CORRESPONDENCE

This department is for the publication of informal communications that are of interest because they are informative and stimulating, and for the discussion of controversial matters. The mandate of this JOURNAL is to disseminate information relating to leprosy in particular and also other mycobacterial diseases. Dissident comment or interpretation on published research is of course valid, but personality attacks on individuals would seem unnecessary. Political comments, valid or not, also are unwelcome. They might result in interference with the distribution of the JOURNAL and thus interfere with its prime purpose.

Regarding Relapse After Long-Term Follow Up of Multibacillary Patients Treated by WHO Multidrug Regimen

TO THE EDITOR:

The article "Relapse After Long-Term Follow Up of Multibacillary Patients Treated by WHO Multidrug Regimen," published in the INTERNATIONAL JOURNAL OF LEPROSY **63** (1995) 195–201, was a strong bomb to all leprosy researchers. The relapse rate reported by Dr. Jamet, *et al.* was so high that it astonished everyone.

I agree to treating some multibacillary (MB) patients with high bacterial indexes (BIs) with a longer duration of MDT. In my work since 1983, all MB patients were treated with MDT until smear negative. To date, there is only one MB patient treated with dapsone (DDS) monotherapy before MDT who relapsed at the end of the third year after 5 years of regular MDT. The mouse foot pad test demonstrated viable organisms. In the neighboring province, however, all of the MB patients were treated with MDT for only 2 years since 1985–1986, and there were two cases who relapsed (private communication). These two cases also had been treated for various durations with DDS monotherapy before MDT. I believe that in my work and in the neighboring province there are many MB patients with a BI of >4.0 before MDT, but the relapse rate was very low in the two areas.

So, the high relapse rate reported by Dr. Jamet, *et al.*, I think, perhaps was caused by irregular MDT treatment. Relapses caused by irregular MDT have occurred in China. Some patients took the tablets into their mouths (facing the doctor) but did not swallow them and disgorged the tablets (behind the doctor's back) for fear of slight side effects caused by the drugs.

Of 35 cases in the article reported by Dr. Jamet, *et al.*, there were 15 who had been treated for various durations with DDS monotherapy before MDT; 5 had been treated with DDS monotherapy followed by various durations of DDS plus rifampin. I do not know how many relapse cases had been given DDS monotherapy before MDT. I found that some relapse cases seemed to be correlated with DDS monotherapy before MDT. Perhaps DDS, as a bacteriostatic monotherapy, before MDT formed a bad living environment for *Mycobacterium leprae,* and changed more *M. leprae* to persisters. When the bactericide (MDT) was given, there was no effect on the many viable persisters, thus causing a late relapse.

A relapsed patient is an infectious source. When leprosy is suspected, it must be quickly confirmed by re-testing the skin smear and skin biopsy to look for solid *M. leprae.* In my experience, some relapse cases after DDS monotherapy may have no obvious new skin lesions, even during the late stage. The active and visible lesions mainly depend on the status of inflammation in the

dermis, such as the number of inflammatory cells, the dilatation of the small blood vessels, and the degree of edema in the dermal layer. In a word, they depend on the cell-mediated immunity of the patient. If a lepromatous patient with a BI of >4.0 does not react to the numerous *M. leprae,* there will be no obvious new skin lesions at all.

I think that if there is an increase in the BI not accompanied by new lesions, the patient must be quickly re-examined by the various methods available today to confirm whether or not she/he had a relapse.

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Dr. Jamet, *et al.* Reply

TO THE EDITOR:

We read with great interest the valuable comments from Dr. Shen Jianping on our article ([1]).

Perhaps it is a reasonable approach to treat multibacillary (MB) patients with high bacterial indexes (BIs) with a longer duration of WHO-recommended multidrug therapy (MDT) if the patients are treated and followed up by a sophisticated institute, such as the Institute of Dermatology in which Dr. Shen is working, because they are able to score correctly the BI of the skin smears. Unfortunately, the quality of skin-smear service in many leprosy control programs is far below the desirable level, and it would required tremendous effort and resources to upgrade the quality of the skin-smear service. We are afraid that it would create enormous confusion in the field if the duration of MDT is variable and depends upon the average BI of the patient before starting MDT. We were very interested to learn that Dr. Shen and his colleagues had very few relapses among their many MB patients with BIs of ≥4.0. If Dr. Shen and his colleagues eventually publish their detailed results, the scientific community would benefit considerably from sharing their experience.

As described in our article ([1]), the patients of this particular group were hospitalized until completion of therapy, and all drugs, including daily dapsone (DDS) and clofazimine, were administered under supervision of medical personnel. Despite supervision, we cannot completely rule out the possibility that occasionally some of these patients did not swallow the drugs (as pointed out by Dr. Shen). Nevertheless, it is very unlikely that the high relapse rate was due to irregularity of MDT. After all, the supervision of drug administration among these patients was better than that in a great majority of outpatients.

Dr. Shen's observations and hypothesis on the relationship between previous DDS monotherapy and relapse after MDT were interesting. But, if this is the case, how does one explain that among the millions of leprosy patients who had been treated with DDS monotherapy before MDT very few of them relapsed?

Finally, we have never seen relapsed patients, especially during their later stage, who did not have obvious new skin lesion(s). In our limited experience, new lesion(s) always occur sooner or later in real relapsed cases. Of course, a suspected relapse should be kept under close surveillance, but there is no need to make a quick decision since, after all, in most cases relapse is not a clinical emergency.

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