Absence of Enhancing Effect of Trimethoprim on the Activity of a Sulfonamide Against *Mycobacterium leprae*

To the Editor:

The activity against *Mycobacterium leprae* of the sulfonamides has been well-documented (Pattyn 1965, Gaugas 1967, Languillon 1964), although the minimal inhibitory concentration (MIC) of these substances is much closer to the blood concentration attainable than is the case with dapsone (Ellard, *et al*, 1972).

Since trimethoprim (TMP) is known to enhance the activity of sulfonamides on a wide variety of microorganisms, we tested the effect of TMP on the activity of a sulfonamide against *M. leprae* in the mouse model.

The continuous method (Shepard 1967) was applied, using strain 12445 previously found to be fully senstitive to dapsone (Pattyn, *et al*, 1972). At the end of the observation period acid-fast bacilli were counted in foot pad harvests from two to three mice individually, and in one or more pools of three foot pads; furthermore, three to six foot pads were examined histologically.

The sulfonamide used was sulfadimethyloxazole (Grüenthal). The results can be summarized as follows:

Concentrations of chemotherapeutics in food

% Sulfa	Result	Sulfa % + TMP %	Result
1	A	1 + 0.2	A
0.1	A	0.1 + 0.02	A
0.01	I	0.01 + 0.002	I
0.001	I	0.001 + 0.0002	I
DDS 0.01			

A = active on *M. leprae*
I = inactive

The MIC of this sulfonamide is higher than those found for other sulfonamides by Ellard, *et al* (1970). It thus appears that TMP does not enhance the activity of sulfadimethyloxazole aginst *M. leprae*. Knowing that TMP alone was inactive (Shepard 1972), this result was not entirely unexpected.

Apart from the importance of this finding for the treatment of human leprosy, this result might also indicate—together with the previous finding of Shepard (1967) that the antibacterial activity of dapsone is only partially antagonized by para-aminobenzoic acid—that the mode of action of sulfones and sulfonamides is not on the pathway of the folic acid synthesis in *M. leprae*.

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