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THESIS

FOR THE DEGREE

OF M.D.

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THE CUTANEOUS AND THE OPHTHALMIC REACTIONS IN THE DIAGNOSIS OF TUBERCULOSIS WITH NOTES ON 100 CASES

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Typist,

Miss P. Whyte,

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MCMVIII.

Ophthalmic Reaction

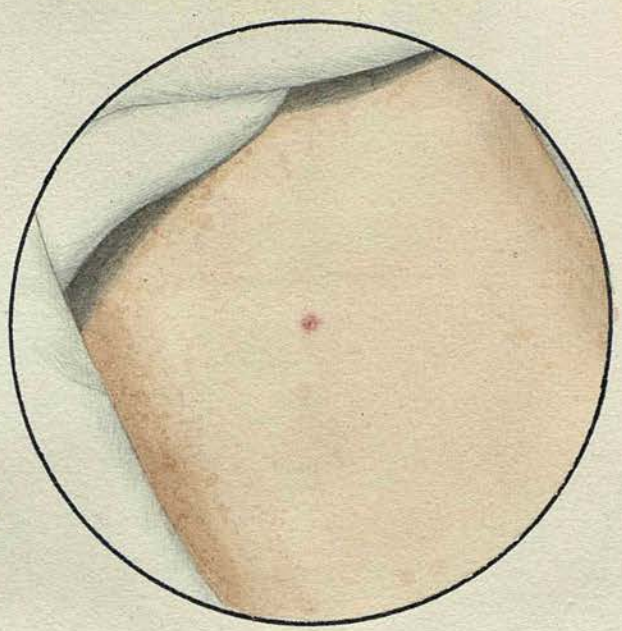
At The End Of Six Hours.


J. C. Brodie

Cutaneous Reaction .

A. After Twenty-four Hours.

B. On The 3rd Day.



A.

B.

J.C. Brodie.

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I.

Introduction.

Von Pirquet's cutaneous reaction to tuberculin and Calmette's ophthalmo-reaction have of late been attracting a considerable degree of attention, and numerous articles have appeared in the various medical journals giving the experiences of different writers. I have collected a number of these articles and have noted the results and opinions of the various authors.

By the kindness of Dr. Philip, whose resident physician I then was, I have been able to perform one or both tests on 100 of his patients in the Royal Infirmary, Edinburgh.

For Von Pirquet's cutaneous test I have used either Koch's pure Old Tuberculin or the solution advised by Von Pirquet, viz:-

Koch's Old Tuberculin	1 Part
Carbolic Glycerine (5%)	1 "
Solution of Sodium Chloride (·85%)	2 Parts

With either the procedure has been the same. First the skin was purified with Sulphuric Ether and then scarified just as for vaccination, drawing no blood if possible; then a small piece of cotton-wool, soaked in the solution, was laid on the scarification and left on for five minutes, after which it was removed and the part covered with dry cotton-wool.

The upper arm was the part selected and at the end of twenty-four hours the cotton wool was removed and the scarified area examined. If a reaction was present there was redness of the area with more or less marked infiltration, best appreciated by gently running the finger over the part and so feeling for any slight raising as compared with the surrounding skin.

For Calmette's ophthalmic test, I have used Tuberculin prepared by the "Institut Pasteur" of Lille according to Calmette's formula. It is issued in a liquid form (0-5%) or as a dry powder, to 5 milligrammes of which distilled water is added - 20 drops making the 0.5% solution and 10 drops the 1%. Calmette prepares his tuberculin solution by precipitating tuberculin with 95% alcohol and then dissolving the dry powder as above. The directions accompanying the tuberculin supplied are as follows:-

"Let one or two drops fall on the conjunctiva of one eye of the patient to be tested, by preference towards the inner angle, and keep the eyelids apart for a moment. The person so treated will feel no pain or inconvenience. If he is not a tuberculous subject no reaction will be produced."

"If he is afflicted with tuberculosis, no matter how slightly, the lower conjunctiva palpebrarum and the caruncula of the eye treated will commence to redden from the third hour. The injection of the vessels is slowly accentuated and accompanied by epiphora. After six hours the caruncula begins to swell and the eye becomes covered by a slight fibrous exudation, which gathers in filaments in the inferior conjunctival sac."

"The maximum reaction is observed between the 6th and 13th hour."

"It is not accompanied by any elevation of temperature. No chemosis is produced nor any pain felt; the only unpleasantness is the epiphora which disappears, and all is again in its usual order after two or three days. The intensity of the reaction will be realized by a comparative examination of the eye which has not received the Tuberculin."

On the 19th of June, 1907 Calmette published his first paper on the ophthalmic reaction, but previously (on the 3rd June) Wolff-Eisner of Vienna had announced to the Society of Medicine of Berlin that a drop of diluted tuberculin put into the eye produced an inflammatory reaction. At the same time, however, he was not able to state anything as to its diagnostic value, and so Calmette's name is the one which is now usually associated with the reaction.

Before giving my own results with the tests I think it well to give some extracts from recent literature on the subject.

II.

Extracts from Literature.

Shennan, (Scottish Medical and Surgical Journal, April 1908) reviews Von Pirquet's Cutaneous Reaction and its Modifications.-

Von Pirquet (Vienna) had been engaged in extended studies on the nature of vaccination against small-pox, and in the course of these had discovered or rediscovered much that is new and important.

Amongst other things, he found that even after repeated vaccination complete immunity practically does not exist. However often a man is inoculated, a rapidly disappearing small papule appears regularly after

about twenty-four hours, whereas in primary vaccination the papule develops for the first time after three or four days.

From the early vaccinal reaction (vakzinale Frühreaktion) one may be certain that the individual concerned has been vaccinated at a still earlier period. This early reaction V. Pirquet designates "allergic," indicating under the term "allergy" the altered reaction which the organism manifests against infective agents or substances already known to it. He regards it as an "antikörper" reaction, which develops on the vaccinal toxin meeting with the corresponding anti-body already existing in the skin.

Allowing that the vaccinal "early reaction" permits one to infer a previous vaccination, V. Pirquet thought that other infective diseases after once attacking an individual, should at a later date furnish an allergic reaction, and indicated as specially suitable diseases tuberculosis, typhus abdominalis and diphtheria.

In the first place, he investigated this principle in tuberculosis, and from a study of nearly 1000 cases soon determined the high diagnostic value of the method.

For the purposes of the reaction the tuberculin is introduced into the outer part of the skin, the superficial layers being removed so as to give access to the lymph spaces in the skin. V. Pirquet employs diluted tuberculin, and states that the dilution to which the reaction is positive is in a constant relationship to the diameter of the local lesion, so that by measuring this one may estimate quantitatively the susceptibility of the individual. In practice he recommends the use of a 25 per cent. tuberculin, and that this be inoculated on the skin of the arm.

The operation is closely analogous to that of vaccination, and the result is also comparable to the local reaction in Jennerian vaccination.

V. Pirquet found that 88 per cent. of his tuberculous children reacted positively, the reaction being given most clearly in cases of bone tuberculosis and scrofula, and that the remaining 12 per cent. were cachectic or suffering from miliary tuberculosis, or had been inoculated too near the fatal issue. Ten per cent. of clinically non-tuberculous children reacted positively. Other authors state that 15 per cent. of clinically non-tuberculous children give a positive reaction, and are of the opinion that this almost certainly points to the existence of tuberculosis in a latent form, arguing from the statements made that 15 per cent. of apparently non-tuberculous children in the first two years of life coming to post-mortem examination show hidden tuberculous lesions, e.g., caseous glands.

V. Pirquet at first concluded that the reaction was only applicable in the case of children in the first year of life. On account of the prevalence of tuberculosis in older children and adults these almost without exception give the reaction. Nevertheless he expressed the opinion that the reaction might later be of practical value even in adults when we learned to estimate the delicacy of the local reaction, its time of onset and extent, and the proper dilution of tuberculin to employ. This has, in point of fact, been accomplished to a great extent, and a reaction in the distinctly non-tuberculous adult can in most cases be distinguished from that occurring in a tuberculous adult, In later papers V. Pirquet states categorically that a positive reaction in children denotes the presence of tuberculosis, and that in adults tuberculosis may be definitely

excluded if they fail to react.

The different points are best considered separately.

(a) The Material used in Inoculating the Skin.- Von Pirquet's original fluid was made up as follows:- Koch's old tuberculin, 1 part; 5% carbolic glycerine, 1 part; sodium chloride (0·85%,) 2 parts. Junker found that 5% glycerine was not free from irritating properties, so substituted 3% glycerine in 0·5% carbolic acid. This author as well as M. Oppenheim came to the conclusion that a 10% dilution produced a more delicately graded reaction. Mainini used a 1·2% dilution, but Junker inclines to think this too weak. Reuschel uses both concentrated tuberculin and 25% tuberculin, as in this way he finds it easier to estimate the value of a weak reaction. He strongly recommends the former. Goebel and Nagelschmidt consider that it does not matter whether one uses a diluted or a strong tuberculin. Lignières, Vallée, F. Arloing, Bandler and Kreibich use concentrated tuberculin. Most authors have used V. Pirquet's original 25% dilution.

Et. Burnet precipitates the tuberculin with alcohol, and redissolves it in salt solution, so that 50 mgm. is contained in 1 c.c. of the solution, but states that it is not necessary to use such a strong solution.

Moro, finding that his 25% tuberculin produced frequently general and distant reactions, as well as the local one, employed an ointment of equal parts of tuberculin and anhydrous lanolin, which he applied to the unbroken skin.

We may conclude that the best dilution of tuberculin is between 10 and 25%, though stronger tuberculin may be employed in the manner to be later indicated.

(b) Methods and Choice of Localities for Inoculation.-

V. Pirquet inoculates over the inner aspect of the forearm. At first he used a dentist's "rose-burr" so as to remove uniform amounts of superficial epithelium, and leave a punched out rounded spot, not necessarily extending down to the corium or drawing blood. A vaccine lancet or other similar instrument may be used to produce the slight excoriation required. More than one excoriation, separated from each other by at least 5 c.m., should be made; a small single drop of the diluted tuberculin placed upon one area, and a drop of the carbolic glycerine menstruum free from tuberculin upon the other, which serves as a control. Reuschel places a drop of concentrated tuberculin on one excoriation, 25% tuberculin on a second, and the third is left as a control. After drying in the air, the area is covered with a little cotton-wool.

Modifications.- Nagelschmidt soaks up the concentrated tuberculin, after ten to twenty seconds' application, with cotton-wool, and by this procedure usually avoids any general reaction.

Moro and Lignières find that it is not necessary to excoriate the skin surface. The first rubs his ointment of tuberculin on the skin beneath the xiphi-sternum, or on the skin of the breast near the nipple. Lignières simply shaves the surface with a safety razor - thus avoiding accidents in nervous children - and after removing all remaining soap and drying, rubs a few drops of concentrated tuberculin on the surface gently, using a small tampon of cotton-wool in catch-forceps, or the tip of the finger protected by a rubber finger-stall. Slatinéano shaves the surface, and scrapes with a bistoury to the slight effusion of blood, before applying

equal parts of tuberculin and distilled water.

(c) The Reaction.- 1. In tuberculous individuals with healthy skin.-

In a characteristic strong reaction a papule appears in from six to twenty hours, at the site of inoculation. Within forty-eight hours this has become a rounded or coffee-bean-shaped, raised, strongly hyperaemic papule, surrounded by a bright red zone of the size of a florin or half-crown, the margin of which, at first diffuse, becomes after two or three days sharply defined. This two-zoned reaction is to be looked upon under all circumstances as a positive reaction. In advanced stages of the disease the zone may be wanting, or the congestion of the papule may be less marked.

Upon the papule miliary vesicles with turbid contents often develop from the fourth to the eighth day, or even earlier. These break after a few days, and their contents dry up to form a scab.

Junker considers that the papule must remain prominent at least until the fifth day, and that a reaction no longer recognisable on the fifth day should be taken as negative. There should be distinct infiltration of the base.

The principal characteristics to be noted are congestion and oedema, defined margin, constancy, and distinct infiltration.

Occasionally lines of swelling radiating from the papule are seen.

The reaction may be delayed, appearing first on the second or third day. Resolution begins about the fourth to sixth day, with scabbing and formation of superficial scales, the general colour becoming brownish from breaking down of red blood corpuscles, and in about eight to ten days, sometimes longer, the swelling has disappeared. Local pigmentation remains for months. Small cicatrices may remain at the sites of inoculation.

No pain, general increase of temperature, or other general symptoms, should be experienced.

The control areas show slight congestion and local tumefaction, which disappear after twenty-four hours, and even this evidence of slight traumatism may not be distinct.

If the inoculations are repeated in the course of a week or two, even though former reactions have not yet completely resolved, similar phenomena follow, but they appear sooner and disappear sooner on each successive application of the test. Occasionally, when a reaction fails to develop, a repetition of the procedure will elicit it; hence in doubtful cases it is as well to repeat the inoculation.

As in the case of the conjunctival reaction, subcutaneous inoculation of tuberculin revives the local cutaneous reaction, even after a period of some months has elapsed.

The strength of the reaction varies with the strength of the tuberculin, and in all cases gradually lessens towards the close of life, failing to develop from two to eight days before that event.

2. The Reaction in Presence of Tuberculous Disease of the Skin.- In such conditions a hypersensitiveness of the skin is manifested; the reaction is very strongly marked, and usually leads to ulceration of the tuberculous areas.

Advantages of the Reaction.- It can be employed in young children, using, if necessary, in nervous individuals the modifications suggested by Moro or Lignières.

It causes no pain, no increase of temperature or other general reaction. In healthy skin of tuberculous patients it soon disappears,

leaving pigmentation. It can be employed in cases with existent temperature, and may be repeated.

Disadvantages.- Tuberculous patients in a cachectic condition, or suffering from miliary tuberculosis, or approaching their end, give no distinctive reaction, or it fails completely. These disadvantages are also shared by Koch's and Escherich's reactions. Oppenheim noted in adults, and Moro and Doganoff in children, the occurrence of lichenous eruptions resembling very closely lichen scrofulosorum and also phlyctenular conjunctivitis. These were, however, chiefly met with in patients with tuberculous skin disease, and are not of usual occurrence in tuberculous patients with healthy skin.

Von Pirquet (Wein med. Woch. 6th July, 1907) claims that the cutaneous reaction is specific, that is, that it occurs only in those who are tuberculous, and possess specific antibodies. It failed to appear in only 11 of 80 undoubtedly tuberculous children. The exceptions included cases of tuberculous meningitis, advanced pulmonary and general tuberculosis, and chronic tuberculous caries. The patients were all cachectic, or as in the cases of tuberculous meningitis, were first vaccinated a few days before death. Now it is exactly such cases that often fail to react to hypodermic injections of tuberculin, and no more can be expected of the cutaneous reaction than of hypodermic injections. The former is merely a much more convenient and safe method. That non-tuberculous subjects exhibit no reaction was shown by necropsies on 28 previously "vaccinated" children, and in the few cases in which a reaction occurred and a necropsy was subsequently performed tuberculosis was found with one exception. In this death was attributed to the status lymphaticus. In adults the diagnostic value

of the cutaneous tuberculin reaction is much less than in children, because the older the subject the greater is the probability that he has become infected with tubercle, though it may be completely latent. A positive reaction after eight years of age is therefore extremely common, whether tuberculosis is suspected or not. On the other hand, in obviously advanced tuberculosis in adults a negative result is frequent. This fact is comparable to the negative results obtained in cachectic tuberculous children. The method is thus of diagnostic value only in early childhood. Of greater importance are the prophylactic possibilities. If all children were vaccinated with tuberculin every six months the exact date of onset of tuberculosis would be detected, and appropriate treatment could be immediately begun.

Engel and Bauer (Berl. klin. Woch., September 16th, 1907) raise the question whether the skin reaction really only takes place when tuberculosis is present.

Pirquet stated that all his negative cases which died were found post-mortem to be free from tuberculosis. In one case which had give a positive reaction, no specific changes were found, but in as much as this was a case of so-called "status lymphaticus," Pirquet deduces that this condition has an intimate relationship to tuberculosis. The authors have tested the reaction in a large number of children (over 300,) adhering closely to Pirquet's directions. Among 48 infants, 6 gave a definite positive reaction. One of these infants died, and no trace of tuberculosis was found at the post-mortem examination. The status lymphaticus could also be excluded; 4 others of the 6 infants did not show any clinical signs of tuberculosis, were carefully reared under circumstances which

would make tuberculosis in the infant very unlikely, and neither gave the skin reaction at all at a later date, nor did they give a positive reaction to subcutaneous injection of tuberculin. Binswanger has shown that infantile tuberculosis always reacts to test subcutaneous injections. The last infant reacted to the injections with a typical rise of temperature. Further, they tested the reaction in 280 older children, mostly inmates of the municipal children's home in Dusseldorf. Most of the children were over six years of age, and were attending school. A number of them were known to be tuberculous, and all of them gave positive skin reactions.

Of the rest the number of positive reactions could easily have represented the number of tuberculous individuals, since the children were waifs and strays from the lowest quarters, in whom tuberculosis was extremely likely to occur. Further, the reaction showed itself in increasing frequency the older the children were. This led the authors to conclude that there appeared to be a close connexion between the skin reaction and tuberculosis, at all events in children beyond the age of infancy. They, however, do not think that a positive reaction necessarily indicates tuberculosis, especially in infancy. As far as its diagnostic importance is concerned they do not consider that it can take the place of the subcutaneous tuberculin injection, although it may be valuable in determining the frequency of tuberculosis in a given district.

Olmer and Terras have published in "La Presse Médicale" of 18th September, 1907 their results with Von Pirquet's cutaneous test in adults. They divide their cases into three groups -

(1) Tuberculous cases.

(2) Cases other than tuberculous.

(3) Suspected cases.

In group 1. the test has been made on 31 patients all with well-marked signs of tuberculosis. 17 of these gave a well-marked reaction, 3 gave a doubtful reaction. 11 showed a negative result,- some of these were cachectic but several had only local lesions and their general health was good.

10 of the cases in this first group were also tested for Calmette's ophthalmic reaction. In 7 the two tests were positive. 2 which had been negative to the cutaneous were positive to the ophthalmic. 1. gave a negative reaction to both tests, although at an operation tuberculous granulations were seen on the pelvic peritoneum, and there was also pulmonary tuberculosis.

In group 2. out of 17 cases 14 were negative, as was expected but 3 were positive - 2 markedly so and one feebly. One of the marked reactions was also positive to Calmette's test.

In group 3. 3 cases suspected of tuberculosis failed to give a positive reaction to Von Pirquet's test. 2 of these were cases of Addison's Disease while the third was a patient with indolent ulcers on the legs and a cold abscess below the right clavicle. This last case was positive to Calmette's test.

The authors have come to the following conclusions:-

(1) Von Pirquet who used the method first on young children admits that children above the age of 2 years and adults react positively to the cutaneous test even if they have no bacillary lesion. According to several authors, however, as we have seen, the reaction is not constant in the adult as it has been negative 28 times in 51 cases.

(2) 11 tuberculous patients out of 31 did not react, and it has been shown that these were not all cachectic. It was considered that perhaps it was necessary to take into account the condition of the skin more or less resistant. There were individuals with delicate skins who gave most definite and sometimes haemorrhagic reactions.

(3) Certain adults who did not present any appreciable tuberculous lesion reacted very intensely. Von Pirquet, Dufour, Sicard and Burnet have published numerous observations on this point. If only characteristic cases were taken into account these contradictory facts would be perhaps less frequent than had been admitted.

(4) Some subjects who from the clinical point of view appeared to be cured of their tuberculosis and to have no apparent active bacillary lesion, might react positively to the cutaneous and ophthalmic reactions. These diverse statements appreciably diminish the diagnostic value of the cutaneous reaction. A negative result did not permit one to draw any conclusion from the experiment. Had a positive result any practical value? Evidently not, if it had not been shown that the subjects who react under these conditions had latent or attenuated tuberculous lesions; or that one could attribute to an old tuberculosis cured from a clinical point of view a particular condition of the body-fluids and tissues which makes them apt to react to the cutaneous test.

In cases where demonstration of this could be made this test would doubtless retain the value of a specific reaction as faithful as the ophthalmic reaction, but less constant and less precise. But it could not be used in practice except as an indication interesting and useful for the discovery of the truth and not as an absolute proof, capable of

confirming clinical diagnosis.

A communication by Ferrand and Lemaire was published in "La Presse Medicale" of September 28th, 1907 giving clinical and histological details respecting the cutaneous reaction as observed in young subjects. They distinguish three grades of reaction - "feeble," "medium," and "strong." The reaction according to their experience, attains its maximum at the end of 24 hours or even earlier and it lasts a variable time, although in many instances it disappeared in from 5 to 10 days.

The "feeble" reaction is characterised by an erythematous zone of 4 to 6 millimetres with its centre slightly papulous and rather resistant to the finger.

The "medium" reaction has an erythematous zone of 6 to 12 millimetres and the papulous nature of its centre is more evident. The skin covering it is slightly oedematous.

The "strong" reaction is much the same as the "medium" only it is more marked and the erythematous zone is 2 to 3 centimetres in diameter. There is a feeling of elastic resistance to the finger. If the oedema is more marked there is an appearance as of urticaria over the area affected.

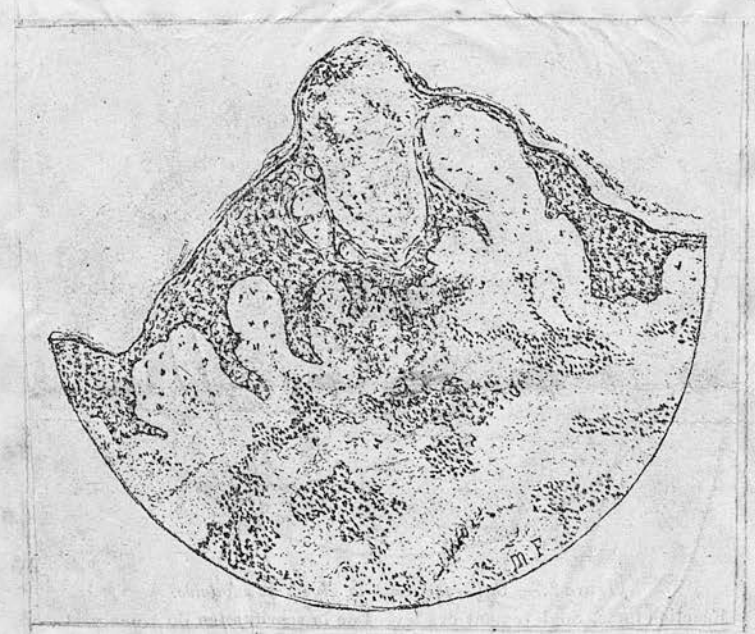
Out of 31 children on whom the cutaneous test had been done and then, several days later, subcutaneous injection of tuberculin given, 6 showed a reappearance or even an exaggeration of the cutaneous reaction on the following day. As regards results - with 18 patients known to be tuberculous, Ferrand and Lemaire obtained 16 positive and 2 negative reactions - both of which were cases of Pulmonary Tuberculosis in the second or third stages. Of the positive results 4 were "light" reactions, 7 "medium" and 5 "strong."

Out of 27 doubtful cases there were 11 negative results and 16 positive, 5 being "light" reactions, 3 "medium," and 8 "strong;" and amongst 55 subjects not clinically tuberculous, 33 were negative and 22 positive - 14 "light," 1 "medium," and 7 "strong" reactions; but out of 21 of these, 9 were positive to the tuberculin subcutaneous test 11 negative and 1 doubtful.

Out of 17 cases negative to the cutaneous reaction, 13 were negative with the ophthalmic reaction and 4 positive.

In 32 cases positive with the cutaneous reaction, 16 were positive to the ophthalmic reaction and 16 negative. 9 cases negative to the cutaneous test were subjected to the subcutaneous injection test and they were all negative; but out of 31 cases positive to the cutaneous test, 25 were positive to the subcutaneous injection, 5 negative, and 1 was doubtful. In all, 29 cases out of 49 were verified by the ophthalmic test and 34 out of 39 by the subcutaneous injection of tuberculin. The 3 tests - ophthalmic, cutaneous, and subcutaneous - were tried on the same cases 32 times. In 20 cases the three were all negative or all positive.

In 11 cases, when the cutaneous and the subcutaneous tests gave the same results, the ophthalmic reaction disagreed once, but this may have been due to the child crying and so washing the tuberculin out of the eye.



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These observers have studied the histology of the cutaneous reaction in 10 children. The changes in the epidermis are as follows:- Along the line of the scarification the epidermis is destroyed to a variable depth and is replaced by a crust in the form of a wedge which penetrates as far as the dermis or stops short at the lower malpighian layers. It is composed of a fibrinous exudate containing numerous leucocytes. When the whole of the epidermis has not been implicated the cellular elements which remain arrange themselves in a layer in front of the wedge-shaped crust. They are composed of cells swollen and elongated, vacuolated in places and separated from each other by an oedema often very important.

The Dermis - The dermis is the seat of an oedema well-marked in all the papillae. One can count on each side of the median crust 15 to 20 papillae elongated or rounded and twice or thrice their original size. They sometimes form large rounded projections infiltrated with serum in which are cells and white globules. Under the scarification and next in importance to it, the tissues of the true skin are affected more or less deeply. They lose their fasciculated texture and become broken up into fine fibrils which unite to form an irregular network, making a sort of reticulated tissue in which are cellular debris and a certain number of degenerated polymorphs. In places, adjoining bundles, still keeping their shape, are granular and stain badly as if degenerated.

