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The Role of Lymph Nodes in Pancreatic Edema

M. Papp, B. Varga and G.B. Makara

Institute of Experimental Medicine, Hungarian Academy of Sciences, Budapest, Hungary

Summary

The pressure in the afferent lymphatic of the in situ perfused peripancreatic (periportal) lymph node of dogs rises with the rate of fluid infusion. A 10 min infusion of 500 ml physiological saline into the superior pancreato-duodenal artery resulted in gross edema of the pancreas. The lymph flow from the cannulated pancreato-duodenal lymphatic and the pressure in the non-transected pancreato-duodenal lymphatics increased. The rise in pancreato-duodenal lymphatic pressure during the intra-arterial infusion was in excess of that observed in either the thoracic duct or the internal jugular vein. Resistance at the peripancreatic lymph nodes to pancreato-duodenal lymph flow may thus be a significant contributing factor in the development of pancreatic edema.

The significance of prelymphatic insufficiency of the intrapancreatic interstitial fluid movement in the development of pancreatic edema is discussed.

The lymphatic pressure in a limb is significantly increased during its active and passive motion (1, 2). The pressure in the afferent lymphatics varies with the rate of perfusion of the tissues that they drain (3, 4). The lymph nodes resist the flow of lymph.

In the early phase of the development of dextran-induced edema of the hindlimb, edema appeared in the popliteal lymph nodes and adjacent tissues. After edema had developed, outflow of lymph from the lumbar lymphatic trunk draining the hindlimbs increased (5). A common mechanism responsible for all the above changes might be the resistance of the lymph nodes to the lymph flow.

Acute serous pancreatitis, produced by obstruction of the pancreatic excretory ducts (6, 7), may often be reversible. Edema of the pancreas may also result from increased capillary filtration. In either case, the pancreatic lymph circulation has a key role in transporting at least part of the fluid being filtered from the blood capillaries or leaking out of the obstructed excretory ducts. This may offer a "safety valve function" for the gland (8). The question therefore arises whether pancreato-duodenal lymph is impeded by the peripancreatic lymph nodes. This would elevate lymph pressure and facilitate pancreatic edema.

Materials, Methods and Results

Seventeen male mongrel dogs (average weight 17 kg, range 11 to 25 kg), were anasthetized intravenously with 0.1 g/kg chloralose. Three groups of animals were studied.

(1.) Pressure/flow relationships in the afferent lymphatics of the periportal lymph nodes near the pancreas were recorded during perfusion in situ with a Harvard infusion pump in 6 dogs. In some cases, the two afferent lymphatics of the lymph node forming a V-shaped anastomosis near the nodes were cannulated.

Thin polyethylene cannulas filled with heparin-saline were introduced into the vessels by advancing their tips toward the common lymphatic, within 1 cm of the lymph node.

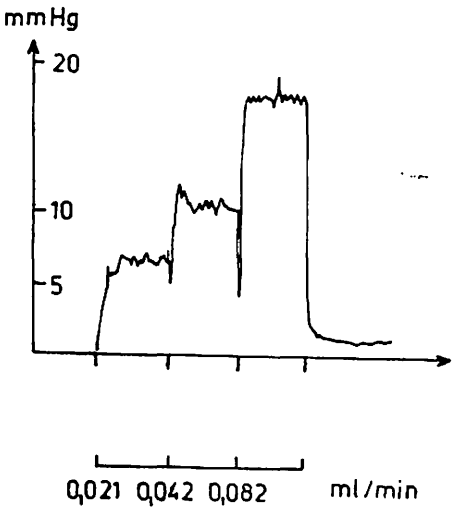


Fig. 1. In situ perfused peripancreatic / periportal / lymph node; pressure-to-flow curve.

When the lymph node had only a single afferent lymphatic, a fine double-barrelled polyethylene cannula was inserted and fixed with its tips within 1 cm of the lymph node. Physiological saline was infused at a constant rate into the free end of one of the cannulas. The intralymph pressure was measured by means of a cannula connected to a *Schwarzer* pressure transducer. Continuous recordings were made with a Physioscript polygraph. The zero reference for pressure was established at about the level of the heart of the supine dog.

The initial infusion was at 0.005 to 0.01 ml/min. This was then doubled each 2 min. up to a rate of 0.1 to 0.3 ml/min.

Graded increments in the amount of fluid infused in situ into the afferent lymphatics of the peripancreatic (periportal) lymph nodes resulted consistently in a proportional increase of intralymphatic pressure (Fig. 1).

