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Regional Distribution of Pulmonary Blood Flow in Normal High-Altitude Dwellers at 3,650 m (12,200 ft)

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Abstract. Simultaneous isotope dilution curves were recorded from the right upper ($\dot{Q}$RUZ) and right lower lung zones ($\dot{Q}$RLZ) by surface scanning in the sitting and recumbent positions in 15 normal high-altitude-born (HAD) males and in 1 HAD female as well as from 3 male newcomers, using 10 μCi of ^{131}I-HSA as a bolus injection into the right ventricle. Similar information was also obtained at sea level from 5 normal males.

The mean percent distribution of total pulmonary blood flow ($\dot{Q}$) to RUZ and RLZ in the two body postures indicate (1) that in the vertical position RUZ in males receives about 17% of $\dot{Q}$ regardless of altitude and elevation in mean pulmonary artery pressure (MPAP) in HAD of 8.6 mm Hg above that extant at sea level; (2) recumbency at high altitude showed $\dot{Q}$RUZ also to be lower than at sea level; (3) elevation in MPAP at altitude has no significant effect on changing the sea-level distribution pattern of pulmonary blood flow.

Key Words
Regional distribution
Pulmonary blood flow
High altitude
Pulmonary hypertension
Alveolar-arterial oxygen gradients ($pA\text{-}aO_2$)

Alveolar-arterial oxygen tension ($pA\text{-}aO_2$) gradients of different magnitude have been documented in both male and female native HADs [1–3] as well as in newcomers of both sexes to the altitudes of 3,650 and 5,200 m (12,200 and 17,200 ft), respectively. The resting mean pulmonary artery pressure (MPAP) increase, associated with residence at altitudes above 10,000 ft, has been thought to favor a more even distribution of pulmonary blood flow particularly to the apices of the lungs [4]. This would provide an explanation for small resting $pA\text{-}aO_2$ gradients observed in the vertical position at high altitude [5, 6] but would not account for the wider gradients established in native HADs by KREUZER *et al.* [2].

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In a study [7, 8] concerned with chronic mountain sickness (CMS/Monge's syndrome), a strikingly different distribution of pulmonary blood flow ($\dot{Q}$), both in the vertical and recumbent positions obtained in these patients, contrasted with that of a small group of normal HADs. It seemed particularly incongruous to us that in patients with CMS the MPAP at rest was 51.5 contrasted with 22.9 mm Hg in the normal native controls, while the $pA\text{-}aO_2$ gradients were significantly wider in the former. The number of observations concerning the normal distribution of $\dot{Q}$ was rather small at the time of the study of the patients with CMS and this prompted us to examine the $\dot{Q}$ distributions in both the vertical and horizontal positions in a larger group of normal HADs. This additional investigation was deemed desirable to provide additional information between normals and patients with CMS, particularly for the vertical distribution of $\dot{Q}$, in the light of preliminary morphometric information concerning normal differences in vascular diameters in upper and lower lobe pulmonary arteries [9] in the normal HADs of La Paz. (Altitude = 3,650 m or 12,200 ft, and mean barometric pressure (P_B) = 496 mm Hg.)

Material and Methods

Table I combines the biometric data, $pA\text{-}aO_2$ gradients, MPAP, mean pulmonary wedge pressures (MPCP) and cardiac indices derived from 15 normal males and 1 female who were born and lived all their lives above the altitude of 12,200 ft, and those of three sea level residents who were studied after 6 h, 3 and 6 months, respectively, of their arrival at La Paz.

Right heart catheterization, for the exclusion of significant congenital heart disease, was performed at the Cardiopulmonary Laboratory of the Instituto Boliviano Biologia de Altura (IBBA), located at the Instituto Nacional de Torax, La Paz. The procedure was thoroughly explained to the patients, particularly the need for the inscription of the isotope-dilution curves while in the vertical position. Detailed hemodynamic and blood gas as well as ventilatory function data of 11 native males have been published elsewhere [8]. In table I are included 7 males from this group, who had sets of data similar to a new group of 8 male normal HADs, whose study was made possible as a result of a second visit recently to Bolivia by one of us (L. C.) and the cooperation of the staffs of IBBA and the Centra de Medicina Nuclear, Hospital de Clinicas Miraflores, La Paz (Dr. L. BARRAGAN).

Table II provides similar data to that shown in table I in 5 normal male studies at the Cardiopulmonary Laboratory, Dalhousie University, Halifax, Nova Scotia prior to the first high-altitude studies in La Paz. The techniques and equipment were similar in both locations and consisted of twin 1-in crystal scintillation probes recessed 2.5 cm in cylindrical 1-in lead collimators which were placed against the right anterior axillary line in the 2nd and 5th right intercostal spaces, respectively. The pulse activity from these probes was simultaneously fed into two counting rate meters and pulse-height discriminators and re-

Table I. La Paz, normals; biometric, blood, $PA\text{-}aO_2$ and hemodynamic data at 12,200 ft (3,650 m), $\bar{x}$ P_B = 496 mm Hg

