Birth Weight and Cardiometabolic Risk

Associations of Birth Weight and Postnatal Weight Gain With Cardiometabolic Risk Parameters at 5 Years of Age

Empar Lurbe, Consuelo Garcia-Vicent, Maria Isabel Torro, Francisco Aguilar, Josep Redon

See Editorial Commentary, pp 1166–1167

Abstract—The present prospective study assessed the impact of birth weight (BW) and postnatal weight gain on blood pressure and metabolic profile during the first 5 years of life. One hundred thirty-nine newborns (63 women) born at term after uncomplicated pregnancies and in the absence of perinatal illness were included. Subjects were divided according to size at birth in small, appropriate, and large for gestational age. After the initial evaluation on the second day of life, infants were followed up at 6 months and 2 and 5 years. Anthropometric parameters and blood pressure were measured at each visit and metabolic assessment was performed at 5 years of age. Among the BW groups, mothers did not differ in terms of age, smoking, and weight gain during pregnancy. BW was a positive determinant of systolic blood pressure at birth. Afterward, current weight was the strongest determinant, becoming significant at 2 years of age and progressively increasing in influence. At 5 years insulin, the homeostasis model assessment index and triglycerides were dependent on BW, current weight, and postnatal weight gain. In addition, BW was positively associated with high-density lipoprotein–cholesterol and inversely so to uric acid. A positive relationship among insulin, blood pressure values, and uric acid was observed even early in life. In conclusion, the acceleration of early infant weight gain may aggravate the effects of low BW. Multiple interactions between hemodynamic and metabolic parameters foreshadow the clustering of cardiometabolic risk factors later in life. (Hypertension. 2014;63:1326-1332.) • Online Data Supplement

Key Words: birth weight ▪ blood pressure ▪ child

The importance of intrauterine and early life events in the development of so-called noncommunicable disorders has been emphasized, contributing to the developmental origins of cardiometabolic disease mainly in adults.1 The phenotypic induction, subtle changes that occur in critical periods of life but have long-ranging effects, leads to changes in the individual programming origins of health or disease. Poor growth in utero contributes to insulin resistance, significant increased risk for type 2 diabetes mellitus, obesity, hypertension, dyslipidemia, and coronary heart disease.2 More recent studies have shown that the postnatal growth pattern in infancy is also an important factor in the expression of later disease.3–6 Indeed, it is a matter of great interest to know how the interaction between pre- and postnatal growth affects the development of cardiometabolic risk factors.

The time immediately before and after birth may be a sensitive period related to programming cardiometabolic risk.7–9 If this is the case, a critical window of opportunity to modify programming can exist during pregnancy and through the first years of life. This topic has gained knowledge mainly from retrospective studies; however, linking early factors with later health can be more assuredly assessed by performing prospective studies.

Those that have analyzed this issue are heterogeneous in terms of postnatal periods of growth and ages at which the potential impact has been assessed.10,11 There are few studies in which metabolic status has been evaluated in early life.12,13

The objective of the present prospective study was to assess the impact of birth weight (BW) and postnatal weight gain on blood pressure (BP) and metabolic profile during the first 5 years of life, using a cohort of newborns born at term after uncomplicated pregnancies.

Methods

Selection of Participants

Newborns born at term (gestational age ≥37 weeks) after uncomplicated pregnancies and in the absence of perinatal illness were randomly invited to participate in the study. One hundred thirty-nine subjects (63 women) were included. Exclusion criteria were multiple gestations, cesarean section, or plan to move out of the area after delivery. Gestational age at birth was ascertained according to the method of Ballard et al.14 The general characteristics of gestation and delivery were obtained from routine obstetric records. The study participants were born in the Hospital General, University of Valencia, Spain. On the second day of life, BP measurements were performed...
on the participants. Subjects were divided according to BW and gestational age in small (SGA), <10th percentile for sex; appropriate (AGA), between 10th and 90th percentile; and large (LGA), >90th percentile. The subjects were followed up at 6 months and 2 and 5 years. In each case, measurements at 6 months were performed within 1 week of the specified date and within 1 month at 2 and 5 years. At birth all parents gave permission for their children to participate in the study and informed consent was obtained. The Committee for the Protection of Human Subjects of the Hospital General approved the study according to the Declaration of Helsinki.