The inflammatory reaction around the zone is important. In the neighbourhood of the track of the inoculation are numerous elongated and irregular cells, some mast-cells, round cells and many polymorphs. But all the cells form a rather compact layer, or even very spread out, in

some of the preparations. This layer is extended in breadth and depth by numerous and large perivascular processes formed almost entirely of small round cells. This constitutes what the authors call the "inflammatory reaction at a distance." It is always present and is independent of the small scarification.

To exclude the possibility of the reaction being due to some of the other substances contained in Von Pirquet's solution and not to the tuberculin the authors performed the test in 100 cases with sterilised glycerine; 100 cases with no application; 9 cases with carbolised glycerine, 20% and 10%; and 3 with pure turpentine - all without any reaction occurring. With sublimated glycerine ($\frac{1}{10}$ %) they had 2 negative reactions and one slight one. With the same substance ($\frac{1}{5}$ %) they had 4 negative reactions and 2 strongly positive. Histological examination of the positive cases showed a reaction which was purely local. The epidermis was destroyed and there were great numbers of degenerated cells and polymorphs, but in the dermis there was no oedema nor cellular infiltration.

On examination of the tissues after inoculating the skin with diphtheria toxine, the authors found that there was no oedema produced. The local reaction was composed almost entirely of an invasion of the tissues by polymorphs, and that there was no "reaction at a distance."

Thus the authors claim to show that Von Pirquet's reaction is histologically distinguishable from any reaction produced by substances other than tuberculin.

Lemaire in "La Presse Médicale" of 2nd November, 1907, says that he finds that the sub-cutaneous injection of Tuberculin causes a reappearance of previous ophthalmic and cutaneous reactions. In several cases he did

a cutaneous test, then gave a sub-cutaneous injection, and then did a second cutaneous test; and he found that the second cutaneous reaction was more marked than the first. Contrary to the observations of Vallée, Lemaire found that a very positive cutaneous reaction occurred in cases where a sub-cutaneous injection of Tuberculin was given at the same time. This agrees with Lépine's observations. (La Presse Médicale, Oct. 26th, 1907.) Lemaire finds also that the ophthalmic reaction is not interfered with by subcutaneous injection of Tuberculin. However in two cases the three tests were made at the same time and the ophthalmic reaction, alone, was negative. But Lemaire thinks that Calmette's test is not always to be depended on (La Presse Médicale, Sep. 28th, 1907.)

He also finds that a general reaction following the cutaneous test is quite exceptional.

In the British Medical Journal of November 23rd, 1907, Austin and Grünbaum state that Von Pirquet's reaction is diagnostic only in young children as a papule develops in almost all adults while it fails in tuberculous subjects shortly before death.

They applied Calmette's test to 70 cases of which 20 were tuberculous. Of these 18 gave a positive reaction and 2 a negative, but one was a patient who died a few days later. Of the other 50 cases none of which were thought to be tuberculous, all were negative.

In "La Presse Médicale" of 19th June, 1907, there is the original article of Professor Calmette of Lille on the opthalmic reaction in tuberculosis. Von Pirquet's cutaneous reaction suggested to him the idea of obtaining a reaction on the ocular mucous membrane. Accordingly, along with two of his pupils, he made his first series of experiments on

25 subjects, 16 of whom were tuberculous and 9 suffered from complaints other than tuberculosis. All of the tuberculous patients gave, without an exception, a positive result, and the 9 other patients all failed to react.

Of the 16 tuberculous patients, 12 had pulmonary tuberculosis, 2 tuberculous pleurisy, 1 tuberculous bronchial glands and 1 was a supposed simple bronchitis. The 9 non-tuberculous cases consisted of sciatica; Bright's Disease; tabes dorsalis; lymphangitis of fore-arm; mitral and tricuspid incompetence; mental confusion; disseminated sclerosis; influenza; rheumatism.

To avoid the irritating effects of glycerine, Calmette used dried tuberculin precipitated by alcohol at 95° C. and then a solution made with distilled water up to 1 : 100. He puts one drop of this solution into one eye of each patient and he uses a freshly prepared solution. 5 or even 3 hours after the instillation there is, in the tuberculous subject, a marked congestion of the palpebral conjunctiva which assumes a bright red tint and becomes the seat of oedema more or less marked. At the same time the caruncle becomes swollen and reddened and is covered with a slight fibrinous exudation.

The injection of the vessels gradually increases and is accompanied by lachrymation. At the end of 6 hours the fibrinous secretion becomes more abundant and collects as filaments in the lower conjunctival sac. The reaction is at its height from 6 to 10 hours after the instillation of the tuberculin. The patients do not complain of any pain, but only of slight discomfort accompanied by a faint burning sensation and disturbance of vision in proportion to the amount of the discharge. There is

no chemosis. The rectal temperature is not appreciably affected. It is easy to appreciate the intensity of the reaction by comparing the affected eye with the other, which has not received the tuberculin.

In infants the congestion begins to disappear at the end of 18 hours and in adults from 24 to 36 hours.

In healthy subjects or in those suffering from some disease other than tuberculosis, instillation of tuberculin causes no reaction. At the most, there is, from 1½ to 3 hours afterwards, a slight redness which soon disappears and is not accompanied by secretion or lacrymation.

Calmette says that this phenomenon is one of great sensitiveness and that it appears much more quickly than the cutaneous reaction which does not appear for 48 hours. He also says that it has not any of the disadvantages of the sub-cutaneous injection of tuberculin.

Prouff "Gazette des Hôpitaux," 25th June, 1907) states that in his first series of 8 cases - 4 known to be tuberculous and 4 thought to be free of tubercle - the 4 tuberculous patients all gave positive ophthalmic reactions, but the other 4 were just as positive. However, one of these latter died a few days later of tetanus, and at the post-mortem an old pleurisy was revealed and on closer examination 2 caseous glands were found one near the trachea and the other in the hilum of the lung.

Four other tuberculous patients all reacted positively to Calmette's test, while with 7 patients, all thought to be free from tuberculosis, 6 were negative and one positive.

Since doing these 2 series, Prouff has applied Calmette's test to 70 persons and all of those who were tuberculous gave a positive reaction, except one case which was moribund.

To try to prove that Calmette's test should be negative in non-tuberculous persons, Prouff, assuming that newly-born children should be free of any trace of tubercle, applied the test to 3 children 2 days' old, 1 one day, and 2 one month, and he found that none of them reacted.

M. Letulle has great faith in the ophthalmic reaction as a means of diagnosis of tuberculosis. In "La Presse Médicale" of 3rd July, 1907, he has written an article expressing his views. He did the test on 50 patients taken at hazard in his wards and 19 of these gave positive reactions. One was a morphomaniac with chronic nephritis and he had numerous subcutaneous abscesses. The autopsy showed the presence of Potts' disease of the lumbar vertebrae, with an unsuspected Lumbar abscess.

A second example of the value of the test was furnished by a patient suffering from very severe typhoid, who developed consolidation of an apex. Convalescence being very slow and unsatisfactory, with evening rises of temperature, tuberculosis was suspected. The test, however, was negative, and events showed it to have been right. Letulle rates the prognostic value of the ophthalmo-reaction as high as the diagnostic importance, and to indicate this quotes the case of a nurse who contracted mild typhoid, in the course of which a small focus of pulmonary consolidation was detected. She made a good recovery, and would have been discharged without more ado but for the positive ophthalmo-reaction, which was taken to mean tuberculous lung mischief, for which a further course of treatment was instituted. In Letulle's opinion the ophthalmo-reaction is of great value in deciding whether a patient with signs of former lung disease is really cured, or whether the tuberculosis is only latent.

Grasset and Rimbaud (Soc. des Sc. Méd. de Montpellier, 5th July, 1907)

found the ophthalmic reaction positive in the following cases:- 4 cases of tuberculosis in which the bacilli were found to be present; 3 in which no bacilli could be found; 5 cases of doubtful tuberculosis and one which was not tuberculous. It was negative in one case of tuberculosis (no bacilli found), 3 doubtful cases and 14 non-tuberculous patients.

Aubaret and Lafon (Gazette Hebdomadaire des Sciences Médicales de Bordeaux 4th August, 1907) have applied Calmette's test to several cases of diseases of the eye:-

(1) Tuberculosis of the choroid - positive reaction. The patient also suffered from pulmonary tuberculosis.

(2) Phlyctenular conjunctivitis - positive reaction.

(3) Phlyctenular conjunctivitis - positive reaction. Patient had enlarged glands in the neck.

(4) Kerato-conjunctivitis - positive reaction - Patient had phthisis also.

(5) Episcleritis - positive reaction. Patient had phthisis.

(6) Phlyctenular ophthalmia - positive reaction.

(7) Double episcleritis - positive reaction.

(8) Parenchymatous Keratitis - positive reaction.

(9) Dacryocystitis - negative.

(10) " "

(11) " "

(12) " "

(13) " "

(14) " "

When the reaction is severe they recommend the use of hot fomentations,

and if the secretion is excessive. of astringent lotions. They tried a solution of adrenaline but did not find it of much use.

They note that Sabrazès has shown that the fibrinous exudate is composed of polymorphs and mucus.

In "La Presse Médicale" of 10th August, 1907, Professor Grasset's results with the ophthalmic test, are given. In 8 cases of supposed tuberculosis the reaction has been positive 7 times and negative once, viz., in a woman suffering from a bilateral bronchitis lasting several months but without tubercle Bacilli in the sputum.

In 15 cases showing no clinical signs of tuberculosis, the reaction was negative 14 times and positive once. This last case was one of epilepsy absolutely free, to all appearance, of any signs of tuberculosis. In 8 doubtful cases the reaction was positive 5 times and negative in 3.

In the same number Comby publishes his results in children. He uses a 1 in 200 solution and out of 132 children, 62 gave a positive reaction and 70 a negative. He obtained autopsies later in 4 of the positive cases and all showed the presence of tuberculosis; and in 7 of the negative and all of these were free from the disease. He describes 3 degrees of the reaction, Slight, Moderate, and Violent, and he also says that one instillation does not prevent a second being positive nor even a cutaneous nor a sub-cutaneous reaction being likewise positive.

Sabrazès and Dupérié (Gaz. hebd. des Sc. Méd. de Bordeaux, 1907, July 1) report a series of cases of the application of the test, and give clinical details. They distinguish the same three grades of reaction, as well as an early (six hours) and a late (twelve hours) reaction. Some of their observations may be summarised: Five cases of phthisis in

different stages, all bacteriologically verified. Reaction early in four, late in one, moderate in four, slight in one. Pyrexia produced in one case. The reaction had no relation to the severity of the tuberculous injection. Two doubtful cases (no bacilli found)- one with signs and symptoms of phthisis, the other with symptoms only, and a history of haemoptysis. The first gives a positive, the second a doubtful reaction. Two cases of pleurisy, one recent, with exposure to tuberculous infection, one of old standing; both gave marked reaction, one early, the other late. Cases of enlarged cervical glands, a consolidation of an apex, osseous tubercle, and senile tubercle also gave a reaction. As regards the cases of cured tubercle, one, an old woman of 75, who was known to have had phthisis years before, gave no reaction; while a second case of healing tuberculosis, in which bacilli had disappeared from the sputum, gave a slight reaction.

Brunetière (Gaz. hebd. des Sc. Méd. de Bordeaux, 1907, July 18th) got negative results in syphilitic eye affections; he counsels caution in applying the test when there is any conjunctivitis.

Dr. Brunetière in "L'Ophtalmologie Provinciale" of August, 1907 reports four cases of eye diseases in which Calmette's test was performed. The first was a case of a man of 20 who had an ulcer at the inner angle of his left eye. It presented all the clinical appearances of a tuberculous ulcer, but the test was negative and examination of the exudate showed the presence of numerous spirochaetes proving the ulcer to be syphilitic.

The second was a case of a woman of 65 with oldstanding iritis. The reaction was negative. The third patient was 16 years old and had an interstitial keratitis. Negative reaction.

The last case was one of choroiditis in a woman of 24 and the reaction was negative.

In "Les Comptes Rendus Hebdomadaires des Séances de la Société de Biologie" of 18th October, 1907, Calmette, Breton and Petit have published results of their experimental work with the ophthalmic reaction.

I. The influence of the injection of tuberculin into healthy animals.

A. Rabbits free from tuberculosis (proved subsequently by autopsy) received into a vein in the ear injections of tuberculin in different doses - 2 and 5 milligrammes and 1 centigramme. 16 hours later a drop of a 1 in 100 solution of tuberculin was instilled into one eye of each animal. 3 hours afterwards there was a visible inflammation of the conjunctiva. 48 hours later the same animals gave a feeble reaction to a drop in the other eye. On the third day none of them gave the reaction.

Other rabbits received doses of 5, 10, 15 or 20 centigrammes - doses usually fatal - but they lived long enough for the reaction to be watched for for 16 hours. Those that had received 5 centigrammes reacted feebly, while with all the others the reaction was negative.

These facts clearly in accordance with what has been observed clinically, show that the local reaction to tuberculin appears when the body contains small doses of the poison but not when it is saturated.

B. Full grown rabbits were given by the mouth various doses of tuberculin - 1 centigramme, 5 centigrammes and 1 decigramme. 12 hours later the ophthalmic test was performed and the resulting reaction was slight and delayed. Two days later they failed to give a reaction. Therefore tuberculin absorbed from the alimentary canal has an effect on the healthy body.

II. The moment at which in Tuberculous Animals the Reaction appears.

Grown rabbits received into the marginal vein of the ear 1 cubic centimetre of a fine emulsion of bovine tubercle bacilli. The ophthalmic test was performed every hour on successive animals and the reaction was found to occur slightly from the 3rd day and then to increase in intensity and then to be negative after 15 to 18 days.

III. Reappearance of the Conjunctival Reaction in healthy or Tuberculous Subjects after a Sub-cutaneous Injection of Tuberculin.

This has already been noted by Slatinéanu in man and by Guérin in animals. Calmette, Breton and Petit have shown that in certain patients suffering from diseases which are not tuberculous, on whom the ophthalmic test had been practised 8 days previously but with a negative result, a redness of the caruncle and conjunctiva appeared a few hours after a subcutaneous injection of 2 milligrammes of tuberculin. The reaction disappeared in 24 hours.

This false reaction seems to prove that even in the non-tuberculous, when the tissues have been touched by tuberculin there remains for several days a sensitiveness to that substance.

In the same number of the same magazine Lépine and Charpenel publish some of their observations. They had obtained positive Calmette reactions in three cases in none of which could they find any physical signs of tuberculosis.

One was a case of general paralysis and at the post-mortem they found a fibro-caseous nodule at one apex.

The other two were cases of mental confusion, and in one there was

evidence of a very early tuberculosis, while in the other, aged 34, there were signs of healed tubercle, which to their knowledge had been active at 17.

On the other hand the reaction had been negative in an imbecile showing definite signs of an apical involvement. This patient died of Para-typhoid and the sectio revealed evidence of tuberculosis.

In a series of 24 cases they obtained the following results:-

10 Positive reactions - 2 patients, undoubtedly tuberculous
7 doubtful.
1 no signs of tuberculosis.

14 Negative - - 7 with no signs of tubercle.
6 with dubious signs.
1 with tuberculous glands, healed tubercle of a bone, and slight and inconstant signs of Pulmonary tuberculosis.

In the "British Medical Journal" of October 19th, 1907, there is an article on the Calmette Serum Reaction in Ophthalmology, by Sydney Stephenson. He says that apart from lesions of the eye recognized by all competent observers as tuberculous, there are several others - especially chronic irido-cyclitis, scleritis, and some forms of choroiditis - of which the tuberculous origin is as loudly proclaimed by one school as it is decried by another. The preponderating part unquestionably played by syphilis in the production of many of these affections has, perhaps, tended to render some of us a little blind to the influence of other causes, prominent among which, as he believes stands tuberculosis. How often disseminated choroiditis, indistinguishable by the ophthalmoscope from the form due to syphilis occurs in patients in whom there is no evidence whatever of a

specific taint, acquired or inherited. He feels tolerably confident that the systematic employment of the ophthalmo-reaction will show that no small number of such non-syphilitic cases are in reality due to tuberculosis.

Calmette's serum has already been used in eye work by Painblan, who obtained positive results in a couple of cases of tuberculosis of the conjunctiva. Brunetière had negative results in three cases thought possibly to be of tuberculous origin - kerato-iritis, interstitial keratitis, and exudative choroiditis. Aubaret and Lafon employed the serum in 18 eye cases, including intraocular tuberculosis, phlyctenular conjunctivitis, and keratitis, episcleritis, interstitial keratitis, lacrymal affections, and, lastly, optic papillitis. Brunetière in the course of a second communication, while reaffirming the diagnostic value of the serum, regretted that it could not be applied to every doubtful case.

Stephenson has applied the test to upwards of thirty patients, all of whom were suffering from some disease or affection of the eye. The more important cases may be briefly described as follows:

1. Phlyctenular (Eczematous) Conjunctivitis and Keratitis -

The tuberculous origin of these common affections of the eye has been suspected for years, and the view is widely held at the present day that they are caused by a tuberculous toxin circulating in the blood stream.

The Calmette serum was applied to the eyes of six children, all of whom had been affected with long-standing and relapsing ulceration of the cornea. Only two of the patients manifested tuberculous lesions elsewhere. The ophthalmo-reaction, however, was obtained in every instance. On the other hand, the result was negative once in a case of recent phlyctenular

keratitis. It is to be noted that Aubaret and Lafon elicited the ophthalmo-reaction in 4 healed cases of phlyctenular disease.

2. Choroiditis.- The serum has been applied in 3 cases of choroiditis in young women, free, as far as could be ascertained, from evidences of syphilis, acquired or inherited. In each of these three patients the ophthalmo-reaction was obtained, although in none had a tuberculous focus been found by clinical examination.

3. Interstitial Keratitis.- Of the 8 cases tested, 5 manifested obvious stigmata of inherited syphilis, and it is significant in them that the ophthalmo-reaction was not elicited. On the contrary, in the remaining 3 cases positive results were forthcoming in all.

4. Episcleritis.- One case of episcleritis was tested, with positive reaction to the serum. A suggestion of tuberculosis was given, by the fact that the cervical, inguinal, and axillary groups of glands were somewhat enlarged. Two other cases in women, aged 50 and 28 years respectively, yielded no reaction to tuberculin.

5. Tubercle of Iris.- A female, aged 12 years, was suffering from a disabling affection of the left eye of nearly six months duration. The anterior chamber of the left eye was almost filled with solid-looking, yellowish-grey exudation, so that the pupil could be recognized with difficulty. No clinical signs either of tubercle or of syphilis. The state of the eye was so characteristic, however, that he did not hesitate to diagnose tuberculosis of the iris and ciliary body, of the form described in systematic treatises as "iritis scrofulosa" or "conglomerate tubercle." For that matter, the tuberculous nature of the process was attested by the general reaction that on two occasions followed the

injection of $\frac{1}{1000}$ mg. of tuberculin T.R. It was confirmed later by the action of the Calmette serum. A well-marked reaction came on in nine hours, and persisted for twenty hours.

6. Tubercle of Cornea.- A girl, aged 12 years, had a history that her right eye had been more or less inflamed for about two months. The child's mother suffered from phthisis pulmonalis, and one of her brothers had died at nine months "with lungs badly affected." The patient herself "had brought up blood" on one occasion. Slight photophobia and patchy ciliary redness. Several curious looking deposits lay at different levels in the substance of the cornea, where they formed a kind of mosaic. Their colour was greyish-white, and they might be compared with drops of cold mutton fat. In addition, the rest of the cornea was more or less hazy. Provisional Diagnosis: Tubercle of cornea, probably secondary to a similar condition of the iris and ciliary body. The injection of $\frac{1}{1000}$ mg. of tuberculin T.R. on 2 occasions yielded no definite result, but a rise in temperature to 100.8° F. followed a third injection. Later the serum was applied to the unaffected eye. A reaction was noted in five hours, and this had disappeared completely thirty-one hours after the serum had been used to the eye.

7. Chronic Irido-Cyclitis.- If there be one class of case more than another in which tuberculosis is believed to play a prominent role it is in insidious and recurrent irido-cyclitis in young adults. According to Stock's recent investigations, of 59 patients suffering from chronic irido-cyclitis no fewer than 61 per cent. showed a general reaction after the injection of Koch's older tuberculin, T.V. He had submitted two patients to the tuberculin test and obtained the ophthalmo-reaction in both.

The first patient presented arthritis of the left knee and dactylitis of the left little finger. The injection of 0.005 mg. of tuberculin T.R. was followed by no reaction, local or general. Later the aqueous humour was withdrawn from the left anterior chamber, but bacteriological examination of the fluid was negative as regards the Treponema pallidum and the tubercle bacillus. A second injection of $\frac{1}{750}$ mg. of tuberculin T.R. was succeeded by a slight rise in temperature, together with pain at the site of the needle-prick. A slight reaction was obtained nine hours after application of Calmette serum to one eye. It had disappeared seventeen hours after the application. In the second patient a drop of the Calmette serum produced in sixteen and three-quarter hours a feeling of stiffness and tenderness in the lids, and when she was seen twenty-three and a quarter hours after the application, the appearances were those of a rather marked acute catarrhal conjunctivitis. The reaction had not wholly subsided in four days.

Later the anterior chamber of the eye was tapped and the aqueous humour examined bacteriologically. Preparations treated by the Ziehl Neelsen process, included a few slender rods stained red.

Audeoud (Rev. Med. de la Suisse Rom., October 20th, 1907) reports his results with Calmette's test:

Of 18 obvious cases of tuberculosis in children aged from 8 months to 15 years, a positive reaction was obtained in 12. The exception was a case of tuberculosis of the cheek which had been scraped and was rapidly healing. In 3 cases suspected to be tuberculous a positive reaction occurred in one. In 15 cases obviously non-tuberculous the results were uniformly negative. Some divergences were observed from Calmette's

description. Thus, in six positive cases the reaction was limited to the caruncle, and in one case it was most intense and accompanied by chemosis. In this, however, the child had previously had conjunctivitis. The onset of the reaction after instillation was later than in Calmette's case - between five and forty-eight hours - and the reaction was at its height eight to twelve hours after the appearance of symptoms. The total duration of the reaction was from two to seven days. Contrary to other observers, a slight rise of temperature - never attaining 1°C.- was the rule. The instillation had no ill effects. Audeoud has collected 611 cases thus tested. A positive result was obtained in 94.6 per cent. of the 261 obviously tuberculous cases; in 8.3 per cent. of 303 cases which presented no clinical symptoms of tuberculosis and in 81% of 47 cases in which tuberculosis was suspected.

Lépine in "La Presse Médicale" of 26th Oct., 1907, reports his experiences with the ophthalmic reaction in mental diseases. The results obtained by him confirm the value of the test, and they show its usefulness in mental diseases of doubtful origin, especially in certain cases of mental confusion.

In the same number Lemaire has a note on the cutaneous reaction. He found that if he gave a sub-cutaneous injection of Tuberculin after a positive cutaneous or ophthalmic test then these reactions reappeared, or if still present, were increased in intensity.

If between two cutaneous reactions, he gave a sub-cutaneous injection, then the second reaction was more marked than the first.

Contrary to Vallée, who experimented on animals, Lemaire has seen the cutaneous reaction distinctly positive in cases where a sub-cutaneous injection of Tuberculin was given at the same time.

He has seen, only very occasionally, a general reaction following the cutaneous test; and he has noticed cases positive to the cutaneous test, but negative to the two other tests, show after long observation the presence of tuberculosis.

Kalt (Recueil d'Ophtalmologie, October, 1907,) at a meeting of the Paris Ophthalmological Society, showed a case in which he had used Calmette's tuberculin as a test for tuberculosis of the eye with very unfortunate results. When first seen the right eye showed slight nebulae, extensive synechiae and no red reflex. The inflammation had quieted down, there was no injection, and the whole condition had existed several years. By the aid of this eye he was able to get about. The vision of the left eye had become bad four months ago. In addition to old iritis there was a focus of scleritis, and the tension was + 1. Three months later the left eye was somewhat better, the right remained as when first seen. Some 1 per cent. tuberculin solution obtained from the Pasteur Institute was instilled into the right eye. The next day there was some injection of the eye. Five days later a small patch of scleritis, which was quiescent and of no importance, began to spread till it occupied half the globe, and the upper half of the cornea was infiltrated. The iris became very muddy and there was intense pericorneal injection. The condition resulted in extensive sclerosis of the cornea. Kalt pointed out that the eye had been quiescent for months, and the disease seemed to light up as soon as the serum was instilled.

Knapp, A. (Arch. of Ophthalm., March, 1908) records a case where typical tuberculous interstitial keratitis followed the use of Calmette's serum. The patient had a superficial keratitis in the right eye of two

months duration. Of 8 siblings, 5 had died - one aged 4 days, twins at 2 days, one of meningitis at 10 months, one miscarriage; 3 living healthy children. The patient had no enlarged glands, no diseased bones or joints. The right cornea presents a broken-down, superficial infiltration; photophobia marked; a chronic ulcer formed on the lid margin. One drop of 1 per cent. tuberculin solution was instilled into the left healthy eye. Six hours later the lids were red and swollen and the child was in great pain. There was severe general reaction, the temperature rising to 100.4°. Ten days later corneal infiltrations appeared. They were arranged in three groups near the temporal margin, consisting of discrete masses, with new formed blood vessels. These coalesced, forming patches 2 mm in diameter. This typical tuberculous process in the cornea came on in a healthy eye after the use of tuberculin solution.

