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# Iodine

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## Drug Levels and Effects

### Summary of Use during Lactation

Iodine is an essential trace nutrient for all infants that a normal component of breastmilk. Infant requirements are estimated to be 15 mcg/kg daily in full-term infants and 30 mcg/kg daily in preterm infants.[1] Breastmilk iodine concentration correlates well with maternal urinary iodine concentration and may be a useful index of iodine sufficiency in infants under 2 years of age, but there is no clear agreement on a value that indicates iodine sufficiency, and may not correlate with infant thyroid function tests.[2-4] A milk iodine value of 100 to 200 mcg/L has been suggested to indicate adequate iodine status in lactating women,[5] although a range as wide as 60 to 465 mcg/L has been proposed.[4] Systematic reviews and studies on iodine nutrition found that iodine in breastmilk is adequate in iodine-sufficient countries, but in countries with iodine fortification of foods, many mothers did not obtain adequate iodine and that additional supplementation was desirable.[6-10] In iodine-deficient areas, supplementation of breastfeeding mothers with iodine appears to be more effective than direct supplementation of the infant in reducing infant iodine deficiency.[11] In the United States, a total iodine intake of 290 mcg daily is recommended during lactation; the WHO recommends a total intake of 250 mcg daily.[9] The American Thyroid Association recommends that breastfeeding women should supplement their diet with a daily oral supplement that contains 150 mcg of iodine, but sustained iodine intake while breastfeeding that exceeds 500 to 1100 mcg daily should be avoided.[12] Vegan and vegetarian mothers appear to have reduced iodine concentrations in their milk and should use iodine supplements.[13] A survey in the United States between 2011 and 2014 found that only 19% of lactating women used a dietary supplement that contained iodine.[14] One study found improved neurodevelopment is the infants of mothers who received 150 mcg of iodine daily during breastfeeding, but a dose of 300 mcg daily did not further improve the outcome.[15]

The use of excessive amounts of iodine in the mother near term and during breastfeeding (e.g., seaweed soup) can increase breastmilk iodine levels and cause transient hypothyroidism in breastfed infants.[16-19] Supplementing mothers with Grave disease in appropriate doses potassium iodide usually does not adversely affect their breastfed infants, although a few may develop mild hypothyroidism.[20,21] The absorption of iodine can be marked after application to open wounds or mucous membranes. Exposure of mothers to unnecessary iodine who are or will be breastfeeding should be avoided or minimized to the extent possible by avoiding its use

on maternal mucous membranes (e.g., vaginal use, wound therapy), avoiding prolonged contact time, avoiding repeated applications, and applying it to the smallest possible surface areas of the body. It is possible that maternal exposure to iodine near term could interfere with thyroid studies done as a part of newborn screening tests.

When treating lactating people after radiation exposure, one dose of potassium iodine 130 mg is recommended at the lowest threshold exposure of >5 Gy to minimize the risk of blocking thyroid function in the fetus or nursing infant. In cases of severe contamination in lactating people, repeat dosing may be given and nursing neonates should be monitored for signs of illness.[22]

## Drug Levels

Iodine is a normal mineral in breastmilk that is essential for the infant's thyroid. Iodine concentrations are highest in colostrum, declining gradually as lactation progresses. The amounts of iodine in breastmilk vary with maternal iodine intake and possibly with genetic variants in the NaI symporter and its activity may be increased by breastfeeding.[23,24] The WHO recommends that lactating women have urinary iodine levels of 100 mcg/L. Others have suggested a breastmilk iodine reference range between 60 and 450 mcg/kg.[9]

*Maternal Levels.* A study of 97 iodine-sufficient women in Switzerland compared two analytic methods. The ICP-MS standard curve method found a median iodine concentration of 245 mcg/kg in pooled milk samples from 25 women while the ICP-MS 129-I isotope ratio method found a median concentration of 183 mcg/kg in pooled milk samples of 66 women.[25]

A study of 36 breastmilk samples from 18 different states in 2003-04 found a mean iodide breastmilk concentrations of 63.3 mcg/L (range 4.5 to 162 mcg/L).[26] Another study of 108 breastmilk samples from 10 women by the same authors found a mean iodide concentration of 87.9 mcg/L (range 3.1-334 mcg/L), and a median concentration of 55.2 mcg/L.[27] The reason for the differences in iodine values between these two studies and the above studies is not clear.

