Changes in the Distribution of Ventilation and Perfusion Associated with Separation from Mechanical Ventilation in Patients with Obstructive Pulmonary Disease

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A trial of separation from mechanical ventilation may induce an abnormal respiratory pattern and a maldistribution of ventilation-to-perfusion ratios (VA/Q), especially in patients with chronic obstructive pulmonary disease. This study was designed to assess the effects of three different modes of ventilation on the distribution of global and also regional VA/Q in eight patients with chronic obstructive pulmonary disease recovering from acute respiratory failure who remained dependent on mechanical ventilation after more than 5 days of attempted separation from the ventilator. VA/Q distribution was assessed using the multiple inert gas and isotopic scanning methods after 30 min each of controlled mechanical ventilation (CMV), 10 cmH2O inspiratory pressure support, and spontaneous breathing (SB). Controlled ventilation was provided at a respiratory rate ranging from 12 to 18 breaths per min and a tidal volume of 8 ml·kg⁻¹. In comparison to CMV, SB resulted in a decrease in tidal volume (from 512 ± 144 to 301 ± 102 ml, P < 0.01), and an increase in respiratory rate (from 15.5 ± 3.2 to 27.3 ± 15.0 breaths per min, P < 0.05), which increased dead space (+7.1% of minute ventilation), cardiac output (+36%), and the perfusion to areas of low VA/Q (+8.5% of cardiac output) (P < 0.05, P < 0.001, and P < 0.05, respectively). Isotopic scans revealed a horizontal craniocaudal difference of VA/Q in all modes, with the lowest VA/Q zones at the basal part of the lungs (mean basal VA/Q 0.58 in SB and 1.05 in CMV). During SB, this craniocaudal difference of VA/Q was highly correlated to the dispersion of perfusion (dispersion around the mean [log SDQ], r = 0.87, P < 0.01). Moreover, the patients with the smallest tidal volume during SB showed the lowest caudal VA/Q ratios (r = 0.88, P < 0.01), the largest craniocaudal gradient in VA/Q (r = 0.77, P < 0.05), and the largest amount of perfusion in the areas of low VA/Q ratios (r = -0.71, P < 0.05). We conclude that in our patients, the change from CMV to SB, induced an abnormal breathing pattern with small tidal volumes. This resulted in a maldistribution of VA/Q ratios that was not improved by pressure support at a level of 10 cmH2O. (Key words: Critical care. Lung, function: ventilation-perfusion ratios; respiratory failure. Ventilation: mechanical; inspiratory pressure support; spontaneous breathing.)

SEPARATION FROM MECHANICAL VENTILATION may be difficult in patients with chronic obstructive pulmonary disease (COPD) recovering from acute respiratory failure. Factors such as increased airway resistance and increased dead space can induce respiratory muscular fatigue, resulting in decreased tidal volume (VT) and inefficient ventilation. These conditions intensify the work of breathing, increase its metabolic cost, and increase the patient's cardiac output. Torres et al. investigated the consequences of the separation from controlled mechanical ventilation (CMV) in patients with COPD and reported changes in the distribution of ventilation. Inspiratory pressure support (IPS) is now commonly provided to ease the transition from mechanical to spontaneous breathing (SB). This mode acts by exerting an adjustable level of positive pressure to the airways during inspiration. IPS increases minute ventilation and decreases cardiac output.

The aim of this study was to evaluate pulmonary gas exchange abnormalities at the time of discontinuation of mechanical ventilation in patients with COPD, using two different methods of measuring ventilation-to-perfusion ratios (VA/Q): the conventional inert gas technique, which quantifies the changes in VA/Q distributions, and an isotopic scanning method. It was expected that the isotopic method would help localize the regions of the lungs responsible for the VA/Q abnormalities.

Materials and Methods

We studied patients with COPD (table 1) in our intensive care unit who were recovering from an acute respiratory failure and in whom either tracheal intubation or tracheostomy had been performed. Included in the study were eight consecutive patients meeting the following criteria: the existence of an obstructive disease documented by lung function tests or a history of a heavy smoking (> 50 pack-years) with lung distention on the chest roentgenogram. At the time of the study, these patients remained dependent upon mechanical ventilation after more than 5 days of attempted separation from the ventilator but could sustain at least 1–3-h periods of SB.

Our protocol was approved by our local ethics committee, and informed consent was obtained in all cases.

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Received from the Service de Réanimation Médicale, the Service de Médecine Nucléaire, and INSERM U296, Hôpital Henri Mondor, Créteil, France. Accepted for publication June 28, 1991. P.R. was on leave from Institut für Anästhesiologie, Heinrich Heine Universität, Düsseldorf, Federal Republic of Germany.

