RELATIONSHIP BETWEEN THE RATES OF SYNTHESIS OF THE PHOSPHOLIPIDS OF THE BILE AND BLOOD IN THE LIVER AFFECTED BY A PATHOLOGICAL PROCESS

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The authors have previously shown [5] that during the development of a pathological process (hepatitis without jaundice) in the liver, the rate of synthesis of the phospholipids secreted with the bile in the liver is considerably lowered. With a disturbance of the normal circulation of bile in dogs with a fistula into the gall bladder and with ligation of the bile duct (leading to partial loss of bile) these changes were still more severe.

In the present investigation, the rate of synthesis of the phospholipids of the blood was studied in the same experimental conditions. These investigations were to provide additional material for determining the relationships between the phospholipids of the bile and the blood [6-10].

EXPERIMENTAL METHOD

The conduct of the experiments and the technique of the biochemical investigation of the bile and blood were described in the previous communication [5]. Besides the total phosphorus, the lipid phosphorus and their radioactivity were determined in the blood serum; the specific activity of these fractions was calculated by the method described previously [2].

EXPERIMENTAL RESULTS

As indicated in the previous communication [5], the incorporation of P^{32} into the phospholipids of the bile took place during the first few hours after its administration into the alimentary tract. In the same experiment the P^{32} was detected at later periods in the phospholipids of the serum. The specific activity of this fraction reached its maximal level (1.4-1.8) after 18-20 h.

In contrast to the corresponding indices of the bile, the values of the specific activity of the total phosphorus of the blood serum and of the phospholipids from it (taken 24 h after administration of P^{32}) changed only insignificantly throughout the period of investigation in a given animal.

The concentration of total and lipid phosphorus in the blood serum taken on the same day as the P^{32} was given and on the next day varied within small limits throughout the period of investigation. Only in some dogs, mostly those with a fistula into the gall bladder and with ligation of the bile duct, the concentration of total phosphorus fell sharply a few days before death, for example form 14 to 8 mg %, while the phosphorus of the phospholipids fell correspondingly from 10 to 5 mg %. In this case, cirrhosis of the liver and ascites were often found at autopsy.

The values of the specific activity of the phosphorus of the bile and the phosphorus of the serum phospholipids of the dogs Ryzhik and Karo 24 h after administration of P^{32} at various times after the operation are given in Fig. 1. It follows from these results that the specific activities of the bile fell steadily whereas the specific activities of the serum phospholipids remained unchanged.

It is also clear from Fig. 1 that in the early periods after the operation, the specific activity of the bile phospholipids was considerably higher than the specific activity of the blood serum, whereas in the late stages after the operation, the activity in the bile was lower. Similar results were obtained in the other dogs, including those in which hepatitis developed as the result of infection from the biliary tract and also as a result of toxicosis caused by administration of carbon tetrachloride.

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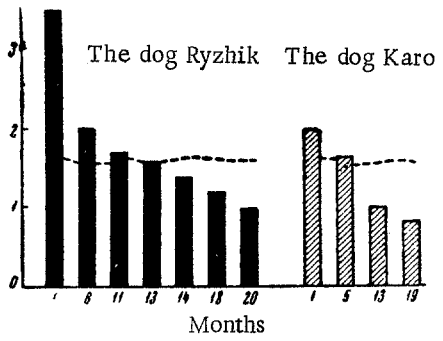

Fig. 1. Dynamics of changes in specific activities of phospholipids of the bile and phospholipids of the blood serum in dogs at different times after operation. Here and in Figs. 2 and 3: black columns – without ligation of the common bile ducts; shaded columns – with ligation of the ducts; along the axis of abscissas – times after operation (in months); along the axis of ordinates – specific activities.

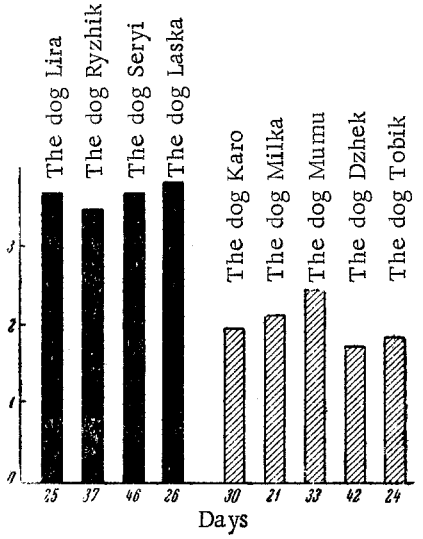

Fig. 2. Specific activities of phospholipids of the bile obtained from dogs 24 h after administration of P^{32} on the 20th-40th day after operation.

