### Hyperthyroidism

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### Thyrotoxicosis

#### Symptoms

- Weight loss, despite increased appetite
- Sweating, heat intolerance
- Tachycardia, atrial fibrillation
- Frequent loose stools
- Emotional lability, restlessness, tremor
- Weakness, fatigue, dyspnea on exertion
- Graves’ ophthalmopathy

#### Definition of Thyrotoxicosis

- A low or undetectable TSH in the setting of clinical hyperthyroidism
  - May be present with a normal Free T4 and T3
  - Rarely can be mediated by TSH: normal or elevated TSH in the setting of elevated Free T4 and/or T3

#### Cardiac Effects of thyrotoxicosis

- Tachycardia, widened pulse pressure and elevated systolic blood pressure
- Atrial fibrillation
  - 8% of all patients develop this
  - 15% of those 70-79 develop in first 30 days
- Heart Failure
  - Occurs in 6% of thyrotoxic patients
  - Felt to be rate-related cardiomyopathy
### Physical Exam Findings

- Tachycardia, systolic HTN
- Pressured speech, being “fidgety”
- Exophthalmos, lid lag, scleral show
- Goiter, thyroid nodule or tender thyroid
  - Bruit over goiter pathognomonic for Graves’
- Warm, sweaty skin that may be “smooth”
- Fine tremor, brisk reflexes

### Critical diagnostic test: $^{131}$I Uptake and Scan

<table>
<thead>
<tr>
<th>Low iodine uptake</th>
<th>High iodine uptake</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Thyroiditis</td>
<td>- Graves’ disease</td>
</tr>
<tr>
<td>- Exogenous</td>
<td>- Toxic MNG</td>
</tr>
<tr>
<td>- Ectopic</td>
<td>- Toxic adenoma</td>
</tr>
<tr>
<td>- Iodine-induced</td>
<td>- “hashitoxicosis”</td>
</tr>
<tr>
<td>- amiodarone</td>
<td>- TSH-mediated</td>
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</table>

## Suspect thyrotoxicosis:

- TSH
  - TSH <0.1 hypothyroidism
    - Radiiodine Uptake and scan
  - TSH 0.1-0.4 Subclinical hyperthyroidism
  - TSH >0.4 Normal

## Graves’ Disease

- Autoimmune hyperthyroidism
- Caused by antibodies that activate the TSH receptor
  - TSH receptor Ab's and Thyroid Stimulating Immunoglobulin
- “Hashimoto’s” antibodies usually also present: Anti thyroid peroxidase Abs
Graves’ Disease

- Peak incidence 30-50yo
- Strong familial predisposition
- Female:male 9:1
- 15-25% remission rate with medical management
  - Usually in patients with mild disease on presentation

Radioiodine uptake and scan in Graves’ disease:

- Uptake is high usually >50%
- Scan shows diffuse, symmetric uptake
Graves’ Disease Ophthalmopathy 
Exophthalmos (Proptosis)

Toxic Adenoma and 
Toxic MNG

- Focal hyperplasia of thyroid follicular cells with functional capacity which is independent of TSH regulation
- More common in those >50yo
- Localized, somatic activating mutation of the TSH receptor gene
- Rarely if ever spontaneously remits
- Can be associated with isolated T3 toxicosis
Radioiodine Scan of Toxic Multinodular Goiter

Uptake % may be WNL
Scan shows patchy, heterogeneous uptake

Antithyroid Medications, cont

• PTU – comes in 50mg tablets
  ✓ Start at 100mg or 150mg TID
  ✓ Non-compliance with TID dosing frequent
• Methimazole – 5mg and 10mg tablets
  ✓ Start at 20-30mg qd x 5d then can frequently decrease to 10mg per day
• If they’ve been on these meds for 12mo and still hyper, the thyrotoxicosis is NOT going away – move to definitive therapy

Treatment: Medications

• Beta blockade for symptomatic relief of palpitations and cardio-protection
• Thionamides: PTU and Methimazole
  ✓ PTU: more inconvenient TID dosing
  ✓ Methimazole: Once daily
  ✓ 5% develop pruritic rash
  ✓ With longer exposure of higher doses, agranulocytosis and elevated LFTs

Treatment: $^{131}$I

• In Graves disease, goal should be total ablation of thyroid gland
  ✓ Typical doses of 10-22mCi
• TMNG, can try to ablate hyperfunctional nodule(s) and leave remaining normal tissue intact
• Takes 6 weeks to 6 months for ablation
• Very safe: used since 1950’s with no increased incidence cancer or leukemia
**Radiation Safety**

- 3 foot (arm’s length) distance x 3 days
  - Should avoid small children completely
- Avoid exposure to body fluids for 7 days
- Avoid pregnancy for 6-12 months
- Actual radiation dose/exposure is very small: similar to flying in a plane from Columbus to San Francisco and back!

