Common Endocrine Problems Seen in Primary Care
Part 1
41st Semi-annual Temple Family Medicine Review Course
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Section of Endocrinology
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Objectives

1. Understand the basic approach to management of commonly seen thyroid diseases-
   • Hyperthyroidism
   • Hypothyroidism

2. Select appropriate imaging studies for hyperthyroidism and hypothyroidism

3. Review the initial approach to evaluation of hypercalcemia

4. List indications for surgical treatment of primary hyperparathyroidism
Clinical Vignette 1
A 56 year old woman is seen in your office for palpitations.

Palpitations: have persisted x 3 months
She also complains of weight loss of 10lbs in the last 3 months.

She had recent episodes of diarrhea after a course of antibiotics. She has increased sweating associated with hot flashes since menopause 4 years ago, but thinks this may be worse recently.
BP 160/73 | Pulse 100 | Temp 98.9 °F | Resp 16 | BMI 23.12 kg/m2

Constitutional: Thin appearing
HENT: Normocephalic and atraumatic. Temporal wasting.
Eyes: Conjunctival injection bilaterally. Mild lid retraction and stare.
Neck: supple. No JVD. No tracheal deviation.
Thyromegaly (R > L). Bruit +. No cervical adenopathy. No stridor.
Cardiovascular: Regular rate, rhythm. Normal heart sounds.
Pulmonary: Effort and breath sounds normal. No wheezes or rales.
Musculoskeletal: 1+ edema up to knees
Neurological: Alert, oriented to person, place, and time. Tremor ++
Bilateral brisk reflexes. Tongue fasiculations ++
Skin: No rash. No erythema.
Psychiatric: Normal mood and affect. Judgment, thought content and behavior normal
Frequent principal symptoms of hyperthyroidism

- Nervousness
- Heat insensitivity
- Sweating
- Weight loss
- Tachycardia
- Palpitations
- Muscle weakness
- Moist skin
- Increased appetite
- Sleepless
- Tremor
- Goiter
- Bruit over thyroid
- Diarrhea
Would you expect this patient to have infiltrative thyroid ophthalmopathy?

**Eye Changes due to Thyrotoxicosis**
- Spasm of the upper lids
  - (stare and lid lag)

**Autoimmune Ophthalmopathy**
- Periorbital edema/chemosis
- Proptosis/exophthalmos
- Impairment of extraocular muscles
Clinical findings in Graves’ disease

- **Ophthalmopathy**
- **Diffuse goiter**
- **Infiltrative dermopathy**
  (pretibial myxedema)
<table>
<thead>
<tr>
<th></th>
<th>Normal range</th>
<th>10.2.17</th>
<th>10.3.17</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH 3\textsuperscript{rd} generation</td>
<td>0.4 – 4.5 mIU/L</td>
<td>0.01 (L)</td>
<td>0.01 (L)</td>
</tr>
<tr>
<td>FT3</td>
<td>2.3-4.2 pg/ml</td>
<td></td>
<td>&gt;20.0 (H)</td>
</tr>
<tr>
<td>FT4</td>
<td>0.8-1.9 ng/dl</td>
<td></td>
<td>7.4 (H)</td>
</tr>
</tbody>
</table>
Assessment and Plan

Thyrotoxicosis
Most likely Grave’s disease

- Start methimazole 30mg daily
- Start atenolol 50 mg daily

- CBC and differential, CMP
- T3, FT4, Thyroid stimulating immunoglobulin

- Consider NM thyroid uptake and scan
Treatment of Graves’ Disease

- Control symptoms with beta blockers
- Beta-adrenergic blockade should be given to elderly patients with symptomatic thyrotoxicosis and to other thyrotoxic patients with resting heart rates > 90 bpm or coexistent cardiovascular disease.

