# Instruments & Methods

## Detection of Macrosomia by the Individual Fetal Growth Curve Assessment Method

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**The value of the Rossavik growth model [$P = c(t)^{k + s(t)}$] was evaluated in 39 patients with singleton pregnancy who had neonatal weight outcome above the 90th percentile of our birth weight distribution for gestational age. Individual fetal growth curve standards for head and abdominal circumferences, femur diaphysis length, and weight were determined from the data of two scans obtained before 26.1 weeks' gestation and separated by an interval of at least 5 weeks. Projected crown-heel lengths were calculated from projected femur diaphysis length values. Comparisons between actual and predicted birth characteristics were expressed by the Growth Potential Realization Index (GPRI) and Neonatal Growth Assessment Score (NGAS). Excessive growth at birth was seen in almost all cases as indicated by high GPRI for weight and abdominal circumference and abnormal NGAS values. In eight of the 33 patients who delivered after 38 weeks, excessive growth was detected only by comparing birth characteristics to their predicted values at 38 weeks' gestation. Our data suggest that individual growth curve standards may identify several patterns of excessive fetal growth that could represent different pathophysiologic mechanisms, ie, failure to terminate growth after 38 weeks versus a defect in a still unknown growth regulator. The individual fetal growth curve standards method gives additional information and discriminates well between normal and excessive fetal growth. *(Obstet Gynecol 77:793, 1991)***

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The fetal growth model developed by Rossavik (Patterns and principles of fetal growth [thesis]. University of Oslo, 1982:186) specifies individual growth curve standards for various fetal anatomical parameters using the data from serial second-trimester ultrasound scans.[1–8] The general form of the Rossavik equation is:

$$P = c(t)^{k + s(t)},$$

in which $P$ is the anatomical parameter, $k$ is a fixed coefficient determined by the anatomical characteristics of the parameter being measured,[4] $c$ is related to genetic regulators of growth,[5,6] $s$ appears to represent an unknown regulatory system that modifies genetically determined growth,[5] and $t$ is the duration of growth of the parameter.[1]

Experience with the model has shown the following: 1) Birth characteristics in normally growing fetuses can be accurately predicted from only two second-trimester scans separated by an interval of at least 5 weeks[9–13]; 2) normal fetuses show relatively limited variability in their projected individual growth curves[9]; and 3) little change in growth occurs after 38 weeks.[7,8] Although the method is capable of separating normal infants from those with evidence of intrauterine growth retardation,[14] there has been little information on its value in excessive fetal growth. For this reason, we evaluated the performance of the Rossavik growth model on a sample of pregnant women who had large for gestational age (LGA) infants as indicated by cross-sectional standards. The findings of the study were compared with those previously obtained in normally growing fetuses.[10,13]

### Materials and Methods

The study group consisted of 39 consecutive women with singleton pregnancies who met the following criteria: 1) ultrasound dating by crown-rump length before 14 weeks' gestation, 2) two ultrasound scans between 15–26 weeks separated by an interval of at least 5 weeks, and 3) live birth with birth weight above the 90th percentile of the birth weight distribution as a function of gestational age previously established for the York County, Pennsylvania population.[15] The



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women were predominantly white (white 84.7%, black 12.8%, Hispanic 2.5%). Ten (25.6%) were middle class and 29 (74.4%) were indigent women. Delivery occurred between 34.7–41.9 weeks' gestation. Thirty-three (84.6%) of the 39 women delivered at or after 38 weeks. There were 18 female and 11 male infants.

Other characteristics of the patient sample, expressed as means and ranges, were: maternal age 24.1 years (16–40), parity 1.4 (0–8), maternal weight at the last menstrual period 163 lb (103–272), weight gain before 26 weeks 1.1 lb/week (−0.3–2.4), and weight gain after 26 weeks 1.3 lb/week (0.19–4.2). Of the 39 women, 12 (30.8%) were diabetics (five insulin-dependent and seven gestational diabetes); 11 (28.2%) had a history of one or more macrosomic infants (birth weight more than 4000 g). Of the five patients with insulin-dependent diabetes, one had chronic hypertension and chronic nephropathy.

