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Developmental, Genetic, and Environmental Components of Lung Volumes at High Altitude

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ABSTRACT Vital capacity and residual lung volume (in terms of 1/min or ml/m^2 of body surface area) of 357 subjects (205 males, 152 females) was evaluated in La Paz, Bolivia, situated at 3,750 m. The sample included: (1) 37 high altitude rural natives (all male), (2) 125 high altitude urban natives (69 male, 58 female), (3) 85 Bolivians of foreign ancestry acclimatized to high altitude since birth (40 male, 45 female), (4) 63 Bolivians of foreign ancestry acclimatized to high altitude during growth (30 male, 33 female), and (5) 47 non-Bolivians of either European or North American ancestry acclimatized to high altitude during adulthood (24 male, 23 female). Results indicate that (1) all samples studied, irrespective of origin or acclimatization status, have larger lung volumes than those predicted from sea level norms; (2) the high altitude rural natives have significantly greater lung volumes (vital capacity and residual lung volume) than the high altitude urban natives and all the non-native high altitude samples; (3) males acclimatized to high altitude since birth or during growth attain similar lung volumes as high altitude urban natives and higher residual lung volumes than subjects acclimatized to high altitude during adulthood but lower than the high altitude rural natives; (4) females acclimatized to high altitude since birth or during growth attain similar lung volumes as subjects acclimatized to high altitude during adulthood; (5) age at arrival to high altitude is inversely related to residual lung volume but not vital capacity; (6) among subjects acclimatized to high altitude during growth, approximately 20–25% of the variability in residual lung volume can be explained by developmental factors; (7) among high altitude rural and urban natives, it appears that approximately 20–25% of the variability in residual lung volume at high altitude can be explained by genetic traits associated with skin reflectance and genetic traits shared by siblings; and (8) vital capacity, but not the residual lung volume, is inversely related to occupational activity level. Together these data suggest that the attainment of vital capacity at high altitude is influenced more by environmental factors, such as occupational activity level, and body composition than developmental acclimatization. On the other hand, the attainment of an enlarged residual volume is related to both developmental acclimatization and genetic factors. Am. J. Hum. Biol. 9:191–203, 1997.

A prominent feature of high altitude natives residing in the Himalayas and the Andes is their enlarged lung volume (Hurtado, 1932, 1964; Frisancho, 1969; Mueller et al., 1978; Greksa et al., 1987; Droma et al., 1991). An ongoing question is the extent to which this characteristic reflects differences in acclimatization based on genetic differences, or simply reflects population differences in adaptation based on environmental factors. In other words, the extent to which

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this characteristic is acquired or genetic is not well defined. In an earlier study, the hypothesis was advanced that the enlarged lung volume of high altitude natives is the result of a developmental adaptation to high altitude hypoxia (Frisancho, 1975). This hypothesis was based upon the finding that Peruvian sea level subjects, raised since childhood at high altitude, attained lung volumes similar to high altitude natives, but Peruvian and U.S. sea level natives, who resided at high altitude for as long as 2 years, attained lower lung volumes than the high altitude natives. Due to the fact that there has been a great deal of admixture among Peruvian populations, it is possible that the similarity between the sea level Peruvians raised (during childhood) at high altitude and the high altitude natives may be due to their genetic similarities rather than reflect a developmental factor. One productive way of answering this question is to study populations who do not share the same genetic makeup as the high altitude natives. For this reason, the lung function of foreigners (Europeans and North Americans) acclimatized to high altitude during adulthood, Bolivians of foreign ancestry acclimatized to high altitude either since birth or during growth, and high altitude natives living in the rural and urban areas of La Paz, Bolivia was studied.

METHODS AND MATERIALS

Sample

Lung volumes were evaluated in 357 subjects (205 males and 152 females), 13–49 years of age, who were exposed to high altitude either since birth, during growth, or at adulthood, as well as high altitude natives living in the urban and rural areas of La Paz, Bolivia. The study included five samples (Table 1):

1. 37 high altitude rural natives (HARN) residing in the village of Taucachi situated at 4,100 m outside of La Paz
2. 125 high altitude urban natives (HAUN) (69 male, 58 female)
3. 85 Bolivians of foreign ancestry acclimatized to high altitude since birth (AHAB) (40 male, 45 female)
4. 63 Bolivians of foreign ancestry acclimatized to high altitude during growth (AHAG) (30 male, 33 female)
5. 47 non-Bolivians of either European or North American ancestry acclimatized to high altitude during adulthood (AHAA) (24 male, 23 female)

Anthropometry

The subjects were evaluated through standard anthropometric techniques (Weiner and Lourie, 1981; Frisancho, 1990), which included stature and weight. The body mass index (BMI, kg/m^2) was computed. Body surface area was estimated using the equation of DuBois and DuBois (1916). Measurements of skin reflectance were made with a Photovolt Reflectometer, Model 575. Reflectance readings were made following the same procedures used in a previous study (Frisancho et al., 1981). This included measurements with two filters identified as triamber and trigreen. The filters have transmission peaks of approximately 600 nm (triamber) and 550 nm (trigreen) (Conway and Baker, 1972; Frisancho et al., 1981). At least two readings at the inner arm distal to the axillary region were obtained for each participant. Reflectance readings given by both filters were averaged for each subject.

Lung function

Lung volume and capacity values were obtained by the technical personnel of the Respiratory Department of the Instituto Boliviano de Biologıa de Altura (IBBA) situated at an altitude of 3,750 m. Measurements were taken using a recording 13 lite spirometer (Warren Collins, Braintree, MA) while subjects were in a sitting position and followed the general guidelines given with the instrument for measurements using helium. In view of the fact that measurements of lung function taken at IBBA are considered the standard reference for high altitude studies in the Andes, their protocols were strictly followed. The present study reports on three measurements: vital capacity, residual lung volume, and total lung volume. Total lung capacity was calculated as the sum of vital capacity and residual volume.

