



**Paper for discussion: Draft Executive Summary of SACN's  
Draft Report on 'The influence of  
maternal, fetal and child nutrition on the  
development of chronic disease in later  
life'**

**Agenda item: 3**

Please see attached a draft summary for the report on 'The influence of maternal, fetal and child nutrition on the development of chronic disease in later life'. This has been written following public consultation of the draft report and has considered relevant comments raised by respondents (comments received from the consultation are also circulated for information – see paper SACN/10/15).

The draft summary is being presented to the Committee for the first time, so members are asked to focus their discussion on this paper, alongside discussion of the draft recommendations (see separate paper SACN/10/13).

## THE INFLUENCE OF MATERNAL, FETAL AND CHILD NUTRITION ON THE DEVELOPMENT OF CHRONIC DISEASE IN LATER LIFE

### EXECUTIVE SUMMARY

#### Background

1. Cardiovascular disease, type 2 diabetes and cancer, are leading causes of death in the UK and present a major contemporary public health challenge. Many chronic diseases are diet-related and therefore the nutritional status of the population has potential implications for the health of future generations.
2. Fetal life and early childhood are periods of rapid growth and development during which imbalanced nutrient supply may alter body structure and function in a way that increases later risk of chronic disease. In girls such changes may additionally modify ability to meet the nutritional stresses associated with reproduction.
3. Understanding the effects of imbalanced nutrient supply at critical periods of development requires consideration of experimental and observational evidence. A wealth of observational evidence has reported associations between nutritional status in early life and adult chronic disease. Experimental evidence suggests causality and offers insight into mechanisms.

#### Terms of Reference

4. The Department of Health asked the Scientific Advisory Committee on Nutrition (SACN) to review the influence of maternal, fetal and child nutrition, including growth and development in utero and up to the age of 5 years, on the development of chronic disease later in the life of the offspring. SACN was also asked to identify opportunities for nutritional intervention that may address these risks.

#### Methodology

5. The review has been undertaken by SACN's Subgroup on Maternal and Child Nutrition (SMCN). The epidemiological evidence has been reviewed in accordance with the principles described in the SACN working document, *A Framework for the Evaluation of Evidence* [Scientific Advisory Committee on Nutrition, 2002].
6. The Committee has not considered the impact of reproduction on the mother's own later health nor has it considered the impact of smoking, alcohol and other environmental exposures on the offspring. It nevertheless stresses their importance.
7. The Committee has focussed attention on cardiovascular risk and cancer as the leading causes of mortality but recognises growing evidence that early life nutritional exposures affect many other outcomes. These include asthma, muscle function, dental health, neurological function, cognition and mental health.
8. Where available, the Committee considered systematic reviews and meta-analyses of relevant studies, with subsequently published individual studies or trials considered separately. In the absence of reviews, the Committee identified relevant retrospective or prospective studies and trials. The Committee finally considered experimental studies in humans and animals in order to explore mechanisms.

## **Growth in fetal life and infancy**

9. Normal growth and development is characterised by a regulated increase in the dimensions, mass and functional complexity of tissues and organs. These processes require a sufficient supply of energy and nutrients and can be disturbed by imbalanced nutrient supply. It is hypothesised that resultant inter-individual differences in the pace and timing of early growth and development become expressed as differences in body composition, metabolic and physiological function, thereby influencing later chronic disease risk.
10. Experimental studies in animals have demonstrated the existence of “critical periods” in early development during which alteration of nutrient supply may alter structure and function irreversibly. This phenomenon has been labelled “nutritional programming”. Understanding it requires a developmental perspective that links nutrient requirements and supply to the composition and distribution of tissues deposited during growth, and to the attainment of functional or metabolic capacity at the whole body and cellular level.
11. Many determinants of fetal growth are established before conception. A woman achieving pregnancy with low nutritional reserves increasingly depends on her current dietary intake to meet the needs of her pregnancy and subsequent lactation. Her nutritional status at the start of pregnancy therefore influences her ability to support the needs of her fetus and her baby.
12. Although widely considered an indicator of pregnancy outcome, birthweight is influenced by many variables other than fetal nutrient supply. These include maternal height, weight, parity, and exposure to toxins such as alcohol and tobacco smoke. Moreover, fetuses may achieve comparable birthweight through different gestational growth trajectories and consequently vary in their body composition and metabolic capacity.
13. Maternal physiological adaptations normally buffer fetal nutrient supply as maternal nutrient intake fluctuates. However, these adaptations may be insufficient under extreme conditions such as famine; fetal nutrient supply is then restricted. The timing of gestational nutrient restriction influences the nature of chronic disease risk in a way that can be related to the known sequence of fetal organs and tissue development.
14. When intrauterine growth restriction occurs the offspring frequently displays an acceleration of early postnatal growth. This is known as “catch-up” (or “compensatory”) growth. In these circumstances the relative amounts of tissue deposited may vary from normal. Such disproportionate growth may give rise to long-term alteration of body composition and metabolic competence, thereby amplifying disease risk.
15. The pattern of feeding in infancy also influences the rate of growth and the type of tissue deposited. Early postnatal nutrient exposure alters hormonal axes and thus has the potential to modify body composition in a way that tracks from fetal life or infancy onwards. The extent to which genetic and ethnic variation influences these processes is currently not clear..

