

## **Bacillaemia in leprosy and effect of multidrug therapy**

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*Summary* Twenty-five patients of bacilliferous leprosy (17 LL, 8 BL) were studied by the modified haemolysis method for occurrence of bacillaemia and its clearance after two multidrug therapy regimens. Acid-fast bacilli were found in 76% of all patients and in 88.2% LL and 50% BL patients. Bacillaemia occurred with significantly reduced frequency in patients with type II reaction. Acid-fast bacilli were demonstrable in peripheral blood after 1 month in one patient on MDT of an Indian Working Group and 3 lepromatous patients on WHO multidrug therapy. However, bacillaemia could not be demonstrated in any patients after 2 and 3 months of treatment with both regimens.

### **Introduction**

Bacillaemia, the finding of lepra bacilli in peripheral circulation, has been a topic of investigation since the turn of the century.<sup>1</sup> Initially bacillaemia was demonstrated in lepromatous leprosy,<sup>2,3</sup> recently, it has been documented even in tuberculoid leprosy.<sup>4,5</sup> The bacillaemia has been attributed to multisystem involvement in lepromatous leprosy.<sup>4</sup> It was planned to study the occurrence of bacillaemia in lepromatous patients and assess the efficacy of multidrug therapy regimens in the clearance of bacillaemia.

### **Materials and methods**

Twenty-five untreated patients having bacilliferous leprosy (LL/BL) formed the study group. There were 22 males and 3 females, with an age range of 16–58 years (mean 37.5). Ridley–Jopling classification was followed.<sup>6</sup> A haemogram, urinalysis, chest skiagram, hepatic and renal function tests were carried out before starting therapy in all cases.

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## BACILLAEMIA STUDIES

Three samples of blood at 12-hr intervals were collected before starting the treatment. Repeat samples were taken at 1, 2 and 3 months in the first 10 patients and at 2 week intervals 1, 2 and 3 months after treatment in the remaining 15 patients. A total of 2 blood samples were collected at 12-hr intervals for the follow-up studies for bacillaemia, and a modified haemolysis method<sup>7</sup> was used for study. Briefly, 5 ml of blood was drawn from the antecubital vein and transferred to a heparanized vial (10 iu/ml). One millilitre of blood from the above was transferred to a half test-tube and the cells were disintegrated by ultrasonic vibrations (800 KHz) for 30 s. One millilitre of sterile distilled water was added and the sample was sonicated again for 30 s. This step was repeated to get a final volume of 4 ml. The same procedure was repeated with the remaining 4 ml of blood to make a final volume of 20 ml. It was centrifuged at 10,000 rpm for 30 min at 10°C in a propylene centrifuge tube. The supernatant was removed, and the deposit was washed and centrifuged again with 20 ml of sterile distilled water at the same speed for 20 min. The deposit was suspended in 1 ml of distilled water and a bacillary count done using the pinhead method.<sup>8</sup> The smears were made for Ziehl-Neelsen staining and studied under an oil-immersion microscope.

## TREATMENT AND FOLLOW UP

*Group I.* The 10 consecutive patients (7 LL, 3 BL) were treated with WHO multibacillary regimen consisting of rifampicin 600 mg and clofazimine 300 mg once a month given under supervision, and dapsonsone 100 mg daily and clofazimine 100 mg on alternate days, self-administered.<sup>9</sup>

*Group II.* The 15 consecutive patients (10 LL, 5 BL) were treated with the India Working Group's multibacillary MDT consisting of intensive therapy with rifampicin 600 mg, clofazimine and dapsonsone 100 mg daily for 15 days and continued on the maintenance phase like the WHO multibacillary regimen.<sup>10</sup> The bacteriological and morphological indices (BI and MI) were repeated at 1, 2 and 3 months after therapy.

## Results

The mean duration of the disease in 25 patients was 3.4 years. The average bacteriological (BI) and morphological (MI) indices were 3.9 + /3.28% and 3.3/1.07% in LL and BL patients respectively. Seventeen patients of lepromatous leprosy (LL) included 12 polar lepromatous (LLp), 4 subpolar lepromatous leprosy (LLs), and 1 with histoid leprosy. Five LL patients had Type II reaction. The patients in group I and II were comparable in age, sex, duration, type of disease and average BI and MI. Bacillaemia was found in 19 (76%) out of 25 patients, 15 (88.2%) were LL out of 17 taken up and 4 (50.0%) were BL out of 8 patients taken up (Table 1). No statistically significant difference

**Table 1.** Bacillaemia in multibacillary leprosy

Type of leprosy	No. studied	No. (%) showing bacillaemia
LL	17	15 (88.2)
BL	8	4 (50.0)
Total	25	19 (76.0)

$$\chi^2 = 2.7; p > 0.05.$$

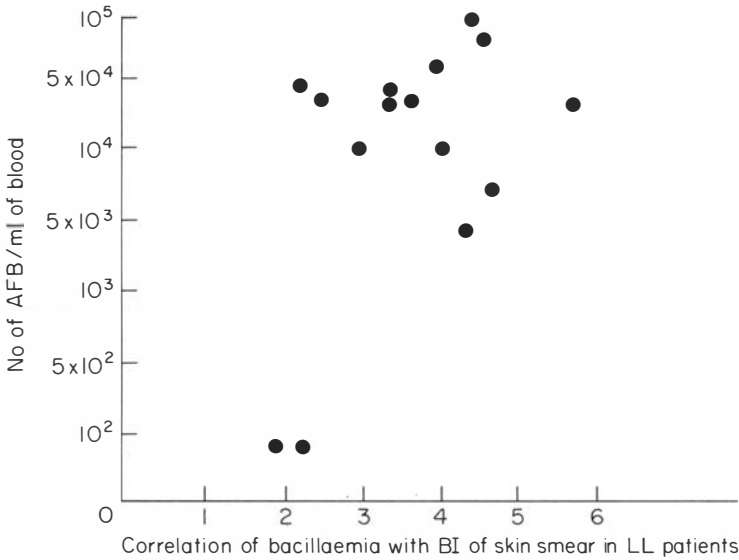


Figure 1.

