TRANSFORMATION OF TWO BORDERLINE-LEPROMATOUS LEPROSY CASES TO TUBERCULOID, WITH HEALING[1]

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INTRODUCTION

One of us (J.M.M.F.) has completed 32 years of leprosy work in the leprosy service of the Carrasco Hospital, and the others of us have had more than 20 years. This privileged situation of being able to follow up the evolution of our patients for long periods has enabled us to collect some observations on the different aspects of the disease which we believe should be given publicity.

We commence with two cases of transformation from a condition diagnosed as lepromatous—but evidently, in retrospect, borderline—to frank tuberculoid and apparent cure, whose evolution we followed for 26 and 20 years, respectively. It will be appreciated that the basis of classification of types and groups has changed during this period, which began before the Cairo congress, and modern terminology is employed in this report. The following are the clinical histories, in summary form.

Case 1.—Maria G., Argentinian, female, single, 25 years of age.

January 1934. Diagnosis: Indeterminate.—The patient presented herself at the clinic with well-delimited erythematous macules, clear in the centers, the size of the palm, located on the left breast, the abdomen, and the right arm. Similar but smaller lesions were seen on the right leg.

Bacteriologic examination: Positive (1+). Lepromin reaction: Negative.

Chaulmoogra treatment started.

July 1936. Diagnosis: Reactional tuberculoid/borderline.—For a long time the patient had discontinued treatment (chaulmoogra) when she presented herself with disseminated polymorphous lesions on the body and limbs, of erythemato-violaceous color. Some of the lesions were simple spots (*manchas*) with diffused borders, while others were well-infiltrated plaques with clear-cut borders.

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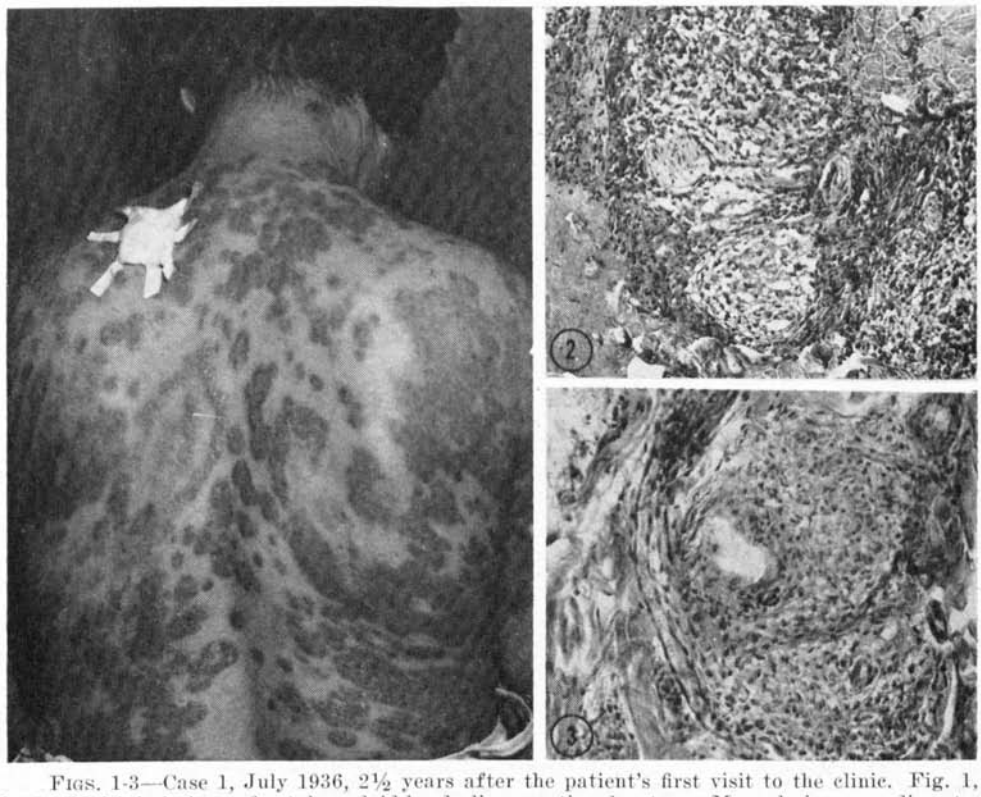
[1]Case No. 1 of this report was presented to the Argentina Leprology Society at a meeting held on November 18, 1960, and Case 2 at the November 29, 1960, meeting of the society.

The lesions on the back (Fig. 1) from which a biopsy specimen was taken (location indicated by the dressing), were very abundant and of various forms but mostly frank tuberculoid. Centrally, just to the left of the midline, was a large, pointed oval ring which apparently surrounded an immune area, within which secondary lesions of limited extent had arisen in the reaction. Slight disturbance of the general condition, with rise of temperature and feeling of weakness.

