Associations of Parental, Birth, and Early Life Characteristics With Systolic Blood Pressure at 5 Years of Age
Findings From the Mater-University Study of Pregnancy and Its Outcomes

Debbie A. Lawlor, PhD, MSc, MBChB; Jake M. Najman, PhD, BA; Jonathan Sterne, PhD, BSc; Gail M. Williams, PhD, BSc; Shah Ebrahim, Dm, MSc, FFPHM; George Davey Smith, DSc, MD, FFPHM

Background—We examined the associations of a range of parental and early life characteristics with systolic blood pressure at 5 years of age.

Methods and Results—Information from 3864 children who were followed up prospectively from their mother’s first antenatal clinic assessment was used. Maternal age, body mass index, and smoking during pregnancy were all positively associated with offspring systolic blood pressure at 5 years of age. The systolic blood pressure of children whose mothers had smoked throughout pregnancy was on average 0.92 mm Hg (95% CI 0.17 to 1.68) greater than that of children whose mothers had never smoked, after full adjustment. Children who had been breast fed until at least 6 months had lower systolic blood pressure than those who were breast fed for a shorter duration. Paternal body mass index and child’s weight, height, and body mass index were all positively associated with blood pressure at age 5.

Conclusions—Because childhood blood pressure tracks into adulthood, interventions aimed at early life risk factors, such as quitting smoking during pregnancy, breast feeding, and prevention of obesity in all family members, may be important for reducing the population distribution of blood pressure and thus cardiovascular disease risk. (Circulation. 2004;110:2417-2423.)

Key Words: blood pressure ■ child ■ etiology ■ smoking ■ breast feeding

Blood pressure in adult life is positively and linearly associated with cardiovascular disease, but blood pressure in childhood may also influence cardiovascular disease risk through the mechanism of blood pressure “tracking” into adulthood and through promotion of the development of premature atherosclerosis. Even blood pressure measurements made in late adolescence are associated with increased risk of cardiovascular disease over 40 to 50 years of follow-up. Furthermore, downward secular trends in blood pressure, seen in most developed countries, have occurred in all age groups, with a recent systematic review finding that important declines in blood pressure levels have taken place in 5- to 34-year-olds for at least the last 50 years.

Although treatment of high blood pressure is beneficial, treated and well-controlled hypertensive adults still have a substantial excess mortality rate and reduced survival rates compared with normotensive people, which makes identification of the means of preventing hypertension in earlier life an important objective. Available studies on the determinants of blood pressure in childhood have been small, some have suboptimal cross-sectional designs, and they have produced inconsistent results. The aim of the present study was to assess the influence of parental, intrauterine, and childhood factors on blood pressure at 5 years of age in a large cohort of Australian children who have been followed up since their mother’s first antenatal clinic visit.

Methods
Participants
The Mater-University study of pregnancy and its outcomes (MUSP) is a prospective study of 8458 (99% of the 8556 invited) women (and their offspring) who received antenatal care at a major public hospital (Mater Misericordiae Hospital) in South Brisbane between 1981 and 1984. Mothers were interviewed at their first antenatal clinic visit, 3 to 5 days after birth, 6 months after birth, and 5 years after birth. When the children reached 5 years of age, a physical examination of the children was undertaken. University and state ethics committee approval was obtained for the study.

Measurements
Birth weight data were abstracted directly from obstetric records, and continuous estimates of birth length and head circumference were...
made from measurements categorized in 8 groups in these records. Ethnicity, maternal height, past obstetric history, marital status, maternal education, maternal weight at first antenatal visit, and maternal estimate of her own prepregnancy weight and paternal height and weight were abstracted from the obstetric records or interview at the first clinic visit. Maternal smoking status was recorded at 3 stages (prepregnancy, first antenatal visit, and during the last trimester); women were grouped into those who quit smoking during pregnancy, smoked throughout pregnancy, or never smoked. The baby’s weight and breast-feeding status at 6 months were obtained from the mother’s report. Household income at birth, 6 months, and 5 years was used to categorize offspring into 3 categories of early life income: consistently poor (below average income at all 3 periods), largely middle income, or high income (above-average income at all 3 periods).

At 5 years, blood pressure was measured as the mean of 2 readings taken 5 minutes apart with a digital sphygmomanometer and appropriate cuff, with the child seated and at rest. The average of 2 measures of the child’s weight, lightly clothed, with a scale accurate to 0.2 kg, was used in all analyses. Height was measured with a portable stadiometer, and triceps skinfold thickness was measured with standard skin calipers.

