Thyroid Disorders

A Pharmacy Approach to Managing Patients’ Thyroid Health
Disclosure

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Overview

- Understand the thyroid and its hormones
- Thyroid disease in focus
  - Hypothyroidism
  - Hyperthyroidism
  - Thyroid nodules
  - Thyroid cancer
Objectives

• Learn how to more effectively manage the health of your patients with thyroid disease
  – Recognize the different types of thyroid disease and their typical symptoms
    • *Do the patient’s symptoms suggest hyper- or hypothyroidism?*
  – Know how hypothyroidism is diagnosed and treated
    • *Should this patient be screened for hypothyroidism?*
    • *Are they effectively treated and regularly monitored?*
  – Understand how pregnancy affects management of hypothyroidism
    • *What should your patient treated with levothyroxine know when planning a pregnancy or upon becoming pregnant?*
The Facts on Thyroid Disease

Affects 1 in 10 Canadians

50% Undiagnosed

2.5 million Adults

Congenital Hypothyroidism 1 in 1700 children

By age 35 the incidence of hypothyroidism increases greatly in women

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The incidence of hypothyroidism increases greatly in women by age 35.
THE THYROID
Understanding The Thyroid

• Anatomy
  – Butterfly-shaped gland
  – Located in the neck, just below the larynx

• Histology
  – Made up of hollow sacs called follicles which produce thyroid hormones

• Thyroid follicles secrete two hormones
  – Thyroxine (T4) and tri-iodothyronine (T3)
Thyroid Hormones

- Action of thyroid hormones
  1. Increase metabolic rate
  2. Increase body temperature (calorogenic effect)
  3. Increase lipolysis and reduce blood cholesterol
  4. Enhance the action of norepinephrine and epinephrine
  5. Together with growth hormone and insulin, act to accelerate body growth

- Most cells have receptors for thyroid hormones
  - As a result, these hormones have broad systemic effects

The thyroid is the only endocrine gland that stores its hormones in large quantities – normally about 100-days’ worth.

Thyroxine is also called tetra-iodothyronine because it contains four atoms of iodine, whereas tri-iodothyronine contains three.
Why not use T3 as a treatment?

About 93% of the hormone secreted from the thyroid is thyroxine (T4).

Treating hypothyroidism with T4, which is converted to T3 in the target tissues, mimics the natural process in the body.

Thyrocytes?

Epithelial cells in the thyroid gland that produce and secrete thyroid hormones

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T4 Conversion to T3

- Thyrocytes primarily secrete T4 which is converted to T3 at the site of action
  - T3 is metabolically more active than T4
  - Peripheral tissues have enzymes that convert T4 to T3 by removing one iodine atom

Levothyroxine (L-thyroxine) is a synthetic hormone identical to T4.
THYROID DISEASE

Affects 1 in 10 CANADIANS
2.5 million ADULTS
50% UNDIAGNOSED
Hypothyroidism

- Primary hypothyroidism
  - Autoimmune thyroiditis (Hashimoto’s disease)
  - Congenital hypothyroidism
  - Iodine deficiency
  - Infiltrative diseases (viral and bacterial)
  - Iatrogenic forms (thyroid surgery, radioiodine, neck irradiation)
- Secondary hypothyroidism
  - Less common
  - Deficiency in pituitary hormone secretion
  - Deficiency in thyrotropin-releasing hormone (TRH)

What is hypothyroidism?

“Failure of the thyroid gland to produce sufficient thyroid hormone to meet the metabolic demands of the body.”

Gaitonde et al. (2012)

What is TRH?

TRH, produced by the hypothalamus, stimulates the release of thyroid-stimulating hormone (TSH) from the pituitary.

Autoimmune thyroid disease is the most common cause of hypothyroidism.
Hashimoto’s Thyroiditis (HT)

- Chronic inflammation of the thyroid first described over a century ago
- Most common initial clinical manifestation is an enlargement of the thyroid gland (goiter)
- Pathology
  - White blood cell (WBC) infiltration of the thyroid
  - WBCs mediate autoimmune destruction of thyrocytes
- Can occur in isolation or along with other autoimmune diseases (e.g., type 1 diabetes)

Women are at least 8-times more likely than men to have HT.
Incidence of CH is approximately 1:1700 newborns. Incidence is nearly double in twin births (1:876) vs singletons (1:1765), and even higher with multiple births (1:575).

