Volume 39, Number 2
Printed in the U.S.A.

Pattern of Leprosy Reactions in Uganda

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Acute reactional episodes in a great variety of forms are part of the clinical picture of leprosy. Some of the milder allergic reactions have been described as favorable, although a nuisance factor, but they are painful and distressing to the patient. In this paper I would like to present the most common as well as rare forms of reaction seen in our patients in Uganda, and outline their treatment.

Predominant is the low resistance tuberculoid type, with multiple lesions, negative skin smears and moderately positive lepromin reactions. The majority of patients with severely mutilated limbs, belong to the tuberculoid-borderline type.

Clinically and histologically the polar types of tuberculoid and lepromatous leprosy, are comparatively rare. In high resistance tuberculoid leprosy strongly positive to lepromin, reactions may be severe, but restricted to one or few of the existing lesions, which become erythematous and infiltrated, and desquamate (Fig. 1). Borders, wholly raised or papular, are always well defined. In highly infiltrated lesions a hypopigmented vague "halo" may extend outside the darker border. Ulcerating skin lesions are more common in the tuberculoid-borderline than in the tuberculoid high resistance type. Severe face edema of angioneurotic type was seen in an Indian patient with a small tuberculoid lesion in the zygomatic region. In the tuberculoid low resistance type, the severity of reaction varies according to the position in the leprosy spectrum; many skin lesions and many nerves are involved.

Local reaction is usually milder, but mutilation more extensive because of multiple nerve involvement and anesthesia (Fig. 2). The worst cases are those with lesions involving the central part of the face. Swelling of the upper lip (Fig. 3), nose and lower eyelids is longlasting and does not respond readily to the usual treatment, including steroids. When swelling subsides, burning and tingling sensations with trigeminal causalgia are very distressing. Congestion of the nasal mucosa often causes difficulty in breathing. Skin smears in our cases of low resistant tuberculoid leprosy, even during reactions, are always negative.

Tuberculoid-borderline leprosy has multiple lesions, mostly of tuberculoid appearance, with some lepromatous infiltrations. Commonly the first lepromatous-like infiltration (but fairly well defined) is on the edge of one or both nostrils and on one ear. During reaction the whole ear (usually one) may become swollen.

Skin smears from the nose and ear infiltrations are positive during reaction, with low BI and MI and usually no globi present. In cases with initial lepromatous-like infiltrations, smears from the rest of the tuberculoid-like lesions, are negative. The

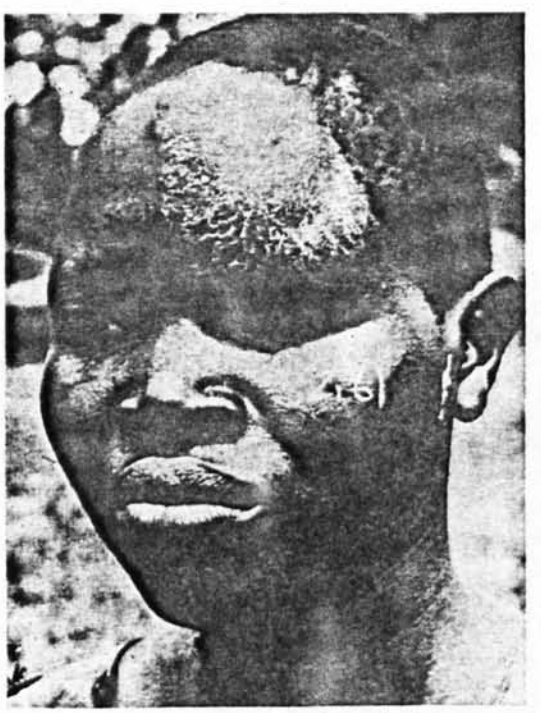

FIG. 1. High-resistance tuberculoid lesion in reaction.

