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PRENATAL NUTRITION

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Impact of Maternal Nutrition on Fetal Development

Expectant mothers have increased nutritional needs. Meeting these needs helps ensure sufficient maternal gestational weight gain, which is related to appropriate fetal weight gain. Adequate levels of both ensure the best pregnancy outcomes. Supplementation with micronutrients (zinc, calcium, magnesium, vitamin A, folate, iron, vitamin C and iodide) improves nutritional status during pregnancy. Prenatal nutrition is thought to exert key effects on fetal development as well as, later in life, on disease susceptibility, and even central nervous system function. It is equally important that mothers continue to ensure appropriate nutritional intake while they are breast-feeding. Information on this population is also addressed in this article.

Nutrition is perhaps the most influential non-genetic factor in fetal development.[1] Maternal body composition, nutritional stores, diet, and ability to deliver nutrients through the placenta determines nutrient availability for the fetus.[1] Prenatal nutrition influences fetal growth, normal development of physiological function[2] and gestational weight gain (GWG). GWG is a complex progression that supports fetal growth and development. Maternal physiology and metabolism as well as placental metabolism also influence GWG. Maternal homeostasis changes can alter placental structure and function, influencing fetal growth.[3]

During the 1960s, high rates of infant mortality, disability and mental retardation in the US were realized to be a function of low birth weight. By 1970, the National Academy of Sciences reported that restricted weight gain for pregnant women was associated with increased risk of low-birth-weight infants. In 1990, the Institute of Medicine (IOM) established weight-gain ranges for pregnant women, which were extensively adopted in the US to improve infant birth weights.[4]

In 2009, the IOM and Health Canada revised their guidelines to reflect the relevance of maternal body composition before conception. More women of childbearing age are severely obese, making maternal health concerns as well as infant birth size both relevant for maternal weight. Additionally, women become pregnant at an older age and more commonly enter pregnancy with chronic conditions (e.g. hypertension or diabetes), increasing the risk of pregnancy complications.[3] (Table 1)

During pregnancy, maternal weight gain affects fetal growth.[4] Small neonate size at birth is attributable to poor growth and shortened gestation, and the most unfavourable outcomes occur in the most immature infants. Low rate of pregnancy weight gain is associated with increased risk of preterm birth[4], whereas low second- or third-trimester weight gain has been shown to be associated with spontaneous preterm delivery risk.[5]

Two factors related to maternal nutrition show a positive connection with infant birth weight: maternal prepregnancy body mass index (BMI, defined as weight/height^2) and weight gain during pregnancy. Women with low prepregnancy BMI are at increased risk for preterm birth and intrauterine growth retardation (IUGR). However, women with low prepregnancy BMI are at increased risk of preterm delivery only if they fail to gain adequate weight.[5]

Appropriate GWG within target ranges can help improve maternal and fetal health.[6] Inadequate GWG has been associated with low birth weight (<2500 g) and gaining more weight than recommended with high birth weight (>4000 g) and postpartum weight retention. Data from the Canadian Maternity Experiences Survey 2006[7] show that pregnant women who gain less weight than recommended are likely to give birth to infants weighing less than 2500 g vs. normal-weight (2500 to <4000 g), full-term infants (44% vs. 24%, respectively).[8]

Many Canadian women gain well above the recommended weight gain ranges as well.[6] Based on the same 2006 survey[7], 55% of overweight, 41% of normal weight and 26% of underweight women fall into this group. A majority of women (58%) who gain more weight than recommended deliver infants weighing 4000 g or more.[8]

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Nutrition During Pregnancy and Breast-Feeding

A complete balanced diet to support healthy fetal growth and development is required for the nutritional demands of pregnancy.

Maternal nutrition determines birth weight outcomes as well.[6] Low-protein diets are associated with adverse outcomes and should be avoided.

Breast-feeding women also have increased nutritional needs. Energy requirements are actually higher during breast-feeding vs. pregnancy.

To ensure proper nutrition, pregnant and breast-feeding women should eat a healthy diet, including multiple nutritious foods, and consume the recommended number of servings from the four major food groups of the Canadian Food Guide.

