Iodine is a trace element required in the diet to support various physiological functions. It is found primarily in plants grown in iodine-sufficient soil and in seafood, particularly kelp and saltwater fish. The World Health Organization (WHO) reports that despite efforts at salt iodization, 2 billion people (approximately 29%) worldwide are iodine deficient. Health effects of iodine deficiency are substantial, and deficiency is currently the leading cause of brain damage. In addition, hypothyroidism, goiter, cretinism, cognitive and neurological disorders, gastric cancer, and breast disease have been associated with iodine deficiency. The recommended daily allowance for iodine in adults is 150 μg (0.15 mg) per day, and it is 220 μg per day in pregnant women and 290 μg daily in lactating women. Although recent reports suggest that the United States population is iodine sufficient, other data indicate that subclinical deficiency could exist.

Iodine Deficiency

Salt iodization began in the 1920s in the United States in response to the prevalence of goiters in certain populations in iodine-deficient areas. The upper Midwest and Great Lakes regions were termed the “goiter belt” because 30% to 40% of the population had goiters in 1922. Universal salt iodization was adopted worldwide in 1993 in efforts to reduce iodine deficiency disorders. Despite the large intake of sodium in the American diet from processed foods, sufficient iodine intake is still questionable because many processed foods do not use the iodized form of salt.

According to the guidelines established by WHO, the mean urinary iodine concentration, which is used as an indicator of iodine status, should not be greater than 10 μg/dL, and no more than 20% of the population should have levels less than 5 μg/dL. The National Health and Nutrition Examination Surveys (NHANES) monitor urinary iodine levels in the US population. Between NHANES I (1971-1974) and NHANES III (1988-1994), the median urinary iodine concentration decreased in the US population by 50%, and excretion of iodine of less than 5 μg/dL increased by 4.5-fold. Furthermore, 6.7% of pregnant mothers and 14.9% of women of childbearing age had urinary iodine excretion below 5 μg/dL. NHANES (2001-2006) indicated that iodine levels in pregnant women in the United States were only borderline sufficient. The most recent report from NHANES 2001-2002 shows that the mean urinary iodine excretion has stabilized.

Iodine deficiency can be caused by numerous factors, including soil erosion causing low levels in foods and water sources. Consumption of large amounts of foods known as goitrogens, such as cruciferous vegetables, cassava, millet, and soya flour, can also affect iodine uptake and utilization. Furthermore, restrictive diets also play a role. Dietary salt restriction is recommended as a first-line therapy for the 74.5 million people in the United States with hypertension. Also, data suggest that 25% of vegetarians and 80% of vegans are iodine deficient. In addition, halogen elements found in the environment are similar to iodine in structure and compete for uptake and utilization. Vitamin A, iron, and selenium deficiency can also exacerbate conditions caused by iodine deficiency.

Competition for Iodine Uptake

Iodine is absorbed from the intestines in the form of iodide. It is primarily taken up from the circulation by the thyroid and...
iodide is also concentrated in breast tissue, gastric mucosa, eyes, the cervix, salivary glands, epidermis, and choroid plexus. Iodine is an element that belongs to the halogen family, which also includes fluorine, chlorine, bromine, and astatine. The halogens are similar in structure and can replace each other in physiological reactions.

**Bromine**

Bromine is used as an insecticide, fumigant, flame-proofing agent, water purifier, emulsifier in soft drinks, and dough softener and is found in fire extinguishers, pharmaceuticals, and bromated vegetable oil. Bromine has been shown to displace iodine in the body. Animal models indicate that bromine ingestion decreases iodide accumulation in the thyroid and skin and in the mammary glands in lactating rats. Additionally, bromide increases iodide excretion by the kidneys, which can influence the pool of iodide in the thyroid.\(^\text{10}\) Also, bromide has been shown to reduce iodine concentration in the mammary glands of lactating rats, to pass through the milk to the offspring, and to affect thyroid function in the offspring.\(^\text{11}\) Research also indicates that bromide can induce goiter with decreased iodine concentration in the thyroid. Supplementation with iodine and selenium has been shown to decrease by 50% the amount of bromine taken up by the thyroid compared with that in rats without selenium and iodine supplementation.\(^\text{12}\)

