Mechanical work of breathing during maximal voluntary ventilation

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Milic-Emili, Joseph, and Marcello M. Orzalesi. Mechanical work of breathing during maximal voluntary ventilation. J. Appl. Physiol. 85(1): 254–258, 1998.—With the use of the esophageal balloon technique, the working capacity of the respiratory muscles was assessed in four normal subjects by measuring the work per breath (W) and respiratory power (W˙) during maximal voluntary ventilation with imposed respiratory frequencies (f) ranging from 20 to 273 cycles/min. Measurements were made in a body plethysmograph to assess the work wasted as a result of alveolar gas compressibility (Wg). In line with other types of human voluntary muscle activity, W decreased with increasing f, whereas W˙ exhibited a maximum at f of ~100 cycles/min. Up to this f value, Wg/W was small relative to W. With further increase in f, the Wg/W ratio increased progressively, amounting to 8–22% of W at f of 200 cycles/min.

Methods

The experiments were made in four healthy men, highly trained as subjects in respiratory studies. Their physical characteristics and values of vital capacity (VC) and total lung capacity are given in Table 1. The study was approved by the local Ethics Committee. All subjects gave informed consent.

Esophageal pressure (Pes) was measured as previously described (14). The volume displacement of the lungs (volume change due to displacement of gas through the airways plus volume change due to compression or expansion of alveolar gas) was measured with a body plethysmograph (13) with a resistance to flow of <0.01 cmH₂O·l⁻¹·s⁻¹. Flow of gas at the mouth was measured with a Silverman pneumotachograph connected to a pressure transducer (Sanborn Instrument, Waltham, MA). The resistance to flow offered by the pneumotachograph and connecting tube was ~0.1 cmH₂O·l⁻¹·s⁻¹. Volume displacement of the lungs and Pes changes were displayed on an X-Y oscilloscope and photographed. Volume displacement of the lungs and flow of gas at the mouth were recorded by a direct-writing oscilloscope (Poly-Viso, Sanborn Instrument).

Experiments were made with the subjects seated in the plethysmograph. MVV measurements were performed at various f values, with inspiratory duty cycle of 0.5. This was achieved by pacing the inspiratory and expiratory durations with a metronome. At each imposed f (range: 20–273 cycles/min), the subjects were instructed to breathe as forcefully as possible for 15 s. Three representative breaths were analyzed at each f. At the end of each MVV maneuver, the subjects were asked to inhale to total lung capacity, and this was used to place the volume-Pes loops within the VC (19, 20). The static volume-pressure curve of the lungs and the relaxation volume-pressure curve of the chest wall were obtained as previously described (15, 18).

The positive mechanical work done during inspiration (Wı) and per breathing cycle (Wı + ɛ) were obtained by the method illustrated in Fig. 1, which has been previously described in detail (9, 15). The tidal volume displaced in and out of the lungs during a breathing cycle (Vı) was obtained by measuring the vertical distance between the points of zero flow at the mouth on the volume-pressure loops obtained during MVV (Fig. 1). The total change of thoracic gas volume during the breathing cycle (Vı'), which includes the change due to compressibility of alveolar gas, was obtained by measuring the vertical distance between the uppermost and lowermost points of the pressure-volume loop. The Vı determined according to Fig. 1 closely corresponded to the Vı measured at the mouth by integration of the flow signal. As shown in Fig. 1, the difference between Vı' and Vı was due virtually entirely to compression of alveolar gas during expiration. As a result, Wı represented virtually entirely the work done by the inspiratory muscles in overcoming static elastic recoil of the respiratory system and resistive forces of the lung. In contrast, during expiration, there was an additional component of elastic work due to Wg, which was dissipated as heat (crosshatched area in Fig. 1) (9). As a result, the work done during expiration (We) included both a resistive component (hatched area in Fig. 1) and Wg.

Although it has been long recognized that measurement of work of breathing during maximal voluntary ventilation (MVV) by the usual procedure (i.e., maximum voluntary effort for 15 s) is theoretically of importance in assessing the maximal working capacity of the respiratory muscles, only few measurements have been reported (7, 15). Furthermore, in these studies, the measurements were confined to MVV at spontaneous breathing frequencies, and the work due to compressibility of alveolar gas (Wg) was not allowed for.