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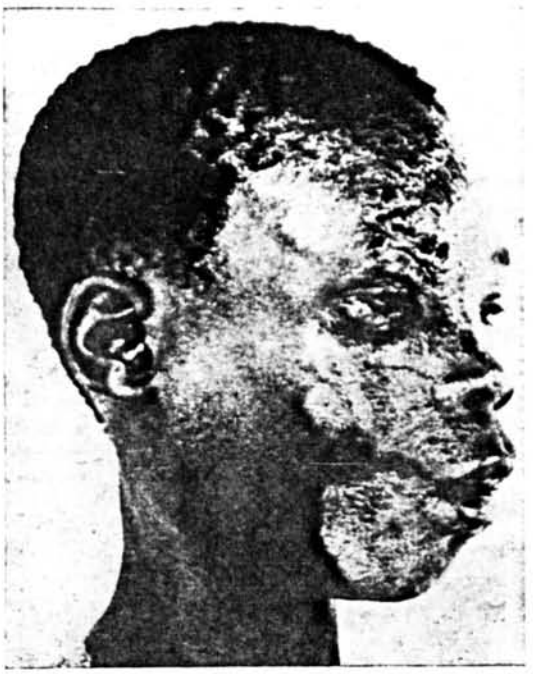

FIG. 2. Tuberculoid low-resistance with central face lesion and involvement of both eyelids.

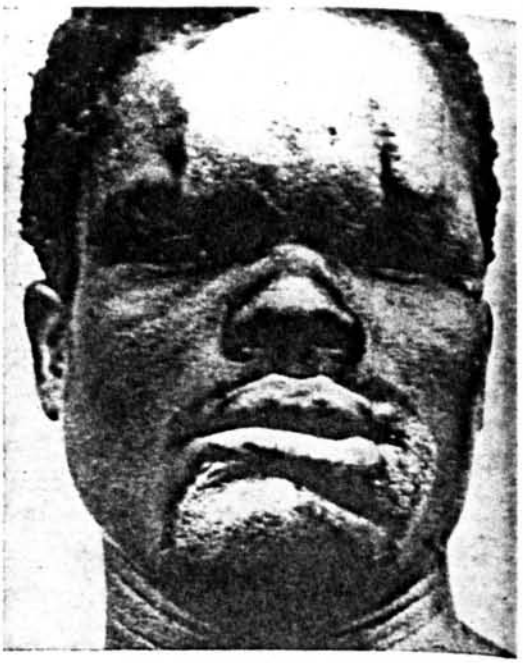

FIG. 3. Tuberculoid lesion with beginning of facial paralysis, which recovered.

lepromin test is weakly positive.

Reactions in tuberculoid-borderline leprosy, as in other borderline forms, are very severe, but local. Skin lesions may ulcerate (Fig. 4), healing subsequently with contracting scars. Hands and feet become swollen and painful (stasis hands) (Fig. 5), and extensive and severe damage leads to sudden paralysis, often symmetrical, of upper and lower limbs. In one case (Fig. 5a) fibrosis of the thumb pad and web developed after prolonged swelling of a tuberculoid lesion on the hand. Tuberculoid-borderline leprosy is the most multilating form of leprosy in Uganda.

Tuberculoid-borderline leprosy usually responds to treatment with corticosteroids, but withdrawal of prednisone may be stormy and prolonged. Ulcerated tuberculoid skin lesions heal best under topical cortisone application. Peripheral nerve involvement is either in the trunk at the site of predilection or in the cutaneous ramifications leading to the lesion (Figs. 6, 8, 10 and 11). Never damage, most extensive in all forms of borderline leprosy (BT, BB,

FIG. 4. Tuberculoid-borderline ulcerating lesion.

FIG. 5. Tuberculoid-borderline lesions with very swollen, painful hands.

FIG. 5a. Stasis hand in tuberculoid-borderline leprosy during reaction with fibrotic thumb.

