

THE FATE OF THE GIANT CELLS WHICH FORM IN THE
ABSORPTION OF COAGULATED BLOOD SERUM IN
THE ANTERIOR CHAMBER OF THE RABBIT'S EYE.

By LUDVIG HEKTOEN.

PLATE LI.

In this article it is the purpose to describe briefly the results of some experiments which show that the multinucleated giant cells which form during the absorption of foreign bodies in the tissues may divide into viable cells.

Concerning the extensive literature about giant cells—their formation, function and fate—reference is made to the article in this Journal by the writer entitled “The Fate of Giant Cells in Healing Tuberculous Tissue as observed in a Case of Healing Tuberculous Meningitis,”* in which it is pointed out that giant cells in tuberculous tissue, under certain conditions, undergo progressive changes and separate into small living cells.

THE EXPERIMENTS.

Small pieces of sterile, solidified blood serum, such as is ordinarily used as a culture medium, were inserted under aseptic precautions and cocaine anæsthesia into the anterior chambers of several healthy rabbits' eyes through a small incision in the sclera near the corneal margin. Once a bit of sterile potato was introduced. These operations were skilfully made for me by Dr. Cassius D. Westcott, Instructor in Ophthalmology in Rush Medical College, and I wish to thank him for his kind aid.

After perfecting the technique the operations were followed by but little reaction; in some instances the vessels in the sclera were congested for three or four days, the cornea rather cloudy, the anterior

* *The Journal of Experimental Medicine*, iii (1898), 21.

chamber turbid, and more or less photophobia was apparent. Soon after their implantation a small greyish white rim would become visible around the foreign bodies, which gradually disappeared until, if allowed, only a small, greyish, semi-opaque thickening in the inner surface of the cornea remained. In a few cases the blood serum was gradually dissolved without any accumulation taking place around it, the cornea and anterior chamber remaining perfectly clear. In the case of the bit of potato and when pieces of dry and hard serum were used, the absorption always proceeded slowly and with well-marked anatomical changes.

The animals were killed at intervals of from a few days to six or more weeks after the operation. The eyes were fixed in corrosive sublimate and the piece of cornea and iris, including the site of the foreign body, embedded in paraffin, cut serially, fixed on the slide and stained with hematoxylin and eosin, van Gieson's stain, etc.

THE HISTOLOGICAL EXAMINATION.

Comparatively slight attention was given the study of the early changes. Suffice it to say that the emigration of leucocytes from the vessels of the iris took place to a limited extent only, at least in the cases in which bits of solid blood serum are concerned. The leucocytes present were of the polymorphonuclear variety, and they appeared to become loaded early with granules of serum, after which some of them returned to the iris, in which a few collections of such cells were found. In the later stages of the resorptive process leucocytes were not observed.

The new cells produced come almost wholly, it would seem, from the layer of polyhedral cells clothing the inner surface of the posterior elastic lamina (Descemet's membrane) and the anterior surface of the iris. The posterior lamina itself generally remains quite intact. The new cells, which are round, oval or polyhedral, accumulate around the foreign body and penetrate into its interior, generally breaking it up, so that there is formed a mass of cells which adheres to the elastic layer and encloses the granular detritus of the coagulated serum. Most of the cells take up granules into the interior of their cytoplasm, often to such an extent that the nucleus and the entire cell appear as

if buried beneath the granular mass. The serum granules, whether free or intracellular, are easily recognizable because of their brownish or golden yellow color (derivatives of hæmoglobin pigment).

During this time there are formed a small number of multinucleated giant cells or plasmodial masses, which appear, as far as these observations show, to result from fusion of many small cells. These giant cells do not differ in form and in their general characteristics from those ordinarily observed in connection with the absorption of sterile foreign bodies elsewhere. Their size and the number of nuclei, which are scattered uniformly throughout the body of the cell, vary considerably. In the earlier stages the cells are loaded with serum granules and are of circular outline (Plate LI, Fig. 1); later when the foreign body has been largely removed the giant cells become oval or oblong, due, it would seem, to the pressure of the new fibres that in the meantime have formed around them (Plate LI, Fig. 3).

