Splanchnic Tissue Oxygenation: Estimation by Thoracic Duct Lymph PO_2 [1]

C. L. Witte, W. R. Cole, R. H. Clauss and A. E. Dumont *

Departments of Surgery, Washington University School of Medicine, St. Louis, Missouri, and New York University School of Medicine, New York City, N. Y., USA.
Lymphology 1, 109–116 (1968)

Internal respiration or gas exchange of oxygen and carbon dioxide between capillary blood and tissue cells involves diffusion through intervening tissue fluid (8) and depends on the partial pressure or fugacity gradient of these dissolved gases in plasma and extracellular fluid (2). Excess interstitial fluid from the small bowel and liver is transported mainly to the thoracic duct, and in animals at rest or under anesthesia forms the bulk of thoracic duct lymph (4, 11). Therefore, thoracic duct lymph oxygen tensions were studied in patients at rest and in experimental animals under anesthesia to assess oxygen exchange in splanchnic tissues.

Methods

A: Experiments in dogs

Fifteen mongrel dogs (10–12 kg) were studied. General anesthesia was induced by intravenous pentobarbital (24 mg/kg) or Myotal (0.5 cc/kg). Respiration was controlled with succinyl choline and endotracheal positive pressure ventilation. The thoracic duct was cannulated in the right chest with polyethylene tubing. The spleen was removed and the portal vein was cannulated via the splenic or mesenteric vein. Right atrium, hepatic vein and aorta were cannulated via the femoral vein, external jugular vein and femoral artery respectively. In one dog the liver and small intestine were regionally perfused in situ at constant blood flow and oxygenation by an extracorporeal heart-lung machine. All samples of blood and lymph were collected anaerobically and gas content measured with an Instrumentation Laboratory gas analyzer (Model 113).

Blood and thoracic duct lymph oxygen tensions were determined in four groups of dogs before and after:

Group I (four dogs): Increased fractional content of oxygen in the inspired air (FI O_2) $> 21\%$.
Group II (four dogs): Induced cardiac arrest by intracardiac secobarbital.
Group III (two dogs): Ligation of the hepatic and superior mesenteric arteries.
Group IV (three dogs): Intravenous administration of sodium cyanide (0.5 mg/kg). In one dog the small bowel and liver was regionally perfused.

[1] Supported by grants from USPHS (HE-09073 and HE-11904), The John A. Hartford Foundation, Inc., the Missouri Heart Association, and the Institute of Medical Education and Research of St. Louis City Hospital.

* Dr. DUMONT is a recipient of the USPHS Research Career Development Award.

Control observations were made in these dogs prior to experimental manipulation and in two other dogs similarly prepared for 60 minutes.

B: Clinical observations

In 15 patients, including 10 with hepatic cirrhosis (post-necrotic or nutritional), the cervical portion of the thoracic duct was cannulated under local anesthesia. Five patients served as control subjects, one with calculous biliary tract disease without hepatic cirrhosis, one normal volunteer, and three with heart disease. The three patients with heart disease had undergone intensive medical therapy prior to cardiac surgery for correction of rheumatic valvular disease. At the time of study, clinical assessment including blood gas analysis indicated adequate ventilation and minimal circulatory congestion. In patients with cirrhosis, nine had markedly deranged tests of liver function, four had prominent ascites, and seven had previously bled from esophageal varices. One patient had massive ascites without jaundice and chemical tests of liver function were within normal limits.

Blood samples were obtained from the femoral or brachial artery, and superior or inferior vena cava in all patients, and in five patients indirectly from the portal circulation via the umbilical, omental or mesenteric vein during laparotomy or from the spleen during splenoportography. Samples of blood and thoracic duct lymph were analyzed for PO_2 before and after increasing the fractional concentration of oxygen in inspired air (FI O_2) $> 21\%$ (four patients, including two with cirrhosis), after intravenous administration of 20 units of vasopressin (five patients with cirrhosis), after intravenous administration of glucagon (0.03 mg/kg) in one patient with cirrhosis, and after side-to-side portacaval shunt for bleeding esophageal varices in two patients with cirrhosis.

