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ELASTASE ACTIVITY IN EXPERIMENTAL PANCREATITIS

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A most important role in the pathogenesis of acute pancreatitis is played by the pancreatic enzyme elastase, which occupies a special place among tissue proteolytic enzymes of animals and man in its ability to hydrolyze one of the most inert tissues of the body, the scleroprotein elastin.

Since the discovery of elastase [5], the pathobiochemical spectrum of its action has been widely studied. Elastase is characterized not only by a marked elastolytic effect [16] and a proteolytic action on hemoglobin, fibrin, and albumin [6], but also by a certain lipolytic activity [9, 13]. Accordingly, elastase may have a much more traumatic effect than trypsin, carboxypeptidase, and lipase [2, 6]. However, the results of investigation of the elastolytic activity of the blood in acute pancreatitis are contradictory, evidently because different methods were used to produce the pancreatitis and to determine elastase [6, 11, 12, 15]. Meanwhile, the problem of the inhibitory property of the blood relative to elastase and the mechanism of production of its inhibitor still remains unsolved [13, 16]. In particular, investigations [8, 10, 14] have revealed a marked fall in the elastase concentration in the general circulation compared with its concentration in the portal blood flow and an unchanged level of inhibitor in these systems. Furthermore, elastase is not inactivated in the pancreas when its concentration rises. The explanation of these phenomena may lie in the active role of the liver in the production of inhibitor and reduction of the elastolytic activity of the blood.

The object of this investigation was to study relations of elastase with its inhibitor in the blood and also with lactate dehydrogenase (LDH) isozymes, which reflect the state of the liver function during the development of acute pancreatitis.

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TABLE 1. Blood Elastase Activity (in μg/ml/min) in Experimental Pancreatitis (M ± m)

Experimental conditions	Initial value	Time of investigation, h			
		1	3	7	12
Pancreatitis	1,19±0,22 (n=16)	2,94±0,52* (n=11)	3,4±0,42* (n=11)	3,4±0,48* (n=8)	3,57±0,46* (n=4)
Control (n = 5)		0,96±0,5	0,94±0,55	1,02±0,54	1,47±0,28

*Here and in Table 2, changes statistically significant compared with initial values.

TABLE 2. Blood Level of Elastase Inhibitor (in μg/ml/min) in Experimental Pancreatitis (M ± m)

Experimental conditions	Initial value	Time of investigation, h			
		1	3	7	12
Pancreatitis	3,86±0,042 (n=16)	2,15±0,49* (n=11)	1,82±0,36* (n=11)	1,55±0,47* (n=8)	1,5±0,54* (n=4)
Control (n = 5)		4,19±0,53	3,88±0,78	3,74±0,82	3,50±0,50

EXPERIMENTAL METHOD

Experiments were carried out on 16 mongrel dogs of both sexes weighing 17-20 kg. The control group comprised five dogs. A model of pancreatitis was created in 11 animals by the commonly used method [4], by injecting autologous bile into the accessory pancreatic duct in a dose of 0.5 ml/kg body weight. Blood analyses were performed immediately after premedication (initial) and 1, 3, 7, and 12 h after induction of pancreatitis or laparotomy in the control group. Activity of elastase and its inhibitor was determined by the method in [12] and activity of LDH and its isozymes by the method in [13] in Yurkov's modification [3]. Unlike most other investigators, we considered that blood samples should be taken by catheterization of the right chambers of the heart and not the femoral veins, so as to eliminate the reducing effect of the lungs on pancreatic enzymes.

EXPERIMENTAL RESULTS

All the animals with experimental pancreatitis died after 6 to 14 h. At autopsy severe hemorrhagic pancreonecrosis was found. The pancreas was considerably enlarged with extensive confluent areas of hemorrhage, necrosis, and stains of steatonecrosis. The diagnosis of pancreonecrosis was confirmed histologically in all cases. The peritoneal cavity contained 150-350 ml of highly blood stained exudate and paresis of the stomach and small intestine and swelling of the liver were present. The direct cause of death was cardiopulmonary failure.