Bacteriologic examination: Positive (2+), bacilli abundant. Lepromin reaction: Negative.

Histopathology: In some fields one can see follicular structures of the reactional tuberculoid type, with abundant bacilli, and marked cellular edema—evidenced by vacuolization consequent on formalin fixation (Fig. 2). In other fields the structure is frankly lepromatous (Fig. 3).

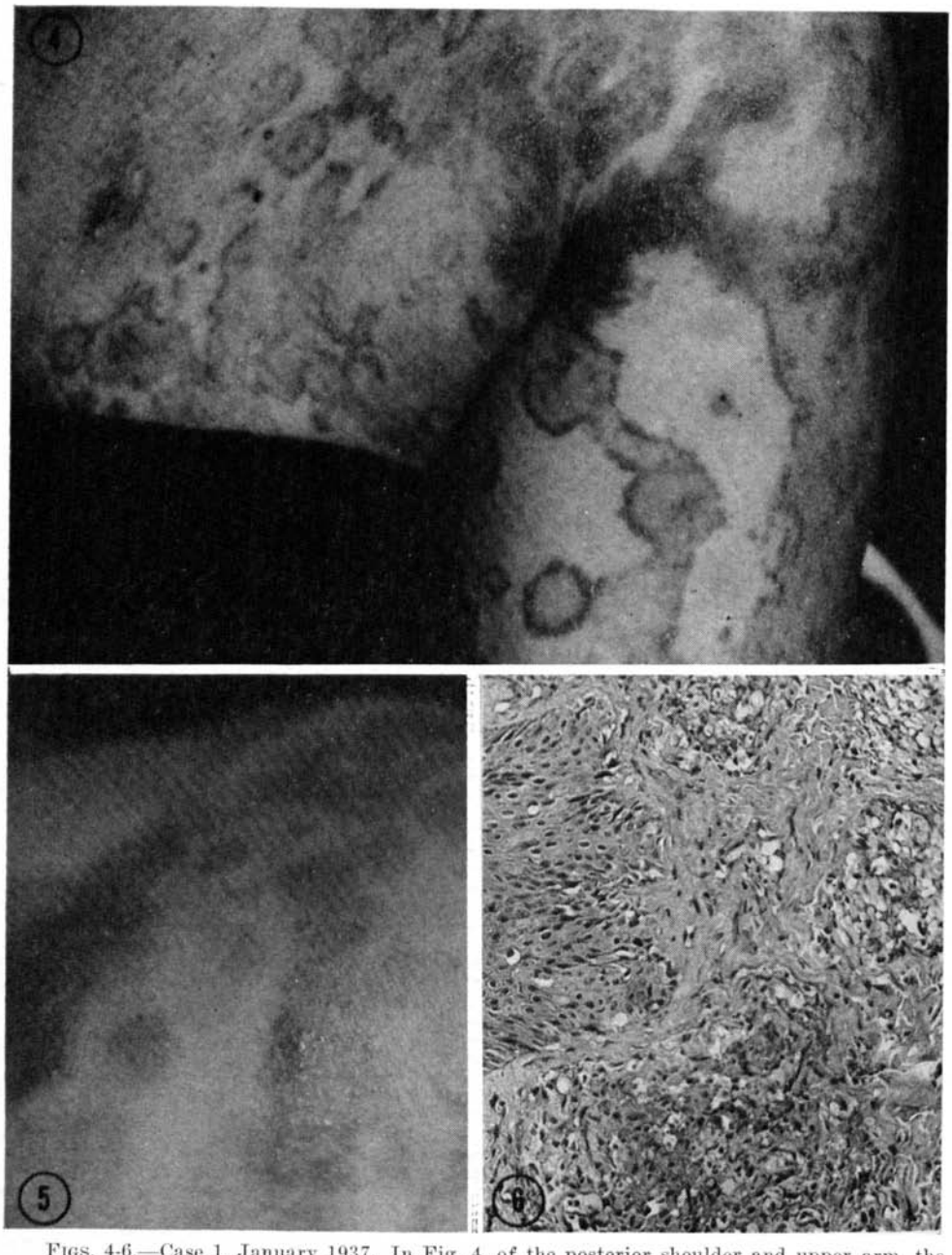


FIGS. 1-3—Case 1, July 1936, 2½ years after the patient's first visit to the clinic. Fig. 1, back. Multiple lesions of a tuberculoid-borderline reactional nature. Many lesions are discrete, in normal-looking skin, while others are merged into less clearly defined plaques. To the left of the central line of the mid-back is an ovoid linear lesion apparently surrounding an immune area in which nondiscrete secondary lesions have developed.

