

A THESIS

on

THE DIAGNOSIS OF PULMONARY TUBERCULOSIS IN ITS EARLY STAGES

presented by

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THE DIAGNOSIS OF PULMONARY TUBERCULOSIS IN ITS

EARLY STAGES.

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CHAPTER 1.

When John Bunyan called consumption the "Captain of the men of Death" he stated a truism which held good in his day and remains to the present. One in every nine of all deaths is due to Tuberculosis. An estimation based on the census report of the United States for 1890 gives the proportion of persons infected with tubercle in that country as 1 in 60 of the total population (Vaughan).

At a low estimate one can say that at least 150,000 persons die annually in the United States from some form of tuberculosis - Osler (1).

In 1913 the total death rate of England and Wales was 504,795 persons, of these, 49,476 were due to tuberculosis - a decrease of 575 compared with the returns of 1912, and of 5.129 compared with the average of the previous five years.

The death rate of 1913 is less than that of any previous year and forms 9.8% of the mortality from all causes. Compared with the average rate of mortality for the five years 1906-1910, the standardized mortality of

1913 shews a reduction of 15 per cent which is a decrease of 2% compared with 1912 and 9% compared with the year 1911. This fall in death rate is of course most satisfactory, and is due to the provision of dispensaries to combat the disease. Up to the end of June 1914, 296 dispensaries were established in England and Wales and 177 tuberculosis officers appointed.

Although improvement has been made I calculate that nearly 1% of the population of England and Wales are still afflicted with this condition.

Tuberculosis therefore remains in the very front rank of diseases which require consideration, and the desirability of every possible effort, by Medical practitioner and layman alike to stamp out this scourge, is self evident.

The statistics of mortality in any given area do not give any definite idea of the large percentage of population who are partially or permanently disabled by the disease and are thus very severely handicapped in the struggle for existence.

I have estimated that in any one year, the number of persons suffering from the disease is six times the number of deaths in that period. If, as stated above, the mortality from the disease in 1913 was 49,476 then the number of persons suffering from active tuberculosis in England and Wales during that

year was nearly 300,000. I have estimated that on an average 80% of deaths resulting from tuberculosis are due to the pulmonary variety.

In every community a human life is, or should be, an asset and is of the greatest importance not only to the state but also to the household. An idea of the economic loss sustained can be roughly obtained from the fact that the vast majority who die of pulmonary tuberculosis do so between the ages of 15 and 65 years when life is at its high water mark. I have calculated that, of the 80% who die of this variety of the disease, less than 4% are under the age of 15 years and only 5% are over the age of 65 years.

It must however not be inferred from this that deaths from tuberculosis are a negligible quantity in youth and old age because such is not the case. It should be borne in mind that these figures refer to pulmonary tuberculosis only, moreover 9% of deaths from this cause at the extremes of life, when applied to the phthisis mortality of a large community such as England and Wales is a factor that has to be reckoned with.

Stanley Barnes, whose pathological experience has a range of over 1,500 post mortem examinations has stated that in more than half the cases there was evidence of lung lesions which he regarded as tubercular. These estimated cases do not include persons whose death was due to tuberculosis. The

experiences of numerous other pathologists coincide with the above and have been reported from time to time.

The statement that tuberculosis should be looked upon as a curable condition is fortified by the fact that the tubercle bacillus is so often found, during post-mortem examination, in the bodies of those who, in the wards, were not considered to have been suffering from this disease. Incidentally this also shews a looseness on the part of medical men, in examining cases clinically, which is greatly to be deplored, moreover accumulative evidence shews that cases of undoubted tuberculosis on being treated have not only improved but recovered.

Among all classes, but particularly among the so-called working classes, the rapidity of onset of pulmonary tuberculosis is such that often considerable destruction of lung tissue has taken place before the physician has an opportunity of examining the patient. The history of the cases follows well known lines. The patient complains that he took a chill or had influenza, pleurisy or bronchitis some time previously, and since then has had a severe cough which has refused to yield to the various mixtures he has obtained from the chemist. He adds that he has lost weight and is feeling generally run down. This initial lowering of vitality

effecting both the lung tissue and the general system is the stage at which the tubercle bacillus begins to grow and develop and this is the time when it is so essential for a correct diagnosis to be made and proper treatment commenced. It is becoming generally recognised that this disease if discovered and treated in the early stages can be cured. Bardswell (2) shews, that the earlier the stage at which treatment begins the better the chance of recovery. This is now looked upon as a fact by all authorities on the subject.

In consequence of this it is absolutely essential to be methodical in making a diagnosis of tuberculosis. Newer methods have been added to the old ones and the latter have in recent years been improved upon.

The literature in the last decade shews the extensive interest which is being taken in the subject and in the new methods that have been introduced for the diagnosis and treatment of what is termed the "white scourge".

In this connection I may state that an experience of a number of years in practice in South Africa taught me that the native, more particularly the raw product, is peculiarly susceptible to the disease, and as this applies to all nations and races the term "Universal Scourge" would be a very much more appropriate one. It is not possible to base a

a diagnosis on any one particular method whether it be an old or new one.

It is only by applying every available method that we are able to get a result which is of sufficient importance clinically to justify us in giving a definite opinion on a case.

I am unable in the time at my disposal, to review every method of diagnosis and I propose to deal only with the most important and outstanding ones.

The classification which I shall use, in my description of the various stages of the disease in this thesis, is the Turban-Gerhardt classification.

CHAPTER 11.

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HISTORY.

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It is necessary to go very carefully into the history of the patient and his family, and wherever possible, to get his statements confirmed.

The origin of the infection may very often be traced to a relative and the family history is of the greatest importance because of this.

The fact that the tubercle bacillus may lie dormant for an extended period should not be lost sight of. All cases of illness with which the patient has been in contact should be enquired into. Special care should be taken to ascertain the exact date of death, from consumption or other tubercular disease, of any near relative or associate. All illness from childhood upwards should be asked about.

It is well known that certain complaints of childhood predispose of tuberculosis. For this reason a history of the patient having had morbillis, pertussis bronchitis, pleurisy, pneumonia etc is often of importance; the duration of the illness and any after effects should be noted.

These facts can be more easily obtained in the case of young persons whose parents are available for

the purposes of questioning. Special care should be taken to enquire into any illnesses that were considered to be due to the bacillus of tubercle.

A knowledge of the habits, occupation and social standing of the patient, with a view to finding causes such as dissipation drink, trouble, worry and insufficient food is essential. These lower the vitality and render the system more liable to attack by the tubercle bacillus. The history of the present illness, with special reference to the dates when the various symptoms appeared, should be carefully noted.

SYMPTOMS.

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Many persons, who appear to be perfectly well and healthy and who state that they feel absolutely nothing the matter with them, shew marked signs of tuberculosis on physical examination.

The symptoms of pulmonary tuberculosis are very numerous. Among the most important are the following:-

PULSE. An increase in the pulse is common in phthisis. -----
A pulse rate of 100 per minute, even without fever, is not unusual. This increase however, if persistent, indicates that the condition is a grave one.

In 60 cases of tuberculosis of the lungs in all stages, I found 37 with a pulse rate of 100 or over

per minute.

Table No. 1 shews these 60 cases divided into three stages and indicates the number in each stage, and the percentage with a definitely accelerated pulse rate.

TABLE. 1.

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	Number of Cases	Number with a pulse rate of over 100.	Percentage
Stage I.	28	15	54%
Stage II.	9	6	66%
Stage III.	23	16	69%

TEMPERATURE. This is very valuable from a diagnosis standpoint. In the early stages this may be normal but in the later stages of tuberculosis pyrexia is very frequently a well marked symptom. Increases usually occur between 6.0 a.m. and 8.0 p.m. but they are by no means confined within these limits and may occur at any time. It is suggested that when making a diagnosis the temperature should be taken every two

hours during the day and four hourly at night.

If the rise is only moderate the patient should be allowed a certain amount of exercise and any variations in the temperature carefully noted.

It is pointed out by Wilkinson (3) that an increase of temperature after meals is of importance.

The thermometer may be placed either in arm pit, the mouth, or the anus. The armpit is not reliable and should not be used for this purpose especially when it is necessary to record small variations in temperature.

The mouth is better but care should be taken to train the patients to breathe through the nose when the measurement is being taken in this situation.

The most accurate results are undoubtedly obtained from the anus and, although an inconvenient method, it should be employed whenever possible.

EMACIATION. This is a well recognized symptom

and every patient should be weighed once a week on a particular day and at the same hour. The loss of weight, to which the disease owes its name, is gradual and continues progressively as long as the condition spreads.

DYSPEPSIA, Loss of appetite and Languor often appear
in the early stages.

SWEATING is a common symptom, very disagreeable to
the patient. It may occur at any time during sleep
but early morning sweating is what is usually
complained of. It may occur at any stage of the
disease.

COUGH. This is an early and important symptom which
when occurring in young men and girls should never
be disregarded even when it is only slight. A dry
cough may be the first sign of the onset of phthisis.

EXPECTORATION. This varies in the different stages
becoming more copious as the disease progresses.

There may be no sputum at all in the initial stage.

HAEMOPTYSIS. is one of the most important signs of
tuberculosis of the lungs. Röpke (4) has estimated
the occurrence of haemoptysis in the initial stage
at 50% among those actively engaged in work. In the
60 cases of phthisis in all stages mentioned in
Table 1. I found that 29 had a history of
Haemoptysis.

Table 11. indicates three stages of the disease
and shews the number and percentage, with a
history of haemorrhage from the lungs, in each stage.

TABLE 2.
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	Number of Cases	Number with a history of Haemoptysis.	Percentage
Stage I.	28	9	32%
Stage II.	9	5	56%
Stage III.	23	15	65%

PAIN if any, is generally due to a localized

 pleurisy at the apex. Rheumatism of the
 shoulder may be really a deferred pain from an
 apical pleurisy. If the pain is due to
 tuberculosis it is constant and does not change
 from place to place.

LARYNGEAL CATARRH. Wilkinson (5) lays stress

 upon this as an early symptom of pulmonary
 tuberculosis. It tends to cause hoarseness and
 has been called pretuberculosis as it is not in
 itself a tuberculosis condition.

PHYSICAL SIGNS.
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In the early stages of pulmonary tuberculosis it is often very difficult to detect physical signs; as the disease progresses they become more and more marked until in the late stages they are quite distinct and of the greatest use for the purposes of diagnosis. Method is again essential - first examine the chest by inspection, then palpation, percussion, and auscultation. Allbutt and Rolleston (6) contend that the primary lesion consists of a small nodule or group of nodules situated somewhat below the extreme apex of the lung. This is not accepted by all authorities. Jordon (7) states that the more frequently starts at the roots and extends along branchings of the large bronchial tubes. Clinically, however, experience points to the apex of the lung as the situation in which the initial trouble is most frequently found and it is sound practice to commence there.

INSPECTION. Always examine the supra-clavicular regions first as a slight flattening here is the earliest sign obtainable. Flattening below the clavicle and shoulder-drop appear at a later stage and are caused by a wasting of the pectorals, the deltoid, and certain other muscles as the disease

extends.

PALPATION. By means of this it is possible to determine the relative expansion of different parts on opposite sides of the chest. It is as well to palpate the cervical region for enlarged glands. Too much importance should not be attached ^{to} their presence in children, as enlarged cervical glands are quite common in childhood.

PERCUSSION. This is as important as auscultation and should be most carefully done. The value does not depend on the quality of the percussion note alone; a careful comparison with the corresponding part on the opposite side of the chest wall being equally as important.

The percussion stroke should be light; the pleximeter being the digital phalanx, rather than the second phalanx, on account of its being more easy to apply to the fossae above and below the clavicles.

Wenzel (8) found that in percussing the apices of the lungs the difference of pitch in the supra- and infra-clavicular fossae are considerably enhanced if the patient is placed with his bare back perpendicularly against a stone wall. I have tried this method with excellent results, especially in the early stages where physical signs are difficult to detect.

For the comfort of the patient it is

advisable to place a small towel between his bare back and the wall so as to prevent its coming into contact with the cold surface. With the patient in this position, holding his breath after a deep inspiration, it is often possible in percussing the apical regions to detect differences in the note on the two sides which were not recognisable by percussion in the ordinary way.

To detect enlargement of the mediastinal glands by percussion in the region between the scapula and the spine it is of advantage to make the patient bend over a table with his chest in contact with its surface.

Krönig (9) has discovered a method which he calls the topographical percussion of the apices.

