The role of nutrition in pregnancy

ANNE CLARK MPS, MB ChB, FRANZCOG, FRCOG, CREI

Good nutrition in pregnancy is crucial for the baby's health and to reduce the likelihood of pregnancy complications. It also reduces the risk of the child developing diseases such as diabetes and heart disease when they reach adulthood.

The World Health Organization (WHO) now rates acquired diseases such as cardiovascular disease and diabetes, as leading causes of death worldwide.[1] Suboptimal nutrition during pregnancy predisposes women and their children to these diseases. The resulting epigenetic changes are then transmitted to, and therefore affect, subsequent generations – that is, the woman's grandchildren. Good nutrition in pregnancy is an important and noninvasive method of reducing the risks of developing these conditions and improving the health of Australians into the future. GPs are ideally placed to identify and treat any pregnant women at risk of nutritional deficiencies, often in conjunction with other health professionals involved in the women's care.[2]

MedicineToday 2015; 16(12): 16-22
Updated January 2016

Dr Clark is Medical Director at Fertility First, Centre for Reproductive Health, Sydney, NSW.

Intrauterine environment and epigenetic changes

Intrauterine life is a time of rapid growth and development of organs and systems. The quality and quantity of a mother's diet during pregnancy can exert permanent, powerful effects on the developing tissues of her baby.[3] These effects are called 'programming' and they can affect a person's risk of developing noncommunicable diseases in adulthood, including coronary heart disease, type 2 diabetes, asthma, lung disease, some mental health conditions and some forms of cancer.[4,5]

The association between the intrauterine environment and later health is often referred to as the 'Barker hypothesis' after the finding by the epidemiologist Dr David Barker. He found that in utero conditions have a permanent conditioning effect on the body's metabolism leading to chronic diseases later in life.[6] More than 20 years ago, Barker reported that lower birth weight was associated with increased coronary mortality.[6] The concept of 'programming' was first introduced in 1991 to describe the process by which exposure to environmental insults or stimuli during critical phases of fetal development can trigger adaptations that result in permanent changes in physiology and organ development.[7]

'Programming' occurs via epigenetic changes, which are changes that occur when individual genes are switched on or

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KEY POINTS

- A woman's suboptimal nutrition during pregnancy affects the development and health of her child into adulthood.
- The process occurs via epigenetic changes that alter the 'programming' of developing organs and tissues.
- Suboptimal nutrition in utero can also result in these changes being transmitted to the woman's grandchildren.
- Nutritional deficiencies can reduce a woman's chance of conceiving and increase the likelihood of complications during pregnancy.
- The proportion of women with nutritional deficiencies is high.
- Nutritional testing and supplementation of women at risk is simple.

off, rather than changes in the overall DNA sequence itself.[8] This results in a change in phenotype rather than genotype, but one which can be inherited by subsequent generations.

The epigenetic changes cause tissue 'remodelling' that results in reduced tissue growth and/or functional capacity, as shown in the Figure.[3] As a consequence, organs such as the pancreas may have reduced capacity to compensate for the age-related degeneration of tissues, and this leads to decreased tissue function and hormone production (e.g. insulin) over time.

Similarly, epigenetic changes due to adverse environmental factors such as smoking can be transmitted through the father's sperm, although that topic is not dealt with in this article.[9]

Clinical consequences of nutritional deficiencies in pregnancy

The placenta is the primary determinant of nutrition to the baby; fetal growth is mainly determined by how effectively the placenta supplies nutrients from the mother. Maternal nutrition, particularly her intake of vitamin D and folate, influences the development of the placenta and its blood supply. A woman's nutritional deficit or excess can alter the size of the placenta in relation to the size of the baby, with irreversible consequences for the baby's developing organs.[10]

A study of children conceived during the Dutch famine in 1944 to 1945, when the Nazi forces blockaded food supplies into Holland, has shown that nutritional deprivation at different stages of pregnancy results in different diseases being more prevalent in adulthood.[11] This is presumably as a consequence of which organ system was developing most at that time.[10] Women who experienced famine in the first trimester of their pregnancies had babies who were heavier at birth than normal. These babies then had greater risks as adults

