Original Article

Nutrition before birth, programming and the perpetuation of social inequalities in health

Vivienne Moore1 BSc(Hons), MPH, PhD and Michael Davies2 BA(Hons), MPH, PhD

1Department of Public Health, University of Adelaide, Adelaide, Australia
2Reproductive Medicine Unit, Department of Obstetrics and Gynaecology, University of Adelaide, Adelaide, Australia

The need to explain social inequalities in health has led to the theory that chronic disease is due, in part, to a legacy of adverse experiences in early life. Epidemiological studies show consistently that individuals who are small at birth have an increased risk of cardiovascular disease in adulthood. There is growing consensus that this association reflects a causal relationship and is not simply the product of bias or confounding. The concept of programming is invoked as the biological mechanism; birth size is thus a proxy for fetal programming. Recent findings suggest that fetal programming interacts with the post-birth environment. The adverse exposures that are thought to underlie and potentiate programming cluster in socially patterned ways, thus creating substantial inequalities in health. Experiments in animals demonstrate that nutritional interventions before or during pregnancy can produce programming phenomena in the offspring, sometimes without an impact on birth size. However, the extent to which maternal nutrition contributes to programming in contemporary developed countries is uncertain.

Introduction

Throughout the life course, an individual’s health is associated with his or her social circumstances; biological processes occur within a social context. Differences in adult lifestyle are an inadequate explanation for social inequalities in health, even from a traditional public health perspective, which recognizes the need to look beyond the individual to the social and cultural forces that shape behaviour. The search for a more complex understanding of how social inequalities in health arise has taken diverse directions. One of those directions concerns the legacy of early life experiences, and in that sphere, one theory focuses on the pre-birth environment.

According to the ‘fetal origins’ theory of adult disease, physiological adaptations that occur when a baby is undernourished before birth lead to increased susceptibility to chronic disease in later life. This process is referred to as ‘programming’. When first proposed by Barker and Osmond in the late 1980s,1 the theory was regarded as radical, although the idea that experiences in early life might have lasting consequences for health is not new.2-6

In the present paper, the connection between the issue of health inequalities and the fetal origins theory is traced. The epidemiological research undertaken in relation to the fetal origins theory is summarized and the evidence for a nutritional basis to fetal programming is examined. Finally, the relevance of the concept of programming for understanding social inequalities in health is considered.

The search for explanations for social inequalities in health

The initial conjecture that chronic disease had origins in early life was prompted by the need to explain the paradox that ‘diseases of affluence’ disproportionately affect the poorest people in developed countries. By the mid-1980s, it was widely recognized that social gradients in health were only partly due to differences in adult lifestyle. This was most clearly demonstrated in the Whitehall study of civil servants.7,8 Other explanations for socioeconomic differentials in health were required.

That was the rationale given by Barker and Osmond for the work presented in their seminal paper in 1986.1 Drawing on ecological data, they suggested that ‘poor nutrition in early life increases susceptibility to the effects of an affluent diet’. To invoke a nutritionally based explanation for inequalities in health was extraordinary at that time. As noted by James et al.,9 diet was usually dismissed as a possible cause of inequalities in health in developed country settings because of the rarity of classic nutritional deficiencies.

A somewhat broader statement was made in Barker and Osmond’s next paper on the subject: ‘past differences in

Correspondence address: Dr Vivienne Moore, Department of Public Health, University of Adelaide, Adelaide, Australia. Tel: +61 8 8303 4605; Fax: +61 8 8223 4075 Email: vivienne.moore@adelaide.edu.au
maternal health and physique and in the postnatal environment . . . may be determinants of current differences in adult mortality’.10 Five years later, after the publication of supportive findings from two cohort studies, Barker reviewed the work and concluded that ‘the seeds of inequalities in health in the next century are being sown today – in inner cities and other communities where adverse influences impair the growth, nutrition and health of mothers and their infants’.11