The principle underlying this method is that it is not conducive to favourable results to imagine a border at the summit of the apex but that it is much better to project the sound as a broad band over the shoulder girdle. The sound waves are projected in a manner not unlike the projection of light rays by a projection lens, the actual conditions prevailing at the apex being projected on to an enlarged surface. Just as the use of a lens is often an improvement on the naked eye so also in this case it is an advantage to enlarge the minute surface at our disposal by this

method of projection.

In direct percussion of the apex to ascertain its highest point, the differences may not be determined in early disease owing to the fact that the apex may be retracted a few tenths of an inch only. But if Krönigs method is applied there will be found a distinct narrowing of the band which passes over the shoulder in front and behind, representing the projection of the pulmonary sound.

In this method, percussion is performed from the middle line outwards until you come to the tissues. Percussion is then continued in an outward direction until the note reveals an absence of pulmonary sound. The narrowest part of the band produced by the projection of the pulmonary sound is, as a rule, 3 C.M. above the clavicle and the width of the band should be measured in this situation.

In healthy individuals the band in this situation is at least 4 C.M. in width; in disease of the apex there is a decrease. In normal cases the pulmonary sound ceases in a sharp line whereas an indistinct and indefinite border is frequently found in affections of the apices.

RIVIERE (10) discussing the percussion note in

cases of pulmonary tuberculosis has drawn attention to the following changes which according to him are regularly found in the condition:- These changes consist in characteristic bands of percussion impairment, of constant position, shape and size, present over both lungs and which are found before any other physical signs are appreciable. He considers these to be of reflex origin and not due to tuberculosis deposits in the lung beneath, and may be produced by approximate means in the normal chest.

Posteriorly he described two areas of impaired resonance in both lungs - the upper between the apex and a level marked by the interval between the first and second dorsal vertebrae and the lower, between the levels of the fifth and seventh dorsal spines and extending outwards over the scapular regions.

In the early stages these areas of increased dullness are only recognizable by gentle percussion and by the heightened pitch of the percussion note. He believes that the explanation of these symmetrical areas of lessened resonance lie in a reflex contraction of the lungs caused by any inflammatory irritation of the lung parenchyma, but, because of their

very early appearance in pulmonary tuberculosis they are to be regarded as of great diagnostic importance in this disease.

Riviere makes the following summary :-

(a) That the earliest signs obtainable in cases of pulmonary tuberculosis are those which fall under the heading of percussion changes.

(b) That those changes are of characteristic position, shape and size, and that they are of reflex origin;

(c) That they are in no way specific or peculiar to tubercle, but are evidence of an inflammation of the lung parenchyma.

(d) That they bear no relation to the distribution of the pulmonary lesions save indicating the side of disease, or of most advanced disease, and in the case of an early focus, its level in the lung to a rough extent.

AUSCULTATION. It is advisable to examine the chest twice when this method, for the detection of physical signs, due to tuberculosis of the lungs, is used. On the first occasion concentrate on the breath sounds with a special reference to a comparison on the two sides, and afterwards go carefully over the chest again with a view to finding râles or other adventitious sounds. Feeble localised breath sounds are often the earliest manifestation of phthisis, Harsh breathing

and prolonged expiration are other early signs. Normally the breath sounds at the right apex are harsher than the left, and it should also be borne in mind that vocal resonance is normally greater on the right side.

In the second part of examination the whole attention should be given to the discovery of ^{rales}rales. In the early stages these are difficult to detect being few in number and only occurring on inspiration. They have a dry crackling sound and can be intensified by making the patient breathe more deeply.

Localized pleurisy at the apex is generally an indication of tubercle and this should be remembered when friction sounds are found on auscultation in this situation.

Mitchell Bruce (11) says that the percentage of cases in which an attack of pleurisy is followed by pulmonary tuberculosis is variously estimated by different observers.

It is, according to Clifford Allbutt (12), safe to say, from a review of a large number of the statistics open to us that all "idionathic" pleurisies in persons, say, over five years, 50% are tuberculous, As regards child life he holds that not more than one in ten are tuberculous, but, on the other hand, he has stated that in elderly persons pleurisy is often due to this cause.

Mitchell Bruce is more conservative in his statement

and uses the term "large percentage", for whether the pleurisy is latent or marked by severe pain and effusion, it is too frequently followed by disease of the lung, at an interval which varies widely from a few months to nearly a quarter of a century.

Examples of the interval quoted by him from cases of his own are three, five, eight, twelve, fifteen, and twenty-one years.

LARYNGEAL EXAMINATIONS. For the purposes of diagnosis the Laryngoscope is sometimes very valuable. Early signs being present without any change in the voice.

Killian (13) has devised a new method of directly inspecting the larynx which he has termed suspension laryngoscopy and which is very useful in cases of tuberculosis.

OTHER CONDITIONS.
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Fishberg (14) has called attention to the following point which should be borne in mind, viz :-

That abnormal signs at the apex may have some other cause than the tubercle bacillus. He classifies such conditions in three groups :-

1. Collapse indurations, found chiefly in mouth breathers.
2. Apical Catarrh after influenza in the emphysematous or in those who follow dusty

occupations.

3. Apical indurations found in persons with heart lesions.

The first of these is the most important. One apex, generally the right, is retracted, dull, with harsh or bronchial breathing and crepitations. This is due to prolonged nasal obstruction with mouth breathing, a catarrhal condition is present and the expectoration is profuse and may be blood streaked, the general health of the patient, however, is fairly good and he is able to remain at work.

In those mouth breathers who follow dusty occupations, the dust, not being filtered, reaches the apex of the lung and causes repeated attacks of catarrh followed by fibrosis and contraction.

These conditions can be distinguished from tuberculosis by the history of colds and nasal obstruction and the fact that no tubercle bacilli are found in the sputum. Moreover there is an absence of fever, loss of weight, tachicardia, and fatigue, and the general health of the patient is pretty good.

Mitral disease is often mistaken for phthisis, abnormal signs, crepitations etc, are found at the apices, and the sputum may be blood stained - the absence of tubercle bacilli in the sputum, and of the constitutional symptoms of tuberculosis make

the differential diagnosis comparatively easy.

INFLUENZA AND TUBERCULOSIS. Jex-Blake (15) has drawn attention to the relation of influenza to tuberculosis, and from his enquiries at the Brompton Hospital extending over three or four years, has come to the conclusion that influenza is an acute bronchitis set up in many cases by the tubercle bacillus and other microbes rather than by the B.influenzae.

Out of 416 cases of pulmonary tuberculosis examined by him 264 gave some history of influenza. These figures make it reasonable to suppose that influenza rather than being a predisposing cause is more often tuberculosis itself; the early symptoms, like a rise of temperature, pains, headache, and prostration are common to both diseases.

CHAPTER 111.
=====Rontgen-ray Examination.
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This is a product of recent years and has become very popular.

Albers-Schoneberg (16) compares the advantages obtained by the examination of consumptive patients by means of X-rays with older methods. He states that the Rontgenographic diagnosis of phthisis is on a par with percussion but is inferior to auscultation. Catarrhal conditions cannot be recognised but the foci of infiltration can be detected before they are revealed by percussion. He considers that the X-rays will often be the deciding factor in questionable cases.

Wenchebach (17) states that the improvement in Rontgen-ray apparatus which makes it possible to take instantaneous radiographs of the chest, and the introduction of the stereoscopic method has revolutionized the methods of chest examination in the prompt diagnosis of early phthisis.

Williams (18) detects a noticeable limitation of movement of the diaphragm on the affected side, even in mild cases, and considers this an important point in the early diagnosis of the disease.

Lawson (19) asserts that experience has not only substantiated the X-ray claims of sixteen years ago, but exalted and glorified them, until now it may be said that the consultant who in the diagnosis of a difficult and obscure lung condition, has not brought them to his aid has failed alike in his duty to himself and to his patient. He is of opinion that in an early doubtful apical pulmonary lesion, a screen examination invariably shews restricted diaphragm movement less translucency and a failure to light up the apex on deep respiration if early phthisis is present.

Walsham and Overend (20) deal with the cause of Williams' sign in its relation to the nerve supply. They consider that the limitation of diaphragm movement etc is due to a reduction in the duration and amplitude of the inspiratory wave, with a definite measure of protection and rest for the diseased areas of the lung.

Leonard (21) says that it is possible to detect bronchial gland enlargements and areas of infiltration about the roots of the lungs where neither percussion or auscultation can reach and before bacteriological examination has determined the cause of the condition.

Riviere (22) points out that radiography goes far to confirm the opinions that phthisis is merely the final stage of a childhood infection seeing

that it discloses as a rule old disease of bronchial and pulmonary glands which appears to spread along the bronchial branches into the lung and especially towards the apex. He lays stress on the importance of utilizing the X-ray method in addition to other methods, in order to confirm the diagnosis in early and doubtful cases, and also to determine the extent of the spread of the disease, and to show if the other side is affected or not.

Jordon (23) makes the assertion that in at least 40% of all cases of tuberculosis of the lungs the disease starts as a well defined peri-bronchial thickening. From the hilus the disease spreads in all directions, but most rapidly along the ascending and descending branches of the main bronchus.

On reaching the apex it spreads so rapidly that very soon the apex appears clinically to be the chief seat of the invasion. In the majority of cases there are no physical signs until the apex has become involved, the disease at the hilus being so deep seated that it escapes detection from without.

Jordon (24) says that this peri-bronchial phthisis may reach an advanced stage without revealing any signs of its presence by the usual methods of physical examination of the chest. He concludes that the only known method of making an early diagnosis in these cases is by means of Rontgen-rays.

Bissell and Richards (25) examined 219 cases, the majority of which shewed indefinite signs and came to the conclusion that the medical profession should be taught not to depend on physical signs either for a positive or negative diagnosis of early pulmonary tuberculosis. They state that a negative X-ray diagnosis is as valuable and perhaps more conclusive than a positive one, and are of opinion that tuberculosis at the hilus is usually secondary to a focus in the lung.

Melville (26) discovered a new sign in X-ray diagnosis of phthisis.

In the normal lung during full inspiration the expansion of the apices is equal, and above the clavicle it is possible to see the posterior ends of at least the two upper ribs, also the two intercostal spaces are equal width.

In lessened expansion, due to tubercle, not only is there less of the ribs visible but the space between the first and second ribs is obliterated. He states that, in screening, it is important to place the central X-ray accurately at the level of the third costal cartilage with the sternum.

The records of sixty cases I examined by Röntgen-rays shewed twelve which gave a positive reaction to tuberculin tests although no focus of disease in the chest could be discovered by physical examination. In seven of these cases the

X-ray shewed distinct peri-bronchial thickening at the root of one or both lungs which could not be mistaken for the normal hilus shadow.

In a number of cases with marked disease, which in percussion and auscultation appeared to be localized to one or both apices, there was considerable thickening at the roots of the lungs.

On examining these cases again subsequent to the X-ray examination no signs of disease could be found over the areas of thickening. In these cases apparently the thickness of normal lung substance between the area of consolidation and the chest-wall is accountable for the normal sounds, and does not allow of any abnormal sounds, from the diseased parts, being heard.

On account of the frequency of this thickening at the hilum I have paid particular attention to percussion in the interscapular region at the level of the roots of the lungs in suspicious cases, and have found definite dullness on each side of the spine in this region in cases which, on X-ray examination in an oblique position shewed thickening in the posterior mediastinum.

In two cases the Rontgen-rays revealed shadows near the base of the lung when no sign of the disease could be discovered by physical examination. These shadows must represent foci of

of disease centrally situated and with a considerable amount of healthy lung tissue surrounding them.

In one case definite shadows were shown near the hilum of the right lung indicating old standing disease which had healed while towards the apex evidences of small cavities pointed to a fresh infection.

In this case physical signs were very definite and coincided with the results obtained from the screening but the interest in the X-ray negative lay in finding these indications of old standing and recent disease in the same lung.

In examining X-ray plates the differences seen in Chronic Bronchitis, Silicosis, and Tuberculosis, are very well marked.

In Chronic Bronchitis the peri-bronchial thickening shews itself as an exaggeration of the normal tree like branchings of the bronchi the edges of which are inclined to be blurred and illdefined.

In Silicosis, I found on examining a large number of these cases from the Rand Mines in Johannesburg, that the peri-bronchial thickening had a streaky appearance resembling Chronic Bronchitis but that the borders were more defined- probably due to the desposition of the Silica along the bronchi and to there being a pure fibrosis and

less diffuse inflammation.