BL), follows the usual pattern. Most common is high ulnar damage, with or without involvement of the low median, peroneal, tibialis posterior and upper branch of the facialis nerve. Comparatively rare is high radial damage with dropped wrist and lower facialis involvement with drooped mouth corner.

Motor and sensory loss is not always proportional to the enlargement and palpable fibrosis of the peripheral nerve trunk. Acute enlargement of cutaneous branches of the ulnar and radial nerves at the wrist, of the peroneal superficialis nerve of the foot, (Fig. 9), and of the auricular nerve (Fig. 7) are most common after reactions or at the beginning of DDS treatment, even

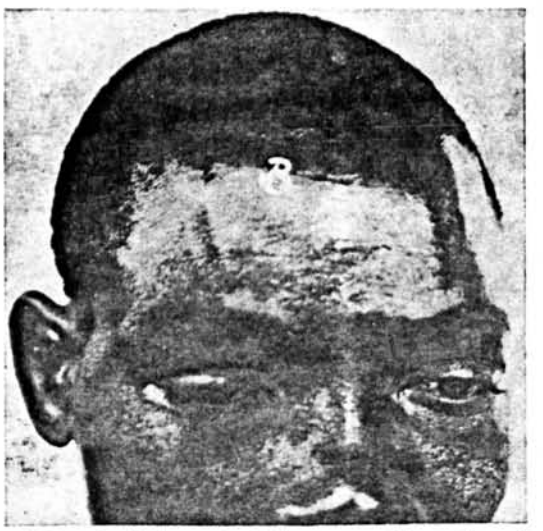

FIG. 6. Tuberculoid leprosy with enlarged frontal nerves.

FIG. 7. Tuberculoid leprosy. Auricular nerve abscess with equally enlarged facialis. Facial paresis.

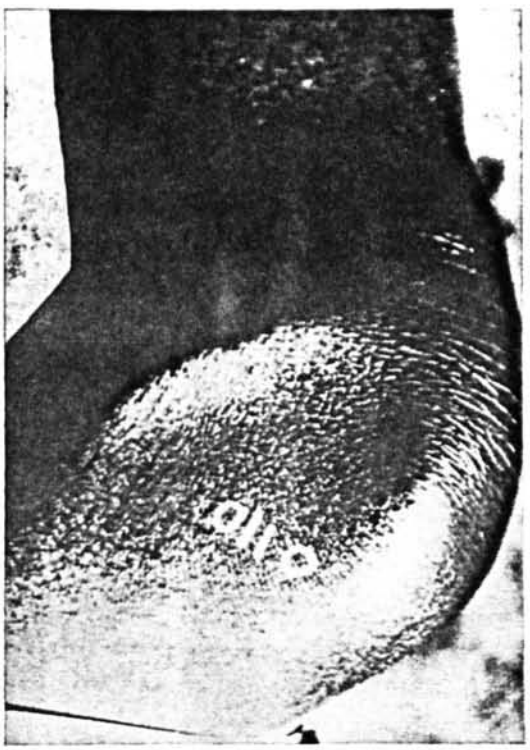

FIG. 8. Tuberculoid leprosy. Enlarged cutaneous branch leading to the lesion.

FIG. 9. Enlarged fibrotic peroneal nerve in tuberculoid leprosy.

when the main nerve trunks are little involved. The patient may or may not complain of pain, and with no other reaction symptoms only frequent routine examination will reveal the presence of these enlarged nerves.

Neuritis of the tibialis posterior causes severe pain and inability to walk. In the hands, median nerve neuritis is more painful than ulnar, while radial and peroneal nerve damage may be practically painless.

