INTERNATIONAL JOURNAL OF LEPROSY

VOLUME 16, NUMBER 4 OCTOBER-DECEMBER, 1948

THE "SPOTTED" LEPROSY OF LUCIO [1,2] (LA LEPRA "MANCHADA" DE LUCIO)

AN INTRODUCTION TO ITS CLINICAL AND HISTOLOGICAL STUDY

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Rafael Lucio, in collaboration with Alvarado, published in 1852 an original description of leprosy entitled "A Short Treatise on the Disease of San Lazaro, or Elephantiasis of the Greeks" (11). They described three forms of the disease, each of them regarded as very different from the others, namely, the nodular, the anesthetic, and the "manchada" or "lazarine." Their study pertained especially to the last of these forms, which they believed to occur only in Mexico, and they described it as characterized by "red and painful spots on the skin" (*manchas rojas y dolorosas en la piel*) and by its greater seriousness.

[1] Presented at the Fifth International Congress of Leprosy, on April 7, 1948. This English edition is based on a translation made by a member of the Congress secretariat, with a final revision by the authors.—EDITOR.

[2] The Spanish word "manchada" signifies primarily "spotted, speckled, stained." The best English term for "lepra manchada," we feel, is "spotted leprosy." The alternative term "lazarine leprosy" which was employed by Lucio and Alvarado has for many years been applied by various writers in other countries to ulcerative tuberculoid leprosy, and perhaps also to other clinical forms of the disease presenting ulcerations, sloughing areas or simple bullae. It has therefore become confused and, in our opinion, unsuitable for use in modern leprology. It seems desirable, nevertheless, that a distinctive term be adopted for this peculiar clinical form of lepromatous leprosy which has been described in Mexico, and we propose to denominate it "pure diffuse lepromatosis with outbreaks of multiple necrotizing vascularitis" (lepra "manchada" o "lazarina" Lucio y Alvarado, 1852).

According to Lucio's description the cases of "lepra manchada" differ greatly from the others. The patients first notice numbness and then impairment of sensation in the hands and feet; later on they begin little by little to lose their eyebrows, eyelashes, and finally their body hair. Years afterward the typical red and painful episodic lesions begin to appear. At first there are only a few of them; then they occur in small outbreaks (*brotes*) ; and with the passage of time and after repeated acute eruptions or stages the lesions become more numerous and important. They predominate on the extremities, and only in the advanced cases are they widely disseminated. In number, size and shape these lesions are variable, often being triangular or irregular; they average 15 days in duration.

Lucio described these acute lesions as highly characteristic and of a typical evolution. At first the lesion is pinkish, ill-defined and painful, and sometimes it is infiltrated. A few days later it shows a darker center which does not disappear under pressure. This center soon approaches the surface, and there forms a small, very thin, dry, brown scab which finally drops off to leave an insignificant scar. In larger and more inflammatory elements there is formed a dark, flaccid blister which bursts, leaving a deep ulceration with jagged edges surrounded by an inflammatory zone. In addition, particularly on the legs, there are secondary pyoderma lesions and chronic cellulitis which complicate the condition.

The complete absence of nodules was also emphasized by Lucio, as well as the occurrence of a progressive and destructive rhinitis, shining eyes and lack of ostensible ocular symptoms. He insisted, too, on certain systemic symptoms, and also certain digestive, respiratory and circulatory complications. He pointed out, finally, that the prognosis is poor, and that death occurs sooner than in other forms of leprosy.

In spite of the excellent description given by Lucio and Alvarado, their denomination of this special form was misunderstood, and its existence was doubted or denied. Consequently, this very peculiar clinical picture is not included in either the older or contemporary treatises on leprosy, and usually it is not even mentioned as a bibliographic reference. Even in Mexico, in spite of the fact that several authors of his generation referred to it, Lucio's work was gradually forgotten, so that during the first of this century Mexican physicians did not identify "lepra manchada." On the other hand, certain contemporary writers (Pardo-Castelló, Rodriguez, and others) have employed the

alternative name used by Lucio and Alvarado, "lazarine leprosy," in describing very diverse aspects of the disease.

In 1938, one of us (Latapí) re-identified the form described by Lucio while studying leprosy cases in the "Dr. Ladislao de la Pascua" Dispensary in Mexico City, and from that time on its study has been continued and an effort has been made to fit it into the frame of modern leprology (7-10). Today, "Lucio's leprosy" is well known by all Mexican leprologists and by some foreign ones. It deserves recognition and investigation because of its frequent occurrence in our country, its relatively great malignity and transmissibility, and the scientific problems which it presents.[3]

Additions have been made to the original description. We have studied a most essential fact in the clinical picture, one which was not noticed by Lucio; de Jesús Gonzalez grasped it in part upon observing the aspect of the eyelids. This essential fact is that the fundamental condition in this clinical form is a diffuse, generalized cutaneous infiltration. Succulent and myxedematoid at first, especially in the face and hands, or atrophic and ichthyosiform years later, it is always the clinical and anatomical basis upon which the other episodic symptoms develop. We have also described the rosacea-like variety which shows, in addition, reddening and telangiectasis.

