

## ORGAN SPECIFICITY OF ACTION OF HUMORAL FACTOR

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After partial hepatectomy in rats the number of mitoses in the liver and salivary gland is increased. After unilateral nephrectomy mitotic activity is increased in the remaining kidney and also in the salivary gland. This confirms data indicating the relative organ specificity of the humoral factor appearing after partial resection of an organ: proliferative activity is intensified not only in the homonymous organ, but also in other organs, although to a lesser degree.

Many investigations have shown that the serum of animals undergoing partial resection of an organ affects growth and regeneration of organs homonymous with those resected [2, 6-8, 10-13, 15]. However, some workers have described that growth-stimulating substances discovered in the body of partially hepatectomized rats stimulate proliferation in other organs also, notably in the cornea and kidney [1, 10].

In this investigation mitotic activity was studied in various organs of partially hepatectomized and nephrectomized rats.

### EXPERIMENTAL METHOD

Three series of experiments were carried out on 215 noninbred male albino rats with a mean weight of 125 g (series I) and 170 g (series II and III). In operations on the experimental animals, either two-thirds of the liver was removed by the method of Higgins and Anderson [14] (series I and III) or one kidney was excised (series II). The control animals underwent a corresponding mock hepatectomy and nephrectomy. A small piece of the left lateral lobe of the liver (3% of the weight of the whole organ) was removed from the control animals to the experiment of series I.

Operations on the rats were performed between 3.30 and 7.30 A. M. and the animals were sacrificed between 6 and 9.30 A. M., i.e. at the time of the highest daily increase in mitotic activity in the liver and kidney [3-5], 25 and 48 h (series I), 27 h 30 min-28 h 30 min (series II and III) and 50 h (series II) after the operation.

Subsequently, on the 3rd, 7th, 10th, 14th, and 21st day after operation, the liver, kidney, and submandibular salivary gland were weighed. The cornea, liver, kidney, and submandibular gland were fixed in Carnoy's fluid. Total preparations were made from the cornea, and the other organs received the usual histological treatment. Mitoses were counted with an MB-3 binocular microscope (objective 90 $\times$ , ocular 7 $\times$ , window in ocular diaphragm 7 $\times$  7 mm) in 15 000 corneal epithelial cells, in 10 000-12 000 secretory epithelial cells of the salivary gland and main portion of the tubular epithelium of the kidney, and in 6 000 liver cells.

The mitotic index (MI) reflected the number of mitoses per thousand cells (promille). Statistical analysis of the data was by the Student-Fisher method.

### EXPERIMENTAL RESULTS

In the animals of series I 25 h after partial hepatectomy, when according to figures given by V. P. Sidorova [9] MI in the liver of these rats was very high (46%), a marked and statistically significant ( $P=0.01$ ) increase in the number of mitoses was also observed in the salivary gland. Removal of small

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TABLE 1. MI in submandibular Gland of Rats After Partial Hepatectomy (Series I)

Amount of tissue removed (in percent)	Time after operation (in hours)	Number of animals	MI (in %)	
			subman-dibular gland	liver (data of Sidorova [3])
61	25	7	2.67	46
3	25	8	0.77	0.3
64	48	8	0.08	21

pieces of liver was not accompanied by such a sharp change in proliferative activity. MI in the liver 48 h after operation had fallen to 21%, and in the salivary gland 0.08% (Table 1).

As Table 2 shows, the submandibular salivary gland reacted in the same way to unilateral nephrectomy (series II). The increase in mitotic activity in the kidney to 5.4%, 50 h after the operation was accompanied by an increase in the mitotic index in the salivary gland to 2.6% ( $P=0.013$ ).

However, both in series I and in series II, stimulation of proliferative processes in the salivary gland was only transient because in contrast to the liver and kidney it did not lead to a statistically significant increase ( $P=0.17$ ) change in the weight of the organ.

It is interesting to note that the increase in MI in the kidney and liver took place at different times after the operation: 25 h after partial hepatectomy and 50 h after unilateral nephrectomy. This indicates that the observed activation of mitoses in the salivary gland was not directly connected with the effect of trauma. The simultaneous increase in the number of mitoses in the salivary gland and liver or in the kidney shows that mitoses in these organs were induced by the same factor appearing in the animals undergoing operation not at the time of increased mitotic divisions of liver and kidney, cells as is generally considered, but long before it. Humoral factor evidently appeared during the first few hours after partial hepatectomy, but after nephrectomy, if the durations of the periods S, G<sub>2</sub>, and M in the kidney and liver are taken to be approximately equal [17], it evidently appeared later.

The marked response of the salivary gland to partial hepatectomy and unilateral nephrectomy suggests that the organ-specificity of action of humoral factor is relative. Its organ-specificity effect is shown by the more marked and prolonged stimulation of mitotic activity in the homonymous organ than in the salivary gland.

The possibility is not ruled out that sensitivity of organs varies to growth stimulators with nonspecific action, i.e., the threshold concentration of this factor in the blood is not identical for them. Possibly, a large measure of the disagreement observed in the literature concerning the action of humoral factor is due, first, to the fact that the authors did not investigate the strength of the responses in the injured organ at the time of investigation (in the parabiont, or pregnant female), and second, to the fact that serum for investigation was taken too late after the operation, at the time of maximal mitotic activity in the resected organ.

TABLE 2. MI in Organs of Rats Undergoing Unilateral Nephrectomy or Partial Hepatectomy

Type of operation	Time after operation (in hours)	Time of day	MI (in %)									
			kidney		cornea		salivary gland			liver		
			experiment	control	experiment	control	experiment	ment	control	experiment	ment	control
Unilateral hepatectomy (series II)	27 1/2-28 1/2	7 h	0.11	0.06	10.8	8.5	0.45	0.35		1.7	0.23	
		30 min										
	27 1/2-28 1/2	9 h	0.11	0.09	17.6	13.4	0.13	0.11		0.5	1.31	
Partial hepatectomy (series III)	50	9 -	5.4	2.4	14.0	11.0	2.6	0.40		0.2	0.13	
	27 1/2-28 1/2	7 -	0.09	0.23	8.6	13.1	0.07	0.07		20.1	0.13	
	27 1/2-28 1/2	9 -	0.21	0.25	10.0	15.0	0.10	0.03		10.0	0.23	
		15 min										

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