EFFECT OF PARTIAL HEPATECTOMY ON THE NUMBER OF SOMATOTROPHS IN THE RAT ADENOHYPOPHYSIS

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Two-thirds of the liver was removed by the method of Higgins and Anderson from male rats weighing 100-150 g. The adenohypophyses from rats undergoing partial hepatectomy or a mock operation or from rats left intact were studied 2, 4, 8-10, and 25 h and 2, 3, 6, 10, 14, and 21 days after the operation. A significant increase in the number of somatotrophs was found 8-10 h after partial hepatectomy, but 25 h after the operation they were fewer in number than in rats undergoing the mock operation. The number of somatotrophs in the adenohypophysis of the partially hepatectomized rats returned to normal on the second day after the operation and thereafter remained substantially unchanged. The results suggest that somatotrophic hormone plays a role in the regulation of repair processes in the liver.

Key words: partial hepatectomy; somatotrophs; adenohypophysis.

Doubts have been expressed about a role of somatotrophic hormone (STH) in the regulation of regeneration in the liver even until very recently, for regeneration of this organ can take place in the absence of the pituitary even after extensive partial hepatectomy. Removal of the pituitary affects only the rate of the course of liver regeneration [2, 3, 9].

Since hypophysectomy is a traumatic procedure, reflected in the state of the liver, other methods had to be sought to study the role of STH in the regeneration of that organ [4, 6, 8].

A cytological investigation was made of the anterior lobe of the intact pituitary in rats undergoing partial hepatectomy. Attention was concentrated on a quantitative study of the somatotrophs at different times after the operation.

EXPERIMENTAL METHOD

Young noninbred male rats weighing 100-150 g were used. The animals were divided into three groups. In group 1 (65 rats) partial hepatectomy was performed by the method of Higgins and Anderson; in group 2 (40 animals) a mock operation was performed, consisting of laparotomy, exteriorization of the left lateral and central lobes of the liver, and their replacement; in group 3 (19 rats) no operation was performed. All operations on the rats of the first two groups were performed at 9-11 a.m. Groups of 5-6 animals from each group were sacrificed, again always during the morning, at the following times: immediately after partial hepatectomy, and 2, 4, 8-10, and 25 h and 2, 3,6,10, 14, and 21 days thereafter.

The animals were decapitated and the pituitary removed and fixed for 3 h in a mixture of a saturated solution of mercuric chloride (9 parts) with neutral 40% formalin (1 part). Paraffin sections 4 μ thick were stained with azan by Heidenhain's method. In this method, which with certain modifications is still used today by histologists for the differential staining of the pituitary [7], acidophilic cells (somatotrophs, lactotrophs) can be distinguished from basophilic cells (thyrotrophs, gonadotrophs, adrenocorticotrophs) and chromophobes.

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TABLE 1. Numbers of Various Types of Cells – Somatotrophs (S), Basophilic Cells (B), and Chromophobes (C) per-Field of Vision in Adenohypophyses of Rats Undergoing Operations and Intact Rats (M ± m)

Time after operation	Partially hepatectomized				Undergoing mock operation				Intact			
	S	B	C	total	S	B	C	total	S	B	C	total
0 h	6,9±0,1	1,7±0,2	11,6±0,4 [1]	20,1±0,4	7,6±0,3	1,9±0,3	11,3±0,4	20,8±0,6	8,1±0,2	1,2±0,1	10,1±0,3	19,4±0,2
2 h	9,3±0,4	1,8±0,1	9,3±0,1 [2]	20,5±0,5	—	—	—	—	—	—	—	—
4 h	8,7±0,5 [3]	1,9±0,8	11,1±0,3	22,6±0,4	8,0±0,6	1,9±0,2	11,5±0,1	20,4±0,3	—	—	—	—
8–10 h	11,7±0,7 [4]	1,9±0,2	6,7±0,3	20,6±0,8	8,3±0,6 [5]	1,5±0,05	11,6±0,3	21,4±0,2	—	—	—	—
25 h	5,1±0,3 [6]	1,5±0,1	12,6±0,9	19,6±1,0	8,1±0,3	1,5±0,08	11,7±0,03	21,3±0,3	—	—	—	—
2 days	7,9±0,2 [7]	1,7±0,1	11,5±0,1	21,1±0,3	8,7±0,3 [8]	1,6±0,2	11,1±0,3	21,4±0,4	7,9±0,3	1,2±0,1	11,1±0,2	20,2±0,5
3 »	8,3±0,2	1,6±0,1	11,6±0,3	21,5±0,3	—	—	—	—	—	—	—	—
6 days	7,6±0,8	1,3±0,3	11,4±0,4	20,3±0,4	—	—	—	—	—	—	—	—
10 »	7,0±0,5	1,9±0,05	10,6±0,4	19,5±0,5	—	—	—	—	—	—	—	—
14 »	7,6±0,3	1,6±0,1	11,8±0,1	21,4±0,1	—	—	—	—	—	—	—	—
21 days	7,3±0,3	2,0±0,2	11,3±0,3	20,6±0,3	—	—	—	—	—	—	—	—

Legend. Small numbers denote values to be compared for which criteria of significance was calculated: for C, $P_{1-2}=0.023$; for S, $P_{3-4}<0.009$, $P_{4-5}<0.008$, $P_{6-7}<0.001$, $P_{7-8}=0.006$.

