Thyroid Nodules & Cancer: New Concepts

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Past President, American Association of Clinical Endocrinologists
Disclosure & Thanks

• Nothing to disclose
• My sincere thanks for the invitation to be with you today
• This presentation is based on new evidence & recent guidelines
Objectives

Thyroid nodule
- Predictors of malignancy
- FNA results
- Management of FN
- Follow-up of benign nodule
- MNG

Thyroid ca
- Incidence & prevalence
- Initial evaluation & Tx
- RRA
- Follow-up
Thyroid Nodule Facts

- Prevalence 5% by palpation, 30-50% by US, with almost 100 million people in U.S.
- 350,000 new nodules will be diagnosed this year
- More common in women & elderly, with I-def, and after radiation
- 95% are benign
Thyroid Nodule

Case 29-year-old woman is referred for a recently discovered thyroid nodule; she is asymptomatic and has no history of radiation; thyroid palpation shows a solitary, firm 2x2 cm left lobe nodule; serum TSH is 1.3 mIU/L

What is the next appropriate test?

A. FNA biopsy
B. US exam
C. Radioisotope scan
D. A trial with T4 and TSH suppression
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Q What is the next appropriate test?

A. FNA biopsy
B. US exam
C. Radioisotope scan
D. A trial with T4 and TSH suppression
29-Year-Old Women

Recommendation

Thyroid sonography should be performed in all pt with known thyroid nodules

Endocr Pract, 2010
29-Year-Old Woman

Which of the following is not a predictor of malignancy in this patient’s thyroid nodule?

A. History of childhood head-neck radiation
B. Serum TSH level
C. Serum calcitonin (CT) level
D. Nodule size and number
29-Year-Old Woman

Q Which of the following is not a predictor of malignancy in this patient’s thyroid nodule?

A. History of childhood head-neck radiation
B. Serum TSH level
C. Serum calcitonin (CT) level
D. Nodule size and number
Evidence: Radiation & Thyroid Cancer

- Radiation before age 15
- $\geq 10$ rads
- CA may develop 30-40 yr after exposure
- Main cause is EBR or radioactive fall out
- Most common ca is PTC

Nat Clin Pract 1:82, 2006
Evidence: Serum TSH & Cancer

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>TSH (mIU/L)</th>
<th>Malignancy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>0.3</td>
<td>8.1</td>
</tr>
<tr>
<td>40</td>
<td>0.5</td>
<td>8.4</td>
</tr>
<tr>
<td>40</td>
<td>1.0</td>
<td>9.4</td>
</tr>
<tr>
<td>40</td>
<td>3.0</td>
<td>14.6</td>
</tr>
<tr>
<td>40</td>
<td>5.0</td>
<td>21.9</td>
</tr>
<tr>
<td>40</td>
<td>6.0</td>
<td>26.4</td>
</tr>
</tbody>
</table>

Boelaert K et al: JCEM, 2006

Evidence: Nodule Size & Cancer

402 pt
Non-palpable nodules

US-FNA

Nodule 10 mm 9.1%
Malignant
Nodule >10 mm 7.0%

Papini et al: JCEM, 2002
## Evidence: Nodule Number & Cancer

<table>
<thead>
<tr>
<th>Study (yr, location)</th>
<th>Individuals (no.)</th>
<th>Definition of nodularity</th>
<th>FNA technique</th>
<th>Cancer rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>McCall et al (1986 U.S.)</td>
<td>442</td>
<td>Scan/Hx</td>
<td>Palpation</td>
<td>17, 13</td>
</tr>
<tr>
<td>Sachmechi et al (2000 U.S.)</td>
<td>443</td>
<td>Scan</td>
<td>Palpation</td>
<td>8, 10</td>
</tr>
<tr>
<td>Papini et al (2002 Italy)</td>
<td>494</td>
<td>US</td>
<td>US</td>
<td>9, 6</td>
</tr>
<tr>
<td>Deandrea et al (2002 Italy)</td>
<td>420</td>
<td>US</td>
<td>US</td>
<td>6, 7</td>
</tr>
</tbody>
</table>
Serum CT Measurement

A number of reports show that routine CT measurement in pt with thyroid nodules leads to detection of unsuspected, early MTC. With regards to CT screen, which is not correct

A. It may detect small MTC, potentially curable by thyroidectomy
B. Unstimulated basal CT level of 100 ng/dL is highly suggestive of MTC
C. Unavailability of pentagastrin in U.S. severely limits utility of CT screen
D. Routine CT screen is not a cost-effective practice
Serum CT Measurement

