ON "HYPODERMITIS NODULARIS LEPROMATOSA RECIDIVANS" (ERYTHEMA NODOSUM LEPROTICUM) (*)

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The two following cases, recently under observation in our Service, are good examples of what is called "leprotic reaction" of the erythema nodosum type "erythema nqdosum leproticum", which we in 1956, proposed(15) to call *recurrent lepromatous nodular hypodermitis (panniculitis).* Both cases are in the initial *clinical* stage of leprosy: Case I is certainly in the incipient manifestations of initial leprosy, Hl, transient to the invading stage, H2, of our evolutionary scheme of 1953 (16). Case II is in a more advanced stage, probably already in its second generalized manifestation of the disease.

OBSERVATION I

N.° 29.061 (20-3-1958), a man, 27 years old, white, single, a medical student, born and residing in Rio de Janeiro.

His father died of tuberculosis of the lungs In 1951, his mother is alive and well, has a brother 16 years old in good health. In 1954, he had a radiological image of a lung condensation, long since disappeared.

Ill for three weeks, with a fever of 38, 5°C — 39°C. A longilineal type, of healthy aspect and weighing 60 kilograms. No subjective manifestations. Some lymph-nodes could be felt.

Dermatological lesions: small papulo-tubercles in the right ear lobe. Zones of tawny coloured pigmentation, not clearly delimited cn the trunk. The dominant feature being a nodular eruption on the back part of the arms, and above all, on the anterior aspect of the thighs and legs. The nodules are of various sizes, ranging from the size of a bean to that of a cherry stone, more or less deep-seated and covered with skin of a bruised looking colour.

Mantoux positive 1:10.000. Positive finding of Hansen bacilli in the ear lobe. Biopsy *N.*° 223.711 (Prof, H. Portugal) : lepromatous dermo-hypodermie infiltrate with bacilli. Figures 1, ï and 3, show within the dermo-hypodermic limit reactional agglomerates of lepromatous nodular panniculitis in the course of organization (Virchow cells, some giant cells of "foreign-body" type, "banal" inflammatory infiltrate consisting of, principally, lymphocytes and polynuclears).

OBSERVATION II

N.º 29.253 (10-4-1958), a woman, 54 years old, white, married, housewife, born in Hungary and resident in Rio de Janeiro for 34 years.

Her husband's brother had leprosy. She suffered from a tumour in the glabella which was treated with x-ray, resulting in a certain degree of the falling of the eyebrows. She had had a rash in 1957 then attributed to urticaria (.7)

She had been ill for a month with fever and a rash that still persists, and despite the treatment with antibiotics and anti-allergics prescribed by her private physician, the febrile period lasted for three weeks. The patient is normolineal, very thin, with eruptions on the limbs, which are particularly pronounced on the thighs (Figs. 4 and 5), consisting of nodules of various sizes, averaging from 15 to 20 millimeters in diameter; isolated or joining to form plaques where the skin becomes darkish red in colour, with slight peeling in the older lesions. The nodules were painful at the beginning and somewhat pruriginous in the final stage. After

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a month's evolution the patient come to us for consultation. We found that the nodules were in all stages of development, from the final reabsorption phase, to that when the nodules had just begun to appear. The lymph-nodes appeared to be normal on touching.

Positive finding of nansen bacilli in the nasal mucus (numerous globs). Biopsy (N.º 1.014) showed us the following alterations (Figs. 6, 7, 8 and 9). In the dermis above all in the middle and deep parts, there was a moderate peri-vascular ant peri-glandular infiltration, consisting of some vacuolated cells, of lymphocytes and plasmocytes; the vessels, in general, were dilated.

In the hypodermic could be seen nodular and massive infiltrates, organizes around the vessels and sometimes occupying all a lobe of fat. These infiltrates arc polymorphous and consist of vacuolated cells of the Virchow cell type and o1 plasmocytes, lymphocytes, fibroblasts and sometimes giant cella of foreign body type. There are also polynuclear neutrophils, although not very numerous. The vessels show a certain degree of proliferation of their walls which appear to be thick and infiltrated by leukocytes. The preparations coloured by the Ziehl-Wade method Show numerous bacilli in the interior of foamy cells, as much as in the dermis as in the hypodermia.