In Tuberculosis the appearance is more of a mottled character.

Cases of Silicosis with Tuberculosis added shew both the streaky and the mottled appearance and in these the prognosis is very bad, whereas, a pure silicosis may recover and often does if the patient leaves the mine and goes farming, when the Tubercle bacillus attacks the lung as well the patient declines rapidly and treatment appears to be of no avail.

In regard to the disease at the apices, the physical signs are usually so well defined that it is doubtful whether X-rays can add to the information obtained from a carefully made physical examination.

CHAPTER IV.Examination of the sputum for Albumen.

The presence of Albumen in the Sputum has in recent years received considerable attention as a means of assisting diagnosis in the early stages of phthisis.

Vercesi (27) states that he found Albumen almost invariably in 121 sputa, both in acute and chronic parenchymatous processes in the lungs; In 76 cases of pulmonary tuberculosis the reaction was positive in 75 cases, while acute and chronic bronchitis hardly ever showed any trace of albumen.

Prorok (28) as a result of 800 investigations respecting the presence of albumen in the sputum, states that he invariably found positive albumen reaction in pulmonary tuberculosis, putrid bronchitis with bronchiectasis, gangrene of the lungs and pneumonia. Albumen was generally absent in cases of chronic bronchitis and bronchial asthma. Frequently however traces could be demonstrated in the latter diseases.

Busnikowa (29) is of opinion, as a result of detailed experiments that the albumen test is only positive in the case of pulmonary tuberculosis, pneumonia crouposa, bronchopneumonia and gangrene,

that is to say, in the case of diseases of the parenchyma of the lungs.

Peskow (30) found as a result of 67 examinations a positive albumen reaction at the commencement of pulmonary tuberculosis. The albumen test in the case of bronchitis is negative.

Brunner (31) proved that the albumen reaction of the sputum, so long as the latter is fresh and is not mixed with anything, is positive in the case of pulmonary tuberculosis. It is, however, occasionally negative in the case of fibrous tuberculosis.

Gantz and Hertz (32) come to the following conclusions after having examined 125 cases :-

1. The albumen reaction is a very simple method of analysis and takes up so little time that it should be constantly applied as a help in the diagnosis of phthisis.
2. The albumen reaction is to a certain degree considered to be specific because it is the expression of inflammation or disease of the lung.
3. In bronchial catarrh the albumen reaction is negative.
4. Lung tuberculosis, both at the commencement and in the later stages, gives a more or less distinct appearance of a positive albumen reaction - an exception is made in the fibrous forms of tuberculosis.
5. In pneumonia and lung infarct the albumen reaction is positive.

6. Diseases of the lung, even of a slight degree, give a distinctly positive albumen reaction. In doubtful cases of early lung tuberculosis, when tubercle bacilli cannot be found in the sputum, the diagnosis may be made by a positive albumen result.

Ritter (33) has made the statement, that a single negative albumen reaction is certain evidence of the absence of tuberculosis.

Scott (34) denies Ritter's statement and contends that a negative reaction may occur about 10 per cent of pulmonary tuberculosis cases and for this reason considers that the test is of more value for prognosis than for early diagnosis.

Biernacki (35) goes further than the simple qualitative estimation. He determines the percentage of albumen present by Esbach's method and finds that tubercle sputum contains albumen in quantities varying from .06 per cent to .8 per cent, the average being .2 to .4 per cent. Larger quantities are present in the last stages of the disease. He states that some cases of bronchitis, often associated with emphysema, give a positive reaction.

As a rule the amount present in these cases is a mere trace which cannot be estimated, and in seven cases he found amounts varying from .03 per cent to .15 per cent. He finds that the presence of albumen in these catarrhal conditions not complicated by tuberculosis depends on disease of the heart and vascular system.

Biernacki, from his investigation arrives at the following conclusions :-

1. The absence of albumen in the sputum proves that the disease has affected the bronchial tissues only, its presence shews that the lung tissue is involved.
2. If the albumen reaction is negative the presence of active tuberculosis can be excluded.
3. In active tuberculosis the reaction is positive almost without exception.
4. The presence of .2 per cent or more of albumen gives the reaction a positive tubercular character if other inflammatory conditions can be excluded. From a clinical point of view such exclusion is comparatively easy.

I have examined the sputa of 39 cases for albumen and have estimated that the quantity present in positive cases.

The sputa is prepared in the manner described by Roger and Levy-Valehsi (36) as follows :-

An ounce of water is added to an equal quantity of fresh, bloodless, and as far as possible saliva-free expectoration. The sputum should be collected early in the morning in a sterilized sputum mug and the patient should be made to gargle his throat with cold boiled water before expectorating.

The test should be done within twelve hours of collecting the sputum. To the sputum diluted with an equal quantity of water add a few drops of 3%

Acetic Acid until litmus paper indicates that the mixture has become acid, then add three more drops of acid and beat up thoroughly with a glass rod to allow the acetic acid to precipitate all the mucine; filter and add one drop of acetic acid to the filtrate to see if any mucine remains.

If muddiness appears the mixture is again filtered, the process being repeated until the mixture becomes quite clear. Now apply one of the tests for albumen. The nitric acid test is the best although Roger and Levy-Valensi use Potassium Ferrocyanide for this test.

For estimating the amount of albumen in the sputum I use Esbach's method for determining the amount of albumen in Urine. The number of grammes per litre is indicated by the level of the albumen in Esbach's albuminimeter and in order to arrive at the percentage it is necessary to divide this by ten. It should also be remembered that the sputum was diluted with an equal quantity of water and to allow for this the result must be multiplied by two. This gives the actual percentage of albumen in the sputum analysed. I found albumen present in 100% of 35 sputa all of which contained tubercle bacilli. The amount varied from a trace to 1.6 per cent, the average being .35 per cent. I found that the worse the case was, the larger the percentage of albumen. In the 35 cases in which a positive albumen result

was obtained a diagnosis of active tuberculosis had been made in each case by other means as well and the results are shown in Table 3.

TABLE 3.

=====

Stage of Disease. (Turban Gerhardt classification)	Number of cases	Number with albumen present in sputum	Number with albumen absent from sputum	Amount present	Average amount
Stage I.	8	8	0	Varying from a trace to .55%	.19%
Stage II.	6	6	0	Varying from a trace to .6%	.29%
Stage III.	21	21	0	Varying from a trace to 1.6%	.35%

In five cases there was a negative albumen reaction although a diagnosis of latent pulmonary tuberculosis had been made in each case.

The results in four nontubercular sputa were as follows :-

Three cases of chronic bronchitis did not shew even a trace of albumen, and in one case of pneumonia the sputum before and for some days after the crisis contained about .6 per cent; after which the albumen disappeared.

The above results shew that in simple bronchial affections albumen is absent, and its presence indicates that lung substance is involved.

I am of opinion that the albumen test is of value in deciding whether a positive reaction to tuberculin tests is associated with an active or inactive pulmonary tuberculosis, the albumen reaction being present in the active condition and absent in the latter.

I agree with Schmey (37) whose opinion of the value of the albumen reaction is as follows :-

1. A negative albumen reaction speaks with certainty against the presence of an active tuberculous lesion.
2. A positive albumen reaction proves the presence of active tuberculosis, when other diseases of the lung tissue, such as pneumonia, infarct, and gangrene, are excluded.
3. As the albumen reaction appears in quite early cases of pulmonary tuberculosis, it is especially adapted for early diagnosis. He also suggests the

following :-

- (a) If the albumen reaction and the Von Pirquet reaction are both positive, then there is active tuberculosis.
- (b) An albumen negative reaction and a Von Pirquet positive reaction prove an inactive latent or healed tuberculosis.
- (c) An albumen positive and Von Pirquet negative reaction prove a nontuberculous trouble.
- (d) If the albumen and Von Pirquet reactions are both negative pulmonary tuberculosis can be entirely excluded.

Schmey (38) says that the appearance of albumen in the sputum of tuberculosis patients is the result of a toxic irritation, emanating from the tubercular focus, which sets in as soon as the bacilli have settled down in the tissues and commenced to multiply.

Ridge and Treadgold (39) found that albumen disappears from the sputum in cases of pulmonary tuberculosis which has been cured. Continued absence of the albumen as well as of bacilli indicate absence of ^{Active} tuberculosis.

ORTHOSTATIC ALBUMINURIA.

Lücke and Oturm (40) investigated orthostatic albuminuria and its importance from a diagnostic standpoint. They examined 140 tuberculosis cases for

The presence of this condition, and found that 102 gave a positive albumin reaction in their urine after they had been standing for one hour. Sixty belonged to the first stage, fifty to the second, and thirty to the third stage.

Positive reaction was obtained in fifty-three from the first, thirty-two from the second, and seventeen from the third stage. Eight control individuals all, after standing for an hour, remained free from albumen in the urine. The authors believe that orthostatic albuminuria in tuberculous individuals is to be attributed to toxic irritation of the kidneys. No changes could be found, after standing, in the haemoglobin content or in the number of erythrocytes. On the other hand, the pressure in the pulse was shown to be lowered. In the urinary deposit of tuberculous patients exhibiting orthostatic albuminuria tubercle bacilli were found on several occasions. A casual connection between tuberculous disease and the albuminuria produced by standing may be assumed to exist in the majority of cases of orthostatic albuminuria.

Chalier (41) found orthostatic albuminuria in 73% of initial cases of tuberculosis.

CHAPTER V.
=====Examination of Sputum for Tubercle Bacilli.
=====

Koch discovered the Tubercle Bacillus in 1882 and since that date the presence of this Bacillus in the sputum has been looked upon as the deciding indication in favour of pulmonary tuberculosis. From the diagnostic standpoint however the tubercle bacillus is only of secondary importance as it is not found in early or incipient tuberculosis. Whereas, its presence is a definite proof of tuberculosis of the lungs in an advanced stage, its absence does not signify that the patient may not be suffering from the condition in its earlier stages.

Tubercle bacilli are only found in the sputum after they have caused caseation which on breaking through the mucosa allow of the bacillus entering a bronchus and thus infecting the sputum. Generally the disease has been present for some time before this caseation occurs, and after it has occurred it is easy to understand that a comparatively large number of bacilli may be present and escape detection by the methods of microscopical investigation at present in use.

Table 4 has been drawn up by me to show how rarely tubercle bacilli are found in the early stage of the disease compared with the frequency with which they

are found in the later stages.

I examined the sputa of 56 cases of undoubted active tuberculosis and the table shews the number of patients in each stage and also the number and percentage whose sputa shewed the tubercle bacillus on examination after using the ordinary ziehl-neelsen stain and, if this gave no result, using antiformin or one of the other methods described in this chapter.

TABLE IV.

=====

	Number of Patients	Number with Tubercle Baccilli in Sputum.	Percentage.
Stage I.	19	2	11%
Stage II.	16	12	75%
Stage III.	21	19	90%

Nowadays tubercle bacilli in the sputum indicates an open tubercular lesion in lung, and from the time of its appearance the question of the possibility of a mixed infection arises.

If streptococci pneumococci or the bacillus of influenza are found in a tubercular sputum the prognosis is bad. Notwithstanding what has been said above, the discovery of the tubercle bacillus is of the greatest importance, because to the busy general practitioner who has not a great deal of time to devote to the very fine methods of physical examination or other scientific methods of diagnosis, the presence of the bacillus in the sputum at once proves the condition to be pulmonary tuberculosis.

Technique of Examination :-

The method to be employed in collecting sputum for examination has already been dealt with in Chapter IV.

Sticker (42) has recommended the use of .2 grams of iodide of potassium, in order to bring about a catarrh artificially in cases without expectoration but I do not advise this method.

Emetics have been given in the early morning to patients without expectoration and the vomit searched for masses of expectoration but no good results have been obtained from this method. The contents of the sputum-mug are poured into a glass dish which is placed on a black surface, great care should be exercised in choosing the part for examination.

The centre of an opaque, grey, hard, fragment

caseous or necrotic in appearance should be picked out with forceps and smeared on a previously warmed slide, a rusty looking piece should not be neglected but starchy food particles should be carefully avoided. After drying and fixing by passing through a bunsen flame one of the following staining methods are employed:-

1. The ordinary Ziehl-neelsen method which is quite the best. When dealing with a number of slides I employ a simple and cheap device which saves much time. A couple of glass rods an inch and a half apart, are placed across the sink, the ends being fixed into wooden blocks.

