

*On the specificity of Luotest in Leprosy

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Introduction

Meirowsky (1909), inspired by the well studied phenomenon of allergic reactions in tuberculosis (Tuberculin test) tried to develop a similar skin test for syphilis. His test material was prepared from human syphilitic organs, and he reported reactions obtained in syphilitics similar to those of the Tuberculin test.

Numerous authors contributed to this subject, but results were equally confirmatory and contradictory, thus not permitting a proper judgement of this test.

The next important improvement was arrived at when Noguchi (1911) freed the preparations from organic matter by preparing a suspension of pure treponemal cultures, which he called Luetin. Again many authors contributed to the subject and summarising their results, the Cultureluetin gave in some way more reliable results than the Organluetin.

But it should be always kept in mind that the skin of syphilitics seems to be more sensitive, even to react with unspecific substances, such as milk, tuberculin, agar, adrenalin, etc. Busacca (1922) when injecting 0,1 ml. sterile gelatine of 37°C reported 207 positive, 41 doubtful and 44 negative reactions obtained on 292 syphilitic patients. The results of the Wassermann reaction were 240 positive and 52 negative.

The judgement is further rendered more difficult as certain drugs, especially compounds of iodine, are able to sensitise a non-syphilitic organism to produce a positive skin reaction with such preparations.

All these results of intensive research may be summarised by stating that Luetin preparations may be of some help in diagnosing cases of late seronegative syphilis, cerebrospinal and hereditary syphilis, but the diagnostic value of Luetin cannot stand a comparison with seroreactions.

Seroreactions may often be influenced by Luetin, as negative reactions may be changed towards positivity after repeated injections (Mueller and Planner, 1921). The authors explain this reversal as a reaction of the Luetin with syphilitic foci in the body, thus stimulating the production of antibodies giving reaction with the antigens used in seroreactions.

The subject has been revived by Rottmann in several reports since 1942, using a preparation obtained from syphilitic rabbit testes named Luotest. Rottmann (1948), Grillmayr (1949), and Csonka (1950) claim high specificity of results, and that diagnosis was arrived at only by help of Luotest in several cases.

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When considering all these facts it should be always borne in mind that they were arrived at from prevalent syphilitic material.

Kaufmann and Wolfram (1950) tested Luotest on a random like material of 770 syphilitic and 200 non-syphilitic patients and were unable to maintain the above claims. They report that Luotest in its different batches was not uniform, and that the skin reactions are to be considered only as moderately specific. Positive readings of reinoculations as well as a reversal of negative seroreactions are not accepted by them as sufficient evidence for the diagnosis of syphilis.

Marshak and Rothman (1951) report their preliminary results of a more purified and standardised preparation, named Treponemin test on 30 patients and 20 rabbits infected with syphilis. Positive readings in man were obtained from secondary syphilis onwards, and in 12 of the 20 rabbits.

Further it is commonly known that there is no strict correlation between immunity of the skin and immunity of the humoral sphere. (Kassowitz 1924, Schmid 1938).

These above referred results were mainly arrived at in countries of moderate climate. Before transferring such results as valid for the tropics with fundamental changes as regards climate, racial composition and diseases (Grillmayr 1950, unpublished paper, read before Sect. A., Ceyl. Ass. of Science), critical investigations should be done to study the local conditions before human beings are labelled to suffer from a social disease.

It seemed therefore to be of interest to study the specificity of Luotest on patients suffering from leprosy, a disease which is known to interfere with the seroreactions of syphilis, especially in the lepromatous type.

Methods

Luotest was supplied by the manufacturer (Federal Serum Institute, Vienna, Austria). The patients suffering from leprosy (Leprosy Hospital, Hendale) were carefully examined for syphilis and paraluic seroreactions (Schmid and Thillainathan, 1951). The seroreactions used were complement fixation (Wyler's technique, 1928), Standard Kahn reaction (1928) and Cardioplipin slide flocculation (Kline 1947) test.

The procedure prescribed for Luotest was strictly followed. Luotest was injected intradermally (0, 2 ml.) on the volar side of the forearm. Reactions were read after 24 and 48 hours. In the material investigated no reaction persisted longer than 48 hours. The injection was repeated on both forearms 6 days after the first injection in the same manner, as well, and the reactions read. Eight days after the second injection, blood was drawn from the patients for seroreactions.

Results

The investigation was done on 175 patients, including 5 cases of syphilis, and 4 cases with a history of yaws. Out of this number, 144 patients without clinical signs or history of syphilis or yaws completed the trial (Table I).

Due to an outbreak of smallpox in the vicinity of the Leprosy Hospital, the number investigated had to be limited to the above 175 patients.

