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THE STATUS AFTER FIVE YEARS OF NEURAL LEPROSY CASES STUDIED IN CEBU¹

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INTRODUCTION

The immediate objective of the studies of the skin lesions of neural leprosy recently published by one of us (H. W. W.)

¹This article is the first of a series of five that deal with follow-up observations of neural-type cases of leprosy at Cebu, in the Philippines. Published with the approval of the Director of Health.

with several colleagues (4) was to establish on clinical and histological grounds their relationships with each other. At the same time it was hoped that follow-up observations might be made in order to learn what changes the cases would undergo and thus perhaps to add to an understanding of the course and prognosis of the different varieties of that type of the disease. This has been possible with the group that was studied by the present writers at Cebu, in the Philippines (1a).

Most of the cases referred to had been under observation for five years when last examined in September, 1938. Those from the Cordova survey were first seen and were biopsied in 1933 (2), though our first joint examination of them was made in 1934. It was then that we biopsied those from the Cebu Skin Dispensary, but with only a few exceptions they had then attended the clinic for a year or more. Reexaminations were made by us jointly at two-year intervals, in 1936 and 1938, but the Cordova cases were also examined twice in 1935 by one of us (J.N.R.), who had relatively frequent opportunities to observe most of the dispensary cases.

Five years is not, of course, a sufficiently long time to determine the ultimate outcome in cases of neural leprosy—i.e., to decide if those that have cleared up will remain permanently cured, or if those that have not recovered will do so later, or will progress indefinitely as of the present form, or will undergo conversion to the lepromatous type. However, the period is not an insignificant one, and the changes that have taken place in some of these cases are interesting.

As for the various factors, intrinsic and extrinsic, that may have influenced the course of the disease in these patients we can say little. Referring specifically only to antileprosy treatment, the Cordova group as a whole had none, few if any of them having taken advantage of the possibility of receiving injections by the local sanitary inspector. The dispensary patients reported for treatment entirely at will; a few did so faithfully and regularly but most of them were quite negligent or came too infrequently to have derived much benefit. Furthermore, because of the necessary conservatism in dosage of outpatient treatment few patients received a large amount of the drug in any given period. In consequence we would say that, in a large majority of the cases, the changes that occurred were not materially influenced by medication.

Our follow-up to 1938 included 46 of the original 52 cases, though five of the other six were reexamined one or more times. One of these six patients died, the others moved away. No less than five of the total (about 10 percent) became bacteriologically positive and were hospitalized; they are included in this report but will be dealt with in detail in later ones. All of the others have remained bacteriologically negative. In our reexaminations further biopsy specimens were taken when there seemed to be any real point in doing so; in 1936 we took 22 specimens from 18 of the nonhospitalized cases and several from the latter, and, in 1938, 12 from 10 cases.

In the original report on these cases they were grouped according to the nature of the individual lesions under study. In the present one the different groups are discussed as such, with special mention of the more interesting individual cases. The case numbers are those of the earlier report, which should be consulted for further data and especially for the pictures showing the previous condition, though some of them are reproduced here. The original grouping of lesions is still considered valid in the main, especially since its principal features were adopted in formal classification by the Cairo congress (1). We are inclined, however, to give increased emphasis to the neglected "papulate" condition, which comprises the least degree of those lesions whose morphological features can be said without hesitation to be due to tuberculoid changes.

PRESENT STATUS OF THE LESIONS AND CASES STUDIED

1. ANESTHETIC, NONMACULAR AREAS

The three lesions in this group (Cases 1 to 3), were solitary anesthetic areas without visible cutaneous change, but they were not all of the same history. (a) In two cases (Nos. 1 and 3) there had been no visible local change up to the time of the first biopsy. The former has remained without any further development, the area of anesthesia persisting. In the latter (from which the original specimen showed only slight round-cell accumulation, with possibly a little subtuberculoid change), a macule appeared later. Unfortunately it had been greatly disturbed, clinically and histologically, by intradermal injections before we could biopsy it; now only residual changes are present. (b) In the third case (No. 2) the anesthesia was residual of a macule that had disappeared four years before it

was biopsied in 1934. This area is still without surface change, but it has enlarged and polyneuritic changes in the same hand have increased considerably.

Comment.—These cases illustrate certain of the developments that nonmacular anesthetic areas may undergo: (a) no change over a period of years, (b) development of a macule (which may be amenable to local treatment), and (c) extension of the area—this last seen in the case that previously had had a macule and in which there had been polyneuritic changes, which also increased, the case thus behaving like an active “pure neural” one.²

2. RESIDUAL MACULES

(a) *Macules without atrophy.*—In seven lesions (Cases 4 to 10) of the thirteen that were classed as residual the process had not been severe enough to cause obvious atrophic changes (i.e., mild scarring). All of these lesions have remained completely inactive and most of them have disappeared; and most of the patients (including one that had a new suspicious skin lesion in 1936) are quite negative. However, in one case there is now a slight suspicious lesion, and in two cases polyneuritic manifestations have developed.

The suspicious lesion found in 1936 (Case 10), an obviously recent small “lichenoid” group of papulations with a palish halo (Plate 8, fig. 1), was removed entire. Sections show an interesting macrophage-type infiltration, undoubtedly recent, probably but not certainly leprotic of “indeterminate” character, with only a suggestion of a tendency to undergo tuberculoid differentiation. Bacilli not demonstrable.

The case with new suspicious lesions (Case 4) was also rebiopsied in 1936, from beside the first scar, with essentially negative findings; the lesion was (see Fig. 3 of the former report) and still is quite residual. There are now, however, a few small pale, faintly roughened spots on the right shoulder (Plate 8, fig. 2) the largest of which was removed. Sections of it show rather slight changes, mostly large round-cell infiltration, not pathognomonic. No acid-fast bacilli have been found, but one nonacid-fast organism was seen that morphologically could not be distinguished from a leprosy bacillus.

