

Altitude and Infant Growth in Bolivia: A Longitudinal Study

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ABSTRACT The growth of 79 healthy, well-nourished lowland (400 M) and highland (3600 M) Bolivian infants was analyzed in a longitudinal study through the first postnatal year. Compared to low altitude infants, the high altitude infants were found, by analysis of covariance controlling for size at the previous exam, to be significantly shorter at birth, 1 and 6 months, while they were significantly lighter only at birth and 1 year. Recumbent length gain was slower in the high altitude infants in the early months of life, while weight gain did not differ between altitudes. The observed lower weights at high altitude throughout the first year appear to be due to a persistence of lower weights seen at birth and not to postnatal growth retardation. Significantly greater triceps and subscapular skin-fold thickness measurements were found in the highland group, despite their smaller length and weight. The possible causes and implications of the greater fat accumulation in the highland infants are discussed.

The physical environment at extreme high altitudes above 3000 M imposes numerous stresses on the human populations that reside there. The most prominent stresses are hypobaric hypoxia, low ambient temperatures, low relative humidity, limited nutritional base, and high background cosmic radiation. Studies of human growth and development under these environmental stresses have shown reduced body size at all postnatal ages and suppressed growth rate, especially during puberty. These observations have been reported for populations living in the South American Andes, the Ethiopian Highlands, and the Asian Himalayas, Tien Shan, and Pamirs (Frisancho, 1978).

Although the environmental effects on achieved growth appear at all ages from birth to adulthood, the importance of early growth experience on later development should be recognized. If poor growth during infancy lays the foundation for later growth failure, then intervention to improve growth during an early age may be an effective measure to prevent

later growth failure. Furthermore, if exposure to hypoxic stress during the early growing years is important to the development of physiological adaptations to this stress (Frisancho, 1975), then provision of an optimal growth pattern may be essential to the expression of these developmental adaptations.

How the growth of highland children is affected by the individual environmental stresses of hypoxia, cold, undernutrition and disease is not clearly understood. Most studies of child growth in less developed nations have demonstrated that chronic undernutrition and disease can affect growth. It is reasonable to assume that these have also been important factors affecting child growth in high altitude areas, especially since nearly all of these areas are located in less developed countries. Child growth at high altitude, however, can be affected by other environmental stresses such as hypoxia and cold. Identifying the impact of these stresses independent of the effects of

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malnutrition and disease has been a problem in the past. Several studies have reported a persistence of small size (Haas, 1973, 1976) and reduced growth rates (Beall, 1976) during infancy in highland Peruvian populations receiving preventive medical care which presumably controlled some of the effects of malnutrition and poor health. A difference in achieved height and weight was also found in a cross-sectional comparison of healthy highland and lowland Peruvian children of the same body composition (Haas, 1981).

Considering the importance of infancy as a period during which the foundation for future growth is established, a longitudinal study of the development of healthy, well-nourished Bolivian infants was conducted to investigate the effect of altitude differences on growth. The major objective of this study was to test the hypothesis that high altitude infants achieve a smaller size and grow more slowly than lowland children when adequate health and nutritional support is available.

METHODS

A sample of 79 Bolivian infants was examined at regular intervals between birth and one year of age. Forty of the infants (16 males, 24 females) came from the city of La Paz at 3600 M above sea level; 39 (18 males, 21 females) came from the city of Santa Cruz at 400 M. The infants were recruited from among mothers who had been examined during the eighth prenatal month as part of a larger project on maternal adaptation during pregnancy at high altitude (Haas, 1980). All mothers were invited to participate in the postnatal follow-up examinations. Infants who served as the cohort were assessed as being full term at delivery according to the neurological and clinical criteria of Dubowitz et al. (1970), delivered without complications, and regularly participated in all scheduled examinations up to 12 months of age. They are, by the nature of the research design and prospective sampling bias, a select group of healthy infants. The infants were from lower and middle socioeconomic classes and mixed ethnic background. Sixty-five % of the La Paz infants and 49% of the Santa Cruz infants were classified as Indian. The remaining infants were of *mestizo* or European ancestry. Examinations were conducted on the infants at birth, 1, 3, 6, 9, and 12 months

postnatally. At each visit the child was examined by a pediatrician, a health history was obtained and an infant feeding questionnaire was completed. Mothers were instructed in proper preventive health care and nutrition, and breastfeeding was encouraged. All children were eligible for free pediatric care for the duration of the study, and mothers were urged to bring them to the pediatrician for any health problems. Vaccinations, vitamin and mineral supplements, and medication were also provided to all subjects when needed. All of these procedures were designed to maintain the children in both cities at good levels of health and nutritional status.