A number of reports show that routine CT measurement in pt with thyroid nodules leads to detection of unsuspected, early MTC. With regards to CT screen, which is not correct

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B. Unstimulated basal CT level of 100 ng/dL is highly suggestive of MTC

C. Unavailability of pentagastrin in U.S. severely limits utility of CT screen

D. Routine CT screen is not a cost-effective practice
# Evidence: CT Screening

<table>
<thead>
<tr>
<th>Author, yr</th>
<th>Country</th>
<th>Pt (no.)</th>
<th>Tx (no.)</th>
<th>MTC No.</th>
<th>MTC %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pacini, 1994</td>
<td>Italy</td>
<td>1,385</td>
<td>52</td>
<td>8</td>
<td>0.6</td>
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<tr>
<td>Rieu, 1995</td>
<td>France</td>
<td>697</td>
<td>15</td>
<td>4</td>
<td>0.8</td>
</tr>
<tr>
<td>Vierhapper, 1997</td>
<td>Austria</td>
<td>1,062</td>
<td>213</td>
<td>6</td>
<td>0.6</td>
</tr>
<tr>
<td>Niccoll, 1997</td>
<td>France</td>
<td>1,167</td>
<td>1,167</td>
<td>18</td>
<td>1.4</td>
</tr>
<tr>
<td>Ham, 2001</td>
<td>Korea</td>
<td>1,448</td>
<td>?</td>
<td>10</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Conclusions: Routine serum calcitonin screening in patients undergoing evaluation for thyroid nodules appears to be cost effective in the United States, with C/E comparable to the measurement of thyroid stimulating hormone, colonoscopy, and mammography screening.
CT Screening

Recommendation

• AACE: Measurement of nonstimulated CT level is a useful test in the initial evaluation of thyroid nodules
  \[\text{Endocr Pract, 2010}\]

• ATA: No recommendation for or against routine measurement of serum CT
  \[\text{Thyroid, 2009}\]
29-Year-Old Woman

Case
Thyroid US showed a solitary, 2.0 x 1.5 x 1.5 cm solid, hypoechoic nodule; US-guided FNA showed a benign, colloid nodule

Which is the appropriate follow-up plan for this pt?

A. No follow-up necessary for this benign nodule
B. Repeat TSH & US in 6-18 mo
C. Repeat TSH, US & FNA in 6-18 mo
D. Begin T4 suppression therapy and repeat TSH & US in 6-18 mo
29-Year-Old Woman

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Follow-Up of Benign Thyroid Nodule

Recommendation

- Benign nodules should be followed by palpations, repeat US & TSH in 6-18 mo
- Routine T4 Rx is not recommended
- Repeat US-FNA if $\geq 50\%$ increase in nodule volume demonstrated

Endocr Pract, 2010
US Examination

Which of the following sonographic features is not suggestive of malignancy?

A. Irregular nodule borders
B. Increased, chaotic vascular flow
C. Microcalcifications
D. Tall > wide dimensions
E. Eggshell calcifications
US Examination

Q Which of the following sonographic features is not suggestive of malignancy?

A. Irregular nodule borders
B. Increased, chaotic vascular flow
C. Microcalcifications
D. Tall > wide dimensions
E. Eggshell calcifications
50-year-old woman is seen because of a right neck mass discovered on self-exam; there is no prior Hx neck radiation; on exam, a firm 2.0 cm right thyroid nodule is palpable; TSH is 2.0 mIU/L; US showed a predominantly solid, hypervascular 2.0 x 2.0 x 1.8 cm nodule; left OK

FNA showed hypercellularity, no colloid and microfollicles consistent with follicular neoplasm (FN)

What should you order next?
A. Repeat FNA with US guidance
B. Obtain BRAF marker
C. Order a thyroid $^{123}$I scan
D. Surgical consultation
Thyroid Nodule

Case

50-year-old woman is seen because of a right neck mass discovered on self-exam; there is no prior Hx neck radiation; on exam, a firm 2.0 cm right thyroid nodule is palpable; TSH is 2.0 mIU/L; US showed a predominantly solid, hypervascular 2.0 x 2.0 x 1.8 cm nodule; left OK

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What should you order next?

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B. Obtain BRAF marker
C. Order a thyroid $^{123}\text{I}$ scan
D. Surgical consultation
Follicular Neoplasm

Recommendation

Follicular or Hürthle cell neoplasm has a risk of malignancy 15-25% and should be removed

NCI Thyroid FNA State of the Science Conf:
Diagn Cytopathol, 2008
50-Year-Old Woman

What is the optimal surgical treatment of this pt?

