Thyroid Nodules and Thyroid Function Test
what you need to know

By Mandy Hansen PA-C
Thyroid Nodules

- More common in women than men ~4:1
- 3-7% adults have palpable nodules
- 20%-76% adults have non-palpable thyroid nodules
- 95% of thyroid nodules are benign
- A thyroid nodule in a child is 2-4 times more likely to be cancerous.
Causes of Thyroid Nodules

- Benign goiter
- Chronic lymphocytic thyroiditis
- Cyst
- Follicular adenomas
- Subacute thyroiditis
- Differentiated thyroid carcinoma
- Poorly differentiated carcinoma
- Anaplastic carcinoma
- Thyroid lymphoma
- Metastatic tumors
- Sarcoma, teratoma, lipoma, hemangioma (rare)
Fun Fact

- Chinese merchants taught Europeans that eating sea weed cured goiter.
- Sea weed has a high iodine content, but it was not until 1812 that connection was made.

*Dr. T Balasubramanian*: Thyroid Historic perspective July 2011
How to work up a thyroid nodule?
Fig 1. Flowchart indicating a scheme for the diagnosis and management of palpable thyroid nodules. Associated Key Recommendations shown in parentheses: FNA, fine-needle aspiration; MNG, multinodular goiter; TSH, thyrotropin; US, ultrasonography.
Not all thyroid nodules are alike
History

- Family history of benign or malignant disease
- Radiation to neck
- Genetic disorders
  - MEN 2
  - Familial papillary thyroid tumors
  - Familial adenomatous polyposis or FAP
  - Cowden's disease
- Trouble swallowing
- Feeling of choking
- Hoarseness
- Trouble breathing (particularly when laying flat on back)
Increased Risk of Malignancy

- History of head and neck radiation
- Family history of medullary thyroid carcinoma, multiple endocrine neoplasia type 2, or papillary thyroid carcinoma
- Age <14 or >70 years
- Male sex
- Growing nodule firm or hard consistency
- Cervical adenopathy
- Fixed nodule
- Persistent dysphonia
- Dysphagia
- Dyspnea
Are we having fun yet?
Physical Exam

Inspection

- Have patient sitting
- Note any sign of prior surgical procedure
- Note if trachea is midline
- Have patient swallow water while look up to visualize thyroid moving, note any nodules
- Note patients voice in response to questions
Palpation

- Can go from anterior approach or posterior approach
  - Posterior
    - Locate the cricoid cartilage and the suprasternal notch
    - Move hands just laterally to feel under the SCM for the thyroid
    - Ask the patient to swallow a sip of water to feel the gland move up and down
    - Feel for enlarged lymph nodes
    - Appreciate the inferior border: note texture, mobility, tenderness, and presence of a nodule
  - Thyroid nodules generally have to be $\geq 1$ cm to appreciate
  - Physical exam detects about 10% of thyroid nodules
  - Risk of cancer is similar in solitary nodule versus multinodular goiter (MNG)
Thyroid exam video

- [http://www.youtube.com/watch?v=krXoyP5j5lk](http://www.youtube.com/watch?v=krXoyP5j5lk)
- (2:10 to 4:00)
Basic tests to order

- **Thyroid function test**
  - TSH, Free T4
    - Low TSH is associated with decreased probability of malignancy
  - Calcitonin is not a routine lab
    - Check if patient has a history of or suspicious family history of MEN or MTC.
    - Can be elevated in patients with pulmonary or pancreatic endocrine tumors, kidney failure, autoimmune disease of thyroid, or if using a PPI.
    - Can also be elevated with alcohol consumption, smoking, and sepsis

- **Imaging**
  - U/S with biopsy if indicated
Ultra Sound

- It is the most image sensitive test
- All patients with palpable thyroid nodules or multinodular goiter (MNG) should have an U/S.
- 50% of thyroid glands with a palpable nodule have additional nodules found on U/S
- Nodules that is >1cm or has suspicious features should be biopsied
- Risk that a single nodule is cancerous = ~4-5%
U/S Report & When to biopsy

- Two or more suspicious characteristics greatly increase risk of thyroid cancer

**Suspicious Characteristics:**
- Hypoechogeticity
- Microcalcifications
- Irregular nodule margins*
- Blurred margins*
- Increased blood flow
- Evidence of tumor invasion*
- Regional lymph node metastases*
- More tall than wide

*very suspicious
Fig. 2. Strength of indication for fine-needle aspiration (FNA) biopsy of thyroid nodules on the basis of ultrasonography (US) findings.
U/S guided FNA

- http://www.youtube.com/watch?v=E3urLT-q4m4
  (2:55-3:19)
Colloid nodule: has abundant watery and or inspissated colloid. Risk of malignancy < 1%

Indeterminant lesion, favor benign: some institutions would categorize this as benign with a note that specimen was suboptimal. Risk of malignancy 5-10%

Follicular Lesion: cellular specimen without nuclear or cellular atypia that would be suspicious for follicular neoplasm. Risk of malignancy <10%
Pathology Report cont.