All children were measured at birth and 1 month by the same person (J.D.H.). All subsequent measurements were made by 3 pediatricians; one physician (J.P.) conducted all of the postnatal measurements from 3 to 12 months in La Paz, while 2 physicians (G.P. and J.Y.) divided the anthropometry of 3-to 12-month-old infants in Santa Cruz. All three physicians were trained by the anthropometrist who took the first two measurements. Training stressed minimization of systematic and random measurement error with quality control checks performed on subsamples of infants at 1 month and 12 months of age. Interobserver and intraobserver error were within acceptable values of below 10% of total sample variance with no change in measurement error between the two quality control periods.

All infants were measured either in a hospital outpatient examination office (La Paz) or in a private physicians' offices (Santa Cruz). The following measurements are used in the present analysis. Weight was taken on a pediatric beam balance calibrated weekly with a standard series of weights and recorded to the nearest 25 g. Crown-heel or recumbent length was taken with an infant measuring board (Olympic infa-length) and recorded to the nearest millimeter. Triceps and subcaplar skinfolds were measured with Lange calipers according to standard procedures (Weiner and Lourie, 1969) and recorded to the nearest 0.5 millimeter.

RESULTS

Table 1 presents the mean achieved weights, and weight increments at each visit for male

TABLE 1. Mean weights and weight increments during the first year in Bolivian high altitude (La Paz) and low altitude (Santa Cruz) infants¹

Age (months)	Males		Females	
	La Paz n = 16	Santa Cruz n = 18	La Paz n = 24	Santa Cruz n = 21
	Weight (g)			
Birth	3019 ± 367	3478 ± 487	3007 ± 395	3315 ± 404
1	3918 ± 600	4242 ± 594	3813 ± 514	3992 ± 366
3	6114 ± 579	6492 ± 600	5613 ± 827	5739 ± 620
6	7780 ± 786	8210 ± 768	7459 ± 1130	7594 ± 877
9	8547 ± 850	9238 ± 1031	8282 ± 1091	8492 ± 1051
12	9270 ± 1107	10326 ± 1214	9045 ± 1107	9503 ± 1219
	Weight increment (g/yr)			
Birth				
1	11442 ± 7405	9417 ± 4072	10073 ± 3902	8350 ± 4504
1-3	12734 ± 2974	13272 ± 3290	10570 ± 2658	10307 ± 2787
3-6	6837 ± 2199	6805 ± 2112	7297 ± 1971	7108 ± 1940
6-9	3003 ± 1608	4136 ± 2269	3371 ± 2160	3662 ± 2007
9-12	2738 ± 1722	4068 ± 2693	2892 ± 1410	3877 ± 1468

¹Means ± S.D.

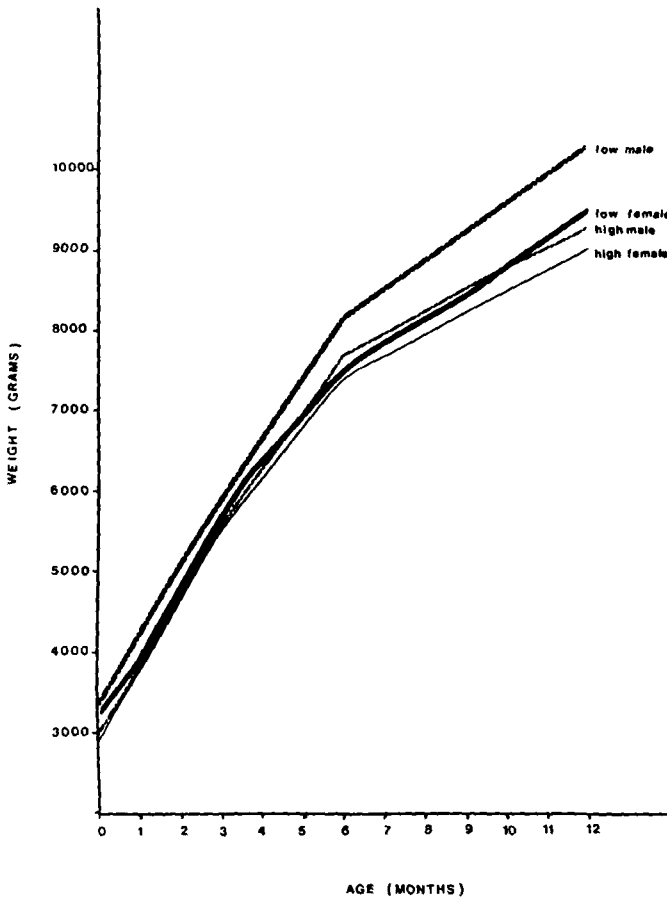


Fig. 1. Distance growth curves of weight for high and low altitude Bolivian infants.

and female infants in La Paz and Santa Cruz. Figure 1 presents these values as distance growth curves. At birth, weight is significantly lower at high altitude for both sexes. The mean birth weights for both altitude groups are 75 to 100 g lighter than the respective means for the larger sample of newborns from which this cohort was drawn (Haas, 1980). This selective bias for smaller infants in the study cohort is not statistically significant and appears to be equal in both altitude groups. Altitude differences in weight at the postnatal examinations appear to persist throughout the first year, especially in male infants.

