ROLE OF ENDOGENOUS REGULATORS IN COMPENSATION AFTER SALIVARY GLAND RESECTION

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KEY WORDS: compensation; salivary gland; regulation of hyperplastic processes.

In response to resection of a salivary gland total compensatory stimulation of the glandular tissue cells takes place not only in the injured, but also in the intact, contralateral gland [1]. The mechanism of this response has not been studied. It has been shown indirectly that nonspecific high-molecular-weight products migrate from the gland tissue into the blood stream, whereas this does not take place with tissue-specific or antigenic substances [2]. Macrophages are known to play a very important role in the elimination of dying cells, and in the process of their activity they secrete factors known as monokines. Some of them have a local action (local mediators). Others (circulating mediators) leave the blood stream and give rise to various effects [5]. The question accordingly arises: are these substances, which play a regulatory role in compensation processes, nonspecific breakdown products of cells and the intercallular matrix, or are they circulating monokines.

The aim of the present investigation was to study the ways and times of entry of these breakdown products into the blood stream, for these substances play the role of endogenous regulators of compensatory processes arising in the glandular tissue in response to trauma.

EXPERIMENTAL METHOD

Experiments were carried out on 97 noninbred male rats weighing 140-160 g. Trauma was inflicted by the method described previously [4], namely resection of 20% by weight of the right submandibular salivary gland (SMSG). The lactate dehydrogenase (LDH; EC 1.1.1.27) isozyme spectrum was studied by the method in [7]. Relative percentages of isozyme fractions were calculated on a Statron 301E integral densitometer (East Germany). The total LDH in heparinized blood plasma obtained after decapitation of the animals was determined on a Cobas instrument (Roche, Belgium). The following parameters were studied on a micro-Astrup apparatus: hydrogen ion concentration (pH), partial pressure of carbon dioxide (pCO_2), and buffer bases. The partial pressure of oxygen (pO_2) was determined with an electrode of Clark type, mounted in the micro-Astrup apparatus. The sublingual and submandibular salivary glands, lying within a common capsule together with the regional lymph nodes, were removed for morphological survey study. Material was fixed in neutral formalin. Paraffin sections 5 μ thick were stained with hematoxylin and eosin. All manipulations on the control and experimental rats were performed under pentobarbital anesthesia (50 mg/kg). The significance of the results was estimated by Student's t test for difference series [3].

EXPERIMENTAL RESULTS

In the experiments of series I at autopsy 1 h after trauma marked arterial hyperemia of the lymph node nearest to the injured gland could be seen. After 24 h, edema of the cellular tissue, congestion of the blood vessels, and focal leukocytic infiltration with traces of fibrin were observed microscopically around the lymph nodes. The same picture was found beneath the capsule of the lymph nodes. Edema and areas of leukocytic infiltration and necrosis were found in the superficial muscle of the neck. After 1 day trophic changes were observed in the cells of the terminal portions in the zone of injury in the traumatized salivary gland and also in its central part, progressing to necrosis but with preservation of individual inter-

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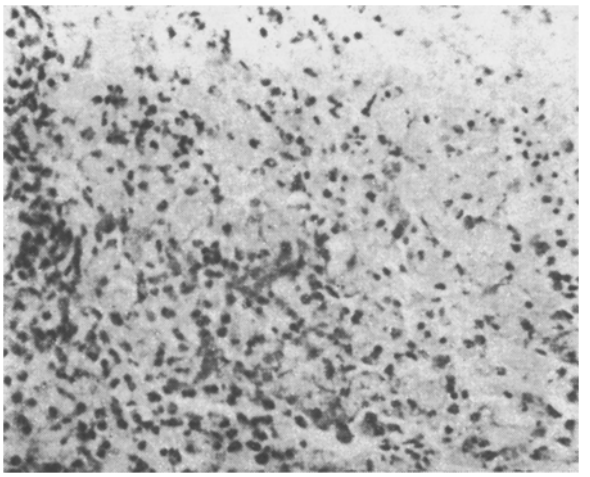

Fig. 1. Necrosis of terminal portions of submandibular salivary gland. Hematoxylin and eosin. 200 ×.

