La Paz - Bolivia

Chapter 43

Cardio-respiratory studies in chronic mountain sickness (Monge's syndrome)

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Contrasted with the healthy and well adapted mountain dwellers of high altitude, certain residents of the Peruvian and Bolivian Andes occasionally develop the well-defined clinical syndrome of chronic mountain sickness. A full description of this illness stems particularly from the elegant accounts of Monge in 1928 (11), and in the Andes of South America it is commonly referred to as Monge's syndrome. In subsequent accounts chronic mountain sickness has been depicted as an example of loss of acclimatization in mountain dwellers to the altitude of their birth, possibly as a result of loss of peripheral chemoreceptor sensitivity to altitude hypoxia (1, 5, 6, 16).

Chronic mountain sickness is insidious in its onset and is usually first recognized in high altitude residents by deepening central cyanosis and progressive polycythemia far in excess of that acceptable as normal for the altitude. In La Paz, as well as elsewhere in the Andes, patients with Monge's syndrome are first seen by hematologists because hemoglobin, red cell counts, and hematocrits exceed the means of normal mountain dwellers by more than 2 standard deviations. For example, in Bolivia a hemoglobin of 23.0 g% is arbitrarily thought to point to chronic mountain sickness in residents of the Bolivian altiplano living between 12–15,000 ft.

Although heart or lung diseases do not predispose to the development of chronic mountain sickness, severe pulmonary hypertension is the rule in the fully established syndrome. Diminished tolerance to carbon dioxide is normal in newcomers, producing large increases in V_E during 5% CO_2 loading. This differs from the great tolerance for CO_2 in chronic mountain sickness while single-breath oxygen tests reveal diminished hypoxic drive in Monge's syndrome, contrasted with an hypoxic drive in acclimatized newcomers that continues at constant intensity (5).

The current study was prompted by the finding of increased mean resting minute ventilations V_E (BTPS) in patients who showed the criteria of chronic mountain sickness, particularly central cyanosis and polycythemia. None of the patients showed evidence of right ventricular failure, but all had obvious pulmonary hypertension.

Demonstration in Monge patients of a lowered PAO_2 and PaO_2 and marked pulmonary hypertension in the presence of V_E higher than in the control population seemed incongruous; an investigation was therefore undertaken which concentrated in particular on measurements of physiological dead space and ventilation/perfusion relationships as tested by alveolar-arterial oxygen, CO_2 gradients and simple isotope lung scans.

MATERIAL AND METHODS

Patients who attended the Hematology Sec-

tion of the Institute because of severe polycythemia were asked to take part in the ventilation studies as a separate group. Clinical review showed that the one female and 19 male patients of this series were free from obvious lung disorders and congenital or valvular heart diseases which might have contributed to the obvious deep central cyanosis, secondary polycythemia or the pulmonary hypertension common to them all. For the purpose of statistical analysis, the cardiopulmonary physiological measurements of the Monge group were compared with similar data from the only control group available, namely 14 normal males born and constantly resident at or above the altitude of La Paz, Bolivia (i.e. 12,200 ft. or 3,650 m; mean barometric pressure (PBA) = 486 mm Hg). Social data and hemoglobin values of the 2 groups are shown in Tables 43–1 and 43–2.

All resting respiratory studies were carried out in recumbency and after a 15–min period of reclining. Vital capacities ($\dot{V}_C$), FEVI, resting minute ventilation ($\dot{V}_E$), respiratory frequency (f/min), tidal volume ($\dot{V}_T$), minute oxygen consumption ($\dot{V}O_2$) and carbon dioxide elimination ($\dot{V}CO_2$) were obtained routinely. All gas volumes are expressed as $\dot{V}$ or $\dot{V}$(BTPS) in ml, l/min, or l/min/m^2, except for $\dot{V}O_2$ and $\dot{V}CO_2$ which are given at STPD (standard temperature at 0°C/760 mm Hg/dry). BTPS (body temperature/ambient barometric pressure full water vapor saturation) and STPD factors were calculated each day in view of considerable temperature fluctuations in the unheated medical school building, as well as wide swings in barometric pressure, using:

$$\text{STPD} = \frac{273}{273 + ta} \times \frac{PBA - PH_2O_{ta}}{760}$$

$$\text{BTPS} = \frac{273 + 37}{273 + ta} \times \frac{PBA - PH_2O_{ta}}{PBA - 47}$$

Where PBA = ambient barometric pressure (mm Hg)
ta = ambient temperature
PH_2O_{ta} = water vapor pressure at ta

Oxygen and carbon dioxide contents of expired air (FEO_2 and $FECO_2$) were analyzed in duplicate by the Roughton-Scholander technique. Hemoglobin content of arterial blood samples was measured photometrically. Arterial blood oxygen tension (PaO_2) determinations were made by polarography using the Clark electrode attachment of the Radiometer micro-Astrup assembly. Arterial blood pH determinations at 37°C were made with the Radiometer glass electrode, while arterial blood PCO_2 ($PaCO_2$) was calculated from pH of blood tonometered with 3.7 and 7.4% CO_2 gas mixture and the Sigaard-Anderson alignment nomogram. Oxygen saturations of arterial blood samples were read off the Severinghaus blood dissociation nomogram utilizing PO_2 of the blood sample and allowing for temperature and pH effects.

Alveolar oxygen (PAO_2) and CO_2 tensions ($PACO_2$) were derived from end-tidal air sampled continuously at the mouth after prolonged exhalation through a Rudolph valve and a 5 ft rubber hose attached to the expiratory port of the valve. The end-tidal air, sampled at the rate of 30 ml/sec, was simultaneously analyzed for oxygen in a Beckman C_2 paramagnetic oxygen analyzer and for CO_2 content in an Onera 80 infrared CO_2 analyzer. Both instruments were calibrated before each measurement with known gas mixtures (i.e. N_2 for zero, 10% O_2 in room air, 5% CO_2 in room air, 10% CO_2 in room air and 100% O_2).

Physiological dead space ($\dot{V}_{DS}$) in ml was calculated from the Bohr equation, using either $PACO_2$ or $PaCO_2$. The resultant dead spaces are designated $\dot{V}_{DS}$ I and $\dot{V}_{DS}$ II, respectively. Resting alveolar ventilation [($\dot{V}A$(BTPS)] was obtained from $\dot{V}_A = \dot{V}_E - \dot{V}_{DS}$ ($\dot{V}_{DS}$ = minute dead space ventilation BTPS), as well as from $\frac{\dot{V}CO_2 \times .863}{PaCO_2} = \dot{V}A$. $\dot{V}_{DS}$ calculations were corrected for apparatus dead space.

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, Bolivia, and in 5 normal males of Group III at sea level at the Cardiopulmonary Laboratory, Dalhousie University, Halifax, Nova Scotia, Canada, prior to the first high altitude studies in La Paz, Bolivia. One inch crystal scintillation probes recessed 2.5 cm in

cylindrical one inch lead collimators were placed against the right anterior axillary line in the second and fifth right intercostal spaces respectively. The pulse activity from these probes was simultaneously fed into 2 counting rate meters and pulse height discriminators and recorded on a twin pen, double channel, 12–inch strip chart recorder at a paper speed of 25 mm/sec. Approximately 10 μ Ci 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 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 radioactivity curves from the right upper and lower lung 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 a) the mean activities provided by digital readout and shift in baseline from background activity at 5 and 10 min respectively following the injection and b) the shift in baseline from the delivery of 2μCi of ^{131}I HSA into a standard of 1000 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 pulmonary blood flow to right upper and lower lung zones for the 2 different body positions was calculated on the basis that the areas of the 2 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 percent of regional pulmonary blood flow through the same areas. Assuming that mixing of the isotopes indicator in the ventricular chambers is complete it can be shown that the ratio of a regionally partitioned quantity of indicator (I_R) to the total amount of indicator injected (I_T) is the same as the ratio of the regional blood flow ($\dot{Q}_R$) to total cardiac output ($\dot{Q}$); 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. (4, 14).

RESULTS

Clinical Aspects of Monge's Syndrome:

Table 43–1 shows that the average age of the chronic mountain sickness patients was twice that of the available control group of male native mountain dwellers (Table 43–2). In height, weight and body-surface area, the Monge patients also exceeded the corresponding mean values of the controls. Their larger frames, age notwithstanding, pointed towards ethnic differences from the control group of predominantly Indian background. The latter were all lifetime residents above 12,200 ft while 3 Monge patients were born at sea level but had lived in or near La Paz for at least 8 years. Fifteen patients with Monge's syndrome were lifetime residents of La Paz.

A breakdown of ethnic backgrounds is shown in Table 43–3. Two-thirds of the control group are genuine altiplano Indians and only the female Monge patients were of similar background. All of the 19 male patients had some Caucasian forbears. Similar ethnic analyses were carried out by Monge in 1943 (11) in patients with chronic mountain sickness and he suggested that a shorter genetic exposure to the effects of high altitude may play a part in the loss of adaptation to high altitude anoxia.

