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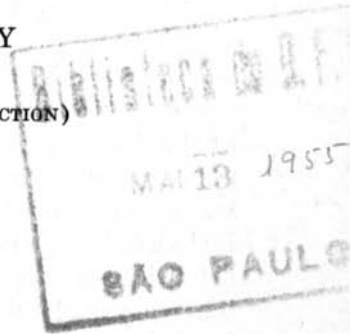
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REACTIONAL STATES IN LEPROSY

LEPRA REACTION
TUBERCULOID REACTIVATION (TUBERCULOID LEPRA REACTION)
REACTIONAL TUBERCULOID LEPROSY
BORDERLINE (LIMITANTES) LESIONS¹

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The term "lepra reaction" is used by many authors as a general one to designate a class of processes which are entirely different clinically and pathologically, whereas others use it in a more limited sense. It is therefore highly desirable that an understanding be arrived at. The following presents our views on the matter.

If "lepra reaction" were to be used in the generic sense it would comprise three groups of clinical phenomena: (1) The classical lepra reaction, a syndrome similar to that of erythema nodosum, erythema multiforme, erythema exudativa, etc., a condition exclusive to the lepromatous type; (2) reactional tuberculoid leprosy, which some authors call "tuberculoid lepra reaction," including the transitional lesions; and (3) the outbreaks (*surtos*) of acute reactivation and exacerbation of the disease,² occurring in any of its clinical forms. This list of these clinical phenomena shows how varied they are in their pathogenic significance.

¹ A translation from the Portuguese, approved by the authors. This is a solicited contribution, requested at the time of the meeting of the WHO Expert Committee late in 1952 and prepared before the Madrid congress, the publication delayed by the translation.—EDITOR.

² The term "surto," frequently used in the original manuscript, is usually but none-too-satisfactorily rendered "outbreak," sometimes as "episode." Item (3) above, originally reading, "Os surtos agudos de reativação, acutização, exacerbção da moléstia..." has been somewhat simplified here and later, because there is no English equivalent for the word "acutização" and because the idea is sufficiently covered without it.—EDITOR.

The first of these conditions, "lepra reaction" proper—often, if unfortunately, called "erythema nodosum leprosum"—is an intercurrent event which occurs only in cases of the lepromatous type. Its clinical and structural aspects are familiar, but little or nothing is known about its pathogenesis, mechanism or significance. Is it a phenomenon of allergy or parallergy? Is it due to some kind of sensitization, either specific to the Hansen bacillus or paraspecific due to heteroallergization by the Koch bacillus or some other organism? It is even a debated question whether it is ultimately beneficial or injurious.

The second kind, reactional tuberculoid leprosy (RTL), constitutes a variety of the tuberculoid form, perfectly individualized by its clinical, bacteriological, immunological and structural aspects. It is not an intercurrent event as lepra reaction is; it is an incontestible clinical variety of the disease. As a "reaction" it has only the fact of its acute and abrupt appearance, in contrast with the other varieties of the tuberculoid type, whose onset is slow and whose evolution is more or less chronic. Also included here are the transitional, *limitantes* lesions, the "borderline" condition of Wade, which undoubtedly constitutes a form apart from the reactional tuberculoid condition, although it almost always originates from it.

The third group comprises all the acute episodes of activation and aggravation of the disease,² occurring in cases in a state of chronic evolution, or in a stationary phase, whatever may be the type of the case. The appearance of these reactional phenomenon in such cases always signifies clinical worsening. The normally chronic evolution of the disease is speeded up, or the quiescent state is interrupted, and the lesions are aggravated.

It seems to us illogical to group phenomena of varied nature, clinical aspect, and significance under "lepra reaction," using the term in a generic sense. Rather we would reserve the term for the classical condition, intercurrent in lepromatous leprosy, as indicated. For the acute phenomena of aggravation of the disease which occur in any and all of the clinical forms, we employ the terms acute activation, or acute reactivation, or clinical exacerbation.²

Otherwise, the classical concept of "lepra reaction" should be abandoned. If this should be done, the term being used generically to designate all of the acute episodes in the evolution of leprosy, it would be necessary to use "erythema nodosum" for the reactional phenomena occurring in lepromatous leprosy—and we believe that term not suitable for the purpose.

What is essential and fundamental is that it be recognized that there exist acute phenomena which are varied in their pathogenic significance. On one hand—a clinical fact—there is the kind which is intercurrent in a given clinical type lepra reaction. This is an event which has defied the ingenuity of leprologists to explain. The condition is precipitated by causes apparently of the most varied nature, even emotional. Its course

is variable; some cases improve under specific therapy while others become worse; indeed, the condition may be precipitated by the treatment itself. Its treatment is limited to palliation of the acute symptoms, there being no treatment that is specific, all or none may give results. The condition may constitute a serious complication for the patient because, apart from the symptoms and damage it causes, it often necessitates interruption of treatment. Dependent on type and intensity, it may even lead to a fatal ending. The fact that the patient, having one or more attacks of this acute condition, which is commonly repeated, relapsing (*recidivante*), may subsequently show improvement of his clinical lesions constitutes another unanswered problem in the pathogenesis and pathology of leprosy.

