

ON THE IMPORTANCE OF SELENIUM FOR THYROID HEALTH

Over the past several years the Iodine deficiency epidemic has received lots of publicity in the the clinical nutrition literature. Many clinicians are now using supplemental iodine for the treatment of many thyroid and ‘extrathyroidal’ conditions associated with iodine deficiency, including hypothyroidism, breast cancer, fibrocystic breast disease and atherosclerosis. Selenium, often under emphasized, is a very critical nutrient involved in many stages of thyroid hormone synthesis and peripheral conversion. In states of selenium deficiency the thyroid gland is exposed to increased levels of oxidative stress, potentiating auto-immune thyroiditis (AIT), as well as a significant decrease in the peripheral conversion of the iodinated thyroid hormones. In this newsletter we will discuss the often overlooked, but critically important, mineral selenium and its relationship to iodine in thyroid function and peripheral hormone conversion.

Iodine is an essential nutrient for thyroid hormone synthesis as well as many ‘extrathyroidal’ body tissues and organ systems, including the skin, breasts, brain, and gastrointestinal tract-more on this next month. In the US, the current RDA for Iodine is 150 mcg/ day, the bare minimum intake to prevent Goiter. The RDA is 100 times less than that consumed on average by the Japanese, which are believed to be the healthiest people in the world (Abraham 2002). According to Dr. Brownstein, a physician in the Midwest that routinely tests and records Iodine levels on nearly every patient, more than 96% of his patient’s are Iodine deficient (unpublished). For a detailed look into the Iodine deficiency epidemic and treatment guidelines read Dr. David Brownstein’s book, “Iodine: why you need it, why you can’t live without it”, 3rd edition, available through DSD International.

Forms of Iodine: Potassium Iodide (KI) & Iodine (I₂)

There are two forms of Iodine, molecular or elemental *iodine*, I₂, and the potassium salt form called *iodide* KI (potassium Iodide). Different tissues concentrate different forms of iodine. The thyroid gland and skin utilizes iodide (KI) while the breast and prostate tissue utilize and store Iodine (I₂) (Brownstein 2008). Thus clinicians have opted to use a combination product containing both

forms of iodine when repleting iodine in patients.

Regulation of Iodine uptake: the NIS

Iodine uptake occurs via the sodium/iodine symporter (NIS) which is found in the thyroid, stomach, salivary gland, mammary glands, pituitary, pancreas, testis, ovary, adrenals, heart, thymus, lungs, and colon (Braverman 2003). The NIS is regulated by TSH. **“In an iodine deficient state plasma T4 production is decreased and TSH increases to ‘trap iodine’ via increasing NIS expression on cell membranes”.** (BIANCO, SALVATORE et al. 2002). From a serology standpoint, compensated iodine deficiency is no different from that of a hypothyroid state as *both are characterized by elevated TSH and low T4*. So is all the hypothyroidism that clinicians see simply due to an Iodine deficiency or does the thyroid gland suddenly go through ‘midlife crisis’ and produce less hormone (T4), causing TSH to increase?

With that as a brief introduction to Iodine, lets start the next section on Selenium with a quote from (Schomburg and Köhrle 2008) **“While iodine is needed as the eponymous constituent of the two major thyroid hormones T3 and T4, Selenium is essential for the biosynthesis and function of a small number of selenocysteine (Sec)-containing selenoproteins implicated in thyroid hormone metabolism and gland function”**

Selenoproteins are enzymes that have a selenocysteine moiety in their active site, 35 of which have been identified (Rayman 200). Selenoproteins influence three broad areas of cell biochemistry through their function as antioxidants, redox status, and modification of thyroid hormone metabolism via conversion of the pro-hormone T4 to the active T3 (Beckett and Arthur 2005). The three selenoproteins pertinent to this discussion are:

Thioredoxin reductase TRx: helps control intracellular redox state, protecting cells against oxidative stress, particularly hydrogen peroxide (H₂O₂)

Deiodinase enzymes: catalyze the peripheral conversion of inactive T4 to active thyroid hormone, T3. Three have been identified, termed D1-D3

Glutathione reductase (GPx): reduces

hydrogen peroxide damage in the thyroid gland, six isoenzymes have been identified in humans.

