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Oxygen Tension of Nearly pure Pulmonary Lymph in Unanesthetized Sheep

N.C. Staub and E.L. Schultz

Cardiovascular Research Institute and Department of Physiology, University of California, San Francisco, California 94143

Bergofsky (1, 2) measured the oxygen tension (Po_2) of thoracic duct (TD) lymph and equated it with average tissue Po_2. Other workers have made similar comparisons for kidney (3) and intestinal tract (4).

Said and *Banerjee* (5) used this concept to calculate the fraction of lung lymph in right lymphatic duct (RLD) lymph in anesthetized dogs. They found the average Po_2 = 75 torr; the same as the average arterial Po_2 and considerably higher than TD Po_2. Using standard mixing equations, assuming pure lung lymph Po_2 equaled alveolar gas Po_2 and non-respiratory lymph equaled TD Po_2, they computed that 53% of RLD lymph came from the lung.

Recently, *Meyer* and *Ottaviani* (6) made similar Po_2 measurements both for RLD and TD normally and in acute edema. They confirmed the apparently high Po_2 in RLD lymph and calculated that most of RLD lymph came from the lung. Assuming body lymph Po_2 equaled mixed venous Po_2, they concluded that 15% of TD lymph originated in the lung. Since TD flow greatly exceeded RLD flow, the net result was that about two thirds of pulmonary lymph entered the thoracic duct both in normal and edematous conditions.

Unfortunately, both RLD and TD lymph have traversed lymph nodes and *Mayerson* (7) has shown that small molecules (molcular weight < 1,000) equilibrate completely during lymph node transit.

Because of the importance of lymph gas tension in the lung and elsewhere, wo have reassessed the oxygen tension of pulmonary lymph obtained from four unanesthetized sheep with chronic lymph catheters. We devised an oxygen-impermeable, external catheter system and measured steady state Po_2 repeatedly over several hours. Our finding is that the average Po_2 of nearly pure lung lymph is very similar to that of mixed venous blood. It is not related to the tissue Po_2 at its source.

Material and Methods

In four young adult, female, Suffolk sheep we cannulated the major efferent duct of the caudal mediastinal lymph node (CMN) using heparin-impregnated silastic tubing as previously described (8, 9, 10). Beginning about one week after the cannulation when lymph flow had stabilized, we prepared an external, gas-tight sheath for the lymph cannula.

A diagramatic representation of the cannula system is shown in Fig. 1. A thick gum rubber sleeve was glued to the sheep's skin using branding cement. The main sheath was glass tubing heat-molded to approximately the natural shape of the silastic catheter. The inside

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diameter of the glass tube was sufficient to leave a 0.5 mm diameter air space around the silastic catheter. After inserting the glass sheath into the rubber sleeve, the dead space between the glass sheath and the silastic catheter was filled with a warm 3% agar solution and allowed to solidify. The distal tip of the silastic lymph catheter was attached to a short polyethylene sleeve just large enough to hold the tip of a 70 µl heparin-coated glass sampling tube.

After 2-4 hours to allow equilibration between the agar and the lymph flowing through the silastic catheter, we collected 70 µl lymph samples and measured these immediately in a micro-oxygen electrode system (Radiometer Model E5046, Copenhagen). The collection time for individual lymph samples ranged between 20 and 30 seconds. The reason for the gas tight arrangement was so the sleeve could be removed and the animals used for other experiments.

Each experiment lasted 1-2 hours, during which repeated samples of lymph were measured. At approximately one hour intervals, we withdrew blood samples from the pulmonary artery (mixed venous) and left atrium (systemic arterial) and measured their Po_2 in the same electrode system. The catheters through which these materials were drawn had been implanted at prior surgery.

