THE NOGUCHI LUETIN REACTION

Thesis for the degree of M.D.

by

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M.D. London 1914
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Two colour sketches by an artist and one photograph with notes are included.
Syphilis, owing to its association with sexual immorality, presents more difficulty to the clinical investigator than other lesions he is called upon to diagnose. Setting aside cases of malingering, none are so often the occasion of falsehood on the part of the patient. In implying difficulty one does not refer to the primary condition, where the cause is usually apparent, but to the obtaining of a history of the disease in the later secondary and tertiary symptoms, in the parasyphilitic lesions, and in congenital syphilis.

The reaction introduced by Professor Wassermann was at once hailed as a likely relief for the physician from the sordid and troublesome cross-examination which he is compelled to use in the case of a patient imbued with a false and misplaced modesty. Its value in estimating the adequacy of treatment was recognised. But disappointment with it as an infallible guide has been expressed. It is found positive in conditions other than syphilitic. Samples of the same blood labelled with different names have been sent to the same pathologist and have afforded contradictory results. Samples of the same blood sent to different pathologists have also been reported on as giving positive and negative reactions. In the same case the/
the reaction varies at times in an unaccountable way.

Much of this confusion may be due to ignorance of the factors involved in the reaction and to inexperience on the part of the pathologist. Though no one can gainsay the usefulness of the reaction, the fact remains that a simpler one is much to be desired.

Von Pirquet, who introduced the cutaneous reaction for tuberculous disease, foresaw the possibilities of a cutaneous reaction in syphilis when the virus of the disease could be obtained in pure culture and the accomplishment of this by Noguchi of New York was followed by his introduction of such a reaction.

Previous Work with Skin Reactions.

But mention must be made of other skin reactions for syphilis, carried out by workers previous to this.

Neisser obtained a skin reaction which showed the formation of a papule by using extract of syphilitic liver, but did not set much store on it owing to the fact that he obtained a similar reaction with normal liver.

Meirowski used extracts of syphilitic foetal liver but obtained reactions in non-specific cases which were much the same as those he obtained in specific cases.

Tedeschi made use of material taken from fresh syphilitic lesions. He ground up portions of tissue in sterile water, made an extract at a temperature of 60°C and filtered this through a Berkefeld filter till
it was devoid of germs. He experimented with this but controlled his results only by taking monkeys and rabbits. No normal cases were used so that his results lose any value they might have possessed.

Ciuffo used extracts from the liver, spleen and kidney of cases of hereditary syphilis. His findings were unsatisfactory, the reactions not being limited to luetic cases.

Nobl had the same experience.

Nicolas, Favre and Gautier prepared glycerin extracts from foeti affected with hereditary syphilis, and used their preparations for cutaneous and intracutaneous reactions. Of ten patients, one showed a negative reaction, four doubtful or weak, and five strongly positive reactions. The non-syphilitic cases without exception showed negative reactions. Other workers could not confirm these results.

Fontana tried a variety of substances for intracutaneous tests:
1. A glycerine extract of mucous patches with abundant spirochaetes which he called syphilin.
2. 10% solution of sodium glycocollate in sterile distilled water.
3. Lecithin, in the form of phospho plasmin.
4. Extract of normal guinea-pig's heart.

Taking as positive reaction a distinct nodular infiltration his results were:
1. In 40 Syphilitic cases - 16 + Syphilin (34 + Wassermann.)

16 Non-Specific cases - 2 + Syphilin.

2. With Sodium Glycocollate solutions less than a third of the cases which showed positive Wassermann reactions were accompanied by a positive reaction.

3. Lecithin injections produced positive reactions in only 16.3% of undoubted luetic cases.

4. Three cases of syphilis reacted positively to injection with extract of guinea pig's heart. Two Normal cases reacted positively out of ten.

We must now consider in full the intracutaneous reaction produced by isolated dead spirochaetes.

Noguchi's work.

In August 1911 Hideyo Noguchi published his account of the cultivation of the treponema pallidum in pure culture which he had been successful in making. Instead of using the syphilitic tissues of human beings he used the testicular tissue of rabbits, after inoculating this with human spirochaetal tissue. His culture-medium was serum-water (1 part serum to 3 parts distilled water), to which he added sterile rabbit tissue - usually kidney, testicle, or heart. Strict anaerobic conditions were important in obtaining the first generation. A slightly alkaline condition - achieved by using the serum and tissue mentioned above, was also/
also necessary. The temperature for successful cultivation was between 35°C and 37°C. In serum water tissue the pallidum grew at the bottom of the medium and did not extend very far. It commenced to multiply after 48 hours and grew slowly for four or five weeks. Noguchi applied his discovery of the methods for obtaining a pure culture of the treponema pallidum to this end - to obtain a reaction by using a pure culture free from animal tissue.

**Preparation of Luetin.**

Two strains of the treponema pallidum are prepared, one in a fluid, the other in a solid medium. Pure cultures were allowed to grow for periods of six, twelve, twenty-four, and fifty days at 37°C under anaerobic conditions.

One in ascitic fluid in which there was also a piece of sterile placenta, the other in ascitic fluid agar also containing placental tissue.

Spirochaete-containing portions of the agar columns were then cut out, the tissue removed and the portions of agar ground up in a sterile mortar. This thick paste was diluted by adding gradually the fluid medium, which also contained great numbers of the pure organism. The perfectly liquid emulsion so formed was heated in a water bath at 60°C for sixty minutes, and 0.5 per cent carbolic acid was added. Under a dark field microscope, 40 - 100 dead treponema pallida could be/
be seen. No infection could be produced in rabbits, it was a harmless mixture. He kept it in a refrigerator when not in use.

**Control.** A similar emulsion with uninoculated medium.

**Intra dermic injection.** Noguchi used both rabbits and men to show the results.

In **Rabbits** the hair on the lower side of the back is shaved off and 0.05 c.c. of emulsion injected. The same amount of control substance is also injected at some distance from this site in the same region in the rabbit.

In **human beings** the upper arm is chosen for injection - left for emulsion, right for control. Alcoholic sublimate solution was used previous to injection to sterilise the skin. The epidermic layer sharply raised up from the cutis and having the appearance of a pale swelling - which goes down in ten to fifteen minutes - is that of the successful injection.

**Reaction Result.**

Noguchi divides his results into Negative and Positive.

