Effect of Birth Weight on Blood Pressure and Body Size in Early Adolescence

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Abstract—The fetal programming theory that birth weight contributes to blood pressure or body size in later life is examined in this study. A prospective longitudinal study was conducted on subjects who were examined as newborns and prospectively interviewed and re-examined at 11 to 14 years old. Low birth weight (<2500 g) was present in 36% of the sample. The adolescent examination included measurements of blood pressure (BP), both auscultation and oscillometric methods; anthropometrics (height, weight, and body mass index [BMI]); health status; and health behaviors. Data were analyzed on 250 subjects. Correlation coefficients of birth weight with all BP measures were nonsignificant, except for the last auscultated diastolic BP (r=0.19, P<0.01), which had a positive relationship. The simple correlation coefficients of birth weight with adolescent body size were significant and positive for weight and BMI. After multiple linear regression analyses with adjustments for age, Tanner stage, and gestational age, there was no significant effect of birth weight on adolescent weight or BMI. No significant correlations were detected for ponderal index at birth with adolescent measures. This study, which includes a substantial portion of low-birth-weight cases (36%), indicates that birth weight does not correlate negatively with later BP. These results do not support the low-birth-weight theory and indicate that childhood factors that are more proximal have a greater effect on adolescent BP than intrauterine factors. (Hypertension. 2004;43:203-207.)

Key Words: blood pressure ■ adolescence

Cardiovascular diseases are the leading causes of morbidity and mortality in the United States. These disorders emerge from an interplay of genetic and environmental factors and appear to be rooted in childhood. A number of publications have reported data supporting an additional causal theory, in which an interaction of the intrauterine nutritional environment with fetal growth also contributes to expression of cardiovascular disease in later life. According to this theory, an impaired intrauterine environment that deprives the fetus of optimal nutrient delivery programs the fetus to express, in later life, ischemic heart disease, type 2 diabetes mellitus, hypertension, and stroke.1–3 Suboptimal intrauterine nutrition would restrict fetal growth and result in lower birth weight. Thus, low birth weight has become the clinical marker of a suboptimal intrauterine environment and a possible risk factor for future chronic disease.

Despite the appeal of this novel hypothesis, it still lacks complete scientific evidence in humans. There is a substantial body of retrospective data from the Barker group4 and elegant experimental investigations in animals5 that support the fetal programming theory. However, data from epidemiological and clinical investigations have not consistently supported the theory. A significant inverse relationship between birth weight and blood pressure (BP) has been reported from several studies.6–8 In children, some investigators have detected a decrease in systolic BP (SBP) from −1.48±0.23 to −2.80 mm Hg7 for each 1-kg increase in birth weight. Alternatively, others have found a weak8 or no9,10 relationship of birth weight with BP during adolescence or in adults. Overall, there is, as yet, limited evidence in humans demonstrated by prospective data that birth weight as an indicator of the fetal environment contributes significantly to BP level in later life.

We investigated the fetal programming theory in a study of a sample of children who were examined as newborns and re-examined in early adolescence. This sample is racially diverse and represents a large range of birth weights. The purpose of this study was to determine if birth weight is a significant determinant of BP or body size in early adolescence.

Methods

This study is a prospective longitudinal investigation on children who were examined as newborn infants and re-examined at ages 11 to 14 years. The cohort of children on which this study is based was developed in 1988. Observational data on perinatal parameters, including birth weight, length, gestational age (GA) at birth, and BP, were obtained for newborn infants who were admitted to well-baby nurseries or to neonatal intensive care units during a 3-month period in 1988. Newborn units in 14 different hospitals participated.11 Data on 1160 infants represented a range of birth weight (<750 to >4000 g) and GA (24 to 42 weeks); 32.8% had low birth weights (<2500 g).
g). Race distribution was 58% black, 27% white, and 13% Hispanic. All data were based on direct measurements by trained staff. GA at birth was ascertained according to the method of Ballard et al.\textsuperscript{11} Ponderal index (PI = w/t^3, where w = weight and t = length) was computed as a measure of adiposity or thinness at birth.

A second examination of children from this cohort was performed between ages 11 and 14 years. Written informed consent was obtained from a parent and signed assent was obtained from the child at enrollment. Contact was achieved with the parent or caretaker of 414 subjects. Of those contacted, 250 (61%) were enrolled for the adolescent assessment. The reasons the remaining 164 were not enrolled were: the family no longer lived in the region (74), foster care (7), death (31), or parent declined participation (52). Deceased cases were from neonatal intensive care nurseries, wherein the deaths were attributed to complications of prematurity, sepsis, or complex congenital anomalies.

