TITLE: Effects of blood PO_2 on Hypoxic Pulmonary Vasoconstriction

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Introduction: Mixed venous oxygen tension influences hypoxic pulmonary vasoconstriction (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 ($P\bar{v}O_2$) on the pulmonary pressor 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, $P\bar{v}O_2$. 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 $P\bar{v}O_2$ of 40 mmHg, to obtain a steady baseline. The O_2 tension to the perfusate was then either reduced or increased; when the perfusate $P\bar{v}O_2$ 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 $P\bar{v}O_2$'s in random order.

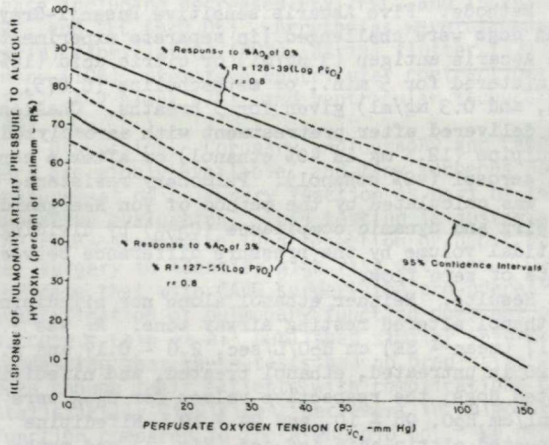
Each response was calculated as a percent of its own maximum response when both the PAO_2 and the $P\bar{v}O_2$ were approximately zero.

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

General Conditions (Mean ± SE, n=10)

Wt.	Hct	pH	PCO_2	Temp.	Flow	Lung
g	%	U	mmHg	°C	ml/min	Water
300	18	7.31	36.2	36.5	12.68	4.8
±17	±1	±0.01	±0.2	±0.3	±0.59	±0.2

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 $P\bar{v}O_2$. The alveolar PO_2 was not influenced by the perfusate PO_2. The observed increase of response with decreased $P\bar{v}O_2$ 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 $P\bar{v}O_2$. In the present study the use of large ventilatory flow relative to perfusate abolished the indirect influence of $P\bar{v}O_2$. The result therefore demonstrates a direct effect of the $P\bar{v}O_2$ in enhancing or attenuating HPV.

Conclusion: In the isolated rat lung there is an inverse relationship between log $P\bar{v}O_2$ and the constrictor reponse to alveolar hypoxia. HPV is therefore directly determined by both $P\bar{v}O_2$ and PAO_2.

References

1) Hauge A. Acta Physiol.Scand. 1969. 76.121 1969. 2) Hyman A.L. et.al. J Appl Physiol 51:1009.81

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