All women were examined using a real-time sector scanner equipped with a 3.5-MHz transducer (ATL Mark III 450 PV real-time system [Advanced Technology Laboratories, Bellevue, WA], Diasonics Wide View, or DRF-400 scanner [Diasonics, Inc., Milpitas, CA]). All measurements were obtained by technician or physician ultrasonographers. Our ultrasound technique and the fetal weight estimation procedure have been described in previous publications.[7,9,10]

Individual fetal growth curve standards were determined for each of the 39 LGA fetuses, using the Rossavik growth model. Values for start points and coefficients $c$ and $s$ were determined for each fetus for abdominal circumference (AC), head circumference (HC), fetal diaphysis length (FL), and head and abdominal cubes from slope values calculated from data obtained in two scans before 26.1 weeks, using the equations previously presented.[10] Values for the coefficient $k$ were determined using start points based on data obtained before 26.1 weeks.[9] The means and standard deviations (SDs) of the coefficient $c$ were calculated for the five parameters and compared with the means of $c$ obtained from previously described fetuses with normal growth.[10] The differences between means were evaluated by the independent $t$ test (two-tailed comparison).

Neonatal weight, FL, HC, and AC values predicted at the actual birth age were calculated using the appropriate growth models. Predicted parameter values at 38 weeks were also obtained for the 33 women who delivered between 38.1–41.9 weeks. Crown-heel length values were calculated from the predicted FL measurements[16] using the equation:

$$\text{Crown-heel length} = 2.585 + 6.135(\text{FL}) + 0.048(\text{FL})^2.$$

All infants were examined within 24 hours of delivery. The parameter values predicted from ultrasound measurements before 26.1 weeks were compared with the weight, fronto-occipital circumference, AC (at the superior border of the umbilicus), and crown-heel length measured at birth in each infant. To evaluate the growth achieved by each individual fetus, the Growth Potential Realization Index (GPRI) values were determined for each parameter in every fetus, using the following equation[13]:

$$\text{GPRI} = \frac{\text{actual birth parameter value}}{\text{predicted birth parameter value}} \times 100.$$

Before calculation, the predicted values for AC were multiplied by 0.841 to compensate for systematic errors resulting from differences between the methods used in obtaining ultrasound and neonatal measurements.[13] For the 33 women who delivered after 38 weeks, GPRI values were obtained using the parameter values predicted both at 38 weeks and at the actual gestational age of birth.

The mean GPRI values (and SDs) were calculated and compared with 100% using the $t$ test. The ranges included all GPRI values. The individual GPRIs for the 39 LGA infants were compared with the ranges of GPRI values previously determined by Deter et al[13] for AC, HC, and weight in fetuses with normal growth. The proportions of GPRI values above normal ranges were calculated.

The GPRI values for weight, AC, and HC were then combined to calculate the Neonatal Growth Assessment Score (NGAS) for each individual fetus, using the following equation[14]:

$$\text{NGAS} = \sqrt{(\text{GPRI}_{\text{WT}}-100)^2+(\text{GPRI}_{\text{AC}}-100)^2+(\text{GPRI}_{\text{HC}}-100)^2}.$$

The individual NGAS values for these infants were then classified as a function of the NGAS boundary value of 14.7, which separates normally and abnormally growing fetuses.[14]

All GPRI and NGAS evaluations were performed by using parameter values predicted at the actual birth age and after replacing those by the parameter values predicted at 38 weeks in patients who delivered after 38 weeks.

All statistical evaluations were made using standard statistical methods on an IBM 50 PC with software developed at York Hospital. $P \leq .05$ indicated statistical significance.

## *Results*

The 39 infants in this study had birth weights above the 90th percentile of the York birth weight distribu-

**Table 1.** Coefficient *c* Used to Specify Fetal Growth Models in Fetuses With Neonatal Weight Outcomes That Were Appropriate or Large for Gestational Age

| Parameter | Coefficient *c* (cm or $cm^3$/wk) | | | | | |
|---|---|---|---|---|---|---|
| | Normal fetuses ($N$ = 70) | | Large for gestational age fetuses ($N$ = 39) | | | |
| | Mean | SD | Mean | SD | Group comparison* | Power† |
| Abdominal circumference | 1.0547 | 0.2017 | 1.0788 | 0.2371 | NS | 13.6% |
| Head circumference | 0.6817 | 0.0724 | 0.6855 | 0.0979 | NS | 0.8% |
| Femur diaphysis length | 0.2211 | 0.0355 | 0.2332 | 0.0434 | NS | 44.0% |
| Head cube | 0.0121 | 0.0035 | 0.0125 | 0.0045 | NS | 12.3% |
| Abdominal cube | 0.0320 | 0.0192 | 0.0359 | 0.0255 | NS | 20.9% |