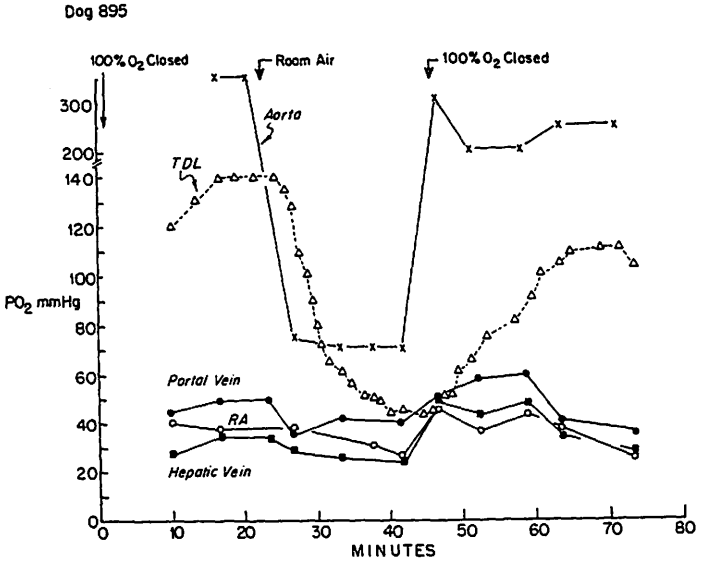

Fig. 1 PO_2 in blood and thoracic duct lymph (TDL) of a dog after increasing the fractional concentration of oxygen in the inspired air. TDL PO_2 is normally slightly higher than right atrium (RA) or splanchnic venous PO_2.

Results

Control values of thoracic duct lymph oxygen tension ($P_t O_2$) in dogs averaged 47 mm Hg and invariably were higher than the oxygen tension in portal ($P_{pv} O_2$), hepatic ($P_{hv} O_2$) or central systemic ($P_{ra} O_2$) venous blood, but lower than arterial oxygen tension ($P_a O_2$).

Group I – Increased $FI O_2$ above 21% raised $P_a O_2$, $P_{pv} O_2$, $P_{hv} O_2$, $P_{ra} O_2$ and $P_t O_2$ and exaggerated the difference between lymph and all three venous oxygen tensions (Fig. 1). The response in lymph was prompt and usually occurred within 60 seconds after supplemental oxygen was administered.

Group II – Cessation of heart beat and respiration produced a progressive diminution in $P_t O_2$ but only minor changes initially in $P_a O_2$, $P_{pv} O_2$, $P_{hv} O_2$ and $P_{ra} O_2$ (Fig. 2). If the experiment was continued more than 20 minutes a "paradoxical" increase in $P_t O_2$ occurred which eventually equilibrated with $P_a O_2$.

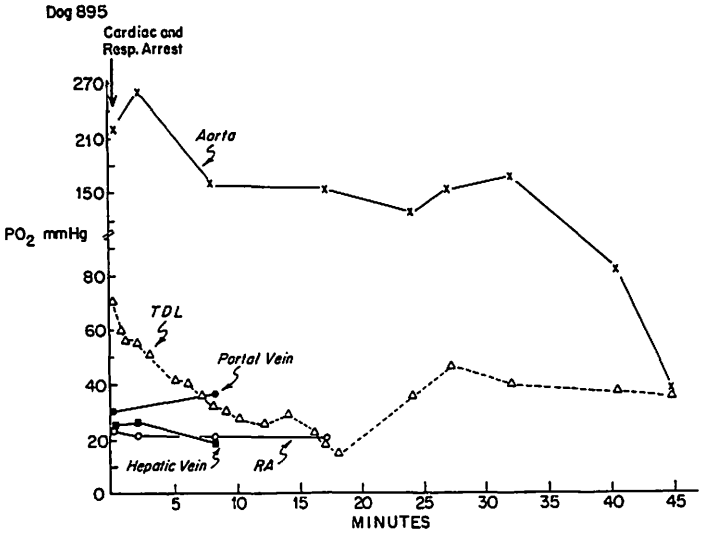

Fig. 2 PO_2 in blood and thoracic duct lymph (TDL) of a dog after induced cardiac arrest. Initially TDL PO_2 progressevely decreases as PO_2 in major blood vessels is largely unchanged. As oxidative metabolism ceases "paradoxical" increase in TDL PO_2 occurs.

