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Influence of Mixed Venous Oxygen Tension ($P\bar{V}_{O_2}$) on Blood Flow to Atelectatic Lung

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The influence of mixed venous oxygen tension ($P\bar{V}_{O_2}$) on blood flow to the atelectatic left lung was studied at normal and reduced cardiac outputs (CO) using extracorporeal veno-venous bypass in six pentobarbital anesthetized, mechanically ventilated dogs. Aortic and left pulmonary artery flows; airway, left atrial, central venous, pulmonary, and systemic arterial pressures; hemoglobin, arterial, and mixed venous blood gases were measured. The blood flow reduction observed in atelectasis was altered by the $P\bar{V}_{O_2}$. Approximately 50% of blood flow was diverted away from atelectatic lung when $P\bar{V}_{O_2}$ was low (24 ± 2 mmHg) or normal (46 ± 2 mmHg) (mean left lung blood flow [$\dot{Q}_L$%] was 23.2 ± 4.6% with low $P\bar{V}_{O_2}$ and 19.0 ± 3.4%, with normal $P\bar{V}_{O_2}$). When $P\bar{V}_{O_2}$ was increased to greater than 100 mmHg, diversion of blood flow away from atelectatic lung did not occur and $\dot{Q}_L$% was nearly the flow expected for normoxic ventilated left lung (mean $\dot{Q}_L$% = 40.4 ± 5.9%). Shunt ($\dot{Q}_S/\dot{Q}_T$%) was significantly greater when $P\bar{V}_{O_2}$ was high than when it was normal or low (mean $\dot{Q}_S/\dot{Q}_T$% = 51.7 ± 5.6%, 31.0 ± 3.1%, 26.0 ± 3.4% with high, normal, and low $P\bar{V}_{O_2}$, respectively). Mean Pa_{O_2} was significantly greater when $P\bar{V}_{O_2}$ was high than when $P\bar{V}_{O_2}$ was normal or low, despite the increase in $\dot{Q}_L$% and $\dot{Q}_S/\dot{Q}_T$% (Pa_{O_2} = 327 ± 25 mmHg, 220 ± 32 mmHg, 115 ± 21 mmHg with high, normal, and low $P\bar{V}_{O_2}$, respectively). A 40% reduction in cardiac output significantly decreased transmural pulmonary artery pressure but did not affect Pa_{O_2}, $\dot{Q}_S/\dot{Q}_T$%, or $\dot{Q}_L$%. The mechanism of blood-flow reduction to atelectatic lung is therefore hypoxic pulmonary vasoconstriction, determined by the $P\bar{V}_{O_2}$. The contribution of mechanical factors in reducing blood flow to atelectatic lung in the open chest is small. (Key words: Heart: cardiac output. Lung: hypoxic pulmonary vasoconstriction; shunting. Oxygen: blood levels.)

BLOOD FLOW GENERALLY DECREASES to areas of lung that become atelectatic,[1,2] thereby reducing pulmonary shunt and preventing hypoxemia. The mechanism of blood flow reduction in atelectasis is believed to be hypoxic pulmonary vasoconstriction (HPV).[1,3–6] While the alveolar oxygen tension ($P_{A_{O_2}}$) is the primary stimulus for HPV in the ventilated lung, with atelectasis the oxygen tension of most lung tissue approaches the mixed venous oxygen tension ($P\bar{V}_{O_2}$). This study examines the hypothesis that in atelectatic lung, the stimulus for HPV is the $P\bar{V}_{O_2}$.

Methods

ANESTHESIA

Six female mongrel dogs (mean weight 22 ± 1.3 kg) were anesthetized with intravenous pentobarbital (30 mg/kg supplemented with 25–50 mg every 30 min). The trachea was intubated with a 10-mm cuffed tube and muscle paralysis ensured with intravenous pancuronium (0.05 mg/kg, supplemented with 0.2–0.5 mg every 30 min). The lungs were ventilated with humidified 100% O_2 at a tidal volume of 25 ml/kg and rate of 10/min via one side of a dual-piston Harvard® ventilator. Inspired CO_2 was added to keep end-tidal P_{CO_2} at 30–35 mmHg. A peripheral vein was cannulated and Normosol® (Abbott Labs, Na = 140 mEq/l, K = 5 mEq/l, Mg = 3 mEq/l, Cl = 98 mEq/l, acetate = 27 mEq/l, gluconate = 23 mEq/l) was administered at rates estimated to be sufficient to maintain euvolemia (100–250 ml/h). A Foley catheter was inserted to measure urine output. Body temperature was measured via a thermister probe inserted into the right femoral vein and was maintained at 37 ± 1°C with heating lamps, pads, and heated humidified inspired O_2.