	Age years	Height cm	Weight kg	Hb g	RBC millions	HKt %	$PA\text{-}aO_2$ mm Hg	MPAP mm Hg	MPCP mm Hg	Cardiac index L/min/BSA
Group I,	17	164	55	15.8	6.1	50.3	2.7	22.0	6.0	3.7
male,	18	160	60	16.3	5.8	51.1	2.4	22.0	5.0	3.9
n=15	20	163	54	16.1	5.8	50.9	2.5	21.0	7.0	3.3
	19	168	62	16.0	7.0	52.1	3.1	24.0	8.0	3.8
	22	165	65	15.8	5.9	50.1	2.1	23.0	6.0	3.4
	19	162	62	16.3	6.1	53.1	1.9	22.0	6.0	3.8
	20	171	64	15.9	6.3	52.0	2.3	23.1	7.0	3.6
	23	167	59	18.2	5.9	51.9	2.9	23.0	6.0	3.4
	20	165	69	17.0	6.9	59.3	3.1	24.0	8.0	3.8
	22	157	60	16.8	5.4	50.7	2.7	24.0	8.0	3.5
	21	155	61	15.9	6.2	52.1	2.1	21.0	6.0	3.6
	20	163	64	15.7	5.8	49.8	2.0	19.0	5.0	3.4
	17	168	62	18.0	7.0	54.8	3.3	23.0	6.0	3.9
	23	160	58	15.8	6.0	50.7	2.9	19.0	5.0	3.3
	18	159	63	17.0	6.3	53.0	3.0	24.0	7.0	3.6
$\bar{X}$	19.9	163	61.2	16.4	6.2	51.8	2.5	22.3	6.4	3.6
SD ±	2.0	4.4	3.8	0.80	0.22	1.5	0.41	1.7	1.1	0.21
Group II, female, n = 1	26	152	56	14.9	5.1	47.0	2.7	23.0	7.0	3.0
Group III,	44[1]	173	70	15.8	5.2	50.0	3.1	23.0	6.0	3.7
male, new-	31[2]	183	81	14.9	5.3	48.0	4.0	–	–	–
comers, n = 3	24[3]	176	73	16.1	5.9	53.1	21.0	–	–	–
$\bar{X}$	33	177	75	15.6	5.5	50.4	3.1	2.3	6.0	3.7
SD ±	10	5.1	5.7	0.62	0.38	2.6	0.95	–	–	–

[1] Time at altitude: 6 months
[2] Time at altitude: 6 h.
[3] Time at altitude: 3 months

Table II. Sea level normals; biometric, blood, PA-aO_2 and hemodynamic data at sea level (altitude = 50 ft; $\overline{X}$ P_B = 756 mm Hg)

	Age years	Height cm	Weight kg	Hb g	RBC millions	HKt %	PA-aO_2 mm Hg	MPAP mm Hg	MPCP mm Hg	Cardiac index (Fick) L/min/BSA
Group IV,	44	173	70	15.1	5.0	46.0	15.0	14.0	6.0	3.6
male,	27	165	63	14.8	4.9	44.0	16.0	15.0	4.0	3.3
n = 5	28	184	78	15.2	5.2	47.0	17.0	15.0	6.0	4.0
	23	171	76	15.3	5.1	45.0	16.0	13.0	5.0	3.7
	31	181	74	15.0	4.8	44.0	12.0	16.0	6.0	3.6
$\overline{X}$	31	175	72	15.1	5.0	45.4	15.2	14.6	5.4	3.6
SD±	8	7.7	5.9	0.2	0.2	1.5	1.9	1.1	0.9	0.25

corded on a twin-pen, double-channel, 12-in, strip-chart recorder at a paper speed of 25 m/sec. Approximately 10 μCi of ^{131}I-HSA (iodinated human serum albumin) were placed into the dead space of a No. 8 Cournand cardiac catheter, the tip of which was freely mobile in the cavity of the right ventricle. At the signal of injection, the isotope was flushed as a bolus into the mid-right ventricle with about ten times its volume of normal saline. The time constants of the rate meters were set at 0.1 sec and the inscription of the radioactive curves from the right upper (RUZ) and lower lung (RLZ) zones at identical preset gains, continued from the injection signal to the onset of recirculation. The total activity in counts/sec injected (I_T) 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 min, respectively, following the injection. The difference in the two readings, if significant, was expressed as a mean and compared with I_T derived from the delivery of 2 μCi of ^{131}I-HSA[1] into a standard of exactly 1,000 ml of saline. All analyses are derived from pairs of time-concentration curves obtained simultaneously from the right lung zones in each patient, first in recumbency and about 15 min later from the sitting vertical position. The percentage distribution of $\dot{Q}$ to RUZ and RLZ for the two different body positions was calculated on the basis that the areas of the two regional time-concentration curves represent the quantities of partitioned indicator or their respective activities arriving in the right upper zone (I_{RUZ}) and in the right lower zone (I_{RLZ}) at the same time and that their respective fractions are similar to the percentage of regional pulmonary blood flow ($\dot{Q}_R$) through the same areas. Assuming that mixing of the isotope indicator in the ventricular chambers is complete, it can be shown [12, 13] that the ratio of a regionally partitioned quantity of indicator (I_R) to the total amount of I_T injected is the same as the ratio of the $\dot{Q}_R$ to $\dot{Q}$, thus it only becomes necessary to derive the percentage of I_T that reaches the respective lung zones for the calculation of $\dot{Q}_R$ to be completed. The percentage of I_T that reaches the respective lung zones for the calculation of $\dot{Q}_R$ to be completed. The percentage of I_T reaching the RUZ i. e., I_{RUZ} and that to the RLZ i. e., I_{RLZ} were derived as follows:

1 ^{131}I-HSA was made available by Dr. L. BARRAGAN, Director, Center of Nuclear Medicine, Hospital de Clinicas, La Paz.

$$I_{RUZ} = \frac{\text{area of curve of RUZ}}{\text{area of } \dot{Q}} \times I_T,$$

or

$$I_{RLZ} = \frac{\text{area of RLZ}}{\text{area of } \dot{Q}} \times I_T,$$

where I_T is the total number of counts injected.

$$Q_{RUZ} = \frac{I_{RUZ} \times 60}{\text{area of } \dot{Q}}$$

$$\dot{Q} = \frac{I_T \times 60}{\text{area of } \dot{Q}}$$

$$\dot{Q}_{RUZ} = \frac{I_{RUZ}/\text{area } \dot{Q}}{\dfrac{I_T}{\text{area } \dot{Q}}} = \frac{I_{RUZ}}{I_T}.$$

Similarly

$$\frac{\dot{Q}_{RLZ}}{\dot{Q}} = \frac{I_{RLZ}}{I_T}$$

or percent of I_T distributed to regional flowbeds/I_T is similar to $\frac{Q_R}{\dot{Q}}$.

