# FORMATION OF MAST CELLS IN THE SKIN OF ALBINO RATS

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The origin of the mast cells is uncertain. It is still disputed whether they are an independent cell form or whether they are merely a specific morpho-functional stage in the process of development and activity of other cell forms of the connective tissue [3, 9]. Even those authors who recognize mast cells as an independent specialized cell variant are in total disagreement about their original forms. As precursors of the formed mast cells, lymphocytes, histiocytes, and fibroblasts have been named [2, 7, 8, 10, etc.]. The formation of mast cells has been described in albino rats from the lymphoid cells of the omentum [5], the pericytes during aseptic inflammation in the skin [4], and from the special wandering cells isolated from the mesenchyme in the early stages of ontogenesis [6].

The object of the present investigation was to study the formation of mast cells in the connective-tissue basis of the skin in albino rats.

## EXPERIMENTAL METHOD AND RESULTS

In preparations of transverse sections of the skin of young and adult animals a conspicuous feature is the presence of large, intensively stained mast cells, situated in the deep layers of the dermis and in the subcutaneous connective tissue (Fig. 1). These cells contain the large metachromatic granules characteristic of the albino rat, which are usually so numerous that the cell nucleus becomes difficult to distinguish. Often the granules appear to be scattered from the cell into the surrounding ground substance. The intensive metachromasia of the granules (especially at low pH values of the solution of the thiazine dyes), the bright staining with Takeushi's reaction for sulfate-containing mucopolysaccharides, the bright staining by Hale's method and with alcian blue confirm that the granules of the mast cells of the form described contain sulfate-containing mucopolysaccharides.

By means of supplementary control methods (as in the scheme for differential histochemical analysis of mucopolysaccharides proposed earlier by the author [1]) it can be concluded that most of the compounds consists of heparin. However, the partial suppression of the staining of the mast cells after treatment of the sections with testicular hyaluronidase demonstrates that heparin is not the only member of the mucopolysaccharides in the granules of the mast cells. They also contain compounds closely similar to or identical with hyaluronic acid and chondroitin sulfate C. The results of staining the granules of the mast cells by Hale's method and with alcian blue are interesting. When these methods are used, only the cortical layer frequently is stained in the granules of the mast cells, and their central zone remains unstained. As a result the granules become characteristically vesicular in appearance.

With combined staining methods of the type of alcian blue–neutral red or the PAS reaction–Hale's method, the nonhomogeneity of the granules is clearly seen: some of the granules are stained an intensive blue color by the alcian blue (or by Hale's method), whereas other granules show a marked affinity for neutral red (or give a clear PAS-positive stain). Finally, the category of mast cells which is being described in characterized by a marked PAS-positive reaction of their granules. The intensity of the color produced in the PAS reaction is much greater than the intensity of staining of mature bundles of collagen fibers.

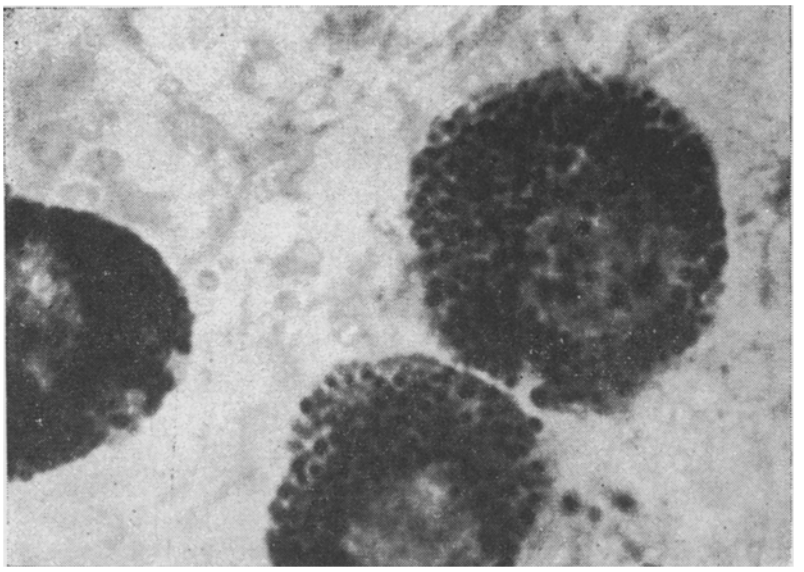

Fig. 1. Mast cells of the subcutaneous connective tissue of an albino rat. Photograph. Vital staining with toluidine blue. Objective 90×, ocular 15×.

A completely different type of mast cell is observed in the superficial layers of the dermis, in the connective tissue of the subepidermal zone. These are cells which, in their morphological characteristics, are similar to young fibroblasts, and in preparations stained with hematoxylin-eosin they are often indistinguishable from the latter. The nuclei of these cells, like those of fibroblasts, are poor in chromatin and contain 3-4 nucleoli. Tiny metachromatic granules can be seen in the cytoplasm, sometimes in large numbers but never filling the whole cytoplasm. As a rule the granules are situated mainly at the periphery of the cytoplasm (Fig. 2). Characteristically, in the same preparations, stained with azure II—eosin or with toluidine blue, the granules of these cells and those of the mast cells in the deep layers of the dermis are different in color. Whereas the granules of the cells in the deep layers are stained a reddish-violet or a pure violet color, those in the cells of the subepidermal layer are a pure and brighter shade of red. The perinuclear zone of the cells is usually free from granules. The granules of the cells of this category are moderately stained by Hale's method, they give a marked reaction for sulfate esters (by Takeushi's method), but they are hardly stained by alcian blue and they fail completely to give a PAS-positive reaction. It is interesting that the author never once saw granules liberated from the mast cells of the subepidermal zone.

