CONTENT OF SERUM PROTEINS AND NUCLEIC ACIDS IN THE LIVER OF RABBITS WITH TOXIC HEPATITIS AND CIRRHOSIS

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In toxic hepatitis and cirrhosis of the liver produced in rabbits by injection of carbon tetrachloride a marked decrease is observed in the RNA content in the liver and an increase in transaminase activity and in the γ-globulin concentration in the blood serum, accompanied by a decrease in the albumin content. Morphologically, progressive degenerative and cirrhotic changes are observed.

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One manifestation of the toxic action of hepatotropic poisons, including carbon tetrachloride, is a considerable disturbance of nucleic acid and protein metabolism [1-3, 10, 14, 18, 19].

The object of the present investigation was to study changes in the content of serum proteins and nucleic acids in the liver of animals with toxic hepatitis and cirrhosis.

EXPERIMENTAL METHOD

Experiments were carried out on 50 noninbred rabbits of both sexes weighing from 2.5 to 3 kg. For 6 months the animals were fed with carbon tetrachloride, alternating with periods of rest, in the manner described by Rubetskii and Korotkina [8]. The experimental animals were divided into three groups. One course of poisoning was given in group 1 (10 rabbits), two courses in group 2 (12 rabbits), and three courses of poisoning in group 3 (9 rabbits). Intact animals acted as controls.

The total protein content was determined in serum obtained from blood taken from the marginal vein of the ear at the beginning, middle, and end of the period of poisoning, protein fractions were estimated by electrophoresis on paper in veronal buffer (μ=0.1) for 6 h at a voltage of 240 V, and activity of glutamate-oxaloacetate and glutamate-pyruvate transaminases (GOT and GPT) was determined by Paskhina's method [5]. The animals were sacrificed after the 1st, 2nd, and 3rd periods of poisoning. The liver was quickly removed and placed in liquid nitrogen, after which the content of RNA and DNA in the tissue homogenates was estimated quantitatively and seseparately by the method of Tsanev and Markov [9]. The liver was examined morphologically.

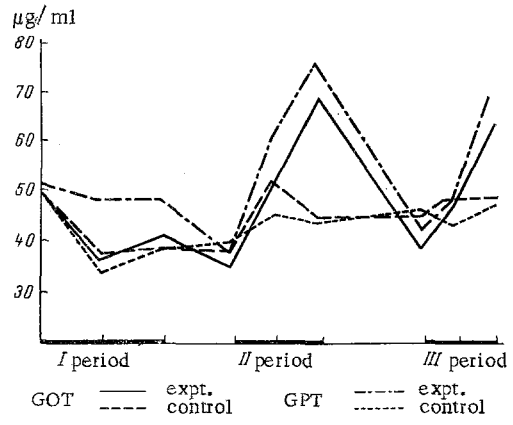

Fig. 1. GOT and GPT in rabbits with toxic hepatitis and cirrhosis (activity expressed in μg pyruvate/ml blood serum).

EXPERIMENTAL RESULTS

The character of changes in protein, protein fractions, transaminase activity of the blood serum, and nucleic acid content in the liver during the period of poisoning is illustrated in Table 1 and Figs. 1 and 2.

In the first period of poisoning, no significant changes were found in any of these indices. Morphologically, degenerative changes affecting the liver parenchyma with

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TABLE 1. Content of RNA and DNA (in mg% P) in 1st, 2nd, and 3rd Periods of Poisoning with Carbon Tetrachloride

Group	Period of poisoning					
	1-st		2-nd		3-rd	
	RNA	DNA	RNA	DNA	RNA	DNA
Control	39,3±3,2	19,3±3,4	35,3±2,2	24,0±2,6	32,1±1,7	19,5±1,6
Experimental	38,0±1,3	24,7±1,4	27,3±1,2	19,7±0,9	25,7±1,5	22,5±1,0
P	>0,05	>0,05	<0,05	>0,05	<0,02	>0,05

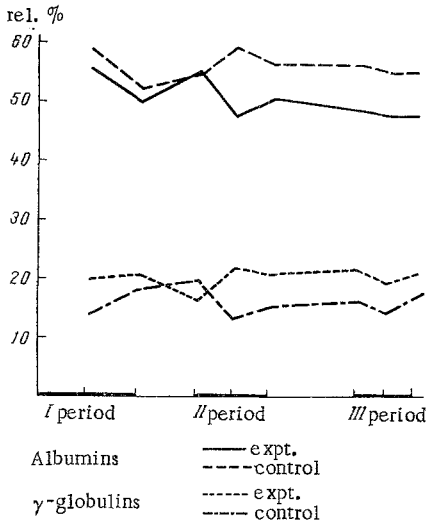

Fig. 2. Serum albumins and γ-globulins in rabbits with toxic hepatitis and cirrhosis.

infiltration of the tissue by lymphoid cells were observed at the periphery of the lobule. Hyperplasia of the Kupffer cells and the initial stages of scar formation in the connective-tissue sheaths around the blood vessels and of the reticular fibrils in the intertrabecular spaces were observed.

In the second period more severe changes were observed: a decrease in albumins and an increase in the γ-globulin fraction of the serum proteins, a decrease in the RNA content in the liver. GOT and GPT activity was considerably increased. The liver cells showed vacuolar degeneration; individual cells and the periphery of the lobule were necrotic, others grossly hypertrophied; binuclear cells appeared and the number of mitoses was increased. Young forms of fibroblasts and lymphoid cells were seen in the young connective tissue in the areas of necrosis and degeneration. Diffuse invasion of the liver by fibrous bands was observed. During the rest period, the composition of the blood proteins did not return to normal.

The third period of poisoning gave rise to no new changes in the protein composition of the blood serum. The RNA content in the liver remained low. A new and sharp increase in GOT and GPT activity was observed. Morphologically, extensive degenerative changes were observed in the liver, with large areas of necrosis, structural changes in the liver parenchyma, organization of pseudolobules, and closer approximation of the triads. The young connective tissue surrounding the lobules was richly infiltrated with lymphoid cells.

In all periods of poisoning there were no significant changes in the content of α- and β-globulin fractions. The total protein content likewise showed to significant change.

Hence, during prolonged poisoning of rabbits with carbon tetrachloride considerable changes are observed in the nucleic acid content in the liver and also in the serum albumin and γ-globulin content. Because of the importance of the protein-synthesizing function of the liver [1, 7, 14, 18, 19], it can be postulated that changes in the serum albumin content in the blood of the animals are the result of disturbance of the ability of the parenchymatous cells of the liver to synthesize this type of protein. The more prolonged administration of carbon tetrachloride (two periods of poisoning) causes a permanent dysproteinemia associated with more marked disturbances of metabolism of the liver cells; this conclusion is confirmed by the histological picture of the liver. The marked degenerative changes connected with disturbance of permeability of the cell membranes and necrosis of the liver cells can also be judged from the serum GOT and GPT activities, which increase sharply in the 2nd and 3rd periods of poisoning [6, 11, 17]. It is interesting to note that changes in the serum albumin content and RNA content of the liver take place in the same direction in the first period of poisoning. In the second and third periods these changes are more marked and also in the same direction. In other words, the decrease in RNA content is accompanied by a decrease in albumin production. This fact is in agreement with the hypothesis of Jacob and Monod [12], according to which the level of synthetic processes in the cell is determined by its RNA content. The increase in γ-globulins may reflect immunological changes in the body [4, 8, 15, 16].

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