SENSITIZATION TO TUBERCULIN INDUCED
BY LEPROMIN

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INFLUENCE OF LEPROSY ON THE TUBERCULIN REACTION

The influence of leprosy on the lepromin reaction has been demonstrated and confirmed in many investigations. On the other hand, the influence of *M. leprae* on the tuberculin reaction has not awakened much interest, and the literature on this subject is by no means abundant. Wade⁽¹⁾ has discussed it in a well documented paper, and one of us (J.M.F.) presented his personal experience and views on the occasion of the Third Argentine Congress on Tuberculosis⁽²⁾.

Convit and his associates⁽³⁾ admit that infection by leprosy may interfere in the sensitization to tuberculin. In 1952 they observed persons in contact with lepers in a rural district in Venezuela and found only 8 per cent tuberculin positive cases in lepromin negative individuals and 46.6 per cent in lepromin positive subjects. In a recent paper Convit⁽⁴⁾ confirms his former findings, stating that there are 3 per cent Mantoux positive (D.P.P. 5U) in lepromin negative, and 45 per cent in lepromin positive individuals.

Lowe and McNulty⁽⁵⁾ have studied immuno-allergic relations between leprosy and tuberculosis in natives of Nigeria. Their results, as they themselves point out, are contradictory, because although in anergics to lepromin the percentage of tuberculin positives (59.4 per cent) was lower than in the healthy population (75.2 per cent), it was slightly above that found in cases of tuberculoid leprosy (55 per cent).

Hodler and Zitti⁽⁶⁾ have reported recently the results of their investigations on the influence of *M. leprae*, *M. lepraemurium* and *M. tuberculosis* on sensitiveness to tuberculin in guinea pigs. They have shown that *M. leprae* and *M. lepraemurium* sensitize guinea pigs to tuberculin, with maximum intensity at thirty and sixty days respectively; later sensitiveness declines and disappears. Tuberculin hypersensitiveness induced in guinea pigs by *M. lepraemurium* is the same as that induced by BCG. They conclude that tuberculin hypersensitiveness in guinea pigs inoculated with *M. leprae* and *M. lepraemurium* depends on two factors: (a) the capacity of the macrophages of destroying these bacilli, lysis of which provokes tissue reaction and hypersensitiveness; and (b) the similarity in the chemical structure of some of the antigenic fractions of *M. leprae* and *M. lepraemurium*, which is responsible for cosensitization.

PERSONAL EXPERIENCE

MATERIAL AND METHODS

As the results of previous investigations, carried out by one of the authors of this paper, on the influence of lepromin on tuberculin reaction, were not conclusive, it was decided to repeat the tests, increasing the number of cases.

Observations were made in a group of eighteen children, aged 3 months to 8 years, lodged in a home, and who had had no known contact with lepers; they were Mantoux negative at 1 : 10.

Crude tuberculin, prepared at the Malbran Institute of the National Ministry of Health, was used in concentrations of 1 : 1,000, 1 : 100, and 1 : 10. Two types of lepromin, both prepared by Dr. A. Serial and A. R. Mercau, were used: (a) bacillary, obtained by chloroform extraction according to Dharmendra's method; (b) whole, prepared by the Mitsuda-Hayashi method.

A single intradermal injection, in doses of 0.1 to 0.2 c.c., in the right scapular region, was given in four cases; this was repeated at 48-hour intervals, once in twelve cases and twice in two cases. Sensitiveness to tuberculin (Mantoux 1 : 10) was tested from the third week after the injection of lepromin, and periodically after that. However, for reasons outside our control, this could not be done at regular intervals in all cases as had been planned in order to determine exactly at what moment the Mantoux reaction became positive.

Cases classified as tuberculin negative were given a Mantoux test for at least three months following the lepromin injection, except in one instance in which the child was withdrawn before this period was up. The Mantoux reaction was read at 24 and 48 hours, the latter being considered as the final result. It was taken as positive when an infiltrated erythematous halo of not less than 10 mm. diameter was observed.

RESULTS

Results are given in the Table. In 8 (44.4 per cent) of the 18 cases the negative Mantoux became positive after the lepromin injection. The majority of the cases became positive between the sixth and seventh week after the lepromin injection; one became positive in 20 days, and in another, which could not be tested regularly, a positive Mantoux was seen only after 130 days.

Positive Mantoux reactions following lepromin injection are similar in appearance and evolution to those induced by BCG vaccination. Reactions of erythematous or erythematous-violaceous type, with discrete infiltration, predominated. Frequently erythema was more marked at 24 than at 48 hours. In all cases, except Nos. 1 and 2, positivity was slight. In several cases an erythematous halo without infiltration was observed; there were considered as negative.

In those cases in which it was possible to follow the course the course of tuberculin allergy it was found to be transitory, since

after a few weeks the reactions became negative.

To illustrate the findings notes corresponding to some of the cases included in the Table are given here:—

No. 1

Maria P., aged 2 years 6 months. Routine clinical and X-ray examination: negative.

- 8.11.1951: Mantoux 1 : 10 negative (-).
- 27.11.1951: 0.2 c.c. whole lepromin intradermally.
- 30.11.1951: do.
- 27.12.1951: Mantoux 1 : 10, negative (-).
- 10. 4.1952: Mantoux 1 : 10 positive (+).
- 21. 4.1952: Mantoux 1 : 10 positive (+). In the scapular region two scars corresponding to the Mitsuda reaction (++) were observed.
- 21. 5.1952: Mantoux 1 : 10 positive (+). Clinical and X-ray examination, normal.
- 21. 6.1952: Mantoux 1 : 10 negative (-).
- 5. 7.1952: Mantoux 1 : 10 negative (-).