The results of investigation of blood elastase in animals of the control group and with experimental pancreatitis are given in Table 1.

The elastase concentration in the blood (Table 1) was increased as early as 1 h after induction of pancreatitis and reached a maximum 3 h after the beginning of the experiment; it remained at a level three times higher than initially until death of the animals. The blood elastase level in dogs of the control group remained virtually unchanged for 7 h and did not begin to rise until after 12 h.

The development of experimental pancreatitis was thus accompanied by a marked increase in the elastolytic activity of the blood, which may have been largely maintained by a fall in the inhibitory power of the blood. Data on the concentration of elastase inhibitor in the blood of dogs with experimental pancreatitis and animals of the control group are given in Table 2.

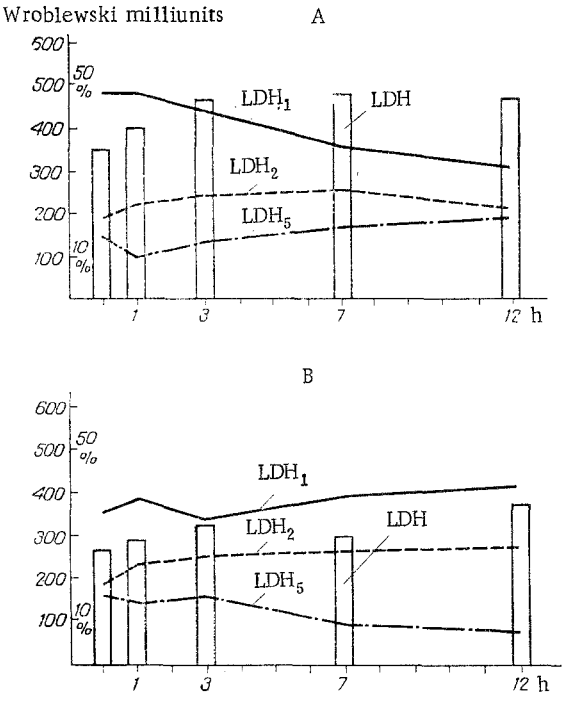

Fig. 1. Total LDH activity (in Wroblewski milliunits) and activity of its isozymes (in %) in the blood of dogs with experimental pancreatitis (A) and in the control (B). Abscissa, time of investigation (in h); ordinate: on left — total LDH (in Wroblewski milliunits), right — percentages of LDH fractions.

The results of determination of blood levels of elastase inhibitor indicate a steady decline in its concentration by 50% or more compared with the initial value and, correspondingly, with the increase in elastolytic activity during the development of experimental pancreatitis. These results differ from those of previous investigations [2] and they contradict the view [7] that elastase inhibitor prevents determination of elastase in the blood.

The fact that changes in the concentration of elastase and its inhibitor were opposite in direction suggests that their sources of production differ. An active role in the synthesis of elastase inhibitor is evidently played by the liver which, as an organ very rich in elastin, would soon suffer from the destructive action of elastase. In this investigation the state of the liverfunction was estimated by determination of LDH. The results of investigation of LDH during the development of pancreatitis are shown in Fig. 1. Analysis of activity of LDH and its isozymes showed that 1 h after induction of pancreatitis the total LDH level increased and this increase continued until the end of the experiment. It was accompanied by redistribution of LDH isozyme activity. The proportion of fraction 1 fell until the 3rd hour of development of pancreatitis, whereas the proportion of fraction 2 increased after the lst hour. The proportion of fraction 4 and, in particular, of fraction 5 increased considerably toward the end of the experiment. These data are similar to those obtained previously [1] and they reflect the development of a serum biochemical syndrome of liver cytolysis.

The elastolytic activity thus rises progressively in experimental pancreatitis and shows no tendency to fall spontaneously as a result of depression of the inhibitory power of the blood. Disturbance of liver function can be regarded as one cause of the decrease in production of elastase inhibitor.

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