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An Electron Microscopic Study of the Small Cutaneous Vessels in Lepromatous Leprosy[1]

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Histologically, *Mycobacterium leprae* have been found in the endothelial cells of cutaneous vessels, as described by many authors ([1, 4, 5, 8–10]). The small vessels themselves show endothelial proliferation and protrusion of the cytoplasm into the lumen, and the larger vessels exhibit fibrosis and homogenization of the vessel wall. This has been described extensively by Coruh and McDougall ([4]) in 100 patients with lepromatous leprosy. Similar alterations have been seen in the vessels of cutaneous nerves. Job ([7]), for example, saw a marked invasion of endothelium in several endoneural vessels, and Boddingius ([2, 3]) also found a "hyaline zone" around endoneural vessels.

The corresponding ultrastructural features in the dermal microvasculature with endothelial swelling, increased endothelial and pericytic processes, and with hypertrophy of the basal lamina were described by Turkel, *et al.* ([12]), who found mycobacteria only in the endothelial cells. The results of our present study show mycobacteria on both sides of the basal lamina and confirm the important role of the dermal vessels in the multiplication and propagation of *M. leprae.*

PATIENTS AND METHODS

Six untreated patients with lepromatous leprosy were examined (2 from Ethiopia, 3 from India, and 1 from Laos). The diagnosis in each case was confirmed by clinical and bacteriologial examination and by skin biopsy. The skin biopsies were taken under local anesthesia. Immediately after each biopsy, the tissue was fixed in 5% glutaraldehyde in 0.1 M phosphate or cacodylate buffer (pH 7.2). After rinsing with buffer, a postfixation was done in 2% OsO_4 and potassium dichromate solution. After dehydration in alcohol and propylene oxide, the specimens were embedded in Durcopan®. A post-staining was performed with uranyl acetate and lead citrate; some probes also were contrasted with 2% phosphotungstic acid and 1% uranyl acetate in 70% alcohol.

RESULTS

Under the electron microscope, changes can be seen not only in the superficial capillaries of the papillae corii but also in the arterioles and arteries of the superficial arterial plexus and in the venules of the superficial venous plexus. As a sign of inflammation, an exudate can always be found.

Endothelial cells. The endothelial cells are swollen, partly separated from neighboring cells, and they extend into the lumen (Fig. 1). The surface shows many folds and finger-like protrusions (Fig. 2). The nucleus also is enlarged and often it is grooved. Many bundles of tonofibrils lie in the cytoplasm, circularly around the nucleus. Many mycobacteria are seen in the endothelial cells (Fig. 3). They are enclosed in vacuoles of different sizes and smaller ones may fuse together. Inside the vacuoles the bacteria are surrounded by a floccular fluid. The mycobacteria look intact and viable. Sometimes the membrane of the endothelial cells ruptures to the lumen, setting the mycobacteria free into the vessel (Fig. 4) where they may be phagocytosed by monocytes (Fig. 5).

Basal membrane. The basal membrane is thickened and shows several layers. Amorphous material can sometimes be found between the concentric lamellae.

Muscle cells and pericytes. Mycobacteria can be found in the smooth muscle cells (Fig. 6) of the vessels as well as in the pericytes (Fig. 7). They also look viable. As can the endothelial cells, the pericytes may rupture after intensive multiplication of the

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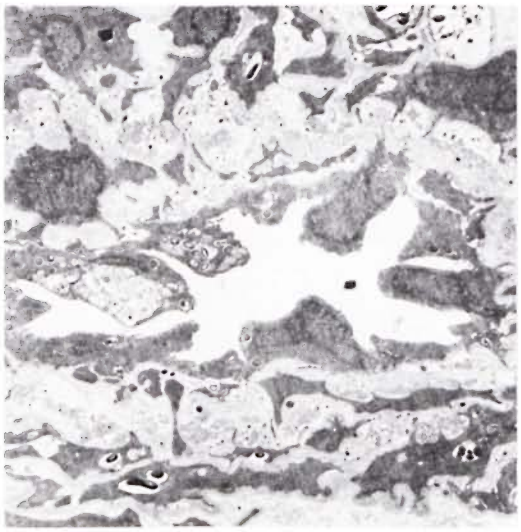

FIG. 1. Transverse section of dermal vessel. Protruding endothelial cells are loaded with mycobacteria (original magnification ×4000).

