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Book Reviews

The following translation from the original publication in German was made by a medical student from Muenster during a period of clinical training in Oxford, September 1982. Editor

Das Mykobakterium Leprae Und Die Mesenchymreaktion Des Integumentes Bei Lepra Lepromatosa Und Interpolarer Lepra (Mycobacterium leprae – Mesenchymal Reaction of the Skin in Lepromatous and Dimorphous Leprosy), by M Bierther, EM Lemmel, KF Schaller, D Schranz. Ernst-Rodenwaldt Institute, Koblenz. In cooperation with the German Leprosy Relief Association. 41-page monograph, paperback, illustrated with 72 electron micrographs, 1978.

This study aims to correlate different structural appearances of *Mycobacterium leprae* with the clearly distinguishable mesenchymal reactions of the skin in lepromatous and dimorphous leprosy by electron microscopy. Additionally, the authors discuss the morphologically distinctive basic mechanisms of the anti-infectious response.
The main headings are as follows: 1. Sites and fine structure of leprosy bacilli, and 2. Mesenchymal reaction of the skin: in the exudative phase; in the phase of bacterial phagocytosis and digestion; in the phase of circumscribed granulomatous reaction.

The work is based on the electron microscopical examination of skin biopsies taken from 6 untreated patients with lepromatous leprosy and 3 untreated patients with dimorphous leprosy. Diagnosis was confirmed by clinical examination and histopathology.

The biopsies were pre-fixed for 4–12 h with 5% glutaraldehyde in 0.1 M phosphate or cacodylate buffer (pH 7.2); sent to Koblenz in the buffer; fixed with 2% OsO_4 and 1% $K_2C_2O_7$ solution; dehydrated in alcohol and then embedded in durcupan after 12–23 days. Because this method renders the nucleus-equivalents of the bacilli invisible, the biopsies of 3 patients were fixed in 1% OsO_4 solution plus 1 M CaC_2 immediately after taking.

During the following dehydration in the increasing alcohol series the uranyl contrast methods of Wohlfarth-Bottermann in 70% alcohol was used. The findings can be summarized as follows:

1. *Sites and fine structure of dividing and resting leprosy bacilli*

M. leprae was detected on the skin surface in 2 cases, in 1 case it could be found in the orifice of a skin appendage and in all cases it was present in the corium, intra – as well as extracellularly.

In lepromatous leprosy the bacilli were predominantly rod-shaped, whereas in dimorphous leprosy mainly bigger forms with invaginations of the cytoplasmic membrane, vacuoles and membrane bodies in the cytoplasm could be seen. The nucleus equivalents show a reticular pattern of the DNA, which lies in an electron-dense nucleoplasm. The nucleoplasm is connected with the cytoplasmic membrane through the cytoplasm by numerous channels.

2. *Mesenchymal reaction of the skin*

Morphological changes of capillaries and their involvement in the cellular defense against the leprosy infection. The endothelial cells show an increase in volume, enlargement of their nucleus and disintegration of the cellular association. They can protrude into the vessel and obstruct its lumen. Their cytoplasm contains numerous morphologically different vacuoles containing leprosy bacilli, which appear to be structurally unchanged. Some biopsies show rupture of the cytoplasmic membrane and release of *M. leprae* into the capillary.

Similar changes can be seen in the adventitial and smooth muscle cells of the vessels. This process leads to destruction of these structures; finally only remains of endothelial and smooth muscle cells are found. In the periphery, fibroblasts produce amorphic base-substance and collagen fibrils which push forward towards the former vessel centre.

Morphology, activity and phagocytic capacity of macrophages and their failure to digest M. leprae *in the exudative phase.* Big macrophages with the typical morphological signs of increasing activation (increase in number of lysosomes, ergastoplasm profiles) are the predominant cell type. Their caryoplasm shows characteristic spherical inclusions which might reflect the functional changes of the nucleus due to the presence of leprosy bacilli. Precondition for the endocytosis of *M. leprae* is a close contact between the bacillus and the macrophage which can occur on the whole surface. The mycobacterium gets surrounded by an ingestion vacuole which is subsequently taken into the cytoplasm. The bacilli appear to be completely unaltered, they are even able to multiply themselves and get into the interstitial space after destruction of the macrophage. The digestion of *M. leprae* is accompanied by a marked change in the cellular picture.

