External thoracic restriction, respiratory sensation, and ventilation during exercise in men

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Harty, Helen R., Douglas R. Corfield, Richard M. Schwartzstein, and Lewis Adams. External thoracic restriction, respiratory sensation, and ventilation during exercise in men. J. Appl. Physiol. 86(4): 1142–1150, 1999.—Multiple factors may contribute to the dyspnea associated with restrictive ventilatory disease (RVD). Simple models that examine specific features of this problem are likely to provide insight into the mechanisms. Previous models of RVD utilizing elastic loads may not represent completely the impact on pulmonary and chest wall receptors derived from breathing at low thoracic volumes. The purpose of this study was to investigate the sensory consequences of breathing at low lung volumes induced by external thoracic restriction in an attempt to further elucidate the etiology of dyspnea in this setting. Ten men were studied, with and without an inelastic corset applied at residual volume (restriction resulted in mean reductions in vital capacity, functional residual capacity, residual volume, and forced expired volume in 1 s of 44, 31, 12.5, and 42%, respectively). During 10-min steady-state exercise tests (at a workload set to achieve ~65% maximum heart rate), restriction resulted in significant increases, compared with control, in minute ventilation (61 vs. 49 l/min), respiratory frequency (43 vs. 23 breaths/min), and visual analog scale measurements of respiratory discomfort (65 vs. 20 mm). Alveolar hyperventilation (end-tidal P CO₂ = 39 vs. 44 Torr for control) and mild O₂ desaturation (arterial blood O₂ saturation = 93 vs. 95% for control) occurred. Hypoxemia,atelectasis, increased work and effort of breathing, or a decrease in the volume-related feedback from chest wall and/or lungs could be responsible for the increased dyspnea reported. External thoracic restriction provides a useful model to study mechanisms of dyspnea in RVD.

Restrictive disease; mechanisms

Dyspnea (shortness of breath) on exertion represents a major debilitating symptom for patients with cardiorespiratory disease and is associated with exercise limitation and deterioration in quality of life. This general symptom is reported in a wide variety of pathophysiological states, and a better understanding of the basis of dyspnea in different conditions could lead to improved symptom management in individual patients.

Patients with either chronic obstructive pulmonary disease (COPD) or restrictive ventilatory disorders demonstrate a degree of exercise limitation that broadly correlates with the severity of their condition (7). Both groups report dyspnea as a major reason for stopping exercise. Despite this, the pattern of ventilatory response during exercise is quite different; although the pattern is quite broad, restrictive disorders lead to a rapid, shallow pattern of breathing sometimes associated with alveolar hyperventilation (4, 29, 36, 37), whereas COPD is associated with a more normal pattern of breathing with alveolar hypoventilation in some patients (17, 32). As a means of experimentally simulating constrained ventilation during exercise in healthy subjects, investigators have used external resistive loads to mimic COPD (5, 8, 10, 11, 14). Models of restrictive ventilatory disorders (i.e., diseases resulting in reduced compliance of the lungs and/or chest wall) have employed either external elastic loads or external thoracic and/or abdominal restriction to mimic aspects of these diseases (12, 22, 23). These models differ considerably in that elastic loading may not induce a large reduction in lung volume, whereas external thoracic restriction induces changes in chest wall compliance. In both conditions, the ventilatory pattern observed during exercise is consistent with that seen in the corresponding disease state. In addition to defining the ventilatory response to exercise during external resistive loading, El-Manshawi et al. (14) have documented the effect on dyspnea. However, the effect of external resistive loading on dyspnea during exercise has not been studied.

Multiple physiological mechanisms contribute to dyspnea in various disease states (27). Patients with restrictive ventilatory disorders may experience dyspnea as a result of stimulation of pulmonary receptors secondary to interstitial inflammation, fibrosis, or collapse of alveoli at low lung volumes. Afferent information from fusimotor muscle spindles within the intercostal muscles, golgi tendon organs, or joint receptors within the rib cage may also be altered as a consequence of reduced tidal excursions at low thoracic volumes. Alteration in gas exchange and the increased sense of effort associated with mechanical loads will also play a role in the genesis of dyspnea in some patients. Models of restrictive ventilatory disorders that employ elastic loads are unlikely to reproduce the effects on pulmonary and chest wall receptors associated with ventilation at low lung volumes. Although tissue volume may be increased in restrictive disorders characterized by interstitial inflammation and fibrosis, radiographic assessment of these patients with a mod-
ererate-to-severe disease invariably demonstrates a reduction in thoracic volume. This finding is typically not present in models that employ elastic loads achieved by air rarefaction. External thoracic constriction, however, has the potential to reproduce this as well as many of the other conditions that may contribute to dyspnea in these patients.

