

LEPROMIN TEST IN CONTACTS, WITH PARTICULAR
REFERENCE TO POSITIVE BACTERIOLOGICAL
FINDINGS

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Within the past two decades numerous publications have appeared describing the lepromin test and discussing its significance in leprosy cases and in other connections. Various workers have departed from the original (Hayashi) method of preparing lepromin with a view to improving the antigen, the most recent variety being Dharmendra's defatted bacillus suspension (2). In all of this work relatively little attention has been given to the significance of the positive and negative reactions in contacts.

At the clinic of the Acworth Leprosy Home, where contacts of leprosy patients are examined clinically and bacteriologically as a routine, it has been possible to test a number of contacts with the Dharmendra lepromin as made by us, and to observe the results in almost all of those tested.

In a previous paper (3) dealing with the results of the bacteriological examination of contacts who showed no clinical lesions, it was reported that 25 were found positive for acid-fast bacilli in smears made from the skin. Our finding of bacilli in such individuals has subsequently been confirmed by Dr. V. R. Khanolkar (5), who found the bacilli in sections prepared from skin biopsy specimens of some of the contacts.

Recently, Bose, Hadler and Sen (1) repeated this work in contacts at the Leprosy Department of the School of Tropical Medicine in Calcutta, and failed to confirm our findings. They, however, used the slit method of obtaining material for examination and not the deep biopsy method described by us.

In our paper referred to, it was mentioned that 9 of these contacts were tested with defatted lepromin and that all of them gave positive reactions. No test, however, had been made at that time of contacts who were negative for bacilli. Subsequently we have attempted to test as many contacts as possible, and the present paper records the results of the test in contacts without clinical lesions examined during the year 1949, with particular reference to positive findings of bacilli in the skin.

METHOD

The Dharmendra type of lepromin was used, 1 mgm. of the dried extracted bacilli in 10 cc. of a 0.5 per cent solution of phenol in saline. This preparation was injected in doses of 0.1 cc. into the skin of the forearm. The results were observed after 24 and 48 hours, and 1, 2 and 3 weeks. Every time a fresh stock of the lepromin was prepared it was first tested on tuberculoid and lepromatous cases of leprosy. Examples of the results of such preliminary tests are given:

1. M. K., male, age 25 years. Tuberculoid leprosy, with thick, red, indurated and well-defined lesions; left ulnar nerve enlarged. Bacteriologically negative. Lepromin reaction: Early, erythema with edema 20 mm. in diameter. Late, nodule at the end of the third week, 8 mm., with central caseation.

2. G., male, age 45 years. Tuberculoid leprosy in reaction, with raised, circumscribed, succulent lesions, subsiding under promin treatment. Nerves supplying the lesions were thickened. Bacteriologically positive. Lepromin reaction: Early, erythema with edema, 12 mm. in diameter. Late, nodule at the end of the third week, 5 mm.

3. A. S. K., male, age 20 years. Early lepromatous, with erythematous, nonanesthetic diffuse areas containing large numbers of bacilli. The injected lepromin was completely absorbed within 24 hours; no late reaction occurred.

THE POSITIVE REACTIONS

The early reaction.—A raised erythematous area more than 5 mm. in diameter was regarded as an early positive reaction. The reactions observed measured from 5 to 30 mm. A smaller area around the site of injection was usually more raised than the whole erythematous area, and was edematous. The early positive reactions reached the maximum 24 to 48 hours after the injection, and showed signs of shrinking and centralization into a hard nodule thereafter.

Late reaction.—This reaction consists of a firm nodule, 3 to 10 mm. in diameter, usually reaching the maximum size 3 weeks after the injection. In some of our cases the nodule softened in the center, ulcerated and formed a scab. The nodule of a late positive reaction requires several weeks for complete absorption.

All patients who gave an early reaction also developed the late one. In one case the early reaction was negative, but a late reaction appeared and the case was included among the positives.

BACTERIOLOGICAL EXAMINATION

In all cases the method of preparation and examination of smears was the same as previously described. With regard to taking skin clips, however, a slight modification suggested by Dr. Khanolkar was introduced. This method has been described in an addendum to another article as reprinted (4).

RESULTS OF THE LEPROMIN TEST IN RELATION TO
BACTERIOLOGICAL FINDINGS

The results of the test in contacts in relation to bacteriological findings in smears made from the skin of the same persons are given in Table 1.