Newborn Screening
A positive TSH test is confirmed with a repeat TSH as well as a free thyroxine blood test.

Given the importance of early treatment of congenital hypothyroidism, TSH testing is part of newborn screening.

Congenital Hypothyroidism (CH)

• CH is a thyroid hormone deficiency present at birth
• Primary hypothyroidism
  – Defect of thyroid gland development
  – Disorder of thyroid hormone synthesis
• Secondary (central hypothyroidism)
  – Deficiency of thyroid stimulating hormone (TSH)
Hyperthyroidism

• In hyperthyroidism, thyroid hormone levels are significantly elevated
  – Affects 1% of all individuals during their lifetime

• Primary causes
  1) Excessive stimulus of the thyroid
     • Grave’s disease, TSH-secreting adenoma
  2) Autonomous function of the thyroid
     • Benign thyroid adenoma, toxic multi-nodular goiter, thyroid cancer with functioning metastases
  3) Thyroiditis
     • Painful thyroid enlargement with systemic inflammatory symptoms
     • Often followed by transient hypothyroidism
     • Believed to be the result of a viral infection

• Thyrotoxic crisis (thyroid storm)
  – Potentially life-threatening syndrome that is usually the end result of severe and sustained thyrotoxicosis

Grave’s Disease

“An autoimmune disorder in which antibodies stimulate the TSH receptor, increasing thyroid hormone production.” Bahn et al. (2011)
Goitre, Thyroid Nodules & Cancer

- **Goitre**
  - An enlargement of the thyroid gland
  - Clinical issues affecting the patient
    - Local compression (trouble breathing or swallowing), cosmetic concerns, thyroid dysfunction, possible malignancy

- **Thyroid nodules**
  - Palpation detects in 6% of women and 2% of men
  - Majority are small, benign nodules or cysts
    - Only 5 to 10% are malignant

- **Thyroid cancer**
  - Most start as thyroid nodules
  - Mean age at diagnosis is 45 years

"The thyroid gland is the largest pure endocrine gland in the body. Its prodigious blood supply makes thyroid surgery a painstaking endeavor."

Marieb et al. (2012)

**Thyroid Cancer**

98% 5-year survival rate with early detection

--

Approximately 4600 Canadian women and 1400 men are diagnosed with thyroid cancer each year.
• Thyroid disease affects 1 in 10 Canadians or more than 2.5 million people  
  – About 50% of these individuals have not been diagnosed

• Thyroid hormones have diverse and significant effects on metabolism and growth  
  – Dysfunction therefore results in a broad constellation of symptoms

• Hypothyroidism  
  – Autoimmune thyroiditis is the most common cause of hypothyroidism

• Hyperthyroidism  
  – Elevation of thyroid hormones

• Thyroid cancer affects about 6000 Canadians a year  
  – Very high 5-year survival rate if detected early
HYPOTHYROIDISM

Symptoms

HYPOTHYROIDISM accounts for 90% of thyroid disease
By age 35, the incidence of hypothyroidism increases greatly in women.

**ATA/AACE Guidelines**

recommend screening for hypothyroidism at 35 years of age and every 5 years thereafter.

**Prevalence of Hypothyroidism**

The Prevalence of Hypothyroidism Increases with Age

- **18-24**
- **24-34**
- **35-44**
- **45-54**
- **55-64**
- **65-74**
- **>74**

**Hypothyroidism (%)**

- Male
- Female

- **Age (years)**
  - 18-24
  - 24-34
  - 35-44
  - 45-54
  - 55-64
  - 65-74
  - >74

**ATA: American Thyroid Association**

**AACE: American Association of Clinical Endocrinologists**
Patient Consult

What additional questions would you ask if your patient described these symptoms?

Are these symptoms new?

Are they getting worse?

Has your doctor ever diagnosed you with hypothyroidism or an underactive thyroid?

Is anyone in your family treated for this condition?

