The First 1000 Days

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The period between conception and two years – the first 1000 days – represents a window of opportunity to influence lifelong health. *In utero*, exposure to adverse environmental factors during critical periods of development has a lifelong impact on disease risk; nutrition is one such factor. Maternal obesity and excessive gestational weight gain increases an infant's risk of future obesity and related metabolic disease. Growth and feeding during the first year of life may also have life-long consequences. Nutrition during the first 1000 days is a key factor impacting later health.

Introduction

The first 1000 days refers to the period of time between conception and a child's second birthday. The term 'the first 1000 days' was possibly first coined by a non-profit organisation launched by Hilary Clinton in 2010, when she was US Secretary of State (http://thousanddays.org/about/). This organisation recognises the window of opportunity this period presents to future health, and seeks to enable a healthy first 1000 days for mothers and children globally.

The study of the foetal effects on disease risk has been a subject of research for over 50 years.[1] One of the best known proponents was the late Professor David Barker who advanced the theories of 'the foetal origins of disease' and the 'thrifty phenotype'.[2] This evolved to become the study of the developmental origins of health and disease (DOHaD), and has been subject of intense study in recent years, in tandem with the increased understanding of epigenetics; a peer reviewed journal of the same name was launched in 2008.

In the current article, the DOHaD concept will be explained with an emphasis of the role of nutrition, along with examples of the powerful influence of diet and nutrition during the first 1000 days; the context is the developed world.

Developmental origins of health and disease (DOHaD)

Non-communicable diseases (NCDs), including cardiovascular disease, diabetes and cancer, account for more than 60% of all deaths worldwide,[3] making them the leading cause of mortality. The risk of developing these diseases is an interaction between genetics, a variety of lifestyle and environmental factors which act across the lifespan.[4] Adverse environmental factors (including nutrition, stress, smoking, infection) have the potential to disturb processes of cell proliferation and differentiation, or to alter patterns of epigenetics during critical periods of development and may result in irreversible changes that alter the risk of disease in later life.[4] This encapsulates the DOHaD concept;[3] it has shown how the foetal environment, either nutritionally deprived or excessive, increases the risk for child and adult obesity and all the associated sequelae. A recent review has summarised current knowledge on how such adverse metabolic conditions perinatally programme hypothalamic pathways which control energy homeostasis and the associated mechanisms.[5]

DOHaD has public health implications, and an understanding and wide recognition by policy makers, and public acceptance, is crucial to the reduction of NCDs.[6] Whilst there is much work to be done, the World Health Organisation's (WHO) 2012 global targets and recommendations for the nutrition of mothers and infants is an example of the attention this area is commanding.[7]

Influence of diet and nutrition in the first 1000 days

Pregnancy and infancy are characterised by rapid growth, development and maturation of organs and systems. The quality of the diet eaten, or the quantity of nutrients consumed, by the pregnant woman or infant during the first year of life can make a lasting impact on the development. These effects are termed 'programming', a term first used by Professor Alan Lucas (UK) and, as above, are an important risk factor for NCDs.[7] The effects of programming are more marked at times of particularly rapid development, e.g. the final trimester of pregnancy.

Pregnancy

Dutch Famine during Second World War

This tragedy, during the winter of 1944-1945 in the west of The Netherlands, has resulted in some important findings. Women who were exposed to famine while pregnant gave birth to infants who were at greater risk of obesity, glucose intolerance, hypertension and coronary heart disease than individuals born before or after the famine. Furthermore, the risk varied according to the timing and intensity of the insult.[8] Exposure to famine during the early stages of gestation was associated with a greater prevalence of coronary heart disease and obesity.[9] Offspring exposed to famine during mid trimester were more at risk of renal dysfunction,[10] and those exposed during the last trimester had greater levels of Type 2 diabetes and glucose impairment compared to contemporaries not exposed to famine whilst *in utero*.[11]

Diet in pregnancy

The link between maternal nutrition and foetal growth in well-nourished populations is conflicting[4] but it is clear that the balance of micronutrients in the diet of the pregnant woman is important and the consequences of low folic acid intake, for instance, are well documented.[2] Another example of the impact of micronutrient intake during pregnancy is seen in the Amsterdam Born Children and their Development (ABCD) cohort. Women with the lowest vitamin D status 25 (OH) had a higher risk of a small for gestational age baby. Interestingly, there was a link between vitamin D status and level of education, with low education levels associated with low vitamin D status and *vice versa*; weight status, with overweight women having lower vitamin D levels; season, with lower levels of vitamin D seen in women who conceived in the winter.[12]

The influence of diet during pregnancy is also seen in the prospective Southampton Women's Study. In this cohort it was apparent that a higher maternal intake of omega-6 (not omega-3) polyunsaturated fats in late pregnancy was associated with an increase in fat mass at four and six years of age.[13]

An Irish intervention study (ROLO) randomised an at risk group of pregnant women to a low glycaemic or a no intervention diet to investigate whether diet could reduce the incidence of macrosomia (excessive birth weight).[14] There were no significant differences in birth weight or birth centile between the two groups but there was significantly lower maternal weight gain during pregnancy in the intervention group and lower rates of glucose intolerance. This study indicated that diet had a positive effect on important factors that affect future metabolic risk for the offspring.

