

Growth and Fatness at Three to Six Years of Age of Children Born Small- or Large-for-Gestational Age

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ABSTRACT. *Objective.* To compare young children 3 to 6 years of age who were born small-for-gestational age (SGA; <10th percentile for gestational age) or large-for-gestational age (LGA; ≥90th percentile) with those who were born appropriate-for-gestational age (10th–89th percentile) to determine whether there are differences in growth and fatness in early childhood associated with birth weight status.

Design and Methods. National sample of 3192 US-born non-Hispanic white, non-Hispanic black, and Mexican-American children 3 to 6 years of age (36–83 months) examined in the third National Health and Nutrition Examination Survey and for whom birth certificates were obtained. On the birth certificates, length of gestation from the mother's last menstrual period was examined for completeness, validity, and whether the pattern of missing ($n = 141$) and invalid data ($n = 147$) on gestation was random. Gestation was considered invalid when >44 weeks, or when at gestations of ≤35 weeks, birth weight was inconsistent with gestation. To reclaim cases with missing or invalid data on gestation for analysis, a multiple imputation (MI) procedure was used. MI procedures are recommended when, as in this case, a critical covariate (length of gestation) is not missing at random, and complete-subject analysis may be biased. Using the results of the MI procedure, children were categorized, and growth outcome was assessed by birth weight-for-gestational age status. The growth outcomes considered in these analyses were body weight (kg), height (cm), head circumference (cm), mid-upper arm circumference (MUAC; cm), and triceps and subscapular skinfold thicknesses (mm). The anthropometric outcomes first were transformed to approximate normal distributions and converted into z scores (standard deviation units [SDU]) to scale the data for comparison across ages. Outcomes at each age then were estimated using regression procedures. SUDAAN software that adjusts variance estimates to account for the sample design was used in analysis for

prevalence estimates and to calculate regression coefficients (in SDU).

Results. Over these ages, children born SGA remained significantly shorter and weighed less (–0.70 to –0.60 SDU). Children born LGA remained taller and weighed more (0.40–0.60 SDU). For weight and height among LGA children, there was a divergence from the mean with age compared with those born appropriate-for-gestational age (10th–89th percentile). Head circumference and MUAC followed these same patterns. The coefficients for MUAC show values for SGA children fairly consistently at about –0.50 SDU and children born LGA show increasing MUAC from +0.40 to +0.50 SDU from 36 to 83 months of age. As with weight, there is a trend toward increased MUAC coefficients with age. Measures of fatness (triceps and subscapular skinfolds), which are more prone to environmental influences, showed less association with birth weight-for-gestational age status. Only a single age group, the oldest (6 years of age) group showed a significant deficit in fatness for children born SGA. For children born LGA, there was an increase in fatness at both the triceps and subscapular sites after 3 years of age.

Conclusion. These findings on a national sample of US-born non-Hispanic white, non-Hispanic black, and Mexican-American children show that children born SGA remain significantly shorter and lighter throughout early childhood and do not seem to catch up from 36 to 83 months of age. LGA infants remain longer and heavier through 83 months of age, but unlike children born SGA, children born LGA may be prone to an increasing accumulation of fat in early childhood. Thus, early childhood may be a particularly sensitive period in which there is increase in variation in levels of fatness associated with size at birth. These findings have implications for the evaluation of the growth of young children. The results indicate that intrauterine growth is associated with size in early childhood. Particularly, children born LGA may be at risk for accumulating excess fat at these ages. Birth weight status and gestational age may be useful in assembling a prognostic risk profile for children. *Pediatrics* 1999;104(3). URL: <http://www.pediatrics.org/cgi/content/full/104/3/e33>; blacks, birth weight, growth, large-for-gestational-age, multiple imputation, Mexican-Americans, National Health and Nutrition Examination Survey, small-for-gestational age, whites.

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ABBREVIATIONS. BWGA, birth weight-for-gestational-age; SGA, small-for-gestational age; LGA, large-for-gestational age; AGA, appropriate-for-gestational age; NHANES III, third National Health and Nutrition Examination Survey; MI, multiple imputation; MUAC, mid-upper arm circumference; SDU, standard deviation units.