Group III – Ligation of hepatic and superior mesenteric arteries produced a similar sequence to Group II (Fig. 3).

Group IV – Intravenous sodium cyanide increased $P_t O_2$. The most sustained response was obtained during regional perfusion of small bowel and liver by an extracorporeal pump and oxygenator which circumvented the undesirable side effect of myocardial depression and altered cardiac output (Fig. 4).

In patients with cirrhosis of the liver $P_a O_2$ was decreased and $P_t O_2$ was usually lower than central or portal venous PO_2 or the reverse of control values in patients and dogs (Fig. 5). Portacaval shunt operation did not alter these findings in two patients with nutritional cirrhosis (Fig. 5). In addition, after oxygen administration

the rise in $P_t O_2$ was less than in control subjects and portal venous PO_2 remained abnormally high (Fig. 6). After intravenous administration of vasopressin, thoracic duct lymph and portal venous PO_2 decreased. In one patient with cirrhosis glucagon also produced a fall in $P_t O_2$ (Fig. 5).

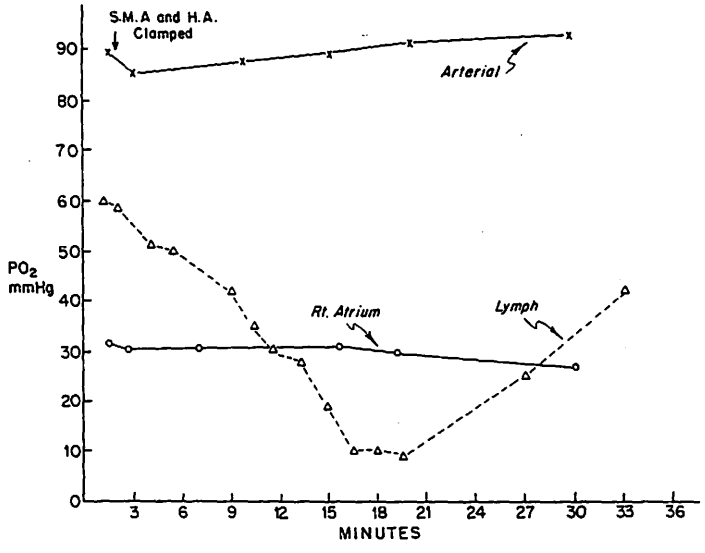

Fig. 3 After ligation of hepatic and mesenteric arteries in dog splanchnic capillary perfusion essentially ceases and thoracic duct lymph (TDL) PO_2 initially decreases. The late rise is probably related to decreased oxidative metabolism (see Fig. 2).

Discussion

Effective tissue oxygenation and cell function ultimately depend on adequate capillary perfusion and gas exchange of oxygen and carbon dioxide between capillary plasma and tissue cells. If mean capillary blood flow and oxygen content remain constant, a "steady-state" distribution of PO_2 within a tissue theoretically depends on the metabolic rate (M in ml O_2/ml tissue/sec) the linear distance for diffusion (x) and the diffusion coefficient in cm^2/sec (D) or[2]

$$d(O_2)/dt = D\, \partial 2\, [O_2] / \partial x^2 \quad - M$$

Ordinarily, thoracic duct lymph originates predominantly from the lower half of the body, At rest, however, it is derived almost exclusively from the liver and extrahepatic portal bed as lymph flow from the immobile lower extremities is practically nil (7). A small contribution arises from the kidneys, but ligation of both renal arteries in this experimental model has no effect on thoracic duct lymph flow or oxygen tension (10). Consequently, changes in thoracic duct lymph oxygen tension, particularly in conjunction with simultaneous changes in arterial, splanchnic and central venous oxygen tension probably reflect the net exchange of oxygen in splanchnic tissues.

Although differing proportions of lymph in the thoracic duct may arise in the liver and extrahepatic portal bed (e. g. in hepatic cirrhosis before and after portacaval shunt), the mean oxygen tension in splanchnic viscera may still be represented by thoracic duct lymph PO_2.

