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The importance of socioeconomic and nutritional conditions rather than altitude on the physical growth of prepubertal Andean highland boys

P. Obert†, N. Fellmann†, G. Falgairette†, M. Bedu‡, E. Van Praagh†, H. Kemper§, B. Post§, H. Spielvogel¶, V. Tellez¶, A. Qintela§ and J. Coudert†

†Laboratoire de Physiologie de la Performance Motrice, Aubière, France
‡Laboratoire de Physiologie-Biologie du Sport, Clermont-Ferrand, France
§Faculty of Human Movement Sciences, Amsterdam, The Netherlands
¶ORSTOM/Instituto Boliviano de Biologia de Altura, La Paz, Bolivia

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Summary. The aim of this work was to study the effect of hypoxic stress on the physical growth of prepubertal Bolivian boys (10–11·5 years of age) of the same socioeconomic and nutritional conditions. The subjects consisted of 143 boys living in La Paz (altitude 3600 m, $n = 67$) and Santa Cruz de la Sierra (altitude 420 m, $n = 76$). Among the boys studied at high altitude, 23 were from a high socioeconomic background (HA1) and 44 from a low socioeconomic background (HA2). The group studied at low altitude consisted of 47 boys from a high socioeconomic background (LA1) and 29 from a low socioeconomic background (LA2). A scientific evaluation of the nutritional status of the boys was realized from specific anthropometric characteristics (height, body weight, upper arm muscle circumference, body fat mass and body mass index) and haematological (haematocrit, haemoglobin, serum iron, serum ferritin, red cell protoporphyrin, transferrin saturation) and biochemical (total serum protein, albumin and prealbumin) parameters. At high as at low altitudes, the biometric characteristics of boys from a low socioeconomic background were significantly lower than those of boys from a high socioeconomic background. The physical growth of HA2 and LA2 boys was delayed by approximately 2 years. All the boys had biochemical and haematological parameters within the normal range. Boys from a low socioeconomic background were considered as marginally undernourished and those from a high socioeconomic background as well-nourished. Within the same socioeconomic class there was no nutritional difference between highland and lowland boys. Similarly, and this is the most important feature of this study, there was no difference for the overall biometric characteristics between highland and lowland boys of the same socioeconomic and nutritional status. Therefore, it appears that when socioeconomic and nutritional conditions are taken into account, there is no effect of hypoxic stress on the physical growth of prepubertal Andean highland boys.

1. Introduction

Numerous studies have been realized in the Andes on the effect of altitude on human growth. Nearly all of them have reported that the growth in height and weight of highland boys is delayed compared to sea-level norms (Frisancho and Baker 1970, Beall, Baker, Baker and Haas 1977, Frisancho 1978, Mueller, Schull, Schull, Soto and Rothhammer 1978, Stinson 1980, Schutte, Lilljeqvist and Johnson 1983; Greksa, Spielvogel, Paredes-Fernandez, Paz-Zamora and Caceres 1984). The smaller size of highland children appears to be due to a smaller size at birth (Haas, Moreno-Black, Frongillo, Pabon, Pareja, Barnegaray and Hurtado 1982) and a slow growth period (Frisancho and Baker, 1970, Frisancho 1978). Several studies have reported that this growth retardation at high altitude is principally the result of hypoxic stress (Frisancho and Baker 1970, Frisancho 1978, Mueller *et al.* 1978, Stinson 1980). Other investigations have, however, suggested that other factors such as genetic, nutritional or socioeconomic factors could also be involved (Hoff 1974, Malina 1974, Frisancho, Borkan and Klayman 1975; Clegg, Pawson, Ashton and Flinn 1972, Stinson 1982, Spielvogel and Caceres 1985, Leonard 1989). The lack of a control population of similar ancestry and socioeconomic and nutritional status at low altitude did not allow any conclusions on the effect of hypoxic stress alone. The predominance of the effect of nutritional stress is strongly supported by the fact that the physical growth pattern usually described in studies on Andean highland children is similar to that of undernourished lowland children (Manocha 1972, Béhar 1981, Buschang and Malina 1983, Spurr, Reina and Barac-Nieto 1983, Martorell 1985).

The aim of this work was to study the effect of hypoxic stress on the physical growth of prepubertal Bolivian boys by means of the comparison of lowland and highland boys matched for ethnic origin and nutritional and socioeconomic factors.