As we do not accept — as we shall explain later, the conception with interpret these cases as erythema nodosum or the classic interpretation of the "leprotic reaction" which attributes the acute eruption to various concurrent causes among them and chiefly the influence of "specific" drugs (*) but on the contrary, we attribute our nodular hypodermitis (pannieulitis) to the evolution of leprosy itself, we are treating both cases in an active manner by employing simultaneously: a) a preparation of streptomycin and dihydro-streptomycin (1 gr. in intramuscular injection on alternate days) and b) a preparation of sulfone plus hydrazide given orally. The first case, at the end of one month, was practically cleared of all his nodules. The second case, began to get better, not only as regards lesions, but also In general health.

Let us present our own personal opinion about these lesions and about their true nosographical classification.

To our way of thinking, these lesions, so frequent in lepromatous patients, and known as "leprotic reaction" or erythema nodosum leproticum, constitute, in reality, one modality of a special evolutionary variety of lepromatous leprosy, a clinical and anatomical sub-type, that we have already proposed calling *recurrent leprornatous nodular hypodermitis (panniculitis).* Although its structure is analogous to classic erythema nodosum, there are various characteristics and circumstances which permit a complete differentiation of the two types, as follows:

1. — The juxtaposition of a lepromatous infiltrate, in general pre-existent, in contiguity to or mixed with the acute-sub-acute inflammation responsible by the clinical symptoms analogous, up to a certain point, to those of erythema nodosum.

2. — The recurring tendency which only exists under exceptional circumstances in classic erythema nodosum. Certain lepers can reiterate this syndrome during almost their life-time, at variable intervals. As in lesions of fixed erythema, the tendency for repetition in the same spot can be noted, reserve being made regarding the more acute cases, where dissemination of lesions in parts not affected before, can be discerned.

3. — The sclerosing reaction of the tissues giving place to a special kind of interstitial fibrosis which WADE called attention to, in his study of histopathology of leprotic erythema nodosum (20) and which is responsible for its peculiar clinical aspect (xiloidoderma of SOUZA LIMA) (7), recalling the texture of tissues that appeared on the buttocks of lepers after being treated for many years with injections of chaulmoogric preparations. We can also imagine that there is a certain similarity between this form of leprosy and fibrous tuberculosis, which is also characterized by sclerosing tendencies of the tissues that come into contact with tuberculous products. We would thus have a fibrous leprosy making a *pendant* to the fibrous tuberculosis of the classical authors.

(*) These two cases are really beyond question, as they are both virgin cases without their having received before any antl-leprotic treatment.

4. — The extraordinary frequency of this pseudo-erythema nodosum in lepers: BECHELLI (1), in 190 isolated lepers, in one day alone, discovered that 71 had this clinical type, erythema nodosum leproticum, in all phases of evolution. Contrarily, erythema nodosum of the tubercular or streptococcal origin (to cite only the two more common causes of this syndrome), without being rarities, appear only in scanty numbers even in the largest dermatological services.

5. — The experiments of SCHUPPLI (17) who administering sulfathiazole to lepromatous patients, could not provoke the appearance of erythema nodosum but rather symptoms of acute lepromatization (' `). It is known that sulfathiazole is a drug capable, clinically and experimentally, of provoking a typical syndrome of erythema nodosum presenting, in the respective dermic-hypodermic lesions the radiated granuloma of MIESCHER (8) that this author considered a pre-requisite of true erythema nodosum. The difference is thus plearly defined; sulfathiazole, capable of frequently provoking typical lesions of erythema nodosum in a variety of patients, when administered to lepers, in 10 cases out of 11, does not provoke this reaction, but an acute lepromatous eruption with accentuated general symptoms connected, possibly, with bacillemia.