The focus of this study was to investigate the effects of a reduction in lung volume and chest wall movement on the response to steady-state exercise in normal subjects. By correlating changes in respiratory discomfort associated with exercise during external thoracic restriction with objective ventilatory measures, we hoped to provide further insight into the neuromechanical basis of respiratory discomfort. A secondary aim of this study was to elucidate whether the specific sensations associated with mechanical restriction are similar to those reported by patients with restrictive respiratory disorders (13, 26, 34). By taking this approach, we hope to develop a model of restrictive pulmonary disease that can be used to examine systematically the interrelationships between altered pulmonary mechanics and exertional dyspnea.

METHODS

These studies were undertaken with the approval of the Ethics Committee of the Riverside Health Authority and are in accordance with the Declaration of Helsinki (1989) of the World Medical Association. All subjects gave informed written consent but were unaware of the specific aims of the study.

Subjects

Twelve male subjects (age range 20–34 yr) were studied on two occasions separated by an interval of between 3 and 10 days. Three of the subjects were smokers, and another three were ex-smokers; none of the subjects had any history of cardiopulmonary disease. Six of the subjects had previously participated in studies involving exercise testing and/or assessment of respiratory sensations.

On the first occasion, subjects performed an exercise test to exhaustion on an electrically braked cycle ergometer (Godart 18070, Gould Instrument Systems, Essex, UK). On the second occasion, subjects performed two exercise tests at a constant workload set to achieve ~65% of their maximum heart rate (HR) attained during the progressive exercise test. This constant-workload level was chosen to induce a ventilatory response to exercise that approximated the threshold for dyspnea in the unrestricted exercise but was sufficiently low that subjects would be likely to complete the second exercise test in the presence of the added thoracic restriction.

Measurement Techniques and Protocols

Cardiorespiratory measurements. Cardiorespiratory variables were measured at rest while the subject was seated on the bicycle ergometer and then throughout each of the exercise tests. Inspiratory and expiratory airflow rates were measured via a mouthpiece (with nose clip applied) connected to a Fleisch pneumotachograph (no. 3 head with MP45/CD12 transducer, Validyne, Northridge, CA; total dead space = 70 ml; resistance 0.1 cmH2O·l−1·s−1). From the airflow signal, breath-by-breath analysis of respiratory frequency (f), tidal volume (VT), and inspired minute ventilation (V̇I) was performed by using an on-line computerized respiratory gas analysis system (Respiratory Gas Analyzer, Buxco, Sharon, CT). Post hoc estimates of alveolar ventilation (V̇A) were computed by using the formula [V̇O2 (ml) = 138 + 0.777 VT] proposed by Jones et al. (24) to predict the physiological dead space volume (V̇D), although it must be noted that these estimates are open to potential error.

Respired gas was sampled continuously from a port in the mouthpiece and analyzed in the majority of studies by using an infrared gas analyzer (#455 Capnograph, PK Morgan, Kent, UK). In a few experiments, a mass spectrometer (Airspec QP9000, Case Medical, Kent, UK) was used. Both analyzers were calibrated with the same calibration gas. Breath-by-breath estimates of end-tidal PCO2 (PETCO2) were obtained via the automated respiratory gas analysis system.

Instantaneous HR was derived from an electrocardiogram. An estimate of arterial blood O2 saturation (SaO2) was assessed continuously by using pulse oximetry via an ear probe (Biox 3700e, Ohmeda, Herts, UK).

Pulmonary function tests. Each subject had lung volumes estimated with the use of a standard helium dilution technique coupled with a slow vital capacity maneuver to yield total lung capacity (TLC), residual volume (RV), and functional residual capacity. Forced spirometry was undertaken, giving values for forced expired volume in 1 s (FEV1) and forced vital capacity. Hypocapnic maximum voluntary ventilation was determined over a 12-s period. All of these tests were completed by using commercial pulmonary function testing equipment (Benchmark, PK Morgan).

