THE SKIN LESIONS OF NEURAL LEPROSY
III. OBSERVATIONS IN CHINA

By H. W. WADE, M.D.
Leonard Wood Memorial Laboratory
Culion, Philippine Islands

AND N. D. FRASER, M.B., CH. B., D.T.M. & H.
English Presbyterian Mission Hospital
Swatow, Kwangtung, South China[1]

INTRODUCTION

Late in 1934 the writers undertook to extend to Chinese patients, in the Swatow region of South China, the study of the skin lesions of neural leprosy which had recently been begun at Cebu, in the Philippines, by Wade and Rodriguez (6). Material was collected in (*a*) the leprosy clinic at the English Presbyterian Mission Hospital in Swatow, (*b*) a recently-established clinic in the country town of Iam-tsao, and (*c*) the Swatow Municipal Leper Asylum. At about the same time material was obtained from a few cases in Shanghai.

A brief statement regarding the institutions concerned seems desirable. In 1867 a leper refuge was established in connection with the mission hospital in Swatow, in which region the disease is a serious problem (1). Later this refuge was discontinued, and treatment of a routine nature was given at an outpatient clinic. In 1928 this clinic was reorganized (N.D.F.) and an attempt was made to treat and observe each case individually. Under the circumstances, which are similar to those under which most mission hospitals in China operate, this work has had to be done on a severely practical basis, and primarily for the relief of patients; the records of the clinic are correspondingly limited.

In Iam-tsao, thirty miles from Swatow, a clinic had been started only a few weeks previously to extend antileprosy work to the country district and, in a way, to serve as a proving-ground for methods of such extension (1). Popular interest in it had led to the registration of 60 cases in the first month. At the time our material was taken, the patients were still being examined and injected in an old temple, utterly lacking in facilities for such work.

[1]Recently transferred to the English Presbyterian Mission Hospital, Swabue, Kwangtung, South China.

At the Swatow Municipal Asylum, a walled compound located on a very small, hilly island in the bay, there were about 100 inmates, most of them beggars picked up on the city streets by the police, and many of them had been there for long periods. The institution was supposed to be visited once a week by an official physician, who had received no special training for leprosy work, but the patients showed little evidence of having been treated.

MATERIAL STUDIED

In most of the cases seen in these institutions the disease had assumed such a form or had advanced to such a stage that the patients had been impelled to appear voluntarily at the clinics for treatment, or had been picked up by the authorities and sequestrated in the asylum. Consequently the number of early or slight cases among them was relatively small, and the group as a whole differs radically from the Cebu group dealt with in the preceding report of this series as regards duration, advancement and the occurrence of polyneuritic changes. We were particularly interested in detecting cases that would exemplify those forms that are recognizable clinically as "tuberculoid leprosy," because little was known about its occurrence in China. However, to permit making a contribution to the comparative study of the leprides we included as many cases as we could with simpler ones and we also included all of the atypical cases of doubtful classification that were encountered. In total, 38 cases were biopsied, from several of whom two specimens were taken.

At the hospital in Swatow, in two clinic periods, about 80 patients were seen. Most of them had been under treatment for periods varying up to several years, and many had undergone some degree of improvement, some to a point that made it impossible to say with certainty just what their lesions had been like originally. Of this group 19 were biopsied. At Iam-tsao none of the patients had been treated for more than a very few weeks, though a few had begun to show some apparent improvement. Among the 45 that appeared on the day of our visit comparatively few were of immediate interest, but among them there were some excellent lesions; 6 cases were biopsied. At the Municipal Asylum surprisingly few of the 75 inmates seen were of interest. In the great majority of them the disease was advanced, and most of them were active cutaneous-type cases; 9 were selected for biopsy.

In Shanghai, which is not an endemic leprosy center, a clinic was being operated at that time in the Hongkew district by the Chinese Mission to Lepers. Of the 80 patients registered 25 were

seen and 4 selected for biopsy, which was done for us at the Henry Lester Institute of Medical Research. Several patients of interest were also seen at the dermatological clinic of the Chinese Red Cross Hospital, but none of them is available for inclusion in this report. Reiss has recently published reports on several cases from that clinic (3).

The cases selected for study had to be dealt with rapidly. Those seen at the clinics had appeared for routine treatment and could not be detained long, and at the asylum our visit was necessarily brief. In consequence the examinations and the notes made were unavoidably incomplete, but photographs were made of most of the lesions biopsied. The condition of the superficial cutaneous nerves was not specially investigated, though note was made of grossly enlarged ones encountered. Obvious "polyneuritic" changes (paralyses, contractures, etc.) were also noted, but lack of notation does not signify absence of enlargement of nerve trunks or peripheral anesthesia. The bacteriological smears were examined at once, and in one instance (an atypical case) the examination was repeated. The histological examinations were made later at Culion on the same lines as in the study of the Cebu cases, the slides being identified only by number and no reference being made to the clinical notes.

CLASSIFICATION OF THE CASES

The classification of the leprides employed in this series of studies (6, 7) having been developed after the work here reported was done, there has been some difficulty in designating on that basis all of the lesions examined from the 35 cases to be considered.[2] However, the data available, with particular reference to the photographs in several instances, has sufficed to permit making quite accurate class diagnoses. These are summarized in Table 1. It is to be understood that, a main purpose of the study being to compare the pathological changes of the different clinical varieties of the leprides, the assignment of the cases has been as of the lesion (or part of lesion) examined as it appeared at the time of examination, rather than of the case as a whole. On the latter basis Case 21, for example, would have been classed as of major grade rather than minor.

Of the "residual and quiescent" group one case can be considered "abortive incipient"; the other two had evidently retrogressed from more active conditions. One of the "simple active" lesions had also been more severe (Case 5) and another possibly so (Case 8). Con-

[2] Three cutaneous-type cases that were biopsied for reasons not connected with this study are not included in this report.

sidering the cases that were clinically tuberculoid, it has seemed best to separate the active and retrogressive ones except as regards the group with "papulate" lesions, some of which were active and others retrogressive. The thirteen active tuberculoid cases of the more familiar kinds (including one with nerve abscess, which is not common in this region) have presented no difficulties. Of the six cases in the retrogressive group, two had obviously been of the major grade, but there was no evidence that the others had been more than minor; one may have been of the papulate variety.

TABLE 1. *Clinical classification of the lesions studied, by sources.*

Groups	Sources of Cases				Total (±225 cases examined)
	Presbyterian Hospital (±80 cases examined)	Iam-tsao Clinic (±45 cases examined)	Municipal Asylum (±75 cases examined)	Hongkew Clinic (±25 cases examined)	
1. Quiescent or residual	2	—	—	1	3
2. Simple, active.....	1	—	5	1	7
3. Papulate (minor tuberculoid).....	2	—	1	—	3
4. Minor tuberculoid (ordinary).....	3	4	1	—	8
5. Major tuberculoid...	2	1	—	1	4
6. Retrogressed tuberculoid.....	5	—	—	1	6
7. Atypical cases.....	2	—	2	—	4
TOTALS.....	17	5	9	4	35

PRESENTATION OF CASES

For the purposes of this report it seems desirable to present the most pertinent data in tabular form (Table 2), rather than in the manner employed in the preceding report. The notations are necessarily very brief, but to some extent they are amplified and discussed in the next section of the article. After all, to convey a definite impression of the morphology of the lesions it is necessary to rely more on the photographs than on description. The four cases included in the "atypical" group, being of special interest, are dealt with more fully than the others, but no attempt is made to do more than record the findings.

The sources of the cases are indicated in the table as follows: PH = Presbyterian Hospital, IT = Iam-tsao, MA = Municipal Asylum,

TABLE 2. *Summary of clinical features and histological findings of lesions studied.*

Numbers, serial and record	Sex and age	Classification and duration	Lesions biopsied	Other lesions	Histological findings
			Residual or quiescent lesions		
1 PH-3	M 20	N1 7 yrs.	Small, flat, smooth, hypochromic, of buttock; apparently residual. (No Fig.) No smear.	None	Slight fibrosis, no inflammatory change; healed lesion.
2 PH-2	M 52	N3– 18 yrs.	Large, somewhat atrophic, inactive, of both shoulders. Fig. 1. B– (two).	Other lesions, mostly similar; a few very slightly raised and reddish. (Polyneuritic changes.)	Slight fibrosis, both specimens; one with very slight round-cell, perivascular.
3 HK-4	M 40	N2– 10 yrs.	(*a*) Somewhat atropic, inactive, of thigh. Fig. 2. (*b*) Diffusely reddish, of chin. B–.	Right cheek reddish, noninfiltrated; other macules quiescent. (Polyneuritic changes.)	(*a*) Slightest round-cell only. (*b*) Chronic inflammatory only.
			Simple, active		
4 MA-9	M 38	N3 (?)	Large, slightly atrophic, of arm; slight erythema in places. Fig. 30. B–.	Numerous small reddish to pale patches, atypical. (Polyneuritic changes.)	Tuberculoid, minimal, residual.
5 HK-1	M 47	N2– 5 yrs.	Noninfiltrated, atrophic, scarred, slightly erythematous in places. (*a*) Scapula, (*b*) buttock. Fig. 3. B–.	Others more or less similar. (Polyneuritic changes.)	(*a*) Tuberculoid, slight, residual(?). (*b*) Less tuberculoid, superficial only. Some fibrosis in both.
6 MA-3	F 25	N2– 16 yrs.	Large, well-demarked, pale, perceptible infiltration, slight erythema, of scapula. Fig. 4. B–.	Several, mostly entirely inactive, at most faintly erythematous.	Very slight tuberculoid, not inactive; some lymphoid infiltration.

