itary hypothalamic homogenate does not restore normal insulin release in response to elevation of the glucose concentration in the medium (Table 2). This indicates that the pituitary participates in hypothalamic control of the endocrine function on the pancreas in rat fetuses.

These results are in good agreement with the writer's previous observations on restoration of reactivity of the B-cells of decapitated fetuses after combined incubation with the adenohypophysis and its hormones [8], and also with data in the literature on the effect of the pituitary gland and its trophic hormones on pancreatic B-cell function in adult animals [4, 5, 9, 10].

It can be postulated that fetal pancreatic B-cells, unlike the corresponding cells of adult animals, are refractory to direct humoral hypothalamic influence, and that humoral connections between the hypothalamus and pancreas in rat fetuses are maintained through the participation of the pituitary.

LITERATURE CITED

1. M. S. Mitskevich and A. Ya. Sapronova, Zh. Évol. Biokhim. Fiziol., 17, 127 (1981).
2. M. S. Mitskevich, O. N. Rumyantseva, E. V. Proshlyakova, and G. P. Sergeenkova, Ontogenez, 1, 631 (1970).
3. G. H. Brouwer, M. S. Lamtey, and J. M. Martin, Life Sci., 30, 703 (1982).
4. J. Brunstedt and J. H. Nielsen, Acta Endocrinol. (Copenhagen), 96, 498 (1981).
5. S. Dunmore, J. Morton, A. Beloff-Chain, and G. Taylor, Biochem. Soc. Trans., 11, 201 (1983).
6. A. Jost, C. R. Acad. Sci. (Paris), 225, 322 (1947).
7. M. Khip, L. Lautala, H. Akerblom, et al., Life Sci., 33, 2311 (1983).
8. M. S. Mitskevich and A. Ya. Sapronova, Endokrinologie, 79, 227 (1982).
9. J. H. Nielsen, Endocrinology, 110, 600 (1982).
10. J. Pierluissi and J. Campbell, Diabetologia, 18, 223 (1980).
11. F. Rohner-Jeanrenaud and B. Jeanrenaud, Ann. Endocrinol., 44, 217 (1983).

EXPERIMENTAL EXOGENOUS ACTIVATION OF THE KININ-FORMING SYSTEM AND FUNCTIONAL MORPHOLOGY OF GASTRIC FUNDAL GLANDS

I. V. Sukhodolo, L. N. Batsula, T. I. Fomina, and L. A. Bogatyreva

UDC 612.325:612.323/-06.612.321.018:577.175.85

KEY WORDS: kallikrein-kinin system; enzyme activity; cells of fundal glands; gastric mucosa.

Control over gastric function is maintained by many mechanisms, among which not the least important is the kallikrein-kinin system (KKS) [3, 5]. Different states of the KKS (activation and inhibition) are reflected differently in the excretory, secretory, and motor activity of the stomach [2]. The KKS plays a definite role in gastroenteric pathology, for the number of its various components changes in chronic gastritis, in peptic ulcer, and in nonspecific ulcerative colitis [3, 6-8].

Components of the KKS are found in the gastric mucosa, gastric juice, and mucus [10-12], and their quantity varies in the gastrin, histamine, and insulin tests [1, 4]. However, no definite opinion has yet been formed on the effect of activation of the KKS on the functional morphology of the intact gastric mucosa.

The dynamics of histochemical parameters of function of the parietal and chief cells, and the surface and pit epitheliocytes of the fundal glands of the rat stomach was studied in the present investigation during activation of the KKS by kallikrein.

Central Research Laboratory, Tomsk Medical Institute.

Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 100, No. 11, pp. 528-530, November, 1985. Original article submitted February 15, 1985.

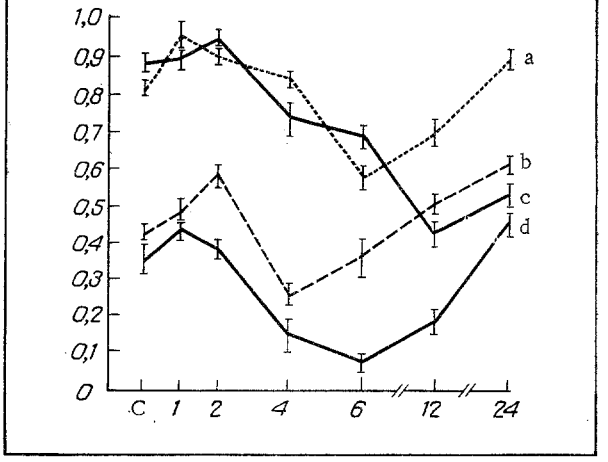

Fig. 1. Changes in enzyme activity in chief cells of fundal glands and of AP in endotheliocytes of mucosa after injection of kallikrein. Abscissa, time after injection of kallikrein (in h); ordinate, enzyme activity (in conventional optical density units); C) control; a) AP, b) NADP-TR, c) G6PDH.

