MORPHOLOGY AND PATHOMORPHOLOGY

CHANGE IN THE TRANSITIONAL EPITHELIUM IN THE CASE OF REPARATIVE REGENERATION

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The study of epithelial reparative regeneration brought us to the problem of how wounds heal. Epidermal regeneration has been the facet of this problem most completely studied. But there are very few works concerning regeneration of the transitional epithelium [4, 11, 14, 16]. The experimental works of recent years that have been done on the transitional epithelium have especially not posed or resolved the problems of regeneration [1, 2, 5, 7, 8, 9, 15].

N. G. Khlopin and his colleagues have shown that the epidermal tissues are stratified and vertically anisomorphic. The transitional epithelium is normally a stratified, polyserial, mucous-producing sheet. Under experimental conditions, in tissue cultures, it produces true stratified structures and even forms intercellular bridges [5, 6].

The purpose of this work was to study certain features of reparative regeneration in the bladder epithelium, proceeding from recent ideas concerning the epithelial tissues.

EXPERIMENTAL METHODS

The work was done on 28 rabbits. The celiac cavity and the bladder were opened by operation. The mucous membrane of the bladder was cauterized in 4-5 places with a red-hot metal plate, or else small sections were cut from it. The damage area was from 4 × 4 to 6 × 6 mm. As a rule, the underlying connective tissue was injured as well as the epithelial sheath, and, in some cases, the musculature of the bladder was also damaged.

The animals were sacrificed at intervals ranging from 12 hours to 15 days after the operation. The bladder was fixed while distended and processed for histological examination. We prepared sections stained with hematoxylin-eosin, iron hematoxylin, mucicarmine and eosin-azure, and also flattened, total preparations. These last were stained with iron hematoxylin according to a method of our own [5].

EXPERIMENTAL RESULTS

Scabs formed immediately on the seared places. During the first hours, dystrophic and necrobiotic changes predominated on the epithelial layer, along the edge of the burn and for some distance from it – vacuolization of the cytoplasm, abnormal nuclei, etc. In the connective tissue underlying the scab and for some distance from it, a marked inflammatory reaction was observed. The vessels became dilated, edema developed, inflammatory leucocytic infiltrations and small foci of hemorrhage appeared.

After 12 hours, the first mitoses appeared in the basal cell layer, receding a little from the edge of the burn. Their number had sharply increased after 24 hours. The mitotically dividing cells were rounded. Later on, the number of mitoses continued to increase, and dividing cells were found in the basal and middle cell layers. The volume of the cells and nuclei noticeably increased. Among the basal elements, one could see leucocytes and macrophages infiltrating from the connective tissue. Erthrocytes were also found, but they occurred more often in small masses.

Fig. 1. Regeneration of the bladder epithelium 2 days after the burn. Burn located on left. Marginal portion of regenerate. The structure of the epithelial layer, becoming simplified, has lost the trizonal structure characteristic of the transitional epithelium. Mitosis. Stained with hematoxylin-eosin. Magnification 320.

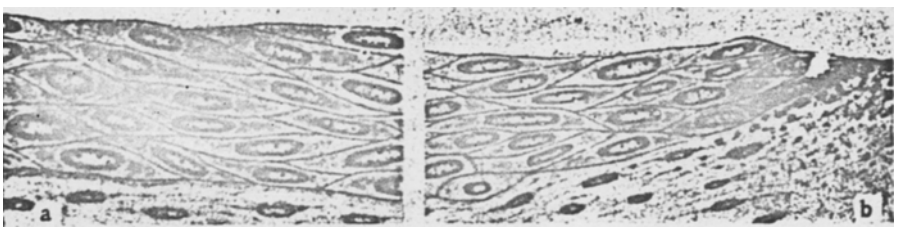

Fig. 2. Regeneration of the bladder epithelium 3 days after the burn. Epithelial layer has become multilayered in structure. The cells of all the layers are compressed and do not show visible difference of differentiation. Magnification 400. a) regenerate portion some distance from edge; b) edge portion of regenerate.

The death and sloughing of the differentiated cells of the superficial layer, as well as some of those of the middle layers, and the vigorous multiplication of the basal elements led to change in the structure of the layer. Its cell elements became more or less uniform and basophilic. The vertical anisomorphic character disappeared. The epithelial layer became less differentiated (Fig. 1).

By the end of the third day, there was a marked epithelial advance towards the damage. An epithelial thickening formed around the scab. One could see on vertical sections that, in the marginal portions of the epithelial regenerate, the cells of all the layers were compressed and oriented towards the direction in which the epithelium was moving, and that their horizontal dimensions had become considerably more vertical. The epithelium moved forward along the developing granulation tissue. In these places, the epithelium acquired the structure of a poorly differentiated, multilayered epithelium with 6-9 layers, with no expressed vertically

anisomorphic character; the cells of all the layers became compressed (Fig. 2). The epithelial regenerate, coming across the scab, either formed an incrustation and became considerably thicker, or, moving up under the scab, became wedge-like in shape (in cross-section).

