Treating Hypothyroidism*

In this issue we have a landmark educational article by Mr. Eric K. Pritchard, an electrical engineer by trade, on the guidelines and policy statements related to the diagnosis and treatment of hypothyroidism. Pritchard eloquently discusses the need for mainstream medicine to think well beyond thyroxine- the only treatment for patients with primary hypothyroidism. His paper sets a new bar with respect to how all clinicians should approach the conundrum of treating patients with full-blown hypothyroidism as well as those along the "spectrum" of thyroid dysfunction.

Orthomolecular clinicians have long recognized the need to treat patients for symptoms suggestive of hypothyroidism even when blood tests show normal levels of thyroid-stimulating hormone (TSH), and free levels of thyroxine (T4) and triiodothyronine (T3). As a companion to Pritchard's educational piece, I felt it prudent to include in this editorial a review of the different types of hypothyroidism (Table 1), as well as the specific orthomolecular treatments that optimize thyroid physiology and peripheral thyroid metabolism.

Primary Hypothyroidism

Intrinsic disease of the thyroid gland is the major cause of primary hypothyroidism because it results in decreased thyroid hormone production. The most common cause of primary hypothyroidism is autoimmune thyroiditis (Hashimoto's thyroiditis), with other less frequent causes being post-partum (usually develops two to 10 months after delivery), subacute granulomatous thyroiditis (inflammatory or viral syndrome), medications (e.g., lithium), and iatrogenic causes (e.g., thyroidectomy and external neck irradiation).[1]

Subclinical Hypothyroidism

This results when the intrinsic pathologic process to the thyroid has not progressed enough to become full blown.[1]

Sub-laboratory Hypothyroidism

This results when a patient presents with many of the common signs and symptoms of hypothyroidism, but lacks the requisite abnormal thyroid test results.[2]

Euthyroid Sick Syndrome

Another category of hypothyroidism is the euthyroid sick syndrome (ESS) or low T3 syndrome.[3-5] This category is reserved for patients with severe systemic illnesses (e.g., hepatic cirrhosis, myocardial infarction, and nephrotic syndrome), and these patients are usually hospitalized. It is distinctively different from the other categories of hypothyroidism. This condition is reflected by a low normal to decreased serum T4, a decreased serum T3, an increased serum reverse T3, and normal to low serum TSH.

The human organism in severe systemic illness attempts to achieve homeostasis by increasing the production of reverse T3 as a means to conserve energy, thus reducing metabolism. Patients can acquire this syndrome during caloric deprivation, acute illness, or surgery. The accompanying changes in thyroid function tests reflect effects by various cytokines and circulating inhibitors.

ESS does not require treatment to augment thyroid function; rather, once the disease in question improves with appropriate medical treatment, the syndrome resolves, as do the abnormal thyroid results, with the normalization of serum reverse T3 being the most important and integral to prognosis.

Wilson's Temperature Syndrome (WTS)

Wilson's temperature syndrome (WTS) is another category of hypothyroidism not to be confused with the ESS. This syndrome is best characterized by low oral temperatures and clinical improvements from a specific protocol involving sustained release triiodothyronine (SR-T3) and sometimes a combination of vitamin, minerals and herbal medicines.[6,7] Patients given the WTS protocol do not have ESS, and do appear to benefit from SR-T3 therapy.

Table 1. Classification of Hypothyroidism

Primary Hypothyroidism (auto-antibodies may be present and are helpful in determining the etiology)	**Subclinical Hypothyroidism**	**Sub-laboratory Hypothyroidism**	**Euthyroid Sick Syndrome**	**Wilson's Temperature Syndrome**
Majority of clinical signs and symptoms of hypothyroidism are present	Some clinical signs and symptoms of hypothyroidism are present	Some clinical signs and symptoms of hypothyroidism are present	Signs and symptoms of non-thyroid systemic illness	Low oral temperatures along with some signs and symptoms of hypothyroidism
Increased TSH	Increased TSH	Normal TSH	Low-to-Normal TSH	Normal TSH
Decreased Free T4	Normal Free T4	Normal Free T4	Decreased Serum T4	Normal Free T4
Decreased Free T3	Normal Free T3	Normal Free T3	Decreased Serum T3 and Elevated Reverse T3 (most prominent findings)	Normal Free T3