Regarding the polyneuritic changes mentioned, one case (No. 9) has slight thickening and tenderness of the right ulnar nerve, with moderate atrophy of the fingers and contraction of the small one. In the other case (No. 7) the right peroneal is much thickened and very tender and there is some disturbance of sensation and function of the leg when the patient is tired.

²In this connection may be mentioned a case—(R. B., previously reported by one of us (3) and to be presented more fully elsewhere—in which there was at first only an anesthetic area on the elbow that never did become macular, but in which several bacteriologically positive lesions appeared later on other parts of the body.

(b) *Macules with atrophy*.—Of the six cases in this group (Nos. 11 to 16) five have been followed to 1938. None now shows any evidence whatever of activity, except possibly a doubtful thickening of a single nerve trunk in one instance.

In one case (No. 11) there was a peculiar soft bulging of the anesthetic lesion-area due to marked changes affecting both the elastic and collagenous fibers of the dermis. These changes seem to be irreparable, for the condition still persists (Plate 8, fig. 3; compare with Fig. 2 of previous report). A similar condition has developed in the arm area of another patient (Case 23) following the subsidence of an active major tuberculoid lesion, which suggests that the lesion in the present case was of that nature when active.

Comment.—It may be that the proportionately numerous cases in this whole group that have remained without further manifestations are really cured. The fact that none of those in the subgroup with atrophic changes show manifestations of activity, whereas such manifestations are seen in some of those in which the lesions were not atrophic, suggests that lesions which cause the more severe damage to the skin—lesions which when active were very likely of definitely tuberculoid type and not “simple”—may on the whole be the more favorable as regards permanent healing.

3. SIMPLE MACULAR LEPRIDS

In this group of lesions, neither residual in appearance nor clinically tuberculoid, we attempted to distinguish (a) those that were quiescent or retrogressive, and (b) the active and progressive ones. This was done mainly on the grounds of presence or absence of erythema, but also taken into consideration were the general appearances as regards color changes, character of surface, elevation or palpable infiltration, and differentiation from the surrounding normal skin.

(a) *Quiescent simple macules*.—The eight cases placed here (Cases 17 to 24) were further divided according to whether or not tuberculoid changes were found (serial sections) in the original specimens.

(1) From three cases the specimens were nontuberculoid. In one (Case 19, recently dead of tuberculosis) the lesion in 1936 was residual and barely perceptible. In another (Case 17) it has remained surprisingly unchanged, the 1938 photograph (Plate 8, fig. 4) showing much the same details of outline and about the same color contrasts as that taken in 1934 (Fig. 5 of previous report). In the third (Case 18) it has progressed slightly but in a peculiar manner.

In this last case the lesion, originally a broken up or conglomerate area (Plate 8, fig. 5), had become somewhat larger and more definitely macular by 1936, with in parts a distinct "spotty" tendency, and in 1938 numerous isolated pale points had developed at some distance from it, the affected area as a whole being spotty rather than macular (Plate 8, fig. 6). Biopsied in both years, the specimens still show only slight round-cell accumulation around the superficial blood vessels.

(2) The histologically tuberculoid though clinically simple macules came from five cases, two of which are now quite negative though both patients neglected treatment.

In one of them (No. 22) the solitary lesion, now residual, progressed for a year or more and became mild minor tuberculoid. In the other (Case 24) the lesion, also solitary, was removed entire, without recurrence. Though it was "simple" in appearance when it was biopsied, it had previously been elevated and histologically the condition corresponds more to a minor tuberculoid than to a simple lepid.

The other three cases have undergone interesting developments and two have had to be hospitalized. One of the latter (Case 23), previously with two irregularly outlined macules (see previous Fig. 8) and only a trace of tuberculoid change histologically, suffered a reaction condition early in 1936 and the macules abruptly developed into large, bacteriologically positive, major tuberculoid plaques. Case 21, in which the disease was advancing in 1935, has now become lepromatous. These cases will be reported in more detail later.

In the third one (Case 20) there has been an unusual development. Some of the lesions, including the large biopsied one (previous Fig. 7), had retrogressed more or less in 1936 but others had progressed and new active ones had appeared. A specimen from one on the back (Plate 9, fig. 7) showed very slight tuberculoid changes, like the original one, and a few atypical bacillary forms were found in sections. By 1938 there was marked improvement, most of the macules having faded almost completely, but at the same time there had appeared numerous small new ones, very superficial, some faintly raised and slightly pinkish. Curiously, several of them were inside the limits of old, faded areas (Plate 9, fig. 8). Histologically one of them shows round-cell accumulation about the superficial plexus vessels, with slight but definite tuberculoid differentiation, without demonstrable bacilli; there is little evidence of the earlier invasion.

Comment.—Of this whole group of supposedly quiescent simple lesions only one-half actually retrogressed, which illustrates the difficulty of distinguishing those which will do that. Even the histological examination will not necessarily indicate what may happen. One solitary nontuberculoid lesion has remained curiously unchanged and another has progressed somewhat, while two of the tuberculoid ones have cleared up.

The development in Case 20 of new lesions within the otherwise more or less residual areas of old macules is rather intriguing because it is contrary to the rule that an area once affected by a lepid is not again invaded. This condition differs markedly from the "spotty" foci that sometimes develop, by the abortive, recrudescence process to be discussed later, within the margins of macules that are still more or less active. Whether or not these new, secondary lesions arose by recrudescence or by reinfection from a distant focus we cannot venture to say.³

(b) *Active simple macules.*—The lesions of this subgroup of eleven cases (Nos. 25 to 35) were originally divided into: (a) flat, with marginal erythema, (b) flat, with diffuse erythema, (c) slightly raised, with marginal erythema and (d) slightly raised, without erythema. These subdivisions are not emphasized here; it has been found more significant to group the cases on the basis of the number of lesions that existed.