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TABLE 1. Clinical Characteristics of Patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Size (cm)</th>
<th>Weight (kg)</th>
<th>Etiology of Failure</th>
<th>FEV₁/FVC</th>
<th>PaO₂ (mmHg)</th>
<th>PaCO₂ (mmHg)</th>
<th>Duration of Ventilation after the Study (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>76</td>
<td>F</td>
<td>149</td>
<td>65</td>
<td>Pneumonia</td>
<td>65</td>
<td>41</td>
<td>81</td>
<td>7</td>
</tr>
<tr>
<td>2</td>
<td>76</td>
<td>F</td>
<td>147</td>
<td>85</td>
<td>Cardiac failure</td>
<td>64</td>
<td>39</td>
<td>77</td>
<td>9</td>
</tr>
<tr>
<td>3</td>
<td>68</td>
<td>M</td>
<td>171</td>
<td>66</td>
<td>Postoperative</td>
<td>51</td>
<td>45</td>
<td>71</td>
<td>8</td>
</tr>
<tr>
<td>4</td>
<td>72</td>
<td>F</td>
<td>160</td>
<td>51</td>
<td>Pneumonia</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>61</td>
<td>M</td>
<td>170</td>
<td>68</td>
<td>Postoperative</td>
<td>52</td>
<td>49</td>
<td>60</td>
<td>6</td>
</tr>
<tr>
<td>6</td>
<td>70</td>
<td>F</td>
<td>156</td>
<td>41</td>
<td>Pneumonia</td>
<td>48</td>
<td>50</td>
<td>55</td>
<td>6</td>
</tr>
<tr>
<td>7</td>
<td>77</td>
<td>M</td>
<td>178</td>
<td>64</td>
<td>Postoperative</td>
<td>49</td>
<td>50</td>
<td>58</td>
<td>5</td>
</tr>
<tr>
<td>8</td>
<td>67</td>
<td>M</td>
<td>189</td>
<td>70</td>
<td>Pneumonia</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>6</td>
</tr>
</tbody>
</table>

A dash indicates that basal lung function tests were not available. Nevertheless, these two patients had an history of previous respiratory failures with artificial ventilation, and a typical lung distortion was observable on the chest x-ray at the time of the study. These findings strongly support the diagnosis of chronic obstructive pulmonary disease. FEV₁ = forced expiratory volume in 1 s; FVC = forced vital capacity.

All patients had indwelling pulmonary artery (7-Fr, Edwards) and radial arterial catheters. They were monitored by electrocardiography (ECG). Hemodynamic and ECG data were continuously displayed on an oscilloscope (Hewlett Packard 78552A). At the time of the study, seven patients had a clear chest roentgenogram and one had a residual opacity in the left lung.

MODES OF VENTILATION

We compared the effects of CMV, IPS, and spontaneous ventilation (without positive end-expiratory pressure) on pulmonary gas exchange and on cardiac output, with respect to V̇A/Q. We used a conventional volume-cycled ventilator (Servo 900C, Siemens) including a filter-humidifier device at the Y piece (Ultisper*, Pall Laboratories). The flowmeters of the ventilator were calibrated prior to the study. We kept the fractional inspired oxygen concentration constant (range, 0.30–0.45) to maintain an arterial oxygen tension greater than 100 mmHg, as measured by blood gas analysis (ABL 30, Radiometer, Copenhagen). CMV was characterized by a respiratory rate ranging from 12 to 18 breaths per minute, a ratio of the duration of inspiration to the duration of the total respiratory cycle of 33%, and a V̇T of 8 ml·kg⁻¹. IPS was provided at a level of 10 cmH₂O, with the minimal trigger level available (−1 cmH₂O). This level of pressure support has been reported to eliminate efficiently the resistance of the endotracheal tube and to decrease slightly the work of breathing.¹⁰ SB and pressure support ventilation were studied in random order, and controlled ventilation was studied last, and served as the control mode.

V̇T was recorded on a paper chart recorder (Gould ES1000) from the analog signal of the ventilator and was averaged over 2 min during a period of steady-state ventilation. Minute ventilation during each mode was calculated as the product of V̇T and respiratory rate. Arterial and mixed venous blood samples were collected for standard blood gas analysis. Cardiac output was determined using the thermodilution technique. The distribution of ventilation and of perfusion (V̇A/Q ratios) and the percent shunt or dead space during each ventilatory mode were determined using the inert gas⁹ and isotopic scanning⁹ techniques. Each mode was studied for 30 min, followed by a 30-min period of rest during CMV before study of the next mode. The same sequence of ventilation was followed during the isotopic study performed 4 h later.