Vital capacity. After the spirometer was filled with a sufficient amount of oxygen, the subject (in a sitting position) breathed normally into a mouthpiece for about 3 minutes, during which time the tidal volume and respiratory frequency were measured. The product of these two values gives ventilation per minute. The subject was asked to take a deep breath and a forceful expiration and inspiration. This task was performed at least

TABLE 1. Anthropometric characteristics of male high altitude rural natives (HARN), high altitude urban natives (HAUN), Bolivians of foreign ancestry acclimatized to high altitude since birth (AHAB), Bolivians of foreign ancestry acclimatized to high altitude during growth (AHAG), and foreigners acclimatized to high altitude during adulthood (AHAA) studied for lung function in La Paz, Bolivia (3,750 m)

	High altitude rural native (HARN)		High altitude urban natives (HAUN)		Acclimatized since birth (AHAB)		Acclimatized during growth (AHAG)		Acclimatized during adulthood (AHAA)	
	Mean	Adjusted mean ± SE	Mean	Adjusted mean ± SE	Mean	Adjusted mean ± SE	Mean	Adjusted mean ± SE	Mean	Adjusted mean ± SE
N	37		49		45		30		24	
Age (yrs)	34.8	n.a.	21.9	n.a.	22.4	n.a.	22.3	n.a.	32.2	n.a.
Age at arrival (yrs)	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	8.2	n.a.	27.3	n.a.
Residence at altitude	34.8	n.a.	21.9	n.a.	22.3	n.a.	14.0	n.a.	5.0	n.a.
Weight (kg)	58.2	54.4 ± 1.6	60.8	62.3 ± 1.1**	63.2	64.5 ± 1.3**	64.3	65.7 ± 1.6**	70.6	67.9 ± 1.8**
Height (cm)	160.5	160.9 ± 1.2	168.4	168.3 ± 0.8**	170.4	170.3 ± 1.0**	173.8	173.6 ± 1.2**	173.7	174.0 ± 1.4**
BMI (kg/m^2)	22.6	21.2 ± 0.5	21.4	22.0 ± 0.3	21.7	22.2 ± 0.4	21.3	21.8 ± 0.5	23.4	22.4 ± 0.5
SA (m^2)	1.6	1.6 ± 0.02	1.7	1.7 ± 0.02**	1.7	1.8 ± 0.02**	1.8	1.8 ± 0.02**	1.8	1.8 ± 0.03**
Sum of skinfolds (mm)	41.4	36.3 ± 3.2	48.5	50.6 ± 2.2**	50.8	52.6 ± 2.6**	45.9	47.8 ± 3.2*	54.8	51.11 ± 3.7**
Lean body mass (kg)	49.9	48.2 ± 1.2	49.8	50.4 ± 0.8	51.6	52.2 ± 1.0*	52.1	52.7 ± 1.2**	56.4	55.23 ± 1.3**
Fat weight	8.3	6.2 ± 1.1	11.1	11.9 ± 0.7**	11.6	12.3 ± 0.9**	12.2	13.0 ± 1.0**	14.2	12.68 ± 1.2**
Percent fat (%)	13.8	12.2 ± 1.3	17.8	18.5 ± 0.9**	17.8	18.4 ± 1.1**	18.2	18.8 ± 1.3**	19.4	18.2 ± 1.5**
Bio-impedance (Ω)	468.6	486.2 ± 9.4	525.4	518.4 ± 6.3**	520.2	513.9 ± 7.6*	517.7	511.2 ± 9.3	494.1	506.7 ± 10.7
Occupational activity (1–3)	2.8	3.0 ± 0.1	2.2	2.1 ± 0.9**	2.0	1.9 ± 0.1**	2.2	2.1 ± 0.1**	2.0	2.2 ± 0.2**
Reflectance (%)	25.9	25.4 ± 0.6	32.3	32.6 ± 0.6**	38.2	38.4 ± 0.5**	38.8	40.0 ± 0.7**	41.2	40.8 ± 0.8**
$Log_{(10)}$ reflectance	1.4	1.4 ± 0.8	1.5	1.5 ± 0.8	1.6	1.6 ± 0.7	1.6	1.6 ± 0.9	1.6	1.6 ± 1.0

n.a. = not applicable; BMI = body mass index; SA = body surface area.
*Significantly ($p < 0.05$) different from HARN.
**Significantly ($p < 0.01$) different from HARN.

three times, and the highest value was chosen.

Residual volume. The measurement of residual volume included evaluations of functional residual capacity (FRC), which was obtained by computation:

$$FRC = V_{added} \times F_{BTPS} \times \frac{Ch1\ (Ch2\text{-}Ch3)}{Ch3\ (Ch1\text{-}Ch2)}$$

where V_{added} is the volume of air added to the spirometer, F_{BTPS} is the conversion factor to correct the values of atmospheric temperature and pressure saturation (ATPS) to body temperature pressure saturation (BTPS), and Ch1, Ch2, and Ch3 are the concentrations of helium read at various points in the rebreathing period.

The protocol for measuring residual volume consisted of four steps. First, the spirometer was emptied and then filled with 600 ml of helium, and when the concentration reached approximately 7–8%, the value was recorded as Ch1. Second, the spirometer's bell was emptied, and when it became stabilized was filled again with 2 L of ambient air (V_{added}), after which the bell was turned on. Once this mixture attained a new equilibrium, the concentration of helium was recorded as the Ch2 value, and the volume present was inscribed on the paper record as a reference line for terminating the test. Third, approximately 1.5 L of 100% oxygen was then added to the system, and this volume was inscribed on the paper. Then the subject began breathing through the mouthpiece with a nose clip in place and then switched into the rebreathing system at normal end expiration. Fourth, the subject continued rebreathing until the oxygen consumed brought the end-tidal expiratory point in the respiratory cycle to the inscribed reference line. The stable helium concentration, after the subject was switched out of the rebreathing circuit, was noted as the Ch3 value. Finally, the FRC was calculated using the above-mentioned formula. Residual volume was calculated as the difference between the expiratory reserve volume and functional residual capacity.