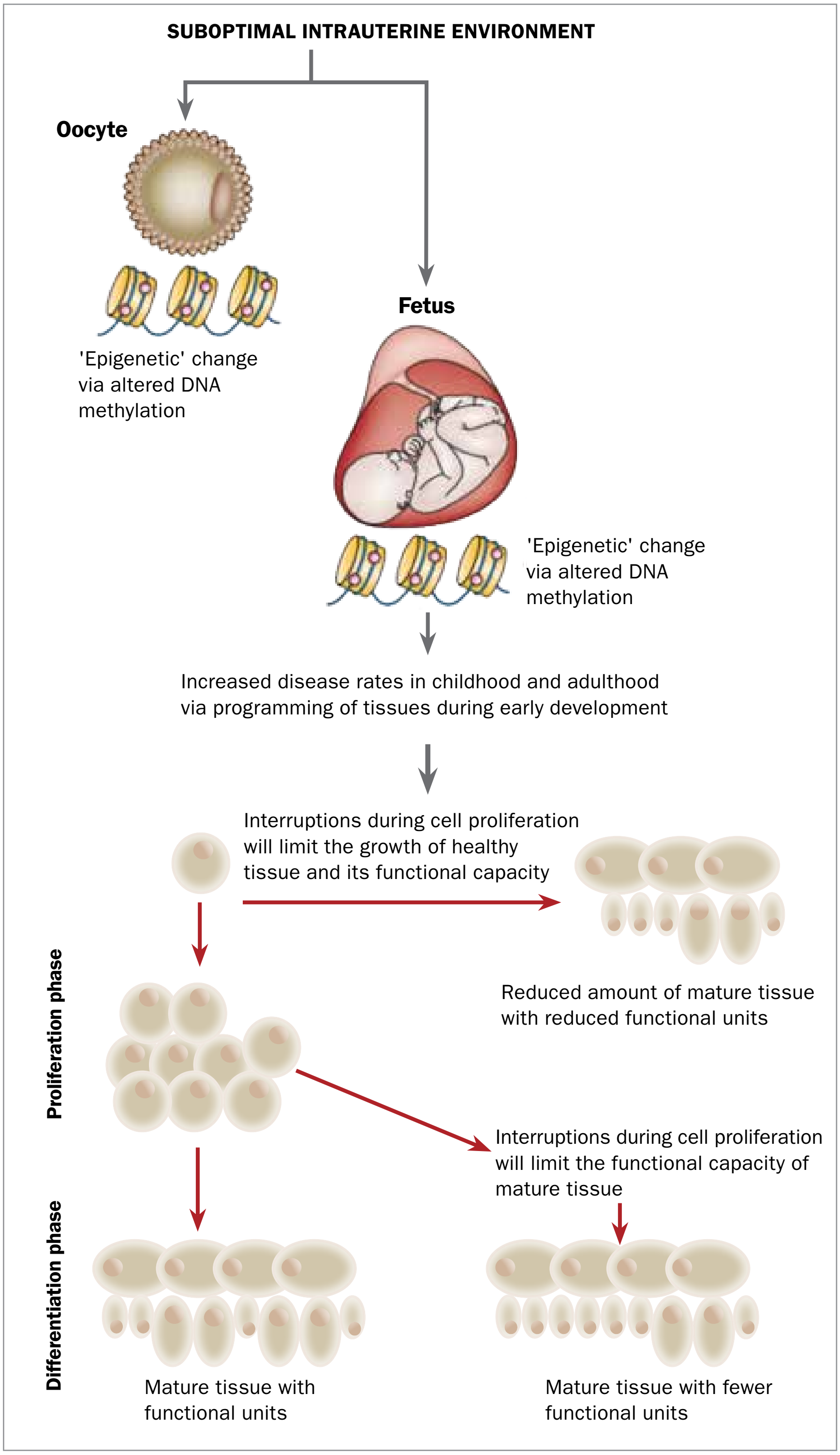

Figure. Tissue changes and remodelling that occurs if environmental factors, including less than optimal nutrition, affect the proliferation of different cells of different organs during development in utero.[3]

of developing heart disease, increased levels of circulating lipids and blood clotting factors, and obesity compared with those not exposed to the famine.[3,11] Babies of women exposed to famine in the second trimester were more likely to develop impaired renal function as adults. In utero exposure to famine in the third trimester was associated with an increased risk of glucose intolerance and type 2 diabetes in later life.

