# MECHANISM OF THE PROTECTIVE ACTION OF SYMPATHETIC DENERVATION ON DEVELOPMENT OF EXPERIMENTAL STAPHYLOCOCCAL SIALOADENITIS

V. V. Mikhailov and A. G. Rusanova

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KEY WORDS: submandibular salivary glands; membrane potential; staphyloccoccal sialoadenitis; sympathetic denervation.

From the earliest stages of development of staphylococcal sialoadenitis an increase in the concentration of catecholamines (adrenalin and noradrenalin) is observed in the gland tissues [5]. Since catecholamines stimulate histidine decarboxylase activity [3, 6] and thereby potentiate histamine production, it might be supposed that catecholamines may play an important role in the pathogenesis of sialoadenitis, for an increase in their concentration in the gland tissue could change the permeability and electrogenic properties of the cells [7, 8].

The object of the present investigation was to discover whether preliminary sympathetic denervation can weaken changes in the membrane potential (MP) level of the duct and acinar cells of salivary glands in staphylococcal sialoadenitis.

## EXPERIMENTAL METHOD

Experiments were carried out on 43 noninbred rats of both sexes weighing 70-100 g, divided into five groups: group 1) rats with staphylococcal sialoadenitis produced by injecting staphylococcal toxin (produced by the N. F. Gamaleya Institute of Epidemiology and Microbiology, 50 mg of the dry toxin, 1/2500 MLD) under sterile conditions in a dose of 0.6 mg/kg body weight (volume 0.1 ml, dissolved in physiological saline) beneath the capsule of the submandibular salivary glands; group 2) animals with sialoadenitis in which sympathectomy (removal of the superior cervical sympathetic ganglion) was performed under sterile conditions 7 days before injection of staphylococcal toxin in the same dose; group 3) animals undergoing mock sympathectomy (control); group 4) animals subjected to sympathectomy; group 5) intact rats. The criterion of successful sympathectomy was the development of ptosis of the upper lid of the ipsilateral side. Development of sialoadenitis was characterized by typical manifestations – hyperemia, edema, condensation, and distention of the capsule of the salivary gland. The operations and acute experiments on animals of all groups were carried out under pentobarbital anesthesia (40 mg/kg, intraperitoneally). MP of cells of the submandibular salivary glands was recorded by the method described previously in situ [4]. The criterion of differentiation of the cells into acinar and duct cells was the value of MP, which varied from 6 to 36 mV in the former and amounted to 36 mV or more in the latter [10]. Experiments on animals with staphylococcal sialoadenitis were carried out 2 and 24 h after injection of the toxin. The results were subjected to statistical analysis [1].

## EXPERIMENTAL RESULTS

In rats with intact sympathetic innervation a marked fall in the level of polarization of the acinar and duct cells was observed 2 h after injection of the toxin beneath the capsule of the salivary gland, and before the appearance of external signs of sialoadenitis (Table 1). It can be concluded from a study of the relative percentages of acinar and duct cells that even at this stage the reduction in the number of duct cells takes place on account of pathological changes leading to depolarization and consequent inclusion of these cells in the "acinar" group. This was most clearly manifested 24 h after injection of the staphylococcal toxin, when there was a sharp decline in the MP level in the group of acinar cells and, in particular, in the group of duct cells.

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TABLE 1. MP (in %) of Different Types of Submandibular Salivary Gland Cells at Different Stages of Staphylococcal Sialoadenitis and Sympathetic Denervation

| Cells | MP intervals, mV | Intact gland (1) | Sympathetic denervation of gland (2) | Staphylococcal sialoadenitis | | Staphylococcal sialoadenitis together with sympathetic denervation | |
|---|---|---|---|---|---|---|---|
| | | | | 2 h (3) | 24 h (4) | 2 h (5) | 24 h (6) |
| Acinar | 6—10 | 8,4 | 13,6 $P$ | 16,4 ($P_{1-3}<0{,}01$) | 22,8 $P^{***}P_2$ | 12,8 $PP_1P_2$ | 14,9 $P^*P_1P_3^*$ |
| | 11—15 | 11,8 | 14,4 $P$ | 15,0 $P$ | 23,2 $P^{***}P_2^*$ | 17,5 $PP_1P_2$ | 16,2 $PP_1P_3$ |
| | 16—20 | 20,8 | 16,9 $P$ | 25,0 $P$ | 19,4 $P\,P_2$ | 19,5 $PP_1P_2$ | 20,2 $PP_1P_3$ |
| | 21—25 | 16,3 | 15,3 $P$ | 17,1 $P$ | 15,2 $PP_2$ | 15,2 $PP_1P_2$ | 12,7 $PP_1P_3$ |
| | 26—30 | 14,1 | 13,1 $P$ | 9,1 $P$ | 8,4 $P^*P_2$ | 12,8 $PP_1P_2$ | 16,3 $PP_1P_3$ |
| | 31—35 | 9,5 | 6,7 $P$ | 9,1 $P$ | 7,6 $PP_2$ | 7,0 $PP_1P_2$ | 9,6 $PP_1P_3$ |
| Total percent of cells | | 80,6 | 80,0 | 92,5 $P^{***}$ | 96,6 $P^{***}P_2^*$ | 84,8 $PP_1P_2^{**}$ | 89,9 $P^{**}P_1^{**}P_3^{**}$ |
| Duct | 36—40 | 5,7 | 4,5 $P$ | 3,8 $P$ | 2,1 $P^*P_2$ | 7,0 $PP_1P_2$ | 3,2 $PP_1P_3$ |
| | 41—45 | 4,2 | 6,1 $P$ | 1,4 ($P_{1-3}<0{,}05$) | 1,3 $P^*P_2$ | 2,3 $PP_1P_2$ | 3,5 $PP_1P_3$ |
| | 46—50 | 3,4 | 4,2 $P$ | 1,0 $P$ | — | 2,7 $PP_1P_2$ | 2,6 $PP_1P_3$ |
| | 51—55 | 3,0 | 3,2 $P$ | 1,0 $P$ | — | 1,2 $PP_1P_2$ | 0,4 $P^*P_1{}^*P_3$ |
| | 56—60 | 1,9 | 1,0 $P$ | 0,3 $P$ | — | 1,2 $PP_1P_2$ | 0,4 $PP_1P_3$ |
| | 61—65 | 0,4 | 1,0 $P$ | — | — | 0,4 $PP_1P_2$ | — |
| | 66—70 | 0,8 | — | — | — | 0,4 $PP_1P_2$ | — |
| Total percent of cells | | 19,4 | 20,0 | 7,5 ($P_{1-3}<0{,}001$) | 3,4 $P^{***}P_2^*$ | 15,2 $PP_1P_2^{**}$ | 10,1 $P^{**}P_1^{**}P_3^*$ |
| Total number of cells recorded | | 263 | 313 | 287 | 237 | 257 | 228 |

