

The Distribution of *Mycobacterium leprae* in Different Structures of the Skin*

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A survey of the various components of the skin for the presence of acid-fast bacilli in 100 cases of lepromatous and borderline leprosy is reported. Bacilli were found to occur in the nerves, macrophages, arrectores pilorum muscles, hair follicles, blood-vessel walls, and the epidermis, in that order. Bacilli were not present in the sweat and sebaceous glands. The frequent occurrence of *Myco. leprae* in the endothelial cells lining the blood vessels is an interesting observation and supports the haematogenous spread of the bacilli. The location of bacilli in the hair follicles and epidermis suggests a possible mode of exit of the bacilli through these structures. *Myco. leprae* appear to remain dormant in the nerves and arrectores pilorum muscles, even in clinically regressed cases, and could possibly account for the relapse of the disease.

The intracellular distribution of *Mycobacterium leprae* within the macrophages of the skin lesions of leprosy has been known for a long time. As long ago as 1879 Neisser gave an accurate description of the distribution of the bacilli within the macrophages (Fite and Wade, 1955). The location of the lesions in the nerves was also an early finding. Dehio pointed out as early as 1897 that the peripheral branches of the nerves within the skin are the initial sites of involvement by *Myco. leprae*. Reviewing the subject, Fite (1943) refers to the observations of several early authors who reported finding acid-fast bacilli (A.F.B.) in various components of the skin in leprosy lesions. The macrophages in the leprosy granuloma, and the nerves in the skin, are the commonest locations in which to look for the presence of A.F.B. when examining sections of skin from leprosy lesions. Careful search, however, reveals bacilli in other structures of the skin, though to a lesser extent. This paper records observations during a systematic study to define the various structures of the skin in which A.F.B. are present in leprosy.

Materials and Methods

The material on which this study was based consisted of sections of 100 consecutive biopsy specimens of skin lesions of leprosy, all of which contained A.F.B. Paraffin sections, 5 μ in thickness, suitably stained, were examined in great detail. All the appendages, nerves, and blood vessels in each specimen were meticulously searched for acid-fast bacilli, multiple sections from each biopsy specimen being studied in most cases. The entire stretch of epidermis was carefully examined for A.F.B. and a quantitative assessment of acid-fast organisms

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in each biopsy specimen was attempted. These specimens had earlier been classified in accordance with the schedule adopted by Ridley and Jopling (1962), using both the clinical criteria and histological findings.

Observations

The distribution of A.F.B. in the various components of the skin is shown in Table 1.

TABLE 1

No. of cases	20	19	12	49	100
Macrophages	20	19	12	35	86
Nerves	20	19	12	49	100
A. P. muscles	20	16	11	30	77
Blood vessels	13	12	7	1	33
Epidermis	6	1	1	0	8
Hair follicles	15	10	8	5	38
Sweat glands					
Sebaceous glands					

MACROPHAGES

Bacilli were present in the macrophages in 86 cases. The macrophages, or the "lepra cells" as they are called in leprosy lesions, are phagocytic cells derived from the tissue histiocytes. In the early and active lesions the macrophages were seen to contain granular eosinophilic cytoplasm; these cells contained large numbers of bacilli. In the older lesions, on the other hand, the cells were highly vacuolated, the cytoplasm presenting a foamy appearance. Fewer bacilli were present in such cells, and further the organisms were highly fragmented and dustlike.

NERVES

All the cases showed acid-fast bacilli in the nerves. Bacilli were present both in the lepra cells within the nerves and in the Schwann cells (Fig. 1). In the lepromatous and near-lepromatous cases, which showed macrophages in considerable numbers within the nerve, bacilli were found in greater numbers, often as large bundles or globi. In nerves which were totally destroyed and replaced by exudate cells, as in the near tuberculoid cases, bacilli were not seen or were extremely rare, whereas nerves which were partially destroyed showed small groups of bacilli amidst the intact fibres. In 9 cases, nerve was the only tissue structure that showed *Myc. leprae*. In these cases the organisms were very few, and occurred singly or in very small groups.

