Micropuncture Measurement of Microvascular Pressures in Isolated Lamb Lungs During Hypoxia

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To study the effect of alveolar hypoxia on the pulmonary circulation of the newborn, we determined the longitudinal distribution of vascular pressures and the distribution of blood flow in isolated blood perfused lungs of newborn lambs during normoxia and hypoxia. We also examined the effect of hypoxia on the slope and intercept of the vascular pressure–flow (P/Q) relation. In 14 lungs, we used the micropipette servonulling technique to measure pressures in 20–80 μm subpleural arterioles and venules during normoxia and hypoxia at constant blood flow. In 5 other lungs, we used radiolabelled microspheres to determine the effect of hypoxia on regional distribution of blood flow. Under baseline normoxic conditions, segmental pressure drops in arteries, microvessels, and veins were approximately equal. During hypoxia pulmonary artery pressure always increased, resulting in a 60% increase in total vascular resistance. All segmental pressure drops increased with hypoxia. Arterial and venous pressure drops increased by 80 and 70% respectively, contributing almost equally to the increase in total pulmonary vascular resistance. Regional distribution of blood flow was uniform during normoxia and was unchanged during hypoxia. Hypoxia increased both the slope and intercept of the P/Q relation significantly, with an increase in fluid filtration rate. We conclude that in the newborn lamb alveolar hypoxia leads to pulmonary arterial and venous constriction, resulting in increased microvascular pressure and fluid filtration. (Circulation Research 1986; 59:398–404)

In adult animals alveolar hypoxia results in predominantly pulmonary arterial constriction, though there is evidence to suggest that microvessels and veins also constrict. In the newborn lamb, there is a possibility that significant pulmonary venous constriction occurs with hypoxia. Alveolar hypoxia results in increased lung lymph flow with a decrease in lymph protein concentration in the newborn lamb, different from what occurs in adult sheep indicating an increase in microvascular pressure for fluid filtration. The exact mechanism by which microvascular filtration pressure increases is not known. Pulmonary venous constriction would result in increased pressure in fluid filtration sites upstream from the site of constriction. An alternate explanation for the increase in microvascular pressure during hypoxia is that a more vigorous constriction of pulmonary arterioles in the bottom of the lung may divert an increased flow of blood to fewer vessels in the upper regions of the lung, thereby increasing the hydrostatic pressure in those vessels.

In this study, in isolated, perfused lungs of the newborn lamb, we have used direct lung micropuncture to determine the longitudinal distribution of microvascular pressures and used the radiolabelled microsphere technique to measure the regional distribution of blood flow, both during normoxia and hypoxia. In addition, we determined the slope and intercept of the vascular pressure–flow relation during normoxia and hypoxia. Our findings indicate that in the newborn lamb during acute alveolar hypoxia arteries and veins constrict to the same degree, contributing equally to the increase in total pulmonary vascular resistance.

Materials and Methods

Isolated Lung Preparation

We used the lungs of 19 newborn lambs whose age and body weight averaged 8.1 ± 3.2 days (5–11 days) and 4.55 ± 1.55 kg respectively. The lambs received Ketamine 25 mg/kg body wt. intramuscularly, and breathed 100% oxygen during placement of catheters. Via a neck incision under local anesthesia with 2% Lidocaine, catheters were inserted into the carotid artery and right atrium and an endotracheal tube tied into the trachea. After checking that the lambs’ blood pH and gas tensions were within normal limits, 25 mg/kg body wt. of pentobarbital sodium and heparin sodium (Liquaemin, Organon) 1000 IU/kg, were injected intravenously and the lamb rapidly exsanguinated through the carotid artery catheter. During exsanguination, we infused 5% dextran 70 in Ringer’s lactate to obtain an adequate volume of blood. The drained blood was collected to prime the perfusion circuit. Via a midline sternotomy, the superior and inferior vena cavae were tied near their entry into the right atrium and the heart and lungs removed and weighed. Cannulas (silastic tubing, 3/16 in. i.d., 5/16 in. o.d. Dow Corning Corp, Mich.) filled with 5% dextran in Ringer’s lactate solution were tied into the pulmonary artery via the right ventricle and into the left atrial appendage. By occluding the distal pulmonary artery with a vascular clamp, we prevented air bubbles from entering the lungs. The ductus arteriosus, aortic root, andazygous veins were ligated and a ligature placed...
around the atrioventricular groove to occlude the lumen of the ventricles. In the newborn lamb, as the ductus arteriosus and foramen ovale are patent, the systemic veins and aorta have to be tied off to prevent leakage of blood. The lungs were placed on a plexiglass table, the vascular cannulae connected to the perfusion circuit, and the endotracheal tube attached to a source of gas supply. The average time interval from death of the lamb to perfusion of the lungs was 12 minutes.

