EFFECTS OF ALTERED PATTERNS OF VENTILATION AND OF INCREASED CARDIAC OUTPUT ON BLOOD FLOW TO A COLLAPSED LUNG IN ANAESTHETIZED, CLOSED-CHEST DOGS

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The major cause of a reduction in blood flow through an underventilated area of lung is hypoxic pulmonary vasoconstriction (HPV), but in collapsed areas of lung this mechanism may be augmented by the increase in Pco2 resulting from the equilibration of the lung with mixed venous blood [1]. In most patients with acute lung disease the application of a positive end-expiratory pressure (PEEP) re-expands collapsed alveoli and so decreases intrapulmonary shunt (Qs/Qt). However, in some patients, particularly those with predominantly unilateral lung disease, PEEP may have the opposite effect [2-6]. There is evidence that the increase in Qs/Qt is associated with an increase in blood flow to the damaged lung [7] and it is believed that the redistribution of flow results from the increase in alveolar capillary pressure produced by compression of the pulmonary capillaries in the ventilated alveoli. This increases the driving pressure across the areas of lung not exposed to this pressure and so increases Qs/Qt [8-10].

There is experimental evidence that an increase in the mean airway pressure (Paw) applied to a ventilated lung can shift blood flow to a collapsed lung in dogs with a closed chest [11] or to a collapsed left lower lobe in dogs with an open chest [12,13]. However, in a recent series of investigations in dogs with an open chest an increase in Paw produced by the application of PEEP or an increase in inspiratory:expiratory time ratio failed to alter the distribution of blood flow from the ventilated right lung to the left lower lobe when the latter was insufflated with oxygen, 7% oxygen in nitrogen, or subjected to collapse [14]. Since the redistribution of flow from a collapsed area of lung is less when the chest is closed than when it is open [15–17], we decided to repeat the studies in a closed-chest preparation with normal and increased blood volume, using measurements of right-to-left shunt as an index of flow through the collapsed lung.

SUMMARY

Right-to-left shunt (Qs/Qt) was measured by the SF6 and oxygen methods in 13 anaesthetized closed-chest dogs intubated with a double-lumen endobronchial tube. Collapse of the left lung increased Qs/Qt from 10% to 23%, suggesting that blood flow to the left lung had been reduced by about 60%. Increasing right lung mean airway pressure by the alteration of the inspiratory:expiratory time ratio or the application of PEEP produced a small but non-significant increase in Qs/Qt with significant increases in arterial and mixed venous carbon dioxide tensions, and arterial to right lung end-tidal carbon dioxide tension difference. Fluid loading during collapse increased cardiac output and pulmonary vascular pressures, but Qs/Qt did not differ significantly from the normovolaemic collapsed state. Increasing the right mean airway pressure in this condition had no effect on Qs/Qt or carbon dioxide tensions.

MATERIALS AND METHODS

Thirteen mongrel dogs (17–29 kg) were anaesthetized with thiopentone 30 mg kg–1 following premedication with Hypnorm (fentanyl citrate...
0.315 mg ml⁻¹ and fluanisone 10 mg⁻¹ (Janssen) i.m. in a dose of 0.06 ml kg⁻¹. After tracheal intubation with a 10-mm i.d. cuffed plastic tube, the lungs were ventilated with the right-hand side of the double bellows-in-box system (fig. 1) at 10 b.p.m., the tidal volume being adjusted to give an end-tidal carbon dioxide concentration of 4.5–5%. Anaesthesia was maintained with 1.5% halothane in oxygen during surgery and, thereafter, with a continuous infusion of Hypnorm 0.13 ml kg⁻¹ h⁻¹ plus 0.2–0.5% halothane to the right lung. The dogs remained in the supine position throughout the study. Blood loss was replaced by the infusion of Haemaccel (Hoechst, U.K., Ltd) and any non-respiratory acidosis corrected by the infusion of 8.4% sodium bicarbonate to maintain a base excess of 0 ± (SD) 2.0 mmol litre⁻¹. A carotid arterial cannula was inserted to permit the measurement of arterial pressure, blood-gas tensions and haematocrit. The ECG and oesophageal temperature were monitored throughout.