6. — The opinion of MIESCHER revives, in a certain manner, the doctrine of TROUSSEAU, and rejects the current concept of poly-etiology of erythema nodosum considering it as "eine infektiiise affektion sui generis" (even when it appears in connection with another disease), characterized by the forming of a highly specific granulomatous picture, the radiated granuloma. As to the occurence of the latter in erythema nodosum leproticum opinions of the histo-pathologists differ; RATH (18), MELLO (in about 150 cases, apud RATH) (18), PEPLER (12) and WADE (20) never found then, while PORTUGAL (14) in 9 cases out of 10, observed formations "very similar" to radiated granuloma, which was also observed by ORBANEJA (11). On the other hand, it appears difficult to admit the coincidence of the two diseases in view of the frequency of erythema nodosum in lepromatous cases (only in them but almost never in tuberculoids).

* * *

At the same time as we, other authors have tried to discriminate between true erythema nodosum and "leprotic reaction" of the erythema nodosum type — our *"reccurent lepronzatous nodular hypodermitis* (panniculitis).

In this fashion RATH (18) thought that the name "erythema nodosum" given to this intercurrent situation was not an appropriate one. MIRANDA (9) also considered the name of "erythema nodosum" occuring in leprosy to be unjustifiable, and above all, PEPLER and his collaborators (8) who presented an excellent histopathological study based on 20 cases, proposed to designate it as "Panniculitis nodosa leprosa" and affirmed that the two principal differing characteristics between the classic erythema nodosum and panniculitis nodosa leprosa would be; a) frequent abcessing of the latter, which is very rare in the former and; b) the presence of Miescher's granuloma in the first and its absence in the second. *"Recurrent lepromatous nodular hypodermitis* (panniculitis)" seems to us to be a more appropriate name than that chosen by PEPLER because:

1. — Hypodermitis is the name universally used after the works of Gougerot and his school for inflamatory lesions of the hypodermis;

(*) Acute lepromatization is a second form of "leprotic reaction" characterized by a febrile state and by the appearance of numerous new lepromata with aggravation of leprosy, in consequence of the lepromatous state. It is, truly and simply, not a "reaction" but acute leprosy, a stage of acute evolution (see: Souza Lima and Maurano (7) (page 52). It is entirely different from our *recurent* iepromatous *nodular hypodermitis (panniculitis)* Which would warrant even a relatively favourable prognosis.

2. — Only just recently VILANOVA (19) studying a new clinical type of his own creation, a "sub-acute migrant nodular hypodermitis" completely revised the general concept of the nosological group of lesions referring to the hypodermis and the ill defined boundary between the dermis and the hypodermis, plainly justifying the adoption of the designation of hypodermitis;

3. — It defines in a satisfactory manner:

a) the deep localization of the lesions;

b) its etiology and;

c) its principal clinical characteristic as being *recurrent.*

We are ourselves convinced that *recurrent lepromatous nodular hypodermitis* (panniculitis) represents a special evolutionary modality, a sub-type, not quite so serious as common lepromatous leprosy with its chronic lepromatous eruptions sometimes turning into leonine leprosy and being able to produce acute on sets of intensive and extensive lepromatization, showing myriads of bacilli, as much as in old lesions as in new ones.

In our *hypodermitis* (panniculitis) on the contrary, we have lepromas or diffuse lepromatous infiltrates which are first substituted, at least in part, by unspecific inflammatory infiltrates, and after by fibrous tissue that take the place of them in consequence of the evolutionary onsets, acute-sub-acute in character, and one of the consequences of which is the diminishing or even the absence of bacilli in the inflammatory foci. It could be conceived perhaps, as a first possibility opened to the lepromatous organism, with which the HANSEN bacilli live almost in symbiosis, *symbiotic leprosy* (16), to dominate. the growth of mycobacteria. In this way an answer has been positively given to the celebrated question raised so frequently by leprologists: "Does leprotic reaction benefit the leper?" (*)

As a matter of fact these cases have an evolution which is a little more favourable than common lepromatous leprosy, in consequence of a beginning of defense which becomes organized and which WADE (20) had a good inkling of, when he noted the existence, between the web of fibres in old cases of *recurrent lepromatous nodular hypodermitis* (panniculitis), of clustered histiocytes, indicating perhaps, the transition of the cytological formula of the infiltrate, in the sense of a tuberculoid leprosy — *antagonic* leprosy (16). It is also understandable why the frequency of these cases seems greater after the general application of sulfone treatment; evidently, the bacteriostatic treatment acts in the same way as the beginning organic defense, enabling the leper to counteract the bacilli invasion by means of a mechanism which we do not know completely and which interpretation, for this reason, has varied according to the doctrines of the authors who have written on this subject.

