obstruction (FEV₁, 1.44 liters, 51 percent predicted; FRC 4.20 liters, 168 percent predicted).

Rib cage and abdomen anteroposterior movements were determined using linearized respiratory magnetometers. The volume calibration of rib cage and abdomen movement was achieved during isovolume maneuvers.

Inspired intercostal muscle electrical activity was recorded with a bipolar needle electrode introduced into the second anterior intercostal space about 5 cm from the edge of the sternum. The electromyographic activity was integrated using a third-order low pass filter to produce a moving time average.

Respiratory stimulation was produced by rebreathing a gas mixture of 7 percent CO₂ in oxygen. The end-tidal CO₂ concentrations were measured with an infrared analyzer and tidal volumes were recorded by electrical integration of the signals from a pneumotachograph.

Resistive loading during inspiration was achieved by placing wire-mesh screen discs with a resistance of 12 cm H₂O/liter/sec in the inspiratory line of the circuit.

All subjects were studied in the sitting and in the supine positions. In the sitting position, both in normal subjects and COPD patients, there were proportional increases in rib cage and abdomen displacement with increasing tidal volume, so that during free rebreathing, the rib cage contribution to tidal volume remained unchanged. The rib cage contribution to tidal volume was 56 ± 6 percent in normal subjects and 51 ± SE 6 percent in COPD patients. At low tidal volumes in the supine position, rib cage displacement was less than abdomen displacement. However, as tidal volume increased there were progressive increases in the rib cage contribution to tidal volume. At a tidal volume of 1 liter, the rib cage contribution was 37 ± SE 6 percent in normal subjects and 33 ± SE 7 percent in COPD patients.

These results indicate that in patients with moderately severe airway obstruction, there are no systematic differences from normal in the pattern of rib cage and abdomen movement despite hyperinflation of the lungs and alterations in the resting length of the inspiratory muscles.

Integrated intercostal muscle electrical activity increased proportionally during progressive hypercapnia in the normal subjects and COPD patients. Also, there were linear relationships between intercostal muscle electrical activity and rib cage volume displacement suggesting that intercostal muscle contraction plays a role in the outward movement of the rib cage during inspiration. In six of eight normal subjects and in five of seven COPD patients, the rib cage displacement for a given amount of intercostal muscle activity was greater in the sitting as compared to the supine position. These observations support the view that particularly in the upright position contraction of the diaphragm also contributes to expansion of the rib cage.

Resistive loading during inspiration had no effect on the relative rib cage and abdomen contributions to tidal volume in either normal subjects or COPD patients. In both sitting and supine positions, there was, however, a greater amount of intercostal muscle electrical activity for a given rib cage volume displacement during resistive loading than during unloaded breathing and this increase was quantitatively the same both in normal subjects and COPD patients.

Changes in intercostal muscle electrical activity with hypercapnia (ΔIEc/ΔPCO₂) were greater in normal individuals during resistive loading than during free rebreathing (169 ± SE 15 percent in the sitting position and 177 ± SE 14 percent in the supine position). In the COPD patients ΔIEc/ΔPCO₂ also increased during resistive loading but the change was significantly smaller (130 ± SE 8 percent in the sitting position, 128 ± SE 10 percent in the supine position) than that noted in the normal subjects.

The normal pattern of thoracoabdominal movement is preserved in patients with moderately severe airway obstruction even during external resistive ventilatory loading. The subnormal intercostal muscle EMG response to resistive loading in the COPD patients seems to represent a defect in nonchemical respiratory control which is not specifically related to any abnormality in respiratory muscle action or movement of the thorax.

REFERENCES


Control of Hyperpnea Associated with Increased Dispersion of VA/Q*

Craig E. Juratsch, Ph.D., and Brian J. Whipp, Ph.D.

Chronic obstructive pulmonary disease in man is characterized by an increased dispersion of alveolar ventilation to perfusion ratios (VA/Q). This condition typically results in hypoxemia, but in certain patients, particularly those with disease of mild to moderate severity, arterial PCO₂ may not be increased. As maldistribution of VA/Q normally predisposes to hypoxemia, this results in decreased ventilation to perfusion ratios in some regions of the lung. The increased dispersion of VA/Q in COPD patients may be associated with a decrease in ventilation to perfusion ratios in the lower regions of the lung and an increase in ventilation to perfusion ratios in the upper regions of the lung. This results in a redistribution of ventilation and perfusion away from areas with high ventilation to perfusion ratios and toward areas with low ventilation to perfusion ratios.

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capnia, West has predicted that ventilation must be increased under these conditions to effect isocapnia presumably by stimulation of "the chemoreceptors." To date, however, there has been no experimental corroboration of such a scheme. The purpose of the present study was to investigate the chemical control mechanisms of the hyperpnea consequent to increased dispersion of $V_A/V$. We have, in the first instance, produced maldistribution of perfusion without impaired airway mechanics to simplify the interpretation of the ventilatory responses.

