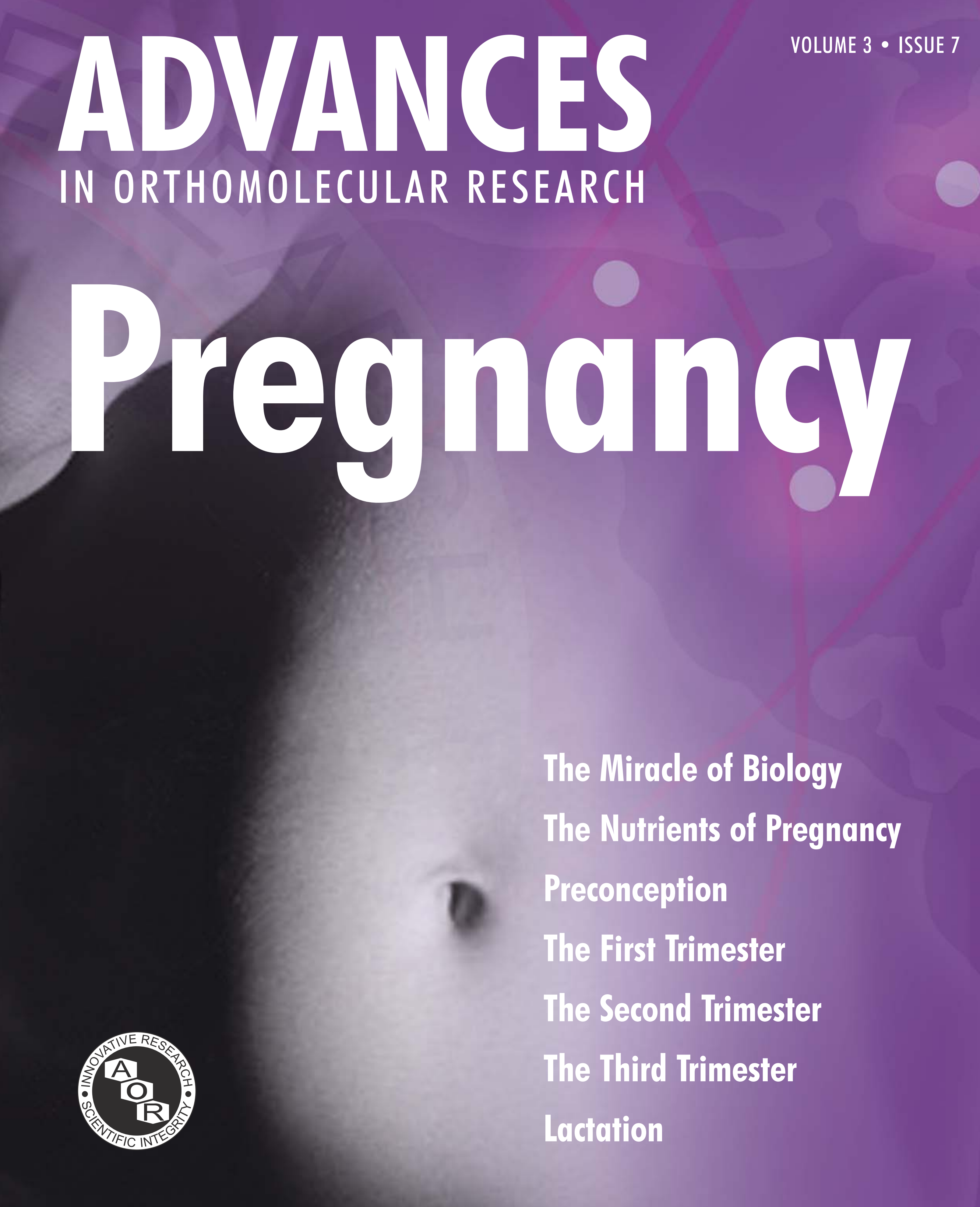

VOLUME 3 • ISSUE 7

ADVANCES
IN ORTHOMOLECULAR RESEARCH

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INNOVATIVE RESEARCH
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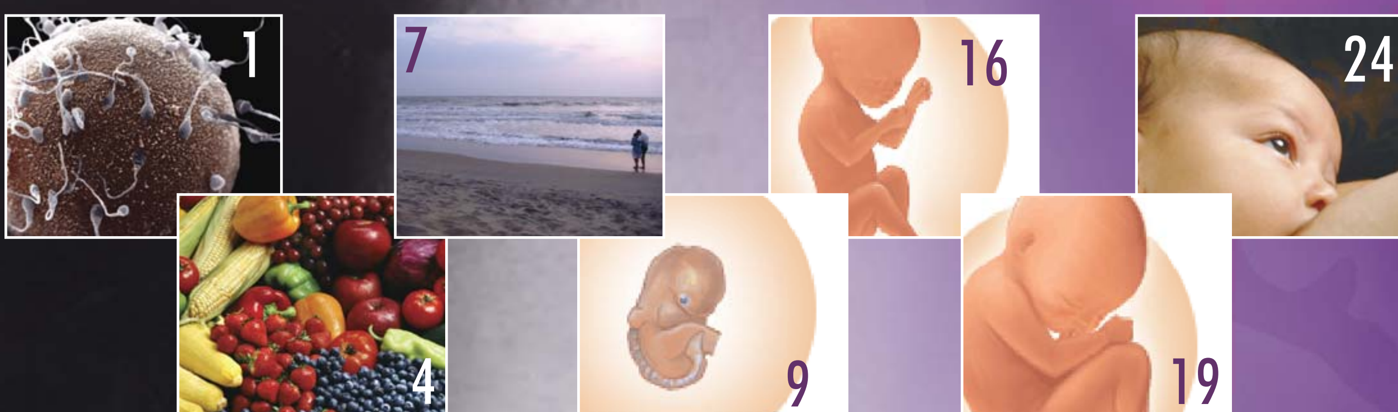

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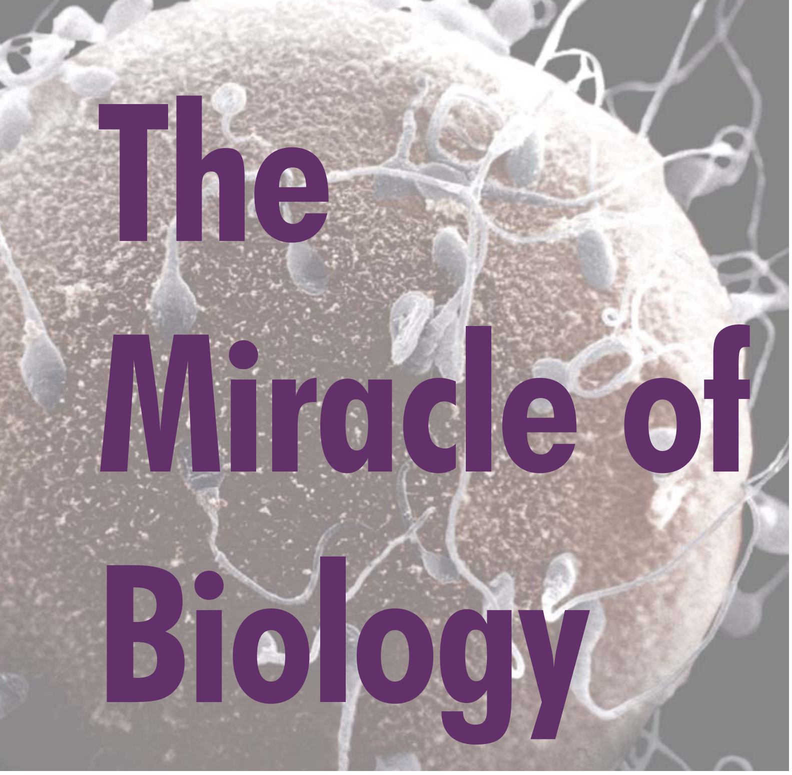


The Miracle of Biology

Most of us want and eventually will have children. After all, they are the miracle of life – a miracle that is not without its challenges. Pregnancy and delivery are sometimes difficult – in the United States, roughly one third of all pregnancies are unsuccessful. In the developing world, childbirth remains a leading cause of mortality for mother and child. It takes 14 to 17 hours to deliver the average first-born child – enough time to fly from Vancouver to Sydney. Yet the birth canal is only eight centimetres long. It is not surprising that women around the world request help during labor. Evolution has let us down, stuck between the compromise of a pelvis that must bear the weight of an upright stature and an opening through which babies are delivered; the middle ground has led to the difficulties women experience today. Nonetheless, most unassisted pregnancies are successful, but conception, pregnancy and fetal development remain delicate biological processes.

Although biology can be unkind, there is reason to rejoice – all biological processes, no matter where they may occur or how vital they may be, can be influenced, corrected or improved. After all, that is the premise behind modern science and as our understanding grows so do our possibilities. Simple interventions have lead to incredible improvements, which is why pregnancy warrants healthy lifestyle choices and adequate nutrition. Folate supplementation and fortification has significantly reduced the rates of neural tube defects and saved countless lives and spared families from the agony of congenital malformations. Iron status is commonly inadequate in pregnancy with deficiencies estimated to affect 20% of women in developed countries and 56% of mothers-to-be in the developing world.[1] According to the World Health Organization, iodine deficiency has left 20 million people worldwide with brain damage. The benefits go far beyond the prevention of deficiencies; one study has even shown that DHA supplementation during pregnancy improved IQ in four-year-old children. Unfortunately, the potential of optimal nutrition during pregnancy is still largely unknown but it is estimated that stem cells (generic cell that can specialize to form the various tissues of the body) undergo 47 cellular divisions from conception to adulthood but only five take place after birth. Without question, adequate or inadequate nutrition during pregnancy have lifelong consequences.

The beauty of pregnancy is universal; a parental joy forever remembered. It is truly miraculous that the union of two people can lead to the creation of a new being, in which traits of both parents are found. From one cell, a person grows, developing a unique physique and personality. Exceptional individuals that deepen our understanding, improve our circumstances, and leave a heritage of new values and possibilities. Individuals that have written the Declaration of Independence, sailed across oceans, built the pyramids of Giza, walked in space, developed modern medicine and grown into loving parents that would risk life and limb for their children.

There are also biological miracles; the achievements seen during gestation often initially seem unsurpassable and the growth of the fetus is at times unbelievable. Pregnancy is the truest testament to our capacity to adapt. The complexity of the tasks at hand combined with the high success rate relay the greatness of pregnancy. For 9 months, body systems meant to maintain homeostasis for one adjust to the growing needs of another. Maternal nutritional reserves ensure adequate fetal supply. From sperm and ovum an average six pound and 18 inches long baby is born. Within nine months, the fetus must develop and growth to the point where it is capable of leaving the mother and maintaining it's own life support systems. During this period, the uterus increases in weight by more than 20 times, blood volume increases by roughly 30% and respiration increases by approximately 20% - all to accommodate fetal needs. Gestation is a period during which the fetus is vulnerable and fetal needs take precedent over maternal requirements. For instance, if the mother's calcium intake is insufficient, calcium will be mobilized from the maternal skeleton to ensure adequate fetal accretion. A successful pregnancy depends on adequate nutriture. Regulatory agencies such as the World Health Organization, the US Institute of Health and Health Canada all make recommendations for safe and effective dietary goals during pregnancy. Recommended Daily Intakes and Upper Tolerable Levels have been established for most vitamins, minerals and some of the other important nutrients throughout pregnancy and lactation.

Nutrition during Pregnancy and Fetal Programming

Nutritional deficiencies are common during pregnancy. Studies looking at nutritional markers demonstrate that inadequate nutriture is common and that the risk of insufficiencies increases as gestation progresses.[2] Even in women taking prenatal supplement formulas, deficiencies commonly develop.[3]

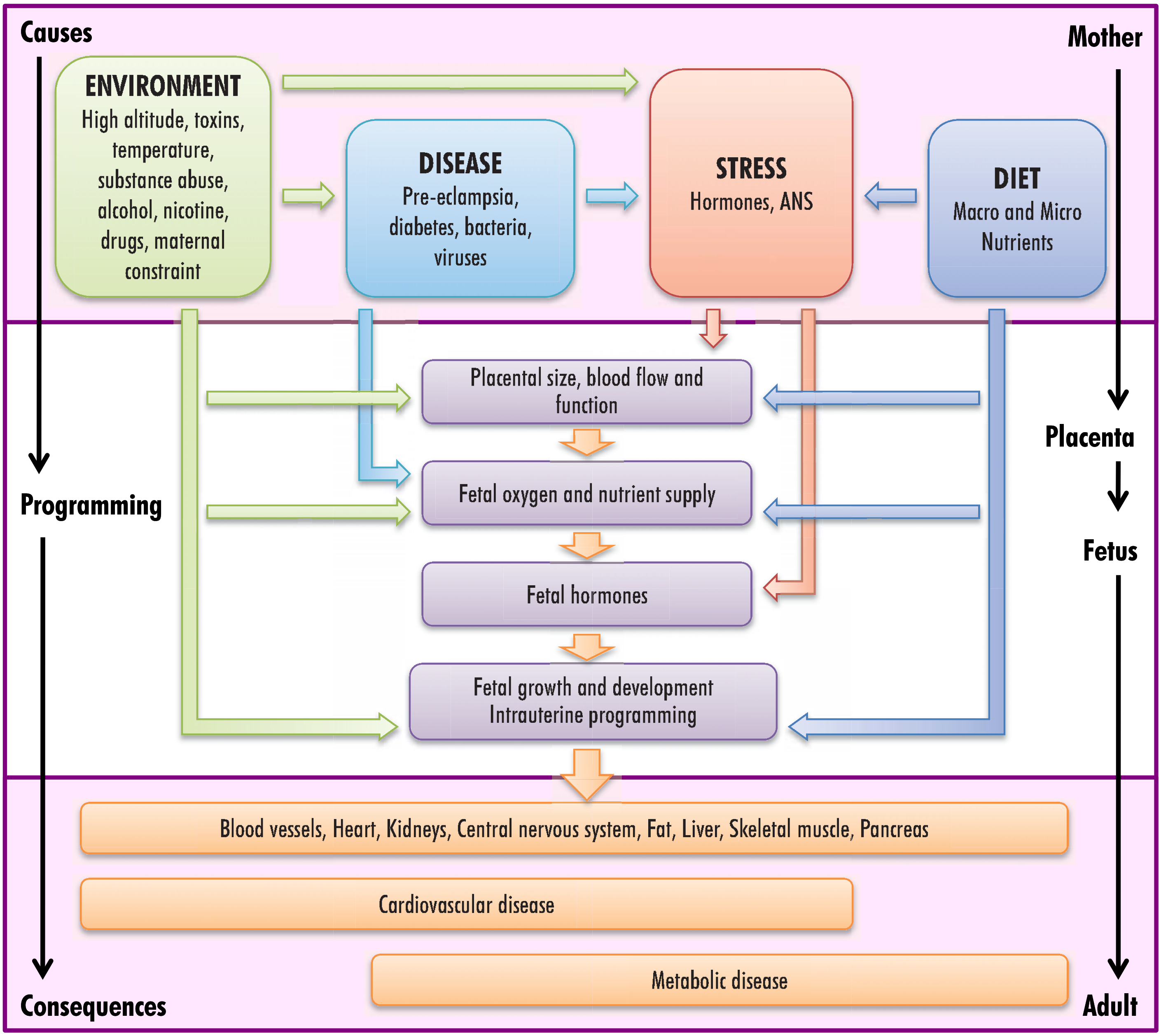


Figure 1. Fetal programming, its causes and consequences. Source: Adapted from Abigail, 2006

