now known that the administration of low doses of dapsone is not advisable in order to minimize the emergence of sulfone resistant bacilli.

2) Through the use of this experimental model, no vaccine has been discovered, so far, to prevent leprosy, and neither could the possible preventive activity of BCG be exactly evaluated.
3) With this experimental model it is not possible definitively to resolve the controversy as to whether or not nonsolid leprosy bacilli are viable.
4) With this experimental model it is not possible definitively to resolve the controversy as to whether or not environmental temperature is the main factor in the growth of *M. leprae*.
5) In this experimental model it has not been possible to determine the mechanism of action of sulfones against *M. leprae*.

In our view the fundamental limitation in this experimental model is that we are dealing with a normal animal. *M. leprae* are inoculated into normal mice which lack the biochemical alterations characteristic of the lepromatous condition. Without these biochemical changes, limited bacillary multiplication can occur, as it does in the foot pads of normal mice, but disseminated infection or disease cannot take place.

In summary, it seems to us that any experimental model which ignores the biochemical alterations characteristic of lepromatous leprosy will inevitably be limited in its applicability. This seems to be the case with Shepard's method in addition to the technical limitations outlined earlier.

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Reply to Dr. Bergel's Letter to the Editor

To the Editor:

The Editor has asked me if I wish to reply to Dr. Bergel's letter. I am reluctant to do so because I believe that communications of this sort too easily degenerate into useless exchanges of personally motivated assertions. The only really suitable scientific communication is a full-scale publication with adequate description of methods, full presentation of results, cogent discussion, and conclusions; the paper should be published in a journal that requires review by knowledgeable scientists before possible revision and acceptance. The reader is thereby provided with the evidence that he needs to form his own conclusions about what has been written in the paper.

If I did not reply to the statements of Dr. Bergel, however, some readers might conclude that I have at least partially accepted his assertions. To avoid such confusion let me simply state that, with one exception, I think all of the limitations and observations listed by Dr. Bergel are either wrong (entirely or in substantial part) or trivial. The exception, of course, is his first limitation; as far as I know, no one has claimed that the experimental *M. leprae* infection in normal mice resembles human lepromatous disease histologically. The concentration of *M. leprae* in mice is usually lower, but the values in mouse-foot-pad lesions and in human lepromatous tissue overlap.

Because Letters to the Editor often are political rather than scientific, the reader is well-advised to consider their purpose. I have given the reason for my reply. It may be that Dr. Bergel feels that the infection

of normal mice with *M. leprae* provides evidence against his theories, which emphasize the harmful effects of pro-oxidant diets. If so, this is most unfortunate because the experimental infection in the mouse and the similar infection in the rat provide opportunities to explore the effect of diet on leprosy. I feel that this experimental area has been ignored much too long. In my own case, discussions with experts in the area have been discouraging because of stated difficulties in experimentally reproducing the usual types of human malnutrition in the mouse or rat. Dr. Bergel's nutritional theories are unique, however, and I believe that they are testable experimentally with these systems. He may be discouraged from proceeding by his belief that values that do not have a normal frequency distribution cannot be analyzed statistically (his limitation number 3). Fortunately, nonparametric methods are entirely suitable for such distributions ([1]). An approach through incisive experimentation would be most helpful. Many observers have been impressed by the association of endemic leprosy with inadequate nutrition.

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HLA Antigens and Leprosy

TO THE EDITOR:

The broad spectrum of clinical forms of leprosy, ranging from tuberculoid to lepromatous leprosy, is determined by the underlying degree of cell-mediated immunity of the host; specific immune response genes (Ir), linked to HLA genes in the major histocompatibility complex, could play a significant role in conditioning the host's susceptibility and/or the type of leprosy.

Many previous population studies of the association of HLA antigens with leprosy, whether tuberculoid or lepromatous, carried out in different ethnic groups failed to show conclusive results, but the family studies of de Vries, *et al.* ([1,2]) have indicated an HLA-linked genetic influence on the course of *M. leprae* infection. On the other hand, the study of Stoner, *et al.* ([4]) has evidenced the absence of an HLA-linked genetic defect underlying the *in vitro* unresponsiveness of lepromatous leprosy patients to *M. leprae* antigens.

We have studied the distribution of HLA antigens in 32 unrelated Italian Caucasian lepromatous leprosy patients and in 210 healthy, unrelated individuals of the same ethnic background. Patients and controls were typed for 52 HLA antigens of A, B, and C loci by the standard NIH Terasaki lymphocytotoxicity microtechnique. The HLA specificities tested were those recognized by the VII Histocompatibility Workshop.

BW52, BW38, and B7 appeared to have an increased frequency in patients when compared to controls (χ^2 with Yates' correction: 5.4, $p < 0.025$; 5.0, $p < 0.05$; 4.7, $p < 0.05$, respectively), but multiplying the significance values by the number of antigens tested ([3]), the differences were no longer significant. Thus our findings do not agree with any one of the previous population studies carried out whether among Caucasian or non-Caucasian ethnic groups. It is likely that the typing of many more patients for HLA-D and DR loci will probably provide more conclusions about some HLA-linked genetic influence on susceptibility to leprosy and/or on the clinical course of this disease.

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