

Subclinical Hypothyroidism: A Review, with Treatment Considerations

by Todd A. Born, ND

Definition

Albeit it is somewhat controversial as to whether subclinical hypothyroidism exists, technically subclinical thyroid disease (SCTD) is defined as serum free T(4) and free T(3) levels within their respective reference ranges in the presence of abnormal serum TSH levels. Most often, patients present with vague, nonspecific symptoms that are suggestive of hypothyroidism, but on many occasions, attempts to identify patients clinically, via laboratory values, have not been successful – conventionally, at least.¹

Epidemiology

Depending on the source, the prevalence ranges from 4% to 15%.² From 1988 to 1994 (I could not locate more current data), in the US National Health and Examination Survey (NHANES III), excluding known thyroid disease, 4.3% of 16,533 people had subclinical hypothyroidism. As we age, prevalence increases. It is present more often in females than males, and lower in blacks than in whites.³

Etiology⁴

The causes of subclinical hypothyroidism are the same as those of overt hypothyroidism.

Most patients have Hashimoto's thyroiditis with elevations of antithyroid peroxidase antibodies (anti-TPO). Other major causes include prior ablative or antithyroid drug therapy for Graves' disease; prior partial thyroidectomy; radiation therapy with Hodgkin lymphoma, leukemia, or brain tumors; inadequate T4 replacement therapy for overt hypothyroidism; and drugs impairing thyroid function.⁵

Diagnosis

Diagnosis is based on blood tests. It may occur with the presence or absence of mild symptoms of hypothyroidism.

In my opinion and experience, to increase the precision of the diagnosis, serum TSH, FT3, and FT4 should be tested. However, in circumstances where there is a strong indication for T4 therapy, such as pregnancy or infertility, T4 and/or T3 replacement should be initiated if TSH is elevated and/or the individual is symptomatic.

Consequences of Subclinical Hypothyroidism

A substantial proportion of patients will eventually develop overt hypothyroidism. Studies have shown in 10 to 20 years of follow-up, the cumulative incidence of overt hypothyroidism ranges from 33% to 55%.^{6,7}

Subclinical hypothyroidism has been associated with an increase in cardiovascular risk factors, markers of inflammation, vascular reactivity, endothelial function, and carotid intima media thickness.⁸⁻¹⁰ Some subjects have been observed to have diastolic dysfunction, along with increased peripheral vascular resistance.¹¹

Other comorbidities may also exist. For example, in a cross-sectional study, nonalcoholic fatty liver disease (NAFLD) was correlated with serum TSH levels. Thirty percent of individuals had ultrasonographic findings of NAFLD (versus 20% of controls), while 20% had abnormal liver enzymes.¹²

Management

Virtually all experts recommend treatment with serum thyrotropin (TSH) concentrations >10 mU/L. The routine

treatment of asymptomatic patients with TSH values between 4.5 and 10 mU/L remains controversial.¹³

Some groups suggest treatment in patients with subclinical hypothyroidism and TSH levels greater than 10 mU/L, given the data linking atherosclerosis and myocardial infarction, along with increased risk of progression to overt hypothyroidism.

There are few reported data showing benefit or harm of thyroxine (T4) treatment in patients with TSH values between 4.5 and 10 mU/L. A clinical consensus group (comprising representatives from the Endocrine Society, American Thyroid Association (ATA), and the American Association of Clinical Endocrinologists) did not recommend routine treatment for such patients, but recommended monitoring TSH levels every 6 to 12 months.¹⁴

Treatment Goals⁴

The goal of therapy is to reduce the patient's serum TSH concentration into the normal reference range, as well as improve symptoms. 1.4 mU/L is the mean serum TSH for the general US population, with 90% having serum TSH levels <3.0 mU/L. Many experts recommend a therapeutic TSH target of 0.5 to 2.5 mU/L in young and middle-aged patients, while a TSH target of 3 to 5 mU/L may be appropriate in patients over age 70 years.

Integrative and Holistic Approach

Throughout my training as a naturopathic doctor, I was indoctrinated with "don't treat the numbers, treat the patient." Typically in our view, subclinical hypothyroidism is a mild elevation in TSH (this value varies amongst various CAM providers, but typically $\geq 2.5 \mu\text{U/L}$

ml, but less than 10 µU/ml), but may also be based more on clinical symptoms.¹⁵ These patients don't meet the criteria for hypothyroidism via standard hormone tests per se (i.e., free or total T3 and free T4), but yet present clinically as hypothyroid.¹⁶

The question then arises, to treat or not to treat with thyroid hormone? I believe this needs to be taken on a case-by-case basis, but studies do show that patients generally have an improved sense of well-being, and measurable lipid and cardiac abnormalities tend to improve.^{17,18} For those with thyroid autoantibodies, it may also prevent progression of the autoimmune process with thyroid replacement.¹⁹

In my opinion, investigation of other organic etiologies that overlap hypothyroid symptomatology should be excluded first, before initiating thyroid hormone replacement. Iron deficiency anemia, hypercortisolemia, and adrenal hypofunction are just a few examples.