- Treat hyperthyroidism with anti-thyroid drugs
  - Methimazole- preferred, except contraindicated in 1st trimester of pregnancy
  - Propylthiouracil
- Radioiodine Therapy
- Thyroidectomy
- The long-term quality of life following treatment was found to be the same in patients randomly allocated to one of the three treatment options

Endocr Pract. 2011 May-Jun;17(3):456-520
The 2 hour uptake is 51% and the 24-hour uptake is 75%.
Markedly elevated values for this laboratory in the range of hyperthyroidism.
The thyroid gland is diffusely enlarged approximately 4 times normal in size. The uptake is slightly heterogeneous. No dominant nodules are identified.
The right lobe measures 68 x 34 mm and the left lobe measures 66 x 34 mm. The estimated size of the gland is 77cc or approximately 77 grams.
Commonly seen pattern on Thyroid Uptake and Scans

<table>
<thead>
<tr>
<th>Disease</th>
<th>Uptake</th>
<th>Scan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Graves' Disease</td>
<td>Very high</td>
<td>Diffuse uptake</td>
</tr>
<tr>
<td>Toxic multinodular goiter</td>
<td>Slightly high or normal</td>
<td>Heterogeneous image with foci of increased uptake</td>
</tr>
<tr>
<td>Toxic adenoma</td>
<td>High or normal</td>
<td>Hot nodule with the rest of gland suppressed</td>
</tr>
<tr>
<td>Subacute thyroiditis</td>
<td>Low or zero</td>
<td>Mild diffuse uptake</td>
</tr>
</tbody>
</table>

Williams Textbook of Endocrinology Chapters 11, 12, 13
Hyperthyroidism with normal or high uptake

- Graves' disease
- Toxic adenoma
- Toxic multinodular goiter
- TSH-producing pituitary adenoma
- Hyperemesis gravidarum
- Trophoblastic disease

Hyperthyroidism with near absent uptake

- Subacute granulomatous (de Quervain's) thyroiditis
- Painless thyroiditis (silent thyroiditis, lymphocytic thyroiditis)
- Postpartum thyroiditis
- Amiodarone
- Radiation thyroiditis
- Excessive LT4 replacement
- Intentional suppressive therapy
- Factitious hyperthyroidism
- Ectopic hyperthyroidism: Struma ovarii
- Metastatic follicular thyroid cancer

Williams Textbook of Endocrinology Chapters 11, 12
Clinical Vignette 2
A 38 year old female complains of severe pain on the anterior neck. She is febrile and complains of nervousness, sweating and palpitations. Other symptoms include: fatigue for the last 1 month
BP 155/90 | Pulse 104 | Temp 100 °F | Resp 15 | BMI 24 kg/m2

Constitutional: Normal appearance
HENT: Normocephalic and atraumatic.
Eyes: She has mild stare, mild lid retraction. Normal conjunctiva.
Neck: Supple. No tracheal deviation present.
Thyromegaly (diffuse). No bruit. No cervical adenopathy. No stridor.
Cardiovascular: Regular rate, rhythm. Normal heart sounds.
Pulmonary: Effort and breath sounds normal. No wheezes or rales.
Musculoskeletal: Normal ROM and no edema
Neurological: Alert, oriented to person, place, and time. Mild tremor + Bilateral brisk reflexes. No tongue fasciculations
Skin: No rash. No erythema.
Psychiatric: Normal mood and affect. Judgment, thought content and behavior normal
Thyroiditis with thyroid pain and tenderness

- Subacute thyroiditis
  (DeQuervain’s, granulomatous, giant cell, non-suppurative)
- Infectious (suppurative) thyroiditis
- Radiation thyroiditis
- Trauma induced
- Hemorrhage into a thyroid nodule

Thyroiditis without thyroid pain and tenderness

- Hashimoto’s
  (autoimmune, silent, lymphocytic) thyroiditis
- Postpartum thyroiditis
- Drug-induced thyroiditis
- Riedel’s (fibrous) thyroiditis
# Laboratory data

<table>
<thead>
<tr>
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<th>Normal range</th>
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<tr>
<td>TSH 3rd generation</td>
<td>0.4 – 4.5 mIU/L</td>
<td>0.01 (L)</td>
<td>0.01 (L)</td>
</tr>
<tr>
<td>T3</td>
<td>76-181ng/dl</td>
<td></td>
<td>260 (H)</td>
</tr>
<tr>
<td>FT4</td>
<td>0.8-1.9 ng/dl</td>
<td></td>
<td>2.2 (H)</td>
</tr>
</tbody>
</table>
Subacute thyroiditis

- Also called granulomatous, DeQuervain’s, giant cell, non-suppurative thyroiditis

- Characterized by neck pain, a tender diffuse goiter, and a predictable course of thyroid function evolution.

- Hyperthyroidism is typically the presentation followed by euthyroidism, hypothyroidism, and ultimately restoration of normal thyroid function.