(1) In six instances the lesions were solitary. Three of the cases—and the only ones with supposedly active lesions to do so—have become clinically quite negative, and a fourth one (Case 34) was retrogressive when last seen. Of the remaining two cases, one has progressed and the other (Case 28) has become lepromatous; that one will be reported later.

Of the cases that have cleared up, the macule of one (Case 33), quite superficial, disappeared within a year or so. In another (Case 25) there was progression for a year but recession thereafter. The third one (Case 31) took longer to subside but the condition was more severe histologically. Though apparently simple when biopsied it had evidently retrogressed from minor tuberculoid, but a second specimen in 1936 showed only remnants of that condition.

In the case that has progressed (No. 30) a few new small papular lesions had developed in 1936 in the neighborhood of the original one (former Fig. 11), in the specimen from which a few bacilli had been found. In 1938 these papules were not found but there were three new ones in the same region. Sections show the usual perivascular infiltration with a little early tuberculoid differentiation; a few bacilli were demonstrated in sections and in smears from the biopsy cut.

(2) In contrast with the preceding group are the five cases that had multiple macules. None of them has cleared up. Some of their lesions have shown progression while others have retrogressed simultaneously, these changes affecting entire macules or only parts of macules. In two cases new lesions have appeared,

³The Kahn test in this case has been reported positive (3+) but the significance of that fact is not known.

and in one the condition has progressed to the minor tuberculoid stage of the disease.

The most favored of these cases (Case 35) is as a whole distinctly better than at first, despite differences of the changes in different lesions (Plate 9, figs. 9 to 12). Another (Case 27) is at least no worse, for though the lesion seems more marked in parts it has retrogressed in other parts and has not increased materially in size (Plate 10, figs. 13 and 14). A few bacilli were found, in 1936, in one of two new biopsy specimens from the former case and none in one from the latter, which indicates that prognosis could not always be based on such findings.

However, both of the two cases in which the disease has progressed, with new lesions of the same type, gave original (1934) specimens in which bacilli were found. A few were also found in a second specimen taken in 1936 from one (Case 26), but the biopsied lesion (former Fig. 9) seems much the same as before except that it has extended somewhat. Bacilli were also present in the two specimens taken in 1936 and 1938 from the other case (No. 32), the appearance of which is not satisfactory as regards ultimate prognosis (Plate 10, figs. 15 and 16). In all instances the organisms were few and not readily found.

The fifth case (No. 29, examined for us by Dr. M. Carreon, in Iloilo), originally with large reddish areas on the arms, histologically slight tuberculoid, now has many widely distributed lesions of the same appearance and one that is "markedly raised, with a granular border"—obviously tuberculoid, probably of minor grade. Several nerves are thickened, and atrophic changes of one hand have developed.

Comment.—Not surprisingly, our diagnosis of active lesions seems on the whole to have been more accurate than that of quiescent ones. Nevertheless, some of these cases have cleared up without further progression. There doubtless is some significance in the fact that none did so that had multiple lesions. The existence of only a solitary lesion is not necessarily a guarantee of good prognosis, for one such case has become lepromatous; but it is to be noted that the original lesion was peculiar, being diffusely erythematous and of rather indistinct outline. The marked progression in one of the cases and ultimate development of a frank tuberculoid condition is also of some interest.

4. PAPULATE (TUBERCULOID) LEPRIDS

The nine cases in this group (Cases 36 to 44) represent a condition which is not generally included in descriptions of leprosy, though it has been emphasized in the preceding studies (1a). Morphologically there were macules, solitary or otherwise, which were more or less retrogressed or even definitely residual except for the presence of tuberculoid papules, or aborted papulations, or residua of that condition. In four instances the papules

were few, and those lesions we called "paucipapulate"; in the others they were numerous, "multipapulate."

Two main kinds of papulate lesions are met with, differing in appearance and significance. One of them, which includes the "lichenoid" lesions, is active and progressive, tending to form ordinary tuberculoid leprids. The other, to which our material is confined almost exclusively, represents an attempt at recrudescence or progression in otherwise flat recessive lesions. In them the populations occur typically (a) at the margins of the macules, often in circinate fashion. Occasionally they may be (b) inside the margins, constituting focal recrudescence in tissue that has been passed over by the advancing front of the infection, but commonly the process is abortive and actual papules are not formed. Finally, they may occur (c) as new foci outside and beyond the edge of the lesion ("colonial" development). In any event, the populations represent more or less isolated, focal attempts to reestablish or to extend activity in spite of factors that tend to overcome elsewhere or that have succeeded in doing so.

The papules may be firm and discrete, with little loss of color, but often lesions which are papulate (especially the multipapulate ones) are predominantly "spotty" because of small, diffusely pale spots that may contain papules, or may once have had them, or that may represent an abortive attempt to produce that change (see Figs. 15 to 27 of previous report). When in a circinate lesion the papulate elements are active, numerous and close together, it may perhaps be difficult to decide whether to put the lesion in this group or to class it as ordinary minor tuberculoid (see Plate 10, fig. 17).

The four cases called "paucipapulate" (Cases 36—former Fig. 15—and 37, 38, and 39), all had solitary macules; in three the papules were clinically active and frankly tuberculoid histologically, but in the fourth they were retrogressive and histologically almost residual. The lesions of three have long since vanished and that of the fourth was clearing up when it was last seen, in 1935, one year after the biopsy. Even anesthesia has disappeared in one instance.