TABLE 1.—*Results of the lepromin test in 184 contacts without clinical lesions, with reference to the bacteriological findings.*

Bacteriological status	No. of cases	No. tested with lepromin	Results of the lepromin test		
			Positive	Negative	Not observed
Positive	54	49	42	5	2
Negative	130	62	0	62	—
Totals	184	111	42	67	2

In our second article (4) it was shown that the 25 individuals with positive skin smears were from a total of 254 contacts examined, which gives a frequency rate of 9.8 per cent. That report comprised all cases dealt with in our earlier work, up to 1949. The 184 cases of the present report, of which no less than 54, or 29.3 per cent, were found positive, are those examined in 1949. These examinations are now made more intensively and carefully than at first, and the incisions for the removal of skin specimens are deeper.

It will be seen that of the 54 contacts without clinical lesions from which acid-fast bacilli were found in smears, 49 were tested with lepromin; but the results in 2 could not be observed. Of the 47 that were observed, 42, or 89 per cent, gave positive reactions while only 5 were negative. These negative reactors were all children. Of the 42 positive reactors, 34 were adults and 8 were children.

On the other hand, of the 62 cases whose smears were found negative and who were tested with lepromin, none gave a positive response. However, as will be seen one individual gave different results later.

DEGREE OF LEPROMIN REACTION IN RELATION TO THE
NUMBER OF BACILLI FOUND

The relationships between the number of bacilli found in the skin smears and the results of the lepromin tests are shown in Table 2. It will be noted that the extent of the positive reactions,

whether early or late, was in inverse proportion to the numbers of bacilli found. In practice it was found that the detection of bacilli in strongly positive reactors was much more difficult than in the weakly positive ones, success being attained sometimes only on the third or even the fourth examination.

TABLE 2.—*Relationship of degree of the positive early and late reactions to the numbers of bacilli found in the skin smears.*

Number of bacilli	No. of cases	Size of the reaction in mm.	
		Early	Late
11-25	8	5.6	3.2
6-10	17	12.2	4.5
2-5	17	18.1	7.2

FOLLOW-UP OF CONTACTS

The difficulties experienced in keeping under observation persons who are of normal appearance, and who unlike hospitalized patients have all the liberties of normal citizens, are well-nigh insurmountable. The molestation involved in the snippings of skin and scrapings of the nose that periodical examinations entail militates against the repeated attendance of such individuals. However, it was possible to keep under observation a few of the contacts including some of those involved in our previous report, and as a result the following findings were made.

(1) *Bacillus-positive contacts not tested with lepromin.*—These cases, the earliest ones detected, were not tested with lepromin. One developed hypopigmented nonanesthetic areas positive for bacilli after a period of one and one-half years.

(2) *Bacillus- and lepromin-positive contacts.*—Out of a total of 51 such cases (9 previously recorded, and the 42 of this report), 6 developed lesions after a period of from 7 months to 2 years. Two of these patients developed small, hypopigmented, circumscribed areas that were slightly raised and showed impairment of tactile and thermal sensation; in two of them bacilli were found in the lesions, but not in the other two. The lepromin test was repeated when these lesions were observed, and all six patients showed positive reactions.

(3) *Bacillus- and lepromin-negative contacts.*—One of these patients, a child 8 years old, was found after a period of nearly

one year to give a positive reaction to lepromin, and on bacteriological examination bacilli were then found in the skin.

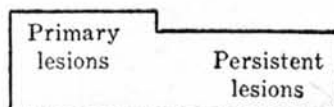
DISCUSSION

The following facts stand out clearly from the work done so far with regard to contacts. (a) Adult contacts in whom the lepromin reaction was positive showed bacilli in the skin. (b) Adult contacts who were negative to lepromin did not show bacilli in the skin. (c) Of 13 children positive for bacilli in the skin, 8 were positive and 5 negative to lepromin. (d) One individual who was negative for bacilli and did not react to lepromin, a child 8 years of age, was after one year found positive to lepromin and also positive for bacilli. (e) Six individuals who were positive for bacilli and reactive to lepromin developed leprosy lesions during a period of from 7 months to 2 years. One bacillus-positive contact who was not tested for lepromin developed leprosy lesions after a period of one and one-half years.