Infants born small, defined as low birth weight-for-gestational-age (BWGA), generally catch up over the first 6 months, whereas the growth of large infants slows.^{1,2} After this initial period of growth compensation, body weight and height have been shown to track through childhood within birth weight categories in several large US studies.^{3–6} A number of smaller, prospective studies also have demonstrated that BWGA status, both small and large, is associated with growth status through infancy and childhood up to 6 to 8 years of age.^{7–13} Whether growth in early childhood (3–6 years of age) is associated with fetal growth and growth status at birth when length of gestation is taken into account has not been demonstrated for an ethnically diverse sample of US-born children. The objective of this study was to compare the growth of non-Hispanic white, non-Hispanic black, and Mexican-American children born small-for-gestational age (SGA; birth weight <10th percentile for gestational age) and large-for-gestational age (LGA; ≥90th percentile) with the growth of normal birth weight children (appropriate-for-gestational age [AGA]) at 3 to 6 years of age.

MATERIALS AND METHODS

Design and Sample

Nearly 40 000 people ≥2 months of age representative of the US civilian, noninstitutionalized population, were selected to participate in the third National Health and Nutrition Examination Survey (NHANES III; 1988–1994) conducted by the National Center for Health Statistics, Centers for Disease Control and Prevention.¹⁴ The analyses reported here focus on NHANES III children from 36 months of age, the age at which measures of height generally are preferred over recumbent length, to 83 months of age (3–6 years). The anthropometric measurements available for these ages include weight, standing height, head circumference, and anthropometric measurements of body composition (mid-upper arm circumference and triceps and subscapular skinfolds).

A total of 4262 children were sampled in the target age range. A household interview, usually with a parent respondent, was completed for 4121 of these children (96.7%). Informed consent was obtained from parents or guardians at the time of interview to seek birth certificates for these children. Health examinations including an anthropometric measurement component were given to 3878 children (91.0%), usually within 2 to 4 weeks of the interview. Among the examined children, 3653 of 3878 (94.1%) were US-born.

Birth Certificates

Birth certificates were sought from the reported states of birth and positively matched for 3428 (93.8%) of the US-born children. Excluded were 5 cases with missing birth weights, 5 cases in which sex was discrepant between the birth certificates and NHANES III, and 83 children who were twins or triplets. The sample then was restricted to non-Hispanic white, non-Hispanic black, and Mexican-American children. Children of all other races/ethnicities ($n = 143$) were excluded, because the reference data used to categorize BWGA¹⁵ are specific for the race (white vs black) given on birth certificates. The final analytic sample was 3192 children.

Using procedures used earlier,^{16,17} length of gestation determined from the mother's last menstrual period as reported on the birth certificate was examined for validity. Gestation was considered invalid when >44 weeks ($n = 72$) and when, at gestations of ≤35 weeks, birth weight was inconsistent with gestation ($n = 75$).¹⁵ Gestation from the last menstrual period was missing for 141 cases. Because we have shown previously that differences in growth relating to preterm delivery do not contribute to the overall group differences among BWGA groups after the first year,¹⁶

very preterm and preterm deliveries were not excluded from the analyses.

However, an examination of the pattern of missing and invalid gestations indicated that gestation was not missing or invalid at random.^{18,19} Gestation was more likely to be missing or invalid (>44 weeks) if the infant was Mexican-American, currently residing in an urban area or in the West census region, and when the interview was conducted in Spanish. Gestation was more likely to be considered invalid because it was inconsistent with birth weight (early for size) for non-Hispanic blacks and for those living in rural areas or in the South census region. Because these factors (race/ethnicity and urban/rural dwelling) are known also to be associated with the dependent variables (childhood growth status and body composition), there was concern that an analysis of the sample for whom data were complete (complete-subject analysis) would yield results that were biased.

