

## Acid-fast Bacilli in the Bone Marrow of Leprosy Patients<sup>1, 2</sup>

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In leprosy *Mycobacterium leprae* is found throughout the body, including the reticuloendothelial system as well as the skin and peripheral nerves. Hirschberg and Biehler<sup>(2)</sup> stated that bacilli were seen in large numbers in the bone in lepromatous leprosy. Gass and Rishi<sup>(1)</sup> on examining the bone marrow in autopsy and surgical specimens of bones found acid-fast bacilli in 17 out of 21 "mixed" cases, but no bacilli were seen in the bones of 48 neural cases. Lowe and Dharmendra<sup>(4)</sup> searched sternal puncture aspirates of 50 patients for the presence of acid-fast bacilli; of 32 patients with cutaneous leprosy 16 had acid-fast bacilli in the sternal aspirate, i.e., 50 per cent. Of 18 nerve leprosy cases only one case was found to have acid-fast bacilli in a bone marrow smear.

The following study of the relationship of acid-fast bacilli in bone marrow preparations to the bacterial index, classification of the disease, duration of the disease, age and sex distribution, and hemopoietic activity of the bone marrow, has been under way at the Schieffelin Leprosy Research Sanatorium for 18 months.

### MATERIAL AND METHODS

In 413 consecutive admissions to the medical service at the Schieffelin Leprosy

Research Sanatorium a bone marrow aspirate obtained by sternal puncture was spread immediately on several glass slides and fixed and stained with the Leishman and carbol fuchsin stains. It is possible that a few bacilli may be conveyed by the sternal puncture needle as it goes through the skin, if the skin contains bacilli, and this may appear in the aspirate. To minimize this possibility, the stilette in the sternal puncture needle was kept flush with the tip of the needle and not disturbed until the needle had pierced the periosteum and was fixed to the sternum. It seems unlikely that a large number of bacilli could have been conveyed from the skin to the marrow in the use of this method. Moreover, those cases where less than ten bacilli were found in ten fields examined, were reported as negative for acid-fast bacilli. At the time the sternal puncture was made, blood was collected by venepuncture for estimation of hemoglobin, packed cell volume, serum B12, folic acid and iron.

Skin smears for acid-fast bacilli were taken by Wade's technic from eight sites (ears two, cheek two, chin, arm, back and buttock) and graded by Cochrane's method from 0 to 6+.

Of the 413 patients, 235 had lepromatous, 33 borderline, 82 tuberculoid, 10 purely neural, and 53 indeterminate leprosy (Table 1). In all cases the clinical classification was confirmed by histologic examination of representative skin and/or nerve lesions, and in the majority by biopsy of the Mitsuda lepromin reaction at three weeks.

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TABLE 1. *Distribution of patients according to classification.*

Classification	Number of patients
Lepromatous	235
Borderline	33
Tuberculoid	82
Purely neural	53
Indeterminate	10
	413

## RESULTS

**1. Acid-fast bacilli in the bone marrow.**

Acid-fast bacilli were found in 110 out of 235 lepromatous cases, five out of 33 dimorphous cases, none out of 82 tuberculoid cases, none out of 10 purely neural cases, and two out of 53 indeterminate cases whose skin smears were negative (Table 2).

There was no apparent relationship to age or duration of the disease (Table 3). There appeared to be a direct relationship between the presence of acid-fast bacilli

in the bone marrow and the bacterial index on skin smear; the higher the bacterial index, the more likely the finding of acid-fast bacilli in the bone marrow (Fig. 1).

The morphology of the bacillus was variegated. In patients with a large number of bacilli in the skin smears there was a preponderance of intracellular rod forms, although in practically all the specimens that contained acid-fast bacilli in bone marrow preparations, granular and coccoid forms were seen.

No definite relationship could be established between exacerbated states of the disease and the presence or absence of bacilli in the bone marrow in this series. This problem is being studied further.

**2. Hemoglobin and acid-fast bacilli in bone marrow.** Of the 235 lepromatous patients, 47 had hemoglobin values of less than 9 gm.; 30 of these (i.e., 64%) had acid-fast bacilli in the bone marrow.

**3. Megaloblastic change in the marrow.** This was seen in 27 per cent of the 235

TABLE 2. *Acid-fast bacilli in bone marrow according to classification.*

Classification	Acid-fast bacilli		Total	Percentage
	Present	Not present		
Lepromatous	110	125	235	47
Borderline	5	28	33	15
Tuberculoid	—	82	82	—
Indeterminate	2	51	53	4
Purely neural	—	10	10	—

TABLE 3. *Acid-fast bacilli in bone marrow in relation to age and duration of disease.*

