Birthweight and arterial stiffness and blood pressure in adulthood—Results from the Amsterdam Growth and Health Longitudinal Study

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Accepted 4 August 2003

Background The association between low birthweight and increased blood pressure in later life has repeatedly been confirmed. Increased arterial stiffness may be an underlying mechanism for this phenomenon. This study investigated whether birthweight was related to blood pressure and local and regional arterial stiffness.

Methods In 281 subjects (161 women), with a mean age of 36, blood pressure was measured. The diameter, distension, and local pulse pressure of three large arteries were measured simultaneously using ultrasound imaging. Local and regional arterial compliance and distensibility were calculated. Information on birthweight was retrieved with a questionnaire.

Results Linear regression analyses showed a 3.3 mmHg lower systolic blood pressure (SBP) and a 1.8 mmHg lower diastolic blood pressure (DBP), per 1 kg higher birthweight. These associations were statistically significant after adjustment for adult weight. Birthweight was significantly and positively related to carotid arterial compliance (P = 0.050), but less so to brachial (P = 0.114) and femoral arterial compliance (P = 0.058). However, after adjustment for adult height, the strength of these associations decreased. Birthweight was not related to arterial distensibility. The association between birthweight and arterial compliance could only partly explain the association between birthweight and blood pressure.

Conclusions Lower birthweight is related to increased blood pressure, and increased arterial stiffness. However, the latter relationship can only partly explain the association between birthweight and blood pressure. Therefore, mechanisms other than arterial stiffness contribute to the birthweight—blood pressure relationship.

Keywords Birthweight, blood pressure, arterial stiffness
fetal growth and local estimates of arterial stiffness, such as
distensibility and compliance. Such a study could be highly
informative, since the arterial tree is not uniform and some beds
can be more susceptible to risk factors than others. Moreover,
and in the perspective of the current debate on the fetal origins
hypothesis, it is interesting to know whether or not adult
weight or height have modifying or confounding effects. If so,
then it is not birthweight alone which is important, but also
adult weight or height.

Therefore, the aims of this study were to investigate whether,
in a healthy adult population born at term: (1) birthweight is
related to blood pressure, (2) birthweight is related to regional
and local (carotid, brachial, and femoral) estimates of arterial
stiffness, and (3) whether the association (if any) between
birthweight and blood pressure can be explained by an
association between birthweight and arterial stiffness.

Methods
Study design and subjects
The population described in this study were all participants of
the Amsterdam Growth and Health Longitudinal Study
(AGAHLS). This cohort study started in 1976 with a group of
615 healthy boys and girls, with a mean age of 13.1 years. Its
main goal was to investigate the natural development of
growth, health, fitness, and lifestyle. Earlier performed drop-out
analyses showed no selective drop-out with respect to
anthropometric measures, fitness, diet, and physical activity, as
measured in 1985, when subjects had a mean age of 22 years.11
More detailed information about the AGAHLS has been
described elsewhere.11–13 All participants were born between
1961 and 1965 and were residents of The Netherlands. In the
year 2000, at a mean age of 36.5 years, 378 subjects visited the
Vrije Universiteit for assessment of birthweight, anthropometry,
blood pressure, and large artery stiffness properties. Of those,
341 subjects had birthweight data available. Most of these
341 subjects retrieved information about their birthweights from
a birth certificate, a birth announcement card, or something
similar (195 subjects); others had to retrieve the information
from their parents (129 subjects).14–17 The remaining
17 subjects did not mention the source of the information and
were excluded from the analyses. Another 43 subjects were
excluded for analyses: 29 subjects who were born preterm
(gestational age <37 weeks [29 subjects]) were excluded since being born
preterm may have independent effects on adult health or
the relationship between birthweight and adult health (for
instance blood pressure) might be different in subjects born
preterm.9,19,20 Twins were excluded because twins have
different fetal growth patterns, which might cause error when
analysing the relationship between birthweight and adult blood
pressure and arterial stiffness.