Arterialized venous blood samples. In four of the subjects, during the tests performed before and with thoracic restriction, estimates of arterial blood-gas levels were obtained from samples of arterialized venous blood. Heparinized blood was sampled via an indwelling cannula from a dorsal hand vein with the hand submerged in a water bath maintained at 43°C. Duplicate samples were obtained over the final 2 min of the 10 min of constant-workload exercise in each condition. The technique was based on that described and validated by Forster et al. (15) and McLoughlin et al. (30).

Subjective assessments of respiratory discomfort. Subjects were asked to quantify their sensation of respiratory discomfort every 30 s throughout each test by using an electronic 100-mm visual analog scale (VAS), as described previously (1). The extremes of the sensation of respiratory discomfort were represented by the two ends of a linear visual display; these were specifically described as “no respiratory discomfort” and “the worst imaginable respiratory discomfort.” After each of the exercise tests, subjects were debriefed by using a standard interview technique to obtain qualitative information related to sensations of respiratory discomfort and breathing pattern. Initially we asked each subject to comment on the experience of the exercise test. This was followed by more specific questions dealing with possible respiratory and nonrespiratory sensations. In particular, subjects were asked to identify up to three descriptors, from a list of 20, which best described their respiratory discomfort (34).

Thoracic restriction. Constriction of the rib cage was achieved by using an incompressible corset (designed to provide support for thoracic vertebrae); this both reduced resting lung volume and restricted rib cage expansion. An appropriately sized corset was selected for each individual and applied around the chest with the upper edge at the level of the axillae and the lower edge at the level of the lowest rib in the lateral position. The corset was secured as tightly as possible with the aid of Velcro straps after subjects had expired to RV.

Experimental protocol. Before the progressive exercise test on the first day, subjects were familiarized with the experimen-
ventilation during unencumbered breathing and external thoracic restriction in 10 healthy male subjects

Table 1. Measurements of static lung volumes and indexes of forced spirometry and maximum voluntary ventilation during unencumbered breathing and external thoracic restriction in 10 healthy male subjects

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>TLC, liters</th>
<th>FRC, liters</th>
<th>RV, liters</th>
<th>FVC, liters</th>
<th>FEV1, liters</th>
<th>MVV, l/min</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>U</td>
<td>R</td>
<td>U</td>
<td>R</td>
<td>U</td>
<td>R</td>
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<tr>
<td>1</td>
<td>7.79</td>
<td>4.70</td>
<td>3.87</td>
<td>2.76</td>
<td>1.64</td>
<td>1.74</td>
</tr>
<tr>
<td>2</td>
<td>7.01</td>
<td>5.24</td>
<td>2.98</td>
<td>2.50</td>
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<tr>
<td>3</td>
<td>6.84</td>
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<td>3.62</td>
<td>2.76</td>
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<td>3.80</td>
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<td>2.78</td>
<td>2.30</td>
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</tr>
<tr>
<td>5</td>
<td>9.12</td>
<td>6.01</td>
<td>4.95</td>
<td>3.36</td>
<td>2.53</td>
<td>2.25</td>
</tr>
<tr>
<td>6</td>
<td>7.05</td>
<td>4.29</td>
<td>3.04</td>
<td>2.35</td>
<td>1.11</td>
<td>0.91</td>
</tr>
<tr>
<td>7</td>
<td>8.47</td>
<td>6.19</td>
<td>4.01</td>
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<td>1.61</td>
</tr>
<tr>
<td>8</td>
<td>7.83</td>
<td>4.96</td>
<td>4.23</td>
<td>2.60</td>
<td>1.15</td>
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<td>3.99</td>
<td>3.19</td>
<td>1.63</td>
<td>1.62</td>
<td>1.10</td>
</tr>
<tr>
<td>10</td>
<td>7.32</td>
<td>4.26</td>
<td>3.37</td>
<td>2.29</td>
<td>1.40</td>
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<td>3.78</td>
<td>2.61</td>
<td>1.62</td>
<td>1.40</td>
</tr>
<tr>
<td>±SD</td>
<td>±0.80</td>
<td>±0.84</td>
<td>±0.66</td>
<td>±0.47</td>
<td>±0.47</td>
<td>±0.41</td>
</tr>
<tr>
<td>P value</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.04</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

TLC, total lung capacity; FRC, functional residual capacity; RV, residual volume; FVC, forced vital capacity; FEV1, forced expired volume in 1 s; MVV, maximum voluntary ventilation; U, unencumbered breathing; R, external thoracic restriction.