With regard to the four cases with the multipapulate circinate condition, the biopsied lesions of three have completely cleared up and two of the patients (Nos. 41—former Figs. 20 and 23—and 43) are now quite negative clinically. As for the other two, in the one with the most active lesions (Case 44) the previous condition has all but cleared up, but a few new palish papules or spots have appeared in the area of the cheek lesion (Plate 10, figs. 17 and 18) and on the buttock. Specimens taken in 1936 and 1938 show corresponding diminution of abnormality. Though the original lesions

of Case 42 have quite disappeared, there has appeared on another part of the body a small, active, nonpapulate macule that in appearance is similar to those shown in Figs. 2 and 6. Histologically it is apparently leprotic, subtuberculoid in nature; bacilli not demonstrable.

A third kind of papulate lesion existed in the ninth case of this group (Case 40). The macule, a very irregular, solitary one on the buttock, was studded generally with a follicular papulation due to concentration of tuberculoid changes around the hair follicles. This condition, we assume, represented focal persistence rather than a recrudescence of the process. The lesion progressed somewhat for a time and became much less irregular, but is now quite recovered, clinically and histologically (Plate 11, figs. 19 and 20).

Comment.—The outcome in these cases confirms the opinion, expressed in our first report, that the "recrudescent" form of the papulate condition is of good prognosis. In most instances the lesions have cleared up, leaving only residual changes or none that are visible. In only one case has there been any really new development, and that probably unimportant.

5. ORDINARY MINOR TUBERCULOID LEPRIDS

Only four cases (Nos. 45 to 48) represented this variety of the leprids. All of them were in the smaller Cordova group, which fact we are not inclined to attribute to any local peculiarity of the disease but rather to the results of treatment of similar lesions in cases that attend the Cebu dispensary.

One patient (Case 46), who had a single large lesion on the thigh (former Fig. 31), seems to be completely recovered. After a year or so of progression and another of recession there was, in 1935, only a little recrudescent papulation at the edge of the area, and now there is not even anesthesia. The lesion of Case 45 that was biopsied (former Fig. 29) increased for at least two years, afterward progressing in parts but with rather more retrogression elsewhere. In the meantime other lesions, two of them papulate, have quite disappeared.

On the other hand, in Case 47 there has been only temporary improvement at one period. The margins of the original large area on the thigh and leg (former Fig. 1) have advanced and are still active, and small macules have appeared on the face. However, the lesions are all too inconspicuous to show well in photographs (Plate 11, fig. 21) and the disease has progressed so slowly that the patient does not really seem any worse off now than five years ago. Nevertheless, a few bacilli were found in the 1938 biopsy sections and even in a smear from the specimen, though all previous examinations were negative.

The fourth case (Case 48), the only one with bacteriologically positive smears in 1933, was hospitalized shortly thereafter and became major tuberculoid. Later he was paroled as apparently recovered, but recently he has

become reactivated and is now one of those border-line cases between the tuberculoid subtype of neural leprosy and the lepromatous type. This unusual case will be reported more fully elsewhere.

Comment.—The developments in this obviously inadequate group suggest that lesions of the minor tuberculoid class tend to progress slowly for years, though some of them clear up spontaneously. It may be that the developments would have been more favorable had active treatment, particularly by the intra-dermal route, been taken by the patients who did not improve.

6. MAJOR TUBERCULOID LEPRIDS

This group (Cases 49 to 52) was no larger than the last but more varied. One case was a marked one of acute "tuberculoid reaction," bacteriologically positive; one was also fairly recent, with an active solitary lesion of the face; a third had two retrogressive lesions and the fourth showed at the time only residual changes. Only one of the three that remained under observation now presents noteworthy lesions.

This case, the one in reaction (No. 49, former Fig. 32) was included in the study group in 1936 and so has been followed for only two years. Hospitalized at that time, the boy is now paroled but as will be shown in a later report the condition is not inactive, though the lesions are no longer of major tuberculoid grade.

In the case with the lesion of the face (No. 51), the area was no longer distinguishable in 1936 but the supraorbital nerve under it was thick. A specimen taken then shows only traces of tuberculoid change in the skin, but the nerve is caseous tuberculoid. In 1938 there was no apparent abnormality except for the paralysis of the orbicularis, which had increased. (Plate 11, figs. 23 and 24).

Comment.—The improvement that has occurred in the three cases with solitary or few major tuberculoid lesions is typical of that which is usual in cases of that kind.⁴

7. NONLEPROTIC CONTROL LESIONS

The nonleprotic lesions that were included in the first report are mentioned here only to say that none of the persons involved has shown any evidence of leprosy.

DISCUSSION

Our observations during the five years that these cases have been followed up give, first and foremost, emphasis to the slowness with which changes ordinarily take place in lesions

⁴Observations in a group of active tuberculoid cases with multiple, bacteriologically positive lesions, studied at the Eversley Childs Treatment Station, will be reported in a later article of the present series.

of the kind studied. Even with steady improvement it may take years for an active lesion to become residual and disappear, while on the other hand when the disease progresses without radical change of form, the rate of extension of the lesions is usually so slow that after several years a patient may seem little worse off than before.

More interesting, though less fortunate, are those cases that undergo change of form. That happened in five of our group (10 percent), one showing rapid extension and intensification of the process with the development of a minor tuberculoid lesion, two undergoing reaction and becoming major tuberculoid, and two suffering direct transformation to the lepromatous type. Detailed discussion of these cases is reserved for later reports.

Another feature of these observations is the emphasis given to the difficulty of determining at a given time those simple macules that are definitely quiescent. Actually residual lesions can be distinguished with more certainty—none that we so classified have shown any further activity, though in a few cases there have been other manifestations of progression of the disease,—and on the other hand the frankly active ones are easily recognized. It is the intermediate group that is most difficult.

