Hemoglobin Concentration of Pastoral Nomads Permanently Resident at 4,850–5,450 Meters in Tibet

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ABSTRACT This paper presents data on the hemoglobin concentration of a sample of 103 pastoral nomads who are lifelong residents of Phala, at 4,850–5,450 m, on the northern plateau of the Tibet Autonomous Region of the Peoples' Republic of China. This native population resides at the highest altitude of which we are aware and is thus exposed to the most extreme chronic hypoxic stress. However, they do not exhibit the most pronounced physiological adaptations, i.e., hemoglobin concentrations exceeding those found in all other high-altitude populations. Adult male and female mean hemoglobin concentrations of 18.2 and 16.7 gm/dl, respectively, were found. These data, in conjunction with earlier studies of ethnic Tibetans living at 3,400 m, demonstrate a pattern of increasing hemoglobin concentration (erythrocytosis) at increasing altitude of residence in the Himalayas and Tibet. At the same time, however, the hemoglobin concentration is lower than that found among Andean highlanders. These new data raise the possibility of quantitative population differences in hematological adaptation to high altitude hypoxia.

This paper presents data on the hemoglobin concentration of a sample of pastoral nomads who are lifelong residents at 4,850–5,450 m on the northern plateau (the changtang) of the Tibet Autonomous Region of the Peoples' Republic of China. As the highest native resident population of which we are aware, the nomads of Phala District are exposed to the most extreme habitual hypoxic stress and are expected to manifest the most pronounced physiological adaptations, i.e., hemoglobin concentrations exceeding those found in all other high-altitude populations.

MATERIALS AND METHODS

The sample is drawn from the population of Phala, Tsatsey Chu, Namring Zone, Tibet Autonomous Region, Peoples' Republic of China. The sole inhabitants are pastoral nomads native to the area who reside in camps of one to four yak-hair tents at altitudes from 4,850 to 5,450 m, move sites several times a year, and earn their livelihood in the traditional way by herding yak, sheep, goats, and horses. Only a few of these nomads had descended to 3,900 m during winter trading trips, and just one individual had visited a site as low as 3,500 m. A 99% sample of the 183 people living in nine camps at altitudes from 4,850 to 5,250 m was obtained in June–July, 1986. This represents 71% of the total population of the district. Time constraints prevented sampling of the remaining camps.

A finger-stick blood sample for immediate analysis of hemoglobin concentration was obtained from 110 of the 111 participants aged 15 years and older. Hemoglobin concentration was measured by the cyanmethemoglobin technique using the battery-operated Ames M-1000 miniphotometer (accurate to within 0.5 gm/dl) (Fraser and McCall, 1979). Each value represents the average of two readings each of duplicate samples. The average difference between the Ames M-1000 and a Coulter Counter Model S-Plus-VI maintained in calibration at Cleveland Metropolitan General Hospital according to rec-

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ommendations of the manufacturer was within the accuracy range of the M-1000 miniphotometer, that is, <0.5 gm/dl, both before and after data collection.

Information on health status was provided by individuals' reports of symptoms, together with our observations, plus the behavior exhibited while living at close quarters in the nomad camps. Pulmonary function was assessed using the Respiradyne pulmonary function monitor, a battery-operated, solid-state, self-calibrating instrument providing measurement of forced vital capacity and forced expiratory volume in 1 sec and their ratio, the forced expiratory volume percent of forced vital capacity (FEV%).

This report is based on a subsample of 103 Phala nomads who are not pregnant, had not delivered a baby within the last year, and have not altered their activities because of symptoms of lung disease. The average age of the 47 males is 39 ± 15 years (range 16–76), and the average age of the 56 females is 41 ± 19 (range 16–82).

RESULTS

Figure 1 presents the frequency distribution of Phala nomads' hemoglobin concentrations. The mean male hemoglobin concentration of the Phala nomads is 18.2 ± 1.9 gm/dl (n = 47), and the mean female hemoglobin concentration is 16.7 ± 1.5 gm/dl (n = 56). There is no association with altitude in the 300 m span of these nine camps, nor is there an association with age or with measures of body size and nutritional status, including weight, height, and the weight/height ratio among males or females.

