

THE LEPROMIN TEST IN TUBERCULOUS PERSONS IN A NON-ENDEMIC AREA

by

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Opinions vary as to the nature of the lepromin reaction. Some workers consider that it represents an allergic response, indicating hypersensitivity to some component of *Mycobacterium leprae*. The failure to react of patients with active lepromatous leprosy is explained by assuming that anergy has been produced by overwhelming dosage. Others regard the reaction as non-specific, attributable to irritation of the tissues by a foreign substance.

Assuming the response to be allergic and specific it should be rarely encountered in areas where leprosy is rare. Several workers, however, have demonstrated high proportions of positives in such areas. As a result, the theory of specificity has been broadened by the assumption that lepromin contains a protein identical or closely similar to tuberculo-protein. In other words, positive results in non-endemic areas are to be explained by prior infection, not with *M. leprae* but with *Mycobacterium tuberculosis*.

Certain studies carried out in non-endemic areas may be mentioned. Cummins and Williams (1) in England found 6 positives among 25 mental patients, or 25 per cent, using lepromin diluted five times. They note that all patients showed positive tuberculin tests. Dubois (2) in Belgium found 15 of 29 persons to be reactors, or 51 per cent, if a reading of 3 mm, or more is accepted as positive. Boncinelli (3) in Italy reported 22 positives among 44 patients with various dermatoses, or 50 per cent. Six of his patients suffered from tuberculosis of the skin. Fernández (4) in Paris found 33 reactors among 42 patients with various dermatoses, or 79 per cent. Eleven of his patients had tuberculosis of the skin.

Radna (5) adduced evidence pointing directly to non-specificity of the lepromin test and to a lack of correlation with the tuberculin test. He tested 100 healthy persons, all negative to tuberculin, belonging to an area where leprosy is very rare, and found that 94 reacted to lepromin. He tested also 25 persons with cachexia caused by infestation with intestinal parasites and found only one who reacted to lepromin.

On the other hand, Dharmendra and Jaikaria (6) found only 36 per cent of 270 inhabitants of a leprosy-free village in the Punjab, India, to be lepro-

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min-positive, as contrasted with 59 per cent of 295 inhabitants of a highly endemic district in West Bengal. Furthermore, they report necrosis and ulceration in the latter group whereas such reactions were not observed in the area free from the disease. In the West Bengal group, 55 per cent of 136 tuberculin-positive individuals were positive to lepromin as against only 15 per cent of 124 tuberculin-negatives. Interpretation of this apparently positive correlation between the two tests is rendered difficult because the comparison does not take into account the differences in age constitution of tuberculin-positive and tuberculin-negative respectively. The authors emphasize the opposite conclusion because of the occurrence of lepromin reactions in 19 persons negative to tuberculin.

In addition to the well-known Mitsuda or late reaction to which the above-mentioned studies refer, which reaches its maximum in from three to four weeks in the form of a papule or a nodule, there is an early reaction, sometimes called the "Fernández phenomenon," which is considered positive when an area of erythema of 10 mm. or more, with or without infiltration, appears from 24 to 72 hours after injection.

Earlier workers had noticed the early reaction but Fernández (7) was the first to show its relationship to the Mitsuda reaction. He found agreement between the two phenomena in 92 per cent of leprosy patients and their contacts. Fernández and Olmos-Castro (8) also found that of healthy non-contacts only 2 per cent showed an early reaction, while the late reaction was evident in 38 per cent.

The present study was undertaken to obtain further information on the response of persons in a non-endemic area, including both early and late reactions.

The lepromin was prepared at the Instituto Lleras of Colombia according to the technic of Hayashi as modified by Mitsuda. Injections were made intradermally in the anterior surface of the right arm, the dose being 0.1 cc. Readings were made at the end of 48 hours and during the fourth week. The early reaction was considered positive if there was 10 mm. or more of erythema; the late reaction if the papule or nodule measured at least 4 mm.

The first group studied comprised 13 adult patients attending the Skin and Cancer Hospital of New York Post-Graduate Medical School and Hospital, New York City. The results of the tests are given in table 1.

It will be noted that of the 13 patients, 10 were tuberculin-positive. Of these, 9 showed early positive reactions to lepromin, and, of 9 observed in the fourth week, 8 showed late positive reactions to lepromin. The three patients who were tuberculin-negative were negative to lepromin both at 48 hours and later. All three suffered from Boeck's sarcoid in which anergy to tuberculin is considered to be the rule. A fourth patient with this disease had a weakly positive reaction to tuberculin, was negative to lepromin on the early reading, but did develop a positive Mitsuda reaction.

