

Iodine, a Critically Overlooked Nutrient

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Iodine is a trace element required by the body for an increasing number of identified physiologic functions. This element belongs to the halogen family of elements, a group of highly reactive nonmetals that includes fluorine, chlorine, bromine, and astatine. Iodine is found naturally in large amounts in seafood such as kelp and saltwater fish. Most iodine intake in the United States is from iodized table salt. Iodation of salt in the United States began in the 1920s in response to the large number of goiters in certain populations in areas where soil and water levels of iodine were low. The upper Midwest and Great Lakes region, where the incidence of goiter was as high as 30–40% in 1922, was named the “goiter belt.”¹

Currently, the recommended daily allowance (RDA) of iodine for adults is 150 µg/day, for pregnant women 220 µg/day, and for lactating women 290 µg/day, and although some studies indicate that Americans’ iodine intake is adequate, many other studies suggest a prevalence of subclinical iodine deficiency.

In this regard, it is worth considering that although many Americans consume large amounts of sodium in processed foods, many such foods do not use the iodized form of salt, and even if they do, research suggests that only 10% of the iodide in iodized salt is bioavailable.² Moreover, with cautionary recommendations that Americans limit their sodium intake, an adequate intake of iodine is of concern because iodine deficiency is associated with numerous abnormalities including hypothyroidism, goiter, cretinism, cognitive disorders, neurologic disorders, and breast disease. Iodine deficiency is especially hazardous in pregnant women, developing fetuses, and newborn infants because of its ability to cause irreversible damage to fetuses and newborns.

The World Health Organization (WHO) has established that the mean urine iodine concentration should not exceed 10 µg/dL, and should be less than 5 µg/dL in no more than 20% percent of a population. The National Health and Nutrition Examination Surveys (NHANES), which periodically measure urine iodine concentrations to evaluate iodine status in the population of the United States, indicate that it has an adequate iodine intake. Moreover, because the adult RDA for iodine is 150 µg/day, and goiter is controlled with only 0.05 mg of iodide per day, many

scientists believe that iodine intake is sufficient. However, between NHANES I (1971–1974) and NHANES III (1988–1994), Americans’ median urine iodine concentration decreased by 50%, while a low urine excretory level of iodine, of less than 5 µg/dL, increased by 4.5-fold in this same period. Monitoring of high-risk groups showed that 6.7% of pregnant women and 14.9% of women of childbearing age had a urine excretory level of less than 5 µg/dL of iodine.³ The most recent NHANES (NHANES IV: 2001–2002) indicated that the mean urine excretory level of iodine has stabilized since NHANES III.⁴

The RDA for Iodine

The suggested daily RDA of 150 µg/day for iodine may be influenced by the fear that an excess of iodine can cause diseases including hyperthyroidism, hypothyroidism, goiter, rashes, and iodine allergy. However, most of these reactions are caused by pharmacologic doses of iodine. Some research has linked iodine excess to autoimmune thyroid disease, which can cause both hypo- and hyperthyroidism,^{5,6} but such autoimmune disease has been increasing during the same period in which iodine intake has been decreasing in the United States.⁷ A high intake of iodine, largely in the form of seaweed, is also typical in the Japanese population, which has generally good overall health. Research has found that the typical Japanese diet has a daily intake of elemental iodine ranging high as 13.8 mg.⁸

Historically, physicians have prescribed iodine in a dose of 0.1–0.3 mL of Lugol’s solution, a 5% solution containing 50 mg of iodine and 100 mg of potassium iodide per milliliter, thus providing 12.5–37.5 mg of the elemental iodine needed to treat iodine deficiency disorders and promote overall well-being.^{8,9} In order to minimize the risk of reactivity to iodine, assays of thyroid function should be done before supplementation with iodine is undertaken in any patient.