INERT GAS STUDY

For practical considerations, we performed the inert gas study before isotopic scanning. Patients lay supine when we determined the V̇A/Q distribution during each ventilatory mode. Therefore we used the six–inert-gas technique described by Wagner et al.¹¹ In brief, after achieving a stable condition where V̇T did not vary more than 15% in the selected mode, we infused six inert gases (sulfur hexafluoride, ethane, cyclopropane, enflurane, diethyl ether, and acetone) dissolved in isotonic sodium chloride into a large peripheral vein of the patient’s arm at a constant rate of 4 ml·min⁻¹. After 30 min of infusion and under steady-state conditions, arterial and mixed venous blood samples were drawn and transported to the laboratory for immediate analysis. Mixed expired gases were collected from the expiratory port of the ventilator by means of a heated mixing box. The expiratory tubing and valve were heated by a heating coil wrapped around these components. The concentrations of inert gases in the blood and expired gas samples were measured using gas chromatography (models 427 and 489, Packard).

ISOTOPICT STUDY

The isotopic study was performed 4 h after the inert gas study. Between these two periods the patients’ lungs were ventilated with CMV. The isotopic imaging was performed in the Nuclear Medicine Department. Patients lay supine, their backs facing a γ camera detector (Compagnie Générale de Radiologie, Paris, France) equipped with a medium-energy collimator and linked to a com-
puter (Sopha, Paris, France) for image processing. Regional $V_A/Q$ ratios during each mode were measured for both lungs by two sequential scintigrams. The first provided a map of ventilation using $81mKr$ according to the method of Amis and Jones. $81mKr$, a short-lived radio-
nuclide ($t_{1/2} = 13$ s, $\gamma$-emission energy = 190 keV), was produced by a $81mRb$ generator and pumped to the inspiratory limb of the ventilator at a constant rate of 300
ml·min$^{-1}$. The second scintigram provided the perfusion scan via $99mTc$-labeled albumin macroaggregates. The $99mTc$ was injected into a peripheral vein of the patient's arm in gradually increased doses for three trials (1, 2, and 4 mCi). Just before the second and third $99mTc$ injection, we recorded regional background $\gamma$ emission by performing a blank acquisition. The background emission was subtracted from the subsequent $99mTc$ scan. Scintigraphy of each mode was followed by a 30-min period of rest during CMV.

For each study, at least 200,000 corrected counts of the posterior view were collected into the computer memory in a 64 × 64 matrix and stored on magnetic tape. Because the energy of the $\gamma$ emission is different for each isotope ($81mKr = 190$ keV; $99mTc = 140$ keV), we applied a 20% window to each energy spectrum peak to separate one isotope emission from another. The scans were displayed on a video monitor after background emission subtraction.

The boundaries of the lungs were then drawn electronically under visual control to determine the regions of interest. Each scan was normalized to its corresponding flow (i.e., ventilation or perfusion). The $64 \times 64$ matrices were then contracted into $32 \times 32$ matrices to improve statistical analysis. Each entry in the matrix of the $81mKr$ scan was divided by that of the corresponding $99mTc$ scan to provide a $V_A/Q$ map of each ventilatory mode.

The view of the two lungs was then divided into three compartments of the same height along the craniocaudal axis. The mean $V_A/Q$ in each of the three zones (apical, mid-, and basal) was calculated (fig. 1). In order to evaluate the craniocaudal gradient of $V_A/Q$, we computed the difference between the apical and the basal mean $V_A/Q$ for each patient.

### Statistical Analysis

All results are expressed as the mean ± the standard deviation. The overall difference between mean values of gas exchange parameters and inert gas data were compared using a two-way analysis of variance in order to separate the mode effect from the patient effect. The differences in isotopic regional mean $V_A/Q$ were assessed by a three-way analysis of variance to separate between the patients the effect of the mode of ventilation and that of the differences between regional distribution. Internal comparisons between means were performed in all cases by Tukey's tests for repeated measurements. Linear regressions by the least-squares method were used to assess linear relationship between pairs of variables.