SURGERY–MONITORING

The animal was placed in the supine position and the chest opened via a median sternotomy. Electromagnetic flow probes (Micron Instruments, Inc.), previously calibrated *in vitro,* were placed around the ascending aorta and left pulmonary artery. A side-hole catheter was placed in the main pulmonary artery via a right ventriculotomy. A right femoral artery catheter, left atrial catheter, and central venous catheter were placed. The left femoral artery and vein were cannulated to form an adjustable arteriovenous fistula. The transducers were zeroed at the midcardiac level and calibrated to mmHg or cmH_2O as appropriate.

SURGERY–AIRWAY

A Kottmeier double-lumen endobronchial tube was placed via a subcricoid tracheostomy and complete lung

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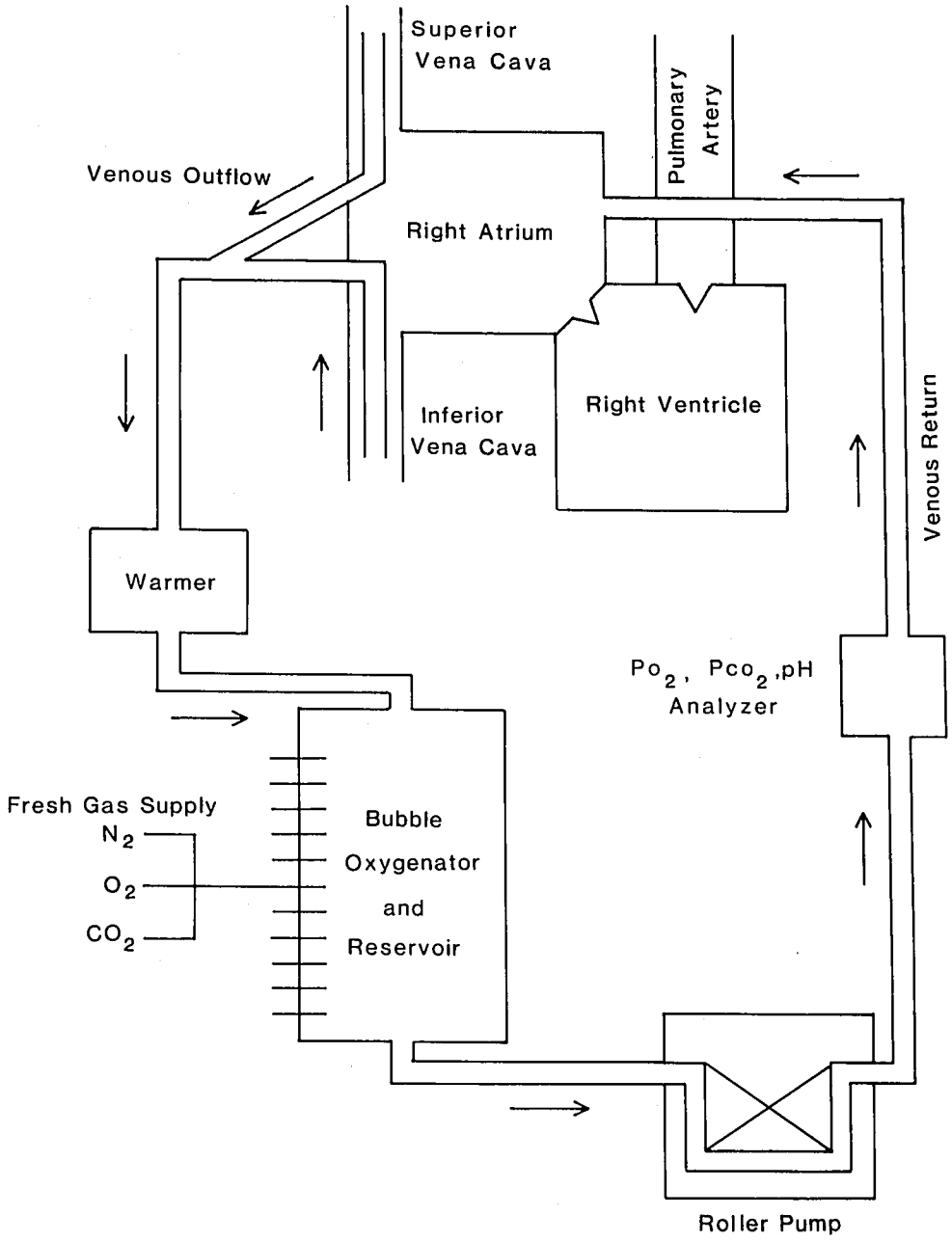

