

# Science Brief: Dairy in Pregnancy and Lactation

## Quality nutrition in the first 1,000 days benefits maternal health and helps the child thrive

The importance of nutrition in the first 1,000 days – from conception to about 2 years of age – cannot be overstated and has been a leading topic of much research in recent years.<sup>1-5</sup> When becoming pregnant, women undergo several hormonal, metabolic and physiological changes. Throughout pregnancy and lactation, energy and nutrient requirements are increased to support normal development and health of the fetus and infant. Optimizing nutrition during this period is critical for maintaining pregnancy, placental function and lactation,<sup>2,5,6</sup> and is especially important for neural system development in utero and after birth.<sup>1,3,7-9</sup>

In the first 1,000 days, the brain grows more rapidly than any other time in a human’s life.<sup>10</sup> While all nutrients are necessary for brain growth, inadequate consumption of key nutrients during this stage can lead to lifelong deficits in brain function even despite subsequent nutrition repletion.<sup>11</sup> Evidence from preclinical (animal) research and human clinical research has convincingly shown that such deficits during pregnancy can have irreversible adverse effects on a child’s lifelong neurocognitive function.<sup>1,2,7,8,12,13</sup> In 2018, the American Academy of Pediatrics published a policy statement, *Advocacy for Improving Nutrition in the First 1,000 Days to Support Childhood Development and Adult Health*, which identified 3 macronutrients and 11 micronutrients as key nutrients for early brain development (**Table 1**).<sup>3</sup> For several of these nutrients, a deficiency early in life has been linked to long-term health consequences.<sup>1,3,7</sup>

**Table 1.** Nutrients of concern from key pediatric and health organizations for the general public, women of reproductive age, women who are pregnant or lactating and/or infants.

2020-2025 Dietary Guidelines for Americans <sup>14</sup>
<p><b>Nutrients of concern for the general public:</b> Calcium, vitamin D, potassium and fiber</p>
<p><b>Nutrients of concern for pregnant and lactating women:</b> Iron, folate, choline and iodine</p> <p>With vegetarian or vegan dietary patterns, there is potential risk for insufficient consumption of iron, choline, zinc, iodine, vitamin B12 and long-chain polyunsaturated fatty acids [eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)]. Pregnant women should consult with a healthcare provider to determine whether and how much supplementation of these nutrients is needed.</p>
<p><b>Nutrient of potential concern for young women of reproductive age:</b> Vitamin B12</p>

## American Academy of Pediatrics<sup>3</sup>

### 2018 policy identified 14 key nutrients that support neurodevelopment:

Protein,<sup>a,b</sup> long-chain polyunsaturated fatty acids,<sup>a</sup> carbohydrates, zinc,<sup>a,b</sup> copper,<sup>a</sup> iron,<sup>a</sup> choline,<sup>a,b</sup> folate,<sup>a</sup> iodine,<sup>a,b</sup> selenium,<sup>b</sup> vitamin A,<sup>b</sup> vitamin B12,<sup>b</sup> vitamin B6 and vitamin K.

For several nutrients (including iodine, choline, vitamin B12), deficiency early in life has been linked to the potential for long-term health consequences.

## World Health Organization<sup>15</sup>

Iodine deficiency remains the single greatest cause of preventable brain damage and mental retardation worldwide. For several nutrients (including iodine, choline, vitamin B12), deficiency early in life has been linked to the potential for long-term health consequences.

<sup>a</sup>Nutrients that meet the principles for demonstrating a critical or sensitive period during development.

<sup>b</sup>Nutrients for which dairy foods are important dietary sources.

Leading pediatric and health organizations recognize the importance of several micronutrients, including iodine, choline and Vitamin B12, during pregnancy and lactation for early growth and development (**Table 1**). For the first time, the 2020-2025 Dietary Guidelines for Americans (DGA) included nutrition guidance for pregnant and lactating women.<sup>14</sup> The guidelines identified calcium, vitamin D, potassium and fiber as nutrients of public health concern for all Americans, including pregnant and lactating women. Iron, folate, choline and iodine were noted as specific nutrients of concern for pregnant and lactating women and vitamin B12 as a nutrient of potential concern for young women of reproductive age. The DGA also noted that vegetarian or vegan dietary patterns during pregnancy and lactation may increase risk for inadequate consumption of certain nutrients, specifically iron, choline, zinc, iodine, vitamin B12 and potentially the long-chain polyunsaturated fatty acids (eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]) (**Table 1**).

