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Respiratory mechanics and gas exchange in postobstructive pulmonary vasculopathy

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ABSTRACT: Chronic unilateral pulmonary artery ligation induces formation of new bronchial collateral vessels in the affected lung. These vessels form precapillary anastomoses with the pulmonary circulation and the lung is perfused with arterial blood. Inspired gas is diverted to the contralateral lung to maintain the ventilation/perfusion ratio ($\dot{V}_A/\dot{Q}$) and gas exchange. This study was designed to determine the mechanism responsible for this shift of ventilation, which has not previously been investigated.

We studied six dogs, before and 6 months after ligation of the left main pulmonary artery. We measured pulmonary resistance (R_L) and elastance (E_L), minute ventilation ($\dot{V}_E$), O_2 consumption ($\dot{V}_{O_2}$) and CO_2 production ($\dot{V}_{CO_2}$) of the right and left lungs. We also examined the effect of CO_2, atropine and isoproterenol on R_L and E_L.

In the lung with ligated pulmonary artery: 1) $\dot{V}_E$ was significantly reduced; 2) R_L and E_L were increased and were unresponsive to CO_2, atropine and isoproterenol; and 3) $\dot{V}_{O_2}$ decreased more than $\dot{V}_{CO_2}$ and, consequently, respiratory quotient (RQ) was greater than 1.

We conclude that, with chronic pulmonary artery obstruction, ventilation shifts to the contralateral lung because of an increase in R_L and E_L not related to airway smooth muscle tone.

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Postobstructive pulmonary vasculopathy (POPV) is defined as the vascular changes resulting from chronic unilateral ligation of one pulmonary artery. Based on early studies in the literature [1–3], and our own recent findings [4–6], the principal characteristics of POPV are: 1) a marked rise in bronchial blood flow to the lung with the ligated artery, associated with proliferation of new bronchial collaterals around pulmonary vessels and airways; 2) precapillary anastomoses between the bronchial collaterals and pulmonary vessels; 3) a doubling of total pulmonary vascular resistance of the lobes with POPV, associated with peripheral muscularization and increased medial thickness in pulmonary arteries; 4) hyperreactivity of the pulmonary arteries to serotonin and of the pulmonary veins to histamine; and 5) normal parenchyma except for mild focal fibrosis.

Since, in the lung with POPV, the pulmonary capillaries are perfused with oxygenated blood from the bronchial arteries rather than deoxygenated blood from the pulmonary artery, ventilation of that lung should contribute little to gas exchange. Previous studies of the acute (<1 day) effects of pulmonary artery occlusion [7–10] showed that, upon cessation of gas exchange, alveolar CO_2 fell, the airways constricted and lung impedance increased. As a result, inspired gas was diverted to the contralateral lung and arterial oxygen tension (Pa_{O_2}) and arterial carbon dioxide tension (Pa_{CO_2}) were maintained without the need for an increase in minute ventilation ($\dot{V}_E$). The bronchoconstriction could be prevented by administration of CO_2 or isoproterenol to the lung with the occluded pulmonary artery, but not by vagotomy or atropine [8], suggesting a direct effect of hypocapnia on airway smooth muscle.

Very few studies have examined the effects of chronic pulmonary artery obstruction on lung function. In the first 2–4 weeks postligation, lung volume is reduced by atelectasis but the pressure-volume relationship is essentially normal when corrected for lung volume. By 2 months, the atelectasis resolves and lung volume returns to normal [11]. Nevertheless, 3 months or more postligation, ventilation of the affected lung remains reduced [12, 13].

Several questions regarding lung mechanics during long-term pulmonary artery obstruction remain unanswered. Firstly, the reason for the continued low ventilation of the lung with the ligated pulmonary artery has not been determined. Secondly, in all previous studies, the pulmonary artery was ligated through an ipsilateral thoracotomy, and the contribution of adhesions between visceral and parietal pleurae to the results has not been considered.

We hypothesized that after long-term pulmonary artery ligation, the shift in ventilation from the lung with the

ligated artery to the contralateral lung was not due to hypocapnic bronchoconstriction, but to other mechanisms, such as: 1) increased airway smooth muscle tone, due, for example, to increased vagal activity or release of mediators; 2) increased thickness of airway smooth muscle; or 3) morphological changes (*e.g.* focal fibrosis) in the lung parenchyma.

