JOURNAL OF APPLIED PHYSIOLOGY
Vol. 39, No. 3, September 1975. *Printed in U.S.A.*

Effect of altitude relocations upon $AaDo_2$ at rest and during exercise

JULIO C. CRUZ, L. HOWARD HARTLEY, and JAMES A. VOGEL
US Army Research Institute of Environmental Medicine, Natick, Massachusetts 01760

CRUZ, JULIO C., L. HOWARD HARTLEY, AND JAMES A. VOGEL. *Effect of altitude relocations upon $AaDo_2$ at rest and during exercise.* J. Appl. Physiol. 39(3): 469–474. 1975.—The supine pulmonary venous admixture (shunt) has been measured at Cerro de Pasco, 4,350 m altitude in eight subjects native to high altitude (HAN) under resting condition. Alveolar-arterial O_2 tension difference ($AaDo_2$) was also determined at rest and during exercise. The same subjects were studied again after 10 days' sojourn at sea level in Lima at 150 m altitude. They were compared with four subjects from sea level (SLN) who were studied first at Lima and after 2 and 10 days at Cerro de Pasco. At altitude, $AaDo_2$ was smaller in HAN than SLN both at rest and during exercise. Shunt was the same in both groups. It is concluded that HAN show more even ventilation/perfusion relationship ($\dot{V}A/\dot{Q}$) at altitude, probably due to their high pulmonary artery pressure. On the contrary, SLN show less even $\dot{V}A/\dot{Q}$ on altitude exposure, since their shunt decreased 37%. At sea level, HAN increased their $AaDo_2$ due partially to an increase of 110% in their shunt, and in part due to less even $\dot{V}A/\dot{Q}$ as shown by augmented VD/VT ratios. Each group tended to have a more effective gas exchange in its own environment.

pulmonary venous admixture; alveolar gas exchange; high-altitude natives

THE EFFECTIVENESS OF THE LUNGS in the process of blood oxygenation can be estimated by measuring the alveolar-arterial O_2 pressure difference ($AaDo_2$). The factors which are responsible for the $AaDo_2$ are *1*) diffusion limitation, *2*) true venous admixture (shunt), and *3*) uneven distribution of the ratios of alveolar ventilation to the blood lung perfusion ($\dot{V}A/\dot{Q}$). The $AaDo_2$ has been found to be less in high-altitude natives than sojourners (12, 18). Although the data of Kreuzer et al. (19) indicated just the opposite, the large gradient observed by them has been attributed to unrecognized pulmonary disease in some of their subjects (22).

Oxygen and carbon monoxide diffusion capacities through the lung (DL_{O_2}, DL_{CO}) have been measured by various investigators (7, 11, 28, 34) and found to be greater in high-altitude natives than in sea-level natives. The purpose of this paper is to evaluate the extent of pulmonary arteriovenous (a-v) shunt and to infer the contribution of the $\dot{V}A/\dot{Q}$ relationship to the low $AaDo_2$ of high-altitude natives. This was approached by directly estimating the shunt with the administration of 100% O_2, and determining the changes in $AaDo_2$ with exercise and sea-level sojourn in high-altitude natives. A group of sea-level natives were also studied by the same techniques and at the same altitudes.

MATERIAL AND METHODS

Eight subjects who were native to elevations above 4,000 m (HAN) were studied first at Cerro de Pasco (4,350 m) in the highlands of Peru, and again after 10 days of sojourn at sea level (Lima, 150 m). They were compared with four medical students native to sea level (SLN) who were of comparable age, but whose height and weight averaged more than HAN. The physical characteristics of both groups are given in Table 1. All subjects were considered to be healthy by physical and radiological examinations. The SLN were examined first at sea level and again after 2 and 10 days of sojourn at altitude. All subjects were carefully informed of the nature of the procedures and its complications, and they gave written consent.

Resting studies were performed with the subjects in the supine position. One hour prior to the measurements a 10 cm polyethylene catheter was inserted percutaneously into the brachial artery and the antecubital vein. Cardiac output was determined by the injection of a bolus of 5–7.5 mg of indocyanine green into the venous catheter, the tip of which was at the axillary vein. Dye curves were inscribed by drawing arterial blood at 30 ml/min through a recording densitometer. The subjects breathed through a large-bore mouthpiece and an Otis-McKerrow valve. Expired gas was collected for 5 min in Douglas bags and measured in a Tissot spirometer, and then analyzed for O_2 and CO_2 fraction using the micro-Scholander technique. Arterial blood samples were taken at the time of oxygen uptake. These samples were analyzed for oxygen content and saturation by the Van Slyke procedure and for gas tensions with the appropriate electrodes (Instrumentation Laboratory).

Exercise studies were performed in the sitting position on a mechanically braked bicycle ergometer (Monark) at a pedal rate of 50 rpm. Work loads were used which had been determined from several preliminary exercise studies to approximate 50, 75 and 100% of maximal oxygen uptake. Maximal oxygen uptake was determined by performance of increasing work loads until the oxygen uptake did not increase despite an increase in work intensity.

