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Diabetogenic Effect of Dapsone

TO THE EDITOR:

The isoniazid (INH) acetylator phenotype of 79 Brazilian leprosy patients, mostly Caucasoids (22 Negroids), which included 45 males and 34 females, 47 of them with diabetes mellitus (26 males and 21 females, 12 of them Negroids), was assessed by means of Eidus, *et al.*'s method ([2]). All of them were under dapsone therapy for at least 5 years. The same procedure for investigating the INH-acetylator phenotype was applied to 30 Brazilian Caucasoids with diabetes mellitus but without leprosy (14 males and 16 females).

The frequency of the slow INH-acetylator phenotype among the 32 nondiabetic leprosy cases (47%) did not differ significantly from that found among the 30 diabetic individuals without leprosy (53%) or among Brazilian Caucasoids (57%; N = 119) and Negroids (50.4%; N = 115) with pulmonary tuberculosis ([1]). In contrast, the slow INH-acetylator phenotype predominated among the 47 diabetic leprosy patients (76.6%), this frequency being significantly higher than that seen among the nondiabetic leprosy patients, the diabetic persons without leprosy, or the patients with pulmonary tuberculosis.

Regression analysis applied to the data recorded on the leprosy cases has shown that the blood level of glycosylated hemoglobin does not depend upon age, sex, duration of the disease, or years of dapsone therapy, but it is correlated to both the slow INH-acetylator phenotype and the fasting plasma glucose.

The results presented here indicate that diabetes mellitus has no influence on the INH-acetylator phenotype, since the frequency of slow INH-acetylators found among the diabetic individuals without leprosy was almost identical to that observed among nondiabetic Brazilian Caucasoids or Negroids. On the other hand, since the blood level of glycosylated hemoglobin is associated with the slow INH-acetylator phenotype, while the *in vivo* acetylation of dapsone depends on the same acetyltransferase used for acetylating INH ([3–6]), one would infer that slow INH-acetylator leprosy patients when under dapsone therapy would be more exposed to an undescribed diabetogenic effect of this drug than fast INH-acetylators. This fact would explain the high frequency of slow INH-acetylators among the diabetic leprosy patients.

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Effect of Preformed Immune Complexes on the Course of *Mycobacterium leprae* Infection in Normal Mice

TO THE EDITOR:

Normal mice infected with *Mycobacterium leprae* in the foot pads show a limited multiplication. Dissemination of infection is seen in immunosuppressed animals, i.e., the thymectomized and irradiated ([9]) and nude mouse ([7]) and the nude rat ([4]). The severe immunosuppression seen in these animals does not simulate human leprosy before or during the course of the disease. Out of the many known and unknown factors operating in the causation of the depressed cell-mediated immunity in lepromatous leprosy, one is the presence of immune complexes (IC). The IC, in turn, are capable of producing specific immunodepression by blocking the recognition of *M. leprae* antigen by lymphocytes. In addition, IC might have multiple other effects on the whole array of immuno-competent cells ([2]) and, subsequently, dissemination of infection may involve other systems.

In the present study, 4-week-old, closely bred, Swiss albino mice (Lacca strain) were divided into two groups: Group I, composed of 55 normal control mice, and Group II, composed of 55 mice which were inoculated in the right foot pad with *M. leprae* (1×10^4 AFB/foot pad) obtained from biopsy specimens of untreated lepromatous patients. Both the control (NC) and infected (NI) mice were each divided into two batches, i.e., 0dIC (N = 30) and 3mIC (N = 25), depending upon the period at which IC were administered: at zero day (0d) or at 3 months (3m) post-inoculation with *M. leprae*. A large number of animals were used as a precautionary measure because of their high mortality rate. Five mice each were sacrificed periodically at 3-, 6-, and 9-month intervals from the 0dIC batches and at 6- and 9-month intervals from the 3mIC batches, since the data for the remaining period were obtained from a study conducted and published earlier ([13]) wherein the procedures for foot pad inoculation, harvesting, and counting of bacilli were also mentioned.

Freeze-dried *M. leprae* (obtained as a gift from IMMLEP) were sonicated to prepare antigen ([6]), and healthy rabbits were immunized to raise the anti-*M. leprae* serum (AMLS). The production of antibodies against *M. leprae* antigens was confirmed by immunodiffusion. The zone of equivalence (ZE) was determined as described by Roitt ([10]). The tube containing 240 μg of *M. leprae* antigen gave maximum precipitate and was taken as the ZE. Twice the ZE gave complexes in 2× antigen excess. AMLS was adsorbed with homogenized human skin tissue and also with *M. bovis* (BCG), *M. tuberculosis* (H37Rv), and *M. avium*. IC were prepared *in vitro* by incubation of the *M. leprae* antigen and the AMLS. IC in 2× antigen excess (1 mg protein) were administered in 0.3 ml of saline intravenously (i.v.) every week for 1 month starting at day 0 and at 3 months after *M. leprae* inoculation into foot pads.

The kidney, liver, sciatic nerve, skin, earlobes, snout, and tail tip of all sacrificed animals were fixed in 10% Formol saline.