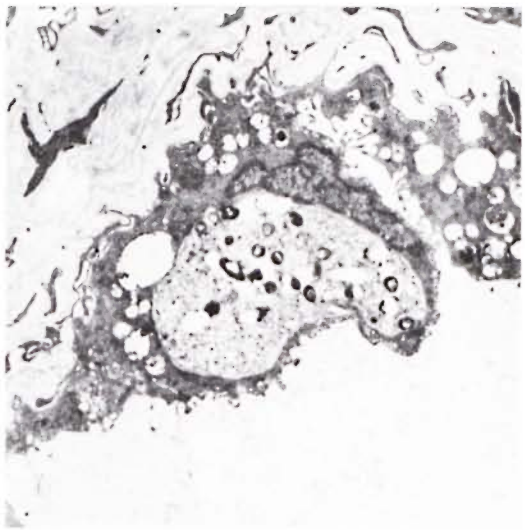

FIG. 3. Enlarged endothelial cell with large vacuole containing mycobacteria and floccular material (original magnification ×4000).

mycobacteria, and mycobacteria can be found in the exudate around the vessels. The pericytes also show signs of activation; they are enlarged.

Surroundings. Around the vessels the number of macrophages is increased; near the vessels they still look like monocytes (Fig. 8). With increasing distance from the vessels, they show more and more signs of activation: the number of lysosomes increases, as well as the amounts of pseudopodia and membranous folds. These membranous folds are often connected distally by plasmatic bridges. The ergastoplasm is seen more distinctly. Inclusion bodies can be noticed in the nucleoplasm. These active macrophages are seen to phagocytose mycobacteria.

Degenerative changes. Some of the ves-

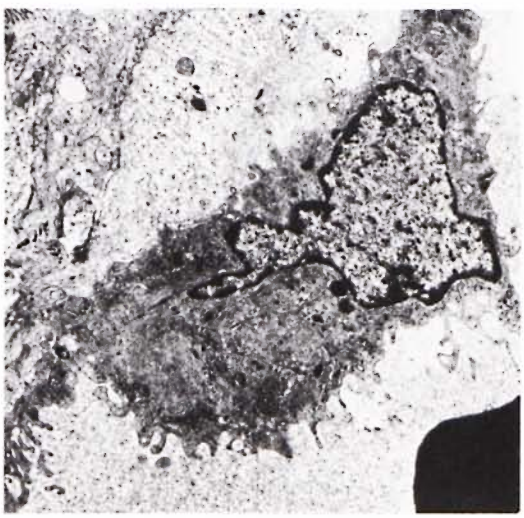

FIG. 2. Enlarged and activated endothelial cell (original magnification ×10,000).

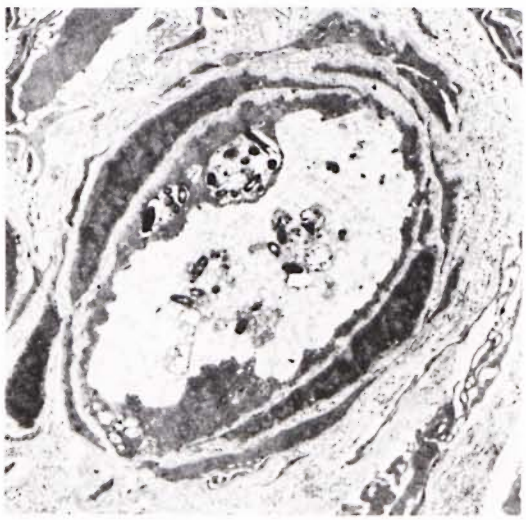

FIG. 4. Capillary with mycobacteria both in endothelial cells and in the lumen (original magnification ×4000).

