DDS-resistant Leprosy

TO THE EDITOR:

With reference to the paper by Almeida, et al. on "DDS-resistant Infection Among Leprosy Patients . . ." appearing in the September 1983 issue of the JOURNAL (pp. 366– 373), the following comments are offered:

Firstly, exclusion of 149 "not screened cases," 198 "absentees," and cases with less than 80% treatment from analysis introduces a bias in estimation. Taking overall treatment regularity as criteria for comparison does not appear to be correct since it does not discriminate the treatment regularity in the crucial initial period of treatment in a patient.

In their paper, "prevalence" is worked out as a percentage of the total number of cases "fully studied" over an unspecified period of time; whereas "incidence" is expressed as the average annual percentage of total person-years of treatment experience. It is like cutting the cake to suit the needs of the situation. If we cut a lamb into a certain number of pieces, we do not get that number of lambkins, only lamb chops considered to be a culinary delicacy. Use of person-years to work out rates in Tables 2 and 3 seems unnecessary and makes it difficult to apply statistical tests for comparison, in the way they are presented. "Prevalence" and "incidence" figures are projected in many papers on studies on DDS-resistance. Can someone elucidate the appropriate methodology for a study to find out prevalence and especially incidence rates of DDS resistance? We are in total disagreement with the interpretation of the findings in Table 3. Cases with less than 50% treatment as well as those with 50-79% treatment should have been included. If, after their inclusion, the results were found to be similar to what is projected in the table, the

one way it could be interpreted is that in cases on low initial doses of DDS, the occurrence of DDS-resistant infection seems to be postponed or delayed; it appears to be quicker in cases on higher initial doses.

In their discussion, the following statements are made which invite comments:

a) "attainment of smear negativity appears to be a favorable prognostic sign, indicating a significantly reduced risk of DDS-resistant infection"—Risk of DDS-resistant infection cannot be assessed by comparing the "prevalence" figures given earlier.

b) "Patients deteriorating on DDS treatment are likely to harbor a greater proportion of DDS-resistant *Mycobacterium leprae* than those improving on DDS treatment"—This is not supported by any finding presented in the paper. It could be stated the other way also. Carrying out more frequent serial harvests using more animals in each MFP experiment, to find out how soon DDS-resistant infection is identified in patients and also noting the multiplication factor in such positive test harvests, may perhaps give an indication of the relative proportions of resistant and sensitive organisms in such patients.

c) "the demonstration of DDS-resistant *M. leprae* by the mouse test (Ref) should not be regarded as synonymous with failure of response to DDS monotherapy"—It depends on what one accepts as response to treatment. This statement could be countered by stating that the (apparent) response to DDS monotherapy should not be regarded as insurance against subsequent development of DDS-resistant disease on continued DDS monotherapy, using the same argument put forth by the authors in the first part of the paragraph on page 371.

The criteria for growth in mouse experiments in their study do not seem to conform to the accepted standards established by the WHO Workshop held in 1979. With reference to Almeida, *et al.* "Response to Dapsone (DDS) ... 1960s vs 1970s":

The statement in their discussion that "although negative findings cannot be used to disprove hypotheses, these data do not support the claim that DDS-resistant infections have been increasing in frequency since the introduction of DDS monotherapy" is grossly misleading and irrelevant to the findings presented in the paper. We got similar findings on the analysis of data on cases treated in the 1960s and 1970s in our field area at C.L.T. & R.I. which are being published in another journal. These findings only show that the overall level of efficacy of DDS in the treatment of leprosy in either period was not very high, and this might still be reduced if the relapses among them are included in the computation. However, the efficacy does not appear to have diminished over the years. This finding only supports the case for inclusion of DDS in the multidrug regimens recommended and accepted for treatment of leprosy in the present context.

With reference to Almeida, *et al.* "Results of Long-term Domiciliary DDS Monotherapy for Lepromatous Leprosy . . . ":

The use of surviving LL cases only in the analysis in this paper introduces bias and hence limits the value of the findings. A better method would be cohort analysis. It is known that mortality is higher among lepromatous cases who do not respond to treatment and worsen clinically.

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