On the other hand there are banal phenomena, acute or subacute, in the course of evolution of this chronic disease: a simple, rapid, progressive evolution which does not constitute a problem for the physician except for the clinical worsening of the case, which always happens.

When the phenomenon of reactivation occurs in cases of the circinate or marginate tuberculoid variety,³ whether or not accompanied by the appearance of new lesions of the same type, it cannot at the time be confused with what we call "reactional tuberculoid leprosy." The latter we regard as a clinical variety of tuberculoid leprosy which has nothing of "reaction" but its acute onset. They are not the same thing; they constitute entirely different clinical entities. This distinction was not made in the reports in which reactional conditions in tuberculoid leprosy were first recognized (6, 3), nor is it made by all writers today.

The purpose of this article is to focalize the fundamental characters of: (a) tuberculoid reactivation, an acute or subacute process which occurs in the chronic evolution of the circinate or marginate tuberculoid variety and which, besides modifying its classical clinical aspects, equally modifies its structure and sometimes even its prognosis; (b) reactional tuberculoid leprosy (RTL), distinguished as a separate variety of the tuberculoid form; and (c) the borderline (*limitantes*) lesions whose features—especially the evolutive one—justify the placing of the cases in an intermediate group between the tuberculoid and the lepromatous forms.

CLINICAL ASPECTS

TUBERCULOID REACTIVATION

In the acute exacerbation occurring in the circinate variety of tuberculoid leprosy, the pre-existing lesions become active and sometimes increase in size, and new lesions may appear; these are always structurally identical with the old ones (Figs. 1-4). Involvement of the nerves is frequent in this phase of the disease. This condition is well described by Souza Lima and Maurano (3):

³ This refers to the "minor" variety.—EDITOR.

In patients with this type of tuberculoid lesions, sometimes of many years duration, we are struck by the contrast [between this acute condition and the kind of reaction in] the lepromatous type. This one is of relatively weak intensity, often giving the impression of being a purely local phenomenon.

The eruption is discrete, *never* (italics ours) causing general disturbance. It starts insidiously, slowly, and the patient becomes aware of it only on noting a more or less distinctly infiltrated erythematous plaque on his face, either in the superciliary or malar region, or on the jaw or the lip. This is the sign by which it can be recognized; and it is also evident at the same time that changes are taking place in the pre-existing circinate leprids, changes which will be noticed by the patient only later.

In the period of the reaction state the lesions are more infiltrated [then before] and more erythematous, that being the predominant color. At the same time, some of the pre-existing lesions will have increased in size. The central area may undergo less marked changes, but it also may become more erythematous and exhibit a certain degree of infiltration.

This condition is variable as to duration and intensity. If the reactivation is slight and of short duration, it may be seen only in the pre-existing lesions. At the other extreme there may occur relapses so intense that there is transformation from the marginate variety to the truly reactional picture.

Souza Lima and Maurano noted that these reactions of the circinate leprids, besides prolonging their duration, accelerate their centrifugal spread. They may also lead to severe nerve involvement and consequent trophic changes, insidiously and without change in the size of the nerves. These things do not improve the prognosis as regards recovery without deformities.

Bacteriologically, the lesions usually remain negative. This is one of the features that differentiate this phenomenon from reactional tuberculoid leprosy, in which positivity—although transitory—is almost the rule.

Lepromin reactivity is usually not modified, remaining positive in most cases. It may eventually become negative if there is transformation to the reactional variety, but even then that is not invariable.

REACTIONAL TUBERCULOID LEPROSY

The acute condition in which there appear the lesions of polymorphous aspect which characterize the reactional tuberculoid variety of leprosy (RTL) may be primary, but usually it is secondary in indeterminate or even tuberculoid cases (circinate variety in reactivation). When they are primary they constitute the initial manifestations of the disease. When they are secondary they constitute an abrupt mutation of type of the disease from indeterminate to tuberculoid, or from one variety of tuberculoid to another.

In either case the lesions consist of tubercles, nodules, plaques (Figs. 7 and 8) or even erythrodermic exanthems (Figs. 5 and 6), isolated or conglomerated, with predominance of one or another of the elements that constitute the distinctive picture of the condition. This RTL variety

occurs in susceptible individuals with unstable resistance, which conditions the benign or malignant evolution of the case. It is not an intercurrent condition. If the lesions disappear and are cured, the leprosy is equally cured. On the other hand, the condition may become borderline, as will be seen. The clinical and other characteristics of this variety of the tuberculoid type are distinctive.

As regards onset, the reactional tuberculoid leprids are as has been said—generally secondary to pre-existent lesions of the indeterminate kind, whether cutaneous (macules) or neuritic (areas of anesthesia). Alternatively, the case may have been of an atypical tuberculoid variety, or—more rarely—of the circinate variety in relapse of exacerbation. On the other hand the condition may be primary, appearing “*d’emblée*” in apparently healthy individuals, the eruptive outbreak constituting the first manifestation of the disease.

The clinical lesions of RTL are very varied, but those that have been mentioned are especially noteworthy. The nodules and tubercles are usually rounded, superficially located, varying as regards infiltration from moderate to succulent and in color from erythematous or erythematoviolaceous to wine color, distributed in a more or less generalized fashion over the entire tegument. When these elements predominate the patient has a syphilitic aspect. The plaques are of variable sizes, from 2-3 cm. to 8-10 cm. in diameter, of the same color as the nodules and usually markedly infiltrated. They are well demarcated from the surrounding healthy skin, this being one of the features that differentiate these plaques from the borderline lesions, the outer borders of which merge gradually into the surrounding skin.

