Continuous Positive-Pressure Ventilation: Effects on Systemic Oxygen Transport and Tissue Oxygenation

JOHN S. LUTCH, M.D., and JOHN F. MURRAY, M.D., F.A.C.P., San Francisco, California

In this study we examined the effects of continuous positive-pressure (CPP) ventilation at 0, 5, and 10 cm H₂O end-expiratory pressure on systemic oxygen transport (cardiac index times arterial oxygen content) and peripheral tissue oxygenation. We studied 19 patients, divided into 3 groups, who required mechanically assisted ventilation: 5 had normal lungs; 10 had decreased lung or chest wall compliance, or both; and 4 had chronic obstructive pulmonary disease. The alveolar-arterial oxygen tension difference narrowed, and hence arterial oxygen content tended to improve in most patients as expiratory pressure increased. Systemic oxygen transport fell in all groups, however, owing to a significant reduction in cardiac index. Despite the fall in oxygen transport, no significant changes occurred in oxygen consumption, respiratory quotient, pH, or mixed venous oxygen tension. We concluded that CPP ventilation significantly decreases cardiac output and oxygen delivery but that total body tissue oxygenation was probably not impaired.

In recent years use of continuous positive-pressure (CPP) ventilation* has become an important adjunct to the therapy of patients whose acute respiratory failure is characterized by a large alveolar-arterial oxygen tension difference and a reduced compliance (1, 2). By applying positive pressure during expiration, a higher functional residual capacity is maintained (3), which prevents alveolar and small airways closure and may open units that were previously collapsed; in addition, CPP ventilation may reduce interstitial and alveolar edema by increasing interstitial pressure, causing subsequent reabsorption of extravascular fluid. Both these factors—increasing the functional residual capacity and redistributing the extravascular fluid—are responsible for the improved arterial oxygen tension (arterial Po₂) commonly observed after application of CPP ventilation. Any improvement in arterial Po₂ from CPP ventilation allows a reduction in the concentration of oxygen in the inspired air that is necessary to achieve a given arterial Po₂ level. Lowering inspired oxygen is desirable because it may prevent lung damage, which has been associated with the prolonged administration of gas mixtures of high oxygen concentration (4). Courmand and associates (5) have shown that intermittent positive-pressure ventilation leads to a reduction in cardiac output because an elevation of mean airway and pleural pressures impairs venous return. Since, on the one hand, CPP ventilation increases pressures during both inspiration and expiration, an even further deterioration in cardiac output may occur with CPP ventilation; but, on the other hand, arterial Po₂, and thus arterial oxygen content, may improve. The result of the interaction of these two variables is reflected by the actual amount of oxygen delivered to the peripheral tissues—the systemic oxygen transport (6). Change in systemic oxygen transport, which is computed as the product of cardiac output and arterial oxygen content, thus represents the net cardiorespiratory effect of CPP ventilation. We decided to determine, first, how CPP ventilation influences systemic oxygen transport, and, second, if changes occurred in oxygen delivery, whether they adversely affected peripheral tissue oxygenation.

Patients and Methods

SELECTION OF PATIENTS

A total of 20 studies were performed on 19 pa-
All patients required mechanically assisted ventilation by either tracheostomy or endotracheal tube. The patients were subdivided into three groups on the basis of clinical criteria (history, physical examination, and chest X ray), blood gases (alveolar-arterial oxygen tension difference, breathing 100% oxygen), and mechanical properties of the lung (peak airway pressure required to produce a tidal volume of 10 to 16 ml/kg body weight) at the onset of the study.

The first group consisted of five patients who were comatose and without spontaneous respirations because of an acute drug overdose. These patients have been designated as the “normal” group because they had no clinical or radiological evidence of active pulmonary disease; in addition, their initial arterial Po2, levels while breathing 100% oxygen were greater than 550 mm Hg, and the peak airway pressures required to achieve a tidal volume of 10 to 16 ml/kg body weight were less than 21 cm H2O. All patients recovered from their illnesses and were discharged from the hospital.

The second group consisted of four patients with “chronic obstructive pulmonary disease.” Two of these patients had severe emphysema and had required permanent tracheostomy before admission. The other two patients had chronic bronchitis and were very obese. They all required controlled ventilation because of an acute deterioration of their clinical status. At the time of study, none had radiologic evidence of pulmonary infiltration. Their initial alveolar-arterial oxygen tension differences were moderately abnormal, but their peak airway pressures were normal. Three of the patients in this group ultimately died.