Numbers, serial and record	Sex and age	Classification and duration	Lesions biopsied	Other lesions	Histological findings
7 MA-2	F 20	N1 5 yrs.	Extensive, of upper back; very slight elevation and erythema. (No Fig.) B–.	Others, similar or entirely quiescent.	Tuberculoid, very slight, a few small foci, apparently residual.
8 MA-6	M 57	N2– (?)	(*a*) Flat, coarse-texture, slight erythema, of scapula. (*b*) Small diffusely reddish, nearby. Fig. 5. B–.	Others, similar, mostly residual. (Polyneuritic changes.)	(*a*) Tuberculoid, slight; some round-cell. (*b*) More infiltration, minimal tuberculoid.
9 PH-12	M 33	N2 10 yrs.	Diffusely reddish, slightly thickened, of face. Fig. 6. B–.	Two large, ordinary macules elsewhere, with erythema. (Polyneuritic changes.)	Tuberculoid, slight, small foci at different levels; considerable round-cell.
10 MA-7	M 32	N1+ (?)	Flushed, slightly infiltrated in places of face. (No Fig.) B–.	Large, quiescent or residual, buttocks and thighs.	Tuberculoid, moderate, active, mostly deep; moderate round-cell.
			Papulate minor tuberculoid lesions		
11 PH-9	M 34	N1 6 yrs.	Small, ill-defined, flat except minutely micropapulate at edge, of lower chest. Fig. 7. B–.	Others, larger and more grossly papulate.	Tuberculoid, slight, mostly superficial, not residual.
12 PH-15	F 16	N1+ 7 mos.	Irregular, pale, flat but minutely papulate, slight erythema, of arm. Fig. 8. B–.	Others on back and buttocks, similar but more conspicuously papulate; pink area face.	Tuberculoid, slight, mostly superficial, not residual.
13 MA-4	M 38	N2– (?)	(*a*) Narrow, coarsely papulate, linear, of chest. (*b*) Similar, less regular, of shoulder. Figs. 9 and 10. B–.	Others very similar, body and arms.	Tuberculoid, moderate, in narrow zone; superficial fibrosis inside that zone.

Numbers, serial and record	Sex and age	Classification and duration	Lesions biopsied	Other lesions	Histological findings
			Minor tuberculoid lesions		
14 IT-2	F 24	N2 9 yrs.	Narrow, moderately raised zone, of lower back. Figs. 11 and 12. B–.	Others on body and extremities; face involved.	Tuberculoid, moderate, mostly in deeper layers.
15 IT-3	F 28	N2– 10 yrs.	Slightly infiltrated, irregular-surfaced, band-like, of back. Fig. 13. B–.	Others elsewhere similar; face involved. (Polyneuritic changes.)	Tuberculoid, moderate, active, mostly deep; numerous small superficial foci.
16 IT-1	F 24	N2– 8 yrs.	Well defined, uniform, band-like, of thigh. Fig. 14. B–.	Similar one on other thigh. (Polyneuritic changes.)	Tuberculoid, moderate, active; superficial foci few and very small.
17 PH-17	F 33	N2– 3 yrs.	Similar but retrogressive(?), of scapula. (No Fig.) B–.	Others, buttock and thighs.	Tuberculoid, slight, mostly deep; retrogressive.
18 IT-5	M 38	N2– 2 yrs.	Small, circular, raised; beginning central depression, of chest. Fig. 15. B–.	One other lesion, of foot. (Polyneuritic changes.)	Tuberculoid, rather slight, mostly deep, considerable round-cell.
19 PH-5	M 28	N1+ 6 yrs.	Large area, of arm, margin irregular of edge and surface, erythematous. (Reaction?) Fig. 16. B–.	Several elsewhere, some suggestive of major tuberculoid.	Tuberculoid, fairly marked, all levels; superficial foci sufficient to form papulations.
20 MA-1	F 38	N2 (?)	Irregular, somewhat raised, similar to preceding, of forearm. (No Fig.) B–.	Others similar elsewhere. (Polyneuritic changes.)	Tuberculoid, moderate, numerous small foci in all levels.
21 PH-19	F 22	N1+ 18 mos.	Small, annular, moderately raised, of thigh. Fig. 17. B–.	Others on lower leg. A major lesion on foot. (See comments.)	Tuberculoid, moderate, slight round-cell superficially.

Numbers, serial and record	Sex and age	Classification and duration	Lesions biopsied	Other lesions	Histological findings
			Major tuberculoid cases, active		
22 IT-4	M 23	N2– 1 yr.	Large, red, abruptly raised plaque on left face; reaction. Fig. 19. B–.	Similar but smaller elsewhere, some scaling. (Polyneuritic changes.)	Tuberculoid, marked, active, all levels; large foci merging.
23 PH-13	M 36	N1 1 yr.	Extensive, abruptly raised, plaque on left face, extending to right. (No Fig.) B–.	None	Tuberculoid, fairly marked, active, mostly in upper one-third of skin.
24 HK-3	M 17	N2– 2 yrs.	(*a*) Extensive red plaque covering most of face. Fig. 20. (*b*) Annular scaling lesion, of shoulder. (See Fig. 18.) B–.	Numerous, mostly annular, scaling, not massive; one on neck (Fig. 21). (Polyneuritic changes.)	Tuberculoid, (*a*) fairly marked. (*b*) Less marked, consistent with appearance.
25 PH-7	M 15	N1+ 9 mos.	Abscess, left great auricular; extensive plaque of cheek. Fig. 22. B–.	None except sharply circumscribed nodulations of left ear.	Tuberculoid, with typical central necrosis and softening.
			Retrogressive tuberculoid lesions		
26 PH-1	M 22	N2 10 yrs.	Extensive, atrophic, scaly of thigh and buttocks (ex minor). Fig. 23. B–.	Another on arm; pinkish macules face. (Polyneuritic changes.)	Tuberculoid, moderate, inactive; foci mostly in deeper levels.
27 PH-18	F 50	N1+ (?)	Large, atrophic, ichthyotic, ill-defined, of left leg; (ex minor). Fig. 24. B–.	None	Tuberculoid, moderate, mostly deep, apparently retrogressive.
28 PH-14	F 42	N2– 12 yrs.	Irregular-surfaced, diffusely reddish, of shoulder (ex papulate?). Fig. 25. B–.	Others, varied, elsewhere; a red one on cheek.	Tuberculoid, minimal, residual.

Numbers, serial and record	Sex and age	Classification and duration	Lesions biopsied	Other lesions	Histological findings
29 HK-2	M 21	N1+ 2 yrs.	Large, irregular, hyperpigmented, of thigh (ex minor?). Fig. 26. B–.	Several, all more or less completely retrogressed.	Very slight round-cell; no definite tuberculoids but a few apparent residual.
30 PH-10	M 36	N1 (?)	Old macule, of hand; upper margin slightly raised, area thin, atrophic (ex major). Nerve enlarged. Fig. 27. B–.	None	Tuberculoid, fairly marked, all levels, larger foci deep; not inactive.
31 PH-11	M 23	N2– 1 yr.	Scarred, marginally thickened, of right ankle (ex major). Nerve enlarged. Fig. 28. B–.	Another, smaller, on left ankle; small macule on forehead. (Polyneuritic changes.)	Tuberculoid, marked, all levels. Nerve branches in subcutis markedly affected.
			Atypical cases		
32 PH-4	M 16	N1+ 1 yr.	Small, reddish area of thigh. Fig. 29. B–.	(See comments.)	Tuberculoid, moderate, atypical; much round-cell.
33 MA-5	M 28	N3– (?)	Large, pale, with atypical minor zone, of chest. Fig. 31. B+.	(See comments.)	Tuberculoid, rather marked, probably modified by reaction.
34 PH-6	M 40	CN? 9 mos?	(*a*) Abruptly raised, oval, of neck. (Fig. 32.) B+. (*b*) Small, annular, of thigh. Fig. 33. B+++.	(See comments.)	Marked granulomatous changes, atypical, transitional to lepromatous(?).
35 MA-8	M 25	N3– (?)	Curious, reddish, irregularly infiltrated, rough-surfaced, of arm. Fig. 34. B.+	(See comments.)	Moderate infiltration, undifferentiated; becoming lepromatous(?).

and HK = Hongkew clinic, Shanghai. The symbol + or − after the general classification symbol (e.g., N1+) signifies a high or low grading in the degree indicated by the numeral. The symbols B+ and B− refer to the bacteriological findings. "Polyneuritic changes" indicates that notation was made of changes of that general nature; they are given in the comments on the cases. Statements regarding infiltration (i.e., elevation), irregularity, and erythema refer only to the marginal portions of lesions unless stated or obviously otherwise. The descriptive terms "active," "retrogressive," etc., in the histological data signify only the interpretation of the microscopic picture, the examination having been made, as stated, without reference to the data on the clinical lesion concerned. The term "round-cell" means in general small round-cell (lymphoid) infiltration, though usually there is an admixture of large cells of the macrophage type.

COMMENT ON CASES

The data given in Table 2 are amplified or discussed here.

1. RESIDUAL AND QUIESCENT LESIONS.

CASE 1.—This old, solitary lesion, apparently inactive and so slight that a photograph was not made, proved to be merely an example of persistence of hypochromia over a healed lesion. The case was, obviously, "aborted incipient."

CASE 2.—This case, under treatment for seven years, had improved markedly, though there was atrophy and contracture of both hands and left foot-drop. The skin lesions (Fig. 1) had probably once been infiltrated, but how much so cannot be told. The histology is in keeping with its apparently healed condition.

CASE 3.—This case was also of long duration, with thickening of the ulnars, anesthesia of one hand and partial paralysis of the lower lids. The thigh lesion biopsied (Fig. 2) was probably never much infiltrated; its residual appearance is reflected in the microscopic findings. The chin was of quite different appearance, reddish and seemingly infiltrated. The significance of the banal chronic inflammatory change found there is uncertain.

2. SIMPLE ACTIVE LESIONS

CASE 4.—The large arm lesion that was biopsied (Fig. 30) was much like the preceding two except for a little marginal erythema in places. Histologically there is only minimal change, the lesion virtually residual. On the back, upper arms and elsewhere there were very numerous lesions that would have been more interesting to study. These were irregular pale areas, the smaller more or less rounded, diffusely outlined, reddish in color but often with smaller pale centers, the larger more irregular, pale, with reddish, ill-defined but very slightly raised edges. These lesions are so similar to those of (atypical) Case 32 that, though the case must be placed here, the photograph is put with that of the latter one for comparison.