(2.) In 4 dogs, a polyethylene cannula filled with saline was introduced into one duodenal branch of the superior pancreato-duodenal artery, and its tip was advanced into the trunk of the artery without interfering with the flow of blood in it. Evans blue solution injected through this cannula aided visualization of the pancreato-duodenal lymphatics draining the portion of the gland supplied by this artery. A fine polyethylene tube was inserted through an incision in the wall of the lymphatic. The tip of the tube was directed peripherally.

Lymph was collected in 10-min fractions (9). To increase filtration of fluid from blood capillaries and thus to increase interstitial fluid, 0.5 liter of physiological saline was infused in the course of 10 min into the superior pancreatico-duodenal artery by means of a Harvard peristaltic pump. Two periods were studied prior to the arterial infusion, one simultaneously with the infusion, and two further periods after stopping the infusion. Gross edema of the pancreas resulted.

The flow of lymph from the pancreato-duodenal lymphatics was enhanced in all 4 dogs. Lymph flow was increased to 2 to 10 times the preinfusion values. The lymph flow gradually decreased on stopping the intra-arterial infusion (Tab. 1).

(3.) In 7 dogs a duodenal branch of the superior pancreato-duodenal artery was cannulated and the portion of the pancreas supplied by the artery and lymphatics was visualized as in (2) above. Two anastomosing branches of the pancreato-duodenal lymphatic were selected. A fine polyethylene cannula was introduced into one branch and advanced to the common lymphatic without interfering with its lymph flow. The other lymphatic vessel was left intact. By raising the free end of the filled Evans blue saline container above the level of the animal, a small bolus of dye was seen to enter the common lymphatic vessel and node, thereby identifying the regional lymph node. The free end of the

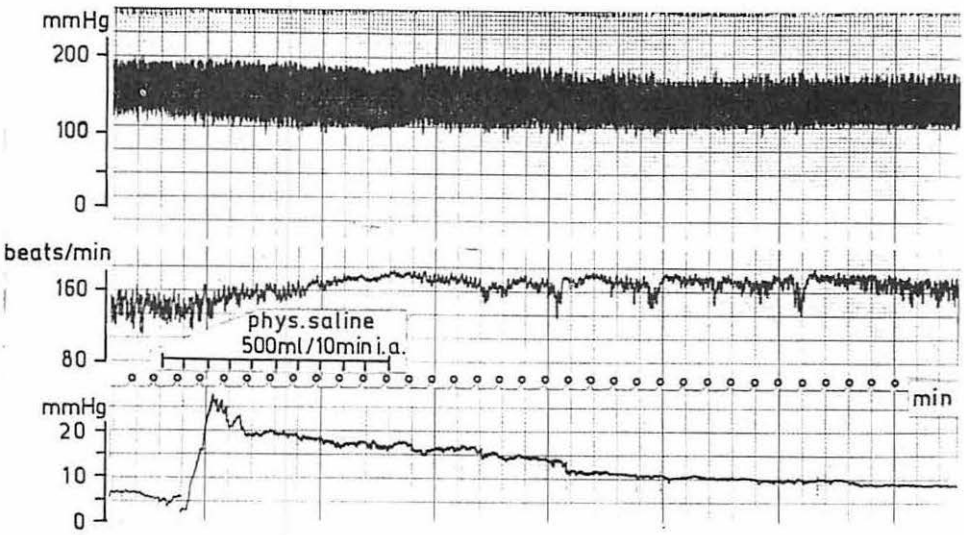


Fig. 2. Physiological saline (500 ml) infused into the superior pancreatico-duodenal artery increased pressure in the pancreatico-duodenal lymphatic (lower tracing) while having no appreciable effect on arterial blood pressure (upper tracing) and heart rate (middle tracing).

cannula was connected to a Statham pressure transducer. Pressure within the pancreato-duodenal lymphatic vessel was recorded simultaneously with pressure in the femoral artery in 2 dogs, with the internal jugular venous pressure in 1 dog and with the thoracic duct pressure in 4 dogs. Thoracic duct pressure was recorded through a polyethylene cannula which had been inserted into the proximal stump of the sectioned left cervical lymphatic trunk by advancing the tip of the cannula to the thoracic duct. Pressures were recorded using *Statham* transducers and *Hellige* Multiscriptor. Saline was infused in the superior pancreato-duodenal artery as above.

