Respiratory energetics during exercise at high altitude
Fabio Cibella, Giuseppina Cuttitta, Salvatore Romano, Bruno Grassi, Giovanni Bonsignore and Joseph Milic-Emili

You might find this additional information useful...

This article cites 35 articles, 17 of which you can access free at:
http://jap.physiology.org/cgi/content/full/86/6/1785#BIBL

This article has been cited by 2 other HighWire hosted articles:
Limits of human lung function at high altitude
R. B. Schoene
[Abstract] [Full Text] [PDF]

The last ""oxygenless"" ascent of Mt Everest
D M Bailey
[Full Text] [PDF]

Medline items on this article's topics can be found at http://highwire.stanford.edu/lists/artbytopic.dtl
on the following topics:
Physiology .. Exertion
Medicine .. Exercise
Medicine .. Respiration
Medicine .. Lungs

Updated information and services including high-resolution figures, can be found at:
http://jap.physiology.org/cgi/content/full/86/6/1785

Additional material and information about Journal of Applied Physiology can be found at:
http://www.the-aps.org/publications/jappl

This information is current as of April 19, 2005.
Respiratory energetics during exercise at high altitude

FABIO CIBELLA,1 GIUSEPPINA CUTTITTA,1 SALVATORE ROMANO,1 BRUNO GRASSI,2 GIOVANNI BONSIGNORE,1 AND JOSEPH MILIC-EMILI3

1Istituto di Fisiopatologia Respiratoria del Consiglio Nazionale delle Ricerche, Palermo 90146; 2Istituto di Tecnologie Biomediche Avanzate del Consiglio Nazionale delle Ricerche, Milan, Italy 20100; and 3Meakins-Christie Laboratories, McGill University, Montreal, Quebec, Canada H2X 2P2

Cibella, Fabio, Giuseppina Cuttitta, Salvatore Romano, Bruno Grassi, Giovanni Bonsignore, and Joseph Milic-Emili. Respiratory energetics during exercise at high altitude. J. Appl. Physiol. 86(6): 1785–1792, 1999.—The purpose of this study was to assess the effect of high altitude (HA) on work of breathing and external work capacity. On the basis of simultaneous records of esophageal pressure and lung volume, the mechanical power of breathing (Wrs) was measured in four normal subjects during exercise at sea level (SL) and after a 1-mo sojourn at 5,050 m. Maximal exercise ventilation (VEmax) and maximal Wrs were higher at HA than at SL (mean 185 vs. 101 l/min and 129 vs. 40 cal/min, respectively), whereas maximal O2 uptake averaged 2.07 and 3.03 l/min, respectively. In three subjects, the relationship of Wrs to minute ventilation (Ve) was the same at SL and HA, whereas, in one individual, Wrs for any given Ve was consistently lower at HA. Assuming a mechanical efficiency (E) of 5%, the O2 cost of breathing at HA and SL should amount to 26 and 5.5% of maximal O2 uptake, whereas for E of 20% the corresponding values were 6.5 and 1.4%, respectively. Thus, at HA, Wrs may substantially limit external work unless E is high. Although at SL VEmax did not exceed the critical Ve, at which any increase in Ve is not useful in terms of body energetics even for E of 5%, at HA VEmax exceeded critical Ve even for E of 20%.

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

http://www.jap.org 8750-7587/99 $5.00 Copyright © 1999 the American Physiological Society 1785
Table 1. Anthropometric characteristics and pulmonary function data of subjects at sea level

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>Age, yr</th>
<th>Ht, cm</th>
<th>Wt, kg</th>
<th>FVC, %pred</th>
<th>FEV1, %pred</th>
<th>FEV1/FVC, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>34</td>
<td>175</td>
<td>74</td>
<td>120</td>
<td>123</td>
<td>85</td>
</tr>
<tr>
<td>2</td>
<td>33</td>
<td>184</td>
<td>100</td>
<td>98</td>
<td>103</td>
<td>86</td>
</tr>
<tr>
<td>3</td>
<td>35</td>
<td>175</td>
<td>70</td>
<td>120</td>
<td>113</td>
<td>78</td>
</tr>
<tr>
<td>4</td>
<td>35</td>
<td>172</td>
<td>60</td>
<td>88</td>
<td>91</td>
<td></td>
</tr>
</tbody>
</table>

FVC, forced expiratory vital capacity; FEV1, forced expiratory volume in 1 s. Predicted values are from Quanjer et al. (32).