Our objectives in the present study were to: 1) minimize pleural adhesions, which could alter lung mechanics, by ligating the pulmonary artery through a contralateral thoracotomy; 2) ascertain whether a chronic shift of ventilation to the contralateral, normal lung occurred in our model; 3) determine the mechanism of the ventilation shift (if any) by measuring lung resistance (R_L) and elastance (E_L); and 4) evaluate the contribution of reversible airway constriction to the changes in R_L and E_L by administering CO_2, atropine and isoproterenol.

Materials and methods

We examined lung mechanics and gas exchange in six adult mongrel dogs weighing 25.9±1.1 kg (mean±SEM), free of respiratory or other diseases. All six animals were studied before and after ligation of the left main pulmonary artery (see below). For the sake of brevity, the animals with the ligated left pulmonary artery will be referred to as "ligated" dogs and the lung as the "ligated" lung. Animal Care and Use Committee approval was obtained for the experimental protocol.

Surgical procedure for pulmonary artery ligation

Ligation of the left main pulmonary artery was carried out as described previously [4, 14]. Briefly, the animals were anaesthetized with pentobarbital sodium (25 $mg \cdot kg^{-1}$), intubated and ventilated with 100% O_2. They were placed in the left lateral decubitus position and, with the use of sterile surgical techniques, a right thoracotomy was performed. The left main pulmonary artery was ligated just beyond its bifurcation from the main artery. The chest was closed in layers and the lung reinflated with temporary insertion of a chest tube. Postoperative care and medication were provided by the McIntyre Animal Resources Centre.

Physiological measurements

The animals were anaesthetized with intravenous pentobarbital sodium (25 $mg \cdot kg^{-1}$), intubated, placed in the supine position, and ventilation with a dual-output constant-volume ventilator (model 618, Harvard Apparatus, Sough Natick, MA, USA). A small catheter was placed in a peripheral upper limb vein for fluid and drug administration. Anaesthesia was maintained with additional doses of 2.5 $mg \cdot kg^{-1}$ pentobarbital sodium at approximately 1 h intervals. The intravenous catheters were sterile, and the endotracheal and oesophageal tubes were clean.

Flow ($\dot{V}$) at the airway opening was measured using a pneumotachograph (Fleisch No. 1) and a piezoresistive differential pressure transducer (MicroSwitch 163PC0036, Honeywell, Scarborough, ON, Canada). A tapered plastic cannula with two side-ports was used to connect the pneumotachograph to the endotracheal tube. Through the first port, airway opening pressure (Pao) was measured with a differential transducer (MicroSwitch 143PC030). Through the second port, we inserted the sampling catheter of a mass spectrometer (model MGA 1100, Perkin-Elmer Medical Industries, Pomona, CA, USA) to measure the fraction of expired O_2 (F_{EO_2}) and CO_2 (F_{ECO_2}). Oesophageal pressure (Poes) was measured with a balloon-catheter system attached to a differential pressure transducer (MicroSwitch 143PC030). The oesophageal balloon was filled with 1 ml air, and its position adjusted to ensure that changes in Poes and Pao were similar when the animal breathed spontaneously against a closed airway [15]. Before ligation, $\Delta Poes/\Delta Pao$ was 1.01±0.01; after ligation, $\Delta Poes/\Delta Pao$ was 1.01±0.07 (mean±SEM).

All measured signals ($\dot{V}$, Pao, Poes, F_{EO_2} and F_{ECO_2}) were amplified and passed through 8-pole Bessel low-pass antialiasing filters (902LPF, Frequency Devices, Haverhill, MA, USA) having a corner frequency of 30 Hz. The filtered signals were digitized at 100 Hz with a 12-bit analogue-to-digital converter (DT2801-A, Data Translation, Marlboro, MA, USA) and stored on a 386 personal computer using the LABDAT data acquisition software (RHT-Infodat, Montréal, QC, Canada).