This clinical form of leprosy we have attempted to place within the lepromatous type of today, naming it "pure and primitive diffuse lepromatosis (Lucio and Alvarado, 1852)." The "red and painful areas" we have designated "Lucio's phenomenon," using also the synonym "erythema necrotisans" which brings out its analogy to erythema multiforme and erythema nodosum. These cutaneous outbreaks are a secondary, episodic condition which we regard as a variety of lepra reaction produced by multiple, acute, necrotizing vascularitis.

Other investigators have contributed to our present knowledge of this condition. Gonzalez Urueña (6) described the special type of cephalic alopecia which is often found, and which had already been observed by Escalona and Palomo (1). Gonzalez Chavez (4) showed how abundant *M. leprae* are in smears from

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[3] It is known that this variety of leprosy occurs in Costa Rica. According to the available abstract of a clinical note sent to the Havana Congress by Romero, Brenes Ibarra and Follas, of that country (see THE JOURNAL **16** (1948) 280), 70 per cent of the leprosy cases seen there are lepromatous, and of them 45 per cent (or 31.5 per cent of all cases) are of the diffuse form—and real nodular cases are so scarce that there is difficulty in getting material for the preparation of lepromin.—EDITOR.

the nasal mucous membranes and infiltrated skin, and how rare they are in the lesions of "erythema necrotisans"; and the same author obtained strong and practically constant positive results with all the serological reactions for syphilis. Rico (16) found the red-cell sedimentation to be always accelerated, much more than in nodular cases. Martinez Baez (12) studied the histopathology of the Lucio phenomenon in some of its phases, and verified the basic lepromatous structure with vascular and acute perivascular lesions going on to necrosis. Medina (13) observed, for the first time, a special reaction to lepromin in diffuse lepromatous cases with acute episodes.

We have observed the Lucio form of leprosy in 15 to 20 per cent of our clinical material in Mexico City, and occasionally also in Jalisco and Sinaloa. Our attention was drawn to the healthy initial aspect of these patients and to their subsequent rapid and profound deterioration; we have seen many die within a few years, with extensive ulcerations and in a cachectic state. We have insisted that their state is aggravated by most active treatments (antisyphilitic treatment, iodides, toxoids), and especially by chaulmoogra in any form, which hastens the advent of death. On the other hand we have witnessed real resurrections within a short while after the beginning of sulfone treatment. That treatment, after a crisis of the Herxheimer type which sometimes requires careful handling, apparently controls spectacularly the previously tragic situation.

The purpose of presenting this paper before the present Congress is to draw the attention of the members to Lucio's "manchada" leprosy, both as originally described and in its present broader features, as well as to solicit opinions on the concept now held in Mexico about this "pure and primitive diffuse lepromatosis with multiple necrotizing vascularitis." We are making a methodical study of it, intended to be as complete as possible and to include dermatological and general clinical studies, pathological studies of the skin and internal organs, and immunological investigations. We will try to go more deeply into its epidemiological aspects in connection with the problem of its special geographic distribution, and to determine its final place in leprology and in general pathology.

We present here only a part of the general study which has already been made. This study includes, on the one hand, the clinical and histopathological aspects of the cutaneous lesions—the chronic and diffuse as well as the acute and limited ones—which are observed, and on the other hand the lesions provoked

in these patients by the intradermal injection of lepromin and other antigens. In summary the following may be said:

(1) The diffuse cutaneous infiltration (Figs. 1 and 2), already described as either succulent or atrophic according to the stage of progression, which shows a diffuse dysesthesia and an abnormal histamine reaction and which is accompanied by alopecia of the eyebrows, eyelashes, body hair and even the hair of the scalp, is histologically of lepromatous nature but of a special form (Figs. 8 and 9). This form can be differentiated from the classical nodular one by the following features: discreet epithelial alterations in the "succulent" phase, a tendency to slight atrophy and hyperkeratosis in the later "dry" phase; new formation of blood vessels in the dermis; moderate but constant infiltration of typical Virchow cells around the dermal vessels, without nodule formation in this region; and, finally, the existence in the subcutaneous layer of large nodules of the infiltrate, and chronic inflammatory phenomena around the large vessels.

