AMERICAN JOURNAL OF HUMAN BIOLOGY 4:17–26 (1992)

Respiratory and Hematological Adaptations of Young and Older Aymara Men Native to 3600M

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ABSTRACT This paper reports the results of a study designed to test the hypothesis that an inevitable concomitant of aging at high altitudes is chronic mountain sickness resulting from excess erythrocytosis secondary to exaggerated hypoxemia caused by aging processes in the respiratory system. It compares age differences in respiratory system function in oxygenating the blood measured as percent O_2 saturation of arterial hemoglobin during wakefulness and sleep and in erythrocytosis measured as hemoglobin concentration in 17 young (22–35 years) and 16 older (47–68 years) rural and urban resident Bolivian Aymara men, healthy lifelong residents of 3,500–4,000 m who were tested at 3,600 m. The results do not support the hypothesis. Older urban men are significantly more hypoxemic during wakefulness and sleep than young urban men, while there are no age differences in the degree of hypoxemia among the rural residents. However, older urban men do not have the higher hemoglobin concentration predicted by the hypothesis. Both urban and rural older men have lower hemoglobin concentration than their young counterparts, a finding not attributable to age differences in nutritional status or testosterone concentration. Despite their relatively low hemoglobin concentration, older men have estimated arterial O_2 content in the normal sea level range for young men and in this sense retain the capacity to adapt to high altitude at least through the seventh decade of life.

The characterization of biological aging as reduced capacity to adapt to environmental stress and maintain homeostasis (Comfort, 1979; Shock, 1977) has adverse implications for populations living under chronic stress, such as high altitide residents. Many adaptations to lifelong hypobaric hypoxia involve the respiratory system, one with marked functional decline during adulthood at sea level (Klocke, 1977). A widely cited hypothesis states that an inevitable concomitant of aging at high altitudes is chronic mountain sickness resulting from excess erythrocytosis secondary to an exaggerated hypoxemic state caused by aging processes in the respiratory system (Sime et al., 1975). This hypothesis was based on a study of 21 Andean high altitude natives from 4–41 years of age and, therefore, confounded growth and aging processes. A priori it seems unlikely that this population, with adaptations to high altitude hypoxia at stages of life from intrauterine through young adulthood, would exhibit a universal loss of adaptation in middle and old age. Yet, physiological theories of aging noted above predict some loss of adaptive capacity and evolutionary theories of aging argue that natural selection may have maximized fitness of young, rather than older, adults (Weiss, 1981). Thus, testing the aging and chronic mountain sickness hypothesis can provide perspective on these theoretical descriptions of the aging processes, on adaptation to high altitude throughout the lifespan, on the interaction of the biological aging processes with disease, and on the health of older high altitude natives.

This paper reports the results of a study designed to test the aging and chronic mountain sickness hypothesis (Sime et al., 1975) by measuring age differences in respiratory system function and hematological adaptation in young (22–35 years) and older (47–68

Received November 8, 1990; accepted February 4, 1991.

years) Bolivian Aymara men, healthy lifelong residents of 3,500–4,100 m who were tested at 3,600 m. It presents data on 1) percent O_2 saturation of arterial blood during wakefulness and sleep, a summary measure of respiratory system function in transferring O_2 to the blood, and 2) hemoglobin concentration, elevated adaptively at high altitude and pathologically in chronic mountain sickness. The results of the study do not support the hypothesis. Rather than developing chronic mountain sickness, healthy older men retain the capacity to adapt to high altitude at least through the seventh decade of life.

METHODS

Healthy young adult (age 22–35 years, n = 17) and older (age 47–68 years, n = 16) Aymara men were invited to participate in a study entailing two nights of sleep in a laboratory for measurement of waking and sleep-related arterial O_2 saturation, pulmonary function, and endocrine and hematological tests. Because of the potential importance of inherited aspects of high altitude adaptation, the sample was restricted to men of Aymara descent. Recognizing the difficulty in categorizing an individual's heritage, a conservative approach used the following individual and parental characteristics to select participants: birthplace in a traditionally Aymara locale, speaks Aymara only or Aymara and Spanish, and has traditionally Aymara surnames. Emphasis was given to the first two criteria because some adopt Hispanic surnames. Each participant also met the following requirements: born and raised above 3,000 m altitude, permanent resident at 3,500–4,000 m, less than one week below 3,500 m in the year prior to the study, and no employment in the interior of mines. (One 68 year old who had worked in a gold mine between the ages of 16 and 19 was the exception to the last requirement.) Only non-obese, healthy (determined by a medical examination focusing on the cardiovascular and pulmonary systems), non-hypertensive individuals who were not engaged in shift work were included in the study. Life-style, smoking, and sleep histories were obtained by interview in Aymara or Spanish. Eight participants were rural agriculturalists recruited when visiting hospitalized friends or family in La Paz and the remainder were urban residents, mostly students and hospital workers, their friends and families. The study was limited to males because of their greater risk for chronic mountain sickness owing to higher frequency of nocturnal hypoxemia and higher hemoglobin concentration relative to females. These characteristics indicate that a sample of males provides the most efficient test of the hypothesized relationship.