Napier, A. (Glasgow Med. Journal, January, 1908) brings forward two more cases which appear to show that, even when Calmette's serum is followed by no reaction, it may bring about a change of local conditions which causes the eye to respond sharply to the introduction of a small dose of tuberculin into the general circulation. Case 1. A man aged 50 had a drop of sterile solution of tuberculin instilled into the right eye on October 21st, 1907. This was followed by no reaction. On October 26th $\frac{1}{10}$mg. of new tuberculin T.R. was injected; no reaction, local or general. October 29th, 1.mg. new tuberculin; no reaction. November 2nd, 5mg. new tuberculin injected; next day - thirteen days after the instillation of Calmette's serum - there was an acute reaction in this eye, and in this eye alone. The second case is a very similar one.

Kalt, in "La Presse Médicale" of 2nd November, 1907, reports the

case of a man aged 64 who for 8 months previously had suffered from irido-choroiditis of the right eye, and from sclero-keratitis of the left. The instillation of a drop of a 1% solution of tuberculin into the right eye was followed by hyperaemia of the conjunctiva, but several days later the infiltration of the sclerotic and the cornea increased considerably and the vision became much worse. There was no reaction in the other eye. He also reports the case of a child with tuberculous iritis in which the instillation of tuberculin led at the end of a week to a serious recrudescence of the disease, which, he says, could not be foreseen.

In the British Medical Journal of Dec. 7th, 1907, MacLennan publishes his results with the ophthalmo-reaction with a view to ascertaining the accuracy of Calmette's claims. He has made over 100 observations, 70 with the Calmette tuberculin, 25 with the "old" and 10 with the "new" tuberculin. The amount of reaction is most variable, and, it does not bear a demonstrable relation to the severity of the lesion from a clinical point of view. Some of the most pronounced reactions were in cases in which there were no physical signs or clinical evidence of the presence of tubercle. An occasional over-violent reaction is the only drawback to the test that he has observed. Perhaps it may be eliminated by giving always in the first instance a weaker solution, say a 1 in 200, as a preliminary test. Indeed, Comby seems to have found that this strength of solution was, in a large series of tests applied to children, as reliable as the stronger solution, His own experience tends to confirm this view, as it will be seen by a reference to the summary of cases. It should be mentioned, however, that Oliver and Terras, who tried a solution of Calmette's tuberculin 1 in 150, obtained, in adults, only doubtful results.

The analysis of his cases brings out these facts:

1. That for the most part the claims advanced by Calmette for his test are fully justified; (2) that the test apparently reveals the presence of tuberculous lesions that are quite benign and unsuspected from a clinical point of view, as well as those that are more obvious; (3) that in those cases in which a subcutaneous injection of "old" tuberculin has given a positive or negative reaction the same result has followed the application of the ophthalmic test; (4) there seems some evidence that a solution of the "old" tuberculin may answer equally well. The results of his observations may be thus summarized:

I. Calmette's Tuberculin.- The dried preparation, dissolved in distilled water, 1 in 100, was employed in 37 cases of disease with well-marked evidence of tubercle, or that were clinically suspected to be tuberculous. These may be thus classified:

(a) Twenty-five cases, all known to be tuberculous. With two exceptions all of these reacted positively in from two and a half to ten hours. One of the two negative results was in a child with lupus, who cried when the solution was instilled; the other was a case of scrofuloderma with an extensive and extending lesion. In this latter case the test was applied to each eye with a negative result. In the majority of these tuberculous cases the reaction began in about three hours, and was usually at its height in about ten hours. Occasionally it was delayed till the second day. In about a quarter of them the reaction was severe, associated with considerable lacrymation and some exudation, and the conjunctivitis in some instances lasted for a week or ten days. As has been already noticed by some observers, he found that there was, in a few cases, a recrudescence of a disappearing oculo-reaction when a hypodermic injection of Tuberculin

was given.

(b) Cases Suspect.- Twelve of these were subjected to the test. It was negative three times - for exampla, pyelitis, synovitis, and tuberculous hip (quiescent for two years); and positive in the following: Delayed resolution in pneumonia, fistula, chronic diarrhoea, chronic bone disease, chronic cough without physical signs, fractured femur with tuberculous family history, diabetes with prolonged expiration at apex, asthma and pleurisy, and sacral abscess.

II. Twenty cases clinically tuberculous tested with a 1 in 200 solution of Calmette's tuberculin. The reaction was positive in all except in one case of multiple sacral abscess. This case was demonstrated to be tuberculous at a later period, as the discharge inoculated into rabbits produced typical tuberculous lesions. Twelve of these cases had previously given a positive reaction to the stronger solution (1 in 100), but the reactions to the weaker solution were equally characteristic, and in no case was it too severe.

III. Twenty cases, apparently free from tuberculous lesion, were subjected to the Calmette test (1 in 100). Of these cases, 4 gave a positive reaction, the remainder being negative.

IV. Twenty-five cases were subjected to the test with a 1 in 100 of the "old" tuberculin of Koch. Of 14 clinically tuberculous, 12 reacted positively and 2 negatively; the remainder, which gave a negative result, showed no signs of tubercle. Ten of the positive cases had given previously the same reaction to the 1 in 100 solution of Calmette.

V. Ten cases treated with 1 in 100 solution of the "new" tuberculin gave doubtful or negative results, quite unlike that produced by the Calmette solution or the "old" tuberculin solution.

To ascertain if the reaction was alone produced by the preparation of Calmette, he also tried a 1 in 100 solution in distilled water of the old tuberculin of Koch on many of the same cases that had been previously tested by the Calmette preparation. This was done long after every trace of the reaction produced by the Calmette solution had disappeared, and on the eye hitherto untreated. In most of these cases the results were identical. But a solution of the "new" tuberculin of a similar strength gave him either negative or very doubtful results. In some of those cases distinctly tuberculous there was with it a minute amount of redness, but not a characteristic reaction. According to Calmette, the presence of glycerine or carbolic acid in the "new" or "old" tuberculin vitiates the test by their irritating actions. He does not believe that this is correct, for if it be considered that in the solutions he used of these preparations carbolic acid or glycerine could not have been present in more than ½ to 1 %, this action may be discounted. To decide the matter, however, he instilled into many healthy eyes 1% solutions of phenol and glycerine, without evoking the slightest redness, lacrymation, or swelling of the caruncle.

This test shows that while the great majority of cases obviously tuberculous gives a positive reaction, a smaller proportion, undoubtedly tuberculous in character, fails to give any result. Mantoux has tried the test in 200 apparently healthy children, and it was only positive in 8%.

He points out, with reason, that latent tuberculous affections must be more frequent than this figure would seem to indicate. In dealing with children, however, the validity of the test depends on the absence of fear. If the child is afraid, and cries, the tuberculin is washed out of the

eyes and no result follows. While, therefore, the ophthalmo-reaction is a valuable contribution to our means of diagnosing tuberculosis, on account of its simplicity and freedom from constitutional disturbance, it must not be interpreted, either when negative or positive, as conculsive of the absence or presence of the disease. It is, however, quite as reliable as the hypodermic injection, and his cases support this view, which is also held by Sicard and Descomps. These two writers, indeed, believe it to be more certain than the hypodermic injection or the other new test, the cuto-reaction; while Prouff, Grasset, and Rimbaud are also favourable to it.

Probably the hypodermic injection of tuberculin will often give reactions which would fail to be elicited by the ophthalmic test, because it is almost certain that hitherto the doses of tuberculin administered have been much too large. Such doses are always toxic, and are likely to be followed by reactions in the tuberculous and non-tuberculous alike, though of course the latter are not so susceptible. The sub-cutaneous injection of tuberculin - either the "old" or the "new" preparation of Koch - if repeated frequently enough and in graduated doses, with careful observation of the temperatures and local reactions, is a trustworthy negative and positive test. The very "slight reactions" are not infrequently overlooked, and the accuracy of the test is thus impugned. But the application of the test is troublesome, and there are several well-known risks associated with its employment. The constitutional disturbance is often very severe, and formerly, before its dose was properly adjusted, it often did a great deal of harm. Besides, the method is painful for children and often very distasteful to adults. In many instances permission to carry it out is absolutely refused. Hence the value of the ophthalmo-reaction, which promises to be as accurate while free from the disadvantages of the sub-

cutaneous method.

The comparative delicacy of the test may be gauged from the results published by Letulle, who, in 75 tuberculous cases tested, got a positive ophthalmo-reaction in all except 3; 2 of these 3 were moribund, while the third recovered. These results are interesting. If, during a chronic tuberculosis, any antitoxin is, as one would expect it to be, developed, then the failure of the reaction in the two of Letulle's cases may have been due to an immunity imparted to the tissues, or else to the fact that vitality was too low to give any inflammatory reaction.

It is clear that if this test proves, on further experience, to be reliable, it will be a valuable aid to the early diagnosis of tuberculosis in obscure cases, and more especially in dealing with children. The success of modern methods of treatment depends on the early diagnosis of phthisis and other tuberculous affections. When a lesion is presenting clinically well-marked physical signs and symptoms, and its tuberculous nature has frankly declared itself, it is often too late to intervene with any prospect of success.

Undoubtedly a far larger proportion of the apparently healthy than we imagine are the victims of latent tuberculous affections. The observations made in the post-mortem room, or when the abdomen is opened for surgical purposes, amply bear this out, and the frequent evidence we have of bygone and completely-healed tuberculous lesions demonstrates that tuberculosis is an eminently curable disease. Any test that can help us to make our diagnosis earlier, and so to institute treatment at a stage when it would be effective, would be of the greatest importance to the physician and the public. Probably if the disease is to be stamped out, our best chance of exterminating it is to recognize it in the young and in its preclinical

stage. If segregation of the tuberculous ever becomes a practical question, might not school children who exhibited suspicious symptoms and who gave a positive ophthalmo-reaction be segregated and kept under observation?

Some rather interesting points suggest themselves from a study of his results. In a few cases not suspected to be tuberculous, but whose family history was bad, he obtained pronounced reactions. Is it possible that this reaction not only reveals the presence of an actual lesion, but also a condition of tissue which is susceptible to the development of tuberculosis? What is the meaning of this reaction? Clearly to the conjunctiva of the tuberculous it is an irritant. To the eye of the healthy it is bland. He has been rather surprised to get a positive reaction in some cases of lupus that had been treated by the subcutaneous injections of the "old" tuberculin, from the smallest to the largest doses, till all local and general reactions had ceased. In such cases one would have expected that the tissues would have acquired an immunity to tuberculin. Are we to assume from this test, when positive, that there is always present an actual tuberculous lesion, or may we get it in the absence of a lesion in those susceptible to the disease? This point can only be settled by prolonged observation and by following the future history of those cases in which the ophthalmo-reaction has been positive. Parallel results are obtained by the cuto-reaction of Von Pirquet. Here, again, the introduction of tuberculin into the skin causes in the tuberculous a characteristic lesion. The tuberculin proves itself an irritant to the skin in the same way as to the conjunctiva. Both in the case of the eye and the skin the action is an evidence of tissue resistance to tuberculin in the tuberculous. Is the tuberculin elaborated in the living tissue the same as that manu-

factured in vitro? One would expect that tuberculin instilled into the eye, scratched into the skin, or injected hypodermically, would "react" only in the healthy, for is not the reaction a sign of tissue resistance that we would expect to find better developed in the healthy than in the unhealthy? It seems apparent that tuberculin, or some other toxin developed in the tuberculous, imparts to the tissues a resistance to to tuberculin, as expressed by the inflammation in the eye or skin, that is absent in the healthy. Von Pirquet holds that the reaction is due to the presence of an antibody.

Chantemesse, in a paper read at the Académie de Médecine (July, 1907), described an analogous reaction in enteric fever to a strong solution of typhoid toxin. The toxin was precipitated by absolute alcohol, and the powder obtained dissolved in distilled water ($\frac{1}{50}$ mg. in mj). In non-typhoid cases in from two to three hours there occurred a slight redness and lacrymation, a reaction which was quite evanescent, all trace of hyperaemia disappearing in from four to five hours. But in enteric cases the reaction was much more pronounced, and at its maximum in from six to twelve hours, and remained till the following day. When very severe it even lasted for two to three days. There was hyperaemia, lacrymation, and a sero-fibrinous exudation - in all respects very similar to the ophthalmo-reaction of Calmette. No constitutional disturbance was observed. Chantemesse could not affirm whether this reaction is, or is not an early sign of enteric, but the reaction has been got in the eye of rabbits injected 48 hours previously with enteric bacilli.

Notes on 121 cases tested with Calmette's Tuberculin, by Webster, and Kilpatrick, (British Medical Journal, 7th December, 1907.)

Altogether they have attempted the reaction in 123 instances, 6 of which were in presumably healthy individuals used as controls, the remaining 117 being in individuals actually suffering from or else suspected to have pulmonary tuberculosis. In all but the first few of their observations they have used the dry form of tuberculin made into a solution with distilled water

In two cases of presumably healthy individuals some slight reddening of the lower palpebral conjunctiva was noticed after two days at least had elapsed since the date of inoculation. In five cases the palpebral conjunctiva was noticed to redden as early as the second hour, but in two cases at least this may have been due to the irritation produced by rubbing the eye, because the degree of injection diminished shortly afterwards, but the individuals themselves denied touching their eyes. They noticed that in many cases the first indication of any reaction was afforded by the plica semilunaris, which is situated just to the outer side of the caruncle, and the swelling and slight reddening which this undergoes occupies a fairly prominent place throughout the whole of the reaction: In one case this fold was the only part of the conjunctiva to show any signs of reaction, and in this particular individual it was evidenced not so much by reddening (present only in a slight degree) as by swelling, especially obvious when the two eyes were compared. By the fourth hour from the time of inoculation 15 more cases commenced to show the reaction, and from this hour onwards the remaining cases giving the reaction commenced to show some slight reddening, the longest latent interval between the placing of the drop in the eye and the time when the reaction was first noticed being twenty hours; unfortunately a night intervened and they were unable to note the onset

of the maximum reaction. In the most severe case the maximum reaction was noticed to be present sixteen hours after the application of the test. The reaction in some slight cases lasted only two days, but in the more severe as long as a week, and even longer. The palpebral conjunctiva usually reddened before the ocular and throughout shows a greater degree of reaction, leading in many cases to swelling; the caruncle was usually the last place to show any sign of reaction, but in one case it was apparently the only place to show any reaction at all. The majority of the patients did not complain of any pain, but noticed some slight discomfort in the inoculated eye, best described in their own words as "it feels as if there was a little grit in my eye," there was also a general complaint of watering of the eye, accompanied by epiphora, which lasted for a varying period and was of varying severity, corresponding usually with the severity of the reaction. In only the most severe reactions was there any purulent discharge, it was only noticed in 5 cases, but nearly all the patients giving the reaction complained either of a slight amount of discharge or else that their eyelids on the inoculated side were glued together when they awoke on the morning following the day when their eyes were inoculated. It was probably due to the fibrinous exudation which occurs normally during this reaction and not to any purulent discharge.

Five patients complained of a little intolerance of light; they were those who gave the most severe reactions. In some cases complaint was made of a soreness at the back of the nose, which made the patient feel as if he had caught cold; in only one of these cases was there any rise of temperature, and the question naturally arises whether, before the epiphora commenced, some of the tuberculin solution diluted by the lacrymation had been washed down the nasal duct into the nose and thence into the pharynx.

The fact that the soreness was first noticed in the morning of the day following the application lends a little colour to this view.

Despite the statement that there is no general reaction, 7 of the cases showed very definite rises of temperature after inoculation. In 4 the temperature went up on the evening of the day when the solution was applied, but in the others it was noticed in the evening of the following day; it was not accompanied by any headache or malaise, and these patients were not those who exhibited the greatest amount of local reaction. The temperature quickly came down to its usual level in all the cases.

One patient after recovering from the reaction caused by the tuberculin became affected with the phlyctenular conjunctivitis to which tuberculous individuals are especially prone.

Altogether they tried the reaction in 123 persons, the majority exhibiting signs of pulmonary tuberculosis; in these the amount of lung involved and the degree of its activity varied very much; many were in a comparatively early stage of pulmonary tuberculosis and not expectorating at all, so that they could not attempt to find the tubercle bacilli; it is in cases such as these that the reaction if it prove to be reliable will be of most value.

It was found convenient to group the cases with regard to the ophthalmo-reaction into: (1) Those which gave a definite reaction. (2) Those which did not give a reaction. (3) Doubtful cases in which the subjective symptoms - for example, epiphora and a feeling of grit in the eye - were present, but in which there were no objective symptoms or only very doubtful reddening of the palpebral conjunctiva.

Out of the 121 individuals 4 were presumably healthy. Of these 2 did not give any reaction and 2 gave doubtful reactions; one of these had had

pleurisy with effusion twice and the other had had a cough for the last twelve months, but neither had been submitted to a physical examination. Both were exceedingly anxious to have the reaction tried again. One case giving a doubtful reaction ten days earlier gave a definite one when inoculated again, whilst the other gave a most intense reaction with some swelling of the eyelids, the second inoculation in this case taking place eight days after the first.

Forty-three cases of pulmonary tuberculosis with very definite physical signs and with tubercle bacilli present in the sputum were subjected to the test, and in every case a positive result was obtained which was absolutely definite.

Of the remaining cases, 58 had comparatively definite signs of pulmonary tuberculosis, one lobe of lung being affected in the majority. In all these cases the disease, by observation of the temperature chart, was judged quiescent, and in none of them had any bacilli been recently found in the sputum. The results were somewhat contradictory. In 36 cases definite reactions were observed; in 18 cases no reaction to Calmette's test was observed; whilst in the remaining 4 cases doubtful results were obtained. These results naturally suggest that this reaction will indicate slight degrees of activity when the temperature chart indicates none at all, but only the future with many more results will show this. One case, however, was very suggestive, since bacilli were isolated from his sputum about a month ago; but recently repeated examinations have failed to reveal any bacilli. This patient did not give any reaction.

The remaining 16 individuals were all doubtful cases of suspected pulmonary tuberculosis without any definite physical signs, and without

any expectoration or sputum from which no bacilli have been isolated. They all, however, had a suggestive history. From these 6 gave a very definite reaction, whilst 7 gave no reaction at all; the remaining 3 gave doubtful results, consisting of subjective signs only.

Summary of Results:-

All definite cases with definite bacilli in the sputum gave the reaction. In cases with physical signs of pulmonary tuberculosis but quiescent as judged by temperature, some gave the reaction and some did not, and there was no obvious cause for this variation.

In doubtful cases some gave the reaction, some did not; some were indefinite.. In presumably healthy individuals two reacted and two did not, but in the absence of physical examination no evidence for or against the presence of tuberculosis in those who gave the reaction could be offered.

It was difficult to draw any conclusions as to the relation between the intensity of reaction as compared with the amount of lung involved, that is, the extent of the tuberculous lesion.

In five cases very severe reactions were obtained, and these cases presented marked differences in the physical signs. The most intense reaction of all was obtained in one of the control cases - an individual who was unaware that he had any tuberculosis, and who, because he gave an indefinite reaction when first inoculated asked them to repeat it 8 days later; he refused to have any physical examination, but he had no symptoms beyond a slight cough for the last twelve months.

A severe reaction also occurred in the case of a patient with advanced and extensive pulmonary tuberculosis, whose temperature chart was satisfactory when he did not attempt any exercise, but whose condition,

judged by its irregularity whenever he attempted exertion, appeared a little unstable. His case, however, was complicated by the presence of a large amount of albuminuria ascribed to a tuberculous kidney. This patient had no adventitious sounds in the lungs.

Another case giving a severe reaction was that of a woman with doubtful disease at one apex and severe and persistent pleuritic pain on that side, accompanied by a friction sound; her temperature was little raised (about 1°F.) above what it should be. Since she was subjected to the ophthalmo-reaction some adventitious sounds made their appearance at the apex, and rendered the diagnosis more definite.

From these cases the difficulty in determining any relation between the amount of tuberculosis present and the degree of reaction will be apparent.

As regards the intensity of reaction as compared with the degree of activity shown by the tuberculous disease, a similar difficulty exists for the cases with the highest temperatures, and therefore the most active tuberculosis did not show the most intense reactions.

As examples of this, the case of the presumably healthy individual may be mentioned first. In this person his temperature for the short time that he was under observation was quite normal, never rising above 98.4°F., and yet he gave the most marked reaction of all. Whether the fact that it was the second inoculation within eight days has anything to do with this or not cannot be stated. The case of the woman, already mentioned, who gave a severe reaction, also illustrates the difficulty, for she showed no marked degree of activity, her temperature being 1°F. above the proper range; out of the total number of cases on which observations were made 24 were classed as subacute cases of pulmonary tuberculosis. Of the 24

cases, 7 gave a fairly severe reaction, but 17 gave only an ordinary amount of reaction, such as the majority of the cases classed as quiescent showed. In the classification of cases with regard to their activity the temperature chart was their guide throughout.

From the above results it seemed to them that this reaction gives some promise of utility, but its reliability could only be ascertained by a much more extended series of observations on both healthy and tuberculous individuals. The chief value seemed to lie in the fact that they obtained the reaction in several cases in which the presence of tuberculosis was suspected, but where there were no definite signs of it; whether it has any value in recognizing the quiescence of a tuberculous lesion cannot be stated, for some cases judged quiescent gave the reaction, and others also judged quiescent did not.

Dr Boyd (Scottish Medical and Surgical Journal, December, 1907,) gives notes of a few cases where the ophthalmic reaction has proved of diagnostic value:-

A girl, aged 18, was admitted to the Deaconess Hospital said to be suffering from chlorosis. She was profoundly anaemic, but the colour index was normal. The opsonic index was 0·8. There was considerable emaciation, some night sweating, and a slight evening rise of temperature. The abdomen was somewhat distended and resistant. Abdominal tuberculosis was suspected. Calmette's reaction was positive. The patient subsequently developed obvious signs of tuberculous peritonitis with ascites.

Man, age 26, seen first in the waiting-room of the Royal Infirmary, and subsequently in Ward 28 while in charge for Dr Byrom Bramwell, complained of emaciation and change in colour of the face , lips &c.

There was some emaciation, a history of occasional vomiting, and marked purplish-black pigmentation of the lips and buccal mucous membrane. The pigmentation was not marked about the axillae or genitals, but was present in scars upon the hands and body.

Diagnosis.- Addison's disease. Calmette's reaction positive.

Child, age 8, admitted to Ward 30, under Dr Bramwell's care, complaining of pains in the abdomen, headaches and sweating.

A week before admission the abdomen had begun to swell. The abdomen on admission was prominent, there was some ascites, and enlarged glands could be made out on palpation. Calmette's reaction positive.

Boy, age 14, admitted to Ward 28, under the care of Dr Bramwell, suffering from spastic paraplegia. He had never been a strong child, and had a history of a former pleurisy. On examination the signs were those of spastic paraplegia. Distinct prominence of the third dorsal spine was noted, and on pressing on the top of the head pain could be elicited in the region of the third and fourth dorsal vertebrae.

Diagoisis.- Tuberculous disease of the spine; spastic paraplegia. Calmette's reaction positive.

In all the control cases where the patient obviously did not suffer from a tuberculous affection the reaction was negative.

Dr Boyd says that one might hesitate to use it in a case of acute tuberculosis. The resistance of the conjunctiva must undoubtedly be lowered for the time being, and if any tubercle bacilli were in the circulating blood it is conceivable that they might attack the conjunctiva during the period of lowered resistance. Cases of acute tuberculosis, however, are not those in which the reaction is most required as an aid to diagnosis. It is the obscure chronic cases which at times present such difficulty of

diagnosis, and it is in these cases that the reaction should prove useful and free from danger.

In the British Medical Journal of Dec. 7th, 1907, there is an article by H. Downes of the Bellefield Sanatorium, Lanark. He used the ophthalmic test upon 22 unquestionable cases of pulmonary phthisis, upon 1 "cured" case, and on 2 apparently healthy controls.

Of the 22 tuberculous cases, 12 gave a positive reaction, whilst 10 gave no result. The reaction varied from a slight, though definite, reddening of the caruncula and plica semilunaris to a well-marked muco-purulent conjunctivitis. There were no general symptoms, and the local effects had entirely subsided in three days. In six hours after the application there was nothing to be seen, but within twenty-four hours the maximum effect had been obtained. The "cured" patient, who had shown no symptoms of phthisis for eighteen months, gave a negative reaction, and the 2 controls were also negative.

So far as they go, these results support the conclusions of Mr L.J. Austin and Dr O.F.F. Grünbaum, as expressed at the recent meeting of the Royal Society of Medicine, that the test is valuable but not infallible. These gentlemen report a positive reaction in 18 out of 20 cases believed to be tuberculous, and a negative reaction in 50 non-tuberculous cases. Dr J.E. Squire, quoting Mount Vernon results, shows a uniformly positive reaction in all tuberculous cases, and Mr S. Stephenson reports favourably on the results in 50 cases.