A Swan–Ganz catheter was introduced via the right external jugular vein for measurement of pulmonary artery pressure (P_{PA}), pulmonary capillary wedge pressure (PCWP) and for the sampling of mixed venous blood. Catheters in the left external jugular vein and femoral artery were used for cardiac output estimations by dye dilution, and a saline solution equilibrated with 20% sulphur hexafluoride (SF₆) in nitrogen was infused continuously to a femoral vein for the measurement of intrapulmonary shunt.

Tracheotomy was performed and one limb of a double-lumen endobronchial tube (35-French gauge National Catheter Corp.) introduced to the left main bronchus, whilst airway pressure was monitored to confirm correct positioning. Separation of the two sides was confirmed by pressurizing the right limb of the tube whilst the left was connected to an under-water seal. The two limbs of the tube were then connected to the two bellows-in-box systems and tidal volumes adjusted to produce equal end-tidal carbon dioxide concentrations on each side. The values of PEEP were then adjusted to match the mean airway pressures. The second stage bellows were compressed by a Nuffield AVS 200 ventilator (Penlon Ltd, Abingdon) which had been modified to provide an extended range of inspiratory times. The efficiency of the ventilator circuit was checked before use on a model lung.

**Design of study**

The study consisted of 10 stages, a set of cardiovascular and respiratory measurements being taken at each stage with a right lung P_{F_{102}} of 1.0. During the first stage (1), both lungs were ventilated with an P_{F_{102}} of 1.0 with an inspiratory:expiratory (I:E) time ratio of 1:2. The left lung was then collapsed by occluding the left endobronchial tube, and 30 min later a second set of measurements was obtained (2). Further sets of measurements were made as follows: (3) during ventilation of the right lung with an I:E ratio of 2:1; (4) with an I:E ratio of 1:2, but with positive end-expiratory pressure added to produce the same mean airway pressure (P_{AW}) as the 2:1 ratio; (5) with an I:E ratio of 1:2 but with PEEP increased to double the P_{AW} (fig. 2). The collapsed lung was then re-expanded and ventilated with oxygen to provide a second control measurement (6). Thereafter, left lung collapse was re-instituted and Haemaccel infused to increase PCWP to 16–20 mm Hg. A set of measurements was then obtained with each of the four conditions of ventilation outlined above, a period of 30 min being allowed for stabilization between successive readings (7–10). The position of the endobronchial tube and the area of collapse were confirmed at autopsy in all animals.

Changes in the perfusion of the collapsed area of lung were estimated by shunt measurements using both oxygen and SF₆ methods. The oxygen shunt (\( \dot{Q}_{s}/\dot{Q}_{t_{O_2}} \)) was calculated from the following equation:

\[
\dot{Q}_{s}/\dot{Q}_{t_{O_2}} = \frac{(C_{O_2}' - C_{O_2})}{(C_{O_2}' - C_{O_2}) + (C_{O_2} - C_{O_2})}
\]
The end-pulmonary capillary-to-arterial oxygen content difference ($C_{a\text{O}_2} - C_{a\text{O}_2}$) was calculated from the oxygen saturation derived from the Severinghaus nomogram [18], the haemoglobin (measured by the cyanmethaemoglobin technique) and a combining factor of 1.39. The end-pulmonary capillary $P_{a\text{O}_2}$ was assumed to equal alveolar $P_{a\text{O}_2}$ ($P_{a\text{O}_2}$) and was calculated from the simplified alveolar air equation:

$$P_{a\text{O}_2} = P_{\text{TO}_{a}} \times \frac{P_{a\text{CO}_2}}{0.8}$$

whilst the arterial-to-mixed venous oxygen content difference ($C_{a\text{O}_2} - C_{a\text{O}_2}$) was measured directly with a Lex-O$_2$-Con analyser, thus minimizing errors from variations in the oxygen dissociation curve.