Two women were given potassium iodide orally. One was given 325 mg orally 3 times daily to a total of 3.6 grams and the other was given 650 mg orally 3 times daily to a total of 4.6 grams. Milk samples were obtained after the eighth and eleventh doses in the first woman and 2 hours after the last dose in the second woman. The first woman had milk iodide concentrations of about 33 and 29 mg/L and the second had a concentration of about 38 mg/L.[28] The analytic method used in this old study was insensitive and imprecise by modern standards.

A woman developed an abdominal wall abscess 1 week after having a cesarean section. The abscess was treated with systemic antibiotics and the wound was packed with 60 sq. cm of iodine tampons, containing about 10.5 mg of iodine. On day 29 postpartum, her milk iodine was 4410 mcg/L (normal range 29 to 490 mcg/L). Her iodine therapy was stopped, and 2 days later milk iodine was about 1400 mcg/L; by day 40 postpartum, it was about 1000 mcg/L. By day 60 postpartum, the milk level was below 100 mcg/L.[29]

The mother of a 31-week preterm infant packed her cesarean section wound with iodine-soaked gauze because of wound dehiscence and infection. Her breastmilk iodine concentration at 3 weeks postpartum was 1911 mcg/L (upper limit of normal 185 mcg/L).[30]

The mothers of 31 preterm Korean infants was measured for iodine concentration on week 1, 3 and 6 postpartum. Korean mothers have elevated iodine levels from large amounts of dietary iodine in brown seaweed soup during the first month postpartum. Median breastmilk iodine levels were 2529, 1153 and 822 mcg/L at the 3 times, respectively.[16]

A mother used an iodine antiseptic on her episiotomy wound for 10 to 12 days postpartum. At 15 days postpartum, her milk iodine level was 300 mcg/L (normal 100-200 mcg/L).[31]

A mother ate large amounts of seaweed soup imported from China for the first 10 days postpartum to increase her breastmilk supply. Breastmilk iodine levels were much higher during the time of seaweed consumption at 878 mcg/L total iodine compared to 188 mcg/L 4 weeks later and 144 mcg/L 7 weeks later.[18]

A study in northern Spain compared the milk iodide level of mothers taking a normal diet, including iodized salt and seafood (n = 14), with mothers on the same diet plus a supplement of 200 mg daily of potassium iodide (n = 46). The median breastmilk iodide levels from supplemented mothers of preterm infants was 0.172 mg/L in the supplemented mothers compared to 0.128 mg/L in the unsupplemented mothers. The median breastmilk iodide levels from supplemented mothers of full-term infants was 0.178 mg/L in the supplemented mothers compared to 0.117 mg/L in the unsupplemented mothers. No statistical difference was found between preterm and full term milk iodide in either the supplemented or unsupplemented group. The authors conclude that in this iodine-sufficient area, unsupplemented mothers excrete sufficient amounts of iodide in breastmilk.[32]

Sixteen lactating women were administered 752 mcg of potassium iodide (572 mcg iodine) in the morning after an overnight fast. They also ingested an additional 36 to 685 mcg of dietary iodine during the study period. Breastmilk samples were obtained at baseline and every hour for 8 hours. Breastmilk iodide increased from an average of 46 mcg/L at baseline to a peak of 354 mcg/L. Peak iodine levels in milk occurred at an median of 6 hours (range 5 to 7 hours) after the dose of iodine.[33]

A study in Thailand compared mothers supplemented with 200 mcg daily of iodine daily to unsupplemented mothers. Breast milk samples were collected from 57 lactating women, 33 of whom received iodine supplementation during pregnancy. The median breastmilk iodine concentration at 2 months postpartum was significantly higher in the supplemented mothers (109 mcg/L) than in unsupplemented mothers 70 mcg/L).[34]

A study in Iran, which is considered iodine deficient, compared iodine breastmilk content between control mothers and those supplemented with cow's milk fortified with 150 mcg of iodine per cup. Both groups used iodized salt. Iodine levels in breastmilk were greater in the supplemented group than in the control group at 10, 14 and 30 days, with the median levels ranging from 210 to 242 mcg/L compared to the control group which had median levels ranging from 142 to 162 mcg/L at the same times.[35]