- **Follicular Neoplasm**: cellular specimen with predominant microfollicular pattern with minimal to no colloid, or shows unusual findings such as trabecular pattern or mitotic figures or necrosis. Risk of malignancy 30%

- **Hurthle Cell Neoplasm**: cellular specimen exclusively composed of Hurthle cells with little colloid. Risk of malignancy 15-45%

- **Suspicious for malignancy**: specimen is just short of a malignant call. Risk of malignancy 60-75%

- **Malignant Neoplasm**: Risk of malignancy 97-99%
Incidentally found thyroid nodules on:

- CT or MRI: thyroid nodules found have uncertain risk of malignancy
  - Should have U/S preformed
- PET: when found have a higher risk of malignancy
  - Should have U/S and FNA
- Nodules found by sestamibi scans have a higher risk of malignancy
  - Should have and U/S

U/S is the answer!!!
What’s Next?
Fig 1. Flowchart indicating a scheme for the diagnosis and management of palpable thyroid nodules. Associated Key Recommendations shown in parentheses. FNA, fine-needle aspiration; MNG, multinodular goiter; TSH, thyrotropin; US, ultrasonography.
Indications for Surgery

- Cancer or suspicion of cancer
- Compression symptoms
  - Hoarseness
  - Choking sensation
  - Trouble swallowing
  - Shortness of breath when supine
- Feeling of tightness around neck
- Others become a discussion
  - Progressive enlargement of thyroid nodule
  - Failure of medical management of hyperthyroidism
  - Nodule >3-4cm
Surgery

- Cancer or goiter → total thyroidectomy
  - Surgery ~2 hour
  - Will stay over night in the hospital
  - About 2 weeks for recovery
  - Urgency depends on type of thyroid cancer
- If not cancerous and is reasonable do thyroid lobectomy
  - Benefits
    - Less likely to need thyroid hormone replacement afterwards
    - 1 ½ hours
    - Only on one side (vocal cords and parathyroid glands)
    - Shorter recovery (slightly)
  - Risk
    - Voice nerve
    - Parathyroid glands
The surgical pathology shows cancer—what now?
Thyroid Cancer

- One of the more common types of cancer
- Peak incidences of thyroid cancer for women: 40-44yo, men: 65-69yo
- Has increased faster than that of any other malignancy
- 25-year mortality if <40 y/o with papillary cancers < 2% after surgical therapy

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Estimated New Cases</th>
<th>Estimated Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder</td>
<td>72,570</td>
<td>15,210</td>
</tr>
<tr>
<td>Breast (Female – Male)</td>
<td>232,340 – 2,240</td>
<td>39,620 – 410</td>
</tr>
<tr>
<td>Colon and Rectal (Combined)</td>
<td>142,820</td>
<td>50,830</td>
</tr>
<tr>
<td>Endometrial</td>
<td>49,560</td>
<td>8,190</td>
</tr>
<tr>
<td>Kidney (Renal Cell) Cancer</td>
<td>59,938</td>
<td>12,586</td>
</tr>
<tr>
<td>Leukemia (All Types)</td>
<td>48,610</td>
<td>23,720</td>
</tr>
<tr>
<td>Lung (Including Bronchus)</td>
<td>228,190</td>
<td>159,480</td>
</tr>
<tr>
<td>Melanoma</td>
<td>76,690</td>
<td>9,480</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>69,740</td>
<td>19,020</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>45,220</td>
<td>38,460</td>
</tr>
<tr>
<td>Prostate</td>
<td>238,590</td>
<td>29,720</td>
</tr>
<tr>
<td>Thyroid</td>
<td>60,220</td>
<td>1,850</td>
</tr>
</tbody>
</table>

From American Cancer Society
Differentiated Thyroid Cancer (DTC)
- Arise from the follicular cells
- ~60,000 new cases each year in the US (about .02% of population)
- Women > Men (by 3x)
- Peak around age 35-50
Differentiated Thyroid Cancer (DTC)

