Determinants of Blood Pressure in Preschool Children
The Role of Parental Smoking

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Background—Hypertension is the leading risk factor for cardiovascular disease. Although accumulating evidence suggests tracking of blood pressure from childhood into adult life, there is little information regarding the relative contributions of genetic, prenatal, biological, behavioral, environmental, and social determinants to childhood blood pressure.

Methods and Results—Blood pressure and an array of potential anthropometric, prenatal, environmental, and familial risk factors for high blood pressure, including parental smoking habits, were determined as part of a screening project in 4236 preschool children (age 5.7±0.4 years). Smoking was reported by 28.5% of fathers and 20.7% of mothers, and by both parents 11.9%. In addition to classic risk factors such as body mass index, prematurity, low birth weight, and parental hypertension, both systolic (+1.0 [95% confidence interval, +0.5 to +1.5] mm Hg; P=0.0001) and diastolic blood pressure (+0.5 [+0.03 to +0.9] mm Hg; P=0.03) were higher in children of smoking parents. Parental smoking independently affected systolic blood pressure (P=0.001) even after correction for other risk factors, such as body mass index, parental hypertension, or birth weight, increasing the likelihood of having a systolic blood pressure in the top 15% of the population by 21% (2% to 44%; P=0.02).

Conclusions—In healthy preschool children, parental smoking is an independent risk factor for higher blood pressure, adding to other familial and environmental risk factors. Implementing smoke-free environments at home and in public places may provide a long-term cardiovascular benefit even to young children. (Circulation. 2011;123:292-298.)

Key Words: blood pressure ■ hypertension ■ pediatrics ■ risk factors ■ smoking

A
rtinal hypertension is probably established early in life.1–3 An increasing body of evidence suggests tracking of blood pressure (BP) from childhood into adulthood.2 The individual BP "channel" in childhood and its tracking into adult life is believed to be a complex function of numerous genetic, biological, behavioral, environmental, and social determinants.3–5 Obesity, which tends to co track along with BP from adolescence to adulthood, is a major determinant of BP in the second decade of life.6,7 In addition, socioeconomic conditions may play an independent important role even in childhood.3

Clinical Perspective on p 298

It is unknown at which minimal age BP becomes a sensitive readout of the various intrinsic and extrinsic determinants of vascular tone and a valid predictor of long-term cardiovascular risk. To elucidate whether casual BP measurements provide meaningful information about risk factor exposure at a very young age, we performed a population-based study in a large sample of preschool children aged 5 to 6 years.

Particular emphasis was laid on the role of passive smoking, a readily modifiable environmental factor. Because passive smoking in this age group is usually due to living with smoking parents, the smoking habits of mothers and fathers were recorded in detail and correlated with BP findings.

Methods

In Germany, children approaching school age undergo a compulsory assessment of physical and cognitive maturation organized and performed by the regional health authorities. In the Rhein-Neckar district in the southwestern part of Germany, up to 5000 kindergarten children are examined each year. In the Heidelberg Kindergarten Blood Pressure Project, BP measurements, additional anthropometric assessments, and a detailed medical and social history were added to the default examination schedule. The project was conducted from February 2007 until October 2008 in preschool children. All children attending the last year of kindergarten were eligible to enter the study. The study fulfilled the criteria of the Declaration of Helsinki and was approved by the Ethics Committee of the Medical Faculty at Heidelberg University. Parents and children were informed about the study by oral and written information and gave written informed consent and verbal assent.

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BP and Clinical Measurements

Measurements were performed in a quiet and temperate room. Children were measured without shoes in light garments. Weight and height were measured with the use of electronic scales (at 0.1 kg) and fixed stadiometers (at 0.1 cm). The body mass index (BMI) was calculated as weight divided by the height squared (kg/m²). BMI centiles were derived from German reference data, and standard deviation scores by age and gender were calculated by the LMS method of Cole and Green.

The BP measurements were performed by a team of 8 carefully trained nurses whose adherence to the measurement protocol was assessed regularly. After 5 minutes of rest, sitting BP was measured 3 times by auscultatory aeroid sphygmomanometry, with the use of an appropriate cuff size adapted to arm circumference according to standardized procedural guidelines. BS standard deviation score values were calculated, and elevated BP was defined according to American reference data.

Triceps and subscapular skinfold thickness measurements at the right-hand side were taken with the use of Harpenden calipers. Three readings were obtained, and the mean values were used to calculate percent body fat by the formula of Slaughter et al.