In line with the force-velocity relationship of muscle, Agostoni and Fenn (1) demonstrated that the maximal inspiratory work that a subject can achieve decreases with increasing speed of air movement. This implies that during MVV the mechanical work per breath (W) should decrease with increasing respiratory frequency (f), because the respiratory muscles will have less time to mobilize chemical potential energy for their performance of work (1). Furthermore, with augmenting frequency, an increasing fraction of W should be wasted in compressing and expanding alveolar gas (9).

In the present study, we have assessed the working capacity of the respiratory muscles by measuring the W and respiratory power (W˙) during MVV with imposed f values ranging from 20 to 273 cycles/min. Measurements were made in a body plethysmograph to assess the work due to compressibility of alveolar gas, Wg. Respiratory work W was measured by using the esophageal balloon technique.
The mean pressures developed during inspiration (\(P_i\)), expiration (\(P_e\)), or the whole breathing cycle (\(P_{i+e}\)) were obtained as ratio of \(W_i\), \(W_e\), and \(W_{i+e}\) to \(V_T\).

The present measurements of work of breathing do not include work done in overcoming the flow resistance of the chest wall, inertia, antagonistic activity of respiratory muscles, or chest wall distortion (6, 11-12, 17). Because the resistance of the chest wall is very small (3), the resistive work on the chest wall should be negligible. The same should probably apply to inertial work (12). In contrast, during MVV, the respiratory muscles exhibit substantial antagonistic activity (15, 17), and, in general, there is considerable chest wall distortion (11).

Values reported are means ± SD. Regression analysis was performed by using the least squares method.

### Table 1. Physical characteristics and values of vital and total lung capacities of the subjects studied

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>Age, yr</th>
<th>Weight, kg</th>
<th>Height, cm</th>
<th>Vital Capacity, liters BTPS</th>
<th>Total Lung Capacity, liters BTPS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>31</td>
<td>72</td>
<td>176</td>
<td>6.48</td>
<td>8.22</td>
</tr>
<tr>
<td>2</td>
<td>38</td>
<td>72</td>
<td>178</td>
<td>4.36</td>
<td>6.03</td>
</tr>
<tr>
<td>3</td>
<td>42</td>
<td>80</td>
<td>186</td>
<td>5.46</td>
<td>7.41</td>
</tr>
<tr>
<td>4</td>
<td>42</td>
<td>86</td>
<td>187</td>
<td>6.83</td>
<td>8.91</td>
</tr>
</tbody>
</table>

### RESULTS

As shown in Fig. 2, \(V_T\) decreased progressively with increasing \(f\). If VC is the \(V_T\) at \(f = 0\), the experimental relationship between \(V_T\) and \(f\) can be described with good approximation by the following rectangular hyperbola

\[
V_T = (b'VC - a'f)/(b' + f) \tag{1}
\]

The values of the constants \(a\) and \(b\) for the four subjects studied were calculated by the method of least squares. The fit of the experimental data to Eq. 1 was good in all individuals studied (r > 0.83; P < 0.01).

The relationship between \(V_T'\) and \(f\) can also be described by an expression similar to Eq. 1

\[
V_T' = (b'VC - a'f)/(b' + f) \tag{2}
\]

The fit of the experimental data to Eq. 2 was good in all subjects, with \(r\) ranging from 0.83 to 0.87 (P < 0.01). It should be noted that no specific meaning is attached to the constants derived in this study: they are merely used to describe in tabular form the approximate character of the experimental plots.

The difference between \(V_T'\) and \(V_T\), which was due almost entirely to gas compression during expiration (Fig. 2), increased with increasing \(f\). While at low \(f\) the difference between \(V_T'\) and \(V_T\) was negligible, this was not the case at higher \(f\) values: at \(f\) of 100 cycles/min, the average value of \(V_T\) for the four subjects was 6% lower than that of \(V_T'\) (range: 4–10%); at \(f\) of 200 cycles/min, \(V_T\) was, on average, 20% lower than \(V_T'\) (range: 14–25%). In subject 4, at \(f\) of 273 cycles/min (highest \(f\) attained in the present experiments), \(V_T\) was 33% lower than \(V_T'\).

The function relating MVV to \(f\) was obtained by multiplying both sides of Eq. 1 by \(f\). Figure 2 shows the relationship of MVV to \(f\) for subject 2. The MVV increased with \(f\) until a maximum (MVV max) was reached, decreasing progressively thereafter. The values of MVV max, together with the corresponding frequencies for the four subjects, are given in Table 2. MVV max...
was attained at frequencies ranging from 108 to 138 cycles/min. It should be noted that the maxima of MVV were rather blunt, so that over a relatively wide range of frequencies MVV was nearly constant (Fig. 2).