2. Method

The study was conducted in Bolivia. This Latin American country is considered to be at a middle level of development. The investigations were carried out at high altitude (HA) in La Paz (altitude 3600 m) and at low altitude (LA) in Santa Cruz de la Sierra (altitude 420 m). In common with other Latin American cities, La Paz and Santa Cruz de la Sierra have in the past 30 years undergone a rapid growth due, in part, to an influx of population from rural areas. The result has been the development of poor neighbourhoods ('barrios') which have sprung up in successive layers around the periphery of each city. The reduced socioeconomic and hygienic conditions of these 'barrios' result in a high incidence of undernutrition among the children.

The subjects were studied at HA in the Instituto Boliviano de Biologia de Altura (IBBA) and at LA in the Centro Nacional de Enfermades Tropicales (CENETROP).

2.1. Subjects

The subjects consisted of 143 prepubertal boys. After explanation of the purposes of the study, and what was expected of the children, written consent was obtained in each case. Every boy underwent a thorough physical examination and was questioned about his medical history by a team paediatrician. The children ($n = 3$) who were not in good health were referred to a physician or a medical clinic for further care. Age was recorded to the nearest month, and only boys of 10–11·5 years old were recruited. The boys' exact ages were checked by using their official birth certificates. The sexual maturation was determined as described by Tanner (1962) and only prepubertal boys (Tanner stage I and orchidometry < 6 ml) were selected. Moreover, boys with obesity ($n = 11$) and anaemia ($n = 14$) of parasitic origin were excluded. In addition, a determination of the ethnic origin of the boys was realized from an analysis of paternal and maternal surnames (Schull and Rothmaner 1977, Ferrell, Bertin and Barton 1980). At high as well as at low altitudes, boys of European ancestry who were recent dwellers were suppressed. The results of the analysis showed that boys of HA1 and LA1 groups were exclusively composed of boys of Spanish ancestry (of families who have a long history of residence in Bolivia) while the HA2 and LA2 groups were composed of boys of both Spanish and Amerindian (nearly essentially Aymara) ancestry. Such an analysis presumably underestimated the proportion of boys of Amerindian ancestry in the two groups of low socioeconomic status. In fact, some Aymara families, in order to have better social conditions, changed their Aymara surnames into Spanish surnames (Mueller *et al.* 1978). However, the underestimation is presumably the same at high and low altitudes. Thus, one can reasonably consider that HA1 and LA1 boys are of the same genetic background, and that there are minor genetic differences between HA2 and LA2 boys.

At both high and low altitudes the children were grouped according to socioeconomic status. They were judged to belong to the lower or to the upper socioeconomic level, from the location and kind of dwelling, and the type of school they attended (private or free public schools). Children from a high socioeconomic background attended a private school and mostly lived in the centre of La Paz and Santa Cruz de la Sierra (highland boys, $n=23$, HA1; lowland boys, $n=47$, LA1). Children from a low socioeconomic background attended a public school and lived in the poor suburbs ('barrios') of the town where there were very poor levels of hygiene and a high incidence of malnutrition among the children (highland boys, $n=44$, HA2; lowland boys, $n=29$, LA2).

All the boys presented here were born and raised at the place where they were studied.

2.1.1. Anthropometric characteristics. The anthropometric characteristics were used to assess the past and present nutritional status of the boys. They included height (H), body weight (BW) and upper arm circumference. Skinfold thicknesses (biceps, triceps, subscapular and suprailiac) were determined with a Harpenden skinfold caliper. The equation of Durnin and Rahaman (1967) was used to determine the percentage of body fat mass. Lean body mass (LBM) was determined from weight and body fat mass. An index of body mass (BW/H^2) was calculated for each boy. Upper arm muscle circumference (UAMC) was calculated following the method of Jelliffe (1966).

2.1.2. Haematological and biochemical analysis. The current nutritional status of HA1, HA2, LA1 and LA2 boys was also assessed from haematological and biochemical analyses. They were realized from a venous blood sample (10 ml) which was drawn from the antecubital vein. Samples were taken between 9 and 12 a.m.

The iron status was assessed by measuring the concentrations in the plasma of the following parameters: haematocrit (microhaematocrit method), haemoglobin (Drabkin method), serum iron (spectrophotometry), serum ferritin (ELISSA system), red cell protoporphyrin (haematofluorimetry), total iron binding capacity (TIBC, colorimetric method) and transferrin saturation (serum iron: TIBC).