(2) The secondary condition which occurs in these cases, and which we have called the Lucio phenomenon, presents various phases (Figs. 3 to 7). The primary phase of erythema is an acute, inflammatory, nonspecific phenomenon of an alterative, vascular and proliferative nature, which appears within the basic diffuse lepromatous structure. There are seen inflammatory changes of the perithelial polyblasts, mobilization of histiocytes, dilatation and at the same time necrosis of capillary vessels, beginning secondary alteration of the superficial dermis and the epithelium.

In the later phase of erythema, when the dark center of the lesion has appeared, one sees the same process in a more advanced stage (Fig. 10). There are frank necrosis of the capillaries (Fig. 11) and the development and later limitations of a secondary dermo-epidermal necrosis. The dry-scab stage evidences itself as a limited and dry secondary necrosis of the upper epithelial layers, and by degeneration and depigmentation of those which may remain.

When the evolution is toward a blister, the necrotic and edematous process is intense, accompanied by the nonhemorrhagic accumulation of liquid (Figs. 12 and 13); the reactional inflammation at the margin is marked, as in the clinical picture. In the ulcer which results from a bulla (Figs. 6 and 7, and 14 and 15) the loss of substance is marked. The surface is covered by a thick fibrinous membrane with numerous polymorphonuclear leukocytes in its meshes, as a screen against the entrance

of pyogenic micro-organisms. The reparative process is intense, with marked connective-tissue proliferation. The whole process is a nonspecific inflammatory one, originally vascular and necrotic, with a later tendency to peripheral fibrosis.

(3) The diffuse lepromatous case showing the Lucio phenomenon gives a special response to integral lepromin, first observed by Medina, which we consider quite different from the Fernández reaction frequently found in tuberculoid cases in the 24-48-hour period. This Medina reaction, as we call it, is already well-defined within the first four to six hours, and is still present after two or more days. It is a little less strong with bacillary lepromin than with the ordinary whole suspension ("integral lepromin").

The appearance and evolution of this reaction to lepromin recall the spontaneous Lucio phenomenon, but the central necrotic area does not have an irregular or triangular shape. Almost identical results are obtained when streptococcal and staphylococcal antigens are used for the test; with other antigens, only false positive reactions of a few hours' duration occur (simple traumatic reaction?).

Histologic study of the Medina reaction lesion, after 4 to 48 hours, reveals the aspect of an acute inflammatory process which differs in important respects from that of the Fernández 48-hour reaction. In the former, one observes, from the first few hours, a predominance of polymorphonuclear leucocytes and a relative abundance of eosinophiles in the cellular infiltrate, and also edema and necrosis of the collagen, the process ending with the formation of an intradermal abscess.

Because of this response to the injection of lepromin, it has been said (Medina, Mom) that leprosy cases of the Lucio form give positive early lepromin reactions, and that consequently they contravene the rule that this allergic phenomenon does not occur in lepromatous leprosy. The reaction which is observed is disconcerting at first, but the facts of the matter must be studied carefully and without prejudice before a final interpretation is arrived at. A correct understanding may be of importance to leprology, and even to general pathology. For this reason an analysis of the reaction is included in a separate paper (16)

dealing with the present interpretation of the Lucio form of leprosy.[4]

CONCLUSIONS

1. The existence in Mexico of a special clinical form of leprosy, described by Lucio in 1852 under the name of "manchada" or "lazarine" leprosy but later forgotten for more than half a century, was verified in 1938 by Latapí. He renewed its study and introduced it into the present frame of leprology, calling it a "pure and primitive diffuse lepromatosis with outbreaks of multiple necrotizing vascularitis."

2. Modern Mexican leprologists have recognized the individuality of this interesting clinical form, have confirmed Lucio's excellent description, particularly as to the "red and painful 'manchas' undergoing necrosis," and have completed its description, which includes diffuse infiltration of the skin, telangiectasis, cephalic alopecia, positive bacteriologic findings, false positive serological reactions for syphilis, lepromatous structure, vascular location of the acute lesion, and a special reaction to lepromin. They have related its repeated outbreaks to the well known "lepra reaction," observed its curious geographic distribution, and witnessed the relatively high malignity which Lucio ascribed to it. Finally, they have been privileged to witness its remarkable control and spectacular improvement by sulfone treatment.