**Anthropometric Parameters and Biochemistry**

At birth and at 6 months, weight and length were measured by trained nurses. Length was measured in the supine position. At 2 and 5 years, body weight was recorded to the nearest 0.1 kg using a standard beam balance scale with the subjects wearing light indoor clothing and no shoes. Height was recorded to the nearest 0.5 cm using a standardized wall-mounted height board. Body mass index (BMI) and the corresponding SD were calculated with BMI being the weight in kilograms divided by the square of the height in meters. Subjects with a BMI ranging from the 85th to 95th percentile were defined as being overweight. Obesity was defined as having a BMI above the 95th percentile.

At 5 years of age a metabolic assessment was performed under fasting conditions in the early morning. Peripheral blood samples were obtained to measure glucose by the glucose oxidase method (Beckman Glucose Analyzer, Beckman Instruments, Fullerton, CA), insulin (Pharmacia Insulin RIA kit; Uppsala, Sweden), lipid profile, and uric acid. The homeostatic model assessment (HOMA) index was calculated by dividing the product of insulin (microunits per milliliter) and glucose (millimoles per liter) by 22.5.

**Casual BP Measurements**

At birth, 6 months, and at 2 and 5 years, nurses measured the BP 3 consecutive times using a Dinamap (Pro Care, GE Medical Systems Information Technologies, Inc, Milwaukee, WI) oscillometric recorder. The mean of the 3 measurements was taken as the casual BP. For measurements taken ≤24 months of age, the subjects were in the supine position or in the care provider’s lap, in a state of quiet sleep or quiet wakening. At subsequent visits, the child was seated. The proper cuff, placed on the left arm, was selected according to each subject’s upper arm length; the cuff extended completely around the arm and the bladder width covered at least two thirds of the upper arm.

**Statistical Analysis**

Differences in anthropometric, BP, and metabolic parameters among SGA, AGA, and LGA groups were assessed using ANOVA with Bonferroni correction for multiple comparisons. Associations between parameters were assessed using Pearson correlation coefficient. Multiple linear regression analysis, using BP values and metabolic parameters as dependent variables and BW, current weight, weight gain from birth to 6 months, birth to 2 years, and from birth to 5 years, as independent variables, was calculated. Sex and height were included in the multiple regression analysis.

**Results**

**General Characteristics of the Study Population**

Of the 169 subjects who were invited to participate, 15 refused the invitation and 10 did not have complete follow-up data. One hundred thirty-nine white subjects (76 men and 63 women) who fulfilled the inclusion criteria and had all their data recorded were included in the present analysis.

In relation to the general characteristics of the mothers, there were no differences among groups on mother’s age (mean age, 32.0±4.6 years; P=0.499), smoking habits (no smokers 66% and heavy smokers 6.2%; P=0.988), and weight gain during pregnancy (mean, 12.7±3.6 kg; P=0.851). Mean gestational age was 38.7±1.2 weeks, and the average BW was 3.0±0.6 kg. About BW, there were 37 (26.6%) SGA (BW, 2.3±0.3 kg), 82 (60%) AGA (BW, 3.1±0.4 kg), and 20 (14.4%) LGA (BW, 4.0±0.3 kg). Although at birth the rate of breastfeeding was 63% and was similar for all groups, it was only maintained until month 6 in 7%.

At 5 years of age, 27% of all subjects were obese. In LGA, AGA, and SGA, the prevalence was 50%, 25%, and 18%, respectively (P=0.03). Averages of BP values were 95.0±9.2/55.9±8.1 mmHg for systolic and diastolic BP, respectively. All subjects were normotensive, and only 1 was in the high–normal range specific for sex, age, and height. Biochemistry profile was the following: fasting glucose, 83.0±7.1 mg/dL; fasting insulin, 7.8±5.4 μU/mL; HOMA index, 1.6±1.2; total cholesterol, 172.4±29.8 mg/dL; high-density lipoprotein (HDL) cholesterol, 53.3±12.0 mg/dL; low-density lipoprotein-cholesterol, 101.3±26.7 mg/dL; log-triglycerides, 1.9±0.20 mg/dL; and uric acid, 3.9±0.8 mg/dL. Four children had a HOMA index >4 and no child in the entire cohort developed or met criteria for diabetes mellitus.

