Iodine in Human Milk: Perspectives for Infant Health
Richard D. Semba, M.D., M.P.H., and François Delange, M.D.

Iodine is essential for normal growth, mental development, and survival of infants. The main source of iodine for breastfeeding infants is the iodine found in human milk. Despite the importance of iodine for infant health, there have been limited studies addressing human milk iodine concentrations. The newly recommended Adequate Intake of iodine for infants is 110 μg/day for infants 0–6 months and 130 μg/day for infants 7–12 months. Further studies of human milk iodine are needed to ensure that iodine prophylaxis is providing sufficient iodine for mothers and infants worldwide.

**Introduction**

Iodine is essential for synthesis of thyroid hormones, normal growth, mental development, and survival. In 1990, an estimated 1.6 billion people worldwide consumed inadequate amounts of iodine and were at risk for iodine deficiency disorders. Iodine deficiency is the leading cause of preventable mental retardation in the world and has been linked with adverse birth outcomes, including stillbirth, spontaneous abortion, and increased perinatal and infant mortality. The infant brain develops rapidly, especially from birth until the end of the second year, and thyroid hormone is essential for normal brain development. Thyroid hormones appear to ensure the coordination of developmental events through regulation of oligodendroglial and neuronal differentiation and cell death.

Iodine is considered unique among the trace elements in milk because it is avidly concentrated by the mammary gland. The iodine status of breastfeeding infants is largely dependent upon the iodine content of breast milk. In many developing countries, the risk of iodine deficiency among infants is high, especially in areas with a high prevalence of goiter that lack widespread use of iodized salt. The goals of this paper are to provide a brief historic overview of the issue, to summarize the published scientific literature on human milk iodine concentrations, and to discuss the need for further investigations of human milk iodine worldwide.

**Historic Background**

Iodine was discovered in 1811 when Bernard Courtois (1777–1838), a saltpetre manufacturer, burned seaweed and observed violet vapors and black crystal formation. This substance was named iodine by the French chemist Joseph Louis Gay-Lussac (1778–1850) after the Greek word for “violet.” Early advocates for the use of pure iodine as a remedy for goiter included William Prout (1785–1850) and Jean-François Coindet (1774–1834). In 1831, Jean Baptiste Boussingault (1802–1887), an agricultural chemist, promoted the use of naturally iodized salt for prevention of goiter. A method for measuring the quantity of iodine was devised in 1851 by H. Rabourdin. Gaspard Adolphe Chatin (1813–1901) improved Rabourdin’s method to detect minute amounts of iodine, and after measuring iodine in water, soil, air, and foods, Chatin concluded that lack of iodine in drinking water was the cause of goiter and cretinism. Iodine prophylaxis for goiter was implemented by public health authorities in parts of France in the 1860s. By the late 19th century, the geographic distribution of endemic goiter and cretinism was recognized to extend around the world, with detailed accounts available from many countries in Europe. The presence of iodine in milk was demonstrated as early as 1859. In 1924, Theodor von Fellenberg, working in the Bureau of Hygiene in Berne, devised a micro-method of iodine determination based upon the principles of Rabourdin and Chatin, and this method and its adaptations were widely applied to the measurement of iodine in early studies of human milk.

**Metabolism and Physiology of Iodine**

Dietary iodide, the inorganic form of iodine, is rapidly absorbed in the stomach and intestine. Iodate, the form of iodine used in iodized salt, is reduced to iodide in the gut and rapidly absorbed in the bloodstream. Iodide circulates freely in the blood, not bound to proteins, and it is trapped by the thyroid and kidney. Iodine is excreted by the kidney; the concentration of urinary iodine correlates

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well with the intake of iodine. The human body contains approximately 15–20 mg of iodine, of which 70–80% is found in the thyroid gland. The thyroid traps iodine through an active transport mechanism known as the iodine pump, and iodine trapping is regulated by thyroid stimulating hormone (TSH), or thyrotrophin, which is released from the pituitary gland. The iodine content of the thyroid is generally related to iodine intake. In the situation where the iodine supply has been abundant, the thyroid may contain 10–20 mg of iodine, but in a situation of chronic iodine deficiency, the thyroid may contain as little as 200 μg of iodine.

