Are Weaning Infants at Risk of Iodine Deficiency Even in Countries with Established Iodized Salt Programs?

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Abstract

Because iodine deficiency (ID) during infancy can irreversibly impair neurodevelopment and increase mortality, it is critical that dietary iodine is adequate in this vulnerable group. Lactating mothers consuming iodized salt can transfer adequate iodine to the infant via breast milk, but during the weaning period, infants are at risk for ID for several reasons: (1) requirements per kg bodyweight for iodine and thyroid hormone during infancy are higher than at any other time in the life cycle; (2) experts recommend no extra salt (iodized or not) be given to infants during the first year; (3) cow’s milk (a major source of dietary iodine in many countries) is also not recommended for infants during the first year; and (4) iron deficiency, a common disorder during infancy, can impair iodine metabolism and reduce thyroid hormone production. For many weaning infants in industrialized countries, iodine fortified into commercial infant foods becomes important. This has recently been demonstrated in Switzerland, where a long-standing iodized salt program provides adequate iodine to pregnant women and school-age children, but new national data suggest weaning infants not receiving iodine-containing commercial baby foods have inadequate iodine intakes. Thus, even in countries with effective iodized salt programs, infants may be at risk of ID during weaning and may need additional dietary and/or supplemental sources of iodine.

Iodine deficiency (ID) during early life may cause irreversible damage to the developing brain [1]. In regions of moderate-to-severe ID, many infants and pregnant women have low circulating levels of thyroid hormone [2]. Thyroid hormone is required for normal neuronal migration and myelination of the brain during fetal and early postnatal life. Hypothyroidism during these
critical periods can cause mental retardation and neurological abnormalities [3]. Prevention of ID during infancy not only improves neurodevelopment, it may also reduce infant mortality. In a randomized, placebo-controlled trial of oral iodized oil (100 mg iodine) in Indonesian infants (n = 617) treated at ≈6 weeks of age, there was a 72% decrease in risk of infant death [4]. Similarly, in a large cross-sectional study in Indonesia, use of adequately iodized salt was associated with a lower infant mortality rate [5]. The potential adverse effects of mild-to-moderate ID during infancy remain unclear, as no well-controlled studies have tested the effects of iodine repletion at this age. However, infant requirements per kg bodyweight for iodine and thyroid hormone are much higher than later in life. Even in areas of iodine sufficiency, a newborn's thyroidal iodine reserve is small, only ≈300 μg [6], and thyroxine turnover is high, with estimated production rates of 5–6 μg/kg bodyweight per day in infancy [7]. Thus, the infant needs a regular supply of dietary iodine to maintain euthyroidism.

National programs to control ID should therefore emphasize this vulnerable period. In most countries, the most effective strategy against ID is salt iodization because salt is one of few foodstuffs regularly consumed by most of the population through the year [8]. Since 1990, a major global effort has increased the number of households using iodized salt from <20% to >70%, dramatically reducing ID [9]. However, the International Council for the Control of Iodine Deficiency Disorders (ICCIDD) estimates 1.88 billion individuals globally still have an insufficient iodine intake, including nearly 1/3 of all school-age children, and ID remains a public health problem in 32 countries [10]. ID is not only a problem in developing regions; it also affects many industrialized countries. About 50% of continental Europe remains mildly iodine deficient, and iodine intakes in other industrialized countries, including the US, the United Kingdom and Australia, have fallen in recent years. ID has reappeared in Australia and the United Kingdom, mainly due to declining iodine residues in milk products because of decreased iodophor use by the dairy industry. In the US, the median UI is 160 μg/l (95% CI: 146–172), still adequate but half the median value of 321 μg/l found in the 1970s [11], and pregnant women who consume few dairy products may be at risk of ID [12]. In most industrialized countries, because 70–90% of salt consumption is from purchased processed foods, if only household salt is iodized, it will not supply adequate iodine. In order to successfully control ID, it is critical that the food industry use iodized salt whenever possible [13]. If both household and industry salt are iodized, salt iodization can deliver adequate iodine to most age groups, including children and adults. Whether it can also deliver adequate iodine during infancy is, however, uncertain [14].