Total lung capacity. Total lung capacity is vital capacity + residual volume. Based on this information, the proportion of residual volume to total lung capacity [(residual volume/total lung volume) $\times$ 100] was calculated for each subject. The lung volumes (corrected for BTPS) were expressed in ml/m^2 of body surface area.

Estimates of altitude-associated effects

To determine the altitude-associated effects on lung volumes, the lung volumes of each subject were also compared with lung volumes (expressed as ml/m^2 of body surface area) derived from sea level norms (Polgar and Promadhat, 1971; Polgar and Weng, 1979). The difference between the expected and observed values were the major analytical variables.

Estimates of occupational activity level

The subjects were asked about their participation in organized sports and physical activity (i.e., soccer, basketball, swimming, bicycling, tennis, and hiking). Each participant was specifically asked how many times per week he/she participated in an organized athletic activity. Based on this information, the subjects were classified into three groups: *Low level:* sedentary individuals who did not regularly practice any sport (although some subjects were occasionally involved in organized activities such as dance groups); *medium level:* individuals who participated in organized sports on a given school or college team, but such activity took place less than 3 times per week; *high level:* individuals whose employment was characterized by a high level of daily activity (e.g., agricultural workers), or subjects who were members of organized sports teams at school or college and the activity occurred more than 3 times per week (e.g., basketball, swimming, and soccer team members).

Statistical analysis

The data were analyzed using parametric and nonparametric procedures. First, because there were significant differences in the age of the samples and age is correlated with anthropometric dimensions and lung volumes, all inter-sample comparisons were adjusted for age by covariance analysis. Second, the variables that were not normally distributed were converted to z-scores (normalized) or logarithmic transformations in order to determine the statistical significance of the observed differences and inter-relationships.

RESULTS

General characteristics

Tables 1 and 2 give the general characteristics of the samples. As expected, the Bolivians of foreign ancestry acclimatized to high altitude during development (AHAG) differed significantly in age at arrival and length of residence at high altitude from high altitude urban natives (HAUN) and Bolivians of foreign ancestry acclimatized to high altitude since birth (AHAB). In terms of body size for males, all four groups were significantly taller and heavier than high altitude rural natives (HARN). Similarly, the HAUN and AHAB were significantly shorter than AHAG and foreigners acclimatized to high altitude during adulthood (AHAA). In terms of skin color, the Bolivians of foreign ancestry acclimatized to high altitude since birth (AHAB) or during development (AHAG), did not differ from foreigners acclimatized to high altitude during adulthood (AHAA), but all three samples were significantly lighter (i.e., higher skin reflectance values) than high altitude rural natives (HARN). In males, high altitude rural natives (HARN) had significantly higher scores of occupational activity than the four samples. On the other hand, in females the scores for occupational activity level of high altitude urban natives was significantly lower than those of the subjects acclimatized to high altitude during growth (AHAG) and during adulthood (AHAA).

Lung volumes

Figure 1 illustrates lung volumes of the five samples compared with that expected at sea level. These data show that all samples, irrespective of origin or acclimatization status, have larger lung volumes than those predicted from sea level norms. Furthermore, the increase is more evident in vital capacity than in residual lung volume and is greater among the high altitude rural natives than in the other samples.

Table 3 presents the non-adjusted and age-adjusted means and standard errors for vital capacity, residual volume, and total lung volume for males and females, expressed as simple milliliters of air or as ml/m^2 of body surface area. The following points are evident. Vital capacity (adjusted for body surface area) of high altitude urban natives (HARN) is significantly greater than that of high altitude urban natives (HAUN) and Bolivians of foreign ancestry acclimatized to high altitude since birth (AHAB), during development (AHAG), or during adulthood (AHAA). However, in terms of residual lung volume, foreigners acclimatized during adulthood (AHAA) have significantly ($P < 0.05$) lower residual volumes than all other groups. Bolivians of foreign ancestry acclimatized to high altitude since birth (AHAB) and during development (AHAG) attain similar residual lung volumes as that of HAUN but lower than that of HARN. Values for total lung volume follow the same pattern. The relative size of the residual lung volume is also significantly ($P < 0.01$) smaller in the foreigners acclimatized during adulthood (AHAA) compared with the HARN or HAUN.

Table 4 presents lung volumes for females where vital capacity is expressed in absolute terms (ml) or adjusted for body size (ml/m^2) and age is quite similar in all four samples. The residual lung volume and total lung volume follow the same pattern. Similarly, the relative size of the residual lung volume is also significantly ($P < 0.01$) smaller in the foreigners acclimatized during adulthood (AHAA) when compared with the HAUN.

DISCUSSION

Lung volumes and developmental response

A unique feature of high altitude natives is their enlarged residual lung volume. The fact that AHAB and AHAG had residual lung volumes that were similar to high altitude natives suggests that this characteristic, to a large extent, is the result of developmental acclimatization to high altitude (Frisancho et al., 1973; Frisancho and Greksa, 1989). As illustrated in Figure 2, among Bolivians acclimatized to high altitude during development (AHAG), about 20% (r = .44) of the variability in residual lung volume can be explained by age at arrival to high altitude. On the other hand, variability in vital capacity is not influenced by variability in age at arrival to high altitude (r = 0.19 of males and 0.18 for females). Additionally, as shown in Figure 1, in males the altitude-associated increase in residual lung volume compared with sea level norms is inversely related to acclimatization status, so that those subjects acclimatized during growth attain similar values as those of high altitude natives (HAUN). On the other hand, the increase in vital capacity is not related to acclimatization status. Similarly, the inverse relationship between an altitude-re-

TABLE 2. Anthropometric characteristics of female high altitude urban natives (HAUN), Bolivians of foreign ancestry acclimatized to high altitude since birth (AHAB), Bolivians of foreign ancestry acclimatized to high altitude during growth (AHAG), and foreigners acclimatized to high altitude during adulthood (AHAA) studied for lung function in La Paz, Bolivia (3,750 m).