CASE 5.—Superficially the scapular lesion of this case (Fig. 3) was fairly similar to the preceding two, except for more evidence of scarring and a tendency of the follicles to gape. It was a retrogressed infiltrated one, but its progression when

examined (if the slight erythema at the edge really signified activity and progression) was of the simple, noninfiltrated kind, hence it is placed in this category. Histologically the condition seems residual rather than active. The specimen from the other lesion biopsied, clinically similar, shows even less suggestion of activity. Both ulnars enlarged, with left ulnar neuritis and numbness, a year previously.

CASE 6.—This macule, the only flat, smooth-surfaced (nonatrophic) one in the group (Fig. 4) shows more round-cell (lymphoid) infiltration than is usual, but there are small but distinct epithelioid foci in several of the cellular collections, which are in the usual relations with the vascular and glandular structures. The condition was probably not indolent.

CASE 7.—This lesion was fairly similar to that of Case 5. The specimen was apparently taken from an inactive portion, but it suffices at least to show that the condition was essentially tuberculoid.

CASE 8.—Whether the condition of the larger area biopsied (Fig. 5, A) was due to previous infiltration cannot be said; the coarse-grained, shiny appearance, without evidence of actual fibrosis, may result from simple macules. The small red area (Fig. 5, B) was evidently more recent and active, apparently an earlier less differentiated stage of the condition. Some paralysis of facial muscles.

CASE 9.—The lesions on the body were marginally erythematous, but only the diffuse reddish one on the face showed any perceptible infiltration. That lesion is difficult to distinguish in the photograph (Fig. 6), but the edge can be made out above and parallel to the line of the left jaw. The amount of round-cell infiltration, moderate but more than usual for these lesions, suggests activity, but the appearance of the tuberculoid foci does not. Both ulnars and great auricular enlarged; slight lid drop. The lesions in this case subsided considerably under treatment in the next few months.

CASE 10.—This case differed from the preceding one in that the extensive areas on the buttocks and thighs showed no signs of activity, while the flushed areas on the face are indistinguishable in the photograph. Nevertheless, the histological change is much more marked, so much so that on microscopic grounds alone the lesion would be classed as diffuse minor tuberculoid. Its deep location in the nonstratified skin structure of this region presumably explains the relatively slight outward change.

3. PAPULATE MINOR TUBERCULOID LESIONS

CASE 11.—The macule biopsied (Fig. 7, A) was slight as regards size, degree of hypochromia and size of papulation. It was nonerythematous, apparently retrogressive, which seems common in leprides of this class (see preceding report). Histologically the tuberculoid foci, typically superficial for the most part, do not appear inactive. It seems quite possible, that, unless the process was interfered with, the lesion may have become as marked as the more grossly papulate one of the loin (Fig. 7, B).

CASE 12.—The lesion biopsied (arm, Fig. 8) seemed inactive, retrogressive, but as in Case 11 the tuberculoid foci in the sections do not have that appearance. They are, as before, mostly superficial, though the specimen does not include any that could have produced the papulations seen clinically.

CASE 13.—The lesions of this case (Figs. 9 and 10), were rather exceptional. (Compare Cebu Case No. 44.) Many of the papules were large, and adjacent ones had merged. The recovered area was surprisingly normal in appearance. Irre-

gular outward extension, often with discrete foci outside of the marginal zone ("colonial" development) is conspicuous, and the sections are of considerable interest in that connection.

4. MINOR TUBERCULOID LESIONS, ORDINARY

CASE 14.—Though most of the lesions of this striking case were quite typically minor tuberculoid (Figs. 11 and 12), some were in part papulate. The one on the left breast had been modified by pressure of the breast-band. The amount of the granulomatous change present is in keeping with the degree of the lesion biopsied. Margins of mocules disappeared subsequently with intradermal and intramuscular injections. No new lesions appeared.

CASE 15.—In this case the lesions (Fig. 13) were less raised and less irregular of surface than in the preceding one (much of the granuloma being deeper in the skin), and they varied in width from minimal ("linear") to the band-like lesions of the following cases. Left ulnar and both auriculars enlarged, some contracture of both hands.

CASE 16.—The prominent, band-like margination, of fairly uniform width, in the nonretrogressed parts of these lesions (Fig. 14) seems to be fairly common in China. The deep location in the skin of the greater part of the granuloma obviously explains the smooth surface. Both ulnars enlarged and one hand rather markedly contracted.

CASE 17.—This lesion was only partly outlined by a band-like zone, the elevation of which was less than in Case 16, and the pathological changes are also less marked. The condition was evidently retrogressive.

CASE 18.—The skin involvement in this case was comparatively recent; chief complaint was anesthesia of the feet and lower parts of the legs; both peroneals were enlarged and there was foot-drop, right. Histologically there is more round-cell infiltration than usual. Clinically the lesion examined (Fig. 15) did not resemble those of the preceding cases except as regards degree of elevation and character of surface; but it seems probable that if it had expanded sufficiently and the central recovery had continued, it would ultimately have presented the same features. Actually it disappeared later under treatment.

CASE 19.—This lesion (Fig. 16) is more familiar than the preceding ones, differing from them both morphologically and in its obvious activity. The irregularity of the outer edge and surface is common in actively progressive lesions in which much of the granulomatous process is superficial. (When the patient first came to the clinic the lesions were in a reaction state and were thought to be lepromatous, but smears were negative.) Polyneuritic changes were noted as present but not recorded.

CASE 20.—This case was similar to the preceding one but much less marked.

CASE 21.—Considered as a whole, this case would go into the major tuberculoid class because on the right foot and ankle there was an area of that kind—large, thick, red, shiny, with some epidermal scaling (reaction), and with a thickened nerve in relation to it. It is placed here because the lesion biopsied (Fig. 17) was clinically and histologically of the minor grade. It serves to demonstrate the lack of a sharp demarkation between these two categories of cases. (See also Cebu Case 50.) The biopsied macule, and others like it, all cleared up later under treatment.


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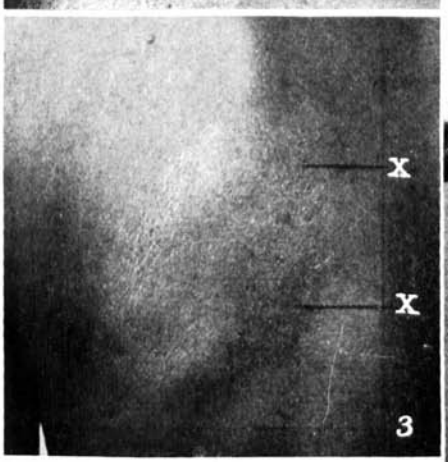
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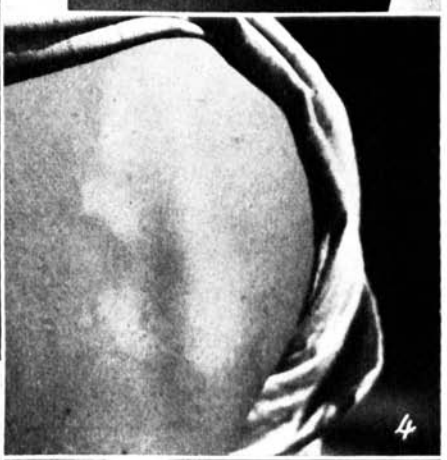
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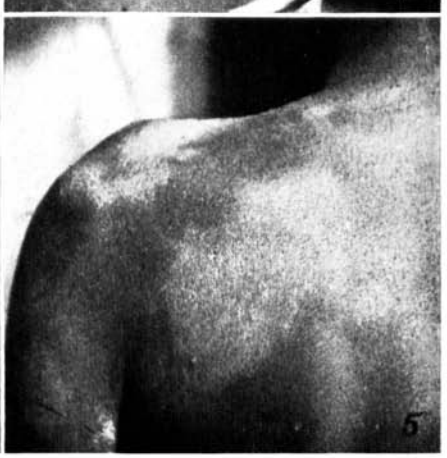
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PLATE 27

FIG. 7. Small, ill-defined macule on lower right chest (A), retrogressive in appearance but with minute, scattered micropapulations at edge. (Compare larger, more frankly papulate lesion at B.) *Histology:* Slight tuberculoid, mostly superficial, not residual in appearance. Case 11.

FIG. 8. Palish, noninfiltrated lesion of right arm (also of back), of quiescent appearance except for fairly conspicuous micropapulations in parts of the periphery. *Histology:* Slight tuberculoid, mostly superficial, apparently not inactive. Case 12.

FIG. 9. Very narrow and abrupt (linear), coarsely papulate marginal zone on chest. *Histology:* Moderate degree tuberculoid change, superficial. Case 13. (See Fig. 10.)

FIG. 10. Shoulder and upper arm of same patient as Fig. 9. Lesion clinically and histologically similar.

FIG. 11. Narrow, moderately raised, irregular, minor tuberculoid lesions on and above gluteal region, etc. In a part of one lesion the zone is broken up, coarsely papulate. *Histology* (solid zone): Moderate tuberculoid. Case 14.

FIG. 12. Chest and abdomen of same patient as Fig. 11. Lesion on abdomen in places much interrupted, coarsely papulate. That on left breast modified by pressure of breast band.

