Thyroid Do’s and Don’ts

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Special thanks to Dr. Cary N. Mariash

Thyroid Gland Overview

- Hypothalamus-pituitary-thyroid axis
- Thyroid anatomy
- Thyroid hormone synthesis, iodine
- Thyroid hormone action
- Thyroid evaluation
- Goiter
- Hyperthyroidism - symptoms, signs, treatment
- Hypothyroidism - symptoms, signs, treatment
- Thyroid physical examination

Thyroid Feedback Loops

TRH
Thyrotropin-Releasing Hormone
hypothalamus

TSH
Thyroid Stimulating Hormone
pituitary

T4, T3
Thyroxine, Triiodothyronine
thyroid

Regulates energy expenditure and more

Gross Anatomy

Importance of Iodine

Iodide (I\(^{-}\)) ingested. Trapped by the thyroid.
Oxidized to iodine (I\(^{\circ}\)) by thyroid peroxidase.
Thyroid makes thyroglobulin, secretes it into colloid.
Iodine is added to tyrosines in thyroglobulin to make T4 and T3. Stored until needed.
Iodine Deficiency
- Iodine derives from ocean sources, evaporates into clouds → rain
- Regions far from ocean have low iodine in soil
- Regions covered longest by glaciers have low iodine in soil
- One billion people live in iodine deficient (mountainous and glaciated) areas.
- Need 100 µg/d to avoid hypothyroidism and goiter

Thyroid Hormone System
- Thyroid gland secretes T4 (85%) and T3 (15%).
- Thyroid hormones bound to carrier proteins in blood. Bound hormones not active.
- Free T4 and T3 taken up by tissues.
- T4 is converted to T3, the active hormone in tissues. T3 then released into blood, carried to other tissues.
- T4 and T3 levels part of feedback loops to regulate the hypothalamus and pituitary.

Functions of T3
- Increases oxygen consumption
- Increases metabolic rate
- Increases heat production
- Increases protein fat, and cholesterol synthesis and degradation
- Increases drug and anesthesia metabolism
- Increases tone of sympathetic nervous system
- Essential for normal brain development in infancy

Thyroid Testing
- TSH
- free T4
- T3
- radioactive iodine uptake - function
- radioactive iodine scan - anatomy
- antithyroid antibodies
- thyroid stimulating immunoglobulins

Low Radioactive Iodine Uptake
- Missing gland
- Defect in iodide trap
- Thyroiditis (damaged gland)
- Exogenous T4 or T3 (TSH suppressed)
- Recent high iodine load
- Anti-thyroid drugs

What Makes a Goiter?
(enlarged thyroid)
- Hyperthyroidism:
  - Thyroid-stimulating immunoglobulins (TSI)
  - Autonomous nodules escape controls
- Primary Hypothyroidism:
  - High TSH
- Euthyroid:
  - Thyroid defect; high TSH overcomes the problem; circulating T4, T3 normal
Prevalence of Thyroid Dysfunction

<table>
<thead>
<tr>
<th>Condition</th>
<th>Prevalence</th>
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<tbody>
<tr>
<td>Hypothyroidism</td>
<td>2%</td>
</tr>
<tr>
<td>Mild Hypothyroidism</td>
<td>5-15%</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>0.2%</td>
</tr>
<tr>
<td>Mild Hyperthyroidism</td>
<td>2-8%</td>
</tr>
</tbody>
</table>

Thyroid Hormone Excess

- **General**: weight loss, heat intolerance
- **Eyes**: lid lag, stare
- **Heart**: increased heart rate and contractility
- **Vascular**: vasodilation
- **Skin**: warm, smooth, moist
- **GI**: increased appetite, absorption, motility; frequent, soft stools
- **Skeleton**: increased bone turnover
- **Neuromuscular**: hyperactivity, tremor, increased muscle contraction, rapid reflex relaxation, weak

