Immediate Postnatal Growth Is Associated With Blood Pressure in Young Adulthood

The Barry Caerphilly Growth Study

Yoav Ben-Shlomo, Anne McCarthy, Rachael Hughes, Kate Tilling, David Davies, George Davey Smith

Abstract—There is a consistent inverse association between birth weight and systolic blood pressure; however, few studies have been able to examine the immediate postnatal period. We have examined whether accelerated postnatal growth predicts adult systolic and diastolic blood pressure. We followed up participants from the Barry Caerphilly Growth Study. Blood pressure data were obtained on 679 of the original 951 subjects (73%) aged ~25 years. Both multivariable linear regression and spline models were used to examine the association among weight, length, and growth velocities with systolic blood pressure and diastolic blood pressure. Both statistical approaches showed that birth weight was inversely associated with systolic blood pressure. Only the spline models found that immediate (0 to 5 months) weight gain (β coefficient: 1.29 mm Hg; 95% CI: 0.36 to 2.23; \(P=0.007\)) and weight gain between 1 year and 9 months to 5 years (β coefficient: 1.44 mm Hg; 95% CI: 0.31 to 2.57; \(P=0.01\)) were independently associated with systolic blood pressure, whereas only immediate weight gain (β coefficient: 0.74 mm Hg; 95% CI: 0.08 to 1.41; \(P=0.03\)) was associated with diastolic blood pressure. This is the first study to demonstrate that only immediate postnatal growth predicts diastolic blood pressure in term births, whereas it adds further evidence that both birth weight and postnatal growth are associated with systolic blood pressure in support of both the fetal origins and growth acceleration hypotheses. (Hypertension. 2008;52:1-7.)

Key Words: blood pressure ■ birth weight ■ cohort study ■ growth and development ■ public health

It has been argued that the origin of many adult chronic diseases lies in the early intrauterine experience of the fetus, which programs anatomic, physiological, and endocrine pathways leading to cardiovascular and other diseases. However, fetal growth is just 1 period of development, and influences acting across other phases of the life course may be of similar importance. Evidence cited supporting the fetal origins of adult disease comes from the consistent inverse association between birth weight and blood pressure seen in both developed and developing world populations. The clinical importance of this association remains controversial with suggestions that the magnitude has been overestimated because of publication bias, may be because of genetic effects, and may have resulted from the inappropriate adjustment for adult body size. The strengthening of the birth weight association by adjustment for later size has been interpreted as providing evidence that postnatal “catch-up” growth or centile crossing, rather than prenatal development, is the more critical event, and evidence from the long-term follow-up of randomized trials of breast and formula milk has led to the “growth acceleration hypothesis”; more rapid catch-up growth, particular in the immediate postnatal infancy period and related to nutritional supplementation, rather than poor uterine development, per se, is the key component of the early life blood pressure association. However, although there are >50 studies comparing birth weight with later blood pressure, there are few that have information on growth in childhood and later blood pressure and none, to our knowledge, that have very detailed measures of postnatal and early childhood growth with adult measures of blood pressure. We have examined the fetal origins and growth acceleration hypotheses by examining whether different growth patterns in early life are associated with adult blood pressure.

Methods

The Barry Caerphilly Growth Study is a follow-up of a randomized, controlled trial undertaken from 1972 to 1974 in 2 small towns in South Wales, United Kingdom. The original trial participants were

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For birth weight, we were specifically interested in testing the accelerated early growth hypothesis.9 These time points were chosen because we were specifically interested in testing the accelerated early growth hypothesis.9 Because of the multitude of measurements, we reduced the number of time points for blood pressure. Simple linear regression models to account for potential confounders: (1) adjusting for adult age, sex, room temperature, and observer; (2) as in 1 but with mutual adjustment for all of the growth measures; (3) as in 2 but with the addition of maternal and paternal weight and height and parental social class in childhood; and (4) as in 3 but with the addition of maternal smoking and adult waist:hip ratio, the latter of which may act as an intermediary between earlier growth and adult blood pressure. We choose waist:hip ratio as our measure of adiposity, because it was a stronger predictor of blood pressure than body mass index, waist circumference, and sagittal abdominal diameter.

Results

Of the 951 subjects who completed the original study, 23 were untraceable or had died or emigrated; 679 (73%) of the remaining 928 agreed to attend the adult follow-up clinic. Male subjects were heavier than female subjects for all 14 of the time points in childhood (P<0.001). They also had higher SBP and DBP (P<0.001; Table 1). We have shown previously that younger maternal age, unclassified social class, and lighter birth weight predicted loss to follow-up (see Reference 14 for detailed analysis).

