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CORRESPONDENCE

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Analysis of a Trial of Dapsone vs Placebo in Lepromatous Leprosy[1]

To the Editor:

This letter is sent in order to present data gleaned retrospectively from a controlled trial of dapsone *vs* placebo in lepromatous leprosy. Although a comparison of dapsone and a placebo based on an experimental design incorporating the recently acquired understanding of the morphology of *Mycobacterium leprae* might yield more informative results, such a comparison is not likely to be carried out now, because current standards of medical practice and investigation do not permit the use of a placebo in a controlled trial of antibacterial chemotherapy in lepromatous leprosy.

Although a fall of the morphologic index (MI, the per cent of *M. leprae* in a bacillary preparation that are uniformly and brightly stained) has been demonstrated ([5]) to be an accompaniment of effective chemotherapy in lepromatous leprosy, a comparison of the MI during treatment with an effective therapeutic agent with that during treatment with a placebo had not been made. The opportunity to make such a comparison presented itself recently when Dr. Chapman H. Binford, Medical Director of the Leonard Wood Memorial, permitted us to review biopsy material from the Memorial's cooperative chemotherapy trials in lepromatous leprosy.

This review was limited to those patients treated at the Eversley Childs Sanitarium near Cebu, the Philippines, in the first Leonard Wood Memorial trial ([2]). Unstained paraffin sections of the skin biopsy specimens of the 20 per cent of the patients who had received the least prior sulfone therapy were obtained from the Leprosy Registry of the Armed Forces Institute of Pathology, stained at the same time by a modification of the Fite-Faraco procedure ([3]), coded with a series of random numbers, and examined. The MI was measured by the method previously described ([4]), in pre- and posttreatment sections from 12 of the 47 patients assigned to the dapsone group and 13 of the 52 assigned to the placebo group. Because prior sulfone therapy was denied for only two patients in the dapsone group and four in the placebo group it was not possible to limit the review to previously untreated patients.

The MI's measured in the 50 sections, listed in the accompanying table, were subjected to an analysis of variance ([1]), which indicated no significant difference between the pretreatment MI's of the two groups of patients, whereas the difference between the post-treatment MI's of the two groups was statistically significant. Analysis of these data by the chi square technic ([1]) indicated that the number of post-treatment MI's less than 1 is significantly greater in the dapsone group than in the placebo group, whereas the number of pre-treatment MI's less than 1 is not significantly different for the two groups.

This study yields the expected results, viz., that the MI falls with effective treatment, and that a decrease of the MI is not a feature of ineffective therapy. That the data are not more convincing requires comment. A high MI was not, of course, a condition for admission to the therapy trials, nor was prior sulfone therapy ground for exclusion from the trial. Thus the number of patients most suitable for analysis of changes in the MI is reduced by 40 per cent. Because more sulfone pretreatment and a shorter period of dapsone therapy

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TABLE 1. *Morphologic index.*

Dapsone		Placebo	
Pretreatment	Posttreatment	Pretreatment	Posttreatment
	Female patients		
2.0	0	0	0
0	0	4.0	1.7
1.0	0.3	3.3	0.7
[3.0][a]	0	2.7	[0]
		7.0	0.7
Mean 1.5	0.1	3.4	0.6
	Male patients		
(0)[a]	0	2.7	0.3
2.0	0.3	2.0	0.7
3.3	0	3.0	0
0.3	0.3	0	1.7
0	0.7	0.7	2.3
2.7	0	0.7	3.3
1.0	[0]	0.3	4.3
[0.8]	0	2.3	2.7
Mean 1.3	0.2	1.5	1.9

[a] MI's enclosed in brackets are based on the examination of 100 bacilli; those enclosed in parentheses are based on the examination of 200 bacilli; all other MI's are based on the examination of 300 bacilli.

characterized the trial in the two remaining institutions in which a placebo was employed, there seems little likelihood of obtaining more revealing data by the examination of additional sections.

Finally, it is apparent that seven of the placebo group experienced a decrease of the MI during treatment similar to that of the dapsone group. It may be argued that decrease of the MI is not restricted to effective therapy, or that it is entirely a random phenomenon. The report already cited ([5]) and unpublished data from this laboratory and that of Dr. Charles C. Shepard of the Communicable Disease Center suggest, on the other hand, that the decrease of the MI is a useful criterion of effective therapy, and the method of measuring the MI employed in this study has been validated ([4]). It is apparent, furthermore, that the MI increased in only one of the five dapsone patients beginning therapy with an MI less than 1, whereas it increased, and to a greater degree, in four of the five placebo patients beginning therapy with an MI less than 1. One wonders if the patients may have had access to an illicit supply of sulfone. Doull's report ([2]) states that blood dapsone levels were measured in a portion of the patients, but no results of these measurements are presented.

In summary, retrospective analysis of a early trial of dapsone *vs* placebo in lepromatous leprosy by the measurement of the MI on the sections of biopsy specimens obtained before and after 48 weeks of treatment, confirms the greater effectiveness of dapsone. It is regretted that the results are not more striking, because it is no longer possible to carry out a prospective comparison of dapsone *vs* placebo.

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