The presenting symptoms of the majority of patients with chronic mountain sickness, as shown in Table 43–4, consisted of effort dyspnea, insomnia and headaches.

The most significant physical signs are summarized in Table 43–5. Apart from plethora and central cyanosis, the most frequently present physical signs were third degree, or drumstick clubbing of the fingers and palpable pulmonary valve closure. Significant systemic hypertension was conspicuous by its absence.

Electrocardiographic and chest x-ray patterns were quite variable in the 20 patients with chronic mountain sickness and are summarized in Table 43–6. Right axis deviation (RAD) is not specific for this group, inasmuch as it is often seen in normal people in La Paz. Incomplete or complete RBBB is usually absent in the normal population and its presence in 11 of the 20 patients of this group is distinctly unusual. Frank right ventricular hypertrophy was seen in

TABLE 43–1. SOCIAL AND CLINICAL DATA OF 20 PATIENTS WITH MONGE'S SYNDROME.

Sex	Age	Height (cm)	Weight (kg)	BSA (m^2)	Birthplace	Ethnic Background (parents) ♂	♀	Haemoglobin (g)
M	63	165	64	1.71	La Paz	S	S	27.4
M	54	168	66	1.75	La Paz	S	I	24.3
F	38	154	69	1.67	La Paz	I	I	23.2
M	48	176	81	2.00	La Paz	S	S	26.5
M	63	176	66	1.80	India (in La Paz 17 yrs.)	English	English	28.4
M	39	168	65	1.73	La Paz	S	S	25.0
M	51	167	55	1.61	La Paz	S	S	25.6
M	40	170	72	1.81	La Paz	S	I	24.1
M	50	167	67	1.74	La Paz	S	S	29.2
M	45	169	72	1.81	Poland (in La Paz 20 yrs.)	Jewish	Russian	21.9
M	47	173	80	1.01	La Paz	S	S	26.2
M	55	171	78	1.89	Mexico City (in La Paz 8 yrs.)	I	S	23.8
M	52	166	61	1.66	La Paz	I	S	25.3
M	49	168	72	1.80	Santa Cruz (in La Paz 16 yrs.)	German	S	23.6
M	55	175	89	2.06	La Paz	S	I	24.7
M	62	176	64	1.81	La Paz	Arabic	S	26.9
M	56	177	73	1.91	Altiplano	I	S	24.6
M	60	168	61	1.72	La Paz	Scandinavian	S	28.1
M	62	176	81	2.01	La Paz	S	I	25.9
M	36	175	70	1.84	La Paz	S	I	28.8
$\bar{X}$ (Mean)		51	170.25	70.28	1.83			25.73
S.D. ±			5.56	7.02	0.127			0.88
S.E. ±			1.57	1.95	0.032			0.29

BSA = Body surface area; S = Spanish; I = Indian.

TABLE 43–2. SOCIAL AND CLINICAL DATA OF 14 NORMAL MALE RESIDENTS OF LA PAZ (CONTROL GROUP).

	Age	Height (cm)	Weight (kg)	BSA (m^2)	Birthplace	Ethnic Background (Parents) ♂	♀	Haemoglobin (g)
	39	174	60	1.71	Oruro	S	I	16.5
	40	176	59	1.69	Potosi	S	I	17.0
	17	164	55	1.58	La Paz	I	I	15.8
	18	160	60	1.00	La Paz	I	I	16.3
	20	163	55	1.58	La Paz	I	I	16.1
	19	168	65	1.72	La Paz	I	I	16.0
	22	168	62	1.69	Altiplano	I	I	15.8
	19	165	59	1.63	Altiplano	I	I	16.3
	20	162	69	1.72	La Paz	I	I	15.9
	23	171	58	1.71	La Paz	I	I	18.2
	20	167	60	1.66	Oruro	S	S	17.0
	20	177	75	1.90	La Paz	S	I	15.7
	32	157	63	1.61	La Paz	I	I	17.0
	22	166	67	1.73	La Paz	S	S	17.5
Mean	24	167	61.93	1.68				16.51
S.D. ±		5.88	5.48	0.036				0.696
S.E. ±		1.54	1.46	0.009				0.186

BSA = Body surface area; S = Spanish; I = Indian.

TABLE 43–3. ETHNIC BACKGROUNDS.

	Spanish ♂	*Spanish ♀*	*Indian ♂*	*Indian ♀*	*Other Races ♂*	*Other Races ♀*
Control Group (N=14)	5 (36%)	2 (14%)	9 (64%)	12 (86%)	—	—
Monge Patients (N=20)	11 (55%)	12 (60%)	4 (20%)	6 (30%)	5 (25%)	2 (10%)

TABLE 43–4. PRESENTING SYMPTONS OF PATIENTS WITH CHRONIC MOUNTAIN SICKNESS (MONGE'S SYNDROME).

Sympton	*Number*	*Sympton*	*Number*
Asthenia		Insomnia	7
Arthralgia	2		
Cough	3	Intermittent	
Chest Pain	1	Claudication	1
Disorientation	1	Palpitation	
Dyspnoea		and oedema	1
Rest	2	Sputum	0
Effort	20	Syncope	1 (2 x)
Headache	13	Vertigo	2

N = 20

TABLE 43–5. PHYSICAL SIGNS IN PATIENTS WITH CHRONIC MOUNTAIN SICKNESS (MONGE'S SYNDROME)

Physical Sign	*Number*	*Physical Sign*	*Number*
Conjunctival		Basal Ejection	
Plethora	20	Systolic Murmur	1
Central		Graham Steel	
Cyanosis	20	Diastolic Murmur	3
Finger Clubbing	13	Lung Signs	2
	(3°)	Oedema	0
"A" Wave	4	Range of	115–165
Palpable pulmonary		B.P.	65–90
valve closure	12		
Fixed P2	7	Splenomegaly	2
Third heart sound	2		

N = 20

30% of the patients and correlated well with the physical signs of pulmonary hypertension.

Chest radiographs showed old and presumably tuberculous scars in 3 patients. The right ventricle was prominent in 5 and dilated pulmonary arteries were visible in three. Translucent upper zones, affecting in particular the right upper lobe, were seen in 6 patients.

Reduced chemoreceptor senstivity to hypoxia, tested by the single-breath Dejours' oxygen test, was demonstrable in 17 of the 20 patients with Monge's syndrome (5). Totally negative responses were found in all 20 patients with 5% CO_2 loading for one min. This produced no discomfort and failed to change resting V_E.

TABLE 43–6. ELECTROCARDIOGRAPHIC AND CHEST X RAY PATTERNS IN 20 PATIENTS WITH CHRONIC MOUNTAIN SICKNESS (MONGE'S SYNDROME)

EKG Patterns:	
Right atrial hypertrophy	5
RAD axis > 125°	20
IRBBB	4
RBBB	7
R in VI and RVH	6
Chest Radiographs:	
Old TB	2 apical scars 1 basal focus
RV++	5
PA++	3
Upper lobe translucency	6

IRBBB = Incomplete right bundle branch block
RBBB = Right bundle branch block
RV = Right ventricle
PA = Pulmonary arteries

Hematological Studies:

Polycythemia, a predictable adaptive response to high altitude hypoxia, relates well to the decreased arterial oxygen tension. The arterial blood of altitude dwellers carried slightly more oxygen than at sea level, mainly as a result of the greater hemoglobin concentration. This average increase is reflected in the data derived from the 14 normal males and represents the typical finding of a well adapted population to the altitude of La Paz, Bolivia. Table 43–7 depicts the normal erythrocyte values as well as the widely different data in the Monge group. Blood volume calculations during the ^{131}IHSA studies are summarized in Table 43–8.

Respiratory Function at Rest:

Table 43–9 summarizes the resting minute volumes (V_E) and indicates that the average resting minute ventilation of the patients with Monge's syndrome apparently exceeds that of the control group. This difference is, however, statistically not significant. The average

TABLE 43–7. HAEMATOLOGICAL DATA

		Haemoglobin (g)	*RBC (millions)*	*Haematocrit (%)*	*WBC*	*Uric Acid (mg)*
Native Male Residents (N=14)	Mean	16.51	6.1	50.3	6,891	7.9
	S.D. ±	0.696	0.3	1.9	—	—
	S.E. ±	0.186	0.02	0.5	—	—
Monge Patients (N = 20)	Mean	25.73	7.1	72.1	5,971	8.2
	S.D. ±	0·88	0·6	3·1	—	—
	S.E. ±	0.29	0.2	0.7	—	—

Altitude = 3,650m; Mean PBA = 486 mm Hg; Mean PIO2 = 96 mm Hg.

frequency of ventilation is the same in both groups and the increase in $\dot{V}_E$ of the Monge group results from the utilization of a larger tidal volume.

Table 43–10 depicts the means concerning $\dot{V}O_2$ and $\dot{V}CO_2$ in the 2 groups. While the Monge group shows means for oxygen consumption and carbon dioxide elimination which appear to be greater than those for the controls, this difference is statistically not significant. The difference in $\dot{V}O_2$ also disappears when expressed as $\dot{V}O_2$/kg and shows that the larger $\dot{V}O_2$ in the Monge patients is directly related to the larger body mass.