A. Ipsilateral lobectomy
B. Total thyroidectomy
C. Lobectomy followed by completion Tx if cancer found
D. Lobectomy, intraoperative frozen section, and more surgery based on FS report
50-Year-Old Woman

What is the optimal surgical treatment of this pt?

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B. Total thyroidectomy
C. Lobectomy followed by completion Tx if cancer found
D. Lobectomy, intraoperative frozen section, and more surgery based on FS report
Match FNA Diagnosis with Reported Malignancy Risk on Cytologic Exam

Malignancy risk

1. <3%
2. 99%
3. 20-30%
4. <1%

Answers

A. 4
B. 3
C. 2
D. 1
Large MNG

With arms raised pt had facial congestion and reported pain – this represents

A. Jod-Basedow phenomenon
B. Plummer’s sign
C. Pemberton’s sign
D. Sister Mary Joseph sign
With arms raised pt had facial congestion and reported pain – this represents

A. Jod-Basedow phenomenon
B. Plummer’s sign
C. Pemberton’s sign
D. Sister Mary Joseph sign
Multinodular Goiter (MNG)

Case

64-year-old woman with a long Hx of a goiter reports increasing neck pressure, DOE and recent sleep apnea; 2 previous FNAs were benign.

Exam shows a euthyroid woman with a moderately enlarged diffuse goiter; serum TSH is 0.2; FT4 1.6; chest x-ray shows marked tracheal deviation; chest CT with contrast demonstrates a huge goiter.
Case: Radioiodine uptake (RAIU) was 8% at 24 hr (n=15-28%).

Q: With regards to the management of this pt’s large goiter, which is correct?

A. T4 suppressive Rx is both safe & effective
B. Data show that most MNGs remain stable in size & function
C. Either surgical thyroidectomy or $^{131}$I after rhTSH is effective in improving symptoms
D. Follow-up without Rx seems reasonable
64-Year-Old Woman with MNG

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Evidence: Natural History of MNG

Goiter and Age

<table>
<thead>
<tr>
<th>Age at presentation</th>
<th>n=</th>
<th>Mean thyroid volume (SE) (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>14</td>
<td>40</td>
</tr>
<tr>
<td>31-40</td>
<td>34</td>
<td>80</td>
</tr>
<tr>
<td>41-50</td>
<td>26</td>
<td>120</td>
</tr>
<tr>
<td>51-60</td>
<td>18</td>
<td>160</td>
</tr>
<tr>
<td>&gt;60</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>

Goiter and Duration

<table>
<thead>
<tr>
<th>Duration of goiter (years)</th>
<th>n=</th>
<th>Mean thyroid volume (SE) (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>36</td>
<td>0</td>
</tr>
<tr>
<td>31-40</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td>41-50</td>
<td>15</td>
<td>80</td>
</tr>
<tr>
<td>51-60</td>
<td>17</td>
<td>120</td>
</tr>
<tr>
<td>&gt;60</td>
<td>14</td>
<td>160</td>
</tr>
</tbody>
</table>

Goiter Size and TSH

Evidence: Results of $^{131}$I Rx in MNG

Nygaard B et al: BMJ, 1993
Bonnema SJ et al: JCEM, 1999
Effect of 0.1 mg rhTSH on 24-Hour RAIU
Comparison of the 24, 48 and 72-Hour Interval

Mean relative \( \uparrow \) in 24 hr RIAU (%)

- 24 hr: 111%, \( P=0.027 \)
- 48 hr: 83%, \( P=0.30 \)
- 72 hr: 62%, \( P=0.50 \)

Increased Goiter Volume Reduction with rhTSH Augmented $^{131}$I Therapy


Bonnema et al: JCEM, 2007

Relative mean goiter volume (%)

- Goiter <100 mL
  - Conventional $^{131}$I at 1 year: Gain 35%
  - +0.3 mg rhTSH at 1 year: Gain 56%
  - P=0.002

- Goiter >100 mL
  - Conventional $^{131}$I at 1 year: Gain
  - +0.3 mg rhTSH at 1 year: Gain
  - P<0.001
How Do You Manage a 52-Year-Old Woman with a 50-80 gm Asymptomatic Nontoxic MNG?