RESULTS

Ten of the twelve subjects were able to complete the 10-min constant-workload exercise test in both the unencumbered and thoracic restriction conditions. The two subjects who failed to complete the exercise test with thoracic restriction both identified pain as a reason for stopping; one subject also reported extreme respiratory discomfort as a reason for cessation of exercise. Data from these subjects were excluded from further analysis.

Pulmonary Function Tests

The values obtained with pulmonary function testing at rest during unencumbered breathing and with thoracic restriction are shown for each individual in Table 1. For the unencumbered condition, each subject was within two SDs of his predicted normal value based on age, height, and weight for each of the pulmonary function indexes measured. With thoracic restriction, statistically significant reductions in all lung-function variables were noted.

Cardiorespiratory and Respiratory Discomfort Responses to Exercise

The group mean levels of respiratory variables and subjective estimates of respiratory discomfort are shown in Figs. 1 and 2. For both unencumbered breathing and thoracic restriction, the data are averaged over 30-s periods for 2 min of resting breathing before exercise and for the 10 min of constant-workload exercise.

At rest, there were no statistically significant differences in mean $P_{\text{ETCO}}$ or $S_{\text{aO}}$ between the two experimental conditions; however, $\bar{f}$ was significantly higher and $V_{\text{T}}$ significantly lower (resulting in a significantly higher resting $V_{\text{E}}$) during thoracic restriction compared with during unencumbered breathing. No subject reported respiratory discomfort at rest during unencumbered breathing, whereas they all gave positive ratings...
with thoracic restriction even before the onset of exercise; the mean difference was statistically significant. Estimates of resting mean (±SE) \( \dot{V_A} \) revealed that there was a significant difference between the unencumbered (9.0 ± 0.6 l/min) and restricted (12.1 ± 1.4 l/min) conditions (P = 0.03). There was no significant difference in mean resting HR between unencumbered breathing and restricted conditions (77.4 ± 5.1 vs. 82.2 ± 5.3 beats/min; P = 0.23).

During the final 2 min of steady-state exercise performed at the same workload during unencumbered breathing and thoracic restriction, there were statistically significant differences for all the variables depicted in Figs. 1 and 2. In addition, estimates of mean (±SE) \( \dot{V_A} \) indicated that this was significantly higher for the restricted (51.6 ± 3.8 l/min) compared with the unencumbered breathing (43.3 ± 2.5 l/min) condition (P = 0.009). At a pulmonary ventilation level of 40 l/min when breathing was unencumbered, the mean (±SE) respiratory discomfort score was 3.2 ± 1.3 compared with the restricted condition for which the mean respiratory discomfort score was 35.8 ± 7.1. This difference was highly significant (P < 0.001). Mean HR during steady-state exercise was also significantly different between the free-breathing and restricted conditions (132.2 ± 5.5 vs. 141.2 ± 4.5 beats/min; P = 0.01).

To assess whether the degree of respiratory discomfort reported was related to an individual’s ventilatory pattern response to restriction, individual regression and multiple linear regression analyses were performed. No statistically significant correlation was found between the change in respiratory sensation and the changes in any of the primary variables measured (\( \dot{V_I}, \dot{V_T}, f, \dot{S_aO_2}, \dot{P_{CO_2}}, \) and HR).

**Arterialized Venous Blood-Gas Measurements**

Table 2 gives the results of blood-gas analysis of arterialized venous blood and corresponding PET\(_{CO_2}\) levels in four subjects at rest and in steady-state exercise during unencumbered and restricted breathing. Duplicate blood measurements were always within 1 Torr for PCO\(_2\) except in one case when the difference was 1.9 Torr; PO\(_2\) and pH measurements also showed good reproducibility. In all cases, measurements of PO\(_2\) indicate that samples were adequately arterialized for PCO\(_2\) measurements to be representative of arterial.

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Fig. 1. Group mean levels (±SE) of tidal volume (\( V_T \)), respiratory frequency (\( f \)), and inspired minute ventilation (\( V_I \)) in 10 subjects with (●) and without (○) external thoracic restriction before and during exercise. P values show level of significance comparing 4 × 30-s values at rest and end of exercise by using ANOVA.

