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Early Developmental Conditions and Reproductive Success in Humans: Downstream Effects of Prenatal Famine, Birthweight, and Timing of Birth

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ABSTRACT Growth, survival, and breeding success of individuals in populations of wild mammals are influenced by the climatic and nutritional conditions that individuals experience during their early development. Recent findings have shown that early conditions also have consequences for subsequent survival and reproductive performance in humans. Environmental conditions which affect early development of individuals, such as the quality and quantity of nutrition received in utero and infancy, predict the onset of many chronic diseases in adulthood, affect longevity and may also influence a range of measures of reproductive performance in both food-limited and contemporary Western human populations. These associations are proposed to result from foetal programming, where a stimulus or insult during a critical period early in life may permanently affect body structure, physiology, and metabolism. Here I review studies showing how birthweight, season of birth, or exposure to prenatal starvation affect different aspects of an individual's subsequent reproductive success in humans and the growth, survival, and reproductive performance of the offspring produced. I show that early maternal and environmental conditions can have a large impact on human reproductive strategies and fitness that can span across generations. Am. J. Hum. Biol. 15:370–379, 2003.

While genetic factors explain part of the individual variation in phenotypic quality and reproductive success (Roff, 1992; Stearns, 1992), a significant role is also played by the environment (McNamara and Houston, 1996). The environmental factors that may influence an individual's investment in reproduction and breeding success include both the climatic conditions and food abundance around the time of breeding (Mousseau and Fox, 1998) and the conditions around the breeder's time of early development (Henry and Ulijaszek, 1996; Lindström, 1999; Metcalfe and Monaghan, 2001). While the former have received considerable attention in human studies relating current reproductive investment and success to the prevailing local ecological settings (e.g., Bereczkei and Dunbar, 1997; Lummaa et al., 1998a; Strassmann and Clarke, 1998; Borgerhoff Mulder, 2000; Lycett et al., 2000), the environmental conditions that an individual is born into, or the conditions that prevail before an individual is even born, are often ignored when trying to explain variation in different reproductive strategies between individuals and the reproductive success that they gain in their lifetime.

Variation in early environment of individuals can be caused by seasonality of climatic and food conditions, which may lead to differential development of individuals born at different times of the year, during different breeding seasons or to mothers of differential condition. Long-term studies on natural populations of wild mammals have shown that growth, survival, and reproductive success can be influenced by the climatic, hormonal, and nutritional conditions that individuals experience during their pre- and postnatal growth period (Lindström, 1999; Metcalfe and Monaghan, 2001). First, ecological variables, which affect maternal condition via changes in nutrition (such as population density and climate), can have consequences for offspring birthweight and survival (Albon et al., 1987; Clutton-Brock et al., 1992; Keech et al., 2000; Cameron et al., 1993). Second, birthweight can impose life-long downstream effects on reproduction and survival in adulthood. For example, in female red deer (*Cervus elephus*),

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weather conditions during an individual's early development before birth affect its subsequent survival, fecundity, offspring size, and, finally, its lifetime reproductive success (Albon et al., 1987; Kruuk et al., 1999). Similarly, birthweight is a significant determinant of mating success and total lifetime reproductive success in red deer males, with heavier-born males being more successful in gaining breeding success than lighter ones (Kruuk et al., 1999). These effects may further generate subsequent downstream effects on the survival and reproductive success of the offspring of these individuals (Lummaa and Clutton-Brock, 2002), creating correlations between breeding success of mothers and offspring. Experimental studies in controlled conditions on rodents have verified these findings (Huck et al., 1987; Meikle and Westberg, 2001).

Evidence from studies on wild animals further shows that the relationships between early development and breeding success or survival in adulthood can have important demographic consequences. In some animal populations, rising population density depresses early growth and this leads to increased mortality or reduced fecundity of individuals at later stages of their life-span. For example, in the Soay sheep (*Ovis aries*) population of St Kilda in Scotland, high overwinter numbers of sheep are associated with reduced birthweight of offspring in spring and with density-dependent changes in neonatal mortality (Clutton-Brock et al., 1992). In other cases, as in Scottish red deer, early development is influenced by density-independent factors such as climate. Here, fluctuations in early development may lead to inter-cohort differences in breeding success or survival (Albon et al., 1987; Rose et al., 1998). Where several 'good' or 'bad' cohorts occur in succession as a consequence of stochastic environmental variation, populations may increase or decrease as a result (Albon et al., 1987).

