ON THE SOUTH AMERICAN CLASSIFICATION OF THE FORMS OF LEPROSY

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When the Sociedade Paulista de Leprologia designated me to discuss here the subject of the South American classification, it was obviously the intention to take advantage of this opportunity to present the experiences acquired in several years of practical application of this classification. A full and frank discussion of the experiences of different centers should bring out the difficulties encountered and lead to the means of solving them; it should consider its inconveniences and possible defects and at the same time recognize its advantages. My task is to initiate the debate as a co-author of the classification, setting forth what I have learned in the long period of its use.

We are happy to say that, as a whole, the South American classification is entirely satisfactory. Nevertheless, as was unavoidable, some of its particular aspects need to be revised in order to make it effective. It seems to me that there are four points which merit special emphasis: (1) the criteria of the division of the fundamental forms; (2) the difficulties of the incharacteristic form; (3) the phenomena of mutation of form with respect to the classification; and (4) the problem of the borderline (*limitantes*), intermediate and relapsing lesions.

1. CRITERIA OF DISTINCTION OF THE FUNDAMENTAL FORMS

In the concept of the majority, the basis of the distinction of the three fundamental forms is a triple one: clinical, structural and immunobiological, this last generic term signifying all of the mechanisms of defense that the organism has available. It is evident, however, that in reality the division depends entirely upon the immunobiological conditions inherent in each patient, for that determines the structure of the lesions by which the disease manifests itself objectively. In other words, the clinical manifestations and their structure are dependent upon this special condition of the organism.

It has been accepted, virtually *a priori* that the immunobiological conditions of the cases are revealed by the results

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[1] *Revista brasileira de Leprologia* **13** (1945) 135-142. Translation of a report made at a joint conference held in Tres Corações, Minas Gerais, June 1945, approved by the author. For the most part the original phraseology is adhered to closely, although a few incidental passages have been deleted.

of the Mitsuda-Hayashi reaction, so that to each form there is attributed an approximate index of positivity and negativity. Practice, however, has shown that were it not for the lepromatous form, with its almost constant negativity, the results of the Mitsuda reaction would be indecisive, and that the approximate indices attributed to the tuberculoid and incharacteristic forms are far from correct. Look first at the tuberculoid form, considered especially by the Argentinians as presenting 100 per cent positivity to the reaction, the index of which was reduced to 90 per cent in the South American classification. Now, studying about one thousand cases of this form, we have found the positivity to be only 70 per cent; and we did not adopt the usual criterion of considering as practically negative the doubtful and weakly positive reactions, in which case [the figure] would have been somewhat lower. To this is to be added the instability of the results in the same patient, which in relatively short periods may change from negative to positive, from weakly to strongly positive, from strongly to weakly positive, and even from positive to negative, without any modification in the clinical condition to explain the variations; and, moreover, the absolute lack of sgnificance of the results in cases of the incharacteristic form, the later evolution of which cannot be predicted by the reaction.

All of this indicates that the matter needs careful review, if not new studies; [and in the meantime the reaction] should not be included unconditionally as a basic criterion of the distinction of the fundamental forms of leprosy. At the same time there should be a correction of the exaggeration of some specialists who attribute to it greater significance than the clinical and structural features, ignoring the evidence of tuberculoid morphology and structure simply because the Mitsuda reaction is negative.

In line with the indices relative to the Mitsuda reaction there are in the general picture of the classification those of bacilloscopy, among which that of the tuberculoid form figures as 98 per cent and 95 per cent negativity, respectively, for the nasal mucosa and the lesion. The averages of positivity of the nasal mucosa and the lesion scrapings in cases of this form seem to me incorrect; I believe it would not be exaggerating it to raise them to 20 per cent, which would doubtless alter, to a certain degree, the prevailing concept regarding the prophylaxis of this form.

2. DIFFICULTIES OF THE INCHARACTERISTIC FORM

The three-way division, as opposed to the dual one of the Cairo classification, i.e., the idea of two polar forms and an intermediate one, is most in accord with the facts, especially when one studies the evolution of a large number of patients. This will be shown later, after making a few remarks on the incharacteristic form.

This designation has been criticized from the viewpoint of philology as poorly conceived and not in agreement with realities [but] the term is supported by popular usage, and that makes language in spite of the grammarians and philologists. It is asserted that it is not proper to call it incharacteristic, because it is one of quite well-characterized symptomatology, with lesions of definite structure. If we consider, however, the most important aspect under which we can view this form, that of evolution, it is evident that this term is better than any other. In fact, in considering a patient of this form, well characterized by the cutaneous lesions, with the typical structure, who of us can predict its evolution? Nobody, however experienced a leprologist he may be. Neither from the morphological aspect of the lesion, nor from the results of bacilloscopy, or even from the Mitsuda reaction, can we obtain evidence as to whether the case will transform to the tuberculoid form, or to the lepromatous form, or if the lesions will regress.

From this point of view, this so characteristic form is absolutely incharacteristic, and it is in this sense—besides the structural one since the structure of its lesions is inspecific or incharacteristic—that the term was chosen.