Energy Requirements During Pregnancy and Breast-Feeding

During pregnancy, energy demands increase during the second and third trimesters. Women with normal body weight at onset of pregnancy need approximately an additional 340 kilocalories/day during the second trimester and 452 kilocalories/day during the third trimester. These extra kilocalories help support adequate GWG as well as fetal growth and development (Table 2).[9]

Breast-feeding women also have increased energy requirements, which are dependent on the amount of milk a woman produces and how quickly she loses weight gained during pregnancy. During the first year of breast-feeding, women need approximately 350 to 400 additional kilocalories/day.[9]

Micronutrient Intake Related to Pregnancy Outcomes

In developing countries, where micronutrient deficiencies are routine, increasing micronutrient intake (by supplementation or increased micronutrient-rich food consumption) is associated with significantly increased birth size and IUGR reduction in women with low prepregnancy BMI.

One study in Chile[10] showed that in underweight women, infant birth weight was significantly higher in subjects receiving energy (milk powder) with micronutrient supplement than those receiving energy supplementation alone. The percentage of IUGR infants was significantly lower in subjects receiving energy plus micronutrient supplement. Later analysis suggested that the risk for IUGR in subjects receiving micronutrient plus energy supplement was significantly lower than for subjects receiving energy supplementation alone.[5]

Ramakrishnan et al.[11] investigated the relationship between micronutrient status and pregnancy outcome. They drew the following conclusions: evidence (typically from developed countries) shows better pregnancy outcomes from zinc, calcium and magnesium supplementation; vitamin A supplementation may be connected to increased birth weight and decreased maternal mortality; even though prevention of neural tube defects with folate supplementation and increased hemoglobin with iron supplementation are well substantiated, evidence showing whether folic acid and iron supplementation decrease other unfavourable pregnancy outcomes is limited; vitamin C deficiency may play a role in preterm delivery etiology; and severe maternal iodine deficiencies cause mental retardation and cretinism, but evidence is lacking for cases of marginal iron deficiency.

Balanced nutritional supplementation may be advantageous. Supplementation can provide for increased nutritional needs for kilocalories, protein, vitamins and minerals. In cases where the health care professional suspects suboptimal nutritional intake, it is important to provide advice to help this patient. In addition to advice on healthy eating, the use of a nutritional supplement containing kilocalories, protein and other essential nutrients can help ensure that nutritional needs are met and reduce associated health risks.

Table 1. Recommended Weight Gain in Singleton Pregnancies

The following table shows the rate of total weight gain recommended for singleton pregnancies based on a woman's prepregnancy BMI

Prepregnancy BMI	Mean[a] rate of weight gain in the 2nd and 3rd trimester		Recommended[b] total weight gain	
	kg/week	lb/week	kg	lbs
BMI <18.5 (underweight)	0.5	1.0	12.5–18	28–40
BMI 18.5–24.9 (normal weight)	0.4	1.0	11.5–16	25–35
BMI 25.0–29.9 (overweight)	0.3	0.6	7–11.5	15–25
BMI ≥30.0[c] (obese)	0.2	0.5	5–9	11–20

[a] Rounded values.
[b] Calculations for the recommended weight gain range assume a gain of 0.5 to 2 kg (1.1 to 4.4 lbs.) in the first trimester.
[c] A lower weight gain may be advised for women with a BMI of 35 or greater, based on clinical judgement and a thorough assessment of the risks and benefits to mother and child.

Adapted from Health Canada. Canadian Gestational Weight Gain Recommendations, January 2010. Available at: http://www.hc-sc.gc.ca/fn-an/nutrition/prenatal/qa-gest-gros-qr-eng.php. Accessed: November 12, 2010.