### Results

**VENTILATION, BLOOD GASES, AND CARDIAC OUTPUT**

The effects of SB and IPS on respiratory variables, arterial, and mixed-venous blood gas tensions and cardiac output were significantly different from those of CMV for all variables except minute ventilation (table 2). $V_T$ during SB was on average 41% less (30.1 ± 10.2 vs. 51.2 ± 14.4 ml, $P < 0.01$) and respiratory rate 76% greater (27.3 ± 15.6 vs. 15.5 ± 3.2 breaths per min, $P < 0.05$) than during controlled ventilation. Despite a minute ventilation in spontaneous mode equal to that in the controlled mode, the corresponding alveolar ventilation was reduced presumably because of a 18% increase in dead space-$V_T$ ratio (dead space ventilation [$V_D/V_T$]) (table 3). IPS led to results similar to those of SB. Slight changes in arterial oxygen tension occurred among the three modes, whereas arterial carbon dioxide tension significantly increased, by 18% from CMV to SB (from 41.4 ± 10.5 to 48.7 ± 10.7 mmHg, $P < 0.05$) and by 19% from CMV to IPS (from 41.4 ± 10.5 to 46.9 ± 10.5 mmHg, $P < 0.05$). Oxygen consumption and cardiac output were 20 and 36% greater ($P < 0.001$) and the arteriovenous difference in oxygen content 15% less ($P < 0.05$) during spontaneous ventilation than during controlled ventilation. IPS yielded values of oxygen consumption and cardiac output similar to those of SB. When data from all three modes of ventilation were pooled, significant correlations were found between cardiac output and arteriovenous difference in oxygen content ($r = -0.44, P < 0.05$) and between cardiac output and oxygen consumption ($r = 0.63, P < 0.001$).

### INERT GAS STUDY

During the calculation of the $V_A/Q$ distribution, the residual sum of squares value below which 50 and 90%
of sets laid were 3 and 9, respectively. Moreover, the residual sum of squares was less than 10 for each ventilatory mode in all but one patient, in whom it reached 23 during CMV. This outlying sum of squares was not perfectly stable during CMV, contrary to those of all other subjects studied.

**Distribution of Ventilation**

The transformation of the retention and excretion of the six gases into a continuous distribution showed that the ventilation was distributed primarily in the range of \(V_A/Q\) between 0.1 and 10 and did not vary significantly between modes of ventilation in this central range of \(V_A/Q\) ratios (table 3). However, the distribution of ventilation in regions of \(V_A/Q\) above 100, i.e., \(V_D/V_T\), differed significantly by mode. \(V_D/V_T\) was high during all three modes but still 18% greater during SB and IPS than during CMV (on average 45.7 ± 7.1 and 45.5 ± 7.2% vs. 38.6 ± 8.2%, respectively, of total ventilation, \(P < 0.05\), table 3). Nevertheless, the differences in \(V_D/V_T\) across modes apparently were not large enough to induce significant differences in either the mean \(V_A/Q\) for ventilation or the dispersion around the mean (log SD\(_V\)).

Looking at individual values, we found a positive relationship between \(V_D/V_T\) obtained in CMV and that observed in SB (\(r = 0.73, P < 0.05\)). A similar correlation was found between log SD\(_V\) measured in CMV and log SD\(_V\) measured in SB (\(r = 0.83, P < 0.01\)). Hence, the patients who experienced the largest abnormalities in \(V_D/V_T\) and the widest distribution of ventilation when they were changed to spontaneous mode were those who already had the largest dead space during the preceding period of controlled ventilation.

**Distribution of Perfusion**

Changes in the distribution of perfusion were more striking than those of ventilation (table 4). During SB and IPS, one patient had an unimodal distribution of perfusion limited to the central zone of \(V_A/Q\) ratios (0.1 < \(V_A/Q\) < 10). Another showed a unimodal distribution that included mainly the central zone of the \(V_A/Q\) scale but also partially overlapped into the region of low \(V_A/Q\) ratios. The six other patients had a bimodal distribution of perfusion, where more than 5% of the perfusion was directed

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**Table 2. Gas Exchange, Cardiac Output, and Ventilation**

<table>
<thead>
<tr>
<th>Mode</th>
<th>Row</th>
<th>(P_{A02}) (mmHg)</th>
<th>(P_{A02}) (mmHg)</th>
<th>(C_{O2-T02}) (vol.-100 m(^3))</th>
<th>(V_{A02}) (ml/min)</th>
<th>(Q_T) (l/min)</th>
<th>(V_T) (ml)</th>
<th>RR (breaths per min)</th>
<th>(V_0) (l/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SB</td>
<td>1</td>
<td>96.4 ± 21.8</td>
<td>48.7 ± 10.7</td>
<td>4.46 ± 0.79</td>
<td>269 ± 55</td>
<td>5.81 ± 0.85</td>
<td>301 ± 102</td>
<td>27.3 ± 15.0</td>
<td>7.08 ± 1.40</td>
</tr>
<tr>
<td>IPS</td>
<td>2</td>
<td>101.3 ± 24.9</td>
<td>46.9 ± 10.5</td>
<td>4.66 ± 0.82</td>
<td>265 ± 52</td>
<td>5.55 ± 1.06</td>
<td>349 ± 78</td>
<td>24.5 ± 10.1</td>
<td>7.87 ± 1.88</td>
</tr>
<tr>
<td>CMV</td>
<td>3</td>
<td>105.2 ± 26.6</td>
<td>41.4 ± 10.0</td>
<td>5.26 ± 1.20</td>
<td>224 ± 43</td>
<td>4.27 ± 0.76</td>
<td>512 ± 144</td>
<td>15.5 ± 5.2</td>
<td>7.44 ± 1.79</td>
</tr>
</tbody>
</table>

Statistical comparisons between rows (mode effect)

NS * * ↑ ✦ ✦ ✦ ✦ NS

Patient effect

★ P < 0.01.