The other parameters included total serum protein (colorimetric method), albumin (radial immunodiffusion method) and prealbumin (turbidimetry).

2.1.3. Statistical analyses. The statistical analyses were realized on a Macintosh Classic computer. The data are expressed as means and standard deviations. The effects of socioeconomic status (SE) and altitude (A) were tested for by using two-way analysis of variance (ANOVA, Stat View SE+graphics package program). Statistical significance was chosen as $p<0{\cdot}05$.

3. Results

3.1. Anthropometric characteristics

The biometric characteristics of the boys are presented in table 1. For overall body dimensions there was a highly significant effect of socioeconomic status ($p<0{\cdot}001$) but no effect of altitude and no statistically significant interactions between A and SE except for UAMC.

Table 1. Biometric characteristics of HA1, HA2, LA1 and LA2 boys.

	HA		LA		Two-way ANOVA probability
	SE+ HA1 ($n=23$)	SE− HA2 ($n=44$)	SE+ LA1 ($n=47$)	SE− LA2 ($n=29$)	
Height (cm)	140 ± 7	131 ± 5	141 ± 5	132 ± 6	A:NS, SE: <0.001 A × SE:n.s.
Weight (kg)	37 ± 9	30 ± 4	36 ± 5	31 ± 4	A:NS, SE: <0.001 A × SE:n.s.
BFM (%)	21.3 ± 5.8	16.5 ± 3.3	21.3 ± 4.5	17.8 ± 3.6	A:NS, SE: <0.001 A × SE:n.s.
LBM (kg)	29 ± 5	25 ± 2	28 ± 3	25 ± 3	A:NS, SE: <0.001 A × SE:n.s.
UAMC (cm)	19.5 ± 2.2	17.4 ± 1.2	18.7 ± 1.3	17.8 ± 1.3	A:NS, SE: <0.001 A × SE: <0.05
BMI (kg cm^{-2})	18.6 ± 2.9	17.2 ± 1.7	17.9 ± 1.8	17.6 ± 2.2	A:NS, SE: <0.05 A × SE:n.s.

Values are means ± SD; n = number of subjects; HA, high altitude; LA, low altitude; SE+, high socioeconomic status; SE−, low socioeconomic status; BFM, body fat mass; LBM, lean body mass; UAMC, upper arm muscle circumference; BMI, body mass index; ANOVA, analysis of variance; A, altitude; SE, socioeconomic status; n.s., not statistically significant.

Table 2. Haematological and biochemical parameters.

	HA		LA		Two-way ANOVA probability
	SE+ HA1 ($n=23$)	SE− HA2 ($n=44$)	SE+ LA1 ($n=47$)	SE− LA2 ($n=29$)	
Haematocrit (%)	45.9 ± 2.8	45.7 ± 2.1	42.4 ± 2.3	39.9 ± 2.2	A: <0.001, SE: <0.05 A × SE:n.s.
Serum iron (μg l^{-1})	1660 ± 700	1340 ± 320	1540 ± 520	1060 ± 330	A: <0.05, SE: <0.001 A × SE:n.s.
Hb (g l^{-1})	153 ± 8	150 ± 9	135 ± 9	128 ± 12	A: <0.001, SE: <0.05 A × SE:n.s.
Ferritin (μg l^{-1})	77 ± 49	52 ± 30	58 ± 41	33 ± 18	A: <0.05, SE: <0.01 A × SE:n.s.
ST (%)	39 ± 14	29 ± 6	30 ± 9	25 ± 7	A: <0.001, SE: <0.001 A × SE:n.s.
RCP (μg l^{-1})	271 ± 52	287 ± 80	319 ± 72	326 ± 82	A: <0.05, SE:n.s. A × SE:n.s.
Total protein (g l^{-1})	76 ± 6	75 ± 7	75 ± 4	79 ± 4	A:NS, SE:n.s. A × SE:n.s.
Albumin (g l^{-1})	48 ± 3	48 ± 4	46 ± 4	45 ± 4	A: <0.05, SE:n.s. A × SE:n.s.
Prealbumin (mg l^{-1})	238 ± 50	195 ± 63	235 ± 37	201 ± 35	A:NS, SE: <0.001 A × SE:n.s.

Values are means ± SD; n = number of subjects; HA, high altitude; LA, low altitude; SE+, high socioeconomic status; SE−, low socioeconomic status; Hb, haemoglobin; ST, saturation transferrin; RCP, red cell protoporphyrin; ANOVA, analysis of variance; A, altitude; SE, socioeconomic status; n.s., not statistically significant.

