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Developmental Components of Resting Ventilation Among High- and Low-Altitude Andean Children and Adults

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ABSTRACT This paper evaluates the age-associated changes of resting ventilation of 115 high- and low-altitude Aymara subjects, of whom 61 were from the rural Aymara village of Ventilla situated at an average altitude of 4,200 m and 54 from the rural village of Caranavi situated at an average altitude of 900 m. Comparison of the age patterns of resting ventilation suggests the following conclusions: 1) the resting ventilation (ml/kg/min) of high-altitude natives is markedly higher than that of low-altitude natives; 2) the age decline of ventilation is similar in both lowlanders and highlanders, but the starting point and therefore the age decline are much higher at high altitude; 3) the resting ventilation that characterizes high-altitude Andean natives is developmentally expressed in the same manner as it is at low altitude; and 4) the resting ventilation (ml/kg/min) of Aymara high-altitude natives is between 40–80% lower than that of Tibetans. Am J Phys Anthropol 109:295–301, 1999. © 1999 Wiley-Liss, Inc.

Previous studies on the ventilatory characteristics of high-altitude natives were limited to documenting either lung volume (Hurtado, 1964; Frisancho, 1975; Frisancho et al., 1997; Greksa et al., 1985; Droma et al., 1991) or the hypoxic ventilatory response (HVR) (Chiodi, 1957; Severinghaus et al., 1966; Weil et al., 1971; West, 1982; Lefrancois et al., 1968, 1969; Pasquis et al., 1971; Mortola et al., 1990, 1992; Lahiri et al., 1976; Byrne-Quinn et al., 1972; Ge et al., 1994a,b; Hackett et al., 1980; Zhuang et al., 1993; Curran et al., 1995; Beall et al., 1997). However, there is no information about the development of resting ventilation. With this purpose, we compared the age-associated changes in resting ventilation of low- and high-altitude Bolivian Aymara natives.

MATERIALS AND METHODS

Study population sites

The study was conducted in two locations, one at low altitude and the other at high altitude.

High altitude. This study was conducted during June–July 1997 in the rural Aymara village of Ventilla situated in the Bolivian altiplano, 50 km from the city of La Paz, at an average altitude of 4,200 m.

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Low altitude. This study was conducted during June–July 1998 in the rural Aymara village of Caranavi situated in the Bolivian lowlands, 50 km from the city of Santa Cruz, at an average altitude of 900 m.

Sample

The study's sample consisted of 118 subjects ranging in age from 11–35 years, of whom 63 were high-altitude natives and 55 low-altitude natives. To recruit subjects, informal arrangements were made with the community leaders of Ventilla and Caranavi, who invited children and their parents to participate in the study. This study's research team included a physician (R.S.) who was in charge of determining health status and excluding unhealthy individuals. The protocol for this study was approved by a Human Subjects Review Committee at the University of Michigan and the Bolivian Institute of Biology and Altitude (IBBA).

Measurements

Pulmonary ventilation. The measurements of pulmonary ventilation were obtained as part of a metabolic study. Resting pulmonary ventilation was measured with a calorimeter (Teem 100, Metabolic Analysis System, AeroSport, Inc., Ann Arbor, MI). This instrument has a built-in pneumotach that takes continuous microsamples of expired air. The procedure includes breathing through a face mask into a pneumotach. The measurements displayed on the calorimeter include: minute-by-minute volume of oxygen consumption (VO_2), carbon dioxide produced (VCO_2), ventilatory volume, barometric temperature pressure saturation (BTPS) (VEb) in liters per minute, and ventilatory volume, standard temperature pressure and dryness (STPD) (VEs) in liters per minute. A two-point calibration was performed before each day's test: every morning of the study, the calorimeter was calibrated with reference to room air, and a gas mixture (16.0% O_2 and 5.02% CO_2, exactly). It should be noted that the present measurement of ventilation refers to total ventilation (VE, liters/min), which encompasses both dead space and alveolar ventilation and is therefore only a crude measure of effective alveolar ventilation.

Finally, the values of ventilation were expressed as liters per minute and further adjusted for body weight as milliliters per kilogram of body weight per minute (ml/kg/min).