The slides are placed on these rods and a strong solution of carbol-fuchsin poured onto them. The bunsen flame is then applied until a head of steam arises and after five minutes staining the slides are washed rapidly and decolorised with 25% Hydrochloric Acid for at least ten minutes, and longer if possible. I have had excellent results after leaving the slides in Hydrochloric Acid solution for several hours. Wash in water and if there is any fear of the sputum having been contaminated by other acid-fast bacilli of which there are a considerable number of varieties, the slide should now be decolorised with absolute alcohol for a couple of minutes. The reason for this is that the tubercle bacillus is both

"acid-fast" and "spirit-fast" whereas these other "acid-fast" bacilli become decolorised on treatment with alcohol. . In staining urinary deposits for tubercle bacilli this should always be done as the "acid-fast" smegma bacillus which has a very similar morphological characteristics is readily decolorised if treated with absolute alcohol for one minute. Brown (43) however contends that no staining method differentiates tubercle bacilli from smegma bacilli and advises the use of cultural methods for this purpose.

After this, the slide is again washed, and counterstained with Löffler's Methylene blue for 20 to 50 seconds, now wash, blot dry in air and examine with an oil immersion lens of 1/12th inch focus for five minutes unless of course positive results are obtained in a shorter time.

2. Herman's method may be employed - use 3% Crystal Violet in 95% alcohol mixed with three volumes of 1% ammonium carbonate as mordant and stain with this for a few minutes, wash, treat with 10% nitric acid and then absolute alcohol. Counterstaining with 3% chrysoidin is useful in bringing out metachromatic spore-like granules and branching forms.

3. Another method, the picrin method, is strongly recommended by Horace Wilson (44).

It is as follows :- Stain with Carbol-fuchsin,

warm, but without too much heat; pour off the stain without washing and pour on picric acid alcohol (consisting of equal parts of saturated solution of picric acid and alcohol) after three seconds wash with 60% alcohol; treat with 15% nitric acid till yellow (30 seconds) wash again with 60% alcohol, counterstain with picric acid-alcohol till lemon coloured, and wash with distilled water and dry gently at low heat. The bacilli are thrown out very conspicuously against the yellow background.

Concentration methods :- If the results are negative

 one of the following concentration methods may be employed :-

"The tubercle bacilli usually occur in nests in clumps of sputum and these concentration methods dissolve the mucous and collect together any bacilli that may be present".

A. Uhlenhuth and Xylander's Antiformin method (45).

The details of this are as follows :- The sputum is mixed with 15% of antiformin, placed in a stoppered bottle and shaken violently for two or three minutes to break up the sputum, then put in a incubator for 15 to 60 minutes until the mucous part is dissolved and becomes a watery fluid.

This is centrifugalised for about fifteen minutes until all the deposit has sunk to the bottom of the tube. After decanting the deposit may be washed in normal saline solution and again centrifugalised, a loopful of the

upper layer of the deposit is then spread out on a slide, fixed and stained in the usual way, except that on account of the harsh treatment of the bacillus with the caustic, instead of putting the carbol-fuchsin on the slide and heating it, it is better to put some of the stain into a test tube, bring to the boil and pour it on the slide. It is also necessary for the same reason to decolorise with a weaker hydrochloric acid solution (10%) as the stronger solution tends to remove the colour from the bacillus as well.

Antiformin is prepared as follows :- Liquor Sodae Chlorinatae (Labarraque's solution) is first made by adding Chlorinated lime to sodium carbonate and an equal part of 15% sodium hydrate is added to the solution thus formed.

One part of antiformin to five parts of sputum is sufficient, but one to four may be used in the case of very tenacious sputum. The advantages of the antiformin are :-

1. It has less effect on the staining properties of tubercle bacilli than any other material used in concentration methods.
2. Breaks up the sputum rapidly.
3. Dissolves all organisms immediately except the "acid-fast" ones.
4. If applied in a not too concentrated form and not too long it does not kill the tubercle bacillus.

This is a useful quality if it is desired to cultivate the organism on suitable media of which, it may be noted here, the most satisfactory are :-

1. Dorset's plain egg medium ; made by adding one part of sterilized .85% sodium chloride solution to three parts of egg which has been carefully mixed and strained through gauze.

2. Glycerine egg (Labenau) Medium : one part of 6% Glycerine in .85% sodium chloride solution added to three parts of egg, and a few drops of alcoholic basic fuchsin added to colour it pink. This is of advantage in aiding the detection of early or scanty growths.

3. Frugonis animal tissue method : soak fresh rabbits lung or other tissue in .85% sodium chloride solution containing 6% glycerine for one hour and then sterilize by autoclaving at 120° C for 45 minutes and then supported over the surface of 6% glycerine bouillon. Cultures for tubercle bacilli are impracticable without concentration, and the antiformin method should always be used.

B. Biederts concentration method for mucous,
 atypical, scanty sputum. In this method an alkaline substance is used in the preparation of the slide and therein it resembles the antiformin method:-
 15 C.C. of sputum is mixed with 30 C.C. of water in a beaker. Stir constantly and add four to eight drops of 10% solution of caustic soda. Boil slowly,

and at the same time add 60 to 90 C.C. of water until the mixture becomes thin in consistence. Now centrifugalise, or stand for two or three days, **Mix ~~with~~** the sediment with a little egg albumen and smear on to a slide. Biedert recommends the egg albumen to fix because without it the deposit is very liable to wash off the slide during the staining process. I found the same difficulty when using the antiformin method and over came it by heat and mixing the sediment with some glairy transparent mucous from the sputum, this is quite as efficacious as egg albumen and the necessity for procuring the latter substance is obviated. Biedert then stains for tubercle bacilli in the ordinary way except that he stains with carbol fuchsin for 8 minutes instead of 5 minutes.

C. Van Ketel's method is of value when the sputum is watery, copious or purulent. 100 C.C. of sputum is mixed with 5 C.C. of liquid carbolic acid and shaken thoroughly.

The mixture is then centrifugalised or left standing for 24 hours. The sediment is removed with a pipette and a film is made in the ordinary way. After drying in air, passthrough a flame and wash in chloroform for one to three minutes. Again wash in water, blot and pass through flame. Stain with carbol-fuchsin and counter-stain with methylene blue.

D. Another satisfactory method is the Mulhauser-Czaplewski method for concentrating bacteria.

Shake up the sputum with four to eight times its volume of $\frac{1}{2}$ per cent solution of sodium hydrate in a stoppered bottle. When the mixture has become a smooth mucilaginous fluid add a few drops of phenol-phthalein solution and bring the pink mixture thus formed to the boil. Then add drop by drop a 2 per cent solution of acetic acid stirring constantly until the pink colour is just discharged. If the least excess of acid is added over that just sufficient to cause the pink colour to disappear Mucin will be precipitated. Now centrifugalize, smear sediment on a slide and stain for tubercle bacilli.

The concentration methods described above, of which antiformin is the most useful, are of value to the general practitioner who has neither the time nor the opportunity for staining and examining many slides. By concentrating the bacilli he gets positive results where by the ordinary method he would get negative ones. For the experts these methods have not always the same advantage because he knows almost by intuition whether a sputum is tubercular or not, and long practice has taught him to recognize the particles which contain the largest number of bacilli and which will give the best results on

staining and examination. In examining the slides care should be taken not to mistake stain deposits in cracks or scratches on the glass for the rodlike bacilli of tubercle.

If negative results are obtained by examination by the above methods we still have the test of animal inoculation which is the most reliable of all.

Guinea pigs are the best for this purpose, and the necessity for taking out a vivisection licence should not be lost sight of. Some of the suspected material is mixed with 3 C.C. of sterile salt solution and injected intra-peritoneally into the animals, which are killed in from four to six weeks and the organs examined for deposits of tubercle bacilli. Some experimenters place a small quantity of the sputum in the sub-cutaneous tissues of the thigh or groin, a small skin incision having been made which is afterwards closed up with colodion.

The neighbouring lymphatic glands become first enlarged and then caseous. The animal loses weight and generally dies within six weeks if not previously killed.

Tubercle bacilli in the sputum may be demonstrated by this method when all others have proved a failure. Oppenheimer (46) injected urine suspected of

containing tubercle bacilli into the livers of experimental animals; he was able by this method to reduce the time taken for the experiment to fifteen days, and in the case of very virulent material to five days.

Examination of the faeces.
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Tubercle bacilli have been demonstrated in the faeces of phthisical patients before tuberculosis of the intestines shewed itself. They are due to sputum being swallowed.

A quantity of the faeces is mixed with 20 C.C. of a 15 per cent solution of antiformin and well broken up until an emulsion is formed. Another 20 C.C. is added, and after standing for two hours, the creamy sediment which forms is pipetted off and examined and stained in the usual manner.

Philip and Porter (47) report having examined 109 specimens of faeces; 42 shewed no tubercle bacilli in the sputum, but 29 of them gave evidence of tubercle bacilli in the faeces. Of 24 cases which had no sputum, 17 shewed tubercle bacilli in the stools; therefore in certain cases this method is of value.

Examination of the blood.
=====

Rosenberger (48) in 1909 first drew attention to the fact that it was possible to demonstrate tubercle bacilli in the blood of most cases of

phthisis, even in the early stages.

Kirashige (49) examined the blood of 155 cases of milder and more severe cases of pulmonary tuberculosis and demonstrated the presence of the bacilli in every case.

Sturm (50) found tubercle bacilli in the blood of 44 ----- per cent of cases in the first stage of pulmonary tuberculosis, in 38 per cent of cases in the second stage and in 48 per cent in the third stage.

Other observers have not been able to discover them in early cases in the blood, but have been successful in the later stages.

Lippman (51) took 10 C.C. of blood from a patient, and having added 3 per cent of acetic acid, centrifuged the mixture. To the deposit he added antiformin, incubated it at a temperature of 37° C and again centrifuged.

He obtained tubercle bacilli in films obtained from the deposit of 53 per cent of advanced cases, in 33 per cent of second stage cases, but was unable to discover any in early cases.

Rogers and Murphey (52) investigated fifty cases of tuberculosis in different stages, by the Kurashige-Schmitter method, which is as follows :- Add 1 C.C. of blood to 5 C.C. of 3 per cent acetic acid, centrifuge for half an hour, dissolve the sediment in 5 C.C. concentrated antiformin and add 5 C. C. absolute

alcohol, again centrifuge, wash in distilled water, centrifuge once more, make a slide and stain. Bachmeister (53) refers to finding tubercle bacilli in the blood of healthy persons and insists that this is a manifestation of pseudo-tuberculosis.

Veribizier (54) after very careful study has come to the conclusion that it is quite erroneous to believe that blood of tuberculous patients contains tubercle bacilli in even as many as 25% of the cases. The bactericidal power of the blood serum is adequate even in such patients.

Serum Diagnosis :- Although it is difficult to obtain tubercle bacilli in the blood of early cases of phthisis, certain methods have been adopted to aid the diagnosis of early phthisis by the estimation of the opsonic index of the serum and by the accurate estimation of the agglutinins usually present in the blood. The tuberculo opsonic index does not, in health, fall below 0.8 or rise above 1.2. Indices persistently above or below these levels point to tuberculosis.

Another method is that of the fixation of the complement; The latter is dealt with by Dudgeon, Meek and Weir (55). Antigens used are extracts of sputum and tissues, tuberculin, and tubercle bacilli. In every case where a patient was under

treatment with tuberculin, the reaction was positive. It was always negative in persons who were only in contact with tuberculous people.

Nesfield (56) could not find antibodies in acute

tuberculosis. He shows the relation between the antibody content and the opsonic index, and he believes the leucocyte is a very delicate test for the amount of free antibody in the serum.

Glover (57) considers that the complement-fixation reaction, the estimation of the tuberculo-opsonic index, and the subcutaneous injection of test doses of tuberculin rank with the sputum examinations as the most reliable tests of tuberculosis. He carefully investigated 47 cases by the above methods and the results of his study of Serum reactions shewed that-1. Positive complement fixation is strong presumptive evidence of active or quiescent disease.

2. Positive complement fixation plus a positive opsonic index is definite evidence of active disease.

3. A positive opsonic index is definite evidence of active or quiescent disease.

4. Negative complement fixation is in nine cases out of ten evidence against active disease.

5. Negative complement fixation plus a negative opsonic index is almost definite evidence against

active disease.

