after blood loss the number of CFU-F rises sharply [5]. It is noteworthy that in the first 6 h after irradiation in a dose of 150 R the number of CFU-F in the bone marrow increased to twice their number immediately after irradiation; the nature of the sources from which the CFU-F are recruited remains unexplained.

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CHANGES IN MITOTIC ACTIVITY OF HEPATOCYTES AND RESORPTION OF NECROTIC AREAS DURING INDUCTION OF CIRRHOSIS OF THE LIVER

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Cirrhosis of the liver was induced in rats weighing 120-140 g by administration of CCl_4 for 2 months. Iodinated oil was injected through the spleen of the experimental and intact animals to produce embolism of the branches of the portal vein and foci of necrosis in the liver tissue. The volume of the necrotic foci and the mitotic activity of the hepatocytes were determined. In cirrhosis of the liver the necrotic foci were resorbed more rapidly. The increase in the mitotic index on the second day after injection of the iodinated oil was greater in the control rats. The results suggest the appearance of a new cell clone in the liver which is responsible for resorption of the necrotic tissue and the reduction in mitotic activity of the hepatocytes in animals during development of cirrhosis of the liver.

KEY WORDS: cirrhosis of the liver; necrotic foci; proliferation in the liver.

Many investigations indicating the high proliferative potential of liver tissue have now been published. For instance, after removal of two-thirds of the liver the weight of the residual part doubles after 50 h. After partial hepatectomy repeated 12 times on rats, with the removal of 71 g liver tissue in the course of 1 year (natural weight of the liver 17.5 g), the histological structure of the organ was fully restored and the mean weight of the liver in these rats was 13.8 g [4, 5]. Meanwhile, during the development of experimental cirrhosis of the liver induced by CCl_4, after the precirrhotic period (about 2 months in rats) the proliferative power of the hepatocytes becomes inadequate and, although the volume of the necrotic areas is reduced, a marked increase is observed in the amount of connective tissue, with the formation of irreversible cirrhosis of the liver [2, 3].

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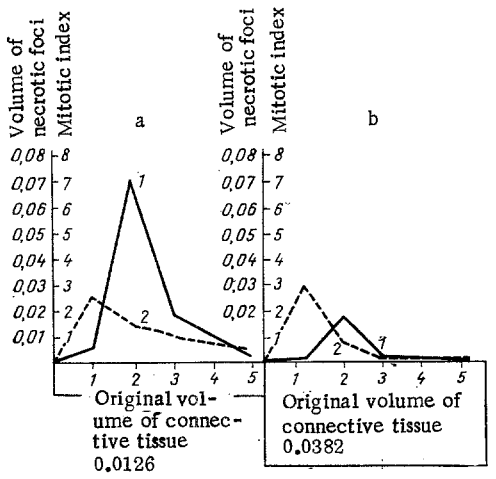

Fig. 1. Decrease in mitotic activity of hepatocytes and acceleration of resorption of necrotic areas in the liver during development of cirrhosis: a) control, b) experiment; 1) mitotic index, 2) volume of necrotic foci. Abscissa, days after injection of iodinated oil; ordinate, volume of necrotic foci (in fractions of volume of whole liver) and mitotic index (in %).

In this connection it was interesting to study how the proliferative power of the hepatocytes and the functional state of the connective-tissue cells change, so far as resorption of necrotic areas in the liver is concerned, in the early stages of development of cirrhosis.

EXPERIMENTAL METHOD

Experiments were carried out on 50 male albino rats weighing 120-140 g, divided into two groups with 25 animals in each group. Before the main experiments began, for 2 months the animals of group 1 (experimental) received CCl_4, and interval of 15 days followed, and then the animals of both groups received an injection of 0.25 ml iodinated oil into the spleen, to produce embolism of the portal vein and foci of necrosis in the liver tissue. The animals were decapitated between 9 and 9:30 a.m. on the first, second, third, and fifth days after injection of the oil. To determine the original volume of connective tissue before the oil was injected, five animals were killed at each time. The volume of mature connective tissues and the volume of the foci of necrosis of hepatocytes with granulation tissue were determined by the point counting method [1]. The mitotic index was determined by counting the number of mitoses in 12,500 hepatocytes.