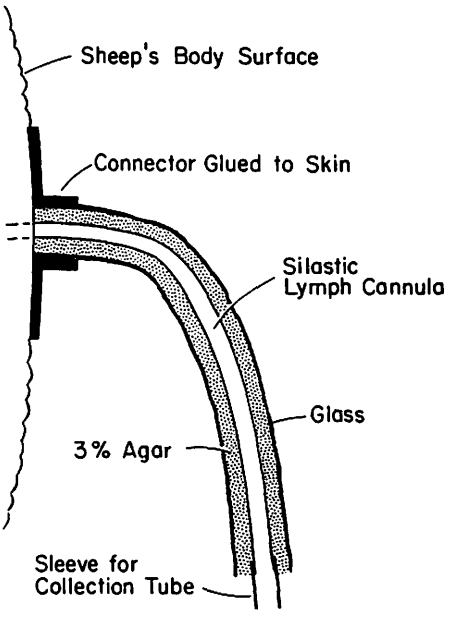

Fig. 1 Schema of gas-tight sheath for lymph catheter. A gum rubber connector was glued to the sheep's skin with branding cement and a bent glass tube (I.D. = 3 mm) inserted into it. The gas space between the silastic catheter and glass sheath was carefully filled with hot 3% agar. No air bubbles were permitted. The plastic sleeve at the distal end was 0.5 cm long and provided a tight junction between the catheter and the tip of the glass micro-sampling tube.

In model experiments we measured the penetration of oxygen through the walls of polyethylene tubing that had been used by prior investigators (5, 6). A reservoir bottle of tap water was degassed by means of bubble equilibration (11). Fluid flowed at known rates from a side arm of the bottle through a 30 cm length of polyethylene tubing (Clay-Adams, Parsippany, N.J., No. PE190; I.D. 0.12 cm, O.D. 0.17 cm). The fluid flowed from the tubing directly into the oxygen electrode which was operated at room temperature, approximately 23°C.

Results

The table shows the individual results in our four sheep, together with our group averages and those of *Said* (5) and *Meyer* (6).

The lymph samples Po_2 varied somewhat; the range and average values are listed. In every individual sample of lymph, the Po_2 was well below that of arterial blood (left atrial blood) although somewhat above mixed venous blood (pulmonary artery sample). Overall lung

Table 1 Steady state pulmonary artery, left atrial and lung lymph oxygen tensions in four unanesthetized sheep, together with comparisons with published literature.

Sheep No.	Oxygen Tension (torr) Lung Lymph Average (range)	Pulmonary Artery	Left Atrium
A. Individual			
S6-72	74 (62 - 80)	34	104
S13-72	57 (50 - 61)	42	90
RS4-72	58 (42 - 69)	50	90
S36-72	35 (32 - 42)	29	92
B. Series averages			
1. This series 4	56	39	94
2. Said (5) 8	86	37	92
3. Meyer (6) 15	75	33	75

lymph oxygen tension averaged 56 torr compared to a mixed venous oxygen tension averaging 30 torr and arterial blood oxygen tension averaging 94 torr. Since the blood gas tensions in our study are nearly identical with those of *Meyer* (6)' the large difference between the measured lung lymph oxygen tensions must be accounted for.

Both *Meyer* and *Said* had used gas-permeable polyethylene tubing to collect RLD and TD lymph. We studied the effect of volume flow rate through polyethylene tubing on the change in oxygen tension of fluid passing through the cannula. Room air Po_2 was 150 torr; that of the fluid entering the tubing < 1 torr. Fig. 2 summarizes the results. In PE 190 tubing there is a hyperbolic (inverse) relation between volume flow rate and change of oxygen tension. At high volume flow rates, such as those in the thoracic duct (60 ml/hr), the change in oxygen tension is very small; about 5 torr. At the slow flow rates of RLD lymph (< 10 ml/hr) the increase in oxygen tension is nearly 50 torr, and very sensitive to flow rate. The open circle in Fig. 2 is the change in oxygen tension for the length of plyethylene used by *Meyer*; the oxygen tension increased nearly 20 torr. The increase in oxygen tension for the smaller and thinner wall tubing (PE90, I.D. .09 cm, O.D. 0.13 cm) used by *Said* and *Banerjee* (5) is not shown on the graph but is proportionally greater at all flow rates.

Discussion

In sheep most lung lymph flows through the caudal mediastinal node lymphatic (12). This node also receives systemic contributions from esophagus and thoracic wall although these are very slight. Variable systemic components from below the diaphragm have been removed in the preparatory surgery. Thus, both by anatomical and physiologic tests (*Staub*, to be published) the CMN lymph is nearly all (95% or more) of pulmonary origin. The steady state lymph flow from this node averages about 5 ml/hr (8).