Barker and his colleagues participated in the recent Independent Inquiry into Inequalities in Health in the UK, chaired by Sir Donald Acheson. Their advocacy is evident in the Acheson report,12 particularly in the sections on mothers and children. Overall, the Inquiry placed considerable emphasis on early life as a formative period for many health-related phenomena. In this respect, its findings were not dissimilar to the Black report published 20 years earlier.13,14

At the same time as Barker was developing what might be considered a ‘materialist’ explanation for inequalities in health, other perspectives were being offered. Of note, as a contrasting and also very influential view, is the psychosocial explanation expounded by Marmot.15 The central premise of Marmot’s work is that an individual’s sense of control and position in the social hierarchy are important pathways to disease, through physiological and metabolic changes induced by sustained biological responses to stress. At first, these two positions appeared to be competing, but recent developments suggest they are not incompatible and may work together.

Size at birth and health in later life
Initially, the evidence for early life influences on later health was indirect and open to interpretation. Barker and Osmond simply observed that in England and Wales, regions that had high infant death rates at the beginning of the twentieth century, tended to have high rates of coronary heart disease some 60 years later.1

However, since then, findings from at least eight cohort studies have confirmed an association between small size at birth and increased risk of cardiovascular disease in adulthood.16-23 The results from one cohort study are not supportive.24 Analyses have generally been restricted to individuals born at term, thus the association does not reflect an influence of prematurity.

The first findings by Barker and his colleagues were obtained from the Hertfordshire and Sheffield cohorts in England.16-18 These cohorts were established retrospectively, using collections of archived birth records pertaining to individuals who are now middle-aged, elderly or deceased. Among the more recent findings are those from two extremely large cohort studies that were undertaken by other researchers.

One is the Nurses’ Health Study in the USA, a cohort of over 120,000 women born between 1921 and 1945, who were registered nurses in 1976 and responded to a postal questionnaire.22 Thereafter, information about cardiovascular events was sought from the women every 2 years, and in 1992 the women were asked to report their birthweights. Analysis of data for over 70,000 women showed that birthweight was inversely related to the incidence of non-fatal coronary heart disease and stroke. The risk of cardiovascular disease, adjusted for age and several other factors, was 50% higher (95% confidence interval 1.1–2.1) among women whose birthweight was less than 5 lb (2.3 kg) compared to women in the referent category whose birthweight was approximately 8 lb (3.6 kg). The risk among women who weighed more than 10 lb (4.5 kg) at birth was 30% lower than that of the referent group (95% confidence interval 0.5–1.0). Between these extremes, the risk was not statistically different from that of the referent group. In this respect, the results contrast with those for the men and women of Hertfordshire, where the risk of death from cardiovascular disease fell progressively as birthweight increased, so that individuals whose birthweight was low but well within the ‘normal’ range were affected.17

The other example is the work of Leon et al. with a cohort of over 14,000 men and women born in Uppsala, Sweden, between 1915 and 1929.23 In the mid-1990s, Leon and colleagues traced over 97% of the cohort members and ascertained whether or not they were still living, and the cause of death for those who had died. The likelihood of death from cardiovascular disease decreased as birthweight increased. Among men, each 1 kg increment in birthweight reduced the risk by 20% (95% confidence interval 0.71–0.91); among women, the same increment in birthweight was associated with a 25% reduction in the risk of cardiovascular disease (borderline statistical significance). The Uppsala cohort contained complete information on gestational age, and analyses clearly showed that being small for gestational age, rather than actual weight, was linked to the risk of cardiovascular disease.

Associations between size at birth and clinical risk factors for cardiovascular disease, such as elevated blood pressure, abnormal lipid profiles and blood clotting factors, have also been investigated.25 Blood pressure has been studied extensively and systematic reviews indicate that the association with birthweight is robust.26,27 Results concerning other risk factors are fewer and seem to be less consistent.

