

MORPHOLOGICAL CHANGES IN THE MUCOUS MEMBRANE OF THE SMALL INTESTINE FOLLOWING ADMINISTRATION OF ACTH AND HYDROCORTISONE

L. K. Leonova

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The effects of hormones on the morphological and functional state of the intestinal epithelium is a problem of considerable interest at the present time. Several authors have shown that corticosteroids influence the mitotic activity of the intestinal epithelium and the secretion of the goblet cells [1, 8, 11, 12]. The stress reaction associated with changes in the hormonal balance is accompanied by obvious macroscopic changes in the mucous membrane of the small intestine [13].

The object of the present investigation was to make a more detailed study of the morphology of the jejunal mucous membrane in the presence of an excess of ACTH and hydrocortisone in the body, corresponding to some extent to a state of stress.

Experiments were carried out on 40 female albino rats weighing from 76 to 125 g. The animals were subdivided into three groups. The rats of group 1 received ACTH once daily in a dose of 4 units/100 g body weight; the animals of group 2 received hydrocortisone in a dose of 2.5 mg/100 g body weight; the rats of group 3 were controls. The animals were sacrificed 2, 5, and 10 days after the beginning of administration of the hormones. Parts of the small intestine were taken at a distance of 0.5-1 cm from the duodenum, not later than 5 min after the heart had stopped. The material was fixed in Bouin's and Carnoy's fluids. Paraffin sections were stained by Masson's method. Polysaccharides were detected by the PAS reaction and ribonucleoproteins by Brachet's method. A three-color reaction [9] was also used for the simultaneous detection of DNA, polysaccharides, and proteins.

EXPERIMENTAL RESULTS

The epithelium of the mucous membrane which was investigated from the portion of the jejunum of the control animals was in various phases of its functional state. In some control rats the epithelium was firmly in contact with the basement membrane of the villi throughout its extent, while in others it was partially detached. In the stroma of the mucous membrane, together with the usual elements of the loose connective tissue, cells could be seen with acidophilic granules, numbering 3-5 per field of vision under the high power of the microscope.

After administration of ACTH and hydrocortisone the changes developing in the mucous membrane had much in common. From the second day after the experiment began, marked accumulation of epithelium was observed on the surface of the villi, where it was thrown into folds, and accompanied by a larger number of detached epithelial cells in the lumen of the jejunum compared with the control animals. After administration of the hormones for 5 days the intensity of detachment of the epithelium increased appreciably, and detachment of whole sheets of lining cells was observed in all the animals of this group.

After administration of hormones for 10 days, the detachment of the epithelium from the surface of the villi became less active. However, in the basal pole of some of the cells of the crypts, above the zone of mitoses, coarse oxyphilic granules appeared. In other cells in the same area, large basophilic granules accumulated.

Comparison of the results of the histochemical reaction showed that the oxyphilic granules contained protein of the histone type, ribonucleoproteins, and a polysaccharide complex. The basophilic granules included the same components except the polysaccharides, and were revealed during the PAS reaction by counterstaining with hematoxylin. The granules, initially situated in the basal pole of the cells, gradually

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Fig. 1. Sphere-cells above the zone of mitoses in a crypt of the rat's jejunum 10 days after administration of ACTN. a) Dense granule (in the center of a granular sphere). Masson's method. Magnification 500x.

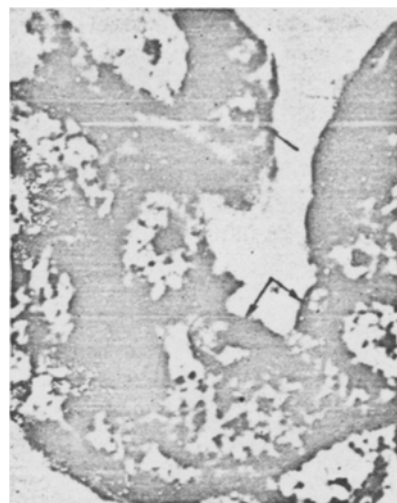


Fig. 2. Sphere cells with nuclei displaced to the apical pole after administration of hydrocortisone for 10 days. Masson's stain. Magnification 1200x.

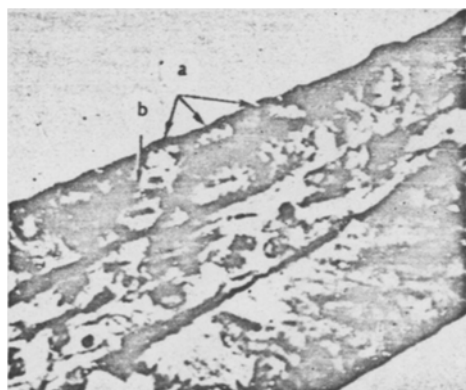


Fig. 3. Sphere-cells in the epithelium on the surface of a villus after administration of ACTH for 10 days. a) Nuclei lying horizontally beneath the apical membrane; b) granular spheres. Masson's stain. Magnification 500x.

accumulated and occupied an ever-increasing part of the cytoplasm, assuming the shape of a granular sphere. In the center of the sphere a large, dense granule could be seen, not giving a reaction for DNA, and surrounded by a lighter zone, almost free from granules (Fig. 1). As the granules accumulated, the nucleus was displaced into the apical pole of the cell, where it assumed a horizontal position and sometimes was sickle-shaped (Fig. 2). The structure of the cells as described above evidently was the final stage of their unusual differentiation. Because of their distinctive shape, they were called sphere-cells.

Subsequently the fully formed sphere-cells in the epithelium of the middle portion of the crypts migrated into the terminal portion, and sometimes onto the surface of the villi (Fig. 3). Collections of these cells in the crypts of the mucous membrane developed locally and were distributed irregularly along the course of the jejunum. Following administration of ACTH for 10 days, formation of sphere-cells took place more intensively than after administration of hydrocortisone for the same period.

The stroma of the mucous membrane appeared reduced and to contain fewer cells after administration of the hormones for 5 and 10 days. Cells with vacuolic granules were observed at the rate of 1 or 2 per field of vision.

The results showed that ACTH and hydrocortisone increase the intensity of desquamation of the intestinal epithelium 2 and 5 days from the beginning of administration, and thus stimulate the formation of the solid part of the intestinal juice. This relationship was confirmed by investigation of the intestinal juice in experiments on dogs [5, 7].

The appearance of these distinctive granules in the epithelium of the crypts demonstrated considerable changes in the intracellular metabolism during prolonged administration (10 days) of the hormones, and the irregularity of the distribution of the sphere-cells could be explained by the general principle

of the phase-structure of the secretory activity of the small intestine along its length [2]. In accordance with this phase structure the epithelium is in different functional states [6], and this may evidently account for the variation in sensitivity of its individual areas to the action of hormones. The possibility is not ruled out that substrates accumulating in the sphere-cells are intended for secretion into the blood stream (such as serotonin, secretin, etc.). This suggestion rests on the basal arrangement of the granules and on results showing that under the influence of ACTH and hydrocortisone the permeability of the limiting membranes is reduced [3, 10], which possibly accounts for the delay in the evacuation of these products from the cell into the blood stream.

The observed decrease in the number of cells and reduction of the stroma of the mucous membrane of the small intestine are associated with the inhibitory effect of the glucocorticoid hormone of the adrenals on the biological activity of connective tissue [4].

In conclusion, the unusual nature of the differentiation of the intestinal epithelium must be stressed, its final stage being represented by the sphere-cells arising after prolonged administration of the hormone.

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