Fall Update 2013: Endocrine Surgical Oncology

Thyroid Cytopathology: Weighing In The Bethesda System

In partnership with:
BC Cancer Agency
UBC Department of Surgery
The Royal College of Physicians and Surgeons of Canada

Saturday, November 2, 2013
Four Seasons Hotel
791 West Georgia, Vancouver, BC
Conflicts

- No financial consideration
Bias

• Work in the Canadian environment where litigation is less

• Thyroid cytology is often referred in by small group of well trained endocrinologist or radiologists

• Thyroid pathology is acted on by a small number of thyroid surgeons
The Problem

Fine Needle Aspiration Biopsy of right thyroid showing groups of thyroid follicles and colloid.

Hyperplasia vs. thyroid neoplasm.
Can not rule out a low grade thyroid malignancy.
Clinical correlation recommended.
The Problem

Fine Needle Aspiration Biopsy of right thyroid showing groups of thyroid follicles and colloid.

Hyperplasia vs. thyroid neoplasm.

Can not rule out a low grade thyroid malignancy.

Clinical correlation recommended.

No Surgery

Surgery
Pathologists don’t understand clinicians and they don’t understand us
Bethesda system

- National Cancer Institute (NCI) Thyroid Fine Needle Aspiration State of the Science Conference
- October 22 and 23, 2007 in Bethesda, Maryland
- Co-hosted by Susan J. Mandel and Edmund S. Cibas
Bethesda system


Diagnostic terminology and morphologic criteria for cytologic diagnosis of thyroid lesions: A synopsis of the National Cancer Institute Thyroid Fine-Needle Aspiration State of the Science Conference (pages 425–437)
Zubair W. Baloch, Virginia A. LiVolsi, Syl L. Asa, Juan Rosai, Maria J. Merino, Gregory Randolph, Philippe Vielh, Richard M. DeMay, Mary K. Sidawy and William J. Frable

The Bethesda System For Reporting Thyroid Cytopathology.
Cibas ES, Ali SZ;.
Available from: http://ajcp.ascpjournals.org/content/132/5/658.full.pdf
The Bethesda System For Reporting Thyroid Cytopathology. Definitions, Criteria and Explanatory Notes
Ali SZ, Cibas ES
Bethesda system

Background
Definition
Criteria
Explanatory notes
Bethesda system

1. Nondiagnostic / Unsatisfactory
2. Benign
3. Atypia of Undetermined significance / Follicular Lesion of Undetermined Significance
4. Follicular neoplasm / Suspicious for follicular neoplasm +/- Hurthle cell
5. Suspicious for Malignancy
6. Malignant
Bethesda system

1. Unsatisfactory
2. Benign
3. Atypia of Undetermined Significance
4. Suspicious for Follicular Neoplasm
5. Suspicious for Malignancy
6. Malignant
Stratification of the risk of malignancy

- Benign 0-3%
- AUS 5-15%
- Susp. FN 15-30%
- Susp. PTC 50-75%
- Malignant 93-95%
Bethesda system

1. Unsatisfactory (Risk 1-4%)
2. Benign (0-3%)
3. Atypia of Undetermined Significance (5 to 15%)
4. Suspicious for Follicular Neoplasm (15-30%)
5. Suspicious for Malignancy (50-75%)
6. Malignant (97-99%)
Table 2: The Bethesda System for Reporting Thyroid Cytopathology: Implied Risk of Malignancy and Recommended Clinical Management

<table>
<thead>
<tr>
<th>Diagnostic Category</th>
<th>Risk of Malignancy (%)</th>
<th>Usual Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nondiagnostic or Unsatisfactory</td>
<td>1-4</td>
<td>Repeat FNA with ultrasound guidance</td>
</tr>
<tr>
<td>Benign</td>
<td>0-3</td>
<td>Clinical follow-up</td>
</tr>
<tr>
<td>Atyopia of Undetermined Significance or Follicular Lesion of Undetermined Significance</td>
<td>5-15</td>
<td>Repeat FNA</td>
</tr>
<tr>
<td>Follicular Neoplasm or Suspicious for a Follicular Neoplasm</td>
<td>15-30</td>
<td>Surgical lobectomy</td>
</tr>
<tr>
<td>Suspicious for Malignancy</td>
<td>60-75</td>
<td>Near-total thyroidectomy or surgical lobectomy</td>
</tr>
<tr>
<td>Malignant</td>
<td>97-99</td>
<td>Near-total thyroidectomy</td>
</tr>
</tbody>
</table>

FNA, fine-needle aspiration.
* Adapted with permission from Ali and Cibas.
† Actual management varies.
‡ Estimate extra.
§ In the case of a solitary nodule rather than a primary thyroid malignancy, surgery may not be indicated.