Age	Duration of disease in years											
	1		1-3		3-5		5+		Not known		Total	
	+ <sup>a</sup>	- <sup>b</sup>	+	-	+	-	+	-	+	-	+	-
0-5	—	—	—	—	—	—	—	—	—	—	—	—
6-15	1	2	1	2	—	3	1	1	2	1	5	9
16-20	3	1	2	2	7	2	2	5	3	4	17	14
21-25	—	2	2	2	8	8	9	9	3	—	22	21
26-30	—	3	2	3	4	4	11	11	3	4	20	25
31-35	1	4	2	2	3	1	10	11	—	5	16	23
36-40	—	—	3	1	—	2	9	6	—	2	12	11
41-50	—	1	3	1	2	2	7	12	2	1	14	17
51 & over	—	1	—	—	1	—	2	4	1	—	4	5
Total	5	14	15	13	25	22	51	59	14	17	110	125

<sup>a</sup>+ = Acid-fast bacilli present

<sup>b</sup>- = No acid-fast bacilli

lepromatous patients; 48.3 per cent (i.e., nearly half) of the patients who had megaloblastic marrow had acid-fast bacilli in the bone marrow. Thus the presence or absence of acid-fast bacilli in the bone marrow did not appear to be an important factor in the pathogenesis of megaloblastosis in this series.

4. **Acid-fast bacilli in the bone marrow of patients with negative skin smears.** It is of considerable interest and significance to note that out of 38 lepromatous leprosy patients who were bacteriologically negative, as judged by skin smears, four had acid-fast bacilli in the bone marrow smear. Among eight dimorphous cases that were negative bacteriologically on skin smear, one had acid-fast bacilli in the bone marrow; in 2 cases among 53 skin-smear-negative indeterminate acid-fast bacilli were found in the marrow.

#### DISCUSSION

This study confirms the already well known fact that one frequently can find acid-fast bacilli in the bone marrow of lepromatous patients with positive skin smears. In this series, 47.0 per cent of all lepromatous patients had acid-fast bacilli in the marrow. As expected, the higher the number of bacilli in the skin smear, the higher the incidence of acid-fast bacilli in the bone marrow.

A few less well recognized facets have been brought to our notice in this study. There is no definite relationship between the duration of the disease, age, and sex distribution, and the incidence of acid-fast bacilli in the bone marrow. There was no rise in the number of cases with acid-fast bacilli in the bone marrow among patients who had exacerbation of the disease as compared to those who did not have such exacerbation.

The finding of acid-fast bacilli in the bone marrow in four out of 38 lepromatous cases, one out of eight patients with dimorphous disease, and two out of 53 with indeterminate disease, all of whom had no bacilli on routine skin smears, is interesting. It suggests that bacilli in the viscera may take much longer to be eliminated than the bacilli in the skin.

RELATIONSHIP BETWEEN AFB IN BONE MARROW & BACTERIAL INDEX IN 235 LEPROMATOUS PATIENTS

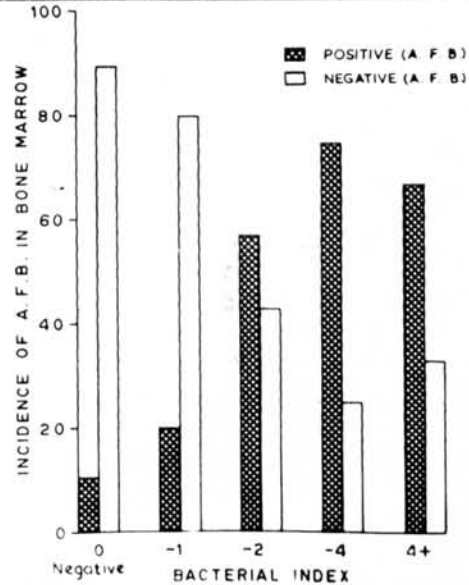


FIG. 1. Relationship between acid-fast bacilli in bone marrow and bacterial index in 235 lepromatous patients.

It was a surprise, besides, to find many solidly staining rods in a number of the bone marrow smears, in view of the concept that higher temperature is inimical to the growth of the lepra bacillus; it is well known that the temperature of the bone marrow is usually 2°-3°F above the skin temperature. The morphology of the bacilli in the bone marrow and the viscera is being studied in greater detail to verify this preliminary observation, because of the far-reaching implications of such a finding in relation to our understanding of the pathogenesis and variegated clinical pattern of leprosy and sites of predilection of nerve damage in leprosy.

These observations, viz., (a) the presence of acid-fast bacilli in the bone marrow of patients with negative skin smears, and (b) the presence of solidly staining rod forms of acid-fast bacilli in the bone marrow, tend to point out that leprosy bacilli may remain dormant in the reticuloendothelial system in the body for long periods of time and be responsible, in some measure, for reactivation of the disease either

when specific treatment is stopped prematurely or when the immunologic balance between host and bacillus is upset by some unforeseen or ill-understood mechanism. If that be the case, the need for prolonged treatment becomes more readily apparent and rational.

