

RSP 01391

Origins of differences in hemoglobin concentration between Himalayan and Andean populations*

A. R. Frisancho

Center for Human Growth and Development, University of Michigan, Ann Arbor, MI 48109, U.S.A.

(Accepted for publication 21 November 1987)

Abstract. Mean hemoglobin concentration of 3511 adult males derived from 19 studies of Andean male permanent residents and 10 studies of Himalayan male permanent residents were compared with reference to partial pressure of inspired oxygen. The regression equation (weighted for sample size) of $P_{I_{O_2}}$ and hemoglobin concentration of the Andean miners is significantly ($P < 0.01$) greater than that of the Andean and Himalayan non-miners. However, the relationship of $P_{I_{O_2}}$ and Hb is similar in the non-mining Andean and Himalayan samples. These findings suggest that the observed differences in hemoglobin concentration between Andean and Himalayan samples are due, in part, to the inclusion of miners in the Andean samples. The higher barometric pressure associated with the north latitude location of the Himalayans may also contribute to decrease the hypoxic stress in the Himalayas. The present data suggest that Andeans and Himalayans have a similar hemopoetic response to hypoxic stress.

Altitude; Andes; Hemoglobin; Himalayas

The relationship between altitude and hemoglobin concentration has been well-established (Hurtado *et al.*, 1945; Reynafarje, 1957). However, recent studies have indicated that the relationship of altitude and hemoglobin is less marked in the Himalayas than in the Andes (Morpurgo *et al.*, 1979; Beall *et al.*, 1983; Beall and Reichsman, 1984). These differences could be due to either variability in hypoxic stress or actual population differences. First, at the same altitude the hypoxic stress in the Himalayas is less than in the Andes. Various investigations have pointed out that because of its north latitude location the barometric pressures in the Himalayas at the same altitude are considerably higher than in the Andes (Haldane and Prieste, 1935; Pugh, 1957; West *et al.*, 1983).

Second, the lower hemoglobins of the Himalayans could be related to the fact that some of the Andean subjects studied were residents of mining communities (Hurtado *et al.*, 1945; Reynafarje, 1957; Cosio, 1973; Santolaya *et al.*, 1981). Since miners are

* Dedicated to Professors Paul T. and Thelma S. Baker on the occasion of their retirement.

Correspondence address: Dr. A. Roberto Frisancho, Center for Human Growth and Development, 300 N. Ingalls, University of Michigan, Ann Arbor, MI 48109, U.S.A.

known to suffer from a variety of chronic respiration disorders, including silicosis and chronic mountain sickness (Ruiz, 1973), which impairs oxygen transport, any evaluation of the role of hypoxia in hemoglobin response needs to take this factor into account (Frisancho, 1983; Garruto and Dutt, 1983). Therefore, there is a need to reevaluate the hemopoetic responses to altitude of Himalayan and Andean populations. Hence, with this purpose the relationship of partial pressure of oxygen in the inspired air ($P_{I_{O_2}}$) and hemoglobin concentration of Andean and Himalayans is compared through regression analysis.

Method

From the literature data were selected on hemoglobin concentration of 3511 males derived from 29 adult samples living permanently in the Andes and the Himalayas. The samples included only adult males living permanently at a given altitude, irrespective of ethnic admixture.

The Andean group included 19 sample means with a total of 3133 subjects belonging to Quechua, Aymara and Mestizo ethnic groups living in the Andes of Peru, Bolivia, and Chile (Hurtado *et al.*, 1945; Reynafarje, 1957; Cosio, 1973; Ruiz, 1973; Frisancho *et al.*, 1975; Chiodi, 1978; Arnaud *et al.*, 1979; Santolaya *et al.*, 1981; Winslow *et al.*, 1981; Clench *et al.*, 1982; Garruto and Dutt, 1983; Tufts *et al.*, 1985). Based on the information given in each report, the Andean samples were classified as living in either mining or non-mining areas, irrespective of whether they actually worked as miners.