Metabolism of Iodine

Iodide is removed from circulating blood primarily by the thyroid gland and kidneys. The body can also concentrate iodide in the salivary glands, breast tissue, gastric mucosa, and choroid plexus, among other sites. Sodium/iodide transporters—protein molecules also known as “symporters”—take up iodide from the

blood into the thyroid across a concentration gradient that may be as high as 50-fold, and concentrate the iodide in the cells of the gland to a level adequate for hormone synthesis. This iodide is incorporated into precursors that are transformed into thyroxine, or T₄, a hormone secreted primarily by the thyroid, which is converted in peripheral tissues to the hormone tri-iodothyronine or T₃, which regulates growth and cellular metabolism. Because the enzyme responsible for the conversion of T₄ to T₃ is selenium-dependent, selenium deficiency decreases this conversion. The average adult thyroid gland in an iodine-sufficient area contains 15 mg of iodine.¹⁰

Iodine Deficiency

An enlarged thyroid, or goiter, is the most overt sign of iodine deficiency. Hypothyroidism from iodine deficiency presents with a decrease in T₃ and T₄ and an increase in thyroid-stimulating hormone (TSH), thyroglobulin, and reverse T₃, an inactive form of thyroid hormone generated by the removal of an iodine group from thyroxine. Symptoms of hypothyroidism include fatigue, dry skin, hair loss, weight gain, cognitive impairment, and depression.

Several factors can cause iodine deficiency. As already noted, low levels of iodine in the soil or water in particular areas may cause this deficiency, as may salt-restrictive diets. Intake of large amounts of cruciferous vegetables, cassava, millet, and soya flour is another source of iodine deficiency, through the goitrogenic substances known as C-glycosylflavones (C-GFs), and this will also affect thyroid function. Additionally, vitamin A and iron deficiency, as well as the selenium deficiency noted earlier, can exacerbate iodine deficiency.¹⁰ Intake of particular elements that compete with iodine for uptake and utilization, such as chlorine, fluorine, and bromine, may also be a factor.

Diagnosis of Iodine Deficiency

Studies indicate that 90% of ingested iodine is eventually excreted in the urine. According to the WHO, median urine iodine levels should exceed 10 µg/dL in "iodine sufficient" populations. Iodine deficiency is commonly identified by measuring urinary iodine excretion. Urinary iodine excretion may also be expressed in relation to creatinine excretion, as µg of iodine per g of creatinine. Levels of thyroxine, TSH, thyrotropin, and thyroglobulin have also been measured as indicators of the adequacy of in vivo iodine concentrations, and some investigators believe that measuring thyroglobulin is a more accurate indicator of such concentrations than is measuring urine iodine levels.¹² Other researchers have reported that measurements of TSH and T₄ are inaccurate indicators of iodine adequacy in "iodine-sufficient" populations.¹³

Bromine

Halogens other than iodine are important factors in health because they can displace iodine in physiologic reactions. Bromine has replaced iodine for use as a dough softener in bread-making, and is also an environmental contaminant found in both food and water. Studies of thyroid function in rats indicate that with increased intake, bromine replaces iodine in this organ.¹⁴ Animal studies also suggest that in the presence of an iodine-deficient state, bromine may induce hypothyroid symptoms of decreased thyroxine synthesis and increased thyroid-gland size, as well as decreasing iodine concentrations in the skin.¹⁴ Studies with pregnant and lactating rats have demonstrated that increased bromine intake decreases the iodine content of mammary tissue, decreases T₄ in both mothers and offspring, and decreases the body weight of offspring. Bromine also increases the renal excretion of iodine in these animals.¹⁴ Treating rats with bromine has been shown to induce goiter and decrease the thyroid iodine concentration, while supplementation with iodine and selenium has been found to reduce by 50% the amount of bromine taken up by the thyroid as compared to that in rats without such supplementation.¹⁵

Perchlorate inhibits thyroid function by inhibiting iodine uptake by the thyroid at doses of 200 mg/day or more.