FIG. 1. Schematic diagram of veno-venous extracorporeal bypass. Total venous return was collected from the superior and inferior venae cavae, passed through a bubble oxygenator, where it was oxygenated or deoxygenated, and then pumped back into the right atrium via a roller head pump. Variation of the oxygenator gas was accomplished by adjusting N_2, O_2, and CO_2 flow meters. A small sample of blood was withdrawn continuously from the reservoir for P_{CO_2}, P_{O_2}, and *p*H analysis.

isolation verified by direct visualization. Left lung atelectasis was induced and the right lung ventilated with 100% O_2. Right lung tidal volume was adjusted to provide peak airway pressures of 15–20 cmH_2O. Inspired CO_2 was added or the respiratory rate adjusted to maintain an end-tidal P_{CO_2} of 30–35 mmHg. Expired gases flowed through a gas-mixing cone before venting to atmosphere via an underwater seal providing 5 cm water of PEEP.

Inspired and mixed expired oxygen tensions were measured (IL® #407 oxygen analyzer). Inspired, end-tidal, and mixed expired CO_2 tensions were measured (Godart® Capnograph). The analyzers were calibrated with gases of known composition and were corrected for barometric pressure, temperature, and water vapor to body temperature (BTPS) conditions.

VENO-VENOUS BYPASS

Figure 1 shows the bypass circuit in schematic form. The circuit contained a bubble oxygenator (Shiley®), with gas supply regulated by N_2, O_2, and CO_2 flow meters. Oxygenator gas O_2 and CO_2 tensions were measured (IL® oxygen analyzer and Godart® Capnograph). The fluid prime and blood from suction were passed through a Bentley® cardiotomy and a Pall Ultrapor® 40-μm blood

filter, respectively, before entering the bubble oxygenator. A Sarns® Inc. roller head pump, calibrated *in vitro* each day, pumped the blood into the animal through 0.95-cm Tygon® tubing. Blood temperature was monitored in the reservoir and was controlled by a Cardiovascular Instrument® water heater. Blood was withdrawn continuously from the reservoir, pumped through a Radiometer® PHM27 Blood Gas Monitor for P_{CO_2}, P_{O_2}, and *p*H analysis and returned to the venous side of the oxygenator.

The animal was anticoagulated with heparin 500 units/kg, with supplemental doses determined by activated clotting times (Hemochron® 400). The pump was primed with 1,000 ml Normosol® and 500 ml dog blood. Heparin (2,500 units) was added to the blood prime, and the CPD anticoagulant was reversed with $CaCl_2$ (250 mg) to avoid hypocalcemic myocardial depression. Large-bore cannulae were placed in the right atrium and superior (SVC) and inferior (IVC) venae cavae. The azygos vein was ligated at its insertion into the SVC. Total extracorporeal veno-venous bypass was established with all venous return collected from the SVC and IVC, passed through the bypass circuit, oxygenated or deoxygenated, and reinfused into the right atrium. The animals occasionally required stabilization with $NaHCO_3$ and a 2-μg bolus of epinephrine at the start of bypass.

Carbon dioxide was supplied to the oxygenator to maintain normocarbia. Additional Normosol® or blood was added to the pump, if required, to replace insensible, blood, and urine losses during the study. $NaHCO_3$ was administered to correct base deficits calculated from measured arterial blood *p*H and P_{CO_2} values. The right lung was hyperinflated periodically to prevent microatelectasis.