Results

Table III summarizes the means and standard deviations of $pA\text{-}aO_2$, MPAP, MPCP and cardiac indices of the three groups from the altitude of La Paz and those of sea level group IV, who provided the comparison of the regional distribution of $\dot{Q}$ for the two body positions.

MPAP of 22.3 mm Hg, now regarded as normal for the altitude of La Paz [6, 10] exceeds the sea level MPAP by 7.7 mm Hg. No differences obtained in regard to MPCP and cardiac index and this also accords with previous observations [10, 11]. The resting mean $pA\text{-}aO_2$ of 2.5 mm Hg for La Paz is clearly much smaller than that for sea level and the magnitude of this decrease in $pA\text{-}aO_2$ gradient is related to the corresponding reduction in gradient between $PIO_2 + PAO_2$ extant at 12,200 ft and the approximation of PAO_2 there to that of normal PaO_2, both being close to the shoulder of the oxygen dissociation curve.

Examples of isotope indicator dilution time concentration curves recorded simultaneously from the right upper and right lower lung zones in recumben-

Table III. Means and standard deviations of $PA\text{-}aO_2$, MPAP, MPCP and cardiac indices of the four groups studied for regional distribution of $\dot{Q}$ using the RUZ and RLZ

Groups	Age years	$PA\text{-}aO_2$ mm Hg	MPAP mm Hg	MPCP mm Hg	Cardiac index (Fick) L/min/BSA
Group I, HAD, males, n = 15					
$\bar{X}$	19.9	2.5	22.3	6.4	3.6
SD	2.0	0.41	1.7	1.1	0.21
Group II, HAD, female, n = 1	26	2.9	23.0	7.0	3.0
Group III, newcomers, male, n = 3					
$\bar{X}$	33	3.1			
SD	10	0.95			
Group IV, sea level, males, n = 5					
$\bar{X}$	31	15.1	14.6	5.4	3.6
SD	8	0.2	1.1	0.9	0.25

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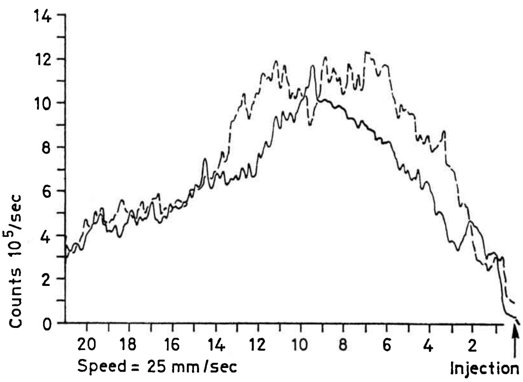

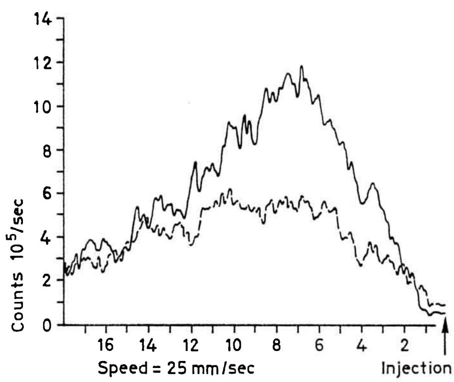

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Fig. 1. Simultaneously recorded ^{131}I-HSA isotope dilution curves from RUZ (-----) and RLZ (———) in recumbent male HAD. Ratio of $\frac{\text{area RUZ}}{\text{area RLZ}} = 0.83$.

Fig. 2. Simultaneously recorded ^{131}I-HSA isotope dilution curves from RUZ (-----) and RLZ (———) of male HAD in vertical position. Ratio of $\frac{\text{area RUZ}}{\text{area RLZ}} = 0.59$.

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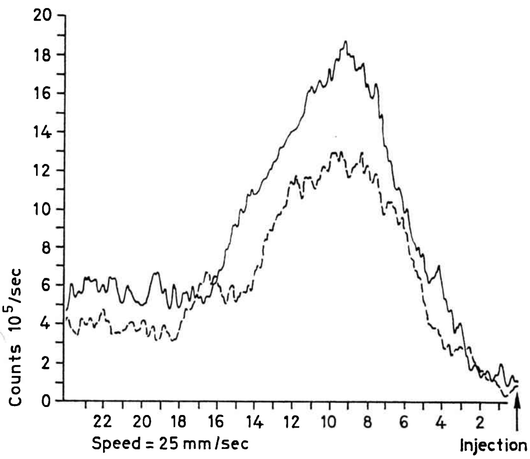

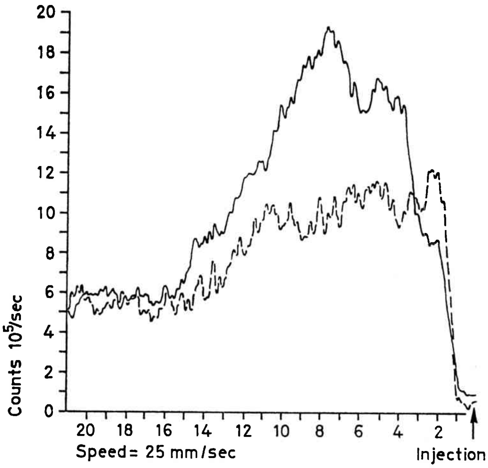

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Fig. 3. Simultaneously recorded ^{131}I-HSA isotope dilution curves from RUZ (-----) and RLZ (———) of female HAD in recumbency. Ratio of $\frac{\text{area RUZ}}{\text{area RLZ}} = 0.93$.

Fig. 4. Simultaneously recorded ^{131}I-HSA isotope dilution curves from RUZ (-----) and RLZ (———) of female HAD in vertical position. Ratio of $\frac{\text{area RUZ}}{\text{area RLZ}} = 0.67$.