Assessment of Cardiovascular Risk Factors

Birth weight and length of the studied children were documented. Moreover, parents were asked to complete a structured questionnaire about disorders during pregnancy (pregnancy-associated diabetes mellitus or hypertension), tobacco smoking during pregnancy, mother’s and father’s current weight and height, age, cardiovascular risk factors (arterial hypertension, diabetes mellitus, or tobacco smoking), educational level, and occupational status. Passive smoking was recorded by self-reporting of the parents (current smoking status and amount of cigarettes per day). Parents were considered hypertensive if they reported having been told by a physician that they had elevated BP or were currently treated for arterial hypertension. Finally, previous and current cardiovascular disorders/events in the family were noted.

Statistical Analysis

Data are expressed as mean±SD. Categorical variables were compared with the χ² test. Student t tests were used for 2-group comparisons, and ANOVA followed by Student-Newman-Keuls tests were used for multiple comparisons. Parametric or nonparametric tests were used to analyze subgroups values, as appropriate. Associations between individual parameters were evaluated by Spearman correlation analysis. Multiple linear regression analysis was performed to assess the relative impact of all potential factors influencing childhood BP. Stepwise multivariable linear regression analysis was performed to identify the most significant independent correlates of systolic and diastolic BP. The associations were checked for linearity, heteroscedasticity, and outliers (by the respective features in the REG and ROBUSTREG procedures of the SAS software). The impact of categorical variables was quantified by calculating odds ratios by logistic regression analysis. Corrections were made for the number of parents who were hypertensive, obese, or smokers (none, 1, or both) and for parental gender.

All statistical analyses were performed with the use of the SAS package (version 9.2; SAS Institute, Cary, NC). Graphs were produced with the use of Sigmplot (SYSTAT Software Inc, San Jose, CA). Significance was assigned at P<0.05.

Results

Subject Characteristics

From February 2007 to October 2008, 4236 white children were examined. The mean age was 5.7±0.4 years (range, 4.0 to 7.5 years), and 48.5% were girls. The characteristics of the children at the time of study and at birth are depicted in Table 1. A total of 8.4% of the children had a mild chronic condition (ie, asthma, atopic dermatitis, allergy), and 3.8% were taking medications (mainly antiallergic and antiasthmatic drugs) at the time of evaluation. One percent of all children were either prescribed medications or suffered from chronic disorders that might exert some effect on BP. These included 3 children with asthma receiving chronic glucocorticoid or β-sympathomimetic therapy, 3 children with diabetes mellitus, 2 with hypercholesterolemia, and 1 with thyroid hormone substitution. These children were not excluded in order to have an unbiased, representative sample of preschool children, but the presence of chronic disease/medication was included as a potential factor of influence.

Parent Characteristics

A total of 4185 completed questionnaires were returned. The parents’ characteristics are presented in Table 1. A large fraction of the fathers or mothers was currently smoking (28.5% of fathers, 20.7% of mothers; 33.4% for at least 1 parent and 11.9% for both parents; Table 2). The proportion of smokers was higher among obese parents (BMI >30 kg/m²) (28.4% versus 21.1%; P<0.05) and among parents with lower educational (42.6% versus 13.0%; P<0.0001) or occupational level (31.4% versus 10.0%; P<0.0001).

Effectors of BP

Anthropometry, Gender, and BP

A strong linear correlation between BP and children’s height and BMI was observed (Table 3). Obese children (BMI >95th percentile) displayed significantly higher systolic and diastolic BP values than lean children (BMI <85th percentile). BP was intermediate in overweight children as defined by BMI 85th to 95th percentile. Systolic BP was significantly lower in girls than in boys (−1.1 [−1.6 to −0.64] mm Hg; P<0.0001).

Prenatal Risk Factors

Children born preterm or with low birth weight showed significantly higher systolic BP values than children born at term or children with birth weight >2500 g. Children exposed to maternal smoking during pregnancy displayed significantly higher systolic BP values than unexposed children, and children of mothers with pregnancy-related hypertension showed significantly higher systolic and diastolic BP levels.

Parental and Environmental Risk Factors

Offspring of hypertensive parents showed higher BP values than children of normotensive parents. Similarly, BP was higher in children of obese parents than in children of nonobese parents. Children from families with at least 1 obese parent exhibited significantly higher standardized BMI than children with nonobese parents.

A lower educational level of the parents was correlated with higher systolic BP values of the offspring.

