Kent Holtorf, MD

Director, Holtorf Medical Group and Holtorf Medical Group Affiliate Centers; Founder and Director, National Academy of Hypothyroidism

How Does the Diagnosis and Treatment of Hypothyroidism Differ from Other Thyroid Diseases?

While the standard of care for most thyroid diseases has little controversy and is supported by a consistent consensus among practitioners, there is significant controversy regarding the essentially two standards of care for the diagnosis and treatment of hypothyroidism. The old standard of care for the diagnosis of hypothyroidism was based on a simplistic model that requires a patient to have a high TSH in order to be diagnosed with hypothyroidism, while a normal TSH indicates euthyroidism (normal tissue thyroid levels) and a suppressed TSH indicates hyperthyroidism (too much thyroid hormone). The problem is that over the last several years, hundreds of studies have demonstrated that this old standard missed the presence of hypothyroidism in the majority of patients, especially those who suffer from chronic illness such as depression, diabetes, obesity, chronic fatigue syndrome, fibromyalgia, or any other condition associated with chronic inflammation as well those with a significant exposure to plastics, pesticides, or other toxins, which potentially includes the majority of the population.

The majority of physicians believe that there must be an elevated TSH in order to make the diagnosis of hypothyroidism. If a patient meets this narrow definition of hypothyroidism, the old standard method of treatment involved treatment with inactive thyroid hormone (T4), which is generally titrated up until the TSH is normalized. The patient is then felt to be euthyroid (have normal thyroid levels). This method, which is practiced by the majority of physicians, is criticized as suboptimal, at best. Additionally, this simple treatment strategy is not followed by a very large (and growing) respectable minority of physicians. Because a significant percentage of physicians are not following the standard guidelines used by the majority of physicians, this respectable minority should not be considered to be practicing outside the standard of care for deviating from the standard diagnostic and treatment guidelines for hypothyroidism. Many alternative methods of diagnosis and treatment of hypothyroidism are evidence-based and backed by numerous published and peer-reviewed studies and taught at numerous CME approved major medical conferences.

While a review of the latest (2014) American Thyroid Association (ATA) Guidelines for the Treatment of Hypothyroidism is beyond the scope of this comment, the large respectable minority of physicians believe that the guidelines are based on a number of flawed premises. One is that the TSH level is an accurate measure of the thyroid activity in the cells of the body. The TSH level is an accurate marker for the T3 level in the pituitary, but hundreds of studies demonstrate that this age-old dogma is only accurate for a theoretical completely healthy patient with no chronic illness, including obesity, depression, stress, and the conditions listed above. Hundreds of studies demonstrate that with any physiologic or emotional stress, the T3 level in the pituitary increases (reducing TSH levels) while the T3 levels in the cells of the rest of the body are decreased. This results in secondary/tertiary hypothyroidism (hypothalamic/pituitary dysfunction), where a low TSH is associated with low peripheral thyroid cellular concentrations if any of the above conditions exist. The ATA Task Force (authors of the latest guidelines) admittedly state that the guidelines do not pertain to those with secondary/tertiary hypothyroidism, but do not state that the majority of the population have some degree of secondary/tertiary hypothyroidism.See: Holtorf, K. Peripheral Thyroid Hormone Conversion and Its Impact on TSH and Metabolic Activity. J Restor Med 2014;23:30-52. Holtorf, K. Thyroid Hormone Transport into Cellular Tissue J Restor Med 2014;3(1):53-68. Schwartz E, Holtorf K. Hormone replacement therapy in the geriatric patient: Current state of the evidence and questions for the future: Estrogen, progesterone, testosterone, growth hormone and thyroid hormone augmentation in the geriatric clinical practice: Part 1. Clinics in Geriatric Medicine 2011;27:541-559. Schwartz E, Morelli V, Holtorf K. Hormone replacement therapy in the geriatric patient: Current state of the evidence and questions for the future: Estrogen, progesterone, testosterone, growth hormone and thyroid hormone augmentation in the geriatric clinical practice: Part 2. Clinics in Geriatric Medicine 2011;27:561-575.

The ATA Task Force's literature review may have missed pertinent studies. For instance, studies that showed dramatic results with straight T3 (rather than the recommended standard treatment with T4) appear to have not been considered. The ATA Task Force used a team of translational scientists to translate basic science into clinical relevance, but they may not have considered the local control of thyroid activity, conversion of T4 to T3 (deiodinase activity), thyroid transport, and the many studies that show why it is impossible to get normal levels of T3 in the tissues if only T4 replacement is used, all of which forms the basis of the alternative treatment regimens used by a large respectable minority of physicians.