Multiple Imputation (MI) Procedure

To reclaim the cases ($n = 288$) with missing or invalid gestation for analysis, a MI procedure was used.^{18,19} MI is a method of handling nonresponse that retains the primary advantages of single imputation but avoids its drawbacks by replacing each missing datum with two or more values drawn randomly from a distribution of likely values. MI procedures are recommended when, as in this case, a critical covariate (length of gestation) is not missing at random, and complete-subject analysis may be biased.¹⁹

Gestation was imputed (5 imputations) using a regression including race/ethnicity, infant sex, mother's height and age, cigarette smoking, parity, family size, mother's race, and state of residence. A total of 267 of the 288 (92.7%) missing or invalid gestations were predicted using this model. Only 21 cases could not be reclaimed because of concurrent missing data (mother's height and cigarette smoking), leaving a final sample of 3171 for analysis of outcome.

BWGA Categories

To categorize BWGA status, a reference based on 1989 vital statistics¹⁵ was used in which infants are categorized separately by race (white vs black) and within race by infant sex (male vs female) and maternal parity (infants of primiparas vs multiparas). Infants designated by NHANES III as non-Hispanic white were categorized using the reference percentiles for whites, and infants designated as non-Hispanic black were categorized using the reference percentiles for blacks.¹⁵ Mexican-American infants were categorized using the percentiles for whites consistent with the approach used to derive the reference data.¹⁵

SGA indicating intrauterine growth retardation was defined as a BWGA below the 10th percentile, AGA from the 10th to 89th percentile, and LGA or macrosomia at or above the 90th percentile. For the complete-subject sample ($n = 2904$) with complete or valid information for gestation, the prevalence of SGA was 10.4% ± 1.1%, AGA was 77.7% ± 2.0%, and LGA was 11.9% ± 1.1%. For the sample with complete or valid information for gestation, the prevalence of very preterm delivery (<33 weeks) was 1.4% ± 0.4%, preterm delivery (33 to 36 weeks) was 5.8% ± 0.7%, and term was 92.9 ± 0.8%.

Age Groups and Anthropometry

The children were grouped into four age groups: 36 to 47 months (3 years), 48 to 59 months (4 years), 60 to 71 months (5 years), and 72 to 83 months (6 years) based on age at examination. At 72 to 83 months, the group included 39 children who were 84 months ($n = 35$) or 85 months ($n = 4$) at the time of examination but who had been interviewed at 83 months of age.

The anthropometric measurements considered in these analyses were body weight (kg), height (cm), head circumference (cm), mid-upper arm circumference (cm), and triceps and subscapular skinfold thicknesses (mm). The body measurements were recorded after standard anthropometric protocols.^{20,21}

Other Variables

Maternal parity was based on number of previous births reported on the birth certificate. Categories of race/ethnicity were based on parental self-reports from NHANES III using US Bureau of the Census definitions.¹⁴ Other variables used only to determine the pattern of missing or invalid gestation and in the imputation

regressions were taken from both birth certificates and NHANES III data. These included mother's age, race, and state of residence from the birth certificate; mother's height, smoking during pregnancy, family size, language of interview, and region of residence were taken from NHANES III. The distributions relative to birth weight status of maternal variables used only to impute gestation are not reported.

Statistical Methods

Sample weights were used to account for the oversampling and unit nonresponse. SUDAAN software, which uses a Taylor series expansion to adjust variance estimates to account for the sample design, was used to estimate standard error (SE) of the prevalence data and background characteristics.^{22,23}

Because the distributions can be skewed, the anthropometric variables were transformed before analysis.^{24,25} Body weight, mid-upper arm circumference (MUAC), and triceps skinfolds were transformed to an approximate normal distribution using a power transformation of $-1/\sqrt{x}$. Subscapular skinfolds were transformed using a negative reciprocal ($-1/x$) to minimize the effects of very large values of the subscapular skinfold. Height and head circumference were not transformed, because both are nearly normally distributed at these ages.^{26,27}

To control for group differences (race/ethnicity and sex) and scale the values for comparison across ages, the anthropometric variables were converted into z scores²⁸ (mean: 0; SD: 1) internally within the sample age, sex, and race/ethnicity groups. By normalizing the distributions, percentiles corresponding to the z scores (standard deviation units [SDU]) can be estimated using the area under the normal curve. Assuming normality, a z score or SDU of zero represents both the mean and the median; the 10th and 90th percentiles are -1.28 SDU and $+1.28$ SDU, respectively.

