Iodine and Iodide: Functions and Benefits Beyond the Thyroid
by Shana Rheault, MS, Stephen Olmstead, MD, Janet Ralston, BS, and Dennis Meiss, PhD

Introduction
A great misconception is that iodine’s sole function in the body is to act as an essential component of thyroid hormones. The thyroid gland is not the only organ to concentrate and organize iodine. Accumulating evidence suggests there are many extrathyroidal benefits of iodine including maintaining the integrity of the mammary gland, antioxidant functions, anti-tumor activities, detoxification, immune system strengthening, and protection against potentially pathogenic bacteria. Since iodine is essential to every cell in the human body and has several biological functions beyond maintaining normal thyroid function, a reevaluation of "iodine sufficiency" is warranted. Thirty years ago, Americans consumed twice as much iodine as they do today, but the average daily intake of 240 μg is still above the reference daily intake (RDI) for iodine (150 μg), which is nearly one hundred times less than populations consuming non-Western-style diets.1 Because the whole body, not just the thyroid gland, needs iodine, most Americans would benefit from consuming larger quantities of dietary inorganic iodine.

Extrathyroidal Benefits
Deficiency of dietary iodine causes a spectrum of disorders including goiter, hypothyroidism, mental retardation, cretinism, and varying degrees of other growth and developmental abnormalities.2 The world’s leading cause of preventable brain damage is iodine deficiency.3 The World Health Organization (WHO) speculates that iodine deficiency disorders affect 740 million people worldwide and that nearly 35%, about two billion, of the world’s population are iodine-deficient.4 In an effort to prevent deficiency-related disorders, the WHO and other world health policymakers subscribe to similar optimal reference daily intakes of 100-199 μg iodine per day.4 While this amount has preventative activity, it may be far from the optimal amount. In fact, the optimal intake of iodine has never been determined. While the thyroid is known as the principal user of iodine in the body, recent biological research has discovered several organs that actively concentrate iodine including the stomach mucosa, mammary glands, salivary glands, thymus, choroid plexus, kidney, joints, arteries, and bones.13 The lactating mammary gland and salivary glands concentrate iodine almost to the same degree as the thyroid gland does. Growing evidence now suggests iodine provides several extrathyroidal benefits when consumed in larger quantities.

Dietary Sources
From 1971 through 1994, data from National Health and Nutrition Examination Survey (NHANES) have demonstrated a surprising reduction in the average American dietary iodine intake.6 Even though there was a decrease in iodine intake, the amount ingested was still considered sufficient.6 However, iodine deficiency rose tenfold to 8.1% of men and 15.1% of women throughout this period.6 Caucasian females between the ages of 40 and 49 years had the highest incidence of iodine deficiency at 25.5%.6 These results suggest that iodine deficiency is again becoming significant in the United States.

Even though dietary habits and iodine consumption of Americans have dramatically changed in the last century, the amount of iodine consumed by the average American is still considered sufficient by the Food and Nutrition Board of the Institute of Medicine.1 Extensive use of iodine in the dairy industry or as a dough conditioner in bread making is a thing of the past. For many Americans, iodized salt is the most significant contributor to their daily iodine consumption. However, over the last 25 years, salt consumption in America has decreased 65%.1 The consumption of eggs, which contain iodine-rich yolks, has also been reduced because of cholesterol concerns. Another study recently reported the significance of iodine lost in sweat, suggesting previous studies have underestimated the implications of iodine loss during exercise.7 Unlike the amount of research done on electrolyte replacement, little has been done on iodine replacement in athletes.7

Insufficient iodine intake and sustained loss have significant implications to overall health.7 The Japanese consume iodine in milligram quantities compared to the microgram amounts consumed by Americans.1 Equally startling is that Japanese women, who have among the highest iodine intake in the world, have the lowest rate of breast cancer mortality compared to US women who have the highest.1 Japanese women who adopt a Western-style diet have higher rates of breast cancer than women consuming traditional Japanese diets.1 Compared to the US, Japan has a higher life expectancy and the world’s lowest infant mortality rate.1 While no direct conclusions about the health benefits of iodine can be drawn from these data, they do suggest that increased iodine is not only safe, but may also provide additional benefits not obtained with current Western-style diets.
Iodine vs Iodide

Iodine Function in Humans

Iodine exists in nature in several inorganic forms including iodates (IO₃⁻), iodides (I⁻), and organic monoatomic iodide (I). Naturally occurring molecular iodine (I₂) is rarely, if ever, encountered. Molecular iodine must be synthesized usually by reacting either sodium or potassium iodide. Tincture of iodide, the usual source of iodine for purposes of supplementation, may be made using either sodium or potassium iodide according to United States Pharmacopoeia specifications. Both sodium and potassium iodide enhance the solubility of molecular iodine. There are also organic man-made forms of iodine that are extremely toxic and should not be mistaken for the forms listed above. Inorganic iodine consumed in large amounts is well tolerated. Several grams of iodine may produce acute toxicity, but this is a rare occurrence. The greatest amount of natural iodine is found in our oceans. Foods of marine origin concentrate iodide and have higher concentrations than terrestrial plants and animals.