Figure 2 presents velocity growth curves for weight in the four groups. The weight increment is expressed in grams per year. There appears to be very little altitude difference in rates of growth for either sex except during the first month when highland infants gain more weight than lowland infants. Large variances in incremental rates characterize all groups throughout the first year.

Table 2 presents the mean value for achieved growth in recumbent length and the incremental growth rates over the first year. Figure 3 presents the distance growth curves for the same data. The high altitude infants appear smaller than the low altitude infants at all ages up to 12 months. Figure 4 presents velocity growth curves for recumbent length in the four samples. The major altitude differences in rates of growth appear in the first month when lowland infants' grow more rapidly, an observation that runs counter to first-month weight gains which favor the highland infants. Altitude differences in growth of triceps and subscapular skinfold thicknesses are presented in Table 3 and Figures 5 and 6. High altitude infants are clearly fatter at all ages beyond three months.

While the results presented thus far constitute actual means and standard deviations, they do not represent an unbiased view of the growth differences between subgroups at any given age. In order to test whether the dif-

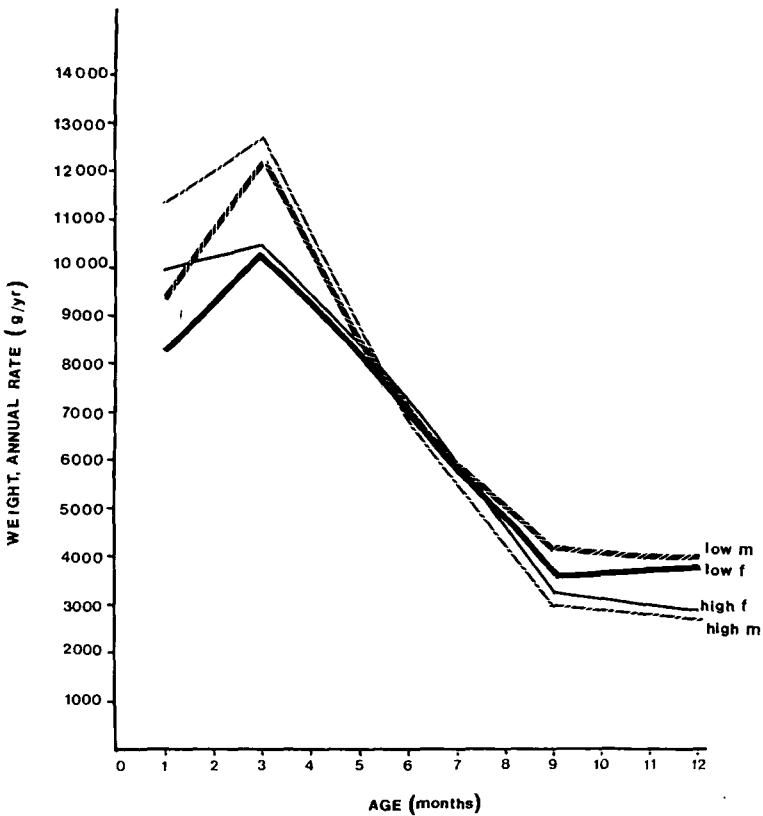


Fig. 2. Velocity growth curves of weight for high and low altitude Bolivian infants.

TABLE 2. Mean recumbent length and recumbent length increments during the first year in Bolivian high altitude (La Paz) and low altitude (Santa Cruz) infants^a