The function of Deiodinase enzymes

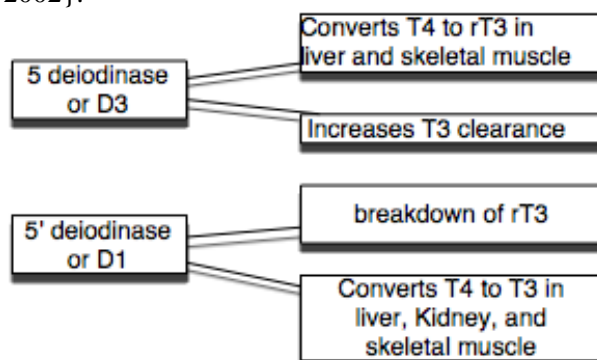
The thyroid gland secretes Thyroxine (T4) and Triiodothyronine (T3) in ratios of 11:1 or 91% T4 and 9% T3 (G J Beckett, 1992,).

“T4 is a pro-hormone, requiring 5′monodeiodination to produce the active tri-iodothyronine (T3)...more than 80% of plasma T3 is produced by 5′deiodination-a selenoprotein- in the peripheral tissues” (BIANCO, SALVATORE et al. 2002)

There are three deiodinase enzymes, labeled D1, D2, and D3. D1 or 5′ deiodinase, is found in high concentrations in the liver, kidney and muscle tissue, and has a selenocysteine residue in its active site removing the 5′ (prime) iodine from T4 (thyroxine) to produce the active T3 hormone, and participates in the breakdown of reverse T3 (rT3) {Arthur, 1990}. Selenium deficiency decreases D1 conversion of T4 to T3 and repletion increases it the activity of D1 to increase (Kohrle 2005). D2 primarily is found in the brain, pituitary, thyroid, and brown adipose tissue and converts the thyroid hormone used by the CNS. D3 or 5 deiodinase, is found in the liver and muscle tissue and converts T4 to rT3, and is up-regulated by cortisol and stressful situations such as critical illness (Peeters, Wouters et al. 2005). Elevated rT3 and low T3, T4 and TSH has been termed euthyroid sick syndrome (ESS) or nonthyroidal illness syndrome (NTIS) and has been associated with selenium deficiency (GROOT 1999).

It is important to note the relationship between D1 and D3 as they both have 2 roles: the D1 enzyme increases T4 to T3 conversion and increases rT3 clearance, and D3 increases T4 to rT3 production and increases T3 clearance(Figure 1.) (Peeters, Wouters et al. 2005). Thus when D3 is active, a marked decrease in free T3 will occur, contributing to NTIS. Factors that increase D1 activity include thyroid, steroid, and growth hormones, cAMP and factors that decrease D1 activity include glucocorticoids, the cytokines TNF-alpha, IL-1 beta, and Interferon gamma, NF- κ B activation, selenium deficiency and fasting {BIANCO, 2002, p05620}. Factors that increase D3 activity include starvation, critical illness, 17- β estradiol (E2), progesterone, pro-inflammatory

cytokines, and high levels of stress hormones, such as cortisol and catecholamines (Gangemi, Garino et al. 2008 WASCO, 2003). During fasting or illness free T3 is reduced by 90% and total rT3 is increases up to 3 fold, with an indictable change in TSH {BIANCO, 2002}.



Selenium supplementation and Deiodinase function

Selenium supplementation in the form of selenomethionine has been shown to increase T4 to T3 conversion, by supporting the D1 deiodinase enzymatic activity (Rayman 2000). For example BEHNE et al measured D1 activity by analyzing the amount of T3 converted from T4 (by D1 in the liver in units of pmol/hour) in two groups of rats; selenium deficient rats and rats given 300 mcg Se/kg (selenomethionine). The rate of T4 to T3

