Abstract—Low birth weight has consistently been associated with increased adult blood pressure. The relative importance of childhood growth is, however, less well established. This study examined sex-specific associations between childhood growth and adult blood pressure in 2120 subjects born from 1921 to 1935 in Reykjavik who were recruited into a longitudinal study in 1967–1991. Size at birth and growth at regular intervals between 8 and 13 years were collected from national archives. Hypertensive males did not differ from normotensive males at birth but were increasingly taller and of higher body mass index between 8 and 13 years. No differences in adult height were observed between hypertensive and normotensive males. For boys, growth-velocity (change in growth per year) for body mass index and height between 8 to 13 years was positively associated ($P<0.05$) with adult blood pressure. The association for body mass index-velocity was fully accounted for by concurrent body size, whereas height-velocity was independent of birth weight and concurrent body size. Males in the highest compared with the lowest tertile in the height-velocity distribution had 66% increased risks of hypertension (95% CI: 15% to 139% increased risks of hypertension) corresponding with 5.0 mm Hg increase (95% CI: 1.5 to 8.5 mm Hg increase) and 3.1 mm Hg increase (95% CI: 1.1 to 5.0 mm Hg increase) in systolic and diastolic blood pressures, respectively. Hypertensive females weighed less at birth but did not differ markedly from normotensive girls between 8 and 13 years, and no association was observed for growth-velocity. In conclusion, rapid linear growth between 8 and 13 years predicts elevated adult blood pressure in boys. This association is likely to reflect relatively early onset of puberty among hypertensive males. (Hypertension. 2011;58:8-15.)

Key Words: hypertension ▪ blood pressure ▪ growth ▪ puberty ▪ uric acid ▪ cohort studies

Low birth weight has consistently been associated with modest increase in blood pressure at adult age.1,2 It has been suggested that this association might be related to reduced nephron numbers and increased arterial stiffness among growth-restricted infants.1 Examining the relative importance of postnatal growth with respect to adult blood pressure has, however, been addressed in less detail. Some studies have suggested that the association between fetal growth and adult blood pressure might be modified by the rate of postnatal growth.3,4 This has, for example, been demonstrated in a longitudinal study from Finland, where a pattern of low birth weight followed by either relatively slow or rapid growth was observed in subjects diagnosed hypertensive late or early (more severe) in adult life, respectively.3 Other studies have concluded that postnatal growth may be an independent predictor of adult blood pressure.5,6

Although epidemiological studies have consistently reported an inverse association between birth weight and adult blood pressure, a recent study using standardized meta-regression analysis combining 20 Nordic birth cohorts (n=197 954) observed a U-shaped rather than inverse linear association over the full range of the birth weight distribution.2 Furthermore, a considerably stronger effect size was observed for females compared with males. On the basis of these observations, it is reasonable to assume that the relative importance of postnatal growth might also be sex specific and birth weight dependent.

The mean birth weight in the North Atlantic is among the highest reported in the world.2,7 In light of increased prevalence of macrosomia and childhood obesity,8,9 studying the relative importance of childhood growth among high birth weight infants is of considerable public health interest. We have reported previously a modest inverse association between birth weight and adult hypertension among females but not males born in Reykjavik in the early 20th century.7 The aim of this study was to follow up on these subjects to examine the association between childhood growth and adult blood pressure.
Materials and Methods

Study Population

The source data for this analysis are a cohort of 4601 singleton subjects used in our previous study on size at birth and adult blood pressure.7 These subjects were born in Reykjavik between 1914 and 1935 and were living in Reykjavik when recruited into a longitudinal study conducted at the Icelandic Heart Association between 1967 and 1991.10 Anthropometric measurements of children aged 8 to 13 years were initiated at the 2 main schools in Reykjavik in 1929 (birth year: 1921). This resulted in exclusion of 782 subjects born before 1921. An additional 1699 subjects were excluded because they were not found in clinical records collected from the 2 main Reykjavik schools. This dropout resulted in a total of 2120 subjects being available for analyses, or 46% of the source data.

Exposing this attrition further we found no indications that this sample reduction might lead to distortion in the outcome measure or in anthropometric measures at birth and adult age. As an example, the 2120 individuals who entered the analyses did not differ markedly from the 2481 individuals who did not enter with respect to (entering versus not entering, mean values) the following: birth weight (3.74 versus 3.75 kg); adult body mass index (BMI; 25.7 versus 25.6 kg/m²), and height (172 versus 171 cm), as well as systolic blood pressure (SBP; 134 versus 136 mm Hg) and diastolic blood pressure (DBP; 86 versus 86 mm Hg).

