# TUBERCULOID LEPROSY; ITS TRANSFORMATION TO THE LEPROMATOUS TYPE*

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It seems still to be an unsettled question whether or not tuberculoid leprosy may transform to the lepromatous form of the disease. Querangel des Essarts and Lefrou (13) believe that the leprids and the lepromata have fundamentally the same architecture and etiology, representing two extremes of the same process. There are intermediate stages and, quite frequently, there is transition from the leprid form to that of leproma. Schujman (15), writing on the evolution and immunology of tuberculoid leprosy, calls tuberculoid leprosy the allergic type, always lepromin positive, in contrast to the lepromatous type which is the anergic one; hence it is a special type showing specific resistance against the disease and is immutable even under the most resistance-lowering factors that could favor its transformation into a lepromatous-type case. He does not know of any convincing publication proving the evolution of a tuberculoid leprosy into a lepromatous type. Cochrane (2) has recently expressed doubt that true tuberculoid cases, with positive lepromin reactions, undergo transformation, but Lowe (7, 8, 9, 10, 16) is convinced that that change often occurs. Wade, who has written extensively on tuberculoid leprosy, which he regards as a subtype of neural leprosy, has not denied the possibility of its transformation into the lepromatous form; and, while the present paper was under preparation, he and Rodriguez (17, 18) have reported instances of such transformation into borderline cases, but they draw attention to the lack of reports of well-substantiated cases of actual transformation.

## REPORT OF CASE

Because of the assertion of certain writers that tuberculoid leprosy never undergoes transformation to the lepromatous type,

*This article in the main part constitutes a reprinting, in condensed form approved by the author, of one which appeared in the *Monthly Bulletin, Bureau of Health*, Manila, **20** (1940) 263-276. There has been added a second case, heretofore not published, with photographs of it.

of the uncertain stand taken by others, and of the apparent lack of definite information on the subject, the present case is considered to be of interest. It is being reported as one that has undergone that change within a period of six years since the first observation. Several other cases of like nature have been observed during the last ten years, but they are not presented because the earlier records are incomplete, due to the fact that at that time our experience with tuberculoid leprosy was meager and attention had not as yet been particularly called to it. Others are withheld because, though they are now considered lepromatous, with nodules and diffused, dark-colored infiltrations of the skin, histological specimens from sites near those of the former biopsies still show the tuberculoid histology, with bacilli. Still others are recalled which were of the kind that we now term tuberculoid leprosy, in which the lesions—and also the bacilli in the cases that were found bacteriologically positive—rapidly disappeared and, after a variable number of years, the disease apparently relapsed and the patients now have advanced lesions of the lepromatous type.†

For the purpose of this report a case is considered histologically to be of tuberculoid nature when the sections show a more or less marked collection of small round cells, alone or with large mononuclears, in follicular or tubercle formation, even in the absence of giant cells. A case is considered histologically lepromatous when sections show macrophage invasion with abundant globi of *M. lepra* in or outside of the cells.

## CASE REPORT

CASE Z.B., admitted August 29, 1933. History: A reddish lesion the size of a grain of corn appeared on the bridge of the nose about 1932, followed after a week by a generalized reddish macular eruption. The lesions retrogressed but reappeared three months before admission, this time accompanied by anesthesia, dryness and scaling of the lower part of the right leg and over the macules.

*Examination on admission.*—Pinkish macular eruptions all over the body, tending to clear up in the centers to leave pale atrophic areas with slightly elevated pinkish circinate borders. These are especially numerous on the cheeks and ears, where they are confluent. (Figs. 1 and 2.) Both ulnar nerves moderately thickened, common peroneals markedly so. Hypoesthesia of the ulnar side of forearms and dorsum of hands. Anesthesia of the distal portion of legs, dorsa of feet and centers of macules. Nasal mucosa congested, thickened and edematous on both sides of the septum and on the right inferior turbinate. Right testis enlarged. Inguinal and femoral glands moderately enlarged.

