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EFFECTS OF POSTURE ON PULMONARY DIFFUSION CAPACITY AND REGIONAL DISTRIBUTION OF PULMONARY BLOOD FLOW IN NORMAL MALE AND FEMALE HIGH ALTITUDE DWELLERS AT 3650 m. (12,200 ft)

H. Spielvogel, E. Vargas, G. Antezana, L. Barragan, L. Cudkowicz*

Instituto Boliviano de Biologia de Altura
Universidad Mayor de San Andrés, La Paz

* Department of Medicine, Wright State University, School of Medicine, Dayton, Ohio, U.S.A.

Previously reported observations (1, 2) concerning the distribution of pulmonary blood flow in high altitude dwellers (HAD) at La Paz, Bolivia (= 496 mmHg, altitude 3650 m or 12,200 ft) were confined to the right upper lung (RUZ) and right lower lung zones (RLZ). Simultaneous isotope dilution curves, derived from these lung zones by surface scanning in the sitting and recumbent postures, revealed in male HAD a distribution of about 17 % of cardiac output ($\dot{Q}$) to RUZ sitting contrasted with 26.0 % in recumbency. This is almost identical with the flow distribution to RUZ in sitting sea-level males (1) and appears to be uninfluenced by the elevation in mean pulmonary artery pressure (MPAP) of 7.7 mmHg at La Paz above that extant at sea Level.

By contrast, observations in a sitting young high altitude woman, showed a more even distribution of $\dot{Q}$ to the RUZ than in vertical male HAD, namely a QRUZ of 21.6 %. This observation as well as independently conducted steady state pulmonary diffusing capacity measurements DL_{CO} at altitude, which showed sex difference in the vertical position, prompted us to extend the observations of the distribution of pulmonary blood flow at the altitude of 3650 m (12,220 ft) to both lungs, by specifically recording additional isotope indicator dilution curves from the left upper (LUZ) and the left lower lung zones (LLZ) from the two body postures. At the same time more information was sought concerning the differences in DL_{CO} between sexes when studied in corresponding body positions. This seemed particulary germane in the light of the apparent agreement that newcommers to altitude, either on short or long term sojourns, do not increase their DL_{CO}, (3, 4) while native high altitude residents appear to have higher DL_{CO} (5). It is of interest in that regard that Remmer and Mithoefer (6) showed only an increase in DL_{CO} in La Paz, but were unable to demonstrate this at 4500 m in HAD. The reaction rate between oxyhemoglcbin (HbO_2) and carbon monoxide is generally assumed to be the same in HAD as in sea level man in spite of a demonstrable reduction in oxygen affinity at high altitude stemming from the increased concentration of 2 - 3 DPG in red cells which also may change carbon monoxide ↔ HbO_2 reaction rate kinetics. In addition DM_{CO} may be increased because HAD polycythemia reduces the distance between red blood cells and the capillary wall in lung capillaries. Presumably this also applies to newcomers who show correspondingly high Hb without significant increases in DL_{CO}. Consequently it seems reasonable to us, when comparisons are made in DL_{CO} between HAD and sea level natives, to carefully correct DL_{CO} for Hb, body surface area (BSA) and in view of apparent sex differences, identify subjects by sex and the posture used during measurements of DL_{CO}.

The purpose of this study rests in the identification of specific patterns in the distribution patterns of pulmonary blood flow in male and female HAD, which are calculated to provide additional explanations for the apparent differences found in magnitudes of DL_{CO} in the vertical posture betwen male and female HAD. A clue could thus emerge to illuminate the curious predilection of chronic mountain sickness for male HAD (7).

MATERIAL AND METHODS

Table 4 gives the means of biometric data for 15 HAD males and 8 HAD women, who cooperated in this study. Mean age, height, weight, BSA, Hb and hematocrit (Hkt%) are different, as expected between the 2 groups, who were all born and lived their total lives at or above the altitude of 3650 m (12,200 ft) and are physically fit and normal.

The distribution of pulmonary blood flow was studied in accordance with the methods already detailed (1, 2) and involved right heart catheterization. This was performed at the Cardio-Pulmonary Laboratory of the Instituto Boliviano de Biología de Altura (IBBA) located at the Instituto Nacional de Tórax, La Paz, Bolivia.