6. A repeatedly negative opsonic index is definite evidence against active disease.

Glover sums up the results of his researches as follows :-

1. That about 62% of cases coming under observation as supposed early phthisis, but with no bacilli in the sputum prove to be negative; nevertheless,
2. That such negative cases may present clinical signs of impairment of percussion note, breath sounds, and resonance at, at least, one apex; and
3. That moist sounds in such cases are almost invariable absent; therefore
4. It is not justifiable to diagnose active tuberculosis on the strength only of impairment of one apex.
5. That active disease confined to one apex, with a repeatedly negative sputum, is not common;
6. That where moist sounds are present, further investigation is needed to exclude or confirm the presence of active disease.
7. That when this investigation takes the form of the complement-fixation reaction along with the estimation of the opsonic index (if necessary, repeatedly), a final diagnosis can be made without recourse to test injections of tuberculin.

Ascolis thermo-precipitin reaction :-

Fagindli (58) describes a method of applying this test which consists in mixing sputum with chloroform, incubating, and then replacing the chloroform by a saline. The filtrate is then run on to the surface of Vallée's anti-tuberculous serum and after keeping in an incubator for half an hour, a ring forms at the junction line if the case is one of pulmonary tuberculosis.

Examination of the sputum for elastic fibres.

Boil a quantity of sputum with an equal volume of liquor potassae and allow the resultant liquid to settle. On examining the deposit microscopically elastic fibres can be detected, if they are present, no staining being required.

This method was used before the discovery of the tubercle bacillus. The presence of fibres indicate breaking down of lung tissue and the test is of no use in the early stages of the disease.

CHAPTER VI.Von Pirquet's Cutaneous Reaction.

This is a method of diagnosis, introduced by Von Pirquet (59) in 1907, and consists of the application of tuberculin to small areas of scarified skin.

Von Pirquet originally used Koch's old tuberculin diluted to the extent of 25% with .5 per cent Carbolic Acid in normal saline solution.

Undiluted old Tuberculin is now used.

Method of application of the test. The flexor aspect of the forearm is first cleansed with alcohol. Two drops of tuberculin are then allowed to fall on the skin about five inches apart. The skin within each drop is then scarified with a sterilised Von Pirquet needle. In scarifying, the needle is applied vertically and rotated; only the superficial layers of the skin are removed and blood should not be drawn. A control scar within a drop of 20 per cent glycerine in normal saline solution should be made between the two previous marks, the needle being carefully sterilised before doing so.

Appearance after applying the test:-

Traumatic reaction :- A traumatic reaction is seen after about an hour as a result of the operation.

This redness generally disappears in an hour or two.

The traumatic reaction is the same in the control area as in the others.

Positive reaction :- This shews as a redness in -----
 three or four hours but is not seen at the control spot. The redness increases for about twenty four hours when a red papule, surrounded by a hyperaemic area of vivid ^{red} colour, develops at the site of inoculation.

The diameter of the papule varies within wide limits - from one to twenty millimeters. A few vesicles may appear around the papules. After a while the papule and surrounding hyperaemia disappears leaving a small pigmented area.

Negative reaction :- When the reaction is negative -----
 the result is similar to that at the control spot, a small scab due to the scarification of the skin is generally all that is left after twenty four hours.

The reaction may vary very considerably. It may reach a maximum and almost disappear in twenty four hours or it may increase gradually for three or four days and then decrease very slowly.

Wolff-Eisner (60) is of opinion that this slow increase or slow decrease indicates a latent lesion and calls it a "late reaction".

If a negative reaction is obtained it is well to repeat the experiment after a few days interval when it is possible that a positive reaction

may appear in cases of latent tuberculosis.

Von Pirquet (61) found that in some cases after repeating the inoculation the reaction became more marked, and a previously negative result became positive. Some investigators hold that all cases with a negative reaction will become positive in time - if the test is applied often enough.

Wolff-Eisner (62) considers that the positive result of the reaction when repeated indicates the presence of latent tubercular centres.

Dael's (63) has demonstrated the specific action of tuberculin, by this method, in cut sections of the papules which shew typical tubercular nodules having giant cells surrounded by epithelioid and round cells.

The test may fail

- (1) in general tuberculosis.
- (2) in the final stages of tuberculosis.
- (3) in cases of tuberculosis complicated by another disease.
- (4) in general cachexia.
- (5) during an attack of measles and some other acute transient conditions.
- (6) when a tolerance of tuberculin has been developed due to subcutaneous injections.

Table 5 shews the results of Forty-three Von Pirquets tests performed by me with undiluted old

Tuberculin.

As laid down above, if the test spots were similar in appearance to the control spots at the end of 24 hours, the result was looked upon as negative.

Traces of a positive reaction were regarded as being present, if, at the end of 24 hours, there was distinctly more hyperaemia at the test spots than at the control, without any evidence of papule formation. In such cases the test should be repeated but for the purposes of this table the first application of the test only is taken into account.

If a papule formed, its diameter was measured at the end of 24 hours and the result charted. Each case was clinically diagnosed as Tuberculosis, and placed in stages according to the Turban-Gerhardt classification.

See over.

TABLE V.

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TABLE V.

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Turban-Gerhardt Classification	Stage 1.	Stage 2.	Stage 3.
Number tested	20	7	16
Number giving a positive reaction	20 100%	6 86%	12 75%
Number giving a negative reaction	0	1 14%	4 25%
Number giving traces of a reaction	1 5%	1 17%	3 25%
Number with papules 2-4 mm in diameter - slight reaction	5 25%	2 33%	6 50%
Number with papules 5-9 mm in diameter - moderate reaction	7 35%	3 50%	3 25%
Number with papules 10 mm or more in diameter - strong reaction.	7 35%	0	0

The above table shews that a large majority of clinically tubercular patients give a positive reaction to the Von Pirquet test. The strongest

reactions only occur in cases in Stage 1 of the disease and the number of positive reactions decrease in percentage as the stages of the disease advance.

Wolff-Eisner (64) states that a positive reaction indicates the existence of the capacity to react, whereas failure to react indicates a lack of this capacity. He considers that a negative reaction in a case of undoubted tuberculosis is to be regarded as an ominous sign, whilst a positive reaction indicates that the reactive capacity is present, or in other words, that the body is still capable of fighting against the disease.

Szaboky (65) confirms the view that a negative Von Pirquet in a patient with undoubted tuberculosis, as a rule means a bad prognosis.

The decrease of this reactive capacity does not necessarily correspond to the stage which the disease has reached, although on the first glance at the Table this appears to be the case. This must be attributed to the fact that, as a rule, a patient with slight disease resists infection, and therefore possesses full reactive capacity, whereas, in a patient with advanced pulmonary tuberculosis, the reactive capacity has been worn out in the struggle.

The inference is that a negative reaction in Stage 1 indicates the patient's inability to fight

the disease and that he will rapidly get worse and die, also a marked positive reaction in an advanced stage would indicate that the disease is inhibited or almost inactive and that the patient may live for years.

Mary Lincoln (66) states that in 80% of cases giving a positive Von Pirquet reaction the results were verified by the opsonic index; that the Von Pirquet and Calmette reactions agreed in 92% of non-tubercular cases, in 69% of cases of bone and joint tuberculosis, and in 64% of cases of lung tuberculosis; She found that the more advanced the disease the smaller is the percentage of positive results obtained with tuberculin tests.

Non-Tubercular Cases :-

Wolff-Eisner (67) has pointed out that out of 192 of his cases, apparently free from tuberculosis, 96 gave a positive reaction to the Von Pirquet test. All these patients were under treatment for other diseases, and did not shew any sign or symptom of tuberculosis, Doubtless in these so-called healthy persons many had latent and healed up or inactive tuberculous lesions.

Bandler and Kreibick (68) obtained 38 Cutaneous reactions out of 62 healthy individuals.

This frequent response to the cutaneous reaction in apparently healthy persons, has forced some observers

to the conclusion that the reaction is of little or no use for diagnosis.

Citron (69) for example, regards the reaction as useless.

Wolff-Eisner (70) considers that the frequent appearance of a positive reaction in apparently healthy people is due to the fact that the cutaneous reaction indicates the presence in the body of inactive as well as active tuberculosis; he states that an inactive and encapsuled tubercular centre may not be discovered by clinical examination and may give rise to no symptoms, and therefore the patient is considered clinically healthy. He brings forward postmortem evidence to support this view. In five cases giving no reaction, no traces of tuberculous change could be found on postmortem examination, whilst the autopsy on eight giving a positive reaction revealed tuberculous changes in each one, six being cases with old, capsules and healed up tubercular centres in different parts of the body.

In Childhood. The mainstay in the diagnosis of active pulmonary tuberculosis, viz, the presence of tubercle bacilli in the sputum can in no way be depended upon in the case of children, since the lesions do not as a rule communicate with the bronchi, and even in definite pulmonary tuberculosis the sputum is often not obtainable.

Therefore a considerable amount of reliance has to be placed upon tuberculin tests. It would however appear evident that because of the great frequency with which a positive reaction is obtained it can be of no great assistance, except in infants, in the diagnosis of tuberculosis. A negative reaction is of much more value for with certain reservations it shews that tuberculosis may be excluded.

In infants and children under the age of 3 years a positive reaction means the presence of active tuberculosis because in these there is no possibility of old or latent disease. A negative result may be regarded as definite proof of the absence of any tubercular lesions.

O.F.Rogers (71) gives his opinion of the value of the Von Pirquet test, derived from the cases of 50 children under the age of 3 years who had given a positive reaction. Before the age of 2 years a positive reaction seems to be an indication that the life of the child is likely to be short. The mortality among all children up to the age of 10 who react to the test is much higher than that of normal children.

Many authorities believe that the great majority of children under twelve years of age are infected with tuberculosis in some form, and they consider that the question of practical importance is not the frequency of the occurrence but how often the condition is an

active one requiring treatment. In this respect the Von Pirquet test is looked upon by S.W. Mc Lellan (72) and others as being of great value.

CONCLUSIONS.

Von Pirquet (73) states that the positive result of the reaction indicates with certainty the presence of active or inactive tuberculous changes. He found that in each of 31 children giving a positive reaction there were tuberculous changes, at any rate caseated glands, at the post-mortem.

Comby (74) performed post-mortem examinations on 58 cases who had given a negative reaction and in none was there any evidence of tuberculosis, whilst at the post-mortem examination on four who had given a positive reaction tuberculosis changes were found in each case.

In regard to infants Wolff-Eisner (75) states that newly born children never without exception give a positive reaction, and that tubercular changes are never found post-mortem in the first infant stage, whereas as age increases the number of positive reactions also increase, and, at the same time, there is an increase in the number of tuberculous discoveries. He also states that healed up cases of tuberculosis have not been known to occur

before the age of three or four years. Rodziejewsky (76) after performing 368 autopsies in children writes that the Von Pirquet test is specific for tuberculosis. He also finds that there is no such thing as an inactive form of tuberculosis in young children, therefore if a child gives a positive reaction it suffers from an active form of the disease. Stadelman (77) gives his judgment on the reaction in the following sentences :- " The justification of a suspicion of tuberculosis by the reaction can only, of course, in the first instance be found in the course of the disease and in clinical observation, which naturally has to extend over a fairly long period, so that a final opinion cannot be given easily and within a very short time. In a number of cases, however, we have actually succeeded, and I may express satisfaction at the fact that our critical and objective judgment in all cases correspond with the result of the reaction. Lapage (78) is a firm believer in Von Pirquet's tests. He considers the method more suitable although not quite so reliable as the subcutaneous one. A reaction indicates that the subject has been infected but does not mean that the disease is progressive or active. A marked reaction in a healthy person may be of

good import and need not bear a similar interpretation. A negative result may follow the test in children infected with tuberculosis:-

- (1). If the disease is advanced
- (2). If there is cachexia
- (3). In very acute disease
- (4). In mixed infections or cases complicated by acute disease.

A negative result does not exclude Tuberculosis for some definitely tuberculous patients react on the third attempt, and others fail to after several trials.

Mc Lellan (79) gives ^{his} conception of the general opinion in regard to the test as follows :-

1. That as a proof of active tuberculosis after the age of three years it is unreliable.
2. That under the age of three years a positive or negative result can only be accepted as a proof of the presence or absence of disease with many reservations.
3. That the younger the child the greater is the reliance that may be put on the result.

Conclusion.

I sum up the value of the test as follows :-

1. As far as cases of definite tuberculosis is concerned the reaction is of greatest value from the prognostic stand point.
2. The deductions to be drawn from a positive reaction are that the patient has been at some time or is now infected by the tubercle bacillus.