The infusion of saline into the superior pancreato-duodenal artery resulted in gross edema of the pancreas, and in spontaneous contractions of the duodenum in all 7 dogs in this group. The pressure in the pancreato-duodenal lymphatic increased in 6 of the dogs. The lymphatic pressure reached its maximal value during the infusion, and then returned gradually to the preinfusion levels after the intra-arterial infusion was stopped. (Fig. 2). Arterial blood pressure was not affected by the infusion.

Intraarterial infusion did not appreciably affect the pressure in the thoracic duct or in the internal jugular vein; (Fig. 3). Pressure in the pancreato-duodenal lymphatics also increased during intra-arterial infusion in dogs with unaltered thoracic duct pressure (Fig. 4). Intra-arterial infusion elevated the pressure in the pancreato-duodenal lymphatic to a greater value than in the thoracic duct. (Fig. 5, 6). Marked increases in pancreato-duodenal lymphatic pressure were obtained at elevated arterial pressures (Fig. 7).

Repetition of the infusion of physiological saline into the superior pancreato-duodenal artery produced a somewhat smaller rise in pancreato-duodenal lymphatic pressure, although thoracic duct pressure increased to considerably higher values than during the first infusion.

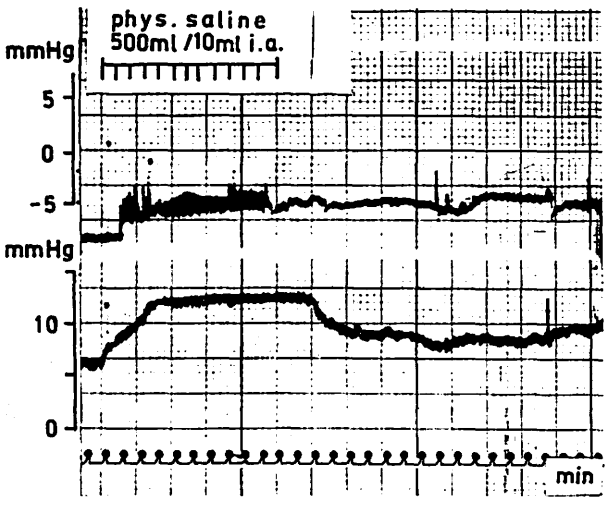
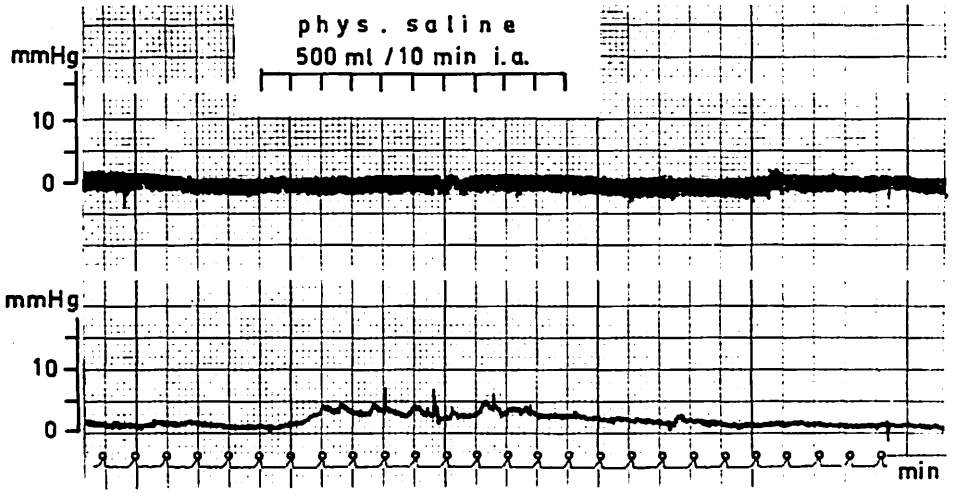


Fig. 3 Physiological saline, 500 ml/ 10 min, infused into the superior pancreatico-duodenal artery caused the pressure in the pancreatico-duodenal lymphatic, lower tracing, to rise earlier and more substantially than in the internal jugular vein, upper tracing.

Fig. 4 Physiological saline, 500 ml/ 10 min, infused into the pancreatico-duodenal artery increased pressure in the pancreatico-duodenal lymphatic, lower tracing, while not affecting pressure in the thoracic duct, upper tracing.