The third group of 10 patients, in whom a total of 11 studies were performed, had a variety of acute pulmonary illnesses. We defined this group as having “stiff thorax” (including either lung or chest wall) syndrome.” The diagnoses of these patients included aspiration or bacterial pneumonia, or both (4), severe flail chest with pneumonia (1), idiopathic fibrosis (1), and severe pulmonary edema (4). These disorders were characterized by a large alveolar-arterial oxygen tension difference and a high initial peak airway pressure necessary to achieve a given tidal volume. Their average age was 55 years, and none had a history of lung disease before hospitalization. All patients in this group ultimately died from their diseases.

Figure 1 shows how the three groups of patients can be distinguished on the basis of their initial alveolar-arterial oxygen tension differences and peak airway pressures.

**STUDY DESIGN**

All patients were studied in the supine position, and all had been receiving mechanical ventilation with a pressure-cycled Bird Mark 7 respirator. For the study of CPP ventilation we used an Emerson volume respirator. The patients adapted well to the change in respirator, and none required sedation. To achieve a given end-expiratory pressure, wide-bore, low-resistance tubing from the expiratory outlet was immersed under water to produce 5 and 10 cm H2O expiratory pressure. The sequence of administration of 0, 5, and 10 cm H2O expiratory pressures was randomized for each patient. A tidal volume between 10 and 16 ml/kg body weight was selected for each patient. Respiratory rate was adjusted to control arterial carbon dioxide tension and to maintain it at the same level observed before beginning the study. Once selected, the settings on the respirator were not altered throughout the experiment. After each testing period the patients were disconnected from the Emerson respirator and placed back on the Bird respirator (without changing the original settings) so that they could be suctioned and be given general care.

**MEASUREMENTS**

Each patient had a large central venous pressure catheter inserted via a brachiocephalic vein into either the superior vena cava or the right atrium. A second catheter was placed in the brachial artery of the other arm for sampling of arterial blood and for measurement of blood pressure by means of a Statham P23db strain gauge, suitable amplifier, and Honeywell recorder. The electrocardiogram was monitored throughout the experiment.

All measurements were performed at the end of a 30-minute period of ventilation with 100% oxygen delivered from a reservoir system to the Emerson ventilator. Oxygen consumption was measured directly by the conventional basal metabolic rate technique. Toward the end of the 30 minutes of washout with oxygen, a 9-liter spirometer containing a carbon dioxide absorber was connected to the respirator and the patient, as shown in Figure 2. All sources of leaks were eliminated, and the apparatus was also checked for leaks before and after each study. Oxygen consumption was measured over a 5-minute period.

Within 1 minute after the measurement of oxygen consumption, expired gas was collected in a meteorologic balloon over a period of 4 minutes while the total number of respirations was counted. The volume of gas was measured in a Tissot spirometer, and tidal volume and minute ventilation were calculated. The carbon dioxide concentration of expired gas was measured by the Scholander technique, and the carbon dioxide pro-

![Image](http://annals.org/)

**Figure 1.** The relationship between initial alveolar-arterial oxygen tension difference ((A-a)dO2) and initial peak airway pressure for each patient. COPD = chronic obstructive pulmonary disease; STS = stiff thorax syndrome.
duction was computed. Respiratory quotient was obtained by dividing carbon dioxide production by oxygen consumption.

During the measurement of oxygen consumption, arterial blood was sampled for 1 minute. It was analyzed within 30 seconds for pH, arterial PCO₂, and arterial PO₂, with Radiometer, Severinghaus, and Beckman electrodes, respectively. Arterial PO₂ (mm Hg) was corrected for the patient’s temperature. Arterial oxygen saturation (SO₂) was then computed with the Severinghaus nomogram (7). For each level of expiratory pressure, hemoglobin concentration (Hb) of arterial blood (g/100 ml) was measured by the cyanmethemoglobin method. Arterial oxygen content (CaO₂, in ml/100 ml) was then calculated by the formula: arterial CaO₂ = arterial SO₂ × (Hb × 1.34) + (arterial PO₂ × 0.003).