3. The frequency of a positive occurrence in healthy persons instead of indicating that the reaction is of no use, shews that tuberculosis in some form or other either active or inactive, is more prevalent than is generally considered to be the case. And that although latent, inactive, healed or any tubercular condition not necessitating treatment required little consideration. Still, on account of the possibility of these conditions lighting up afresh, the fact that a positive Von Pirquet reaction is obtained is of considerable interest and some importance.

4. A marked positive reaction in an advanced case indicates inhibition of the disease and the immediate prognosis is a good one.

5. A repeated negative result while not definitely excluding tuberculosis may be looked upon in persons with no clinical evidence of the disease, as being practically nontubercular.

6. In definitely tubercular cases a negative result is evidence of rapidly spreading disease.

7. In childhood - the younger the patient the more valuable is the test.

In infants and very young children a positive reaction indicates active tuberculosis. A negative one means that there is no tuberculosis present.

From my experience and study of this condition I am of opinion the tubercle bacillus has a greater affect on infant mortality than is generally recognised.

The mortality in infants under one year of age in England and Wales in 1913 reached the comparatively low but enormous figure of 95.608 or 18.9% of the total death rate, corresponding to a mortality of 108 per 1000 births or 13 per 1000 births below the average of the previous ten years.

The tubercle bacillus in some form or other either slightly or virulently attacks the great majority of infants and young children, and by lowering their vitality lowers their power of resistance to all and sundry organisms enabling these to take a toll which they would have less chance of doing if the child were tubercle-free. For this reason I consider that the Von-Pirquet test is most important and of the greatest value from the point of view both of prognosis and treatment in diseases of infancy and early childhood.

A severe cold or an influenzal attack in young children is probably generally due to the tubercle bacillus. If the condition becomes progressive it is diagnosed as tuberculosis and as such accounts for a considerable percentage

of the death rate from all causes in children. If the infant recovers, its vitality is lowered and it may and often does succumb to some other condition, while if the patient reaches adult life, the fact that he was infected by the bacillus of Tubercle in his early years explains the positive Von Pirquet reaction so often got in healthy persons.

8. The Von Pirquet test is also of great value in determining the initial dose of tuberculin for sub-cutaneous injection either in diagnosis or treatment. If the reaction is marked, thus shewing that the patient is very sensitive to tuberculin, the initial dose given is small, if the reaction is slight or negative the dose is larger. In this way it is possible to avoid severe reactions at the commencement of a course of subcutaneous injections.

CHAPTER VII.The quantitative Von Pirquet Reaction.

Ellermann and Erlandsen (80) have endeavoured to obtain quantitative information as regards the amount of tuberculin-sensitiveness present in a person infected with tubercle. They formulated a method by which the sensitiveness of the patient can be determined by a series of measurements and the result expressed numerically.

This method, which has been simplified by Morland (81) allows of a standard of comparison between different cases and makes it possible for the progress of a patient to be estimated numerically at different periods during a course of treatment.

For the purposes of this test, the apparatus for the qualitative Von Pirquet plus four dilutions of old Tuberculin viz 1%, 4%, 16% and 64%, is all that is necessary.

A drop of each dilution is allowed to fall on the forearm at distances of one inch apart. The weakest dilutions are placed distally in order to prevent a stronger solution being carried to a proximal point by the lymphatics and thus making the results unreliable.

The skin is scarified in the ordinary way within

each drop. The needle should be carefully sterilized between each scarification to prevent the different dilutions being conveyed from one spot to another. The diameters of the papules which form are measured in millimeters at the end of twenty four and forty eight hours and the results charted. The papule alone is measured, not the hyperaemia surrounding it, and the diameter of the actual scarification is deducted as irrelevant.

A cheap and useful instrument for measuring the diameter of the papules can be made as follows :-

A small magnifying glass is fixed by means of four wire legs to a piece of glass on which a number of millimeter squares are marked. By placing the piece of marked glass over the papule and looking at it through the magnifying end the diameter of the papule is very easily obtained.

The average size of each papule is then found - a papule of 4 millimeters in diameter after twenty four hours and 8 millimeters after forty eight hours would have an average diameter of 6 millimeters.

Papule size:- Add the averages of the four papules

together and divide the result by four the figure obtained is known as the "Papule Size".

Papule Difference - The difference in diameter

between the average size of the successive papules, that is, between the 1% and 4%, and 4% and 16%, and the 16% and 64% results, is then ascertained, the sum of these three differences is divided by three and the figure obtained is called the "papule difference".

Reference must then be made to the table worked out by Erlandsen (82) which has been simplified by Morland (83). By comparing the figures, representing the papule difference and papule size, with this table the numerical expression of the sensitiveness of the patient is obtained.

In Morland's table the sensitiveness values range from 14 to over 5000. Ellermann and Erlandsen look upon the value 100 as the crucial one clinically; the active cases of tuberculosis are above this figure, and ^{the} inactive or latent ones are below it. Morland (84) states that the determination of the quantitative Von Pirquet test is of the greatest importance for diagnosis and as a guide to treatment. He says that the test is to be used (1) in deciding whether an existent tuberculosis is in such a condition as to require treatment; (2) as a guide to the progress of the case - if favourable, the figure soon falls below the crucial limit; (3) in concluding or excluding the presence of tuberculosis where the diagnosis is doubtful; (4) in determining

the initial dose of tuberculin for a therapeutic course (where the figure is high and the sensitiveness accordingly great, a small dose should be chosen to begin with); and (5) in standardising any particular preparation of the tuberculin and comparing two or more preparations.

In order to avoid fallacies in drawing a conclusion from the result of the test, Morland (85) calls attention to the following points:- (1) The Von Pirquet reaction tends to disappear in advanced cases of tuberculosis and in military tuberculosis of rapid course.

(2) The reaction is constantly absent during the first ten days of measles and in some other transient acute conditions (3) The sensitiveness value tends to remain high long into convalescence from bone and glandular tuberculosis.

(4) In the negative phase of a tuberculin reaction the figure may be very high, but it is remarkable how rapidly the large papules disappear as the positive phase sets in.

I have performed the quantitative test in forty two cases and have recorded the results in Table 6.

Several cases shewing a negative Von Pirquet reaction have been omitted.

TABLE VI.

Sensitiveness value. (Morlands Table)	Cases in Stage 1.	Cases in Stage 2.	Cases in Stage 3.
Below 100	3	1	1
100 to 500	8	3	3
500 to 1000	5	1	1
1000 to 2000	3	1	3
above 2000	4	1	4

With regard to the three cases in Stage 1. giving a figure below 100, Ellermann and Erlandsen would look upon these as inactive. I think this is probably correct. The two cases in Stages 2 and Three however are not inactive.

I employed tuberculin for purposes of treatment in 10 cases with a sensitiveness value of over 100 before treatment commenced. The patients were mostly in Stage 1. and the results are shown in Table 7.

TABLE VII.

Sensitiveness value at beginning of treatment.	Very good progress made during treatment.	Fairly good progress made during treatment.	Not good progress made during treatment.
100 to 500	4	1	0
500 to 1000	1	0	0
1000 to 2000	1	0	0
above 2000	1	1	1

In Table 6, of the 37 cases with a sensitiveness value of over 100, 58% were between 100 and 500, whereas Table 7 shews that of the 10 cases which had undergone treatment 50% gave a figure between 100 and 500. This shews that patients with a low sensitiveness value are those whose course of treatment is most quickly completed.

I consider that the nearer the sensitiveness value is to 100 the shorter the period of time necessary to complete treatment.

Also the progress under treatment with tuberculin is more satisfactory and successful in those cases

with a low sensitiveness value at the beginning.

Moreover I find that when treatment is successful the sensitiveness value falls and in many cases ends up below the 100 mark.

As very small differences in measurements of the papules make considerable differences in the figures of sensitiveness value, I am of opinion that test is of no value in the third stage cases where the papules are usually so small that it is almost impossible to measure them accurately. This applies to many cases in Stage 2 as well.

I think that the test may prove of some use in Stage 1 cases, but my observations are not sufficiently extensive to venture a definite opinion in the matter.

THE OPHTHALMIC REACTION.

The ophthalmic reaction is merely an adaption of the cutaneous one.

It was first introduced by Wolff-Eisner and immediately afterwards in a safer form by Calmette (86).

It consists of placing a minute quantity of tuberculin into the eye. In cases of tuberculosis a marked reaction is produced on the conjunctiva. Calmette recommends a purified tuberculin got by precipitating old tuberculin with alcohol. The precipitate is dried and 10 m.g.m. are dissolved in 1c.c. of sterile water or normal saline solution.

In performing this test one drop of the solution is placed in the space between the lower lid and the eyeball. The lid should be held down for a short while to ensure distribution of the fluid over the conjunctiva and to prevent the patient immediately closing the eye thus extruding the tuberculin.

The eye is then examined at intervals of eight twelve, twenty-four and forty-eight hours and any differences in the appearance of the two eyes carefully noted. A positive reaction is indicated by redness and swelling of the conjunctiva, most marked at the semilunar folds and caruncle.

The reaction is often severe and gives rise to

considerable pain and inconvenience.

If the test is applied to an eye with any disease present, the patient may lose his eyesight. I strongly advise trying all other tests before proceeding to use this one.

TREPERCUTANEOUS REACTION.

This test was introduced by Moro (87) and consists in the application to the skin of an ointment composed of Koch's old tuberculin mixed with lanoline, the strength being 5 c.c. of a tuberculin fluid to 5 grms of lanoline. A small piece, about the size of a pea, is rubbed into the skin for about five minutes, a control being made with pure lanoline.

A positive reaction appears in from twenty-four to forty-eight hours and shews itself in the form of numerous small papules. The local reaction is not accompanied by any general symptoms.

Moro claims that a positive reaction is as conclusive for a present or previous tuberculous infection as is that obtained by the conjunctival or the Von Pirquet reaction.

A negative reaction with Moro's test cannot be regarded as excluding the possibility of tuberculosis.

SUBCUTANEOUS INJECTIONS OF TUBERCULIN.
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"I believe I am not going too far in assuming that tuberculin for the future will constitute an indispensable agent in diagnosis".

These words were written by Koch (88) in November 1890.

Since that time the subcutaneous injection has been extensively used for diagnostic purposes although in recent years the practice is not so general as it used to be, many observers condemning it as being far too dangerous.

Sahli⁽⁸⁹⁾ states that it should never be used, while Comac Wilkinson (90) advocated its use only when tubercle bacilli are absent from the sputum.

Gelien and Hamman (91) conclude from a study of the subsequent history of 1000 cases who received the tuberculin tests, that they are of value only in reference to the condition of the patients at the time they are given.

Fowler (92) considers that tuberculin is always dangerous and specially so when fever is present.

Virchow, it will be remembered, attacked tuberculin soon after its introduction and said it caused a scattering of the tubercle bacilli - this however he modified later.

L. Rabmowitsch (93) found tubercle bacilli in the blood of tuberculous animals after the tuberculin test, when previous examination had been negative.

Bacmeister (94) examined the blood of fifteen patients during the height of the tuberculin reaction and obtained positive results by animal inoculation in four.

Ravogli (95) who lost two patients as a direct result of the subcutaneous injection of tuberculin regards the use of tuberculin, for any other than diagnostic purposes, as in the Von Pirquet and Moro tests, as dangerous. He deprecates its internal use even in the smallest doses.

Whatever may be said against its use however, its diagnostic value is undoubted, and our knowledge today of the widespread distribution of tuberculosis is largely due to this method of diagnosis.

Hayling Coleman (96) makes the following statement:-

"Tuberculin is an important aid to diagnosis, whereby we can be positive in cases where, without it, we should still be in doubt. It is in discovering tubercle in its early curable stages that our chief hope lies in dealing with a disease whose annual death rate is equal to 75% of our total killed for the first year of the War. I am aware that some hold the use of tuberculin for diagnosis to be risky but their reasons when examined do not convince; the ability to diagnose tubercle in its early stages is of such

paramount importance that, even if there were some slight risk it would be justified".

Technique :- A combination of asepsis and accurate doses is essential. For this reason I recommend the use of Messrs Burroughs Wellcome & Co's all-glass aseptic syringe which can be taken to pieces and boiled, and is specially designed for substances like tuberculin which have to be given accurately in minute doses. The barrel and piston are about twice the length of the ordinary hypodermic syringe and the former is clearly engraved with numbered graduations of 1 to 10 between which are marked half graduations each equivalent to .05 c.c. Both piston and nozzle are of deep blue glass so that the position of the piston can be determined with the greatest precision. A platinum iridium needle should be used, as it can be repeatedly flamed without rusting or blunting. The syringe should in the first instance, be sterilized by boiling and then immersed in absolute alcohol so as to be always ready for use. When required the syringe is washed out with boiled water, after use it is again washed and returned to the alcohol.