Correlations of this kind between environmental variables and individual survival and/or breeding success may arise as a consequence of at least three different kinds of causal mechanisms. First, an environmental variable (such as population density, or starvation) may exert a direct effect on early growth, which, in turn, affects juvenile mortality and reproductive performance (Fig. 1a). Alternatively, the environmental variable may have independent effects on early growth and juvenile mortality (Fig. 1b). And, third, it may generate interactions between early growth and juvenile mortality, for example so that population density does not depress growth but strengthens the effects of growth on survival (Fig. 1c). Effects of all three kinds can be found in the same population; for example, in red deer density-related changes in juvenile mortality are caused partly by a rise in mortality across all phenotypes, partly by density-dependent changes in birth date, and partly by a strengthening of the effects of birthweight on survival (Clutton-Brock et al., 1992).

There is accumulating evidence that effects of early development on later growth, health, and survival also occur in human populations (Lummaa and Clutton-Brock, 2002). For example, early environmental conditions, such as the quality and quantity of nutrition received in utero and infancy, may predict the onset of chronic diseases in adulthood, such as coronary heart disease and noninsulin-dependent diabetes mellitus (Barker, 1994; O'Brien et al., 1999). Furthermore, timing of birth has been shown to influence an individual's longevity (Moore et al., 1997; Doblhammer and Vaupel, 2001) and final height in adulthood (Weber et al., 1998). In fact, some of the most detailed and long-term datasets on the effects of early environmental conditions on later life events are available for humans. However, although the impact of early conditions on later-life disease patterns in humans have been recognised for public health, their role in determining reproductive success and fitness have rarely been considered before. In this article, I review evidence from the current literature on the downstream effects of early growth on survival and breeding success in human populations and examine the role of variation in early environmental conditions in determining an individual's lifetime reproductive success and fitness across generations.

HOW DO DOWNSTREAM EFFECTS OF EARLY CONDITIONS ON LATER LIFE EVENTS ARISE?

During foetal growth and development, different tissues of the body grow during differing crucial periods of rapid cell division. The foetal programming hypothesis (Lucas, 1991) proposes that changes in nutrient and hormonal conditions at these times could

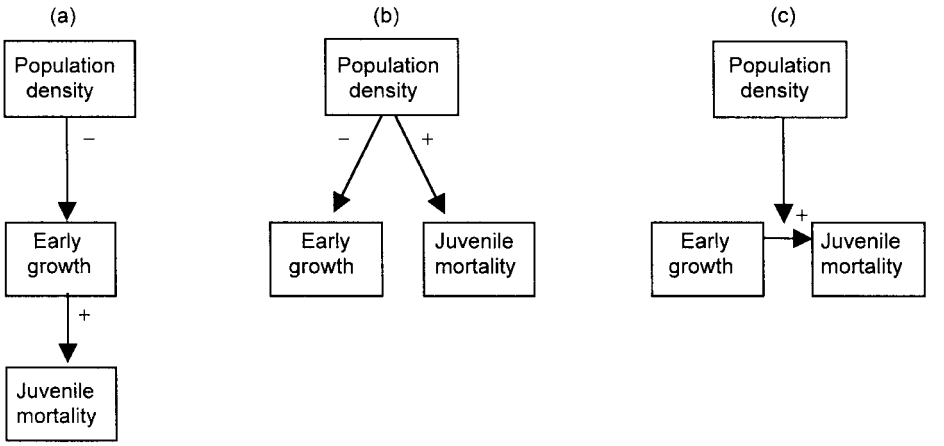

Fig. 1. Examples of how correlations between early conditions, growth, and subsequent survival can arise. The diagram presents three ways in which an environmental variable (here rising population density) can affect juvenile survival: (a) population density depresses early growth and this raises mortality; (b) high population density has independent effects on early growth and mortality; (c) population density does not depress growth but strengthens the effects of growth on survival (modified, with permission, from Clutton-Brock et al., 1992).

