

South Australian Paediatric Clinical Guidelines

Vitamin & mineral supplementation in Pregnancy

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The Royal Australian and New Zealand College of Obstetricians and Gynaecologists College Statement C-Obs 25 2008 has been used to inform this practice guideline

Introduction

- > Although, in the general population, a healthy balanced diet should largely obviate the need for vitamin and mineral supplementation, pregnancy and lactation create extra nutritional demands that, for some individuals, may make supplementation advisable (RANZCOG 2008)

Vitamins

Folate

- > Folic acid deficiency is associated with megaloblastic anaemia and birth defects (especially neural tube defects)
- > All women should take preconceptual folic acid (500 micrograms [0.5 mg] folate daily) while attempting pregnancy to reduce the risk of neural tube defects
- > As 50 % of pregnancies are unplanned, when contraception is not being used, a dose of 500 micrograms daily should be taken
- > From September 2009, all bread (except organic bread) is fortified with folate; however women are still advised to take supplements

Food sources of folate

- > Fortified cereals
- > Soy
- > White beans
- > Chickpeas
- > Lentils
- > Yeast extract (e.g. vegemite)
- > Green leafy vegetables
- > Sunflower seeds

Indications for measurement

- > Routine measurement of red cell folate (RCF) is not required unless:
 - > Increased MCV (> 100 fL but may be of the order of 120 fL)
 - > Poor diet
 - > Prolonged hyperemesis / poor oral intake in pregnancy
 - > GIT pathology (celiac disease, Crohn's disease, gastric bypass etc)

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Dosage

- > The standard dose recommended for all women is 500 micrograms (0.5 mg) folate daily for one month before conception and during the first three months of pregnancy
- > Where there is an increased risk of folate deficiency and NTD (see list below), advise 5 mg daily dose throughout the pregnancy. Women with an increased risk include:
 - > Women taking an anticonvulsant medication which is liver enzyme inducing (for further information, please see PPG, Epilepsy and pregnancy management)
 - > Pre-existing diabetes mellitus
 - > Multiple pregnancy
 - > Haemolytic anaemia
 - > Family history of NTD or women with a child with NTD
 - > Women with known MTHFR mutation

Vitamin B¹²

- > Vitamin B₁₂ is essential for infant neurodevelopment. Undiagnosed maternal vitamin B₁₂ deficiency may result in irreversible neurological damage to the breastfed infant. Although maternal vitamin B₁₂ deficiency is uncommon, the majority of women with deficient B₁₂ levels are asymptomatic (Ministry of Health 2006)

Food sources of vitamin B¹²

- > Red meat
- > Oysters, clams
- > Trout
- > Salmon
- > Chicken / poultry
- > Eggs
- > Milk

Indications for measurement

- > Routine measurement of vitamin B₁₂ is not required; however vitamin B₁₂ screening is indicated if any of the following exist:
 - > Increased MCV (> 100 fL but may be of the order of 120 fL)
 - > Vegetarian or vegan diet (long term)
 - > GIT pathology (coeliac disease, Crohn's disease, gastric banding / bypass etc)
 - > Family history of vitamin B₁₂ deficiency or pernicious anaemia
 - > Falling platelet count (< 100 x 10⁹ / L)
- > Except in strict vegans, true vitamin B₁₂ deficiency is unlikely despite the increased requirements of pregnancy due to the extent of vitamin B₁₂ stores

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Diagnosis

- > Measurement of serum vitamin B₁₂ is the standard test
- > Serum B₁₂ levels should be interpreted in relation to clinical symptoms, because the test measures total, not metabolically active vitamin B₁₂ and there is a large 'grey zone' between the normal and abnormal levels

Treatment

- > Oral replacement of vitamin B₁₂ is the treatment of choice in most cases, including pernicious anaemia
- > Women who have significant neurological symptoms, however, should receive initial intramuscular injections of 1000 micrograms vitamin B₁₂, followed by oral doses of 1000 - 2000 micrograms per day. The duration of treatment depends on the cause of deficiency
- > Hydroxocobalamin produces higher and more prolonged serum levels of vitamin B₁₂ than cyanocobalamin when given by intramuscular injection in the same dosage. Hydroxocobalamin disperses more slowly from the site of injection than cyanocobalamin, is more strongly bound to plasma proteins and accumulates in the liver to a greater extent
- > In strict vegans 1000 micrograms of vitamin B₁₂ by intramuscular injection may be given at 3 monthly intervals to prevent the development of vitamin B₁₂ deficiency
 - > Alternatively, oral vitamin B₁₂ (cyanocobalamin) 250 - 500 micrograms daily may be given for the duration of the pregnancy

