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Determinants of Blood Pressure in Preschool Children
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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

Arterial 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 cotrack 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.[5]

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,[8,9] the smoking habits of mothers and fathers were recorded in detail and correlated with BP findings.

Methods

Subjects

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/m^2). BMI centiles were derived from German reference data,[10] and standard deviation scores by age and gender were calculated by the LMS method of Cole and Green.[11]

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.[12] BP standard deviation score values were calculated, and elevated BP was defined according to American reference data.[12]

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.[13]

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 χ^2 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 Sigmaplot (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 2. 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/m^2) (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

Table 1. Characteristics of 4236 Preschool Children

	Boys (n=2181)	Girls (n=2055)	P
Characteristics at time of investigation			
Age, y	5.74±0.44	5.67±0.44	
Height, cm	117.8±5.4	116.2±5.3	
Height SD score	−0.14±1.11	−0.25±1.07	
Weight, kg	22.0±3.8	21.3±3.7	
Body fat, %	15.6±4.9	19.5±5.2	
BMI, kg/m^2	15.8±1.9	15.7±1.9	
BMI SD score	0.03±1.0	0.0±1.0	
Percent BMI <85th/85–95th/>95th percentile	86.1/7.8/6.1	85.1/9.5/5.5	
Height SD score by BMI <85th/85–95th/>95th percentile	−0.21[a]/0.12[b]/0.57[c]*	−0.34[a]/0.11[b]/0.47[c]*	
Systolic BP, mm Hg	100.7±7.7	99.6±8.0	<0.0001
Systolic BP SD score	0.48±0.70	0.56±0.76	0.0004
Systolic BP, mm Hg, by BMI <85th/85–95th/>95th percentile	100.1[a]/104.2[b]/105.5[b]*	98.9[a]/102.1[b]/105.5[c]*	<0.0001/<0.005/NS
Diastolic DP, mm Hg	61.8±6.3	62.1±6.5	NS
Diastolic BP, SD score	0.62±0.55	0.61±0.60	NS
Diastolic BP, mm Hg, by BMI <85th/85–95th/>95th percentile	61.4[a]/63.4[b]/65.0[c]*	61.7[a]/63.1[b]/65.9[c]*	NS/NS/NS
Characteristics at birth			
Birth weight, g	3398±588	3279±546	
Birth length, cm	51.7±3.2	51.0±3.1	
Gestational age, wk	39.0±2.1	39.1±2.0	
Preterm (<37 gestational weeks), %	9.3	8.6	
Small for gestational age (birth weight <10th centile), %[14]	10.5	11.2	
Low birth weight (<2500 g), %	10.2	11.2	

Numbers are mean±SD or percentage unless indicated otherwise.
*Different letters denote significant differences between subgroups (P<0.05).

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.

Table 2. Characteristics of Parents

	Mother	Father	Both
Age, y	36.5±5.1	39.5±5.6	
Height, cm	166.4±6.6	179.6±7.3	
Weight, kg	66.3±13.2	84.7±13.4	
BMI, kg/m^2	24.0±5.8	26.2±3.7	
Obesity (BMI >30), %	10.2	12.1	2.3
Arterial hypertension, %	4.0	9.2	0.7
Smoker, %	20.7	28.5	11.9
No. of cigarettes per day	11.6±6.4	13.9±7.5	18.2±11.6
Educational level, %			
Primary school	20.5	26.8	
Secondary school	35.1	24.2	
>Secondary school	44.4	49.0	
Occupational level, %			
Manual workers	22.4	40.5	
Nonmanual workers	59.9	32.8	
University graduates	17.7	26.7	

Values are mean±SD or percentage.

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

Table 3. Univariate and Multivariable Linear Regression Analyses of Factors Affecting Systolic and Diastolic BP

