Optimizing the Thyroid by Meredith MacKay, MSc, RHN

The importance of the thyroid gland in sustaining optimal human health is well documented. It is also well known that iodine is a critical component to thyroid gland hormones. What is significantly less recognized is the interaction and importance of other minerals in the functioning of the thyroid gland, such as selenium, copper, zinc and iron. Additionally, the effects of specific foods, such as soy and cruciferous vegetables, on the thyroid is uncertain and generally misinformed; as such, these foods are usually eliminated from the diet when any thyroid issues begin to manifest, despite the various health benefits of these foods. With this article, we will dive into the world of the thyroid – starting with a brief understanding of how exactly the thyroid gland functions, endocrinologically, the building blocks required for optimal thyroid gland function, how and why a goiter forms, and what is meant by goitrogenic in terms of food and other chemicals.

The biochemistry of the thyroid gland is complex. It is controlled by the pituitary gland in the brain via hormones. Thyroid stimulating hormone (TSH) is sent from the pituitary to the thyroid gland to stimulate the production of thyroid hormones and pro-hormones. These pro-hormones (T4) and hormones (T3) are converted back and forth by iodothyronine de-iodinase enzymes (IDIs) in the body, and T3 hormones from the thyroid binds travel through the body, binding to receptors in various tissues to control gene expression (2). The metabolism of thyroid hormones and their target tissue responses depend on a variety of enzymes (such as IDIs), proteins and minerals.(2)

Iodine Plays a Key Role

Iodine is found most commonly, and in highest concentration, in the ocean - there is very little iodine found in the soil, relatively speaking. (3) The trace mineral is essential for the production of thyroid hormones and pro-hormones, yet approximately 800 million people in the world are affected by iodine deficiency disorders, including goiters, hypothyroidism, mental retardation and a spectrum of other growth and development abnormalities. (1) Since iodine is so critical to thyroid hormone production, it is the mineral most likely to affect thyroid gland function. Approximately one billion people worldwide live in areas that are at risk for iodine deficiency; of these, approximately 211 million have goiters. (2) Iodine-deficient areas are generally found in countries such as Africa, South Asia and Central Asia; however, countries in Europe, including France, Italy, and Germany, are now also considered to be iodine deficient. Even though North America is considered to be "iodine affluent", recent population surveys in the US show that approximately 36 percent of women of childbearing age are iodine deficient. (4) Subclinical hypothyroidism is defined as elevated circulating levels of TSH with normal circulating levels of T3 and T4. (6a) In mild deficiencies, such as subclinical hypothyroidism, normal thyroid hormone levels still occur, due to the enlargement of the thyroid gland (goiter), (5) which is the most recognized symptom of iodine deficiency. There are other manifestations of iodine deficiency as well, which are referred to as iodine deficiency disorders. (5) These occur most often in children and infants due to maternal iodine deficiency, and effects include hearing loss, brain damage, learning disabilities and myelination disorders. (6)

Pregnancy and lactation both increase iodine loss, which increases the risk for goiters, even after cessation of lactation. (5) Iodine deficiency can lead to hypothyroidism, anovulation, infertility, gestational hypertension, spontaneous first trimester abortion and stillbirth. (7) It is also a risk factor for thyroid carcinoma in animal and humans studies. (8-11) During pregnancy, mild hypothyroidism due to iodine deficiency is associated not only with goiters, but also lowered IQ and cognitive defects in children. (12, 13) In areas where goiters are prevalent, supplemental iodine given to infants has been shown, by skin testing, to normalize immunity, suggesting a role for iodine in immune function. (14) The thyroid gland and hypothalamic/pituitary/thyroid axis begins functioning in a fetus at 11 weeks, and T4 levels are expressed gestationally at 18 to 20 weeks to ensure the optimal development of the fetal nervous system. (5) Studies in the US assessing maternal hypothyroidism and lowered IQ in children found that iodine deficiency is linked to fetal brain damage and other neurological defects, including diminished IQ, spasticity, ataxia and deaf-mutism. (15) Iodine is also critical during lactation for continued neurological development in the infant. (16)

In Japan, the consumption of sea vegetables is very high. Sea vegetables are an excellent source of iodine, thus the estimated average intake of dietary iodine in Japan is 30 to 80 times higher than the estimated average intake in the US. (17) Japan has a lower incidence of goiters (18) than North Americans and it is hypothesized that the high intake of iodine has a protective effect for both breast cancer and thyroid diseases, (17) as iodine stores are actually higher in mammary tissue than even in the thyroid gland. (19)

The thyroid tissue sodium-iodide symporter protein stores iodide from extracellular fluid in the body within the thyroid gland, in order to produce the required concentration of iodine for the iodine-based thyroid hormones. (5) The iodide molecules move across the membrane into the cell where they are oxidized by thyroid peroxidase enzyme (TPO), then bound to tyrosine, and these mono- and di-iodotyrosines become the precursors to thyroid hormones T3 and T4. (figure 1 [5]) (20)