The decrease in left lung blood flow observed with atelectasis before bypass was obliterated by the onset of bypass. This effect may be due to surgical trauma, cardiovascular instability, or acute hemodilution and was a transitory phenomenon. Therefore, high and low mixed venous oxygen tensions were alternated every 10 min until the hypoxic pulmonary vasoconstrictor response returned. The experimental manipulations were not begun until consistent and stable left-lung blood-flow responses were observed with high and low $P\bar{v}_{O_2}$, usually 1–2 h after the establishment of total bypass.

Experimental Design

Each animal was exposed to all of the experimental manipulations in a counterbalanced sequence: normal $P\bar{v}_{O_2}$ (46 mmHg) at the prebypass cardiac output (75 $ml \cdot min^{-1} \cdot kg^{-1}$), low $P\bar{v}_{O_2}$ (20–30 mmHg) at a lower (50 $ml \cdot min^{-1} \cdot kg^{-1}$) and a higher (100 $ml \cdot min^{-1} \cdot kg^{-1}$) cardiac output (CO), and high $P\bar{v}_{O_2}$ (105–135 mmHg) at the same lower and higher CO. The desired $P\bar{v}_{O_2}$ was achieved by adjusting the N_2 and O_2 flows to the pump oxygenator. The cardiac output was raised to 100 $ml \cdot min^{-1} \cdot kg^{-1}$ by increasing pump flow and opening the arteriovenous fistula to yield adequate venous return and reduced systemic vascular resistance. The cardiac output was lowered by reducing pump flow.

Measurements

After 20 min of each phase, the following measurements were recorded: temperature, O_2 and CO_2 tensions of the right lung (inspired and mixed expired P_{O_2} and P_{CO_2}, and end-tidal P_{CO_2}) and the pump oxygenator gas; aortic and left pulmonary artrial blood flow; and airway, left atrial, central venous, pulmonary, and systemic arterial pressures. These measurements were recorded on an eight-channel Grass Polygraph® and the values noted at the end-expiration phase of the respiratory cycle. Arterial and mixed venous blood gases were collected simultaneously for *p*H, P_{CO_2}, and P_{O_2} analysis using an IL® Model 113 ultramicro blood gas analyzer. The erythrocyte hemoglobin content was calculated as total hemoglobin minus plasma hemoglobin measured by cyanmethemoglobin determination.[7] At the end of the study, the bypass pump flow was discontinued and the animal exsanguinated. The heart, lungs, and abdomen were inspected for gross pathology.

Calculations

The following calculations were made from the recorded data. Right pulmonary artery blood flow was calculated from total cardiac output ($\dot{Q}_T$ = pump flow) minus left pulmonary artery flow ($\dot{Q}_L$). Thus, our calculation of $\dot{Q}_R$ included coronary and bronchial blood flow. The percentage of blood flow to the left and right lungs was expressed as percentage of total flow ($\dot{Q}_L$% and $\dot{Q}_R$%, respectively). Pulmonary perfusion pressure (PP) was calculated as mean PAP minus mean LAP in mmHg. Left, right, and total pulmonary vascular resistances in $dyn \cdot cm^{-5} \cdot s$ were calculated by (PP × 80) divided by respective lung blood flow in L/min. Alveolar oxygen tension of the right lung was calculated from measured inspired O_2 tension corrected for barometric pressure, water vapor pressure, and Pa_{CO_2}. Blood O_2 contents (Cb_{O_2}) were calculated from the measured O_2 tension and hemoglobin concentration using the equation:

$$Cb_{O_2} = (1.34 \times Hb \times \% \text{ sat}) + (Pb_{O_2} \times 0.0031)$$

where Cb_{O_2} = blood oxygen content in ml/dl blood, 1.34 = O_2 capacity of hemoglobin in ml/g Hb, Hb = hemoglobin in g/dl blood, % sat = percentage saturation, Pb_{O_2} = blood oxygen tension in mmHg, and 0.0031 = dissolved O_2 in $ml \cdot mmHg^{-1} \cdot dl^{-1}$ blood. Percentage saturation, corrected for *p*H and temperature, was cal-

TABLE 1. Effects of Cardiac Output (CO) and $P\bar{V}_{O_2}$ on Blood Gases and Pulmonary Hemodynamics During Left-lung Atelectasis