The values of Wrsmax in Table 2, which correspond to VEmax during incremental exercise, were established according to Eq. 1 by using the individual values of b and c constants.
and c in Fig. 1. On average, $\dot{W}_{r_{max}}$ was 222% higher at HA than at SL ($P < 0.03$).

Figure 2 (top) depicts the average values of $\dot{V}O_{2_{r_{max}}}$ at $VE_{max}$ (Table 2) for different values of E (5–20%). $\dot{V}O_{2_{r_{max}}}$ was established by using the average values of $W_{r_{max}}$ in Table 2; in these calculations we used four different values of E because values ranging from 5 to 20% have been reported in the literature (1, 8, 21, 25, 30). Figure 2 (bottom) shows the values of $\dot{V}O_{2_{r_{max}}}$ expressed as a percentage fraction of $V_{O2_{tot_{max}}}$. The $\dot{V}O_{2_{r_{max}}}$ are higher at HA than SL. The difference is more pronounced when $\dot{V}O_{2_{r_{max}}}$ is expressed as a fraction of $V_{O2_{tot_{max}}}$ because at HA the latter is lower than at SL (Table 2).

The curves shown in Fig. 1 are of ever-increasing slope, i.e., the mechanical power required per unit increase in $VE$ ($dW_{r}/dVE$) increases progressively with increasing $VE$. The relationship between the $dW_{r}/dVE$ and $VE$, obtained by differentiating Eq. 1 with respect to $VE$, is given by

$$dW_{r}/dVE = 2b\dot{V}E + 3c\dot{V}E^2$$  \hspace{1cm} (2)

Equation 2 implies that the additional $\dot{V}O_{2_{r}}$ per unit of additional $VE$ ($d\dot{V}O_{2_{r}}/dVE$) becomes greater the larger the $VE$ (see below).

Figure 3 depicts the relationship of $V_{O2_{tot}}$ during the incremental exercise and $VE$ in subject 3 at SL and HA. The values of $V_{O2_{tot}}$ for any given $VE$ were lower at HA than at SL. Similar results were obtained in subjects 1, 2, and 4. In all instances, the following polynomial equation closely fit ($r^2 \geq 0.99$) the relationship between $V_{O2_{tot}}$ and $VE$ both at SL and HA

$$V_{O2_{tot}} = a' + b'VE + c'VE^2$$  \hspace{1cm} (3)

The individual values of the constants in Eq. 3 at SL and HA are given in Table 3. 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.

As shown in Fig. 3, the slope $dV_{O2}/dVE$ decreased with increasing $VE$ both at SL and HA. The relationship of $dV_{O2}/dVE$ to $VE$ can be obtained by differentiating Eq.
The individual relationships of \( \frac{dV_{O2\text{tot}}}{dV_{E}} \) to \( V_{E} \) at SL and HA are depicted in Figs. 4 and 5, respectively. These relationships were computed according to Eq. 4 by using the individual values of the constants \( b' \) and \( c' \) in Table 3. In all instances, the \( \frac{dV_{O2\text{tot}}}{dV_{E}} \) slope decreased progressively with increasing \( V_{E} \), indicating that the additional energy uptake per unit of increase in \( V_{E} \) diminished with augmenting \( V_{E} \). In contrast, as implied by Eq. 2, the additional \( V_{O2\text{rm}} \) per unit increase in \( V_{E} \) \( (\frac{dV_{O2\text{rm}}}{dV_{E}}) \) increased progressively with augmenting \( V_{E} \). This is shown by the dashed-line isopleths in Figs. 4 and 5, which were computed for three different values of \( E \) by using a modification of Eq. 2

\[
\frac{dV_{O2\text{rm}}}{dV_{E}} = 2bE^{-1}V_{E} + 3cE^{-1}V_{E}^2
\]

Clearly, when \( \frac{dV_{O2\text{rm}}}{dV_{E}} = \frac{dV_{O2\text{tot}}}{dV_{E}} \) (6), any further increase in \( V_{E} \) will result in less energy \( (O_{2}) \) available for doing “useful” external work (e.g., cycling) because the respiratory muscles will use all the additional \( O_{2} \) provided by the increased \( V_{E} \) (18, 29). Therefore, the \( V_{E\text{crit}} \), corresponding to the limiting value in Eq. 6, should represent the \( V_{E\text{max}} \) available for useful external work (18, 29).

