Commentary: The meaning of thrift

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According to the Oxford dictionary, ‘thrifty’ means many things: ‘wisely economical, industrious, thriving, prosperous’. The term ‘thrifty phenotype’1 was used as a contrast to the ‘thrifty genotype’.2 The thrifty genotype hypothesis for type 2 diabetes proposed that diabetogenic genes persist at high levels in populations because they somehow confer a survival advantage in times of nutritional deprivation. There is little evidence to support such a speculation and the genes have not been found. The speculation rested on the stereotypic model of type 2 diabetes as a disease of high intakes of energy-dense food, physical inactivity and obesity. Across India, however, recently described as ‘the world capital of diabetes’, the disease occurs in vegetarians who are physically active and not obese.3 A deeper scientific inquiry is now needed to stem the rising epidemic of a disorder which affects 366 million people around the world and will soon affect 552 million people.4

The thrifty phenotype hypothesis built on the work of the late Nick Hales who advocated that type 2 diabetes originates in deficient insulin secretion.1 He pioneered the study of insulin precursors, importantly 32–33 split proinsulin. He pointed out that people with type 2 diabetes have a reduced early insulin response to oral glucose, indicating insulin deficiency.
His ideas converged with a new realization that cardiovascular disease and type 2 diabetes are initiated in utero. The resulting thrifty phenotype hypothesis proposed that malnutrition in foetal and early infant life is detrimental to the development of the beta cells in the endocrine pancreas, which synthesize insulin. Defects in the structure and function of the islets containing beta cells predispose to the later development of type 2 diabetes, especially if obesity, ageing, physical inactivity and other processes lead to insulin resistance in later life.

So what is the biology of thrift, its causes and consequences? Like other living creatures, humans are plastic as they develop. They have insufficient resources to perfect every aspect of their development. The availability of resources, importantly nutrition, sets the structure and function of their bodies for life, a phenomenon known as ‘programming’. During development there are critical periods during which each system or organ has to mature. These periods are often brief; they occur at different times for different systems; and for most systems they occur in utero. During critical periods a system is highly sensitive to the environment. The baby has a hierarchy of developmental priorities. Brain growth is at the top of this hierarchy, whereas the development of organs such as the kidney and lungs, which do not function in utero, are towards the bottom. There may also be genetically determined developmental priorities that vary between ethnic groups. Babies in India, for example, prioritize the accumulation of visceral fat, which may help them survive.

The more limited a baby’s resources are, the more economical in resource allocation, or thrifty, it may have to be. But, this seems to predispose it to disease in later life, especially if it encounters stressors along the way. This predisposition could reflect reduced functional capacity or altered metabolic settings and hormonal responses. The fundamental biological reasons why thrift initiates disease are not known. A thrifty strategy is likely to affect more than one organ or system whose critical periods occur around the same time. Furthermore, human development is choreographed by the interplay between different systems. Insulin is a major foetal growth hormone, and reduced insulin production could have secondary consequences for the development of a range of systems. Such changes in the harmony of growth may lead to comorbidity in later life, exemplified by the metabolic syndrome. Comorbidity is an important health issue: for example, in the USA only 17% of people with coronary heart disease have that disorder alone. People with different comorbidities may have followed different paths of development. The foeto-placental growth of people who later develop hypertension with diabetes differs from that of people with hypertension alone.

Thrift enables a baby to survive and thrive. Two aspects of thriving are the quality and amount of growth. Babies have to divide their resources between the two and this must be a delicate balance. Better quality growth leads to less disease, to less osteoporosis for example, and to better quality tissues, heart muscle for example. Bigger babies have lower death rates after birth than smaller ones. Whatever their evolutionary origins may be, the thrifty responses of the human foetus have long-term costs that include more disease, less well-being and shorter lifespan.

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References