Doubtless, it is this form which will present the greatest difficulties to the clinician in the practical application of the classification. Two things should be borne in mind. In the first place, there are lesions of incharacteristic aspect that present positive bacilloscopy, which suggests the lepromatous form. Sometimes the structural findings confirm this supposition at other times, surprisingly, there are structures which are phases of organization of the tuberculoid granuloma; and in still other cases we find structures which, were it not for the presence of germs, would be unspecific.

In this contingency I believe that the classification should be incharacteristic, in spite of the positive findings, until by evolution the case becomes one or the other of the polar forms.

The great difficulty, however, lies in the cases called neural

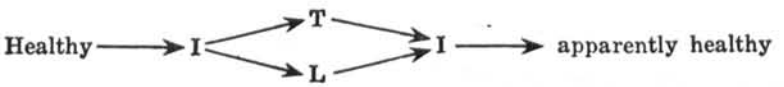
incharacteristic, that is, patients showing the effects of involvement of the nervous system without any cutaneous manifestations. For these it is nearly impossible to solve the question and place them in one of the three forms, because in most instances they present no nerve accessible to biopsy, which would solve the problem, and we cannot depend on the other elements of classification. Some leprologists depend upon the result of the Mitsuda reaction, considering a case as incharacteristic neural when it is Mitsuda negative and as tuberculoid neural when it is positive, granting that lepromatous neural cases are rare. This is a practical way of solving the question [i.e., to call it incharacteristic] although doubtless over-simple and subject to error, but that is without serious consequences. Here we have an aspect of the South American classification which to me seems extremely difficult, except for cases with caseation of the nerve which determines them [as tuberculoid].

3. MUTATION OF FORM AND THE SOUTH AMERICAN CLASSIFICATION

The most important evidence of the success of the South American classification, with its three fundamental forms, two polar and one intermediate, lies in the phenomenon of mutation of forms. Under the older classifications and the modern one of Cairo this is aberrant and incomprehensible, in spite of its frequency. When viewed in the light of the South American classification, however, it is normal, clear and comprehensible.

It is a fact that if we study the clinical history of a large number of patients, observed for long periods of time, we find that the evolution of the disease invariably proceeds by a series of transformations, gradual or abrupt, which convert [the cases] in accordance with their immunobiological conditions from the intermediate incharacteristic form into one or the other of the polar forms, tuberculoid or lepromatous, only to return thereafter to the incharacteristic form, now residual. Thus leprosy describes a constant evolutive cycle, which we call the normal one, with a phase of progression passing from the symptomatology of the incharacteristic form to one of the polar forms, in which it remains for a variable time, constituting the stable period, and then, after a regressive phase in which the characters of the acquired polar form are degraded, it returns to the initial incharacteristic aspect, until finally, by the disappearance of all symptoms the patient becomes again a healthy,

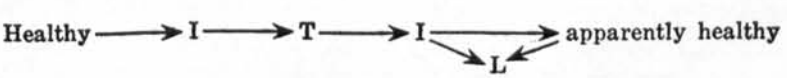
or apparently healthy, individual. This course can be indicated by the following scheme:



It is also true that a certain number of patients seem not to follow this normal evolutive cycle, the disease apparently manifesting immediately one of the polar forms, either by an acute outbreak (*surto*) or by ordinary symptoms of the tuberculoid or lepromatous form. In our opinion these cases only apparently deviate from normal; in reality they go through an incharacteristic phase which passes unperceived.

If the normal evolutive cycle of leprosy is an undisputable confirmation of the success of the three-way division of the South American classification, it is necessary also to consider those quite numerous cases in which the evolution is anomalous, the condition transforming from one polar form to the other. This constitutes the quite frequent transformation from tuberculoid to lepromatous, and the very rare transformation from lepromatous to tuberculoid.

Regarding the former, the conversion of the tuberculoid form into lepromatous, we have a collection of cases which permit us to assert with assurance, based on clinical and structural documentation, that the process first pursued the normal cycle—that is, changing from incharacteristic into tuberculoid and from that back to incharacteristic—but was followed, sometimes after the total disappearance of all the lesions as if the patient were a healthy individual, by the beginning of a second cycle, under the influence of unknown factors, this time orientating to the lepromatous form, according to the following scheme:



Regarding the latter, the transformation from lepromatous into tuberculoid, there is no need to emphasize its rarity. We have at present under observation in the Sanatorio Padre Bento a case in which this mutation is in progress; it is the first of which we have knowledge with the indispensable clinical and structural documentation. The patient is an old woman from whom all of the symptoms of the lepromatous form disappeared gradually, and after some years of apparent inactivity

there began to appear first the manifestations of the incharacteristic form, large achromic lesions which later became erythemato-hypochromic with slight erythema and marginal infiltrations. At this time we made a biopsy and found structures corresponding to the phases of organization of the tuberculoid granuloma. At present she is in this state of transformation. Until now, however, the evolutive cycle has developed according to the concept of the polar forms, with a period of abeyance in the incharacteristic form:

$$I \longrightarrow L \longrightarrow I \longrightarrow T$$

It is obvious that when we refer to the clinical aspect of these transformations, the structural aspect is included.

