Pancreaticoduodenal Lymph Flow and Lipase Activity in Acute Experimental Pancreatitis

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Activity of the pancreatic digestive enzymes in thoracic duct lymph has been shown to increase in man after pancreatic stimulation by secretin (3, 5), impaired passage of the pancreatic juice into the duodenum (5), surgical trauma to the pancreas (5) and in the dog following ligation of the excretory ducts of the pancreas (4, 13, 16, 17, 19), enhancement of pancreatic secretion (1, 10, 19, 23) and injection of bile (6, 7, 18, 19) and trypsin (20, 21) into the pancreas. Thus, pancreatic secretion has a lymphatic pathway through which enzymes are continuously delivered into the thoracic duct.

Lymphatic drainage of pancreatic digestive enzymes is implicated in the pathogenesis of acute pancreatic necrosis, as occlusion of the thoracic duct and secretory ducts of the pancreas in dogs leads to necrosis of this organ and augments the extension of the necrosis of adipose tissue adjacent to the pancreas (16). It has also been suggested that lymphatic drainage from the thoracic duct is of therapeutic benefit in experimental acute pancreatitis (20, 21) as well as in acute (3) and subacute (4) and chronic (3) pancreatitis in man. It has been shown that pH of the pancreatic tissue in the rabbit is higher than in other tissues (8).

Determination of thoracic duct lymph flow and enzyme activity allows only indirect conclusions to be drawn as to the changes in pancreatic lymph flow in acute pancreatitis. Accordingly in the present work, the values of acid-base balance in the pancreaticoduodenal lymph were studied in dogs with and without anesthesia, as well as the effect of acute pancreatitis on flow and lipase activity of pancreaticoduodenal lymph.

Materials and Methods

Thirty-two mongrel dogs of both sexes, weighing 14 kg on the average, were fed with meat and were divided into three groups.

(i) In 12 dogs, the femoral region was locally anaesthetized and femoral arterial and venous blood samples were withdrawn anaerobically for determination of acid-base balance.

The dogs (i; ii; iii) were anaesthetized with chloralose (0,1 g/kg body weight), after food deprivation for 16 hours, and following tracheal intubation, spontaneous inhalation of oxygen was allowed by a Dräger Romulus anesthesia apparatus. At laparotomy, a polyethylene cannula was inserted into the duct of Santorini. The duodenal portion of the superior pancreaticoduodenal vein was ligated and a polyethylene cannula was intro-

duced through the stump of the vein into the main trunk. A thread was passed under the proximal segment of the vein where it enters the splenic vein. During withdrawal of blood samples, this thread was gently pulled. The pancreaticoduodenal lymph vessels were cannulated with polyethylene tubes. These lymphatics drained a 3 to 5 cm segment of the pancreas representing 1/3 to 2/5 part of the organ including the portion of the pancreatic body lying adjacent to the ascending part of the duodenum, and the area near the tail. The ascending part of the duodenum was also drained by these lymphatics. The thoracic duct was cannulated in the neck (i). Arterial blood samples were withdrawn from the femoral artery; the contralateral artery serving for blood pressure measurement by a mercury manometer.

(i) In 12 animals subjected to the study of acid-base balance, determinations were repeated between the 60th and 90th min of chloralose anaesthesia. Blood samples were withdrawn from the femoral artery and pancreaticoduodenal vein, and lymph samples from the thoracic duct and pancreaticoduodenal lymphatics. All blood and lymph samples were analysed with a Micro-Astrup equipment (Radiometer, Copenhagen).

(ii) In 8 dogs, 8 to 10 ml of bile obtained from the same animal, and (iii) in 12 dogs the same amount of sunflower oil were injected into the pancreas at a pressure higher than 50 cm of water, through the cannulated Santorini's duct. Pancreaticoduodenal lymph was collected over a period of 45 min prior to the intrapancreatic injection of bile or sunflower oil, and for 70 to 90 min thereafter, into heparinized tubes kept in an icy bath. Lymph flow was computed for 45 min. At the end of the lymph collection periods, blood was withdrawn from the pancreaticoduodenal vein. Lipase activity in blood and lymph was assessed by the method of *Weber* (25).

Table 1 Mean pH, base excess (BE), standard bicarbonate (St. bicarb.) and pCO_2 values in blood and lymph determined with the Micro-Astrup equipment in dogs before and after anesthesia.

