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CYTOLOGICAL FEATURES DISTINGUISHING GROWTH OF THE RAT LIVER IN THE EMBRYONIC AND NEONATAL PERIODS AND DURING REGENERATION

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Embryonic and neonatal growth of the liver was studied in August rats and compared with growth of the regenerating liver of adult animals in the early stages after partial hepatectomy (22, 48, and 72 h after removal of two thirds of the organ). The mitotic activity and area of the nuclei of the hepatocytes were determined and the number of binuclear cells counted. Several general principles were discovered in the dynamics of the changes in the cytological parameters of embryonic and neonatal growth of the intact liver and growth of the regenerating liver of adult rats in the early stages after resection.

KEY WORDS: Embryonic and neonatal liver; regeneration; hepatocytes.

Studies of the growth and development of the liver in the early stages of ontogeny have recently been published [2,3]. However, many aspects of the cytological processes taking place under these circumstances remain inadequately explained and require clarification and further study. Meanwhile, regeneration of the liver after resection takes place to some extent through cytological processes which are the same as those found in the organ during its normal growth [1].

It was therefore thought worthwhile to make a comparative cytological study of growth of the embryonic and neonatal liver and of the regenerating adult liver in the early stages after resection.

EXPERIMENTAL METHOD

Rats of the August strain were used. The liver of embryos (of the 19th-20th day of gestation), newborn rats (until 3 h after birth), and day-old animals and the regenerating liver of adult rats (weighing 191 ± 29 g) from which two thirds of the liver had been removed, was investigated. The hepatectomized rats were killed 22, 48, and 72 h after the operation. At each time of study four to six animals were chosen. The liver (intact and regenerating was weighed. Material was fixed in Carnoy's fluid; the number of mitotically dividing hepatocytes in 6000 cells was counted in histological sections 5 μ thick, stained with hematoxylin and eosin. The mitotic index (MI) was expressed in promille. The number of binuclear hepatocytes was counted in 2000 cells and

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TABLE 1. Parameters of Growth of Intact and Regenerating Rats Liver (M ± m)

Liver	Number of animals	MI (in $^0/_{00}$)	Area of hepatocyte nuclei (in μ^2)	Number of binuclear cells (in %)
Intact:				
embryonic	4	0,09±0,002	27,5±0,32	0,29±0,09
neonatal	6	0,70±0,072	23,8±0,48	0,20±0,029
of day-old rats	6	0,33±0,054	23,8±0,25	0,94±0,182
Regenerating				
22 h after operation	4	1,7±0,54	50,4±4,3	2,45±0,33
48 h after operation	4	22,5±3,6	38,4±1,8	0,46±0,086
72 h after operation	5	8,9±0,83	37,1±1,30	0,86±0,146

expressed as a percentage. The diameter of the nuclei also was measured with an ocular micrometer, and their area was calculated in square microns. The numerical results were subjected to statistical analysis by the Fisher–Student method.

EXPERIMENTAL RESULTS

A study of mitotic activity in the liver of the embryonic, neonatal, and day-old rats (Table 1) showed that MI of the embryonic liver was $0.09^0/_{00}$, and it increased to 0.70 $^0/_{00}$ by 3 h after birth (P = 0.000), after which it fell in the day-old rats to 0.33 $^0/_{00}$ (P = 0.006). The embryonic and neonatal liver contained a few binuclear cells. They were most numerous in the liver of the day-old rats, namely 0.94% (P = 0.019). The nuclei of the hepatocytes of the embryonic liver were a little larger (27.5 μ^2) than in the newborn and day-old rats (23.8 μ^2; P = 0.000).

Similar changes were observed in the regenerating rat liver (Table 1). The highest mitotic activity was observed 48 h after resection, namely 22.5 $^0/_{00}$ (P = 0.001). The hepatocyte nuclei were largest 22 h after the operation, and they were somewhat smaller in size after 48 and 74 h (P = 0.03), due to the formation of new young cells by mitosis, which were smaller than the undividing hepatocytes, on the second and third day after the operation. The number of binuclear cells started to rise on the third day after partial hepatectomy over their level at 48 h, the figures being 0.86 and 0.46% respectively (P = 0.06).

If the growth and development of the liver in young rats at the early stages of ontogeny is compared with regeneration of the adult rat liver in the early stages after partial hepatectomy, many common features can thus be observed in the changes in the cytological parameters of growth: mitotic activity, number of binuclear cells, and dimensions of the hepatocyte nuclei. In the writers' opinion, the reason for these common features is that in the intact neonatal and the regenerating adult liver similar factors apply. The first such factor is physiological shock, which is observed during birth, and the stress evoked by the removal of a large quantity of liver tissue. The second similar factor is an increase in mass: In the case of the intact neonatal liver this is by physiological growth, whereas during regeneration of the resected liver it is regenerative growth.

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