Arguably of more interest than results concerning single risk factors, is the association between birth size and a cluster of conditions that are now recognized as a syndrome. The conditions are diabetes (or impaired glucose tolerance), hypertension and abnormal lipid profiles. Individuals with this ‘metabolic syndrome’ (sometimes called syndrome X) have an increased risk of death from ischaemic heart disease. Associations between small size at birth and metabolic syndrome appear to be especially strong.28 In the Hertfordshire cohort, 30% of the men whose birthweight was less than 5.5 lb (2.5 kg) had metabolic syndrome at around 64 years of age. The prevalence of the syndrome fell progressively as birthweight increased, to a low of 6% among men whose birthweight was greater than 8.5 lb (3.9 kg).29
Cohort studies can suffer from bias introduced through the selection of subjects or the attrition of subjects over time. Critics appropriately challenged the early findings on these grounds. In the Hertfordshire study, for example, the results are based on less than half of those individuals named in the birth records.17 However, in contrast, follow up for the Uppsala cohort was almost complete.23

Historically, but to a lesser extent now, small babies were likely to be born into families in disadvantaged circumstances. Those children would have grown up in a social environment in which they were more likely to be exposed to and adopt lifestyles adverse for cardiovascular health. Thus it was important to examine the extent to which associations between size at birth and health in later life were due to confounding by socioeconomic status.

This issue has been examined carefully using the accepted techniques of stratification and adjustment.22,23 When a cohort is separated into social groups (for example, based on the family’s circumstances at the time each individual was born), associations between size at birth and adult health are evident within each social group. When the influence of socioeconomic status on health is statistically partitioned out, an independent association between birth size and adult health is still apparent. Likewise, when the effects of specific adult behaviours are partitioned out, the association remains.

These approaches to examining confounding are limited by the accuracy with which the potential confounder can be measured. In this case, the potential confounder is social position, a dynamic, multifaceted construct, which is imperfectly captured by variables such as educational attainment and occupation. This has led some to argue that, despite surviving the standard degree of scrutiny, there may be residual confounding by social class.30 It is entirely possible that there is some residual confounding, but it seems unlikely that refined dimensions of social class could entirely eliminate the association. In the Nurses’ Health Study,22 for example, the confounding effects of many socioeconomic and lifestyle variables were examined, including smoking, alcohol consumption, saturated fat consumption, physical activity, use of hormone replacement therapy, height, body mass index, waist-to-hip ratio, the occupations of the mother and father, whether or not the mother smoked when the subject was a child, and the father’s education. Inclusion of most of these variables in the analyses did not appreciably change the magnitude of the relative risks.

It is also unlikely that the associations between birthweight and later health are principally due to genetic inheritance. Evidence from intergenerational studies of similarity in birthweights, embryo-transfer studies, cross-breeding in animals and other experiments suggests that birthweight is largely determined by the supply of nutrients and oxygen to the fetus.31,32 Nevertheless genes do have some influence on birthweight,33 and could have some role in these associations.

Overall, the weight of evidence tends to support a direct link between size at birth and health in later life. Several groups have now issued consensus statements to that effect.34,35 Nevertheless, there are many uncertainties in the detail. One area of uncertainty is the biological mechanism involved, although programming is the conceptual candidate.

Programming

Programming is a well-established biological and developmental phenomenon. It refers to the process whereby an event or exposure that occurs during a critical or sensitive period has a lasting impact.36 In its general form, programming is not confined to the period before birth, but can also occur in postnatal life.

There are numerous naturally occurring instances of programming. For example, the incubation temperature of the egg determines the sex of the American alligator.37 If the egg is incubated at 30°C the alligator will be female, but if the incubation temperature is 33°C, the alligator will be male. Between these two incubation temperatures, there are varying probabilities of the alligator being either female or male.