One inch crystal scintillation probes recessed 2.5 cm in cylindrical 1 inch lead collimators were placed against the left anterior axillary line in the 2nd and 5th lef intercostal spaces respectively. The pulse activity from these probes was simultaneously fed into 2 rate meters and pulse height discriminators, and recorded on a twin pen double channel 12 inch strip chart recorder at a paper speed of 10 mm/sec.

Approximately 80 μ Ci of ^{113}Indium labelled albumin were placed into the dead space of a No. 8 Cournand cardiac catheter, the tip of which was freely mobile in the cavtiy of the right ventricle. At the signal of injection the isotope was flushed as a bolus into the mid-right ventricle with about 10 times its volume of normal saline. The time constants of the rate meters were set at 0.1/sec and the inscription of the isotope indicator dilution curves from the left upper and lower lung zones at identical pre-set gains, continued from the injection signal to the onset of recirculation. The total activity in counts/second of injected isotope (IT) for each study was derived from the same probes, from the mean activities provided by digital readout and shift in baseline from background activity at 5 and 10 minutes respectively following the injection and from the shift in baseline after the delivery of 13.5 μ Ci of ^{113}Indium into a standard of exactly 1000 mls of saline. All analyses were derived from pairs of time concentration curves obtained simultaneously from the left lung zones with each patient first in recumbency and 15 minutes later from those recorded in the sitting vertical position. The percentage distribution of Q to LUZ and LLZ for the 2 body positions was calculated on the basis that the areas of the regional time concentration curves represent the quantities of partitioned indicator (IT) or their respective activities, arriving in left upper zone (I Luz) and left lower zone (I LLZ) at the same time and that their respective fractions are similar to the percent of regional Q coursing through the same areas. The basis of these assumptions have been previously published (8, 11). The measurements of DL_{CO} were carried out in 15 male and 8 female HAD separately in recumbency and in the vertical position using the steady state technique (9).

RESULTS

Distribution of Pulmonary Blood Flow (Q) to the Left Lung

Inspection of the isotope indicator dilution time concentration curves recorded simultaneously from LUZ (continuous lines) and LLZ (interrupted lines) in the vertical male HAD show markedly smaller areas for QLUZ (see Figs. I & II) than in female HAD, who in the vertical position yielded LUZ and LLZ areas of similar magnitude (Fig. III) while in recumbency the areas of LUZ and LLZ in both male and female are approximately equal (Figs. IV, V, VI).

Table 1 provides the means of areas of LUZ and LLZ in cm^2, obtained by electronically integrated planimetry in recumbency and in the vertical positions for the two sexes. The means of ratio of LUZ Area/LLZ Area in recumbency is 0.91 in males and 0.93 in females respectively. In the vertical position the means of ratio of the curve areas was 0.58 in males and 0.89 in female HAD.

Table 2 summarizes the means of regional distribution of Q to the left lung in the 2 groups of HAD. It shows that in the vertical position male HAD have a mean QLUZ of 0.86 L/min or 16.9 % of Q contrasted with a mean QLLZ of 1.63/min or 31.8 % of Q. In female HAD the vertical distribution of Q to LUZ is greater with a mean QLUZ of 0.98 L/min or 22.5 % contrasted with a mean QLLZ of 1.15 L/min or 21.1 % of Q. In recumbency QLUZ in male and female HAD are similar. i.e. 22.8 and 21.1 % of Q respectively.

Table 3 summarizes the percent distribution of total Q to four lung zones in normal HAD, derived from RUZ and RLZ of a previous study (1) and for the left lung from the current investigation. In male HAD in the vertical posture the means of QRUZ and QLUZ are 17.5 and 16.9 % of Q while the means in recumbency for QRUZ and QLUZ were 25.9 and 22.8 % respectively. In female HAD in the vertical position the means for QRUZ and QLUZ were 21.6 and 22.5 % while in recumbency they measured 29.0 and 22.1 % respectively. The change in QLUZ in female HAD with posture thus seems insignifiant.

