

BORDERLINE TUBERCULOID LEPROSY¹

BY H. W. WADE, M.D.

*Medical Director, Leonard Wood Memorial
Culion Leper Colony*

AND J. N. RODRIGUEZ, M.D.

*General Supervisor of Regional Treatment Stations
Bureau of Health, Manila*

One of the questions regarding tuberculoid leprosy that remains to be answered satisfactorily is whether or not cases definitely of that nature may undergo change to the lepromatous type, and if so by what process. The reason for the continued uncertainty regarding this matter may, perhaps, be that the time since this phase of the disease began to be studied with care has not been long enough for many cases to be followed individually through their natural courses. At any rate, those workers who are convinced that the transformation does take place have not published detailed descriptions of cases, without which those who have not observed the phenomenon may well remain unconvinced. It is not questioned that neural cases of the "simple" subtype, with flat macular lesions, do undergo this unfavorable development, especially those in which lesions are not well defined (11), or in which the lepromin reaction is negative (3), but it does not necessarily follow that actual tuberculoid cases may do so.

There was a time when some writers, including Jadassohn himself, held the opinion that the tuberculoid tissue reaction in leprosy was intermediate between, on the one hand, the banal chronic inflammatory infiltration which was long supposed to be characteristic of the ordinary lesions of "simple" maculo-neural cases, and, on the other hand, the classical lepromatous condition. A few cases which may perhaps be interpreted as having undergone the change in question may be found in the literature of the period around the end of the last century. That, however, was long before there had been much study of tuberculoid leprosy, and especially before there was available any evidence of the kind which the lepromin, or Mitsuda, reaction affords. The established fact that that reaction is strongest in the most typical and

¹This article is the fifth of a series dealing with follow-up observations of neural-type cases at Cebu, Philippines.

marked tuberculoid cases, but completely negative in typical lepromatous cases, indicates that the tuberculoid process is in a direction opposite to rather than tending toward the lepromatous one; it evinces a high reactivity on the part of the tissues and, therefore, most students of the matter agree, a resistance that would have to be broken down.

The situation today is that a few writers assert that the change in question does take place, while others hold the contrary; more of us, probably, are uncertain and awaiting definite proof of the first view or the many long and careful observations that alone can substantiate the other. The only specific report of supposed evolution of leprids to lepromata that we know of is one by Querangel des Essarts and Lefrou (9), who described what they took to be this change in two cases. However, as Schujman (15) points out, it seems much more probable that the condition was merely one of reaction in tuberculoid lesions. Not only may such lesions easily be mistaken clinically for lepromata but, unhappily, the histological picture may be equally confusing.

Prominent among those who hold that the change does occur is Lowe, who in replying to an inquiry on the subject in 1936 (4) stated categorically that he had seen tuberculoid cases become lepromatous. Later (5) he wrote:

Sometimes the tuberculoid lesion forms the center of a spreading leprotic² infiltration of the skin, but when this becomes at all marked the infiltration of the original lesion often subsides and it remains as a depressed area in the middle of a typically leprotic lesion teeming with bacilli. Generally speaking, we find that the existence of tuberculoid lesions (as also of marked cutaneous nerve thickening and nerve abscess which often accompany them) appears to be incompatible with the simultaneous existence of the leprotic infiltration in any marked degree. If the case becomes a C2 or C3 case the tuberculoid lesions disappear. On the whole, however, the existence of tuberculoid lesions is evidence of high resistance to leprosy, and we find that in comparatively few patients showing these lesions does the disease progress to the cutaneous type.

Elsewhere in the same year (6) he mentioned, hardly conclusively, the histology of the change:

In lesions in which this change occurs the following phenomena are seen. The number of bacilli increases and this change is accompanied by the development of "foamy" changes in the cells. The Langhan's giant cells disappear, and the focal arrangement of the granuloma is lost, because of the development of the more diffuse lepromatous change.

In the following year, after further experience in Calcutta, he asserted (17) that the lepromatous change happens in perhaps 25

² Meaning, in this connection, lepromatous.

or 30 percent of tuberculoid cases; the change in type of lesion starts at the margins of the tuberculoid macules and is at first localized there, but later it may become diffuse and affect the whole body. In his clinic it has long been the practice to classify more or less informally the more marked tuberculoid reaction cases, at least temporarily, as "N?C" (16, 17). By this is indicated uncertainty as to their status and prognosis, occasioned by their atypical, unfavorable clinical appearance and the frequently positive bacteriological findings.

In a recent publication (7) Lowe speaks of the greater frequency with which transformation occurs in Burmese patients than in Indians:

A considerable number of cases were seen [in Burma] in which the lesions were either "reacting" tuberculoid lesions in which smears showed an abnormally large number of bacilli, or else were lepromatous lesions developing from a previously existing tuberculoid lesion. In addition there were many patients in whom the lesions were definitely of lepromatous type, but the peculiarly localised nature of the lesions and their peculiar distribution, and the fact that involvement of cutaneous nerves supplying the lesions was found, indicated very strongly that these lepromatous lesions had developed from previously existing tuberculoid lesions. This phenomenon, tuberculoid reaction being followed by lepromatous change, is sometimes seen in Indians, but in Burmans it appears to be much more common. It is this intermediate type of case met with so commonly in Burma which is so difficult to classify.

It is of particular interest in connection with the present report that this author speaks of these cases as "intermediate." So far, however, he has not recorded any of them specifically.

Ryrie also believes that tuberculoid cases undergo transformation, insisting that the tuberculoid process is often harmful because of exhaustion of the protective forces. As a result of his experience of the severity of tuberculoid reaction among Chinese patients in Malaya he has said (12) that he had ceased to regard tuberculoid leprosy as a manifestation of resistance but considered it a potentially dangerous sensitization—"tissue vindictiveness rather than tissue defence." Later (13), in describing ulcerative tuberculoid leprosy, he stated that the ultimate prognosis is bad, that most of his cases had degenerated in a year or two to the lepromatous form with rapidly spreading lesions, and added:

No one observing the clinical progress of the condition would speak of this phase of tuberculoid leprosy as representing general bodily resistance to the disease. In its whole course and ultimate prognosis the word "resistance" seems out of place. If, however, we consider the tuberculoid process as essentially a phase of tissue-resentment, a reaction to the presence of

the infecting organism that is lacking in the cutaneous type of the disease, then we can picture a condition or sequence of conditions that vary from the relatively meek protest of the lesser forms or degrees of the tubercloid type of lesion, through the more striking forms sometimes called "Calcutta leprosy," to the tissue mania, so to speak, of the acute ulcerative condition here described. If the underlying factor of the condition in the last of these stages is to be considered as "resistance," it is resistance so violent and overdone that it damages the patient and often prepares the way for the transition to cutaneous leprosy.

It happens, however, that none of a group of his cases, some of them old, that were examined with him in 1937 by one of us (H.W.W.) was clinically lepromatous at that time, despite the fact that foamy-celled lepromatous foci were found in sections of some of the biopsy specimens; nor had any of them become definitely of that nature when reviewed a year later.

More recently Muir (8) has exemplified the kind of evidence that is usually depended upon in this matter, in the statement that traces of old tubercloid lesions may be found in cases which have become lepromatous, or that reference to previous records may show that this change has taken place. He illustrated the condition with a photograph of a lesion called a tubercloid leprid replaced by lesions of the lepromatous type, and in description of it said that a lepromatous lesion had developed in the flattened center of a residual tubercloid leprid and that numerous lepromatous macules were present in previously unaffected skin. But, for reasons that will become apparent, we believe that lesion to be an example of the "relapse tubercloid" type to be discussed, the case probably being what we here call a "borderline" one.

Considering now the contrary view, Schujman (14), who initiated the inquiry referred to above, indicated at that time doubt that transformation occurs. Further experience with tubercloid leprosy as it occurs in Argentina has convinced him that it does not (15); he holds that tubercloid cases may either improve to total cure or persist as such for long periods. Fernandez, of the same organization, remarked in a study of tubercloid lepra reaction (2) that in none of the twelve cases observed by him had there been a change toward the nodular form.

Cochrane (1), working in South India, seems also to have become convinced that tubercloid cases do not undergo transformation. He expressed the opinion that the results of the lepromin test in reaction cases "makes unacceptable the view that tubercloid leprosy may become lepromatous." He regards cases with lesions that "simulate those of tubercloid leprosy" but in

which the lepromin reaction is negative as belonging to an intermediate variety; as a rule they undergo recovery but occasionally pass into the lepromatous form.