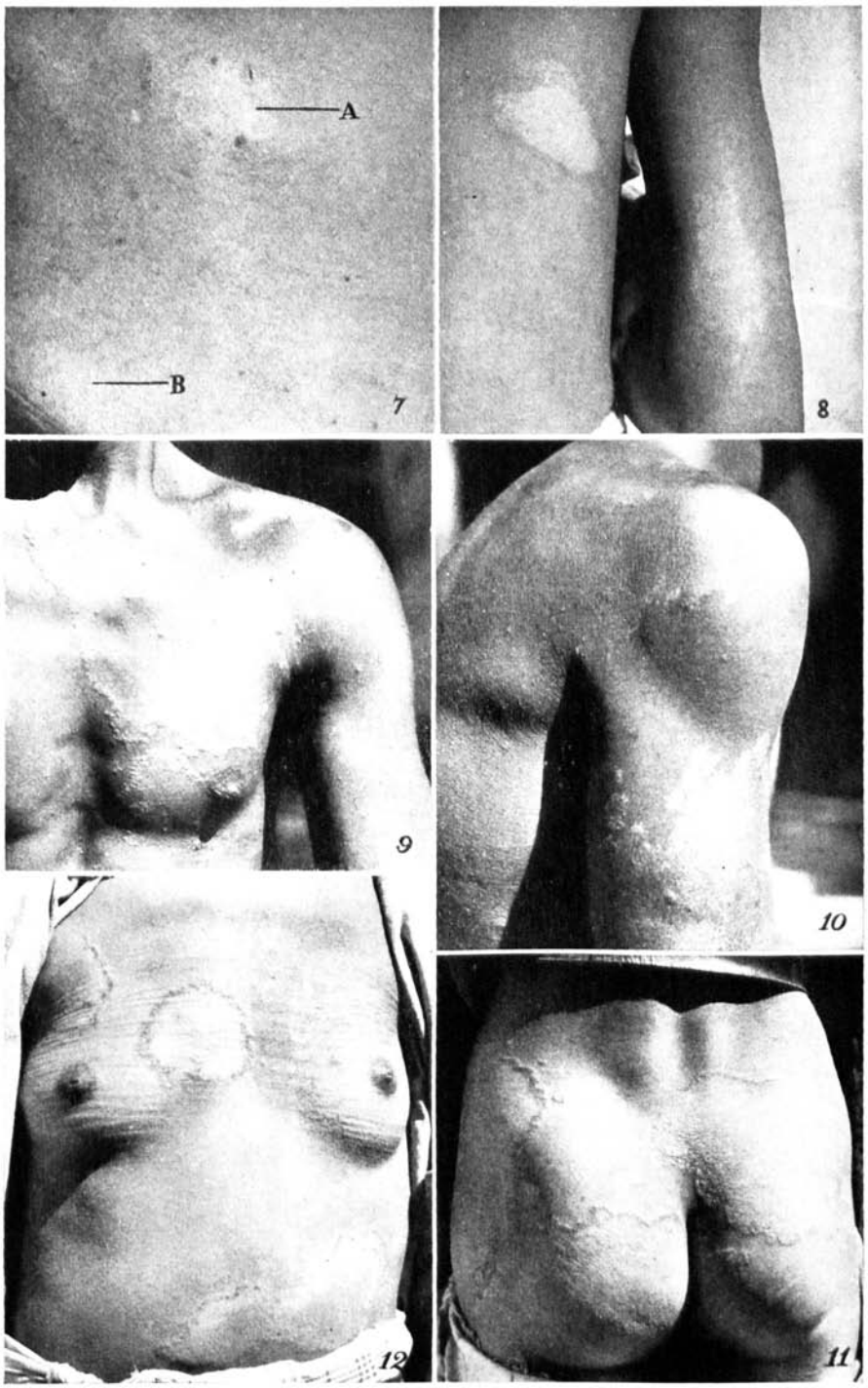

PLATE 27

PLATE 28

FIG. 13. Lesions of back with conspicuous marginal zones, rather irregular as to outline, width, degree of infiltration and surface. *Histology:* Moderate tuberculoid, active. Case 15.

FIG. 14. Lesion on posterior aspect of thigh with, in upper part, band-like margin like that in Fig. 13 but more raised smooth and uniformly wide; less marked and distinct below. *Histology:* Moderate tuberculoid, very little in superficial layers. Case 16.

FIG. 15. Small lesion on chest (X), apparently an early lesion of the same kind as the foregoing, with beginning central recession. *Histology:* Rather slight degree tuberculoid, with considerable round-cell infiltration. Case 18.

FIG. 16. Extensive area on arm, with irregular, rather markedly raised and erythematous margin, post-reactional. *Histology:* Fairly marked tuberculoid. Case 19.

FIG. 17. Small, recent, rather superficial and irregular lesion of thigh, with a daughter (?) lesion near it. One of several secondary lesions in a case with a major tuberculoid area of the foot. *Histology:* Slight to moderate tuberculoid changes, with some round-cell infiltration in papillary layer. Case 21.

FIG. 18. A lesion of the buttock somewhat similar to that in Fig. 17, but more marked, in another major tuberculoid case (see Figs. 20 and 21); marked erythema and scaling due to (subsiding) reaction. Not biopsied; a similar lesion on shoulder showed fairly marked tuberculoid changes. Case 24.

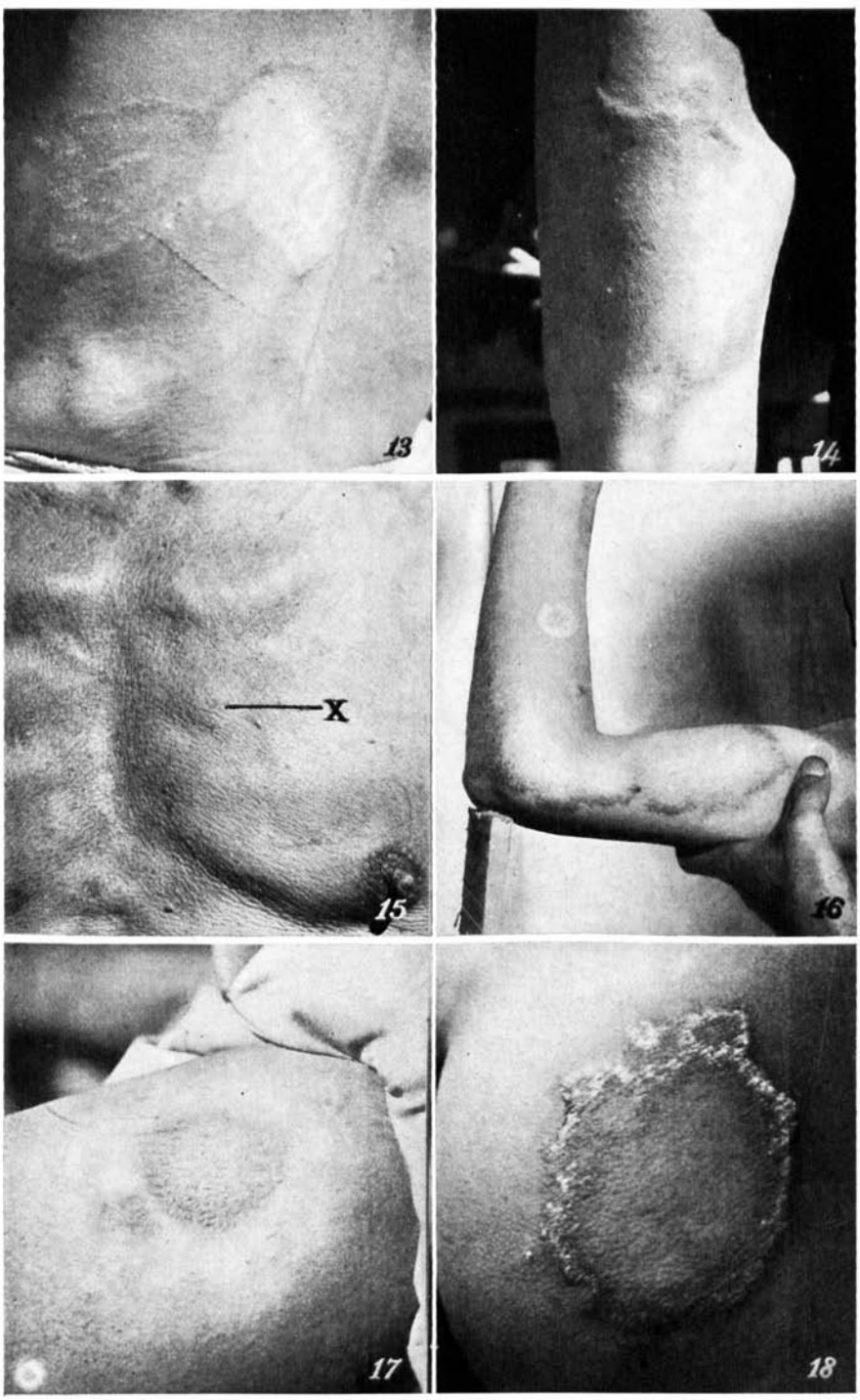

PLATE 28

PLATE 29

FIG. 19. Typically thickened, abruptly limited, extensive major tuberculoid plaque of face, involving eyelid, etc., with small nodulations resembling lepromata on chin and right cheek. Ears not involved. *Histology:* Marked tuberculoid, active. Case 22.

FIG. 20. Very extensive, deep red, plaque-like lesion covering entire right side of face (including eyelids), forehead and chin and extending far to the left and on to the neck; reaction condition. (See also Figs. 18 and 21.) *Histology:* (specimen from forehead): Fairly marked tuberculoid. Case 24.

FIG. 21. Lesion on back of neck, scaling from reaction, extending into the occipital scalp. Same case as Figs. 20 and 18.

FIG. 22. Abscess of left great auricular nerve (A) and marked enlargement of the cutaneous colli (B), in patient with extensive major tuberculoid infiltration involving the entire side of face. *Histology:* Tuberculoid change with necrosis and softening. Case 25.

5. MAJOR TUBERCULOID LESIONS

CASE 22.—This case was in a reaction state, with scaling of some of the lesions. The plaque of the face (Fig. 19) is fairly typical of the major tuberculoid affection of that part, as were the smaller lesions which might easily have been mistaken for lepromatous nodules; the ears, as frequently happens, were not affected. The histological changes are correspondingly marked. One of the ulnars was enlarged, with weakness of the hand. That condition, as well as the skin lesions, later improved greatly under treatment.

CASE 23.—Much of this lesion (no Fig.) was discolored by treatment (Dr. Brangwin), but the rest was of the bright red color typical of these lesions. Iodized esters had been given intradermally but the treated areas were not of the usual color. Methylene blue had also been administered intravenously and some of it had, apparently, been taken by the injected areas but not by the rest. The specimen, taken from a part that had not been injected, does not show the lesion at its maximum.

