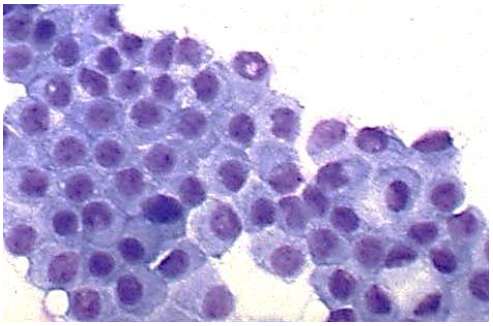
Prepared by Kurt Schaberg

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**

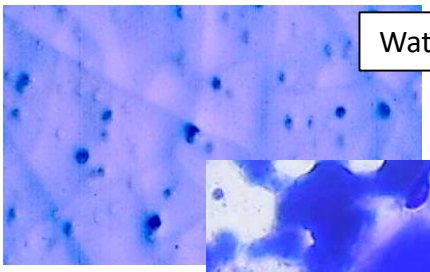
Ideally, follicular epithelium should be in nice big, flat ("monolayered") sheets, with evenly spaced ("Honeycomb-like") dark, round nuclei with uniformly granular chromatin.

Benign Follicular Nodule

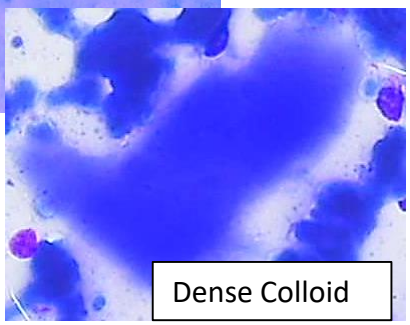
Histologically represent nodular goiter, adenomatoid nodules, and colloid nodules.
Variable amounts of: **colloid, bland follicular cells, Hürthle cells, and macrophages.**
Should be <u>sparse to moderately cellular</u> with a good amount of colloid (easiest to see on diff-quick)

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

Cystic degeneration: macrophages, "reparative" stretched cells



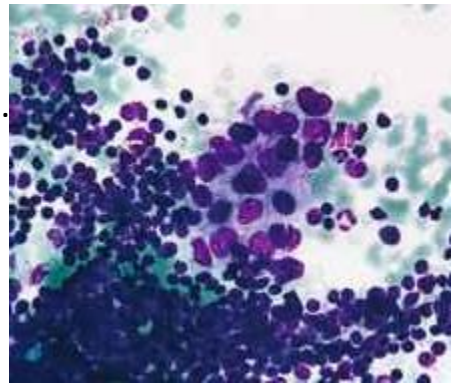
Watery Colloid



Dense Colloid

Lymphocytic Thyroiditis

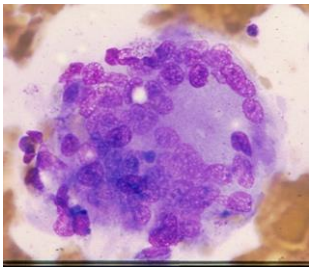
Hypercellular smear with **abundant, polymorphic lymphocytes**.
Hürthle cell metaplasia common (Large cells with abundant granular cytoplasm and prominent nucleoli).
Advanced cases may be hypocellular (due to fibrosis).
Often middle-aged women with associated circulating autoantibodies.