Analyses of the growth and body composition variables were performed using SUDAAN regression procedures.²³ Eight separate indicator variables were created representing SGA and LGA for each of the four age groups and were entered into a single regression with the anthropometry z scores as the dependent variables. Regression coefficients (\pm SE) in SDU from results of the MI for gestation were combined using the equations of Little and Rubin¹⁶ and were tested for statistical significance ($\alpha = .05$) from zero (AGA reference). As expected, the intercepts from the regression equations representing the mean for the AGA reference did not differ significantly from zero in any analysis.

Comparison of coefficients for the outcomes generated in complete-subject analyses compared with the results using the MI procedures showed that there was little difference in magnitude by reclaiming the 267 cases but that the inclusion of the additional cases did reduce sufficiently the variance of the estimates so as to strengthen statistical significance. Only results using the MI procedure are reported here.

RESULTS

The background characteristics of the sample ($N = 3192$) are presented in Table 1 and are estimated using the statistical weights for examined children to account for the complex sample survey design.²² Births to primiparous women represent $>40\%$ of the children. The proportion of low birth weight (<2500 g, both preterm and term) is 10%; just over 10% are macrosomic (≥ 4000 g).

The growth outcomes include measures of overall body mass and size (weight and MUAC), linear measurements (height and head circumference), and measures of fatness (triceps and subscapular skinfolds). Weight in early childhood shows the clearest pattern of association with BWGA status. This is not unexpected, because deviations in weight form the bases of the classification (Fig 1). Children born SGA stay at ~ -0.70 SDU for weight from 36 to 83 months of age (Table 2). Children born LGA increase in size over these ages from $+0.40$ to $\sim +0.70$ SDU (Fig 1).

The coefficients for MUAC show values for SGA

TABLE 1. Distribution* of US-born non-Hispanic White, non-Hispanic Black, and Mexican-American Singletons by Selected Characteristics 36 to 83 months of Age, NHANES III, 1988–1994

	Sample N	Weighted %	SE
Chronological age (mo)			
36–47	942	26.0	1.1
48–59	872	23.1	0.9
60–71	878	25.5	1.3
72–83	500	25.5	1.6
Race/ethnicity			
Non-Hispanic white	940	72.2	1.7
Non-Hispanic black	1,122	18.0	1.5
Mexican-American	1,130	9.8	0.9
Infant sex			
Male	1,563	52.3	1.5
Female	1,629	47.7	1.5
Birth order			
First born	1,273	43.6	1.4
Second born	943	32.6	1.4
Third+ born	976	23.8	1.3
Birth weight			
Low birth weight (<2500 g)	413	10.0	0.6
Normal (2500–3999 g)	2,498	79.8	1.1
Macrosomic (≥ 4000 g)	281	10.2	0.8

* $N = 3192$. Characteristics are estimated using the statistical weights to account for the complex sample survey design.

