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
- 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

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

Thyroid Stimulating Hormone (TSH)
Measurement of TSH has become the principal test for the evaluation of thyroid function in most circumstances. A TSH value within the reference interval excludes majority of cases of primary overt thyroid disease. 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.
Table 1: Causes of high thyroid-stimulating hormone (TSH)

1. Hypothyroidism
2. Recovery from severe illness
3. Pituitary excess due to pituitary tumours causing secondary hyperthyroidism (very rare)

Table 2: Causes of low thyroid-stimulating hormone (TSH)

1. Hyperthyroid State
   A. Both T3 and T4 elevated
      i) Graves’ disease
      ii) Toxic multinodular goiter
   B. Only T3 elevated with normal T4
      i) T3 toxicosis (e.g. Autonomous nodule)
      ii) Exogenous T3 ingestions (liothyronine)
   C. Only T4 elevated with normal T3
      i) Hyperthyroidism patient with nausea, vomiting and starvation causing decreased conversion of T4 to T3

2. Hypothyroid State
   i) Pituitary or hypothalamic disease (both T4 and T3 low)

3. Euthyroid State
   i) Sick euthyroid (both T3, T4 low, rT3* elevated)
   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.  
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, 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.

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. Elevated 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%. Every year, 2% to 5% of patients with subclinical hypothyroidism progress to overt hypothyroidism. In recent reviews, thyroid hormone therapy for subclinical hypothyroidism did not result in improved survival or quality of life. 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 pregnancy19,20 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 Throxine 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 annual22 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. If initial testing is normal, repeat testing is unnecessary, unless there is a change in clinical condition.

References

3. Thyroid Foundation of Canada. Health Guides on Thyroid Disease http://www.thyroid.ca/Guides/HG02.html#1, Accessed March 5 2009.
23. The Endocrine Society Guidelines on Thyroid disease in pregnancy, J Clin Endocrin Metab. 2007;92(8):S1-S47.
List of Abbreviations

<table>
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<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>TSH</td>
<td>Thyroid stimulating hormone</td>
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<td>ESS</td>
<td>Euthyroid sick syndrome</td>
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<td>fT3</td>
<td>Free triiodothyronine</td>
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<td>fT4</td>
<td>Free thyroxine</td>
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<td>PPT</td>
<td>Post-partum thyroiditis</td>
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<td>rT3</td>
<td>Reverse T3 (Triiodothyronine)</td>
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<tr>
<td>TPO</td>
<td>Thyroid peroxidase</td>
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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

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The Clinical Practice Guidelines (the "Guidelines") have been developed by the Guidelines and Protocols Advisory Committee on behalf of the Medical Services Commission. The Guidelines are intended to give an understanding of a clinical problem, and outline one or more preferred approaches to the investigation and management of the problem. The Guidelines are not intended as a substitute for the advice or professional judgment of a health care professional, nor are they intended to be the only approach to the management of clinical problems.