A study in Ethiopia compared administration of capsules containing 225 mcg of iodine given once daily to the provision of iodized salt containing 35 mcg/gram of iodine to mothers who were breastfeeding. At the end of 6 months no difference was found in median breastmilk iodine concentrations between the two groups. Forty-five percent of women had breastmilk iodine levels above 120 mcg/L, which is the level recommended for adequate infant iodine intake. The authors considered the two methods to be equivalent.[36]

Twenty-three mothers in Japan were treated with potassium iodide for Graves disease. Doses were adjusted to maintain normal thyroid function; the median dose was 50 mg daily (range 10 to 100 mg/day). The median breastmilk iodine level was 15.05 mg/L (range 0.831 to 72 mg/L).[20]

Thirty-six women in the Netherlands took a supplement containing 150 mcg of iodine daily during pregnancy and for 4 weeks postpartum. Milk samples from 33 of the women analyzed at 4 weeks postpartum contained 1.2 micromoles/L (304 mcg/L; range 0.05 to 3 micromoles/L).[37]

A study in Iran randomized mothers to receive placebo (n = 51), 150 mcg (n = 50) or 300 mcg (n = 43) of iodine daily as potassium iodate for 12 months. Milk iodine levels were measured at 1, 2, 4, 6, and 12 months postpartum. In mothers who received iodine, median breastmilk iodine over the 12-month period was greater than in the placebo group. The iodine concentration was 1.39 times higher in the 300 mcg group than that in the 150 mcg group. Iodine milk levels slowly trended downward and at 12 months postpartum, levels in all groups was about 150 mcg/L.[7]

Fifty-seven women in Iceland had foremilk iodine levels measured at 5.5 months postpartum. The median breastmilk iodine content was 84 mcg/L (IQR: 48 to 114 mcg/L).[38]

A study in China compared lactating women from four cities, two with an average drinking water iodine of 57.5 mcg/L and two with an average of 464.8 mcg/L. Median milk iodine levels in the milk of women was 312 mcg/L from the low iodine cities and 1006 mcg/L from the high iodine cities. Living in the high-iodine area for more than 5 years was a strong predictor of breastmilk iodine sufficiency or excess.[39]

Mothers in Tianjen, China, where iodized salt is consumed, had breastmilk iodine levels measured at 1, 4, 8, 12, 16 and 24 weeks postpartum. At 1 week postpartum, 634 mothers participated and their mean maternal breastmilk iodine was 365 mcg/L (median 225 mcg/L). By 24 weeks postpartum, 151 mothers participated and breastmilk iodine levels had steadily decreased to a mean of 80 mcg/L (median 121 mcg/L). The authors judged these values to be adequate for infant nutrition.[40]

A study in New Zealand compared the breastmilk iodine concentrations of women taking an iodine supplement (n = 35) to those who were not (n = 52). Mothers who took an iodine supplement had a median milk iodine level of 84 mcg/L and those who took no supplement had a median milk iodine level of 62 mcg/L.[10]

One hundred thirteen mothers who donated milk at a Spanish milk bank had their milk iodine measured on 4 consecutive days. Mothers were 1.5 to 49.4 months postpartum, 83% had a full-term infant and 56% took iodine supplements ranging from 40 to 200 mcg daily. The median iodine concentration in the samples was 148.5 mcg/L and 70% of the mothers had a milk iodine concentration less than the desired intake for preterm infants of 200 mcg/L.[41]

A study of breastmilk iodine concentrations in 25 exclusively breastfeeding pairs found that milk samples taken in the afternoon or after midnight are most representative of iodine concentrations. The iodine concentration in milk was associated with recent iodine intake and maternal 24-hour urinary iodine excretion was the best predictor of breastmilk iodine concentration.[42]

A small study of vegan, vegetarian and omnivore nursing mothers found that vegan and vegetarian women had lower milk iodine concentrations than omnivores and that maternal supplementation with iodine with prenatal vitamins resulted in higher breastmilk iodine concentrations. The authors concluded that iodine supplementation is important in vegan and vegetarian mothers.[13]