Important vitamins and minerals to assess in pregnancy

Iodine, vitamin D, folate, vitamin B12 and iron are important for maternal health and the development of the baby, as well as for the later health of the unborn baby. These vitamins and minerals are therefore the most important to assess during pregnancy. Table 1 shows the National Health and Medical Research Council (NHMRC) recommendations of nutrient levels for pregnant women in Australia, nutritional sources of these vitamins and minerals and the women most likely to be at risk of deficiencies during pregnancy.[2,12]

Nutritional deficiencies of these vitamins and minerals can reduce a woman's chance of conceiving.[13,14] These deficiencies can also increase the likelihood of women developing complications during pregnancy, as well as increasing the risk of disease during childhood and adulthood (Table 1).[15-17]

A study of 7486 women in Australia across all pregnancy categories found that a significant number of women had nutrient levels below the nationally recommended levels of intake.[18] At the author's clinic, 65% of all new female patients presenting for fertility assessment and treatment (n = 7368 in the past five years) have nutritional deficiencies that would impact on fertility and the short- and long-term health of the child (Table 2).[19] Patients are advised to correct these deficiencies as the first step in their treatment program.

Ideally, a healthy balanced diet would negate the need for mineral and vitamin supplementation during pregnancy.

TABLE 1. NHMRC RECOMMENDATIONS OF NUTRIENT LEVELS FOR PREGNANT WOMEN IN AUSTRALIA[17]

Nutrient	Recommended levels for Australian women	Recommended daily supplementation	Dietary sources	At-risk women/pregnancies
Iodine	150 μg/day	150 μg	Dairy products (2 to 3 serves per day) Eggs (1 to 2 serves per week) Seafood (1 to 2 serves per week)	All pregnant women, particularly those • with a low dietary iodine intake • who smoke • who consume alcohol
Vitamin D	75 nmol/L	1000 to 4000 IU	Seafood (2 to 3 serves per week) Eggs (1 to 2 serves per week) Mushrooms exposed to sunlight (3 to 4 mushrooms per day)	• Women with dark skin • Women with a body mass index of >30 kg/m^2 • Women who wear sunscreen on a regular basis • Women who do not expose their skin to sunlight • Women with medical conditions or taking medications that affect vitamin D metabolism and storage • Younger women
Folate and vitamin B12 (low-risk deficiency)	Red blood cell folate: 300 to 1500 nmol/L Vitamin B12: 300 to 740 pmol/L	Folic acid: 0.4 to 0.5 mg Vitamin B12: 125 to 2000 μg	Vegetables (green leafy) Red meat Nuts and legumes	• Women in lower socioeconomic groups • Indigenous women • Women in rural areas • Younger women • Multiparous women • Women with a body mass index of >30 kg/m^2
Folate and vitamin B12 (high-risk deficiency)	Red blood cell folate: 300 to 1500 nmol/L Vitamin B12: 300 to 740 pmol/L	Folic acid: 5 mg Vitamin B12: 2.6 μg	Vegetables (green leafy) Red meat Nuts and legumes	• Women with a reproductive or family history of neural tube defects • Women who have had a pregnancy affected by neural tube defect • Women taking antiepileptic medication • Women diagnosed with diabetes • Women with a body mass index of >30 kg/m^2 • Women at risk of folate deficiency, e.g. *MTHFR* gene mutation • Women who are strict vegans can be low in vitamin B12
Iron	Haemoglobin: >110 g/L Ferritin: >12 μg/L	27 to 45 mg	Vegetables (green leafy) Red meat Foods high in vitamin C to assist in iron absorption	• Women who are vegetarians • Multiparous women • Women with a short pregnancy interval • Women with severe morning sickness • Women who consume a poor diet

Abbreviation: MTHFR = methylenetetrahydrofolate reductase.