alter expression of the foetal genome, leading to permanent effects on a range of physiological processes (Fig. 2). Even brief periods of malnutrition can permanently reduce the numbers of cells in the organs undergoing crucial growth at the time of food restriction. It has been hypothesised that the foetus might monitor its environment and set growth projections according to nutrient availability. In an environment with poor nutrient supply, for instance, it would be advantageous to be small. Offspring with placental insufficiency or impaired nutrition might 'interpret' their environment as being nutrient poor and, perhaps irreversibly, set themselves up for shorter stature (see Barker, 1994).

There are at least three possible, not necessarily completely mutually exclusive, mechanisms for how this memory of the early event is stored and later expressed (McCance and Widdowson, 1974). First, the early nutrient environment of a developing cell line might permanently alter gene expression, so that cellular progeny will have the 'message' passed on to them. Second, early nutrition might affect distribution of different cell types, and, finally, early nutrition could permanently influence cell numbers. Although these changes are beneficial to survival under poor nutritional conditions, they might be detrimental under conditions of normal or overnutrition and might lead to increased risk of several later-life diseases. For instance, people who are small or thin at birth but who are obese as adults tend to have a higher risk of noninsulin-dependent diabetes mellitus and impaired glucose tolerance in adulthood. There is some evidence that their 'poor' foetal growth resulted in a reduced number of pancreatic β-cells and a diminished capacity to make insulin, making them less able to withstand the stress of becoming obese as adults (Godfrey, 1998).

These often permanent changes in the body structure, physiology, and functioning as a consequence of the prevailing nutrient and hormonal conditions during early stages of development may carry consequences for lifetime reproductive success of individuals in several ways. First, they may directly influence reproductive performance through effects on, e.g., female and male fertility rates or growth and development of babies. Second, they may indirectly modify reproductive success by affecting mating success (e.g., via changes in body proportions which are known to be important for both male and female mate choice in humans (e.g., Tovee et al., 2002)), or by influencing length of reproductive lifespan (e.g., by causing increased mortality at reproductive ages). However, despite the increasing number of studies showing relationships between early growth, nutrition, and climatic conditions and future

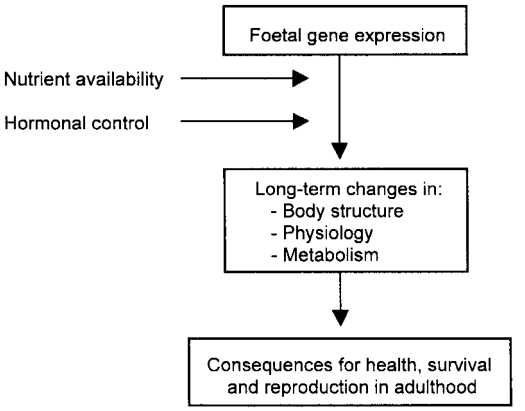

Fig. 2. Schematic presentation of the mechanism how early nutrition may cause long-term downstream effects on adulthood health, survival, and reproduction.

reproductive performance, the long-term consequences of early environmental conditions for reproductive success in adulthood are still often poorly understood at the physiological level.

HOW ARE EFFECTS OF EARLY DEVELOPMENT STUDIED IN HUMANS?

The human studies examining long-term effects of early developmental conditions on the subsequent health, survival, and reproduction of individuals can be divided into three main categories: 1) Studies examining normal individual variance in birth size or early growth rate after birth in a (usually industrialised) population and linking this to probability of an event (such as suffering from a certain disease) happening in adulthood (e.g., Eriksson et al., 2001; Phillips et al., 2001). 2) Studies comparing later life events of individuals who were born to mothers suffering from starvation to individuals whose mothers were well-nourished while pregnant (e.g., comparison of individuals born before, during, and after a short famine (e.g., Ravelli et al., 1998; Stanner et al., 1997) or comparison of offspring born to well-nourished mothers and mothers following a diet or suffering, e.g., from anorexia nervosa (Bulik et al., 1999). 3) Studies concentrating on populations living in a seasonal environment and comparing the life events of individuals born during different times of the year and therefore experiencing differing early developmental conditions (e.g., Moore et al., 1997; Doblhammer and Vaupel, 2001; Lummaa and Tremblay, submitted).

