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Title : $P_{\bar{v}}O_2$ AS A DETERMINANT OF HYPOXIC PULMONARY VASOCONSTRICTION

Authors : Pirlo, A., M.D.; Benumof, J., M.D.

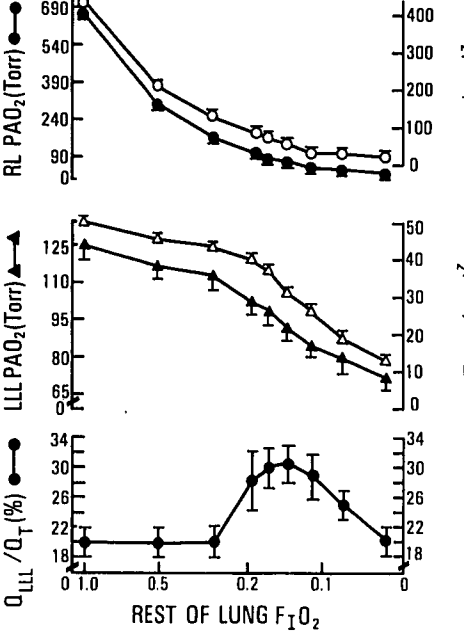
Affiliation: Anesthesia Research Laboratory
University of California, San Diego
La Jolla, California 92093

Introduction. When only a small segment of the lung is normoxic and the remaining large segment of the lung is hypoxic, systemic hypoxemia occurs and there is only a minimal amount of blood flow redistribution away from the large hypoxic compartment over to the small normoxic compartment.[1] The mechanism of the failure of the large hypoxic compartment to effectively shift blood flow is unknown but it has been suggested, based on calculations, that the systemic hypoxemia causes a markedly decreased mixed venous PO_2 ($P_{\bar{v}}O_2$) which, in turn, causes a decrease in the small "normoxic" compartment alveolar PO_2 (P_AO_2) to a level which illicits offsetting or competing small compartment hypoxic pulmonary vasoconstriction (HPV). The purpose of this experiment was to directly test this hypothesis by measuring P_aO_2, $P_{\bar{v}}O_2$, large (hypoxic) and small ("normoxic") compartment P_AO_2 and large and small compartment blood flows during stepwise decrements in large compartment F_IO_2 from 1.0 to 0.06.

Methods. Eight mongrel dogs were anesthetized with intravenous pentobarbital 25 mg/Kg, intubated and ventilated with 100% O_2. Following a left thoracotomy, electromagnetic flow probes were placed around the main and left lower lobe (LLL) pulmonary arteries. LLL blood flow is expressed as a fraction of the cardiac output ($\dot{Q}_{LLL}/\dot{Q}_t$). Femoral artery, pulmonary artery (P_{pa}) and left atrial (P_{la}) pressures were measured directly. The LLL bronchus was cannulated distal to a ligature and ventilated independently and synchronously with the rest of the lung (RL) with room air. Compartmental tidal volumes and external deadspaces were manipulated so that both ventilated compartments had equal airway pressures and ET_{CO_2}=5%. The respiratory rate was adjusted to achieve P_aCO_2 = 40 torr. The experimental sequence consisted of decreasing, in a stepwise manner, the RL F_IO_2 from 1.00 to 0.50, 0.30, 0.21, 0.18, 0.15, 0.12, 0.09, and finally to 0.06; after each stepwise decrement in RL F_IO_2 produced a new steady state (stable cardiac output, $\dot{Q}_{LLL}/\dot{Q}_t$ and P_{pa}) arterial, mixed venous and mixed expired ($\bar{E}$) CO_2 and O_2 were analyzed. RL and LLL P_AO_2 were calculated according to the formula: $P_AO_2=P_IO_2 - [(P_aCO_2/P\bar{E}CO_2)(P_IO_2-P\bar{E}O_2)]$. All results are expressed as mean $\pm$ SE and were analyzed by paired t analysis with $p<0.05$ considered significant.

Results. As the RL F_IO_2 was progressively decreased to 0.15, $\dot{Q}_{LLL}/\dot{Q}_t$ increased and RL P_AO_2, P_aO_2, $P_{\bar{v}}O_2$ and LLL P_AO_2 decreased. When RL F_IO_2 = 0.15, RL P_AO_2 = 66 torr, P_aO_2 = 54 torr, $P_{\bar{v}}O_2$=31 torr, and LLL P_AO_2 = 91 torr. When RL F_IO_2 was progressively decreased below 0.15, $\dot{Q}_{LLL}/\dot{Q}_t$ decreased and RL P_AO_2, P_aO_2, $P_{\bar{v}}O_2$ and LLL P_AO_2 decreased further. $\dot{Q}_{LLL}/\dot{Q}_t$ was significantly increased during RL F_IO_2 between 0.21 and 0.12 compared to RL F_IO_2=1.0. Cardiac output was signinficantly increased during RL F_IO_2 0.15-0.06 compared to RL F_IO_2=1.0 whereas P_{pa} was significantly increased during RL F_IO_2 0.30-0.06 compared to RL F_IO_2 = 1.0.

Discussion. The increase in $\dot{Q}_{LLL}/\dot{Q}_t$ as RL F_IO_2 was decreased towards 0.15 was ably due to RL HPV. The decrease in $\dot{Q}_{LLL}/\dot{Q}_t$ as RL F_IO_2 was decreased below 0.15 was presumably due to offsetting, competing, concomitant LLL HPV. The fact that $\dot{Q}_{LLL}/\dot{Q}_t$ started to decrease precisely at the LLL P_AO_2 expected to begin to cause LLL HPV strongly implicates LLL HPV as the cause of the late (RL $F_IO_2<0.15$) decrease in $\dot{Q}_{LLL}/\dot{Q}_t$. In view of the fact the LLL F_IO_2 was constant (room air) the progressive decrease in $P_{\bar{v}}O_2$ must have caused the progressive decrease in LLL P_AO_2. These findings indicate that if decreases in RL F_IO_2 cause secondary decreases in P_aO_2, which cause tertiary decreases in $P_{\bar{v}}O_2$, which cause quantenary decreases in "normoxic" lung P_AO_2, then $P_{\bar{v}}O_2$ is an important determinant of the magnitude of the HPV response. Thus any of several therapeutic interventions which increase $P_{\bar{v}}O_2$ even a few torr (above 31 torr in our experiment) may confer a critical benefit to a patient by enhancing pulmonary autoregulation. Such therapeutic interventions include decreased O_2 consumption, increased cardiac output, increased F_IO_2 and extracorporeal membrane oxygenation.



References: 1. Johansen I, Benumof JL: Anesthesiology 51:3S:369, 1979