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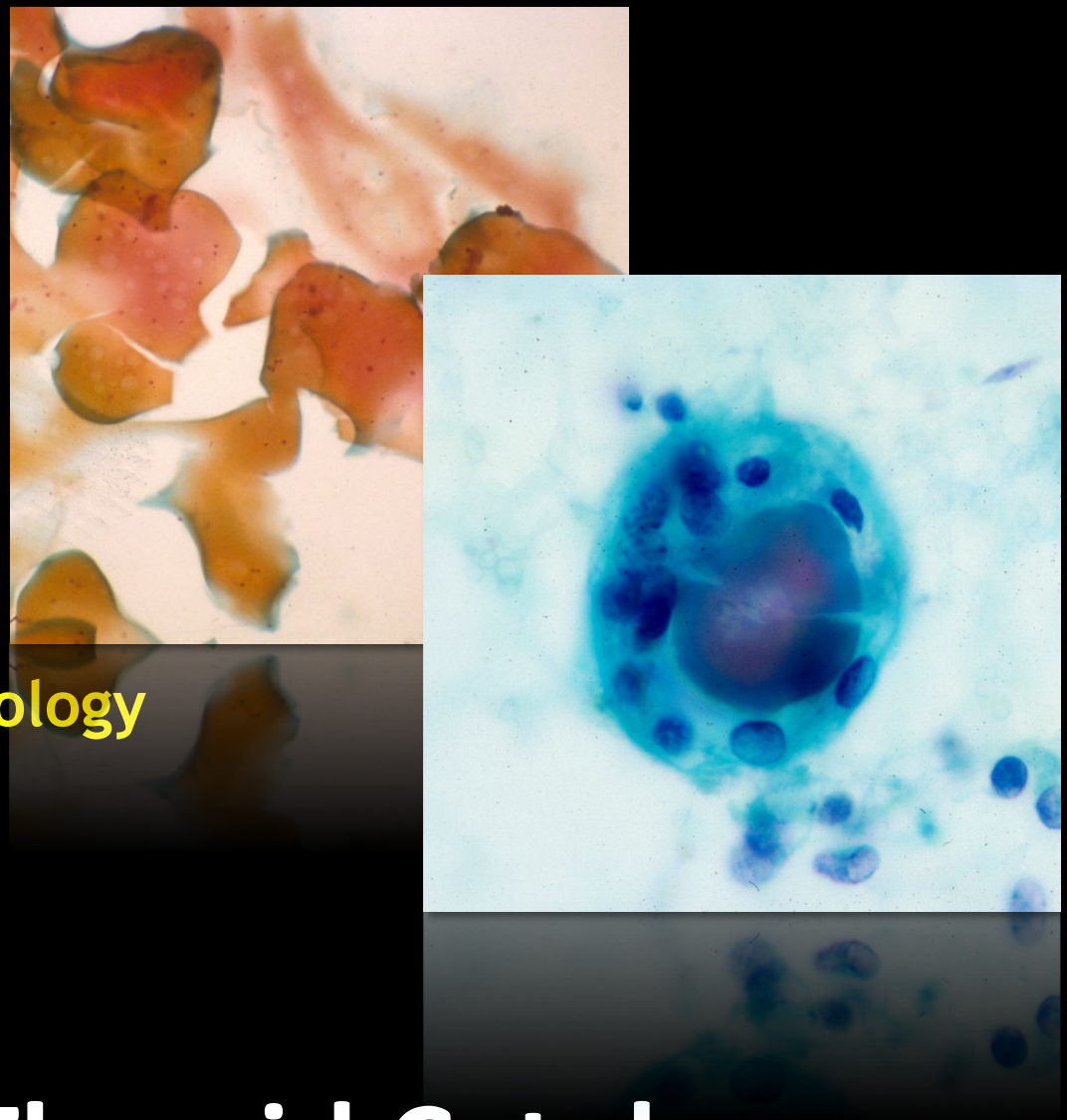
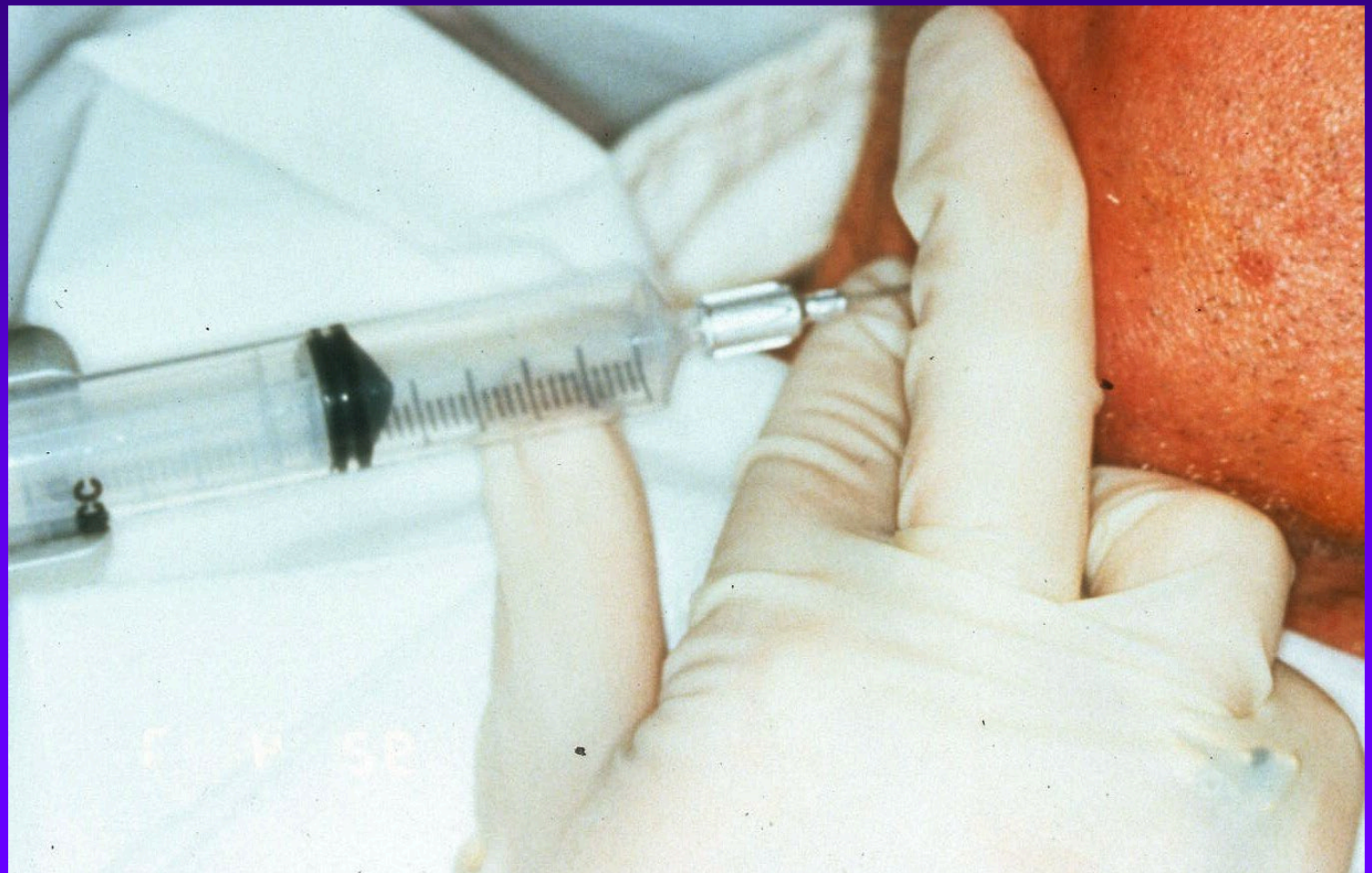
@BFAQUIN



Essentials in Thyroid Cytology

Thyroid FNAs are Among the Most Common Non-GYN Cytology Specimens



Thyroid FNA:
Used for U/S TIRADS 4 & 5 Nodules

"FNA is the most accurate and cost-effective method for evaluating thyroid nodules."

The American Thyroid Association Guidelines Taskforce

Thyroid FNA Processing: Many Options!

TECHNIQUE AND PROCESSING:

- 3-5 separate passes per nodule
- Ethanol-fixed smears
- Air-dried smears
- Liquid based preparations
- Cell block
- Rinsings in saline or cytolyte

MGH: 4-6 fixed smears + 1 Thin-Prep

BWH: 1-2 Thin-Preps

BIDMC: 1 Thin-Prep

The 3rd Edition of the Bethesda System for Reporting Thyroid Cytopathology

ROM IN BETHESDA 3rd Edition

3rd Ed Category	3rd Ed. ROM
Non-Diagnostic	13% (5-20%)
Benign	4% (2-7%)
AUS	22% (13-30%)
Follicular Neoplasm	30% (23-34%)
Follicular Neoplasm: Oncocytic FN	30% (23-34%)
Suspicious for Malignancy	74% (67-83%)
Malignant	97% (97-100%)

NORMAL THYROID ELEMENTS:

COLLOID

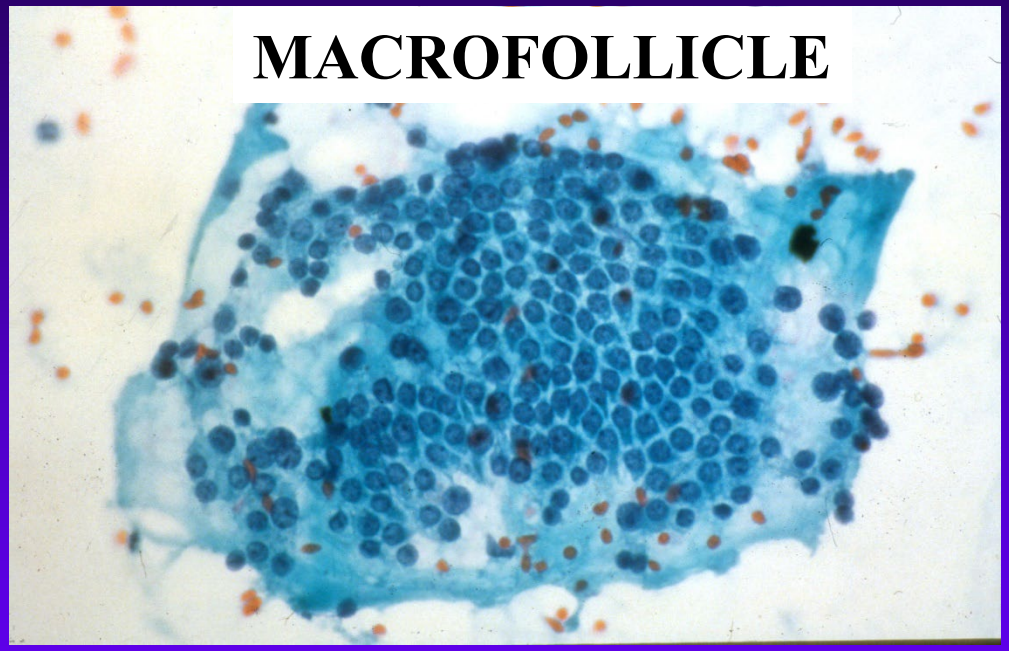
FOLLICULAR CELLS

COLLOID

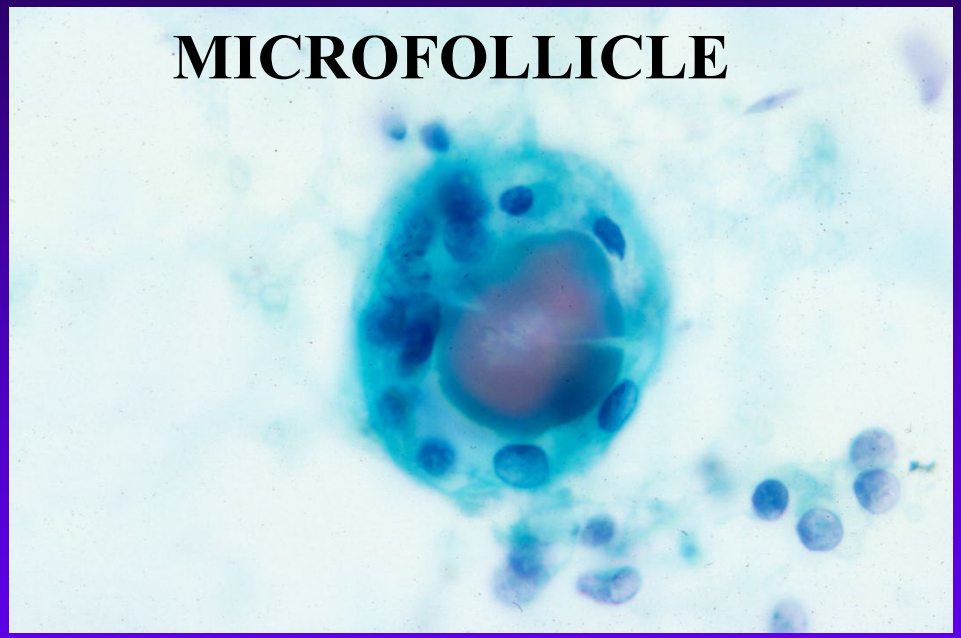
Usually a benign feature

MACROFOLLICLES VS MICROFOLLICLES

MACROFOLLICLE



MICROFOLLICLE

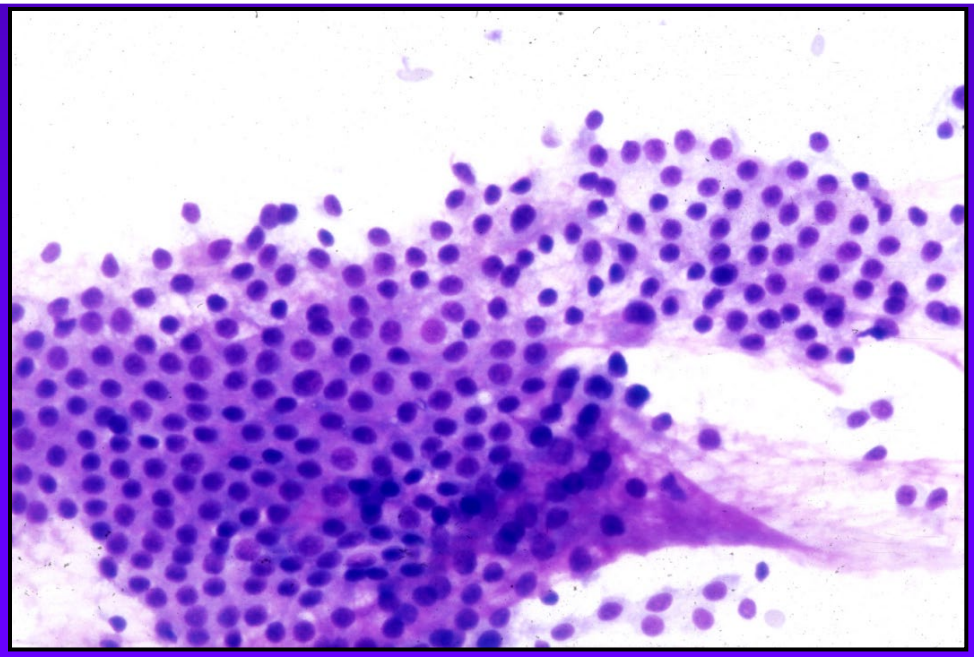


Cytologic Reporting of Follicular Lesions

A majority of thyroid FNAs are BENIGN!

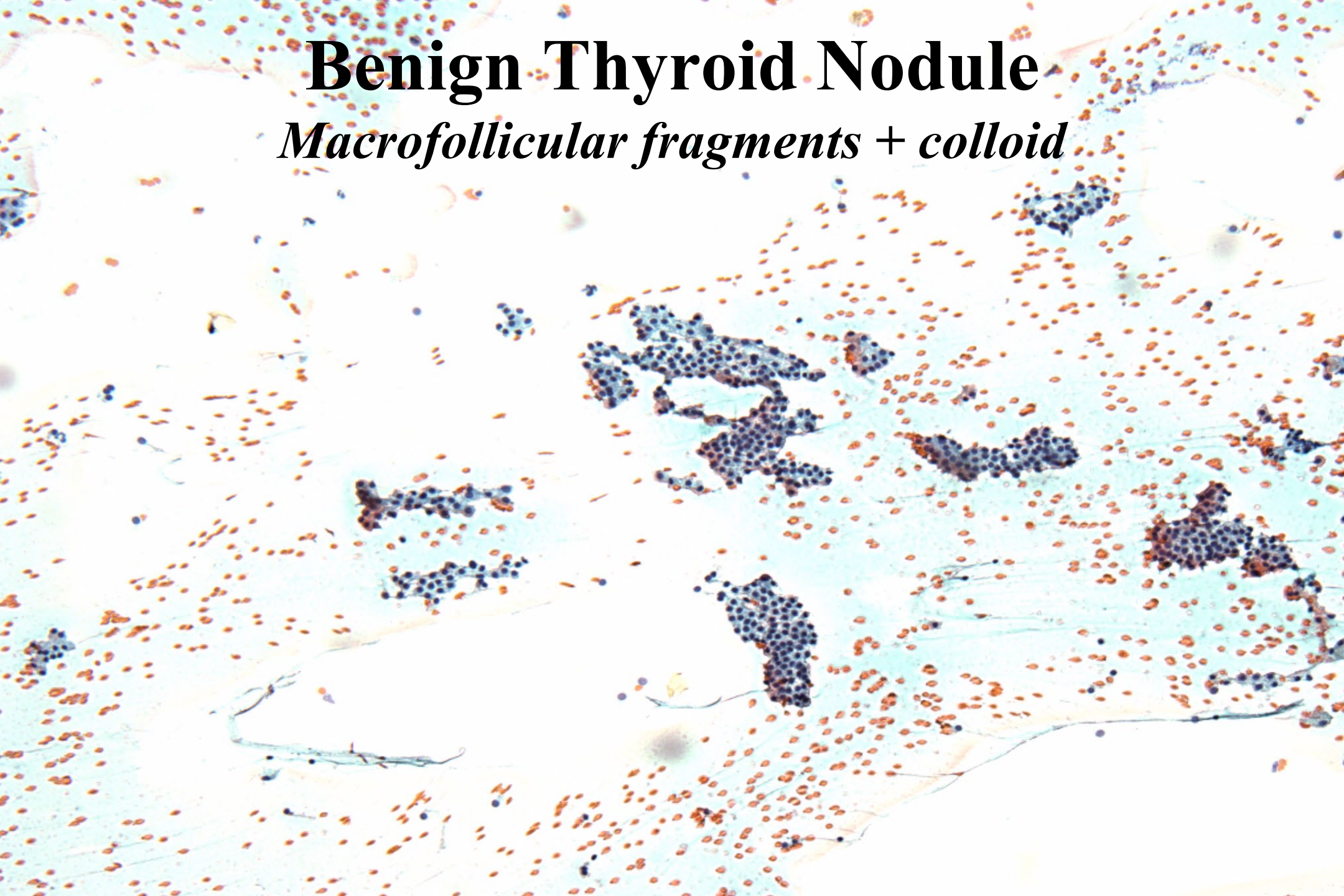
60-70% of thyroid FNAs

- **BENIGN**
  - **Macrofollicles and colloid, consistent with a benign thyroid nodule.**