(*) Davidson and Koolj In a recent article (4) concluded that "erythema nodosum leproticum is not a favourable sign", basing their deductions on a meticulous statistical study. It is curious that the basis of their investigation gives an entirely different Impression from that they arrived at. As a matter of fact, of the 97 cases considered "arrested" (absence of clinical activity and negative bacterioscopic examination over a period of 12 months), 74 belonged to the erythema nodosum group and 23 to the group without erythema nodosum, that is, the erythema nodosum group presented more than three times of the "arrested" cases than the common chronic lepromatous leprosy group. The fact that the group with erythema nodosum leproticum had more than 4 deaths and the other group none, is explained, in part, by the numerical difference itself 74:23 (the group of 23 should give 1,2 deaths and gave 0, which does not appear significant to us). The greatest argument put forwcrd by the authors is that the erythema nodosum leproticum group took on an average 72 months to become negative, while the other group took 57 months to become negative. It seems to us that the recurring characteristic of this evolutionary type of leprosy, can, perhaps, in itself explain the difference.

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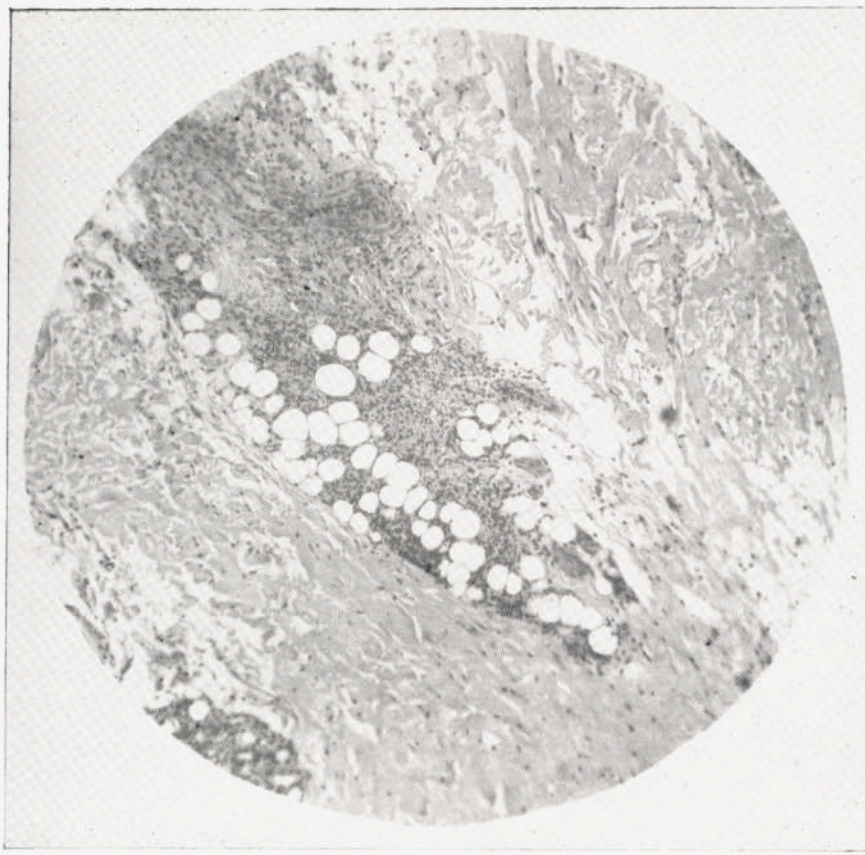
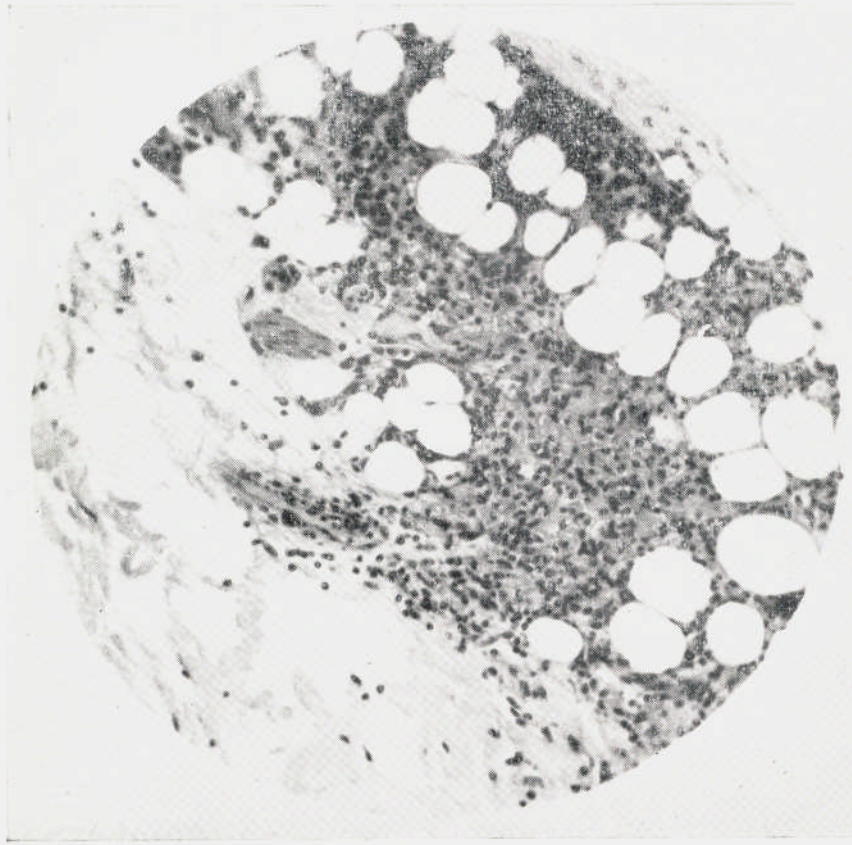


