

## Hypertension Editors' Picks Pediatric Hypertension

The Editors

The following articles are being highlighted as part of *Hypertension's* Editors' Picks Series. Pediatric hypertension has become an area of increased interest over the past decade. Clinical skills in recognizing and diagnosing asymptomatic primary hypertension in childhood have improved, and recent epidemiological reports demonstrate that the prevalence of childhood hypertension is increasing. Recent clinical and translational research have led to insights that move beyond just considering high blood pressure in childhood a primordial risk factor for hypertension in later adulthood. Interest has extended to exploring effects of early life experiences that modify cardiovascular development and metabolic function throughout the lifespan. For our readers, we have collated 16 full length articles, related to the evolution of primary hypertension, that were published in our Journal between January 2014 and February 2015. These articles include epidemiological, clinical, and translational science investigations that explore relationships of fetal programming and early childhood exposures with cardiovascular development and hemodynamic regulation in later life. Together the articles published in *Hypertension* represent forward movement in understanding the fetal and childhood origins of hypertension-related cardiovascular disease.

### Efficacy of Atomoxetine Versus Midodrine for the Treatment of Orthostatic Hypotension in Autonomic Failure<sup>1</sup>

#### Abstract

The clinical presentation of autonomic failure is orthostatic hypotension. Severely affected patients require pharmacological treatment to prevent presyncopal symptoms or frank syncope. We previously reported in a proof of concept study that pediatric doses of the norepinephrine transporter blockade, atomoxetine, increases blood pressure in autonomic failure patients with residual sympathetic activity compared with placebo. Given that the sympathetic nervous system is maximally activated in the upright position, we hypothesized that atomoxetine would be superior to midodrine, a direct vasoconstrictor, in improving upright blood pressure and orthostatic hypotension-related symptoms. To test this hypothesis, we compared the effect of acute atomoxetine versus midodrine on upright systolic blood pressure and orthostatic symptom scores in 65 patients with severe autonomic failure. There were no differences in seated systolic blood pressure (means difference=0.3 mmHg; 95% confidence interval, -7.3 to 7.9;  $P=0.94$ ). In contrast, atomoxetine produced a greater pressor response in upright systolic blood pressure (means difference=7.5 mmHg; 95% confidence interval, 0.6–15;  $P=0.03$ ) compared with midodrine. Furthermore, atomoxetine (means difference=0.4; 95% confidence interval, 0.1–0.8;  $P=0.02$ ), but not midodrine (means difference=0.5; 95% confidence interval, -0.1 to 1.0;  $P=0.08$ ), improved orthostatic hypotension-related symptoms as compared with placebo. The results of our study suggest that atomoxetine could be a superior therapeutic option than midodrine for the treatment of orthostatic hypotension in autonomic failure.

### Distensibility of the Aorta and Carotid Artery and Left Ventricular Mass From Childhood to Early Adulthood<sup>2</sup>

#### Abstract

In adults, arterial distensibility decreases with age and relates to changes in cardiac left ventricular mass. Longitudinal data on changes in arterial distensibility from childhood to adulthood are lacking. Our aim was to study the effect of age and sex and low-saturated fat dietary counseling on arterial distensibility from childhood to early adulthood. In addition, we assessed the association of arterial distensibility with left ventricular mass. Distensibility of the abdominal aorta and common carotid artery was measured repeatedly at ages 11, 13, 15, 17, and 19 years ( $n=395-472$ ) in an atherosclerosis prevention trial (Special Turku Coronary Risk Factor Intervention Project [STRIP]). Aortic and carotid distensibility decreased with age (both  $P<0.0001$ ). In boys, distensibility values were generally lower ( $P<0.0001$ ) and showed steeper decrease by age (age and sex interaction: both  $P<0.01$ ). The low-saturated fat dietary counseling given in STRIP was not significantly associated with arterial distensibility. Left ventricular mass increased with age ( $P<0.0001$ ), and it was greater in boys ( $P<0.0001$ ). In conclusion, a marked age-related decrease in vascular distensibility was found already at this young age, and this decrease was more pronounced in boys than girls. The longitudinal progression of aortic and carotid distensibility was related with changes in left ventricular mass.

