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EARLY CARDIOMETABOLIC RISK FACTORS IN CHILDREN AND YOUNG PEOPLE

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Key Points

- The antecedents of atherosclerosis and cardiovascular disease commence early in life and are progressive leading to early vascular ageing.
- Mortality after 24 years of follow-up of 11 year-old children was 75% higher in those with the worst glucose intolerance and 55% higher in those with hypertension.
- Obstructive sleep apnea risk increase 12% for each unit of BMI increase.
- Obesity with its metabolic sequelae is driving the appearance of cardiovascular risk at an ever earlier age.

The events that lead to the development of atherosclerosis and cardiovascular disease are progressive, with antecedents that commence early in life – even in the immediate pre- and post-natal periods. They result from genetic susceptibilities and environmental "hazards" that eventually culminate in clinical events. The earlier, more frequent and more severe development of obesity has already been shown to produce metabolic disorders such as type 2 diabetes at an earlier age than hitherto, and now commonly affects adolescents and even younger children; it can be expected that similar trends in cardiovascular disease will be seen. A clear relationship between adiposity (measured by body mass index [BMI]), intra-abdominal (visceral) fat, plasma leptin and hypertension and dyslipidemia is already apparent at age 9-11 years [1].

A recent report on a cohort of 4,857 American Indian children without diabetes (mean age, 11.3 years; 12,659 examinations) born between 1945 and 1984, found that after a mean follow-up of 23.9 years, there were 166 deaths from "endogenous" causes. Among children in the highest quartile of glucose intolerance, death rates were increased by 73% compared to the lowest quartile; the presence of hypertension in childhood increased the risk of premature death by 55% [2]. These risks have been characterized as "early vascular ageing" [3] and can be further defined by the presence of arterial stiffening related to the state of low level but chronic inflammation that exists in obesity (Table).

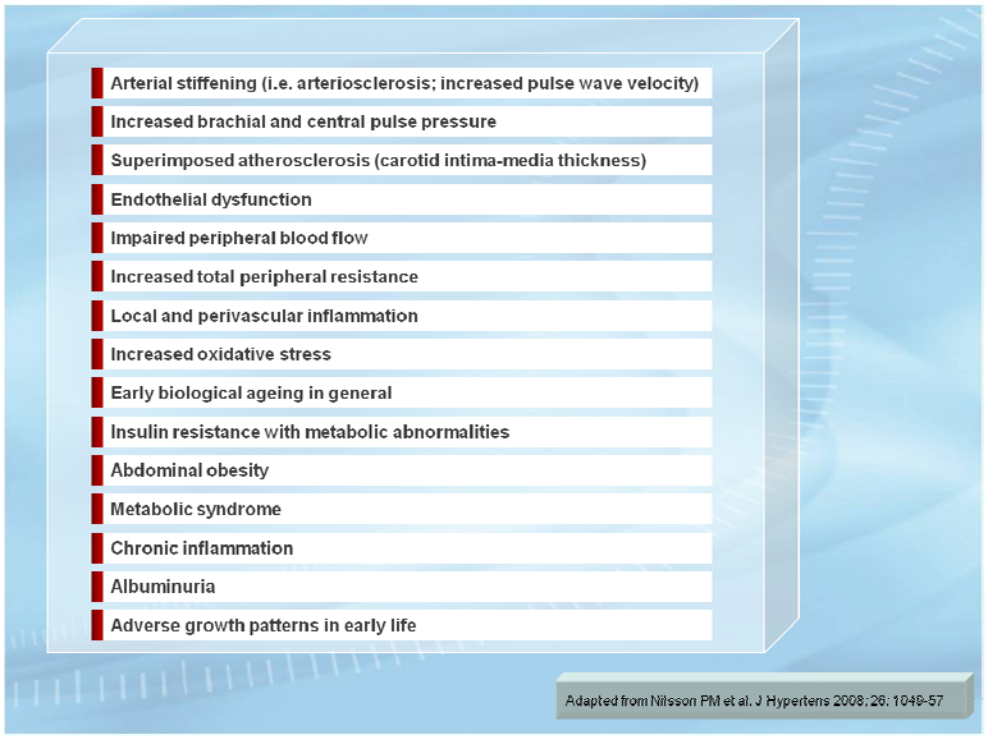

Table: Component of the early vascular ageing (EVA) syndrome and associated conditions.

Further data attest to the impact of early childhood adiposity and later cardiovascular and metabolic risk [4] with relative risks of 4.8-5.8 in boys and girls respectively for later metabolic syndrome (20-year follow-up) by highest to lowest quartile for waist circumference at age 7-15. A number of studies have shown that the young already have evidence for atherosclerosis [5], 1 in 6 teenager donors for heart transplant had significant coronary artery lesions [6]. Evidence from the Bogalusa Heart Study showed that as the number of cardiovascular risk factors increased so did the severity of asymptomatic coronary and aortic atherosclerosis [7]. A systematic review found the presence of type 1 diabetes, dyslipidemia, hypertension and renal failure in childhood consistent disease risks for increased carotid intima-media thickness. In terms of incident cardiovascular events before the age of 60, a 1-unit increase in BMI raised the risks by 3-7% at age 7, and 12-15% by age 13 [8].