Pairs of volunteers slept for two nights in the Neurology Service of the Instituto Boliviano de Bologia de Altura, Hospital de Clinicas, La Paz, Bolivia, altitude 3,600 m, P_b 500 torr, between January and April 1987. Data were obtained on two nights in order to exclude a possible first night effect. Virtually all participants were asleep 10–20 minutes after "lights out," slept for eight hours both nights, and reported a good night's sleep. There were no significant differences between nights in any of the sleep-related variables.

Percent O_2 saturation of arterial hemoglobin during wakefulness was measured every 30 seconds for 20 minutes prior to sleep both nights using a Criticare Systems finger pulse oximeter model 501+. The average of these observations was used as the waking percent arterial O_2 saturation.

Percent O_2 saturation during sleep was measured using the Vitalog system of recording ear pulse oximetry (Biox IVA; Ohmeda Corp.) for each volunteer throughout the two nights of sleep, accumulated continuously, and stored for transfer to a microcomputer after each night using the Vitalog Home Monitoring System (Vitalog PMS-8, Vitalog Corp.), a microprocessor based portable monitoring system. Data from both nights were averaged for analysis. Percent O_2 saturation of arterial hemoglobin during sleep was accumulated as percentage of total sleeptime in a series of categories of oxygen saturation: above 90%, 90–85%, 85–80%, and so on.

A validation study simultaneously recording the signal on a Grass polygraph found that the Vitalog system computer program processes and/or stores signals in a way that slightly overestimates percent O_2 saturation (Gyulay et al. 1987). We conducted a pilot study to compare results obtained with the Vitalog and formal polysomnography and found no systematic differences. Waking baselines recorded by the Vitalog averaged 3.5% higher than the waking baseline obtained with the Criticare 501+. This recording anomaly explains the few men who were

reported as spending some sleeptime at percent O_2 saturation higher than during wakefulness. The waking baseline measured with the Criticare rather than the Vitalog is reported because it provides an accurate and comparable measure of the level of waking percent O_2 saturation, while trends and drops in percent O_2 saturation during sleep accurately tracked and measured with the Vitalog system are reported.

Forced vital capacity, tidal volume, and ventilation frequency were measured using a Collins Modular Lung Analyzer following the manufacturer's specifications and converted to body temperature and ambient pressure (saturated) (BTPS). Height and weight were measured following published protocols (Cameron et al., 1981). A venipuncture blood sample for immediate analysis of hemoglobin concentration and subsequent analysis of plasma ferritin and folate concentrations was obtained from each participant and analyzed as described elsewhere (Beall et al., in press; Kamen and Caston, 1974).

STATISTICAL ANALYSIS

The variables described above are normally distributed and not skewed. Two-tailed t-tests for independent samples and analyses of variance were used to test age and residence differences in sample means and correlation-regression analyses were used to test variable associations. A summary measure of O_2 saturation during sleep was calculated as the percent of total sleeptime above 90% O_2 saturation, where lower percentages reflect greater hypoxemia. Estimated arterial O_2 content in ml O_2/100 ml blood was calculated as hemoglobin concentration multiplied by 1.34 multiplied by percent O_2 saturation and divided by 100. Weight-for-height was calculated as weight in kilograms divided by stature in meters. Minute ventilation was calculated as tidal volume multiplied by ventilation frequency. Iron deficiency was defined as a plasma ferritin $\leq$ 12 ng/dl (Cook and Finch, 1979). Folate deficiency was defined as a free folate concentration $\leq$ 6 ng/ml).

