GUIDELINES & PROTOCOLS
ADVISORY COMMITTEE

# Thyroid Function Tests: Diagnoses and Monitoring of Thyroid Function Disorders in Adults

Effective Date: January 1, 2010

## Scope

This guideline applies to:
- the detection of thyroid dysfunction in adults (individuals 19 years of age and over)
- monitoring adult patients treated for thyroid function disorders.

**Diagnostic Codes:** 244 (Hypothyroidism), 242 (Hyperthyroidism)

## Prevention and Risk Factors

**Routine thyroid function testing is not recommended in asymptomatic adults.** However, testing may be indicated when non-specific signs and symptoms are present in patients at risk for thyroid disease.

**Risk factors for thyroid disease**[1]
- personal history of thyroid disease
- strong family history of thyroid disease
- diagnosis of autoimmune disease
- past history of neck irradiation
- drug therapies such as lithium and amiodarone
- women over age 50
- elderly patients
- women 6 weeks to 6 months post-partum

## Diagnosis/Investigation

**Signs/Symptoms**[1,2,3,5,6]

| Hypothyroidism | Hyperthyroidism |
|---|---|
| • Weight gain<br>• Hair loss<br>• Lethargy<br>• Menstrual irregularities (menorrhagia)<br>• Cognitive impairment<br>• Depression<br>• Constipation<br>• Goitre<br>• Dry skin<br>• Cold intolerance | • Weight loss<br>• Hair loss<br>• Palpitations / Tachycardia / Atrial fibrillation<br>• Menstrual irregularities (amenorrhea/oligomenorrhea)<br>• Widened pulse pressure<br>• Nervousness and tremor<br>• Muscular weakness<br>• Goitre<br>• Heat intolerance, diaphoresis, clammy hands<br>• Hypertension |

## Tests

**Thyroid Stimulating Hormone (TSH)**
Measurement of TSH has become the principal test for the evaluation of thyroid function in most circumstances.[2] **A TSH value within the reference interval excludes majority of cases of primary overt thyroid disease.**[3] If TSH is abnormal, confirm the diagnosis with free T4 (fT4). Where risk factors exist, consider free T3 (fT3) when fT4 is normal and thyrotoxicosis is suspected. Laboratories in BC usually retain specimens for 5 to 7 days in case add-on testing is required. See Tables 1 and 2 for potential causes.

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| Table 1: Causes of high thyroid-stimulating hormone (TSH) |
|---|
| 1. Hypothyroidism<br>2. Recovery from severe illness<br>3. Pituitary excess due to pituitary tumours causing secondary hyperthyroidism (very rare) |

| Table 2: Causes of low thyroid-stimulating hormone (TSH) |
|---|
| 1. Hyperthyroid State<br>A. Both T3 and T4 elevated<br>i) Graves' disease<br>ii) Toxic multinodular goiter<br>B. Only T3 elevated with normal T4<br>i) T3 toxicosis (e.g. Autonomous nodule)<br>ii) Exogenous T3 ingestions (liothyronine)<br>C. Only T4 elevated with normal T3<br>i) Hyperthyroidism patient with nausea, vomiting and starvation causing decreased conversion of T4 to T3 |
| 2. Hypothyroid State<br>i) Pituitary or hypothalamic disease (both T4 and T3 low) |
| 3. Euthyroid State<br>i) Sick euthyroid (both T3, T4 low, rT3* elevated)<br>ii) Drugs such as glucocorticoids, octreotide, and dopamine |

*rT3: Reverse T3 (Triiodothyronine)

## Free Thyroxine (fT4) and Free Triiodothyronine (fT3)

**Measurements of fT4 and fT3** have replaced measurements of total T4 and total T3 levels. Laboratories are permitted to substitute free hormone assays when total T3 or T4 have been ordered. **Measurement of fT3 in patients with suspected hyperthyroidism is rarely indicated.** This is reserved for situations where hyperthyroidism is suspected clinically and TSH is suppressed, but the fT4 is not elevated.[5] **Measurement of fT3 is not indicated in hypothyroidism.**

More frequent measurement of thyroid function may be useful when there is a discrepancy between the results of the initial thyroid function test and clinical findings. In most cases, repeating the same test is less useful than ordering a different test (e.g. if a TSH result does not appear to correlate with the patient's clinical status, it may be more appropriate to follow with a fT4 measurement). Consultation with a laboratory physician is appropriate when the test results do not correlate with clinical findings.