The strength of association between standardized SBP and DBP with weight at each time point is shown in panel A of the Figure. We used the standardized measures rather than actual values, because the mean and SD of DBP are smaller than those of SBP, so effects look weaker simply because

Table 1. Basic Descriptive Data on Anthropometric Measures and Adult Blood Pressure by Gender

<table>
<thead>
<tr>
<th>Variable</th>
<th>Men (n=362)</th>
<th>Women (n=318)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Weight, kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth</td>
<td>3.44</td>
<td>0.49</td>
</tr>
<tr>
<td>3.0 mo</td>
<td>6.42</td>
<td>0.73</td>
</tr>
<tr>
<td>1.5 y</td>
<td>12.1</td>
<td>1.3</td>
</tr>
<tr>
<td>5.0 y</td>
<td>19.1</td>
<td>2.3</td>
</tr>
<tr>
<td>Adult measures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>25</td>
<td>0.7</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>123.5</td>
<td>11.1</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>71.5</td>
<td>7.6</td>
</tr>
<tr>
<td>Waist:hip ratio, ×100</td>
<td>63.5</td>
<td>5.1</td>
</tr>
</tbody>
</table>

The second approach was more complex, using a within-subject analysis of all 14 childhood measurements in developing a linear spline random-effects model with 2 knots (thus dividing follow-up into 3 time periods, each with its own gradient). This accounts for repeated measures on the same individuals. The 4 between-subject random effects from the spline model are, thus, a within-subject summary of an individual’s growth curve from birth to 5 years, denoting the deviance from the average predicted birth weight and the deviance from the average predicted growth rate (kilograms per year) for each of the 3 time periods. These are defined as “immediate weight velocity” (between birth and 5 months), “infant weight velocity” (between 5 months and 1 year and 9 months), and “childhood weight velocity” (between 1 year and 9 months and 5 years). These variables were converted into z scores so that the sizes of the coefficients were directly comparable. Analyses of the adult outcome measures were undertaken using linear regression with the 4 random effects (the deviance from the average predicted birth weight and the deviance from the average predicted growth rate for each of the 3 time periods) as exposures. Additional details of this model are reported elsewhere.13

We examined the effects of early growth with 4 incremental models to account for potential confounders: (1) adjusting for adult age, sex, room temperature, and observer; (2) as in 1 but with mutual adjustment for all of the growth measures; (3) as in 2 but with the addition of maternal and paternal weight and height and parental social class in childhood; and (4) as in 3 but with the addition of maternal smoking and adult waist:hip ratio, the latter of which may act as an intermediary between earlier growth and adult blood pressure. We choose waist:hip ratio as our measure of adiposity, because it was a stronger predictor of blood pressure than body mass index, waist circumference, and sagittal abdominal diameter.

Statistical Analysis

We used 2 different approaches to model the effects of prenatal and postnatal growth on adult blood pressure. Simple linear regression was used to examine the effects of early growth on later blood pressure. Because of the multitude of measurements, we reduced the data by only including measures at birth, 3.0 months, 1.5 years, and 5.0 years. These time points were chosen because we were specifically interested in testing the accelerated early growth hypothesis.9 For birth weight, internal z scores were derived for all of the births that took place between 36 and 44 weeks gestation and were standardized by sex and gestational age (in weeks). For the other growth measures, internal z scores were standardized by sex and age at the time of the measurement for all of the children in the original study.

The strength of association between standardized SBP and DBP with weight at each time point is shown in panel A of the Figure. We used the standardized measures rather than actual values, because the mean and SD of DBP are smaller than those of SBP, so effects look weaker simply because
There was no effect with DBP. Ponderal index showed a similar pattern to birth weight, although it appeared more bimodal with a second peak around 3 years, although this could have been a chance fluctuation ($P=0.12$ for SBP). Given the similarity between the weight and ponderal index pattern, we have chosen to only present the detailed models for birth weight.