Age (months)	Males		Females	
	La Paz n = 16	Santa Cruz n = 18	La Paz n = 24	Santa Cruz n = 21
	Recumbent length (cm)			
Birth	49.1 ± 1.60	50.2 ± 2.05	48.2 ± 1.65	49.5 ± 1.70
1	52.2 ± 1.86	54.7 ± 1.94	52.1 ± 1.61	53.7 ± 1.84
3	60.0 ± 2.22	62.6 ± 1.80	58.9 ± 2.01	60.4 ± 2.02
6	64.8 ± 2.56	68.0 ± 2.77	63.3 ± 2.30	66.5 ± 2.16
9	68.8 ± 1.93	71.5 ± 2.30	67.9 ± 2.56	69.7 ± 2.49
12	73.2 ± 2.08	74.5 ± 2.61	72.3 ± 2.32	73.2 ± 1.99
	Recumbent length increments (cm/yr)			
Birth	39.0 ± 16.21	55.0 ± 15.71	49.3 ± 10.54	52.8 ± 13.50
1	45.0 ± 7.21	46.9 ± 9.20	39.8 ± 7.48	39.4 ± 10.27
1-3	20.0 ± 7.62	21.3 ± 7.31	17.3 ± 5.68	23.4 ± 5.81
3-6	15.7 ± 5.65	13.8 ± 4.83	19.7 ± 9.81	12.7 ± 6.68
6-9	16.9 ± 3.84	11.2 ± 5.33	16.5 ± 3.95	13.6 ± 4.28

^aMeans ± S.D.

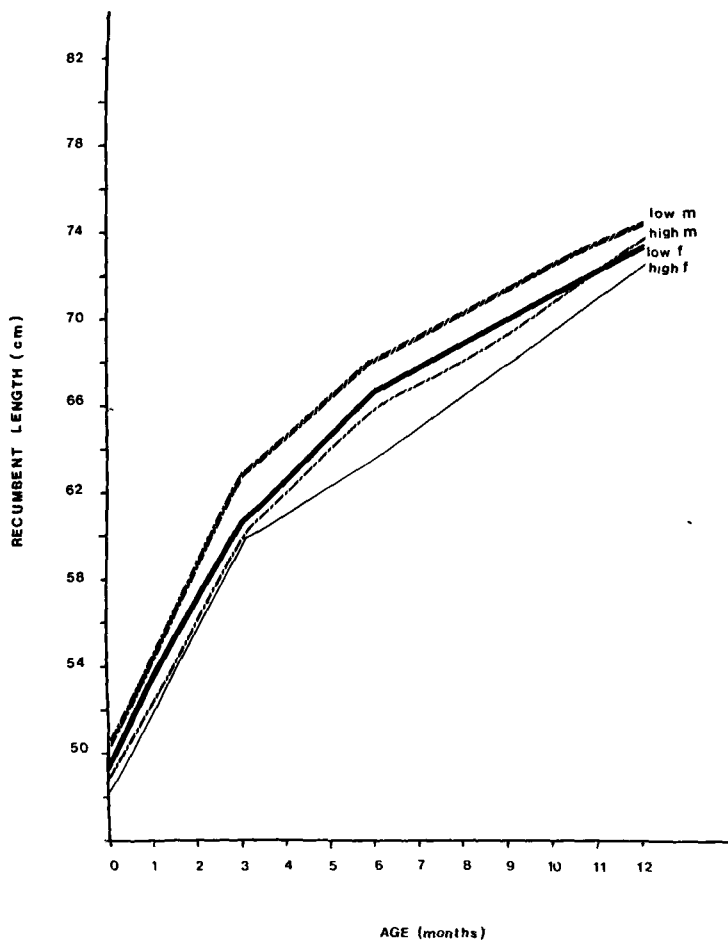


Fig. 3. Distance growth of recumbent length for high and low altitude Bolivian infants.

ferences in achieved growth between sexes and altitude groups are significant, it is important to recognize that size at any specific examination or age is related to some degree to the size of the child at previous examinations. Therefore, in order to test for statistical differences between groups at each age after birth, several analyses of covariance were performed in an effort to control for differences in previous growth. Tables 4 and 5 present a summary of the results of this analysis. The adjusted means for weight and crown-heel length are presented after controlling for covariation in several parameters. In Table 4, it can be seen under column A that when weight is compared between high and low altitude at each post-natal age after controlling for the covariation in weights at the previous examination and possible sex differences, the only age at which significant altitude differences occur is at birth and 12 months. Since birth weight is so different between the two groups, it was used as a sole covariate in the second analysis for which the adjusted means are presented in column B. The results are essentially the same as reported for the previous analysis, except that

weight differences at 12 months are no longer statistically significant. In order to control for variation in weight that is associated with variation in crown-heel length at the same age and weight at previous examinations, another analysis of covariance was performed. The results of this analysis are presented in column C, where the adjusted means at each age can be interpreted as "weight-for-length" or weight for a similar crown-heel length and a similar weight at the previous examination. Significant altitude differences persist in weight-for-length at birth and 12 months in favor of lower weight at high altitude. However, at 1 through 9 months, the high altitude infants tend to be heavier than the low altitude infants at a comparable length and previous exam weight, although the differences are only significant at 1 month.