A Negative result consisted in the following - after twenty-four hours a slight erythema appeared at the point of injection. This faded within forty-eight hours and left no induration. A small papule occasionally/
occasionally formed in 24 - 48 hours but this receded within 72 hours, no induration being left behind.  

Positive Results were divided into three classes:-

Papular Forms.

Pustular "

Torpid "

The Papular Form.

Within 24-48 hours a large raised reddish indurated papule, 5-10 m.m. in diameter, appeared. Round it was a diffuse zone of redness and it showed marked telangiectasis. For three or four days the size and degree of induration of the papule increased and then the inflammatory process began to recede. The colour of the papule gradually became dark bluish-red.

In one week the induration disappeared but in some cases a trace of the reaction persisted, especially in congenital syphilis and in cases of secondary syphilis under regular mercurial treatment where there were no manifest lesions when the skin test was made.

The Pustular form.

As above until the fourth or fifth day, when the indurated, round papule became oedematous and multiple miliary vesicles sometimes formed. Softening of the centre occurred and in twenty-four hours a vesicle formed which was finally purulent. This ruptured, dried up, and the crust fell off in a few days. This reaction was seen mostly in cases of tertiary syphilis as well as in cases of secondary or hereditary syphilis treated/
treated with salvarsan.

The Torpid form.

In some cases an apparently negative reaction occurred till the 10th day when the pustular reaction manifested itself. It was seen in one case each of primary and hereditary syphilis and in two cases of secondary syphilis. All of these were under mercurial treatment.

Constitutional Effects.

Slight rise of temperature took place for a day in positive cases.

Three tertiary cases and one hereditary case showed general malaise, loss of appetite, and diarrhoea.

Nature of the Reaction.

Noguchi is of the opinion that this reaction, when positive, is due to an "allergic" (von Pirquet) or anaphylactic condition of the body and therefore of the skin. It is developed in patients who have had the disease for some time and is not produced where the spirochaetes are at their prime but in such cases as those of the later secondary stage, especially where weakened by vigorous treatment.

Other workers hold that it is merely a "pathologically sensitive" condition of the skin itself produced by the syphilitic virus. Neisser gives to it the name of "Umstimmung" and instances the occasional reaction/
reaction obtained at the control site with the uninoculated medium. Noguchi, however, replies that the reaction in these cases is always much larger and more emphatic at the luetin site.

Candidate's experience with Luetin.

It occurred to me on reading accounts of this test that it might be useful in military work, and I wrote to Noguchi asking for some of the Luetin and some of the uninoculated medium as control. He was good enough to send me enough Luetin to test over sixty cases, but said he had now discontinued the use of a control emulsion, "as my experience has shown that it is superfluous".

Technique.

The upper arm of each patient was used and the site chosen was the deltoid insertion. The skin was rendered aseptic by the use of a solution of corrosive sublimate in absolute alcohol (1 in 1000). This was allowed to dry. The needle of a 3/4 c.c. Record syringe was then passed as superficially as possible into the skin with the flute-like point facing outwards until it had just disappeared. The Luetin was then injected slowly till a small, white, warty blister was raised and the needle withdrawn. Care to keep the needle-point and luetin bottle and its cork sterile was maintained between injections by passing them through/
through the flame of a spirit lamp.

The amount of luetin required on each day of inoculation was poured into a small specially sterilized test tube. The syringe was also sterilized each day - the needle-point, as mentioned above, being flamed between each case.

The variety of syringe was that commonly used for tuberculin injections - the \( \frac{1}{2} \) c.c. measurement being divided up into ten parts and each of these into five, so that each mark on the syringe barrel registered .01 c.c., and thus a dosage of .07 could be given easily.

The Luetin itself was like any bacterial emulsion in appearance - whitish and cloudy, but translucent.

**Microscopically.**

Spirochaetes in varying numbers were seen but much fewer than the 40 - 100 per field which Noguchi and Ziegel described. The Luetin during use was ascertained to be sterile from time to time.

**Observation.**

All cases were under observation for three weeks or longer. Forty-four were seen every day for ten days. Sixteen were seen every two days.

**CASES.**

In the first eleven cases, I followed the instructions in Noguchi's letter, using .07 c.c. of equal parts of Luetin and normal saline solution, i.e. .035 c.c. of Luetin.

1. Andrew Russell Scott. 47. Ward 31, R.I.E.

**History.** Diagnosed as Tabes Dorsalis: had shooting pains, absence of knee jerks, anaesthetic patches, girdle sensation, gastric crises. Argyll-Robertson pupil/
pupil present, commencing optic atrophy, ataxia, Rombergsism. No history of primary or secondary syphilis.

Treatment. No antisyphilitic treatment.

Wassermann reaction. 'Negative'.

Luetin reaction. Negative.

Slight induration present at site of inoculation when seen on first, second, third and fourth days. No reddening.


History. Diagnosed as Lymphadenoma. Glands swollen in neck, axilla and groin and very hard on palpation.

No luetic history.

Luetin reaction. Negative.

There was some induration at the site of inoculation for several days, and marked reddening, but no sign of a raised papule.


History. Exposed to infection three months before. On slitting up the oedematous prepuce an extensive superficial ulcer was found involving the whole front part of the glans penis, with some induration in the neighbourhood of the frenum. Glands enlarged.

Papular rash.

Treatment. Two injections of Neo Salvarsan had been given/
given before the reaction was tried.

**Wassermann Reaction.** Eleven days before reaction - a "doubtful positive" reaction was obtained.

The day after the Luetin test an "absolute positive" reaction was obtained.

**Luetin reaction,** was negative.

Slight induration was felt where the inoculation had been done.

4. Andrew Edmonds. 49. Ward VA. R.I.E.

**History.** Suspicious case. Diagnosed as having a gumma on the chin. Tonsils and fauces congested. Mucous patches in mouth. Right epitrochlear gland palpable.

**Treatment.** No treatment for syphilis.

**Wassermann Reaction.** Applied three days after Luetin test - was "absolute positive".

**Luetin Reaction.** Negative.

Induration and slight reddening at site of inoculation, disappearing in four days.


**History.** Exposed to infection a month before. Soft sores on labia. Condylomata round anus. Rash - papular and pustular - on neck, chest, back and limbs. Tonsils large and congested.

**Previous treatment.** Three injections of Neo Salvarsan.

**Mercurial inunction.**

**Wassermann reaction.** Twelve days before Luetin test - was/
was "nearly negative" - having been "absolutely positive" on two previous occasions.
Luetin reaction was quite negative - no induration or reddening being seen after the third day.

