

Symposium Paper

Relative Leg Length as a Biological Marker to Trace the Developmental History of Individuals and Populations: Growth Delay and Increased Body Fat

A. ROBERTO FRISANCHO*

Department of Anthropology, University of Michigan, Ann Arbor, Michigan 48104

ABSTRACT The purpose of this study was to determine whether differences in leg length index are related to differences in body fat. The study included a cross-sectional sample of 21,021 subjects ranging in age from 2 to 90 years who had anthropometric information and poverty income ratio that participated in the third National Health and Nutrition Survey (NHANES III) of the United States conducted during 1988–1994. Of the total 21,021 participants, 7,810 were non-Hispanic white (3,900 men and 3,910, women), 8,134 were African-American black (3,127 men and 2,889 women) and 6,237 were Mexican-American (3,221 and 3,016 women). In both males and females and in all three ethnic groups and across socio-economic status (measured by the poverty income ratio) a low leg length index is associated with increased body fat (measured by skinfold thickness) when compared with those with high leg length index. It is postulated that a low leg length index reflects the consequence of negative environmental conditions leading to growth delay. Previous studies indicate that individuals exposed both during development and adulthood to under-nutrition respond through inter-related physiological mechanisms oriented at improving energetic efficiency and low oxidation of fat. These interrelated compensatory physiological adjustments work together to promote fat storage among growth delayed individuals or populations. *Am. J. Hum. Biol.* 19:703–710, 2007. © 2007 Wiley-Liss, Inc.

Previous studies have shown that an adverse intra-uterine environment, as measured by birth weight, is associated with more subcutaneous and abdominal fat and less lean body mass in adulthood. For example, studies among populations with low socio-economic status in England, Gambia, India, and survivors of the Dutch Famine of World War II have shown that low birth weight is associated with higher frequency of diabetes type II, hypertension, and obesity (Ravelli et al., 1976, 1999). This finding led to the development of the hypothesis of the Fetal programming or Thrifty Phenotype of adult disease (Barker, 1998; Hales and Barker, 2001; Lampl and Jeanty, 2004). However, not only does fetal exposure to malnutrition need to be considered but also the postnatal development. Longitudinal studies have shown that leg length is the most important component responsible for the rapid growth of stature during childhood and adolescence (Krogman, 1972; Scammon, 1930; Tanner, 1978), which is also evident in cross-sectional anthropometric data. As shown in Figure 1 the leg length during childhood and adolescence grows very rapidly and contributes more to the variability in stature than trunk size that grows very slowly. In

general, a relatively long leg implies a rapid growth and the influence of positive environmental factors during childhood and adolescence. Conversely, relatively short legs imply a slow growth and the influence of negative environmental factors during childhood and adolescence. In other words, relative leg length is a sensitive and specific marker of developmental conditions. In 2001 analysis of the anthropometric and socio-economic data of Mexican-Americans (that participated in the Hispanic Health and Nutrition Examination Survey from 1982–1984) shows that poverty income index is more associated with leg length index than with sitting height (Frisancho et al., 2001). Accordingly, we proposed that measurements of relative leg length could be used to trace the developmental history of children and adults (Frisancho et al., 2001). The purpose of this study is to determine whether differences

*Correspondence to: A. Roberto Frisancho; Department of Anthropology, University of Michigan, 1085 S. University, Ann Arbor, MI 48104. E-mail: arfrisan@umich.edu