Legend. P) Significance of differences from intact gland, $P_1$) significance of differences from sympathetic denervation of gland, $P_2$) significance of differences from staphylococcal sialoadenitis (2 h), $P_3$) significance of differences from staphylococcal sialoadenitis (24 h); P without asterisk – differences not significant, with one asterisk – $P < 0.05$, with two asterisks – $P < 0.01$, with three asterisks – $P < 0.001$.

However, the fact that a sharp decrease in the value of MP was observed in the group of cells supports the conclusion that considerable changes took place not only in the duct cells, but also in the acinar cells. In control experiments (five rats, 259 cells recorded), in which the solvent alone was injected, changes of this kind in the MP level were not present and the cell composition corresponded to the normal state ($P < 0.5$).

Later, at the same times, the same parameters were studied in previously sympathectomized animals with staphylococcal sialoadenitis. Table 1 shows that 2 h after injection of the toxin MP values recorded in the animals' acinar and duct cells did not differ significantly from normal. Considerably smaller changes in MP level also were observed 24 h after injection of the toxin in sympathectomized rats compared with rats with an intact innervation of their salivary glands and receiving the toxin.

These results indicate a reduction in the pathological action of staphylococcal toxin on secretory cells of the submandibular salivary glands despite the fact that sympathectomy itself has no significant effect on the level of polarization of acinar and duct cells (Table 1). So far as the mechanism of the protective action of sympathectomy on the development of staphylococcal sialoadenitis is concerned, first, sympathectomy induces a neuroparalytic arterial hyperemia and improves the blood supply to the salivary glands, thereby promoting rapid elimination of the injected staphylococcal toxin from the gland tissue. Second, after sympathectomy secretion of the salivary glands is enhanced, and in this case the injected toxin can be removed with the saliva. Finally, the possibility cannot be ruled out that protein synthesis and the concentration of catecholamines are appreciably reduced in the gland tissue of sympathectomized rats, the excitability of the gland cells is modified [2], and this may lead to a reduction in the pathogenic effect of staphylococcal toxin on epithelial cells of the salivary glands.

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# CONCENTRATION OF BIOGENIC AMINES IN STOMACH TISSUES OF RATS WITH REDUCED GASTRIC CIRCULATION

L. K. Gavrovskaya, V. M. Sedov, A. K. Gusyakov, and E. N. Kharchevnikova

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Clinical experience shows that a reduction in the blood flow in the celiac artery as a result of stenosing diseases is the cause of ischemic changes in the stomach and duodenum: atrophic gastritis and duodenitis, gastroduodenal ulcers [6, 8, 11]. After surgical removal of the cause of ischemia these changes do not always regress, and accordingly additional pharmacological correction of these states is required. Under these circumstances the complex mechanisms of development of structural and functional lesions of the gastric (GM) and duodenal mucosa must be taken into account. Biogenic amines – histamine, serotonin, catecholamines – are of great importance in the metabolic organization of gastric function and in the development of gastric pathology [1, 4, 12].

The object of this investigation was to study the concentrations of biogenic amines in the stomach tissues of rats with chronic reduction of the gastric circulation.

## EXPERIMENTAL METHOD

Experiments were carried out on 300 male rats weighing 250-300 g deprived of food for 2 days. Under ether anesthesia stenosis of the celiac artery was produced by constricting its lumen by 50% of its initial diameter (0.8 ± 0.007 mm). The control group consisted of animals in which the stenosis was discontinued immediately after its creation. The animals were removed from the experiment after 3 h and 1, 2, and 7 days. A macroscopic study of GM was undertaken. The concentrations of histamine [14], serotonin [15], and adrenalin and noradrenalin [5] in the stomach wall were determined.

## EXPERIMENTAL RESULTS

Chronic ischemia of the gastric wall was found to cause marked degenerative changes in GM. In all cases erosive gastroduodenitis and ulcers were found in the fundal part of the stomach. The ulcers after 3 h of the experiment were punctate, and the mucosa was edematous with venous congestion. On the 1st day the ulcers increased in size on account of necrotic areas of mucosa and a very small quantity of hemorrhagic contents was present in the lumen of the stomach. On the 2nd day these changes progressed further: The ulcers penetrated as far as the serous membrane, they often perforated, and the mucosa was ischemic. By the 7th day the

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