WHITE BILE AS A SECRETION OF THE LIVER CELLS

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Experiments on animals with a fistula of the gall bladder and with or without ligation of the bile duct show that white bile appears in response to feeding the dog with egg yolk mixed with milk and water. Such bile contains no bilirubin and a reduced content of certain other bile components, notably phospholipids and sulfur-containing substances.

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In earlier investigations [2-4] I showed that a distinct parallel is found between the concentrations of individual components of bile. Concentrations of these components may be either increased or decreased by means of foods or pharmacological agents. For instance, if an excess of glucose or adrenalin is given, the concentration of phospholipids and bilirubin in the bile of dogs increases. Conversely, administration of insulin sharply reduces the content of phospholipids and bilirubin is the bile.

Very demonstrative changes in the bile chemistry follow feeding of dogs with peptone, meat, meat broth, or egg yolks. In a series of experiments along these lines after 2-3 h of secretion an almost colorless bile was formed, with a negligible content of bilirubin, phosphorus, and solids. These changes were reversible. There are indications in the literature that colorless bile is produced by dogs in response to certain food stimuli [1]. It follows that, in contrast to the phenomenon of white bile observed by clinicians in diseases of the biliary tract, bile of unusual composition may also be found in physiological states if the activity of the liver cells is modified.

It was therefore decided to make a detailed study of the white bile phenomenon in an attempt to discover the mechanism of its appearance. An isotope method was used.

EXPERIMENTAL METHOD AND RESULTS

Experiments were carried out on dogs with a gall bladder fistula, and with or without ligation of the common bile duct. On the day before the experiment the dogs were given methionine-S^{35} mixed with milk and water. On the day of the experiment bile was collected from the fasting animals for 3-4 h. The dogs were then given the yolks of 5-10 eggs mixed with milk (100 ml) and water (50 ml) and the collection of bile continued for the next 5 h. The volume of bile and its radioactivity were measured. The level of radioactivity of the fasting bile 24 h after administration of methionine-S^{35} varied within narrow limits. On the subsequent days the radioactivity of the bile gradually diminished.

In some experimental dogs feeding with egg yolks caused considerable changes in the composition of the bile. The color of the bile became weaker or completely disappeared, and the bilirubin concentration fell almost to 0. Secretion of colorless bile continued for 1.5-2.5 h, after which its color was gradually restored, although at the end of the experiment (5-6 h later), the bile was still weaker in color than before administration of egg yolks to the animals. The radioactivity of the bile resulting from administration of methionine-S^{35} the previous day was absent in the period of secretion of colorless bile and returned when the bile again became colored (Fig. 1). The volume of bile varied within the limits observed in control experiments, or was very slightly increased. This increase precludes any explanation of the disappearance of color and labeled compounds from the bile by its dilution.

During the period of secretion of colorless, nonradioactive bile the level of radioactivity of the blood serum and of the serum proteins remained unchanged.

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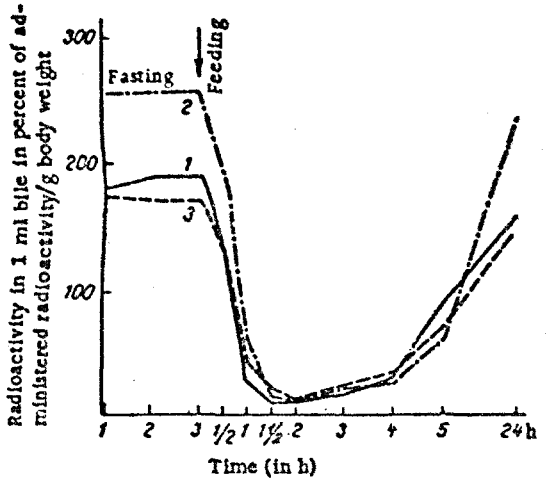