**Table 3. Inert Gas Results: Ventilation Distribution**

<table>
<thead>
<tr>
<th>Mode</th>
<th>Row</th>
<th>Mean (V_A/Q)</th>
<th>Log SD(_V)</th>
<th>0.1 &lt; (V_A/Q) &lt; 10 (%)</th>
<th>10 &lt; (V_A/Q) &lt; 100 (%)</th>
<th>(V_D/V_T) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SB</td>
<td>1</td>
<td>1.59 ± 0.68</td>
<td>0.71 ± 0.23</td>
<td>53.4 ± 7.1</td>
<td>1.80 ± 4.58</td>
<td>45.7 ± 7.1</td>
</tr>
<tr>
<td>IPS</td>
<td>2</td>
<td>1.59 ± 0.40</td>
<td>0.65 ± 0.22</td>
<td>53.5 ± 7.7</td>
<td>0.65 ± 1.18</td>
<td>45.5 ± 7.2</td>
</tr>
<tr>
<td>CMV</td>
<td>3</td>
<td>1.80 ± 0.87</td>
<td>0.75 ± 0.35</td>
<td>58.0 ± 11.7</td>
<td>3.09 ± 4.92</td>
<td>38.6 ± 8.2</td>
</tr>
</tbody>
</table>

Statistical comparisons between rows (mode effect)

NS NS NS NS NS *1–3

Patient effect

★ P < 0.01.

★ P < 0.05.

★ P < 0.001.

Mean \(V_A/Q\) and distribution (log SD\(_V\)) of ventilation and their partitioning to different \(V_A/Q\) ranges.

SB = spontaneous breathing; IPS = inspiratory pressure support ventilation; CMV = controlled mechanical ventilation; NS = not significant.

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Mean \( \dot{V}_A/Q \) and distribution (log SDQ) of perfusion and their partitioning to different \( \dot{V}_A/Q \) ranges.  
SB = spontaneous breathing; IPS = inspiratory pressure support ventilation; CMV = controlled mechanical ventilation; NS = not significant.

to regions characterized by low \( \dot{V}_A/Q \) ratios (0.005 < \( \dot{V}_A/Q \) < 0.1). In these patients, a clear demarcation centered around the \( \dot{V}_A/Q \) boundary of 0.1 was observed. The lower limit for low \( \dot{V}_A/Q \) regions was set at 0.005.

The amount of perfusion in the regions of low \( \dot{V}_A/Q \) was higher during spontaneous ventilation (15.0 ± 10.6%) than during CMV (6.1 ± 8.4%) or IPS (8.9 ± 8.5%, \( P < 0.05 \)) (see example in fig. 2). The changes in perfusion within the low \( \dot{V}_A/Q \) regions also reflected in a significantly lower mean \( \dot{V}_A/Q \) for perfusion during SB and IPS than during CMV (0.45 ± 0.25 and 0.51 ± 0.16 vs. 0.76 ± 0.27, respectively, \( P < 0.01 \)). In contrast, the average change in the dispersion of perfusion (log SDQ) between modes that included the whole range of \( \dot{V}_A/Q \) did not reach significance (\( P = 0.09 \)). Nonetheless, considering individual values, we found a good relationship between the amount of perfusion in the low \( \dot{V}_A/Q \) range (0.005 < \( \dot{V}_A/Q \) < 0.1) and log SDQ (\( r = 0.90, P < 0.01 \)).

This suggests that the increased perfusion to low \( \dot{V}_A/Q \) regions is accompanied by an increase in the dispersion of perfusion and therefore is due not only to an overall shift of the perfusion on the \( \dot{V}_A/Q \) diagram. Of note, while breathing spontaneously, the patients with the smallest \( V_T \) had the most abnormal distribution of \( \dot{V}_A/Q \). This is shown in figure 3 by the significant negative correlation (\( r = -0.71, P < 0.05 \)) between the amount of perfusion in the range of low \( \dot{V}_A/Q \) ratios and \( V_T \). Shunt, in contrast, remained low and similar in the three modes. We found no correlation between values of perfusion in the low \( \dot{V}_A/Q \) regions during CMV and the corresponding values obtained in SB. Similarly, no correlations were found between these two modes of ventilation for individual values of log SDQ.