### Statistical Analysis

Student’s t test and χ² tests were used to compare characteristics of those who did and did not attend the examinations at age 5. Blood pressure measurements were adjusted for gender and age, using the child’s exact age in days at examination. Multiple linear regression was used to assess the associations of exposures with systolic blood pressure at age 5, with adjustment for potential confounding and mediating factors. To examine possible nonlinear associations, graphs of the relationships between exposures and outcomes were plotted, and quadratic terms, for continuous variables, were included in regression models. F-tests were used to examine interactions between the effects of size at birth and size at age 5 on blood pressure. Systolic and diastolic blood pressures were correlated (Pearson’s correlation coefficient 0.56 [95% CI 0.54 to 0.58]), and there were no substantive differences between the associations with systolic blood pressure presented in this report and similar associations with diastolic blood pressure (data not presented).

### Results

Among the 8456 maternal participants, there were 7223 singleton live births discharged alive from hospital and not adopted. Of these, 3864 (53%) attended the examination at 5 years of age. Table 1 shows the differences in parental and childhood characteristics between those who did and did not attend at 5 years.

The mean (SD) systolic blood pressure of participating children was 104.0 (9.7) mm Hg. Table 2 shows age- and gender-adjusted linear regression coefficients for each of the exposures on systolic blood pressure at age 5.

### Maternal Factors

Table 3 shows associations between maternal characteristics and offspring blood pressure with adjustment for potential confounding and mediating factors. Only children with complete data on all covariates were included in analyses; blood pressure did not differ between those with and those without

### Table 1. Differences in Parental and Birth Characteristics of Children Who Attended Examination at 5 Years and Those Who Did Not

<table>
<thead>
<tr>
<th>Maternal characteristics</th>
<th>Children Who Attended 5-Year Examination (n=3864)</th>
<th>Children Who Did Not Attend 5-Year Examination (n=3359)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>25.0 (5.1)</td>
<td>24.1 (5.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prepregnancy weight, kg</td>
<td>58.2 (11.4)</td>
<td>57.7 (11.4)</td>
<td>0.05</td>
</tr>
<tr>
<td>Height, cm</td>
<td>162.3 (6.4)</td>
<td>162.5 (6.6)</td>
<td>0.49</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>22.0 (4.1)</td>
<td>21.8 (4.0)</td>
<td>0.03</td>
</tr>
<tr>
<td>Smoker in last trimester, %</td>
<td>35.3</td>
<td>44.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>First pregnancy, %</td>
<td>38.9</td>
<td>42.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Single, %</td>
<td>8.0</td>
<td>13.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Educated to less than 10th grade, %</td>
<td>17.5</td>
<td>19.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Family income &lt;$10 400 during year of pregnancy, %</td>
<td>30.6</td>
<td>40.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>White, %</td>
<td>94.3</td>
<td>89.5</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Paternal characteristics*</th>
<th>Children Who Attended 5-Year Examination (n=3864)</th>
<th>Children Who Did Not Attend 5-Year Examination (n=3359)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight, kg</td>
<td>74.1 (12.4)</td>
<td>73.2 (12.7)</td>
<td>0.006</td>
</tr>
<tr>
<td>Height, cm</td>
<td>176.6 (7.7)</td>
<td>176.0 (8.6)</td>
<td>0.004</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>23.7 (3.5)</td>
<td>23.7 (5.6)</td>
<td>0.7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Birth/infant characteristics</th>
<th>Children Who Attended 5-Year Examination (n=3864)</th>
<th>Children Who Did Not Attend 5-Year Examination (n=3359)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age, wk</td>
<td>39.4 (1.7)</td>
<td>39.2 (2.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Birth weight, g</td>
<td>3401.8 (523.3)</td>
<td>3319.6 (586.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Birth length, cm</td>
<td>51.8 (3.0)</td>
<td>51.5 (3.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Birth head circumference, cm</td>
<td>34.8 (1.5)</td>
<td>34.7 (1.6)</td>
<td>0.002</td>
</tr>
<tr>
<td>Still breast feeding at 6 months, %</td>
<td>32.0</td>
<td>25.8</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are mean (SD) or percent. *Reported by mother.
complete data. Maternal age, body mass index, height, and smoking throughout pregnancy were all independently and positively associated with offspring blood pressure. The positive association with maternal age was present even when the analyses were restricted to first births: 0.50 (95% CI 0.08 to 1.08) mm Hg per increase in 1 SD of maternal age, although this was slightly weaker than the association among all other women (0.95 [95% CI 0.53 to 1.36]; \( P \) for difference \( 0.21 \)).