## Influence of Maternal Angiogenic Factors During Pregnancy on Microvascular Structure in School-Age Children<sup>3</sup>

### Abstract

Reduced placenta growth factor (PIGF) levels and higher soluble fms-like tyrosine kinase (sFlt-1) levels in mothers during pregnancy may have persistent effects on vascular structures in their offspring. We examined whether angiogenic factors during pregnancy also affect childhood retinal microvasculature in a population-based prospective cohort study among 3505 mothers and their children. We measured in the first and second trimester of pregnancy, maternal PIGF and sFlt-1 levels. At the age of 6 years, we measured childhood retinal arteriolar and venular calibers from digitized retinal photographs. We performed multiple linear regression models taking account for maternal and childhood socio-demographic and lifestyle-related characteristics, birth characteristics, and childhood current body mass index and blood pressure. We observed that first trimester maternal PIGF and sFlt-1 levels were not associated with childhood retinal arteriolar caliber. Lower second trimester maternal PIGF levels, but not sFlt-1 levels, were associated with narrower childhood retinal arteriolar caliber (difference:  $-0.09$  SDS (95% confidence interval,  $-0.16, -0.01$ ), per SDS decrease in PIGF). This association was not explained by maternal and childhood socio-demographic and lifestyle-related characteristics, birth characteristics, or childhood current body mass index and blood pressure. Maternal PIGF and sFlt-1 levels in the first or second trimester were not associated with childhood retinal venular caliber. Our results suggest that lower maternal second trimester PIGF levels affect the microvascular development in the offspring, leading to narrower retinal arteriolar caliber in childhood. Further studies are needed to confirm these findings and to explore the underlying mechanisms and long-term cardiovascular consequences.

## Long-Term Blood Pressure Variability Throughout Young Adulthood and Cognitive Function in Midlife: The Coronary Artery Risk Development in Young Adults (CARDIA) Study<sup>4</sup>

### Abstract

Whether long-term blood pressure (BP) variability throughout young adulthood is associated with cognitive function in midlife remains uncertain. Using data from the Coronary Artery Risk Development in Young Adults, which recruited healthy young adults aged 18 to 30 years (mean age, 25 years) at baseline (Y0), we assessed BP variability by SD and average real variability (ARV) for 25 years (8 visits). Cognitive function was assessed with the Digit Symbol Substitution Test (psychomotor speed test), the Rey Auditory Verbal Learning Test (verbal memory test), and the modified Stroop test (executive function test) at follow-up (Y25). At the Y25 examination, participants ( $n=2326$ ) had a mean age of 50.4 years, 43% were men, and 40% were black. In multivariable-adjusted linear regression models, higher ARVSBP, ARVDBP, and SDBBP were significantly associated with lower scores of Digit Symbol Substitution Test (beta [SE]:  $-0.025$  [0.006],  $-0.029$  [0.007], and  $-0.029$  [0.007], respectively; all  $P<0.001$ ) and Rey Auditory Verbal Learning Test (beta [SE]:  $-0.016$  [0.006],  $-0.021$  [0.007], and  $-0.019$  [0.007], respectively; all  $P<0.05$ ) after adjustment for demographic and clinical characteristics and with cumulative exposure to BP through Y0 to Y25. Neither SDBP nor ARVBP was associated with the Stroop score. The associations between ARVBP or SDBP and each cognitive function test were similar between blacks and whites except for 1 significant interaction between race and SDSBP on the Digit Symbol Substitution Test ( $P<0.05$ ). Long-term BP variability for 25 years beginning in young adulthood was associated with worse psychomotor speed and verbal memory tests in midlife, independent of cumulative exposure to BP during follow-up.