Table 2 shows the regression coefficients for birth weight and weight at 3.0 months, 1.5 years, and 5.0 years for both SBP and DBP. There was little difference if the intervention arm was included in the model, because this did not predict blood pressure. Gestational age alone did not predict either SBP ($P=0.40$) or DBP ($P=0.17$). Adjustment for the later growth measures increased the inverse association between birth weight and SBP, although this was somewhat attenuated in the final model that also included adult waist:hip ratio as a potential intermediary. All of the associations with DBP were compatible with chance. A further analysis using birth length and height found that only height at 5 years showed a positive association with SBP (model 4 height at 5 years $\beta$ coefficient: $1.93$; 95% CI: 0.52 to 3.34; $P=0.007$), whereas birth length showed an association with DBP (model 4: birth length $\beta$ coefficient: $-0.88$; 95% CI: $-1.74$ to $-0.02$; $P=0.05$). We repeated model 2 but also included the trial intervention arm to ensure that this did not alter our results; the $\beta$ coefficients for SBP with birth weight and weight at 3.0 months, 1.5 years, and 5.0 years were $-1.67$, 0.69, $-0.08$, and 0.99, respectively, which were almost the same as the results in Table 2. Results for DBP were hardly altered after including the intervention arm into the models.

The correlations among the 4 standardized weight measures were moderately high (between 0.30 and 0.72), but this was much weaker for the birth weight and spline coefficients (between 0.05 and 0.48), with the correlation between birth weight and immediate weight velocity only being 0.07. The spline models revealed different patterns of results (Table 3). Although birth weight remained inversely associated with SBP, immediate postnatal growth between 0 and 5 months, although this was somewhat attenuated in the final model that also included adult waist:hip ratio as a potential intermediary. All of the associations with DBP were compatible with chance. A further analysis using birth length and height found that only height at 5 years showed a positive association with SBP (model 4 height at 5 years $\beta$ coefficient: $1.93$; 95% CI: 0.52 to 3.34; $P=0.007$), whereas birth length showed an association with DBP (model 4: birth length $\beta$ coefficient: $-0.88$; 95% CI: $-1.74$ to $-0.02$; $P=0.05$). We repeated model 2 but also included the trial intervention arm to ensure that this did not alter our results; the $\beta$ coefficients for SBP with birth weight and weight at 3.0 months, 1.5 years, and 5.0 years were $-1.67$, 0.69, $-0.08$, and 0.99, respectively, which were almost the same as the results in Table 2. Results for DBP were hardly altered after including the intervention arm into the models.

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The results with birth length and height found that immediate height gain (fully adjusted $\beta$ coefficient: $1.50$; 95% CI: 0.46 to 2.53; $P=0.005$) and childhood height gain (fully adjusted $\beta$ coefficient: $1.78$; 95% CI: 0.45 to 3.12; $P=0.009$) were positively associated with SBP, similar to weight gain and, if anything, even stronger. Only infant height gain predicted DBP ($\beta$ coefficient: $0.73$; 95% CI: 0.02 to 1.47; $P=0.05$). There was no evidence of sex differences in the associations between early growth and blood pressure using either method.
In the light of our differential findings we went back and repeated the simple models, now using the data from the 6-month visit rather than the 3-month visit. The simple model found no real evidence of an effect of weight at 6 months with SBP (β coefficient: 0.56; 95% CI: −0.25 to 1.38; P = 0.17); however, this strengthened after adjustment for the other time points (β coefficient: 1.14; 95% CI: −0.08 to 2.36; P = 0.07) but was still consistent with chance. Similarly, with DBP the simple model for weight at 6 months was weaker than that from the spline model (β coefficient: 0.40; 95% CI: −1.17 to 0.97; P = 0.17). After mutual adjustment, this effect again strengthened, and the size of the coefficient was stronger than what we found with the spline model, although the size of the P value was very similar (β coefficient: 1.12; 95% CI: 0.27 to 1.97; P = 0.01). In the fully adjusted model (model 4), weight at 6 months remained a predictor of DBP (β coefficient: 1.12; 95% CI: 0.17 to 2.08; P = 0.02).

### Discussion

This is the first study that has modeled detailed growth trajectories over the first 5 years in relation to blood pressure in adult life. No other studies, that we know, have such detailed measures over the first few years of life and over 20 years of follow-up. We have shown that a more sophisticated approach to modeling growth periods was more sensitive in identifying effects on SBP than the conventional approach of adding anthropometric parameters at arbitrary ages, although the findings with DBP were broadly similar. This approach models changes in growth velocity rather than anthropometry.

