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A Follow-Up Study of Multibacillary Hansen's Disease Patients Treated with Multidrug Therapy (MDT) or MDT + Immunotherapy (IMT)[1]

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Hansen's disease presents a broad spectrum of clinical and histopathological manifestations which reflect the nature of the individual's immune response to *Mycobacterium leprae*. This spectrum of clinical manifestations includes two polar types of infection, lepromatous leprosy (LL) and tuberculoid leprosy (TT), as well as intermediate borderline forms of disease ([17]). To simplify field work, the World Health Organization (WHO) classifies leprosy patients according to the bacillary load as multibacillary (MB) patients, with an elevated bacterial load, and paucibacillary (PB) patients, who present negative or weak bacilloscopy.

Cell-mediated immunity (CMI) plays a major role in resistance and protection to intracellular infection. In leprosy, as in other intracellular infections, CMI depends on the ability to develop an effective T-cell-mediated immune response against the microorganism. This cellular reactivity is low or absent in MB patients; negativity persists for many years after chemotherapy in most patients.

Tissues infected with *M. leprae* contain large amounts of phenolic glycolipid-I (PGL-I), which is a highly specific antigen of the microorganism. Antibody levels against PGL-I are frequently used to follow up the therapeutic response and elimination of the bacillary load in patients under treatment ([2, 6, 13]).

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M. leprae is an obligate intracellular pathogen that invades and multiplies within monocytes/macrophages, activating the metabolic burst and the production of toxic radicals. High levels of nitrite in serum have been associated with several pathologies ([19, 20]) and provide an indirect measurement of nitric oxide (NO) production by endothelial cells, activated macrophages and neurons ([9, 11]).

Because of bacterial resistance induced by monodrug therapy, it has been necessary to develop and implement effective multidrug treatment of leprosy patients ([1, 7, 23]). In the Institute of Biomedicine, Caracas, Venezuela, MB leprosy patients are treated with multidrug therapy (MDT), with or without simultaneous immunotherapy (IMT) with a combined vaccine containing heat-killed *M. leprae* plus BCG. An effort is made to systematically follow the two groups for a period of 5 years or more, with repeated clinical, histopathological and immunological evaluations.

In a previous study, we evaluated the immune responses of patients submitted to IMT+MDT before treatment and after a 5-year follow up ([16]). In our present study, we report an annual follow up for at least 5 years of CMI and levels of serum antibody to PGL-I in MB patients treated with MDT alone as well as with MDT+IMT. The preliminary results of the determination of serum nitrite levels in both MB and PB patients are also reported.

MATERIALS AND METHODS

Patients and treatments. All patients were adults and were classified according to WHO criteria. MDT with dapsone (DDS), rifampin and clofazimine was administered using WHO protocols ([24]). IMT, as described previously by Convit, *et al.* ([7]), was

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