Arterial stiffness
Properties of the right common carotid (CCA), brachial (BA),
and the common femoral arteries (CFA) were obtained with a
B+M-mode ultrasound scanner equipped with a 7.5 MHz
linear array transducer (Pie Medical, Maastricht, The Netherlands).
The ultrasound scanner was connected to a personal computer
-equipped with an acquisition system and a vessel wall
movement detector software system (Wall Track System 2, Pie
Medical, Maastricht, The Netherlands). This integrated device
enables measures of arterial diameter, distension, and pulse
wave transit time.21,22 All subjects had abstained from
smoking and caffeine-containing beverages on the day the
measurements were performed. At the time of measurement of
arterial properties, subjects had been resting in a supine
position for 15 minutes in a quiet, temperature-controlled
room.

Local arterial stiffness
The mean diameter (D) and distension (∆D) of three
consecutive measurements on each artery, and the mean local
pulse pressure (∆P) (described below) of three measurements
obtained at approximately the moment of those measurements,
were used to estimate distensibility and compliance as
follows:23

\[
distensibility = \frac{(2\Delta D \cdot D + \Delta D^2)}{(\Delta P \cdot D^2)} \text{ in } 10^{-3} \text{ kPa}^{-1} \quad (1)
\]

\[
compliance = \pi \cdot (2D \cdot \Delta D + \Delta D^2)/4\Delta P \text{ in } \text{mm}^2 \text{ kPa}^{-1} \quad (2)
\]

Distensibility is the fractional change in arterial cross-sectional
area per unit change in (local) pulse pressure, i.e. it describes
the amount of diameter expansion expressed as percentage
of the initial diameter of the artery in relation to the force
that causes the expansion (transmural pressure). Compliance
is defined as the absolute change in cross-sectional area per unit
of transmural pressure. Distensibility is therefore a measure of the
elastic properties of an artery whereas compliance is a measure
of the local vessel capacity to store extra volume (i.e. buffering
capacity).24

Regional stiffness
While measuring diameter and distension, the time delay
between the foot of the distension waveforms and the R-wave
of the simultaneously recorded ECG, i.e. the pulse wave transit
time (TT), was determined for each artery. Each recording
included 3–7 heartbeats and the mean TT of three recordings
in each artery where calculated. The carotid pulse wave TT was
then subtracted from the femoral pulse wave TT to obtain the
carotido-femoral TT. We used this carotido-femoral TT (in ms)
as an indicator of regional stiffness.25 The TT of a pulse wave
from the carotid to the femoral artery is negatively related
to mean arterial stiffness over this segment and closely related
to carotido-femoral PWV, as length of the carotido-femoral segment divided by the segment pulse wave TT. Measurement of this length (usually performed with a tape measure over the subject’s body surface) may introduce error. We therefore used the carotido-femoral transit time adjusted for sitting height in the analyses (and not height, avoiding the error introduced by ‘long trunk-short legs’ or ‘short trunk-long legs’ variability among subjects). Due to technical reasons (deficient ECG signalling tracing), data on PWV was available only on 234 subjects (133 women). Subject without this information did not differ significantly from the ones included with regard to birthweight, adult body weight, height, body mass index (BMI), systolic blood pressure (SBP), and diastolic blood pressure (DBP).

**Blood pressure**

Throughout the entire period of ultrasound imaging, SBP, DBP, and mean blood pressure were assessed (mean is used) in the left arm at 5-minute intervals with an oscillometric device (Colin Press-Mate, model BP 8800, Komaki-City, Japan). Brachial artery pulse pressure was defined as SBP minus DBP, and pulse pressure at the common carotid and femoral arteries was calculated by calibration of the distension waveforms. This method of calibration is based on the observation that mean arterial pressure is constant throughout the large artery tree and that DBP does not change substantially. Distension waveforms were assessed at the target (i.e. the carotid and femoral arteries) and at the reference artery (i.e. the brachial artery). Based on these distension waveforms and on pulse pressure measured at the reference artery, pulse pressure was calculated at each target artery as follows: \[PP_{target} = PP_{reference} \times CF\] (Calibration factor), where \(CF = \left[\frac{PP_{reference} - DBP_{target}}{DBP_{reference}}\right]^{-1}\). This means that mean arterial pressure can be calculated from the area under the pressure curve divided by time, an similarly using the distension waveforms instead.