ARRECTORES PILORUM MUSCLES

Bacilli were present in the arrectores pilorum muscles in 77 cases. In some of these cases the muscles were infiltrated by the exudate cells, which replaced them to a varying extent. In such cases, bacilli were present in large numbers, but they were mainly in the macrophages infiltrating the muscles; in several cases, however, bacilli were seen in the uninfiltreated muscles. They were usually found in small

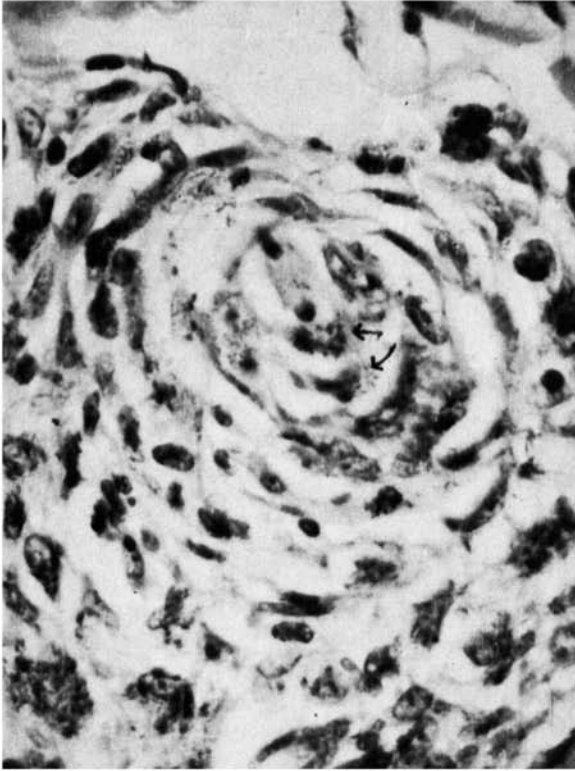


Fig. 1. Cross section of a nerve within a lepromatous granuloma showing numerous acid-fast bacilli in the Schwann cells.

groups in thin spindle-shaped collections parallel to the nucleus of the muscle fibre (Fig. 2). The shape of the bacillary collection conformed to the contour of the cell, and the relation of the bacillary cluster to the nucleus indicated that the bacilli were present within the muscle cells.

BLOOD VESSELS

Perivascular collections of exudate cells were seen mostly in specimens from patients with lepromatous leprosy. Some of the cases also showed infiltration of the walls of the blood vessel by the lepra cells. These contained numerous bacilli throughout the thickness of the blood vessel wall, and were located mainly in the macrophages infiltrating the vessel. In some of the sections, blood vessels without any infiltration of their walls by macrophages showed acid-fast bacilli in the endothelial cells lining the lumen (Fig. 3). Some of these cells were loaded with bacilli and were seen budding out and projecting into the lumen.

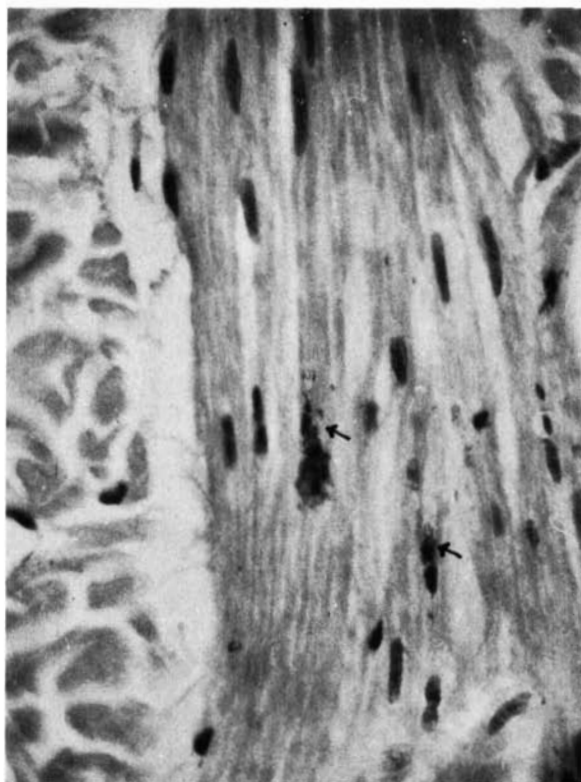


Fig. 2. Bacillary clumps within the arrectores pilorum muscles seen as spindle-shaped bundles and lying parallel to the nucleus.