The cells described are very numerous in the superficial layers of the dermis, but particularly so in the parts of the dermis lying nearest to the region of a healing wound and in parts situated above a polyvinyl sponge grafted into the subcutaneous connective tissue. In these cases the number of such cells reaches 14-16% of the total number of cells in this zone (except the endothelial cells). In the deeper parts of the skin the number of mast cells usually does not exceed 1-2% of the total number of cells in the deep layers. None of the cells characteristic of the subepidermal zone are present in the deep portions, and in turn, in the subepidermal zone there are none of the typical mast cells with numerous large granules, so characteristic of the deep portions of the skin and the subcutaneous connective tissue.

If preparations of transverse sections of the skin are examined in the direction from the superficial to the deep layers of the dermis, all the intermediate cell forms can be seen—from the cells of the surface zone to the mast cells of the deeper portions. The deeper in the dermis the mast cells are found, the larger their granules, the more numerous they are, and the more brightly they stain by Hale's method and by alcian blue; the PAS-positive staining of the granules correspondingly appears and increases in intensity. Some granules are extracellular in position. Finally, some granules become vesicular in appearance, a feature characteristic of the mast cells of the deep portions of the dermis only.

The impression is created that the mast cells in the skin of albino rats begin to be formed in the subependymal zone from cells morphologically similar to young fibroblasts and situated more often near the blood vessels. These developing forms of mast cells, which may conventionally be called young mast cells, then migrate into the deeper

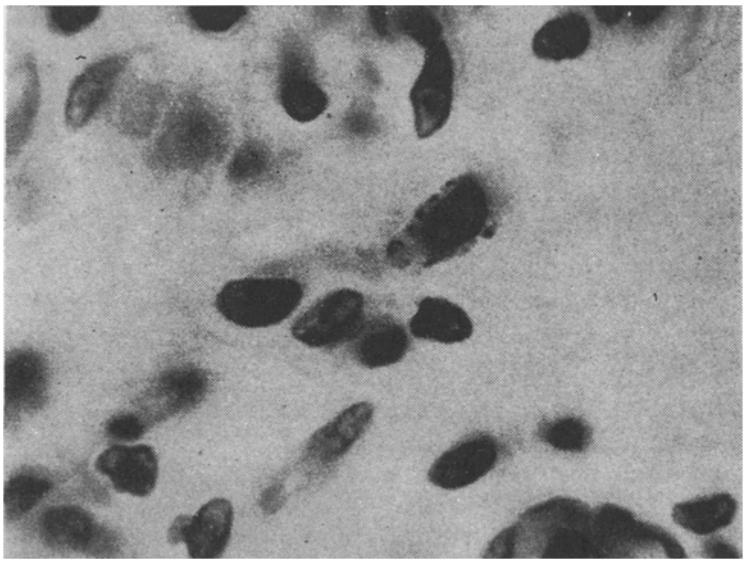

Fig. 2. Young form of mast cell in the subepidermal portion of the skin of an albino rat. Photomicrograph. Azure–eosin. Objective 90X, ocular 10X.

layers of the dermis, and as they migrate they differentiate and gradually become changed into adult mast cells. This is expressed morphologically by an increase in the dimensions of the cells themselves, by an increase in the number of granules, and by changes in their staining properties.

Comparison of the histochemical features distinguishing the granules of the young and adult forms of mast cells shows that those of the young forms contain mucopolysaccharides with a large number of more active acid groups than the granules of the adult mast cells. The change in the tone of the metachromatic staining, and the appearance and increase in the intensity of the PAS-positive staining show that in the process of maturation of the mast cells a loss or blocking of the free acid groups takes place, primarily of the free sulfate groups. It may be postulated that in the process of formation of the mast cells heparin synthesis begins somewhat sooner than the synthesis (or arrival from outside) of histamine. This leads to the appearance of granular structures in the cytoplasm containing mucopolysaccharides with active, free sulfate groups. Subsequently, in the course of formation of the heparin–histamine complex, some of the sulfate groups are apparently fixed, and this causes a corresponding change in the staining properties of the granules of the mast cells.

It may thus be concluded from these results that the mast cells in the skin of albino rats are formed from cells in the subepidermal zone. These cells are morphologically similar to young forms of fibroblasts and they can be regarded as a specialized (topographically isolated) cambial reserve for new generations of mast cells.

During the study of connective tissue developing in a polyvinyl sponge grafted beneath the skin the formation of new mast cells was never observed, despite the presence of numerous cells of young fibroblasts type in the developing connective tissue. Meanwhile, in the dermis itself (above the grafted sponge), in its subepidermal portions, the number of young mast cells was considerably increased. This suggests that the original fibroblast-like cells of the subepidermal zone either possess unique possibilities of development, distinguishing them from the other fibroblastic elements and determining their differentiation into mast cells, or they are similar to all other fibroblastic cells but it is assumed that in this case certain special conditions are necessary for their transformation into mast cells, and in the skin these conditions exist only in the most superficial, subepidermal portions of the dermis. It is difficult to say at present which of these hypotheses is closer to the truth. Further investigations are necessary to solve the problem of the origin and the functional role of the enigmatic mast cells.

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**All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of the first issue of this year.**

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