AN HYPOTHESIS EXPLAINING SOME ASPECTS OF THE PATHOGENESIS OF NERVE INVOLVEMENT IN LEPROSY

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It is well-known that an immunological (cellular and/or humoral) defense can be induced against a number of organs. These cellular or humoral responses are often specific for certain species or organs. To achieve this one injects experimental animals intracutaneously with certain tissues or extracts, emulsified in Freund's adjuvant (Milgrom, F. and Witebsky, E., 1962). The part played by this adjuvant is not fully understood. It is supposed that the killed mycobacteria are necessary to provoke a chronic proliferative inflammatory infiltrate, while the paraffin oil is probably necessary to maintain a depot in the skin over a prolonged period, a condition apparently necessary for this type of sensitization. The antigens present in this infiltrate are in their turn responsible for the specific cellular response. It is likely that the mycobacteria also play a part as "Carrier" of tissue antigens (Milgrom, F., and Witebsky, E., 1962). In this way it has been possible to produce aspermatogenesis, neuritis and contact allergy, after immunization with respectively testicular tissue, nerve tissue and chemical compounds all administered in Freund's adjuvant. Both humoral and cellular forms of immunological response often play a part in these experimental auto-immune processes. However, it is assumed that especially the specific lymphocytic immune response is responsible for the ultimate pathological process.

In leprosy, two forms, tuberculoid and lepromatous are distinguished. In the tuberculoid form the lepromine test (Mitsuda) is strongly positive: an extract prepared from the lepromatous tissue inocculated intracutaneously produces a nodular infiltrate after 3 – 4 weeks. Reactions after 24 – 48 hours (Fernandez) are also observed. The tuberculin test is sometimes positive. This might be explained either on the basis of a cross reaction between the related antigens (*M. leprae and M. tuberculosis*) or as a sign of concomitant or previous tuberculous infection. It has also been noted that patch tests with contact allergens are positive in sensitized patients suffering from tuberculoid leprosy.

In lepromatous leprosy the situation is entirely different: the lepromin test after 24 – 48 hours and the Mitsuda-reaction are always negative; patients are usually unable to develop positive tuberculin or patch tests (Turk, J.L., 1970). While in tuberculoid leprosy the Reticular Endothelial System (R. E. S.) is still sufficiently functioning to produce a lymphocytic immune response, the R. E. S. in lepromatous leprosy is impaired and a lymphocytic immune response is usually absent. (Turk, J.L., 1970, Katz, S. I. et al 1971).

The histology is in keeping with the immunology: tuberculoid granulomas with epitheloid cells, surrounded by lymphocytes in tuberculoid leprosy and infiltrates consisting mainly of foamcells (histocytes filled with *M. leprae*) in lepromatous leprosy.

We propose the following hypothesis. In leprosy the nerve fibres in the skin are primarily invaded by *M. leprae* (a situation comparable to inocculation with Freund's adjuvant containing emulsified nerve tissue). The *M. leprae* provoke a chronic proliferative inflammatory granuloma in the skin, analogous to the chronic process produced by the mineral oil and paraffin of Freund's adjuvant. In tuberculoid leprosy in which the R. E. S. is at least partially intact there is a lymphocytic tissue response directed against nerve tissue as well as against *M. leprae*. As a consequence patients suffering from tuberculoid leprosy often present early in the disease with acute, extensive nerve involvement while *M. leprae* are absent with standard methods of examination.

In lepromatous leprosy by contrast the R.E.S. is deficient and the lymphocytic immune response is inadequate. Hence, all delayed type reactions, lepromine, tuberculin, and patch tests are mitigated or negative. As a consequence acute extensive nerve involvement is absent and *M. leprae* abound in the skin. Chronic neuritis usually occurs insiduously after several years, not as an auto-immune process (as in tuberculoid leprosy) but rather as the result of the chronic continuous presence of *M. leprae* in the nerves.

To test this hypothesis an extract from nerve tissue should be prepared of a strength to which normal individuals do not respond on interdermal testing. Then leprosy patients are challenged with this extract. We presume that patients with lepromatous leprosy will not show a reaction owing to impaired lymphocytic immunity, while patients with tuberculoid leprosy should show a strong response producing an infiltration and papule after 24 – 48 hours.

TRUE or FALSE

Melanocytes in hair follicles are more sensitive to irradiation during their resting phase than in their actively dividing state unlike most other cell populations in the body.

(Answer page No. 197)