A comparison of women who quit smoking during pregnancy (\( n = 401 \)) and those who continued (\( n = 1191 \)) suggested that quitting during pregnancy could prevent the adverse effect of maternal smoking during pregnancy on offspring blood pressure. The fully adjusted difference (quitters minus persistent smokers) was \(-0.69 \) (95% CI \(-1.80 \) to 0.42) mm Hg. However, because of small numbers, this difference was imprecisely estimated.

### Paternal Factors

The association of paternal factors with offspring blood pressure was assessed in 3000 offspring with complete data on all variables considered in the fully adjusted model. Blood pressure did not differ between those with complete data and the remainder. Each SD (4.56 kg/m²) increase in paternal body mass index was associated with an age- and gender-adjusted increase in offspring blood pressure of 1.15 (95% CI 0.71 to 1.56) mm Hg. With adjustment for family income during the year of pregnancy, together with maternal characteristics (age at first antenatal visit, body mass index, height, body mass index.)
TABLE 3. Multivariable Associations of Maternal Characteristics With Offspring Systolic Blood Pressure at Age 5 Years

<table>
<thead>
<tr>
<th>Maternal Characteristics</th>
<th>Regression Coefficient (95% CI) of Systolic Blood Pressure (mm Hg) per Maternal Risk Factor</th>
<th>Adjusted for Potential Mediating Factors (on the Causal Pathway)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adjusted for Potential Confounding Factors</td>
<td>Adjusted for Potential Mediating Factors (on the Causal Pathway)</td>
</tr>
<tr>
<td></td>
<td>Child’s Age (Days) and Gender</td>
<td>Child’s Age (Days), Gender, Other Maternal Characteristics, and Birth Weight</td>
</tr>
<tr>
<td>Age at first antenatal visit (per SD, 1 SD=5.2 y)</td>
<td>0.63 (0.28 to 0.97)</td>
<td>0.80 (0.38 to 1.22)</td>
</tr>
<tr>
<td>Prepregnancy body mass index (per SD, 1 SD=4.01 kg/m²)</td>
<td>0.78 (0.46 to 1.10)</td>
<td>0.65 (0.20 to 0.91)</td>
</tr>
<tr>
<td>Maternal height (per SD, 1 SD=6.5 cm)</td>
<td>0.37 (0.01 to 0.72)</td>
<td>0.41 (0.04 to 0.78)</td>
</tr>
<tr>
<td>Smoking throughout pregnancy (difference: yes/never smoked)</td>
<td>0.73 (0.00 to 1.47)</td>
<td>0.88 (0.10 to 1.65)</td>
</tr>
<tr>
<td>Smoking immediately before pregnancy but not at end (difference: yes/never smoked)</td>
<td>0.02 (−1.00 to 1.05)</td>
<td>0.10 (−1.00 to 1.20)</td>
</tr>
<tr>
<td>Single (yes/no)</td>
<td>0.31 (−1.14 to 1.71)</td>
<td>0.46 (−1.09 to 2.00)</td>
</tr>
<tr>
<td>Low education (&lt;10th grade) (difference: yes/no)</td>
<td>1.02 (0.15 to 1.91)</td>
<td>0.85 (−0.12 to 1.82)</td>
</tr>
<tr>
<td>Family income &lt;$10 400 during year of pregnancy (difference: yes/no)</td>
<td>0.51 (−0.21 to 1.17)</td>
<td>0.63 (−0.11 to 1.36)</td>
</tr>
<tr>
<td>White (yes/no)</td>
<td>0.78 (−0.82 to 2.39)</td>
<td>0.63 (−1.00 to 2.25)</td>
</tr>
</tbody>
</table>

Mean systolic blood pressure (95% CI) by birth order among 3-year-old children, adjusted for maternal age in pregnancy and child’s age (days) and gender. BP indicates blood pressure.

