

EXTERNAL SECRETORY ACTIVITY OF THE LIVER  
AND PERIODIC BILE SECRETION IN DOGS  
WITH ACUTE EXPERIMENTAL PANCREATITIS

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Acute experimental pancreatitis in dogs induces considerable changes in the bile-forming function of the liver and the activity of the biliary apparatus. The disturbances of bile formation are characterized by a reduction in the quantity of bile and in its concentration of the lipid complex, cholic acid, and phospholipids during the first 5-10 days from the beginning of the disease, followed by an increase in the quantity of bile and an increase in or return to the normal concentration of the above-mentioned components in it (11-20 days). Their total content secreted during the experiment increases considerably at these times. The normal levels are restored by the 30th-40th day. The disturbance of bile secretion is expressed as absence of periodic fluctuations in the early stages. Periodic bile secretion may also be absent later, despite restoration of normal periodic movements. The degree and duration of the disturbances of bile formation and secretion depend on the clinical course of the disease.

Considering data in the literature on combined involvement of organs of the hepato-pancreatico-duodenal system in pathological processes [3, 7] and observations of frequent morphological and functional changes in the liver in acute pancreatitis [1, 5, 8, 10-12], it was considered important to study experimentally the character of the influence of this disease on bile formation and secretion.

EXPERIMENTAL METHOD

Experiments were carried out on three groups of mongrel dogs weighing 12-16 kg. Of the three dogs in group 1, two had fistulas of the cystic duct in conjunction with cholecystectomy by Nesterin's method [9] and one dog had a fistula of the gall bladder by Schiff's method. All the dogs in addition had duodenal fistulas. The external secretory function of the liver was estimated from the concentration of the lipid complex, determined quantitatively by an electrophoretic method [9], of cholic acid (by the method of Reinhold and Wilson [13]), and phospholipids (as total phosphorus [2], determined by the method of Fiske and Subbarow in the modification of Zamychkina and Grodzenskii [4]), in the bile.

In the nine dogs of group 2, periodic bile secretion was studied. Recordings were made of the periodic motor activity of the stomach and intestine and of the volume of periodic secretion escaping from the fistulas of the duodenum (seven dogs) and jejunum (two dogs), after which the concentration of the lipid complex and cholic acid was determined in the secretion by the methods mentioned above.

In the three dogs of group 3 with a fistula of the cystic duct (one dog) and fistulas of the gall bladder (two dogs), a control laparotomy was performed to discover the effect of the operation and the postoperative program on the external secretory function of the liver and on bile secretion.

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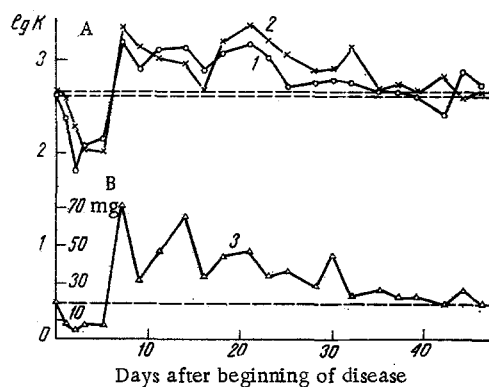


Fig. 1

Fig. 1. Dynamics of changes in content of lipid complex (1), cholic acid (2), and total phosphorus (3) in 3-hourly portions of bile from dogs of group 1. Graph A—logarithmic scale; graph B—numerical scale.

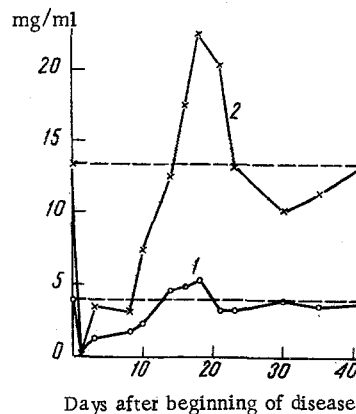


Fig. 2

Fig. 2. Dynamics of changes in concentration of lipid complex (1) and cholic acid (2) in duodenal secretion of dog of group 2.

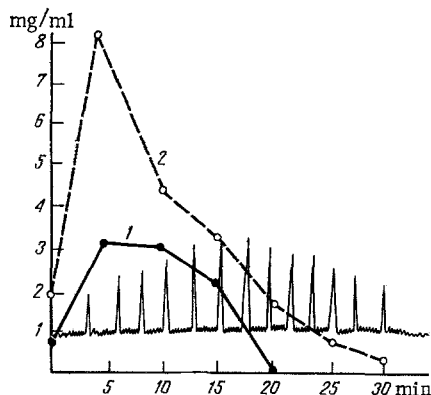


Fig. 3. Changes in concentration of lipid complex (1) and cholic acid (2) in duodenal secretion of dog of group 2 during period of work of the stomach.