Fig. 2. Group mean levels (±SE) of end-tidal PCO\(_2\) (PET\(_{CO_2}\)), arterial blood O\(_2\) saturation (\( \dot{S_aO_2} \)), and respiratory discomfort in 10 subjects with (●) and without (○) external thoracic restriction before and during exercise. P values show level of significance comparing 4 × 30-s values at rest and end of exercise by using ANOVA.
With corresponding measurements of PETCO₂ during at rest and during steady-state exercise in 4 subjects with corresponding measurements of PETCO₂ during unencumbered breathing and thoracic restriction.

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>Unencumbered Breathing</th>
<th>Thoracic Restriction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PO₂, Torr</td>
<td>PCO₂, Torr</td>
</tr>
<tr>
<td>1</td>
<td>7.39, 75.5</td>
<td>45.1</td>
</tr>
<tr>
<td>Rest</td>
<td>7.32, 80.6</td>
<td>45.6</td>
</tr>
<tr>
<td>Exercise</td>
<td>7.39, 80.2</td>
<td>38.6</td>
</tr>
<tr>
<td>2</td>
<td>7.35, 90.5</td>
<td>38.2</td>
</tr>
<tr>
<td>Rest</td>
<td>7.38, 85.1</td>
<td>43.9</td>
</tr>
<tr>
<td>Exercise</td>
<td>7.38, 87.2</td>
<td>46.1</td>
</tr>
<tr>
<td>3</td>
<td>7.41, 70.4</td>
<td>42.5</td>
</tr>
<tr>
<td>Rest</td>
<td>7.36, 71.8</td>
<td>46.0</td>
</tr>
</tbody>
</table>

Blood-gas measurements are the average of 2 samples collected within a 30-s period; end-tidal PCO₂ (PETCO₂) measurements are the average of 10 consecutive breaths within same period. Subject 2 had missing blood-gas values during exercise with thoracic restriction.

PCO₂ (24); pH values at rest were also consistent with those expected in arterial blood from subjects with normal acid-base status.

In three subjects for whom all data were available, the average blood PCO₂ at rest during unencumbered breathing was 43.8 Torr compared with an average PETCO₂ level of 39.2 Torr. With restriction, the corresponding values were 42.4 and 37.6 Torr, respectively. With unencumbered breathing during exercise, the average blood PCO₂ was 45.9 Torr, whereas the average PETCO₂ was 46.5 Torr. With restricted breathing during exercise, the average blood PCO₂ was 43.8 Torr compared with a mean PETCO₂ level of 42.0 Torr. Taken together, these estimates of arterial PCO₂ in three subjects indicate an increase from rest to exercise but a lower PETCO₂ during exercise with thoracic restriction compared with unencumbered breathing. Furthermore, PO₂ was lower, both at rest and during exercise, in all subjects during restricted compared with unencumbered breathing.

Qualitative Descriptions of Respiratory Discomfort

During exercise with unencumbered breathing, all subjects reported that the level of exercise was well within their capacity. Nine subjects reported that the exercise was associated with little or no respiratory discomfort (3 subjects gave VAS ratings of zero throughout exercise), with one subject indicating substantial discomfort (VAS ratings of 70 mm) at the end of exercise. The only other symptom volunteered was an awareness that breathing had increased (2 subjects). During restricted breathing at rest, eight subjects reported that they had difficulty in the act of breathing; five subjects reported a slight ache or pain, four subjects reported a restricted or tight sensation, and three subjects reported a need for more air. During exercise with restricted breathing, seven subjects reported that they were short of breath or needed more air, six subjects reported an ache or pain, and two subjects reported difficulty in the act of breathing. The responses to identifying specific descriptors of respiratory discomfort during unencumbered and restricted breathing are summarized in Table 3.