Chlorine

Perchlorate, an environmental contaminant often used in fertilizers, is a known competitive inhibitor of the iodine/sodium symporter and is known to inhibit thyroid function by inhibiting iodine uptake by the thyroid at doses of 200 mg/day or more.¹⁶ Perchlorate is often consumed in plants such as lettuce and leafy greens, and in drinking water and milk. Studies have found that the majority of dairy milk samples and all samples of breast milk tested contained perchlorate. A recent study demonstrated a mean perchlorate level in breast milk of 10.5 µg/L, suggesting that the average breast-fed infant consumes more than twice the recommended maximum daily level of perchlorate established by the National Academy of Sciences.¹⁷

Studies of perchlorate levels in drinking water and their relation to diseases in the United States have provided conflicting results. Several studies have measured thyroid hormone values as indicators of the health effects of perchlorate in drinking water, and have found no effect.¹⁸ One study did find a statistically significant increase in newborns' TSH levels in an area where all samples of drinking water were contaminated with perchlorate, as compared to the TSH levels of newborns in an area without such contamination.¹⁹ Some researchers suggest that the combination of perchlorate with other competitors of the iodine/sodium symporter, such as nitrates and thiocyanate, as well as the combination of perchlorate with iodine itself, increases the risk of thyroid-related disease.²⁰ A further study, of the incidence of attention-deficit/hyperactivity disorder (ADHD), autism, and the academic performance of fourth

graders in areas with and without perchlorate contamination did not find a statistically significant difference in these conditions in the two groups. However, this study did not take into account the residence locations of mothers at the time of gestation, or their individual perchlorate exposure.²¹

Fluorine

Fluorine, a halogen like bromine and chlorine, is commonly added to drinking water and used as a component of dental products for decreasing the risk of caries. Research on possible effects of fluorine on the thyroid gland has given controversial results. However, some animal studies have shown that increased intake of fluoride can decrease serum T3 and T4 levels in iodine-deficient mice.²²

Iodine Deficiency and Thyroid Disease

Maternal hypothyroidism during pregnancy can result in preeclampsia, miscarriage, and early rupture of membranes, abnormal fetal growth, perinatal morbidity, and neonatal death. Early fetal brain development beginning at the 15th week of gestation relies on thyroxine from the mother, and maternal hypothyroidism can produce fetal brain damage, cretinism, and a decreased intelligence quotient. Cretinism, a severe neuropathology caused by iodine deficiency, is marked by gross mental retardation along with varying degrees of shortness of stature, deaf-mutism, and spasticity. Because of decreased iodine retention, preterm infants, in whom renal function is not fully developed, require twice the daily intake of iodine for normal infants. To decrease these risks, the WHO in 2001 suggested an increased iodine intake for infants and an increased iodine content in infant formula.²³

Iodine Deficiency and Breast Disease

Besides being important in thyroid function, iodine is required for the normal growth and development of breast tissue. The high level of iodine intake by Japanese women, noted earlier, has been associated with a low incidence of both benign and cancerous breast disease in this population. Evidence links iodine deficiency with an elevated risk of breast, endometrial, and ovarian cancer.²⁴ Antiproliferative iodolactones in the thyroid may be responsible for this effect.²⁵ Although autoimmune antibodies directed against thyroid peroxidase have been associated with a better prognosis in breast cancer,²⁶ thyroid supplementation may increase the risk of breast cancer²⁷—a subject that remains in debate. In vitro studies have found that molecular iodine inhibits induction and proliferation and induces apoptosis in some human breast cancer cell lines, as well as exhibiting antioxidant activity.²⁸

Benign, fibrocystic breast disease is also associated with iodine deficiency. Blocking of iodine with perchlorate in the mammary

tissue of rats has been found to cause histologic changes indicative of fibrocystic breast disease, as well as precancerous lesions.²⁹ Conversely, iodine supplementation has been shown to ease mastalgia. Supplementation with 3 or 6 mg/day of molecular iodine significantly decreased pain reported by patients, as well as physicians' assessments of pain, tenderness, and nodularity in benign breast disease, with a dose of 6 mg/day providing significant reduction of pain in more than 50% of patients.³⁰