Collection of Growth Data

Information on birth outcomes was extracted from the midwives’ birth records, which included data on infant sex, birth weight (recorded with precision of ±50 g), length from crown to heel (in centimeters), and information on singleton versus multiple births. Information on childhood growth between 8 and 13 years of age was collected from school health records, where weight, height, and date of measurement for each child were recorded each year by a school nurse.

Collection of Adult Data

At enrollment participants were asked to fill out a standardized questionnaire covering a number of health, social, and lifestyle factors,10 including information on the history of familial hypertension and current use of antihypertensive medication. Clinical examinations were performed at the Icelandic Heart Association Heart Preventive Clinic in Reykjavik. Subjects arrived for examination between 8:30 to 10:30 AM in a fasting state. Blood pressure was measured once in sitting position by a trained nurse after 5-minute rest. SBP and DBP were measured to the nearest 2 mm Hg, with a mercury sphygmomanometer Erkameter wall model (Erka, Bad Tölz, Germany) using a cuff size of 12×23 cm.13 The same type of instrument was used throughout the study. A blood sample was also drawn at clinical examination, and serum triglycerides, total cholesterol, and fasting blood glucose were quantified as described previously.12,13

Exposure Measures

Primary measures of exposure were height and BMI between the ages of 8 and 13 years. Childhood growth was quantified as the mean change in the relevant growth measure per year as either height-velocity (change in height per year) or BMI-velocity (change in BMI per year) for the whole period between 8 and 13 years, as well as for the age periods 8 to 10 years and 11 to 13 years.

Outcome Measures

The primary outcome measure, hypertension, was defined according to World Health Organization guidelines14 as SBP ≥140 mm Hg and/or DBP ≥90 mm Hg and/or use of antihypertensive medication. In addition, SBP and DBP, entered as continuous variables, were used as secondary outcome measures.

Because different hypertension subtypes may have different etiologies, the growth pattern of participants classified into 3 distinct hypertension subtypes were explored. These subtypes were as follows: (1) use of antihypertensive medication before clinical examination (previously diagnosed hypertension); (2) being moderately hypertensive at clinical examination, defined as SBP between 140 to 159 mm Hg and/or DBP 90 to 99 mm Hg, with no previous use of antihypertensive medication; and (3) being severely hypertensive at clinical examination, defined as SBP ≥160 mm Hg and/or DBP ≥100 mm Hg with no previous use of antihypertensive medication.

Statistical Analyses

The mean and SD were used to describe characteristics of study participants. For dichotomous outcomes, univariate and multivariate logistic regression were used, whereas linear regression was used for continuous outcomes. As a measure of an association, we used F test (type III) for continuous outcomes and χ² test (type III) for dichotomous outcomes. Associations were examined for males and females separately. All of the analyses were performed using SAS version 9.1 (SAS Institute, Inc, Cary, NC).

To determine whether height-velocity or BMI-velocity was an independent predictor of adult hypertension, these growth measures were examined in univariate analyses and then adjusted for birth weight and anthropometric measures at adult age. Although adjustment for anthropometric measures at adult age may lead to spurious results when examining the effect of earlier growth on blood pressure,13 such an adjustment is relevant to determine whether the effect of childhood growth may be independent of or mediated through later body size.

Associations between childhood growth and adult hypertension that were stable with respect to birth weight and adult body size were then examined in more detail, both with respect to SBP and DBP and with respect to the timing of the effect (8 to 10 years or 11 to 13 years). For these analyses, we identified and included the following as covariates: birth weight (dichotomous: <3.5, 3.5 to 3.0, 4.0 to 4.5, and >4.5 kg), birth year (dichotomous: 3-year intervals from 1921 to 1935), age at clinical examination (continuous), history of familial hypertension (binary variable), and growth measure at the start of the period under examination. Birth weight and the growth measure at the start of the growth period were included to account for potential confounding because of birth weight and previous childhood growth. Birth year was included to account for potential changes in environmental factors over time; history of familial hypertension and age at clinical examination were included because they are known risk factors for adult hypertension.16,17

