ON THE INFLUENCE OF THE CENTRAL NERVOUS SYSTEM ON CELL DIVISION

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Recently, the role of the nervous system in the regulation of the regenerative processes and its influence on the proliferative processes and on the origin and growth of new formations has been the subject of many works. Since the processes of cell division are closely associated with these complex biological phenomena, one can suggest that nuclear and cell division depend on the condition and function of the nervous system.

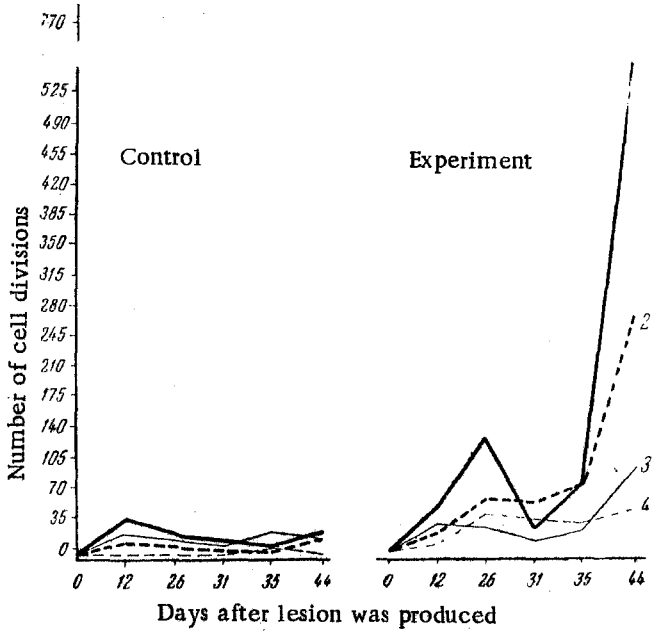

Figure 1. Intensity of cell divisions during healing of experimental lesions in dog No. 23. 1) number of mitoses in epidermis; 2) number of amitoses in epidermis; 3) number of mitoses in connective tissue; 4) number of amitoses in connective tissue.

As early as 1880, M. D. Lavdovsky, studying the morphological changes of salivary gland secretory cells caused by long stimulation of a tympanic string by induction current, showed that, in this case, the number of mitoses in the cells increased.

In recent years, works have appeared in which the authors made tests to approach the study of cell division

processes from new directions, taking into account the functional condition of the entire body and especially, the influence of the nervous system [1, 2, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13].

However, the way in which the nervous system influences cell division processes is still not clear. According to some authors [9], the number of mitoses decreases under conditions of denervation, while, according to others [7], denervation intensifies cell division.

Studying the effect of spinal cord transection on the healing processes of cutaneous lesions in dogs [13], one author points out the sharp change in cell division activity in connection with the broken nerve links. This observation was the basis for a more profound study of the central nervous system's influence on the processes of cell division.

The spinal cord in dogs was completely transected at the level of the V lumbar vertebra, thereby disturbing the connection of the hind legs with the central nervous system.

A lesion was experimentally induced on one of the denervated legs. A similar lesion was made on the front leg, which served as the control. Material for histological examination was resected at different intervals – from the 1st to the 79th day. The pieces were fixed in 10% neutral formalin and imbedded in celloidin. Hematoxylin combined with eosin, picro-indigo-carmine or picrofuchsin, iron hematoxylin or a combination stain of iron hematoxylin and Mallory's mixture were used as the stains. 36 dogs were operated upon and clinically observed. Material obtained from 25 animals was histologically processed. The cells in a dividing condition were counted in material obtained from 5 dogs. Beginning the 4th day after the lesion had been induced and ending the 44th day, the mitoses and amitoses were counted on 5 sections at each stage of the wound process. Both in the experiment and in the control, from 20 to 80 sections from each animal were examined individually, sections of the epidermis, its derivatives, and the adjoining connective tissue. The lack of any difference in the rate of cell divisions in the normal skin of the anterior and posterior extremities and in the tissues of the lesions in these extremities, not preliminarily denervated, was established by special observation.

Analysis of the data resulting from the cell division computations showed that the average ratio of the number of mitoses in the tissues of the control to the number of experimental lesions fluctuated from 1 : 2 to 1 : 18; the ratio of amitoses, from 1:10 to 1:98. In the connective tissue, this ratio fluctuated from 1:1.5 to 1:6 for mitoses and from 1:8 to 1:66 for amitoses (see Table 1).

Figure 1 shows the curves of cell division intensity characterizing the changes at the early stages of healing. In the control lesions, the number of dividing cells increased considerably until the 12th day, when they gradually decreased until the 31st day, i.e., until the lesion was completely epithelialized, to the normal physiological level. In the experimental lesion, mitotic and especially amitotic activity of the cells increased steadily according to the stage of the wound process, showing the active epithelial proliferation.