	Unanesthetized	Chloralose anesthesia			
	pH	pH	BE mEq/l	St. bicarb. mEq/l	pCO_2 mm Hg
Femoral artery	7.28 ± 0.009[1] (7)	7.16 ± 0.018 (12)	−11.00 ± 1.45	16.72 ± 0.73	77.09 ± 12.00
Femoral vein	7.22 ± 0.008 (12)	–	–	–	–
Pancreaticoduodenal vein	–	7.14 ± 0.019 (12)	−13.42 ± 1.28	16.08 ± 0.51	92.16 ± 12.00
Pancreaticoduodenal lymph	–	7.39 ± 0.015[2] (12)	−4.85 ± 1.98[3]	20.45 ± 1.50[3]	31.80 ± 3.10
Thor. duct. lymph	–	7.22 ± 0.23 (7)	−1.83 (3)	22.83 (3)	98 (3)

[1] mean ± S.E.M.; [2] $p < 0.001$; [3] $p < 0.05$; () = number of dogs.

If lymph from the pancreaticoduodenal lymphatics was chylous, or arterial blood pressure fell below 70 mm Hg, the animal was excluded from the study.

At the end of lymph collection periods, in the 12 dogs without pancreatitis (i) and in some of the treated with autologous bile (ii), 3 to 4 ml of Evans-blue were injected into the pancreas, via the cannulated Santorini's duct. Lymphatics draining the pancreas rapidly stained with the dye. Following intraductular injection of bile pancreaticoduodenal lymphatics stained yellowish, indicating that the collected lymph in fact was derived from the pancreas. Biopsy specimens were taken from the pancreas for routine histological examination to verify acute pancreatitis.

Results of measurements pertaining to acid-base balance (i) were evaluated by variance analysis, while the data concerning lymph flow and lipase activity (ii, iii) were analysed by Student's t-test.

Results

Bicarbonate level and pH of the pancreaticoduodenal lymph was higher, while pCO_2 lower than the same parameters in arterial ($P < 0.05$) and venous ($P < 0.01$) blood obtained from the same dog while awake and in arterial blood and thoracic duct lymph obtained during anesthesia (Table 1). Pancreaticoduodenal lymph flow was 0.03 ml/min and flow was not affected by intrapancreatic injection of bile but was significantly decreased by sunflower oil (Table 2). Lipase activity measured in the pancreaticoduodenal lymph derived from the intact pancreas was 300 to 400 IU/1,000 ml, while in pancreaticoduodenal venous effluent it was 100 to 250 IU/1,000 ml of plasma. Injection of bile caused an almost tenfold increase of activity both in lymph and plasma, the average value in lymph being statistically significantly higher than in the plasma ($P < 0,05$). Oil increased lipase activity in blood plasma about 3 times (Table 3). Bile as well as sunflower oil caused gross pancreatic edema, and eventually acute necrosis of the gland (Fig. 1).

Table 2 Mean pancreaticoduodenal lymph flow (ml per 45 min) in dogs after intraductal injection of bile and sunflower oil.

Treatment	Before	After
Bile	1.29 ± 0.24[1] (8)	1.09 ± 0.25 (8)
Oil	1.35 ± 0.14 (12)	0.69 ± 0.11[2] (12)

[1] mean ± S.E.M.; [2] $p < 0.01$; () = number of dogs.

Table 3 Mean lipase activity (IU/1000 ml) in pancreaticoduodenal lymph and venous plasma in dogs after intraductal injection of bile and sunflower oil.

Treatment	Before				After			
	Lymph		Blood plasma		Lymph		Blood plasma	
Bile	410 ± 164[1]	(6)	115 ± 95	(6)	4601 ± 1089[3,4]	(5)	1167 ± 184[2]	(5)
Oil	285 ± 92	(5)	247 ± 124	(6)	413 ± 92	(5)	818 ± 182[3]	(6)

[1] mean ± S.E.M.; [2] $p < 0.01$; [3,4] $p < 0.05$; () = number of dogs.