RESULTS

The older men are more hypoxemic than their younger counterparts as indicated by 1.4% lower average O_2 saturation during wakefulness (Fig. 1, Table 1) and 22% lower percent of total sleeptime above 90% O_2 saturation (Fig. 2, Table 1). Some older men had

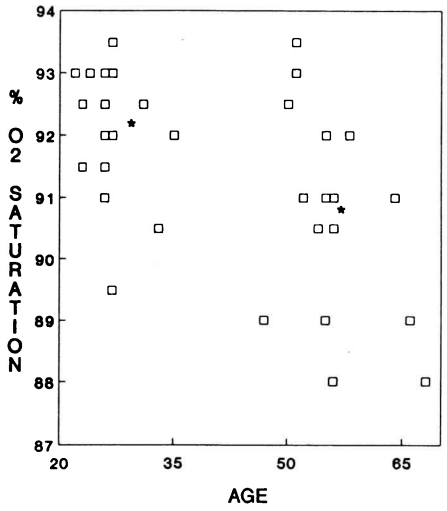


Fig. 1. Waking percent O_2 saturation plotted against age (*mean values for young and older men).

percent O_2 saturation during wakefulness and sleep as high as the highest observed in young men while others had percent O_2 saturation below the lowest observed in young men. Within age groups, greater hypoxemia during wakefulness is also associated with greater hypoxemia during sleep (older men: $r = .84$, $P < .05$; young men: $r = .51$, $P < .05$). Percent O_2 saturations are lower than the waking baseline during portions of sleeptime. Men with waking saturations of 90% or higher spend an average of 42% $\pm$ 23 (n = 16 young) and 53% $\pm$ 28 (n = 11 older) sleeptime below 90% saturation. However, few experienced profound hypoxemia during sleep. The lowest recorded percent O_2 satu-

TABLE 1. Age differences in percent O_2 saturation and hemoglobin concentration of young and older Bolivian Aymara men tested at 3,600 m

	Young (n = 17) Mean $\pm$ S.D.	Older (n = 16) Mean $\pm$ S.D.
Waking percent O_2 saturation	92.1 $\pm$ 1.1	90.7 $\pm$ 1.7**
Percent sleeptime above 90% O_2 saturation	57 $\pm$ 23	35 $\pm$ 29*
Hemoglobin concentration (gm/dl)	17.4 $\pm$ 0.6	16.4 $\pm$ 1.0**

*$P < .05$, t-test.
**$P < .01$, t-test.

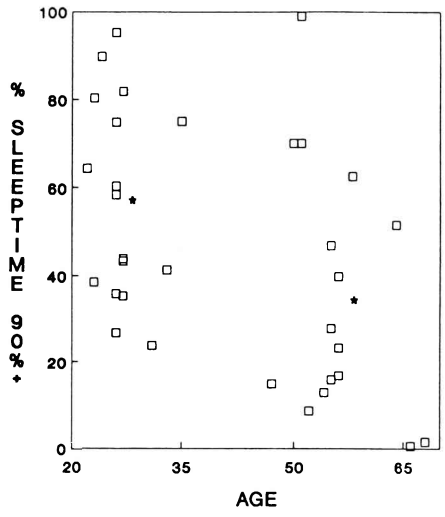


Fig. 2. Percent sleeptime above 90% O_2 saturation plotted against age (*mean values for young and older men).

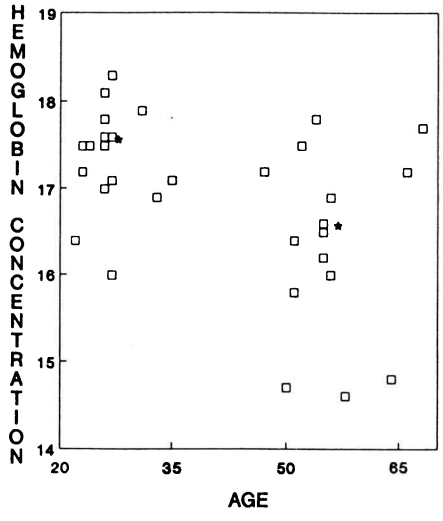


Fig. 3. Hemoglobin concentration plotted against age (*mean values for young and older men).

rations average 81% ± 6 (young) and 77% ± 5 (older). For sea level comparison, the waking O_2 saturations of the Bolivian high altitude natives average 5.2% (older) and 3.7% (young) below a median of 95.9 ± 1.2% for a healthy sample age 18–70 years monitored continuously for an average of 22 hours using the Criticare oximeter. In this sample, percent O_2 saturation did not vary with age or with sleep/wake state (Strohl et al., 1989).