Children exposed to parental smoking at home had higher systolic and diastolic BP than unexposed subjects (Figure 1). The number of cigarettes smoked by the mothers, but not paternal cigarette consumption, was correlated linearly with systolic BP (r=0.06, P<0.03).

Gender did not influence the risk factor profile significantly; however, the influence of passive smoking on BP was expressed more in boys than in girls. Administration of steroids and/or β-sympathomimetics in children with asthma...
was associated with a significantly higher systolic and diastolic BP. No difference in the prevalence of asthma or bronchitis was found for children from smoking or nonsmoking families.

Detailed information on the effect sizes of individual risk factors on BP is given in Table 4.

**Multivariable Analysis of Risk Factors**

Full adjustment for potential confounders by multivariable regression analysis identified gender, height, BMI, birth weight, gestational hypertension, parental smoking, and parental hypertension as significant correlates of systolic BP. Diastolic BP was affected by gender, height, BMI, birth weight, and parental hypertension (Table 3).

Stepwise multivariable linear regression analysis was performed to identify the most significant independent effectors of BP. Systolic BP was associated with gender, BMI, height, birth weight, gestational hypertension, parental hypertension, and parental smoking. Diastolic BP was associated with gender, BMI, height, birth weight and parental hypertension (Table 3). The likelihood of having a systolic BP >1 SD above the mean was independently increased with higher BMI, lower birth weight and height, hypertensive parents, and parental smoking. Higher BMI, parental hypertension, and lower birth weight and height were associated with a slightly increased likelihood of a higher diastolic BP (Table 5).

Moreover, systolic and diastolic BP progressively increased with the cumulative number of parent-related risk factors (parental obesity, hypertension, and smoking) (Figure 2). The mean difference between children without any risk factors and those with the maximum number of risk factors is shown in Figure 3.
and children with 3 cumulative risk factors was 3.2 (1.1 to 5.3) mm Hg ($P=0.003$) for systolic and 2.9 (1.2 to 4.6) mm Hg for diastolic BP ($P=0.001$).

**Discussion**

Very few studies have addressed the distribution and determinants of BP in preschool children. This study, designed primarily to evaluate the miscellaneous factors influencing BP in childhood, demonstrates that the multifactorial dependency of BP on familial, prenatal, and environmental influences is manifest as early as at preschool age.

A unique finding of this study is the novel evidence for a BP-raising effect of environmental nicotine exposure in children as young as 4 to 5 years of age. The effect of passive smoking remained significant when we corrected for all other relevant child- and parent-related risk factors and prenatal circumstances. The adjusted likelihood to be in the top 15% of systolic BP distribution was increased by 21% in children exposed to passive smoking. Adverse consequences of active and passive tobacco exposure on cardiovascular functions have been demonstrated widely in adults. These include increased BP and heart rate, decreased exercise tolerance, coronary vasoconstriction, endothelial dysfunction, elevated blood carboxyhemoglobin concentration, and an increased risk of thrombosis. In children, passive tobacco smoke exposure has been associated with altered endothelial function and arterial morphology, however, an influence of passive smoking on childhood BP has not been reported previously. Notably, a quantitative relationship was established for maternal, but not paternal, cigarette consumption. This difference might be due to the fact that mothers are more likely to smoke predominantly at home, whereas fathers tend to consume the bulk of cigarettes at the workplace. Moreover, the effect size of passive smoking was found to be higher in boys than in girls. Whereas in adolescents or adults a sex-preferential susceptibility of males to cardiovascular risk factors is well established and is related to differential sex steroid effects on the vasculature, a similar difference in preschool children would require one to assume gender-specific genetic predisposition or prenatal programming of vascular reactivity. Although clinical and experimental evidence for such a phenomenon is currently lacking, this area may be an interesting field of future research.

At least at the univariate level, the association of tobacco exposure with early childhood BP encompassed maternal gestational smoking. This finding is in agreement with
mortality has been demonstrated convincingly. Second, childhood BP consistently tracks into adult life. Although the relative contributions of genetic and environmental factors and the effect of reversibility of the latter on long-term BP tracking and adult cardiovascular health are far from understood, avoiding or removing potentially irreversible adverse factors as early as possible is a reasonable approach. Furthermore, children whose parents smoke are themselves more likely to smoke in the future. Finally, passive smoking in children not only may compromise long-term cardiovascular health but has also been shown to affect lung function, constituting an important cause of childhood pulmonary obstructive diseases.

