

INTERNATIONAL JOURNAL OF LEPROSY

VOL. 6

APRIL-JUNE

No. 2

ACUTE ULCERATIVE OR SLOUGHING TUBERCULOID LEPROSY

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The condition of acute ulcerative tuberculoid leprosy here discussed was first noted by the writer in Sungei Buloh in 1932, at which time he was unaware of the unique character of this phase of the disease. Since then over twenty cases have been treated here, a sufficient number to enable one to become familiar with the essential clinical features and course of this process. The present description, in which a recent case is reviewed, is written partly to draw attention to the condition, because of its interest in itself and of the desirability of learning whether its occurrence is really as limited as it seems to be, and partly to record my experience of its treatment.

Acute ulcerative tuberculoid leprosy is of special interest for two reasons. One is that it appears to shed additional clinical light on the tuberculoid process of the disease. The other is its remarkable response to hydnocarpus treatment, which has what appears to be a truly specific effect upon it.

The process begins with the usual flare-up or "reaction" of acute tuberculoid leprosy, the lesions being multiple and consisting of raised inflamed plaques, and marginal zones around central areas of partially anesthetic skin (Figs. 1 and 2, and others). As in ordinary acute tuberculoid leprosy, the lesions often appear on the sites of old and apparently inactive simple leprides. The onset, though not as rapid as that of lepra fever ("lepra reaction" of cutaneous leprosy), may be and often is by no means slow, and

multiple angry looking lesions may appear where no special activity was observed forty-eight hours before. The lesions have a definite tendency to spread into the relatively immune areas of the body, which are normally free from cutaneous involvement (Fig. 16). There may be low fever and malaise, and unless suitable measures are taken there may be considerable mental depression.

The frank sloughing stage which is the subject of this note may develop in any of three ways: (a) After about a week a fine exfoliation is seen on the surfaces of the lesions; the appearance is as if cigarette ash had been dusted finely over them (Fig. 3). It should be noted that the process may stop at this scaly stage or at any further point short of complete sloughing. In progressive cases the exfoliation gradually becomes more gross until large tatters of dead epithelium hang from the lesion areas (Fig. 4), and under them can be seen the raw surfaces of the acute tuberculoid areas. Shallow ulcerations appear here and there, beginning usually at pressure points, and they gradually deepen and spread. (b) There may be little or no exfoliation. The lesions in these cases become more and more inflamed, tense and shiny, until the thinned-out epithelium gives way and ulceration proceeds. (c) The ulcerative stage may be preceded by the appearance of tiny engorged venules on the lesion surfaces. In two cases I have noted punctate hemorrhages, and in one case larger ones, as in scurvy; it may be added that the condition is unaffected by vitamin C. In one case I have seen autogenous, nonpurulent blisters.

Rapidly developing exfoliation is, in our experience here, the commonest mode of onset. Whatever the premonitory signs, however, once the ulceration starts it spreads and deepens until the whole of the acute tuberculoid tissue sloughs away. Where the lesion was marginate this process leaves a broad band of ulceration around the central anesthetic area, and where there was no flat central anesthetic area the lesion becomes a massive ulcer (see Figs. 14 and 15). Under ordinary hospital conditions there is no pus; I have had no experience with untreated cases. The edges are well defined, the base appears rather darker than ordinary granulation tissue, is friable, bleeds easily and has a coarse, lumpy appearance. The developed ulcerated area is more than a half centimeter in depth. This means that eyelids and ears are destroyed when they are affected (see Plate 15). The central anesthetic areas may become gangrenous, but as a rule

there is sufficient blood supply to maintain their vitality. The ulceration is confined strictly to the active tuberculoid tissue.

The patient loses weight rapidly and looks—and is—extremely ill. The task of dressing considerable areas over the arms, legs, face and trunk is a very awkward one, and the patient experiences difficulty in finding a posture of any comfort. Small children suffering from this condition tend to cry continuously, and even in adults the sight of the large ulcerated areas causes a good deal of mental distress. In the earlier cases that were under my treatment the dressings had to be renewed day after day for months on end, with little sign of recovery and with increasing cachexia and hopelessness on the part of the patient.

Recovery without the treatment to be described is extremely slow. The stage of ulceration may persist from three to seven months (as in the patient shown in Figs. 12 to 15), to be followed by a protracted convalescence. Considerable distortion of the face may result, and perforation and erosion of the ears, the appearance being like that of severe scarring from burns. On the trunk can be seen broad circular bands of scar tissue surrounding the central anesthetic areas.