DHEA-S looks at adrenal function, and the stress hormone cortisol (secreted from the adrenal cortex) inhibits T4 to T3 conversion.²⁰ T4 to T3 also need cofactors of iron (Fe), zinc (Zn), methylcobalamin (B12), and selenium (Se) to convert.²¹ If FT3 is low or low normal, while FT4 is normal, you might consider a cofactor conversion issue. In order for thyroid hormone to be functionally produced, tyrosine and iodine also need to be present.²²

Once I have ruled out iron deficiency anemia, metabolic syndrome, diabetes and frank hypothyroidism, and the diagnosis "subclinical hypothyroidism," is determined, I institute the following treatments before using thyroid hormones. I have seen improvements in TSH, FT4, and FT3 values in over 100 patients, and more importantly, improvement in most if not all of the patient's health concerns.

- proper sleep hygiene
- stress management
- exercise
- contrast hydrotherapy (water therapy) to regions over the thyroid and suprarenal glands
 - Consists of 3 min hot, 30 seconds cold, in sets of three, three times daily. Always end on cold.
 - The theory is that this acts as a pumping mechanism and stimulates the glands.

- high-potency multivitamin/mineral combination, including RDA of iodine (varies from 90 mcg to 290 mcg depending on age, pregnancy, and lactation)²³
 - Provides cofactors for T4/T3 conversion.
- adaptogenic botanical medicines (beyond the scope of this discussion)
 - These have traditional use, as well as evidence regarding their efficacy to assist the body's ability to "adapt" to stress, improve stamina, energy, and mood.²⁴⁻²⁶
- DHEA supplementation if DHEA-S is low or low normal for age and gender²⁷

Conclusion

Subclinical hypothyroidism is becoming increasingly prevalent in the US, especially when one considers the ubiquity of endocrine disruptors in our environment, role of chronic stress, and poor dietary choices.²⁸ Many patients seek out integrative/CAM providers because they don't feel listened to and/or their symptoms may be brushed off and ignored.

This article has (hopefully) opened the door to the view that this may be an overlooked etiology for a patient's health concerns, and appropriate treatment may improve not only laboratory values but quality of life.

Notes

1. Bembien DA, Hamm RM, Morgan L, et al. Thyroid disease in the elderly. Part 2. Predictability of subclinical hypothyroidism. *J Fam Pract.* 1994;38(6):583.
2. Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. *Arch Intern Med.* 2000;160(4):526.
3. Hollowell JG, Staehling NW, Flanders WD, et al. Serum TSH, T(4), and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). *J Clin Endocrinol Metab.* 2002;87(2):489.
4. Ross DS, Cooper DS, Mulder JE. Subclinical hypothyroidism. UpToDate. August 2015. Accessed Sept. 11, 2015.
5. Biondi B, Cooper DS. The clinical significance of subclinical thyroid dysfunction. *Endocr Rev.* 2008;29(1):76.