	High altitude urban natives (HAUN)		Acclimatized since birth (AHAB)		Acclimatized during growth (AHAG)		Acclimatized during adulthood (AHAA)	
	Mean	Adjusted mean ± SE	Mean	Adjusted mean ± SE	Mean	Adjusted mean ± SE	Mean	Adjusted mean ± SE
N	56		40		33		23	
Age (yrs)	22.7	n.a.	20.56	n.a.	21.38	n.a.	32.81	n.a.
Age at arrival (yrs)	n.a.	n.a.	n.a.	n.a.	8.44	n.a.	28.63	n.a.
Residence at altitude	22.6	n.a.	20.52	n.a.	12.93	n.a.	4.18	n.a.
Weight (kg)	55.4	55.5 ± 1.1	53.60	54.25 ± 1.27	55.99	56.45 ± 1.38	58.57	56.39 ± 1.87
Height (cm)	156.8	156.8 ± 0.8	158.51	158.36 ± 0.99	162.65	162.54 ± 1.08**	163.08	163.60 ± 1.46**
BMI (kg/m^2)	22.5	22.6 ± 0.4	21.28	21.59 ± 0.43	21.14	21.35 ± 0.47*	21.99	20.96 ± 0.64*
SA (m^2)	1.5	1.5 ± 0.02	1.53	1.54 ± 0.02	1.59	1.60 ± 0.02**	1.62	1.60 ± 0.03
Sum of skinfolds (mm)	68.6	68.9 ± 2.5	67.98	69.13 ± 3.04	62.30	63.12 ± 3.31	69.61	65.74 ± 4.49
Lean body mass (kg)	40.6	40.7 ± 0.7	39.45	39.79 ± .86	42.16	42.40 ± 0.94	44.60	43.47 ± 1.27
Fat weight	14.8	14.9 ± 0.8	14.1	14.5 ± 0.9	13.8	14.0 ± 1.0	14.0	12.9 ± 1.4
Percent fat (%)	26.1	26.2 ± 1.0	26.2	26.4 ± 1.2	24.3	24.5 ± 1.3	23.1	23.4 ± 1.8
Bio-impedance (Ω)	566.6	565.2 ± 8.4	600.2	594.8 ± 10.1*	586.3	582.4 ± 11.0	551.7	570.1 ± 14.9
Occupational activity (1–3)	1.8	1.8 ± 0.1	1.90	1.80 ± 0.12	2.18	2.11 ± 0.13	2.09	2.42 ± 0.18**
Reflectance (%)	33.4	33.4 ± 0.4	36.95	37.03 ± 0.53**	38.15	39.21 ± 0.58**	40.33	40.06 ± 0.78**
$Log_{(10)}$ reflectance	1.5	1.5 ± 0.01	1.57	1.57 ± 0.01**	1.57	1.57 ± 0.01**	1.60	1.60 ± 0.01**

n.a. = not applicable; BMI = body mass index; SA = body surface area.
*Significantly ($p < 0.05$) different from HAUN.
**Significantly ($p < 0.01$) different from HAUN.