DISCUSSION

None of several possible extraneous sources of variation in hemoglobin concentration appears to have influenced the parameters of the nomad distribution. They are ethnic Tibetans, and there is no admixture with populations with a different history of high-altitude exposure. The Phala nomads reside at the highest habitual altitude of which we are aware, have no exposure to low altitude, and engage in a traditional mode of subsistence. They are not a recent colony, nor are they a transient population measured during acute or intermittent exposure to very high altitude activity such as mining or mountaineering. Thus variation in genetic background and pattern of exposure to high altitude does not influence hemoglobin concentration.

Iron deficiency is unlikely, because meat is the main dietary item during the winter months and is eaten almost daily throughout the year. Household survey data indicate that, in 1985, families slaughtered an average of 2.5–5.5 sheep/goats, and 0.2 yak per person over 5 years of age. Although slaughtering is seasonal, meat is dried and thus is available for later consumption. Hunting of mountain goat and antelope takes place

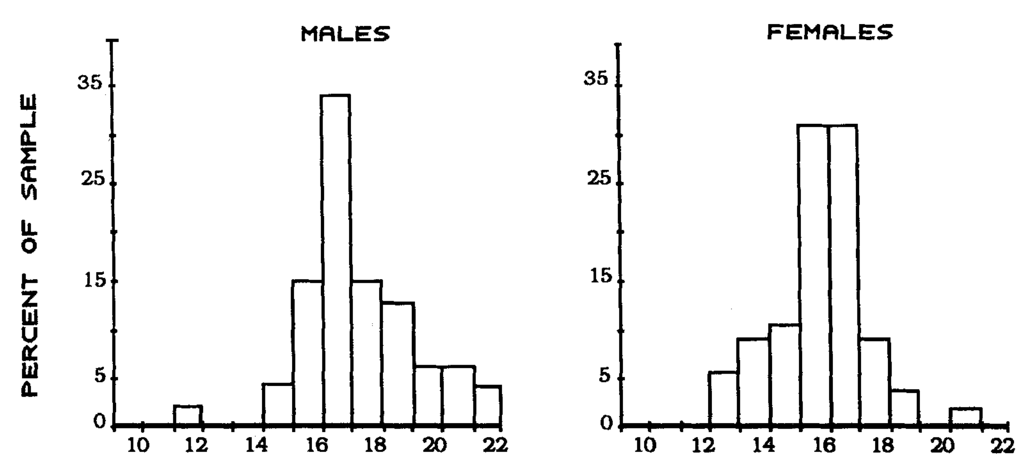

Fig. 1. Frequency distribution of hemoglobin concentrations among Phala nomads.

throughout the year and supplements the domestic meat intake. Folate deficiency is also unlikely, since barley and dairy products including yogurt, butter, and cheese are also eaten daily.

If disease, especially lung disease, exacerbates high-altitude hypoxemia, abnormally high hemoglobin concentration can result. However, high hemoglobin concentration and poor lung function are not directly associated in this sample. There is no association between hemoglobin concentration and FEV% in this sample. The three men observed to have altered their habitual activities in response to symptoms of lung disease (e.g., coughing throughout the day or marked shortness of breath following mild exertion) had a hemoglobin concentration of 18.0 gm/dl. Although these men are excluded from the present analysis to conform to the standard protocol of reporting nominally healthy individuals, their inclusion would not have changed the results.

Smoking can exacerbate hypoxemic stress. Although about half the males and one quarter of the females smoke, the hematological characteristics of smokers and nonsmokers do not differ. Few would be considered heavy smokers. Most men smoke three to five cigarettes per day, a few occasionally smoke 10–20 per day, and women smoke one or two per day. Cigarette consumption may be nil for months when the supply is exhausted. Overall, therefore, the hemoglobin distribution of Phala nomads is probably not due to undernutrition, lung disease, or smoking.

Comparing the Tibetan nomads from Phala with a large, medically screened, healthy sample from an indigenous (nonrefugee) Tibetan agropastoral population residing 1,800 m lower, at 3,250–3,560 m, in Upper Chumik, Nepal, reveals a generally greater erythrocytosis at the higher altitude (Kolmogorov-Smirnov $z = 3.5$ for males, $z = 4.2$ for females; $p < 0.001$ in both cases). Forty-four percent of Phala males and 38% of Phala females lie above the normal range of variation about the Upper Chumik mean (2 SD). The Phala mean male and female hemoglobin concentrations of 18.2 and 16.7 gm/dl are significantly higher than the Upper Chumik means of 16.1 and 14.6 gm/dl (one-tailed $t = 11.8$ for males, 19.9 for females; $p < 0.001$).