The anthropometric parameters at birth, 6 months, 2 and 5 years according to size at birth are shown in Table 1. Overall, weight gain during the first 6 months, 2 and 5 years were 3.7±0.8, 12.6±2.7, and 18.4±5.1 kg, respectively. No differences in weight gain were observed among the 3 BW categories at any time. At the end of the study period, SGA children had significantly lower weight as compared with those who were LGA, despite the fact that no differences in height were observed. Both BMI and BMI Z score were significantly lower in the SGA when compared with the LGA. No differences were observed between SGA and AGA children at 2 years of age or thereafter.

**BP Values**

Systolic BP values at birth, 6 months and 2 and 5 years of age are in Figure S1 in the online-only Data Supplement, grouped by BW categories (Figure S1A) and by weight tertiles (WT) at 5 years (Figure S1B). SGA children have the lowest values of systolic BP at birth as compared with the other 2 groups. At 6 months of age and thereafter, however, systolic BP was not different among groups, despite the fact that weight was still lower in the SGA. In contrast, differences existed in systolic BP among tertiles of weight at 5 years.

The determinants of systolic BP at each assessment were analyzed using a multiple regression analysis, which included systolic BP as the dependent variable and sex, BW, and weight and height at the time of measured BP as independent variables. The determinant coefficients, R², in each of the observational points are in Figure S1C. During follow-up, BW was a positive determinant of systolic BP only at the time of birth. In contrast, current weight is the strongest determinant, becoming significant at 2 years of age and progressively increasing its influence to R² 0.17 at 5 years of age.

**Metabolic Parameters**

Glucose and insulin values, HOMA index, lipid profile, and uric acid were measured in fasting conditions at 5 years of age. Grouped by BW categories, the SGA had significantly lower levels of HDL (SGA, 49.1±11.3 mg/dL; AGA, 53.6±10.0 mg/dL; LGA, 58.6±17.1 mg/dL; P<0.04) when compared with that for the LGA (P=0.04), and higher levels of uric acid.
Table 1. Anthropometric Parameters at Birth, 6 Months and 2 and 5 Years Grouped by Birth Weight Condition