EPIDERMIS

Although not very common, bacilli were also seen in the epidermis, where they were present in small clusters in the prickle cells and more superficially in the keratin layer. In one case, a fairly large number of A.F.B. was found in the keratin layer. The possibility of these bacilli being saprophytic mycobacteria could not be ruled out in this case. However, the bacilli in the deeper layers of the epidermis within the prickle cells were highly suggestive of *Myco. leprae*.

HAIR FOLLICLES

The occurrence of acid-fast bacilli in the hair follicles in 38 cases out of 100 in the present study was an interesting observation. The number of bacilli was quite appreciable, being present in many instances as large groups or as globi. They were observed mostly in the epithelial cells in the root of the hair (Fig. 4). Occasionally, bacilli were also seen in the space between the epithelial cells and the hair shaft.

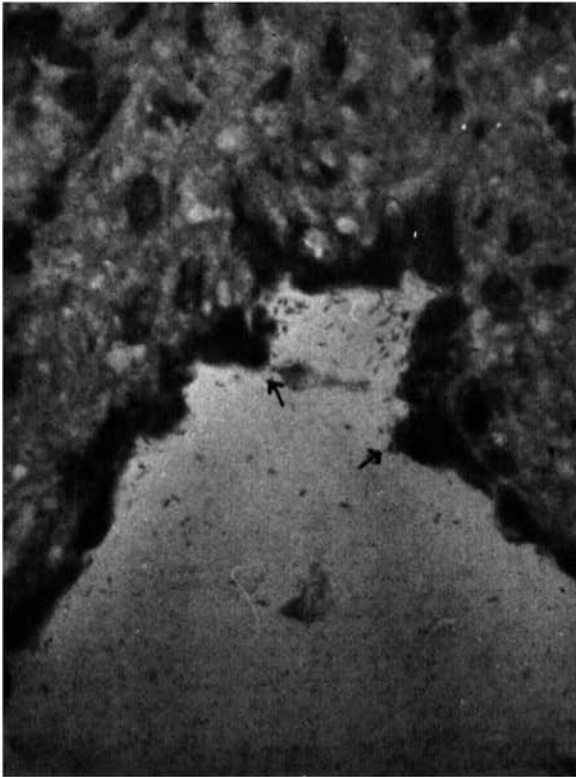


Fig. 3. Endothelial cells lining a blood vessel, loaded with acid-fast bacilli and seen to project into the lumen.

SWEAT GLANDS

Although the sweat glands are often infiltrated by lepromatous granuloma, it was interesting in this study that in no case were bacilli found in the epithelial cells of the sweat-glands or in their lumen. The cytoplasm of the epithelial cells of sweat glands frequently showed acid-fast granular material; but the size and shape of these granules precluded the possibility of their being bacteria.

SEBACEOUS GLANDS

None of the cases examined showed acid-fast bacilli in the sebaceous glands.

The distribution of bacilli in various types of leprosy is shown in Table 2.

From Table 2 it may be seen that the arrectores pilorum muscles contained acid-fast organisms in 8 out of 17 cases of borderline tuberculoid leprosy. In the other types of active cases of leprosy examined, practically all showed bacilli in the arrectores pilorum muscles. In contrast to this, the occurrence of bacilli in the blood vessel wall was a feature restricted mainly to cases of LL and BL leprosy, although interestingly, one case of BB type and one case of BT also showed

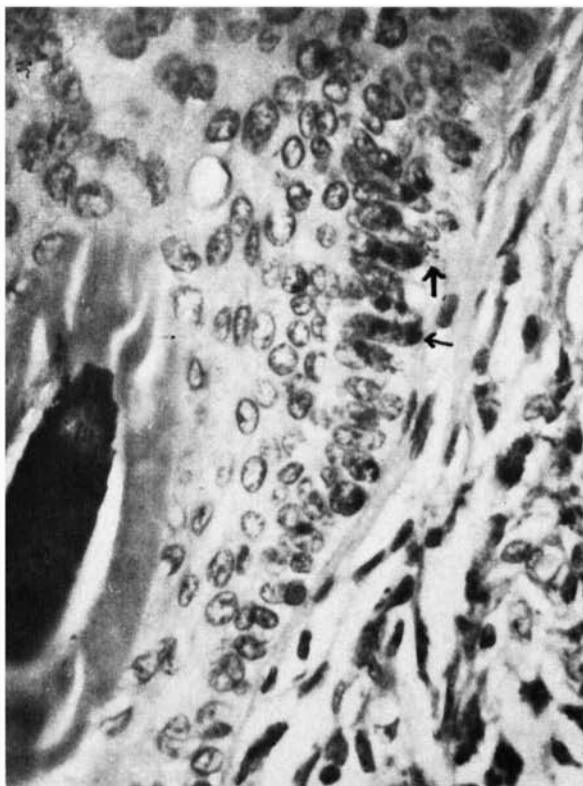


Fig. 4. Hair follicle showing bacillary clumps within the epithelial cells.