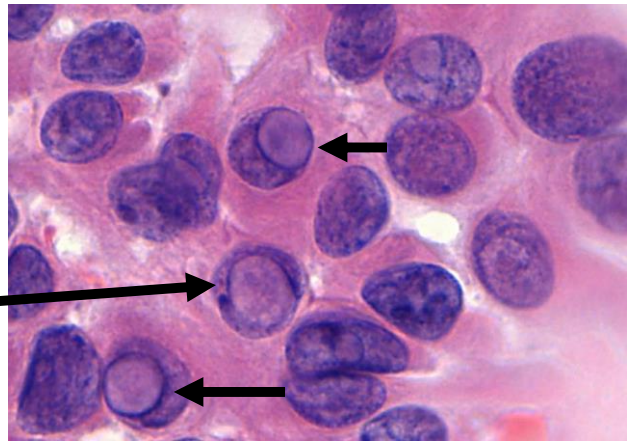
Granulomatous Thyroiditis

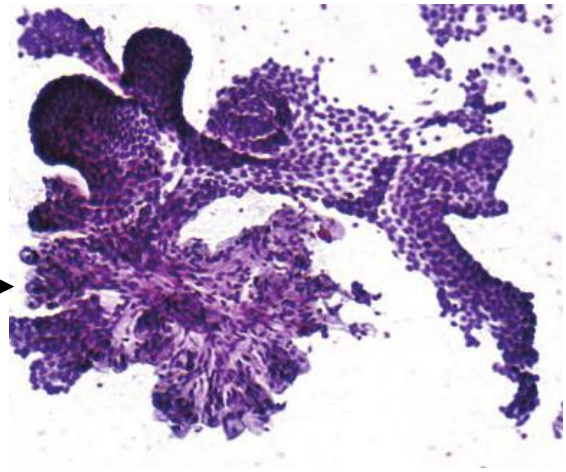
Aka subacute or de Quervain's

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



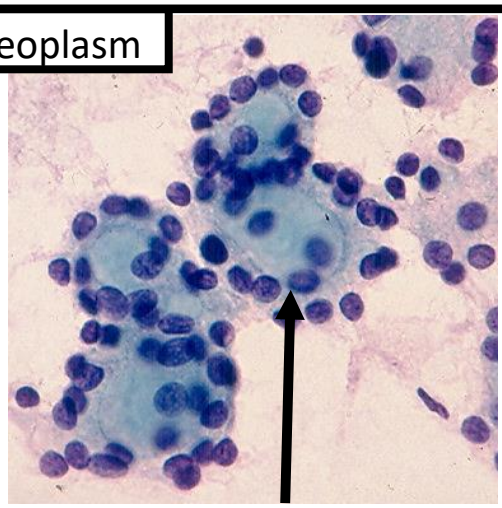


Most common malignant thyroid neoplasm
Relatively good prognosis. Spreads via lymphatics.

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!)

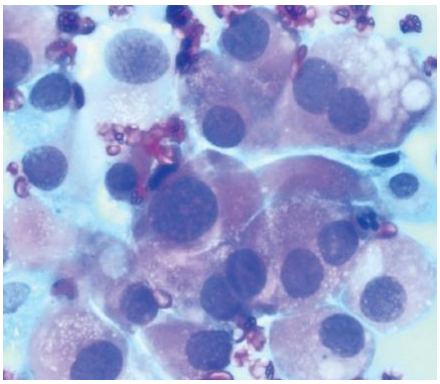
Moderately or **Markedly cellular**
Significant alteration in follicular architecture
→ Repetitive **microfollicular pattern** or cell crowding/overlapping in trabeculae
→ **Minimal colloid**
Minimal cytologic atypia.

Microfollicle: less than 15 cells arranged in a circle that is at least 2/3 complete

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)

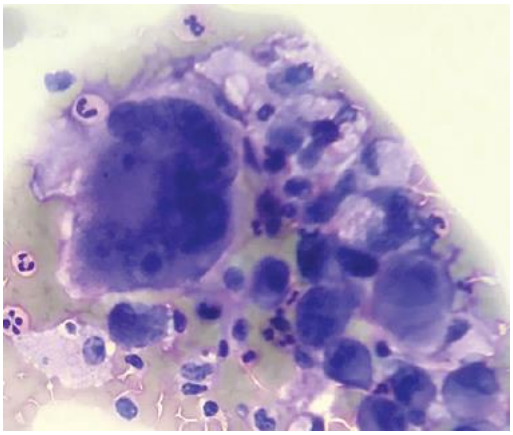
Medullary Carcinoma



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.

Papillary Thyroid Carcinoma:
MAPK Pathway
BRAF (most classic PTC's)
V600E (most common)
RAS (associated with follicular variant & NIFTP)

Medullary Carcinoma:
RET (think MEN2A&B)

Follicular Neoplasms:
RAS most common
PAX8/PPARG
PTEN

Poorly Differentiated and Anaplastic
TP53
CTNNB1
(and others mentioned above)

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