Japanese workers have long been convinced of the ultimate good prognosis of all cases with positive lepromin (Mitsuda) reactions. In a report of follow-up observations of cases that had given atypical reactions ten years previously, Igarashi and F. Hayashi (3) make no mention of such a development. They indicate how unexpected it was that an ordinary neural case, with a typical positive reaction, had become lepromatous later.

We ourselves have seen lepromatous development take place in three cases of our Cebu study group (11), but they, too, were neural-type cases with simple, flat macules.³ It is supposed to be the bacteriologically positive, major tuberculoid case of reaction type that is most liable to undergo that change. In none of that kind which we have had under observation—relatively few in numbers, it is true—has it occurred as yet. There have, however, been occasions when we were more or less inclined to believe that it had happened; but actually the cases were in what it seems appropriate to call a “borderline” condition, still essentially of tuberculoid nature but apparently approaching the lepromatous, uncertain as to actual classification and ultimate prognosis. In such a state, perhaps, are the “intermediate” cases to which Lowe refers, and probably those to which Cochrane applies the same term though he specifies for them a negative lepromin reaction.

REPORT OF CASES

Of the three cases to be reported here, two were of the tuberculoid group hospitalized in the Eversley Childs Treatment Station at Cebu that we took under observation in 1936, but they were not included in our recent report of that group (19) because of their uncertain status, in which they still persist after another year. The third one was included in our report on the development of major tuberculoid cases from lesser forms (18), but at that time it had relapsed and seemed to be in a borderline condition, discussion of which was postponed until further observations could be made. The lesions, which had some features suggestive of the lepromata

³In the sections of the original biopsy specimen from one of these cases, the only one that was properly biopsied, several small tuberculoid foci were found. That finding, however, common in clinically simple lesions, does not of course justify classing the case as tuberculoid. The finding of a very few bacilli in these sections, unusual for that kind of lesion, was perhaps significant of the change to come.

but others that were highly atypical of them, we here designate as of "relapse tuberculoid" type.⁴ One of the two cases first mentioned has had lesions of this type, but in other respects they are peculiar unto themselves. Our observations of these cases have been occasional, usually annual, but they have sufficed to establish their principal features.

CASE I. BORDERLINE PAPULAR ERUPTIVE CONDITION

This case, which presented several though not extensive tuberculoid lesions of quite ordinary appearance when admitted to the Cebu leprosarium in 1936, has been atypical in its course in that since those lesions subsided the picture has been dominated by a repeated papular eruption of peculiar nature. Of interest is the evident attempt that for a time lesions of that eruption made to progress as tuberculoid leprids. With the present condition, and with histological findings that have varied considerably but that on the whole are indeterminate, the status of this case is decidedly uncertain.

Previous history.—The patient, P.O., a male Filipino aged 15, was admitted in March, 1936. A numb area on the right leg had been noticed three years before, and two years later small, red, infiltrated macules appeared there and on the left cheek and left hip. These enlarged, the one on the cheek becoming diffused and that on the leg receding centrally, leaving an infiltrated margin. *Condition on admission* (Dr. J. G. Tolentino): A large thick red plaque on right leg and smaller ones on left leg, left hip and right elbow; red areas on the face, the left cheek with central infiltration; ears turgid; also, scattered generally, numerous pale, slightly reddish papules. No perceptible enlargement of nerve trunks, but anesthesia of right hand, medial side; also of the larger skin lesions. Smear (cheek) 4+. Admission diagnosis: Leprosy, C1-N1.

First examination, September, 1936.—When we saw this patient there was a new erythematous patch on the right arm, extending from the original raised macule near the elbow to the wrist; where not modified by local injections it was reddish, shiny, very slightly raised and coarsened in texture, but apparently subsiding (Plate 18, fig. 1). The original larger lesions were all modified by treatment. The scattered papules, perhaps 60, were raised, rather flat and faintly reddish under brown, from pin-head to 1.5 cm. in size, the largest on the right arm and buttocks. In places some of them had apparently enlarged and become more diffused (Plate 18, fig.

⁴The term "relapse tuberculoid lesions" is used in this connection instead of "secondary" because, though in a way they are secondary, the latter term is used more generally and a distinctive one is needed. The form "relapsed" is not applied to them for they are not merely previous lesions reactivated, though they are in a peculiar relation to them. The case as a whole is of course "relapsed." It is not to be understood, however, that all relapsed tuberculoid cases will have lesions of this special kind. Many will present only new leprids of the ordinary kinds, but the "relapse" type is seen only in relapsed cases.

2). Right ulnar moderately enlarged, right peroneal slightly; no enlarged cutaneous nerves found. Smears: left cheek again 4+; shortly afterward six smears were all positive, 1+ to 3+.

Biopsies: (a) a large papule, left buttock; (b) the new reddish lesion, right forearm. Smears from sites 1+, though small globi present. Histology: Lesion (a), fairly marked changes, rather superficial, recorded as of lepromatous appearance but not definitely so, certainly without tuberculoid characteristics, possibly an undifferentiated reaction lesion. Bacilli numerous in places, sometimes invading nerves and in some of the more heavily bacillated cells occurring in clumps, sometimes even with small globi. Lesion (b), no significant abnormality except a little large-cell infiltration around the superficial vessels. A few bacilli found, none in nerves in the deeper layers.

Up to this point the clinical condition did not differ greatly from that in other cases of tuberculoid leprosy. As the several earlier plaques had subsided an extensive new area had developed on the arm. However, the indeterminate appearance of this lesion, and that of some elements of the multiple papular eruption, raised a question of the status of the case, but the condition as a whole (including the unilateral nerve affection of the limbs on which there were skin lesions) did not resemble a lepromatous one. The histological picture in the papular lesion removed was puzzling, certainly not of tuberculoid characteristics, but the very slight changes and the scarcity of bacilli in the large lesion of the arm sufficed to allay any suspicion that the case might have undergone lepromatous transformation.

Interim.—There was apparently no development in the next nine months worthy of note. In the one bacteriological examination made (October, 1936) six smears were all positive, 1+ to 3+.

Second examination, June, 1937.—The previous macular areas were now indistinguishable. The papular lesions, which had increased greatly in numbers, had for the most part receded, leaving small, pale, residual spots. In some parts, however, there were several less pale, raised, palpably infiltrated flat ones, chiefly on the upper part of the trunk. A few on the buttocks were erythematous, but the others were more of a more brownish tint. Interestingly, some of these "papules" on the trunk and elsewhere had enlarged somewhat and showed beginning central retrogression (Plate 18, fig. 3). A group of such lesions was found high on the posterior surface of the right arm (Plate 18, fig. 4), and lower down a further extension of this development, namely, a group of three small, delicate circinate lesions, with extremely narrow, raised edges that were finely papulate. Right ulnar now markedly thickened, with some atrophy of hand. Smears (three): positive, all 4+.

Biopsies: (a) a small circinate lesion on the right arm; (b) an enlarged, oval papule above the right scapula; (c) one of the extended ones with beginning central recession on the right arm. Histology: Lesion (a), a nice tuberculoid specimen, of slight to moderate degree, with very few bacilli.

Lesion (b), like the first one of 1936, apparently though not definitely non-foamy lepromatous, with no suggestion of tuberculoid differentiation. Bacilli abundant (3+), mostly in groups, both in parallel and dispersed, with occasionally an apparent globus. Lesion (c), seemingly quite definitely of lepromatous character, even to a lack of cellular invasion of some of the nerves in the areas of infiltration, though they contain numerous bacilli. Elsewhere bacilli are very numerous, though somewhat less so than in the second specimen.

At this stage the case was decidedly peculiar. The larger lesions had all disappeared and the active process consisted solely of the low papular eruption, new lesions of that kind having continued to appear. Most of them had receded or become actually residual but some had enlarged, a few showing more or less central recession, suggestive of tuberculoid leprids. One group of them had progressed to the narrow-margined circinate stage—minor tuberculoid but miniature, both in size and degree of elevation. Histologically one of these circinate lesions showed definite tuberculoid structure, with typically sparse bacilli. One of the other two specimens, (in both of which bacilli were numerous) was indeterminate, but the third seemed to be nonfoamy lepromatous, giving weight to the suspicion that the case was becoming of that nature. Note was made, however, that if that had happened the condition was peculiar, with important features against that diagnosis.

