DAPSONE COMPLIANCE USING ISONIAZID-MARKED FORMULATION

Sir,

In *Lepr Rev*, 1983; **54:** 317–25, Stanley *et al.*[1] describe their investigation of dapsone compliance using an isoniazid-marked formulation in conjunction with the determination of dapsone/creatinine (D/C) ratios in urine. Their basic idea is to determine the mean D/C ratios in the urines of individual patients under conditions of full compliance which—in their procedure—is not established by a period of supervised dapsone intake, but by the detection of 2 isoniazid metabolites in the urines. Once an estimate of the individual's mean 'compliant' D/C ratio has been obtained, his compliance can be followed by comparing the D/C ratios in further urine samples with this estimated mean. The paper gives an example of such comparisons in which numbers of missed doses are calculated based on a fall in D/C ratios by about 50% every 27 h.

I have considerable doubts about the validity of this procedure because of the following:

1 The urine of a patient who would have missed yesterday's dapsone dose, but would have taken today's dose correctly, would be equally positive in the marker test for compliance as the urine of a fully compliant patient.

2 The 'compliant' D/C ratios of individuals in this study had on average a variation about the mean of 'only' $\pm 12\%$, but in more than a quarter of the individuals the lowest D/C 'compliant' ratio was less than 73% of the highest one, the percentage that is used to discriminate between full compliance and one missed dose.

3 Because of the 'small' variability in the 'compliant' D/C ratios all marker-positive urines were considered to be due to dapsone intake that same morning. However, at least the lower D/C 'compliant' ratios referred to under point 2 could quite well be interpreted as being due to dapsone intake on the previous day.

4 Previous studies of half-lives of dapsone in man have reported considerable variation, with ranges from 11–53 h and means varying from 18–38 h.[2–4] Calculations in individuals should therefore be based on individual half-lives and not on a mean value.

In view of the points raised above, such calculations of numbers of missed doses as presented in the paper are of little value. But even if it could lead to valid calculations, to introduce an isoniazid-marked formulation would seem equally far-fetched as hospitalization for the purpose of establishing full compliance when estimating the 'compliant' D/C ratios of individual patients. A few days of supervised intake of dapsone at home combined with health-education could be a simple and productive alternative.

I would certainly not envisage the isoniazid-marked formulation in conjunction with the determination of D/C ratios as a 'much improved standard approach to monitoring the dapsone compliance of out-patients', as is suggested by the authors. A standard approach should be simple and cheap, but none the less valid. In my current experience, the urine spot test employing filterpaper impregnated with a modified Ehrlich's reagent, which was recommended by the WHO Expert Committee on Leprosy as early as 1966,[5] fully qualifies for this purpose. A slightly revised account of this test is published in the April 1984 issue of *Tropical Doctor*.[6]

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