I have not seen a fatal case, but I have little doubt that secondary sepsis would occur if extreme care were not taken, because the raw ulcerating areas may be very large indeed. A point of considerable interest is that even at the worst stages the erythrocyte sedimentation rate is unexpectedly low.

The ultimate prognosis is bad. Most of the cases that I have seen degenerate in a year or two to the cutaneous stage, with rapidly spreading lesions.¹ One case under observation just now, however, after undergoing three years ago the worst attack of acute ulcerative tuberculoid I have ever seen, has now developed fresh acute tuberculoid lesions. Some cases, however, apparently remain static, showing only the residual scarring without undergoing cutaneous or other change.

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

¹Some of the cases of which photographs are used to illustrate this article were examined specially with Wade in February, 1937, and were found histologically to be undergoing or to have undergone lepromatous change, though not sufficiently to be clinically recognizable with certainty at the time.

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 tuberculoid 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.

The treatment of this condition is important. The first cases that I had to handle were given a rich, high-vitamin diet to combat the cachexia, and antiseptic dressings and later stimulating ointments of various kinds were employed in dealing with the actual ulcerations. For that purpose a large number of preparations was used, but the response in every case was extremely disappointing. Little or no benefit was derived, and in some cases the ulceration gradually increased. The first case that I saw here several years ago remained openly ulcerative for over seven months, leaving scarring deformities causing grotesque distortion of the face (Figs. 12 to 15). Until a year or so ago I had found no treatment that influenced the course of this form of leprosy.

The worst possible treatment is to give fluorescein or phthalic acid. This will inevitably increase the ulceration, and in cases on the verge of ulceration will precipitate that condition. All of the phthalic acid derivatives are definitely contraindicated. Calcium gluconate may be given in appropriate doses intravenously; it does no harm and may help a little.

The only effective treatment is hydnocarpus oil, given in large doses inside and out. Give subcutaneously 1 cc. of hydnocarpus oil for every ten pounds of body weight, twice a week, and if necessary increase the dose up to 1 cc. for every five pounds. Along with this apply daily, and lightly massage in, hydnocarpus ointment in liberal quantities over the ulcerated areas. Leave a thick coating of it on the ulcer bed, and also impregnate the inner dressings with it. The preparation used here is:

Hydnocarpus oil 3 drachms	(10.00 cc.)
Eucalyptus oil 1 drachm.....	(3.25 cc.)
Zinc oxide 50 grains.....	(3.33 gm.)
Dettol, pure 1/2 drachm.....	(2.00 cc.)
Vaseline, yellow, ad 1 ounce.....	(28.00 gm.)

The response of acute ulcerative tuberculoid leprosy to this treatment is, relatively speaking, dramatic; it is the most convincing demonstration I have seen of the specific efficacy of hydnocarpus oil. The cachexia ceases and the ulcerations heal, sometimes with surprising rapidity.

The description of this condition that I have given is of the virulent form as it is seen in the wards of Sungei Buloh. Less severe and more localized forms occur, but the process described is more or less typical. I have seen it only in our Chinese patients, never in the Malays or Indians. It is not common; out of about twelve hundred Chinese three or four cases occur annually. Wade, who has had exceptional opportunities to observe leprosy in various parts of the world, has informed me that he has not seen anything like it anywhere else—and acute ulcerative tuberculoid leprosy in its typical form as we see it would not be readily missed.

REPORT OF CASE

The following case history illustrates a number of the salient features of the condition:

Lim Kan, a Chinese hawker, aged 65 years, was admitted to the hospital on March 30, 1937, complaining of low fever of a week's duration. Examination revealed raised acute tuberculoid lesions all over the face, trunk and arms. There were residual evidences of an old lobar pneumonia, but no other abnormality. Weight 134 lbs. Laboratory findings: Blood negative for Malaria (three examinations). Hemoglobin 60%. Stools negative (three examinations). Urine: specific gravity 1020; a few epithelial cells and lime crystals. Wasserman and Kahn tests negative. Sedimentation index 16. Smears from the lesions negative for leprosy bacilli.