6. Elizabeth Davidson. 20. Ward 20, R.I.E.


Treatment. Mercurial inunction previously for primary infection. Four injections of Neo Salvarsan.

Wassermann reaction. Twelve days previously - "absolute positive".
Luetin reaction. Quite negative - no induration or reddening seen after the third day.

7. Jessie Waddell. 29. Ward 20, R.I.E.

History. Date of exposure - 7 years ago. Eye became painful a month before. Patient was suffering from acute photophobia and iritis.

Treatment. Mercurial inunction previously.
Neo salvarsan about four hours before Luetin test tried.

Wassermann reaction. Blood taken on same day as Luetin test was "absolute positive".
Luetin reaction. Doubtful. On the second day of inspection the inoculation area showed hardening with some oedema round it and was painful. These signs disappeared in five days. The result might be called doubtful.
8. Ellen Hart. 28. Ward 20, R.I.E.

History. Syphilitic sore a year before with a fresh infection four months before test.

A large irregular sore on right labium. Old macular rash visible on body - papular and pustular on forehead and scalp.

Treatment.

Mercury pills and one injection of Neo salvarsan had been given at previous infection. Neo salvarsan was given on day of test, about four hours before. Wassermann reaction. Two days after luetin test was "absolutely positive" and another sample of blood taken nine days after was also "absolute positive". Luetin reaction was doubtful. Slight induration and reddening showed for a few days after injection. On the fourth day these signs were increased slightly and began to disappear on the seventh day. On the tenth day some pigmentation was left at the inoculation area.


Treatment. Mercurial inunction. Neo salvarsan, two injections, one a week before, the other on the day of inoculation about four hours before. Wassermann Reaction. One twelve days before test was "nearly positive".

Second, five days before, was "absolutely positive".

Third/
Third, two days after test, was "absolutely positive". Fourth, nine days after test, was "absolutely positive". Luetin reaction. Quite negative, only slight induration for three days. No reddening.

10. Thomas Letton. 23. Ward VA, R.I.E.  
History. Congenital syphilis, ulceration of nose and palate.  
Treatment. Three injections of Neo salvarsan previously.  
Wassermann reaction. "Absolute positive".  
Luetin reaction. Doubtful. Slight reddening and induration at inoculation site for four days only. Nothing observed till seventeen days after the application of the test when a large purplish injection about 1 c.m. in diameter appeared at the inoculation site and faded away again in four days. No vesicle or pustule developed.

Treatment. None before test.  
Wassermann reaction. Four days after test "positive". Luetin reaction. Quite negative. Induration for three days. No reddening.
I was disappointed with the results - three doubtful positive reactions - obtained in the foregoing cases, as I felt that some of them were cases which should have produced signs of a reaction if the test was to be of service. Concluding that possibly the dosage had been rather small, I used Noguchi's original method of injecting .07 c.c. of the Luetin alone and discontinued the sterile saline solution.

12. Agnes Millar. 23. Ward 20, R.I.E.

History. Infection - three months before. Had sores on labia, mucus patches on under surface of tongue, ulceration and congestion of the fauces.

Treatment. Practically none before the reaction was tried. Salvarsan had been given about five hours before on the same day.

Wassermann reaction. Blood taken two days after the reaction showed an "absolute positive" reaction. "Absolute positive" reactions one day and eight days after test.

Luetin reaction was negative. There was no reddening. The indurated spot felt below the skin in the region of the needle-puncture disappeared in three days.


See No. 8, previous series, for clinical notes.

Luetin reaction was negative. No reddening was observed/
First Artist's water-colour sketch, to illustrate case No. 15, on the fourth day. It shows the typical pustular reaction obtained in the majority of the cases.
17.

observed on this occasion. Induration disappeared in four days.


History. Infection six weeks before. Sores about labia. Roseolar rash on body.

Treatment. Neo salvarsan a day before test.

Wassermann reaction.

Five days before test, "absolute positive".
One day after test, "absolute positive".
Seven days after test, "absolute positive".

Luetin reaction. Negative. Induration for three days. No reddening.

15. Jessie Waddell. Syphilitic Iritis, see No. 7.

Treatment. Neo salvarsan day before test.

Wassermann reaction. Day before test - "absolute positive".

Luetin reaction. Positive. Distinct reddening, 1 c.m. in breadth, seen at site of inoculation on first day of inspection, which increased in intensity. On the third day a whitish area showed itself in the centre and on the fourth a pustule made its appearance. This had broken by the sixth day. A crust formed in the centre by the tenth day. Three weeks after a small scab with induration was still present at the inoculation site.

16./
16. Mrs Ramsay, 32. Ward 20, R.I.E.

History. Infection six months before. Several soft sores about labia. Marked rashes of different type seen on body. Mucous patches in mouth and on fauces.

Treatment. Mercurial inunction. Three injections of Neo salvarsan before test.

Wassermann reaction.

First. Fifteen days before test - "absolute positive".
Second. Eight days before test - "Positive, § lysed".
Third. The day before test - "Positive, § fixation".
Fourth. Six days after test - "Positive, § lysed after 24 hours."

Luetin reaction. Positive.

After 48 hours a distinct elevated papule was seen at the point of inoculation, slightly reddened.

After 72 hours, a whitish centre appeared, but though the induration remained constant for ten days, the white centre never became a pustule but gradually disappeared. In three weeks all traces of the reaction had disappeared.

The following eleven cases were inoculated at Piershill barracks. All were free from signs of disease when inoculated.

17. Gunner Hicks.


Treatment. Mercurial injections = 1 gr. of mercury were/
19.

were given into gluteal region, starting five months ago, to the extent of 15 grains of mercury.

Two injections of salvarsan, the last three months before.

Wassermann Reaction. Five months before - "Positive".

Four days before - "Negative".

Luetin reaction. Negative. Slight induration for four days. No reddening.

18. Gunner Hewitt.

History. Infected seven months before. Glands enlarged. Roseolar rash.

Treatment. Two injections of salvarsan. Eight grains of mercury in weekly injections of 1 grain.

Wassermann reaction. Two months before test - "Positive".

Two days before test - "negative".

Luetin reaction. Negative. Some indurations at site of injection. On the third day slight redness which had disappeared by the fifth day.


History. Had a hard sore on the prepuce seven months before test was applied. Glands enlarged. Macular rash on skin. Tonsils ulcerated. Condylomata.

