

# VARIED INCREASE IN MASS OF LOBES OF THE LIVER AFTER REPEATED PARTIAL HEPATECTOMY

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Partial hepatectomy was performed three times at monthly intervals on female albino rats weighing 100 g. At the first operation 70% of the mass of the organ was removed, at the second operation 32% of the regenerating liver, and at the third operation 24% of the liver regenerating for a second time. During regeneration after the first resection there was a uniform increase in mass of the residual lobes. After the second and third operation this uniformity was disturbed. In the liver after one operation, just as in the intact organ, the weight of the upper and lower halves of the caudate lobe of the liver was the same. In the liver regenerating after the second operation the weight of the lower part of the caudate lobe was 1.5-1.8 times greater than the weight of the upper part of the same lobe. The histological structure of these parts of the liver and the dimensions of the nuclei of their hepatocytes were identical. In this case the uniformity of the distribution of mitoses is evidently disturbed in the various parts of the regenerating liver.

Regeneration of the rat liver after a single partial hepatectomy takes place on account of a regular increase in mass of the lobes remaining after resection [14]. In the present investigation the problem of whether this rule applies after repeated resections was examined.

## EXPERIMENTAL METHOD

Experiments were carried out on 50 noninbred female albino rats weighing on the average 100 g before the experiment began. The experimental animals were divided into three groups: 1) rats undergoing a single hepatectomy and sacrificed 2 and 3 months after the operation; 2) rats undergoing two hepatectomies and sacrificed 2 months after the second operation; 3) rats undergoing three operations and sacrificed 1 month after the third resection. The intervals between the resections were of 1 month's duration. The first operation was carried out by the method of Higgins and Anderson [6], with removal of the left lateral and central lobes of the liver. At the second operation the upper part of the right lobe of the liver was removed, equivalent to about 32% of the weight of the regenerating organ. At the third operation the lower part of the right lobe of the liver was removed - on the average 24% of the mass of the liver regenerating a second time. Intact rats sacrificed 1, 2, and 3 months after the beginning of the experiment acted as the control.

At sacrifice the liver and its individual lobes were weighed (with an accuracy of 10 mg). Pieces of the various lobes of the liver were fixed in Carnoy's fluid and 10% formalin and embedded in paraffin wax. Sections 7 $\mu$  in thickness were stained with hematoxylin and eosin and by Mallory's method. The nuclei of the mononuclear hepatocytes were measured with a screw-operated ocular micrometer. Altogether 200 nuclei in each lobe were measured. Statistical analysis of the results was carried out in accordance with the recommendations of Palkovitz and Fischer [7].

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TABLE 1. Weight Relationships between Lobes of the Liver

Group of rats	Num- ber of rats	Weight of liver (in g)	Weight of lobes of liver (in percent)					
			left lat- eral	central	right lateral		caudate	
					upper	lower	upper	lower
Control rats killed after beginning of experiment:								
after 1 month .....	5	4,65±0,46	30,1±1,1	35,7±1,1	15,9±0,6	9,3±1,1	4,5±0,2	4,4±0,4
» 2 months .....	5	6,70±0,4	31,4±0,8	35,3±0,4	16,6±0,8	8,8±0,6	4,0±0,7	4,0±0,6
» 3 months .....	5	5,65±0,4	31,2±1,3	36,2±0,6	15,2±1,2	8,3±0,6	4,8±0,1	4,3±0,6
Experimental rats:								
Group 1, killed 2 months after op- eration .....	5	6,30±0,7			47,5±0,9	27,5±1,4	12,0±0,6	14,9±1,4
Group 1, killed 3 months after op- eration .....	9	5,45±0,2			47,3±2,2	28,0±2,4	12,0±1,0	12,7±0,5
Group 2 .....	6	5,70±0,3				44,9±2,2	22,1±1,7	33,0±1,7
Group 3 .....	8	7,30±0,2				28,5±3,7	25,8±1,6	45,7±3,1

TABLE 2. Dimensions of Nuclei of Mononuclear Hepatocytes in Upper and Lower Parts of Caudate Lobe of Normal and Regenerating Liver

Liver studied	Number of rats	Area of nucleus (in $\mu^2$ )	
		lower part of caudate lobe	upper part of caudate lobe
Normal	5	84±1,6	80±0,6
Regenerating: once	5	87±1,6	87±2,0
twice	5	83±1,6	85±2,5
3 times	8	91±1,2	93±2,3

## EXPERIMENTAL RESULTS

After the first operation complete restoration of the weight of the regenerating liver took place through a uniform increase in mass of the lobes remaining after the resection (Table 1). After three resections the uniformity of the increase in weight of the individual areas of the repeatedly regenerating liver was disturbed. One month after the third operation the weight of the regenerating liver was  $7.3 \pm 0.2$  g (weight of the liver of the control rats  $6.7 \pm 0.4$  g). The relative weight of the repeatedly regenerating liver was  $3.2 \pm 0.1\%$  ( $3.3 \pm 0.1\%$  in the control). Regeneration of the liver after the third operation took place on account of an increase in the mass of the caudate lobe and also of proliferation of the stump of the right lobe left behind after the operation. The dimensions of the caudate lobe of the thrice regenerating liver were 8-12 times greater than normally. The rate of increase in mass of the lower part of the caudate lobe differed from that of the upper part of this lobe. In the intact liver the weight of the lower part of the caudate lobe was equal to the weight of the upper part of the same lobe. Two and 3 months after the first partial hepatectomy the weight of the upper and lower parts of the caudate lobe also were the same. In the liver regenerating for the third time, the weight of the lower part of the caudate lobe was 1.8 times greater than the weight of the upper part of the same lobe ( $P = 0.001$ ; Table 1).

Meanwhile, histological investigation of the upper and lower halves of the caudate lobe of the thrice regenerating liver showed no appreciable differences either in the state of the sinusoids or in the quantity of connective tissue. The nuclei of the hepatocytes in different parts of the liver also were equal in size (Table 2).

Similar results were obtained on investigation of the liver after a second hepatectomy (Tables 1 and 2).

The phenomenon of variation in growth of different parts of the liver after extensive partial hepatectomies has been observed in experiments on rabbits by Ponfick [8] and Meister [2]. Facts are also available which indirectly point to differences in the contribution of different parts of the liver to its regeneration. Zhenevskaya [1], for example, describing the formation of outgrowths on the wound surface of the rat liver after removal of half of the total mass of the organ, pointed out that these outgrowths are formed only from the residue of the middle lobe of

the liver and never from the residue of the left lobe. Sidorova [3] observed projections of the parenchyma on the wound surface of the liver in cocks after injury to the right lobe but never found projections of this type after injury to the left lobe. Solopaev [5], in experiments on dogs, found that after surgical injury to the right lobe of the liver the disturbances of bile secretion were more severe than after similar operations on the left lobe.

Comparison of the results of these experiments with those described by other workers suggests that under certain conditions different parts of the liver may respond differently to injury. Presumably under these conditions the uniformity of distribution of mitoses in different parts of the regenerating liver is disturbed. In particular, there are good grounds for postulating that after repeated partial hepatectomy the mitotic activity in the lower part of the caudate lobe of the liver must be perceptibly higher than in the upper part of that lobe. The widespread view that different parts of the liver grow at an equal rate during regeneration of the organ is thus apparently valid in by no means every case, and it is in need of revision.

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