## Monitoring

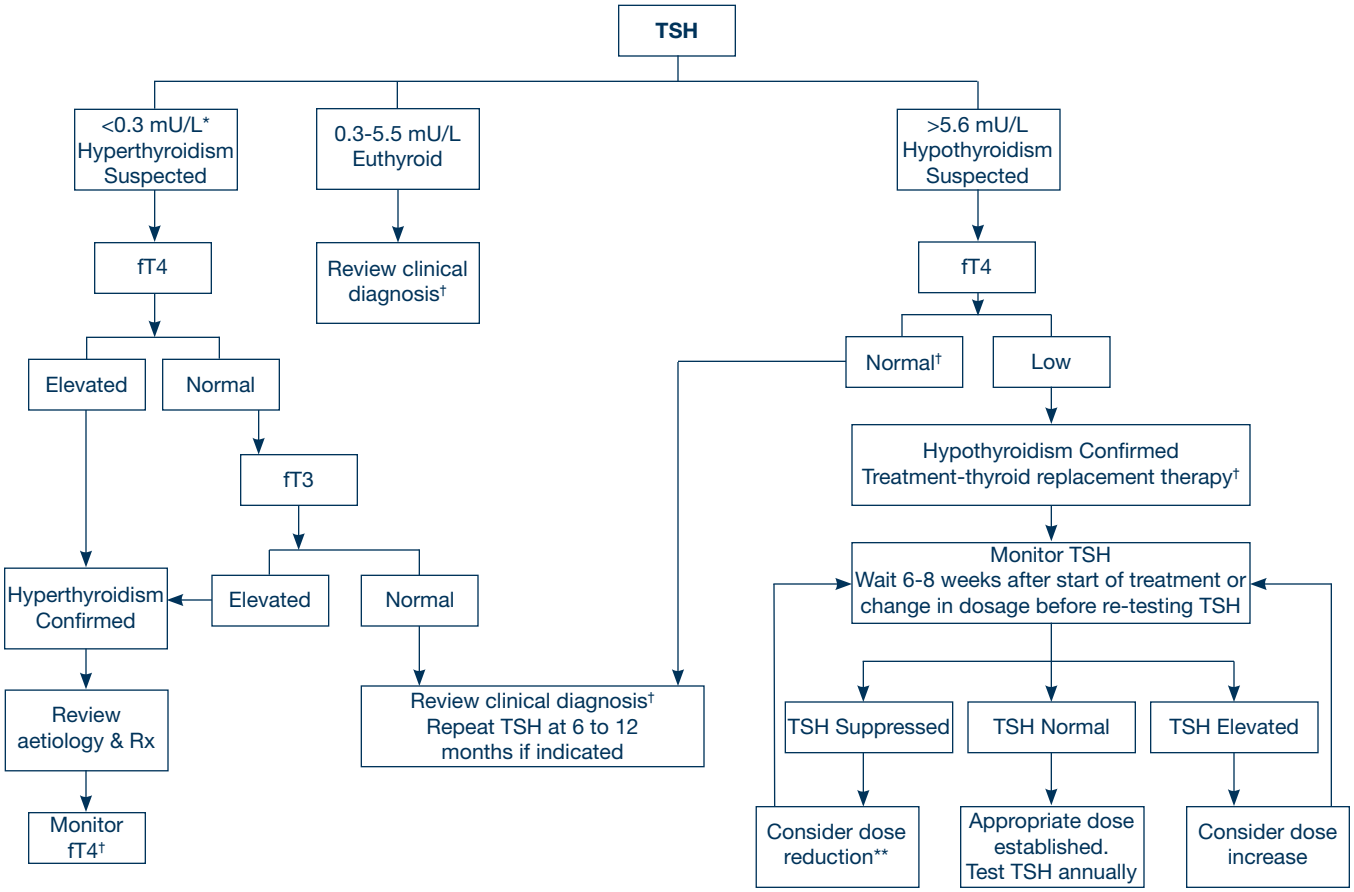
**Hypothyroidism: Since TSH values change slowly,[6] frequent repeat testing is unnecessary.** TSH may be repeated after at least 6-12 weeks following a change in thyroid hormone replacement dose or a change in a patient's clinical status. Once the TSH has normalized with treatment, it should be checked annually unless clinically indicated. This would confirm adequacy of treatment dose and compliance with therapy.

