PROPOSAL REGARDING MB MDT

Editor,

Since the first sulphones were used in the 1940s, leprosy treatment has come a long way. In particular, the introduction of multidrug therapy (MDT) has been a success story. The factor missing in several countries in the 1980s was wide coverage in terms of percentage of patients treated with MDT. There is no doubt that the developments in leprosy treatment and the large reduction in global prevalence over the last 16 years are very exciting.

From the patient's point of view, perhaps the most exciting development has been progressive shortening of treatment due to the increased efficacy of MDT. Both patients and leprosy control programme managers would welcome even further reduction of treatment duration, as long as it has equal efficacy to the currently accepted global standard: 24-month fixed-duration MDT for multi-bacillary (MB) patients.

This is exactly the issue in the debate concerning the new 12-month MB MDT regimen recently recommended by the WHO. Along with many others, including Dr Patrick Lynch (see this issue), I am concerned that, while the efficacy of this regimen may be sufficient for some categories of MB patients, it would not be sufficient for others.

Dr Lynch draws attention to the Institut Marchoux Study,[1] which reported on the increased rate of relapse even with the previous 24-month regimen. We have also observed this after the introduction of the current 24-dose fixed-duration treatment. Before the introduction of clofazimine, the cumulative incidence of ENL was up to 25% in BL and 50% in LL patients. Thanks to clofazimine these percentages have now been more than halved. It is well known that such reactions can lead to irreversible nerve damage, blindness and other severe impairments.

The argument put forward in some WHO publications in favour of reducing the duration of MDT for all MB patients has been that highly smear positive (HSP) patients are nowadays rare. We have observed an increase in the risk of ENL reaction after the introduction of the current 24-dose fixed-duration treatment. There are three flaws to this argument. First, relapse from leprosy is not like relapse from other infectious diseases, such as amoebic dysentery or even malaria. Each leprosy relapse could spell social disaster for the person involved and also for their whole family. Second, the success of the MDT campaign is partly due to the trust that has been built up in the 'community', that leprosy can be cured. Often new cases present because they have heard that leprosy can be cured from others who have (had) the disease. An increased frequency of relapses could jeopardize this trust. Third, and most importantly, MB patients are most likely to relapse with multibacillary disease. It may take years in individual cases before the diagnosis of relapse is made. All the time they may be a source of infection in the community, creating a new pool of infection at a time when the battle against leprosy might otherwise have been in its final stage.

I contend that HSP leprosy is not rare in several of the currently most endemic countries. For example, in Nepal, where more than 50% of new cases are MB, the percentage of HSP cases has ranged from 7% to 40% in various large projects across the country. With case detection statistics of over 6000 per year, HSP cases cannot be called rare, even in absolute numbers. In our field programme in the Western Region of Nepal, 73% of the patients are classified 'MB'. Most (~80%) have a skin smear done at diagnosis. Out of 2346 new cases registered in recent years and who had a skin smear taken, 308 (13%) had an initial smear of >3+.

The figures published in the *Weekly Epidemiological Record* (WER) of 2 May 1997 (vol. 72, no. 18) also show that HSP patients are not rare. About 17% of 142,844 new MB cases reported in 1995 were HSP (BI >3+). If the data from India are considered separately, 25% of MB and 13% of all cases in the remaining countries had an initial BI of >3+. In many endemic countries the number of HSP patients is large enough to warrant our special concern. Table 3 in the quoted issue of the WER shows that in 1995, India registered an estimated number of 8842 new cases who were HSP, Brazil registered 5388, Indonesia 1507, Nepal 1374, Ethiopia 1329 and Madagascar 980. Because of the lack of (adequate) skin smear facilities in the field programmes in many of these countries, these figures may well be underestimates.

As stated by Waters in his editorial in the June issue of *Leprosy Review*,[2] 12 months of MB MDT is likely to be adequate for smear negative MB cases (or even for those whose smears are 1–2+). However, I am not aware of any current scientific evidence showing that 12 months of MDT has an equal or better treatment efficacy to the standard 24-month regimen for HSP MB cases. For this reason, it should be considered unethical to treat such patients with the shortened regimen.

Not many leprologists would recommend 12 months treatment to a patient if they knew the patient's skin smears were 4, 5 or 6+. The solution would seem easy: treat all HSP cases with 24-month MDT and all other MB cases with the 12-month regimen. One problem, however, is that in many field situations, smears are no longer done. Establishing reliable skin smear services has been notoriously difficult and with the advent of the 24-month fixed-duration regimen, many (including the WHO) no longer recommended that skin smears be done. All MB patients would receive the same treatment, regardless of their initial smear.

This means that in many field programmes, we no longer know who is (highly) smear positive and who is not. If the 12-month regimen is to be considered currently unethical for HSP patients, and I propose that it should, then it also becomes unethical to treat any MB patients with this regimen, as long as it is not possible to determine their bacteriological status. I therefore propose that we continue

treating all MB patients with a 24-month regimen, unless it is known that their initial highest BI is less than 3+.

Many countries have already implemented the new shortened regimen. Perhaps this was done without giving adequate consideration to the ethical issues involved. In such circumstances, I would recommend that the new treatment guidelines be modified as suggested above. An exception could perhaps be made for countries and areas where HSP patients are genuinely rare, say, less than 2% of the new cases.

It is accepted best practice in medicine only to implement a new treatment regimen after its efficacy and safety have been adequately demonstrated in scientifically conducted randomized controlled trials. Such trials would compare the efficacy and safety of the new treatment or regimen with the currently accepted treatment. According to Ji in his recent editorial in Leprosy Review,[3] such a trial is underway, testing the new 12-month MB MDT against the current 24-month regimen. Let us hope that in a few years time, after an adequate surveillance time has been completed, we will have evidence that MB MDT can be further shortened.

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References

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