<table>
<thead>
<tr>
<th>Rx</th>
<th>LATS (%)</th>
<th>ATA (%)</th>
<th>ETA (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Rx</td>
<td>39</td>
<td>36</td>
<td>28</td>
</tr>
<tr>
<td>T4</td>
<td>21</td>
<td>56</td>
<td>52</td>
</tr>
<tr>
<td>( ^{131}\text{I} )</td>
<td>7</td>
<td>1.4</td>
<td>5.8</td>
</tr>
<tr>
<td>Surgery</td>
<td>28</td>
<td>6.4</td>
<td>10</td>
</tr>
</tbody>
</table>

JECM 90:117, 2005
 Thyroid Cancer Facts

• Fastest growing ca in U.S.; increased 3.8% per year 1992-2001
• 8th most common ca in women
• 44,000 new cases this year; prevalence 350,000
• PTC is the commonest cause of death (50%) due to thyroid ca
Thyroid Cancer

Relative Frequency

- Follicular: 9%
- Medullary: 4%
- Hürthle: 1%
- Anaplastic: 1%

National Cancer Database: SEER Registry
Thyroid Cancer Incidence 1973-2002

Papillary Thyroid Cancer 1988-2002

Thyroid Cancer Incidence and Mortality 1973-2002

Davies L and Welch HJ: JAMA 295:2164, 2006
Papillary Thyroid Cancer (PTC)

- Most common endocrine malignancy
- 80% of new cases worldwide
- F:M 2:1, mean age at Dx 30-40 year

Typical Case
Typical Presentation of PTC & FTC

- Painless mass
- Discovered on routine exam or by pt
- Stable over several mo
- Normal thyroid function
- Diagnosed by FNA (PTC) or suspicious (FTC)
Papillary Thyroid Carcinoma (PTC)

Case  28-year-old woman is found to have a 1.5 cm right thyroid nodule on routine pre-pregnancy examination; FNA biopsy showed nuclear changes suspicious for PTC; serum TSH is 0.8 mIU/L

Q  What additional preop test should you order?

A. Serum thyroglobulin (Tg)
B. Radioisotope scan
C. Thyroid US
D. Neck CT with contrast
Papillary Thyroid Carcinoma (PTC)

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B. Radioisotope scan
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D. Neck CT with contrast
28-Year-Old Women with PTC

Recommendations

Preop neck US for the contralateral lobe and cervical (central & lateral neck compartments) lymph nodes is recommended for all pt undergoing Tx for a malignant FNA

Thyroid, 2009
28-Year-Old Woman with PTC

Case
Thyroid US showed a 1.4 x 1.0 x 1.0 cm solid right nodule with microcalcifications; the left lobe appeared normal and no adenopathy was identified.

What is the surgical procedure of choice in the case?

A. Right lobectomy
B. Near-total or total Tx only
C. TTx plus central compartment (level VI) dissection
D. Either B or C
28-Year-Old Woman with PTC

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What is the surgical procedure of choice in the case?

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C. TTx plus central compartment (level VI) dissection
D. Either B or C
Initial Surgery

Recommendation

• For pt with thyroid ca >1 cm, the initial surgical procedure should be a NTTx or a TTx

• Tx without CND may be appropriate for small (T1 or T2) nod-neg PTC

• Therapeutic central compartment (level VI) neck dissection with clinically involved central or lateral neck nodes should accompany TTx

Thyroid, 2009
28-Year-Old Woman with PTC

Case
Total Tx showed a 1.3 x 1.0 x 0.9 cm FV PTC; no abnormal nodes were identified at surgery

Appropriate postop care should include

A. Radioiodine remnant ablation (RRA) using 100 mCi $^{131}$I
B. RRA using 30 mCi $^{131}$I
C. No RRA; start T4 Rx with target TSH <0.01 mIU/L
D. No RRA; start T4 Rx with target TSH 0.1-1.0 mIU/L
28-Year-Old Woman with PTC

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C. No RRA; start T4 Rx with target TSH <0.01 mIU/L
D. No RRA; start T4 Rx with target TSH 0.1-1.0 mIU/L
28-Year-Old Woman with PTC

Recommendation

- RAI is not recommended for pt with unifocal ca <1 cm without higher risk features
- Maintenance of TSH at 0.1-0.5 mIU/L is appropriate for low-risk patient

Thyroid, 2009
Goals of Initial Rx

• Remove primary disease and involved lymph nodes
• Minimize morbidity
• Provide info for accurate staging
• Facilitate $^{131}$I Rx
• Minimize risk of ca recurrence
Preoperative Evaluation

- Neck US for contralateral lobe and cervical nodes
- Additional scanning not necessary
- Finding of metastatic disease rarely alters need for Tx
- Routine Tg measurement not recommended
Case

40-year-old man is referred 2 mo after a left thyroid lobectomy for a 2.0 cm follicular lesion. Pathologic exam showed the lesion to be a follicular adenoma; in addition, a 0.8 cm PTC was discovered in the resected lobe. No nodes were removed at Tx.