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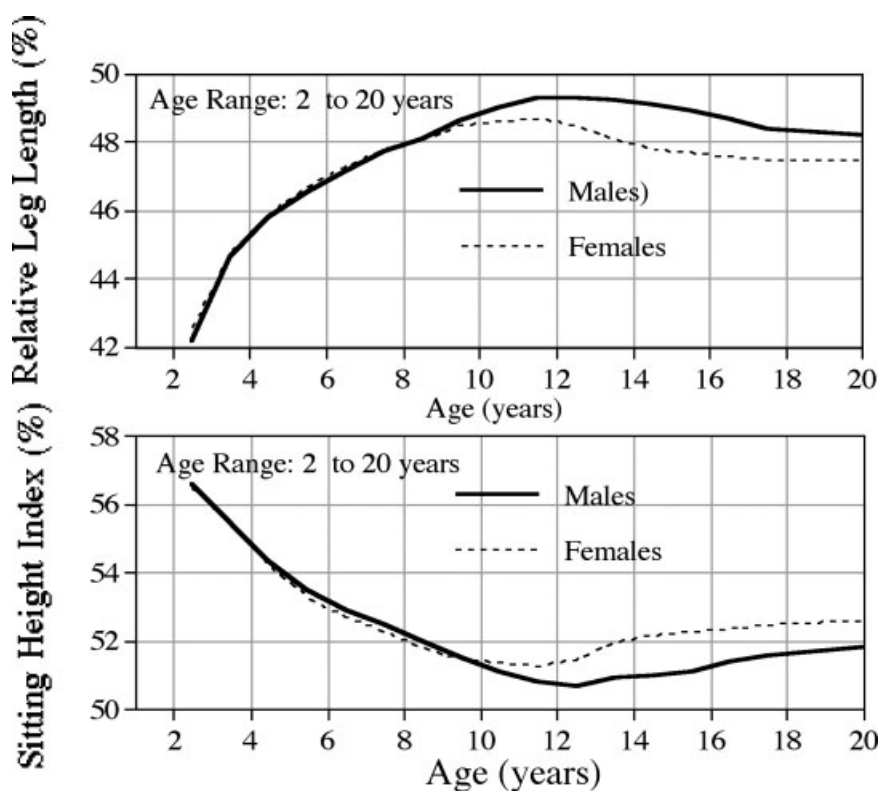


Fig. 1. Relative growth of leg length and trunk height. The leg length during childhood and adolescence grows very rapidly and contributes more to the variability in stature than trunk size that grows very slowly. Adapted from: Frisancho (2007).

in body fat are related to differences in leg length index among the populations of the third National Health and Nutrition Survey (NHANES III) studies during 1994–1998.

STUDY POPULATION AND METHODS

Sample

The study included a cross-sectional sample of 21,021 subjects ranging in age from 2 to 90 years who had participated in the third National Health and Nutrition Survey (NHANES III) of the United States conducted during 1988–1994 by the National Center for Health Statistics to evaluate the health and nutritional status of the noninstitutionalized US population and in whom data on anthropometric variables values had been collected. Of the total 21,021 participants, 7,810 were non-Hispanic white (3,900 men and 3,910 women), 8,134 were African-American black (3,127 men and 2,889 women)

and 6,237 were Mexican-American (3,221 and 3,016 women).

Anthropometric measurements

The anthropometric measurements included stature (cm), sitting height (cm), and sum of skinfold thickness (mm) at four body sites: triceps, subscapular, supra-iliac, and thigh. Leg length and leg length index (%) were derived by computation:

- Leg length (cm) = Stature- sitting height.
- Length index (%) = [(leg length/stature)*100]

Using as reference the new anthropometric reference (Frisancho, 2007) the participants were classified into two groups of leg length index (%):

- a. Low leg length index (%) = Z-score < -1.036 the age and sex-specific reference of leg length index (%)

TABLE 1. Comparison of mean sum of four skinfold (triceps, subscapular, suprailiac, and thigh) thickness (mm) adjusted for age and body mass index through analysis of variance for participants ranging in age from 2 to 20 years with low total leg length index and high total leg length index below and above poverty income ratio derived from the third National Health and Nutrition Examination Survey (NHANES III) conducted during 1988–1994

	Low leg length index*		High leg length index*		Significance
	N	Mean ± SE	N	Mean ± SE	
Males: Non-Hispanic White					
Below Poverty Income Ratio	72	44.5 ± 2.9	10	29.9 ± 2.3	<i>P</i> < 0.01
Above Poverty Income Ratio	479	41.3 ± 0.9	74	33.8 ± 2.2	<i>P</i> < 0.01
Males: Non-Hispanic Black					
Below Poverty Income Ratio	143	38.2 ± 2.0	237	31.1 ± 0.9	<i>P</i> < 0.01
Above Poverty Income Ratio	139	35.1 ± 1.8	255	35.7 ± 1.3	N.S.
Males: Mexican-American					
Below Poverty Income Ratio	349	42.0 ± 1.8	60	35.2 ± 2.1	<i>P</i> < 0.01
Above Poverty Income Ratio	311	46.5 ± 1.4	65	38.8 ± 2.2	<i>P</i> < 0.01
Females: Non-Hispanic White					
Below Poverty Income Ratio	86	50.0 ± 2.7	14	47.4 ± 8.1	<i>P</i> < 0.10
Above Poverty Income Ratio	511	51.3 ± 1.1	74	45.2 ± 2.2	<i>P</i> < 0.01
Females: Non-Hispanic Black					
Below Poverty Income Ratio	128	51.7 ± 2.5	270	46.3 ± 1.4	<i>P</i> < 0.01
Above Poverty Income Ratio	115	60.6 ± 2.9	299	47.3 ± 1.4	<i>P</i> < 0.01
Females: Mexican-American					
Below Poverty Income Ratio	352	53.1 ± 1.4	70	42.3 ± 2.1	<i>P</i> < 0.01
Above Poverty Income Ratio	328	57.0 ± 1.5	60	40.0 ± 2.1	<i>P</i> < 0.01