The means of vital capacity (V_c/l) and its subdivision, IRV, (inspiratory reserve volume) show statistically significant reduction in the Monge group, but the expiratory reserve volumes (ERV) in the 2 groups were similar (Table 43–11). The reductions in vital capacity and IRV in the Monge patients are probably related to changes in functional residual capacity (FRC) and total lung capacity (TLC). A few measurements made in 4 controls and in 4 Monge patients yielded means for FRC of 2.85l in the Monge patients and 3.01l in the controls, while the mean of TLC was 6.48l in the 4 controls and 5.81l in the 4 Monge patients. The difference in means of V_c, FEV_1, and also for TLC, are probably related to the differences in age and build of the 2 groups, rather than associated heart or lung disease in the Monge group.

Data concerning the differences in the 2 groups for alveolar-arterial blood gas tensions and arterial pH are summarized in Table 43–12. Contrasted with the normal control group, the patients with Monge's syndrome showed statistically significant decreases in arterial pH and arterial oxygen saturation. The latter appears as a consequence of a reduction in mean PaO_2 to 47.9 mm Hg compared with that of 56.7 mm Hg for the control group. While the alveolar PCO_2 means are not significantly different, there is a striking and statistically significant difference in the means of the arterial PCO_2 ($PaCO_2$); namely, 43.5 mm Hg in the Monge patients and 34.7 mm Hg for the normals. The latter figure, while lower than that normally extant at sea level, is typical for normal residents at an altitude above 12,000 ft (3,600 m). The corresponding higher mean $PaCO_2$ of 43.5 mm Hg, together with the reduction in arterial pH, implies that the Monge group at that altitude has respiratory acidosis which stems from alveolar hypoventilation, identical resting minute ventilations (Table 43–9) and similar PAO_2 and $PACO_2$ notwithstanding. Apart from this critical reduction in effective alveolar ventilation in the Monge group, as evidenced by the elevation in mean $PaCO_2$ and a significantly wider mean PA-aCO_2 of 8.1 mmHg, there also exists a wider PA-aO_2 gradient of 8.6 mm Hg

TABLE 43–8. BLOOD VOLUME CALCULATIONS DURING 131_I HSA STUDIES

		Total Blood Volume (liters)	*Plasma (liters)*	*Erythrocytes (liters)*
Male Native Residents (N=6)	Mean	5.72	2.14	3.58
Monge (N=6)	Mean	6.91	2.38	4.53

TABLE 43–9. RESTING MINUTE VENTILATION

		Ht (cm)	Wt (kg)	BSA (m^2)	V_E (STPD) (l/min)	V_E (BTPS) (l/min)	f/min	V_T (BTPS) (ml)	V_E (STPD) (l/min/m^2)	V_E (BTPS) (l/min/m^2)	V_T (BTPS) (ml/m^2)
MNR	Mean	167.1	61.9	1.68	5.21	10.1	16.7	598	3.5	6.0	356
(N= 14)	SD±	5.88	5.48	0.036	1.04	2.09	3.11	139	0.6	1.2	83
	SE ±	1.54	1.46	0.009	0.23	0.46	0.83	37	0.2	0.3	22
M	Mean	172.5	72.5	1.83	6.15	11.8	16.8	707	3.3	6.5	386
(N=20)	SD±	2.99	9.18	0.127	0.93	1.28	5.16	144	0.60	1.3	96
	SE±	0.72	2.31	0.032	0.26	0.35	1.31	41	0.16	0.4	27
	P	<0.1	<0.02	<0.01	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1

MNR = male native residents; M = Monge; Altitude = 3,650 m; P_B = 486 mm Hg; Temp = 18.5°C. $\bar{X}$ STPD = 0.592; $\bar{X}$ BTPS = 1.1135.

TABLE 43–10. RESTING OXYGEN CONSUMPTION (ml/min).

		$\dot{V}_{CO_2}$(STPD)	$\dot{V}_{O_2}$(STPD)	RQ	$\dot{V}_{O_2}$/BSA	$\dot{V}_{O_2}$/kg
Male Native	Mean	216.1	232.2	0.97	137.3	3.7
Residents	S.D. ±	59.9	61.7	0.11	39.1	1.1
(N=14)	S.E. ±	16.1	17.9	0.03	10.4	0.3
	Mean	264.3	284.1	0.95	155.2	3.9
Monge	S.D. ±	84.3	122.1	0.12	52.5	1.2
(N = 20)	S.E. ±	21.8	24.9	0.03	13.2	0.3
	P	<0.1	<0.1	<0.5	<0.5	<0.5

Altitude = 3,650m; P_B = 486 mm Hg; Temp. = 18.5°C. $\bar{X}$ STPD=0.592, $\bar{X}$ BTPS=1.1135.

which differs significantly from the mean of 2.9 mm Hg in the controls.

In the calculations of physiological dead space $PACO_2$ was utilized for V_{DS} I and $PaCO_2$ for V_{DS} II. The normal group showed a mean difference (ΔV_{DS} I − V_{DS} II) of only 5.0 ml, while a mean difference of 12.0 ml was found in the Monge group. $\dot{V}_{DS}$ II was, therefore, used for the calculation of dead space ventilation ($\dot{V}_{DS}$ II liters/min) and alveolar ventilation ($\dot{V}_A$ II liters/min) the latter being derived from $\dot{V}_A$ II (BTPS) = $\dot{V}_E$ (BTPS) − $\dot{V}_{DS}$ II(BTPS).

TABLE 43–11. LUNG VOLUMES (L/BTPS)

		V_C	ERN	IRV
Male Native	Mean	4.9	1.3	3.0
Residents	S.D. ±	0.81	0.23	0.67
(N=14)	S.E. ±	0.22	0.06	0.13
	Mean	4.1	1.1	2.4
Monge Patients	S.D. ±	0.58	0.16	0.50
(N=20)	S.E. ±	0.15	0.03	0.11
	P	<0.05	<0.1	<0.05

V_C = Vital capacity; ERV = Expiratory reserve volume; IRV = Inspiratory reserve volume.

Table 43–13 shows that mean $\dot{V}_A$ II so calculated is significantly smaller in the Monge group, while no statistically significant difference could be demonstrated between the resting minute ventilations [$\dot{V}_E$ (BTPS)] of the 2 groups. The gross reduction, in effective alveolar ventilation in the Monge patients appears to be the result of a significantly larger V_{DS} II, the mean of 406 ml exceeding 205 ml in the normal controls. The $\dot{V}_D$II/V_T ratio of 0.33 in the controls is within normal limits, while in the Monge group this ratio increases to 0.57 because of the larger V_D II. Calculation of $\dot{V}_A$ III, derived from $\frac{\dot{V}CO_2 \times .863}{PaCO_2}$, also shows

TABLE 43–12. RESTING ALVEOLAR-ARTERIAL BLOOD GAS TENSIONS AND GRADIENTS

		$PECO^*_2$	PAO^*_2	$PACO^*_2$	$PaCO^*_2$	PaO^*_2	$PA\text{-}aO^*_2$	$PA\text{-}aCO^*_2$	Bicarb mM	pH	Arterial Sat.%
MNR	Mean	22.1	59.6	33.3	34.7	56.7	2.9	1.4	21.7	7.3991	89.7
	S.D. ±	2.59	3.14	2.84	2.38	2.39	1.11	0.98	1.47	0.027	3.91
	S.E. ±	0.69	0.85	0.76	0.63	0.64	0.33	0.26	0.39	0.007	0.97
M	Mean	15.6	56.5	35.4	43.5	47.9	8.6	8.1	24.2	7.3481	82.8
	S.D. ±	4.11	2.97	2.62	2.41	3.34	2.14	1.2	1.96	0.056	4.11
	S.E. ±	1.04	0.77	0.61	0.59	0.86	0.54	0.3	0.50	0.014	1.09
	P	<0.01	<0.1	<0.1	<0.01	<0.01	<0.01	<0.01	<0.02	<0.05	<0.02

MNR = Male Native Residents (N = 14); M = Monge (N = 20);*mm Hg; Altitude = 3,650 m; $\bar{X}$ PB = 486 mm Hg

similar reduction in the mean of effective alveolar ventilations in the Monge group. The slightly lower mean values for $\dot{V}_A$ III of both normals and the Monge patients is probably accounted for by a consistent error in calculated instrumentation dead space during the 4–min air collections, in which a simple two-way Hans-Rudolph valve was used with the additional side arm rubber hose for alveolar air sampling. The error arising from the differences in calculated and actual instrumentation dead space applied equally to both populations and does not affect the calculations used in deriving the means for $\dot{V}_A$ III of the 2 groups.