Some problems are related to each of these approaches. The studies comparing individuals born with differing birthweight generally expect that most of the variation in birthweight of babies is caused by environmental conditions prevailing during gestation and use birthweight as a proxy for foetal nutrition, although part of this variation is likely to be of genetic origin given that the foetal genome affects human growth potential in utero (Carr-Hill et al., 1987). The causes for differences in birthweight between individuals are usually not known, and therefore the specific potential environmental factors affecting early growth rate also remain unidentified. This may pose a problem, as it has been suggested that low birthweight and some health problems in adulthood (such as diabetes and hypertension) may all be products of the same genotype (Hattersley and Tooke, 1999). Studies comparing life events of identical twins born with differing birthweight (but sharing the same genotype and social settings) may avoid some of these problems, but such studies are still scarce (but see, e.g., IJzerman et al., 2000). Studies comparing later events of individuals born or fertilised during a famine to individuals born and fertilised before or after the famine may suffer from a lack of power in detecting any effects of the prenatal starvation, as it is usually impossible to determine how affected each pregnant woman was by the famine and whether all the mothers giving birth during the famine actually suffered from malnutrition. Studies examining health, survival, or reproduction of individuals born during different seasons of the year and therefore encountering different early developmental conditions can be more sure that the early environment of the compared individuals differed, but in this case it is often difficult to tell what it is in a particular time of birth that imposes effects on early development and growth of individuals. Finally, few studies so far have managed to convincingly show a particular time of the early development (some time after birth vs. some time during gestation vs. conception vs. even before this) that is most sensitive for insult or stimuli causing downstream effects on later life events and the exact mechanism for such long-term effects.

HOW DO EARLY CONDITIONS CREATE VARIATION IN LIFETIME REPRODUCTIVE SUCCESS?

In the following, I address three alternatives for how any differences in reproductive success or fitness between individuals exposed to differing conditions during their own early development may arise: 1) through their own differential survival rates; 2) through their own differential reproductive success; and 3) through differences in the survival and reproductive output of their offspring.

Effects on survival rate

To date, there is a considerable amount of evidence from humans that low birthweight, reduced early growth rate, or exposure to prenatal starvation can increase an individual's risk of contracting several diseases and health problems in adulthood (Barker, 1994; O'Brien et al., 1999) and affect subsequent survival probability. For example, recent studies in Europe, North America, and some 'developing' countries have shown that low birthweight and other indices of abnormal foetal growth in babies born at term are linked with a whole host of problems later in life. These include, for example, a higher prevalence of glucose intolerance (reviewed in Phillips, 1998), hypertension (Law and Shiell, 1996), and vascular disease (Eriksson et al., 2001). Furthermore, longitudinal studies have also found links between early development and measures of ageing (Sayer et al., 1998) and functions of the immune (McDade et al., 2001a,b) and respiratory systems (Shaheen et al., 1999; Lopuhäa et al., 2000). These findings suggest that poor early environmental conditions may be associated with an increased likelihood of suffering from a wide range of adulthood diseases and premature ageing.