The thyroid, a highly vascularized organ, contains follicles consisting of thyroid cells surrounding colloid. The main constituent of the colloid is thyroglobulin, a storage form of thyroid hormones. Iodine is an essential constituent of thyroid hormones 3,5,3',5'-tetraiodothyronine, thyroxine (T₄), and triiodothyronine (T₃). Thyroglobulin is synthesized from amino acids in thyroid cells and moves into the colloid. Iodide moves into the colloid of the thyroid by passive diffusion. In the colloid, iodide is oxidized by hydrogen peroxide from the thyroid peroxidase system and combines with tyrosine in thyroglobulin to form monoiodotyrosine (MIT) and diiodotyrosine (DIT). MIT and DIT continue oxidation and couple to form iodothyrosines. The iodinated thyroglobulin is absorbed back into thyroid cells by pinocytosis and subsequently undergoes proteolysis, releasing T₃ and T₄ into the blood.

Iodine metabolism and the synthesis of thyroid hormones are regulated by complex interactions involving the brain, pituitary, thyroid, and iodine intake. Iodine uptake by the thyroid, synthesis of MIT and DIT, and secretion of T₃ and T₄ are regulated by TSH, which is secreted by the pituitary. Secretion of TSH, in turn is regulated by the level of circulating TSH as well as by thyrotrophin-releasing hormone (TRH), which is secreted by the hypothalamus. TRH release is influenced by neurotransmitters such as adrenalin, noradrenalin, serotonin, and dopamine. Further details of this complex regulation can be found elsewhere.22

In the blood, T₃ and T₄ are bound by different proteins produced in the liver, such as transthyretin, albumin, and thyroid-binding globulin (TBG). Approximately three-quarters of T₄ is normally bound to TBG. T₃ is found in much higher concentrations in the blood than T₄, and most of the T₃ in plasma is derived from peripheral tissues where it is generated by monodeiodination of T₄. Other metabolic derivatives of thyroid hormones, such as rT₃ and 3,3'-diiodo-L-thyronine, are also found in the blood. Three deiodinases have been identified that catalyze monodeiodination of the outer ring.23 Further deiodination of the inner ring deactivates T₃ and T₄.

During pregnancy, thyroid volume and function adapt in a physiologic manner to meet the increased demands for iodine. In areas of low or moderate iodine intake, thyroid volume increases during pregnancy, whereas thyroid volume does not increase during pregnancy among women with sufficient iodine intake. The renal clearance of iodide is increased during pregnancy, which contributes to the increased iodine requirement during gestation.24 Free T₄ decreases by approximately 15% in the second and third trimesters of pregnancy among women from iodine-replete areas.25 In iodine-deficient areas, the decline is much more marked: up to 30% starting during early gestation.26 The transplacental passage of maternal thyroid hormones is greatly limited by enzymatic deiodination of thyroid hormones by the placenta. Fetal thyroid follicular cells are capable of iodotyronine synthesis by the end of the first trimester of pregnancy, but TSH and T₃ are at extremely low concentrations in fetal serum until 18–20 weeks of gestation.27 TBG, TSH, total T₄, and free T₄ concentrations progressively increase and plateau in fetal serum at 35–37 weeks gestation. Although thyroid hormones are essential for fetal development, including the development of the brain, there is a paucity of quantitative data from humans on the timing of fetal thyroid hormone production and utilization by various tissues of the fetus.28