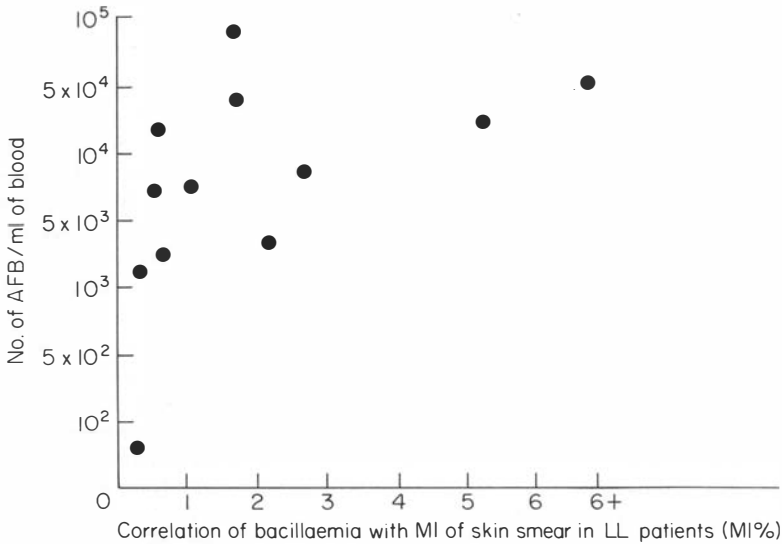


Figure 2.

was found in the frequency of bacillaemia in lepromatous and borderline lepromatous leprosy ( $\chi^2=2.24$ ;  $p>0.05$ ). However, there was a statistically significant difference in the frequency of bacillaemia in patients with and without Type II reaction ( $\chi^2=4.48$ ;  $p<0.05$ ), as only 3 out of 5 patients with Type II reaction showed bacillaemia. The correlation between bacillaemia and bacteriological index was good (Figure 1) and no correlation was demonstrated between bacillaemia and morphological index in slit-skin smears (Figure 2).

**Table 2.** Bacillaemia clearance after multidrug therapy

Type of MDT	Type of leprosy	No. studied	No. of patients showing bacillaemia after MDT			
			2 weeks	1 month	2 months	3 months
WHO (1982)	LL	7	ND	3	0	0
	BL	3	ND	0	0	0
Indian Working Group	LL	10	1	1	0	0
	BL	5	1	0	0	0
Total		25	2	4	0	0

ND, not done.

The bacilli could not be demonstrated in peripheral blood 2 and 3 months after therapy in all the patients. However, bacilli were still demonstrable after 1 month in 3 out of 7 LL patients on WHO-MDT regimen (Group I) and in 1 out of 10 LL patients on the Indian Working Group regimen (Group II) (Table 2). The clearance of bacillaemia after 1 month of each of the two MDT regimens was not different ( $\chi^2 = 2.24$ ,  $p > 0.05$ ) though it seems that the Indian Working Group regimen resulted in earlier clearance. There was no significant reduction in BI, however MI was reduced to zero after 3 months of MDT.

## Discussion

Bacillaemia occurs in 67–100% patients of bacilliferous leprosy.<sup>2-4,11</sup> The frequency of demonstration of bacillaemia has progressively increased with the modification of methodology.<sup>4,7,12,13</sup> Circulating bacilli were found in 92–100% patients with lepromatous leprosy (LL)<sup>4,11</sup> compared to our finding of 88.2%. However, in borderline lepromatous leprosy (BL) bacillaemia occurs less frequently<sup>4</sup> but there is apparently no direct correlation between frequency of bacillaemia and the bacteriological and morphological indices.<sup>3,4</sup> There was apparently good correlation between BI of slit-skins smear and bacillaemia in our patients. Sankara Manja *et al.*<sup>13</sup> also reported similar results.

Bacillaemia occurred with lower frequency in LL patients with Type II reaction compared to LL patients without reaction and the difference was statistically significant ( $\chi^2 = 4.48$ ;  $p < 0.05$ ). A similar finding has been reported earlier.<sup>2,14,15</sup> It may be due to stimulation of cell-mediated immunity in Type II reaction resulting in the increased clearance of bacilli.<sup>16</sup>

Drutz *et al.*<sup>2</sup> reported gradual clearance of bacillaemia over a 4-month period after dapsone monotherapy. The extracellular bacilli cleared first followed by intracellular bacilli. Subsequently, Ramu *et al.*<sup>17,18</sup> assessed bacteraemia in 36 LL patients at weekly intervals for 4 weeks after putting patients on 4 drug regimens, namely dapsone alone, dapsone and clofazimine, dapsone and isoniazide, and dapsone and rifampicin. They observed that bacillaemia disappeared after one week in the dapsone and rifampicin regimen, while it took 3 weeks with the other regimens. Bacillaemia cleared in all patients by 2 months with different multibacillary regimens in our study. The 15 days intensive multibacillary therapy did not show significant advantage in clearance of bacillaemia. The exact pathogenesis of clearance of bacilli from peripheral circulation in the presence of a heavy bacterial load in skin is not known. Probably the administration of drugs results in immediate bacteriostasis and thereby prevents the further multiplication and overspill from involved vasculature into the circulation. The immunostimulatory effect of antileprotics has been suggested as another possible factor.<sup>17,19</sup>

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