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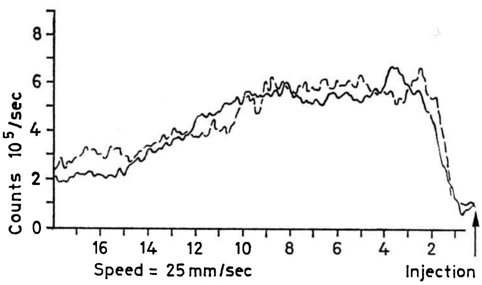

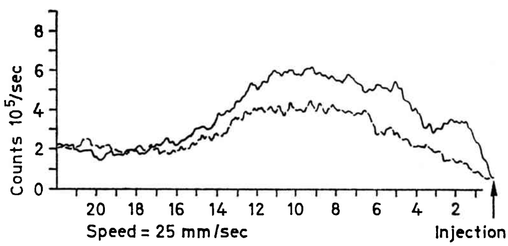

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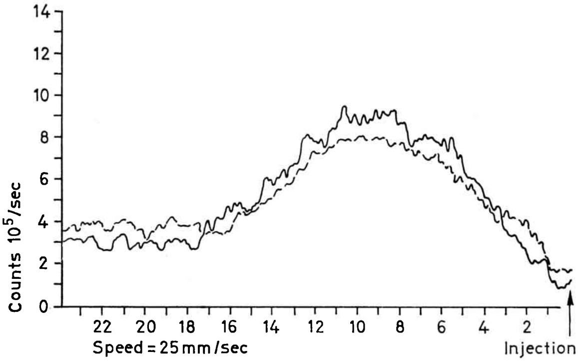
Fig. 5. Simultaneously recorded ^{131}I-HSA isotope dilution curves from RUZ (-----) and RLZ (———) of normal male newcomer to La Paz in recumbency. Ratio of $\frac{\text{area RUZ}}{\text{area RLZ}} = 0.93$.

Fig. 6. Simultaneously recorded ^{131}I-HSA isotope dilution curves from RUZ (-----) and RLZ (———) of normal male newcomer to La Paz in vertical position. Ratio of $\frac{\text{area RUZ}}{\text{area RLZ}} = 0.71$.



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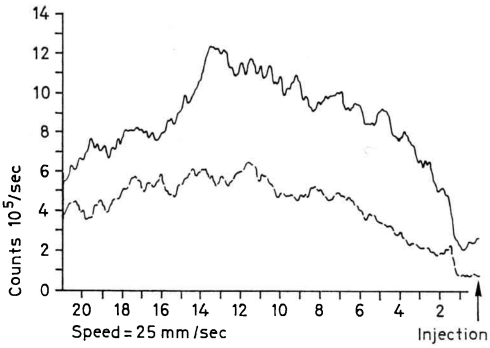

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Fig. 7. Simultaneously recorded ^{131}I-HSA isotope dilution curves from RUZ (-----) and RLZ (———) of a normal recumbent male at sea level. Ratio of $\frac{\text{area RUZ}}{\text{area RLZ}} = 0.97$.

Fig. 8. Simultaneously recorded ^{131}I-HSA isotope dilution curves from RUZ (-----) and RLZ (———) of a normal male in sitting position at sea level. Ratio of $\frac{\text{area RUZ}}{\text{area RLZ}}$ = 0.55.

cy and in the vertical positions are shown in figures 1 and 2 for a normal male HAD; in figures 3 and 4 for a normal female HAD; in figures 5 and 6 for a male newcomer acclimatized to La Paz after 3 month's residence; in figures 7 and 8 for a normal male studied similarly at sea level.

Table IV provides the areas of RUZ and RLZ in cm^2 in recumbency and in the sitting positions for the four examples as well as the ratios of area RUZ/area RLZ for the same body positions. Males native to sea level or to high altitude show the largest reduction in perfusion of the RUZ, the means of the ratios being 0.59 at altitude and 0.55 at sea level, respectively.

Table IV. Areas of isotope curves from RUZ and RLZ and their ratios in 2 body positions

Groups	Recumbency		Sitting		Recumbency	Sitting
	area RUZ cm²	area RLZ cm²	area RUZ cm²	area RLZ cm²	areas RUZ / areas RLZ	areas RUZ / areas RLZ
Group I, male natives, fig. 1, 2	115.49	139.4	62.37	105.66	0.83	0.59
Group II, native female, fig. 3, 4	182.36	196.63	163.04	253.24	0.93	0.67
Group III, male newcomers, fig. 5, 6	60.16	64.96	49.15	68.52	0.93	0.71
Group IV, males, sea level, fig. 7, 8	104.01	106.25	79.54	147.05	0.97	0.55

Areas have been derived in cm^2 by electronically integrated planimetry. Groups I–III were tested in La Paz, at 12,200 ft.

Table V provides the individual data used in the calculations of the regional distribution of $\dot{Q}$ in the vertical position for all four groups. The means show that the percentage distribution of isotope is practically the same as the $\dot{Q}_{RS}$. At sea level, the $\dot{Q}$RUZ of normal males received 17.0 ± 0.34 % of $\dot{Q}$ while the $\dot{Q}$RLZ obtained 30.8 ± 1.44 % of $\dot{Q}$. At the altitude of La Paz, normal males showed a similar distribution in the vertical posture, in that $\dot{Q}$RUZ was 17.5 ± 1.27 % while that of $\dot{Q}$RLZ amounted to 29.4 ± 1.3 % of total $\dot{Q}$ (fig. 9).

In the one female studied at La Paz, $\dot{Q}$RUZ exceeded the mean for males by 4.6 %. $\dot{Q}$RUZ equalled 21.6 % while $\dot{Q}$RLZ was 31.2 % (fig. 10).

The observations in 3 male newcomers, each one having a different exposure period to the altitude of 12,200 ft (3,650 m) showed a mean $\dot{Q}$RUZ of 19.7 ± 0.78 % and a mean $\dot{Q}$RLZ of 28.5 ± 0.87 % (fig. 11).