†Such a case is the one which is here added to the original report.

Six smears (both sides of septum, both ear-lobes, both cheeks) all negative. Biopsy (right forearm): Tuberculoid leprosy (Fig. 8); sections negative for bacilli. Four other smears made a month later were also negative.

*November 10, 1933:* The face and ears show pinkish patches which are soft, slightly wrinkled and subsiding. The papulomacules found all over the body are pale, depressed in the center, elevated and granular at the borders. Nasal mucosa congested. Four smears (right side of septum, both earlobes, both cheeks) all negative. Six more made two weeks later, including four from skin lesions on extremities and body, all negative.

*December 28, 1933:* The skin lesions have now subsided markedly, most of them being level with the skin. Those on the upper part of the body and upper extremities have shiny, slightly elevated borders and atrophic centers. Nasal mucosa congested but intact. Four smears from skin lesions negative.

*February 2, 1934:* The skin lesions are depressed, atrophic areas except those on the face, which are still slightly indurated. Those on the body and extremities have brownish, irregular, nonelevated borders. Three smears negative.

*April 13, 1934:* The original lesions have left atrophic, slightly depressed brownish patches surrounded by pale areas. Two smears (from cheeks) negative.

The patient was released with a clinical certificate and went to his home province, where he had no further treatment. He was not seen again for more than five years, until he came back to the hospital in a fairly advanced stage of the disease.

*December 5, 1939* (Figs. 3 and 4): The ears and face are markedly infiltrated, irregular, with beginning nodule formation on the ears, malar eminences, nose and chin; these lesions are of a dark brownish color. There are numerous hazy, shiny, slightly wrinkled, pale patches all over the arms, chest, abdomen, back, buttocks, and thighs, surrounded by hazy brownish areas. On the suprascapular and the deltoid areas, the posterior aspect of the arms, and generally over the body are irregular, shiny, brownish areas, in some places slightly thickened and in others distinctly infiltrated, forming tiny nodules, either raised or flattened, which give the skin a rough, irregular surface. On the distal part of the arms, lateral to the cubital fossae, the skin is irregular, brownish, with small, dark brownish, papular eruptions, and the skin as a whole is diffusedly thickened, especially noticeable when pinched between the fingers. The fingers are swollen and shiny at the tips. The palms and soles are thickened and infiltrated. The right ulnar nerve is moderately thickened, both common peroneals markedly so. There is moderate ichthyosis of the distal portion of the legs. The pale areas are not anesthetic, but the distal thirds of the legs are insensible to both light touch and pain.

Eight smears (both earlobes, right septum, right cheek, chin, forehead and forearm in two places) all strongly positive (4+). Biopsy (November 6, 1939): Histologically lepromatous (Fig. 9); section positive for bacilli, with plenty of globi (Fig. 10). Lepromin test: Negative up to the fourth week.

*Summary.*—This protocol is of a case in which the first lesion of leprosy appeared in 1932, a small reddish eruption which was followed in a week by generalized reddish macular areas; these lesions underwent retrogression but reappeared in a year. He was then admitted to this institution, but as he was bacteriologically negative, and the lesions receded, he was paroled after seven months. The previous history, the nature of the skin lesions as seen on admission, the repeatedly negative bacteriological examinations, the histological findings and, finally, the rapid resolution of the lesions, together show that the case was a tuberculoid one (of the annular form of Wade and Schujman) which was in reaction but in process of retrogression at the time of admission. The evidence is believed to be ample, even though the lepromin test was not made at that time.

Five years and eight months after he was paroled, he returned in an advanced condition. As may be seen from the description on readmission, and the photographs taken then, he now presents clinically the distinguishing features of the lepromatous type. While some of the old lesions can still be traced in the form of hazy, shiny, wrinkled patches, in many places they have been replaced by diffused thickened patches of brownish infiltration, without any demarcation or border, and by small coffee-colored nodules. Ordinary bacteriological smears show numerous bacilli with many globi. A skin section taken a few millimeters from the former biopsy now shows macrophages filled with acid-fast bacilli, and there are numerous globi inside and outside the cells. Finally, the lepromin reaction is negative.