4. BORDERLINE OR INTERMEDIATE LESIONS AND RELAPSING LESIONS

When we consider the cases of transformation from tuberculoid into lepromatous and the process by which that mutation is effected, we find a small proportion [of them]. which go to contradict all our doctrines and open a breach in the South American classification.

We have 13 patients whose histories, clinical and structural, show indisputably that mutation of form may proceed directly from tuberculoid to lepromatous, without an intermediate period in the incharacteristic form. Thus the evolutive cycle is simplified, as follows:

$$I \longrightarrow T \longrightarrow L$$

This is an incontestible fact, the number [of cases being] sufficiently large to be taken into account.

On the other hand, there were found in these 13 patients points of contact in both the morphological and structural aspects. All were previously listed in the tuberculoid form, reactional variety, and all of the cutaneous manifestations presented as belonging to the group called borderline, or intermediate, lesions and thus to the group of lesions of relapse.

As we know, these lesions have a special character, showing at the same time characteristics of both the tuberculoid and the lepromatous forms. They are infiltrated and well delimited from the healthy skin around them; their color tends to be somewhat ferruginous; the bacilloscopy is temporarily positive, this temporary positivity being, however, much more prolonged than in the common reactional leprids.

With regard to structure the same thing is repeated. The anatomic substrate of these lesions is the tuberculoid granuloma, but with the peculiarity that bacilli are found in greater numbers than is customarily the case in reactional leprids, although much fewer than in lepromatous lesions.

Examining the acute eruption by which they originate, we find a character that approximates the lepromatous form in spite of the tuberculoid structure. The acute eruption is accompanied by disturbance of the general condition of the patients, with high fever whose curve surpasses in both duration and intensity that which is found in an acute outbreak of erythema nodosum or multiforme. Moreover, it is also accompanied by marked edema of the feet and hands, a condition which is more or less constant in the acute reactions of the lepromatous form. In some cases the evolution of the reaction proceeds normally, like that in the reactional tuberculoid form. In others, as in the 13 mentioned, there occurs direct conversion from the tuberculoid to the lepromatous form. The Mitsuda reaction does not furnish indications; some cases are Mitsuda-negative, others positive.

It is evident that these cases present at the same time characteristics of the lepromatous and the tuberculoid forms. They cannot properly be put into the lepromatous form, nor would we feel satisfied in labelling them tuberculoid. They are in a border (*limite*) zone, between one and the other.

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To finish, I propose the following questions:

1. Should the results of the Mitsuda reaction be excluded as a basic criterion of the distinction of the fundamental clinical forms of leprosy, or should they be held in reserve until new and more accurate studies demonstrate the true significance and value of this reaction?

2. Should the present indices of bacilloscopy be changed?

3. What term could be substituted for the present term incharacteristic?

4. What are the elements which can be used for the classification of the neural subtypes of the fundamental forms?

5. Should or should not the phenomena of mutation of form, normally observed in almost all cases, be included as basic criteria of the distinction of the fundamental forms?

6. How should the limitant lesions and those of relapse be regarded in classification? Should they be included in the

tuberculoid or the lepromatous form, or should they be placed separately in a new group?

OPINIONS ON SOUZA LIMA'S REPORT

This "well considered and judicious" report, it was stated editorially,[1] which brought out "the first doubts on the fundamentals of the classification," aroused so much interest that committees representing the São Paulo, Minas Gerais, and Rio de Janeiro groups and also the Argentine workers were appointed to render opinions on them. The communications from these committees and separate ones of certain individuals, and Souza Lima's report itself, were all published together. The opinions, it was concluded, showed "that the so-called South American classification emerged victorious in its first public debate, and that the doubts regarding details which still exist can be perfectly adjusted . . . ."

In the next issue[2] the majority opinions were summarized editorially as follows (the questions not repeated here):

There was not, nor could there be, unanimity in the proposed solutions of the doubts raised in the Tres Corações report, but in general it can be said that the replies are concordant, although differing here and there in the interpretation of facts.

Question No. 1: Use the results of the Mitsuda reaction as a basic criterion for the distinction of the fundamental forms of leprosy, although recognizing its imperfections and causes of error.

Question No. 2: Change the indices of bacilloscopy.

Question No. 3: Retain the term "incharacteristic form."

Question No. 4: The results of the Mitsuda reaction.

Question No. 5: Do not take into account the phenomena of mutation in the basic criteria of the distinction of fundamental forms.

Question No. 6: (There is no concordance in the answers which would permit establishing a majority opinion.)

This editorial also enumerates a number of points raised in the opinions rendered which should be the subject of new studies:

(*a*) The concept of mutation.

(*b*) The intermediate reactional phase, epituberculoid reaction.

(*c*) Separation of the reactional tuberculoid from the tuberculoid form.

(*d*) Lepra reaction in the incharacteristic form (Argentina committee).

(*e*) The borderline (*limitante*) reactional episode.

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[1] *Rev. brasileira Leprol.* **13** (1945) 133-134.

[2] *Rev. brasileira Leprol.* **13** (1945) 299-300.