Table VI shows the data for the four groups used in the calculation of $\dot{Q}_{RS}$ to the RUZ and RLZ, respectively, in recumbency.

At sea level in normal males, the mean for $\dot{Q}$RUZ was 28.6 ± 0.8 % while that for $\dot{Q}$RLZ was practically identical at 28.5 ± 1.02 %. In normal native males at La Paz the mean for $\dot{Q}$RUZ was slightly less, namely 25.9 ± 1.5 % and the mean for $\dot{Q}$RLZ exceeded that for sea level by 2.5 %, the mean being 30.0 ± 1.35 % (fig. 9).

Table V. Comparisons of regional distribution of $\dot{Q}$

Groups	No.	I_T	Area RUZ	Area RLZ	$\frac{I_{RUZ}}{I_T} \times 100$	$\frac{I_{RLZ}}{I_T} \times 100$
Group I	1	14.4	2.64	4.42	18.3	30.8
HAD male, n = 15	2	14.6	2.53	4.31	17.4	29.0
	3	14.0	2.89	4.57	20.3	32.7
	4	14.5	2.46	4.34	16.8	30.1
	5	14.6	2.63	4.46	17.9	30.6
	6	14.3	2.43	4.22	17.1	29.5
	7	14.9	2.66	4.50	17.6	30.2
	8	13.9	2.28	4.18	16.5	30.0
	9	13.6	2.17	4.31	15.9	31.7
	10	12.9	2.09	4.16	16.3	32.1
	11	13.9	2.33	4.37	16.9	31.6
	12	13.6	2.49	4.41	18.3	32.5
	13	15.0	2.56	4.54	17.0	30.2
	14	14.0	2.68	4.49	19.2	32.1
	15	14.6	2.31	4.27	15.8	29 5
Mean $\bar{X}$		14.2	2.48	4.36	17.4	30.8
SD ±		0.4	0.21	0.13	1.2	1.2
Group II						
HAD female, n = 1	1	14.7	3.11	4.54	20.8	30.9
Group III	1	15.1	2.87	4.23	19.1	28.0
Male newcomers,	2	15.0	3.01	4.17	20.0	27.9
n = 3	3	14.7	2.93	4.31	20.2	29.3
Mean $\bar{X}$		14.8	2.94	4.24	19.8	28.4
SD ±		0.38	0.07	0.07	0.59	0.78
Group IV	1	14.0	2.35	4.19	16.8	30.0
Males at sea level,	2	13.8	2.29	4.24	16.6	30.7
n = 5	3	13.7	2.39	4.09	17.5	29.9
	4	13.1	2.22	4.39	17.0	33.5
	5	13.4	2.32	4.11	17.3	30.8
Mean $\bar{X}$		13.6	2.31	4.22	17.04	31.0
SD ±		0.35	0.064	0.125	0.36	1.46

Area RUZ, area RLZ, area $\dot{Q}$ = counts in million/sec of ^{131}I-HSA; $\dot{Q}_{RUZ}$ from $\frac{I_{RUZ} \times 60}{\text{area } \dot{Q}}$; $\dot{Q}_{RLZ}$ from $\frac{I_{RLZ} \times 60}{\text{area } \dot{Q}}$; $\dot{Q} = \frac{I_T \times 60}{\text{area } \dot{Q}}$. $\bar{X}$ P_B = Barometric pressure; 760 mm Hg at sea level, 496 mm Hg at 3,650 m (12,200 ft).

in normals at altitude (3,650 m) and sea level in vertical position

Area $\dot{Q}$	$\dot{Q}$/L/min	$\dot{Q}_{RUZ}$/ L/min	$\frac{\dot{Q}_{RUZ}}{\dot{Q}} \times 100 = \dot{Q}$, %	$\dot{Q}_{RLZ}$/ L/min	$\frac{\dot{Q}_{RLZ}}{\dot{Q}} \times 100 = \dot{Q}$, %
1.54	5.6	1.03	18.3	1.72	30.8
1.61	5.3	0.95	17.8	1.57	29.6
1.49	5.7	1.17	20.4	1.84	32.4
1.57	5.5	0.93	17.0	1.66	30.1
1.48	5.9	1.06	18.1	1.83	30.6
1.61	5.3	0.91	17.0	1.57	29.5
1.48	6.1	1.08	17.7	1.82	30.1
1.53	5.5	0.89	16.2	1.64	30.0
1.29	6.3	1.01	16.1	2.01	32.0
1.63	4.8	0.77	16.0	1.54	32.1
1.59	5.2	0.81	17.0	1.66	31.8
1.36	6.0	1.10	18.5	1.95	32.6
1.81	4.9	0.85	17.3	1.50	30.6
1.75	4.8	0.92	19.1	1.54	31.9
1.51	5.8	0.91	15.8	1.70	29.4
1.55	5.5	0.96	17.5	1.70	29.1
0.13	0.47	0.11	1.27	0.16	1.3
1.83	4.7	1.02	21.6	1.47	31.2
1.47	6.2	1.17	18.8	1.74	27.9
1.51	5.9	1.19	20.2	1.67	28.1
1.46	6.0	1.20	20.1	1.77	29.5
1.48	6.0	1.19	19.7	1.73	28.5
0.03	0.15	0.015	0.78	0.05	0.87
1.51	5.5	0.93	17.0	1.67	30.4
1.43	5.8	0.96	16.5	1.78	30.7
1.36	6.1	1.06	17.4	1.81	29.5
1.47	5.4	0.90	16.8	1.78	33.3
1.43	5.7	0.97	17.1	1.72	30.3
1.44	5.7	0.96	17.0	1.75	30.8
0.056	0.27	0.06	0.34	0.056	1.44

