IV. Oxygen Transport System Before and After Exposure to Chronic Hypoxia

G. Ferretti[1], *U. Boutellier*[1] *, *D. R. Pendergast*[2], *C. Moia*[1], *A. E. Minetti*[1], *H. Howald*[3], *and P. E. di Prampero*[1,4]

[1]Department of Physiology, University of Geneva Medical School, Geneva, Switzerland
[2]Department of Physiology, State University of New York at Buffalo, Buffalo, NY, USA
[3]Research Institute of the Swiss School of Physical Education and Sports, Magglingen, Switzerland
[4]Institute of Biology, University of Udine, Udine, Italy

Abstract

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Maximal $\dot{V}O_2$ on the treadmill ($\dot{V}O_2$max) and on the bicycle ergometer ($\dot{V}O_2$peak), maximal cardiac output ($\dot{Q}$max), by a CO_2 rebreathing method, maximal heart rate (HRmax), blood hemoglobin concentration (Hb), and hematocrit (Hct) were measured on six subjects before (B) and 3 weeks after (A) prolonged exposure to chronic hypoxia. It was observed that after high-altitude exposure $\dot{V}O_2$max, $\dot{V}O_2$peak, and $\dot{Q}$max were lower ($P < 005$) than before [A: 4.13 ± 0.67; 3.28 ± 0.41 and 16.89 ± 2.49 (l/min ± SD); B: 4.39 ± 0.39; 3.53 ± 0.34 and 21.81 ± 1.27, respectively], whereas Hb and Hct were larger (A: 162 ± 8 g/l and 0.46 ± 0.02; B: 142 ± 7 and 0.41 ± 0.02) and HRmax was unchanged (178 ± 7 vs 175 ± 9 bts/min). Thus, the calculated stroke volume of the heart and the Hb flow at $\dot{V}O_2$ peak were lower in A than in B (95 ± 15 vs 124 ± 7 ml and $2{,}723 \pm 307$ vs $3{,}129 \pm 196$ g/min) ($P < 0.05$, respectively), whereas the arteriovenous O_2 difference was greater in A than in B (195 ± 16 vs 162 ± 19 ml O_2/l; $P < 0.05$). At any given submaximal work load, $\dot{V}O_2$ and HR were the same in B and in A, whereas $\dot{Q}$ was lower in A by ~ 2–3 l/min. However, because of the increased Hb, leading to a higher arterial O_2 content, at any work load the O_2 flow remained unchanged.

Key words

maximum O_2 consumption, cardiac output, limiting factors, hemoglobin, blood O_2 concentration

Introduction

In chronic hypoxia both maximal oxygen uptake ($\dot{V}O_2$max) (5, 21, 22) and maximal cardiac output ($\dot{Q}$max) (4, 16, 18, 19) are known to be reduced. However, according to Cerretelli (5), "$\dot{Q}$max does not appear to be reduced enough to justify the decrease of $\dot{V}O_2$max observed both breathing air and, particularly, oxygen." In fact, in chronic hypoxia the drop in $\dot{V}O_2$max is associated with an increase in blood hemoglobin concentration (Hb) (5), a fact that tends to maintain the maximal hemoglobin flow, $\dot{M}_{Hb}$, in spite of the reduced $\dot{Q}$ max. Also, upon return form altitude increased Hb is not accompanied by an equivalent rise in $\dot{V}O_2$max (4).

It is generally inferred from these data that the function of the O_2 transport system is preserved by altitude acclimatization, and therefore it does not limit $\dot{V}O_2$max both at altitude (chronic hypoxia) and during the first days upon return to sea level (acclimatized subjects in normoxia, a condition here defined as acute normoxia). This conclusion is opposite to that believed to apply in normoxia for subjects not acclimatized to altitude (3). Surprisingly enough, this implies that the circulatory limits to $\dot{V}O_2$max described in normoxia shall disappear completely with chronic hypoxia. The relations between oxygen transport system and $\dot{V}O_2$max after prolonged exposure to high altitude therefore deserve further studies.

The aim of the present paper is to describe the changes in $\dot{V}O_2$max and in the O_2 transport system (cardiac output and hemoglobin flow) observed upon return from prolonged exposure to high altitude.