Composite B-group vitamins

- > Studies have found that vitamin B₆ reduces the severity of nausea but not vomiting in the first trimester. Vitamin B₆ was also associated with a decrease in the risk of dental decay in pregnant women. However, studies failed to show a positive effect on other obstetric and neonatal outcomes, and the risk of adverse events was difficult to assess. Consequently, there is no strong evidence to support routine vitamin B₆ supplementation in pregnancy (RCOG 2011)
- > Similarly, due to minimal data on the benefits and harms of supplementation with vitamin B₁, B₂, B₃, B₅, B₇, and B₁₂, there is no strong evidence to support supplementation with any of these vitamins during pregnancy (RCOG 2011)
- > Hyperhomocysteinaemia is the most common thrombophilia with approximately 1.5 % of the population being homozygous for the MTHFR mutation and 25 % heterozygous. The thrombophilic tendency is minimised by an adequacy of folate, riboflavin, B₆ and B₁₂. In the absence of any screening for this condition, some clinicians advise that all women should ensure an adequate intake of these vitamins (RANZCOG 2008)

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Vitamin D

- > Studies of pregnant women in Australia and New Zealand have found a disturbing frequency of vitamin D deficiency. Women at increased risk include those with reduced sunlight skin exposure (e.g. veiled women, those who use sunscreen on a regular basis and dark-skinned women).
- > Vitamin D deficiency is known to be an important risk factor for the development of osteoporosis in later life.
- > For further information on screening for vitamin D deficiency and vitamin D supplementation, refer to PPG Vitamin D deficiency (antenatal screening of at risk mothers and prevention of deficiency in their infants)

Vitamin K

- > Vitamin K is a fat soluble vitamin crucial to the production of many proteins involved in the coagulation process
- > Vitamin K may be administered in late pregnancy to women with proven cholestasis of pregnancy, due to reduced vitamin K absorption (see PPG, Obstetric cholestasis). It is also recommended from 36 weeks gestation for women on some anticonvulsant medication (liver enzyme-inducing), although recent evidence casts doubt on the need for this (see PPG, Epilepsy and pregnancy management)
- > Vitamin K supplements have also been suggested for women at risk of having low levels in the first trimester e.g. on liver enzyme-inducing antiepileptics

Food sources of vitamin K

- > Spinach
- > Brussel sprouts
- > Green salad vegetables
- > Broccoli
- > Plant oils (e.g. canola oil)

Other vitamin supplementation

- > There is little evidence to support routine supplementation of the fat soluble vitamins A & E, and excessive quantities of fat soluble vitamins may be harmful
- > Pregnant women should be informed that vitamin A supplementation (intake above 10,000 units of Retinol) may cause birth defects and therefore should be avoided. Pregnant women should be informed that liver and liver products may contain high levels of vitamin A, and therefore consumption of these products should also be avoided (NICE 2010)
- > Betacarotene, the vegetable form of vitamin A is not associated with an increased rate of birth defects
- > Vitamin C is an essential water soluble vitamin found widely in fruits and vegetables. A low intake of vitamin C may be associated with complications of pregnancy such as preeclampsia, anaemia and intrauterine growth restriction. However, there is not enough evidence to determine if supplementation with vitamin C (either alone or in combination with other vitamins e.g. vitamin E) is beneficial in pregnancy (Rumbold & Crowther 2005)

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Minerals

Iron

- > The iron demands of pregnancy are particularly pronounced due to the expanded red cell volume, blood loss around the time of delivery and the demands of the developing fetus and placenta. Iron supplementation will generally be recommended for women at particular risk of iron deficiency. This includes vegetarians and women with a multiple pregnancy. All women should have their haemoglobin level checked at the first antenatal visit and again at approximately 28 weeks' gestation and any anaemia investigated and treated. Routine iron supplementation is not recommended in every pregnancy.
- > For further information on iron deficiency anaemia see PPG, anaemia in pregnancy

Calcium

- > Providing there is no vitamin D deficiency, a balanced diet will have sufficient calcium for pregnancy and lactation. If the woman avoids dairy in her usual diet, and does not consume alternative high calcium food (e.g. calcium enriched soya milk), calcium supplementation is advisable (RDI 1200 mg / day)
- > A systematic review found calcium supplementation almost halved the risk of pre-eclampsia, reduced the risk of preterm birth and occurrence of the composite outcome 'death or serious morbidity'. The effect was greatest for women with low baseline calcium intake. There were no other clear benefits, or harms (Hofmeyer et al. 2010)

