

**Assessment of Thyroid Nodules**  
**(AACE.com for Guidelines)**  
**March, 2007**

**Prevalence:** palpable 3-7% (6.4% of women and 1.5% of men); ultrasound ~50%  
More common in elderly and those with iodine deficiency or radiation exposure;  
~5% of evaluated nodules are diagnosed as malignant

**Symptoms:** infrequent - dysphagia, dysphonia, pressure, pain, or hyperthyroidism

- 1) No clear relationship between nodule histologic features or size and symptoms
- 2) Most symptoms turn out **not** to be caused by the thyroid nodule(s)
- 3) Sudden pain is commonly due to hemorrhage into a cystic nodule
- 4) Rapid enlargement of a nodule can be anaplastic carcinoma or primary lymphoma

**Clinical Features:**

- 1) Firm or hard, solitary or dominant thyroid nodule that clearly differs from the rest of the gland
- 2) Solitary nodules are **not** significantly more likely to be cancer than nodules in MNGs
- 3) Small differentiated thyroid cancers are frequently **devoid** of alarming clinical characteristics

**Family History:** Familial medullary thyroid carcinoma (MTC), MEN-2, familial papillary thyroid tumors, familial polyposis coli, Cowden disease, and Gardner's syndrome

**Summary - Symptoms or Signs That Warrant Further Investigation:**

- Prior head and neck irradiation
- Family history of MTC or MEN2
- Age <20 years or >70 years
- Male sex
- Growing nodule or nodule >10 mm
- Firm or hard consistency of nodule; ill-defined nodule margins on palpation
- Cervical adenopathy
- Fixed nodule on examination
- Dysphonia, dysphagia, and cough

**Ultrasound** is the first step in diagnosis: (Cancer is **not less common** in nodules <10 mm)

- 1) Microcalcifications: small intra-nodular punctate hyper-echoic spots with scanty posterior acoustic shadowing (Specificity for cancer: 85-95%) (Sensitivity: 30-60%)
- 2) Irregular or micro-lobulated margins (Spec: 83.0% to 85.0%) (Sens: 55-75%)
- 3) Hypervascularity & chaotic arrangement of intra-nodular vascular images (Spec: 81%) (Sens: 74%)  
(i.e. arteriovenous shunts and tortuosity of vessel course)
- 4) Degenerative changes and multiple fluid areas
- 5) Extracapsular growth: Extension of irregular hypo-echoic lesions beyond the thyroid capsule  
(Invasion of pre-thyroid muscles, posterior extra-capsular growth, or infiltration of the recurrent laryngeal nerve demand immediate cytologic assessment)
- 6) Complex or Cystic Lesions: Most complex thyroid nodules with a dominant fluid component are benign. However, US-FNA should be done because papillary carcinomas can rarely be cystic.
- 7) Suspicious Cervical Adenopathy: Enlarged rounded lymph nodes with no hilum, but with cystic changes, micro-calcifications, or chaotic hypervascularity are always biopsied.

Hypo-echoic appearance (a decreased echogenicity in comparison with the surrounding parenchyma, similar to that of the cervical strap muscles) **+ one of the first 3 US findings** above indicates a subset of **non-palpable** thyroid nodules that are high risk for cancer

Additional suspicious criteria:

- 1) Rounded appearance
  - 2) “More tall (anteroposterior) than wide (transverse)” shape of the nodule
  - 3) “Marked hypo-echogenicity” of a solid lesion (hypo-echoic compared to the cervical muscles)
- The presence of 2 suspicious criteria reliably identifies most neoplastic lesions (~90% of cases)

**It is generally possible to restrict the number of US-FNA procedures to about a third of the impalpable thyroid nodules.**

### **Summary: Recommendations for the Evaluation of Thyroid Nodules**

1) Ultrasound evaluation:

**Not recommended** (*grade C*):

- a) As screening test in the general population or
- b) In patients with normal thyroid on palpation and low risk for thyroid cancer

**Recommended** (*grade C*):

- a) For high-risk patients (familial thyroid cancer, MEN2, or external irradiation)
- b) For all patients with palpable thyroid nodules or MNG
- c) For those with adenopathy suggestive of a malignant lesion