Hayling Coleman prefers needles made like dentists injection needles. He says "the needles (supplied in sterilized tubes) are separate from the mount to which they can be readily attached; by using these one always has a sharp point and can use a new needle every time if advisable. I always keep platinum -

iridium needle in reserve, but they get blunt far too readily".

TUBERCULIN:- Koch recommended old Tuberculin and

 this has been most commonly used for diagnosis. It is a solution chiefly of the exotoxins, prepared by filtering a sterilized tubercle culture through porcelain. Numerous modifications of this have been placed on the market. In late years the Hochster Farbwerke has introduced a new variety called Koch's Albumose-Free Tuberculin, which I used for subcutaneous injections. In manufacturing this preparation bacilli of the human type are grown in a medium free from all albumoses and peptones. The advantages over Koch's old Tuberculin claimed for it are the specific character of the reaction induced and the exclusion of anaphylactic symptoms, in consequence of the absence of non-specific proteins. Albumose-free tuberculin is used in exactly the same manner as old tuberculin and corresponds with it in regard to its active value. I am of opinion that it is quite as trustworthy as old tuberculin from a diagnostic standpoint, and has the advantage that the constitutional disturbance following its injection is less severe although the rise of temperature is equally well marked.

In using it I make a dilution of 1 in 100 and another of 1 in 1000 with .5% of carbolic acid

solution with the former dilution each 1/10 graduation on the hypodermic syringe represents .001 c.c. and with the latter (1-1000) each division represents .0001 c.c. of the undiluted tuberculin.

SITE OF THE INJECTION. The injection should be into loose connective tissues so that the swelling which follows will not be too painful. The extensor surface of the forearm, the upper arm, or the back in the region of the lower ribs are all excellent positions. The injection is subcutaneous, not cutaneous or intramuscular.

The skin must be carefully cleansed with alcohol before giving the injection.

After the operation the puncture in the skin should be closed with a small piece of cotton wool soaked in collodion.

PRECAUTIONS:- Before applying this test it is necessary to take the temperature of the patient every three hours for at least three days. As soon as the temperature is found to be normal or nearly so, the injections may be commenced. If possible it is good practice to keep the patient in bed for at least two days before giving a diagnostic injection.

If the mouth temperature is over 99° F the patient should be put to bed until the temperature has been normal for at least three days, and then the injection may be given.

After the injection the patient should be kept in bed

for not less than twenty-four hours and the temperature noted at the same hours as before the injection, and also at any time that the patient complains of feeling unwell or suffers from symptoms indicating a rise in temperature.

It should be borne in mind that in Women a pre-menstrual rise in temperature occurs, and the onset of menstruation should be enquired about in female patients in order to avoid confusing this with the rise of temperature due to tuberculin.

DOSE. I apply the dosage, advocated by Koch for old

Tuberculin, to the albumose-free product.

For adults of good physique the initial dose is .001 c.c. If no result the second dose given is .002 c.c. If still no reaction .005 c.c. is injected. Failure with this leads to the fourth dose of .01 c.c. If there is strong presumptive evidence that the patient has tuberculosis in spite of failure to react to .01 c.c. the latter may be repeated in a fortnight.

If the absence of reaction is continuous the case may be looked upon as non-tuberculous.

An increased second, third, or fourth dose should never be given if there is a rise of temperature after the preceding injection. After, even, a very slight rise the same dose should be repeated on the temperature returning to normal.

The initial dose in weakly adults and children is

reduced to one quarter or even less - but the maximum dose is .01 as in ordinary adults. I invariably do a Von Pirquet test as a guide to the initial dose for a subcutaneous injection. If the cutaneous tests shows marked sensitiveness on the part of the patient to tuberculin the initial subcutaneous dose may be reduced to one tenth, one twentieth or even less.

Subcutaneous injections are contra-indicated in advanced cases of tuberculosis.

Intervals between injections. As a rule three days should elapse between each injection. If a marked rise of temperature occurs no further injection is required. A slight rise generally subsides quickly and a repeat of the same dose should be given after an interval of three days provided always that the temperature has become normal.

The Tuberculin Reaction:- The following signs occur when the patient with pulmonary tuberculosis in any stage, is given an injection of tuberculin :-

1. Local Reaction. There may be no local reaction at all or a painful, red swelling may shew itself which increases until the third day and then gradually disappears. It may occur in one or both of two ways, either first as a thickening and sometimes a distinct redness and oedema in the subcutaneous tissue or second as the needle tract reaction - due to the escape of a very small quantity of tuberculin into the skin itself - producing a vivid redness round the

puncture and at times a painful nodule as well.

2. Temperature reaction:- This is very easy to recognise. As a general rule the reaction is regarded as positive if the temperature rises one degree or more above the highest point noted before the injection.

The reaction may be looked upon as slight - up to 100° F.

Moderate - up to 102° F.

Marked - over 102° F.

The temperature usually begins to ascend in from six to twelve hours after the injection but it may occur earlier or later, in some cases even after 24 hours. The duration of the fever varies considerably. Typically it rises rapidly, falls slowly, and lasts for about twenty-four hours.

3. General or Constitutional Reaction:- If marked this may be indicated by rigors, dizziness, headache, pains in limbs and joints, nausea, palpitation, sleeplessness, thirst, anorexia, fatigue and depression; even very slight reactions may be accompanied by headache, loss of appetite, malaise, nausea and perhaps vomiting. These symptoms vary in intensity and do not always follow the temperature curve. Even a severe reaction subsides quickly and is often followed by a feeling of improvement in general health.

4. Focal Reaction. This is due to changes in, or near,

the tubercular foci, and may shew itself in the form of subjective symptoms, such as pain in chest, cough and dyspnoea and as objective symptoms e.g. increase of expectoration, blood stained streaks in the sputum, increased dullness on percussion, increase of râles etc.

Contra-indications :-

1. The chief contra-indication is a mouth temperature of over 99.5°F . This is due to the fact that alterations in temperature make the correct interpretation of an increase in temperature, following the injection of tuberculin, an impossibility.
2. It is contra-indicated naturally in cases where there is a definite history, where the clinical signs are positive and the bacillus has been demonstrated in the sputum, Here the test is superfluous and dangerous.
3. Recent haemoptysis is a contra-indication of importance. **Such** cases must be rested in bed till all expectoration of blood has stopped for some days, before giving a diagnostic injection of tuberculin. Hayling Coleman however states that he has never known harm follow an injection in these cases, and contends that the haemoptysis occurs in spite of the treatment, not in consequence of it.
4. The test should not be used in case of organic cardiac disease, but this does not apply to functional disturbances of the heart so frequently found in early tuberculosis.

5. True Nephritis is a contra-indication - hence the necessity for examining the urine - more particularly in the direction of a quantitative urea estimation - before tuberculin administration. The albumen test is useless in nephritis - Simple and transient albuminuria being frequently diagnosed as nephritis. Large numbers of men have recently been discharged from the army suffering from nephritis - who have had no lesion of the kidneys whatever.
6. The possibility of an irritative action in cases of epilepsy should always be borne in mind and an endeavour, to elicit a history of this condition, should be made before proceeding to give an injection of tuberculin.
7. Severe hysteria and neurasthenia are sometimes a contra-indication, because in such cases temperature variations are produced by slight physical disturbances even when tuberculosis is absent.
8. The slightest suspicion of military tuberculosis is a strong contra-indication, also cases of extensive ulceration of the intestine with evident extension to the peritoneum.
9. Feeble or convalescent patients immediately after severe disease should not be subjected to the test until recovery is quite complete.
10. In persons with apoplectic possibilities, severe diabetes, marked arterio-sclerosis and amyloid disease of the abdominal organs the test should be avoided. Speaking generally, the indications for the employment

of the tuberculin test — are :-

- A. Clinically doubtful cases - to confirm diagnosis.
- B. Cases presenting difficulties in differential diagnosis.

The test should not be looked upon as an alternative to other diagnostic methods, but should be employed when these fail to give a definite decision.

It is the final diagnostic procedure.

The reaction is slight, as a rule, and the symptoms disappear in a day or two if the patient is kept in bed.

If properly applied there is very little risk while from the diagnostic standpoint its value is undoubted.

Wilkinson (97) states that, after an experience extending over 20 years, he has not yet seen a serious effect from the use of tuberculin as a diagnostic agent; he also declares that it is absolutely reliable.

A rise of temperature of 1° F or more is considered to constitute a positive reaction, but the importance of local and general symptoms should be borne in mind. Even if there is only a slight rise of temperature, the development of these symptoms must be regarded as suggestive and warranting further injections after the reaction has subsided.

Koch (98) wrote that by means of tuberculin it is possible to diagnose doubtful cases of incipient

phthisis, even when on account of the absence of the bacilli and elastic fibres or regular physical signs, definite information concerning the nature of the lesion cannot be obtained. He also stated that healthy persons, or patients suffering from diseases other than tuberculosis, react, either not at all, or scarcely at all, after a dose of .01 c.c. of tuberculin.

Röpke (99) states that the subcutaneous tuberculin test is the sovereign diagnostic method.

Waterhouse (100) writes that in his experience the subcutaneous injection of tuberculin is a trustworthy test and gives accurate results in 99% of cases.

Muller (101) says that the injection of tuberculin is the most reliable specific test. In animals, if the fever rises promptly to 41°C or over after the first injection tuberculosis is present in 98% of cases.

Hammon (102) draws conclusions from observations on over 5000 cases at the Phipps Dispensary and believes that the reaction is specific and that a negative reaction is decisive information.

Bandelier and Roepke (103) declare that a positive reaction shows the presence of tuberculosis without giving indications with regard to its activity or the reverse. They say (104) that if a positive reaction is obtained, other weighty evidence, either from clinical signs or the patients history, is

necessary before it can be positively concluded that the patient is the subject of active tuberculosis. The subcutaneous injection of tuberculin must be regarded as the most reliable and most scientific of the tuberculin diagnostic methods; a positive reaction indicates the presence in almost all cases of a tubercular infection, either active or latent, whilst a negative reaction excludes the possibility of such infection.

Hayling Coleman (105) says that those who have used tuberculin most are those most strongly convinced of its value, and their conviction increases as time goes on.

My experiences are given below in Table VIII. This record does not include advanced cases which do not require diagnostic injections. It may be added however that, as in the case of the Von Pirquet reaction, patients in the last stages of the disease do not respond to the subcutaneous test.

Albumose-free tuberculin was used in each case, in and the cases divided into the way already laid down, five different classes as follows :-

Class I. Those with tuberculin bacillus in their sputum, discovered on microscopical examination. These cases are undoubtedly cases of tuberculosis.

Class II. Those whose sputum contained .2% or more of albumen. I stated in chapter IV. that, if

pneumonia, gangrene of the lung and heart disease are - - - excluded, a patient with the above per centage of albumen in his sputum must be regarded as suffering from active tuberculosis.

I have omitted cases with less than .2% of albumen as some authorities, already referred to, claim to have found traces of albumen in the sputum of patients suffering from bronchitis.

Class III. Patients who, on the evidence revealed by clinical examination, history, and symptoms, were looked upon as suffering from active tuberculosis.

Class IV. Patients shewing signs of changes in the lung on physical or X-ray examination but who were considered to be cases of latent and not active disease.

Class V. Patients in whom physical examination and the X-rays failed to discover **changes** in the pulmonary tissues but who on account of ill-health, or symptoms which suggest the possibility of tuberculosis, were regarded with suspicion.

TABLE VIII.

Class of Case.	Number of patients.	Number giving a positive reaction at first or subsequent injection.	Number failing to react even after .01 c.c. albumen-free tuberculin had been injected.
1. Tubercle Bacilli in Sputum.	10	10	0
2. .2% or more of albumen in sputum.	15	15	0
3. Clinically active tuberculosis.	28	28	0
4. Clinically latent tuberculosis.	16	12	4
5. Suspicious cases with no signs on X-ray or physical examination	10	6	4

An analysis of this table shews that, of the patients in the first three classes, all of whom were considered to be actively tubercular, 100 per cent

gave a positive reaction.

Of the latent cases (class 4) exactly 75 per cent gave a positive result.