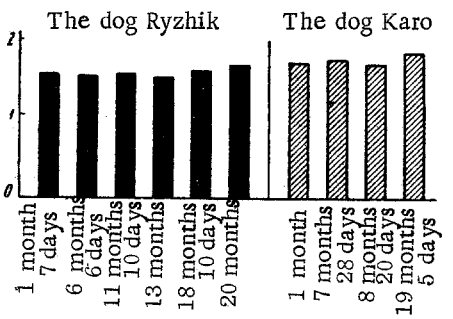

Fig. 3. Specific activities of phospholipids of the blood serum of dogs at various times after the operation.

The specific activities of the bile phospholipids in the dogs with ligation of the bile ducts changed sooner after the operation than in the dogs without ligation of the bile ducts. At the same time, the specific activities of the serum phospholipids of both groups of dogs showed only very slight variations both in the early and the late periods after the operation (Figs. 2 and 3).

The steady decrease in the specific activities of the dog's bile in the course of development of the pathological process in the liver, while the specific activities of the phospholipids of the blood serum remained at the same level, indicates that the pathways of biosynthesis of the lecithin of the bile and blood in the liver are different.

The results obtained may be useful for explaining the pathogenesis of the hyperphospholipemia in mechanical jaundice. Different opinions have been expressed in the literature regarding the nature of the hyperphospholipemia in jaundice. Some authors believe that hyperphospholipemia in acute hepatitis with jaundice is the result of the increased synthesis of the phospholipids of the blood in the liver. Others consider that the hyperphospholipemia is the result of a disturbance of the lipid metabolism in the liver (inability of the liver to utilize the lecithin of the blood). This view became widespread because until very recently it was assumed that the lecithin of the bile is derived from the lecithin of the blood.

The results described above do not agree with this view. As reported earlier [3,4], investigations using the method of isotope dilution showed that when P^{32}-labeled bile phospholipids are introduced into the alimentary tract, their direct transfer to the newly secreted bile is not observed. Similar results have been obtained by other workers [7,10].

The authors' earlier investigations showed that, in patients with parenchymatous hepatitis accompanied by jaundice, the concentration of total phosphorus and of phosphorus of phospholipids in the blood serum rises [2]. In rabbits, after ligation of the bile duct in the period of development of jaundice the concentration of total phosphorus in the serum and the concentration of phosphorus of phospholipids from the serum are increased. Several days after ligation of the bile duct, a relatively constant level of phospholipids and of bilirubin was maintained in the blood of some rabbits. A few days before death of the animal, the concentration of these substances in the blood fell. With severe liver damage (cirrhosis) no hyperphospholipemia was observed [2].

On the basis of the view that the biosynthesis of the phospholipids of the blood and bile in the liver takes place as two independent processes, it may be concluded that the hyperphospholipemia in jaundice of any origin is the result of flooding of the blood with bile phospholipids. The absence of hyperphospholipemia when severe lesions of the liver are present is associated with the marked inhibition of synthesis of the bile phospholipids in the liver.

Consequently, the hyperphospholipemia in jaundice is not dependent on whatever creates the obstruction to the entry of phospholipids from the blood into the bile but, on the contrary, on the inflow of phospholipids from the bile into the blood. This conclusion may be drawn from present observation on the dogs in which, because of liver damage, "white bile" appeared, not containing bilirubin or phospholipids. If an obstruction to the outflow of bile was created in such dogs, they did not develop hyperphospholipemia as in the case of the animals with cirrhosis of the liver.

Evidently, the level of the phospholipids in the blood in jaundice may fall not only as a result of restoration of the outflow of bile from the liver into the intestine, but also during the period of deterioration of the functional state of the liver and of its bile-forming capacity, when the bile synthesized in the organ becomes poorer and poorer in phospholipids.

It may thus be concluded from the results of these investigations that the rate of incorporation of P^{32} into the lecithin of the bile and blood is not the same. The incorporation of P^{32} into the lecithin of the bile takes place during the first few hours after its administration by mouth in the form of sodium phosphate, while its incorporation into the lecithin of the blood serum takes place 18-20 h later. In the period of development of hepatitis without jaundice in the dogs, a gradual fall in the specific activities of the bile is observed. The rate of incorporation of P^{32} into the lecithin of the bile also falls. Meanwhile the specific activity of the lecithin of the blood serum shows only very slight variations throughout the period of investigation.

Because the rate of synthesis of the phospholipids of the bile in the liver is dependent on the functional state of this organ, the influence of disturbances of the bile-forming function of the liver on the level of the hyperphospholipemia in jaundice can be understood.

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