Methods

Maximal Oxygen Uptake

The maximal oxygen uptake ($\dot{V}O_2$max) was measured during treadmill running on a + 10% grade and during cycling. On the treadmill each subject ran first at 6 km/h for 5 min. Subsequently, he performed 3 to 5 runs of 3 min duration at increasing speed (from 7.5 km/h to a maximum of 13.5 $km \cdot h^{-1}$). At the end of each work level blood samples were taken from the antecubital vein for lactate determination (Kontron, enzymatic method, 17), then the speed was increased by steps of 1.5 km/h. Expired air was collected

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* Present address: Department of Physiology, University of Zurich, CH-8057 Zurich, Switzerland

Table 1 Physical characteristics and $\dot{V}O_2max$ before and after the expedition

Subj.	Age (yrs)	Height (cm)	Weight (kg)		$\dot{V}O_2max$ (l · min−1)		$\dot{V}O_2max$ (ml · min−1 · kg−1)	
			Before	After	Before	After	Before	After
GF	50	176	71.4	66.5	4.49	4.28	62.9	64.4
LM	37	179	76.0	73.0	4.53	4.46	59.6	61.1
MR	44	167	66.6	63.2	3.62	2.86	54.3	45.3
RA	38	177	69.7	64.9	4.38	4.09	62.8	63.0
RM	30	174	79.7	74.7	4.65	4.22	58.3	56.5
WP	44	183	75.3	77.0	4.67	4.84	62.0	62.9
$\bar{x}$	41	176	73.1	69.9	4.39	4.13	60.0	58.9
SD	7	5	4.8	5.7	0.39	0.67	3.3	7.2
Δ%			−4.4		−5.9		−1.9	
t			−3.09		−2.05		−0.66	
2*P*			< 0.05		< 0.10		NS	

Table 2 Peak $\dot{V}O_2$ on the bicycle and the hemodynamic parameters before and after the expedition

Subj.	$\dot{V}O_2peak$ (l · min^{-1})		$\dot{Q}max$ (l · min^{-1})		HRmax (min^{-1})		SV (ml)		$(Ca\text{-}\bar{C}v)O_2$ (ml O_2/l)	
	Before	After	Before	After	Before	After	Before	After	Before	After
GF	3.80	3.19	22.58	14.53	176	180	128	81	168	220
LM	3.48	3.75	23.44	20.88	176	181	133	115	148	180
MR	2.89	2.58	21.05	14.54	172	176	122	83	137	177
RA	3.50	3.28	22.54	15.84	180	180	125	88	155	207
RM	3.66	3.26	21.24	16.95	188	184	113	92	172	192
WF	3.82	3.62	19.98	18.60	160	164	125	113	191	195
$\bar{x}$	3.53	3.28	21.81	16.89	175	178	124	95	162	195
SD	0.34	0.41	1.27	2.49	9	7	7	15	19	16
Δ (%)	−7.1		−22.6		+ 1.7		−23.4		+ 20.4	
t	−2.05		− 4.62		1.52		− 5.12		4.32	
2*P*	< 0.10		< 0.01		NS		< 0.01		< 0.01	

in three Douglas bags during the last 1.5 min of each work and subsequently analyzed for gas composition (A-52 Applied Electrochemistry O_2 meter and LB-2 Beckman CO_2 meter) and volume (Singer dry gas meter). The average value of the three $\dot{V}O_2$ measurements was taken as the $\dot{V}O_2$ of the test. Heart rate was measured continuously by ECG. The following criteria were used for establishing that $\dot{V}O_2max$ had indeed been attained: (1) an increase in $\dot{V}O_2$ of less than 2% between two successive runs; (2) the attainment of maximal heart rate (Δ HR < 5 min^{-1}); (3) blood lactate exceeding 7 mM at the end of the highest work load; (4) subject's exhaustion.

On the bicycle ergometer a maximal work load corresponding to 90% of $\dot{V}O_2max$ on the treadmill (3) was chosen. Four exercise levels were then selected, corresponding to 25%, 50%, 75%, and 100% of the calculated maximal work load. At each work load steady-state O_2 consumption was measured by standard open circuit method, as described above. The highest measured $\dot{V}O_2$ value was retained as the maximal O_2 uptake on the bicycle ergometer ($\dot{V}O_2peak$).