The Role of Selenium

Concentrations of selenium are higher in the thyroid gland than almost any other tissues in the body, with the exception of the kidneys and the liver, implying that selenium has an important function within the thyroid gland. (2) Selenium can also exert effects on thyroid hormone metabolism in tissues other than the thyroid (21) – which is different from iodine, as iodine's effects are confined strictly to the thyroid gland. Three different selenium-dependent IDIs, types I, II, and III, can activate and inactivate thyroid hormones, making selenium as essential in normal development, growth and metabolism as iodine. (1) Selenium's essential action in the thyroid is due in large part to the seleno-proteins that regulate thyroid hormone synthesis, conserve thyroid integrity during oxidative stress and control metabolism of hormones in tissues outside the thyroid gland, where the pro-hormone T4 is converted to the biologically active hormone T3 or its inactive isomer rT3. (21-23) Studies in selenium and iodine deficient populations have shown that

coexistence of these deficiencies leads to increased TSH levels and are a major contributor to the development of goiters. (24a) In populations with coexisting deficiencies, iodine supplementation is required in conjunction with selenium supplementation in order to prevent thyroid damage from iodine supplementation alone. (25)
In animal models, selenium-deficient animals with increased T4 and decreased T3 concentrations have also shown that selenium plays a role in thyroid hormone metabolism, independent of iodine. (2) This role relates to a decrease in hepatic and renal IDI type II (IDII) activity (the process of converting T4 to T3). (2) Levels of T4, T3, and rT3 are also regulated by two different IDIs Type II (IDII) and type III (IDIII); both of which contain selenium. IDII is expressed in different tissues than type I IDI and is found most often in the brain, central nervous system, brown adipose tissue and in the pituitary gland – its metabolic function depends on T2, which is produced from T4 de-iodination catalyzed by IDII (21-24). IDIII catalyzes inner ring de-iodination which converts T4 to inactive rT3 and catabolizes T3 to produce inactive T2, therefore expression of the three de-iodinase enzymes can control the concentration of thyroid hormones presented to specific tissues. (21, 24)

In selenium deficiency, selenium reserves are prioritized for specific tissues and for different seleno-enzymes within a tissue. Concentrations of selenium and seleno-enzymes are lower in liver, kidney and muscle; however, concentrations in the brain and endocrine organs (e.g. thyroid) are maintained during deficiency, implying that specific seleno-proteins are maintained at the expense of others, likely to preserve the higher priority functions of metabolism during selenium deficiency. (25a) Selenium deficiency can exacerbate hypothyroidism and goiters from iodine deficiency (2) because selenium is found bound to cysteine, as a selenocysteine molecule, in the centre of enzymes that protects the thyroid from free radical damage. (1)
In addition to iodine and selenium, zinc is important for thyroid function, with complex roles involving the synthesis of hormones and the mechanism of action of the hormones. In animal models zinc deficiency has been shown to lead to lower T3 levels, however results are inconclusive. (27, 28) Iron and copper status are also linked to lowered T3 levels in both animal and human research. (29, 30)

Are Goitrogens Problematic?

There are phytochemicals found in some foods that have been traditionally thought to diminish functioning of the thyroid gland and leads to the development of goiters – thus these compounds are termed goitrogenic.

The two most commonly known foods with goitrogenic properties are soy and cruciferous vegetables. In soy, it is the isoflavones daidzein and genistein which are believed to act as inhibitors of thyroid peroxidase enzyme. (31) Soy isoflavonoids are hypothesized to affect the thyroid hormone feedback system by interfering with biosynthesis, secretion and metabolism. (32) However, a review of fourteen trials (33) concluded that *only modest, if any, hormonal effects on the thyroid, followed a soy-rich diet*. **Also, additional risk factors, particularly iodine deficiency, are required before consuming soy could induce even a small degree of anti-thyroid effects.** (34) Recent studies have shown that soy supplementation did not affect thyroid end

points and were not associated with changes in serum thyroid hormone concentrations. (35) Given the well documented health benefits of flavonoid phytonutrients in general, and the isoflavones daidzein and genistein in particular - which include antioxidant, antihypertensive, hypocholesterolemic, anti-cancer, immunomudulatory, anti-diabetic, and anti-obesity activities, as well as improved bone health (36) - the benefit of including soy foods in the diet would likely far outweigh any possibility of negative effects on the thyroid.

Cruciferous vegetables contain thioglucosides which have been reported to breakdown into goitrogens and induce thyroid tumors in rats. (37) However, more recent studies have concluded that the possible detrimental effects of cruciferous vegetables on thyroid diseases are not supported by epidemiological studies in well-nourished populations. (38) Besides goitrogenic substances, cruciferous vegetables contain many phytonutrients, such as flavonoids, phenols, isothiocyanates, which inhibit carcinogens, and have anti-cancer properties. (39) Most cruciferous vegetables are also sources of carotenoids, such as β-carotene, and other antioxidants, which protect against various types of cancers. (26) Like soy, if there are marginally unfavorable thyroid effects of cruciferous vegetables on very specific iodine- and selenium-deficient populations, those effects are far outweighed by the protective effects of the many other phytonutrients found in this family of vegetables.

It is also important to note that there are many drugs, pesticides and chemicals that have goitrogenic effects with no beneficial effects to counter the negative effects: lithium (a popular drug used to treat mental illness), phenylbutazone (a non-steroidal anti-inflammatory [NSAID] drug), and pollutants such as thiocyanates, phthalates ester derivatives and perchlorates, which can be found in our food supply, and may play a role in thyroid diseases. (38, 41) Generally these chemicals interfere with the metabolism of iodine in the body, such that the body is unable to produce the iodine-containing thyroid hormones. Perchlorates in particular, inorganic anions naturally occurring in soil, which are also produced synthetically, are a competitive inhibitor of the sodium-iodide symporter and are capable of inhibiting iodide uptake, causing the suppression of T3 and T4 hormones. (42) Studies have found significant contamination of groundwater from perchlorates throughout western North America. (42) These chemical compounds, with no health benefits are likely a much greater source for thyroid concern than any naturally occurring, live, good quality soy or crucifer plant.

When looking to improve thyroid health it is important to eat a balanced diet containing lots of fresh fruit and vegetable, legumes, whole grains and especially sea vegetables to ensure adequate intake of iodine, selenium, zinc, copper and iron and to avoid processed foods, chemicals, pollutants and unnecessary medications that may inhibit the body's ability to metabolize the fundamental nutritional building blocks of the thyroid.

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