The granules of solid blood serum without and within the cells gradually disappear, largely, it would seem, by means of a process of intracellular digestion or solution; in some of the giant cells as well as in the smaller cells occur vacuoles in the cytoplasm containing granules; some of the serum, but not much, is also transported into the iris by leucocytes.

Simultaneously with the destruction or removal of the foreign granules the uninuclear and multinuclear cells begin to show further and progressive changes that ultimately lead to the formation of a layer of tissue which much resembles the cornea in structure. These changes begin first and are farthest advanced at the periphery of the cell mass, extending little by little throughout the central parts.

The changes consist in the production of a fibrillated intercellular substance, or stroma, while at the same time the cells become spindle-shaped and elongated, the nuclei more slender and fusiform. All the stages in this transformation of embryonal cells to mature tissue, during which the granules of serum are destroyed, can be quite readily traced. In the later stages the fibrillæ of the new stroma are gathered together into interlacing bundles of considerable thickness (Plate LI, Figs. 2 and 3), the general course of which is parallel with

that of the corneal lamellæ, from which they are separated by the intact posterior elastic lamina. While the course and arrangement of these new fibres are identical with those of the cornea, yet the new lamellæ are not so thick and densely interwoven as those in the cornea and they stain more deeply with eosin. This new tissue, the free surface of which becomes covered by a distinct endothelial lining, may finally appear as a mere rounded or pyramidal-shaped thickening on the posterior surface of Descemet's membrane (Plate LI, Fig. 4), or it may unite the cornea with the iris, especially if the foreign body found a resting place in the irido-corneal angle.

Lying in the spaces of the new tissue, sometimes apparently upon its fibres, are small cells like connective tissue cells, occasionally cells containing granules as well as free heaps of serum detritus and, in the stages not too far advanced, multinucleated giant cells in the process of separation into uninuclear cells.

It has already been stated that in the earlier stages the giant cells are more or less circular and the margins smooth and even. As the fibrillated stroma forms about them they may in many cases become oval and even distinctly oblong (Plate LI, Fig. 3), simultaneously with the disappearance of the serum, the long diameter corresponding to the direction of the fibres of the stroma. At this time they are usually entirely, or almost entirely, free from granules of serum; occasionally there may be vacuoles containing granules in the protoplasm. It should be emphasized that there are no signs of degeneration in the giant cells; the cytoplasm is reddish when stained by eosin and sometimes finely granular, but often it appears dense and homogeneous; the nuclei stain perfectly, and in one instance a dividing nucleus in the daughter star stage was observed in a giant cell.

As the serum disappears more or less distinct lines of cleavage become visible in the giant cells, at first most marked at the periphery; the margin is not smooth and even, but is fringed by the spindle-shaped projections of partly separated cells which seem to have a tendency to arrange themselves parallel with the fibres of the stroma (Plate LI, Fig. 3). Single uninuclear cells exactly similar to these partly detached masses are occasionally found about the giant

cells. In some giant cells, especially those encountered in the older and firmer parts, there are lines of separation throughout their entire extent (Plate LI, Fig. 3), running in such a manner that single nuclei surrounded by more or less cytoplasm are completely or incompletely mapped out; it is noteworthy that in these cells the lines of cleavage map out more or less distinctly spindle-shaped cells, the long axes of which correspond in direction to the fibres of the stroma. Occasionally the lines separating a nucleated mass are so broad and well marked that it appears as though a distinct cell were lying in a vacuole; the cytoplasm of such giant cells especially seems firm and condensed; the splitting up apparently takes place more slowly, and the impression is received that this may all be caused by the pressure exerted upon the giant cell by the fibrillated stroma in which it is enclosed, or that the cytoplasm is being transformed into the same sort of substance as the fibres of the stroma. The separation of small cells nevertheless continues, because in the older tissue are found small giant cells containing a few—three or four—nuclei and embedded in a dense capsule of nucleated fibrous tissue, without any traceable evidences of nuclear disintegration or of destruction of the giant cells by phagocytes.

When the serum is absorbed rapidly and the giant cells lie in the broad and loose meshes of the new-formed fibrillated tissue, the lines of cleavage may be quite complete, so that single nuclei, surrounded by an irregularly shaped bit of cytoplasm, are split off and imperfect giant cells result, which are surrounded by uninuclear small cells that fit the depressions and elevations on the remnant of the subdividing plasmodial mass. Uninuclear cells thus produced present no signs of necrobiosis and can be traced by means of transition stages into the elongated and flattened cells above described as lying in the new-formed tissue. Nuclear and protoplasmic detritus, as well as evidences of immigration of small cells or leucocytes into giant cells, are not to be observed.