The fetus is dependant on the maternal supply of nutrients. During gestation, the maternal dietary intake is of utmost importance to support growth during the prenatal period. Epidemiological studies demonstrated that inadequate growth throughout gestation influences long-term health in the infant,[4] leading to increases in Type 2 diabetes, hypertension and several other diseases later in life (see figure 1 and Box 1).[5] This appears to be an adaptive mechanism. For example, in the case of Type 2 diabetes, if nutriture is insufficient during pregnancy, the fetus adapts by down regulating the expression of enzymes required for glucose metabolism, effectively reducing the need for glucose and increasing the chances of survival in a nutrient-poor environment. The process is known as fetal programming.[6] Problems occur when glucose metabolism has been compromised in a high caloric environment. In such cases, fetal programming is counterproductive as an inability to use glucose effectively increases the risk of developing Type 2 diabetes later on in life. Although fetal programming remains poorly understood, the body of evidence pointing towards a link between gestational nutrition and adult health continues to grow.

Box 1. Adult Diseases Associated with Suboptimal Intrauterine Conditions
Source: Abigail (2006)

Physiological System	Disease
Cardiovascular System	Hypertension Coronary Heart Disease Stroke Atherosclerosis Coagulation disorders Pre-eclampsia
Metabolic System	Impaired glucose tolerance Insulin resistance Dyslipidemia Obesity Type 2 diabetes
Reproductive System	Polycystic ovary syndrome Early onset of puberty/menstrual cycles Early menopause
Respiratory System	Chronic obstructive pulmonary disease Asthma
Endocrine System	Hypercortisolism Hypothyroidism
Nervous System	Neurological disorders Schizophrenia Dementia
Skeletal System	Osteoporosis

The Nutrients of Pregnancy

Some nutrients are essential for life. Vitamins, by definition, cannot be produced endogenously but are essential for life and normal metabolism. Similarly, orthomolecules are indispensable for health but may or may not be produced by the body. Minerals, antioxidants, phytonutrients, elements and macronutrients, although not always recognized as indispensable, exert a multitude of essential functions in the human body.

As metabolic requirements increase during pregnancy and lactation, so do nutritional needs. The Dietary Reference Intakes as established by the Food and Nutrition Board of the Institute of Medicine are a testament to increased nutritional requirements during pregnancy. As such, those nutrients have overt advantages throughout pregnancy because they are required for maternal metabolism, but are far more important for the support of normal fetal growth and development. Specific Dietary Recommended Intakes are shown in Tables 1a and 1b.

Clinical Trials and Prenatal Formulas

The benefits of supplementation during gestation have not always been reflected by the applied research.[7] There is a simple explanation: prenatal nutritional support tends to increase birth weight. For example, studies have demonstrated that pantothenic acid, sodium and vitamin E supplementation appear to increase birth weight.[8] Iron, iodine, calcium, folate, vitamin A, and vitamin C maternal intakes also influence offspring size.[9] Therefore, the benefits of supplementation in developing countries may be grossly underestimated simply because larger babies are more difficult to deliver (see figure 2). In countries where medical interventions for pregnancy complications are lacking, nutritional support may cause more difficult deliveries and result in an apparent lack of benefit.

Table 1a. Dietary Reference Intakes (DRIs): Vitamins

Source: Food and Nutrition Board, Institute of Medecine, National Academies

Age (years)	Vit A (μg/d)	Vit C (mg/d)	Vit D (μg/d)	Vit E (mg/d)	Vit K (mg/d)	Thiamin (mg/d)	Riboflavin (mg/d)	Niacin (mg/d)	Vit B6 (mg/d)	Folate (μg/d)	Vit B12 (μg/d)	Vit B5 (mg/d)	Biotin (μg/d)	Choline (mg/d)
Pregnancy														
14-18	750	80	5	15	75	1.4	1.4	18	1.9	600	2.6	6	30	450
19-30	770	85	5	15	90	1.4	1.4	18	1.9	600	2.6	6	30	450
31-50	770	85	5	15	90	1.4	1.4	18	1.9	600	2.6	6	30	450
Lactation														
14-18	1200	115	5	19	75	1.4	1.6	17	2	500	2.8	7	35	550
19-30	1300	120	5	19	90	1.4	1.6	17	2	500	2.8	7	35	550
31-50	1300	120	5	19	90	1.4	1.6	17	2	500	2.8	7	35	550

The situation is not the same in developed countries where medical care is readily available. Prenatal nutrient formulas are not meant to facilitate labour but designed to ensure the short and long term health of both the mother and child.

Birth weight is one of the most important outcome measures of pregnancy; since low birth weight increases the infant's risk of mortality and morbidity.[10] Low birth weight infants, although easier to deliver, are at risk for several complications and have lower rates of survival. In Canada and the United States, no factor is more significant than a low birth weight in predicting infant and fetal mortality (see Table 2).[11]

In addition, there is clear evidence showing that birth weights are also correlated to the incidence of several adult diseases such as diabetes (see Table 3) and

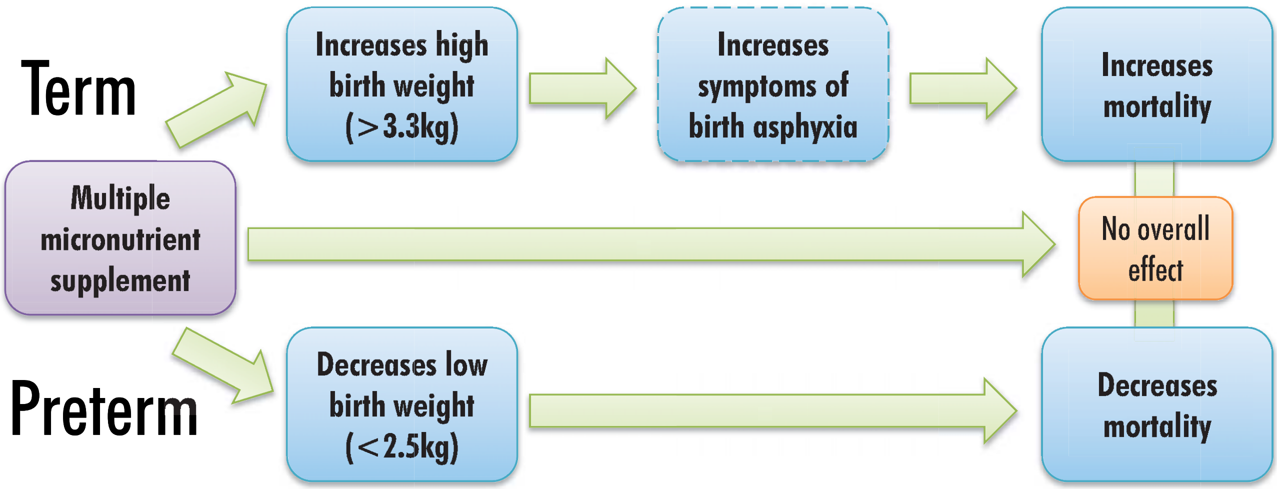


Figure 2. Possible explanation for reported lack of an overall effect of nutrient supplementation on infant mortality. Source: redrawn from Christian (2003).

Table 1b. Dietary Reference Intakes (DRIs): Minerals

Source: Food and Nutrition Board, Institute of Medecine, National Academies

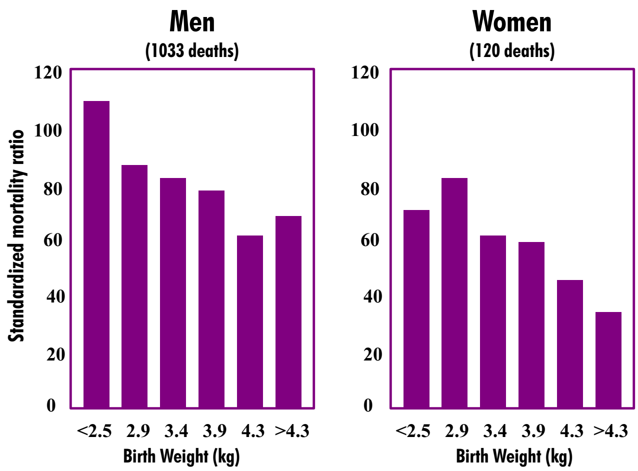
Age (years)	Calcium (mg/d)	Chromium (μg/d)	Copper (μg/d)	Fluoride (mg/d)	Iodine (μg/d)	Iron (mg/d)	Magnesium (mg/d)	Manganese (mg/d)	Zinc (mg/d)	Phosphorus (mg/d)	Selenium (μg/d)	Molybdenum (μg/d)	Potassium (g/d)	Sodium (g/d)
Pregnancy														
14-18	1300	29	1000	3	220	27	400	2	12	1250	60	50	4.7	1.5
19-30	1000	30	1000	3	220	27	350	2	11	700	60	50	4.7	1.5
31-50	1000	30	1000	3	220	27	360	2	11	700	60	50	4.7	1.5
Lactation														
14-18	1300	44	1300	3	290	10	360	2.6	13	1250	70	50	5.1	1.5
19-30	1000	45	1300	3	290	9	310	2.6	12	700	70	50	5.1	1.5
31-50	1000	45	1300	3	290	9	320	2.6	12	700	70	50	5.1	1.5

Table 2. Causes of neonatal deaths in developing countries vs. United States (1999)
Source: Rouse (2003) & CDC

Cause of neonatal death in developing countries	Proportion of all newborn deaths (%)	Cause of neonatal death in US	Proportion of all US newborn deaths (%)
Birth asphyxia	21.1	Low birth weight	23.1
Pneumonia	19.0	Congenital defects	20.8
Neonatal tetanus	14.1	Maternal complications	7.4
Congenital anomalies	11.1	Respiratory distress syndrome	5.6
Birth injuries	10.6	Complications of placenta	5.4
Prematurity	10.3	Sepsis of newborn	3.5
Sepsis and meningitis	7.2	Atelectasis	3.4
Others	5.1	Birth asphyxia	3.1
Diarrhea	1.5	Neonatal hemorrhage	2.6
		Others	25.1
Total	100	Total	100

cardiovascular conditions (see Graphs 1 & 2).[12] Most importantly, studies demonstrate that without prophylaxis, roughly 75% of pregnant women suffer from a deficit of at least one vitamin.[13]

Let us not forget that nutritional supplementation during pregnancy in developing nations remains one of the most cost effective ways to prolong life by preventing pregnancy related mortality. For instance, it is estimated that it would cost between $1.80 and $18 to save one infant through iodine supplementation. This is far less than other already established preventive interventions such as tetanus prevention at a cost of $27 to $115 per child saved.[14]



Graphs 1 & 2. Coronary heart disease death rates, according to birth weight. Source: Redrawn from Godfrey, 2000.

Table 3. Prevalence of type 2 diabetes in 370 men aged 59-70 according to birth weight
Source: Godfrey (2000)

Birth Weight (lbs)	Odds ratio of type 2 diabetes or impaired glucose tolerance
< 5.5	6.6
5.5 – 6.5	4.8
6.5 – 7.5	4.6
7.5 – 8.5	2.6
8.5 – 9.5	1.4
> 9.5	1

Preconception

Although half the pregnancies in the United States are unplanned, preconception can be viewed as a time to build nutritional reserves. This is a particularly opportune time for a healthier lifestyle and better dietary behaviors. Any supplementation should be limited to nutrient intakes that are safe during the first trimester of pregnancy. Indeed, by the time mom knows that she is pregnant; the embryo is likely to be several days, if not weeks, old. The embryo is most sensitive to environmental changes during early pregnancy. Supplementation must therefore be restrained during this period.

Most couples have a strong desire to have children, the latest survey of Australian women reported that 71.4% of women want one or two children and 19.2% wish for three or more children, leaving 9.3% of women not wanting children.[15] Unfortunately, almost a quarter of couples experience fertility issues. Infertility is the inability to conceive after attempting to become pregnant for 12 or more months. Forty to fifty percent of the difficulties are related to women, 30% are related to men, 20 to 30% are combinations of factors affecting both partners, and 15% of infertility is of unknown cause. Female reproductive physiology is far more complex than men's, which makes the preconception period an excellent opportunity to provide nutrients to support female reproductive function. Depending on their age, 7- 28% of women experience reproductive difficulties.[16]

Body weight and body composition influence fertility. For instance, the Frisch hypothesis postulates that menarche will not occur until at least 17% of body weight is fat.[17] Weight variations lead to abnormal reproductive ability in women. Women who over exercise or lose the equivalent of 10 to 15% of their normal body weight tend to become amenorrheic (absence of menstruation). Overweight women are also prone to amenorrhea.[18] It is not surprising that weight influences fertility; the increased metabolic requirements of pregnancy require sufficient energy reserves for successful outcomes. Furthermore, infant birth weights are correlated to survival and birth weights are also correlated to maternal weight at conception.[19] Maternal weight is not only important for conception but also for a successful pregnancy.