Interim.—In February, 1938, two of three smears were positive, both 2+. In April a reaction occurred that lasted until June. Another one had occurred a short time before we saw the patient again.

Third examination, September, 1938.—The condition as a whole was neither improved nor was it greatly aggravated. Evidently resulting from the recent reactions, a pinkish macule had reappeared on the left cheek and the earlobes again showed slight infiltration. Elsewhere there were numerous new small lesions of the usual kind, the most active-looking ones on the thighs. Chiefly on the lower back and buttocks were others that were less noticeably raised, most of them with little or no erythema. The greater part of these lesions, everywhere, were flat and more or less residual, entirely pale or with a hyperpigmented zone around a pale spot. In the photograph (Plate 19, fig. 5) the latter kind look like scabies scars, but actually that appearance was due to local intradermal injections, which apparently had stimulated hyperpigmentation around the lesion foci. Atrophy of hand had increased. Smears (five): all positive, those from the cheek and a papule on the loin 4+.

Biopsies: (a) a reddish, slightly raised flat papule below the left gluteal fold; (b) a pale, slightly raised one on the lower back. Smears from sites positive. Histology: Lesion (a), changes slight, practically entirely superficial—fairly general large round-cell infiltration about the vessels of the subpapillary plexus and diffusely above, very little below, quite without distinctive differentiation. Surprisingly many bacilli present, very numerous

in places and often extracellular, indicating inadequacy of the cellular response. Lesion (b), more marked but of the same undifferentiated character. Bacilli even more abundant (3+), with much close, parallel clumping.

The papular eruption, still the most notable feature, now showed no extended, annular or circinate forms; i.e., there was no attempt to produce anything suggestive of tuberculoid leprids, and those previously seen had disappeared. The infiltration of the ears—if not the condition of the cheek, which was unilateral—seemed suggestive of lepromatous change, as did the numbers of bacilli found in smears. Yet the condition as a whole continued to be very far from that of lepromatous leprosy, and the reaction that had occurred only a few days previously has to be considered. The fact that both of the papular lesions biopsied showed an undifferentiated condition, but with bacilli in surprising abundance, left the case no less uncertain as to status than before. It was evident from the subsidence of so many of the papular lesions that a continued stubborn effort was being made to hold the infection in check, but from the repeatedly occurring new lesions and the inadequacy of the cellular response and lack of differentiation in them it was still highly doubtful that the ultimate prospect was at all hopeful.

Interim.—In April, 1939, smears were recorded as positive (2+) from four out of five sites. A lepromin injection was made in July by one of us (J.N.R.) during a visit to Cebu, but through a misunderstanding it was not read; the patient, however, states that no papule developed at the site so evidently it was negative. The findings in two examinations made this year (August and October) are combined as of one.

Fourth examination, 1939.—The case, though not inactive, was in a period of relative quiescence, and the patient seemed to be in excellent condition. The lesion on the left cheek was only a faint, ill-defined macule some 7 cm. across, locally injected; the ears showed no definite abnormality (Plate 19, fig. 6). Most of the papular lesions and residual spots previously seen had quite disappeared, though there are still numerous rather faint ones, mostly not elevated and pale; but some were slightly pinkish, varying in size from pin-head to 5 to 8 mm., flat or only very slightly elevated. The photograph of the back (Plate 19, fig. 7) suggests the presence of small annular lesions larger than any previously seen, but the appearance is due to hyperpigmentation around pale spots. One, dome-shaped, about 5 mm. in diameter, was found on the medial surface of the right forearm. A group of pale, raised scars forming a discontinuous band on the lower right chest (Plate 19, fig. 8) was ascribed by the patient to herpes zoster.

No *biopsy* specimen was taken, the condition not seeming sufficiently active or different from before to warrant the further molestation at this time. Smears (four): strongly positive, 2+ to 4+.

Summary.—This case, after an observation period of three

years, early in which the original tuberculoid leprids disappeared and throughout which there has been a repeated and at times more or less continuous appearance of a papular eruption, these lesions always positive for bacilli and usually quite strongly so, still remains of uncertain status. In one period (1937) some of the lesions showed centrifugal extension and central recession, an evident attempt to progress as do the ordinary tuberculoid leprids, and one of them proved to be tuberculoid histologically. But that attempt was abandoned, and since then the papules have appeared and disappeared without further development, usually responding quickly to single local injections of chaulmoogra drugs. On the other hand nothing of the usual appearance of the lepromata has appeared. On each of the three annual examinations at which biopsies were made one or more of the specimens were found to be of indeterminate nature. At the time when one proved to be tuberculoid another seemed quite certainly to be lepromatous, yet neither of the two obtained in the following year was definitely of that kind. If it is correct to recognize a borderline condition, tuberculoid approaching lepromatous, this case is certainly to be so classified. The boy has developed normally and seems to be strong and in excellent general health, and when last seen the disease was relatively quiescent, but the prognosis remains uncertain. In view of the continued failure to overcome the infection (and especially if, as seems to have been the case, the lepromin test made in 1939 was negative) it cannot be said to be favorable.

CASE 2. PAPULAR ERUPTION AND RELAPSE TUBERCULOID LESIONS

An interesting feature of this case, at the outset, is that the disease began more than twelve years before the time of this report, and that between the time of his first hospitalization in Manila (in 1927) and the relapse that brought him to the Cebu leprosarium (in 1934) there was a period of some five years of apparently complete recovery. Undoubtedly tuberculoid on the first occasion but not of more than minor grade, the condition was of major degree after the abrupt, reactional recrudescence. Repeated reactions have occurred since then, with decided aggravation of the disease and considerable departure from the original form, yet after five years it cannot be said what the outcome will be.

Previous history.—The patient, D.A., a male Filipino aged 28, sturdy and well-nourished, was admitted in April, 1934, a relapsed case. *First hospitalization:* Entered San Lazaro Hospital, Manila, in June, 1927, with a "diffuse macule," light red in color, slightly thickened especially at the border, on the left malar region extending to the frontal. Six months

previously a red area had appeared on the face; still earlier anesthesia of the dorsum of the right foot had been noticed. Smears positive. Diagnosis: Early nodular leprosy. *Progress:* A year later (July, 1928) macular areas were recorded on the cheeks, forehead and right scapular region. Ulcers of nasal septum, ulnar nerves slightly thickened. Recession occurred and the patient was paroled in August, 1929.

Interim.—There were no further manifestations of the disease until February, 1934, two months before the patient was rehospitalized. Relapse was abrupt, initiated with red areas on the right leg and left foot; others appeared elsewhere later. A generalized papular eruption occurred suddenly, with fever, about three weeks before admission.

Condition on admission (Dr. Tolentino).—The reaction, now of two months duration, was still manifest. Areas of dusky red infiltration over both knees, on both legs posteriorly and on left hand; also left ear. Numerous ham-colored papular lesions everywhere, measuring from 2 mm. to nearly 1 cm. Nasal septum ulcerated. Ulnar and peroneal nerves moderately thickened, great auriculars slightly. Smears positive. Admission diagnosis: Leprosy, C2. *Progress:* In August, four of seven smears were positive; three months later all were negative. The patient was placed on the negative list in January, 1935; there were chocolate-colored scars on legs, left palm slightly livid, face and ears flushed, left earlobe with a purplish papule and numerous small reddish-brown papules on trunk and extremities, some with wrinkled surfaces. All of the eight bacteriological examinations made that year were negative, but the patient was not paroled. Beginning in January, 1936, from one or two to five smears were found positive on each of five occasions, though never more than 1+. No change in the clinical appearance was recorded.

First examination, September, 1936.—When this case came under our observation the previous large lesions were represented by hyperpigmented, slightly depressed areas. Externally on the right leg there was a new large, irregular patch, reddish, infiltrated and scaly but ill-defined (Plate 20, fig. 10), and a similar small area (3 cm.) was on the right elbow. Cheeks smoothly thickened and slightly flushed, without definite lesions; earlobes had localized red thickenings. Scattered all over the body were raised, reddish, papular lesions with ill-defined edges, most of them modified by injection (Plate 20, fig. 9). Slight paralysis of muscles of both eyes, with frequent twitching of the upper lip and left cheek. Ulnar nerves thickened but soft; common peroneals considerably so, left one slightly tender; superficial branch of left radial also thickened.