The ATA Task Force discusses the fact that much is being learned about how genetic defects in deiodinases (T4 to T3 conversion) may lead to poor patient satisfaction with T4 replacement. However, the task force did not discuss the dramatic effect that occurs on deiodinases (in addition to genetic effects) with a wide-range of chronic illnesses, all resulting in reduced cellular levels of T3. The conclusions of the task force are probably correct for a theoretical patient that has no illness, is not overweight, is not stressed, has no depression, and has never dieted, which makes the guidelines inaccurate for all those except the healthiest individuals.

A few notes on the ATA Task Force's major recommendations: regarding the recommendation on the use of T4 in those with depression and have a normal TSH, the task force recommended against treatment, stating that due to a paucity of evidence treatment success was not assured. The task force may not have considered numerous studies, including one of the largest

Malpractice or Negligence Liability: Thyroid Disorders and Conditions

Table of Contents

Introduction

Expert Analysis
Stephen Falk, MD, FACS
Robert M. Bernstein, MD, FACE
R. Thomas Zoeller, PhD
Kent Holtorf, MD

The Perspectives: Improve Your Strategy
Attorneys
Physicians and Health Providers
Insurers
Employers and Risk Managers

Practice the Technique: Checklists
Attorney Checklist
Physician Checklist
Insurer Checklist
Employer Checklist

Alternative Dispute Resolution

Reasons To Reach Settlement

Reasons To Go To Trial

Jury Awards and Settlements

Thyroid Disorders and Conditions

Law and Medicine Resources

studies ever done on the treatment of depression, which included the use of T3 in those with a normal TSH. With over 4000 patients, The Star*D Report is the largest trial comparing antidepressant effectiveness for depression. It found that 66% of patients fail to respond to antidepressants or have side-effects severe enough to discontinue use. Of those who do respond, over half will relapse within one year. The trial found that T3 was effective even when other medications-such as citalopram (Celexa), bupropion (Wellbutrin), sertraline (Zolft), venlafaxine (Effexor), or cognitive therapy-were not. Thyroid replacement with T3 was shown to be 50% more effective, even with the less than optimal dose of 50 mcg, under direct comparison with significantly less side effects than commonly used therapeutic approaches with antidepressants. See: **National Institutes of Mental Health, Questions and Answers about the NIMH Sequenced Treatment Alternatives to Relieve Depression (STAR*D) Study-All Medication Levels (November, 2006).**

The task force did not mention that the *International Journal of Neruopsychopharmacology*, published a double blind placebo control trial of 50 patients with normal thyroid function as defined by a normal TSH (1.5 +/- 0.8). The patients were randomized to receive 25 mcg of T3 or placebo in addition to antidepressant therapy. The study found almost a two-fold increase in response rate with T3 and a 4.5 times greater likelihood of experiencing a positive response at any point over a six-week period with the addition of T3. Side effects were higher in the placebo group on 10 out of 11 criteria including a significant increase in nervousness with the placebo group. See: **Posternak M et al, A pilot effectiveness study: placebo-controlled trial of adjunctive L-triiodothyronine (T3) used to accelerate and potentiate the antidepressant response, *International Journal of Neruopsychopharmacology* (February, 2008).**

The task force did not mention a study by Tammas Kelly and Daniel Lieberman that investigated the effectiveness of T3 for the treatment of biopolar disorder in 160 patients that had failed to respond to an average of 14 medications used to treat their bipolar disorder. T3 was found to be well tolerated and 84% experienced significant improvement and 33% had a full remission. Again, this is in patients who had not previously responded to numerous medications. One patient who was switched to standard T4 therapy for cost reasons experienced a return of symptoms, which resolved with the reintroduction of T3. See: **Tammas Kelly and Daniel Z. Lieberman, The use of triiodothyronine as an augmentation agent in treatment-resistant bipolar II and bipolar disorder NOS, Journal of Affective Disorders 116 (2009) 222–226.**

