PROLIFERATION OF CELLS OF THE LARGE SALIVARY GLANDS OF THE RAT DURING REPARATIVE REGENERATION

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The object of this investigation was to study the special features distinguishing reparative regeneration in the salivary glands with a protein and a mucous type of secretion. The mitotic division of the cells was investigated after thermal injury to the submaxillary and sublingual glands of the rat, which have a protein [10-12] and mucous [11] type of secretion respectively.

EXPERIMENTAL METHOD

Experiments were conducted on 60 sexually mature albino (male) rats weighing 250-300 g. In aseptic conditions about 33-50% of the submaxillary and more than 50% of the sublingual gland was destroyed by means of a hot metal plate, unilaterally. The material was fixed during the morning at intervals of between 15 min and 60 days after the operation [8-10]. The sections were treated by the usual histological and certain histochemical methods. The numerical results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

Mitotic division of the epithelial cells began 24 h after injury in the submaxillary gland and 48 h after injury in the sublingual gland. The first mitoses were found in the secretory cells of the terminal portions, after which the cells of the ducts began to divide. In both the sublingual and the submaxillary glands the role of the cells of the acini and the efferent ducts in the proliferative processes after injury was almost identical. The mitotic activity of the cells of the efferent duct system on the wound surface of the submaxillary gland 54 h after trauma was 11.7 ± 0.9, and the activity of the cells of the terminal portions 11.4 ± 0.5. The corresponding figures for the sublingual gland were 5.7 ± 0.4 and 5.3 ± 0.8. On the whole the level of the mitotic activity in the epithelial cells of the submaxillary gland was higher than in the sublingual.

As several authors have pointed out [1, 6], the nuclei of very many epithelial cells become greatly enlarged in the first stages of regeneration. The results of measurements now showed that they increased in size in the ratio 1 : 2 : 4. This is directly dependent on their ploidy [8] and it agrees with the modern view of the role of endomitosis and polyploidization in regenerative processes [3]. No evidence could be obtained in this material to indicate direct (amitotic) division of the cells during regeneration, as has been reported in the literature [4].

In the process of regeneration of the submaxillary and sublingual glands mitoses were observed not only in the epithelial structures invading the granulation tissue at the site of injury, but also in parts of the glands not apparently involved in the inflammatory process. The relative importance of mitotic cell division at the wound surface and some distance from it may be considered. To elucidate this problem, the localization of epithelial cells dividing by mitosis at different stages of the regenerative process was strictly determined. Sections cut through salivary glands placed side by side, with a visible site of injury and a well defined zone of reactive changes, were projected by means of a microscope and two mirrors on to a sheet of white paper. When drawings were made, not only the outlines of the glands were included, but also a number of morphological structures – the connective-tissue septa of the lobules, and the large and middle-sized ducts. It was thus easy to identify the topography of the preparations when magnified under the immersion lens (objective 90 ×, ocular 7 ×), when the positions of the cells undergoing mitotic division were marked accurately on the paper.

Drawings of three sections are shown in the figure. Comparison of them shows that during both the period of increase of mitotic activity and the period of its gradual decline, proliferative processes in the epithelial cells arose mainly at the wound surface, where the epithelial tubes invaded the granulation tissue at the site of injury. To

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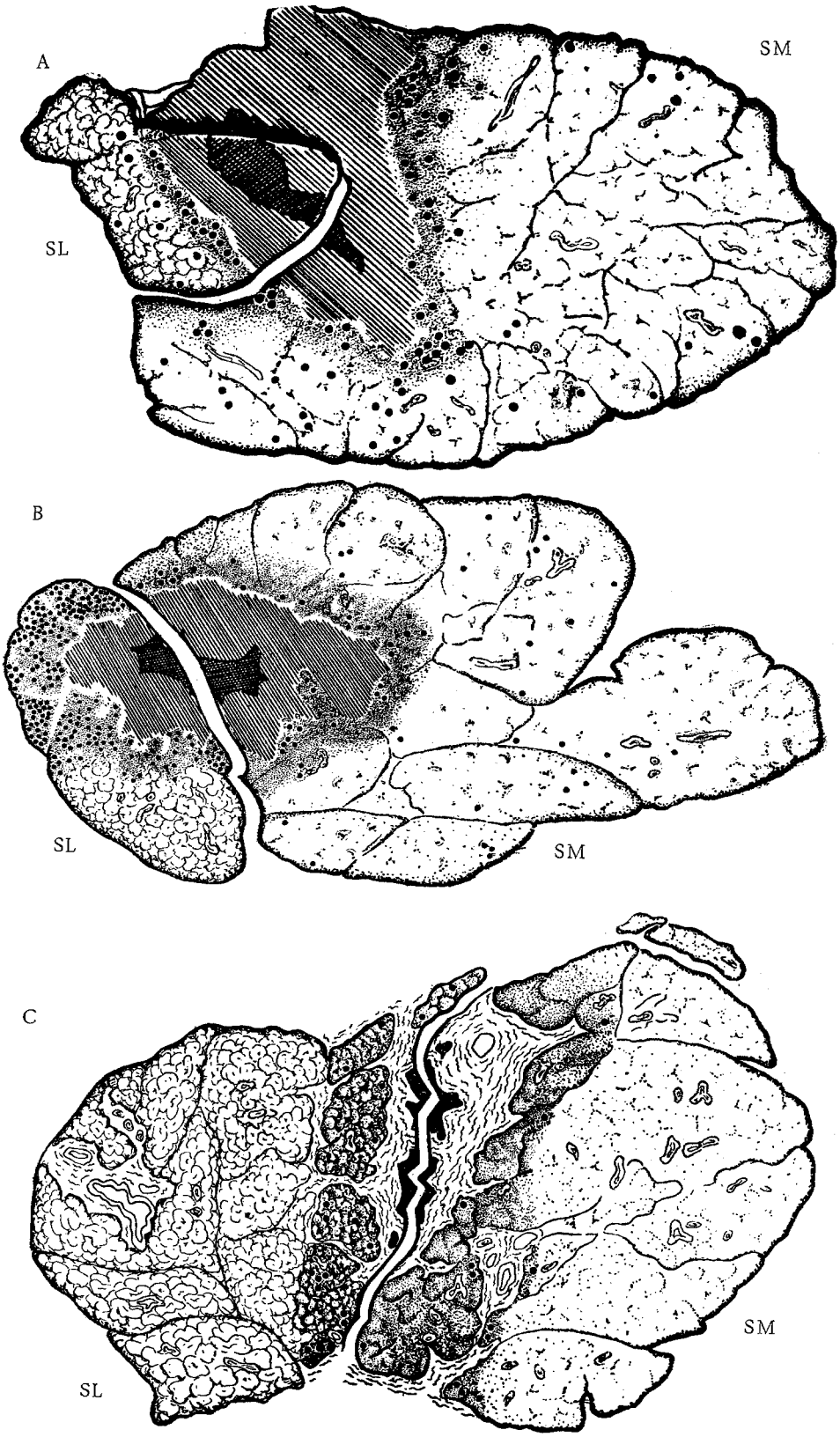

