Effects of iodine deficiency in pregnancy

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**A B S T R A C T**

Dietary iodine requirements are increased in pregnancy due to increased thyroid hormone production, increased renal iodine losses, and fetal iodine requirements. Adverse effects of iodine deficiency in pregnancy include maternal and fetal goiter, cretinism, intellectual impairments, neonatal hypothyroidism, and increased pregnancy loss and infant. Dietary iodine requirements remain increased in lactation due to the concentration of iodine in breast milk. Iodine deficiency remains a significant global public health problem. Excess iodine ingestion in pregnancy, while a relatively uncommon problem, may also have adverse fetal effects. However, the safe upper limit for chronic iodine ingestion in pregnancy and lactation is not currently well defined.

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**Introduction**

Adequate maternal iodine intake is required for the synthesis of thyroid hormones that are important for normal fetal and infant neurodevelopment. This review will discuss iodine metabolism, homeostasis, and nutritional recommendations for pregnancy and lactation.

**Dietary iodine requirements in pregnancy**

After oral ingestion, iodide is rapidly absorbed through the stomach and duodenum. Plasma inorganic iodide is then transported through the circulation to be either taken up by the thyroid in varying amounts (5–100% of absorbed iodine), depending on the iodine supply and the functional state of the thyroid [1], or renally excreted. The normal thyroid gland contains approximately 10–20 grams of iodine [2].

Iodine is needed for the production of thyroid hormones, which increases by approximately 50% starting in early pregnancy. In early gestation the thyroid is stimulated not only by thyroid-stimulating hormone (TSH) but by human chorionic gonadotropin (hCG), which also binds to and stimulates the thyroidal TSH receptor [3]. Serum hCG levels peak at 9–11 weeks gestation. In addition, high estrogen levels in pregnant women increase serum thyroxine binding globulin (TBG) concentrations by 1.5-fold, increasing the levels of bound circulating total triiodothyronine (T3) and thyroxine (T4), and requiring an increase in thyroid hormone production in order to maintain free, or unbound, thyroid hormone levels [4]. Type 3 deiodinase (D3), which inactivates thyroid hormones by removing the inner ring iodine from T4 and T3, is present in high concentrations in the placenta, making it an independent site of iodine metabolism [4]. Maternal iodine readily crosses the placenta to the fetus. Starting at about 20 weeks gestation, the fetus requires this iodine supply for its own thyroid hormone production [5]. Finally, another reason for increased maternal iodine requirements in pregnancy is the increase in glomerular filtration rate. Because iodine is passively excreted by the kidney, increased maternal renal glomerular filtration results in increased losses of ingested iodine [6].

Women in iodine sufficient regions typically begin pregnancy with adequate intrathyroidal iodine stores and are able to meet the increased demands of pregnancy as long as they maintain optimal iodine intake. However, in iodine deficient regions, women may begin pregnancy with inadequate intrathyroidal iodine stores which are rapidly depleted [3,7,8]. Because of increased thyroid hormone production, increased renal iodine losses, and the fetal iodine requirements in pregnancy, dietary iodine requirements are higher in pregnancy than they are for non-pregnant adults (Table 1).

Median urinary iodine concentrations can be used to assess population iodine status [9]. Thresholds for median urinary iodine sufficiency have been identified for populations, but not for individuals, given significant day-to-day variation of iodine intake [10]. Population iodine sufficiency is defined by median urinary iodine concentrations 100–199 μg/L in non-pregnant adults and 150–249 μg/L in pregnant women [11].

**Consequences of iodine deficiency in pregnancy**

Consequences of iodine deficiency are most severe for pregnant women and their fetuses, and include goiter, cretinism, intellectual
Table 1
Recommended dietary iodine intakes.