The anguish of infertility can be alleviated by several nutrients shown to be beneficial for those who are not able to conceive. Just as appropriate energy stores are necessary for normal reproduction, so are stores for other essential nutrients. Any nutritional inadequacies during this precarious period may preclude new beginnings. Nutritional support was shown to improve fertility in women with reproductive difficulties. In a double-blinded placebo controlled study, 15 women trying unsuccessfully to conceive received dietary supplementation while another 15 women received a placebo. Thirty-three percent of the women receiving the dietary supplement were pregnant within three months while none of the women in the placebo group conceived.[20]

Nutrients with significant benefits related to successful conception include:

Vitamin B12

Vitamin B12 deficiency leads to pernicious anemia, which in turns leads to infertility in men and women. Normal reproductive function returns after supplementation. It appears that a deficiency in vitamin B12 leads to higher homocysteine levels and hypercoaguability, which may lead to fetal loss.[21]

Folate

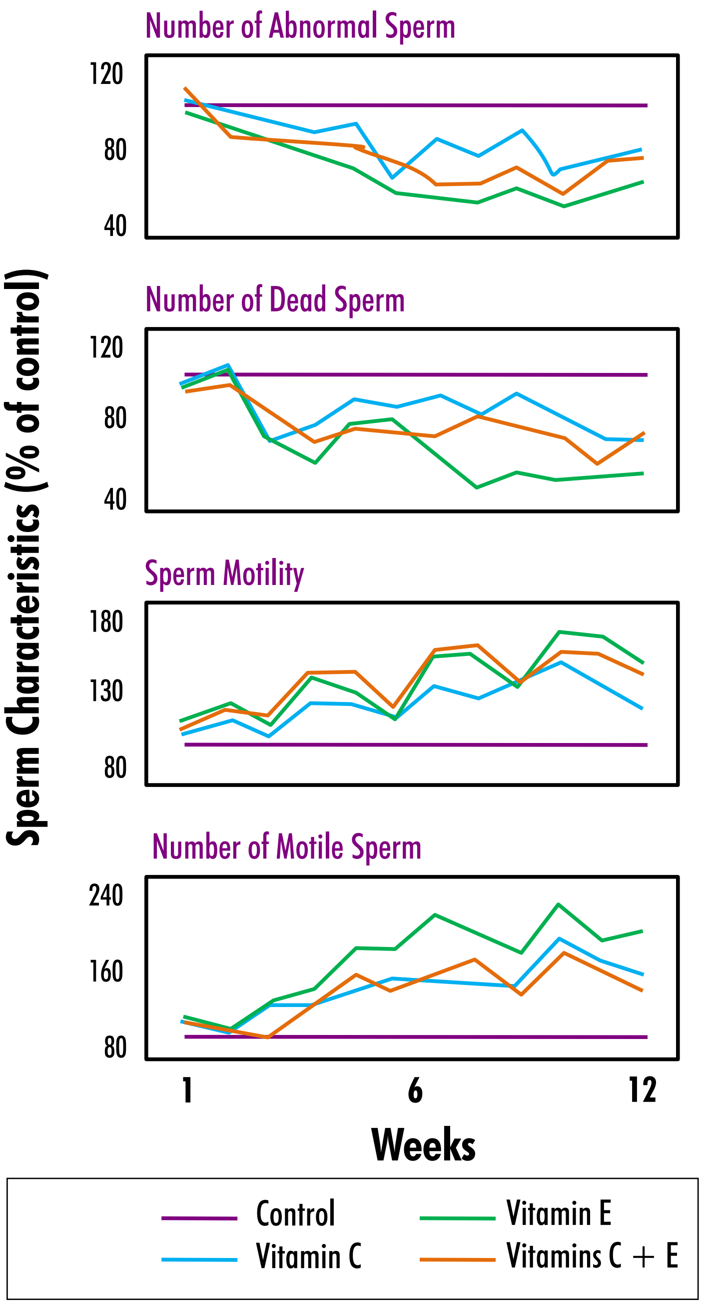
Folate deficiency may be the reason behind some cases of infertility. In case reports, three infertile celiac disease patients showing signs of folate deficiency all became pregnant after folate supplementation.[22] In animal models, diets deficient in folic acid reduce fetal implantation in the uterus by 50% while increasing pregnancy loss,[23] congenital defects and growth retardation.[24]

Selenium

In males, selenium deficiency is linked to decreased testosterone biosynthesis. In animals, deficiencies lead to abnormal and immobile sperm.[25] The role of selenium in female reproduction may be related to the enzyme glutathione peroxidase, a powerful antioxidant that protects cellular membranes from oxidation.[26]

Zinc

Second essential trace element in importance after iron, zinc is needed for fetal development and dietary needs during pregnancy are heightened. Zinc is required for spermatogenesis and ovogenesis, which explains why 40% of infertile women in a French study were deficient in zinc.[27]



Graphs 3-6. Changes in total abnormal and dead sperm, sperm motility index and total motile sperm during treatment of rabbits with Vitamin C, Vitamin E and their combination.

Oxidative Stress and Reproduction

In health, antioxidants and pro-oxidants should always remain balanced in our body. If this delicate equilibrium is upset, serious consequences may be experienced especially in couples wanting to conceive. Increases in reactive oxygen species may affect both the fertilization and implantation of eggs.[28-29] Oxidative stress may also be related to pathologies which themselves lead to reproductive difficulties and female reproductive tract pathologies such as endometriosis and pre-eclampsia.[30-31] Although more research is needed to uncover the extent and the implications of excessive oxidative stress or insufficient antioxidant defenses in cases of infertility, increasing evidence suggests that free radicals may be at fault in female reproductive difficulties.

Antioxidants, such as vitamin C and vitamin E, may be important nutrients for the treatment and prevention of infertility. In the human body, vitamin C concentrations are highest in the pituitary, adrenals, testes and ovaries.[32] In males, vitamin C deficiency has been linked to low sperm counts and reduced sperm motility. Not surprisingly, vitamin C and vitamin E supplementation improves sperm quality (see Graphs 3 to 6).[33] In women, high concentrations of vitamin C in the ovaries may support rapid follicular growth, collagen synthesis and the development of the corpus luteum (necessary for fetal implantation).[34] Large amounts of vitamin C are required during pregnancy, and it was suggested in 1973 that all pregnant women should be supplementing their diet with at least 500 mg of vitamin C.[35] Current recommended daily intakes for vitamin C are 80 mg per day with the upper tolerable level set at 2000 mg.

The First Trimester

The first 13 weeks of pregnancy

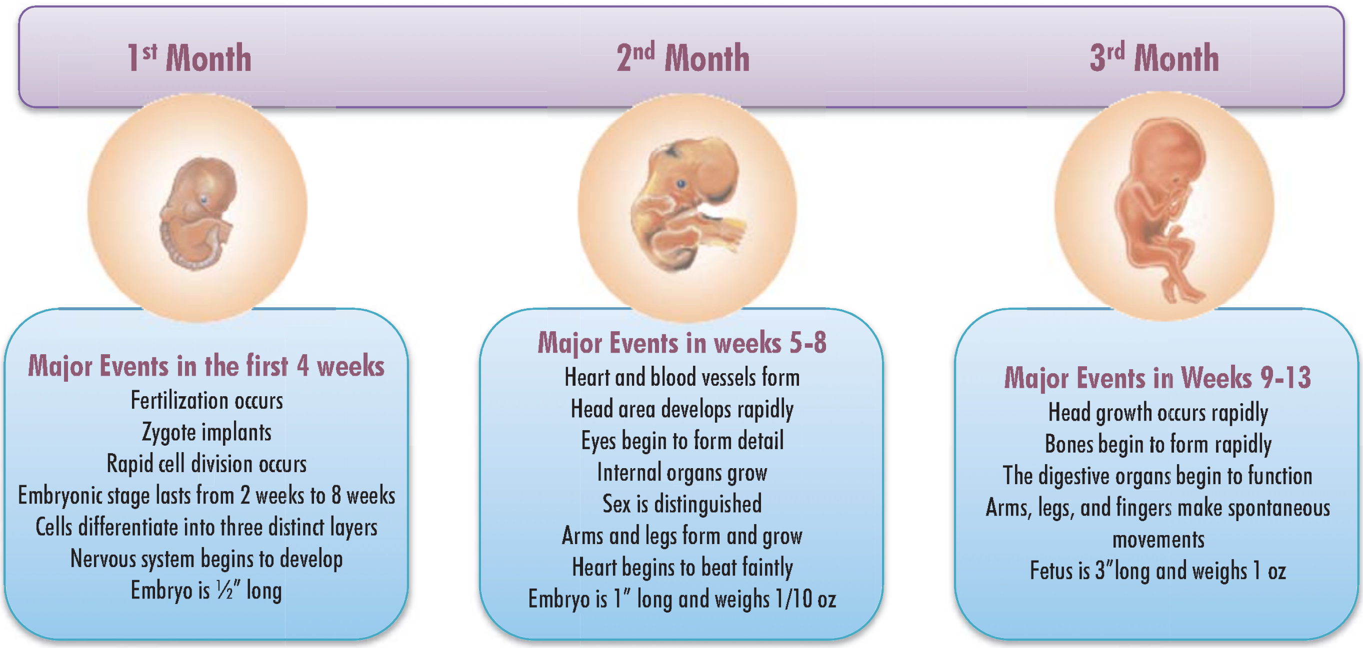


Figure 3. Fetal development in the 1st trimester

Developmental Milestones

Everything begins with conception. Every month, during the middle of the menstrual cycle, a mature follicle is swept into one of the uterine tubes (the passage connecting the ovaries to the uterus) where it awaits the arrival of sperm. The ovum is the female reproductive cell and it matures in follicles found in the ovaries that respond to hormonal influences. The release of the mature ovum from the ovaries is brought about by a surge in luteinizing hormone. The ovum contains half the genetic material found in human cells, the other half comes from the sperm. Fertilization occurs in the uterine tubes. The sperm travels from the vagina through the cervical canal; into the uterus and finally up the uterine tube, where the egg is found. The sperm then enters the egg, and the genetic material from the sperm and the ovum are combined and develop into a morula containing several cells. Conception must occur within 24 hours of ovulation.

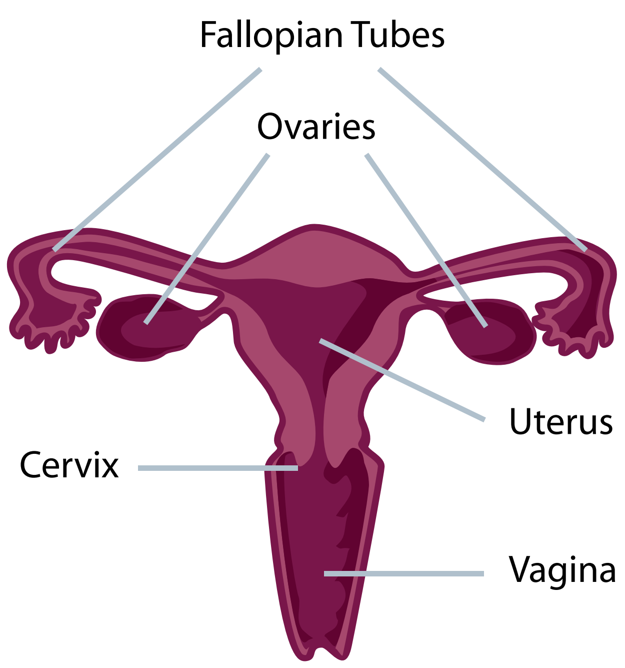


Figure 4. The female reproductive system.

The morula enters the uterus where it implants after several days and becomes a developing embryo. The embryo produces hormones that halt the menstrual cycle, permitting continued growth. The placenta, the organ that unites the mother and the child, supports embryonic growth by allowing exchanges between maternal and fetal blood. By the end of the fourth week of gestation, the heart, digestive system and spinal cord begin to develop. By the 22nd day of pregnancy, the embryonic heart begins to beat. By week 7 the embryo is the size of a raspberry. By the end of the 8th week, the eyes, the face and the teeth are developing. By two months the fetus is constantly moving and webbed fingers are clearly perceptible.

By the end of the first trimester, most of the organs are formed; arms, legs, toes and fingers are shaped and the eyes are almost completely developed.

Growing Pains

Baby is growing fast, and this rapid growth together with the hormonal changes required to support it are causing havoc for mom. During the first trimester, it is common for women to experience nausea and vomiting, dizzy spells, constipation, fatigue, heartburn and food cravings; most of which are related to hormonal changes. Raging hormones are also responsible for the dreaded emotional instability, mood swings and impatient tendencies.

The Challenges of the First Trimester

The fist trimester is a precarious period. It is the time where the fetus is the most susceptible to changes and disruptions to its environment. Nutritional deficiencies but also exposure to toxins and teratogens (a substance that may cause birth defects) will be most harmful during this period of rapid growth and organogenesis (the formation of organs).

Other possible problems include miscarriages. Eighty percent of miscarriages occur in the first trimester and affect 15% to 20% of all pregnancies.[36] Miscarriages may be related to maternal or fetal causes. Genetic anomalies affecting the fetus are the main cause of spontaneous abortions or miscarriages.

The first trimester is also likely to leave mom feeling queasy. Indeed, a Canadian study has reported nausea in 74% of pregnant participants. Roughly 80% of women will begin to feel nauseated between the fourth and seventh week post catamenia. In all but ten percent of women, the condition resolves by the 20th week and usually remains benign. In one of every 200 pregnancies, vomiting becomes serious causing electrolyte imbalances and significant weight loss, posing a health risk to the mother and child.

A Note about Morning Sickness

There are those who adhere to the view that morning sickness is a protective mechanism and that the safest nourishment for the fetus comes from the breaking down of maternal tissues. According to this hypothesis, morning sickness occurs during organogenesis, a time when the fetus is most fragile.

Although interesting, this view remains problematic. Indeed, it does not explain why some women remain nauseous throughout pregnancy, a phenomenon that is clearly detrimental. There is also the impasse of the vast array of clinical evidence pointing out common maternal nutritional deficiencies during pregnancy leading to unfavorable growth and negative outcomes for the fetus.

