

# Commentary: Birthweight and coronary heart disease in a historical cohort

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A challenge to the idea that coronary heart disease originates through slow growth *in utero* and during infancy is that malnutrition during development is characteristic of the Third World, while the disease is a new Western disorder the incidence of which rises as populations become affluent. The ‘fetal origins’ hypothesis was first put forward in an attempt to explain the paradox that while coronary heart disease increases with rising prosperity, it is more common in poorer areas of Western countries and among poorer peoples.<sup>1</sup> For the disease to occur two influences seem to be necessary, one associated with poverty and the other associated with affluence.

Morley *et al.*<sup>1</sup> have examined for the first time mortality from coronary heart disease in a cohort born in the 19th century. The people were born in a charity hospital in Melbourne, Australia, between 1857 and 1900: they were born into poverty and most remained impoverished throughout their lives. Low birthweight was not related to coronary heart disease. One suggested explanation for the absence of an association regularly found in more modern cohorts is that people ‘programmed’ for coronary heart disease died in infancy. An astonishing 50% of the traced cohort died before the age of 1 year. Only 14% of these weighing <6 pounds at birth survived to age 40 years compared with 41% of those weighing 8 pounds or more.

The issue of selective mortality cannot be taken further. Setting it aside leaves the question of what else could have obscured an association between low birthweight and coronary heart disease. If low birthweight denoted the occurrence of poverty in the cohort, what influence might have been associated with affluence? The obvious candidate is the high energy Western diet. But at what stage of life might the effects of this diet be critical—in adult life or during development? Is there evidence that the cohort was exposed to it?

The original description of the fetal origins hypothesis proposed that poor nutrition in early life increases susceptibility to the effects of the Western diet in later life.<sup>2</sup> This suggestion brought with it the idea that while people may be made vulnerable to coronary heart disease by poor early growth and development, they are not doomed, irrespective of their later environment and lifestyle. Evidence that now supports this concept includes observations in the Hertfordshire cohort, where the link between low birthweight and coronary heart disease was first established. Among men in the cohort who weighed <7 pounds at birth a high saturated fat diet was associated with an unfavourable blood lipid profile.<sup>3</sup> There was no similar association among men with birthweights >7

pounds. This interaction may reflect the effects of poor liver growth *in utero* among people with low birthweight. The liver has a major role in the regulation of cholesterol homeostasis.

Another possibility is that the Western diet exerts its adverse effects during gestation. The Helsinki cohort studies showed that men who were thin at birth were at increased risk of coronary heart disease. The risk, however, was much higher among men born to mothers who were short but overweight, with a high body mass index. This led to a new explanation for the rise and fall of coronary heart disease.<sup>4</sup> Short thin (and probably undernourished) mothers have small babies who in adult life have low rates of coronary heart disease. Such may have been the case in 19th century Melbourne. As nutrition improves mothers become heavier but not taller. Their children have high rates of heart disease. As nutrition improves still further mothers become taller and heavier and maternal fatness no longer increases the risk of disease. In the absence of data on maternal body size this cannot be explored further in the Melbourne cohort.

In the Helsinki cohort thinness at birth was a stronger predictor of heart disease in men than low birthweight. Among women short length at birth was the strongest predictor. Weight at birth is a crude indicator of fetal growth. The same birthweight can result from different paths of growth, which are accompanied by differences in the proportional size of different organs and lead to different long-term disease outcomes in adult life.<sup>5</sup> A difference between fetal growth in developing countries and in Western countries is that in the former retarded growth tends to be proportional, with reduction in head size, length, and tissue soft mass. In Western countries disproportionate growth prevails with babies being either thin or stunted at birth. Low birthweight may, therefore, have different outcomes in different settings.

A high-energy diet may have important long-term effects during childhood. In the Helsinki cohort, the boys and girls who later developed coronary heart disease were small at birth, thin at 2 years but, thereafter, increased rapidly in weight and body mass index.<sup>6</sup> Rapid gain in body mass index after infancy must reflect better availability of food. If it follows a period of poor nutrition and growth it leads to insulin resistance and hypertension, two risk factors for coronary heart disease. From the data available about living conditions in Melbourne it seems likely that rapid compensatory weight gain in childhood would have been uncommon.

The study by Morley *et al.* highlights concerns about what the United Nations refer to as the ‘double burden’ of malnutrition.<sup>7</sup> ‘While undernutrition kills in early life, it also leads to a high risk of disease and death in later life’. Part of this double burden may depend on the co-existence of underweight and overweight. In the world, 170 million infants and young

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children are underweight. At the same time childhood obesity is becoming a recognized problem. 'These issues are still perceived to be separate. In reality both are often rooted in poverty and co-exist in communities and even the same households in most countries'. And even, they might have added, in the same individuals at different stages of their lives.

## References

- <sup>1</sup> Morley R, McCalman J, Carlin JB. Birthweight and coronary heart disease in a cohort born 1857–1900 in Melbourne, Australia. *Int J Epidemiol* 2006;**35**:880–85.
- <sup>2</sup> Barker DJP, Osmond C. Infant mortality, childhood nutrition and ischaemic heart disease in England and Wales. *Lancet* 1986;**i**:1077.
- <sup>3</sup> Robinson SM, Batelaan SF, Syddll HE, Aihie Sayer A, Dennison EM, Martin HJ, Barker DJP, Cooper C and the Hertfordshire Cohort Study Group. Combined effects of dietary fat and birth weight on serum cholesterol concentrations: the Hertfordshire Cohort Study. *Am J Clin Nutr* 2006;**84**:230.
- <sup>4</sup> Scrimshaw NS. The relation between fetal malnutrition and chronic disease in later life. *BMJ* 1997;**315**:825–26.
- <sup>5</sup> Harding J. The nutritional basis of the fetal origins of adult disease. *Int J Epidemiol* 2001;**30**:15–23.
- <sup>6</sup> Barker DJP, Osmond C, Forsén TJ, Kajantie E, Eriksson JG. Trajectories of growth among children who have coronary events as adults. *N Engl J Med* 2005;**353**:1802–09.
- <sup>7</sup> United Nations Standing Committee on Nutrition. 33rd Annual Session, Geneva, Switzerland, 13–17 March 2006.