During the oxygen consumption measurement, cardiac output was measured by the dye dilution technique, using indocyanine green and a Gilford densitometer. Dye was injected through the central venous catheter while blood was withdrawn from the brachial artery. The method of Stewart and Hamilton was used to compute the cardiac output (8). Cardiac index (liter/min per m² body surface area) was obtained by dividing cardiac output by body surface area.

Systemic oxygen transport (ml/min per m² body surface area) was computed as the product of cardiac index and arterial oxygen content. Mixed venous oxygen content and arterial-venous oxygen difference were calculated from the Fick equation, using the patient’s cardiac output, oxygen consumption, and arterial oxygen content. Since the measurements of both cardiac output and oxygen consumption are subject to errors of 10% to 15%, calculations derived from these values may be in error by as much as 20% to 30%. Mixed venous oxygen tension (mm Hg) can be calculated from mixed venous oxygen saturation (mixed venous content/Hb × 1.34) and the Severinghaus nomogram; in addition to incorporating the errors implicit in the derivation of venous oxygen content, this method assumes that venous pH equals arterial pH and a normal oxyhemoglobin dissociation curve. Despite these limitations, we believe that technical and analytical factors are likely to cause errors in the same direction in a given patient and that changes in intracellular pH and inorganic phosphates will be constant. Because each patient serves as his own control, relative changes will be valid, but derived values for mixed venous oxygen tension will underestimate the actual ones because our patients’ oxyhemoglobin dissociation curves were probably shifted to the right.

The tension of inspired oxygen was measured in a specimen collected while the arterial blood gas was sampled; the alveolar oxygen tension was calculated by the alveolar gas equation (9) and the alveolar-arterial oxygen tension difference computed. The right-to-left shunt fraction was calculated by the standard shunt formula (10).

Physiologic dead space fraction, or wasted ventilation, was calculated using the Enghoff modification of the Bohr equation (11). The 10-ml dead space of the Emerson respirator was ignored.

We computed “effective dynamic compliance,” reflecting the mechanical properties of the lung and chest wall, by dividing tidal volume by the difference between peak inspiratory pressure and expiratory pressure.

Within each group, changes were evaluated by means of the Student’s t test. A probability value less than 5% (P < 0.05) is considered “significant.”

Results

Table 1 contains the blood gas and hemodynamic measurements for each group of patients at 0, 5, and 10 cm H₂O expiratory pressure.

**NORMALS**

Data for this group showed that after the applica-
Table 1. Results of Continuous Positive-Pressure Ventilation

<table>
<thead>
<tr>
<th>Pressure (cm H$_2$O)</th>
<th>ml/cm H$_2$O</th>
<th>%</th>
<th>VD/VT</th>
<th>pH</th>
<th>Arterial Pco$_2$</th>
<th>Arterial Po$_2$</th>
<th>(A-a) do$_2$</th>
<th>Arterial Oxygen Content</th>
<th>Cardiac Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>69</td>
<td>27</td>
<td>7.46</td>
<td>31</td>
<td>594</td>
<td>51</td>
<td>17.4</td>
<td>4.2</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>101</td>
<td>2.1</td>
<td>0.028</td>
<td>1.8</td>
<td>14.8</td>
<td>15.9</td>
<td>1.52</td>
<td>0.54</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>8.2</td>
<td>3.2</td>
<td>0.015</td>
<td>1.4</td>
<td>14.9</td>
<td>13.7</td>
<td>1.52</td>
<td>0.48</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>78</td>
<td>30</td>
<td>7.43</td>
<td>32</td>
<td>601</td>
<td>42</td>
<td>17.4</td>
<td>3.4†</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>4.8</td>
<td>4.3</td>
<td>0.021</td>
<td>1.5</td>
<td>17.8</td>
<td>18.5</td>
<td>1.58</td>
<td>0.59</td>
<td></td>
</tr>
</tbody>
</table>