Furthermore, although the embryo is most vulnerable to contaminants during organ development, it is also most vulnerable to inadequate nutrition at this time and several clinical trials have demonstrated that supplementation during early development can reduce the incidence of congenital malformations, folate being a famous example.

Favorable Nutrients during the First Trimester

Vitamin D for Adult Disease Prevention

The role of vitamin D for bone health has been well studied. Unfortunately, other roles for the vitamin are poorly understood and the exact requirements have not been identified. There is, however, growing evidence that vitamin D plays a significant role in health and disease prevention that extend far beyond the skeletal system. Better vitamin D nutriture during pregnancy has recently been linked to a reduced risk of immune disorders such as multiple sclerosis,[37] rheumatoid arthritis and chronic disease susceptibility later in life.[38] It has been hypothesized that low prenatal vitamin D levels lead to fetal imprinting, increasing the risk for cancer, schizophrenia, insulin dependent diabetes, immune disorders and other adult health outcomes.[39] Epidemiological evidence linking multiple sclerosis and vitamin D deficiency includes an increased prevalence of the disease at higher latitudes, an association with spring births (lower maternal sun exposure in second and third trimester) and promising results in animal models of the condition.[40] Vitamin D is synthesized through the skin's exposure to UV light. Higher latitudes and spring births would lead to lower sun exposure during gestation and would reduce the vitamin D available during fetal development.

Vitamin D supplementation during pregnancy may be required given the prevalence (reported at 12%) of hypovitaminosis D in women of childbearing age in the United States. Furthermore, pregnant women have higher requirements for vitamin D due to fetal requirements and a tendency to reduce outdoor activity and sun exposure.[41] Vitamin D supplementation during pregnancy was recommended in 1991, but received little attention.[42]

Biotin deficiency is Teratogenic

Clinical studies have documented that biotin deficiency may be common during pregnancy.[43] Indeed, urinary excretion of 3-hydroxyisovaleric acid, shown to be elevated in early pregnancy, is a sign of decreased activity of a biotin dependent enzyme.[44] Although vitamin deficits may occur during pregnancy, biotin status may be more worrisome. Animal studies have demonstrated that biotin deficiency is teratogenic. Ninety four percent of pups born to biotin deficient dogs were malformed despite the fact that there were no observable signs indicating an abnormal pregnancy.[45] Similarly, all offspring of mice rendered deficient in biotin suffered from cleft palate and limb shortening.[46] It appears that biotin is required for cellular proliferation as demonstrated by the biotin uptake in replicating lymphocytes, which is 300-700% that of non-proliferating cells.[47] Biotin requirements increase during fetal development - a period of intense cellular growth. Therefore, a marginal deficiency could cause abnormal cellular replication and congenital malformations due to anomalies in fatty acid metabolism (biotin is a cofactor in fatty acid production and oxidation).

Too Much Vitamin A must be Avoided

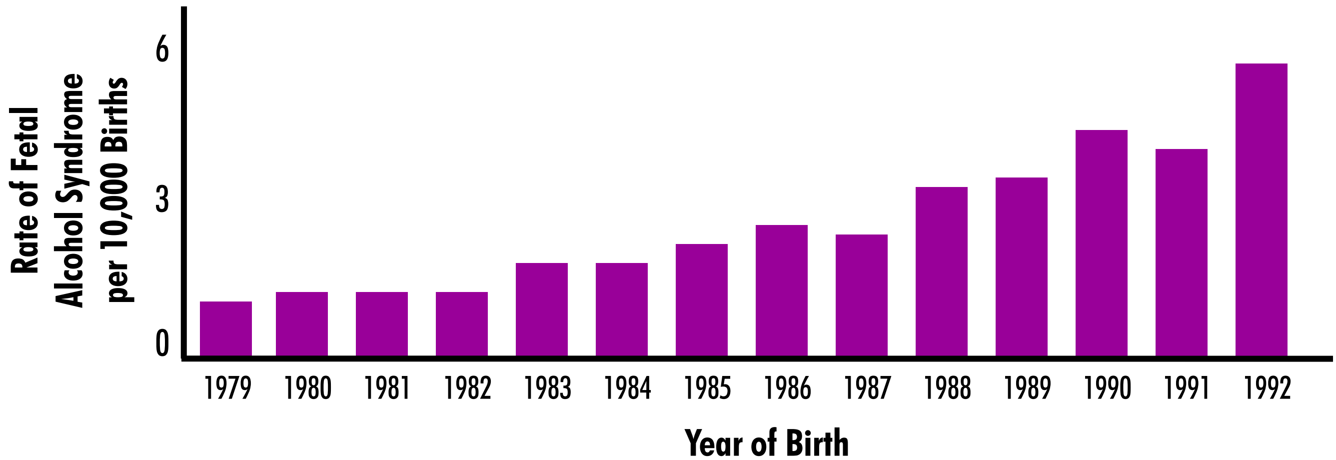
Chronic consumption of high doses of vitamin A must be avoided, especially during pregnancy. In non-pregnant adults, preformed vitamin A in amounts of roughly 5000 IU per day was shown to increase the risk of bone fracture.[48-49] During pregnancy, the consequences of high dose vitamin A supplementation are dire with birth defects reported in one out of every 57 women taking 10,000 IU or more per day of preformed vitamin A.[50] Women taking more than 10,000 IU of preformed vitamin A per day are almost five times more likely to give birth to a malformed infant.[51] Beta-Carotene is not teratogenic and appears to be a much safer alternative to preformed vitamin A supplementation.[52]

There are benefits to vitamin A supplementation during pregnancy. Lower vitamin A levels are seen in habitual abortions.[53] Vitamin A supplementation may also prevent night blindness during and after pregnancy, a significant problem in developed countries. Night blindness is indicative of inadequate vitamin A nutriture and is associated with a two to four-fold increase in maternal mortality.[54]

Vitamin B3 Protects the Developing Brain

Fetal exposure to alcohol is the number one cause of non-genetic mental retardation in developed countries. Maternal alcohol consumption can lead to Fetal Alcohol Syndrome, a condition with the following possible features: congenital heart disease, growth retardation, feeding problems, and disorganization of neurons[55] leading to serious neurological disorders such as hyperactivity, learning and memory deficits, psychosis, depression, and schizophrenia.[56] The incidence of Fetal Alcohol Syndrome is estimated at 1 out of every 100 newborn children in the United States.[57] A single episode of binge drinking leads to the death of thousands of fetal neurons[58] explaining the toxicity seen with ethanol consumption. It has been suggested that vitamin B3 may have neuroprotective activity in the developing brain. Research has also shown that vitamin B3 protects the nervous system from free radicals.[59]

In the latest study, researchers from Cornell University examined the possible benefits of vitamin B3 for the prevention of ethanol-induced neurodegeneration in mice.[60] The results are encouraging. Vitamin B3 reduced injuries to neurons and "inhibited the decrease in the number of neurons following ethanol exposure during early postnatal development" an effect that appears to be related to mitochondrial protection.[61] Most importantly, the research uncovered that vitamin B3 is capable of preventing hyperactivity and memory impairment in animals exposed to ethanol in utero making vitamin B3 the first treatment with demonstrated efficacy at the cellular, molecular and behavioral level for the prevention of ethanol induced neuronal apoptosis (cellular death).



Graph 7. Reported incidence rate of fetal alcohol syndrome, by year of birth, from the Birth Defects Monitoring Program of the Centers for Disease Control and Prevention, 1979-1992.

Of course, pregnant women should always avoid alcohol. Unfortunately, fetal exposure to ethanol is widespread (see Graph 7) despite the 1989 imposed label warning for all alcoholic beverages in the United States: "According to the Surgeon General, women should not drink alcoholic beverages during pregnancy because of the risk of birth defects." One explanation is that alcohol exposure may be occurring before the mother knows she is pregnant. In Project Viva which enrolled 2 128 pregnant women, 70% reported alcohol consumption after their last menstrual period but before learning they were pregnant while eight percent continued consuming alcohol once they realized they were pregnant.[62]

Ginger and Vitamin B6 for Morning Sickness

More than half of pregnant women experience nausea and vomiting of pregnancy especially in the first trimester. The rapidly increasing production of the human chorionic gonadotropin (HCG) hormone by the placenta may be to blame. Indeed, it is thought that the hormone stimulates the vomiting center in the brain, triggering nausea and the vomiting reflex.

Ginger is a well-known antiemetic and several studies have documented its efficacy at reducing the symptoms of morning sickness with significant improvements in nausea and retching after four days of supplementation with 1500mg of ginger daily.[63] The studies have also demonstrated that ginger does not adversely affect the fetus; birth weights, gestational age and APGAR scores (a test designed to quickly evaluate a newborn's physical condition) were not affected in newborns when the mother was giving ginger as a treatment for nausea and vomiting.

Vitamin B6 is essential for neurotransmitter synthesis, lipid metabolism and protein synthesis. During pregnancy, vitamin B6 was shown to prevent dental decay[64] and is effective at reducing the nausea and vomiting of pregnancy.[65] A study looking at the comparative effectiveness of vitamin B6 and ginger found significant improvement in nausea and a reduction of vomiting episodes in both treatment groups.[66]

Homocysteine levels, Folate, Vitamin B12, Inositol, Choline and Neural Tube Defects

Homocysteine

Homocysteine is a highly toxic by-product of normal metabolism and is known to be a risk factor for vascular disorders. During pregnancy, rising homocysteine levels are associated with increasing risks of serious complications such as preeclampsia, placental abruption and thrombosis.[67]

Homocysteine accumulation is in some ways similar to folate deficiency as folate derivatives are required to recycle homocysteine. Therefore, elevated homocysteine levels are also indicative of deficient methylation because homocysteine is recycled through methylation. DNA also needs to be methylated throughout fetal development.[68] Changes to DNA methylation may be responsible for gene silencing, and thus it has been hypothesized that improper DNA methylation may be responsible for fetal programming and prolonged changes in cellular function.[69]

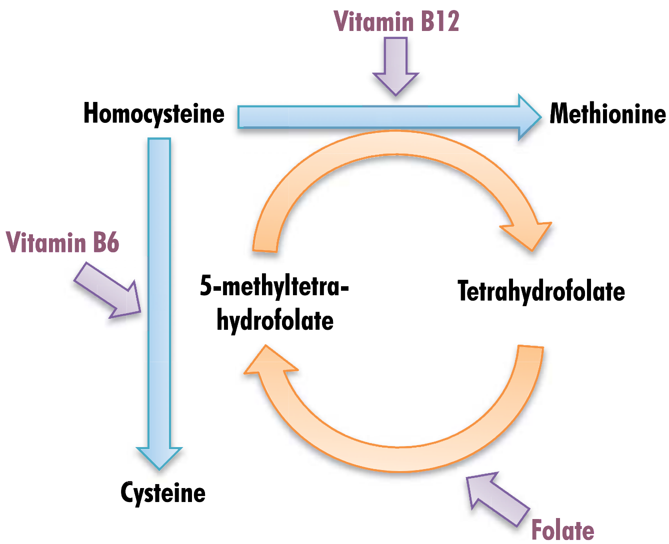


Figure 5. The Methyl Cycle. Source: Redrawn from Ray and Laskin (1999)[70]

The etiology behind neural tube defects (NTD) remains unclear. The process of neural tube closure is also poorly understood. The latest model suggests two sites of fusion (see Figure 6).[71] It is thought that inadequate folate status due to insufficient intake or irregular genes may increase the risk of abnormal cellular division leading to birth defects. It has also been observed that women carrying fetuses with NTD have mildly elevated homocysteine levels. Both homocysteine levels and NTD are influenced by genetic and nutritional factors.[72]

Folate

Most pregnant women are aware of the importance of folate during pregnancy. The vitamin was examined in the 1960's and 1970's for it potential in reducing neural tube defects (NTD). NTD are a common but serious congenital defect where the neural tube of the embryo - the structure that develops into the central nervous system - does not grow normally. Although genetics are a significant contributing factor to the development of NTD, environmental factors are also fundamental to the disorder. NTD are amongst the most common birth defects causing serious disability and mortality. About one in 33 infants born in the United States will be affected by birth defects ranging from NTD to cleft palate or lips and cardiac malformations. Studies have demonstrated that high dose folate supplementation (10 mg/day) prevented recurrence of orofacial clefts in populations at high risk for the malformation.[73-74] Folate also reduced the incidence of congenital heart defects.[75]

It is estimated that folate supplementation alone would decrease neural tube defects by 50%[76] and the risk of malformations by 30-60%.[77] However, because embryonic development including neural tube formation occurs early during gestation (neurulation occurs between the 17th and 30th post-conception days)[78], folate supplementation must begin before conception. This is why it is currently recommended that all women who could become pregnant should supplement their diet with folate. By the time women realize they are pregnant, it is often too late to prevent NTD. The increased folate demands throughout pregnancy are often not met through the diet. Furthermore, supplemental folate is 1.7 times more bioavailable than food folate,[79] strengthening the support for folic acid supplementation throughout pregnancy.

