A New Look at Intrauterine Growth and the Impact of Race, Altitude, and Gender

Pam Thomas, RN*; Joyce Peabody, MD*; Virginia Turnier, MD*; and Reese H. Clark, MD*‡

ABSTRACT. ***Background.*** **Growth curves described in the 1960s are used to classify neonate intrauterine growth as normal or abnormal. Our objective was to determine whether continued use of these curves is appropriate.**

Methods. **From 1996 to 1998, we collected birth weight, length, head circumference, estimated gestational age (EGA), gender, race, and place of birth (<4000 feet or ≥4000 feet) on 27 229 neonates to evaluate the effects of each on intrauterine growth and the diagnoses of small for gestational age (SGA) and large for gestational age (LGA). We compared the gestation-specific growth parameters derived from our sample with those reported in 1966 and 1969.**

Results. **Gestational age had the largest influence on each growth parameter. Race and gender both had effects on birth weight. Female neonates were smaller than male neonates, and black neonates were smaller than Hispanic and white neonates at each EGA.**

For neonates with an EGA <30 weeks, our data had a smaller variance and lower average weights, lengths, and head circumferences than those reported in 1966 and in 1969. For neonates >36 weeks, the variance was similar, but our curves showed that neonates in our sample were larger and heavier. Use of the older growth curves to classify neonates as SGA, LGA, and appropriate for gestational age (AGA) led to significantly different rates of each by gender and race.

Conclusions. **Intrauterine growth patterns previously described and commonly used to classify neonates as AGA are inaccurate for use in current populations and lead to gender- and race-specific diagnoses of SGA and LGA that are misleading.** ***Pediatrics*** **2000;106(2). URL: http://www.pediatrics.org/cgi/content/full/106/2/e21;** ***neonates, growth, race, gender.***

ABBREVIATIONS. SGA, small for gestational age; LGA, large for gestational age; AGA, appropriate for gestational age; EGA, estimated gestational age.

In the late 1960s, 2 landmark articles described intrauterine growth patterns for the first time.[1,2] Two subsequent studies reported that disproportionate growth at a given gestational age was related to neonatal mortality risk.[3,4] These important articles have led to the nearly universal use of reference growth curves to characterize an infant's growth relative to gestational age for the last 30 years. This practice has been based on the recognition that variance of growth relative to gestational age, either undergrown (small for gestational age [SGA]) or overgrown (large for gestational age [LGA]), predicts short-term morbidity and mortality. However, there are 2 reasons why the accuracy of the standard reference curves for identifying high-risk neonates needs reevaluation. First, the plot curves of earlier studies[1,2] were based on a small and biased population sample, particularly at low gestational ages. Second, because of increased attention to nutritional issues affecting pregnancy and improved identification and management of factors adversely impacting fetal well-being, one might expect to observe positive changes in intrauterine growth patterns since the 1970s.

Our purpose was to determine whether the continued use of these growth curves is appropriate or whether curves based on a larger, less biased, and more current sample were significantly different. In addition, we evaluated the risk of death as related to gestational age and birth weight to determine whether the previous risk identifiers were applicable to current populations.

METHODS

Pediatrix Medical Group, Inc uses a research data system to generate a daily medical record document. The data entry portion of our database system is located as close to the patient as space allows and provides the caregivers (neonatologist and/or neonatal nurse practitioner) with direct access to the computer system. Information for this study was collected from 85 hospitals using the research data system. The neonatal units are located throughout the United States at various altitudes. The information is entered by the patient's caregiver.

Between March 1, 1996 and December 31, 1998, we collected data on 27 229 neonates cared for at 85 of our nurseries from admission until discharge. Data collected included birth weight, length, and head circumference. In addition, we collected data on race, gender, and altitude. To evaluate the effect of altitude, we compared neonates born at units located ≥4000 feet above sea level with neonates born in units <4000 feet above sea level. We used 4000 feet based on our previous assumption that below this altitude standard, sea level growth curves could be used to classify neonates as SGA, appropriate for gestational age (AGA) or LGA. In addition, we compared neonates born in Denver area hospitals with neonates born in our other sites to see whether infants born at >5000 feet above sea level have different growth patterns.