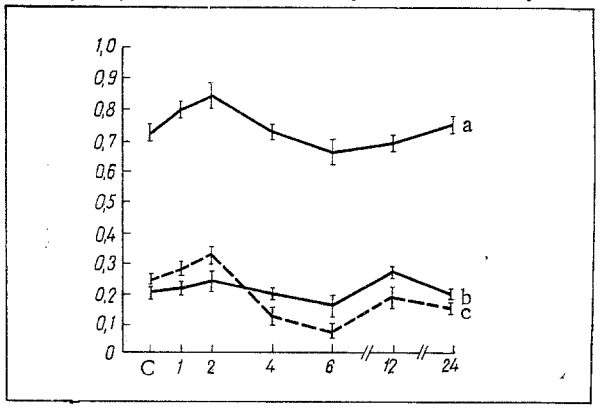

Fig. 2. Changes in enzyme activity parietal cells of gastric fundal glands: a) SDH, b) LDH, c) NAD-TR, d) MDH. Remainder of legend as to Fig. 1.

EXPERIMENTAL METHOD

Experiments were carried out on 50 male Wistar rats weighing 200-220 g. Kinin production was activated by a single intraperitoneal injection of kallikrein (0.6 U/g) (from Winthrop, USA). The control animals were given a single injection of physiological saline.

The control and experimental animals were decapitated 1, 2, 4, 6, 12, 24, and 48 h after the injection. Pieces of stomach wall were frozen with liquid nitrogen, and activity of succinate (SDH), lactate (LDH), and NAD-dependent malate dehydrogenases (MDH), of NAD- and NADP-tetrazolium reductases (NAD-TR, NADP-TR), glucose-6-phosphate dehydrogenases (G6PDH), and alkaline phosphatase (AP) was determined in frozen sections by the usual histochemical methods. Neutral (PAS reaction) and acid (by Steedman's method) mucopolysaccharides (MPS) also were determined. Survey sections were stained with hematoxylin and eosin.

Enzyme activity was determined cytophotometrically in conventional optical density units on the LYUMAN I-3 microscope in transmitted light. The numerical results were subjected to statistical analysis by Student's test.

EXPERIMENTAL RESULTS

A single injection of kallikrein induced phasic changes in functional activity of the rat fundal gland cells.

Hyperemia of the blood vessels in all layers of the stomach wall and slight edema of the foveolar stroma were observed 1 h after injection of kallikrein, and these changes persisted until the 4th hour. By the 2nd hour of the experiment, in vessels in the region of the floor of the fundal gland and submucosa, pavementing of the polymorphonuclear leukocytes

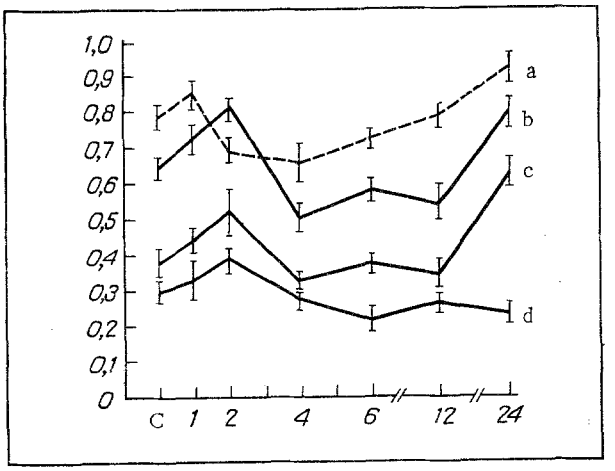

Fig. 3. Changes in enzyme activity and content of PAS-positive substances (PAS^+) in surface and pit epitheliocytes after injection of kallikrein: a) PAS^+, b) SDH, c) MDH, d) G6PDH. Remainder of legend as to Fig. 1.