To calculate the shunt the subjects breathed 100% oxygen for 15 min through the same setup used in room air measurements. During the last 2 min, arterial blood samples were taken for oxygen content and gas tensions, and dye dilution curves of cardiac output were recorded. $\dot{V}o_2$ was

TABLE 1. *Physical characteristics of subjects*

Subj	Age, yr	Height, m	Weight, kg	Hematocrit, %
		Sea level		
Vel	22	1.70	72	45.5
Ris	21	1.74	75	43.8
San	20	1.87	76	44.3
Rea	21	1.73	67	43.8
Mean	21.0	1.76	72.5	44.4
±SE	±0.4	±0.04	±2.0	±0.4
		High altitude		
Bra	21	1.59	56.1	51.5
Val	20	1.60	56.2	55.5
Jan	19	1.55	63.0	58.7
Roj	20	1.56	51.1	47.6
Lec	25	1.68	75.5	46.5
Pad	20	1.55	59.0	47.5
Tri	20	1.65	55.1	52.4
Zar	28	1.66	69.0	49.4
Mean	21.6	1.61	60.6	51.1
±SE	±1.1	±0.02	±2.9	±1.5
P	<0.70	<0.01	<0.05	<0.02

assumed to be the same as previously measured breathing room air.

The alveolar oxygen tension was calculated from the alveolar gas equation using the Pa_{CO_2} and the respiratory quotient. During 100% oxygen breathing this formula was modified as follows: $P_{A_{O_2}} = P_{I_{O_2}} - Pa_{CO_2}$. The shunt was calculated as $\dot{Q}s/\dot{Q}t = (P_{A_{O_2}} - Pa_{O_2}) \times 0.0031/[Ca_{O_2} - C\bar{v}_{O_2} + (P_{A_{O_2}} - Pa_{O_2}) \times 0.0031]$ where $\dot{Q}s/\dot{Q}t$ is the ratio of the magnitude of the shunt to total pulmonary blood flow and 0.0031 is the Bunsen O_2 solubility coefficient at 37°C. Mixed venous oxygen content was calculated as $C\bar{v}_{O_2} = Ca_{O_2} - \dot{V}O_2/\dot{Q}$ where $\dot{V}O_2$ is the oxygen uptake and $\dot{Q}$ = cardiac output. Dead space-to-tidal volume ratio (V_D/V_T) was calculated using Pa_{CO_2} according to the formula $V_D/V_T = (Pa_{CO_2} - P_{E_{CO_2}})/Pa_{CO_2}$. All symbols which are used are those commonly accepted as standard (24) and those recently approved by the International Union of Physiological Sciences Committee on Nomenclature (5).

RESULTS

Data obtained while breathing 100% oxygen at rest in the supine position appear in Table 2. Values for ventilation, O_2 and CO_2 tensions, Ca_{O_2}, pH, V_D/V_T, and heart rate obtained in HAN are shown in Table 3, and for SLN in Table 4. More extensive cardiovascular measurements in these subjects are reported elsewhere (35, 36).

Studies at high altitude. Pulmonary ventilation was greater in HAN than in SLN at rest ($P < 0.05$). The arterial P_{CO_2} was not different between the two groups. During exercise, the pulmonary ventilation was different between the groups only during heavy work loads, and at an O_2 uptake of 2.4 l/min the greater values of SLN were statistically significant ($P < 0.02$). This $\dot{V}O_2$ represents maximal oxygen uptake to SLN at altitude but only 78% of $\dot{V}O_{2\,max}$ for HAN. Therefore the higher ventilation of SLN is in part due to more intensive work. The mean values of $AaDo_2$ at rest were smaller in HAN than in SLN ($P < 0.02$) and during all levels of exercise (Fig. 1). The pulmonary a-v shunts at supine rest were similar in both groups (Table 2).

Sea-level natives did not show significant changes in the resting values of $AaDo_2$ with altitude exposure, but during exercise they were clearly greater for a given O_2 uptake compared to sea-level determinations (Fig. 1). No difference between the 2nd and 10th day was found. Pulmonary a-v shunt was 37% lower ($P < 0.05$) than sea-level control (Table 2).

Studies at sea level. Ventilation was lower at sea level as compared with altitude measurements in both groups, at rest and during exercise. No significant differences were found in ventilation at sea level between the groups either at rest or during exercise. The mean $AaDo_2$ increased in HAN both at rest and during exercise ($P < 0.01$) when they moved to sea level (Fig. 1), and the pulmonary a-v shunt increased from their high-altitude control (Table 2) by 110% ($P < 0.001$).

DISCUSSION

Alveolar-arterial O_2 pressure difference ($AaDo_2$) apparently increases in acute exposure to altitude (27). However data from the literature (12, 15, 16, 21, 26) indicate that $AaDo_2$ decreases toward control values with more prolonged stay (Fig. 2). Our data suggest that this may also occur during exercise (Table 4).

Studies at high altitude. The usual difference in resting ventilation between high-altitude natives (HAN) and sea-level natives (SLN) at altitude observed by others (18, 23, 31) was not seen in this study. This was due to the fact that both groups of subjects ventilated more than is usual at 4,350 m.