The ATA guidelines state that a suppressed TSH indicates overtreatment and there is significant and dramatic risk if the TSH is suppressed when on thyroid replacement, including atrial fibrillation (a-fib) and osteoporosis. These risks are claimed to be grossly overstated and disputed by a large respectable minority of physicians who state that such risks are not supported by the medical literature. For instance, the perceived risk of a-fib with a suppressed TSH is essentially based on one commonly cited study by Sawin. See: Sawin CT, Geller A, Wolf P, et al. Low serum thyrotropin concentrations as a risk factor for atrial fibrillation in older persons. NEJM 1994;331(19):1249-52. The ATA guidelines state, “For example, in one study, patients > age 65 with serum TSH levels <0.1 mIU/L, the majority of whom were taking L-T4, had a three-fold increase in the risk of atrial fibrillation over a 10 year observation period compared to euthyroid controls.” See: Jonklaas J, Bianco AC Bauer AJ, et al. Guidelines for the treatment of hypothyroidism: Prepared by the American Thyroid Association Task Force on Thyroid Hormone Replacement. Thyroid 2014;24(12):1670-751. This statement is criticized as being incorrect and grossly misleading. As an initial criticism, only 5.7% of study individuals were on thyroid replacement, not the majority, as stated. Of the 115 patients on thyroid replacement (compared to 1892 not on thyroid replacement), 36 (31%) had a suppressed TSH. There were, however, no cases of atrial fibrillation in these patients. This data thus indicates that there is no increased risk of a-fib among people who have a suppressed TSH on thyroid hormone replacement and actually shows protection against a-fib if the TSH is suppressed with those on thyroid hormone replacement. The findings support the known increase risk of a-fib in those with chronic illness, including cardiovascular disease and congestive heart failure, due to secondary and tertiary hypothyroidism.

The task force also did not mention studies that demonstrate that hypothyroidism significantly increases the risk of a-fib and that the use of T3 in those with low serum T3 reduces the risk of a-fib. See: Klemperer JD, Klein IL, Ojamaa K, et al. Triiodothyronine therapy lowers the incidence of atrial fibrillation after cardiac operations. Ann Thorac Surg 1996;61:1323-9. The same can be said of the risk of osteoporosis in those on thyroid hormone replacement with a suppressed TSH. The ATA guidelines do not cite the largest and most rigorous studies and meta-analyses that demonstrate an extremely low risk of osteoporosis with even TSH suppressive doses of thyroid replacement. In fact, the risk of osteoporosis is much higher with the simple use of antidepressants when compared to those with suppression of TSH with thyroid replacement.

In summary, the diagnosis and treatment of hypothyroidism has at least two major standards of care. Because of this, the large but minority group of physicians who do not follow the standard guidelines should not be considered to be practicing outside the standard of care.

Kent Holtorf, M.D. is the medical director of the **Holtorf Medical Group** and the nation-wide Holtorf Medical Group Affiliate Centers. He is also founder and director of the non-profit **National Academy of Hypothyroidism (NAH)**, which is dedicated to dissemination of new information to doctors and patients on the diagnosis and treatment of hypothyroidism.

Dr. Holtorf has personally trained numerous physicians across the country in the use of bioidentical hormones, hypothyroidism, complex endocrine dysfunction, and innovative treatments of chronic fatigue syndrome, weight loss, fibromyalgia, and chronic infectious diseases, including Lyme disease.

He is a fellowship lecturer for the American Board of Anti-Aging Medicine, the Endocrinology Expert for AOL Health, and is a guest editor and peer-reviewer for a number of medical journals, including *Endocrine, Postgraduate Medicine* and *Pharmacy Practice*. Dr. Holtorf has published a number of peer-reviewed endocrine reviews including on the safety and efficacy of bioidentical hormones, inaccuracies of standard thyroid testing, testosterone replacement for men and women, the diagnosis and treatment of growth hormone deficiency, the diagnosis and treatment of adrenal dysfunction in chronic fatigue syndrome and fibromyalgia, peripheral thyroid hormone conversion and its impact on TSH and metabolic activity, and the clinical applications of thyroid hormone transport into cellular tissue.

He has helped to demonstrate that much of the long-held dogma in endocrinology is inaccurate. He is a contributing author to Denis Wilson’s just published *Evidenced-Based Approach to Restoring Thyroid Health*.

He has been a featured guest on numerous TV shows, including CNBC, ABC News, CNN, EXTRA TV, Discovery Health, The Learning Channel, The Today Show, The Doctors, Dr. Dean Edell, Glenn Beck, Nancy Grace, Fox Business, ESPN, Rush Limbaugh, CBS Sunday Morning, Sean Hannity, So Cal News, and quoted in numerous print media including the Wall Street Journal, Los Angeles Times, US New and World Report, San Francisco Chronicle, WebMD, Health, Elle, Better Homes and Garden, US Weekly, Forbes, Cosmopolitan, New York Daily News, Self magazine, among many others.

WORDSWORTH LAW PUBLICATIONS, INC.
220 Fifth Avenue Suite 900, New York, NY 10001
(212) 213-0222