It is noteworthy that sex differences are significant in the two-way analysis of variance model at three months for models that control for birth weight (column B) and present length and previous weight (column C) and at 9 months after birth weight is controlled (column B). In all models males are heavier than females;

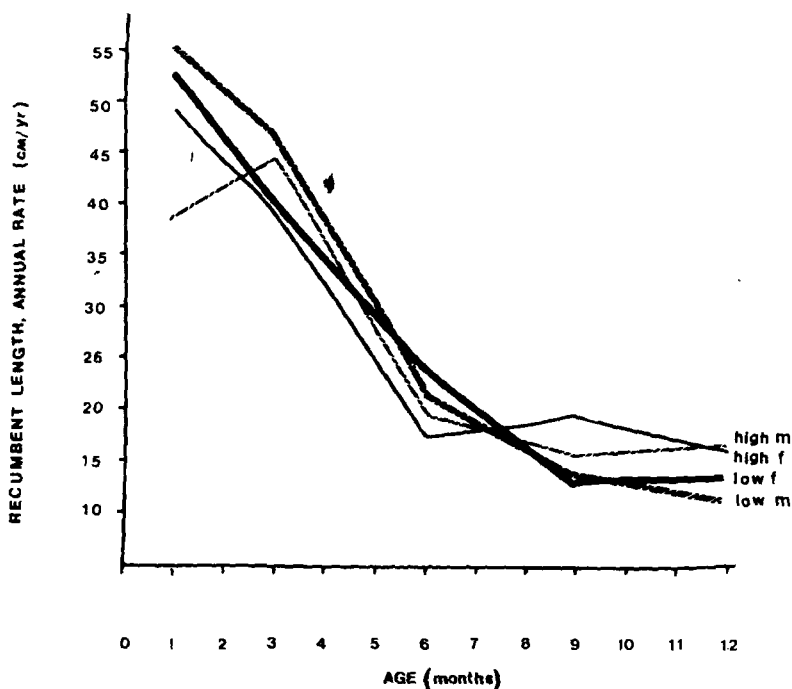


Fig. 4. Velocity growth curves of recumbent length for high and low altitude Bolivian infants.

TABLE 3. Mean triceps and subscapular skinfolds during the first year in Bolivian high altitude (La Paz) and low altitude (Santa Cruz) infants¹

Age (months)	Males		Females	
	La Paz n = 16	Santa Cruz n = 18	La Paz n = 24	Santa Cruz n = 21
	Triceps (mm)			
Birth	4.2 ± 0.63	3.8 ± 1.82	4.1 ± 0.70	3.8 ± 1.03
1	6.3 ± 1.83	6.9 ± 1.26	6.4 ± 1.35	7.0 ± 1.74
3	9.8 ± 2.04	9.7 ± 1.70	10.0 ± 2.25	9.3 ± 1.74
6	11.5 ± 1.37***	8.6 ± 2.20	11.9 ± 2.15***	9.2 ± 2.54
9	12.7 ± 2.09***	9.6 ± 2.82	12.6 ± 3.02***	9.1 ± 2.56
12	13.2 ± 2.31***	8.3 ± 2.44	14.0 ± 3.22***	8.1 ± 2.02
	Subscapular (mm)			
Birth	3.7 ± 0.70	3.7 ± 1.17	4.0 ± 0.79	3.7 ± 1.05
1	7.4 ± 2.85	6.5 ± 1.35	6.2 ± 1.64	6.6 ± 1.88
3	9.8 ± 2.01*	8.1 ± 1.32	9.6 ± 2.23*	8.1 ± 2.00
6	9.6 ± 1.37***	7.8 ± 1.47	10.3 ± 1.90***	8.0 ± 2.05
9	9.5 ± 2.13*	7.7 ± 1.70	10.3 ± 2.33**	8.1 ± 2.00
12	9.6 ± 2.29**	7.2 ± 1.40	11.4 ± 2.80***	7.4 ± 1.46

¹Means ± S.D.

Significance of altitude difference for each sex:

* = sig. 0.05.

** = sig. 0.01.

*** = sig. 0.001.

TABLE 4. Adjusted mean weights (g) for La Paz and Santa Cruz infants during the first year (sexes combined)

Age at exam	A Weight adjusted for weight at previous exam			B Weight adjusted for birth weight			C Weight adjusted for present length and weight at previous exam		
	La Paz	Santa Cruz	sig.	La Paz	Santa Cruz	sig.	La Paz	Santa Cruz	sig.
Birth	3012 ¹	3390 ¹	a	3012 ¹	3390 ¹	a	3115 ²	3284 ²	a
1 month	4010	3949		4010	3949		4079	3878	a
3 months	5942	5955	b	5958	5939	b	6043	5951	b
6 months	7732	7730		7744	7717	b	7860	7599	b
9 months	8529	8692		8523	8698	b	8622	8597	
12 months	9364	9648	a	9269	9745		9382	9629	a

¹Unadjusted.