CASE 24.—The case was in a late reaction condition and the face plaque, which involved even the eyelids (Fig. 20), was dark red. With the exception of one lesion on the neck that extended into the occipital scalp (Fig. 21), those elsewhere were annular, red and scaling (Fig. 18), and were of a grade that might be called marked minor, especially in view of the conspicuous superficial focalization. Histologically the condition (two specimens) is not as marked as is often seen in major lesions. From the history the case evidently began as an ordinary simple macular one. Ulnar nerves enlarged, hands anesthesic, some paralysis of face including lids.

CASE 25.—This case is exceptional, nerve abscess being rare in South China. Below the frankly abscessed great auricular the cutaneous colli stood out so conspicuously (Fig. 22) that it must have been at least necrotic. Sections confirm the tuberculoid nature of the abscess. A specimen was not obtained from the cheek lesion with which the nerve condition was associated, but it must certainly have been major tuberculoid. The sharply circumscribed nodulation of the ear, easily mistaken for a leproma, is quite typical of that condition. Since the specimen was removed the face lesion has improved greatly.

6. RETROGRESSED TUBERCULOID LESIONS

CASE 26.—This lesion (Fig. 23) was probably of the minor grade at its maximum. The degree of atrophic change is unusual. The histological findings are in keeping with the incompletely retrogressed but apparently inactive condition. Both great auriculars and ulnars enlarged, hands somewhat atrophied, right one contracted.

CASE 27.—The macule in this case—the only one present—was essentially similar to that of the preceding one, but it was somewhat less clearly defined and its general appearance (Fig. 24) was greatly affected by the ichthyotic changes that commonly occur in lesions of the leg.

CASE 28.—This lesion was not typical because of the flushed appearance and irregular coarsening of the more or less atrophic surface, which in part had the appearance of retrogressed papulation (Fig. 25). Whether at its height it was papulate or of the ordinary minor tuberculoid kind cannot be said.

CASE 29.—From the history this case was certainly of tuberculoid type at one time, but the lesions had retrogressed so much that they cannot be classified as to degree. The marginal zone of the one biopsied (Fig. 26) was hyper- rather than

hypopigmented, and the central portion was darkened by home medication. The specimen is almost negative histologically; possibly it was taken from a point inside of the marginal zone.

CASE 30.—The affected area, extending from the wrist onto the fingers (Fig. 27), was well marked at its upper and lateral limits but diffused off over the fingers. Over most of the area the skin was unusually atrophic and thin. From the history, the gross enlargement of the dorsal branch of the ulnar nerve, and the degree of histological change in the part biopsied (wrist), as well as the degree of atrophy, it is certain that the lesion had been a major one.

CASE 31.—This lesion was essentially similar to the preceding one. The saphenous nerve (Fig. 28) was greatly enlarged for an extraordinary distance above the macule. The specimen removed includes nerve branches in the subcutis that are greatly affected, the nerve tissue quite replaced by the tuberculoid granuloma. Anesthesia of both feet, obviously due to involvement of trunk nerves.

Because of the special features of the four cases classified as atypical, they are described here in some detail, though some of them cannot be discussed as conclusively as they deserve.

7. ATYPICAL CASES

CASE 32.—The skin lesions, said to be of only four months duration, were distributed over rather extensive, fairly symmetrical areas of the buttocks and thighs (Fig. 29). They consisted of numerous irregular, more or less diffused patches, some isolated and others merging, some reddish and others pale, none distinctly raised. In a few of the larger of them repigmentation was evident. Polyneuritic changes: both great auricular nerves and right ulnar enlarged. Small anesthetic patch on right elbow; also three enlarged cutaneous nerves posteriorly on right forearm, though no skin lesion of arm was observed. Smear from thigh negative. Biopsy of one of the reddish lesions. *Histology:* Tuberculoid, moderate degree, atypical. On the whole rather marked changes throughout, but round-cell accumulation greatly in excess of the tuberculoid condition. Numerous small epithelioid foci in the papillary layer, usually with a few small round-cells and more numerous large mononuclears, which are sometimes abundant. Only one large giant cell found, with a few small ones. Numerous larger foci of infiltration in the deeper layers, in the usual relations, none of which contain typical tuberculoid foci, though there are numerous cells of epithelioid type.

Comment.—Clinically some of the lesions were undoubtedly of the nature of leprides (compare Cebu Case 27), but others, especially the smaller, reddish, diffused ones, were of indeterminate appearance and the possibility of lepromatous change had to be considered. The large number of them and their generally small size bespeaks a general, hematological distribution, perhaps of "reaction" nature (compare Case 4). Histologically the lesion, definitely tuberculoid, is obviously active, but one that may be expected to settle down to the usual tuberculoid state. It seems probable that the older, more definitely lepridic lesions arose in similar fashion.

CASE 33.—Large pale macules on arms and left chest. The chest lesion (Fig. 31) was perfectly flat and nonerythematous toward the shoulder, with irregular, streaming edges. Elsewhere there was a narrow, uniformly wide, moderately raised marginal zone, most marked along the lower border. The surface of this zone was fairly smooth except near the axilla, but in its outer portion and for some distance beyond it the skin was shiny, coarsened in texture, and reddish-brown to bronzy in color. Duration of disease obviously long; facial paralysis and deformities on hands. Smear positive, but bacilli extremely few. Biopsy of the margin described. *Histology*: tuberculoid, rather marked, more superficial than deep. In the papillary layer, which is fairly completely involved, there are ordinary epithelioid-cell foci and also diffusion of cells of apparently the same type. In places some lymphoid accumulation, but nowhere marked. No suggestion of lepromatous change.

Comment.—Clinically this lesion was similar in form to several of the "band-like" minor tuberculoid ones studied, but the peculiar color (present also in the arm lesions) and the diffusion of the outer edge suggested a reaction condition which might be undergoing transformation, and it was recorded as "probably cutaneous." The finding of bacilli in the smear was in keeping with the first part of this assumption, but they were far too few to support the second. Histologically there is no indication of lepromatous transformation.

CASE 34.—Conspicuous extensive infiltration, apparently lepromatous, of face, ears and elsewhere. Posteriorly on the neck a group of five oval, abruptly raised lesions, flat-topped but of irregular "granular" surface (Fig. 32). On the thighs and elsewhere numerous rather small, moderately elevated, erythematous annular areas, discrete and merging, edges irregular and sloping off to the normal skin in a manner suggestive of lepromata but not diffused, rather marked coarsening of the skin grain, and central resolution in all but the smallest (Fig. 33). Smears from the thigh strongly positive, with occasional small globi. One from neck (first examination) negative; others made later showed a very few bacilli from the lesion first examined and numerous ones from two others. *Histology* (two specimens): Marked, atypical granulomatous lesions. In the specimen from a neck lesion definite, discrete epithelioid (i.e., tuberculoid) foci are found superficially, but most of the granuloma is a mixture of small and large round cells, the latter usually predominating, with no tendency to tuberculoid formation but rather toward the nonvacuolate lepra-cell type. The nerves, however, are affected in a way more suggestive of a lepride than a leproma. The thigh specimen shows no definite tuberculoid tendency; otherwise it is similar to the other lesion.

Comment.—Clinically this case was apparently a mixed one. From the appearance of the face and ears (the latter seen in Fig. 32) it would have been passed without question as of cutaneous type. From the neck lesions alone it would have been called tuberculoid, and the bacteriological findings from that part were appropriate for such a lesion in a state of reaction. Morphologically the leg lesions were atypical but seemed more probably tuberculoid than lepromatous, but the bacteriological findings were suggestive of the latter

condition. The histology indicates that the case was intermediate, transitional to the cutaneous type. However, it is to be added that the patient has continued under treatment, though irregularly, and that the lesions of the face have subsided until the appearance approximates normal, with some improvement of the condition of the legs. If the face lesions were actually lepromatous this result must be considered remarkable.

CASE 35.—Extensive pale areas on the legs and reddish ones on the arm, with mutilation of the hands, case apparently of ordinary neural type, of long duration. Most of the skin lesions were ordinary macules, apparently quiescent or residual, but posteriorly on the arm was one of curious appearance (Fig. 34). It was diffusely reddish, fairly well demarked above but diffusing off below, dry and superficially atrophic (Fig. 34; complicating condition at elbow), not distinctly infiltrated marginally but definitely so and of coarsened appearance well inside the margin, much more marked in some places than others. Smear positive, bacilli few. Biopsy of marginal region. *Histology:* Moderate perivascular infiltration throughout the papillary plexus, mostly large round cells, with tendency to apparent epithelioid change but without tuberculoid focalization. Larger collections in the deeper levels, in some of which were cells distinctly of lepra-cell appearance, though nonvacuolated. Apparently a slight leproma.

Comment.—There was no suspicion that this case was not an ordinary neural one of long duration. The evident but slight infiltration and the irregular coarsening of the surface of the lesion were assumed to be due to irregular scarring effects of the ordinary lepridic process, and much of the condition was probably due to that process (cf. Figs. 23, 24 and 25). The finding of a few bacilli was unexpected. The slight apparent (but not typical) lepromatous change found microscopically indicates a partial, perhaps recent transformation. It would be interesting to know whether a specimen from one of the more infiltrated areas would have shown a more definitely lepromatous condition. It is particularly regrettable that no subsequent history can be obtained.

DISCUSSION

General findings.—This inquiry has been limited by the brief observation of the patients on a study basis, but the material serves the actual purposes of the inquiry. These were, first, to observe frank tuberculoid leprosy in China, and, second, to contribute to the comparative study of the leprides as a whole.

With regard to the first point, it is clear that the conditions which can be recognized clinically as tuberculoid are not infrequent in China, and that they occur in all the usual forms. Including two of the atypical cases, 23 of this general class were found among approxi-

mately 225 cases of all kinds seen, and at least 7 of these cases were or had been of the major variety. It is to be understood, however, that this proportion, 10 percent, is of no statistical value as regards general incidence.