- Caused by a viral infection or a postviral inflammatory process
Other tests in the evaluation of thyroiditis

• Thyroglobulin is released along with thyroid hormone in subacute, painless, and palpation thyroiditis

• An elevated Tg can be caused by any form of thyroid inflammation/destruction, hyperthyroidism or certain thyroid cancers.

• ESR may be greater than 100 mm/hr in subacute thyroiditis (normal < 20 mm/hr).

• Thyroid Ultrasound (US) - Rarely necessary for thyroiditis
• Consider if unsure of diagnosis to rule out other causes of anterior neck pain
  – Infectious thyroiditis- abscess
  – Hemorrhage into thyroid cyst
  – Rapidly enlarging thyroid nodule/cancer
Treatment and course of subacute thyroiditis

• Thyrotoxicosis
  – Usually mild or asymptomatic
  – Can use low dose beta blocker to control heart rate, anxiety, tremor

• Pain
  – NSAIDS at high doses (800 mg ibuprofen q 8 hrs)
  – May need corticosteroids
  – Usual course is 4-8 weeks

• Usually resolves in weeks to months
• A subset of patients develop permanent hypothyroidism and they usually have positive TPO antibodies
• Usually become euthyroid when gland regenerates
A 61 year old woman complains of increasing fatigue over the last 5 months. She has gained 10 pounds during this interval.

She has cold intolerance, mild constipation, and dryness of skin and hair.

She fallls sleep easily.

She has noted puffiness of upper eye lids.

Thyroid gland cannot be palpated.

What is the possible diagnosis?
<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Symptoms</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slowing of metabolic processes</td>
<td>Fatigue and weakness</td>
<td>Slow movement</td>
</tr>
<tr>
<td>Cold intolerance</td>
<td>Bradycardia</td>
<td></td>
</tr>
<tr>
<td>Dyspnea on exertion</td>
<td>Delayed relaxation of tendon reflexes</td>
<td></td>
</tr>
<tr>
<td>Weight gain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cognitive dysfunction</td>
<td>Slow speech</td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accumulation of hyaluronic acid</td>
<td>Coarse skin</td>
<td></td>
</tr>
<tr>
<td>Hoarseness</td>
<td>Puffy facies</td>
<td></td>
</tr>
<tr>
<td>Edema</td>
<td>Periorbital edema</td>
<td></td>
</tr>
<tr>
<td>Reduced secretion from sweat and sebaceous glands</td>
<td>Dry skin</td>
<td></td>
</tr>
<tr>
<td>Diminished O2 requirement and decreased production of erythropoietin</td>
<td></td>
<td>Normocytic, normochromic anemia</td>
</tr>
</tbody>
</table>

Williams Textbook of Endocrinology Chapter 13
Causes of Hypothyroidism

• Primary Hypothyroidism
  – Hashimoto’s disease
  – Treatment for hyperthyroidism (anti-thyroid drug, RAI)
  – Thyroid surgery
  – Hypothyroid phase in subacute thyroiditis
  – Drugs- amiodarone, glucocorticoids, interleukin 2, tyrosine kinase inhibitors
  – Iodine deficiency/excess
  – Congenital hypothyroidism

• Secondary Hypothyroidism (Pituitary TSH deficient)

• Tertiary (TRH deficient)

• Resistance to thyroid hormone (inherited)
Diagnosis of Hypothyroidism

- **Primary hypothyroidism**
  - High TSH
  - Low Free T4

- **Secondary and tertiary hypothyroidism**
  - Low or low normal TSH
  - Low Free T4

- **Free Hormone** is metabolically active and determines thyroid status versus total hormone which is largely bound to binding proteins.

- **Total T3** Principal use is diagnosing and following Thyrotoxic patients, *NOT* Hypothyroid patient

- **Free T3** Not as reliable as Total T3

Keys to diagnosing Autoimmune Thyroid disease

Elevated anti-thyroid antibody titers

• Anti-thyroglobulin antibodies (TgAb): Does not correlate with hypothyroidism

• Antimicrosomal/anti-thyroid peroxidase antibodies (TPOAb): Correlate with the development of hypothyroidism

• TSH receptor antibodies (TSHRAb) : Used in the diagnosis and monitoring of Graves’
  – Thyroid Stimulating Immunoglobulin (TSI)
  – Thyrotropin Binding Inhibitory Immunoglobulin (TBII)