The SF$_6$ shunt ($\dot{Q}_s/\dot{Q}_{t\text{SF}_6}$) was calculated from the ratio of arterial to mixed venous SF$_6$ contents [19]. Synchronous 5-ml samples of arterial and mixed venous blood were taken in duplicate into heparinized glass syringes, and then equilibrated at 20 °C with 20 ml of 100% nitrogen at atmospheric pressure for 30 min. The supernatant gas was analysed in 5-ml aliquots using an electron capture detector on a Perkin–Elmer Sigma 3B chromatograph. By using suitable carrier gas flows, sharp peaks of SF$_6$ distinct from those of oxygen could be recorded, the peak heights being proportional to the concentration of SF$_6$ in each sample.

Cardiac output was measured ($\dot{Q}_t$) (dye dilution) by injecting cardio-green (Sigma Chemicals Ltd) to the pulmonary artery, the area under the curve recorded by a CO-10R cardiac output monitor (Waters Instruments Inc.), $\dot{Q}_t$ being calculated from the formula:

$$\dot{Q}_t = \frac{\text{amount of dye (mg)} \times 60 \times 0.856}{\text{calibration peak height} \times \text{width at } \frac{1}{2} \times 100 \text{ factor of curve peak height}}$$

The coefficient of variation of duplicate estimations was less than 7%.

Statistical analysis

Each of the recorded variables was analysed using the two-way analysis of variance. Comparison of individual stages was by Student’s $t$ test at the 5% level. Related comparisons were grouped and the required level of significance adjusted for the number of comparisons using Sidak’s inequality [20]. The reduction in the number of comparisons in the later stages of the study was the result of technical problems and other local difficulties which prevented completion of the full experimental programme.

RESULTS

The only significant difference between the two control stages was that mixed venous oxygen tension ($P_{v\text{O}_2}$) was lower at stage 6 than stage 1 (table I). Collapse of the left lung resulted in a reduction in arterial $P_{a\text{O}_2}$, an increase in both SF$_6$ and oxygen shunts, and a reduction in mean carotid arterial pressure ($P_{\text{CA}_a}$) (table II). Increasing right mean airway pressure ($P_{aw}$) from 4.5 to 13.1 mm Hg during collapse had no effect on $\dot{Q}_s/\dot{Q}_{t\text{SF}_6}$ (fig. 3), but increased mean pulmonary artery pressure ($P_{p\text{a}}$), and arterial and mixed venous $P_{co\text{O}_2}$, $P_{v\text{co}_2}$, the values during the high value of PEEP (stage 5) being significantly higher than those during stage 2. The arterial-to-right lung end-tidal $P_{co\text{O}_2}$ difference also increased from 0.7 kPa at stage 2 to 1.4 kPa at stage 5.

Fluid loading by the infusion of Haemaccel 1–2 litre over a period of 15–20 min (stages 7–10)
**TABLE I.** Blood-gas tensions, right end-tidal PCO₂ (Pf CO₂) and arterial to end-tidal PCO₂ differences (Pₐ CO₂-Pf CO₂) at each stage of the experiment (mean±SEM). V = ventilation; C = collapse; FL = Fluid loading. Right lung conditions: i.e ratio: P and PP signify PEEP at two different values. n = Number of observations. *Significant differences (P < 0.05) between stages shown in parentheses