Five normal subjects

<table>
<thead>
<tr>
<th>Pressure (cm H$_2$O)</th>
<th>ml/cm H$_2$O</th>
<th>%</th>
<th>VD/VT</th>
<th>pH</th>
<th>Arterial Pco$_2$</th>
<th>Arterial Po$_2$</th>
<th>(A-a) do$_2$</th>
<th>Arterial Oxygen Content</th>
<th>Cardiac Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>43</td>
<td>47</td>
<td>7.48</td>
<td>40</td>
<td>434</td>
<td>209</td>
<td>18.8</td>
<td>2.4</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>47</td>
<td>4.8</td>
<td>0.029</td>
<td>1.6</td>
<td>12.7</td>
<td>12.2</td>
<td>1.18</td>
<td>0.52</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>54</td>
<td>4.8</td>
<td>0.026</td>
<td>1.4</td>
<td>70.1</td>
<td>33.1</td>
<td>1.18</td>
<td>0.49</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>3.6</td>
<td>4.8</td>
<td>0.022</td>
<td>0.0</td>
<td>26.5</td>
<td>42.2</td>
<td>1.19</td>
<td>0.44</td>
<td></td>
</tr>
</tbody>
</table>

Four patients with chronic obstructive pulmonary disease

<table>
<thead>
<tr>
<th>Pressure (cm H$_2$O)</th>
<th>ml/cm H$_2$O</th>
<th>%</th>
<th>VD/VT</th>
<th>pH</th>
<th>Arterial Pco$_2$</th>
<th>Arterial Po$_2$</th>
<th>(A-a) do$_2$</th>
<th>Arterial Oxygen Content</th>
<th>Cardiac Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>28</td>
<td>61</td>
<td>7.40</td>
<td>40</td>
<td>177</td>
<td>445</td>
<td>14.1</td>
<td>3.5</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>3.0</td>
<td>2.5</td>
<td>0.027</td>
<td>3.5</td>
<td>40.1</td>
<td>50.0</td>
<td>0.51</td>
<td>0.60</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>29</td>
<td>60</td>
<td>7.40</td>
<td>39</td>
<td>209</td>
<td>414</td>
<td>14.2</td>
<td>3.1</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>36</td>
<td>64†</td>
<td>7.39</td>
<td>41</td>
<td>206</td>
<td>387</td>
<td>14.1</td>
<td>2.8†</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>3.1</td>
<td>2.6</td>
<td>0.023</td>
<td>3.2</td>
<td>47.7</td>
<td>60.2</td>
<td>0.402</td>
<td>0.46</td>
<td></td>
</tr>
</tbody>
</table>

Nine patients with stiff thorax syndrome

*Values shown are means ± SE, which is listed below the mean. VD/VT = dead space to tidal volume ratio; (A-a)dO$_2$: difference; A-V = alveolar venous oxygen content difference; Qs/Qt = shunt fraction.

The results of continuous positive-pressure ventilation (CPP) show significant changes in cardiac index and arteriovenous oxygen difference at an expiratory pressure of 10 cm H$_2$O. A significant fall in cardiac index occurred at 5 cm H$_2$O. Mean mixed venous oxygen tension fell; however, with the wide variation of changes and the small size of the group, the change was not statistically significant. No change occurred in blood pressure, respiratory quotient, oxygen consumption, pH, wasted ventilation, or arterial Pco$_2$.

**CHRONIC OBSTRUCTIVE PULMONARY DISEASE**

In this group of four patients significant changes in cardiac index and arteriovenous oxygen difference were produced by 10 cm H$_2$O pressure. Although arterial oxygen content increased slightly because of a narrowing of the alveolar-arterial oxygen tension difference, cardiac index fell proportionately more; therefore, systemic oxygen transport decreased significantly at 10 cm H$_2$O.

The elevated pH and normal arterial Pco$_2$ values indicate either that the patients had had compensated carbon dioxide retention and had been "hyperventilated" or that they had an uncompensated metabolic alkalosis caused by factors such as diuretic administration or potassium depletion.

The low effective dynamic compliance for this group of obstructed patients is explained by the fact that this measurement was performed under dynamic rather than static conditions. Systemic blood pressure, respiratory quotient, oxygen consumption, mixed venous oxygen tension, wasted ventilation, pH, and arterial Pco$_2$ did not change significantly with increased expiratory pressure.