Symptoms of Hypothyroidism

- These nonspecific symptoms can make diagnosis difficult
- A patient with new, progressive or multiple symptoms…
  - …is more likely to have hypothyroidism

Fatigue
Cold intolerance
Constipation
Depressed mood
Lethargy
Weight gain
Poor appetite
Hoarseness
Weakness
Muscle pain
Joint pain
Dry skin
Hair loss
Clinical Presentation in Elderly

Symptoms of hypothyroidism in the elderly differs from younger patients

- Memory loss & confusion
- Decrease in cognitive function
- Weight gain
- Sleepiness
- Dry skin
- Constipation or incontinence

Specific Signs in Elderly

- Ataxia
- Non-joint pain/muscle ache
- Carpal tunnel syndrome
- Falling

Is it aging or hypothyroidism?

Elderly patients may have fewer symptoms of hypothyroidism than younger adults.

Symptoms are often subtle and vague and may be incorrectly attributed to ‘normal’ aging.

Ataxia

A neurological sign consisting of a lack of voluntary coordination of muscle movements.

May cause poor coordination, unsteady walk and difficulty with fine motor skills (e.g., writing).
## Consequences of Untreated Hypothyroidism

### Cardiovascular
- Increased cardiovascular mortality
- Hypertension
- Increased vascular resistance
- Reduced cardiac output

### Neurologic
- Impaired intellectual function
- Depression
- Slowed speech
- Headache
- Memory loss in elderly
- Bradycardia
- Hypothermia

### Fertility & Pregnancy
- Irregular menstruation
- Anovulation & impaired fertility
- Higher rate of spontaneous abortion
- Impaired neurological development
- Developmental delay
- Reduced growth

### Women’s Health
- Predominantly older patients
- Bradycardia
- Hypothermia
- High mortality rate
- Severe hypotension
- Multiorgan failure

### Newborn
- Impaired neurological development
- Developmental delay
- Reduced growth
Cardiovascular Consequences

- Increased cardiovascular (CV) mortality
  - Most strongly associated with overt hypothyroidism
  - Evidence of increased CV risk with subclinical hypothyroidism is less clear

- Hypertension
  - Three-fold more prevalent in patients with overt hyperthyroidism vs euthyroid subjects
  - Contributing factors include an increase in peripheral vascular resistance and arterial stiffness
  - Poorly controlled by conventional antihypertensive medications but improves upon obtainment of euthyroid state

- Impaired left ventricular diastolic function
  - Slowed myocardial relaxation/impaired ventricular filling

- Hypothyroidism not associated with atrial fibrillation (AF)
  - 2014 publication of the Framingham Heart Study found no increased risk of AF
Neurologic Consequences

• All intellectual functions are slowed in hypothyroidism

• Common presentation
  – Loss of initiative, memory deficits, lethargy, somnolence, headache
  – Memory loss in elderly patients may be mistaken for senile dementia

• Psychiatric disorders are common
  – Typically paranoid or depressive type and may induce agitation

• Cerebral hypoxia due to circulatory alterations
  – May predispose to confusion and syncope
  – May be prolonged and can lead to stupor or coma
Reproductive Consequences

• Preconception
  – Diminished libido and anovulation
  – Progesterone secretion is inadequate
  – Excessive and irregular breakthrough menstrual bleeding
  – Impaired fertility

• Pregnancy
  – Increased risk of spontaneous abortion and preterm delivery
  – Other risks
    • Anemia, preeclampsia, placental abruption, low birth weight

• Newborn
  – Impaired neurologic & physical development
  – Manifested by delay in reaching normal developmental milestones (e.g., holding up head, sitting, walking, and talking)
Myxedema Coma – Consequence of Severe Hypothyroidism

• Nearly exclusive to elderly population
  – More common in winter months

• Life-threatening condition characterized by
  – Hypothermia, bradycardia, hypotension, altered mental status
  – Multisystem organ failure

• Risk factors
  – Advanced age, underlying major organ system diseases
  – Exposure to cold, infection, trauma
  – Use of central nervous system depressants or anesthetics
  – Long-standing thyroid hormone deficiency
HYPOTHYROIDISM

Diagnosis

SERUM TSH is the primary screening test for thyroid dysfunction.
TSH Testing

• TSH is a sensitive measure of thyroid dysfunction
  – Accurately detects common causes of hypothyroidism and hyperthyroidism

