OBJECTIVE

Alberta clinicians optimize laboratory testing for the investigation and management of primary thyroid dysfunction

TARGET POPULATION

Adults and children with suspected or confirmed primary thyroid dysfunction

EXCLUSIONS

Neonatal patients

Asymptomatic, seemingly healthy individuals having a periodic exam

RECOMMENDATIONS

PRACTICE POINT

Thyroid stimulating hormone (TSH) is the most sensitive and specific test for the investigation and management of primary thyroid dysfunction

- ✓ Order TSH as the single best initial test to diagnose primary hyperthyroidism and hypothyroidism when symptoms are present (See Table 1, for at-risk see Table 2)
- X DO NOT test patients who are asymptomatic, seemingly healthy, having a periodic exam

Symptoms of Hypothyroidism	Symptoms of Hyperthyroidism
• Weight gain • Lethargy • Cold intolerance • Menstrual irregularities • Depression • Constipation • Dry skin	• Palpitations/ tachycardia/ atrial fibrillation • Widened pulse pressure • Nervousness and tremor • Heat intolerance • Weight loss • Muscular weakness • Usually goiter is present

Table 1: Symptoms of Hypothyroidism and Hyperthyroidism

- ✓ Follow Category 1 for patients having suspected primary thyroid disease
- ✓ Follow Category 2 when patients are taking thyroid hormone replacement and dosage needs monitoring
- ✓ Follow Category 3 when patients are receiving thyroxine therapy for thyroid cancer
- ✓ Follow Category 4 when patients are pregnant and receiving thyroid hormone replacement
- ✓ Follow Category 5A or 5B when patients are receiving lithium or amiodarone
- X DO NOT order TSH for suspected pituitary disease. FT4 is recommended
- X DO NOT use TSH as an indicator of thyroid status in patients with severe non-thyroidal illness (e.g., CCU, ICU, acute severe psychiatric illness)

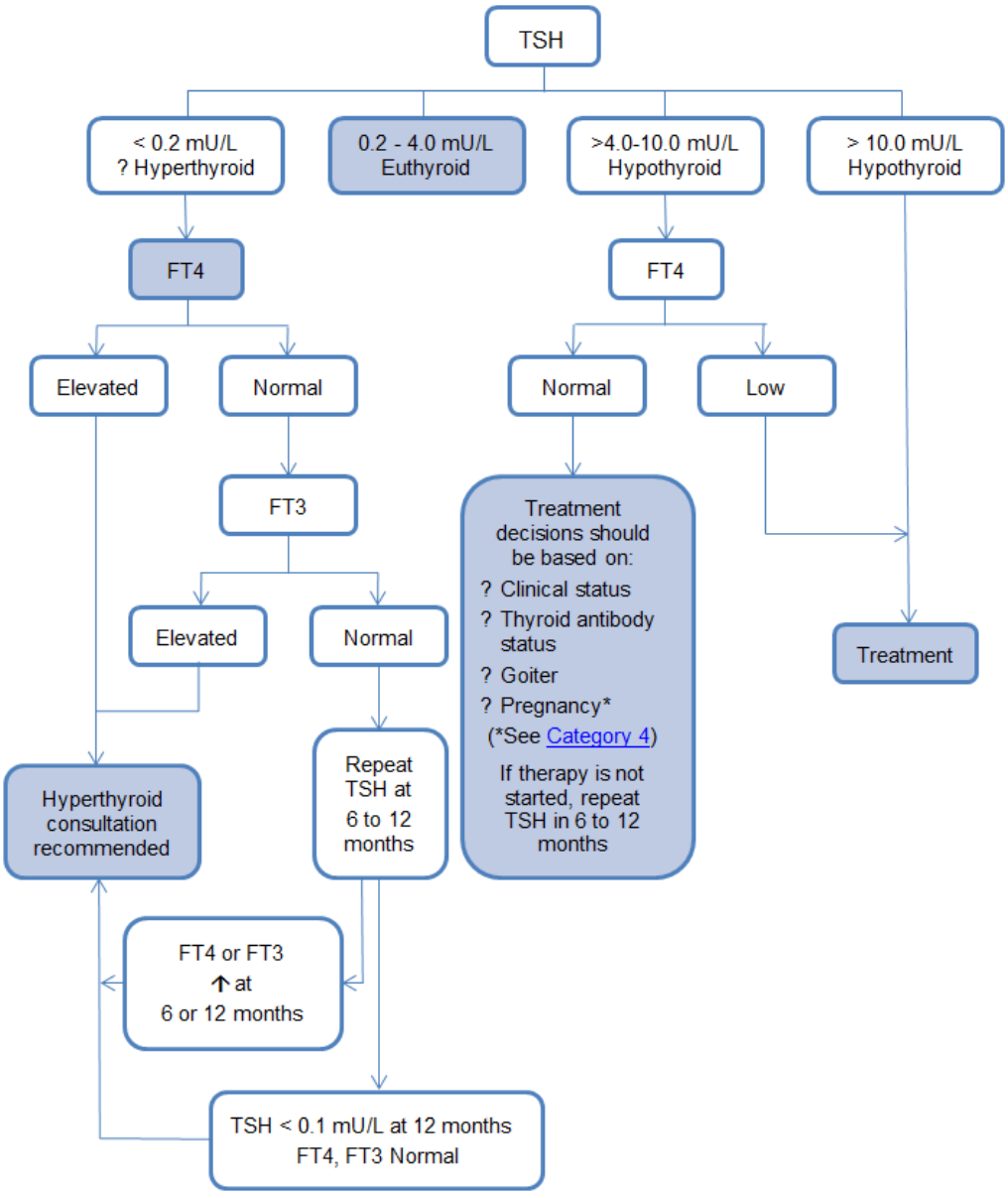
X DO NOT rely on TSH alone within three months of therapy for hyperthyroidism with radioactive iodine as it may not reflect the clinical status. Use FT4 in addition to TSH during this period.

