3B). Under these conditions normalization of the membrane-bound calcium level also was blocked (Fig. 3C, 3).

PGE_2 thus blocks recovery of the native shape of platelets, possibly by inactivating the mechanism maintaining membrane-bound calcium at a definite level in the cell.

PGE_1 thus leads to recovery of the native shape of platelets, whereas PGE_2 alters that shape. Taking this into account and also the importance of changes in the shape of platelets for aggregation, it can be postulated that prostaglandins of the E group exert their action on aggregation through their effect on mechanisms, probably calcium-dependent, controlling the shape of platelets.

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ROLE OF THE PARASYMPATHETIC NERVOUS SYSTEM IN PROLIFERATION OF CORNEAL EPITHELIAL CELLS IN RATS AFTER INJURY TO THE SUBMAXILLARY SALIVARY GLAND

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KEY WORDS: corneal epithelium of rats; cell proliferation; botulinus toxin; muscarinic acetylcholine receptor; trauma to submaxillary salivary gland.

Proliferation of the corneal epithelial cells is enhanced after injury to internal organs as a result of the production of nonspecific growth stimulators [2]. However, trauma to organs leads to significant changes in the function of the autonomic nervous system. This evidently plays an important role in the changes taking place in cell proliferation after trauma, for proliferation is inhibited when autonomic dystonia develops, with predominance of the sympathetic division of the nervous system [3]. However, there is little information on the influence of the parasympathetic division of the nervous system on cell proliferation [1, 5]. To study this problem, however, is interesting because after injury to the preganglionic (decentralization) and postganglionic (denervation) neurons dystrophic changes do not develop equally [4].

On the basis of existing data showing the high level of proliferation of the corneal cells and the presence of many adrenergic and cholinergic receptors among them, it was decided to study how corneal proliferation is modified after blocking, initially of preganglionic, and later of postganglionic neurons and how total pharmacologic stimulation and blockade of muscarinic acetylcholine receptors is reflected in proliferation, in the absence and during the formation of nonspecific growth stimulators as a result of trauma to the submaxillary salivary gland (SMSG).

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EXPERIMENTAL METHOD

Experiments were carried out on female Wistar rats weighing 80 g. Selective blockage of the parasympathetic neurons of SMSG was induced by subcutaneous injection of type A botulinus toxin, in a dose of 0.05 mg in 0.1 ml of physiological saline (1 MLD for mice is 0.0001 mg) into the region of the right gland. It has been shown that if the toxin is injected in this way activity of the parasympathetic innervation zone of the ipsilateral gland is inhibited [4]. In the course of 3-6 days a decentralization effect is created under these circumstances as a result of injury to the preganglionic neurons, but later injury of the postganglionic neuron develops and signs of denervation appear [6]. The rats were killed in experiment 1 on the 6th day after poisoning, during the first half of the day, and in experiment 2 on the 9th day, during the second half of the day. Accordingly there were differences between the initial levels of proliferation in the control groups. Pilocarpine and atropine (1 mg/kg) were injected in a volume of 0.2 ml from the 6th through the 9th day of experiment 2, intraperitoneally, at 9 a.m. and at 1 and 5 p.m. The last injection was given 4 h before sacrifice, together with colchicine (3 mg/kg, from Merck, West Germany). The formation of nonspecific growth stimulators was induced by resection of about one-fifth of the right SMSG under pentobarbital anesthesia (50 mg/kg). Unlike other workers [1, 5], who injected a single dose of pilocarpine and atropine and who disregarded the duration of the mitotic cycle, we killed the rats after this interval (3 days for the cornea), enucleated the eyes, and fixed them in Carnoy's fluid. The prophase and c-mitosis indices were calculated in promille after examination of total preparations of the cornea, made in the usual way. The significance of differences at the $P \leq 0.05$ level was determined by Student's t test.

EXPERIMENTAL RESULTS

It will be clear from Fig. 1A that in the early periods when mainly preganglionic neurons were injured, proliferative activity in the cornea was unchanged. In the late periods (Fig. 1B), however, the intensity of proliferation was appreciably increased as a result of the development of trophic changes in the postganglionic neurons. This result indicates that division of the corneal cells depends on the functional state of the parasympathetic nervous system in the zone of injection of the toxin, although the toxin itself has no cytopathogenic action [4].