The DL_{CO} in the Sexes at High Altitude

The means of biometric data of the 2 groups of male and female HAD, studied by the steady state DL_{CO} technique are shown in Table 4. The mean age of females exceeded that of males by 6.4 years and differences are also apparent with regard to height, weight and BSA. Female HAD show a mean Hb of 15.3 g contrasted with a mean Hb in males of 16.4 g. A similar difference emerges in respect of Hkt%.

Effects of Posture on DL_{CO}

Table 5 depicts the means of uncorrected DL_{CO} in recumbency and in the vertical positions of male and female HAD. The mean of 34.83 mls/min/mmHg in recumbent males falls to a mean of 27.97 ml/min/mmHg or by 19.7 % on sitting up. This contrasts with a mean reduction in Q to RUZ + LUZ of male HAD of 26.9 %. In female HAD the DL_{CO} in recumbency changes with vertical posture from a mean of 28.25 to 26.69 mls/min/mmHg or by 5.5 %. This contrasts with a reduction of 11.9 % in Q to RUZ + LUZ with the adoption of the vertical position in female HAD.

Thus the change in Q to the upper lung zones in both sexes exceeds by about 7 % the changes demonstrable in DL_{CO} with posture, which in females is 14.2 % less than in males.

Corrections of DL_{CO} for BSA and Hb

Because of the significant difference between the sexes with regard to height, weight, BSA and Hb, the measurements in recumbent and vertical DL_{CO} were expessed as DL_{CO}/BSA or diffusion indices and corrected for the differences in Hb by applying correction factors (10), fig. VII.

Table 6 shows the means for diffusion indices in the sexes. The male HAD DL_{CO} index is larger than that for sea level males. After correction for Hb it reduces from 21.5 to 18.7 mls/min/mmHg in recumbency. However, with adoption of the vertical posture DL_{CO}/BSA now falls to a mean of 14.9 mls/min/mmHg which brings it below that of vertical males at sea level.

In the female the corrected DL_{CO} index also changes with vertical posture namely from a mean of 17.1 to 15.9 mls/min/mmHg.

Fig. VIII shows that the effect of correction for Hb or DL_{CO} is significant inasmuch as the sea level DL_{CO} and that for altitude are now similar in males for both recumbency and the vertical position, while in female HAD the corrected DL_{CO} in the vertical position is significantly higher than in vertical females at sea level.

DISCUSSION

Differences PA - aO_2 gradients, while small, exist between male and female HAD at La Paz and at Chacaltaya (5200 m or 17,200 ft) (11). They are smaller in resting females and increase in both sexes on effort. To our knowlege the significant increase in physiological dead space and the widening of PA - aO_2 gradients above 10 mmHg found in male patients with chronic mountain sickness (CMS) is probably unknown or exceedingly rare in females HAD (12). Similary, high altitude pulmonary edema appears to spare women and suggest that V/Q mismatching and significant alveolar hypoxia seldom occur in female HAD. This may stem from the better distribution of pulmonary blood flow to the upper lung zones in high altitude women in the vertical position. No obvious and specific structural differences obtain in regard to regional morphology of the pulomonary vasculature. It is of interest that the ratios of number of distal and proximal pulmonary arterioles are the same in upper and lower lung lobes. There is a difference, however, concerning the size of medial area of normal right upper lung lobe arteries when compared with similary distributed right lower lobe arteries. The total cross sectional area of upper lobe arterial media is significantly greater (2). Since this regional difference applies to both sexes, no anatomical explanation emerges concerning the better upper lung zone perfusion in female HAD.

The MPAP of La Paz is approximately 22.8 ± 0.4 mmHg for both normal male and female HAD (13). Thus increase in perfusion pressure at rest of 7.7 mmHg in the pulmonary artery at La Paz over that found in normals at sea level has no obvious part to play in ensuring the more even distribution in pulmonary blood flow to the upper lung zones apparent in female HAD.