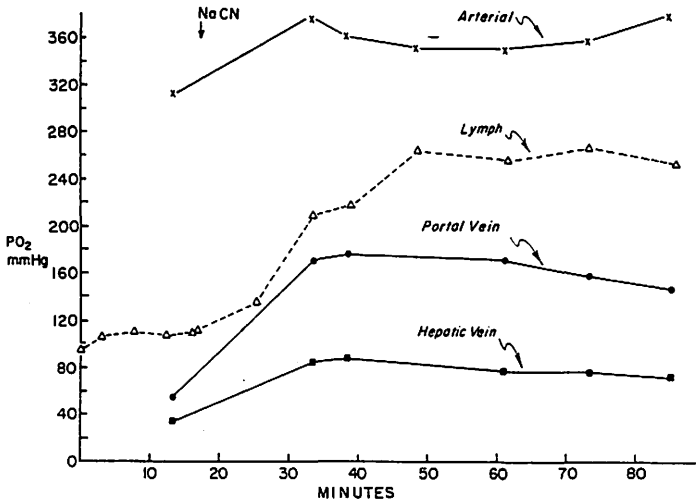

Fig. 4 Effect of intravenous sodium cyanide (NaCN) on blood and thoracic duct lymph (TDL) PO_2 of a dog during in situ regional perfusion of small intestine and liver by extracorporeal pump and oxygenerator. Constant temperature, splanchnic blood flow and oxygenation were maintened. PO_2 and pH in arterial perfusate, portal vein and hepatic venous return were determined simultaneously and splanchnic, liver and intestinal oxygen consumption estimated by the Fick principle. The rise in TDL PO_2 is accompanied by a decrease in liver and intestinal oxygen consumption.

In dogs breathing room air, mean splanchnic tissue PO_2 as measured in thoracic duct lymph is approximately 45–50 mm Hg. After oxygen administration tissue PO_2 rises as D, x, M and capillary blood flow are probably largely unchanged. Intravenous sodium cyanide inhibits oxidative metabolism (M), and oxygen, though still available, is not consumed. Lymph PO_2 correspondingly increases toward arterial oxygen tension (Fig. 4). Reduction of blood flow by induced cardiac arrest, interruption of major splanchnic arteries, and probably hemorrhage (9) produce splanchnic tissue or lymph "hypoxia" by restricting the amount of oxygen reaching capillaries. Once mitochondrial death ensues or oxidative metabolism (M) ceases, an increase in lymph PO_2 occurs as in cyanide poisoning.

In control patients thoracic duct lymph PO_2 is 55–60 mm Hg. This range for $P_t O_2$ is slightly higher than in dogs and is explained by the higher mean arterial PO_2 in human subjects breathing room air. After oxygen supplementation in the inspired air, a similar increase in thoracic duct lymph PO_2 occurs (Fig. 5).

In patients with hepatic cirrhosis, on the other hand, arterial PO_2 is decreased and thoracic duct lymph PO_2 is usually decreased (mean $P_t O_2$ = 30 mm Hg) and lower

than central and portal venous PO_2. These findings suggest the presence of chronic "hypoxia" in the liver and/or small intestine in this disease. Increased tissue oxygen consumption (M) for the low $P_t O_2$ seems an unlikely explanation as oxygen administration fails to correct the reversed portal venous-lymph PO_2 relationship (Fig. 6). Rather, the high portal venous PO_2 and low thoracic duct lymph PO_2 suggests impairment of oxygen "delivery" by (1) circumvention of capillary circulation through mesenteric and hepatic arteriovenous shunts (5, 6), (2) lowered diffusion coefficient (D) or an increase in the linear distance of diffusion (x) between capillary endothelium and cell wall from increased capillary filtration or tissue edema secondary to hepatic postsinusoidal obstruction, and (3) hepatic desmoplasia with a mechanical block of oxygen diffusion similar to alveolar-capillary block in pulmonary interstitial fibrosis. The circumstances favoring diminished oxygenation in cirrhosis are probably unaltered by portacaval shunt. Accordingly, thoracic duct lymph PO_2 remains abnormally low after this operation.