X DO NOT use thyroxine suppression therapy for thyroid nodules or euthyroid nodular goiter

*CATEGORY 1: SUSPECTED HYPER OR HYPOTHYROIDISM**

*For patients receiving thyroid hormone therapy follow Category 2

- Patients with thyrotoxicosis usually have a TSH value < 0.1 mU/L
- Thyroid antibodies are indicated in cases of hypothyroidism (TSH > 4 mU/L) due to suspected autoimmune thyroid disease. Serum antibody (anti TPO) testing should only be performed once for the diagnosis. Serial testing has no clinical utility.



CATEGORY 2: TSH USE IN THYROXINE THERAPY FOR TREATMENT OF HYPOTHYROIDISM

- ✓ Use L-Thyroxine for thyroid replacement. DO NOT use T3, T3/T4 combinations, or desiccated thyroid
- ✓ Target TSH in euthyroid range*
- ✓ Wait for TSH equilibration – TSH equilibration requires eight to 12 weeks after any thyroxine dosage change
- ✓ Order a yearly TSH once a stable dose is achieved – yearly TSH is sufficient

**Patients on thyroxine therapy with TSH < 0.2 mU/L may have increased health risk*

CATEGORY 3: TSH USE IN MONITORING THYROXINE THERAPY IN THYROID CANCER

- ✓ Target: Achieve suppressed TSH (< 0.1 mU/L) in moderate to high risk patients, and TSH 0.1 – 0.5 mU/L in low risk patients,[1] to prevent re-growth of cancer