Both inter-observer reliability and intra-observer reliability were good. For instance the reproducibility as assessed by inter-observer coefficients were on average: diameter, 2.9% (carotid), 4.6% (brachial), and 2.8% (femoral); and distension, 6.4% (carotid), 27.7% (brachial), and 24.2% (femoral); and carotido-femoral TT 12.3%.

**Potential covariates/effect modifiers—Adult weight and height**

Body weight (to the nearest 0.1 kg) and body height (to the nearest 0.001 m) were measured according to standard procedures, with subjects dressed only in underwear.

**Statistical analyses**

Multiple linear regression analyses were used to assess the relationship between birthweight on the one hand and blood pressure and arterial stiffness estimates on the other. The associations were assessed firstly with adjustment for sex (and mean blood pressure in the case of analyses with stiffness estimates as outcome variables) (model 1), and secondly with additional adjustment for adult weight and/or height. The level of significance for the associations between birthweight and the outcome variables was set at \(P < 0.05\).

To analyse whether an observed association between birthweight and blood pressure can be explained by an association between birthweight and arterial stiffness, stiffness estimates were added to the models with birthweight and blood pressure.

It was then analysed whether or not sex was an effect modifier in the relationships of interest. When the interaction showed a \(P\)-value < 0.1, results were presented separately for men and woman.

All analyses were carried out with the Statistical package of Social Sciences, version 10.1. for Windows (SPSS, Inc, Chicago, IL).

**Results**

Characteristics of all subjects (n = 281) are presented in Table 1. Mean birthweight in men (3.54 kg) was slightly higher than in women (3.42 kg). Mean birthweight of subjects who collected their birthweight from their parents’ memory (3.56 ± 0.52 kg, adjusted for sex), was slightly higher than the mean birthweight of subjects who had written documents (3.43 ± 0.48 kg, adjusted for sex). This was most probably due to the tendency to report rounded to higher numbers (e.g. 3.5 kg instead of 3.4 kg) when no written documents were available.

Table 2 shows that birthweight was inversely related to both SBP as well as DBP. After adjustment for adult weight (model 2), but not after adjustment for adult height, these associations became stronger and statistically significant. Since total body weight comprises both fat and lean mass, it was further analysed which of these body composition components cause the strengthening of the association between birthweight and blood pressure. In the AGAHLS, data was available on fat mass, lean mass (as estimated by the Durnin and Womersley equations), and body fat distribution (waist-to-hip ratio). For both SBP and DBP, adjusting for fat mass instead of body weight resulted in almost the same effect estimates. The model including lean mass instead of body weight resulted in slightly lower regression coefficients for birthweight. The model including waist-to-hip ratio differed the most from the model including adult height and weight. All results were reported for men and women together, because no interactions were found between birthweight and sex.

Table 3 shows that birthweight was significantly and positively associated with carotid compliance, an association that was mainly due to the association of birthweight with the diameter of this artery. However, after adjustment for current weight or height the association decreased and was no longer significant.

Birthweight was positively associated with the diameter of the brachial artery. This association remained significant when adult height was introduced into the model, but not after further adjustment for adult weight.

Birthweight was inversely and significantly associated with the local pulse pressure of the femoral artery. The relationship between birthweight and femoral compliance was borderline significant (\(P = 0.058\)), but decreased when height was introduced into the model (model 2).

Birthweight was associated with regional stiffness in a different fashion for men and women (\(P = 0.021\) for interaction between birthweight and sex). For women the association was in a positive direction, while for men the association was equally strong but negative.
Next, analyses were performed to study the mediating effect of all stiffness estimates used in this study on the relationship between birthweight and SBP. Results showed that adding femoral compliance into the model which already included birthweight as a determinant, sex and weight as covariates, and SBP as an outcome, changed the regression coefficient of birthweight from $-3.31$ mmHg/kg to $-2.41$ mmHg/kg ($P = 0.045$). Adding carotid or brachial compliance instead of femoral compliance resulted in smaller changes in the regression coefficient (to $-2.60$ mmHg/kg and $-2.83$ mmHg/kg respectively).

