

Considerations in evaluating the thyroid gland in a primary care setting

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ABSTRACT

The evaluation of the thyroid can be a very involved process. A misinterpretation of the results of a thyroid function test can lead to serious complexities in a patient's management and outcome. The nuances in diagnostic approaches necessitates that standardized protocols for assessing thyroid function are established. A number of factors may impact how the thyroid functions and these factors must be considered when interpreting the results of a thyroid function test. Unfortunately, many clinicians only observe a cursory analysis of thyroid function. Primary care physicians, in particular, must be aware of these practice deficiencies and hopefully increase the detection of thyroid anomalies with greater accuracy at this first level of clinical contact.

Keywords: 5'iodinase, Biotin, metabolic, T3, T4, thyroid disorders, triiodothyronine, TSH, thyroid stimulating hormone, thyrotropin-releasing hormone, thyroxine, TRH, thyroxine-binding protein

Introductory Statement Basic Thyroid Anatomy and Physiology

The thyroid gland is a butterfly-shaped endocrine organ located in the anterior neck.^[1,2] It begins to form about 24 days after fertilization, making it the first endocrine gland to develop during the gestational period.^[1,3,4] The thyroid gland weighs about 25 grams and has two pear-shaped lobes surrounding the anterolateral aspects of cervical trachea. The primary function of the thyroid is to secrete Triiodothyronine or T3 and Thyroxine or T4, the active and inactive forms of thyroid hormones, respectively. These hormones regulate metabolism and contribute significantly to normal body development and function.^[1,2]

The thyroid gland is responsible for several metabolic functions. The wide list of functions that the thyroid gland

affect is a compelling reason why primary care physicians should have a clear understanding of its role and functions and pathophysiology. Further, an increased awareness of thyroid diseases and its associated comorbidities at the primary care level will significantly reduce practice deficiencies. Moreover, with this increase in awareness there can hopefully be an early detection of these thyroid anomalies with greater accuracy and clinical astuteness at this first level of clinical contact.

The thyroid gland has a very competent regulatory system which uses a negative feedback loop to maintain normal thyroid function. The body responds to increased levels of thyroid hormones by inhibiting the release of Thyroid Stimulating Hormone (TSH) from the anterior pituitary. Thyroid hormone production and release is stimulated through the hypothalamic-pituitary axis. The hypothalamus influences the release of thyrotropin or TSH from the anterior pituitary by secreting Thyrotropin-releasing hormone (TRH).^[2] Overall, normal thyroid function is achieved by the opposing forces of TRH and T3, which ensures a euthyroid state.^[1] Though the thyroid hormone is made up of about 90% T4, T3 hormone is two to ten times more bioactive.

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To regulate this issue, the target tissues contain 5'-iodinase, which is found in target tissues, convert the iodine-containing T4 into T3.^[2,3] Both hormones are mainly transported through the blood stream by Thyroxine-Binding Globulin (TBG).^[1]

Thyroid hormones increase basal metabolic rate, glucose absorption, proteolysis, lipolysis, and gluconeogenesis.^[4,5] They play a significant role in increasing stroke volume and heart rate, and ultimately cardiac output. In early life, thyroid hormones contribute to growth, maturation of bones, and growth plate fusion.^[1]

TSH as a Relatively Poor Standalone Thyroid Diagnostic Tool

A growing number of physicians are using the TSH as a sole diagnostic tool to evaluate thyroid disorders. This poor practice method is limited and shows no efficacy in diagnosing a majority of thyroid problems. Clearly, this dissonance in evaluating thyroid health will affect the health care of the population as many will be misdiagnosed or undiagnosed. There is poor diagnostic value in detecting any problems with T4 conversion to T3 when using TSH as a sole measure of accessing thyroid disorders.

Reviewing the Thyroid Panel

The various hormones secreted by the thyroid gland, the multiple endocrine glands and hormones involved in its negative feedback loop, and the many tissues, structures, hormones and biochemical and metabolic pathways involved in overall thyroid function, can make the thyroid evaluation a very intricate process.

TSH and Free T4 (FT4) are best suited to assess the thyroid function in a healthy population with no past medical history of thyroid disease.^[6] However, TSH and TT4 (Total T4) are best used in the assessment of hypothyroidism and hyperthyroidism.^[6] Both T3 and Free T3 (FT3) are limited in confirming hypothyroidism. Levels of these hormones are often normal in persons with hypothyroidism and are therefore poor in confirming a hypothyroid state. Moreover, 80% of T3 comes from the deiodination of T4. In a hypothyroid state, the anterior pituitary releases TSH which causes the thyroid to produce more T4.^[2] The increase in T4 causes a concomitant increase in T3. Similarly, if a person is taking supplemental Levothyroxine (L-T4), their serum T3 levels remain stable as a result of this conversion process. Therefore, measuring the T4 level with the TSH offers a better tool for evaluating hypothyroidism.^[2,6]