All volunteers were measured both under fasting and nonfasting conditions. The fasting measurements were made in the morning before breakfast. The nonfasting measurements were made in the afternoon, at least 3 hr after the first measurement. Each subject after the first measurement was given breakfast. The ventilation measured in the morning under fasting conditions was highly correlated ($r = 0.95$) with the ventilation obtained in the afternoon under nonfasting conditions. However, because ventilation is, in part, determined by metabolic rate, and metabolic rate increases following a meal, for the present analysis we used only the ventilation obtained under fasting conditions.

After a 10-min resting period, each subject was fitted with a face mask that was connected to the calorimeter while they were sitting and were confortably clothed. The volunteers were instructed to relax and breathe normally. Once a steady breathing state was reached, usually within 5 min, the minute-by-minute measurements were done for an average of 30 min.

Arterial oxygen saturation (SaO_2). SaO_2 was measured continuously with an Omeda Biox 3700 Pulse Oximeter (Ohmeda, Boulder, CO). This instrument updates and displays arterial oxygen saturation (SaO_2) of hemoglobin and pulse rate (every 4–6 beats). The noninvasive photocell sensor was placed on the index finger (occasionally, when readings were erratic, the sensor was placed on the earlobe). The average of the first and last 5 min of the readings were recorded. In addition, arterial systolic and diastolic blood pressures were measured manually with a sphygmomanometer before and after the test. The average blood pressures are reported here.

Anthropometric measurements. Standardized measurements of height and weight (Frisancho, 1990; Lohman et al., 1988) were obtained for each participant.

Respiratory function. The forced vital capacity (FVC) was measured using a Vitalograph respirometer (Micro Spirometrics, Inc.,

TABLE 1. Anthropometric and ventilatory characteristics of Andean natives ranging in age from 11–35 years

	Males		Females	
Age range	High altitude, mean ± SE	Low altitude, mean ± SE	High altitude, mean ± SE	Low altitude, mean ± SE
11–20 years				
N	28	28	16	17
Age (years)	15.3 ± 0.4	16.5 ± 0.5	16.2 ± 0.8	14.6 ± 0.6
Height (cm)	154.1 ± 2.4	157.5 ± 2.3	148.5 ± 1.8	152.0 ± 1.6
Weight (kg)	46.6 ± 2.1**	53.1 ± 2.3	48.3 ± 2.3	50.1 ± 2.4
BMI (kg/m^2)	19.3 ± 0.4*	21.0 ± 0.5	21.7 ± 0.7	21.5 ± 0.7
FVC (liters)	4.5 ± 0.2	4.2 ± 0.2	3.9 ± 0.2	3.7 ± 0.1
FVC (ml/cm)	28.9 ± 1.2**	26.2 ± 1.0	26.8 ± 1.0**	25.3 ± 0.8
SaO$_2$ (%)	90.8 ± 0.6*	97.9 ± 0.3	90.9 ± 0.6*	96.9 ± 0.4
Resting ventilation (liter/min)	13.6 ± 0.4*	8.5 ± 0.6	11.6 ± 0.3*	9.7 ± 0.4
Resting ventilation (ml/kg/min)	305.9 ± 13.8*	170.1 ± 18.3	249.9 ± 14.7**	215.3 ± 7.7
21–35 years				
N	7	34	12	12
Age (years)	26.7 ± 1.7	27.7 ± 0.8	27.5 ± 1.7	26.6 ± 1.5
Height (cm)	162.2 ± 1.7	164.9 ± 1.0	147.7 ± 1.1	150.5 ± 1.5
Weight (kg)	60.7 ± 2.1	64.4 ± 1.2	49.7 ± 1.2*	61.6 ± 3.0
BMI (kg/m^2)	23.1 ± 0.7	23.7 ± 0.4	22.8 ± 0.6*	27.1 ± 1.0
FVC (liters)	5.4 ± 0.2	4.8 ± 0.1	3.8 ± 0.1	3.7 ± 0.1
FVC (ml/cm)	33.0 ± 1.1**	29.2 ± 0.8	26.0 ± 0.6	24.8 ± 0.8
SaO$_2$ (%)	91.7 ± 1.1*	97.9 ± 0.3	91.4 ± 0.7*	97.3 ± 0.3
Resting ventilation (liter/min)	14.2 ± 0.4*	8.9 ± 0.5	11.1 ± 0.5	11.3 ± 0.7
Resting ventilation (ml/kg/min)	232.3 ± 7.3*	142.0 ± 8.2	222.1 ± 7.5*	185.5 ± 8.6

*$P < 0.01$.
** $P < 0.05$.