Thyroid hormones are essential during the period of rapid development in the fetus and young infants, and T₃ receptors are widely expressed in the brain and other organs. Two families of high-affinity thyroid hormone receptors (TR) have been identified: TR-α and TR-β. Of the two TR-α isoforms, TR-α₁ binds thyroid hormone and TR-α₂ does not. Both TR-β isoforms bind thyroid hormone. TR isoforms are differentially expressed in brain and tissues, and brain gene expression is modified by thyroid hormones through TR, including that of Purkinje cells, telencephalic neurons, oligodendrocytes, and cerebellar granule cells.10 Thyroid hormones play an important regulatory role in the secretion of growth hormone29 and bone cell growth and differentiation.30 Some of the consequences of inadequate maternal iodine status during fetal development are miscarriages, stillbirths, congenital anomalies, impaired brain function, cretinism, and goiter.1-4,12 Infants are born with little iodine storage. In full-term infants, the neonatal thyroid contains approximately 100 μg of iodine under conditions of iodine sufficiency.29 Further sources of iodine in human milk are necessary to meet the demands for iodine during infancy.

**Physiology of Iodine Secretion in Human Milk**

The mammary gland is able to concentrate iodide during pregnancy and lactation,30,31 and this concentrating mechanism appears to ensure an adequate supply of iodine to the newborn.32 Iodine in human milk is often found at concentrations that are 20–50 times higher than plasma.32,33 Sodium iodide symporter (NIS), an intrinsic membrane pro-
tein, mediates the transport of iodide into the thyroid. Iodide transport is a sodium-dependent process that can be blocked by perchlorate and thiocyanate. The NIS gene has been isolated and cloned. The sodium iodide symporter also appears to control iodide uptake by the mammary gland, and expression of NIS increases during lactation. The main mechanism for iodide transport is probably the sodium-dependent mechanism, but an alternative anion-exchange pathway has also been identified.

Early studies showed that after radioiodide administration, the level of activity of iodine in milk could rise much higher than the plasma concentration. Nearly 80% of total iodine in mature human milk is in the form of iodide (I⁻), and the remainder is organic iodine. T₃ and T₄ are present in milk and constitute a small proportion of the total iodine in human milk. Early studies demonstrated the biologic iodination of milk proteins, that the mammary gland forms monoiodotyrosine, diiodotyrosine, and other iodinated compounds, and that the site of iodination is primarily within alveoli. T₄ was described in human milk, and subsequent studies using radioimmunoassay showed that T₄ usually occurs in very low concentrations of <2 µg/L. Most reports show that T₄ occurs in human milk in low concentrations of <0.05 µg/L. Although one case report suggested that breastfeeding reduced cretinism in an athyrotic infant, a subsequent case series did not confirm that breastfeeding alone was sufficient to ameliorate cretinism among infants. In general, the concentrations of T₃ and T₄ appear to be insufficient to constitute a significant source of thyroid hormones for neonates, but human milk appears to supply the iodine needed for the neonate to make thyroid hormones. Tracer studies also suggest that milk thyroxine is largely destroyed in the gut of suckling animals.

Prolactin stimulates iodide accumulation in cultured murine mammary glands and appears to stimulate the expression of NIS. A recent study suggests prolactin acts via the polyamine pathway to regulate iodide uptake and incorporation into the mammary gland. Seasonal variation has been observed in the iodine content of cows’ milk, but no seasonal variation has been noted in iodine concentrations in human milk. None of the human studies to date have been specifically designed to examine seasonal variation in human milk iodine. Iodine deficiency has been associated with dysplasia and atypia in the rat mammary gland, suggesting that iodine is important in maintaining the structural integrity and function of the mammary gland.

The secretion of ¹³¹I in human milk has been described in several reports that provide insight into the metabolism of iodine. Ingestion of diagnostic tracer doses of ¹³¹I is followed by almost complete absorption from the gastrointestinal tract. A large proportion of ¹³¹I is taken up by the thyroid gland in the euthyroid individual, and smaller amounts are concentrated in the salivary glands, gastric mucosa, choroid plexus, ciliary body, and sweat glands. In a lactating woman, ¹³¹I is concentrated against a plasma gradient, and significant uptake of radioactive iodine has been observed in the thyroid of infants who are breastfeeding from mothers receiving ¹³¹I. It has been suggested that the use of ¹³¹I for imaging studies be avoided during lactation because of the long period (approximately 40 days) in which ¹³¹I is found in appreciable quantities in milk.