These lesions exhibit a peculiar, constant and distinctive feature in their localization. Those of the face are located by choice in the malar and superciliary regions, on the forehead, the lips, and the jaw. On the upper lip they frequently invade the naso-labial mucosa and semi-mucosa. Frequently a large plaque covers the upper part of one-half of the face, involving the eye and in time leading to lagophthalmos. Other preferred and distinctive localizations are the palmar and planter regions. More bizarre locations are the scrotum, the anus, the nipple, and the soft palate. When the condition is generalized, the scalp may also be involved.

The type of lesion called erythrodermic, less frequent, consists of an extensive plaque involving all of a segment of an upper or lower limb, covering it like a sleeve (Fig. 6). In color it is intensely erythematous or wine colored; the infiltration is of more moderate degree than in the other lesions described. These areas exhibit desquamation, sometimes marked, especially when receding.

The number of the lesions and the intensity of the RTL outbreak are very variable. In general the lesions are of exanthematic nature, with involvement of most of the skin surface; more rarely they are

localized, with few eruptive elements. The condition practically never appears with only one of these types of lesions; usually all three types—nodular, plaque-like, and erythrodermic are associated. These reactional tuberculoid leprids may appear during the outbreak, but more often they are secondary and late. The condition may involve the nerves, leading to muscular atrophy.

The bacteriological findings help to differentiate this condition from the other tuberculoid varieties, for the lesions are almost always positive from the beginning of the eruption. Even the nasal mucosa may be positive, although less frequently. Positivity, however, is transitory, depending largely upon the duration of the condition. Sometimes the lesions become negative after 3 to 6 months; at other times they remain positive for 8 to 12 months. The duration of positivity—as of the outbreak itself—is very variable, apparently depending upon the degree of resistance of the individual.

Lepromin reactivity may likewise undergo variation, there being practically always a relationship with the bacteriological findings. Thus at the beginning the results of the test are usually negative, becoming positive as the condition declines. Some cases, however, are positive from the onset, corresponding to an initial bacteriological negativity.

The evolution of the reactional tuberculoid leprids is always acute and rapid, as compared with the other tuberculoid varieties. Once the eruptive outbreak has started the lesions tend to acquire, and to be stabilized in, their own distinctive morphology. As said, the morphology is very variable, but one of the various forms of cutaneous elements predominates until the long period of regression begins. The lesions then become disinfiltated, flattening out, and at the same time become more pigmented, from erythematous-violaceous to dark maroon. With the leveling, atrophy begins to appear, quite pronounced in some cases. The pigmentation ultimately disappears, and hardly anything is left but the atrophy, which in some cases is almost pathognomonic.

In a certain proportion of RTL cases, however, the first outbreak does not retrogress completely. The lesions become flat, but they remain erythematous and without atrophy, and are persistently bacteriologically positive. In these cases new outbreaks are liable to occur, old lesions becoming infiltrated again while new ones appear. With this there is some disturbance of the general condition, with fever or a subfebrile state, pains and edema of the principal joints, and general malaise. These are the cases which sooner or later tend to transform to the borderline form, and from that to the lepromatous type.

The reactional tuberculoid variety is the least stable form of the tuberculoid type of leprosy. The uncertain prognosis depends on the state of resistance or of sensitization of the organism. If the sensitization persists without giving rise to a state of resistance (i.e., if the lepromin reaction remains negative) the case has a tendency to new

outbreaks and unfavorable developments. On the other hand, if the resistance increases (i.e., if the lepromin reaction becomes positive) the tendency is toward recovery, which may be entirely spontaneous.

THE *LIMITANTES* OR "BORDERLINE" GROUP⁴

Observation of cases of the reactional tuberculoid variety reveals the existence of a group which, clinically and otherwise, can be differentiated as having much similarity to certain lepromatous lesions. To this group Wade (7, 8) considering especially the peculiar morphology of the lesions, which as has been said taper off at the edges instead of being sharply delimited, and also the fact that they are markedly and persistently positive bacteriologically, gave the name of "borderline"—that is, marginal (*limitantes*)—because they present features of both of the two polar forms, tuberculoid and lepromatous. The fact that such lesions occur frequently with repetition of the reactional tuberculoid outbreaks explains why they were also called "lesions of relapse." Subsequently, however, it was found that some cases may be of this kind from the outset.

The most important fact that led to the individualization of cases with these lesions, as an unstable intermediate group between the reactional tuberculoid form and the lepromatous type, is the frequency with which they evolve to the latter kind. This position is justified for various other reasons, clinical, bacteriological, immunological and histological.

Clinically the appearance of the lesions may be the same as those of the reactional tuberculoid variety, especially when primary (Figs. 9-12). In this case the distinction is based mainly on coloration—the superimposition of a characteristic sepia, yellowish-rusty to reddish-erythematous color characterizing them. This is one of the things that accounts for their relation with lepromatous lesions.