Pulmonary vascular pressures and flows, available in patients with Monge's syndrome, are compared in Tables 43–14 and 43–15 with similar data derived from 11 native male patients living in or above La Paz and free from cardiopulmonary disorders. The mean values in this group have been published elsewhere (5) and represent the first normal studies of this kind for the altitude of La Paz (12,200 ft; 3,650 m). The means in the 2 Monge patients show reductions in pH of the respective bloods as well as lower PO_2 and saturations compatible with respiratory acidosis from alveolar hypoventilation and venous admixture. The mean O_2 contents are grossly increased in the Monge patients as a result of a mean hemoglobin of 26.5 g contrasted with 15.8 g in the controls. The cardiac output is similar in both groups while the mean cardiac index is smaller in the Monge patients because of their larger body surface areas. A reduction in heart rate is responsible in the Monge patients for the apparently larger mean stroke volume. Both patients with Monge's syndrome show marked pulmonary hypertension with mean MPAP 100% higher than in the controls. The wedge pressures are similar in the 2 groups while mean PVR and PAR were 215% and 260% above the

TABLE 43–13. RESTING DEAD SPACES AND ALVEOLAR VENTILATION

		$\dot{V}_T$ (ml)	$\dot{V}_{DS}I$ (ml)	$\dot{V}_{DS}II$ (ml)	$\dot{V}_{DS}I\text{-}\dot{V}_{DS}II$ (ml)	$\dot{V}_D II/\dot{V}_T$	$\dot{V}_{DS}II$ L/min	$\dot{V}_A II$ L/min	$\dot{V}_A III$ L/min	$\dot{V}_E$ L/min
MNR	Mean	598	200	205	5.0	0.33	3.6	6.5	5.9	10.1
	S.D.±	139	30	45	1.0	—	0.62	1.58	1.11	2.09
	S.E.±	37	10	12	0.2	—	0.17	0.43	0.21	0.46
M	Mean	707	394	406	12.0	0.57	6.8	4.9	4.7	11.88
	S.D.±	144	89	122	2.1	—	1.48	1.51	1.19	1.28
	S.E.±	41	22	41	0.3	—	0.36	0.39	0.22	0.35
	P	<0.1	<0.01	<0.01		<0.01	<0.01	<0.02	<0.02	<0.1

MNR = Male Native Residents (N = 14); M = Monge (N = 20); Altitude = 3,650 m; PB = 486 mm Hg; Temp. = 18.5°C; $\bar{X}$ STPD = 0.592; $\bar{X}$ BTPS = 1.1135; $\dot{V}_A$ II = $\dot{V}_E$ − V_{DS} II; V_{DS} I uses $PaCO_2$; V_{DS} uses $PaCO_2$; $\dot{V}_A$ III $= \frac{VCO_2}{PaCO_2} \times .863$

TABLE 43–14A. ARTERIO-VENOUS O2 DIFFERENCES

		Pulmonary Artery Blood				Systemic Arterial Blood				
		PO_2 (mmHg)	pH	O_2 Content (vol.%)	Sat.%	PO_2 (mmHg)	pH	O_2 Content (Vol.%)	Sat.%	A-VO_2 Diff. (Vol.%)
Male Native Residents (N = 11)	Mean	37.6	7.358	15.2	72.0	60.2	7.417	18.93	89.6	3.71
	S.D. ±	1.1	0.003	1.3	10.13	7.11	0.003	1.54	4.39	0.91
	S.E. ±	0.2	0.001	0.23	2.54	1.63	0.001	1.37	0.84	0.20
Monge (N = 2)	Mean	36.5	7.288	22.2	68.9	50.7	7.382	26.3	83.8	4.1

TABLE 43–14 B. CARDIAC OUTPUT AND HAEMOGLOBIN PERCENTAGE

		Q Fick+	Cardiac Index*	f/min	Stroke Vol. (ml)	Stroke Index (ml/m2)	Haemoglobin (g)
Male Native Residents (N = 11)	Mean	5.71	3.85	86.0	67.3	45.0	15.8
	S.D. ±	1.29	0.31	12.6	23.1	12.1	—
	S.E. ±	0.32	0.05	2.8	5.2	2.7	—
Monge (N = 2)	Mean	5.98	3.3	71.0	84.5	46.8	26.5

+ = Liters/min; * = Liters/min/m2

TABLE 43–15. RESTING RIGHT HEART AND PULMONARY VASCULAR PRESSURES AND RESISTANCES.

		RAP (mm Hg)	RVP (mm Hg)	MPAP (mm Hg)			PCP (mm Hg)			PVR	PAR
				S	D	$\bar{X}$	S	D	$\bar{X}$		
MNR	Mean	3.8	36.7/0	38.0	14.5	22.9	10.1	4.2	6.8	312.0	219.7
	S.D.±	1.4	—	10.31	3.9	5.21	3.98	2.11	2.32	91.1	94.4
	S.E. ±	0.3	—	2.47	0.76	1.34	1.07	0.46	0.59	21.4	21.6
M	Mean	7.8	76.0/–3.0	74.0	41.0	51.5	12.1	5.1	7.5	668.5	568.3

MNR = Male Native Residents (N = 11); M = Monge (N = 2); RAP = Right atrial pressure; RVP = Right ventricular pressure; MPAP = Main stem pulmonary artery pressure; PCP = Pulmonary wedge pressure; PVR = Pulmonary vascular resistance (dynes-/sec/cm^{-5}); PAR = Pulmonary arterial resistance (dynes/sec/cm^{-5}); S = Systolic; D = Diastolic; $\bar{X}$ = Mean.

means for the controls. The mean pulmonary artery pressure of 22.9 mm Hg in the control group is, of course, well above the mean of 14.0 mm Hg normally found at sea level.

The effects of oxygen breathing on MPAP and PCP over a 4–min period are summarized in Fig. 43.1. In the controls MPAP declined steadily from 22.9 to 16.0 mm Hg during the 4 min of observation, while the MPAP in the 2 Monge patients fell from 51.5 to 34.0 mm Hg, a drop of 33%, which is similar to the 30% drop in the controls. No significant changes could be detected in either group for mean PCP.

Figure 43–2 shows the effect of exercise over a 4-min period. In the Monge patients MPAP rose from 51.5 to 93.0 mm Hg, or by 81%, while in the controls the corresponding rise in MPAP was from 22.9 to 49.0 mm Hg, an increase of 109%. PCP rose from a mean 6.8 to 9.8 mm Hg (44%) in the controls and from 7.5 to 8.9 (20%) in the Monge group.

Acetyl choline infused for 4 min into the

pulmonary artery at the rate of 5 μ g/min. produced a drop in MPAP of 4.9 mm Hg (16.8%) in the controls, which is less than the drop observed during oxygen breathing, while the mean PCP fell from 6.8 to 5.4 mm Hg—a change of 17%. A drop in MPAP with acetyl choline was observed in one patient with Monge's syndrome, amounting to 8.5 mm Hg or 16%. No change occurred in PCP.

The Distribution of Pulmonary Blood Flow.

Table 43–16 summarizes the means and standard deviations of pA−aO2, MPAP, MPCP, and cardiac indices of the 3 groups from the altitude of La Paz and those of sea level Group III, who provided the comparison of the regional distribution of pulmonary blood flow for the 2 body positions.

MPAP of 22.3 mm Hg., now regarded as normal for the altitude of La Paz, 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. The resting mean pA − aO_2 gradient is related to the corresponding reduction in gradient between PI O_2 + PA O_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 (stippled lines) and right lower lung zones (continuous lines) in recumbency and in the vertical positions are shown for a normal male high altitude dweller (HAD) in Figs. 43–3 and 43–4, for a normal male studied similarly at sea level, in Figs. 43–5 and 43–6 whereas 43–7 depicts similar curves from a male patient with CMS.

Table 43–17 provides the means of areas of RUZ in cm^2 in recumbency and in the sitting positions for the 4 groups as well as the means

