

THE LATE LEPROMIN REACTION IN
SUBSIDED LEPROMATOUS CASES

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INTRODUCTION

The lepromin test is the only immunologic test of value in leprosy. Although it is of little if any value in establishing a diagnosis of leprosy, yet it throws valuable light on the prognosis of a case of leprosy. A positive late, or Mitsuda, lepromin reaction indicates a good prognosis and it is usually observed in noninfectious cases, but a negative one indicates lack of body resistance and inability on the part of the infected tissues to cope with the bacillary invasion. The vast majority of lepromatous cases give negative results with the test, although some workers have reported that in a small number of such cases the results may be positive and that in these cases clinical improvement is seen more frequently than in lepromin-negative cases.

With respect to subsided lepromatous cases, Hayashi (⁶), Lagrosa (⁷), Rodriguez (⁸), Schujman (¹⁰) and Sato and Fukuda (⁹) have each reported the occurrence of positive late reactions.

Figueredo (⁴), in a study of 68 lepromatous cases, observed a significant development of lepromin positivity in 15 subsided lepromatous cases after sulfone treatment (1+ in 13, and 2+ in 2).

Dharmendra and Mukerjee (²), in their observations of 17 lepromatous cases which had subsided and become bacteriologically negative under hydnocarpus therapy, observed positive *early*, or Fernandez, reactions in 3 (strongly positive in 1 and weakly positive in 2). Dharmendra and Mukerjee (³) further investigated the matter, and expressed the view that a definite positive early reaction is seldom seen in lepromatous cases under treatment with sulfones or under any other medicament, but a slight increase in early reactivity to lepromin may often be encountered with the subsidence of the disease process; but this increase is not sufficiently marked for the reaction to be called positive.

On the other hand, Davey (¹) reported that the lepromin reaction changed from negative to positive in 11 of 17 cases after 5 to 10 months of treatment with sulphetrone. Fiol *et al.* (⁵) also reported that the re-

action to lepromin became positive in nearly 10 per cent of 125 patients which they had treated with Promin for over a year.

It is rather difficult to reconcile the views and observations on the subject recorded by different workers from different countries. However, the observations made so far were mainly of clinical nature, and have rarely been corroborated by histopathologic studies. This may partly be responsible for divergent conclusions. With a view to correlating the occurrence of the clinically positive late reaction and its histologic picture, a study has been made on 17 subsided lepromatous cases in the Leprosy Department of the School of Tropical Medicine, Calcutta, and the results of this study are presented.

PRESENT STUDY

The present study involved 17 patients with lepromatous leprosy who had been attending the outpatients' department for a long time and were consistently bacteriologically negative as ascertained by multiple-smear examinations at regular intervals. All of these cases have been under sulfone therapy for 2 to 9 years, and clinical subsidence and bacteriologic negativity have been maintained for 2 to 4 years. In 15 of the 17 cases the classification had been confirmed by histologic examination of biopsy material from the skin lesions; of the remaining 2 cases, one had shown the picture of an atypical leproma, and the other one was of borderline histology.

The initial lepromin tests were made with Dharmendra's "defatted" antigen when the patients first came under observation. The results, read after 24 hours, had been negative in 15 cases, and positive in 2 (one of which is Case 3 of this report). Subsequent lepromin tests were made with the Mitsuda-Hayashi antigen (modified by Wade), on those patients who were still maintaining the subsidence. Readings were recorded after 24 hours, and at the end of the 1st, 2nd and 3rd weeks. Biopsy of the site of lepromin injection of each patient was made either between the 3rd and the 4th weeks after the lepromin injection, or at the end of the 4th week. Similar biopsies, to serve as controls, were also performed on tissue taken either adjacent to the site of the lepromin injection or from the corresponding part on the other side of the body.

FINDINGS

No early reaction with the Mitsuda-Hayashi (Wade) lepromin was seen in any of the 17 cases. The late reactions were negative in 15, doubtful in 1 (Case 2), and weakly positive in 1 (Case 3). The initial lepromin reaction with Dharmendra's antigen in these two cases was negative in one (Case 2), and positive in one (Case 3).

Histopathologic studies of the biopsy specimens from the sites of lepromin injection, taken after 3 weeks, showed negative results in 14, and positive results (i. e., formation of tuberculoid foci) in 3 cases. Of

these 3 cases in which a histologically-positive reaction was observed, the first was a frank lepromatous case (Case 5), the second atypical lepromatous (Case 2), and the third one (Case 3) a borderline case.

The findings in the 3 cases in which the histologic picture indicated a positive lepromin reaction are given below. In these cases, subsidence has been maintained for periods of 2 or 4 years.

