FORMATION OF THE REGENERATION STIMULUS AFTER TRAUMA TO THE SUBMANDIBULAR SALIVARY GLAND AND LIVER AFTER PRELIMINARY TOTAL SYMPATHETIC INACTIVATION

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Injury to the liver, salivary glands, and other organs leads to an increase in the intensity of physiological proliferation not only in the injured organ [1, 2], but also in corneal cells, far away from the site of injury [3]. It is not yet clear whether this activation of proliferation is brought about entirely by stimulators formed in the injured tissues or whether the sympathico-adrenal system, activated by trauma, takes part in this process [7].

Accordingly it was interesting to study to what extent proliferation of the corneal epithelial cells is modified during posttraumatic regeneration of the submandibular salivary gland (SMSG) and of the liver when activity of the sympathico-adrenal system is inhibited.

EXPERIMENTAL METHOD

Experiments were carried out on Wistar rats of both sexes weighing 80 ± 5 g. The animals were divided into seven groups: in groups 1 and 2 20-30%, respectively, of the weight of the SMSG and liver was resected without the arrest of bleeding; 3) control (animals undergoing mock operations); 4) thermal burn of the liver (the area of the burn and size of the wound after resection of the liver were identical); 5) blood loss (0.5% of the body weight) by bleeding from the femoral vein; 6) total inactivation of the sympathico-adrenal system by means of diphtheria toxin (a single intraperitoneal injection of 0.75 mg/kg); 7) resection of SMSG after poisoning the rats with diphtheria toxin. All operations were performed under pentobarbital (50 mg/kg) anesthesia. Since the duration of the generative cycle in the corneal epithelium was 72 h, enucleation of the eyes and their fixation in Carnoy's fluid were carried out in all experiments after the end of this time. Colchicine (3 mg/kg, from Merck, West Germany) was injected into the animals 4 h before sacrifice. The index of mitoses and of C-mitoses (MI_{col}) were calculated in promille after examination of total preparations of the cornea stained with hematoxylin. The results were subjected to one-factor dispersion analysis [5].

EXPERIMENTAL RESULTS

As Table 1 shows, resection of part of the SMSG and the liver and a thermal burn of the liver (experiments of series I) are accompanied by an appreciable rise in MI_{col} of the corneal cells. Since bleeding develops during operations on glandular tissues and since, according to existing data [8], this may lead to an increase in erythropoietin production and to nonspecific stimulation by erythropoietin of proliferation, a control experiment was carried out (series II) with determination of the precise role of bleeding in stimulation of proliferation of the corneal cells. However, the results in Table 1 show that bleeding comparable in volume with that arising during trauma to SMSG, by itself stimulates proliferation. Confirmation was obtained that the traumatized SMSG and liver liberate humoral stimulators, unconnected with an increase in erythropoietin production.

Since during trauma an increase is observed in the activity of the sympathico-adrenal system, the mediators of which affect the intensity of proliferative processes, trauma was

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TABLE 1. Results of One-Factor Dispersion Analysis of MI_{col} in Corneal Epithelium of Rats 72 h after Various Forms of Trauma (M ± m)

Series of experiments	Group of animals	Type of operation	MI_{col} in experiment, % of control	Factors considered in experiment, %	Number of animals	F	P	Postdispersion analysis of comparison of pairs by F criterion: comparison with control	P	comparison between groups	P
I	1	Trauma to SMSG	+92	92±4	28	65,34	<0,01	$F_1 = 8,16$	<0,01	$F_{1-2} = 0,12$	>0,05
	2	Trauma to liver	+206					$F_2 = 19,55$	<0,01	$F_{1-3} = 0,98$	>0,05
	3	Burns of liver	+158					$F_3 = 11,27$	<0,01	$F_{2-3} = 0,86$	>0,05
II	4	Blood loss	+19	83±8	26	35,88	<0,01	$F_4 = 0,71$	>0,05	$F_{4-5} = 11,73$	<0,01
	5	Trauma to SMSG	+86					$F_5 = 15,29$	<0,01	—	—
III	6	Trauma to SMSG	+72	82±5	34	45,65	<0,01	$F_6 = 3,80$	<0,05	$F_{6-7} = 0,19$	>0,05
	7	DT	+57					$F_7 = 2,95$	=0,05	$F_{6-8} = 0,65$	>0,05
	8	Trauma to SMSG + ST	+42					$F_8 = 1,36$	>0,05	$F_{7-8} = 0,02$	>0,05

inflicted on SMSG under conditions of total blocking of noradrenergic neurons and chromaffin cells (cathecholamine producers) by diphtheria toxin. Initially the experiment was carried out on intact rats poisoned with diphtheria toxin. They showed that 48 h after poisoning, in the phase of development of bradycardia, diarrhea, atony of the skeletel muscles, and other signs of relative insufficiency of tone of the sympathetic nervous system, MI_{col} of the corneal cells was appreciably increased. This increase was evidently connected with a fall in the cathecholamine level in the tissues and abolition of their inhibitory action on cell proliferation [4].

It was next decided to study whether the stimulation effect is changed after partial reaction of SMSG, performed after blocking of the sympathico-adrenal system and chromaffin cells by the toxin. As Table 1 shows, in this case summation of activating influences on proliferation was not observed.

The absence of stimulation against the background of poisoning cannot be regarded as the result of the cytotoxic action of the toxin on the corneal cells, for injection of the same dose of toxin into intact rats increased MI_{col} by a greater degree than during trauma in previously poisoned animals. This last result is evidence that trauma to SMSG against the background of chemical desympathization of the gland evidently leads to a decrease in the ability of the injured glandular cells to produce growth stimulators. Another possibility can also be accepted: Reduction of the effect of growth stimulators against the background of inhibition of activity of the sympathico-adrenal system such as is observed, for example, during inhibition of production of erythrocytic chalone by pharmacological blocking of the sympathico-adrenal system [6].

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