In only one-half of the macules that we called quiescent has the disease failed to advance, which simply emphasizes the fact that very inactive-looking leprids may really be indolently active. One of those in which no tuberculoid change was found histologically (in the serial sections) has progressed slightly. Three of the five that showed tuberculoid changes have undergone interesting developments, one of them becoming lepromatous, while a fourth progressed for a year and then retrogressed; it would seem that as long as definite tuberculoid histology is present it cannot be said that a lesion may not progress, or become reactivated. Even the site of a mere anesthetic area may develop a visible macule unless it is histologically quite residual; and even then, as evidenced by one case, the anesthesia may extend and other neural changes develop, presumably because of lesions confined to the nerves themselves.

With regard to the lesions that we classed as active, three out of the eleven cases improved steadily, but that does not necessarily imply that the lesions in question were not active when first examined. In general, more marked tuberculoid changes were found in sections of the macules called active than

in those that seemed quiescent, but even when simple leprids are retrogressive slight tuberculoid changes persist in them so long that the histological examination alone cannot be relied upon to determine their status.

On the other hand these observations as a whole indicate the frequency with which lesions of whatever class—and indeed the cases themselves—may be expected in time to clear up even with little or no treatment. As is shown in Table 1, 29 of the 46 lesions followed to 1938 (63 percent) have disappeared or are only residual, and we are certain that this has happened in some of the other cases. Of these 29 patients only one (a papulate case) took treatment fairly regularly, while 19 took none or only a negligible amount. On the other hand, of the 10 patients whose lesions got worse (found only in the simple macular and minor tuberculoid groups) only one took more than a negligible amount of treatment. The 7 patients whose lesions either remained stationary or improved but did not clear up did better in this respect, one-half of them being in the upper bracket. It certainly is not to be concluded that treatment is to be ignored in neural leprosy, for it is not possible to distinguish the cases that will improve spontaneously from those that will not.

TABLE 1. *Changes in cases followed to 1938, with special reference to the lesions biopsied.*

Lesion Group	Cases		Changes of lesions			
	Original number	Number seen in 1938 ^a	Residual or gone	Improved not residual	Stationary	Worse
1. Anesthesia only	3	3	3 ^b	—	—	—
2a. Residual, without atrophy	7	7	7 ^c	—	—	—
2b. Residual, with atrophy . . .	6	5	5	—	—	—
3a. Simple, quiescent	8	7	2 ^d	1 ^e	1	3
3b. Simple, active	11	10	3	1	1	5
4. Papulate	9	8	7 ^f	1 ^g	—	—
5. Minor tuberculoid	4	4	1	—	1	2
6. Major tuberculoid	4	2	1	1	—	—
TOTALS	52	46	29	4	3	10

^a Not including cases followed for from one to three years.

^b Not considering purely neural changes.

^c In one instance (Case 4) the original lesion is gone but a slight new one present in 1938. Two cases (Nos. 7 and 9) with aggravated polyneuritis.

^d Lesion removed entire in one case (No. 24).

^e New recent lesions have developed (Case 20).

^f Including Case 42, now with a new solitary lesion.

^g Case 44; only a little left, but not wholly inactive.

In the difficult matter of prognosis, which is naturally influenced by many other factors than treatment, our observations indicate the importance of two features: (a) the type of the lesions, and (b) their number or extent. With regard to the former, it seems evident that there are required information regarding the clinical appearance of the lesions *at their maximum* and an understanding of the pathological changes in them. There is evidence that, up to a certain point at least, the more marked the tuberculoid response to the infection—that is, the more active the tissue reaction—the better the prognosis. The major tuberculoid cases with few lesions showed the recovery that we have come to expect of that condition. It would seem that the minor tuberculoid lesions, with less marked tissue reaction, are more prone to persist for long periods of time, though as a class they respond well to active treatment. In this connection there seems to be reason to believe that patients with residual lesions showing more or less permanent atrophic changes, indicating relative severity when active (i.e., the clinical tuberculoid condition) have a better chance of remaining free from further trouble than those with nonatrophic residual macules. On the other hand the “simple” lesions seem more prone to persist indefinitely. We have gained an impression that it is such cases, especially when the lesions are of the less differentiated type histologically, that are most liable to undergo change of form to the lepromatous type.

Considering the second of the factors mentioned, the degree of involvement of the skin, it seems clear that, whether the lesion be simple or tuberculoid, there is a much better chance that a case will clear up when there are only one or a very few leprids (i.e., the lesser N1 cases) than when such lesions are multiple and extensive. That is rather strikingly brought out in the active simple group, in which four of six with solitary lesions have cleared up or are really improved, while only one of the four with multiple ones has improved.

This leads to the question of localization or limitation of the infection in this form of leprosy. It may or may not be simple coincidence that there was no further manifestation of the disease in one patient (Case 24) after complete removal of the small solitary lesion which histologically was relatively marked tuberculoid. In another patient (Case 10) a very small lichenoid lesion (Plate 8, fig. 1) was removed entire in 1936, with no recurrence. It was so recent and histologically undif-

ferentiated that we cannot be certain that it was leprous, since bacilli could not be demonstrated, but at least we could not give it any other diagnosis. On the other hand, in one instance (Case 34) a small, active pinkish macule was only partly removed, and in the succeeding two years, until the patient emigrated, there was a little progression at the sides of the scar (Plate 11, fig. 22). It seems probable that if the entire lesion had been excised there would have been no further activity.

An intriguing though common feature of the process of improvement in this form of leprosy is the way in which forces favorable and antagonistic to the disease process vary locally from place to place. Inactivation and healing in one lesion may occur simultaneously with progression in another, and such differences occur even in different parts of the same lesion. Perhaps the most interesting phenomenon of this kind is the papulate condition seen in several of our cases. That particular process is clearly dependent upon very limited, colony-like, and usually quite temporary, recrudescence of the lesion-process in cases that on the whole are relatively antagonistic to it. This kind of lesion is not generally recognized in descriptions of leprosy. Though it is similar at least in structure to the "lichenoid" and similar forms by which lesions are sometimes initiated, it differs in significance in that with the latter form the patient's forces of resistance are insufficient to prevent the condition from progressing to establish one of the more ordinary leprids.