With regard to the other feature of the inquiry, the findings are in essential agreement with those obtained in Philippine cases studied in Cebu (7) though the cases were on the whole of much greater duration and advancement, with correspondingly conspicuous polyneuritic changes, and several had grossly enlarged cutaneous nerves. The 34 skin lesions biopsied in 31 cases (not including the "atypical" ones) all fall, with a single exception, within the scheme of lepride classification developed during these studies. Furthermore, with the exception noted, the specimens from all lesions that presented definite clinical evidence of activity showed tuberculoid changes of some degree.

Source-distribution of cases.—The distribution as regards sources of the cases dealt with is not without interest. Among the 45 seen in the Iam-tsao clinic, which were fresh, practically unmodified by treatment, five were of frank tuberculoid nature, but there were none with simple, retrogressed or quiescent lesions. On the other hand such lesions were fairly numerous among the patients at the long-established clinic at the hospital in Swatow. At the Municipal Asylum, where treatment was nominal, if any, the few doubtless retrogressive cases seen were not entirely inactive but, unexpectedly, no case of the major variety was found there, though lesions of that kind are especially striking and the patients therefore particularly apt to be recognized as lepers.

A similar absence of major lesions among old institution cases has been noted by one of us (H.W.W.) at St. Joseph's Asylum at Shek-lung, between Hong Kong and Canton, an institution with about 700 inmates most of whom had been apprehended by the authorities of Canton.[3] Out of 320 patients looked over (170 men and 150 women, the latter being practically all of the female population), only 23 had definite leprides of any kind. In only 5 were they obviously tuberculoid, and none was of the major form.

Special features.—It seems interesting that six of the eight minor tuberculoid cases were in females, while all but one of the major

[3]This observation was made possible by the cooperation of the director, the Rev. J. Marsigny, and the Sisters in charge of the dormitories, and by the assistance of the Rev. J. A. Sweeney and Dr. H. Blaber of the leper asylum of the Catholic Mission at Kong Moon.

lesions seen were in males. Though the sex ratio of all cases dealt with in this report (1 to 1.8) approaches the general sex ratio of the Swatow clinic (1 to 2.6), and though at Shek-lung 12 males out of 171 and 11 females out of 150 were noted as having macular lesions, there remains a question whether sex may influence the frequency of the different varieties of the frankly tuberculoid leprides.

The group of lesions studied is, as stated, on the whole essentially similar to those of the Cebu group, though none of the latter had the rather striking "band-like" variety exemplified by Case 16 (Fig. 13). This lesion is striking in its uniformity of width and the abruptness of the inner edge of the infiltrated zone. This feature is not unique—it has been seen by one of us in South Africa (5) and elsewhere—but it remains interesting that in some cases the process should subside as abruptly as it develops, instead of doing so gradually and irregularly.

Certain of our cases illustrate the lack of sharp differentiation of "tuberculoid leprosy" from lesser forms, though some writers set it apart as a special form of the disease (4). In two cases that had frank major tuberculoid lesions (Nos. 21, Fig. 17, and 24, Figs. 18, 20 and 21) there were other lesions that, taken by themselves, could only have been called minor. The gap between the ordinary minor tuberculoid and the simple varieties is bridged by the papulate lesions. More or less similar intermediate cases were seen in the Cebu cases.

Two cases with lesser-degree lesions of the face exemplify the difficulty of determining from outward appearances alone the extent of the actual changes in that area. In one the lesion, though histologically slight, is distinguishable in the photograph (Case 9, Fig. 6), largely because of the color difference, but the more severe one (Case 10) cannot be identified in the picture. The nonstratified nature of the skin of the face apparently affects the morphology of the lesions. The chin, presumably for mechanical as well as structural reasons, is a particularly difficult area; one would hesitate to predict the findings in, for example, the apparently infiltrated one in Case 9 (Fig. 6). The one chin lesion that was biopsied (Case 3), diffusely reddish and noninfiltrated, is the only lesion in otherwise typical cases that is not histologically tuberculoid.

Lymphoid infiltration.—Other lesions which seem probably to be related to the one just mentioned are certain ones that showed, besides more or less tuberculoid focalization, more than the usual amount of round-cell (lymphoid) infiltration. These cases are No. 6

(Fig. 4), a simple macule, and No. 15 (Fig. 13), a minor tuberculoid one, both apparently progressing; Nos. 8 and 9 (Fig. 5) with simple, diffusely erythematous macules of the face; and No. 18 (Fig. 15) with a small, evidently recent minor tuberculoid lesion. Though this condition suggests activity of a sort, it is not necessarily present in all "active" lesions (e.g., Cases 13 and 14, Figs. 9 and 11); not even in marked ones in—or at least recently in—a reaction condition (Cases 15 and 34, Figs. 19 and 31).

The larger of the lesions biopsied in Case 8 (Fig. 5) showed changes much like that of Case 6, but the small, diffusely erythematous one showed much more round-cell accumulation and only minimal tuberculoid change. The red one of the atypical Case 32 (Fig. 29) also showed much round-cell change, though more of the tuberculoid condition. Both of these lesions were, in all probability, early, morphologically undifferentiated macules, which suggests that the nontuberculoid chin lesion of Case 3 might have shown that condition later. A question that arises in this connection is whether a lesion that is apparently undergoing lepromatous change but that has a conspicuous lymphocytic element, like those in Case 35 (Figs. 32 and 33), may be expected to become a true leproma, which is so different in character.

Significance of erythema.—Unexpectedly little abnormality was found in certain of the noninfiltrated lesions that were noted as being to some extent erythematous and therefore presumably active. In Cases 5 and 7 (redness slight and marginal), and in Case 28 (diffusely red) the microscopic changes were slight and did not have the appearance of activity seen in the specimens from Cases 6, 7, 8 and 12, and also atypical (early lepromatous?) lesion of Case 35. It would seem that the vasomotor disturbances which are not uncommon in the leprides when they are active may persist after activity ceases, and consequently that slight erythema does not necessarily indicate activity (i.e., progression) any more than lack of it necessarily indicates quiescence.

Atrophy of the skin.—With regard to the permanent changes of the skin—atrophy, sometimes actual scarring, and hypochromia—there is reason to conclude that there is no clear or regular relation between their degree and the clinical variety of the lepride that causes them. It is true that the most marked lesions of this kind (Cases 30 and 31, Figs. 27 and 28) were caused by major tuberculoid lesions, but it is not uncommon to see lesions of that variety subside with little or no permanent change. A marked, very superficial condition

such as that in Case 13 (Fig. 9, chest) may leave the recovered area surprisingly normal in appearance, yet another of much the same grade may cause considerable damage, as in Case 14 (Fig. 11, gluteal region), but at the same time it may fail to do so in another area in the same patient (Fig. 12, abdomen). Similar though less marked contrasts may be seen even among the simple, relatively noninfiltrated macules, as in Cases 6 and 9 (Figs. 4 and 5). It would seem that in the causation of these changes, which are due more to injury of the superficial web of fine elastic-tissue fibers than to fibrosis, there are several factors which apparently include not only the quantitative degree of the infiltration but also the duration of the lesion, the area involved, and very probably some obscure qualitative element of the tissue reaction.

Involvement of cutaneous nerves.—Though special attention was not paid to the condition of the cutaneous nerves, five of the cases (Nos. 21, 25, 30, 31 and 32) were noted to have enlarged ones, our series differing decidedly from the Cebu group in this respect. In four cases these nerves (three of them shown in the illustrations, Figs. 22, 27 and 28), were undoubtedly necrotic. They were distributed to areas with lesions of the major tuberculoid variety, which seems quite definitely to be preeminently responsible for the production of nerve lesions of this grade.

In the fifth case lesser-degree enlargement of nerves of the arm was noted, though no skin lesion of the part was observed. This brings up the question whether such seemingly independent enlargement of cutaneous nerves results (*a*) from previous skin lesions that have completely disappeared, which is sometimes energetically denied by the patients, or (*b*) from actual but outwardly imperceptible lesions of the skin, presumably limited to the deeper layers since the pigment and surface are unaffected, or (*c*) independently of skin involvement by deposition of the causative organism from the blood, which Rabello holds is not the case (2).

Polyneuritic changes.—The association of polyneuritic changes (peripheral anesthesia, muscular atrophy, etc.) with ordinary macular skin changes is a part of the usual picture of neural-type leprosy of long duration and is illustrated by several of our cases. There seems to be, however, a tendency in some quarters to believe that such neural disturbances are not a part of the picture of "tuberculoid leprosy." It is true that on the whole they are not commonly seen in cases observed in the more recent stages, and furthermore there may be biological factors that lessen the frequency (or severity) of nerve trunk lesions in such cases, but there remains a question of what

would be seen of that nature in cases of duration comparable to that at which they occur in cases that start with ordinary macules. Of our six major cases (four active and two retrogressed) three showed such changes. Of the fourteen other tuberculoid cases (including the papulate ones) five had them.

Treatment.—Little is to be said on the subject of treatment in this connection. No survey of the group has been made since our material was taken, but certain patients are known to have improved markedly, supposedly as a result of treatment, in spite of irregular attendance at the clinic. These cases are No. 18, with a small lesion of the chest (Fig. 15); No. 21 (Fig. 17), with a major tuberculoid lesion that was not biopsied; Nos. 22 and 23 (Figs. 19 and 22), both major tuberculoid; and No. 34. The fact that the apparently lepromatous condition of the face and ears of this last case (Fig. 32) should have subsided seems most remarkable, and it raises serious doubt that it was really of that nature.

There is a point of some interest in Case 23 (major tuberculoid, face). Methylene blue injections had not caused discoloration of the parts of the lesion which had not been injected locally with iodized chaulmoogra ethyl esters, but the parts that had been injected had taken up some of the dye. It would seem as if the cells which infiltrate a lesion in response to the presence of the oily drug are capable of taking up the dye, while those that form the tuberculoid granuloma are not, though they are of similar origins.