The magnitude of change in the differences between DL_{CO} measured in the vertical posture over that in recumbency in male HAD is approximately 7. 2 % below the means of the postural difference for Q distribution. Inasmuch as a similar change in magnitude of difference in DL_{CO} and Q distribution, namely 6.4 %, obtains in female HAD also, our Q distribution measurements and those for DL_{CO} identify the changing magnitude in blood flow to the 4 major distribution zones of the lungs with posture. Regardless of similar MPAP in the sexes at La Paz, the upper lung distribution zones in the vertical position appear to be at least 15 % larger in females than in male HAD.

RESUME

Le présent travail complète une étude antérieure sur la distribution de la perfusion entre les parties haute et basse du poumon chez les sujets résidents permanents d'altitude (La Paz 3.650 m - P_B 496 mmHg). Les premières observations portaient sur la distribution du débit dans le poumon droit (fig. 9) ; cette fois, c'est la distribution dans le poumon gauche qui a été mesurée et, ceci, compartivement chez la femme et l'homme.

- les résultats confirment la discrétion des changements de la répartition du débit lors du passage de la position couchée à la position assise chez la femme ; alors que chez les hommes, il y a une réduction de 25 % environ de la perfusion de la partie haute (fig. 10).

- les modifications de la répartition du débit sanguin pulmonaire ont été confrontées à celle de la diffusion du CO (DL_{CO}), corrigée pour la surface corporelle et la concentration d'hémoglobine : chez les sujets mâles DL_{CO} diminue de 19.7 % en position verticale (7.2 % de moins que pour le débit) ; chez les sujets de sexe féminin, la différence n'est que de 5.5 % (6.4 % de moins que pour le débit). La perfusion et DL_{CO}, en position verticale, sont ainsi significativement plus grandes chez la femme du niveau de la mer, alors qu'une telle différence se retrouve dans l'autre sexe (fig. 11).

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Effects of posture on pulmonary diffusion capacity and regional distribution of pulmonary blood flow in normal male and female high altitude dwellers at 3 650 m

H. SPIELVOGEL, E. VARGAS, G. ANTEZANA, L. BARRAGAN, L. CUDKOWICZ

Figures 1 to 11

Tables 1 to 6

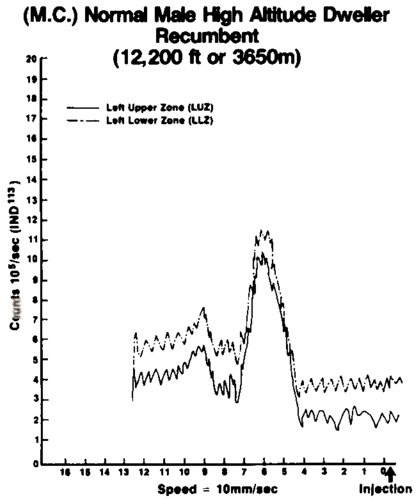

Fig. 1 (M.C.) -

Shows Indium indicator dilution curves simultaneously recorded from the left upper (continuous line) and left lower lung zones in a male HAD sitting up. The total activity (I LUZ) is less than in (I LLZ).

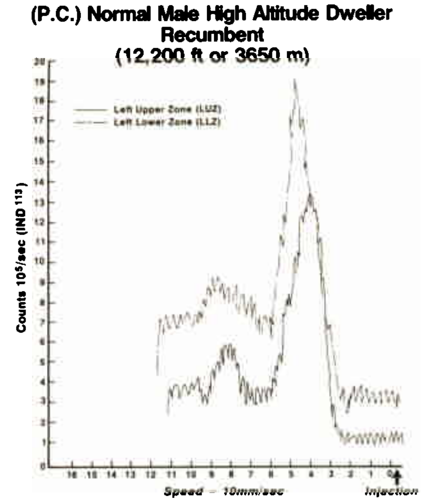

Fig. II (P.C.) -

Shows Indium indicator dilution curves simultaneously recorded from the left upper (continuous line) and left lower lung zones in a male HAD sitting up. The total activity (I LUZ) is less than in (I LLZ)