This study shows that the $AaDo_2$ of HAN is clearly less than SLN, both at rest and during exercise at high altitude (Fig. 1). This finding is in agreement with the published observations of others (12, 18, 31). The greater diffusion capacity of the lung for O_2 (7, 34) and CO (7, 11, 28) in

TABLE 2. *Data obtained during 100% oxygen breathing at rest*

Subj	Place of Study	$P_{A_{O_2}}$, mmHg	$AaDo_2$, mmHg	Ca_{O_2}, vol %	$(Ca-Cv)_{O_2}$, vol %	$\dot{Q}$, l/min	$\dot{Q}s/\dot{Q}t$, %
High altitude	Cerro de Pasco	390 ±2.3	119 ±9.7	23.96 ±0.57	7.01 ±0.39	5.17 ±0.30	5.0 ±0.4
	Lima (after 10 days)	676 ±0.7	210 ±5.5	23.26 ±0.57	5.63 ±0.27	5.43 ±0.27	10.5 ±0.4
(8)	Cerro de Pasco vs. Lima, *P*	<0.001	<0.001	<0.025	<0.020	<0.60	<0.001
Sea level	Lima	670‡ ±2.0	177 ±32.1	21.50 ±0.20	5.37 ±0.22	7.27 ±1.01	9.1 ±1.2
	Cerro de Pasco (after 2 days)	385 ±0.5	118 ±3.6	21.35† ±0.57	5.44* ±0.50	6.56 ±0.74	6.4 ±0.6
(4)	Cerro de Pasco (after 10 days)	388 ±2.9	120 ±7.2	21.90* ±0.61	6.27 ±0.33	5.54 ±0.32	5.7 ±0.5

Values are means ± SE. Means were significantly different from the high-altitude group at the corresponding place of study. * $P < 0.05$. † $P < 0.02$. ‡ $P < 0.005$.

TABLE 3. *Pulmonary gas exchange at rest and during exercise in high-altitude natives studied at Cerro de Pasco and Lima*

		Rest	Exercise 1	Exercise 2	Max Exercise
$\dot{V}_{EBTPS}$, l/min	Cerro de Pasco	21.44 ± 2.33	69.11 ± 6.13	106.12 ± 5.34	151.57 ± 9.54
	Lima	11.61 ± 0.81	51.85 ± 2.63	74.07 ± 3.79	135.14 ± 8.28
Pa_{CO_2}, mmHg	Cerro de Pasco	24.5 ± 1.7	24.1 ± 0.9	22.9 ± 0.8	21.5 ± 0.7
	Lima	34.2 ± 1.3	37.1 ± 1.1	34.3 ± 1.3	31.1 ± 1.4
Pa_{O_2}, mmHg	Cerro de Pasco	55.0 ± 2.5	50.6 ± 1.1	46.9 ± 1.1	47.1 ± 1.4
	Lima	94.1 ± 3.5	90.6 ± 2.5	91.1 ± 2.3	96.1 ± 1.4
Ca_{O_2}, vol %	Cerro de Pasco	21.88 ± 0.76	21.08 ± 0.59	20.25 ± 0.42	20.02 ± 0.37
	Lima	20.81 ± 0.47	21.61 ± 0.50	21.65 ± 0.46	23.05 ± 0.55
pH	Cerro de Pasco	7.540 ± 0.013	7.509 ± 0.012	7.455 ± 0.009	7.379 ± 0.012
	Lima	7.460 ± 0.013	7.411 ± 0.009	7.386 ± 0.017	7.288 ± 0.014
V_D/V_T, %	Cerro de Pasco	31.7 ± 4.3	18.8 ± 2.4	12.7 ± 1.6	10.3 ± 1.9
	Lima	38.7 ± 1.7	27.6 ± 2.9	19.1 ± 2.2	17.0 ± 2.7
Heart rate, beats/min	Cerro de Pasco	62.1 ± 3.1	110.3 ± 3.5	150.8 ± 3.6	176.4 ± 3.0
	Lima	53.6 ± 0.9	101.8 ± 3.6	139.1 ± 4.9	179.2 ± 2.9

Values are means ± SE.

TABLE 4. *Pulmonary gas exchange at rest and during exercise in sea-level subjects studied at Lima and Cerro de Pasco*