Birth Order
There was a J-shaped association between birth order and blood pressure (P for quadratic term=0.002; Figure 1). With adjustment for age and gender, blood pressure at age 5 was 0.60 mm Hg (95% CI 0.43 to 1.34) mm Hg. Further adjustment for birth weight did not alter this association, but additional adjustment for weight and height of the offspring at age 5 years attenuated it to 0.63 (95% CI 0.15 to 1.07) mm Hg. Each SD (8.15 cm) increase in paternal height was associated with an age- and gender-adjusted increase in offspring blood pressure of 0.57 (95% CI 0.20 to 0.93) mm Hg (P<0.001). With full adjustment for all potential confounding and mediating factors, this attenuated to the null: 0.05 (95% CI −0.35 to 0.45) mm Hg.

Birth Size and Breast Feeding
Table 4 shows the associations between birth size and systolic blood pressure among 2989 children with complete data on all variables included in the fully adjusted models. Blood pressure did not differ between those with and without complete data. Additional adjustment for potential confounding factors (maternal and paternal characteristics and socioeconomic position) did not substantively alter the weak positive associations between birth size and blood pressure. Additional adjustment for weight or body mass index at age 5 did not alter the associations (data not shown). However,
1-SD (1.6 kg/m²) increase in body mass index was associated with a 1.33 mm Hg (95% CI 1.19 to 1.43) increase in systolic blood pressure in age- and gender-adjusted models (Table 2), and this association attenuated to the null in fully adjusted models.

**Childhood Height, Weight, and Body Mass Index**

The positive associations between the child’s height, weight, and body mass index at age 5 and their blood pressure at age 5 (Table 2) were not substantively altered by additional adjustment for maternal and paternal body mass index and height, maternal age during pregnancy, smoking during pregnancy, educational attainment, family income, and birth weight. The fully adjusted change in blood pressure for a 1-SD (1.6 kg/m²) increase in body mass index was 3.37 mm Hg (95% CI 2.99 to 3.75); and for a 1-SD (5.5 cm) increase in height, it was 2.52 mm Hg (95% CI 2.13 to 2.92 mm Hg). Triceps skinfold thickness at age 5 was only weakly positively associated with systolic blood pressure in age- and gender-adjusted models (Table 2), and this association attenuated to the null in fully adjusted models.

**Life Course Influences on Blood Pressure at Age 5**

A model containing the child’s gender, age in days, weight, and height at the time of blood pressure examination explained 19% of the variation in the child’s blood pressure at age 5. The final regression model, which additionally included maternal age, body mass index, smoking throughout pregnancy, educational status, family income during the year of pregnancy, paternal body mass index, birth order (quadratic term), and breast feeding history, explained 27% of the variation.

**Discussion**

Maternal and paternal factors, together with aspects of pregnancy, breast feeding, and childhood body build, were independently associated with systolic blood pressure at age 5 years.

**Study Strengths and Limitations**

Strengths of this study are the detailed maternal and obstetric data, the large size, and the prospective follow-up. The loss to follow-up was 47%, and the offspring who were not examined at age 5 were more likely to have mothers who were smokers and who were socioeconomicly disadvantaged. This selective follow-up would only lead to the present results being an exaggeration of the true effect if the associations were in opposite directions or markedly weaker in nonresponders, which seems unlikely. Paternal size was based on maternal report. Any misclassification is likely to be nondifferential and therefore would tend to dilute the associations. Measurement error in birth length and head circum-

### TABLE 4. Multivariable Associations of Birth Size With Offspring Systolic Blood Pressure at Age 5 Years

<table>
<thead>
<tr>
<th>Child’s Age (Days) and Gender</th>
<th>Child’s Age (Days), Gender, and Gestational Age*</th>
<th>Child’s Age (Days), Gender, Gestational Age, Maternal and Paternal Characteristics, and Socioeconomic Position†</th>
<th>Adjusted for Potential Confounding Factors</th>
<th>Adjusted for Potential Mediating Factor (on the Causal Pathway)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight (1 SD=557.5 g)</td>
<td>0.20 (−0.18 to 0.58)</td>
<td>0.36 (−0.09 to 0.81)</td>
<td>−0.31 (−0.78 to 0.14)</td>
<td></td>
</tr>
<tr>
<td>Birth length (1 SD=2.96 cm)</td>
<td>0.22 (−0.21 to 0.65)</td>
<td>0.27 (−0.18 to 0.73)</td>
<td>−0.22 (−0.67 to 0.23)</td>
<td></td>
</tr>
<tr>
<td>Birth ponderal index (1 SD=3.97 kg/m²)</td>
<td>−0.16 (−0.61 to 0.28)</td>
<td>−0.16 (−0.60 to 0.22)</td>
<td>−0.12 (−0.58 to 0.32)</td>
<td></td>
</tr>
<tr>
<td>Head circumference (1 SD=1.59 cm)</td>
<td>0.01 (−0.46 to 0.45)</td>
<td>0.01 (−0.46 to 0.47)</td>
<td>−0.34 (−0.80 to 0.12)</td>
<td></td>
</tr>
</tbody>
</table>