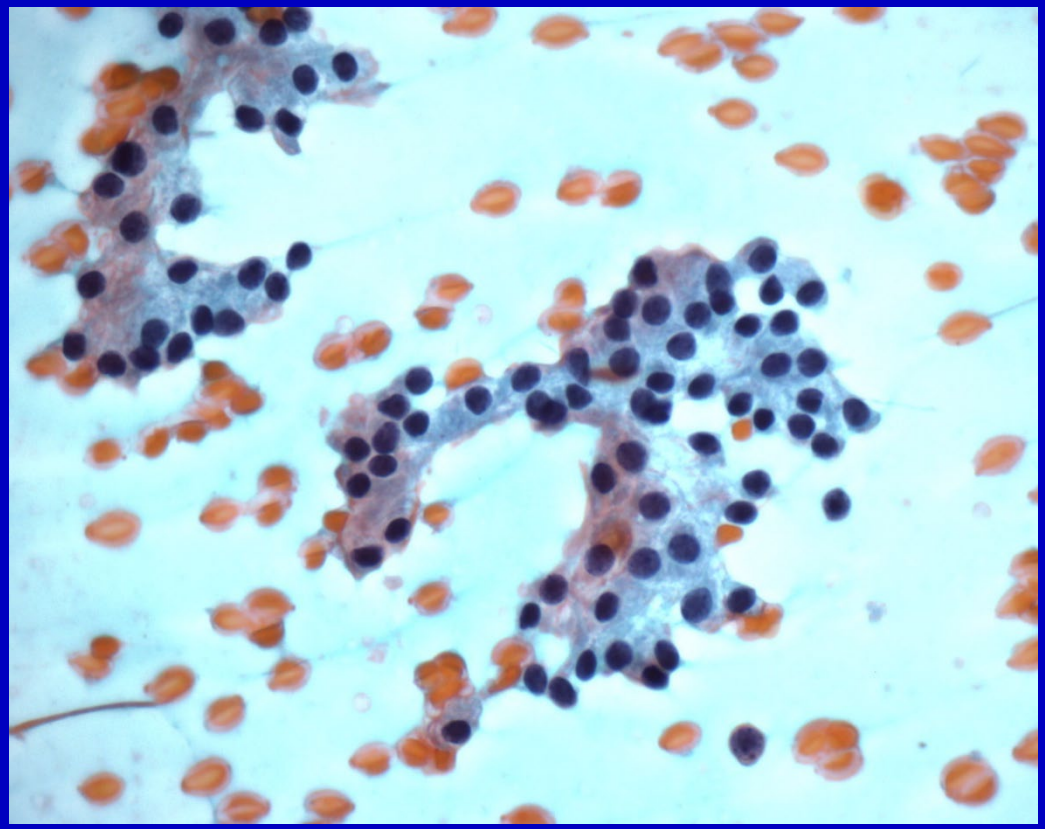
Benign Thyroid Nodule

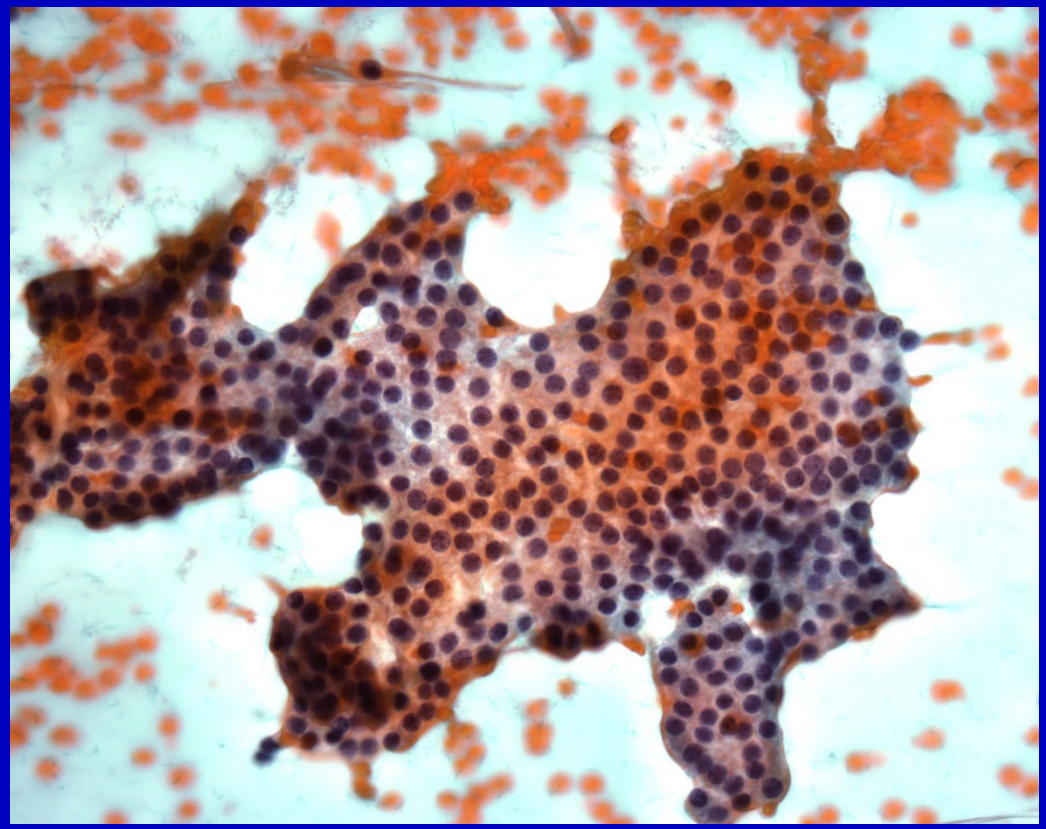
Macrofollicular fragments + colloid



Benign Thyroid Nodule

Flat macrofollicular fragments



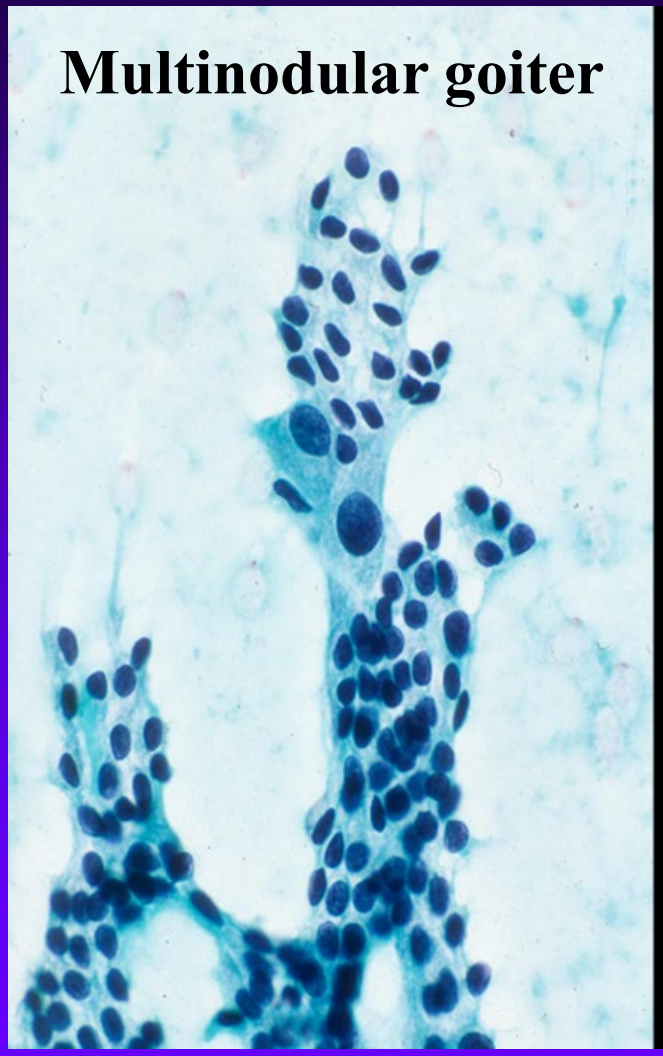


KEY POINT

- **Benign =**
  - **Macrofollicular fragments**
  - **Colloid**

Benign Atypia in Follicular Lesions

- Atypia is generally not a useful feature in the evaluation of follicular thyroid lesions
- Mild to moderate atypia is common



Why are some thyroid FNAs signed-out as NON-DIAGNOSTIC?