The Himalayan group included 10 sample means with a total of 378 subjects belonging to ethnic groups referred to as Tibetans, Sherpas, Tamills, and Ladakhis, living in the Himalayas (Pugh, 1966; Guleria *et al.*, 1971; Bharadwaj *et al.*, 1973; Adams and Shresta, 1974; Adams and Strong, 1975; Morpurgo *et al.*, 1979; Samaja *et al.*, 1979; Beall and Goldstein, 1987). The mean hemoglobins for male Phala Nomads between 4850 and 5450 m living in the Himalayas recently studied by Beall and associates (Beall and Goldstein, 1987) are also included here.

Since it is not high altitude that causes hypoxia but the associated low barometric pressure, we have analyzed the relationship of hemoglobin concentration to the partial pressure of inspired O_2 rather than to altitude. Based on the altitude given in each report, the barometric pressures (Torr) in all studies were derived using the tables of International and Aviation Organization Standard Atmosphere (Manual of ICAO, 1968). The partial pressure of O_2 in the inspired air ($P_{I_{O_2}}$) was calculated following standard procedures. The relationship of $P_{I_{O_2}}$ and hemoglobin concentration was evaluated using regression analyses. Because of the variability in the sample size the regression equation of $P_{I_{O_2}}$ on Hb was weighted for sample size differences.

Results and Discussion

Table 1 summarizes the data on hemoglobin concentration, altitude and inspired P_{O_2} of the 29 samples. It is quite evident that at a given altitude or inspired P_{O_2} the Andeans

TABLE 1

Hemoglobin concentration of high altitude permanent residents living in mining and non-mining areas in the Andes and the Himalayas by altitude and partial pressure of oxygen in inspired air.

Mean alt. (m)	Reference	N	Pop.	Pressure (Torr)		Hemoglobin (g/dl)	
				P _B	P _{O₂}	Non-mining (Mean ± SD)	Mining (Mean ± SD)
1200	Cosio, 1973	104	Andean	658	128	-	14.8 ± 1.3
2300	Cosio, 1973	168	Andean	578	111	-	15.4 ± 1.4
2800	Santolaya <i>et al.</i> , 1981	270	Andean	536	103	-	17.4 ± 1.2
3200	Clench <i>et al.</i> , 1982	103	Andean	516	98	16.8 ± 1.8	-
3400	Beall and Reichsman, 1984	126	Himalayan	502	95	16.1 ± 1.2	-
3475	Cosio, 1973	408	Andean	493	94	-	18.0 ± 1.5
3600	Arnaud <i>et al.</i> , 1979	85	Andean	487	92	18.2 ± 1.1	-
3657	Adams and Shresta, 1974	52	Himalayan	484	92	16.8 ± 1.4	-
3650	Guleria <i>et al.</i> , 1971	25	Himalayan	484	92	14.7 ± 1.3	-
3692	Bharadwaj <i>et al.</i> , 1973	23	Himalayan	482	91	18.0 ± 1.5	-
3700	Tufts <i>et al.</i> , 1985	499	Andean	481	91	18.8 ± 1.4	-
3720	Cosio, 1973	271	Andean	480	91	-	17.8 ± 1.3
3740	Hurtado <i>et al.</i> , 1945	40	Andean	480	91	-	18.8 ± 1.5
3840	Frisancho <i>et al.</i> , 1975	40	Andean	470	89	17.2 ± 1.2	-
3900	Bharadwaj <i>et al.</i> , 1973	24	Himalayan	468	88	18.3 ± 2.4	-
3900	Samaja <i>et al.</i> , 1979	13	Himalayan	468	88	17.0 ± 1.9	-
4000	Adams and Strong, 1975	28	Himalayan	462	87	17.0 ± 1.3	-
4050	Pugh, 1966	22	Himalayan	459	86	17.1 ±	-
4100	Ruiz, 1973	414	Andean	456	86	-	18.5 ± 1.5
4200	Garruto and Dutt, 1983	44	Andean	450	85	17.3 ± 1.5	-
4260	Ruiz, 1973	234	Andean	445	84	-	18.4 ± 1.7
4260	Clench <i>et al.</i> , 1982	60	Andean	445	84	17.6 ± 1.7	-
4460	Clench <i>et al.</i> , 1982	70	Andean	440	82	18.4 ± 1.6	-
4521	Chiodi, 1978	96	Andean	430	80	-	19.3 ± 1.8
4540	Hurtado <i>et al.</i> , 1945	83	Andean	430	80	-	20.1 ± 2.0
4540	Winslow <i>et al.</i> , 1981	46	Andean	430	80	-	20.2 ± 2.3
4600	Clench <i>et al.</i> , 1982	98	Andean	426	79	18.7 ± 1.6	-
4950	Morpurgo <i>et al.</i> , 1979	18	Himalayan	408	79	16.8 ± 1.6	-
5050	Beall and Goldstein, 1987	47	Himalayan	401	78	18.2 ± 1.9	-