Fig. 2, photomicrograph of a field of the biopsy specimen, showing edematous tuberculoid elements of reactional nature. Fig. 3, another field of the same section, showing a frankly lepromatous structure.

January 1937. Diagnosis: Borderline-lepromatous.—Having been unable to continue chaulmoogra treatment in the previous six months,

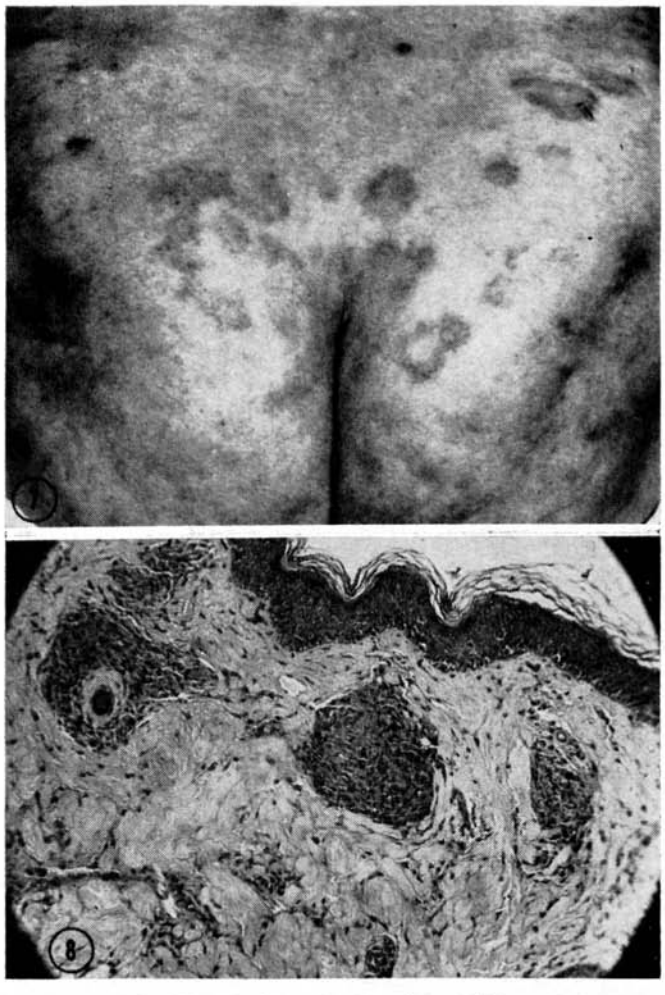
the patient presented herself at the clinic with lesions of variegated forms (Fig. 4). Some of them were spots and plaques of lepromatous



FIGS. 4-6.—Case 1, January 1937. In Fig. 4, of the posterior shoulder and upper arm, the lesions are of very different nature, largely geographic with infiltrated borders. An unusual feature is the papuloid aspect of some of the solid lesion areas.

Fig. 5, lepromatous lesions of the back, midline, of very different character from those seen in Fig. 1.

Fig. 6, photomicrograph, shows the lepromatous character of the biopsied lesion.



FIGS. 7 and 8.—Case 1, July 1945. Fig. 7 shows the newly-developed lesions on the buttocks, of tuberculoid aspect.

Fig. 8 is a photomicrograph which confirms the tuberculoid nature of lesions existing at this time.

type, markedly infiltrated with diffused borders and of sepia color. In places, as in Figs. 4 and 5, some of the lesions were of papuloid aspect. There was subacute iritis in the right eye.

Bacteriologic examination: Strongly positive (abundant bacilli). Lepromin reaction: Negative.

Histopathology: The lesion biopsied proved to be of typical lepromatous structure (Fig. 6).

The diagnosis of lepromatous was made at this time, not only because of the clinical aspect of some of the lesions, but also because of the occurrence of iritis, which of necessity is a lepromatous lesion, and this diagnosis was supported by the histologic findings in the specimen examined.

June 1945. Diagnosis: Tuberculoid.—From 1937 to 1944 the patient took chaulmoogra treatment regularly, and all of her lesions had improved. In 1944 she was started on sulfone treatment (Diasone), and