	Cardiac Output 50 ml·min^{-1}·kg^{-1} = 1,240 ± 30 ml/min		Cardiac Output 100 ml·min^{-1}·kg^{-1} = 2,140 ± 70 ml/min	
	Low $P\bar{V}_{O_2}$	High $P\bar{V}_{O_2}$	Low $P\bar{V}_{O_2}$	High $P\bar{V}_{O_2}$
$P\bar{V}_{O_2}$ mmHg	21 ± 2	107 ± 12	28 ± 2	135 ± 36
Pa_{O_2} mmHg	115 ± 18*	326 ± 29	115 ± 29*	329 ± 28
$\overline{PAP}$ mmHg	14.2 ± 1.6	12.0 ± 1.2†	19.3 ± 1.6	13.4 ± 2.8
PP mmHg	9.9 ± 1.8	7.7 ± 0.6	13.6 ± 2.2	9.7 ± 1.6
PVR Left dyn·cm^{-5}·s	5,640 ± 2,500	1,480 ± 320	2,260 ± 680	920 ± 160
PVR Right dyn·cm^{-5}·s	790 ± 110	1,000 ± 260	710 ± 70	640 ± 110
PVR Left:right ratio	6.4 ± 2.1*	1.9 ± 0.5	3.1 ± 0.8*	1.6 ± 0.3

Pa_{O_2} was significantly lower and PVR left:right ratio was significantly higher with reduced $P\bar{V}_{O_2}$ at both levels of cardiac output. $\overline{PAP}$ was significantly higher with the higher cardiac output. Significant difference ($P < 0.05$): *indicates that indicated value at high $P\bar{V}_{O_2}$ is significantly different than the value at low $P\bar{V}_{O_2}$; †indicates that the mean of the values during low CO is significantly different from the mean of the values under high CO.

Abbreviations: $\overline{PAP}$ = mean pulmonary artery pressure; PP = pulmonary perfusion pressure; PVR = pulmonary vascular resistance.

culated from a nomogram for canine hemoglobin.[8] End-capillary oxygen tension (Pc'_{O_2}) was assumed equal to alveolar O_2 partial pressure. The percentage venous admixture or shunt ($\dot{Q}_S/\dot{Q}_T$) was calculated by the following equation:

$$\dot{Q}_S/\dot{Q}_T = (Cc'_{O_2} - Ca_{O_2})/(Cc'_{O_2} - C\bar{V}_{O_2})$$

where Cc'_{O_2} = end-capillary O_2 content, Ca_{O_2} = arterial O_2 content, and $C\bar{V}_{O_2}$ = mixed venous O_2 content.

STATISTICS

The data were analyzed by a within-subjects two-factor analysis of variance (ANOVA), which compared the effects of manipulating $P\bar{V}_{O_2}$, cardiac output, and their interaction on left-lung blood flow, shunt, pulmonary vascular resistances, pulmonary arterial and perfusion pressures, arterial oxygenation, and general experimental conditions. Because cardiac output did not alter $\dot{Q}_L$%, $\dot{Q}_S/\dot{Q}_T$% and Pa_{O_2}, these data for low and high $P\bar{V}_{O_2}$ at the two cardiac outputs were averaged and compared with normal $P\bar{V}_{O_2}$ by a one-way ANOVA and the Neuman-Keuls test for comparison of differences between means. A $P < 0.05$ was deemed significant for all statistical measurements. Results are expressed as mean ± SE.

Results

The general experimental conditions were constant throughout the study (body temperature = 37.2 ± 0.1°C, hemoglobin concentration = 8.0 ± 0.4 g/dl, arterial *p*H = 7.33 ± 0.01, Pa_{CO_2} = 41 ± 1 mmHg, $P\bar{V}_{CO_2}$ = 45 ± 1 mmHg, BE = −4 ± 1 mEq/l, mean airway pressure = 7.2 ± 0.1 cmH_2O, mean systemic arterial BP = 77 ± 2 mmHg, and mean left atrial pressure = 5.3 ± 0.5 mmHg).