As shown in Fig. 3, \( P_I, P_E, \) and \( P_{I+E} \) developed by the respiratory muscles decreased approximately linearly with increasing \( f \)

\[ P = P_0 - cf \]  

(3)

where \( P_0 \) is the intercept of \( P \) at \( f = 0 \), and \( c \) is the slope of the curve. The regressions were statistically significant in all instances (\( P < 0.02 \)), except for the inspiratory data of subject 3. With this exception, the correlation coefficients ranged from 0.63 to 0.85.

As \( W = P \cdot V_T \), from Eqs. 2 and 3 it follows that

\[ W = (P_0 - cf)(b'V_C - a'f)/(b' + f) \]  

(4)

Figure 4 depicts the relationship of \( W_I \) and \( W_{I+E} \) to \( f \) for subject 2, which was computed according to Eq. 4. Similar relationships were obtained in the other three subjects. Both \( W_I \) and \( W_{I+E} \) decreased progressively with increasing \( f \). The \( W_I \) ranged between 20 and 40% of the total work per breath.

At low frequencies (<100 cycles/min), \( W_{g'} \) was a very small fraction of total work per breath (Table 3). At \( f \) of 100 cycles/min, it ranged between 3 and 10%, whereas at 200 cycles/min it ranged from 8 to 22%. Almost all \( W_{g'} \) was due to compression of alveolar gas during expiration (Fig. 1).

By multiplying both sides of Eq. 4 by \( f \), the function relating \( W \) to \( f \) is obtained. As shown in Fig. 4, both \( W_I \) and \( W_{I+E} \) increased with \( f \) until a maximum \( W_{I+E} \) was reached. The maximal values of \( W_I \) and \( W_{I+E} \) with the corresponding \( f \) values for the four subjects are given in Table 2. Both maxima were blunt.

### DISCUSSION

Measurement of mechanical work of breathing during MVV is useful for assessing the working capacity of the respiratory muscles. In line with other types of human voluntary muscle activity (1), the \( W_I \) and \( W_{I+E} \) decreased progressively with increasing \( f \), whereas the respective power outputs exhibited maxima at discrete \( f \) values.

In agreement with previous observations (2), \( V_T \) during MVV decreased with increasing \( f \), whereas MVV increased until a maximum was reached, decreasing progressively thereafter (Fig. 2). The frequencies at \( MVV_{max} \) ranged from 108 to 138 cycles/min (Table 2). It should be noted that at \( MVV_{max} \) the \( f \) values were higher than those attained during maximal exercise (40–60 cycles/min).

According to Eq. 1, \( V_T \) (and consequently MVV) is zero when \( f \) equals \( b'V_C/a' \). Such limiting value of \( f \),

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>MVV(\text{max}, \text{l/min} )</th>
<th>( W_I\text{max}, \text{kg·m·min}^{-1} )</th>
<th>( W_{I+E}\text{max}, \text{kg·m·min}^{-1} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>196 (108)</td>
<td>84 (79)</td>
<td>255 (100)</td>
</tr>
<tr>
<td>2</td>
<td>196 (125)</td>
<td>79 (105)</td>
<td>348 (111)</td>
</tr>
<tr>
<td>3</td>
<td>176 (129)</td>
<td>57 (140)</td>
<td>213 (89)</td>
</tr>
<tr>
<td>4</td>
<td>208 (138)</td>
<td>88 (151)</td>
<td>226 (137)</td>
</tr>
</tbody>
</table>

Table 2. Maximal values of MVV, \( W_I \), and \( W_{I+E} \) during MVV

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>Respiratory Frequency, cycles/min</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>50</td>
</tr>
<tr>
<td>1</td>
<td>0.3</td>
</tr>
<tr>
<td>2</td>
<td>6.3</td>
</tr>
<tr>
<td>3</td>
<td>2.4</td>
</tr>
<tr>
<td>4</td>
<td>1.3</td>
</tr>
</tbody>
</table>