2) Ultrasound reporting criteria (*grade C*):

- a) Describe position, shape, size, margins, content, echogenic pattern, and the vascular pattern
- b) Identify the nodule at risk to be malignant, and stratify the nodule with an US risk score
- c) Identify the nodules for FNA biopsy

3) No US-FNA: Nodules <10 mm without suspicious US findings or high-risk history (*grade C*)

4) Recommend US-FNA:

- a) Any nodule with a history of neck irradiation or family history of MTC or MEN2 (*grade C*)
- b) All hypoechoic nodules  $\geq 10$  mm with irregular margins, chaotic intra-nodular vascular spots, a more-tall-than-wide shape, or micro-calcifications (*grade B*)
- c) Extra-capsular growth or abnormal cervical nodes no matter the size of the lesions (*grade B*)
- d) Complex thyroid nodules (sample the solid component before fluid drainage) (*grade C*)

5) Thyroid Incidentalomas:

Repeat US in 6-12 months and “regularly” thereafter (*grade D*)

6) MRI and CT are not indicated in routine nodule evaluation (*grade C*)

7) Radioisotope Scan:

Useful if the TSH level is low (i.e. to evaluate hyperthyroidism)  
Hot or “warm” nodules almost never cancer

Causes of Thyroid Nodules
<i>Benign</i>
Multinodular goiter
Hashimoto’s thyroiditis
Simple or hemorrhagic cysts
Follicular adenomas
Subacute thyroiditis
<i>Malignant</i>
Papillary carcinoma
Follicular carcinoma
Hürthle cell carcinoma
Medullary carcinoma
Anaplastic carcinoma
Primary thyroid lymphoma
Metastatic malignant lesion

## Thyroid Nodules

### Questions:

- 1) A 25 year old, previously healthy woman reports that her mother has been diagnosed with “thyroid disease”. Which of the following should you do and in what order:
  - a) Lab: TSH and free T4
  - b) Thyroid ultrasound
  - c) Palpate her neck along with your usual physical exam
  - d) Thyroid scan and uptake
  - e) Neck CT
  - f) Thyroid biopsy
  - g) Take a complete thyroid history
  
- 2) A 71 year old man reports that he has felt a lump in his neck and you discover a 1.5 cm thyroid nodule in a “lumpy” gland. There are no enlarged nodes. Which of the following should you do and in what order:
  - a) Lab: TSH and free T4
  - b) Thyroid ultrasound
  - c) MRI
  - d) Thyroid scan and uptake
  - e) Neck CT
  - f) Thyroid biopsy
  - g) Take a complete thyroid history
  
- 3) A 45 year old woman presents with tachycardia, diaphoresis, and nervousness for the preceding 3-4 months. She has a large multi-nodular goiter and sinus tachycardia. Which of the following should you do and in what order:
  - a) Lab: TSH and free T4
  - b) Thyroid ultrasound
  - c) Radioactive iodine ablation
  - d) Thyroid scan and uptake
  - e) Neck CT
  - f) Thyroid biopsy
  - g) Take a complete thyroid history

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- d) Thyroid scan and uptake
- e) Neck CT
- f) Thyroid biopsy
- g) Take a complete thyroid history

ANSWER: g, c, then maybe a

(‘a’ is optional unless the patient shows signs or symptoms of hyper- or hypothyroidism – you should have a low threshold for obtaining thyroid studies)

No imaging is recommended unless you palpate a nodule. Exceptions: the mother has been diagnosed with MEN-2, FTC, etc., or the patient has been exposed to neck irradiation.

2) A 71 year old man reports that he has felt a lump in his neck and you discover a 1.5 cm thyroid nodule in a “lumpy” gland. There are no enlarged nodes. Which of the following should you do and in what order:

- a) Lab: TSH and free T4
- b) Thyroid ultrasound
- c) MRI
- d) Thyroid scan and uptake
- e) Neck CT
- f) Thyroid biopsy
- g) Take a complete thyroid history

ANSWER: g, a, b

Almost all thyroid nodules  $\geq 10$  mm should be biopsied unless the patient has a short life expectancy. If the patient is hyperthyroid, you can consider a thyroid scan before