Figure 2, a shows the epidermal outgrowth, with 8 dividing cells visible in the field of vision. Mitotic forms were found in both the horny cells of the epidermis and in the marginal cells of the basal layer on top of the epithelial wedge (Fig. 2, b).

The data presented clearly show that the number of dividing cells in both the epidermis and the connective tissue was much greater in the lesion cut off from the central nervous system than in the control lesion, and that the greatest increase was in the number of amitoses.

In the experimental lesions, along with the usual amitotic forms found on the majority of sections, massive fragmentation was usually found, which led to the formation of multinuclear elements, having from 3 to 12 nuclei (Fig. 3).

It should be particularly noted that denervation causes more active cell division in the epidermis and its derivatives than in the connective tissues. Dividing cells appeared in the epidermal derivatives, although, normally, they occur there extremely rarely (for example, the glandular and myoepithelial cells of the sweat glands).

Along with the increased number of cell divisions in the tissues of the denervated lesion, signs of epidermal simplification and of a disturbance in the correlative relations of the epithelium and connective tissue appeared rather early. The epidermis lost its specific differentiation; its cells, especially in the horny layer, increased in size and stained less intensely, and their cytoplasm became cloudy. The intercellular spaces grew

TABLE 1

Change in Cell Division Intensity Under Conditions of Denervation

No. of animals	Epidermis						Connective tissue					
	Mitoses			Amitoses			Mitoses			Amitoses		
	Control	Experiment	Ratio	Control	Experiment	Ratio	Control	Experiment	Ratio	Control	Experiment	Ratio
3	132	835	1:6,3	21	456	1:21,7	63	203	1:3,2	8	61	1:7,6
6	213	408	1:1,9	15	213	1:14,2	49	191	1:3,8	2	16	1:8,0
23	59	1 041	1:17,6	6	588	1:98,0	32	196	1:6,1	2	132	1:66,0
24	109	589	1:5,4	23	607	1:26,4	34	62	1:1,8	3	23	1:7,6
30	146	747	1:5,1	8	76	1:9,5	56	76	1:1,3	2	19	1:9,5

Figure 2. Numerous mitoses in epidermal outgrowth of skin (a). Dog No. 23, skin of experimental leg 44 days after production of lesion. Objective 20, ocular 7x; b) mitosis in cell of basal layer on top of epithelial wedge. Dog No. 23, skin of experimental leg, 26 days. Objective imm. 90, ocular 10 x.

Figure 3. Nuclear fragmentation in horny layer of epidermis. a, b, c) in dog No. 23, experimental leg, 34th day. Objective imm. 90, ocular 15 x; d) - skin of experimental leg in dog No. 24, 29th day. Objective imm. 90, ocular 10 x.

much larger, and the epidermis became reticulated in places. One could often see huge nuclei, two or three times as large as ordinary nuclei, in the epithelial sheet. Active epithelial proliferation and disappearance of the basal membrane caused infiltrative growth of the epidermis, whose cells formed tongue-like forms which penetrated considerably deeply into the underlying connective tissue (Fig. 4). Some epithelial cells pulled away from the epithelial wedges and became much larger in size with a large nucleus and a weakly-staining, foamy cytoplasm.

As a working hypothesis, one may propose that,

when there are more mitoses than amitoses in denervated lesions, the epidermis grows infiltratively (a shaft of mitotically dividing cells perpendicular to the surface of the skin), which causes it to grow into the underlying connective tissue in tongue-like forms. When there are more amitoses than mitoses, the epidermis only thickens, and does not develop the typical infiltrative growth.

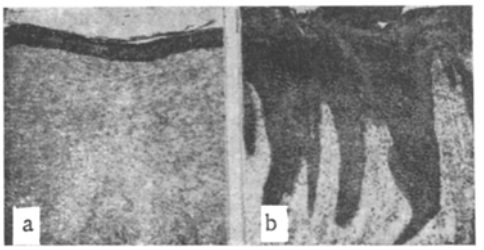

Figure 4. General view of vertical cross-section of lesion. Dog. No. 23, 26th day. Objective 8 x, ocular 7 x. a) control; b) experiment.

In any case, there is no doubt that sectioning the spinal cord causes a great increase in the number of cell divisions during the regeneration of cutaneous lesions.

The data presented allow the assumption that the central nervous system has a regulating effect on cell division, and that, when its impulses are excluded, the amitotic activity especially, as well as mitotic activity of the cellular elements are disinhibited.

That the number of dividing cells increased when the spinal cord of a dog was cut, as occurred in the experiments described, agrees with results obtained on axolotls by N. A. Ioff, who, although he did not study cell divisions directly, came to the same conclusion on the basis of observations on the healing of wounds.

SUMMARY

The effect of section of the spinal cord on cell division in the tissues of cutaneous lesions has been studied. Observations of 25 myelotomized dogs have shown, that in case of cutaneous lesions disruption of tissue innervation caused augmentation of cell division and intense infiltrative growth of the epidermis. These phenomena are connected with correlated disturbed relations of the epithelial and connective tissues.

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