The question arises whether this phenomenon is connected with acetylcholine receptor activity. First an attempt was made to influence proliferation by injecting pilocarpine, a stimulator of muscarinic acetylcholine receptors, into rats. However, the results showed that stimulation of muscarinic acetylcholine receptors while the function of the postganglionic neurons remains intact does not change the level of proliferation. Injection of pilocarpine likewise did not stimulate proliferation after the development of trophic changes in the parasympathetic neurons in the zone of injection of the toxin. These findings show that pharmacologic excitation of muscarinic acetylcholine receptors evidently does not affect the level of proliferation of corneal cells whether the parasympathetic innervation of tissues located in the zone of injection of the toxin is intact or injured by the toxin.

It was decided next to study how total blocking of muscarinic acetylcholine receptors by atropine is reflected in cell division. Experiments showed that after systematic injection of atropine, proliferation was actually stimulated even more (by 23 ± 5%) than when the postganglionic neurons were injected in the late periods after injection of botulinus toxin (Fig. 1B). Injections of atropine into the poisoned rats at this period, incidentally, reduced the stimulating effect of the toxin on proliferation (by 28 ± 9%). Pharmacologic blockage of muscarinic acetylcholine receptors can thus stimulate proliferation if the parasympathetic innervation of the tissue is intact. After injury to the tissue the action of atropine is reversed and it acquires the property of inhibiting proliferation of corneal cells when stimulated beforehand.

The next step was to make a similar investigation of proliferation in the corneal epithelium after trauma to SMSG. As Fig. 1A and B show, after partial extirpation of the gland tissue proliferation in the cornea was increased by 20 ± 3% (experiment 1) and by 96 ± 18% (experiment 2). Despite diurnal and seasonal fluctuations, stimulation of muscarinic acetylcholine receptors caused inhibition of proliferation (by 27 ± 4% in experiment 2), whereas blocking of muscarinic acetylcholine receptors by atropine increased it in the same experiment by 31 ± 9%.

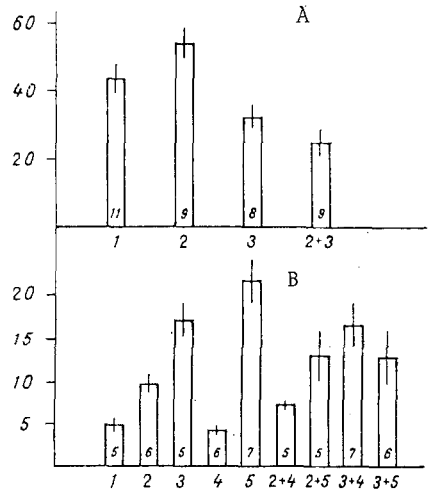

Fig. 1. Role of muscarinic acetylcholine receptors in proliferation of corneal epithelial cells in rats. Abscissa, groups of rats; 1) control; 2) trauma to SMSG; 3) botulinus toxin; 4) pilocarpine; 5) atropine. Ordinate, mitotic index (in %). A) Experiment 1; B) experiment 2. Numbers inside columns show number of corneas.

It can thus be concluded that the parasympathetic nervous system has a restraining effect on cell proliferation. This is manifested both in the intact organ (corneal epithelium) and when regeneration is stimulated as a result of trauma to SMSG.

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LIPOPROTEIN METABOLISM IN THE LIVER AND INTESTINAL WALL OF RABBITS AFTER A SINGLE LOADING WITH SUNFLOWER OIL AND CHOLESTEROL

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KEY WORDS: lipoprotein metabolism; intestinal wall; liver; sunflower oil; cholesterol.

Besides many other factors, an increase in the degree of risk of the onset of cardiovascular diseases is associated also with elevation of the blood cholesterol (CS) concentration. CS enters the blood mainly from the liver and intestine in the composition of lipoproteins (LP), which are its principal transport form. Accordingly, when mechanisms of pathogenesis of hypercholesteremia are studied, the necessity arises for investigation of pathophysiological changes in LP formation and metabolism in the liver and cell wall. Existing data in the

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