Tab. 1 The Effect of the infusion of physiological saline, 500 ml, 10 min, into the superior pancreatico-duodenal artery on the pancreatico-duodenal lymph flow, mg, 10 min.

Number of dogs	Body weights: kg	Pancreatico-duodenal lymph flow mg, 10 min				
		Before phys. saline infusion	During phys. saline infusion		After phys. saline infusion	
		Periods: I.	2.	3.	4.	5.
1	16	63	53	68	233	187
2	16	186	125	961	749	544
3	13	73	103	210	222	112
4	11	319	131	1786	1389	472
Range:	11–16	63–319	63–131	68–1786	222–1389	112–544
Mean:	14	160	103	756	648	328

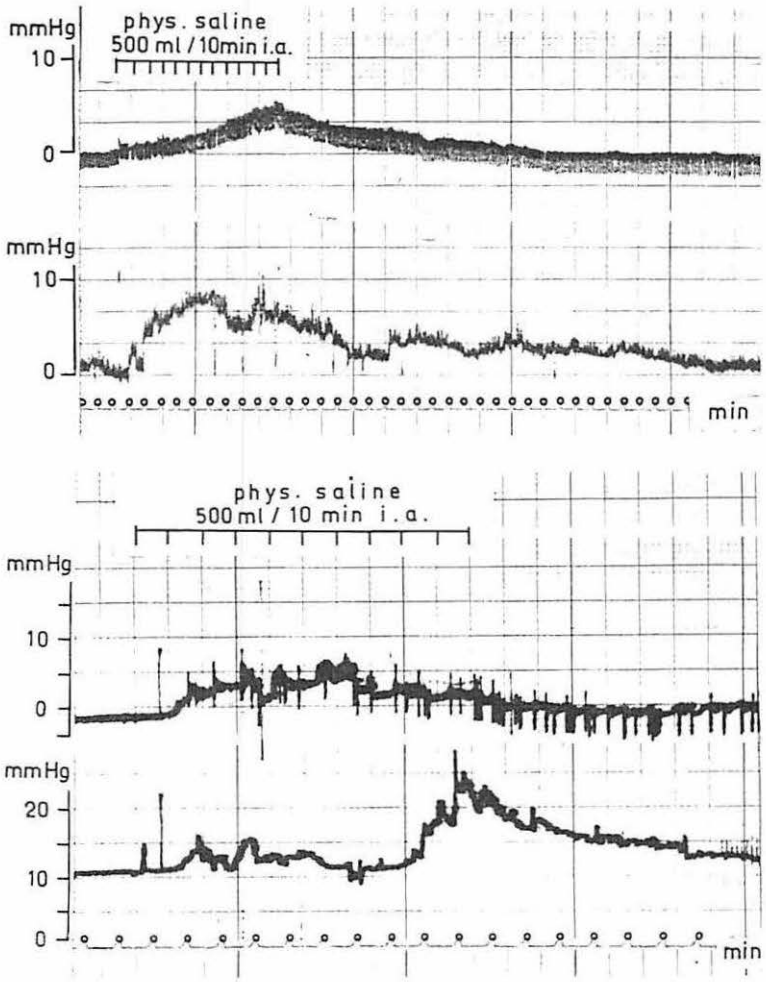


Fig. 5,6 Physiological saline, 500 ml/10 min, infused into the superior pancreatico-duodenal artery caused the pressure in the pancreatico-duodenal lymphatic, lower tracing, to rise more markedly than in the thoracic duct, upper tracing; furthermore, pressure already decreased in the thoracic duct when it attained its maximum in the pancreatico-duodenal lymphatic.

Discussion

Physiological saline infused at a relatively high rate into the superior pancreato-duodenal artery must have substantially increased the amount of fluid filtered across the capillary wall in the pancreas, owing to a rise in hydrostatic and a drop in oncotic pressure. The abundant capillary filtrate increased tissue fluid and led to an apparent edema of the pancreas. The lymphatic flow out of the transected pancreato-duodenal lymphatic increased. The pressure rise in the non-transected pancreato-duodenal lymphatic vessels, indicated a central resistance to flow. An increase in the rate of infusion also increased the pressure in the afferent lymphatic of the *in situ* perfused peripancreatic