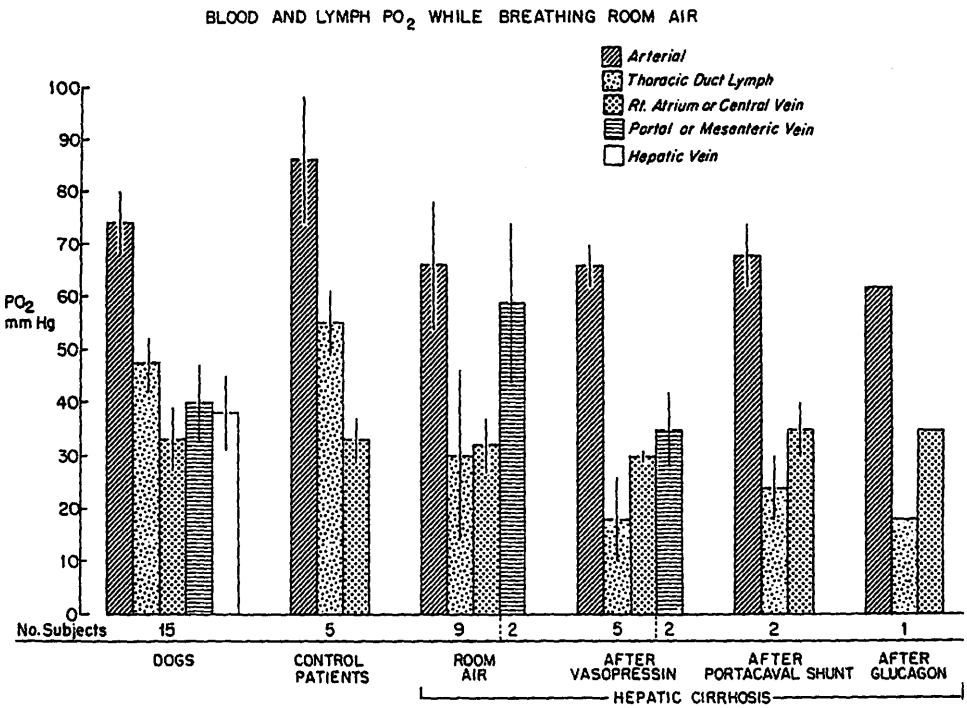

Fig. 5 PO_2 in blood and thoracic duct lymph (TDL) of patients with hepatic cirrhosis and control subjects. Note the low TDL PO_2 and reversed relationship to venous PO_2 which is unaltered by portacaval shunt in hepatic cirrhosis. Administration of glucagon or vasopressin in cirrhosis promotes a pronounced decrease in TDL PO_2.

Previous observations on hepatic oxygen metabolism in man have demonstrated that patients with cirrhosis have a limited capacity to respond to increased functional activity with a rise in splanchnic blood flow (1). In this instance, increased cellular

metabolism is offset predominantly by wide extraction of oxygen content (aortic–hepatic vein) rather than by increased splanchnic blood flow (3), and oxygen supply available to splanchnic tissue is thereby limited. As a result, administration of glucagon, a hormone capable of doubling splanchnic oxygen consumption in cirrhosis (3), and administration of vasopressin which reduces splanchnic blood flow, rapidly lead to very low thoracic duct lymph PO_2.

These preliminary studies suggest that oxygen tension in thoracic duct lymph represents the mean splanchnic tissue oxygen tension and provides a way of estimating an important unknown, namely, the oxygen tension in the region of actively metabolizing cells.

