FORMATION OF HEPATIC LOBULES IN THE REGENERATING LIVER

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The area of hepatic lobules was measured in the liver of rats after three successive partial hepatectomies carried out at intervals of 1 month. After the first resection, hypertrophy of the lobules was observed. After subsequent resections there was no increase in the degree of hypertrophy of the lobules. This shows that new lobules are formed during regeneration of the liver.

Regeneration of the liver after partial hepatectomy takes place through division and hypertrophy of the cells throughout the remaining mass of the organ [3]. However, the mechanism of regeneration of the liver at the level of its structural units has not yet been explained. Some workers consider that regeneration hypertrophy of the liver in adult animals takes place through enlargement of pre-existing hepatic lobules [1, 2, 4], while others claim that new hepatic lobules can be formed during regeneration of the liver [5, 6], and that this process is intensified after repeated resections of liver tissue [7].

In the investigation described below the formation of new hepatic lobules after one and several partial hepatectomies was studied.

EXPERIMENTAL METHOD

Experiments were carried out on 120 noninbred female albino rats weighing initially 100 g. Partial hepatectomy was performed once on the rats of one group, twice on the rats of a second group, and three times on the rats of a third group. The operations were repeated at intervals of 1 month. At the first operation the left lateral and central lobes of the liver were removed by the method of Higgins and Anderson. At the second resection, the upper part of the right lobe was removed. The weight of the tissue removed on this occasion was 2100 g, amounting to 32% of the weight of the regenerating liver. At the third operation, the lower portion of the right lobe was removed. The weight of tissue removed at this third operation was 1750 g, or 24% of the liver regenerating for the second time. To determine the boundaries of the hepatic lobules, the arterial system of the liver was injected with a mixture of ink and gelatin as described by Sidorova [4]. The rats were sacrificed 1, 2, and 3 months after the operation. The weight of the regenerating liver was determined. The length and width of the lower caudal lobe was measured and the area of cross section of the lobe determined. This will conventionally be called the area of the lobe. The outlines of the hepatic lobules were traced from tangential sections of the lower caudal lobe by means of an

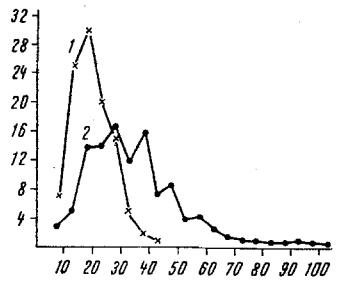

Fig. 1. Changes in size of hepatic lobules 1 month after first operation: 1) control; 2) experiment. Abscissa: area of lobules (in conventional units); ordinate: number of lobules (in %).

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TABLE 1. Changes in Size of Lower Caudal Lobe of Liver and Its Lobules after Single and Repeated Regeneration of the Liver

Groups of rats	Number of rats	Area of lower caudal lobe (in percent of control)		Number of hepatic lobules measured	Area of hepatic lobule (in percent of control)	
		mean	limits of variations		mean	limits of individual variations of mean values
One month after first operation. . .	5	293	215-365	517	174	146-211
Two months " " . . .	6	232	173-373	404	156	128-193
Three months " " . . .	9	273	155-355	529	179	152-208
One month after second operation .	6	480	350-632	655	201	126-266
Two months " " .	5	400	222-686	522	153	104-216
One month after third operation . .	8	545	1023-328	1478	172	100-228

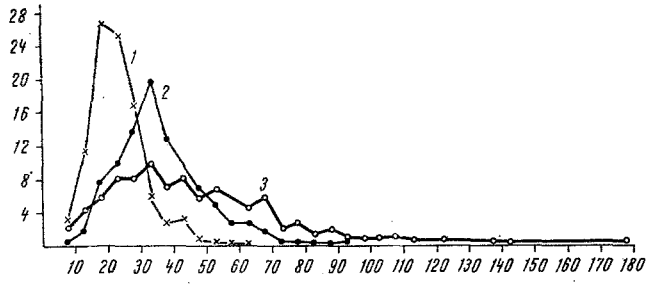

Fig. 2. Changes in size of hepatic lobules 1 month after second operation: 1) control; 2) liver after single hepatectomy; 3) liver after second hepatectomy. Abscissa and ordinate: as in Fig. 1.