**STIFF THORAX SYNDROME**

Cardiac index fell and arteriovenous oxygen difference increased significantly at 10 cm H$_2$O expiratory pressure in this group. In 8 of 11 studies at 5 cm H$_2$O and in 9 of 11 studies at 10 cm H$_2$O, alveolar-arterial oxygen tension difference decreased. The degree of improvement in alveolar-arterial oxygen tension difference was about the same for all patients in the group, and, further, the responses to expiratory pressure did not correlate with initial values, shown by the right-hand scale of Figure 3. Similarly, initial cardiac index (left-hand column of Figure 3) did not relate to the change in alveolar-arterial oxygen tension difference produced by CPP ventilation.

Because of the slight fall in measured hemoglobin concentration at 10 cm H$_2$O, arterial oxygen content rose less than would be anticipated from the improvement in alveolar-arterial oxygen tension difference alone. The low initial values of arterial oxygen content reflect a reduction in hemoglobin concentration from overexpansion of plasma volume or reduction in red cell mass, or both. Systemic oxygen transport...
Table 1. (Continued)

<table>
<thead>
<tr>
<th>ml/100 ml</th>
<th>ml/min • m² BSA</th>
<th>%</th>
<th>ml/min</th>
<th>mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.4</td>
<td>742</td>
<td>3.9</td>
<td>0.87</td>
<td>247</td>
</tr>
<tr>
<td>0.26</td>
<td>135.8</td>
<td>1.18</td>
<td>0.025</td>
<td>32.9</td>
</tr>
<tr>
<td>3.8</td>
<td>673</td>
<td>3.7</td>
<td>0.85</td>
<td>256</td>
</tr>
<tr>
<td>0.30</td>
<td>117.2</td>
<td>1.04</td>
<td>0.027</td>
<td>33.1</td>
</tr>
<tr>
<td>4.3†</td>
<td>597†</td>
<td>2.6</td>
<td>0.84</td>
<td>250</td>
</tr>
<tr>
<td>0.39</td>
<td>127.7</td>
<td>1.08</td>
<td>0.010</td>
<td>32.6</td>
</tr>
<tr>
<td>5.8</td>
<td>465</td>
<td>10.0</td>
<td>0.91</td>
<td>263</td>
</tr>
<tr>
<td>0.70</td>
<td>114.8</td>
<td>1.02</td>
<td>0.071</td>
<td>81.3</td>
</tr>
<tr>
<td>6.0</td>
<td>425</td>
<td>7.8</td>
<td>0.93</td>
<td>257</td>
</tr>
<tr>
<td>0.54</td>
<td>115.0</td>
<td>1.62</td>
<td>0.067</td>
<td>81.4</td>
</tr>
<tr>
<td>6.9†</td>
<td>394†</td>
<td>6.9</td>
<td>0.92</td>
<td>267</td>
</tr>
<tr>
<td>0.53</td>
<td>101.5</td>
<td>2.01</td>
<td>0.051</td>
<td>78.1</td>
</tr>
<tr>
<td>5.6</td>
<td>503</td>
<td>27.0</td>
<td>0.88</td>
<td>258</td>
</tr>
<tr>
<td>0.80</td>
<td>80.2</td>
<td>4.2</td>
<td>0.019</td>
<td>21.9</td>
</tr>
<tr>
<td>6.3</td>
<td>452</td>
<td>23.1</td>
<td>0.89</td>
<td>266</td>
</tr>
<tr>
<td>0.90</td>
<td>76.2</td>
<td>3.50</td>
<td>0.018</td>
<td>27.0</td>
</tr>
<tr>
<td>5.4†</td>
<td>407†</td>
<td>21.5</td>
<td>0.88</td>
<td>247</td>
</tr>
<tr>
<td>0.87</td>
<td>65.4</td>
<td>3.37</td>
<td>0.027</td>
<td>20.9</td>
</tr>
</tbody>
</table>

† P < 0.05.

significantly decreased at 10 cm H₂O, owing to the reduction in cardiac index. Only at 10 cm H₂O did shunt fraction significantly fall. It should be noted that this decrease is the result not only of the improvement in alveolar-arterial oxygen tension difference but also of the widening in arteriovenous oxygen difference associated with a fall in cardiac output. The relationship between cardiac index and shunt fraction is represented in Figure 4; there is a significant correlation (r = 0.50) between the decrease in cardiac index due to expiratory pressure and the decrease in shunt fraction.

