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 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

---

**Commentary: Birthweight arterial stiffness and blood pressure: in search of a unifying hypothesis**

Ian B Wilkinson\(^1\) and John R Cockcroft\(^2\)

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
with brachial \( (P = 0.114) \) or femoral \( (P = 0.058) \) compliance. However, after adjustment of the results for current height there was no association between birthweight and compliance. Moreover, there was no relationship between birthweight and distensibility in any vascular bed. The authors suggest that differences in arterial stiffness in their cohort can only partially explain the relationship between birthweight and blood pressure.

Is the original hypothesis still viable, or is there a piece of the jigsaw still missing or perhaps, most importantly, have the authors measured the correct parameters? Arterial compliance represents the change in volume (diameter or area) of a vessel for a given change in pressure and is an index of stiffness, whereas distensibility is the relative change in area for a given change in pressure and provides information about vessel elasticity. Although the two parameters are related, they do not necessarily change in a similar way. Indeed, with age brachial artery compliance decreases, whereas distensibility does not. Relatively few data exist concerning the predictive value of distensibility and compliance whereas aortic pulse wave velocity (inversely related to aortic distensibility) has been shown to predict outcome in patients with hypertension, \(^5\) diabetes, \(^6\) end stage renal failure, \(^7\) and older healthy individuals. \(^8\) Perhaps, therefore, assessment of aortic pulse wave velocity would have been more appropriate in te Velde’s study.

Although te Velde et al. present data relating birthweight to both systolic (SBP) and diastolic blood pressure (DBP) measured peripherally they show no data for peripheral pulse pressure (the difference between SBP and DBP). This is potentially important because systolic and, to a larger degree, pulse pressure depends on large artery stiffness (and cardiac output) whereas DBP and MAP depend more on peripheral resistance. Previous data suggest a relationship between pulse pressure measured in the arm and low birthweight. \(^9\) Moreover, recent data from the MRC national survey of health and development suggest that birthweight is, in agreement with many other studies, associated with SBP but not DBP, \(^10\) suggesting that perhaps low birth weight predisposes to systolic rather than systolic/diastolic hypertension. SBP and pulse pressures also vary throughout the arterial tree, and aortic pulse pressure relates more closely to left ventricular mass and carotid intima-media thickness than brachial pulse pressure, suggesting that central pulse pressure may be a better predictor of risk, which was recently confirmed in a cohort of patients with end-stage renal failure. \(^11\) Therefore, it would be of considerable interest to investigate the relationship between aortic pulse pressure, birthweight, and arterial stiffness. Fortunately, non-invasive assessment of aortic blood pressure is now possible using a validated transfer function with the SphygmoCor system. \(^12\) This also allows calculation of the augmentation index (AIx), a composite measure of wave reflection and arterial stiffness that independently predicts future cardiovascular risk in selected patient groups. \(^13\) In a recent study Lurbe et al. \(^14\) used the SphygmoCor system to generate, non-invasively, central aortic waveforms in 219 healthy children aged 7–18 years. Their results showed a significant inverse correlation between birthweight and AIx, and also a negative correlation between birthweight and aortic SBP. Suggesting that children with low birthweights exhibit haemodynamic changes associated with increased large arterial stiffness at an early stage, supporting the hypothesis that large arterial stiffening is, indeed, an important link between low birthweight and the risk of developing hypertension in later life. Whether early detection of arterial stiffening in children or young adults will allow for the development of intervention strategies designed to prevent the development of hypertension in such individuals is an important question and one that will need addressing in the future. In the meantime it may be that we need to search no further than subtle changes in arterial stiffness already detectable in children and adolescents to explain the predisposition to develop hypertension associated with low birthweight.

References


\(^3\) Martin CN, Greenwald SE. Impaired synthesis of elastin in the walls of aorta and large conduit arteries during early development as an initiating event in the pathogenesis of systemic hypertension. Lancet 1997;350:953–55.