Cardiac Output

Steady-state cardiac output during cycloergometric exercise ($\dot{Q}$) was determined by means of a CO_2 rebreathing method (10) in the course of the same protocol as for the determination of $\dot{V}O_2peak$. A mass spectrometer (Centronic 200 MGA) was used for gas analysis. The CO_2 rebreathing traces were followed on paper (Grass 7D), stored on discs, and subsequently analyzed by a computer (IBM XT 286). The $\dot{Q}$ calculations were performed in a blind manner by a technician not involved in this study. At each work load three determinations of $\dot{Q}$ were performed, and the mean value was retained and utilized in subsequent data analysis. The highest measured $\dot{Q}$ value was taken as the maximal cardiac output ($\dot{Q}max$). During the same protocol heart rate (HR) was measured by cardiotachography. The stroke volume of the heart (SV) was calculated as the ratio of $\dot{Q}$ to HR. The overall arteriovenous difference for oxygen, $(Ca\text{-}Cv\text{-})O_2$, was calculated as the ratio of $\dot{V}O_2$ to $\dot{Q}$.

Hematologic Data

Blood hematocrit (Hct) and hemoglobin concentration (Hb) were determined by standard laboratory techniques. The hemoglobin flow ($M_{.Hb}$) was then calculated as the product of Hb times $\dot{Q}$.

Subjects

Six subjects, all experienced climbers who participated in the 1986 Swiss Expedition to Mount Everest, volunteered for the present study and signed an informed consent. Their physical characteristics appear in Table 1. They were tested in Magglingen ($\dot{V}O_2max$) and in Geneva ($\dot{Q}$) before departure and 3 weeks after return to sea level. Details

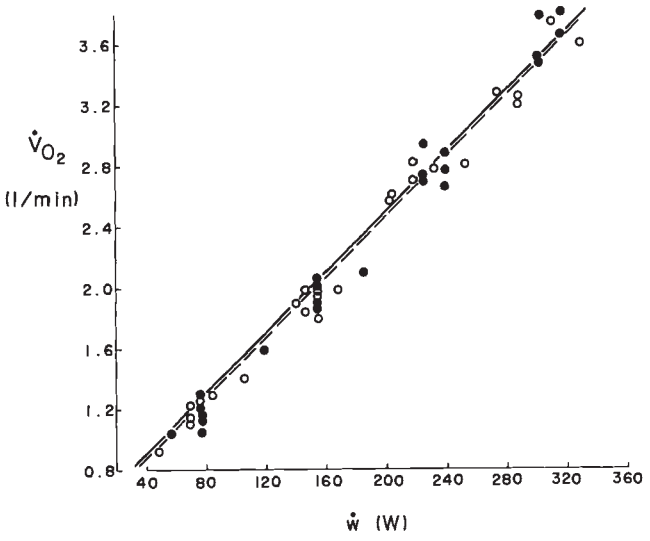

Fig. 1 O_2 consumption ($\dot{V}O_2$) as a function of the work rate ($\dot{w}$) in B (●) and in A (○). In B, $\dot{V}O_2 = 0.44 + 0.010\,\dot{w}$, $r = 0.993$, $n = 24$. In A, $\dot{V}O_2 = 0.32 + 0.011\,\dot{w}$, $r = 0.993$, $n = 24$. The two equations are not statistically different ($2P > 0.10$ for both the slope and the intercept).

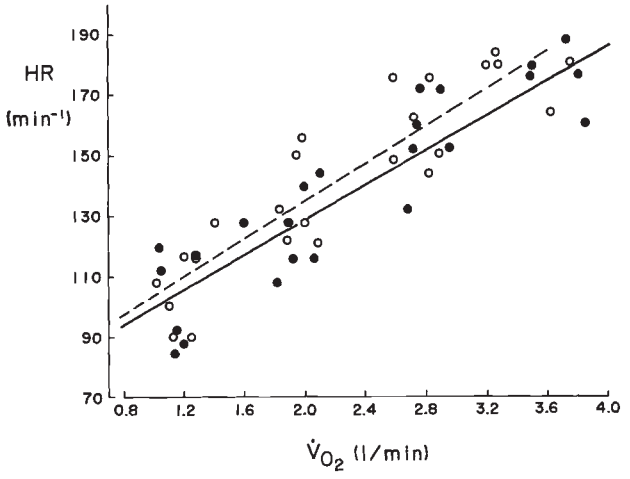

Fig. 2 Heart rate (HR) as a function of $\dot{V}O_2$ in B (●) and in A (○). In B, $HR = 71.44 + 28.45\,\dot{V}O_2$, $r = 0.905$, $n = 24$. In A, $HR = 72.66 + 31.07\,\dot{V}O_2$, $r = 0.894$, $n = 24$. The two equations are not statistically different.

of expedition and altitude exposure timing appear in paper I (7).