### Table 2. Association Between Birth Weight and Weight in Infancy and Childhood (z Score) With Adult SBP and DBP

<table>
<thead>
<tr>
<th>Variables</th>
<th>Model 1 (n=623)</th>
<th></th>
<th>Model 2 (n=567)</th>
<th></th>
<th>Model 3 (n=480)</th>
<th></th>
<th>Model 4 (n=474)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>βCoefficient</td>
<td>95% CI</td>
<td>P</td>
<td></td>
<td>βCoefficient</td>
<td>95% CI</td>
<td>P</td>
<td></td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth weight*</td>
<td>−0.94</td>
<td>−1.77 to −0.11</td>
<td>0.03</td>
<td>−1.61</td>
<td>−2.60 to −0.61</td>
<td>0.002</td>
<td>−1.47</td>
<td>−2.57 to −0.37</td>
</tr>
<tr>
<td>Weight at 3.0 mo</td>
<td>0.21</td>
<td>−0.60 to 1.02</td>
<td>0.61</td>
<td>0.70</td>
<td>−0.42 to 1.82</td>
<td>0.22</td>
<td>0.47</td>
<td>−0.79 to 1.72</td>
</tr>
<tr>
<td>Weight at 1.5 y</td>
<td>−0.34</td>
<td>−0.46 to 1.15</td>
<td>0.40</td>
<td>0.07</td>
<td>−1.35 to 1.21</td>
<td>0.92</td>
<td>0.44</td>
<td>−0.98 to 1.85</td>
</tr>
<tr>
<td>Weight at 5.0 y</td>
<td>0.77</td>
<td>−0.03 to 1.57</td>
<td>0.06</td>
<td>0.97</td>
<td>−0.24 to 2.19</td>
<td>0.12</td>
<td>0.76</td>
<td>−0.66 to 2.18</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth weight*</td>
<td>−0.47</td>
<td>−1.06 to 0.11</td>
<td>0.11</td>
<td>−0.81</td>
<td>−1.51 to −0.12</td>
<td>0.02</td>
<td>−0.85</td>
<td>−1.63 to −0.08</td>
</tr>
<tr>
<td>Weight at 3.0 mo</td>
<td>0.21</td>
<td>−0.35 to 0.77</td>
<td>0.46</td>
<td>0.74</td>
<td>−0.04 to 1.53</td>
<td>0.06</td>
<td>0.56</td>
<td>−0.33 to 1.44</td>
</tr>
<tr>
<td>Weight at 1.5 y</td>
<td>0.02</td>
<td>−0.55 to 0.58</td>
<td>0.96</td>
<td>−0.18</td>
<td>−1.08 to 0.73</td>
<td>0.70</td>
<td>0.07</td>
<td>−0.93 to 1.07</td>
</tr>
<tr>
<td>Weight at 5.0 y</td>
<td>0.09</td>
<td>−0.47 to 0.64</td>
<td>0.75</td>
<td>0.11</td>
<td>−0.74 to 0.97</td>
<td>0.79</td>
<td>0.11</td>
<td>−0.89 to 1.11</td>
</tr>
</tbody>
</table>

### Table 3. Association Between Birth Weight and Immediate, Infant, and Childhood Weight Velocities (z Score) With Adult SBP and DBP

<table>
<thead>
<tr>
<th>Variables</th>
<th>Model 1 (n=600)</th>
<th></th>
<th>Model 2 (n=498)</th>
<th></th>
<th>Model 3 (n=498)</th>
<th></th>
<th>Model 4 (n=498)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>βCoefficient</td>
<td>95% CI</td>
<td>P</td>
<td></td>
<td>βCoefficient</td>
<td>95% CI</td>
<td>P</td>
<td></td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth weight*</td>
<td>−0.88</td>
<td>−1.76 to 0.01</td>
<td>0.05</td>
<td>−1.13</td>
<td>−2.22 to −0.05</td>
<td>0.04</td>
<td>−1.17</td>
<td>−2.27 to −0.08</td>
</tr>
<tr>
<td>Immediate (0 to 5 mo)</td>
<td>1.17</td>
<td>0.35 to 2.00</td>
<td>0.006</td>
<td>1.29</td>
<td>0.36 to 2.23</td>
<td>0.007</td>
<td>1.22</td>
<td>0.28 to 2.17</td>
</tr>
<tr>
<td>Infant (5 mo and 1 y and 9 mo)</td>
<td>0.43</td>
<td>−0.39 to 1.26</td>
<td>0.30</td>
<td>0.19</td>
<td>−0.84 to 1.23</td>
<td>0.72</td>
<td>0.15</td>
<td>−0.91 to 1.21</td>
</tr>
<tr>
<td>Child (1 y and 9 mo and 5 y)</td>
<td>1.00</td>
<td>0.15 to 1.84</td>
<td>0.02</td>
<td>1.44</td>
<td>0.31 to 2.57</td>
<td>0.01</td>
<td>1.31</td>
<td>0.16 to 2.46</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth weight*</td>
<td>−0.38</td>
<td>−1.00 to 0.24</td>
<td>0.23</td>
<td>−0.56</td>
<td>−1.33 to 0.21</td>
<td>0.16</td>
<td>−0.57</td>
<td>−1.35 to 0.21</td>
</tr>
<tr>
<td>Immediate (0 to 5 mo)</td>
<td>0.62</td>
<td>0.04 to 1.21</td>
<td>0.04</td>
<td>0.74</td>
<td>0.08 to 1.41</td>
<td>0.03</td>
<td>0.72</td>
<td>0.04 to 1.39</td>
</tr>
<tr>
<td>Infant (5 mo and 1 y and 9 mo)</td>
<td>−0.31</td>
<td>−0.89 to 0.26</td>
<td>0.29</td>
<td>−0.27</td>
<td>−1.00 to 0.47</td>
<td>0.47</td>
<td>−0.25</td>
<td>−1.00 to 0.50</td>
</tr>
<tr>
<td>Child (1 y and 9 mo and 5 y)</td>
<td>0.13</td>
<td>−0.46 to 0.72</td>
<td>0.67</td>
<td>0.59</td>
<td>−0.21 to 1.40</td>
<td>0.15</td>
<td>0.50</td>
<td>−0.32 to 1.32</td>
</tr>
</tbody>
</table>