FIG. 1 — OBS. I — N.° 29.061 (X72)



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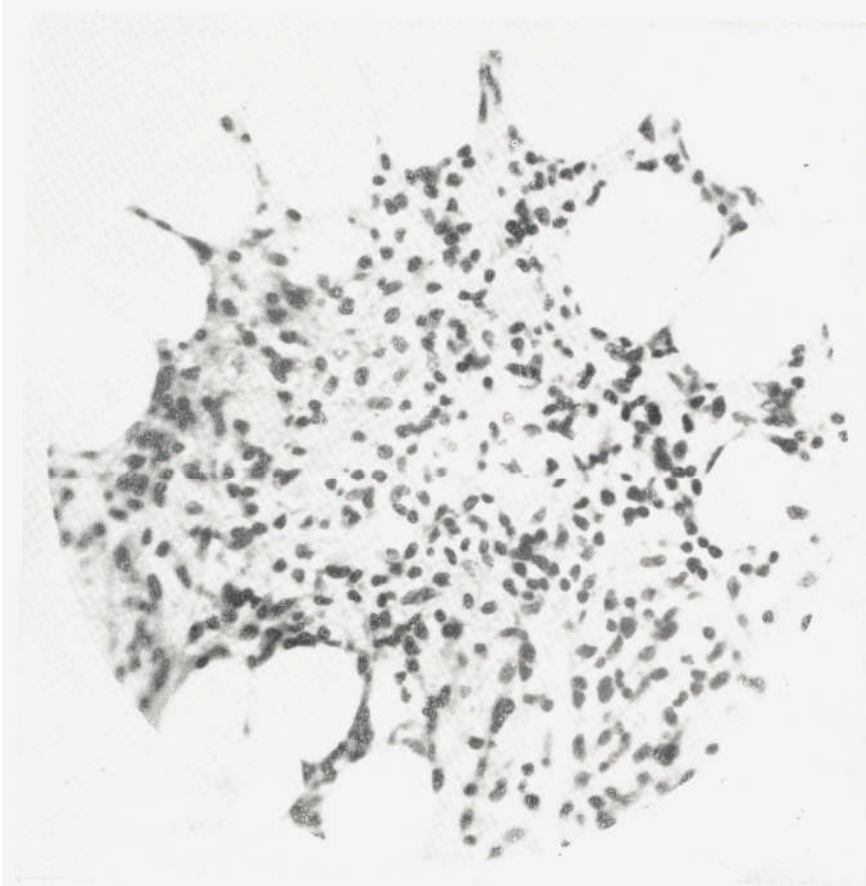