Nerve abscesses, also common in chil-

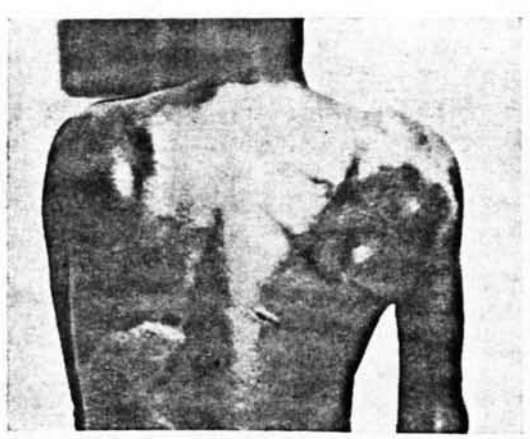

FIG. 10. Tuberculoid lesions with enlarged nerves on the trunk. Very rare.

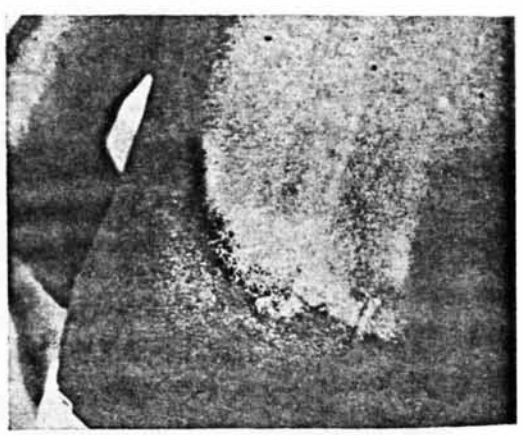

FIG. 11. Single tuberculoid lesion on the back, with two enlarged nerves. Great diagnostic value.

FIG. 12. Multiple nerve abscesses along an involved cutaneous nerve in tuberculoid leprosy.

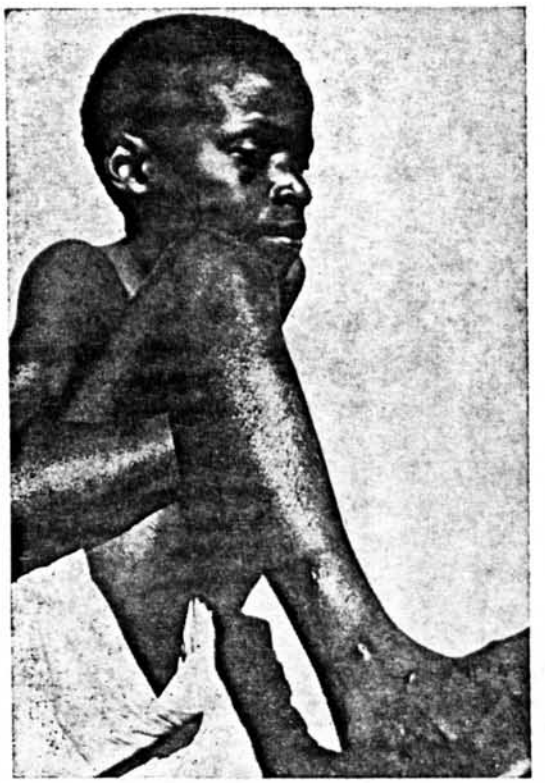

FIG. 13. Multiple peroneal abscesses after reaction in boy with *single* tuberculoid lesion on the face.

dren, appear several weeks after reaction and are often multiple along the involved nerve (Fig. 12). In one case five nerve abscesses appeared in the superficial peroneal nerve in a boy with a single tuberculoid lesion on the face (Fig. 13). Epitrochlear lymph glands may be enlarged, suppurating, and fused with ulnar nerve abscesses.

In all forms of borderline leprosy reactions are either upgrading or downgrading. Upgrading or reversal are healing reactions, with increase in lymphocyte-mediated immunity, where histologically not only lymphocytes but also epithelioid and giant cells appear and the MI remains low or negative. In downgrading reactions (Fig. 14), in which, because of lowered resistance, a sudden increase in lesions, as well as in bacillary and morphological indices, takes place, lymphocytic and epithelioid focal infiltration is replaced by histiocytic dispersed or massive granuloma. All borderline cases need careful treatment of both reactional state and leprosy, especially when reaction is downgrading.