The phenomenon has also been the subject of experimental investigation. For example, in the 1950s, Levine showed that mature rats that had been handled daily between birth and weaning tolerated physiological stress better than rats that had not been handled as pups.38 Levine thought that the differences he observed were due to changes in the reactivity of the central nervous system. Meaney et al.39 later repeated Levine’s experiment and found evidence of differences in the gluco-corticoid receptor system in the hippocampus and frontal cortex of the handled and non-handled rats.

According to the fetal origins theory, programming of chronic disease occurs when there is an imbalance between the supply of nutrients and the nutritive needs of the developing fetus. Under these circumstances, the metabolism of the fetus reacts in ways that are adaptive in the short-term, but potentially disadvantageous in the longer-term. Growth of the fetus may be slowed and this may result in reduced size at birth.

More fundamental changes are thought to occur at the level of organ structure or physiological function. These changes may be due to the altered distribution of cell types or the re-setting of hormonal feedback. For example, one feedback loop that may be affected by the fetal environment is that governing the hypothalamic–pituitary–adrenal axis. This could be re-set in such a way that, throughout life, the release of gluco-corticoids in response to stress is greater and circulating gluco-corticoids are at higher levels than normal. Since cortisol can increase blood pressure and impair glucose tolerance, this may eventually increase the risk of cardiovascular disease.28

Birth size is thus a proxy for fetal programming. As such, the findings of the epidemiological studies described can be interpreted as evidence of programming. However, birthweight may not be a sensitive marker of programming, which will mean that the impact of programming on later health is underestimated by these studies.
Barker and his colleagues have attempted to improve their analyses by using other phenotypic measures, such as thinness at birth. Body proportions at birth are thought to reflect nutritional conditions at different times of gestation, and hence provide better indicators of programming than birthweight. However, this assumption is questionable as supportive data are patchy. For example, Kramer et al. studied almost 9000 infants born in Canada and found no evidence of distinctly proportional and disproportional growth retardation.40 Harding suggested that growth trajectory might be a more useful indicator of adverse programming,41 although this requires repeated measurements of the size of the baby prior to birth.

A growing body of work is attempting to elucidate the changes in structure and function attributable to programming. For example, it has been shown that men who were thin at birth have reduced rates of glycolysis in their muscles.42 In a study undertaken in Adelaide, young men who were thin at birth were found to dispose of glucose in a different manner to their peers, compensating for reduced insulin sensitivity by an increase in insulin secretion and a greater degree of glucose-mediated glucose disposal.43

Programming by nutrition

Poor nutrition before birth is suggested to give rise to altered programming.25 Exposure to high levels of maternal stress hormones has also been proposed as a source of programming,44 and effects have been demonstrated in animals.45 This is not necessarily a separate pathway, as maternal gluco-corticoids are elevated in response to a variety of adverse conditions, such as psycho-social stress, bacterial infection and pre-eclampsia, and thus may mediate nutritional effects.46

Experiments in animals (mainly rats, but also guinea pigs and sheep) show that changes to maternal nutrition before or during pregnancy can produce elevated blood pressure and impaired glucose tolerance in offspring.47 Much of this research has been undertaken over the past decade, motivated by epidemiological studies. Two dietary manipulations have been the focus of these experiments: (i) an isocaloric low protein diet; and (ii) varying degrees of reduced energy intake. Recently, it has been shown that even a very short low protein diet; and (ii) varying degrees of reduced energy intake. Recently, it has been shown that even a very short

In fact, until now, it was commonly thought that growth of the human baby was unaffected by variations in maternal nutrition, except in extreme situations of poverty or famine. Early observational studies and unsuccessful trials of nutritional interventions seemed to bear this out. However, a reappraisal of this body of work suggests these null results may be a reflection of the quality of the research more than a realistic assessment of any relationships.49–51

Kramer and Kramer et al. have undertaken several reviews of many studies on nutrition and birthweight.50,51 They make an important distinction between low birthweight due to prematurity and low birthweight due to restricted growth, as these outcomes have different aetiologies (and, probably, different long-term consequences). In the most recent review, Kramer et al. summarize the public health importance of the many factors that affect birthweight using the concept of population-attributable risk; this amalgamates information on the risk conferred by a factor and how widespread that factor is.51 Thus, in a developed country in which approximately 25% of women smoke, smoking has the greatest attributable risk for restricted fetal growth. This is followed by low weight gain during pregnancy, first pregnancy, low pre-pregnancy body mass index, short stature and ethnic origin. Three of these factors have a connection with the nutrition of the mother (four, if differences in the diets of smokers and non-smokers are included).