Figure 1. Function of D1 and D3 in the peripheral conversion of T3 and rT3

conversion in selenium deficient rats was 5 pmol/hour vs 134 pmol/hour in Se supplemented rats, a 27 fold increase in T4 to T3 conversion (BEHNE, KYRIAKOPOULOS et al. 1992). These same authors found that low iodine status also decreased liver D1 activity, reducing T4 to T3 conversion, but adding selenium to iodine deficient rats normalized the D1 conversion of T4 to T3. *Selenium deficiencies can act in concert with iodine deficiency to impair thyroid hormone metabolism and when used together they can have an enhanced response to prophylactic treatment of the two nutrients* (Zimmermann and Köhrle 2002). When both iodine and selenium are used together in deficient humans, the serology normalizes to that observed of a euthyroid state, including increased TSH, T3, and decreased T4, suggesting

that there is an increased activation of deiodinase enzymes and conversion of T3 (B, JE et al. 1991). Zinc and iron are also important minerals for adequate T3 hormone receptor binding (Daniel and Dieck 2004). According to many peer reviewed studies cited in this paper, selenomethionine is the most bioavailable and preferred form of selenium to supplement.

Oxidative Damage in thyroid hormone production

In the lumen of thyrocytes thyroperoxidase (TPO) requires high levels of hydrogen peroxide (H_2O_2 - a free radical) for iodide oxidation during the iodination of tyrosyl residues on thyroglobulin (TgB). This can create a increase in H_2O_2 and increased oxidative damage to the thyroid gland, causing apoptosis and necrosis in thyroid cells, contributing to the development of hypothyroidism (Song, Driessens et al. 2007). Synthesis of H_2O_2 appears to be the rate limiting step in thyroid hormone synthesis, and is *regulated through the action of thyroid stimulating hormone (TSH)* (Beckett and Arthur 2005). High levels of TSH increase generation of H_2O_2 , increasing cytotoxic and oxidative damage to the thyroid gland (Kohrle 2005).

“Some epidemiological studies have suggested that the increased generation of H_2O_2 caused by the high TSH associated with iodine deficiency, together with the loss of thyroidal selenoperoxidase activity due to concurrent Se deficiency, produces the marked thyroid atrophy found in myxoedematous cretinism” (Beckett and Arthur 2005)

Protecting the thyroid gland from oxidative stress

As described earlier, there are two important selenoenzymes that function as antioxidants in the thyroid gland, Glutathione reductase (GPx) and thioredoxin reductase (TRx). In states of adequate selenium status GPx and TRx protect the thyrocytes from oxidative damage by decreasing excess levels of H_2O_2 and lipid hydroperoxides (Duntas 2006). In states of selenium deficiency, the normal exposure to H_2O_2 is cytotoxic, and is associated with DNA damage, thyroid cancer and autoimmune thyroiditis (AIT) (Demelash, Karlsson et al. 2004 Leonidas H. Duntas , 2006).

Selenium treatment in Autoimmune

thyroiditis (AIT)

Many papers have been published demonstrating an immunological benefit in AIT via a reduction in anti-TPOAb titers through the use of selenium. The mechanism of action is thought that selenium repletion leads to an increased level of GPx production, thus increased antioxidant status in the thyroid gland (Turker and Karapolat 2008).

Discussion

Iodine and selenium should be used together when managing thyroid conditions because both iodine excess and iodine deficiency, in the absence of adequate selenium status, will increase oxidative stress in the thyroid gland. As stated earlier the physiological adaptation in an iodine deficient state is an increase in plasma TSH, enabling the body to increase expression of the NIS in an attempt to ‘trap’ as much iodine as possible for thyroid hormone synthesis. Since TSH also directs H_2O_2 synthesis an Iodine deficient state and concomitant elevations in plasma TSH will increase production of H_2O_2 in the thyroid gland, and without proper selenium status to promote adequate synthesis of the endogenous antioxidant enzymes GPx and TRx, the increased H_2O_2 synthesis will likely lead to increased oxidative damage to DNA and the cellular membranes in the thyrocytes (Figure 2). The consequences of the above include increased risk of AI, thyroid gland atrophy, and necrosis. Furthermore, iodine repletion (in a deficient state) will cause an increase in thyroid

hormone synthesis and TPO activity, naturally increasing thyrocyte H₂O₂ levels for the catalyzed iodination of tyrosine on TgB. If iodine repletion occurs in a state of selenium deficiency, when raw