Results

Body Weight and $\dot{V}O_2$max

Individual data of body weight (BW) and $\dot{V}O_2$max before (B) and after (A) the expedition appear in Table 1. BW was 73.1 ± 4.8 kg in B and 69.9 ± 57 kg in A ($2P < 0.10$). $\dot{V}O_2$max was 4.39 ± .039 l ± min^{-1} in B and 4.13 ± 0.67 l·min^{-1} in A. In A the decrease in $\dot{V}O_2$max was slightly greater ($\Delta\ \dot{V}O_2max = -5.9\%$; $2P < 0.10$) than the drop in BW. Once standardized per Kg of BW, $\dot{V}O_2$max decreased from 60 ± 3.3 ml·min^{-1} in B to 59 ± 7.2 ml·Kg^{-1}·min^{1} in A ($2P > 0.10$). At the highest speed Lab was 7.68 ± 3.03 mM and 8.29 ± 1.43 mM in B and A, respectively, the difference being not significant ($2P > 0.10$).

On the bicycle ergometer the maximum measured $\dot{V}O_2$ ($\dot{V}O_2$ peak) was 3.53 ± 0.34 l·min^{1} in B and 3.28 ± 0.41 l·min^{-1} in A (Table 2), i. e., 80.4% and 79.4% of $\dot{V}O_2$max, respectively. The corresponding work loads were 295 ± 29 and 281 ± 43 W in B and A, respectively ($2P > 0.10$). The decrease in $\dot{V}O_2$ peak in A was slightly greater than that in $\dot{V}O_2$max ($\Delta\ \dot{V}O_2$ peak $= -7.1\%$; $2P < 0.10$). At any given submaximal work load, equal values for $\dot{V}O_2$ were found in B and in A (Fig. 1), the net mechanical efficiency being 0.267 ± 0.022 and 0.254 ± 0.019, respectively.

Hemodynamic Parameters

Individual data of heart rate on the bicycle ergometer (HR) in B and in A are plotted in Fig. 2 as a function of $\dot{V}O_2$. The resulting linear relationships are not statistically different ($2P > 0.10$). Maximal HR was 175 ± 9 min^{-1} in B and 178 ± 7 in A ($2P > 0.10$).

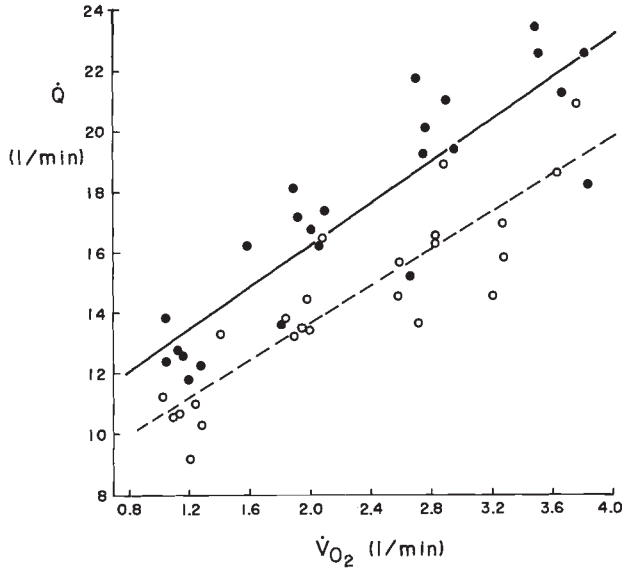

Fig. 3 Cardiac output ($\dot{Q}$) as a function of $\dot{V}O_2$ in B (●) and in A (○). In B, $\dot{Q} = 9.264 + 3.50\,\dot{V}O_2$, $r = 0.881$, $n = 24$. In A, $\dot{Q} = 7.495 + 3.05\,\dot{V}O_2$, $r = 0.886$, $n = 24$. The two lines appear to be parallel. ($2P > 0.10$ for the slope, and $2P < 0.10$ for the intercept).