Birth weight, by definition, was recorded (to the nearest gram) during the admission process in the neonatal intensive care unit. The caregiver recorded length and head circumference at birth on admission of the patient. Both were recorded to the nearest tenth of a centimeter. Estimated gestational age (EGA) was defined as the best estimate of the neonatologist of gestational age, based on obstetrical history, obstetrical examinations, prenatal ultrasound, and postnatal physical examinations. This best estimate was re-

From *Pediatrix Medical Group, Inc, Fort Lauderdale, Florida; and ‡Duke University, Durham, North Carolina.

Received for publication Jan 20, 2000; accepted Feb 22, 2000.

Reprint requests to (R.H.C.) Director of Research, Pediatrix Medical Group, Inc, 1301 Concord Terrace, Ft Lauderdale, FL 33323-2825. E-mail: reese_clark@pediatrix.com

corded to the closest week. Gender was recorded as male, female, or unknown during the admission process. If unknown was changed to male or female before discharge, the entry reflected this. Race was recorded based on maternal race or ethnic origin. The choices within the computerized database were black, white, Hispanic, Native American, Asian, and other. A research associate monitored data collected on patient admission and discharge. On discharge, data were sent to a common database. There are no patient identifiers in this common dataset. We queried the database for the data elements outlined above and checked them for outliers and then performed our analyses.

First, we compared the intrauterine growth curves for weight, length, and head circumference that were derived from our database with published standards (Usher and McLean[2] in 1969 and Lubchenco et al[1] in 1966) that are commonly used in neonatal care units. Second, we evaluated the effect of race, gender, and altitude on gestational age, specific birth weight, length, and head circumference using a multivariate analysis of variance, where race, gender, and altitude were each evaluated with gestational age for effects on each growth parameter.

Third, we used the published reference standards to classify neonates as SGA, LGA, and AGA. When the care provider entered birth weight and gestational age, the computer determined whether the neonate's birth weight fell outside the 90th percentile limits for the assigned gestational age based on the reference curves. For hospitals located ≥4000 feet above sea level, the weights used at each gestational age to define the 10th and 90th percentiles were derived from the reference curves published by Lubchenco et al[1] and circulated by Mead Johnson and Company (Evansville, IN). For sites located below 4000 feet, we used weights derived from curves initially published by Usher and McLean[2] and modified by Babson and Benda[5] and circulated by Ross Products Division (Abbott Laboratories, Columbus, OH). Neonates with a weight less than the 10th percentile were labeled SGA; those with a weight greater that the 90th percentile were labeled LGA. We expected each subgroup of race, gender, and altitude to have ~10% of their neonates classified as SGA or LGA using the previously published reference curves. To evaluate this hypothesis, we looked at the percentage of neonates classified as AGA, LGA, and SGA by race, gender, and altitude at birth using χ^2 analysis.

To complete the comparison of our growth curves to nationally used standards, we compared the mortality rates for neonates cared for at our units on a continuum of gestational age and birth weight as reported by Lubchenco et al.[4] Our goal was to determine whether mortality rates were higher in neonates labeled SGA or LGA using definitions of SGA (<10%) and LGA (>90%) derived from our datasets.