Bethesda system

1. Unsatisfactory (Risk 1-4%)
2. Benign (0-3%)
3. Atypia of Undetermined Significance (5 to 15%)
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5. Suspicious for Malignancy (50-75%)
6. Malignant (97-99%)
Nondiagnostic / Unsatisfactory
Adequacy

• 5-6 groups, each with 10 or more cells (1)
• 10 groups, each with 20 or more cells (2)
• 6 groups on at least 2 of six aspirates (3)
• 8 groups, on at least 2 slides (4)


As cited by Auger M from CSC “Practice guidelines for fine Needle Aspiration Cytology of the thyroid” http://cap-acp.org/guidelines_fine_needle_aspiration.cfm
Adequacy

...if the pathologist needs to count the number of cells present in the smears, then I believe the specimen is unsatisfactory.

Adequacy

“How can I tell if the specimen is adequate unless it is diagnostic of the lesion being aspirated?”

Unidentified Pathologist SPH (2009)

“It is my responsibility to determine whether the specimen is adequate for diagnosis”

Blair Walker (2013)
Bethesda system

1. Unsatisfactory (Risk 1-4%)
2. Benign (0-3%)
3. Atypia of Undetermined Significance (5 to 15%)
4. Suspicious for Follicular Neoplasm (15-30%)
5. Suspicious for Malignancy (50-75%)
6. Malignant (97-99%)
Benign

• Benign nodules have:
  – Macro follicules, colloid, cystic change
<table>
<thead>
<tr>
<th>American Thyroid Ass. Guidelines</th>
<th>NCI Malignancy risk</th>
<th>Literature Malignancy risk</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inadequate</td>
<td>Nondiagnostic</td>
<td>2-9% or 37-54%</td>
<td>Repeat</td>
</tr>
<tr>
<td>Benign</td>
<td>Benign</td>
<td>&lt; 1%</td>
<td>0.8-3.4%</td>
</tr>
<tr>
<td>Indeterminate, Follicular lesion of undetermined significance</td>
<td>Follicular lesion of undetermined significance</td>
<td>5-10%</td>
<td>Lobectomy</td>
</tr>
<tr>
<td>Indeterminate, Follicular lesion of undetermined significance</td>
<td>Follicular lesion of undetermined significance</td>
<td>5-10%</td>
<td>Lobectomy</td>
</tr>
<tr>
<td>%</td>
<td>Malignant</td>
<td>Total</td>
<td>Reference</td>
</tr>
<tr>
<td>2.4%</td>
<td>6</td>
<td>246</td>
<td>Hamburger JL (1987) Arch Intern Med 147:97-9</td>
</tr>
<tr>
<td>0.8%</td>
<td>2</td>
<td>235</td>
<td>Chehade JM (2001) 7:237-43</td>
</tr>
</tbody>
</table>
Suspicious for follicular neoplasm

• Or Follicular neoplasm +/- Hurthle cell

Neoplastic nodules have:
  – Microfollicules
  – *No colloid, not cystic,*

• Follicular carcinomas are ONLY diagnosed on histology
  – *Never “malignant”*
St. Paul’s data

Suspicious for Follicular Neoplasm

<table>
<thead>
<tr>
<th>Final Diagnosis</th>
<th>N</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>236</td>
<td>78%</td>
</tr>
<tr>
<td>Carcinoma</td>
<td>67</td>
<td>22%</td>
</tr>
</tbody>
</table>

Follicular Carcinoma 7%
PTC 6%
Medullary Carcinoma <1%
Micro PTC 8%

Bethesda system

1. Unsatisfactory (Risk 1-4%)
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Malignant

- Papillary thyroid carcinoma

- Medullary, Anaplastic, Lymphoma, etc
Malignant- Papillary thyroid carcinoma

- Classic papillary thyroid carcinomas are easy
- Follicular variants are subtle and arbitrary