3. We have attempted in this paper to summarize the essential facts pertaining to the Lucio form of leprosy, to pay homage to its discoverer, and to present part of the work being done on the subject in Mexico. This is the part which refers to the comparative clinical and histopathological study of the diffuse

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[4] From complementary studies we now feel that lepromatous "lepra reaction" (with acute cutaneous lesions of erythema multiforme, erythema nodosum or erythema necrotisans types) and the special Medina response to lepromin are but, respectively, the spontaneous and experimental expressions of a bacterial hypersensitiveness entirely unrelated to the tuberculin-type hypersensitiveness which is found in tuberculoid leprosy. We think that "lepra reaction" and the Medina response are in some way more closely related to the so-called Shwartzman type of bacterial hypersensitiveness. The primary vascular damage, as well as the necrotic nature and rapid course of the whole process (4 to 6 hours), are in support of this belief. Therefore, we are not dealing with allergic phenomena *sensu strictu*, since they are not specific but are apparently elicited by a synergic bacterial mechanism. In this case the development of this mechanism seems to depend upon the association of cocci of secondary infections with the Hansen bacilli.

cutaneous infiltration, which we have found to be different from the classical nodular type, and of the acute episodic lesions which are essentially dependent upon an acute vascularitis, and for which Latapí has proposed the name "Lucio's phenomenon" or "erythema necrotisans." Finally, we have included a preliminary statement regarding the Medina reaction, a special response to lepromin in these patients.

ACKNOWLEDGMENTS

We are grateful for the unlimited cooperation given us by Drs. Obdulia Rodriguez and María Concepcion Estrada in the preparation of this paper, as well as for the previous or present collaboration in various scientific aspects of this subject given to us by Drs. Alfonso González Chavez, Demetrio Sodi Pallares, Manuel Medina Ramírez, Silvestre Rico Venegas and Jose Baez Villaseñor.

REFERENCES

1. ESCANOLA, ERNESTO. La reacción leprosa. La Prensa méd. mexicana (1941) 127-130 (Sept. 15).
2. FERNANDEZ VAUTRAI, RAÚL. Comentarios sobre a chamada lepra lazarina. Rev. brasileira Leprol. **9** (1941) 263-269.
3. GONZALEZ, JOSE DE JESUS. Contribución al Estudio en México de la Lepra. Tesis. Facultad de Medicina de México. México, 1897.
4. GONZALEZ C. IGNACIO. Estudio de los granulocitos sanguíneos de los leprosos. Arch. Latino-Americano Card. y Hem. (1943) (May).
5. GONZALEZ URUEÑA, JESUS. La Lepra en México. El Ateneo, Buenos Aires, Argentina, 1941, 806 pp.
6. GONZALEZ URUEÑA, JESUS. Alopecía leprosa en México. Rev. Sifilog., Leprol. y Dermatol. **2** (1945) 73-100 (June).
7. LATAPÍ, FERNANDO. Manifestaciones agudas de la lepra. Rev. Med. **18** (1938) 526-538 (Oct.).
8. LATAPÍ, FERNANDO. Lepra. La Prensa méd. mexicana **11** (1946) 1 (Jan.).
9. LATAPÍ, FERNANDO. Clasificación de la lepra; tipo, grupo, forma y caso. V. Congr. Internat. de Lepra, Havana, Cuba, April 1948.
10. LATAPÍ, FERNANDO and CHEVEZ, AGUSTIN. Interpretación actual de la lepra de Lucio. V. Congr. Internat. de Lepra, Havana, Cuba, April 1948.
11. LUCIO and ALVARADO. Opúsculo sobre el Mal de San Lázaro o Elefancíasis de los Griegos. M. Murguía y Cía, México, 1852, 53 pp.
12. MARTINEZ BAEZ, MANUEL. Nota preliminar sobre la histopatología de las manifestaciones cutáneas de la "forma de Lucio" de la lepra. Gac. Méd. méxicana (1942) (June); Rev. Fac. Med. **10** (1942) 610-622.
13. MEDINA, R. M. Personal communication (1944).

14. OBERMAYER, M. E. Diffuse lepra. Ann. West. Med. & Surg. **1** (1947) 225-231 (Aug.).

15. PARDO CASTELLO, V. and CABALLERO, G. M. Lazarine leprosy, a peculiar monosymptomatic form of leprosy. Arch. Dermat. & Syphilog. **23** (1931) 1-11 (Jan.).

16. RICO VENEGAS, SILVESTRE. Nota acerca del índice de sedimentación globular en las diferentes formas clínicas de la lepra. La. Prensa méd. mexicana (1941) 135 (No. 9, Sept. 15).

17. RODRIGUEZ, J. N. and WADE, H. W. Bullous tuberculoid leprosy; report of a case with a discussion of lazarine leprosy. Internat. J. Leprosy **8** (1940) 333-334.

DESCRIPTION OF PLATES

PLATE 20

FIG. 1. Pure diffuse lepromatous leprosy. Permanent diffuse edematoid swelling of the entire face—"healthy" appearance—with progressive loss of eyebrows and eyelashes but complete lack of nodule formation. (Courtesy of Dr. S. Rico.)