In borderline lepromatous leprosy the combination of massive infection by *M. leprae* with circulating antibodies and a certain amount of cell-mediated immunity with local allergy, is responsible for prolonged general lepra reactions of ENL type, with severe nerve damage, as in tuberculoid leprosy. A reactional state of many months, even one to three years' duration, is more damaging in borderline than in polar lepromatous leprosy.

Lepromatous leprosy reactions are of two different types: (1) acute leprosy exacerbation, and (2) erythema nodosum leprosum, with the whole spectrum of different clinical pictures.

Acute leprosy exacerbation in patients (Fig. 18) who did not take treatment or became resistant to it, may be very similar to

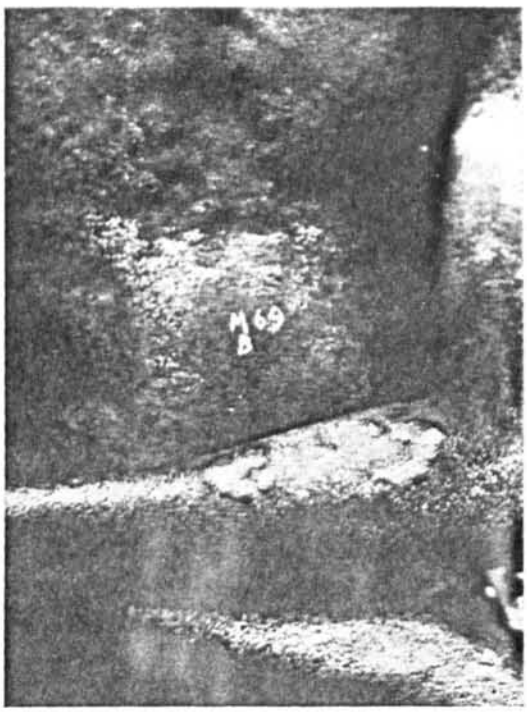

FIG. 14. Lepromatous infiltration that developed in a tuberculoid-borderline patient during downgrading reaction. *M. leprae* present only in the forearm infiltration.

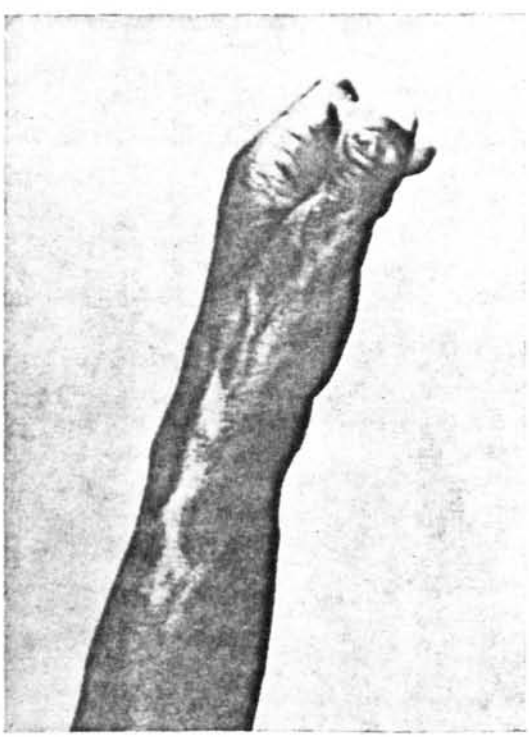

FIG. 15. Hypopigmentation after hyaladecortisone injections along the enlarged nerve.

FIG. 16. The most common picture of moderate ENL.