living in mining areas have significantly higher hemoglobin concentration than the Andeans not living in mining areas. As shown in fig. 1A the difference in hemoglobin concentration between those living in mining areas and those living in non-mining areas increases with altitude. In contrast, fig. 1B shows that Andeans not living in mining areas have a similar hemoglobin concentration to that of the Himalayans. These findings suggest that, contrary to previous assertions (Morpurgo *et al.*, 1979; Beall *et al.*, 1983; Beall and Reichsman, 1984), both Andeans and Himalayans have a similar hemopoetic response to hypoxic stress.

Since mining is associated with pollution, which in turn can accentuate hypoxia, the enhanced polycythemia of Andeans living in mining areas probably represents a response to the compound stress of mining and altitude. As previously indicated (Frisancho, 1981), from the point of view of functional adaptation high polycythemia represents either only a temporary response to hypoxia made by sea-level natives who are partially acclimatized to high altitude or an exaggerated response to the compound stress of pollution associated with mining and high altitude hypoxia. On the other hand,

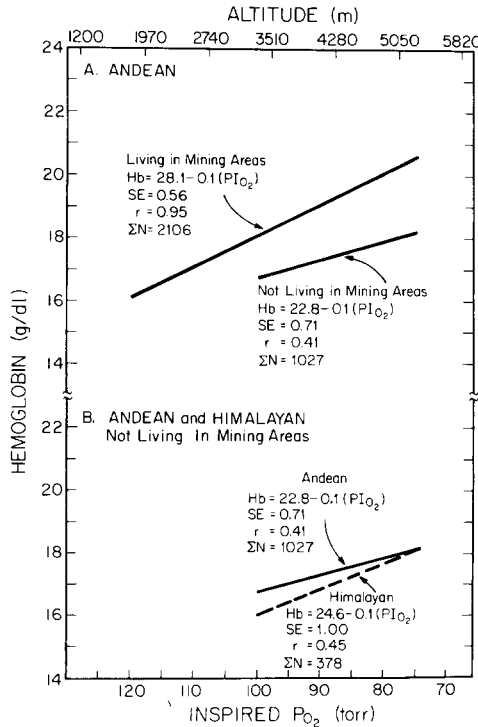


Fig. 1. Increase in hemoglobin concentration (g/dl) associated with a decrease in the partial pressure of inspired O₂ (P_IO₂). Note that among Andeans the increase in Hb is significantly greater in the samples living in mining areas than in those not living in mining areas. On the other hand, the increase in Hb is similar in both Andeans and Himalayans not living in mining areas.

a complete functional adaptation like that exhibited by Andeans not living in mining areas and Himalayans requires only a moderate polycythemic response. This is because acclimatization to high altitude is attained not only through hemopoetic response but through physiological and morphological adaptations acquired during the developmental period.

