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## FUNCTIONAL MORPHOLOGY OF GASTRIN-PRODUCING CELLS IN DIFFERENT PHASES OF PERIODIC GASTRIC ACTIVITY IN DOGS

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UDC 612.325.019:599.742.1].086

**Key words:** stomach; periodic activity; gastrin-producing cells

Periodic activity (PA) of the gastrointestinal tract is one of the most demonstrative rhythms of the body [1-3]. An essential role in the neurohumoral mechanisms of regulation of alternation of the phases of PA, namely a period of relative rest (PR) and a period of work (PW), is played by the peptide component [3, 4, 7]. Data on changes in the blood gastrin concentration (BGC) during alternation of the phases of PA are highly contradictory [2, 4], although a circadian rhythm of BGC has been found in man and in animals [5, 8, 10].

We studied the ultrastructure of gastrin-producing cells of the antral mucosa of the canine stomach in different phases of PA, in the fasting state.

### EXPERIMENTAL METHOD

Material for electron-microscopic and morphometric investigation was taken from 10 mongrel dogs with fistulas of the body and pyloric part of the stomach. Alternation of the phases of PA was studied by recording gastric motor activity on the drum of a kymograph by a combined hydraulic and pneumatic transmission system.

Food stimulation consisted of feeding the dogs with minced meat, and 20 min later biopsy specimens were taken from the mucosa of the antral part of the stomach.

Material taken in the middle of PR and PW, and also 20 min after food stimulation was fixed in a 4% solution of paraformaldehyde in Hanks' buffer (pH 7.4), cooled to 4°C, postfixed with OsO<sub>4</sub>, dehydrated, and embedded in a mixture of Epon and Araldite resins. Ultrathin sections were stained with lead citrate and uranyl acetate, examined in the JEM-100CX microscope, and photographed under magnification of 8000. Morphometry of the negatives was carried out on a semiautomatic "MOP-Videoplan" image analyzer ("Reichert," Austria). The number of secretory granules (SG) per square micron area of the cytoplasm of a gastrin-producing (GPC), the area of each type of SG, the maximal diameter and relative area of each type of SG,

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Central Research Laboratory, Tomsk Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR E. D. Gol'dberg.) Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 109, No. 4, pp. 410-412, April, 1990. Original article submitted March 20, 1989.

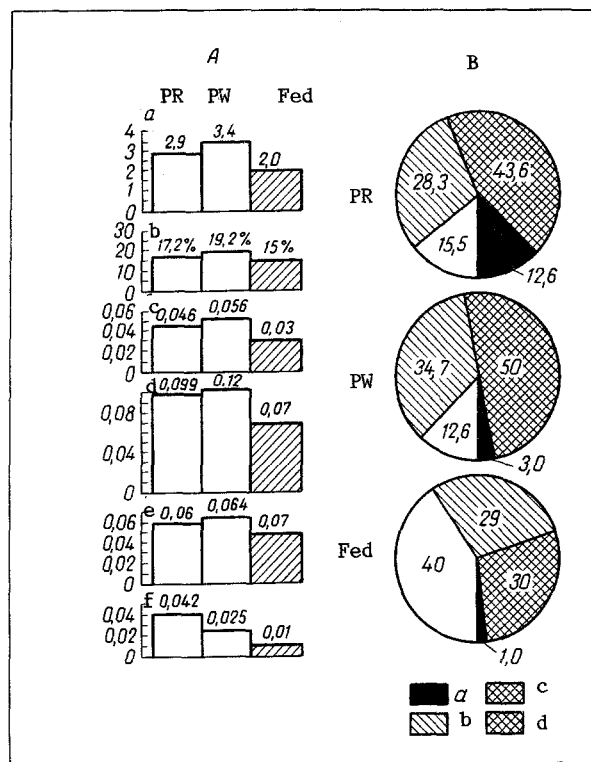


Fig. 1. Morphometric characteristics of SG in GPC on dogs during PA in the fasting state and after feeding. A: a) Concentration (in  $g/\mu^2$ ), b) relative area of SG of all types (in %), c-f) average area of SG of each type (in  $\mu^2$ ): c) SG 1, d) SG 2, e) SG 3, f) SG 4; B) relative areas of SG of all types (in %) in cytoplasm of GPC during PR and PW and after feeding (fed). Legend: a-d) the same as to Fig. 1A.

and also integral values (for SG of all types represented in GPC). The numerical results were subjected to statistical analysis and histograms constructed by a standard program incorporated in the computer of the instrument.