From these measurements, using ANADAT data analysis software (RHT-Infodat, Montréal, QC, Canada), we calculated the following parameters: 1) transpulmonary pressure (P_L)=Pao-Poes; 2) tidal volume (V_T) by numerical integration of flow; 3) minute ventilation ($\dot{V}_E$) by multiplying V_T by frequency; 4) carbon dioxide production ($\dot{V}_{CO_2}$) from $\int F_{ECO_2} \times \dot{V} \times dt$; and 5) oxygen consumption ($\dot{V}_{O_2}$) from $\int F_{EO_2} \times \dot{V} \times dt$.

The mechanical parameters lung resistance (R_L) and elastance (E_L), were determined by fitting the equation:

$$P_L = R_L\dot{V} + E_LV + PEEP \quad (1)$$

to the data by multiple linear regression. In this equation, positive end-expiratory pressure (PEEP) is a constant that accounts for non-zero pressures at end-expiration; in fact, in these experiments, PEEP was not different from zero.

Experimental protocol

Firstly, we studied the mechanics and gas exchange of the whole lung, after intubating the trachea with a 9 mm endotracheal tube. Measurements were made in duplicate during one minute intervals of spontaneous breathing to obtain values of $\dot{V}_E$, $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$, and during one minute intervals of mechanical ventilation at a tidal volume (V_T) of 404±11 ml and a frequency of 11.4±0.6 $breaths \cdot min^{-1}$ to obtain R_L and E_L.

Secondly, we studied the mechanics and gas exchange of the right and left lungs separately by replacing the endotracheal tube with a double-lumen tracheal tube (Willy Rusch AG, Waiblingen, Germany). Complete separation of the two lungs was ascertained by briefly ventilating one lung with 20% helium in room air, whilst measuring the expired gas composition of the contralateral lung with the mass spectrometer to ensure that no helium crossed over. We then repeated the mechanics and gas exchange measurements, *i.e.* RL, EL, $\dot{V}_E$, $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$, under baseline conditions. Measurements on right and left lungs were made sequentially, in random order. For the measurements of RL and EL, both lungs were mechanically-ventilated by a dual-output ventilator at a frequency of 12.7±0.7 breaths·min^{-1}; left lung VT was 177±7 ml, right lung VT was 184±5 ml. During spontaneous breathing, the lung not being studied was open to the room. Fraction of inspired oxygen (F_{IO_2}) was 0.21 at all times.

We measured the pressure-flow relationship between 0 and 1 *l*·s^{-1} in both lumens of the Rusch tube and fitted a polynomial to the data points. The resulting equations were, for the left side, $P=6\dot{V}+32\dot{V}^2$ and, for the right side, $P=3\dot{V}+54\dot{V}^2$. From these equations, the pressure drop and the resistance of the tube were calculated under baseline conditions during mechanical ventilation. A linear fit to the data gave an approximate resistance value.

To ascertain whether there was reversible bronchoconstriction, we tested the effects of the following: 1) 5% CO_2 delivered for 5–10 min to the left lung only; 2) atropine (0.04 mg·kg^{-1}) [8] administered as an intravenous bolus over 1 min, whilst monitoring any change in pulse rate; 3) isoproterenol, 0.4 mg, aerosolized with 10 *l*·min^{-1} room air using a Hudson nebulizer and delivered to the left lung only [16]. Between the CO_2, atropine and isoproterenol administrations, a set of control measurements were made to ensure a return to baseline conditions.

We followed the above protocol on all six animals to obtain preligation data. The animals then underwent ligation of the left main pulmonary artery (see above). After an interval of 5.9±1.1 months, the animals were anaesthetized as described previously, and the above protocol repeated to obtain postligation data.

Statistical analysis

Results are given as mean±SEM. Statistical significance was assessed by analysis of variance for paired data (block analysis) or, when appropriate, by Student's paired t-test using a proprietary software program (Systat Inc., Evanston, IL, USA). Values of p less than 0.05 were considered significant. Separate comparisons were made for: 1) the differences between right and left lungs; 2) the effect of left main pulmonary artery ligation on right and left lungs; and 3) the effects of CO_2, atropine and isoproterenol. For the relationship between the shift of ventilation and RL and EL, we calculated Spearman's rank correlation coefficient using the aforementioned software program.