The perfusion circuit (Figure 1) was filled with approximately 250 ml of blood. We added heparin to make a final concentration of 30 IU heparin/ml of blood. The perfusate was kept at 38–39° C (the body temperature of lambs) with a heat exchanger (Mini-prine, Travenol Labs., Ill.) and a filter in the circuit (Ultipore, Pall Biomedical, New York) continuously filtered clots and bubbles. A thermistor probe placed at the outlet of the heat exchanger allowed continuous monitoring of the temperature. To decrease pulsations, a bubble trap was placed before the pulmonary arterial cannula and a Starling resistor in the circuit prevented pressures from rising above 80 cm H₂O. Blood was circulated by a roller pump (Integral variable drive, Cole Parmer) through the pulmonary artery into the lungs and back through the pulmonary veins into a venous reservoir. We calibrated the roller pump by timed collections of the outflow. We continuously measured pulmonary arterial and left atrial pressures with pressure transducers (Gould Statham P23) that were connected to polyethylene tubing, the tips of which were located in the pulmonary arterial and left atrial cannulas. Zero reference level for vascular pressures was the top surface of the lung (the site of all micropunctures). Left atrial pressure was set by adjusting the height of the venous reservoir; the pulmonary arterial pressure was controlled by adjusting blood flow. We sampled blood from the venous reservoir or the pulmonary artery cannula via a T-piece and measured perfusate O₂ and CO₂ tensions and pH every 10 minutes using standard electrode techniques (Radiometer BMS 3MIC2, Copenhagen) and adjusted pH to 7.40–7.50, when necessary, by the addition of sodium bicarbonate. Perfusate hematocrit and glucose concentrations (by Dextrostix) were monitored every 20 minutes, and blood glucose concentration was kept between 90 and 130 mg/dl by periodic addition of 50% glucose in water.

Initially, we perfused the collapsed lungs at a low flow rate, then increased the flow gradually as the lungs were inflated. We ventilated the lungs with appropriate gas mixtures between micropuncture and during micropuncture we kept the lungs steadily inflated at an airway pressure of 7 cm H₂O.

**Experimental Protocol**

During a baseline normoxic period, the lungs were ventilated by hand at 25/5 cm H₂O airway pressure (inspiratory and expiratory pressures), 25 times a minute with a gas mixture of 30% O₂, 6% CO₂, and 74% N₂ for a few minutes, then switched to a constant airway pressure of 7 cm H₂O. We adjusted blood flow to maintain pulmonary artery pressure at 30 cm H₂O and adjusted the height of the venous reservoir to maintain left atrial pressure at 8 cm H₂O. Lungs were perfused under Zone 3 conditions, i.e., the left atrial pressure was kept greater than airway pressure throughout the height of the lungs. Once established, blood flow was kept constant for the rest of the experiment. Blood flow averaged 84 ± 20 ml/kg body wt./min (404 ± 87 ml/min) during micropuncture. During this period, in 14 lungs, we measured pressures by the micropipette servonulling technique in the 20–80 μm diameter subpleural arterioles and venules. After initial filling of the microvascular bed, subsequent decreases in the volume of blood in the reservoir were taken to represent fluid accumulation in the lungs. For the hypoxic period, the lungs were ventilated at the same airway pressures and rate with a gas mixture containing 8% O₂, 6% CO₂, and 86% N₂ until the blood P O₂ decreased below 50 torr, then switched to a constant airway pressure of 7 cm H₂O. We tried to puncture the same or adjacent microvessels during the hypoxic period as during normoxia. In 6 lungs, after adjusting blood flow and vascular pressures in the baseline normoxic period, we measured microvascular pressures during hypoxia first, followed by pressure measurements during normoxia.