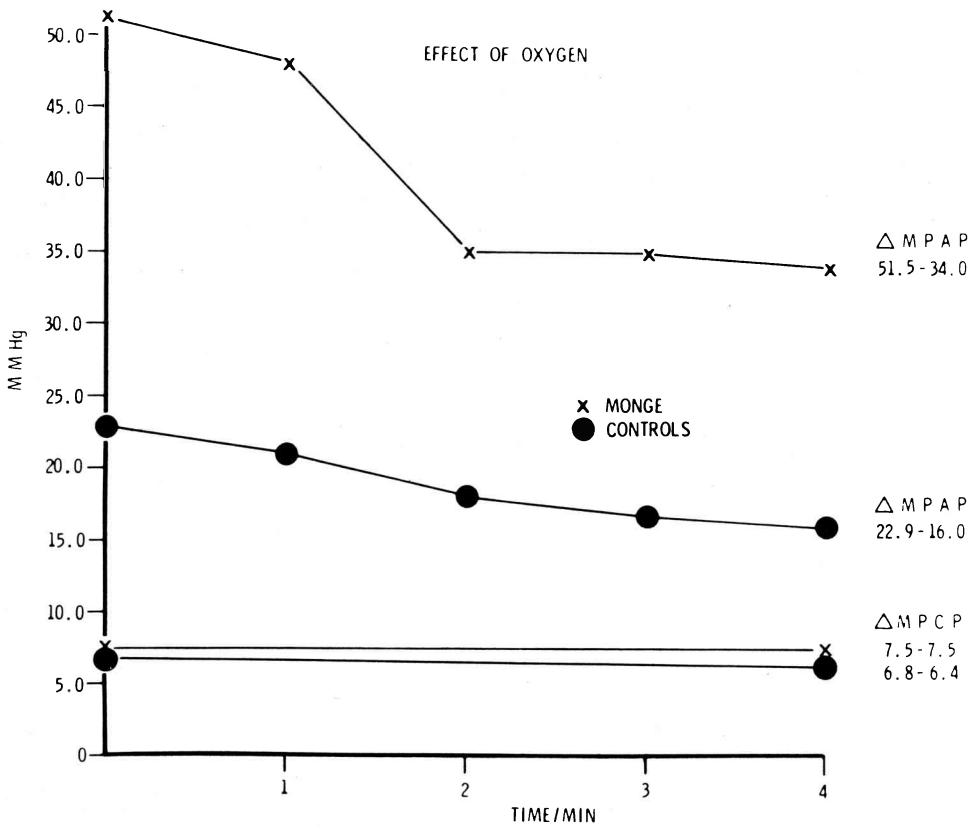

FIG. 43–1. The effect of oxygen breathing on MPAP and PCP is shown over 4 min. In the normal native males, MPAP falls steadily by 30% from the resting mean. In the Monge group, the mean drop in MPAP took place at 2 min of O_2 breathing and amounted to 33%. No change was demonstrable in respect of MPCP.

TABLE 43–16. PA−aO2, MPAP, MPCP, AND CARDIAC INDICES OF THE FOUR GROUPS

	N	Age	PA-aO2	MPAP	MPCP	Cardiac Index (Fick)
Group I Males H.A.D.	15					
$\bar{X}$		19.9	2.5	22.3	6.4	3.6
S.D.		2.0	0.41	1.7	1.1	0.21
Group II Male Newcomers	3					
$\bar{X}$		33	3.1			
S.D.		10	0.95			
Group III Males of Sea Level	5					
$\bar{X}$		31	15.1	14.6	5.4	3.6
S.D.		8	0.2	1.1	0.9	0.25
Group IV CMS	12					
$\bar{X}$		51	8.6	51.5	7.5	3.85
S.D.		12	2.14			0.31

H.A.D. = High Altitude Dweller; PA-aO2 = Alveolar-arterial oxygen gradient; MPAP in mm Hg = Mean pulmonary artery pressure; MPCP in mm Hg = Mean pulmonary capillary pressure; Cardiac Index in L/min/BSA; CMS = Chronic Mountain Sickness.

of ratios of Area RUZ/Area RLZ for the same body positions. Males native to sea level or to high altitude show similar reductions in perfusion of the RUZ, the means of the ratios being .59 at altitude and .55 at sea level respectively, while the largest reduction in the mean of these ratios obtained in 12 patients with chronic mountain sickness.

Table 43–18 provides the individual data used in the calculations of the regional distribution of pulmonary blood flow in the vertical position for all 4 groups. The means show that the percentage distribution of isotope is practically the same as the regional blood flows. At sea level the right upper zone ($\dot{Q}$RUZ) of normal males received 17.0 ± 0.34 percent of total cardiac output ($\dot{Q}$) while the right lower lung zone ($\dot{Q}$RLZ) obtained 30.8 ± 1.44 percent of total $\dot{Q}$. At the altitude of La Paz normal males showed a similar distribution in the vertical postures, in that $\dot{Q}$RUZ was 17.5 ± 1.27% while that of $\dot{Q}$RLZ amounted to 29.1 ± 1.3% of total $\dot{Q}$. The CMS group IV showed a mean $\dot{Q}$RUZ of only 7.7 ± 1.81% and a $\dot{Q}$RLZ of 29.0 ± 1.69%.

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%.

Table 43–19 shows the data for the 4 groups used in the calculation of regional blood flows 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 1.5%, the mean being 30.0 ± 1.35%. The patients with CMS in Group IV showed a much reduced mean $\dot{Q}$RUZ, namely 11.1 ± 0.41 while $\dot{Q}$RLZ was 24.1 ± 1.2 (see Fig. 43–7).

In group II the mean values in recumbency for the 3 male newcomers to high altitude were 26.3 ± 0.8% for $\dot{Q}$RUZ and 28.2 ± 0.7% for $\dot{Q}$RLZ respectively.

Autopsy Studies:

The differences in perfusion patterns observed

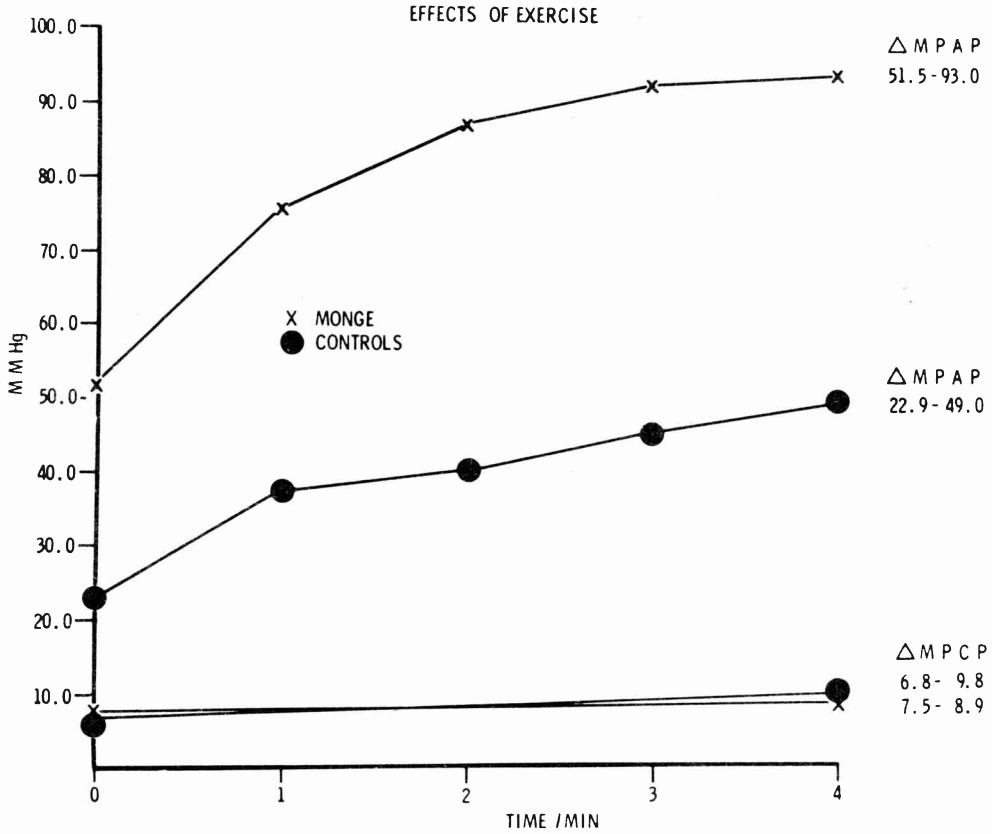

FIG. 43–2. Exercise, consisting of straight leg raising over 4 min, shows a 109% increase in mean MPAP in the normals and an 81% elevation in MPAP in the Monge patients. The MPCP rose by 44% in the controls and by only 20% in the Monge group.

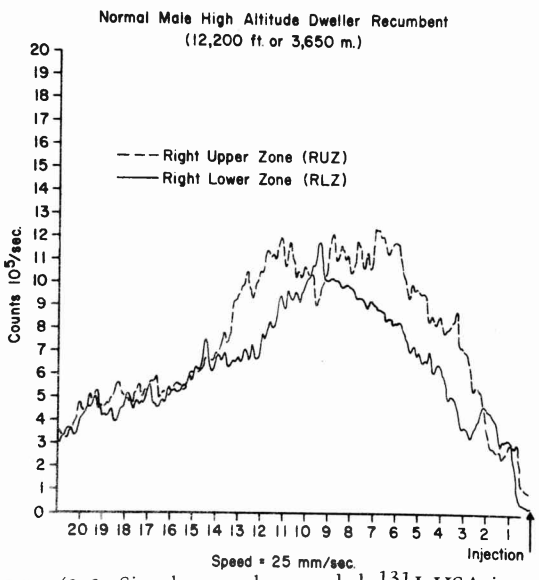

FIG. 43–3. Simultaneously recorded ^{131}I HSA isotope dilution curves from RUZ and RLZ in recumbent male HAD.

$$\text{Ratio of } \frac{\text{Area RUZ}}{\text{Area RLZ}} = 0.83$$

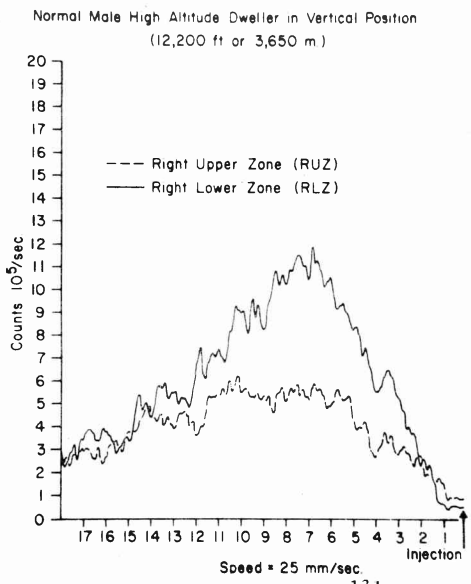

FIG. 43–4. Simultaneously recorded ^{131}I HSA isotope dilution curves from RUZ and RLZ of male HAD in vertical position.

$$\text{Ratio of } \frac{\text{Area RUZ}}{\text{Area RLZ}} = 0.59$$

TABLE 43–17. MEANS OF RUZ AND RLZ AND THEIR' RATIOS IN SITTING AND RECUMBENT POSITIONS IN FOUR GROUPS.