FIGURE 1. Case 3. Low-power view showing an encapsulated follicular patterned lesion (A). B, high-power view showing follicles of varying sizes and areas of sclerosis. C, D, high-power views showing follicles with and without nuclear features of papillary carcinoma.
<table>
<thead>
<tr>
<th>American Thyroid Ass. Guidelines</th>
<th>Benign</th>
<th>Nondiagnostic</th>
<th>Indeterminate, suspect for neoplasm</th>
<th>Indeterminate, suspect for neoplasm</th>
<th>Indeterminate, suspect for neoplasm</th>
<th>Indeterminate, suspect for neoplasm</th>
<th>Malignant</th>
<th>Cyst</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>False +ve</td>
<td>Total</td>
<td>Reference</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.1%</td>
<td>1</td>
<td>32</td>
<td></td>
<td>Baloch et al (2001) 25:231-4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0%</td>
<td>0</td>
<td>11</td>
<td></td>
<td>B Kuru (2008) surgery 143:835-6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lobectomy +/- frozen section or repeat FNA &amp; total thyroidectomy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>100%</td>
<td></td>
<td>96-99%</td>
<td></td>
<td>Total thyroidectomy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10-15%</td>
<td></td>
<td></td>
<td></td>
<td>Repeat aspiration, surgery if undefined or solid component</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Bethesda system

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Atypia of Undetermined Significance

- Or Follicular lesion of Undetermined Significance (FLUS)
Atypia of Undetermined Significance

1. Some microfollicles but not enough for “Suspicious for follicular neoplasm”
2. Cellular Hurthle cell lesion
3. Artifacts resulting in follicular cell atypia, cyst atypia and treatment effect
4. PTC-like features in benign lesions (Hashimoto’s, hurthle cells)
5. Too many lymphocytes
Suspicious for Malignancy

- Likely papillary thyroid carcinoma but not enough
  - Arbitrary threshold for PTC in follicular variants
  - Atypical cysts
  - Hashimoto’s clear cell change
The Problem

• Why be wrong?
  – Favor *Atypia of undermined significance*
  – Favor *Suspicious for PTC over Malignant*
Bethesda system

• Can it be done?

• Need
  – Buy in
  – Department wide usage
  – Recognition of the “stratification of risk” concept
  – Application of criteria
### St. Paul’s data Distribution

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number</th>
<th>Distribution percentage</th>
<th>Literature incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nondiagnostic</td>
<td>513</td>
<td>23%</td>
<td>10%</td>
</tr>
<tr>
<td>Benign</td>
<td>1355</td>
<td>61%</td>
<td>60%</td>
</tr>
<tr>
<td>AUS</td>
<td>167</td>
<td>8%</td>
<td>8%</td>
</tr>
<tr>
<td>FN</td>
<td>89</td>
<td>4%</td>
<td>9%</td>
</tr>
<tr>
<td>Susp. M</td>
<td>44</td>
<td>2%</td>
<td>4%</td>
</tr>
<tr>
<td>Malignant</td>
<td>60</td>
<td>3%</td>
<td>7%</td>
</tr>
<tr>
<td>Total</td>
<td>2228</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Cases with follow-up</td>
<td>Cases with malignant histology on follow-up</td>
<td>Cancer risk</td>
</tr>
<tr>
<td>-----------------</td>
<td>----------------------</td>
<td>---------------------------------------------</td>
<td>-------------</td>
</tr>
<tr>
<td>Nondiagnostic</td>
<td>50</td>
<td>7</td>
<td>4%*</td>
</tr>
<tr>
<td>Benign</td>
<td>80</td>
<td>5</td>
<td>6%</td>
</tr>
<tr>
<td>AUS</td>
<td>49</td>
<td>11</td>
<td>22%</td>
</tr>
<tr>
<td>Susp.FN</td>
<td>38</td>
<td>12</td>
<td>31%</td>
</tr>
<tr>
<td>Susp. M</td>
<td>18</td>
<td>17</td>
<td>84%*</td>
</tr>
<tr>
<td>Malignant</td>
<td>41</td>
<td>40</td>
<td>98%*</td>
</tr>
<tr>
<td>Total</td>
<td>286</td>
<td>104</td>
<td>36%</td>
</tr>
</tbody>
</table>
## St. Paul’s data