Salivary glands of a rat 2 (A), 6 (B), and 15 (C) days after injury. During reproduction of the drawings the sublingual gland (SL) has been detached from the submaxillary gland (SM) to improve clarity. The site of direct injury is cross-hatched; the areas of the gland undergoing necrosis are shaded with oblique lines, and the surrounding zone of reactive changes is slightly darkened. Attention is drawn to the position of the mitoses (black dots) and the new lobules of the glands, in the layer of connective tissue filling the site of injury (C). Rest of explanation in text.

Mitotic Activity (MC) of Cells of the Submaxillary and Sublingual Salivary at Different Stages of the Regenerative Process (in %)

Time after operation (in days)	Submaxillary gland				Sublingual gland			
	at the edge of the injured area		at a distance from injured area		at the edge of the injured area		at a distance from injured area	
	total no. of cells counted	MC	total no. of cells counted	MC	total no. of cells counted	MC	total no. of cells counted	MC
3	18 000	18,5±0,29	30 000	0,6±0,03	18 000	12,3±0,26	30 000	0,6±0,03
5	18 000	5,5±0,12	30 000	1,8±0,03	18 000	33,8±0,45	30 000	3,2±0,06
8	18 000	3,8±0,10	30 000	1,3±0,03	12 000	7,5±0,19	30 000	0,8±0,04
15	18 000	1,1±0,07	30 000	0,1±0,01	18 000	2,4±0,08	30 000	0,6±0,02

confirm this conclusion quantitatively, all the mitoses were counted in the zone of reactive changes, on the one hand, and at points distant from the site of injury, on the other, in each of the investigated glands 3, 5, 8, and 15 days after injury. Altogether 6000 cells at the site of injury and 10,000 cells some distance away were counted in three rats at each time (for technical reasons, after 8 days the cells in the zone of injury to the sublingual gland were counted in two rats). The results of these counts are given in the table.

As the table shows, at all stages of regeneration the intensity of the proliferative processes at the points remote from the site of injury was much less than that at the wound surface. The difference between the number of mitoses in the focus of injury and the number at a distance from it was significant in all the periods of the investigation ($P < 0.001$). It may therefore be concluded that the regeneration of the submaxillary and sublingual glands after their thermal injury takes place mainly by epimorphosis (growth per appositionem [6]). The role of endomorphosis or regeneration hypertrophy (growth per intussusceptionem) in the process of regeneration of the salivary glands in adult male rats after thermal injury is much less important. This conclusion cannot be extended to the reparative regeneration of other organs or even to the same glands in other experimental conditions.

After 15 days complete newly formed lobules of the submaxillary and sublingual glands were seen in the mature granulation tissue now filling the area of necrosis. After 30-60 days, they had differentiated to form acinar portions of serous and mucous character. The development of these newly formed structures is very reminiscent of the postnatal development of the sublingual [7] and submaxillary glands [9]. As might be expected, from findings described by many authors [6, 2, 4], 60 days after injury the site of the burn was filled with fibrous tissue, in which small lobules of regenerating gland were observed. Some of the newly formed structures, especially those which had lost their connection with the ducts of the old parenchyma, showed degenerative changes and signs of resolution; others remained viable in appearance.

SUMMARY

Reparative regeneration of the submaxillary and sublingual salivary glands was studied on 60 sexually mature male albino rats in periods from 15 min to 60 days after a thermal lesion. Proliferation of cells was effected by way of mitotic division. Accurate account of the place of arrangement and number of mitoses in the epithelial cells at all stages of the regenerative process has shown that proliferative processes develop mainly at the wound surface. The level of the mitotic activity of terminal portions and in the system of outlet ducts at the wound surface is approximately the same. Numerous adhesions and trabeculae forming as a result of dedifferentiation and proliferation of epithelial cells grow into the granulation tissue filling the site of the defect. Small lobules of the submaxillary and sublingual glands with an ordinary structure form on the site of the lesion. They are connected with the general system of outlet ducts.

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