STRUCTURE OF THE REGENERATING LIVER AFTER RESECTION IN RATS OF DIFFERENT AGES

V. F. Sudorova

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During regeneration of certain internal organs of vertebrates after resection, the morphogenetic reactivity may vary [1, 6]. This is due to several causes, one of which may be the presence or absence of processes of formation of new structural and functional units in the organ at the moment of injury (lobules in the liver, alveoli in the lung, nephrons in the kidney, and so on).

In most internal organs of mammals the process of development of new structural and functional units diminished with age; it can be observed only at the earliest stages of postnatal ontogenesis. This may account for the fact that in adult animals resection of part of an organ—the liver, lung, or kidney—does not lead to the development of new structural components in the organ, but to hypertrophy of those already existing [2–4].

For these reasons the determination of the reaction of an organ to injury from the age aspect is particularly interesting.

The object of the present investigation was to study the structure of the regenerating liver after partial hepatectomy in rats in the early postnatal period of development.

EXPERIMENTAL METHOD

In the experiments of series I, the left lateral and central lobes of the liver were removed from young rats aged 7, 14, and 24–28 days by the method of Higgins and Anderson. The mass of liver tissue removed amounted to 66% of the total weight of the organ. In each age group there were 5–7 rats undergoing the operation and 4–5 control animals.

The young rats undergoing operation at the age of 7–14 days were sacrificed 1.5 months after partial hepatectomy, and the rats undergoing the operation at the age of 24–28 days were sacrificed 6 months later. The control animals were sacrificed at the same time as the experimental. In the experiments of series II (repeated) partial hepatectomy was carried out on rats aged 10 and 24 days. The experimental and control animals of both age groups were sacrificed at the same time, 1.5 months after the operation.

The outlines of the individual lobules of the liver were traced by means of a special technique, described previously [4], in the experimental and control animals. The liver was then fixed in 10% formalin. Sections were cut on a freezing microtome. By means of a drawing apparatus the outlines of the individual lobules of the liver were drawn and their area was determined. In each animal the area of 40–50 lobules was measured. The results obtained were analyzed statistically by the Fisher–Student method.

EXPERIMENTAL RESULTS

As the results of the experiments of series I show, the age of the animal at operation was of decisive importance in determining the final structure of the regenerating liver.

The liver of rats undergoing partial hepatectomy at the age of 7 and 14 days was practically indistinguishable in structure from the liver of the intact animal: most of the lobules of the liver were the same size as in the controls ($P = 0.6$, difference not significant). This was seen particularly clearly when the dimensions of the lobules were broken down into separate classes. Lobules with an area of 140–240 mm² (magnification 28×) were included in class 1, those with an area of 260–360 mm² in class 2, those with an area of 380–480 mm² in class 3, and those with an area of 500–600 mm² in class 4, and so on.

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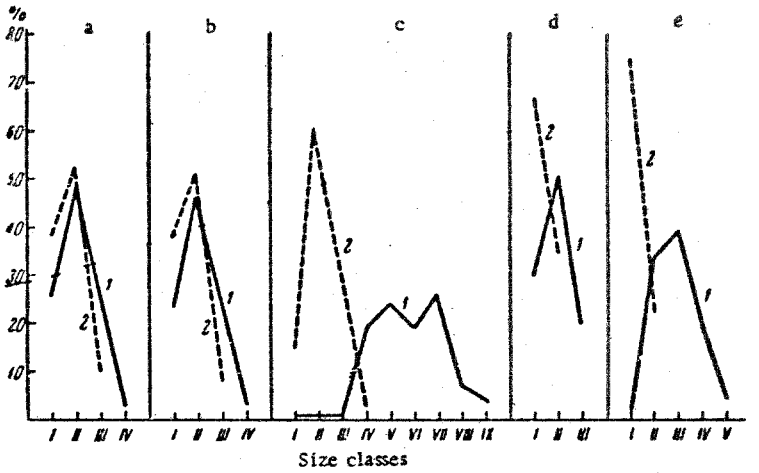

Fig. 1. Relationship between dimensions of hepatic lobules, broken down into classes, in the regenerating and intact liver of rats. Partial hepatectomy was performed at the age of 7 (a), 14 (b), 24-28 (c), 10 (d), and 24 days (e). All the experimental animals were sacrificed at the same time as the controls, 6 months after the operation. 1) Experiment, 2) control.

In the animals undergoing operation at the age of 7 and 14 days, the lobules belonged by their size to the first four classes, mostly to class 2, while in the control (intact) rats they belonged to the first three classes, again mostly to class 2 (Fig. 1, a and b).