### ISOTOPE STUDY

The mean \( \dot{V}_A/Q \) ratios of each lung region (apical, mid-, and basal) were significantly lower during SB than during IPS and significantly lower during IPS than during CMV (\( P < 0.001 \)) (fig. 1). For instance, the \( \dot{V}_A/Q \) ratio in the basal region during SB was nearly half that observed for the same region during the CMV. A significant trend (\( P < 0.001 \)) also appeared in the spatial partition of \( \dot{V}_A/Q \) along the craniocaudal axis with all three modes: the \( \dot{V}_A/Q \) ratios significantly decreased from the apex to the base of the lung. Furthermore, as figure 3 shows, the \( \dot{V}_A/Q \) of the bases was highly and positively dependent on the size of the \( V_T \) during SB. A clear relationship was found also between the size of the \( V_T \) and both the magnitude of the craniocaudal gradient in \( \dot{V}_A/Q \) (\( r = -0.77, P < 0.05 \)) and the magnitude of the caudal \( \dot{V}_A/Q \) ratio (\( r = 0.88, P < 0.001 \)).
VENTILATION-PERFUSION RATIOS

Comparison Between the Inert Gas and the Isotope Results

We compared the perfusion in the low-\( \dot{V}_A/\dot{Q} \) units obtained from the inert gas method to the regional heterogeneity of \( \dot{V}_A/\dot{Q} \) ratios by plotting the craniocaudal difference in \( \dot{V}_A/\dot{Q} \) against the log SD\(_Q\) (r = 0.87, P < 0.01). Figure 4 shows a significant correlation between these two parameters during SB. Moreover, during SB, we found a good correlation between the isotopic \( \dot{V}_A/\dot{Q} \) of the bases versus the perfusion of the low \( \dot{V}_A/\dot{Q} \) units by the inert gas technique (r = -0.82, P < 0.05) (fig. 4). This suggests that low \( \dot{V}_A/\dot{Q} \) units identified by the inert gas technique were located at the bases.

Discussion

Our study was designed to evaluate the changes in ventilation and perfusion distribution under three different modes of ventilation. We added an isotopic scanning method to the inert gas technique in order to localize the \( \dot{V}_A/\dot{Q} \) abnormalities during spontaneous ventilation. When changing from controlled to spontaneous ventilation, our patients developed a shallow breathing pattern with an increased respiratory rate and a low \( V_T \). Concomitantly, they increased cardiac output. Considering average values for the eight patients, the distribution of perfusion was significantly shifted toward lower values. Moreover, during SB, isotopic dispersion of \( \dot{V}_A/\dot{Q} \) cor-

**FIG. 3.** Linear regression of pulmonary blood flow to regions with low \( \dot{V}_A/\dot{Q} \) (0.005 < \( \dot{V}_A/\dot{Q} < 0.1 \)) versus \( V_T \) (P < 0.05) (left) and of \( \dot{V}_A/\dot{Q} \) base versus \( V_T \) (P < 0.01) (right), using individual values from the eight patients in spontaneous breathing. Inert gas method: Low \( \dot{V}_A/\dot{Q} = \) percentage of the perfusion distributed in units with \( \dot{V}_A/\dot{Q} \) comprised between 0.005 and 0.1. Isotopes: \( \dot{V}_A/\dot{Q} \) base = basal \( \dot{V}_A/\dot{Q} \) expressed as a ratio to the overall \( \dot{V}_A/\dot{Q} \) of the lung. \( V_T = \) tidal volume.

**FIG. 4.** Linear regression of diff. \( \dot{V}_A/\dot{Q} \) versus log SD\(_Q\) (P < 0.01) (left) and of \( \dot{V}_A/\dot{Q} \) base versus low \( \dot{V}_A/\dot{Q} \) (P < 0.05) (right), using individual values from the eight patients in spontaneous breathing. Isotopes: Diff. \( \dot{V}_A/\dot{Q} = \) algebraic difference between the mean isotopic \( \dot{V}_A/\dot{Q} \) of the apices and that of the bases. \( \dot{V}_A/\dot{Q} = \) basal \( \dot{V}_A/\dot{Q} \) expressed as a ratio to the overall \( \dot{V}_A/\dot{Q} \) of the lung. Inert gas method: Low \( \dot{V}_A/\dot{Q} = \) percentage of the perfusion distributed in units with \( \dot{V}_A/\dot{Q} \) comprised between 0.005 and 0.1. Log SD\(_Q\) = Log of standard deviation for perfusion.
related with Log SDQ from the inert gas technique. The
regions with a low V̇A/Q were located at the bases of the
lungs (fig. 1). The size of the VT was the major deter-
mnant for these changes and correlated with perfusion
in the low V̇A/Q range, the decrease of basal V̇A/Q ratios,
and the widening of the isotopic cranio-caudal gradient.
Hence, an abnormal respiratory pattern in SB probably
accounts for the V̇A/Q heterogeneities in this mode.