NS = not significant ($P > .05$).
* Comparison of mean coefficients *c* (independent *t* test, two-tailed comparison).
† Probability of rejecting the null hypothesis when it is false, at significance $P = .05$.

tion as a function of gestational age.[15] The means (± SD) for weight, AC, HC, and crown-heel length of these infants at birth were: 4294 ± 410 g, 35 ± 2.2 cm, 35.5 ± 1.4 cm, and 52.6 ± 2.0 cm, respectively. The mean gestational age at birth was 39.3 weeks (range 34.7–41.9).

Table 1 compares the mean coefficient *c* of these 39 infants for AC, HC, FL, and head and abdominal cubes with those of previously described fetuses with normal neonatal weight outcome.[10] Although the mean *c* values of the LGA fetuses were slightly greater, the numbers of patients required in each group to make the differences between means significant at a probability of 0.05% and a power of 80% would have been 1200 for AC, 7000 for HC, 164 for FL, 1580 for head cube, and 500 for abdominal cube.

Table 2 compares the GPRI and NGAS values of the 39 infants with the values observed in normally growing fetuses.[13] When birth occurred after 38 weeks, these growth outcome variables were calculated using parameter values predicted at 38 weeks. Before 38 weeks, the parameter values predicted at the actual birth age were used for the calculations. The mean GPRI values for the 39 infants were significantly above 100% for all parameters. All the individual GPRI values for weight, and, with one exception, for AC, were above the ranges of GPRI values observed in normally growing fetuses.[13] Only 33.3% of the GPRI values for HC were above the normal range. All the individual NGAS values calculated from GPRI values were above 14.7, the value that discriminates between normal and abnormal growth.[14]

Table 3 shows the same calculations using parameter values obtained exclusively at the actual birth age. Of the 33 infants who delivered after 38 weeks, eight had normal GPRI values for weight and HC and normal NGAS values. Six of the these eight infants also had a normal GPRI for AC. The 25 other infants had NGAS values compatible with abnormal fetal growth. These data indicate that the eight infants with a normal NGAS value continued to grow according to their individual growth curves after 38 weeks. Among the mothers of these eight infants, four (50%) had a history of one or more macrosomic infants and four had no apparent risk factor for macrosomia. Of the 31 women with large NGAS values before or after 38 weeks, 12

**Table 2.** Growth Potential Realization Index and Neonatal Growth Assessment Score Calculated for 39 Large for Gestational Age Infants, Using Parameter Values Predicted at 38 Weeks*

| Outcome variable | Normal value (Baylor)[13,14] | Outcome variable value | | | | |
|---|---|---|---|---|---|---|
| | | Mean (%) | $P$† | SD (%) | Range (%) | Abnormal values |
| GPRI (%) | | | | | | |
| AC | 91–107 | 119.9 | ≤.01 | 6.3 | 107–135 | 38/39 (97.4%) |
| HC | 95–105 | 103.1 | ≤.01 | 3.8 | 97–115 | 13/39 (33.3%) |
| Weight | 91–108 | 135.3 | ≤.01 | 16.1 | 110–192 | 39/39 (100.0%) |
| CHL | | 103.3 | ≤.01 | 5.2 | 91–118 | |
| NGAS (AC, HC, weight) | ≤14.7 | 41.3 | | 16.0 | 15.6–98.8 | 39/39 (100.0%) |

GPRI = Growth Potential Realization Index; AC = abdominal circumference; HC = head circumference; CHL = crown-heel length; NGAS = Neonatal Growth Assessment Score.
* When birth occurred after 38 weeks, the GPRI was calculated by comparing the birth characteristics with parameter values predicted at 38 weeks and not at the actual birth age.
† Comparison of mean GPRI with 100% (*t* test).