Iodine Deficiency and Cognitive and Neurologic Disorders

T3 and T4 are particularly important for myelination of the developing brain. Hypothyroidism during pregnancy and lactation causes numerous neurologic and cognitive deficits. A study of schoolchildren with mild iodine deficiency found that urine iodine levels above 100 µg/L were associated with significantly higher IQ scores, while levels below 100 µg/L increased the risk of an IQ below 70.³¹ The same study also found that consuming noniodized salt and drinking milk less than once daily increased the risk of an IQ below the 25th percentile.³¹ Another study found that children from severely iodine-deficient areas had IQ scores that were 12.45 points below average.³² A small study comparing the prevalence of ADHD in children from a mildly iodine-deficient area and a moderately iodine-deficient area found that 68.7% of those from the latter area had a diagnosis of ADHD, as compared with an absence of this diagnosis in the children from the mildly iodine-deficient area, and that IQ scores were lower in the moderately deficient area. Of the children with ADHD, 63.6% were born to mothers who had become hypothyroxinemic in early gestation.³³

Studies have also suggested that iodine deficiency affects hearing. Children in a mildly iodine-deficient area who had elevated serum thyroglobulin levels had higher auditory thresholds for sound of higher frequencies than did children with lower thyroglobulin levels.³⁴ Another comparative study, of children from a severely iodine-deficient and a mildly iodine-deficient region, found that the former group had lower thyroxine levels, higher TSH levels, and lower scores on achievement motivation tests, and were slower learners than the latter group.³⁵

Research on endemic cretinism from congenital iodine deficiency has shown specific severe neurologic deficits including deaf-mutism and a varying degree of bilateral hearing loss, as well as dysarthria, mental deficiency, spasticity of the proximal lower extremities, rigidity, and bradykinesia. In some cases strabismus and kyphoscoliosis were also present.³⁶

Iodine Deficiency and Gastric Cancer

Iodine deficiency has been linked to an increased risk of gastric carcinoma. One study demonstrated an increased prevalence of gastric cancer and an increased risk of atrophic gastritis in areas with a greater-than-average prevalence of iodine-deficiency-

Benign, fibrocystic breast disease is associated with iodine deficiency.

related goiter. The researchers also reported that competitive inhibitors of intracellular iodine transport, such as nitrates, thiocyanate, and salt increased the risk of gastric cancer.³⁷ Another study found a significant correlation between decreased mean urinary iodine levels and prevalence data for stomach cancer, as well as a greater frequency of severe iodine deficiency in stomach cancer than in controls.³⁸ There is also evidence for lower levels of iodine in cancerous gastric tissue than in surrounding normal tissue.³⁹

Treatment of Iodine Deficiency

The American Thyroid Association (ATA) recommends that iodine supplementation of 150 µg/day be given to all pregnant and lactating women, and suggests that all prenatal vitamin supplements contain 150 µg of iodine.⁴⁰ Based on this recommendation, it may be possible to extrapolate this increased need to the general population. Considering that the consumption of iodine from food sources in Japan exceeds by more than 10-fold the minimally recommended ATA figure for daily iodine intake, there arises the issue of adjusting iodine-intake recommendations to optimal levels, rather than to a level that is marginally sufficient to prevent overt thyroid disease. As with far too many nutrients, the 1940s approach of dosing at marginal levels to prevent “breakthrough” disease fails to consider that a specific nutrient, such as iodine, does not have a single limited role, such as preventing goiter.

Conclusion

Iodine has been used for many other purposes than those named here. It is, for example, still widely used as an antibacterial and antifungal agent and topical antiseptic. One notable use for iodine is radiation exposure. Potassium iodide tablets are often distributed to individuals living near nuclear power plants in case of a radiation-releasing nuclear accident. This is because immediate supplementation with potassium iodide will block the absorption of radioactive iodide into the thyroid gland.

Iodine deficiency is a worldwide concern with serious consequences to health. Although endemic goiter is decreasing, overt iodine deficiency continues to exist in some areas. With the increased presence of other halogens in food and water supplies, relative iodine deficiency is a growing concern. Perhaps with increasing knowledge of the physiologic functions that require iodine, it will be possible to sharpen the definition of an adequate iodine intake. As with vitamin D, folic acid, the omega-3 fatty acids, and other nutrients recognized as deficient in the Western diet, subclinical iodine deficiency may then become a thing of the past. We recommend that before supplementation is begun with iodine at levels above those of its dietary intake, testing be done to rule out thyroid cancer, autoimmune disease, or other thyroid pathology; this should include testing for iodine saturation, thyroid peroxidase, antithyroglobulin antibodies, TSH, and free T3 and free T4, with thyroid ultrasound examination and other tests as indicated by the patient’s clinical presentation. □