The glass-coated, agar-filled sheath we have developed offers an efficient gas-tight seal except at the distal tip where the lymph samples are taken. It is our opinion that the correct Po_2

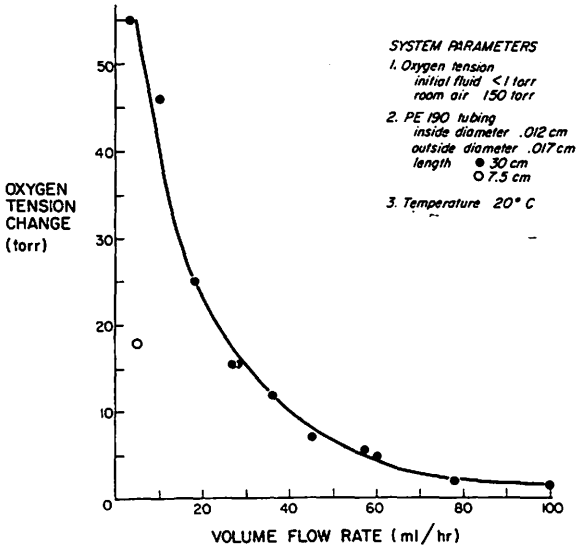

Fig. 2 Change in oxygen tension in water as a function of volume flow rate through gas-permeable polyethylene tubing for the conditions shown.

of lung lymph is actually the lowest measured value obtained in each animal (32-62 torr) rather than the average as reported here. Any break in technique such as a slight uncovering of the silastic catheter tip or a microbubble in the system would tend to increase the Po_2 in the lymph.

The only possible cause for a decrease in Po_2 in the slowly flowing lymph would be if oxygen consumption by lymphocytes were significant during transit through the catheter, during collection and before measurement. Based on lymph flow rates and the volume of our silastic catheter, we estimate the transit time through the catheter is 1 minute. Collection time was less than 1 minute and measurement time in the electrode is about 2 minutes. It is difficult to measure the rate of oxygen consumption of the lymph in these studies. We incubated samples of lymph for periods up to one hour, but have as frequently found increases in Po_2 as decreases. It is unlikely that a significant fall in Po_2 would have occurred in the short time of these experiments. This is particularly true because the Po_2 was just as low in situations where the lymph flow was high as in those where it was low.

On two occasions, we measured the Po_2 of lymph from the silastic catheter without the glass sheath. The Po_2 was nearly that of room air, as would be expected from the very high oxygen permeability of silastic tubing.

Meyer and *Ottaviani* (6) used a 10 cm length of PE190 polyethylene tubing for their right lymphatic cannulations. *Said* and *Banerjee* (5) used a 10 cm length of the smaller, thinner-walled PE90 tubing. It is clear from the data in Fig. 2 that the flow rates of RLD lymph these investigators reported, together with the air-exposed lengths of gas permeable tubing are sufficient to account for the increased lymph Po_2 they found.

We conclude that the oxygen tension in lymph taken from large ducts cannot be used as a measure of the oxygen tension in the tissue of origin. Direct sampling of small lymphatics as they leave organs (3) may give better estimates of tissue gas tensions. But even there, it is incumbent upon the investigator to prove that there was no uptake of oxygen through the exposed thin-walled lymph vessel itself or in his collecting system.

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N.C. Staub,MD. and E.L. Schultz,B.A., Cardiovascular Research Institute and Department of Physiology, University of California, San Francisco, California 94143

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Restoration of the Primary Immune Response and Prevention of Wasting by Pregnancy in Neonatally Thymectomized Female Rats

K. Borum

Institute of Pathology, University Hospital, Lund, Sweden and Institute of Medical Anatomy A, University of Copenhagen, Denmark

Summary

Pregnancy restored the impaired immune capacity of neonatally thymectomized rats towards normalcy, as measured by the serum haemolysin response to sheep red blood cells (SRBC). Pregnancy also prevented the development of the wasting syndrome in these animals. The beneficial effect of one pregnancy lasted at least five months.

In 1965 *Osoba* (1) reported the interesting observation that the depressed immune reactivity of neonatally thymectomized female mice was restored to normal by pregnancy. In eight out of nine thymectomized mice a normal serum haemagglutinin titer following the administration of SRBC was found after one or more pregnancies, which also gave protection against wasting.

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