SDU for Weight

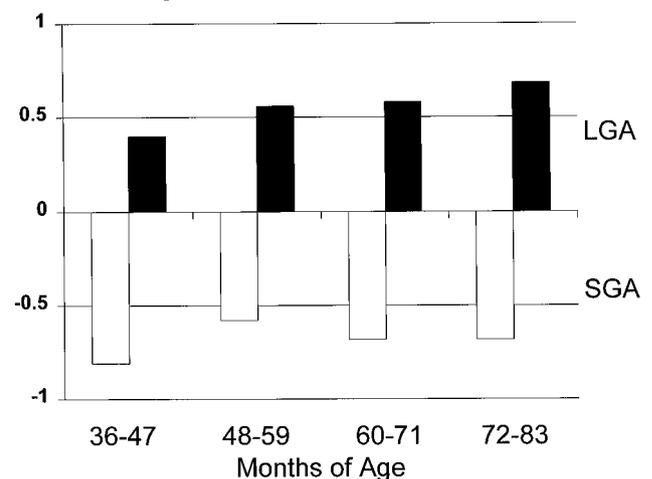


Fig 1. Regression coefficients in SDU (z scores) for body weight for children born SGA and LGA compared with children born AGA (z score: 0). All coefficients are different from zero at $P < .01$ with the exception of the coefficient for LGA children 48 to 59 months of age, which is significant at $P < .05$.

children fairly consistently at ~ -0.50 SDU and children born LGA show increasing MUAC from $+0.40$ to $+0.50$ SDU from 36 to 83 months of age (Table 2). As with weight, there is a trend toward increased MUAC coefficients with age.

The results for height (Fig 2) and head circumference show coefficient patterns that are similar to measures of body size. All coefficients are significantly different from zero with the exception of that for height for the children born LGA at 48 to 59 months of age (Table 2). For both height and head circumference children born LGA seem to show a tendency to deviate from the mean with age, but particularly for head circumference the trend is not as sharply linear.

TABLE 2. Regression Coefficients in SDU for Child Growth Status at 36 to 83 months* of Age by BWGA Status, NHANES III, 1988–1994

	SGA		LGA	
	β	SE	β	SE
Weight				
36–47 mo	−0.81	0.17‡	0.40	0.09‡
48–59 mo	−0.58	0.15‡	0.56	0.25‡
60–71 mo	−0.68	0.21‡	0.58	0.14‡
72–83 mo	−0.68	0.18‡	0.68	0.20‡
Mid-upper arm circumference				
36–47 mo	−0.62	0.18‡	0.37	0.17‡
48–59 mo	−0.31	0.15‡	0.46	0.21‡
60–71 mo	−0.48	0.19‡	0.51	0.13‡
72–83 mo	−0.55	0.14‡	0.54	0.25‡
Height				
36–47 mo	−0.69	0.10‡	0.33	0.12‡
48–59 mo	−0.54	0.14‡	0.38	0.24
60–71 mo	−0.59	0.21‡	0.43	0.16‡
72–83 mo	−0.57	0.14‡	0.66	0.19‡
Head circumference				
36–47 mo	−0.68	0.14‡	0.29	0.13‡
48–59 mo	−0.64	0.14‡	0.49	0.20‡
60–71 mo	−0.57	0.12‡	0.36	0.15‡
72–83 mo	−0.60	0.17‡	0.63	0.21‡
Triceps skinfold				
36–47 mo	−0.18	0.17	0.09	0.13
48–59 mo	−0.15	0.16	0.29	0.10‡
60–71 mo	−0.07	0.13	0.33	0.16‡
72–83 mo	−0.49	0.11‡	0.63	0.23‡
Subscapular skinfold				
36–47 mo	−0.21	0.18	0.05	0.16
48–59 mo	−0.19	0.15	0.38	0.18‡
60–71 mo	−0.13	0.21	0.28	0.15
72–83 mo	−0.22	0.13‡	0.56	0.24‡

* N = 3171.

† Regression coefficient in SDU significantly different from zero at $P < .05$.

‡ Regression coefficient in SDU significantly different from zero at $P < .01$.

Measures of fatness, which are more prone to environmental influences and measurement error, show less association with BWGA status (Table 2). The coefficients are significant for triceps and subscapular skinfolds indicating a relative deficit in fatness only at 72 to 83 months (6 years) of age for children born SGA. For children born LGA, skinfolds are progressively higher from 4 years of age onward especially at the triceps site (Fig 3).