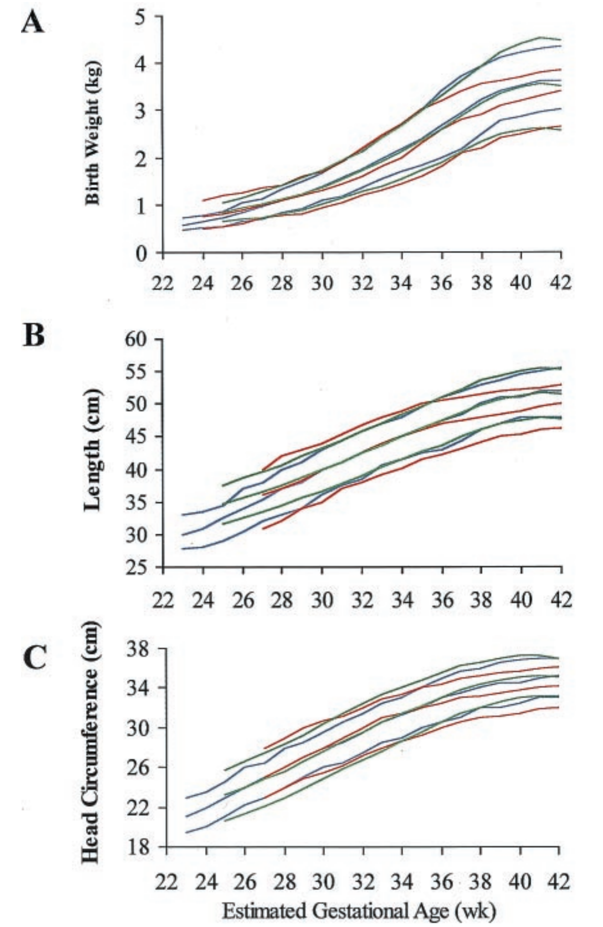


Fig 1. Differences in growth curves. Blue lines are the 10th, 50th, and 90th percentile curves plotted from data in the Pediatrix Medical Group, Inc, database. Green lines are the 3rd, 50th, and 97th percentile curves plotted from the data of Usher and McLean.[2] Red lines are the 10th, 50th, and 90th percentile curves plotted from the data of Lubchenco et al.[1] Curve A indicates birth weight; B, birth length; and C, birth head circumference.

RESULTS

Our dataset included 27 229 records. Gender assignment was available on 27 028 (missing on 201). The sample included 11 918 female and 15 110 male neonates. Data on race were recorded on 25 041 neonates; 4531 (18.1%) were black, 4951 (19.8%) Hispanic, 634 (2.5%) Asian, 76 (.7%) Native American, and 14 102 (58.9%) white neonates. Most (91%) were cared for at neonatal intensive care units <4000 feet above sea level, and most (83.5%) were classified as having a weight that was AGA.

Growth curves generated from our data were significantly different from those reported in 1969 by Usher and McLean[2] and in 1966 by Lubchenco et al[1] (Fig 1). For neonates <30 weeks of EGA, our data had a smaller variance and lower average weights, lengths, and head circumferences than those reported previously (Fig 1). In neonates >36 weeks of EGA, the variance was similar, but our curves showed that neonates in our sample were larger and heavier than neonates reported by Lubchenco et al,[1] but similar to the neonates reported by Usher and McLean[2] (Fig 1). For neonates between 30 and 36 weeks, data plotted from our patient population were similar to both previously published growth curves.

Gestational age had the largest influence on each birth parameter, and there was a significant increase for each additional week of gestation up to 40 weeks of EGA. Both race and gender had gestational age-independent effects on birth weight (Fig 2). Although neonates born at higher altitude were slightly lighter, altitude did not have a significant gestational age-independent effect on any of the birth parameters (Fig 2). At each specific week of gestation, female neonates had lower average birth weights, lengths, and head circumferences than male neonates (Fig 2). Racial comparisons showed that black neonates were consistently shorter and had lower birth weights than Hispanic and white neonates. Although the differences were consistent for race and gender, they were small. Female neonates were, on average, 95 g lighter, .6 cm shorter, and had head circumferences that were .6 cm smaller than male neonates. White and Hispanic neonates were, on average, 90 g larger, .4 cm longer, and had head circumferences that were .4 cm larger than black neonates. Both gender and