The aging and chronic mountain sickness hypothesis (Sime et al., 1975) predicts that more hypoxemic individuals, i.e., the older men, will compensate by producing more hemoglobin. However, the older men have an average hemoglobin concentration 1.0 gm/dl *lower* than the young men (Table 1, Fig. 3). The highest hemoglobin concentrations (17.8 among older and 18.3 gm/dl among young) are well below the suggested 22 gm/dl cutoff for polycythemia at this altitude (Tufts et al., 1985). For sea level comparison, these mean hemoglobin concentrations are roughly 13% higher than those observed in healthy, well-nourished, samples of young (20–49 years) and older (50–70 years) men who average 15.4 gm/dl and 14.6 gm/dl, respectively (Viteri et al., 1972).

Although the predicted differences are not observed among groups with different levels of hypoxemia, the predicted relationship may occur *within* the older age group. The more hypoxemic older men have higher hemoglobin concentration during sleep (Fig. 4, $r = -.74$, $P < .01$) and wakefulness (not plotted, $r = -.56$, $P < .05$). In contrast, hemoglobin concentration of young men does not vary systematically throughout the observed range of hypoxemia during sleep (Fig. 4, $r = .25$, $P > .05$) or wakefulness (not plotted $r = .32$, $P > .05$).

The negative association between hemoglobin concentration and hypoxemia among

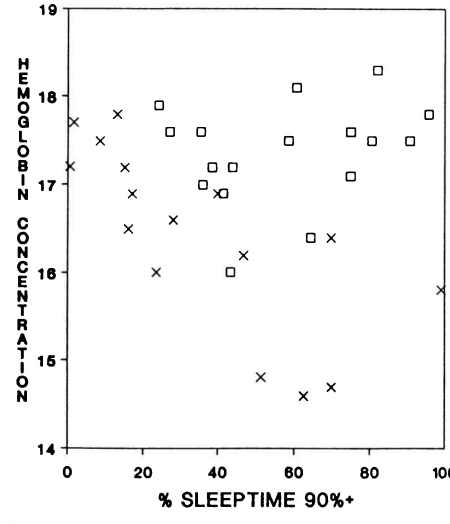


Fig. 4. Hemoglobin concentration plotted against percent sleeptime above 90% O_2 saturation for older and young men.

TABLE 2A. Rural-urban and age differences in percent O_2 saturation, hemoglobin concentration, pulmonary, and nutritional characteristics of Bolivian Aymara men tested at 3,600 m

	Rural residents		Urban residents	
	Young (n = 3) Mean	Older (n = 5) Mean	Young (n = 14) Mean	Older (n = 11) Mean
Waking percent O_2 saturation	91.5	92.0	92.5	90.1
Percent sleeptime above 90% O_2 saturation	54	63	58	22
Hemoglobin concentration (gm/dl)	16.9	15.7	17.5	16.7
Weight-for-height (kg/m)	35.7	37.5	36.5	37.8
Log plasma ferritin (ng/ml)	1.9	2.0	1.9	2.1
Free folate concentration (ng/ml)	—	13.8	11.4	9.6
FVC (L, BTPS)	5.5	4.9	5.4	4.7
FEV_1 (L, BTPS)	4.0	3.5	4.4	3.2
Minute ventilation (L, BTPS)	11.9	14.4	13.2	10.6
Arterial O_2 content (ml O_2/100 ml blood)	20.7	19.4	21.6	20.2
Systolic blood pressure (mm Hg)	123	110	125	124
Diastolic blood pressure (mm Hg)	69	76	81	85
Resting heart rate (f/min)	57	60	65	63

TABLE 2B. Analysis of variance testing for main effects and interaction of residence and age on measures described in Table 2A

