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Urine Thyroid Assessment

Clinical Information for Professionals

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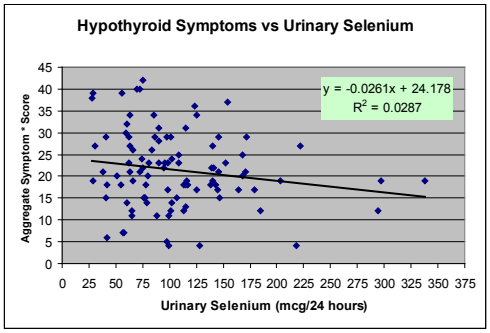
Importance of Thyroid Assessment

By some estimates, as many as 2 million Canadians may have undiagnosed thyroid disease. Thyroid disease refers to both hypo and hyperthyroidism, but hypothyroidism is by far the most common. Even mild hypothyroidism can have significant health consequences, making early detection a health priority.

Urinary Thyroid Assessment

The Urinary Thyroid Assessment measures unconjugated non-protein bound triiodothyronine (T3), unconjugated non-protein bound thyroxine (T4) and selenium in a 24 hour urine collection. There are several reasons why a urinary thyroid assessment may be beneficial:

- A specimen collected over a 24 hour period may better reflect the average thyroid gland output, since thyroid gland activity varies through the day.
- Quantities of T3 and T4 in a 24 hour urine are significantly higher than those found in a single serum sample, so levels can be more reliably measured. Measurement of free T3 and T4 in serum is inherently difficult.
- Selenium is a cofactor for 5′-deiodinase, the enzyme required to convert T4 to T3. A low 24 hour urinary selenium level likely correlates with selenium intake[1] and urinary selenium is also reflective of supplemental selenium.[2] As shown in the figure below once the urinary selenium levels rise above 100 mcg/24 hours, the average symptom score begins to decline. This trend suggests that patients who are replete in selenium experience fewer hypothyroid symptoms.



Laboratory Methodology

There are several different methodologies used to measure T3 and T4 in urine (e.g. radioimmunoassay[3], liquid chromatography mass spectrometry). The method used for this assay is liquid chromatography mass spectrometry.

Note: The Urinary Thyroid Assessment is not a substitute for serum testing in the diagnosis of thyroid illness; it is meant to assist clinicians in the evaluation of patients whose clinical presentation is not readily explainable by measurement of serum thyroid parameters alone. See back page for a discussion of serum TSH and free T3 and T4 measurements.

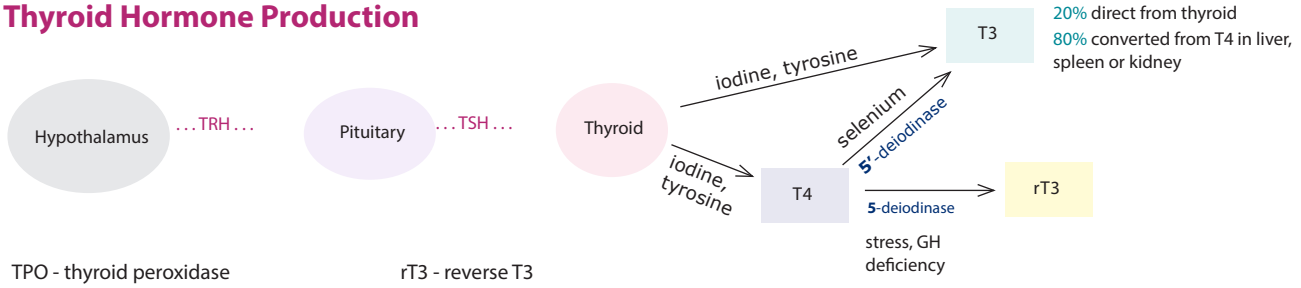
Triiodothyronine (T3)

Thyroxine (T4)

Selenium

Urine Thyroid Assessment correlates with clinical signs of hypothyroidism

Thyroid Hormone Production



TPO - thyroid peroxidase
TSH - thyroid stimulating hormone
TRH - thyrotropin releasing hormone
GH - growth hormone

rT3 - reverse T3
T3 - triiodothyronine
T4 - thyroxine

Condidtions and Symptoms Associated with Hypothyroidism

Cardiovascular Disease: Some studies suggest that total cholesterol rises incrementally with rises in TSH,[4] while others refute that finding.[5] C-reactive protein and homocysteine levels are increased in hypothyroidism.[6,7] Blood pressure is also often elevated.[7] These laboratory changes are markers of increased cardiovascular disease risk.

Weight Gain/ Fatigue: Hypothyroidism results in decreased metabolism, which in turn may lead to weight gain. Slowed speech, slowing of physical functions, and dull facial expression can also occur.

Skin, Hair, Musculoskeletal: Dry skin, roughness and thickening of skin on hands, forearms or elbows, hair loss, thinning eyebrow hair, and/or a puffy, swollen face (particularly under the eyes). Also, muscle cramps in calves, toes, fingers, diaphragm, thighs and upper arms plus rheumatoid pain, joint, tendon and muscle swelling and stiffness.

Depression: Risk of depression is four times greater for elderly patients suffering from sub-clinical hypothyroidism than from overt hypothyroidism.[9] General slowing of mental functions is another feature of hypothyroidism.

Headache: Migraine and tension headaches can be associated with hypothyroidism.

Constipation: A hard bowel movement less than once every 2 days may indicate hypothyroidism.

Cold intolerance: Hands and feet are cold to touch, and patient frequently feels chilled.