ATELECTASIS WITH NORMAL $P\bar{V}_{O_2}$ AND CARDIAC OUTPUT

When the $P\bar{V}_{O_2}$ was normal (46 ± 2mmHg) and the CO at prebypass level (1,680 ± 75 ml/min), $\dot{Q}_L$% was 19.0 ± 3.4%, $\dot{Q}_S/\dot{Q}_T$% was 31.0 ± 3.1%, and Pa_{O_2} = 220 ± 32 mmHg. Mean pulmonary artery pressure was 15.3 ± 1.1 mmHg, pulmonary perfusion pressure was 9.4 ± 1.4 mmHg, and the ratio of left:right lung pulmonary vascular resistance was 5.1 ± 1.0.

EFFECTS OF CARDIAC OUTPUT

Cardiac output was raised to 2,140 ± 70 ml/min (100 ml·min^{-1}·kg^{-1}) with the open arteriovenous fistula and increased pump flow. It was decreased to 1,240 ± 30 ml/min (50 ml·min^{-1}·kg^{-1}) by closing the fistula and reducing pump flow. Lowering CO by 40%, significantly reduced $\overline{PAP}$ from 19.3 ± 1.6 to 14.2 ± 1.6 mmHg with low $P\bar{V}_{O_2}$ and 13.4 ± 2.8 to 12.0 ± 1.2 mmHg with high $P\bar{V}_{O_2}$ ($P < 0.05$; see table 1). Despite this decrease in transmural $\overline{PAP}$, the reduction in CO did not significantly affect Pa_{O_2}, $\dot{Q}_L$%, or $\dot{Q}_S/\dot{Q}_T$% (table 1, fig. 2). Left lung PVR, right lung PVR, and the PVR left:right ratio were not altered significantly by change in CO.

EFFECTS OF $P\bar{V}_{O_2}$

A broad range of $P\bar{V}_{O_2}$ was obtained by changing the gas supply to the oxygenator (table 1). $P\bar{V}_{O_2}$ was reduced to 21 ± 2 mmHg with the lower CO and to 28 ± 2 mmHg with the higher CO. $P\bar{V}_{O_2}$ was raised to 107 ± 12 mmHg and 135 ± 36 mmHg at 50 and 100 ml·min^{-1}·kg^{-1} CO, respectively.

When $P\bar{V}_{O_2}$ was low, $\dot{Q}_L$% was reduced but was not different from that observed with normal $P\bar{V}_{O_2}$ (mean $\dot{Q}_L$% = 23.2 ± 4.6%, see fig. 2). Raising the $P\bar{V}_{O_2}$ to