Results

Mean age of study participants at recruitment was 51 years with an SD of 6 years (range: 36 to 65 years). Comparison between normotensive and hypertensive males (Table 1) revealed nonsignificant differences in birth weight, birth length, and adult height. Hypertensive females had significantly lower birth weight compared with normotensive females. At 10 years of age, the prevalence of overweight as defined by Cole et al18 was 2.1% and 4.8% for males and females, respectively. The prevalence of underweight at 10 years19 corresponding with adult BMI <18.5 kg/m² was 7.9% and 8.9% for males and females, respectively. At recruitment, hypertensive males and females had elevated levels of fasting blood glucose, serum triglycerides, and total cholesterol compared with normotensive subjects.

The association between BMI-velocity and height-velocity between 8 and 13 years for males is shown in Table 2. A positive association was observed for both BMI-velocity (P=0.0006) and height-velocity (P=0.0006) with respect to adult hypertension in unadjusted analyses. For BMI-velocity, adjustment for birth weight had minor impact, whereas additional adjustment for adult BMI eliminated the associa-
The association for height-velocity was more stable with respect to adjustment for both birth weight and adult BMI ($P=0.008$), with an adjusted odds ratio of 1.49 (95% CI: 1.04 to 2.13) when comparing the highest with the lowest tertile in the velocity distribution. The association was also stable after further adjustment for adult height ($P=0.01$; data not shown).

Height-velocity between 8 and 13 years for males was then explored without adjustment for anthropometric measures at adult age (Table 3). Those analyses revealed that the association with hypertension ($P=0.21$). The association for height-velocity was more stable with respect to adjustment for both birth weight and adult BMI ($P=0.008$), with an adjusted odds ratio of 1.49 (95% CI: 1.04 to 2.13) when comparing the highest with the lowest tertile in the velocity distribution. The association was also stable after further adjustment for adult height ($P=0.01$; data not shown).

### Table 1. Characteristics of Study Participants

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Normotension (n=469)</th>
<th>Hypertension (n=616)*</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight, kg</td>
<td>2120</td>
<td>2.02 (0.53)</td>
<td>3.79 (0.59)</td>
<td>0.34</td>
</tr>
<tr>
<td>Birth length, cm</td>
<td>2119</td>
<td>2.53 (2.3)</td>
<td>2.72 (2.7)</td>
<td>0.06</td>
</tr>
<tr>
<td>Weight at 10 y, kg/m²</td>
<td>2116</td>
<td>3.10 (4.0)</td>
<td>3.16 (4.5)</td>
<td>0.02</td>
</tr>
<tr>
<td>Height at 10 y, cm</td>
<td>2118</td>
<td>137.7 (5.5)</td>
<td>138.5 (6.0)</td>
<td>0.02</td>
</tr>
<tr>
<td>Overweight at 10 y, %‡</td>
<td>2114</td>
<td>1.4</td>
<td>2.7</td>
<td>0.16</td>
</tr>
<tr>
<td>Underweight at 10 y, %§</td>
<td>2114</td>
<td>6.9</td>
<td>8.6</td>
<td>0.30</td>
</tr>
</tbody>
</table>

At recruitment, mean (SD) or %

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Normotension (n=645)</th>
<th>Hypertension (n=390)*</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>2120</td>
<td>49.8 (5.2)</td>
<td>50.2 (5.6)</td>
<td>0.25</td>
</tr>
<tr>
<td>Adult height, cm</td>
<td>2119</td>
<td>178.6 (5.9)</td>
<td>187.7 (6.6)</td>
<td>0.84</td>
</tr>
<tr>
<td>Adult BMI, kg/m²</td>
<td>2115</td>
<td>25.0 (3.3)</td>
<td>27.1 (3.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>2120</td>
<td>123 (9)</td>
<td>151 (18)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>2120</td>
<td>80 (5)</td>
<td>96 (10)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fasting blood glucose, mg/dL</td>
<td>2116</td>
<td>80.1 (10.9)</td>
<td>85.4 (18.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Serum cholesterol, mmol/L</td>
<td>2117</td>
<td>6.3 (1.0)</td>
<td>6.4 (1.1)</td>
<td>0.01</td>
</tr>
<tr>
<td>Serum triglycerides, mmol/L</td>
<td>2040</td>
<td>1.2 (0.6)</td>
<td>1.6 (1.1)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

The table shows the dichotomous comparison between normotensive and hypertensive subjects. BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure.