Certain features of involvement of the nerves might be discussed. For example, workers in India lay much stress upon thickening of the cutaneous nerves that supply the areas of the leprids, due to direct extension upward of the tuberculoid process. In our 1936 examinations we gave particular attention to this matter and our findings confirmed previous experience that, in the Philippines, important thickening of the cutaneous nerves in relation to the leprids is uncommon. In only one of the major tuberculoid cases (Case 51) was a notably affected superficial nerve found; histologically it was typically tuberculoid, with caseation.

A related feature that we have encountered is polyneuritic affection of a single extremity, on which there has been a leprid. In such an event the question arises whether the deep nerve trunk was affected by continuity through the cutaneous nerve and lateral spread from that part of the trunk to parts

that supply the muscles, or by accidental metastatic seeding from the blood stream. If the latter course is the actual one, it seems a strange coincidence that in not less than four of our cases there is unilateral polyneuritis of the same members that have had macules, and not a single definite instance of that affection in a limb without a macule. If the lesion does reach the trunks by way of the cutaneous nerves it often, if not usually, does so—in Philippine cases—without producing gross enlargement of those nerves.

Other questions are raised by some of these cases. One is why in some instances anesthesia should persist for years after a macule disappears, or even increase, as in Case 2, while in other instances it clears up entirely in time. In the former case is there damage to the cutaneous nerve above the lepride—without perceptible thickening—and not in the latter? Another question is whether an area of anesthesia without macule formation is due to an occult lesion in the skin itself or to disturbance confined to the cutaneous nerve. If the latter is possible, may the pathological condition extend in retrograde fashion to involve the skin? Specifically, was the macule that developed secondarily in Case 3 due to involvement of the skin that had been there, imperceptible, from the outset, or was it a secondary development starting from the cutaneous nerve? These latter questions may be academic, but they are of some interest because so many patients—at least in the Philippines—say that the first manifestation of the disease is numbness or anesthesia in some localized area.

SUMMARY

Although five years is much too short a time to determine the final outcome in cases of the neural type of leprosy, interesting changes have been observed in many of the 52 cases of the group that we began to study in 1933 and 1934.

Of three cases with only anesthetic areas over normal-looking skin, one has shown no change whatever; in another the anesthetic area became a macule; and the last, whose neural manifestations were secondary to a macule that had disappeared four years previous to the initial examinations, now has progressive polyneuritic changes but no skin lesions.

Thirteen patients exhibited residual macules, seven of them without atrophy of the involved skin. Four of the latter have

become quite negative; one shows new suspicious lesions which, however, failed to show changes pathognomonic of leprosy; two others have developed polyneuritic manifestations. Among the six cases with residual macules that showed atrophy, none of the five that were fully followed up shows any evidence of activity. It seems that leprids which cause severe enough damage to the skin to cause atrophy (lesions that probably were clinically tuberculoid when most active) are of more favorable prognosis than those that do not produce such effects.

We originally divided the simple macular leprids into active or progressive and quiescent or retrogressive, depending chiefly on the presence or absence of erythema and elevation. (a) Of the eight patients who had apparently quiescent macules of this class, the lesions have become residual in three, remained unchanged in one, showed slight progression in one, advanced to a major tuberculoid lepid in one; in the seventh it became lepromatous. The eighth patient was of particular interest, presenting extensive lesions some of which were retrogressive at the same time that new ones showing a few bacilli kept appearing. Thus some of the macular leprids which were believed to be quiescent were in reality indolently active. (b) Developments in the eleven patients who had clinically active simple macules indicate that the number of such macules has some significance as regards prognosis. Of the six cases with solitary macules, four became quite negative, although one continued to progress and one became lepromatous. On the other hand none of the five cases with multiple lesions has cleared up.

What we have described as the recrudescence type of the papulate tuberculoid lepid was represented by nine cases. All have cleared up, leaving only residual lesions, except one patient in which a small active macule has recently appeared. This group taken as a whole has shown the most favorable course of all those under observation.

Only four cases were classified as having ordinary minor tuberculoid leprids. One seems to have completely recovered, the second has a large lesion which has progressed in parts but retrogressed in others, the third is very slowly progressive, while the fourth has become reactivated after passing through a major tuberculoid phase with apparent recovery.

The four cases in the major tuberculoid group have all shown marked retrogression during the observation period, though indications of activity have persisted in one.

We are indebted to Dr. Fidel C. Plantilla, now in charge of the Cebu Skin Dispensary, for use of the records there and for material assistance in connection with the reexamination of patients, and to Dr. Ricardo S. Guinto, assistant epidemiologist of the Leonard Wood Memorial, for his part in the follow-up of the Cordova cases in 1934 and 1935.

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DESCRIPTION OF PLATES

PLATE 8

FIG. 1. A suspicious new lesion of lichenoid type, histologically of "indeterminate" nature but presumably leprosy. Removed entire, it did not recur. Case 10 (1936).

FIG. 2. Suspicious small, recent lesions, the largest of them found histologically to show only large round-cell infiltration, but probably leprotic. (Compare Fig. 7.) Case 4.

FIG. 3. Permanent soft bulging of the anesthetic area of skin, site of a lesion, presumably marked tuberculoid, healed several years ago (compare Fig. 2 of previous report). Case 11.

FIG. 4. A macule which has undergone practically no change, in outline or otherwise, in the four years since it was biopsied (compare Fig. 5 of former report). Case 17.

FIGS. 5 and 6. Comparing the original appearance of the lesion of Case 18, a small discontinuous area of irregular outline and inactive appearance (Fig. 6 of former report), with its condition four years later. It is now almost entirely "spotty," micropapulate. (The scars of first two biopsy wounds are evident.)