In both B and A the relationship between cardiac output ($\dot{Q}$) and $\dot{V}O_2$ can be approximated by a straight line (Fig. 3). The two lines have almost indentical slope but different intercepts ($2P < 0.10$) so that at any given submaximal work load, $\dot{Q}$ is lower in A by ~ 2–3 l·min^{-1}. Maximal $\dot{Q}$ ($\dot{Q}$max) was 21.81 ± 1.27 l·min^{-1} and 16.89 ± 2.49 l·min^{-1} in B and A, respectively (Table 2), the difference ($\Delta\dot{Q}max = -22.6\%$) being highly significant ($2P < 0.01$).

Since HR is the same in B and in A, the drop in $\dot{Q}$ must be due to an equivalent reduction in stroke volume (SV). Maximal calculated SV was 124 ± 7 ml in B and 95 ± 15

Table 3 Hematologic variables before and after the expedition

Subj.	Hb ($g \cdot l^{-1}$)		HCt (%)		$\dot{M}_{Hb}$ ($g \cdot min^{-1}$)	
	Before	After	Before	After	Before	After
GF	140	168	41	48	3161	2441
LM	145	157	41	43	3399	3278
MR	130	168	40	48	2884	2443
RA	146	170	40	46	3291	2693
RM	145	159	44	45	3080	2695
WF	148	150	42	44	2957	2790
$\bar{x}$	142	162	41	46	3129	2723
SD	7	8	2	2	196	307
Δ (%)	+14.1		+12.2		−13.0	
t	3.75		3.52		− 4.22	
$2P$	< 0.05		< 0.05		< 0.01	

ml in A (Table 2), the value in A being 23.4% less than in B ($2P < 0.01$).

Maximal arteriovenous differences for O_2, $(Ca-\bar{C}v-)O_2$, were about 20% higher in A than in B, amounting to 162 ± 19 ml O_2/l and to 195 ± 16 ml O_2/l, respectively ($2P < 0.01$). When $(Ca-\bar{C}v)O_2$ was expressed relative to the maximal blood O_2-carrying capacity, the calculated values were much closer (0.84 ± 0.087 and 0.90 ± 0.072 in B and A, respectively) but still significantly different ($2P < 0.10$).

Hematologic Data

Blood hemoglobin concentration (Hb) and hematocrit (Hct) are given in Table 3. Hb was 142 ± 7 $g \cdot l^{-1}$ in B and 162 ± 8 $g \cdot l^{-1}$ in A. Similarly, Hct increased from 41 ± 2% in B to 46 ± 2% in A. Thus, Hb and Hct were 14.1% and 12.2% greater in A than in B, the difference being significant in both cases ($2P < 0.10$).

The relationship between the hemoglobin flow, $\dot{M}_{Hb}$ and $\dot{V}O_2$ is described in Fig. 4. For submaximal $\dot{V}O_2$ values, no difference between B and A was observed, the two lines being statistically equal ($2P > 0.10$).

However, since the reduction in $\dot{Q}$max was greater than the increase in Hb, the maximal hemoglobin flow, $\dot{M}_{Hb}$, max = max ± Hb, appeared to be 13% lower in A (2,723 ± 307 $g \cdot min^{-1}$) than in B (3,129 ± 196 $g \cdot min^{-1}$) ($2P < 0.01$).