During both normoxia and hypoxia, we examined the vascular pressure–flow relation of the lungs. We chose blood flow rates ranging from 80 to 620 ml/min as this range of flow rates usually yielded a linear pressure–flow relation (correlation coefficient >0.99) (Figure 3). Left atrial pressure was kept at 8 cm H₂O and airway pressure 7 cm H₂O (Zone 3 conditions). Flow rate was increased in discrete steps every 30 seconds by adjusting the pump speed and pulmonary artery pressure was recorded.

The duration of each experimental period was between 1 and 1.5 hours and the total perfusion time did not exceed 3 hours. The lungs, except for the site of micropuncture, and the venous reservoir were covered with gas tight plastic, to prevent diffusive losses of CO₂ from the blood.

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**FIGURE 1.** Perfusion circuit for lamb lungs. Blood is warmed and filtered before entering the lungs. A Starling resistor prevents pressures before rising above 80 cm H₂O in the circuit.
Estimation of Fluid Filtration Rate

During baseline, once vascular pressures and blood flow were constant, we noted the level of blood in the venous reservoir. Subsequently, during perfusion, we added blood to the venous reservoir every 10 minutes to keep the level constant. By noting the volume of blood added to the reservoir, we could approximately estimate the rate of weight gain in the lungs. There was no leakage of blood from the lungs during perfusion. At the end of the experiment, the heart and lungs were drained of blood, removed, and weighed again, so that we could calculate the total weight gain during the experiment.

Microvascular Pressure Measurement

To measure lung microvascular pressures we micropunctured the lung using the technique described by Bhattacharya and Staub. We used a pipette puller to make micropipettes from glass tubing (vertical pipette puller model 700D, David Kopf, Tujunga, Calif.) and bevelled the tip to a diameter ranging between 2 and 4 \( \mu \text{m} \) on a pipette beveller (Diamond Abrasive plate, David Kopf). As the pleura of the lamb is thick, and the arterioles are situated deep beneath the pleura, a thick glass tubing (i.d. 0.6 mm, o.d. 1.2 mm, Frederick Hauer and Co., Me.) was used to construct sturdy pipettes, with the taper length ranging between 200 and 300 \( \mu \text{m} \). We filled the pipette with 1.2 M NaCl solution colored with green dye (Guinea Green B, Aldrich Chemical Co., Inc.) and connected it to a servonulling pressure measuring system (model 4A, Instruments for Physiology and Medicine, San Diego). The dye enabled us to see the tip of the pipette easily and to perform a dye flow test during micropuncture. To facilitate micropuncture of the lung, the lung surface was stabilized by lightly placing a metal ring (attached to a stand) on the pleura; the ring also held a pool of normal saline on the lung surface for obtaining the zero reference pressure. We then viewed the lung surface through a stereomicroscope (Zeiss) at \( \times 80 \) or \( \times 120 \) magnification with illumination from a cold light source (Intralux 5000, American Volpi, Auburn, N.J.). Subpleural venules, ranging from 10 to 250 \( \mu \text{m} \) in diameter are numerous and easily visible, especially near the lung edges; on the other hand only a few arterioles, ranging from 20 to 100/\( \mu \text{m} \) in diameter were visible and were found in a random distribution on the lung surface. Also, venules are more superficial and, hence, easier to micropuncture. We micropunctured 20- to 80-\( \mu \text{m} \) diameter arterioles and venules and chose these sites as it permitted us to compartmentalize the pulmonary circulation into three segments: arteries (pulmonary artery to 20-\( \mu \text{m} \) arteriole), microvessels (<20-\( \mu \text{m} \) vessels), and veins (20-\( \mu \text{m} \) vein to left atrium).