Biopsies: (a) the scaly lesion on the right leg; (b) a papular lesion on upper back. Smears from sites: (a), positive, only 1+ but with small globi containing at most 3 or 4 bacilli; (b), negative. (Error? Labels reversed?) Histology: Lesion (a), slight tuberculoid, a few small foci in all levels, not active in appearance; a very few bacilli found. Lesion (b), slight tuberculoid, confined to a part of the papillary layer; bacilli found in considerable numbers in places.

As in the usual course of tuberculoid leprosy, the lesions present on admission subsided quite rapidly and all bacteriological examinations were negative for more than a year. What led to the

return to the positive state early in 1936 is not evident, but the condition that we found later in that year suggests that the patient had experienced one of the occasional reactions that have marked his progress since then. As yet, however, there was nothing to mark the case as exceptional; with the clear-cut, though slight, tuberculoid changes found in the biopsy specimens from both large and small lesions it appeared to be an ordinary one with delayed resolution.

Interim.—Six weeks later (October, 1936) the papular lesions were recorded as subsiding, faint and pinkish, like tinea flava; the active lesion of the right leg was still reddish, but the one on the right elbow had subsided almost entirely. Of six bacteriological examinations only one was completely negative; in May, 1937, all smears were positive though as usual only 1+.

Second examination, June, 1937.—The hyperpigmented areas were apparently quite residual. The reddish one on the right leg was now smooth but presented small, brownish-red areas of somewhat suspicious appearance. Scattered generally were many small, reddish, slightly elevated spots of the "papular" eruption that had appeared from time to time, in continual succession rather than in crops; some were oval or elongate and many were discolored by injections. Bacteriologically they were ordinarily 1+, seldom 2+. One intradermal injection, it was said, would serve to clear up one of them. Partial paralysis and atrophy of left hand. Face as before.

Biopsy: a specimen of a new papular lesion high on left thigh, obtained after persuasion. Smear from site 1+. Histology: slight infiltration (large round-cell) in the papillary layer, focal but undifferentiated, neither tuberculoid nor suggestive of leproma; deep, beside a nerve, a tuberculoid focus was found. Bacilli present in some numbers, with occasional small globi.

On the whole the condition did not seem much changed from the previous year. With new papules arising as old ones subsided the case seemed on the whole to be in a state of equilibrium, the infection neither being overcome nor becoming materially progressive. Some parts of the leg lesion that was active when previously seen were suggestive of a lepromatous development, but hardly more than in color. Bacilli were seldom very numerous in smears, nor were they so in sections of the biopsy specimen obtained from a recent papule. Histologically that lesion was for the most part focal but undifferentiated, but since a single small tuberculoid focus was found the weight of evidence was for that nature of the process.

Interim.—For most of the next year, the patient says, he improved until there were only a few lesions left, they not very noticeable. Smears, however, were persistently positive (seven examinations) though never strongly so until June, 1938, when, after he took a week's absence without leave, three of the four positive ones were 2+. In July he left again for a month, returning a few days after the onset of a febrile reaction.

Third examination, September, 1938.—Besides remnants of the old large lesions and residua of the papular eruption, some pale, others hyperpigmented or discolored by injections, there were new fresh lesions that had appeared in the recent reaction, all of rather bright reddish color, moderately elevated and diffuse of outline. Many of them were papular, but on the forearms, wrists, thighs and legs were fairly large elevated patches. The face showed more disturbance than before, the cheeks with some irregular infiltration and erythema and the alae nasi thickened and red. Nerve trunks much as before, with some tenderness. Smears (four): all 2+.

The new lesions on the forearms and wrists were of special interest. They were quite thick, symmetrically placed but irregular in shape and somewhat complicated, on the whole suggestive of tuberculoid plaques except that peripherally for the most part they diffused off into the surrounding skin (Plate 20, fig. 11). The outline of each of those on the wrists was indented at one place by an area of normal looking skin; and against this area, in conspicuous contrast to the condition elsewhere, the elevation stopped abruptly. Those on the forearms were in part annular, containing small, normal-looking, noninfiltrated areas; against them, too, the elevation stopped abruptly. The patient stated that all of the unaffected areas so demarked were the sites of previous lesions. These new lesions, and those on the lower extremities, were in part hypoesthetic; the papular ones were hyperesthetic.

Biopsy was refused, but later the patient permitted two specimens to be taken. Unfortunately they were lost in transit.

The new development, which resulted from a reaction a month or so before the examination, while the patient was away, was looked upon at that time as of uncertain nature. Morphologically the new large lesions described seemed rather suggestive of transformation, chiefly because of the diffusion of their outlines; yet they were far from typical of lepromatous infiltrations. A striking feature was the arrangement in relation to, without intrusion into, areas said to be the sites of previous lesions, at which places the elevation ended abruptly. These new lesions were decidedly atypical of either leprids or lepromata, but if they were the latter the case was peculiar, for one thing, in that the multiple papular eruption was in no way essentially different from before. The loss of the two specimens that the patient finally gave is particularly regrettable.

Interim.—Characteristic of the case is the fact that when the patient was biopsied in January, 1939, the lesions that four months before had been selected for study had receded so much that they were no longer suitable, but that new ones, both large and small had appeared. Two to four smears were positive in each of three examinations between February and June, usually 1+, seldom 2+. Two examinations were made by us this year, with different findings.

Fourth examination, August, 1939.—The marked reaction lesions seen in 1938, and those that developed afterward, had subsided, the areas being quite indefinite and showing only slight flushing, with no perceptible infiltration.

The body was studded practically all over by the old papular eruption, most of the spots more or less discolored by intradermal treatment, but there were no fresh papules.

Interim.—Shortly afterward seven smears were all found negative and the patient was given leave. Two weeks later (September) he returned, as in 1938, in a state of reaction. Smears were then positive (1+).

Fifth examination, October, 1939.—Of the new lesions resulting from the recent reaction, the most numerous were in the scapular and subscapular regions (15 to 20 on each side), and over the right loin (about 10); a few were on the chest and abdomen. Some were small, papular, but many consisted of larger, rather diffusely outlined, slightly elevated reddish areas. A few of the latter were circular and more elevated, but most of them were elongate, some oval and others appearing as more or less serpiginous streaks. Some showed central depression, and thus they were superficially suggestive of a tuberculoid eruption with central recession. However, the elevation terminated around these small central flat areas much more abruptly than peripherally (Plate 21, figs. 12 and 13), and it is therefore to be suspected that they were actually halos around previously affected areas—"relapse tuberculoid" lesions similar except in size to the interesting ones seen in 1938. For the most part, however, the new lesions seemed to be entirely independent of old lesion areas. The areolae were involved, the left one with irregular infiltration and elevation of a zone of uniform width extending about 12 mm. from the nipple itself and extending about 3 mm. beyond the pigmented area (Plate 21, fig. 12); the right one was similarly but less markedly affected.

Biopsy: A small new lesion in the right subscapular area. Histology: a particularly interesting picture, due to the fact that by accident the section was cut parallel to the surface and in consequence the foci of cellular infiltration (vasculo-neural tracts) are cut transversely and are rather uniformly scattered throughout. The smallest of these accumulations consist almost entirely of large macrophage-type cells, undifferentiated, but within many of those of larger size are discrete epithelioid foci—typical small tuberculoids. In the largest areas the epithelioid element is correspondingly conspicuous. Here and there are giant cells, usually very small. This is definitely a tuberculoid development.

Summary.—After a period of some five years following apparent recovery from the first stage of the disease, this case relapsed by reaction and, except for a negative period of one year, it had remained more or less active for more than five years at the time of our last examination. As in the preceding case, the main lesions that were present on readmission subsided quite completely, but new ones have continued to appear, mainly as a result of the several reactions. Most of them have been of the atypical papular kind, of limited duration and easily controlled by treatment, that have for so long been the only active manifestations in the preceding case, but at no time did they show any evidence of an attempt to progress in the manner of tuberculoid macules. In one period, however, several larger lesions of the "relapse tuberculoid" type

appeared, some of them at least in relation to previously affected areas; these, too, subsided quite rapidly, eliminating any suspicion that they might have been lepromatous. (It cannot be said if the lesions that appeared in 1934 were of this nature, but at least there is no indication that they had any relation to the areas that had been occupied by the original ones.) When the patient was seen last the multiple eruptive elements had departed considerably from their usual small, rounded papular form, being larger and usually elongate, even more diffuse of outline than usual. Some of them had small, flat, central areas, the sharp margination and pale color of which indicated that they were the sites of previous papules, the zones around them thus being extraordinarily small lesions of the "relapse" type. Histologically the specimen obtained was partly undifferentiated but essentially tuberculoid. The course of this case has been discouraging and the ultimate prognosis is uncertain. It remains to be seen what significance is to be attached to the histological findings in the last biopsy specimen.