DISCUSSION

The objective of these analyses was to compare the growth status of children 3 to 6 years of age born SGA (<10th percentile BWGA) and LGA (\geq 90th percentile) with those born AGA. We show that there are effects of BWGA status on measurements of body mass and size (weight and MUAC) and linear measurements (height and head circumference) in early childhood from 36 to 83 months of age. The coefficients (z scores) for children born SGA remain at fairly consistent levels below the mean. However, for children born LGA, there is increasing deviation from the mean (AGA reference: 0) with age. Measures of MUAC follow this pattern. The levels of deficit in height are fairly consistent across the ages for children born SGA, and there is again an increase in the SDU with age for children born LGA. Mea-

SDU for Height

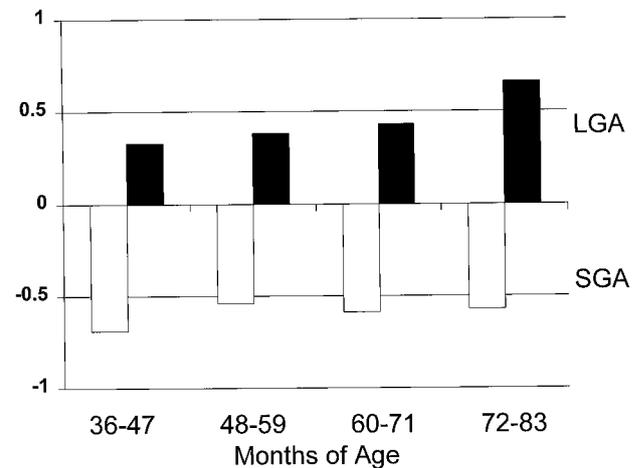


Fig 2. Regression coefficients in SDU (z scores) for height for children born SGA and LGA compared with infants and children born AGA (z score: 0). All coefficients are different from zero at $P < .05$, with the exception of those for LGA at 48 to 59 months of age, which is not significant.

SDU for Triceps Skinfold

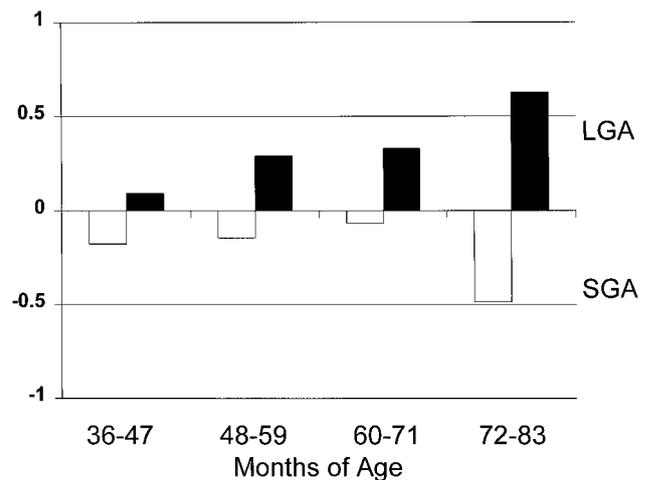


Fig 3. Regression coefficients in SDU (z scores) for triceps skinfold thicknesses for children born SGA and LGA compared with infants and children born AGA (z score: 0). Coefficients are not statistically different from zero (at $P < .05$) for SGA children with the exception of that at 72 to 83 months of age. For LGA children, the coefficients are significant for the 48- to 59-month, 60- to 71-month, and the 72- to 83-month groups.

asures of head circumference followed this same pattern based on BWGA status.

These findings are in agreement with the few large US studies that have considered the entire range of birth weight and demonstrated that weight and length or height status based on size at birth (independent of gestation) tend to track during early childhood.^{3–6} Smaller clinical studies that have followed SGA infant growth prospectively have also consistently found significant differences attributable to SGA status in childhood and beyond.^{7–9}

