Dr. Katoch's Response

TO THE EDITOR:

We are writing in response to a letter by Dr. Jopling regarding our paper entitled "Comparison of three rifampin-containing regimens in paucibacillary patients" (4). Dr. Jopling has raised certain questions about our lepromin testing results. Firstly, the antigen used in our studies is Dharmendra antigen as standardized by Sengupta, *et al.* (5). The final concentration of this antigen is 10 million bacilli per ml. This number of bacilli gives a good early and late Mitsuda reaction, with an additional advantage that ulcerations with standard antigen are fewer and more superficial than with a higher concentration of *Mycobacterium leprae* as recommended internationally. We agree with Dr. Jopling that induration of 3 mm or more is recommended as positive reaction with standard Mitsuda lepromin containing 160 million bacilli per ml. However, the size of the nodule of a positive late reaction will vary with the strength of the antigen depending upon the number of bacilli per ml and their integrity. We have fixed a 5-mm induration as the criterion depending upon experience with our preparation. Other workers (2) have also used a 5-mm induration at 4 weeks as the positive criterion for the Mitsuda reaction. With our preparation and with this criterion, we never get a negative response in tuberculoid (TT) and never a positive response in lepromatous (LL) cases. Most of the borderline tuberculoid (BT) cases are also positive; only a few BT cases are negative and this applies to histopathologically confirmed cases also. We have not recorded the doubtful positive results and cannot speculate what their response might have been had we used Mitsuda antigen with a higher concentration of bacilli and/or with 3 mm as the criterion of positivity. However, we do agree that some of our BT and indeterminate (I) cases who are negative by our criteria might have been Mitsuda positive by the international criteria. On the other hand, responses of less than 5 mm with a lepromin preparation containing 160 million bacilli have been considered to be nonspecific (1). Our lepromin was recently prepared so the effect of storage is highly unlikely. Lepromin negativity in BT leprosy has been reported by other workers as well (3). We agree that the late Mitsuda response helps to some extent in classifying leprosy cases but, on the basis of our experience, we feel that the clinical criteria of classifying TT, BT, and I cases as paucibacillary as recommended by the World Health Organization (WHO) is adequate for treatment purposes. In our experience, lepromin positivity has not been found to be of much prognostic significance in paucibacillary patients once these cases are on multidrug therapy (MDT). As detailed in our paper and from subsequent follow up, we have not found any relationship between lepromin positivity and a) response to MDT, b) spontaneous subsidence after stopping the treatment, and c) occurrence of relapses (4).

Lepromin (Mitsuda) positivity and response to MDT. It was observed in our paper (4) that out of 66 lepromin-positive patients (Regimen I) only 52 responded to 6 months of MDT; whereas of 12 lepromin-negative patients of Regimen I, 10 responded to 6 months of MDT, showing thereby that the lepromin status in this group of patients did not influence response to therapy.

The spontaneous subsidence of activity after stopping the treatment also was not influenced by lepromin (Mitsuda) positivity. It may be recalled that 25 patients remained active at 6 months of MDT, at the time of cessation of therapy (Regimen I). Of these patients, 18 worsened with progression of the disease and among these 18 patients, 14 were lepromin (Mitsuda) positive. This, thereby, shows that disease activity did not subside spontaneously even in lepromin-positive patients when the treatment was stopped at 6 months.

The number of relapses occurring in subsided cases was also not influenced by lepromin positivity as is evident from our present study and further follow up. Out of 65 patients who subsided after 6 months of MDT (Regimen I of our study), 5 have re-

lapsed in 2 years of follow up after stopping treatment; 4 of these 5 patients were lepromin (Mitsuda) positive.

On the other hand, the significant observation of our study was that by further continuation of treatment with dapsone for another 6 months (Regimen II of our paper), no worsening of the disease status was observed in any of the paucibacillary cases, whatever their classification or immunological status. Further, the incidence of relapses was also minimized.

We thank Dr. Jopling for his valuable comments, and hope that our reply will clarify the questions raised by him.

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Allergy and Immunity in Leprosy: Are these Concepts Becoming Obsolete?

TO THE EDITOR:

Science advances by observation and experiment. For both of these, technology is necessary and when it is inadequate, progress may be retarded. However, as investigators into artificial intelligence (AI) are now finding, conception and creativity are also required, but the ideas that these introduce may not be immediately susceptible to confirmation or refutation by existing techniques. In the absence of new ideas, not only may real advances be blocked, but false conclusions may be reached due to persistent misinterpretation of observations and experimental results already obtained.

In the exact science of inorganic chemistry, Stenberg, *et al.* ([9]) pointed out that the solid-state chemistry of superficially mundane A_2BX_4 compounds with β-K_2SO_4-related structures was "*a can of worms*" characterized by prolific polymorphism and, despite careful single-crystal X-ray diffraction studies, *persistent uncertainty* about exact space groups and atom positions. They referred to *50 years of (confusing) literature* and proposed that *wrong structural models might have been refined* (my italics).

It is tempting to believe that similar considerations may apply in the less exact science of "leprology." The interesting editorial by Maier ([5]) gives an excellent review of knowledge of the subject to date, but appears at several points to avoid addressing some crucial longstanding problems. Although on p. 133 Maier states: "There is as yet no immunological explanation for tuberculoid leprosy, in which cell-mediated responses to *M. leprae* seem to be intact." He then cites two possibilities for the appearance of this form of the disease: "Firstly, there may be a delay before the onset of cell-mediated immunity so that when it appears the bacilli are established in vulnerable tissues which are then damaged by the inflammation. Secondly, cell-mediated immunity could be directed against antigenic components which are released only by or-