Fig. 3. Regeneration of the bladder epithelium 12 days after burning. Redifferentiation of the regenerate. The layer has again acquired the structure of the transitional epithelium. Stained with hematoxylin-eosin. Magnification 465.

The regenerating transitional epithelium approached the damage in a multilayered sheet. As N. A. Shevchenko [10] has shown, such a method of regeneration is characteristic of the cutaneous type of epithelia. Thus, this feature also emphasizes that the transitional epithelium belongs to the tissues of the epidermal type.

In a series of cases, moreover, buried inflammatory growths of the epithelium were observed. It grew deep inside, like massive rods. Sometimes, one could see a group of cells which had separated from the rod next to it. Such cell complexes became spherical in form. They have been described by A. Brunn [12], and are known in the literature as "Brunn's nests." When a foreign body was placed in the rabbit bladder, we observed buried inflammatory growth of the epithelium to develop. In this case, structures which are known in human pathology as cystic and glandular cystitis [7] also formed. R. Giani [15] also observed the buried development of the transitional epithelium with the formation of cysts.

In some places, during the wounded stages of the regenerative process, erythrocytes and lumps of detritus were seen in the surface layers of the epithelial sheet, between and inside the cells. Sometimes they were piled up, like coins, in columns. These epithelial cells replete with erythrocytes and heaps of detritus were later sloughed. The presence of erythrocytes in the cells of the transitional epithelium has been described by A. V. Cornil and P. Carnot [14] and by A. S. Lezhava [3]. By the 6th-8th day, the newly-formed epithelial sheet had already covered a considerable portion of the injury. In those places where the scab still remained, the advancing epithelium scaled it off.

In those cases where the mucous membrane had been cut, the picture was generally the same as that described above. The picture differed in that the scab was smaller, the injury more quickly covered over, the inflammatory symptoms were less marked and there were no dystrophic changes in the cells.

In the case of the burns, the scab usually fell off on the 10th-12th day, and the whole region of the former injury was sealed by the newly-formed epithelial sheet at about the same time. The place of the burn could be recognized by unevenness in the mucous membrane and by a stellate scar.

Mucous formation in the transitional epithelial sheet of the rabbits was usually weakly expressed. On the preparations stained with mucicarmine, drops of mucous could be seen in the cells of the interstitial and integumentary zones. The cytoplasm of the cells in the integumentary zone became a diffused light pink shade. In the regenerating portion of the transitional epithelium, the formation of mucous was slightly greater, and more drops of mucous were observed. In the marginal portion of the regenerate and in the epithelial incrustation

which abutted against the scab, cells were often found containing many small drops of mucous in their cytoplasm.

On the vertical sections, one could trace in detail those changes in the newly-formed epithelial sheet which were connected with the onset of redifferentiation. In its youngest portion (the most central), the cells of all the layers were compressed and arranged in 4-5 layers. The epithelial sheet was considerably thinner here than in the peripheral part of the former injury. The thickening of the sheet towards the periphery was due to the increased number of cell rows and to the increase in the vertical dimensions of the cells and to their changed shape. From being compressed and parallel to the surface, they became isoprismatic and then highly prismatic. They became more clearly defined, and the cell zones became more evident. The large cells of the integumentary zone were the largest cellular elements in the sheet. There were some polynuclear elements in the sheet. The cells of the interstitial and basal zones resumed their proper forms; basal branches appeared in them, and their apical ends became thickened and rounded off. The number of mitoses decreased at about this time (Fig. 3).

The changes in the epithelial sheet were closely associated with the character of the changes in the underlying connective tissue. The exudative phase of inflammation was replaced by the proliferative. The epithelial sheet advanced along the poorly differentiated granulation tissue. According to the stage of maturity, a loose binding of collagenous bundles was formed in it. On the 15th-16th day, the damaged portion of the bladder mucous membrane was more or less completely restored.

Our data, as well as the data of other experimental works studying the transitional epithelium give a sufficiently complete characterization of this tissue.

Normally a stratified-polyserial, mucous-producing, vertically anisomorphic sheet in the rabbit, the transitional epithelium loses its characteristic trizonal structure during the process of regeneration. The structure of the sheet becomes simplified and, in the marginal portions of the regenerate, poorly differentiated and multilayered. The cells of all the layers of such an epithelium are compressed. In this case, we are not dealing with metaplasia, but, according to the terminology of V. G. Garshin, with transitory changes connected with the processes of inflammation and regeneration. Later, during redifferentiation, the regenerate again acquires the structure natural to the transitional epithelium.

Therefore, in the case of transformations under experimental conditions, the transitional epithelium not only shows certain general histotypical properties characteristic to the epidermal type of tissue, but also retains to a known degree its own specific features, by which one can distinguish it from other related tissue of the epidermal type , during growth and proliferation.

SUMMARY

Studies of the reparative regeneration of the mucous membrane epithelium in the urinary bladder after a restricted burn or extirpation have revealed certain peculiarities of this process. The data obtained show that the transitional epithelium has under the conditions of regeneration certain histotypical properties characteristic of the epidermal tissue in general.

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