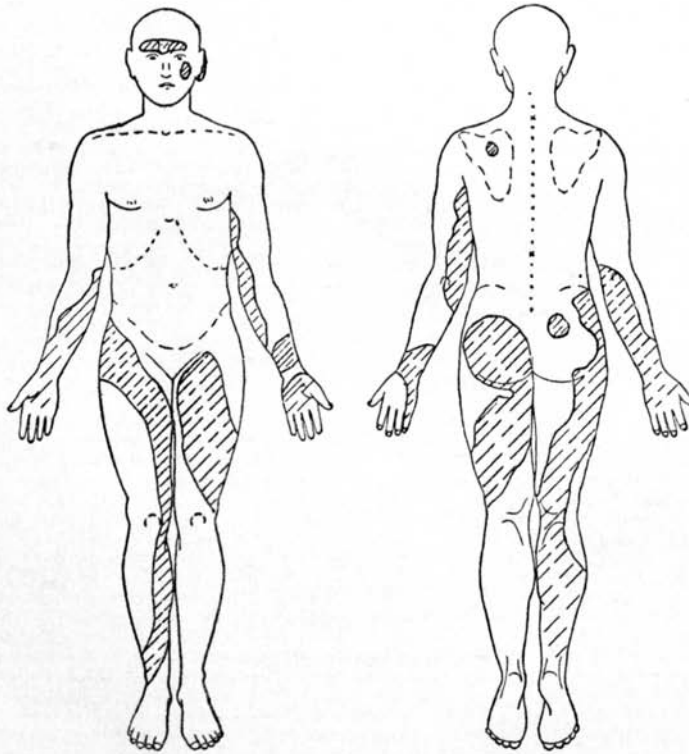
CASE 3. PHASE OF RELAPSE TUBERCULOID LESIONS

This case, a remarkable one of many vicissitudes, we classed as "borderline" in 1938 (18, Case 2) because of its clinical and histological appearances at that time, shortly after it had relapsed, with abrupt development of extensive new lesions. After that, following an extraordinary further reactional condition that will be described separately (10), the condition has again subsided quite completely, in the manner typical of tuberculoid reaction, so that for the present at least its status is not in doubt. It is nevertheless included here with respect to the phase of relapse, because it exemplifies most strikingly an "intermediate" condition that is borderline at least in the sense that it is readily mistaken for lepromatous transformation, its lesions illustrating well the "relapse tuberculoid" kind seen on a small scale in the preceding case.

Previous history.—Recapitulating the history to 1938, the patient, T.C., encountered in the Cordova survey in 1933 at the age of 20, had then extensive, active minor tuberculoid lesions on the buttocks and thighs which had spread with extraordinary rapidity. Smears 3+; bacilli also numerous in sections, which showed typical active tuberculoid changes. The *second phase* was one of aggravation of the condition to the major tuberculoid form as a result of an acute febrile reaction which occurred three months later and incapacitated the patient for two months. The previously affected areas flared up, including parts that had resolved, and many new lesions developed. Their distribution at the time of hospitalization in March, 1934, is shown in Text-fig. 1. Trophic changes had appeared by then, mostly affecting the hands. Admission diagnosis: C2-N2. The *third phase*, that of recession, progressed so rapidly that when the patient was transferred to Cullion four

months later most of the skin lesions had flattened, and all continued to recede, but smears continued occasionally to be positive until the middle of 1936. Paroled in March, 1937.

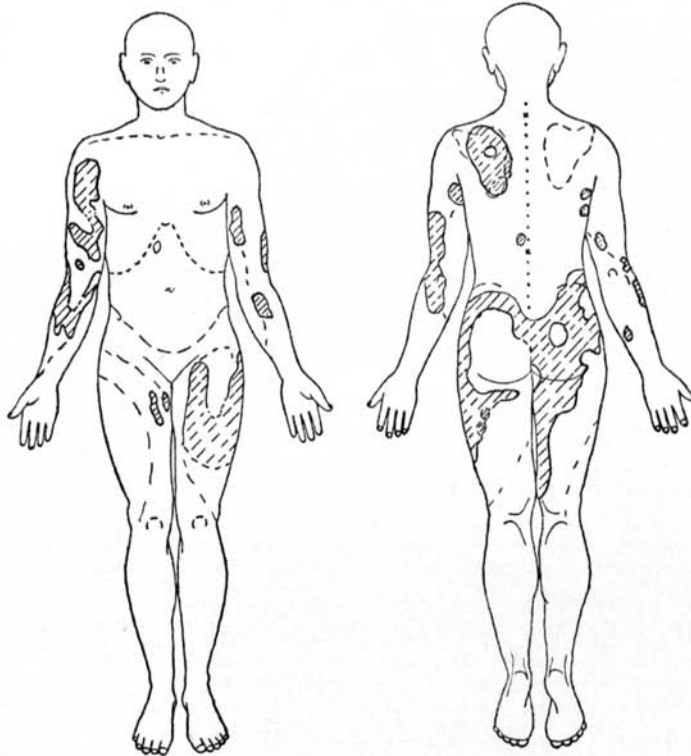
So far the case was simply an ordinary one of reaction tuberculoid leprosy, of interest mainly in the fact that it had been seen and examined histologically while it was of minor grade, in the unusual severity of the reaction that caused it to evolve to the major grade, and in the rapidity with which the lesions subsided after hospitalization, in spite of which bacilli did not disappear entirely for a long time. It began to be an outstanding one in our experience when, after a period of more than two years without manifestations of the disease, there developed the condition to be described.



TEXT-FIG. 1. Diagram showing approximately the location of the lesions of the reaction tuberculoid phase of the disease in Case 3, from sketches made by Dr. R. S. Guinto in September, 1933, when the patient was first seen, and by Dr. J. G. Tolentino, in March, 1934, when the patient was admitted to the leprosarium.

Relapse phase.—Seen at Cordova in September, 1938, eighteen months after parole, the patient had suffered an abrupt relapse, and extensive new lesions had appeared. Three weeks previously a large boil had developed

over the left knee, accompanied by high fever, headache and chills, and on the third day large red areas bloomed forth and evolved rapidly. Previous to that time, he asserted, there had been no manifestations since he left Culion. The lesions consisted of widely distributed acute, erythematous patches, more or less elevated and rather rough-surfaced, a few of them small but others very extensive. Their distribution is shown in Text-fig. 2.



TEXT-FIG. 2. Diagram of the lesions of the relapse phase of the disease in Case 3, in September, 1938, showing their intimate relation to but usual avoidance of areas affected previously.

On the right side a vast area extended from above the iliac crest down over the buttock onto the posterior and medial surfaces of the thigh, nearly to the popliteal fossa (Plate 22, figs. 16 and 17). It did not extend around onto the anterior surface, but there, in the inguinal region, were two small but prominent isolated patches. Central over the buttock, and also externally on the right hip and from there down over the thigh posteriorly, were areas of quite normal-appearing or slightly hypopigmented skin against which the infiltration terminated abruptly. These areas were the sites of major tuberculoid plaques in the previous active phase of the disease.

On the left side the buttock area, previously affected but now not participating, was surrounded over fully three-quarters of its circumference by a prominent active lesion that extended from the hip region upward

and inward as a rather narrow zone limited at about the iliac crest, and just below the gluteal fold extended medially as a narrow but particularly elevated peninsula (Plate 22, figs. 18 and 19). This lesion area, also to be described as vast, covered almost the entire hip and extended downward over the external and latero-posterior surfaces of the thigh to the knee; anteriorly it turned upward to the inguinal region. At its lower limit toward the knee it shaded off gradually and became indistinct.

There were similar though less extensive patches of irregular shapes anteriorly on the right arm and posteriorly on the left one. Anteriorly on the right forearm (Plate 21, fig. 14) two prominent bands converged to meet below the cubital space, at which point the infiltration was relatively slight. On the upper arm was another very irregular lesion, roughly S-shaped, almost separated into two by a zone that was only slightly infiltrated (more prominent when photographed later). The large one on the left arm was less irregular. These lesions, too, were all diffused in parts of their peripheries, but abruptly marginate in other parts where they adjoined previously affected immune areas. Another fairly large lesion was in the left scapular area (Plate 21, fig. 15), and appearing as a sunken island in it was a rounded "immune" area. Along the lower and medial edges of the lesion were two distinct, prominent patches, and above them a less prominent one; elsewhere the active condition was less conspicuous, tending to merge off into the normal skin. There were a few relatively small lesions elsewhere on the back, but only one was found on the anterior surface.