**METHODS**

Healthy, adult mongrel dogs of both sexes, weighing between 18 and 24 kg were studied, anesthetized with a mixture of chloralose (64 mg/kg) and urethane (48 mg/kg). Dogs were prepared for study by inserting a specially designed triple lumen balloon catheter (Edwards Laboratories) into the pulmonary artery. The balloon was maintained in stable position in the main pulmonary artery by wedging the extended tip of the catheter in a small branch of the pulmonary artery. Maldistribution of the pulmonary blood flow was induced by nonocclusive inflation of the balloon in the main pulmonary artery to levels that do not significantly affect cardiac output. A second catheter was placed in the ascending aorta. Thus, both pulmonary artery pressure (distal to the balloon) and aortic pressure were monitored and discrete aortic blood samples drawn for measurement of blood gases. In addition, an indwelling $P_{CO_2}$ electrode (General Electric, with a time constant of response of approximately 20 seconds) was placed, nonocclusively, in the femoral artery. During these studies, the dogs breathed through a tube placed in a permanent tracheostomy. A Hans-Rudolph unidirectional valve was connected to the tube. Respired flow was measured with a heated pneumotachograph (Fleisch) located on the expiratory side of the valve and connected to differential strain gauge transducer. Expired $CO_2$ and $O_2$ were measured by mass spectrometry (Perkin-Elmer).

The ventilatory responses to maldistribution of pulmonary blood flow induced by balloon inflation was studied in four dogs both before and after bilateral carotid body resection (CBR).

**RESULTS**

Characteristically, the partial inflation of the intrapulmonary artery balloon in the intact dog induced hyperpnea (Fig. 1, Table 1) with no significant increase

**Table 1—Ventilatory and Blood Gas Responses to VA/Q Maldistribution Induced by Intra-Pulmonary Arterial Balloon Inflation in Dogs**

<table>
<thead>
<tr>
<th></th>
<th>Intact (mean ± SEM)</th>
<th>Carotid Body Resected</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before Inflation</td>
<td>During Inflation</td>
</tr>
<tr>
<td>$V_E$ (L/min)</td>
<td>5.04 ± 1.20</td>
<td>7.47** ± 1.42</td>
</tr>
<tr>
<td>$T_{1/2}$ (sec)</td>
<td>11 ± 0.03</td>
<td>0.51** ± 0.02</td>
</tr>
<tr>
<td>$V_D/V_T$</td>
<td>0.32 ± 0.04</td>
<td>0.57** ± 0.06</td>
</tr>
<tr>
<td>$P_{O_2}$ (mm Hg)</td>
<td>69 ± 4</td>
<td>57** ± 6</td>
</tr>
<tr>
<td>$P_{E_{CO_2}}$ (mm Hg)</td>
<td>36 ± 4</td>
<td>22** ± 3</td>
</tr>
<tr>
<td>$P_{CO_2}$ (mm Hg)</td>
<td>31 ± 3</td>
<td>30** ± 3</td>
</tr>
<tr>
<td>$\Delta P_{CO_2}$ (max) (mm Hg)</td>
<td>1.08 (30 sec)</td>
<td>1.90 (90 sec)</td>
</tr>
<tr>
<td>pH</td>
<td>7.39 ± 0.02</td>
<td>7.39 ± 0.02</td>
</tr>
</tbody>
</table>

**P < 0.05**

† Only two dogs studied after CBR.

‡ Discrete blood samples taken in the steady state.

The peak change in $P_{CO_2}$ in the transient phase, from the indwelling $P_{CO_2}$ electrode.

**Figure 1.** Normal dog: Ventilatory, alveolar gas and arterial $P_{CO_2}$ responses to inflation of balloon (between the vertical lines) in the main pulmonary artery of dog with intact chemoreceptors anesthetized with chloralose-urethane. Note that the hyperpnea is associated with sustained alveolar hypocapnia and a transient arterial hypercapnia.
in PaCO₂ in the steady state. With the onset of balloon inflation Vₚ rose rapidly within two or three breaths, reaching a steady state which averaged 2.27 L/min above control levels (P < 0.05), within 1.5-2.0 minutes. The response involved both Vₚ and f and invariably resulted in a significant reduction of PₚTPCO₂ (Fig 1 and 2). The halftime of the Vₚ response was 11 seconds. After deflation of the balloon, Vₚ returned to control levels with a time course similar to the onset response (Fig 1). The indwelling Pco₂ electrode demonstrated that PaCO₂ consistently increased, transiently reaching a maximum of about 1.0 mm Hg above control levels after approximately 30 seconds of balloon inflation (Fig 1, Table 1). As a consequence, the arterial to end-tidal Pco₂ difference increased significantly (P < 0.05) and was associated with an increase in the dead space to tidal volume ratio (P < 0.05), (Table 1). Arterial Po₂ also decreased in all animals, averaging a fall of 12 mm Hg (P <0.05).