*Data show SBP ≥140 mm Hg and/or DBP ≥90 mm Hg at recruitment or the use of hypertensive medication before recruitment.

†Data show $\chi^2$ test for familial hypertension and underweight and overweight at 10 y; Wilcoxon rank test for blood glucose, cholesterol, and triglycerides; otherwise F test.

‡Cutoff values as derived by Cole et al (see Reference 19) correspond with having adult BMI <18.5 kg/m².

§Cutoff values as derived by Cole et al (see Reference 18) correspond with having adult BMI <17 kg/m².

### Table 2. Growth-Velocity (or Change in Growth/Year) in Males Between the Ages of 8 and 13 y in Relation to Adult Hypertension (Mean Age: 50 y)

<table>
<thead>
<tr>
<th>Growth-Velocity</th>
<th>Unadjusted, OR (95% CI)</th>
<th>Adjusted for Birth Weight, OR (95% CI)</th>
<th>Adjusted for Birth Weight and Adult BMI, OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI-velocity between 8 and 13 y, Δ kg/m² per y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tertile 1</td>
<td>(0.22)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Tertile 2</td>
<td>(0.41)</td>
<td>1.2 (0.85 to 1.69)</td>
<td>1.2 (0.87 to 1.71)</td>
</tr>
<tr>
<td>Tertile 3</td>
<td>(0.66)</td>
<td>1.94 (1.38 to 2.75)</td>
<td>1.95 (1.38 to 2.76)</td>
</tr>
<tr>
<td>$P$ for effect†</td>
<td>0.0006</td>
<td>0.0006</td>
<td>0.21</td>
</tr>
<tr>
<td>Height-velocity between 8 and 13 y, Δ cm/y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tertile 1</td>
<td>(4.5)</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Tertile 2</td>
<td>(5.1)</td>
<td>0.95 (0.68 to 1.33)</td>
<td>0.93 (0.66 to 1.30)</td>
</tr>
<tr>
<td>Tertile 3</td>
<td>(6.1)</td>
<td>1.76 (1.25 to 2.48)</td>
<td>1.74 (1.23 to 2.45)</td>
</tr>
<tr>
<td>$P$ for effect†</td>
<td>0.0006</td>
<td>0.0006</td>
<td>0.008</td>
</tr>
</tbody>
</table>

Crude associations and associations adjusted for anthropometric measures at birth and at adult age are presented. OR indicates odds ratio; BMI, body mass index. Adult hypertension was defined as systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg and/or the use of hypertensive medication.

*Data show the median in each tertile (Δ in kg/m² or centimeters per year).

†Data show $\chi^2$ test type III.
Table 3. Covariate-Adjusted Associations Between Height-Velocity and Adult Blood Pressure in Males (Mean Age: 50 y)

<table>
<thead>
<tr>
<th>Height-Velocity* (Median-Value)†</th>
<th>Hypertension, OR (95% CI)‡</th>
<th>SBP, Δ (95% CI), mm Hg</th>
<th>DBP, Δ (95% CI), mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 to 10 y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tertile 1 (4.4)</td>
<td>1.00 Referent</td>
<td>Referent</td>
<td>Referent</td>
</tr>
<tr>
<td>Tertile 2 (5.1)</td>
<td>0.84 (0.59 to 1.20)</td>
<td>−2.0 (−5.5 to 1.5)</td>
<td>−1.0 (−3.0 to 0.9)</td>
</tr>
<tr>
<td>Tertile 3 (5.9)</td>
<td>0.97 (0.68 to 1.41)</td>
<td>0.8 (−2.8 to 4.4)</td>
<td>0.4 (−1.6 to 2.4)</td>
</tr>
<tr>
<td>P for effect§</td>
<td>0.60</td>
<td>0.29</td>
<td>0.34</td>
</tr>
<tr>
<td>11 to 13 y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tertile 1 (4.2)</td>
<td>1.00 Referent</td>
<td>Referent</td>
<td>Referent</td>
</tr>
<tr>
<td>Tertile 2 (5.5)</td>
<td>1.27 (0.90 to 1.79)</td>
<td>0.4 (−3.0 to 3.8)</td>
<td>0.7 (−1.2 to 2.6)</td>
</tr>
<tr>
<td>Tertile 3 (7.5)</td>
<td>1.73 (1.21 to 2.46)</td>
<td>4.6 (1.1 to 8.1)</td>
<td>2.7 (0.8 to 4.7)</td>
</tr>
<tr>
<td>P for effect§</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
</tr>
<tr>
<td>8 to 13 y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tertile 1 (4.5)</td>
<td>1.00 Referent</td>
<td>Referent</td>
<td>Referent</td>
</tr>
<tr>
<td>Tertile 2 (5.1)</td>
<td>0.87 (0.61 to 1.24)</td>
<td>−0.8 (−4.3 to 2.7)</td>
<td>0.3 (−1.6 to 2.3)</td>
</tr>
<tr>
<td>Tertile 3 (6.1)</td>
<td>1.66 (1.15 to 2.39)</td>
<td>5.0 (1.5 to 8.5)</td>
<td>3.1 (1.1 to 5.0)</td>
</tr>
<tr>
<td>P for effect§</td>
<td>0.001</td>
<td>0.002</td>
<td>0.003</td>
</tr>
</tbody>
</table>