EXPERIMENTAL RESULTS

Microscopic examination showed that the volume of connective tissue before injection of the oil was 0.0382 of the volume of the whole liver in the animals of group 1 and 0.0126 in the animals of group 2. After injection of the iodinated oil into the spleen and the formation of emboli in the branches of the portal vein, necrotic areas of liver tissue appeared in the animals of both groups and occupied part of the lobule from the periphery to the central vein, and evidently corresponded to Rappaport's acinus. Infiltration with cells consisting chiefly of lymphocytes, histiocytes, and solitary macrophages was observed in these areas. The volume of the necrotic foci appearing on the first day was approximately the same in the experimental (0.0298 of the volume of the whole liver) and control groups (0.0242). However, the dynamics of resorption of the necrotic areas differed. In the experimental group, for instance, maximal cellular infiltration and the greatest volume of the necrotic foci were observed on the first day, on the second day the volume of the necrotic foci was greatly reduced (0.0088), by the third day it was 0.0004 of the total volume of the liver, and the necrotic foci had almost completely disappeared on the fifth day after injection of the oil (Fig. 1). In the control group, despite the somewhat smaller volume of the necrotic foci appearing after injection of the oil, they were resorbed much more slowly than in the experimental group. For instance, on the second day the volume of the necrotic foci was 0.0143 of the volume of the whole liver, by the third day it was 0.0092, and on the fifth day 0.0048 (Fig. 1).

Investigation of the mitotic activity showed a very small increase in both the experimental and control groups (on the first day in both cases 0.05%), followed by a considerable rise in the control group to 7.1% on the second day and a gradual fall to 1.8% on the third day and 0.1% on the fifth day. In the experimental group the maximal, but lower, rise of mitotic activity also was observed on the second day after injection of the oil, to 1.7%; it fell to 0.2% on the third day and to zero on the fifth day (Fig. 1).

Investigation of the dynamics of resorption of the necrotic areas in the liver of the intact animals and animals in the early stage of development of cirrhosis thus revealed more rapid resorption of the necrotic areas arising following embolism of the branches of the portal vein after injection of an oily solution into the spleen in the animals of the experimental group. In the writer's opinion, this result can be explained by the appearance of a new clone of cells in the liver after administration of CCl_4 for 2 months, or by an increase in the number of local cells responsible for the resorption of necrotic foci. Meanwhile, in the early stages of cirrhosis of the liver the proliferative power of the epithelial component was reduced.

The results thus suggest that the formation of cirrhosis of the liver leads to a decrease in the mitotic activity of the hepatocytes and to the appearance of a new clone of connective-tissue cells, which are capable

of resorbing necrotic masses more rapidly and thus stimulating the development of the connective tissue of the liver.

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LYMPH NODE AND SPLEEN MORPHOLOGY IN GNOTOBIOTIC RATS

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The lymph nodes, spleen, and adrenal cortex of 12 gnotobiotic and 12 control Wistar rats were investigated by the ordinary histological and histochemical methods. Absence of the normal microflora was shown to inhibit the development of the zone of B lymphocytes of the lymph node and to cause thickening of the adrenal cortex and enlargement of the lipid inclusions in its cells; no effect on the structure of the lymphoid follicles of the spleen could be found. Inhibition of lymphopoiesis in the rat lymph node takes place as a result of absence of direct microbial stimulation and its mechanism involves a hormonal principle. These factors have no effect on lymphopoiesis in the spleen, which is stimulated within the organ itself.

KEY WORDS: gnotobiotic animals; lymph nodes; spleen; adrenals.

Lymphoid tissue is known to maintain the normal immunological homeostasis of the organism [1]. Ecological factors, among which an important place is occupied by microorganisms, have a great influence on the structure of the lymphoid organs. Gnotobiotic animals are the only objects by which the action of the microbial factor on the systems of the body can be standardized; the need thus has arisen for the organs of such animals to be studied with a view to determining their norms and studying the role of the microbial factor in the histophysiology of the tissue of the protective lymphoid system.

The importance of the normal microbial factor for the state of the lymphoid tissue and adrenal cortex was studied.

EXPERIMENTAL METHOD

The mesenteric lymph node, spleen, and adrenal cortex of 12 gnotobiotic Wistar rats aged 4 months were studied. Gnotobiotic animals were obtained from the Laboratory of Experimental Biological Models, Academy of Medical Sciences of the USSR. Similar organs were investigated from ordinary conventional animals of the same strain. Material was fixed in Carnoy's fluid and in 10% formalin solution. Sections 5-7 μ thick were stained with hematoxylin and eosin, for RNA by Brachet's method with the appropriate control, for free iron in the spleen by Perls' method, and for lipids in the adrenal cortex by Sudan III and IV.

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