PATHOGENIC BASES OF THE SOUTH AMERICAN CLASSIFICATION OF LEPROSY*

by

MOACYR DE SOUZA LIMA; JOSE BARBA RUBIO; LAURO DE SOUZA LIMA, and PAULO RATH DE SOUZA**

The present work which is being presented at this Pan-American Congress of Leprosy represents the synthesis of our observations in the laboratory and in the clinic, and of our effort to represent in schematic form the pathogenesis of leprosy, in relation to the immunology and the histopathologic structure of the lesions, with a view to explaining the mutations from one to the other of the polar forms of the South American classification. Such mutations, which form one of the most discussed topics about this disease, are fortunately getting rarer from day to day as our knowledge about them advances.

According to our point of view, after the implantation of the *M. leprae* in the body of the human host through various routes of invasion, we find that the bacillus remains principally in the interstitial connective tissue, capable of a long period of survival, although unable to multiply actively unless it succeeds in penetrating into living cells.

We know, on the other hand (according to Bordet), that the principal response of the host to the invading organism consists of phagocytosis. This process in leprosy, according to our understanding, can be complete (phagocytosis with lysis) or incomplete (phagocytosis without lysis) by macrophages or histiocytes. These, which are fundamentally from the perivascular adventitious cells of the reticulo-endothelial system, multiply and are transformed into polyblasts or inflammatory macrophages, according to Maximow and Bloom, who also attribute this property to the lymphocytes and monocytes. In our opinion, these cellular elements give origin to the characteristic cellular reaction of leprosy, whether the results be the epithelioid cells or the Virchow cells of the lepromas.

Now, the first fundamental phenomenon observed is the difference in the behavior or reaction of the histiocytic cells in the presence of the *M. leprae*. In some cases, these cells remain indifferent, that is, there is no reaction on the part of the components of the reticulo-endothelial system (the uncharacteristic form). In others, the histiocytic cells multiply considerably; they mobilize and

---

*Read at the Second Pan-American Conference on Leprosy, Rio de Janeiro, Brazil, October 19-27, 1946.

**From the Leprosy Service, São Paulo, Brazil.

prepare themselves to phagocytose; in other words, they react to the presence of *M. leprae,* and present different histological structures which are, however, quite typical (lepromatous and tuberculoid forms of the South American classification).

Analysing further the phenomenon of phagocytosis, we observe that although the histiocytic cells (epithelioid cells and Virchow's cells) seem to us, as already stated, to have the same origin, nevertheless they show differentiation later on. One group can effect *complete* phagocytosis (phagocytosis with lysis) of the *M. leprae,* while a second group produces *incomplete* phagocytosis (phagocytosis without lysis). Hence, when under influences as yet unknown, complete phagocytosis is effected, a tuberculoid granuloma is formed, consisting of epithelioid and giant cells, with destruction of the *M. leprae* (according to the law of Jadassohn-Lewandowsky), thus constituting the clinical polar type of tuberculoid leprosy.

When, on the other hand, the histiocytic elements (macrophages) do not dissolve or digest the *M. leprae,* and are limited simply to phagocytosing them, then the typical foamy cell of Virchow is produced. The phagocytosed organisms multiply within the vacuoles of the protoplasm and the multiplication may be so rapid and prolific as to destroy the cells, producing compact masses constituting the globi. Clinically, this type presents the other polar type—the lepromatous—of the South American classification.

We must also emphasize the added observation that in lepromas and lepromatous infiltrations, epithelioid cells in variable numbers are likewise present, but are usually few in number. This fact has already been noted in Minas Gerais by Rodrigues Vieira, an observation which supports our viewpoint and which appears to us to explain fully the observed facts. In effect, since the epithelioid cells and the Virchow cell have the same origin, it is natural that in the leproma, mixed with the preponderating Virchow cells, some epithelioid cells should be present, distinguished by the lack of vacuolization and not containing any bacilli. This last may be due to the fact that they have not yet been invaded or that they have the faculty of complete phagocytosis.

However, it is certain that biological phenomena are never as schematic or absolute as we represent them, and there must exist a gamut of histological variations or stages (which are, however, not clinical types) (or which cannot be differentiated clinically—Ed.) between the two polar types with the result that no two patients can ever be identical. The same patient may exhibit tissue changes consisting of a mixture of practically antagonistic charac-

teristics which may confuse the clinician and apparently undermine even such a scientifically based classification as the South American.

But further detailed study of this phenomenon indicates that the presence of a few epithelioid cells is both justified and logical and is precisely the proof of the rational and scientific basis of the South American classification which is based on clinical, immunological, and histological grounds.

Finally, we have observed exceedingly few cases in which the phenomenon of phagocytosis, particularly the lytic function, is not present in distinctly polar extremes, but rather, whereas some cells completely destroy the bacilli, others merely engulf them or are themselves destroyed by the bacilli. The resulting structure shows a multitude of epithelioid cells, scarcely forming tubercular or nodular arrangement (hence more or less diffused), with a few lymphocytes, accompanied by vascular dilation, interstitial edema, and absence of giant cells. Some of the epithelioid cells are so similar to the Virchow cells that the histologist, on a study of the structure alone, is unable to decide whether the lesion is tuberculoid or lepromatous. To complicate matters, there are found in such sections, after acid-fast staining, more bacilli than could be expected from a similar advancement of tuberculoid lesion and less than in a similar degree of lepromatous infiltration.