At SL, in all four subjects the \( \frac{dV_{O2\text{tot}}}{dV_{E}} \) curves in Fig. 4 did not cross any of the corresponding \( \frac{dV_{O2\text{rm}}}{dV_{E}} \) isopleths (with the exception of the 5% \( E \) curve in subject 1). Thus, at SL, in most instances \( V_{E\text{max}} \) did not exceed \( V_{E\text{crit}} \) even for \( E \) as low as 5%. In contrast, at HA, \( V_{E\text{max}} \) in three subjects was beyond \( V_{E\text{crit}} \) for all the \( E \) levels considered (5–20%) (Fig. 5). Only in subject 1 was \( V_{E\text{max}} \) below \( V_{E\text{crit}} \) for all \( E \) levels considered, except 5%. This individual, however, exhibited the lowest increase in \( V_{E\text{max}} \) at HA relative to SL.

DISCUSSION

This study provides the comparison of the Wrs during exercise at SL and after a sojourn at HA. In the present study, the relationship of Wrs to \( V_{E} \) at SL (Fig. 6) was similar to previous observations (2, 8, 18, 24). In all of these studies, Wrs was determined by using the same approach.

In three subjects, the relationship of Wrs to \( V_{E} \) at HA was essentially the same as at SL (Fig. 1, A, C, and D). In subject 2, however, the values of Wrs were lower at HA than SL, the difference becoming more pronounced with increasing \( V_{E} \) (Fig. 1B). The latter results are similar to those obtained by Petit et al. (31) in two normal subjects studied in a decompression chamber at simulated altitude of 5,000 m (rapid ascent). They attributed the decrease in Wrs at altitude to decreased air density. On this basis, Wrs should have decreased in all of our subjects at HA. This was not the case in three of them. Accordingly, density per se cannot explain the present results.

Contrary to the present results and those of Petit et al. (31), Thoden et al. (36) found that, at 3,100 m, Wrs, at any given \( V_{E} \), was actually higher than at SL. However, their results are questionable in view of the fact that a 16-cm-long esophageal balloon was used, giving rise to artifacts in assessment of pleural pressure (26).

In a discussion of the effects of altitude on Wrs, it should be stressed that our measurements of Wrs represent the power expended in overcoming Raw (18).
There are no measurements of Raw during exercise at HA. During resting breathing, Cruz (9) found a 7% decrease in Raw in six subjects exposed to 4,350 m for 3 days; Mansell et al. (17) found a 29% decrease in seven subjects exposed to 5,366 m for 30 days; and Gautier et al. (12) found a 14% decrease in nine subjects exposed to 3,457 m for 6 days. Thus, at least at rest, Raw decreases at HA. In contrast, in three of our subjects during exercise W˙rs did not change appreciably with altitude, suggesting that Raw was not altered at HA. Apart from air density (31, 37), however, there are several mechanisms that could affect Raw at HA. First, the hypoxia and hypocapnia present at altitude may cause an increase in Raw as a result of bronchoconstriction (16, 28). Such an effect may become more important during exercise at HA, when hypocapnia and hypoxia become more severe (35). In this connection it should be noted that, in the acute experiments by Petit et al. (31), Ve was increased by rebreathing from a spirometer initially filled with 100% O2. In this way, hypoxia was avoided, whereas the arterial PCO2 increased progressively during the rebreathing run. The latter should have promoted bronchodilatation (28). Second, Gautier et al. (12) suggested that at HA there is bronchodilatation because of a change in activity of the β2-adrenergic and/or -cholinergic systems. Increased levels of catecholamines at HA have been reported (39), and these could increase during exercise. Third, the engorgement of the pulmonary vascular bed and interstitial pulmonary edema, which may occur at HA (14), could lead to increased Raw. Fourth, changes in end-expiratory lung volume, breathing pattern, and shape of the V profile over a breath (pneumotachogram) may also affect W˙rs at any given Ve (15, 22, 25). Thus the effect of altitude on W˙rs depends on the balance among the above-mentioned mechanisms, which varies among individuals. In subject 2 the decrease in W˙rs at HA could have resulted from both decreased air density and bronchodilatation. In the other three subjects, hypoxic and hypocapnic bronchoconstriction, as well as increased Raw because of pulmonary engorgement-interstitial edema, may have prevailed. However, at rest, none of our subjects had clinical evidence of pulmonary edema (cough, rales, tachycardia, and so on) (33). It should be noted, however, that according to West (38), interstitial edema is likely to develop during exercise at HA. Finally, it should be noted that W˙rs for a given Ve depends on the breathing pattern and shape of the pneumotachogram, being least for constant Ve (15, 25). During exercise at

Table 3. Values of constants a', b', and c' in Eq. 3 of subjects at sea level and high altitude