A central problem to monitoring iodine status in infancy is the iodine requirement for this age group has not been well defined. The US Institute of Medicine [15] estimated an adequate intake (AI) for infants because there was not sufficient scientific evidence to calculate an Estimated Average Requirement. The AI, 110 μg and 130 μg/day for ages 0–6 and 6–12 months, respectively, is derived
from the mean iodine intake of healthy infants fed human milk, based on a median breast milk iodine content (BMIC) of 146 μg/l in US women in the early 1980s [15]. But because iodine intakes in the US population were excessive at that time, the BMIC used to set the AI was at the upper end of the range of 78–167 μg/l reported for iodine-sufficient countries [16]. Although high maternal iodine intakes can result in high BMIC, iodine intakes by the infant greater than requirements will simply be excreted in the urine. Thus, iodine requirements during lactation should be based on infant balance studies, and a single small balance study in Belgian infants found iodine retention was 7.3 μg/kg per day [17]. If the reference bodyweight at 6 months of age is 7 kg [15], an infant at this age would be in positive balance at a daily intake of ≈50 μg. The WHO has set a Recommended Nutrient Intake (RNI) of 90 μg/day for iodine during infancy [8]. But clearly more data are needed, preferably from a large, carefully controlled balance study, to better define the iodine requirement during infancy.

Lactating mothers consuming iodized salt transfer iodine to the infant via breast milk. During lactation, the mammary gland actively concentrates iodine via the Na/I symporter [18] and secretes it into breast milk. Because the gland is able to concentrate iodine, iodine supply to the newborn via breast milk may be at least partially maintained even during maternal ID [19]. However, a recent New Zealand study in iodine-deficient mothers reported a significant fall in BMIC during the first 6 months of lactation [20]. In contrast, in iodine-sufficient lactating women in the US with a median urinary iodine concentration (UIC) of 114 μg/l, the median BMIC was 155 μg/l [21]. A review of BMIC in iodine-sufficient countries found a wide range of mean or median concentrations, from 50 μg/l in Finland to 270 μg/l in the US, but sample sizes were small and not representative [16].

Although breast milk can supply adequate iodine to infants, as they are weaned from breast milk, usually in the second half of the first year, their dietary iodine intakes may fall. With the exception of some sea foods, the native iodine content of most foods is low [22, 23]. Residues from iodophors used during dairying and transport of milk can increase the iodine content of dairy products [13]. But iodized salt, either used in the household or added to processed foods, is the primary source of iodine in the diets of many countries. For example, the two main sources of dietary iodine in the US and Switzerland are bread containing iodized salt and dairy products [23, 24]. However, iodized salt may not contribute significantly to infant iodine intakes because pediatricians and nutritionists recommend no extra salt (iodized or not) be given to infants during the first year. After breastfeeding for 6 months, mothers are encouraged to feed their infants home-prepared complementary foods (CF) without added salt [25, 26]. Moreover, cow’s milk (a major adventitious source of dietary iodine in older children) is also not recommended for infants during the first year [26].

Thus, for many weaning infants in industrialized countries, iodine added to commercial infant foods becomes an important iodine source. In the New
Zealand Total Diet study, which simulated typical diets, iodine-containing infant formula/foods provided 60% of iodine intakes for infants older than 6 months [27]. In the US Total Diet Study, 90% of iodine intake in infants older than 6 months was provided by infant formula/foods and dairy products [28].

In national programs to control ID, regular monitoring of iodine status in target populations is important to detect both low and excessive intakes of iodine. For monitoring, WHO recommends using the median UIC from a representative sample of spot urine collections to classify a population's iodine status [8]. Because >90% of dietary iodine eventually appears in the urine, UIC is an excellent indicator of recent iodine intake. In monitoring programs, it has been traditionally assumed that if the general population is iodine sufficient, infants will be also iodine sufficient. But this assumption has not been rigorously tested as there have been no national studies assessing infant iodine status in countries with established iodized salt programs where the general population has adequate iodine intakes. One reason for the lack of data in infants is the difficulty of obtaining spot urine samples to measure UIC. However, a simple noninvasive method for collection of spot urine samples from infants has recently been developed and validated [29]. An absorbent pad (e.g. a feminine hygiene pad that is free of iodine) is inserted inside the diaper and the infant is breastfed. Several milliliters of urine absorbed by the pad can be aspirated into a syringe for measurement. WHO recommendations state a median (m)UIC ≥100 μg/l in a representative population of infants indicates they have adequate iodine nutrition [8].