Serum TSH is 0.5 mIU/L on T4; Tg 2.2 ng/dL; Tg Ab neg; thyroid US shows a surgically absent L lobe, a normal R lobe, and no adenopathy

Based on current recommendations what do you suggest?

A. Observation with periodic US, TSH & Tg measurement
B. 100 mCi RAI with follow-up
C. Completion Tx, 50 mCi RAI and follow-up
D. Completion Tx, 100 mCi RAI and follow-up
**Case**

A 40-year-old man is referred 2 mo after a left thyroid lobectomy for a 2.0 cm follicular lesion. Pathologic exam showed the lesion to be a follicular adenoma; in addition, a 0.8 cm PTC was discovered in the resected lobe. No nodes were removed at Tx.

Serum TSH is 0.5 mIU/L on T4; Tg 2.2 ng/dL; Tg Ab neg; thyroid US shows a surgically absent L lobe, a normal R lobe, and no adenopathy.

**Q**

Based on current recommendations what do you suggest?

A. Observation with periodic US, TSH & Tg measurement

B. 100 mCi RAI with follow-up

C. Completion Tx, 50 mCi RAI and follow-up

D. Completion Tx, 100 mCi RAI and follow-up
50 Year Old with Micro-PTC

Recommendation
Completion Tx should be offered to those for whom a TTx would have been recommended if the Dx was available before initial surgery – this includes all pt except small (<1 cm), unifocal, intrathyroid, node-neg, low-risk tumors

Thyroid, 2009
Evidence: Papillary Thyroid Microcarcinoma

- Accounts for 30-50% of PTC
- Mean tumor size, 5-6 mm
- Prevalence 10% (2-30%)
- Nodal metastasis 20-40%
- Multicentricity 30-40%
- Bilaterality 20%
PTC

Case  53-year-old woman is evaluated because of a 2.5 cm R lobe nodule and an enlarged R level III node; FNA of both nodule & node show typical PTC

From your knowledge of TNM staging, her disease is?

A. Stage I  
B. Stage II  
C. Stage III  
D. Stage IV
Case 53-year-old woman is evaluated because of a 2.5 cm R lobe nodule and an enlarged R level III node; FNA of both nodule & node show typical PTC

Q From your knowledge of TNM staging, her disease is?

A. Stage I
B. Stage II
C. Stage III
D. Stage IV
### AJCC Staging for DTC – pTNM

<table>
<thead>
<tr>
<th>Stage</th>
<th>&lt;45 yr</th>
<th>&gt;45 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Any T, any N, M0</td>
<td>T1, N0, M0</td>
</tr>
<tr>
<td>II</td>
<td>Any T, any N, M1</td>
<td>T2, N0, M0</td>
</tr>
<tr>
<td>III</td>
<td>–</td>
<td>T3, or N1a, M0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2, N1a, M0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T3, N1a, M0</td>
</tr>
<tr>
<td>IV, A, B, C</td>
<td>–</td>
<td>T4a, N0, M0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Any T, any N, M1</td>
</tr>
</tbody>
</table>

| T1: | ≤2 cm, T2: >2 to ≤4 cm, T3: >4 cm |
| T4a,b: | Extending beyond thyroid capsule |
| N0: | No lymph node metastasis, N1a,b: LN metastasis |
| M0: | no distance metastasis; M1: Distant metastasis |
Compartment-Oriented Neck Dissection
Based on her presentation, what is the recommended surgical approach?

A. Lobectomy plus ipsilateral neck dissection
B. Total Tx
C. Total Tx plus CND
D. Total Tx plus CND and lateral neck dissection
53-Year-Old Woman

Based on her presentation, what is the recommended surgical approach?