FIG. 2. Diffuse infiltration of the hand in the early or "succulent" stage. (Pure diffuse lepromatosis has occasionally been confused with myxedema.)

FIG. 3. "Lepra manchada" of Lucio and Alvarado. A typical acute outbreak of the "red and painful spots" which those authors described as a special—"spotted" or "lazarine"—form of leprosy. This is now regarded as an episodic phase, a multiple necrotizing angiitis, of diffuse lepromatous leprosy. (Courtesy of Dr. S. Rico.)

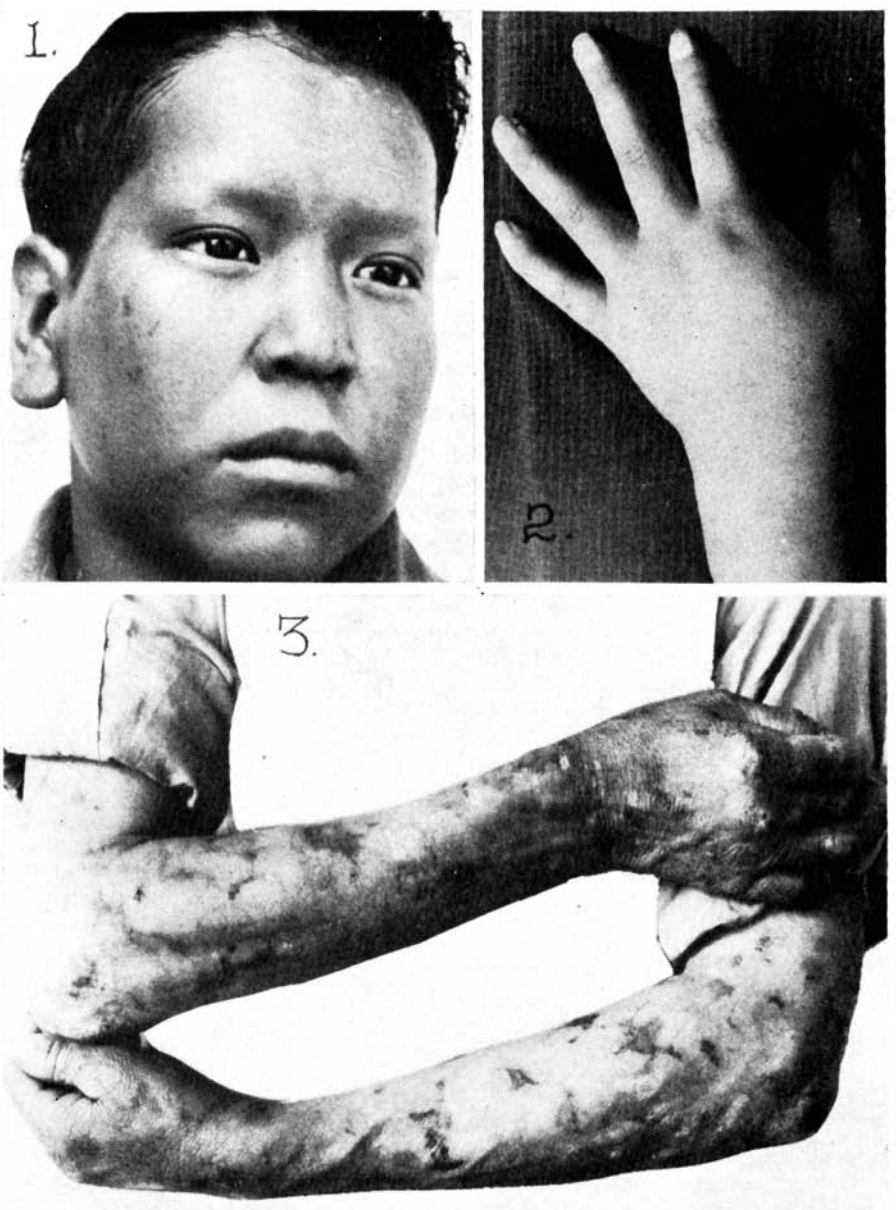

PLATE 20

PLATE 21

FIG. 4. The "Lucio phenomenon" or "erythema necrotisans" (Latapí). A crop of acute lesions showing different stages of the condition, the total picture of which comprises initial erythema, pseudo-purpura, dry brownish necrotic scab with consecutive superficial scar, or bullae formation with extensive sloughing and deep ulceration. (Courtesy of Dr. S. Rico.)