3.2. *Haematological and biochemical analyses*

The haematological and biochemical parameters are presented in table 2. Haematocrit and haemoglobin concentrations followed a similar pattern with a highly significant effect of altitude ($p < 0 \cdot 001$), a moderate but significant effect of socioeconomic status ($p < 0 \cdot 05$) and no significant interactions between A and SE. For serum iron and ferritin concentrations there were a highly significant effect of socioeconomic status ($p < 0 \cdot 001$), a moderate effect of altitude ($p < 0 \cdot 05$) and no significant interactions between A and SE. Only altitude has a significant effect ($p < 0 \cdot 05$) on red cell protoporphyrin concentrations. For transferrin saturation there were highly significant effects of socioeconomic status ($p < 0 \cdot 001$) and altitude ($p < 0 \cdot 001$) but no significant interactions between A and SE.

Neither altitude nor socioeconomic status have an effect on serum total protein concentrations. For albumin concentrations there was a moderate but statistically significant effect of altitude ($p < 0 \cdot 05$) but no effect of socioeconomic status and no significant interactions between A and SE. Finally, for prealbumin concentrations there was a highly significant effect of socioeconomic status ($p < 0 \cdot 001$) but no effect of altitude and no interactions between these two factors.

4. Discussion

The most important feature of the present study is that altitude has no effect on the physical growth of prepubertal Andean boys when socioeconomic and nutritional status are taken into account (table 1). Impaired growth traditionally reported in prepubertal Andean highland boys, as is the case for HA2 in this study, is certainly the result of reduced socioeconomic and nutritional conditions, with hypoxia playing a negligible role.

The evaluation of the nutritional status of boys was realized from specific anthropometric characteristics and haematological and biochemical parameters. Our anthropometric characteristics show that HA1 and LA1 boys are well-nourished and HA2 and LA2 boys are marginally undernourished. The biometric characteristics are those commonly used in nutritional anthropometry (Jelliffe 1966, Waterlow 1972, 1973; Eveleth and Tanner 1976). Height and weight are among the most used criteria. Several classifications have been realized from these parameters in order to evaluate the nutritional status of a child (Gomez *et al.* 1956, Waterlow 1972). The principle of these classifications is to compare the weight and height of the child with a standard reference established for well-nourished children of the same age. The well-known criteria, height for age, give an indication of impaired growth and are a reflection of past nutritional status (Waterlow 1972, 1973). Measurements derived from height and weight such as weight/height or weight/height^{2}have also been widely used (Visweswara and Singh 1970, Waterlow 1973, Cole, Donnet and Standfield 1981). These citeria are an index of alteration in body proportions and composition and are a reflection of current nutritional status (Visweswara and Singh 1970, Cole *et al.* 1981).

The statistical analysis realized in this study on weight and height showed that, at both high and low altitudes, children from a high socioeconomic background (HA1, LA1) were significantly ($p < 0 \cdot 001$) taller and heavier and had a higher ($p < 0 \cdot 05$) body mass index (BMI = weight/height^2) than those from low socioeconomic background (HA2, LA2). Comparison of weight and height of HA1, LA1, HA2 and LA2 boys with the NHCS reference standard (Hamill, Drizd, Johnson, Reed, Roche and Moore 1979) and Latin American norms (Johnston, Borden and McVean 1973) showed that HA1 and LA1 boys were within the normal range for well-nourished boys of the same age. HA2 and LA2 boys were, however, much smaller and lighter than these two standard references (height 10th percentile and weight 25th percentile as regards the NHCS reference standard). The physical growth of these boys was delayed by approximately 2 years. In spite of socioeconomic effect ($p < 0 \cdot 05$), the BMI values of all the boys were in the normal range for well-to-do boys (Sempé 1979, Rolando-Cachera, Cole, Sempé, Tichet, Rossignol and Charraud 1991). Studies in which children were found to have low weight and height for age but normal weight for height have concluded that the physical growth retardation of the children was the result of past malnutrition, which occurred primarily during prime infancy (Béhar 1981, Spurr *et al.* 1983, Martorell 1985, Trowbridge, Marks, Lopez de Romana, Madrid, Boutton and Klein 1987). This should probably be the case in the present study for HA2 and LA2 boys. Upper arm muscle circumference and skinfold thicknesses at selected sites (biceps, triceps, subscapular and suprailiac) are also commonly used in nutritional anthropometry because they reflect protein and calorie reserves (Jelliffe 1966, Jelliffe and Jelliffe 1969, Frisancho and Garn 1971). Numerous studies have shown in children that these reserves are depressed in the case of protein–calorie restriction (Jelliffe and Jelliffe 1969, Frisancho and Garn 1971; Gurney, Jelliffe and Neill 1972). In the present study, at both high and low altitudes, boys of high socioeconomic status had a significantly ($p < 0 \cdot 001$) higher upper-arm muscle circumference and body fat mass (calculated from four skinfold thicknesses) than those of low socioeconomic status. In spite of these differences the upper arm muscle circumference and body fat mass values of HA1, LA1, HA2 and LA2 boys were found to be within the normal range for well-nourished boys of the same age (Sempé 1979, Frisancho 1981). Nevertheless, these results indicated that the diet between groups of high and low socioeconomic status is different. Indeed, dietary information in boys of this study was obtained by Post (Post, Kemper, Lujan, Parent and Coudert 1992). These authors showed that mean energy and nutrient (protein, fat) intake were marginal in boys from low socioeconomic backgrounds. It therefore appears that HA2 and LA2 boys are chronically marginally undernourished.