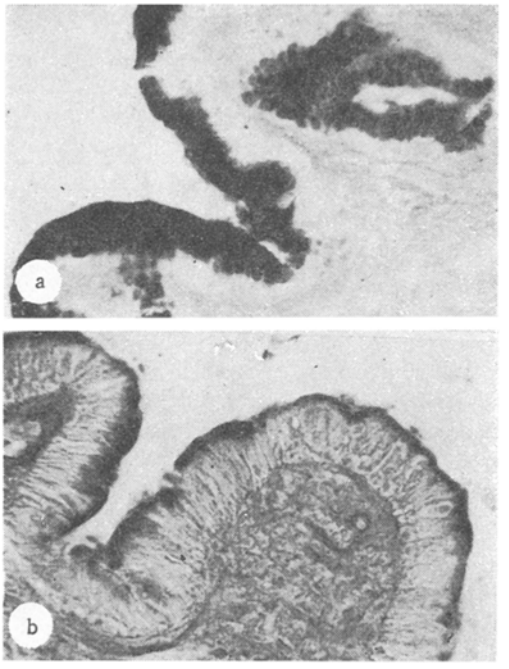

Fig. 4. Rat stomach: a) content of acid MPS in surface and pit epitheliocytes in control; b) increase in content of acid MPS in surface and pit epitheliocytes during activation of kinin production; Steedman's reaction; 500×.

was observed, and later, after 4 h, some cells were located outside the vessels, in the stroma between the glands. At this time an increase in the number of perivascular mast cells was observed, and by the 24th hour they had spread throughout the mucosa.

A single injection of kallikrein caused phasic changes in AP activity in the endotheliocytes of the mucosa (Fig. 1), in activity of oxidation-reduction enzymes in the parietal cells (Fig. 2), and of enzymes responsible for protein synthesis in the chief cells (Fig. 1) and mucus formation in the surface and pit cells (Fig. 3). Increased production of acid (Fig. 4) and neutral MPS by the surface and pit epitheliocytes, and also the visually detectable hyperproduction of mucus by the accessory cells will be noted. By the 48th hour after injection all the parameters studied returned to their original values.

Injection of kallikrein was thus definitely reflected in the functional state of cells of the gastric fundal glands. The most important finding, in our opinion, was the very marked activation of mucus formation by the surface and pit epitheliocytes and the accessory

cells. This is evidently one mechanism of the antiulcerogenic action of kallikrein preparations.

The effect of a single injection of kallikrein on activity of the parietal cells cannot be interpreted unequivocally, for the period of their increased functional activity (1-2 h after injection of kallikrein) was replaced by a phase of very drastic inhibition (after 4-6 h), followed again by activation (until the 24th hour). This pattern is in agreement with the results of physiological experiments on dogs, in which 24 h after injection of kallikrein the periodic gastric motor activity of the animals disappeared and acid contents were found in the stomach in the fasting state.

Activation of kinin production due to injection of kallikrein is evidently accompanied by a series of staggered changes in the systems of several different biologically active substances, capable of acting on receptors of the fundal gland epitheliocytes (histamine, gastrin, serotonin, other peptides). Meanwhile there are no adequate grounds for rejecting the direct action of individual components of the KKS on the functional activity of gastric glands and their internal secretory apparatus.

LITERATURE CITED

1. I. V. Bogatel'nikov et al., Patol. Fiziol., No. 1, 51 (1979).
2. V. N. Vasil'ev, "Secretory and excretory functions of the stomach during disturbance of salivary gland activity," Author's Abstract of Dissertation for the Degree of Candidate of Medical Sciences, Novosibirsk (1981).
3. A. D. Vizir et al., Ter. Arkh., No. 10, 74 (1981).
4. G. I. Dorofeev, N. M. Leshchenko, E. I. Tkachenko, and V. M. Luft, Sov. Med., No. 7, 21 (1981).
5. V. T. Ivashkin, Metabolic Organization of Gastric Functions [in Russian], Leningrad (1981).
6. G. N. Ilysheva et al., Klin. Med., No. 2, 13 (1979).
7. G. T. Kerimov et al., Azerb. Med. Zh., No. 2, 39 (1977).
8. I. V. Stepanova et al., Vrach. Delo, No. 10, 21 (1974).
9. V. D. Sukhodolo et al., in: The Functional Role of Surface-Active Substances [in Russian], Chernovtsy (1975), p. 21.
10. R. Geiger et al., Hoppe-Seyler's Z. Physiol. Chem., 358, 931 (1977).
11. M. Kobayashi et al., Jap. J. Pharm., 28, 1681 (1978).
12. M. Kobayashi et al., Jap. J. Pharm., 30, 705 (1980).