FIG. 5. The necrotic stage of a typical acute lesion on the thigh. The black necrotic area is somewhat triangular in shape and fairly well defined. Below it and slightly to the right is a similar lesion in its initial, erythematous phase. Enlargement of the subcutaneous veins, a feature recorded by Lucio, is conspicuous. The background of these changes is a diffuse lepromatous skin involvement in the advanced, atrophic stage. (Courtesy of Dr. S. Rico.)

FIG. 6. Multiform cutaneous lesions of Mexican "lazarine" leprosy. During the advanced stage, in untreated cases of diffuse lepromatous leprosy, the new initial vascular lesions are constantly accompanied by multiple necrotic ulcerations, pyogenic crusts and more or less deep scars.

FIG. 7. Chronic ulcers in an old case of diffuse lepromatous leprosy, a frequently-seen condition resulting from the necrotic vascular process. The swelling of the legs is related to long-standing lymphangitis and cellulitis due to repeated secondary infections. (Courtesy of Dr. S. Rico.)

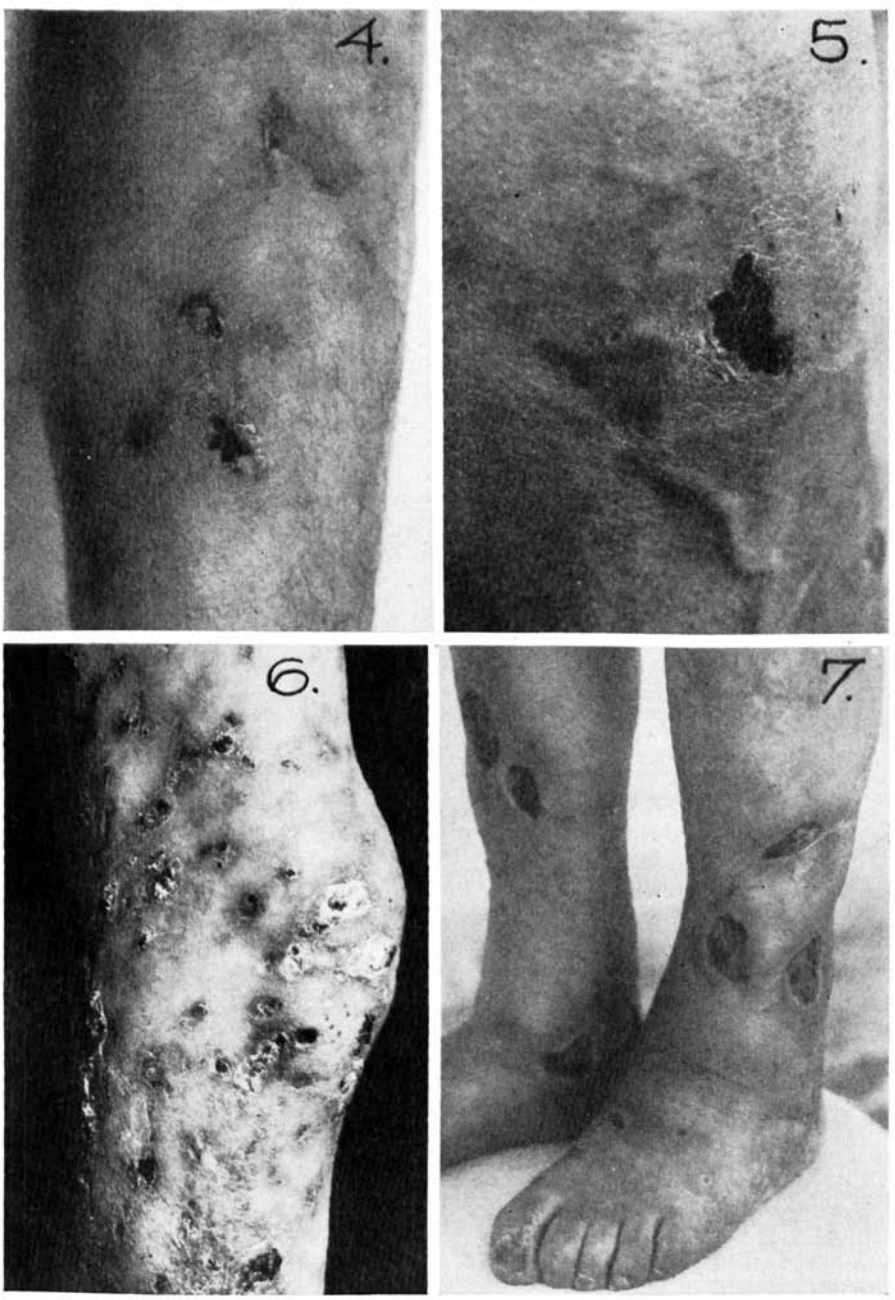

PLATE 21

PLATE 22

FIG. 8. Histology of the pure diffuse lepromatous leprosy in an early stage. Note the edema of the dermis and the diffuse perivascular infiltration by typical lepromatous Virchow cells, with normal epidermis.