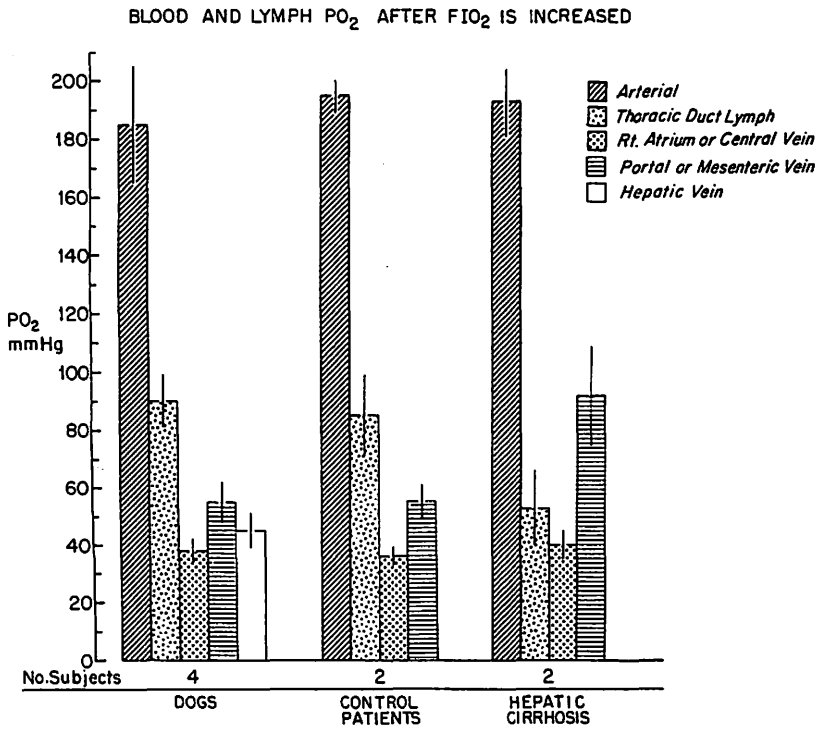

Fig. 6 PO_2 in blood and thoracic duct lymph (TDL) after increasing the fractional concentration of oxygen in the inspired air in patients with hepatic cirrhosis and control subjects. After oxygen administration, TDL PO_2 in hepatic cirrhosis is lower than values in control subjects and is lower than portal venous PO_2.

Summary

Effective tissue oxygenation depends on adequate capillary perfusion and exchange of oxygen between capillary plasma and tissue cells. The exchange of oxygen in turn depends on the partial pressure gradient between plasma and interstitial fluid. Since excess interstitial fluid from the splanchnic area is transported by the thoracic duct as lymph, PO_2 determinations were made in patients and dogs on lymph from the thoracic duct and blood from the aorta, right atrium, hepatic and portal veins to assess oxygen exchange between blood and splanchnic tissues.

Thoracic duct lymph PO_2 ($P_t O_2$) is normally higher than systemic or splanchnic venous PO_2 and lower than arterial PO_2, and probably represents the mean splanchnic tissue oxygen tension. In dogs, after oxygen administration $P_t O_2$ rises promptly as oxygen tension in arterial blood increases. Administration of sodium cyanide inhibits oxygen consumption and $P_t O_2$ accordingly increases toward arterial PO_2. Reduction of splanchnic blood flow by induced cardiac arrest and ligation of the hepatic and superior mesenteric arteries initially lowers $P_t O_2$ by restricting the amount of oxygen reaching capillaries. As cellular death progresses and oxidative metabolism decreases a delayed increase in $P_t O_2$ occurs.

In patients with hepatic cirrhosis, $P_t O_2$ is decreased and is lower than central and portal venous PO_2. This difference is accentuated by administration of vasopressin (decreases splanchnic blood flow) and glucagon (increases hepatic oxygen consumption) and is largely unaffected by portacaval shunt. These observations suggest that assessement of $P_t O_2$ may help to elucidate other clinical disorders in which oxygen exchange in splanchnic tissues is impaired.

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Roy H. Clauss, M. D., Charles L. Witte, M. D., William R. Cole, M. D., Departments of Surgery, Washington University School of Medicine, St. Louis City Hospital, 1515 Lafayette, St Louis. Allan E. Dumont, M. D., Department of Surgery, New York University School of Medicine, 550 First Avenue, 16 New York, N. Y. USA

Complications of Lymphography

P. R. Koehler

The Edward Mallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis, Missouri, USA

Lymphology 1, 116–120 (1968)

In this report the summary of questionaires concerning the more serious complications associated with lymphography will be presented.

Material

326 questionaires were mailed to members of The International Society on Lymphology and to authors of publications dealing with lymphography. Eighty-three investigators returned these questionaires. In 10 instances the questionaires were returned blank since more than one was sent to the same department.