Genes Nutr (2007) 2:31–32
DOI 10.1007/s12263-007-0004-y

PROCEEDINGS

Metabolic programming during pregnancy: epidemiological studies in humans

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Published online: 21 September 2007

Fetal growth and later disease

Epidemiological evidence gathered over the past 15 years has shown that impaired fetal growth affects susceptibility to cardiovascular disease and type II diabetes in adult life. Across a wide variety of populations, lower birth weight, and thinness at birth, is associated with an increased risk of development of these conditions. These associations are evident within the normal range of birth weight, and are not explained by effects of extreme growth retardation, by differences in gestational age at birth, or by differences in adult lifestyle [1].

Interaction of fetal with postnatal experience in influencing disease risk in adult life

In recent studies of individuals whose postnatal growth was described in detail, the effects of poor fetal growth on later disease have been shown to be compounded by continued poor growth in infancy, but followed by rapid weight gain in childhood. Amongst Finnish men and women, an increased risk of coronary heart disease was seen in those who were thin at birth and in infancy, but who gained weight rapidly after the age of 2 years [3].

The influence of different pathways of growth on later health has also been described in a study of young Indian adults [4]. The pattern of growth associated with impaired glucose tolerance or diabetes in adult life was characterised by thinness between birth and the age of 2 years, but followed by rapid weight gain in childhood and a relatively high body mass index at the age of 12 years.

The significance of a single measure of BMI, or of being overweight, at any age, in relation to cardiovascular disease and impaired glucose tolerance, therefore differs according to earlier pathways of growth—and some individuals may be more vulnerable to the effects of excess body weight as a result of their early experience.

Vulnerability to stressors in adult life

Follow-up of individuals who differ according to their pathways of fetal and postnatal growth has provided evidence that responses, and therefore vulnerability, to the effects of adverse influences in adult life are conditioned by early growth. For example, in the American nurses' health study, the highest risk of coronary heart disease was found among women who had low birth weight but who had a high body mass index as adults [7].

Among a group of Finnish men born between 1934–1944, low income was associated with increased rates of coronary heart disease as would be expected [2]. However, the association differed according to thinness at birth, defined by the ponderal index (birth weight/length^3); the adverse effects of low income were only seen among the men who were thin at birth.

This suggests that individuals, whose growth in early life was impaired, are more vulnerable to the effects of stressors acting in adult life. These findings are consistent

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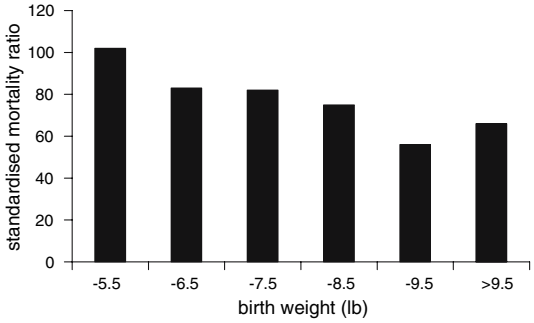


Fig. 1 Mortality from coronary heart disease before 65 years in 10,141 men in Hertfordshire

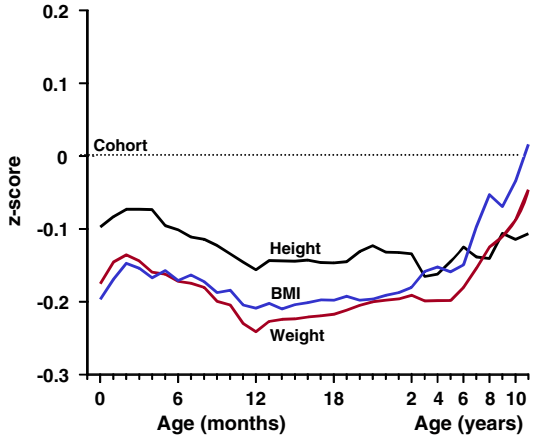
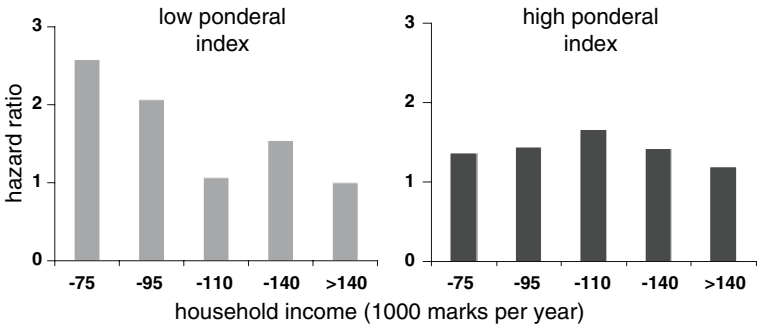


Fig. 2 Mean z scores for length and body mass index among boys who later developed coronary heart disease: Helsinki cohort 1934–1944

Fig. 3 Hazard ratios for coronary heart disease in men according to ponderal index at birth and household income in adult life



with the ideas of Dubos who wrote that "the effects of the physical and social environments cannot be understood without knowledge of individual history" [5].

Personalised nutrition

Such heterogeneity, originating in early life, in response to stressors in adult life may also apply to the effects of diet—raising the possibility that variations in adult diet will have different metabolic effects among adults who differ in their early experience. There is some experimental evidence to support this idea. For example, in guinea pigs, modest restriction of maternal diet during pregnancy, and impaired fetal growth has been shown to lead to an altered response to a high cholesterol diet among male adult offspring [6]. If responses to adult diet are conditioned by early growth, this could help to explain the inconsistent cross-sectional relationships found between diet and health. It would also have importance for considerations of personalised nutrition. Dietary advice for optimal health in adult life may differ according to early experience. (Figs. 1, 2, 3)

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