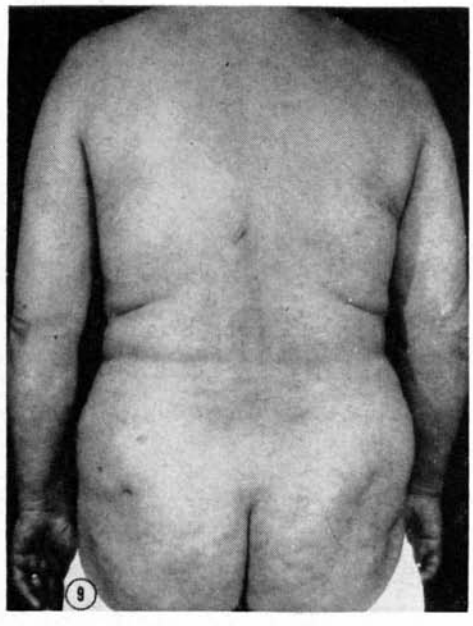


FIG. 9.—Case 1, January 1948, after 3 years of active sulfone treatment. Posterior aspect of the patient, showing complete absence of clinically active lesions, only a few pigmented residual spots remaining. (The patient was quite clear of residuae, and 2+ lepromin positive, when last seen, in 1960.)

the great majority of the lesions had subsided, only erythematoviolaceous spots remaining. In June 1945 she presented herself at the clinic with lesions on the buttocks, which were infiltrated with well-defined borders and of erythemato-violaceous color (Fig. 7).

Bacteriologic examination: Negative. Lepromin reaction: Negative.

Histopathology: Inflammatory foci of follicular pattern in the upper dermis composed of epithelioid cells and lymphocytes (Fig. 8).

January 1948. Absence of lesions.—At this time the patient was free from clinically active lesions; only a few residual pigmented spots could be seen (Fig. 9). She had taken regular and intensive sulfone treatment during the intervening 3 years.

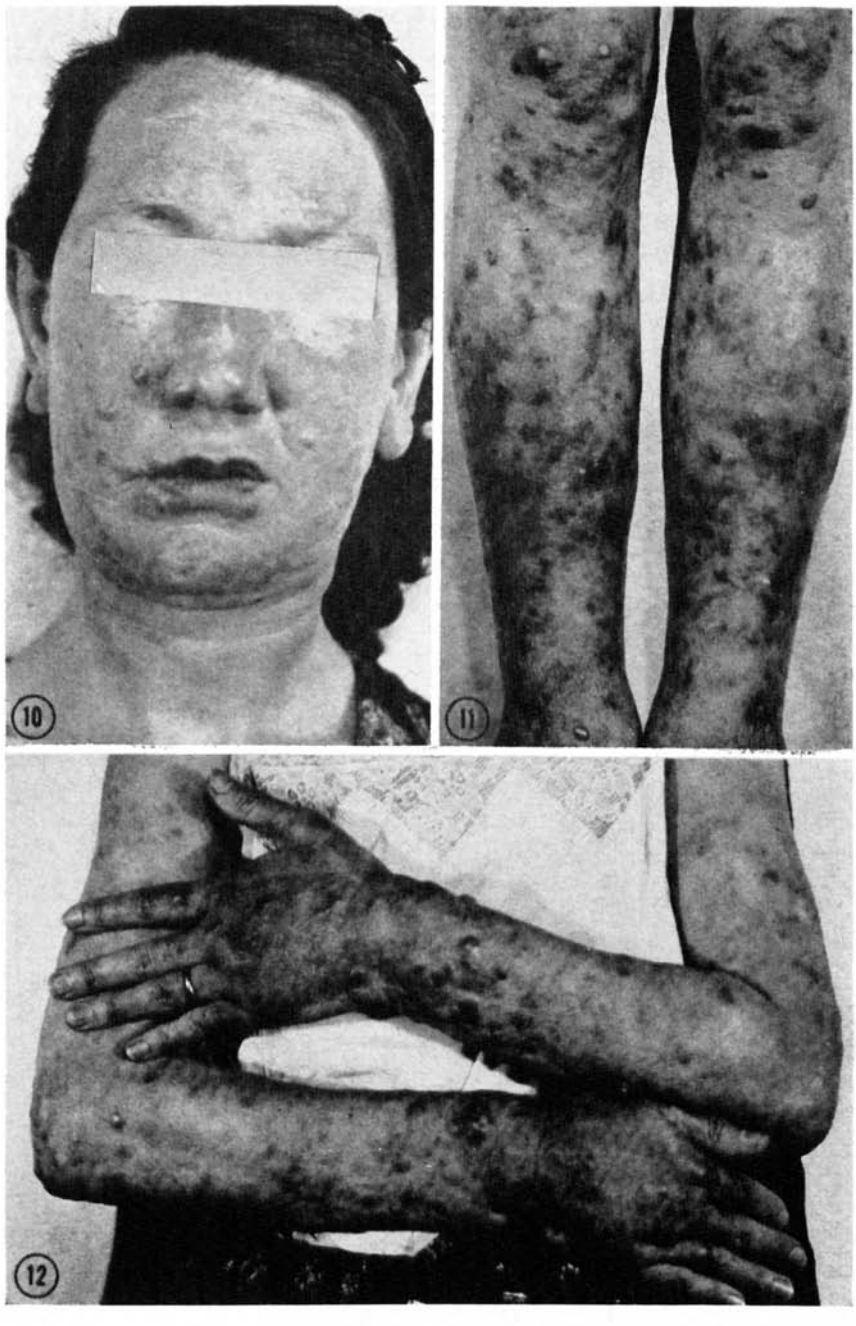
Bacteriologic examination: Negative. Lepromin reaction: Weakly positive.