Treatment. No salvarsan but has had twenty-one grains of Mercury in injections.

Wassermann reaction. A month before test - was "positive".

Luetin/
Luetin reaction. Positive.

The day after injection - redness and induration were present at the site of inoculation. On the second day a whitish centre began to appear in the reddish papule which on the fourth day had become definitely pustular. On the seventh day this had broken down and a crust had formed in the centre of the red papule which was about 5 mm. in diameter. A week later the reddish area had diminished slightly but had a scab in the centre.

20. Driver Law.

History. Infection seven months before test.
Indurated sore behind corona. Glands enlarged.
Macular rash front and back. Slight reddening of fauces.

Treatment. Had salvarsan and three injections of mercury and then deserted.

Wassermann reaction. "Positive", taken some time before inoculation.

Luetin reaction. Positive.

On the second day of inspection a reddish papule had appeared. On the fourth day a whitish centre had appeared which, on the seventh day, was definitely pustular. On the tenth day this had broken down and yellowish crusts had formed. Twenty-one days after, there was still a scab with a thin margin of reddening.

21./

History. Infection two and a half months before.
Small indurated sore on glans. Glands enlarged.
Slight injection of fauces.

Treatment.
First injection of salvarsan two months before.
Second injection of salvarsan one month before. Ten grains of mercury in weekly injections.

Wassermann reaction. Before first injection of salvarsan, was "positive".

Luetin reaction. Was distinctly negative. Slight induration at site of inoculation for four days, with no reddening.

22. Driver Sheppard.

History. Infection two years and seven months before inoculation. Chancre on corona. Bubo, right groin.
Roseolar eruption on trunk.

Treatment. Had a full course of mercurial treatment as it used to be carried out in the Army:-
27 grains of mercury.
First dose of salvarsan one year and three months ago.
Second dose of salvarsan two months ago.
Third dose of salvarsan eleven days before test.

Wassermann reaction. Three months before was "positive".

Luetin reaction. Positive.

Redness and induration appeared at the site of inoculation on the first day and persisted for four days/
days and then the colour faded slightly. Twelve days after, however, a pustule formed, broke down, became crusted, and was evident as a reaction three weeks after.

23. Driver Allanson.

History. Infection four months before. Indurated sore on under surface of prepuce. Discrete papular rash on chest and back.

Treatment. Weekly mercurial injections and two doses of salvarsan - the last one month before test.

Wassermann reaction. "Positive" - one month before inoculation.

Luetin reaction. Was quite negative. Slight induration for four days and no reddening.

24. Driver Parsons.

History. Infection three years and one month before. Had a primary sore, though only a scar was visible when treatment was started five months later. Roseolar rash. Tonsils, fauces, pharynx, inflamed and ulcerated.

Treatment. Full course of Mercurial injections - 27 gr. No salvarsan.

Wassermann reaction. Ten months before was "positive". Four months before was "negative".

Luetin reaction. Negative. Showed reddening and induration till the fourth day, when these signs had almost disappeared.

25./
25. Driver Banks.

History. Infection four years and a month ago. 

Treatment. Full mercurial course - 27 gr. mercury.

Two injections of salvarsan given subsequently, owing to Wassermann reaction being positive.

Wassermann reaction.

Fifteen months before - was "positive".

Three months before - was "negative".

Luetin reaction. Positive.

A red indurated papule appeared on the first day. On the second there were signs of commencing pustular change in the centre and on the fourth day a pustule had formed which broke down, and on the tenth crusts were seen to have formed with a ring of reddening round extending to about 5 m.m. This gradually faded. Three weeks after a scab was still present at the point of inoculation and some induration round it.


History. Infection three years ago. Sore on scrotum and hard sore under penis. Roseolar rash on trunk and extremities.

Treatment. Not started till five months after infection. A full course of mercurial injections - 27 gr. Two injections of salvarsan.

Wassermann/
Wassermann reaction.

Ten months before inoculation - "positive".

Three months before inoculation - "negative".

Luetin reaction. Negative. Slight induration for three days. No reddening.

27. Driver Tyler.

History. Contracted two years and four months before inoculation. Hard sore on prepuce. Glands generally enlarged. Roseolar rash on trunk.

Treatment. Twenty-one grains of Mercury in injections. Salvarsan fourteen months before inoculation.

Wassermann reaction.

Twelve months before inoculation - "weakly positive".

Three months before inoculation - "negative".

Luetin reaction. Negative.

On the second day reddening and induration were present at the site of inoculation. On the fourth these signs had lessened and on the fifth day they had disappeared.


History. Infected nine years ago and treated at the time by Mercury pills. At present suffering from a doubtful condition of the hip-joint, provisionally diagnosed as "Charcot's" disease from the disorganised appearance of the joint on X-ray examination.

Wassermann/
25.

**Wassermann reaction.** "Doubtfully positive".

**Luetin reaction.** Negative.

Induration for three days. No reddening.

29. **David Peter.** Ward 31, R.I.E. (Control case)

**History.** A year ago a swelling appeared in his neck. Others have since appeared in the neck and the left axilla. On removal by frequent operations they were found to be sarcomatous.

No history of syphilis.

**Luetin reaction.** Doubtfully positive.

Reddening and induration appeared on the first day after inoculation. On the second day there was some oedema surrounding the site of inoculation. On the third day both reddening and oedema were less. On the tenth day, a pustule had appeared at the inoculation site which, by the twelfth day, had broken and a scab formed. Patient stated that he scratched his arm and the reaction certainly looked a little brighter in colour than the usual "torpid" reaction.

30. **Russell Scott.** Ward 31, R.I.E. See previous case, No.1, with weaker Luetin.

**Luetin reaction.** Negative. No reddening and slight induration for three days.

31. **Sergeant Miller.** Military Hospital, Edinburgh

**History.** Suffering from Interstitial Keratitis, possibly congenital as he has no history of specific disease/
disease. Thinks it was due to cigarette ash blowing into his eye. It started three months ago.

Treatment. No previous anti-syphilitic treatment.

Wassermann reaction. 'Positive' 3 weeks after test.

Luetin reaction. Positive.

An indurated red papule appeared at the inoculation site the day after injection. This showed a white centre on the fourth day and then the reactive signs seemed to lessen, but reappeared a fortnight after, when a pustule developed, broke, crusted and went on to the formation of a scab which was present three weeks after.