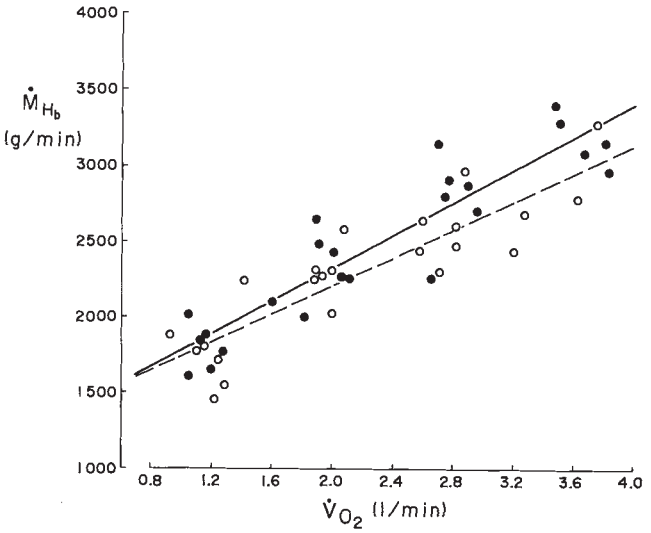

Fig. 4 Hemoglobin flow ($\dot{M}_{Hb}$) as a function of $\dot{V}O_2$ in B (●) and in A (○). In B, $\dot{M}_{Hb} = 1239 + 540\,\dot{V}O_2$, $r = 0.915$, $n = 24$. In A, $\dot{M}_{Hb} = 1280 + 463\,\dot{V}O_2$, $r = 0.881$, $n = 24$. The two equations are not statistically different.

Discussion

Maximal O_2 Consumption and Maximal Cardiac Output

The maximal O_2 consumption ($\dot{V}O_2$max) in B appeared to be greater than that of sedentary untrained subjects of the same age (2) and equal to that of world-class climbers (15). The observed values of $\dot{V}O_2$max and of maximal cardiac output (Table 2) permit a classification of the present subjects as nonathletic well-trained individuals (6). These data therefore confirm the conclusions drawn by Oelz et al. (15) that a very high $\dot{V}O_2$max is not the most critical physiological parameter required for successful Himalayan climbers. Actually, the best climbers in the world and the present subjects, who incidentally failed to reach the summit of Mt. Everest, have the same $\dot{V}O_2$max.

Upon return from the expedition, absolute $\dot{V}O_2$max was slightly but significantly lower than before departure, whereas specific $\dot{V}O_2$max (in $ml \cdot min^{-1} \cdot kg^{-1}$) was practically unchanged. In conditions similar to those of the present study, Cerretelli (4) found slightly higher values of $\dot{V}O_2$max after acclimatization. He observed, however, that $\dot{V}O_2$max was less than that expected, ceteris paribus, from the observed increase in blood hemoglobin due to acclimatization. His data are confirmed also by the present study, showing that $\dot{V}O_2$max did not incrase in A in spite of a 14% increase in blood hemoglobin. Such an increase, in fact, was offset by a concomitant 23% reduction in maximal cardiac output, resulting in a reduced maximal hemoglobin flow.

On the bicycle ergometer the peak observed $\dot{V}O_2$ values were 20% lower than treadmill $\dot{V}O_2$max, both in B and in A. This might be due to either the exercise mode or to the characteristics of the ergometer. In fact, (1) since during cycling the working muscles are contracted for a longer time than in running, lactate starts accumulating in muscles at lower work loads; and (2) during cycling a smaller muscle mass is utilized than during running.

$\dot{Q}$max in A appears to be markedly reduced with respect to B (Table 2). This reduction is much greater than that of $\dot{V}O_2$max, suggesting that an increased $(Ca-\bar{C}v)$ O_2 partially compensates for the reduced $\dot{Q}$max. The rather low $\dot{Q}$max values observed in A may raise some doubts. However, the measurements of $\dot{Q}$max in the present study have been obtained by means of a CO_2 rebreathing technique reported to be very reliable with respect to other methods (10). In addition,

1. the $\dot{Q}$ vs $\dot{V}O_2$ relationship in B is not significantly different from previous values reported in the literature (6)
2. $\dot{Q}$max is pretty close to the average values reported in the literature for trained nonathletic subjects (9)

Table 4 O_2 transport before (B) and after (A) the expedition

$\dot{V}O_2$ ($l \cdot min^{-1}$)		$\dot{Q}O_2$ ($l \cdot min^{-1}$)		$\dot{V}O_2/\dot{Q}O_2$ (Ca-Cv)O_2		$\dot{W}$ (%)
B	A	B	A	B	A	
1.14	1.15	2.40	2.27	0.48	0.51	25
1.88	1.86	3.11	3.06	0.60	0.61	50
2.65	2.63	3.59	3.41	0.74	0.77	75
3.53	3.28	4.19	3.65	0.84	0.90	100

O_2 uptake ($\dot{V}O_2$ flow ($\dot{Q}O_2$) and extraction ($\dot{V}O_2/\dot{Q}O_2$) at given submaximal loads (W.). $\dot{Q}O_2$ is calculated from Hb, assuming that 1 g of Hb links 1.34 ml O_2.