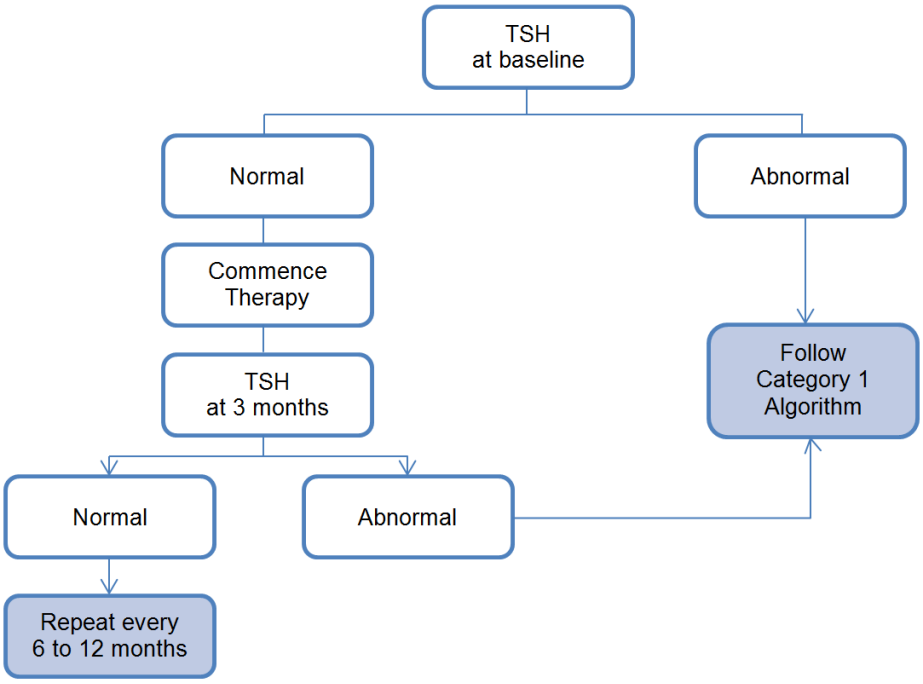
CATEGORY 4: PREGNANCY

PRACTICE POINT

Subclinical hypothyroidism in the mother may lead to cognitive impairment in the infant. Achieving euthyroidism prior to pregnancy is ideal.

- ✓ For patients receiving thyroxine replacement:
  - Order TSH when pregnancy is confirmed and repeat every four to six weeks (due to increased demand for thyroxine during pregnancy)
  - Thyroxine dose can be adjusted as required every six weeks based on TSH levels
  - Target: TSH 0.2- 2.5 mU/L in the first trimester, and 0.2 – 3.5 mU/L after 20 weeks gestation[2] (Category 2)
- ✓ Recommend a TSH receptor antibody (TRAB) level for patients with a history of Grave's disease
- ✓ Consult endocrinology if TRAB ≥ 5 x normal

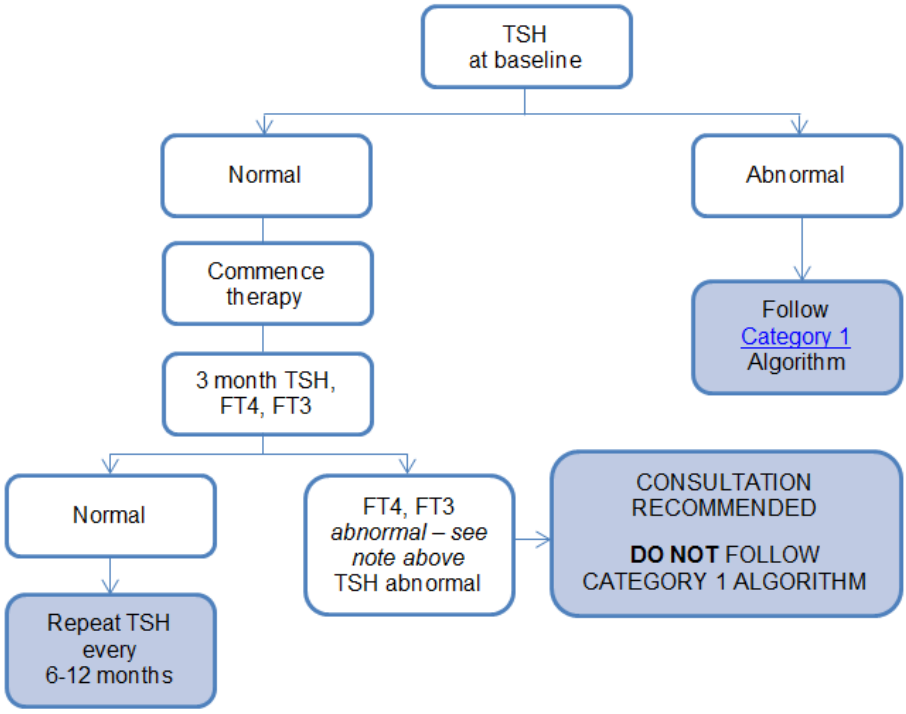
CATEGORY 5A: PATIENTS RECEIVING LITHIUM



CATEGORY 5B: PATIENTS RECEIVING AMIODARONE

Amiodarone may cause elevated FT4 in the presence of normal TSH (drug effect to inhibit T4 to T3 conversion)