TABLE 1. Reactions to lepromin and tuberculin in 13 patients with various skin diseases.

Diagnosis	Number of cases	Number with positive reaction to		
		Mantoux	Lepromin	
			Early	Late
Boeck's sarcoid	4	1	0	1
L. vulgaris	6	6	6	5
Tuberculoid	1	1	1	*
Scrofuloderma	2	2	2	2
TOTAL	13	10	9	8

* Not read.

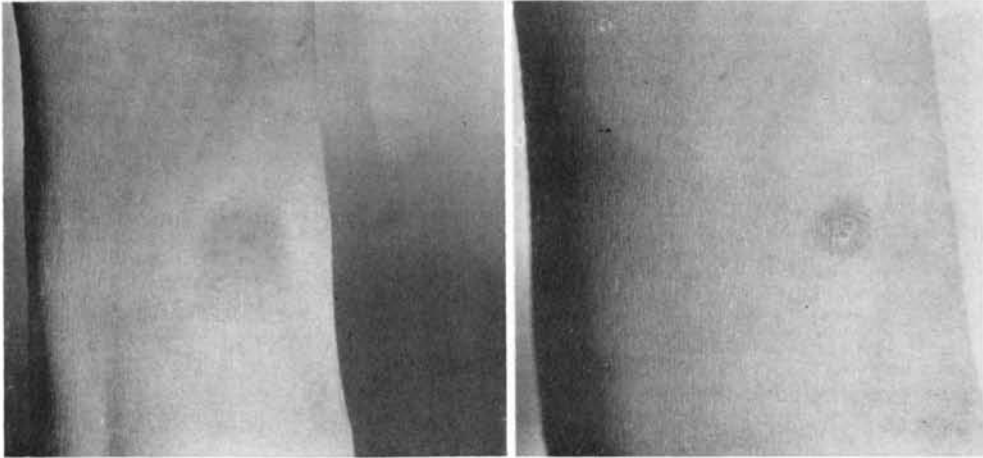
The second group studied comprised 108 patients at Seaview Hospital, New York, 70 of whom were Negroes. Of the group, 42 were under 6 years of age, 32 from 6 to 11 years, 27 from 11 to 20 years, and 7 over 20 years. All had pulmonary tuberculosis, for the most part of the primary type and all of the remainder were sputum-negative. This group is especially interesting because of the large proportion of children. In table 2, comparison is made between the late reactions obtained at Seaview and those obtained by Dharmendra and Jaikaria (6).

TABLE 2. Comparison of Mitsuda reactions in tuberculous patients at Seaview Hospital, N. Y., with those found in West Bengal and the Punjab, India.

Age in Years	Healthy persons in W. Bengal (highly endemic area)			Healthy persons in the Punjab (non-endemic area)			Tuberculous patients at Seaview		
	Number Tested	Number Positive	Per Cent Positive	Number Tested	Number Positive	Per Cent Positive	Number Tested	Number Positive	Per Cent Positive
0-5	60	13	21	50	7	14	42	19	45
6-10	80	29	36	42	9	21	32	16	50
11-20	67	48	71	60	16	27	27	10	37
Total	207	90	43	152	32	21	101	45	44