However, the developing baby places extra nutritional demands on the mother and many studies have shown a high proportion of pregnant women will require supplementation. It is important that any woman who requires supplementation during pregnancy does not stop after the first trimester as has been traditional in the past.

Iodine

Iodine deficiency during pregnancy is the leading preventable cause of intellectual impairment in children around the world. Iodine is a key component of the thyroid hormones that are crucial for brain development, particularly during gestation and early life.[15] During pregnancy the thyroid gland produces 50% more of the thyroid

TABLE 2. IMPACT OF NUTRITIONAL DEFICIENCIES ON FERTILITY, PREGNANCY OUTCOMES AND LONG-TERM HEALTH IN A POPULATION OF WOMEN AT FERTILITY FIRST CLINIC, SYDNEY

	Iodine deficiency	Vitamin D deficiency	Folate and vitamin B12 deficiency and/or raised homocysteine levels	Iron deficiency
Proportion of new patients affected (n = 7368)	57%	45%	19%	3%
Cause of infertility	Can be a contributing factor	Yes	Yes	Yes
Cause of long-term adverse health effects for children and adults	Yes – irreversible reduction in IQ of up to 13 points, and increased risk of birth defects and autism	Yes – increased risk of rickets, multiple sclerosis and schizophrenia	Yes – increased risk of neural tube defects, asthma, autism and depression	Yes – increased risk of anaemia when born, and reduced IQ and behavioural development
Increased miscarriage rate	Yes	Yes	Yes	N/A
Pregnancy complications increased	Yes	Yes	Yes	Yes – if deficiency is significant
Gestational hypertension	Yes	Yes	Yes	N/A
Placental abruption	N/A	N/A	Yes	N/A
Intrauterine growth restriction	N/A	Yes	Yes	N/A
Preterm birth	N/A	Yes	Yes	Yes – if deficiency is significant
Low birth weight	Yes	Yes	Yes	Yes – if deficiency is significant
Stillbirth	Yes	N/A	Yes	Yes – if deficiency is significant

Abbreviation: IQ = intelligence quotient; N/A = not available.

hormones than usual, so a woman's iodine intake must be increased to accommodate that. The most serious outcome of iodine deficiency during pregnancy is cretinism, characterised by severe mental retardation and physical deformities. Meta-analyses have shown that milder forms of iodine deficiency result in an average 10 to 13.5 point reduction in intelligence quotient (IQ).[5,20] Unfortunately, adequate iodine intake later in childhood cannot reverse the neurocognitive damage caused by even mild maternal iodine deficiency in pregnancy.[21]

In the past, most dietary iodine came from dairy foods such as milk and cheese and the use of iodised salt in cooking and at the table. However, people today are adding less salt to their food and/or replacing iodised salt with rock or sea salt, which contain negligible amounts of iodine. The increasing use of manufactured foods, for which iodised salt is not required in Australia, is also a factor. Mandatory use of iodised salt in bread commenced in 2009 but many women eat very little bread now.[22] Eggs and seafood are other sources of dietary iodine.

The NHMRC recommends supplementation of 150 μg/day of iodine to ensure that all pregnant women obtain adequate iodine intake.[12] Women should not take kelp (seaweed) supplements or kelp-based products because they may contain varying levels of iodine and may be contaminated with heavy metals such as mercury.

Vitamin D

More than 60% of women in the reproductive age group are now considered to be vitamin D deficient. This is attributed to changing lifestyle factors, including increased use of sunscreens for skin protection, increased time spent indoors at both work and home, and increasing maternal obesity. In the author's clinic, more than 50% of women presenting for fertility treatment have mild to severe vitamin D deficiency.