32. Private Lovie. Military Hospital, Edinburgh.

(Control case)

History. Suffering from scalding of the legs with septic change. No history of syphilis and no anti-syphilitic treatment.

Luetin reaction. Negative.

Slight induration and reddening at the control site for four days.

33. Corporal Pemberton. Military Hospital, Edinburgh.

(Control case)

History. Suffering from fractured fibula. No history of syphilis and no anti-syphilitic treatment.

Luetin reaction. Was quite negative. Slight induration, but no reddening was present at the inoculation site for three days.

34. Private Ewart. Military Hospital, Edinburgh.

(Control case)

History/
Photograph showing the state of the same reaction a fortnight after. There was still discolouration and swelling.
Second Artist's water-colour sketch to illustrate case

No. 35. Tabes. It shows the reaction as seen on the third day. It was the most vigorous reaction obtained and confirms Wolfschon's statement as to the emphatic character of the positive reaction when obtained in Tabes. This was one of the two cases in which slight constitutional disturbance took place.
History. Admitted suffering from a sprained ankle. No history of syphilis and no anti-syphilitic treatment. Luetin reaction. Was negative. Slight induration but no reddening was present at the inoculation site for three days.

35. James Prentice. 47. Ward 31, R.I.E.

History. Six years ago he began to have trouble with walking and has since then developed the typical symptoms of Locomotor Ataxia.

Had syphilis twenty-three years ago, but no anti-syphilitic treatment.

Wassermann reaction. "Absolute positive".

Luetin reaction. Markedly positive.

On the first day of inspection there was slight redness and swelling at the inoculation site. On the second day there was some oedema round this. On the third day there was the appearance which Howard Fox described in some of his reactions, of "an incipient furuncle" with a yellow spot on the surface, which broke on the fourth day and became crusted. The whole reaction was about one inch in diameter with some lymphangiectasis around.

In his case a slight constitutional change was observed. On the second day of inspection a rise in the axillary temperature to 99°F. was observed from an average temperature previously of 97.4°. It was 98.6°F. on the third day and on the fourth day again 99°F./
99°F. It returned to 97.4° on the fifth day.

It is instructive to compare this case with the two following, which were done on the same day in succession to No. 35 as control cases, absolutely the same methods being used.


History. Complained of rheumatic pains in the right shoulder joint. No history of syphilis and no anti-syphilitic treatment.

Luetin reaction. Negative.

No reaction was observed. Slight induration was present at the inoculation site for three days, but no redness.

37. David McRoberts. Ward 31, R.I.E. (Control case)


Luetin reaction. On the first day there was some redness and oedema round the inoculation site which suggested the haemolytic change which I have seen occurring in doing the haemolytic test for carcinoma which Elsberg, of New York, introduced three years ago. On the second day of inspection this had almost disappeared. On the third day there was no trace of the reaction. Reaction - Negative.

38. James Inglis. 25. Ward VA.

History. Sore on penis six years ago. This was not/
not well treated. Numerous ulcers, the result, apparently, of a rupial eruption, appeared on various parts of the trunk four to five weeks before inoculation.

**Treatment.** Had Neo salvarsan three days before inoculation.

**Wassermann reaction.** "Doubtful positive" - § lysed after 24 hours - four days before Luetin inoculation.

**Luetin reaction.** Was negative on the second and fourth days after inoculation, and as long as he was under observation.


**History.** Sore on penis nine years ago, was treated with boxes of Mercury pills. Five years ago a rupial eruption appeared on his body. Five months ago the eruption appeared again.

**Treatment.** No constitutional treatment.

**Wassermann reaction,** was not done before inoculation.

**Luetin reaction.** Negative on second and fourth days of inspection, and as long as he was under observation.


**History.** Infected 5-6 weeks ago. Sore on penis. Macular rash on body. Condylomata and sore throat.

**Treatment.** Neo salvarsan three days before inoculation.

**Wassermann reaction.**

Three days before inoculation "absolute positive".

Ten days before inoculation "absolute positive".

Luetin/
Luetin reaction.

Negative on second and fourth days of inspection, and as long as he was under observation.

41. Private Wright. Military Hospital, Edinburgh.


Treatment. Course of mercurial injections. Two injections of salvarsan eleven months ago.

Wassermann reaction. Three months before inoculation negative.

Luetin reaction. Negative.

Slight reddening and induration at inoculation site twenty-four hours after, but these signs disappeared in four days.

42. Private Jamieson.

History. Contracted disease three years and two months before. Primary sore, small, on dorsum of prepuce. Lymphatic glands generally enlarged. Mucous patches on pharynx and at angle of mouth. Tonsils congested. Rash on trunk.

Treatment. Eleven months before inoculation had had 36 grains of mercury in injections of one grain weekly. Two injections of salvarsan two months and one month before inoculation respectively.

Wassermann reaction. Three months before inoculation, "positive"/
"positive".

Luetin reaction. On first day of inspection a definite papule was seen, with a whitish centre. On the second day of inspection this was more pronounced. Up till the fourth and on the seventh day the character of the reaction was that of a papule with a vesicle in the centre.


Treatment. Has had a course of mercurial injections - 27 grains of mercury - and two injections of salvarsan, nine and eight months before inoculation. Wassermann reaction. A month before inoculation was "negative".

Luetin reaction. Positive.

On the second day there was a distinct reddened papule with a whitish centre. Up till the fourth day and on the seventh day the reaction was in the form of a papule with a vesicle in the centre.

44. Private Lloyd. Military Hospital, Edinburgh. History. Contracted disease three years and two months before. Primary sore on penis. Glands enlarged generally. Macular rash on skin. Patches on/
on tonsils. In spite of a course of 29 grains of mercury by injection, a tertiary ulcer appeared on the forehead four months before inoculation, but this healed after two doses of salvarsan.

Treatment. As above: salvarsan was given four and three months before inoculation.

Wassermann reaction.

Four months before inoculation - "positive".

Luetin reaction. Negative.

Slight reddening and induration at inoculation site twenty-four hours after inoculation. These signs disappeared in four days.

The next series of sixteen cases was done at the Royal Edinburgh Asylum, West House. Thirteen of these were diagnosed as general paralysis of the insane, one as cerebro-spinal lues, one as chronic mania with a history of lues, and one as an alcoholic paranoia also with a history of lues.

45. Thomas Service. 37.

History. Two years in the asylum. Grandiose ideas, marked slurring speech, muscular tremors, is now an advanced case of general paralysis of the insane.