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n=139)</th>
<th>SGA (n=37)</th>
<th>AGA (n=82)</th>
<th>LGA (n=20)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>At birth</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight, kg</td>
<td>3.0±0.6</td>
<td>2.3±0.3</td>
<td>3.1±0.4*</td>
<td>4.0±0.3†</td>
<td>0.000</td>
</tr>
<tr>
<td>Length, cm</td>
<td>48±2.3</td>
<td>46±1.6</td>
<td>49±1.7*</td>
<td>51±1.3†</td>
<td>0.000</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>12.80±1.84</td>
<td>11.05±1.23</td>
<td>12.98±1.27*</td>
<td>15.51±1.23†</td>
<td>0.000</td>
</tr>
<tr>
<td>PI, kg/m³</td>
<td>2.6±0.33</td>
<td>2.4±0.25</td>
<td>2.6±0.28*</td>
<td>3.1±0.28†</td>
<td>0.000</td>
</tr>
<tr>
<td>6 mo</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight, kg</td>
<td>7.8±1.0</td>
<td>6.9±0.6</td>
<td>7.9±0.9*</td>
<td>8.5±1.2*</td>
<td>0.000</td>
</tr>
<tr>
<td>Length, cm</td>
<td>67±2.5</td>
<td>65±1.8</td>
<td>68±2.2*</td>
<td>68±3.6*</td>
<td>0.000</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>17.2±1.7</td>
<td>16.3±1.3</td>
<td>17.4±1.7*</td>
<td>18.5±1.5†</td>
<td>0.000</td>
</tr>
<tr>
<td>PI, kg/m³</td>
<td>2.6±0.26</td>
<td>2.5±0.22</td>
<td>2.6±0.26</td>
<td>2.7±0.30*</td>
<td>0.011</td>
</tr>
<tr>
<td>Weight gain, kg</td>
<td>3.7±0.8</td>
<td>3.5±0.5</td>
<td>3.8±0.9</td>
<td>3.7±1.1</td>
<td>0.227</td>
</tr>
<tr>
<td>2 y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight, kg</td>
<td>12.8±2.1</td>
<td>11.8±2.0</td>
<td>12.9±1.9*</td>
<td>14.0±2.5*</td>
<td>0.003</td>
</tr>
<tr>
<td>Height, cm</td>
<td>87±3.4</td>
<td>85±3.5</td>
<td>87±3.2*</td>
<td>89±3.3*</td>
<td>0.004</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>16.2±1.9</td>
<td>16.2±1.8</td>
<td>17.0±1.8</td>
<td>17.8±2.3*</td>
<td>0.010</td>
</tr>
<tr>
<td>BMI Z score</td>
<td>0.09±1.25</td>
<td>0.38±1.19</td>
<td>0.19±1.18</td>
<td>0.56±1.47*</td>
<td>0.032</td>
</tr>
<tr>
<td>Weight gain, kg</td>
<td>12.7±2.7</td>
<td>11.9±1.6</td>
<td>12.8±2.9</td>
<td>13.3±3.3</td>
<td>0.257</td>
</tr>
<tr>
<td>5 y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight, kg</td>
<td>21.5±5.1</td>
<td>19.9±6.2</td>
<td>21.4±4.5</td>
<td>24.1±5.1*</td>
<td>0.028</td>
</tr>
<tr>
<td>Height, cm</td>
<td>111±5.3</td>
<td>109±6.1</td>
<td>111±5.1</td>
<td>112±4.6</td>
<td>0.104</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>17.3±2.8</td>
<td>16.4±3.4</td>
<td>17.3±2.7</td>
<td>19.0±2.4*</td>
<td>0.018</td>
</tr>
<tr>
<td>BMI Z score</td>
<td>0.89±1.39</td>
<td>0.26±1.57</td>
<td>0.94±1.29</td>
<td>1.85±0.89*</td>
<td>0.001</td>
</tr>
<tr>
<td>Weight gain, kg</td>
<td>18.4±5.1</td>
<td>17.5±6.2</td>
<td>18.4±4.6</td>
<td>20.3±4.8</td>
<td>0.235</td>
</tr>
</tbody>
</table>

Weight gain; birth to 6 mo, birth to 2 y, birth to 5 y. AGA indicates adequate for gestational age; BMI, body mass index; LGA, large for gestational age; PI, ponderal index; and SGA, small for gestational age.

*Significant differences with the SGA, P<0.05.
†Significant differences with the AGA, P<0.01.

(SGA, 4.3±0.8 mg/dL; AGA, 3.7±0.7 mg/dL; LGA, 3.7±0.8 mg/dL; P<0.02) when compared with those for the AGA (P=0.02) and LGA (P=0.03). Although a trend to higher levels of insulin existed, it was nonsignificant (SGA, 8.8±6.1 μU/mL; AGA, 7.6±5.4 μU/mL; LGA, 6.8±4.0 μU/mL; P=0.46) and were similar for the HOMA index (SGA, 1.7±1.4; AGA, 1.5±1.4; LGA, 1.4±1.1; P=0.46).

Metabolic parameters at 5 years when grouped by WT were the following: insulin (low WT, 6.6±5.3 μU/mL; middle WT, 6.5±3.6 μU/mL; high WT, 9.8±5.9 μU/mL; P<0.01), HOMA index (low WT, 1.4±1.2; middle WT, 1.3±0.8; high WT, 2.0±1.3; P<0.01), and triglycerides (low WT, 72±33.6 mg/dL; middle WT, 69±35.6 mg/dL; high WT, 100±52.6 mg/dL; P=0.04). The highest WT had significantly higher levels when compared with the middle WT (insulin, P=0.03; HOMA, P=0.03; and triglycerides, P=0.01) and also when compared with the low WT (insulin, P=0.03; HOMA, P=0.03; and triglycerides, P=0.02).