• T4 and T3 may also be measured concurrently
  – Can confirm the significance of an abnormal TSH level
  – Defines the severity of thyroid dysfunction
  – Assists in the determination of the underlying cause

• Other possible tests
  – Thyroid autoantibody titers
    • Confirm a diagnosis of autoimmune thyroiditis
    • Evaluate the severity of Graves' disease

Value of TSH Testing

“*In most patients with primary thyroid gland dysfunction, measurement of a single TSH level permits an accurate classification of the thyroid status.*”

*Kim M, Ladenson P. (2012)*
Free T4?
Most T4 is bound to serum proteins. Free T4 refers to thyroxine that is not protein bound.

Screening for hypothyroidism
Start at 35 years of age and every 5 years thereafter

* Upper limit of normal values for T4 will vary by laboratory. Typical normal range of 9-20 pmol/L in adults.
Medications Impacting Thyroid Function Testing

• Impact TSH secretion
  – Dopamine agonists
  – Glucocorticoids
  – Somatostatin analogues (octreotide and lanreotide)

• Impact T4 and T3 secretion
  – Amiodarone, lithium
  – Tyrosine kinase inhibitor (sunitinib, sorafenib)
  – Iodide (dietary supplements, radiological contrast agents)

• Modify binding of T4/T3 to plasma proteins
  – Estrogen, methadone, clofibrate, 5-fluorouracil, perphenazine, tamoxifen
  – Glucocorticoids, androgens
  – Furosemide, salicylates, phenytoin, carbamazepine, NSAIDs, heparin

Heparin/Low-Molecular Weight Heparins

The potential for heparin to raise free thyroid hormone levels (i.e. T3 & T4) was first observed in patients undergoing hemodialysis.

Administration of heparin results in a rapid (< 15 min) and pronounced (≤ 5-fold) increase in FT4.

Measurement of FT4 and FT3 is best avoided in patients treated with heparin; however, when indicated, it is recommended that the blood sample be taken > 10 h after the last dose of heparin.
HYPOTHYROIDISM

Treatment

**L-thyroxine** was first isolated in **1914** by Dr. Edward Kendall at the Mayo Clinic.

Kendall EC. JAMA 1915; 64(25):2042-3.
Levothyroxine is the mainstay of treatment

**Overt Hypothyroidism**
- Should be treated

**Subclinical Hypothyroidism**
- Consider treatment if:
  - Symptoms of hypothyroidism
  - Anti-thyroid Abs
  - CV disease

Guideline recommendation for desiccated thyroid hormone
- No evidence showing preference to levothyroxine
- “…desiccated thyroid hormone should not be used for the treatment of hypothyroidism.” [Recommendation 22.4, pg 1220]
Treatment Targets

TSH Target Range

0.45 - 4.12 mIU/L

Levothyroxine has a narrow therapeutic range. Careful dose titration is necessary to avoid over- or under-treatment.

Overtreatment can lead to thyrotoxicosis (severe hyperthyroidism).

A survey of > 52,000 patients treated with levothyroxine found that 5.8% had a TSH < 0.1 mIU/L.

Treatment not working?

“Poor adherence to levothyroxine therapy is the most common cause of persistently elevated TSH levels in patients on adequate doses of thyroid hormone.”

Gaitonde et al. (2012)

Claims database of 37,600 adults with hypothyroidism

Only 68% were adherent
Levothyroxine Dose Titration

- Dose and rate of administration depends on indication
  - Always individualized according to patient response (symptom improvement) and TSH tests

- Clinical and laboratory (TSH) evaluations
  - 6 to 8 week intervals (2 to 3 weeks with severe hypothyroidism)
  - Dose adjusted by 12.5 to 25 mcg increments until TSH is normalized and signs and symptoms resolve

- Few patients require doses > 200 mcg/day
  - Inadequate response to 300 to 400 mcg/day is rare
  - Suggests malabsorption, poor adherence, and/or drug interactions

Dose in children
In general, despite a smaller body size, the dose (on a weight basis) required to sustain full development and general health is higher than in adults.