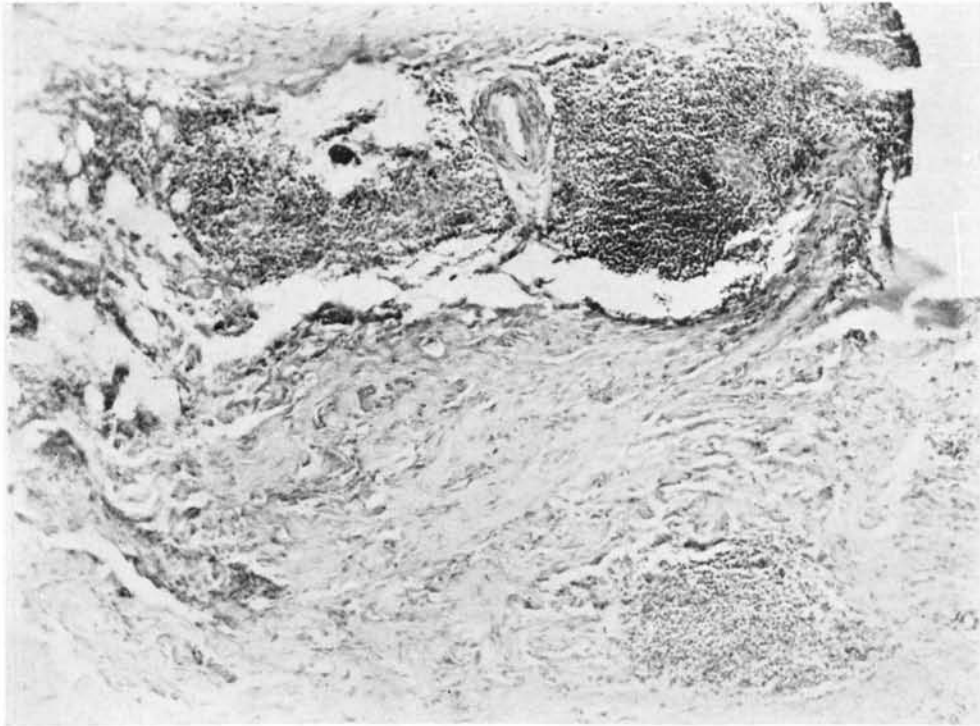
The data of table 2 show that in the Indian areas studied, the proportions with positive Mitsuda increase with age. Also the proportion positive in each age group is much higher in the endemic than in the non-endemic area. Among tuberculous patients at Seaview the proportions positive in the two younger age groups are much higher than in the corresponding age groups in the endemic area of W. Bengal. In the age group from 11 to 20 years the proportion positive among the Seaview patients is higher than in the Punjab but much lower than in the West Bengal area.

A possible explanation is that there actually exists an allergic condition common to tuberculosis and leprosy. All the Seaview patients were tuberculin-positive, which according to this theory would lead to a high propor-



Early reaction of Fernández

Mitsuda late reaction with necrosis



Positive Mitsuda test after 2 months, showing tuberculoid structure

tion of lepromin-positives even in the younger ages. The results of the tuberculin tests are not given for the West Bengal area, but it may be that tuberculosis is likewise much more prevalent there than in the Punjab.

In table 3 a comparison is made between the Fernández and the Mitsuda phenomenon for the 108 patients tested at Seaview.

TABLE 3. *Fernández and Mitsuda phenomena in tuberculin-positive patients.*

Type of reaction	Number tested	Number positive	Per cent positive
Fernández phenomenon	61	43	70.4
Mitsuda phenomenon	108	50*	46.2

*14 of these reactions showed necrosis.

It is clear from table 3 that the Fernández phenomenon, like the Mitsuda is not a specific reaction indicative of prior infection with *M. leprae*, because the possibility of such infection can be excluded in consideration of this group.

The second fact to be noted is that the proportion of early reactions to lepromin at Seaview is much higher than was found among healthy persons (2 per cent) by Fernández and Olmos-Castro (8), and among healthy persons (5 per cent) by Dharmendra and Jaikaria (9).

Attempts have been made to show that the Fernández phenomenon is related to hypersensitiveness to tuberculin. Fernández himself (10) demonstrated that of a group of healthy persons showing a negative Fernández phenomenon, a majority gave a positive reaction after being sensitized by injection of killed *M. tuberculosis*, suspended in oil. Thus it is possible that the explanation of the high proportion of positives among Seaview patients may lie in the fact that all were tuberculin-positive.

The agreement between the early and late lepromin reactions was not nearly so close in the two groups of the present study as has been reported in leprosy patients by Fernández (7) and others. Combining the two groups and omitting 47 patients on whom 48 hour observations were not made, there remain 74 patients. Of 52 who showed the Fernández phenomenon, 32 or 61 per cent had a positive Mitsuda, while of 22 who were Fernández-negative, 7 or 32 per cent had a positive Mitsuda.

SUMMARY

1. Of ten patients, with various dermatoses, attending the outpatient clinic at New York Skin and Cancer Hospital, all reacted positively to tuberculin. Of this group 9 showed early and 8 late positive reactions to lepromin.
2. Of four patients with Boeck's sarcoid, three reacted negatively to tuberculin and to lepromin. The fourth was weakly positive to tuberculin,

negative to lepromin on the early reading but did develop a positive Mitsuda reaction.

3. Of 108 tuberculous patients at Seaview Hospital, 70.4 per cent were positive to lepromin on the early reading and 46.2 on the late reading. This high proportion of Fernández positives may be due to the fact that all individuals were tuberculin positives. If so, comparative figures for Mitsuda positives would indicate that the Mitsuda reaction is less affected by cosensitization with *M. tuberculosis* than is the Fernández reaction.

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