## REPORT OF SECOND CASE
### (ADDENDUM)

The following case came under observation a little later than the previous one, and presents an interesting contrast to it clinically and bacteriologically, both before and after the transformation had taken place. The first case was one of tuberculoid leprids of moderate degree, believed to be in retrogression from a reaction, and negative bacteriologically. The present case was a major tuberculoid one in a state of chronic reaction, past the height of its severity as shown by marked scaling of the lesions, and was bacteriologically positive.

CASE E. S., admitted May 8, 1935. History: About a year previously he felt numbness on the left forearm. The region became swollen and a large reddish scaly eruption rapidly appeared. Similar but smaller eruptions appeared simultaneously on the face and neck, and later above the left elbow.

After six months other reddish eruptions appeared all over the body. Both feet and the lower half of the legs became anesthetic.

*Examination on admission.*—The condition is illustrated by Fig. 5. There are depigmented macules with distinct borders on the chest and buttocks. The ears, right upper eyelid and brow, elbows, left forearm and arm are covered by reddish scaly infiltrations with sharp margins. Both knees are also reddish and thickened. Round reddish eruptions with sharply delimited borders are scattered all over the skin surface, most of them the size of a grain of corn, with many as large as a pigeon's egg. Some of these are drying up and are scaly. Ulnar and great posterior auricular nerves are slightly thickened. Areas of anesthesia on the left forearm, both legs and feet.

Two smears (right cheek and chin), positive (4+). Biopsy (right forearm): Tuberculoid leprosy (Fig. 11); sections positive for bacilli.

*November 25, 1935:* The skin infiltrations have subsided markedly, leaving pinkish wrinkled patches which are still slightly elevated. Seven smears (both sides of the septum, left helix, chin, left mandible, chest and right buttock) all negative except the left mandible, which is positive (2+).

*December 20, 1935:* Earlobes flushed and slightly thickened but soft. Skin shows numerous atrophic, depressed, pale or light brownish areas. Seven smears (right septum, both earlobes, right brow, nasal bridge, both forearms), all negative. A month later five smears were again all negative.

*March 13, 1936:* Septum moderately congested, mucosa intact. Skin over the glabella is tense, shiny and flushed. Earlobes flushed, but soft and velvety. The lesions on the face appear as depressed brownish atrophic patches surrounded by a narrow zone of pale areola. Those on the upper and lower extremities and abdomen now appear as depressed grayish patches, surrounded by brownish borders. Six smears negative.

*June 12, 1936:* There are pinkish macules on both sides of the face, and the skin at the left angle of the mouth is slightly elevated, pinkish and shiny. The chin and earlobes are of the same appearance and are slightly thickened on palpation. On the back of the neck are shiny, wrinkled, elevated and pinkish macules. Of seven smears from various sites one, from the chin, is positive (1+).

*November 4, 1936:* No clinical description available. Five smears (left earlobe, left eyebrow, chin, back, right forearm) all markedly positive (4+).

*March 7, 1940:* At this time, more than three years after the last record here noted, the appearance is of a marked, lepromatous case, as shown in Fig. 6. Biopsy (right forearm, from near the scar of the first one): Leproma (Fig. 12). Sections show many giant cells and abundant bacilli in large globi (Fig. 13). Lepromin test: negative up to the fifth week.

*August 16, 1940:* The patient is rather emaciated and pale, and the bony framework, especially of the chest, is prominent. He has had two accesses of hemoptysis, the last about a year ago. Pulmonary findings of advanced tuberculosis. The nasal mucosa is thickened and pale, the right side of the septum being eroded. The entire body is almost completely covered by brownish diffused infiltrations of varying thickness, the borders gradually merging with the few remaining areas of apparently uninvolved skin (see Fig. 9). The infiltrations are especially marked on the ears,

face, chest, abdomen, lower part of the back and all extremities. The upper part of the back shows less involvement. The skin is everywhere shiny, and the less infiltrated lesions are dry and wrinkled. The superficial nerve trunks are not prominently thickened and there is only slight atrophy of the muscles of the hands. Ten smears all markedly positive (4+).