Signs and Symptoms of Hyperthyroidism

<table>
<thead>
<tr>
<th>Symptom</th>
<th>%</th>
</tr>
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<tbody>
<tr>
<td>Nervousness</td>
<td>99</td>
</tr>
<tr>
<td>Sweating</td>
<td>91</td>
</tr>
<tr>
<td>Heat Intolerance</td>
<td>89</td>
</tr>
<tr>
<td>Palpitations</td>
<td>89</td>
</tr>
<tr>
<td>Fatigue</td>
<td>88</td>
</tr>
<tr>
<td>Weight loss</td>
<td>85</td>
</tr>
<tr>
<td>↑ appetite</td>
<td>65</td>
</tr>
<tr>
<td>Hyperdefecation</td>
<td>33</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sign</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tachycardia</td>
<td>97+</td>
</tr>
<tr>
<td>Goiter</td>
<td>97+</td>
</tr>
<tr>
<td>Skin changes</td>
<td>97</td>
</tr>
<tr>
<td>Tremor</td>
<td>97</td>
</tr>
<tr>
<td>Thyroid bruit</td>
<td>77</td>
</tr>
<tr>
<td>Eye signs</td>
<td>71</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>10</td>
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</table>

Causes of Hyperthyroidism

<table>
<thead>
<tr>
<th>Disease</th>
<th>Mechanism</th>
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<tbody>
<tr>
<td>Graves’ Disease</td>
<td>Thyroid stimulating IgG</td>
</tr>
<tr>
<td>Toxic multinodular goiter</td>
<td>?</td>
</tr>
<tr>
<td>Toxic adenoma</td>
<td>TSH receptor mutation</td>
</tr>
<tr>
<td>Thyroiditis</td>
<td>Viral, immune destruction (inflammation)</td>
</tr>
<tr>
<td>Drug induced</td>
<td>Iodine, amiodarone</td>
</tr>
<tr>
<td>Hamburger toxicosis, T4, T3 ingestion</td>
<td>Exogenous hormone</td>
</tr>
<tr>
<td>Pituitary adenoma</td>
<td>Excess TSH (rare)</td>
</tr>
</tbody>
</table>
Graves’ Disease

Causes ~75% of hyperthyroidism
- Familial: 10X more common in women
- Autoimmune. Thyroid stimulating immunoglobulins stimulate thyroid receptor
- Gland enlarges. Smooth goiter.
- T4, T3 high; TSH low. Radioiodine uptake high
- Eye muscles often infiltrated with mucopoly-saccarides and lymphocytes --> double vision

Thyroiditis
- Destruction of thyroid follicle epithelium, Leakage of T4, T3, so hyperthyroid initially
  - Autoimmune
  - Viral
  - Radiation
  - Drugs (amiodarone)
- Low radioiodine uptake (damaged gland)

Indications for Rx of Subclinical Hyperthyroidism

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>INDICATIONS FOR REDUCING THE DOSE OF THIOXINE IN PATIENTS WITH EXOGNOSIS SUBCLINICAL HYPERTHYROIDISM</th>
</tr>
</thead>
<tbody>
<tr>
<td>New atrial fibrillation, angina, or cardiac failure</td>
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<tr>
<td>Accelerated loss of bone density</td>
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<tr>
<td>Oligomenorrhea, amenorrhea, or infertility</td>
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<tr>
<td>Non-specific symptoms such as tiredness, hyperreflexia, and palpitations</td>
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<tr>
<td>Borderline high serum triiodothyronine concentration</td>
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Toft NEJM 345, 2001

Treatment of Hyperthyroidism

- Radio-active iodine (70% in USA)
  - > 50% later hypothyroid not during pregnancy
- Anti-thyroid drugs (29% in USA)
  - inhibit steps in T4 synthesis
  - rash, neutropenia, GI effects, LFTs (10%)
- Surgery (1% in USA)
  - if large goiters
  - anesthetic, bleeding, recurrent laryngeal nerve, parathyroid damage
Hypothyroidism

- Primary - thyroid defect
  T4, T3 low; TSH high
- Secondary - pituitary defect
  T4, T3 low; TSH low or low normal
- Tertiary - hypothalamic defect
  Low T4, T3; TSH any level but TSH not functional