<table>
<thead>
<tr>
<th>Stage</th>
<th>Left</th>
<th>Right</th>
<th>n</th>
<th>P_a CO₂ (kPa)</th>
<th>Pₐ CO₂ (kPa)</th>
<th>P_f CO₂ (kPa)</th>
<th>P_f CO₂ (kPa)</th>
<th>P_f CO₂ (kPa)</th>
<th>(P_a CO₂ - P_f CO₂) (kPa)</th>
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</thead>
<tbody>
<tr>
<td>1 V 100% O₂</td>
<td>1:2</td>
<td>13</td>
<td>61.8±2.9*</td>
<td>4.3±0.1</td>
<td>7.5±0.3</td>
<td>5.4±0.2</td>
<td>3.9±0.2</td>
<td>0.3±0.2</td>
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</tr>
<tr>
<td>2 C</td>
<td>1:2</td>
<td>13</td>
<td>26.9±2.4* (1, 6)</td>
<td>5.0±0.2</td>
<td>6.5±0.3</td>
<td>6.0±0.2</td>
<td>4.3±0.2</td>
<td>0.7±0.2</td>
<td></td>
</tr>
<tr>
<td>3 C</td>
<td>2:1</td>
<td>13</td>
<td>28.9±2.4* (1, 6)</td>
<td>5.8±0.2* (1, 6)</td>
<td>6.0±0.3* (1)</td>
<td>6.9±0.2* (1)</td>
<td>4.9±0.2* (1, 6)</td>
<td>1.0±0.2</td>
<td></td>
</tr>
<tr>
<td>4 C</td>
<td>2:2P</td>
<td>12</td>
<td>23.5±2.6* (1, 6)</td>
<td>5.7±0.2* (1, 6)</td>
<td>6.1±0.3* (1)</td>
<td>7.0±0.2* (1, 6)</td>
<td>4.9±0.3* (1, 6)</td>
<td>0.9±0.2</td>
<td></td>
</tr>
<tr>
<td>5 C</td>
<td>2:2PP</td>
<td>11</td>
<td>23.3±2.5* (1, 6)</td>
<td>6.6±0.2* (1, 2, 6)</td>
<td>6.2±0.3* (1)</td>
<td>7.6±0.2* (1, 2, 6, 7)</td>
<td>5.3±0.3* (1, 2, 6)</td>
<td>1.4±0.2* (1)</td>
<td></td>
</tr>
<tr>
<td>6 V 100% O₂</td>
<td>1:2</td>
<td>11</td>
<td>65.6±3.1</td>
<td>4.3±0.2</td>
<td>6.4±0.4* (1)</td>
<td>5.5±0.2</td>
<td>3.9±0.2</td>
<td>0.4±0.2</td>
<td></td>
</tr>
<tr>
<td>7 C+FL</td>
<td>1:2</td>
<td>10</td>
<td>35.9±2.6* (1, 6)</td>
<td>5.2±0.2</td>
<td>6.6±0.3</td>
<td>5.8±0.2</td>
<td>4.4±0.3</td>
<td>0.7±0.3</td>
<td></td>
</tr>
<tr>
<td>8 C+FL</td>
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<td>9</td>
<td>28.3±3.0* (1, 6)</td>
<td>5.6±0.3* (1, 6)</td>
<td>6.2±0.3</td>
<td>6.2±0.3</td>
<td>5.0±0.3</td>
<td>0.6±0.3</td>
<td></td>
</tr>
<tr>
<td>9 C+FL</td>
<td>2:2P</td>
<td>9</td>
<td>32.7±3.0* (1, 6)</td>
<td>5.6±0.3* (1, 6)</td>
<td>6.4±0.3</td>
<td>6.2±0.3</td>
<td>5.0±0.3</td>
<td>0.7±0.3</td>
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</tr>
<tr>
<td>10 C+FL</td>
<td>2:2PP</td>
<td>8</td>
<td>35.2±3.6* (1, 6)</td>
<td>5.9±0.3* (1, 6)</td>
<td>6.9±0.4</td>
<td>6.5±0.3</td>
<td>5.9±0.3* (1, 2, 6, 7)</td>
<td>0.0±0.3* (5)</td>
<td></td>
</tr>
</tbody>
</table>

**TABLE II.** Shunt as measured by SF₆ (Qt) /QT₉₆ and oxygen (Qt /QT₉₆) techniques, cardiac output (Qt), mean pulmonary artery (P₉₆) and pulmonary capillary wedge (PCWP) pressures, mean carotid artery pressure (Pc), right lung mean (Paw), peak (peak Pmaw), and end-expiratory (r PEEP) pressures for each stage of the experiment (mean±SEM). V = Ventilation; C = collapse; FL = Fluid loading. Right lung conditions: i.e ratio: P and PP signify PEEP at two different values. n = number of observations. *Significant differences (P < 0.05) between stages shown in parentheses

