Splanchnic Tissue Oxygenation: Estimation by Thoracic Duct Lymph $P_O_2$

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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 ($F_I O_2 > 21\%$).
- 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.

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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 $P_{O_2}$ before and after increasing the fractional concentration of oxygen in inspired air ($F_{I O_2} > 21\%$) (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.

![Diagram](image.png)

**Fig. 1.** $P_{O_2}$ in blood and thoracic duct lymph (TDL) of a dog after increasing the fractional concentration of oxygen in the inspired air. TDL $P_{O_2}$ is normally slightly higher than right atrium (RA) or splanchic venous $P_{O_2}$.
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 $F_{i}O_{2}$ 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 $P_{a}O_{2}$.

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 $P_{O_{2}}$ 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 \( P_1 O_2 \) was less than in control subjects and portal venous \( P_1 O_2 \) remained abnormally high (Fig. 6). After intravenous administration of vasopressin, thoracic duct lymph and portal venous \( P_1 O_2 \) decreased. In one patient with cirrhosis glucagon also produced a fall in \( P_1 O_2 \) (Fig. 5).

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 \( P_1 O_2 \) 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:

\[
\frac{d (O_2)}{dt} = D \frac{s^2 \left[ O_2 \right]}{8x^2} - M \frac{O_2}{t}
\]

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 oxygenator. Constant temperature, splanchnic blood flow and oxygenation were maintained. 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 PtO\(_2\) 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 PtO\(_2\) = 30 mm Hg) and lower.
than central and portal venous $P_{O_2}$. 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 $P_{O_2}$ seems an unlikely explanation as oxygen administration fails to correct the reversed portal venous-lymph $P_{O_2}$ relationship (Fig. 6). Rather, the high portal venous $P_{O_2}$ and low thoracic duct lymph $P_{O_2}$ 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 $P_{O_2}$ remains abnormally low after this operation.

**Fig. 5** $P_{O_2}$ in blood and thoracic duct lymph (TDL) of patients with hepatic cirrhosis and control subjects. Note the low TDL $P_{O_2}$ and reversed relationship to venous $P_{O_2}$ which is unaltered by portacaval shunt in hepatic cirrhosis. Administration of glucagon or vasopressin in cirrhosis promotes a pronounced decrease in TDL $P_{O_2}$.

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 PO2.

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.

**BLOOD AND LYMPH PO2 AFTER FIO2 IS INCREASED**

![Graph showing PO2 levels 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 PO2 in hepatic cirrhosis is lower than values in control subjects and is lower than portal venous PO2.]

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, PO2 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 $P_tO_2$ ($P_tO_2$) is normally higher than systemic or splanchnic venous $P_O_2$ and lower than arterial $P_O_2$, and probably represents the mean splanchnic tissue oxygen tension. In dogs, after oxygen administration $P_tO_2$ rises promptly as oxygen tension in arterial blood increases. Administration of sodium cyanide inhibits oxygen consumption and $P_tO_2$ accordingly increases toward arterial $P_O_2$. Reduction of splanchnic blood flow by induced cardiac arrest and ligation of the hepatic and superior mesenteric arteries initially lowers $P_tO_2$ by restricting the amount of oxygen reaching capillaries. As cellular death progresses and oxidative metabolism decreases a delayed increase in $P_tO_2$ occurs.

In patients with hepatic cirrhosis, $P_tO_2$ is decreased and is lower than central and portal venous $P_O_2$. 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 assessment of $P_tO_2$ may help to elucidate other clinical disorders in which oxygen exchange in splanchnic tissues is impaired.

References

4 Morris, B.: The hepatic and intestinal contributions to the thoracic duct lymph. Quart. J. Exper. Physiol. 41 (1956), 318
10 Witte, C. L.: Personal observations

Complications of Lymphography

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

Material

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