Hyperthyroidism: Diagnosis and Treatment

Family Practice Refresher Course

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Objectives

Review diagnosis and management of

• Graves
• Hot nodules
• Toxic nodular goiter
• Thyroid storm
Hyperthyroidism

- 24 y.o. with weight loss, proptosis, palpitations, heat intolerance and amenorrhea
- 80 y.o. with fatigue and thyroid nodule
- 65 y.o. with longstanding goiter and dysphagia
- 40 y.o. with neck and ear pain and heat intolerance
Thyrotoxicosis

- Weight loss, tremor, fatigue, amenorrhea, palpitations, heat intolerance, hyperdefecation
- Apathetic thyrotoxicosis in elderly
- FT$_4$ levels do not always correlate with symptoms
DDx Hyperthyroidism

<table>
<thead>
<tr>
<th>Condition</th>
<th>FT_4</th>
<th>TSH</th>
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<tbody>
<tr>
<td>Graves</td>
<td>↑</td>
<td>↓</td>
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<tr>
<td>Hot nodule</td>
<td>↑</td>
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<tr>
<td>Thyroiditis</td>
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<tr>
<td>Toxic goiter</td>
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A thyroid scan and/or iodine uptake can help determine etiology
Graves Disease

Diffuse increased uptake of radioactive iodine or technetium
Toxic Nodular Gland

Multiple nodules
Enlarged gland
Heterogeneous uptake with hot and cold nodules
Hyperfunctioning (Hot) Nodule

- Rarely malignant
- Many are euthyroid
- Remainder of gland suppressed
Subacute Thyroiditis
Graves

TSIG
↓
thyroid hormone synthesis
↓
↑ T₄  ↑ T₃
↓
suppressed TSH

Thyroiditis

inflammation
↓
release of thyroid hormone
↓
↑ T₄  ↑ T₃
↓
suppressed TSH
↓
thyroid hormone synthesis
Graves Disease

- Autoimmune
- Thyroid stimulating antibodies bind to TSH receptors
- Diffuse smooth thyroid enlargement
- Orbitopathy in 5-10%
- $\uparrow$ RAI uptake
- $\uparrow$ free T$_4$, $\downarrow$ TSH
Graves Ophthalmopathy

- Diplopia
- Proptosis
- Exophthalmos
- Periorbital swelling
- Bilateral or unilateral
- Pulse 120, DTRs 4+, diffuse tremor, anxious.
- Palpitations
- Heat intolerance
- Hyperdefecation
Graves

• Work-up
  - FT$_4$, TSH
  - Thyroid stimulating immunoglobulin (TSIG)
  - TSH receptor antibodies
  - don’t routinely need T$_3$

• Treatment
  - methimazole
  - propylthiouracil
  - radioactive iodine
  - surgery
Radioactive Iodine

- Gland destruction
- TSH receptor antibodies persist after treatment
- Avoid RAI in patient with severe Graves ophthalmopathy
- Single dose effective in 90%
- Most become hypothyroid after 2-3 months, time course variable
Methimazole

- Decreases thyroid stimulating immunoglobulin levels and blocks $T_4$ synthesis
- 30–40% have spontaneous remission after 1 year of therapy
- Agranulocytosis – rare
- Cholestatic hepatitis – rare
Propylthiouracil (PTU)

- Decreases conversion of $T_4$ to $T_3$
- TID dosing
- Use in 1st trimester of pregnancy
Surgery

- Recurrence is possible
- Potential hypocalcemia and recurrent laryngeal nerve damage
- Use for nodules or extremely large glands
A 24 yo with Graves disease was treated with RAI 9 months ago. Her free T4 was 3.1 (↑) at diagnosis. Palpitations and heat intolerance are gone, her periods are regular, and her weight has normalized.

FT$_4$ 1.4 (nl)  
TSH 0.05 (↓)

Which of the following should you recommend?

A. Start methimazole  
B. Another dose of RAI  
C. Measure T3  
D. No intervention
In Graves TSH may remain suppressed for months after treatment

Don’t make post-treatment decisions on TSH alone
A 50 yo has a 1-month history of tremor, palpitations, and heat intolerance. His pulse is 100, the thyroid is smooth and tender, and he has no proptosis.

FT$_4$ 2.1 ($\uparrow$)
TSH 0.01 ($\downarrow$)

What should you do next?

A. Thyroid scan
B. Check T$_3$
C. Ultrasound
D. Repeat TFT’s in 6 weeks
Subacute or Painless Thyroiditis

- Painful gland, ear pain
- Elevated ESR
- Mild hyperthyroidism
- Hyperthyroid phase followed by transient hypothyroidism
- Usually resolves without Rx
- Occurs postpartum too
Subacute Thyroiditis
A 25 yo nursing assistant has a 2 month history of palpitations. She is trying to lose weight. On exam her thyroid is not palpable and she has a fine tremor.

FT₄ 2.1, TSH 0.01, thyroglobulin ↓

What is the most likely diagnosis?

A. Graves
B. Surreptitious use of T₄
C. Subacute thyroiditis
D. Hot nodule
A 75 y.o. has lost weight, has palpitations and has noted declining energy. On exam his thyroid is smooth and not enlarged.

His TSH is 0.01 (0.2-4.2). The FT$_4$ is 1.2 (0.9-1.5).
What is the next step?