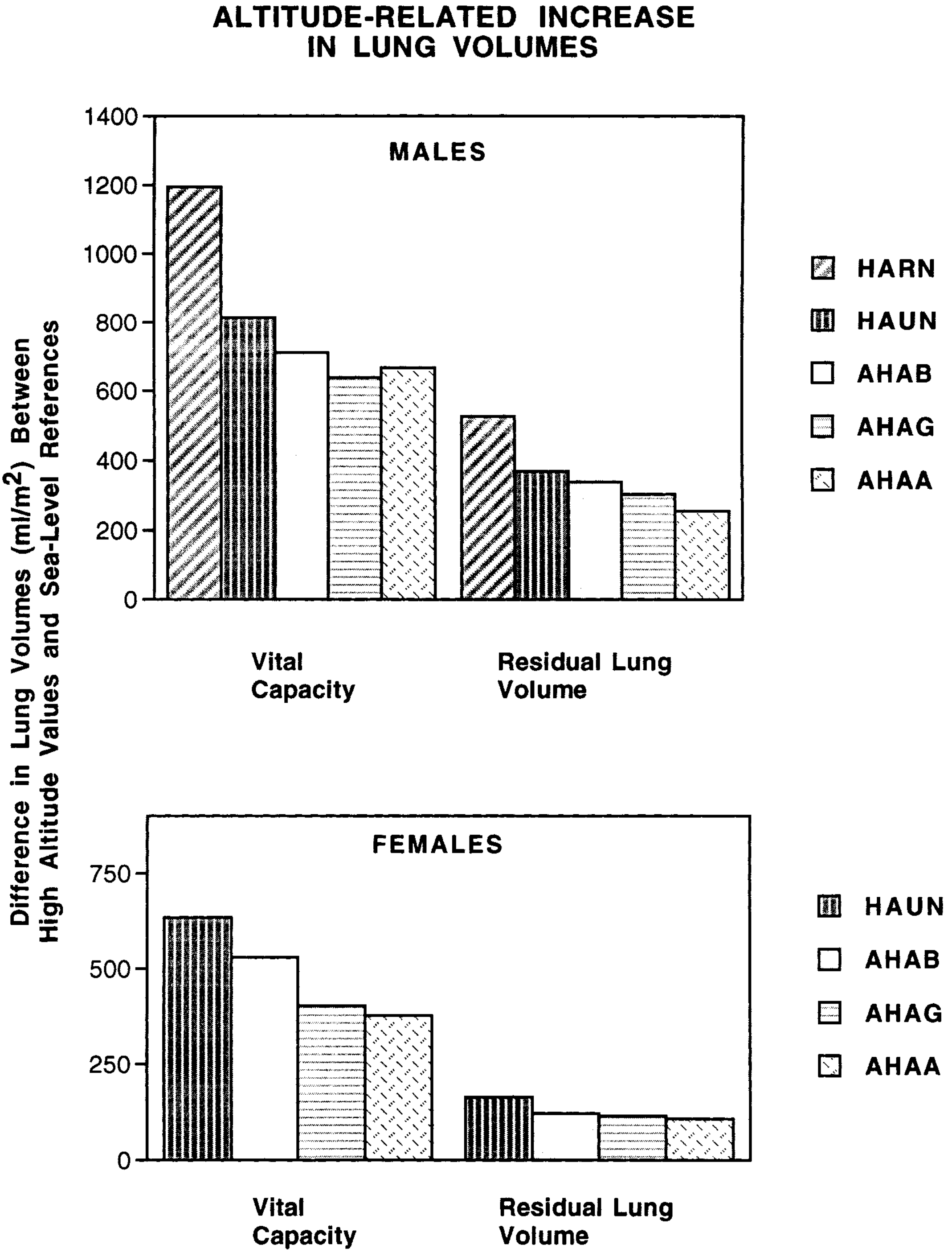

Fig. 1. Altitude-associated increase in lung volumes among high altitude natives and subjects acclimatized to high altitude. In both males and females the increase in residual lung volume is significantly greater among the subjects acclimatized to high altitude during growth (AHAG) than in subjects acclimatized during adulthood (AHAA).

TABLE 3. Age-adjusted lung volumes of male high altitude rural natives (HARN), high altitude urban natives (HAUN), Bolivians of Foreign Ancestry Acclimatized to high altitude since birth (AHAB), Bolivians of foreign ancestry acclimatized to high altitude during growth (AHAG), and foreigners acclimatized to high altitude during adulthood (AHAA) studied in La Paz, Bolivia (3,750 m)

	High altitude rural native (HARN)		High altitude urban natives (HAUN)		Acclimatized since birth (AHAB)		Acclimatized during growth (AHAG)		Acclimatized during adulthood (AHAA)	
	Mean	Adjusted mean ± SE	Mean	Adjusted mean ± SE	Mean	Adjusted mean ± SE	Mean	Adjusted mean ± SE	Mean	Adjusted mean ± SE
N	37		69		45		30		23	
VC (ml)	5253.9	5266.1 ± 123.9	5206.4	5201.7 ± 82.5	5199.5	5195.4 ± 100.0	5327.0	5322.7 ± 121.8	5411.3	5419.3 ± 142.7
RV (ml)	1807.1	1715.0 ± 75.5	1719.8	1755.4 ± 50.2	1724.4	1755.2 ± 60.9	1734.8	1766.9 ± 74.2	1661.0	1600.5 ± 86.9
TLV (ml)	7061.0	6981.1 ± 175.2	6926.3	6957.1 ± 116.6	6924.0	6950.7 ± 141.4	7061.8	7089.6 ± 172.2	7072.3	7019.8 ± 201.8
VC/SA (ml/m^2)	3281.3	3348.3 ± 57.1	3082.0	3056.2 ± 38.0*	3003.5	2981.1 ± 46.1*	3007.9	2984.6 ± 56.1*	2944.5	2988.4 ± 65.7*
RV/SA (ml/m^2)	1127.5	1095.1 ± 41.6	1017.9	1030.4 ± 27.7	993.8	1004.6 ± 33.6	978.3	989.61 ± 40.9	905.3	884.0 ± 47.9‡
TLV/SA (ml/m^2)	4408.9	4443.4 ± 83.7	4099.9	4086.6 ± 55.7*	3997.2	3985.7 ± 67.6*	3986.2	3974.2 ± 82.3*	3849.8*	3872.5 ± 96.4*
RV/TLV (%)	25.5	24.5 ± 0.7	24.6	25.0 ± 0.1	24.6	24.9 ± 0.5	24.5	24.9 ± 0.7	23.54	22.9 ± 0.8†

*Significantly different from HARN ($p < 0.01$).
†Significantly from HARN, AHAB, and AHAG ($p < 0.05$).
‡Significantly from HARN, HAUN, AHAB, and AHAG ($p < 0.05$).
VC = vital capacity; RV = residual volume; TLV = total lung volume; SA = surface area.

TABLE 4. Age-adjusted lung volumes of female high altitude urban natives (HAUN), Bolivians of foreign ancestry acclimatized to high altitude since birth (AHAB), Bolivians of foreign ancestry acclimatized to high altitude during growth (AHAG), and foreigners acclimatized to high altitude during adulthood (AHAA) studied in La Paz, Bolivia (3,750 m)

	High altitude urban natives (HAUN)		Acclimatized since birth (AHAB)		Acclimatized during growth (AHAG)		Acclimatized during adulthood (AHAA)	
	Mean	Adjusted mean ± SE	Mean	Adjusted mean ± SE	Mean	Adjusted mean ± SE	Mean	Adjusted mean ± SE
N	56		40		33		23	
VC (ml)	3950.6	3946.5 ± 64.9	3886.9	3869.9 ± 78.5	3938.9	3926.8 ± 85.2	3898.9	3988.0 ± 115.6
RV (ml)	1305.5	1311.7 ± 32.0	1279.1	1304.4 ± 38.7	1379.2	1397.2 ± 42.0	1281.4	1280.0 ± 57.0
TLV (ml)	5256.2	5258.2 ± 85.6	5166.1	5174.4 ± 103.4	5318.1	5324.0 ± 112.3	5180.3	5168.0 ± 152.4
VC/SA (ml/m^2)	2565.6	2560.7 ± 31.6	2527.7	2507.7 ± 38.1	2472.4	2458.1 ± 41.4	2405.0	2492.5 ± 56.2
RV/SA (ml/m^2)	847.7	850.8 ± 18.3	831.7	844.2 ± 22.2	864.9	873.8 ± 24.1	791.9	800.1 ± 32.7
TLV/SA (ml/m^2)	3413.3	3411.5 ± 41.5	3359.4	3351.8 ± 50.2	3337.2	3331.9 ± 54.5	3196.9	3292.3 ± 74.0
RV/TLV (%)	24.8	24.9 ± 0.4	24.8	25.3 ± 0.5	25.8	26.12 ± 0.5	24.62	24.3 ± 0.7

See Table 3 for abbreviations.