<table>
<thead>
<tr>
<th>Stage</th>
<th>Left</th>
<th>Right</th>
<th>n</th>
<th>Qt /Qt₉₆ (%)</th>
<th>Qt /Qt₉₆ (%)</th>
<th>Qt (litre/min)</th>
<th>P₉₆ (mm Hg)</th>
<th>PCWP (mm Hg)</th>
<th>P₉₆ (mm Hg)</th>
<th>P₉₆ (mm Hg)</th>
<th>peak Pmaw (mm Hg)</th>
<th>r PEEP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 V 100% O₂</td>
<td>1:2</td>
<td>13</td>
<td>10.1</td>
<td>12.3</td>
<td>2.4</td>
<td>13.4</td>
<td>5.8</td>
<td>110.4</td>
<td>4.9</td>
<td>17.8</td>
<td>0.9</td>
<td></td>
</tr>
<tr>
<td>2 C</td>
<td>1:2</td>
<td>13</td>
<td>12.0</td>
<td>12.4</td>
<td>2.1</td>
<td>12.2</td>
<td>2.8</td>
<td>83.5</td>
<td>4.5</td>
<td>18.4</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>3 C</td>
<td>2:1</td>
<td>13</td>
<td>20.9</td>
<td>21.0</td>
<td>1.9</td>
<td>15.0</td>
<td>5.3</td>
<td>82.0</td>
<td>7.4</td>
<td>17.6</td>
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<tr>
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<td>2:2P</td>
<td>12</td>
<td>26.2</td>
<td>23.6</td>
<td>2.0</td>
<td>16.0</td>
<td>6.1</td>
<td>86.6</td>
<td>7.5</td>
<td>19.9</td>
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</tr>
<tr>
<td>5 C</td>
<td>2:2PP</td>
<td>11</td>
<td>28.9</td>
<td>27.4</td>
<td>2.0</td>
<td>23.3</td>
<td>8.2</td>
<td>78.7</td>
<td>13.1</td>
<td>24.7</td>
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</tr>
<tr>
<td>6 V 100% O₂</td>
<td>1:2</td>
<td>11</td>
<td>5.6</td>
<td>8.5</td>
<td>2.2</td>
<td>16.0</td>
<td>7.5</td>
<td>104.2</td>
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</tr>
<tr>
<td>7 C+FL</td>
<td>1:2</td>
<td>10</td>
<td>26.9</td>
<td>26.4</td>
<td>4.1</td>
<td>30.0</td>
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<td>2:1</td>
<td>9</td>
<td>32.3</td>
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<td>31.6</td>
<td>19.5</td>
<td>110.6</td>
<td>9.0</td>
<td>18.9</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>9 C+FL</td>
<td>2:2P</td>
<td>9</td>
<td>28.9</td>
<td>30.2</td>
<td>4.5</td>
<td>33.7</td>
<td>20.5</td>
<td>112.5</td>
<td>8.9</td>
<td>22.2</td>
<td>4.0</td>
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<tr>
<td>10 C+FL</td>
<td>2:2PP</td>
<td>8</td>
<td>35.8</td>
<td>31.5</td>
<td>4.3</td>
<td>30.8</td>
<td>23.9</td>
<td>100.4</td>
<td>13.7</td>
<td>25.8</td>
<td>9.5</td>
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doubled cardiac output and produced significant increases in $P_{PA}$ and mean pulmonary capillary wedge pressure (PCWP), but no significant change in $P_{VA}$ or $P_{VAO}$. $Q_S/Qt$ at stage 8 was significantly higher than at stage 2, but otherwise there were no differences in $PaO_2$ and $Q_S/Qt$ after transfusion. There were no significant changes in these measurements or in $P_{Aco_2}$, $P_{Vco_2}$, $P_{VO_2}$, $P_{PA}$, PCWP or $Qt$ in response to the application of different patterns of ventilation to the right lung. There were no significant changes in pH which remained within the limits $7.34 \pm (SD) 0.06$ throughout the experiment. Complete collapse of the left lung was confirmed at autopsy in all animals and a little oedema was present in the dependent regions of both the left and right lungs in four dogs.

DISCUSSION

These results show that there was a significant increase in right-to-left shunt after the induction of left lung collapse, but that the percentage shunt was not altered by changes in the pattern of ventilation applied to the right lung. Fluid loading to a degree which resulted in significant increases in cardiac output and pulmonary vascular pressures during left lung collapse did not alter the percentage shunt. Subsequent changes in the pattern of right lung ventilation during the period of fluid loading also failed to alter the shunt.