*Summary.*—This case was admitted in 1935 with markedly positive lesions in ordinary smears and in histological sections, the lesions appearing as reddish thickened areas of various sizes with well circumscribed borders. Seven months later the lesions had subsided, leaving pale or pale brownish atrophic areas that were bacteriologically negative.

He remained negative for six months, after which (June, 1936) clinical activation of the lesions on the face and nape of the neck as pinkish macules was noted, and the chin was found weakly positive (1+). After a further period of five months—eleven months after he had been found negative—the lesions had advanced and smears were again strongly positive (4+). The rapid unfavorable development seems to have been influenced by lowering of resistance due to pulmonary tuberculosis.

The section from one of the lesions taken soon after admission showed a massive tuberculoid structure, with the presence of bacilli. After the period of recession and bacteriological negativity, generalized skin infiltrations gradually and steadily developed, and another skin section taken from beside the site of the first specimen, more than five years later, shows a leproma with massive globi and the presence of foamy cells and of great numbers of giant cells. The lepromin reaction at this stage was negative.

## REMARKS

According to the definition contained in the report of the International Congress held at Cairo in 1938 (5), the essential feature of a leproma is an accumulation of "lepra cells" which may show little differentiation from the original form (macrophages) or may contain globi, or may undergo multiple vacuolation to produce the Virchow cells and contain numerous bacilli. According to this definition, therefore, the second biopsy made in the first case, a few millimeters from the first one after more than five years, showed a lepromatous transformation of what was formerly a tuberculoid lesion. The lepromin or Mitsuda test, made soon after the last admission and inspected weekly for a month, was negative. This alone is strong evidence that the case is now lepromatous. Essentially the same features are presented by the second case.

If it be agreed that the condition in these cases was tuberculoid when they were first admitted, and that now they are lepromatous, as shown clinically, bacteriologically, histologically and immunologically, the fact is of particular interest since there is as yet, so far as I am aware, no convincing record of such a transformation. The evidence that this transformation can take place is of particular significance because Manalang has repeatedly claimed, with regard to the pathogenesis of the leprous lesion, that the tuberculoid condition is a stage in its development which precedes the bacillus-laden leproma. That a single tuberculoid case of leprosy does transform in this way, or even that several cases do so, is not proof that all lepromatous cases pass through a tuberculoid stage. Such a transformation may be exceptional. It is to be recalled that many cases of tuberculoid leprosy are observed in India and Japan; and there are no less than 160 of them under observation in the San Lazaro Hospital yearly. The evolution of the lesion in leprosy is so slow that it may take many years for an individual case to develop fully into a lepromatous type.

Manalang (12) pointed out three years ago the necessity of observing cases carefully and continuously for many years in order to observe such a development. Wade has pointed out in an editorial (3) that such studies and observations are tedious and time-consuming, often difficult to make because of the distraction of our immediate activities, and may even be impossible, but that it must be done if our knowledge in leprosy is to be made precise. It is believed that if such observations could be made for generations—should they be confined to adults—few cases would be seen to transform into the fully developed lepromatous type.