Table VI. Comparisons of regional distribution of pulmonary blood

Groups	No.	I_T	Area RUZ	Area RLZ	$\frac{I_{RUZ}}{I_T} \times 100$	$\frac{I_{RLZ}}{I_T} \times 100$
Group I	1	14.1	3.68	4.44	26.1	31.5
HAD male, n = 15	2	14.7	3.49	4.31	23.7	29.6
	3	14.2	3.88	4.61	27.3	32.3
	4	14.8	3.74	4.31	25.3	29.2
	5	14.9	3.96	4.51	26.4	30.2
	6	14.9	3.61	4.27	24.2	28.7
	7	14.0	4.01	4.51	26.9	30.3
	8	13.8	3.41	4.19	24.7	30.2
	9	13.9	3.87	4.31	27.9	30.9
	10	15.3	3.64	4.19	23.6	27.4
	11	15.8	3.81	4.38	24.1	27.7
	12	15.3	4.01	4.41	26.1	28.7
	13	14.8	4.21	4.56	28.4	30.8
	14	14.8	3.91	4.51	26.5	30.5
	15	14.9	3.62	4.21	24.4	28.2
Mean $\bar{X}$		14.7	3.79	4.38	25.7	29.7
SD±		0.54	0.22	0.14	1.55	1.41
Group II						
HAD female, n = 1	1	14.8	4.27	4.55	28.7	30.7
Group III	1	14.9	3.94	4.22	26.5	28.3
Male newcomers,	2	15.2	3.86	4.19	25.4	27.5
n = 3	3	14.9	4.02	4.30	26.9	28.9
Mean $\bar{X}$		15.0	3.94	4.24	26.3	28.2
SD±		0.17	0.08	0.06	0.78	0.70
Group IV	1	14.3	4.05	4.18	28.3	29.2
Males at sea level,	2	14.9	4.11	4.21	27.7	28.3
n = 5	3	13.6	3.97	4.08	28.9	30.1
	4	15.0	4.25	4.27	28.4	28.6
	5	15.1	4.01	4.08	26.7	27.1
Mean $\bar{X}$		15.6	4.08	4.16	28.0	28.7
SD±		0.63	0.11	0.08	0.84	1.11

Area RUZ, area RLZ, area $\dot{Q}$ = counts in millions/sec of ^{131}I-HSA; $\dot{Q}_{RUZ}$ from $\frac{I_{RUZ} \times 60}{\text{area } \dot{Q}}$; $\dot{Q}_{RLZ}$ from $\frac{I_{RLZ} \times 60}{\text{area } \dot{Q}}$; $\dot{Q} = \frac{I_T \times 60}{\text{area } \dot{Q}}$. $\bar{X}$ P_B = Barometric pressure; 760 mm Hg at sea level, 496 mm Hg at 3,650 m (12,200 ft).

flow in normals at altitude (3,650 m) and sea level in recumbency

Area $\dot{Q}$	$\dot{Q}$, L/min	$\dot{Q}_{RUZ}$/ L/min	$\frac{\dot{Q}_{RUZ}}{\dot{Q}} \times 100 = \dot{Q}$, %	$\dot{Q}_{RLZ}$/ L/min	$\frac{\dot{Q}_{RLZ}}{\dot{Q}} \times 100 = \dot{Q}$, %
1.47	5.8	1.51	26.1	1.81	31.4
1.58	5.6	1.32	23.6	1.03	29.2
1.39	6.1	1.68	27.7	1.99	32.7
1.48	6.0	1.15	25.2	1.74	29.2
1.42	6.3	1.67	26.6	1.91	30.3
1.54	5.7	1.40	24.6	1.66	29.2
1.27	7.1	1.88	26.5	2.14	30.1
1.40	5.9	1.46	24.9	1.79	30.4
1.15	7.2	2.02	28.1	2.25	31.2
1.74	5.2	1.26	24.3	1.44	27.8
1.69	5.5	1.35	24.5	1.56	28.4
1.35	6.8	1.79	26.3	1.96	28.9
1.73	5.1	1.46	28.6	1.58	31.6
1.81	4.9	1.30	26.7	1.49	30.4
1.44	6.1	1.51	24.7	1.75	28.8
1.50	6.0	1.54	25.9	1.78	30.0
0.18	0.68	0.22	1.5	0.23	1.35
1.77	5.0	1.45	29.0	1.54	30.6
1.39	6.3	1.69	26.4	1.82	28.4
1.37	6.7	1.71	25.5	1.84	27.4
1.40	6.4	1.73	27.0	1.85	28.8
1.39	6.5	1.71	26.3	1.84	28.2
0.015	0.17	0.02	0.75	0.015	0.72
1.38	6.2	1.76	28.4	1.81	29.1
1.34	6.7	1.84	27.5	1.89	28.1
1.17	7.0	2.05	29.0	2.09	29.9
1.56	5.8	1.63	28.2	1.64	28.3
1.52	5.9	1.57	26.9	1.61	27.2
1.39	6.32	1.77	28.6	1.81	28.5
0.155	0.52	0.19	0.81	0.20	1.02

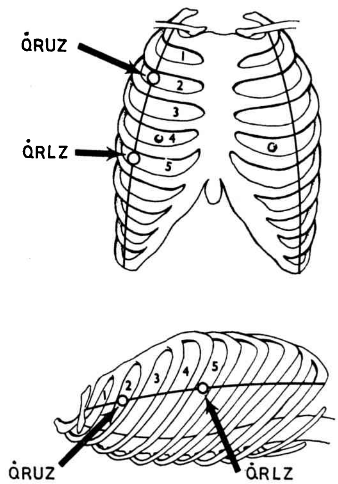

Fig. 9. Mean percent distribution of Q̇ to RUZ and RLZ are shown in normal males at altitude and at sea level in vertical positions (a) and in recumbency (b). In the vertical position, the distributions are the same at sea level and altitude.