Endocr Pract. 2011 May-Jun;17(3):456-520
Autoimmune Thyroid Disease: 20 Year % Probability of Developing Hypothyroidism

- TPOAb (+) with TSH of 3-4 have less than 50% chance of developing hypothyroidism over 20 years;
- TPOAb (-), <20%

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>TSH (mIU/liter)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>1</td>
<td>6</td>
<td>1</td>
<td>6</td>
<td>3</td>
<td>13</td>
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<td>30</td>
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<td>8</td>
<td>2</td>
<td>8</td>
<td>3</td>
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<td>10</td>
<td>2</td>
<td>11</td>
<td>4</td>
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<td>13</td>
<td>3</td>
<td>13</td>
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<td>60</td>
<td>3</td>
<td>17</td>
<td>3</td>
<td>17</td>
<td>7</td>
<td>31</td>
</tr>
<tr>
<td>70</td>
<td>4</td>
<td>21</td>
<td>4</td>
<td>21</td>
<td>9</td>
<td>37</td>
</tr>
</tbody>
</table>

Indications for testing for autoimmune thyroid disease

- Evaluating patients with subclinical hypothyroidism

- To identify autoimmune thyroiditis when nodular thyroid disease is suspected to be due to autoimmune thyroid disease

- Evaluating patients with recurrent miscarriage, with or without infertility
<table>
<thead>
<tr>
<th></th>
<th>Normal range</th>
<th>3.21.17</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH 3rd generation</td>
<td>0.4 – 4.5 mIU/L</td>
<td>38 mIU/L (H)</td>
</tr>
<tr>
<td>FT4</td>
<td>0.8-1.9 ng/dl</td>
<td>0.3 ng/dl (L)</td>
</tr>
</tbody>
</table>
Treatment of Hypothyroidism

- TSH is the primary diagnostic test and is used to assess adequacy of thyroid hormone replacement.
- In central hypothyroidism, free T4 should guide dose adjustments.
- Patients with hypothyroidism should be treated with L-thyroxine monotherapy.
- Evidence does not support using L-thyroxine and L-triiodothyronine combinations or desiccated thyroid hormone.
- Patients whose serum TSH levels exceed 10 mIU/L are at increased risk for heart failure and cardiovascular mortality, and should be considered for treatment with L-thyroxine.

Treatment of Subclinical Hypothyroidism

- Symptoms suggestive of hypothyroidism
- Positive TPOAb or
- Evidence of atherosclerotic cardiovascular disease, heart failure, or associated risk factors for these diseases

- Initial L-thyroxine dosing is generally lower than in overt hypothyroidism.
- Daily dose of 25 to 75 µg should be considered, depending on the degree of TSH elevation.

When should TSH levels be measured in patients being treated for hypothyroidism?

• Established hypothyroidism: TSH measurements done at 4-8 weeks after initiating treatment or after a change in dose.

• Once an adequate replacement dose has been determined, periodic TSH measurements should be done after 6 months and then at 12-month intervals, or more frequently based on clinical judgment.
# Recommendations of Six Organizations Regarding Screening of Asymptomatic Adults for Thyroid Dysfunction

<table>
<thead>
<tr>
<th>Organization</th>
<th>Screening recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Thyroid Association</td>
<td>Women and men ≥35 years of age should be screened every 5 years.</td>
</tr>
<tr>
<td>American Association of Clinical Endocrinologists</td>
<td>Older patients, especially women, should be screened.</td>
</tr>
<tr>
<td>American Academy of Family Physicians</td>
<td>Patients ≥60 years of age should be screened.</td>
</tr>
<tr>
<td>American College of Physicians</td>
<td>Women ≥50 years of age with an incidental finding suggestive of symptomatic thyroid disease should be evaluated.</td>
</tr>
<tr>
<td>U.S. Preventive Services Task Force</td>
<td>Insufficient evidence for or against screening</td>
</tr>
<tr>
<td>Royal College of Physicians of London</td>
<td>Screening of the healthy adult population unjustified</td>
</tr>
</tbody>
</table>
Clinical Vignette 4
• A 66 year old woman is seen in your office for a routine visit. She offers no complaints.
• She takes hydrochlorothiazide 25 mg and lisinopril 20 mg daily for hypertension and metformin 1000 mg twice daily for diabetes.

