TITLE: Effects of blood PO$_2$ on Hypoxic Pulmonary Vasconstriction

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Introduction: Mixed venous oxygen tension influences hypoxic pulmonary vasconstriction (HPV). Its effect may be indirect by altering PAO$_2$, or a direct stimulation of the pulmonary artery.

The purpose of the present study was to examine the direct effect of perfusate oxygen tension (PO$_2$) on the pulmonary pressure response to constant alveolar hypoxia. Method: Adult female rats (wt.330 ± 17g) were anesthetized with pentobarbital (30 mg/kg i.p.). A tracheostomy was performed and the lungs were ventilated by a Harvard Rodent Ventilator at 180 mls/min with PEEP of 2 cm. water. The heart and lungs were exposed via a mid-sternal incision. Heparin (100 IU) was injected intracardially.

A metal cannula was tied into the pulmonary artery and a venous catheter was inserted into the left ventricle. The heart and lungs were suspended in a humidified and temperature controlled chamber. The isolated lungs were perfused at constant temperature with a solution of 50% heparinized rat blood (obtained from donor rats) and 50% physiological salt solution plus 3% albumin. The perfusate was pumped from a water jacketed reservoir through a Kolobow oxygenator. From this circuit, perfusate was diverted at a constant rate into the PA of the isolated lungs by a Harvard peristaltic pump. The effluent returned to the reservoir by gravity.

The perfusing solution was equilibrated with 0, 3, 6, 10 and 21% oxygen containing 5% CO$_2$. The lungs were ventilated with 21, 0 and 3% O$_2$ containing 5% CO$_2$. The ventilation to perfusion volumes/min were 10:1. pH and temperature were held constant. Measurements consisted of ventilation, airway pressure, and mixed inspired and expired PO$_2$, and PCO$_2$. PAP, hematocrit, pH, flow of the perfusate; and finally water/dry weight of the lungs.

Study Design: For thirty minutes the isolated lungs were ventilated with a PO$_2$ of about 150 mmHg and perfused with a PO$_2$ of 40 mmHg, to obtain a steady baseline. The O$_2$ tension to the perfusate was then either reduced or increased; when the perfusate PO$_2$ had reached a new steady state the lungs were challenged with 0% or 3% O$_2$ for 5 minutes alternating with 21% O$_2$. This procedure was repeated with PO$_2$'s in random order.

Each response was calculated as a percent of its own maximum response when both the PAO$_2$ and the PVO$_2$ were approximately zero.

Results: The general conditions of the study are shown in the Table.

<table>
<thead>
<tr>
<th>General Conditions</th>
<th>Mean ± SE, n=10</th>
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<tr>
<td>Wt. Hct pH PCO$_2$ Temp. Flow Lung g % U mmHg °C ml/min Water</td>
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<tr>
<td>300 18 7.31 36.2 36.5 12.68 4.8</td>
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<td>±17 ±1 ±0.01 ±0.2 ±0.3 ±0.59 ±0.2</td>
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The figure shows that there is a highly significant ($p<0.001$) inverse relationship between the pulmonary artery pressure response to alveolar hypoxia and the log PVO$_2$. The alveolar PO$_2$ was not influenced by the perfusate PO$_2$. The observed increase of response with decreased PVO$_2$ represents a direct effect of perfusion oxygen tension on HPV.

Discussion: It has been shown by a number of investigators (1,2) that the mixed venous O$_2$ tension can influence the constrictor response to alveolar hypoxia, but the effect is generally believed to be an indirect one resulting from changes of PAO$_2$, secondary to PVO$_2$. In the present study the use of large ventilatory flow relative to perfusate abolished the indirect influence of PVO$_2$. The result therefore demonstrates a direct effect of the PVO$_2$ in enhancing or attenuating HPV.

Conclusion: In the isolated rat lung there is an inverse relationship between log PVO$_2$ and the constrictor response to alveolar hypoxia. HPV is therefore directly determined by both PVO$_2$ and PAO$_2$.

References
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