Treatment. No antisyphilitic treatment.

Wassermann reaction. In the case of blood and cerebro-spinal fluid was "partially positive". Another test, eight days after inoculation, was positive to the extent of fifteen doses.

Luetin/
Luetin reaction. Negative.

On first day of inspection the inoculation site showed redness and some induration. On the fourth day of inspection the redness had disappeared, and only some induration was felt. This was still felt on the seventh day but had almost disappeared.

46. Hugh McFarlane. 43.
History. Two years ill. Slurring speech, muscular tremors, depression, control of organic reflexes impaired. No scars on genitalia or signs of old lues.

Treatment. No anti-syphilitic treatment.

Wassermann reaction. "Positive in blood and cerebrospinal fluid" a month before inoculation.

Luetin reaction. Negative.

Redness at site of inoculation was observed on first day of inspection. Some ecchymosis was seen round this on the fourth day of inspection. On the seventh there was nothing to be seen or felt.

47. James Mothersole. 41.
History. Ill for two years. Had a chancre twenty years ago, treated with black wash. No secondaries, excitable, talkative but incoherent and rambling. Left pupil shows Argyll-Robertson phenomenon.

Treatment. No anti-syphilitic treatment save that mentioned above.

Wassermann/
Wassermann reaction. "Positive" in blood and cerebro-spinal fluid, to the extent of "twelve doses".

Luetin reaction. Positive.

A red indurated papule was present on first day of examination, with a white point in the centre. On the third day this was more pronounced. On the fifth day a red papule was still present. On the seventh day it had almost faded away.

48. William Geddes Houston. 33.

History. Ill for two years. Served in army. Tongue tremulous, speech thick, gait ataxic.

Treatment. No antisyphilitic treatment.

Wassermann reaction. Six months before inoculation was "positive" in blood. Eight days after inoculation another test was positive to the extent of thirty doses.

Luetin reaction. Negative.

Very slight redness with induration seen on first day of inspection. Both these signs had disappeared on the third day of inspection.

49. George Aikman. 29.

History. Subject to grandiose ideas and excitable. Admitted to asylum after an outburst, the result of sexual intercourse with his fiancée - who had been treated for lues and a gumma of the breast.

Treatment. No antisyphilitic treatment.

Wassermann/
Wassermann reaction. Two and a half months before inoculation, was "positive" though "not well marked" in the cerebro-spinal fluid. In the blood it was negative.

Luetin reaction. Was positive.

Showed redness on first day of examination.

On the fifth day quite a definite red papule was present. On the seventh day a white centre could be seen. The day after inoculation the axillary temperature rose to 99.8° in the evening but returned to the normal on the succeeding morning. No other signs were noted.

50. Albert Hughson.

History. Had lues. His affection started with speech difficulty. Has also muscular weakness and tremors. Gait affected.

Treatment. No antisyphilitic treatment.

Wassermann reaction. In blood "positive to five doses", in cerebro-spinal fluid "positive to ten doses". Eight days after the inoculation another test showed a positive reaction to the extent of twelve doses.

Luetin reaction. Doubtful.

On first day of inspection there was no redness but slight induration. On the third day of inspection there was what might be described as a "slight wheal" but no redness. On the fifth day this induration was/
was fading and no redness present.


**History.** General paralysis started three to four years before. Muscular weakness. Ataxia. Absence of reflexes and speech difficulties present. No history of syphilis.

**Treatment.** No antisyphilitic treatment.

**Wassermann reaction.** Distinctly "positive in blood and cerebro-spinal fluid".

**Luetin test.** Positive.

On first day of inspection a red papule was seen. On the third day of inspection a distinct white centre to the papule had formed. On the fifth day of inspection the whole reaction had faded slightly. On the seventh day it had almost completely faded but there was still some induration present.

52. David Hood.

**History.** Admitted as a case of Toxic Insanity which passed into a state of mania. As his pupillary reactions are becoming sluggish and the Wassermann "tends to become positive", the diagnosis is veering towards that of General Paralysis of the Insane. He does not admit syphilitic disease.

**Treatment.** No antisyphilitic treatment.

**Wassermann reaction.** Was "positive in cerebro-spinal fluid but partial in the blood". Eight days after inoculation/
inoculation another test showed a positive reaction to the extent of seven doses.

**Luetin reaction.** Negative.

Slight redness and indurations were present on the first day of inspection but these signs had almost faded by the fifth.

**53. James Muir.**

**History.** General paralysis of the Insane in the third stage. No history of lues.

**Treatment.** No antisyphilitic treatment.

**Wassermann reaction.** In blood and cerebro-spinal fluid, was "positive to the extent of 15 doses".

**Luetin reaction.** Positive.

On the first day of inspection a reddish papule was seen with a white centre. On the third day this was seen to be more distinct in character and was pustular in character on the fifth day. On the seventh day the redness round about had faded slightly.

**54. Thomas Oswald.**

**History.** General paralysis of the Insane. Has had several "congestive" attacks. No history of syphilis.

**Treatment.** No antisyphilitic treatment.

**Wassermann reaction.** "Positive in blood and cerebro-spinal fluid to the extent of ten doses".

**Luetin reaction.** Positive.

On first day of inspection a papule with a white centre/
centre was observed which grew more marked in character till the fifth day of inspection, when it began to fade.


History. Case of advanced general paralysis. Cannot give a good history. Has been a sailor.

Treatment. No antisyphilitic treatment.

Wassermann reaction. "Positive to the extent of ten doses in the cerebro-spinal fluid, to the extent of five in the blood". Eight days after inoculation another test was positive to the extent of 15 doses.

Luetin reaction. Negative.

Slight redness and slight induration which had almost faded on the fourth day of inspection.

56. Thomas Scott. 10.

History. Case of congenital syphilis - his mother being a patient of the same asylum and suffering from general paralysis.

Had congestive attacks four years before. Has now deficient mentality and commencing optic atrophy.

Treatment. No antisyphilitic treatment.

Wassermann reaction. Markedly "positive in brain and spinal cord to the extent of fifteen doses".

Luetin reaction. Positive after eight days. No signs were observed till the seventh day of inspection when a red indurated papule about 10 m.m. in diameter made its appearance.

This/
This case is interesting from the fact that a Luetin reaction done some time previously was said to be negative.

William Watson. 39.

**History.** Ill for seventeen months. Has had, in addition to the usual symptoms of general paralysis, congestive seizures. Has well-marked scars from tertiary ulcers on the legs.