Results

The values of RL, EL, $\dot{V}_E$, $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ of the whole lung were within normal limits and were not significantly altered by ligation of the left main pulmonary artery (figs 1 and 2).

When we looked at the right and left lungs separately (figs 3–5), the changes induced by the ligation became apparent. Before ligation baseline RL was 14.8±2.6 $cmH_2O{\cdot}l^{-1}{\cdot}s$ in the left lung, slightly higher ($p<0.05$) than in the right lung, 13.6±1.1 $cmH_2O{\cdot}l^{-1}{\cdot}s$ (fig. 3). Baseline EL (fig. 4) was also higher on the left side than on the right (40.0±5.2 and 29.2±4.0 $cmH_2O{\cdot}l^{-1}$ ($p<0.001$), respectively), because of the smaller size of the left lung [17], with VT being the same on both sides. The higher RL and lower EL of the left lung are consistent with previous observations [18].

After ligation of the left main pulmonary artery (figs 3 and 4), the main finding was a significant increase in RL ($p<0.001$) and EL ($p<0.02$), in the left lung. In addition, there was a small but statistically significant ($p<0.05$) increase of right lung RL; right lung EL did not change with ligation.

The estimated *in situ* tube resistance on the left side was 12.0±0.3 $cmH_2O{\cdot}l^{-1}{\cdot}s$ before and 12.8±0.2 $cmH_2O{\cdot}l^{-1}{\cdot}s$ after ligation. On the right side, the values were 12.3±0.2 and 13.7±0.3 $cmH_2O{\cdot}l^{-1}{\cdot}s$, respectively. These data indicate that most of the measured resistance was due to the endotracheal tube.

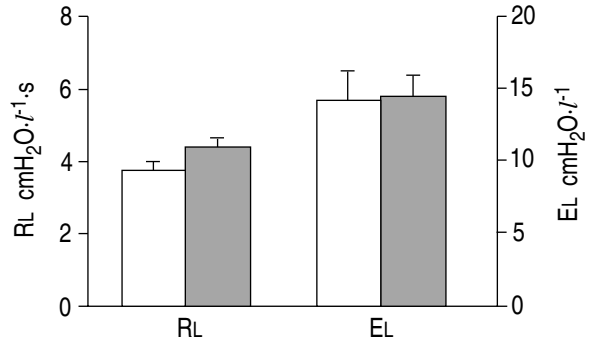

Fig. 1. – Effect of left pulmonary artery ligation on pulmonary resistance (RL) and elastance (EL) of the whole lung (mean±SEM). Note small, albeit not statistically significant, rise in resistance after ligation of left pulmonary artery. ▭ : preligation; ▬ : postligation.

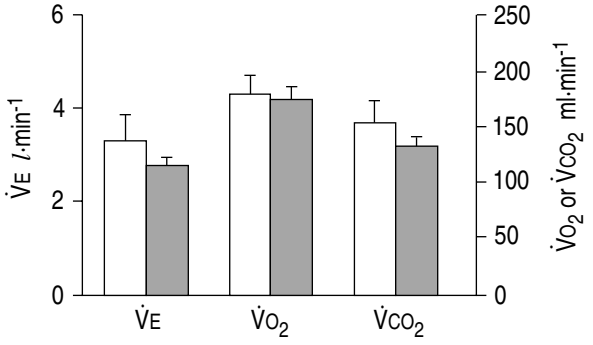

Fig. 2. – Minute ventilation ($\dot{V}_E$), O_2 consumption ($\dot{V}_{O_2}$) and CO_2 production ($\dot{V}_{CO_2}$) of the whole lung (mean±SEM) were not significantly altered by ligating the left pulmonary artery. ▭ : preligation; ▬ : postligation.