Other features noted were contracture and deformity of the hands, affecting all of the fingers, with marked atrophy and some deformities of both members, more on the right side than the left. The ulnar nerves were only moderately thickened, however; the right peroneal was markedly so. Smears (buttocks): 2+ and 3+.

Biopsies: (a) from the upper edge of the lesion zone above the left buttock, to include lesion and normal skin (it was found later that the surgeon failed to include any of the actual lesion); and (b) the lower edge of that zone, including lesion and the normal-looking immune skin. Smears from sites positive, 1+ and 2+. Histology: In a part of specimen (b) is a rather marked granuloma, mostly in the superficial zone, relatively little deeper, lowest levels not affected. The elongate character of the essential cells, and the penetration of the masses everywhere by fine, irregular strands of collagenous material, led to a diagnosis of nonfoamy leproma, and it is still impossible to characterize it otherwise. Bacilli here were found to be very numerous (3+). The part that came from the central, immune area shows certain residual changes, by far the most prominent being fibrosis of the subpapillary layer. Specimen (b), actually taken from the unaffected skin, shows very slight round-cell infiltration at a few points, mostly in the sub-papillary layer. Unexpectedly, bacilli were fairly numerous (2+).

Subsequent course.—The patient was reexamined for us about two months later by Dr. R. S. Guinto. From photographs made then (the first lot had proved unsatisfactory) it is evident that over much of their less infiltrated parts the lesions had undergone some recession. Smears: seven from skin areas, including earlobes, all positive, 1+ to 3+; nasal septum, 4+.

Since the later developments are to be described elsewhere, it is suffi-

cient to say here that another reaction had occurred by the time the patient entered the Cebu leprosarium after another six weeks (December 1, 1938). For the most part the lesions described above were then noted as bluish-red, flat or only slightly elevated, but parts of them had become reactivated and new lesions had appeared, including rather extensive ones of the face and ears. A smear was 4+. In still another reaction a remarkable bullous, ulcerating condition developed, after which all lesions subsided, apparently completely, and when the patient was seen in 1939 the condition seemed again to be entirely quiescent. A biopsy specimen, however, showed residual tuberculoid foci beneath the zone of fibrosis.*

Character of the relapse lesions.—Emphasis is to be placed on certain features of the “relapse lesions” that were so striking in this case (and to a less extent in the preceding one) wherein they differed from ordinary tuberculoid leprids. (a) The principal one is their diffusion into the previously unaffected skin, in which respect they looked more like lepromata than leprids. (b) No less arresting was the contrary condition of abrupt and conspicuous margination around—or against—the areas which had been affected by the previous active phase of the disease, which areas with perhaps a few exceptions did not participate in the new activity. This appearance was again the reverse of what is ordinarily seen in tuberculoid plaques, in most of which (barring certain band-like kinds, hardly to be confused with the lesions under discussion) slope off gradually to the resolved central areas. The facts that almost all of the new lesions, at this stage of the relapse, were in immediate proximity to the old areas, and that generally the infiltration was more marked there than at a distance, are not the least interesting features of the case. (c) The unusual irregularity of elevation, as well as of extension, of the new lesions is also noteworthy. A much larger proportion of the affected areas were only moderately thickened than markedly so, and in many places the condition was relatively slight. This fact, together with the common diffusion of the edge toward the normal skin, made it difficult at times to determine with any accuracy the exact limits of the areas involved, and impossible to demonstrate them satisfactorily in photographs. These lesions, clearly, had morphological features very unlike those of lepromatous infiltrations, as was their sudden development. Despite the histological findings in the one useful specimen, which permit no other microscopic diagnosis than that of a nonfoamy leproma, the later reac-

*It was reported by Dr. Tolentino in May, 1940, after this report was in press, that the patient was still bacteriologically positive in various places (1+ to 3+), and that new lesions had appeared in April around some of the scars.

tional phenomena and subsequent recession serve effectively to rule out any possibility that the case as a whole had undergone transformation.

DISCUSSION

These cases, obviously, are not presented as illustrating the process by which tuberculoid leprosy undergoes transformation to the lepromatous type, for none of them has done so yet. If that change occurs—a possibility which we would by no means deny—it may well be that it is in some quite different way, or that the process may differ among different peoples. Nor are they presented with any idea that they are wholly typical of actual borderline cases as seen elsewhere; in fact the two that are persistently in that condition may be very unusual. All three of them, however, have at one time or another in their long and varied courses aroused in us more or less strong suspicion that they were undergoing change of type, and they present features of interest in connection with that question.

One feature of the first two is the fact that the original frank tuberculoid leprids receded and disappeared more or less completely. A second feature of them is that the repeated eruptions by which the disease process was continued thereafter consisted predominantly of peculiar papular lesions, entirely so in Case 1. A third feature is the confusing kind of lesion, shown by its clinical behavior unquestionably to be a leprid rather than a leproma, that the second case has exhibited and that characterized the third one during the relapse phase here dealt with.

Regarding the recession of the earlier frank tuberculoid lesions, Lowe asserts that that happens when a case becomes lepromatous. That is entirely reasonable, for the tissue reactivity that produces the lesion of tuberculoid leprosy—and also that of the positive lepromin reaction—is lacking in lepromatous leprosy, and if in a tuberculoid case it should be lost the lesions that depend upon it could hardly be maintained. At the same time it is true that ultimate subsidence of lesions is characteristic of the reaction tuberculoid case itself. Furthermore, local variations of the process, retrogression of some lesions while others progress and new ones appear, is a common phenomenon in any variety of neural leprosy. It does not follow, therefore, when in cases of the kind under discussion old lesions subside coincidentally with the development of new ones, that the latter are necessarily of fundamentally different nature.

As for the secondary papular lesions, eruptions of that kind

constitute a conspicuous feature of active tuberculoid leprosy as it occurs in Cebu (19). Whether or not the frequency with which they occur in that place is a regional peculiarity we cannot say. The condition does occur elsewhere, of course, but the infrequent references to it indicate that it is not at all prominent in the picture of tuberculoid leprosy as seen by other workers. As for the condition under discussion, Lowe does not mention such lesions in his statements regarding "intermediate" or converted cases. However, in the picture which Muir published (8) there is evidence of them around the main lesion, and it seems possible that the "numerous lepromatous macules" seen all over the previously unaffected skin may have been, then or originally, of that nature.

The papules in ordinary tuberculoid cases are as a rule fairly prominent and discrete. They were often so in our two persistently borderline cases (Plate 18, figs. 1 and 2), but usually they were diffuse of outline and low. In ordinary acute cases, again, they as a rule subside sooner or later without enlarging, though they sometimes do that. The same holds for these borderline cases, though certainly in Case 1 in 1937, and apparently in Case 2 when it was last seen, a tendency to spread was evident in some of the lesions. Histologically these lesions in the borderline cases differ from those in the ordinary ones, in which they are of tuberculoid structure, in that most of those examined were of indeterminate character. At the time when extension of lesions was evident in Case 1, the specimen from one of them seemed quite definitely to be lepromatous, while on the other hand that from one of the few that had succeeded in becoming delicate, miniature circinate leprids proved to be of clear-cut tuberculoid histology. These findings at least signify a conflict of forces.

The larger lesions here designated as of "relapse tuberculoid" type are certainly not peculiar to Philippine cases. Because of their generally atypical appearance, however, and also because quite regularly they are bacteriologically positive and often highly so, it is probable that they are usually mistaken for leprids transformed to lepromata. Repeatedly in the past we have seen this condition—an apparent leproma diffusing off into the normal tissue through most or all of the periphery, but surrounding or bordering upon a sharply demarked uninvolved area, this appearance being the reverse of the typical abrupt outward limit of major tuberculoid patches and the gradual sloping off inwardly as their centers retrogress. When Lowe, after mentioning a transitional stage, describes the converted lesion as showing "a depressed area in the

middle of a typically leprotic lesion teeming with bacilli," the suspicion is strong that he has these lesions in mind. That description would apply to the one which Muir pictured except for the secondary development within parts of its central area. The transitional stage referred to we have not seen. In our cases the original tuberculoid leprids had subsided completely, the relapse lesions around them developing later as a reactional condition. The facts that the latter subsided as only reactional leprids do, with corresponding change in the bacteriological findings, is the best possible proof that they could not have been lepromata despite the fact that the histology of the single useful specimen secured (Case 3) does not permit any other diagnosis than that of nonfoamy leproma. The problem of the histology of these atypical reaction lesions in general cannot be gone into here.