The use of shunt measurements to provide an estimate of regional perfusion in the closed-chest preparation is dependent on a number of assumptions. The first is that the shunt measured in the control period during ventilation with an $F_{IO_2}$ of 1.0, is equally distributed between the two lungs so that there is a shunt of approximately 5% in each. The second assumption is that the right lung shunt is not affected by collapse of the left lung or by subsequent alterations in the right lung airway pressure. This assumption is probably not justified because the right lung transpulmonary pressure would have been increased by the application of PEEP and by the greater subatmospheric pleural pressure resulting from the collapse of the left lung [15,21], and this would have tended to reduce dependent zone collapse in the lung subjected to PEEP. If the shunt in the right lung had been reduced by the increased transpulmonary pressure, the actual increase in left lung blood flow in response to increased right airway pressure would have been greater than the measured increase in shunt, thus accentuating the trend observed in the shunt measurements. The third assumption is that the measured shunt does not include extrapulmonary sources of shunt. It is known that the oxygen method measures total right-to-left shunt from both intra- and extrapulmonary sources. However, the SF₆ shunt measures only intrapulmonary sources of shunt resulting from alveoli with a $V_A/Q_A$ ratio of less than 0.05 [19]. The oxygen shunt values should, therefore, have been higher than the SF₆ shunt values throughout the investigation. However, although there was a good correlation between the two measurements (fig. 4), SF₆ shunts were consistently higher than the oxygen shunts, and the difference increased at higher shunt values.

There are a number of possible causes for this discrepancy. One is that the mixed venous SF₆ values may have been over-estimated as a result of non-linearity of the electron capture detector. However, care had been taken to assess the linearity of the analytical system before the
The onset of HPV in response to collapse of the left lung resulted in a biphasic reduction in arterial $P_{O_2}$. This reached its lowest value 5–10 min after clamping the endobronchial tube and increased to a plateau value 20–30 min after initiating the collapse. Presumably, the initial decrease in $P_{A_{O_2}}$ was associated with the decrease in alveolar $P_{O_2}$ as the oxygen in the alveoli was consumed, whilst the secondary increase in $P_{A_{O_2}}$ was caused by the reduction in blood flow to the collapsed lung caused by HPV.

If it is assumed that the initial shunt during bilateral oxygen ventilation (10%) was equally divided between the two lungs, and that the 5% shunt in the right lung was not changed by the onset of collapse in the left lung, then the contribution of the left lung collapse to the total shunt (stage 2) would have been $23 - 5 = 18\%$. Since 45% of the total pulmonary blood flow is normally distributed to the left lung of a dog [22,23], this would represent a reduction in left lung flow of $(45 - 18)/45 = 60\%$, a value which is close to the 61–66% reduction in flow previously observed during lobar collapse in open-chest animals in this laboratory [1,14,24]. This suggests that these animals had an active HPV response.

There are three factors which may affect the diversion of flow in such a preparation. First, the magnitude of flow diversion in response to hypoxia is inversely related to the volume of lung made hypoxic [25], so that whole lung collapse in the closed-chest animals should produce a smaller proportional reduction in flow and, consequently, a relatively higher $Q_s/Q_t$, than lobar collapse in the open-chest animals. Second, collapse of a segment of lung in the closed-chest animal results in a greater numerical value of subatmospheric pressure over the collapsed segment. This increases the transmural pressure difference which tends to expand the extra-alveolar vessels, with a consequent reduction in regional pulmonary vascular resistance [17,26,27]. Furthermore, the reduction in left lung volume results in a reduction in intrapleural pressure which may increase the transpulmonary pressure across the ventilated right lung and so decrease vascular conductance at capillary level in this lung, thus also tending to increase $Q_s/Q_t$ [21]. The third factor is that in the closed chest, transmural filling pressures and cardiac output are greater than in the open-chest preparation. Since the cardiac output in the normovolaemic state was about 2.2 litre min$^{-1}$ in...
the present experiments, and approximately 1.4 litre min\(^{-1}\) in previous open-chest experiments [14], this should have maintained a higher blood flow to the ventilated lung and so tended to reduce \(\dot{Q}_s/\dot{Q}_t\). Since both Takaro [11] and Benumof and colleagues [12] observed decreases in hypoxic lung flow in the region of 36% in the closed-chest preparation, it seems reasonable to conclude that there must have been a substantial increase in vascular tone in the collapsed lung during the present investigations.