Iron status was assessed in this study by means of specific parameters (Bainton and Finch 1964, Cook, Finch and Smith 1976, Sauberlich 1983). There was a moderate but significant ($p < 0 \cdot 05$) effect of socioeconomic status on haematocrit and haemoglobin concentrations. In spite of this, haematocrit and haemoglobin values of highland (HA1, HA2) and lowland (LA1, LA2) boys were within the normal range for well-nourished children of the same age studied at high altitude (Wittembury and Monge 1972, International Nutritional Anemia Consultative Group 1981) and low altitude (Viteri, de Tuna and Guzman 1972, Dallman and Siimes 1979, Garn, Ryan and Owen 1981), respectively. There was also a significant effect of altitude ($p < 0 \cdot 001$) on these two parameters. This is in accordance with previous studies which reported greater values for haemoglobin and haematocrit in highland boys than in their lowland counterparts (Favra, Ramas, Reyrafarje, English, Finne and Finch 1969; International Nutritional Anemia Consultative Group 1981). This phenomenon is the result of an increased red cell production (polycythaemia) due to hypoxic stress. A significant effect of socioeconomic status ($p < 0 \cdot 01$) was found for all the other haematological parameters except red cell production (RCP). Despite this, all the boys had values for serum iron, ferritin, RCP concentrations and ST similar to those reported for well-nourished children (Geigy 1963, Viteri *et al.* 1972, Koerper and Dallman 1977, Deinard, Schwartz and Yip 1983, Palazzari, Matiniak and Schulz 1986). There was therefore no incidence of iron deficiency in any of the four groups studied.

Total protein, albumin and prealbumin concentrations have been traditionally used as indicators of protein–energy malnutrition. In spite of the effects of altitude (albumin:$p < 0 \cdot 05$) or socioeconomic status (prealbumin:$p < 0 \cdot 001$), values for these parameters were in each group similar to those reported for well-to-do children (Linhares, Round and Jones 1986, Mahu, Valteau, Suquet, Meskens, Saly, Lebas, Isautier, Gerard, Caillens, Cristides, Potier de Courcy, Galacteros and Turquet, 1988). There was therefore no severe protein–energy deficiency in the present study. This is in accordance with a study realized in marginally undernourished Brazilian boys (Desai, Waddell, Dutra, Dutra de Oliveira, Duarte, Robazzi, Cevallos Romero, Desai, Vichi, Bradfield and Dutra de Oliveira, 1984).

To conclude, it appears that when socioeconomic and nutritional conditions are taken into account, there is no effect of hypoxic stress on the physical growth of prepubertal Andean highland boys. Impaired growth previously reported in several studies on prepubertal Andean highland boys is therefore primarily the result of reduced socioeconomic and nutritional conditions, with hypoxia playing a negligible role. However, further investigations in older subjects would be necessary to validate this statement during the entire growth period.

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Address for correspondence: Pr Jean Coudert, Laboratoire de Physiologie-Biologie du Sport, Faculté de Médecine, place H. Dunant, BP 38-63001, Clermont-Ferrand, France.