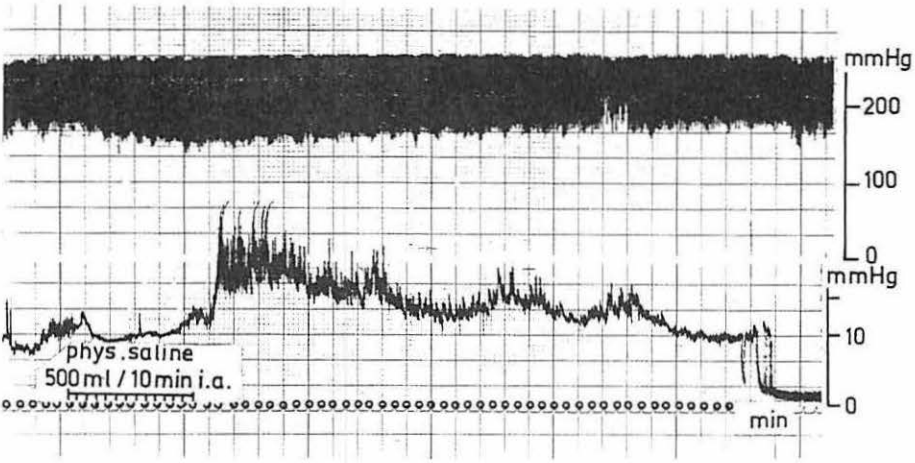


Fig. 7 Physiological saline, 500 ml/10 min, infused into the superior pancreatico-duodenal artery increased pressure in the pancreatico-duodenal lymphatic, lower tracing; arterial blood pressure, upper tracing.

(periportal) lymph node. These results permit the conclusion that in the pancreas an increase in the volume of fluid that filtered across the capillary wall augments the lymph flow in the pancreato-duodenal lymphatics and is associated with a rise of lymphatic pressure. This is probably due to the resistance to flow through the peripancreatic lymph nodes (3).

Pressure in a lymphatic vessel may be increased when a central resistance to the lymph flow is present. Such a resistance to lymph flow might develop not only because of the regional lymph node, but through an increased central venous pressure (10). This possibility could be ruled out since the pancreato-duodenal lymphatic pressure rose above either the central venous or thoracic duct pressure. Furthermore, repeated infusion into the superior pancreato-duodenal artery resulted in smaller rises of pressure in the pancreato-duodenal lymph vessel although the increase in pressure either in the internal jugular vein or the thoracic duct was appreciably greater. The failure of pancreato-duodenal lymphatic pressure to rise to the previous level on repeated infusion can be accounted for by the distension of peripancreatic lymph nodes due to augmented lymph flow.

The present observations thus indicate that pancreatic edema caused by either increased transcapillary filtration or by retention of pancreatic juice might have a dual mechanism. First, the large amounts of fluid accumulating in the interstitial space pass relatively slowly (11, 12) across the capsular barriers of the pancreas and thus reach the lymphatic system only after a considerable delay, i.e., there is a prelymphatic insufficiency of interstitial fluid movement. This mechanism may be responsible for the development of edema in cases where the interstitial fluid has a high protein concentration. The failure of the pancreato-duodenal lymph flow to increase in the early phase of bile-induced acute pancreatitis, despite marked pancreatic edema, may be due to prelymphatic insufficiency of interstitial fluid movement across the capsular barriers (9, 11). The other mechanism contributing to the formation of pancreatic edema resulting from increased capillary filtration may be the resistance of the peripancreatic nodes to lymph flow.

Based on their experiments using intravenously injected labelled erythrocytes, *Sim et al.* (13) suggested that acute experimental pancreatitis may be aggravated by lymphatic obstruction by red cells in the intrapancreatic lymphatics and in the peripancreatic lymph nodes. This observation was not confirmed in our experiments using labelled red blood cells injected into the major pancreatic duct of the intact pancreas (14). The discrepancy between these two series of observations may have been due to the circumstance that the above authors (13) were working with very low values of counts per minute both in blood and in the peripancreatic lymph nodes, which involve a much greater experimental error.

We suggest that in acute pancreatitis, prelymphatic insufficiency of intrapancreatic interstitial fluid movement is a significant factor in the development of edema of the pancreas. A contributing factor could be the obstruction of pancreato-duodenal lymph flow by the peripancreatic lymph nodes after cessation of the prelymphatic insufficiency of interstitial fluid movement.

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M. Papp, B. Varga and G.B. Makara, Institute of Experimental Medicine, Hungarian Academy of Sciences, 1083 Budapest, Hungary