- **Papillary Thyroid Cancer**
  - Most common type of thyroid cancer (79% of all thyroid cancers)
  - 10 year survival rate nearly ~95%
  - Typically slow growing and predictable, can remain in thyroid gland and regional lymph nodes for years

- **Follicular Thyroid Cancer**
  - About 13% of all thyroid cancers
  - Slightly more aggressive than papillary thyroid cancer
  - 5 year survival rate nearly 100%

- **Hurthle Cell Thyroid Cancer**
  - Sometimes it is put in a sub-category under Follicular thyroid cancer
  - About 4% of all thyroid cancers
  - Radioactive iodine does not work as well in these cancers
Medullary Thyroid Cancer
- 4% of all thyroid cancers
- CEA and Calcitonin are useful tumor markers
- More aggressive than differentiated thyroid cancers
- 20-25% are familial
- 10 year survival rate 50-80% (tightly linked to early detection)

Anaplastic Thyroid Cancer
- 2% of all thyroid cancers
- Often hallmarked by sudden enlargement of goiter
- Resistant to therapy
- Median survival 3-6 months (5yr survival 7%)

Radio Active Iodine (RAI) does not work with the above cancers.
## Survival Rates

### Papillary Thyroid Cancer

<table>
<thead>
<tr>
<th>Stage</th>
<th>5-Year Relative Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>near 100%</td>
</tr>
<tr>
<td>II</td>
<td>near 100%</td>
</tr>
<tr>
<td>III</td>
<td>93%</td>
</tr>
<tr>
<td>IV</td>
<td>51%</td>
</tr>
</tbody>
</table>

### Follicular Thyroid Cancer

<table>
<thead>
<tr>
<th>Stage</th>
<th>5-Year Relative Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>near 100%</td>
</tr>
<tr>
<td>II</td>
<td>near 100%</td>
</tr>
<tr>
<td>III</td>
<td>71%</td>
</tr>
<tr>
<td>IV</td>
<td>50%</td>
</tr>
</tbody>
</table>

### Medullary Thyroid Cancer

<table>
<thead>
<tr>
<th>Stage</th>
<th>5-Year Relative Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>near 100%</td>
</tr>
<tr>
<td>II</td>
<td>98%</td>
</tr>
<tr>
<td>III</td>
<td>81%</td>
</tr>
<tr>
<td>IV</td>
<td>28%</td>
</tr>
</tbody>
</table>

*Based on patients diagnosed 1985 to 1991

*Based on patients diagnosed 1998 to 1999

Numbers from AJCC Cancer Staging Manual (7th ed).
# Thyroid Carcinoma


<table>
<thead>
<tr>
<th>Table 1</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Tumor (T)</strong></td>
<td></td>
</tr>
<tr>
<td>Note: All categories may be subdivided: (A) solitary tumor, (b) multifocal tumor (the largest determines the classification).</td>
<td></td>
</tr>
<tr>
<td>TX</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor 2 cm or less in greatest dimension limited to the thyroid</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor more than 2 cm but not more than 4 cm in greatest dimension limited to the thyroid</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor more than 4 cm in greatest dimension limited to the thyroid or any tumor with minimal extrathyroid extension (e.g., extension to sternothyroid muscle or perithyroid soft tissues)</td>
</tr>
<tr>
<td>T4a</td>
<td>Tumor of any size extending beyond the thyroid capsule to invade subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve</td>
</tr>
<tr>
<td>T4b</td>
<td>Tumor invades prevertebral fascia or encases carotid artery or mediastinal vessels</td>
</tr>
<tr>
<td>All anaplastic carcinomas are considered T4 tumors.</td>
<td></td>
</tr>
<tr>
<td>T4a</td>
<td>Intrathyroidal anaplastic carcinoma—surgically resectable</td>
</tr>
<tr>
<td>T4b</td>
<td>Extrathyroidal anaplastic carcinoma—surgically unresectable</td>
</tr>
<tr>
<td><strong>Regional Lymph Nodes (N)</strong></td>
<td></td>
</tr>
<tr>
<td>Regional lymph nodes are the central compartment, lateral cervical, and upper mediastinal lymph nodes.</td>
<td></td>
</tr>
<tr>
<td>NX</td>
<td>Regional lymph nodes cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Regional lymph node metastasis</td>
</tr>
<tr>
<td>N1a</td>
<td>Metastasis to Level VI (pretracheal, paratracheal, and prelaryngeal/Delphian lymph nodes)</td>
</tr>
<tr>
<td>N1b</td>
<td>Metastasis to unilateral, bilateral, or contralateral cervical or superior mediastinal lymph nodes</td>
</tr>
<tr>
<td><strong>Distant Metastasis (M)</strong></td>
<td></td>
</tr>
<tr>
<td>MX</td>
<td>Distant metastasis cannot be assessed</td>
</tr>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis</td>
</tr>
</tbody>
</table>

**Stage grouping:** Separate stage groupings are recommended for papillary or follicular, medullary, and anaplastic (undifferentiated) carcinoma.