*Low leg length index (%) = Z-score < -1.036 the age and sex-specific reference of leg length index (%). Frisancho, 2007.

*High leg length index (%) = Z-score > +1.036 the age and sex-specific reference of leg length index (%). Frisancho, 2007.

- b. High leg length index (%) = Z-score > +1.036 the age and sex-specific reference of leg length index (%).

Socio-economic status

Socio-economic status was inferred from the poverty income ratio (PIR). The Poverty statistics are based on family income and family size using Bureau of the Census poverty thresholds, which are updated annually by the U.S. Bureau of the Census to reflect changes in the Consumer Price Index for all urban consumers (CPI-U). In general poverty status is based on family income, family size, number of children in the family, and for families with two or fewer adults, the age of the adults in the family. Families or individuals with income below their appropriate thresholds are classified as PIR of 1. Conversely, families or individuals with income above their appropriate thresholds are classified as PIR of 2.

Age groups and statistical analysis

To compare the mean values of subcutaneous fat the participants were classified into two groups: (a) nonadult that includes individuals ranging in age from 2 to 20 years hereafter referred to as children and (b) adult that includes individuals ranging in age from 21 to 90 years hereafter to as adults. It should be

noted that because the Z-scores for leg length index were calculated with reference to sex-specific 1 year age intervals any changes concentrated in one cohort, for instance, early childhood does not affect the comparisons of the outcome variable such as sum of skinfold thickness. However, to avoid the effects of collinearity of age and body mass index and leg length index the analyses of variance using ANOVA of the outcome variable were adjusted for age and body mass index. Although NHANES III used stratified, multistage probability cluster sampling, sample weights were not used in this analysis. The disadvantages of using weights in analyses of this kind of sample were discussed by Korn and Graubard (1991). Statistical analyses were performed using the software Statview version 5 of SPSS.

RESULTS AND DISCUSSION

The relationship of leg length index to sum of four skinfold thickness (mm) is shown Tables 1 and 2 and in Figures 2 and 3. From these data it is evident that in both children and adults, males and females and in all three ethnic groups and across socio-economic status (measured by the PIR) a low leg length index is associated with significantly greater amount of body fat (measured by skinfold thickness) than their counterparts with high

TABLE 2. Comparison of mean sum of four skinfold (triceps, subscapular, suprailiac, and thigh) thickness (mm) adjusted for age and body mass index through analysis of variance for participants ranging in age from 21 to 90 years with low total leg length index and high total leg length index below and above poverty income ratio derived from the third National Health and Nutrition Examination Survey (NHANES III) conducted during 1988–1994