In previous studies there have been variable changes in the distribution of pulmonary blood flow in response to unilateral changes in \(P_{aw}\). Thus Sanchez de Leon and colleagues [13] found that the application of 10 cm H\(_2\)O PEEP to the ventilated lung increased the lobar to total blood flow ratio (\(\dot{Q}_l/\dot{Q}_t\)) from 8 to 15% during left lower lobe collapse in dogs with an open chest, whilst Benumof and co-workers [12] reported that an increase in PEEP to the ventilated lung from 2 to 10 cm H\(_2\)O resulted in an increase in \(\dot{Q}_l/\dot{Q}_t\) from 10 to 23% when the chest was open and from 10 to 12% when the chest was closed. Takaro [11] demonstrated an increased flow to a hypoxic-hypercarbic lung when a constant pressure difference of 15 or 25 cm H\(_2\)O was applied for 20 s to the opposite hyperoxic lung. These results contrast with our previous open-chest studies which showed no increase in \(\dot{Q}_l/\dot{Q}_t\) in response to increases in \(P_{aw}\) of 3-4 mm Hg produced by the addition of PEEP or change in 1:1 ratio, and with the present studies when even greater changes in \(P_{aw}\) failed to produce a change in \(\dot{Q}_s/\dot{Q}_t\) during unilateral collapse in the closed chest.

There are a number of possible causes for the lack of change in the present studies. First, the increase in \(P_{aw}\) may have been less than that applied in other studies. Our increases in \(P_{aw}\) (4.5 to 7.4 to 13.1 mm Hg) were similar to the changes produced by increasing PEEP from 2 to 10 cm H\(_2\)O [12,13], but less than the 15 and 25 cm H\(_2\)O difference in pressure between the two lungs applied by Takaro [11]. Benumof and co-workers [12] found that the change in \(\dot{Q}_l/\dot{Q}_t\) was much less in the closed-chest group (\(\dot{Q}_l/\dot{Q}_t\) 9.5-12.3%) and in our studies such a shift of flow could have been concealed by a reduction in \(\dot{Q}_s/\dot{Q}_t\) in the ventilated lung in response to the increase in \(P_{aw}\). A second possibility is that the HPV response may have been stronger in our investigations than in those reported by other authors. In the experiments reported by Takaro [11], a 5% oxygen–5% carbon dioxide–90% nitrogen mixture was used to produce HPV in one lung, and this resulted in a 36% reduction of \(Q_l/\dot{Q}_t\), the increase in \(\dot{Q}_s/\dot{Q}_t\) in response to hypoxia being from 15.4 to 36%, in contrast to our increase from 10% to 23%. The importance of HPV in opposing the effects of PEEP is illustrated by studies in dogs with experimental left lower lobe pneumonia in which the application of 12 cm H\(_2\)O PEEP increased \(Q_l/\dot{Q}_t\) from 24 to 37% [28]. These authors found that there was little diversion of blood flow away from lobes with high bacterial counts and attributed the marked shift in blood flow in response to PEEP to a reduction in HPV in the acute stages of the disease.

There have been a number of reports of a reduction in arterial \(P_O\), in patients subjected to PEEP [2,3]. This may be caused by an increase in the proportion of blood passing through intrapulmonary shunt pathways, but may also result from a reduction in mixed venous \(P_O\) secondary to a reduction in cardiac output in the presence of an unchanged \(\dot{Q}_s/\dot{Q}_t\) [29,30]. However, a number of authors have recorded increases in \(\dot{Q}_s/\dot{Q}_t\) in response to PEEP in patients with predominantly unilateral disease [4–6], and Kanarek and Shannon [7] obtained measurements which confirmed the redistribution of flow to the damaged lung in response to 5 and 15 cm H\(_2\)O PEEP in one patient who had been subjected to trauma and who had developed unilateral pneumonia. It is known that trauma to the lung can release prostacyclin which inhibits HPV [31]. HPV is also inhibited by endotoxin [32]. It is thus possible that the shift of blood flow in these patients may have been associated with a poor HPV response.