A. Lobectomy plus ipsilateral neck dissection
B. Total Tx
C. Total Tx plus CND
D. Total Tx plus CND and lateral neck dissection
53-Year-old Woman

Recommendation

Therapeutic lateral neck compartment lymph node dissection should be performed for pt with biopsy-proven metastatic lateral cervical adenopathy

Thyroid, 2009
53-Year-Old Woman

**Case**
Tx showed a 2.5 cm PTC with minimal extension thru the capsule; 2 of 8 level VI and 2 level III nodes were metastatically involved

**Q**
What is your recommendation for further Rx?

A. Defer RRA, start T4 suppressive Rx and follow

B. Rx with 100 mCi $^{131}$I, start T4 Rx and follow
53-Year-Old Woman

**Case**

Tx showed a 2.5 cm PTC with minimal extension thru the capsule; 2 of 8 level VI and 2 level III nodes were metastatically involved

What is your recommendation for further Rx?

**A.** Defer RRA, start T4 suppressive Rx and follow

**B.** Rx with 100 mCi $^{131}$I, start T4 Rx and follow
53-Year-old Woman

Recommendation

RAI ablation is recommended for selected pt with 1-4 cm cancers who have documented lymph node mets

Thyroid, 2009
Limitations of Staging Systems

- 42 yo with T1 N1b M0 is stage I
- 46 yo with T1 N1b M0 is stage IVA
- 40 yo with diffuse distant mets is stage II
- Do not incorporate molecular or histologic info
- Predict death but not recurrence
<table>
<thead>
<tr>
<th></th>
<th>Very low</th>
<th>Low</th>
<th>Intermediate</th>
<th>High</th>
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</thead>
<tbody>
<tr>
<td><strong>Age at Dx</strong></td>
<td>Any age</td>
<td>&lt;45</td>
<td>&lt;45</td>
<td>&gt;45</td>
</tr>
<tr>
<td><strong>Tumor size (cm)</strong></td>
<td>&lt;1</td>
<td>1-4</td>
<td>&gt;4</td>
<td>&gt;4</td>
</tr>
<tr>
<td><strong>Histology</strong></td>
<td>Classic</td>
<td>Classic</td>
<td>PTC</td>
<td>Unfavorable</td>
</tr>
<tr>
<td><strong>Lymph</strong></td>
<td>No</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><strong>Distant</strong></td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Endocrinol Metab Clin N Am 37:419, 2008
Evidence: Survival by pTNM Stage, 1940-1990

- I (60%)
- II (21%)
- III (18%)
- IV (1%)

Surviving PTC (%)

Yr after initial treatment

n=1,851
P<0.0001
Evidence: Tumor Recurrence in 359 (23.5%) Among 1,528 Patients Followed with Median 16.6 Years.
Evidence: Overall Outcome in PTC

Mortality

Recurrence

Occurrence (%)

Yr postop

5 10 15 20 25

2% 4% 5% 5% 5%

8% 11% 12% 13% 14%
Radioiodine Remnant Ablation (RRA)

- Aimed to eliminate post-surgical thyroid remnant
- Satisfactory result is absence of visible uptake on follow-up WB5
- May decreases recurrent loco-regional disease
- Best use minimum RAI doses (30-100 mCi)
53-Year-Old Woman with PTC

What is the preferred way to achieve RRA in this patient?

A. By THW (thyroid hormone withdrawal)
B. By rhTSH administration
C. By either THW or rhTSH; both are equally effective
53-Year-Old Woman with PTC

Q What is the preferred way to achieve RRA in this patient?

A. By THW (thyroid hormone withdrawal)
B. By rhTSH administration
C. By either THW or rhTSH; both are equally effective
Evidence: Comparison of RRA Using THW vs rhTSH

Elisio R et al: JCEM, 2009
66-year-old woman underwent a total Tx for a large MNG; pathologic report showed multiple benign adenomatous nodules; incidentally noted were 3 foci of PTC, 2 (0.1 & 0.6 cm) in the left and 1 (0.4 cm) in the right lobe.

In additional to T4 Rx and periodic exam, what else do you recommend?

A. 30 mCi $^{131}$I for remnant ablation (RA)
B. 50 mCi $^{131}$I for RA
C. 100 mCi $^{131}$I for RA
D. No $^{131}$I Rx is necessary
RRA

Case

66-year-old woman underwent a total Tx for a large MNG; pathologic report showed multiple benign adenomatous nodules; incidentally noted were 3 foci of PTC, 2 (0.1 & 0.6 cm) in the left and 1 (0.4 cm) in the right lobe

Q

In addition to T4 Rx and periodic exam, what else do you recommend?