Changes in breathing pattern and pulmonary gas ex-
change during the removal of assisted ventilation are
common.13 Gilbert et al.14 showed that shallow breathing
occurred in patients with COPD within the first 30 min
of being disconnected from the ventilator. They reported
spirometric and blood gas values similar to those we report
and found their patients unable to sustain increased re-
spiratory work. Brochard et al.15 also observed that blood
gas and spirometric findings were abnormal in the same
type of patients during disconnection from the ventilator.
They reported that increasing levels of pressure support
increased the VT, normalizing the respiratory pattern.

In our study, IPS yielded results close to those for SB.
This could be due to the relatively low level of pressure
support (10 cmH2O) we used. Indeed, the VT achieved
during IPS was only 16% higher than that observed under
SB. Fiantro et al.10 reported that an IPS ranging from 4
to 6 cmH2O is needed to cancel the resistances of the
endotracheal tube. Consequently, we chose an IPS level
10 cmH2O, expecting this supplementary positive pres-
sure to be able to relieve our patients from the resistive
load of the endotracheal tube and partly to relieve them
from their intrinsic resistive and elastic respiratory
charges. We chose a similar level of IPS for all patients
in order to standardize this parameter throughout the
study. This level appeared to be insufficient to efficiently
improve spontaneous ventilation. Nevertheless, if a higher
level of IPS had been used, one may suppose that VT and
perhaps V̇A/Q distributions would have been closer or
even equal to those observed under controlled ventilation,
thereby suppressing any difference between these two
modes. This highlights the problem of choosing the ade-
quate IPS level in such a comparative protocol. Due to
these methodologic restrictions, most of the results we
discuss here will consider SB and IPS together.

Several mechanisms may explain the changes in the
distribution of V̇A/Q we observed during both spontane-
ous and IPS ventilation. First, V̇D/V̇T was significantly
during SB and IPS compared to that during CMV.
Consequently, the distending effect of large VTs on air-
ways reported under controlled ventilation, which should
have increased dead space16 in our patients, was probably
overwhelmed during spontaneous ventilation by the de-
leterious effects of shallow breathing, which reduced VT
and increased the V̇D/V̇T. Interestingly, individual pro-
files could be identified for the parameters describing the
distribution of ventilation by inert gases (log SDV and
V̇D/V̇T). Indeed, the patients who had the largest abnor-
malities in CMV were those who were the most abnormal
for these parameters in SB. Because all patients suffered
from relatively severe COPD (table 1), one may postulate
that they showed the hallmarks of a disturbed distribution
of ventilation even during CMV.

Second, combined with the regional changes in venti-
lation, the increase in cardiac output during the sponta-
neous mode which was correlated with an increase in ox-
ygen consumption and a decrease in arteriovenous oxygen
content difference is likely to have amplified the changes
in distribution of V̇A/Q, by overperfusing zones of low
V̇A/Q. The shunt perfusion (in regions of V̇A/Q under
0.005) did not rise as did perfusion in areas of low V̇A/
Q (between 0.005 and 0.1) during SB or IPS. In fact, the
dependence of shunt on cardiac output has been reported
for higher values of shunt than those we obtained.17

The distribution of both ventilation and perfusion were
larger than normal (log SD > 0.5)19 in our patients but
were consistent with those reported by Wagner et al.,18 in
patients with COPD. Changes in V̇A/Q distribution from
one ventilatory mode to another also have been studied by
Dantzker et al.19 in awake patients being disconnected
from mechanical ventilation after coronary artery bypass
graft surgery. During intermittent pressure ventilation,
they found a consistent shunt and a variable degree of
V̇A/Q inequality by the inert gas technique, while SB re-
sulted in a lower mean V̇A/Q ratio without any change
in shunt or V̇A/Q dispersion. Because cardiac output re-
mained stable, they attributed these changes to the pre-
dominant effect of hypoventilation.

These findings need to be compared to those of Torres
et al.,3 who studied eight patients with COPD during the
separation from mechanical ventilation. Part of their study
was conducted at a maintenance fractional inspired oxy-
gen concentration of 0.4, as was ours. The change from
controlled to SB induced a marked reduction of VT, an
increase in respiratory rate, and an increase in Q̇T. This
resulted in increased perfusion of the regions of low V̇A/
Q and a lower mean V̇A/Q for perfusion without signifi-
cant increase in log SDQ. At the same time, the mean
V̇A/Q for ventilation decreased and log SDV increased.
Hence the results of both studies are close to ours for
perfusion but demonstrated marked changes in the dis-
persion of ventilation from CMV to SB.

