MULTIDRUG THERAPY: REPLY TO LETTERS

Editor,

Exactly 1 year after publication of my Editorial, 'Why multidrug therapy for multibacillary leprosy can be shortened to 12 months,[1] in *Leprosy Review*, two 'Letters to the Editor'[2,3] related to my Editorial appeared in the June 1999 issue. I would like to reply to these letters.

It is correct that, as Mr Lynch[2] has pointed out, an article of which I was a co-author proposed prolonging the duration of MDT for those MB patients who had an average BI $\geq$ 4·0 before MDT.[4] This proposal was based on our observation that the risk of relapse was closely correlated with the bacterial load of the patient, and was significantly greater among patients with BI $\geq$ 4·0 before MDT or $\geq$ 3·0 at the end of MDT.[4] The proposal was logical, but we knew that it was not feasible. On the other hand, Mr Lynch completely ignored our alternative proposal, which was also presented in the same article. We concluded that, from an operational point of view, it is not necessary to introduce a lengthy duration of MDT for a small number of special cases;[4] we thought that MB patients with an initial average BI $\geq$ 4·0 are relatively few, that, in the great majority of relapses, the patients' organisms would remain susceptible to rifampicin and clofazimine, and that tremendous efforts to upgrade the quality of skin-smear services for detecting patients with a BI $\geq$ 4·0, would be required. For these reasons, my colleagues and I did not recommend prolonged duration of MDT for patients with an initial high BI in an article[5] published separately.

Although I continue to believe that the potential risk of relapse is higher among patients with an initial BI $\geq$ 4·0, I have no reason to challenge the low relapse rates reported by control programmes.[6] In fact, we attributed the low relapse rates to the small proportion of patients with BI $\geq$ 4·0 in the field.[4]

With respect to the WHO/CTD/LEP/94.1 document,[6] because the average duration of follow-up was relatively short at the time this document was published in 1994, it was, of course, necessary to emphasize the need to interpret the findings with 'great caution'.[4] However, by the time I prepared my Editorial 4 years later, no significant increase in the relapse rate had been observed. Was it not then reasonable to quote the document as one of the references demonstrating a low relapse rate from routine control programmes?

Various adjectives, e.g. 'relatively few',[4,5] 'rare'[7] and 'relatively scarce',[1] have been employed to emphasize the fact that patients with a high initial average BI are few. Both Mr Lynch and Dr Van Brakel disagreed with this assessment. Mr Lynch[2] stated that, among the MB cases registered in the Dhanusha District, almost 10% had a BI $\geq$ 4·0. However, there is a difference between registered cases and previously untreated cases. If he were to demonstrate that 10% of the newly detected and previously untreated MB cases in the Dhanusha District have an average BI $\geq$ 4·0, I would certainly agree with Mr Lynch that such a frequency is not 'relatively scarce' or 'rare'; in this case, the adjective 'relatively few' appears more appropriate.

Dr Van Brakel also stated[3] that high smear positive (HSP) patients are not rare, but his definition of high smear positivity is > 3 +, a value approximately 10% of our cut-off point, $\geq$4·0. It is not possible to compare the numbers of patients at risk employing two so different criteria.

Because of the lack of evidence showing that 12 months of MDT is as efficacious as the standard

24-month regimen for HSP MB cases, Dr Van Brakel considered that it is unethical to treat such patients with the shortened regimen, and proposed to continue treating all MB patients with the 24-month regimen.[3] Many of us heard the same criticism when MDT was first introduced in the early 1980s, and again, when the fixed duration, 24-month regimen was recommended in the early 1990s.

I am pleased to learn that our report of the correlation between high relapse rate and high initial BI of patients[4] caught the attention of Mr Lynch and Dr Van Brakel and their colleagues in Nepal, and was a source of concern to them. However, if our observation was valid, even the 24-month regimen may be too short to prevent relapse among MB patients with high initial BI;[4] should this be the case, is it 'ethical' to propose continuing the 24-month regimen for all MB patients? I am disappointed that, 4 years after it was reported, the correlation between relapse rate and bacterial load has yet to be confirmed or denied by other investigators. Because they are dealing with a significant number of MB patients with high initial BI, both Mr Lynch and Dr Van Brakel could provide valuable information regarding this issue.

Shortened MDT regimen may be associated with higher relapse rate, and one of the objectives of chemotherapy research is to identify the shortened possible duration of treatment without significantly compromising its efficacy. After the publication of the Seventh Report[7] of the WHO Expert Committee on Leprosy, in terms of duration of treatment, there are two alternative regimens for MB patients, either 12 or 24 months. For individual national leprosy programme, the final choice of the regimen is the responsibility of the national authorities, particularly the programme managers. To avoid unnecessary confusion in the field, whenever possible the two MB regimens should not be employed simultaneously in the same programme. Whatever the regimen being implemented, detection and treatment of relapse is always part of the daily activities of the national programme, and should be incorporated in the training, case-holding, supervision and monitoring. On the other hand, relapse is almost unavoidable after treating hundreds and thousands of patients with MDT. All of us should fully accept the few relapses that may occur from patients with a high initial BI and treat those patients who do relapse with a further course of MDT,[1] and there is no reason to exaggerate the consequence of relapse in leprosy.

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References

[1] Ji B. Why multidrug therapy for multibacillary leprosy can be shortened to 12 months (Editorial). *Lepr Rev*, 1998; **69:** 106–109.
[2] Lynch P. Multidrug therapy (Letter to the Editor). *Lepr Rev*, 1999; **70:** 70–71.
[3] Van Brakel WH. Proposal regarding MB MDT (Letter to the Editor). *Lepr Rev*, 1999; **70:** 71–73.
[4] Jamet P, Ji B, and the Marchoux Chemotherapy Study Group. Relapse after long-term follow-up of multibacillary patients treated by WHO Multidrug regimen. *Int J Lepr*, 1995; **63:** 195–201.
[5] Ji B, Levy L, Grosset JH. Chemotherapy of leprosy: progress since the Orlando Congress, and prospects for the future. *Int J Lepr*, 1996; **64:** S80–S88.
[6] WHO Leprosy Unit. Risk of relapse in leprosy. WHO Document. WHO/CTD/LEP/94.1.
[7] WHO Expert Committee on Leprosy. Seventh Report. *WHO Technical Report Series, No. 874.* Geneva: World Health Organization, 1998.