		Rest	Exercise 1	Exercise 2	Max Exercise
$\dot{V}_{EBTPS}$, l/min	Lima	10.24 ± 0.56	33.41 ± 3.35	60.14 ± 8.62	121.09 ± 10.64
	Cerro de Pasco (2 days)	14.48 ± 3.69	34.17 ± 2.54	55.50 ± 10.38	145.14 ± 13.09
	Cerro de Pasco (10 days)	14.25 ± 2.41	41.16 ± 1.95	60.38 ± 10.03	138.74 ± 11.50
Pa_{CO_2}, mmHg	Lima	39.3 ± 2.3	39.2 ± 1.8	39.5 ± 1.9	34.5 ± 3.0
	Cerro de Pasco (2 days)	28.2 ± 1.1	28.6 ± 1.5	25.4 ± 1.7	20.3 ± 2.4
	Cerro de Pasco (10 days)	23.7 ± 1.3	22.8 ± 1.4	22.5 ± 1.1	18.9 ± 1.5
Pa_{O_2}, mmHg	Lima	92.9 ± 2.6	90.1 ± 1.5	84.2 ± 2.9	88.6 ± 5.8
	Cerro de Pasco (2 days)	41.5 ± 1.4	40.4 ± 1.9	38.2 ± 1.4	40.4 ± 1.4
	Cerro de Pasco (10 days)	47.6 ± 1.8	45.6 ± 2.8	44.1 ± 2.2	47.3 ± 3.0
Ca_{O_2}, vol %	Lima	19.61 ± 0.53	20.54 ± 0.31	21.12 ± 0.46	21.50 ± 0.50
	Cerro de Pasco (2 days)	16.77 ± 1.10	16.84 ± 1.07	16.82 ± 0.98	16.56 ± 0.92
	Cerro de Pasco (10 days)	19.06 ± 0.60	19.31 ± 0.66	18.84 ± 0.56	18.75 ± 0.64
pH	Lima	7.413 ± 0.033	7.396 ± 0.013	7.365 ± 0.014	7.275 ± 0.026
	Cerro de Pasco (2 days)	7.468 ± 0.044	7.480 ± 0.007	7.492 ± 0.016	7.393 ± 0.021
	Cerro de Pasco (10 days)	7.512 ± 0.018	7.505 ± 0.009	7.493 ± 0.010	7.354 ± 0.026
V_D/V_T, %	Lima	29.9 ± 4.3	22.3 ± 3.9	19.3 ± 4.8	21.3 ± 8.3
	Cerro de Pasco (2 days)	27.2 ± 2.0	16.3 ± 1.6	14.7 ± 1.6	10.5 ± 3.2
	Cerro de Pasco (10 days)	23.0 ± 2.1	11.2 ± 3.4	12.3 ± 1.4	8.0 ± 1.2
Heart rate, beats/min	Lima	71.3 ± 3.6	109.8 ± 7.1	146.3 ± 10.6	185.3 ± 3.6
	Cerro de Pasco (2 days)	94.7 ± 5.3	117.8 ± 3.2	133.7 ± 2.4	178.8 ± 1.0
	Cerro de Pasco (10 days)	75.8 ± 2.6	115.5 ± 4.5	135.5 ± 5.2	150.8 ± 3.6
$AaDo_2$, mmHg	Lima	11.5 ± 0.27	11.0 ± 2.1	16.3 ± 1.3	20.0 ± 4.4
	Cerro de Pasco (2 days)	14.5 ± 2.1	15.5 ± 2.3	22.6 ± 2.3	28.5 ± 2.3
	Cerro de Pasco (10 days)	12.7 ± 2.1	16.5 ± 2.6	18.8 ± 3.0	22.8 ± 3.7

Values are means ± SE.

HAN than SLN at altitude would explain in part their small $AaDo_2$. However, estimates of $AaDo_2$ due to $D_{L_{O_2}}$ are negligible breathing air or low oxygen (6, 33). The supine rest pulmonary a-v shunt determined at altitude in both groups shows no statistically significant difference. Therefore, the shunt contribution to the $AaDo_2$ should be similar in both groups (see below). Thus, we infer that HAN have a better $\dot{V}_A/\dot{Q}$ than SLN at altitude. In contrast, SLN at altitude have a lower pulmonary a-v shunt (Table 2) and no change in $D_{L_{CO}}$ (4, 8, 12, 20, 37). It seems probable therefore that the unchanged $AaDo_2$ we have observed after 10 days at altitude reflects changes in $\dot{V}_A/\dot{Q}$. A similar conclusion was reached by Haab et al. (14) by measuring CO_2 and N_2 gradients at altitude. Determinations of regional lung $\dot{V}_A/\dot{Q}$ ratios with radioactive gases have shown that $\dot{V}_A/\dot{Q}$ alterations are taking place in both sea-level sojourners (9) and altitude natives of North America (10) in relation to sea-level controls. The $\dot{V}_A/\dot{Q}$ changes observed by them would be expected to occur, as explained in our discussion.

Studies at sea level. After 10 days' sea-level sojourn, HAN increased their $AaDo_2$ at rest and during exercise as compared with their altitude control (Fig. 1). However the values obtained were not different from those of SLN. This interesting finding, not reported before, could be explained in part by an increase of 110% in pulmonary a-v shunt. The magnitude of this shunt however was not different from the SLN values (Table 2). Another possible explanation for the large $AaDo_2$ at sea level of HAN would be the change of $\dot{V}_A/\dot{Q}$ as suggested by their higher V_D/V_T ratios shown at sea level ($P < 0.05$).

