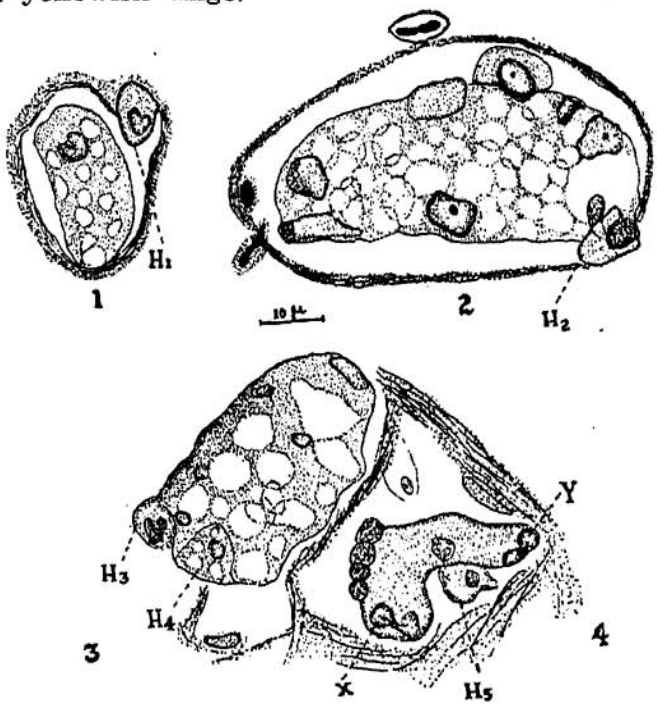
FORMATION OF MULTINUCLEAR CELLS IN LEPROUS LESIONS

ARE Langhan's giant cells described in tuberculoid leprosy comparable to multinucleated vacuclate giant cells seen in lepromata? Is the marginal arrangement of nuclei a necessary criterion for comparison? Are we seeing entirely specific types? The recent publication by Cowdry[1] of photomicrographs showing giant cells in rat leprosy attracted me to this problem. Are these giant cells the product of mere multiplication of nuclei or are they formed by fusion of discrete cells? Some interesting results obtained in this direction are described below.

The material studied was a skin clipping obtained through the kindness of Dr. Shama Rao, Leprosy Officer to the Government of Hyderabad. This is a small nodule showing in smears bacilli with "seed row" arrangement of granules (see Subramaniam[2]). The material was fixed in Regaud's fluid and attempts to stain the bacilli with Ziehl-Neelsen technique resulted in a thorough failure. Various modifications of the technique were employed but the pictures obtained of the bacilli lacked clarity and were, therefore, rejected. The sections were then bleached with potassium permanganate and oxalic acid and stained in iron hæmatoxylin.

The vacuolate lepra cells do occur only in the deeper layers of the dermis. In the series of sections examined by me they were never observed in the papillary layer. Other skin clippings from the same patient were fixed in various fluids and of all the fixatives only formalin gives clear pictures of the bacilli. In Zenker the bacilli take the stain but they lack clarity. The curious fact observed was that while masses of bacilli could be observed in the papillary layer in formol material, often touching the lowermost layer of the epidermis, no Virchow cells could be discovered in that layer. All gradations of vacuolation leading to the typical foamy Virchow lepra cells have been observed in the series of sections. These cells occur in spaces in the connective tissue network and always have a clear area surrounding them. In Fig. 1 is shown a lepra cell with vacuolation, but with only one nucleus. Near it and lying in the clear area surrounding it is a histiocyte (H_1). Fig. 2 is that of a giant cell showing marginal arrangement of nuclei. Such an arrangement, therefore, is not characteristic of giant cells in tuberculoid leprosy alone. Photomicrographs 9 and 10 of Cowdry[1] show a similar arrangement of nuclei in lesions of the rat. In this slide which was not counterstained, the nuclei alone are stained and the cytoplasm is yellow. The nuclei are irregular in shape and in a few what look like nucleoli occur. At H_2 could be seen a histiocyte lying in close contact with the giant cell. The cytoplasmic outline of the histiocyte could just be made out and in its non-vacuolate cytoplasm could be observed a few refractile granules having a yellowish tinge.



In Figs. 3 and 4 are illustrated a giant cell with vacuolation and another without any foamy appearance lying side by side. At H_3 is a histiocyte with distinct outlines lying in close contact with the giant cell. It has a cordate nucleus and its cytoplasm is light pink being stained by eosin. At H_4 is another which gives one the impression that it is just fusing with the giant cell. Its cytoplasm is vacuolated, but its outline is very clear.

Separated from the above cell by only a clear space is a non-vacuolate giant cell (Fig. 4) whose disposition and irregular outline reminds one of text-figures of connective tissue unicellular histiocytes. Most of the nuclei are at the margin and those at X and Y are suggestive of amitotic division. At H_5 is another cell which only careful examination reveals as distinct from the giant cell. Its cytoplasm and nucleus exactly simulate the staining reactions of the giant cell.

Mitsuda[3] from his study of the lepra cells in various organs suggests "that in the majority of cases, the lipoid substance is produced in the cell as opposed to its origin from bacilli that have entered there". Cowdry[1] describes "rosette" formation in rat leprosy but unlike in the human globi, he states, that there is no "schleim" associated with these "rosettes". We have in the literature a variety of grades. (1) Giant cells with bacilli and lipoid as seen in lepromata. (2) Giant cells without schleim but with bacilli as in rat leprosy. (3) Vacuolated cells with lipoid but with no bacilli as observed by Mitsuda in the mesenteric lymph glands of man and (4) Giant cells with no bacilli or lipoid as seen in major leprides.

This leads one to the question whether

these varying types may after all not be the different expressions of one and the same type of cell? In the connective tissue of the skin one finds a variety of cells. All these various forms have been considered by many cytologists as transitional forms between the small lymphocytoid and monocytoid cells to the histiocytes on the one hand and between histiocytes and fibroblasts on the other.

In infection and inflammation it is the histiocytes that are mobilized as active phagocytes. These active elements are capable of not only storing colloidal acid and basic dyes but also droplets of fat and lipoid. Accumulation of lipoid, therefore, in lepra cells appears to be not a new phenomenon at all. When mobilized the histiocytes assume a variety of shapes. Giant cells have been frequently noticed in the peritoneal exudates of rabbits injected with repeated doses of lithium carmine. Maximow[4,5] recorded that in tissue cultures these polyblasts may fuse to form giant cells.

Observations presented by me show that giant vacuolate cells are formed more commonly by addition of active cells with no sign of vacuclation to cells which have already assumed a foamy appearance. Such a phenomenon leads one to the conclusion that there is an attempt on the part of the active macrophages to reinforce those which are being immobilized by the bacilli engulfed by them. The formation of giant cells which show no vacuclation and occurrence in such cells of amitotic division indicate that fusion may not be the only method of origin of such cells.

The reaction of the organism shown in tuberculoid leprosy differs widely from that of the lepromatous variety. It is perhaps in consonance with this difference that we find a difference in the formation and nature of the giant cells. Is it not possible then, that these variations observed in structure and mode of formation of giant cells in various types of leprosy are after all the different expressions of one and the same type of cell to different conditions encountered?

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