Beyond limited energy intake, the aspects of maternal nutrition that have received most attention are the micronutrients, calcium, folate, zinc and long-chain fatty acids. Randomized controlled trials have generally not demonstrated the benefits of supplementation, contrasting with the positive associations reported from observational studies. Kramer et al. suggest this may be because specific micronutrient intakes are correlated with other aspects of diet, and believe there is a need for more sophisticated research in this area.51

So the research on women’s nutrition and birth size does not give clear indications of what aspects of maternal nutrition might underpin programming, other than general support for restricted energy intake being a factor. It offers little insight as to the reproductive consequences of poor dietary quality, although maternal obesity is associated with increased risk of complications during pregnancy and an abnormally heavy baby.52 Obese women also have reduced fertility and increased risk of miscarriage.53

The other limitation on use of this research as an evidence-base is that, as mentioned previously, birthweight and other birth dimensions are not necessarily very sensitive indicators of programming. Therefore, the role of nutrition in programming may be missed by studies that simply consider the effects of nutrition on birth size. This is highlighted by some of the animal studies in which changes to maternal nutrition programmed the physiology of the offspring, although there was no observable impact on birth size.57 In a developed country setting, where the nutritional problem is more likely to be one of ‘cheap’ energy, rather than restricted
energy, it is possible that adverse programming will occur without overt changes in size at birth.

Greater insight may be gained through studies that directly link aspects of maternal nutrition to health outcomes in offspring. However, relatively few such studies have been undertaken in humans.

One opportunity to examine relevant data has arisen from the Dutch famine that occurred during World War II under the German occupation. Over the winter of 1944–1945, food was especially scarce and rations fell to 400–800 calories (17–33 kJ) per day. Results published over 25 years ago indicated that severe under-nutrition of the mother in late pregnancy led to a reduced size of the baby at birth. Later, under-nutrition of the mother early in pregnancy was associated with increased obesity in male offspring at around 20 years of age. In a more recent follow-up study of 700 individuals born in one Amsterdam hospital, glucose tolerance was assessed. Impaired glucose tolerance was most common among individuals whose mothers were experiencing late pregnancy when the famine began. Individuals conceived during or after the famine also had increased risk of impaired glucose tolerance, compared to those born before the onset of famine. Of relevance to the present argument, the differences between these groups in terms of glucose tolerance at the age of 50 years were much larger than the differences in birthweight.

A study of individuals who were born in and around Leningrad when it was under siege during World War II had contrasting findings. There were no differences in blood pressure, lipid profiles or glucose tolerance between subjects born before the siege, those born during the siege, and those born outside the city around the same time. However, increased rates of endothelial dysfunction and a stronger relationship between obesity and blood pressure were observed among subjects who were in utero during the siege.

In rural Gambia, there is a period of famine every year when it rains, known as the ‘hungry season’. Season of birth was not related to cardiovascular risk factors in 219 adults who had maintained their traditional lifestyle, although the rate of early adult death (mainly due to infectious diseases) was markedly elevated among those born in the hungry season.

A handful of studies have documented a link between aspects of maternal nutrition in less extreme conditions, and later health of the offspring. Only one study has been able to consider the outcome of death from coronary heart disease. The others have examined clinical risk factors, usually blood pressure.