²Adjusted for present length only.

a = Altitude difference significant at p < 0.05.

b = Sex difference significant at p < 0.05.

TABLE 5. Adjusted mean recumbent length (cm) for La Paz and Santa Cruz infants during the first year (sexes combined)

Age at exam	A Recumbent length adjusted for previous recumbent length			B Recumbent length adjusted for recumbent length at birth			C Recumbent length adjusted for birth weight		
	La Paz	Santa Cruz	sig.	La Paz	Santa Cruz	sig.	La Paz	Santa Cruz	sig.
Birth	48.6 ¹	49.8 ¹	a	48.6 ¹	49.8	b	49.1	49.2	a
1 month	52.6	53.6	a	52.6	53.6	a	52.5	53.7	a
3 months	60.1	60.6	b	59.7	61.0	a,b	59.8	61.0	a,b
6 months	64.8	66.3	a	64.3	66.7	a,b	64.2	66.8	a
9 months	69.5	69.2		68.7	70.1	a,b	68.6	70.2	a
12 months	73.6	72.9	a	72.9	73.5	b	72.8	73.6	

¹Unadjusted.

a = Altitude difference significant p < 0.05.

b = Sex difference significant at p < 0.05.

all of the adjusted means reported in Table 4 and 5 control for the sex differences that exist at each age. No significant statistical interactions were observed between altitude and sex.

When recumbent length is compared between high and low altitude infants after controlling for various covariates in Table 5, the pattern of altitude differences is somewhat different than that observed for weight. After controlling for recumbent length at the previous examination (column A), significant altitude differences in length can be observed at 1, 6 and, 12 months. While high altitude La Paz infants are shorter at the younger ages, they are longer at 12 months. Since recumbent length at birth is significantly smaller at high altitude, it was employed as a covariate to compute the adjusted means in column B. In this analysis, the high altitude infants are shorter than low altitude infants at all ages up to 9 months. A similar analysis was performed, ex-

cept with birthweight replacing recumbent length at birth as the covariate, and the results are presented in column C. If compared at the same birth weight, length is significantly smaller at high altitude for the ages between 1 and 9 months.

To test whether energy reserves, as measured by sum of triceps plus subscapular skinfolds, have an effect on weight gain and length gain, the data were subjected to analysis of covariance. In the resulting model, the sum of skinfold thicknesses at each visit served as a covariate which was held constant between groups while the altitude effect on growth rate during the subsequent interval was tested for statistical significance. The relationship between skinfold thickness at any one examination and subsequent growth was not significant at any age during the first year in either La Paz or Santa Cruz. Therefore, the altitude differences in growth rate presented in

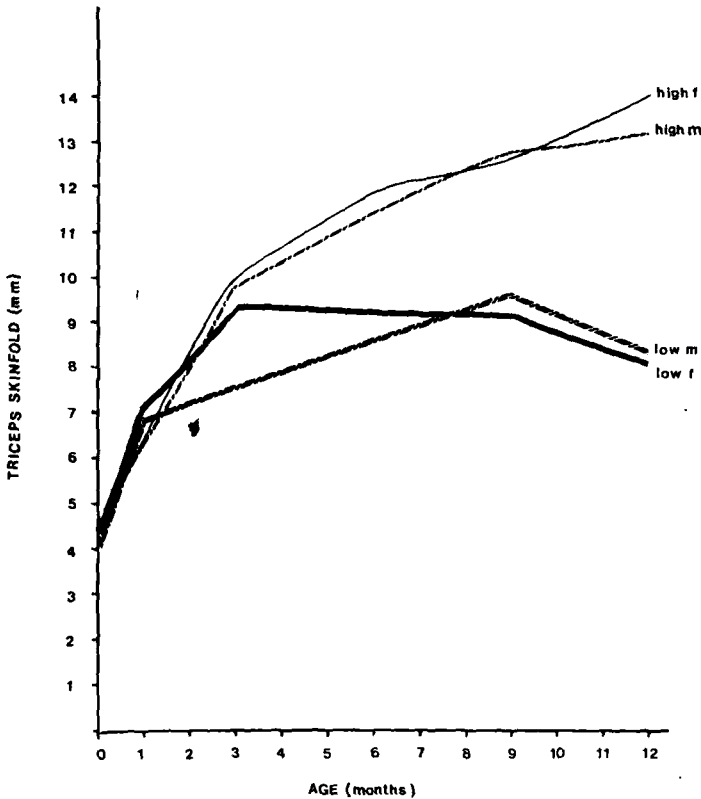


Fig. 5. Distance growth curve for triceps skinfold thickness in high and low altitude Bolivian infants.