TABLE 1. Parameters of Acid-Base Balance in Mixed Arteriovenous Blood 1 h after Resection of Salivary Gland

Parameter	Control (n = 6)	Experiment (n = 6)	P
pH	7,34±0,001	7,37±0,03	>0,05
pCO_2, mm Hg	48,3±0,4	43,0±6,0	>0,05
SB, meq/liter	25,3±0,9	24,0±0,8	>0,05
BE, meq/liter	−1,1±0,2	−0,8±0,4	>0,05
BB, meq/liter	47,1±0,7	47,0±1,0	>0,05
pO_2, mm Hg	35,5±1,6	34,2±15,3	>0,05

lobular ducts and terminal portions beneath the capsule (Fig.1). Edema, and focal infiltration by leukocytes, macrophages, and histiocytes were visible in these regions beneath the capsule. Serous inflammation was present around the capsule. Away from the site of trauma the terminal portions remained intact but there was some edema of the stroma. The morphological investigation thus showed that the consequences of resection of SMSG are necrosis of gland tissue, the formation of breakdown products, their release into the humoral medium, and migration of leukocytes into this zone. Macroscopically, one of the early manifestations of trauma is hyperemia of the regional lymph nodes. In the next series of experiments, it was therefore decided to compare morphological and functional features of the tissues of SMSG and lymph nodes.

The enzyme LDH was chosen as marker passing from the injured gland into the blood and lymph, for, first, it is one of the few enzymes that is selectively transported by lymph [8] and, second, it consists of five different isozymes, the relative percentages of which differ individually for different tissues. The relative percentages of LDH isozymes in SMSG, a lymph node, and the blood of healthy rats, obtained in this investigation, are shown in Fig. 2.

In the experiments of series II the total LDH concentration in the blood was determined at different times after resection of SMSG. It will be clear from Fig. 3 that soon after trauma there was a significant increase in the quantity of LDH, which was most marked 1 h after trauma. It can be concluded from these results that salivary gland breakdown products enter the bloodstream 30 min after injury to the gland. Under these circumstances, however, no significant changes were found in the parameters of the acid-base balance of the blood (Table 1).

Taking sacrifice after 1 h as the reference point, in the experiments of series III the LDH isozyme spectrum was studied in the injured and intact salivary glands and in the regional lymph nodes. This marker revealed a considerable change in function of the gland parenchyma. In the injured glands the content of LDH_4 and LDH_5 was increased whereas that of LDH_1 was re-