### Iodine, choline and vitamin B12 are critical nutrients for brain development in early life, yet pregnant and lactating women may be at risk for under-consuming these nutrients

Specific to iodine, the World Health Organization (WHO) states that iodine deficiency remains the single greatest cause of preventable brain damage worldwide.<sup>15</sup> However, a 2017 U.S. survey of obstetrician members of the American Medical Association (n=277) and midwife members of the American College of Nurse-Midwives (n=199) revealed that about one-third of participants did not know about the importance of maternal iodine adequacy for fetal brain development or thought that iodine deficiency was not harmful for the fetus.<sup>16</sup> In addition, although prenatal multivitamins were recommended by almost all participating health professionals, few specifically recommended those that contain iodine: 75% of survey participants prescribed lower amounts of iodine than recommended by health professional organizations or did not recommend iodine supplementation for women prior to or during pregnancy and lactation.<sup>16</sup> This may be due to a lack of knowledge about iodine nutrition and an absence of specific guidelines by some obstetrical and midwife organizations (e.g., American College of Obstetricians and Gynecologists

[ACOG]) to ensure adequate iodine consumption during pregnancy. Nutrition education is needed for healthcare professionals to ensure awareness of the importance of adequate iodine consumption – and other nutrients critical to cognitive development – before and during pregnancy and lactation.

## Iodine

Iodine is essential for many metabolic processes in the body, such as metabolic regulation and thermogenesis.<sup>13,17,18</sup> An indispensable component of thyroid hormones, iodine is critical for normal neurodevelopment during pregnancy and early in a child's life.<sup>13,17,18</sup> In particular, thyroid hormones are required for proper development of nerve cells in the brain (i.e., neurogenesis), structural formation of brain regions (i.e., neuronal migration) and nerve cell maturation, including axonal and dendritic formation and growth, synaptogenesis and myelination. Iodine cannot be synthesized by the body, making it an essential nutrient that must be obtained through the diet.<sup>19-22</sup> When consumed, most iodine is absorbed across the digestive tract and is either used by the thyroid gland for thyroid hormone synthesis or by the kidney for urinary excretion. Importantly, about 90% of the iodine that is absorbed is excreted within 24 hours, emphasizing the importance of adequate nutrition to maintain proper levels of this essential micronutrient in the body.

Dairy milk and other dairy foods are significant contributors to iodine adequacy in the diet.<sup>23-25</sup> Other commonly consumed foods that contain iodine include fish, eggs and iodized salt (in countries where iodine fortification is voluntary or mandatory). According to the DGA, women who do not regularly consume foods providing iodine (dairy, eggs, seafood) and/or do not use iodized salt are more likely to have insufficient intakes of iodine and may need to increase intake from dietary supplements. In the U.S. and many European countries, dairy milk and other dairy foods have been shown to be major dietary sources of iodine during pregnancy and lactation and in women of childbearing years, and higher consumption of dairy milk and other dairy foods by pregnant women and women of childbearing years has been shown to increase the likelihood of iodine sufficiency.<sup>26-29</sup> This suggests that women who consume little or no milk and dairy foods may be at increased risk for iodine deficiency. Furthermore, breastmilk iodine content is dependent on maternal iodine intake and is the sole source of iodine for exclusively breastfed infants.

