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## The fetal and infant origins of adult disease

### *The womb may be more important than the home*

A hundred years ago, when tuberculosis and rheumatic heart disease were common, the proposition that the childhood environment affects adult health would have been self evident. This proposition may still hold, even though infective disease has given place to degenerative disease.

Studies in Norway, Finland, Britain, and the United States have shown that death rates from cardiovascular disease are inversely related to adult height, and geographical differences in cardiovascular mortality are related to past differences in infant mortality.<sup>1-7</sup> These findings have been interpreted as evidence that adverse living conditions during childhood, such as poor housing and diet, increase the risk of ischaemic heart disease.<sup>4</sup> Case-control studies have generally supported this<sup>8-12</sup>: patients with myocardial infarction have higher infant death rates among their siblings,<sup>8,9</sup> are more likely to come from larger families, and are more likely to have fathers who were unemployed.<sup>10</sup> Now studies in Finland show that men with ischaemic heart disease had worse socioeconomic conditions in childhood (p 1121)<sup>12</sup>—an observation also made in Britain.<sup>9</sup>

The completeness of infant mortality records in England and Wales from 1911 onwards has allowed detailed geographical comparisons of the relation between infant mortality 70 years ago and mortality from cardiovascular disease today. Differences in the death rates from cardiovascular disease among the 212 local authority areas of England and Wales are closely related to past differences in neonatal mortality.<sup>6,13</sup> Most neonatal deaths were associated with low birth weight, and rates were high in areas where mothers had poor health and high death rates during childbirth.<sup>14,15</sup> These findings suggested that research should be redirected towards the intrauterine environment rather than the environment in later childhood—housing, family income, diet, and other influences. The Medical Research Council employed a historian to search for old records of birth

and infancy. In Hertfordshire health visitors recorded the birth weight of all babies born in the county from 1911 onwards and visited their homes periodically throughout infancy. Follow up studies of the men and women born 60 and more years ago show that those who weighed more at birth and, if they were breast fed, at 1 year, had lower death rates from ischaemic heart disease and stroke.<sup>16</sup> The differences in death rates were large.

We are beginning to identify processes that link fetal and infant growth with cardiovascular disease. A recent study of 449 men and women aged 50 years who had been born in one hospital in Preston, England, showed that their current blood pressure and risk of hypertension were strongly related to their placental and birth weight.<sup>17</sup> Pressures were highest when birth weight had been lower than expected from placental weight. Discordance between placental and birth weights may be interpreted as fetal growth failure. Its causes are unknown, but maternal nutrition is an obvious suspect.

These epidemiological findings point to the importance of long term programming in early life and parallel findings in clinical and animal research. For example, the composition of infant food has been shown to have an important effect on motor development in preterm babies,<sup>18</sup> and programming of lipid metabolism by early feeding has been shown in baboons.<sup>19</sup> Knowledge of the fetal processes that may determine programming is beginning to emerge.<sup>20</sup> A recent symposium heard evidence that diseases other than cardiovascular disease may also be determined by the maternal environment.<sup>21</sup> Schizophrenia and obstructive lung disease are two examples.

The old model of adult degenerative disease was based on the interaction between genes and an adverse environment in adult life. The new model that is developing will include programming by the environment in fetal and infant life.

D J P BARKER

Director,  
MRC Environmental Epidemiology Unit,  
University of Southampton,  
Southampton General Hospital,  
Southampton SO9 4XY

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