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>a'</th>
<th>ml O2/min</th>
<th>b'</th>
<th>ml O2/l</th>
<th>c'</th>
<th>ml O2/l²</th>
<th>r²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sea Level</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>-23</td>
<td>47.7</td>
<td>-0.22</td>
<td></td>
<td>0.99</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>-33</td>
<td>41.6</td>
<td>-0.13</td>
<td></td>
<td>0.99</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>-264</td>
<td>61.3</td>
<td>-0.22</td>
<td></td>
<td>0.99</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>-386</td>
<td>60.5</td>
<td>-0.25</td>
<td></td>
<td>0.99</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>-177 ± 179</td>
<td>52.8 ± 9.7</td>
<td>-0.21 ± 0.05</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High Altitude</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>-61</td>
<td>24.7</td>
<td>-0.082</td>
<td></td>
<td>0.99</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>20</td>
<td>20.7</td>
<td>-0.058</td>
<td></td>
<td>0.99</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>-110</td>
<td>26.5</td>
<td>-0.063</td>
<td></td>
<td>0.99</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>-184</td>
<td>25.6</td>
<td>-0.076</td>
<td></td>
<td>0.99</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>-84 ± 86</td>
<td>24.4 ± 2.6</td>
<td>-0.070 ± 0.011</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

See RESULTS for details.
SL, normal subjects tend to adopt a quasi-constant V̇E pattern, minimizing Ẇrs (15). Whether this also occurs at HA is not known.

In line with previous reports (7, 34, 35), at HA the values of Ẇmax and VO₂max were lower than at SL, whereas VEmax was higher (Table 2). At HA there was also a marked increase in Ẇrsmax, which averaged 222%. It should be noted, however, that our estimates of Ẇrsmax have limitations because they were based on the assumption 1) that the relationship between Ẇrs and VE obtained during constant-load exercise (Fig. 1) is the same for incremental exercise and 2) that at HA Eq. 1 can be extrapolated up to VEmax. In fact, at HA the values of VEmax attained during constant-load exercise were in most instances lower than those achieved during incremental exercise (on average, 145 vs. 185 l/min), whereas at SL such difference was small (98 vs. 101 l/min). To our knowledge, there are no reports in which Ẇrs during constant-load exercise and incremental exercise was compared. It has been shown, however, that in a given subject the relationship of Wrs to VE is similar 1) during different types of exercise (treadmill or bicycle ergometer) (12) and 2) during exercise and rebreathing (26). Furthermore, at SL the relationships of Wrs to VE reported in the literature are close in general (Fig. 6), despite the fact that progressive exercise (2) or exercise with constant loads was used (Refs. 8, 22; present study). Thus it seems reasonable to assume that the relationships of Wrs to VEmax should not differ substantially between constant-load and incremental exercise. The validity of our estimates of Wrs based on extrapolation of Eq. 1 to VEmax (see assumption 2 above) is supported by a study in which the relationship of Wrs to VE was studied in five healthy subjects 1) at different levels of constant-load exercise, in which VEmax averaged 143 l/min; and 2) during rebreathing, in which VEmax attained 185 l/min (23). Although, with rebreathing, higher values of VE were achieved than during exercise, all data fit a single function (Eq. 1), indicating that the value of constants b and c in Eq. 1 does not change at very high VE. This provides indirect support for our extrapolations. Although our estimates of Ẇrsmax may not be entirely valid, it is unquestionable that this value is much higher at HA than SL, and that at HA most individuals exceed VEcrit during maximal exercise because VEmax is much greater than VEcrit (Fig. 5).

In a classic review of Wrs, Otis (29) introduced the concept of VEcrit. However, in calculating the function between dWrs/dVE and VE, he made a mathematical error, obtaining a value of bVE + cVE² instead of 2bVE + 3cVE² (Eq. 2). Hence his computation of VEcrit is not valid. Nevertheless, his approach provided the kernel for the estimation of VEcrit by Margaria et al. (18) and in the present study. In two young subjects exercis-
ing at SL on a treadmill or bicycle ergometer, Margaria
et al. found that VEcrit was lower than VEmax even for E
of 20%. Using the same approach, we found that at SL,
even for E as low as 5%, only one subject approached
VEcrit during maximal exercise, whereas in the other
three subjects VEcrit was well beyond VEmax (Fig. 4).
These results are consistent with those of Aaron et al.
(1, 2), who, using a different approach, concluded that
at SL healthy young subjects (n = 8) in general do not
reach VEcrit even during maximal exercise. In this
study, E amounted to ~10%. It is noteworthy that the
subjects in the work by Aaron et al. exhibited higher
values of VEmax and VO2max (on average, 153 l/min and
2.88 l/min, respectively) than those in the present
study. In fitter subjects, the decrease in dVO2/dVE with
increasing VE (Eq. 5) should be smaller than in less-fit
subjects, reflecting a smaller VE at any given VO2.
Accordingly, VEcrit should be higher in fitter subjects.