Furthermore, worthy of note is the relationship between BP values and metabolic parameters in the entire study population (Table S1). A positive relationship between office systolic BP and insulin, HOMA index, and log-triglycerides was observed.

Relationship Between Anthropometric, BP, and Metabolic Parameters at 5 Years of Age

Correlation coefficients between birth and current weight, as well as weight gain during the first 6 months and 2 and 5 years, with systolic and diastolic BP and metabolic parameters are shown in Table 2. BW was related to metabolic parameters, positively to HDL-cholesterol and inversely to uric acid. Weight at 5 years was positively related to systolic and diastolic BP, fasting glucose, insulin, HOMA index, and log-triglycerides. The impact of weight gain in the first 6 months of life was not related to BP or to metabolic parameters. In contrast, growth after 6 months influenced several of the parameters at 5 years of age. Although weight gain in the first 2 years was related to systolic and diastolic BP at 5 years, weight gain across the 5 years was related not only to systolic and diastolic BP values but also to metabolic parameters, insulin, HOMA index, and log-triglycerides.

The influence of the anthropometric parameters and growth gain on both BP and metabolic parameters was sought by multiple linear regression analysis (Table 3). BW was independently and inversely related to insulin, HOMA index, and uric acid. Weight at 5 years was an independent determinant of office systolic BP, insulin, HOMA index, and uric acid. Furthermore, weight gain throughout the study period was related to insulin and HOMA index, independent of current weight. The concurrent influence of both BW and current weight on insulin and HOMA index is shown in the Figure (A and B), respectively. Subjects were divided according to BW conditions and current WT, and the insulin and the HOMA index were calculated for each of the interaction groups. For
Two recent prospective studies have analyzed the importance of early postnatal growth. The study by Hof et al21 shows that the magnitude of BMI at 9 months might be a useful measure in youth healthcare practice for identifying at a young age those children with increased risk for obesity and hypertension later in life. Likewise, Skilton et al22 observed that early postnatal weight gain from birth to 18 months is independently associated with childhood overweight and obesity, excess central adiposity, and greater arterial wall thickness at 8 years of age. The present study collected a group of children born at term after a noncomplicated pregnancy and in the absence of perinatal illness. The subjects were followed up using a detailed protocol, which included both anthropometric and BP measurements at 6 months, 2 and 5 years, as well as a metabolic assessment at the final examination. The proportion of subjects that did not complete all the scheduled visits was minimal. The observed BP values and changes over time were in agreement with previous studies in which BP at birth was positively related to BW, and a rapid rise in BP during the first months of life was present.22–24 As the age of the subjects increased, BP became progressively dependent on body size while the impact of BW disappeared. Previous studies, including some from our group, have demonstrated an inverse relationship between BW and systolic BP. These studies, however, included older children25,26 and adults.7,27 The present data collected show that the relevant factor associated with BP values at 5 years is the corresponding weight and the total weight gain during the study. Chiolero et al28 observed that weight changes during any age period since birth have substantial impact on BP during childhood and adolescence, with BP being more responsive to recent than to earlier weight changes. In other studies it has been demonstrated that both early and late catch-up growth is associated with increased systolic BP in adolescence29 and the effect of change in relative body size on adult BP was more pronounced after the age of 11 years than in earlier childhood.30 All these studies are consistent with the importance of change in weight on the level of BP.

Specific attention has been paid to the exact time of growth acceleration and its association with BP values. The impact of critical periods during the first 2 years of life has not been demonstrated consistently. It is worthy to note that although SGA subjects were still smaller than LGA ones at 5 years,
BP values were similar among groups. Whether subjects born SGA will have a faster BP tracking, which becomes significant after 5 years of age, needs to be further assessed.

