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Commentary: Components in the interpretation of the high mortality in the county of Finnmark

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The weather in Northern Norway is severe. Anders Forsdahl describes 'polar nights, harsh cold and long winters' that force people to spend much of their time indoors. He himself, however, put his long winters to good use, reflecting on why the adult population of Finnmark, far above the Arctic Circle, has such high death rates. He quickly disposed of smoking and genes as possible explanations. He concluded that since economic and social conditions in Finnmark were similar to those in other parts of Norway, its 25% higher adult mortality rates must be a legacy of its history, of events during the childhood or adolescence of the adult population. This was the first of two platforms on which he developed his hypothesis. Like most good ideas it had occurred to others before him. Studying adult mortality in Britain before 1920, Derrick had shown that each succeeding generation displayed a lower mortality at all ages from childhood to old age.[1] He concluded that 'each generation is endowed with a vitality peculiarly its own, which persistently manifests itself through the succeeding stages of its existence'. The pre-war development of ideas about generation effects has been reviewed by Kuh and Davey Smith.[2]

To develop his hypotheses Forsdahl turned his attention to a single municipality within Finnmark, Sor-Varanger. His findings are described in this issue of the *International Journal of Epidemiology*. He established by 'research mainly based upon personal knowledge' that the population had a sizeable Finnish minority, second or third generation immigrants. Death rates among these Finnish people were much higher than those among the non-Finnish population, the excess deaths being mainly due to coronary heart disease. There were no explanations to be found in differences in adult lifestyles, but historically the Finnish population had occupations associated with poor living conditions, had lived in more crowded homes, and had been more vulnerable to periodic famine. Forsdahl estimated infant mortality from information in the archives of Sor-Varanger and found that, until the Second World War, rates were higher among Finnish than non-Finnish people. He concluded that poor living conditions in childhood and adolescence contributed to coronary heart disease. As an example of the long-term consequences of poor childhood living conditions he cited the persisting poor health of young men who survived prisoner of war camps. He recognized that, since coronary heart disease is a western disease, affluence had also to play a role. This was the second platform of his hypothesis. In his best known paper he suggested that 'great poverty in childhood and adolescence followed by prosperity is a risk factor for arteriosclerotic heart disease'.[3]

Forsdahl did not develop his ideas further. His observations did not allow him to determine whether poor living conditions were especially harmful at certain times in childhood and adolescence or to specify what aspects of poor living conditions were important. Ten years previously Geoffrey Rose had reported that siblings of patients with coronary heart disease had stillbirth and infant mortality rates that were twice as high as those of controls.[4] Rather than interpreting this as an association with poor living conditions in childhood he concluded that 'ischaemic heart disease tends to occur in individuals who come from a constitutionally weaker stock' a conclusion foreshadowing the discovery that coronary heart disease is associated with low birthweight. During this period, McCance and Widdowson, working at Cambridge University, were showing, in experimental animals, that undernutrition before or shortly after birth profoundly and permanently modifies the morphology and physiology[5,6] of the body. (In later years Widdowson readily accepted the concept that coronary heart disease may originate through undernutrition *in utero*.) Had Forsdahl been aware of these developments his work might have progressed further. It was analyses of neonatal and post-neonatal mortality in England and Wales[7] that first showed that coronary heart disease is associated with past infant mortality because it originates in poor conditions *in utero*, rather than poor conditions in childhood, though these contribute.[8] The geographical distribution of cardiovascular disease was more closely related to neonatal mortality, that is deaths in the first month after birth, than to post-neonatal deaths from one month to one year. Since, in the past, high neonatal mortality was strongly associated with low birthweight and was used as a marker of maternal undernutrition this observation suggested that low birthweight was associated with later coronary heart disease, an association that subsequent longitudinal studies have now established.[9–13]

Forsdahl's best known paper is entitled 'Are poor living conditions in childhood and adolescence an important risk factor for arteriosclerotic heart disease?'.[3] The short answer is that they are not. Questions raised by Finnish migrants in Norway are now being answered by studies of Finnish residents in Finland, using the archives in Helsinki. It has taken 8 years for Eriksson and colleagues, in collaboration with the Southampton group, to assemble a cohort of 15 000 men and women born in Helsinki whose size at birth was recorded, together with their living conditions and growth through childhood.[13] Now answers are appearing and the picture is clear. Coronary heart disease,

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hypertension and Type 2 diabetes are associated with paths of growth that are broadly similar though different in detail. Low birthweight, or shortness or thinness at birth, are followed by poor infant growth but thereafter rapid growth, so that body weight returns to around the average for all the children.[13–15] Rapid growth is generally associated with good nutrition and good living conditions. People who were small at birth remain biologically different through life because of the persisting constraints and adaptations that accompany slow early growth. Their different morphology and physiology leads them to respond differently to the biological[13] and social environments in later life.[16] Rapid postnatal growth has costs about which we know little, but examination of a sample of subjects in the Helsinki cohort may illuminate these. Thus the discontinuity in nutritional experience that leads to later disease does not seem to be primarily poor nutrition in childhood and adolescence followed by good or excess nutrition in adult life, as Forsdahl proposed. Rather it is poor nutrition *in utero* and during infancy, the so-called 'fetal' phase of endocrine control of growth,[17] followed by improved nutrition in the second phase of growth, which begins in early childhood.

In the long Norwegian evenings and the no-doubt dusty archives of Sor-Varanger, Forsdahl realized that differences in cardiovascular mortality rates are not driven by the adult environment, though this may contribute to them. This realization takes its place in a body of knowledge that is changing the way we think about the environmental causes of cardiovascular disease.[18] In the past we sought causes that acted in adult life and hastened destructive processes; the formation of atheroma, rise in blood pressure and loss of glucose tolerance. This model, however, has a limited ability to explain the ecology of coronary heart disease. What is now emerging is a new 'developmental' model. The causes to be identified act on the baby. In responding to them the baby ensures its continued survival and growth but at the cost of cardiovascular disease in later life.

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