DISCUSSION

The primary aim of this study was to investigate the effects of a reduction in lung volume and chest wall movement on the response to steady-state exercise in normal subjects to evaluate the use of external thoracic restriction as a model of restrictive ventilatory disease (RVD). Such a model may provide valuable insights into the basis of exercise-induced dyspnea specifically when the requirements for increases in V̇t cannot be met readily and when lung volumes are reduced. Whereas earlier studies in exercising normal subjects have described the ventilatory response to external thoracic restriction (22, 23), the present study is the first attempt to investigate the effect of experimentally induced restrictive loading on dyspnea. We found that a level of thoracic restriction sufficient to reduce lung function by a degree equivalent to moderate clinical impairment resulted in rapid, shallow breathing accompanied by a mild alveolar hyperventilation. This pattern is typical of the ventilatory response to exercise observed in patients with RVD, although the severity and thus observed response of such disorders is broad ranging. The marked increases in respiratory discomfort are also characteristic of this condition, although the pathophysiological changes that give rise to the respiratory discomfort associated with RVD are again broad ranging.

In considering the appropriateness of our experimental arrangement as a model of RVD, it is important to acknowledge that our restriction was extrathoracic rather than intrapulmonary. Thus the external thoracic restriction may be more akin to pathological conditions such as kyphoscoliosis and other chest wall deformities rather than to interstitial lung diseases such as alveolitis, although ventilation in both cases is
associated with breathing from lower lung volumes. An alternative approach would have been to use external elastic loading employing rarefaction. Utilizing an elastic load of 14.0 cmH₂O/l provided by an 80-liter metal drum, D'Urzo et al. (12) studied the performance of progressive exercise to exhaustion. At workloads similar to those achieved in our study, there was no significant difference in $V_{\text{i}}$ or $P_{\text{CO}_2}$, although comparable changes in $V_T$ and $f$ were found. Models that employ elastic loads may not reproduce the reduced lung volumes (functional residual capacity, RV) characteristic of many patients with restrictive ventilatory disorders. In the present study, we have observed a pattern of ventilatory responses to exercise similar to those of a group of patients with interstitial lung disease in whom exercise was limited by dyspnea (20). These patients had similar decreases in lung function ($FEV_1 = 64\%$, TLC = 67% predicted), and, at maximal exercise, some evidence of alveolar hyperventilation was observed, with an average $V_T$ of 1.1 liter and $f$ of 44 breaths/min. By comparison, our subjects ($FEV_1 = 58\%$, TLC = 62% of their normal value) reported high levels of respiratory discomfort (70 mm) with evidence of hyperventilation at a $V_T$ of 1.46 liter and $f$ of 42.5 breaths/min in the presence of external thoracic restriction. Although the patient group was older (47 vs. 26 yr, this study), the workload and HR achieved at peak exercise were similar in the two studies, and both groups showed some arterial desaturation during exercise (range 4–13% in patients; 0–7% in normal subjects with restriction).

The relatively rapid, shallow breathing pattern that we observed with thoracic restriction led to a significant increase in $V_{\text{i}}$ compared with that seen during normal exercise. In addition, we saw a significantly lower $P_{\text{ETCO}_2}$ suggesting a higher level of $V_{\text{A}}$ with restriction; this suggestion is supported by our direct estimations of $V_{\text{A}}$, although such estimations are open to potential error. In a previous study on exercising healthy subjects, Hussain and Pardy (22) reported no difference in $P_{\text{ETCO}_2}$ between thoracic restriction (similar in magnitude to the present study) and control conditions; these authors also documented no difference in $V_{\text{i}}$ between the two conditions. However, in their study subjects were exercising at 80% of maximum power output (compared with 65% in our study), and there was electromyographic evidence of diaphragm muscle fatigue, suggesting an inability to maintain the required ventilatory response. Thus the failure of their study to demonstrate alveolar hyperventilation may be explained by the extreme workload of their experimental condition. Hyperventilation and hypocapnia during exercise have been observed in some studies in patients with interstitial lung disease (29, 36), and our model is consistent with these observations. We were concerned that, in the present study, measurements of $P_{\text{ETCO}_2}$ may not be representative of arterial levels, particularly in the presence of rapid breathing (38). In an attempt to gain further data on this point, we repeated these studies in a few subjects with measurements of arterialized venous blood $P_{\text{CO}_2}$.

Although these data were limited in number, they confirmed the pattern seen for $P_{\text{ETCO}_2}$ in that, with thoracic restriction, the increase in $P_{\text{CO}_2}$ from rest to exercise was less than that observed in the unencumbered state. This supports the idea of a relative alveolar hyperventilation during constant workload, i.e., low-intensity exercise, in the presence of thoracic restriction. It is possible that this alveolar hyperventilation results from stimulation of pulmonary receptors (see below) or is a response to the breathing discomfort itself.

