Iodine Insufficiency: A Global Health Problem?\textsuperscript{1,2}

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\section*{ABSTRACT}

As a result of collaborative efforts with international organizations and the salt industry, many developing and developed countries practice universal salt iodization (USI) or have mandatory salt fortification programs. As a consequence, the prevalence of iodine deficiency decreased dramatically. The United States and Canada are among the few developed countries that do not practice USI. Such an undertaking would require evidence of deficiency among vulnerable population groups, including pregnant women, newborns, and developing infants. Government agencies in the United States rely heavily on data from NHANES to assess the iodine status of the general population and pregnant women in particular. NHANES data suggest that pregnant women in the United States remain mildly deficient. This is important, because the developing fetus is dependent on maternal iodine intake for normal brain development throughout pregnancy. Professional societies have recommended that pregnant and lactating women, or those considering pregnancy, consume a supplement providing 150 \( \mu \text{g} \) iodine daily. The United States and Canada collaborate on the daily recommended intake and are also confronted with the challenge of identifying the studies needed to determine if USI is likely to be beneficial to vulnerable population groups without exposing them to harm. \textit{Adv. Nutr.} 4: 533–535, 2013.

\section*{Introduction}

Iodine is an essential nutrient required for reproduction and growth. The only known function of iodine is synthesis of thyroid hormone (TH)\textsuperscript{5}. TH has pleiotropic effects, affecting multiple biological processes. Successful pregnancy and continued normal development of newborns and infants are among the most important outcomes.

Various international agencies (e.g., WHO, the International Committee for the Control of Iodine Deficiency Disorders Global Network, the Micronutrient Initiative, the Global Alliance for Improved Nutrition, and UNICEF) are credited with working with governments and the salt industry in many countries to dramatically reduce iodine deficiency globally since the 1990s. However, despite enormous progress, several research gaps remain and there are still opportunities to improve iodine status, especially of the most vulnerable population groups.

The spectrum of iodine deficiency does not recognize international borders. Prior to the introduction of iodine fortification programs, the prevalence of iodine deficiency was largely determined by the iodine content of the soil. Before the 1920s, a goiter belt was identified across the northern United States, especially around the Great Lakes. Voluntary iodization of table salt was initiated and was effective in reducing the incidence of goiter. About the same time, salt iodization was gradually introduced in Switzerland and iodine deficiency was largely eliminated (1). Today, universal salt iodization (USI), the iodization of all salt consumed by humans and animals, is highly cost effective and remains the mainstay of iodine deficiency prevention efforts worldwide. However, the United States does not have USI. Only \( \sim 70\% \) of table salt sold is iodized, and the majority of U.S. salt intake is from processed foods that are not produced with iodized salt.

\section*{Assessment of iodine status}

Iodine intake is a key determinant of iodine status but is difficult to assess. FFQs (used to assess the type, quantity, and frequency of foods and supplements consumed) exist, but food composition tables for iodine are not readily available. Instead, urinary iodine concentration (UIC) is almost universally used as a proxy for population intake. This index is based on the assumption that most (\( \sim 90\% \)) of the iodine consumed from foods and supplements is absorbed and that the amount excreted in the urine reflects recent intake.
WHO has set criteria for the assessment of school-age children and pregnant and lactating women based on UIC. The population UIC cutoff values expressed as μg/L for school-age children are: <20 (severe deficiency), 20–49 (moderate deficiency), 50–99 (mild deficiency), 100–199 (optimum), 200–299 (risk of iodine-induced hypothyroidism), and ≥300 (risk of adverse health). The corresponding values for pregnancy are: <150 (insufficient), 150–249 (adequate), 250–499 (more than adequate), and ≥500 (in excess of amount to control deficiency). Recent data suggest that using the median values of school-age children to represent the entire population, including pregnant, women is likely inappropriate and requires further consideration (2).

Iodine status is also reflected by measures of thyroid function, including circulating concentrations of thyroid-stimulating hormone (TSH). Testing is performed in newborns in many parts of the world to screen for congenital hypothyroidism. WHO has indicated that TSH concentrations >5 mIU/L should occur in <3% of newborns in iodine-sufficient populations. An important caveat is that the newborn testing must be performed >48 h after birth to be valid, because there is a normal physiological surge in infant TSH concentrations after birth.