Lafon and Lautier (Gaz. Hebd. des Sci. Méd., December 22nd, 1907,) consider that there are many cases of very slight ophthalmo-reaction whose significance must remain doubtful. They have employed cytological examination of the conjunctival secretion in these cases. The normal

secretion contains very few cells - a few epithelial cells, and here and there a polynuclear leucocyte. In cases of negative reaction there is no change in the number or character of the cellular elements. But when the reaction is positive, even feebly so, there is a marked increase in the number of the polynuclear leucocytes in the secretion. The leucocytes appear an hour or two after the clinical manifestation of the reaction. Some authorities have attributed the doubtful conditions under discussion to frequent touching of the eye, whether by the patient himself or the observer. The author thinks that irritation caused thus would not cause an increase in the number of polynuclear leucocytes. Some people, too, have attributed these conditions to the glycerine with which the tuberculin-test liquid of the Paris Pasteur Institute is made up. But the instillation of $\frac{1}{10}$ glycerine into normal and tuberculous eyes does not cause any change in the conjunctiva or in its secretion. Certain people, the subjects of slight chronic conjunctival infections, have in their conjunctival secretion a considerable number of polynuclear leucocytes, without showing any reddening of the conjunctiva, or any lacrymation or any muco-purulent discharge. But these chronic infections of the conjunctiva are nearly always bilateral. The technique employed by the authors is very simple: the lower lid is pulled down, the end of a Pasteur pipette is applied to the cul-de-sac; the secretion is drawn up and placed on a slide, is dried, fixed and stained, and examined with an oil-immersion lens.

In the British Medical Journal of December 28th, 1907, 2 cases of bilateral reaction are reported by Sydney Long:

Out of a series of 40 cases a well-marked reaction occurred in both eyes with two patients. In both instances one drop only of a 1% solution of Calmette's serum was used. The first case was one of early pulmonary

tuberculosis, with tubercle bacilli in the sputum. Six hours after the drop had been put into the right eye a well-marked reaction was seen; and twenty-four hours later a very distinct reaction was visible also in the opposite eye, and this did not pass off until four days later.

The second case was one of chronic discharge from both nostrils of three years' duration in a boy aged 14. In this instance also the reaction in the left eye was not evident until about forty-eight hours after the drop had been put into the right eye, which latter gave a very marked positive reaction.

Paul Eisen (Beiträge zur Klinik der Tuberkulose, 1907, Heft 4) has tried the ophthalmo-reaction in 82 cases. Forty-five of the cases were the subjects of phthisis of which 19 were in StageI (Turban), 10 in Stage II and 16 in Stage III. All Stage I cases, in which the diagnosis was doubtful were confirmed by tuberculin injection. Positive reaction was obtained in 66 % - namely, 78.9 per cent. of the cases in Stage I,70 per cent, in Stage II, and 50 per cent, in Stage III. This diminution of the number of positive results with the increased stage of the disease corresponds to the results obtained by tuberculin injection, and shows the ophthalmo-reaction to be a specific tuberculous reaction. In one negative case a rise of temperature was noticed only after the first instillation. Nine cases examined were suffering from pleurisy, this being the sole symptom, no joint affections being present. Of these, 4 gave a positive reaction - that is, 44.4 per cent. Here again 1 negative case showed a rise in temperature, only after the first instillation. Of 17 cases suffering from various diseases, but, so far as could be ascertained, non-tuberculous, 31.1 per cent. gave a positive reaction. Finally, 11 healthy subjects were

tested. Of these none gave a positive reaction, either objectively or subjectively. The redness and swelling of the positive reaction, as well as the mostly quite trivial subjective troubles, always disappeared in one to two days. In only one case they lasted six days and then disappeared, leaving the eye quite normal. Two cases which had had conjunctivitis in childhood required special treatment. These cases led the author subsequently to inquire for any former conjunctivitis before applying the test.

On the whole, the ophthalmo-reaction, in not a few cases, failed to reach the same degree of exactitude obtained by sub-cutaneous injections of tuberculin. The results in cases of pleurisy were particularly disappointing, as in these cases the sub-cutaneous injection of tuberculin is to be avoided. The author, nevertheless, holds that it may become an important addition to the means of diagnosis, when, by further trials, the method of using tuberculin has been regulated as regards dose, etc., and further knowledge of contraindications has been gained.

F. Köhler (Deut. med. Woch., 1907, No. 50, p. 2082) has tested 175 lung cases with old tuberculous solutions of 1 %, 2 %, and 4 %; of the cases 169 were certainly clinically tuberculous, 5 were doubtful, and one was not tuberculous. Of the first group, 83 (51 per cent) reacted to 1 %, 66 (41 per cent) to 2 % after 1 % had failed, and 13 (8 per cent) reacted to 4 % after the weaker solutions had failed; 8 of the certainly tuberculous (4.7 per cent) gave no reaction. Of the 5 doubtful cases 2 reacted to 1 % and 3 to 2 % solutions. The clinically non-tuberculous case reacted to 4 per cent solution.

Schenek and Seifert (Munch. med. Woch., No. 47) found 50 per cent of their non-tuberculous cases react.

L. Meille (Rassegna di Terapia, Turin, 1907,) reports his results in 18 patients, 11 of them known to be suffering from tuberculosis; 9 of these gave a marked ophthalmo-reaction; while the other 2 (who were being treated with large doses - 3 to 5 my.- of tuberculin given sub-cutaneously) gave no reaction. The other 7 cases, all free from any tuberculous infection as far as could be seen, gave no ophthalmo-reaction. Meille recommends this method of diagnosis strongly as being simple, trustworthy, and harmless.

In a long paper, Wolff-Eisner and Teichmann (Berl. klin. Wchnschr., 1908, January 13) endeavour to prove that in man, when the ophthalmo-reaction is strong early in the disease, the promnosis is good, and bad when it is feeble or absent. A strong reaction in advanced tubercle also points to a favourable outlook. Levy (Deutsche med. Wchnschr., Leipzig, 1908, January 16) finds out of forty-one tuberculous patients that 85 % gave a positive reaction, out of fifty-four doubtfully tuberculous patients 60 % gave a positive reaction, while in 235 non-tuberculous patients only a percentage of 2·5 was positive.

In the British Medical Journal of Feb. 15th, 1908, Parkes Weber reports that he finds that patients with tuberculous meningitis, and advanced pulmonary tuberculosis fail to give the reaction. He reports that some observers have found 10 % of apparently non-tuberculous hospital cases to give a positive reaction. He believes this percentage would have been much higher if the test had been tried, not on non-tuberculous hospital patients suffering from various complaints, but on apparently healthy persons who have to irritate their eyes by sitting up late every night to read and write by artificial light. He knows five medical men who have tried this test or had it tried on themselves, but in all these

apparently healthy doctors a positive result was obtained; in three the reaction was violent, and in the other two it was relatively slight, and occurred only after a second instillation of Calmette's tuberculin, the result of the first test (in the other eye) having been negative.

One of these five medical men had a small tuberculous nodule (resulting from an accidental rather deep inoculation at a post-mortem examination on a case of advanced pulmonary tuberculosis) removed from a finger seventeen years ago, but he has had no symptoms of any form of tuberculosis since then, and Calmette's test has been proved to give a negative result in cases of old, obsolete, and "cured" tuberculous lesions. In regard to the strength of the tuberculin fluid used for the test in these cases, it was either the 1 per cent. strength recommended by Calmette or considerably weaker. In one instance another drop of the same tuberculin fluid which excited a violent ophthalmo-reaction in a medical man failed to produce any reaction whatever in the eye of a man (a patient of his own) with the characteristic clinical signs of active tuberculosis of the upper part of one lung, whose sputum, moreover, contained tubercle bacilli.

Much light is thrown on such anomalous results of the test by a recent communication of Waldstein to a meeting of the Wissenschaftl. Gesellschaft deutscher Aerzte in Böhmen on January 15th. He has observed violent reactions as a result of the test in some cases of follicular conjunctivitis and even in ordinary chronic conjunctival catarrh, whereas the result of the test has been completely negative in some other affections of the eye, notably in tuberculosis of the iris.

In the Medical Press, Feb. 19th, 1908, Walsh reports a non-typical case of Lupus diagnosed by Calmette's Tuberculin test. Patient complained of a rash of two months duration on nose and face. This rash was one of

the borderland kind so far as appearances went; one of those transition forms on which the French writers lay a good deal of stress. In these atypical eruptions it is impossible for even the most experienced to be certain of the diagnosis, except under prolonged observation. The rapid settlement of diagnosis, therefore by so simple a method as that afforded by Calmette is obviously of considerable practical value. In this case the balance of probabilities lay in the supposition that the skin rash was of a tubercular nature. Although it may, of course, happen that a patient may have a non-tubercular skin rash, but may furnish the ophthalmic reaction of Calmette owing to latent tuberculosis elsewhere. There was no reason to suspect the latter condition. The patient was accordingly informed that it was desirable to repeat the scraping at an early date.

At present there is much doubt as to the precise relation of lupus erythematosus to tuberculosis. Several cases of that malady, however, have been already found to give the ophthalmic reaction. An interesting case of Bazin's disease (erythema induratum) in a young woman, aet, 21, with a tuberculous family history (two aunts on mother's side). Dr J.M.H. MacLeod obtained a positive reaction of an acute character coming on six hours after the instillation of one drop of Calmette's solution into the conjunctiva.

As regards Calmette's test used for various diseases, two recent American writers, Drs. Frank Smithier and R.P. Walker have fully published a collection of cases by French writers, in which a positive reaction was obtained in 176 out of 185 cases clinically tuberculous, with 9 negative reactions. Of 28 cases doubtfully tuberculous, 21 gave positive and 7 negative reactions. Of 188 persons suffering from disease not tuberculous, and including a proportion of apparently normal individuals, 186

gave negative and only 2 positive reactions.

Roe in the British Medical Journal of February 22nd, 1908, states that he finds cases tested by the Calmette method have given varying results. It one case it cleared up the diagnosis in a difficult case, and had the effect of making the stethoscopic signs much more apparent. Crepitation was easily heard where before it had been very slight and doubtful, and he has been told by the medical officer of one of our largest sanatoriums that this is not unusual. In a second case, when the history and examination led him to regard the case as tuberculous, there was a negative result.

In the same number, Gibb gives his results: Out of 170 cases, 3 % of those apparently non-tuberculous gave the reaction. Some 15 consecutive cases of the type which Dr Weber describes as suitable controls were tested. These were adults using their eyes for many hours by day and night for microscopic work, reading, and writing. All were apparently healthy. None gave a reaction. A 1 % solution, less than eight hours old, was used, and the identical solution, used on patients, gave reactions.

2 of Dr Weber's cases he can explain. He has proof that a reaction obtained only after a second application of test, even though it be applied to the opposite eye, is no evidence of a tuberculous lesion.

As regards his second point, several of the patients to whom the test has been applied have had chronic conjunctivitis, and this has in no way interfered with the result, positive or negative.

It is certainly wise not to try the test in an eye that is acutely inflamed for several reasons: (1) The difficulty of observing the result; (2) the likelihood of changes in the natural course of the conjunctivitis misleading one; (3) the possibility of an additional irritant, even

though not specific, causing an exacerbation. He has tried the test in other forms of eye disease, filamentary and interstitial keratitis, irido-cyclitis, and chorociditis, and have found the results to agree in the main with results in other cases.

Maitland Ramsay in the "Lancet" of March 7th, 1908 reports as a warning a case of a girl aged 12 who had a superficial vascular ulceration of the right cornea. She had had a similar attack in the other eye two years before. There were no signs of tubercle in the lungs or abdomen.

1 drop of a 1 % solution of tuberculin was instilled into the sound eye, in which there was a faint nebula, the result of a previous ulceration. Within 24 hours the reaction was violent and the cornea became vascular, and at its centre it was abraded. The discharge lasted for over a month and then gradually subsided, leaving, however, a considerable opacity in the centre of the cornea.

In the Boston Medical and Surgical Journal of March 12th, 1908, Dr Malcolm Mackay has recorded the following case of prolonged conjunctivitis following Calmette's reaction. A woman came under observation on Nov. 23rd, 1907, complaining of "rheumatism" of the left knee. For one and a half years she had been troubled with a good deal of pain upon walking, although active and passive movements while sitting down were practically painless. At night she was often kept awake by aching in the joint and at times was awakened by the pain. Examination showed moderate diffuse swelling in and about the joint which was held slightly flexed but could be straightened. There was no redness or heat and the patella was not floating, although lateral movements produced a soft crepitus. There was marked tenderness over the head of the tibia at the external tuberosity about three-quarters

of an inch below the articular surface. A cough had existed more or less for two years and there was a family history of tuberculosis. Examination revealed a "pulmonary lesion" and evidence of old spinal disease at the lower dorsal and upper lumbar region. A few tubercle bacilli were found in the sputum. As the patient wished the diagnosis of tuberculosis to be confirmed by an expert she was sent to one, and on Dec. 14th one drop of Calmette's 1 per cent. solution was placed in the right eye. The reaction promptly appeared and was very marked; photophobia, lacrymation, and gumming of the eyelids were very troublesome. A lotion of boric acid was used and the condition remained about the same for ten days and then subsided. On Jan. 20th there was recrudescence; the conjunctiva was red and the eye was partly closed. On the 25th the inflammation was severe, the bulbar and palpebral conjunctiva being involved with chemosis and gumming of the lids. Boric acid and zinc drops were prescribed and a boric acid ointment was applied to the lids which developed a row of small pustules. On February 26th, more than ten weeks after the instillation, the conjunctiva was red and there was slight photophobia with some narrowing of the palpebral fissure. The conjunctivitis was confined to the eye into which the tuberculin was put. The patient had never previously had any trouble with her eyes.

Gebhardt (Pester-Medizin-Chir. Presse, March 15th, 1908) has tested the conjunctival reaction in 198 cases. He used tuberculin in a 3 % solution of boric acid, and limited his cases to those in which no inflammation was present in the eyes, and in which the lacrymal duct was perfectly healthy. In no case did the inflammation extend to the eyeball or become purulent. In 64 cases of definite tuberculosis, surgical and

medical, he obtained a positive result in 58 per cent. In 16 cases of suspicious tuberculosis he obtained a positive reaction in 50·6 per cent. In 118 cases of other diseases he obtained a positive reaction in 18·6 %. In cases of pulmonary tuberculosis in the first stage (10 cases,) a positive result occurred in 80 per cent., in the second stage (13 cases) 100 per cent. In more advanced stages the large amount of toxin in the organism produces immunity, as has also been shown to occur in animals. The results of eleven observers of 360 cases of suspicious tuberculosis are averaged, showing a positive reaction in 50·3 per cent.(varying from 30·7 per cent to 81·0 per cent,) and also of eleven observers of 670 cases in which tuberculosis was not suspected, showing a positive reaction in 15·2 per cent. (varying from 1·1 per cent. to 60·0 per cent.). Five observers are quoted who, in cases which had given a positive reaction in life, on section found no tuberculous lesion. The author concludes:- (1) That in severe cases where tuberculosis is certain no reaction is obtained because the organism, impregnated with toxin, is immune. (2) A positive reaction may be produced by other toxins than the tuberculous, so that it cannot be looked upon as specific.

In the Lancet of April 4th, 1908, Dr Sturrock of the Midlothian and Peebles asylum gives his results with Calmette's test on asylum patients.

One girl with active phthisis and four patients with quiescent phthisis gave a positive reaction.

91 patients of poor nutrition but with no definite proof of tuberculosis reacted positively. Nearly 50 % of his patients gave a positive reaction, and 2 who he says were very healthy gave marked reactions.

In the Scottish Medical and Surgical Journal for April, 1908, Dr Lovell Gulland publishes his results with Calmette's test on the patients at the Royal Victoria Hospital for consumption. He lays stress on the fact that if the test is negative it should be repeated before an opinion is given. The following are his results:-

		Sex	Age	State of Lungs	Active or Quiescent	T.Bs.	Reaction	Onset	Duration
1.	R.E.	M.	23	Marked double apical . .	Active	×	Marked	3 hrs.	3 days
2.	J.B.	M.	17	Very slight double apical	Quiescent	No Sptm.	Slight	3 hrs.	3 days
3.	D.P.	M.	22	Marked double apical . .	Active	×	Definite	3 hrs.	4 days
4.	A.M.	M.	25	" " " . .	Active	×××	Doubtful		
5.	G.P.	M.	22	Mainly right apical . .	Quiescent	×	Absent		
6.	W.A.	M.	22	Slight double apical . .	Quiescent	---	Marked	8 hrs.	5 days
7.	W.C.	M.	32	Double apical . . .	Quiescent	×	Definite	7 hrs.	4 days
8.	J.G.	M.	24	Mainly left upper & Lower	Active	× ×	Marked	6 hrs.	4 days
9.	A.H.	M.	43	Very advanced case . .	Active	×××	Absent		
10.	H.P.	M.	47	Cavity left apex . .	Quiescent	---	Absent		
11.	L.B.	F.	18	Slight double apical . .	Quiescent	No Sptm.	Very slight	26 hrs.	1 day
12.	J.M.	F.	27	Marked double apical . .	Active	××	Slight	24 hrs.	2 days
13.	A.M.	F.	13	Slight " " . .	Quiescent	No Sptm.	Absent		
14.	M.N.	F.	20	Mainly left apical . .	Active	×	Absent		
15.	L.T.	F.	25	Very advanced . . .	Active	××	Very slight	24 hrs.	36 hours
16.	C.T.	F.	24	Well-marked double . .	Active	×	Slight	9 hrs.	3 days
17.	J.W.	F.	18	Marked double apical . .	Active	×	Slight	24 hrs.	2 days
18.	T.G.	M.	35	" " " . .	Active	×	Very slight	24 hrs.	4 days
19.	R.M.	M.	22	Advanced case . . .	Active	×	well marked	5 hrs.	5 days
20.	F.R.	M.	22	Mainly right apex . .	Quiescent	No Sptm.	Slight	5 hrs.	2 days
21.	J.M.	F.	28	Marked double apical . .	Active	×	Absent		
22.	E.W.	F.	18	" " " . .	Active	×	Marked	5 hrs.	4 days
23.	W.B.	M.	31	" " " . .	Active	×	Slight	2 hrs.	3 days
24.	G.P.	M.	38	Slight " " . .	Quiescent	---	Slight	24 hrs.	2 days
25.	M.M.	F.	18	" " " . .	Quiescent	No Sptm.	Definite	4 hrs.	3 days
26.	J.F.	F.	17	Marked " " . .	Active	No Sptm.	Absent		
27.	A.B.	M.	16	" " " . .	Quiescent	No Sptm.	Very slight	8 hrs.	1 day
28.	R.R.	M.	30	" " " . .	Active	×	Marked	3 hrs.	4 days
	Repeats.								
4.	A.M.			. . . . .	. . .		Definite	7 hrs.	2 days
13.	A.M.			. . . . .	. . .		Slight	3 hrs.	2 days
5.	G.P.			. . . . .	. . .		Slight	8 hrs.	1 day
11.	L.B.			. . . . .	. . .		Marked	3 hrs.	3 days
9.	A.H.			. . . . .	. . .		Definite	7 hrs.	2 days

Dr Harrison Butler in the British Medical Journal of 18th April, 1908, states that his personal experience with Calmette's test has been very favourable. He has tried it in 5 or 6 cases of iritis and choroiditis which he did not believe to be tuberculous in nature but which might have been, and not one of them reacted positively. In another case of eczema of the brow a severe reaction was obtained, and as the child was apparently healthy he regarded the indication as false. But he had to take the child into the wards again, and this time she had a typically hectic temperature. He has not been able to find any tuberculous focus yet, but he thinks that a hectic temperature taken with a positive ophthalmo-reaction makes the presence of tubercle very probable. A second trial gave no reaction, but probably the tube, which had been opened some ten days previously, was not active, for it failed to elicit a reaction from three undoubted cases of surgical tuberculosis, which have since reacted to a second tube of serum.

Calmette's reaction is useful in cases of cerebral compression. Some months ago he had two cases of undoubted cerebral disease in the wards. The first case had severe optic neuritis, headache, vomiting, vertigo, and fits. She was almost blind, and had lost all sense of smell. She had been very deaf for some years. He concluded that she had a gumma somewhere in the anterior part of the brain. She did not improve under iodides in large doses, so she was readmitted, and ultimately very successfully decompressed. This case gave a negative reaction, and the subsequent history showed that the tumour was not a tuberculous one.

The second case, had headache, optic neuritis, and vomiting, with severe retraction of the head. She was pale and tuberculous-looking.

The reaction was in her case positive, and he considered that she had tuberculous meningitis. This patient unfortunately discharged herself, and he has lost sight of her.

A third cerebral case is of great interest. A man was sent in suffering from headache, vertigo, and vomiting. He had old-standing, quiescent tuberculous disease of the ankle. He had slight optic neuritis, and he gave a positive ophthalmo-reaction. Shortly afterwards he developed all the signs of typical tuberculous meningitis, and died.

All the cases of obvious tuberculosis in which he has performed the test have given a positive result, but in one the reaction was merely subjective, he could see no inflammation, but the patient, a medical man, assured him that his eye was glued up when he wakened in the morning, the serum having been put in the last thing at night. The case was one of tuberculous kidney, which has since been excised. Tubercle bacilli were found in the urine.

He has so far seen only one very slight reaction in an apparently healthy individual, although he has tried several, including himself and his whole family. Dr Butler also mentions the following cases:-

No. 1. Old-standing, advanced phthisis. Tubercle bacilli in sputum; slight reaction to 0·5 per cent. solution. This case gave a similar reaction three months previously.

No. 2. Tuberculous knee. Slight result with 0·5 per cent., very marked with 1 per cent.

No. 3. Tuberculous ankle. Doubtful with 0·5 per cent., good with 1 %.

No. 4. Tuberculous ankle. Slight with 0·5 per cent., very good with 1 per cent.

No. 5. Periostitis of tibia. No result with either; the case is

probably non-tuberculous.

No. 6. Abscess of Lung, with consecutive empyema. No result with either strength of solution.

No. 7. Case of Cystitis and Probable Nephritis. Patient is suspected to be tuberculous, but no bacilli have so far been found in the urine. The reaction to 0·5 was very slight. Splendid reaction to 1 per cent., with filamentous exudate.

One or two of the cases reacted to the weak solution after twenty-four hours. The serum was placed in the eye last thing at night; next day there was a very slight and doubtful reaction, but on the second day it became marked.

J. Eyre, B. Wedd, and A. Hertz have tested 138 cases - 63, or about half, gave a positive reaction, and of these the majority were unquestionably tuberculous. Two cases almost certainly tuberculous gave no reaction. A case of meningitis, which died thirty hours after the test, did not react, although tubercles were found on the meninges, but this harmonizes with the view now held that no reaction is to be expected during the last week of life.

P. Brons obtained an excessive reaction in 5 cases. He holds that the ophthalmo-reaction has dangers of its own, and should not be used indiscriminately. Butler regards it merely as a help in diagnosis, not as an infallible guide. It is not nearly so accurate as the injection of tuberculin, but it is probably as useful an indicator as is Widal's reaction in typhoid.

Marique, working at the Hôpital St. Pierre, at Brussels, has tested 76 in-patients in the children's surgical ward with tuberculin placed in the conjunctival sac (Journal Med. de Brux., July, 1908.)

He used 0·5 per cent solution, prepared according to Calmette's formula. The summarized results are as follows: 29 patients suffering from definite and certain surgical tuberculosis gave 24 positive reactions, or 82·7 per cent.; 47 children who were considered upon clinical grounds to be free from tubercle gave 13 positive reactions, or 27 per cent. Among the tuberculous cases which did not react were: (1) A non-cachectic infant suffering from multiple osteitis; (2) a "white swelling" of the knee not suppurating when tested, but which suppurated later on; (3) a case of chronic ulcer of the foot gave no reaction, but three weeks later developed tuberculous meningitis, verified by autopsy. Some of the reactions were so very violent and prolonged that Marique has abandoned the method. He concludes that it is too unreliable and uncertain to justify the very real risks.

Harrison Butler (British Medical Journal, 8th August, 1908,) was formerly of the opinion that Calmette's reaction, though sometimes obtained in the non-tuberculous, and sometimes not obtained in the certainly tuberculous, was a useful aid to diagnosis, and that if the eye used for the test were healthy there was no danger to be feared from a ½ or a 1 % solution of tuberculin. Three of the cases, however, which he quoted have since done so badly that he is now of the opinion that the dangers are very real, and that, as the reaction is by no means conclusive, it is hardly a justifiable method of diagnosis. The history of the case is shortly as follows:

Case I.

R. S., aged 4, female, had been in the Coventry and Warwickshire Hospital for a month suffering from a disease of the ankle, which was regarded as tuberculous in nature. Both eyes were absolutely normal.

On March 6th a drop of 0·5 per cent solution of Calmette's tuberculin

was placed in the right eye. No change was noticed. On March 9th the instillation was repeated with a 1 per cent. solution. The next day there was a decided reaction. The caruncle was swollen and the eye injected. This conjunctivitis became rapidly worse; there was a copious discharge and intense inflammation. Later there was chemosis and some swelling of the right eyelids. The conjunctiva was turgid and thickened, and the condition of the lids was very similar to that seen in some varieties of trachoma. This intense conjunctivitis gradually yielded to treatment, but much photophobia and lacrymation persisted.