### Iodine Content of Human Milk

Although the presence of iodine in human milk has been known since the mid-19th century, most reports on the concentration of iodine in human milk began to emerge in the 1920s from Switzerland, Germany, and New Zealand. There has been a dearth of reports on the iodine content of human milk in the world’s scientific literature, despite the importance of iodine to infant health (Table 1). The existing studies of iodine in human milk have not determined whether there are within-feed or diurnal variations of iodine concentrations in human milk. Generally, these studies show that the mean iodine content of human milk is relatively low (9–32 µg/L) in women from areas with a high prevalence of goiter, and among women diagnosed with goiter (13–18 µg/L). The prevalence of cretinism can reach 5–15% among breastfeeding populations that have a high prevalence of goiter.

Human milk iodine concentrations are higher in areas where salt iodization occurs, with median concentrations of 146 µg/L reported from North Carolina in an often-cited study by Gushurst and colleagues, and 92 µg/L reported in Eskilstuna, Sweden. These studies suggest that salt iodization is largely effective in increasing the human milk iodine content. Median human milk iodine concentrations were also found to be higher among women who received supplements containing iodine compared with women who received no supplements, although a recent study from Italy showed no impact of iodine supplementation upon milk iodine in well-nourished women. None of these studies were actual randomized, controlled clinical trials of iodine supplements, but rather, milk iodine concentrations were measured in women who reported use or no use of iodine supplements during pregnancy. In Germany, relatively higher milk iodine was reported among mothers who took 200 µg iodine/day during pregnancy, but compliance and duration of supplementation were not described.

The iodine concentration in human milk is highest in colostrum and then it appears to decrease and remain steady in mature milk. In human colostrum, iodine concentrations of approximately 200–400 µg/L have been reported. Thyroid function in lactating women ap-
Table 1. Reports of the Iodine Content of Human Milk