Edinger's drawing apparatus with magnification of 27 times. Sections at the same relative distance from the capsule were always chosen for investigation. The drawn outlines of the lobules were cut out and weighed on torsion scales.

RESULTS

The dimensions of the lower caudal lobe in the hepatectomized animals were unchanged with age. No age changes likewise were detected in the area of the hepatic lobules. The dimensions of the hepatic lobules in the intact liver varied from 5 to 65 conventional units. Only single large lobules were present. The mean area of the hepatic lobule in the intact liver was 21 conventional units.

The weight of the regenerating liver one month after the first partial hepatectomy was the same as normal. The area of the lower caudal lobe one month after the operation averaged 293% compared with the control. The increase in size of the lower caudal lobe was accompanied by hypertrophy of the hepatic lobules on the average by 74% (Table 1; Fig. 1). No statistically significant differences were found in the size of the lower caudal lobe or of the hepatic lobules composing it between groups of rats sacrificed 1, 2, and 3 months after the first partial hepatectomy. The weight of the regenerating liver was likewise the same as in the control one month after the second operation. The area of the lower caudal lobe was 480%. Compared with the liver after a single partial hepatectomy, the number of large hepatic lobules in the liver regenerating after the second hepatectomy was increased. The area of some lobules was as much as 180 units. However, there were few large lobules, and the mean area of the hepatic lobule from the liver after the second hepatectomy was the same as that in the liver after the first hepatectomy, namely 201% (Table 1; Fig. 2).

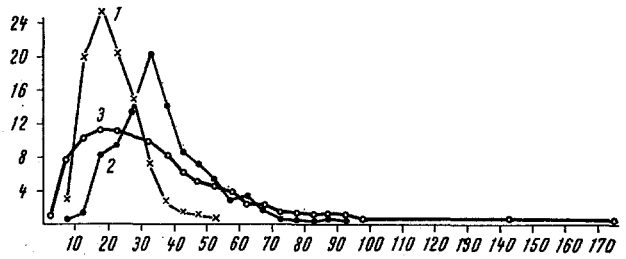

Fig. 3. Changes in size of hepatic lobules 1 month after third operation: 1) control; 2) liver after first hepatectomy; 3) liver after third hepatectomy. Abscissa and ordinate: as in Fig. 1.

The dimensions of the lower caudal lobe and of its component hepatic lobules two months after the second resection were the same as one month after the repeated operation(Table 1). After the third operation, further hypertrophy of the residual liver took place. The weight of the regenerating liver 1 month after the third operation was 30% greater than the weight of the liver in the control rats. The area of the lower caudal lobe was increased compared with the control on the average by 445%, although considerable individual variations were present. However, the mean area of the hepatic lobule after the third resection of the liver was increased by only 72% compared with the control (Table 1). Individual lobules were greatly hypertrophied, but most of the hepatic lobules were no larger than those in the intact liver. In addition, a few hepatic lobules of smaller size than in the intact liver were found in the liver after the third hepatectomy. A characteristic feature of the thrice hepatectomized liver was thus a shift to the left of the variance curve, toward a decrease in size of the hepatic lobules (Fig. 3).

The dimensions of the hepatic lobules varied in different parts of the liver. Large and small lobules were arranged in groups. The mosaic character of distribution of hepatic lobules of different sizes in the liver injected with ink could be seen with the naked eye. The focal distribution of small and large hepatic lobules occurred in the liver regenerating after the first and second hepatectomy, but with an increase in the number of resections it became more pronounced. It is evidently associated with the pattern of ramification of blood vessels in the liver.

In regeneration hypertrophy of the liver, after single and repeated resection of the organ, hypertrophy of the hepatic lobules thus takes place, but it does not increase in degree after repeated resections, and hypertrophy of the hepatic lobules lags considerably behind hypertrophy of the liver as a whole. In some cases, but not all, this lag can be observed after the first operation. It becomes much more marked after the second resection. It must therefore be concluded that during regeneration of the liver, hypertrophy of the hepatic lobules is accompanied by the formation of new lobules, and this latter process increases in intensity after repeated operations.

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