Early in April an elongated phlyctenule was present at the outer aspect of the corneo-scleral margin. This condition did not improve with yellow ointment, but gradually got worse. At the end of April, just inside the phlyctenule, there were three distinct patches of interstitial keratitis, and in the very centre of the cornea an ulcer appeared the size of a large pin's head, which stained deeply with fluorescein. The eye was put under atropine and tied up. This ulcer proved very chronic, but neither it nor the interstitial keratitis showed any tendency to spread. After a fortnight's treatment with atropine, yellow oxide of mercury was added to the ointment, and the condition gradually cleared up.

At the present time there is a small central nebule, the rest of the cornea is clear, and the eye is no longer injected.

As a result of the instillation of tuberculin, a typically tuberculous process was set up in a perfectly healthy eye, and the central nebula will considerably reduce the visual acuity of the eye.

This case is strictly comparable to one which has been published by Arnold Knapp, (Archives of Ophthalmology, March, 1908.)

Case II.

B. M., aged 7, was admitted to the hospital on March 2nd suffering from a disease of the knee, probably tuberculous in nature. Both eyes were absolutely normal. On March 9th a drop of 1 per cent. solution of Calmette's tuberculin was placed in the right eye. This was followed by a violent reaction.

The conjunctivitis developed rapidly and became very chronic with much thickening of the palpebral conjunctiva. Early in April a very chronic phlyctenule appeared, just as in the last case, which did not yield to yellow oxide. Only now, late in May, has the condition cleared up, and there is still some lacrymation and photophobia. Fortunately in this instance there was no implication of the cornea.

Case III.

A little boy, with a tuberculous ankle. A drop of ½ per cent solution was used and no reaction followed. A second of 1 per cent. was given. The result was a violent muco-purulent conjunctivitis in both eyes which became chronic and resisted all treatment for two months. In fact there was no improvement till the weather permitted the boy to be out of doors nearly all day. In this case also there was no pre-existing eye disease.

Erlanger, Zeitschrift für Augenheilkunde, April, 1908, has carried out a series of tests with a very weak solution (1 to 10,000) of tuberculin. He considers that when there is any pre-existing ocular disease whatever it is most dangerous to use a strong solution until the 1 to 10,000 solution has been tried and has failed. He has obtained a reaction in several cases with this dilute reagent.

Considering, therefore, that the test is often deceptive and may do

grave damage to the eye Butler thinks it hardly justifiable to use it any longer. He has abandoned the method, and is now employing injections of old tuberculin (P.G.) to help to decide the question as to whether a disease is or is not tuberculous in nature.

In a recent case of interstitial keratitis and choroiditis which, upon clinical grounds, was considered to be almost certainly syphilitic, but which, in spite of full doses of mercury, was rapidly going from bad to worse, he obtained a typical reaction both general and local, and was able to decide that the disease was tuberculous, and that it should be treated with tuberculin. He says that Calmette's reaction would have only decided that the patient was tuberculous; the injection of P.G. gave a clear local reaction, and pointed to the ocular lesion being tuberculous.

In the "Medical Press" of August 12th, 1908, Parkes Weber gives further results with Calmette's Ophthalmo-reaction. In thirty cases in which the presence of tuberculosis was established (tubercle bacilli in the sputum), or made probable by clinical examination, the reaction was positive in 24 (very slightly or doubtfully positive in one of them) and negative in six. Of these six, however, at least four were advanced cases of pulmonary tuberculosis, in which it is now generally recognised that a positive reaction is not to be expected. In all these four cases the probably grave prognostic significance of the absence of reaction was confirmed by the patient's subsequent death and the advanced tuberculous lesions found at the post-mortem examination.

In 39 clinically non-tuberculous cases the ophthalmo-reaction was negative in 29 and positive in 10. One of these 10 cases, a man with pulmonary emphysema and chronic bronchitis, who gave an only slight and

transient reaction, subsequently died from cardiac insufficiency, and at the necropsy, as far as the examination went, no evidence of tuberculosis was discovered beyond some old scarring of both pulmonary apices. The most acute reaction that he has observed was in a young woman, aet, 25, who persuaded someone to try the reaction in her own eye. In three hours' time after the instillation of a drop of Calmette's tuberculin (one per cent. fluid) there was already obvious conjunctival reddening, and on the next day the ocular conjunctiva was so intensely injected that it looked almost like a sheet of blood, but she quite recovered. In this case there were no signs or symptoms of pulmonary or glandular tuberculosis, nor any family history of the disease, but he believes there was a special local irritability (excessive sensitiveness) in the conjunctivae.

Weber says that it is now well known that even in apparently quite healthy persons, when the result of the first instillation of tuberculin is negative, a second instillation, ten days or so later on, often gives a decidedly positive reaction. In two of the above mentioned cases of advanced pulmonary tuberculosis, in which no reaction followed a first instillation, a second instillation produced a slight positive reaction. The first instillation does not seem to be followed by this heightened conjunctival sensibility in every case; in two or three of his cases no reaction followed a second instillation.

A point of great scientific interest - which, however, he has not himself been able to confirm - is that the ophthalmo-reaction can be employed to test whether a tuberculin preparation, when given by the mouth or by the rectum, has been absorbed from the alimentary canal into the blood-stream. If the tuberculin has been absorbed into the blood the

conjunctiva, on which a week or two previously Calmette's ophthalmo-reaction has been tried, should become reddened, just as it would become were tuberculin to be injected under the patient's skin. A recurrence of conjunctivitis (in the eye in which the ophthalmo-reaction has been tried), when the patient is afterwards subcutaneously "inoculated" with tuberculin, is of extreme theoretical importance, as in his opinion it furnishes an explanation for the spontaneous recurrences of conjunctivitis which have been occasionally observed in tuberculous patients a week or more after the Calmette test has been employed. In such cases it is he believes an "auto-inoculation" with tuberculin which, having the same effect as the subcutaneous injection of tuberculin, reproduces the ophthalmo-reaction, or even lights up a chronic conjunctivitis in the tested eye.

Dr Klieneberger, (Konigsberg) considers that, although the ophthalmic test is of great value in the early diagnosis of Tuberculosis, it indicates the presence of tuberculosis when manifest only, and not in latent or healed forms.

Dr. Klieneberger's observations have shown him that many cases of definite tuberculosis do not react to a first instillation of tuberculin, while a repeated instillation produces an especially violent reaction, which, however, is not available as a proof. In 17 cases of tuberculosis, (in which T B was present) seven did not react, two were doubtful. Of these 7 cases, 2 were in the second, and 1 in an early stage of the disease. He therefore considers that not only in advanced stages, but also in the first and second stages, the ophthalmic reaction may fail.

He gives statistics of 61 cases, treated with repeated instillations of Koch's 1 % solution and also Calmette's preparation.

Group I. Of 9 cases of definite tuberculosis, all reacted to a second instillation, none of whom , with one exception, had reacted to the first. The second reaction was much more pronounced.

Group II. Of 6 suspected cases, only two reacted positively to second instillation. They had also shown slight reaction at first trial.

Group III. Out of 64 unsuspected cases, 36, i.e., 56·25% reacted - a surprising result. 16 cases showed very violent reaction, swelling of lid, chemosis, etc. 28 of these cases had shown not the slightest trace of reaction at the first instillation, and the remaining cases little or none. Dr. Klieneberger considers that this result must not be taken as indicating so high a percentage of latent tuberculosis, but he affirms, that the exceeding violence of the reaction is the result of a local hypersensitiveness induced by repeated instillations. He considers that the method of repeated instillations is therefore faulty as a test.

Drs. Wiens and Günther give the results of their investigations in relation to the ophthalmic reaction in tuberculosis. They followed Calmette's method, using dried tuberculin in sterilised water. Their statistics are as follows:-

In a series of 12 cases, Group I. contained 9 unsuspected cases. Group II. contained 1 doubtful case. Group III. was composed of 2 definite cases of tuberculosis.

Group I. In 3 cases only was the reaction negative. All the others showed a characteristic reaction. In two, additional signs of blood were noticeable in the conjunctiva sclerae, as in typical pneumococcic conjunctivitis.

Three cases of positive reaction are analysed, as of special interest,

one being a case of spinal tumour, one of poliomyelitis, and one of multiple sclerosis. In none of these three cases, had there been any suspicion of tuberculosis.

Group II. The single case in this group was one of inflammation of knee joint. There were no lung symptoms, yet the reaction was particularly pronounced.

Group III. One case of early progressive tuberculosis gave a positive reaction. Another case in a seemingly stationary, but more advanced stage showed no reaction.

As in the above series, the reaction was too violent, the 1 % solution was reduced to a ½%, and trial was made in a series of 38 cases. These are similarly grouped.

Group I. containing 24 cases, presented a negative reaction with one exception, which is fully described. It was the case of a man of 30 years of age, who had suffered from frequent conjunctivitis and had indeed a predisposition thereto. The first instillation produced no reaction. The second, two and a half months later, produced violent reaction. Rontgen inspection of lungs showed no tuberculosis.

Group II. containing 5 suspected cases, included 2 negative cases, two of doubtful apical affection, and one of anaemia with suspicion of tuberculosis of bowels. Of the two showing positive reaction, one was a case of doubtful apical tuberculosis, the other of scrofula with superficial keratitis. The latter proved of special interest and is described in detail. The patient was suffering from an affection of the cornea in the left eye. Instillation was made in the healthy eye, and produced

typical scrophulous keratitis. The lung condition was normal.

Group III. Of 9 possible cases, 7 positive reactions were obtained. Of the two negative cases, one was that of incipient disease, the other of galloping consumption. Amongst other cases, not classified, two patients in advanced stages, showed no reaction. Two cases of children with eye affection showed a particularly violent reaction. From this, the authors affirm that in no case of conjunctivitis should the test be made. The general conclusion drawn is that only very seldom the ophthalmic reaction fails in cases of known pulmonary tuberculosis.

Dr. Kohler considers that, though 95% of cases of pulmonary tuberculosis show the ophthalmic reaction, it remains to be proved to what extent the same reaction is present in non-tuberculous subjects. Investigations have proved that in advanced tuberculosis, the reaction is wanting.

Cohn has frequently found the ophthalmic reaction to Original Tuberculin in cases of typhus.

Dr. Comby has made repeated instillations in a series of 20 children at intervals of a few days, several weeks and even months. Those who had reacted to the test continued to do so in the same degree, and those in which no reaction had been obtained, presented none. The reaction did not vary in cases where hypodermic injections or skin-inoculations of tuberculin had been made.

Dr. Comby found that children with latent tuberculous infection answered as positively to the test as those in definite and advanced stages. Tuberculous meningitis gave positive reaction in all phases, as did cases of surgical tuberculosis, including Pott's disease, coxalgia, spina ventosa, etc. Dr. Comby has taken special pains to obtain proof of the

certainty of the test by observation and post-mortem examination.

He emphasizes the point that the test should only be made when both eyes are in a clean and healthy condition, any blepharitis, keratitis, conjunctivitis being contra-indications to its employment. Besides the danger of aggravating any pre-existent ophthalmia, the observer can draw no definite conclusions as to his test. Finally, it is necessary to examine closely for slight reaction and to delay for late reaction, in some cases as long as 48 hours.

Dr. Mainini discusses the Von Pirquet and Wolff-Eisner tuberculin reactions. He remarks on the fact that reaction is sometimes positive in adults in cases where no tuberculous process is present. He considers that this may be due to a tuberculous infection at some other time.

He gives his own statistics in reviewing a series of 208 cases. He used a solution of old tuberculin, 1 × 80 in strength. He inoculated in two spots on the lower arm, making a very slight cutaneous scratch, and allowing a drop of the solution to dry into the scratch. The second mark served as control. His statistics are divided into three groups as follows:-

I. Cases of Tuberculosis, showing T B.

II. Cases of suspected Tuberculosis.

III. Cases where no suspicion of Tuberculosis is present.

Group I.

Of 23 patients, 9 acted positively. The remaining four were in advanced stages of tuberculosis with severe marasmus.

Group II.

Of 74 patients, 67 showed positive reaction. Of the 7 remaining, 2 died of cachexia, 1 proving to be a case of pulmonary and spinal tuberculosis, the other that of miliary tuberculosis. One had

previously reacted to a tuberculin injection, and later to the cutaneous test, but at this trial showed no reaction. Four remain unexplained.

Group III. This group consisted of 111 cases in which no cause for suspecting tuberculosis was present. They included various illnesses. 89 reacted positively, 22 negatively. It is difficult to prove with certainty the correctness of the test in such miscellaneous cases, but Dr. Mainini is inclined to consider that the test is of such great sensibility that the slightest latent, or even healed seat of disease may be indicated by its use.

With regard to Wolff-Eisener's ophthalmic test, Dr. M. used 5 % old tuberculin solution, considering (contrary to Calmette) that the glycerine contained in the solution was quite harmless, and also preferring the stronger solution to a diluted one. He describes the course of the ophthalmic reaction also in detail, and divides his statistics into the same groups as above.

Group I. Of 12 cases, 11 reacted.

Group II. Of 32 cases, 26 reacted.

Group III. Of 56 cases, 8 reacted.

In group I. the exceptional case was one of cachexia. In group II. 6 of the exceptional cases included 2 old men with pleuritis, 1 with probable spinal tuberculosis, and one with pleuritis with high fever. The two remaining cases were one tuberculous meningitis, and one dry pleurisy. In comparing the results of the two different tests, the first two groups are almost in complete agreement. But in comparing the third

groups, we find that 89 % reacted positively to Von Pirquet's test, while only 14·2% showed ophthalmic reaction.

Dr. Mainini remarks in explanation of the seeming contradiction, that the skin is much more likely than the substance of the conjunctiva to contain the specific properties which serve to produce a reaction. As a proof of this, he cites the fact that a second instillation into the eye at a short interval, often produces a reaction, the sufficient amount of the hypothetically specific substances being then present. In conclusion he sums up as follows:-

1. The cutaneous, as well as the ophthalmic reaction give with great constancy proof of tuberculosis, except when the disease is in advanced stages.

2. The specific value of this reaction is probable but not proven. The value of the cutaneous reaction in suspected cases of tuberculosis is six times as high as that of the ophthalmic reaction.

3. The ophthalmic reaction is significant of an active tuberculous process, the cutaneous reaction in addition points to a latent tubercle.

Nicolas and Gauthier (Ann. de dermat. et de syph., Paris, 1907, December) have specially investigated the Skin and Ophthalmic Reactions in three groups of skin diseases - (1) In patients affected with typical cutaneous tuberculosis, lupus vulgaris, tuberculosis verrucosa; (2) in skin diseases susceptible of presenting special relations with tuberculosis, lupus erythematosus, prurigo, etc.; (3) in patients taken at random, under hospital treatment for syphilis, varicose ulcers, eczema, etc., in order to determine in a certain degree the value of the method. For the skin reaction a single inoculation was made on the forearm with 1 drop of a 1% solution of tuberculin. The reaction attained its maximum usually at

the end of twenty-four, rarely of forty-eight hours. The intensity differed from a simple redness of the margins of the scarifications to a voluminous, markedly infiltrated papule with tendency to ulcerate. The duration of the complete evolution of the more pronounced cases might last as long as three weeks, in the less so from four to fifteen days. Of the first group of nine cases all gave a positive reaction. Of the second, seven with four positive and three negative reactions. Of the third, twenty-eight with nineteen negative, two doubtful, and seven positive reactions. One can only grant a relative value to the information furnished by the skin reaction, so long at least as it is not proved that, in persons clinically healthy, positive reactions reveal a latent tuberculosis. On the contrary, negative reactions appear to them to have a greater value, since all the tuberculoses clinically appreciable, yet not in an advanced or grave phase, gave positive reactions. With respect to the ophthalmic reaction, a 1 per cent. specially prepared solution was employed. Most of the reactions were gone in ten days, but in one phlyctenular keratitis supervened, and had not completely disappeared twenty-five days after. This was quite unexpected, as the eyes had previously been healthy. Of the patients tested in this way, those clinically tuberculous gave of ten examples nine positive and one doubtful reaction; while of nine not clinically tuberculous, eight gave negative reactions and one positive. The most which can be claimed for these procedures is the establishment of probable tuberculosis, and the cutaneous method is the one to be selected as always painless; the ophthalmic is frequently disagreeable for the patient, and may possibly entail regrettable complications.

R. Bing records the results obtained in Baginsky's children's clinic

in Berlin with von Pirquet and Wolff-Calmette's tuberculin reactions (Berl. klin. Woch., March 16th, 1908). Dealing with the cutaneous reaction first, he has records of 241 children in whom the test was applied. Of these 19 were undoubtedly tuberculous, and of these 14 gave a positive and 5 a negative result. This would yield a positive result in 73.7 per cent. of the undoubted tuberculous cases. Thirty-six children were regarded as suspicious of tuberculosis and 69 per cent. of them gave a positive reaction. Among 186 not tuberculous children, 34 gave a positive reaction, that is, 18.2 per cent. The 5 negative cases of the first group included 4 cases of tuberculous meningitis and 1 of miliary tuberculosis.

Pirquet has pointed out that the reaction may prove negative in advanced cases of tuberculous affections. But among the positive cases, Bing found 2 advanced cases of tuberculous meningitis and 2 cases of miliary tuberculosis. In comparing the number of children who reacted to the cutaneous application of tuberculin, according to their ages, it appears that the frequency increases steadily from 19.3 per cent. in the first year of life to 56.2 per cent. between the ages of 12 and 14. In all the fatal-ending cases in which a positive reaction was obtained the diagnosis of tuberculosis could be confirmed post mortem. The last 100 cases were further controlled by the ophthalmo-reaction to tuberculin, Calmette's original 1 per cent. and 1.5 per cent. solutions being used for this purpose. The 6 cases of undoubted tuberculosis yielded 50 per cent. of positive and 50 per cent. of negative reactions, 15 suspicious cases showed 40 per cent. of positive against 60 per cent. of negative results, while among the 79 not tuberculous cases, only 1 gave a positive reaction and all the others - that is, 98.8 per cent - gave negative reactions.

Among the undoubted tuberculous cases, only 1 showed a difference between the two reactions. This was a case of tuberculous meningitis, and gave a positive reaction with Pirquet and a negative with Calmette. Much more marked differences were noted in the second group. Bing considers that Pirquet's reaction reveals every tuberculous focus in the body, save the very advanced ones, while the ophthalmo-reaction only shows those which are active and which are not advanced. He further records that, contrary to the experience of Cohn, none of the cases of enteric fever gave a conjunctival reaction. He regards the cutaneous reaction as quite safe, while the same cannot be said of the ophthalmo-reaction.

In the Lancet of April 18th, 1908, it is reported that Dr. Kremer has made a series of comparative observations in order to ascertain whether Calmette's and Pirquet's reactions were of equivalent value or not. He divided the individuals into three distinct groups - namely, cases of tuberculosis with positive clinical symptoms, cases of suspected tuberculosis, and non-tuberculous cases. In each group the observations were made at the same time. The first group consisted of 33 cases, of whom 17 were treated by Pirquet's method of cutaneous inoculation with tuberculin and 16 were treated by Calmette's method of instillation of a drop of a solution of tuberculin of 1 per cent. into the conjunctival sac. Pirquet's method gave 15 positive and two negative results while Calmette's method gave 12 positive and four negative results. The patients included cases of meningitis, peritonitis, lupus, cold abscess, caries of bone, pulmonary tuberculosis, and lymphoma of the neck. The last named cases gave negative results by Pirquet's method whilst Calmette's method failed to produce any reaction in these as well as in the cases of lupus and caries of bone.

The second group consisted of 35 cases, 18 of which were treated by Pirquet's method with 15 positive results, whilst 17 were treated by Calmette's method with 12 positive results. The patients comprised cases of bronchitis, pleuritis, anaemia, and catarrhal disease of the lungs. The third group consisted of 25 cases free from any suspicion of tuberculosis. Of this group 14 patients were treated by Pirquet's method with four positive results whilst 11 were treated by Calmette's method with two positive results. Dr. Kremer took care to select cases as much as possible similar to each other for the control tests. Wherever possible both tests were used in the same individual at the same time. Pirquet's reaction sometimes showed itself five hours after the inoculation but as a rule, the effect was produced in 24 hours and lasted from four to six days. Once it was visible for 11 days. Calmette's reaction occurred, as a rule, six hours after application but in one instance only after 24 hours; it lasted mostly from four to five days but in two instances for eight and 12 days respectively. In five cases the cutaneous reaction was positive whilst the ocular reaction failed to show the presence of tuberculous disease, and in four cases the eye was severely affected for some days. Dr. Kremer therefore concludes that of the two methods the cutaneous one is the more trustworthy, the easier, the less severe, and the less painful.

Louis Hamman (Arch. of Intern. Med., June, 1908,) states that the cutaneous reaction is too delicate an indicator to be of any value in diagnosis unless the reaction be negative, which he says it seldom is in adults. The eye reaction, according to him, gives results more nearly in accordance with clinical experience, but at the same time it is by no means absolutely certain.

Hammerschmidt (Med. Klinik, June 7th, 1908) advises that both

Calmette's reaction and Pirquet's test of inoculation by scarification of the skin should be used coincidently, in order that one may neutralize the mistakes of the other. He has tried this double test in 500 cases, the great majority of which were healthy people. For Calmette's reaction, one drop of not more than 1% old tuberculin, disolved in 0.5 per cent. phenol solution was instilled into one eye, and for control, a drop of 0.5 per cent phenol solution into the other.

For Pirquet's test, the arm, after being rubbed with 60% alcohol, was touched with a drop of a 20% solution of old tuberculin, and then on the same place a cross was scratched with a new boiled steel pen. A second scratch was made in another part for control. Pirquet's test was positive in 140 cases (28 per cent.), and of these 140 cases Calmette's reaction was positive in 97 (19.4 per cent.) Beyond a slight twitching sson after the scarification, and while the pustule was developing, Pirquet's test produced no local or general disturbance. In the ophthalmo-reaction, there was no pain on instillation, and never any considerable inflammation of the bulbar conjunctiva - at the most there was a slight redness of that part covered by the lower lid. Subjective disturbances were observed five times, and consisted of slight pricking and burning. Only once were cold bandages required for some hours; in this case Pirquet's reaction was very weak. The ophthalmic changes appeared twelve to fourteen hours after instillation; the Pirquet result in twenty to twenty-four hours, or even later. A late pustule, as described by Stadelmann, occurred in only 5 or 6 cases. When Calmette was positive Pirquet was also always positive, but the reverse was often not the case. Although tuberculin was in many cases injected sub-cutaneously after the tests for therapeutic purposes, in no case did the eye become again inflamed. Reaction always occurred

in cases where it was to be expected, and frequently in cases where tuberculosis was suspected. In strong people the reaction was quicker than in weak, but in the latter the duration was greater. In by far the greater number of cases the pustule appeared directly after or coincidently with the ophthalmo-reaction.

The statistics so far published show that C. is + in from 78 to 99.3 per cent. Petruschky's report shows that P. is + in all cases except those of advanced and of manifestly healed tuberculosis. That the 28 per cent. or 19.4 per cent. giving a + reaction does not correspond to the percentage of people with tuberculous lesions (92 to 96 per cent.) is explained by the fact that the reaction is the sign of active, not healed disease. In 13 cases where C. was + and P. at first -, P. was repeated several times before a reaction followed; in 2 cases four times. In 7 of these 13 cases the after clinical course gave evidence of tuberculosis. The author ascribes the peculiarities possibly to a difference in capacity of individuals to react to tuberculin, possibly to an alteration in the capacity of the same individual at different times. The technique could hardly be to blame, since this was the same in all cases. When tuberculin was also injected subcutaneously, the reaction was not weakened; P. was in 3 cases marked, while C. was unaltered.

Hammerschmidt does not agree that a subcutaneous injection always shows reaction after inoculation by scarification. In one case repeated inoculations were tried as a therapeutic measure. From fourteen inoculations a reaction was obtained eleven times. The patient felt improvement, gained 1 kilogram in weight in fourteen days, and the amount of haemoglobin rose from 72 per cent. to 83 per cent., a result which is an

encouragement to further trials of the treatment. The author concludes (1) that a negative result speaks with great probability against tuberculosis. (2) That a positive result speaks with still greater probability for tuberculosis. He thinks that the combined Calmette and Pirquet tests may completely and fully replace the diagnostic injections.

In the Edinburgh Medical Journal for June, 1908, there is a review by Dr. Fowler of the Specific Tests for Tuberculosis. There are four tests, or rather three and one modification. (1) The oculo-reaction, or conjunctival reaction, (2) The cutaneous reaction of Pirquet. (3) The subcutaneous reaction ("stich-reaction"). Hamburger supports this as the most certain method of diagnosing tuberculosis. The injection of 1 mgrm. of old tuberculin under the skin of a tuberculous individual produces local swelling and redness; sometimes much smaller doses ($\frac{1}{10,000}$ to $\frac{1}{100}$ mgrm.) also give the reaction. (4) Moro's salve reaction is simply a variation of the cutaneous reaction. He finds that if an ointment consisting of 5 c.c. old tuberculin, and 5 grms. anhydrous lanoline be rubbed into the skin of a tuberculous subject, slight dermatitis ensues. Heinemann has tested this on a series of patients, and shows that it gives practically the same results as the instillation of tuberculin into the eye, without the discomfort attending the latter.