n=2989 with complete data on all variables included in fully adjusted models.

*Age (in days) and gender of child plus gestational age (continuous).

†As above (†) plus height at age 5 years (continuous).

‡As above (‡) plus height at age 5 years (continuous).
Obesity and Childhood Blood Pressure
Parent’s body mass index and child’s weight and body mass index were positively and independently associated with childhood systolic blood pressure at age 5. Although these associations may reflect a genetic predisposition to obesity and high blood pressure, they are also likely to be strongly influenced by family diet and physical activity levels. Our findings, together with those of others, highlight the importance of childhood and family obesity as a determinant of higher blood pressure in childhood.

Maternal Smoking, Maternal Age at Pregnancy, and Childhood Blood Pressure
An important finding in the present study is the association between maternal smoking and higher blood pressure in offspring. This result is consistent with that of 1 other large cross-sectional study and a smaller prospective cohort study, although a second small (n = 518) prospective study found no association between maternal smoking and offspring systolic blood pressure at age 5 to 9 years. To the best of our knowledge, this is the first study to suggest that the offspring of women who quit smoking during pregnancy have no higher blood pressure at age 5 than the offspring of women who never smoked. These results should be replicated in other studies. However, they provide further evidence to suggest that programs that support mothers to stop smoking during pregnancy are beneficial to both their health and the future health of their offspring.

Our finding of a positive association between maternal age during pregnancy and offspring blood pressure is consistent with 1 other study and with a recent study assessing this association in the newborn period. Because a positive association between maternal age and blood pressure persisted when analyses were restricted to first-born children, the trend, in industrialized countries, to delay first birth until the late 20s and early 30s may result in an upward shift in the population distribution of blood pressure in future generations.

Birth Order and Childhood Blood Pressure
One previous study has shown that blood pressure increases with the number of siblings. The J-shaped association between birth order and systolic blood pressure found in the present study may reflect the similarly shaped association between parity and coronary heart disease in older women. Multiparous women tend to be more insulin resistant than other women. These disturbances of pregnancy may be associated with greater blood pressure in their offspring. The higher blood pressure in first-born compared with second-born children may be related to maternal age. Preeclampsia and high blood pressure are more common in first pregnancies, and offspring of women who experience these complications are more likely to have higher blood pressure and obesity in later life. If these mechanisms do explain the observed association between birth order and systolic blood pressure, interventions to control metabolic disturbances during pregnancy would be expected to reduce offspring blood pressure.

Birth Size, Infant Feeding, and Childhood Blood Pressure
Although birth size did not influence blood pressure at age 5, it is possible that such effects only become apparent with increasing age. The emergence of a weak inverse association between birth weight and systolic blood pressure with additional adjustment for contemporary height suggests that accelerated linear postnatal growth may influence systolic blood pressure, although we found no evidence of an interaction between birth size and contemporary size in the present study.

The protective effect of breast feeding on childhood blood pressure has also been reported in other observational studies and in a 13-year follow-up of premature infants who took part in an infant feeding trial. Breast feeding may be associated with lower blood pressure through a hormonal effect, may be related to levels of sodium in infant formulas, or may be due to beneficial effects of the long-chain polyunsaturates in breast milk.

Study Implications
The individual regression coefficients for early life exposures on blood pressure at age 5 years found in the present study are modest, with the largest being for the child’s weight at the time of blood pressure measurement. However, together, these maternal, paternal, infancy, and childhood characteristics explained more than 25% of the variation in systolic blood pressure at age 5; if we had been able to allow for within-subject variation, this estimate may have been larger. Further research is required to examine the effect of these early life exposures on adult disease outcomes. Such effects may cumulatively have important public health implications.

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References


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