The adolescent assessments were conducted by trained research nurses during a visit to the child’s home. Research nurses were not considered nurses during a visit to the child’s home. Research nurses were not considered nurses during a visit to the child's home. Research nurses were not considered nurses during a visit to the child's home. Research nurses were not considered nurses during a visit to the child's home. Research nurses were not considered nurses during a visit to the child's home. Research nurses were not considered nurses during a visit to the child's home. Research nurses were not considered nurses during a visit to the child's home. Research nurses were not considered nurses during a visit to the child's home. Research nurses were not considered nurses during a visit to the child's home. Research nurses were not considered nurses during a visit to the child's home. Research nurses were not considered nurses during a visit to the child's home. 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examined the relationship of PI at birth, a measure of thinness at birth, with adolescent BP. Figure 2 provides these data, which also demonstrate no statistically significant relationship of PI at birth with adolescent SBP. There was also no significant correlation of PI with BP in the subgroup of term infants ($r=-0.05$, $P=0.61$). Correlation analyses, adjusted for GA and adolescent age, were performed on birth weight and PI versus SBP and DBP from each set of measurements. There were no significant correlations of PI with any BP measurement. There were also no statistically significant correlations for birth weight with the BP measurements, with the exception of diastolic BP4. The correlation coefficient for the final DBP (BP4), an auscultated BP measurement, was $r=0.19$, $P<0.01$, which is a positive relationship.

Analyses were conducted to determine if there was a relationship of birth weight with measurements of adolescent body size. Table 2 provides the simple correlation coefficients for PI with adolescent measures. For birth weight and GA, the correlation coefficients were statistically significant with height, weight, BMI, and the age-adjusted height and weight percentiles. These correlation coefficients were also positive, indicating that higher birth weight and higher GA correlate with greater height, weight, and BMI in adolescence.

Separate multiple linear regression models were built using 5 a priori designated adolescent parameters as dependent variables (height, weight, BMI, and gender-specific height and weight percentile ranks) to determine the relative influence and predictability of birth parameters on adolescent body size. Adolescent age, Tanner stage, and GA were forced into all models to adjust for the possible effects of these confounders on adolescent size and birth-weight analyses. In each of these models, birth weight was entered first as a continuous variable and next as a categorical variable grouped in 500-g increments as follows: <1500 g, 1500 to 1999 g, 2000 to 2499 g, 2500 to 2999 g, 3000 to 3500 g, and >3500 g. These results are provided in Table 3. In all 5 models, weight as a categorical variable was slightly more significant, but in no model was birth weight a statistically significant predictor of adolescent body size. The only significant relationship with adolescent size was in models 1 and 2, in which adolescent height is associated with birth length, and adolescent height percentile rank is associated with length at birth.

### Discussion

This study on the effect of newborn parameters on adolescent BP and body size detected no statistically significant inverse relationship of birth weight with adolescent BP. A significant correlation was detected for birth weight with the final DBP, but this relationship was positive, which is contrary to the low-birth-weight hypothesis. Although the simple correlation coefficients detected significant positive correlations of birth weight with adolescent weight and BMI, this relationship was no longer significant in multivariate analyses that adjusted for adolescent age and gestational age. Thus, there was also no evidence detected to support the theory that low birth weight is a determinant of obesity in adolescence.

The results of this study are contrary to recent, as well as previous, reports on the low-birth-weight theory. Walker et al. found a significant negative relationship of birth weight with later BP in children in Jamaica aged 11 to 12 years. They also found that the current weight was the strongest predictor of SBP in the adolescents. A study on young adult men in Denmark detected a significant inverse relationship of birth weight with BP. However, this relationship was only significant when adjusted for current BMI. In a study of very young children, Whincup et al. reported a graded inverse relationship of birth weight with BP in children aged 3 years. For each kilogram increase in birth weight, there was a decrease in SBP of 1.91 mm Hg and a decrease in DBP of 1.42 mm Hg. Again, a statistically significant relationship was achieved only after adjustment for current weight and BMI. Others have not detected the inverse relationship between birth weight and BP in later life. Stein et al. examined this question in a sample of young adults (mean age: 24 years) in Guatemala who had participated in a longitudinal study from birth. They found that in women there was a significant but positive association of birth weight...
Overall birth-weight groups (birth weight < 2.5 kg). The data were analyzed in the two cohorts of low-birth-weight subjects was conducted by Donker et al. Two separate cohorts were conducted on samples that have birth weights in the range of 2.5 kg. The data were analyzed in the two cohorts of low-birth-weight subjects was conducted by Donker et al.

Most of the clinical and epidemiological studies have been conducted on samples that have birth weights in the range of 2.5 kg. The data were analyzed in the two cohorts of low-birth-weight subjects was conducted by Donker et al.