Tables 1 and 2 were essentially unchanged after controlling for variation in adiposity.

DISCUSSION

The persistence of small size in healthy high altitude infants compared to low altitude infants confirms the findings from previous studies of infant growth at high altitude (Haas, 1976, 1981; Beall, 1976). However, when analyzed from a longitudinal perspective it appears that many of these altitude differences are not so striking. Specifically, the increments of growth in weight and recumbent length suggest very little altitude difference in growth rate. The achieved growth in weight and length at any given age is highly dependent upon size at the previous examination. When previous weights are controlled statistically, altitude differences in weight fail to be significant except at 12 months. The same type of statistical control for recumbent length at the previous

exam yields significant altitude differences at 1, 6, and 12 months. However, the interpretation of these trends is unclear since highland children tend to be shorter in the early months but taller by 12 months.

Further analyses reveal that much of the variation in size throughout the first year of life is related to size at birth. The impact of low birth weights at high altitude seem to be long lasting, since altitude differences in weight at any postnatal exam is reduced to non-significance if the La Paz and Santa Cruz infants are compared at similar birth weights.

Another example of the long term impact of variation in birth weight at high altitude was reported by Beall (1981). In this study of infant mortality risk relative to birth weight at high and low altitude in Peru, Beall concluded that a lower optimal birth weight exists at high altitude. This suggests that the consequences of being smaller at high altitude are not as

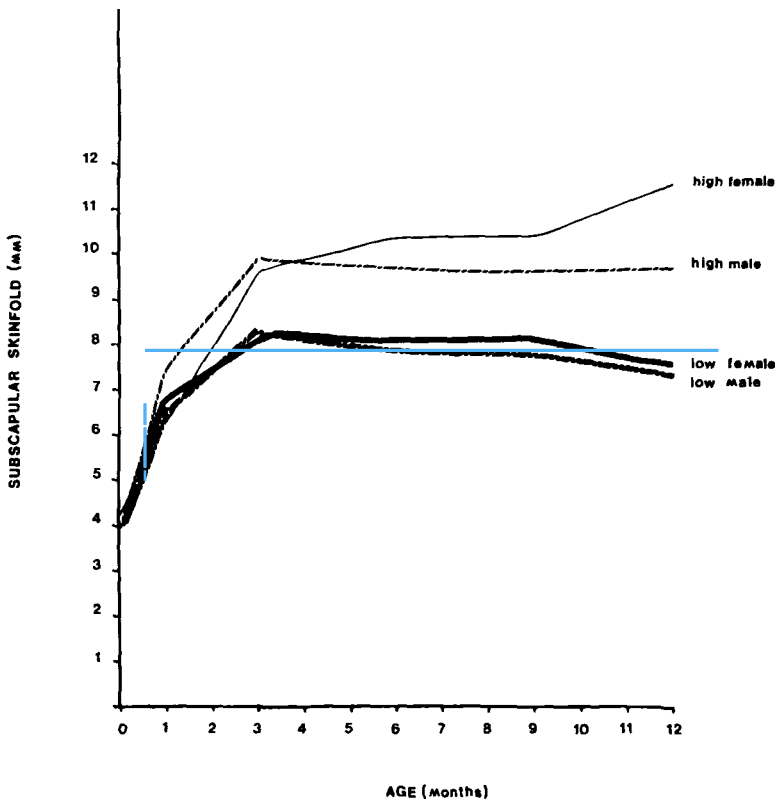


Fig. 6. Distance growth curve for subscapular skinfold thickness in high and low altitude Bolivian infants.

severe as being of a comparable weight at low altitude. The present study, however, suggests that postnatal growth of healthy infants is no different between high and low altitudes if birth weights are similar. Both studies suffer from sampling bias that precludes speculation as to the reason for this apparent discrepancy in the long term effects of variation in birth weight at high altitude. Beall's study deals only with hospital births and only infant deaths that are reported in official registries. The present study also deals only with hospital births and is not adequately represented by low birth weight infants to evaluate subsequent growth in those infants who are also at high risk of infant death, irrespective of altitude.

While birth weight differences between altitudes appear to account for much of the differences in subsequent growth of body weight, the same cannot be said for recumbent length. Birth lengths also differ between altitude groups, but do not influence the subsequent altitude differences in recumbent length.

In general, these patterns suggest a greater effect of altitude on linear growth rather than on body mass. Postnatal weight measurements adjusted for length support this supposition, since highland La Paz infants actually have a greater, but generally nonsignificant, weight when compared to low altitude infants of the same length up to 9 months of age. A similar pattern has been reported for healthy, well-nourished Peruvian infants at high altitude where the mean weight-for-height was at about the 90th percentile and mean recumbent length was at the 10th percentile of the U.S. reference standards (Haas, 1981).