### Table 1

Characteristics of the population (at age 36 years)

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birthweight (kg)</td>
<td>3.54 (0.46)</td>
<td>3.42 (0.52)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>84.2 (10.7)</td>
<td>68.1 (10.0)</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.84 (0.06)</td>
<td>1.71 (0.06)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.8 (2.7)</td>
<td>23.4 (3.3)</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg) (supine)</td>
<td>121.6 (10.6)</td>
<td>111.3 (10.9)</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg) (supine)</td>
<td>66.6 (7.0)</td>
<td>62.8 (7.1)</td>
</tr>
<tr>
<td>Mean arterial pressure (mmHg) (supine)</td>
<td>85.6 (7.7)</td>
<td>78.7 (8.3)</td>
</tr>
</tbody>
</table>

#### Common carotid artery

<table>
<thead>
<tr>
<th></th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter (mm)</td>
<td>7.18 (0.48)</td>
<td>6.55 (0.52)</td>
</tr>
<tr>
<td>Distension (µm)</td>
<td>0.63 (0.13)</td>
<td>0.51 (0.12)</td>
</tr>
<tr>
<td>Local pulse pressure (mmHg)</td>
<td>53.0 (8.0)</td>
<td>45.7 (7.8)</td>
</tr>
<tr>
<td>Compliance (mm²/kPa)</td>
<td>1.05 (0.23)</td>
<td>0.92 (0.26)</td>
</tr>
<tr>
<td>Distensibility (10⁻³/kPa)</td>
<td>26.0 (5.4)</td>
<td>27.2 (6.8)</td>
</tr>
</tbody>
</table>

#### Brachial artery

<table>
<thead>
<tr>
<th></th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter (mm)</td>
<td>4.51 (0.52)</td>
<td>3.53 (0.47)</td>
</tr>
<tr>
<td>Distension (µm)</td>
<td>0.20 (0.11)</td>
<td>0.17 (0.09)</td>
</tr>
<tr>
<td>Local pulse pressure (mmHg)</td>
<td>55.2 (6.5)</td>
<td>48.6 (6.5)</td>
</tr>
<tr>
<td>Compliance (mm²/kPa)</td>
<td>0.20 (0.10)</td>
<td>0.15 (0.08)</td>
</tr>
<tr>
<td>Distensibility (10⁻³/kPa)</td>
<td>13.2 (9.5)</td>
<td>15.9 (9.5)</td>
</tr>
</tbody>
</table>

#### Common femoral artery

<table>
<thead>
<tr>
<th></th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter (mm)</td>
<td>10.6 (0.98)</td>
<td>8.88 (1.00)</td>
</tr>
<tr>
<td>Distension (µm)</td>
<td>0.22 (0.11)</td>
<td>0.23 (0.10)</td>
</tr>
<tr>
<td>Local pulse pressure (mmHg)</td>
<td>54.9 (9.2)</td>
<td>49.4 (9.7)</td>
</tr>
<tr>
<td>Compliance (mm²/kPa)</td>
<td>0.51 (0.23)</td>
<td>0.52 (0.24)</td>
</tr>
<tr>
<td>Distensibility (10⁻³/kPa)</td>
<td>5.8 (3.1)</td>
<td>8.5 (4.4)</td>
</tr>
<tr>
<td>Carotid-femoral transit time (ms) (corrected for sitting height)</td>
<td>78.8 (2.79)</td>
<td>78.7 (2.59)</td>
</tr>
</tbody>
</table>

Data are means (SD).

### Table 2

Regression coefficients ($β$) and 95% CI for the relationship between birthweight (kg) and systolic (SBP) and diastolic (DBP) blood pressure