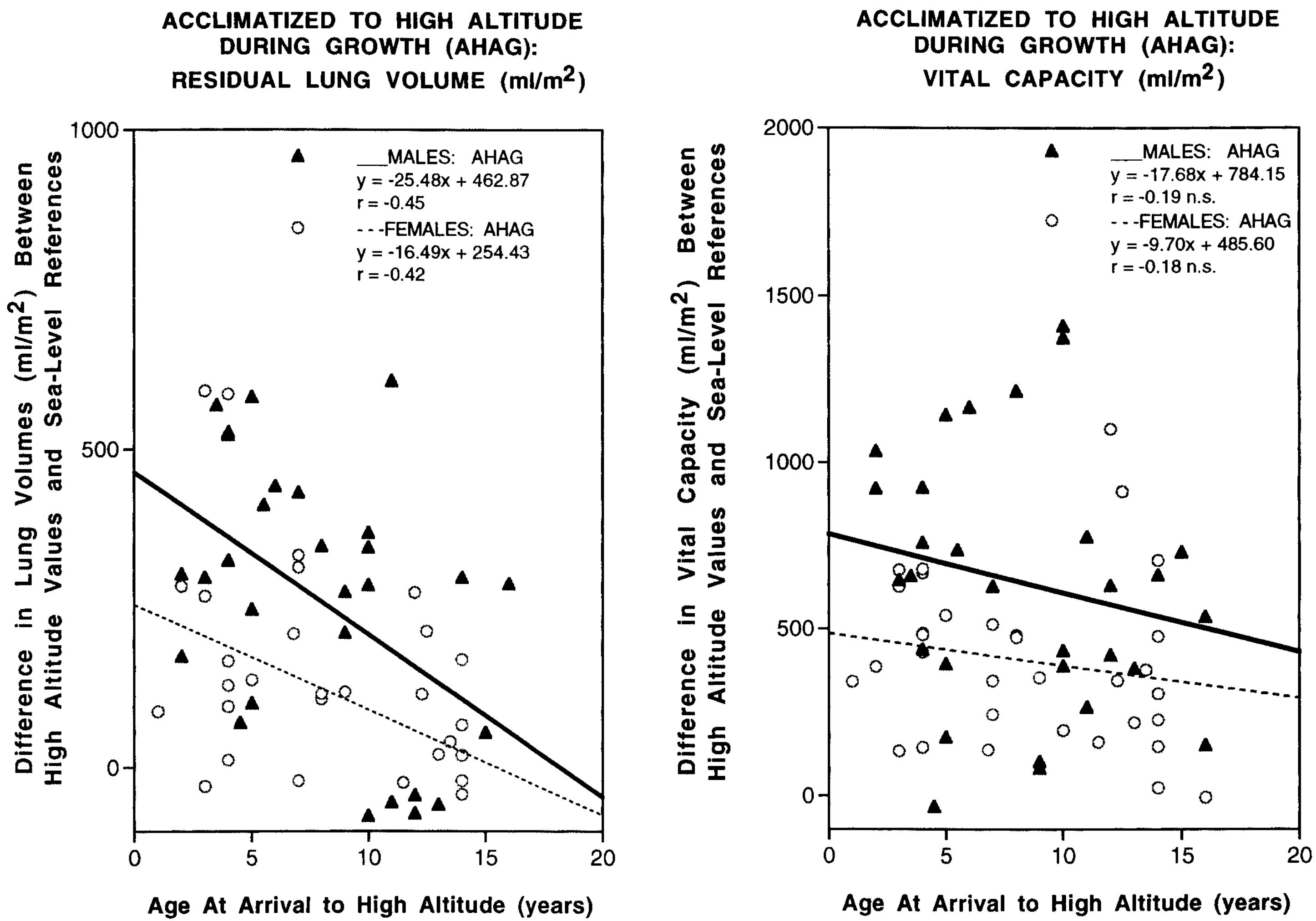

Fig. 2. Relationship of residual lung volume (ml/m^2) and vital capacity (ml/m^2) to age at arrival to high altitude. While the altitude-associated increase in residual lung volume is inversely related to age at migration to high altitude, the vital capacity is not.

TABLE 5. Correlation coefficients (r) of the log of mean skin reflectance (%) and measures of lung volumes (expressed as ml/m² of surface area) at high altitude for males and females

Variables	High altitude rural native (HARN) M (r)	High altitude rural native (HARN) F (r)	High altitude urban natives (HAUN) M (r)	High altitude urban natives (HAUN) F (r)	Acclimatized since birth (AHAB) M (r)	Acclimatized since birth (AHAB) F (r)	Acclimatized during growth (AHAG) M (r)	Acclimatized during growth (AHAG) F (r)	Acclimatized during adulthood (AHAA) M (r)	Acclimatized during adulthood (AHAA) F (r)
Vital capacity (m/m^2)										
Log skin reflectance (%)	−0.10	n.a.	−0.17	−0.19	−0.22	0.08	0.12	−0.08	0.01	0.16
Residual volume (m/m^2)										
Log skin reflectance (%)	−0.52*	n.a.	−0.42*	−0.30†	−0.17	−0.14	0.01	−0.09	−0.10	0.23
Total lung volume (m/m^2)										
Log skin reflectance (%)	−0.32†	n.a.	−0.31†	−0.28†	−0.23	0.02	0.09	−0.11	−0.02	0.22
(Residual volume/total lung volume) 100 (%)										
Log skin reflectance (%)	−0.49*	n.a.	−0.42†	−0.16	−0.08	−0.16	0.10	−0.08	−0.09	0.18

†$p < 0.05$, *$p < 0.01$.

lated increase in lung volumes and acclimatization status is not well defined in females. This differential response of females is puzzling. It is quite possible that it may be related to variability in occupational physical activity and body fat. Although the relationship of occupational variability and lung volumes was the same in males and females, the range of variability in occupational activity level and body fat was greater in females than in males. Therefore, since lung volumes are related to body composition and activity level, it is possible that the difference in occupational activity and body fat may override altitude acclimatization effects.