## Impaired Cardiovascular Structure and Function in Adult Survivors of Severe Acute Malnutrition<sup>5</sup>

### Abstract

Malnutrition below 5 years remains a global health issue. Severe acute malnutrition (SAM) presents in childhood as edematous (kwashiorkor) or nonedematous (marasmic) forms, with unknown long-term cardiovascular consequences. We hypothesized that cardiovascular structure and function would be poorer in SAM survivors than in unexposed controls. We studied 116 adult SAM survivors, 54 after marasmus, 62 after kwashiorkor, and 45 age/sex/body mass index-matched community controls who had standardized anthropometry, blood pressure, echocardiography, and arterial tonometry performed. Left ventricular indices and outflow tract diameter, carotid parameters, and pulse wave velocity were measured, with systemic vascular resistance calculated. All were expressed as SD scores. Mean (SD) age was  $28.8\pm 7.8$  years (55% men). Adjusting for age, sex, height, and weight, SAM survivors had mean (SE) reductions for left ventricular outflow tract diameter of 0.67 (0.16;  $P<0.001$ ), stroke volume of 0.44 (0.17;  $P=0.009$ ), cardiac output of 0.5 (0.16;  $P=0.001$ ), and pulse wave velocity of 0.32 (0.15;  $P=0.03$ ) compared with controls, but higher diastolic blood pressures (by 4.3; 1.2–7.3 mmHg;  $P=0.007$ ). Systemic vascular resistance was higher in marasmus and kwashiorkor survivors (30.2 [1.2] and 30.8 [1.1], respectively) than controls (25.3 [0.8]), overall difference 5.5 (95% confidence interval, 2.8–8.4 mmHg min/L;  $P<0.0001$ ). No evidence of large vessel or cardiac remodeling was found, except closer relationships between these indices in former marasmic survivors. Other parameters did not differ between SAM survivor groups. We conclude that adult SAM survivors had smaller outflow tracts and cardiac output when compared with controls, yet markedly elevated peripheral resistance. Malnutrition survivors are thus likely to develop excess hypertension in later life, especially when exposed to obesity.

## Maternal Parity, Fetal and Childhood Growth, and Cardiometabolic Risk Factors<sup>6</sup>

### Abstract

We examined the associations of maternal parity with fetal and childhood growth characteristics and childhood cardiometabolic risk factors in a population-based prospective cohort study among 9031 mothers and their children. Fetal and childhood growth were repeatedly measured. We measured childhood anthropometrics, body fat distribution, left ventricular mass, blood pressure, blood lipids, and insulin levels at the age of 6 years. Compared with nulliparous mothers, multiparous mothers had children with higher third trimester fetal head circumference, length and weight growth, and lower risks of preterm birth and small-size-for-gestational-age at birth, but a higher risk of large-size-for-gestational-age at birth ( $P<0.05$ ). Children from multiparous mothers had lower rates of accelerated infant growth and lower levels of childhood body mass index, total fat mass percentage, and total and low-density lipoprotein cholesterol than children of nulliparous mothers ( $P<0.05$ ). They also had a lower risk of childhood overweight (odds ratio, 0.75; 95% confidence interval, 0.63–0.88). The risk of childhood clustering of cardiometabolic risk factors was not statistically significantly different (odds ratio, 0.82; 95% confidence interval, 0.64–1.05). Among children from multiparous mothers only, we observed consistent trends toward a lower risk of childhood overweight and lower cholesterol levels with increasing parity ( $P<0.05$ ). In conclusion, offspring from nulliparous mothers have lower fetal but higher infant growth rates and higher risks of childhood overweight and adverse metabolic profile. Maternal nulliparity may have persistent cardiometabolic consequences for the offspring.

## Associations of Blood Pressure Change in Pregnancy With Fetal Growth and Gestational Age at Delivery: Findings From a Prospective Cohort<sup>7</sup>

### Abstract

Hypertensive disorders of pregnancy are associated with intrauterine growth restriction and preterm birth. However, the associations of patterns of blood pressure change during pregnancy with these outcomes have not been studied in detail. We studied repeat antenatal blood pressure measurements of 9697 women in the Avon Longitudinal Study of Parents and Children (median [interquartile range], 10 [9–11] measurements per woman). Bivariate linear spline models were used to relate blood pressure changes to perinatal outcomes. Higher systolic, but not diastolic, blood pressure at baseline (8 weeks of gestation) and a greater increase in systolic and diastolic blood pressure between 18 and 36 weeks of gestation were associated with lower offspring birth weight and being smaller for gestational age in confounder-adjusted models. For example, the mean difference (95% confidence interval) in birth weight per 1 mmHg/week greater increase in systolic blood pressure between 18 and 30 weeks was  $-71$  g ( $-134$  to  $-14$ ) and between 30 and 36 weeks was  $-175$  g ( $-208$  to  $-145$ ). A smaller decrease in systolic and diastolic blood pressure before 18 weeks and a greater increase between 18 and 36 weeks were associated with a shorter gestation (percentage difference in gestational duration per 1 mmHg/week greater increase in systolic blood pressure between 18 and 30 weeks was  $-0.60\%$  [ $-1.01$  to  $-0.18$ ] and between 30 and 36 weeks was  $-1.01\%$  [ $-1.36$  to  $-0.74$ ]). Associations remained strong when restricting to normotensive women. We conclude that greater increases in blood pressure, from the 18-week nadir, are related to reduced fetal growth and shorter gestation even in women whose blood pressure does not cross the threshold for hypertensive disorders of pregnancy.