In this series, 64 per cent of 47 lepromatous patients who had hemoglobin values less than 9 gm., had acid-fast bacilli in the bone marrow. The numbers are too small, however, for generalization. It is possible that the presence of acid-fast bacilli in the bone marrow may interfere with hemopoiesis by the following mechanisms:

- (a) by causing replacement of hemopoietic tissue in the bone marrow by leprous granulomata<sup>(3)</sup>, as in leukemia, carcinomatosis, etc.,
  - (b) by bringing about a "toxic depression" of the bone marrow, and
  - (c) by competition of the lepra bacillus for available hematinic principles, such as B12 and folic acid, and thereby bringing about a conditioned deficiency of these vitamins.
- Such a mechanism may be partly responsible for the otherwise unexplained high incidence (27% of all lepromas) of megaloblastosis that was found in this series.

These fascinating facets of hematologic changes merit further study.

#### SUMMARY

1. Twenty-seven per cent of 413 leprosy patients, representing the various types of leprosy, were found to have acid-fast bacilli in bone marrow aspirates.

2. Of these 413 patients, 235 were lepromatous; among them 47.0 per cent had acid-fast bacilli in the bone marrow.

3. There was a direct relationship between the incidence of acid-fast bacilli in the bone marrow and the number of bacilli seen in skin smears: the greater the number of bacilli in skin smears, the higher the incidence of acid-fast bacilli in the bone marrow.

4. Acid-fast bacilli of variegated morphology were seen in the bone marrow, ranging from solidly staining rods lying intra- and extracellularly to granulated and fragmented bacilli. The intracellular rods were more common among the highly positive lepromatous cases.

5. In 10.5 per cent of 38 lepromatous cases, one out of eight borderline cases, and two out of 53 indeterminate cases in which skin smears were negative, acid-fast bacilli were present in the bone marrow.

6. Twenty-seven per cent of lepromatous patients had megaloblastic bone marrow.

7. The clinical, pathologic and therapeutic significance of these findings is discussed.

#### RESUMEN

1. Veinte y siete por ciento de 413 enfermos de lepra, que representan varios tipos de lepra, se encontraron tener bacilos ácido-resistentes en la médula ósea aspirada.

2. De los 413 pacientes, 235 eran formas lepromatosas; de ellos el 47.0 por ciento tenía bacilos ácido-resistentes en la médula ósea.

3. Hubo una relación directa entre la incidencia de bacilos ácido-resistentes en la médula ósea y el número de bacilos observados en frotis de la piel: cuanto mayor fué el número de bacilos en los frotis de la piel, mayor fué la incidencia de bacilos ácido-resistentes en la médula ósea.

4. Se observaron bacilos ácido-resistentes de variada morfología en la médula ósea, que variaron desde bastones firmemente teñidos ubicados intra y extra celularmente a bacilos granulados y fragmentados. Los bastones intracelulares fueron mas comunes entre las formas lepromatosas altamente positivas.

5. En 10.5 por ciento de los 38 casos lepromatosos, uno en ocho formas borderline, y dos de 53 formas indeterminadas en los cuales el frotis de la piel era negativo, presentaron bacilos ácido-resistentes en la médula ósea.

6. En 27 por ciento de los enfermos lepromatosos, la médula ósea era de tipo megaloblástico.

7. Se discute el significado clínico, patológico y terapéutico de estos hallazgos.



## RÉSUMÉ

1. Chez 27 pour cent parmi 413 malades de la lèpre, atteints des divers types de la maladie, on a trouvé des bacilles acido-résistants dans des ponctions de moëlle osseuse.

2. De ces 413 malades, 235 étaient lépromateux; parmi ceux-ci, 47.0 pour cent avaient des bacilles acido-résistants dans la moëlle osseuse.

3. Il y avait une relation directe entre l'incidence de bacilles acido-résistants dans la moëlle osseuse et le nombre de bacilles observés dans les frottis cutanés; l'incidence de bacilles acido-résistants dans la moëlle osseuse était d'autant plus élevée que les bacilles dans les frottis cutanés étaient plus abondants.

4. On a observé dans la moëlle osseuse des bacilles acido-résistants d'une grande variété dans leur morphologie, depuis des bâtonnets se colorant uniformément et situés dans les cellules ou au dehors, jusqu'à des bacilles fragmentés et granuleux. Les bâtonnets intracellulaires étaient plus courants parmi les cas lépromateux fortement positifs.

5. Chez 10.5 pour cent des 38 cas lépromateux, chez un border-line parmi 8 étudiés, et chez deux de 53 cas indéterminés, chez lesquels les frottis cutanés étaient négatifs, on a trouvé des bacilles acido-résistants dans la moëlle osseuse.

6. Vingt-sept pour cent des malades lépromateux avaient une moëlle osseuse mégalo-blastique.

7. On discute la signification de ces observations des points de vue clinique, pathologique et thérapeutique.

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