It must be emphasized that the so-called clinical lepers among adults, to which the tuberculoid cases discussed by various writers belong, are the filtered cases—the resistant ones, or benign infections, a portion of a great number who have been infected in childhood, of whom a greater or lesser proportion have long since become lepromatous. Attention is called to the reports made by certain Philippine writers (4, 14, 6) based on careful and painstaking observations made among children. In their descriptions of the early lesions in children, they refer to a group of leprids and to the frankly clinical tuberculoid cases as described by various authors, which lesions have been shown by Manalang (11) and Chiyuto (1) to have either perivascular round cell infiltration or the tuberculoid histology. If these are the early lesions, then

it must follow that the leproma in an advanced case of leprosy is the end result of these lesions. The follow-up of infected children who are living outside of institutions is impracticable, and many of them may develop through the different stages of the disease unnoticed. But leprosaria and kindred institutions like Welfareville, near Manila, to which contact children of lepers are transferred and where they are continuously observed, offer ideal opportunities for systematic and continued follow-up. The children at Welfareville were not separated from their leprous parents at birth, and a few of them become bacteriologically positive each year. Some have already been reported by the last-named authors, and it is hoped that more reports on these children of lepers that have become lepromatous and were thoroughly observed during the different stages of their evolution will appear from time to time.

## SUMMARY AND CONCLUSIONS

Mention is made of contradictory opinions of different authors regarding the occurrence of transformation of established cases of tuberculoid leprosy to the lepromatous form of the disease. Two cases of tuberculoid leprosy which have undergone that transformation after coming under observation are presented. These cases, together with the clinical, bacteriological and histological studies of other authors, seem to agree with the opinion of Manalang that tuberculoid leprosy is a stage in the evolution of leprosy, not immutable as asserted by Schujman. It is indicated that such transformation among adult tuberculoid cases is rare because they represent the filtered resistant ones, or benign infections. Continued follow-up and life-long study of contact children born of leper parents in institutions is indispensable if we are to know the evolution of leprosy.

## ACKNOWLEDGMENT

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## DESCRIPTION OF PLATES

### PLATE 6

FIG. 1. Case Z.B., photograph taken August, 1933. The skin lesions appear as round, reddish, elevated areas surrounded by pale outer borders. Their centers show a tendency to subside and become paler, of annular appearance.

FIG. 2. Posterior view of the same patient. Multiple lesions of the same character.

FIG. 3. Same case, photograph taken in December, 1939. Traces of the previous lesions are visible as hazy, dry, pale areas. There are lepromatous lesions of the face and ears, and dark diffused infiltrations of the arms and forearms. The scar indicated by the letter A is that of the biopsy made in 1933; B and C are those of biopsies made in 1939.

FIG. 4. Posterior view, showing the numerous small nodulations occurring in diffused lepromatous infiltration.