<table>
<thead>
<tr>
<th>Year</th>
<th>Location</th>
<th>n$^1$</th>
<th>Mean$^2$ (SD or SEM$^3$) or range (ng/L)</th>
<th>Remarks</th>
<th>Investigator</th>
</tr>
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<tbody>
<tr>
<td>1926</td>
<td>Berne</td>
<td>–</td>
<td>50</td>
<td></td>
<td>Fellenberg$^{21}$</td>
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<tr>
<td>1926</td>
<td>Stuttgart</td>
<td>12</td>
<td>15–150</td>
<td></td>
<td>Scheurlen$^{24}$</td>
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<tr>
<td>1926</td>
<td>Munich</td>
<td>2</td>
<td>490–440</td>
<td>1 Day after iodine supplement</td>
<td>Maurer &amp; Diez$^{23}$</td>
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<td>1927</td>
<td>New Zealand</td>
<td>14</td>
<td>28</td>
<td>Goitrous area</td>
<td>Hercus &amp; Roberts$^{26}$</td>
</tr>
<tr>
<td>1931</td>
<td>New Zealand</td>
<td>4</td>
<td>43</td>
<td>Nongoitrous area</td>
<td>Hercus et al.$^{77}$</td>
</tr>
<tr>
<td>1933</td>
<td>Boston</td>
<td>10</td>
<td>124</td>
<td>Nongoitrous area</td>
<td>Turner$^{78}$</td>
</tr>
<tr>
<td>1933</td>
<td>Düsseldorf</td>
<td>9</td>
<td>145</td>
<td>Goitrous area</td>
<td>Eyckerman$^{79}$</td>
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<tr>
<td>1934</td>
<td>Vienna</td>
<td>–</td>
<td>75</td>
<td>5 Days after delivery</td>
<td>Leipert$^{80}$</td>
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<tr>
<td>1934</td>
<td>Lwow</td>
<td>4</td>
<td>82–450</td>
<td>Colostrum</td>
<td>Elmer &amp; Rychlik$^{91}$</td>
</tr>
<tr>
<td>1969</td>
<td>Providence</td>
<td>4</td>
<td>45–50</td>
<td>5 Days after delivery</td>
<td>Man &amp; Benotti$^{82}$</td>
</tr>
<tr>
<td>1983</td>
<td>Paris</td>
<td>1</td>
<td>70</td>
<td>Case report</td>
<td>Texier et al.$^{83}$</td>
</tr>
<tr>
<td>1983</td>
<td>California</td>
<td>16</td>
<td>142 ± 81$^4$</td>
<td></td>
<td>Bruhn &amp; Franke$^{84}$</td>
</tr>
<tr>
<td>1984</td>
<td>North Carolina</td>
<td>37</td>
<td>146$^5$</td>
<td>Mature milk</td>
<td>Kosta et al.$^{85}$</td>
</tr>
<tr>
<td>1984</td>
<td>Paris</td>
<td>68</td>
<td>82</td>
<td></td>
<td>Gushurst et al.$^{86}$</td>
</tr>
<tr>
<td>1984</td>
<td>Germany</td>
<td>50</td>
<td>18$^1$</td>
<td>Mothers with goiter</td>
<td>Etling &amp; Gehin-Fouque$^{41}$</td>
</tr>
<tr>
<td>1986</td>
<td>Brussels</td>
<td>91</td>
<td>95</td>
<td>5 Days after delivery</td>
<td>Biernaux$^{84}$</td>
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<td>1986</td>
<td>Verona</td>
<td>23</td>
<td>48 ± 2$^4$</td>
<td></td>
<td>Heidemann et al.$^{90}$</td>
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<td>1986</td>
<td>Göttingen</td>
<td>41</td>
<td>25</td>
<td>Recent salt iodization</td>
<td>Delange et al.$^{29}$</td>
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<tr>
<td>1988</td>
<td>Zaire</td>
<td>143</td>
<td>13</td>
<td>Salt iodization present</td>
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<tr>
<td>1988</td>
<td>Jena</td>
<td>52</td>
<td>12</td>
<td>Severe goiter, no therapy</td>
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</tr>
<tr>
<td>1989</td>
<td>Brussels</td>
<td>10</td>
<td>1267</td>
<td>After topical povidone iodine</td>
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</tr>
<tr>
<td>1989</td>
<td>Brussels</td>
<td>91</td>
<td>95</td>
<td></td>
<td>Delange &amp; Bürgi$^{91,92}$</td>
</tr>
<tr>
<td>1989</td>
<td>Paris</td>
<td>68</td>
<td>82</td>
<td>Area with endemic goiter</td>
<td>Delange &amp; Bürgi$^{91,92}$</td>
</tr>
<tr>
<td>1989</td>
<td>Stockholm</td>
<td>60</td>
<td>93</td>
<td></td>
<td>WHO/IAEA$^{93}$</td>
</tr>
<tr>
<td>1989</td>
<td>Madrid</td>
<td>69</td>
<td>77</td>
<td></td>
<td>WHO/IAEA$^{93}$</td>
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<tr>
<td>1989</td>
<td>Freiburg</td>
<td>41</td>
<td>25</td>
<td>Area with endemic goiter</td>
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<td>1989</td>
<td>Sicily</td>
<td>31</td>
<td>27</td>
<td></td>
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<tr>
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<td>1989</td>
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<td>11</td>
<td>57</td>
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<tr>
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<td>Nigeria</td>
<td>7</td>
<td>62</td>
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<tr>
<td>1990</td>
<td>Guatemala</td>
<td>25</td>
<td>60</td>
<td></td>
<td>WHO/IAEA$^{93}$</td>
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<tr>
<td>1990</td>
<td>Wellington</td>
<td>14</td>
<td>145</td>
<td>&lt;30 Days after delivery</td>
<td>Johnson et al.$^{94}$</td>
</tr>
<tr>
<td>1992</td>
<td>Sicily</td>
<td>11</td>
<td>32 ± 7$^4$</td>
<td>Goitrous area</td>
<td>Vermiglio et al.$^{95}$</td>
</tr>
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<td>1994</td>
<td>Denmark</td>
<td>95</td>
<td>34$^4$</td>
<td>No iodine supplements</td>
<td>Norh et al.$^{96}$</td>
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<td>1995</td>
<td>Ankara</td>
<td>25</td>
<td>109 ± 50$^3$</td>
<td>Iodine supplements</td>
<td>Gökman &amp; Dagh$^{97}$</td>
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<tr>
<td>1999</td>
<td>Italy</td>
<td>10</td>
<td>150 ± 90$^3$</td>
<td>30 Days after delivery</td>
<td>Chierici et al.$^{94}$</td>
</tr>
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<td>1999</td>
<td>Korea$^7$</td>
<td>39</td>
<td>892 ± 1036$^3$</td>
<td>4 Weeks after delivery</td>
<td>Moon and Kim$^{99}$</td>
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<td>1999</td>
<td>Thailand</td>
<td>75</td>
<td>51$^3$</td>
<td>Taking seaweed supplement</td>
<td>Pongpaew et al.$^{100}$</td>
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<tr>
<td>1999</td>
<td>Germany$^8$</td>
<td>40</td>
<td>55 ± 58$^1$</td>
<td>Without iodine supplements</td>
<td>Seibold-Weiger et al.$^{101}$</td>
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</table>