While tracking iodine status at the individual and population level has critical public health implications, there are important gaps and limitations in the U.S. and globally to do so. Considered the current gold standard, WHO recommendations monitoring the iodine status of populations via urinary iodine concentrations (UIC) in spot urine samples. This is a widely used methodology to assess population iodine status in regional surveillance, epidemiology and clinical research.<sup>15</sup> For example, NHANES research utilizes the WHO criteria to classify iodine status by the median UIC as a proxy for iodine consumption in U.S. populations.<sup>26,27,30-32</sup> Yet, since most iodine absorbed by the body is readily excreted in the urine, UIC is considered a sensitive marker of current, but not long-term (i.e., habitual), iodine consumption or thyroid function. As such, UIC is not a reliable indicator of iodine status in individuals, and currently there are no valid biomarkers to assess the iodine status of individuals. Tracking of iodine status through assessment of dietary patterns may be an important method to complement UIC data. Until recently, the iodine content of foods in the U.S. and many countries has been lacking in food databases that are used to assess nutrient consumption in the general public. In 2020, a collaboration of the USDA, the Food and Drug Administration (FDA) and the Office of Dietary Supplements (ODS) led to the development and release of a database containing iodine content of nationally representative foods and dietary supplements (available at FoodData Central, [www.ars.usda.gov/mafcl](http://www.ars.usda.gov/mafcl)),<sup>23-25</sup> which revealed the iodine content of some foods can vary considerably. Sources of variability include the iodine content in soil, irrigation practices, and, for dairy products, the iodine in the cows' diets and/or iodophor sanitizers used to keep cows' udders healthy.<sup>33,37</sup> The iodine content of commercial seaweeds is particularly variable (16 to 2,984 ug/g), and although rarely consumed in the U.S., the consumption of some seaweeds can lead to excessive iodine intakes.<sup>33-35</sup>

In the U.S., the iodine status of most of the population is considered adequate: however, evidence from NHANES research indicates that pregnant women may have mild or borderline iodine deficiency.<sup>26-29</sup> During pregnancy, many hormonal and metabolic changes occur that influence thyroid-related functions. Notably, thyroid hormone production is increased by 50% and placental uptake of maternal thyroid hormones begins early in gestation; thus, iodine requirements are increased during pregnancy.<sup>17</sup> This increased iodine requirement is vital to cognitive development of the fetus during the first half of pregnancy, because fetal neural system development depends on the transfer of maternal thyroid hormones across the placenta.<sup>13</sup> Many health professional organizations in the U.S. and globally recommend that women who are planning to become pregnant and women who are pregnant or lactating take a daily dietary supplement containing 150 ug of iodine.<sup>36-38</sup>

Although evidence is limited, mild-to-moderate iodine deficiency in women of childbearing years and lactating women also may lead to adverse effects on neurocognitive development of the fetus and young child.<sup>18,39</sup> In addition, an emerging body of literature, largely from observational studies, indicates that mild-to-moderate iodine deficiency during pregnancy also may be associated with deficits in neurocognitive development well into the childhood years.<sup>17,18</sup> It is well documented that when maternal iodine consumption during pregnancy is severely deficient, deficits in cognitive development of the child are potentially irreversible.<sup>17,40-43</sup> More research, particularly well-designed, adequately powered cohort studies and randomized controlled trials (RCTs), is needed to better understand neurocognitive outcomes in children of mothers with mild-to-moderate iodine deficiency before and during pregnancy and lactation. The development of robust, validated biomarkers to accurately evaluate iodine status both at the individual and population level will be instrumental to these efforts.

## Choline

Choline supports a diverse number of metabolic and structural functions in the body.<sup>44-46</sup> While choline is notably known as a vital component of cellular one carbon (1-C; **Table 2**) metabolism as a methyl donor, choline also is essential in the body for cholinergic neurotransmission and lipid and cholesterol transport, and plays a structural role in cell membranes (i.e., phosphatidylcholine, sphingomyelin). Humans can synthesize choline, but not in sufficient amounts to meet choline needs across the lifecycle.

At current consumption levels, dairy foods along with meats and eggs are the top 3 food sources of choline.<sup>45,47,48</sup> Food sources of choline include animal-based foods (e.g., meat, eggs and dairy foods) as well as some plant-based foods. Choline is present in foods in both fat-soluble and water-soluble forms, with animal and plant foods generally being rich in fat- and water-soluble forms, respectively.<sup>44</sup> Human milk contains mainly water-soluble forms (primarily phosphocholine and glycerophosphocholine) as does dairy milk (primarily glycerophosphocholine). Choline consumption from dietary supplements has historically been limited because it is commonly absent (or present only in low amounts) in most supplements,<sup>14,49</sup> although that may be changing.