Dose in elderly
Older patients may require < 1 mcg/kg/day.
Starting dose is typically 25-50 mcg/day and dose titration is 12.5-25 mcg/day (per 6-8 weeks).
Drug Interactions with Levothyroxine

- Many drugs affect levothyroxine pharmacokinetics
  - Antacids, bile acid sequestrants, calcium, iron, orlistat
    - Reduce absorption of levothyroxine
  - Oral anticoagulants
    - Increased anticoagulant activity (carefully monitor)
  - Antidepressants
    - Therapeutic/toxic effects of both drugs may increase
    - Adding sertraline in patients stabilized on levothyroxine may result in increased levothyroxine requirements
- Oral hypoglycemic agents and insulin
  - Levothyroxine may increase dose requirements
  - Careful monitoring of blood glucose when levothyroxine started, or dose is changed.

The above list is not comprehensive and levothyroxine product monographs should be consulted for complete details.

Other Interactions

Digitalis glycosides
Serum digitalis levels may decrease when a patient becomes euthyroid, necessitating an increase in the dose of digitalis glycosides.

Ketamine
Concurrent use may cause marked hypertension and tachycardia.

Growth hormones (GH)
Excessive use of thyroid hormones with GH may accelerate epiphyseal closure. However, untreated hypothyroidism may interfere with growth response to GH.
Treatment targets and monitoring requirements are significantly changed in pregnancy

- TSH upper limits of normal during pregnancy are lower

- Target TSH levels by trimester
  - 1st 2.5 mIU/L
  - 2nd 3.0 mIU/L
  - 3rd 3.5 mIU/L

- TSH monitoring is also more frequent in pregnant patients with treated hypothyroidism
  - Every 4 weeks during the first half of pregnancy because levothyroxine dose adjustments are often required
  - At least once between 26 and 32 weeks gestation
Summary - Hypothyroidism

- Guidelines recommend screening for hypothyroidism at age 35 and every 5 years thereafter
  - At age 35 the incidence of hypothyroidism increases greatly in women

- Common symptoms
  - Fatigue, cold intolerance, constipation, depressed mood
  - Presentation in elderly differs from younger adults

- Untreated hypothyroidism has significant negative effects on cardiovascular health, neurologic functioning, reproduction and fetal development

- Readily diagnosed using a TSH test

- Treated with levothyroxine
  - Narrow therapeutic window requires careful dose titration and TSH monitoring

- Women planning a pregnancy or who are pregnant require more frequent TSH monitoring and have different TSH targets
HYPERTHYROIDISM
Symptoms, Diagnosis and Treatment
### Symptoms of Hyperthyroidism

<table>
<thead>
<tr>
<th>Nervousness and irritability</th>
<th>Exophthalmos</th>
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<tr>
<td>Palpitations and tachycardia</td>
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<tr>
<td>Heat intolerance</td>
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<td>Sweating</td>
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<td>Tremor</td>
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<td>Weight loss</td>
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<td>Frequent bowel movements</td>
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<td>Dyspnea</td>
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<td>Insomnia</td>
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<td>Vision changes</td>
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<td>Fatigue</td>
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<td>Muscle weakness</td>
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### Thyrotoxicosis

Refers to the combination of clinical features arising from elevated levels of thyroid hormones.

May be due to hyperthyroidism or non-hyperthyroid conditions.

#### Hyperthyroidism
- A type of thyrotoxicosis caused by excessive thyroid hormone
- However, the terms ‘hyperthyroidism’ and ‘thyrotoxicosis’ are often used interchangeably

#### Grave’s disease
- A cause of hyperthyroidism
- Thyroid may be enlarged to 2- to 3-times normal size
- Associated with additional ocular symptoms
  - Sensation of grittiness, eye discomfort, and excess tearing
  - Eyelid retraction
  - Exophthalmos (bulging eyes)
Consequences of Untreated Hyperthyroidism

**Cardiovascular**
- Tachycardia
- Atrial fibrillation
- Angina
- Hypertension
- Peripheral edema
- Heart failure

**Ocular**
- Exophthalmos
- Diplopia (double-vision)
- Peripheral field defects
- Corneal damage
- Optic nerve compression
- Vision loss

**Skeletal**
- Osteopenia
- Hypercalciuria
- Mild hypercalcemia
- Slight increase fracture risk
Graves's Disease

The probable diagnosis in a patient with a symmetrically enlarged thyroid, recent ophthalmopathy, and moderate/severe hyperthyroidism.