Lung volumes and skin reflectance

Previous studies have demonstrated that skin color as measured by skin reflectance is under genetic control (Harrison, 1961). It has been shown that variability in skin color reflectance is the result of the additive effects of 3–5 loci (Byard, 1981) and that 50–70% of the variability in skin reflectance is due to a heritable additive genetic component (Frisancho et al., 1981; Post and Rao, 1977). Based on this information, Greksa (1992) has used measurements of skin reflectance to evaluate the role of genetic factors in the acquisition of lung volume in high altitude subjects. As such, skin reflectance can be used as a proximate marker of genetic differences.

As shown in Table 5, in both the high altitude rural and urban natives (HARN and HAUN), residual lung volume but not vital capacity is inversely related to skin color reflectance (Fig. 3). These data suggest that about 20–25% of the variability in residual lung volume at high altitude can be explained by genetic factors associated with skin color, while variability in vital capacity is probably related more to environmental than genetic factors. On the other hand, among females skin color reflectance is not correlated with residual lung volume. Due to the fact that the Bolivians of foreign ancestry were selected specifically so as not to include subjects with indigenous admixture, there is, as expected, no correlation between lung volumes and skin reflectance.

Lung volumes and sibling similarities

Among the Bolivians acclimatized to high altitude since birth and during growth (AHAB and AHAG), sibling correlation coefficients for residual lung volume are significant (Table 6). Although not statistically significant within the high altitude urban natives (HAUN), there is a positive relationship among siblings. These data together suggest that in general 21–27% of the variability in residual lung volume at high altitude may be explained by genetic factors shared by siblings.

Lung volumes and occupational activity

Tables 7 and 8 compare lung volume by occupational activity level for males and females. These data show that in both males and females, there is a direct relationship between occupational activity level and vital capacity, so that the higher the occupational activity level, the higher the vital capacity

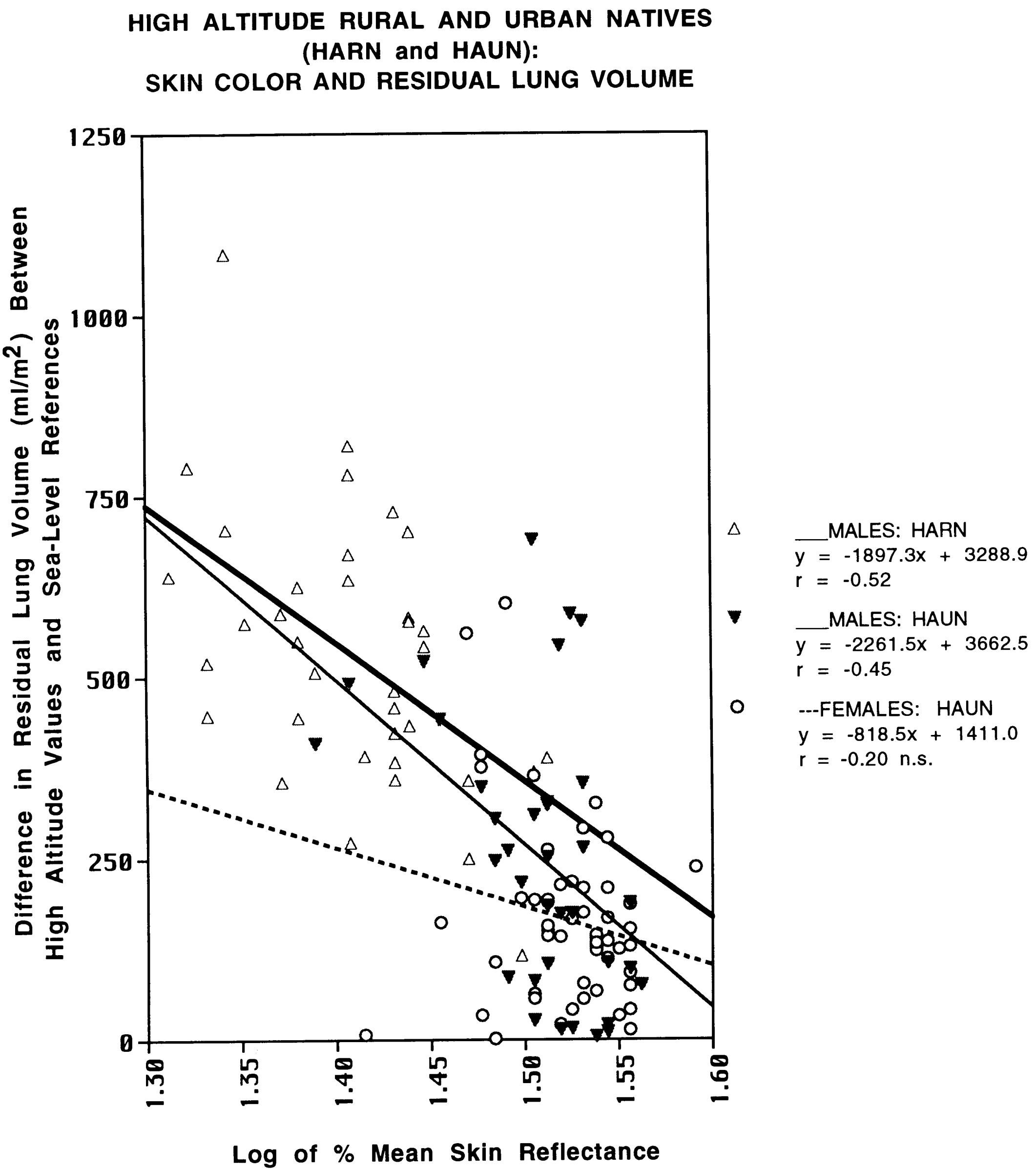

Fig. 3. Relationship of skin reflectance color and residual lung volume (ml/m^2). Inverse relationship between skin color and residual lung volume (ml/m^2) in high altitude urban and rural natives.