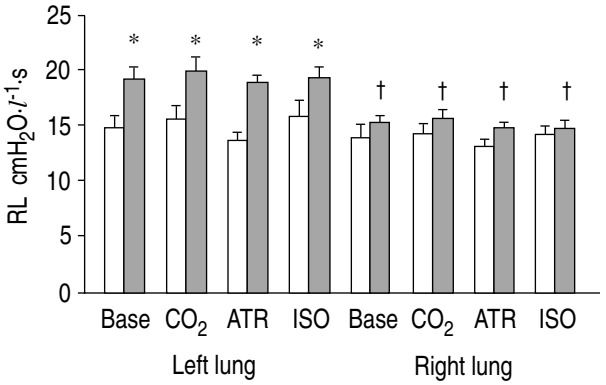

Fig. 3. – Pulmonary resistance (R_L) of the left lung (mean±SEM) increased substantially after ligation. There was also a small, but significant, rise in the R_L of the contralateral right lung. Note the absence of an effect of CO_2, atropine (ATR) and isoproterenol (ISO) on R_L on either side. Base: baseline. ▭: preligation; ▬: postligation. *: p<0.01; †: p<0.05, postligation *vs* preligation.

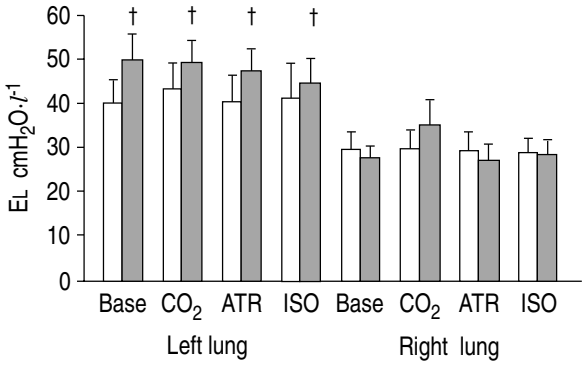

Fig. 4. – Lung elastance (E_L) (mean±SEM) increased only in the left lung after ligation of the left pulmonary artery. CO_2, atropine (ATR) and isoproterenol (ISO) had no effect. Base: baseline. ▭: preligation; ▬: postligation. †: p<0.05, postligation *vs* preligation.

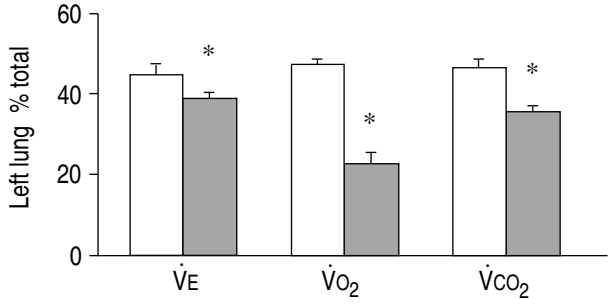

Fig. 5. – Effect of ligation on minute ventilation ($\dot{V}_E$), O_2 consumption ($\dot{V}_{O_2}$), CO_2 production ($\dot{V}_{CO_2}$) expressed as percentage of total (mean±SEM). Note that $\dot{V}_E$, $\dot{V}_{CO_2}$ and to a greater extent $\dot{V}_{O_2}$ in the left lungs fell significantly after ligation. ▭: preligation; ▬: postligation. *: p<0.01.

Inhalation of CO_2 and isoproterenol and the intravenous administration of atropine had no bronchodilating effect in either the right or left lungs, before or after ligation. Neither R_L (fig. 3) nor E_L (fig. 4) differed significantly from baseline values for any of the agents.

Data for $\dot{V}_E$, $\dot{V}_{O_2}$, $\dot{V}_{CO_2}$ are illustrated in fig. 5. To control for variations in the level of anaesthesia, values were expressed as a percentage of total. Prior to ligation, the left lung contributed 45±2% of the total $\dot{V}_E$, 47±1% of total $\dot{V}_{O_2}$, and 46±2% of total $\dot{V}_{CO_2}$. After ligation, left lung $\dot{V}_E$ fell significantly to 39±1% of total. In addition, despite perfusion of the pulmonary capillaries with arterial blood, the ligated left lung contributed 22±3% of total $\dot{V}_{O_2}$ and 35±1% of total $\dot{V}_{CO_2}$ (p<0.01 *versus* preligation).