	Residence			Age			Residence × age		
	df	MS	F	df	MS	F	df	MS	F
Waking percent O_2 saturation	1	3.8	2.3	1	19.0	11.7**	1	10.2	6.2*
Percent sleeptime above 90% O_2 saturation	1	2,928	5.6*	1	5,029	9.7**	1	2,852	5.5*
Hemoglobin concentration (gm/dl)	1	3.9	6.6*	1	5.5	9.2**	1	0.3	0.4
Weight-for-height	1	3.1	0.2	1	24.7	1.9	1	10.4	0.8
Log plasma ferritin concentration (ng/ml)	1	.04	0.4	1	.20	2.0	1	.0	.0
Free folate concentration (ng/ml)	1	43.2	1.5	1	18.7	0.6	1	—	—
FVC (L, BTPS)	1	3,774	17.1**	1	4,460	20.2**	1	439	2.0
FEV_1 (L, BTPS)	1	48	0.1	1	8,408	20.3**	1	726	1.8
Minute ventilation (L, BTPS)	1	13,243	1.6	1	16,711	2.0	1	34,164	4.2***
Estimated arterial O_2 content (ml O_2/100 ml blood)	1	4.1	4.7*	1	15.1	17.6**	1	.0	.0
Systolic blood pressure (mm Hg)	1	449	4.4*	1	127	1.3	1	208	2.1
Diastolic blood pressure (mm Hg)	1	418	7.4*	1	33	0.6	1	65	1.2
Resting heart rate (f/min)	1	0.2	.0	1	134	4.3***	1	28	0.9

*$P < .05$, **$P < .01$, ***$P = .05$.

older men is due to those in the lower right hand quadrant of Figure 4, i.e., with percent O_2 saturation during sleep in the upper range of the young men and much lower hemoglobin concentrations. Because four of the six men are rural residents, hypoxemia during sleep and wakefulness was re-examined for rural-urban differences. The greater hypoxemia among older men described in Figures 1 and 2 accurately represents only an urban pattern. Older urban men average 90.1% waking O_2 saturation and spend just 22% of sleeptime above 90% O_2 saturation compared to an average waking O_2 saturation of 92.5% and 58% of sleeptime above 90% O_2 saturation among young urban men (Tables 2A, 2B). In contrast, there are no age differences in hypoxemia during wakeful-

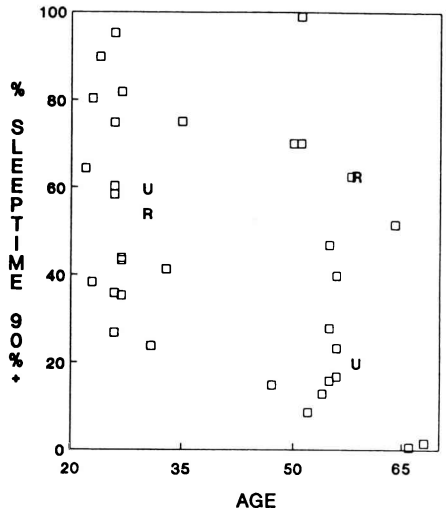


Fig. 5. Percent sleeptime above 90% O_2 saturation for young and older urban (U = mean) and rural (R = mean) men.

ness or sleep among rural men. Rural men of both age groups resemble young men in degree of hypoxemia (Tables 2A, 2B). The aging and chronic mountain sickness hypothesis predicts that the greater hypoxemia of older urban men would be associated with higher hemoglobin concentration, while the similar hypoxemia of young and older rural men would be associated with similar hemoglobin concentrations. However, older urban residents have 0.8 gm/dl lower hemoglobin concentration than young urban men. Similarly, older rural residents have 1.2 gm/dl lower hemoglobin concentration than young rural men. Rural men have lower mean hemoglobin concentration than their urban agemates.

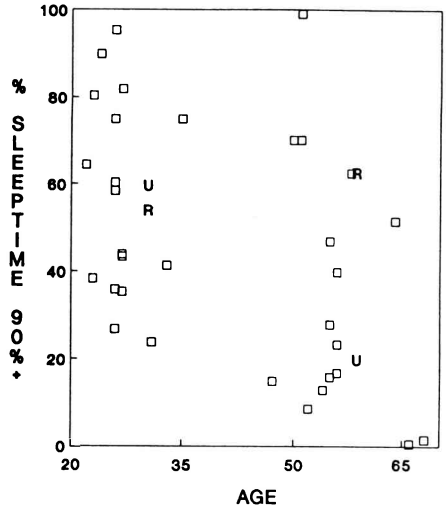
DISCUSSION

The results of this study offer no support for the hypothesis that when the usual age-related changes in the respiratory system occur at high altitude they inevitably lead to chronic mountain sickness, a disease characterized by extremely high hemoglobin concentration (Sime et al., 1975). Instead older men have lower hemoglobin concentration. Aging changes have occurred in the lungs as illustrated by the 11–13% lower forced vital capacity (FVC) and 12–27% lower forced expiratory volume in one second (FEV_1) of older men (Tables 2A, 2B). Arterial percent O_2 saturation is affected only in the older urban sample perhaps due to a 25% lower minute ventilation compared to rural older men. Older urban men have 20% lower minute ventilation than young urban men whereas older rural men have 20% higher minute ventilation than young rural men (Tables 2A, 2B).