**Hyperthyroidism:** To monitor patients on treatment for Graves' disease or other causes of hyperthyroidism, allow at least three months before repeating TSH levels since pituitary secretion of TSH may be suppressed for prolonged periods following hyperthyroidism. If a biochemical measurement of thyroid status is required during this time period, fT4 is preferred.[1,6]

**Hypothalamic or pituitary disease:** TSH is only useful as a measure of thyroid disease if the hypothalamic-pituitary-thyroid axis is intact. When pituitary or hypothalamic disease is suspected, fT4 measurement is preferred to assess adequacy of thyroid replacement therapy.

**Algorithm for Thyroid Function Tests for Diagnosis and Monitoring in Symptomatic Patients With Intact Hypothalamic-Pituitary-Thyroid Axis**

(This algorithm does not apply to patients with Euthyroid Sick Syndrome or subclinical thyroid disease.)




* Patients with thyrotoxicosis usually have a TSH value of <0.1 mU/L.
** Excess replacement does increase the risk of osteoporosis and arrhythmias, especially in elderly subjects.
† Immunoassays for thyroid function tests are subject to analytical interference due to heterophile antibodies, TSH isoforms, or preanalytic factors.

**Note: Consultation with the lab physician is recommended when the test result is in conflict with the clinical presentation.**

**Subclinical Thyroid Disease**

Typically patients with subclinical thyroid diseases are asymptomatic, but have a TSH outside the reference interval and a free thyroxine within the reference interval.

In **subclinical hypothyroidism**, the TSH level may be borderline elevated in the presence of normal levels of fT4.[7] Treatment for subclinical hypothyroidism is recommended when:

- TSH greater than 10mU/L;
- TSH is above the upper reference interval limit, but ≤10 mU/L and any of the following are present:
  - elevated thyroid peroxidase (TPO) antibodies
  - goitre
  - strong family history of autoimmune disease
  - pregnancy (see pregnancy section below)

The prevalence of **subclinical hypothyroidism** in the general population is between 4% and 8%.[8] Every year, 2% to 5% of patients with subclincal hypothyroidism progress to overt hypothyroidism.[9] In recent reviews, thyroid hormone therapy for subclinical hypothyroidism did not result in improved survival or quality of life.[9,10] Monitoring of TSH in untreated patients at 12 month intervals is indicated. Routine screening for subclinical

hypothyroidism is not recommended. Clinicians should have a low threshold for obtaining a serum TSH in women who have vague suggestive symptoms, who are pregnant or anticipating becoming pregnant, or who have a strong family history of autoimmune thyroid disease.

In **subclinical hyperthyroidism**, the TSH level may be borderline suppressed in the presence of normal levels of fT4. Subclinical hyperthyroidism is less common, with a prevalence of 0.6% -1.1%.[12] In elderly patients with TSH <0.1 mU/L, the relative risk for atrial fibrillation increases threefold.[13-15] Post-menopausal women with subclinical hyperthyroidism may have an increased rate of bone loss. In the elderly there is a higher cardiovascular risk and an increased risk of fracture. Patients with atrial fibrillation and osteoporosis should be screened for hyperthyroidism. Treatment of subclinical hyperthyroidism should be considered in the elderly.[16] Patients with subclinical hyperthyroidism due to multi-nodular goitre or functioning adenoma are unlikely to normalize and are therefore more likely to benefit from treatment. Follow up testing with TSH and fT4 6-12 months later is recommended.[17]

## Thyroid Disease in Pregnancy

**a) Pre-pregnancy and early pregnancy:** TSH screening for hypothyroidism is indicated in women who are planning pregnancy or are in early pregnancy if they have a goitre or strong family history of thyroid disease.[18] If hypothyroidism has been diagnosed before pregnancy, treatment should be adjusted to achieve a TSH level not higher than 2.5 mU/L before pregnancy[19,20] and T4 re-measured within 30-40 days.[20]

**b) Pregnancy:** A high index of suspicion for thyroid disease during pregnancy is warranted. Research data support a possible connection between untreated maternal hypothyroidism and neuropsychological impairment in the offspring.[19-22] **TSH may be suppressed as a normal finding within the first trimester of pregnancy. A normal fT4 generally excludes hyperthyroidism.**[1] Thyroxine replacement dosage may increase by 25-50% during pregnancy, particularly in the first trimester. In patients on thyroxine replacement, measurement of TSH at least during each trimester is recommended.[23] It is recommended that thyroxine dose be adjusted to keep TSH between 0.5-2.5 mU/L in the first trimester and 0.5- 3.0 mU/L in the second and third trimesters.[22] Hyperthyroid patients should have specialist consultation when contemplating pregnancy or during pregnancy.