Nearly all the authors speak favourably of the reliability of the tests. Almost the only exceptions are Olmer and Terras, who appear to have been unfortunate in getting eleven negative results out of thirty-one trials on tuberculous adults with Pirquet's test. It is unanimously agreed that all the tests fail in advanced cases of tuberculosis, in general miliary tuberculosis, and in tuberculous meningitis. Pirquet's test (the cutaneous reaction) differs from the oculo-reaction in this respect,

that a large number of clinically healthy adults (up to 80 or 90 per cent. according to some observers) react positively, this being much higher than in the case of the oculo-reaction. The test is, therefore, chiefly valuable in children under 2 years. This difference in delicacy is explained by Mainini and others, on the assumption that a positive cutaneous reaction is evoked by any latent deposit of tubercle, while for a positive oculo-reaction an active focus is required. This supposition is scarcely justified; all that we can say is that the cutaneous reaction is so delicate as to be robbed of much of its value as a diagnostic of clinical tuberculosis in the adult.

Statistics of the oculo-reaction.-

Collating the results given by Moro, Heinemann, Mainini, Schröder and Kaufmann, Damask, Blum, Cohn, Levi, Schenk and Seiffert, and Wollf, we find that of 404 tuberculous persons, 327 gave a positive reaction; of 215 patients suspected of tubercle 130 gave a positive reaction; of 716 patients clinically non-tuberculous 123 reacted positively. These figures relate to adults; for children we have Audeoud and Machard. Of 290 tuberculous children 271 reacted; of fifty suspects, forty reacted; of 310 non-tuberculous, twenty-six reacted. The percentage of positive results in adults, tuberculous, suspect, and non-tuberculous respectively, are 80, 60, and 17; in children, 93·4, 80, and 8·4. It seems, therefore, that the test is one on which both positively and negatively a considerable degree of reliance can be placed, particularly in children below the age of 12.

Statistics of the Cutaneous Reaction.-

For adults, collating Mainini, Wollf, and Goebel, we have tuberculous

persons ninety-six, of whom eighty-four reacted; suspects, 195, of whom 137 reacted; clinically non-tuberculous, 128, of whom 101 reacted. As to children, Goebel, Ferrand and Lemaire, Bing, and Pirquet give 128 tuberculous with ninety positive reactions; sixty-eight suspects with forty-four positive reactions; and 93 non-tuberculous with fifty-seven positive reactions. The percentage in this case are 87, 70, and 80 for adults; 70, 66, and 19 for children.

Comparisons of the two tests, and of both with the results of injections of tuberculin, have been instituted by several observers. Wollf, who is a partisan of injections, which are not, he asserts, dangerous, found that, taking doubtful cases of tuberculosis, a much larger proportion reacted definitely to injections than to either the Calmette or Pirquet test. He found on X-raying a number of suspicious lung cases which had not given the cutaneous reaction, that changes could be detected in the thorax notwithstanding. His method of applying the tuberculin test is to begin with $\frac{1}{10}$ mgrm., increasing to 1, 2, 5, or 10 mgrms., with two-hourly temperature observations. Ferrand and Lemaire found that the result of the cutaneous reaction, whether positive or negative, was confirmed by the ophthalmo-reaction in twenty-nine out of 49 cases; it was confirmed by tuberculin injection in thirty-four out of thirty-nine cases. It is not very easy to compare the results of different observers, owing to the different methods of control they have adopted, but the general result seems to be that both subcutaneous and cutaneous inoculation are much more delicate tests than the oculo-reaction, and that their usefulness is somewhat detracted from by the fact that they reveal the latent or obsolete tubercle which apparently lurks in so many clinically healthy adults in

a much greater degree than does the oculo-reaction.

Prognostic value of tuberculin reactions.-

The general impression is that the intensity of these reactions is to some extent inversely proportional to the severity of the disease. Detri regards the disappearance of response in a patient who has previously reacted as ominous. Wolff-Eisner and Teichmann have paid special attention to this aspect of the question. They hold that the cutaneous reaction has a typical course, which depends on the gravity and progress of the disease. They divide the reaction into three groups:- (1) Marked reaction, which sets in within four to six hours after inoculation, and reaches its height twenty to twenty-four hours later, and diminishes at the third or fourth day. This occurs in incipient tubercle, and in the first and second stages of favourable cases. (2) Mild reaction, beginning about six hours after inoculation, reaching its acme in ten hours, and disappearing on the second day. This is characteristic of the third stage of tuberculosis, and of bad cases in the first and second stages. (3) Late and continued reaction, beginning about six hours after inoculation, reaching a height very slowly, and persisting for a week. This is met with in patients who show no clinical signs of tuberculosis. Of the oculo-reaction, only the first and second types are met with.

Effect of repeated inoculations.-

If in a suspicious case the test is negative or doubtful, it is the natural impulse to try it again, but to do so introduces a complication of rather a curious nature. This is bound up in the question of super-sensitisation, or anaphylaxis, a phenomenon which has been extensively studied in connection with "serum disease," and which for the present purpose we may define as an increased sensitiveness to the second and

subsequent inoculations with a serum. Pirquet suggests the term "Allergie" to denote this increased sensitiveness, and "Allergie tests" have been employed in a number of cases. Perrand and Lemaire are among those who report the recurrence of the ophthalmo-reaction, on a curative dose of tuberculin being given weeks after the test has been applied. Klieneberger found that on a second test being applied 76 per cent. of the clinically non-tuberculous show the ophthalmo-reaction. Dufour, however, found that two successive instillations into different eyes always yielded concordant results, though the second reaction might be more severe; with two successive instillations into the same eye, the first being negative, the second was sometimes positive; with three or more instillations the first being negative, the later ones were sometimes positive on the same eye, but not in the opposite one. Anaphylaxis is therefore local.

Is the oculo-reaction free from danger?-

Many German writers have reported severe conjunctivitis, etc., following Calmette's test, and most of them speak warningly on the subject. "Scrofulous" children are especially liable. Possibly, however, this preponderance of bad results is due to the fact that Höchst's dry tuberculin is tenfold the strength of Calmette's preparation. Lapersonne states that the conjunctivitis is usually due to saprophytes; the Koch-Weeks bacillus was only once found. He has seen persistent lacrymation, pannus, and keratitis followed by irido-cyclitis after the test. If there has been any ulceration of the cornea the reaction is very likely to provoke a relapse. The usefulness of the test in ophthalmic work is therefore limited. It should be employed sparingly in the aged.

The reaction is relatively often positive in typhoid patients (Damask and others.) The numbers are, however, few. The lesions of the skin are

said to be characteristic, and cannot be reproduced by mechanical or chemical irritants (Ferrand and Lemaire.) The cytology of the exudate has been studied by Lafon, who finds that there is a more marked polymorphous leucocytosis than in conjunctivitis, and thinks this may decide doubtful cases. Various attempts have been made to utilise these tests to shorten the time required to determine the result of diagnostic animal inoculation, but without success. Cattle react; rabbits react in six or eight weeks, guinea-pigs do not respond either to Pirquet's or Calmette's test.

With the object of testing the efficiency of the ophthalmo-tuberculin reaction in cattle, McCampbell and White (Journal of Experimental Medicine, March 1st, 1908) carried out the following series of experiments: The cattle used in the tests were divided into three classes. Class A, five animals, which reacted to the tuberculin test in February, 1907; Class B, five animals, which reacted to the tuberculin test in September, 1907; Class C, twenty animals, which were used as control, and to which the tuberculin test applied in November, 1906, showed no reaction. The first method tried was the administration of tuberculin as prepared by Calmette. This method was found to be of no use. With tuberculin obtained from the Bureau of Animal Industry, United States Department of Agriculture, definite results were obtained.

All the cows in Classes A and B showed the reaction, and one cow in Class C - an animal which had not been regularly tested with tuberculin owing to its continued high temperature. Class A showed the most profuse exudate and the most typical reaction. With the exception of the one animal in Class C, none of the animals in this class showed the reaction. The conculsions the authors draw from their experiments are as follows:

The ophthalmo-tuberculin reaction is of some value for diagnosis of tuberculosis in cattle. The reaction is more pronounced in those animals which have not been recently tested with tuberculin. The ordinary tuberculin test does not seem to interfere to any great extent with the ophthalmo-tuberculin test, at least within four weeks, but occasionally it absolutely prevents a second reaction during a period of from six weeks to a year. With the ophthalmo-tuberculin test one reaction probably inhibits a second reaction for the same period of time. In cattle recently tested with tuberculin by the subcutaneous method the ophthalmo-tuberculin reaction is only slightly reduced in its intensity. No constitutional disturbance being noticed in any of the cattle tested, it is obvious that the instillation of tuberculin into the eye does not produce the general reaction which in some cases attends the subcutaneous injection of tuberculin.

G. Joannovics and G. Kapsammer (Berl. klin. Woch., November 11th, 1907) write an article on the diagnosis of tuberculosis by experiments on animals. Bloch published, during the course of last year, the details of a method of determining by animal experiment whether a material is tuberculous or not within a short time with absolute certainty. They found that Bloch's method enables one to diagnose doubtful cases of tuberculosis by animal experiment within fourteen days.

They next turned their attention to Pirquet's method. They tested this method on 20 guinea-pigs which had been rendered tuberculous, and also on four healthy guinea-pigs. The same animals were subjected to the ophthalmo-reaction, which Wolff-Eisner and later Chantemesse, have introduced. The tuberculous animals did not yield results which could be distinguished from the healthy animals with Pirquet's test, while 2 out of 19 tuberculous animals reacted slightly to the introduction of tuberculin

into the eye, the remainder being unaffected save one, which, curiously enough, showed a reddening of the ear (not eye). Further, they introduced pure, undiluted tuberculin into the eyes of 22 tuberculous guinea-pigs without producing any effect.

It thus appears that Pirquet's skin reaction with tuberculin, Wolff-Eisner's ophthalmo-reaction with tuberculin, and Chantemesse's ophthalmo-reaction with tuberculin precipitated by alcohol, are useless for guinea-pigs. This has already been found, and the results of the experiments do not in any way clash with the claims which Calmette has made for the ophthalmo-reaction in human tuberculosis.

III.

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IV.

Cases.

The following cases were taken at random from amongst the patients in the Wards, but I was careful not to perform Calmette's test on any patient whose eyes were not healthy or who had any history of previous disease. At the end of each case I have mentioned which test was performed and the result. As regards Von Pirquet's test, in some cases I have used pure old Tuberculin (Koch) and in these cases I have mentioned it, but in all the other cases v. Pirquet's solution was used.

For Calmette's test, Calmette's solution was used, except in a few cases and in these the other solution is given. The dilution is also

mentioned and the result of the test. I have divided the results with Calmette's test as follows:-

A. Positive

I. Slight Reaction

II. Marked "

III. Purulent "

IV. Delayed "

B. Negative.

C. Doubtful.

The numbers placed after the positive reactions (at the ends of the cases) refer to the degree of the reaction, as above.

A Slight Reaction consists in a slight but distinct redness and swelling of the caruncle and plica semilunaris with slight hyperaemia of the palpebral conjunctiva. To detect this a careful comparison should be made of both eyes. This reaction lasts, as a rule, for 2 or 3 days.

A Marked Reaction consists in great redness of the conjunctiva with considerable swelling and redness of the caruncle and plica, with sometimes a fibrinous deposit. There is also more or less oedema of the lower eyelid. The patient may complain of a "gritty" feeling in the eye. The reaction is very evident and it usually persists for from 5 to 7 days.

A Purulent Reaction is more intense and also there is a purulent secretion.

A Delayed Reaction is one not appearing till 12 hours and more after the instillation of the tuberculin.

A. Forty-Seven Tuberculous Cases giving Positive Reactions:

Gonorrhoeal Rheumatism.

R. S. m. History- 5 weeks ago patient had an attack of gonorrhoea which was followed a week later by a double gonorrhoeal conjunctivitis. Three weeks ago he began to complain of pain and swelling in his left knee and ankle.

Respiratory System. Marked dulness at both apices with bronchial breathing and increased vocal resonance. Slight dulness in each interscapular region with harsh vesicular breathing with prolonged expiration.

Haemopoietic System. Numerous enlarged glands in the neck, axillae and right groin.

Von Pirquet's test. (Pure Old Tuberculin) Positive. Slight redness and infiltration of scarified area. 29th July, 1908.

Pulmonary Tuberculosis.

A. R. m. aet 32.

History - Up till six months ago patient was in good health but then he "caught a cold," and ever since then he has had a cough and a spit, and latterly he has had several attacks of haemoptysis.

Respiratory System. Dulness with bronchial breathing and crepitations at the right apex. Haemoptysis.—Sputum contains Tubercle Bacilli.

Von Pirquet's test, (pure Old Tuberculin) Positive.

Slight infiltration and redness of scarified area. 27th August 1908.

Abdominal Tumour. (Carcinoma of Caecum)

D. B. m. aet 38.

History - For the last four years patient has had attacks of severe pain in the right side of his abdomen with swelling of that region, pain and swelling lasting 5 or 6 hours and then gradually disappearing.

Alimentary System. Palpable tumour of size of hen's egg in the right hypochondrium.

Respiratory System. Dulness at right apex with harsh vesicular breathing. Harsh vesicular breathing at apices of both lower lobes.

Haemopoietic System. A few slightly enlarged glands in the neck.

V. Pirquet's test, (Pure Old Tubeeculin) Positive. 27th August, 1908. Slight but definite redness and infiltration.

Neuritis of Arm & Pleurisy:

P. G. m. Aet. 31 History - Patient for the last 12 months has complained of pains in his left side and left arm, due he thinks to frequent wettings at his work. Patient has had Rheumatism, Pleurisy and Bronchitis.

Nervous System. Marked tenderness over left median and ulnar nerves with thickening of these nerves.

Respiratory System. Dulness at both apices with broncho-vesicular breathing at right & harsh vesicular with prolonged expiration at the left. Coarse friction at left base.

Haemopoietic System. Enlarged glands in neck and axillae.

v. Pirquet's test (Pure Old Tuberculin) Positive. 20th July, 1908. Very marked reaction - redness and infiltration with slight surrounding vesicle formation. (Patient was getting Pot. Iodide 10 grains t.i.d. at the time)

Pulmonary Tuberculosis:

J. B. m. Aet 56 History - About six months before admission patient complained of an aching pain in his left shoulder and there gradually developed a cold abscess in this situation. Patient for several years has had a"winter-cough." Two years previously, he had "dry pleurisy."

Respiratory System. Marked dulness at both apices with harsh vesicular breathing with prolonged expiration. Rhonci and crepitations at apices. Sputum contains almost a pure culture of Tubercle Bacilli.

v. Pirquet's test. October 12th, 1907. Positive Slight Reaction.

Pleurisy with Effusion.

A. S. m. Aet 25. History - Three weeks ago, patient began to suffer from general weakness with pains in the chest. He was also very short of breath.

Respiratory System. Absolute dulness on the left side of the chest reaching as high as the 4th interspace in the anterior axillary line. The breath sounds are absent over this area. Breath sounds are harsh vesicular with prolonged expiration over the part of the left lung above the dull area.

V. Pirquet's test November 21st, 1907. Positive

" " " " 27th " "

" " " December 10th " "

Slight redness and infiltration.

Aortic & Mitral Disease.

Mrs T. Aet 39. History - For last seven years patient has been short of breath on exertion. Lately she has been getting very weak and

short of breath. Previous illnesses - Rheumatic Fever, 3 times, at 11, 18, and 24.

Circulatory System. Systolic and Diastolic Aortic murmurs. Mitral Systolic murmur.

Respiratory System. Dulness + 1 at left apex. Bronchial breathing at both apices. No accompaniments.

Calmette's test. (1:200) February 28th, 1908. Positive I. Caruncle and Plica swollen and slightly reddened. Some oedema of lower lid.

Bright's Disease.

B. M. m. Aet, 54 years. History - Three months ago patient got a bad cold and after this he noticed that he easily became short of breath and that his ankles and eyelids became swollen. He also was passing less urine than usual.

Urinary System. Urine - 1028 acid. Albumin 7·895 gr. per oz. Blood. Urea 10 gr. per oz. Granular and hyaline casts.

Respiratory System Dulness + ½ at both apices with harsh vesicular breathing with prolonged expiration - occasional rhonchi.

Calmette's test (1:150) 3rd March, 1908. Negative.

" " " 4th March, " Positive II.

Plica and Caruncle swollen and inflammation of conjunctiva. Some fibrinous deposit with sensation of prickling in the eye. Slight oedema of the lower lid.

Bright's Disease.

G. B. m. Aet, 28. History - Three weeks ago, patient's feet began to swell and also he had a cough and spit. Two weeks ago he began to

have frequency of micturition. Previous illnesses - Acute Bright's Disease, 5 years ago.

Urinary System. Urine - 1020. acid albumin 3·7 gr. per oz.
Urea 4 gr. per oz. Granular & fatty casts.

Respiratory System. Dulness + 1 at right apex
" + 2 " left "

Bronchial breathing at apices. Occasional sibilant rhonchi all over the chest.

Calmette's test, (1:150) 3rd March, 1908. Positive IV. Reaction did not appear till 27 hours after the instillation. Reaction well-marked, swelling of caruncle and plica and inflammation of conjunctiva with fibrinous deposit. Oedema of lower lid. Some prickling sensation in the eye.

Disseminated Sclerosis.

A. C. m. Aet, 18 years. History - Patient, 3 months ago, felt his right foot heavy and walked with a limp. This has gradually got worse and he has become less steady on his feet.

Nervous System. Anaesthesia to touch over area above left eye. Loss of vibration sense below both knees. Knee-jerks exaggerated and Babinski's sign present. Lateral nystagmus present.

Respiratory System. Dulness + 1 at left apex and supra-scapular region, Broncho-vesicular breathing at both apices. No accompaniments.

Calmette's test, (1:200) February 22nd, 1908. Positive II. Considerable injection and swelling of the conjunctiva and caruncle with some swelling of the lids.

Gastric Ulcer.

Mrs W. Aet, 26. History - For the last two years patient has suffered from indigestion, vomiting & headache. Occasionally she has vomited a dark brown fluid. Has had a cough and spit all the winter. Previous illnesses - Three years ago both ovaries were removed for ovarian disease.

Alimentary System. Slight pain and resistance in the epigastrium.

Respiratory System. Dulness +1 at right apex with bronchial breathing
" +2 " left " " " "
No accompaniments.

Calmette's Test (1:150) 3rd March, 1908. Positive II.
Caruncle and plica swollen and reddened. Conjunctiva reddened. Lacrymation Slight puffiness of lower lid. Slight prickling sensation in the eye.

Aortic and Mitral Regurgitation.

J. B. m. Aet, 58 years. History - Three months ago patient was suddenly seized at his work with shortness of breath, but this was recovered from in half an hour. After this, however, he suffered from severe cough which has continued. On the night before admission to hospital he had another attack of shortness of breath which was very severe. Previous Illnesses - Rheumatism, 20 years ago, Gonorrhoea, 30 years ago.

Circulatory System. Mitral systolic and aortic systolic and diastolic murmurs.

Respiratory System. Dulness + 2 at right apex and infraclavicular region.
" + 1 " left " " "
" Bronchial breathing at apices and crepitations over the whole of both lungs.

Calmette's Test (1:200) 4th March, 1908. Positive IV.

Reaction delayed - 24 hours. Reaction slight - slight "sandy" feeling in the eye. Caruncle and Plica swollen and slightly reddened.

Sciatica.

J. R. m. Aet, 68. History - Seven months ago patient began to suffer from pain across his sacrum and about a month later it spread down to the back of his hip.

Respiratory System: Dulness + 2 in right infra-clavicular region with bronchial breathing and fine crepitations.

Calmette's Test (1:150) 4th March, 1908. Positive II.

Caruncle and Plica swollen. Distinct inflammation of the conjunctiva with some fibrinous deposit on it. Oedema of lower lid, and slight sensation of prickling in the eye.

Pulmonary Tuberculosis.

C. S. f. Aet, 20. History - Eight years ago patient caught a cold which settled on her chest and it continued for two years. Later she suffered from dyspnoea and cough.

Respiratory System - Dulness + 1 at right apex.

" + 2 " left "

Bronchial breathing at both apices with occasional sibilant rhonchi.

Calmette's Test (1:150) 4th March, 1908. Negative.

Calmette's test (1:150) 13th March, 1908. Positive II.

Caruncle and Plica reddened and swollen, and conjunctiva inflamed. Some fibrinous deposit. Slight oedema of the lower lid.

Hysteria.

G. F. m. Aet, 65. History - Present illness began one year ago with weakness of the left leg, and later the right arm was affected. Later he began to suffer from headaches and giddiness.

Respiratory System: Dulness + 1 at right apex.

" + 2 " left suprascapular region.

Bronchial breathing over these areas.

Calmette's test (1:100) 6th March, 1908. Positive II.

Caruncle and Plica swollen, Conjunctiva, inflamed. Oedema of the lower lid.

Mitral and Aortic Disease.

J. A. m. Aet, 57. History - Two months ago patient began to suffer from shortness of breath on exertion. This has gradually got worse and he now has a cough as well. There has been blood in the spit. Family History - One sister died at 26 of consumption.

Circulatory System: Mitral diastolic and aortic diastolic murmurs.

Respiratory System: Dulness + 1 at both apices and in the right infra-clavicular region and at the right base. Bronchial breathing at the apices.

Calmette's Test (1:150) March 13th, 1908. Positive II.

Caruncle and Plica swollen and reddened. Conjunctiva inflamed, some fibrinous deposit. Slight oedema of the lower lid.

Sub-acute Bright's Disease.

J. G. m. Aet, 43. History - Patient got a chill at his work a week ago, and after it noticed that his face and feet were beginning to swell and he also complained of headaches. Previous Illnesses - Scarlet Fever.

Respiratory System: Dulness + 1 at both apices.

" + 1 in right interscapular region

with V.R. + 1 and harsh vesicular breathing with prolonged expiration.

Haemopoietic System: A chain of slightly enlarged lymphatic glands on either side of the neck and several enlarged glands in the groins.

Calmette's Test (1:100) May 1st, 1908. Positive I.

Caruncle swollen and reddened and conjunctiva slightly hyperaemic.

Bronchitis with Dilated Heart:

T. G. m. Aet, 30. History - Cough for the last 6 months, but 5 days ago it became very much worse and he became very short of breath.

Respiratory System: Dulness + 1 at both apices with bronchial breathing. Coarse crepitations and sonorous rhonchi heard all over the chest.

Calmette's Test(1:100) May 1st, 1908. Positive I.

Conjunctiva reddened and caruncle swollen and reddened, slight reaction.

Sub-acute Bright's Disease.

T. C. m. Aet, 31. History - Twelve weeks ago patient noticed that his ankles were swollen, but before this he felt in his usual health. Later he became short of breath and suffered from severe headaches.

Urinary System: Urine contains albumin, blood and pus, and there are epithelial, granular and hyaline casts.

Respiratory System: Dulness at both apices with harsh vesicular breathing with prolonged expiration.

Haemopoietic System:

Slightly enlarged lymphatic glands in the neck, axillae and groins.

Calmette's Test (1:100) 2nd June, 1908. Positive I.

Slight redness and swelling of conjunctiva, Plica and caruncle.

Mitral Incompetence.

J. B. m. Aet, 46. History - Six weeks before admission to hospital patient began to suffer from constant pain in the lower part of the abdomen; and later he became very short of breath.

Circulatory System: Mitral systolic murmur and an enlarged heart.

Respiratory System: Slight dulness at both apices extending as far down as the angles of the scapulae. Breathing harsh vesicular with expiration prolonged, but bronchial at the right apex. No accompaniments except a few coarse crepitations at the right base.

Haemopoietic System: Slightly enlarged glands in the neck and groins.

Calmette's Test (1:100) 6th July, 1908. Positive II.

Redness and swelling of caruncle, plica and conjunctiva with oedema of the lower lid. The reaction was still evident at the end of 3 weeks.

Lobar Pneumonia and Phthisis.

C. G. m. Aet, 47. History - Patient, who had been attending the hospital on account of a carbuncle, 2 days ago felt very feverish and noticed a rash all over his body, and he was then admitted to hospital.

Respiratory System: Absolute dulness over the whole of the left lower lobe with high pitched bronchial breathing, increased vocal resonance and fremitus. When this had cleared up there remained an area at the apex of the left lower lobe where there was dulness, amphoric breathing,

and whispering pectoriloquy. There was also dulness at both apices with broncho-vesicular breathing.

Haemopoietic System. Chain of slightly enlarged glands on each side of the neck and in each axilla.

Calmette's Test (1:100) 10th July, 1908. Positive I. Conjunctiva, caruncle and plica, reddened and swollen.

Chronic Bright's Disease:

W. M. m. Aet, 36. History - Patient states that his illness began with a sudden pain in his abdomen a fortnight before his admission to hospital. Three days later, his abdomen began to swell and this has continued.

Respiratory System: Dulness at both apices with bronchial breathing at the right and harsh vesicular with prolonged expiration at the left.

Haemopoietic System: Slightly enlarged glands in neck, axillae and groins.

Urinary System: Urine contains granular and hyaline casts.

Calmette's Test. (1:100) on 2nd June, 1908. Positive II. Great amount of swelling and injection of caruncle, plica and conjunctiva, with some fibrinous deposit. Marked oedema of the lower lid.

Chronic Bright's Disease.

P. M. m. Aet, 42. History - Three weeks before admission patient caught a chill and since then he has had swelling of his ankles and puffiness of his eyelids.

Urinary System: Frequency of micturition. Urine contains albumin and a few fatty casts.

Respiratory System. Dulness at right apex with harsh vesicular breathing with prolonged expiration.

Haemopoietic System: Enlarged glands in neck, axillae and groins.