Just as the present study found greater waking hypoxemia in the older urban, but not rural, residents, some previous studies reported greater hypoxemia among older men while others did not. Greater waking hypoxemia among older people has been reported in some studies at sea level (reviewed in Horvath and Borgia, 1984; Naefeh et al., 1987) and 3,900 m altitude (Beall and Goldstein, 1990), while an absence of age differences has also been reported at sea level (Strohl et al., 1989) and 4,850–5,450 m (Beall and Goldstein, 1990).

The finding of lower hemoglobin concentration among older men has not been reported previously among high altitude natives, although it has been reported among sea level natives sojourning at high altitude (Dill et al., 1963, 1969). No age differences in hemoglobin concentration were found in several other studies (Beall and Reichsman, 1984; Beall et al., 1987; Garruto, 1973; Chiodi, 1978), while one study reports an increase in average hemoglobin concentration with age in Peruvian miners (Monge et al., 1990). Subclinical lung disease resulting from longer exposure to the mining environment could lead to higher hemoglobin concentration in the older age groups (Frisancho, 1988). Two studies that report higher average hematocrit among older adult males compare children to young and middle aged adults, extrapolating through adulthood the increases in hematocrit during growth (Sime et al., 1975; Whittembury and Monge, 1972). This procedure would clearly be misleading for height or weight and is equally inappropriate for hematocrit.

The lower hemoglobin concentration of older rural and urban men in the present study is not explained by lower testosterone concentration (Haboubi et al., 1988) because young and older men do not differ in mean testosterone concentration (Beall et al., in press). Nor is the lower hemoglobin concentration of the older men explained by poorer nutrition. There are no age differences in nutritional status measured by mean weight-for-height, plasma ferritin (one young urban resident is iron deficient), or free folate concentrations (no participants are folate deficient) (Tables 2A, 2B).



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Selection criteria for inclusion in the study probably do not bias the study toward older men with abnormally low hemoglobin concentration. While the criterion of health excludes men with frank chronic mountain sickness and biases against the inclusion of individuals with very high hemoglobin concentration values, if a trend toward higher values existed among the still healthy older men, this group would have higher hemoglobin concentration. That it does not, suggests that the trend does not exist. The possibility that occult chronic disease in these apparently healthy individuals or selective survivorship of those with lower hemoglobin concentration of the older men cannot be evaluated with the available data.

Lower hemoglobin concentration at older ages has been observed in some, but not all, studies at sea level, usually at older ages than included in this study (e.g., Viteri et al., 1972; Nilsson-Ehle et al., 1989). The existence of an age-related decline in hematopoietic reserve has been hypothesized (Haboubi et al., 1988; Lipschitz et al., 1984; Nilsson-Ehle et al., 1989) and it is possible that this decline is accelerated under conditions of chronic hypoxic erythropoietic stress. However, the rural-urban differences in hemoglobin concentration among the older men plus the existence of cases of excessive erythrocytosis among older men (e.g., Monge et al., 1990) indicate some remaining hematopoietic reserve.

In addition to reasons for hemoglobin concentration depression among older men, reasons for hemoglobin concentration elevation among young men can be evaluated. The most likely cause is excessive smoking (Smith and Landaw, 1978). Cigarette smoking is light in this sample. Just one young man smokes as frequently as daily, while 8 of the 17 do not smoke at all. Similarly, just one older man smokes as frequently as daily, while 7 of the 16 do not smoke at all. Five of the rural residents do not smoke and the rest smoke less than one cigarette per week. Smokers do not have higher hemoglobin concentrations.

The finding that percent O_2 saturation during wakefulness is not related to hemoglobin concentration in this sample of healthy Aymara men at 3,600 m is in agreement with findings from rural Tibet at 4,850–5,450 m (Beall and Goldstein, 1990) and 3,700 m in Peru (Hultgren et al., 1965), although not those from a U.S. mining town at 3,100 m where an inverse association was found (calculated from data in Weil et al., 1968).