To micropuncture venules, we positioned the pipette at a 30° angle to the pleural surface, whereas to puncture arterioles we approached the pleura with the pipette at a 45° angle. We identified venules by observing the direction of flow of red blood cells from small vessels into larger ones; for arterioles blood flowed from a large vessel into a smaller one. As arterioles are deepseated, a dye flow test was essential to determine the direction of blood flow.

We accepted microvascular pressure measurements that fulfilled the criteria reported by Bhattacharya and Staub (Figure 2):

1. reproducible zero reference pressure obtained both before and after the pressure measurement;
2. an immediate response in the microvascular pressure tracing when either the pulmonary artery or left atrial pressure is perturbed;

![Figure 2](http://circres.ahajournals.org/) Microvascular pressure tracing in a 50 \( \mu \text{m} \) venule. a) When left atrial pressure is raised, venular pressure follows closely, returning to baseline afterward; b) during the dye flow test (see text for details), pressure tracing is lost transiently; c) on increasing the servonull gain, pen goes into oscillations, returning to baseline afterward.
3. immediate washout of injected dye from the pipette by the flowing blood, indicating that the pipette tip was lying freely in the vessel lumen;
4. a pressure measurement that is independent of small changes in the optimal servonull gain setting, indicating that the pipette tip is in liquid.

Blood Flow Measurements

In 5 lungs, we used the radiolabelled microsphere technique, to determine the distribution of blood flow within the lungs during normoxia and hypoxia. During each experimental period, when vascular pressures and blood flow were stable, we made two injections of 15-µm-diameter radionuclide microspheres, 15 minutes apart. The microspheres were injected rapidly retrograde to blood flow, through a thin catheter inserted via a T-piece into the perfusion circuit 15 cm from the pulmonary artery. This created turbulence, allowing for adequate mixing of the microspheres. Following the injections, we stopped blood flow, clamped the trachea at 7 cm H₂O airway pressure, and froze the lungs in liquid nitrogen. The average height of the lungs was 9 cm. We cut the lungs into 1-cm-thick horizontal slices. At the top of the lung, the site of micropuncture, we cut a 1-mm horizontal slice of the subpleural region of the lung. Each slice was cut into approximately 1-cm² pieces and the anatomical location of each piece noted. All lung pieces, including the top 1-mm slice, were weighed, then placed in a multiple channel gamma counter (1282 Compu Gama, LKB Wallace) for radionuclide counting of the four tracers (³²P, ⁴¹Ca, ⁸⁶Sr, ⁴¹Co). Later, the lung pieces were dried in an oven at 70-80° C for 72 hours and reweighed. We calculated the fractional blood flow to each slice and expressed it as ml·min⁻¹·g dry lung⁻¹.

Data Analysis

Results shown are mean values ± SD for each group of lungs. We used an analysis of variance for multiple comparisons and the paired t test for comparisons between normoxic and hypoxic periods. Linear regression analysis was used to determine correlation between blood flow and lung height. For the pressure–flow points we performed linear regression analysis and obtained a slope and intercept in each lung for both normoxic and hypoxic periods. We compared mean data for both slopes and intercepts from the two experimental periods, using a paired t test, and accepted a p value of <0.05 as indicative of statistical significance.