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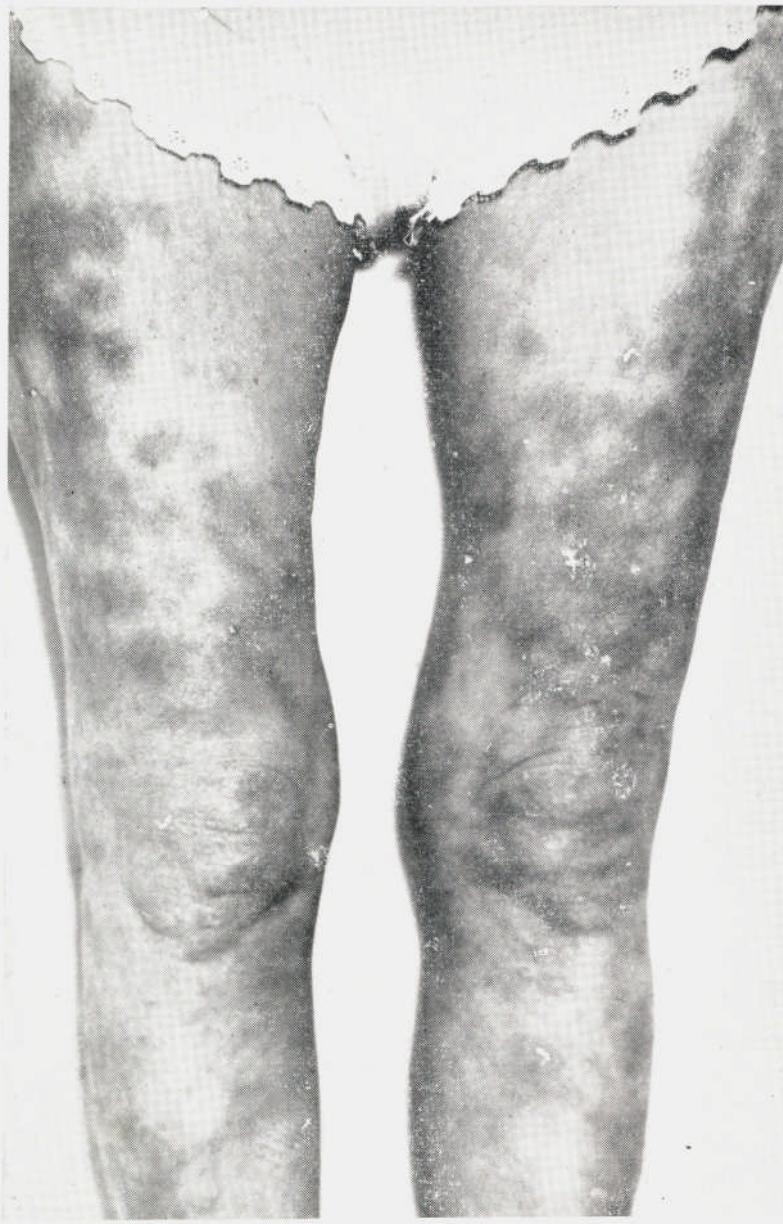