January 1960. Complete regression.—The patient was completely free from lesions, even more so than when the 1948 picture was made. There were no muscular atrophies, and only some scars on the hands due to burns could be seen. In the interval she had continued to take sulfone treatment, although intermittently.

The lepromin reaction was now 2+ positive. She was definitely discharged, 26 years after her first consultation.

CASE 2.—Lucia P., Argentinian, female, single, 20 years of age. First seen in September 1940, the patient stated that her disease first appeared in 1936 with erythematous macules on the trunk and arms. The father also had leprosy, of the lepromatous type.

On further investigation of her history before she was seen at the



FIGS. 10-12.—Case 2, September 1940, four years after onset. Fig. 10, face. Extensive involvement is evident, with several peculiarly discrete small nodules presumably of lepromatous nature. Only the outer parts of the eyebrows have been lost.

Fig. 11, legs. Extensive spotty involvement, many spots apparently residuae of previously elevated lesions. A few discrete fresh little nodules, as on the face, are seen on the knees and the left ankle. Fig. 12, arms. Particular extensive involvement of forearms, wrists and hands, with elevated nodules of various sizes, some of them large and tending to confluence.

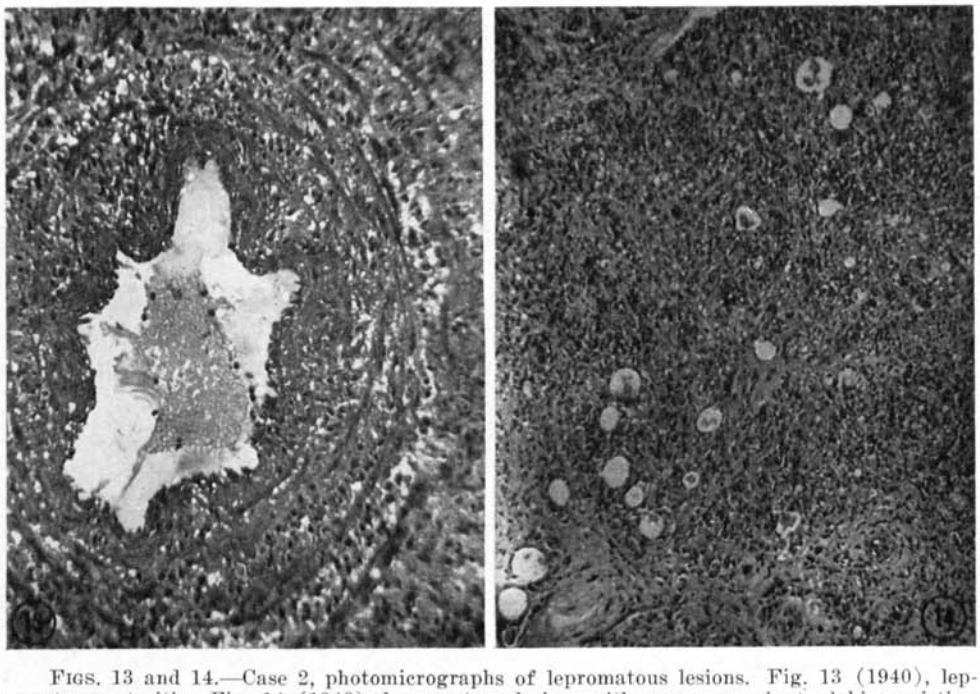
clinic, it was learned that she had consulted a dermatologist and was treated with chaulmoogra for 1½ years after which, her condition greatly improved, she abandoned treatment. In 1938 she married against advice, and in the following year had a child. Forty days later she observed new "nodules"—obviously a reactional condition, presumably of tuberculoid type—and these lesions augmented progressively, evidently through borderline to lepromatous.

September 1940. Lepromatous.—At this time, when the patient first presented herself at the clinic, the condition was taken to be definitely advanced (L2) lepromatous, but with lesions peculiarly disseminated widely over the integument as if by reactional episodes (Figs. 10, 11 and 12). She was admitted to the Carrasco Hospital and she remained there under chaulmoogra treatment for some three months, until December 1940, after which she continued treatment as an outpatient. While in the hospital, nodules were excised from the arms and forearms for use in preparing lepromin. Chaulmoogra treatment was begun.