A small but statistically significant increase in wasted ventilation occurred at 10 cm H₂O expiratory pressure, but arterial Pco₂ remained constant. As in the other groups of patients, no change occurred in blood pressure, pH, respiratory quotient, oxygen consumption, or mixed venous oxygen tension.

Figure 5 shows that the three groups can be distinguished by their initial shunts and ratios of wasted ventilation to tidal volume. The patients in the stiff thorax syndrome group have the severest abnormalities of ventilation and perfusion and are clearly separate from the normal group. Those patients in the chronic obstructive pulmonary disease group have moderately abnormal shunt fractions and ratios of wasted ventilation to tidal volume. Shunt fractions greater than 15% were associated with wasted ventilation to tidal volume ratios of at least 50%.

Figures 6 and 7 show the change in cardiac index and systemic oxygen transport for all three groups at each level of expiratory pressure. The amount of decrease in each of these two variables was proportionately nearly the same for all groups.

No complications, such as pneumothorax, occurred as a result of the study.

Discussion

For the first time we have performed a detailed study on the effects of CPP ventilation on systemic oxygen transport and tissue oxygenation in comatose "normal" subjects and in patients who required mechanical ventilation. Although the alveolar-arterial oxygen difference narrowed, and hence arterial oxygen content improved in most patients with increased levels of expiratory pressure, systemic oxygen transport decreased, owing to a significant reduction in cardiac index. Despite the fall in systemic oxygen transport, which was significant at 10 cm H₂O in all groups, tissue oxygenation was not impaired, as evidenced by the lack of changes in oxygen consumption, respiratory quotient, pH, systemic blood pressure, or mixed venous oxygen tension. Although we applied each level of expiratory pressure for a relatively brief period, both the cardiac and respiratory effects of CPP ventilation have been shown to occur well within the duration of our observations (2, 12).
EFFECTS ON ARTERIAL OXYGEN

Continuous positive-pressure ventilation probably improves arterial oxygenation by preventing the collapse of small airways and alveoli during expiration. Use of expiratory pressure, large tidal volumes, or periodic sighing have been recommended to prevent alveolar closure and subsequent shunting of blood (13). Collapse tends to occur, in part, because surface forces are increased in alveoli as the result of either depletion or alteration of the surface active lining (surfactant) at the air-liquid interface. During the application of expiratory pressure the lung is ventilated from a higher position on its pressure-volume curve, thereby increasing functional residual capacity; if terminal lung units are held open, the arterial $P_{O_2}$ will increase. With more prolonged use, CPP ventilation may also improve the arterial $P_{O_2}$ by reducing tissue and alveolar edema through an increase in interstitial pressure which provides a "barrier" to the extravasation of fluid. Any improvement in arterial $P_{O_2}$, in the presence of a stable or increasing cardiac output, means that lower inspired oxygen concentrations can be maintained, which will diminish potential lung damage from oxygen toxicity.

Although most of the patients studied had some improvement in their alveolar-arterial oxygen tension differences, shunt fraction decreased significantly only in the stiff thorax syndrome group at 10 cm H$_2$O expiratory pressure. The mechanism for this change may have been the result of either the opening and ventilating of previously closed units that were the sites of shunts or the redistribution of blood flow away from shunt pathways. The improvement in shunt fraction, however, correlated with a significant decrease in cardiac index. In some of the patients in the stiff thorax syndrome and chronic obstructive pulmonary disease groups, as increasing expiratory pressure was applied, alveolar-arterial oxygen tension difference changed very little, yet shunt fraction decreased. This apparent paradox is explained by the fact that arterial oxygen tension should fall if cardiac output, and, hence, mixed venous oxygen content, alone is reduced; therefore, if arterial $P_{O_2}$ remains stable despite a fall in cardiac output, the amount of blood shunted must have decreased.
Figure 5. The relationship between initial shunt fraction \( \frac{Q_s}{Q_T} \) and wasted ventilation to tidal volume ratio \( \frac{V_d}{V_T} \) for all patients. COPD = chronic obstructive pulmonary disease; STS = stiff thorax syndrome.