Results

Hematocrit of the lambs, prior to volume expansion with 5% dextran in Ringer’s lactate averaged 22.3 ± 2.7%. Blood Po₂ averaged 146 ± 18 torr during the normoxic period and 43 ± 6 torr during the hypoxic period; blood PCO₂ was 38 ± 6 torr throughout the experiment. Simultaneous blood samples drawn from the venous reservoir and the pulmonary artery cannula had the same Po₂. Perfusion hematocrit rose from 17.0 ± 3.5% to 18.0 ± 4.0% during hypoxia, possibly due to fluid accumulation in the lungs. Blood pH and blood glucose concentration were stable during the normoxic period but tended to fall during hypoxia, needing adjustment.

Microvascular Pressures in Normoxic and Hypoxic Lamb Lungs

Total pressure drop across the pulmonary circulation was 22.1 ± 2.1 cm H₂O. The pressure drop in the arterial segment was 33 ± 13%, in microvessels 29 ± 12% and in veins was 38 ± 9% of the total pressure drop, indicating that the arteries, microvessels and veins contribute approximately a third each to the total pressure drop across the pulmonary circulation. (See Table 1).

During hypoxia pulmonary artery pressure always rose; for the group of lungs, pulmonary artery pressures rose from 30.0 ± 3.0 to 43.0 ± 5.7 cm H₂O; a 60% increase in total pulmonary vascular resistance. Arteriolar and venular pressures also increased. The pressure drop in the arterial segment increased by 80%; in microvessels by 15%, and in veins by 70%.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Pulmonary artery (cm H₂O)</th>
<th>Arteriole (20–80 µm)</th>
<th>Venule (20–80 µm)</th>
<th>Left atrium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normoxia</td>
<td>30.0 ± 3.0</td>
<td>22.7 ± 2.4</td>
<td>16.4 ± 2.3</td>
<td>8.0 ± 0.0</td>
</tr>
<tr>
<td>∆P</td>
<td>7.3</td>
<td>6.3</td>
<td>8.4</td>
<td></td>
</tr>
<tr>
<td>R%</td>
<td>33.2%</td>
<td>28.6%</td>
<td>38.2%</td>
<td></td>
</tr>
<tr>
<td>Hypoxia</td>
<td>43.0 ± 5.7‡</td>
<td>29.8 ± 3.4‡</td>
<td>22.4 ± 3.4‡</td>
<td>8.0 ± 0.0</td>
</tr>
<tr>
<td>∆P</td>
<td>13.2</td>
<td>7.4</td>
<td>14.4</td>
<td></td>
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<tr>
<td>R%</td>
<td>37.7%</td>
<td>21.1%</td>
<td>41.1%</td>
<td></td>
</tr>
</tbody>
</table>

Results are mean values ± SD.

∆P, pressure drop in vascular segments.
R%, % of total pressure drop in vascular segments.
*Pressures in cm H₂O, relative to pleural pressure (atmospheric) at level of micropuncture. Blood flow was constant at 84 ± 24 ml/kg body wt/min.
†Number of punctured vessels.
‡p < 0.05.
Arterial and venous pressure drops increased almost equally, contributing equally to the total increase in pressure drop across the pulmonary circulation. As arterial and venous pressure drops increased more than the pressure drop in the microvessels during hypoxia, the microvessels represent a smaller fraction (21%) of the total pressure drop than the arteries (38%) and veins (41%).

**Fluid Filtration Rate**

During normoxia, the lung invariably gained weight at an average rate of 0.5 ± 0.6 g/min. During hypoxia, the rate of weight gain increased in all lungs, some lungs gaining weight more rapidly than others, an average rate of 1.2 ± 1.0 g/min. At the end of the experiments, the lungs had gained 30–60% of their initial weight. Airway edema did not occur in any of the lungs.

**Vascular Pressure-Flow Relation of Lamb Lungs During Normoxia and Hypoxia**

Typical pressure–flow relation in a lamb lung during normoxia and hypoxia are shown in Figure 3. The effect of hypoxia invariably was an increase in the slope and intercept of the pressure flow curves. During hypoxia, the mean slope of the P/Q relation increased from 0.049 ± 0.014 to 0.068 ± 0.019 cm H$_2$O·ml·min$^{-1}$ ($p<0.05$), and the mean intercept increased from 11.3 ± 2.9 to 21.3 ± 5.9 cm H$_2$O ($p<0.05$).