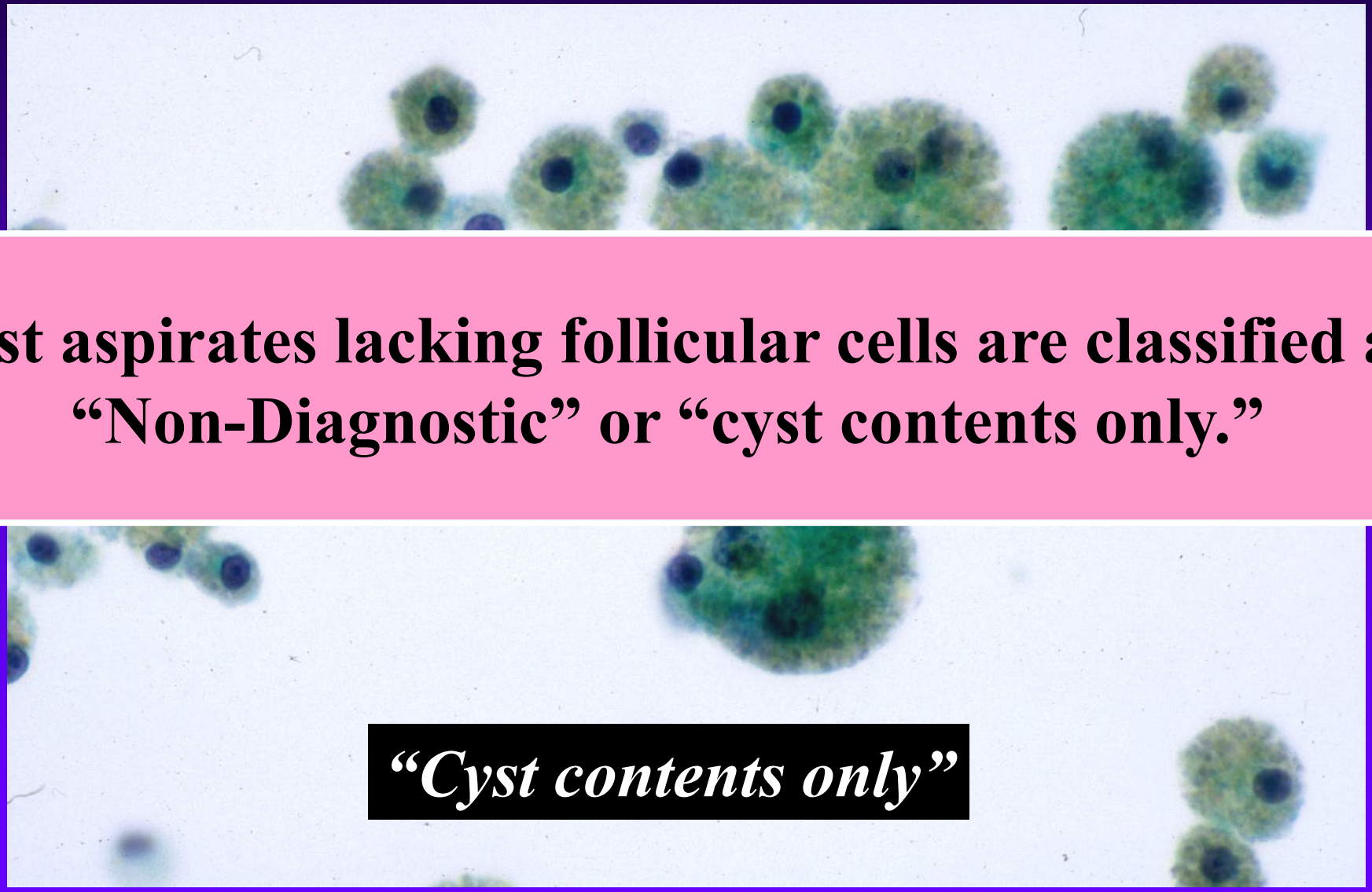
KEY POINT

Criteria for Adequacy

Satisfactory smears: At least six groups of follicular cells with at least 10 cells per group

- **Approx. 5-20% of thyroid FNAs are Non-Diagnostic.**

Non-Diagnostic Thyroid FNAs Will Usually Get a Repeat FNA



Cyst aspirates lacking follicular cells are classified as "Non-Diagnostic" or "cyst contents only."

EXCEPTION TO ADEQUACY RULE:

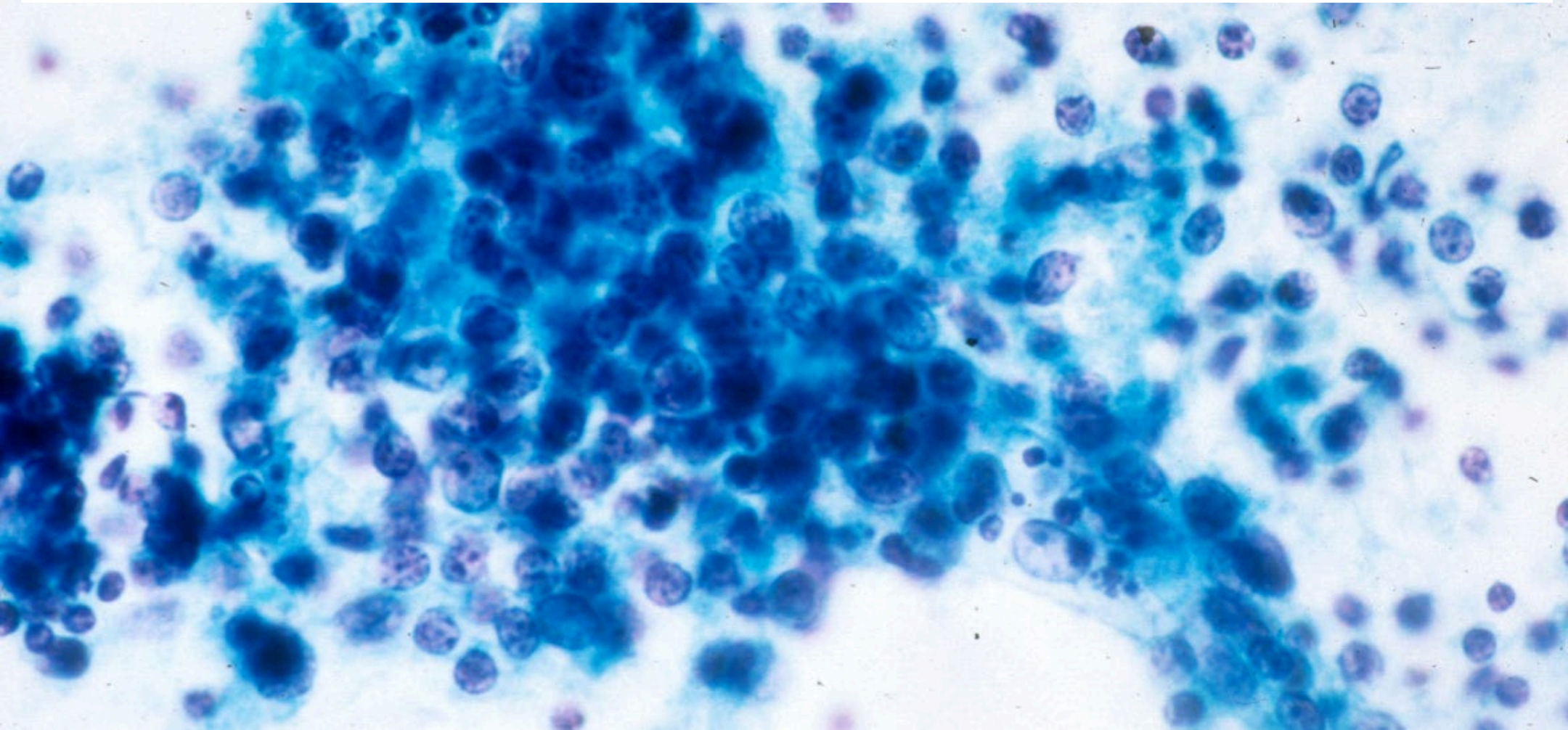
Colloid Nodule

Thyroid FNAs with abundant colloid only, can be placed into the BENIGN category.

EXCEPTION TO ADEQUACY RULE:

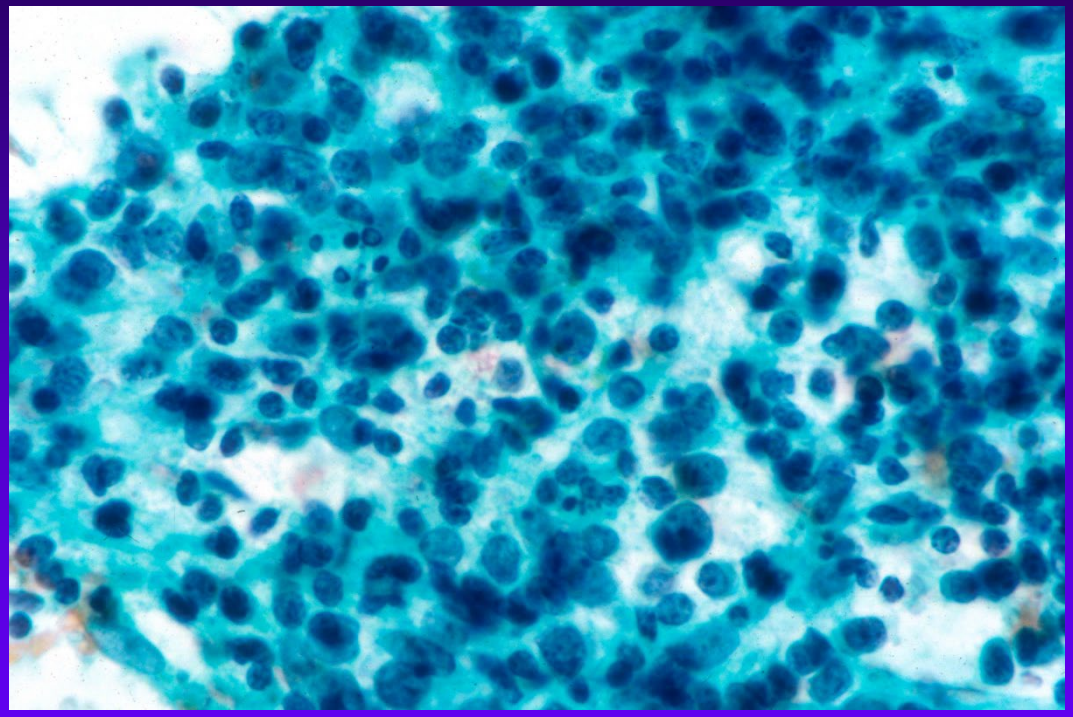
Inflammation only

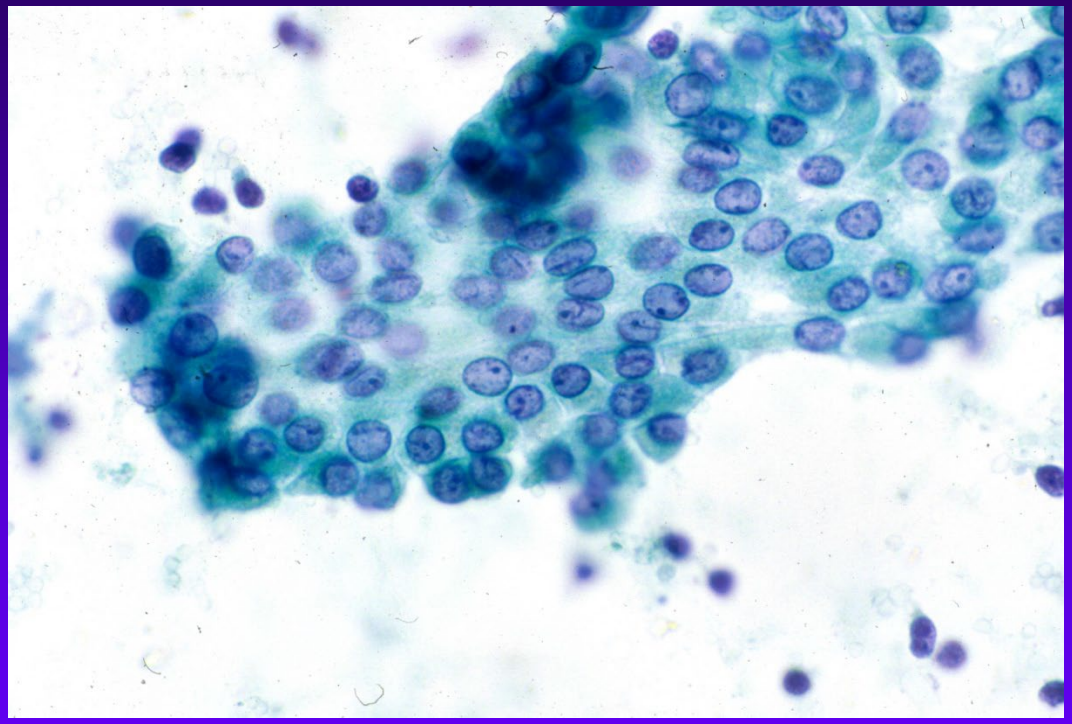
Thyroid FNAs with abundant inflamamtory cells only, can be placed into the BENIGN category.



HASHIMOTO'S THYROIDITIS

Lymphocytes + Oncocytes





3rd Edition of Bethesda System for Thyroid

The Indeterminate Thyroid FNA Comprises 15-30% of All Thyroid FNAs
Many are NIFTP !!!

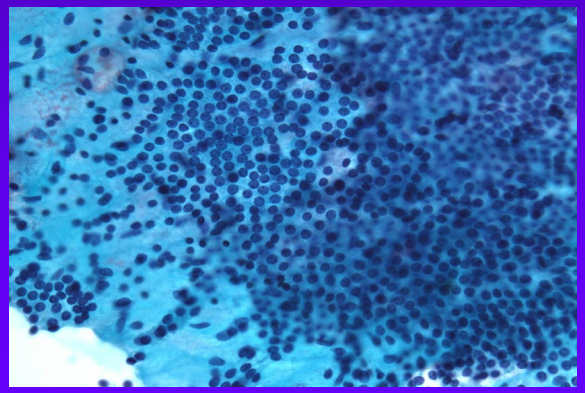
Category	Management	Implied Risk of Malignancy (%)
Non-Diagnostic	Repeat FNA	5-20%
Benign	Follow-up	2-7%
AUS- (*Nuclear atypia vs Other*)	Repeat FNA Lobectomy Surveillance Molecular Test	13-30%
Follicular Neoplasm	Lobectomy Molecular Test	23-34%
Follicular Neoplasm: Oncocytic FN	Lobectomy Molecular Test	23-34%
Suspicious for Malignancy	Lobectomy/ Total Thyroid Molecular Test	67-83%
Malignant	Lobectomy/ Total Thyroid	97-100%

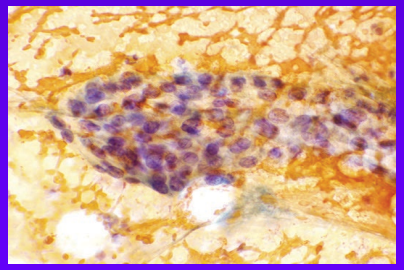
What is Atypia of Undetermined Significance? (AUS)

TBSRTC: AUS in 2024

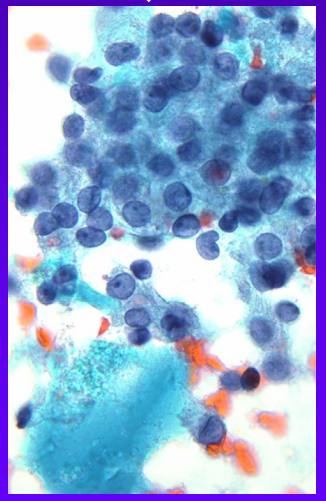
16 Years Old Now!!!