Common Symptoms of Hypothyroidism

- fatigue
- depression
- sensation of coldness
- headache
- muscle cramps
- constipation
- joint and soft tissue aches
- swelling
- stiffness

Importance of Conversion of T4 to T3

T3 is the active hormone at thyroid hormone receptor sites, but T4 is the main hormone produced by the thyroid. Conversion of T4 to T3 is therefore an important process for ensuring proper thyroid function. The diagram above shows how the body produces and maintains T3 levels. The following factors influence the conversion of T4 to T3:

- A low carbohydrate diet can impair conversion of T4 to T3.
- Low levels of growth hormone impair conversion of T4 to T3, and increase levels of the inactive reverse T3 hormone.
- Presence of toxic elements like cadmium and mercury poison the 5'-deiodinase enzyme and prevent conversion of T4 to T3.
- Excess cortisol stimulates the conversion of T4 to the inactive reverse T3 hormone.
- Selenium is required as a cofactor in the conversion of T4 to T3, and low levels of selenium are associated with increased hypothyroid symptoms.

Hyperthyroidism

Symptoms of hyperthyroidism can include weight loss, increased appetite, nervousness, restlessness, heat intolerance, increased sweating, fatigue, frequent bowel movements, menstrual irregularities in women, and goiter. Approximately 75% of cases of hyperthyroidism are due to Grave's disease. Hyperthyroidism is usually treated with anti-thyroid medications, radioactive iodine (which destroys the thyroid and stops the excess production of hormones), or surgery to remove the thyroid.

Hormone	Potential Interventions	
Triiodothyronine (T3) **M: 238 - 459 ng/g creatinine** **F: 283 - 486 ng/g creatinine**	**Nutritional supplements to consider** • **Iodine, tyrosine** required to make T3 in thyroid gland • **Selenium** needed to convert T4 to T3 in kidney, liver and spleen • **7-keto DHEA** has been shown to increase levels of free T3 in obese patients.[10] • **Guggul** (Indian frankincense) increases production of T3.[11,12] • **Ashwagandha** may increase T3 levels.[13] • **Adaptogens** may normalize cortisol levels and prevent cortisol induced suppression of TSH.	**Supplement** with liothyronine (T3) sustained release compounded T3, or natural thyroid extracts. **Lifestyle considerations** • Reduce stress as stress and high cortisol levels can suppress TSH release thereby reducing T3 production. • Cortisol also stimulates conversion of T4 to inactive reverse T3.
Thyroxine (T4) **M: 296 - 725 ng/g creatinine** **F: 237 - 658 ng/g creatinine**	**Nutritional supplements to consider** • **Iodine, tyrosine** required to make T4 in thyroid gland • **Ashwagandha** may increase T4 production.[13] • **Fucus** (bladderwrack) is high in iodine. Contamination with cadmium and arsenic is possible.[14] **Supplement** with levothyroxine (T4), compounded combined T4 and T3, or natural thyroid extracts.	**Lifestyle considerations** • Reduce stress: high cortisol and high levels of stress can suppress TSH release and thereby reduce T4 production. **Dietary considerations** • Reduce soy intake: soy can antagonize release of T4 from storage granules in thyroid.
Selenium **M: 52 - 97 ng/g creatinine** **F: 58 - 128 ng/g creatinine**	**Protocol Considerations** • **Selenium** supplementation may be necessary if selenium levels in a first morning or 24 hour urine are low or low-normal. • An above range result for selenium may indicate excessive selenium supplementation. • Follow-up urine, serum or hair analysis for selenium levels should be considered for out of range	

Testing Patients Who Supplement with Thyroid Hormone

Treatment with T4 and/or T3 results in increased urinary excretion of these hormones. The urinary thyroid hormone test can therefore be used for qualitative monitoring purposes - that is, to verify absorption and compliance. At this time, the correlation between the clinical picture and the 'on-therapy' urine T3 & T4 levels has not been fully evaluated. Therefore, we do not recommend that this test be used as the only means to titrate dosing of T3 or T4 containing products. If you intend to use this test to monitor thyroid hormone therapy, please discuss with our Medical Director prior to retesting. Health care professionals should be guided by the patient's clinical response.

Thyroid Testing Options

Serum TSH is an excellent marker of thyroid function but has the following limitations:

- The normal ranges for serum TSH are quite broad. Most laboratories consider 0.35 mU/L to 5.0 mU/L to be normal, and some physicians will not treat a TSH less than 10mU/L. However, a British study showed that TSH >2.0 mU/L is associated with increased risk of developing overt hypothyroidism later in life.[15] Thus, many instances of hypothyroidism could be missed because the range is so broad, and because the importance of having low TSH is overlooked.
- Normal TSH may not represent optimal T3 levels in all tissues, particularly when T4 is supplemented:
  - Saravanan found that patients whose TSH was lowered by T4 had significantly impaired psychological wellbeing compared to controls.[16] And, Alevizaki showed that hypothyroid patients had low SHBG and low T3 (additional laboratory indicators of hypothyroidism) even after their serum TSH was normalized by T4 replacement.[17]
- High cortisol levels arising from physical or psychological stress or synthetic glucocorticoids may normalize TSH levels, thereby masking hypothyroidism. (TSH appears normal when it would be elevated in the absence of high cortisol).
- Animal studies suggest that cadmium may lower TSH levels and mask hypothyroidism (TSH appears normal when it would be elevated in the absence of cadmium).[18]

What about Serum Free T3 and T4?

In theory, free T3 and free T4 are good indicators of thyroid function since low levels trigger the pituitary to produce more TSH. However, the following factors may limit their usefulness:

- levels of free T3 and T4 in serum are extremely low, and reliability of free T3 and T4 measurements at low levels is questionable.
- free T3 is the active hormone, but levels change in response to fasting, presence of acute or chronic non-thyroid disease, and with age. This makes free T3 measurements too variable to be clinically useful.

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