In addition to the observed impact of prenatal and current nicotine exposure, our study confirmed height, obesity, low birth weight, and parental hypertension as independent determinants of BP in early childhood.

Not unexpectedly in this young age group, we identified strong associations of BP with body height and BMI. BMI and height together explained almost 12.4% of the variation of systolic BP, with a weaker effect on diastolic BP. Obese children were almost twice as likely to have a high-normal or elevated systolic BP. These findings are in close agreement with previous studies dealing with the relationship between BMI and BP in childhood.

Since the first description by Barker et al of the association of low birth weight with high BP in adult life nearly 2 decades ago, the hypothesis of prenatal priming of postnatal BP was essentially confirmed by a majority of studies, albeit with variable effect size. Our study adds to this body of evidence. In our population-based sample, we observed a highly significant but quantitatively small effect of birth weight, explaining ≈1% of the variation in systolic BP at preschool age with a weak additional independent association of gestational hypertension with childhood systolic BP.

Parental obesity, hypertension, and lower educational and occupational status were all associated with childhood BP but

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**Table 4. Increase of Systolic and Diastolic BP by Presence of Defined Prenatal, Parental, or Environmental Risk Factors in Comparison to Children Without the Respective Risk Factor**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Prevalence, %</th>
<th>Systolic BP Mean (95% CI)</th>
<th>Diastolic BP Mean (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prematurity</td>
<td>9.0</td>
<td>+1.4 (0.5–2.3)</td>
<td>+1.2 (0.4–2.1)</td>
</tr>
<tr>
<td>Birth weight &lt;2500 g</td>
<td>10.7</td>
<td>+0.9 (0.1–1.6)</td>
<td></td>
</tr>
<tr>
<td>Maternal smoking during pregnancy</td>
<td>8.0</td>
<td>+1.1 (0.2–2)</td>
<td></td>
</tr>
<tr>
<td>Gestational hypertension</td>
<td>5.6</td>
<td>+2.5 (1.4–3.5)</td>
<td>+1.2 (0.4–2.1)</td>
</tr>
<tr>
<td>Obesity (BMI &gt;95th percentile)</td>
<td>5.8</td>
<td>+6.0 (5.0–7.0)</td>
<td>+3.8 (3.0–4.7)</td>
</tr>
<tr>
<td>Overweight (BMI 85–95th percentile)</td>
<td>6.3</td>
<td>+3.6 (2.8–4.3)</td>
<td>+1.7 (1.0–2.4)</td>
</tr>
<tr>
<td>Chronic medication (eg, steroids or β-sympathomimetics)</td>
<td>1.0</td>
<td>+2.2 (0.5–3.9)</td>
<td>+2.3 (0.9–3.7)</td>
</tr>
<tr>
<td>Parental hypertension</td>
<td>12.5</td>
<td>+2.1 (1.4–2.9)</td>
<td>+1.5 (0.9–2.1)</td>
</tr>
<tr>
<td>Parental obesity</td>
<td>17.7</td>
<td>+1.2 (0.5–1.8)</td>
<td>+1.3 (0.8–1.8)</td>
</tr>
<tr>
<td>Parental smoking</td>
<td>33.4</td>
<td>+1.0 (0.5–1.3)</td>
<td>+0.5 (0.03–0.9)</td>
</tr>
<tr>
<td>Lower parental educational level</td>
<td>44.3</td>
<td>+1.3 (0.8–1.8)</td>
<td></td>
</tr>
</tbody>
</table>

CI indicates confidence interval.
highly interrelated. Of these variables, only parental hypertension emerged as an independent risk factor, suggesting a major role of genetic determinants of childhood BP.

Importantly, parental smoking, hypertension, and obesity appear to act synergistically on BP in preschool children; mean BP increased progressively in proportion to the cumulative number of risk factors present. The absolute BP difference observed between children without any risk factors (“healthy lifestyle” families) and those accumulating 3 risk factors was 3.2 mm Hg for systolic and 2.9 mm Hg for diastolic BP, corresponding to almost half of a standard deviation of the BP distribution in the total population. Because BP differences related to risk factors also tend to amplify from infancy to adulthood, the observed impact of modifiable risk factors even at preschool age is a major concern, and comprehensive interventions that seek to reduce the cardiovascular risk burden early in life by promoting lifestyle changes in all family members may prove essential for lowering the cardiovascular disease risk of future generations.

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Disclosures

None.

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