At 10 cm H\(_2\)O 2 of 11 patients in the stiff thorax syndrome group had a mild deterioration of their alveolar-arterial oxygen tension differences (77 and 25 mm Hg, respectively) with an increase in their shunt fraction (9.8% and 3.7%, respectively). Analysis of their dye dilution curves failed to demonstrate the presence of an intracardiac shunt. However, increased right-to-left shunting still could have been caused by flow through a patent foramen ovale, since this site of shunting is best detected by an inferior, rather than superior, vena cava dye injection (14). An increase in shunt fraction could also occur through an alteration of ventilation-perfusion relationships, either by blood flow shifting to nonventilated units or by ventilation decreasing in previously well ventilated areas.

The significant increase in wasted ventilation in the stiff thorax syndrome group at 10 cm H\(_2\)O can also be explained by alterations in the distribution of ventilation with respect to perfusion; in this case, some alveoli may have been overventilated relative to their perfusion, or blood flow may have been redistributed away from ventilated alveoli. Arterial P\(_{CO_2}\) did not rise, as might have been anticipated from the increased wasted ventilation, but either an improvement in shunt fraction or a small decrease in carbon dioxide production could have offset any change in arterial P\(_{CO_2}\) predicted on the basis of an increase in wasted ventilation alone (15).

HEMODYNAMIC EFFECTS

Although it is generally alleged that cardiac output is not affected by CPP ventilation in patients with stiff thorax syndrome, our results show that cardiac index did indeed fall—and fell by nearly the same percentage in every group of patients. At 10 cm H\(_2\)O the decrease in cardiac index was statistically significant in all three groups (Figure 6). As in our studies, the results of other investigations suggest that the reduction in cardiac output can be related to the mean level of end-expiratory pressure; McIntyre, Laws, and Ramachandran (3) found no change in cardiac output using 5 cm H\(_2\)O, but Kumar and associates (2) noted a significant reduction with the use of 13 cm H\(_2\)O. Moreover, Colgan, Barrow, and Fanning (16) recently reported that a greater reduction in cardiac output occurred with CPP ventilation achieved by expiratory flow resistance than with an expiratory plateau of positive pressure.

Cardiac output should fall when positive pressure is used to inflate the lungs and distend the chest wall, and the magnitude of the effect is related to the change in mean intrapleural pressure and to its influence on venous return. If a patient's lungs are stiff, more pressure is required to inflate them, but the "extra" pressure is dissipated across the lungs and not transmitted to the pleural space, unless the limits of lung distensibility have been reached. At any given lung volume intrapleural pressure is...
the same in patients with normal and noncompliant lungs, and therefore any change in lung inflation from end-expiratory pressure would cause a comparable change in intrapleural pressure in the two conditions. These relationships are shown in the studies of Uzawa and Ashbaugh (12); when they ventilated dogs with noncompliant lungs with positive end-expiratory pressures, higher pleural pressures were found than when the same animals were ventilated using 0 (atmospheric) end-expiratory pressures.

We would expect, therefore, that a patient with normal or stiff lungs who is ventilated with large tidal volumes from an initially low functional residual capacity or has his functional residual capacity raised by application of CPP ventilation will experience a predictable fall in cardiac output because of impairment of venous return that depends on the change in mean intrapleural pressure. If the thoracic wall is noncompliant (structural disorder or muscle spasm from pain or injury), much higher inflation pressures are required, and intrapleural pressures will be correspondingly greater. Other factors, such as peripheral venous volume and right atrial filling pressure, changes in pulmonary vascular resistance from lung disease, and extent of lung inflation, will also modify the cardiac response to CPP ventilation.

Effective dynamic compliance may change with added expiratory pressure because breathing at higher lung volumes could open lung units and should distend airways. Since no change in dynamic compliance occurred in the three groups studied, we can infer that the patients were breathing on the relatively linear segment of their combined lung and chest wall pressure-volume curves.

No change occurred in systemic blood pressure with increasing expiratory pressure, despite the fall in cardiac output, indicating that baroreceptor mechanisms were intact and adequate to increase systemic vascular resistance. The reported depressant effect of intermittent positive-pressure ventilation on peripheral vasoconstrictor reflexes (17) was not observed in our patients.

EFFECTS ON SYSTEMIC OXYGEN TRANSPORT

Systemic oxygen transport was significantly reduced at 10 cm H2O expiratory pressure in all three groups. Even though arterial oxygen content increased slightly owing to a narrowing of the alveolararterial oxygen tension difference, the cardiac index decreased proportionately more, which accounts for the significant reduction in systemic oxygen transport. This impairment of oxygen delivery is the most critical measure of the overall cardiopulmonary effect of CPP ventilation.