Orthomolecular Support

The therapeutic administration of orthomolecules can support thyroid physiology and even the peripheral metabolism of thyroid hormones. Rats on a copper-deficient diet for 35 days were shown to be deficient in the thyroxine 5'-monodeiodinase enzyme (converts T4 to T3 within the liver and brown adipose tissue).[8] This resulted in an increase in serum cholesterol levels, a decline in plasma T4 concentrations, and lowered body temperatures. The effects of copper deficiency on thyroid metabolism have not been corroborated in humans.

A deficiency of iron is relatively common in clinical practice. Patients can either present with iron deficiency anemia (microcytic anemia and low ferritin levels) or with iron deficiency without anemia (absent microcytic anemia and low ferritin levels). The majority of such patients complain of being persistently tired and generally feel unwell. Of course, the severity of these symptoms is dependent on the severity of their low of iron stores. There might be a relationship between iron deficiency and impaired thyroid function. In a human study (n=11), women who were made iron deficient, had reduced metabolic heat production during acute cold exposure.[9] Their abnormal responses to acute cold exposure ceased when they were adequately replete with iron. It does appear that adequate iron status is involved in the peripheral metabolism of thyroid hormones, but its mechanism requires further study.

Based on research data, selenium plays a role in ensuring proper peripheral conversion of T4 to T3, and also reduces autoimmunity directed against the thyroid gland. In a double-blind, placebo-controlled trial (n=36) of elderly subjects with normal thyroid functioning, the selenium-treated subjects had improvements in selenium indices (e.g., increased glutathione peroxidase activity), a decrease in T4, and a trend toward normalization of the T3/T4 ratio.[10] In a study published in 2007, the daily use of 200 mcg of selenium (as l-selenomethionine) for

six months resulted in statistically significant reductions in serum anti-thyroid peroxidase levels.[11] An observational study in 2008 assessed the therapeutic effects of 50-100 mcg of selenium daily to women undergoing autoimmune thyroiditis therapy.[12] This study lasted for 14 months and had a five month follow-up period. During the supplementation trial, there was an increase in serum selenium by 45%, an increase in glutathione peroxidase by 21%, and a decrease in anti-thyroid peroxidase antibodies by 76%. When selenium supplementation was withdrawn, these improvements reversed. A 2010 systematic review and meta-analysis concluded that selenium supplementation for three months resulted in significantly lower anti-thyroid peroxidase antibodies, and a significantly higher probability of reporting improvements in wellbeing and/or mood.[13] These results suggest that selenium supplementation can reduce autoimmunity directed against the thyroid gland, and improve wellbeing and/or mood if supplemented for at least three months. By supplementing for six months, there should be further decreases in anti-thyroid peroxidase antibodies.

Studies have demonstrated that both vitamin C and E favorably influence hepatic 5'-deiodinase only under circumstances where there is increased lipid peroxidation and decreased liver antioxidant-enzyme activity. More study is needed to determine how these antioxidants impact thyroid function, especially among patients with deficient levels of these antioxidants and/or with thyroid illness.

Animal studies have been able to demonstrate that zinc deficiency is associated with declines in the levels of serum T3 and free T4, as well as reductions in type I 5'-deiodinase activity.[14,15] A human study evaluating zinc-deficient disabled hypothyroid patients showed that zinc sulphate supplementation (4-10 mg/kg of body weight for 12 months) normalized levels of serum T3, decreased levels of reverse T3, and normalized the thyrotropin-releasing hormone-induced TSH reaction.[16]

Conclusion

Much more research is needed to determine the specific orthomolecules (including doses) that correct abnormal thyroid physiology and defects in peripheral thyroid metabolism. Additionally, we need to be able to quantify more precisely via laboratory studies and relevant clinical evaluations the different types of thyroid-related illness; essentially, moving beyond primary hypothyroidism as the only thyroid illness worthy of treatment. The good news for us clinicians is that this journal will continue to provide emerging information on this complicated subject. I also recommend that our readers consider looking into another organization, the Association for the Advancement of Restorative Medicine (www.restorativemedicine.org), which has been publishing and presenting conferences on the different types of hypothyroidism for years. They have done a tremendous job at evolving the paradigm of T4-only treatment for primary hypothyroidism into new paradigms of care for euthyroid patients having low body temperatures and other signs and symptoms.