**Blood Flow Distribution in Lamb Lungs During Normoxia and Hypoxia**

Blood flow distribution along a vertical gradient in 5 lamb lungs (Figure 4) was uniform during normoxia (blood flow = 0.13; height + 10.2, $r = 0.32$, $n = 50$) and unchanged during hypoxia (blood flow = 0.13; height + 9.3, $r = 0.36$, $n = 50$).

Blood flow in the top millimeter of lung, the site of micropuncture was similar to the lower slices of the lungs and remained unchanged during hypoxia. Blood flow was 15 ± 5% lower in the subpleural regions than in the center of the lungs, both during normoxia and hypoxia.

**Discussion**

**Estimates of Segmental Vascular Resistance**

Under baseline conditions, total vascular resistance in the isolated lamb lung is significantly higher than that reported in the isolated dog,\textsuperscript{16} cat\textsuperscript{3} and rabbit.

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**FIGURE 3.** Typical vascular pressure flow data in a lamb lung during normoxia and hypoxia. With hypoxia, the slope and intercept of the pressure–flow line invariably increased. Normoxia: slope 0.043 cm H$_2$O·ml·min$^{-1}$, Pressure intercept: 14.5 cm H$_2$O, $r = 0.99$. Hypoxia: slope 0.087 cm H$_2$O·ml·min$^{-1}$, Pressure intercept: 20.9 cm H$_2$O, $r = 0.99$.

**FIGURE 4.** Blood flow distribution in 5 lamb lungs during normoxia and hypoxia. Blood flow was uniform with lung height both during normoxia and hypoxia. Bars, mean values; lines, SD.
Lung. However, the calculated resistance in the microvascular segment, determined from micropuncture pressure measurements, is similar in all the lungs. The increased resistance in the lamb lung is due to a higher resistance in the pulmonary arteries and veins. Similarly, in lungs of neonatal rabbits (3–4 weeks old) using the micropuncture technique, we found a significantly higher resistance in arteries and veins than in adult rabbits. The distinctive feature of the neonatal pulmonary circulation appears to be a higher resistance in the arterial and venous segments. A high basal vasomotor tone and differences in the structure of the vessels in the neonatal lamb lung may in part explain the higher arterial and venous resistance. Also, as basal pulmonary vascular resistance is lower in the living animal than in the isolated lamb lung, it is possible that various vasoconstrictive agents released during the experimental procedure may be contributing toward the high arterial and venous resistance.

The fractional resistance imposed by the arteries, microvessels, and veins is approximately equal in the neonatal lamb lung, whereas in the adult lungs, fractional resistance is greatest in the microvessels (65% in rabbits, 80% in dogs). It appears that if total pulmonary vascular resistance is high, then the contribution of the microvascular segment to total resistance is low.

Though a low venous resistance has been reported in adult lungs using the micropuncture technique, other investigators have reported a significant resistance in veins, either by direct measurement of pressures in small veins using catheters or by morphometric measurements of the vasculature.

Sites of Hypoxic Vasoconstriction

In our experiments, alveolar hypoxia consistently resulted in a significant increase in arterial and venous resistance, with a small increase in resistance in microvessels. There is some evidence for venous constriction during hypoxia from earlier studies: Rivera-Estrada et al. demonstrated a rise in pulmonary artery wedge pressure without a change in left atrial pressure in hypoxic open-chested dogs; and Morgan et al., by simultaneously measuring pulmonary venous and pleural pressures, reported an increase in venous transmural pressure during hypoxia in intact dogs. More recently, Hakim et al., using the arterial and venous occlusion technique, reported a predominant increase in resistance in the middle segment of the dog lung during hypoxia. If the middle segment includes vessels as small as arterioles up to 500 μm in diameter, then our data using the micropuncture technique are very consistent with that of Hakim et al. Similarly, in the hypoxic cat lung, Nagasaka et al. reported an increase in venous resistance, though the increase in resistance in arteries was three times that in veins. In the lamb, the increase in resistance in veins and arteries was equal. Therefore, in comparing our data in the lamb lung with data from studies in adults, it appears that, though venous constriction may occur during hypoxia in the adult, the magnitude of venous constriction is greater in the neonate.

