Respiratory energetics during exercise at high altitude

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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 (W˙rs) 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 Wr 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 Wr to minute ventilation (VE) was the same at SL and HA, whereas in one individual, Wr 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, Wr 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 energetic economy (E) for E of 5%, at HA VEmax exceeded critical VE even for E of 20%.

chronic hypoxia; respiratory muscles; muscle efficiency; work of breathing

IT HAS LONG BEEN RECOGNIZED that ventilation (VE) at rest and for a given exercise level is higher at altitude than at sea level (SL) (34, 35). As a result, breathing is often felt to be “difficult” at altitude, as aptly stated by Reinhold Messner (20) in describing his approach to the summit of Mt. Everest (8,848 m) together with Peter Habeler, the two being the first humans to climb Mt. Everest breathing ambient air and not using supplementary bottled oxygen: “Breathing becomes such a strenuous business that we scarcely have strength to go on.” This quotation vividly suggests that VE and work of breathing (Wrs) contribute to the limitation of exercise performance at high altitude (HA).

At HA, maximal exercise VE (VEmax) is considerably higher than at SL (35). This should lead to increased mechanical power of breathing (Wrs) and O2 consumption by the respiratory muscles (Vo2rm). The increase in Wrs, however, should be attenuated by a decrease in airway resistance (Raw) because of lower density. In fact, in two normal subjects studied in a decompression chamber at various simulated altitudes (rapid ascent), ranging from 34 to 7,500 m, Petit et al. (31) found that Wrs at any given VE decreased progressively with increasing altitude. These authors attributed the changes in Wrs to decreased air density. Surprisingly, there is only one report concerning Wrs during exercise at HA, which was carried out in seven normal subjects at an altitude of 3,100 m (36). Contrary to expectations, in this study Wrs at any given VE was found to be slightly higher at HA than SL. However, because a 16-cm-long esophageal balloon was used, the measurements of Wrs are questionable. Indeed, 16-cm-long balloons necessarily extend into the upper one-third of the esophagus, and hence false values of pleural pressure may be recorded (26).

Information concerning Wrs at HA is also important to establish if, as a result of the very high exercise values of VE at HA, VEmax exceeds the critical value (VEcrit) at which any increase in VE is not useful in terms of the energetic economy of the body because the O2 gained is less than that required for the increased Wrs (29). At SL, according to Aaron et al. (2), VEcrit in general is not attained by healthy young subjects even during maximal exercise.

Accordingly, in the present investigation, we measured Wrs during exercise in four normal subjects at SL and after a 1-mo stay at 5,050 m. Furthermore, we have assessed whether VEcrit is attained during exercise at HA.

METHODS

Four healthy male subjects (aged 33–35 yr) were studied during exercise at SL and after a 1-mo stay at 5,050 m in the Italian Pyramid Laboratory “Ardito Desio” in the high Khumbu Valley, close to the Mt. Everest Base Camp, in Nepal (barometric pressure = 410 Torr). The same subjects also participated in a study dealing with exercise endurance at this altitude (7). Two subjects (subjects 1 and 2) led a sedentary lifestyle, whereas subjects 3 and 4 were physically active on a recreational basis. Table 1 lists their anthropometric characteristics and baseline lung function data. Subject 2 weighed 119% of predicted normal weight. The study was approved by the institutional Ethics Committee. All subjects gave informed consent.

The same apparatus was used at SL and altitude. In each subject, the total body O2 uptake (Vo2tg) was measured with the open-circuit method (MedGraphics; Medical Graphics, St. Paul, MN) during incremental cycle ergometer exercise both at SL and at HA. After sitting for a few minutes at rest on a braked cycle ergometer (Monark Ergomedic 818 E; Monark Exercise, Varberg, Sweden), the subjects performed the incremental exercise. Starting at 30 W, the external power was increased stepwise by 30 W every 4 min until exhaustion, defined as the inability of subjects to maintain the imposed pedaling frequency (60 rpm). The latter was continuously
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>
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<tr>
<td>2</td>
<td>33</td>
<td>184</td>
<td>100</td>
<td>98</td>
<td>103</td>
<td>86</td>
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<td>3</td>
<td>35</td>
<td>175</td>
<td>70</td>
<td>120</td>
<td>113</td>
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</tr>
<tr>
<td>4</td>
<td>35</td>
<td>172</td>
<td>60</td>
<td>88</td>
<td>96</td>
<td>91</td>
</tr>
</tbody>
</table>