	Low leg length index*		High leg length index*		Significance
	N	Mean ± SE	N	Mean ± SE	
Males: Non-Hispanic White					
Below Poverty Income Ratio	77	68.4 ± 3.4	16	52.9 ± 4.5	<i>P</i> < 0.01
Above Poverty Income Ratio	1073	66.8 ± 0.7	174	61.9 ± 1.7	<i>P</i> < 0.01
Males: Non-Hispanic Black					
Below Poverty Income Ratio	49	61.9 ± 4.3	173	48.2 ± 1.8	<i>P</i> < 0.01
Above Poverty Income Ratio	157	69.0 ± 2.1	520	58.4 ± 1.2	<i>P</i> < 0.01
Males: Mexican-American					
Below Poverty Income Ratio	290	64.5 ± 1.3	35	56.4 ± 3.9	<i>P</i> < 0.01
Above Poverty Income Ratio	535	66.7 ± 1.0	54	61.4 ± 3.6	<i>P</i> < 0.05
Females: Non-Hispanic White					
Below Poverty Income Ratio	120	88.3 ± 3.0	27	75.0 ± 5.4	<i>P</i> < 0.10
Above Poverty Income Ratio	963	89.6 ± 0.9	185	80.3 ± 2.1	<i>P</i> < 0.01
Females: Non-Hispanic Black					
Below Poverty Income Ratio	65	102.3 ± 3.7	216	83.6 ± 2.3	<i>P</i> < 0.01
Above Poverty Income Ratio	138	98.9 ± 2.5	322	86.6 ± 1.8	<i>P</i> < 0.01
Females: Mexican-American					
Below Poverty Income Ratio	265	97.6 ± 1.7	35	82.6 ± 4.9	<i>P</i> < 0.01
Above Poverty Income Ratio	432	93.8 ± 1.4	31	86.4 ± 5.7	<i>P</i> < 0.01

*Low leg length index (%) = Z-score < -1.036 the age and sex-specific reference of leg length index (%). Frisancho, 2007.

*High leg length index (%) = Z-score > +1.036 the age and sex-specific reference of leg length index (%). Frisancho, 2007.

leg length index when compared to those with high leg length index. Birth cohort studies in England indicate that environmental influences during development are greater for growth in leg length than trunk growth (Wadsworth et al., 2002). It is postulated that a low leg length index reflects the consequence of negative environmental conditions leading to growth delay. Hence, it can be assumed that a low leg length index is a biological indicator of negative environmental factors during development resulting in delayed growth. Conversely, a high leg length index is as an indicator of a positive environmental factor during development resulting in advanced growth. Epidemiological studies in England indicate that adult differences in leg length are associated with significant differences in the components of the metabolic syndrome such as glucose intolerance, insulin resistance and hypertension (Bray et al., 2006; Gunnell, 2001; Gunnell et al., 2001, 2003). Anthropometric studies in Brazil and Mexico indicate that growth stunted individuals were associated with higher BMI and obesity than in non-growth stunted adults (Florencio et al., 2003; Velazques-Melendez, 2005).

Experimental studies in animals indicate that nutritional restriction during early development is associated with an increase drive to eat and a reduced expenditure of energy; a

higher caloric efficiency linked with suppressed lipid utilization; and a preferential lipid accumulation in adipose tissue accompanied by adipocyte hyperplasia (Dulloo and Girardier, 1990, 1993; Jones and Friedman, 1982; Jones et al., 1986; Jones et al., 1984; MacLean et al., 2004, 2006). Likewise, laboratory studies of humans exposed to drastic caloric restriction resulting in rapid weight loss are associated with a sustained reduction in resting metabolic rate (Brehm et al., 2005; Elliot et al., 1989; Weyer et al., 2000, 2001). In both animals, exposed to calorie restriction these interrelated compensatory adjustments work together to promote rapid and efficient weight regain.

The relative amounts of the macronutrients oxidized by an individual are reflected in the respiratory quotient (RQ), i.e., the ratio between carbon dioxide (CO₂) produced and oxygen (O₂) consumed. In general, a high RQ, indicating a relatively low fat oxidation will tend to cause increased fat deposition over time, since the oxidation of 1 g of fat is equivalent to 9 kcal, while 1 g of carbohydrate is equivalent to 4 kcal. Longitudinal studies indicate that a low oxidation of fat (high RQ) in the fasting state is a significant predictor of substantial weight gain in non-obese white men (Seidell et al., 1992). Studies in post-obese subjects indicate that reduced fat oxidation is related to subsequent body weight gain

