Acknowledgment. We are grateful to Mrs. K. Jayanthi for secretarial help and to Mr. T. Peter Sathesh and Mr. B. Vijayakumar for technical assistance. The study was financed by the American Leprosy Mission International, Greenville, South Carolina, U.S.A.

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Staging Nerve Involvement in *M. leprae* Infection

TO THE EDITOR:

It is assumed that leprosy is primarily an infectious disease of the peripheral nerve even though skin manifestations remain an important clinical sign of the disease. The nerve may be affected alone (pure neural) or may be the first site to be involved (primarily neural), the other possibility being concomitant skin and nerve involvement.

Briefly, *Mycobacterium leprae* infection cannot be conceived without nerve involvement. Leprosy neuropathy is essentially a neuritis. The inflammatory reaction within the nerve contributes to the pathogenesis of leprous neuropathy through a variety of effector mechanisms ([8]). It is assumed that in leprosy an immunopathological mechanism plays an important role in the pathogenesis of nerve damage ([5]). Staging this nerve involvement is important in order to find a new therapeutic approach for the prevention of clinical neuropathy. We propose the following four steps:

1. Subclinical stage I, which may be called stage of involvement, can be considered as characterized by an inflammatory reaction within the nerve trunk ("neuritis") but as yet without either subjective or objective manifestations. However, it may be assumed that during this stage the immunopathological mechanism has been triggered.

2. Subclinical stage II, which may be called the stage of nerve damage. We consider that this stage may be accompanied or not by subjective clinical manifestations such as pain or tenderness, but loss of function is absent. Manifestation of pain seems to be related to the rate and kind of nerve fiber degeneration ([2]). This stage may not be associated with pain and tenderness in the so called "silent neuropathy" (we have previously proposed the expression of "silently arising clinical neuropathy") ([3]).

3. Clinical stage I, which may be called stage of destruction. This clinical stage may be described as characterized by loss of function, but with possible recovery.

4. Clinical stage II, this is the stage of scarring; recovery is not possible.

Pearson and Ross ([4]) assume that as much as 30% of the nerve fibers have to be destroyed before sensory impairment becomes detectable. In the same line of thought, Weller and Cervos-Navaro ([7]) underline that a large proportion of nerve has been damaged before the appearance of clinically detectable neurological deficit.

We think that prevention of clinical neuropathy (meaning destruction of more than 30% of nerve fibers) has to be addressed at the subclinical stage. How can this early subclinical stage be recognized? Is there any indicator clinical sign contemporary to the subclinical neuropathy? In animal models, Crawford, *et al.* ([1]) have demonstrated

that the hypopigmented skin macule is an indicator of a hypersensitivity reaction to sensory nerve myelin. McDougall ([6]) has put forward an attractive theory on the mechanism of hypopigmentation in leprosy. He relates the hypopigmentation as a consequence of free radical formation during the cell-mediated immune response. We may assume that a hypopigmented skin lesion is, therefore, an early indicator of the immunopathological mechanism affecting the nerve trunk.

The above-mentioned hypothesis allows us to raise questions on the possible modalities of preventive therapy to be established for patients without clinically detectable loss of nerve function but classified on the basis of skin lesion.

How important is the close association between the subclinical neuropathy and the skin lesion? Can we consider that in leprosy the earliest skin lesion may be considered a forerunner of clinical neuropathy?

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Detection of Antibodies Toward Secreted Mycobacterial Antigen 85 in Untreated Leprosy Patients' Sera

To the Editor:

Leprosy is an insidious disease that affects two million persons worldwide (1993) and continues to present a public health problem in various parts of the world. The efforts carried out by the World Health Organization (WHO) to eliminate leprosy by the year 2000 have been based mainly on monitored multidrug treatment ([3]), which includes the use of new diagnostic, prevention and disease classification methods.

Mycobacterium leprae is one of the first human pathogens to have been described, but the impossibility of its cultivation *in vitro* has impeded the isolation and characterization of its various antigenic components. It would be extremely important to determine the role these antigens may play in the immunopathology of the disease, both in humoral and cellular responses.

The chemical structure of *M. leprae* is complex. Considering the high degree of homology between this bacterium and *M. bovis* ([1]), in this study we analyze the humoral response to *M. bovis* secreted anti-