At sea level, very low percent O_2 saturation during sleep has been found to be an important stimulus to erythropoiesis (e.g., Moore-Gillon et al., 1986). The finding that percent O_2 saturation during sleep is not related to hemoglobin concentration in this high altitude sample may be due to the absence of severe desaturation. In one case where this relationship was observed, high altitude polycythemia patients at 3,100 m in the U.S., polycythemia spent an average of almost 200 minutes sleeptime below 80% O_2 saturation (Weil et al., 1978). Treatment with respiratory stimulants caused a modest improvement in average saturation and abolished the episodes of severe desaturation, resulting in a decrease in hematocrit. In contrast to those high altitude patients, just 17 of the 33 healthy high altitude natives in the present study spent any sleeptime at saturations this low. Only 5 of the 17 spent more than five minutes below 80% O_2 saturation; the longest period was 55 minutes.

Contrary to the prediction of the aging and chronic mountain sickness hypothesis (Sime et al., 1975), the greater hypoxemia of older urban men is not associated with any general trend toward higher hemoglobin concentration that might reflect a process leading to an exaggerated polycythemia or chronic mountain sickness that would reflect a loss of high altitude adaptation. Instead, the present findings raise the opposite question: Is the *lower* hemoglobin concentration of older high altitude native men, relative to young men, evidence of reduced adaptive capacity?

Defining optimal values for healthy life at high altitude has been problematic because elevated hemoglobin concentrations can have simultaneously negative consequences for O_2 delivery due to increased viscosity and positive consequences due to increased O_2 content (e.g., Winslow, 1982; Winslow and Monge, 1987). An approach to the question is to compare the estimated arterial O_2 content, a function of percent O_2 saturation and hemoglobin concentration. This is significantly lower among older high altitude native Aymara men than young (Tables 2A, 2B); yet, the values of 19.4 and 20.2 ml O_2/100 ml blood differ little from the sea level reference value of 20.4 for young men (Altman and Ditmer, 1971). In this sense, the observed hemoglobin concentrations, 8 and 14% elevated over sea level (Viteri et al.,

1972), are adaptive because they restore sea level values of estimated arterial O_2 content. Determining the consequences for O_2 supply and delivery requires measurement of blood volume and cardiac output in future studies. It is hypothetically possible that the lower hemoglobin concentration in older men leads to lower blood viscosity, larger cardiac output, higher blood flow, and maintenance of delivery of the same amount of oxygen to the tissues as their younger counterparts.

These findings argue against the stated hypothesis that normal time-dependent processes in the lung will inevitably result in excessive erythrocytosis. These findings suggest, instead, that additional factors are necessary to precipitate the disease. Epidemiological data reveal that the prevalence of excessive erythrocytosis among miners at 4,300 m increases more than four-fold in prevalence from 6.8% at 20–29 to 33.7% at 50–59 years (defined as hemoglobin concentration > 21.3 gm/dl, Leon-Velarde et al., 1990) and clinical data give the impression that chronic mountain sickness is more common among middle aged than young adults (Heath and Williams, 1989; Winslow and Monge, 1987). The high prevalence of young miners with excessive erythrocytosis suggests that the mining occupation may be generally associated with a high risk of this disease. A higher prevalence of cardiopulmonary disease in older age groups could be the additional stress accounting for the higher prevalence of excess erythrocytosis and chronic mountain sickness among older Andean high altitude natives. Slight impairments in cardiopulmonary function causing hypoxia that might be insignificant at sea level may be capable of initiating the development of chronic mountain sickness (Winslow and Monge, 1987) when superimposed upon high altitude hypoxia exacerbated by age-related hypoxia.

The rural-urban contrast in hypoxemia and hemoglobin concentration raises the question of the relevant influences in the urban environment that appear to accelerate aging changes in the function of the respiratory system and its ability to oxygenate blood and also appear to raise hemoglobin concentration. The small sample of rural men poses important issues about differential aging processes; yet they must be interpreted cautiously because the study was not designed to test rural-urban differences. It does not appear that sample bias (considered in detail in Beall et al., in press) accounts for the findings. The eight rural residents in the present sample do not differ in weight-for-height, plasma ferritin, and hemoglobin concentration from a larger sample of 99 rural Aymara men of the same age range residing in the same area.