	Recumbency		*Sitting*		*Recumbency*	*Sitting*
	Area RUZ CM^2	*Area RLZ* CM^2	*Area RUZ* CM^2	*Area RLZ* CM^2	*Areas RUZ / Areas RLZ*	*Areas RUZ / Areas RLZ*
Group I Male Native LA PAZ (12,200 ft) (Figs. 43–3 and 43–4)	115.49	139.4	62.37	105.66	.83	.59
Group II Male Newcomers LA PAZ (12,200 ft)	60.16	64.96	49.15	68.52	.93	.71
Group III Male Sea Level (Figs. 43–5 and 43–6)	104.01	106.25	79.54	147.05	.97	.55
Group IV C M S (Chronic Mountain Sickness)	18.21	191.46	16.36	184.81	.095	.089

Areas have been derived in cm^2 by electronically integrated planimetry.

TABLE 43–18. COMPARISONS OF REGIONAL DISTRIBUTION OF PULMONARY BLOOD FLOW IN NORMALS & C M S* AT ALTITUDE (3,650m) AND SEA LEVEL IN VERTICAL (SITTING) POSITION.

	I_T = counts/10^6/min	AREA RUZ	AREA RLZ	$\frac{IRUZ}{IT} \times 100$	$\frac{IRLZ}{IT} \times 100$	AREA $\dot{Q}$	$\dot{Q}$ L/min	$\dot{Q}$RUZ L/min	$\frac{\dot{Q}RUZ}{Q} \times 100 = \%\dot{Q}$	$\dot{Q}$RLZ/L/min	$\frac{\dot{Q}RLZ}{\dot{Q}} \times 100 = \%\dot{Q}$
Group I Male H.A.D. N = 15											
Mean		2.48	4.36	17.4	30.8	1.55	5.5	.96	17.5	1.70	29.1
S.D. ±		.21	.13	1.2	1.2	.13	.47	.11	1.27	.16	1.3
Group II Male Newcomers N = 3											
Mean	14.8	2.94	4.24	19.8	28.4	1.48	6.0	1.19	19.7	1.73	28.5
S.D. ±	.38	.07	.07	.59	.78	.03	.15	.015	.78	.05	.87
Group III Males at Sea Level N = 5											
Mean	13.6	2.31	4.22	17.04	31.0	1.44	5.7	.96	17.0	1.75	30.8
S.D. ±	.35	.064	.125	.36	1.46	.056	.27	.06	.34	.056	1.44
Group IV C M S N = 12											
Mean	14.8	0.73	4.38	9.8	30.3	1.45	6.94	0.53	7.7	2.09	29.0
S D ±	0.41	.02	0.7	0.2	1.29	0.32	1.1	0.04	1.81	0.61	1.69

* C M S = Chronic Mountain Sickness

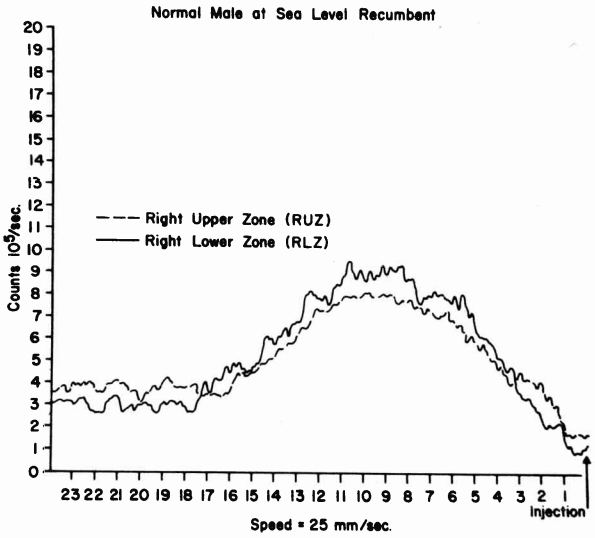

FIG. 43–5. Simultaneously recorded ^{131}I HSA isotope dilution curves from RUZ and RLZ of a normal recumbent male at sea level.

$$\text{Ratio of } \frac{\text{Area RUZ}}{\text{Area RLZ}} = 0.97$$

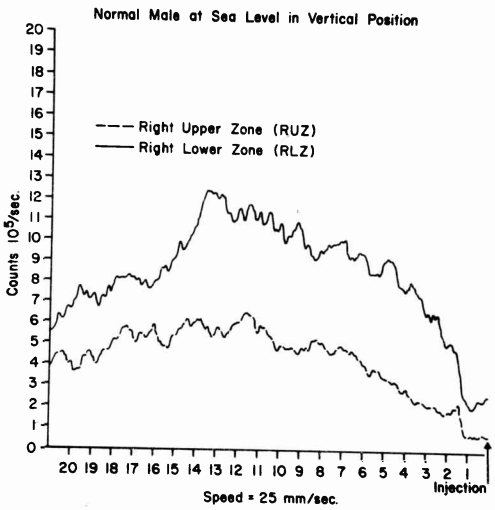

FIG. 43–6. Simultaneously recorded ^{131}I HSA isotope dilution curves from RUZ and RLZ of a normal male in sitting position at sea level.

$$\text{Ratio of } \frac{\text{Area RUZ}}{\text{Area RLZ}} = 0.55$$

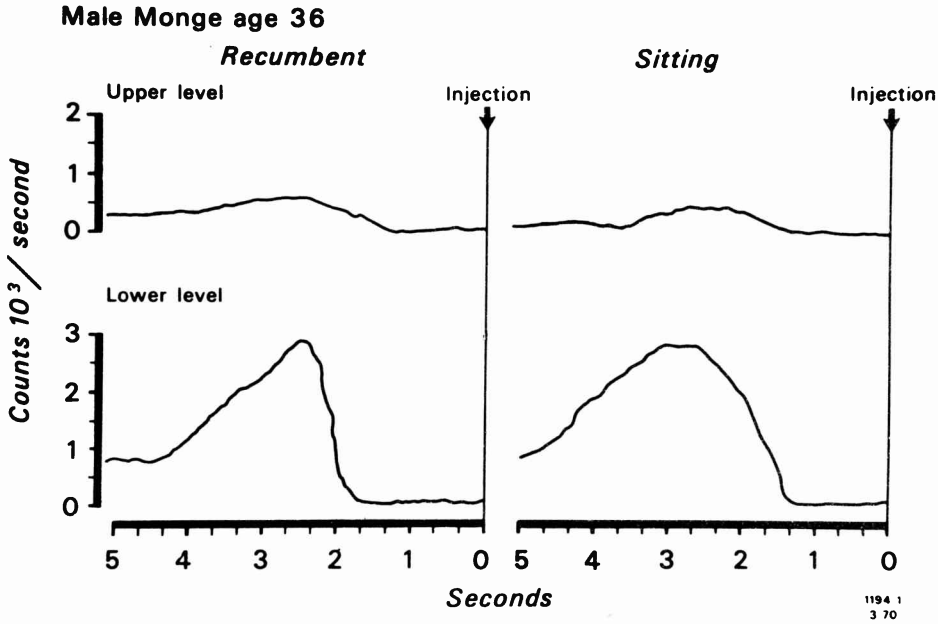

FIG. 43–7. Simultaneously recorded ^{131}I HSA isotope dilution curves from RUZ and RLZ of a male patient with chronic mountain sickness (Monge CMS) both in recumbency and in sitting positions. The QRUZ is very small and ratios of $\frac{\text{Area RUZ}}{\text{Area RLZ}}$ are less than 0.1 in both positions.

TABLE 43–19. COMPARISONS OF REGIONAL DISTRIBUTION OF PULMONARY BLOOD FLOW IN NORMALS AND IN C M S* AT ALTITUDE (3,650m) IN RECUMBENCY.