<table>
<thead>
<tr>
<th>Covariates</th>
<th>SBP (mmHg)</th>
<th>95% CI</th>
<th>DBP (mmHg)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>$-1.54$</td>
<td>($-4.09, 1.01$)</td>
<td>$-0.9$</td>
<td>($-2.57, 0.77$)</td>
</tr>
<tr>
<td>Sex, adult weight</td>
<td>$-3.31^{**}$</td>
<td>($-5.75, -0.879$)</td>
<td>$-1.85^{*}$</td>
<td>($-3.49, -0.21$)</td>
</tr>
<tr>
<td>Sex, adult weight, adult height</td>
<td>$-3.05^{*}$</td>
<td>($-5.51, -0.60$)</td>
<td>$-1.55$</td>
<td>($-3.19, 0.08$)</td>
</tr>
<tr>
<td>Sex, adult height, adult fat mass</td>
<td>$-3.01^{*}$</td>
<td>($-5.45, -0.56$)</td>
<td>$-1.54$</td>
<td>($-3.17, 0.08$)</td>
</tr>
<tr>
<td>Sex, adult height, adult lean mass</td>
<td>$-2.73^{*}$</td>
<td>($-5.24, -0.21$)</td>
<td>$-1.34$</td>
<td>($-3.01, 0.33$)</td>
</tr>
<tr>
<td>Sex, adult height, adult waist to hip ratio</td>
<td>$-2.04$</td>
<td>($-4.72, 0.63$)</td>
<td>$-1.12$</td>
<td>($-2.86, 0.64$)</td>
</tr>
</tbody>
</table>

* $P < 0.05$, ** $P < 0.01$. 

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Table 3 The regression coefficients (β) and 95% CI for the relationships between birthweight and adult arterial stiffness estimates

<table>
<thead>
<tr>
<th></th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β</td>
<td>95% CI</td>
<td>β</td>
</tr>
<tr>
<td><strong>Common carotid artery</strong>a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diameter (mm)</td>
<td>0.162**</td>
<td>(0.046, 0.279)</td>
<td>0.121*</td>
</tr>
<tr>
<td>Distension (μm)</td>
<td>0.017</td>
<td>(−0.013, 0.046)</td>
<td>0.001</td>
</tr>
<tr>
<td>Local pulse pressure (mmHg)</td>
<td>−0.378</td>
<td>(−2.205, 1.449)</td>
<td>−0.810</td>
</tr>
<tr>
<td>Distensibility (kPa⁻¹)</td>
<td>0.260</td>
<td>(−1.108; 1.627)</td>
<td>−0.047</td>
</tr>
<tr>
<td>Compliance (mm²/kPa)</td>
<td>0.057*</td>
<td>(0.000; 0.114)</td>
<td>0.034</td>
</tr>
<tr>
<td><strong>Brachial artery</strong>a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diameter (mm)</td>
<td>0.144*</td>
<td>(0.028, 0.259)</td>
<td>0.138*</td>
</tr>
<tr>
<td>Distension (μm)</td>
<td>0.010</td>
<td>(−0.014, 0.033)</td>
<td>0.005</td>
</tr>
<tr>
<td>Local pulse pressure (mmHg)</td>
<td>−0.632</td>
<td>(−1.969, 0.705)</td>
<td>−0.950</td>
</tr>
<tr>
<td>Distensibility (10⁻³/kPa)</td>
<td>0.809</td>
<td>(−1.395; 3.012)</td>
<td>0.719</td>
</tr>
<tr>
<td>Compliance (mm²/kPa)</td>
<td>0.017</td>
<td>(−0.004; 0.038)</td>
<td>0.013</td>
</tr>
<tr>
<td><strong>Common femoral artery</strong>a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diameter (mm)</td>
<td>0.181</td>
<td>(−0.054, 0.416)</td>
<td>0.091</td>
</tr>
<tr>
<td>Distension (μm)</td>
<td>0.009</td>
<td>(−0.015, 0.034)</td>
<td>0.003</td>
</tr>
<tr>
<td>Local pulse pressure (mmHg)</td>
<td>−2.751**</td>
<td>(−4.827; −0.676)</td>
<td>−2.727**</td>
</tr>
<tr>
<td>Distensibility (10⁻³/kPa)</td>
<td>0.616</td>
<td>(−0.268; 1.499)</td>
<td>0.465</td>
</tr>
<tr>
<td>Compliance (mm²/kPa)</td>
<td>0.053</td>
<td>(−0.002; 0.108)</td>
<td>0.036</td>
</tr>
<tr>
<td>Transit time in carotido-femoral segment (ms)b</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>−4.365</td>
<td>(−9.517; 0.787)</td>
<td>−4.368</td>
</tr>
<tr>
<td>Women</td>
<td>3.895</td>
<td>(−0.649; 8.439)</td>
<td>3.861</td>
</tr>
</tbody>
</table>

Model 1: adjusted for sex; model 2: adjusted for sex and adult height; model 3: adjusted for sex, adult weight, and height.

a All models adjusted for mean arterial pressure.

b Models are adjusted for sitting height.