**Chlorine**

Chlorine is an environmental contaminant found in fertilizers, cleaning products, insecticides, pharmaceuticals, and plastics and is used in water purification. Perchlorate is a water-soluble compound used in fertilizers, rocket fuel, fireworks, and other explosives. Perchlorate has been shown to affect thyroid function by inhibiting iodine uptake by incorporation into thyroid hormones. Perchlorate is a competitive inhibitor of the iodide/sodium symporter (NIS), which concentrates iodine in the thyroid cells. This means that perchlorate can reduce the uptake of iodide in the thyroid and cause decreased thyroid function.\(^\text{13}\) In fact, the sodium iodide symporter has a 30-fold greater affinity for perchlorate than for iodide. Thus, perchlorate when present is much more likely to be taken up into the thyroid gland than iodide.\(^\text{14}\)

Research has shown that in iodine-deficient women, higher levels of perchlorate in the urine were associated with increased thyroid stimulating hormone (TSH) and decreased thyroxine (T4) levels.\(^\text{15}\) Another study revealed that all the breast milk samples and the majority of dairy milk samples contained perchlorate. The mean perchlorate levels in breast milk samples was 10.5 μg/L, which implies that the average breast-fed infant perchlorate intake is more than double the recommended maximum daily “safe” level according to the National Academy of Science.\(^\text{16}\) Although the research on perchlorate is inconsistent, some research revealed a significant increase in newborn TSH levels in an area with 100% perchlorate-contaminated drinking water compared with newborns in an area without perchlorate contamination.\(^\text{17}\) Chloride is a major component of iodized salt, where it competes with iodide for absorption. Research suggests that only 10% of iodide in iodized salt is bioavailable because of the chloride content.\(^\text{18}\)

**Fluorine**

Fluorine is found in drinking water, dental treatments, air conditioning and refrigeration, and nonstick coating such as Teflon. Research has demonstrated that excess fluorine intake increases the incidence of thyroid diseases and lower anthropometric indices in children.\(^\text{19}\) Other studies indicate that consumption of drinking water with raised fluorine content modulates the pituitary–thyroid axis resulting in an increase in TSH levels and a decrease in triiodothyronine (T3) levels.\(^\text{20,21}\) Although the research is inconsistent, animal models also show that increased intake of fluoride can cause an increase in thyroid hormones, particularly in iodine-deficient mice.\(^\text{22}\)

**Health Effects of Iodine Deficiency**

**Thyroid and Cognition**

Physiologically, the need for iodine is critical for optimal thyroid function. Iodide is taken up through the thyroid cell membrane via sodium/iodide transporters, where its concentration is 20 to 50 times higher than that in plasma. The average adult thyroid contains 15 mg of iodine in an iodine-sufficient area.\(^\text{23}\) Iodine is incorporated into thyroid hormone precursors, that combine resulting in the formation of thyroxine (T4) and triiodothyronine (T3). A goiter, or enlarged thyroid, is the initial sign of iodine deficiency. Iodine deficiency results in hypothyroidism with low levels of triiodothyronine and thyroxine and elevation of TSH, thyroglobulin, and reverse triiodothyronine test levels. Iodine deficiency is of particular importance in pregnant and lactating women. Maternal iodine deficiency and hypothyroidism is detrimental to the developing fetus, which relies on maternal thyroxine for normal development. Significant maternal iodine deficiency and hypothyroidism can result in cretinism, a condition characterized by mental retardation, neurological defects, and growth abnormalities.

Researchers evaluated the relationship between iodine deficiency and intelligence quotient (IQ) in school children. This study showed that children with urinary iodine levels above 100 μg/L had a significantly higher IQ, whereas children with urinary iodine levels less than 100 μg/L had an increased risk of having an IQ below 70. This study also found that consuming noniodized salt and drinking milk less than once per day increased the risk of having an IQ below the 25th percentile.\(^\text{24}\) Similarly, children from severe iodine-deficient areas had a loss in IQ scores of 12.45 points compared with children from iodine-sufficient areas.\(^\text{25}\)

Attention-deficit hyperactivity disorder (ADHD) has also been studied in relation to iodine deficiency. This study found
that 68.7% of the children from a moderately iodine-deficient area were diagnosed with ADHD, compared with no children diagnosed from a mildly deficient area. IQ scores were also lower in the moderately deficient area compared with scores for children in the mildly deficient area. Of the children diagnosed with ADHD, 63.6% were born to mothers who had become hypothyroid in early gestation. A similar study compared children from a severely iodine-deficient area to children from a mildly iodine-deficient area. This study demonstrated that children in the severely iodine-deficient area had lower thyroxine levels and higher TSH levels. Furthermore, the children were slower learners and had lower scores on achievement motivation tests compared with children from the mildly iodine-deficient area. Another study evaluated psychomotor development in children from a moderately iodine-deficient area. This study found that children in this area born to mothers with a free thyroxine level in the bottom 25th percentile had more than double the risk of developmental delay at 18 and 24 months of age.