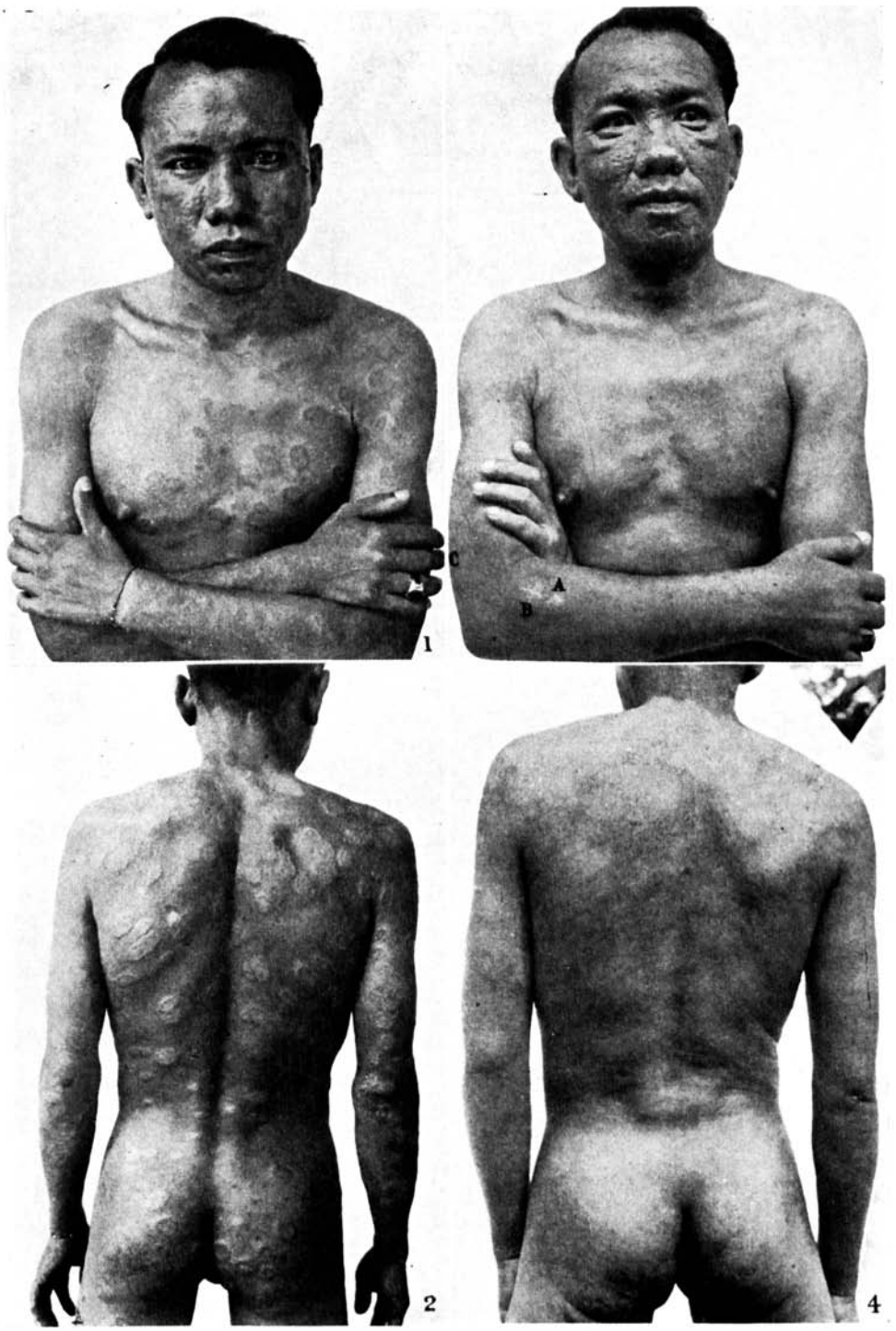


PLATE 6

PLATE 7

FIG. 5. Case E. S., photograph taken in May, 1935. Massive reddish, scaling infiltration on the left forearm, with many small round nodular lesions on various parts of the body, especially conspicuous on the face, with involvement of the ears.

FIG. 6. Same case, photograph taken in March, 1940. Extensive diffused lepromatous infiltrations, practically generalized.

FIG. 7. Another picture of the face of this patient, taken in August, 1940.