Auburn, ME). The respirometer was adjusted for changes in room temperature before each measurement. The subjects were asked to inhale as completely as possible and then exhale to the maximum in one continuous motion. These respirometric measurements were repeated three times, and the highest of the three values was recorded.

Analysis

The ventilations and FVC were adjusted for body size. The ventilations were adjusted for body weight and expressed as ml/kg/min, while the FVC were adjusted for body height and expressed as ml/cm. All analyses were performed using Statview 5.0 (SAS Institute Inc., Cary, NC). The statistical significance of differences in anthropometric and ventilation variables between high- and low-altitude samples was assessed by an analysis of variance test applied separately to each sex and age group. The age trends in resting ventilation were analyzed using regression equations, whereby age was the independent variable and resting ventilation was the dependent variable. The statistical significance of differences in slopes of resting ventilation values were assessed by two-sample t-test.

RESULTS

Table 1 gives the mean values for the anthropometric and respiratory data. Among youth, the high-altitude subjects tended to be smaller in body size than their counterparts from low altitudes. On the other hand, the high-altitude boys and girls tended to have systematically higher values of forced vital capacity than the low-altitude youths. Similarly, the arterial oxygen saturation was significantly lower at high altitude. In contrast, from the youngest age measured, 11 years, to the age of 20 years, the resting ventilation, especially when expressed as ml/kg/min, was significantly higher among the high-altitude than the low-altitude subjects. Similar differences were observed among adults in terms of arterial oxygen saturation and resting ventilation.

Observation of the individual data indicates that ventilation declines from 11 years (the youngest age measured) until about age 20 years, but thereafter remains unchanged in both populations. Hence, the age-trend analysis excludes those over age 20 years. As shown in Figures 1 and 2, the age-associated decline in resting ventilation in both males and females follows the same pattern at low

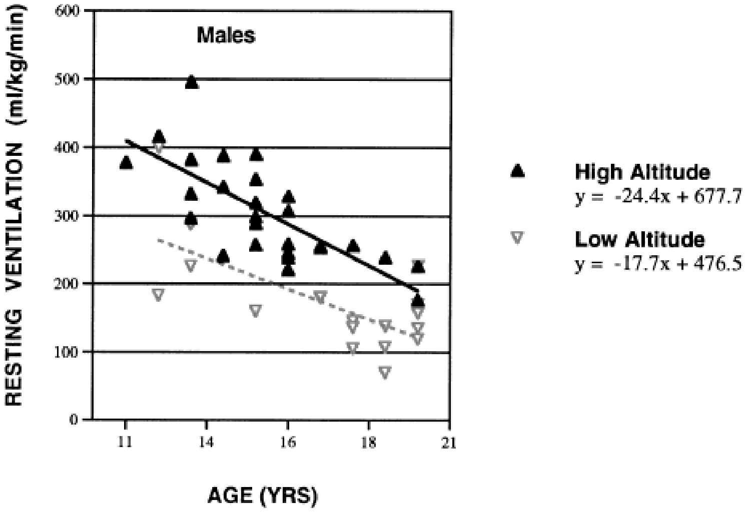

Fig. 1. Relation of resting ventilation and age among high-altitude Aymara native males. Both at high and low altitude, the age-associated decline in resting ventilation follows the same pattern.