Morphologically these disseminated intermediate lesions appear as large plaques and nodules of varied sizes, with borders sometimes well-defined and sometimes indefinite, and with infiltration ranging from moderate to succulent. At times the character of the outer limit is an important differential element because, instead of being clear-cut, it diffuses and merges into the surrounding skin. Internally, this same border exhibits a special aspect: it embraces, as a relapse eruption, an area where previously there was a reactional lesion. The new lesion surrounds the site of the old one, and therefore its inside edge is well-defined, in contrast to the outer edge. In this case the lesion consists of a more or less broad border, less infiltrated than the lesions from which they originated, surrounding a central area in which the skin may be of normal appearance or slightly atrophic (Figs. 13 and 14). In these outbreaks, in

⁴ Only in the heading of this section and one other place in the original manuscript does the term "borderline" appear; elsewhere "*limitantes*" is used. Since that word has no exact counterpart in medical English, it is usually rendered as "borderline" in this translation.—EDITOR.

which also the lesions are polymorphous, there may be new ones of various sorts and sizes with the peculiar coloration that has been described.

The bacteriological findings again are characteristic. The lesions are more markedly and more persistently positive than are those of RTL. As for the immunological factor, the lepromin reaction is constantly negative.

HISTOPATHOLOGICAL ASPECTS

LEPRA REACTION

Although a study of the dermatological elements peculiar to this intercurrent phase of lepromatous leprosy is not within the scope of this article, its histopathological aspects are summarized here to serve as a basis for comparison with the lesions in which we are especially interested.

Sections of the elements of "lepra reaction" exhibit vascular dilatation accompanied by interstitial edema and exudation of polymorphonuclear leucocytes, and sometimes eosinophiles in variable numbers. This exudate, according to the findings of other investigators and our own experience, is always in relation with lepromatous infiltrations of greater or lesser degree, sometimes very slight. If slight they may not have been clinically discernable until made visible by the reactional outbreak. This may lead to the erroneous impression that lepra reaction lesions occur in normal skin.

It is noteworthy that these lepromatous infiltrates are always conspicuously regressive, with foamy Virchow cells markedly vacuolated by lipids and with picnotic nuclei, and usually containing relatively small numbers of granular bacilli. In the course of the reaction these lesions are invaded and markedly disturbed by the polymorphonuclears and the edema fluid.

These infiltrates must have preceded the exudative phenomenon of the reaction. Being granulomatous lesions, they could not be produced as quickly as the latter. The regressive aspect, which is constant, must also have existed before the reaction, for the same reason.

The exudation of polymorphonuclear leucocytes is rapid and transient, so that these elements may no longer be found in reaction lesions removed late, although we may find numerous lymphocytes in place of them. After the reactional condition has passed, the exudative elements all disappear but the lepromatous infiltrations which were invaded by them still remain.

Briefly, in terms of histopathology "lepra reaction" in the clinical sense can be defined as an exudative process with implantation of polymorphonuclear leucocytes as an intercurrent condition on the substrate of a pre-existing granulomatous (lepromatous) process. The pathogenesis of lepra reaction is obscure, but it all happens as if, at a certain time, there occurs in regressive lepromatous lesions some leucotactic substance the nature and origin of which—whether bacillary or cellular—is unknown.

The fact that the exudative phenomenon is constantly associated with a lepromatous lesion is one of the reasons why we regard as unsuitable the terms "erythema nodosum," which has often been applied to this intercurrent condition of lepromatous leprosy. However, the finding by Portugal, Carneiro and Zeo (2) of the same histopathological element (radiating granuloma) in the lesions of lepra reaction which Miescher considered specific for the authentic erythema nodosum, makes the matter worthy of a more thorough investigation.

TUBERCULOID REACTIVATION

The histopathological changes of the "tuberculoid reaction" consist simply of an intra-and intercellular edema of the typical tuberculoid granuloma (Figs. 15 and 16). The latter, being a well-known histopathological structure, will not be described here. Although in the tuberculoid reactivation phase the cells of the granuloma appear vacuolated, the examination for lipids is always negative.

This picture can obviously be confused with that of reactional tuberculoid leprosy (see below), except that in the latter we do not find the typical tuberculoid granuloma. In many instances this permits the histopathological differential diagnosis between the two conditions.

As for the bacteriological findings, these lesions differ in no respect from the typical tuberculoid granulomas. Most of them are negative, and when bacilli are found they are usually few.

REACTIONAL TUBERCULOID LEPROSY

In the lesions of this form of leprosy the histopathological examination reveals a chronic inflammatory infiltrate, of variable intensity, composed mainly of epithelioid cells. In the most typical form of this structure the epithelioid cells are grouped chiefly in peri-or paravascular locations, forming rounded, nodular agglomerates (Figs. 17 and 18). These are distributed along the papillary body, accompanying the lower edge of the epidermis, and they also extend more deeply in relation to the vessels or nerves and the cutaneous appendages. When the intensity of the process is great, these fundamental nodules may be seen to have fused or to have formed infiltrative cords of various sizes.

An important aspect of these lesions is that, in keeping with the succulent appearance of the gross lesions, they are infiltrated by edema fluid. The edema is seen both inside the epithelioid cells and between them. The fluid also insinuates itself between the collagenous fibers, an interstitial edema. The edematous epithelioid cells have a frankly vacuolated appearance, while the intercellular fluid makes the infiltrates appear loosened and dissociated.