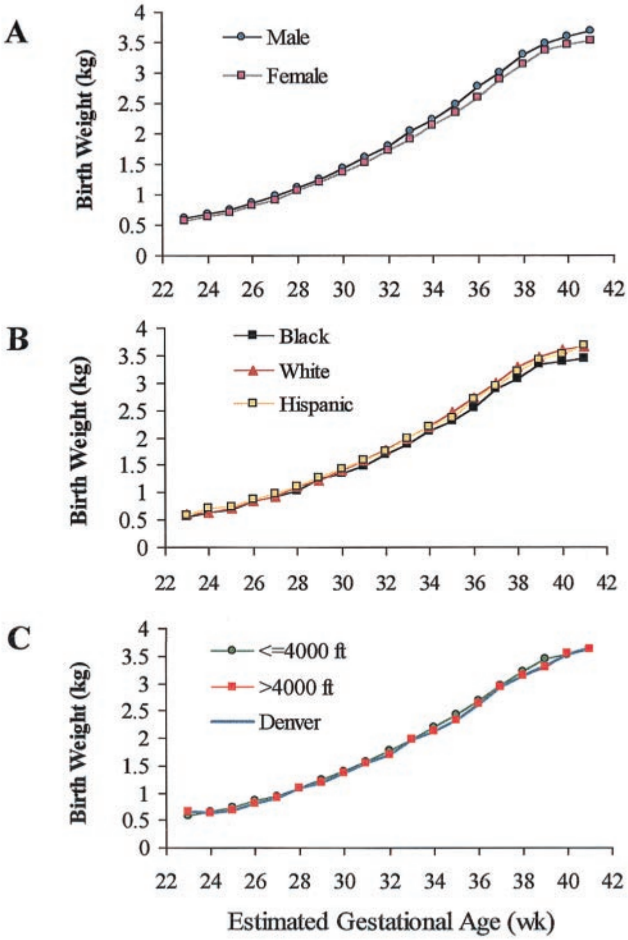


Fig 2. Growth curves of average birth weight for each gestational age by gender (A), race (B), and altitude of place of birth (C).

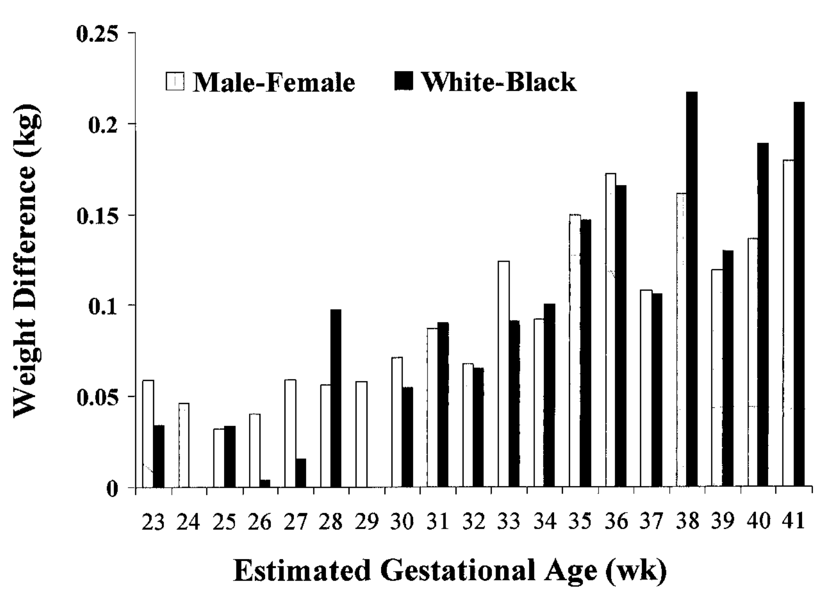
racial differences increased with gestational age (Fig 3). The only growth parameter significantly affected by race and gender independent of gestational age was birth weight. Head circumference and length differences by race and gender were consistent across gestational age. However, these differences were small and not statistically different.