## Adverse Childhood Experiences Are Associated With Detrimental Hemodynamics and Elevated Circulating Endothelin-1 in Adolescents and Young Adults<sup>8</sup>

### Abstract

Growing evidence suggests that adverse childhood experiences (ACEs) increase the risks for coronary heart disease and hypertension in mid and late adulthood. We previously reported that early life stress induces a hyperreactive endothelin-dependent cardiovascular phenotype in a rat model. In the present study, we evaluated whether exposure to ACEs is associated with greater peripheral resistance, arterial stiffness, blood pressure, or elevated circulating endothelin-1 levels in humans. In 221 healthy adolescents and young adults (mean age, 21 years; range, 13–29 years), we found a graded association of ACE exposure with plasma endothelin-1 levels, of which on average 18% and 24% were higher in participants with 1 ACE and  $\geq 2$  ACEs, respectively, compared with those with no ACEs ( $P=0.001$ ). Participants with moderate/severe exposure to ACEs ( $\geq 2$  ACEs) had significantly higher total peripheral resistance index (+12%), diastolic blood pressure (+5%), and pulse wave velocity (+9%) compared with those who were not exposed. These associations were independent of age, race, sex, body mass index, and childhood socioeconomic status. Our results indicate that early life stress promotes cardiovascular disease risk, specifically detrimental vascular and cardiac function, detectable in young adulthood.

## Racial Differences in Sensitivity of Blood Pressure to Aldosterone<sup>9</sup>

### Abstract

Blacks in comparison with whites are at risk for a more serious form of hypertension with high rates of complications. Greater sodium retention is thought to underlie the blood pressure (BP)-determining physiology of blacks, but specific mechanisms have not been identified. In a prospective observational study of BP, 226 black children and 314 white children (mean age, 10.6 years) were enrolled initially. Assessments were repeated in 85 blacks and 136 whites after reaching adulthood (mean age, 31 years). The relationship of BP to plasma aldosterone concentration in the context of the prevailing level of plasma renin activity was studied in blacks and whites. In a secondary interventional study, 9- $\alpha$  fludrocortisone was administered for 2 weeks to healthy adult blacks and whites to simulate hyperaldosteronism. BP responses in the 2 race groups were then compared. Although black children had lower levels of plasma renin activity and plasma aldosterone, their BP was positively associated with the plasma aldosterone concentration, an effect that increased as plasma renin activity decreased ( $P=0.004$ ). Data from black adults yielded similar results. No similar relationship was observed in whites. In the interventional study, 9- $\alpha$  fludrocortisone increased BP in blacks but not in whites. In conclusion, aldosterone sensitivity is a significant determinant of BP in young blacks. Although its role in establishing the risk of hypertension is not known, it could be as relevant as the actual level of aldosterone.

## Associations of Birth Weight and Postnatal Weight Gain With Cardiometabolic Risk Parameters at 5 Years of Age<sup>10</sup>

### Abstract

The present prospective study assessed the effect 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 into 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.

## Salt Intake of Children and Adolescents in South London: Consumption Levels and Dietary Sources<sup>11</sup>

### Abstract

Since 2003/2004, the United Kingdom has implemented a salt reduction campaign; however, there are no data on salt intake in children as assessed by 24-hour urinary sodium, the gold standard method, to inform this campaign. We performed a cross-sectional study involving South London school children across 3 age tiers: young children (5- to 6-year olds), intermediate-aged children (8- to 9-year olds), and adolescents (13- to 17-year olds). Dietary salt intake was measured by 24-hour urinary sodium excretion and compared with newly derived maximum salt intake recommendations. In addition, dietary sources of salt were assessed using a 24-hour photographic food diary. Valid urine collections were provided by 340 children (162 girls, 178 boys). The mean salt intakes were 3.75 g/d (95% confidence interval, 3.49–4.01), 4.72 g/d (4.33–5.11), and 7.55 g/d (6.88–8.22) for the 5- to 6-, 8- to 9-, and 13- to 17-year olds, respectively. Sixty-six percent of the 5- to 6-year olds, 73% of the 8- to 9-year olds, and 73% of 13- to 17-year olds had salt intake above their maximum daily intake recommendations. The major sources of dietary salt intake were cereal and cereal-based products (36%), which included bread (15%), meat products (19%), and milk and milk products (11%). This study demonstrates that salt intake in children in South London is high, with most of the salt coming from processed foods. Much further effort is required to reduce the salt content of manufactured foods.