	Q̇RUZ, % of Q̇		Q̇RLZ, % of Q̇	
	sitting	recumbent	sitting	recumbent
Male HAD	17.5±1.27	25.9±1.5	29.4±1.3	30.0±1.35
Males at sea level	17.0±0.34	28.6±0.8	30.8±1.4	28.5±1.0

In group III, the mean values in recumbency for the three male newcomers to high altitude were 26.3±0.8% for Q̇RUZ and 28.2±0.7% for Q̇RLZ (fig. 11) while Q̇RUZ in the female at La Paz measured 29.0% and Q̇RLZ 30.6% of Q̇ (fig. 10).

Discussion

Resting minute volume ($\dot{V}_E$) of ventilation increases at high altitude, particularly above 3,000 m, and gradually levels out in newcomers at a $\dot{V}_E$ consistently above that normal for sea level [11]. By contrast with normal male HAD, acclimatized male newcomers accomplish this increase in $\dot{V}_E$ by moving larger tidal volumes rather than changing their sea level respiratory

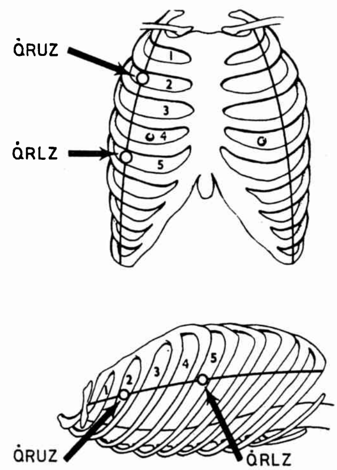

Fig. 10. Percent distribution of Q̇ to RUZ and RLZ are shown here in a normal female HAD in the vertical position (a) and in recumbency (b). The reduction in Q̇RUZ in the latter is less than in the males.

Q̇RUZ, % of Q̇		Q̇RLZ, % of Q̇	
sitting	recumbent	sitting	recumbent
21.6	29.0	31.2	30.6

frequency. Their arterial carbon dioxide ($paCO_2$) tensions are thus lower and arterial oxygen tensions (paO_2) higher than in male HAD. Such differences are less obvious between native and newcomer females at similar altitudes [3]. Increased ventilatory responses to the hypoxia of high altitude reduce the oxygen gradient between the inspired (PIO_2) and alveolar oxygen (PAO_2) tensions and that of pulmonary capillary blood (pO_2), thereby approximating paO_2 to mean pAO_2. Small pA-aO_2 gradients might therefore be anticipated in healthy individuals at high altitude, in the absence of unfavorable effects of altitude on (1) $\dot{V}_A/\dot{Q}$ equilibrium; (2) pulmonary diffusing capacity for oxygen (D_LO_2); (3) right to left veno-arterial shunting. Apart from an assumption that these three variables do not change significantly from sea-level values, a concomitant increase in MPAP at altitudes above 3,000 m is in itself also calculated to ensure a narrow pA-aO_2 gradient

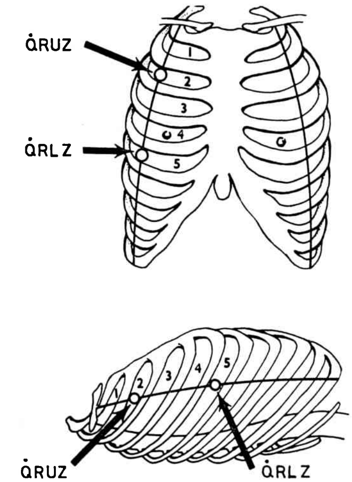

Fig. 11. Mean percent distribution of $\dot{Q}$ to RUZ and RLZ in male newcomers to La Paz in vertical position (a) and in recumbency (b) $\dot{Q}$RUZ in the vertical position is slightly in excess of that of male HAD.

	$\dot{Q}$RUZ, % of $\dot{Q}$		$\dot{Q}$RLZ, % of $\dot{Q}$	
	sitting	recumbent	sitting	recumbent
	19.7±0.78	26.3±0.8	28.5±0.9	28.2±0.7

in that better perfusion of the lung apices and a more uniform $\dot{V}_A/\dot{Q}$ distribution ensue from the associated pulmonary hypertension [14].

If $\dot{V}_A/\dot{Q}$ distribution is to remain constant in newcomers to high altitude, the increase in $\dot{V}_A$ has to be matched by a similar rise in $\dot{Q}$ and this has been demonstrated during acute exposure to altitude [15]. Increases in $\dot{Q}$ of newcomers are however transient, and soon return to sea-level values [15, 16]. Normal HAD of both sexes show resting cardiac indices similar to normal sea-level dwellers and $\dot{Q}$ rises in HAD on effort, as it does at sea-level, in relation to the exercise load [11]. By contrast, newcomers after acclimatization were found in some studies [17, 18] to show reductions in maximum $\dot{Q}$ for similar exercise loads at altitude, principally as a result of minimal increases in stroke volume and strikingly higher heart rates. This pattern of difference in newcomers possibly reflects a persistence of the marked sympathetic activity from the initial hypoxic stress of altitude. Raised blood catecholamine levels have been demonstrated [19] at high altitude and are thought to be responsible for the elevated metabolic rate [20] and the interesting cutaneous circulatory patterns demonstrated in La Paz by MARTINEAUD *et al.* [21].

Regional distribution of $\dot{Q}$ has been examined for the renal [22] coronary [23, 24] hepatic [25] and cerebral circulations [26] in HAD and newcomers and was found to be variable in regard to length of exposure to altitude, arterial blood gas tensions and hydrogen ion concentrations. In mammals, a general augmentation in capillary density [27] is thought to favor oxygen diffusion at tissue level, but measurements of pulmonary diffusing capacity (D_LCO) at altitude in newcomers showed no increase over that established at sea level at rest or exercise at corresponding work loads. Exercising at altitude at work loads in excess of 360 kg/m depicted invariably falls in paO_2 and widening of $pA\text{-}aO_2$ gradients in the presence of a rise in ventilatory equivalent for oxygen ($\dot{V}_A/\dot{V}O_2$). These observations in newcomers differ, from those found in HAD, particularly in regard to D_LCO in healthy HAD who showed a 20- to 30-percent increase above that of sea-level controls [28, 29]. This increase applies to both the alveolar membrane component (D_M) and capillary blood volume (V_c). The increase in D_M and in V_c is attributed to recruitment of larger numbers of pulmonary capillaries, from a higher mean MPAP at altitude, aiding blood flow to the otherwise poorly perfused lung apices at sea level.

