Reply to Dr H. W. Wheate's Letter

Sir,

While I appreciate the compliment paid by Dr Wheate on my Editorial in *Leprosy Review* (1978, **49,** 97) on "Combined Therapy in Principle and Practice for the Control of Dapsone Resistance", I fully accept his assessment that the very large pool of lepromatous leprosy throughout the world who are already on dapsone monotherapy, represent the major source from which ever increasing numbers of patients with dapsone resistance (secondary) will inevitably emerge in the next decade. Therefore, while accepting that all newly diagnosed cases of lepromatous leprosy be initiated on combined therapy to prevent them ever developing resistance to dapsone, the more immediate and greater source of dapsone-resistant lepromatous patients will evolve from the vast pool of past lepromatous patients given dapsone monotherapy.

In an attempt to halt or significantly reduce the risk of dapsone resistance emerging in these lepromatous patients Dr Wheate rightly proposes that they should all be given a short course of additional antileprosy drugs while remaining on dapsone, and continuing afterwards on dapsone monotherapy. While I fully accept the additional antileprosy drugs recommended by Dr Wheate for this short course "intervention-combined therapy" as regards their efficacy, practicability and relative low cost, I believe they need to be defined in more detail than outlined in Dr Wheate's letter. Thus, while continuing dapsone 100 mg daily the patients would receive, supervised, one dose of rifampicin 1500 mg and a 6 months course of 150 mg daily thiosemicarbazone (thiacetazone). After completion of this 6 months treatment with thiosemicarbazone (thiacetazone) the patients would continue on daily dapsone 100 mg. In addition, at the time of the beginning of the course of intervention therapy and from then onwards, Dr Wheate recommends, if locally practicable, the administration of acedapsone 225 mg by injection every 3 months. The introduction of acedapsone is to ensure that *all* patients are receiving some dapsone, whether or not they are taking unsupervised dapsone by mouth.

Finally Dr Wheate states that this intervention regimen has the advantage of allowing the use of both rifampicin and thiosemicarbazone (thiacetazone) again in combination with clofazimine in the unlikely event of the patients relapsing with dapsone resistance. Unfortunately, I think Dr Wheate is being too optimistic in assuming that such relapses could only be due to the emergence of dapsone resistance strains of *Mycobacterium leprae.* Such relapses could unfortunately be now due to the emergence of strains of *Mycobacterium leprae* resistant to rifampicin or thiosemicarbazone.

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