### Clinical Effect of Naturally Random Allocation to Lower Systolic Blood Pressure Beginning Before the Development of Hypertension<sup>12</sup>

#### Abstract

Systolic blood pressure (SBP) rises approximately linearly with age in most societies. The cause of this rise is unclear. We tested the hypothesis that SBP is causally associated with the rate of rise in SBP with age by evaluating the effect of 12 polymorphisms associated with lower SBP on the age-related rate of rise in SBP in a series of meta-regression analyses involving  $\leq 199\,477$  participants in 63 studies. We then evaluated the effect of these polymorphisms on the odds of coronary heart disease in 22\,223 case and 64\,762 control subjects and compared it with the effect of lower SBP observed in both prospective cohort studies and blood pressure-lowering randomized trials. All 12 polymorphisms were associated with both lower SBP and a slower age-related rise in SBP. The weighted mean effect of these 12 polymorphisms was associated with a 0.32-mmHg lower SBP ( $P=1.79\times 10^{-7}$ ) and a 0.093-mmHg/decade slower age-related rise in SBP ( $P=3.05\times 10^{-5}$ ). The effect of long-term exposure to lower SBP on coronary heart disease mediated by these polymorphisms was 2-fold greater than that observed in prospective cohort studies ( $P=0.006$ ) and 3-fold greater than that observed in short-term blood pressure treatment trials ( $P=0.001$ ). We conclude therefore that SBP seems to be causally associated with the rate of rise in SBP with age and has a cumulative effect on the risk of coronary heart disease.

### Childhood Cardiometabolic Outcomes of Maternal Obesity During Pregnancy: the Generation R Study<sup>13</sup>

#### Abstract

Maternal prepregnancy obesity is associated with impaired cardiometabolic health in offspring. Whether these associations reflect direct intrauterine causal mechanisms remains unclear. In a population-based prospective cohort study among 4871 mothers, fathers, and their children, we examined the associations of both maternal and paternal prepregnancy body mass index (BMI) with childhood body fat distribution and cardiometabolic outcomes and explored whether any association was explained by pregnancy, birth, and childhood factors. We measured childhood BMI, total body and abdominal fat distribution, blood pressure, and blood levels of lipids, insulin, and C-peptide at the age of 6 years. We observed that higher maternal and paternal prepregnancy BMI were associated with higher childhood BMI, total body and abdominal fat mass measures, systolic blood pressure, and insulin levels and lower high-density lipoprotein cholesterol levels ( $P<0.05$ ). Stronger associations were present for maternal than paternal BMI, with statistical support for heterogeneity between these associations. The associations for childhood fat mass and cardiometabolic outcomes attenuated after adjustment for childhood current BMI. Compared with children from normal-weight mothers, those from obese mothers had increased risks of childhood overweight (odds ratio, 3.84 [95% confidence interval, 3.01–4.90]) and clustering of cardiometabolic risk factors (odds ratio, 3.00 [95% confidence interval, 2.09–4.34]). Smaller effect estimates for these outcomes were observed for paternal obesity. In conclusion, higher maternal and paternal prepregnancy BMI were associated with an adverse cardiometabolic profile in offspring, with stronger associations present for maternal prepregnancy BMI. These findings suggest that maternal prepregnancy BMI may influence the cardiometabolic health of offspring through direct intrauterine mechanisms.

### Childhood Family Living Arrangements and Blood Pressure in Black Men: The Howard University Family Study<sup>14</sup>