Switzerland has a model iodized salt program that was initiated in 1922; in national surveys in 1999 and 2004, >90% of households were using iodized salt, and school children were iodine sufficient [30, 31]. The objectives of a recent Swiss study [32] were to first measure UIC in a national sample of pregnant women and school children to confirm that the Swiss population remains iodine sufficient, and then to collect UIC data from a nationally representative sample of infants. The mUIC (95% CI) in school children (n = 916) and pregnant women (n = 648) was 120 (120–128) and 162 (144–177) μg/l, respectively, indicating iodine sufficiency in both groups. Spot urine samples were collected from infants at 3–4 days after delivery, at 6 months ± 6 weeks or at 12 months ± 6 weeks. Inclusion criteria for the mother-infant pairs were: (1) full-term, healthy pregnancy; (2) parental residence in Switzerland for ≥12 months before delivery and since delivery; (3) no history of thyroid disorders in the mother; (4) no ingestion of iodine-containing drugs or contrast media during gestation; (5) delivery without use of iodine-containing disinfectants, and (6) no health problems in the infant. Breast milk iodine concentrations (BMIC) were measured in the mothers of the infants at 6 and 12 months. The iodine concentration of commercial infant foods was directly analyzed, including infant formulas, follow-on formulas and commonly-consumed baby cereal products. The relative contributions of BMIC, infant formula milk (IFM) and CF to iodine intakes in the infants were estimated.
Twenty-four participating clinics provided samples from exclusively breast-fed infants on days 3 or 4 after birth (n = 368: day 3, n = 248, day 4, n = 120). Overall, mUIC was 91 μg/l; at day 3, mUIC was 87 μg/l and at day 4, it was 100 μg/l (table 1). Among the mothers, 65% (n = 241) were taking supplements, but only 0.8% (n = 3) were consuming iodine-containing supplements (during pregnancy or currently), and 12% (n = 42) were using non-iodized salt.

For the older infants, eighteen clinics provided 507 infant/mother pairs. The mUICs (95% CI) in the 6- and 12-month-old infants were 91 (79–103) and 103 (92–116) μg/l, respectively, and were not significantly different (table 1). Girls had higher UICs than boys (mUIC, 103 vs. 88 μg/l; p < 0.05). Among the mothers, mUIC was 75 μg/l (95% CI: 69–81) and mBMIC was 49 μg/kg. Fifty-seven percent of the 6-month-old infants and 18% of the 12-month-old infants were being breastfed fully or partly at the time of sampling. Breastfed infants with or without IFM had a lower mUIC than infants not currently breastfed (82 μg/l, n = 196, vs. 105 μg/l, n = 311; p < 0.001). About 60% of all infants were receiving IFM, and their mUIC was higher than in those not receiving IFM (109 μg/l, n = 304, vs. 73 μg/l, n = 203; p < 0.001). Infants (breastfed and/or CF) receiving IFM had higher mUIC than breastfed weaning infants who did not receive IFM (109 μg/l, n = 304 vs. 70 μg/l, n = 131; p < 0.01; fig. 1). Weaned infants not receiving breast milk or IFM did not differ in UIC (89 μg/l, n = 72) from the other two groups. Eighty four percent of mothers were using iodized salt at home, 8% of mothers were not using iodized salt and 8% were unsure; there were no significant differences in UIC of the mothers.

<table>
<thead>
<tr>
<th>Age of the infants</th>
<th>3–4 days</th>
<th>6 months</th>
<th>12 months</th>
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<tbody>
<tr>
<td>Total</td>
<td>368</td>
<td>279</td>
<td>228</td>
</tr>
<tr>
<td>Male/female</td>
<td>171/197</td>
<td>142/136</td>
<td>106/122</td>
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<tr>
<td>UIC, μg/l</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Median (95% CI)</td>
<td>91 (82–99)</td>
<td>91 (79–103)</td>
<td>103 (92–116)</td>
</tr>
<tr>
<td>Range</td>
<td>4–922</td>
<td>11–759</td>
<td>6–951</td>
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<tr>
<td>&lt;20%</td>
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<td>2</td>
<td>3</td>
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<tr>
<td>20–49%</td>
<td>20</td>
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<tr>
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Data from Andersson et al. [32].
or infants among these 3 groups. Among the 6-month-old infants, nearly 4 out of 5 were already receiving CF, and at 6 and 12 months, 7 and 95% of infants were receiving some foods from the family table. The mUIC of infants receiving some iodized salt in CF (103 μg/l, n = 287) was higher, but not significantly different from the mUIC of infants not receiving iodized salt (89 μg/l, n = 189). In a multivariate regression of predictors of UIC in the 6- and 12-month-old infants, BMIC (β = 0.320, p < 0.0001) and current consumption of IFM (yes/no; β = 0.201, p = 0.010) were significant, while gender, age and maternal UIC were not.