**c) Post pregnancy:** After delivery, most hypothyroid women need a decrease in the thyroxine dosage they received during pregnancy.[19,20] Post-partum thyroiditis (PPT) may occur in 5-10% of women, but there are insufficient data to recommend screening of all women. PPT is an auto-immune disorder and the presence of anti-TPO antibodies increases the risk of disease.[24] Women that are TPO antibody positive should have a TSH performed at 3 and 6 months post-partum.[20] PPT is often mild and transient. The disorder may present as hyperthyroidism followed by hypothyroidism and subsequent recovery of normal thyroid function. Some women may present with hypothyroidism without a hyperthyroid interval and may remain hypothyroid. There is an increased incidence of Graves' disease in the post-partum interval and not all hyperthyroidism is post-partum thyroiditis. There is a significant risk for recurrent post-partum thyroiditis in subsequent pregnancies. Women with a history of PPT have an increased risk of developing permanent primary hypothyroidism in 5-10 years post PPT episode. Evidence suggests an annual[20] TSH in these patients.

### Euthyroid Sick Syndrome

In Euthyroid Sick Syndrome (ESS) the hypothalamic-pituitary-thyroid axis is affected by a nonthyroid illness. The syndrome is acute, reversible, and occurs commonly after surgery, during fasting and in many acute febrile illnesses, and after acute myocardial infarction. Malnutrition, renal and cardiac failure, hepatic diseases, uncontrolled diabetes, cerebrovascular diseases, and malignancy can also produce abnormalities in thyroid function tests.[4] These changes may be observed in up to 75% of hospitalized patients.[25]
Almost any condition that can make a person ill can cause ESS, and the elderly are more susceptible because of multiple co-morbid conditions. Any abnormality in hormone level is possible, although usually fT3 and fT4 are low and TSH could be low or normal. As patients recover from their illness, TSH may normalize or become elevated. **Ideally, thyroid function tests should not be performed during non-thyroid illness**, but this may not be practically applicable, so any abnormal results should be interpreted with caution and with a realization that ESS is the most likely explanation for the finding rather than true thyroid disease. TSH levels must be interpreted with caution in hospitalized individuals unless values are below 0.1 or above 20 mU/L.[2] Thyroxine replacement has not been beneficial and should not be used in patients with ESS.[4,25]

## Rationale

Considering the high prevalence of thyroid disease, particularly hypothyroidism in women, and the fact that some studies have shown that affected women may benefit from early treatment, it is recommended that clinicians maintain a high index of suspicion and investigate individuals with vague symptoms that could be related to thyroid dysfunction.[26] **If initial testing is normal, repeat testing is unnecessary, unless there is a change in clinical condition.**

## References


1 Toward Optimized Practice Clinical Practice Guideline Working Group. Clinical Practice Guideline: Investigation and Management of Primary Thyroid Dysfunction. Toward Optimized Practice Program, Edmonton: AB, 2008 Update.

2 Dufour D. Laboratory Tests of Thyroid Function: Uses and limitations. Endocrinol Metab Clin N AM. 2007;36:579-594.

3 Thyroid Foundation of Canada. Health Guides on Thyroid Disease http://www.thyroid.ca/Guides/HG02.html#1, Accessed March 5 2009.

4 Rehman S, Cope D, Senseney A, et al. Thyroid Disorders in Elderly Patients, S Med J 2005;98(5):543-549.

5 Ont Assoc of Medical Laboratories. Guideline for the Use of Laboratory Tests to Detect Thyroid Dysfunction CLP 015, Revised July 2007.