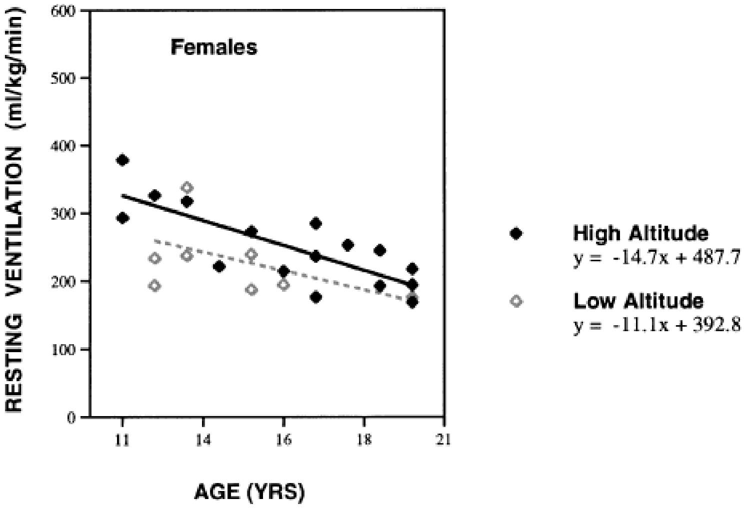

Fig. 2. Relation of resting ventilation and age among high-altitude Aymara native females. Both at high and low altitude, the age-associated decline in resting ventilation follows the same pattern.

altitude and high altitude. However, the per-year rate of decline of ventilation as indicated by the difference in slope is higher at high altitude than at low altitude. At high altitude in males, the ventilation declined by approximately 24 ml/kg/min per year, which is significantly larger than the 18 ml/kg/min decline at low altitude ($P < 0.05$). In females at high altitude, the ventilation declined by about 15 ml/kg/min, which is again significantly higher than the 11 ml/kg/min decline at low altitude ($P < 0.05$) (Fig. 2). The age decline of ventilation is similar in both lowlanders and highlanders, but the starting point and therefore the age change are much higher at high altitude. In contrast, in adulthood, there was no statistically significant age-associated decrease in ventilation in either the high- or low-altitude population samples.

DISCUSSION

This is the first study that documents the development of resting ventilation at high and low altitudes. Furthermore, it demonstrates the age-associated decline in resting ventilation is similar at high and low altitudes. The only difference is that the resting ventilation starts from a high point at high altitude, but the rate of decline per

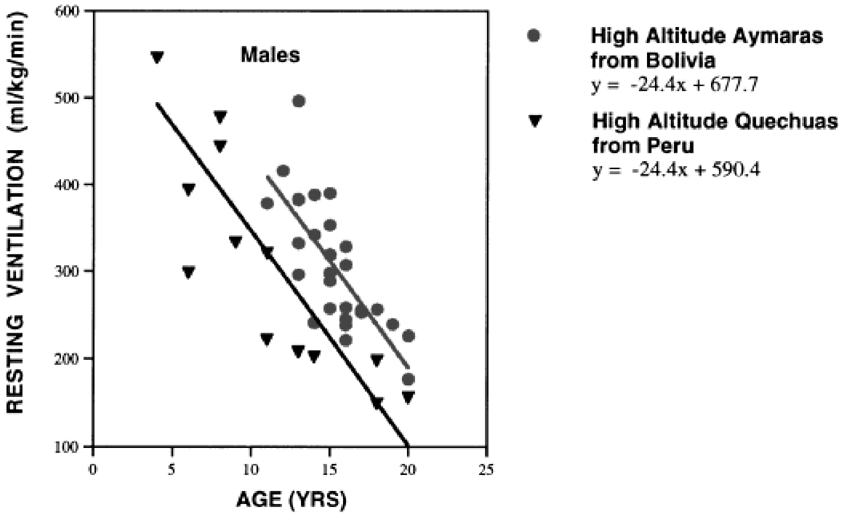

Fig. 3. Comparison of age-associated decline of resting ventilation among high-altitude Aymara compared to high-altitude Quechua natives reported by Sime (1973). Note that the decline in resting ventilation among high-altitude Quechua natives from Peru is almost identical to that observed among high-altitude Aymara from Bolivia.

