ARE DAPSONE HYPERSENSITIVITY REACTIONS DOSE RELATED?

Sir,

I would be surprised if there are many leprologists who would disagree with the often repeated concern regarding dapsone hypersensitivity reactions. Numerous publications in the past five years from many countries have commented on the frequency as well as the severity of this phenomenon and most have concluded with some hypotheses as to the reason for the presumed increase in incidence of dapsone hypersensitivity in one or other of its manifestations.

I am stimulated to reply to the paper by Richardus & Smith[1] on the recent observation of the recovery of a ten-year-old boy with full blown dapsone syndrome in the south east of Nepal. He is the thirteenth case of dapsone hypersensitivity (fortunately none fatal) in the past two years from this leprosy control project, which currently has a total of 4645 patients on treatment, 59% of whom are on standard WHO multidrug therapy. With two exceptions all of these patients were started on full dose dapsone monotherapy and hence developed their problem before rifampicin or rifampicin and clofazimine were commenced. It can be seen from Smith's paper[2] that two of the three fatalities we reported to him from Zambia were in patients who were still on monotherapy at the time of their catastrophic drug reaction and this has similarly been reported over many years.[3 6]

It would therefore suggest to me that the combination of dapsone with other antileprosy drugs, as has been suggested elsewhere, is not a factor in the possible increase in dapsone hypersensitivity. The high starting dose of dapsone given almost universally to all patients is probably a more significant factor. The idea that a reduced dose of dapsone may lessen the incidence of side-effects is certainly not new.[3] Additionally it was considered that the dapsone syndrome virtually disappeared with the subsequent lowering of the initial dose, for example to 25 mg weekly.[6] A small average body

weight population, such as the Nepalese, Burmese, Thais, etc. may be even more at risk from starting on full dose dapsone.[7] Where health workers are not sufficiently alert to the problem, or where the patient stays at home, it may initially be the case that further doses of dapsone are consumed after the presenting features of hypersensitivity occur and this may also result in more serious manifestations and possibly increase the likelihood of a fatal outcome.

I think we would see fewer and less severe problems if we started adults at 50 mg per day and children at 25 mg per day and only after a period of four weeks on this dose assumed the standard WHO recommended dose.

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