In this stage (which we repeat is not a clinical form), should be included the limiting, intermediary, and relapsed lesions, delineated and studied by Drs. Lauro Souza Lima and de Souza Campos, as well as the lepromatous lesions with a large number of epithelioid cells mixed with the Virchow cells, with tendency to nodular formation (focalization—Ed.).

In these stages where there are relative phenomena of complete as well as incomplete phagocytosis, certain cells have the power of dissolving the *M. leprae* (as in tuberculoid leprosy), while others are destroyed by the bacilli (as in lepromatosis). These two types of reactions are mixed in such a way that if the phenomenon of lysis and complete digestion eventually takes place, the final result would be the tuberculoid form; whereas if the destruction of the cells by the bacilli predominate, that is, if the phagocytosis remains definitely incomplete, the patient will present the lepromatous form.

To this transitional stage or aspect where the structural and bacillary characters of both polar forms mix and in which the patient is in unstable stage, waiting for the outcome of the interaction between the cells and the bacilli, in order to label its clinical form, prognosis, etc., we the authors, propose the title of "transi-

tional," because in effect it is a transitional structural stage between the two polar forms. It can become epithelioid or lepromatous with equal ease. In other words, it is in a stage of reaction and implies a transitory, unstable, and confusing stage, without indicating in any way, the ultimate evolution of the disease.

It cannot be called "tuberculoid type in stage of reaction" because this later is a clinical variety, is already well known and should be continued in the South American classification, possessing as it does, its own clinical, structural, and bacillary findings, whereas our "transitional" phase, without being a clinical form, merely indicates an immuno-histologic aspect, which includes in part the "tuberculoid type in stage of reaction," the so-called "limiting, intermediary, and relapsed lesions," and finally, the other forms which, starting as typical lepromatous lesions, by the action of modern drugs, or through other factors, begin to show structures with large numbers of epithelioid cells, some appearing to be Virchow cells, with tendency to nodular formation (focalization—Ed.) indicating an inclination towards the epithelioid forms, without, however, indicating the final outcome of the lesions.

These changes we explain in the following way: beginning with a tuberculoid form in a stage of reaction (reacting tuberculoid) with typical structure, nodular (focal) and well defined, then for unknown reasons the second function of phagocytosis (lysis) can no longer be effected by the cells, there begin to appear cells which are frankly foamy, and the nodular structure is lost. If such foamy cells reach a sufficient number, and if, at the same time, the bacilli become so numerous as to dominate the picture, the lesion becomes frankly lepromatous, as shown by new clinically lepromatous lesions in the patient. On the other hand, we can have a lepromatous case, with typically lepromatous sections of the skin, numerous bacilli in globi, where phagocytosis is incomplete (phagocytosis without lysis) followed by destruction of the cells of Virchow. Let us now suppose that this incomplete phagocytosis is not absolute, that is, there co-exist also some cells that produce lysis, so that destruction of the cells and bacilli co-exist although there is more of the latter, then, thanks to the action of drugs or for co-existing reasons, complete phagocytosis with lysis superimpose to the extent of dominating the picture. If this process continues, we will witness the clinical, immunological, and structural change from lepromatous to the tuberculoid.

And if these changes operate as we have described, there is no reason for surprise when in the same section we see both leproma-

tous and follicular structures, considered rare at the present time, but observed and defended by one of us (Lauro de Souza Lima).

At the beginning of this article, we stated that the structure of leprosy is shown in two ways. In one, there is absolute absence of reaction on the part of the reticulo-endothelial system (pure uncharacteristic type) while in the other, there is intense reaction on the part of that system with complete or incomplete phagocytosis (tuberculoid and lepromatous type). But in still other cases, it is observed that although clinically they still present uncharacteristic erythematous, hypochromic or simple erythematous forms, histologically, there is noted a difference from the typical uncharacteristic-type structure in that there is already noted a slight histiocytic reaction, the beginning of a response on the part of the reticulo-endothelial system. This feature separates such cases from the pure uncharacteristic form, nor can they be included in the group of frank histiocytic reacting forms, thereby subdividing schematically the uncharacteristic type into two subgroups, namely, the pure uncharacteristic group and the typical uncharacteristic group. These two subtypes cannot be differentiated clinically, but the second (typical) is characterized by slight histiocytic response, some with a few Virchow cells and others, with tendency to tuberculoid formation. Previously these two subtypes were known as pre-leproma and pre-tuberculoid respectively.

If in this group of clinically uncharacteristic type with slight histiocytic reaction, the epithelioid cells increase considerably to dominate the picture, and in addition complete and absolute phagocytosis takes place, then the clinical, structural, and immunologic development towards the tuberculoid type takes place. If the increase in the activity of the reticulo-endothelial system is incomplete, the change is towards the lepromatous type.

Retrogressive changes in the lepromatous or tuberculoid types in which they lose their typical structures until what remains is simple unspecific infiltration, without reaction of the reticulo-endothelial system with an occasional extra *M. leprae* between the fibrils of the peripheral nerve fibers, are evidences of a transformation of the tuberculoid or lepromatous type to the uncharacteristic type. In this condition, however, there still exists a potentiality towards later new transformations to the polar types. This stage is entirely different from the residual cicatrix of the cured tuberculoid cases, or of the residual lesions of the uncharacteristic and lepromatous patients who are already cured, which show no evident pathogenic

potentiality, but are merely scars of extinguished pathologic processes.