TABLE 2

No. of cases	35	12	2	11	11	17	12	100
Macro	35	12	2	10	11	8	8	86
Nerves	35	12	2	11	11	17	12	100
A.P. muscles	31	12	2	9	10	8	5	77
Blood vessels	22	8	—	2	—	1	—	33
Epidermis	7	1	—	—	—	—	—	8
Hair follicles	25	6	1	1	1	—	—	38

A.F.B. in the blood vessels. In like manner, the occurrence of acid-fast organisms in the epidermis and hair follicles was restricted mainly to cases of leprosy of the LL and BL types.

An interesting observation was the distribution of bacilli in regressed cases of leprosy. Histologically, these cases, which had been under treatment for a long

time, were typed as regressed because the picture was essentially non-specific, being composed of collections of a few lymphocytes. In 9 of these cases skin smears were found to be bacteriologically negative.

Bacilli were present in the nerves in all the cases, but the frequent occurrence of bacilli in the arrectores pilorum muscles and hair-follicles is an interesting feature.

Discussion

The predilection of *Myc. leprae* for nerves is a well-known and established fact (Iyer and Desikan, 1968). The observation by Khanolkar (1955) of acid-fast bacilli in the nerves of early lesions of leprosy confirms the fact that leprosy is essentially neural in inception. The phagocytic propensity of Schwann cells and their affinity for leprosy bacilli have been demonstrated in tissue culture by Lumsden (1964). It appears from the present study that the leprosy bacilli remain in the Schwann cells long after they disappeared from other locations. The Schwann cells even seem to afford some protection to the bacilli from chemotherapy, as evidenced by the fact that bacilli were found in the nerves in all the clinically regressed cases. These bacilli, remaining dormant in the Schwann cells, could be responsible for relapse of the disease.

The presence of acid-fast bacilli in the arrectores pilorum muscles was pointed out earlier by Neves (1961), and Harman (1968) found the bacilli not only between the smooth muscles, but also within the cells themselves. The electron-microscopic observations of Job *et al.* (1969) confirmed the location of the bacilli within the muscle cell. The muscle cell, therefore, seems to be another host cell for the leprosy bacillus. The bacilli in the muscle are often seen as solid forms, and on this ground Pearson *et al.* (1970) conclude that the organisms multiply in the muscles in the early stages and persist in them after apparent cure. In the present study, bacilli were found in the arrectores pilorum muscle in 4 out of 9 cases in which the skin smears were negative.

The presence of bacilli in the endothelial cells lining the blood vessels in one-third of the cases provides evidence for the spread of leprosy by the blood stream. It is clear that the bacilli can multiply in the endothelial cells, since the cells were loaded with the organisms and were seen to bulge into the lumen. From this situation, the bacilli could be released by the bursting of the cells, be thrown into the blood stream and so carried to distant sites. Recent observations by Padma (unpublished) at this Institute have provided supporting evidence for such a contention. Acid-fast bacilli in the endothelial cells of blood vessels in several internal organs have been reported and haematogenous spread accounts for the occurrence of miliary lepromatous lesions in organs like the liver, spleen and adrenal glands (Desikan and Job, 1970).

The hair follicle is another common structure showing acid-fast bacilli. The organisms are found mainly in the epithelial cells of the hair root, and to a lesser extent within the hair follicle. Prickle cells away from the hair follicles also show acid-fast bacilli, although in smaller numbers. The superficial location of bacilli in the epidermis and hair follicles suggests a possible mode of exit of the bacilli from the body. Periaswamy (1968), who also found the bacilli in large numbers in these locations, demonstrated the presence of bacilli on the surface of the skin by a method of pooling and concentration.

A striking negative finding in the present study was the absence of bacilli in the

sweat and sebaceous glands. Sweat has been thought to be a vehicle of exit of the bacilli, but the observations in the present study offer no support for this contention.

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