Birth weight symposium

Maternal nutrition as a determinant of birth weight

T Stephenson, M E Symonds

Maternal nutrition, encompassing maternal dietary intake, circulating concentrations, uteroplacental blood flow, and nutrient transfer across the placenta, influences birth weight

THE CONTRIBUTION OF MATERNAL NUTRITION TO BIRTH WEIGHT

Birth weight is correlated between half siblings of the same mother but not of the same father[1] because of the greater contribution of the maternal genotype and environment.[2] As summarised in table 1, the latter includes maternal nutrition.

MATERNAL NUTRITION AND CLINICALLY SIGNIFICANT INTRAUTERINE GROWTH RESTRICTION

In the narrow sense, "maternal nutrition" describes the pregnant woman's diet. The effects of severe macronutrient deficiency depend on the stage of gestation. During the Dutch famine of 1944–1945, a 50% reduction in energy intake during the first trimester was associated with increased placental weight but no change in birth weight.[4] Maternal undernutrition in late gestation was associated with reduced placental and fetal weights.

"The effects of severe macronutrient deficiency depend on the stage of gestation."

Embryo transfer and litter reduction experiments similarly show that maternal environment predominantly influences later fetal growth.[5] Although macronutrient deficits in later pregnancy would be expected to exert greatest impact on birth weight (the human fetus weighs only 20% of term weight at 24 weeks[3]), catch up growth often occurs.[6 7] In contrast, the earlier in postnatal life that undernutrition occurs, the more likely it is to have permanent—that is, programming—effects.[8] In normal pregnancies of malnourished women, dietary supplementation during late pregnancy increases birth weight.[9]

MATERNAL NUTRITION AND VARIATION WITHIN THE NORM: THE BARKER HYPOTHESIS

In developed countries, dietary macronutrient or micronutrient deficiency are rarely thought to be responsible for clinically significant impaired fetal growth.[10] Lower birth weight is associated with lower social class, but although it is often assumed that this is nutritional, there are many confounders such as smoking and genetic factors. Recent human pregnancy studies do not confirm the dietary hypothesis,[11 12] but these studies have been criticised.[13] Contemporary studies in Australia, however, indicate that nearly 30% of women who deliver babies with a low birth weight (< 2500 g) suffer from eating disorders.[14] Experimentally increasing maternal nutrition in sheep enhances birth weight.[13]

Epidemiological studies have shown that size at birth and/or placental weight predict adult disease.[15 16] The hypothesis that variations in maternal diet within the normal range can lead to concomitant variations in birth weight and hence to later disease remains the subject of intense debate. These studies are criticised because of possible confounding factors. However, later blood pressure is independent of maternal blood pressure and smoking,[17] social class at birth, adult social class, later cigarette smoking, and obesity.[15] In the Hertfordshire cohort,[18] birth weight is unrelated to social class either at birth or currently.[15] Moreover, birth weight was not associated with lung cancer or deaths from non-cardiovascular causes, which may also be expected to be influenced by social class and lifestyle.

Table 1 Genetic and environmental contributions (%) to birth weight variation (adapted from James & Stephenson[3])

Genetic	
Maternal genotype	20
Fetal genotype	16
Fetal sex	2
Total genetic contribution	38
Environmental	
General maternal environment	18
Immediate maternal environment	6
Maternal age and parity	8
Unknown environmental influences	30
Total environmental contribution	62

FETAL SUBSTRATE SUPPLY

So far, this review has focused on the mother's dietary intake. In the wider sense, maternal "nutrition" encompasses the complete supply line of maternal intake, circulating concentrations, uteroplacental blood flow, and nutrient transfer across the placenta.[3] Experimental reduction of the number of placentomes in sheep results in a smaller fetus,[19] as does reduction in uterine artery blood flow.[20] Maternal smoking[21] and pre-eclampsia are associated with lower birth weight.[22] Nutritional or vascular factors probably account for the association between lower birth weight and placental anomalies, twin-twin transfusion syndrome, and maternal diseases (respiratory, cardiac, renal, and collagen).[23] Nutrition is a dominant influence on insulin-like growth factor-I concentrations prenatally,[24] and the correlation between birth weight and insulin-like growth factor-I[25] is further evidence that nutrition, in this broader sense, is a determinant of birth weight.

However, most fetuses with clinical intrauterine growth restriction have a reduced placental to birth weight ratio, suggesting that the fetus adapts to improve placental transfer when the placenta is pathologically small. In contrast, in Barker's studies of predominantly healthy (and surviving) infants from 50 years ago, it was men with a high placental to birth weight ratio who had highest death rates from cardiovascular disease,[15] suggesting different mechanisms. The association between maternal anaemia and increased placental weight[26 27] could be linked by nutrition or oxygen delivery.

In the Dutch famine, dietary restriction during early gestation increased the placental to birth weight ratio and resulted in a much greater risk of adult coronary heart disease and obesity.[28] In a sheep model, maternal nutrient restriction between early to mid gestation resulted in increased placental weight but not fetal weight at term.[29]

HOW COULD MATERNAL NUTRITION PROGRAMME RISK IN LATER LIFE DESPITE A BIRTH WEIGHT IN THE NORMAL RANGE?

