**FNA of Thyroid**

*Follicular Lesion/Atypia of Undetermined Significance*

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**Diagnostic Categories Proposed by Bethesda System/NCI Thyroid Conference**

1. Benign
2. Follicular lesion of US/Atypia of US
3. Follicular Neoplasm
4. Suspicious for Malignancy
5. Malignant
6. Non-diagnostic

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**Introduction**

- No standards existed for reporting thyroid FNAs
- Different classification schemes based on personal/institutional preferences and biases
- Discord between pathologists and clinicians on perceptions of terminology used in reporting thyroid FNAs

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**Diagnostic Terminology and Reporting Session 2006**

- Surveyed 133 clinicians (Endocrinologists, Surgeons, Thyroid specialists)
- Implications of FNA DX on management options
  - Non-diagnostic → 98% repeat FNA
  - Suspicious → 96% surgery
  - Indeterminate → 58% repeat FNA, 32% surgery
  - Atypical → 37% repeat FNA, 52% surgery
- “Indeterminate” was confused with ND in most cases. “Atypical” was too ambiguous and treated as “Susp.” in over ½ of cases

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**Justifications for Bethesda System Diagnostic Categories**

- FNA has become the standard of care for initial workup of thyroid nodules
- Most clinicians use FNA results in conjunction with clinical findings to guide treatment
- Clinicians generally utilize FNA to provide a relative risk of malignancy, from which they can base their management decisions
- The proposed diagnostic categories are important in providing a risk of malignancy to clinicians and patients → Surgery vs. follow-up

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**NCI Conference/Bethesda Classification**

<table>
<thead>
<tr>
<th>Diagnostic Categories</th>
<th>Risk of Malignancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>&lt; 2-3 %</td>
</tr>
<tr>
<td>Follicular lesion of US/AUS</td>
<td>5-10 %</td>
</tr>
<tr>
<td>Neoplasm (Follicular / Oncocytic)</td>
<td>20-30%</td>
</tr>
<tr>
<td>Suspicious for Malignancy</td>
<td>50-75%</td>
</tr>
<tr>
<td>Malignant</td>
<td>100 %</td>
</tr>
<tr>
<td>Non-diagnostic</td>
<td>= 12 % (BMH)</td>
</tr>
</tbody>
</table>
What is your diagnosis?

**Case 1:**

A. Nodular goiter  
B. Follicular neoplasm  
C. Indeterminate  
D. Suspicious

**Differential Diagnosis of Follicular Lesions**

- Hyperplastic/adenomatoid nodule  
- Follicular Neoplasm  
- Follicular variant of Papillary carcinoma

**Nodular Goiter/Hyperplastic Nodule**

- Abundant colloid  
- Variable cellularity  
- Oncocytic metaplasia  
- Degenerative changes

**Follicular Neoplasm**

**Cytologic Criteria**

- High cellularity  
- Scant colloid  
- Prominent microfollicles and/or syncytial fragments (> 50-75% of cells)  
- Significant nuclear overlapping and crowding  
- Monotonous cell population
Microfollicles

- <15 cells arranged in circle that is at least two-thirds complete
- Microfollicles + no atypia → low cancer risk (6%)
- Microfollicles + abundant colloid + absence of nuclear overlap → 0% cancer

Follicular Neoplasm
Cytologic Criteria

- Uniform enlargement >2X RBC
- Coarse and clumped chromatin
- ± Prominent nucleoli
- ± Severe nuclear pleomorphism

Follicular Lesion of US (FLUS)
Cytologic Features

- Major differential diagnosis is HN vs. FN
- High cellularity, scant colloid
- Admixture of flat sheets and microfollicles/syncytia
- Smears from different passes show a spectrum ranging from “benign” to “possible FN”
- Minimal nuclear overlapping and crowding
- Low cellularity, but prominent microfollicles and nuclear overlap (highly vascular lesions)
Specimen consisted predominately of blood
- Rare groups of follicular cells
  - Clue: abundant blood with rare microfollicles or syncytia

Follicular Lesion/Atypia of Undetermined Significance (FLUS)
- Cytology not convincingly benign, yet degree of cellular or architectural atypia is not sufficient for diagnosis of “FN”
- Some cases are due to a compromised specimen, i.e. low cellularity, poor fixation, obscuring blood
- Avoid overuse of this category
  - Ideally < 7% of thyroid FNAs

Clinical Implications and Management
- Benign
  - ≤ 5% cancer risk
  - Clinical/periodic US exams @ 6-18 month intervals, for at least 3-5 years
  - Repeat FNA if significant increase in nodule size
- Follicular neoplasm
  - 20-30% cancer risk
  - Lobectomy

Clinical Implications and Management
- FLUS 10% cancer risk
  - Approximately 10% cancer risk
  - Repeat FNA, correlate with clinical and radiologic findings
  - If repeat FNA is “Atypical” or worse → consider surgery
  - NOT equivalent to “Susp. for malignancy” (50-75% cancer risk)
Suspicious for PTC

- Cancer risk = 75%

Management options:
1. Lobectomy
2. Lobectomy + intra-operative consult
   - Helpful in additional 30% of cases
     (Baloch 2002)
3. Total thyroidectomy

Summary

- Use of "diagnostic categories" is encouraged, but Dx should be qualified, when applicable, with appropriate differential diagnosis
- The use of the term "Atypical" or "Indeterminate" as a stand alone diagnosis is not recommended. Its meaning is not standardized and may be interpreted in different ways
- Recommendations for follow-up may be included in the report, if acceptable to clinicians