In humans, the various ingested forms of iodine are reduced in the gut and are absorbed as iodide. Once in the bloodstream, iodide is transported throughout the body and eventually removed by the thyroid gland and the kidney. The thyroid gland takes up around 60 µg of iodide from circulation daily to use in the production of the thyroid hormones triiodothyronine (T₃) and thyroxine (T₄). These hormones are synthesized, stored, and released from the thyroid when needed. After binding to target tissues, the thyroid hormones regulate a number of physiologic processes, including growth, development, metabolism, and reproductive function.

In states of iodine deficiency, the thyroid enlarges, which increases its surface area and its iodine trapping efficiency. More severe cases of iodine deficiency can result in hypothyroidism and decreased fertility. A recent study of the mammary gland, showed that iodine contributes to the maintenance of its normal integrity. As opposed to the thyroid gland, which selectively accumulates iodide, the mammary gland favors iodine, suggesting that different chemical forms of iodine exhibit different functions in various organs. In human breast carcinoma tissue, iodine levels are significantly lower in surrounding tissue in the breast containing the tumor. Fibrocystic breast disease (FBD) is characterized by microcysts, fibrosis, epithelial hyperplasia, and painful lumpy breasts in reproductive-aged women.

In a review of three clinical trials, which determined the response of patients with FBD to different forms of iodine, researchers reported molecular iodine was superior to protein-bound iodide and sodium iodide when treating FBD. In one study, 74.5% of the women with FBD treated with 0.08 mg molecular iodine per kilogram showed improvement with microcysts disappearing within five months. Other forms of iodine were less efficient and included side effects such as iodine poisoning (iodism) and acne. These data substantiate studies showing iodine, rather than iodide, is the preferred form of iodine to support breast health. In addition to forming thyroid hormones, iodine in thyroid and mammary tissue can be incorporated into lipid molecules, called iodolipids, which regulate cell metabolism and proliferation and possibly have an anti-proliferative role in breast tissue.

Antioxidant and Anti-Tumor Effects of Iodine

The antioxidant properties of inorganic iodine were first revealed in kelp, when it was shown to neutralize hydrogen peroxide and prevent hydroxyl radical formation. The researchers also noted that kelp absorbed increased amounts of iodine when placed under oxidative stress. Since then, an ancestral antioxidant function has been proposed for life forms from primitive marine algae to vertebrates. In cells, iodide can act as an electron donor in the presence of hydrogen peroxide and peroxidase enzymes to prevent free radical formation. Iodine atoms iodinate amino acids, lipids, and other membrane or nuclear components, making them less reactive to free oxygen radicals. In mammals, dietary iodides have shown antioxidant activity in the eyes, an ability to defend brain cells from lipid peroxidation, and an increased antioxidant status of human serum. Iodine has also been shown to induce apoptosis in cancer cells both in vivo and in vitro. The administration of iodine-rich kelp was found to significantly delay the occurrence of chemically induced tumors in animals. The direct uptake of inorganic iodine by DMBA-induced breast tumor tissue in animals significantly suppressed tumor growth. Human breast cancer and genetically modified lung cancer cell lines have been shown to undergo apoptosis in the presence of inorganic iodine. Iodine was also shown to limit the growth of iodine-accumulating tumor xenografts compared with non-iodine-accumulating tumors in animals. Studies suggest that high iodine intake is associated with lower occurrence of breast cancer, while lower intake is associated with higher occurrence of breast cancer. The incidence of breast cancer is three times greater in people with goiters resulting from iodine deficiency. Epidemiological studies have reported increased prevalence of gastric cancer in iodine-deficient Italian populations. With increased dietary consumption of iodine-rich foods, these Italian populations have shown decreased incidences of gastric cancer. Researchers speculate this effect is due to the iodide-concentrating ability of the stomach, which uses iodide's antioxidant qualities to protect the cells from damage caused by lipid peroxidation.