In the present study, the increase in ventilation observed during exercise with thoracic restriction was accompanied by a paradoxical decrease in $S_{\text{aO}_2}$. Again, this finding is consistent with the hypoxemia often seen in patients with restrictive lung disorders during exercise (29). It seems probable that the arterial desaturation we observed resulted from ventilation-perfusion inequalities, perhaps related to atelectasis. Support for the view that atelectasis was present in our subjects comes from the finding that mean RV was reduced during thoracic restriction.

A feature of the present study was the marked increase in the degree of the respiratory discomfort reported in the presence of thoracic restriction, which was more than a reflection of the increased ventilation level, as a significant difference exists between the two conditions at a ventilation level of 40 l/min. All the subjects reported respiratory discomfort at rest, and this increased dramatically over the 10-min period of exercise. Indeed, in designing the study we chose a relatively mild level of exercise because pilot experiments had indicated subjects would be unable to complete the tests at a higher workload secondary to profound respiratory discomfort. These findings are again consistent with what is widely documented in patients with restrictive lung disease, in whom dyspnea is often reported at rest, and are regarded as major factors contributing to exercise limitation (29).

It is interesting to consider the physiological mechanisms that underlie the respiratory discomfort experienced by our subjects. One possibility is that the arterial hypoxemia we observed may have been responsible. Support for this comes from a recent study in patients with interstitial lung disease in whom prevention of arterial hypoxemia during incremental exercise improved performance (20). However, inspection of our data identified four subjects with minimal changes in $O_2$ saturation, who reported marked respiratory discomfort, and an additional subject with the maximum degree of desaturation (7%), who reported the lowest increase in discomfort. In addition, preliminary data from two subjects have shown that supplemental $O_2$ during exercise sufficient to correct the hypoxemia did not alter the amount of respiratory discomfort recorded during exercise in the presence of external thoracic restriction.

Another possibility to account for the respiratory discomfort is the increased sense of effort associated with the act of breathing against the added external restriction. This view is supported by the qualitative
descriptors identified by the subjects when questioned further on their primary sources of respiratory discomfort (see below) and is likely to be mediated via the tendon organs sensing changes in the respiratory pressures generated. Ventilation is proportional to inspiratory muscle shortening, and the mechanical properties of the chest wall and lungs are altered in the presence of the added restriction. No attempt was made to measure these during exercise as the addition of an esophageal balloon may have induced other aspects of respiratory discomfort, which may have been misleading. At rest, however, added thoracic restriction has been shown to increase lung elastic recoil because of an increase in the surface tension of the alveolar lining layer and increase the apex-to-base pleural pressure gradient because of regional changes induced in chest wall compliance (25, 35). Subjects also indicated “inspiratory difficulty” as one of the causes of the respiratory discomfort experienced, suggesting that changes in airways resistance may have been in some part responsible. Previous studies at rest have shown that external thoracic restriction produces a reduction in airway caliber, resulting in an increase in airway resistance, upstream of the restriction (25, 35). However, these findings are in contrast to those of Douglas et al. (11) and Scheidt et al. (33) in which chest wall strapping produced increases in maximal air flow due in part to decreased airways resistance. These studies also demonstrated similar changes in airways resistance when subjects voluntarily breathed at low lung volumes in the absence of strapping. Such changes in airways caliber, in association with increases in static recoil pressure of the lung, led the authors to speculate about the possible contribution of an increase in the surface tension of the alveolar lining, possibly related to breathing at low lung volume, to these physiological observations. Similarly, changes in alveolar compliance and consequent atelectasis could be playing a role in the dyspnea associated with chest wall strapping in our study.

In this study, we did not measure individual muscle group activity and cannot comment on the possible existence of respiratory muscle fatigue. However, many of the subjects commented on a midline-type pain similar to a “stitch,” which may have indicated some diaphragmatic muscle fatigue and could have given rise to the increased respiratory discomfort reported. However, if this were the case, we might have expected to see a hyperventilatory response and increased Pco2; there was no evidence for this. Accessory respiratory muscles may have been brought into play to maintain diaphragm length and force of contraction, and previous studies have shown that respiratory discomfort develops with increased accessory muscle usage (3). Further work is required to confirm this.