3. the calculated $(Ca–\bar{C}v)O_2$ difference for A is within the expected physiological range.

Chronic exposure to hypoxia increased Hb and Hct (see Table 3), consistent with the data reported by others (3–5). However, the remarkable decrease in Qmax (–22%, Table 2) more than compensated for the increased Hb and Hct so that O_2 transport by blood convection ($\dot{Q}O_2$) was smaller in A than in B (–13%). This clearly explains why $\dot{V}O_2$max did not increase in A. On the contrary, after the finding that chronic hypoxia deteriorates muscle function, as shown by the reported decrease in mitochondrial density and in the activity of oxidative enzymes (12, 13), one should expect a greater decrease in both $\dot{V}O_2$max and $\dot{V}O_2$ peak than in $\dot{Q}O_2$. This was not the case in the present study since $\dot{V}O_2$max and $\dot{V}O_2$ peak decreased by 6%–7% only. Therefore, the deteriorated muscle function had to be compensated for by some other factor than facilitated O_2 flow. Such a factor could be the increased capillary density consequent to the reduced muscle fiber size (12), which enhances O_2 diffusion from the capillaries to the mitochondria.

Regulation of O_2 Transport at Submaximal Exercise

At any submaximal work load, the muscles take up as much oxygen as they need, either in normoxia, or in acute hypoxia, chronic hypoxia, and acute normoxia (present subjects in A), irrespective of CaO_2. By contrast, at any given work load, $\dot{Q}$ in A is 2–3 l/min less than in B so that the relationship between $\dot{Q}$ and $\dot{V}O_2$ in acute normoxia is shifted downward (Fig. 3). On the other hand, in acute hypoxia (20) the $\dot{Q}$ vs $\dot{V}O2$ relationship is shifted upward, whereas after acclimatization to chronic hypoxia, the $\dot{Q}$ vs $\dot{V}O_2$ relationship is the same as in normoxic conditions (4, 16, 18, 19).

The series of events determining the reported shifts of the Q/vs $\dot{V}O_2$ relationship can be described as follows. When PIO_2 is suddenly decreased, e. g., from 159 to 97 Torr (20), SaO_2 at a 100 W work level decreases from 0.96 to 0.71. Therefore, $\dot{Q}O_2$ decreases, and O_2 extraction increases, thus leading to a lower $P\bar{v}O_2$. Prehypoxic values of $\dot{Q}O_2$, O_2 extraction, and $P\bar{v}O_2$ are then reestablished by a corresponding increase in $\dot{Q}$, which compensates for the decreased SaO_2. These series of adjustments result in a $\dot{Q}$ vs $\dot{V}O_2$ relationship shifted upward. If the exposure to hypoxia is prolonged, the synthesis of erythropoietin is stimulated (1, 8), which in turn increases Hb. This adaptation tends to increase $\dot{Q}O_2$, to reduce O_2 extraction, and to increase $P\bar{v}O_2$. The readjustment of these parameters leads to a corresponding reduction in $\dot{Q}$ so

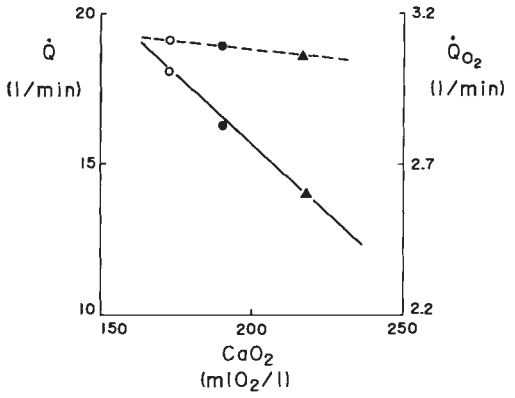

Fig. 5 Cardiac output ($\dot{Q}$, left ordinate, continuous line) and O_2 flow ($\dot{Q}O_2$, right ordinate, dashed line) as a function of CaO_2 at a work rate of 140 W (50% of present subjects' $\dot{V}O_2$peak). O, acute hypoxia, from Stenberg et al. (22). ● and ▲ are the present data in normoxia and acute normoxia, respectively.