Maternal obesity

Given the current increasing rates of adult obesity, maternal obesity will pose an ever greater threat.

Maternal obesity is associated with a negative effect on foetal development, birth outcomes and obesity risk.[15] In a newly published comprehensive systematic review on risk factors for childhood obesity in the first 1000 days, higher maternal pre-pregnancy BMI and excess gestational weight gain were consistently shown to be associated with later childhood obesity.[16] The mechanisms through which maternal obesity exerts a programming effect are not fully elucidated but it is apparent that maternal obesity results in chronic inflammation and oxidative stress.[17] Animal models suggest that neuronal regulation of appetite and food intake, adipose tissue physiology and altered energy metabolism and inflammation are the primary mechanisms that negatively influence future obesity risk.[18] Obesity is associated with insulin resistance and the development of gestational diabetes.

The 'over-nutrition' that occurs during gestational diabetes results in rapid foetal growth in particular body fat. The long-term adverse consequences of gestational diabetes (and obesity) have been widely documented and focusing on maternal health is seen as an important approach to combating the ever increasing burden of NCDs.[18, 19] Changes in foetal growth and body composition may result after the development of gestational diabetes.[17]

Birth weight and infant growth

Maternal over- and under-nutrition has been shown to have detrimental effects on birth weight and subsequent growth in the offspring.[18] In a review of the influence of nutrition in early life and the programming of adult disease, Langley Evans summarises the main studies that have linked low birthweight with an increased incidence of metabolic risk factors in adulthood.[7] Excessive birth weight which is particularly associated with maternal obesity is associated with higher body fat in the off spring and an increased risk of obesity in later life with related metabolic disorders.[17]

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There is evidence that rapid growth in infancy or in early childhood poses a greater risk of adulthood cardiovascular and metabolic disease and diabetes,[20] especially if infants were small at birth;[20] overfeeding is a possibility in formula fed infants. There is an association of accelerated infant growth and childhood and adolescent obesity.[21, 22, 23] Premature babies fed with infant formula resulting in rapid growth has been associated with risk factors for cardiovascular disease in adolescence.[24]

Infant feeding

The short-term benefits of breastfeeding are well documented, but the longer term benefits are less clear and this may be due to methodological issues.[7] The presence of other protective factors consistent with those who chose to breastfeed would be confounding variables. The area is further complicated by a lack of clear definitions in studies surrounding exclusive and partial breastfeeding and how this is recorded, and a lack of clarity if duration of breastfeeding was accounted for.

In 2014, a review summarised the literature on the long-term effects of breastfeeding on major NCDs and their risk factors and is summarised in **Table One**.[25]

Complementary feeding

There does not appear to be a clear association between the timing of complementary feeding and excessive childhood weight, but there is some evidence that early introduction of complementary foods, i.e. before four months of age is associated with obesity risk.[26] Convincing evidence does not exist about the type of weaning foods fed and subsequent disease risk; although, there is some evidence that a higher protein intake at 2-12 months of age is associated with higher body fat in childhood.[27]

The timely introduction of new tastes and textures is important to develop healthy eating habits for the future. Flavour exposure via maternal diet begins in the womb, and continues during breastfeeding,[28] and must be progressed during complementary feeding. It has been shown that a delay in the introduction of textures leads to an increase in fussy eating.[29] Furthermore, this period of time is a particularly sensitive one for the discovery of textures, taste and flavour.[30] In a three country European study, offering vegetables between six and 12 months when children are most receptive was said to be important in the promotion of vegetable consumption in children.[31]

Feeding in the early years

It has been known for some time that the first two years of life are important for the development of healthy eating habits.[32] There has been research into early food experiences[30] given the importance of dietary habits in the development of NCDs. Important influencing factors appear to be repeated exposure, pleasure and the social context,[30] which means that parents and carers have an important role to play in the formation of their child's eating habits. The need for practical tips on the development of healthy eating habits in early life has been recognised in a review of available guidance.[33] There is evidence that food habits track over time; in one longitudinal study,[34] food preferences at the age of two and three were associated with those at the age of eight years. Another longitudinal study on the evolution of food preferences showed that a relationship between vegetable preferences in childhood, adolescence and early adult life was related to vegetable choices in early childhood.[35] Thus, feeding habits in the early years may be an important factor for lifelong health.

Table One: Summary of the Role of Breastfeeding on Major NCDs and their Risk Factors Cited by Kelishadi & Farajian 2014[25]

NCDs	Role of Breastfeeding
Hypertension	Results on the protective effects of breastfeeding are conflicting and remain to be determined in longitudinal studies with long-term follow-up.
Obesity	Many studies show only long-term breastfeeding influences obesity in adulthood. There are still conflicting results with not all studies confirming an association.
Diabetes	Breastfeeding is associated with lower levels of insulin. Fasting blood glucose is inversely proportional to long-chain polyunsaturated fatty acids in skeletal muscle membrane; these fatty acids are found in breastmilk and not in formula. Epidemiological studies are mixed in their findings.
Hypercholesterolemia	The cholesterol content of breastmilk is higher than in formula and it has been observed that breastfed infants have higher mean blood cholesterol in infancy, similar in childhood and lower in adulthood.
Cardiovascular disease	A large body of evidence suggest breastfeeding positively affect high density lipoprotein but results are not always consistent. The duration of breastfeeding is important.

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