On the second day after admission the lesions showed slight epithelial scaling. The exfoliation increased rapidly. After a week the patient complained of persistent pain in the lesions. On the eighth day a shallow pressure-ulcer appeared on the left elbow, and there were renewed complaints of pain or itching over the lesions. After an injection of 10 cc. of hydnocarpus oil and an alkaline bath the patient felt greatly relieved. By the eleventh day the exfoliation had increased considerably, the lesions still remaining angry and tense. On the sixteenth day isolated shallow ulcers began to appear (Fig. 5); these were dressed with hydnocarpus ointment. Sedimentation index 15.5, weight 130 lbs. Smears now found positive. On the eighteenth day 20 cc. of hydnocarpus oil was injected subcutaneously. By the twenty-sixth day the ulcerations had become extensive over the back, arms and legs, the nonulcerated areas appearing dark red, dry and scaly (Fig. 17).

After a month in the hospital most of the acute tuberculoid areas had ulcerated. A biopsy specimen of the ulcerating tuberculoid tissue was taken for histological examination. At the same time 10 cc. of 10 percent cal-

cium gluconate was given intravenously. For the next five days the ulcerated areas exuded blood-stained serum. They were still dressed daily with hydnocarpus ointment. Sedimentation index now 28, weight 120 lbs. On the thirty-third day the sedimentation index was 30 and weight 114 lbs, a loss of 20 lbs. Smears show considerable numbers of irregular bacilli and acid-fast debris.

By the fortieth day signs of healing were evident, and the ulcerative areas had ceased to extend. The few areas of acute tuberculoid tissue still remaining continued to exfoliate profusely. During the next ten days the ulcerated lesions continued to granulate satisfactorily and clearly, and the nonulcerative areas steadily subsided. On the fiftieth day the sedimentation index was 32; the weight was only 100 lbs, a loss of 34 lbs. After that time healing accelerated rapidly.

I have cited this case as typical of the condition under discussion, and a typical example of rapid healing with hydnocarpus oil injections and inunctions. Between the thirtieth and sixtieth days a total of 120 cc. of hydnocarpus oil was injected subcutaneously, in doses of 20 cc. twice a week. To this was added daily inunctions of hydnocarpus ointment over the ulcerated areas. It was during this period of "heroic" treatment that the spread of ulceration and the cachectic process were checked and rapid healing took place. Similar cases treated with any other commonly available method have always continued to ulcerate for months, and have ended up with considerable deformity from deep scarring.

Sections of the biopsy specimen taken from this patient were sent to Dr. H. W. Wade, at Culion, who reported in part as follows:

The lesion is a massive granuloma, of the general type common in reaction tuberculoid lesions, composed of great numbers of closely-packed individual foci, most of which are small though in the deeper portions some are of relatively large size. The epidermis is straightened but not entirely flattened; it is unbroken and nowhere necrotic, though in places it is decidedly thinned and sometimes edematous. The granuloma makes contact with it in only a few places; elsewhere the subepidermal zone shows a scattered cellular infiltration, with not a few polymorphonuclears. The vascular spaces here are much dilated and conspicuous. There is some hemorrhagic extravasation in places; this may have been caused by the surgical manipulation, but it is of interest that some of the veins within the granuloma show edema and degeneration.

The granuloma mass as a whole is made up of focal epithelioid collections but it is diffuse in some places. The foci are as a rule separated only by remnants of the original fibrous tissue; these strands are usually edematous and vascular dilatation is marked throughout. Though the conspicuous element of the granuloma is epithelioid, with many giant cells of various sizes, there are also, as usual, a great many less differentiated cells, rounded, irregular

and elongate. In many places the granuloma cells are in bad condition, their cytoplasm diffused and granular, and often of hydropic appearance. Very few polymorphonuclears are found in the lesion itself, and no lymphoid-cell accumulation. No cells of or suggesting the "foamy" form can be found, but an occasional isolated globus-containing cell is encountered, or a small group of them.

In summary, the lesion is a massive tuberculoid granuloma, obviously a marked reaction condition, with more degenerative tendency than is seen in the ordinary lesions of the kind.

SUMMARY

The process here described as acute ulcerative tuberculoid leprosy appears at present to be unknown outside Malaya, and so far has been found here only in Chinese patients. The condition is essentially a rapid flare-up of acute tuberculoid leprosy, going on to exfoliation (occasionally with punctate hemorrhages), and sloughing out of the tuberculoid tissue. It is accompanied by low fever and rapid loss of weight. Except with specific treatment its progress is intractable and slow, and it leaves considerable deformity and deep scarring.

In my experience the process can be controlled only by very large doses of hydnocarpus oil given subcutaneously, accompanied by inunctions of hydnocarpus ointment to the ulcerated areas. To one who has previously dealt with the condition by other methods, the treatment described is a very convincing, and indeed striking, vindication of the use of hydnocarpus derivatives.