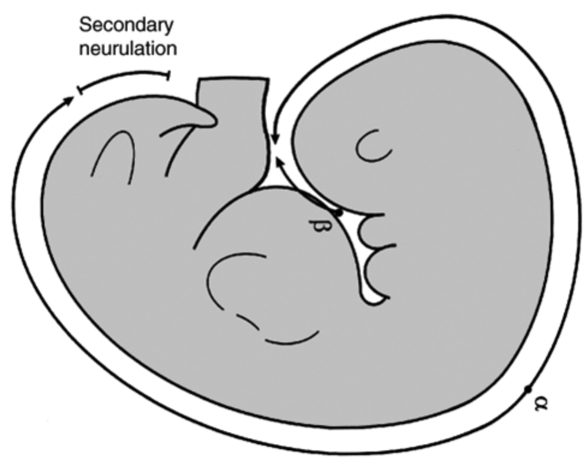


Figure 6. Fusion of the neural tube 25-27 days post-ovulation. Fusion begins at site α and then at site B. Source: Redrawn from O'Rahilly and Muller (2002)[71]

The influence of folic acid on NTD may well be related to homocysteine. Folic acid is a precursor to methylene tetrahydrofolate, the enzyme involved in the remethylation of homocysteine into methionine. Furthermore, of the nutritional factors that regulate homocysteine levels, folate status has the greatest influence.[80]

Inositol

Other nutrients have also shown promise when it comes to congenital defects. Inositol, a lipotrophic factor, helps in the metabolism of fatty acids. Approximately one gram per day of inositol is found in the diet.[81] Inositol is essential for cellular growth. A recent study demonstrates that maternal blood concentrations diminish during the first trimester of pregnancy after which concentrations slowly increase.[82]

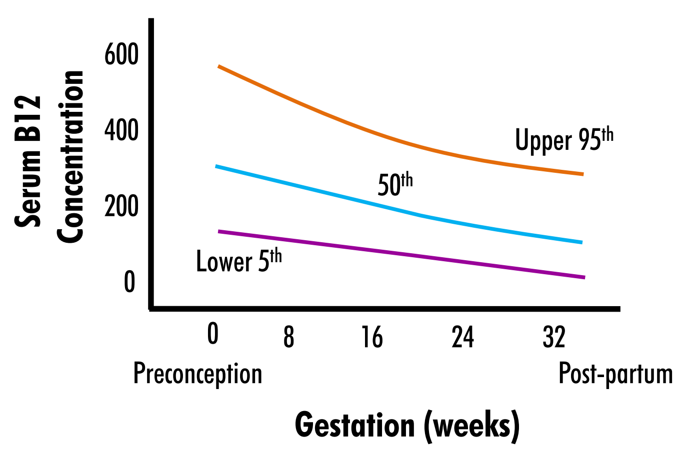
In maternal mice with genetic anomalies leading to neural tube defects in the offspring's that do not respond to folic acid supplementation, shortcomings can be prevented through myo-inositol supplementation early in pregnancy.[83] Unfortunately, approximately 30% of NTD are unresponsive to folate supplementation. There is no current treatment for such situations but inositol may be an effective treatment for folate resistant NTD. Indeed, it appear that supplementation with inositol leads to the activation of a specific protein kinase C (PKC) that may be essential for embryonic development, and particularly for the normal closure of the neural tube. The effect is cancelled by the administration of a PKC inhibitor - a further indication that inositol's benefits are related to PKC activity.

The fist use of inositol supplementation in a mother with a history of folate-resistant NTD resulted in a normal pregnancy and healthy baby with no signs of toxicity for the mother or fetus.[84] The mother was given 500mg of inositol and 2.5mg folate daily starting three months pre-conception and continuing 60 days post-conception. A study from the Netherlands revealed that lower maternal inositol concentrations were linked to an increased risk of cleft lip or palate in the infant.[85] Cleft lips or palate are another common congenital defect that develops between the seventh and 14th weeks of pregnancy. Inositol is also involved in lung surfactant production[86-87] and may be especially beneficial in premature babies. Inositol also reduced retinopathy, death, bronchopulmonary dysplasia and intraventricular hemorrhage in premature infants.[88]

Inositol is beneficial for diabetic pregnancies. The rates of congenital malformations in diabetic mothers are four to five times higher than in normal pregnancies. Congenital defects account for 40% of infant's mortality with diabetic mothers. The exact reason for the defects that affect mostly the heart and nervous system remains unclear, but free radicals, insulin and arachidonic acid deficiency have been suggested as possible underlying factors. In animal studies, inositol reduced the incidence of neural tube defects in diabetic animals by 50%[89], suggesting that inositol depletion may be involved in the pathophysiology.[90] Inositol depletion appears to be the main mechanism behind hyperglycemia-induced embryopathy.[91] However, it is probably best to limit inositol supplementation later on during pregnancy, as inositol may be involved in parturition.[92]

Vitamin B12

Also known as cobalamin, vitamin B12 is essential for health. Vitamin B12 is important for the maintenance of adequate methyl donors. The vitamin is required for the activation of folate, the recycling of homocysteine, fat metabolism, cellular replication and DNA synthesis. Vitamin B12 deficiency leads to neurological deficits, anemia and elevated homocysteine levels. During pregnancy, inadequate cobalamin levels increase the risk of NTD.[93] Vitamin B12 serum concentrations progressively decline during pregnancy (see Graph 8) leading to borderline or deficient levels[94], with low vitamin B12 levels associated with neural tube defects.[95]



Graph 8. Vitamin B12 serum concentration throughout a healthy pregnancy. Upper or 95th, lower or 5th and 50th percentiles of the concentrations of vitamin B12 from preconception, throughout pregnancy, to 6 weeks post-partum. Source: Redrawn from Cikot (2001)[1]

Choline

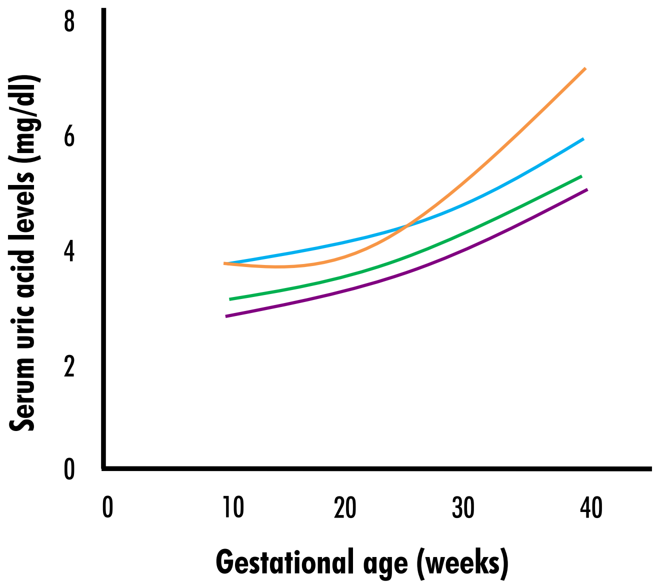
Choline is an essential nutrient involved in the synthesis of phospholipids and neurotransmitters. Choline is also a methyl donor implicated in the metabolism of homocysteine. Animal studies have shown that choline requirements during pregnancy may be difficult to attain through dietary means.[96] Fetal choline requirements are extremely high with plasma concentrations that are three times higher than maternal levels[97-98], which may lead to a diminution of maternal choline stores.[99] Worrisome findings as a study published in the American Journal of Epidemiology revealed that higher dietary intake of choline before conception reduced the risk of NTD, and other congenital defects affecting the nervous system.[100] This explains why the dietary reference intake for choline during gestation was set relatively high at 450 mg per day.

Trimethylglycine

Trimethylglycine (TMG) is another methyl donor inversely related to homocysteine levels, emphasizing its role in pregnancy.[101]

The Dangers of Elevated Uric Acid Levels

Uric acid is a metabolite of protein breakdown. Uric acid is present in the blood and is eliminated via the urine. Associations between elevations of uric acid concentration and preeclampsia were first reported in 1917. Hypotheses behind elevations of serum uric acid levels during pregnancy have revolved around kidney dysfunction and reductions in glomerular filtration rates. Animal studies have revealed that uric acid is an independent risk factor for cardiovascular disease and hypertension[102] suggesting that the molecule itself may play a significant role in fetal and maternal pregnancy related complications. Evidence showing that elevations in uric acid precede the development of preeclampsia[103] supports the view that uric acid leads to preeclampsia and not vise versa. The unfavorable effects of imbalanced uric acid levels go beyond preeclampsia, with studies showing a strong correlation between early pregnancy fetal loss and a diminution of the normal uric acid decline seen in the first trimester of pregnancy. However, this apparent lack of diminution of uric acid levels may simply be due to an inadequate blood volume expansion in early pregnancy.[104]



Graph 9. Predicted mean serum uric acid concentrations after adjusting for serum creatinine.

Purple line: control pregnancy. Green line: women with gestational hypertension and proteinuria without evidence of hyperuricemia at delivery. Blue line: women with gestational hypertension, proteinuria, and hyperuricemia at delivery. Orange line: women with gestational hypertension and hyperuricemia at delivery. Source: Redrawn from Powers (2006)

The Second Trimester

Weeks 13 to 24

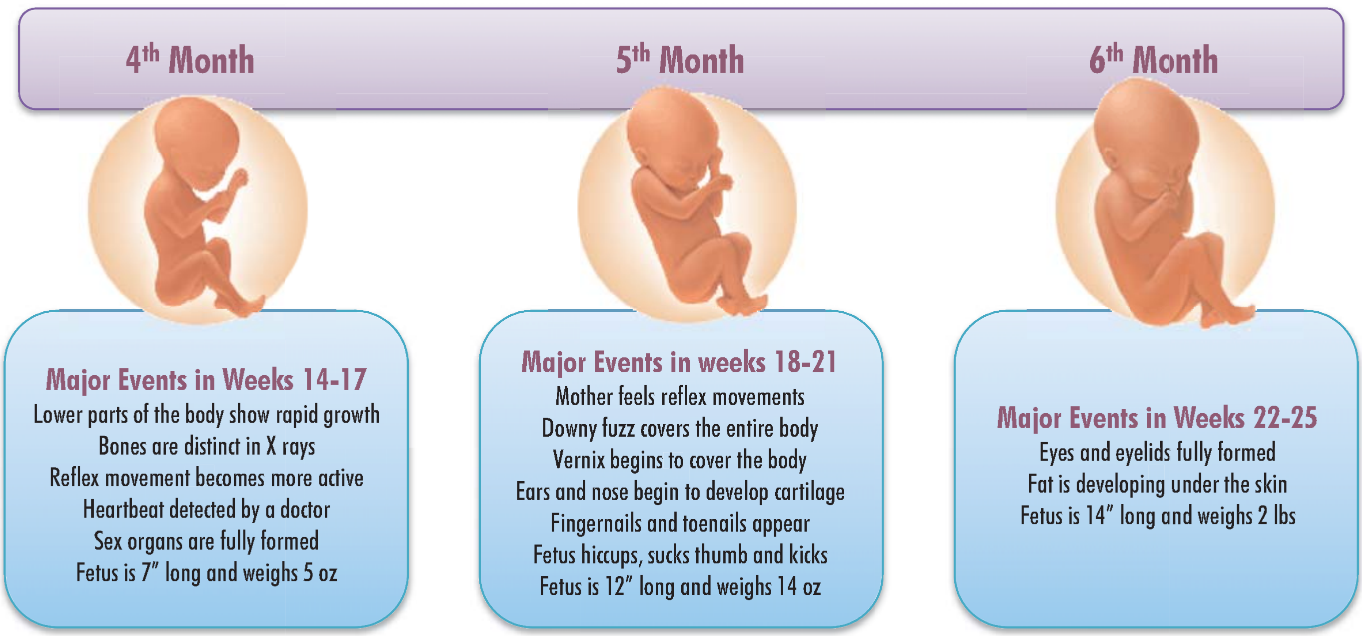


Figure 7. Fetal development in the 2nd trimester

Well-Earned Rest for Mom

During the second trimester of pregnancy mom's physiology has usually adapted to the demands of pregnancy. The ruckus of the first trimester is quietly fading and mom's physical indispositions usually improve.

Baby is Growing

At three months, the fetus is about two inches long and although still mostly transparent, the face is becoming more human like. At four months, baby is 4.5 inches long with a heart that is now pumping over 20 liters of blood per day. Sex is identifiable and reflexes such as swallowing begin to appear. By the end of the 5th month, hair begins to grow, eyebrows and eyelashes appear and organs mature. This is an exciting time for mom who begins to notice fetal movement. By the end of the second trimester, the fetus weighs around two pounds, reaches 11-14 inches in length and can now open his or her eyes.

The Uncertainties of the Second Trimester

The main complications experienced in the second trimester are placental abruption and an incompetent cervix. Monitoring for pregnancy-induced hypertension and anemia is also important during this period.

Beneficial Nutrients during the Second Trimester

Calcium for the Prevention of Pregnancy Induced Hypertension

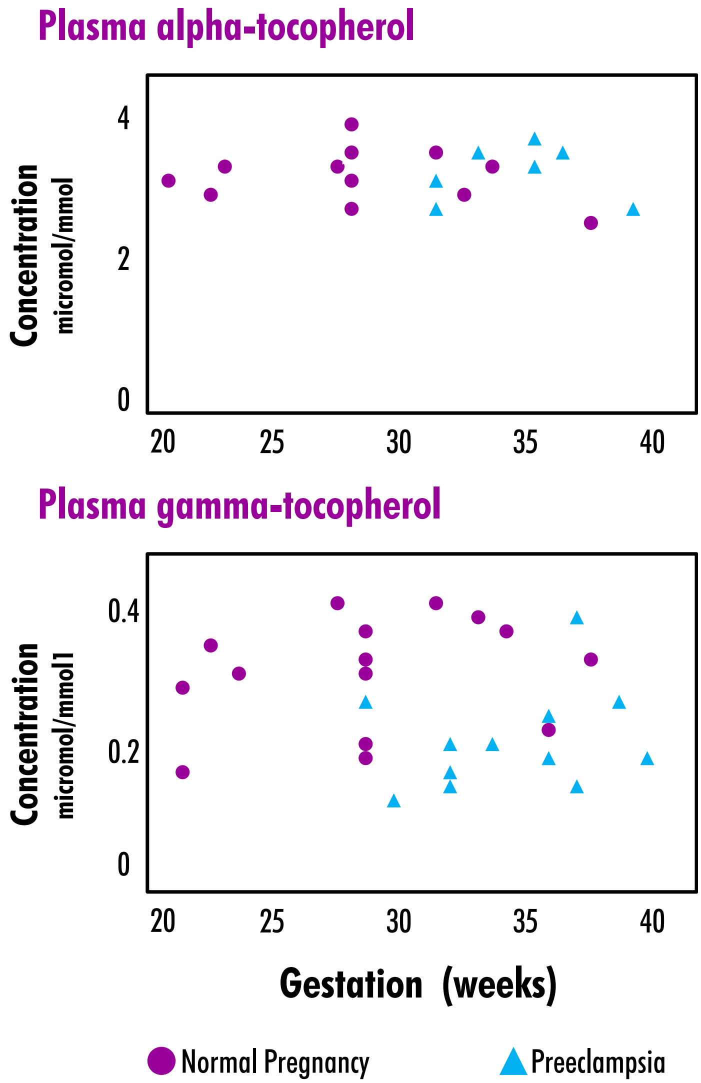
Pregnancy induced hypertension and preeclampsia are closely related. Both conditions are exclusive to pregnancy and affect five to eight percent of all pregnancies.[105] Preeclampsia is characterized by elevations is blood pressure, edema and the presence of protein in the urine. Preeclampsia may progress to eclampsia a serious condition where seizures are present. Despite medical treatment, preeclampsia and eclampsia may be fatal to child and mother.