• Examination is overall normal

Abnormal laboratory data-
• Calcium 10.9 mg/dl (8.5-10.2 mg/dL)
Causes of Hypercalcemia

<table>
<thead>
<tr>
<th>PTH Dependent Hypercalcemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Primary hyperparathyroidism (PHPT)</td>
</tr>
<tr>
<td>2. Tertiary hyperparathyroidism</td>
</tr>
<tr>
<td>3. Familial hypocalciuric hypercalcemia</td>
</tr>
<tr>
<td>4. Lithium-associated hypercalcemia</td>
</tr>
</tbody>
</table>
Causes of Hypercalcemia—non PTH dependant

1. Neoplasms
   PTHrP-dependent
   Other humoral syndromes
   Local osteolytic disease (including metastases)

2. PTHrP excess (non-neoplastic)

3. Excess vitamin D action
   Ingestion of excess vitamin D or vitamin D analogues
   Topical vitamin D analogues
   Granulomatous disease

4. Thyrotoxicosis

5. Renal failure
   Acute renal failure
   Chronic renal failure with aplastic bone disease

6. Immobilization

7. Drugs
   1. Vitamin A intoxication
   2. Milk-alkali syndrome
   3. Thiazide diuretics

8. Adrenal insufficiency

Williams Textbook of Endocrinology Chapter 28
Evaluation of Asymptomatic PHPT

Laboratory:
• Biochemistry panel- calcium, phosphate, alkaline phosphatase, BUN, creatinine
• 25(OH)D
• PTH by second- or third-generation immunoassay

Skeletal assessment:
• BMD by DXA Lumbar spine, hip, and distal 1/3 radius
• Vertebral spine assessment: X-ray or VFA by DXA

Renal assessment
• 24-h urine for: Calcium, creatinine, creatinine clearance
• Stone risk profile: Abdominal imaging by x-ray, ultrasound, or CT scan
Laboratory analysis

- PTH 150 pg/ml (H) 10-65 ng/L
- Calcium 10.9 g/dl (H) 8.5-10.2 mg/dL
- Albumin 4.2 g/dl 3.5 to 5.5 g/dL
- Creatinine 1 g/dl 0.6-1.2 mg/dL
- Urine calcium 320 mg/24 h 35-250 mg/24 h
- Urine Creatinine 1.6 g/24 h 0.63-2.50 g/24 h
- Vitamin D 25 OH 26 (L) 30-100 ng/mL
Guidelines for Monitoring Patients with Asymptomatic PHPT

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum calcium</td>
<td>Biannually DXA, annually (forearm)</td>
<td>Biannually DXA, annually (3 sites)</td>
<td>Annually DXA, every 1–2 y (3 sites)(^a)</td>
<td>Annually Every 1–2 y (3 sites),(^a) x-ray or VFA of spine if clinically indicated (eg, height loss, back pain)</td>
</tr>
<tr>
<td>Skeletal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal</td>
<td>eGFR, annually; serum creatinine, annually</td>
<td>eGFR, not recommended; serum creatinine, annually</td>
<td>eGFR, not recommended; serum creatinine, annually</td>
<td>eGFR, annually; serum creatinine, annually. If renal stones suspected, 24-h biochemical stone profile, renal imaging by x-ray, ultrasound, or CT</td>
</tr>
</tbody>
</table>

\(^a\)
Follow up Laboratory analysis shows:

- PTH 166 pg/ml (H)
- Calcium 12.2 g/dl (H)
- Albumin 4 g/dl
- Creatinine 1.2 g/dl (H)
- GFR 55 ml/min (L)
- Urine calcium 310 mg/24 h (H)
- Vitamin D 25 OH 20 (L)

- T-score is -2.2 at lumbar spine, -2 total hip, femoral neck, and – 3 at the distal 1/3 radius