For model 1, each growth measure is adjusted for adult age, sex, room temperature, and observer; model 2 is as 1, but each growth measure is now mutually adjusted for each other; model 3 is as 2 but with the addition of parental heights and weights and parental social class in childhood; and model 4 is as 3 but with the addition of maternal smoking in pregnancy and adult waist-hip ratio.

*All of the measures have been z scored.
at 1 time point, which, from an etiologic perspective, is the
more relevant exposure. We have specifically identified that
rapid postnatal weight and increases in length in the first 5 to
6 months of life may be important for both future SBP and
DBP independent of fetal growth, weight gain in later
childhood, and adult adiposity. Our associations were present
before any adjustment for adult adiposity and cannot be
dismissed as mere statistical artifact.\(^\text{19}\) Birth weight adjusted
for gestational age showed that the well-documented inverse
association with blood pressure and childhood weight gain
was positively associated with higher SBP.\(^\text{20}\) These data
suggest that both prenatal and postnatal growth patterns are
important and are consistent with both the fetal origins and
growth acceleration hypotheses. We can only speculate on the
possible pathophysiological mechanism behind these associ-
ations, but it has been argued that abnormal patterns of
growth, both prenatally and in the immediate postnatal
period, may have long-term effects on the ratio of elastin
to collagen fibers in the arterial wall.\(^\text{16}\) The effect of postnatal
growth on DBP is relatively novel and may be of clinical
importance, because longitudinal analysis from the Framing-
ham Heart Study has shown that isolated diastolic hyperten-
sion is a very strong predictor of new-onset systolic diastolic
hypertension.\(^\text{17}\)

Several publications have emerged from the long-term
follow-up of randomized, controlled trials of infant feeding,
although these studies only had prehospital discharge mea-
sures at several weeks of age. Preterm infants (130 subjects)
randomly assigned to formula milk compared with banked
breast milk showed greater weight gain before discharge and
had higher mean arterial blood pressure, DBP, and SBP,
although the latter was consistent with chance.\(^\text{8}\) A similar
study recruiting 250 small-for-gestational-age infants, ran-
domly assigned to standard formula, nutrient-enriched for-
mula, or breastfeeding, also found that the nutrient-enriched
group had higher mean arterial pressure and DBP, with a
weaker effect on SBP.\(^\text{18}\) One must be cautious before gener-
alizing the results from preterm and small-for-gestational-age
infants to all term births. Other but not all observational
cohorts have also found positive associations between child-
hood growth and later life blood pressure.