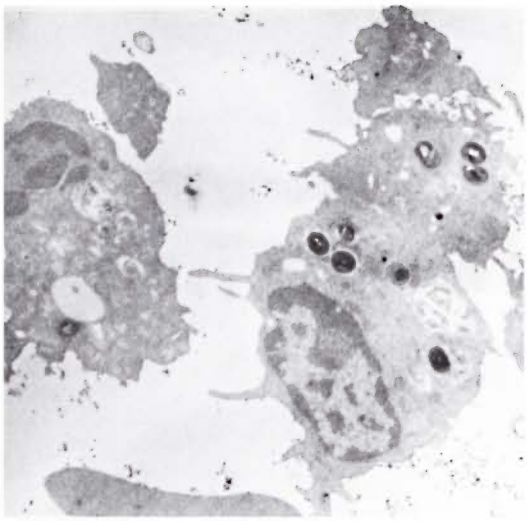

FIG. 5. Blood monocyte containing mycobacteria (original magnification ×8000).

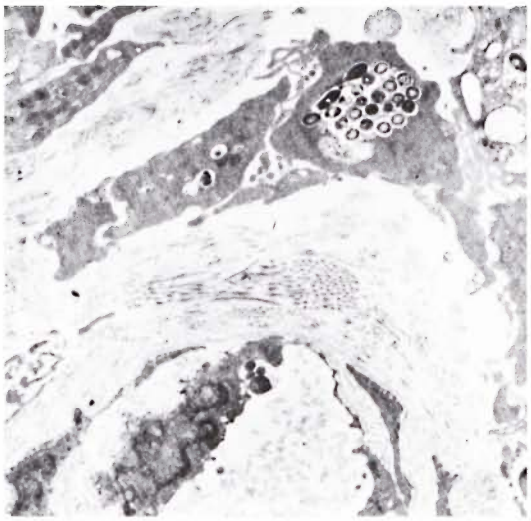

FIG. 7. Pericyte containing mycobacteria (original magnification ×8000).

sels show degenerative changes (Fig. 9). The basal membranes are hypertrophied, and no lumen of the vessel can be seen. Only remnants of muscle cells and pericytes are observed, but these can still contain intact mycobacteria (Fig. 10).

DISCUSSION

The electron microscopic changes we found in the cutaneous vessels of lepromatous leprosy patients are similar to the results of Coruh and McDougall ([4]). The endothelial cells show the typical signs of activation, with hypertrophy and augmentation of the cellular surface. The mycobacteria which are often found in the endothelial cells are extruded into the lumen. Moreover, we could show that the mycobacteria are not only transported free in the blood stream ([6, 11]) but, in some cases, are

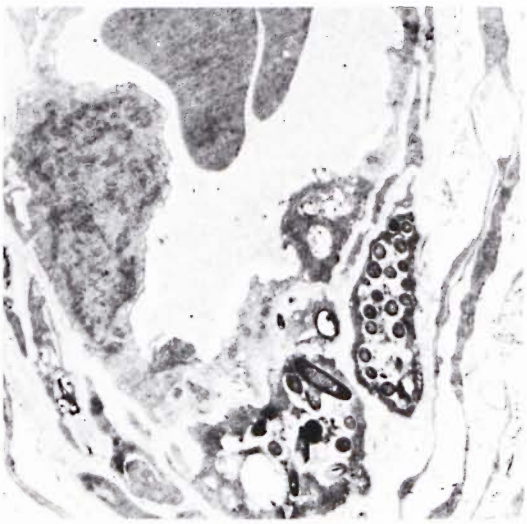

FIG. 6. Transverse section of dermal arteriole. The smooth muscle cells contain mycobacteria (original magnification ×8000).

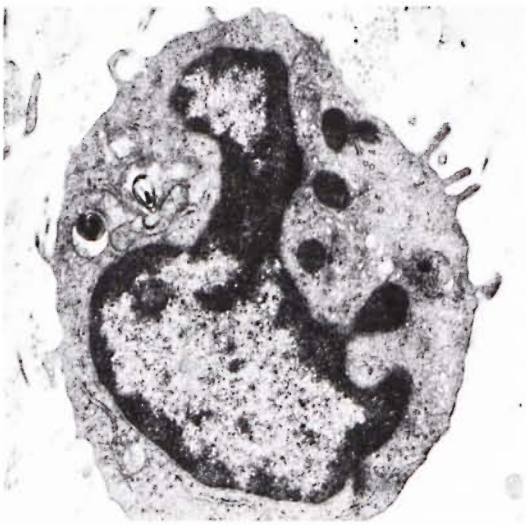

FIG. 8. Macrophage resembling blood monocyte with some mycobacteria (original magnification ×8000).