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>0–6 months*</td>
<td>110</td>
<td>0–5 years 90</td>
<td></td>
</tr>
<tr>
<td>7–12 months*</td>
<td>130</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–8 years</td>
<td>90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9–13 years</td>
<td>120</td>
<td>6–12 years 120</td>
<td></td>
</tr>
<tr>
<td>&gt;13 years</td>
<td>150</td>
<td>&gt;12 years 150</td>
<td></td>
</tr>
<tr>
<td>Pregnancy</td>
<td>220</td>
<td>Pregnancy 250</td>
<td></td>
</tr>
<tr>
<td>Lactation</td>
<td>290</td>
<td>Lactation 250</td>
<td></td>
</tr>
</tbody>
</table>

* More conservative adequate intake levels, rather than recommended dietary allowances, are provided for infants 12 months of age and younger.

Table 2
Tolerable upper limits for iodine exposure.

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>0–12 months</td>
<td>Unknown</td>
<td>Infants 180</td>
<td></td>
</tr>
<tr>
<td>1–3 years</td>
<td>200</td>
<td>Pregnancy 500</td>
<td></td>
</tr>
<tr>
<td>4–8 years</td>
<td>300</td>
<td>Lactation 500</td>
<td></td>
</tr>
<tr>
<td>9–13 years</td>
<td>600</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14–18 years</td>
<td>900</td>
<td></td>
<td></td>
</tr>
<tr>
<td>19–50 years (including pregnant and lactating women)</td>
<td>1100</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Consequences of iodine excess in pregnancy

The safe upper limit of iodine intake in pregnancy is controversial. Following exposure to high iodine levels, the synthesis of T4 and T3 is normally acutely inhibited by a process known as the acute Wolff–Chaikoff effect [26]. The mechanism, although not fully understood, appears to rely on newly formed iodolipids or iododolactones temporarily inhibiting thyroid peroxidase synthesis. If high iodine exposure persists, the thyroid is normally able to escape from the acute Wolff–Chaikoff effect within a few days [27] by downregulation of expression of sodium iodide symporter (NIS), the transporter of iodine into the thyroid [27]. While most pregnant women can maintain normal thyroid function in the setting of high iodine exposure, women with subtle defects in thyroid hormone synthesis, such as those with Hashimoto’s thyroiditis, may be unable to escape from the acute Wolff–Chaikoff effect. Such women can develop iodine-induced hypothyroidism [28]. In addition, the fetal thyroid’s ability to escape from the acute Wolff–Chaikoff effect does not fully mature until approximately 36 weeks gestation [29]. Therefore, a large maternal iodine load could selectively cause fetal hypothyroidism. The U.S. Institute of Medicine recommends an upper limit of 1100 µg dietary iodine daily in pregnancy, while World Health Organization (WHO) more conservatively recommends an upper limit of 500 µg per day (Table 2) [11,30]. The benefits of correcting iodine deficiency far outweigh the risks of supplementation as long as supplementation is not excessive [31].

Iodine in lactation

Following delivery, maternal iodine continues to be the only source of iodine for breastfed infants. NIS is expressed in lactating breast tissue and is responsible for concentrating iodine in colostrum and breast milk [32]. A woman who is exclusively breastfeeding excretes approximately 75–200 µg iodine daily in breast milk and therefore requires increased dietary iodine intake to keep up with losses [33,34]. Recommendations for dietary iodine intake during lactation range from 250 to 290 µg/day, higher than the 150 µg/day recommended for non-pregnant and non-lactating adolescents and adults (Table 1).

Adequate breast milk iodine levels are important for normal neurodevelopment in nursing infants. In iodine-sufficient areas, breast milk iodine concentrations are generally adequate to meet infants’ iodine nutritional needs [35]. However, mothers living in iodine deficient areas may be unable to meet the increased demands for iodine intake. In a recent study, the iodine intake of breastfed infants in iodine-deficient New Zealand remained inadequate even when their mothers were supplemented with 150 µg daily iodine during the first 6 post-partum months [36].
Conclusions

Dietary iodine requirements are increased in pregnancy and lactation. Iodine deficiency remains a significant global public health problem. Excess iodine ingestion in pregnancy, while a relatively uncommon problem, may have adverse fetal effects. However, the safe upper limit for chronic iodine ingestion in pregnancy and lactation is not currently well defined. Because pregnant women and their fetuses are particularly vulnerable to iodine deficiency disorders, urine iodine concentrations should be obtained from pregnant women as part of the routine monitoring of population iodine status.

References