In hyperthyroid states, Total T3 (TT3) has poor diagnostic value in hyperthyroidism except in the evaluation of T3 hyperthyroidism.^[6] TT4 has better diagnostic sensitivity for hyperthyroidism. If a clinical diagnosis is made of hyperthyroidism in the absence of elevated T4 and T3 levels, clinicians should remeasure serum T4 levels in 1-2 weeks. Storage, temperature variances and transportation of blood samples can alter the FT4 level. TT4 levels remain relatively stable under these conditions and,

therefore, remains a significantly better method of confirming clinically suspicious hyperthyroidism than FT4.^[6]

Several medical conditions should be considered when evaluating thyroid function. TSH levels may decrease with primary hyperthyroidism, pituitary/hypothalamic disease, prolonged thyrotroph cell suppression after recent hyperthyroidism in euthyroid or hypothyroid patients, and combination of pulsative TSH secretion (released in a regular pattern or at regular intervals) and analytical precision limits.^[6] Also, drugs such as glucocorticosteroids and dopamine can also decrease TSH levels. TSH suppression and elevation is also observed in the elderly population. It is critical to note that acute or chronic systemic illnesses or non-thyroidal illnesses may also reduce TSH levels.^[6] These include chronic liver poor renal disease, myocardial infarction, burns, sepsis, and malignancy. Poor nutrition and post-surgical period should also be considered.^[6,7,8] TSH levels may be elevated with primary hypothyroidism, Amiodarone use (Amiodarone-induced thyrotoxicosis), poor gastrointestinal absorption because of drugs or disease, testing too soon after increasing dosage of T4, altered T4 clearance, poor drug compliance, recovery phase after severe systemic illness, pituitary thyrotroph adenoma, pituitary resistance to thyroid hormone (central hyperthyroidism), and generalized thyroid hormone resistance.^[9]

T4 may be elevated with hyperthyroidism (increased thyroid hormone synthesis and secretion from the thyroid gland), Graves' disease (the clinical syndrome of excess circulating thyroid hormones, irrespective of the source), early phase of acute thyroiditis, Plummer's disease (toxic thyroid adenoma), Struma ovarii, and in some cases of Luft's syndrome (Hypermetabolic Mitochondrial Miopathy). It may be decreased with primary hypothyroidism due to thyroid failure, secondary hypothyroidism due to pituitary failure or tertiary hypothyroidism due to hypothalamic failure.^[6] A T4 test is needed to properly diagnose secondary hypothyroidism and end organ hormone resistance.^[6] It is also essential when optimizing Thyroxine therapy.^[6]

Interfering Factors in Thyroid Evaluation

It is crucial to note that thyroid function can be influenced by several physiological and nutritional factors. Therefore, it is critical to consider these factors when evaluating thyroid function. Moreover, some medication and supplements can also affect thyroid function. High estrogen levels in pregnancy may increase the levels of total T4 and T3.^[10] This effect caused by high estrogen levels, is also seen in persons using birth controls. Estrogen increases the levels of binding proteins (TBG) and subsequently lead to high levels of total T4 and T3.^[6,7] Therefore, individuals who are pregnant or those who are using birth control pills should be evaluated with both TSH and free T4, as a more accurate marker for thyroid function.^[8]

The use of Biotin, a water-soluble B-vitamin, can falsely cause thyroid function tests to appear abnormal when they are not.^[11]

According to Kummer *et al.* (2016), Biotin therapy can mimic the symptoms of Graves' Disease, the most common form of hyperthyroidism followed by toxic nodular goiter.^[8,9,11] The authors recommend that Biotin be discontinued for at least two days before thyroid tests are conducted.^[9,11]

Clinical Presentation of Thyroid Diseases

Also, it is critical to note that thyroid disease can present in a number of ways with subtle, non-specific symptomatology.^[6,9,12] Some symptoms of hypothyroidism and its related conditions include weight gain, cold intolerance, fatigue, hair loss, dry skin, muscle and joint pain and weakness, depression, insomnia, memory impairment, poor attention span and concentration, forgetfulness, emotional dysfunction, constipation, menstrual and hormone issues, infertility, reduced perspiration, hoarseness and feeling of fullness in the throat, decreased vision and hearing, and paresthesia and nerve entrapment syndromes.^[6,9,12]

Some common symptoms of and its related conditions include nervousness, anxiety, heat intolerance, increase in perspiration, cardiac anomalies (tachycardia and atrial arrhythmia), hyperactivity, lid lag, warm, moist smooth skin, systolic hypertension with a widened pulse pressure, hand tremors, oligomenorrhea, muscle weakness, and unprovoked weight loss.^[6,9,12]

Other Considerations

Repeated thyroid function panels may be indicated when the results are atypical and do not follow the usual hypo/hype state. This trend analysis is crucial in evaluating the compensatory mechanisms. At this stage, no definitive treatment may be pursued.