FIG. 9. Typical Virchow foamy cells in the diffuse lepromatous infiltration of the skin. (Possibility of finding a number of lepra bacilli with special techniques.)

FIG. 10. The acute necrotizing arteritis in a lesion of the "erythema necrotisans" type, in the dry stage, showing focal necrosis of the epithelium and dermis secondary to acute vascular damage.

FIG. 11. The initial vascular damage. Showing the primary necrosis and thrombosis of the terminal dermal arterioles.

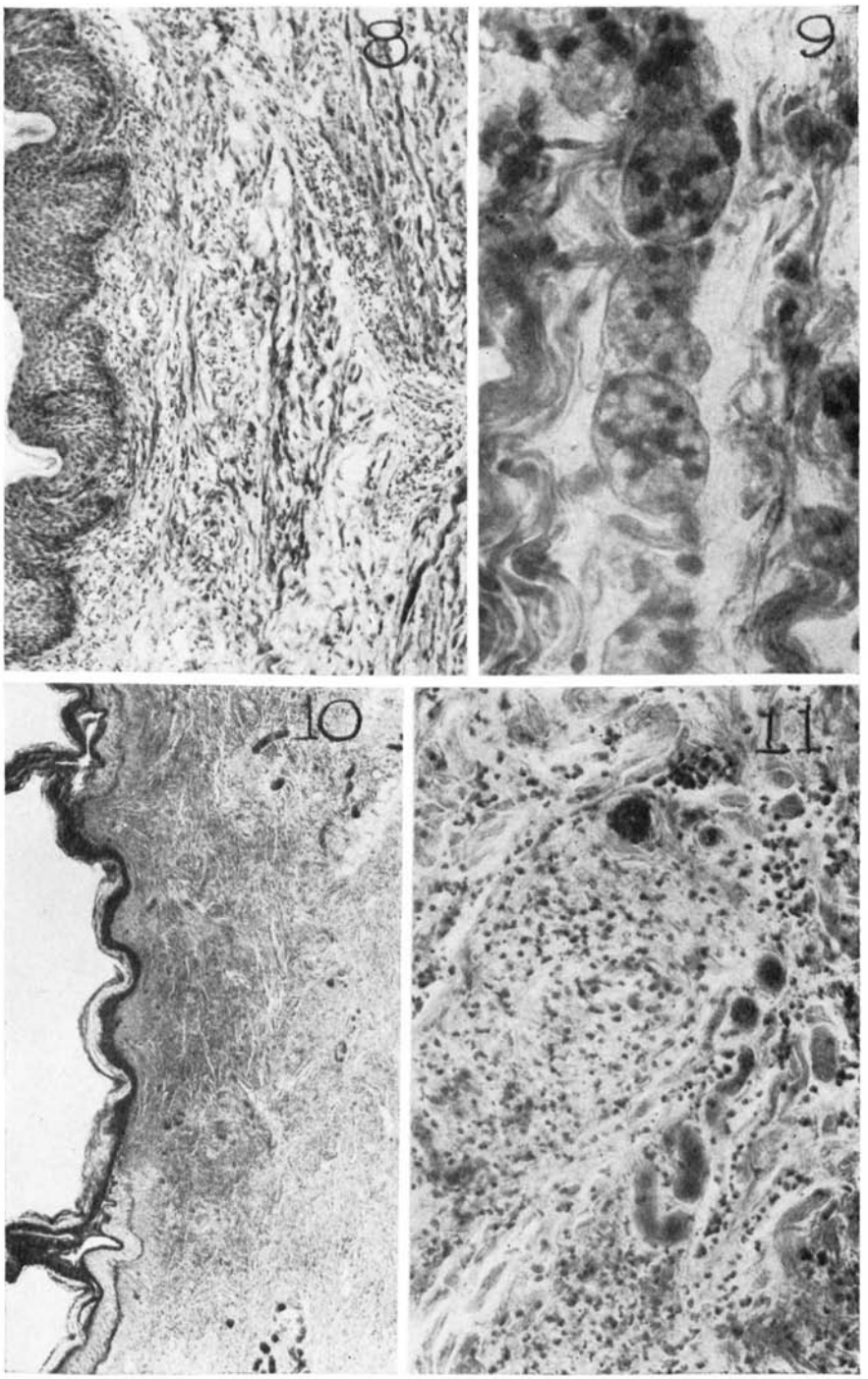

PLATE 22

PLATE 23

FIG. 12. The microscopic appearance of the necrotic bullous type of lesion, with subepidermal serous accumulation secondary to dermal necrosis.