Another factor which may contribute to lower the hemoglobin concentration of the Himalayans is that the barometric pressure because of its north latitude location is higher at the same altitude than in the Andes. Various investigations have pointed out that barometric pressures on mountains in the equatorial or temperate zones are considerably higher than those predicted from ICAO (Haldane and Prieste, 1935; Pugh, 1957; West *et al.*, 1983). For example, Pugh (1957) reports that the barometric pressure reading for Mount Everest at 8888 m was 269 Torr, while the ICAO Standard Atmosphere table gives 236 Torr. This difference of 33 Torr units represents a height of 467 m. The cause for the lower hypoxic stress in the Himalayas appears to be related to its north latitude location, which is associated with higher barometric pressure. As pointed out by West *et al.* (1983), the barometric pressure in the altitude range of 2 to 16 km bulges markedly near the equator. For this reason, and as a result of a combination of complex radiation and convective phenomena, the coldest air in the atmosphere is above the equator. Another effect of the bulge in barometric pressure is that the junction between the troposphere (where all the weather events take place), and the stratosphere (where the temperature of the air is essentially independent of altitude) is much higher near the equator than near the poles. Thus, the barometric pressure is higher (or a given altitude related to hypoxic stress is decreased) in the mountains situated above the equator or toward the poles, and lower (or the altitude related to hypoxic stress is increased) in the mountains situated below the equator. The fact that at a given altitude the barometric pressure is higher in the Himalayas indicates that at an equivalent altitude the Andeans are exposed to greater hypoxic stress than the Himalayans and therefore one would expect that hemoglobin be also higher in the Andeans than in the Himalayans.

References

- Adams, W.H. and S.M. Shresta (1974). Hemoglobin levels, vitamin B₁₂ and folate status in a Himalayan village. *Am. J. Clin. Nutr.* 27: 217-219.
- Adams, W.H. and L.J. Strong (1975). Hemoglobin levels in persons of Tibetan ancestry living at high altitudes. *Proc. Soc. Exp. Biol. Med.* 49: 1036-1039.
- Arnaud, J., J. Quilici, N. Gutierrez and J. Beard (1979). Methaemoglobin and erythrocyte reducing systems in high-altitude natives. *Ann. Hum. Biol.* 6: 585-593.
- Beall, C.M., K.P. Strohl and B.M. Gary (1983). Reappraisal of Andean high altitude erythrocytosis from a Himalayan perspective. *Semin. Respir. Med.* 5: 195-201.
- Beall, C.M. and A.B. Reichsman (1984). Hemoglobin levels in a Himalayan high altitude population. *Am. J. Phys. Anthropol.* 63: 301-306.
- Beall, C.M. and M.C. Goldstein (1987). Hemoglobin concentration of pastoral nomads permanently resident at 4850-5450 m in Tibet. *Am. J. Phys. Anthropol.* 73: 433-438.
- Bharadwaj, H., A. Singh and S. Malholya (1973). Body composition of the high altitude natives of Ladakh. A comparison with sea-level residents. *Hum. Biol.* 45: 423-434.