DETAILS OF CASES

CASE 2 (No. 6335).—This patient, an L_2 case of 1+ bacteriologic positivity, had had the disease for 3 years when admitted for treatment at the clinic. A biopsy specimen taken in 1938 showed an atypical leproma, with a not marked degree of bacillus positivity. First found bacteriologically negative in January 1951, nearly two years before sulfone treatment was begun in October 1952. Negative bacteriologic findings were repeated on 5 occasions to late 1957.

First lepromin test, in June 1940, negative. The subsequent test, in August 1958, gave: early, negative; late, doubtful (erythema 5 mm., induration 3.5 mm.).

The biopsy of the injection site revealed a moderate, compact infiltration in the upper zone of the specimen. The cells were mostly small round cells partly vacuolated, epithelioid and foamy, with a few giant cells in a localized area. Nerves slightly infiltrated. No bacilli found. (Figs. 1 and 2.)

The specimen taken for comparison showed similar findings, but without giant cells.

CASE 3 (No. 10,255).—This patient, also only 1+ for bacilli originally, of 4 years duration when admitted for treatment, was of uncertain classification at that time— $B_2?$ T_2 (reaction). A biopsy specimen taken in January 1954, shortly before treatment was begun, showed a picture of doubtful tuberculoïd reaction, the histologic changes and bacillus positivity of 1+ grade. First found bacteriologically negative in April 1956; also negative in 2 subsequent examinations in 1956 and 1959.

First lepromin test, in March 1954, gave 13 mm. erythema (read as positive) and 3.5 mm. induration. The subsequent test, in September 1958, gave only slight early changes but a weakly-positive late reaction (erythema 10 mm., induration 3 mm.).

The biopsy of the reaction site revealed moderate cellular infiltration in the upper part and more extensive infiltration deeper. The infiltration consisted of small round cells, with epithelioid cells (some vacuolated), and a few giant cells in a localized area. No bacilli found. (Fig. 3 and 4.)

The comparison specimen showed a similar picture, but without giant cells.

CASE 5 (No. 10,597).—An L_2 case, of 2+ bacillus positivity, was of 5 years duration when admitted to the clinic. Put under sulfone treatment in January 1955; first found bacteriologically negative in January 1957, and repeated twice afterward.

First lepromin test, in January 1955, resulted negative, as did the second one in August-September 1958.

The biopsy findings, with both specimens, were the same as those described for the preceding case.¹

¹ A photomicrograph intended to illustrate this case shows a group of giant cells in a focus, but the picture is too flat to show details in reproduction.—EDITOR.

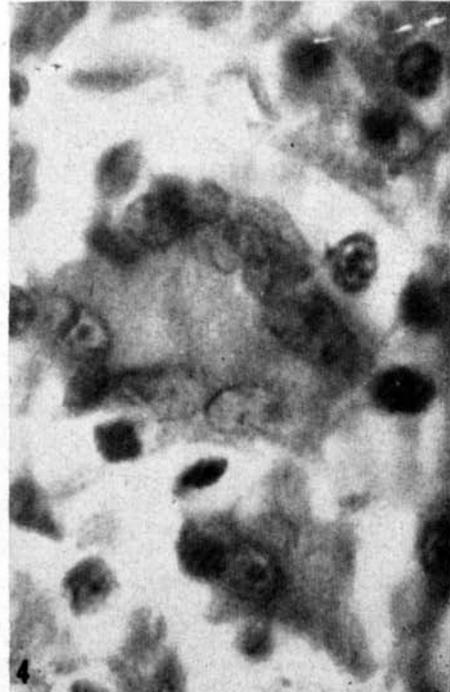
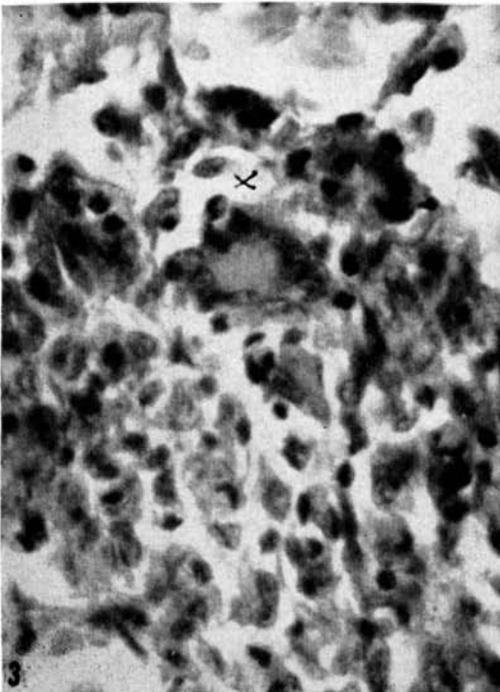
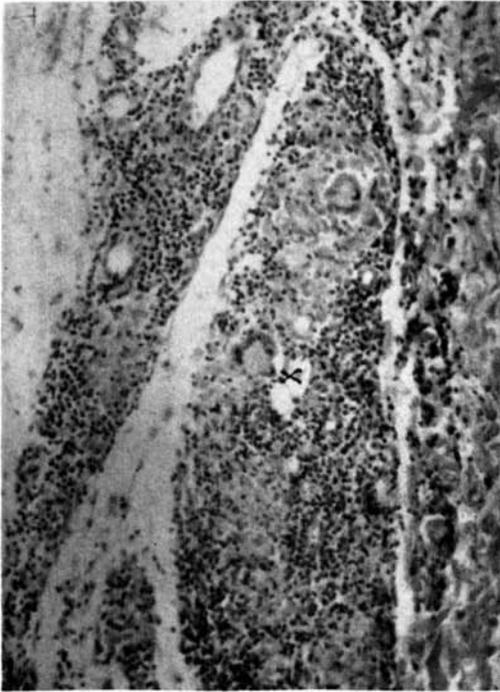
DESCRIPTION OF PLATE