Atypical cases.—Of the four cases set aside as atypical, the biopsied lesion of one (Case 32, Fig. 29) was apparently an early, incompletely established tuberculoid condition, and that of another (Case 33, Fig. 31) proved to be tuberculoid evidently modified (and made bacteriologically positive) as a result of a reaction condition. One case (No. 34, Figs. 32 and 33) seemed to be in an intermediate stage, apparently well on the way to become an advanced cutaneous case, but that that change actually took place seems doubtful from the subsequent history of improvement under irregular clinic treatment. In the fourth case (No. 35, Fig. 34), though it was not suspected of that change, the sections indicated more definitely a lepromatous transformation. Atypical and borderline cases such as these, which are very difficult to classify, offer an interesting field for careful investigation.

SUMMARY

The results of a study of leprides in 35 cases of leprosy, from which 39 biopsy specimens were taken, are reported. All but one of the

lesions from 31 cases (excluding 4 cases classed as atypical) were clinically simple, tuberculoid, or more or less retrogressed, falling into the classification of leprides developed in the course of the present series of studies. Histologically all of them, with the exception mentioned, showed tuberculoid changes in some degree, thus agreeing with the findings of the preceding study of this series.

From the number of cases with clinically tuberculoid lesions of different varieties and in different stages (23 out of about 225 cases examined) it is evident that this form is fairly common in China, at least in the southern region. At least 7 cases were or had been of the major form. Several had an interesting "band-like" form of lesion not seen in the Cebu group but observed elsewhere.

The more marked forms of the tuberculoid lesions were found in clinic cases; they are apparently rare in old institutionalized cases. A suggestion of a sex influence has been noted, the major tuberculoid lesions being almost entirely in males and the active minor forms predominating in females in this small group.

Certain of the cases exemplify the lack of any sharp separation between those with major and with minor lesions, and also between those with minor and with simpler lesions. Other cases exemplify the frequent difficulty of determining the severity of face lesions from outward appearances.

One lesion (from the chin) showed nothing but banal chronic inflammatory changes. Certain others in which such changes (chiefly lymphoid infiltration) were marked or predominant seemed to be incompletely differentiated but essentially tuberculoid in nature. The significance of variations in lymphoid-cell content, both in otherwise typical tuberculoid lesions and in those suspected of undergoing transformation to lepromata, requires elucidation.

There is reason to believe that slight marginal erythema does not necessarily imply activity (i.e., progression) any more than lack of it necessarily implies quiescence.

Superficial atrophy of the skin is discussed. The degree of that condition is apparently dependent upon several factors and does not necessarily indicate the original clinical grade of a retrogressed lesion.

Enlargement of cutaneous nerves of a degree probably due to necrosis was observed in four cases, in one of which the specimen examined was an abscess of the great auricular. In all instances the affected nerves supplied areas involved by major tuberculoid lesions. In a fifth case enlargement of nerves of the forearm was noted, apparently without any skin lesion.

Disturbances due to polyneuritic changes were obvious enough to be noted in several of the cases, including practically one-half of those with major and minor tuberculoid lesions. Whether such changes are any less frequent in tuberculoid cases of long duration than in cases with simpler macules of similar duration cannot be said.

A few observations of interest in the present connection, based on the apparent effects of treatment, are pointed out.

Of four cases classed as clinically atypical, the lesions of two are concluded to have been leprides, one incompletely differentiated and the other disturbed by reaction. The other two seemed to be undergoing lepromatous changes, but that cannot be asserted positively.

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REFERENCES

(1) Fraser, N. D. A village clinic for leprosy treatment. Internat. Jour. Lep. **3** (1935) 204–206.

(2) Rabello, Jr. Données nouvelles pour l'interprétation de l'affection de Besnier-Boeck: rôle de la lèpre. Ann. Dermat. et Syphil. **7** (1936) 571–597; *abstracted in* Internat. Jour. Lep. **5** (1937) No. 3.

(3) Reiss, F. Tuberculoid leprosy amongst Chinese. Delib. IX Cong. Internat. Dermatol., Budapest, 1935, vol. 2; *abstracted in* Internat. Jour. Lep. **4** (1936) 556. Also, Trans. Far Eastern Assoc. Trop. Med., Nanking, 1934.

(4) [Symposium.] Classification and evolution of tuberculoid leprosy. Internat. Jour. Lep. **4** (1936) 369–375; **5** (1937) 96–99.

(5) Wade, H. W. Tuberculoid changes in leprosy. I. The pathology of tuberculoid leprosy in South Africa. Internat. Jour. Lep. **3** (1934) 7–38.

(6) Wade, H. W. The skin lesions of neural leprosy. I. General introduction. Internat. Jour. Lep. **4** (1936) 409–430.

(7) Wade, H. W. and Rodriguez, J. N. The skin lesions of neural leprosy. II. Observations in Cebu. Internat. Jour. Lep. **5** (1937) 1–30.

DESCRIPTION OF PLATES

PLATE 26

FIG. 1. Retrogressed, quiescent, apparently healed macular area on shoulder, with slight atrophy and persistent hypochromia. *Histology:* Practically negative except for slight fibrosis. Case 2.

FIG. 2. Lesion similar to Fig. 1, posterior on thigh. *Histology:* Slight fibrosis with a few round cells near vessels, insignificant; apparently healed. Case 3.

FIG. 3. Macular area over scapula with atrophy and scarring, and a tendency to gaping of follicles, now noninfiltrated but with slight marginal erythema as at points marked (X). *Histology:* Some fibrosis with slight tuberculoid, apparently residual. Case 5.

FIG. 4. Pale, simple macule of common kind in the scapular region; in part slightly erythematous and perceptibly infiltrated at edge. *Histology:* Very slight tuberculoid, apparently not residual, with some round-cell infiltration. Case 6.

FIG. 5. Macule on scapular area with slightly erythematous margin, not infiltrated but of coarsened, relaxed texture and rather shiny (A), and near it a small, diffusely reddish spot (B). *Histology:* (*a*) Slight tuberculoid, with some round-cell accumulation; (*b*) more round-cell infiltration, superficial, with less tuberculoid change, apparently a recent lesion. Case 8.

FIG. 6. Diffusely reddish areas covering much of both cheeks and the forehead, distinguishable in the photograph from the normal only at the slightly elevated edge paralleling the left jaw (X). *Histology:* Slight tuberculoid with considerable lymphocytic infiltration throughout. Case 9.

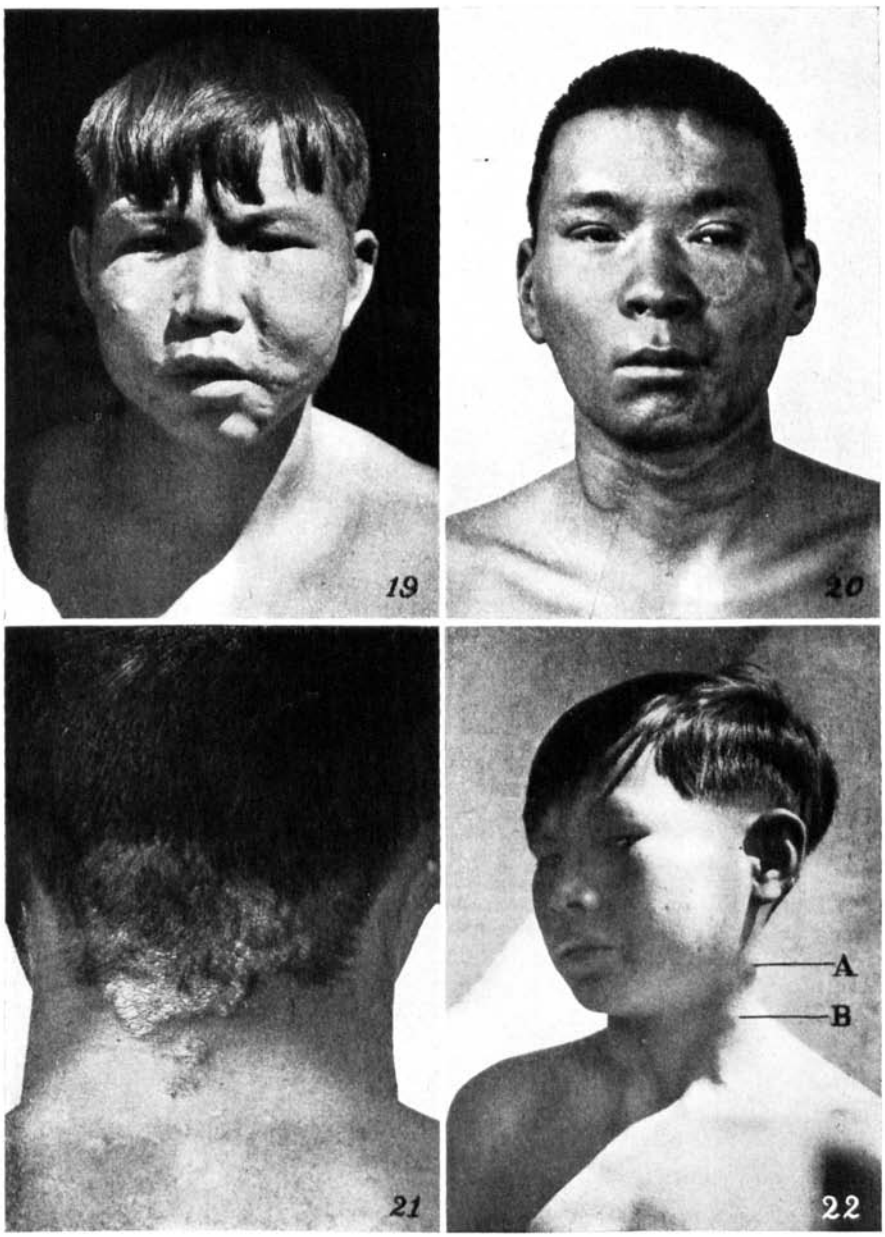


PLATE 29

PLATE 30

FIG. 23. Extensive area of thigh and buttocks, with rather marked atrophy, margin somewhat infiltrated but retrogressive, originally of minor tuberculoid grade. *Histology:* Moderate tuberculoid, apparently inactive. Case 26.