Because our data suggested that female neonates were proportionately smaller than male neonates, and black neonates were proportionately smaller than white and Hispanic neonates, we evaluated the length and head circumference to weight ratios. Length and head circumference to birth weight ratios decreased with increasing gestational age and were also different for race and gender. Male neonates had lower values than did female neonates (length/weight = 20.4 cm/kg vs 21.6 cm/kg and head circumference/weight was 14.2 cm/kg vs 15.1 cm/kg). White and Hispanic neonates had lower values than did black neonates (length/weight = 20.1 cm/kg vs 20.8 cm/kg vs 22.2 cm/kg and head circumference/weight = 14.0 cm/kg vs 14.5 cm/kg vs 15.5 cm/kg). Multivariate analysis showed that gender and racial differences were independent of gestational age ($P <$ .001).

Using the AGA, LGA, and SGA definitions of Lubchenco et al[1] or Babson and Benda[5] to classify neonates admitted to our neonatal intensive care units (see "Methods"), we found that more male neonates were classified as LGA (11.5% vs 7.3%; $P <$ .001 by χ^2) and fewer were classified as SGA (7.3% vs 8.3%; $P <$ .001 by χ^2) than female neonates. Similarly, black neonates were more often classified as SGA (9.1% compared with 6.3% and 6.5%; $P <$ .001 by χ^2) and less often classified as LGA (6.3% compared with 10.4% and 10.5%%; $P <$ .001 by χ^2) than Hispanic and white neonates, respectively. Compared with neonates born at centers <4000 feet above sea level, neonates born at centers ≥4000 feet above sea level were less often classified as LGA (7.9% vs 9.8%) but were classified as SGA at the same rate (7.0% vs 7.1%). Prematurely born (<37 weeks) neonates were rarely classified as LGA (3.8%) and more commonly labeled SGA (8.2%). Term neonates were commonly classified LGA (17.3%) and uncommonly classified as SGA (5.3%).

As anticipated, both birth weight and gestational age were important predictors of death. Although the mortality rates in our cohort are lower than those reported by Lubchenco et al,[1] the relative risk of

Fig 3. The gestational age-specific difference in birth weight between male and female neonates and between white and black neonates. The y-axis is the average weight differences that were calculated from our dataset. The x-axis is gestational age.



death for SGA, AGA, and LGA neonates at each gestational age is similar to those reported by Lubchenco et al.[1] Neonates classified SGA had higher mortality rates at every gestational age. In contrast, LGA neonates had similar or lower mortality risk (Fig 4).

DISCUSSION

The importance of the growth curves described by Usher and McLean[2] or Lubchenco et al[1] over 3 decades ago is proven by the fact that they are commonly used in neonatal units today. They serve as standard references to classify neonates as SGA, LGA, and AGA. Two commercially available medical documentation systems use numbers derived from these curves to automatically assign intrauterine growth classifications (SGA, AGA, and LGA) to patients entered into the database. To assess the applicability of these standards to current patients, we compared data accumulated in our research data system to determine whether our patients were categorized appropriately. We also wanted to determine whether there was a need to correct automated systems for gender, race, and place of birth with regard to altitude. Finally, we wanted to update mortality data relative to intrauterine growth classifications and to see whether the relationship of mortality to intrauterine growth had in any way changed. Our findings require that we carefully reexamine the appropriateness of continued use of growth curves reported by Lubchenco et al[1] and Usher and McLean[2] to classify neonates SGA, LGA, and AGA.

We found significant differences between our growth plots and those reported by Usher and McLean[2] and Lubchenco et al.[1] Table 1 describes the difference in methods used for defining intrauterine growth curves. The most important differences are in the selection of patients to be studied. We performed a population-based study that included all admissions to our neonatal intensive care units. We expected that this would introduce some selection biases into our data for patients who were >33 weeks, because it is possible that near-term neonates who are SGA or LGA may be more likely to be admitted than those who are AGA. However, in our dataset, the most common reason for admission of neonates >36 weeks was to rule out sepsis or respiratory distress, not hypoglycemia or LGA.