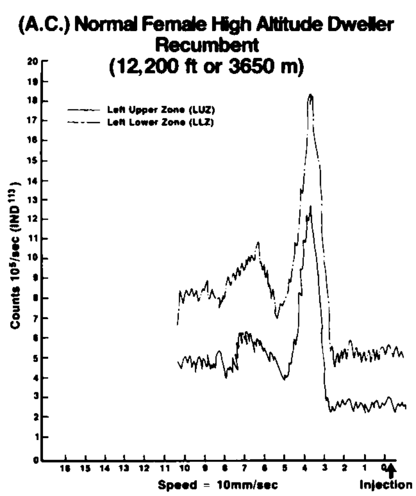

Fig. III (A.C.) -

Shows Indium indicator dilution curves simultaneously recorded from the left upper (continuous line) and left lower lung zones in a female HAD sitting up. The total activity (I LUZ) is almost identical with that of (I LLZ).

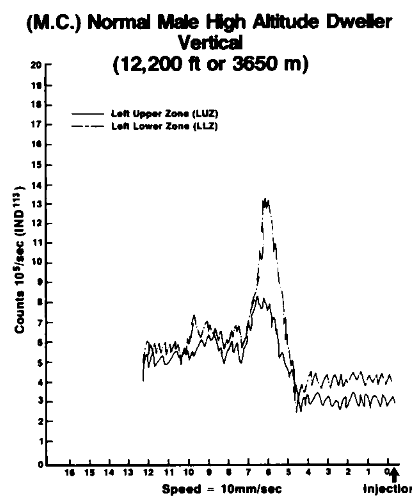

Fig. IV (M.C.) -

This shows Indium indicator dilution curves recorded simultaneously from left upper and left lower lung zones in a male HAD in recumbency. The total activity of (I LUZ) is identical with that of (I LLZ).

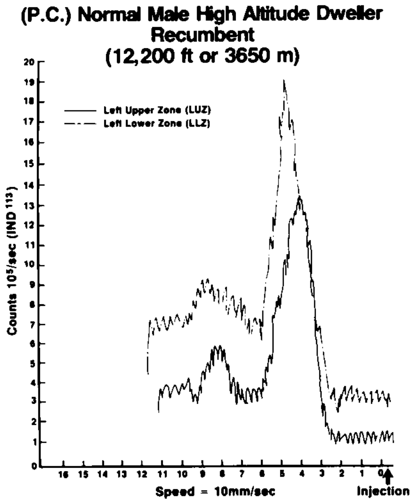

Fig. V (P.C.) -

This shows Indium indicator dilution curves recorded simultaneously from left upper and left lower lung zones in a male HAD recumbency. The total activity of (I LUZ) is identical with that of (I LLZ).

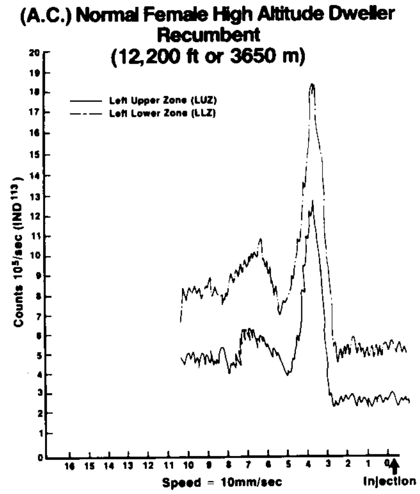

Fig. VI (A.C.) -

This shows Indium indicator dilution curves recorded simultaneously from left upper and left lung zones in a female HAD recumbency. The total activity of (I LUZ) is identical with that of (I LLZ).

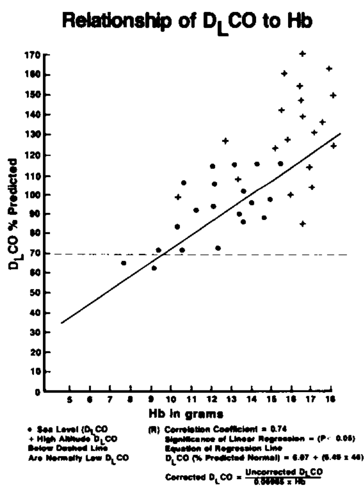

Fig. VII -

The effect of Hb on DL_{CO} at altitude are shown here and indicate that % predicted DL_{CO} appears to vary directly with magnitude of Hb (After Dinakara, et al. (10).