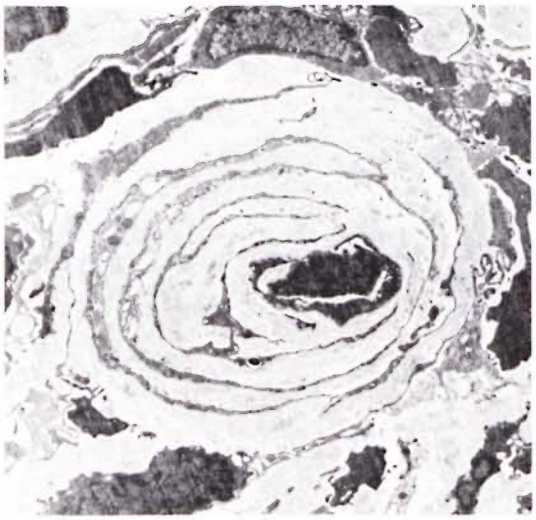

FIG. 9. Obliterated small vessel with some mycobacteria in remnants of pericytes (original magnification ×4000).

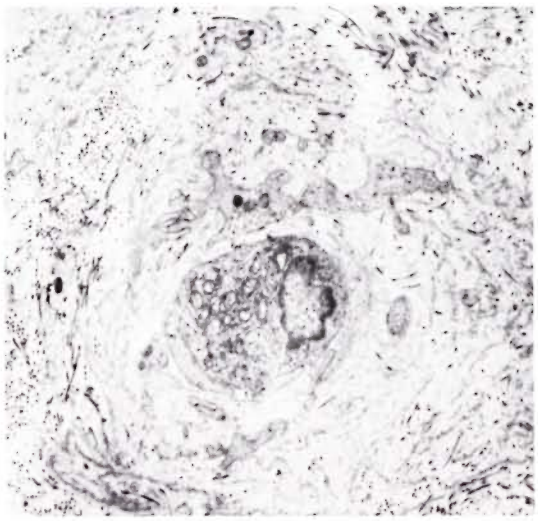

FIG. 10. Final stage of obliteration (original magnification ×4000).

also phagocytosed by blood monocytes which obviously play a role in the spread of the mycobacteria. On the other hand, the mycobacteria can penetrate the vessel wall. Large numbers of mycobacteria are found in the pericytes and muscle cells. Like the endothelial cells, the pericytes show signs of activation. Like the endothelial cells the pericytes may also rupture, discharging the mycobacteria into the interstitium. Here they are phagocytosed by macrophages.

These observations confirm that the small vessels play an important role in the process of disease in leprosy.

SUMMARY

The small dermal vessels play an important role for the propagation of *Mycobacterium leprae*. Bacteria can multiply in the endothelial cells as well as in the pericytes and can enter the blood stream from the endothelial cells and the interstitial space from the pericytes. *M. leprae* can be phagocytosed by blood monocytes.

RESUMEN

Los pequeños vasos dérmicos juegan un importante papel en la propagación del *Mycobacterium leprae*. Las bacterias pueden multiplicarse en las células endoteliales tan bien como en los pericitos y pueden entrar en la corriente sanguínea a partir de las células endoteliales y al espacio intersticial a partir de los pericitos. El *M. leprae* puede ser fagocitado por los monocitos de la sangre.

RÉSUMÉ

Les petits vaisseaux du derme jouent un rôle important dans la propagation de *Mycobaterium leprae*. Les bactéries peuvent se multiplier dans les cellules endothéliales, de même que dans les péricytes; elles peuvent pénétrer dans le courant sanguin à partir des cellules endothéliales et des espaces interstitiels constitués par les péricytes. *M. leprae* peut être phagocyté par les monocytes du sang.

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