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

displayed to the subject. VE (BTPS) and VO₂tot (STPD) were determined breath by breath with a computerized system (CPX; Medical Graphics). VE was calculated by digital integration of the expiratory flow (V), which was measured with a Fleisch no. 3 pneumotachograph (Fleisch; Lausanne, Switzerland) calibrated with a 3-liter syringe. The added dead space of the mouthpiece two-way valve system was 100 ml. The equipment resistance (2-way valve plus tubing and pneumotachograph) was 1.0 cmH₂O·l⁻¹·s⁻¹. Inspired and expired air was continuously sampled at the mouth of the subject and analyzed for O₂ and CO₂ fractions by rapid (90% response time <100 ms) zirconium O₂ (Medical Graphics) and infrared CO₂ (Datex model CX-104) analyzers. The analyzers were calibrated before each experiment with gas mixtures of known composition. O₂ uptake (VO₂) was calculated by using standard mass balance equations. VE and VO₂tot values obtained during the last 30 s of resting breathing and at each work load were averaged.

Two days later, the subjects performed exercise on the cycle ergometer at a constant load, corresponding, respectively, to 75% of SL or HA maximal VO₂ (VO₂max), until exhaustion. At SL the time to exhaustion amounted to 29 ± 10 min, whereas at altitude it was 13 ± 3 min. During the constant-load exercise, V at the mouth was measured with a calibrated pneumotachograph (Fleisch no. 3) connected to a differential pressure transducer (Validyne MP-45, 5 ± cmH₂O; Validyne, Northridge, CA). The pneumotachograph was connected to a large-bore mouthpiece and was heated to prevent condensation. The dead space of the mouthpiece and pneumotachograph system was 65 ml, and its resistance was 0.17 cmH₂O·l⁻¹·s⁻¹ over the experimental range of V. Because V was laminar, it was not affected by density, and hence, at HA, the resistance is not expected to change significantly. Esophageal pressure (Pes) was measured with a balloon-tipped catheter placed in the lower one-third of the esophagus and connected to a calibrated differential pressure transducer (Validyne MP-45, ±80 cmH₂O) referenced to atmospheric pressure (18, 26). Catheters were also attached to the reference side of both manometers, with the length adjusted to balance the opposite sides of the transducer. The position of the esophageal balloon was adjusted by using the occlusion technique proposed by Baydur et al. (5).

All the analog signals were recorded on a four-channel strip-chart recorder (Hewlett-Packard 7754B; Hewlett-Packard, Waltham, MA) and an eight-channel magnetic tape recorder (Hewlett-Packard 3968A) for further playback and analysis.

The V and Pes signals were sampled at 10-ms intervals and stored on a computer (Digital Alpha Station; Digital Equipment, Maynard, MA). From the calibrated V and Pes signals the computer calculated the tidal volume (VT) breath by breath by the integration of inspiratory V, respiratory frequency (f), VE, Wrs, and Wrs, as the product of Wrs × f.

As in previous studies (18, 24, 31), the mechanical work per breath was measured as the area enclosed by the dynamic loops of volume against Pes. Strictly speaking, such measurement represents the resistive work done on the lung per breathing cycle and does not include the work due to inertial forces, compressibility of thoracic gas (13), distortion of the chest wall from its relaxed configuration (4, 25), and the resistive work done on the chest wall. Under the present experimental conditions, the inertial forces are negligible (19), and the work due to compressibility of gas is very small over the range of f used in the present study (27). Because the resistance of the chest wall is very small (10), the resistive work on the chest wall should be negligible (27).