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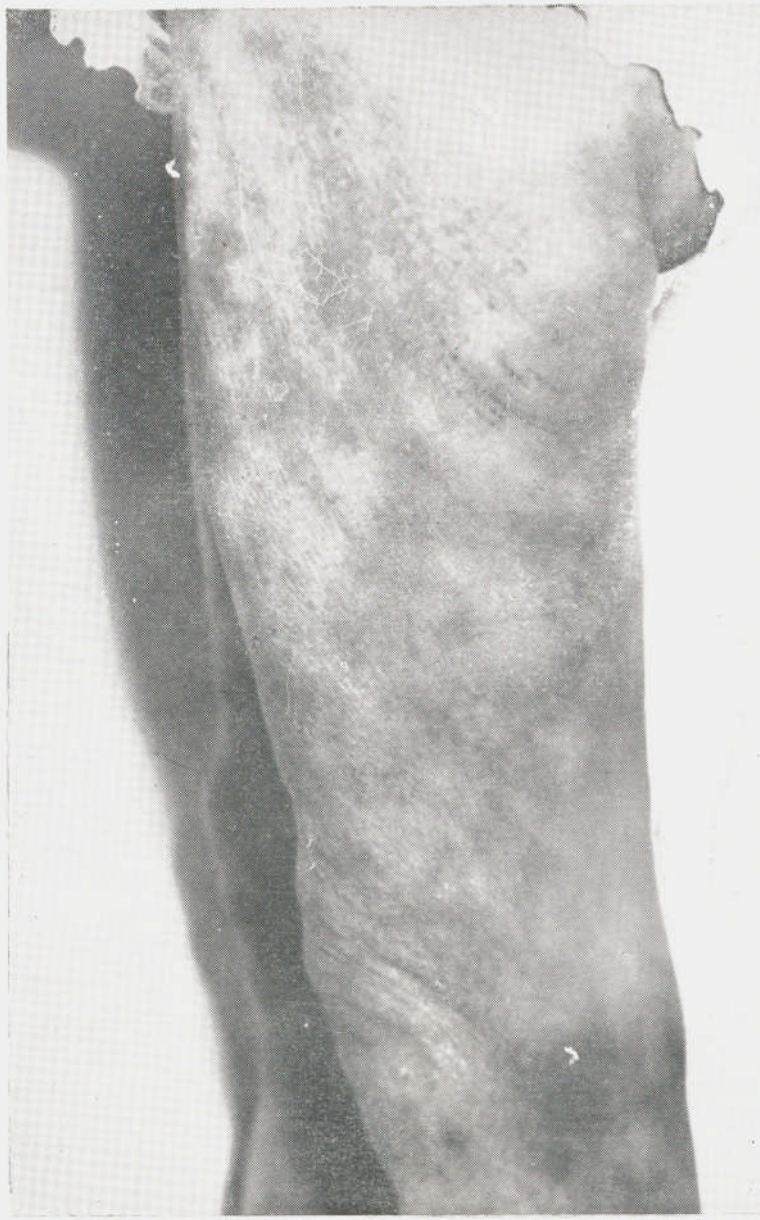

FIG. 5 — OBS. II — N.º 29.253

FIG. 6 — OBS. II — N.° 29.253 (X72)