$^1$ The exact number of subjects was not stated in all studies.
$^2$ Some figures were rounded for consistency in table.
$^3$ Standard deviation.
$^4$ Standard error of the mean.
$^5$ Median noted here because of skewed distribution of values.
$^6$ Infants born <35 weeks gestation.
$^7$ There was a high consumption of seaweed soup among lactating women in this population.
$^8$ All mothers of preterm infants.
pears to depend upon the iodine status of the mother during and after pregnancy, and the uptake of iodine by the mammary gland during lactation may reduce the maternal iodine pool in the situation of inadequate iodine status. The United States, the reported mean values for iodine concentration in mature human milk have varied considerably over the last five decades. A mean iodine concentration of 70 μg/L in human milk was widely quoted in the 1950s and 1960s based upon work by Macy and colleagues. The estimates for the iodine concentration in mature human milk was revised by the Committee on Nutrition in 1985 to a mean (±SD) of 110 ± 40 μg/L. The greater use of iodine by the bread and dairy industries has contributed to an increase in consumption of iodine from foodstuffs.

As is clear from Table 1, most of the published studies of the iodine content of human milk have lacked the sample size and power to determine with sufficient accuracy the proportion of women with inadequate iodine concentrations in breast milk. For example, if a cross-sectional study of human milk iodine were aimed to determine the prevalence of women with inadequate iodine content with an accuracy of ±5%, and the “true” prevalence was 20%, the study would require a sample size of 300 women to obtain an expected value of 20% with a 95% confidence interval of 15.6–25.0%. The insufficient sample sizes in many studies have made it difficult to interpret some results that seem improbable, e.g., the higher human milk iodine found in goitrous areas of Detroit compared with nongoitrous Boston, or the slight differences in human milk iodine between goitrous and nongoitrous areas of New Zealand and Sicily. Many of these studies lacked sufficient sample size and were underpowered to address differences between goitrous and nongoitrous areas.

In the future, from a practical standpoint, most surveys of iodine concentration in human milk will need to draw upon a clinic-based sample of women who are breastfeeding, such as women who could be reached when their infant is seen for childhood immunizations or for a well baby check.