During pregnancy, the baby's concentration of serum 25-hydroxy vitamin D directly reflects that of the mother. Vitamin D deficiency can result in the development of rickets in the first year of life and an increased risk of developing multiple sclerosis and schizophrenia in later life.[23] In Australia, a child born in Tasmania has a seven times greater risk of developing multiple sclerosis than a child born in Queensland as a consequence of lower maternal sun exposure during pregnancy.[23]

Food sources of vitamin D are limited, so sunshine exposure or vitamin D supplementation are the best options during pregnancy. Supplementation with 2000 to 4000 IU/day of oral cholecalciferol is sufficient, depending on serum levels.[24] However, recent research has shown that mushrooms exposed to sunlight for a few hours can also produce vitamin D (which is not destroyed by cooking) and three to four mushrooms a day provide adequate vitamin D supplementation.[25-27]

Folate and vitamin B12

Low folate levels during pregnancy are well known to be associated with an increased risk of neural tube defects in the baby. Less well known is the association with increased risk of autism spectrum disorders.[28] Up to 40% reduction in the risk of autism spectrum disorders has been reported when folic acid supplements are taken preconceptionally or during the first two months of pregnancy.[29-31] A multicentre Australian study has suggested that maternal folate and vitamin B12 intake during pregnancy may reduce the risk of childhood brain tumours, the second most common childhood tumour, particularly in women who drink alcohol while pregnant.[32,33]

Low levels of folate during pregnancy are either due to deficient intake or genetic variants of the methylenetetrahydrofolate reductase (*MTHFR*) gene, which also lead to elevated homocysteine concentrations.

Iron

Iron deficiency is associated with pregnancy complications and may have a negative effect on the intelligence and behavioural development of a child. However, routine iron supplementation is less necessary in Australia compared with some other countries. The NHMRC recommends that women in Australia should not be routinely offered iron supplements but rather be monitored for the development of anaemia and treated as required (Table 1).[12] The NHMRC also recommends that women be made aware that foods rich in vitamin C improve iron absorption, whereas tea and to a lesser extent coffee decrease iron absorption.

If iron supplements are required, gastrointestinal side effects are reduced if they are taken with a meal rather than on an empty stomach. However, the amount of iron absorbed is reduced when taken this way.[34]

Maternal obesity

It is estimated that half the women in the reproductive age group are now overweight or obese.[35] Increased food consumption and the metabolic changes associated with increased weight make it more difficult for a woman to get pregnant and stay pregnant and can cause the epigenetic changes that lead to long-term disease in the child. The dietary patterns, such as high consumption of processed foods, that have led to a woman's increased weight can also be associated with the nutritional deficiencies.

If a woman is encouraged to lose weight it is very important, particularly if rapid weight loss occurs, that conception is delayed. Otherwise, the developing baby can be programmed for birth into a perceived 'famine' environment with increased risks for a 'Barker hypothesis' outcome in adult life. The delay should be one to two years after bariatric surgery and three to six months after consumption of a very low kilojoule diet.

Conclusion

It is now widely accepted that a child's exposure to a suboptimal environment during pregnancy has a long-term effect on the health of that child in adulthood. Type 2 diabetes, cardiovascular disease, some mental health conditions and some forms of cancer have all been reported as being more common after inadequate nutrition or inadequate levels of some vitamins and minerals during pregnancy. Which organs are affected most depends on the stage of pregnancy at which the nutritional deprivation occurs. Excess food consumption and maternal obesity can also have adverse long-lasting effects on the baby's health. Even more concerning, it has been shown that these detrimental consequences can also be transmitted, via epigenetic changes, to the next generation – that is, the woman's grandchildren.

Monitoring and correcting for good nutrition in pregnancy is important to reduce the risks of developing these conditions and increase the health of Australians into the future. MT

Acknowledgement

Dr Clark is grateful for the assistance of Dr Nicola Stark BScMedSci, MScMed(RH&HG), PhD, Senior Embryologist and Research Scientist at Fertility First in the preparation of this paper.

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A list of references is included in the website version (www.medicinetoday.com.au) of this article.

COMPETING INTERESTS: None.

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