Exclusive breastfeeding is universally recommended, including by the most recent DGA for at least the first six months after birth followed by breastfeeding along with complementary foods, including yogurt and cheese, over the next six months.<sup>14</sup> Choline levels in breastmilk increase rapidly between seven and 22 days after birth and thereafter remain relatively stable.<sup>50</sup> The amount of water-soluble choline is similar in breastmilk of lactating women who consume vegetarian, vegan or non-vegetarian diets.<sup>51</sup> Choline levels in preterm breastmilk are notably lower than those in full-term breastmilk.<sup>50,52</sup> and it has been suggested that preterm infants may be choline deficient at birth.<sup>53</sup>

Most Americans, including pregnant and lactating women, fall short of the recommended amounts of choline.<sup>44,54</sup> The recommended intake (Adequate Intake, AI) for choline by women of childbearing years and during pregnancy and lactation is 425, 450 and 550 mg/d, respectively. Average choline consumption during pregnancy, for example, are 70% of the AI. The DGA encourage women who are pregnant and lactating to consume a variety of choline-containing foods across all food groups.<sup>14</sup> This includes the recommended servings from the dairy and protein food groups and from the beans, peas and lentils subgroup to help achieve amounts compatible with the AI. Increasing consumption of dairy foods from the current 1.85 cup-equivalent servings to the recommended 3 cup-equivalent servings per day could help many pregnant women get closer to meeting choline recommendations.

The importance of sufficient choline consumption during pregnancy is becoming increasingly evident from emerging clinical research and a large body of preclinical animal research. Research on potential health benefits associated with maternal choline status and consumption has focused largely on neurocognitive development of offspring in the first few years after birth, and less so on maternal health and pregnancy outcomes. Overall, studies in humans show that higher choline consumption during pregnancy protects against neural tube defects during fetal development and enhances neurocognitive development into early childhood.<sup>55-60</sup> While based on a more limited body of science, daily consumption of 450-1000 mg choline, which is close to the current AI and up to twice the AI, respectively, has been proposed as an adequate range that can both support fetal development<sup>55-60</sup> and improve pregnancy outcomes.<sup>61</sup> Large-scale, long-term clinical trials that are designed to evaluate the impact of a range of choline consumption levels on a broad scope of clinical outcomes and metabolic health markers are needed to establish recommendations for maternal choline consumption for optimal fetal development and reduced risk of pregnancy complications.

**Table 2.** An overview of cellular one carbon metabolism<sup>a</sup>

<p><b>What is one-carbon (1-C) metabolism?<sup>a</sup></b></p> <p>One carbon metabolism is a multi-nutrient metabolic network centered around folate metabolism. Foliates are 1-C (also known as methyl groups) donors and acceptors in the cell, and this transfer of 1-C units supports cellular metabolism (synthesis and breakdown of various compounds, such as DNA).<sup>82</sup></p>
<p><b>What are 1-C metabolism-related nutrients?</b></p> <p>Folate, vitamin B6, methionine, choline, vitamin B12 and betaine<sup>83</sup></p>
<p><b>How is 1-C metabolism, function and nutrient adequacy linked to health outcomes and cognition?</b></p> <p><b>A child's growth and development are metabolically stressful periods characterized in part by increased requirement of 1-C nutrients.</b></p> <p>The nervous system and brain are particularly sensitive to nutrient availability during development.</p> <p><b>Inadequate consumption of these methyl donor nutrients can impact maternal health, pregnancy and birth outcomes; perinatal growth and development and long-term programming effects.<sup>57,84,85</sup></b></p> <p>One suggested mechanism from animal studies and observational studies is the role of dietary methyl donors (i.e., folate, vitamin B12 and choline) on fetal programming via epigenetic regulation involving DNA methylation before and during pregnancy and lactation.<sup>85,96</sup></p>

<sup>a</sup>Adapted from K. Klatt, personal communication, August 16, 2022

## Vitamin B12

Vitamin B12 is a water-soluble vitamin that is important in cellular metabolism and DNA synthesis, the formation of red blood cells and neurocognitive development beginning early in pregnancy.<sup>62</sup> In particular, vitamin B12 is a critical cofactor for two key enzymes in cellular 1-C metabolism pathways (**Table 2**).<sup>62</sup>