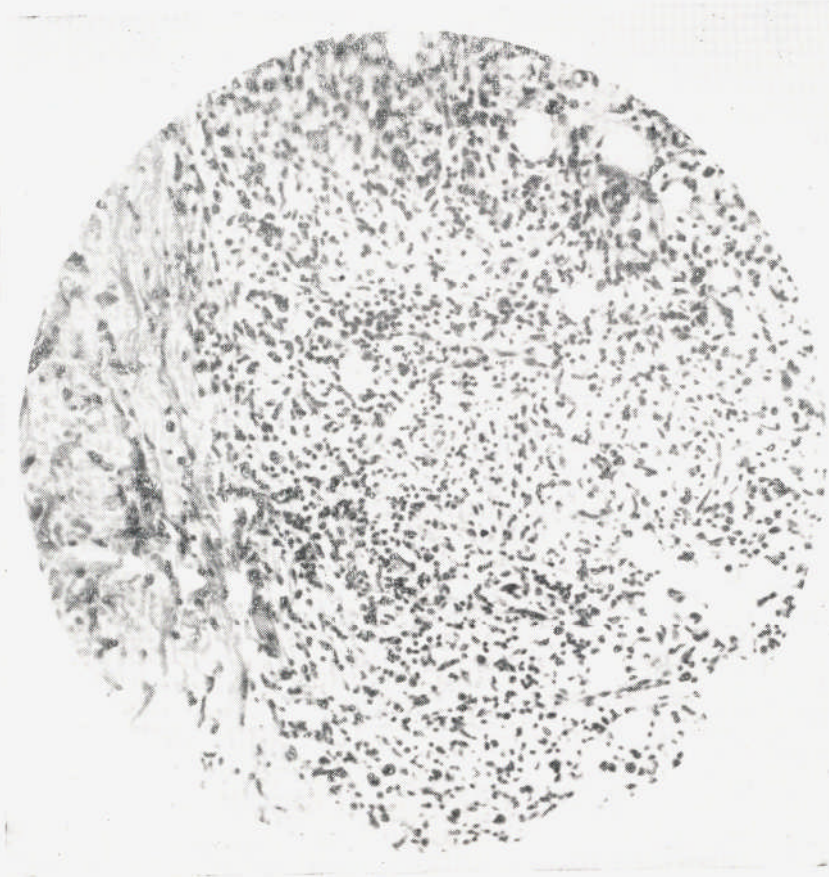

FIG. 7 — OΞS. II — N.° 29.253 (X180)

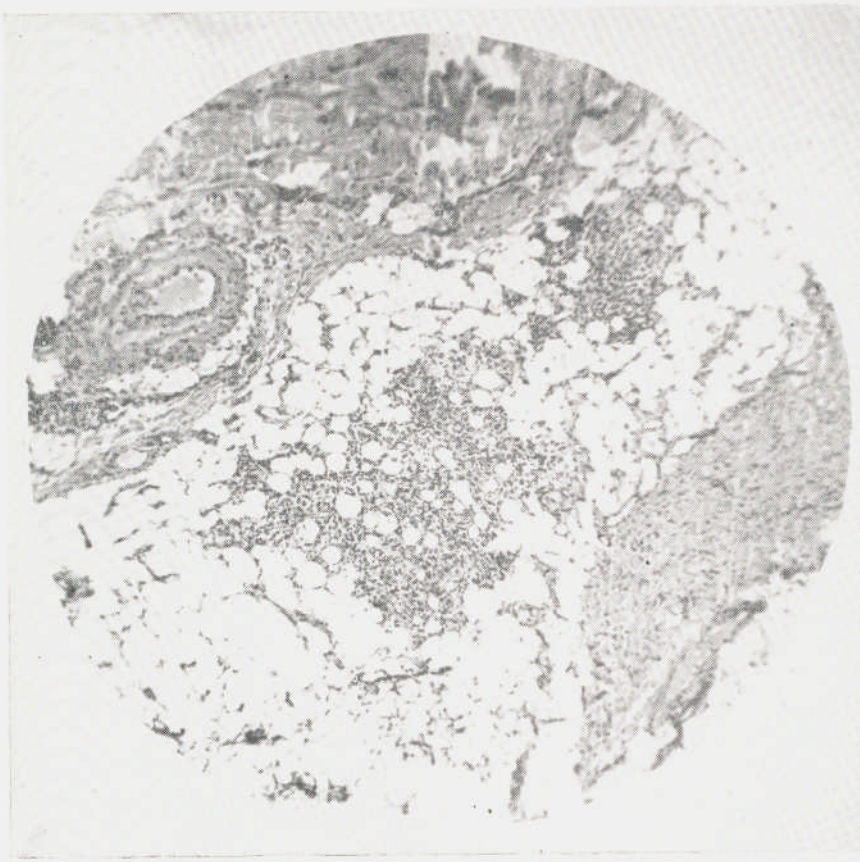

FIG. 8 — OBS. II — N.° 29.253 (X72)

FIG. 9 — OBS. II — N.° 29.253 (X360)