### Cancer risk

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Cases with follow-up</th>
<th>Cases with malignant histology on follow-up</th>
<th>Cancer risk</th>
<th>NCI published cancer risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nondiagnostic</td>
<td>50</td>
<td>7</td>
<td>4 %*</td>
<td>1-4%</td>
</tr>
<tr>
<td>Benign</td>
<td>80</td>
<td>5</td>
<td>6%</td>
<td>0-3%</td>
</tr>
<tr>
<td>AUS</td>
<td>49</td>
<td>11</td>
<td>22%</td>
<td>5-15%</td>
</tr>
<tr>
<td>Susp.FN</td>
<td>38</td>
<td>12</td>
<td>31%</td>
<td>15-30%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>286</strong></td>
<td><strong>104</strong></td>
<td><strong>36%</strong></td>
<td></td>
</tr>
</tbody>
</table>

### Class Risk of Malignancy

<table>
<thead>
<tr>
<th>Class</th>
<th>Risk of Malignancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUS- PTC</td>
<td>30%</td>
</tr>
<tr>
<td>AUS- FL or AUS-FH</td>
<td>12%</td>
</tr>
<tr>
<td>AUS-NOS</td>
<td>14%</td>
</tr>
</tbody>
</table>
Not papillary thyroid carcinoma
St. Paul’s data

Not papillary thyroid carcinoma
Benign
AUS (AUS-FL, AUS-NOS)
Suspicious for follicular neoplasm

No mention of nuclear grooves, nuclear clearing, intra nuclear inclusions, papillary architecture, psammoma bodies
## “Not papillary thyroid carcinoma”
### St. Paul’s data

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Cases with follow-up</th>
<th>Cases with malignant histology on follow-up</th>
<th>Cancer risk</th>
<th>NCI published cancer risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nondiagnostic</td>
<td>50</td>
<td>7</td>
<td>4 + 10%*</td>
<td>1-4%</td>
</tr>
<tr>
<td>Benign</td>
<td>80</td>
<td>5</td>
<td>6%</td>
<td>0-3%</td>
</tr>
<tr>
<td>AUS</td>
<td>49</td>
<td>11</td>
<td>22%</td>
<td>5-15%</td>
</tr>
<tr>
<td>Susp FN</td>
<td>38</td>
<td>12</td>
<td>31%</td>
<td>15-30%</td>
</tr>
</tbody>
</table>

**Diagnosis**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>90%</td>
</tr>
<tr>
<td>Follicular carcinoma</td>
<td>2%</td>
</tr>
<tr>
<td>Papillary Thyroid Carcinoma</td>
<td>7%</td>
</tr>
</tbody>
</table>
St. Paul’s- The warts
Bethesda leakage

A. FNA Thyroid Left - Dominant L thyroid lobe, mixed solid/cystic:

Cellularity limits interpretation

Bethesda terminology: Only a few small groups of benign appearing follicular cells present.
St. Paul’s- The warts

In review 2013

5% use non-standard terminology
Bethesda System

- Benign 0-3%
- AUS 5-15%
- Susp. FN 15-30%
- Susp. PTC 50-75%
- Malignant 93-95%
Bethesda system

1. Unsatisfactory
2. Benign
3. Atypia of Undetermined Significance
4. Suspicious for Follicular Neoplasm
5. Suspicious for Malignancy
6. Malignant
7. Cyst fluid Only
Adequacy

- In my institution about one half of the aspirate the radiologist feel are reported “unsatisfactory” have cystic degeneration.

- Bethesda (NCI) consensus document:
  Diagnosis “cyst fluid only”… “non diagnostic” not “unsatisfactory”

- Canadian Society of Cytology:
  cyst fluid “non diagnostic” with explanation

Auger M from CSC “Practice guidelines for Fine Needle Aspiration Cytology of the thyroid”
Cyst fluid only
(Added to Bethesda terminology)

Risk on malignancy:
- 1-4% in simple, non-complex cysts aspirates.
- 14% in mixed solid and cystic nodules, large cysts (>3cm) and recurring cysts.

Action generally recommended:
- if it recurs excision
Cyst fluid only
(Added to Bethesda terminology)

Entities included in this category:

– Cyst contents without adequate material to diagnose a solid component