

## CORRESPONDENCE

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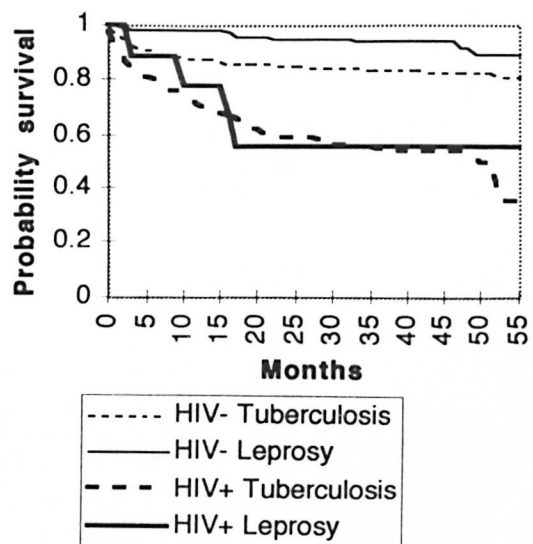
## Survival of HIV-Positive and HIV-Negative Leprosy Patients in Mwanza, Tanzania

TO THE EDITOR:

Little is known on the long-term survival, relapse and incidence of complications among leprosy patients with and without the human immunodeficiency virus (HIV) infection. There are case reports suggesting an association of HIV infection with reversal reaction (RR) and neuritis as well as with increased incidence and mortality due to severe erythema nodosum leprosum (ENL) reactions<sup>(2,4,6)</sup>. There are no reports suggesting that HIV infection predisposes a leprosy patient to relapse following a curative course of treatment. It is important to know whether a difference exists in the outcome of treatment and the risk of complications after treatment in relation to HIV infection.

Between 1 April and 30 September 1991, 120 consecutively diagnosed new and relapsed after multiple drug therapy (MDT), self-reported, multibacillary (MB) and paucibacillary (PB) leprosy patients in the Mwanza region in Tanzania were enrolled in a study of the association of leprosy with HIV infection. The diagnosis, classification, outcome of treatment and survival was assessed under routine program conditions by experienced District Tuberculosis and Leprosy Coordinators (DTLCs). Classification was still based on skin-smear results in addition to the clinical picture. Detailed descriptions of the study methods have been described earlier<sup>(1,3)</sup>. PB patients were

treated with six monthly supervised doses of rifampin and daily self-administered Isoprodian (combination of dapsone, prothionamide and isoniazid) and were assessed after 1 year. MB patients were treated with 24 monthly supervised doses of rifampin and daily self-administered Isoprodian and were assessed after 3 years. The outcome of "Treatment completed" was considered when the patient had finished treatment as



THE FIGURE. Kaplan Meier survival curve for HIV-positive and HIV-negative tuberculosis and leprosy patients enrolled between April and September 1991 in the Mwanza region, Tanzania.

TABLE 1. *Leprosy patients enrolled between April and September 1991 in the Mwanza region, Tanzania, and eligible for analysis; their HIV status and exact p values for differences.*

	No.	HIV+	%HIV+	p Value
Type				
New	114	9	8%	1.000
Relapse	6	0		
Classification				
Paucibacillary	78	3	4%	0.064
Multibacillary	42	6	14%	
Age group (yrs.)				
15-24	12	1	8%	0.002
25-34	27	7	26%	
35-44	36	1	3%	
45-54	19	0		
≥55	26	0		
Sex				
Male	80	6	8%	1.000
Female	40	3	8%	
Disability grading				
No disability	60	6	10%	0.491
Grades 1 and 2	60	3	5%	
Total	120	9	8%	

prescribed. In case of HIV infection, no therapy for HIV was given.

During October and November 1995 a follow-up assessment among the same patients was performed. DTLCs made all possible efforts to interview the patients at their homes or to question their relatives and neighbors and trace patients who had moved in order to establish their current status. Relapses were diagnosed according to the National Tuberculosis and Leprosy Programme protocols.

For patients who had died after completing treatment, the cause of death was determined by verbal autopsy, following the protocol of the adult morbidity and mortality

study performed elsewhere in Tanzania (McLarty, D. Policy implications of adult morbidity and mortality; preliminary report. Dar es Salaam: Dar es Salaam University Medical Faculty, 1993).