BGC was studied in peripheral blood (from the femoral vein) using GASK-PR kits from "CEA-IRE-Sorin" (France), the results were subjected to statistical analysis by the Wilcoxon—Mann—Whitney tests.

To test the validity of the hypothesis relating to fluctuations of BGC and of the morphometric parameters of SG during alternation of the phases of PA, one-factor dispersion analysis was used.

## EXPERIMENTAL RESULTS

The different phases of PA in the fasting state were accompanied by changes in the functional morphology of the GPC, as shown by the morphometric characteristics of SG and fluctuations of BGC.

GPC were characterized by polymorphism of the granules, associated with their maturation. The following types can be distinguished among the SG in GPC: SG 1) "empty," electron-transparent granules, SG 4) dark, electron-dense granules, and two groups of SG of intermediate type (SG 2 — containing traces of electron-dense material or half-filled with it, and SG 3 — completely filled with substance of average electron density). The most widely recognized scheme of the process of granule formation in GPC assumes that the hormone is synthesized in cisterns of the endoplasmic reticulum, that the SG receive their definitive shape in the lamellar apparatus (SG 4), and that SG 4 contains high-molecular-weight forms of the hormone, which is subsequently transformed in SG 3 and SG 2 to low-molecular-weight forms, which separate from SG by diffusion or exocytosis [6, 9].

PR of the stomach is characterized by a decrease in the SG concentration per unit area of cytoplasm of GPC (to  $2.9 \pm 0.04 g/\mu^2$  in PR compared with  $3.4 \pm 0.1 g/\mu^2$  in PW). This tendency also was characteristic of the relative area of SG (Fig. 1).

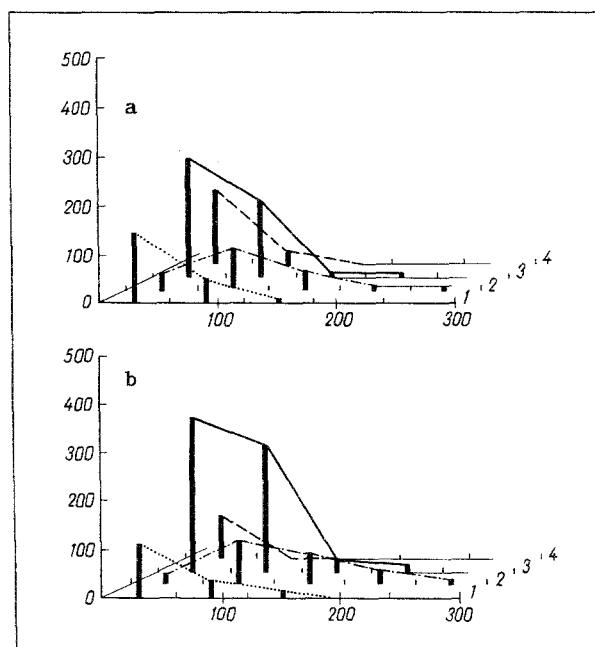


Fig. 2. Histogram of distribution of SG in GPC of mucosa of antral part of canine stomach during alternation of phases of PA. a) PR, b) PW; abscissa, absolute number of SG; ordinate, mean area of SG (in  $\mu^2$ ). 1, 2, 3, 4) Types of granules.

Analysis of histograms of distribution of SG by area indicate the greater variability of this parameter in PW than in PR (Fig. 2). The percentage of SG 1 and the proportion of granules of this type increase with increasing values of average area and maximal diameter, although the statistical mean values of SG 1 in PR were lower than in PW.

SG 2 showed minimal fluctuations during alternation of the phases of PA (Figs. 1 and 2). The number of SG 3 and also their relative area were higher in PW than in PR, whereas values of the mean area and maximal diameter were unchanged.