	I_T = counts/10^6/min	AREA RUZ	AREA RLZ	$\frac{IRUZ}{I_T} \times 100$	$\frac{IRLZ}{I_T} \times 100$	AREA $\dot{Q}$	$\dot{Q}$ L/min	$\dot{Q}$RUZ L/min	$\frac{\dot{Q}RUZ}{\dot{Q}} \times 100 = \%\dot{Q}$	$\dot{Q}$RLZL/min	$\frac{\dot{Q}RLZ}{\dot{Q}} \times 100 = \%\dot{Q}$
Group I											
Male H.A.D.											
N = 15											
Mean	14.7	3.79	4.38	25.7	29.7	1.50	6.0	1.54	25.9	1.78	30.0
SD±	.54	.22	.14	1.55	1.41	.18	.68	.22	1.5	.23	1.35
Group II											
Male Newcomers											
N = 3											
Mean	15.0	3.94	4.24	26.3	28.2	1.39	6.5	1.71	26.3	1.84	28.2
SD±	.17	.08	.06	.78	.70	.015	.17	.02	.75	.015	.72
Group III											
Males at Sea Level											
N = 5											
Mean	15.6	4.08	4.16	28.0	28.7	1.39	6.32	1.77	28.6	1.81	28.5
SD±	.63	.11	.08	.84	1.11	.155	.52	.19	.81	.20	1.02
Group IV											
C M S											
N = 12											
Mean	15.4	0.81	4.49	10.3	29.3	1.42	6.61	0.73	11.1	1.8	24.1
SD±	.71	0.01	.08	0.3	1.66	.161	0.60	0.08	.41	.30	1.2

*CMS = Chronic Mountain Sickness

TABLE 43–20. NUMBER OF DA/PA RATIO (NUMBER OF DISTAL ARTERIES OVER NUMBER OF PROXIMAL ARTERIES).

Cases	*Ratio DA/PA Mean ± S.D.*	*F*	*P*
Control	3.34 ± 1.86	0.1748	N.S.
U L	3.05 ± 1.16		
L L			
C M S			
U L	11.10 ± 5.62	0.3586	N.S.
L L	12.31 ± 3.12		
Control Both Lobes	3.10 ± 1.52		
C M S Both Lobes	11.70 ± 4.47	64.9945	<0.001

in respect of QRUZ in patients with CMS prompted us to seek morphometric vascular information from autopsied lungs at La Paz. A 31 year old female patient without evidence of lung disease and who died from an ovarian neoplasm constitutes the normal control study for the one patient known to have suffered from CMS for at least 3 years and who had a persistent Hb of 27.6 g. He died at 53 years following a massive thrombosis of the superior mesenteric artery. In both instances 1 cm cubes of tissues were obtained from the bronchovascular bundles 10 cm distal from the hilum both from the right upper (RUL) and right lower lobes (RLL). Following standard preparation the cross sectional areas, external and internal diameters and the total number of pulmonary arteries per field at identical distances from the hilum were measured by integrated planimetry and comparisons were made by computer in regard to:

(1) The number of distal (DA) and proximal arteries (PA) per field and their ratios in the RUL and RLL respectively.

(2) The pulmonary artery medial area expressed as a percentage of the total cross sectional area of the vessel.

(3) A correlation analysis between medial area (MA) and the ratio of the internal over the external diameters, as well as between the medial area and the external diameter alone.

Table 43–20 shows that the ratios of DA/PA in the RUL and RLL in the control lung were similar, while in CMS no significant differences obtained in regard to DA/PA ratios of RUL and RLL but the means of the CMS ratio was almost 4 times that of the control lung and the difference in this mean of the ratio in CMS was statistically highly significant.

Table 43–21 summarizes the means of the analysis concerning size of medial area. It shows that in the control lung the medial area of 30 RUL vessels examined, when expressed as a per cent of the total cross sectional area is greater than that of the 30 corresponding RLL vessel and that this difference was statistically highly significant.

This difference is further increased between the RUL and RLL vessels in CMS and this difference is also statistically highly significant. No statistical significance obtains however when the means are compared for the vessels of both lobes of the normal compared with the total number of 60 vessels of both lobes of the CMS patient.

Figure 43–8 shows a typical pulmonary artery from the RUL 10 cm from the right hilum of a normal high altitude dweller. The total cross sectional area is small and a markedly corrugated appearance of the medial coat is evident.

Figure 43–9 shows a typical pulmonary artery from the RLL taken exactly 10 cm from the right hilum. The cross sectional area is much increased suggesting distension of the vessel with a taut appearance of its medial coat, contrasted with the relaxed pattern of the coat in Fig. 43–8.

Figure 43–10 shows a typical RUL artery taken 10 cm from the right hilum in the patient with CMS. There is no evidence of intimal disease and the medial coat has a similar

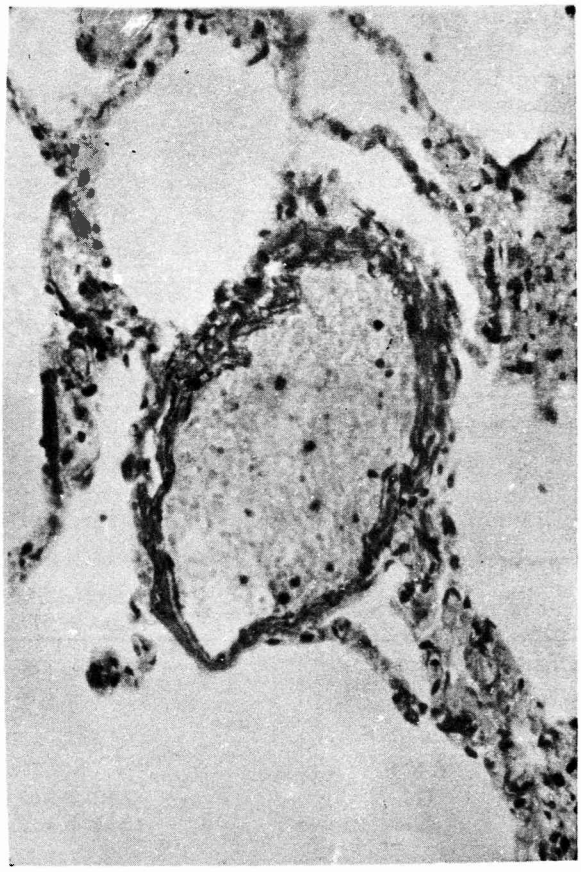

FIG. 43–8. Typical pulmonary artery (normal high altitude dweller) is shown located in the right upper lobe 10 cm from the right hilum. The total cross sectional area is small and a marked corrugated appearance of the medial coat is evident.

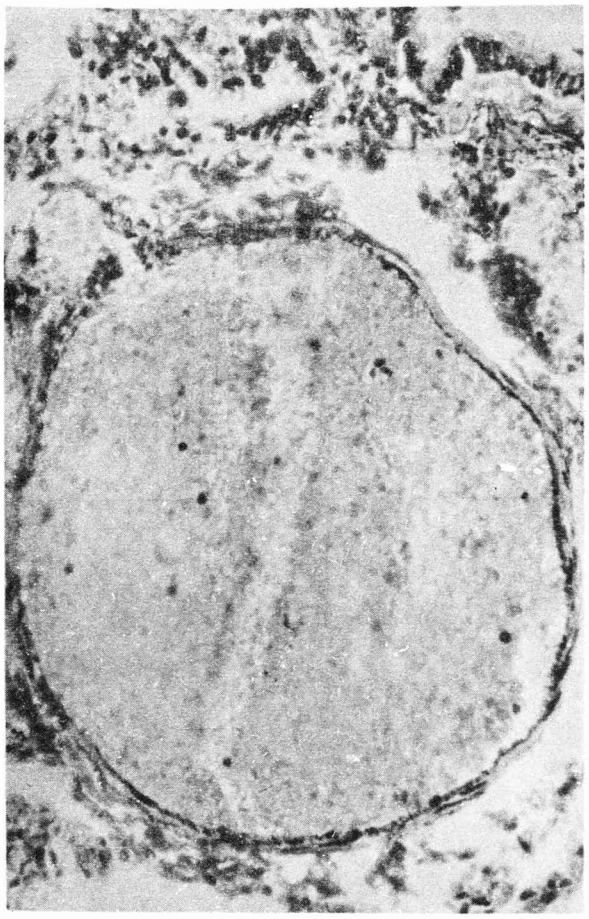

FIG. 43–9. A typical pulmonary artery (normal high altitude dweller) is shown from the right lower lobe and 10 cm from the right hilum. The cross sectional area is much increased suggesting also distension of the artery. Its medial coat is very taut contrasted with that shown in Fig. 43–8.

corrugated appearance as Fig. 43–8 and a small cross sectional area.

Figure 43–11 depicts a RLL pulmonary artery 10 cm from the right hilum from the lung of the patient with CMS. The marked overdistension of this vessel suggests a "balloon" effect with a marked increase in cross sectional area and striking tautness of its medial coat.