Furthermore, at V > 30 l/min, most of the elastic work done during inspiration or expiration is recovered for producing V during the subsequent respiratory phase (18, 24). At V > 30 l/min, the work due to viscoelastic pressure dissipations (11) and the negative work done by the inspiratory muscles during expiration or expiratory muscles during inspiration are negligible (18, 25). Furthermore, the mechanical efficiency of muscles is considerably greater during eccentric than concentric contractions (3), and hence the O₂ cost of negative work is negligible. Accordingly, our estimates of Wrs probably closely approximate the total work per breathing cycle.

The plots of the relationship of Wrs to VE were obtained by averaging VE over intervals of 10 l/min and computing the corresponding values of Wrs (Fig. 1). Wrs was expressed in calories per minute. The O₂ cost of breathing (VO₂bm, ml O₂ STPD/min) was computed by using the following equation:

\[ \text{Wrs} = \frac{W_{\text{O}_2}}{4.825} \]

E is mechanical efficiency and 4.825 is the caloric equivalent of 1 ml O₂ STPD (6, 18).

Values are reported as means ± SD. Regression analysis was performed by using the least squares method. Comparison between data obtained at SL and HA was made by using a paired Student t-test, with the level of significance set at P < 0.05.

RESULTS

The values of Wmax, total body VO₂ (VO₂max), Wrs (Wrsmax), and VE (VEmax) of the four subjects at SL and HA are given in Table 2. In all instances, the values of Wmax and VO₂tot, max were smaller at HA than at SL (on average by 23 and 32%, respectively), whereas VEmax was 83% higher at HA.

Figure 1 shows the relationship between Wrs and VE in the four subjects during the square-wave exercise at SL and HA. In subject 2 (Fig. 1B) Wrs, at any given VE, was higher at SL than HA. In both instances, the data points closely fitted (r² = 0.99) the following equation of Otis et al. (29, 30)

\[ W_{\text{rs}} = bV^2 + cV^3 \]  

(1)

where b and c are constants. The curves corresponding to SL and HA of subject 2 were computed according to Eq. 1 by using the corresponding values b and c in Fig. 1B. In contrast, in the other three subjects, the relationships of Wrs to VE at SL and HA were essentially the same. Accordingly, in these subjects the SL and HA data were pooled, and a single curve was computed according to Eq. 1. The individual values of constants b and c are indicated in Fig. 1, A, C, and D. In all instances, r² was 0.99.

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 in Fig. 1. On average, Wrs max was 222% higher at HA than at SL (P < 0.03).

Figure 2 (top) depicts the average values of VO2rm, max at VE max (Table 2) for different values of E (5–20%). VO2rm, max was established by using the average values of Wrs 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 VO2rm, max expressed as a percentage fraction of VO2 tot, max. The values of VO2 rm, max are higher at HA than SL. The difference is more pronounced when VO2 rm, max is expressed as a fraction of VO2 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 (dWrs/dVE) increases progressively with increasing VE. The relationship between the dWrs-dVE slope and VE, obtained by differentiating Eq. 1 with respect to VE, is given by

\[
\frac{dWrs}{dVE} = 2b\dot{V}E + 3c\dot{V}E^2
\]  

(2)

Equation 2 implies that the additional VO2 rm per unit of additional VE (dVO2 rm/dVE) becomes greater the larger the VE (see below).

Figure 3 depicts the relationship of VO2 tot during the incremental exercise and VE in subject 3 at SL and HA. The values of VO2 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 VO2 tot and VE both at SL and HA

\[
\dot{V}O2_{tot} = a' + b'\dot{V}E + c'\dot{V}E^2
\]  

(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 dVO2/dVE decreased with increasing VE both at SL and HA. The relationship of dVO2/dVE to VE can be obtained by differentiating Eq.