Calmette's Test. (1:100) 2nd June, 1908. Positive II. Redness and swelling of caruncle, plica and conjunctiva and slight oedema of the lower lid.

Dilated Heart:

A. K. m. Aet, 24. History - Patient has for the last eighteen months been very short of breath on exertion and has had attacks of palpitations and tachycardia.

Respiratory System: Slight dulness at the right apex with harsh vesicular breathing with prolonged expiration.

Haemopoietic System: Numerous enlarged glands in the neck, axillae and groins.

Calmette's Test. (1:100) 2nd June, 1908. Positive II. Marked swelling and injection of caruncle, plica and conjunctiva with some fibrinous deposit. Oedema of the lower lid.

Gastritis and Arterio-sclerosis:

J. B. m. Aet, 65. History - For about a year patient has been troubled with vomiting at intervals, and lately this has become much worse. Patient has had a slight "winter cough" for years.

Respiratory System: Slight dulness at right apex with harsh vesicular breathing.

Haemopoietic System: Slightly enlarged glands in neck, axillae, and

groins.

Calmette's Test (1:100) 2nd June, 1908. Positive II.
Great redness and swelling of conjunctiva and caruncle and plica, with some fibrinous deposit. Oedema of the lower lid.

Gastritis:

M. K. f. Aet, 26. History - Ten weeks before admission, patient began to have gnawing pains in the stomach, but no vomiting. Her condition gradually got worse. She had pleurisy 6 years ago and again 2 weeks ago.

Respiratory System: Dulness at both apices with bronchial breathing at the right and harsh vesicular with prolonged expiration at the left. No accompaniments.

Haemopoietic System: A few enlarged glands in the neck.

Calmette's Test. (1:100) 21st May, 1908. Positive I.
Slight swelling and redness of caruncle and conjunctiva.

Gastritis:

E. McP. f. Aet, 21. History - About five years ago, patient began to be troubled with indigestion and vomiting and her condition has gradually got worse.

Respiratory System: Dulness at right apex with bronchial breathing.

Haemopoietic System: Chain of slightly enlarged glands on either side of the neck.

Calmette's test. (1:100) 21st May, 1908. Positive I.
Slight injection and swelling of conjunctiva and caruncle.

Acute Rheumatism:

J. McD. m. Aet, 18. History - A week before admission patient

developed a severe burning pain in his right ankle. Later he felt the pain in his knees and hip, and he became very feverish.

Haemopoietic System: Chain of slightly enlarged glands on either side of the neck.

Respiratory System: Dulness at both apices and in both interscapular regions. Bronchial breathing with crepitations at right apex, and harsh vesicular breathing with prolonged expiration at left apex. In the interscapular regions the breathing is harsh vesicular with expiration prolonged and there are crepitations.

Calmette's test. (1:100) 2nd June, 1908. Positive II. Great injection and swelling of conjunctiva, plica and caruncle, with fibrinous deposit. Oedema of the lower lid.

Cerebral Syphilis:

T. S. m. Aet, 27. History - Patient for the last 12 months has had pains in the head lasting usually for about 6 hours in the day. Six weeks before admission, patient got a wetting and on the next morning he could hardly walk on account of weakness in his legs. He now tends to walk to the left and he frequently has attacks of giddiness. He had syphilis 4 years ago, and has had gonorrhoea 3 times.

Respiratory System: Dulness at both apices with bronchial breathing and a few crepitations at the right; harsh vesicular with expiration prolonged at the left - crepitations also.

Calmette's test. (1:100) 2nd June, 1908. Positive II. Injection and swelling of conjunctiva, caruncle and plica. Some oedema of the lower lid.

Pulmonary Tuberculosis:

R. H. f. Aet, 10 years. History - About 3 mouths before admission patient began to complain of occasional sharp pains in the left side, and she also began to be short of breath on exertion. She has had a cough and spit for some time. She had bronchitis and pneumonia a year ago. Her mother has a cough and spit.

Respiratory System: Dulness at right apex and infra-clavicular region with bronchial breathing. No accompaniments.

Haemopoietic System: Enlarged glands on either side of the neck.

Calmette's test. (1:100) January 20th, 1908. Positive II. Considerable injection and swelling of conjunctiva and caruncle.

Bazin's Disease:

A. T. f. Aet, 15. Present Condition - For the last eight weeks patient has suffered from ulcers on both legs. These ulcers are not deep but are very resistant to treatment. She had a similar condition three years ago. Patient has enlarged glands in the neck and previously has been operated on for a similar condition.

Calmette's test - (1:200) 12th March, 1908. Positive II. Caruncle and plica reddened and swollen. Hyperaemia of the conjunctiva with some fibrinous deposit. Some pain in the eye.

Pulmonary Tuberculosis. Tuberculous Shoulder.

F. McI. f. Aet, 16. History - Six months ago, patient was operated on for a tuberculous shoulder, and during her time in hospital she developed symptoms of waxy disease of the kidney.

Respiratory System: Marked dulness at both apices and in both inter-scapular regions, with broncho-vesicular breathing and increased vocal

resonance.

Haemopoietic System: A few slightly enlarged glands on the right side of the neck.

Calmette's Test - (1:200) 17th September, 1908. Positive. II. Redness and swelling of plica, caruncle and conjunctiva.

V. Pirquet's Test (Pure Old Tuberculin) 21st Sept., 1908. Positive. Distinct redness and infiltration. Post-mortem examination showed that there was tuberculous disease of the right shoulder-joint, and also a few miliary tubercles in both lungs and in the spleen.

Pleurisy with Effusion:

A. B. m. Aet, 18. History - Four weeks ago while at his work, patient felt a sudden pain in his right side, increased by drawing a long breath. This pain continued off and on till 10 days ago when he became short of breath and was unable to work.

Respiratory System: Absolute dulness over the right chest from the 2nd rib downwards with absent breath sounds. Harsh vesicular breathing with expiration prolonged, at the right apex, and vocal resonance and fremitus increased. Chest was aspirated and 52 ozs. removed.

Haemopoietic System: A few slightly enlarged glands in neck and axillae.

V. Pirquet's test. (Pure Old Tuberculin) 22nd Aug., 1908. Positive. Slight redness and infiltration.

Calmette's test, (1:200) 17th September, 1908. Positive. I. Distinct redness and swelling of caruncle, plica and conjunctiva.

Haematuria:

B. H. f. Aet, 21. History - In the last year patient has had pain

in the loins and for the last six months she has noticed that her ankles have been swollen and her eyelids puffy.

Urinary System: Tenderness on palpating the right kidney. Slight pain during micturition. Blood and albumin in the urine, but no casts and no Tubercle Bacilli.

Respiratory System: Dulness at both apices with bronchial breathing.

Calmette's test (1:100) 22nd May, 1908. Positive I. Slight redness and swelling of caruncle, plica and conjunctiva.

V. Pirquet's test, 24th May, 1908. Positive. Slight infiltration and redness.

Dyspepsia.

T. McM. m. Aet, 27. History - Patient for the last nine months has had pains in the stomach after food and occasional vomiting.

Respiratory System: Dulness at both apices with harsh vesicular breathing with expiration prolonged. Vocal resonance increased. No accompaniments.

Haemopoietic System: A few slightly enlarged glands in the neck.

V. Pirquet's test, (Pure Old Tuberculin) 9th July, 1908, Negative.

Calmette's Test, (1:100) 10th " " Positive I. Slight injection and swelling of caruncle and plica.

v. Pirquet's test, (Pure Old Tuberculin) 13th " " Positive. Slight redness of the area of skin and slight infiltration.

Chorea.

A. McB. m. Aet, 8. History - Two weeks before admission to hospital, patient began to have constant mouvements of the right arm and

leg and these mouvements spread to the left arm and leg and also to his face.

Respiratory System: Bronchial breathing with increased vocal resonance at the right apex.

Haemopoietic System: Chain of slightly enlarged glands on each side of the neck.

v. Pirquet's test, 2nd June, 1908. Positive.

Slight reaction.

Calmette's test, (1:100) " " " Positive II.

Redness and swelling of caruncle, plica and conjunctiva with some fibrinous deposit. Some puffiness of the lower lid.

Pulmonary Tuberculosis (advancing).

A. L. m. Aet, 11 years. History - For the last year patient has had a cough and for the last ten months he has suffered from dyspepsia and vomiting. He had measles in infancy.

Respiratory System: Marked dulness at both apices, the dulness extending downwards. Bronchial breathing at both apices with numerous coarse crepitations.

Haemopoietic System: Large numbers of slightly enlarged glands in the neck.

v. Pirquet's cutaneous test, 6th October, 1907. Positive.

" " " " 10th " " Positive.

Calmette's ophthalmic test (Beraneck's Tuberculin 1:100) " II.

16th December, 1907.

Marked swelling and injection of conjunctiva and caruncle.

Phthisis Pulmonalis & Retroperitoneal Tuberculous Glands:

M. S. male, Aet, 20. History - About six weeks ago pain in the back and abdomen began, it has continued constantly ever since. Previous Illnesses: Mumps and measles when a child. Influenza in March, 1907. Right sided pleurisy (dry), April, 1907. General surroundings, satisfactory.

Alimentary System: A mass, tender to the touch, is to be felt in the region of the umbilicus. It pulsates with the aorta but the pulsation is not expansile.

Respiratory System: Dulness + 2 at right apex with Bronchial breathing and crepitations. Vocal resonance + 2. Dulness + 2 at both bases with friction.

Calmette's test, (Béraneck's Tuberculin 1:200) Dec. 15th, 1907. Positive. II.

v. Pirquet's test,	Positive.	"	16th,	"
Calmette's test (1:200)	Positive III.	"	18th	"
" " (1:200)	Positive III.	Jan.	15th	"

Swelling of Caruncle and plica. Marked inflammation of conjunctiva of lower lid with purulent discharge. Oedema of lower lid.

Mitral Incompetence and Adherent Pericardium.

M. R. female, Aet, 19 years. History - Patient has been in hospital previously with the same complaint and was discharged much improved. A week ago patient began to get very breathless and had a cough and she noticed that her abdomen was swollen.

Circulatory System: Systolic murmurs in mitral, aortic and pulmonary areas.

Respiratory System: Nothing to note.

v. Pirquet's test, November 24th, 1907. Positive.

" " " " 29th " "

" " " December 12th " "

Calmette's " (Beraneck's Tuberculin 1:200) 16th " " II.

Marked swelling of caruncle and plica with inflammation of conjunctiva of lower lid. Oedema of lower lid. Post-Mortem examination in this case showed chronic and acute endocarditis of the mitral, Tricuspid and Aortic Valves. General dilitation of all the cavities of the heart. Adherent pericardium (non-tuberculous). Old pleurisy. General chronic Venous Hyperaemia. Old chalky gland in the mesentery in the ileo-colic angle.

Tabes Mesenterica.

A. S. female, Aet, 12 years. History - Present complaint began in April, 1907, with pain in the back which disappeared under treatment at home. As she was losing weight her mother brought her up to hospital for advice. Previous Illnesses - "Kidney Disease" in 1905. Measles when five years old.

Alimentary System: Numerous firm masses can be detected in the abdomen on palpation.

Respiratory System Dulness + 1 at both apices, with bronchial breathing at the right and harsh vesicular with prolonged expiration at the left. No accompaniments.

v. Pirquet's test, Dec. 2nd, 1907. Positive.

Calmette's (1:200) " 12th " " II.

" " " " 14th " " II.

" " " " 17th " " II.

" " " Jan. 9th 1908 " II.

Marked swelling of caruncle and plica with well-marked inflammation of the conjunctiva. Oedema of lower lid.

Genito-Urinary Tuberculosis.

D. M. Male, Aet, 28 years. History - Gonorrhoea three years ago - discharge lasted five months. Six weeks after the gonorrhoea patient began to suffer from frequency of micturition with pain at the end of the act. There was also bleeding.

Genito-Urinary System: Patient has a bi-lateral tuberculous epididymitis. There is albumin, blood and pus in the urine, but no tubercle bacilli have been found. There is great frequency of micturition.

v. Pirquet's test, Jan. 7th, 1908. Positive.

Calmette's " (1:200) " 9th " " II.

Very marked reaction with oedema of the lower lid.

Tuberculous Peritonitis.

N. C. m. Aet, 1 year & 8 months. History - Patient has always been delicate. His mother has noticed that for the last two months the child's abdomen has been greatly swollen.

Respiratory System: Dulness + 1 at left apex with broncho-vesicular breathing.

Alimentary System: Abdomen very tense and swollen. No fluid or enlarged glands to be detected.

v. Pirquet's test. 13th March, 1908. Positive.

Very slight reaction - faint papule.

Calmette's test (1:200) Jan. 16th, 1908. Positive III.

Great swelling of caruncle & plica. Well-marked inflammation of conjunc-

tiva with a purulent discharge. Odema of lower lid.

Pernicious Anaemia. J. M. m. Aet, 51 years. History - About 5 years ago, began to suffer from a raw feeling in his chest followed later by shortness of breath and cough. He has been getting gradually weaker and his complexion has been assuming a yellowish colour, now quite marked.

Respiratory System: Dulness + 1 at left apex, with vocal resonance + 1 and vesicular breathing and a few crepitations.

Haemopoietic System: Blood - R. B. C. 1,684,000. W. B. C. 7,600. H. b. O. 40%. Colour Index - 1.18. Megaloblasts, Poikilocytes, Macrocytes, Microcytes.

Calmette's test, (1:200) February 8th, 1908. Positive I.

" " " " 18th, " " I.

Slight but distinct reaction.

v. Pirquet's test, " 22nd, " "

Post-Mortem revealed old tubercular scarring at left apex and old fibroid pleurisy of right lung.

Genito-urinary Tuberculosis.

A. R. m. Aet, 19. History - About two weeks ago, patient began to suffer from a dull pain in his back. A week later he noticed that the pain was worse when he made his water. A few days ago on waking in the morning he found his legs covered with a purple rash, and later he began to suffer from pains in his joints.

Respiratory System: Dulness + 2 at both apices with bronchial breathing, crepitations and rhonchi.

Urine contains albumin, blood and pus - No T. B. found

Calmette's test (1:200) Jan. 21st, 1908. Positive II. Well-marked reaction.

v. Pirquet's test, Feb. 22nd, " "
Slight redness and infiltration.

Disseminated Sclerosis.

J. M. m. Aet, 28 years. History - Patient 18 months ago began to feel a peculiar numbness in left side of the face. This spread to affect the whole left side of his body. Then the right leg became weak and stiff and later the left. He was unable to walk in the dark. No history of venereal disease, but patient is much exposed to wet and cold.

Nervous System: Knee-jerks greatly exaggerated. Babinski's sign present. Lateral nystagmus present.

Respiratory System: Dulness + 1 with Bronchial breathing at right apex, V. R. + 1. No accompaniments.

v. Pirquet's test, Positive.

Calmette's test, (1:150) 3rd March, 1908. Positive. II. Caruncle and plica reddened and swollen and the lower palpebral conjunctiva much congested and a fibrinous deposit in the conjunctival fold. There is lachrymation, and slight oedema of lower lid. Patient complains of a slight prickling sensation in the eye. Patient two weeks after Calmette's test was done developed a granular conjunctivitis with two or three small corneal ulcers. When seen on the 16th April the affected eye had returned to its natural condition.

Syphilitic Cervical Glands.

G. A. m. Aet, 28. History - Present illness began with weakness

and lassitude. Nine months ago a swelling started in the left side of his neck and it has gradually increased in size and other lumps have made their appearance.

Respiratory System: Nothing to note.

Haemopoietic System: Several firm large masses of glands on the left side of the neck and some smaller enlarged glands on both sides of the neck.

Calmette's test (1:200)	April 27th, 1908.	Negative.
v. Pirquet's test	" " "	"
v. Pirquet's "	May 3rd "	"
Calmette's " (1:200)	" " "	Positive I.

Caruncle and conjunctiva slightly red and swollen.

v. Pirquet's test (Pure Old Tuberculin)	August 27th, 1908.	"

Slight redness and infiltration.

Post-Mortem showed that in the left lung 1½ inches below its apex there was a small cavity, situated posteriorly, surrounded by dense fibrous tissue deeply pigmented. There were numerous old-standing fibrous adhesions over the surface of the left lung.

Tuberculous Peritonitis.

M. D. m. Aet, 10 years. History - Patient seven months ago began to suffer from diarrhoea and at the same time his abdomen began to become protuberant. He has gradually been losing strength.

Respiratory System: Dulness at both apices with bronchial breathing at the right and harsh vesicular at the left.

Alimentary System: The abdomen has a "doughy" feel.

Calmette's test, (1:200) . . April 15th, 1908. Positive.I. Caruncle and plica reddened and swollen. A slight reaction.

v. Pirquet's test (Pure Old Tuberculin) August 8th, 1908. Positive. Slight reaction - some redness with infiltration at the site of inoculation.

B. 11 Tuberculous Cases Positive to either Calmette or v. Pirquet but Negative to the other.

Subacute Bright's Disease.

D. McG. m. Aet, 40. History - A month ago patient began to suffer from excessive fatigue after his work, and two weeks ago his ankles began to swell and his eyelids to be puffy. His urine on examination was found to contain albumin and blood, and also blood, epithelial and granular casts.

Respiratory System: Slight dulness at both apices and left inter-scapular region with harsh vesicular breathing with expiration prolonged.

Haemopoietic System: Numerous slightly enlarged glands in the neck and axillae.

v. Pirquet's test (Pure Old Tuberculin) 22nd August, 1908. Negative.

" " " " " " 27th " " "

Calmette's test (1:200) 17th Sept. " Positive.I. Slight redness and swelling of caruncle and plica.

Hemiplegia.

A. McD. m. Aet, 42. History - A week ago, patient suddenly felt very giddy and then he noticed great weakness in his right arm and leg. Two days later his face became drawn to the left side.

Respiratory System: Marked dulness at both apices and there the breathing is harsh vesicular with prolonged expiration. Vocal resonance is increased.

Haemopoietic System: Several slightly enlarged glands in each side of the neck and in each axilla.

v. Pirquet's test (Pure Old Tuberculin) 27th August, 1908. Positive. Slight redness and infiltration.

Calmette's test (1:200) 21st September, 1908. Negative.

" " " 26th " " "

Aortic Stenosis And Mitral Incompetence.

G. S. m. Aet, 18. History - Five months ago patient had an attack of rheumatic fever with pericarditis and pleurisy with effusion. Since then he has been very short of breath and occasionally he becomes oedematous.

Circulatory System: Aortic and Mitral systolic murmurs.

Respiratory System: Slight dulness at both apices. Bronchial breathing at right apex and harsh vesicular with prolonged expiration at the left.

Haemopoietic System: Enlarged lymphatic glands in the neck, axillae and groins.

Calmette's test (1:100) 13th May, 1908. Positive. I. Slight redness and swelling of caruncle, plica and conjunctiva.

v. Pirquet's test (Pure Old Tuberculin) 21 st Sept., 1908. Negative.

Aortic Stenosis.

A. P. male, Aet, 17. History - Patient six months ago had pleurisy and he has never felt quite well since. He now complains of pain in the stomach.

Respiratory System: Dulness + 1 with bronchial breathing at the right apex.

Haemopoietic System: Several enlarged glands in the groins and axillae.

Calmette's test, (1:200) April 15th, 1908. Positive. I. Caruncle and plica reddened and swollen - slight reaction.

v. Pirquet's test, April 17th, Negative.
" " " " 20th "
" " " " 23 "

Calmette's test, (1:200) May 3rd, Positive I. Slight reaction.

Irritable Dyspepsia and Phthisis.

D. B. male. Aet, 25. History - Fifteen months ago patient caught a cold and ever since then he has had a cough and spit. He has attacks of pain in the stomach, vomiting and diarrhoea. Previous Illnesses - Abscesses in the legs 2½ years ago.

Respiratory System: Cough and expectoration. Dulness + 1 at both apices and in right infra-clavicular region. Bronchial breathing with v. R. + 1 at right apex. Broncho-vesicular breathing at left apex and in right infraclavicular region.

Calmette's test (1:200) April 15th, 1908. Negative.
" " " May 3rd " Positive I. Slight redness of conjunctiva and of caruncle.

v. Pirquet's test May 3rd, 1908. Negative.

Diabetes Insipidus.

J. J. male. Aet, 36. History - Patient began to pass more water than usual about a year ago. He was also very thirsty. Family History - A brother and a sister died of consumption.

Urinary System: Frequency of micturition, especially at night. Urine - 232 ozs.: very pale: 1009, acid: minute trace of albumin.

Respiratory System: Dulness + ½ in the left infraclavicular region. Faint bronchial breathing at both apices. No accompaniments.

Calmette's test (1:150) 10th March, 1908. Positive II. Swelling and redness of the caruncle and plica. Inflammation of the conjunctiva with some fibrinous deposit and lachrymation. Slight oedema of the lower lid. Slight "sandy" feeling in the eye.

v. Pirquet's test. 13th March, 1908. Negative.

Phthisis and Progressive Muscular Atrophy.

J. M. male. Aet, 40 years. History - For the last few weeks patient has had attacks of shiverings and feverishness. For the last week he has suffered from pains in the chest and a cough and spit. Previous Illnesses - Pneumonia, 20 years ago. Pleurisy 12 years ago. Has had a slight cough for years.

Respiratory System: Dulness + 2 at left apex and over the upper half of the left lung posteriorly with bronchial breathing and medium crepitations. Dulness + 1 at right apex and also in the left infraclavicular region with bronchial breathing and medium crepitations.

Nervous System. Atrophy of small muscles of the hands.

Calmette's test (1:150) 3rd March, 1908. Negative.

" " " 4th " " Positive. I.

Slight swelling and redness of caruncle, plica and conjunctiva. "Sandy" feeling in the eye. Some lachrymation.

v. Pirquet's test 9th March, 1908. Negative.

Acute Rheumatism.

C. B. female, Aet, 12. History - Ten days ago patient had an attack of shivering and was feverish. A few days later she began to complain of pains in the joints.

Circulatory System: Mitral Systolic murmur.

Respiratory System: Slight dulness with bronchial breathing and increased vocal resonance, at the left apex.

Calmette's test (1:200) February 28th, 1908. Positive. I.

Caruncle and plica swollen. Conjunctiva on lower lid slightly inflamed.

v. Pirquet's test. March 9th, 1908. Negative.

Tuberculous Peritonitis. M. S. female, Aet, 2. History -

Ever since birth the child has not been strong, and it cries and frets a great deal. About a month ago the mother noticed that the child's abdomen was swollen, and so she brought the child to hospital for advice.

A sister has tuberculous peritonitis.

Alimentary System: Nothing to note beyond the prominence of the abdomen.

Respiratory System: Nothing to note.

v. Pirquet's test (Pure Old Tuberculin) Sept. 1908. Positive.

Marked redness and infiltration of the scarified area.

Calmette's test (1:200) 21 September, 1908. Negative.

" " " 26th " " "

Child cried a great deal.

Secondary Anaemia.

J. W. male. Aet, 25. History - Patient's illness dates from four months ago when he had painful swellings over several of his joints. These recovered but left him very weak. He has had bleeding piles for six years. Previous Illnesses - Rheumatic Fever, 12 years ago. Fistula in ano, 4 years ago.

Respiratory System: Dulness + 1 at left apex with broncho vesicular breathing.

Calmette's test (1:200) February 18th, 1908. Negative.

v. Pirquet's test " 22nd " Doubtful.

Calmette's test " March 6th, " Negative.

v. Pirquet's test (Pure Old Tuberculin) Sep. 21st, Positive. Slight redness and infiltration.

Calmette's test (1:200) 26th September, 1908. Negative.

Pneumonia and Phthisis.

J. F. m. Aet, 47 years. History - For years past patient has suffered from a cough with a slight spit. Two weeks ago he caught a severe chill and from that time he complained of pains in the front of the chest. Previous Illnesses - "Inflammation of the lungs" at 26 years.

Respiratory System: Dulness + 1 at right apex and supra-scapular region.

" + 2 " Left " " " "

" + 2 " right base. "

"

Bronchial breathing at both apices. No accompaniments.

Bronchial breathing with numerous crepitations at right base.

v. Pirquet's test		22nd February, 1908.	Positive
Calmette's	" (1:150)	3rd March "	Negative.
"	" (1:100)	4th " "	Negative.

C. 22 Tuberculous Cases giving no Reaction:

Mitral Stenosis.

P. G. male, Aet, 17. History - For the last three years patient has been short of breath on exertion and has had a cough and spit. A week ago, after a blow on the spine, patient began to suffer from pain in his right side.

Circulatory System: Mitral presystolic and systolic murmurs.

Respiratory System: Slight dulness at right apex and in both inter-scapular regions. Harsh vesicular breathing with prolonged expiration in these areas, accompanied by rhonci and crepitations.

Haemopoietic System: Numerous glands of size of small peas in the neck and axillae.

v. Pirquet's test (Pure Old Tuberculin) 8th August, 1908. Negative.

" " " " " " 22nd " " "

Mitral Stenosis and Rheumatism.

K. H. female. Aet, 17. History - A week ago patient caught cold and following this she had pain in her chest and in several of her joints.

Circulatory System: Mitral presystolic and systolic murmurs.

Respiratory System: Slight dulness at the right apex, with harsh vesicular breathing with expiration prolonged.

Haemopoietic System: Great numbers of slightly enlarged lymphatic glands in the neck and axillae.

v. Pirquet's test (Pure Old Tuberculin) 8th August, 1908. Negative.