Diagnosis of Hyperthyroidism

- Measurement of both TSH and free T4 is used to diagnose hyperthyroidism

Overt Hyperthyroidism
- T4: Increased
- T3: Elevated/Normal
- TSH: Undetectable

Subclinical Hyperthyroidism
- T4: Elevated/Normal
- T3: Increased
- TSH: < 0.1 mIU/L

Periodic TSH monitoring should be considered in younger, asymptomatic patients with TSH levels of 0.1 to 0.5 mIU/L.
Treatment of Hyperthyroidism

• Symptom management
  – Use beta-blockers in patients with resting heart rate > 90 bpm or with cardiovascular disease

• Effect of beta-blocker treatment
  – Decrease in heart rate, systolic blood pressure, muscle weakness, and tremor
  – Improves irritability, emotional lability, and exercise intolerance

• Oral verapamil and diltiazem
  – Used for rate control in patients who do not tolerate or are not candidates for beta-blockers

2011 Guidelines

Hyperthyroidism and Other Causes of Thyrotoxicosis: Management Guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists

Rebecca S. Bahn (Chair),1* Henry R. Busch2, David S. Cooper3, Jeffrey R. Garber4, M. Carol Greaves1,16
Ray Harris,1* Peter Lesslie5,1* Gene McGuigan7,1* Jerry W. Monheim6, Scott A. Rivkees1,16
Douglas S. Ross1, Jula Ann Smith1,16, and Mario N. Stangl

Background: Thyrotoxicosis has multiple etiologies, manifestations, and potential therapies. Appropriate treatment requires an accurate diagnosis, and is influenced by considering medical conditions and patient preference. This article describes evidence-based clinical guidelines for the management of the thyrotoxicosis that would be useful to generalists and subspecialty physicians and others providing care for patients with this condition.

Method: The development of these guidelines was commissioned by the American Thyroid Association in association with the American Association of Clinical Endocrinologists. The American Thyroid Association (ATA) and American Association of Clinical Endocrinologists (AACE) Clinical Guidelines Task Force was created to develop these guidelines. The task force included experts representing a range of medical specialties from endocrinology, geriatrics, pediatric endocrinology, nuclear medicine, cardiovascular medicine, and psychiatry.

Results: The task force in this report identified the evidence base, approach to guideline development, and methodology. The clinical recommendations were developed through a 3-step process: evidence review, draft recommendation development, and expert panel review. The level of evidence and strength of recommendation are rated according to the Grading of Recommendations, Assessment, Development, and Evaluation.

Conclusions: The strength of evidence-based recommendations was developed to aid the care of patients with thyrotoxicosis and to share what the task force believes to be current, rational, and optimal medical practice.

Treatment of Overt Hyperthyroidism

- A number of treatments may be used to manage overt hyperthyroidism in Grave’s disease
  - All have similar efficacy, safety and quality of life post-treatment
  - A number of factors guide the choice of treatment modality

- Radioactive iodine
  - Common therapeutic approach
  - Preferred in patients planning a pregnancy (> 4-6 months), or those with increased risk during surgery

- Anti-thyroid medication (propylthiouracil, methimazole)
  - Used for patients with higher probability of remission (e.g., milder disease, women, small goiters)

- Thyroid surgery (thyroidectomy)
  - Used if symptomatic compression or large goiter (≥ 80 g)
  - In cases of thyroid cancer

Radioactive Iodine

Concentrated in thyroid gland due to selective uptake of iodine.
Destroys thyroid tissue, effectively controlling hyperthyroidism.
Main side effect is post-ablative hypothyroidism.
Summary - Hyperthyroidism

- Excess thyroid hormone levels & suppressed TSH
- Grave’s disease is a common cause of hyperthyroidism
  - Associated with characteristic ocular symptoms (bulging eyes)
- Possible severe consequences of untreated hyperthyroidism
  - Cardiovascular (hypertension, atrial fibrillation, heart failure)
  - Ocular (optic nerve compression, vision loss)
  - Skeletal (osteopenia, fracture risk)
- Symptom management may include beta-blockers
- Overt hyperthyroidism may be treated with radioactive iodine, anti-thyroid medications, surgery

Weight loss
Feeling hot
Fatigue
Palpitations
Vision changes
THYROID NODULES AND CANCER
Thyroid Nodules

• Usually noted by the patient or the physician upon palpitation
  – Often occur with no other complaints
• May be detected incidentally during imaging procedures
• Symptoms of compression (lower neck pain, cough, dyspnea) suggest that a nodule may be malignant

What advice to a patient who has detected a ‘lump’?