Despite the well-documented effects that early development has for health, it is not at present always clear whether this has significant consequences for survival and longevity in a population. Indirect evidence that this might be the case comes from the studies examining the effect of early conditions on age-specific mortality rates or longevity. Such studies suggest that the lifespan of individuals may partly depend on the prevailing climatic and/or food conditions before and immediately after birth. First, studies comparing survival of individuals born during different times of the year show that timing of birth in a seasonal environment can affect survival rates following birth (Lummaa et al., 1998b) and in adulthood (Doblhammer and Vaupel, 2001). Lummaa et al. (1998b) studied variation in a newborn's survival expectation according to month of birth in rural Finnish people living in prehealth-care conditions of the 18th and 19th centuries. Individuals born during summer months, with reduced hygienic conditions, increased risk of infectious diseases, and low availability of food resources for mothers had the lowest survival probability during their first year of life, with boys born during that time of the year having particularly lowered survival, whereas babies born in the autumn following the harvest were most likely to survive through infancy (Lummaa et al., 1998b). Such effects may last throughout life: Doblhammer and Vaupel (2001) found that the month of birth predicted survival after age 50 in 20th century Austria, Denmark, and Australia. These correlations may be related to seasonal variation in birthweight of babies (Ward, 1993), but other mechanisms are possible as well for mediating the effects of early conditions, for these studies could not directly address the causes underlying relationships between timing of birth and mortality.

Another line of evidence for the effects of early developmental conditions on survival comes from studies comparing mortality rates of individuals exposed to starvation during fertilisation or gestation to survival of individuals born to well-nourished mothers. Kannisto et al. (1997) analysed survival of cohorts born in Finland during the severe 1866–1868 famine and during the 5 years preceding and following the famine. Their findings suggest that, although cohorts subjected to prolonged and extreme nutritional deprivation in utero and infancy suffered an immediate rise in mortality in infancy, after the famine had passed mortality rates dropped to normal levels. Using historical records, it is, however, difficult to determine how different the early conditions were that each individual experienced. For instance, if famines were restricted to certain areas within a country or to certain social classes, then it may be that many of the children born during the famine were not exposed to starvation. More direct comparisons come from studies able to measure

weight gain and energy intake of mothers giving birth during differing food conditions. For example, conditions in early life reduced the adult survival prospects of rural Gambians born during the annual wet season with reduced food availability and increased workload and risk of malaria as compared to being born during the dry (harvest) season with better living conditions (Moore et al., 1997). Adult women in the Gambian population experience a negative energy balance and tend to lose 2–4 kg of their body weight during the wet season, whereas during the harvest season this weight is usually regained (Cole, 1993). As a consequence, the weight gain of pregnant women is significantly reduced during the wet season (Cole, 1993). Individuals born during the wet season were up to 10 times more likely to die prematurely in young adulthood, mostly due to infections and pregnancy complications (Moore et al., 1999). The authors suggest a permanent effect of malnutrition on the development of the immune system during foetal growth to be a likely explanation.

Finally, a study on the association between early growth and risk of suicide in adulthood in cohorts born in early 20th century England found that men and women who committed suicide had lower than average rates of weight gain in infancy even after controlling for their current social class and the way they were fed as infants (Barker et al., 1995). As patterns of hormone release by the hypothalamus are known to be imprinted in utero, it was suggested that altered programming could influence both growth in infancy and mood throughout life (Barker et al., 1995).

The current evidence therefore suggests that early developmental conditions may have important consequences for the survival rates of individuals throughout life. Such effects should be large prior to menopause in order to have significant consequences for the lifetime reproductive output of women, for mortality rates after reproductive ages are less important for the reproductive success gained by individuals, and for strength of natural selection (Stearns, 1999). Many of the diseases so far linked to early growth, such as coronary heart disease, tend to affect the part of the population who have mostly passed their reproductive years. At the present, not enough is known about the age-specific mortality rates relative to early development to assess the importance of differential mortality due to early conditions in a satisfactory way, but it appears that, at least under certain conditions, differential reproductive-aged mortality of individuals according to their early conditions may lead to significant differences in their lifetime reproductive success and fitness (Lummaa and Tremblay, submitted).

Effects on reproductive success

Variation in early conditions could also generate individual differences in lifetime reproductive success and fitness if conditions experienced early in life affect development of the organs producing and regulating reproductive hormones (Lumey and Stein, 1997) and/or marriage or mating probability. Despite the large number of animal studies showing that such influences can be important (reviewed in Lindström, 1999), few studies so far have addressed the effects of early developmental conditions on reproductive performance in humans (Lummaa and Clutton-Brock, 2002). However, some recent studies have indicated that associations between early development and subsequent reproductive parameters in adulthood may be common both in food-restricted and Western human populations.