Forsen et al. studied more than 3000 men born in Helsinki between 1924 and 1933. Size at birth was associated with risk of coronary heart disease in adulthood. Coronary heart disease in offspring was also strongly related to the maternal body mass index during pregnancy. The highest rate of death occurred among men who were thin at birth and had a mother who was relatively short and fat. It was suggested that this signified a woman whose family had only become well nourished in recent times.

In other work, low maternal weight gain in late pregnancy was associated with elevated blood pressure of a subgroup of Gambian children. Low maternal weight gain during pregnancy, low haemoglobin and thin triceps skinfold were all associated with elevated blood pressure among children at the age of 11 years in a study conducted in Jamaica. Maternal anaemia and low mean cell volume during pregnancy, but not maternal body mass index, were associated with elevated blood pressure in a group of English children at the age of 4 years.

To our knowledge, there are three studies that have attempted to link maternal dietary intakes to blood pressure of the offspring. McGarvey et al. assessed the diets of approximately 200 pregnant women living on Rhode Island and made repeated measurements of the blood pressure of their infants over the year following birth. Maternal intakes of calcium and potassium were negatively correlated, albeit weakly, with the blood pressure of the child.

Belizan et al. considered the enduring consequences of a supplement administered in a randomized controlled trial. Approximately 600 pregnant women in Argentina participated in a trial to see whether 2 g of calcium per day could prevent pregnancy-induced hypertension. Seven years later, 11% of children whose mothers received the calcium supplement had high blood pressure, compared to 19% of controls (P < 0.05). Interestingly, there were no differences in birthweight between the two groups of children, and the effect persisted after maternal blood pressure during pregnancy was taken into account.

The third study, which spans the longest time period, concerns approximately 200 men and women born in Aberdeen, Scotland, between 1948 and 1954. While pregnant, their mothers completed a dietary survey. At around the age of 40 years, the blood pressures of cohort members were assessed. Where the mother’s intake of animal protein during pregnancy had been less than 50 g per day, there was a positive association between maternal carbohydrate intake and offspring blood pressure. However, the association was negative where maternal intake of protein was more than 50 g per day. The glucose tolerance of cohort members was also assessed. Individuals whose mother had a high intake of protein or fat in late pregnancy had a lower insulin increment than their peers, indicating reduced insulin secretion. This finding possibly reflects an influence of maternal hyperglycaemia in pregnancy.

So far, these results do not have a clear pattern. This may be, in part, because researchers (understandably) have examined data that was to hand, rather than addressing the question comprehensively. As well as considering non-nutritional influences on programming, ways forward might involve a focus on dietary composition or quality, and probably require a better marker of programming than birthweight. Harding suggests using fetal growth trajectory and emphasizes the need to distinguish between maternal nutrition and fetal nutrition. The nutrition received by the fetus depends not only on maternal diet, but also on other factors along the ‘supply line’, including maternal nutrient...
Programming and inequalities in health

Could ‘maladaptive’ programming help to explain social inequalities in cardiovascular disease and diabetes? In developing countries and indigenous groups, where low birthweight is very common, this explanation seems especially relevant. However, we suggest that programming could also play a significant role in perpetuating social inequalities in health in developed countries, such as Australia.

First, it must be acknowledged that, in Australia, social variations in birthweight are relatively modest. The relationship is clearer when socioeconomic status is imputed from personal attributes of the parents rather than postcode. Most of the social variation in birthweight appears to be due to differences in the proportion of babies weighing between 1500 and 2500 g, rather than to differences in the proportion of babies weighing below 1500 g. Babies in the former group are sometimes referred to as ‘moderately low’ birthweight and include growth-restricted babies born at term, while those in the latter group are termed ‘very low’ birthweight and are almost always born very prematurely (and may or may not be growth-restricted). In the present context, this is interesting, because the mechanisms underlying moderately low birthweight are thought to differ from those causing premature birth. In particular, environmental influences are thought to have a more important role in causing moderately low birthweight than premature birth.