6 Kaplan MM. Clinical perspectives in the diagnosis of thyroid disease. Clin Chem 1999;45(8):1377-1383.

7 Ogedebe H. Thyroid function test: a clinical lab perspective. Medical Laboratory Observer, February, 2007:10-19.

8 Muller AF, Bergout A, Wiersinga WM, et al. Thyroid Function Disorders- Guidelines of the Netherlands Association of Internal Medicine. The Netherlands Journal of Medicine. 2008;66(3):134-142.

9 Surks M. Ortiz, E., Daniels, G. et al. Subclinical Thyroid Disease; Scientific Review and Guidelines for diagnosis and Management. JAMA. 2004;291(2):228-238.

10 Villar HCCE, Saconato H, Valente O. et al. Thyroid hormone replacement for subclinical hypothyroidism. Cochrane Datatbase of Systematic Reviews. 2007:3.

11 Fatourechi V. Subclinical Hypothyroidism: An Update for Primary Care Physicians, Mayo Clin Proc. January 2009;84(1):65-7

12 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. 1995;43:55-68.

13 Sawin CT, Geller A, Wolf PA, et al. Low serum thyrotropin concentrations as a risk factor for atrial fibrillation in older persons. N Engl J Med. 1994;331(19):1249-52.

14 Toft AD. Subclinical hyperthyroidism. N Engl J Med. 2001;345(7):512-516.

15 Hoogendoorn E, den Heijer M, van Dijk A. et al. Subclinical Hyperthyroidism: to treat or not to treat? Postgrad Med J. 2004;80:394-398.

16 Biondi B. European Journal of Endocrinology. 2008;159:343–345.

17 Use of Thyroid Function Tests Gidelines Development Group. UK Guidelines for the Use of Thyroid Function Tests, http://www.acb.org.uk/docs/TFTguidelinefinal.pdf, 2006.

18 Fauci A, Harrison TR. Harrison's Principles of Internal Medicine, 17th edition, NY:McGraw-Hill Professional; 2008.

20 Abalovich M, Amino N, Barbour L, et al. Management of thyroid dysfunction during pregnancy and postpartum: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2007;92(8):S1-S47.

21 ATA Public Health Committee Statement. Haddow study of maternal hypothyroidism during pregnancy. Thyroid. 1999;9(9):971-972.

22 Davies TF. The ATA, the Endocrine Society, and the AACE confuse endocrinologists on thyroid disease in pregnancy. Thyroid. 2000;10(2):107.

23 Haddow JE, Palomaki GE, Allan WC, Williams JR, Knight GJ, Gagnon J et al. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. N Eng J Med. 1999;341(8):549-555.

24 The Endocrine Society Guidelines on Thyroid disease in pregnancy, J Clin Endocrin Metab. 2007;92(8):S1-S47.

25 Montero MN. Management of hypothyroidism during pregnancy. Clin Obstet Gynecol. 1997;40(1):65-80.

26 American College of Obstetrics and Gynecologists Practice #37. Bulletin Obstetrics and Gynecology. 2002;100(2).

27 Adler SM, Wartofsky L. The nonthyroidal illness syndrome. Endocrinol Metab Clin North Am. 2007;36:657-72.

28 The Canadian Task Force on the Periodic Health Examination. Screening for thyroid disorders and thyroid cancer in asymptomatic adults. The Canadian Guide to Clinical Preventive Health Care. 1994;612-618; revised 2003.

## List of Abbreviations

| | |
|---|---|
| TSH | Thyroid stimulating hormone |
| ESS | Euthyroid sick syndrome |
| fT3 | Free triiodothyronine |
| fT4 | Free thyroxine |
| PPT | Post-partum thyroiditis |
| rT3 | Reverse T3 (Triiodothyronine) |
| TPO | Thyroid peroxidase |

This guideline is based on scientific evidence current as of the Effective Date.

This guideline was developed by the Guidelines and Protocols Advisory Committee, approved by the British Columbia Medical Association and adopted by the Medical Services Commission.

**The principles of the Guidelines and Protocols Advisory Committee are to:**

- encourage appropriate responses to common medical situations
- recommend actions that are sufficient and efficient, neither excessive nor deficient
- permit exceptions when justified by clinical circumstances

**Contact Information**

Guidelines and Protocols Advisory Committee
PO Box 9642 STN PROV GOVT
Victoria BC V8W 9P1
Phone: 250 952-1347
Fax: 250 952-1417
E-mail: hlth.guidelines@gov.bc.ca
Web site: www.BCGuidelines.ca