Observations in regard to differences in D_LCO, widening of $pA\text{-}aO_2$ gradients particularly during effort at altitude and the fall in paO_2 on effort in normals, raises doubts as to the validity of an assumption for constancy of the aforementioned three parameters at altitude in healthy HAD and newcomers, and the evidence for a more balanced $\dot{V}_A/\dot{Q}$ distribution at altitude remains inconclusive [3, 7, 30].

Increased $pA\text{-}aO_2$ gradients, suggestive of non-uniformity of $\dot{V}_A/\dot{Q}$ have been demonstrated in normals at altitude [2, 31] while other studies are in support of the contrary [3, 5]. The significant increase in physiological dead space (V_{DS}) and the excessively widened $pA\text{-}aO_2$ gradients found in patients with CMS who showed particularly high elevations in MPAP in the absence of other heart or lung disorders, seemed to us to be of particular importance in that $\dot{V}_A/\dot{Q}$ mismatching in the presence of pulmonary hypertension of high altitude [7] was demonstrated by a persistent decrease in perfusion of the RUZs both in recumbency and in the vertical position, using the ^{131}I-HSA technique, detailed again in this present study. The details concerning regional distribution of $\dot{Q}$ in healthy normal males at sea level and in male HAD are entirely confined to the RUZ and RLZ. In the vertical position RUZ receives about 17% of $\dot{Q}$ regardless of altitude and in the presence of a difference in MPAP of 8.6 mm Hg for male HAD (fig. 9). The observations in the three male newcomers, while not supported by measurements of MPAP involve three different exposure periods to high altitude, show a slightly better perfusion of the RUZ in the vertical position, namely 19.7% of $\dot{Q}$. The mean $pA\text{-}aO_2$ of this group is, however, wider than in the male HAD (table III). Similarly, the single observation from the vertical position available in a healthy female HAD, right upper lobe perfusion amounted to 21.6% of $\dot{Q}$ in the presence of a MPAP of 23.0 mm Hg, while $pA\text{-}aO_2$ was of the same magnitude as in the male HAD (table III).

Our method of placing the detectors against the chest wall in recumbency ensured that the separated fields of detection were in the same horizontal plane, approximately 11 cm above the table top, and that the isotope activity counted stemmed from the central perfusion zones of the right upper and lower lobes. In sea-level males, the percent distributions of $\dot{Q}$ to the RUZ and RLZ in recumbency were identical, namely 28.5%, while male HAD in that body position showed a slight difference; the RUZ received 25.9 and the RLZ 30.0% of $\dot{Q}$ (fig. 9). In the male newcomers, altitude perfusion of the RUZ in recumbency was 26.3% compared with 28.2% of $\dot{Q}$ distributed to the RLZ. In the female, recumbency also showed a slightly lower perfusion of the RUZ, namely 1.6% less than to the RLZ. Although these differences appear to be very minor, it is nervetheless of interest that in all our observations conducted at altitude in recumbency, the perfusion of the RUZ was less than at sea level. The similarity in reduction of perfusion to the RUZ in the vertical position of healthy males particularly, both at sea level and at 3,650 m (12,200 ft), suggest that the increase in perfusion pressure in the pulmonary artery at altitude has no part to play in ensuring a more even distribution of $\dot{Q}$ to the upper lung zones. While no studies are available concerning the distribution of $\dot{Q}$ during exercise at altitude, the widening of $pA\text{-}aO_2$ found during effort, when both MPAP and $\dot{Q}$ rise, a persistence of $\dot{V}_A/\dot{Q}$ imbalance is probably contributing also to the fall in paO_2. Increases in pulmonary diffusing capacity during effort at high altitude, attributable to recruitment of additional pulmonary capillaries does not seem to compensate for other factors responsible for the widening in $pA\text{-}aO_2$ gradients on exercise. Additionally, factors other than $\dot{V}_A/\dot{Q}$ mismatching can account for the fall in paO_2 on exercise at high altitude, particularly right to left shunting, inasmuch as 100-percent oxygen breathing at the altitude of 3,800 m was found to produce an abnormally wide pA-aO_2 gradient of 117±10 mm Hg [32] while the pure oxygen breathing in patients with CMS yielded venous admixture shunts of about 24 % [8]. The main routes for lung perfusion in patients with CMS are those of the middle and lower lung zones, regardless of body posture. Exercise pA-aO_2 widen further in CMS patients and

$$\frac{V_{DS}}{V_T}$$

rises above the already abnormally high ratio at rest, indicating either progressive $\dot{V}_A/\dot{Q}$ mismatching or right to left shunting during effort and rising MPAP. In upright man at altitude, the gravity-dependent lung zones contain at any one time the major fraction of the central blood volume, and during effort probably become less compliant in the face of high blood flows [33]. Excessive $\dot{V}_A/\dot{Q}$ mismatching during exercise at altitude becomes, therefore, a distinct possibility if tidal volume distribution is primarily to the upper lung zones.

An additional possibility exists favoring right to left shunting by a diffuse asymptomatic rise in extravascular water in the dependent lung zones in upright man at altitude. Normal hydrostatic force exerted by gravity at the bases of the lungs, exceed that operative at the apices by about 20 cm of water [35] altering the regional differences in MPAP to the extent that closure of small pulmonary vessels and airways ensue from cuffs of perivascular edema and wide swings in intrapleural pressure to positive during expiration. Regional differences in the morphometry of the pulmonary vasculature apply in the upper and lower lung zones of normal human lungs at altitude [9] and an investigation is currently in progress which stems from the finding of such exaggerated regional histological differences in a patient with chronic mountain sickness.

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