Small for gestational age does not necessarily equate with intrauterine growth

Abbreviations: 11β-HSD, 11β-hydroxysteroid dehydrogenase.

restriction. Even if birth weight remains within the normal range, this may conceal a birth weight significantly below genetic potential because of suboptimal maternal or fetal nutrition.[30] Nutritional deprivation redistributes maternal cardiac output away from the uterine vasculature,[31] and a chronic fetal "stress response" to this could permanently reprogramme steroid sensitivity. Fetal overexposure to maternal glucocorticoids may programme hypertension[32, 33] In sheep, dexamethasone treatment during early pregnancy results in persistent hypertension in the offspring.[34]

Sensitivity to glucocorticoids is regulated by expression of the glucocorticoid receptor and 11β-hydroxysteroid dehydrogenase (11β-HSD). 11β-HSD1 catalyses the conversion of cortisone to the more potent cortisol,[35, 36] and 11β-HSD2 does the opposite, "protecting" the fetus from adverse glucocorticoid exposure.[32, 37] The renin-angiotensin system is also regulated by glucocorticoids[38] and is critical to the control of blood pressure during fetal and postnatal life.[39, 40] Increased tissue exposure to cortisol could explain how early reduction in maternal nutrition affects fetal cardiovascular development while birth weight remains within the normal range.

In the sheep model with maternal nutrient restriction in early gestation and increased placental to fetal weight ratio at term,[29] both glucocorticoid and type 1 angiotensin II receptor mRNA expression are increased in the offsprings' adrenal and kidney.[41] Conversely, placental 11β-HSD2 mRNA expression is decreased, which could increase cortisol transfer across the placenta in the absence of any apparent change in maternal cortisol.[42, 43]

CONCLUSIONS

In developing countries, maternal dietary intake can affect birth weight, and intervention helps. In developed countries, epidemiological studies and experiments using animals indicate that modest reductions in maternal food intake could affect survival at birth and longevity, in the absence of pathological changes in birth weight.[44, 45] It appears to be earlier maternal nutrient restriction that increases placental size[29] and alters the expression of genes regulating the glucocorticoid and renin-angiotensin systems.[41]

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Birth weight symposium

Social influences on birth weight

N Spencer, S Logan

Risk factors for low birth weight are strongly influenced by the social environment

Birth weight, like growth, is determined by the complex interplay of genetic and environmental factors. The proportional contribution of these influences is unclear. However, birth weight varies within genetically similar populations,[1–3] suggesting that environmental factors play a significant role. Secular changes in birth weight[4] also suggest an environmental influence. Birth weight also shows a reverse social gradient such that increasing disadvantage is associated with decreasing birth weight.[1–3]

ENVIRONMENTAL FACTORS AFFECTING BIRTH WEIGHT

Environmental factors with a known association with birth weight are nutrition, smoking, maternal ill health, and genital infection. The association of other factors such as stress[5] and exposure to some types of work during pregnancy[6] remains unproven. Other risk factors for low birth weight such as maternal age, although not themselves environmental factors, are strongly influenced by the social environment.

Severe energy restriction during pregnancy, such as occurs in some developing countries[7] and was noted in the 1945 Dutch Hunger Winter[8], reduces birth weight but, randomised controlled trials of nutritional interventions in the index pregnancy have failed to show convincing benefit.[9] Nutrition may exert its effect over a longer period through an effect on maternal growth in childhood[10] and possibly through an intergenerational effect.[11] Adult height has a known association with relative nutritional impairment in childhood,[12] and maternal height is an important determinant of birth weight.[13]

The association of smoking with a reduction in birth weight is well established.[13] Maternal ill health has been associated with reduced birth weight,[14] and genital infection exerts its influence through increasing the risk of preterm delivery.[15]

Evidence for an independent effect of stress is slight, but one study does show stress exerting an effect through increased smoking.[16]

SOCIAL GRADIENT IN BIRTH WEIGHT

Given the importance of birth weight for infant, childhood, and adult health,[17] a 150–200 g social gradient in mean birth weight and 30% of births less than 2500 g attributable to social inequalities[1] is a key public health issue. Reductions in inequalities in infant mortality and many childhood and adult health inequalities, key government health targets,[18] are unlikely to be achieved without a narrowing of the social gradient in birth weight. Interventions to increase birth weight in disadvantaged groups have been largely unsuccessful,[19] and, although mean birth weight has increased,[20] the rate of change is slow and the gradient remains unchanged.

> "Reductions in inequalities in infant mortality and many childhood and adult health inequalities, key government health targets, are unlikely to be achieved without a narrowing of the social gradient in birth weight."

The failure of interventions to influence the social gradient is likely to result from a focus on modifying individual risk factors such as smoking, diet, and infection in the already established pregnancy with the intervention starting around 16 weeks at the earliest. The social gradient in birth weight probably arises as a result of the accumulation and addition of risk and protective factors over time[21] and across generations[11] rather than resulting from risk exposures within the index pregnancy. Poor socioeconomic circumstances in early life may lead to biological vulnerability in later life,[22] and adult health behaviours seem to have socioeconomic roots early in life.[23] A woman whose parents were disadvantaged is more likely to have been low birth weight herself, to have experienced more childhood ill health, to have had a less nutritious diet with adverse effect on her growth, to have started smoking in adolescence and be less likely to quit in early pregnancy, and to come to pregnancy at an earlier age.

Although innovative approaches to smoking cessation and stress reduction may have some effect in the short term, reduction of the social gradient is likely to be a long term goal requiring attention to the nutritional and health status of young children. Of equal importance will be improving the overall social environment in which children grow up so that protective factors, such as maternal education, become more evenly distributed across social groups and risk factors are reduced in disadvantaged groups.

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