Role of pulmonary a-v shunt on $AaDo_2$ with altitude changes. The contribution of $D_{L_{O_2}}$ to $AaDo_2$ breathing air at sea level in resting condition is negligible (6, 33). As mentioned above, even during low oxygen breathing it is very low, i.e., 0.2 mmHg (33), in spite of an increase in $D_{L_{O_2}}$, either by

breathing low oxygen concentration at SL or by going to high altitude (7, 8). Therefore, at rest, regardless of $P_{I_{O_2}}$, $P_{A_{O_2}}$ is in equilibrium with the end capillary oxygen tension ($P_{c_{O_2}}$). Thus, it is possible to calculate the anatomical shunt contribution to AaD_{O_2} with the following equation

$$Sa = (\dot{Q}ns \cdot S_A + Qs\ S\bar{v})/\dot{Q}t$$

where Sa, S_A, and $S\bar{v}$ are oxygen saturations in arterial, pulmonary capillary, and mixed venous blood, respectively. Qns, Qs, and Qt are nonshunted, shunted, and total blood flows, respectively. S_A is read from the dissociation curve at pH_a. $S\bar{v}$ is calculated as described in the equation shown under METHODS. $\dot{Q}t$ is taken from measurements made on the same subjects by dye dilution technique (35, 36) and $\dot{Q}s$ as determined by breathing 100% O_2. The calculations show that in both SLS and HAN the AaD_{O_2} at SL due to the shunt is 2.6 and 2.5 times the actual gradient measured, respectively. Undoubtedly, this is due to the values obtained for the shunt in both groups that were too high. Since no technical problems were recognized, this may be explained by the possibility of atelectasic zones due to the prolonged supine position used (1 h), in addition to the possible role of oxygen itself. Atelectasis may also have been present at altitude.

When pulmonary a-v shunt determinations of SLN at altitude are compared with their sea-level control values, the altitude data represent a 37% reduction ($P < 0.05$). Assuming no change in the a-v shunt with altitude exposure, it can be predicted that its contribution to AaD_{O_2} is less at altitude than at sea level (Table 5). The contribution is even less as the shunt becomes smaller. Unfortunately, the shunt has not been measured at altitude as frequently as AaD_{O_2}. Kronenberg et al. (21) reported a shunt of 11% at 24 h and 7% at 72 h of altitude exposure. The latter value agrees with our 6.4 ± 0.6% determined at 48 h (Fig. 3).

Although the oxygen breathing itself, which is required to determine the shunt, may have obscured any difference that existed while breathing air, the effect seems to be the same in both groups of subjects.

Pulmonary a-v shunt in HAN and SLN were similar at the two elevations and were higher at sea level than at alti-

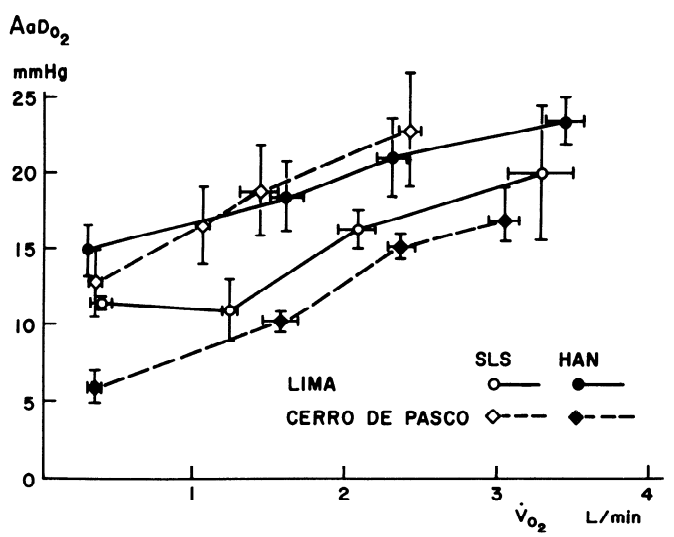

FIG. 1. Alveolar-arterial oxygen tension differences plotted as function of oxygen uptake. Bars are means ± SE. SLS: sea-level subjects; HAN: high-altitude natives. Note that each group tends to have more effective gas exchange in own environment.