Fig. 1

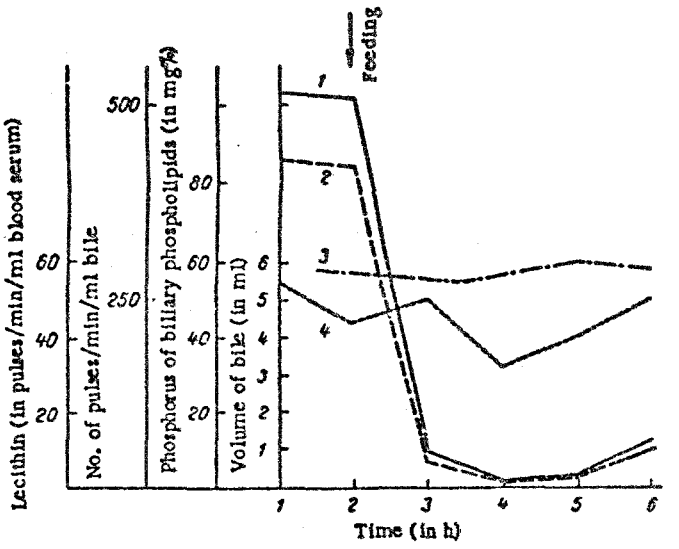

Fig. 2

Fig. 1. Radioactivity of 1 ml bile (in % of administered dose/g body weight). Determination 24 h after administration of methionine-S^{35} to fasting animals and feeding with egg yolks. 1) Dog Zhuk; 2) dog Tobik; 3) dog Tikhii. During operations on the dogs Zhuk and Tikhii the bile duct was not ligated, while the duct of the dog Tobik was ligated.

Fig. 2. Results of experiments on the dog Tikhii. 1) Number of pulses/min/ml bile; 2) phosphorus of biliary phospholipids; 3) number of pulses/min in phospholipids from 1 ml blood serum; 4) volume of bile.

The radioactive sulfur of methionine could exist in the bile in the composition of protein, taurocholic acid, or sulfate. The radioactive components disappeared from the bile secreted in response to administration of egg yolks into the alimentary tract. This suggests the possibility of a sudden but temporary change in the chemical composition of the bile under physiological conditions, and, moreover, under conditions when no changes took place in the chemical composition of the blood according to the indices chosen.

Similar experiments were performed with radioactive phosphorus. On the day before the experiment the dogs with a gall bladder fistula were given a solution of radioactive phosphorus ($Na_2HP^{32}O_4$) to drink. After 24 h and later the whole of the radioactivity of the bile was confined to phospholipids of lecithin type [4, 5]. On the day of the experiment bile was collected for 3-4 h from the fasting animals. Egg yolks mixed with milk were then given. If colorless bile subsequently appeared, no lecithin could be detected in it either chemically or radiometrically. With the appearance of colored bile, radioactive lecithin was again observed in it. However, at the end of the 6th hour of the experiment the bile-forming function of the liver remained abnormal. The lecithin content and radioactivity of the bile were less than in the bile collected initially from the fasting animals. In one experiment, for example, the radioactivity of phospholipids was 500 pulses/min/ml, falling to 60 pulses/min/ml soon after feeding with egg yolks, and 1.5 h after no radioactive phospholipids whatever could be found in the bile. Subsequently the radioactivity gradually returned.

Under these experimental conditions the secretion of white bile was a temporary process and normal bile formation was soon restored. The blood plasma could not have been the immediate source of origin of the white bile, for in contrast to bile the radioactivity level in the blood serum remained unchanged throughout the experiment. The results of an experiment on the dog Tikhii are given in Fig. 2. Similar results were obtained in experiments on various other dogs.

The great importance of the physiological state of the liver for the white bile phenomenon is also apparent from the results of the next series of experiments. In dogs with hepatitis caused by ascending infection from the biliary tract, or by poisoning with carbon tetrachloride, atophan, and other substances, the secretion of a faintly colored, or sometimes colorless bile was often observed. If the dogs were given methionine-S^{35} or P^{32} during this period, secretion of radioactive products in the bile was low. Synthesis

of the biliary components was apparently disturbed. This process was irreversible. At necropsy of the animals cirrhosis of the liver was often observed, sometimes complicated with ascites.

These results show that white bile may be secreted in response to a strictly physiological stimulus such as food of a certain type. In this case the secretion of white bile could be the result of functional changes in the liver, for it was of short duration and the bile soon regained its characteristic features. The origin of this physiological white bile is evidently intrahepatic. In the presence of severe liver disease, white bile also appears, but in this case the process is irreversible and the animal usually dies soon after. However, in these circumstances also the white bile is intrahepatic in origin.

As we know from the literature [6-9], clinicians more frequently encounter white bile during operations on the biliary tract for obstruction by tumor calculi. White bile of this type is a secretion of the cells lining the biliary tract and has nothing in common with true bile. However, in clinical conditions from time to time white bile of intrahepatic origin is seen at operations, and is a product of liver cells damaged by a pathological process (paracholia). It may be that such cases are more common than has been suspected.

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