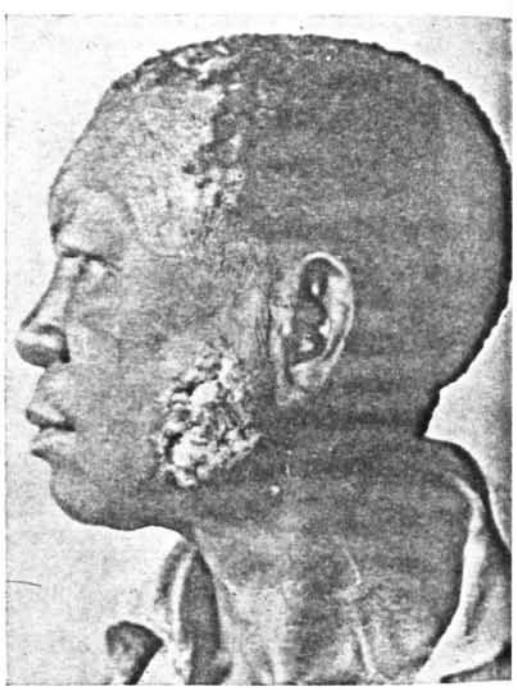

FIG. 17. The same patient as in FIG. 16 developed necrotizing blisters during his last few severe reactions.

FIG. 18. Acute leprosy exacerbation in irregularly treated patient.

FIG. 19. Pustular eruption during reaction. In smear from the pus only *M. leprae* were present.

ENL, with high fever, swellings and neuritis, but new lesions appear and multiplying *M. leprae* give rise to increase in the BI as well as the MI. If the patient was well on the way to recovery before the exacerbation occurred, the clinical and histologic picture may be that of reversal reaction, often with severe nerve involvement, but with bacteriologic and morphologic indices increased. In two recent cases the only clinical symptom of exacerbation was the sudden appearance of an episcleral lepromatous nodule. Prompt specific treatment, if necessary with a different drug, combined with reaction treatment, brings the situation under control.

Erythema nodosum leprosum, an allergic phenomenon, is an autoimmune mechanism, with which the lepromatous patient, full of circulating antibodies, responds to liberated bacillary metabolities. It can be the result of successful treatment, usually after one to two years, when the MI drops considerably. Severe forms of reaction are usually triggered by some additional stress factor, physical or mental, which upsets the shaky state of Selye's adaptation stage and leads to an exhaustion syndrome. The spectrum of ENL ranges from mild to very severe and crippling, from short (two to five days) duration, to a chronic reactional state, in which a patient may become bedridden for one to two years, in spite of intensive treatment, including heavy doses of steroids. In mild form it consists of transitory cutaneous and subcutaneous tender erythematous nodules and vague joint or muscular pains (Fig. 19).

Moderate and severe reactions are always accompanied by high fever. Painful subcutaneous nodules and infiltrations, and swellings of ears, hands and feet, are the most common (Fig. 20). Purple plaques of erythema multiforme reaction, also very tender, leave deeply hyperpigmented patches, similar to those seen in DDS sensitization.

In the pemphigoid form (one patient seen) small, dark-red patches occurred, forming, within a few hours, superficial

FIG. 20. Broken lepromatous nodules during reaction.

blisters, which peeled off when touched, exposing heavily bleeding bases. This stage lasted several months and was extremely painful (Fig. 21).

Pustular eruptions, in which pus contains only leprosy bacilli, are now more frequently encountered (Fig. 19). They usually dry up or peel off without skin damage, but in two cases the eruptions led to superficial necrosis with scar formation on the face (Fig. 17).

Erythema induratum on the dorsum of the hands, with danger of intrinsic-plus deformity, is one of the more distressing forms. It may respond well to local infiltration of Procaine hyalase-cortisone. Joint pain is common; acute exudative arthritis, mostly involving one of the knee joints, might be one of the first symptoms of reaction. Swelling of ankle joints is often a sequel to neuritis of the tibialis posterior. In prolonged swelling of the hands in both tuberculoid borderline and lepromatous cases, coexisting ganglion on the dorsum of the wrist can be seen frequently.