Values for RQ are plotted in figure 6. The left lung before ligation and the right lung before and after ligation had an RQ in the range 0.70–0.75. However, left lung RQ rose to 1.55 after ligation because of preferential exchange to CO_2 over O_2.

To determine if there was a relationship between the shift in ventilation postligation and the observed changes in respiratory mechanics, we plotted the change (postligation minus preligation) in the percentage of total $\dot{V}_E$ going to the left lung against the change in R_L and E_L of the left lung (fig. 7). There was a significant relationship between the change in V_E of the left lung and R_L, but not E_L.

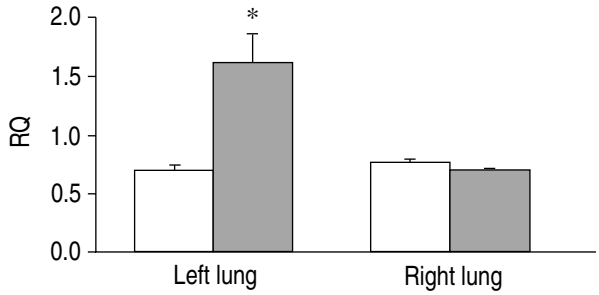

Fig. 6. – Respiratory quotient (RQ) (mean±SEM) rose significantly to values greater than 1 in the left ligated lung. ▭: preligation; ▬: postligation. *: p<0.01, postligation *vs* preligation.

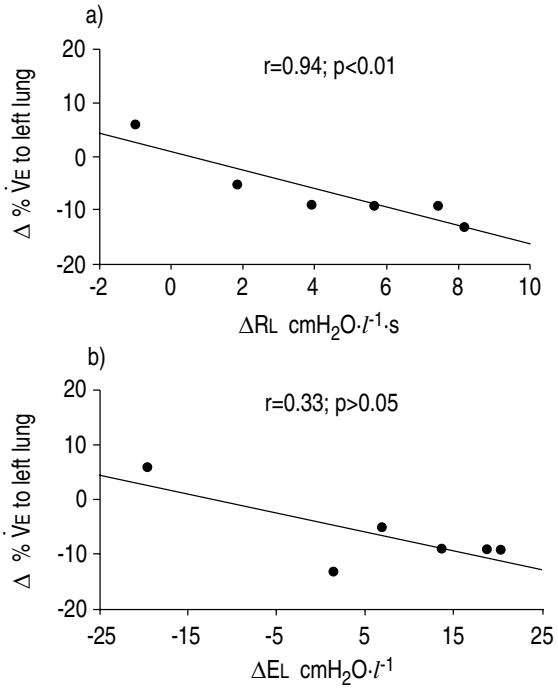

Fig. 7. – Relationship between the change (postligation minus preligation) in the percentage of $\dot{V}_E$ going to the left lung and the change in a) pulmonary resistance (R_L) and b) pulmonary elastance (E_L) of the left lung. Note significant correlation (Spearman's rank correlation test) only for R_L.

Discussion

In this model of POPV, we performed the pulmonary artery ligation through a contralateral thoracotomy to prevent the formation of adhesions between visceral and parietal pleurae, prevent invasion of intercostal blood vessels into the lung, and minimize pleural thickening, all of which could significantly alter lung mechanics and the distribution of ventilation. Despite this, as shown previously [4], the left visceral pleura was still thicker than normal, due to the presence of new bronchial collaterals. The adhesions on the contralateral side were delicate and readily lysed, since there was minimal vascularization [5, 6].

Our previous studies of POPV have focused on the haemodynamics and structure of the pulmonary and bronchial vasculatures [4–6]; however, the effects of POPV are not restricted to the circulation. Gas exchange is also perturbed because, firstly, alveolar capillaries are perfused with bronchial arterial blood and, thus, the driving pressure for exchange of CO_2 and, to a greater extent, for exchange of O_2 with alveolar gas is reduced. Secondly, bronchial blood flow in POPV is only 25–50% of normal pulmonary blood flow [4–6].

In this study of pulmonary mechanics and gas exchange in POPV, our principal findings in the ligated lung were that: 1) ventilation was reduced; 2) R_L and E_L were increased; and 3) a significant portion of gas exchange, particularly for CO_2, was carried out in this lung.