Disease Susceptibility

Accumulated evidence documents that prenatal factors predispose individuals to disease later in life. Negative environmental factors—including suboptimal maternal nutrition—may play a major role. The relationship between low birth weight and disease is an imbalance between fetal demand and maternal supply. The imbalance results in metabolic and endocrine changes, which assist the fetus in the short term by slowing growth and increasing available fuel, but lead to long-term greater risk of metabolic syndrome and cardiovascular disease.[1]

During the mid-1980s, epidemiologist Dr. David Barker and colleagues observed that coronary heart disease rates showed a profound correlation with infant mortality rates earlier in the century.[12] Dr. Barker's observations postulated that low-birth-weight infants might be at increased coronary artery disease risk later in life. Using the National Health Service Register in Britain, Dr. Barker's studies uncovered strong inverse associations between birth (or infant) weights and coronary artery disease deaths. Coronary heart disease death rates declined nearly twofold between those at the lower and upper strata of the weight distribution. Substudies have shown that trends in coronary heart

Table 2. **Estimated Energy Requirements by Life Stage Group**

Estimated energy requirements (Kcals/day)	Pregnant[a]	Breast-feeding
19–30 years (1900 non-pregnant)	1st trimester 1900 + 0	0–6 months' postpartum 1900 + 330
	2nd trimester 1900 + 340	7–12 months' postpartum 1900 + 400
	3rd trimester 1900 + 452	
31–50 years (1800 non-pregnant)	1st trimester 1800 + 0	0–6 months' postpartum 1800 + 330
	2nd trimester 1800 + 340	7–12 months' postpartum 1800 + 400
	3rd trimester 1800 + 452	

[a]The values are approximate. They were calculated for sedentary females using Canadian median heights and weights derived from the median normal BMI.

Adapted from Health Canada. Prenatal Nutrition, May 2010. Available at: http://www.hc-sc.gc.ca/fn-an/pubs/nutrition/guide-prenatal-eng.php. Accessed: November 12, 2010.

disease with birth weight parallel trends in biological risk factors of coronary heart disease, namely, hypertension, type 2 diabetes and metabolic syndrome.[13-15]

The effect of under-nutrition has also been demonstrated in a study of men and women, aged 50 years, who were babies born after the Dutch winter famine of 1944.[16] Follow-up data show that under-nutrition at any stage of gestation is linked with reduced glucose tolerance and insulin resistance in offspring.[14] Transgenerational influences in birth weights were also observed. Women who had been severely undernourished during the first trimester gave birth to (on average) normal birth weight infants, but those infants gave birth to smaller offspring in the following generation.[17]

Key Effects on Early Brain Development

Nutrition is a primary non-genetic factor affecting brain development. The effects of under-nutrition (and malnutrition) on the developing brain are long-lasting, leading to permanent deficits in learning and behaviour.

A predominant cause of hindered fetal brain development is maternal malnutrition, including placental insufficiency. Protein seems to be the most critical element for development of neurological function, and prenatal protein deficiency can impact brain development at critical junctures.[2]

Both nutrition and environment affect the ability and performance of the central nervous system. Maturation of the central nervous system is not linear. A decisive period of development represents a once-only window of opportunity that can neither be repeated nor reversed. The entire developmental period of the brain has subcritical periods, each of which may be disrupted and thereby affect the maturation and organization of the brain.[2]

Nutritional deprivation seems associated with varying degrees of intellectual disturbance such as cognitive impairments and attention deficit disorders. Failure of the fetus to develop optimally because of nutritional deprivation does not lead to immediate brain dysfunction. Rather, consequences can remain hidden, or manifest only as predispositions until a time when the system is stressed by unusual circumstances.[2]

Nutrition is perhaps the most influential non-genetic factor in fetal development. A complete balanced diet to support both maternal and fetal health is necessary throughout pregnancy and breast-feeding. With so much at risk during fetal development, it is crucial to maximize the health of mother and fetus through adequate nutrition. At times, supplementation may be helpful to promote the health of both. Proper nutrition provides the optimal environment for development in all aspects.

Weaning Infants from Breast Milk

The Canadian Paediatric Society (CPS) describes infant weaning as a natural but complex process during development, involving nutritional, immunological, biochemical and psychological components. Natural weaning occurs when an infant accepts nutrition from sources other than breast milk.