FIG. 24. Retrogressed minor tuberculoid lesion of leg; moderately thickened margin (X). Illustrating atypical, ichthyotic appearance often seen in lesions on legs. *Histology:* Moderate tuberculoid, apparently retrogressive. Case 27.

FIG. 25. Irregular-surfaced, somewhat atrophic, merging areas on shoulder, slightly and diffusely reddish, of atypical appearance (ex papulate or minor tuberculoid?). *Histology:* Very slight (minimal) tuberculoid, obviously residual. Case 28.

FIG. 26. Large macular area of thigh, margin very irregular, hyperchromic, slightly and irregularly elevated, much retrogressed. Central area darkened by home medication. Original condition probably minor tuberculoid. *Histology:* Very slight chronic changes, no definite tuberculoid. (Specimen wrongly taken?) Case 29.

FIG. 27. Retrogressive, atrophic macule of hand, ex major tuberculoid. Upper margin (A) moderately raised, but lower extension diffused over fingers. Grossly enlarged dorsal ulnar nerve (B) arises from the area. *Histology* (raised margin): Fairly marked tuberculoid, not inactive. Case 30.

FIG. 28. Scarred macular area on ankle, ex major tuberculoid; raised upper margin (A) poorly shown. Greatly enlarged saphenous nerve (B) extends upward from the lesion. *Histology:* Marked tuberculoid; deep nerve branches markedly affected. Case 31.

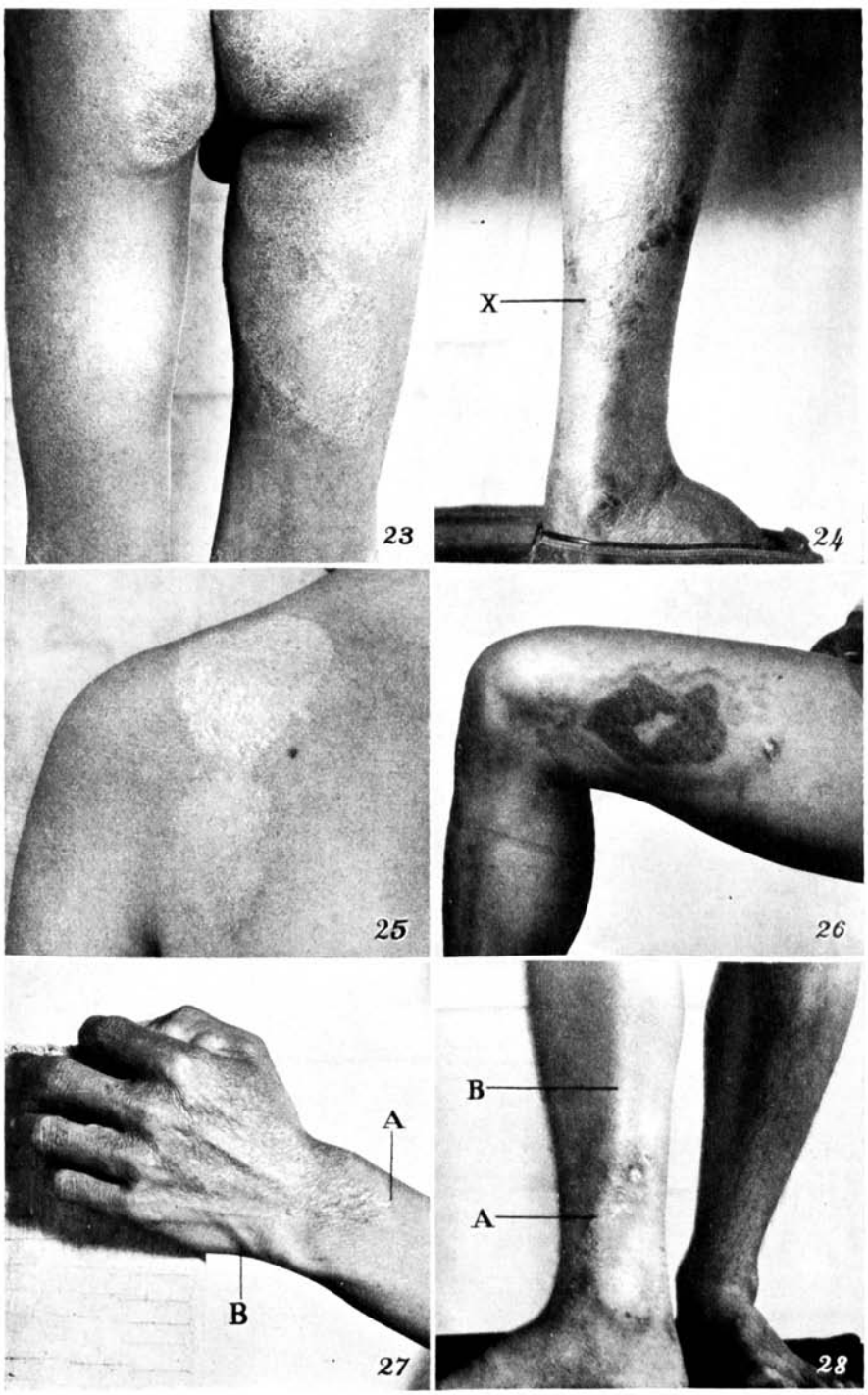


PLATE 30

PLATE 31

FIG. 29. *Atypical case.* Multiple small, non-infiltrated, reddish and pale areas on buttocks and thighs, some isolated and others merging. *Histology:* Atypical, probably tuberculoid but not well defined. Case 32.

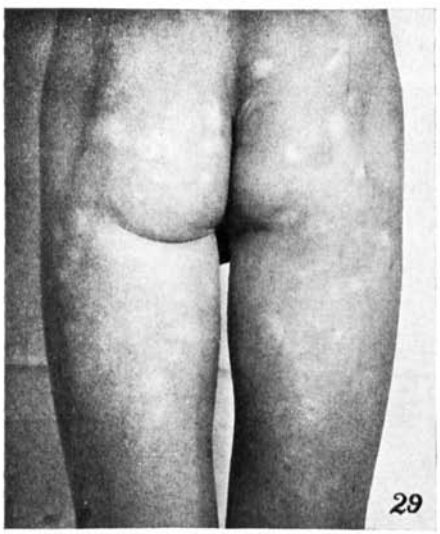
FIG. 30. Multiple small areas apparently similar to those in Fig. 29 (not biopsied). Large, slightly atrophic area of arm, with slight marginal erythema (biopsied). *Histology:* Minimal tuberculoid, evidently residual. Case 4.

FIG. 31. *Atypical case.* Large pale area of left chest, partly outlined by a minor tuberculoid zone of atypical appearance, diffusing off into the normal skin, reddish in the outer portion, with shininess of the contiguous surface. Evidently postreactional. Bacteriologically positive. *Histology:* Rather marked tuberculoid, obviously active and in some respects atypical. Case 33.

FIG. 32. *Atypical case.* A group of oval lesions, abruptly raised, flat-topped but irregular of surface, on neck in case which in some respects seemed ordinary cutaneous. (See ears, also Fig. 33.) Bacteriologically positive. *Histology:* Markedly granulomatous, atypical, tuberculoid tendency in part. Case 34.

FIG. 33. Annular lesions of thigh, same case as Fig. 32. Bacilli very numerous. *Histology:* Atypical granuloma, without tuberculoid tendency.

FIG. 34. *Atypical case.* Extensive macular lesion of curious appearance on arm, slightly erythematous, not infiltrated at the margin but somewhat so in places elsewhere, with considerable atrophic "scarring." *Histology:* Moderate superficial infiltration, undifferentiated but suggestive of lepromatous development. Case 35.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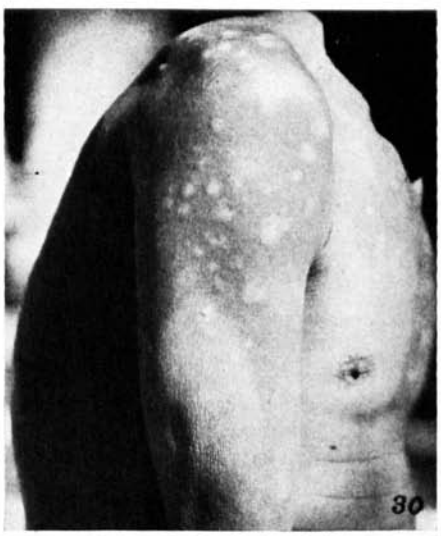
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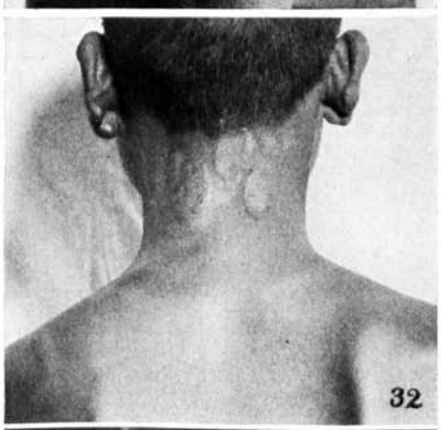
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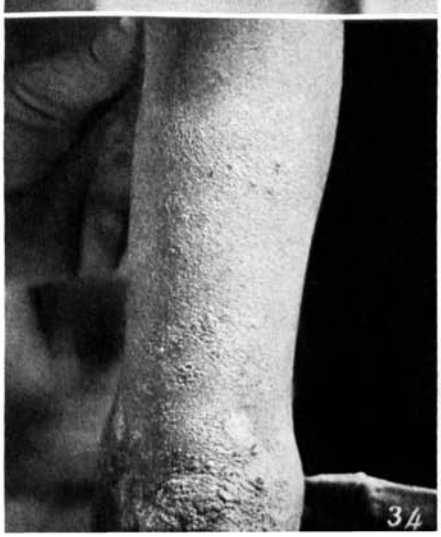
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