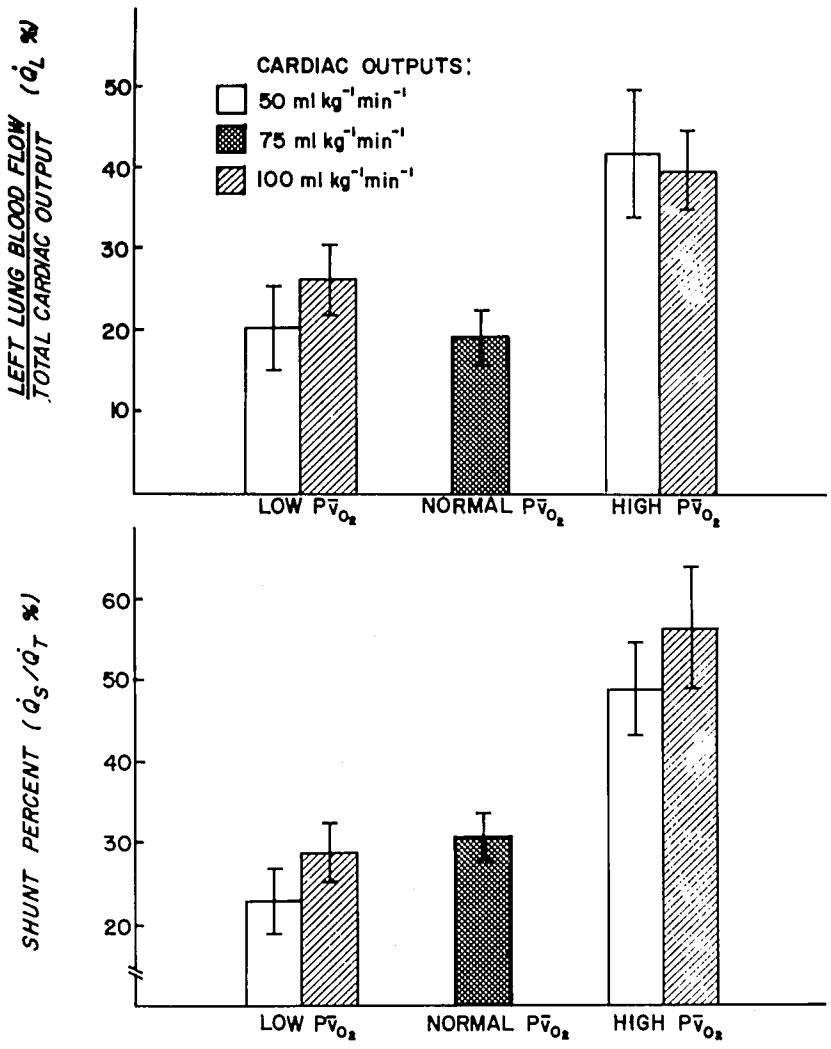

FIG. 2. Effects of $P\bar{v}_{O_2}$ on left-lung blood flow as percentage of total blood flow ($\dot{Q}_L\%$) and shunt per cent ($\dot{Q}_S/\dot{Q}_T\%$) during the left-lung atelectasis. Data from three cardiac outputs (CO) are represented. Cardiac output did not influence either $\dot{Q}_L\%$ or $\dot{Q}_S/\dot{Q}_T\%$. *Upper panel:* $\dot{Q}_L\%$ was 19–25% when $P\bar{v}_{O_2}$ was low or normal. When $P\bar{v}_{O_2}$ was raised to greater than 100 mmHg, $\dot{Q}_L\%$ was increased significantly to 40%, nearly the flow expected for normoxic ventilated left lung. *Lower panel:* $\dot{Q}_S/\dot{Q}_T\%$ was significantly greater when $P\bar{v}_{O_2}$ was high than when it was normal or low.

greater than 100 mmHg significantly increased $\dot{Q}_L\%$ to nearly the flow expected for normoxic ventilated left lung (mean $\dot{Q}_L\% = 40.4 \pm 5.9\%$, $P < 0.001$). Thus, diversion of blood flow away from the atelectatic lung did not occur when $P\bar{v}_{O_2}$ was high.

The $\dot{Q}_S/\dot{Q}_T\%$ observed during left-lung atelectasis also was increased significantly by the high $P\bar{v}_{O_2}$ (fig. 2, mean $\dot{Q}_S/\dot{Q}_T\% = 51.7 \pm 5.6\%$, $P < 0.001$). When $P\bar{v}_{O_2}$ was low, the mean $\dot{Q}_S/\dot{Q}_T\%$ (26.0 ± 3.4%) was not different from $\dot{Q}_S/\dot{Q}_T\%$ when $P\bar{v}_{O_2}$ was normal. Pa_{O_2} was significantly greater when $P\bar{v}_{O_2}$ was high than when $P\bar{v}_{O_2}$ was normal or low, despite the increase in $\dot{Q}_L\%$ and $\dot{Q}_S/\dot{Q}_T\%$ (Pa_{O_2} = 327 ± 25 mmHg with high $P\bar{v}_{O_2}$, 220 ± 32 mmHg with normal $P\bar{v}_{O_2}$, and 115 ± 21 mmHg with low $P\bar{v}_{O_2}$).

Pulmonary perfusion pressure and pulmonary vascular resistances were variable (table 1). Comparing the ratio of left:right PVR demonstrated that when $P\bar{v}_{O_2}$ was low or normal, the left-lung PVR was considerably greater than the right-lung PVR. Raising $P\bar{v}_{O_2}$ significantly lowered the left:right PVR ratio to close to one ($P < 0.05$; table 1).