Appearance of lymphoid cells–phase of increased phagocytosis and digestion. Small lymphocytes which were absent during the exudative phase

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can easily be detected. They seem to leave the capillaries trans-endothelially. They take up appositional contact with the macrophages, indentations can actually be seen. At this stage the macrophages are characterized by intensive digestive processes. Primarily the cell wall remains intact whereas the cytoplasm shows marked features of destruction (osmiophilia). Finally, bacterial cell wall rests can be found in the vacuoles. In the meantime laminated membrane convolutions indicate macrophage degeneration.

These processes point out a mutual dependence; the direction of flow of information however, cannot be detected.

Appearance of mast-cells, amyloid depositions and giant cells. Apart from macrophages, some mast cells can be detected, especially near vessels close to the epidermis. Characteristic features are lysosome-like inclusions which can be stained with Pb-citrate and therefore are easily distinguishable from macrophages. Additionally they do not contain bacilli. Closely under the epidermis lies a homogenous hyaline substance, presumably amyloid. It may be the product of permanent exposition of antigen products of leprosy bacilli to immune competent plasma cells.

Finally, a few giant cells which can be polynuclear and show bacterial inclusions were detected. Their number seems to correlate with the intensity of the infection.

Epithelioid- and giant-cells as a feature of the phase of circumscribed granulomatous formation in dimorphous leprosy. Macrophages are again the predominent type of cell. Additionally to the previously described mesenchymal reactions, however, areas of macrophages forming a granuloma can be seen. The granuloma is surrounded by a macrophagic infiltrate. The macrophages lie along the collagen fibres of the connective tissue which is slightly oedematous. They contain leprosy bacilli and breakdown products and surround nerve fibres, lymph- and blood-vessels.

In the granuloma no phagocytosis could be demonstrated. The membranes of adjacent macrophages show indentations. Inside the granuloma lie big epithelioid cells which still show close relationship to macrophages. On the other hand they have a differently structured chromatin-pattern of the nucleus and a remarkably high number of mitochondriae, which is an obvious sign of intensive metabolism. Additionally, many organelles with a secretory function are present which could be involved in a synthetic process. The authors suggest that foreign substances, which are produced by the chronic stimulus, could be taken up from the interstitial space, metabolized and detoxified and released as less toxic products which would imply a protective function.

In summary. The study confirms that the killing of bacilli depends on cellular defence mechanisms. However, it does not explain the initial reactions caused by *M. leprae.* Although it describes the mycobacterium in different phases, a coherent description of the structural changes of *M. leprae* is still missing. Nevertheless, this study covers the morphological changes and reactions of the skin in lepromatous and dimorphous leprosy at electron microscope level in detail and it should be of great value as a work of reference to researchers in this field.

M W A HENTZE

Tuberculosis in Children by F.J.W. Miller, Published by Churchill Livingstone 1982. Price £8.00, 294 pp

This is a paperback, 14 by 21 cm, and includes an extensive index. It is produced in the series "Medicine in the Tropics". *Part I* is devoted to Basic Facts – 1 Evolution of the primary infection with *Mycobacterium tuberculosis,* 2 Tuberculin sensitivity and the tuberculin test, 3 Epidemiology of tuberculosis, 4 BCG vaccination, and 5 Control of tuberculosis. *Part II* describes Clinical Manifestations under the following headings – 6 The recognition, diagnosis and treatment of tuberculosis in children, 7 Intrathoracic tuberculosis and miliary spread, 8 Oral and alimentary tuberculosis, 9 Tuberculosis of the skin, 10 Tuberculosis of eye and conjunctiva, 11 Superficial tuberculous lymphadenitis, 12 Tuberculosis of the central nervous system, 13 Tuberculosis of bones and joints, 14 Tuberculosis of genital tract and breast, 15 Tuberculosis of the renal tract, 16 Tuberculosis of liver, spleen, haemopoietic system and adrenals, 17 Congenital tuberculosis and infection early in infant life, 18 Tuberculosis in immigrant children in the United Kingdom, 19 Non-tuberculous mycobacterial infections, 20 Tuberculosis in animals. The appendices include information on the examination of gastric contents for AFB, laryngeal swabs, staining of *M. tuberculosis* and other acid-fast bacilli (Ziehl-Neelsen method), and the examination of c.s.f. for AFB. There are many pages of references and a very full index. This book is superb value and should be on the shelves of all dealing with tuberculosis in children and adults.