This is one of the important aspects which differentiate RTL from the typical tuberculoid granulomas. The latter, especially when in the quiescent state and therefore free from edema, present a compact structure with the nonvacuolated epithelioid cells closely packed together. When

in the state of "tuberculoid reactivation" the lesions, although disturbed by edema, retain their tuberculoid aspects, and in most cases this permits their histological differentiation from the lesions of RTL which do not have the typical tuberculoid structure.

Langhans giant cells may be present in variable numbers in the RTL lesions, but they may be completely absent. As a general rule, even when present in some numbers, they are less numerous than in the typical tuberculoid granulomas. Lymphocytes are usually present, also in variable numbers, and without the usual tendency to form halos around the epithelioid nodules. Polymorphonuclear leucocytes, the most characteristic component of the lepra reaction lesions, never appear in the RTL lesions.

Although the epithelioid cells of RTL are frankly vacuolated they never contain lipids, except perhaps some insignificant granules. This fact aids, to a certain extent and without resorting to special stains for fats, in differentiating these cells from the Virchow cells. The edematous, vacuolated epithelioid cell usually has a single large vacuole which causes lateral pressure on the nucleus, which is elongated and bent, whereas the Virchow cell in fatty degeneration appears perforated with smaller vacuoles which give it its foamy appearance, and the nucleus—generally picnotic—may occupy any position in the cell.

The bacteriological findings in the RTL lesions are varied and irregular. Taking different lesions of the same histology, we find some without bacilli, others with few, and still others with many, but on the whole there are considerably more positive than negative lesions. In even the most markedly positive ones the bacilli are less numerous than in active lepromatous lesions. Moreover, they do not show much tendency to form globi, being by preference scattered irregularly inside the cells. Regarding morphology, it is our experience that both normal—i.e., solid—and granular forms may be found, either in the same lesion or different lesions, without any apparent relation to the histological aspect.

The RTL lesions therefore, consist of a granulomatous process approaching the tuberculoid structure to which there is intimately related—and not occurring as an intercurrent event—an exudative process represented only by edema, without the participation of polymorphonuclear leucocytes. The edema is responsible for the succulent microscopic aspects of the lesions, and for their markedly infiltrated clinical aspect.

THE BORDERLINE LESIONS

From the histological point of view the borderline (*limitantes*) lesions of leprosy are those which, because of their microscopic characteristics, cannot be diagnosed with certainty as either lepromatous or reactional tuberculoid. Consequently, they have an intermediate position between the two.

There are two ways by which a lesion may confuse a pathologist, placing him in doubt between these two diagnoses: (1) By the coexistence

in the same lesion, and even in the same histological section, of parts that are lepromatous and parts that are similar to the RTL lesions. There is no superimposition, or, better said, confusion of these two pictures; if they coexist they are independent. Souza Lima and Rath de Souza (4) referred to these lesions, which they began to see after the introduction of sulfone treatment, as "pseudo-exacerbation" of leprosy. (2) By the intimate fusion of the features peculiar to lepromatous leprosy and to reactional tuberculoid leprosy, these appearing in such a confused and superimposed manner as to make it very difficult or even impossible for the examiner to say which of these two kinds of lesions it actually represents. So the pathologist, hesitating between these two diagnoses, and fearful of applying one of them with the risk of being contradicted by the later evolution of the case, prefers to use a less compromising terminology, such as "transitional," "borderline," "*limitante*," etc.

Of the two kinds of borderline lesions mentioned, the second is the one which interests us at the moment, and for this reason it is here considered in further detail.

(a) The general architecture of the infiltrate: As a rule the infiltration is so marked that the essential rounded, nodular structures distinctive of RTL are so compressed and fused that they cannot be distinguished. Consequently, we have an apparently amorphous—or, better said, monomorphous—infiltrate which resembles an intense lepromatous infiltration, a leproma. Sometimes, however, it is possible to make out, here and there, the rounded, nodular structure distinctive of RTL lesions. So it is that, as regards architecture, the borderline lesions sometimes resemble the lepromatous kind, while sometimes the diagnosis leans to the side of reactional tuberculoid leprosy.

(b) Cells: In great part the cells present elongated, curved hyperchromic nuclei, resembling those of the epithelioid cells, frequently with a vacuolated cytoplasm as in the cells of RTL, apparently caused by intracellular edema as in those cells (Figs. 19 and 20). However, mixed with these cells there are also others, in variable numbers, that do not have the epithelioid appearance. These cells present vesicular nuclei and non-vacuolated cytoplasm, and are therefore similar to the nonregressive lepra cells, i.e., the nonfoamy Virchow cells. No tendency to giant cell formation is seen. Lymphocytes and plasma cells may be found in variable numbers, but not polymorphonuclears. The cytological analysis, because of the constant presence and usual predominance of vacuolated cells of the epithelioid type, inclines the histopathologist to classify the lesion on the side of reactional tuberculoid leprosy.

(c) Bacilli: These are always numerous, usually forming globi. This is the most important cause of doubt in the classification of the lesion. In fact, in certain cases in which the lesion, although not perfectly typical, presents an architecture and cytology in favor of RTL, the numbers of bacilli and globi are so great as to justify the diagnosis of borderline lesion.