- Chiodi, H. (1978). Aging and high-altitude polycythemia. *J. Appl. Physiol.* 45: 1019–1020.
- Clench, R., E. Ferrell and W.J. Schull (1982). Effect of chronic altitude hypoxia on hematologic and glycolytic parameters. *Am. Phys. Soc.* 447–451.
- Cosio, G. (1973). Hematic and cardiopulmonary characteristics of the Andean miner. *Bol. Of. Sanit. Panam.* English Edition VII: 26–33.
- Frisancho, A.R., T. Velasquez and J. Sanchez (1975). Possible adaptive significance of small body size in the attainment of aerobic capacity among high-altitude Quechua natives. In: *Biosocial Interrelations in Population Adaptation*, edited by E. Watts, F.E. Johnston and G.W. Lasker. The Hague, Morton, pp. 55–64.
- Frisancho, A.R. (1981). *Human Adaptation: A Functional Interpretation*, 2nd edition. Ann Arbor, University of Michigan Press.
- Frisancho, A.R. (1983). Perspectives on functional adaptation of the high altitude native. In: *Hypoxia, Exercise, and Altitude: Proceedings of the Third Banff International Hypoxia Symposium*, edited by J.R. Sutton, C.S. Houston and N.L. Jones. New York, Alan R. Liss, pp. 383–401.
- Garruto, R.M. and J.S. Dutt (1983). Lack of prominent compensatory polycythemia in traditional nature Andeans living at 4200 meters. *Am. J. Phys. Anthropol.* 61: 355–366.
- Guleria, J.S., J.N. Pande, P.K. Sethi and S.B. Roy (1971). Pulmonary diffusing capacity at high altitude. *J. Appl. Physiol.* 31: 536–543.
- Haldane, J.S. and J.G. Priestley (1935). *Respiration*, 2nd edition. New Haven, Yale University Press.
- Hurtado, A., C.F. Merino and D. Delgado (1945). Influence of anoxemia on the hemopoietic activity. *Arch. Intern. Med.* 75: 284–323.
- Manual of the ICAO Standard Atmosphere (1968). International Civil Aviation Organization. Montreal, 2nd edition.
- Monge, M.C. and C.C. Monge (1966). *High-Altitude Diseases*. Springfield, C.C. Thomas.
- Morpurgo, G., P. Battaglia, N.D. Carter, G. Modiano and S. Passi (1979). The Bohr effect and the red cell 2-3 DPG and Hb content in Sherpas and Europeans at low and high altitude. *Experientia* 28: 1280–1283.
- Pugh, L.G.C. (1957). Resting ventilation and alveolar air on Mount Everest: with remarks on the relation of barometric pressure to altitude in mountains. *J. Physiol. (London)* 135: 590–610.
- Pugh, L.G.C. (1966). A programme of physiological studies of high-altitude peoples. In: *The Biology of Human Adaptability*, edited by P.T. Baker and J.S. Weiner. Oxford, Clarendon Press.
- Reynafarje, C. (1957). The influence of high altitude on erythropoietic activity. *Brookhaven Symp. Biol.* 10: 132–146.
- Ruiz, L. (1973). Epidemiologia de la hipertension arterial y de la Cardipatia isquemica en las grandes alturas: Prevalencia y factores relevantes a su historia natural. Doctoral Thesis Universidad Peruana Cayetano Heredia.
- Samaja, M., A. Veicsteinas and P. Cerretelli (1979). Oxygen affinity of blood in altitude Sherpas. *J. Appl. Physiol.* 47: 337–341.
- Santolaya, R., J. Araya, R. Vecchiola, R. Prieto, R.M. Ramirez and R. Alcayaga (1981). Hematocrito, hemoglobina y presion de oxigeno arterial en 270 hombres y 26 mujeres sanas residentes de altura (2.800 mts.) *Rev. Hosp. Roy H. Glover* 1: 17–29.
- Tufts, D.A., J.D. Haas, J.L. Bear and H. Speivogel (1985). Distribution of hemoglobin and functional consequences of anemia in adult males at high altitude. *Am. J. Clin. Nutr.* 42: 1–11.
- West, J.B., S. Lahiri, K.H. Maret, R.M. Peters and C.J. Pizzo (1983). Barometric pressures at extreme altitudes on Mt. Everest: physiological significance. *J. Appl. Physiol.* 54: 1188–1194.
- Winslow, R.M., C.C. Comge, N.J. Statham, C.G. Gibson, S. Charache, J. Whittenbury, O. Moran and R.L. Berger (1981). Variability of oxygen affinity of blood: human subjects native to high altitude. *J. Appl. Physiol.* 61: 1411–1416.