*Infant Levels.* The preterm infants of Korean mothers with high levels of breastmilk iodine had relative high urinary iodine levels that were thought to be related to high maternal intake of iodine.[16]

A woman developed an abdominal wall abscess 1 week after having a cesarean section. The abscess was treated with systemic antibiotics and the wound was packed with 60 sq. cm of iodine tampons, containing about 10.5 mg of iodine. On day 29 postpartum, her breastfed infant's urine contained 3932 mcg/L of iodine (normal range <185 mcg/L). By day 40 postpartum, the infant's urine iodine level was normal.[29]

The mother of a 31-week preterm infant packed her cesarean section wound with iodine-soaked gauze because of wound dehiscence and infection. The urine iodine level of her 2-week-old breastfed neonate was 684 mcg/L (normal range 42 to 350 mcg/L).[30]

A mother used an iodine antiseptic on her episiotomy wound for 10 to 12 days postpartum. At 15 days of age, her infant had a urinary iodine concentration of 410 mcg/L (normal 100 to 200 mcg/L).[31]

Two mothers originally from Asia (Korea and China) reportedly ate large amounts of soup made from seaweed from their home countries in the postpartum period. The infants of both mothers had elevated urinary iodine levels. The Korean mother continued to eat the soup for several weeks postpartum. Her infant's urinary iodine levels were 391 mcg/L and 690 mcg/L (normal range 100 to 300 mcg/L) at 1 and 2 months postpartum. The Chinese mother ate large quantities of seaweed soup for the first 10 days postpartum to increase her breastmilk supply. Her infant's urinary iodine level at 4 weeks of age was 343 mcg/L or 5055 mcg/gram of creatinine (normal range 100 to 300 mcg/gram).[18]

A study of 46 nursing mothers supplemented with 200 mg of potassium iodide daily measured the iodine content of their breastfed infants' urine. Urine iodide concentrations were 0.365 mg/L among preterm infants and 0.376 mg/L among full-term infants.[32]

A study in Thailand compared mothers supplemented with 200 mcg daily of iodine daily during pregnancy to unsupplemented mothers. At 2 months of age, exclusively breast-fed infants whose mothers received iodine supplementation (n = 11) had greater urinary iodine concentrations (381 mcg/L) than those whose mothers were not supplemented (n = 14; 216 mcg/L).[34]

A study in Iran, which is considered iodine deficient, compared iodine breastmilk content between control mothers and those supplemented with cow's milk fortified with 150 mcg of iodine per cup. Both groups used iodized salt. Although iodine levels in infant urine were greater in the supplemented group than in the control group at 10, 14 and 30 days, these differences were not statistically significant and all infants were iodine sufficient.[35]

A study in Ethiopia compared administration of capsules containing 225 mcg of iodine given once daily to the provision of iodized salt containing 35 mcg/gram of iodine to mothers who were breastfeeding. At the end of 6 months, no difference was found in the median urinary iodine concentrations between the two groups of breastfed infants. The authors considered the two methods to be equivalent.[36]

Twenty-three mothers in Japan were treated with potassium iodide for Graves disease. Doses were adjusted to maintain normal thyroid function. Their 26 infants (1 pair each of twins and triplets) were breastfed, some exclusively and some partially. The median urinary iodine concentration in the infants' urine was 15.65 mg/L (range 0.157 to 250 mg/L). The infants' median free thyroxine level was 1.01 ng/dL (range 0.61 to 1.55 ng/dL) and median thyrotropin level was 2.1 microIU/mL (range 0.6 to 12.3 microIU/mL).[20]

A study of infants between 4 and 6 months of age in Bangkok, Thailand measured urinary iodine levels in exclusively breastfed (n = 19), mixed breastmilk and formula (n = 17) and exclusively formula-fed (n = 35) infants. The median urinary iodine concentrations (UIC) of infants and lactating mothers was 282 and 149 mcg/L, respectively. Breastfed infants had a significantly higher median UIC than formula-fed infants. There was a positive correlation between infant and maternal UIC.[43]

A study in Iran randomized mothers to receive placebo (n = 51), 150 mcg (n = 50) or 300 mcg (n = 43) of iodine daily as potassium iodate for 12 months. Among their breastfed infants, the urinary iodine concentration was >100 mcg/L in all groups at all times with no statistically significant differences between groups.[7]