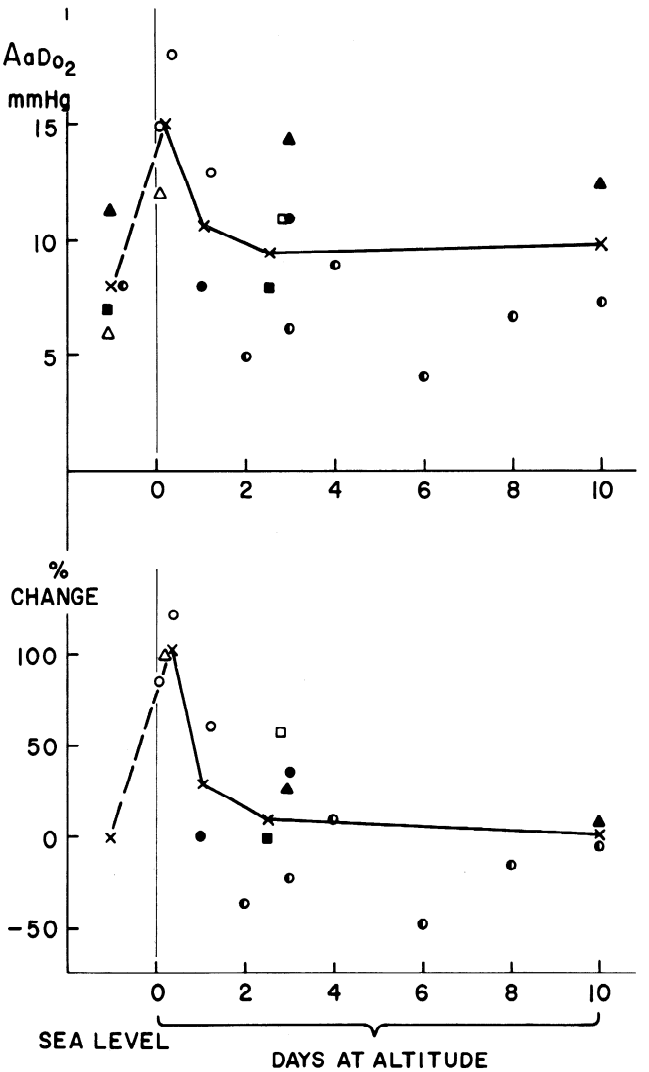

FIG. 2. Alveolar-arterial oxygen tension differences plotted against time of exposure at altitude. Data obtained from the literature: □ = Dempsey et al. (12); ■ = Hansen et al. (16); ○ = Hansen et al. (15); ● = Kronenberg et al. (21); ◐ = Raymond and Severinghaus (26); △ = Reeves et al. (27); ▲ = our data; × = averages. Lower section of figure shows above data expressed as percentage change from sea level control. References 10 and 15 do not have data at sea level. In these cases, percentage changes were calculated using average value for sea level.

TABLE 5. *Predicted AaD_{O_2} (mmHg) due to a-v pulmonary shunt based on $P_{A_{O_2}}$, cardiac output, and arterial pH measured at sea level and altitude*

Place of Study	Total AaD_{O_2}		a-v Shunt					
			2.0%		1.0%		0.5%	
	SLN	HAN	SLN	HAN	SLN	HAN	SLN	HAN
Lima	11.5	14.9	11.2	12.2	5.4	7.1	3.5	4.2
Cerro de Pasco	12.7	6.0	1.8	2.2	0.8	1.2	0.3	0.7

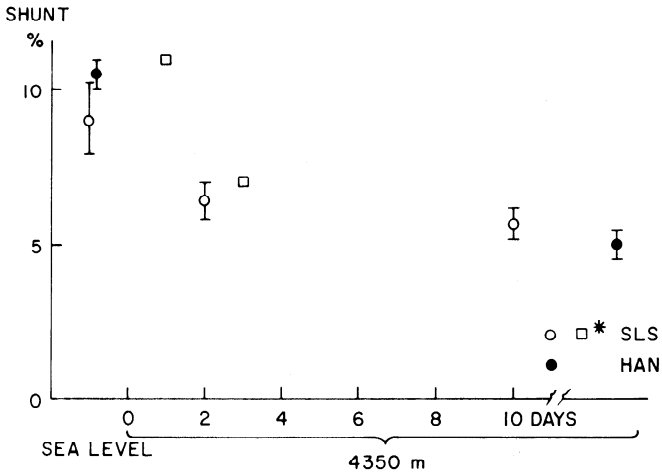

FIG. 3. Pulmonary venous admixture (shunt) plotted as function of time of exposure at altitude. SLS: sea-level subjects; HAN: high-altitude natives. * Averages reported by Kronenberg et al. (21). No significant difference was found between SLS and HAN either at sea level or at altitude.

tude (Table 2). The a-v shunt contribution to the $AaDo_2$ is also similar in both groups at both elevations, regardless of the magnitude of the shunt (Table 5). Therefore, the $AaDo_2$ differences observed between the two groups at altitude is not due to the a-v pulmonary shunt. Since $AaDo_2$ of HAN is smaller than SLN at altitude and the shunt contribution to the gradient is the same, i.e., 4.8 and 4.6 mmHg in SLN and HAN, respectively, the difference left, 7.9 mmHg and 1.4 mmHg from the total $AaDo_2$ measured, is attributed to the $\dot{V}A/\dot{Q}$ effect. The larger DL_{O_2} of HAN, explained by their larger pulmonary volumes (17) and larger alveolar surface area (13) is not expected to contribute to $AaDo_2$ more than SLN since $P_{A_{O_2}}$ will be in equilibrium with P_{CO_2} in both groups at rest.

Role of pulmonary artery pressure and cardiac output changes with altitude translocations. The principal factors that may affect the $\dot{V}A/\dot{Q}$ ratios with altitude translocations are pulmonary artery pressure and cardiac output, and the pattern of change in these two hemodynamic adjustments are different in HAN and SLN. The pulmonary artery pressure is very high at altitude in HAN (3, 25, 29) while it is only slightly elevated in SLN at altitude (1, 21, 32). On the other hand, cardiac output is lower at altitude than at sea level in SLN (1, 32, 36), but not different between the two elevations in HAN (3, 35). Thus, the less even $\dot{V}A/\dot{Q}$ relationship suggested in SLN at altitude may be due to their low pulmonary blood flow in the presence of normal pulmonary artery pressure, while HAN show a better $\dot{V}A/\dot{Q}$ due mainly to their high pulmonary artery pressure in the presence of normal pulmonary blood flow. Less even $\dot{V}A/\dot{Q}$ ratios at sea level in HAN may be explained by their decrease in pulmonary artery pressure (2) in the presence of normal cardiac output (2, 35).