We compared our birth weight data with a similar dataset of 150 000 neonates maintained in the Neo Knowledge data system, and our growth plots for weight are nearly identical. Our average values for birth weight are also very similar to those reported by Brenner et al,[6] who studied 31 202 neonates; Arbuckle et al,[7] who reported data on over 1 million neonates; and Alexander et al,[8] who reported data on over 3 million neonates. We believe the data suggest a role for the publication and circulation of new growth curves that are gender- and race-specific and include a larger sample of very low birth weight neonates. Additionally, a reevaluation of the definitions of AGA, LGA, and SGA based on these new curves may be appropriate.

The Lubchenco et al[1] curves were developed in the mile-high city of Denver, Colorado. Our data suggest that the current use of these curves leads to an overestimation of the number of neonates greater than the 90th percentile and underestimation of the number of neonates less than the 10th percentile, when applied to the general population. Another sampling problem is that the study by Lubchenco et al[1] included a relatively indigent population consisting of white neonates only. Similar problems affect the data reported by Babson and Benda[5] and Usher and McLean.[2] Although Brenner included both white and non-white neonates, 98% of the non-white neonates were black, and 47% of the total population was non-white. The population we studied was ethnically diverse, drawn from cities throughout the United States, and included a large numbers of premature neonates.

Our data support previous findings that intrauterine growth, as measured by birth weight; length, and head circumference, is affected by gender and race.

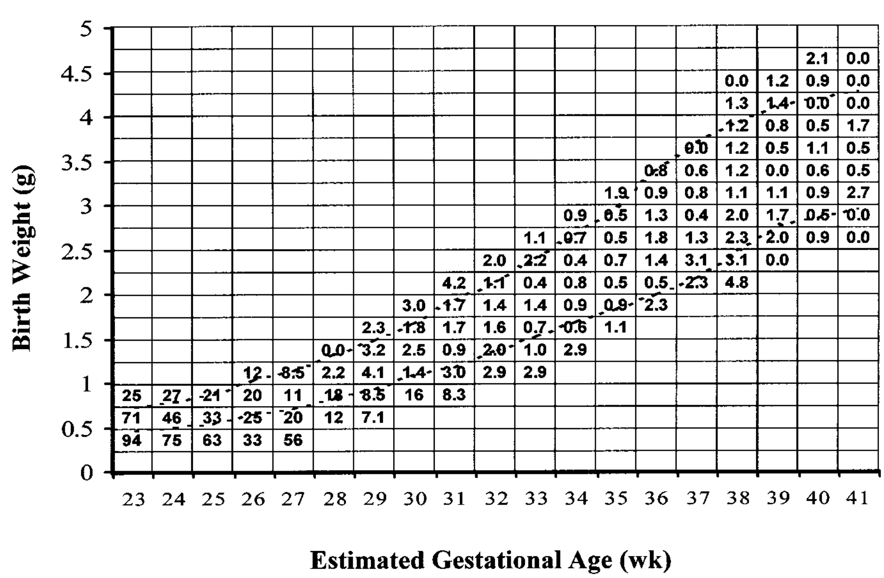


Fig 4. Birth weight- and EGA-specific mortality rates. The dashed lines of the figure represent the 10th and 90th percentile weights based on our cohort. The grid lines are plotted by each gestational age and in 250-g weight increments as previously done by Lubchenco et al.[1] Each number in the box is the percent mortality rate for the grid defined by gestational age and birth weight range.