The total number of cells in a field of vision and the proportion of each of the cell types listed above were determined in the central zone of the lateral part of the adenohypophysis of the experimental and control animals (magnification: ocular 100, objective 90). In each case 30 fields of vision were counted. For convenience in counting the cells the field of vision of the microscope was cut down by means of a window measuring 5×5 mm. The numerical results of counting the various types of cells in the adenohypophyses of the rats undergoing partial hepatectomy and the mock operation and the intact rats were subjected to statistical analysis by the Fisher–Student method.

The regenerating liver was fixed in Carnoy's fluid; paraffin sections 6-8 μ thick were stained with hematoxylin and eosin. The level of mitotic activity of the liver cells was determined 25 h and 2 and 3 days after the operation. The number of mitoses per 3000 cells was counted. The results were expressed per 1000 cells.

EXPERIMENTAL RESULTS

Cells containing small acidophilic granules (somatotrophs) in the pituitary of intact rats were arranged in compact groups close to the connective-tissue septa or blood vessels. Their cytoplasm was packed with dark red granules of secretion.* Completely degranulated forms were rare. The basophilic cells were large, with juicy cytoplasm, filled with large blue granules of secretion; they were less frequently seen than somatotrophs and, as a rule, were arranged singly, often close to clearly distinguishable groups of somatotrophs. By far the greater part of the field of vision was filled with chromophobes, stained pale violet in color.

Sharp dilatation of the capillaries of the adenohypophysis was observed 2-4 h after the operation and the cytoplasm of some somatotrophs and basophilic cells was degranulated and contained little secretion. After 8-10 h the somatotrophs began to contain more secretion and to be arranged regularly along the septa. The cytological picture of the adenohypophysis 25 h after the operation again showed marked changes: there were few somatotrophs and many of them contained few granules of secretion. By the second day after partial hepatectomy somatotrophs were more numerous than previously along the blood vessels although the cytoplasm of many of them still contained little secretion. The histological structure of the adenohypophysis gradually returned to normal after 3-10 days. The adenohypophysis of the hepatectomized rats 2-3 weeks after the operation differed only a little from normal.

Counting the various types of cells in the adenohypophyses of the rats undergoing the operations and the intact rats revealed definite changes in their number at various times after the beginning of the experiment (Table 1). For example, during the first few hours after partial hepatectomy a definite tenden-

*Since these experiments were carried out on males, it was considered that cells containing dark red granules of secretion in their cytoplasm were mainly somatotrophs, for lactotrophs are known [1] to be comparatively rare in males.

cy was observed for the number of somatotrophs to increase ($P_{3-4} < 0.009$), and this in turn led to a decrease in the number of chromophobes in the field of vision ($P_{1-2} = 0.023$). These changes were seen particularly clearly 8-10 h after partial hepatectomy.

The number of somatotrophs fell sharply after 25 h, and the number of chromophobes increased correspondingly. The total number of cells in the field of vision remained practically unchanged.

No significant changes were found 2 days or more after the operation in the adenohypophysis of the partially hepatectomized rats.

The mock operation was not followed by any considerable quantitative variations in the numbers of the various types of cells in the adenohypophysis.

It follows from the data given in Table 1 that no significant fluctuations could be detected in the number of basophilic cells. The increase in the number of somatotrophs, however, evidently may have taken place both through an increase in the quantity of secretion in degranulated forms of the cells of this type and through additional transformation of chromophobes [1].

In the present experiments 25 h after partial hepatectomy the mitotic index of the hepatocytes was 33.7%, falling to 20.96% after two days and to 7.78% after 3 days. These results are evidence of the intensive course of regenerative processes in the liver and the indices of mitotic activity were similar to those observed by the writer previously [2] and to those described by other workers [5].

On the whole the facts presented in this paper indicate that partial hepatectomy undoubtedly has some effect on the histological structure of the adenohypophysis and, in particular, on the cells secreting growth hormone. The accumulation of somatotrophin in the pituitary during the first few hours after the operation of partial hepatectomy (8-10 h) and its subsequent liberation into the blood stream (25 h after the operation) were evidently connected with the need for this hormone to be present both during the period of preparation of the liver cells for reproduction and during the division of their nuclei. The validity of this hypothesis is confirmed by the fact that, first, no such changes were observed during the later periods of regeneration of the liver and, second, they were virtually absent in the adenohypophysis of the animals undergoing the mock operation.

The results of this investigation and the suggestions put forward regarding the role of somatotrophin in the mechanisms inducing the liver to regenerate are confirmed in the literature [4, 6, 8].

Meanwhile, besides the cause of the increased secretion of STH in the adenohypophysis of rats after partial hepatectomy suggested above, the possibility of another must be borne in mind. STH is known to reduce the intensity of stress reactions [1]. In the present experiments the partial hepatectomy undoubtedly acted as a stressor. The increased secretion of STH by the adenohypophysis of the animals undergoing the operations could therefore have been due not only to its participation in the mechanisms of cell proliferation but also to its role in increasing the resistance of the organism to the stress effect of trauma. Further investigations will be carried out in an attempt to differentiate between these factors influencing the cytoarchitectonics of the adenohypophysis.

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