In conclusion, since a small $AaDo_2$ means greater lung effectiveness in the process of blood oxygenation, the data presented in Fig. 1 suggest that each group of subjects achieved a better gas exchange in its own environment.

The authors acknowledge the help of all our technicians and assistants, especially Messrs. Wendell Bradford, Guillermo Hurtado, and Santiago Torres. We also thank Miss Claire Claffey for her aid in typing the manuscript.

This study was supported in part by Defense Research Office US Army Grant G-0001. The opinions or assertions contained herein are the private views of the author(s) and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense. This human research study, in protocol form, was reviewed and approved by the Office of The Surgeon General for the Department of the Army in accordance with Army Regulation 70-25.

J. Cruz is on leave of absence from the Insituto de Investigaciones de la Altura, Universidad Peruana Cayetano Heredia, Lima, Peru.

L. Hartley's address is: Dept. of Medicine, Harvard Medical School, Beth Israel Hospital, Boston, Mass. 02215.

Received for publication 4 October 1974.

REFERENCES

1. ALEXANDER, J. K., L. H. HARTLEY, M. MODELSKI, AND R. F. GROVER. Reduction of stroke volume during exercise in man following ascent to 3,100 m altitude. *J. Appl. Physiol.* 23: 849–858, 1967.
2. BANCHERO, N., AND J. C. CRUZ. Hemodynamic changes in the Andean native after two years at sea level. *Aerospace Med.* 41: 849–853, 1970.
3. BANCHERO, N., F. SIME, D. PENALOZA, J. CRUZ, R. GAMBOA, AND E. MARTICORENA. Pulmonary pressure, cardiac output, and arterial oxygen saturation during exercise at high altitude and at sea level. *Circulation* 33: 249–262, 1966.
4. BARCROFT, J., C. A. BINGER, A. V. BOCK, J. H. DOGGART, H. S. FORBES, G. HARROP, J. C. MEAKINS, AND A. C. REDFIELD. Observations upon the effect of high altitude on the physiological processes of the human body, carried out in the Peruvian Andes, chiefly at Cerro de Pasco. *Phil. Trans. Roy Soc., London, Ser. B* 211: 351–480, 1922.
5. BARTELS, H., P. DEJOURS, R. H. KELLOGG, AND J. MEAD. Glossary on respiration and gas exchange. *J. Appl. Physiol.* 34: 549–558, 1973.
6. CRUZ, J. C. Calculation of oxygen diffusing capacity: a new method. *IRCS, Physiol., Respiration* 2: 1627, 1974.
7. CRUZ-JIBAJA, J. C. *Alveolar Gas Exchange at Altitude.* US Army Med. Res. Rept. DAMD-17-74-G-9383, June 1974.
8. CRUZ, J. C., J. T. MAHER, L. H. HARTLEY, AND R. F. GROVER. Agreement between O_2 and CO diffusing capacity in normoxic and hypoxic conditions at sea level and high altitude. *IRCS, Physiol., Respiration* 2: 1628, 1974.
9. DAWSON, A. Regional lung function during early acclimatization to 3100 m altitude. *J. Appl. Physiol.* 33: 218–223, 1972.
10. DAWSON, A., AND R. F. GROVER. Regional lung function in natives and long-term residents at 3100 m altitude. *J. Appl. Physiol.* 36: 294–298, 1974.
11. DEGRAFF, A. C., JR., R. F. GROVER, R. L. JOHNSON, JR., J. H. HAMMOND, JR., AND J. M. MILLER. Diffusing capacity of the lung in Caucasians native to 3100 m. *J. Appl. Physiol.* 29: 71–76, 1970.
12. DEMPSEY, J. A., W. G. REDDAN, M. L. BIRNBAUM, H. V. FORSTER, J. S. THODEN, R. F. GROVER, AND J. RANKIN. Effects of acute through life-long hypoxic exposure on exercise pulmonary gas exchange. *Respiration Physiol.* 13: 62–89, 1971.
13. GARCIA-OYOLA, E., AND M. SALDANA. Morphometry of the high altitude human lung. *Proc. Int. Union Physiol. Sci.* 11: 339, 1974.
14. HAAB, P., D. R. HELD, H. ERNST, AND L. E. FARHI. Ventilation-perfusion relationships during high altitude adaptation. *J. Appl. Physiol.* 26: 77–81, 1969.
15. HANSEN, J. E., L. H. HARTLEY, AND R. P. HOGAN III. Arterial oxygen increase by high-carbohydrate diet at altitude. *J. Appl. Physiol.* 33: 441–445, 1972.
16. HANSEN, J. E., J. A. VOGEL, G. P. STELTER, AND C. F. CONSOLAZIO. Oxygen uptake in man during exhaustive work at sea level and high altitude. *J. Appl. Physiol.* 23: 511–522, 1967.