### Papillary or Follicular

| Under 45 Years |  |
| Stage I | Any T Any N M0 |
| Stage II | Any T Any N M1 |

### Papillary or Follicular

| 45 Years and Older |  |
| Stage I | T1 N0 M0 |
| Stage II | T2 N0 M0 |
| Stage III | T3 N0 M0 |
| Stage IV A | T4a N1a M0 |
| Stage IV B | T4b N1b M0 |

**Stage IV C** Any T Any N M1

**Anaplastic Carcinoma**

All anaplastic carcinomas are considered Stage IV

| Stage IVA | T4a Any N M0 |
| Stage IVB | T4b Any N M0 |
| Stage IVC | Any T Any N M0 |

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## Medullary Carcinoma

| Stage I | T1 N0 M0 |
| Stage II | T2 N0 M0 |
| Stage III | T3 N0 M0 |
| Stage IVA | T4a N1a M0 |

**Histopathologic Type**

There are four major histopathologic types:

- Papillary carcinoma (including follicular variant of papillary carcinoma)
- Follicular carcinoma (including Hurthle cell carcinoma)
- Medullary carcinoma
- Undifferentiated (anaplastic) carcinoma
Follow Up

- If no cancer and no surgery
  - Usually follow up in 6-18 months
  - Repeat U/S and thyroid function test (TSH, Free T4)
  - Re-biopsy if:
    - nodule significantly increased in size
    - suspicious changes occur
    - Previous biopsy was indeterminate

- If no cancer and a total thyroidectomy
  - Check TFTs in 6-8 weeks
  - Follow with PCP or Endo for TFTs as needed (at least 2x/year)

- If no cancer and lobectomy
  - Check TFT within the next 6 months
  - discuss signs of hypothyroidism.

- If DTC
  - follow up every 6 months for the next 2 years with U/S and TFTs
    (varies by path results)
Are you still awake?
Thyroid Function Tests (TFTs)
Fun Fact

What animal has a impaired thyroid homeostasis?

- Ostrich
- Sloth
- Penguin
- Dingo
Thyroid Hormone Feedback Loop

Hypothalamus

TRH

Pituitary

TSH

Thyroid

T4/T3

Thyroxine and Triiodothyronine
# Thyroid Function Test

<table>
<thead>
<tr>
<th>TSH</th>
<th>T4</th>
<th>T3</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>High</td>
<td>High</td>
<td>Hyperthyroidism</td>
</tr>
<tr>
<td>High</td>
<td>Low</td>
<td>Low</td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td>Low</td>
<td>Normal</td>
<td>Normal</td>
<td>1. Ingestion of T4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2. Less common 1’ hyperthy</td>
</tr>
</tbody>
</table>

- **TSH** (Thyroid Stimulating Hormone)
- **T4** (Thyroxine)
- **T3** (Triiodothyronine)
Thyroid Hormone Replacement

- Synthroid preferred drug
  - name brand preferred for thyroid cancer patients
  - Seems to help keep tighter control of thyroid levels
  - T4 which converts to T3 in the body

- Dosing
  - Full replacement dose---1mcg/kg-1.7mcg/kg
  - Start on the lower end and titrate up
  - Check levels every 6-8 weeks until reach desired level
  - Educate on hyper and hypothyroidism symptoms

- Considerations
  - Take on an empty stomach 1 hour before eating
  - Do not take with other medications
  - Once a day dosing
  - Some people (in few instances say they feel better on cytomel or T3 as well)
Target TSH

- TSH shows overview of levels (like HBA1c)
  - Non cancer patient goal TSH= ~1
  - Depending on stage of cancer varying recommendations on thyroid hormone suppression
    - TSH <1 but >.1
    - More aggressive TSH <.1 but >.01
We are done! Please remember...

文明没有旁观者，
个个都是践行人。

everyone is called on to practice civilized behaviors.