**Infant and Maternal Requirements for Iodine**

The Food and Nutrition Board of the Institute of Medicine has made new recommendations of iodine intake for infants and for pregnant and lactating women (Table 2). The Adequate Intake (AI) is the recommended level of intake for infants, and these estimates were based upon a median concentration of iodine in human milk of 146 μg/L multiplied by an average milk excretion of 0.78 L/day to equal 114 μg/day. The new recommendations also take into consideration iodine balance studies that were conducted in full-term and preterm infants. Positive iodine balance in the young infant, enough to accommodate the increasing iodine stores of the thyroid, is only achieved when the iodine intake is 15 μg kg⁻¹ day⁻¹ in full-term infants and 30 μg kg⁻¹ day⁻¹ in preterm infants. Under these conditions, normative values for iodine in human milk may need to be in the range of 100–200 μg/L, and women who are breastfeeding have a recommended dietary allowance of 200–300 μg of iodine per day. The World Health Organization (WHO) recommends that infants aged 0–12 months receive 90 μg iodine/day (Table 2), compared with the AI of 110 μg iodine/day for infants 0–6 months and 130 μg iodine/day for infants 7–12 months.

The actual intake of iodine in the United States may be higher in infants than the newly established AI. Dietary intake of iodine among typical infants in the United States based on food analysis was estimated to be 575 ± 196 μg/day, which is approximately 4.4–5.2 times the AI, using the AI range of 110–130 μg/day for infants. The Department of Foods and Nutrition of the American Medical Association concluded that there was no evidence for adverse physiologic reactions associated with iodine intakes up to 1000 μg/day in healthy children.

The Estimated Average Requirement (EAR) of iodine for pregnant women is 160 μg iodine/day, based upon iodine supplementation studies in pregnant women. The Recommended Dietary Allowance (RDA) of iodine for pregnant women is defined as the EAR plus twice the coefficient of variation (CV) to cover 97–98% of individuals in this group. Thus, the new RDA for pregnant women is 220 μg iodine/day, which is close to the WHO recommendation of 200 μg iodine/day for pregnant women. For lactating women, the EAR was estimated based upon the average requirement of adolescent girls and nonpregnant women of 95 μg iodine/day and the average daily loss of 114 μg iodine in human milk, giving an EAR of 209 pg/day.

<table>
<thead>
<tr>
<th>Table 2. Recommendations for Iodine Intake (μg/day)</th>
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<tr>
<td><strong>Group</strong></td>
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<tr>
<td>Infants, 0–6 months</td>
</tr>
<tr>
<td>Infants, 7–12 months</td>
</tr>
<tr>
<td>Pregnant women</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Lactating women</td>
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<td></td>
</tr>
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</table>

Note: AI = Average Intake, EAR = Estimated Average Requirement, RDA = Recommended Dietary Allowance.
μg iodine/day.110 The RDA for iodine for lactating women is defined as the EAR plus twice the CV, assuming in this situation a CV of 20%, to give an RDA of 290 μg iodine/day. The current WHO recommendation for lactating women is somewhat less, at 200 μg iodine/day.112

Hypothyroidism can occur among infants who are exposed to excessive amounts of iodine.113 Excessive concentrations of iodine can be found in human milk after application of topical povidone-iodine solution for cesarean section or epidural anesthesia,29,114 and another direct route of exposure of infants is through transcutaneous absorption of iodine antiseptics.115 A thirteenfold increase in breast milk iodine concentration was found after a single application of topical povidone-iodine solution in preparation for cesarean section.116 In Korea, there is a tradition of serving seaweed soup, a rich source of iodine, to lactating women, and among women with this practice, high milk iodine concentrations have been reported; extremely high milk iodine was also found in women taking seaweed health food supplements.99

**Laboratory Methods for Determination of Iodine in Milk**

The conventional methods for measuring iodine in human milk were based upon the methods originally devised by Rabourdin and Chatin, with some modifications.21,79 A closed system was developed by McClendon and colleagues in the 1930s for quantitation of iodine,117 but this method proved to be more difficult to use in subsequent studies. Further microchemical methods were developed that involved colorimetric determinations of iodine in milk.78,118,119 Microchemical methods are relatively tedious and have presented problems in reproducibility owing to losses during alkali digestion or by the presence of substances interfering with colorimetric reactions. Ion-selective electrodes can be used to determine the concentration of iodine in milk,120-122 and this technique is more simple and allows a more rapid measurement than previous chemical procedures. Other methods that have been used for determination of iodine concentrations in milk include x-ray fluorescence spectrometry,120 a kinetic-catalytic method,97 and radioactivation analysis.123 Iodine in milk can also be determined by the colorimetric method of the Sandell-Kolthoff reaction124 using an auto-analyzer,125 provided that the samples are carefully homogenized before being submitted to ashing. Although the newer techniques have made it easier to process large numbers of milk samples, this does not imply that the older data are unreliable. In general, the older data from studies conducted from 1920 to 1940, prior to more widespread use of iodized salt, are consistent with new data from recent studies conducted among populations with and without use of iodized salt.