17. HURTADO, A. Animals in high altitudes: resident man. In: *Handbook of Physiology. Adaptation to the Environment.* Washington, D.C.: Am. Physiol. Soc. 1964, sect. 4, chapt 54, p. 843–860.
18. HURTADO, A., T. VELASQUEZ, C. REYNAFARJE, R. LOZANO, R. CHAVEZ, H. ASTE-SALAZAR, B. REYNAFARJE, C. SANCHEZ, AND J. MUNOZ. *Mechanisms of Natural Acclimatization.* Randolph AFB, Texas: USAF School Aviation Med. Rept. 56-I, 1956.
19. KREUZER, F., S. M. TENNEY, J. C. MITHOEFER, AND J. REMMERS. Alveolar arterial oxygen gradient in Andean natives at high altitude. *J. Appl. Physiol.* 19: 13–16, 1964.
20. KREUZER, F., AND P. VAN LOOKEREN CAMPAGNE. Resting pulmonary diffusing capacity for CO and O_2 at high altitude. *J. Appl. Physiol.* 20: 519–524, 1965.
21. KRONENBERG, R. S., P. SAFAR, J. LEE, F. WRIGHT, W. NOBLE, E. WAHRENBROCK, R. HICKLEY, E. NEMOTO, AND J. SEVERINGHAUS. Pulmonary artery pressure and alveolar gas exchange in man during acclimatization to 12,470 ft. *J. Clin. Invest.* 50: 827–837, 1971.
22. MITHOEFER, J. C., J. E. REMMERS, G. ZUBIETA, AND M. C. MITHOEFER. Pulmonary gas exchange in Andean natives at high altitude. *Respiration Physiol.* 15: 182–189, 1972.
23. MONGE, C. C., R. LOZANO, AND A. CARCELEN. Renal excretion of bicarbonate in high altitude natives and in natives with chronic mountain sickness. *J. Clin. Invest.* 43: 2303–2309, 1964.
24. PAPPENHEIMER, J. R. Standardization of definitions and symbols in respiratory physiology. *Federation Proc.* 9: 602–605, 1950.
25. PENALOZA, D., F. SIME, N. BANCHERO, R. GAMBOA, J. CRUZ, AND E. MARTICORENA. Pulmonary hypertension in healthy men born and living at high altitude. *Am. J. Cardiol.* 11: 150–157, 1963.
26. RAYMOND, L., AND J. W. SEVERINGHAUS. Static pulmonary compliance in man during altitude hypoxia. *J. Appl. Physiol.* 31: 785–786, 1971.
27. REEVES, J. T., J. HALPIN, J. E. COHN, AND F. DAOUD. Increased alveolar-arterial oxygen difference during simulated high altitude exposure. *J. Appl. Physiol.* 27: 658–661, 1969.
28. REMMERS, J. E., AND J. C. MITHOEFER. The carbon monoxide diffusing capacity in permanent residents at high altitudes. *Respiration Physiol.* 6: 233–244, 1969.
29. ROTTA, A., A. CANEPA, A. HURTADO, T. VELASQUEZ, AND R. CHAVEZ. Pulmonary circulation at sea level and at high altitudes. *J. Appl. Physiol.* 9: 328–336, 1956.
30. SALTIN, B., R. F. GROVER, C. G. BLOMQVIST, L. H. HARTLEY, AND R. L. JOHNSON, JR. Maximal oxygen uptake and cardiac output after 2 weeks at 4300 m. *J. Appl. Physiol.* 25: 400–409, 1968.
31. SEVERINGHAUS, J. W., C. R. BAINTON, AND A. CARCELEN. Respiratory insensitivity to hypoxia in chronically hypoxic man. *Respiration Physiol.* 1: 308–334, 1966.
32. SIME, F., D. PENALOZA, L. RUIZ, N. GONZALES, E. COVARRUBIAS, AND R. POSTIGO. Hypoxemia, pulmonary hypertension, and low cardiac output in newcomers at low altitude. *J. Appl. Physiol.* 36: 561–565, 1974.
33. STAUB, N. C. Alveolar-arterial oxygen tension gradient due to diffusion. *J. Appl. Physiol.* 18: 673–680, 1963.
34. VELASQUEZ, T. *Maximal Diffusing Capacity of the Lungs at High Altitudes.* Brooks AFB, Texas: USAF School Aviation Med. Rept. 56–108, 1956.
35. VOGEL, J. A., L. H. HARTLEY, AND J. C. CRUZ. Cardiac output during exercise in altitude natives at sea level and high altitude. *J. Appl. Physiol.* 36: 173–176, 1974.
36. VOGEL, J. A., L. H. HARTLEY, J. C. CRUZ, AND R. P. HOGAN. Cardiac output during exercise in sea-level residents at sea level and high altitude. *J. Appl. Physiol.* 36: 169–172, 1974.
37. WEST, J. B. Diffusing capacity of the lung for carbon monoxide at high altitude. *J. Appl. Physiol.* 17: 421–426, 1962.