FIG. 13. Another view of a necrotic bullous lesion, demonstrating the absence of red and white cells in the bulla.

FIG. 14. The ulcerating stage of a bullous lesion.

FIG. 15. A recent ulceration secondary to a necrotic bulla. The damaged area has lost its epithelium and is covered by a thick fibrinous membrane with numerous polymorphonuclear leucocytes. The reparative process is active, with marked connective-tissue proliferation.

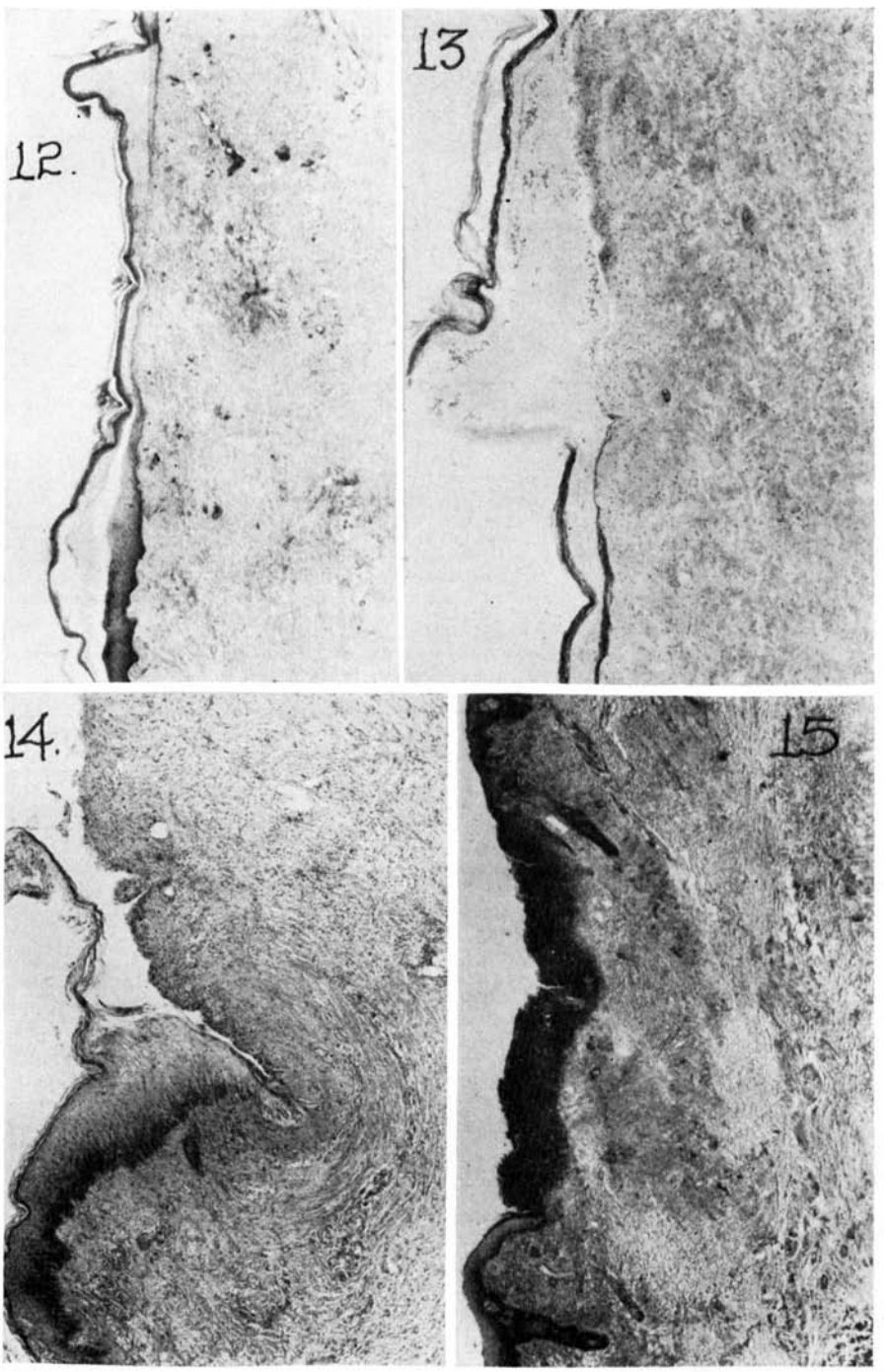

PLATE 23