The knowledge that BW and postnatal growth have an impact on metabolic parameters may add useful data from a clinical point of view. According to previous studies, the metabolic risk after birth in SGA children is the consequence of prenatal programming. Changes in physiology and metabolism, as well as alterations in the sensitivity of tissues, have short-term survival advantages but may have long-term disadvantages when there is a rapid weight gain later. This is a pattern of growth, which is associated with insulin resistance later in life because rapid weight gain may lead to a disproportionately high fat mass in relation to muscle mass. The data from the present study indicate that some traces of insulin resistance can be observed even at 5 years. Levels of insulin, and mainly the HOMA index, which were highest among the SGA children, may be markers of subtle alterations in insulin resistance that will become more evident later on. Indeed, insulin levels increase mainly dependent on body weight, but the HOMA index, a more precise marker of insulin resistance, is elevated in SGA regardless of body weight. Therefore, further factors prone to promote dysregulation in carbohydrate metabolism will enhance the development of insulin resistance in SGA individuals.

At 5 years, BW was inversely related to insulin but not to BP values, which are more dependent on the current weight. Furthermore, uric acid, which was higher in SGA children than in AGA and LGA ones, was also strongly related to insulin, the HOMA index, and triglycerides. Of special interest is the additional information that has emerged from this prospective study. There was a positive relationship between insulin, BP values, and uric acid, even early in life, that is influenced by BW and postnatal growth. The clustering of higher BP values, insulin levels, and uric acid has the potential to increase cardiometabolic risk, indicating that the acceleration of early infant weight gain may aggravate the effects of low BW later in life. The multiple interactions between hemodynamic and metabolic parameters foreshadow the clustering of cardiometabolic risk factors.

The study has to be interpreted within the context of its strengths and limitations. Potential strengths of the study are the following: it is prospective in nature, it includes children born at term, it starts at birth, and it contains several years of follow-up. This is one of the first studies to look at associations between BW and postnatal growth and cardiometabolic parameters early.
in life. The limitations of the study include the small sample size and that data from clinical samples with a large proportion of SGA and LGA are not representative of the general population. This has, however, allowed for a comparison of the 2 extreme BW conditions that have different postnatal growth patterns. Although SGA is more prone to metabolic abnormalities,31 LGA is a marker of in-utero growth permissiveness, has been associated with higher childhood BMI32 and obesity at 5 years. In the present study, BMI percentiles were used to classify overweight, and although BMI is a good measure for overweight, it has limitations as an indirect measure of fat mass. Likewise, insulin levels and the HOMA index were used as surrogate markers of insulin resistance although these measurements can differ in part from the gold standard method to assess insulin resistance, the hyperinsulinemic–euglycemic clamp.33

Perspectives
The present study supports the concept that the early postnatal period is a critical window for individuals who have not only experienced a growth insult in fetal life, reflected by a small size at birth, but also in those who are born large. In fact for SGA children, metabolic alterations manifested by the highest values of insulin, HOMA index, triglycerides, uric acid, and lowest HDL are present even at as early a stage in life as 5 years of age. Moreover, LGA became obese more frequently, with the corresponding risk for comorbidities. Therefore, rapid weight gain in the postnatal period must be taken into consideration not only in SGA children but also in those who are LGA. The window of opportunity for intervention to avoid an unbalanced weight gain is a matter of interest requiring the definition of optimal postnatal growth based on the context of fetal size.

Acknowledgments
We acknowledge the expert assistance of Rachael Dix (Centros de Investigación Biomédica en Red Fisiopatología Obesidad y Nutrición, Spain).

Sources of Funding
The study was partially funded by Centros de Investigación Biomédica en Red Fisiopatología Obesidad y Nutrición (CB06/03), Instituto de Salud Carlos III, Spain; grant numbers PI11/00144 and PI081277, Instituto de Salud Carlos III Spain.

Disclosures
None.

References
What Is New?

- In children born at term after a uncomplicated pregnancy, both intrauterine and postnatal growth exert independent influences on cardiometabolic risk factors at 5 years of age.

What Is Relevant?

- Rapid weight gain in the postnatal period must be taken into consideration not only in small for gestational age children but also in those who are large for gestational age. This information provides a window of opportunity for intervention to avoid an unbalanced weight gain and to reduce the potential increment of cardiometabolic risk later in life.

