

## **Relapse rates and a 10-year follow-up of a 6-week quadruple drug regimen for multibacillary leprosy**

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Accepted for publication 19 March 2002

*Summary* Between 1989 and 1993, 136 multibacillary leprosy patients received a 6-week treatment regimen consisting of daily rifampicin 600 mg, ofloxacin 400 mg, clofazimine 100 mg and a weekly dose of 100 mg minocycline. A previous analysis after a mean follow-up of 4–7 years revealed a relapse rate of 2%, involving six late (after more than 5 years of follow-up) relapses. During the following years, 12 more relapses appeared during years 8–9 of follow-up. A mean follow-up period of 5 years is insufficient to evaluate treatment regimens in multibacillary leprosy. The present regimen cannot be recommended.

### **Introduction**

For many years, we have performed studies on short course treatment regimens for leprosy. When in the late 1980s the bactericidal effects of ofloxacin and minocycline were discovered,<sup>2,3</sup> we initiated a study on a 6-week treatment regimen of multibacillary leprosy using a combination of rifampicin, ofloxacin, clofazimine and minocycline. Favourable results were published in 2000.<sup>1</sup> During 2000 and 2001, however, the number of relapses among previously treated patients increased and forced us to abandon the regimen and to communicate the more recent results.

### **Patients and methods**

Between November 1989 and December 1993, a total of 136 patients participated in the study. Diagnosis was based on clinical and bacteriological examinations and histopathology of a punch skin biopsy.

Treatment consisted of daily (6 days a week) supervised administration of 600 mg rifampicin, 400 mg ofloxacin, 100 mg clofazimine and a weekly dose of 100 mg minocycline. Thereafter, patients were examined once a year in the same way as at intake.

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**Table 1.** Number of relapses in relation to years of follow-up

Years of follow-up	Number of relapses
5	2
6	4
7	2
8	5
9	4
10	1

## Results

By mid-1999, the mean follow-up period of the patients was 4–7 years with a cumulative relapse rate of 2%. From year 6 on, it was increasingly difficult to see the patients annually. At that moment, six late relapses had been diagnosed after, respectively, 72, 96, 96, 103, 106 and 111 months after the start of treatment. During 2000 and early 2001, however, the number of relapses during the 8th and 9th years 8 and 9 increased considerably, bringing the total now to 18 (13%) (Table 1).

The bacillary index (BI) of these patients at the start of treatment was as follows: one had a BI of 3, 12 had a BI of 4 and 5 had a BI of 5. All patients have now been given the WHO multibacillary regimen.

## Discussion

Since there is no possibility yet to distinguish relapses from reinfections (which have been documented in tuberculosis<sup>4,5</sup>), the worst hypothesis has to be applied in the analysis of the results and the cases are to be interpreted as relapses.

There has been much discussion about the incubation time for relapses in leprosy, in particular how frequently they appear after more than 5 years after the start, or the end, of therapy.<sup>6</sup> A WHO report<sup>7</sup> states that 50% of relapses appear within the first 3 years and 75% within the first 6 years after treatment. However, these figures are influenced by the carefulness with which patients are examined. When identical short course regimens were applied in Bamako, Mali, and in Congo Zaire,<sup>8</sup> relapses occurred 18–24 months later in Zaire. This may have resulted from a different awareness of the examiners in the two countries for the early symptoms of relapse, as mentioned by Lienhardt *et al.*<sup>9</sup> In the present study, almost all relapses detected after more than 5 years after the start of therapy were passively detected, i.e. they were diagnosed by the patients themselves. It is possible that in this setting diagnoses were delayed by 1–2 years. However, this does not influence the number of relapses appearing after more than 5 years. This observation shows that to evaluate a treatment regimen in multibacillary leprosy, a mean follow-up period of 5 years is insufficient, since late relapses may appear much later. Whether this is limited to short course regimens only, remains an open question.

The present regimen cannot be recommended for the treatment of multibacillary leprosy.

**References**

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