The adverse response to PEEP seen in patients with predominantly unilateral disease is less obvious in those with diffuse disease [6]. Enjeti and associates [33] have shown that there is a greater reduction in regional blood flow when collapse is restricted to a segment of lung instead of a lobe in closed-chest pigs, and that the application of PEEP does not increase flow to the collapsed segment [34]. On the other hand, Hasan and colleagues [35] found that an increase in \(\dot{Q}_s/\dot{Q}_t\) in acid aspiration injury in dogs occurred at lower PEEP values when the injury was more diffuse than when it was confined to one lung.

The infusion of fluid during lung collapse produced no significant change in \(\dot{Q}_s/\dot{Q}_t\) even though \(\dot{Q}_t\) was doubled, and PCWP was increased to 19 mm Hg. Benumof and Wahrenbrock [36]
found that the vasoconstrictor response to ventilation hypoxia of the left lower lobe in the open chest was halved at this left atrial pressure, whilst in our open-chest experiments $Q_{s}/Q_{t}$ increased from 0.11 to 0.20 as a result of fluid loading to a left atrial pressure of 21 mm Hg [14]. Since the transmural pressure tending to distend the extra-alveolar pulmonary vessels should have been greater in the collapsed lung in the closed chest than in the lobe in the open chest, this adds further weight to the suggestion that the HPV response was very active in our closed-chest animals. However, the increase in $Q_{t}$ resulting from the infusion of fluid was not accompanied by an increase in $P_{\nu O_2}$ or significant reduction in the arterio-venous oxygen content difference in the present experiments. Since there were no large changes in pH or $P_{\text{CO}_2}$ which could have affected the position of the oxygen dissociation curve, this suggests that tissue oxygen consumption increased in parallel with the increase in $Q_{t}$. The lack of change in $P_{\nu O_2}$ might account for the similarity in the shunt measurements made before and after transfusion, for an increase in $P_{\nu O_2}$ is known to increase flow to a collapsed lobe [37, 38]. The increase in $P_{\nu x}$ and PCWP was similar in our open- and closed-chest experiments, but an increase in flow to the hypoxic lobe was only noted in the open-chest experiments where $P_{\nu O_2}$ increased in parallel with the increase in $Q_{t}$. It thus appears that the changes in $P_{\nu O_2}$ may be of more importance in reducing HPV than the change in intravascular pressure when $Q_{t}$ is increased by fluid loading.

Although there were no significant increases in $Q_{s}/Q_{t}$ in response to changes in right mean airway pressure, there was a trend towards an increase in $Q_{s}/Q_{t}$ with increased pressure in the normovolaemic state. The increase in $P_{\text{aw}}$ was associated with an increase in $P_{\text{aco}}$ and in arterial-to-end-tidal $P_{\text{Co}}$ difference, thus suggesting that there was an increase in alveolar deadspace in response to the increase in airway pressure. This provides confirmatory evidence that the increase in airway pressure was having a small effect on flow through the ventilated lung.

It is concluded that the effects of PEEP on the redistribution of blood flow to a collapsed area of lung depend on the relationship between $P_{\text{aw}}$ and intravascular pressures and on the strength of the HPV response. When the latter is active moderate increases in $P_{\text{aw}}$ produced by the application of PEEP or changes in the $I:E$ ratio do not increase flow to a collapsed lung in closed-chest dogs.

ACKNOWLEDGMENTS

This work was supported by the Medical Research Council. The authors thank Messrs M. S. Michael and R. A. Lyons for the statistical analysis. They would also like to acknowledge the skilled technical assistance of Messrs W. A. Ryder, L. A. Jones and R. G. Madgwick, and the secretarial assistance provided by Miss D. J. Rawlings.

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