In the present study, it appears that the excess weight-for-height might be associated with increased fatness at high altitude as indicated by subscapular and triceps skinfolds that are significantly greater than low altitude values after 3 to 6 months of age. As with weight and length, altitude differences after 6 months in skinfolds are diminished if the appropriate skinfold measurement at the previous exam is held constant between altitude groups (analysis not shown). Nonetheless, the persistence through the first year of a pattern of greater adiposity with reduced linear growth at high altitude is an interesting one, which has

not been previously reported. In fact, the opposite trend of reduced adiposity at high altitude has been reported by Haas (1976) for Peruvian infants.

The altitude differences in skinfold measurements are not presently understood, although several explanations are possible. A systematic measurement error is unlikely since a 12 month quality control check showed interobserver random error and bias to be insignificant.

Several possible explanations relate to dietary differences in the two groups. If one assumes that adiposity reflects energy reserves in the form of fat, then it might be inferred that the La Paz infants are better nourished than the lowland Santa Cruz infants of the current study or the lowland and highland Peruvian infants of the earlier study by Haas (1976). Infant feeding patterns do distinguish the present study groups in that La Paz infants are weaned from the breast at a later age (median age of total severance, 12 months) than Santa Cruz infants (median age 7.5 months) and the relationship between feeding practices and growth must await subsequent analysis.

Another aspect of diet that is often overlooked but may be relevant here is water intake. Local pediatricians acknowledge that infants in Santa Cruz, a semitropical environment, generally ingest more water either in the process of formula preparation or as an unmixed supplement. Such practices may lead to food intakes of lower caloric density in the lowland infants.

It could be hypothesized that excess fat gain is a result of allocation of energy to maintain an insulative adipose layer for protection against high altitude cold. However, a review of the literature on human thermoregulation did not uncover evidence for this mechanism operating in infants.

Some of the altitude differences in adipose thickness are probably related to the reduced body surface area at high altitude over which the subcutaneous layer of fat is distributed. La Paz infants with their reduced length and body weight have less surface area. If the same absolute amount of adipose fat were observed in both samples, the infants with the lesser surface area would have deposited fat in layers of greater thickness. Calculations of body surface

area from the Dubois equation, $SA(\text{cm}^2) = \text{weight (kg)}^{0.425} \times \text{length (cm)}^{0.725} \times 0.007184$, were used in conjunction with the average skinfold thickness over six sites to estimate the volume of adipose tissue in the two samples. Computations based on these crude estimates indicate that La Paz infants from 6 to 12 months of age have approximately 25% more adipose tissue than is necessary to maintain a fat volume equal to the Santa Cruz infants of the same ages. Therefore, even accounting for their reduced surface area, the La Paz infants still appear to carry an excess of adipose fat when compared to Santa Cruz infants.

Finally, it is possible that hypoxic conditions may affect growth at the cellular level. In vitro studies have shown that tissues incubated under hypoxic conditions show inhibition of skeletal cell growth and protein synthesis, while cell lipid/cell protein ratios and cellular free fatty acid content increase (Kittlick, 1977; Shaw and Basset, 1976; Lipton, 1977; Gordon et al, 1977). Hunter and Clegg (1973a, b) have shown reduced growth in long bones and caudal vertebrae in experimental animals under hypoxic stress. One could hypothesize that increased fatness at high altitude results from suppressed cellular growth which leads to an excess energy being diverted from cell division and maintenance to fat reserves. Of course the conditions of adequate to excessive energy intakes would be necessary to support excess fatness and such conditions are unlikely to occur in the general Bolivian population, of which the current sample is hardly representative.

CONCLUSION

The results of the present study indicate that the altitude difference in achieved weight and linear growth of healthy, well-nourished infants through the first year of life can be accounted for, in part, by the initial differences seen at birth. Linear growth appears to be affected by high altitude early in the postnatal period while weight gain is not.

High altitude infants also accumulate more subcutaneous fat after the third month. However, the mechanism for this difference in adiposity is not known.

Clearly more research is needed to determine the ideal body composition of the high altitude infants in the Andes. This future research

should address such issues as the consequences of infantile obesity in terms of later growth, the role of adipose tissue in thermal regulation during infancy and early childhood, and the role of changing infant feeding patterns on the development of muscular, skeletal and adipose tissue at high altitude. In addition to these human studies, further experimental studies using appropriate animal models should address the issues of biological mechanisms regulating cellular and tissue growth at high altitude under different dietary regimes.

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