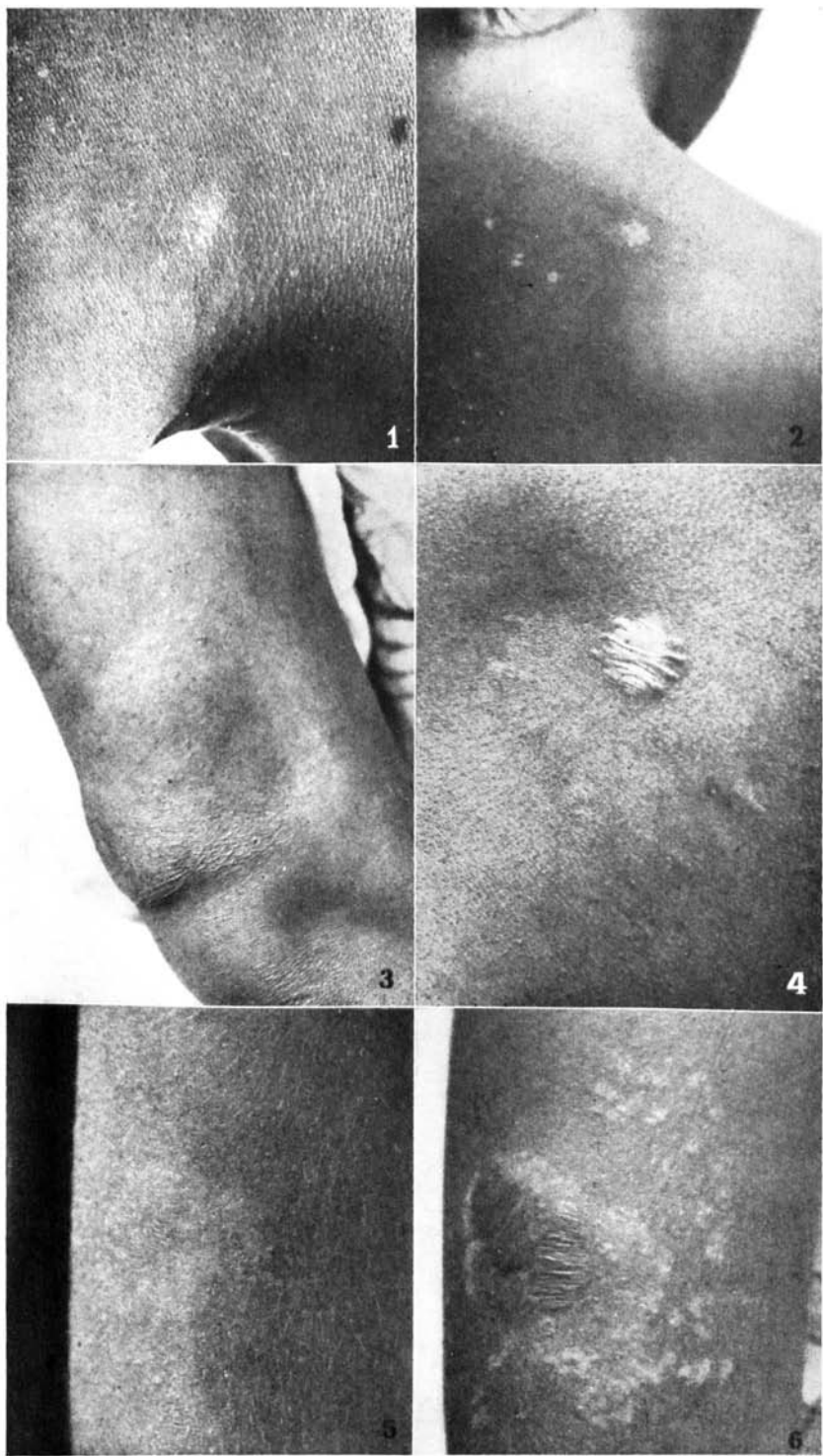


PLATE 8

PLATE 9

FIG. 7. Lesion on back in Case 20, in 1936, when it had spread actively while the one biopsied in 1934 (Fig. 7 of former report) had retrogressed markedly.

FIG. 8. The same macular area, now residual and hardly discernible, but with a small new lesion (similar to but larger than the one shown in Fig. 2) which has developed secondarily in the area previously affected.

FIGS. 9 and 10. The leg lesion of Case 35 as it appeared in 1934 (Fig. 14 of former report) and in 1938. The area involved is much larger than before and the lesion is still active, though very irregular and interrupted. (Compared with Figs. 11 and 12.)

FIGS. 11 and 12. The buttock lesion of the same case, as seen in 1914 (Fig. 13 of former report) and in 1938. It enlarged considerably but, in contrast with the leg lesion shown in the two preceding pictures, it has now undergone marked retrogression. (Scars of two biopsy wounds present.)



PLATE 9

PLATE 10

FIGS. 13 and 14. The lesion of Case 27, comparing the condition in 1934 (Fig. 10 of former report) and in 1938. With apparent regression in places, there is accentuation in others, yet in size and outline the affected area has changed but little.

FIGS. 15 and 16. Showing the general appearance and some of the extended lesions of Case 32 (not previously figured). Bacilli in small numbers were found in all of the biopsy specimens examined, in 1934, 1936 and 1938. The general appearance of the patient and his lesions is such that the prognosis cannot be considered favorable.

FIGS. 17 and 18. Showing the improvement in the face lesion seen in 1934 (Fig. 27 of former report), which at that time was in part papulate and in part minor tuberculoid. Little trace of it now remains, but a few new pale papulations have developed recently. (The same marked improvement, with the same recent papulation, has occurred in the buttock lesion, Fig. 26 of the former report.)