Thirty-two percent of the mothers were taking nutritional supplements (n = 158), but only 3% of women were consuming iodine-containing supplements. The agreement between the labeled and analyzed iodine content of the IFMs and infant cereals was high: the mean (± SD) difference (%) between labeled and measured values was 13.5 ± 9.1% for the formulas and 4.5 ± 2.6% for the cereals. None of the formula milks or cereals exceeded the recommended maxima of 50 and 35 μg/100 kcal [18].

This study is important in that it is the first national representative study assessing infant iodine status in a country with an established long-standing
iodized salt program where school age children and pregnant women have adequate iodine intakes [32]. The mUIC in the infants in this study at 3–4 days and at 6 months was just below the 100 μg/l cutoff that indicates iodine sufficiency in infancy [8]. Infants who were not receiving iodine-fortified IFM during the weaning period were clearly deficient, with an mUIC of ≈70 μg/l. Several reports of mUIC in infants (<2-year-olds) in countries with more than adequate or excess iodine intakes have found higher values than in this study [33–36]. But other studies in European infants have generally reported mUIC similar to the Swiss value [33, 37–40]. In the Swiss infants, only 58% of the 6-month-olds and 18% of the 12-month-olds were being breastfed. Infants who were breastfed and given home-prepared CF (that contain little or no added salt) were at highest risk of low iodine intakes. In Germany, using a dietary model, it was estimated that the iodine intake of an 8-month-old breastfed infant who receives home-prepared CF would be only ca. 45 μg/day compared to ≥125 μg/day in a formula-fed infant who receives commercial CF [41].

An additional factor that may aggravate low iodine intakes in weaning infants is the high prevalence of iron deficiency at this age. Iron deficiency reduces heme-dependent thyroperoxidase activity in the thyroid and impairs production of thyroid hormone. In iodine-deficient children, iron deficiency anemia blunts the efficacy of iodized oil and iodized salt [42]. In pregnant women, poor iron status predicts higher thyroid-stimulating hormone and lower thyroxine concentrations in an area of borderline ID [43]. Thus, iron-deficient infants may be at higher risk of poor thyroid function during low iodine intakes. But there are no published studies of the influence of iron status on thyroid function in infants with ID.

The Swiss study and others raise the concern that specific public health measures, in addition to salt iodization, should be considered to improve iodine intakes at this age. These could include increasing public awareness of the importance of providing at least some iodine-containing infant foods/formula during weaning. Infant food manufacturers should be strongly encouraged to fortify their products with iodine [14]. In Europe, the required level of iodization for IFMs is 10–50 μg/100 kcal (2.5 μg/100 kJ), but for cereal-based and other CFs, there are no requirements for minimum iodization while the allowed upper level is 35 μg/100 kcal [44]. In the US, iodine fortification of infant formula is mandatory at a minimum level of 5 μg/100 kcal (maximum level is 75 μg/100 kcal) [45]. In Germany, it is estimated only ≈50% of CFs are fortified with iodine [41].

Another strategy to increase iodine intakes in weaning infants would be iodine supplementation. Supplementation of lactating women can increase BMIC and could provide additional iodine, particularly during weaning when infants are being partially breastfed. In Danish mothers (n = 147), median BMIC on the 5th day postpartum was significantly higher (57 μg/l) in those receiving supplementation with 150 μg/day of oral iodine, compared to those

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not supplemented (34 μg/l) [46]. In Germany, 60 mothers who received 200 μg/day of oral iodine had significant higher mean iodine concentrations in breast milk (76 μg/l) than those who did not (55 μg/l) [47]. Thus, iodine supplementation of breastfeeding women can significantly improve iodine supply to the newborn. In the Swiss study, supplements containing iodine were consumed by <5% of lactating women. Alternatively, iodine supplements could be given to infants directly, as is often done for iron or vitamin D. Currently, American and European pediatric societies do not recommend iodine supplements for infants on well-balanced diets [48]. Similarly, in countries such as Switzerland with an effective iodized salt program, WHO does not recommend iodine supplementation for infants or lactating women [49]. These recommendations may need to be reconsidered if the Swiss findings are confirmed in other industrialized countries.

References

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