Common reasons given by mothers (or cited by mothers) for mother-led (planned) weaning include: insufficient breast milk, infant growth concerns, painful feedings or breast infection, mother's return to work, new pregnancy, wanting the other parent to administer feedings or infant teeth emerging.[18]

Another study documented results of self-reported data from 1323 mothers who rated the importance of 32 reasons for discontinuing breast-feeding.[19] Regardless of infants' age, the perception that infants were not satisfied by breast milk alone was cited consistently as one of the top 3 reasons mothers decided to discontinue breast-feeding (Table 3).

The CPS recommends screening and educating breast-feeding mothers on how to wean infants off breast milk. The CPS guidelines include the following recommendations[20]:

- Partial weaning can be a good choice by mothers who would like to continue with some breast-feeding after they return to work or school.
- Implement weaning gradually.
- Substitute a cup or bottle (pumped breast milk, formula, cow's milk) for the least favourite feeding. Avoid whole cow milk until infants are at least 9 (preferably 12) months old. Give no more than 720 mL/day. Limit fruit juices to 60 to 120 mL/day.
- Introduce solid foods at 6 months of age. The infant is developmentally ready and greatly benefits from the oral stimulation at this time.
  - Introduce iron-containing foods by 4 to 6 months old, as iron stores accumulated from birth are diminishing by this time. Delaying introduction of solid foods beyond 6 months of age can make the infant more susceptible to iron-deficiency anemia and other micronutrient deficiencies.
  - Offer solid foods at developmentally appropriate times.

Dietary Nucleotide Supplementation

Nucleotides are essential RNA and DNA components in all cells and are said to be important for maturation of the gastrointestinal tract, development of neonatal immune function and growth, and reduced

Table 3. **Reasons for Discontinuing Breast-Feeding as Self-Reported Data from Mothers**

Infant Age	Reasons for Planned Weaning
Within 1st month or between 1st and 2nd months	- Infant's difficulties sucking and latching - Breast milk alone not satisfying infant - Insufficient milk
3 to 8 months old	- Perceived lack of infant satisfaction by breast milk alone (~49% of mothers) - Concern about having enough milk (43% to 54% of mothers) - Infant lost interest in nursing or began to wean themselves
9 months old	- Infant lost interest in nursing or began to wean themselves - Infant not satisfied with breast milk alone - Infant lost interest in nursing - Infant started to bite

Adapted from Canadian Paediatric Society. *Pediatrics* 2008;122:S69-S76.

incidence of infant diarrhea. Dietary nucleotide supplementation in infants may be necessary to enhance nucleotide synthesis.[21]

Nucleotides are available in human milk at concentrations of 72 mg/L, whereas cow's milk contains only about 10 mg/L. Infant formula supplemented with nucleotide levels similar to those of human milk may facilitate maturation and immunoregulatory shifts in some lymphocyte populations consistent with those seen in human milk-fed infants.[22] While evidence supports formula supplementation at levels of at least 33 mg/L, formula supplemented with 72 mg/L shows greater effects.[23]

Additionally, better antibody responses to immunization (*Haemophilus influenzae*, diphtheria toxin and oral polio [OPV] vaccines) have been associated with nucleotide-supplemented infant formula.[23] In 48-week-old infants, serum immunoglobulin A (IgA) concentrations increased in infants fed formula fortified with 72 mg/L nucleotides vs. iron-fortified formula. At subsequent measurements, serum IgA concentrations were higher in infants fed nucleotide-fortified formula.[24]

Study outcomes indicate that infants who received a nucleotide-supplemented formula at 72 mg/L had significantly higher OPV type 1 neutralizing antibody (PV-VN1) responses than infants who received the same formula without nucleotides. PV-VN1 responses in infants fed human milk were not different from infants who were fed the nucleotide-fortified formula.[25] At 12 months of age, normal growth was observed in both groups, and growth was comparable to that of infants fed human milk.

Several studies have reported reduced incidence of diarrhea in infants given dietary nucleotides. In one study, infants fed nucleotide-fortified formula demonstrated a 25% lower risk of diarrhea vs. controls.[24] Other studies report that nucleotide-fortified formulas are associated with fewer episodes of diarrhea over controls.[23,26] An infant recovering from diarrhea could benefit from dietary nucleotides to replace intestinal mucosal cells as well as to help maintain normal growth.[21] ☐

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