Benign

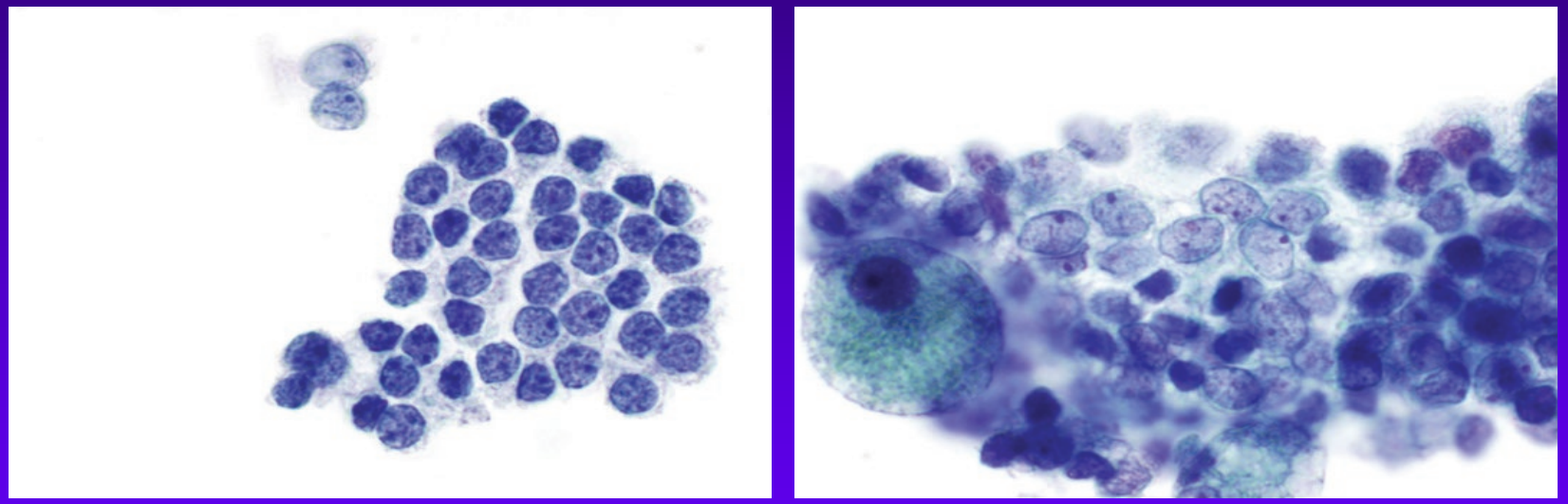




Follicular Neoplasm

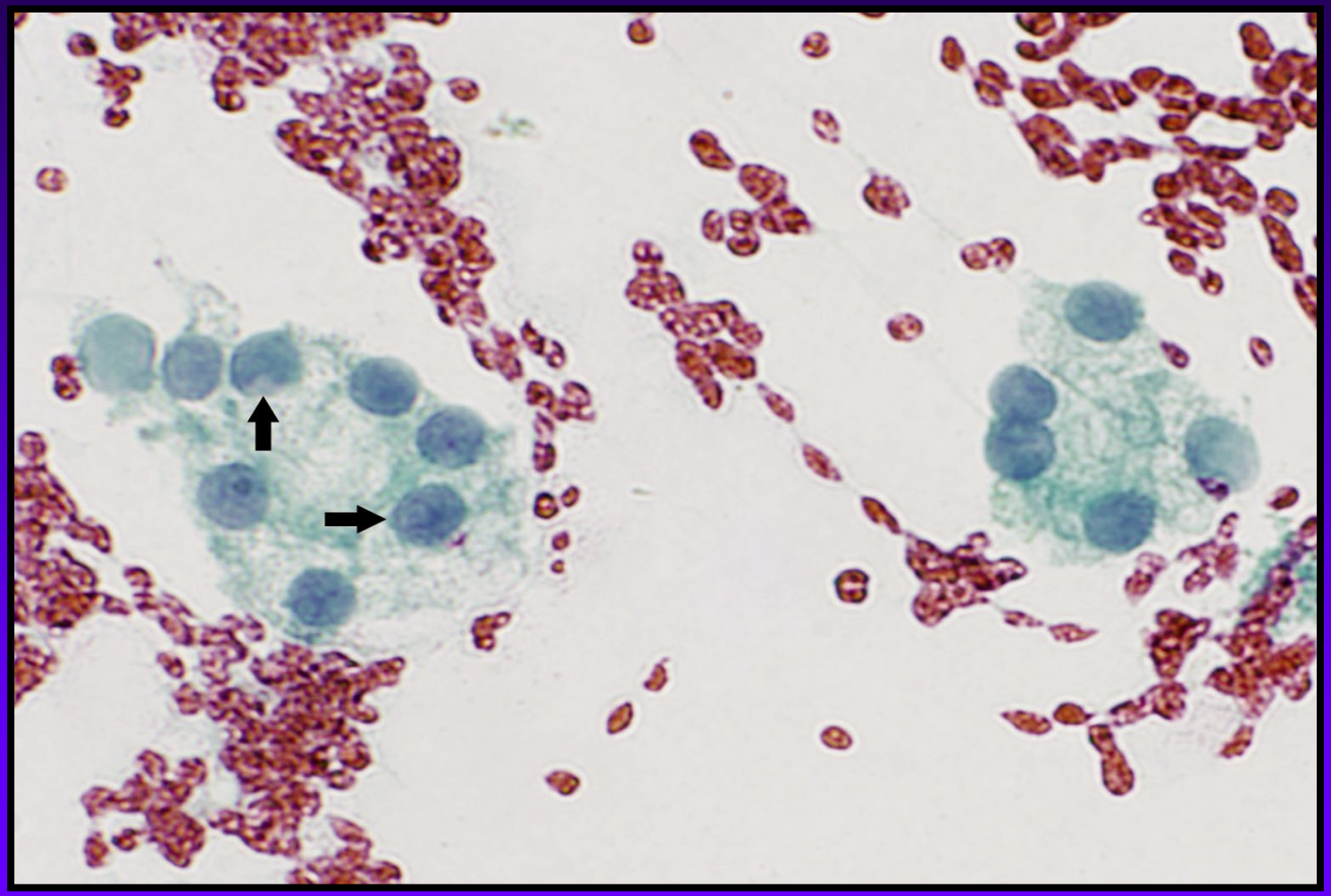


AUS – Nuclear Atypia Scenario: Focal Features of Papillary Carcinoma



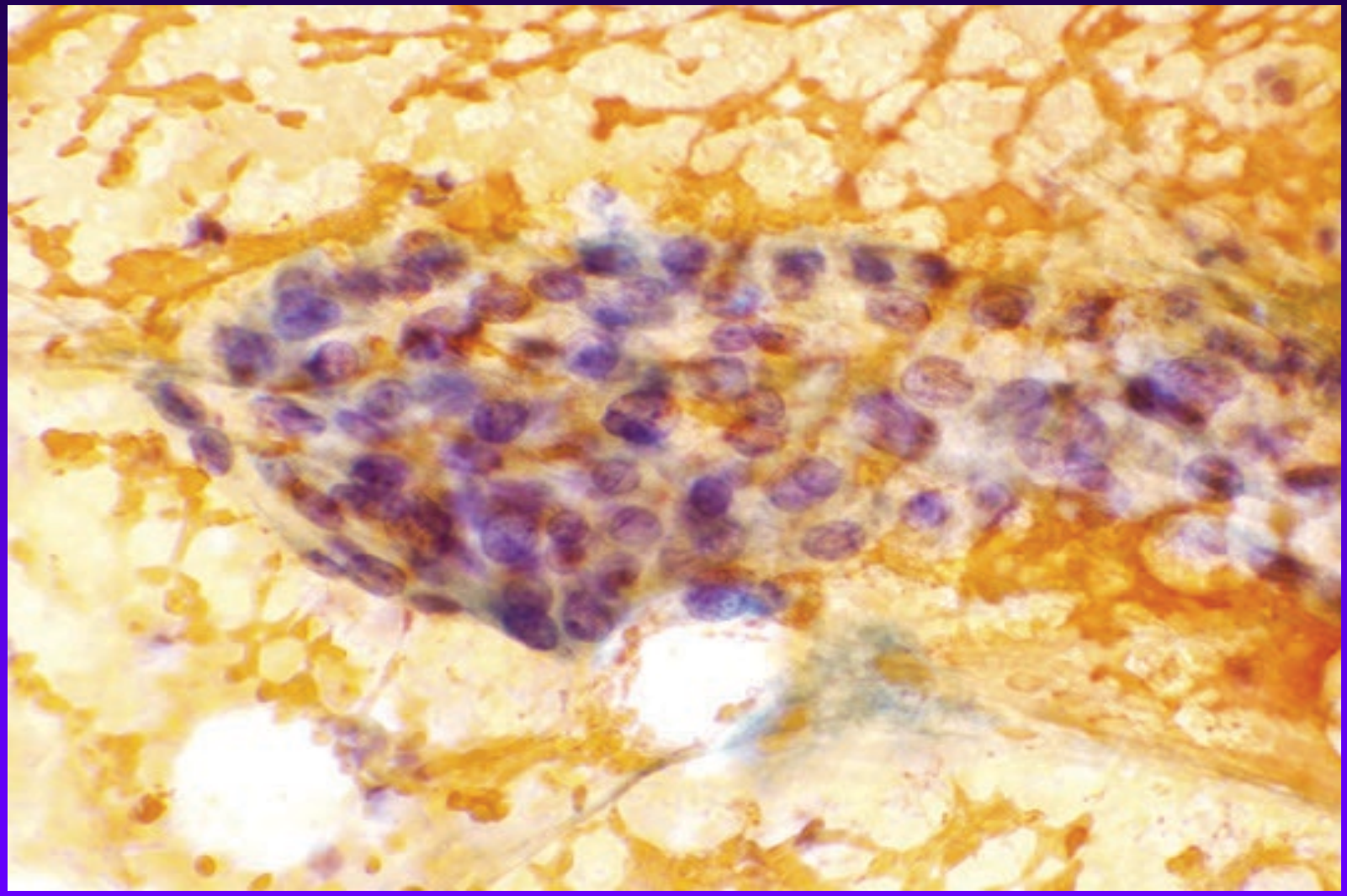
Figs. 4.5 A and B, The Bethesda atlas

AUS – Nuclear Atypia Scenario: Preparation Artifact and Mild Atypia



Air-drying of Pap-stained smear (Fig. 4.2, The Bethesda Atlas)

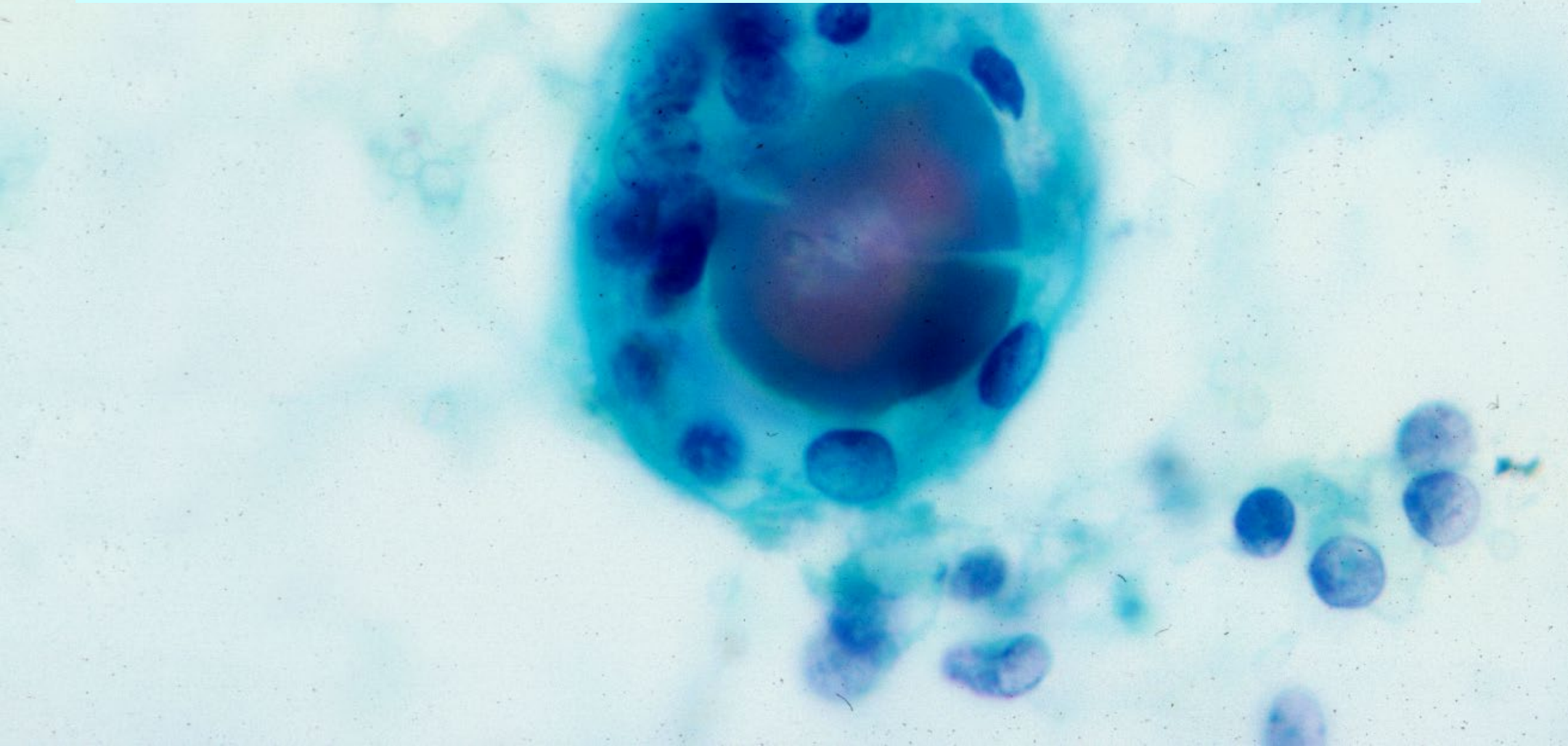
AUS – Nuclear Atypia Scenario: Blood Artifact



Obscuring blood and mild atypia

AUS- Other: Hypocellular but Microfollicular

What features are used to diagnose an FNA as “Follicular Neoplasm?”



FNA as a Screening Test for Follicular Carcinoma

The Riddle

If the criteria for classifying these follicular-patterned lesions are purely histologic, what hope is there for FNA?