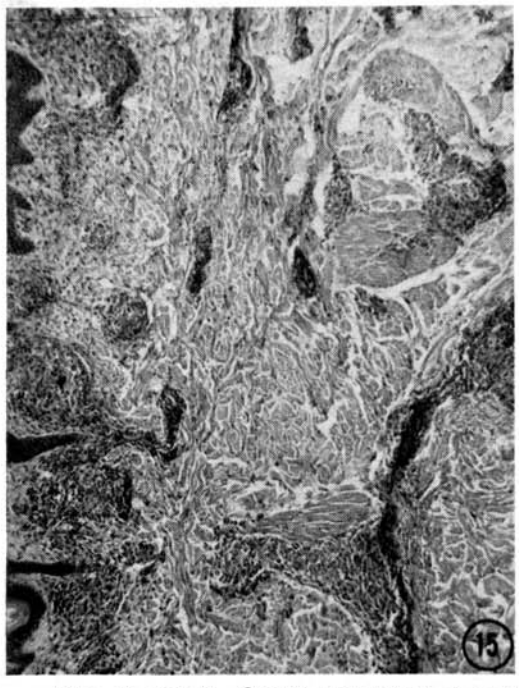
Bacteriologic examination: Frankly positive. Lepromin reaction: Negative.

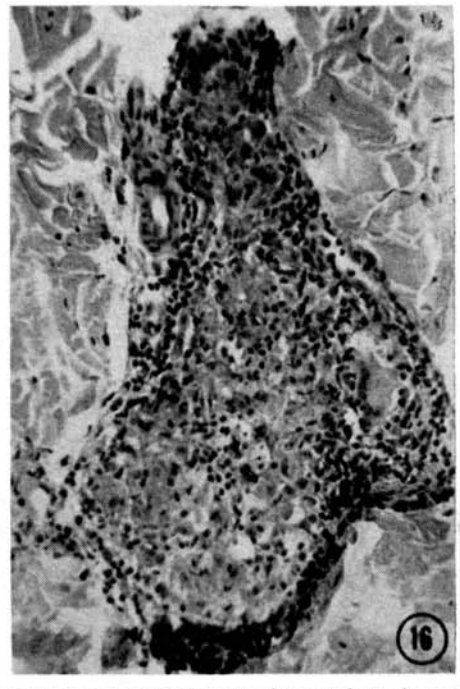
Histopathology: Typically lepromatous structure. The condition is evident in the finding of a lepromatous panarteritis, as shown in Fig. 13.

February 1948. Lepromatous.—After the patient was put under



FIGS. 13 and 14.—Case 2, photomicrographs of lepromatous lesions. Fig. 13 (1940), lepromatous arteritis. Fig. 14 (1948), lepromatous lesion, with numerous giant globi persisting despite regular treatment since 1940 (sulfone treatment since 1946).





FIGS. 15 and 16.—Case 2, April 1959, photomicrographs of a biopsy specimen taken eleven years after the 1948 biopsy was made. Fig. 15, low magnification, showing a zone of small tuberculoid foci superficially in the papillary layer, and a few less discrete foci deeper in the dermis. Fig. 16, high-power view of a complete tuberculoid focus, with one conspicuous giant cell, in the deeper dermis.

therapy she took the chaulmoogra treatment regularly until 1946, when intensive sulfone (Diasone) treatment was begun. Clinically, she had improved markedly, but active lepromatous lesions were still present. On this occasion she was accompanied by her young child, who was found to have a lone nodular lesion of the infantile tuberculoid variety.

Bacteriologic examination: Positive. Lepromin reaction: Negative.

Histopathology: A biopsy specimen taken at that time revealed a typical lepromatous structure persisting, with numerous giant globi (Fig. 14).

July 1951. Residual lesions.—The clinical examination showed erythemato-violaceous residual macules, and abundant cicatricial lesions corresponding to old lepromatous nodules. The sulfone treatment had been continued regularly and intensively. The general condition of health was very good.

October 1958. Reactional tuberculoid.—The patient presented herself at this time, frightened because of the appearance of new lesions a week before. Clinically, there were various erythemato-violaceous, infiltrated plaques with clear-cut borders on her back, right shoulder, lumbar region, buttocks, and face. All of these had the aspects of lesions of the reactional tuberculoid form. She was advised to intensify her sulfone treatment.

April 1959. Reactional tuberculoid in regression.—The process was frankly in regression, but there still persisted infiltrated plaques on the back and buttocks. Sulfone treatment was continued.