Other Functions of Inorganic Iodine

Additional benefits of consuming iodine in milligram amounts are currently being studied. Among these benefits is detoxification. In one study to determine the optimal dose of iodine, women supplemented with 12.5 mg elemental iodine daily showed increased urine levels of mercury, lead, and cadmium after just one day. Although the exact mechanism by which iodine increases immune function is not known, it has long been used therapeutically in various pathologies involving the immune system. Studies have reported that adequate iodine intake is necessary for maintaining normal cell-mediated immunity, suppressing certain autoimmune diseases, and possibly preventing the development of gastric cancer induced by abnormal growth of Helicobacter pylori. The long-term consumption of high-iodide eggs resulted in increased lipid metabolism.

<table>
<thead>
<tr>
<th>Extrathyroidal Functions of Inorganic Iodine</th>
<th>Antioxidant</th>
<th>Suppresses Autoimmunity</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Neutralizes H₂O₂*</td>
<td>Enhances T-cell Adaptive Immunity</td>
<td></td>
</tr>
<tr>
<td>* Scavenges -OH*</td>
<td>Protects Against Helicobacter pylori</td>
<td></td>
</tr>
<tr>
<td>Induces Apoptosis</td>
<td>Detoxification</td>
<td></td>
</tr>
</tbody>
</table>

100 TOWNSEND LETTER – DECEMBER 2008
and thyroid function in animals. Long-term consumption suppressed age-induced lipid peroxide accumulation in the brain, reduced serum cholesterol, and elevated tissue lipoprotein lipase activity, which accompanied a moderate hypotriacylglycerolemia effect. Aging animals fed high-iodide eggs also exhibited higher thermogenic and serum T3 responses to cold, suggesting they were better suited to maintain normal thyroid function than control animals. In a small study of 12 patients with type 1 diabetes mellitus given between 50-100 mg of iodine per day, a decrease in the total amount of medications used to control the diabetes was seen in all patients, and remarkably, six patients were able to stop taking diabetes medication altogether.

### Defining the Optimal Dose

Whole-body iodine sufficiency may require consumption in milligram doses. The current RDI for iodine is 150 μg per day. Although this amount is sufficient in preventing mental retardation, hypothyroidism, goiter, and cretinism in the majority of the population, it does not account for whole-body iodine usage. The RDI was last examined by the Food and Nutrition Board in 2002 and has not changed since 1980. While the RDI gives 1.1 mg per day as an upper limit of iodine intake, it considers only the body’s thyroidal needs and not its extrathyroidal needs. An iodine-deficient person can tolerate between 12.5-50 mg per day without reported adverse side effects, allowing enough iodine in the body to sufficiently cover all needed areas.

Japanese populations living in the coastal regions consume copious amounts of iodine, averaging 13.8 mg daily due to the large quantity of seaweed in their diets. These people are among the healthiest in the world. The RDI of 150 μg per day does not provide the body with sufficient iodine to create normal cell-mediated immunity and to protect from gastric cancer and fibrocystic breast disease.

The mechanisms for these extrathyroidal roles of iodine are not well defined, but it is clear that iodine is needed in parts of the body other than the thyroid. For a generally healthy person living in any area, whether he or she has low or high levels of iodine intake, an amount of 12.5 mg up to 50 mg of inorganic iodine/iodide per day may support full body health. These larger amounts could enhance immune function and in women, contribute to the integrity of normal mammary glands. Although iodine is well tolerated, not everyone should take higher doses. Those who shouldn’t take higher doses include children under 18 and people with thyroid disease, as the risk of subclinical hypothyroidism and autoimmune thyroiditis is greater in this population.

It is imperative that anyone thinking of beginning iodine milligram dose supplementation be evaluated for underlying thyroid disease to evaluate for subclinical hyperthyroidism.

### Conclusion

Americans consume only half the amount of iodine they did 30 years ago and nearly 100 times less than the Japanese. The number of Americans who are iodine deficient has risen tenfold in a 20-year span. With food manufacturers reducing the amounts of iodine in milk and breads, and the number of Americans consuming fewer eggs and table salt, many Americans are not consuming sufficient amounts of iodine. The recommended daily intake 150 μg. This amount is far too low for many Americans. Even though this recommended intake reduces the prevalence of hypothyroidism related to iodine deficiency, it does not take into account whole-body health. Daily iodine intake in the milligram dosage may provide immune system benefit and antioxidant protection. Increased inorganic iodine/iodide has been shown to be safe in healthy adults whether iodine-deficient or not.

The benefits of increased iodine intake may include improvements in fibrocystic breast disease, a decrease in gastric and breast cancer risk, and a reduction in the amount of medication needed to control diabetes mellitus. The antioxidant and antiproliferative effects of iodine on the body may benefit healthy individuals.

### Notes