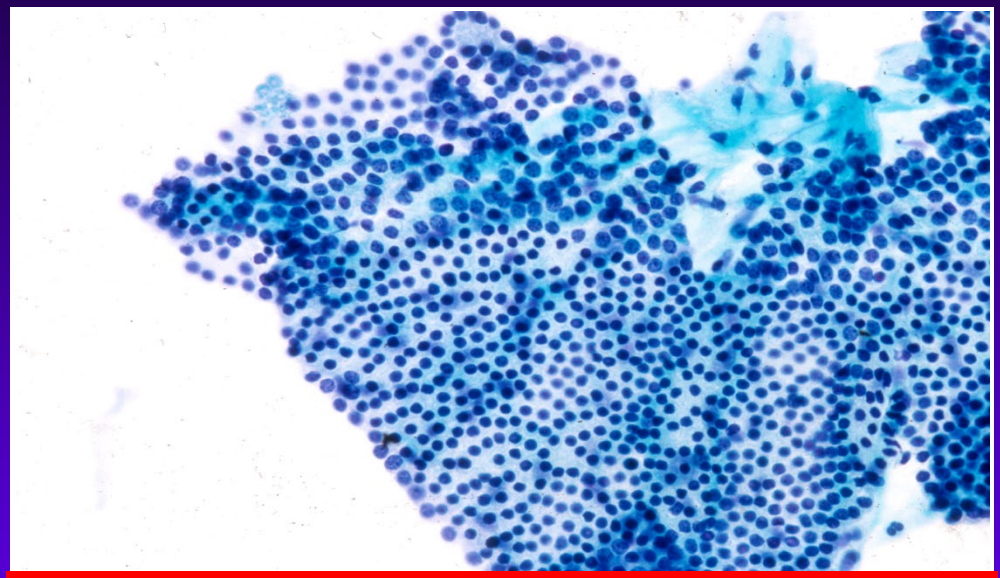
FNA as a Screening Test for Follicular Carcinoma

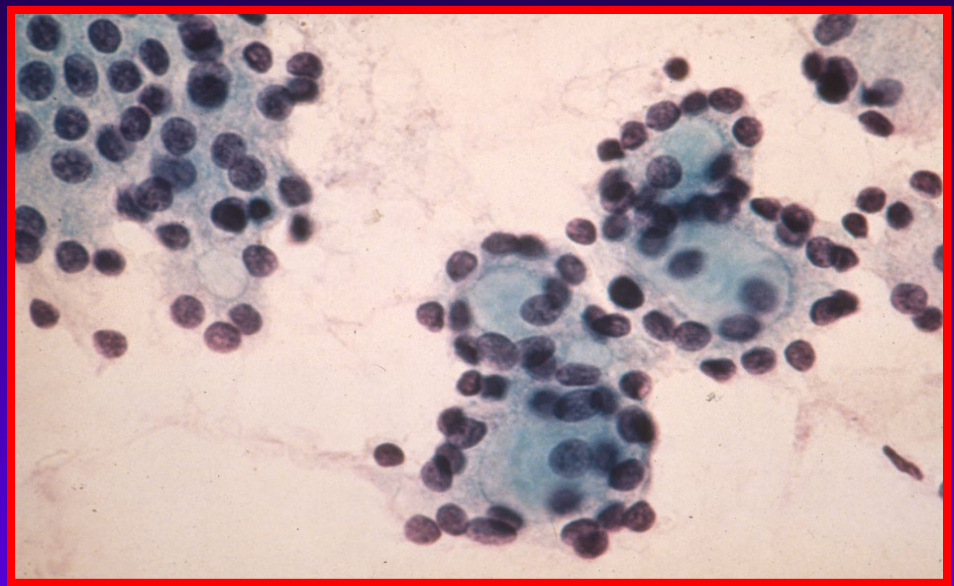
Multinodular goiter
Adenomatous nodule

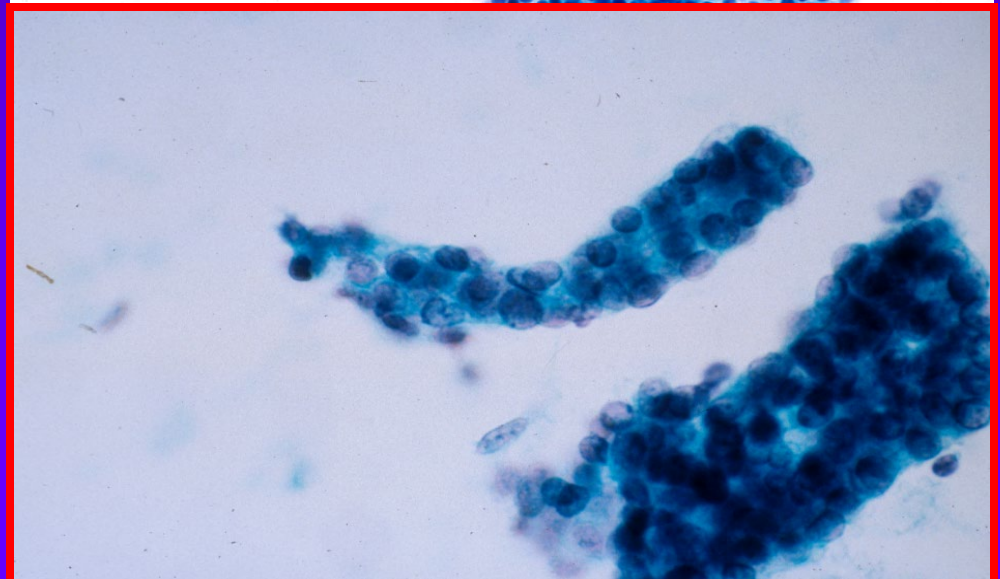
Follicular adenoma
- Macrofollicular
- Microfollicular
- Trabecular
- Solid