6. Vanderpump MP, Tunbridge WM, French JM, et al. The incidence of thyroid disorders in the community: a twenty-year follow-up of the Whickham Survey. *Clin Endocrinol (Oxf).* 1995;43(1):55.
7. Kabadi UM. 'Subclinical hypothyroidism'. Natural course of the syndrome during a prolonged follow-up study. *Arch Intern Med.* 1993;153(8):957.
8. Monzani F, Caraccio N, Kozakowa M, et al. Effect of levothyroxine replacement on lipid profile and intima-media thickness in subclinical hypothyroidism: a double-blind, placebo-controlled study. *J Clin Endocrinol Metab.* 2004;89(5):2099.
9. Kvetny J, Heldgaard PE, Bladbjerg EM, Gram J. Subclinical hypothyroidism is associated with a low-grade inflammation, increased triglyceride levels and predicts cardiovascular disease in males below 50 years. *Clin Endocrinol (Oxf).* 2004;61(2):232.
10. Cikim AS, Ofiaz H, Ozbey N, et al. Evaluation of endothelial function in subclinical hypothyroidism and subclinical hyperthyroidism. *Thyroid.* 2004;14(8):605.
11. Biondi B, Fazio S, Palmieri EA, et al. Left ventricular diastolic dysfunction in patients with subclinical hypothyroidism. *J Clin Endocrinol Metab.* 1999;84(6):2064.
12. Chung GE, Kim D, Kim W, et al. Non-alcoholic fatty liver disease across the spectrum of hypothyroidism. *J Hepatol.* 2012 Jul;57(1):150-156. Epub 2012 Mar 14.
13. Surks MI, Ortiz E, Daniels GH, et al. Subclinical thyroid disease: scientific review and guidelines for diagnosis and management. *JAMA.* 2004;291(2):228.
14. Surks MI, Ortiz E, Daniels GH, et al. Subclinical thyroid disease: scientific review and guidelines for diagnosis and management. *JAMA.* 2004;291(2):228.
15. Pizzorno JE, Murray MT. *Textbook of Natural Medicine.* Churchill Livingstone; 1999:1331.
16. Weetman AP. Hypothyroidism: screening and subclinical disease. *BMJ.* 1997 Apr 19;314(7088):1175-1178.
17. Cooper DS, Halpern R, Wood LC, et al. L-thyroxine therapy in subclinical hypothyroidism. *Ann Intern Med.* 1984;101:18-24.
18. Arem R, Patsch W. Lipoprotein and apolipoprotein levels in subclinical hypothyroidism. *Arch Intern Med.* 1990;150:2097-2100.
19. Cooper DS. Subclinical hypothyroidism. *Adv Endocrinol Metab.* 1991;2a:77-89.
20. Walter KN et al. Elevated thyroid stimulating hormone is associated with elevated cortisol in healthy young men and women. *Thyroid Res.* 2012 Oct 30;5(1):13.
21. Kelly GS. Peripheral metabolism of thyroid hormones: a review. *Altern Med Rev.* 2000 Aug;5(4):306-333.
22. Ehrlich SD. Hypothyroidism [online article]. University of Maryland Medical Center. 2013. <http://umm.edu/health/medical/altmed/condition/hypothyroidism>. Accessed Oct. 12, 2014.
23. Iodine fact sheet for health professionals [Web page]. NIH Office of Dietary Supplements. 2011. <http://ods.od.nih.gov/factsheets/Iodine-HealthProfessional/#en2>. Accessed Oct. 13, 2014.
24. Kelly GS. Nutritional and botanical interventions to assist with the adaptation to stress. *Altern Med Rev.* 1999 Aug;4(4):249-265.
25. Head KA, Kelly GS. Nutrients and botanicals for treatment of stress: adrenal fatigue, neurotransmitter imbalance, anxiety, and restless sleep. *Altern Med Rev.* 2009 Jun;14(2):114-140.
26. Panossian AG. Adaptogens in mental and behavioral disorders. *Psychiatr Clin North Am.* 2013 Mar;36(1):49-64.
27. Kalra S, Kalra B, Nanda G. Dehydroepiandrosterone supplementation in hypothyroidism. *Thyroid Res Pract.* 2006;3(3):71-75.
28. Massart F, Ferrara P, Saggese G. Environmental thyroid disruptors and human endocrine health. In: Springer D, ed. *A New Look at Hypothyroidism.* InTech; 2012. Available at <http://www.intechopen.com/books/a-new-look-at-hypothyroidism/environmental-thyroid-disruptors-human-endocrine-health>. ◆

Dr. Todd A. Born is a naturopathic doctor, and coowner and medical director of Born Naturopathic Associates Inc. in Alameda, California. Dr. Born is the product manager, head of new product development, and scientific advisor for Allergy Research Group LLC and editor-in-chief of its science *Focus Newsletter*. He is a Thought Leader for the UK-based Clinical Education, a free peer-to-peer service that offers clinicians a closed forum to ask clinical questions and receive evidence-based responses by experts in their fields.

Dr. Born graduated from Bastyr University in Seattle and completed his residency at the Bastyr Center for Natural Health and its 13 teaching clinics, with rotations at Seattle-area hospitals. His clinical focus is utilizing integrative medicine to treat chronic disease. He has a strong interest in difficult and refractory cases, gastrointestinal issues, neurological and neurodegenerative disorders, endocrinology, cardiovascular disease and diabetes, autoimmune disease, development and behavioral issues, HIV/AIDS, and geriatrics. He has extensive knowledge and training in the basic medical sciences, physical medicine (osseous manipulation, craniosacral therapy, hydrotherapy, and physiotherapy), botanical medicine, homeopathy, biotherapeutic drainage, Ayurveda, counseling, pharmacology, and diet and nutrient therapies.

Dr. Born may be contacted via dr.born@bornnaturopathic.com or www.bornnaturopathic.com.

When he's not working, Dr. Born enjoys spending time with his wife and son, being in the great outdoors, reading, writing, traveling, and playing with his three rescued Persian cats.