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FUNCTIONAL MORPHOLOGY OF GASTRIC FUNDAL GLANDULOCYTES PERMANENTLY EXPOSED TO BILE

I. V. Sukhodolo, V. D. Sukhodolo, L. N. Batsula, and T. I. Fomina

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Many workers regard regurgitation of bile into the stomach as a factor which is conducive to disturbance of the functional state of the mucosal barrier, to increased reversed diffusion of hydrogen ions, and as a result of this, to the development of ulceration of the mucosa [2, 8, 11].

Meanwhile other workers have obtained evidence of a positive regulatory effect of bile on the motor, secretory, and endocrine functions of the gastroduodenal complex [1, 5, 6, 12, 13] and they consider that bile has a protective action on the gastric mucosa in the presence of hyperchlorhydria [6, 9, 10].

The aim of this investigation was a differential study of the dynamics of mitochondrial enzyme activity in the mucous neck cells and parietal cells and also of the RNA content in the chief cells and vascular permeability in the mucosa of the gastric fundus in rats, in order to assess the functional state of the gastric mucosal barrier and of the morphological substrate of the secretion of acid and digestive enzymes after diversion of all the bile into the stomach.

EXPERIMENTAL METHOD

Experiments were carried out on 47 mature male rats weighing 240-250 g. An anastomosis was formed in the animals between the bile duct and the body of the stomach. The experimental and control (mock operation) rats were decapitated 10, 30, 60, and 90 days after the beginning of permanent diversion of bile into the stomach. Material for investigation was taken after starvation of the animals for 24 h, but with unrestricted fluid intake. After autopsy the gastric mucosa was carefully inspected for macroscopic defects. The subsequent histochemical investigation and preservation of the material were undertaken in accordance with recommendations in [3].

Frozen sections of the mucosa of the body of the stomach were stained for activity of NADH-dependent dehydrogenase (NADH-DH), succinate (SDH), isocitrate (ICDH), and malate dehydrogenases (MDH), and alkaline phosphatase (AlP) and for quantitative determination of RNA and neutral and acid mucopolysaccharides (MPS) by the usual histochemical methods.

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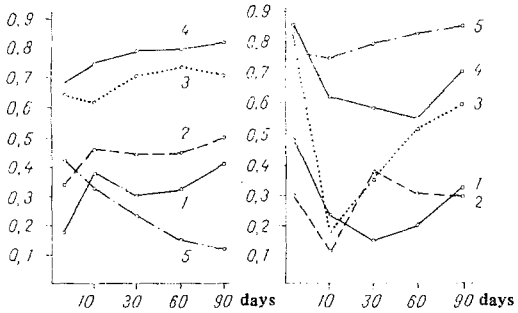

Fig. 1. Changes in ICDH (1), MDH (2), SDH (3), and NADH-DH (4) activity in mucous neck cells and in RNA content (5) in chief cells during diversion of bile into stomach. Here and in Fig. 2: abscissa, time after beginning of experiment (in days); ordinate, optical density of histochemical reaction products (in relative units).

Fig. 2. Changes in ICDH (1), MDH (2), SDH (3), and NADH-DH (4) activity in parietal cells and AlP activity (5) in endothelial cells during diversion of bile into stomach.

Enzyme activity was estimated quantitatively by cytophotometry on the Lyumam-IZ microscope. The numerical data were subjected to statistical analysis by Student's t test on the Nairi-K computer.

EXPERIMENTAL RESULTS

Macroscopically the gastric mucosa of the rats in the early stages of the experiment (10-30 days) showed superficial gastritis, changing to atrophic gastritis later (60-90 days). In all cases much saliva, mucus, and bile was found in the stomach. No erosions or ulcers were found in the mucosa. Histological study showed that 10 days after formation of the anastomosis between the bile duct and stomach signs of hyperproduction of neutral and acid MPS by the epithelial mucous neck cells were present. This was confirmed by quantitative analysis of mitochondrial enzyme activity in the cells studied (Fig. 1). The blood vessels of the mucosa during this period were somewhat hyperemic and AlP activity in the endotheliocytes was depressed, but not statistically significantly ($P > 0.05$). The RNA content in the cytoplasm of the chief cells was reduced. Mitochondrial enzyme activity also was reduced significantly in the parietal cells (Fig. 2).

Edema, accompanied by increased AlP activity, was observed in the mucosa of the body of the stomach 30 days after the experiment began. The complex structure of the fundal glands was disturbed and their deeper portions were dilated. Mitochondrial enzyme activity remained low in the parietal cells compared with the control. The only exceptions were MDH and, to some degree, SDH (Fig. 2).

The width of the band of neutral and acid MPS in the mucous neck epithelial cells and the intensity of their staining were greater at this time than in the control. Quantitative study of the dynamics of the mitochondrial enzymes in the mucous neck epithelial cells demonstrated their continued activation.

The time course of mitochondrial enzyme activity in the surface epithelium and parietal cells remained opposite in direction 60 days after the beginning of the experiment (Figs. 1 and 2). Hyperproduction of neutral and acid MPS by the mucous neck cells continued: The surface of the mucosa and the widened spaces between the pits were filled with large quantities of mucus. Depressed function of the chief cells was reflected in quantitative determination of their RNA.

Atrophic changes in the mucosa of the gastric fundus were a noteworthy feature 90 days after the experiment began.

Mitochondrial enzyme activity in the parietal cells at this time showed a tendency to return to normal, but it still differed from the control level, and in the mucous neck epithelial cells it remained high (Figs. 1 and 2).

Permanent diversion of all the bile into the stomach in rats thus gives rise to various changes in the functional morphology of the gastric glands. These changes are characterized initially by depression of secretory activity of the parietal and chief cells, accompanied by hyperproduction of mucus by the mucous neck cells. Later in the experiment a tendency was found for mitochondrial enzyme activity in the parietal cells to return to normal although functional activity of the epithelial mucous neck cells remained high. The permanent stimulant action of the bile on the mucosa induces intensive functional activity of mucus-forming cells and, probably, their increased wear and tear by analogy with the action of aspirin [7]. It must accordingly be considered that there is a redistribution of differentiating neck cells toward the formation of mucous neck epithelial cells. The deficiency of the neck cell pool in the fundal glands evidently leads to the development of the atrophic changes which were observed in the late stages of the experiment.

It can be concluded from these findings that prolonged diversion of all the bile into the stomach in rats is not accompanied by the development of erosions or ulcers of the fundal mucosa, but it does lead to changes, in various directions, in mitochondrial enzyme activity in the mucous neck cells and parietal cells. From the functional point of view, this picture can be regarded as adaptation of the mucosal barrier to extremal conditions, accompanied by a decrease in the secretion of acid and digestive enzymes.

The dynamics of the histochemical changes in fundal glandulocytes of the stomach in response to irritation of the mucosa with bile indicates the existence of well-marked compensatory mechanisms. The detergent action of bile on the mucosa, without any additional effects weakening the function of the mucosal barrier, is insufficient to cause the development of erosions and ulcers of the gastric mucosa in rats.

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