° P < 0.05; ** P < 0.01.

Discussion

The purpose of this study was to investigate whether, in a relatively healthy and young population, birthweight was related to adult blood pressure and arterial stiffness indicators, and whether adult weight or height modified or confounded these relationships.

We observed that birthweight was indeed negatively associated with both SBP and DBP, which was statistically significant after adjustment for adult weight. The estimates for the effect of birthweight on SBP whether or not adjusted, were comparable with those in other studies.⁵,⁶

The present study was the first in which the relationship between birthweight and stiffness indicators in three large arteries (i.e. common carotid, brachial, and femoral artery) was investigated. Birthweight was positively associated with the compliance of all three arteries investigated, but this decreased after adjustment for adult height. That birthweight was associated with compliance but not with distensibility is most probably due to the association between birthweight and diameter (in carotid and brachial arteries). Compliance and distensibility reflect two different arterial properties, elastic and buffering capacities respectively, and these results suggest that birthweight is more related to the size of the arteries and the buffering capacity than to elasticity.

A further essential question was whether or not the association between birthweight and blood pressure could be explained by the relationship between birthweight and arterial stiffness, as Martyn and Greenwald⁴ have suggested. Adding carotid or brachial or femoral arterial compliance into the model resulted in a reduction of the regression coefficient for birthweight (from −3.31 to −2.60, −2.83, or −2.41, respectively), but the regression coefficients were still significant (P < 0.045). Considering possible inaccuracies in measurement of both birthweight and arterial stiffness, it can still be concluded that arterial stiffness may at most partly explain the relationship between birthweight and systolic blood pressure. Other determinants of blood pressure may therefore play an important role, such as nephron number, kidney function, sympathetic nervous system, and body composition.³⁰–³⁴

Adjustment for adult size

Adjustments for adult size (i.e. weight, height) are controversial in the analyses of the relationships between birthweight and cardiovascular outcomes.⁵⁵,⁶⁶ Adult height can be both a confounder or a mediator in the relationship between birthweight and arterial stiffness. Models not adjusted for adult height would give the more correct estimate for the effect of birthweight if we assume that adult height is a mediator.
independent of current size, and that birthweight was related to cardiac sympathetic activation independently of current weight. The fact that the association between birthweight and arterial stiffness differs from the association between birthweight and blood pressure might suggest different underlying mechanisms.

**Sex difference**

In the present study, an interaction with sex was found for the relationships between birthweight and TT in the carotido-femoral segment. For men an inverse relationship was found, while for women a positive relationship was found. This difference could not be explained by differences in body size, because this difference was also found after correction for body size. However, in a study of Murray et al. a comparable sex difference was observed. Thus there may be a 'true' sex difference, which implies that regional stiffness is different in this respect from local stiffness (as has been measured in the present study in the carotid and femoral artery). That these associations with regional stiffness are different from the associations with local stiffness is possible, since they represent arterial stiffness in different parts of the body. Furthermore, the human arterial tree is not homogeneous, as the distribution of collagen and elastin differs between arteries. If this interaction is genuine, then this may suggest that increased arterial stiffness (as measured with TT) cannot be the exclusive underlying mechanism in the birthweight—blood pressure relationship, since that relationship is not modified by sex. To our knowledge, no other study has reported results on the relationship between birthweight and compliance separately for men and women, and we cannot exclude that the interaction we observed was a chance finding.