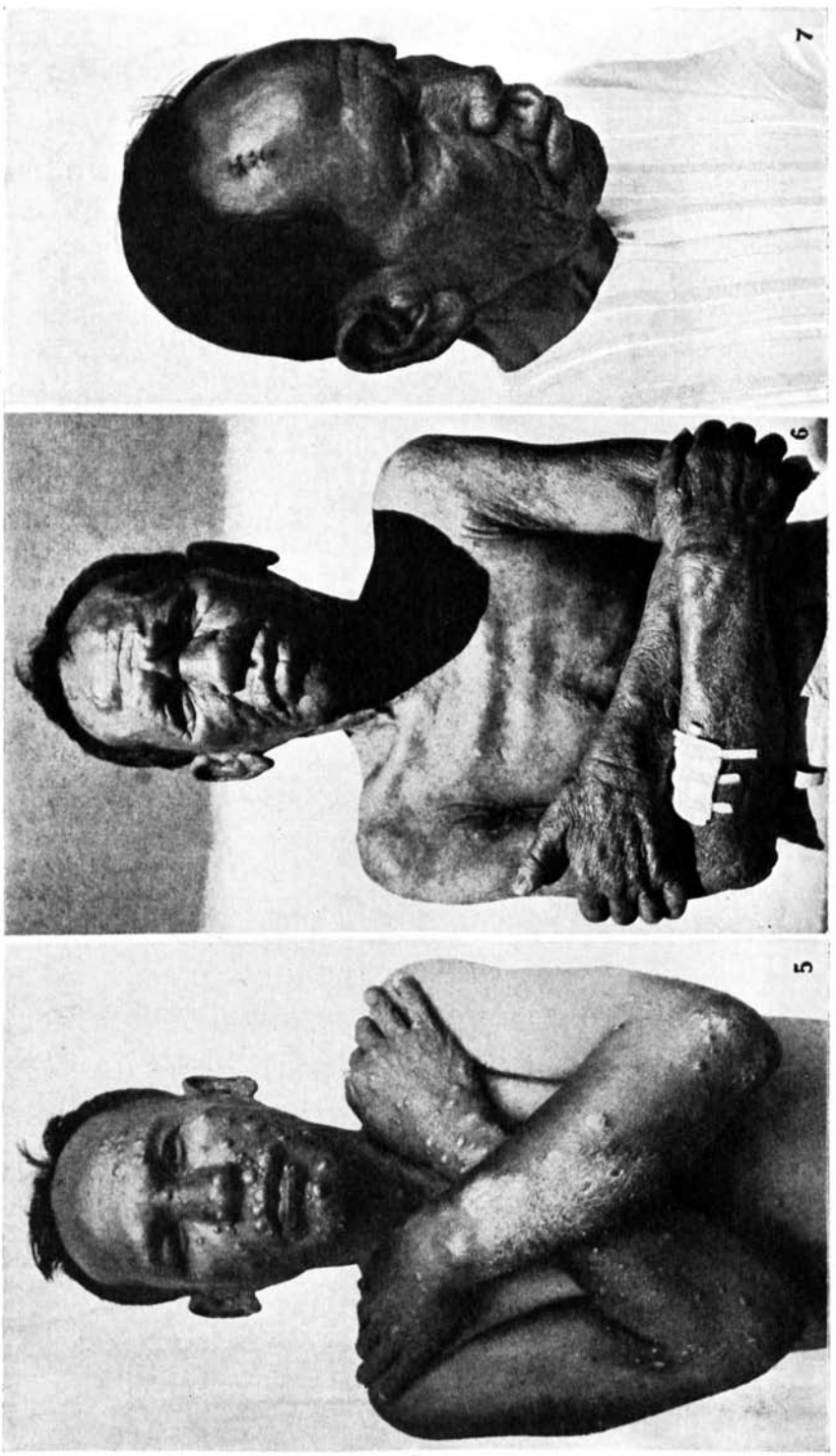


PLATE 7

## PLATE 8

FIG. 8. Photomicrograph of the biopsy specimen from Case Z.B., taken in 1933, showing the characteristic picture of tuberculoid leprosy.

FIG. 9. Photomicrograph of the specimen taken from the same case in 1939, of an infiltration beside the scar of the previous biopsy. Sections stained for bacilli showed them in abundance, often in globi.

FIG. 10. From a section stained by the Ziehl-Neelsen method, same specimen. Showing *M. leprae*, scattered and in large clusters. (Photomicrograph by Valdez, magnification 900×.)

FIG. 11. Low-power photomicrograph of specimen taken in 1935 from Case E.S., the lesion being one of the nodular eruptions seen on the right forearm in Fig. 5. Showing the massive tuberculoid structure.

FIG. 12. Low-power photomicrograph of specimen taken in 1940 from a site near the scar of the first biopsy (see Fig. 6). Section stained by the Ziehl-Neelsen method, showing many globi as black, rounded areas. (Photograph by Dr. J. Mendiola.)

FIG. 13. High magnification of another section of the same specimen, stained by hematoxylin and eosin, showing among other details the presence of giant cells.

