COMMENT

Protein, programming and plumpness: is there a link?

Rachel R. HUXLEY
Heart and Vascular Division, Institute for International Health, University of Sydney, 144 Burren Street, Newtown, Sydney, NSW 2042, Australia

ABSTRACT

Early-life nutrition has been suggested to influence the progression of chronic disease. In this issue of Clinical Science, Ozanne and colleagues argue that the pre- and post-natal diet can have a significant impact on the risk of becoming overweight in later life. Although an intriguing finding that warrants further investigation, it is most likely that the key to stemming the obesity pandemic will depend chiefly on the implementation of effective population-wide strategies that focus on lifestyle modification, both in childhood and in adult life.

In recent years, the idea that nutrition in early neonatal and postnatal life, the fetal-origins hypothesis, could shape an individual's disease risk profile in later life has become increasingly popular. The hypothesis has been used to partly explain the increasing rates of cardiovascular disease and associated disorders, including hypertension and Type II diabetes [1]. However, the evidence linking maternal nutrition and birth size with later disease risk is anything but conclusive, as a recent review of the fetal-origins literature has shown [2]. In that review, the reported inverse association between birthweight and subsequent blood pressure, which has been suggested to provide the strongest evidence in support of the fetal-origins hypothesis, is likely to have been driven chiefly by publication bias, inadequate adjustment for confounders and unduly selective emphasis on small studies [2], problems that frequently plague the epidemiological literature.

In this issue of Clinical Science, Ozanne et al. [3] demonstrate an intriguing association in mice which, after being exposed to a low-protein diet in early-life, subsequently gained less weight on a ‘cafeteria’ style diet. In addition, the growth-restricted offspring of dams that were fed a reduced protein diet during gestation, upon exposure to a standard diet postnatally, exhibited ‘catch-up’ growth that exceeded the body weight of control mice. These findings suggest that nutritional influences, both neonatal and postnatal, can somehow influence or ‘programme’ body weight homoeostasis in subsequent life. Findings which, if true, could have important implications for the ongoing battle against the bulge.

Previous studies in animals have produced conflicting results with regards to the impact of postnatal protein intakes with fat accretion. In rats, postnatal accretion of body fat has been reported to be positively associated with dietary protein intakes [4], whereas, in pigs, the converse has been reported [5]. In several observational studies in human populations, protein intake in infancy and in adolescence has been observed to correlate directly with body mass index (BMI) in subsequent life [6]. However, methodological flaws within these studies, including poor consideration of possible confounding factors and the method of ascertainment of protein intake, requires that these findings should be interpreted with caution.

It might be expected that studies of infant breast-feeding may help to shed further light on this issue, since breast milk typically has approximately a quarter less protein than traditional infant formulas. However, evidence from epidemiological studies that have looked at the impact of breast-feeding on subsequent risk of becoming overweight in later life is again conflicting. Some studies have reported a protective effect of breast-feeding on subsequent risk of becoming overweight [7], whereas other studies have found no association [8].

Key words: birthweight, catch-up growth, obesity, protein.
Correspondence: Dr Rachel Huxley (e-mail rhuxley@iih.usyd.edu.au).

© 2004 The Biochemical Society
Recently, in a large cohort of more than 12,000 individuals followed longitudinally from childhood into adult life [8], breast-feeding was shown to have a protective effect on the later risk of becoming overweight, but the association disappeared after adjustment was made for relevant confounders, such as social class, mother’s BMI and mother’s smoking in pregnancy. This led the authors to conclude that “the method of infant feeding itself is unlikely to influence obesity”. Furthermore, in the only published randomized trial of nutrition in preterms, in which infants were randomly assigned to receive either breast-banked milk or nutrient-enriched formula (which contained more protein), there was no evidence of any difference in BMI among these individuals in adolescence [9].

The second issue raised by the findings from the study by Ozanne et al. [3] concerns the ‘thrifty phenotype’ hypothesis and the potential impact of catch-up growth on subsequent body weight. In essence, the hypothesis proposes that, in response to poor nutrition, the fetus can make physiological adaptations, which, although conferring an immediate survival advantage, may, when exposed to an environment where there is an abundance of nutrition, increase the susceptibility to disease in later life. In the literature, postnatal catch-up growth, often defined as the percentage change in body weight or height from birth, is often used to indicate such nutritional mismatch.

A large number of studies have published associations between catch-up growth with a wide range of adverse health outcomes, including insulin resistance [10], ovarian cancer [11] and coronary heart disease [12]. That postnatal catch-up growth may confer an increased risk of obesity in later life, as suggested by these current findings by Ozanne et al. [3], adds further to this list of risk factors. However, there is an equally abundant literature describing how failure to ‘catch-up’ is similarly adversely related to increased risk of adverse events in later life, including suicide [13] and coronary heart disease [14]. Thus the possible effects of postnatal catch-up growth on health in later life remain unclear and, due to the limitations inherent in observational epidemiology, it may take some time before we are able to distinguish causation from association.

Even if a robust relationship could be demonstrated between the constituents of the postnatal diet with risk of becoming obese in later life, any potential benefit is likely to be modest and heavily outweighed by the obesity-promoting environment to which an increasing number of individuals are being exposed. Reduced levels of physical activity combined with an almost inexhaustible supply of cheap, calorie-laden foods are considered to be the chief suspects responsible for the increased prevalence worldwide of overweight and obesity. And unfortunately, it will not be until we are able to devise and implement effective strategies at the population level that counteract these two factors that we will be able to stem, and hopefully reverse, the tide of the obesity pandemic.

REFERENCES