Because of the smaller size of the left lung [17], its ventilation is normally about 45% of the total [7, 8, 13]. This was true in the present study, since, before ligation, left lung $\dot{V}_E$ was 45±2% of total. Six months after ligation of the left main pulmonary artery, we found that left lung $\dot{V}_E$ had fallen to 39±1% of total, indicating that the long-term loss of pulmonary blood flow is associated with some diversion of ventilation to the contralateral lung. Under similar circumstances, LILKER and NAGY [13] found that left lung $\dot{V}_E$ fell to 34±2% of total. These values are, in turn, somewhat higher than those obtained following acute pulmonary artery obstruction, when left lung $\dot{V}_E$ was 30–33% of total [7, 8].

By what mechanism does the lung regulate the distribution of ventilation after occlusion of the pulmonary artery? Immediately after the interruption of pulmonary blood flow, gas exchange ceases in the affected lung, alveolar CO_2 (P_{ACO_2}) falls, airway smooth muscle constricts [8, 10] and the lung with the obstructed pulmonary artery becomes more difficult to ventilate. The length of time that hypocapnic bronchoconstriction persists after ligation is unknown, but it probably depends on the speed and extent of neovascularization of the lung by bronchial collaterals [3]. Of greater importance, within 2 days of ligation areas of the affected lung become atelectatic and its total lung volume is reduced by 40–50% [11, 19, 20]. The proportion of total ventilation directed to that lung is probably reduced below 30%, but no data are available in the literature for this postligation time period. The atelectasis appears to resolve completely within 2 months [11], and, in previous studies, we found that the lungs were well expanded [4–6]. Nevertheless, 6 months after ligation of the pulmonary arteries, ventilation of the left lung remains low, and, in this study, we found that R_L and E_L were elevated compared with preligation values (figs 3 and 4). Since the changes in left lung R_L correlated with the change in the proportion of $\dot{V}_E$ delivered to the left lung (fig. 7), it is likely that alterations in the mechanical properties of the airways and/or the parenchyma were responsible for the reduction in ventilation of the left lung.

Of the possible mechanisms for the increased R_L and E_L, hypocapnic bronchoconstriction can be ruled out because gas exchange was reinstituted by perfusion of alveolar capillaries with blood from the new bronchial collaterals and we found that end-tidal CO_2 was 5.4±0.4% in the ligated lung. In the contralateral lung, end-tidal CO_2 was 6.6±0.5%. Furthermore, elevation of left lung P_{ACO_2} by addition of CO_2 to the inspired gas did not reduce R_L or E_L. We do not think that airway smooth muscle tone was elevated, since R_L and E_L remained unchanged after administration of atropine and isoproterenol. Despite these observations, airway changes cannot be ruled out entirely, since airway luminal diameter could be reduced by an increase in smooth muscle thickness. Previously, one of us showed peripheral muscularization and medial thickening of the pulmonary arteries in POPV [5]. This may be the result of increased levels of growth factors: indeed, in a previous study, we found increased expression of endothelin, a growth factor as well as a vasoconstrictor, in the endothelium of pulmonary arteries in the ligated lung compared with those in the control, contralateral lung [21]. Since the pulmonary arteries run in close proximity to the airways, it is possible that endothelin or other growth factors might affect airway smooth muscle as well.

Changes in the lung parenchyma could also lead to the observed alteration of lung mechanics. Focal areas of fibrosis have been described in POPV [5, 22]. In addition, the increased number of bronchial collaterals widens connective tissue septa and bronchovascular bundles and causes thickening of the pleura [4, 5]. Since, at normal breathing frequencies, a large part of lung resistance is due to tissue resistance [23, 24], a likely mechanism for the increase in R_L in the ligated lung is increased tissue resistance as the result of these parenchymal changes.

