The Response of the Patient With Leprosy Toward
*Mycobacterium leprae* Injected With Lepromin

A Histopathologic Study Four Hours after Injection

Amado Saul

The varying behavior of the human organism in the presence of *M. leprae* was first recognized by leprologists almost with the first descriptions made of the disease. In 1948, in Havana, the concept of polarity was accepted: the same bacillus produces two totally opposed types, almost two different diseases (6, 19), although afterward the existence of cases with ambiguous characteristics was recognized, justly called interpolar cases (29).

While immunologic studies of leprosy were initiated in 1919, when Mitsuda described the different response of patients toward a suspension of dead bacilli derived from lepromatous nodules, it has been only in the last decade that immunologists have fixed their attention toward this disease, which, as has been said, constitutes a unique immunologic model in pathology. In fact the classification nowadays accepted has as its basis a fundamentally immunologic concept.

Much has been advanced in leprosy immunology that may carry us toward a more rational and logical treatment of patients, to the acquisition of an effective immunization means, and to understanding of the reactionary episodes of lepromatous leprosy, but there is still a great deal to learn (30).

In spite of the fact that the results of recent immunologic studies are frequently contradictory, there is sufficient evidence that the lepromatous case offers a peculiar immunologic dissociation; while it preserves a very good capacity of forming antibodies (humoral immunity), it presents on the other hand, a partial impairment of cell-mediated immune response (CMI) (2, 6, 30, 31, 32, 33, 39).

Evidences in the sense that the delayed hypersensitivity, mediated by immunized thymus-dependent cells, is partially impaired in lepromatous leprosy, are the non-response to lepromin in these cases, the partial or contradictory response to other antigens of fungi and candida and to tuberculin (2, 36, 37, 38), the mild sensitivity to picric acid and to dinitrochlorobenzene (4, 8), the deficient blastic transformation of lymphocytes of lepromatous patients in the presence of phytohemagglutinin and streptolysin O (6, 9, 21, 26, 31), and the replacement of the paracortical area of the lymph nodes of lepromatous patients (usually rich in thymo-dependent lymphocytes) by reticulo-histiocytes, as occurs when treating an animal with antilymphocytic serum, while preserving, on the other hand, a large number of plasma cells, producers of antibodies, in the medulla of the lymph nodes (36, 37).

Furthermore, in lepromatous cases there exists a remarkable increase of immunoglobulins, and, by immunologic methods, antibodies are detected against group-specific antigens (*mycobacteria*, *Poly INb* of *Nocardia brasiliensis*) (7, 8, 11, 13, 22, 28, 40) and of autoantibodies (2, 8, 20), demonstrating the good capacity of the lepromatous patient to form antibodies.

The numerous studies in animals, and others performed in human beings, have fully proved that all things that may depress the CMI favor the development and multiplication of *M. leprae* (thymectomy radiation, antilymphocytic serum); and that, in turn, it is possible to improve the resistance of the animal to leprosy or transfer the sensitivity to lepromin and to other antigens by means of lymphocytes of normal animals (14, 15, 16, 17, 22, 24, 26, 29).

It is accepted that in chronic granulomatous diseases produced by intracellular my...
Saul: Response in Leprosy to M. leprae and Lepromin

Cobacteria, the immunologic mechanism of defense depends on the macrophage function (42, 43). Mycobacteria cannot be eliminated by antibody alone (39). In accordance with these concepts, it is logical to assume that the impairment of the CMI present in the lepromatous case favors the permanence and multiplication of the bacillus and, therefore, the lack of resistance to it. Likewise, the production of humoral antibodies against polysaccharide antigens of the bacillus and the subsequent reaction of antigen-antibody and complement, may explain, by the attraction of polymorphonuclears and release of enzymes, the symptoms of the lepra reaction (erythema nodosum or polymorphous fever, arthralgies, etc.) (23, 30, 39).

In tuberculoid leprosy there are contradictory data, perhaps because in its study no use is made of strictly polar cases; however, these cases conserve a normal immunologic mechanism in the production of both antibodies and immunized cells, which means a more or less rapid destruction of M. leprae and, consequently, a resistance to the disease.

Now at what moment, and where and why does this defect or immunologic deficiency occur in lepromatous cases? This is still a point of study. Do genetic, prenatal and environmental factors interfere therein? This already enters into hypothetic fields.

INVESTIGATION OF THE PRESENCE OR ABSENCE OF M. leprae FOUR HOURS AFTER INJECTION OF INTEGRAL LEPROMIN

His topathologic study of the different responses of leprosy patients to integral lepromin (Mitsuda after 21 days, Fernandez after 24 hours and Medina after six hours) has revealed the presence or absence of bacilli which, beyond doubt, go with the lepromin injected, and this is related to the different immunologic status of the cases. Novales [cited (4)] points out when there are many bacilli after 48 hours, there are also many after 21 days and no true granuloma is formed, but when after 48 hours there are no bacilli at the site of application of lepromin, they will not be present after 21 days, and then a real tuberculoid granuloma is formed. In 1944, Medina reported that some patients with diffuse lepromatous leprosy presented, after six hours, at the site of the integral lepromin injection, a response constituted by erythema, edema and vesiculation that resembled the early phases of Luetic's phenomenon. Afterward, in 1964, when the experiences of Medina were revised again, we verified the fact that this response occurs not only in lepromatous cases but also in some tuberculoid and indeterminate cases, both with lepromin and with tuberculin, and when we made a histologic study of this response, it was verified that in the tuberculoid cases the bacilli injected only six hours before were no longer present, whereas in almost the total number of lepromatous patients, bacilli were found intact (35).

This fact was fully studied afterward (34), and it is precisely the topic of our research and the experiences of that research which we are disclosing in this paper.

MATERIALS AND METHODS

Fifty patients with diverse clinical forms of leprosy and a control group of 50 patients with dermatoses other than leprosy, were subjected to intradermal injections of 0.1 cc of lepromin. Four hours later a search for acid-fast bacilli was made by two methods, a lymph smear and a biopsy of the site of injection of the antigen. The lymph smears were consistently negative. The biopsies, however, revealed the presence of acid-fast bacilli in some cases, but not in others. The results were related with the clinical, bacilloscopic and histopathologic data of each case, and also with the late (21 day) response to lepromin.

RESULTS

The histologic changes found after four hours were invariably the same discrete epidermic alterations, consisting of a moderate acanthosis, if any change at all. In the superficial dermis there was a dilatation and congestion of the capillaries, which were surrounded by small infiltrates of histiocytes and lymphocytes. In the mid-