Table 3. Work done in compressing alveolar gas and not used to move gas out of the lungs, expressed as % total work done by respiratory muscles during MVV at various respiratory frequencies
calculated with the latter equation, ranged from 347 to 550 cycles/min in our four subjects. This corresponds to the highest experimental values of \( f \) reported by Don-}


\[ \text{Jeager and Otis} \] \( \text{pointed out that, as a result of the compressibility of gas in the lungs, the change in thoracic gas volume actually produced by the respiratory muscles during the breathing movements is greater than the volume of gas displaced through the airways. They concluded, however, that at sea level the difference between these two volumes should in general be negligible. The present results show that during MVV the difference between \( V'T \) and \( Vt \) is negligible only at \( f < 100 \text{ cycles/min} \). At higher frequencies, the difference becomes substantial, amounting to \( \sim 20\% \) at \( f \) of 200 cycles/min. The frequency dependence of \( V'T - Vt \) is in agreement with the predictions of \text{Jeager} and \text{Otis}. In line with these authors, \( \text{Wg}/\text{W} \) increased with increasing \( f \). However, at \( f < 100 \text{ cycles/min}, \text{Wg}' \) was very small.

The mean pressure developed by the inspiratory and expiratory muscles during MVV decreased approximately linearly with increasing \( f \) (Fig. 3). This probably mainly reflected the fact that with increased rapidity of the breathing movements the respiratory muscles have progressively less time to approach their full potential force (1). A decline in force with increasing frequency of movements is also found in other forms of human voluntary muscle activity (e.g., pedaling on a bicycle ergometer). It should be noted, however, that during MVV maneuvers at spontaneous \( f \) values the respiratory muscles exhibit considerable antagonistic activity (16). This phenomenon is also found during MVV with imposed \( f \), because it is easier to pace the respiratory movements to the metronome by simultaneous contraction and relaxation of agonists and antagonists. Variability of such antagonistic activity may explain in part the fact that, in some instances, the coefficients of correlation of the regressions of \( P_i \) and \( P_e \) to \( f \) (Eq. 3) were relatively weak.

The expiratory pressures exhibited during MVV were much higher than the critical expiratory pressures at which expiratory flow limitation is reached as a result of dynamic airway compression (5, 8). As a result, during MVV the work of breathing per liter of ventilation (\( V \)) is very high, since the high pressures developed during expiration produce proportionately little flow.

Both the \( \text{W}i \) and \( \text{W}i + \text{E} \) exhibited maxima, which, in general, occurred at lower frequencies than those corresponding to MVV (Table 2). However, since the optima were blunt, the values of \( \text{W}i \) and \( \text{W}i + \text{E} \) attained at the frequencies corresponding to \( \text{MVV}_{\text{max}} \) did not differ appreciably from maximal \( \text{W}i \) and maximal \( \text{W}i + \text{E} \).

The frequency dependence of \( \text{W}i + \text{E} \) may explain in part the differences in total respiratory power output during MVV reported in the literature (Table 4). The values reported by \text{Hesser et al.} (7) may have been lower than in the present study because the MVV was performed with \( f \) of only 65 ± 13 cycles/min. It should also be noted that their measurements did not include \( \text{Wg}' \). According to Table 3, however, this should have been negligible at the frequencies used. By contrast, in the study of \text{Milic-Emili et al.} (15), in which \( \text{Wg}' \) was allowed for, frequencies as high as 180 cycles/min were used. According to the present results, at such frequencies the W output should have been less than maximal. It should be stressed, however, that there is a marked

Table 4. Respiratory variables during MVV reported in the literature

<table>
<thead>
<tr>
<th>No. of Subjects</th>
<th>( \text{W}i + \text{E}_i ) kg m·min(^{-1} )</th>
<th>MVV, l/min</th>
<th>( f ), cycles/min</th>
<th>Ref. No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>233 ± 75</td>
<td>187 ± 35</td>
<td>143 ± 25</td>
<td>16</td>
</tr>
<tr>
<td>8</td>
<td>199 ± 37</td>
<td>193 ± 25</td>
<td>65 ± 13</td>
<td>7</td>
</tr>
<tr>
<td>4</td>
<td>261 ± 61*</td>
<td>194 ± 13*</td>
<td>109 ± 21*</td>
<td>Present study</td>
</tr>
</tbody>
</table>

Values are means ± SD. \( f \), Respiratory frequency. *Values represent \( \text{W}i + \text{E}_{\text{max}} \) and \( \text{MVV}_{\text{max}} \). †Values corresponding to \( \text{W}i + \text{E}_{\text{max}} \).