Table 2. Maximal total power, maximal total body O2 uptake, and maximal ventilation during incremental exercise with corresponding respiratory power of subjects at sea level and high altitude

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>Wmax, W</th>
<th>VO2 tot,max, l/min</th>
<th>VE max, l/min</th>
<th>Wrs max, cal/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>180</td>
<td>2.56</td>
<td>103</td>
<td>33</td>
</tr>
<tr>
<td>2</td>
<td>180</td>
<td>2.81</td>
<td>103</td>
<td>46</td>
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<tr>
<td>3</td>
<td>300</td>
<td>3.74</td>
<td>105</td>
<td>43</td>
</tr>
<tr>
<td>4</td>
<td>240</td>
<td>3.02</td>
<td>94</td>
<td>36</td>
</tr>
</tbody>
</table>

Mean ± SD  225 ± 57*  3.03 ± 0.51†  101 ± 5‡  40 ± 6‖

\( W_{max}, \) maximal external power; \( VO_{2tot, max}, \) maximal total body O2 uptake; \( VE_{max}, \) maximal exercise ventilation; \( W_{rs max}, \) maximal respiratory power. \*P < 0.05, †P < 0.03, and ‡P < 0.01, sea level vs. high altitude. §Computed according to Eq. 1 by using constants in Fig. 1.
3 with respect to $V_E$

$$\frac{dV_{O2r,m}}{dV_E} = b' + 2c'V_E$$

(4)

The individual relationships of $dV_{O2r,m}/dV_E$ 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 $dV_{O2r,m}/dV_E$ 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 $V_{O2r,m}$ per unit increase in $V_E$ ($dV_{O2r,m}/dV_E$) 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

$$dV_{O2r,m}/dV_E = 2bE^{-1}V_E + 3cE^{-1}V_E^2$$

(5)

Clearly, when

$$dV_{O2r,m}/dV_E = dV_{O2r,tot}/dV_E$$

(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 $V_{E,crit}$, corresponding to the limiting value in Eq. 6, should represent the $V_{E,max}$ available for useful external work (18, 29).

At SL, in all four subjects the $dV_{O2r,tot}/dV_E$ curves in Fig. 4 did not cross any of the corresponding $dV_{O2r,m}/dV_E$ isopleths (with the exception of the 5% $E$ curve in subject 1). Thus, at SL, in most instances $V_{E,max}$ did not exceed $V_{E,crit}$ even for $E$ as low as 5%. In contrast, at HA, $V_{E,max}$ in three subjects was beyond $V_{E,crit}$ for all the $E$ levels considered (5–20%) (Fig. 5). Only in subject 1 was $V_{E,max}$ below $V_{E,crit}$ for all $E$ levels considered, except 5%. This individual, however, exhibited the lowest increase in $V_{E,max}$ 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 (Figs. 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), V˙E was increased by rebreathing from a spirometer initially filled with 100% O2. In this way, hypoxia was avoided, whereas the arterial P CO2 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 V˙E (15, 22, 25). Thus the effect of altitude on W˙rs depends on the balance among the above-mentioned mechanisms, which appears to vary 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 V˙E depends on the breathing pattern and shape of the pneumotachogram, being least for constant V˙ (15, 25). During exercise at

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>Sea Level</th>
<th>High Altitude</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>a', ml O2/min</td>
<td>b', ml O2/l</td>
</tr>
<tr>
<td>1</td>
<td>-23</td>
<td>47.7</td>
</tr>
<tr>
<td>2</td>
<td>-33</td>
<td>41.6</td>
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<tr>
<td>3</td>
<td>-264</td>
<td>61.3</td>
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<tr>
<td>4</td>
<td>-386</td>
<td>60.5</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>-177 ± 179</td>
<td>52.8 ± 9.7</td>
</tr>
</tbody>
</table>

See Results for details.
normal subjects tend to adopt a quasi-constant \( V \dot{E} \) pattern, minimizing \( W \dot{rs} \) (15). Whether this also occurs at HA is not known.