	Univariate Regression				Multiple Regression (Full Model)				Stepwise Multiple Regression			
Variable in All Subjects	β	SE	P	Adjusted R^2	β	SE	P	Adjusted R^2	β	SE	P	Adjusted R^2
Systolic BP												
Gender	−0.0045	0.0009	<0.0001	0.0048	−0.9070	0.2771	0.001		−0.9064	0.2587	0.0005	0.0032
BMI	0.0699	0.0039	<0.0001	0.0856	1.0302	0.0887	<0.0001		0.9932*	0.0741	<0.0001	*
Height	0.1840	0.0104	<0.0001	0.0704	0.3143	0.0274	<0.0001		0.3136*	0.0252	<0.0001	*
Gestational age	−0.0195	0.0045	0.0001	0.0050	−0.0109	0.0912	0.9					
Birth weight	−0.0021	0.0011	0.06	0.0006	−1.2256	0.3410	0.0003		−1.2348	0.2458	<0.0001	0.0082
Chronic medications	0.0007	0.0003	0.02	0.0012	1.0493	0.9129	0.3					
Parental hypertension	0.0042	0.0007	<0.0001	0.0094	1.5636	0.4144	0.0002		1.4761	0.3922	0.0002	0.0047
Parental smoking	0.0044	0.0010	<0.0001	0.0049	0.8442	0.3059	0.006		0.7960	0.2706	0.003	0.0025
Parental educational status	−0.0053	0.0009	<0.0001	0.0068	−0.5756	0.3008	0.06					
Parental obesity	0.0026	0.0007	0.0004	0.0028	−0.6233	0.3701	0.09					
Gestational hypertension	0.0021	0.0005	<0.0001	0.0050	1.2959	0.6232	0.04		1.2105	0.5563	0.03	0.0013
Maternal smoking during pregnancy	0.0013	0.0006	0.03	0.0013	−0.1601	0.6138	0.8					
								0.1460				0.1444
Diastolic BP												
Gender	0.0017	0.0012	0.1	0.0003	0.5155	0.2382	0.03		0.5184	0.2203	0.02	0.02
BMI	0.0612	0.0047	<0.0001	0.0439	0.6739	0.0747	<0.0001		0.6663*	0.0623	<0.0001	*
Height	0.1274	0.0131	<0.0001	0.0224	0.1387	0.0235	<0.0001		0.1425*	0.0214	<0.0001	*
Gestational age	−0.0118	0.0055	0.03	0.0010	−0.0616	0.0755	0.4					
Birth weight	0.0004	0.0014	0.7	−0.0002	−0.5819	0.2775	0.04		−0.7047	0.2065	0.0007	<0.0001
Chronic medications	0.0010	0.0003	0.002	0.0020	1.2057	0.7451	0.1					
Parental hypertension	0.0044	0.0009	<0.0001	0.0069	0.9976	0.3771	0.008		1.2337	0.3251	0.0002	0.0003
Parental smoking	0.0030	0.0012	0.01	0.0013	0.1608	0.2686	0.5					
Parental educational status	−0.0048	0.0011	<0.0001	0.0036	−0.1851	0.2619	0.5					
Parental obesity	0.0045	0.0009	<0.0001	0.0058	0.4765	0.3239	0.1					
Gestational hypertension	0.0016	0.0006	0.01	0.0018	0.4277	0.5564	0.4					
Maternal smoking during pregnancy	0.0013	0.0007	0.08	0.0007	−0.0775	0.5314	0.9					
								0.0675				0.0648

β indicates parameter estimate; SE, standard error of estimate.
*Height and BMI have been forced into the model.

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.[15] These include increased BP and heart rate, decreased exercise tolerance, coronary vasoconstriction, endothelial dysfunction, elevated blood carboxyhemoglobin concentration, and an increased risk of thrombosis.[16–19] In children, passive tobacco smoke exposure has been associated with altered endothelial function and arterial morphology[20,21]; 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,[22] 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

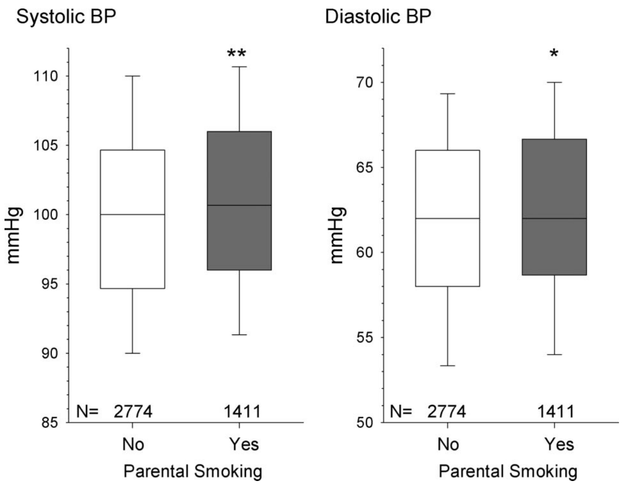

Figure 1. Influence of current parental smoking on BP in preschool children (**P=0.0001, *P<0.05). The boundary of the box closest to zero indicates the 25th percentile, the line within the box marks the median, and the boundary of the box farthest from zero indicates the 75th percentile. Whiskers (error bars) above and below the box indicate the 90th and 10th percentiles.