Thirty-two exclusively breastfed infants and 28 partially breastfed infants in Iceland had urinary iodine concentrations measured at 25 weeks of age. The median urinary iodine concentration was 152 mcg/L (IQR: 79 to 239 mcg/L), with no significant difference between exclusively and partially breastfed infants. The amount of urinary iodine was correlated with the mother’s breastmilk iodine concentration. Estimated infant intake was between 67 and 71 mcg of iodine daily.[38]

A study in China compared lactating women from four cities, two with an average drinking water iodine of 57.5 mcg/L and two with an average of 464.8 mcg/L. Median milk iodine levels in the milk of women was 312 mcg/L from the low iodine cities and 1006 mcg/L from the high iodine cities. The median concentration of urinary iodine of the breastfed infants of the mothers with low iodine levels was 427 mcg/L and 1222 mcg/L in the infants of mothers in the high-iodine group.[39]

Exclusively breastfed infants in Tianjen, China, where iodized salt is consumed, had urinary iodine levels measured at 1, 4, 8, 12, 16 and 24 weeks postpartum. At 1 week postpartum, the mean infant urinary iodine was 281 mcg/L (median 284 mcg/L). Breastmilk iodine levels steadily decreased to a mean of 81 mcg/L (median 213 mcg/L) at 24 weeks postpartum. The authors judged these values to be adequate for infant nutrition.[40]

A study in Aydin, Turkey of 334 mothers and their healthy neonates found a positive correlation between mothers' breastmilk iodine concentration and their infants' urinary iodine concentration. The prevalence of neonatal serum TSH >10 microIU/L, which is suggestive of mild iodine deficiency, was 19%.[44]

A study in New Zealand compared the serum iodine concentrations in the infants of women taking an iodine supplement (n = 35) to those who were not (n = 52). Infants of mothers who took an iodine supplement had a median serum iodine level of 150 mcg/L and infants of those who took no supplement had a median milk iodine level of 86 mcg/L.[10]

## Effects in Breastfed Infants

In Switzerland, a girl born at 29 weeks of gestation with adequate size for gestational age showed negative TSH screening on day 5. Her mother developed an abscess of the abdominal wall 1 week after her cesarian section and the wound was packed with tampons containing about 10.5 mg of iodine. The baby's TSH was elevated to 23 milliunits/L on day 23, and 288 milliunits/L on day 29. Free thyroxine (T4) levels were decreased to 2.8 ng/L and free liothyronine (T3) with 1.52 ng/L, without signs or symptoms of hypothyroidism. Iodine contents of maternal milk and of infant urine were 4.4 mg/L and 3.9 mg/L, respectively. Treatment with levothyroxine was started, breastfeeding was discontinued and disinfection with iodine was stopped. The infant's thyroid function tests normalized after 6 days.[29] The infant's abnormal thyroid function tests were probably caused by maternal iodine use.

The mother of a 31-week, 961 gram preterm infant packed her cesarean section wound with iodine-soaked gauze because of wound dehiscence and infection. She was expressing milk for her hospitalized infant. The infant's thyroid function tests were normal at birth, but at 2 weeks of age, the infant's serum thyroxine was borderline low and TSH levels were elevated. One week later, TSH had increased to 77 milliunits/L and both thyroxine and free thyroxine levels were low. Breastmilk was discontinued and levothyroxine was started. The mother discontinued the iodine packing and 1 week later breastmilk feeding was resumed. At 2 months of age, the infant's thyroid function test were normal while taking levothyroxine.[30]

A study of 31 preterm infants born at 34 weeks gestational age or less was performed in Korea where mothers typically ingest large amounts of seaweed soup during the first month postpartum. Subclinical hypothyroidism was frequently found in the infants with high intake of iodine from breastmilk.[16]

A mother used an iodine antiseptic on her episiotomy wound for 10 to 12 days postpartum. At 15 days of age, her infant had elevated TSH and low free T4 serum levels, an enlarged thyroid gland, and an elevated urinary iodine concentration. The infant's symptoms were probably related to maternal iodine application.[31]

Two mothers originally from Asia (Korea and China) reportedly ate large amounts of soup made from seaweed from their home countries in the postpartum period. Their infants had elevated thyrotropin (TSH) levels when tested at 3 to 4 weeks of age and signs of hypothyroidism. Both were treated with thyroid hormones and regained normal thyroid function.[18]