–Jonathan E. Prousky, ND, MSc
Editor

*Based on material previously published in Prousky J: *Textbook of Integrative Clinical Nutrition.* Toronto, ON. CCNM Press, Inc. 2012;108-112.

References

1. Medscape Reference. Hypothyroidism. Retrieved from: *[http://emedicine.medscape.com/article/122393-overview].*
2. Gaby AR: Sub-laboratory hypothyroidism and the empirical use of Armour thyroid. *Altern Med Rev,* 2004; 9: 157-179.
3. Wartofsky L, Burman KD: Alterations in thyroid function in patients with systemic illness: the "euthyroid sick syndrome." *Endocr Rev,* 1982;3:164-217.
4. Wartofsky L, Burman KD, Ringel MD: Trading one "dangerous dogma" for another? Thyroid hormone treatment of the "euthyroid sick syndrome."

J Clin Endocrinol Metab, 1999; 84: 1759-1760.
5. Mufti TS, Jielani A: Deranged thyroid hormone status in non-thyroid illnesses; sick euthyroid syndrome. *J Ayub Med Coll Abbottabad,* 2006; 18: 1-3.
6. Friedman M, Miranda-Massari JR, Gonzalez MJ: Supraphysiological cyclic dosing of sustained release T3 in order to reset low basal body temperature. *P R Health Sci J,* 2006; 25: 23-29.
7. Wilson ED: Reversing hypometabolic symptoms by normalizing low body temperatures with sustained-release T3 in patients with euthyroid TSH levels. *J Restor Med,* 2012; 1: 64-74.
8. Lukaski HC, Hall CB, Marchello MJ: Body temperature and thyroid hormone metabolism of copper deficient rats. *Nutr Biochemistry,* 1995; 6: 445-451.
9. Lukaski HC, Hall CB, Nielsen FH: Thermogenesis and thermoregulatory function of iron-deficient women without anemia. *Aviat Space Environ Med,* 1990; 61: 913-920.
10. Olivieri O, Girelli D, Azzini M, et al: Low selenium status in the elderly influences thyroid hormones. *Clin Sci* (Lond), 1995; 89: 637-642.
11. Mazokopakis EE, Papadakis JA, Papadomanolaki MG, et al: Effects of 12 months treatment with L-selenomethionine on serum anti-TPO Levels in Patients with Hashimoto's thyroiditis. *Thyroid,* 2007; 17: 609-612.
12. Zagrodzki P, Ratajczak R: Selenium supplementation in autoimmune thyroiditis female patient--effects on thyroid and ovarian functions (case study). *Biol Trace Elem Res,* 2008; 126: 76-82.
13. Toulis KA, Anastasilakis AD, Tzellos TG, et al: Selenium supplementation in the treatment of Hashimoto's thyroiditis: a systematic review and a meta-analysis. *Thyroid,* 2010; 20: 1163-1173.
14. Kralik A, Eder K, Kirchgessner M: Influence of zinc and selenium deficiency on parameters relating to thyroid hormone metabolism. *Horm Metab Res,* 1996; 28: 223-226.
15. Fujimoto S, Indo Y, Higashi A, et al: Conversion of thyroxine into tri-iodothyronine in zinc deficient rat liver. *J Pediatr Gastroenterol Nutr,* 1986; 5: 799-805.
16. Nishiyama S, Futagoishi-Suginohara Y, Matsukura M, et al: Zinc supplementation alters thyroid hormone metabolism in disabled patients with zinc deficiency. *J Am Coll Nutr,* 1994; 13: 62-67.