CONCLUSION.

The conclusion seems warranted that the giant cells formed in the absorption of coagulated blood serum inserted into the anterior cham-

ber of the rabbit's eye subdivide again into uninuclear small cells that take part with other new-formed cells derived from the lining of this space to form a densely fibrillated mass of tissue that resembles quite closely the cornea in its structure.

This demonstration materially strengthens the opinion expressed by the writer in his previous article in this Journal,* that the giant cells in healing non-degenerated tuberculous tissue may separate into small living cells, and that the giant cells of tuberculosis are not necrobiotic elements from the very moment and from the very mode of their formation, as has been the general teaching, especially in Germany.

DESCRIPTION OF PLATE LI.

Fig. 1.—Recent giant cell with rounded and smooth margin filled with granules of serum so that the nuclei are covered over.

Photo-micrograph, 500 diameters, of eosin and hæmatoxylin specimen.

Fig. 2.—Photo-micrograph. Separating giant cell lying in the meshes of new fibrous tissue and surrounded by cells and by a cell mass which appear to have been sundered from the larger mass; distinct lines of cleavage are seen in the smaller as well as in the larger mass, so that small uninuclear cells may be said to be separating.

Same magnification and staining as in Fig. 1.

Fig. 3.—Oblong giant cell with a dense protoplasm in which run distinct lines that subdivide the multinucleated mass into more or less well-marked, small, uninuclear cells. In the centre is a part of a cell lying in a distinct vacuole. From a late stage. To the left of the giant cell and the surrounding thick fibres runs the intact posterior elastic lamina, and to the right is the substance of the iris.

Photo-micrograph with same magnification and staining as in Fig. 1.

Fig. 4.—Fusiform thickening of posterior surface of cornea, due to the formation of a densely fibrillated mass of new tissue after complete absorption of the blood serum. The posterior surface of the new-formed mass is clothed with a single layer of endothelial cells which is continuous with the lining of the posterior surface of Descemet's membrane. Close inspection will show the intact posterior elastic lamina running between the new tissue and the cornea.

Photo-micrograph, 100 diameters, of eosin and hæmatoxylin specimen.

* Loc. cit.

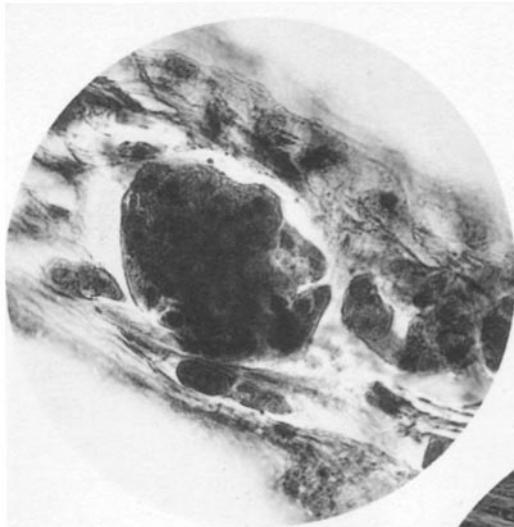


FIG. 1.



FIG. 2.



FIG. 3.

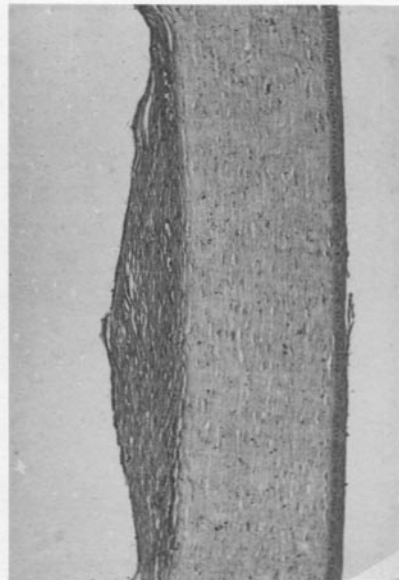


FIG. 4.