After bilateral carotid body resection, the induced Vₐ/Q maldistribution still increased the mean steady state Vₚ by a mean of 2.84 L/min (P <0.05), (Table 1). However, as evidenced by the T1/2 of Vₚ of 46 seconds, the kinetics of the ventilatory response was considerably slowed (Fig 2, Table 1). Consequently, the ability to regulate arterial Pco₂ was impaired, leading to a larger (1.9 mm Hg) peak increase in the transient phase in arterial Pco₂ as shown by the indwelling Pco₂ electrode (Fig 2, Table 1). However, the steady state arterial Pco₂ was still regulated in the steady state in two of the animals and was returning towards control levels in the other two, when the balloon was deflated. The slow kinetics induced by carotid body resection is particularly evident in Figure 2, where the rate of change of alveolar Pco₂, for example, is significantly slower than normal at both the on and off-transient.

**DISCUSSION**

Our results demonstrate that balloon inflation in the main pulmonary artery of the dog causes a redistribution of pulmonary blood flow which results in an increased dispersion of Vₐ/Q. This presumably accounts for the observed transient increase in arterial Pco₂ despite the hyperpnea (without significant increase in cardiac output). Such a response pattern has been suggested by West, but has not, we believe, been demonstrated previously.

The results of this study are consistent with West's contention that "the chemoreceptors" adjust alveolar ventilation to return the increased arterial Pco₂ to normal limits. However, our studies demonstrate that the carotid bodies contribute the dominant proportion of the early dynamic ventilatory response to Vₐ/Q maldistribution; this function can largely be subserved by other slower, presumably central, chemoreceptors in the absence of the carotid bodies. A similar contention has been asserted by Whipp and Wasserman for man. The results of this study are also consistent with the peripheral and central chemoreceptors influencing ventilation in other than a simple additive manner. Vagotomy alone did not appear to impair appreciably the ability of the ventilatory control system to regulate arterial Pco₂ in the steady state of Vₐ/Q maldistribution and hence the mechanism of the hyperpnea appears not to be related directly to the increased pressure in the pulmonary artery during the balloon inflation.

We conclude that balloon inflation in the main pulmonary artery of the dog leads to increased dispersion of Vₐ/Q which, as predicted, causes arterial Pco₂ to increase transiently. Ventilation is stimulated (with the carotid bodies being vital for the normal transient behavior) and reaches a level appropriate to regulate PaCO₂ at the control value; PaO₂ however remains low. These studies, therefore, suggest that when Vₐ/Q relationships become more dispersed, hyperpnea is induced by a CO₂-linked, respiratory feedback mechanism which appears to operate at or close to zero steady state PaCO₂ error.
Effect of Steady State Exercise on Right and Left Ventricular Performance in Chronic Obstructive Pulmonary Disease

Noninvasive Assessment by Radionuclide Angiocardiology


Right and left ventricular response to exercise in patients with chronic obstructive pulmonary disease (COPD) remains to be defined fully. Consequently, exercise cardiac performance was evaluated in 24 patients with COPD and the results compared to data obtained in 20 normal control subjects.

In patients with COPD, forced expiratory volume in one-second (FEV₁) averaged (±SEM) 51±5 percent predicted. Right ventricular (RV) and left ventricular (LV) ejection fractions (EF) were determined noninvasively by first-pass radionuclide angiocardiology at rest and during exercise using a computerized multicrystal scintillation camera and intravenous injections of 99mTc-technetium.1 2 The normal cardiac response to exercise in controls was an absolute increase of ≥ 5 percent in RV EF and LVEF.3 4 In patients with COPD, cardiac performance was measured during relatively steady state upright bicycle exercise at approximately 50 percent maximal workload (range, 25 to 75 watts).

In patients with COPD, RVEF was abnormal at rest (<45 percent) in 8/24 patients. Mean RVEF at rest and exercise was not different (rest, 48±1 percent; exercise 45±2 percent, P<NS). In contrast, LVEF rose from 62±3 percent to 68±3 percent (P<.05). An abnormal RV response to exercise occurred in 20/24 patients, including 12 with normal resting RVEF and all eight with an abnormal resting RVEF. Furthermore, RVEF fell by at least 5 percent with exercise in seven of these 20 patients.

Mean arterial oxygen saturation did not change significantly with exercise. FEV₁ was significantly lower in patients with an abnormal RV response to exercise than in those with normal response (49±5 vs 65±5 percent predicted, P<.05); a similar but not significant difference was demonstrated for resting arterial oxygen tension (65±3 vs 76±5 mm Hg, P NS). Seven patients had an abnormal LV response to exercise, which was unrelated to severity of COPD and probably was due to latent coronary artery disease.

RV dysfunction in COPD may not be present in the resting state, but may become manifest only under physiologic stress such as mild upright exercise. Abnormal exercise RV reserve in COPD occurs most frequently in patients with high degrees of resting obstructive ventilatory impairment.

References


Q. (Woolcock): Did you give your patients oxygen? A. (Matthay): We are planning to do this. It is obviously very important.

Q. (Edelman): Are your data explained by changes in afterload? A. (Matthay): At this point I cannot answer this question for certain, although afterload augmentation by one of several potential mechanisms likely played a significant role in the observed abnormal RV exercise responses in patients with COPD.

Q. (Permutt): I think it is a beautiful piece of work—good correlation with mechanical factors. Is lung hyperinflation increased during exercise? A. (Matthay): Although we did not address this in our exercising patients, we think it likely that lung hyperinflation increases with exercise, causing an increase in RV afterload.

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References