(d) Lipids: The borderline condition has attracted our attention only relatively recently, and we do not yet have definite information regarding the occurrence of lipids in the lesions, whether active or in the phase of involution. In Fig. 20 is shown a borderline lesion diagnosed in 1942 which we examined for lipids with negative results. (In 1950 this patient was lepromatous, confirmed histologically.)

ABSTRACT

In orientation, the authors assert that in its classical sense the term "lepra reaction" applies only to the condition often called "erythema nodosum leprosum," which occurs only in lepromatous leprosy. If however, that term were to be used in a generic sense it would also include two other conditions dealt with especially in this article, (a) what they call "reactional tuberculoid leprosy," considered a distinct clinical variety of the tuberculoid type but actually not a reactional condition at all; and (b) the acute episodes (*surtos*) of activation of the disease occurring in cases of any type. They recognize, furthermore, that cases with the *limitantes* form of lesions, the "borderline" condition of Wade, are a group apart from the reactional tuberculoid variety, although allied to it. In any case, it is fundamental that there are acute phenomena that are intercurrent in a clinical type, and others that represent acute activation or progression of the disease itself.

Specifically with respect to tuberculoid leprosy, this acute activation (tuberculoid lepra reaction) occurs usually in the chronic course of the circinate (minor) form of that type. It should not be confused with "reactional tuberculoid leprosy," which they hold has nothing reactional about it except its acute onset.

The main part of the paper is devoted to (a) tuberculoid reactivation (the lepra reaction in tuberculoid leprosy, or the tuberculoid lepra reaction, of some writers), (b) reactional tuberculoid leprosy (held by the writers to be a distinct clinical variety), and (c) the *limitantes*, or "borderline" condition (which they agree should be distinguished, as a phase intermediate between the tuberculoid and lepromatous types). The clinical features of these conditions are dealt with first, and then the histopathology. The latter section begins, for comparison, with notes on what the authors regard as the classical lepra reaction.

ABSTRACTO

Los autores afirman que en su sentido clásico el término "lepra reaction" se aplica solamente a la condición frecuentemente llamada "erythema nodosum leprosum," la cual ocurre solamente en lepra lepromatosa. Si el término se usa en sentido general, debe incluir otras condiciones tratadas en éste artículo, (a) "reactional tuberculoid leprosy" que se considera una variedad especial del tipo tuberculoide y no es una condición reaccional verdadera; y (b) los episodios agudos (*surtos*) de activación de la enfermedad y que pueden ocurrir en casos de cualquier tipo. Los autores reconocen que los casos con lesiones "limitantes," las "borderline" de Wade, son un grupo distinto

APPENDIX
Summary tabulation of the main features of the conditions discussed.

| | (1) Lepra reaction ('ENL') | (2) Tuberculoïd reactivation | (3) Reactional tuberculoïd leprosy (RTL) | (4) The borderline condition |
|-------------------|--|--|--|--|
| Origin | Acute onset. Intercurrent, in L leprosy only (about 60% of cases). May be initial manifestation. | Slow onset. Intercurrent; appears in the chronic evolution of T leprosy. | Acute onset. Secondary, in macular cases or, rarely, circinate T in reactivation. May be initial manifestation. | Acute onset. Usually secondary to RTL after repeated relapses; may be initial manifestation of the disease. |
| Eruptive type | Lesions similar to erythema nodosum, multiforme, etc. Frequent neuritic, ocular or orchitic complications. Frequently relapsing. | Pre-existing lesions present activated borders. Infiltrated, enlarged, reddish; new lesions may appear. Never abrupt outbreak as in RTL. | Polymorphous lesions (tubercles, nodules, plaques, etc.), reddish or wine-colored, tumid and succulent. Peculiar features of location. | Same aspect as RTL; color tends ferruginous; external borders tends to fade away, inner often abrupt; infiltration less accentuated. |
| General phenomena | Always present when acute (fever, headaches, neuritis, adenopathy, etc.); less marked in chronic form. | Absent. | Rarely acute phenomena; usually sub-acute (subfebrile, moderate joint pains, etc.); sometimes entirely absent. | Almost always present (fever, headache, severe arthritis, etc.); patients frequently confined to bed. |
| Evolution | Tendency to chronicity, with repeated acute and subacute outbreaks; induced changes in local lesions. | Subsides, the case returning to chronic evolution, frequently with increased lesions. With relapse, may evolve to RTL. | The acute phase subsided, usual tendency to clinical cure. With relapse, tendency to become borderline. | The acute phase subsided, lepromatous aspect frequently assumed. Rarely, involution produces or restores RTL characteristics. |
| Bacteriology | Positive as a rule; rarely negative. | Persistently negative. Development of positivity usually coincides with tendency to change to RTL. | Frequently positive while acute (bacilli numerous, globi absent); tends negative with regression. | Usually positive before and during the outbreak (globi). When negative, tendency to regression to RTL. |
| Lepromin reaction | Always negative. | Almost always positive, of greater or lesser intensity. | Nonreactive while acute and B+; positive if without bacilli, increasing with regression. | Practically always and permanently negative. Rare positive reactions of slight intensity. |
| Structure | Acute inflammation, exudative, on pre-existing lepromatous infiltration. Bacilli granular; lipids present. | Classical tuberculoïd, with acute inflammatory phenomena: vascular dilatation, endothelial swelling, edematous dispersion, etc. No lipids; usually no bacilli. | Less typical tuberculoïd, plus other changes of (2), the edema intra- and extracellular with consequent changes. Bacilli almost always found, but lipids absent. | Intermediate between RTL and lepromatous. Bacilli always abundant (globi); re lipids, not yet well studied. |

de la variedad tuberculoide aunque aliado a ésta. De todos modos es fundamental reconocer fenómenos agudos intercurrentes en un tipo clínico, y otros que representan activación o progresión de la enfermedad en sí.