It is possible that in the stiff thorax syndrome group oxygen delivery might not have decreased by the amount we observed if we had studied the effects of breathing lower concentrations of oxygen. Any improvement in arterial oxygen content under the conditions of our study depended mainly on an increase in dissolved oxygen because hemoglobin was in most cases nearly fully saturated at 0 cm H2O. Had a lower concentration of inspired oxygen been used in the study, arterial oxygen content might have increased more, because of an increase in hemoglobin saturation as well as in the dissolved oxygen. Thus, the decrease in cardiac index might have been offset by a more substantial increase in arterial oxygen content, and, as a consequence, systemic oxygen transport could have been influenced far less by CPP ventilation. We purposely chose an inspired concentration of 100% oxygen, so that the effects of CPP ventilation on hypoxia caused by shunting...
rather than that caused by ventilation-perfusion imbalance could be more clearly defined and examined; moreover, most of the hypoxia in patients for whom CPP ventilation has been recommended is caused by shunting.

Another important variable of arterial oxygen content is the hemoglobin concentration. Because prolonged administration of CPP ventilation may reduce edema by shifting alveolar and interstitial fluid into the vascular space, we would predict that the hemoglobin concentration would decrease because of hemodilution. It is noteworthy that in the stiff thorax syndrome group the arterial oxygen content did not increase by the amount anticipated from an improvement in alveolar-arterial oxygen difference owing to a slight fall in hemoglobin concentration. Whether this reflects actual redistribution of extravascular fluid is difficult to ascertain, particularly in short-term experiments. Further studies on the influence of CPP ventilation on pulmonary fluid dynamics are clearly indicated.

PERIPHERAL OXYGENATION

Despite the fall in cardiac index and systemic oxygen transport, mixed venous oxygen tension decreased only slightly in all groups with increasing expiratory pressure. As discussed earlier, our computation of mixed venous oxygen tension may underestimate the actual mixed venous oxygen tension. In our study the expected decrease in mixed venous oxygen tension was offset mainly by a rise in arterial oxygen content and, in a few instances, by a slight fall in oxygen consumption. The opening of or increased flow through peripheral arterial-venous anastomoses may have minimized the tendency for mixed venous oxygen tension to fall.

Since mixed venous oxygen tension reflects total body tissue oxygen tension, we conclude that the reduction in cardiac index and hence systemic oxygen transport did not interfere with overall peripheral oxygenation. Had metabolic acidosis occurred because of a shift from aerobic to anaerobic metabolism, a critical reduction in systemic oxygen transport should have been associated with a change in pH, oxygen consumption, respiratory quotient, or (possibly) blood pressure. As further evidence of the adequacy of overall tissue oxygenation, no change in any of these variables occurred. We should point out, however, that the reduction in cardiac output observed after CPP ventilation was probably accompanied by redistribution of blood flow; thus, there may have been impairment of oxygen delivery and metabolism to some organs that could not be identified by examining “total” body activity.

Clinically, expiratory pressure can be helpful in the management of properly selected patients with respiratory failure; it has been shown to benefit infants with the idiopathic respiratory distress syndrome (18) and patients with the adult respiratory distress syndrome (1); based on pathophysiological considerations, it should also be of particular benefit in patients with “shock lung” (19). It should not be used in patients with obstructive lung disease because of the 50% incidence of complications, mainly pneumothorax and pneumomediastinum, that developed in carefully selected patients (2), and the increased risk of such complications in patients with airways obstruction.

We have shown that in controlled, steady-state experiments, CPP ventilation was attended by a significant decrease in systemic oxygen transport but without any obvious deterioration in peripheral oxygenation. Furthermore, the decrease in oxygen delivery was proportionately the same for each group studied. We emphasize that these are short-term studies and do not answer questions concerning the long-term hazards and benefits of CPP ventilation. However, we have shown for the first time that systemic oxygen transport is influenced by CPP ventilation; therefore, oxygen transport and indicators of peripheral oxygenation should certainly be considered in future studies rather than relying solely on the alveolar-arterial oxygen tension difference to judge its value, as has been the practice.


References


Lutch and Murray • Continuous Positive-Pressure Ventilation 201