**I^131 Therapy: follow-up**

- Draw labs in 4 weeks: FreeT4
  - Every 4 weeks
- Begin Synthroid once FT4 is in the lower part of the normal range
- Synthroid dosing: 1.6mcg/kg

**Thyroid Surgery for Definitive Treatment of Hyperthyroidism**

- Not first choice in most thyrotoxic pts
- Risk of surgical complications
  - Hypoparathyroidism
  - Recurrent laryngeal nerve injury
- Patient must be euthyroid prior to surgery

**Thyroid Surgery**

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Thyroid Surgery

- Treatment of Choice in Select individuals:
  - Severe hyperthyroidism that failed I\(^{131}\)
  - Moderate to severe orbitopathy
    - Could be made worse by radioactive iodine
  - Suspicious “cold” nodule in the setting of hyperthyroidism

Subacute Thyroiditis

- Release of preformed hormone
- Frequently begins in setting of adjacent inflammation
  - URI or other viral illness
- Self limited – typically lasts 6-12 weeks
- May have thyroid tenderness

Subacute thyroiditis, continued

- Will not respond to Antithyroid medications or I\(^{131}\)
- Beta blockade for symptomatic relief
- Radioiodine uptake/scan shows very low percentage uptake - <5%
- Typical three phase response: Hyperthyroidism, then hypo, then recovery
- 10% of patients go on to develop overt hypothyroidism

Figure: 2009 uptodate
**Amiodarone-induced thyrotoxicosis**

- Amiodarone is 33% iodine
- Hypothyroidism is the more common result
- 2% of patients develop thyrotoxicosis
  - Dumping of stored hormone: thyroiditis
    - Lasts 2-6 months
    - Treat with beta blockade, steroids
  - Excess iodine load in Graves' like picture
    - Usually do see a goiter, family history
    - May respond to methimazole

**Subclinical Hyperthyroidism**

- Suppressed TSH with normal FreeT4 and FreeT3
- Etiology similar to overt hyperthyroidism
  - More likely to be TMNG than Graves, however
- 40% remit within one year of diagnosis; rarely does this progress to thyrotoxicosis

**Amiodarone-induced thyrotoxicosis**

- Cannot use radiiodine scan for diagnosis
- Cannot use I\textsuperscript{131} for treatment
- Thyroidectomy may be necessary
  - Not always the best surgical risk patients, though
- Endocrine consult definitely helpful!

**Subclinical Hyperthyroidism**

<table>
<thead>
<tr>
<th>TSH low, FreeT4 And FreeT3 normal</th>
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<tbody>
<tr>
<td>TSH &lt;0.1</td>
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<tr>
<td>TSH 0.1 – 0.4</td>
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- Treat with ATDs
  - Age >65
    - Risk of arrhythmia
      - Or fracture
    - No cardiac disease
      - No bone disease
  - Age <65
    - Observe
Hypothyroidism

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The Ohio State University

Survey of 13K people with no known thyroid disease

- 4.6% hypothyroid
- 4.3% subclinical hypothyroidism
- 0.3% overt hypothyroidism

11% had elevated TPO Ab
10% had elevated Tg Ab

National Health and Nutrition Examination Surveys (NHANES III)

Elevated TSH levels

TSH distribution by age in US
### Clinical Symptoms and Signs

- Fatigue
- Constipation
- Impaired memory
- Depression
- Muscle weakness
- Menstrual disturbance
- Infertility
- Cold intolerance
- Hoarseness
- Goiter
- Periorbital edema
- Weight gain
- Nerve entrapment syndromes
- Bradycardia
- Dry skin

### Associated Conditions

- Laboratory test abnormalities
  - Hypercholesterolemia
  - Hyponatremia
  - Hyperprolactinemia
  - Hyperhomocysteinemia
  - Anemia
  - CPK elevation

### Percentage of patients with hypothyroid symptoms

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Normal TSH</th>
<th>Elevated TSH</th>
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<tbody>
<tr>
<td>More constipated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feeling colder</td>
<td></td>
<td></td>
</tr>
<tr>
<td>More tired</td>
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<td></td>
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<tr>
<td>Slower thinking</td>
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All differences reach statistical significance

Ann Int Med 2000; 160: 526-534

### Consequences of Hypothyroidism

<table>
<thead>
<tr>
<th>Cholesterol Level (mg/dL)</th>
<th>Abnormal TSH Level</th>
<th>Euthyroid</th>
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<tbody>
<tr>
<td>&gt;10</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>&lt;0.3</td>
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<tr>
<td>0.3</td>
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<td>5.1</td>
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<td>&gt;5.1</td>
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<td>&gt;15</td>
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<td>&gt;60</td>
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<tr>
<td>&gt;80</td>
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Radiological Abnormalities

- Pericardial effusion
- Pleural effusion
- Pituitary enlargement

Medications affecting thyroid function

- Amiodarone
- Lithium
- Interferon α, Interleukin 2
- Dopamine, dobutamine
- Glucocorticoids
- Estrogen
- Tamoxifen
- Methadone

- Cholestyramine
- Ferrous Sulfate
- Omeprazole, lansoprazole
- Calcium carbonate
- Phenobarbital
- Rifampin
- Phenytoin
- Carbamazepine

Causes of Hypothyroidism

- Hashimoto’s thyroiditis
- Post-surgical
- Radiation exposure
- Radioactive iodine
- Drugs
- Central hypothyroidism
- Iodine deficiency/excess

Treatment

- T4 replacement
  - 1.6-1.8 mcg/kg (ideal body weight)
  - Elderly, CAD – 12.5 to 25mcg/day
- Check TFTs in 6-8 weeks
- Re-assess at 6 months
- IV dose is 75-80% of PO
**Pediatric Patients**

- 1-3 years old  4-6 mcg/kg
- 3-10 years old  3-5 mcg/kg
- 10-16 years old  2-4mcg/kg
- Once started, probably best to continue therapy until growth and pubertal development are complete

**T3 Therapy**

- Anectodal reports of patients feeling better with it
- Serum half life 12 hours
- Target organs have deiodinases to convert T4 to T3
- Adds another drug to the medication regimen

**T3 levels pre- and post-operatively**

**Symptom scores by serum TSH level**
Screening

- AACE and AAFP – periodic screening of elderly women
- ACP – women >50 years
- ATA – women over age of 35 should be checked every five years
- USPSTF – does not recommend screening adults or children
- “Aggressive case finding in those >60y and others at high risk for thyroid dysfunction”