Lumey and Stein (1997) hypothesised that if prenatal caloric restriction due to nutritional deprivation affects development of the organs responsible for producing and regulating female reproductive hormones, fertility of women exposed to fetal malnutrition would be impaired. They examined whether exposure to acute, severe famine in utero during the Dutch famine 1944–1945 affected a women's subsequent reproduction and found that exposure to fetal famine was sufficient to result in a 300-g decrease in mean birthweight. These individuals with significantly reduced birthweights did not suffer from adverse effects on their subsequent fecundity in adulthood, but they were more likely to give birth to offspring of reduced birthweight (Lumey et al., 1995). This reduced birthweight in the second generation was associated with a high frequency of still-births and early infant mortality (Lumey and Stein, 1997). Thus, in this respect females exposed to the famine in utero had reduced reproductive success compared with those who were born before or after the famine. Other female reproductive

traits can be affected by early nutrition as well. In a follow-up study of women born in England in the first half of the 20th century, Cresswell et al. (1997) found that menstruation ceased at an earlier age in those who had low weight gain during their first year of life, or who were short at birth (but see Treloar et al., 2000, for the opposite result). The authors suggest that poor growth and development in late gestation, a critical time for ovarian follicular development, leads to a smaller peak number of primordial follicles in the ovary, which leads in turn to an earlier menopause.

Ellison (1996) suggested that the levels of ovarian hormonal function in adult women are associated with the tempo of growth and maturation in childhood and adolescence. The relationship between menarcheal age and adult ovarian hormonal function both within and between different human populations is compatible with the current understanding of the mechanisms underlying pubertal maturation of ovarian hormonal function (Ellison, 1996). Functionally, such a relationship could serve the purpose of modulating adult fecundity to chronic environmental conditions. Alternative hypotheses include the possibility that the relationship is not causal but rather reflects either confounded effects of some common cause or the persistence of acute environmental effects through time, but proper testing of such alternative hypotheses would require longitudinal data on migrant populations, changing environments, or secular trends within populations (Ellison, 1996).

Lummaa and Tremblay (submitted) examined the effect of birth month for a range of reproductive traits and the consequences of this for lifetime reproductive performance and eventual fitness of women living in a rural society in 19th century Canada, which experienced conditions of natural fertility. Month of birth had long-term consequences for the subsequent length of these women's reproductive lifespan, age at menopause, number of lifetime live-births, and numbers of children raised to adulthood. Moreover, women born during the 'best' month of the year had over seven grandchildren more born into the population than those women born during the 'worst' month, suggesting that the timing of birth had large effects on subsequent fitness in this rural community. The variation in reproductive success between women born during different months of the year was related to the climatic conditions both at the time of their gestation and birth. Some other studies have also found associations between month of birth and reproductive traits of women, such as early menarche or menstrual disorders (Jongbloet et al., 1994) and fecundability (Nonaka et al., 1990; Smits et al., 1997). These findings suggest that early conditions may play an important role in shaping female reproductive performance across generations.

Far fewer studies have addressed the potential effects of early developmental conditions on the subsequent reproductive success in men. However, some studies indicate that, like in some other large mammals (Kruuk et al., 1999), male mating success in adulthood can be reduced by their adverse early conditions. First, a study on Finnish and English men born in the 1920s and 1930s and belonging to a cohort where marriage was a social norm found that men born with low birthweight were less likely to succeed in marrying in their lifetime (Phillips et al., 2001). This was true irrespective of the men's adulthood size, social class, or age, which could also affect a man's marriage prospects. Second, low fluctuating asymmetry (FA) predicted lower morbidity and more offspring fathered by rural Belize men and was marginally associated with their lower age at first reproduction and larger number of lifetime sex partners (Waynworth, 1998). FA is widely used as a proxy to measure how precisely the genotype generates the phenotype, given that organisms face genetic and environmental perturbations during development (Møller and Swaddle, 1997). However, usually it is not known exactly when and why such developmental instabilities arise, and more direct studies are therefore needed to confirm the possible relationships between early conditions in later mating patterns in men.