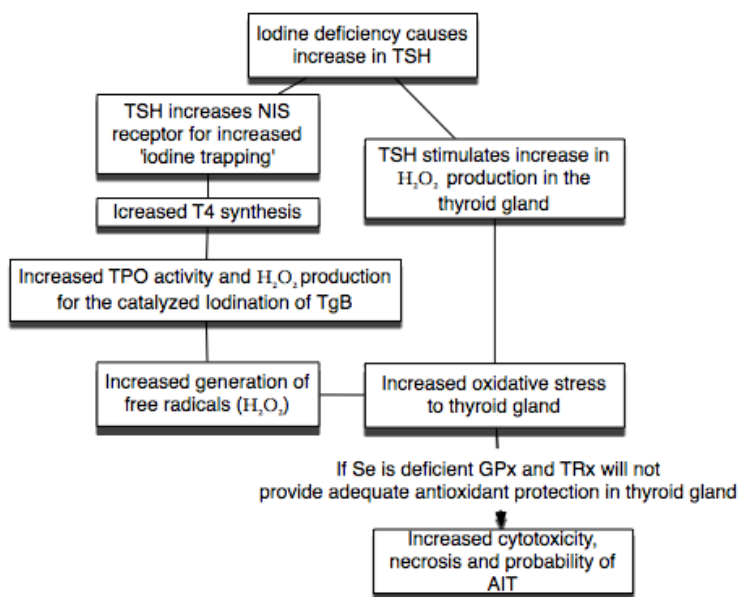


Figure 2. Pathways of hydrogen peroxide induced oxidative stress in the thyroid gland

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Thyroid Product Review

Common symptoms associated with low thyroid function

Meda-

- Depression
- Cognitive dysfunction
- Elevated cholesterol
- Constipation
- Cold intolerance
- Persistent fatigue
- Slow recovery
- Muscle cramps
- Easy bruising

Stim: Broad spectrum thyroid support product containing nutrients that support:

- **Thyroid hormone production:** Iodine, B complex, Amino acids Amino acids (Tyr, Gly, Asp), Bladderwrack, and other herbs
- **Antioxidant protection:** Selenomethionine, Glutathione, Sage, Pellitory
- **Peripheral hormone conversion:** Selenomethionine, Zinc
- **Hormone receptor binding:** Zinc

GTA: Glandular support for thyroid hypofunction. Each capsule of GTA contains 5 mg of desiccated porcine thyroid extract, which has been used for the treatment of hypothyroidism for more than 100 years. Should be used with **Meda-Stim** to give antioxidant support and assist in peripheral hormone conversion of T4 to T3.

Iodizyme-HP: Each 12.5 mg scored tablet contains 5 mg of metallic iodine and 7.5 mg of potassium iodide (potassium carrier is not measured). This is the iodine combination that is recommended by Dr. Abraham and Dr. Brownstein in their written literature

Conditions associated with iodine deficiency

Thyrostim: Contains

- Breast cancer prevention
- Fibrocystic Breast Disease
- Thyroid hypofunction
- Mastitis
- Benign Prostate Hypertrophy
- ADHD
- Autoimmune thyroiditis
- Thyroid Nodules
- Recurrent Infections
- Autism
- Thyroid cancer
-

vitamins, minerals, amino acids and glandulars to assist thyroid hormone synthesis and anterior pituitary function.

- **Thyroid hypofunction secondary to anterior pituitary hypofunction:** commonly the plasma TSH will be decreased below 3.0 along with subjective indications of thyroid hypofunction

Blood Chemistry Case History Webinar Series

This Summer and Fall Dr. Harry Eidenier will be conducting online in-depth case history sessions. Please check the online calendar of events for more details.

Drugs That Don't Work & Natural Therapies That Do!

Seminar July 11th 2009 David Brownstein, MD

Seminar Schedule: July 11, 2009 from 8:30am - 5:30pm Dr. Brownstein

Sandia Resort & Casino

30 Rainbow Road NE • Albuquerque, NM 87113
800.526.9366 For questions or to register by phone call:
(888) 450-5932 or dna9@qwest.net

Teleconference Calendar

Thursday, May 28, 2009

The Gut Part III

Thursday, June 25, 2009

Nutritional approaches to neurological disorders: anxiety, depression, & insomnia

Thursday, July 30, 2009

Integrative Cardiology

All calls will be conducted at 12:00 PM Pacific Standard Time

Please call or email the consultant in your area for lecture notes and call in numbers.

Event calendar can be found online at

www.dsdinternational.com/events



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