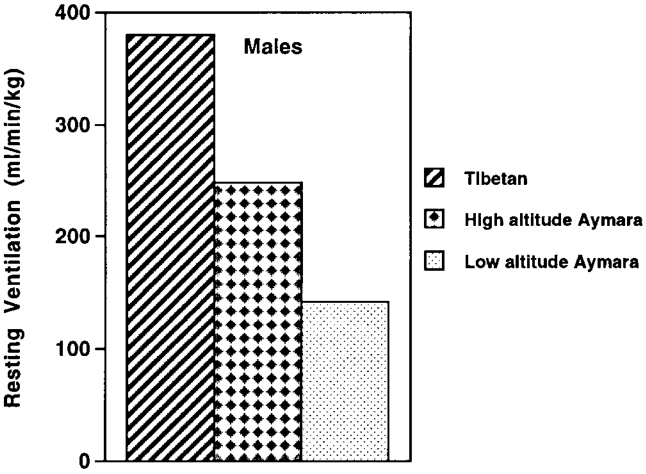

Fig. 4. Comparison of resting ventilation of Aymara and of Tibetan adult males reported by Beall et al. (1997). The Aymara have significantly lower resting ventilation than the Tibetans, but the high-altitude Aymara have higher ventilation than the low-altitude Aymara.

year is quite similar in both locations. The age-associated decline in resting ventilation at high altitude, as shown in Figure 3, is similar to the findings reported by Sime (1973) for high-altitude Quechua samples. Therefore, one can conclude that the resting ventilation that characterizes high-altitude Andean natives is developmentally expressed in the same manner as it is at low altitude (Cotes, 1965).

It should be noted that for most physiological and anthropometric evaluations of highlanders and lowlanders, low altitude is the frame of reference. For ventilation, however, the frame of reference has always been lowland migrants to high altitude, who tend to have higher ventilation than highland natives. Hence, Andean highlanders are described as having a low hypoxic ventilatory response (Chiodi, 1957; Severinghaus et al., 1966; Weil et al., 1971; West, 1982; Lefrancois et al., 1968; Pasquis et al., 1971; Mortola et al., 1990, 1992; Lahiri et al., 1976; Byrne-Quinn et al., 1972; Beall et al., 1997). However, the present study demonstrates that resting ventilation of Andean high-altitude natives is greater than that of lowlanders at low-altitude.

Several studies have demonstrated that Tibetans have a higher HVR than Andeans (Zhuang et al., 1993; Curran et al., 1995). The ventilation for high-altitude Aymara

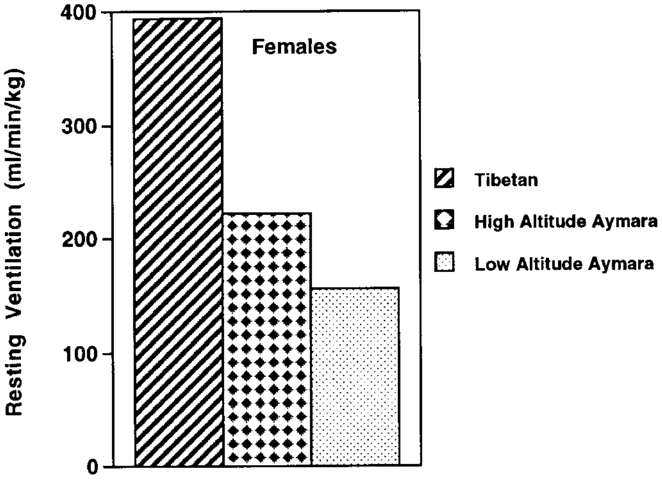

Fig. 5. Comparison of resting ventilation of Aymara and Tibetan adult females reported by Beall et al. (1997). The Aymara have significantly lower resting ventilation than the Tibetans, but the high-altitude Aymara have higher ventilation than the low-altitude Aymara.

adults is quite similar to the values reported for other Aymara high-altitude samples (Beall et al., 1997), and as illustrated in Figures 4 and 5, the Andean high-altitude natives have a lower resting ventilation than high-altitude Tibetans.

The present findings also confirm that high-altitude natives tend to have higher forced vital capacity when expressed per unit of body size (ml/cm), which agrees with previous studies (Hurtado, 1964; Frisancho, 1975; Frisancho et al., 1997; Greksa et al., 1985; Droma et al., 1991). The present findings also confirm that the arterial oxygen saturation is significantly lower at high altitude than at low altitude.

In summary, the present findings suggest that the resting ventilation that characterizes high-altitude Andean natives is developmentally expressed in the same manner as it is at low altitude. Furthermore, it confirms that Andean high-altitude natives have a lower resting ventilation than high-altitude Tibetans.

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