TABLE 6. Sibling correlations (r) for measurements of lung volumes among high altitude urban natives (HAUN) and samples acclimatized to high altitude since birth (AHAB) or during growth (AHAG)

		Lung volumes			
	No. pairs	VC (ml/m^2)	RV (ml/m^2)	TLV (ml/m^2)	(RV/TLV)100 (%)
		(r)	(r)	(r)	(r)
HAUN	7	0.32	0.46	0.50	0.41
AHAB & AHAG	28	0.09	0.52*	0.28	0.27

*Significant at $p < 0.01$.

TABLE 7. Lung volumes (expressed as ml/m^2 of surface area) by occupational activity level among five male samples studied in La Paz, Bolivia (3,750 m)

Occupational activity level	High altitude rural native (HARN) mean ± SE (N = 37)	High altitude urban natives (HAUN) mean ± SE (N = 69)	Acclimatized since birth (AHAB) mean ± SE (N = 45)	Acclimatized during growth (AHAG) mean ± SE (N = 30)	Acclimatized during adulthood (AHAA) mean ± SE (N = 25)
Vital capacity (m/m^2)					
Low	—	2864.44 ± 59.19	2778.57 ± 72.48	2739.62 ± 179.33	2369.67 ± 80.57
Medium	3079.05 ± 80.07	3118.29 ± 52.23	3035.14 ± 68.83	2903.67 ± 35.84	3042.62 ± 115.61
High	3337.15 ± 53.90	3170.48 ± 39.06	3200.53 ± 85.97	3190.29 ± 107.39	3042.97 ± 112.15
Significance	$p < 0.03$	$p < 0.01$	$p < 0.01$	$p < 0.02$	$p < 0.05$
Residual volume (m/m^2)					
Low	—	954.62 ± 85.07	955.76 ± 85.41	965.89 ± 224.87	869.41 ± 45.42
Medium	1164.82 ± 93.37	1044.58 ± 58.58	980.57 ± 45.35	920.38 ± 52.29	900.04 ± 61.72
High	1117.24 ± 31.65	986.97 ± 34.05	1069.67 ± 92.35	983.24 ± 51.08	927.95 ± 21.29
Significance	N.S.	N.S.	N.S.	N.S.	N.S.
Residual volume/total lung volume × 100 (%)					
Low	—	24.54 ± 1.56	25.24 ± 1.58	24.84 ± 3.54	25.09 ± 0.75
Medium	27.21 ± 1.34	24.67 ± 0.90	24.22 ± 0.60	23.92 ± 1.09	22.70 ± 1.17
High	25.04 ± 0.51	23.61 ± 0.61	24.71 ± 1.28	23.54 ± 0.93	23.47 ± 0.79
Significance	N.S.	N.S.	N.S.	N.S.	N.S.

TABLE 8. Lung volumes by occupational activity level among four female samples studied in La Paz, Bolivia (3,750 m)

Occupational activity level	High altitude urban natives (HAUN) mean ± SE (N = 56)	Acclimatized since birth (AHAB) mean ± SE (N = 40)	Acclimatized during growth (AHAG) mean ± SE (N = 33)	Acclimatized during adulthood (AHAA) mean ± SE (N = 22)
Vital capacity (m/m^2)				
Low	2405.15 ± 47.56	2365.31 ± 47.93	2347.50 ± 41.49	2198.88 ± 123.17
Medium	2585.25 ± 36.78	2574.27 ± 54.40	2445.38 ± 53.86	2494.92 ± 81.15
High	2805.39 ± 49.13	2654.82 ± 85.47	2564.90 ± 64.75	2458.57 ± 51.27
Significance	$p < 0.01$	$p < 0.02$	$p < 0.06$	$p < 0.06$
Residual volume (m/m^2)				
Low	820.37 ± 29.59	823.89 ± 22.51	827.42 ± 56.79	755.27 ± 52.36
Medium	871.61 ± 19.71	811.98 ± 21.41	878.15 ± 55.13	774.14 ± 80.50
High	855.42 ± 50.84	892.77 ± 30.77	871.88 ± 45.71	813.29 ± 63.52
Significance	N.S.	N.S.	N.S.	N.S.
Residual volume/total lung volume × 100 (%)				
Low	25.41 ± 0.72	25.86 ± 0.66	25.88 ± 1.18	25.62 ± 1.40
Medium	25.20 ± 0.39	24.04 ± 0.59	26.22 ± 0.96	23.21 ± 1.58
High	23.23 ± 0.96	25.18 ± 0.40	25.31 ± 0.99	24.70 ± 1.54
Significance	N.S.	N.S.	N.S.	N.S.

level. On the other hand, the residual lung volume in any of the subsamples does not appear to be related to occupational activity level. These findings suggest that, to some extent, variability in occupational activity influences more the attainment of vital capacity than of residual lung volume.

CONCLUSIONS

The present study demonstrates that high altitude rural natives have significantly greater lung volumes, especially residual lung volume, than all other samples studied. The present research also indicates that life at high altitude results in an enlargement of both vital capacity and residual lung volume. These data suggest that attainment of an enlarged vital capacity is influenced by environmental factors, such as exposure to high altitude hypoxia and occupational activity, while the attainment of an enlarged residual lung volume seems to be related to both developmental acclimatization and genetic factors.

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