### Iodine utilization during pregnancy

Iodine requirements increase during pregnancy due to a variety of physiologic changes. For example, the glomerular filtration rate increases, resulting in increased maternal urinary iodine excretion. Some investigators have suggested that trimester-specific reference UIC values might be more informative than the current WHO values used to represent all stages of pregnancy. Production of maternal TH also increases by ~50% starting in early pregnancy. TH is required for normal cognitive development, sight, and hearing. Fetal TH production does not start until 14–16 wk; before that time, the fetus is reliant on transplacental passage of small amounts of maternal TH. Assuming that maternal iodine intake and pregancy intrathyroidal stores are adequate, maternal transfer of TH to the fetus continues throughout pregnancy, protecting the fetal brain. TSH typically falls and free thyroxine (FT4) increases in the first trimester of pregnancy, largely due to the influence of human chorionic gonadotropin, which acts as a weak stimulator of the TSH receptor. As human chorionic gonadotropin concentrations fall after wk 10 of gestation, TSH tends to rise. Thus, there is a normal physiologic rise in TSH and drop in FT4 from the beginning to the end of pregnancy that needs to be considered in assessing thyroid function. The upper limit of TSH is considered 2.5 mIU/L in the first trimester and 3.0 mIU/L in the second and third trimesters. Assay-specific, trimester-specific, FT4 reference ranges are recommended for use in pregnancy (3,4).

### Iodine supplementation in pregnancy and lactation

Iodine supplementation of pregnant women is clearly beneficial in severely iodine-deficient regions. Data regarding the effects of iodine supplementation in pregnant women who are moderately to mildly iodine deficient are more limited. Mild iodine deficiency does not appear to affect newborn thyroid function. However, long-term randomized studies examining neurodevelopmental outcomes in children are lacking. Such studies are currently being undertaken in Thailand and India.

Several professional societies, including the American and European Thyroid Associations, recommend that women who are considering pregnancy and those who are pregnant or lactating should take a daily supplement that provides 150 μg of iodine. This recommendation, however, has not been widely implemented in the United States (5).

At birth, newborn intrathyroidal iodine stores are limited to ~300 μg. At the same time, the TH requirements of the developing infant are at their highest per kilogram body weight compared with subsequent growth periods and also at a time when adequate TH remains critical for ongoing neurodevelopment. Thus, newborns and infants are particularly vulnerable to iodine deficiency.

There are relatively few reports of iodine status of breastfed compared with formula-fed infants (6). Exclusively breastfed infants rely entirely on maternal iodine intake, which may include iodine supplements. Optimal breast milk iodine content has not been defined, and there are limited data to date to identify optimal supplementation strategies for lactating women and their infants. Commercially prepared infant foods may contain iodine, but standards vary worldwide. When home-prepared complementary foods are introduced, the addition of iodized salt (sodium iodide) is discouraged due to concerns about excessive sodium intake. In severely iodine-deficient parts of the world, large doses of iodine as iodized oil may be administered to breast-feeding mothers and directly to infants at weaning. WHO recommends a single annual dose of iodized oil of 400 mg/y to lactating women and 200 mg/y to weaning infants. The efficacy of this recommendation is currently being tested in a study conducted in Morocco.

### DRI

In 2001, the Institute of Medicine set an adequate intake for iodine for infants 0 through 6 mo (110 μg/d) and 7 through 12 mo (130 μg/d). The adequate intake for a nutrient is generally taken to be the average intake by full-term infants born to healthy, well-nourished mothers and who are exclusively breastfed. This approach also assumes that breast milk provides an amount of a nutrient that exceeds the infant’s actual requirement during the first and second 6 mo of life. If forthcoming evidence indicates that breast milk intake in the United States and/or Canada does not meet the iodine requirements or ensure proper stores in young and/or older infants, then consideration of developing an estimated average requirement would be appropriate.

In conclusion, inadequate iodine intake during pregnancy and lactation can adversely affect the developing fetus and infant. The health consequences of inadequate intake are largely determined by the timing, degree, and duration of iodine insufficiency. International organizations promote
USI as the primary strategy for achieving iodine adequacy worldwide. USI is not practiced in the United States or Canada, because the efficacy and safety of the intervention has not been evaluated in these countries. With the exception of monitoring UIC of a representative sample of the U.S. population through NHANES, the United States and Canada have not made a substantial research investment relevant to iodine and human health of vulnerable population groups in North America. Such information is important to assess the availability of relevant new information that could inform an update of the DRI for iodine.

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Literature Cited