Although most nodules are benign they should still be evaluated by a physician. This is particularly important if the patient has any signs of hyperthyroidism (weight loss, tachycardia, etc).
Thyroid Cancer

- Most thyroid cancers start as thyroid nodules
  - Often asymptomatic or may be associated with local cervical symptoms or adenopathy

- Three-times more common in women than men

- Papillary and follicular (epithelial) thyroid cancers
  - Arise from epithelium of thyroid follicles
  - Papillary is the most common form

- Other types of thyroid cancer
  - Medullary and anaplastic

- Fine-needle aspiration biopsy conducted to confirm presence of cancer and determine type
Thyroid Cancer - Treatment

• Epithelial cancer
  – Surgery, often followed by radioiodine ablation of remaining thyroid tissue
  – Thyroxine therapy is used post-treatment to restore euthyroidism

• Medullary cancer
  – Surgical resection of the thyroid and regional lymph nodes
  – Lymph nodes involved in 50% of patients at diagnosis

• Anaplastic cancer
  – Aggressive malignant neoplasm
  – Generally unresectable
  – Treated with beam radiation and chemotherapy

ret Proto-Oncogene
In children with this inherited mutation, the risk of medullary thyroid cancer is so high that prophylactic thyroidectomy is advisable.

Anaplastic thyroid cancer
Median survival of 3 to 7 months.
Questions at the Pharmacy Counter
Hypothyroidism and obesity

Overt hypothyroidism is not more common in patients with obesity.

Although hypothyroidism and obesity are often linked, appetite in those with marked hypothyroidism is often suppressed which offsets the decreased metabolic rate.

Even in cases of profound hypothyroidism, the impact of thyroid hormone therapy on weight loss is modest.

Could you please tell me...

• When should I take my dose of levothyroxine?
  – Take with a full glass of water preferably on an empty stomach, 30 to 60 min before breakfast

• What happens if I take my levothyroxine with food?
  – Soybean flour (infant formula), cotton seed meal, walnuts, iron supplements, calcium, calcium-fortified orange juice, and dietary fibre may decrease the absorption of levothyroxine
  – It is best to take levothyroxine on an empty stomach

• Can I use levothyroxine or thyroid supplements for weight loss?
  – Thyroid hormones should not be used for weight loss
  – In patients with a healthy thyroid, doses within the range of daily hormonal requirements are ineffective
  – Larger doses may produce serious or even life threatening side effects, especially when used with medications with anorectic effects
Why do some patients use combination therapy rather than T4 monotherapy?

A study of T4 and T3 combination therapy observed different responses in patients with different genetic subtypes of type 2 deiodinase (the enzyme that converts T4 to T3).

The long-term benefit of combination therapy remains unknown as does the possible benefit of genotyping patients to identify those who might benefit from combination therapy.

...and what about?

- **What is the difference between different brands of levothyroxine?**
  - Health Canada approved labelling and treatment guidelines state that different brands should not be used interchangeably unless TSH is retested and re-titration of the dosage, as necessary, occurs.

- **Why did my doctor switch me to liothyronine? Why did she add it to my levothyroxine?**
  - This medication is also a thyroid hormone called T3 and is used in some patients by itself or in combination with levothyroxine (T4).
  - Some patients require this medication in order to control their hypothyroidism.

- **My doctor said my TSH test was normal but I have some of the symptoms of hypothyroidism; should I be treated?**
  - Patients with symptoms of hypothyroidism, but normal thyroid hormone levels do not benefit from levothyroxine.
  - In fact, treatment confers a substantial risk of hyperthyroidism.

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  - In fact, treatment confers a substantial risk of hyperthyroidism.
Sorry, just a few more questions...