A 21-day-old breastfed (extent not stated) infant presented with unconjugated hyperbilirubinemia. Neonatal TSH screening was normal, but at 21 days it was 87.3 IU/L (normal 0.27 to 4.2 IU/L). Free T4 was 7.3 pmol/L (normal 12 to 22 pmol/L) and the thyroid was slightly enlarged. The infant's parents were of Korean origin and the mother had consumed 3 to 4 bowls of brown seaweed (*Undaria pinnatifidia*) soup daily from the time of birth. The infant's hypothyroidism was probably caused by the high iodine content of the seaweed soup.[17]

Twenty-three mothers in Japan were treated with potassium iodide for Graves disease. Doses were adjusted to maintain normal thyroid function; the median dose was 50 mg daily (range 10 to 100 mg/day). Their 26 infants (1 pair each of twins and triplets) were breastfed, some exclusively and some partially. Twenty-five of the 26 infants had normal thyroid function. One 5-month-old infant presented with subclinical hypothyroidism,

indicated by a blood thyrotropin level of 12.3 microIU/mL, after 1 month of maternal therapy. Two months after potassium iodide discontinuation, the blood thyrotropin level normalized to 2.3 microIU/mL. In other infants, thyrotropin levels deceased over time without discontinuing maternal iodine or breastfeeding.[20] In a follow-on case series, 210 blood samples were obtained from 100 infants (including these 26 infants) who were partially or fully breastfed by 81 mothers taking potassium iodide for Graves disease. Upon measurement of TSH and fT4 were evaluated, 12 infants were found to have subclinical hypothyroidism. In 3 infants, TSH normalized in 2 months after stopping breastfeeding and in 7 others, TSH normalized despite continued breastfeeding and maternal iodine supplementation; 2 were lost to follow-up.[21]

A breastfed Korean infant was found to have an elevated TSH at 15 and 22 days of age and a low free T4 level at 22 days of age. The infant also had markedly elevated urine iodine levels. Her mother had been drinking seaweed soup almost daily during pregnancy and postpartum. The infant was started on levothyroxine and the mother told to feed the infant formula and stop breastfeeding temporarily. The mother resumed nursing at 1 month of age and levothyroxine was at a lower dose until 4 months of age. The infant's thyroid function remained normal up to 12 weeks off of levothyroxine. It is probable that the thyroid dysfunction was caused by excess iodine in breastmilk.[45]

A Dutch infant was referred to specialists on day 8 of life for abnormal congenital hypothyroidism screening. Laboratory results showed repeatedly increased TSH concentrations, with fT4 in the normal range. The infant's mother consumed a bowl of wakame miso soup daily, hijiki or arame seaweed once a week and nori seaweed once a week. In addition, she used *Chlorella* (algae powder) and 'sweet iron' supplements during pregnancy. After discontinuation of seaweed, the infant's TSH concentrations gradually decreased but did not normalize. The fT4 concentrations remained in the normal range. As a result of TSH values being >10 milliunits/L, the mother was strongly recommended to supplement her infant with levothyroxine to prevent long-term complications. However, the mother was reluctant to start supplementation because of normal fT4 concentrations. During 9 months of follow-up, the infant's neurodevelopment was normal.[46]

A study in Tehran, Iran of mothers who planned to exclusively breastfeed their infants randomized mothers to receive placebo (n = 45), 150 mcg (n = 35) or 300 mcg (n = 45) of iodine daily. At 3 years of age, cognitive scores were higher in children whose mothers received 150 mcg daily compared to children whose mothers received placebo. Supplementation with 150 mcg daily had no effect on language or motor development. The 300 mcg dose had no advantage over the 150 mcg dose.[15]

## Effects on Lactation and Breastmilk

Relevant published information was not found as of the revision date.

## Alternate Drugs to Consider

(Skin Disinfection) Chlorhexidine, Benzalkonium Chloride

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# Substance Identification

## Substance Name

Iodine

## CAS Registry Number

7553-56-2

## Drug Class

Breast Feeding

Lactation

Milk, Human

Anti-Infective Agents, Local

Antibacterial Agents