that in chronic hypoxia the relationship between $\dot{Q}$ and $\dot{V}O_2$ is equal to that observed in normoxia (16, 18, 19). A sudden return to sea level, as in the present study in A, moves SaO_2 back to 1. However, since $\bar{Hb}$ is still elevated, this would lead to an increase in $\dot{Q}O_2$ and $P\bar{v}O_2$ and a decrease in O_2 extraction. These changes are modulated by a reduction in $\dot{Q}$. As a result, the $\dot{Q}$ vs $\dot{V}O_2$ relationship in acute normoxia is shifted downward with respect to normoxia (Fig. 3), whereas $\dot{Q}O_2$ and O_2 extraction are practically unchanged (Table 4). Thus, on the one hand, the $\dot{Q}$ vs $\dot{V}O_2$ relationship for a given PIO_2 appears to be affected by changes in the Hb concentration (normal PO_2, normoxia vs acute normoxia; low PO_2, acute hypoxia vs chronic hypoxia). On the other hand, for a given Hb concentration, the $\dot{Q}$ vs $\dot{V}O_2$ relationship is affected by changes in PIO_2 (normal Hb, normoxia vs acute hypoxia; high Hb, chronic hypoxia vs acute normoxia).

In conclusion, at any given work load, $\dot{Q}$seems to be regulated in such a way as to keep $\dot{Q}O_2$ constant, independent of CaO_2. This is shown in Fig. 5, where $\dot{Q}$ and $\dot{Q}O_2$ are plotted as a function of CaO_2, for a work load of 140 W, corresponding to 50% of the present subjects' $\dot{V}O_2$max. $\dot{Q}$ is negatively related to CaO_2: it increases by 93 ml/min per 1 ml/l decrease in CaO_2. On the other hand, the $\dot{Q}O_2$ vs CaO_2 relationship is practically parallel to the abscissa.

On these bases, it is tempting to postulate that, for any given work load, the absolute $\dot{Q}$ level is set not only by the work intensity, but also by CaO_2. If it is so, then

1. the position of the $\dot{Q}$ vs CaO_2 function should be set by (e. g.) $P\bar{v}O_2$-sensitive receptors (11) and/or other peripheral and/or central mechanisms assumed to regulate $\dot{Q}$ as a function of the work intensity
2. the slope of the $\dot{Q}$ vs CaO_2 line of Fig. 5 (93 ml/min per ml/l) indicates the gain of the system, which finely tunes $\dot{Q}$ on the basis of CaO_2
3. the carotid body can be viewed as the sensor organ responsible for this fine tuning.

However, what the carotid body is sensitive to (reduced PaO_2, CaO_2, or carotid body $\dot{Q}O_2$, see 11, 14) is un-

clear: sensitivity to PaO_2 alone is to be ruled out as it would not be compatible with the present data. The stimulation of the receptor, on the other hand, may lead to changes in $\dot{Q}$, mediated by combined changes in the sympathetic and in the vagal activity. Indeed, in the present "acute normoxia" condition (A), HR is essentially the same as in normoxia (B), whereas the SV is lower. This is compatible with a normal sympathetic tone and a reduced vagal tone.

Conclusions

The present experiments have shown that, upon return from a 10-week altitude exposure, $\dot{V}O_2max$ is slightly decreased (−5.9%), whereas $\dot{Q}max$ is decreased by a greater extent (−22.6%), thus, more than compensating for the increase in Hb (+ 14.1%) and in Hct (+ 12.2%). The drop of $\dot{Q}max$ follows a reduction in SV rather than in HR, and it leads to greater $(Ca-\bar{C}v)O_2$ differences. At submaximal exercise, $\dot{V}O_2$ is equal to that in the control condition before departure, whereas $\dot{Q}$ is 2–3 $l \cdot min^{-1}$ lower. The decrease in $\dot{Q}$ compensates for the higher O_2 concentration (or lower, $Pv-O_2$) associated with increased Hb. This allows O_2 transport at any given submaximal work load to be practically constant.

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Dr. G. Ferretti

Dept. of Physiology
C. M. U. Rue Michel-Servet 1
CH-1211 Geneve 4
Switzerland