**Treatment.** Has had several courses of mercurial inunction with Potassium Iodide internally.

**Wassermann reaction.** "Positive in blood and cerebro-spinal fluid" a month before inoculation. Eight days after inoculation another test showed a positive reaction to the extent of seven doses.

**Luetin reaction.** Positive.

Redness appeared at inoculation site a day after. On the third day there was a whitish centre to a red indurated papule. On the fifth day this was more pronounced. On the seventh day, the reaction was seen to be fading.

58. Benjamin Wyllie. 30.

**History.** A case of cerebro-spinal lues with a moderate degree of dementia.

**Treatment.** Has had courses of mercury and potassium iodide but not for six months.

**Wassermann reaction.** Practically negative.

"Partially positive to the extent of four doses in blood/
blood and cerebro-spinal fluid."

**Luetin reaction.** On first day of inspection a red papule was present. On the third day a definite pustule was present which increased in size till the fifth, when it broke. On the seventh it was still a red indurated area with a crusted centre.

59. **John Kinchin.**

**History.** Admitted four years before. Diagnosed as chronic mania. Had an attack of mania seventeen years before.

Admits a soft chancre. Has commencing optic atrophy.

**Treatment.** No antisyphilitic treatment.

**Wassermann reaction.** Negative in blood and cerebro-spinal fluid. Another test eight days after inoculation showed no reaction in cerebro-spinal fluid, but one of +5 in the blood. Practically a negative reaction according to the pathologist.

**Luetin reaction.** Positive.

On the first day of inspection a papule was seen to be present. On the third day a yellow centre appeared, which was more marked on the fifth day of inspection and was definitely pustular in character on the seventh.

60. **David Mitchell.**

**History.** Diagnosed as suffering from alcoholic paranoia but admits an untreated chancre thirty-seven years/
years ago.

Wassermann reaction. Negative.

Luetin reaction. Negative.

Redness and induration appeared on the first day but had quite faded by the fifth day of inspection.

Summary of results.

Of the eleven cases of the First Series:-

One case, No. 10, gave a torpid reaction without the formation of a pustule.

Two were doubtful.

Eight were negative.

Of the forty-nine cases of the Second Series:-

Eight gave papular reactions.

Eight gave pustular reactions.

One on the 12th day gave the torpid pustular reaction as described by Noguchi.

One gave a torpid, papular reaction on the eighth day of inspection.

One gave a papular reaction which faded, and a fortnight after inoculation, a torpid pustular reaction/
reaction appeared.

One gave a doubtful reaction.

Twenty-nine were negative.

Summary of own results in definite affections.

Primary syphilitic cases. None were tested.

Secondary syphilitic cases. Out of ten cases, two showed a positive Luetin reaction and all gave a positive Wassermann reaction.

Tertiary syphilitic cases. In three cases there was no Luetin reaction, all gave a positive Wassermann reaction.

Latent syphilitic cases. In seventeen cases, seven gave a positive Luetin reaction, seven gave a positive Wassermann reaction. In eleven cases the reactions confirmed each other, i.e. 64%.

Congenital syphilis. In three cases, one doubtful positive, and two positive Luetin reactions were obtained. All gave a positive Wassermann reaction.

Parasyphilitic cases. Fifteen cases were tested. Thirteen cases of general paralysis gave seven positive Luetin reactions and one doubtful - 53% positive. These gave eight positive Wassermann reactions - 61% positive.
Two cases of locomotor ataxia gave one positive and one negative result to both Luetin and Wassermann tests.

60% of the Luetin and Wassermann reactions corresponded in parasyphilitic conditions.

Cerebro-spinal lues.

The one case tested gave a very definite reaction but from it one could not confirm Ladislaus Benedek's hypothesis that this condition gives a more pronounced reaction than general paralysis. It seemed to be much the same as those obtained in general paralysis.

In eight cases in which no syphilitic history could be obtained, only one gave a doubtful positive result with Luetin.

Experience of other workers with the Luetin Test.

Noguchi's own results were to obtain a high percentage of positive results in tertiary, latent, and congenital syphilis. He obtained:-

Primary syphilitic cases. One positive result out of five.

Secondary syphilitic cases. 58% positive results.

Tertiary syphilitic cases. 96% positive results.

Latent syphilitic cases. 80% positive results.

Congenital syphilis. 95% positive results.

Parasyphilitic cases. 50% positive results.

In normal cases he had no positive results.

These/
These were not compared with the Wassermann reaction.

Nobl and Fluss obtained these results:

**Primary syphilitic cases.** Two positive out of seven cases.

**Secondary syphilitic cases.** 33% positive results.

**Tertiary syphilitic cases.** One positive result in the one case of tertiary gumma inoculated.

**Latent syphilitic cases.** 56% positive results.

**Parasyphilitic cases.** Two positive results in two cases.

**Congenital syphilis.** One positive result out of three cases.

Three cases out of nine supposed non-syphilitic subjects gave a positive result. Three of these gave a reaction of a doubtful character.

Amongst all the types of syphilis mentioned above, they had a considerable number of doubtful results.

Ziegel found that in hereditary and tertiary syphilis he obtained more than 90% positive reactions, corresponding to 76.78% positive Wassermann reactions.

Gradwohl found that:

**Primary syphilitic cases.** In two undoubted primary cases the Wassermann reaction was positive in both, the Luetin test negative.

**Secondary syphilitic cases.** One out of three cases gave/
gave a positive Luetin reaction. All three gave a positive Wassermann reaction.

**Tertiary syphilitic cases.** 85% gave a positive Luetin reaction. 50% gave a positive Wassermann reaction.

Seven cases only were tested.

**Latent syphilitic cases.** 40% gave a positive Luetin reaction. 20% gave a positive Wassermann reaction.

Five cases were tested.

**Parasyphilitic cases.** 66% Luetin reactions were positive. 100% Wassermann reactions were positive.

In normal cases no positive Luetin results were obtained.

**Daisy Orleman Robinson:**

**Primary syphilitic cases.** No Luetin reaction obtained. 75% positive Wassermann reactions.

**Secondary syphilitic cases.** 57% positive Luetin reactions. 40% positive Wassermann reactions.

**Tertiary syphilitic cases.** 100% positive Luetin reactions. 10% positive Wassermann reactions.

**Congenital syphilis.** 100% positive results with both Wassermann and Luetin reactions.

In non-syphilitic cases no positive Luetin reactions were obtained.
Howard Fox:-

Secondary syphilitic cases. Luetin reaction positive in 40% cases. Wassermann reaction positive in 100% cases.