DISCUSSION

Increased pA − aO_2 gradients, suggestive of non-uniformity of $\dot{V}A/\dot{Q}$ have been demonstrated in normals at altitude (8, 12, 13, 15) while other studies are in support of the contrary (3, 9). The significant increase in physiological dead space (VDS) and the excessively widened pA − aO_2 gradients found in patients with Monge's Syndrome (CMS) who showed particularly high elevations in MPAP in the absence of other heart or lung disorders (5), 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 was demonstrated by a persistent decrease in perfusion of the right upper lung zones, both in recumbency as well as in the vertical position, using the ^{131}IHSA technique, detailed again in this present study. The details thus far concerning regional distribution of pulmonary blood flow in healthy normal males at sea level and in male HAD are entirely confined to the right upper (RUZ) and right lower (RLZ) zones. In the vertical position RUZ receives about 17% of $\dot{Q}$ regardless of altitude and in the presence of a difference in MPAP of 7.7 mmHg for male HAD. The observations in the 3 male newcomers, while not supported by measurements of MPAP and involving 3 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 − aO_2 of this group is, however, wider than in the male HAD. 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 − aO_2 was of the same magnitude as in the male high altitude dwellers.

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 distribution 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 $\dot{Q}$. In the male newcomers to 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 the RLZ. Although these differences appear to

TABLE 43–21. PULMONARY ARTERIAL MEDIAL AREA (M A) EXPRESSED AS PERCENT OF THE TOTAL CROSS-SECTIONAL ARTERIAL AREA.

Cases	*No. of Arteries*	*Medial Area (M A) Median % ± S.D.*	*F*	*P*
Control				
U L	30	19.15 ± 4.35	41.2384	<0.001
L L	30	12.87 ± 3.12		
C M S				
U L	30	21.28 ± 5.50	40.7573	<0.001
L L	30	13.00 ± 4.49		
Control Both Lobes	60	16.01 ± 4.91	1.1613	N.S.
C M S Both Lobes	60	17.14 ± 6.50		

FIG. 43–10. A typical right upper lobe artery (chronic mountain sickness) is shown 10 cm from the right hilum. There is no evidence of intimal disease and the medial coat has a corrugated appearance as in Fig. 43–8.

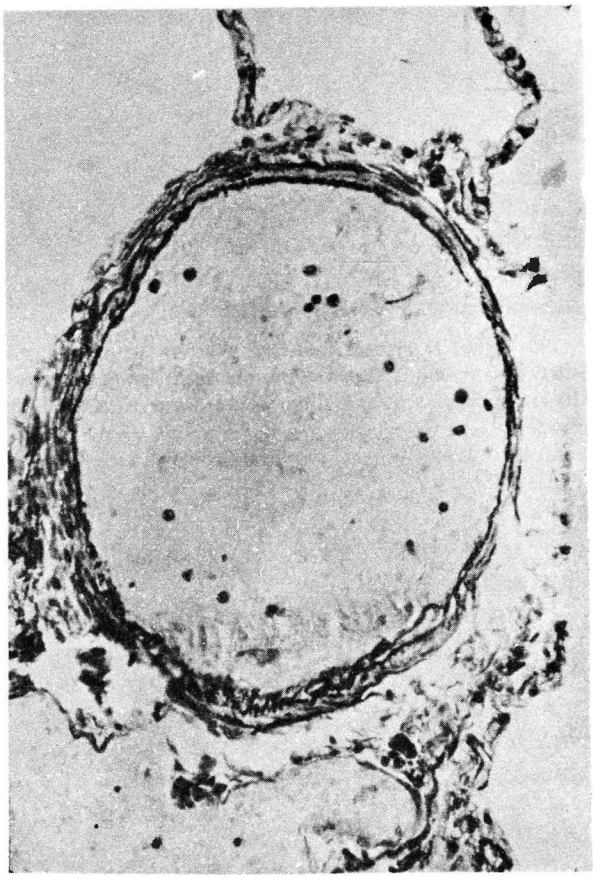

FIG. 43–11. A right lower lobe artery (chronic mountain sickness) is shown 10 cm from the right hilum. The marked overdistension of this vessel suggests a "balloon" effect with a considerable increase in cross sectional area and striking tautness and hyperplasia of its medial coat.

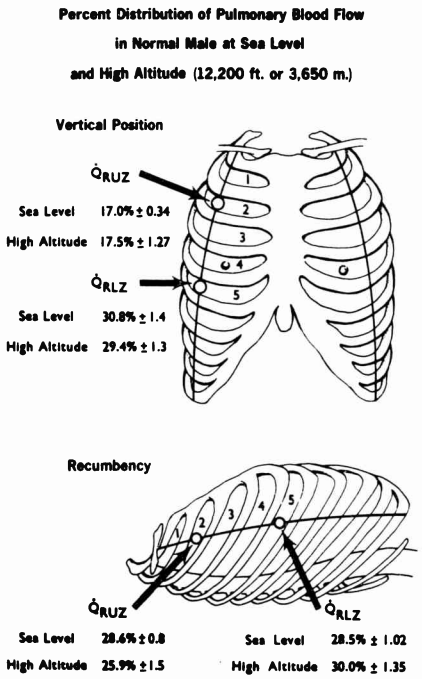

FIG. 43–12. Mean percent distributions of $\dot{Q}$ to RUZ and RLZ are shown in normal males at altitude and at sea level in recumbency and vertical positions. In the vertical position, the distributions are the same at sea level and altitude.

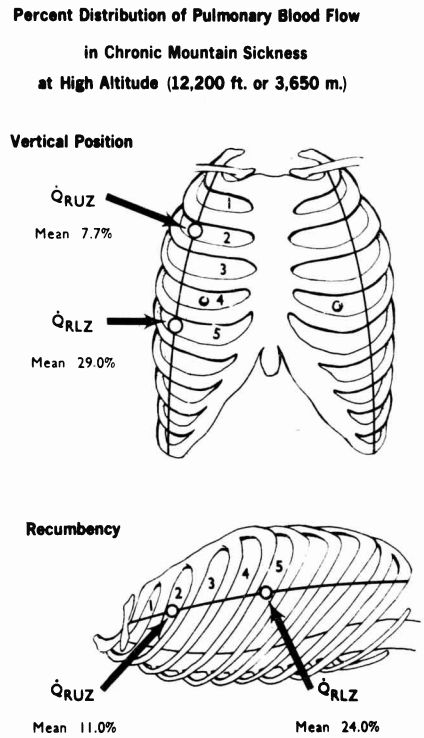

FIG. 43–13. Mean percent distribution of $\dot{Q}$ to RUZ and RLZ are shown in chronic mountain sickness (CMS) in the vertical and recumbent positions. The difference in means for $\dot{Q}$RUZ is significantly less than in normal males at altitude or sea level.

be very minor, it is nevertheless of interest that in all our observations conducted at altitude in recumbency, the perfusion of the right upper zone was less than at sea level. The similarity in reduction of perfusion to the right upper lung zones 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 at rest in the pulmonary artery at altitude has no part to play in ensuring a more even distribution of pulmonary blood flow to the upper lung zones. This is particularly striking in CMS where $\dot{Q}$RUZ is markedly reduced both in the vertical and recumbent position (Figs. 43–12 and 43–13) in the face of a MPAP at rest of above 50 mm Hg.

In the 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 (10). Excessive $\dot{V}A/\dot{Q}$ mismatching during exercises at altitude becomes, therefore, a distinct possibility if tidal volume distribution is primarily to the upper lung zones and would explain the widening of PA − aO2 during effort, so frequently noted above 12,000 ft (13).

Regional differences in the morphometry of the pulmonary vasculature apply in the upper and lower lung zones of normal human lungs at altitude and no actual arterial disease obtains in CMS. 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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SUMMARY

Comparisons with 14 normal, younger, male native residents of La Paz showed that 20 patients with Monge's syndrome have significantly higher mean body surface areas, hemoglobin, resting tidal volumes [VT (BTPS)], and resting minute volumes [$\dot{V}E$ (BTPS)].

If [$\dot{V}E$ (BTPS)] is subdivided into its components of alveolar [$\dot{V}A$ (BTPS)] and dead space ventilations [$\dot{V}DS$ (BTPS)], it becomes apparent that the former is significantly smaller and the latter much larger in the Monge patients than in the controls.

Further differences emerge in that means of physiological dead space, PA–aCO2 and PA–aO2 gradients are increased in the Monge group. Alveolar hypoventilation in the Monge group is evidenced by an elevated mean PaCO2; a lower mean pH of 7.349, a PaO2 of 48.1 mm Hg, compared with 57.7 mm Hg in the normals; and a mean arterial oxygen saturation of 82.8% versus that of 89.7% in the latter.

Simultaneous surface scanning of the right upper and lower lung zones, using a central venous injection of ^{131}IHSA (human iodinated serum albumin), showed a reduction of total isotope activity in the right upper zones of the Monge group, both in the sitting and recumbent positions. A perfusion anomaly of the upper lung zones is postulated to explain the increase in physiological dead space and which appears to be related to a structural difference in the right upper lobe pulmonary arteries contrasted with those in the right lower lobes.

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