Note: The Mantoux may have become positive before April, 1952; the child left the home in December and did not return till April.

No. 2

Stella A., 1 year old. Routine clinical and X-ray examination, negative.

- 9. 3.1952: Mantoux 1 : 10 negative (-).
- 10. 4.1952: 0.2 c.c. whole lepromin intradermally.
- 12. 4.1952: do.
- 22. 5.1952: Mitsuda positive (++) . Mantoux 1 : 10 negative (-).
- 5. 6.1952: Mantoux 1 : 10 negative (-).
- 21. 6.1952: do.
- 5. 7.1952: do.
- 22. 7.1952: do. Erythematous halo without infiltration.

No. 4

Rodolfo S., 6 years old. Routine clinical and X-ray examination, negative.

- 8.11.1951: Mantoux 1 : 10 negative.
- 24.11.1951: 0.2 c.c. whole lepromin intradermally.
- 27.11.1951: do.
- 30.11.1951: do.
- 11.12.1951: Mitsuda positive (++) . Mantoux 1 : 10 negative (-).
- 4. 1.1952: Mantoux 1 : 10 negative (-).
- 25. 3.1952: do.
- 17. 4.1952: do.
- 5. 6.1952: do.

No. 17

Mario P., Argentine. Routine clinical and X-ray examination, negative.

- 8.11.1953: Mantoux 1 : 10 negative (-).
- 30.11.1953: 0.1 bacillary lepromin intradermic.
- 18.12.1953: Mitsuda positive (++) . Mantoux 1 : 10 negative (-).
- 12. 1.1954: Mantoux 1 : 10 positive (+).
- 17. 3.1954: Mantoux 1 : 10 doubtful ($\pm$). Erythematous halo without infiltration.

DISCUSSION

Before discussing the results it is necessary to acknowledge several deficiencies in this investigation. The weakest point is the insufficient control of the course of tuberculin allergy following

lepromin injection; but in children it is not always possible to repeat the tests at as short intervals as they should be. This did not allow accurate determination of the length of the pre-allergic period between the injection of lepromin and the establishment of a positive Mantoux reaction, or of the duration of sensitiveness to tuberculin. In the majority of the cases in which the negative Mantoux became positive, it did so six to seven weeks after the intradermal injection of lepromin. The Mantoux again became negative after a few weeks, but it is not possible to state exactly when it did so. Possibly the number of cases showing a positive Mantoux following lepromin would have been greater if the tests had been carried out more often.

The standard for assessing results of tuberculin tests in work such as is here reported is of decisive importance, but sometimes of difficult application. If the usual standard for classifying erythema and infiltration as positive or negative is strictly adhered to, it is obvious that some reactions do not fulfil the conditions necessary to be considered as positive, yet are not exactly negative. It is certain that some change has been provoked in the organism, but this is not sufficient to be computed in the final result. In this series often the manner of response changed after lepromin injection, but the magnitude or intensity of this change was not sufficient to consider the reaction as positive. Attention should be drawn here to the fact that Long and Favour⁽⁷⁾ consider a tuberculin test as positive when there is some change in the response (erythema or infiltration), whatever its degree, at the site where the antigen has been inoculated.

It is possible that *M. leprae* can induce sensitiveness to tuberculin with greater frequency and intensity than has been observed in the series here reported, in which small quantities of dead bacilli have been used. If, instead, adequate amounts of live bacilli were inoculated, it is almost certain that the proportion of tuberculin positive reactions following inoculation would be greater than that observed after lepromin has been injected. This occurs when *M. tuberculosis* is inoculated; live bacilli (virulent or attenuated) have greater sensitizing activity than dead bacilli.

Owing to the deficiencies of this investigation, striking results have not been obtained. It is possible to state, however, that following intradermal injection of whole lepromin, more than 40 per cent of tuberculin negative cases become tuberculin positive.

SUMMARY

A group of eighteen children, from 2 months to 8 years years old, living in a home without any known contact with lepers,

having a Mantoux 1 : 10 negative, was given 1 to 3 intradermic injection of 0.1 to 0.2 c.c. bacillary and/or whole lepromin. The following results were observed: in 44.4 per cent of the cases the negative Mantoux became positive in six to seven weeks following the injection of lepromin. The appearance and course of the positive tuberculin reaction was similar to that induced by BCG vaccination. In the majority of cases this tuberculin allergy was weak and of short duration.

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Name	Age	Lepromin Used	No. of injections	Result of the lepromin reaction		Result of the Mantoux in days after lepro- min injection
				F*	M	
1—P.M.	2 years	Whole	2	—	++	+130
2—F.M.	5 years	"	3	—	+	+20
3—S.E.	8 months	"	2	—	±	+40
4—S.I.	6 years	"	3	—	+	—240
5—A.S.	1 year	"	2	—	+	—90
6—A.M.	2 years	"	2	—	+	+42
7—L.A.	5 months	"	1	—	—	—100
8—M.R.	2 y. 6 m.	"	2	—	—	—90
9—B.J.	2 years	"	2	—	+	+42
10—W.V.	6 years	"	2	—	—	—90
11—H.S.	4 years	" & bac.	2	—	+	—90
12—S.	6 years	" "	2	—	+	—90
13—S.J.	5 years	" "	2	—	+	—47
14—H.M.	6 years	" "	2	—	+	—50
15—S.B.	5 years	" "	2	—	+	—90
16—M.J.		Bacillary	1	—	—	—90
17—P.M.		"	1	—	—	+47
18—D.S.		"	1	—	—	+47
19—V.F.		"	1	—	+	—42

* F=Early reaction. M=Delayed reaction.

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