Tertiary syphilitic cases. Luetin reaction positive in 60% cases. Wassermann reaction positive in 85% cases.

Latent cases. Luetin reaction positive in 47.8% cases. Wassermann reaction positive in 60.8% cases.

He did not find any correspondence between the degree of the Wassermann reaction and doubtful Luetin reactions.

J. M. Wolfschohn.

Secondary syphilitic cases. Luetin reaction positive in two cases tried. Wassermann reaction also positive in the two cases.

Both cases were in the stage of the maculopapular rash.

Tertiary Syphilitic cases.

Luetin reaction positive in five cases out of six. Wassermann reaction positive in five cases out of six.

Parasyphilitic cases.

Luetin reaction, 18 positive reactions out of 19. Wassermann/
Wassermann reaction, 10 positive reactions out of 19.
Wolfsohn was impressed by the violent character of the reaction in tabes. This I can confirm.

**Latent syphilis.** Luetin reaction positive in 100%. Wassermann reaction positive in 40 - 70%.
Twenty-four cases being tested.

**D. T. Kaliski.**

**Primary & Secondary syphilitic cases.**
Luetin reaction positive in 10% cases. Wassermann reaction positive in 60% cases.

**Tertiary syphilitic cases.**
Luetin reaction positive in 63% cases. Wassermann reaction positive in 76% cases.

**Latent syphilis.** Out of seven cases, the Luetin reaction gave no result, the Wassermann reaction four positive results.

**Congenital Syphilis.**
Luetin reaction gave 1% positive results. Wassermann reaction 10% positive results.

**Parasyphilitic cases.**
Luetin test gave 9% positive results. Wassermann test gave 50% positive results.

**Cerebro-spinal lues.** Luetin test gave 30% positive results.
results. Wassermann test gave 84% positive results.
Amongst control cases, while he obtained no positive Wassermann result, he had twelve cases out of 250 which reacted positively to the Luetin.

G. R. Foster.
The most recent results:
Secondary syphilitic cases. 77% reacted positively to the Luetin test.
Tertiary syphilitic cases. 80% positive Luetin reactions.
Latent Syphilis. 88% positive Luetin reactions.

Ladislaus Benedek.
Tested 81 cases of general paralysis and had 65 positive results - 80.4%.
In three cases of cerebral syphilis, he obtained an exceedingly well-marked reaction and offers it as a means of differential diagnosis between this condition and general paralysis. I cannot confirm this.

Consideration of work done with the Luetin reaction.
There can be no doubt that this reaction is entirely connected with the effects of the Luetin and is not due to septic infection at the needle-puncture. This/
This is borne out by the series of syphilitic and non-syphilitic cases done at the same time.

In no case was the reaction centred round the needle-puncture, but in all cases it was developed exactly where the injection had raised the surface layers of the skin.

One has no difficulty in agreeing with the manifestations in the pustular and torpid forms of the reaction which Noguchi described, but it is difficult to be certain of the form he describes as papular. Different observers may easily obtain different results by interpreting leniently or exclusively the change which occurs after injection at the inoculating site. One's experience with the reaction Elsberg introduced, in which normal human serum was injected subcutaneously and the results noted in carcinomatous and other cases, leads one to pass over some of the appearances as being quite non-syphilitic in production and due to some haemolytic or other change. In preparing the above results, the candidate took up the exclusive attitude and this may account for a lower percentage of positive results than has been obtained by the American workers, except Howard, Fox and Kaliski.

Again, one feels that an uncertain element is introduced in so far as the emulsion does not seem to be standardised precisely. The dosage of .07 c.c. of luetin gave a series of much clearer reactions than .035/
.035 c.c. luetin and the same quantity of saline solution. One is inclined to think the Luetin sent must have been weaker than that originally used by Noguchi and the emulsion sent to Ziegel.

**Effects on the Patient.**

The patients did not complain of any pain or discomfort locally, and in only two cases were there slight constitutional disturbance. The reaction therefore is quite harmless.

**The Value of the Reaction.**

Though the Wassermann reaction is now slighted and no longer regarded as infallible, there can be no doubt from a consideration of the disparity of statistics and one's own experience of the Luetin reaction that it can never take the place of the Wassermann test, which must still remain our surest aid in clinical uncertainty. While the Luetin test is quite simple to use, it takes longer in point of time to arrive at a diagnosis, and it is of very little use in primary and early secondary cases.

**Does it change the Wassermann reaction from a negative to a positive reaction?**

Someone has suggested that this does occur. It is certainly interesting to note that in every case where the Wassermann test was performed (all within a month) after the Luetin test, it was always positive save/
save in one case - No. 59 - where the reaction was + 5 doses - which Dr. Abel informs me is practically negative when we compare it with the reaction obtained in the normal individual of + 5.

Does treatment affect the Luetin reaction?

In five cases of Syphilis absolutely untreated - other than those included under the diagnosis of general paralysis - the reaction was negative. It was difficult to obtain a history of syphilis or its treatment from those suffering from general paralysis, owing to their mental instability.

Four of the five cases dated the infection six weeks, nine years, twenty-three years and thirty-seven years respectively, before the test was applied. The other was a tertiary case in which the date of infection was not ascertained.

Comparison with von Pirquet's reaction.

Compared with such a reaction as that of von Pirquet for Tuberculous disease, it has not the association of so many positive results in cases presumably non-syphilitic. In the few positive reactions so obtained, there has always been the suspicion of a luetic strain. Foster so explained one positive reaction from the fact that the maternal grandmother had been luetic. In spite of such an explanation, the reaction is weakened in importance by these cases. All we can say is that positive results/
results in non-syphilitic cases occur in less than 1%, while von Pirquet's reaction gives more than 50% positive reactions in cases presumably non-tuberculous.

CONCLUSIONS.

1. That the Luetin reaction can never take the place of the Wassermann reaction, which is the most valuable diagnostic test we have in syphilis at present.

2. That the Luetin reaction is of value in confirming the diagnosis by the Wassermann Reaction of cases of Tertiary, Congenital, and Cerebro-spinal syphilis, and of parasyphilitic conditions.

3. That it is quite harmless and produces positive reactions in patients presumably non-syphilitic in less than 1% cases.


3. von Pirquet. The Archives Int. Med. 1911. VII.


