ROLE OF BILE IN DISTURBANCES OF PHOSPHORUS METABOLISM IN OBSTRUCTIVE JAUNDICE

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The rate of absorption of radioactive phosphorus from the intestine is lowered in dogs with obstructive jaundice caused by ligation and division of the common bile duct. After intravenous injection P^{32} the radioactivity of the blood falls more slowly than in healthy animals. The specific activity of phospholipids circulating in the blood plasma is raised in early periods after the operation, but later is lowered because of developing liver damage.

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In a series of papers, K. S. Zamychkina and D. É. Grodzenskii [1-4, 5-12] have described the results of their investigations of the role of the bile-forming function of the liver in lipid metabolism. These investigations demonstrated the importance of the state of liver function for the rate of synthesis of biliary phospholipids (lecithin) in tha organ. The importance of disturbance of the enterohepatic circulation of bile in the genesis of the hyperphospholipemia in obstructive jaundice was also demonstrated. In 1956, K. S. Zamychkina and co-workers [7] found diminished absorption of radioactive sodium phosphate from the alimentary tract in hepatitis of different origin.

In the present investigation we studied absorption of radioactive sodium phosphate ($Na_2HP^{32}O_4$) from the alimentary tract at various stages of development of obstructive jaundice in dogs and the rate of synthesis of the phospholipids circulating in the blood during obstructive jaundice.

EXPERIMENTAL METHOD

Experiments were performed on ten dogs. Obstructive jaundice was produced by ligation and division of the common bile duct. Experiments on the affected dogs began 10-14 days after the operation and observations continued for between 25 and 90 days after the operation.

Radioactive sodium phosphate was given to the fasting dogs in a mixture of milk and water (total volume 150 ml) in a dose of 150-250 pulses/min/g body weight. Blood was taken from the short saphenous vein with the animal in a standing position, 15, 30, 60, 90, 120, 180, and 240 min and 24 h after the beginning of the experiment. Blood serum (0.5 ml) was placed on a foil target and dried at room temperature. The radioactivity of the samples was measured in a B-2 apparatus with a BFL-25 end-type counter. The results of the measurements were expressed as radioactivity per ml blood serum as a percentage of the radioactivity administered per gram body weight. In each successive experiment allowance was made for the residual radioactivity of the blood serum. The rate of absorption and utilization of P^{32} was judged from the dynamics of the changes in radioactivity of the blood serum after administration of P^{32} to the animals The index of the rate of synthesis of phospholipids circulating in the blood stream was the level of specific activity of the phospholipid fraction of blood serum taken 4 and 24 h after oral administration of P^{32} [3]. In the course of the disease, the serum bilirubin was also investigated by Van den Bergh's method, and the total and lipid phosphorus [4] and their radioactivity were determined.

To determine the rate of utilization of P^{32} from the blood, investigations were carried out on 4 of the 10 dogs in which P^{32} in sterile isotonic solution was injected intravenously. Otherwise the experimental conditions were the same as before.

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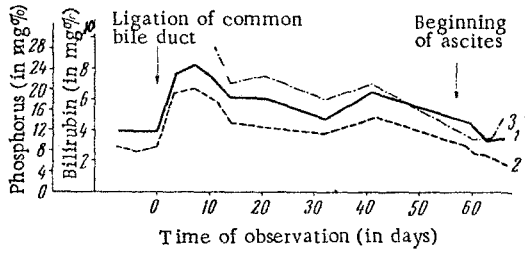

Fig. 1. Changes in blood level of total phosphorus (1), lipid phosphorus (2), and bilirubin (3) during development of obstructive jaundice in the dog Gordets.

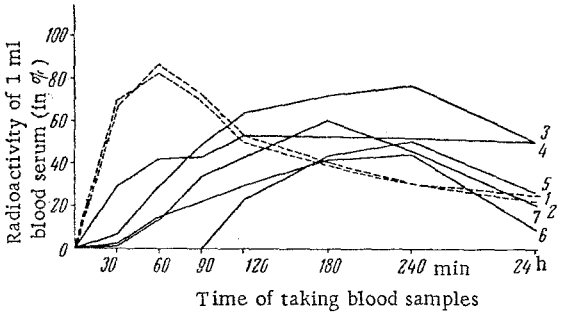

Fig. 2. Level of serum radioactivity after oral administration of P^{32}. 1 and 2) Control experiments (the dog Sharik); 3) 20 days after ligation of common bile duct; 4) 43 days; 5) 62 days; 6) 79 days; 7) 93 days after ligation (the dog Kolobok).

EXPERIMENTAL RESULTS

From the first day after the operation hyperbilirubinemia and hyperphosphoremia developed, mainly on account of phospholipids. The changes observed in the blood components investigated took place simultaneously and followed a parallel course in the same animal (Fig. 1). However, differences were observed between the animals in the times when their bilirubin and phospholipid levels reached a maximum. In some dogs the maximum was observed on the 10th-14th day after operation, and in others on the 30th day or later.

In later stages of the disease, and particularly just before death (sacrifice) of the animals, as well as a fall in the bilirubin level, the total phosphorus and phospholipids of the blood serum also were reduced, often below the control level.

It is clear from Fig. 2 that, by comparison with the controls, the increase in radioactivity of the blood serum after administration of radioactive phosphorus to the animals was slowed in the dogs with jaundice. The maximum of the serum radioactivity was shifted toward later times. The subsequent decrease in the serum radioactivity took place more slowly than in the healthy dogs. These changes in absorption and utilization of P^{32} increased with an increase in the time after formation of obstruction to the flow of bile.

The curves of serum radioactivity after intravenous injection of P^{32} into healthy dogs and dogs with jaundice likewise did not coincide. In the dogs with jaundice the serum radioactivity fell more slowly than in the healthy dogs. This difference began to appear 3 h after injection of phosphate and may be explained not only by the slower absorption of P^{32} from the blood, but also by the increased arrival of P^{32}-labeled compounds from the organs in the blood stream at this time. This is also suggested by the fact that near the end of the animals' life, when irreversible changes had begun in the liver, the curves of serum radioactivity in such animals altered their appearance again: the serum radioactivity was reduced in the late stages after injection of P^{32}.

Investigation of the specific activity of the serum phospholipids 4 and 24 h after oral administration of P^{32} revealed a statisfically significant difference between the healthy and sick animals. The specific activity was higher in the latter. For example, after 24 h the specific activity of the serum phospholipids in the control series averaged 1.4, compared with 2.2 in the experimental series ($P < 0.01$). This confirms the hypothesis put forward earlier by K. S. Zamychkina and co-workers, that in obstructive jaundice the biliary phospholipids enter the blood stream and circulate in it, thereby causing hyperphospholipemia [6, 9, 10].

The increased specific activity of the serum phospholipids is explained by the fact that, as Zamychkina and Grodzenskii found, the phospholipids in the dog's bile in the first 24 h after administration of P^{32} have a higher specific activity than the serum phospholipids, so that if the biliary phospholipids enter the blood stream, the specific activity of the phospholipids contained in the blood must therefore rise [11, 12]. The absence of this effect in the later periods after the operation was the result of advanced damage to the liver caused by prolonged stasis of bile.

In dogs with obstructive jaundice, a decrease in the rate of absorption of radioactive phosphorus from the intestine is thus observed and persists throughout the investigation. After intravenous injection of P^{32} the radioactivity of the blood in the dogs with jaundice falls more slowly than in healthy animals. The

specific activity of the phospholipids circulating in the blood plasma in the early periods after operation is increased, while in the later periods it falls because of developing liver damage.

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