A. 30 mCi $^{131}$I for remnant ablation (RA)
B. 50 mCi $^{131}$I for RA
C. 100 mCi $^{131}$I for RA
D. No $^{131}$I Rx is necessary
66-Year-old Woman with Multifocal Micro-PTC

Recommendation

RAI ablation is not recommended for pt with multifocal cancer when all foci are <1 cm in the absence of other higher-risk features
Evidence: Lack of Impact of RRA on Mortality & Recurrence in Low-Risk PTC Patients

<table>
<thead>
<tr>
<th>Low risk</th>
<th>20-yr mortality</th>
<th>20-yr recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NT/TT alone</td>
<td>NT/TT and RRA</td>
</tr>
<tr>
<td>1970-2000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>0.4%</td>
<td>0.6%</td>
</tr>
<tr>
<td>(n=1,163)</td>
<td>P=0.64</td>
<td>P=NA</td>
</tr>
<tr>
<td>Node negative</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>(n=636)</td>
<td>P=NA</td>
<td>P=0.80</td>
</tr>
<tr>
<td>Node positive</td>
<td>1.2%</td>
<td>0.9%</td>
</tr>
<tr>
<td>(n=527)</td>
<td>P=0.99</td>
<td>P=0.19</td>
</tr>
</tbody>
</table>

Trans Am Clin Assoc 113:241, 2002
Case

62-year-old man underwent TTx 3 yr ago for a 3-cm PTC with a background of lymphocytic thyroiditis; 2 of 6 central compartment (level VI) nodes were metastatically involved. He received 100 mCi of RAI postop and was maintained on T4 150 mcg daily. Last year, serum Tg was <1 ng/dL, Tg Ab negative, and after rhTSH stimulation, WBS was negative and serum Tg 1.2 ng/dL.

Today, examination is normal; serum TSH is 0.1 mIU/L; FT4 1.6 ng/dL; Tg <1.0 ng/dL; TgAb 120 IU/mL.

Q

Which of the following is the best next step?

A. Increase T4 dose to 175 mcg/day
B. US of the neck
C. PET scan
D. Repeat WBS using rhTSH
PTC Follow-Up

Case

62-year-old man underwent TTx 3 yr ago for a 3-cm PTC with a background of lymphocytic thyroiditis; 2 of 6 central compartment (level VI) nodes were metastatically involved. He received 100 mCi of RAI postop and was maintained on T4 150 mcg daily. Last year, serum Tg was <1 ng/dL, Tg Ab negative, and after rhTSH stimulation, WBS was negative and serum Tg 1.2 ng/dL

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Q

Which of the following is the best next step?

A. Increase T4 dose to 175 mcg/day
B. US of the neck
C. PET scan
D. Repeat WBS using rhTSH
62-Year-old Man

Recommendation

• Following surgery, cervical US to evaluate the thyroid bed and central and lateral cervical nodal compartments should be performed at 6-12 mo, and then periodically

• ↓ Ab levels are correlated with disease-free status while ↑ levels suggest persistent disease

Thyroid, 2009
## Comparison of Diagnostic Tests in Thyroid Cancer

<table>
<thead>
<tr>
<th>Test</th>
<th>US-FNA</th>
<th>rhTSH-Tg</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cost ($)</strong></td>
<td>300</td>
<td>1,800</td>
</tr>
<tr>
<td><strong>Time</strong></td>
<td>Single visit</td>
<td>Multiple visits</td>
</tr>
<tr>
<td><strong>TgAb</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Localization</strong></td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

**US-FNA**: US-guided FNA  
**TgAb**: thyroglobulin antibody
Lymph Node Features on US

Likely benign
• Flat or oval
• Echogenic (hilar) line
• Hilar vascular flow in Doppler
• Size varies

Likely malignant
• Rounded AP/T >0.5
• About echogenic line
• Calcifications
• Cystic necrosis
• Chaotic vascularization
Serum Thyroglobulin (Tg)

- Highly thyroid specific, but not tumor specific
- Current assay functional sensitivity $\leq 0.1$ ng/mL
- Tg $<$0.1 on T4 indicates probable cure
- Sensitivity ↑ after TSH stimulation; Tg $>$2 ng/mL suspicious for recurrence
- TgAbs should always be measured; occur in 25% of pt & cause false low Tg
# Value of Serum Tg in Follow-Up

<table>
<thead>
<tr>
<th></th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>None</td>
</tr>
<tr>
<td>Supp Tg</td>
<td>0</td>
</tr>
<tr>
<td>Stim Tg</td>
<td>0</td>
</tr>
<tr>
<td>Tg Ab</td>
<td>0</td>
</tr>
</tbody>
</table>
40-Year-Old Woman with PTC

Case

1 year ago, a 40-year-old woman underwent TTx for a 3.0 cm PTC; 2 of 18 level VI nodes were positive for microscopic PTC; she received 100 mCi $^{131}$I for remnant ablation; post therapy WBS was negative 3 months ago; on T4 150 mcg/day, TSH was 0.01 mIU/L, Tg <0.1 ng/dL, and TgAb neg; neck US showed no adenopathy

Today, her exam is unremarkable

Q

What additional test should be done at this visit?