References

1. Markel H. “When it rains it pours”: Endemic goiter, iodized salt, and David Murray Cowie, M.D. *Am J Public Health* 1987;77:219–229.
2. Abraham GE. The concept of orthoiodosupplementation and its clinical implications. *Original Internist* 2004;11:29–38.
3. Hollowell JG, Staehling NW, Hannon WH, et al. Iodine nutrition in the United States: Trends and public health implications. Iodine excretion data from National Health and Nutrition Examination Surveys I and III (1971–1974 and 1988–1994) *J Clin Endocrinol Metab* 1998;83:3401–3408.
4. Blackburn GL. National Health and Nutrition Examination Survey: Where nutrition meets medicine for the benefit of health. *Am J Clin Nutr* 2003;78:197–198.
5. Prummel MF, Strieder T, Wiersinga WM. The environment and autoimmune thyroid diseases. *Eur J Endocrinol* 2004;150:605–618.
6. Zois C, Stavrou I, Svarna E, et al. Natural course of autoimmune thyroiditis after elimination of iodine deficiency in northwestern Greece. *Thyroid* 2006;16:289–293.
7. Abraham GE, Flechas JD, Hakala JC. Orthoiodosupplementation: Iodine sufficiency of the whole human body. *Original Internist* 2002;9:30–41.
8. Abraham GE, Brownstein D. A rebuttal of Dr. Gaby’s editorial on iodine. *Townsend Letter for Doctors & Patients*, October 2005. Online document at: www.townsendletter.com/Oct2005/gabyrebuttal1005.htm Accessed on April 1, 2007.
9. Jamieson A, Semple CG. Successful treatment of Graves’ disease in pregnancy with Lugol’s iodine. *Scott Med J* 2000;45:20–21.
10. National Academies Press. *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*. 2000. Online document at: www.nap.edu/openbook.php?record_id=10026&page=268 Accessed on April 1, 2007.
11. Gaitan E, Cooksey RC, Legan J. Antithyroid effects in vivo and in vitro of vitexin: A C-glucosylflavone in millet. *J Clin Endocrinol Metab* 1995;80:1144–1147.
12. Simsek E, Safak A, Yavuz O, et al. Sensitivity of iodine deficiency indicators and iodine status in Turkey. *J Pediatr Endocrinol Metab* 2003;16:197–202.
13. Soldin OP, Tractenberg RE, Pezzullo JC. Do thyroxine and thyroid-stimulating hormone levels reflect urinary iodine concentrations? *Ther Drug Monit* 2005;27:178–185.
14. Pavelka S. Metabolism of bromide and its interference with the metabolism of iodine. *Physiol Res* 2004;53(suppl1):S81–S90.
15. Kotozova D, Eybl V, Mihaljevic M, Glatte E. Effect of long-term administration of arsenic (III) and bromine with and without selenium and iodine supplementation on the element level in the thyroid of rat. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub* 2005;149:329–333.
16. Crump C, Michaud P, Tellez R. Does perchlorate in drinking water affect thyroid function in newborns or school-age children? *J Occup Environ Med* 2000;42:603–612.
17. Kirk AB, Martinelango PK, Tian K, et al. Perchlorate and iodide in dairy and breast milk. *Environ Sci Technol* 2005;39:2011–2017.
18. Li Z, Li FX, Byrd D, et al. Neonatal thyroxine level and perchlorate in drinking water. *J Occup Environ Med* 2000;42:200–205.
19. Brechner RJ, Parkhurst GD, Humble WO, et al. Ammonium perchlorate contamination of Colorado River drinking water is associated with abnormal thyroid function in newborns in Arizona. *J Occup Environ Med* 2000;42:777–782.
20. De Groef B, Decallonne BR, Van der Geyten S, et al. Perchlorate versus other environmental sodium/iodide symporter inhibitors: Potential thyroid-related health effects. *Eur J Endocrinol* 2006;155:17–25.
21. Chang S, Crothers C, Lai S, Lamm S. Pediatric neurobehavioral diseases in Nevada counties with respect to perchlorate in drinking water: An ecological inquiry. *Birth Defects Res [A] Clin Mol Teratol* 2003;67:886–892.
22. Zhao W, Zhu H, Yu Z, et al. Long-term effects of various iodine and fluorine doses on the thyroid and fluorosis in mice. *Endocr Regul* 1998;32:63–70.