DESCRIPTION OF PLATES

PLATE 13

FIGS. 1 and 2. Fairly typical "acute tuberculoid reaction." (Yeong Ah Chong, aged 25, No. 4766 (SB-21). Great numbers of tuberculoid lesions, mostly recent and none very large, involving extensively the face, body and extremities, and even the axilla and inguinal regions (see reproduction of color photograph Fig. 16). This case might very well have gone on to the ulcerative stage, but stopped short of that; the most acute stage is past, with only slight erosion in places. Scaling slight except over the relatively large annular lesions above knees. Five out of six smears positive, one (from large lesion on chest) 2+, the others 1+. Histologically typical marked ("major" grade) tuberculoid. (H.W.W.)

FIG. 3. Generalized tuberculoid lesions in the scaling stage, which did not advance to ulceration. The patient (Loke Weng, No. 2591, SB-3) was hospitalized for a month in 1935 and three times in 1936 for "acute tuberculoid reaction"; photograph taken on one of these occasions. (Cf. Fig. 11.)

FIG. 4. Acute exfoliative tuberculoid leprosy in the pre-ulcerative stage. The process was aborted by intensive hydnocarpus treatment.



PLATE 13

PLATE 14

FIG. 5. The case of acute ulcerative tuberculoid leprosy described in the report. Photograph taken in the exfoliative stage, with ulceration commencing at the points marked X. A color photograph taken when the ulceration was more advanced is reproduced in Fig. 17.

FIGS. 6-8. Late results in the case shown in Fig. 5, after the hydnocarpus treatment described. Note the minor degree of scarring as compared with that in cases treated by other methods, shown in Plate 15.

FIG. 9. Same patient as in Fig. 3, healed after hydnocarpus treatment with relatively little obvious scarring, though when examined specially (February, 1937) the face was somewhat irregular from deep fibrosis and some scarring was present in the zones left by the reaction lesions. These zones, of the common marginal type, rather narrow, and of a dull purplish color, marked the body and extremities almost universally and, because of their number and extensive fusion, presented a most confused appearance. (See also color photograph, Plate 16, fig. 18.) Earlobes thickened, suggesting lepromatous change, but one proved bacteriologically negative and the other only 1+. Four other smears 1+. In biopsy specimens keloid-like scarring was found, and a few foci of foamy cells—inactive lepromatous change. (H. W. W.)



PLATE 14

PLATE 15

FIGS. 10 and 11. Showing scarring and deformity after subsidence of the acute ulcerative tuberculoid condition, in a patient treated by other methods than the hydnocarpus oil treatment described, before discovery of the efficacy of the latter. In this case many of the scars become conspicuously keloidal.

FIGS. 12 and 13. Acute ulcerative tuberculoid leprosy of marked severity, incompletely recovered, scaling still present. (Patient No. 2683, SB-4.) Old case, treated by other than the hydnocarpus method. Extensive destruction and mutilation, especially of eyelids and ears, after seven months of ulceration. (Cf. Figs. 9 and 10.) In this instance the cartilage of the ear is perforated, which is unusual; more or less extensive destruction of the marginal soft tissues is not uncommon.

FIGS. 14 and 15. The same patient after healing. Note the extensive scars on right chest and arms in Fig. 14; in this case the entire lesion area on the chest, including the central anesthetic portion, sloughed out. On the other hand, only the broad active margin of the lesion of the back ulcerated away, leaving a broad band of scar tissue (Fig. 15). When specially examined (February, 1937), all of five smears were positive, three of them 2+ and one 3+. Histologically two specimens, from chest and abdomen, were found to be lepromatous, of the intermediate (elongate-cell) type, with numerous bacilli. (H. W. W.)



PLATE 15

PLATE 16

(Reproduction of Dufay color films.)

FIG. 16. Right axilla, chest and face of patient shown in Figs. 1 and 2. Acute tuberculoid reaction, before the ulcerative stage.

FIG. 17. Ulcerative tuberculoid leprosy, patient described in the report. (Cf. Figs. 5-8.) Condition not as marked as in many cases seen in the past; hydnicarpus treatment was started promptly.

FIG. 18. Back of the same patient as in Fig. 9, showing (in the parts that were not over-exposed) the color of the healed zones.

FIG. 19. Back of the same patient as in Figs. 12 to 15.



PLATE 16