In the largest clinical study, Ounsted et al^{10–12} in Oxford conducted a 7-year longitudinal study comparing 238 SGA (18 with gestational ages of <37 weeks), 246 AGA (8 preterm), and 241 LGA (1 pre-

term) white, singleton infants. Follow-up at 4 years^{10,11} and 7 years¹² showed significant differences among the groups in height and weight. The Oxford children born SGA were 3 cm shorter at 4 years of age than were the AGA children and weighed 2 kg less. The children born LGA were taller by 3 cm and heavier by 2 kg.^{10,11} The SGA group was still about 3 cm shorter at 7 years of age, whereas the LGA group was 3 to 4 cm taller. The SGA group was 2 kg lighter and the LGA group 2 to 3 kg heavier than was the AGA group.¹² Our findings on a much larger, national sample of non-Hispanic white, non-Hispanic black, and Mexican-American children clearly confirm these earlier studies on white children on the effects of birth weight status on height and weight in early childhood. However, it should be noted that the weighted NHANES III sample reflects a US population that is primarily non-Hispanic white, and findings may still be most applicable to that group.

Measures of fatness do not show the same association with BWGA status, especially for children born SGA. Overall, for children born SGA, the coefficients for skinfolds are negative, although small and not generally significant through these ages in childhood. Our findings for SGA children ≤ 83 months of age follow on and overlap our previous analyses of the growth outcomes of NHANES III infants and young children 2 to 47 months of age.^{16,17} In previous analyses, we showed that the discrepancies in weight at 2 to 47 months of age among SGA children are attributable primarily to deficits in muscularity.^{16,17} At the earlier ages, there were consistent differences among the BWGA status groups for measures of body size and linear measures, but no comparable differences in levels of fatness for either SGA or LGA children through 3 years of age.¹⁷

However, for children born LGA, there seems to be an increase in fatness after 3 years of age. Because skinfolds are measured less precisely than weight or linear measurements, it might be expected that the relationship of the skinfold levels to birth weight status is attenuated because of measurement error. Reliability estimates for the anthropometric measurements from the two HANES surveys before NHANES III have indicated that skinfold measurements have greater interobserver measurement error than other linear measurements or weight.^{29,30} In fact, in our analyses the magnitude of the coefficients for skinfolds is diminished. Nevertheless, the increasing levels of fatness among LGA children parallel the increase over these ages in weight and MUAC and are thus unlikely to be attributable to measurement error.

Skinfold levels for children born LGA are virtually identical to those of children born AGA at 3 years of age (SDU close to zero), but by 6 years of age, the levels of skinfolds have diverged considerably to $>+0.60$ SDU. This is consistent with findings from the British National Study of Health and Growth of children 5 to 11 years of age in which it was shown that by 5 years of age, birth weight contributed significantly and positively to the variation in triceps and subscapular skinfolds.³¹

Early childhood may be a particularly sensitive

period in which there is increase in the variation in levels of fatness.^{32,33} The development of overweight and increase in fatness among some 4- to 5-year-old children may be associated with the timing of the adiposity rebound, the point at which body mass index (and skinfolds) begins to rise from the childhood trough.³⁴⁻³⁶ Rolland-Cachera et al³⁴ have noted that as many as 30% of all children have their adiposity rebound at as early as 4 years of age, and an earlier adiposity rebound has been associated with both larger size in early childhood and a high-protein diet in very early childhood (2 years of age).³⁵ Children born LGA, because they are both heavier and taller at 4 to 5 years, may be more likely to have an earlier adiposity rebound and show increased fatness at 4 to 6 years of age relative to their more slowly maturing counterparts.^{34,36} This increase in fatness may be of concern if it leads to overweight in childhood, thereby increasing the risk for overweight in adulthood.^{37,38}

The findings reported here on a national sample of US-born non-Hispanic white, non-Hispanic black, and Mexican-American children confirm that children born SGA continue to remain significantly shorter and lighter throughout early childhood, and they do not seem to catch up from 36 to 83 months of age. LGA infants remain longer and heavier through 83 months of age, but unlike children born SGA, children born LGA may be prone to the increasing accumulation of fat in early childhood. Thus, these findings have implications for the evaluation of the growth of young children. Intrauterine growth is associated with size in early childhood, and birth weight status and gestational age may be useful in assembling a prognostic risk profile for children.

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