### Thyroid Cytology

**Adequacy Criteria**

Must see at least 6 groups of well-visualized follicular epithelial cells, each consisting of at least 10 cells.

**Exceptions:**
1. Abundant colloid with radiographic findings compatible with a colloid nodule
2. Abundant inflammation with a solid nodule (lymphocytes, granulomas, or neutrophils)
3. Atypia

Ideally, follicular epithelium should be in nice big, flat (“monolayered”) sheets, with evenly spaced (“Honeycomb-like”) dark, round nuclei with uniformly granular chromatin.

### Benign Follicular Nodule

Histologically represent nodular goiter, adenomatoid nodules, and colloid nodules.

Variable amounts of: **colloid, bland follicular cells, Hürthle cells, and macrophages.**

Should be sparse to moderately cellular with a good amount of colloid (easiest to see on diff-quick)

- Watery colloid – thin, watery, like cellophane
- Dense Colloid – thick, hyaline

Cystic degeneration: macrophages, “reparative” stretched cells

### Lymphocytic Thyroiditis

Hypercellular smear with abundant, polymorphic lymphocytes. **Hürthle cell metaplasia common** (Large cells with abundant granular cytoplasm and prominent nucleoli).

Advanced cases may be hypocellular (due to fibrosis).

Often middle-aged women with associated circulating autoantibodies.

### Granulomatous Thyroiditis

*Aka subacute or de Quervain’s*

Self-limited inflammatory condition, usually diagnosed clinically

Clusters of epithelioid histiocytes (i.e., granulomas) and multinucleated giant cells, often ingesting colloid

Early can have neutrophils and eosinophils. Later have lymphocytes.
**Papillary Carcinoma**

Most common malignant thyroid neoplasm
Relatively good prognosis. Spreads via lymphatics.

**Classic findings:**
- Intranuclear **pseudoinclusions**
- **Powdery**, pale chromatin with marginal micronucleoli
- Enlarged, irregular nuclei
- Longitudinal nuclear grooves
- Dense, **squamoid cytoplasm**
- Multinucleated **giant cells**
- Dense, “**Bubble gum**” colloid
- Septate cytoplasmic vacuoles
- **Papillary structures** w/ and w/o fibrovascular cores

**Some findings, but “not enough”?**
Consider Atypia of Undetermined Significance (AUS) or Suspicious for Malignancy.

**Follicular Neoplasm/Suspicious for Follicular Neoplasm**

Cannot differentiate between Follicular Adenoma and Carcinoma on cytology specimens (need to see capsular or vascular invasion on resection specimen!)

Moderately or **Markedly cellular**
Significant alteration in follicular architecture
→ Repetitive **microfollicular pattern** or cell crowding/overlapping in trabeculae
→ **Minimal colloid**
Minimal cytologic atypia.

**Hürthle Cell Lesions:**
Look for: 1) nonmacrofollicular architecture, 2) absence of colloid, 3) absence of inflammation, and 4) presence of “Transgressing blood vessels”

**Some findings, but “not enough”?**
Consider Follicular Lesion of Undetermined Significance (FLUS)
Medullary Carcinoma
Can be sporadic or inherited (part of MEN 2A&B)
Derived from Parafollicular C cells → stain with Calcitonin!

Moderate to Marked Cellularity. Often discohesive.
Plasmacytoid, polygonal, to spindled cells.
Mild to moderate pleomorphism.
“Salt and Pepper” chromatin.
Granular cytoplasm with small granules.
Occasional intranuclear pseudoinclusions or amyloid fragments

Undifferentiated (Anaplastic) Carcinoma
Extremely aggressive. Poor prognosis.
Classically older women with rapidly growing, hard neck mass → trouble breathing

Variable cellularity. Often discohesive.
Epithelioid to Spindled cells.
Enlarged, pleomorphic nuclei.
Often associated necrosis and inflammation.
Can see osteoclast-like giant cells

The Bethesda System and Genetics
With rare exception, FNAs should be classified into one of the Bethesda Categories.
If you have an equivocal AUS/FLUS case, consider sending for molecular testing.

<table>
<thead>
<tr>
<th>Papillary Thyroid Carcinoma: MAPK Pathway</th>
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<tbody>
<tr>
<td>BRAF (most classic PTC’s)</td>
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<tr>
<td>V600E (most common)</td>
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<tr>
<td>RAS (associated with follicular variant &amp; NIFTP)</td>
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<tr>
<th>Follicular Neoplasms: RAS most common</th>
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<tbody>
<tr>
<td>PAX8/PPARG</td>
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<td>PTEN</td>
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<tr>
<th>Poorly Differentiated and Anaplastic</th>
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<tbody>
<tr>
<td>TP53</td>
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<tr>
<td>CTNNB1</td>
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(and others mentioned above)

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<thead>
<tr>
<th>Diagnostic Category</th>
<th>Risk of Malignancy</th>
<th>Management</th>
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<tbody>
<tr>
<td>I</td>
<td>Unsatisfactory</td>
<td>Repeat US-guided FNA</td>
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<tr>
<td>II</td>
<td>Benign</td>
<td>0-3% Clinical follow-up</td>
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<tr>
<td>III</td>
<td>AUS/FLUS</td>
<td>~5-15% Repeat FNA and/or Molecular testing</td>
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<tr>
<td>IV</td>
<td>Follicular Neoplasm</td>
<td>15-30% Lobectomy</td>
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<tr>
<td>V</td>
<td>Suspicious for Malignancy</td>
<td>60-75% Near total or total thyroidectomy</td>
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<tr>
<td>VI</td>
<td>Malignant</td>
<td>97-99% Thyroidectomy</td>
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