- A renal ultrasound shows bilateral nephrocalcinosis

- What is the further management?
## Guidelines for Surgery in Asymptomatic PHPT

<table>
<thead>
<tr>
<th>Measurement(^b)</th>
<th>1990</th>
<th>2002</th>
<th>2008</th>
<th>2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum calcium (\geq) upper limit of normal</td>
<td>1–1.6 mg/dL (0.25–0.4 mmol/L)</td>
<td>1.0 mg/dL (0.25 mmol/L)</td>
<td>1.0 mg/dL (0.25 mmol/L)</td>
<td>1.0 mg/dL (0.25 mmol/L)</td>
</tr>
<tr>
<td>Skeletal</td>
<td>BMD by DXA: Z-score (&lt;-2.0) (site unspecified)</td>
<td>BMD by DXA: T-score (&lt;-2.5) at any site(^b)</td>
<td>BMD by DXA: T-score (&lt;-2.5) at any site(^b)</td>
<td>A. BMD by DXA: T-score (&lt;-2.5) at lumbar spine, total hip, femoral neck, or distal 1/3 radius(^b)</td>
</tr>
<tr>
<td>Renal</td>
<td>A. eGFR reduced by (&gt;30%) from expected</td>
<td>A. eGFR reduced by (&gt;30%) from expected</td>
<td>A. eGFR &lt; 60 cc/min</td>
<td>B. Vertebral fracture by x-ray, CT, MRI, or VFA</td>
</tr>
<tr>
<td></td>
<td>B. 24-h urine for calcium (&gt;400) mg/d ((&gt;10) mmol/d)</td>
<td>B. 24-h urine for calcium (&gt;400) mg/d ((&gt;10) mmol/d)</td>
<td>B. 24-h urine for calcium (&gt;400) mg/d ((&gt;10) mmol/d) and increased stone risk by biochemical stone risk analysis(^d)</td>
<td>A. Creatinine clearance (&lt;60) cc/min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>C. Presence of nephrolithiasis or nephrocalcinosis by x-ray, ultrasound, or CT</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>(&lt;50)</td>
<td>(&lt;50)</td>
<td>(&lt;50)</td>
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</table>
## Indications for Parathyroid Surgery

<table>
<thead>
<tr>
<th>Measurement</th>
<th>2013</th>
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</thead>
<tbody>
<tr>
<td>Serum calcium (&gt;upper limit of normal)</td>
<td>&gt;1 mg/dL (&gt;0.25 mmol/L)</td>
</tr>
<tr>
<td>Skeletal</td>
<td>A. T-score ≤-2.5 at lumbar spine, total hip, femoral neck, or distal 1/3 radius; or a significant reduction in BMD⁸</td>
</tr>
<tr>
<td></td>
<td>B. Vertebral fracture by x-ray, CT, MRI, or VFA</td>
</tr>
<tr>
<td>Renal</td>
<td>A. CrCl &lt; 60 cc/min</td>
</tr>
<tr>
<td></td>
<td>B. Clinical development of a kidney stone or by imaging (x-ray, ultrasound, or CT)</td>
</tr>
</tbody>
</table>
### EBM Recommendations

<table>
<thead>
<tr>
<th>Evidence Rating</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-adrenergic blockade should be given to elderly patients with symptomatic thyrotoxicosis and to other thyrotoxic patients with resting heart rates in excess of 90 bpm or coexistent cardiovascular disease</td>
<td>Grade A, ++</td>
</tr>
<tr>
<td>Patients whose serum TSH levels exceed 10 mIU/L are at increased risk for heart failure and cardiovascular mortality, and should be considered for treatment with L-thyroxine.</td>
<td>Grade B, +++</td>
</tr>
<tr>
<td>In patients with asymptomatic pHPT, abdominal imaging should be performed for detection of nephrocalcinosis or nephrolithiasis</td>
<td>Grade B, +</td>
</tr>
</tbody>
</table>

# EBM Recommendations

<table>
<thead>
<tr>
<th>Type of grading</th>
<th>Definition of grades</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Strength of the recommendation</strong></td>
<td><strong>A</strong> = strong recommendation (for or against) Applies to most patients in most circumstances Benefits clearly outweigh the risk (or vice versa)</td>
</tr>
<tr>
<td></td>
<td><strong>B</strong> = weak recommendation (for or against) Best action may differ depending on circumstances or patient values Benefits and risks or burdens are closely balanced, or uncertain</td>
</tr>
<tr>
<td><strong>Quality of the evidence</strong></td>
<td><strong>+++</strong> = High quality; evidence at low risk of bias, such as high quality randomized trials showing consistent results directly applicable to the recommendation</td>
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<tr>
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<td><strong>++</strong> = Moderate quality; studies with methodological flaws, showing inconsistent or indirect evidence</td>
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<td><strong>+</strong> = Low quality; case series or unsystematic clinical observations</td>
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