In line with previous reports (7, 34, 35), at HA the values of \( W_{max} \) and \( VO_2_{max} \) were lower than at SL, whereas \( VE_{max} \) was higher (Table 2). At HA there was also a marked increase in \( W_{rs_{max}} \), which averaged 222%. It should be noted, however, that our estimates of \( W_{rs_{max}} \) have limitations because they were based on the assumption 1) that the relationship between \( W_{rs} \) and \( V_{E} \) 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 \( VE_{max} \). In fact, at HA the values of \( VE_{max} \) 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 \( W_{rs} \) during constant-load exercise and incremental exercise was compared. It has been shown, however, that in a given subject the relationship of \( W_{rs} \) 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 \( W_{rs} \) 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 \( W_{rs} \) to \( VE_{max} \) should not differ substantially between constant-load and incremental exercise. The validity of our estimates of \( W_{rs_{max}} \) based on extrapolation of Eq. 1 to \( VE_{max} \) (see assumption 2 above) is supported by a study in which the relationship of \( W_{rs} \) to \( VE \) was studied in five healthy subjects 1) at different levels of constant-load exercise, in which \( VE_{max} \) averaged 143 l/min; and 2) during rebreathing, in which \( VE_{max} \) 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 \( W_{rs_{max}} \) 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 \( VE_{crit} \) during maximal exercise because \( VE_{max} \) is much greater than \( VE_{crit} \) (Fig. 5).

In a classic review of \( W_{rs} \), Otis (29) introduced the concept of \( VE_{crit} \). However, in calculating the function between \( dW_{rs}/dVE \) and \( VE \), he made a mathematical error, obtaining a value of \( 2bVE + cVE^2 \) instead of \( 2bVE + 3cVE^2 \) (Eq. 2). Hence his computation of \( VE_{crit} \) is not valid. Nevertheless, his approach provided the kernel for the estimation of \( VE_{crit} \) by Margaria et al. (18) and in the present study. In two young subjects exercis-
of 20% during maximal exercise, whereas in the other three subjects \(V_{\text{Ecrit}}\) was well beyond \(V_{\text{Emax}}\) (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 \(V_{\text{Ecrit}}\) even during maximal exercise. In this study, E amounted to \(\approx 10\%\). It is noteworthy that the subjects in the work by Aaron et al. exhibited higher values of \(V_{\text{Emax}}\) and \(V_{\text{O2max}}\) (on average, 153 l/min and 2.88 l/min, respectively) than those in the present study. In fitter subjects, the decrease in \(\Delta VO_2/\Delta V_e\) with increasing \(V_e\) (Eq. 5) should be smaller than in less-fit subjects, reflecting a smaller \(V_e\) at any given \(V_{\text{O2}}\). Accordingly, \(V_{\text{Ecrit}}\) should be higher in fitter subjects.

At HA, in three subjects \(V_{\text{Emax}}\) exceeded \(V_{\text{Ecrit}}\) even for E as low as 5%. When \(V_{\text{Ecrit}}\) is reached, any further increase in \(V_e\) will not make more \(O_2\) available to the exercising limb muscles unless the respiratory muscles operate anaerobically. These results suggest that lowlanders have no regulatory mechanism that keeps \(V_e\) within the useful range (\(\approx V_{\text{Ecrit}}\)). Because exercise hyperpnea in native highlanders is less than in lowlanders (35), it is conceivable that they do not exceed \(V_{\text{Emax}}\) during exercise. Highlanders are also endowed with large lungs and hence low Raw. Accordingly, at any given \(V_e\), Wrs should be less than in lowlanders.

Although at 5,050 m \(V_{\text{O2max}}\) was relatively large, even for 5% E the net values of \(V_{\text{O2max}}\) (i.e., the difference between \(V_{\text{O2tot, max}}\) and \(V_{\text{O2max, max}}\)) were sufficient to sustain moderate external exercise. Indeed, according to results in Fig. 2, at E of 5% the net \(V_{\text{O2max}}\) averaged 1.53 l/min, corresponding to 74% of \(V_{\text{O2tot, max}}\) (Table 2). For E of 20% the corresponding value would be 1.93 l/min. At more extreme altitudes, however, \(V_{\text{O2max}}\) 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 \(V_e\) 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 \(V_e\) was lower at HA in only one of four subjects. Although \(V_{\text{O2max}}\) Decreased by 32% on average at HA, \(V_{\text{max}}\) and Wrs increased by 83 and 222%, respectively. As a result, at HA, \(V_{\text{Emax}}\) exceeded \(V_{\text{Ecrit}}\) in three of four subjects. This was not the case at SL in any of the individuals.

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Received 10 August 1998; accepted in final form 21 December 1998.

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