There are other points of contrast between these two Tibetan populations residing at different altitudes. There is no adolescent rise in hemoglobin concentration in Phala, as was found in Upper Chumik. The average hemoglobin concentrations of six Phala males and seven females 15–19 years old are 18.1 and 16.3 gm/dl, respectively, virtually identical to values of 18.2 and 16.7 gm/dl for those 20 years old and older. Nor is there an association between weight and hemoglobin concentration among Phala males as there was among Upper Chumik males. It is not known if these contrasts are attributable to a smaller sample, or whether the patterns observed in Upper Chumik are disrupted by the generally higher hemoglobin concentrations in the Phala sample.

Methodological differences between the two studies do not account for the contrasts. Although hemoglobin concentrations were measured by different techniques in the two studies, because the instrument used in the Upper Chumik study does not measure the upper range of hemoglobin concentrations encountered in Phala, simultaneous measurement of control samples revealed that the average difference between the two instruments was less than the 0.5 gm/dl accuracy of each machine. Another difference concerns screening methods. Inclusion in the Upper Chumik sample was based on medical criteria of health, and inclusion in the Phala sample was based on behavioral criteria. Consequently, the Phala sample could include some individuals who would have been excluded from the Upper Chumik sample. However, neither of these differences would be responsible for the Phala nomads' 2.1 gm/dl higher hemoglobin concentration.

Both the Phala nomads and the Upper Chumik sample have significantly higher hemoglobin concentrations than a low-altitude reference sample screened to eliminate pathological sources of variation. Figure 2 plots the mean hemoglobin concentration of these two ethnic Tibetan samples and a low-altitude reference sample (Viteri et al., 1972) and demonstrates a slight, but statistically significant, increase at 3,250–3,560 m (Upper Chumik) and a marked increase at 5,000 m (Phala). Thus native ethnic Tibetan populations exhibit a hematological response to the stress of hypoxemia. However, although this is qualitatively similar to the response reported for Andean highlanders, the Tibetans' response appears quantitatively smaller.

Figure 2 also plots predicted hemoglobin concentrations derived from two equations

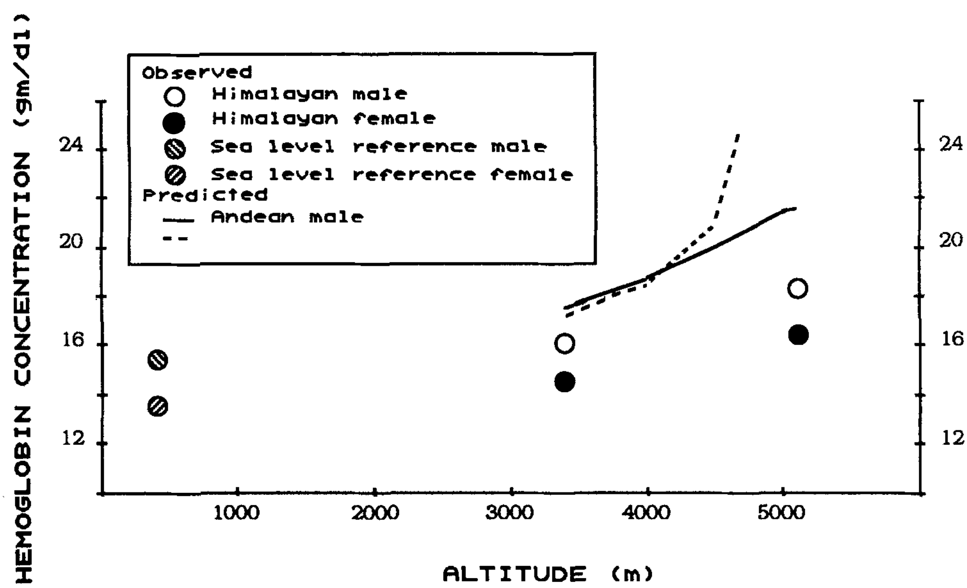

Fig. 2. Relationship between altitude of residence and hemoglobin concentration in selected populations.

describing Andean males and including the altitude span from Upper Chumik to Phala. It illustrates that, although the Phala nomads are the highest native resident population of which we are aware, their hemoglobin concentrations are not the highest. These Andean-based predictions are 9% higher at 3,400 m and at least 37% higher at 5,000 m (Cosio, 1972; Torrance et al., 1970/71). The ethnic Tibetan samples demonstrate clearly that it is possible for healthy individuals to live at high altitude without the degree of erythrocytosis widely known and cited for Andean populations. Consequently, accounting for ethnic Tibetan-Andean differences is a fundamental concern.

