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Letters to the Editor

Dapsone Resistance in Patients with Treated Lepromatous Leprosy

Sir,
The excellent Editorial in your June number (Vol. 49, No. 2) by Dr Rees on “Combined Therapy in Principle and Practice for the Control of Dapsone Resistance” should be widely read and widely applied.

May I make one comment? Dr Rees rightly distinguishes between the two quite different aspects of the problem:

1) To treat established proved dapsone resistance.

2) To prevent the emergence of dapsone resistance by combined therapy.

The latter aspect is the subject of my comment. Dr Rees says “this involves every new lepromatous patient being treated at onset with dapsone on full dosage with at least one companion drug”, and certainly everyone should agree and act on this statement. In my view, however, this is not enough. There are very many lepromatous patients who have been under treatment for many years—regrettably in many cases with unsupervised, and/or inadequate dosage of dapsone—and many of these must be “incubating” dapsone resistance. It is of note, particularly in certain West African countries, that dapsone resistance was until last year considered a minor problem. Now, however, cases are being recognized and the number of such cases will inevitably increase. From the public health point of view, the already treated lepromatous patient presents a more immediate danger of infection, and of the spread of primary dapsone resistance than the previously untreated patient. As Dr Pearson pointed out in Mexico the situation is analogous to that of an epidemic.

We must, therefore, give combined therapy, at least for a short period, to all cases of lepromatous leprosy; and in the very large group of previously treated patients who are attending our clinics, one such short regimen which combines safety and cost-effectiveness would be: Rifampicin 1500 mg in a single dose, with thiosemicarbazone 150 mg daily for 6 months, combined with dapsone 100 mg daily. This may be supplemented if local conditions make it feasible by an injection of acedapsone 225 mg every 3 months.

This regimen has the advantage of allowing us the possibility of using both Rifampicin and thiosemicarbazone or one of the thionamides again in combination with clofazimine if and when proven dapsone resistance emerges; but hopefully it should at least delay this occurrence.

H. W. WHEATE

ALERT
P.O. Box 165,
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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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