#### Abstract

Black men have higher blood pressure (BP) levels and consequently higher prevalence of hypertension compared with men from other ethnic groups in the United States. Socio-familial factors in childhood have been found to play an important role in hypertension, but few studies have examined this relationship among black men. We investigated whether childhood family living arrangements are independently associated with mean BP and hypertension in a cross-sectional sample of 515 unrelated black male participants aged  $\geq 20$  years enrolled in the Howard University Family Study between 2001 and 2008. Black men who lived with both parents compared with the reference group of men who never lived with both parents during their lifetime had lower systolic BP ( $-4.4$  mmHg [95% confidence interval {CI},  $-7.84$  to  $-0.96$ ]), pulse pressure ( $-3.9$  mmHg [95% CI,  $-6.28$  to  $-1.51$ ]), and mean arterial BP ( $-2.0$  mmHg [95% CI,  $-4.44$  to  $0.51$ ]). This protective effect was more pronounced among men who lived with both parents for 1 to 12 years of their lives; they had decreased systolic BP ( $-6.5$  mmHg [95% CI,  $-10.99$  to  $-1.95$ ]), pulse pressure ( $-5.4$  mmHg [95% CI,  $-8.48$  to  $-2.28$ ]), mean arterial pressure ( $-3.3$  mmHg [95% CI,  $-6.56$  to  $0.00$ ]), and a 46% decreased odds of developing hypertension (odds ratio=0.54; 95% CI, 0.30–0.99). No statistically significant associations were found for diastolic BP. These results provide preliminary evidence that childhood family structure exerts a long-term influence on BP among black men.

## Williams Syndrome Predisposes to Vascular Stiffness Modified by Antihypertensive Use and Copy Number Changes in NCF1<sup>15</sup>

### Abstract

Williams syndrome is caused by the deletion of 26 to 28 genes, including elastin, on human chromosome 7. Elastin insufficiency leads to the cardiovascular hallmarks of this condition, namely focal stenosis and hypertension. Extrapolation from the Eln(+/-) mouse suggests that affected people may also have stiff vasculature, a risk factor for stroke, myocardial infarction, and cardiac death. NCF1, one of the variably deleted Williams genes, is a component of the nicotinamide adenine dinucleotide phosphate oxidase complex and is involved in the generation of oxidative stress, making it an interesting candidate modifier for vascular stiffness. Using a case-control design, vascular stiffness was evaluated by pulse wave velocity in 77 Williams cases and matched controls. Cases had stiffer conducting vessels than controls ( $P < 0.001$ ), with increased stiffness observed in even the youngest children with Williams syndrome. Pulse wave velocity increased with age at comparable rates in cases and controls, and although the degree of vascular stiffness varied, it was seen in both hypertensive and normotensive Williams participants. Use of antihypertensive medication and extension of the Williams deletion to include NCF1 were associated with protection from vascular stiffness. These findings demonstrate that vascular stiffness is a primary vascular phenotype in Williams syndrome and that treatment with antihypertensives or agents inhibiting oxidative stress may be important in managing patients with this condition, potentially even those who are not overtly hypertensive.

## The Impact of Malaria in Pregnancy on Changes in Blood Pressure in Children During Their First Year of Life<sup>16</sup>

### Abstract

We established a maternal birth cohort in Ibadan, Nigeria, where malaria is hyperendemic, to assess how intrauterine exposure to malaria affected infant blood pressure (BP) development. In a local maternity hospital, healthy pregnant women had regular blood films for malaria parasites from booking to delivery. Growth and BP were measured on 318 babies, all followed from birth to 3 and 12 months. Main outcomes were standardized measures of anthropometry and change in BP up to 1 year. Babies exposed to maternal malaria were globally smaller at birth, and boys remained smaller at 3 months and 1 year. Change in systolic BP (SBP) during the year was greater in boys than in girls (20.9 versus 15.7 mmHg;  $P = 0.002$ ) but greater in girls exposed to maternal malaria (18.7 versus 12.7 mmHg; 95% confidence interval, 1–11 mmHg;  $P = 0.02$ ). Eleven percent of boys (greater than twice than expected) had a SBP  $\geq 95$ th percentile (hypertensive, US criteria), of whom 68% had maternal malaria exposure. On regression analysis (beta coefficients, mmHg), sex (boys > girls; beta = 4.4; 95% confidence interval, 1.1–7.7;  $P = 0.01$ ), maternal malaria exposure (3.64; 0.3–6.9;  $P = 0.03$ ), and weight change (2.4; 0.98–3.8/1 standard deviation score;  $P = 0.001$ ) all independently increased SBP change to 1 year, whereas increase in length decreased SBP (–1.98; –3.6 to –0.40). In conclusion, malaria-exposed boys had excess hypertension, whereas malaria-exposed girls a greater increase in SBP. Intrauterine exposure to malaria had sex-dependent effects on BP, independent of infant growth. Because infant-child-adult BP tracking is powerful, a malarial effect may contribute to the African burden of hypertension.

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## Disclosures

None.

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