**Discussion**

This literature review shows that the iodine content of human milk is extremely variable, ranging from 9 μg/L in severely iodine-deficient populations to 146 μg/L in North America, where the mean value is estimated at 110 ± 40 μg/L.11,106 The concentration of iodine in breast milk is much higher in colostrum than in mature milk and is closely related to the iodine concentration in urine of both the mother and the infant. Breast milk iodine constitutes another index of the status of iodine nutrition and is particularly important because breast milk is the single source of iodine for millions of breastfed infants in developing countries during the critical period of brain development.

The recommendations for iodine intake in the United States have recently been revised by the Food and Nutrition Board of the Institute of Medicine and take into account studies of iodine in human milk, iodine balance studies, and studies of iodine supplementation in pregnant women.110 The current WHO recommendations for daily iodine intake of 90 μg/day for infants during breastfeeding and 200-300 μg/day for lactating women was estimated to ensure that the iodine content of breast milk is in the range of 100-200 μg/L, i.e., the level that is achieved in iodine-replete populations such as in the United States.86 This level is not achieved in endemic goiter areas and even in many European countries with persistent, mild-to-moderate iodine deficiency.112 The global epidemiology of iodine deficiency disorders has been changing drastically in the last two decades because of the massive implementation of programs of iodine supplementation, especially the systematic use of iodized salt. In addition, a relative increase in the iodine content of cow's milk and meat appear to have contributed to the increase in human milk iodine in the United States66 and in parts of Europe.57

As indicated by a recent WHO, UNICEF, and International Council for Control of Iodine Deficiency Disorders report to the World Health Assembly in 1999,126 of 1.6 billion people living in countries with iodine deficiency disorders, 68% now have access to iodized salt. Of 130 countries affected by iodine deficiency disorders, 104 countries (81%) have an intersectoral coordinating body and 98 (75%) have legislation in place for iodized salt. This constitutes an unprecedented public health success in the field of noncommunicable diseases. Major challenges remain in ensuring the sustainability of salt iodization through monitoring and enforcement. The goals for monitoring include a proportion of 90% of households consuming effectively iodized salt, and urinary iodine in the normal range (median between 100-200 μg/L). The lower level of 100 μg/L is necessary to ensure normal brain development in the fetus and young infant, and the upper level of 200 μg/L is to minimize the occurrence of iodine excess such as iodine-induced hyperthyroidism.127,128 An
additional indicator could include the proportion of lactating women whose breast milk iodine concentration reaches a critical threshold of 100 μg/L.

Conclusions

In areas where iodine deficiency disorders are endemic, it is reasonable to anticipate that effective iodine prophylaxis will result in improved birth outcomes, better infant growth and mental development, and lower infant mortality. Although great progress has been made in improving access to iodized salt worldwide, in many developing countries, noniodized salt continues to be sold in local markets. The monitoring of milk iodine concentrations provides a simple and noninvasive means to assess whether the dietary needs for iodine are being met for both mother and infant. Human milk iodine concentrations are a useful indicator of monitoring the effectiveness of iodine prophylaxis. Further surveys with adequate sample size and power are needed from countries worldwide to assess the adequacy of iodine prophylaxis for maternal and infant health.

Acknowledgments

Supported in part by the National Institutes of Health (HD30042, HD32247), the Fogarty International Center, the United States Agency for International Development (Micronutrients for Health, Cooperative Agreement HRN-A-00-97-00015-00), and the International Council for Control of Iodine Deficiency Disorders.

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