**Breast Disease**

Breast tissue also expresses the iodine/sodium symporter, allowing iodine to be concentrated. Iodine is required for normal growth and development of breast tissue, and is concentrated in breast milk. The iodine/sodium symporter has been shown to be active in lactating breast tissue, benign fibrotic breast changes, and breast cancer. Researchers suggest that the high intake of iodine in Japanese women is associated with the low incidence of benign and cancerous breast diseases in this population. Iodine supplementation has been shown to suppress both the development and size of benign and cancerous growths in breast tissue. Also, there is a strong correlation between breast cancer and thyroid disease, which suggests a possible common link such as iodine deficiency.

Iodine deficiency is associated with increased risk of breast, endometrial, and ovarian cancer. Breast tissue deficient in iodine is more susceptible to the action of carcinogens, and lesions occur earlier and in greater profusion. Additionally, iodine-deficient breast tissue exhibits changes to estrogen receptor proteins, which could play a role in cancer development. Cell studies have demonstrated that in some human breast cancer cell lines, molecular iodine inhibits induction and proliferation, induces apoptosis, and exerts antioxidant activity.

Fibrocystic breast disease is also associated with iodine deficiency. Animal models indicate that blocking iodine uptake results in abnormal tissue changes such as intralobular fibrosis and cystic changes similar to human fibrocystic disease and increases precancerous lesions. Clinical trials have revealed that iodine supplementation improves mastalgia. In that study, physician assessment of pain, tenderness, and nodularity improved and more than 50% of patients receiving 6 mg/d of molecular iodine reported significant overall pain reduction. Other studies have revealed similar findings, showing that 40% to 74% of individuals with fibrocystic breast changes reported improvement in symptoms with iodine supplementation.

**Gastrointestinal Health**

Iodine is also concentrated in the gastric mucosa. Studies have shown that conditions such as atrophic gastritis result in less uptake of iodine by the tissue and are associated with iodine deficiency and goiter. Similarly, individuals with iodine-deficient goiters have an increased risk of atrophic gastritis. Furthermore, iodine inhibitors such as nitrates, thiocyanate, and salt (sodium chloride) have been shown to increase the risk of gastric cancer. Data have shown that goiter is associated with double the risk of gastric noncardia adenocarcinoma, and as iodine intake increases, both the incidence of goiter and stomach cancer decreases. Additional research has revealed that severe iodine deficiency was present in 49% of individuals with stomach cancer as compared with 19.1% of controls.

**Prostate**

Although there is no substantial research in this area, iodine could also play a role in prostate health. The iodine/sodium symporter is present in prostate epithelial tissue. NHANES I Epidemiologic Follow-up Study evaluated the potential association between iodine deficiency and prostate cancer risk. The data showed that individuals with the highest urinary iodine/creatinine ratio had a 29% reduction in prostate cancer risk compared with those with the lowest iodine excretion levels. Furthermore, the study showed a history of thyroid disease doubled the risk of prostate cancer, and those with thyroid disease for greater than 10 years had more than 3 times the risk of prostate cancer.

**Iodine Supplementation**

Controversy remains regarding the optimal daily iodine intake. This could be partly a result of the fear that iodine excess causes conditions such as hypothyroidism, goiter, and rash. Other research suggests that iodine excess is associated with thyroid autoimmune disease leading to both hypothyroidism and hyperthyroidism, despite the fact that autoimmune disease has been increasing during the same time period that iodine intake has been decreasing in the United States.

Historically, physicians over the past century have prescribed iodine in the form of Lugol’s solution, which is a 5% solution of 50 mg iodine and 100 mg potassium iodide per milliliter. Lugol’s solution was prescribed at the dose of 0.1 to 0.3 mL, which contains 12.5 to 37.5 mg elemental iodine for treatment of iodine deficiency disorders and overall well-being. Furthermore, the typical Japanese diet has a daily intake of elemental iodine as high as 13.8 mg.
Conclusion

The prevalence of iodine deficiency is alarming as it results in serious health consequences. The increasing presence of competing halogens in the environment also makes iodine deficiency a widespread health concern. Despite reports of iodine sufficiency, relative deficiencies still exist, which is of particular concern in high-risk populations.

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References