FIG. 1. Photomicrograph of a tuberculoïd focus containing two giant cells, in the reaction lesion of Case 2. Note also the small (subtuberculoïd) group of epithelioid cells in the zone to the left, and a lone giant cell to the right. Hematoxylin and eosin, magnification about 250.

FIG. 2. One of the giant cells (marked x) of Fig. 1. Magnification about 2000.

FIG. 3. Photomicrograph of a tuberculoïd focus containing a giant cell, in the reaction lesion of Case 3. Hematoxylin and eosin, magnification about 550.

FIG. 4. High-power view of the giant cell in Fig. 3. Magnification about 2000.



DISCUSSION

In the 17 cases included in this study, the results of the initial lepromin tests—Dharmendra antigen, 24-hour readings— were negative in 15 and positive in 2. With the subsidence of the disease, there was no change in the lepromin reactivity, as then tested, in 14 cases; in the remaining 3, the subsidence was associated with a change in the lepromin reaction (clinically 2, histologically 3). In one case (Case 2) this was in the direction of an increase in reactivity (from initial negative to doubtful positive). In the second one (Case 3) a positive reaction changed to weakly positive. In the remaining one (Case 5) the lepromin reaction remained clinically negative as before, but the histologic findings were those of a positive late reaction—formation of tuberculoid foci in a localized area. To sum up, positive late lepromin reactions (confirmed by histologic findings) were observed in 3 cases, 1 a typically lepromatous one, 1 atypical lepromatous, and 1 borderline. In these cases subsidence had been maintained for 2 to 4 years under sulfone therapy.

From these observations, we are unable to confirm the reports of other workers regarding the increase in reactivity to lepromin associated with the subsidence of the disease, in any material proportion of lepromatous cases under treatment with the sulfones or any other medicament.

SUMMARY

1. The lepromin reaction with the Mitsuda-Hayashi (Wade) antigen was studied clinically and histologically in 17 lepromatous cases under sulfone treatment in which subsidence had been maintained for periods of 2 to 4 years.

2. Three out of the 17 cases showed positive late lepromin reactions—2 of them clinically and 3 histologically. Of these 3 cases, one had been frank lepromatous, the second atypical lepromatous, and the third borderline.

3. It is concluded that a great majority of subsided lepromatous cases remain negative to lepromin, although a positive reaction— clinical or histologic— may occasionally be encountered in a few such cases.

RESUMEN

1. La reacción a la lepromina con el antígeno de Mitsuda-Hayashi (Wade) fué estudiada clínica e histológicamente en 17 casos lepromatosos sometidos a la sulfonoterapia en los que se había mantenido la atenuación de la dolencia por períodos de 2 a 4 años.

2. Tres de los 17 casos acusaron reacciones positivas tardías a la lepromina—2 de ellos clínica y 3 histológicamente. De estos 3 casos, uno había sido francamente lepromatoso, el segundo lepromatoso atípico y el tercero limítrofe.

3. Se deduce que los casos lepromatosos atenuados en su gran mayoría permanecen negativos a la lepromina, aunque pueda encontrarse de vez en cuando en algunos de esos casos una reacción positiva—clínica e histológica.

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