The striking feature of the resistance or "immunity" of the central or bordering areas that had previously been the sites of typical tuberculoid leprids is a most interesting one. Ordinarily those areas remain wholly free from involvement, but in a few places in Case 3 (notably anteriorly on the right thigh) new plaques occurred in places that are supposed to have been affected before. That, apparently, had occurred in Muir's lesion referred to if, as we assume, it is an example of the relapse tuberculoid leprid. It may be that in such areas the previous lesion-process had not been sufficiently marked to produce complete immunity, for it is known that the sites of previous minor tuberculoid leprids may be involved when the major tuberculoid condition arises by reaction, and that old flat, "simple" macules seem prone to that, though in both instances such lesions are immune to refection by a process of the original degree.

Why it is that the relapse type of lesion is characteristically in immediate relation to an old site is a matter of speculation. That relationship, and the further fact that often the degree of the new lesions is greatest in immediate juxtaposition to those sites (shown clearly in the photographs of Case 3), leads to the thought, wholly unorthodox and paradoxical, that the infecting agent may somehow have been harbored in those supposedly recovered areas—unless it be that the previous infection had made the neighboring tissue especially susceptible to involvement when that agent was again disseminated from wherever it may have lain dormant. We do not advance either of these speculations as an opinion, but it seems not unreasonable to expect that the explanation of so unusual a condition will itself be unusual.

Further with reference to the question of causation, there is in all three cases the factor of reaction. The reason is obvious for the single, severe one in Case 3 (namely, the pyogenic infection), but not for the milder and repeated ones in the two persistently borderline cases. We know of no general or particular "predisposing factors," for both patients are in excellent general condition (see Figs. 6 and 11) and the boy has developed normally. The instability in this respect is real, however, as is evidenced by the repeated reactions suffered by Case 2 when on leave. The facile explanation of "loss of resistance" does not do much explaining. Granted that the disease has been permitted repeatedly to establish many lesions, and bacilli have often if not usually been allowed to become extraordinarily, suspiciously numerous in them. But the ability to control the lesions after a certain stage of development, which is so important a characteristic of ordinary tuberculoid leprosy, has not been lost; on the contrary, existing ones constantly subside even while new ones are being formed. It would probably be more correct to say that there has been only a diminution, or possibly a modification, of resistance. If it is ultimately lost, and the cases really go over the threshold to become lepromatous, it will at least be evident that conversion of the tuberculoid to the lepromatous form of the disease is not a thing easily accomplished, that the influences which make the form as benign as it is are not easily abolished. In any event, the course that these cases has taken indicates that caution is in order in pronouncing a tuberculoid case transformed.

SUMMARY

Three cases which bear on the unsettled question of the transformation of tuberculoid leprosy to the lepromatous type are presented. Two of them have been for long periods in a peculiarly unstable, "borderline" condition, repeatedly suspected of becoming lepromatous. The third one presented, in the phase here dealt with, as at one time one of the others did to a less extent, lesions of peculiar, atypical morphology and histology that are designated as "relapse tuberculoid."

The persistently borderline cases have long been characterized mainly by repeated reactions of more or less mild degree and repeated, at times continuous, eruptions of papular lesions, the earlier large leprids having subsided relatively early in the course of the disease. The papular elements have usually not been discrete, but diffused peripherally, and when acute they have or-

dinarily yielded numerous to abundant bacilli; yet they have regularly receded spontaneously or yielded promptly to local treatment in the way of papular leprids, while the new ones appeared coincidentally or in later eruptions. Histologically most of them have been indeterminate, neither tuberculoid nor frank lepromatous. Seldom have they shown any attempt to enlarge, but that development has been seen. At one time in Case 1 a few become miniature circinate leprids, of clear-cut tuberculoid histology, and the most recent specimen from Case 2 is tuberculoid. Nor have these cases become lepromatous, though the prognosis remains uncertain.

Other lesions of highly atypical, suspicious character appeared during one period in Case 2, and in the third case such lesions were extensive and very striking. With their diffused outlines, abundant bacilli and peculiar histology, they might easily be taken for lepromata; and, with enclosed or adjoining unaffected areas that are known to have been sites of previous major tuberculoid lesions, against which the infiltration is sharply limited, they might seem to have arisen by lepromatous transformation of such earlier lesions; yet they later subsided in the way of leprids. The explanation of the obvious relationship of these "relapse tuberculoid" lesions to the apparently healed, previously tuberculoid areas is a matter of speculation. There is reason to believe that such lesions have at times been taken to be lepromata, thus confusing the picture of transformation of tuberculoid cases if that occurs, which remains to be established satisfactorily.

These cases indicate that caution must be exercised in diagnosing lepromatous transformation of tuberculoid leprosy.

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DESCRIPTION OF PLATES

PLATE 18

FIG. 1. Right arm of Case 1, in September, 1936, showing the recent extensive erythematous, slightly raised patch, more or less modified by local injections, that extended from the elevated lesion which was present in March near the elbow, to the wrist. Several of the papular lesions so conspicuous in this case are seen on the right buttock. Histologically (biopsy site indicated) only slight large round-cell infiltration was found.

FIG. 2. Left hip, etc., showing discrete papular lesions and (above iliac crest) larger, more diffused ones. The papule removed (indicated) suggested histologically a nonfoamy lepromatous condition but was not definitely of that nature.

FIG. 3. Left chest of the same case in June, 1937. The papular lesions, more numerous and less discrete than before, have mostly receded to leave only small, pale residual spots. Some, however, are slightly elevated, and a few of the largest show a tendency to central recession.

FIG. 4. Right back and arms of the same patient, also 1937, showing everywhere numerous papular lesions, some of which have extended, and residual spots. Lesions that have spread are particularly prominent on the arm. One group of three (at A) shows central recession and dimpling. Another group lower down (at B) has gone farther in this development and presents—in miniature as regards both size and elevation—the morphological characteristics of circinate minor tuberculoid leprids. Histologically one of them (indicated) proved to be of that nature. On the other hand one of the upper, dimpled lesions (indicated) seemed quite definitely to be lepromatous, with bacilli correspondingly numerous. A third specimen from the flat, uniform, extended "papule" on the upper back (indicated) was intermediate in appearance, like the one from the buttock taken in 1936.