Anti-Thyroid rx

- PTU
- Methimazole
- Dosing
- Cost
- Side-Effects
- Pregnancy

Causes of Hypothyroidism

Primary (thyroid damage)
- Autoimmune
- Absence of gland
- Congenital thyroid defects
- Radioactive iodine or surgery
- Anti-thyroid drugs

Secondary (pituitary or hypothalamus damage)
- Low TSH

Thyroid Hormone Deficiency

- General fatigue, lethargy, cold intolerance
- Heart ↓ heart rate and contractility
- Vascular vasoconstriction, hypertension
- Skin cool, dry, coarse, puffy around eyes
- GI ↓ motility, constipation
- Reproductive ↓ fertility, heavy menses
- Neuro-muscular slow reflex relaxation, hoarse voice, slowed mentation
- Growth delayed bone age, short stature

Treatment for Hypothyroidism

- Give thyroxine (T4)
- Increase dose slowly
- T4 will be converted to T3 as needed
- Goal - normal TSH and free T4
Prevalence of high TSH

What Is Upper Normal TSH?
- 2007 Surks and Hollowell published a further analysis of the NHANES III data
- The 95% upper limit in 20-29 year olds was 3.56
- The 95% upper limit in the 80+ group was 7.49

Thyroid Physical Exam
- Affect
- Vitals - BP, heart rate, weight loss
- Eyes - lid lag, stare, proptosis, EOM abnormal, diplopia
- Neck - goiter, thyroid bruit
- Skin - texture, temperature
- Extremities - tremor, edema
- Neurologic - reflex relaxation rate, strength

Recommendation
- Measure TSH if:
  - Symptoms are present (especially if new)
  - Goiter
  - Evidence of autoimmune disease
  - Positive family history
- Measure TSH every 5 years if over age 35 (?50)
- If TSH elevated, confirm with repeat TSH and measure free T4
  - Treat if free T4 is low (overt hypothyroidism)
  - If free T4 is normal but other risk factors present, treat
  - May follow if no risk factors and free T4 normal

Arguments Against Treating Mild Hypothyroidism
- Not all studies show increased symptoms
- Lipid reduction is modest
- Significant (~10%) numbers of patients developed symptoms of hyperthyroidism in treatment trials
- Overtreatment may precipitate cardiac disease such as angina and arrhythmia

How Can Dose Requirement Change
- Decreasing input (thyroidal production) of hormone
- Change in absorption
- Change in metabolism
- Change in distribution?
- Change in requirement?
  - Body weight change
  - Aging
Drugs Associated With Altered Dose
- Cholestyramine (1969)
- Antacids
  - Aluminum hydroxide
  - Sucralfate
- Anticonvulsants
  - Phenytoin
  - Phenobarbital
  - Carbamazepine
  - Not valproic acid
- Rifampin
- FeSO₄
- CaCO₃
- Estrogens
- Androgens
- Raloxifene
- GH treatment
- Others (not well documented)
  - Glucocorticoids
  - Propanolol
  - Furosemide/salicylates

Thyroid Replacement rx
- Synthroid
- Levoxyl
- Unithroid
- Levothroid
- Tirosint
- Levothyroxine
- Armour
- Cytomel
- Availability
- Cost

Thyroid Exam
- Observe the neck—any swelling or asymmetry?
- Exam best done while standing behind patient
- Start at just below chin and trace down
- First thing you will feel is the thyroid cartilage
- Next is Cricoid cartilage
- Next are the first two rings of the trachea

Abnormalities
- Tenderness
- Swelling
- Deviation of Trachea
- Difficulty swallowing
- Pressure

Thyroid Exam (continued)
- Lobes of thyroid are just below and right and left of midline
- Have patient take a sip of water and hold in their mouth until you instruct them to swallow
- Notice for fingers on either hand to move when patient swallows
- Any masses should move upward when patient swallows

Remember…
- Order [only] the labs that you understand and can interpret
- Prescribe appropriate rx
- Utilize your specialists
- If you don’t know, ASK!
"THINK THYROID"