TABLE 1. Differences in Patient Populations

	Lubchenco et al[1]	Usher et al[2]	Brenner et al[6]	Pediatrix Medical Group
Dates of measurement	1948–1961	1959–1963	1962–1969	1996–1998
n	5635	300	30 772	27 028
Male neonates	N/A	145	N/A	11 918
Female neonates	N/A	155	N/A	15 110
Race	White	White	White/non-white, 98% of non-white were black	White/Hispanic/black
Socioeconomic level	Medically indigent or partial pay	All	All	All
Altitude	Denver	Sea level	<600 ft	Continental United States—sea level → 5280 ft
Exclusions	Major congenital anomalies	Major congenital anomalies, erythroblastosis, infant of a diabetic mother, and marked fetal malnutrition	None	None
Intervals	Weekly	Grouped at EGA: 24–26 wk, 27–28 wk, 29–30 wk, 31–32 wk	Weekly from 2 through 44 wk	Weekly from 22 through 42 wk

N/A indicates not available.

As reported by Brenner et al[6] and confirmed by Arbuckle et al[7] and Alexander et al,[8] the degree of correction needed for race and gender is gestationally age-dependent. We found that female neonates had higher length and head circumference to weight ratios than male neonates at each gestational age. Similarly, black neonates had higher values for these ratios than did Hispanic and white neonates. These differences became larger with increasing gestational age for both race and gender. We did not find a need to correct for the effects of altitude in the centers providing care within Pediatrix Medical Group, Inc. However, our sample size for neonates born at centers located >4000 feet above sea level is small.

The disparity we observed for race and gender may represent either a biological or pathologic difference. For example, black mothers more often have pregnancy-associated hypertension and their neonates are more often classified as SGA. It may be that our findings can be explained by these pathologic events. That is to say, black neonates have more intrauterine problems with growth retardation and weight is more affected than length and head growth. However, we cannot explain the gender differences within the same race based on pathologic events. It is well known that male children grow differently than female children during adolescence and that this is believed to be attributable to differences in testosterone and estrogen levels. In the same way, we speculate that the gender and race differences we report are biological and/or physiologic rather than pathologic.

We provide a new and current risk evaluation chart that represents the outcomes that can be expected with today's neonatal health care system. Like previous reports, SGA neonates at each gestational age had higher mortality rates than did AGA neonates. In contrast, neonates with weights above the 90th percentile (LGA) based on our growth curves did not always have higher mortality rates. Up to 30 weeks of EGA, LGA neonates had lower mortality rates than did AGA neonates. LGA neonates assigned gestational ages of 30 weeks or more had higher mortality rates than did AGA neonates. We expect that these observations represent some selection bias. It is likely that LGA neonates may, in some cases, be AGA, more mature (later gestational age) neonates. Similarly, we suspect that some SGA neonates are more immature, AGA neonates. Unfortunately, these problems represent a clinical reality, namely, that gestational age can only be estimated, not precisely determined. Figure 4 represents a real world perspective on outcomes of neonates admitted to neonatal intensive care units in the United States and provides the clinician with an estimate of the impact attributable to the classifications of SGA, AGA, and LGA.

CONCLUSION

We suggest that there is a need for updated intrauterine growth curves that are gender- and race-specific. Additionally, we need to reevaluate the definitions of AGA, LGA, and SGA to ensure that neonates are appropriately categorized. Our data suggest that altitude, as an independent variable, may not be so powerful as to warrant altitude-specific curves. Defining indices (eg, birth weight/birth length) based on definitions of growth might decrease the inherent error introduced by estimation of gestational age. Finally, we have initiated a population-based study to evaluate the birth parameters of all neonates born at our sites to determine whether selection bias, introduced by including only admitted patients, has influenced our results.