Abdominal Tumour (Sarcoma)

E. H. female. Aet, 14. History - Patient for the last six months has complained of occasional pains across the lower part of the abdomen and the abdomen has gradually been swelling.

Alimentary System: A large moveable tumour can be felt in the lower part of the abdomen and the abdomen contains free fluid which when aspirated off was of a bright red colour and contained red blood corpuscles and polymorphs.

Respiratory System: Slight dulness at both apices, bronchial breathing at the left and harsh vesicular at the right.

Haemopoietic System: Chain of slightly enlarged glands on each side of the neck.

v. Pirquet's test ~~(Pure Old Tuberculin)~~ 3rd July, 1908. Negative.

" " " (Pure Old Tuberculin) 8th " " "

Jacksonian Epilepsy following Cerebro-spinal Miningitis.

R. S. male, Aet, 6 years. History - In March, 1907, patient had an attack of cerebro-spinal meningitis from which he recovered after 3½ months treatment, but ever since, he has suffered from one-sided convulsions affecting the right arm, leg and face. Previous Illnesses - Whooping cough and Measles at 2½ years.

Respiratory System: Dulness + 2 at left apex with bronchial breathing

and vocal resonance + 2. No accompaniments. Numerous small palpable glands in chains on both sides of the neck.

Calmette's test	(1:200)	December 17th, 1907.	Negative.
"	"	January 12th, 1908.	"
"	"	" 16th, "	"
"	(1:150)	March 13th, "	"

Bright's Disease.

W. W. male. Aet, 50. History - Four months ago, patient caught a bad cold on the chest and following it he had a severe cough. Shortness of breath began three weeks ago and swelling of the ankles five days ago. For last seven weeks has been passing very little water at a time, but there was frequency at night.

Respiratory System: Dulness + 1 in right infraclavicular region with harsh vesicular breathing and prolonged expiration. Dulness + 1 at both apices with vesicular breathing and numerous crepitations.

Circulatory System: Mitral and aortic systolic bruits.

Urinary System: Urine - amount 22 oz. 10 15. acid. Albumin .656 gr. per oz. Blood. Urea 7½ gr. per oz. Epithelial and granular casts and red blood corpuscles.

Calmette's test	(1:150)	3rd March, 1908.	Negative.
"	(1:200)	4th " "	"

Acute Rheumatism.

J. M. male. Aet, 22. History - After a wetting seven weeks ago patient began to suffer from these pains in his joints. Previous Illnesses: Rheumatism, five months ago.

Circulatory System: Presystolic and systolic mitral bruits. Systolic and diastolic aortic bruits.

Respiratory System: Dulness + 1 at right apex with bronchial breathing

Calmette's test (1:200) 6th March, 1908. Negative.

Disseminated Sclerosis.

P. H. male. Aet, 40. History - 1½ months ago patient was suddenly seized with an attack of giddiness and fell to the ground. Since then he has always been more or less giddy, and he staggers as he walks. Previous Illnesses - Acute Pleurisy 26 years ago.

Nervous System: No nystagmus. Slight Rhombergism. Knee-jerks exaggerated. Babinski's sign, present.

Respiratory System: Dulness + 1 at left apex, suprascapular and infra-clavicular regions with bronchial breathing. No accompaniments.

Calmette's test (1:150) 6th March, 1908. Negative.

Myocarditis.

T. P. male. Aet, 42. History - Six weeks ago, patient got a severe wetting. After this he began to suffer from breathlessness and cough and these have gradually got worse. Family History - One brother died of consumption.

Respiratory System: Dulness + 2 at right apex with bronchial breathing and crepitations. Dulness + 1 at left apex with broncho-vesicular breathing.

Calmette's Test (1:150) 13th March, 1908. Negative.

Tuberculous Cystitis.

R. M. male. Aet, 33. History - About a year ago patient began to be troubled with painful micturition and with frequency, and these symptoms have continued up till the present.

Urine. contains albumin and pus. No T. B. found.

Respiratory System: Dulness + 1 with bronchial breathing at the right apex.

Calmette's test (1:200) April 15th, 1908. Negative.
" " (1:100) July 6th, " "

Myocarditis and General Debility.

T. C. male. Aet, 58. History - Patient for the last year has felt himself getting gradually weaker and he has had to give up his work in consequence.

Respiratory System: Dulness + 1 at left apex with bronchial breathing
" + ½ " right " " " "

Haemopoietic System: A chain of enlarged lymphatic glands in each groin and on either side of the neck.

Calmette's test (1:100) May 1st, 1908. Negative.

Influenza.

J. R. male. Aet, 47. History - Three weeks ago patient had a severe attack of Influenza and ever since he has complained of pain in his abdomen and of vomiting.

Respiratory System: Dulness + 1 at both apices with harsh vesicular breathing with prolonged expiration.

Calmette's test. (1:100) May 1st, 1908. Negative.

Influenzal Pneumonia.

R. H. male. Aet, 39. History - Nine days ago patient caught a bad cold and since then he has been complaining of great weakness.

Respiratory System: Dulness at both apices with faint bronchial breathing at right base and broncho-vesicular at left. Harsh vesicular breathing with expiration prolonged at both apices.

Haemopoietic System: No enlarged glands.

Calmette's test (1:100) May 1st, 1908. Negative.

" " " July 10th, 1908. "

Phthisis. Aortic Stenosis.

A. C. female. Aet, 41. History - Two months ago patient began to be troubled with a cough and this has continued up to the present time.

Respiratory System: Dulness + 2 at right apex with bronchial breathin

" + 1 " left " " " "

" + 1 " right suprascapular region with harsh vesicular breathing

" + 1 " " infraclavicular " "

" " " accompanied by a few rhonchi.

Sputum contains numerous elastic fibres but no T. B.

Circulatory System: Aortic and mitral systolic murmurs.

Haemopoietic System: No enlarged glands.

Calmette's test (1:100) April 30th, 1908. Negative.

Aortic Incompetence.

W. W. male. Aet, 68. History - For the last nine months patient has gradually been getting very short of breath and he has been troubled

with a cough. He had rheumatism 14 years ago.

Circulatory System: Double aortic and mitral murmurs with an enlarged heart.

Respiratory System: Marked dulness at both apices with broncho-vesicular breathing.

Haemopoietic System: Numerous enlarged glands in neck and axillae.

Calmette's test. (1:100) 10th July, 1908. Negative.

Aortic Stenosis.

P. McB. male. Aet, 67. History - Patient, who for years has been short of breath, became more so about five years ago and it has gradually got worse. For the last two years he has had a cough and spit.

Circulatory System: Aortic and mitral systolic murmurs.

Respiratory System: Dulness at both apices with bronchial breathing at the right apex. Coarse crepitations and sibilant rhonci heard over the whole chest.

Calmette's test (1:100) 2nd June, 1908. Negative.

Rickets.

M. K. male. Aet, 4 years. History - General languor for the last two years. Patient has been getting much thinner and his appetite is poor. Suffers from severe diarrhoea. Abdomen has been swelling gradually. No previous illnesses. General surroundings - always plenty of fresh air.

Respiratory System: Dulness + 2 at right apex with bronchial breathing and vocal resonance + 2. No accompaniments. Dulness + 1 at left apex with harsh vesicular breathing with prolonged expiration. No accompaniments.

Alimentary System: Nothing to note beyond the distension of the abdomen.

v. Pirquet's test Dec. 2nd, 1907. Negative.
" " " " 6th " "

Calmette's " (Beraneck's Tuberculin 1:200)
Dec. 12th, 1907. Negative.
" " " " " " 17th, " "
" " " " " Jan. 9th, 1908. "
" " " " " " 16th, " "

Mitral Stenosis and Incompetence.

I. P. female. Aet, 10. History - Patient was discharged a year ago from hospital after being treated for the same complaint. Shortly after her return home she became much more short of breath and the cough became very troublesome. Previous Illnesses - Pericarditis in July, 1907.

Circulatory System: Systolic and Diastolic murmurs in mitral area. Systolic murmurs in the other areas.

Respiratory System: Dulness at both apices with bronchial breathing but no accompaniments.

v. Pirquet's test December 20th, 1907. Negative.

Calmette's " (1:200) " 26th, " "

Sub-Acute Bright's Disease.

J. R. male. Aet, 60. History - A fortnight ago, patient caught a severe cold. At this time he noticed that his feet were swollen and his face puffy.

Urinary System: Urine - 1018. acid. Albumin 3·5 gr. per oz. blood. Epithelial and fatty casts.

Respiratory System: Dulness + 1 at left apex with bronchial breathing

Dulness + 1 at right base with dimenished breath sounds. Breath sounds at right abex harsh vesicular with prolonged expiration.

v. Pirquet's test 9th March, 1908. Negative.

Calmette's test (1:200) 13th, " " "

Aortic Stenosis, Mitral Incompetence and Subacute Bright's Disease.

M. S. female. Aet, 17. History - Twelve days ago, patient had an attack of shivering with pain in the chest and over the heart. As these continued in spite of treatment she was admitted to hospital.

Heredity - One sister has cardiac disease and pulmonary tuberculosis.

Circulatory System: Mitral systolic and diastolic murmurs. Aortic systolic murmur.

Respiratory System: Dulness at both apices with broncho-vesicular breathing at the right and harsh vesicular at the left.

Calmette's test (1:150) 13th March, 1908. Negative.

" " (1:100) 1st May, " "

v. Pirquet's test (Pure Old Tuberculin) 13th July, 1908. "

Pulmonary Tuberculosis with Haemoptysis.

D. M. male. Aet, 55.

v. Pirquet's test 13th March, 1908. Negative.

Calmette's test (1:150) " " " "

General Debility.

M. E. female. Aet, 20. History - Since the age of 15 patient has suffered from dsymenorrhoea and menorrhagia. During the last two years she has become very pale and has been very short of breath.

Respiratory System: Slight dulness at both apices, with harsh

vesicular breathing with prolonged expiration. Vocal resonance increased.

Haemopoietic System: Several glands of the size of small peas on either side of the neck.

v. Pirquet's test (Pure Old Tuberculin) 8th August, 1908. Negative.

Calmette's test (1:200) 17th September, 1908. Negative.

Hodgkin's Disease: T. D. male. Aet, 39.

History - About two years ago patient first noticed a small lump on the left side of his neck, and this gradually increased in size and others appeared. For the last year patient has been gradually becoming weaker in spite of treatment and he has been losing weight steadily.

Haemopoietic System: Great numbers of glands on either side of the neck and in the axillae and groins. Spleen is distinctly enlarged, and also the liver.

Respiratory System: Marked dulness at both apices with harsh vesicular breathing with prolonged expiration. Vocal resonance increased.

v. Pirquet's test (Pure Old Tuberculin) 27th August, 1908. Negative.

Calmette's test (1:200) 17th September, 1908. Negative.

D.16 Non-Tuberculous Cases Giving No Reaction.

Infantile Cerebral Palsy.

R. W. female. Aet. 4½. History - The birth of the patient was very prolonged but no "instruments" were used. Some weeks afterwards it was noticed that the child could not use its legs and arms properly and now the limbs are in a very spastic condition.

Respiratory System: Nothing to note.

Haemopoietic System: A few slightly enlarged glands on either side of the neck.

v. Pirquet's test (Pure Old Tuberculin) 8th August, 1908. Negative.

Mitral Incompetence.

I.D. a female. Aet, 12. History - Patient was in ward 17 R. I. E. on account of an injury to the knee and while there she developed a temperature with pain in her knee, supposed to be rheumatic and so she was transferred to ward 33.

Circulatory System: Mitral systolic murmur.

Respiratory System: Nothing to note.

Haemopoietic System: Numerous slightly enlarged glands on the left side of the neck.

v. Pirquet's test (Pure Old Tuberculin) 8th August, 1908. Negative.

Gastric Ulcer.

L. H. female. Aet, 20. History - For the last six months patient has suffered from constant pain in the stomach aggravated by taking food. About an hour after food she frequently vomited and occasionally the vomit was like coffee-grounds.

Respiratory System: Nothing to note.

Haemopoietic System: Slightly enlarged glands in neck and axillae.

v. Pirquet's test (Pure Old Tuberculin) 8th August, 1908. Negative.

Rickets.

A. Mc.C. female. History - Up till four months ago patient was a healthy child but then the child began to be very weak and to have diarrhoea

and its abdomen began to swell.

Osseous System: Prominent frontal and parietal eminences. Femora Tibiae and Fibulae are all bent very much.

Respiratory System: Nothing to note.

Haemopoietic System: No enlarged glands.

v. Pirquet's test (Pure Old Tuberculin) 31st July, 1908. Negative.

Mitral Stenosis. J. M. male. Aet, 18 years. History -

About a year ago patient caught cold and he began to cough and spit and he noticed a little streak of blood in the spit. Two months later he began to get short of breath. Previous Illnesses - Measles as a child.

Circulatory System: Presystolic and Diastolic murmurs in the mitral area.

Respiratory System: Nothing to note.

Haemopoietic System: Numerous enlarged glands on both sides of the neck.

Calmette's test (Béraneck's Tuberculin 1:200) December 14th, 1907. Doubtful Reaction - Slight injection of conjunctiva and slight swelling of caruncle.

Calmette's test (Beraneck's Tuberculin 1:200) Jan. 12th, 1907. Negative.

Transverse Myelitis.

J. G. male. Aet, 34. History - Four years ago patient had his left hip crushed between two buffers. He recovered from this but fourteen months ago his left leg began to tremble under him and it became very weak. Previous Illnesses - Patient denies syphilis but he had a large sore on

his right groin which quickly healed under Potass. Iodide.
Influenza at 17 and again at 19 years of age.

Nervous System: Sensory functions impaired on both legs as are also the motor functions and co-ordination. Knee-jerks exaggerated and Babinski's sign present.

Respiratory System:- No signs of tuberculosis.

Calmette's test (1:150) 3rd March, 1908. Negative.

Aortic Regurgitation.

W. B. male. Aet, 44 years. History - Seven years ago patient began to suffer from throbbing in the neck and also occasional pains in the chest. Two years ago these became more severe. Previous illnesses - Rheumatic pains in right arm seven and a half years ago. Attacks of acute tonsillitis at age of 15. Scarlet fever as a boy. Dry pleurisy 16 years ago.

Circulatory System: Systolic and diastolic aortic murmurs.

Respiratory System: Nothing to note.

Calmette's test (1:150) 3rd March, 1908. Negative.

Mediastinal Tumour.

T. D. male. Aet, 54. History - For the last four months patient has suffered from occasional pains in the right arm on exertion. Two months ago patient was suddenly seized with a sharp pain between his shoulder-blades and though this subsided it left a dull pain which still persists. Previous illnesses - Patient has had a "winter cough" for five or six years.

Circulatory System: Cardiac dulness increased up over the area over the great vessels. 2nd, aortic sound loudly accentuated.

Respiratory System: Percussion note resonant all over the lungs. Breath sounds vesicular with prolonged expiration marked by sibilant rhonchi all over the chest.

Calmette's test (1:150) March 6th, 1908. Negative.

Post-mortem examination revealed a lympho-sarcoma growing in the mediastinum, but no signs of tuberculosis.

Pseudo Angina Pectoris.

E. C. male. Aet, 28. History - A fortnight ago patient was suddenly seized with a severe pain in the left side of the chest and in the left shoulder. Ten days later he had a similar attack.

Circulatory System: Heart is considerably enlarged. No murmurs.

Respiratory System: Nothing to note.

Calmette's test (1:150) 13th March, 1908. Negative.

Chorea.

A. C. male. Aet, 14 years. History - Patient has had the present illness for the last six months. He had a similar attack 7 years previously.

Respiratory System: Nothing to note.

Calmette's test (1:100) April 15th, 1908. Negative.

" " (1:100) May 3rd, " "

Acute Rheumatism.

W. M. male. Aet, 29. History - For a month past patient has had occasional pains in his joints but two days ago the pains became very severe and he was feverish, due he thinks to exposure to cold air after working in a hot engine-room.

Respiratory System:

Nothing to note.

Haemopoietic System: No enlarged glands.

Calmette's test (1:100) May 1st, Negative.

Aortic Aneurism.

J. H. male. Aet, 45. History - Three months before admission, patient got a severe wetting and since then he has been troubled with a cough, pain in the chest, and with shortness of breath. Patient has had syphilis and gonorrhoea.

Circulatory System: Dulness extending from the upper border of the cardiac dulness up to the top of the sternum. Aortic systolic murmur with accentuated second sound. Pulses unequal.

Respiratory System: Slight dulness at both apices. Breathing all over the chest, vesicular with prolonged expiration. Paralysis of left vocal cord.

Haemopoietic System: Enlarged glands in neck, axillae and groins.

Calmette's test (1:100) 7th Jsne, 1908. Negative.

Aortic Incompetence.

K. S. female. Aet, 22. History - Ever since she was ten years of age patient has been short of breath, but it is much worse at times than at others.. She has had chorea ten times.

Circulatory System: Double aortic murmur.

Respiratory System: Nothing to note.

Haemopoietic System: Several enlarged glands in axillae and in the neck.

Calmette's test (1:100) 21st May, 1908. Negative.

Aortic Aneurism.

M. Mc.G. male. Aet, 50. History - About six months ago patient began to be very short of breath on exertion and he has occasionally fainted while at his work.

Circulatory System: Area of dulness extending from the cardiac dulness up to the top of the sternum. Aortic and Mitral systolic and diastolic murmurs.

Respiratory System: Slight dulness at the left apex with harsh vesicular breathing.

Haemopoietic System: Slightly enlarged glands in the neck, axillae and groins.

Calmette's test (1:100) 2nd June, 1908. Negative.

Subacute Rheumatism.

J. M. male. Aet, 45. History - A week before admission patient began to have pains in his head and joints and they have been gradually becoming worse.

Respiratory System: Slight dulness at right apex. Breathing vesicular over the whole chest.

Haemopoietic System: Several enlarged glands in axillae & groins.

Calmette's test (1:100) 1st May, 1908. Negative.

General Debility.

W. L. male, Aet, 3½. History - During the last six months patient has been getting thinner, losing weight, sleeping badly, and his abdomen has been swollen.

Respiratory System: Nothing to note.

Haemopoietic System: Several slightly enlarged glands on either side of the neck.

v. Pirquet's test (Pure Old Tuberculin) 16th Sept., 1908. Negative.

Calmette's test (1:200) 17th September, 1908. Negative.

E. 4 Non-Tuberculous Cases Giving Positive Reactions.

Rheumatoid Arthritis.

A. S. female. Aet, 57. History - Ten weeks ago patient had an attack of phlebitis in the left leg and on recovering from this she began to suffer from severe pain in the left knee. The pain gradually became worse and the knee began to swell and patient was sent to hospital for treatment.

Respiratory System: Slight dulness at the left apex. Breath sounds vesicular all over the chest.

Haemopoietic System: No enlarged lymphatic glands.

v. Pirquet's test (Pure Old Tuberculin) 8th Aug., 1908. Positive. Slight redness and infiltration.

Calmette's test (1:200) 21st September, 1908. Positive I. Slight but distinct redness and swelling of the caruncle, plica and conjunctiva.

Mitral Incompetence and Chorea.

L. D. female. Aet, 11. History - Patient in June, 1907 was in Ward 27, R.I. E. with chorea and she began two weeks ago to show signs of it recurring.

Circulatory System: Blowing mitral systolic murmur.

Respiratory System: Nothing to note.

Haemopoietic System: A few enlarged glands in the neck.

v. Pirquet's test. 17th December, 1907. Positive.

Calmette's test (1:100) 18th Dec., " Positive II.

Marked injection and swelling of caruncle and lower palpebral conjunctiva.

Tabes Dorsalis.

A. R. male. Aet, 51. History - Illness began a year ago with weakness in the legs and unsteadiness in walking. Has pains in the legs.

Nervous System: Girdle sensation across the epigastrium. Knee-jerks absent. Rhombergism.

Respiratory System: Nothing to note.

Calmette's test (1:150) 6th March, 1908. Positive. II.

Caruncle and plica swollen and reddened. Conjunctiva inflamed. Lachrymation. Some fibrinous deposit. Patient feels as if there were a film over the eye. Oedema of both eyelids very pronounced. Patient complains of pain in the eyeball.

v. Pirquet's test. 13th March, 1908. Positive.

Slight pink papule.

Aortic and Mitral Stenosis.

C. F. male. Aet, 20 years. History - A week ago patient was siezed with shivering at his work. Later he had pains in his joints and back. He was very feverish. Previous Illnesses - Rheumatic fever 2½ years ago.

Circulatory System:

Mitral area - presystolic, systolic, and diastolic murmurs. Aortic area - systolic murmur.

Respiratory System: Dulness + 1 at right apex. Breath sounds vesicular - no accompaniments.

Calmette's test. (1:150) 3rd March, 1908. Positive IV. Slight reaction but not appearing till twenty-four hours after the instillation.

* *

These results may be grouped under two heads:-

I. Positive compared with Negative.

II. Those obtained with v. Pirquet's test compared with those obtained with Calmette's.

I. A. Tuberculous Cases.

1. Positive to Calmette or to v. Pirquet - 31 cases
" " both Calmette and v. " - 16 "
" " Calmette but negative to v. Pirquet 7 " - 72·5%.
" " v. Pirquet but negative to Calmette 4 "

2. Negative to Calmette or to v. Pirquet or to both Calmette & v. Pirquet - 22 cases - 27·5%.

B. Non-Tuberculous Cases.

1. Negative to Calmette or to v. Pirquet, or to both Calmette & v. Pirquet - 16 cases - 80%.

2. Positive to Calmette or to v. Pirquet, or to both Calmette and v. Pirquet - 4 cases - 20%.

II. A. Tuberculous Cases.

1. v. Pirquet — Positive - 25 cases - 58%.
   Negative - 18 " - 42%.

2. Calmette — Positive - 48 " - 67·6%.
   Negative - 23 " - 32·4%.

B. Non-Tuberculous Cases.

1. v. Pirquet — Negative - 5 cases - 63%.
   Positive - 3 Cases - 37%

2. Calmette — Negative - 11 " - 68·7%.
   Doubtful - 1 Case - 31·3%.
   Positive - 4 Cases

v. Pirquet's and Calmette's tests were performed on the same patient in 39 cases, and in 28 of these (71·8%) the tests were either both negative or both positive, while in the remaining 11 (28·2%) the results did not correspond - v. Pirquet being positive and Calmette negative in four cases; and v. Pirquet negative and Calmette positive in 7 cases.

In four of the cases which gave positive reactions to both Calmette's and v. Pirquet's tests, post-mortem examination revealed the presence of tuberculosis. In one of these cases - a girl who had given very marked reactions - the evidence of tuberculosis consisted in a large solitary calcareous gland in the abdomen, and signs of old pleurisy. The post-mortem on one case negative to Calmette's test, failed to find any signs of tuberculosis. In only two of all the cases was there a purulent reaction and in each case a 0·5% solution had been used. There were no bad after-effects in either case.

In one case - that of a man with Disseminated Sclerosis who had very little evidence of Pulmonary Tuberculosis - a very prolonged reaction resulted as it was six weeks before all trace of the reaction had disappeared and during its course two or three small corneal ulcers developed as well as a granular conjunctivitis. The strength of the solution in this case was 1:150.

In one case in which v. Pirquet's test gave a very decided reaction, Calmette's test was twice negative, but this was perhaps due to the child crying and so washing away all the solution. One case was one of Bazin's Disease and it gave a positive reaction to Calmette's test.

Two cases of Pulmonary Tuberculosis died within a week after the tests were performed; and they gave positive reactions, though dying cases are supposed to be exceptions to the rule.

In the following table the degrees of reaction are compared in cases of slight and of marked Tuberculosis.

Tuberculosis.				Reaction.
I. Slight. (32 cases)	Slight	v. Pirquet	10 cases	v. Pirquet's sol. - 5. Pure Old Tuberculin 5.
		Calmette	14 "	1:100 - 8. 1:150 - 0. 1:200 - 6.
	Well-marked	v. Pirquet.	0 cases	
		Calmette	15 "	1:100 - 7. 1:150 - 6. 1:200 - 2

II. Well-marked. (25 cases)	Slight	v. Pirquet.	11 cases	v. Pirquet's sol. 7. Pure Old Tuber. 4.
		Calmette	6 "	1:100 - 1. 1:150 - 1. 1:200 - 4.
	Well-marked.	v. Pirquet.	4 cases	v. Pirquet's sol. 1. Pure Old Tuber. 3.
		Calmette	12 cases	1:100 - 4. 1:150 - 2 1:200 - 6

These figures do not allow one to draw any conclusions as to the prognostic value of either test, though some cases of very early tubercle gave most marked reactions while advanced cases gave feeble reactions.

This agrees with what Harrison Butler says in the British Medical Journal of 18th April, 1908 p. 922 - "The intensity of the reaction bears no relationship whatever to the severity of the tuberculous process."

In conclusion it may be stated that according to my results neither test is diagnostic in itself, and that, without further proof, it would be unwise to say that a patient had or had not, tuberculosis according to whether either test was positive or negative. The tests should be looked on as only one piece of evidence, which without more to confirm it would be useless. If the two tests give a similar result then they are more likely to be correct, but even this cannot be relied upon. A negative result with either test appears to be slightly more reliable than a positive one; and Calmette's test has yielded results which are, on the whole, rather more accurate than those obtained with v. Pirquet's.