previous literature demonstrating cardiovascular stress hyperreactivity in babies[23] and higher BP in children of mothers smoking during pregnancy.[24] The effect of prenatal smoking might be mediated by fetal reprogramming of the cardiovascular system in response to adverse global intrauterine growth conditions caused by placental insufficiency.[25]

Hence, the findings of this study suggest that the implementation of strictly smoke-free environments, specifically at home, may be relevant to preserve cardiovascular health not only in the adult, but also in the pediatric, population. Although definite proof for this notion would require a long-term prospective interventional study, early prevention of tobacco smoke exposure is supported by several lines of reasoning. First, the efficacy of providing smoke-free environments to nonsmokers in decreasing their cardiovascular mortality has been demonstrated convincingly.[26] Second, childhood BP consistently tracks into adult life.[2] 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.[12,27,28]

Since the first description by Barker et al[29,30] 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.[31,32] 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

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

		Difference, mm Hg					
		Systolic BP			Diastolic BP		
Risk Factor	Prevalence, %	Mean	95% CI	P	Mean	95% CI	P
Prematurity	9.0	+1.4	0.5–2.3	0.002			
Birth weight <2500 g	10.7	+0.9	0.1–1.6	0.04			
Maternal smoking during pregnancy	8.0	+1.1	0.2–2	0.03			
Gestational hypertension	5.6	+2.5	1.4–3.5	<0.0001	+1.2	0.4–2.1	0.01
Obesity (BMI >95th percentile)	5.8	+6.0	5.0–7.0	<0.0001	+3.8	3.0–4.7	<0.0001
Overweight (BMI 85–95th percentile)	6.3	+3.6	2.8–4.3	<0.0001	+1.7	1.0–2.4	<0.0001
Chronic medication (eg, steroids or β–sympathomimetics)	1.0	+2.2	0.5–3.9	<0.01	+2.3	0.9–3.7	0.001
Parental hypertension	12.5	+2.1	1.4–2.9	<0.0001	+1.5	0.9–2.1	<0.0001
Parental obesity	17.7	+1.2	0.5–1.8	0.0003	+1.3	0.8–1.8	<0.0001
Parental smoking	33.4	+1.0	0.5–1.3	0.0001	+0.5	0.03–0.9	0.03
Lower parental educational level	44.3	+1.3	0.8–1.8	<0.0001			

CI indicates confidence interval.

Table 5. Logistic Regression Analysis of Factors Affecting the Likelihood of Displaying a Systolic or Diastolic BP >1 SD Score (85th Percentile)

	Odds Ratio	95% CI	*P*
Systolic BP >1 SD score			
BMI	1.26	1.20–1.32	<0.0001
Height	0.98	0.96–0.99	0.02
Birth weight	0.65	0.55–0.76	<0.0001
Parental hypertension	1.58	1.25–2.00	0.0001
Parental smoking	1.21	1.02–1.44	0.02
Diastolic BP >1 SD score			
BMI	1.20	1.15–1.26	<0.0001
Height	0.95	0.94–0.97	<0.0001
Birth weight	0.85	0.72–0.98	0.03
Parental hypertension	1.45	1.15–1.82	0.002

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,[33] 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

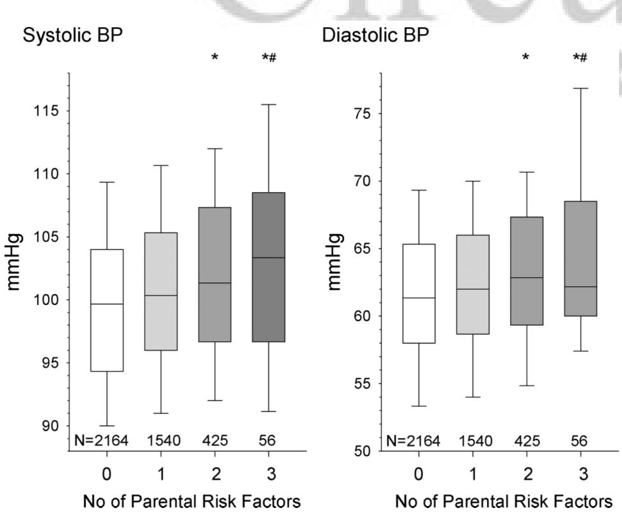

Figure 2. Synergistic effect of parent-related risk factors on BP in preschool children. A progressive increase in systolic and diastolic BP was observed with increasing cumulative number of parental risk factors (obesity, hypertension, smoking) ($P<0.05$ compared with children *without risk factors or #with 1 risk factor).

for lowering the cardiovascular disease risk of future generations.