The Minneapolis Children’s Blood Pressure Study found that
caster rates of weight gain in childhood and adolescence
were both associated with increased SBP.\(^\text{19}\) The Brompton
cohort study found that conditional childhood weight gain,
between 1 and 5 years, showed a positive association with
SBP but not DBP.\(^\text{20}\) Conditional infant weight gain, between
birth and 1 year, showed a weak positive association, which
was totally attenuated after adjustment for adult body mass
index. A Japanese study from Ishikawa found that weight at
age 3 years and weight gain from ages 3 to 20 years were
positively associated with SBP and DBP, whereas an increase
in height from 3 to 20 years was inversely associated with
SBP.\(^\text{21}\) Two Finnish studies found that weight gain during the
first year of life was positively associated with SBP but not
DBP at 7\(^\text{22}\) and 31 years of life.\(^\text{23}\) A retrospective cohort study
of children born between 1934 and 1944 from Helsinki,
Finland, found that hypertensive subjects were lighter at birth
and caught up to average weight by \(\approx 6\) to 7 years, thereafter
being heavier than normotensive subjects.\(^\text{24}\) Although differ-
ent patterns were observed for subjects with diagnosed
hypertension than with undiagnosed hypertension.\(^\text{25}\)

Other studies either show no association\(^\text{26–28}\) or an inverse
association\(^\text{29–32}\) between early life changes in anthropometry
and later-life blood pressure. There are several possible
factors for these divergent findings. There are major differ-
ences in the analytic strategies. For example, a simple
analysis of weight at 1 year in our data set, as in the
Hertfordshire cohort, would find no association between early
growth and SBP. In some studies, the effects or early growth
are attenuated or even reversed after adjustment for a later
measure of growth.\(^\text{33}\) For example, the Pelotas cohort in
Brazil found that weight at 2 years was positively associated
with SBP at 15 years, but after adjustment for weight at 4 and
15 years it can became inversely associated.\(^\text{34}\) Finally, there
may be genuine heterogeneity in the effects of postnatal
growth depending on its social and biological context. So,
rapid infant growth may reflect recovery from fetal growth
restriction and normalization of body weight within a devel-
oping world context or excess growth resulting in infant
obesity in a developed world context.\(^\text{32}\)

One logical explanation for our associations is that
faster postnatal and childhood growth alter an individual’s
trajectory or endocrine status so that he or she is more
likely to be obese or insulin resistant in later life.\(^\text{35}\) In our
study, childhood weight gain was a much stronger predic-
tor of adult body mass index than immediate weight gain,
and neither predicted waist:hip ratio.\(^\text{15}\) It is possible that
postnatal growth operates through a different pathway,
such as the development of the vascular tree.\(^\text{16}\) Greater
weight gain in the first 2 weeks of life was associated with
worse endothelial function between 13 and 16 years among
preterm babies.\(^\text{36}\) We have failed previously to find an
association between birth weight and arterial stiffness in
this cohort,\(^\text{37}\) but we did not examine immediate postnatal
weight gain.

**Strengths and Limitations**
The study has several important strengths. First, we are
unaware of any study with as many as 14 measures of
growth between birth and 5 years and long-term follow-up.
This has allowed us to differentiate different patterns of
growth in early life using our more complex spline
regression methods rather than growth measures at arbit-
rary time points. This may identify potential critical or
sensitive periods for intervention, which are based on
biological growth patterns defined a priori, rather than
examining multiple time points in an ad hoc fashion and
then choosing those that show the largest association with
the outcome. Our approach also allows us to examine
within-subject variations and reduces the problem of
collinearity between repeated growth measures made over
short time periods. It also allows ones to better handle
missing data at any specific time point, which are dropped
in the simpler analysis. However, we did not have growth
data between 6 and 24 years of age. In addition, there was
some inevitable loss to follow-up, which was associated
with lighter birth weight; however, this was relatively small compared with most studies and is unlikely to be related to differences in blood pressure, because the cohort is still young and in good health.

**Perspectives**

These findings suggest that developmental factors acting both prenatally and postnatally may alter future blood pressure. We cannot elucidate the mechanisms underlying these associations. They may reflect a common genetic effect whereby genes that regulate postnatal growth themselves determine blood pressure. They may be the influence of postnatal environmental factors, which could influence an individual’s biological trajectory so that more rapid growth, adaptive in the short-term, could have a maladaptive effect in later life. They could reflect the influence of both genes and environment through epigenetic influences or a gene-environment interaction. Future work needs to explore these possibilities, preferably through an experimental paradigm, e.g., the effect of nutritional supplementation on later blood pressure in humans or animals or by studying known genetic variants that are associated either with blood pressure or growth. This study shows that both birth weight and the immediate postnatal period may be important in determining both SBP and DBP and, hence, the future risk of both essential and isolated systolic hypertension. This highlights the need to consider life course influences on the developmental trajectories of infants, children, and adolescents.

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**Disclosures**

None.

**References**

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