The development of noninvasive methods of examining the structure and function of the vasculature has expanded our knowledge of cardiovascular disease and its risk factors in children. Arterial stiffness can be measured ultrasonically to derive values for pulse wave velocity, brachial distensibility, and for augmentation pressure and index. The methods are reliable and reproducible if performed by well-trained technicians and according to well-defined protocols [9]. In one small survey of young people aged 10-23 years, those with type 2 diabetes had worse measures of arterial stiffness that correlated with intra-abdominal fat assessed by waist circumference, and blood pressure [10]. Another technique used to assess vascular function is flow-mediated dilatation (FMD) – the response of arterial calibre in response to brief ischemia – which in adults has been shown to be an independent and significant predictor for later cardiovascular death and stroke. Its validity in the young is not well established. The presence of low-grade inflammation as evidenced by elevated high-sensitive C-reactive protein levels was however associated with impaired FMD in otherwise healthy children [11].

Another factor that increases cardiovascular risk burden is the presence of obstructive sleep apnea. Although obstructive sleep apnea is much less common in children and adolescents compared with adults, its risk increases by 12% for each unit of BMI increase [12]; when present the risk for metabolic syndrome in adolescents was increased 6-fold [13].

While many of these measures represent endothelial and vascular damage, another component, namely endothelial repair, is seen to be of perhaps equal importance and driving the concept that damage occurs when the endothelium's repair capacity is exceeded (Figure).

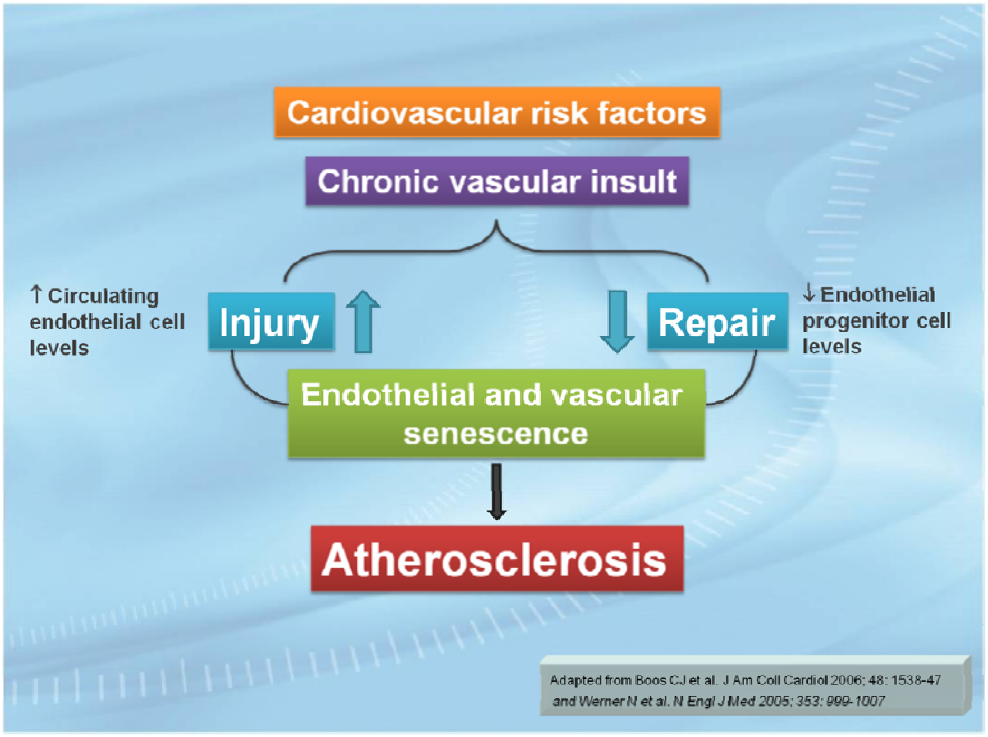

Figure: Exhaustion of endothelial repair capacity

Hill et al. [14] concluded from a study in 2003 that in healthy men, levels of endothelial progenitor cells may be a surrogate biologic marker for vascular function and cumulative cardiovascular risk suggesting that endothelial injury in the absence of sufficient circulating progenitor cells may affect the progression of cardiovascular disease. Preliminary work from our laboratory suggests similar impairment of repair mechanisms in obese children.

It appears that risk factors only previously identified in adult populations exist in children and adolescents, and that the growing prevalence of obesity with its metabolic sequelae are driving the appearance of cardiovascular risk from disorder function and form of the vasculature at an ever earlier age.

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