**Elastic versus muscular arteries**

The relationships between birthweight and compliance and distensibility were assessed in both elastic (CCA) as well as in muscular arteries (BA and CFA). According to the hypothesis postulated by Martyn and Greenwald, it could be expected that effects of fetal growth on the stiffness of an artery should be clearer in elastic arteries, since elastin synthesis is thought to be limited in those with retarded fetal growth or lower birthweight. In support, the association between birthweight and compliance in the elastic carotid artery was somewhat stronger than the association with compliance in the femoral and brachial artery. In the carotid and brachial artery the association was mainly due to the positive association with the diameter (i.e. arterial geometry), while in the femoral artery this was due to the strong negative relationship with local pulse pressure. Increased pulse pressure may result from early wave reflections, which could be caused by changes in small rather than in large arteries. Another factor which influences pulse pressure is stroke volume. Unfortunately, in the AGAHLs population stroke volume was not measured, but heart rate was measured, which could serve as an indicator. Additional analyses showed, however, that birthweight was not related to heart rate (P = 0.245). Thus, from this data it is not clear what caused the relationship between birthweight and pulse pressure in the femoral artery.

**Study limitations**

The method used in this study to measure birthweight may not be as precise as using birth certificates from hospitals. However, several studies have supported the method of retrospective questionnaires. In The Netherlands it is difficult to retrieve information on birthweight and gestation from hospitals, since most mothers give birth to their babies at home. In the population of the AGAHLs 187 subjects (66.5%) were born at home. In additional analyses we observed that the methods used to retrieve information on birthweight (either written documents or parents’ memory) did not affect the associations found (data not shown).
The population of the AGAHLS is a relatively healthy population. Most subjects had normal birthweights. Only a few reported birthweights ≤2.5 kg (7 subjects), which is often considered as low. Therefore, the variation in the main independent variable was relatively small, which may cause difficulties in detecting associations.

Conclusions
Birthweight was significantly and negatively related to SBP, and tended to be positively related to compliance in the carotid, brachial, and femoral arteries. However, the latter finding only tended to be positively related to compliance in the carotid artery. Birthweight was significantly and negatively related to SBP, and adjustments for adult weight increased the association between birthweight and blood pressure, and adjustments for adult height decreased the association with arterial compliance, which suggests that adult weight and height are important to take into account when interpreting these relationships.

Acknowledgements
The AGAHLS is supported by multiple grants from the Dutch Prevention Fund (ZON), Dutch Heart Foundation (NHS), Dutch Ministry of Education and Science, Dutch Ministry of Well Being, Public Health and Sports (VWS), the Dairy Foundation on Nutrition and Health (ZVG), Dutch Olympic Committee/Dutch Sports Foundation (NOC/NSF), Scientific Board Smoking and Health, and Heineken Inc. We would like to thank Eveline Bekkering, who was one of the observers in the ultrasound measurements, and we would like to thank all the men and women who participated in the AGAHLS.

KEY MESSAGES
- This study confirms the often reported birthweight—blood pressure relationship.
- This study shows a positive association between birthweight and compliance (i.e. buffering capacity) of the carotid artery.
- It was also shown that the association between birthweight and compliance can only partly explain the birthweight—blood pressure relationship.

References
7 Kumaran K, Fall CH, Martyn CN, Vijayakumar M, Stein C, Shier R. Blood pressure, arterial compliance, and left ventricular mass: no relation to small size at birth in south Indian adults. Heart 2000;83:272-77.
Arterial stiffness is a major, independent risk factor for the development of cardiovascular disease and also an important predictor of outcome. In addition, increased arterial stiffness may play a role in the development of hypertension. Although a body of evidence already exists linking low birthweight to the development of hypertension in later life, this has recently been challenged. Nevertheless, a unifying hypothesis linking fetal growth retardation to increased arterial stiffness and the future development of hypertension remains an attractive one. To date a number of studies have attempted to test this hypothesis in different populations often with conflicting results. In the study reported in this issue of the International Journal of Epidemiology, te Velde and colleagues address this important issue in 281 subjects enrolled in the Amsterdam Growth and Health Longitudinal Study using measurements of compliance and distensibility in three vascular beds; the carotid, brachial, and femoral respectively. Their results are far from clear cut and somewhat difficult to interpret. The main findings were that birthweight was inversely associated with adult blood pressure even after adjustments, and birthweight was significantly correlated with carotid arterial compliance ($P = 0.050$) but not...