Vitamin B12 consumption is almost exclusively derived from animal foods, including dairy milk and other dairy foods.<sup>63</sup> Other dietary sources include vitamin B12 fortified foods such as ready-to-eat cereals, some nutritional yeasts and dietary supplements (many dietary supplements contain vitamin B12, but in highly variable amounts).<sup>63</sup> According to the DGA, vegetarian and vegan diets may not provide sufficient amounts of vitamin B12 during pregnancy and lactation, for exclusively breastfed infants, and for infants and toddlers due to vitamin B12 intake relying on consumption of animal source foods (and dietary supplements).<sup>14</sup> This aligns with research suggesting that dairy milk and other dairy foods are important dietary sources of vitamin B12 during pregnancy and lactation. For example, an NHANES study showed that pregnant women who consumed 3 or more cup-equivalents of dairy foods daily had higher vitamin B12 intakes than those who consumed 2 cup-equivalents, 1 cup-equivalent or less than 1 cup-equivalent of dairy foods each day.<sup>26</sup> Other NHANES studies also have shown that consumption of vitamin B12 from foods during pregnancy is similar to that of non-pregnant women and in the general U.S. population.<sup>26,64-66</sup>

There are numerous gaps in our current understanding of the vitamin B12 content in breastmilk.<sup>67,68</sup> While limited research indicates that vitamin B12 concentrations in breastmilk can be increased by increasing maternal consumption of B-12-containing foods and with vitamin B12 supplementation during lactation, further research is needed. Overall, a better understanding of sources of variability in breastmilk levels of vitamin B12, specifically maternal blood levels of vitamin B12 and/or methodology for vitamin B12 analyses, is needed. Future research should define reference values for vitamin B12 in human breastmilk, which then will help inform recommendations for vitamin B12 amounts needed during lactation and by infants.

Several published reviews have examined associations between maternal vitamin B12 status before and/or during pregnancy and maternal health, pregnancy and birth outcomes and neurocognitive development of offspring, yet the studies are highly variable in methodology and findings.<sup>62,69-75</sup> Systematic reviews of studies from across the globe, many cross-sectional, report limited and inconsistent evidence for associations between maternal vitamin B12 status and maternal health (including anemia, pre-eclampsia and gestational diabetes).<sup>62,75</sup> Other bodies of literature have shown an increased risk of neural tube defects with low maternal vitamin B12 status<sup>62,71</sup> and that maternal vitamin B12 deficiency during pregnancy may be associated with increased risk of preterm birth and low birthweight in newborns;<sup>72,73,76</sup> yet, findings are inconsistent and more research is clearly needed.

One factor that likely plays a role in the variability among study findings is that vitamin B12 deficiency can be challenging to diagnose, especially in pregnant women.<sup>77,78</sup> The symptoms of vitamin B12 deficiency are not unique to vitamin B12 deficiency, and all of the vitamin B12 status biomarkers typically utilized in health screenings and/or studies are affected by the normal physiological and hormonal changes that take place during pregnancy.<sup>79,80</sup> In addition, a classic symptom of vitamin B12 deficiency, macrocytic anemia, also is a symptom of folic acid deficiency; therefore, high folate status can “mask” vitamin B12 deficiency and supplementation with folate may be recommended.<sup>81</sup>

Overall, more well-designed studies are needed to evaluate the effects of varying degrees of maternal vitamin B12 deficiency and benefits of vitamin B12 consumption or supplementation before and/or during pregnancy and

lactation on neurocognitive development of children. Part of this work will be to clearly define and standardize vitamin B12 biomarker testing and reference ranges for a broad range of populations, including for women before and during pregnancy (each trimester), pregnancy-related complications, different ethnic groups, vegetarians, vegans and for those with pre-existing medical conditions.<sup>77,81</sup>

### **Dairy milk and other dairy foods can help meet recommended amounts of iodine, choline and vitamin B12 during pregnancy and lactation**

Milk, cheese and yogurt are nutrient-rich foods that are important dietary sources of several essential nutrients, including iodine, choline and vitamin B12, for optimal health across the lifespan and particularly for maternal and infant health. Evolving evidence indicates that insufficient consumption of iodine,<sup>17,18,40,41,88,89</sup> choline<sup>24,55-57</sup> and vitamin B12<sup>70,71,90-93</sup> may increase risk for pregnancy complications, preterm birth, low birthweight and/or result in adverse effects on neurocognitive development. Women who are pregnant or lactating, particularly those who do not regularly consume the recommended amounts of dairy foods, may consume inadequate amounts of these nutrients. There is an opportunity to raise awareness about the public health implications of nutrition for early life cognitive development. Dairy foods can be a part of the solution as a nutritious, affordable and accessible source of critical nutrients, including iodine, choline and vitamin B12, to help ensure children have a fair start to a lifetime of wellness.

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