23. World Health Organization and Food and Agriculture Organization Vitamin and Mineral Requirements in Human Nutrition, 2nd ed. 2004. Online document at: http://whqlibdoc.who.int/publications/2004/9241546123_chap16.pdf Accessed April 1, 2007.
 24. Stadel BV. Dietary iodine and risk of breast, endometrial, and ovarian cancer. *Lancet* 1976;1:890–891.
 25. Aceves C, Anguiano B, Delgado G. Is iodine a gatekeeper of the integrity of the mammary gland? *J Mammary Gland Biol Neoplasia* 2005;10:189–196.
 26. Smyth PP. The thyroid, iodine and breast cancer. *Breast Cancer Res* 2003;5:235–238.
 27. Kapdi CC, Wolfe JN. Breast cancer: Relationship to thyroid supplements for hypothyroidism. *JAMA* 1976;236:1124–1127.
 28. Shrivastava A, Tiwari M, Sinha RA. Molecular iodine induces caspase-independent apoptosis in human breast carcinoma cells involving the mitochondria-mediated pathway. *J Biol Chem* 2006;281:19762–19771. Epub 2006 May 5.
 29. Eskin BA, Shuman R, Krouse T, Merion JA. Rat mammary gland atypia produced by iodine blockade with perchlorate. *Cancer Res* 1975;35:2332–2339.
 30. Kessler JH. The effect of supraphysiologic levels of iodine on patients with cyclic mastalgia. *Breast J* 2004;10:328–336.
 31. Santiago-Fernandez P, Torres-Barahona R, Muela-Martinez JA, et al. Intelligence quotient and iodine intake: A cross-sectional study in children. *J Clin Endocrinol Metab* 2004;89:3851–3857.
 32. Qian M, Wang D, Watkins WE, et al. The effects of iodine on intelligence in children: A meta-analysis of studies conducted in China. *Asia Pac J Clin Nutr* 2005;14:32–42.
 33. Vermiglio F, Lo Presti VP, Moleti M, et al. Attention deficit and hyperactivity disorders in the offspring of mothers exposed to mild–moderate iodine deficiency: A possible novel iodine deficiency disorder in developed countries. *J Clin Endocrinol Metab* 2004;89:6054–6060.
 34. van den Briel T, West CE, Hautvast JG, Ategbo EA. Mild iodine deficiency is associated with elevated hearing thresholds in children in Benin. *Eur J Clin Nutr* 2001;55:763–768.
 35. Tiwari BD, Godbole MM, Chattopadhyay N, et al. Learning disabilities and poor motivation to achieve due to prolonged iodine deficiency. *Am J Clin Nutr* 1996;63:782–786.
 36. DeLong GR, Stanbury JB, Fierro-Benitez R. Neurological signs in congenital iodine-deficiency disorder (endemic cretinism). *Dev Med Child Neurol* 1985;27:317–324.
 37. Venturi S, Venturi A, Cimini D, et al. A new hypothesis: Iodine and gastric cancer. *Eur J Cancer Prev* 1993;2:17–23.
 38. Behrouzian R, Aghdami N. Urinary iodine/creatinine ratio in patients with stomach cancer in Urmia, Islamic Republic of Iran. *East Mediterr Health J* 2004;10:921–924.
 39. Gulaboglu M, Yildiz L, Celebi F, et al. Comparison of iodine contents in gastric cancer and surrounding normal tissues. *Clin Chem Lab Med* 2005;43:581–584.
 40. Becker DV, Braverman LE, Delange F, et al. Iodine supplementation for pregnancy and lactation—United States and Canada: Recommendations of the American Thyroid Association. *Thyroid* 2006;16:949–951.
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