Fig. 5. Relationship of total respiratory power to \( \dot{V} \) during maximal voluntary ventilation (top curve) and exercise (bottom curves) for subject 1 (Subj: 1). Nos. on top curve indicate corresponding \( f \) values. Bottom solid curves represent relations obtained during exercise at fixed \( f \) (from left to right) of 20, 40, and 60 cycles/min (see Ref. 16). Each solid curve terminates at symptom-limited maximal exercise. Broken curves extrapolate relations obtained during exercise to the iso-\( f \) points during maximal voluntary ventilation.

Table 5. \( \dot{V} \) and \( \text{W}i + \text{E} \) at different \( f \) values during maximal exercise on bicycle ergometer and MVV of subject 1

<table>
<thead>
<tr>
<th>( f ), cycles/min</th>
<th>( \dot{V}_i ), l/min</th>
<th>( \text{W}i + \text{E}_i ), kg m·min(^{-1} )</th>
<th>( \dot{V}_e ), l/min</th>
<th>( \text{W}i + \text{E}_e ), kg m·min(^{-1} )</th>
<th>( V_{\text{MVV}} ), %</th>
<th>( V_{\text{MVV}}/\text{W}i + \text{E}_{\text{MVV}}, % )</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>78</td>
<td>26</td>
<td>95</td>
<td>128</td>
<td>82</td>
<td>20</td>
</tr>
<tr>
<td>40</td>
<td>122</td>
<td>51</td>
<td>147</td>
<td>191</td>
<td>83</td>
<td>27</td>
</tr>
<tr>
<td>60</td>
<td>133</td>
<td>54</td>
<td>177</td>
<td>222</td>
<td>75</td>
<td>24</td>
</tr>
</tbody>
</table>
intersubject variability in maximal $W_{I+E}$, which in our four subjects ranged between 213 and 348 kg·m·min$^{-1}$ (Table 2).

High values of $V$ may be obtained with submaximal expiratory efforts, as shown in Fig. 5, which depicts the relationship of $W_{I+E}$ to $V$ of subject 1 during MVV and exercise (cycle ergometer) with fixed $f$ values of 20, 40, and 60 cycles/min (from Ref. 16). During exercise, power increased more steeply the lower the value of $f$, presumably because of improvement of the $V_T$ well into the expiratory reserve volume (16). At any given $V$, the power was considerably greater during MVV compared with exercise. Whereas the values of maximal exercise ventilation obtained at the three imposed frequencies amounted to ~80% of the corresponding MVV values, the $W$ during maximal exercise was only 20–27% of the values achieved at corresponding frequencies during MVV (Table 5). This is a further proof that during MVV the $W$ increases disproportionately as a result of dynamic airway compression.

Our measurements of $W$, which essentially represent elastic and/or resistive work, do not include the wasted work due to antagonistic activity of the respiratory muscles and distortion of the chest wall. Normal subjects, with ventilation increased by $CO_2$ inhalation, exhibit antagonistic contraction of the abdominal muscles during inspiration and, as a result, the $W$ based on changes in transdiaphragmatic pressure ($P_{di}$) may exceed up to 20% of that calculated from only $Pes$ (17). During MVV performed at spontaneously chosen $f$, there is marked antagonistic activity of the abdominal muscles during inspiration and of the diaphragm during expiration, as reflected by the fact that 1) during inspiration the abdominal pressure ($P_{ab}$) markedly exceeds the relaxation curve of the chest wall, and 2) during expiration $P_{ab}$ exceeds $Pes$ (15). Indeed, from Fig. 4 in Ref. 15 it can be calculated that in six subjects $W$ based on changes in $P_{di}$ was $74 \pm 33\%$ higher than that based on changes in $Pes$. Similarly, during expiration, $P_{ab}$ was $53 \pm 27\%$ higher than $Pes$, reflecting antagonistic activity of the diaphragm. Although computation of $W$ based on $P_{di}$ may not be entirely valid, this analysis indicates that during MVV the energy wasted due to antagonistic activity of respiratory muscles must exceed 50% of our measured work.

By using the method of Konno and Mead (10), McCool et al. (11) found that most normal subjects performed the MVV maneuver quite far from the relaxation configuration on the Konno-Mead plot. The varied nature of such distortions indicates that different individuals use different strategies to perform the MVV maneuver. This probably results from differences of activation and coordination of various respiratory muscles. In view of this variable behavior, we are unable to estimate the work due to chest wall distortion during MVV. It may be argued, however, that to the extent that the distortion work is mainly elastic in nature, the distorting energy stored during inspiration and expiration should be used to produce flow during expiration and inspiration, respectively.

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