After the initial control investigations acute pancreatitis was induced in the dogs of groups 1 and 2 by injecting bile into the pancreatic duct. The dogs of group 1 received an injection of bile (0.5 ml/kg) obtained from them the previous day, those of group 2 received bile taken at laparotomy from the gall bladder (four dogs received 0.5 ml/kg, five dogs received 0.3 ml/kg). All dogs in group 1 survived; of the four dogs of group 2 receiving 0.5 ml/kg bile one survived, while four of the five dogs receiving 0.3 ml/kg bile survived.

After the operation all the dogs were kept under specified conditions, receiving neither food nor water, with the intestinal fistula remaining open for 48 h, and with daily subcutaneous injection of physiological saline in a dose of 0.5 liter per diem. The existence of pancreatitis in the surviving animals was confirmed by their clinical condition, a significant increase in the serum amylase level, and the results of pathological and histological investigations.

## EXPERIMENTAL RESULTS

The control laparotomy led to a decrease in the quantity and concentration of components of the bile only for the first 2-3 days; on the 3rd-4th day no significant deviations of these parameters from the normal level were observed in the control animals.

Pancreatitis led to significant changes in the external secretory activity of the liver. In the dogs of group 1, phasic changes occurred in the quantity of bile and in the concentrations of lipid complex, cholic acid, and phospholipids in it. In the first 5-7 days from the beginning of the disease these indices fell, but later (10-14-20 days) the quantity of bile increased considerably in all dogs whereas the concentration of the components of the bile in one dog rose significantly, fluctuated in another, and returned to the normal level in a third dog at these times. However, when calculated as the quantity of bile obtained in an experiment lasting 3 h, a significant increase in the content of cholic acid, phospholipids, and lipid complex could be observed (Fig. 1). All these indices returned to normal 30-40 days after the beginning of the disease.

In three dogs of group 2, similar phasic changes occurred in the concentrations of lipid complex and cholic acid (Fig. 2) and in only one dog, after an initial decrease in the levels of these components of the bile during the first 5 days, did they return to normal, but then fall again by almost half. Normal values also were restored on the 26th-40th day from the beginning of the disease. In a dog with a particularly

severe clinical course, but surviving after injection of bile in a dose of 0.5 ml/kg, the concentration of these components of the bile remained low until the 5th month of the disease.

Disturbances (particularly marked if the clinical course of the disease was severe) in the normal ratios between cholic acid and the lipid complex were observed in the dogs of this group; with a high concentration of cholic acid the concentration of the lipid complex could be considerably reduced or it could be absent altogether, and vice versa, indicating serious disturbances of the bile-forming function of the liver.

Investigations of the periodic bile secretion in the absence of digestive activity in the dogs of group 2 showed that the highest concentration of the components of the bile in the periodic intestinal secretion occurred usually in the first 5-10 min after the beginning of a period of work of the stomach; the concentration then fell and reached zero at the end of the period of work of the stomach (Fig. 3).

In acute pancreatitis, secretion of bile into the duodenum in the first 5-7 days either was absent altogether or was constant and not periodic in character; in such cases the concentrations of the tested components of the bile were low. With restoration of periodic motor activity of the stomach the periodic bile secretion also was restored. However, if the clinical course of the disease was severe, bile secretion into the intestine was absent despite the recovery of periodic contractions of the stomach. In a dog surviving this form of pancreatitis, disturbances of bile secretion occurred until 5 months after the beginning of the disease. Secretion of bile into the intestine during the first month was found in only three of 15 experiments, whereas during the second month it was completely absent in two of the nine experiments and in the rest it accompanied 13 of the 15 periods of work recorded. In the third and fourth months of the disease bile secretion was absent altogether in two of the 12 experiments and was recorded in 18 of the 26 periods of work of the stomach studied. In the fifth month, normal secretion of bile into the intestine was restored in this dog.

Consequently, externally normal periodic activity of the stomach and intestine with the change to the chronic form of pancreatitis may take place simultaneously with essential disturbances in the composition of the periodic secretions.

These investigations thus revealed considerable disturbances of the bile-forming function of the liver and in the activity of the biliary system in dogs with acute pancreatitis. In conjunction with observations indicating severe disturbances of the external secretion of the pancreas and changes in the motor and enzyme-secreting function of the duodenum obtained in previous investigations in the writers' laboratory [6], these results suggest a combined lesion of all organs of the hepato-pancreatico-duodenal system in this disease. The mechanisms of the pathological changes affecting the system evidently involve both nervous and hormonal-humoral factors and they require further special study.

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