In our patients, the absence of significant differences
in the dispersion of V̇A/Q for perfusion (log SDQ) and
ventilation (log SDQ) between CMV and SB could be due
to a large interpatient scatter, especially in SB. Never-
theless, these apparent large interpatient differences, at
least for log SDQ, may be explained during SB by the size of
the VT. Indeed, there was a strong correlation between
log SDQ and VT and also between the cranio-caudal gra-
dient in $V_A/Q$ and $V_T$. Using the isotopic scanning technique to localize the regions of low $V_A/Q$, we found a clear gradient in $V_A/Q$ from the apex to the bases of each lung (figure 1). In addition, the mean $V_A/Q$ ratios of the apical, mid and basal zones of the lung were significantly lower during SB than during CMV. When SB was investigated further, we found the excess in perfusion of the low $V_A/Q$ units to be located at the bases of the lungs and to correlate with the size of the $V_T$.

The problem of the spatial partition of abnormal $V_A/Q$ during the separation from mechanical ventilation has to our knowledge never been assessed previously. Only one study, by Parsons et al.,20 has compared the topographic distribution of $V_A/Q$ in different modes of assisted ventilation. However, these authors used $^{133}$Xe to study healthy seated patients during spontaneous, continuous positive-pressure, and intermittent positive-pressure ventilation. They found no significant difference in the distribution of $V_A/Q$ for the three modes. In addition to the obvious differences in study population and scanning technique, their patients were seated, which would make it difficult to distinguish changes in gradient due to $V_A/Q$ abnormalities from the physiologic and gravity-related major vertical gradient in $V_A/Q$ normally observed. In contrast, the isotopic method we used allowed us to attribute the increase in low $V_A/Q$ in the caudal part of the lungs to a low $V_T$ in SB.

A plausible explanation is that impaired diaphragmatic function in our patients with COPD would result in an inability to support the weight of the abdomen21 in the supine position, perhaps favoring these low basal $V_A/Q$ values. In addition, a possible cranial shift of the diaphragm could lead to a reduction in functional residual capacity22 below closing capacity. This would result in intermittent airway closure phenomena in the more caudal parts of the lungs, enhancing low $V_A/Q$.23 Basal airway closure could also increase local airway resistances, inducing a redistribution of inspiratory flow to the apex.24 These physiopathologic hypothesis are supported by the experimental findings of Engel and Prefaut.25 These authors, in an isotopic study of the spatial distribution of $V_A/Q$ ratios in supine volunteers, proved the existence of a craniocaudal gradient in $V_A/Q$ ratios. They also demonstrated that changes in the distribution of $V_A/Q$ ratios could be attributed to airway closure phenomena occurring at low lung volume. Indeed, their subjects who had a closing capacity greater than FRC had a craniocaudal gradient in $V_A/Q$ as high as that observed in our patients during SB. This gradient faded out when lung volume was greater than FRC plus 20% of the total lung capacity. In contrast, when closing capacity was lower than FRC, the craniocaudal gradient was always minimal and did not show consistent change with lung volume.

A methodologic limitation may apply to our isotopic method. Since the bases of the lungs are larger than the apices, the isotopic emission from the most anterior parts of the lungs (the furthest from the camera) may have not been fully detected as a consequence of the attenuation occurring in the lung parenchyma. This theoretical limitation would have favored the analysis of the most posterior basal segments, those closest to the camera. These segments of the lung bases are known to have lower $V_A/Q$ than regions that are less dependent upon gravity, i.e., the anterior parts of the bases. Accordingly, the craniocaudal gradient in $V_A/Q$ would have been magnified. Nevertheless, we used high-energy isotopes, and the absolute lung volume differences between CMV and SB were small. Therefore, we believe that such an attenuation effect, if any, would be comparable in all modes studied and should not explain all the high regional differences in $V_A/Q$ we found.

We conclude that in patients with COPD, the major determinants for the worsening in $V_A/Q$ distribution during SB resulted from a critical alteration of the ventilation pattern due to an increase in respiratory rate and a decrease in $V_T$. This led to development of basal regions with very low $V_A/Q$.

The authors thank Robert Herigault and Annie Dupeyrat for their technical assistance in processing inert gas samples. They are indebted to Winfried von Ehrenburg and Christine Burren for the stylistic correction they brought to the manuscript.

References

10. Faiastro JF, Habib MF, Quan SF: Pressure support compensation for inspiratory work due to endotracheal tubes and continuous positive airway pressure. Chest 93:499–505, 1988
11. Wagner PD, Laravuso RB, Uhl RR, West JB: Continuous distri