- **Can I treat my condition with ‘natural’ desiccated thyroid hormone?**
  - The amount of thyroid hormone varies between desiccated thyroid preparations depending on the brand and whether it is of pig or cow origin
  - These preparations are not well studied in the treatment of hypothyroidism and are not recommended

- **Can I take my levothyroxine at bedtime?**
  - It is usually taken in the morning on an empty stomach
  - However, it may be taken at bedtime at least 4 hours after the last meal
And about pregnancy...

- I am planning on becoming pregnant. Should I have a TSH test to check my thyroid?
  - Experts are divided on this question
  - If you are concerned you might have a thyroid disorder you should talk to your doctor

- I am pregnant, should I have a TSH test?
  - A TSH test should be done early in pregnancy in women at high risk of overt hypothyroidism (OH)

- I am treated with levothyroxine and I just found out I am pregnant. What should I do?
  - Notify your doctor promptly as guidelines recommend that hypothyroid patients receiving levothyroxine who are newly pregnant should increase their dose 25%–30% upon a missed menstrual cycle or positive home pregnancy test

Women at high risk of OH

- History of thyroid dysfunction or surgery
- Age >30 years
- Symptoms of thyroid dysfunction
- Presence of goiter
- TPOAb positivity
- Type 1 diabetes or other autoimmune disorders
- History of miscarriage/preterm delivery
- History of head or neck radiation
- Family history of thyroid dysfunction
- Morbid obesity (BMI ≥ 40 kg/m²)
- Use of amiodarone or lithium, or recent use of iodinated radiologic contrast
- Infertility
- Residing in an area of known moderate to severe iodine insufficiency
CONCLUSIONS
Conclusions

• Thyroid hormones have broad systemic effects
  – As a result, thyroid disease is associated with a large constellation of symptoms and serious long-term consequences if untreated or inadequately controlled

• Hypothyroidism represents 90% of abnormal TSH levels
  – More common in women
  – Incidence increases sharply in women after age 35

• Key symptoms of hypothyroidism
  – Fatigue, cold intolerance, constipation, depressed mood, weight gain

• TSH measurement is the gold-standard of detection and treatment monitoring
  – Levothyroxine is the standard treatment of hypothyroidism
What Role for the Pharmacist?

**TSH Testing**

Direct patients with symptoms of hypothyroidism to request a TSH test from their physician

Consider that the clinical presentation of hypothyroidism in your elderly patients may mimic normal signs of aging

Patients who are not undergoing regular TSH testing are at risk of over- and under-treatment

**Drug Education**

Provide overview of levothyroxine treatment (how and when to take, side effects, drug interactions, treatment expectations, TSH monitoring, follow-up)

Discuss importance of adherence with levothyroxine treatment
What Role for the Pharmacist?

Pregnancy
Discuss changes to treatment and management of hypothyroidism with pregnant patients or women planning a pregnancy
Inform patients with treated hypothyroidism that they will likely need an increase in levothyroxine dose upon becoming pregnant
Confirm with a pregnant patient that she is undergoing the recommended frequency of TSH testing

Overtreatment
Consider the possibility of levothyroxine overtreatment in patients with symptoms of hyperthyroidism
Overtreatment with levothyroxine is common – about 1 in 20 patients
CLICK HERE to complete the LEARNER ASSESSMENT and EVALUATION and receive your CEUs
RESOURCES & REFERENCES
Resources

Thyroid Foundation of Canada
www.thyroid.ca

A non-profit volunteer organization that supports Canadian thyroid patients through awareness, education, and research.

Thyroidsymptoms.ca
www.thyroidsymptoms.ca

A resource for patients with hypothyroidism or who are experiencing symptoms suggestive of hypothyroidism.

Clinical Practice Guidelines
www.thyroid.org/thyroid-guidelines/

Guidelines for the diagnosis and treatment of hypothyroidism, hyperthyroidism, other thyroid disorders and cancer.


ATA. Guidelines for the diagnosis and management of thyroid disease during pregnancy and postpartum. Thyroid 2011; 21(10):1081-125.


Canadian Thyroid Foundation. ‘About Thyroid Disease.’ http://www.thyroid.ca/thyroid_disease.php.


Rastogi MV, LaFranchi SH. Congenital hypothyroidism. Orphanet J Rare Dis 2010;5:17.