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Disclosures

None.

References

1. Bao W, Threefoot SA, Srinivasan SR, Berenson GS. Essential hypertension predicted by tracking of elevated blood pressure from childhood to adulthood: the Bogalusa Heart Study. *Am J Hypertens*. 1995;8:657–665.
2. Chen X, Wang Y. Tracking of blood pressure from childhood to adulthood: a systematic review and meta-regression analysis. *Circulation*. 2008;117:3171–3180.
3. Dekkers JC, Snieder H, Van Den Oord EJ, Treiber FA. Moderators of blood pressure development from childhood to adulthood: a 10-year longitudinal study. *J Pediatr*. 2002;141:770–779.
4. Kelder SH, Osganian SK, Feldman HA, Webber LS, Parcel GS, Leupker RV, Wu MC, Nader PR. Tracking of physical and physiological risk variables among ethnic subgroups from third to eighth grade: the Child and Adolescent Trial for Cardiovascular Health cohort study. *Prev Med*. 2002;34:324–333.
5. Kivimaki M, Lawlor DA, Smith GD, Keltikangas-Jarvinen L, Elovainio M, Vahtera J, Pulkki-Raback L, Taittonen L, Viikari JS, Raitakari OT. Early socioeconomic position and blood pressure in childhood and adulthood: the Cardiovascular Risk in Young Finns Study. *Hypertension*. 2006;47:39–44.
6. Chiolero A, Cachat F, Burnier M, Paccaud F, Bovet P. Prevalence of hypertension in schoolchildren based on repeated measurements and association with overweight. *J Hypertens*. 2007;25:2209–2217.
7. Gutin B, Basch C, Shea S, Contento I, DeLozier M, Rips J, Irigoyen M, Zybert P. Blood pressure, fitness, and fatness in 5- and 6-year-old children. *JAMA*. 1990;264:1123–1127.
8. Mannino DM, Caraballo R, Benowitz N, Repace J. Predictors of cotinine levels in US children: data from the Third National Health and Nutrition Examination Survey. *Chest*. 2001;120:718–724.
9. Cook DG, Whincup PH, Jarvis MJ, Strachan DP, Papacosta O, Bryant A. Passive exposure to tobacco smoke in children aged 5–7 years: individual, family, and community factors. *BMJ*. 1994;308:384–389.
10. Kromeyer-Hauschild K, Wabitsch M, Kunze D. Perzentile f[uml[ur den Body Mass Index für Kinder im Alter von 0 bis 18 Jahren. *Monatszeitschrift Kinderheilkunde*. 2001;149:807–818.
11. Cole TJ, Green PJ. Smoothing reference centile curves: the LMS method and penalized likelihood. *Stat Med*. 1992;11:1305–1319.
12. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. *Pediatrics*. 2004;114:555–576.
13. Slaughter MH, Lohman TG, Boileau RA, Horswill CA, Stillman RJ, Van Loan MD, Bemben DA. Skinfold equations for estimation of body fatness in children and youth. *Hum Biol*. 1988;60:709–723.
14. Voigt M, Fusch C, Olbertz D, Hartmann K, Rochow N, Renken C, Schneider KT. Analysis of the neonatal collective in the Federal Republic of Germany, 12th report: presentation of detailed percentiles for the body measurement of newborns. *Geburtsh Frauenheilk*. 2006;66:956–970.
15. Barnoya J, Glantz SA. Cardiovascular effects of secondhand smoke: nearly as large as smoking. *Circulation*. 2005;111:2684–2698.
16. Celermajer DS, Adams MR, Clarkson P, Robinson J, McCredie R, Donald A, Deanfield JE. Passive smoking and impaired endothelium-