**Table 3.** Growth Potential Realization Index and Neonatal Growth Assessment Score Calculated for 39 Large for Gestational Age Infants, Using Parameter Values Predicted at Actual Birth Age

| Outcome variable | Normal value (Baylor)[13,14] | Outcome variable value | | | | |
|---|---|---|---|---|---|---|
| | | Mean (%) | $P^*$ | SD (%) | Range (%) | Abnormal values |
| GPRI (%) | | | | | | |
| AC | 91–107 | 114.6 | ≤.01 | 7.2 | 99–135 | 33/39 (84.6%) |
| HC | 95–105 | 100.8 | NS | 3.8 | 92–114 | 2/39 (5.1%) |
| Weight | 91–108 | 121.2 | ≤.01 | 17.0 | 96–192 | 31/39 (79.5%) |
| CHL | | 100.2 | NS | 4.7 | 86–111 | |
| NGAS (AC, HC, weight) | ≤14.7 | 27.2 | | 16.8 | 2.9–98.8 | 31/39 (79.5%) |

NS = not significant ($P > .05$); other abbreviations as in Table 2.
* Comparison of mean GPRI with 100% ($t$ test).

(38.7%) were diabetic, seven (22.6%) had a history of one or more macrosomic infants, and 12 (38.7%) had no apparent risk factors. The mean maternal weight at the last menstrual period was slightly higher in the group of women with high NGAS values, ie, 164.7 ± 44.4 versus 158 ± 49.0 lb. However, because of the small size of the sample, the difference between mean maternal weights was not statistically significant ($P > .05$).

## *Discussion*

All the LGA infants in this study exceeded their respective individual fetal growth potential. Excessive fetal growth was evidenced in most cases by high GPRI values for weight and AC and abnormal NGAS values. The fact that only one-third of the infants had accelerated growth of HC as well is consistent with the observations of other authors.[17,18] These symmetrically large infants usually represent the influence of genetic factors or prolonged pregnancy,[17,18] whereas infants with large AC only are more likely to reflect metabolic or other pathologic causes.[18–22] The metabolic effect is particularly well known in diabetes mellitus, in which fetal liver and insulin-responsive soft tissues are stimulated by insulin or substances with insulin-like properties in response to maternal hyperglycemia.[19]

Our study data suggest two patterns of excessive fetal growth. The first pattern appeared to be caused by continued fetal growth after 38 weeks; it is evidenced in the eight infants who had growth outcome variables that were abnormal for 38 weeks, but normal for the actual birth age after 38 weeks. In these infants, a still unknown regulator of growth did not shut off as expected, perhaps for genetic reasons, allowing these fetuses to continue growing along their projected growth curves.[18] This type of defect would only occur after 38 weeks and would be recognized by comparing actual birth characteristics with their respective values predicted at 38 weeks by the individual fetal growth curves method.

The second pattern was seen in the other 31 patients, who had abnormal growth outcome variables at the actual birth age regardless of when they delivered. In these patients, the growth regulator mechanism could be defective for genetic reasons, or overridden by diabetes or occult carbohydrate intolerance not detected by current testing procedures, or by other nongenetic factors.[18] It is interesting that this group included all 12 patients with either insulin-dependent or gestational diabetes.

These differences in growth pattern should also be identifiable by ultrasound before birth. In the first type (continued growth after 38 weeks), differences between actual and predicted ultrasound measurements obtained before 38 weeks would be within the ranges compatible with normal growth.[18] However, scans done after 38 weeks would reveal excessive growth only if the ultrasound measurements are compared with their values predicted at 38 weeks. In the second type (defective growth regulator), deviations between actual and predicted ultrasound measurements in the third trimester would be larger than those usually observed in normal fetuses, regardless of when they were obtained.[18]

Whatever was responsible for the excessive fetal growth in our patients (genetic factor, carbohydrate intolerance, or maternal obesity) became evident in the latter part of gestation.[23] No significant differences were observed in mean $c$ values for any of the parameters between large and normal fetuses,[10] indicating little difference in growth between these two groups during the first 26 weeks of gestation.

The individual fetal growth curves method provides a comprehensive fetal growth evaluation, using the fetus as its own control instead of comparing it with population norms. It can detect when an individual fetus deviates from its genetically determined growth

potential and give useful information on the pathophysiology of the fetal growth anomaly. This new method could be very useful in metabolic acceleration of growth by providing the clinician with feedback on the effect of therapeutic action. For instance, large deviations between actual and predicted ultrasound measurements can prompt the diagnosis of unsuspected gestational diabetes or help regulate an existing carbohydrate intolerance. Correcting these large deviations by effective diet and/or insulin management may prevent macrosomia and avoid related maternal and neonatal complications. Besides its diagnostic capability, the individual fetal growth curves method may be particularly well suited to support the management of fetal growth anomalies when the problems are amenable to correction.

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