3) A 45 year old woman presents with tachycardia, diaphoresis, and nervousness for the preceding 3-4 months. She has a large multi-nodular goiter and sinus tachycardia. Which of the following should you do and in what order:

- a) Lab: TSH and free T4
- b) Thyroid ultrasound
- c) Radioactive iodine ablation
- d) Thyroid scan and uptake
- e) Neck CT
- f) Thyroid biopsy
- g) Take a complete thyroid history

ANSWER: g, a, d; maybe f; followed by c

Hyperthyroidism should be confirmed by lab and RAI uptake; it is likely that the patient has one or more hot nodules which should be ablated if found; however, if there is a cold nodule  $\geq 10$  mm, it should be biopsied BEFORE ablation.

## Management of Papillary and Follicular Thyroid Cancer February, 2007

**FNA:** Malignant → >95% malign (one-stage surgery if patient agrees; 1 in 20 chance → **benign**)  
Indeterminate or Follicular (hyperplastic, adenomas, carcinomas) → **10-20% malignant**  
(2 stage surgery if low risk, 1 stage if high risk; discuss options with patient)  
Benign → **1-2% malignant** (no surgery)

Intra-operative frozen section evaluation is **not** helpful following FNA.

**Note:** 40 year mortality: 10% overall, 30% if tumor clinically evident

Check TSI if there is a positive history of hyperthyroidism or suspicion of Graves D

(TSI stimulates growth of cancer and increases the risk of hyperthyroidism during therapy)

**Criteria for Cancers w/Low Risk for Recurrence** (~80% of differentiated thyroid cancers are low risk)

Basis: Age (<40), female, size (<1, 1-4, >4cm), uni-centric,

No capsule & vascular invasion, positive nodes, or mets

Not Hurthle cell; not papillary tall cell or columnar cells

### **Protocol for Low Risk Cancers:**

- 1) Near-total thyroidectomy (papillary: add nodal dissection); no replacement until after RAI ablation
- 2) When TSH >30, check thyroglobulin (Tg) → ~100-150 mCi to ablate remnant, WBS 4-7 days later  
If TSH does not increase to >30, then use rhTSH to stimulate thyroid tissue  
(100 mCi required for 100% ablation of normal tissue)
- 3) After RAI, start T4 and maintain TSH 0.1-0.4
- 4) At 12 months: check unstimulated Tg (Tg not useful if anti-Tg antibodies are present)
  - a) If Tg undetectable (<2.0), repeat annually
  - b) If Tg is detected → options:
    - i) Repeat in 6 months (consider just monitoring if Tg 2 → 10)
    - ii) Stimulate Tg: switch T4 to T3 for 2 weeks and then stop T3 for 1 week  
When TSH >30, check Tg and “whole body scan” (WBS)  
Consider repeat ablation if scan positive (<sup>131</sup>I → 100+ mCi)  
Consider neck ultrasound if scan negative

### **Protocol for High Risk Cancers:**

- 1) Near-total thyroidectomy (papillary: add nodal dissection); no replacement until after RAI ablation
- 2) When TSH >30, check thyroglobulin (Tg) → ~100-150 mCi to ablate remnant, WBS 4-7 days later  
If TSH does not increase to >30, then use rhTSH to stimulate thyroid tissue  
(100 mCi required for 100% ablation of normal tissue)
- 3) After RAI, start T4 and maintain TSH at detectible level but <0.1
- 4) At 12 months and possibly at 3 or 5 yrs: check stimulated Tg
  - a) If Tg undetectable (<2.0), repeat unstimulated Tg annually
  - b) If Tg is detected → options
    - i) Stimulated WBS
    - ii) Neck ultrasound
    - iii) CT chest (best for lung mets)
    - iv) PET scan (best for neck mets, although ultrasound also good)
    - v) X-rays (lytic lesions) → femur, pelvis, sternum, skull, and vertebrae
    - vi) Consider surgery or external radiation for isolated mets if no iodine uptake

Use of Recombinant Human TSH (rhTSH):

- 1) Requires accurate Tg to equal sensitivity of Thyroxin withdrawal
- 2) Requires a larger dose of  $^{131}\text{I}$  because patient is euthyroid
- 3) Does work following an Iodine load
- 4) Give two doses on consecutive days (~\$1,400)