- ✓ Recommend pre-treatment TSH and three month post treatment TSH, FT4, and FT3



BACKGROUND

PREVALENCE

According to the Canadian Task Force, the Periodic Health Examination community survey results have revealed prevalence rates of overt hyperthyroidism of less than 1.9%, the rates being comparable in elderly populations.[3,4] If "sub-clinical" cases are included, the prevalence rate can be as high as 2.7%. In a well-conducted community study, the annual incidence rate of overt hyperthyroidism was estimated to be two to three per 1,000 women.

The prevalence of hypothyroidism is three times higher among women than in men. The prevalence in an unselected community population of young, middle-aged and elderly individuals is about one to four percent and the estimated annual incidence rate is one to two per 1,000 women.

Surveys of geriatric populations have yielded estimated prevalence rates for overt hypothyroidism of 0.2 percent to 3 percent.[3] Symptom presentation in the elderly may be atypical or absent.[4] The prevalence of subclinical hypothyroidism is estimated to be between 4.0–8.5% of the adult US population without known thyroid disease, and the prevalence increases with age.[5] Up to 20% of women over the age of 60 are estimated to have subclinical hypothyroidism.

RISK FACTORS

Caucasians are more likely to have subclinical hypothyroidism than non-Caucasians. The risk is highest in those with type I diabetes mellitus, a family history of thyroid disease or head/neck cancers treated with external beam radiation. Other risk factors include previous radioactive iodine treatment or thyroid surgery. Interestingly, about 20% of patients on thyroid medications are both over replaced and under replaced. See Table 2.

Patients at Increased Risk for Thyroid Disease
• Women over 45* • Postpartum women • Patients receiving drug therapies such as lithium and amiodarone (Category 5A & 5B) • Patients with other autoimmune diseases such as Type I diabetes • Patients with a strong family history of thyroid disease *Note: *There is evidence to suggest increased risk for thyroid disease in patients over the age of 60*

Table 2: Patients at Increased Risk for Thyroid Disease

MONITORING AND TREATMENT CONSIDERATIONS

Because of the high incidence of thyroid disease, The American Thyroid Association recommends measuring thyroid function on all adults beginning at age 35 years and every five years thereafter noting that more frequent screening may be appropriate in high risk groups.[6]

The treatment of subclinical hypothyroidism has been controversial,[7,8] but more recent data suggest there are increased risks of ischaemic heart disease in untreated patients and that a more

aggressive approach to treatment would be appropriate.[9] In contrast, subclinical hyperthyroidism has more well understood risks of atrial fibrillation and flutter, and so should be more aggressively treated.[10,11]

Thyroid disease in pregnancy requires special attention and follow-up. Of particular concern is the effect of hypothyroidism on the neuropsychological development of the child.[12] Thus, many women on thyroxine replacement therapy will require up to a 50% increase in dosage during their pregnancy. Some authorities have suggested immediate increase in dose upon diagnosing pregnancy to avoid sequelae of hypothyroidism.[13]

Several drugs, that are commonly used, can have significant effects on the thyroid. The drug Amiodarone, by virtue of its two iodine atoms, may induce iodide-like effects of hypo- or hyperthyroidism, with abnormalities being more common if there is underlying autoimmune thyroid disease.

Hypothyroidism is more common than hyperthyroidism.[14,15] Lithium can cause goiter, hypothyroidism, and possibly hyperthyroidism, with hypothyroidism being the most common sequela.[16] Interferon alfa-2b may cause hyper- or hypothyroidism.[17]

For the treatment of thyroid cancer, suppression of TSH (a growth factor for normal and malignant thyroid cells) will reduce recurrence rates of thyroid cancer by approximately 40%,[18] therefore the treatment target is an undetectable TSH.

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For more information see www.topalbertadoctors.org

Guideline Committee

The committee consisted of representatives of family medicine, pathology, endocrinology, clinical biochemistry, laboratory technology and a member of the public.

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