## **Observational evidence about the impact of early life nutrition on later chronic disease**

16. The largest body of observational evidence considers cardiovascular disease (CVD) outcomes such as coronary heart disease, stroke, and type 2 diabetes.
17. Birthweight is commonly regarded as a proxy for fetal nutritional exposure in observational studies. However it reflects the influence of numerous factors on fetal development and does not describe body composition or metabolic competence of the offspring. Its weakness as a measure of offspring nutritional status deserves wider acknowledgment.
18. The few studies of body composition that have been able to resolve separately the fat and lean mass components, suggest that higher birthweight may be associated with relatively greater lean mass in later life, whereas lower birthweight is associated with relatively greater fat mass.
19. The majority of studies looking at the relationship between birthweight and coronary heart disease (CHD) risk show modest inverse associations: studies of CVD risk factors (blood pressure, serum cholesterol) and birthweight also suggest small inverse associations. Taken together, lower birthweight, lower weight at one year, and increased body mass index (BMI) in childhood are associated with an increased risk of CHD.
20. The totality of evidence suggests that lower birthweight is associated with increased risk of subsequent type 2 diabetes. A rapid increase in adiposity after the age of 2 years also increases the risk of type 2 diabetes in adult life.
21. The evidence relating infant feeding practices to subsequent cardiovascular mortality is inconsistent, though infants who are not breastfed tend to have higher blood pressure and serum total cholesterol concentrations in adulthood. They are also at greater risk of type 2 diabetes.
22. Sodium intake at 4-months of age has been associated with systolic blood pressure at the age of 7 years. Similar changes were noted at adolescent follow-up of term infants randomly assigned to low sodium infant formula. These findings suggest that early sodium intake modifies later risk of hypertension.
23. Infants who are not breastfed are more likely to be obese (show increased BMI) in later life.
24. Greater birthweight and faster childhood growth are associated with an increase in risk of certain cancers in later life, notably breast cancer (particularly in pre-menopausal women) and child leukaemia. There is consistent evidence that more rapid height gain during adolescence is associated with later breast cancer risk.

## **Underlying biology, putative mechanisms and their implications**

25. There is little human evidence linking long-term outcome to restriction in the intake of specific nutrients during fetal or early postnatal life. However epidemiological evidence from populations affected by severe food shortage during gestation or early life implies that the timing of nutritional restriction predicts the structural and functional effects observed. These situations have imposed severe generalised restriction in the supply of both macronutrients and micronutrients.

26. Similarly, experimental dietary restriction in pregnant animals suggests that the timing, degree and duration of nutrient restriction exert stronger influences on fetal development than the specific nature of nutrient restriction.
27. Limitation of micronutrient or macronutrient intake sufficient to achieve dietary imbalance in pregnant animal models may alter phenotype through disruption of the normal sequence of tissue development. The consequence of this process is alteration of the offspring phenotype, which may be evident as change in body weight, size, body composition or function. Each may be altered independently, though there are well-described correlations between alteration of function, of organ architecture and of tissue composition.
28. New understanding of the processes by which nutrients may alter gene expression in animal models suggests mechanisms by which nutrient supply to the fetus may induce change in phenotype at the cellular and tissue level. Of particular interest is the observation that imbalance in the supply of those nutrients involved in the methylation cycle may induce change in observable characteristics. For example, epigenetic regulation alters the expression of several hepatic enzymes concerned with intermediary metabolism. It may also alter the endocrinological balance of the mother and feto-placental unit by determining the expression of placental 11 $\beta$ -hydroxysteroid dehydrogenase and of fetal glucocorticoid receptors.
29. These mechanisms have relevance to the observed relationship between impairment of fetal development and physical or emotional stresses imposed on the pregnant mother.
30. Dietary restriction in pregnant animals therefore induces permanent structural and functional changes in the offspring through epigenetic modification of the genome. The role of epigenetics in human disease is becoming more widely appreciated. Altered methylation of DNA has been associated with some cancers and atherosclerosis. Epigenetic effects can also account for inter-generational effects of nutrient restriction observed in pregnant animal models.
31. Despite the accumulating animal evidence no controlled studies in human pregnancy have yet identified maternal dietary interventions that reduce risk of adult chronic disease in the offspring.

### **Implications for maternal and child nutrition in the UK**

32. National studies of diet and nutritional status indicate that excessive consumption of energy, particularly refined carbohydrate and fat, coexists with insufficient intake of vegetable, fruit, and oily fish. In consequence, there is a rising prevalence of obesity, coupled with evidence of low micronutrient status. These observations raise concerns specific to the health of childbearing women and young children.
33. Women aged 19-24 years show poor dietary variety and have low mean intake of certain micronutrients. Consumption of folic acid supplements remains too low amongst women of childbearing age as does the use of vitamin D supplements during pregnancy and lactation, despite evidence of low status. These trends are most marked in low income groups.
34. There is a lack of national data about the dietary intake and nutritional status of pregnant and breastfeeding women, and of children aged less than 18 months. However there is strong evidence that a mother's educational attainment and income predict her dietary choices and infant feeding behaviour.

35. The rising prevalence of obesity in girls and young women represents an important and modifiable risk factor for adverse pregnancy outcome, and for later health outcomes of both the mother and offspring.