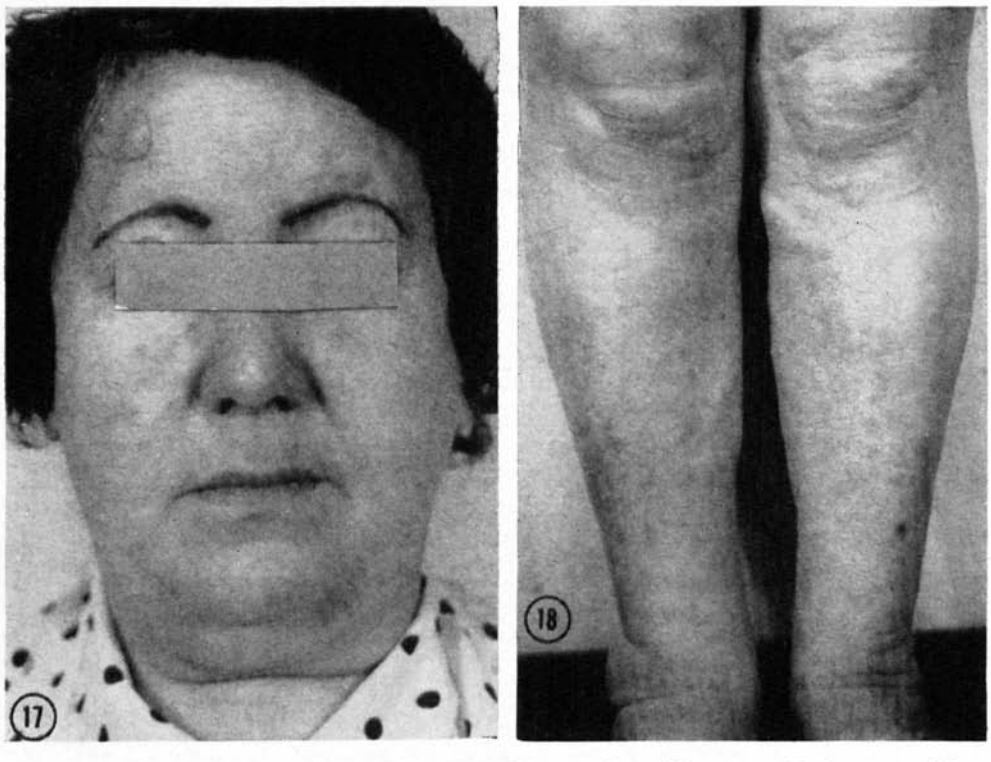
Bacteriologic examination: Negative. Lepromin reaction: Fernandez, negative; Mitsuda, positive, 1+.

Histopathology: A biopsy specimen from a plaque on the back showed clear follicular structures in the papillar layer, especially, and some deeper in the dermis (Fig. 15). In some foci the tuberculoid follicles were complete, with giant cells (Fig. 16).

September 1959. Complete regression.—The face was quite normal in appearance at this time (Fig. 17), in striking contrast with the original condition. Practically no lesions could be found except for several residual spots, violaceous and slightly atrophic, on the arms and legs (Fig. 18).

Bacteriologic examination: Negative. Lepromin reaction: Fernandez, positive, 1+ (Fig. 20); Mitsuda, positive, 2+.

The patient was discharged under observation, nearly 20 years after the first consultation.



FIGS. 17 and 18.—Case 2, September 1959. Fig. 17, face. No trace of lesions remaining. Fig. 18, legs, skin clear of active lesions, with only some residual areas remaining. (Compare with Figs. 10 and 11, pictures taken 19 years before.)

DISCUSSION

The articles of Wade and Rodriguez ([4]) and Wade ([5]), in which was demonstrated the existence of a form of leprosy intermediate between the polar lepromatous and tuberculoid types which the authors called "borderline," represent a valuable contribution to the understanding of the pathology of the disease. This form of leprosy constitutes the link which connects the other forms to each other, which permits a better insight into the phenomena of mutation from one type to the other.

The borderline group was accepted in 1952 by the First WHO Expert Committee on Leprosy ([8]), and was officially incorporated in the classification of the forms of leprosy by the Madrid Congress in 1953 ([2]). In a well-documented article by Gay Prieto ([1]) there is an up-to-date bibliography on the subject.

With the individualization of the borderline group, the structure of a leprous infiltrate is now limited to four possibilities: either it is (*a*) lepromatous (L), or (*b*) tuberculoid (T), or (*c*) borderline (B) (i.e., both lepromatous and tuberculoid), or (*d*) indeterminate (i.e., neither lepromatous nor tuberculoid, and only of microscopic grade, not forming clinical infiltrates).

One of the most important consequences which results from the identification of the borderline group is the necessity of reevaluating the classification of many patients who had been erroneously classified as lepromatous. Wade, with Perrin ([7]), has recently called attention to this matter by presenting a case which had been called lepromatous when first diagnosed as leprosy, but which diagnosis on reevaluation was changed to borderline.