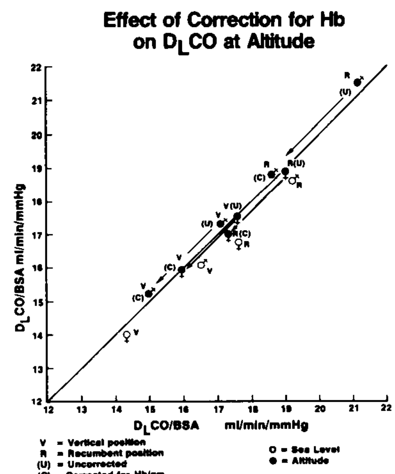

Fig. VIII -

The effect of correction of DL_{CO} for Hb are shown here in both sitting and recumbency in male and female HAD. The corrected DL_{CO} (C) in male HAD are close or below sea level male DL_{CO} in the vertical position.

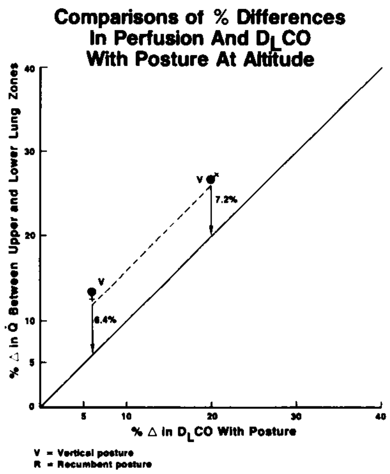

Fig. IX -

This graph shows that the difference in female and male lung upper zones Q̇ is 6.4 and 7.2 % larger than the respective differences in mean DL_{CO} .

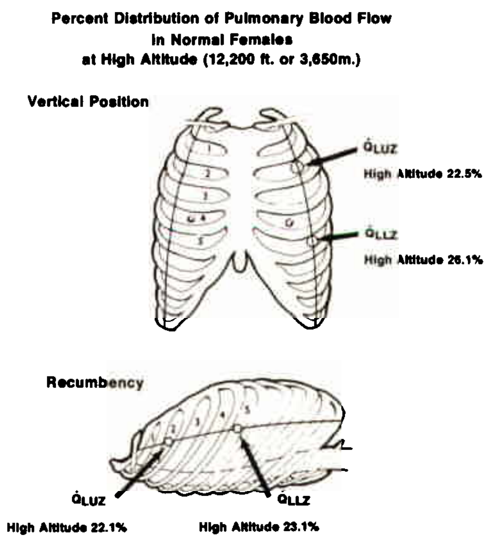

Fig. X -

This summarizes the effect of the vertical posture in % distribution of Q̇ in female HAD.
Q̇ LUZ remains unchanged from that found in recumbency.

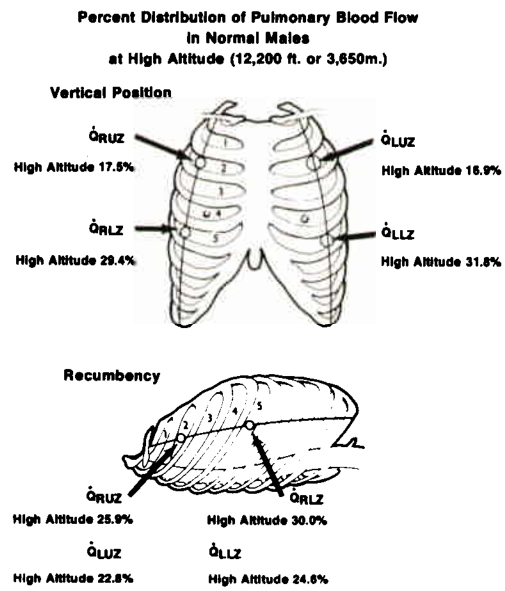

Fig. XI -

This figure summarizes the change in upper zone (Q̇ RUZ) and Q̇ LUZ) distribution in Q̇ in vertical male HAD. The % reduction in upper zone Q̇ while sitting up in male HAD is identical with vertical sea level males.