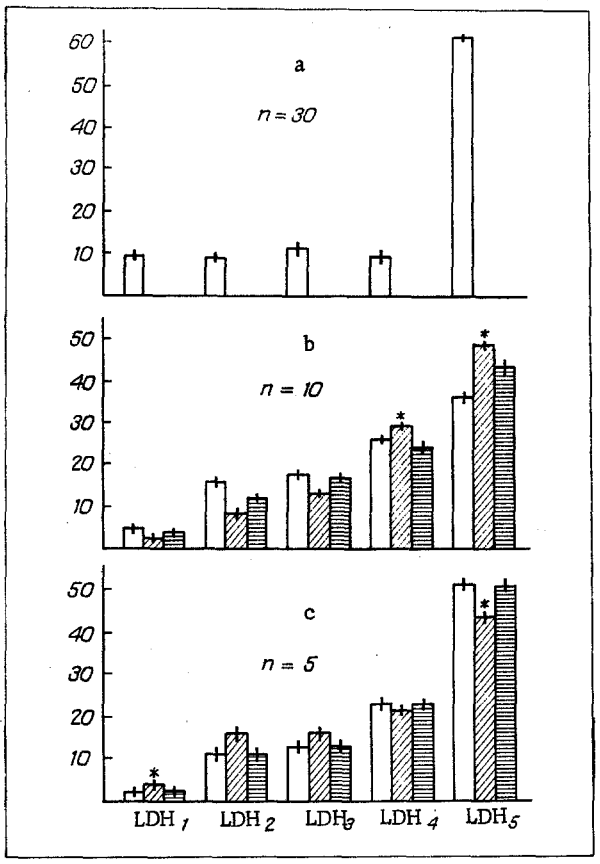

Fig. 2. LDH isozyme spectrum in blood, SMSG, and lymph nodes under normal conditions and 1 h after sialotomy. Abscissa: unshaded columns — control group, obliquely shaded — traumatized SMSG and homonymous lymph node, horizontally shaded — contralateral SMSG and homonymous lymph node; ordinate, relative percentages of individual LDH fractions. a) Blood, b) SMSG, c) lymph nodes. n) Number of measurements. Results differing signfiicantly from control marked by asterisk.

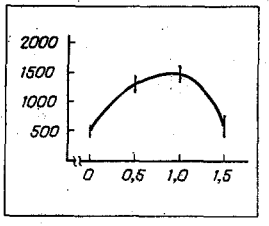

Fig. 3. LDH content in mixed (arteriovenous) blood in the early stages after trauma to SMSG. Abscissa, times of sacrifice (in h); ordinate, LDH concentration (in units/liter).

duced (Fig. 2b). Changes of this kind in the LDH isozyme spectrum can be explained by the development of hypoxia on account of post-traumatic disturbances of the microcirculation, i.e., the isozymes react very quickly to slight changes in tissue metabolism. The results are in agreement with those of the morphological investigation, showing the development of degenerative, necrobiotic, and necrotic changes in the gland parenchyma. The isozyme spectrum of the contralateral (intact) gland at this time remained virtually unchanged.

The symmetrical regional lymph nodes for SMSG under normal conditions have an identical isozyme spectrum. After trauma, an increase in the LDH_1 content and a decrease in that of LDH_5 were observed in the lymph nodes corresponding to this gland, evidence of activation of aerobic processes in this tissue. Meanwhile, in the contralateral lymph nodes (for the intact gland) the relative percentages of individual LDH fractions were unchanged (Fig. 2c).

Changes in the composition of LDH fractions in the injured gland and its regional lymph nodes were completely unsynchronized in character: the content of the LDH_1 fraction fell in the gland and rose in the lymph nodes, whereas the content of the LDH_5 fraction rose in the gland and fell in the lymph node.

Scrutiny of these data sheds new light on our results and, in particular, enables the re-evaluation of data obtained previously [2]. The present investigation confirms that LDH is the right choice for marker. A significant change was found in the total LDH activity in the blood, whereas the physicochemical blood constants (partial pressure of oxygen and carbon dioxide, buffer base concentration) were unchanged. A possible explanation for the absence of antigenic breakdown products of SMSG after trauma, as described in [2], was found. It was shown that the passage of breakdown products into the bloodstream takes place through the lymph node, where these products with antigenic properties are processed (antigenic stimulation). Evidence in support of this view is given by the change in functional properties of the lymphocytes as early as 17 h after trauma [6].

This investigation thus showed that the breakdown products enter the general bloodstream through the regional lymph nodes, and this process can be recorded as early as 30 min after trauma to the gland. Migration of leukocytes into the zone of trauma and macrophagocytosis develop more slowly. In our view, it is evidently the breakdown products of the gland tissue which trigger compensatory hyperplasia [4] in the salivary glands in response to their resection.

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COMPARISON OF MICROCIRCULATORY DISORDERS IN THE PERIMETRIUM OF INTACT AND PREGNANT RATS UNDER THE INFLUENCE OF OXYTOCIN

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The microcirculation is the process by which tissue cells obtain nutrients and get rid of metabolites. Without an adequate microcirculation the normal exchange of materials and the normal functioning of any organ would be impossible [4, 10]. In clinical obstetrics, a leading component in the pathogenesis of many complications of pregnancy is a disturbance of the microcirculation. However, there have been only a few studies of the microcirculation in the uterus [2, 6, 7]. Changes in contractility of the uterus after injection of oxytocin have been studied by many investigators [1, 3, 8]. However, the effect of oxytocin on the microcirculation in the uterus has not previously been studied. The aim of this investigation was to study the microcirculation in the perimetrium under the influence of oxytocin.

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