

**The Overgrowth of the Connective Tissue Cells in Infected Wounds.**

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In a previous paper<sup>1</sup> the author has shown that clean skin wounds close in large part by a moving forward of the epithelial cells of the epidermis. These cells drag the uninjured skin of the border of the wound across the opening to cover it. This movement takes place early and quickly before there is any extensive growth of the connective tissue cells. Such movement leads to the most perfect restoration of the wounded area. The growing connective tissue cells inhibit this movement of the epidermis.

In infected wounds the picture changes; the connective tissue cells grow in excess of the epidermal cells. The question arose whether these connective tissue cells are more resistant to bacteria than the epidermal cells. A careful study of many infected cultures of mesenchyme, connective tissue cells and epithelial cells has shown that this is not true. The only cells which invade areas of the medium infected with bacteria are the lymphocytes and leucocytes. They appear to be little disturbed by the growing bacteria. All fixed tissue cells are strongly inhibited by all of the growing bacterial cells, so far tested.

Having established this fact, it became evident that other peculiarities of the connective tissue cells or the connective tissue of the skin must allow them to show activity in the presence of bacteria where the epithelial layer cannot become active. In studying the difference between the epithelial and connective tissue cells (fibroblasts) in the tissue culture the author has noted<sup>2</sup> that the connective tissue cells transform the fibrinogen of the exudate of the wound into true fibrin. It was also noted that these cells do not destroy this fibrin except in the areas of the wound where they are crowded, and their environment is sufficiently stagnant for them to grow and divide most actively. While the epithelial cells are also able to transform the fibrinogen into true fibrin, they dissolve this fibrin almost as fast as it is formed under the conditions in which they exist in the wound.

In the infected wounds where granulation tissue develops the bacteria grow in the exudate. The connective tissue is the vascular tissue of the wound. In the infected wound fresh fibrinous exudate is being exuded continuously from the blood vessels of the connec-

tive tissue layer. The new exudate moves to the free surface of the wound and pushes out the old infected exudate. The epithelial cells dissolve that part of this exudate which comes into contact with them. They contain no blood vessels and supply no exudate. These cells, quite different from the connective tissue cells, must lie in a fluid which is directly continuous with the infected exudate of the wound. The fibroblasts do not liquify the exudate. The new exudate coming from their blood vessels must be forming continuously between them and the infected exudate without.

Such fresh exudate is an active stimulus for the migration and growth of both the connective tissue cells and the epithelial cells. It became of interest to see, therefore, to what extent it might act also as a shield against substances liberated by the growing bacteria. The effect of bacteria of various kinds upon the growth of heart muscle cells *in vitro* have been studied. The cultures were prepared by placing fragments of heart muscle into layers of plasma which clotted about them. Non-liquifying cultures of bacteria growing in such cultures can inhibit the growth of the heart muscle cells for a distance no greater than 0.55 mm. In cultures of tissues containing bacteria which liquify the medium the inhibiting substances diffuse with the ferment which dissolve the clot. They may also diffuse from the liquified zone for a distance of 0.5 mm., but as a rule they do not penetrate the clot so great a distance.<sup>3</sup>

It became evident, therefore, that the sterile fresh fibrin in a wound may be a very effective barrier against the action of bacteria on the cells. It is possible that the overgrowth of the connective tissue cells in many infected wounds is the direct result of the protection of them by this fibrinous layer. The above experiments show that a layer of this substance greater than 0.5 mm. in thickness can protect the cells from the action of any bacteria which does not grow and invade the exudate faster than it is being laid down anew by the blood vessels.

This is a preliminary report.

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<sup>1</sup> Burrows, M. T., *J. Med. Res.*, 1924, lxxvii, 615.

<sup>2</sup> Burrows, M. T., *Anat. Rec.*, 1917, xi, 355.

<sup>3</sup> For other experiments on the diffusion of substances into clotted plasma, see Burrows, M. T., *Am. J. Anat.*, 1926, xxxvii, 289.