Out of 120 patients enrolled, 42 (35%) had MB leprosy. This proportion has been similar over the years in the Mwanza region. Among these 42 MB patients HIV infection was higher than in the PB patients, although statistically not significant. An association between HIV infection and MB leprosy was reported earlier in a population-based, case-control study of a subset of these patients (those between 15 and 54 years of age), suggesting that HIV is a risk

TABLE 2. *Status at the end of the 55-month observation period of HIV-positive and HIV-negative leprosy patients enrolled between April and September 1991 in the Mwanza region, Tanzania.*

HIV status	Alive/ well	% <sup>a</sup>	Died during treatment	%	Died after treatment	%	Unknown	%	Total
HIV+	5	56%	3	33%	0		1	11%	9
HIV-	101	91%	2	2%	5	5%	3	3%	111
Total	106	88%	5	4%	5	4%	4	3%	120

<sup>a</sup> Percentages are rounded off.

factor for MB leprosy (<sup>1</sup>). The overall HIV seropositivity among the leprosy patients was 7.5% (9/120). The highest HIV seroprevalence was found in the 25 to 34 age group. None of the six cases diagnosed as a relapse of leprosy was HIV-positive (Table 1).

The treatment completion rate for HIV-positive patients was 44% (4/9); for HIV-negative leprosy patients, 85% (94/111). This was due mainly to the differences in mortality in HIV-positives (3/9) and HIV-negatives (2/111), and was statistically significant (odds ratio 5.1, 95% confidence interval 1.1–24.1) also after adjusting for age, sex and disability grading. Adjustment for classification has been omitted because of collinearity between MB leprosy and HIV seropositivity and subsequent mortality.

At the end of treatment five patients had died. At the time of follow up after 55 months, an additional five patients had died, all of whom were HIV-negative at the moment of enrollment into the study (Table 2). Only four patients could not be located for reassessment. Among the 106 patients who could be assessed after 55 months, there was no evidence of relapse or having developed a leprosy reaction after finishing treatment.

The overall mortality of the HIV-positive patients (3/9) was statistically significantly greater than that of HIV-negative patients (7/111). Of the 10 patients who died, 9 were MB and 1 was PB. Verbal autopsies were done for all five patients who had died after treatment (all HIV-negative at time of diagnosis) but not for the five patients who had died during treatment. The reported causes of death were not related to HIV infection or to AIDS: heart failure in two patients, snake bite in the third, and unknown in the fourth patient. In the fifth, a severe case of ENL was the underlying cause of death.

Survival analysis according to the Cox proportional hazard model showed that the probability of dying was significantly associated with HIV infection but not with sex, age group or disability grading. HIV-positive patients had an 8.3 higher chance of dying than did HIV-negative patients.

The higher early mortality after diagnosis could be explained by a more advanced stage of HIV infection in MB leprosy patients at the moment of the diagnosis. This is further supported by a similar survival

curve among HIV-positive tuberculosis patients (<sup>8</sup>) enrolled in the same period in the Mwanza region (The Figure).

Although not confirmed in this study, in Tanzania a higher proportion of MB patients have disability and have a higher mean age at the moment of diagnosis than do PB patients. This suggests that MB patients tend to wait longer before coming forward for diagnosis and treatment (van den Broek, J., Lubango, M., van der Steen, F., Rubona, J. and van Wijnen, A. Prevention of disabilities and rehabilitation of leprosy patients in Tanzania: estimating the prevalence of persons affected by leprosy; unpublished data and Annual Reports 1984 through 1995 of the National Tuberculosis and Leprosy Programme, Tanzania). The long latent period of MB leprosy, in combination with the longer patient delay, would expose these patients longer to the risk of contracting HIV infection before being diagnosed as a leprosy patient. It is also unknown to what extent undiagnosed HIV-positive MB patients may have died before the diagnosis of leprosy was made. We also could not rule out a possible effect of false-positive results of the ELISA in relation to leprosy, as is reported to exist (<sup>5</sup>).

The assumption that HIV infection, in combination with MB leprosy, may lead to more frequent and serious complications of leprosy, such as ENL and RR, could not be confirmed in this study. No relapse or reaction at the time of examination or during the observation period following treatment could be shown to have occurred, contrary to the findings in a group of 18 HIV-positive leprosy patients and 18 HIV-negative matched controls in Kenya (<sup>7</sup>). This finding casts some doubt on the accuracy of the recall of the informants, or the ascertainment of the physical condition of the patients by the interviewers.

The mortality rate among leprosy patients in the 1984 to 1995 annual treatment cohorts of the national data in Tanzania did not show any change. It also has been consistently higher among MB (on the average 3%) than among PB patients (on the average 0.8%). Any effect of the HIV pandemic on a change in the mortality rate during treatment of leprosy could, therefore, not be confirmed by the national data.

The number of patients and deaths in this study was small, and therefore the results should be interpreted with caution.

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## Relapse of Multibacillary Leprosy after Rifampin and Ofloxacin Treatment for 28 Days; a Case Report

TO THE EDITOR:

We report here on what we believe to be the first case of relapse in multibacillary (MB) leprosy following short-course chemotherapy for 28 days with daily doses

of rifampin (R) 600 mg and ofloxacin (O) 400 mg.

The following diagram summarizes the time sequence of events relating to a previously untreated, 30-year-old, male BL-LL patient with an initial bacterial index (BI) of