Específicamente en lepra tuberculoide, ésta activación (tuberculoid lepra reaction) ocurre por lo general en el curso crónico de la forma circinata (menor) de ese tipo. No debe confundirse con "reactional tuberculoid leprosy," la cual nada tiene de reaccional excepto al comienzo.

La mayor parte del trabajo se dedica a: (a) reactivación tuberculoide, (b) lepra reaccional tuberculoide, y (c) los "limitantes" o "borderline" que deben distinguirse como fase intermedia entre los tipos tuberculoide y lepromatosos. Se describen los cuadros clínicos y anatómo-patológicos. Los autores comienzan por describir la reacción leprosa clásica.

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DESCRIPTION OF PLATES

Sources of pictures: Nine of the clinical photographs, Figs. 1, 2, 5-8 and 12-14, and all of the photomicrographs, are from the photography archives of the Instituto Conde de Lara, of the Departamento de Profilaxia da Leprosia. Five of the clinical photographs, Figs. 3, 4 and 9-11, are from the files of the Sanatorio Padre Bento, D.P.L.

PLATE (16)

FIGS. 1-4. Examples of the clinical appearance of tuberculoid reactivation.



PLATE 16

PLATE (17)

FIGS. 5-8. Examples of the clinical appearance of reactional tuberculoid leprosy (RTL).



PLATE (18)

FIGS. 9-12. Examples of the clinical appearance of borderline cases and lesions.



PLATE 18

PLATE (19)

FIGS. 13 and 14. Clinical lesions in borderline cases.

FIGS. 15 and 16. Photomicrographs illustrating the histological structure of acute reactivation of tuberculoid lesions.