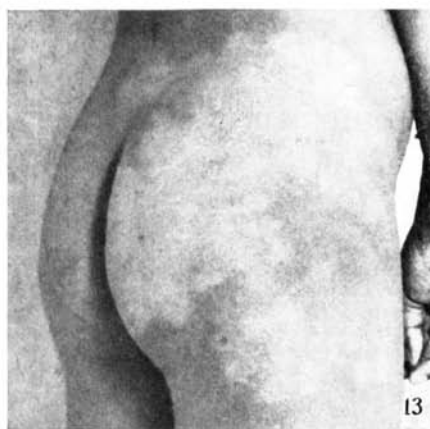


PLATE 11

FIGS. 19 and 20. The unique perifollicular, diffusely papulate lesion of Case 40, as it appeared in 1934 (Fig. 21 of former report) and at present. It is now quite recovered, clinically and histologically, and even on the patient himself its previous outline can be made out only when viewed from a certain angle and distance. (The biopsy scars are in the lower part of the lesion area.)

FIG. 21. The face of the patient with an extensive but slight-degree minor tuberculoid lesion of the thigh (Case 42, Fig. 1 of former report). For at least four years there has been an active macule in the left malar region, increasing steadily in size to measure 5×7 cm., but it is so slight in degree that it cannot be definitely distinguished in the original photograph. A smaller one below the corner of the mouth is more evident, being more elevated and paler—slight minor tuberculoid.

FIG. 22. Showing the spread of a small lesion beyond the scar (right and left) one year after incomplete excision. Originally a pinkish, flat ("simple") macule, the process became more marked, causing irregular elevation—slight minor tuberculoid.

FIGS. 23 and 24. Showing the complete recession of a major tuberculoid lesion of the face, Case 51. Fairly recent and active when first photographed in 1934, very little remained at the time the enlarged supra-orbital nerve was biopsied in 1936 (scar evident), and it now seems entirely recovered, though the paralysis persists.

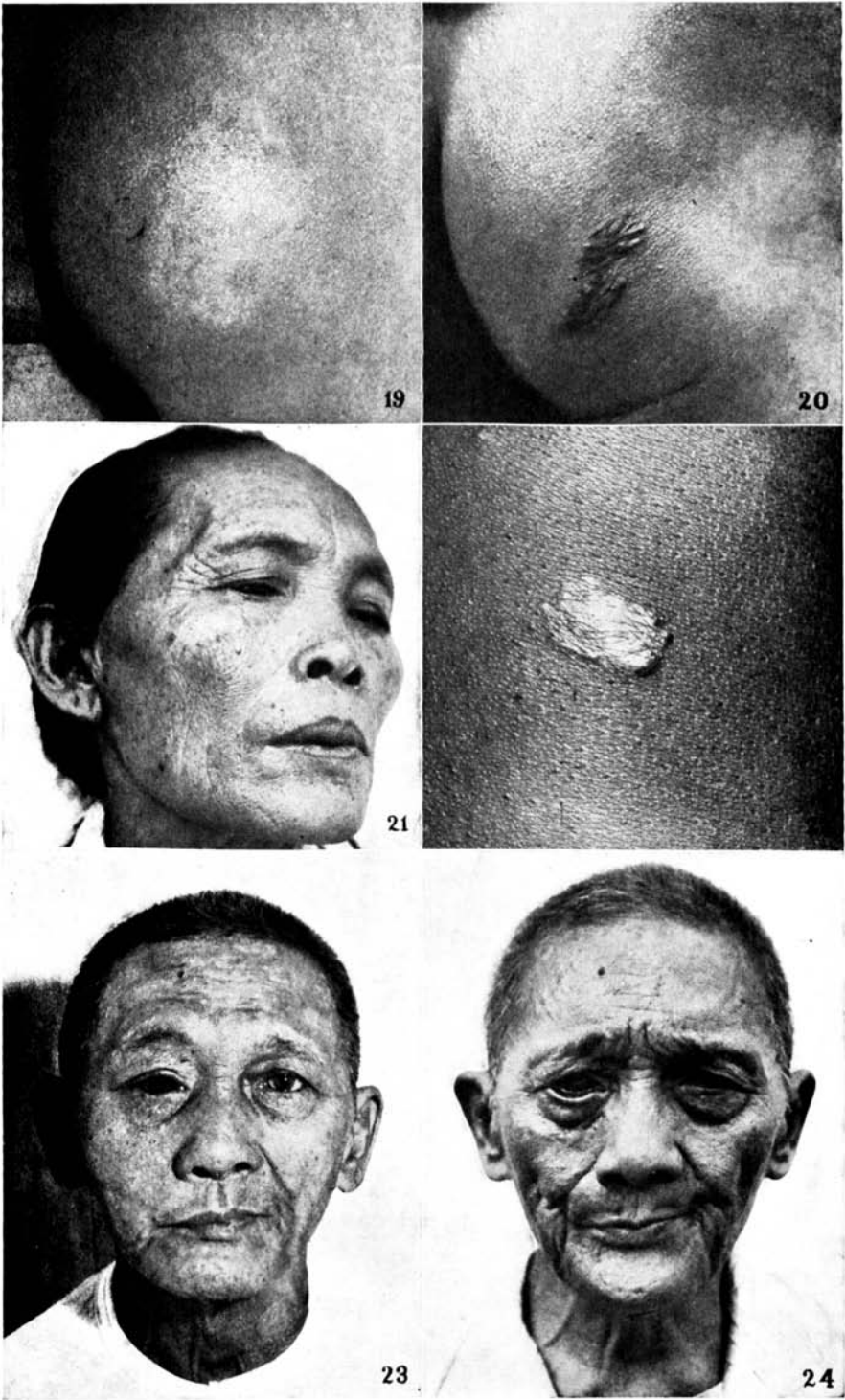


PLATE 11