In contrast, the social gradient for adult conditions, such as cardiovascular disease, is quite marked in Australia. Leaving aside the problem of birthweight as an imperfect indicator of fetal programming, does this mean that programming cannot be contributing greatly to inequalities in health in Australia? On the contrary, we argue that it is likely that programming interacts with the post-birth environment, so that small initial differences in predisposition to disease are amplified over time. Thus, a life-course perspective is necessary to fully appreciate the significance of programming for inequalities in health.

This is most clearly demonstrated in the recent work of Barker et al., with a cohort of men born in Helsinki. The highest risk of coronary heart disease was observed among men who were thin at birth, had accelerated weight gain after infancy, and who had experienced poor living standards in adulthood. Men who were not thin at birth were largely resilient to the effects of low social class or low household income in adulthood.

These findings concerning Finnish men highlight the potentiating role of social circumstances, but do not specify in detail the influential aspects of the social environment. Other work with the same cohort suggests that nutrition in childhood might be a factor. Two growth paths appeared to increase the risk of coronary heart disease for the Finnish men: (i) being thin at birth, but gaining weight rapidly after infancy; and (ii) growing poorly during infancy and remaining thin during childhood. Men who followed either of these growth paths were likely to be short, at least up to the age of 12 years. A number of other studies indicate that the association between birthweight and later cardiovascular disease or diabetes is enhanced among individuals who become obese as adults.

Besides nutrition, other compounding features of the social environment could include constant stress or lack of success. Barker et al. observed that higher educational attainment protected the men who were thin at birth from the harmful effects of low income, and speculated that psychosocial factors may be involved, rather than simply material limitations. This may be a point of convergence with psycho-social explanations for social inequalities in health, as Marmot recognized.

Thus, while fetal programming may create a constitutional vulnerability to chronic disease, this may or may not be realized; an individual’s health destiny will also depend on the conditions experienced following birth. Unfortunately, the adverse exposures that are thought to underlie programming and its amplification cluster in socially patterned ways. Poor nutrition is implicated at several stages, although detailed knowledge of nutritional influences is lacking. However, in general, the theory lends support to broad strategies to improve the nutrition of those in disadvantaged circumstances, especially women and children.

Acknowledgements. We thank Professor Jeffrey Robinson for his comments on the present manuscript.

References
29. Phillips DIW, Barker DJP. The thrifty phenotype hypothesis. In:
28. Phillips DIW. Fetal growth and programming of the hypothalamic-
27. Huxley RR, Shiell AW, Law CM. The role of size at birth and
25. Barker DJP. Mothers, Babies, and Disease in Later Life. London:
24. Eriksson M, Tibblin G, Cnattingius S. Low birthweight and
23. Leon DA, Lithell HO, Vagero D, Koupilova I, Mohsen R,
18. Barker DJP, Osmond C, Simmonds SJ, Wield GA. The relation of
15. Marmot MG. Social differential in health within and between
13. Department of Health and Social Security. Inequalities in Health,
11. Barker DJP. The foetal and infant origins of inequalities in health
10. Barker DJP, Osmond C. Inequalities in health in Britain: specific
9. James WPT, Nelson M, Ralph A, Leather S. The contribution of
8. Phillips DIW, Barker DJP. The foetal and infant origins of inequalities in health in
7. Johnson BM, Nathanielsz PW, eds. Research in Perinatal Medi-
6. Franklin S, Elwood P, Sweetnam P, Yarnell J, Davey Smith G.
5. Marmot MG. Social determinants of health and disease: evidence
3. Dunger DB, Ong KK, Huxtable SJ, Sherriff A, Woods KA,
0. Stein CE, Fall CHD, Kumaran K, Osmond C, Cox V, Barker DJP.


68. Robinson R. The fetal origins of adult disease: no longer just a hypothesis and may be critically important in south Asia. BMJ 2001; 322: 375–376.