The small increase in resistance in microvessels may be explained by the hypothesis that extravascular contractile interstitial cells in the alveolar wall constrict in response to hypoxia resulting in the folding of alveolar walls and increased capillary resistance.

Blood Flow Distribution in the Lung During Hypoxia

In the intact newborn lamb, alveolar hypoxia results in increased blood flow to the lungs as well as a redistribution of blood flow predominantly to the upper and posterior regions of the lung. Thus, in the intact lamb two additional effects might be operative, i.e., an increase in perfused microvascular surface area and an increased microvascular pressure in those vessels that preferentially receive greater blood flow. In our experiments, by keeping blood flow constant and by perfusing the lungs in Zone 3 (with possibly maximal recruitment of blood vessels), we were able to study only the pressor response of the pulmonary circulation to hypoxia. Our data indicate that, under Zone 3 conditions, a condition that might exist in the presence of significant left atrial hypertension, hypoxia does not cause uneven constriction of blood vessels with redistribution of blood flow. In as much as blood flow to the top millimeter of the lung is representative of flow in the vessels that we micropunctured, we can conclude that the increase in microvascular pressures observed during hypoxia were due not to increases in blood flow but to active constriction of blood vessels.

Pressure–Flow Relation During Normoxia and Hypoxia

In every experiment, alveolar hypoxia increased the extrapolated pressure axis intercept as well as shifted the pressure flow line to the left, thus increasing the slope of this line. Since the slope of the linear portion of the pressure–flow line can be taken to represent the resistance of the circulation upstream from the site of critical pressure, our data indicate that hypoxia increased upstream resistance. The intercept of the pressure–flow line (critical pressure) increased with hypoxia. As the critical pressure was always greater than left atrial pressure and as fluid filtration rate increased with hypoxia, the site of critical pressure during hypoxia is probably some place upstream from the left atrium but downstream from sites of fluid filtration, i.e., in either the microvascular or the venous segment. If, indeed, fluid filtration can occur through large pulmonary arteries as suggested by Whayne and Severinghaus, the locus of critical pressure might even be in arteries. By measuring the effects of a change in alveolar pressure on the critical pressure, Sylvestre and co-workers reported that in the hypoxic pig lung the site of critical pressure was in extralveolar vessels at airway pressures <5 torr but in alveolar vessels at greater airway pressures. We did not study the effect of inflation on the site of critical pressure in our experiments. Our pressure–flow data derived from the whole lung are consistent with the data from the micropuncture pressure measurements obtained from the subpleural region of the lung.
Effect of Fluid Accumulation on Microvascular Pressures

By the end of the experiment the lungs had gained 30–60% of their initial weight due to fluid accumulation in the lung. None of the lungs developed airway edema. We have previously shown that interstitial edema alone has no effect on total pulmonary vascular resistance or on microvascular pressures in the adult rabbit lung. Wang et al. have shown in the dog lung that both hydrostatic and increased permeability edema per se had no effect on total and segmental vascular resistance. Only in the presence of airway edema, with an associated increase in hematocrit, total vascular resistance increased, mainly due to an increase in resistance of the middle segment. In our experiments, hematocrit increased by only 1%, which cannot explain the significant increases in total and segmental vascular resistance with hypoxia.

In summary: Our results show that in the newborn lamb, alveolar hypoxia results in pulmonary arterial and venous constriction to the same degree, explaining the increased microvascular pressure and lung fluid filtration observed in hypoxic lambs.

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