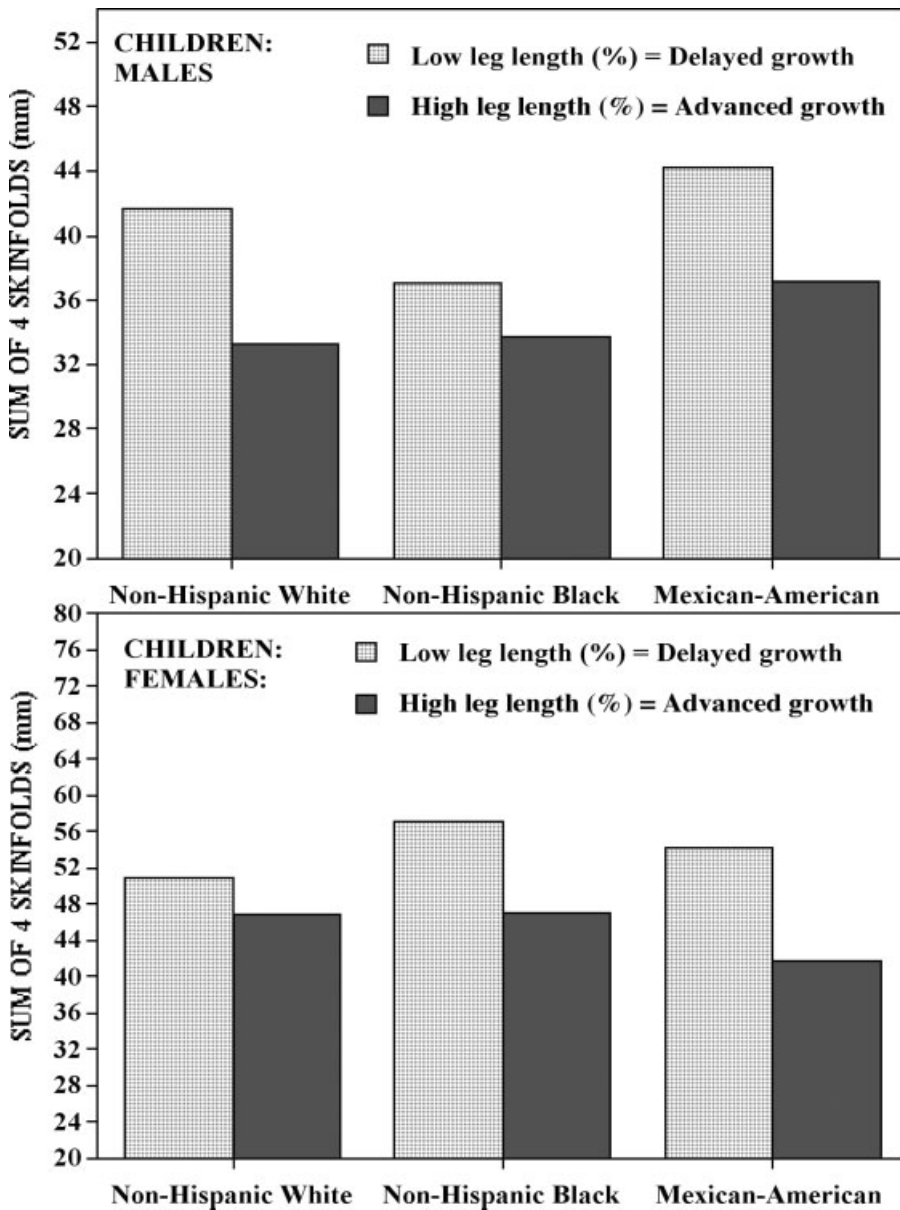


Fig. 2. Increased fatness in children associated with delayed leg length growth. Leg length defined with reference to: Frisancho (2007).

(Froidevaux et al., 1992; Lean and James, 1988; Schutz et al., 1992). Similarly, subjects failing to maintain body weight reduction have lower fat oxidation than those succeeding in keeping their weight down (Froidevaux et al., 1992). Likewise, obese pre-pubertal chil-

dren who were fed a mixed carbohydrate diet had a significantly greater oxidation of exogenous carbohydrate than their lean counterparts (Rueda-Maza et al., 1996). Evaluations of 24-h RQ in Pima Indians fed a weight maintenance diet found that low fat oxidation was