The growth periods examined are at 8 to 10, 11 to 13, and 8 to 13 y of age. OR indicates odds ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure.

* Covariate-adjusted associations were adjusted for height at the start of each growth period, birth weight, birth year, age at clinical examination, and history of familial hypertension.
†Data show the median in each tertile (Δ in centimeters/year).
‡Data are defined as SBP ≥140 mm Hg and/or DBP ≥90 mm Hg and/or the use of hypertensive medication.
§Data show the χ² test type III for hypertension and F test type III for SBP and DBP.

Discussion

In a cohort examining growth in 8- to 13-year-old subjects born 1921–1935 with follow-up between 1967 and 1991 (mean age: 51 years), rapid growth in BMI and height was positively associated with hypertension among males, whereas no association was observed for females. A comparison between hypertensive and normotensive subjects also revealed sex-specific differences with respect to size at birth and childhood age. For males, the association for BMI-velocity between 8 and 13 years was mediated through adult body size, whereas the corresponding association for height-velocity was independent of adult body size and birth weight.
growth up to 11 years among subjects diagnosed hypertensive early (more severe) or late (less severe), respectively. Our results partly support these observations, because both males and females diagnosed at recruitment as mildly hypertensive were shorter and of lower BMI compared with those diagnosed as severely hypertensive. However, in our study, all of the hypertensive males appeared to be following the same trend in growth compared with normotensive males. Results for subjects taking antihypertensive medication are more difficult to interpret, because this group partly resembles severely hypertensive subjects for males but mildly hypertensive subjects for females. This group should, however, be representative, because the prevalence of subjects taking antihypertensive medication in our study was comparable to what was observed in the general population during the recruitment period.

In addition, our findings are not fully compatible with reports suggesting that hypertensive subjects may, in general, be characterized by a pattern of low birth weight followed by accelerated growth in comparison with normotensive subjects. Although increased differences in height and BMI were observed between hypertensive and normotensive males, hypertensive males weight only 30 g less at birth. This modest difference in birth weight might be because of the relatively high mean birth weight in our study population. In contrast to males, hypertensive females weight 100 g less at birth, whereas differences in height and BMI were only observed for those women diagnosed as severely hypertensive. Because both sexes should share the same environment prenatally and postnatally, these sex-specific growth differences are unlikely to share the same etiology.

A positive association between childhood BMI and hypertension, as observed for males in our study, has been reported frequently. Although the association was eliminated after adjustment for adult BMI in our study, these results require cautious interpretation, first because a positive association between childhood BMI and later blood pressure has been observed in studies with shorter temporal separation between childhood BMI and blood pressure and, second, because childhood BMI is a well-established marker for adult overweight and obesity. A recent study examining childhood growth in boys between 7 and 13 years of age using path analysis concluded that, although concurrent body size may be the strongest predictor of concurrent blood pressure, the size of the effect depends on how that body size is achieved.

Absence of an association between childhood BMI-velocity and hypertension for females in our study is noteworthy, because we observed near identical correlations between BMI-velocity and adult BMI for both sexes in our data. Changes in BMI before 8 years or after 13 years of age might, however, be of more importance for females.

The primary finding of this study was the observed positive association between height-velocity and hypertension in males. The fact that hypertensive and normotensive males were of same adult height and the association for height-velocity was confined to the period between 11 and 13 years strongly suggests that the association may be driven by relatively early onset of puberty.