Episcleritis, more often seen than *iritis*, is also one of the first symptoms of lepra reaction. Acute iridocyclitis, comparatively rare, may be complicated by secondary glaucoma.

Lepromatous osteo-periostitis of the tibia is rare; one such case, with frequent prolonged reactions refractory to different treatment schemes, including steroids, thalidomide and B.663, twice developed transitory diabetes. It lasted each time several months, did not respond to high doses of insulin (120 units daily) and each time disappeared suddenly for many months, until the next severe and prolonged reaction. At least the first of these diabetic episodes was not connected with prednisone treatment. The second disappeared, when the patient improved greatly, but while still on a sustenance dose of prednisone (1.5 mgm./day).

Cases of acute laryngeal edema, fortunately not very common, respond to prednisone or tracheostomy.

Acute, very painful neuritis, mostly ulnar, was seen in many cases, usually of many years duration, where the nerve was much enlarged and fibrotic. It seldom responded to local or systemic cortisone; only operation brought permanent relief.

One recent case of lepromatous leprosy after a year and a half of treatment and

FIG. 21. Unusual case of reactional state with pemphigoid blisters, which peeled off, leaving bleeding areas.

severe reaction, developed a large abscess in the ulnar nerve at the elbow, and three smaller ones in peripheral branches of the radial and ulnar nerves on the hand. They healed after operative evacuation.

Diagnostic difficulties may arise during reactions in unusual cases. One of our lepromatous patients, who had transitory lymphadenitis during frequent reactions, suddenly developed a pack of submaxillary glands, which proved to be of tuberculous origin. Another lepromatous-borderline patient, brought in with severe and prolonged reaction with subcutaneous nodules, had some rather unusual looking ones on the feet. Biopsy confirmed suspected Kaposi sarcoma nodules.

A very unusual case of reaction was that of a lepromatous patient, brought to us in reactional state and general cachexia. Repeatedly he developed "cold abscesses" filled with fluid pus. They were very painful but not hot, located in the axillae, groins, abdominal surface, and even forehead. A smear from punctured pus (usually 5-15 ml. per abscess) revealed the presence of multiple globi of leprosy bacilli. Culture on media and inoculation of animals for tuberculosis and other organisms gave negative results (Markarere University). During later reactions the patient had extensive ulcerations on the legs and attacks of jaundice (he was a very heavy drinker). After a year and a half of stormy reactions he is now well, fully working, and taking treatment as an outpatient.

FIG. 22. Severe reaction with hemorrhagic blisters and no necrosis. Last one before steady improvement.

FIG. 23. Exfoliative dermatitis after abuse of DDS.

Each patient has his own, individual pattern of reaction, which starts with the same symptoms of conjunctivitis, arthritis, neuritis or erythematous eruption. It can change during the course of the disease. The last reactions before recovery are often the most severe ones (Fig. 22).

Common causes of severe reactions include the following:

Overdose of DDS, usually the first attempt at self treatment, with 400-600 mgm/day causes severe *exfoliative* dermatitis, neuritis or an acute mental state (Fig. 23). It is extremely difficult to desensitize a patient after exfoliative dermatitis due to abuse of DDS.

Reaction after *small-pox vaccination* in lepromatous cases is usually severe, but short-lasting except when the patient is already in reactional state when vaccinated. Fragmented and solid bacilli appeared during such reaction in one young patient after many months of negative smears. Reactions after *childbirth* were most severe in borderline and borderline-tuberculoid types of leprosy.

Intercurrent infections, severe anemia, and mental and physical stress, are common additional factors, contributing to the severity and frequency of reactions, but heavy habitual drinking is one of the worst, as it tends to change frequent moderate lepromatous reactions into a chronic reactional state.