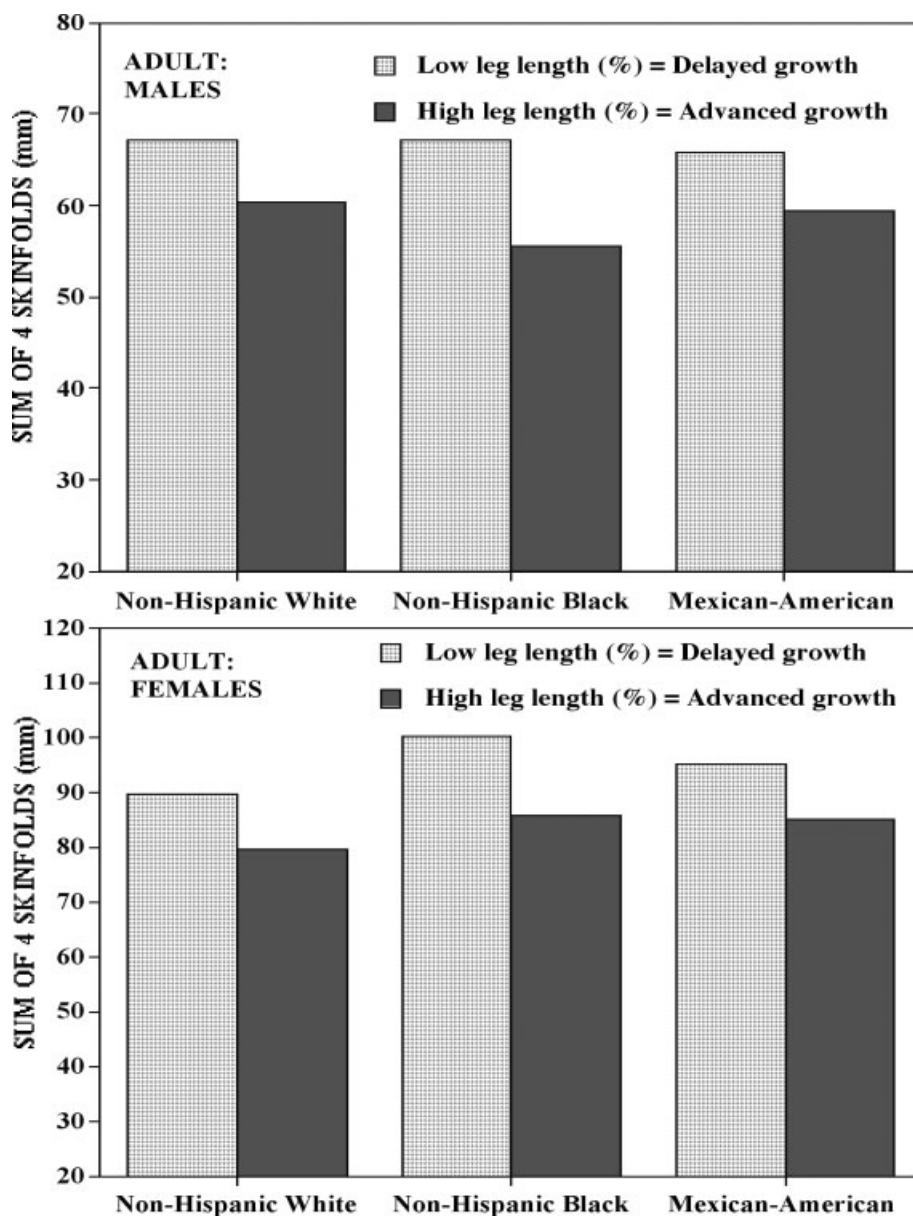


Fig. 3. Increased fatness in adults associated with delayed leg length growth. Leg length defined with reference to: Frisancho (2007).

associated with subsequent weight gain (Zurlo et al., 1990). Furthermore, the low fat oxidation was aggregated in families. These findings suggest that increased adiposity is related to a certain extent to a preferential oxidation of carbohydrate rather than fat.

Studies among Brazilian children indicate that those with delayed growth (i.e. low-height-for age) children had a high RQ, indicating a relatively low fat oxidation that predispose them to weight gain and fat storage than those with advanced growth (i.e. normal

height-for age) (Hoffman et al., 2000). This finding suggests that an increased carbohydrate oxidation and/or low fat oxidation resulting in increased fat deposition is associated with a negative developmental nutritional experience leading to delayed growth.

In sum, it is postulated that a low leg length index reflects the consequence of negative environmental conditions leading to growth delay. Hence, it can be assumed that a low leg length index is a biological indicator of a negative environmental insult during development resulting in delayed growth. Conversely, a high leg length index is as an indicator of a positive environmental condition during development resulting in advanced growth. The fact that growth delayed individuals tend to be fatter than those that had an advanced growth suggest that the interrelated compensatory physiological adjustments such as improved energetic efficiency and the low oxidation of fat associated with exposure to negative environmental conditions work together to promote fat storage among growth delayed individuals or populations.

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