Summary

In a prospective study performed in children born at term, differences in body size at birth were maintained at 6 months of life. By the age of 2 years, the body mass indexes of the small for gestational age group have already caught up with the adequate for gestational age group, whereas the large for gestational age group was still significantly bigger, and which was persistent at 5 years.

Throughout the study, systolic blood pressure was related to weight gain, and at 5 years the heaviest children had the highest systolic blood pressure. Although systolic blood pressure at birth was positively related to birth weight, from then on and until 5 years of age the impact of birth weight was negligible.

Subtle metabolic alterations observed at 5 years of age are dependent on both birth weight, as a proxy of fetal growth, and on weight gain during the postnatal period.

A clustering of higher blood pressure values, insulin levels, and uric acid levels has been observed early in life, indicating the potential to increase cardiometabolic risk later on.
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Hypertension. 2014;63:1326-1332; originally published online March 31, 2014;
doi: 10.1161/HYPERTENSIONAHA.114.03137
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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ASSOCIATIONS OF BIRTH WEIGHT AND POSTNATAL WEIGHT GAIN
WITH CARDIOMETABOLIC RISK PARAMETERS AT FIVE YEARS OF AGE

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Table S1: Correlation coefficients between office systolic blood pressure and metabolic parameters at five years

<table>
<thead>
<tr>
<th>Variable</th>
<th>Office SBP (mmHg)</th>
<th>Glucose (mg/dl)</th>
<th>Insulin (µU/ml)</th>
<th>HOMA index</th>
<th>Total C (mg/dl)</th>
<th>HDL-C (mg/dl)</th>
<th>LDL-C (mg/dl)</th>
<th>Log Trig (mg/dl)</th>
<th>Uric Acid (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Office SBP (mmHg)</td>
<td>0.219*</td>
<td>0.307†</td>
<td>0.315†</td>
<td>0.030</td>
<td>-0.146</td>
<td>0.032</td>
<td>0.204*</td>
<td>0.319†</td>
<td></td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>0.334†</td>
<td>0.436†</td>
<td>0.009</td>
<td>-0.051</td>
<td>-0.024</td>
<td>0.208*</td>
<td>0.167</td>
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</tr>
<tr>
<td>Insulin (µU/ml)</td>
<td>0.990†</td>
<td>0.13</td>
<td>-0.402†</td>
<td>0.006</td>
<td>0.606†</td>
<td>0.463†</td>
<td></td>
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<tr>
<td>HOMA Index</td>
<td>0.011</td>
<td>-0.383†</td>
<td>0.010</td>
<td>0.58†</td>
<td>0.456†</td>
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</tr>
<tr>
<td>T-C (mg/dl)</td>
<td>0.299†</td>
<td>0.846†</td>
<td>0.243*</td>
<td>-0.021</td>
<td></td>
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</tr>
<tr>
<td>HDL-C (mg/dl)</td>
<td>0.052</td>
<td>-0.502†</td>
<td>0.204*</td>
<td>-0.065</td>
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<tr>
<td>LDL-C (mg/dl)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.259†</td>
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<tr>
<td>Log Trig (mg/dl)</td>
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<tr>
<td>Uric Acid (mg/dl)</td>
<td></td>
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</tr>
</tbody>
</table>

T-C Total-cholesterol; LDL-C LDL cholesterol; HDL-C HDL cholesterol *p<0.05, †p<0.01
Panel A: Systolic blood pressure values at birth, 6 months, 2 and 5 years grouped by birth weight categories, SGA, small for gestational age; AGA appropriate for gestational age; or LGA, large for gestational age. * denotes significant differences with the SGA.

Panel B: Systolic blood pressure values at birth, 6 months, 2 and 5 years grouped by weight tertiles at 5 years, * denotes significant differences with the SGA, † denotes significant differences with the AGA.

Panel C: R^2 of the multiple regression model for systolic BP as a dependent variable, and birth weight (dotted line) and current weight (continuous line) as independent variables, adjusted by sex and current height.