In these latent cases it is almost impossible to be certain whether they are tubercular or not without recourse to tuberculin, and the 25 per cent who failed to react are very probably nontubercular cases. Of the ten suspicious cases (class 5) 60 per cent were positive and the remaining 40 per cent failed to react. In each of these ten cases the patient had some condition such as cough or loss of weight which seemed to point to tuberculosis and in view of what has already been written it appears to be reasonable to suppose that each of the six cases giving a positive reaction may have been suffering from active or latent disease with a focus too small to be detected on physical examination, or due to its situation in the bronchial glands, or in some unsuspected organ.

It is interesting to note that in six cases which I have not included in Table VIII, and which shewed signs of active disease on physical examination, each patient has sputum without a trace of tubercle bacilli or albumen and moreover each failed to react to .01 c.c. subcutaneous injection of tuberculin. I therefore diagnosed these cases of chronic bronchitis, which I am still of opinion they were, and my experience leads me to believe that I would have been

justified in diagnosing them as chronic bronchitis on the absence of albumen from their sputum alone. My results, therefore, coincide with Koch's original opinion, and that of other writers already quoted, that a positive reaction indicates tubercular infection while a negative one means the absence of tuberculosis, but as pointed out by Bandelier and Roepke (previously mentioned) a positive reaction does not distinguish between active and latent disease. In the majority of cases the history, symptoms, physical signs, and sputum examination are sufficient to allow of a definite diagnosis being made.

But in very early or difficult cases I believe that the subcutaneous reaction is of very great value and should always be resorted to.

In dealing with the Von Pirquet reaction I mentioned that Von Pirquet found that in some cases when the cutaneous reaction was repeated it increased in strength and became positive where previously it had been negative; I also referred to the fact that Wolff-Eisner considers that the positive result of the reaction, when repeated, indicates the presence of latent tuberculosis.

Wolff-Eisner's (106) explanation of this increased reaction on repetition is, that in a person with an inactive lesion, perhaps long since healed up, the cells of the body for a long period have had no

occasion to react on tubercle bacilli or their products; but that, under the renewed stimulus of the toxins of tubercle bacilli, they re-assume their former reactive capacity. When the test is repeated, therefore, a hypersensibility reaction promptly occurs. Wolff-Eisner states that this view is supported by post-mortem evidence.

Wolff-Eisner's theory should apply equally well to the subcutaneous reaction.

I have gone through the records of the cases dealt with in Table VIII in order to find out whether it was the first or a subsequent injection which gave a positive reaction. The results are embodied in Table IX., and the cases are classified in exactly the same manner as was done in Table VIII.

TABLE IX.

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TABLE IX.

Class of Case.	Number of Patients.	Number giving a positive reaction after first subcutaneous injection.	Number giving a positive reaction after second injection.	Number giving a positive reaction after third injection.	Number giving a positive reaction after fourth or a later injection.	Number failing to react to .01 c.c. albumen-free tuberculin
1. Tubercle Bacilli in Sputum.	10	8 80%	2 20%	0	0	0
2. .2% or more of albumen in sputum.	15	11 73%	3 20%	1 7%	0	0
3. Clinically active tuberculosis.	28	23 79%	5 18%	1 3%	0	0
4. Clinically latent tuberculosis.	16	3 19%	5 31%	3 19%	2 12%	4 25%
5. Suspicious Cases	10	3 30%	1 10%	3 30%	0	4 40%

It will be noticed that a large percentage of the undoubtedly active cases gave a positive reaction after the first injection (Class 1, 80%, Class 2, 73%) , also that the same applies to clinically active cases (Class 3 - 79%); of the clinically latent cases only 15% gave a positive result after the first inoculation. The figures are equally striking with regard to positive reactions obtained from injection subsequent to the first.

In class 1, 20%, Class 2, 27% and Class 3, 21%, failed to give a positive reaction until more than one injection had been given, while of the latent cases 62% failed to react until more than one injection had been given while 25% shewed no result at all - the latter were probably nontubercular.

The conclusions to be drawn, from a study of this table, may be briefly stated by pointing out how tuberculin injections would influence one in the direction of making a diagnosis in the ten patients in class 5, in which only the symptoms of tuberculosis were present.

The two cases reacting after the first injection would probably be cases of active tuberculosis; the one case giving positive results after the second injection would very likely be latent but the diagnosis would be finally based on the continued observations of the patients progress; the three cases reacting after the third injection would also probably

be latent while the four failing to react to .01 c.c. of tuberculin would be classed as non-tubercular.

I consider that very useful diagnostic information may be obtained by carefully observing the interval elapsing between the injections and the onset of fever.

Hollman (107) has shown, however, that this interval differs according as the injection is given in the morning or evening.

I am unable to give an opinion in regard to Hollman's contention as I have not been in the habit of giving injections at the same hour in all cases. I, however, think that wherever possible diagnostic injections should be given at a specified time and suggest 10 a.m. as probably the best for this purpose.

CHAPTER IX.

CONCLUSIONS.

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The conclusions I have come to after a prolonged study of the subject of Pulmonary Tuberculosis with special reference to its early diagnosis will be found embodied in this Thesis, but I propose to briefly recapitulate the crucial points in this chapter in regular sequence :-

My main conclusion is that the hold tuberculosis has on the general public of this Kingdom is a sad reflection on our profession and more especially on the rank and file, usually referred to as General Practitioners.

I have nothing but good to say of that little band of scientific observers and enthusiasts who spend their lives in what, to the popular mind, is obscurity, but whose work lives and to whom, led by Koch, the Medical profession and humanity are indebted for what has already been done in the matter of dealing with the Universal Scourge known as Tuberculosis.

I consider, however, that if the ordinary practitioner took an average interest in, and expended a reasonable amount of ~~his~~ time and trouble on, the finer methods of diagnosis, and treatment, of this condition, instead of, as a rule, relying on Physical Examination and Cod Liver Oil only, many lives would be saved annually.

The argument will no doubt be advanced that much

has been done in late years especially in the direction of establishing Tuberculosis Dispensaries and moreover that it is a matter for the Government to deal with. This is correct; but my contention is that a great deal more can be done, and that it is the business of the Profession to see that it is done.

I have discussed the question with many Tuberculosis Officers and find that for Diagnosis most of them depend entirely on the history, symptoms, physical signs, and staining test for tubercle bacillus - which methods although quite sufficient in the later stages, are often a failure in the earlier ones.

Moreover the fatal results which have in the past occurred through an indiscriminate use of large doses of Tuberculin in advanced cases have scared many of them, to such an extent, that they have either entirely discarded the subcutaneous injection of tuberculin for diagnosis and treatment, or make use of it in such dilution that they fail to get a reaction, and therefore condemn the method as being either dangerous or useless.

I am of opinion that if Great Britain had been forced to expend one hundredth part of the energy and money on the early diagnosis, prompt treatment, and quick cure of Tuberculosis that she has on combating Prussian Militarism, her position as the

world power would in a very few years have been absolutely unassailable.

Every life lost means a loss of capital and energy. Every life saved means added strength. To a nation like ours, with great Dominions overseas calling out for men to come out to help to populate and to develop their enormous resources, the conserving of every life possible is absolutely essential, more especially as after this War the Mother Country and her colonies will become more dependant on each other than ever.

But out of evil good may come, - if the War has awakened the nation, and if, in the future, the right steps are taken to reduce the death rate especially from Tuberculosis.

Destructive Criticism such as the above is, of course, easy enough but, unless a remedy is indicated no good results can be achieved.

I have, therefore, to suggest a method of dealing with the question of Pulmonary Tuberculosis with a view to the speedy reduction of the death rate due to it.

I have examined a large number of the Huts built for housing Troops and Munition Workers. After the War many of these will be available for other purposes, and I propose :-

- 1st. That the number of tuberculosis dispensaries at present established be doubled - that is brought up to 600.

- 2nd. That two huts ^{each} with sufficient air space to contain 20 patients be erected as near as possible to each dispensary.
- 3rd. That these huts be under the charge of the Tuberculosis Officer attached to the dispensary and that two nurses, one day and one night, be constantly in attendance.
- 4th. That every facility possible be given to the Medical Officer-in-Charge to make accurate diagnosis of Pulmonary Tuberculosis in the early stages.
- 5th. That only such early cases as can be cured by the subcutaneous injection of Tuberculin be treated in these huts. All advanced cases being sent to Sanitoria as hitherto.
- 6th. That senior Tuberculosis Officers be retained by the government for the sole purpose of making a regular inspection of these Tuberculosis Huts - their duties being to advise, and supervise the proper administration of Tuberculin in the treatment of these early cases, - the discipline which the whole nation is undergoing will make it possible to have such supervision.

As I have received instructions to proceed to the East with my unit in a few days, it is impossible, in the time at my disposal, to elaborate this scheme as I had intended. But it appears to me that something will have to be done to replete the

wastage caused by the War, and a scheme to save life by a vigorous assault on the bacillus of tubercle is perhaps as good a method as any; Such a scheme would have to follow, broadly, the lines I have laid down, because it is essential to get at the early cases and to treat them vigorously by means of subcutaneous injections of Tuberculin. Cases of pulmonary tuberculosis are not sent to Hospitals or Sanatoria until they are in the later stages, when prospect of a cure has disappeared.

In treating a case with tuberculin it is necessary to have the patient in bed under constant observation, particularly in regard to fluctuations in temperature and pulse rate. It would therefore be necessary either to have hut or other hospital accomodation at the disposal of the Tuberculosis Officer, or for the latter to make daily house to house visits. In doing so he will probably have to cover enormous distances if he is to treat a sufficient number of cases to do any good. Moreover the difficulty of sterilizing the syringe at each house, and the fact that the patient is not under proper supervision makes it impossible to assure getting even moderately accurate records of alterations in temperature and pulse. For these reasons, as well as, because the greater facilities which the tuberculosis officers would have for making accurate diagnosis in the early cases, I submit that my scheme at least merits consideration.

A resumé of outstanding points in the various methods of diagnosis dealt with in this Thesis may not be out of place here :-

1st. History symptoms and physical signs, - These will always be of primary importance, especially in the later stages and from the point of view of the general practitioner.

2nd. Rontgen-ray Examination. - The value of this method lies in the fact that a case on physical examination considered to be purely apical may shew extensive lesions in the substance and at the roots of the lungs when examined by the X-rays.

It is invaluable in suspicious cases and especially in those in which a positive reaction has been obtained with tuberculin, but in which the site of the disease cannot be determined by physical examination, moreover it facilitates differential diagnosis between Tuberculosis, Silicosis, and Chronic Bronchitis.

3rd. Albumen reaction - The quantitative estimation of albumen in the sputum by means of Esbach's test is an extremely useful method especially as it is within easy reach of the busy general practitioner - It may be accepted that, provided gangrene of the lung, pneumonia and heart disease are excluded, the presence of

.2% or more of albumen means that the case is one of pulmonary tuberculosis.

This method also differentiates between Tuberculosis, and Chronic Bronchitis - in which the percentage of albumen, if any, never rises above .2%. It is also of value in deciding whether positive reaction to tuberculin is associated with an active or inactive tuberculosis, - albumen being present in the active condition only.

4th. Examination of Sputum for Tubercle Bacilli-

The ordinary Ziehl-nielsen stain is quite the best while for a concentration method there is no necessity to go beyond the Antiformin one. All others may be looked upon as interesting but of subsidiary importance.

Serum diagnosis etc- reference should be made to Glover's conclusions on pages 53 and 54.

5th. Von Pirquet's cutaneous reaction - This is of great value in children under the age of 3 years and as a guide for dosage in subcutaneous injections of tuberculin. A negative Von Pirquet, as a rule, means a bad prognosis in undoubted tuberculosis - it shews that the capacity to react to the serum is absent. The fact that so many apparently normal persons give a positive Von Pirquet reaction merely bears out Stanley Barnes' statement (Page 5) that there was evidence of

tubercular^{lung} lesions in more than half of the post-mortem cases he has done. Vide also detailed conclusions on pages 67 to 70.

6th. The subcutaneous Injection of Tuberculin in appropriate doses is of the very greatest importance both in the diagnosis and treatment of early cases. From the diagnostic point of view it must be looked upon as the most reliable and scientific of all methods; a positive reaction indicates the presence in almost all cases of tubercular lesions either active or latent, whilst a negative reaction excludes the possibility of such infection. As in the case of the Von Pirquet test the more advanced the disease the smaller the percentage of positive results to tuberculin - the capacity to react being absent, that is to say, the body is no longer capable of fighting against the disease.

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