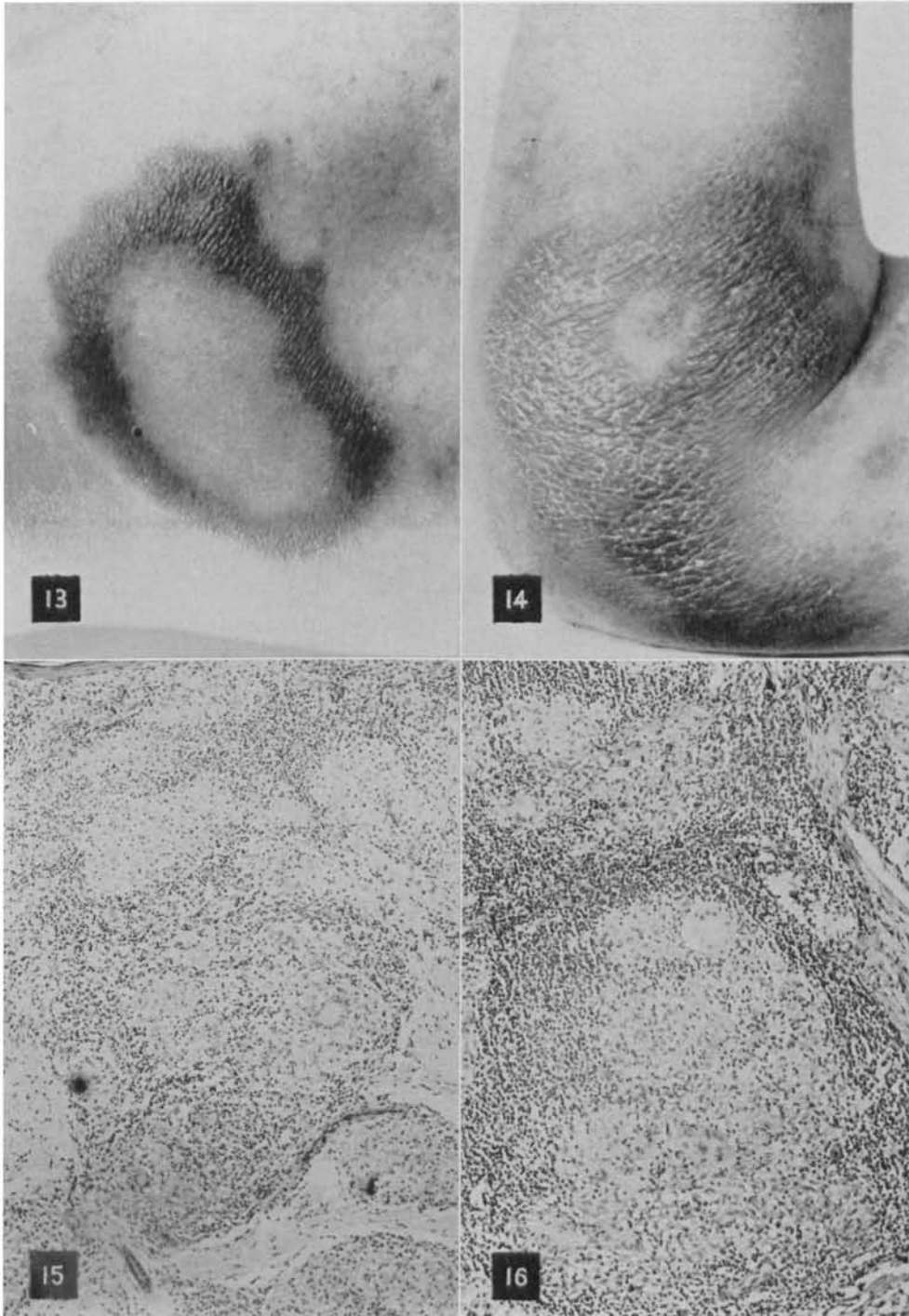


PLATE 19

PLATE (20)

FIGS. 17 and 18. Photomicrographs illustrating the histological structure of reactional tuberculoid leprosy (RTL).

FIGS. 19 and 20. Photomicrographs illustrating the histological structure of borderline lesions.

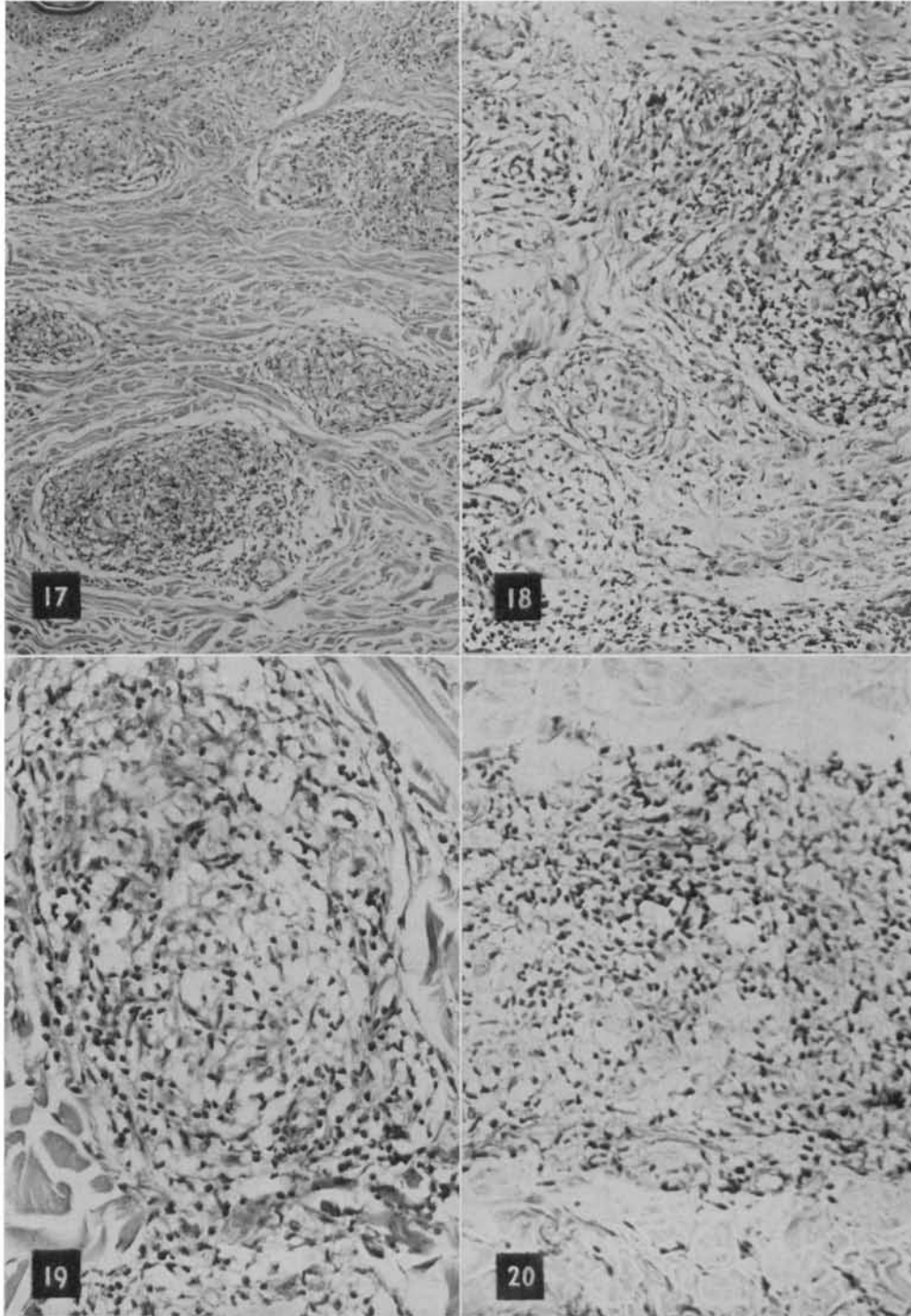


PLATE 20