The discovery of a larger number (23-25%) of lobules of class 3 in the liver of the experimental groups of animals than in the controls (10%) and also the appearance of lobules of class 4 (Fig. 1, a and b) indicate that during regeneration of the liver new hepatic lobules appeared, and hypertrophy of the lobules also took place.

Measurements of the hepatic lobules in the rats undergoing partial hepatectomy at the age of 24-28 days yielded different results: the number of lobules in the experimental groups was 2 or 3 times greater than in the controls ($P < 0.001$). Breakdown of the lobules into classes showed that in the animals of the experimental group classes 3-9 were most commonly present, but in the control animals, lobules of classes 1-4 (Fig. 1, c).

Since the animals undergoing partial hepatectomy at the age of 24-28 days were sacrificed at a longer interval after the operation (6 months) than those undergoing the operation at the ages of 7 and 14 days (1.5 months later), it may be suggested that the larger size of the hepatic lobules in the experimental animals of this group was due to their increase in size during growth of the organ.

For this reason the investigation was repeated, constituting the experiments of series II, similar to series I, but the animals undergoing operation at the ages of 10 and 24 days were sacrificed at the same time as the controls, 1.5 months after the operation.

The results obtained were the same as in the experiments of series I: in the animals undergoing partial hepatectomy at the age of 24 days, the hepatic lobules were hypertrophied compared with those in the controls (Fig. 1, e), while in the animals undergoing operation at the age of 10 days, the dimension of the lobules were close to those in the controls (Fig. 1, d and Fig. 2).

However, as in the experiments of series I, in the young rats undergoing operation at the age of 10 days, besides the formation of new hepatic lobules, partial hypertrophy of the lobules also must have taken place, because the number of large lobules in the liver of the experimental animals was always greater than their number in the controls (Fig. 1, d).

The experimental results described above suggest that the structure of the organ at the time of operation determines its structure during regeneration. Evidently the ability to form new structural and functional units of an organ at the time of operation determines this same

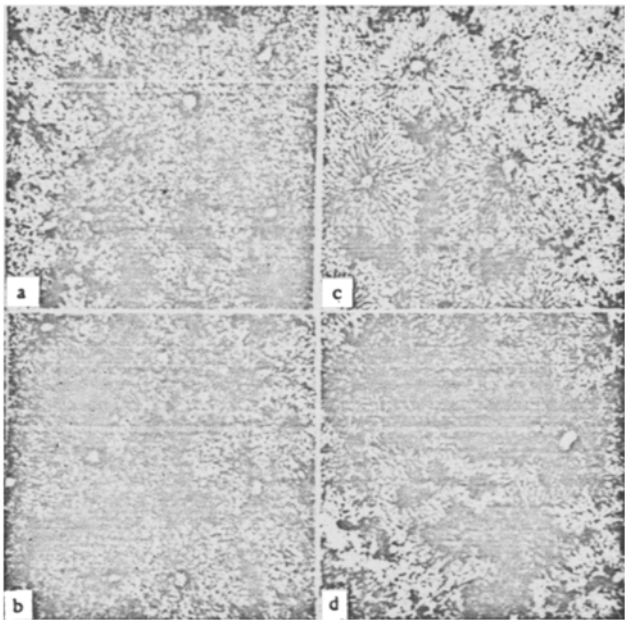

Fig. 2. Structure of the regenerating liver 1.5 months after partial hepatectomy. The dimensions of the lobules of the liver in the animals undergoing operation at the age of 7 days (a) are similar to those in the controls (b); the lobules in the rats undergoing operation at the age of 24 days (d) are hypertrophied by comparison with the control (c).

process in the regenerating organ. In this case, performance of partial hepatectomy on young rats at the ages of 7, 10, and 14 days (the period of ontogenesis when the formation of new hepatic lobules is still possible in the liver [7]) leads to the appearance of hepatic lobules in the process of regeneration of the organ. If, on the other hand, the morphogenetic processes in the ontogenesis of the organ are already complete, clearly they can be manifested only to an extremely slight degree during its regeneration. In fact, after partial hepatectomy on rats over 24 days old, mainly an increase in the size of existing hepatic lobules and not the formation of new lobules was observed. Consequently, the same reaction took place as in adult animals after extensive partial hepatectomy [4].

The results obtained provide experimental confirmation of the author's earlier hypothesis that the processes observed during regeneration of the internal organs of vertebrates (after extensive resections) are closely similar in nature to the processes taking place during the postnatal development of these organs [5].

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