One possibility is that ethnic Tibetan highlanders adapt to hypoxic stress at different steps of the oxygen delivery process. Although data on oxygen transport of Himalayan (mostly ethnic Tibetan) and Andean highlanders are incomplete, a detailed comparison of the information available failed to find any systematic difference between the two populations apart from hemoglobin concentration. This suggests the hypothesis that Himalayan highlanders experience less extreme hypoxemic stress measured as the percent of oxygen saturation of arterial blood, which could result from different breathing patterns and would cause less stimulus to erythropoiesis (Beall et al., 1983).

Another possibility is that the Andean natives in some samples are also responding hematologically to stresses other than high-altitude hypoxia. The Himalayan samples are all drawn from traditional, rural, native populations, who subsist by farming, herding, and trading (see, e.g., Adams and Strang, 1975; Adams and Shrestha, 1974; Beall and Reichsman, 1984). In contrast, virtually all the available Andean data are based on samples of miners and urban workers (see, e.g., Arnaud et al., 1981; Cosio, 1972; Hurtado et al., 1945; Torrance et al., 1971; Tufts et al., 1985; Winslow et al., 1981). These people are likely to have a variety of genetic backgrounds, distinctive diseases, activity patterns, and histories of exposure to altitude, some or all of which may contribute to the elevation of hemoglobin concentration (Garruto and Dutt, 1983). In this context, it is noteworthy that a rural Andean adult male sample following a traditional life-style at 4,000 m has a mean of 17.5 gm/dl, lower than all other Andean samples and insignificantly higher than a Himalayan value of 17 gm/dl at the same altitude (Adams and Strang, 1975; Garruto, 1976; t = 1.4; $p < 0.05$). These data suggest that there may be important differences between Andean traditional rural populations and Andean urban or mining populations. Thus Himalayan-Andean population differences in erythrocytosis may be partly explained by additional stresses encountered by many among the Andean samples.

However, there is also evidence that the Himalayan-Andean differences cannot be explained solely by sample confounding. Another rural Andean combined male and female sample from 3,500 m had an 11% prevalence of hemoglobin concentration over 19 gm/dl, 9% if individuals with a history of severe disease are eliminated, whereas a Himalayan sample at the same altitude has *no* individuals with hemoglobin concentrations over 19 gm/dl (Beall and Reichsman, 1984; Buck et al., 1968). This suggests that the population difference in degree of erythrocytosis is not just an artifact of sample differences.

Finally, although Andean populations are noted for the prevalence of a syndrome, chronic mountain sickness, characterized by very high hemoglobin concentrations and signs of exaggerated hypoxemia, this is very rare in Himalayan populations (Hackett et al., 1984; Heath and Williams, 1977; Huang et al., 1984). The erythrocytosis of Himalayan and Tibetan highlanders conveys a theoretical advantagae in oxygen carrying capacity but does so without raising blood viscosity to a level so high that blood flow and oxygen delivery are decreased and the advantage of erythrocytosis is offset. Significantly, signs and symptoms of the exaggerated hypoxemia that would result from pathologically elevated blood viscosity (e.g., cyanotic appearance) are not present in the nomad sample. None of the Phala nomads had hemoglobin concentrations above 23 gm/dl, a suggested diagnostic cut off point for chronic mountain sickness (Heath and Williams, 1977). Just two had hemoglobin concentrations 0.2 gm/dl above another suggested diagnostic cut off point of 22 gm/dl for polycythemia (Tufts et al., 1985). This suggests that the normal range of Tibetans' hemoglobin concentration, even at 5,000 m, is associated with healthy levels of blood viscosity. In this sense, the erythrocytosis of Himalayan and Tibetan highlanders appears more advantageous than that expected for Andean highlanders at similar altitudes, since it is extremely rare for Himalayan and Tibetan highlanders to achieve hemoglobin concentrations sufficiently far above the sample mean to severely affect blood viscosity, whereas it is more common for Andean highlanders, whose mean hemoglobin concentration is higher.

In summary, the Phala data confirm that some erythrocytosis appears to be a universal adaptive response to permanent residence at very high altitude but also strongly raise the possibility of quantitative population differences in the adaptation to high altitude hypoxia and the question of factors in addition to altitude that may determine the degree of erythrocytosis.

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