The greatest changes during alternation of the phases of PA were exhibited by SG 4: the percentage of granules of this type in PW was reduced by 55 compared with PR. The specific area of SG 4 was reduced by 75% in PW, and the average area of SG was reduced almost by half (Fig. 1).

Analysis of electron micrographs of GPC in different phases of PA showed that the rough endoplasmic reticulum and lamellar apparatus are activated in PW, and together with the decrease in the average morphometric parameters of SG 4, this is evidence in support of more intensive granule formation.

Changes in the functional morphology of GPC in the different phases of PA were combined with fluctuations of BGC located within the different versions of the basal GBC: the acrophase was the middle of PR ( $66.2 \pm 9.1$  pg/ml), whereas the lowest values were determined in PW ( $19.6 \pm 3.7$  pg/ml). Dispersion analysis of the results confirms the hypothesis relating to fluctuations of BGC in association with PA, and demonstrates their high level of significance.

Comparison of the morphometric characteristics of SG and GPC in the different phases of PA in the fasting state with the state after taking food showed that food stimulation causes a marked fall in the concentration of SG in GPC (to  $2.0 \pm 0.1$  g/ $\mu^2$ ). The average area of SG in GPC also was reduced due to a decrease both in statistical mean values of the parameters of SG of all types and of their number. Under these circumstances there was a marked increase in the percentage of SG 1 and SG 2, accompanied by some decrease in the percentage of SG 3 and a considerable decrease (by 94.7%) (Fig. 1). The value of BGC after food stimulation was  $163.2 \pm 13.6$  in SG 4 (Fig. 1). The value of BGC after food stimulation was  $163.2 \pm 13.6$  pg/ml.

Comparison of the morphometric characteristics of GPC after food stimulation with fluctuations in their structure during PA demonstrates a definite difference (Fig. 1).

Incidentally, changes in the functional morphology of GPC in the different phases of PA were not as great as might be expected considering the fluctuations of BGC. This fact may perhaps be explained, first, by the arrival in the blood stream of gastrin from extragastric sources during PA, and second, by a change in the rate of catabolism of the hormone in connection with PA.

Nevertheless, alternation of the phases of PA in the fasting state was accompanied by changes in the functional morphology of GPC in the antral part of the gastric mucosa of the dogs: in PR the hormone evidently diffuses from SG 1 and SG 2 (increased realization of secretion) whereas the secretion potential is unchanged and the reserve increased (an increase in the number of SG 4). PW is characterized by activation of granule formation accompanied by weakening of the release of the hormone from SG.

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## FUNCTIONAL ANATOMY OF THE HUMAN ESOPHAGEAL MUCOSA DURING POSTNATAL DEVELOPMENT

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UDC 612.315:612.642]:66

**Key words:** esophagus; ontogeny; mucous membrane

The study of the human esophageal mucosa has been the subject of numerous publications [1, 2, 4, 6, 10], on account of the special position of the esophagus in the digestive tube [8, 9]. Some investigators have attached great importance to the combined study of the structure of the boundary segments of the esophageal wall, separating functionally different regions of the digestive tube [3, 7, 11, 12]. However, despite the large number of investigations, we could find no information on the dynamics of morphological changes in the mucosa (in successive layers) during postnatal development, confirmed morphometrically.

The aim of this investigation was a morphometric study of the layers of the human esophageal mucosa in the pharyngo-esophageal, aortic-bifurcational, and esophago-gastric segments of the organ in postnatal ontogeny.

#### EXPERIMENTAL METHOD

The layers of the human esophageal mucosa were measured in 2400 serial microscopic preparations varying from 15 to 25  $\mu$  in thickness, from 122 cadavers of persons aged from birth to 90 years. The causes of death were unrelated to diseases of the esophagus. Transverse and longitudinal sections were cut at the level of the pharyngo-esophageal, aortic-bifurcational, and

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Department of Pathological Anatomy, A. V. Vishnevskii Institute of Surgery, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR D. S. Sarkisov.) Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 109, No. 4, pp. 412-414, April, 1990. Original article submitted July 19, 1989.