Zussamenfassung. Ziel der vorliegenden Untersuchung war es, die Auswirkungen der chronischen Höhen-Hypoxie auf das Wachstum von bolivianischen Jungen in der Vorpubertät (10 bis, 11·5 Jahre alt), die unter denselben sozio-ökonomischen und ernährungsmäßigen Bedingungen leben, zu erforschen. Von den 143 untersuchten Kindern lebten 67 in La Paz (3600 m N.N.) und 76 in Santa Cruz de la Sierra (420 m N.N.). Von den Hochlandbewohnern gehörten 23 einer sozial höher stehenden Schicht an, 44 der 'Unterschicht'. Bei den Flachlandbewohnern kamen 47 Jungen aus besseren Verhältnissen, 29 aus der 'Unterschicht'. Der Ernährungszustand der Kinder wurde aufgrund folgender Untersuchungskriterien bewertet: spezifisch antropometrische Parameter waren Körpergröße und -gewicht, Umfang der Oberarmmuskulatur, Fettmasse sowie Körpermassen-Index; also hämatologische Parameter galten Hämatokrit, Hämoglobin, Eisen- und Ferritin-Serum, Rotzellen-Protoporphyrin sowie Transferrin-Sättigung, als biochemische Werte Gesamt-Proteinserum, Albumin und Präalbumin. Die Kinder der Unterschicht, sowohl im Hoch- als auch im Flachland, zeigten bezüglich der biometrischen

Eigenschaften in signifikanter Weise niedrigere Werte als die der sozial höheren Schicht. Die Jungen mit einer sozial schwächeren Herkunft waren denen der höheren Schicht um ungefähr zwei Jahre im Wachstum hinterher. Bei allen untersuchten Personen lagen die biochemischen und hämatologischen Parameter im Normalbereich. Generall konnten die Kinder der Unterschicht als unterernährt, die aus besseren Verhältnissen als gut ernährt bezeichnet werden. Es bestand ferner kein Unterschied in der Ernährung zwischen Hoch- und Flachlandbewohnern bei gleicher sozialer Herkunft. Ebenso - und das erscheint uns das wichtigste Ergebnis der Untersuchung - zeigten sich keine Differenzen bei allen biometrischen Werten zwischen Hochland- und Flachlandkindern bei gleichem sozialen Status und gleichen Ernährungsbedingungen. Berücksichtigt man also die sozio-ökonomischen und ernährungsmäßigen Bedingungen, so ergibt die Untersuchung, daß sich das Phänomen der Höhenhypoxie anscheinend in keiner Weise auf das Wachstum der Andenkinder im Vorpubertätsstadium auswirkt.

Résumé. L'objet de ce travail est d'étudier l'influence de l'hypoxie chronique sur la croissance d'enfants Boliviens prépubères (10–11·5 ans) présentant le même statut socio-économique et nutritionnel. La population de l'étude est composée de 143 garçons vivant à La Paz (altitude 3600 m, n = 67) et Santa Cruz de la Sierra (altitude 420 m, n = 76). A haute altitude, 23 garçons sont issus d'un milieu socio-économique élevé (HA1) et 44 d'un milieu socio-économique bas (HA2). La population étudiée à basse altitude est composée de 47 garçons issus d'un milieu favorisé (BA1) et 29 d'un milieu défavorisé (BA2). Une évaluation de l'état nutritionnel de chaque sujet a été réalisée à partir de paramètres biométriques, hématologiques et biochimiques spécifiques. A haute comme à basse altitude, les caractéristiques anthropomètriques des enfants issus d'un milieu défavorisé sont inférieures à celles des enfants issus d'un milieu favorisé. Les enfants des groupes HA2 et BA2 présentent un retard de croissance d'environ 2 ans. Les caractéristiques hématologiques et biochimiques de l'ensemble des sujets se situent dans les valeurs normales définies pour des enfants sains de même âge. Les enfants originaires d'un milieu socio-économique bas sont considérés comme marginalement dénutris et ceux originaires d'un milieu socio-économique élevé comme bien nourris. Au sein d'une même classe socio-économique, il n'existe pas de différence nutritionnelle entre les enfants natifs de HA et BA. De même, et ceci constitue le résultat le plus important de ce travail, il n'existe pas de différence entre les caractéristiques biométriques des enfants de HA et BA présentant le même statut socio-économique et nutritionnel. Par conséquent, il apparaît que lorsque l'on prend en compte les facteurs socio-économiques et nutritionnels, il n'existe pas d'effet de l'hypoxie chronique sur la croissance d'enfants prépubères originaires des Andes.