

petition between morphine and NA distinguished by an incomplete inhibition effect [1]. In competition of this type a triple complex (receptor-NA-morphine) may be formed. Morphine and NA probably bind with different neighboring groups of the receptor, and this determines their mutual influence on the affinity of the other for the receptor (Fig. 3C, D).

It can be concluded from the results of these experiments that morphine and trimeperidine act on peripheral adrenergic processes in the myocardium. Morphine, however, blocks the uptake of NA whereas trimeperidine stimulates its liberation. In both cases there is an increase in the free NA content in the synaptic space, i.e., the ultimate effect is the same.

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#### EFFECT OF LEVODOPA ON THE HEALING OF NEUROGENIC DEGENERATIVE LESIONS OF THE GASTRIC MUCOSA IN RATS

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Neurogenic degeneration of the gastric mucosa was produced in rats by immobilizing the animals for 3 h and by electrical stimulation. At the end of stimulation hemorrhagic erosions had developed in the gastric mucosa and they were still present 48 h later. Macroscopic and microscopic investigations showed that injections of levodopa into the rats in a dose of 10 mg/kg for 2 days after the end of stimulation accelerated the healing of hemorrhagic erosions of the mucosa.

KEY WORDS: *Neurogenic degeneration; healing; levodopa; gastric ulcers.*

An important role in the development of experimental neurogenic degeneration of the gastric mucosa is played by the sympathetic nervous system and its mediator, noradrenalin [1, 3, 7, 10, 12]. For instance, after electrical stimulation of rats leading to the development of degeneration of the stomach, the noradrenalin level in the organ falls [2]. Administration of the noradrenalin precursor, levodopa, after the end of electrical stimulation led to earlier restoration of the noradrenalin level in the stomach and disappearance of the hemorrhagic erosions.

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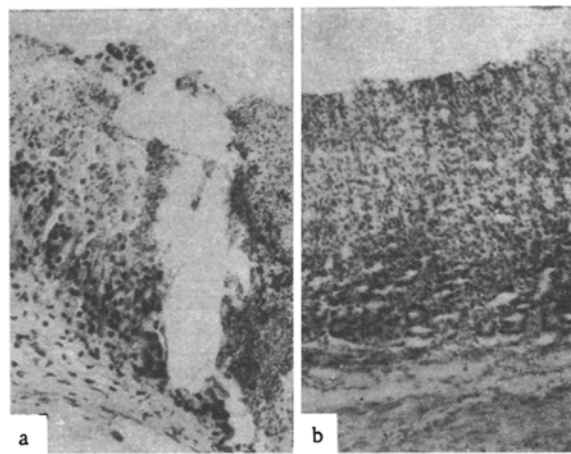


Fig. 1. Gastric mucosa of rats 48 h after end of electrical stimulation for 3 h. Hematoxylin-eosin, 140 $\times$ : a) necrotic changes in stimulated rat; b) gastric mucosa of rat receiving levodopa for 48 h after stimulation.

It was decided to make a simultaneous study of the effect of levodopa on the macroscopic and microscopic picture of degenerative lesions in the gastric mucosa in the course of their healing.

#### EXPERIMENTAL METHOD

Experiments were carried out on 58 noninbred male albino rats weighing 160–220 g. Neurogenic degeneration of the gastric mucosa was produced by electrical stimulation of the immobilized rats for 3 h with a current of square pulses through electrodes inserted into the muscles of the forelimbs [6]. Stimuli were applied from an ÉST-10 square pulse generator [voltage 7 V (to 10 rats), frequency 20 Hz, pulse duration 10 msec]. The rats were deprived of food for 48 h before stimulation. Since no appreciable healing of the hemorrhagic lesions of the gastric mucosa took place during the 48 h after stimulation [8], levodopa was injected intraperitoneally in a dose of 10 mg/kg into the experimental rats over a period of 2 days after the end of stimulation. Levodopa was injected immediately after stimulation, at 10 a.m. and 4 p.m. the next day, and at 10 a.m. and 2 p.m. on the second day. Control animals were stimulated without receiving levodopa. The rats were decapitated 48 h after stimulation. The stomachs were opened along the greater curvature and rinsed with physiological saline. The mucosa was investigated macroscopically for the presence of hemorrhagic lesions and to determine their localization. Since in most cases hemorrhagic lesions were punctate in character, the severity of degeneration of the mucosa was judged from their number. Stomachs for histological investigation were fixed in 10% neutral formalin solution. Pieces of tissue were embedded in paraffin wax and sections were cut to a thickness of 7–8  $\mu$ .

#### EXPERIMENTAL RESULTS AND DISCUSSION

Electrical stimulation of the immobilized rats for 3 h led to the development of hemorrhagic lesions of the mucosa in the fundus of the stomach. No lesions were found in the forestomach or in the pyloric part.

Microscopic examination of the gastric mucosa revealed areas of necrosis (Fig. 1), either superficial or penetrating to the submucosa. In some places foci of necrosis were situated beneath an area of unchanged mucosa. Leukocytes were scattered among the foci of necrosis and some of them had disintegrated. Small groups of leukocytes were often seen along the submucosa. Decomposing blood pigment, dirty yellow in color, was constantly present in the foci of necrosis. The capillaries of the mucosa at the edges of the foci of necrosis were dilated and filled with erythrocytes.

In animals receiving levodopa injections for 48 h after the end of stimulation the number of lesions in the mucosa (1.1; 0.36–1.84) was significantly ( $P < 0.02$ ) less than in the controls (3.3; 1.6–5.0). The results of the microscopic investigations also provided evi-

dence of stimulation of healing of the hemorrhagic erosions. No foci of necrosis were present. In some places in the surface layers of the gastric mucosa dilated capillaries congested with erythrocytes were observed. Foci of edema were present in the submucosa. Discrete areas of inflammatory infiltration were found in the submucosa at the base of the mucosal glands at the boundary with the muscular coat. Small foci of infiltration also were seen in the muscular coat. Sometimes histiocytes, basophils, and mast cells were observed among the adipose tissue in the serous membrane.

According to previous investigations [8] the number of lesions in the gastric mucosa of rats immediately after the end of electrical stimulation is unchanged 48 h later, and a reduction by half takes place only after 3 days. Complete healing of hemorrhagic erosions takes place without scar formation 6 days after the end of stimulation, in agreement with data in the literature [15].

The acceleration of healing of the hemorrhagic erosions in the gastric mucosa by the action of levodopa agrees with the results of the writers' previous investigations in which larger doses of the substances were given [8]. The effect of levodopa can be linked with its role in noradrenalin biosynthesis. Levodopa in a dose of 10-15 mg/kg has been shown to stimulate catecholamine synthesis [4, 11, 13, 16]. Substances preventing interaction between noradrenalin and adrenergic receptors of effector organs by some means or other delay the restoration of the noradrenalin level in the stomach and inhibit the healing of hemorrhagic erosions [9].

Trophic processes are nowadays looked upon as biochemical processes aimed at maintaining the structural integrity and constancy of function of the cells and tissues [3]. Investigations by Anichkov et al. [4] have shown that levodopa interferes with the course of trophic processes in the stomach by preventing the development of disturbances of energy metabolism in neurogenic degeneration. The stimulation of reparative changes under the influence of levodopa can thus be explained by potentiation of the effect of noradrenalin, especially on the process of energy formation in the stomach wall.

The clinical use of levodopa has appreciably increased the percentage of scar healing of gastric and duodenal ulcers [4, 5, 14].

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