TABLE I

Patients of leprosy without syphilis or history of yaws	144																									
Type of leprosy	69 L					69 N						6 LN														
Seroreactions before Luotest	27 +			42 -			14 +			55 -			4 +		2 -											
Luotest reaction	23 -		1 +	3 trace		29 -		4 +	9 trace		5 -	2 +	7 trace		33 -		11 +	11 trace		3 -	1 +	2 trace				
Seroreactions after Luotest	13 -	10 +	1 -	2 -	1 +	26 -	3 +	3 -	1 +	9 -	1 -	4 +	1 -	1 +	4 -	3 +	31 -	2 +	10 -	1 +	10 -	1 +	3 +	1 +	1 -	1 +

Key: L Lepromatous type of leprosy
 N Neural type of leprosy
 LN Mixed type of leprosy

+ Positive
 - Negative

(Cairo nomenclature, Cochrane 1947).

As traces of Luotest reactions are to be reckoned as negative, the distribution of reactions is shown in table II.

TABLE II

Luotest—reaction Type	Pos. Neg.	
	L	5
N	13	56
LN	1	5

Key—see Table I.

From table II it is to be seen that the neural type of leprosy shows far more positive (18.9 per cent.) Luotest reactions, than the lepromatous type (7.2 per cent.). The latter influences more the seroreactions for syphilis. (Table I and III). With regard to seroreactions, the number of reactors before and after the application of Luotest as well as reversals of seroreactions are given in table III.

TABLE III

Type	Seroreactions					
	Before Luotest		After Luotest		Reversals.	
	Pos.	Neg.	Pos.	Neg.	Pos. to Neg.	Neg. to Pos.
L	27	42	15	54	16	4
N	14	55	12	57	6	4
LN	4	2	5	1	—	1

Key—see Table I.

Table III shows that reversals from seropositivity to seronegativity are more frequently seen, than reversals towards seropositivity. As regards the type of leprosy, the lepromatous type interfering more seriously with the seroreactions shows more reversals of such paralytic seroreactions, than the neural type. In both types, however, reversals towards negativity are prevalent.

Six more patients (4L, 2N) had only the first injection of Luotest, and the final blood test. All were negative for Luotest, and showed no reversal of seroreactions (1 pos., 5 neg.). Fifteen further patients (5L, 9N, 1 LN) had both injections of Luotest, but were missing when the blood was to be drawn. Five of them (2 L seropos., 3 N seroneg.) had a positive reaction of Luotest, and one more patient (N, seroneg.) had only one injection of Luotest with a negative result, thus giving a total of Luotest reactions shown in table IV.

TABLE IV

Luotest—reaction Type	Pos. Neg.		Total
	L	7	
N	16	65	81
LN	1	6	7
Total	24	142	166

Key—see Table I.

Five patients had clinical evidence or history of syphilis (1 L, 4 N). All but one, a treated case of syphilis, were seropositive. One of them had a positive reaction of Luotest as well, and the seroreactions of all patients (1 no rebleeding) showed no change after the administration of Luotest.

Four other patients (2L, 2N) with a history of yaws had 2 positive reactions (1 L, 1 N) with Luotest. Their first seroreactions were all positive, but when rebled, one (N. Luotest pos.) reverted to negativity.

Discussion and Conclusions

It can be seen from the above enlisted material that the neural type of leprosy interferes more with the cutaneous reaction for syphilis (Luotest), than the lepromatous type does. These facts clearly involve the need of a most cautious interpretation, and at least when Leprosy is involved, Luotest is deprived of its claimed specificity. In leprosy a reversal of paraluic seroreactions towards negativity is more frequently encountered, than a reversal towards seropositivity. These facts cannot support any specific influence of Luotest as regards a specific stimulus producing antibodies in the humoral sphere then reacting with the antigens for seroreactions, when leprosy is concerned, as an inhibiting action is seen more frequently.

These results are in full agreement with Kaufmann and Wolfram's (1950) conclusions that Luotest is only moderately specific and that reversals of seroreactions are not sufficient evidence of syphilis.

Further a technical difficulty for extensive trials of field testings is involved, as the patients have to be inspected on 2 or 3 subsequent occasions to read the results after each injection. Even in a hospital such as in Hendala it was found impossible to maintain the initial number of patients during the whole trial. This difficulty multiplies for trials outside a hospital.

It may still be possible to develop a reliable skin test for syphilis using certain standardised methods of preparation as outlined for instance by Marshak and Rothman (1951). Anyhow such tests should be given further trials in the tropics as well as in moderate climates.

Finally it may be mentioned that Luotest was tested in the same manner as sera, but gave negative results with complement fixation, Kahn, Cardioplin and Mueller Ballung (Clotting) tests. A positive (+ + +) reaction was obtained with Meinicke antigen (Meinicke-Kvittingen test, 1948).

Summary

Luotest shows no specificity when leprosy is interfering. The neural type of leprosy was found to interfere more with cutaneous reactions than the lepromatous type. The lepromatous type interferes less with cutaneous reactions, but more with seroreactions, which fact is a well known one.

Paraluic seroreactions are more frequently reverted to seronegativity, than negative reactions are reverted to seropositivity.

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