TABLE I

Means of Areas of Isotope Curves From LUZ and LLZ Derived From 2 Body Positions

Group	RECUMBENCY			VERTICAL		
	LUZ Area in cm2	LLZ Area in cm2	Ratio LUZ area / LLZ Area	LUZ Area in cm2	LLZ Area in cm2	Ratio LUZ Area / LLZ Area
Males N = 15 $\bar{x}$	64.34	71.81	0.91	50.16	84.8	0.58
Females N = 8 $\bar{x}$	60.04	64.31	0.93	53.81	61.42	0.89

LUZ = Left upper lung zone
LLZ = Left lower lung zone

TABLE 2

Comparison of Regional Distribution of $\dot{Q}$ To Left Lung at Altitude of 12,200 Ft (3650m)

Group	VERTICAL					RECUMBENCY				
	$\dot{Q}$	$\dot{Q}_{LUZ}$	% $\dot{Q}$	$\dot{Q}_{LUZ}$	% $\dot{Q}$	$\dot{Q}$	$\dot{Q}_{LUZ}$	% $\dot{Q}$	$\dot{Q}_{LLZ}$	% $\dot{Q}$
Males N = 15 $\bar{x}$	5.1	0.86	16.9	1.63	31.8	5.9	1.34	22.8	1.46	24.6
Females N = 8 $\bar{x}$	4.4	0.98	22.5	1.15	26.1	4.8	1.07	22.1	1.13	23.1

$\dot{Q}$, $\dot{Q}_{LUZ}$, $\dot{Q}_{LLZ}$ } in L/min

TABLE 3

% Distribution of Total Pulmonary Blood Flow ($\dot{Q}$) To Four Lung Zones in Normal High Altitude Dwellers (12,200 Ft or 3650m)

Sex	$\dot{Q}_{RUZ}$	$\dot{Q}_{RLZ}$	$\dot{Q}_{LUZ}$	$\dot{Q}_{LLZ}$
Males N = 15 Vertical $\bar{x}$	17.5	29.4	16.9	31.8
Recumbency $\bar{x}$	25.9	30.0	22.8	24.6
Females N = 8 Vertical $\bar{x}$	21.6	31.2	22.5	26.1
Recumbency $\bar{x}$	29.0	30.6	22.1	23.1

RUZ = Right upper lung zone
RLZ = Right lower lung zone

TABLE 4

Biometric Data of D_LCO High Altitude Dwellers

Group	Age years	Height cm	Weight Kg	BSA m^2	Hb grams	HKt %
Males N = 15						
$\bar{x}$	20.9	163	61.2	1.62	16.4	50.8
SD±	3.0	4.4	3.8	0.51	0.8	1.5
Females N = 8						
$\bar{x}$	27.3	156	54.7	1.51	15.3	49.1
SD±	9.6	6.1	4.1	0.18	1.9	0.9

BSA = Body Surface Area in M^2

TABLE 5

Means of D_LCO in High Altitude Dwellers At 12,200 Ft (3650m)

Group	D_LCO Recumbency	D_LCO Vertical	% Difference in D_LCO with Posture	% Difference in perfusion ($\dot{Q}$) between upper and lower lung zones in vertical position
Males N = 15 $\bar{x}$ Average age = 20.9 years	34.83	27.97	19.7	26.9
Females N = 8 $\bar{x}$ Average Age = 27.3 years	28.26	26.69	5.5	11.9

TABLE 6

Corrections Of D_LCO At 12,200 Ft (3650m)

Group	Recumbent D_LCO/BSA = D_LCO Index	Vertical D_LCO/BSA = D_LCO Index	D_LCO % predicted normal from $6.07 + (6.49 \times Hb)$	Corrected $D_LCO = \frac{\text{Uncorrected } D_LCO}{0.06965 \times Hb/BSA}$	
				Recumbent	Sitting
Males N = 15 $\bar{x}$	21.5	17.2	113%	18.7	14.9
Females N = 8 $\bar{x}$	18.8	17.5	109%	17.1	15.9