Food sources of calcium

- > Primarily dairy foods, although bony fish, legumes and fortified foods are also sources of calcium
 - > Milk (reduced / low fat)
 - > Cheese (only hard yellow cheese during pregnancy)
 - > Yoghurt (reduced / low fat)
 - > Calcium fortified soy products, almonds
 - > some legumes e.g. white beans, baked beans
 - > white bait, sardines, the little crunchy bones in canned salmon that are edible

Iodine

- > Iodine is a trace element essential for synthesis of the thyroid hormones; triiodothyronine (T3) and thyroxine (T4). These hormones play a vital role in the early growth and development stages of most organs, in particular the brain.
- > Iodine plays a critical role in neuropsychological development of the fetus throughout gestation and in the first two years of life (NHMRC 2009)
- > The National Iodine Nutrition Survey (2006) has identified that the Australian population is mildly iodine deficient. Iodine uptake by the thyroid is higher in pregnancy and the iodine reserve in the thyroid can decrease to approximately 40 % of preconception levels

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- > From September 2009, Food Standards Australia New Zealand (FSANZ) mandated the fortification of bread with iodised salt (with the exception of organic bread), however this will not provide sufficient dietary iodine intake for pregnant and lactating women (NHMRC 2009)
- > The National Health and Medical Research Council (NHMRC) recommends that all women who are pregnant, breastfeeding or considering pregnancy, take an iodine supplement of 150 micrograms each day (NHMRC 2010)
 - > However, randomised controlled trials to support routine supplementation and dosage are lacking

Food sources of iodine

- > Bread (except organic bread), eggs, meat, dairy products, seafood and seaweed*
- > The amount of iodine varies greatly based on factors such as changes in season and processing practices (NHMRC 2010)
- > The NHMRC (2010) advises that women who are pregnant, breastfeeding or planning pregnancy should not take kelp (seaweed) supplements or kelp based products because they contain varying levels of iodine and may be contaminated with heavy metals such as mercury
- > The availability of iodine in plant foods varies considerably depending on the availability of iodine in the soil in which the plants are grown

Dosage and administration

- > Iodine supplement 150 micrograms daily
- > Clinicians may recommend a multivitamin that contains the recommended daily intake of iodine
- > Women with pre-existing thyroid conditions should be referred for medical review before taking a supplement

Other minerals

- > There is little evidence to support routine supplementation of other minerals in pregnancy such as magnesium, fluoride, zinc or rare minerals (RANZCOG 2008)

Prostaglandin precursor supplementation

Fish (marine) oil

- > Population studies have shown that higher intakes of marine foods during pregnancy are associated with longer gestations, higher infant birth weights and a low incidence of pre-eclampsia. It is suggested that the fatty acids of marine foods may be the underlying cause of these associations (Makrides et al. 2006)
- > Marine oils are a rich source of the n-3 long chain polyunsaturated fatty acids (LCPUFA) eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)
- > These fatty acids are precursors to the 3-series prostaglandins and have been shown to modulate inflammatory and vascular effects
- > Most commercially available fish oils have been processed in a way that strips magnesium along with other heavy metal. Some preparations are marked as mercury tested

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- > However, there is not enough evidence to support the routine use of fish oil supplements during pregnancy to prevent preeclampsia and preterm birth and to increase birth weight (Makrides et al. 2006)

Evening primrose oil

- > There are no studies that assess evening primrose oil consumption in pregnancy (Makrides et al. 2006)
- > > The use of evening primrose oil in pregnancy is of questionable value. It contains that fatty acid gamma-linolenic acid (GLA) which is a metabolic precursor of arachidonic acid (AA). It is AA that would have the biological activity as a precursor to the 2-series prostaglandins. Robust information regarding the conversion rate of GLA to AA does not exist

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Abbreviations

AA	arachidonic acid
DHA	docosahexaenoic acid
e.g.	For example
EPA	eicosapentaenoic acid
et al.	And others
etc	Et cetera
fL	Femtolitre(s)
FSANZ	Food Standards Australia New Zealand
GIT	Gastrointestinal tract
GLA	gamma-linolenic acid
LCPUFA	long chain polyunsaturated fatty acids
MCV	Mean corpuscular volume
mg	Milligram(s)
mL	Millilitre(s)
NHMRC	National Health and Medical Research Council
NTD	Neural tube defects
RANZCOG	Royal Australian and New Zealand College of Obstetricians and Gynaecologists
RCF	Red Cell Folate
RDI	Recommended dietary intake
T3	Triiodothyronine
T4	Thyroxine
Vit	Vitamin

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