Treatment of reactions should be individual rather than schematic. In mild and

moderate cases we give antipyretics, antihistamines, calcium and antimalarials. Antimony injections are given only in moderate and severe lepromatous reactions. Where routine treatment fails, injections of ACTH, intravenously or intramuscularly are given. Systemic corticosteroids, which are fairly safe in tuberculoid reactions, are given in bacilliferous cases with greatest caution and only in the most severe cases. The usual indications are acute severe neuritis, all cases of recent paralysis, iridocyclitis, orchitis, edema of the larynx, and severe reactional state. The necessary sustenance dose in chronic reactional state in some patients was as low as 1 mgm. or 0.75 mgm. of prednisone daily.

B.663 (Lampren) in doses up to 400 mgm./day may or may not check severe reaction, but it keeps the patient on very good specific treatment during the critical stage. Thalidomide is very good but unobtainable in East Africa. Local treatment of involved organs included injection of oily vitamin E in tuberculoid cases, wax compresses and perineural (not intraneural) injections of Procaine-hyalase-cortisone (Fig. 15), subconjunctival injections of corticosteroids in iritis, and opening of nueral abscesses.

Neurolysis (perineurolysis, epineurolysis and fascicular neurolysis) with or without transposition of the nerve, brought to all 30 cases relief from severe pain. Sensory and motor changes improved in the majority of operated patients and remained stationary in the rest, except for one who became slightly worse. A patient with peroneal paralysis, which followed popliteal nerve operation, recovered completely within six months.

Extensive physiotherapy is necessary to avoid mutilation, especially in erythema induratum and stasis hands, and in bedridden patients in severe reactional state. Weakness of extensors of the feet and hands requires temporary splinting.

Throughout the years we have had some unusual, interesting cases of reaction, which cannot be fitted in any of the common patterns.

Although we have in steroids, thalidomide (not available in Uganda), and Lampren powerful weapons to combat reactions and avoid mutilations, there are still patients in whom, in spite of early treatment with all available drugs, we are not able to prevent permanent nerve damage.

SUMMARY

Acute reactional episodes are part of the clinical picture of leprosy. This paper presents a clinical picture of common as well as rare forms of reactions seen in leprosy patients in Uganda.

Predominant is the low-resistant tuberculoid and tuberculoid-borderline type of leprosy. In the lepromatous group the polar type of typical LL is comparatively rare; most lepromatous cases fit clinically and histologically into the L or LB type.

In tuberculoid leprosy, severe ulceration of skin lesions is not common. In central face lesions prolonged swelling of the upper lip and eyelids is usually followed by distressing lacrimation, paresthesia and trigeminal causalgia.

Neuritis: most common is high ulnar, low median and popliteal nerve damage. Motor and sensory loss is not always proportional to the enlargement and palpable fibrosis of the nerve trunk. Enlargement and fibrosis of cutaneous branches of the ulnar, radial, superficial peroneal and auricular nerves are common after reactions, even when the main nerve trunks are little involved.

Nerve abscesses, not very common, appear several weeks after reaction, and are often multiple along the involved nerve. In ulnar nerve abscess local lymph glands may be adherent and suppurating.

Multiple paresis after reaction is found mostly in the tuberculoid-borderline type, as well as prolonged swelling of the hands and feet with subsequent muscular weakness.

Most common in lepromatous leprosy is general reaction with high fever, multiple subcutaneous ENL, swellings on the face and ear lobes, edema of the feet and hands and pain in the joints. Less common are acute gonitis, usually unilateral, orchitis, episcleritis going on to iritis, and erythema induratum of the hands. Cases of pustular eruption and necrotizing blisters are now

more frequently encountered. Acute neuritis (usually ulnar) is seen late in lepromatous cases.

Very rare are cases of acute edema of the throat, and osteoperiostitis of the tibia. We had one case of multiple "lepromatous cold abscesses" (in fluid pus only leprosy bacilli were present) and jaundice.

The pattern of reaction is individual and may change during the disease. All cases of exfoliative dermatitis that were seen were due to abuse of DDS. Common factors contributing to reactions, and outlines of treatment, are described.