The antecedent history of such patients is of much importance for the following reasons. If a primary lepromatous patient—i.e., one who was lepromatous from the onset of his disease, or at least from the time an indeterminate beginning became determinate—is placed under adequate treatment he will slowly improve, but even if his lesions and bacilli disappear he will still be essentially of lepromatous nature, potential or "latent." In case of relapse, he will be lepromatous again, because there had been no mutation of form, no change of background characteristics.

On the other hand, if a patient who presents as lepromatous but was originally tuberculoid and changed because of reactional tuberculoid and borderline phenomena (secondary lepromatous), is placed under adequate treatment he will improve relatively rapidly because he retains, latent, the potentiality of something of the resistance of the original tuberculoid form.

He may even experience while under treatment a mutation of form through an acute episode, that is to say, he may return to the original form and from that stage go on to healing. This phenomenon is called

the "reactional reversal phenomenon" by Wade ([6]). It coincides, up to a certain point, with the process described by Souza Lima ([3]) under the name "pseudoexacerbation."

With respect to Case 2 here reported, we must confess that at first we interpreted it as a mutation of a lepromatous polar form to tuberculoid. But on the suggestion of Wade (personal communication) who suspected, from examination of the photographs, that it might be an example of the reactional reversal phenomenon, we again reviewed the previous history of the patient and found that she had had a reactional phenomenon before reaching the lepromatous stage.

SUMMARY

The authors present two cases of leprosy whose disease began as of an indeterminate form. In later years they presented phenomena of exacerbation of the reactional tuberculoid and borderline type which took them to the secondary lepromatous stage.

Submitted to adequate treatment, both cases ultimately returned to their former tuberculoid form after having experienced a further process of exacerbation, after which their lesions disappeared and the lepromin reaction became positive.

The authors believe these two cases to be examples of the process which Wade calls the "reactional reversal phenomenon."

RESUMEN

Los autores presentan dos casos de lepra que iniciaron su enfermedad por una forma indeterminada. Posteriormente presentaron fenómenos de exacerbación del tipo tuberculoide reaccional y borderline hasta llegar a una etapa lepromatosa secundaria.

Sometidos, a tratamiento adecaudo, ambos casos regresan a su forma tubercloide anterior después de experimentar un nuevo proceso de exacerbación y luego desaparecen sus lesiones y la lepromino reacción se hace positiva.

Consideran a estas dos observaciones, como ejemplos típicos del proceso que Wade ha denominado "reactional reversal phenomenon."

RESUMÉ

Les auteurs présentent deux cas de lèpre chez lesquels la maladie a commencé par une forme indeterminée. Dans les années suivantes, ces malades ont présenté des phénomènes d'exacerbation du type tuberculoïde réactionnel et border-line qui les a menés vers une évolution lépromateuse secondaire.

Soumis à un traitement adéquat, ces deux cas sont revenus finalement à leur forme tuberculoïde antérieure après avoir subi un phénomène d'exacerbation, à la suite duquel leurs lésions ont disparu et la réaction à la lépromine est devenue positive.

Les auteurs croient que ces deux cas peuvent être des exemples de l'évolution que Wade appelle le "reactional reversal phenomenon."

REFERENCES

1. Gay Prieto, J. The concept and limits of borderline leprosy. Internat. J. Leprosy **27** (1961) 442-459.

2. [Madrid Congress] Technical resolutions. Classification of leprosy. Mem. VI Congr. Internac. Leprol., Madrid, 1953; Madrid, 1954, pp. 78-79.
3. de Souza Lima, L. The "pseudoexacerbation" reactional state of leprosy. Mem. III Conf. Panamericana Leprol., Buenos Aires, 1951; Vol. 1, 1953, pp. 184-188; *reprinted, translated in* Internat. J. Leprosy **23** (1955) 429-434.
4. Wade, H. W. and Rodriguez, J. N. Borderline tuberculoid leprosy. Internat. J. Leprosy **8** (1940) 307-331.
5. Wade, H. W. Relapsed and borderline cases of tuberculoid leprosy. Leprosy Rev. **12** (1941) 3-17.
6. Wade, H. W. A tuberculoid-like reaction in lepromatous leprosy; a reactional reversal phenomenon. Internat. J. Leprosy **23** (1955) 443 (editorial).
7. Wade, H. W. and Perrin, S. R. A case of advanced borderline leprosy. Reevaluation of a case originally reported as lepromatous. Internat. J. Leprosy **29** (1961) 460-472.
8. World Health Organization, Expert Committee on Leprosy; First Report. Wld. Hlth. Org. Tech. Rep. Ser. No. 71, 1953, pp. 19-22.