At HA, in three subjects VEmax exceeded VEcrit even for
E as high as 20%. When VEcrit is reached, any further
increase in VE will not make more O2 available to the
exercising limb muscles unless the respiratory muscles
operate anaerobically. These results suggest that low-
landers have no regulatory mechanism that keeps VE
within the useful range (≤VEcrit). Because exercise
hyperpnea in native highlanders is less than in low-
landers (35), it is conceivable that they do not exceed
VEcrit during exercise. Highlanders are also endowed
with large lungs and hence low Raw. Accordingly, at
any given VE, Wrs should be less than in lowlanders.

Although at 5,050 m VO2rm, max was relatively large, even
for 5% E the net values of VO2max (i.e., the difference
between VO2tot, max and VO2rm, max) were sufficient
to sustain moderate external exercise. Indeed, according
to results in Fig. 2, at E of 5% the net VO2max averaged
1.53 l/min, corresponding to 74% of VO2tot, max (Table 2). For E of 20% the corresponding value would
be 1.93 l/min. At more extreme altitudes, however,
VO2rm may severely limit exercise performance (25).

In conclusion, it has been previously shown that,
during rapid ascent to various simulated altitudes
decompression chamber), Wrs at any given VE decreased progressively with increasing altitude, mainly
reflecting decreasing air density (31). In contrast, the
present results show that, after a 1-mo sojourn at 5,050
m, Wrs for any given VE was lower at HA in only one
of four subjects. Although VO2max decreased by 32% on average at HA, VEmax and Wrsmax increased by 83 and
222%, respectively. As a result, at HA, VEmax exceeded
VEcrit in three of four subjects. This was not the case at
SL in any of the individuals.

Address for reprint requests and correspondence: F. Cibella,
Istituto di Fisiopatologia Respiratoria del CNR, via Trabucco 180,
90146 Palermo, Italy (E-mail: CIBELLA@FRPA.IFR.PA.CNR.IT).
Received 10 August 1998; accepted in final form 21 December 1998.

REFERENCES
Oxygen cost of exercise hyperpnea: implications for performance.
changes on the rate of oxygen consumption during negative
5. Baydur, A., P. K. Behrakis, W. A. Zin, M. J. Jæger, and J.
Milic-Emili. A simple method for assessing the validity of the
6. Carpenter, T. M., Tables, Factors and Formulae for Computing
Respiratory Exchange and Biological Transformations of Energy
(4th ed.). Washington, DC: Carnegie Institution of Washington,
1948. (Publ. 303C)
7. Cibella, F., G. Cuttitta, B. Kayser, M. Narici, S. Romano,
and F. Salibene. Respiratory mechanics during exhaustive
submaximal exercise at high altitude in healthy humans. J.
8. Coast, J. R., S. A. Rasmussen, K. M. Krause, J. A. O’Kroy,
R. A. Loy, and J. Rhodes. Ventilatory work and oxygen
consumption during exercise and hyperventilation. J. Appl.
9. Cruz, J. C. Mechanics of breathing in high altitude and sea level
Milic-Emili. Chest wall interrupter resistance in anesthetized
Bono, G. Torri, and J. Milic-Emili. Pulmonary and chest wall
12. Gautier, H., R. Peslin, A. Grassino, J. Milic-Emili, B. Han-
hart, E. Powell, G. Miserochi, M. Bonora, and J. T.
Fischer. Mechanical properties of the lungs during acclimatiza-
13. Jæger, M. J., and A. B. Otis. Effects of compressibility of
alveolar gas on dynamics and work of breathing. J. Appl.
15. Lafondt, C. L., A. E. Minetti, and P. Mognoni. Inspiratory
16. Libby, P. M., W. A. Briscoe, and T. K. C. King. Relief of
hypoxia-related bronchoconstriction by breathing 30 per cent
PV characteristics of human subjects at an altitude of 5,366 m. J.
Mechanical work of breathing during muscular exercise. J. Appl.
19. Mead, J. Measurement of inertia of the lungs at increased
respiratory rate on the mechanical work of breathing during
muscular exercise. Int. Z. Angew. Physiol. Einschl. Arbeits-
meccanico della respirazione durante la rirespirazione. Arch.
work of breathing during exercise in trained and untrained
Lung (2nd ed.), edited by R. G. Crystal, J. B. West, P. J. Barnes,