Discussion

Blood flow generally decreases to atelectatic lung, thereby reducing the expected pulmonary shunt and reducing hypoxemia. This study demonstrates that the blood flow reduction observed in atelectasis was altered by the $P\bar{v}_{O_2}$. When $P\bar{v}_{O_2}$ was normal (46 mmHg) or low (21–28 mmHg), hypoxic pulmonary vasoconstriction (HPV) occurred and approximately 50% of the blood flow was diverted away from the atelectatic lung. HPV was abolished when $P\bar{v}_{O_2}$ was 100–140 mmHg, and the atelectatic lung blood flow was that expected for normoxic ventilated left lung (40%).[2]

Under the conditions of this study (open-chest and nitrogen-washout prior to occlusion), total atelectasis was achieved. This is a convenient model to demonstrate the role of $P\bar{v}_{O_2}$ in hypoxic pulmonary vasoconstriction be-

cause in the absence of alveolar gas, the P_{O_2} of most lung tissue approaches $P\bar{V}_{O_2}$ and becomes the only stimulus for HPV. The atelectasis model, therefore, avoids the interaction between PA_{O_2} and $P\bar{V}_{O_2}$, which has made interpretations difficult in other models using normal lungs,[9–12] alveolar hypoxia,[9,12–14] or oleic acid-injured lungs.[10,11] The stimulus–response curve to alveolar hypoxia is sigmoid with HPV responses evident when PA_{O_2} is less than 100 mmHg, which become maximal when PA_{O_2} is 30–40 mmHg.[15,16] Thus, HPV is maximally stimulated in atelectasis when $P\bar{V}_{O_2}$ is normal or low and $P\bar{V}_{O_2}$ must be greater than 100 mmHg to eliminate its effect. The effectiveness of this response is reduced when the normal lung is ventilated with gas mixtures containing less than 100% O_2. In these circumstances, sufficient reduction of $P\bar{V}_{O_2}$ also may induce vasoconstriction in the ventilated lung.[17] It is of interest that hypoxic pulmonary vasodilation has been reported *in vitro* when the P_{O_2} is less than 30 mmHg,[18] but inhibition of HPV was not observed in the present *in vivo* study.

The HPV responses to left-lung atelectasis observed when $P\bar{V}_{O_2}$ was normal are consistent with previous studies,[2] although the magnitude of the flow diversion was somewhat less and shunt was greater than in the intact dog.[2] This may be due to the use of veno-venous bypass to alter $P\bar{V}_{O_2}$ in this study, with the resultant surgical stress, hemodilution, and anemia.

It has been suggested that the reduced lung volume associated with atelectasis causes mechanical distortion of lung vasculature, which further increases atelectatic lung vascular resistance and reduces blood flow.[19] The present work and that of others[1,4–6,20] indicates this mechanical effect must be small. With high $P\bar{V}_{O_2}$, the blood flow to atelectatic left lung was essentially the same (40%) as that expected for the normoxic ventilated left lung. Thus, HPV is the principal mechanism of blood flow reduction in atelectasis.

Reducing cardiac output by 40% significantly lowered transmural pulmonary artery pressure, but did not affect the HPV response to atelectasis in this study. Shunt varies directly with cardiac output in animals with normal[10,11] or diffusely abnormal lungs[10,11,21,22] because of a mechanical inhibition of HPV by increased pulmonary artery pressure.[21,23,24] However, atelectatic lung perfusion and shunt increased with both high[25] and low[26,27] cardiac outputs in closed-chest models. The increase in atelectatic lung blood flow with low cardiac output from hemorrhage has been attributed to the mechanical effects of atelectasis (both mechanical distortion of vasculature and negative intrapleural pressure causing increased transmural pressure), which cause a disproportionate increase in pulmonary vascular resistance of the ventilated lung.[21,27] When the chest is open, atelectasis is not associated with a negative intrapleural pressure. Reducing cardiac output failed to alter the distribution of lung blood flow in atelectasis in our open-chest model and in a previous study using hypoxic ventilation of a lung.[27]

In summary, approximately 50% of blood flow was diverted away from atelectatic lung when $P\bar{V}_{O_2}$ was low or normal. When $P\bar{V}_{O_2}$ was raised to 100–140 mmHg, the HPV response was abolished and the atelectatic lung blood flow was that expected for normoxic ventilated lung. These results confirm the hypothesis that HPV is a primary regulator of blood flow distribution in the atelectatic lung and that $P\bar{V}_{O_2}$ is the principal stimulus. Other factors such as age, *p*H, P_{CO_2}, lung disease, and the manner of ventilation of nonatelectatic lung are secondary variables that can influence the responses observed but cannot be regarded as initiators of HPV.

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