In patients that are at risk for the development of preeclampsia, calcium supplementation may help reduce blood pressure and may prevent preterm labor.[106] A meta-analysis involving a total of 2412 patients showed that supplementation with calcium lead to a drop of 1.27 mmHg in systolic blood pressure[107] and the latest report suggests that calcium supplementation may halve the risk of preeclampsia.[108] In addition, calcium is beneficial for the infant as shown by a trend towards lower blood pressure in children whose mother had supplemented with calcium during pregnancy.[109]

Tocopherol Levels in Pre-Eclampsia vs. Normal Pregnancy

Vitamin E is much more than α-tocopherol. Although α-tocopherol is found in the greatest quantity in the serum, the seven other molecules, which together form the vitamin E complex, have several important health functions. α-tocopherol is often incapable of accomplishing those roles (see: Introducing Vitamin E "Complex", The Holistic Lifestyle). A paragon also expressed in pregnancy.

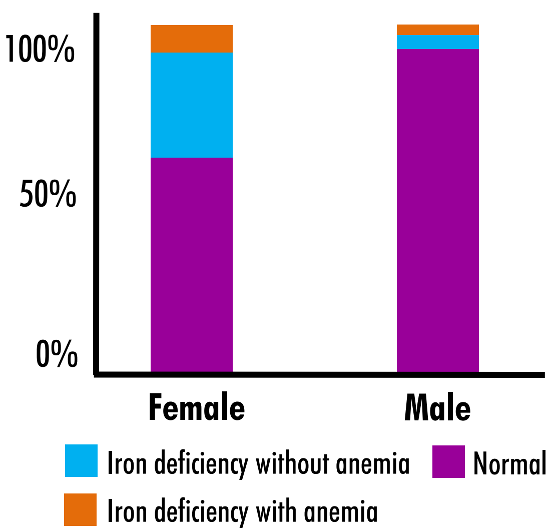
Interestingly enough, whereas most nutrient levels diminish as pregnancy progresses, α-tocopherol levels naturally increase as pregnancy progresses.[110] Although the etiology of preeclampsia remains poorly understood, it has been suggested that oxidative damage to the vascular system may play a significant role in the pathology of the condition which is precisely why research efforts between Japanese and Swedish scientists looked at the relationship between α and γ tocopherol levels in normal pregnancy versus preeclamptic conditions.[111] The results: α-tocopherol levels did not significantly differ between normal and preeclamptic pregnancies; conversely, γ-tocopherol levels were significantly lower in preeclamptic women versus women having normal pregnancies (see Graphs 10 and 11). Furthermore, γ-tocopherol levels were significantly lowered in pregnant versus non-pregnant women.



Graphs 10 & 11. Plasma levels of Alpha and Gamma-tocopherol in normal and pre-eclamptic pregnancy. Source: Ishihara (2004)

The Importance of Iron

After folate, iron is quite possibly the most significant nutrient of pregnancy. Iron deficiency is one of the most common deficiencies especially in women and children. The rates are alarming; in the United States between 1988 and 1994, nine percent of toddlers and nine to 11% of women of childbearing age were iron deficient.[112] In certain specific groups deficiencies are even more frequent. For example, the rates of iron deficiency in recreationally active women reached 29% (see graph 12).[113] However, pregnant women worldwide faired worse than all others groups with anemia, which affects 50-70% of women during pregnancy.[114] The consequences of iron deficiency, especially during rapid development, are disconcerting. Infants are especially susceptible to iron deficiency because of the rapid growth they undergo which explains why iron requirements during pregnancy almost double (see Dietary Reference Intakes, Table 1b). The consequences of iron deficiency are dire, infants with inadequate iron status scored six to15 points lower on mental development test scores, six to 17 points lower on motor test scores, had poorer locomotor skills and had longer looking times on visual recognition memory tests.[115] The unfortunate news is that most studies report that developmental deficits persist even after iron has been replenished.[116] During infancy, the hippocampus (essential for the formation of new memories) and the cortical brain region (necessary for higher brain function such as though and action) are at their peak phase of development. Animal studies have shown that if iron stores are insufficient to support myelin, synapse and dendrite formation, permanent metabolic changes may occur. It appears that iron deficiency impedes and interferes with the arrangement of proteins in the brain, leading to metabolic and structural changes.[117]



Graph 12. Prevalence of iron deficiency with and without anemia as determined by serum ferritin. Source: Sinclair (2005)

Gestational iron deficiency also negatively affects emotional and behavioral attributes. Studies demonstrated that babies born to iron deficient mothers are more irritable.[118] Also, newborns with lower hemoglobin and serum iron levels at birth have lower levels of alertness and soothability which can not be explained by variations in family demographics, low birth weight, gestational age, maternal diabetes or neonatal illness.[119]

The importance of iron is not limited to higher brain function. Higher maternal dietary iron intakes reduced the risk of spina bifida in pregnant Dutch women[120], while iron deficiency anemia leads to low birth weight and premature babies.[121-122] Higher umbilical venous blood iron levels also corresponded with higher placental weights (bigger placentas allow for better transfer of nutrients between mother and child).[123]

Folate Deficiency may predispose to Placental Abruption

The association between folate deficiency and placental abruption remains tentative but several studies have demonstrated that folate deficiency increases the incidence of placental abruption while other studies did not find a significant connection.[124] The mechanism through which folate and placental abruption are related is unknown but may be related to homocysteine levels.

Homocysteine and Placental Abruption

Two studies have shown that women with placental abruption were significantly more likely to have higher levels of homocysteine either when fasting or in post methionine states.[125]

The Third Trimester

Weeks 25 to Birth

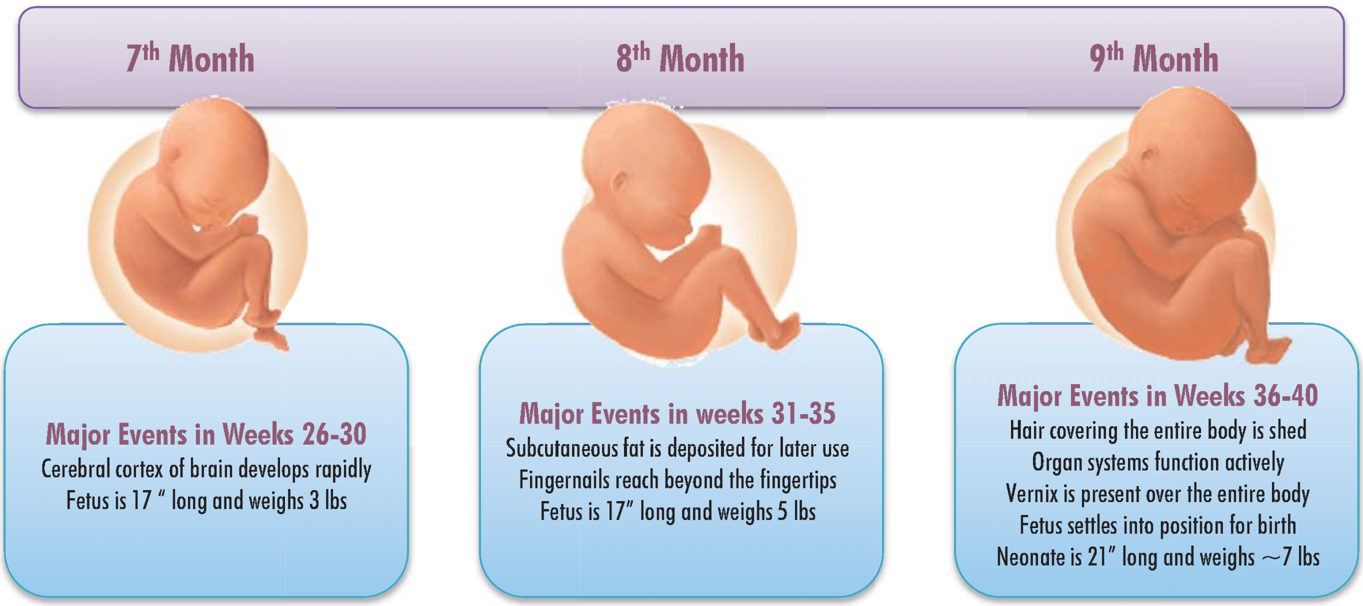


Figure 8. Fetal development in the 3rd trimester

Baby is Maturing

During the third trimester, final developmental milestones must be achieved before the infant is ready for life outside the womb. Taste buds develop, fat layers are deposited, tremendous brain development occurs, the kidneys mature and finally the lungs are ready for their first breath of air. The baby's position in utero also changes; the baby is usually head down and lower in the abdomen, ready for parturition.

Mom is ready for Baby

The added weight of the unborn child weighing about seven pounds at delivery is enough to cause back pain due to the added pressure on the spine and the shift in the center of gravity. Furthermore, the baby is now pulling on several ligaments, which may aggravate the problem. Bone pain can also occur because of the increased presence of progesterone, which relaxes the joint at the center of the two pubic bones, in order to create a larger opening for the baby. Unfortunately, this change may also cause some lumbar discomfort.

The baby is now occupying a large part of the abdomen and may press and push on the stomach causing indigestion but also on blood vessels leading to poor venous return, which in turn may cause edema especially in the legs and feet.

Beneficial Nutrients in the Third Trimester

Maternal Stores are Running Low

This should be no surprise, as baby gets bigger, the nutritional demands also increase and low nutrient levels in mom are commonly seen later in pregnancy. For instance, in a study that looked at vitamin B12 status in pregnancy, it was shown that the lowest levels occur at the end of the third trimester when 43% of the women had low cobalamin levels.[126] However, lower serum vitamin B12 values were not associated with detrimental consequences.[127]

Thiamin Status during the Third Trimester Influences Thiamin Breast Milk Content

Not surprisingly, maternal nutritional status in the months preceding lactation influences breast milk quality. Research published in the British Journal of Nutrition demonstrated a clear association between thiamin status in the third trimester of pregnancy and the concentration of thiamin in breast milk.[128] Thiamin status is especially pertinent in pregnancy; studies suggest that high rates of deficiencies occur in pregnant women and infants.[129-130] The aforementioned study demonstrated that pregnant women with thiamin intakes above the recommended intakes (0.4 mg/4184 KJ + 0.1 mg with a minimum of 1 mg/day) in the third trimester of their pregnancy had higher thiamin levels in their breast milk and were less likely to have breast milk thiamin levels below normal. Women with higher thiamin intakes were also less likely to become severely deficient: only 7.9% of women with adequate intakes developed severe signs of deficiency versus 30.8% of the women who did not meet their thiamin requirements. Previous research demonstrated that supplementation with a multivitamin and mineral supplement containing riboflavin increased breast milk content from 0.48 μmol/L to 0.66 μmol/L after supplementation.[131]

Choline and Fish Oils Encourage the Development of the Nervous System

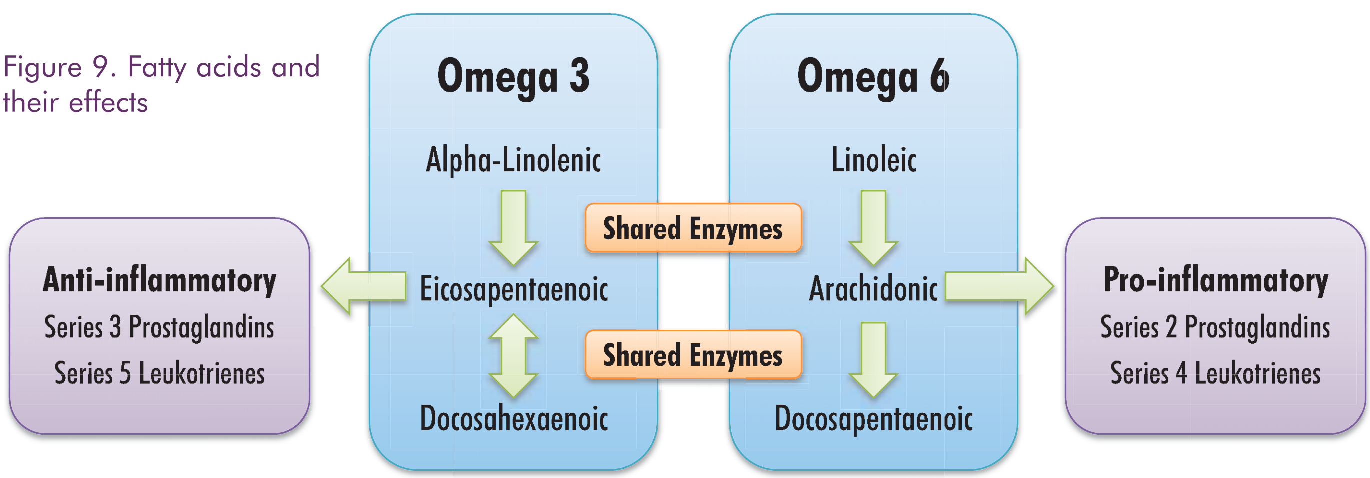
Choline

Choline is a neurotransmitter precursor involved in brain development and memory accretion.[132] Choline is also a structural component of tissues and cellular membranes required for normal cellular growth.[133] Choline is required during pregnancy for the normal growth of the infant and in animal studies maternal choline supplementation increases fetal blood and brain choline. Animal studies reveal that animals receiving choline in utero through maternal supplementation had "long-term facilitative effects on spatial navigation that extend well into adulthood".[134] Further testing demonstrated memory improvements in both recall and acquisition but also in memory capacity.[135] What is even more astonishing is that, unlike control animals, animals receiving prenatal choline-supplementation showed no age-associated decline in choice performance.[136] Choline represents the first possible treatment for the deterioration of cognition in old age. In rodents, brain development is especially sensitive to choline depletion during two periods; one occurs during fetal development at days 12-17 of gestation (normal parturition occurs on day 21), the other during postnatal days 16-30.[137] The mechanism behind choline's ability to influence brain development may be related to a change in the brain's organization that occurs during development and leads to permanent effects on cognition.[138] This effect is so profound that scientists can recognize animals whose mothers received extra choline even when the animals are elderly.[139]