APPENDIX

In addition to the authors, the following physicians participated in the growth study: Harrisburg, PA, K. Lorah; Utica, NY, M. Siriwardena; Wichita, KS, E. Otero, C. Smart; Ft Lauderdale, FL, S. Haskins; Boca Raton, FL, F. Miller; Coral Springs, FL, G. Melnick; Boynton Beach, FL, L. Whetstine; Denver, CO, E. Berman, D. Eichorst, J. Toney, P. Honeyfield; Houston, TX, R. Rivas, H. Pierantoni, E. O'Donnell; Englewood, CO, K. Zarlengo; West Palm Beach, FL, D. Kanter; Virginia Beach, VA, R. Balcom, E. Bollerup; Frederickburg, VA, J. Amin; Spartenburg, SC, V. Iskersky; Watertown, NY, K. Komar; Tarzana, CA, J. Banks; Ventura, CA, J. van Houten; Hoboken, NJ, M. Dyan; Stratford, NJ, J. Coleman; Trenton, NJ, K. Weiss, R. Axelrod; Fountain Valley, CA, A. Esparza; Covina, CA, V. Chundu, G. Martin; San Luis Obispo, CA, J. Martin; Newport Beach, CA, L. Wickham, B. Hannam;

Riverside, CA, M. Leitner; Las Vegas, NV, M. Kaneta; Alexandria, VA, M. Dwyer, L. Goldberg; Albuquerque, NM, R. Nederhoff, S. Swetnam; Aurora, CO, M. Brown; Phoenix, AZ, M. McQueen; Dallas, TX, J. Whitfield, T. Brannon; Roanoke, VA, R. Allen; Dayton, OH, N. Kantor; Ogden, UT, N. Harper; Columbia, SC, S. Ellis; Panama City, FL, D. Sprague; Pensacola, FL, J. Nagel; Reno, NV, G. Yup; Tacoma, WA, J. Mulligan, G. Jordan, R. Knudson; Ponce, PR, E. Ochoa; Barrington, IL, F. Uraizee; Fort Worth, TX, R. Sidebottom, D. Turbeville, M. Stanley; Charleston, WV, S. Maxwell; San Juan, PR, A. Rivera, M. Ortega; Austin, TX, J. Courtney, D. Wermer, J. Scharnberg; San Jose, CA, E. Alderete; Rock Hill, SC, A. Payne; South Bend, IN, R. White; Kansas City, MO, B. Heimes, J. Anderson; Huntington, CA, R. Liberman; Apple Valley, CA, K. Schooley; Elmira, NY, W. Helmuth, J. Felix.

REFERENCES

1. Lubchenco LO, Hansman C, Boyd E. Intrauterine growth in length and head circumference as estimated from live births at gestational ages from 26 to 42 weeks. *Pediatrics*. 1966;37:403–408
2. Usher R, McLean F. Intrauterine growth of live-born Caucasian infants at sea level: standards obtained from measurements in 7 dimensions of infants born between 25 and 44 weeks of gestation. *J Pediatr*. 1969;74: 901–910
3. Battaglia FC, Lubchenco LO. A practical classification of newborn infants by weight and gestational age. *J Pediatr*. 1967;71:159–163
4. Lubchenco LO, Searls DT, Brazie JV. Neonatal mortality rate: relationship to birth weight and gestational age. *J Pediatr*. 1972;81:814–822
5. Babson SG, Benda GI. Growth graphs for the clinical assessment of infants of varying gestational age. *J Pediatr*. 1976;89:814–820
6. Brenner WE, Edelman DA, Hendricks CH. A standard of fetal growth for the United States of America. *Am J Obstet Gynecol*. 1976;126:555–564
7. Arbuckle TE, Wilkins R, Sherman GJ. Birth weight percentiles by gestational age in Canada. *Obstet Gynecol*. 1993;81:39–48
8. Alexander GR, Himes JH, Kaufman RB, Mor J, Kogan M. A United States national reference for fetal growth. *Obstet Gynecol*. 1996;87: 163–168

A New Look at Intrauterine Growth and the Impact of Race, Altitude, and Gender

Pam Thomas, Joyce Peabody, Virginia Turnier and Reese H. Clark

Pediatrics 2000;106;e21
DOI: 10.1542/peds.106.2.e21

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

A New Look at Intrauterine Growth and the Impact of Race, Altitude, and Gender

Pam Thomas, Joyce Peabody, Virginia Turnier and Reese H. Clark

Pediatrics 2000;106;e21
DOI: 10.1542/peds.106.2.e21