In the lung with POPV, perfusion of pulmonary capillaries is re-established after neovascularization by bronchial collaterals, but the capillaries are perfused with arterial blood. Despite this, in the present study we found that the left lung was responsible for 35% of total $\dot{V}_{CO_2}$ and 21% of total $\dot{V}_{O_2}$. These values are approximately twice those obtained by LILKER and NAGY [13]. The difference is probably due to differences in the magnitude of bronchial collateral blood flow. LILKER and NAGY [13] calculated left lung bronchial perfusion ($\dot{Q}br$) using the Fick equation and obtained a value of 94 ml·min^{-1}. In a previous study of POPV in which the duration of ligation was approximately the same as the present one [4], we found that $\dot{Q}br$ was 122 ml·min^{-1} in the left lower lobe (which is about half the left lung [17]) and, therefore, estimate total left lung $\dot{Q}br$ to be 244 ml·min^{-1}. Studies of acute pulmonary artery occlusion

give values for $\dot{Q}br$ of 6 ml·min^{-1} [25], and values of $\dot{V}CO_2$ of 9% total [9].

In this study, the left lung contributed 21% of the $\dot{V}O_2$ and 35% of the $\dot{V}CO_2$ after ligation. How does this occur if the lung is perfused with arterial blood from the bronchial collaterals? The $PaCO_2$ of systemic arterial blood in anaesthetized dogs is about 5.3 kPa (40 mmHg) [13], approximately equal to the $PaCO_2$ of the blood entering the left lung *via* the bronchial collaterals. Therefore, there is a sufficient partial pressure gradient between capillary blood and alveolar gas in the ligated lung to provide a driving force for CO_2 exchange. On the other hand, the oxygen saturation of the blood entering the left lung should be close to maximum and the driving force for uptake of O_2 small. Although we did not measure blood gases, we can assume that blood entering the bronchial circulation has a PaO_2 similar to the systemic PaO_2 in this experimental model, *i.e.* 9.3 kPa (70 mmHg), as measured by LILKER and NAGY [13] in their anaesthetized dogs. Blood leaving the capillaries should have an oxygen tension (PO_2) similar to left lung PAO_2. From the alveolar gas equation and our measured values of end-tidal CO_2 and RQ, we estimate PAO_2 to be about 16.4 kPa (123 mmHg). The maximum increase in O_2 content is then about 4.0 ml O_2 per 100 ml blood. If blood flow through the left lung is ≈250 ml·min^{-1}, the resulting $\dot{V}O_2$ will be 10 ml·min^{-1}. To account for our measured left lung $\dot{V}O_2$ of 35 ml·min^{-1}, either bronchial blood flow is higher than our estimate or the blood entering the pulmonary capillaries is less saturated. The mechanism cannot be ascertained from our data. Finally, since $\dot{V}CO_2$ exceeds $\dot{V}O_2$ in the ligated lung, its RQ is greater than 1 (fig. 6).

The adaptability of the lung to conditions as extreme as the complete cessation of pulmonary blood flow to one lung is evident from this study. After prolonged left pulmonary artery ligation, the $\dot{V}E$, $\dot{V}O_2$, $\dot{V}CO_2$, EL and RL of the entire lung were unchanged compared with preligation values (figs 1 and 2). In addition, although we did not measure arterial blood gases, other studies show that PaO_2 and $PaCO_2$ are also unchanged [13].

Our model of POPV is relevant to at least two situations in clinical medicine. The first is congenital unilateral absence of one pulmonary artery; these patients are often asymptomatic and diagnosed only on routine examination. In two recent reports [26, 27], such patients were found to have normal arterial blood gases and a mild restrictive defect in pulmonary function. Chest X-rays indicated that the affected lung was small and had prominent bronchial collaterals. The second clinical situation relevant to POPV is that of chronic major vessel pulmonary thromboembolism [28–30], where it has been observed that, after the initial acute event, patients improve, although they remain dyspnoeic. Pulmonary function and gas exchange parameters measured prior to thrombarterectomy indicated a significant reduction of PaO_2 and $PaCO_2$ and an increased alveolar-to-arterial O_2 gradient, suggesting greater compromise of gas exchange in these patients than in the animals with POPV [28, 30].

In summary, chronic pulmonary artery ligation produces a shift in ventilation away from the ligated lung as a result of an increase in lung elastance and resistance. In addition, despite perfusion with bronchial arterial blood, a significant proportion of O_2 uptake and CO_2 production occurs in the ligated lung.

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