

# ROLE OF CATECHOLAMINES IN THE DEVELOPMENT OF CORTICOSTEROID LESIONS OF THE GASTRIC MUCOSA

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UDC 616.33-02 [615.557.453.015.2;  
615.357.452

Administration of prednisolone to rats leads to the development of hemorrhages and erosions in the gastric mucosa and reduces mitotic activity substantially. Adrenergic blocking agents (tropaphen\* + propranolol) reduce the harmful action of prednisolone. This is regarded as evidence of the role of catecholamines in the development of trophic disturbances induced by administration of glucocorticoids.

In view of reports of interaction in the body between glucocorticoid hormones and catecholamines and, in particular, of Ingle's [6] concept of the permissive action of glucocorticoids, according to which glucocorticoids facilitate the exhibition of catecholamine action, and following experimental investigation [1, 3] demonstrating the "permissive action" of glucocorticoids in the production of some metabolic disturbances, it was decided to study the role of catecholamines in the development of trophic disturbances developing in the gastric mucosa during administration of glucocorticoid hormones.

In the investigation described below, the level of nutrition of the gastric mucosa, as reflected in macroscopic changes (hemorrhages and erosions), and the mitotic activity of the epithelium lining the surface of the ducts, which is depressed by glucocorticoid hormones, were studied.

## EXPERIMENTAL METHOD

Experiments were carried out on 50 male Wistar albino rats weighing 180-200 g. The animals were divided into 3 groups: group 1 consisted of 10 intact rats (control); group 2 of 20 rats which received prednisolone (Gedeon Richter) by intramuscular injection daily for four days in a dose of 25 mg/kg, dissolved in 0.5 ml physiological saline; group 3 of 20 rabbits which received the  $\alpha$ -blocking agent tropaphen, in a dose of 5 mg/kg, and the  $\beta$ -blocking agent propranolol, in a dose of 0.1 mg/kg, dissolved in 0.5 ml physiological saline, together with prednisolone (25 mg/kg daily for 4 days). Throughout the experiment the animals received a standard diet, but on the last day only water was given. During the 5 h before the end of the experiment, all the animals received an injection of colchicine (Merck) in a dose of 1 mg/kg. At the end of the experiment the animals were anesthetized with ether and the stomach was removed, washed with physiological saline, and stretched out on cork. A strip was cut from the whole length of the lesser curvature, fixed in Carnoy's fluid, and embedded in paraffin wax. Sections, 5  $\mu$  in thickness, were stained with hematoxylin eosin and examined under the microscope with an immersion objective (900 $\times$ ). Mitotic activity was assessed by the mitotic index, i.e., the number of cells in a state of mitosis per 1000 undividing cells. The cells from the epithelium lining the ducts of the pyloric glands, cut sagittally, were counted. In each preparation 200 cells were counted.

\*The tropine ester of  $\beta$ -acetoxyphenyl- $\alpha$ -phenylpropionic acid.

Gastric Department, All-Union Research Institute of Gastroenterology, Ministry of Health of the USSR. (Presented by Academician of the Academy of Medical Sciences of the USSR V. Kh. Vasilenko.) Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 73, No. 5, pp. 31-33, May, 1972. Original article submitted July 20, 1971.

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TABLE 1. Mitotic Activity of Epithelium Lining Ducts of Pyloric Glands under the Influence of Various Factors

Group of animals	No. of animals	Mitotic index	Mean mitotic index	Significance of differences
1 (control)	5	93 105 105 125 150	115,6	—
2 (prednisolone)	6	22 44 44 45 50 58	43,1	$P < 0,05$
3 (prednisolone + adrenolytics)	6	71 75 97 107 146 148	105,6	$P_{1-3} > 0,05$ $P_{2-3} < 0,05$

## EXPERIMENTAL RESULTS

Hemorrhages and erosions in the glandular part of the stomach were found in 17 of the 20 animals receiving prednisolone. They were found, although much less frequently (in three of the 10 rats), in the control group also. Administration of the adrenolytics considerably reduced the frequency of the lesions of the gastric mucosa, which were found in only two of the 20 rats.

The development of gastric lesions in the control animals was evidently due to stressor effects during the operation. Hemorrhages and erosions in the animals receiving prednisolone were perhaps the result of a combination of the harmful action of hormones and of stress factors.

Histological examination of the specimens showed that most mitoses were located in the deep parts of the ducts, and fewer in the intermediate parts. No mitoses were found in the surface epithelium of the ducts. Similar results for the distribution of mitoses were obtained by other workers [2, 4, 6-8].

As Table 1 shows, prednisolone considerably reduced the mitotic activity of the cells of the glandular epithelium. Simultaneous administration of adrenolytics significantly reduced the depressant effect of prednisolone.

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