DHA

Fish lipids, particularly lipids from cold-water fish are high in long chain polyunsaturated fatty acids, especially omega-3 fatty acid of which DHA (docosahexaenoic acid) is a major constituent. DHA is a 22-carbon chain containing 6 unsaturated bonds all of which are in the cis configuration. DHA is an essential part of cellular membranes, specifically in brain and retinal cells - representing roughly 15% of the total fatty acid content of the brain[140] and constituting the predominant fatty acid in the retina.[141,142] This makes DHA especially important

Figure 9. Fatty acids and their effects



during pregnancy, a period of rapid fetal brain development. Furthermore, around 80% of fetal DHA accumulation occurs in the last trimester of pregnancy because this is when the fetus builds up adipose tissue.[143] Unfortunately, this leaves preterm babies without the DHA needed for brain maturation and even 40 weeks post-conception, brain DHA levels in preterm infants remain lower.[144]

Because omega-6 and omega-3 share the same metabolic enzymes and compete with each other, modification of the fatty acid content of the diet also changes the fatty acid content of cellular membranes, which in turns affects cellular function and growth.[145] Breast milk contains higher concentrations of long chain polyunsaturated fatty acids (LCPUFA) than infant formulas. Studies report that breast-fed infants fare better than formula-fed infants when visual acuity and cognitive development are investigated suggesting that LCPUFA are important for the infants' development.[146] Animal studies demonstrated that inadequate omega-3 fatty acid supply in the postnatal period affects nerve growth factors, dopamine production and glucose uptake in the brain.[147] Furthermore, brain hypothalamic DHA levels did not recover in animals given alpha-linoleic acid (precursor to omega-3 fatty acids) for 24 weeks after being fed low levels of omega 3.[148]

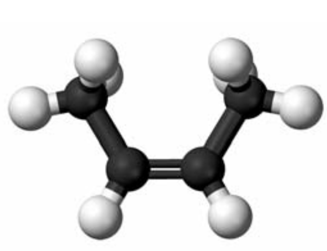
During gestation, LCPUFA are delivered to the fetus via the placenta. Human studies have confirmed that higher maternal omega-3 fatty acid consumption may improve cerebral maturation of the newborn[149] and prevent the recurrence of preterm delivery with fish oil supplementation in the last trimester of pregnancy (providing 920 mg DHA and 1.3 g EPA) reducing recurrences from 33% to 21%.[150] Low seafood consumption, which relates to poor omega-3 fatty acid intakes, throughout pregnancy was also shown to be a strong risk factor for preterm delivery and low birth weight.[151] Associations between maternal blood DHA levels and the baby's sleep patterns were also reported, suggesting that higher maternal blood DHA levels are associated with greater central nervous system maturity in the newborn.[152] Epidemiological data suggests that higher consumption of omega-3 fatty acids throughout pregnancy increases birth weight, head circumference, birth length and the duration of gestation.[153] Animal diets enriched in omega 6 fatty acids and low in omega 3 fatty acids increased blood pressure later on in life.[154] The International Society for the Study of Fatty Acids and Lipids recommends at least 300 mg DHA per day with a total of at least 650 mg combined DHA and EPA during pregnancy.[155] These goals could only be reached in the United States through supplementation, a four-fold increase in fish consumption or functional foods.[156] Furthermore, the concern for an increase in oxidative stress in women given fish oil supplements (unsaturated oils are susceptible to oxidation) has been disproved by Shoji et al. In their study, pregnant women were given 500 mg DHA and 150 mg EPA fared no worse than women not receiving the supplement.[157]

Another interesting observation was inspired by the notion that omega-6 fatty acids tend to promote inflammation while omega-3 fatty acids exhibit anti-inflammatory activity. In a recent study, scientists from three American universities looked at the ratio of omega-6 to omega-3 fatty acid in placental tissues of normal and preeclamptic women.[158] DHA levels were lower in preeclamptic women with a ratio of omega-6 to omega-3 fatty acids roughly twice as high in preeclampsia versus normal pregnancy. The same authors had previously reported lower omega-3 fatty acid concentrations in preeclamptic maternal plasma.[159] In other studies, a 15% increase in the omega-3 to omega-6 ratio reduced the risk of preeclampsia by 46%.[160]

Researchers have reported a 21% reduction of maternal brain DHA levels during animal gestation when dietary supply of the essential fatty acid is low. Previous studies had demonstrated that women with lower blood or breast milk DHA content were more likely to suffer from postpartum depression. It had previously been thought that brain DHA levels did not fluctuate because the nutrient is eagerly preserved. The authors concluded that the high ratio of omega-6 to omega-3 fatty acids in the Western diet might be a risk factor for postpartum depression.[161]

Alcohol inhibits delta-6 and delta-5 desaturases, which suppresses the conversion of linoleic acid and gamma-linolenic acid to arachidonic acid (AA), DHA and EPA. Ethanol also reduces the blood levels of linoleic acid. Alcohol consumption by pregnant women therefore reduces the availability of essential fatty acids to the developing fetus and may partially explain the developmental deficits seen in Fetal Alcohol Syndrome. This also explains why vitamin B3, necessary for delta-6 desaturase activity, exerts neuroprotective activity in fetal alcohol syndrome.[162]

A Note about Trans Fatty Acid Intake during Pregnancy



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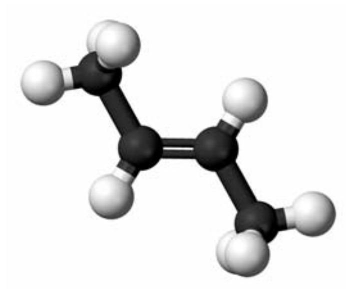


Trans

There are two sources of trans fatty acids (TFA) in our diet: hydrogenated fats and the meat and milk of ruminant animals. In Canada and the United States, during the 1990's, TFA consumption reached 2.5-13g per person per day. Until 2000, 80-90% of dietary TFA came from hydrogenated fats but that percentage has now decreased because the food industry has reduced their use of TFA.[163] Nonetheless, TFA remain widespread in our food supply.

A recent review published in the New England Journal of Medicine advocates the reduction or complete avoidance of TFA if possible.[164] TFA have no nutritional value whatsoever but consumption of TFA reduces HDL cholesterol (the beneficial cholesterol fraction) and increases LDL cholesterol (the unhealthy cholesterol fraction). Health wise, the consequences of the dietary intake of TFA are far worse than the effects seen with saturated fat intake. TFA consumption has serious and severe repercussions on the cardiovascular system. A two percent increase in energy intake from TFA increases the incidence of coronary heart disease by 23% and the adverse effects are seen even with extremely low dietary consumption of TFA – 2 to 7g/day is enough to damage blood vessels.[165] In 2003, cardiovascular disease claimed 910,614 US lives.[166] According to estimates, the elimination of TFA's from the food supply could have saved over 200 000 thousand lives – representing roughly four times the total number of US casualties in the Vietnam war[167] - in 2003 alone.

Unfortunately, the presence of TFAs in our food supply also has repercussions in pregnancy and lactation. As already discussed, both DHA and arachidonic acid (AA) are essential for fetal and infant growth. Sadly, high TFA consumption is consistently linked with lower DHA levels.[168] TFA displace other important dietary fats and are incorporated in cellular membranes where they disrupt function and fluidity. Canadian dietary estimates revealed that pregnant women were consuming on average 3.4 to 3.8 g of TFA per day with intakes as high as 11.3g/day.

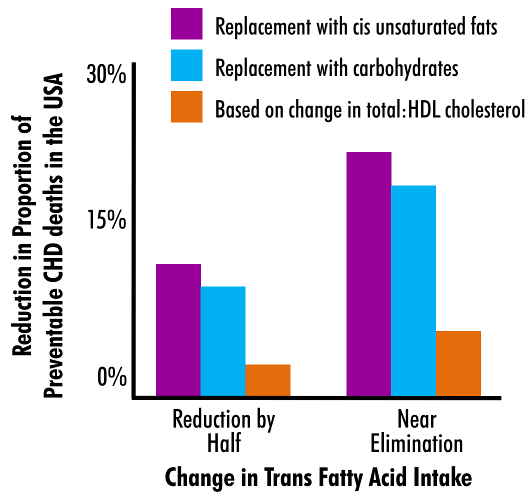
Table 4. Typical Trans Fatty Acid Content of Foods

Type of Food	Trans Fatty Acid Content			
	g/Typical Serving	g/100g	% of Total Fatty Acids	% Daily Energy Intake
Fast or Frozen Foods				
French Fries	4.7 -6.1	4.2 - 5.8	28 - 36	2.1 - 2.7
Breaded Fish Burger	5.6	3.4	28	2.5
Breaded Chicken Nuggets	5	4.9	25	2.3
French Fries, frozen	2.8	2.5	30	1.3
Enchilada	2.1	1.1	12	0.9
Burrito	1.1	0.9	12	0.5
Pizza	1.1	0.5	9	0.5
Packaged Snacks				
Tortilla chips	1.6	5.8	22	0.7
Microwave popcorn	1.2	3	11	0.5
Granola Bars	1	3.7	18	0.5
Breakfast Bars	0.6	1.3	15	0.3
Bakery Products				
Pie	3.9	3.1	28	1.8
Danish	3.3	4.7	25	1.5
Doughnuts	2.7	5.7	25	1.2
Cookies	1.8	5.9	26	0.8
Cake	1.7	2.7	16	0.8
Brownie	1	3.4	21	0.5
Muffin	0.7	1.3	14	0.3
Margarines				
Vegetable shortening	2.7	19.2	19	1.2
Hard (stick)	0.9 - 2.5	6.2 - 16.8	15 -23	0.4 - 1.1
Soft (tub)	0.3 - 1.4	1.9 - 10.2	5 -14	0.1 - 0.6
Other				
Pancakes	3.1	2	21	1.4
Crackers	2.1	7.1	34	0.9
Tortillas	0.5	1.8	25	0.2
Chocolate Bar	0.2	0.6	2	0.1
Peanut Butter	0.1	0.4	1	0.05

Meanwhile, dietary consumption of alpha linoleic acid, precursor to DHA was only 1.6g/day.[169] Furthermore, it has been established that maternal dietary TFA consumption correlates with the newborn TFA plasma levels, which surpass omega-3 levels by more than two-fold.[170]

The situation in breast fed infants is similar. There is a rapid accretion of TFA into breast milk after dietary consumption[171], which leads to a TFA exposure in breast fed infants ranging from 0.7 to 5.4g/day.[172] There is no mechanism to prevent infant exposure to TFA in the mammary glands, in pregnancy as in lactation; maternal TFA intake directly determines the infants' exposure.

In 2003 Canada became the first country to introduce food labeling for TFA. Such labeling has reduced the upper concentration limit of TFA content in breast milk by more than 50% from 18.7g to 8.8g TFA per 100 g human milk... a welcomed change in the right direction.



Graph 13. Estimated Effects of Reducing the Consumption of Trans Fatty Acids on the Incidence of Coronary Heart Disease in the United States. (Source: Mozaffarian, 2006)

Vascular Support: glycine and pycnogenol

Glycine is a non-essential amino acid. However, during pregnancy endogenous production may not be enough to meet the increasing demands due to the rapid synthesis of nucleotides. Therefore, glycine is a conditionally-essential nutrient during pregnancy.[173] Studies demonstrate that a high proportion of women show signs of glycine deficiency.[174]

Glycine may have anti-inflammatory and antioxidant properties. Glycine also provides a methyl group to folic acid for the synthesis of DNA and for the methylation of homocysteine.[175] In animals that were fed a protein-deficient diet, additional glycine helped the mothers adapt to the increased vascular demands of pregnancy protecting the vascular systems of both the mother and fetus - a mechanism that may be related to the reduction of free radicals.[176]

Pycnogenol is an antioxidant extracted from the bark of a pine tree with anti-inflammatory activity and capable of inhibiting several inflammatory messengers. Studies show that pycnogenol is helpful for the management of menstrual cramps, low back and abdominal pain[177], which led to the investigation of the benefits of pycnogenol for the treatment of pain associated with pregnancy by a team of Japanese researchers. One hundred and forty women in their third trimester suffering from low back pain, pelvic pain, hip joint pain, varicose related pain or calf pain were included in the study. Of those, 80 women received 30 mg of pycnogenol with breakfast while the remaining 60 participants did not receive any treatment. The results were impressive, for all symptoms significant improvements were reported two weeks after supplementation began and no unwanted effects were seen in women receiving pycnogenol. Meanwhile, the women who unfortunately found themselves in the control group saw no significant improvements after two weeks except for betterment of inguinal pain, an improvement that subsided after the study had reached its sixth week.[178] Unfortunately, because the control group was not given a placebo, it is difficult to assess the true impact of pycnogenol supplementation for the relief of pain. Indeed, a recent review of the effect of control studies without any treatment in patients suffering from neck pain reveals average improvements of 0.18 while treatment with placebo alone led to much higher improvements with reductions in reported pain sensations reaching 0.5.[179] This means that until a placebo control study is available, the real benefits will be difficult to assess. Furthermore, the safety of pycnogenol in the first trimester of pregnancy has not been established, supplementation with the extract should therefore be limited to later on in the gestational period.

