

DEVELOPMENTAL BIOLOGY

The whole nine months

Michael Sargent examines the evidence that pre-birth experiences shape our lives.

The human uterus is not a tranquil nursery. At least one in 30 babies who make it through have health problems caused by genetic mutations and chromosomal misbehaviour. The fetus is also vulnerable to damaging external pressures that are less well understood. In *Origins*, journalist Annie Murphy Paul reviews the evidence that pre-birth experiences affect our health later in life.

Paul recounts the mid-twentieth-century scandals, involving two drugs given to pregnant women, that made the biomedical community aware that fetuses could be sensitive to medications that are harmless to adults. Thalidomide, which was prescribed for morning sickness and approved for clinical use before it was common to rigorously test drugs for all eventualities, caused abnormal limb development. Diethylstilbestrol, given to prevent miscarriage, triggered a rare cancer in daughters. More fetus-damaging influences have been recognized since, including the neurotoxin methylmercury, alcohol, inhaled tobacco smoke, a number of recreational drugs and some viruses.

Investigations of the factors that affect human fetal development are difficult. But catastrophes can offer key insights. Studies of people conceived during the Dutch 'hunger winter' of 1944–45, at the end of the Second

World War, revealed how a fixed period of malnutrition affected the fetus. Many went on to develop type 2 diabetes and cardiovascular disease prematurely, and were more susceptible to schizophrenia.

Similar problems afflicted those who were conceived during the 1918 influenza pandemic. As well as having higher rates of diabetes and cardiovascular disease compared with a control group, this cohort did less well at school, were smaller as adults and were more likely to be poor. Investigations of nineteenth-century demographic data have also revealed that the season of conception affected the health and longevity of progeny, presumably because vitamin D synthesis triggered by sunshine and folate from fresh vegetables promoted healthy pregnancies.

In-depth studies of the fetal origins of ill health were initiated in the 1980s by David Barker of the University of Southampton, UK. His premise that the fetus is damaged by maternal undernutrition, resulting in



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premature age-related diseases, now has widespread support after a controversial debut.

The fetus responds to poor nutrition by scaling down development. Unnecessary muscle growth is avoided, and excess resources are diverted into fat deposits that can be mobilized after birth when food is scarce. Animal experiments confirm that a diet deficient in protein or certain micro-nutrients is damaging to the fetus.

The resulting epigenetic modification of crucial genes — changes that modify gene expression without altering the DNA sequence — can be transmitted to one or even two generations, Paul notes. So susceptibility to diabetes and heart disease can be passed on from a historical episode of hardship. The optimal nutritional regimen for human fetal development is frustratingly hard to formulate, although Paul's interviewees have strong views. Surveys do show, however, that later health benefits are conferred by a fish-rich diet and supplements of folate and vitamin D.

Paul is particularly fascinated by the evidence that maternal experiences of stress affect the fetus and influence the development of psychological characteristics. She recounts investigations of pregnant women and their progeny who experienced bereavements, Hurricane Katrina, earthquakes, famines and wars. Stress during pregnancy always involves constriction of blood vessels servicing the fetus and elevation of the stress hormone cortisol. The consequences include a risk of reduced birth weight, reduced cognitive and language skills, schizophrenia and premature age-related diseases.

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On a positive note, the author reports that tests show that improved prenatal care and nutrition can raise the IQ of offspring of disadvantaged women. Interestingly, Caesarean delivery is less stressful to the baby than a natural birth, and much less stressful than a birth involving forceps. The special character of the intrauterine environment is revealed in another way by the observation that autism is associated with exposure of the fetus to excess testosterone, although as yet there is no indication of why this should be.

Origins is an absorbing account of how we might be shaped by our early life in the womb — physically, psychologically, even temperamentally. ■

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Malnutrition and stress can affect the physical and psychological development of the fetus.