Intro & Epidemiology

- 4-7% of population have palpable thyroid nodules, 19-67% have incidental nodules on ultrasound
- 5% of palpable nodules are malignant (<1% of nodules cause hypothyroidism or thyrotoxicosis)
- Nodules <1cm are not usually palpable (unless anterior)
- Majority are benign, the key goal is to rule out cancer
- Pain is uncommon (if painful likely benign)

Review of Thyroid Symptoms

- Hyperthyroidism:
  - wt loss (good appetite), anxiety, intolerance to heat, sweating, hair loss, muscle pains, weakness, tremor, irritability/hyperactivity.
  - nervousness, irritability, increased perspiration, palpitations, hand tremors, anxiety, poor sleep, thinning skin, brittle hair, muscle weakness, frequent BM, wt loss, good appetite, menstruation may lighten.
- Hypothyroidism
  - Early (cold intolerance, constipation, wt gain, bradycardia, sweating, muscle/joint pains, dry/itchy skin, thin/brittle fingernails, depression, infertility (cycles irregular), elevated lipids, hyperprolactinemia, galactorrhea.

Risk Factors (“Red Flags”)

- Extremes of age (<20yo or >65yo)
- Male Gender
- Symptoms of local invasion (“dysphagia, neck pain, hoarseness”)
- History of neck radiation
- Family history of thyroid cancer or polyposis (Gardner's Syndrome)

Physical Exam:

- Thyroid exam
- Lymph nodes

Differential Diagnosis

- Solitary:
  - Cyst
  - Thyroid Adenoma (Benign Tumour - "Hot" or "Cold")
  - Thyroid Carcinoma
    - Papillary
    - Follicular
    - Medullary
    - Anaplastic
  - Lymphoma
  - Thyroglossal Duct Cyst
  - Reidel's Struma
- Multiple - Multinodular Goiter

Classification

Benign

- Macrofollicular adenoma (simple colloid) - Benign, but may share features of follicular carcinoma
- Microfollicular adenoma (fetal) - 5% malignant
- Colloid Nodule - most common, no increased risk of malignancy
Inflammatory

- Subacute thyroiditis

Carcinoma

- Usually presents with a solitary palpable nodule
- Types:
  - Papillary (75%)
  - Follicular (10%)
  - Medullary (5-10%)
  - Anaplastic (5%)

Diagnostic Algorithm

- **1st Thing: Is TSH suppressed?**
  - If Low --> Thyroid Scan and Radioactive Iodine Uptake
  - If Not Low --> Thyroid Ultrasound +/- FNA
    - If FNA = Benign --> continue regular F/U
    - If FNA = Insufficient --> Repeat FNA (US guidance)
    - If FNA = Follicular neoplasm or malignant --> Call Surgeon

- **Thyroid Antibody Levels** appropriate in pts with multinodular goitres or autoimmune suspected
- **Calcitonin** Measurement **NOT recommended** (fused to follow disease activity in medullary thyroid cancer)
  - Used to follow disease activity in medullary thyroid cancer.
  - MEN2 or related disorders.
- **Serum Thyroglobulin level**
  - Primary tumor marker with well differentiated thyroid cancer who had thyroidectomy and RAI Ablation.

Based on the American Association of Clinical Endocrinologists (taken from AAFP website)
Diagnostic Tests

- **Ultrasound**
  - ALL patients with new thyroid nodules should undergo U/S to assess:
    - Confirm the presence
    - **Malignant Features**
      - Hypoechoic
      - Hypervascular
      - Microcalcifications
      - Irregular Border
      - Taller than Wide on sagittal view
      - Size > 3cm
    - **Benign Features**:
      - Comet Tail
      - Increased peripheral nodule vascularity
      - Hyperechoic
      - Halo present
• Pure Cyst
  ▪ Presence of additional nodules
  ▪ Lymphadenopathy.
• CT/MRI not indicated, unless suspect substernal goitre or cervical adenopathy or tracheal compression.

• **Radioactive Iodine Uptake Scan (RAI scan)**
  ◦ Useful if euthyroid, but multiple nodules - to see which nodules are concerning
  ◦ Useful if thyrotoxic (low TSH), to see if nodule is cold (risk of cancer) or hot (no risk of cancer)

• **TSH**
  ◦ Based on several studies, correlates with risk of cancer and severity.
    ▪ If TSH is low, indicating overt or subclinical hyperthyroidism, the possibility of hyperfunctioning nodule is increased and should do RAI scan.
    ▪ If TSH is normal or elevated, meets criteria for sampling, need FNA bx. + evaluate for hypothyroidism.
  ◦ Based on one study (J Clin Endocrinol Metab. 2006;91(11):4295.)
    ▪ 2.8, 3.7, 8.3, 12.3, and 29.7 percent for patients with serum TSH concentrations <0.4 mU/L, 0.4 to 0.9 mU/L, 1.0 to 1.7 mU/L, 1.8 to 5.5 mU/L, and >5.5

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<thead>
<tr>
<th>TSH</th>
<th>Risk of Thyroid Ca</th>
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<tr>
<td>&lt;0.4 mU/L</td>
<td>2.8%</td>
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<tr>
<td>0.4 mU/L</td>
<td>3.7%</td>
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<tr>
<td>0.9 mU/L</td>
<td>8.3%</td>
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<tr>
<td>1.0 mU/L</td>
<td>12.3%</td>
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<tr>
<td>1.7 mU/L</td>
<td>29.7%</td>
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• **FNA Biopsy**
  ◦ Any solid & hypoechoic nodules >1cm should be biopsied
    ▪ Or >2cm if mixed (cystic and solid)
  ◦ No biopsy necessary if: (Consider if significant risk factors!)
    ▪ Smaller than 1cm
    ▪ Not growing on annual U/S exam
    ▪ Pure Cyst
    ▪ Hot Nodule

**Pathology**

• Possibilities:
  1. Benign Nodule
  2. Malignant Nodule
  3. Non-Diagnostic Sample
  4. Nodule Suspicious For Malignancy
  5. Follicular Neoplasm
  6. Follicular Lesion of Undetermined Significance

• 5 & 6 = Increased risk --> Generally refer for surgery to excise and pathology.

**Treatment**

• **Call Surgery if:**
  ◦ Malignant Nodules
  ◦ Hypoparathyroidism
  ◦ Recurrent Laryngeal nerve paresis
  ◦ >4cm & ass'd worrisome findings (cervical lymphadenopathy, hoarseness, external radiation, lab findings).
• **Benign Nodules**
Monitor with periodic neck exams & ultrasound (q6-18mo)
- Repeat FNA biopsy recommended if grown in interval (>50% by volume, or >20% in 2-dimensions, or suspicious findings)
- If stable >18mo, can change screening for q3-5y

**Multinodular Goiter**
- In iodine-sufficient areas, has both solid and partially cystic thyroid nodules.
- More common in older patients.
- Over time can grow to require treatment.
- **Dx:**
  - FNA needed to exclude cancer
- **Complications:**
  - Can impinge on esophagus and recurrent laryngeal nerve
    - --> dyspnea, stridor, cough, fullness sensation, hoarseness.
  - Some nodules can become large enough to suppress TSH and make pt thyrotoxic.
- **Tx:**
  - Thyroidectomy if causes compressive symptoms or thyrotoxic.
  - Use methimazole for thyrotoxic pts.
  - Radio-iodine 131I -> decreases size, but not first line. (useful if thyrotoxic, doesn't reliably shrink the gland).