

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 ( $PvO_2$ ) on the pulmonary pressor response to constant alveolar hypoxia.

**Method:** Adult female rats (wt.  $330 \pm 17g$ ) 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  $PCO_2$ ,  $PO_2$ . 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  $PvO_2$ 's in random order.

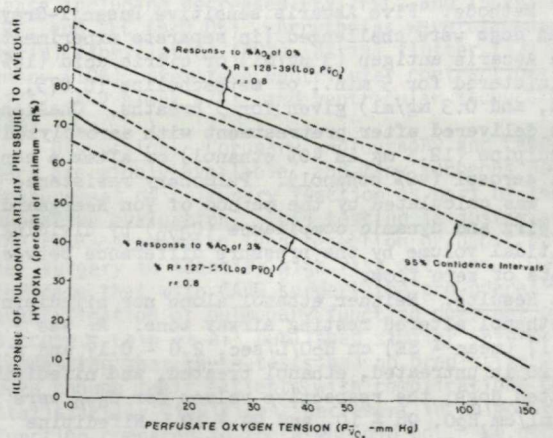
Each response was calculated as a percent of its own maximum response when both the  $PAO_2$  and the  $PvO_2$  were approximately zero.

**Results:** The general conditions of the

study are shown in the Table.

General Conditions		(Mean $\pm$ SE, n=10)				
Wt.	Hct	pH	$PCO_2$	Temp.	Flow	Lung
g	%	U	mmHg	$^{\circ}C$	ml/min	Water
300	18	7.31	36.2	36.5	12.68	4.8
$\pm 17$	$\pm 1$	$\pm 0.01$	$\pm 0.2$	$\pm 0.3$	$\pm 0.59$	$\pm 0.2$

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  $PvO_2$ . 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**

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