### TABLE 3. Predicting Adolescent Body Size

<table>
<thead>
<tr>
<th>Multiple Linear Regression Models</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model</td>
<td>Height</td>
<td>Height Percentile Rank</td>
<td>Weight</td>
<td>Weight Percentile Rank</td>
<td>Body Mass Index</td>
</tr>
<tr>
<td>Overall R²</td>
<td>0.26</td>
<td>0.16</td>
<td>0.27</td>
<td>0.18</td>
<td>0.13</td>
</tr>
<tr>
<td>Overall P value</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Adolescent age*</td>
<td>2.86±0.99 P = 0.004</td>
<td>-11.92±2.89 P &lt; 0.001</td>
<td>0.13±1.54 P = 0.93</td>
<td>-9.31±2.79 P = 0.001</td>
<td>-0.82±0.59 P = 0.17</td>
</tr>
<tr>
<td>Tanner stage</td>
<td>3.41±0.89</td>
<td>11.97±2.58</td>
<td>7.22±1.37</td>
<td>12.04±2.49</td>
<td>2.14±0.53</td>
</tr>
<tr>
<td>Gender†</td>
<td>-0.08±1.26 P = 0.95</td>
<td>-8.07±3.68 P = 0.03</td>
<td>-0.24±1.95 P = 0.90</td>
<td>-0.40±3.54 P = 0.91</td>
<td>-0.29±0.76 P = 0.70</td>
</tr>
<tr>
<td>Gestational age</td>
<td>-0.11±0.21 P = 0.62</td>
<td>0.20±0.63 P = 0.75</td>
<td>0.07±0.33 P = 0.83</td>
<td>0.54±0.60 P = 0.37</td>
<td>0.09±0.13 P = 0.47</td>
</tr>
<tr>
<td>Birth length</td>
<td>0.44±0.19 P = 0.02</td>
<td>1.22±0.56 P = 0.03</td>
<td>0.47±0.30 P = 0.12</td>
<td>0.47±0.54 P = 0.39</td>
<td>0.01±0.12 P = 0.92</td>
</tr>
<tr>
<td>Birth weight group</td>
<td>-0.78±0.64 P = 0.22</td>
<td>-1.14±1.86 P = 0.54</td>
<td>0.32±0.99 P = 0.75</td>
<td>1.47±1.80 P = 0.42</td>
<td>0.34±0.38 P = 0.38</td>
</tr>
</tbody>
</table>

* b: SE(b), P value.
†Gender (1 = male 2 = female).

with adult BMI and DBP; in men, birth weight was not associated with adult BMI, BP, or other cardiovascular risk factors.

Although some investigations have not detected evidence to support the low-birth-weight theory, most reports support this concept to some degree. Reviews that have examined the results of multiple studies that collectively include thousands of persons estimate that a 1-kg increase in birth weight is associated with a 2- to 4-mm Hg lower SBP. Huxley et al recently examined the validity and consistency of this relationship by evaluating the data provided from more than 100 reports on clinical studies. Based on their review, these authors proposed that the findings of statistically significant inverse relationships between birth weight and later BP may be confounded by the effects of random error, particularly in ascertainment of birth weight. Other confounders involved the selective emphasis on particular results and inappropriate adjustment for current weight. These authors concluded that birth weight, as a surrogate measure of the intrauterine environment, had little if any relationship to BP level later in life.

Most of the clinical and epidemiological studies have been conducted on samples that have birth weights in the range of term newborns, with few low-birth-weight infants. Before this report, the investigation that contained the largest portion of low-birth-weight subjects was conducted by Donker et al in the Bogalusa Heart Study. Two separate cohorts were merged, and in a total sample of 1446 subjects 8.1% had low birth weight (<2.5 kg). The data were analyzed in the two birth-weight groups (<2.5 kg and >2.5 kg), separately. Regardless of birth-weight group, no correlation of birth weight and BP was identified, except a weak negative correlation with DBP in black males. Strong correlations were identified between current BMI and current BP in males and females of black and white races. The size of our sample was relatively small; however, our study sample contains a substantial portion (36%) of low-birth-weight subjects. In this prospective study, the data were obtained by direct measurement in both the newborn and adolescent examinations. Multiple measurements of BP level were obtained during uniform and standardized conditions to enable the most valid ascertainment of adolescent BP.

The tracking of birth weight with height, weight, and BMI into late adolescence was investigated in a large study of twins by Pietilainen et al. These investigators identified a significant positive relationship of adolescent body size with birth weight that was also influenced by their parents’ body sizes. Simple bivariate analysis on our data identified a significant and positive effect of birth weight on body size in adolescence. However, after adjustment for adolescent age, Tanner stage, and GA, there was no significant effect of birth weight on adolescent body size. Other factors may be contributing to the small effect of birth weight on BP that has been described in large epidemiologic investigations. Recent reports propose that it is a rapid early postnatal growth rate that contributes to later BP level and BMI. Data from one study suggested that feeding in the early postnatal period could determine future BMI and, hence, BP level. Singhal et al. provided evidence in humans that lower nutrient intakes and consequent slower growth rates in infancy might have more favorable health outcomes in later life. These reports also indicate that the extraterrine environment outweighs the intrauterine environment in effects on later BP.

**Perspectives**

The birth-weight hypothesis has been an interesting and novel concept for investigations on the origins of hypertension and cardiovascular disease. Despite the evidence from experimental studies that alterations in the intrauterine fetal environment can have effects on later life, the evidence in humans has been less clear. The number of reports that supports the birth-weight hypothesis outnumber those reports that are not supportive. However, in those reports that do support the birth-weight hypothesis, the effect has been very small. Few studies have been longitudinal and most have relied on recall or other records for determination of birth weight. The results of this longitudinal investigation do not support the birth-weight or fetal progranming theory.

**Acknowledgments**

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References


21. Reference deleted in proof.