A British study assessing pubertal development at 15 years by medical examination observed a positive association between early onset of puberty and adult blood pressure for males born in the 1950s. The association was also stable with respect to adult body size, and the observed effect size was similar to our study (5 mm Hg for SBP). Reports from Italy and Sweden focusing on growth around pubertal age in subjects born in the late 1980s have also suggested that early pubertal growth might be associated with increased blood pressure among males. In these studies, the associations were either more modest or not present in females.

On the basis of the relative consistency between our results
and the previously mentioned studies, covering diverse populations born throughout the 20th century where environmental factors are likely to have differed markedly, there is reasonable evidence to suggest that early onset of puberty is associated with increased risk of hypertension among males. In contrast to BMI, timing of puberty is not a readily modifiable factor, with estimates suggesting that 70% to 80% of the variation is driven by genetic factors, although environmental factors such as nutrition also play a role.

Concerning mechanism, it is possible that the association between growth around pubertal age and adult blood pressure may be related to changes in serum uric acid. This assumption is supported by a cross-sectional study on 6768 adolescents aged 12 to 17 years, observing a relatively strong positive association between serum uric acid and sexual maturity in males (Pearson $r=0.46$) and height ($r=0.44$) in males. Weaker associations were observed for the same end points in females ($r=0.1$), and serum uric acid was more strongly associated with concurrent blood pressure in males compared with females. These sex-specific difference may potentially relate to the uricosuric effects of estrogen. Furthermore, other studies have consistently observed a positive association between serum uric acid and concurrent blood pressure in children and adolescents, and this association has been observed to persist into adult age.

Under the assumption that uric acid may play a role in our findings, animal studies have provided some mechanistic insight. First, elevated uric acid levels activate the renin-angiotensin system, resulting in decreased NO synthase, renal vasoconstriction, and sodium retention. Second, uric acid has a proinflammatory effect on vascular smooth muscle cells through activation of platelet-derived growth factor, mitogen-activated protein kinase, and cyclooxygenase 2. Activation of these factors then results in increased cell proliferation and preglomerular arteriolopathy. Persistent renal vasoconstriction and preglomerular arteriolopathy then lead to persistent hypertension because of development of salt sensitivity. In this context, it is relevant to note that low birth weight infants have been observed to have increased levels of uric acid and raised blood pressure during childhood.
tion between birth weight and salt sensitivity at adult age has also been reported. The relevance of these findings for later growth remains, however, to be explored, and lack of information on serum uric acid levels during childhood in our study makes the above arguments speculative.

Concerning study limitations, we acknowledge that the generality of our findings may be confined to a white population of relatively high birth weight. Furthermore, study participants were growing up in a period of rapid economic changes, which partly overlapped with the Great Depression. To account for possible temporal confounding, birth year was included as a covariate in our analyses, but this adjustment had minor effect on the association between growth and later blood pressure. Another limitation of our study is that we do not have information on onset of hypertension among those taking antihypertensive medication, which complicates comparison with subjects diagnosed at recruitment. Finally, as with all observational studies, influence of unmeasured confounding can also never be fully excluded.

Perspectives
In a population of relatively high birth weight, rapid growth from 8 to 13 years of age is related to increased risk of hypertension among males but not females. For males, this association appears to be mediated through 2 processes, which include early onset of puberty and accelerated changes in childhood BMI. Although the effect of prenatal and postnatal growth on later blood pressure has been explored in some detail, the potential mechanism behind the sex-specific growth patterns often reported needs to be addressed in more detail.

Acknowledgments
We acknowledge the contribution of the staff at the National Archives of Iceland and the Reykjavik Municipal Archives for their assistance in collection of archived birth records and growth data.

Sources of Funding
This work was supported by the University of Iceland Research Foundation, the Icelandic Fund for Research and Education (RANNÍS), the University of Iceland Students’ Innovation Fund, and the Icelandic Foundation, the Icelandic Fund for Research and Education (RANNÍS), the University of Iceland Research Foundation.

Disclosures
None.

References


Childhood Growth and Adult Hypertension in a Population of High Birth Weight
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Hypertension. 2011;58:8-15; originally published online May 16, 2011;
doi: 10.1161/HYPERTENSIONAHA.111.170985

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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