A further possibility to account for the respiratory discomfort reported in this study is the presence of abnormal afferent information from the lungs secondary to atelectasis. Some evidence that information from lung afferents can lead to dyspnea comes from a few patient studies employing vagal blockade or section (9, 19). However, the fact that these studies were not blinded and the study protocols varied may limit the value of these observations. This afferent information may derive from stimulation of rapidly adapting stretch receptors, which are known to be activated by experimental deflation in animals (6).

As discussed above, a predominant feature of the ventilatory response to exercise during thoracic restriction is the marked decrease in VT, and this may have contributed to the respiratory discomfort experienced. There is considerable evidence that lung volume-related feedback is important in ameliorating the sensation of respiratory discomfort in the presence of increased ventilatory stimulation. Thus Fowler (16) demonstrated marked relief of the discomfort of breathing holding when respiratory movements, which did not improve the abnormal blood-gas status, were made. More recent evidence is provided by Banzett et al. (2) who showed an inverse relationship between respiratory discomfort and VT under constant conditions of hypercapnic-stimulated ventilation. Subsequent studies have failed to elucidate the extent to which this phenomenon depends on afferent feedback from the chest wall (28) or the lungs (21). In addition to the altered afferent feedback from the chest wall, thoracic restriction is likely to result in a reduction in end-expiratory lung volume. Measurements of lung volumes were only made with the subjects at rest in this study. The magnitude of the changes in end-expiratory lung volume during exercise with thoracic restriction and the precise relationship of these changes to the respiratory discomfort experienced remain to be defined.

Irrespective of the underlying mechanisms that give rise to the respiratory discomfort experienced, the pattern of breathing adopted is often one in which respiratory discomfort is minimized, and to this end the respiratory discomfort itself can lead to immediate responses to improve breathing. Adjustments could lead to prolonged hyperventilation or even to a decrease in breathing efforts to reduce discomfort and work of breathing when the cause of the dyspnea cannot be easily eliminated. In this study, we imposed a limit on the degree of chest wall and lung excursion and thus restricted the pattern of breathing that could be adopted. This change would have been rapid in onset (as opposed to the more usual clinical situation in which changes would be of a gradual nature in response to worsening pathology), and, because the subjects could not dictate their own breathing pattern, this too could have had an impact on the dyspnea experienced. It is interesting to note a study by Nishino et al. (31) in which hyperventilation (characterized by a decrease in ventilation and f and a reduction in Pco2 and inspiratory time) was observed in awake subjects in response to heavy chest compression, but the response was absent when the compression was repeated during light anesthesia.

In the present study, we chose to ask subjects to rate their intensity of general respiratory discomfort rather than the more specific term “shortness of breath.” In
this way, we were able to question subjects about the specific qualities of their discomfort associated with exercise and thoracic restriction. With exercise alone, subjects identified “urge to breathe” as the only distinct quality of their discomfort; addition of the restriction generated other qualities including “effort,” “work,” and “hunger” to breathe as primary sources of discomfort. “Constriction” or “tightness” were often reported, although in these studies it seems likely that this was related directly to the external thoracic restriction rather than the tightness commonly associated with asthma (34). Subjects frequently identified “inspiratory difficulty,” “rapid,” and “shallow” as appropriate descriptors of their breathing. Thus the pattern of qualitative response reported with thoracic restriction in exercise in normal subjects is similar to that reported by patients with restrictive lung disease who identified “effort,” “work,” “gasping,” “shallow,” and “rapid” as the key descriptors of their respiratory discomfort (13, 26, 34). It is clear from the above that subjects can sense a number of dimensions related to the act of breathing, but it is impossible from this preliminary study to determine the relative importance of each. Furthermore, whereas the breathing pattern chosen may be selected to minimize overall respiratory discomfort, one type of dyspnea, e.g., “air hunger,” might intensify, whereas another type, e.g., “effort,” is diminished. Further studies are needed to ascertain the relative impact of changes in breathing pattern on these sensations and the priority placed on one or the other in the selection of a given pattern.

In conclusion, external restriction of rib cage expansion in normal subjects during exercise is associated with ventilatory and blood-gas changes as well as respiratory sensations characteristic of RVD. This experimental arrangement provides a useful model to investigate the neuromechanical basis of exertional dyspnea in these patients.

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