In considering management, primary care physicians must also consider cases that fit the criteria for sub-clinical hypothyroidism (SCH).^[12,13] SCH is considered with there is an elevation in TSH but with normal corresponding levels of FT3 and FT4.^[12,13] A diagnosis of mild SCH can be made with TSH levels between 4.0 and 10.0 milli-international units (mIU)/l with normal FT3 and FT4, while levels greater than 10.0 mIU/1 is considered severe SCH.^[12] Mild SCH is associated with some functional cardiac abnormalities including impaired systolic and diastolic cardiac function and vascular dysfunction with impaired endothelial function and increased vascular stiffness.^[12] Mild SCH is also associated with dyslipidemia.^[12] Studies suggest that treating mild SCH with low dose Levothyroxine may improve the cardiac outcome by improving cardiac systolic function, diastolic function at rest and during exercise, cardiac preload, lipid metabolism, systemic vascular resistance, and arterial stiffness.^[12]

TSH levels may be elevated in persons older than 80 years of age. This elevation in TSH in this cohort may be a physiological adaptation to aging and not necessarily SCH. Experts recommend that this factor should be considered when making a diagnosis of SCH.^[12,14]

Conclusion

There is an enormous responsibility placed on primary care physicians as the first point of clinical contact, to be judicious in delivering excellent clinical care and diagnostic precision. The facets of good clinical practice form the foundation from which appropriate specialist referrals are made and from which proper management ensues.

A Quick Recap

1. TSH is a poor standalone thyroid diagnostic test.
2. The thyroid regulates a number of metabolic functions.
3. The thyroid is regulated by a negative feedback loop.
4. The body responds to increased levels of thyroid hormones by inhibiting the release of TSH from the anterior pituitary.
5. The hypothalamic-pituitary axis controls the production and release of thyroid hormone.
6. The hypothalamus influences the release of thyrotropin or TSH from the anterior pituitary by secreting Thyrotropin-releasing hormone (TRH).
7. Normal thyroid function is achieved by the opposing forces of TRH and T3
8. Though the thyroid hormone is made up of about 90% T4, T3 hormone is two to ten times more bioactive.
9. Both T3 and T4 are mainly transported through the blood stream by thyroxine-binding protein
10. T4 is converted into T3 by the 5'-iodinase that is found in target tissues.
11. Biotin supplementation can affect thyroid function
12. High estrogen levels in pregnancy or with the use of birth controls can affect thyroid function.
13. SCH must be carefully evaluated in the elderly population.

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Conflicts of interest

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References

1. Beynon ME, Pinneri K. An overview of the thyroid gland and thyroid-related deaths for the forensic pathologist. *Acad Forensic Pathol* 2016;6:217-36.
2. Costanzo LS. Thyroid hormones. In: Cicalese B., editor. *Physiology*. 4th ed. Philadelphia: Saunders Elsevier; 2010. p. 401-9.
3. Mescher AL. Junqueira's basic histology text & atlas. 12th ed. New York: McGraw-Hill Medical; c2010. Chapter 20, Endocrine Glands; p. 348-70.
4. Khatawkar AV, Awati SM. Thyroid gland-historical aspects, embryology, anatomy and physiology. *IAIM* 2015;2:165-71.
5. Mullur R, Liu YY, Brent GA. Thyroid hormone regulation of metabolism. *Physiol Rev* 2014;94:355-82.
6. Shiva Raj KC. Thyroid function test and its interpretation. *J Pathol Nepal* 2014;4:584-90.

7. Li H, Yuan X, Liu L, Zhou J, Li C, Yang P, *et al.* Clinical evaluation of various thyroid hormones on thyroid function. *Int J Endocrinol* 2014;2014:618572.
8. Santin AP, Furlanetto TW. Role of estrogen in thyroid function and growth regulation. *J Thyroid Res* 2011;2011:875125.
9. De Leo S, Lee SY, Braverman LE. Hyperthyroidism. *Lancet* 2016;388:906-18.
10. Pramanik S, Mukhopadhyay P, Ghosh S. Total T4 rise in pregnancy: A relook? *Thyroid Res* 2020;13:14.
11. Kummer S, Hermsen D, Distelmaier F. Biotin treatment mimicking Graves' disease. *N Engl J Med* 2016;375:704-6.
12. Javed Z, Sathyapalan T. Levothyroxine treatment of mild subclinical hypothyroidism: A review of potential risks and benefits. *Ther Adv Endocrinol Metabol* 2016;7:12-23.
13. Habib A, Molayemat M, Habib A. Elevated serum TSH concentrations are associated with higher BMI Z-scores in Southern Iranian Children and Adolescents. *Thyroid Res* 2020;13:9. <https://doi.org/10.1186/s13044-020-00084-9>.
14. Leng O, Razvi S. Hypothyroidism in the older population. *Thyroid Res* 2019;12:2. <https://doi.org/10.1186/s13044-019-0063-3>.