- Repeat levels in 6 weeks
- Measure $T_3$
- Measure TPO antibodies
- Measure reverse $T_3$
$T_3$ Toxicosis

- Normal free $T_4$ and suppressed TSH
- Symptoms of hyperthyroidism
- Measure total $T_3$ to confirm diagnosis
- Apathetic thyrotoxicosis especially in elderly
During an evaluation for fatigue and muscle weakness an 80 y.o. is found to have a 1.5 cm thyroid nodule. Her exam is otherwise normal. Her TSH is 0.09 (0.2-4.2), the free T₄ is 1.6 (0.9-1.5).

What is the next step in evaluating the nodule?
What is the next step?

A. Ultrasound
B. Thyroid scan
C. Fine needle aspiration
D. TPO antibodies
Hyperfunctioning (Hot) Nodule

- 5-10% of nodules
- Malignancy uncommon
- FNA not required
- When $T_4$ is elevated - surgery or radioactive iodine
A 65 y.o. with lifelong goiter

FT₄ 1.3, T₃ 1.2, TSH <0.01

No dysphagia or palpitations

How to treat?
Multinodular Goiter

- Effects of suppressive therapy are variable
- Thyroid hormone is risky when TSH is low or suppressed
- No need for FNA unless there is a dominant nodule
- Surgery is a good option in some cases
Multinodular Goiter

- Suppressive therapy not uniformly effective
- Cancer risk is the same in solitary nodules and multinodular goiter
- Hyper or hypothyroid
- Dysphagia, hoarseness with substernal extension
- Nodule size and characteristics determine whether FNA is necessary
A 70 yo with steroid-dependent asthma is admitted with CHF, atrial fibrillation, fever, and confusion. She has an enlarged thyroid, and her FT$_4$ is 7 (↑↑). Her ventricular rate is 120. She has received an IV β-blocker and 100 mg hydrocortisone in the ICU.

What should be done next?

A. Radioactive iodine  
B. Propylthiouracil  
C. Cold iodine  
D. Technetium scan  
E. TSH receptor antibodies
Thyroid Storm

- Exaggerated symptoms of hyperthyroidism
- Surgery, infection, iodine load may precipitate
- Block $T_4$ synthesis with PTU, then block $T_4$ release with nonradioactive iodine
- High mortality
- Glucocorticoids and PTU decrease $T_4 \rightarrow T_3$ conversion
22 y.o. in first trimester with weight loss, tremor and tachycardia. The thyroid is enlarged, pulse 110.

FT$_4$ 3.4 (0.9-1.5) and TSH 0.01 (0.2-4.2).
Treatment of Hyperthyroidism in Pregnancy

- Control of thyroid hormone secretion important in reducing preterm delivery, preeclampsia and IUGR
- Propylthiouracil (PTU) in 1st trimester then methimazole (MMI)
- PTU and MMI cross the placenta equally
- MMI associated with scalp defect, aplasia cutis and choanal atresia
During Pregnancy

• Keep FT$_4$ at upper limit of normal and monitor monthly
• High doses of PTU or MMI can lead to fetal goiter or hypothyroidism
• May be able to stop antithyroid agent in later stages of pregnancy
• Breastfeeding is ok with both PTU and MMI
On a wellness screen a 70 y.o. woman has a free $T_4$ of 1.2 (0.9-1.5) and TSH of $<0.05$ (0.2-4.2). She feels fine and her exam is normal. Her thyroid is irregular and mildly enlarged. Her family history is negative for thyroid disease.
Causes of Low TSH

- Elderly
- Acute illness
- Hypopituitarism
- After treatment for thyrotoxicosis
- Early or developing hyperthyroidism
- $T_3$ toxicosis
Evaluation of Low TSH

- **↓TSH**
  - **FT₄**
  - **Normal**
    - **T₃ RIA**
      - Normal
      - High
        - Subclinical Hyperthyroidism
  - **High**
    - Hyperthyroidism
  - **Low**
    - 2° Hypothyroidism
      - T₃ toxicosis
Subclinical Hyperthyroidism

- No symptoms
- Normal FT$_4$
- Normal T$_3$
- ↓ TSH
- Multinodular goiter
- Autonomous nodule(s)
Subclinical Hyperthyroidism

- Exogenous or endogenous
- Prevalence 1-12%
- More common in females
- TSH may normalize spontaneously in 50%
- Progression to overt hyperthyroidism is uncommon
Incidence of Atrial Fibrillation in Subclinical Hyperthyroidism

Percent with Atrial Fibrillation

- TSH ≤ 0.1 mU/L
- TSH 0.1-0.4 mU/L
- TSH ≥ 0.5 mU/L

NEJM 331: 1249, 1994
Risk of Fracture in Women with Low TSH

Odds Ratio

- Hip: TSH 0.5-5.5 = 1.9, TSH 0.1-0.5 = 3.6, TSH <0.1 = 1
- Vertebral: TSH 0.5-5.5 = 2.8, TSH 0.1-0.5 = 4.5, TSH <0.1 = 1
- NonSpine: TSH 0.5-5.5 = 2, TSH 0.1-0.5 = 2.3, TSH <0.1 = 1

Ann Intern Med 2001
• No long term clinical trials have assessed whether therapy improves cardiovascular or bone health in subclinical hyperthyroidism.

• Treat based on risk factors and degree of TSH suppression.
Subclinical Hyperthyroidism

- Low risk, asymptomatic
  - monitor TFT’s every 6-12 months

- High risk
  - elderly, CV disease
  - get DXA scan
  - technetium scan
Questions?