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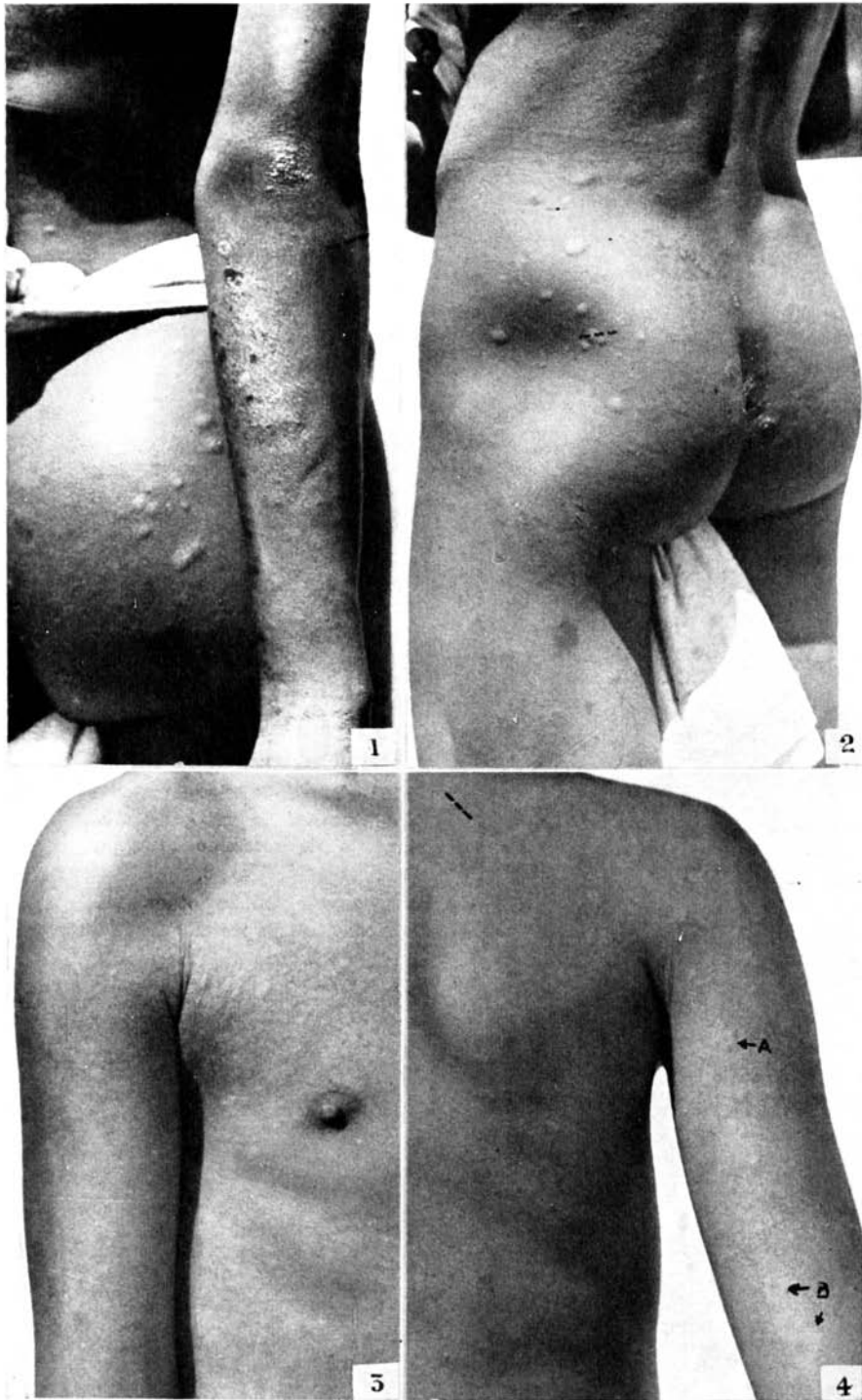


PLATE 18

PLATE 19

FIG. 5. Back of the same patient in September, 1938. Some recent papules are present, but the whole is studded with pale spots of receded ones and fainter residuae of others. Many spots, especially low on the body, being surrounded by zones of hyperpigmentation due to local injections resemble scabies scars. Two lesions were biopsied; histologically both are very undifferentiated, with surprisingly many bacilli.

FIG. 6. Face of same patient, October, 1939, when the condition was relatively quiescent, showing his evident good development and general condition. No trace of the lesion area on the left cheek is evident other than dark spots due to local injection. Ears now show no abnormality.

FIG. 7. Back of same patient, also 1939. No definitely elevated lesions present (scars of several biopsies evident). Zones of hyperpigmentation due to local treatment surrounding pale, residual spots resemble in appearance here small annular lesions.

FIG. 8. Front of body, same patient, showing little other than the keloidal scars low on the right chest ascribed to herpes zoster.

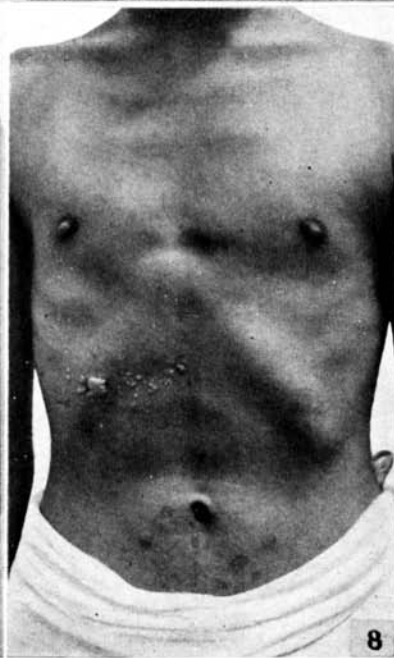


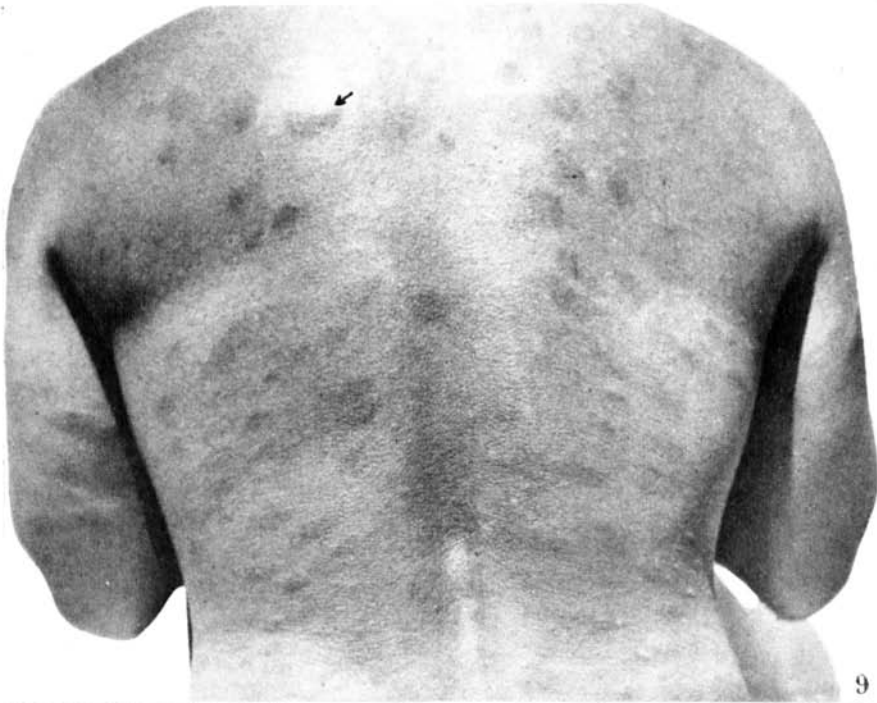
PLATE 19

PLATE 20

FIG. 9. Back of Case 2 as seen in 1936, showing the abundant, frequent recurring of small, more or less diffused papular lesions, some now receded and represented by small pale spots, others discolored and made apparently much larger by local injections. (Compare with Fig. 7, Case 1.) An untreated papule removed (site indicated) showed, like the leg lesion, slight tuberculoid changes but relatively numerous bacilli.

FIG. 10. Right leg of same patient, also 1936, two and one-half years after admission. On the posterior surface is a large hyperpigmented area that represents one of the lesions present in 1934. Externally the large, active, diffused area of more recent involvement, a biopsy specimen from which (site indicated) showed slight tuberculoid changes, with only a few bacilli present.

FIG. 11. Forearms and hands of the same patient, also 1938, showing the large, thickened elevated lesions high on the forearms and over the wrists. The diffused character of most of the peripheral edge of the wrist lesions is evident, and also the contrasting abrupt margination at one place in each of them against areas (marked X) said by the patient to have been the sites of previous lesions. The similarly abrupt termination of the infiltrated zone around the small, noninfiltrated areas in the peripherally diffused plaques high on the forearms, also said to represent previous lesions, is not as well shown.



9



10



11

PLATE 21

FIGS. 12 AND 13. Trunk of the same patient in October, 1939, some six weeks after the last reaction. Numerous in and around the scapular region, less so on the left chest, are slightly elevated, diffusely outlined lesions of various shapes, some round but many more elongate. Several of them appear to have undergone central resolution, but from the abrupt margination of the infiltration around the central areas, in contrast to the condition at the peripheries, it is believed that those areas are actually the sites of old, small lesions, the present ones thus having the essential features of the "relapse tuberculoid" type.

FIG. 14. Showing the new relapse lesions on the right arm of Case 3, in 1938. High on the forearm two prominent bands, the external one extending well above the cubital space, merge below in an area which is less infiltrated except in its lower part. On the upper arm is a roughly S-shaped lesion; the lower half has receded considerably while the narrow connecting band is more prominent than at first. Both lesions show diffuse margination in parts, but stop abruptly where they adjoin areas of previous lesions (best seen where marked, \times). This photograph, and those that follow, were taken some two months after we saw the patient. Scaling has occurred in places, most marked at the shoulder, and decided recession in other parts, including the one mentioned.

FIG. 15. Left back of same case, showing the extensive lesion in the scapular region, with an enclosed immune area (\times). Much recession has occurred except in the two isolated areas over the lower end of the scapular. Lower on the back, near the midline, is a small, prominent new lesion.



PLATE 21