dependent arterial dilatation in healthy young adults. *N Engl J Med*. 1996;334:150–154.
17. Sidney S, Sternfeld B, Gidding SS, Jacobs DR Jr, Bild DE, Oberman A, Haskell WL, Crow RS, Gardin JM. Cigarette smoking and submaximal exercise test duration in a biracial population of young adults: the CARDIA study. *Med Sci Sports Exerc*. 1993;25:911–916.
18. Deanfield JE, Shea MJ, Wilson RA, Horlock P, de Landsheere CM, Selwyn AP. Direct effects of smoking on the heart: silent ischemic disturbances of coronary flow. *Am J Cardiol*. 1986;57:1005–1009.
19. Argacha JF, Adamopoulos D, Gujic M, Fontaine D, Amyai N, Berkenboom G, van de Borne P. Acute effects of passive smoking on peripheral vascular function. *Hypertension*. 2008;51:1506–1511.
20. Kallio K, Jokinen E, Raitakari OT, Hamalainen M, Siltala M, Volanen I, Kaitosaari T, Viikari J, Ronnemaa T, Simell O. Tobacco smoke exposure is associated with attenuated endothelial function in 11-year-old healthy children. *Circulation*. 2007;115:3205–3212.
21. Kallio K, Jokinen E, Saarinen M, Hamalainen M, Volanen I, Kaitosaari T, Ronnemaa T, Viikari J, Raitakari OT, Simell O. Arterial intima-media thickness, endothelial function, and apolipoproteins in adolescents frequently exposed to tobacco smoke. *Circ Cardiovasc Qual Outcomes*. 2010;3:196–203.
22. Mahmud A, Feely J. Effects of passive smoking on blood pressure and aortic pressure waveform in healthy young adults: influence of gender. *Br J Clin Pharmacol*. 2004;57:37–43.
23. Cohen G, Vella S, Jeffery H, Lagercrantz H, Katz-Salamon M. Cardiovascular stress hyperreactivity in babies of smokers and in babies born preterm. *Circulation*. 2008;118:1848–1853.
24. Lawlor DA, Najman JM, Sterne J, Williams GM, Ebrahim S, Davey Smith G. 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. *Circulation*. 2004;110:2417–2423.
25. Nuyt AM, Alexander BT. Developmental programming and hypertension. *Curr Opin Nephrol Hypertens*. 2009;18:144–152.
26. Ong MK, Glantz SA. Cardiovascular health and economic effects of smoke-free workplaces. *Am J Med*. 2004;117:32–38.
27. Wuhl E, Witte K, Soergel M, Mehls O, Schaefer F. Distribution of 24-h ambulatory blood pressure in children: normalized reference values and role of body dimensions. *J Hypertens*. 2002;20:1995–2007.
28. Rosner B, Cook N, Portman R, Daniels S, Falkner B. Determination of blood pressure percentiles in normal-weight children: some methodological issues. *Am J Epidemiol*. 2008;167:653–666.
29. Barker DJ, Bull AR, Osmond C, Simmonds SJ. Fetal and placental size and risk of hypertension in adult life. *BMJ*. 1990;301:259–262.
30. Barker DJ, Osmond C, Golding J, Kuh D, Wadsworth ME. Growth in utero, blood pressure in childhood and adult life, and mortality from cardiovascular disease. *BMJ*. 1989;298:564–567.
31. Taittonen L, Nuutinen M, Turtinen J, Uhari M. Prenatal and postnatal factors in predicting later blood pressure among children: cardiovascular risk in young Finns. *Pediatr Res*. 1996;40:627–632.
32. Uiterwaal CS, Anthony S, Launer LJ, Witteman JC, Trouwborst AM, Hofman A, Grobbee DE. Birth weight, growth, and blood pressure: an annual follow-up study of children aged 5 through 21 years. *Hypertension*. 1997;30:267–271.
33. Law CM, de Swiet M, Osmond C, Fayers PM, Barker DJ, Cruddas AM, Fall CH. Initiation of hypertension in utero and its amplification throughout life. *BMJ*. 1993;306:24–27.

CLINICAL PERSPECTIVE

There is increasing evidence that environmental tobacco exposure has significant effects on cardiovascular health even at a young age. Abnormal arterial morphology and function have been demonstrated in teenagers exposed to second-hand smoking. The age at which cardiovascular effects of passive smoking first become detectable has not been established to date. This population-based study was designed to explore endogenous and exogenous determinants of blood pressure (BP) in preschool children. BP was measured in conjunction with a family health and lifestyle survey in a cohort of 4236 children aged 4 to 6 years. Multifactorial dependency of BP on body stature and familial, prenatal, and environmental influences was observed. Among these factors, exposure to parental smoking was associated with a small but consistent BP-raising effect, which remained significant when adjusted for numerous potentially collinear anthropometric, medical, and social factors affecting BP in the children and their parents, including prenatal conditions. Childhood BP was quantitatively correlated with the daily cigarette consumption of the mothers only, compatible with closer exposure to maternal smoking at home. The findings of this study add an important pediatric perspective to the issue of prevention and containment of active and passive smoking. They complete the picture of tobacco exposure interfering with cardiovascular maturation and health from gestation to adulthood. The benefit of successful primary prevention programs would most likely not be limited to adults but extend even to the youngest family members.