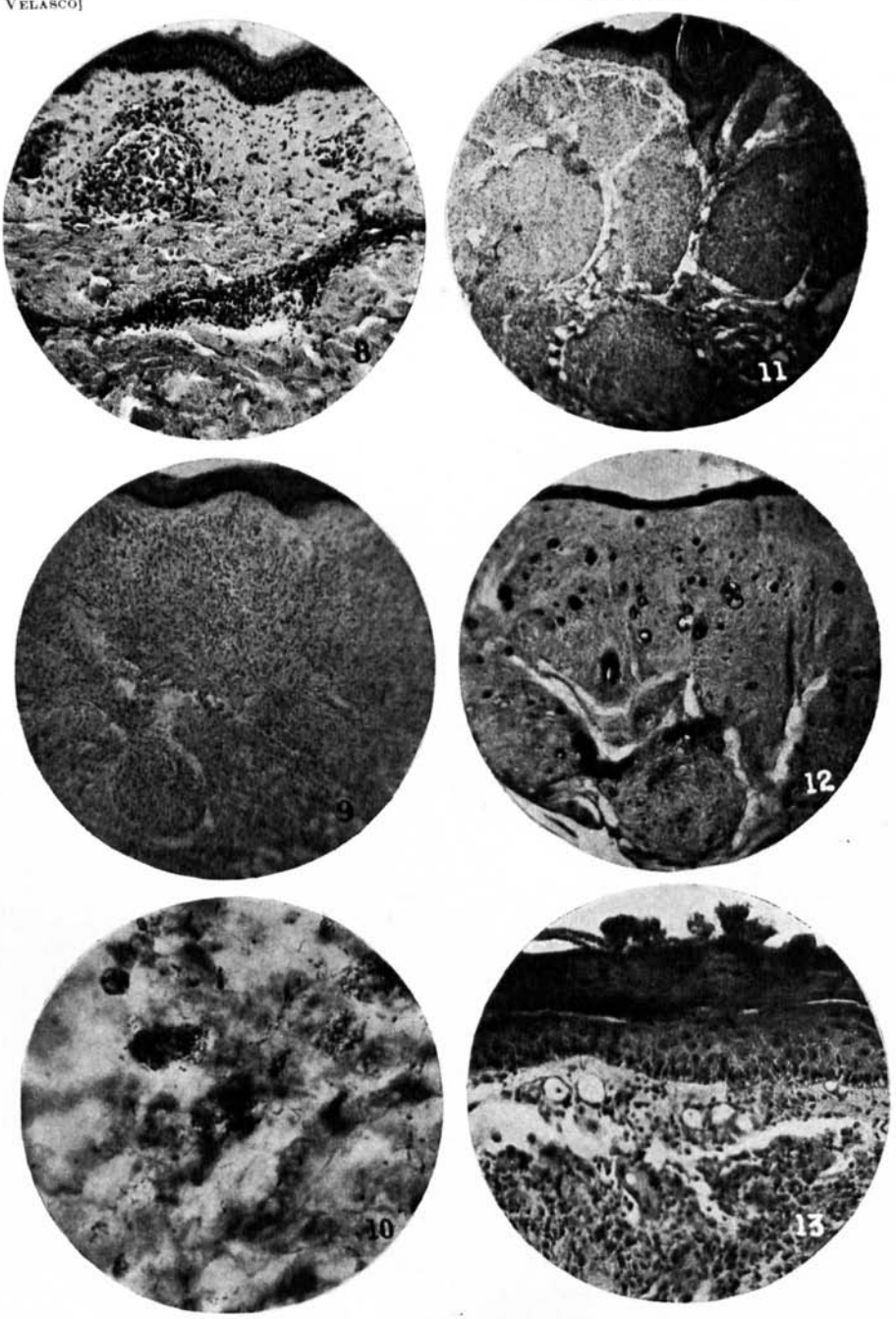


PLATE 8