It is difficult to assess the significance of these findings in a limited number of cases, but a reference to the literature on the earliest lesions may place them in a definite group with regard to the evolution of the disease. The most comprehensive observations on the earliest lesions made in children are those of Lara and associates, summarized in an editorial by Rodriguez (6). Analyzing the various facts observed, Rodriguez concludes by presenting three possibilities with regard to primary lesions. The third possibility reads as follows:

That, at whatever age, the primary lesion in leprosy is essentially tuberculoid in nature, or at least passes early through such a stage, although the lesions of this phase are usually so insignificant as to size and so fleeting in course that they are often missed. Later, other types of lesions, more readily detected and more persistent, may develop.

This sequence may be shown diagrammatically as follows:



Of those with primary lesions, indicated in the first step of the diagram, some—as postulated by Rodriguez—develop “other” types of lesions more readily detected and more persistent,” indicated in the second step. The primary lesion is said to be essentially tuberculoid in nature, whatever the type of persistent lesion that may develop later. This means that the individual

must be lepromin-positive at the stage the primary lesions exist.

What is responsible for the development of the primary lesion? Obviously the lepra bacilli, which must be present in the skin before the primary lesion develops.

What is the condition or state of the individual before a primary lesion develops? Rodriguez states,

An alternative possibility is that the infecting organisms first introduced, before the appearance of any outward manifestation, may serve as a sensitizing antigen so that when lesions do appear they are of the tissue-reactive (i.e., tuberculoid) type.

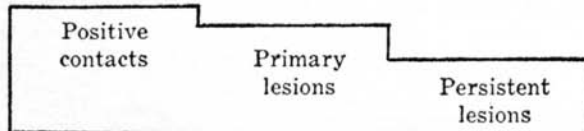
Hence the state of the individual before primary lesions develop is a condition in which the infecting organisms, the bacilli, are present, and the reaction of the tissues to these bacilli is manifested in some form other than as clinical lesions.

This is exactly the condition as exists in the bacillus- and lepromin-positive contacts dealt with in this paper. They show no lesions but harbor the bacilli in the skin, and they manifest the reaction of the tissues to the bacilli in the form of a positive lepromin reaction.

Fernandez, according to Rodriguez, admits that the stage of the primary lesions described by Lara and associates is not the earliest phase of the disease. He is quoted as saying,

It is true that, from the pathological point of view, these [primary] lesions cannot be considered as the real first manifestation of the infection, since it already reflects a state of sensitization of the organism which logically should have been preceded by an earlier morbid stage.

From these considerations the contacts who are bacillus-positive and react to lepromin can be considered to be in a stage which is the forerunner of the one in which primary lesions develop. This stage is represented as the first one in the following diagram.



Further evidence in favor of this assumption is provided by the fact that six of these bacillus- and lepromin-positive contacts developed lesions, two of the "primary" type (small hypopigmented areas without sensory changes but positive for bacilli, with lepromin positivity), and four of the "definite and persistent" type (small hypopigmented, raised areas with sensory changes, two positive and two negative for bacilli, all positive to lepromin). These findings lend support to the views of Rodriguez.

SUMMARY

(1) The results of the lepromin test in contacts with de-fatted lepromin are given.

(2) Adult contacts who gave positive reactions to lepromin were positive for bacilli in the skin, whereas adult contacts who were negative to lepromin were negative for bacilli.

(3) Of 13 children who were positive for bacilli in the skin, 8 were positive and 5 negative to lepromin.

(4) The degree of the positive lepromin reaction is compared with the number of bacilli found, and is shown to be in inverse proportion.

(5) The significance of the positive bacteriological and immunological findings is discussed, and a case is made out for the assumption that these contacts were in a stage which is the forerunner of the phase at which primary lesions develop.

(6) The development of lesions in contacts is discussed.

ABSTRACTO EN ESPAÑOL

El autor relata los resultados de la prueba de la lepromina en sujetos que han tenido "contacto" con pacientes leprosos. Lepromina desgrasada fué usada en todas las pruebas. Aquellos adultos que reaccionaron positivamente a la lepromina demostraron tener bacilos ácido resistentes en la piel (54 casos positivos de 184 sujetos examinados). Los sujetos de reacción negativa también fueron negativos para bacilos en la piel. De 13 niños los cuales fueron positivos para bacilos en la piel, 8 fueron positivos y 5 negativos a la prueba de la lepromina. Si se compara la intensidad de la prueba de la lepromina con el número de bacilos en la piel, la proporción resulta ser inversa. El autor discute los hallazgos y es de opinión que aquellos "contactos" con pruebas positivas tanto inmunológicas como bacteriológicas representan pacientes en la fase inicial antes de desarrollar lesiones primarias.

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