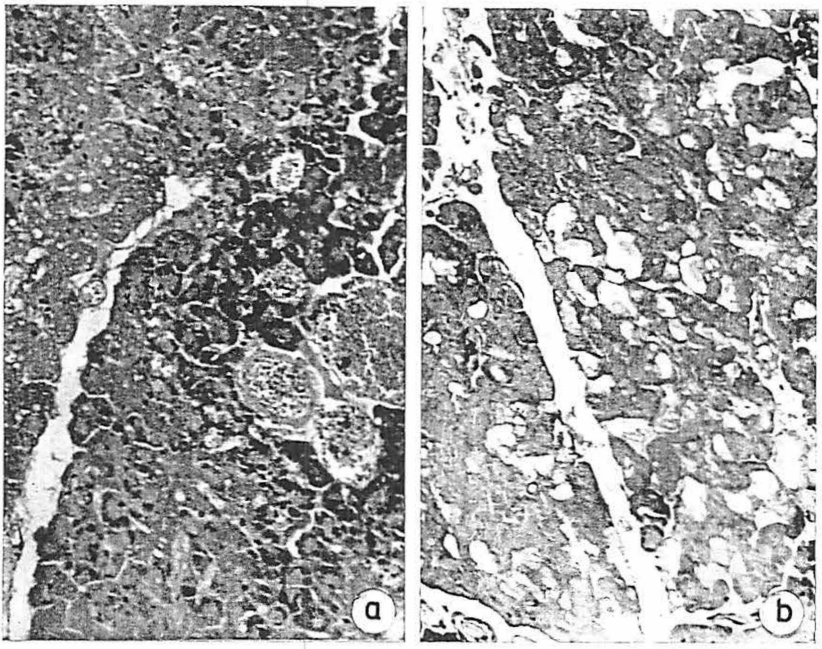

Fig. 1 Microphotogramm showing typical histological changes of bile-induced (a) and sunflower oil-induced (b) acute pancreatitis (haematoxylin-eosin; ×160): Extensive acinar necrosis is present 90 minutes after intraductal injection.

Discussion

The high pH and bicarbonate level in pancreaticoduodenal lymph indicates that lymph thus obtained was indeed derived from the pancreas. In the dog (9) or in the rabbit (8), the pH of the pancreas is higher than that of other tissues.

This finding is most likely attributable to diffusion of bicarbonate from the excretory ducts to the interstitium and further into the lymph.

Injection of bile into the pancreas enhanced the activity of lipase in pancreaticoduodenal lymph and venous blood. Since lipase activity in the lymph increased to values significantly higher than those found in plasma it appears that increased activity of digestive enzymes in thoracic duct lymph following the intraductal injection of bile is of pancreatic, and not of hepatic or jejunal origin (22). In contrast to the observations of others (6, 20, 21) where intraductal injection of bile or trypsin augments the rate of lymph flow from the thoracic duct, the present experiments with intraductal bile injection failed to enhance pancreaticoduodenal lymph flow.

Sunflower oil diminishes pancreaticoduodenal lymph flow. Oil droplets may have obstructed the lymphatics (24) and in our experience lymph flow is also decreased by subsequent necrosis. Absence of a measurable increase in lipase activity of pancreaticoduodenal lymph in the presence of intracellular lipolysis induced by the oil, is most likely due to rapid destruction of acinar cells (3a, 15). Sunflower oil significantly de-

creases pancreatic tissue lipase activity within an hour after administration (14) Increase in blood lipase activity observed after injection of oil probably results from gross outflow of lipase into blood, preceding rapid necrosis of the parenchyma.

Drainage of thoracic duct lymph through a fistula has been found to reduce toxic symptoms accompanying acute pancreatitis (3, 4, 20, 21), probably by diversion of lymph rich in toxic material and enzymes.

However several facts have to be considered when applying this method as a therapeutic measure in acute pancreatitis. If acute pancreatitis is caused by biliary reflux, thoracic duct drainage will be of benefit only if the time lag between reflux and drainage is not longer than a few hours. 24 hours after injection of bile acid into the pancreas the rate of protein synthesis is already substantially reduced (11). Thus at this time there is only an insignificant outflow of enzymes into the lymph. Furthermore, if acute pancreatitis is evoked by reflux of chyme with high triglyceride concentration (12), thoracic duct drainage would not be expected to have an ameliorating effect as pancreatic necrosis is rapid, and the amount of enzymes delivered into the lymph is insignificant even in the early stage of acute pancreatitis.

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Summary

The pH of the pancreaticoduodenal lymph was higher than that in arterial blood obtained from the same dog.

Injection of bile into the pancreas of dogs via the cannulated duct of Santorini increases lipase activity to a higher value in pancreaticoduodenal lymph than in pancreatic venous plasma without change in pancreaticoduodenal lymph flow. Injection of sunflower oil increases activity of lipase in pancreaticoduodenal venous blood plasma but not in pancreaticoduodenal lymph, as pancreaticoduodenal lymph flow diminishes.

These data suggest that thoracic duct lymph drainage may be of therapeutic value in the early stage of acute pancreatitis caused by reflux bile.

Lymphatic drainage is not likely to be beneficial in advanced stages of acute pancreatitis from biliary reflux when pancreatic protein synthesis is impaired, and not in pancreatic self-digestion from reflux of chyme ,as the amount of enzymes delivered into the lymph is minimal.

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Comparative Studies of Lymph and Lymphocytes of the Thoracic Duct and Right Lymphatic Duct I. Normal Dogs*

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Introduction

The thoracic duct drains principally the abdominal viscera and lower extremities, the left upper limb and left side of the head and neck, while the right lymphatic duct drains most of the lungs, serous cavities, right upper extremities and right side of the head and neck.

A comparison of the two systems was made by the simultaneous drainage of lymph from the thoracic duct and right duct which was collected hourly for 5 hours. The purpose of the experiments was to study the rate of flow, lymphocyte content and output, morphologic types of cells and electrophoretic differences in the supernatant fluid of lymph from the two largest lymph systems in the body.

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