A. No tests
B. Repeat WBS after rhTSH
C. Repeat US, Tg and TSH
D. Measure Tg after rhTSH
40-Year-Old Woman with PTC

Case
1 year ago, a 40-year-old woman underwent TTx for a 3.0 cm PTC; 2 of 18 level VI nodes were positive for microscopic PTC; she received 100 mCi $^{131}$I for remnant ablation; post therapy WBS was negative 3 months ago; on T4 150 mcg/day, TSH was 0.01 mIU/L, Tg <0.1 ng/dL, and TgAb neg; neck US showed no adenopathy

Today, her exam is unremarkable

What additional test should be done at this visit?

A. No tests
B. Repeat WBS after rhTSH
C. Repeat US, Tg and TSH
D. Measure Tg after rhTSH
40-Year-Old Woman with PTC

Recommendation

In low-risk patients who have had RRA and negative US and undetectable TSH-suppressed Tg within the first year after Rx, serum Tg should be measured after T4 WD or rhTSH stimulation 12 months after the ablation.
$^{131}$I Treatment

- For locally recurrent or distant mets
- Treat when functioning mets are present
- Usual doses 100-200 mCi given at 6-12 months
- rhTSH-mediated Rx not recommended
- Consider acute & chronic side effects
### Evidence: Pooled Relative Risk of SPM in Thyroid Carcinoma Patients Treated with RAI Relative to Those Not Treated with RAI

<table>
<thead>
<tr>
<th>Type of SPM</th>
<th>Relative risk</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any SPM</td>
<td>1.19</td>
<td>1.04, 1.36</td>
<td>0.010</td>
</tr>
<tr>
<td>Bladder</td>
<td>1.19</td>
<td>0.51, 2.78</td>
<td>0.690</td>
</tr>
<tr>
<td>Breast</td>
<td>0.86</td>
<td>0.64, 1.16</td>
<td>0.324</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>1.74</td>
<td>0.73, 4.17</td>
<td>0.213</td>
</tr>
<tr>
<td>Colon and rectum</td>
<td>1.16</td>
<td>0.77, 1.75</td>
<td>0.472</td>
</tr>
<tr>
<td>Digestive tract</td>
<td>1.17</td>
<td>0.88, 1.54</td>
<td>0.28</td>
</tr>
<tr>
<td>Kidney and renal pelvis</td>
<td>1.39</td>
<td>0.71, 2.72</td>
<td>0.338</td>
</tr>
<tr>
<td>Leukemia</td>
<td>2.50</td>
<td>1.13, 5.53</td>
<td>0.024</td>
</tr>
<tr>
<td>Lung</td>
<td>1.50</td>
<td>0.85, 2.60</td>
<td>0.151</td>
</tr>
<tr>
<td>Melanoma (skin)</td>
<td>0.86</td>
<td>0.43, 1.70</td>
<td>0.655</td>
</tr>
<tr>
<td>Stomach</td>
<td>1.66</td>
<td>0.74, 3.72</td>
<td>0.220</td>
</tr>
</tbody>
</table>

Data from Brown et al and Rubino et al; total number of thyroid cancer survivors included in pooled analysis is 16,502
Sawka A et al: Thyroid, 2009
**131I Facts**

- **Safe dose at one time**: ≤200 mCi
- **Total dose in a lifetime**: ≤800 mCi
- **Side effects**: Dose dependent
- **Second primary malignancies**: Rare
- **Next pregnancy**: 6-9 mo
- **Subsequent pregnancies**: OK
Thyroid nodules are common & commonly benign

Initial evaluation should include TSH, US & FNA

Risk factors for malignancy include TSH level, US appearance & FNA; not nodule size or number

Benign nodule should be followed by repeat US

Cytologically indeterminate or malignant nodule should be excised
Conclusions (2)

- Data suggest ↑ incidence of PTC
- Initial surgical approach of choice is a NTTx or TTx
- RRA is necessary for some low-risk and all high-risk patient
- Long-term follow-up should include TSH, Tg, and US exam
- RAI treatment is appropriate for locally recurrent or distant metastasis