Vitamin B Supplementation for Leg Cramps

Leg cramps, especially at night, are common during the second half of pregnancy. A recent study evaluated the efficacy of several nutrients for the treatment of muscle spasms during pregnancy. The results showed that two weeks supplementation with 500mg calcium carbonate improved muscle cramps by 5.5 folds while 100 mg thiamine plus 40 mg pyridoxine improved muscle cramps by a factor of 7.5 fold.[180]

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Crucial for Breastfed Infants

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Enhances Mood

Reduces the Risk of Developing Cancer

Decreases Blood Pressure

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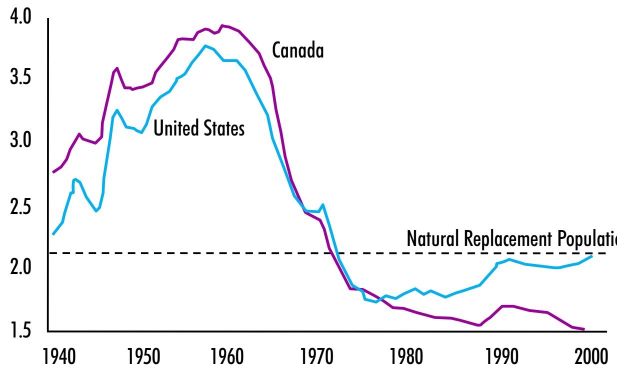
A Note about Birth Rate

The birth rate represents the number of childbirths per thousand people per year. Birth rate is a key factor for population dynamics and for government planning agencies. High birth rates stress the welfare system, family programs and the education system. Low birth rates put pressure on the senior care system and cause a shift that eventually results in less working adults to support the growing aging population.

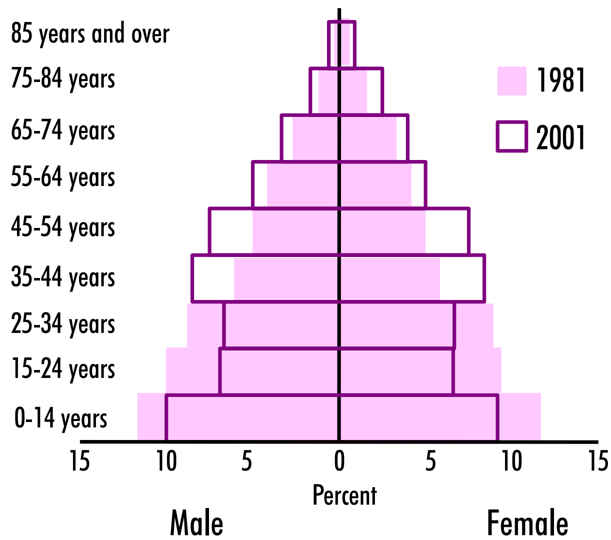
In Canada, the birth rate is slowly declining and has reached an all time low of 10.28% as of 2009. There are many factors at play in this societal change. The main factor relates to couples having children later in life because women are choosing to work longer before deciding to have children. Other factors include government policies, decreasing religious influence against contraception and abortion and economic prosperity.

Average Number of Children per Women
Source: Statistics Canada



North American demographics are heavily influenced by the baby boomer population. In Canada, the now retiring baby boomers constitute roughly one third of the Canadian population. There are currently five working Canadians for every senior but as the baby boomers retire over the next few decades, this ratio will dwindle reaching 2.5 people working for every senior in 2040. The economic pressures are already shifting from schools to the needs of the elderly with extraordinary demands being placed on the health care system. 2010 marks the 65th anniversary of the first of the boomers and health care expenditures have grown to the point where some are predicting the collapse of the entire system. In Ontario for example, 46 cents out of every dollar earned by the province will be invested in health care. And the worst is still to come with costs now increasing by seven percent a year.

Distribution of Canada's Population by Age Group 1981 vs. 2001



Quebec is the only province that has been able to reverse this trend with inexpensive and heavily funded daycare and subsidies in the form of tax relief and generous parental leave programs. Quebec's fertility rate (the number of children per women) is now higher than the Canadian average and has been growing for the last 5 years reaching its highest level since 1976. This is quite a feat considering that in the 1980's Quebec's birth rate was the lowest in Canada and one of the lowest in the world.

Lactation

Baby is finally here and must be fed. Milk production is initiated by the loss of the placenta, which leads to a shard decline in estrogen and progesterone levels. Prolactin and oxytocin are the two hormones central to lactation. Prolactin supports milk secretion while oxytocin, the release of which is stimulated by the suckling of the breast, promotes ejection of breast milk.

Lactation is also beneficial for mom; oxytocin release helps the uterus to return to its normal size. Lactation also suppresses menses through the inhibition of two hormones: LH and FSH thereby preventing another pregnancy and preventing maternal resources from being shared between the newborn and a new developing embryo.

For the newborn, breast milk is far superior to any other food or infant formula. Breast milk contains all the nutrients required for infant growth and development but also immune factors. Passive immunity mediated through the transfer of immune factors and probiotics from maternal breast milk protects the newborn from infections until the infant can mount an adequate immune response on his own. Nutrients in breast milk can be present in concentrations that exceed maternal blood levels - once again demonstrating that infant growth may take precedent over maternal requirements. For example, breast milk folate levels are five to10 times the maternal blood concentrations.[181] In addition, folate levels in women who nursed for more than 6 weeks are significantly lower than the levels seen in women who did not nurse[182], suggesting maternal folate depletion during lactation. Vitamin B12 has a similar course, excretion through breast milk reaching 0.6 mcg/day.[183] It is therefore important to support the maternal nutritional requirements so that both mother and infant can meet their essential nutritional needs.

Beneficial Nutrients during Lactation

Choline

Choline requirements are increased during lactation because high concentrations of choline are present in breast milk.[184] Animal studies also show a greater risk of developing choline deficiency while lactating.[185] Furthermore, in rodents, adequate choline is essential soon after parturition, emphasizing the importance of adequate maternal choline consumption for breastfed infants.

DHA

During lactation, fatty acid delivery to the infant may modify cellular membrane composition, especially in the nervous system, which in turn affects the function of neurons.[186] Long chain polyunsaturated fatty acids are supplied to the infant through breast milk. DHA intake levels in breast milk vary according to dietary intake. For instance, Inuit women eating large amounts of fish, often have breast milk DHA concentrations that are 10 times higher than in their European or North American counterparts.[187] Animal studies have demonstrated that raising the neonates DHA intake increases DHA levels in neurons, glial cells (cells with a supportive role in the nervous system) and in the retina.[188] Since infant formulas are typically lower in DHA than breast milk, formula-fed infants have lower blood and brain DHA levels.[189] This may explain why studies have shown that breast-fed infants have higher IQ's as early as six months after birth, with differences still present at 15 years of age[190-191], and also why studies have shown that breast-fed infants have a better visual acuity prior to six months,[192] suggesting that the impact of DHA on visual development is moderate.[193]

An early study reported that infants receiving a formula with a high EPA oil concentration exhibited worse growth than infants receiving a formula without long chain polyunsaturated fatty acids (LCPUFA).[194]

These results however, were not reported in later studies, which used formulas that contained both omega-3 (DHA, EPA) and omega-6 (GLA, AA) fatty acids. High omega-3 intake, especially EPA, decreases arachidonic acid (AA) levels, also essential for normal growth and development. Further work in the area has revealed that supplementation of formula-fed preterm infants should include a balance of omega-3 to omega-6 fatty acids. Suggestions include DHA levels of approximately 0.4% and AA levels around 0.6% - such levels represent the lowest range of DHA levels found in human milk worldwide but greater amounts have not been evaluated.

DHA supplementation in nursing mothers increases breast milk DHA concentrations and the infants' blood DHA levels. However, DHA breast milk levels above 0.8% resulted in negligible increases in the infant blood DHA levels.[195] Furthermore, maternal supplementation with DHA did not affect breast milk AA or tocopherol levels.[196]

Vitamin K levels are running Low

Transfer of vitamin K from mother to fetus is insignificant. Indeed, cord levels are extremely low and prophylactic vitamin K is administered intramuscularly to newborn infants to minimize the risk of deficiency and prevent hemorrhagic disease of the newborn. A condition which affects newborn infants which was recently renamed "vitamin K deficiency bleeding" and has an incidence of 2.5 to 17.0 per 1000 infants not receiving vitamin K at birth.[197] Vitamin K deficiency in newborn infants is common due to the limited transfer between mom and fetus in utero. Also, the fetal liver is incapable of producing sufficient clotting factors and the intestinal flora of newborns does not produce vitamin K2[198] - a significant source of vitamin K in adults. Vitamin K deficiency is more common in breastfed infants because infant formulas contain higher concentrations of vitamin K than breast milk. However, research has established that maternal vitamin K supplementation significantly raises breast milk concentrations with 5 mg of vitamin K1 per day resulting in breast milk vitamin K levels that correspond to the levels seen in infant formulas.[199] More interestingly however, is the latest information showing that menatetrenone (a type of vitamin K2) concentrations are significantly higher in breast milk than they are in the maternal plasma. This means that menatetrenone is selectively concentrated in breast milk.[200] Nonetheless, the amounts of vitamin K present in breast milk are not sufficient to compensate for the vitamin K given to newborns as a cautionary measure[201] but a Danish study has indicated that weekly oral supplementation of the newborn with vitamin K (without intramuscular vitamin K injection) was an effective measure against vitamin K deficiency bleeding.[202]

Vitamin C in Breast Milk Influences Risk of Atopy

Although the word may not have meaning for them, atopy is the black sheep that all parents dread. With it come the frustrations of allergies, the fright of asthma, the annoyance of rhinitis and the irritation of dermatitis. Atopy is the hereditary and genetic predisposition to immediate allergic reactions, conditions for which the prevalence in Western countries continue to increase. However, genetic expression is influenced by nutritional and environmental factors.[203]

Case in point: vitamin C in breast milk. Vitamin C is one of the main antioxidants found in breast milk. Antioxidants are believed to be a significant factor in atopic diseases. Indeed, allergic reactions lead to inflammation and free radical production. Antioxidants are well known for their ability to curb both free radical production and the inflammatory response.[204] Furthermore, atopic diseases are characterized by the presence of an overabundance of free radicals and allergy sufferers seem to be consuming lesser amounts of antioxidants. Together, those observations motivated Finnish researchers to examine the subject more attentively.

Thirty-four mother and children pairs were selected. All mothers suffered from atopic diseases such as allergic rhinitis, dermatitis and asthma. The infant's progress was monitored throughout the first year of life and breast milk samples were analyzed at one month of age for their antioxidant content. All mothers underwent skin prick allergy testing, in which 68%

experienced positives. Dietary vitamin C intakes were significantly correlated with breast milk vitamin C content and the vitamin C content of breast milk did not differ between women with positive or negative skin prick tests. Although mothers with positive skin prick tests and food hypersensitivities were more likely to have atopic children, the increased presence of vitamin C in breast milk reduced the risk of atopy by an odds ratio of 0.3.[205]

> "Nothing you do for children is ever wasted"
>
> Garrison Keillor

Pregnancy is a time of high metabolic demands. Gestation is a crucial developmental period where inadequate supply of essential nutrients will negatively affect long-term health in the newborn and compromise maternal well-being. The health of the mother and child are dependant on the maternal nutritional status as is the quality of the breast milk. After all, pregnancy and lactation are developmental periods where mom is eating for two.

Pregnancy is characterized by rapid development – a growth spurt that will not be seen at any other time throughout the life span. Unfortunately, rapid growth is also accompanied by vulnerability. The swift pace at which organs and body systems emerge leaves the embryo in a precarious position. Major changes to the fetal environment may disrupt a valuable balance resulting in costly consequences and nutritional deficits also produce serious consequences: growth is altered by deficiencies. The consequences of inadequate nutrition during pregnancy, as illustrated by fetal programming, result in unrecoverable metabolic inadequacies and developmental irregularities. The research is clear; the potential associated with improved nutrition is at no time greater than throughout pregnancy. As folate, iodine and vitamin A saved countless from the complications of congenital malformations, mental deficits and blindness so will vitamin B12, choline and vitamin D in the future.

> Tomorrows are established today and at no time is this truer than during pregnancy

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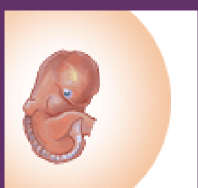
Preconception

Adequate nutrition before pregnancy is important for supporting fertility and building nutritional reserves.

Advanced Prenatal provides essential vitamins and minerals in doses that are safe and effective, before and during pregnancy.

First Trimester



Folate supplementation during the first months of pregnancy dramatically reduces the risk of neural tube defects and other congenital malformations.

Biofolate contains 5-methyltetrahydrofolate, the active form of folate.

Second Trimester

Iron requirements are nearly double during pregnancy. Adequate iron supplies are essential for fetal development.

Ortho-Iron contains a well absorbed form of iron that is easier on the intestines than other forms.

Third Trimester

Omega-3 fatty acids like DHA are essential to support healthy brain development.

Omega Natal is a fish oil concentrate high in DHA and is molecular-distilled to remove contaminants.

Lactation

Breast milk is naturally low in Vitamin D. Health Canada recommends that breastfed infants receive daily vitamin D3 supplementation.

Liquid Vitamin D3 for children provides safe and convenient supplementation for newborns.

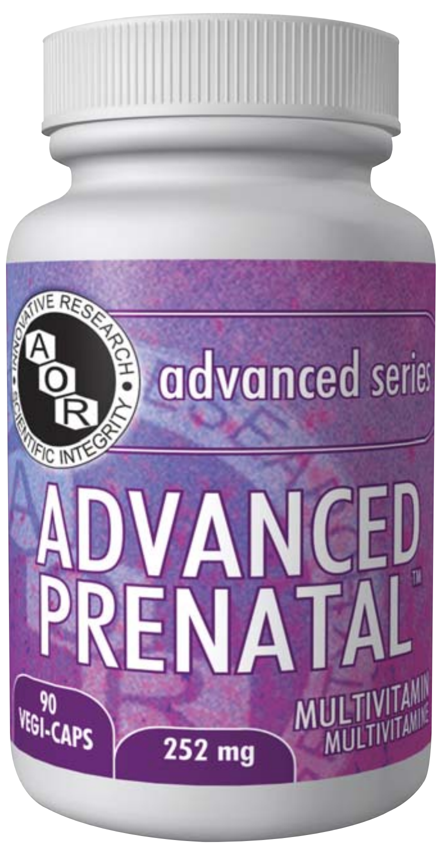
Advanced Prenatal

The Best Prenatal Supplement Available

Prevents pregnancy related deficiencies

Supports fetal growth and health

Provides key nutrients for mom and baby



"Nothing you do for Children is ever Wasted"

Garrison Keillor