All the older urban men were born in rural areas and migrated to the city; five migrated before the age of 20 and the remainder migrated between 20 and 48 years of age. Selective rural to urban migration of men with greater hypoxemia cannot be ruled out with these cross-sectional data. Alternatively, exposure to the urban environment may have accelerated the aging processes in the urban environment. The available data suggest there are differences in activity patterns. Older urban men have significantly lower FVC, higher systolic and diastolic blood pressures, and insignificantly higher resting heart rates than older rural men (Tables 2A, 2B). This is consistent with a hypothesis that different levels of activity and physical fitness may underlie rural-urban differences in respiratory characteristics of older high altitude native men. The higher urban hemoglobin concentation is probably accounted for by the higher urban testosterone concentration (Beall et al., in press).

The findings of the present study also contribute to the literature on inter- and intrapopulation variation in hemoglobin concentration at high altitude. Identification of apparent Andean-Himalayan populations differences in hemoglobin concentration and hematocrit at high altitude (e.g., Beall et al., 1983; Beall and Reichsman, 1984) has prompted a number of attempts to explain this variation (e.g., Frisancho, 1988; Ballew et al., 1989; Beall et al., 1987, 1990, submitted). Explanatory hypotheses for the apparently higher hemoglobin concentration of Andean high altitude natives include the possibility of profound hypoxemia during sleep, ethnic admixture, history of exposure to high altitude, and life-style. The present study demonstrates clearly that profound hypoxemia does not occur in healthy Andean high altitude natives and cannot account for higher Andean hemoglobin concentration. The rural-urban difference in hemoglobin concentration found in the present study occurs in a sample where ethnic admixture and history of exposure to high altitude have been controlled and, therefore, these factors probably do not account for higher Andean hemoglobin concentration. The implication is that some aspect of life-style or of the

rural-urban environment is an important determinant of hemoglobin concentration. This possibility receives additional support from the first study describing an urban Himalayan sample (Moore and Sun, 1990). It reported a mean hemoglobin concentration in a sample of young Tibetan students that was 1.3 gm/dl higher than rural Himalayan samples at similar altitudes. The picture emerging from these new data suggests that the Andean-Himalayan differences in hemoglobin concentration are explained partly by population differences in life-style that have not yet been adequately identified. At the same time, direct comparison of similar rural samples from the Andes and the Himalayas found higher hematocrit among the Andean high altitude natives, indicating the likely existence of population differences in response to high altitude hypoxia (Winslow et al., 1989).

In summary, the findings of this study fail to support the aging and chronic mountain sickness hypothesis (Sime et al., 1975) that aging at high altitude is accompanied by a loss of adaptive capacity and a trend toward development of chronic mountain sickness and excess erythrocytosis. Although natural selection may have acted to maximize the fitness of young adults, it does not necessarily follow that older adults are poorly adapted. Age-related decrease in lung function does occur at high altitude; however, the functional capacity of young adult men apparently includes sufficient "reserve" that its loss does not inevitably compromise the adaptation of older men. These findings illustrate the potential influence of social and/or environmental influences on the aging processes and high altitude adaptation while indicating that healthy older rural and urban men are adequately adapted to high altitude hypoxia in the sense of maintaining O_2 content similar to sea level values at least through the seventh decade of life.

ACKNOWLEDGMENTS

The project was supported by grant awards to C.M. Beall from the American Federation for Aging Research and the Western Reserve College Research Initiatives Program and by National Institutes of Health grant awards HL02011 and HL42215 to K.P. Strohl. Criticare Systems, Inc. loaned a Criticare Oximeter Model 501+ to the project. The staff of the Vitalog Corporation was very helpful. Dr. L.P. Greksa provided guidance at all stages of the project.

The project benefited greatly from the scientific and technical advice of many people. It was conducted in affiliation with the Instituto Boliviano de Biologia de Altura, Drs. P. Desjeux and G. Antezana, Directors, which generously provided space and services. Dr. H. Spielvogel provided much appreciated guidance. We gratefully acknowledge the invaluable contributions of the research assistants who recruited, organized, and monitored the study participants throughout many long nights: E. Apaza, E. Caceres, F. Duran, F. Fortun, S. de Valverde, A. Yujra, and G. Yujra. Drs. E. Loza and F. Duran performed many of the physical exams. G. Castillo performed the pulmonary function tests. Finally, we are grateful to the study volunteers for participating.

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