Effects on quality of offspring

Finally, early developmental conditions could generate differences in fitness between individuals if the adverse early development reduced the long-term survival and reproductive performance of the offspring produced by individuals suffering from early starvation or other factors interfering with their early development. Experiments on other mammals have shown that early conditions may affect reproductive success

across generations. For example, daughters of food-restricted golden hamster females (*Mesocricetus auratus*), themselves reared on ad libitum diets, may produce smaller litters and relatively fewer sons over their lifetime than daughters of females that were not food-restricted (Huck et al., 1987).

There are almost no studies conducted on humans that directly examine how early developmental conditions of parents affect the long-term survival and reproductive success of their offspring. Hackman et al. (1983) found that maternal birthweight was significantly related to pregnancy weight gain, baby's birthweight, gestational duration, and the baby's need for neonatal intensive care in modern Americans. Mothers who weighed 2 kg or less at birth were at elevated risk of poor own pregnancy outcomes, even if their babies did not weigh less than babies of heavier-born mothers. This suggests that factors interfering with intrauterine growth could have an impact on the next generation of babies, and if their birthweight is reduced as a consequence of their mother's adverse early developmental conditions, they may in turn have reduced survival and reproductive success in adulthood. Indeed, it appears that the blood pressure level in some Western human communities depend partly on the early nutritional experience of the previous generation of mothers (Barker et al., 2000). In addition, Lummaa and Tremblay (submitted) found that the lifetime number of children born alive to Canadian women in the 20th century depended on the time of year that their mother was born, and therefore on the early developmental conditions of the previous generation.

CONCLUSIONS

Most of the evidence for the relationship between early nutrition and survival or reproduction in adulthood comes from follow-up and comparison of babies born with different weights to Western mothers who are generally not food-limited. Normal individual variation in fetal size and thinness at birth appear to have implications for health throughout life, possibly via just subtle changes in the maternal–placental supply of nutrients. These new observations challenge the view that the foetus is little affected by changes in maternal nutrition, except in circumstances of famine. Conducting studies on Western populations living in relatively modern settings is, however, likely to result in difficulties in observing effects of adverse foetal conditions on later reproductive performance. Reasons for this lie in the wide practice of family planning and consequent limited fecundity, availability of contraception or possibility of medical treatment for low fertility, and nonrestricting food conditions in most of the postwar Western countries. These factors are bound to smooth individual variation in reproductive traits. It is therefore predicted that long-term effects of fetal malnutrition on later life-history traits are most easily detected in populations living in nonmodern, harsh conditions and experiencing a food-limited environment. However, due to an extreme paucity of data, such studies are at the present very rare, and the lack of studies on food-limited human populations may account for the fact that only some of the reproductive consequences of early development detected in other mammals have thus far been documented in humans.

The demographic consequences of correlations between early development and subsequent survival or breeding success in humans are still unclear. In most human populations these may be relatively small compared to more food-limited populations of nonhuman mammals, and since the effect of early conditions may only become apparent in the following generation over 20 years later, such effects may be difficult to detect in humans even if they played a significant role. However, the consequences of early development may be substantial for some components of the population. There is already firm evidence that early development can affect susceptibility to a range of diseases in later life, including diabetes, stroke, and asthma probability (Barker, 1994; O'Brien et al., 1999). Contrasts between Western and 'developing' world medicine availability and healthcare are likely to have reinforcing effects on population fertility and mortality trends, given that food-restricted people are predicted to exhibit greater effects of early development on downstream effects on survival and reproduction, especially if the food conditions later improve (Eriksson et al., 2001). Gaining a deeper understanding of the medical, demographic, and evolutionary aspects of downstream effects of early development in humans depends crucially on establishment of individual-based long-term studies, especially on populations of developing

countries. Ultimately, such data can serve to advise on the best strategy to enhance both adult and offspring survival in different environments.

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