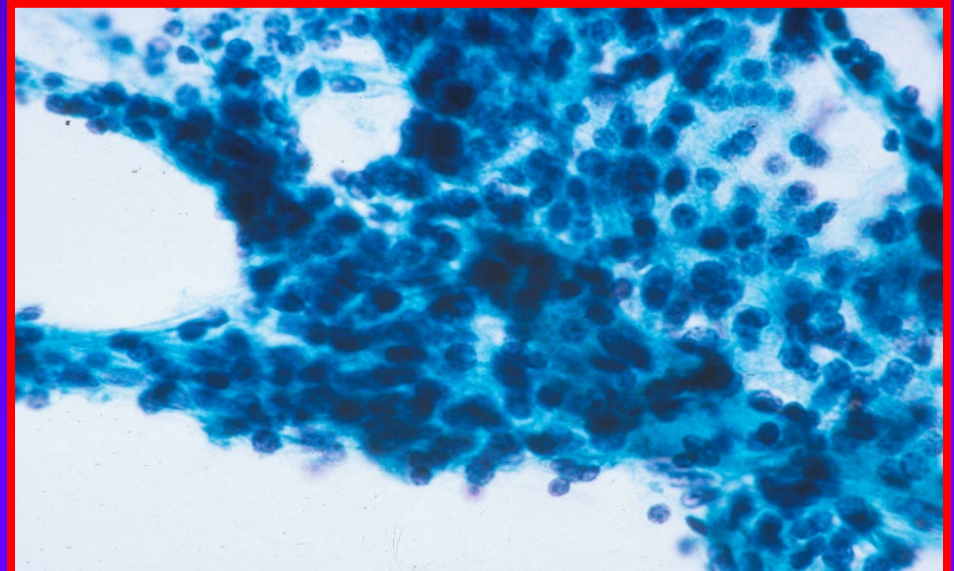
Follicular carcinoma

FNA as a Screening Test for Follicular Carcinoma









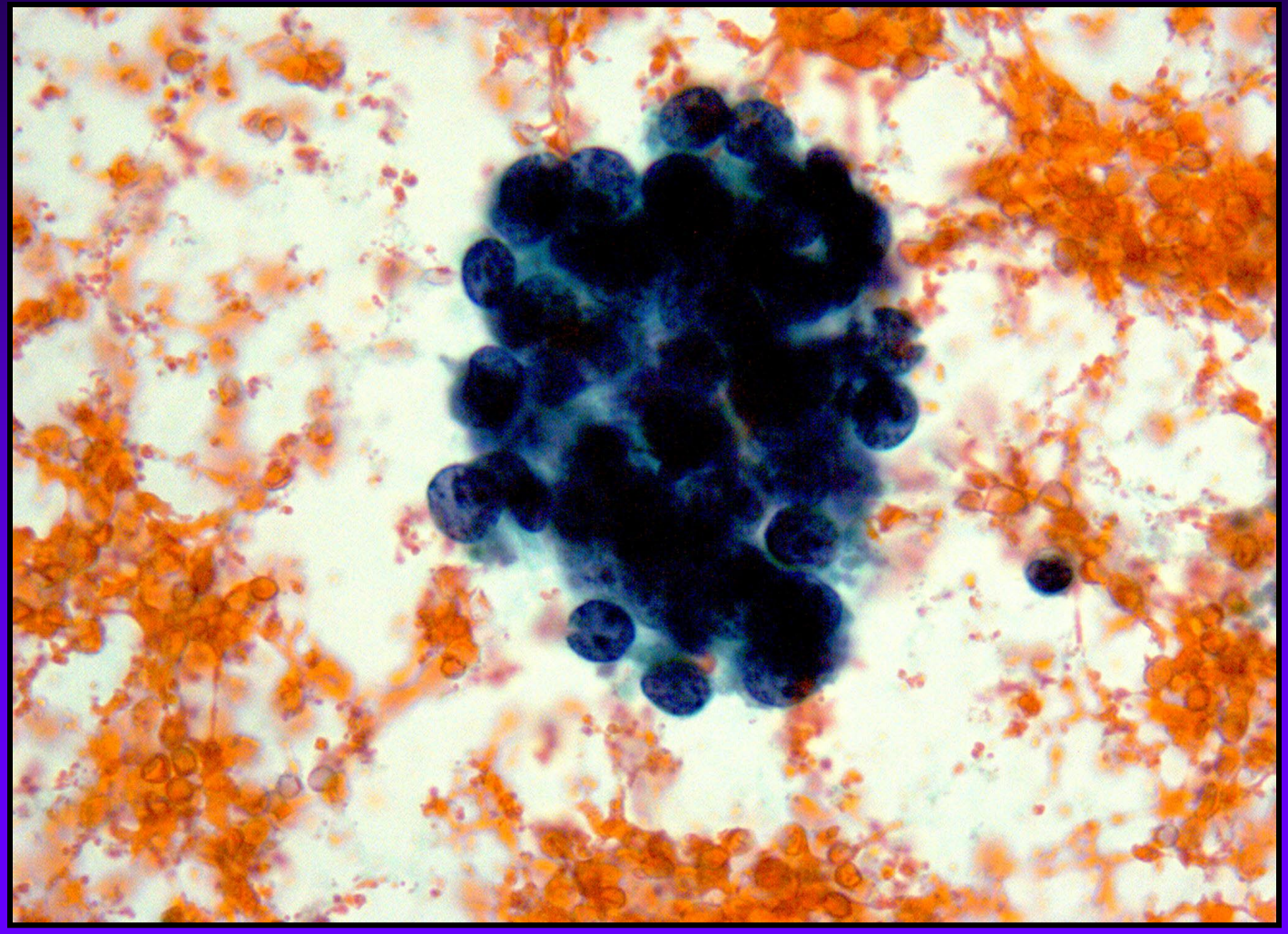
KEY POINT

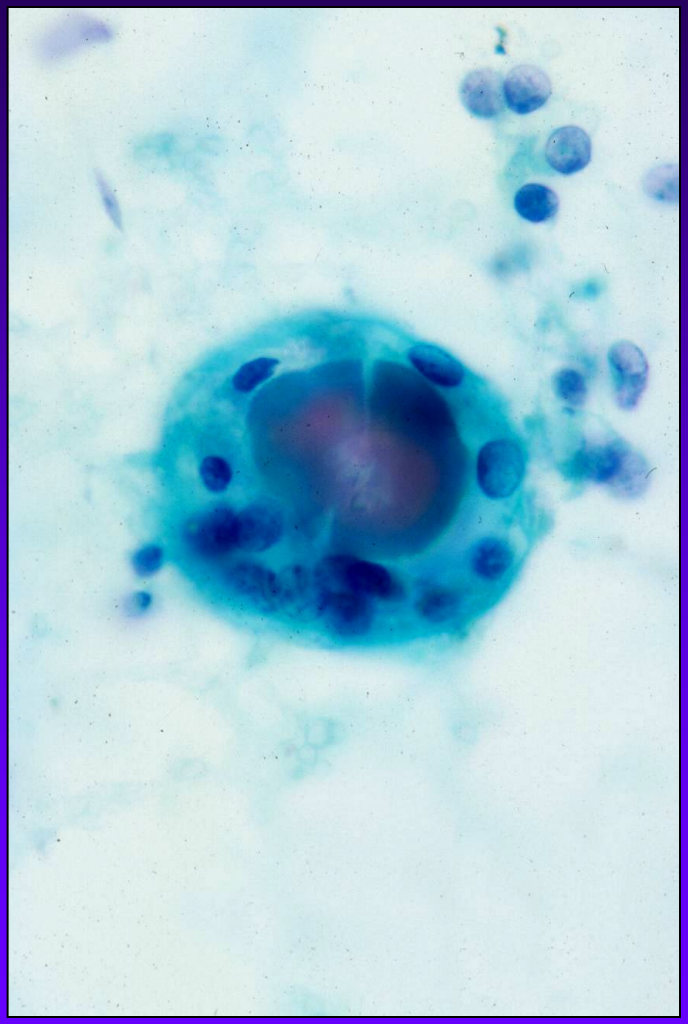
One microfollicle is NOT enough!

- **All follicular lesions are a mixture of micro- and macrofollicles.**

- **Focus on the predominant pattern.**

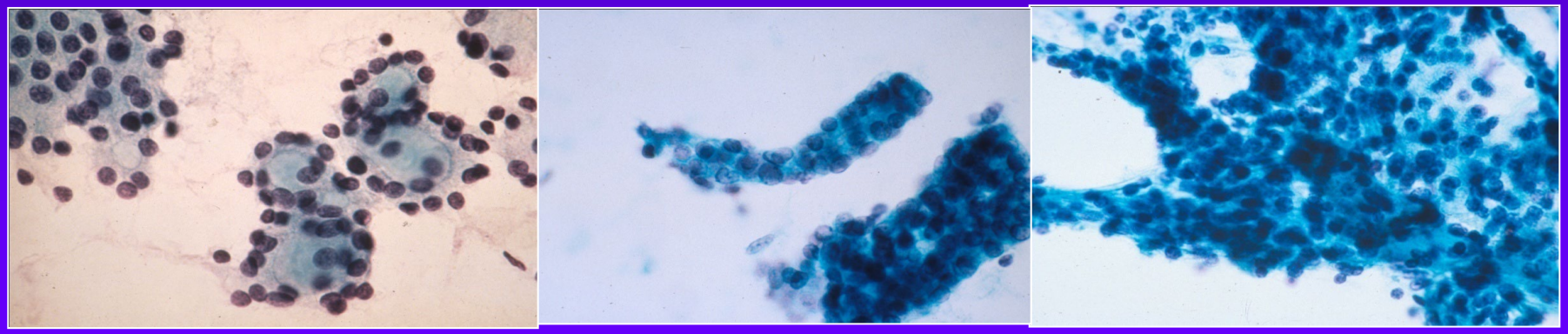
Follicular Neoplasm:
2-8% of All Thyroid Aspirates





Cytologic Reporting of Follicular Lesions

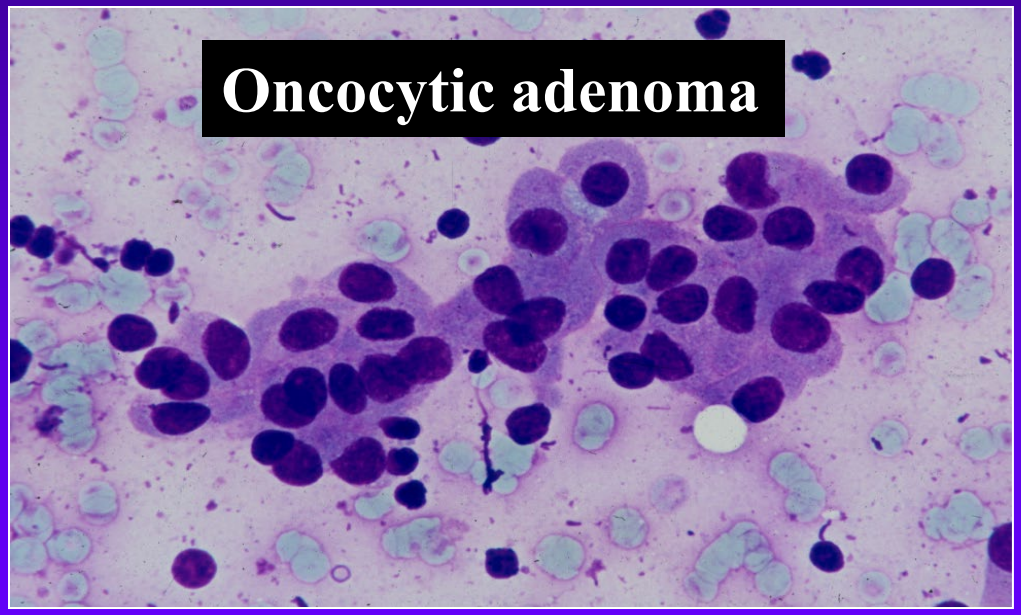
- **FOLLICULAR NEOPLASM (+/- Oncocytic Features)**
  - ***Note: Distinction between a follicular adenoma and follicular carcinoma is not possible based upon cytologic material.***

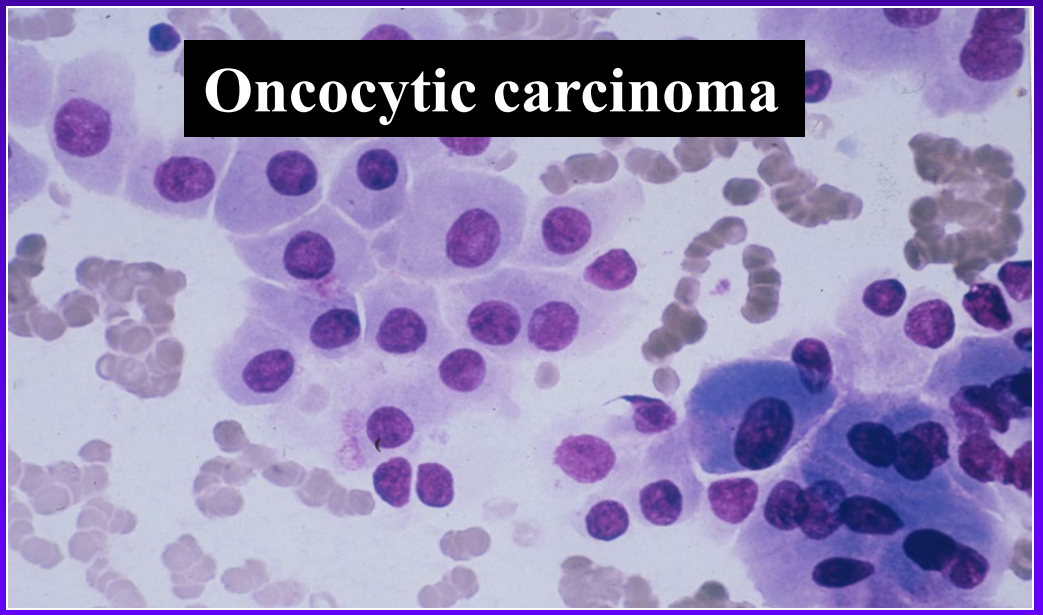



What are the features used to diagnose an FNA as “Oncocytic Follicular Neoplasm?”

FNA OF ONCOCYTIC NEOPLASMS

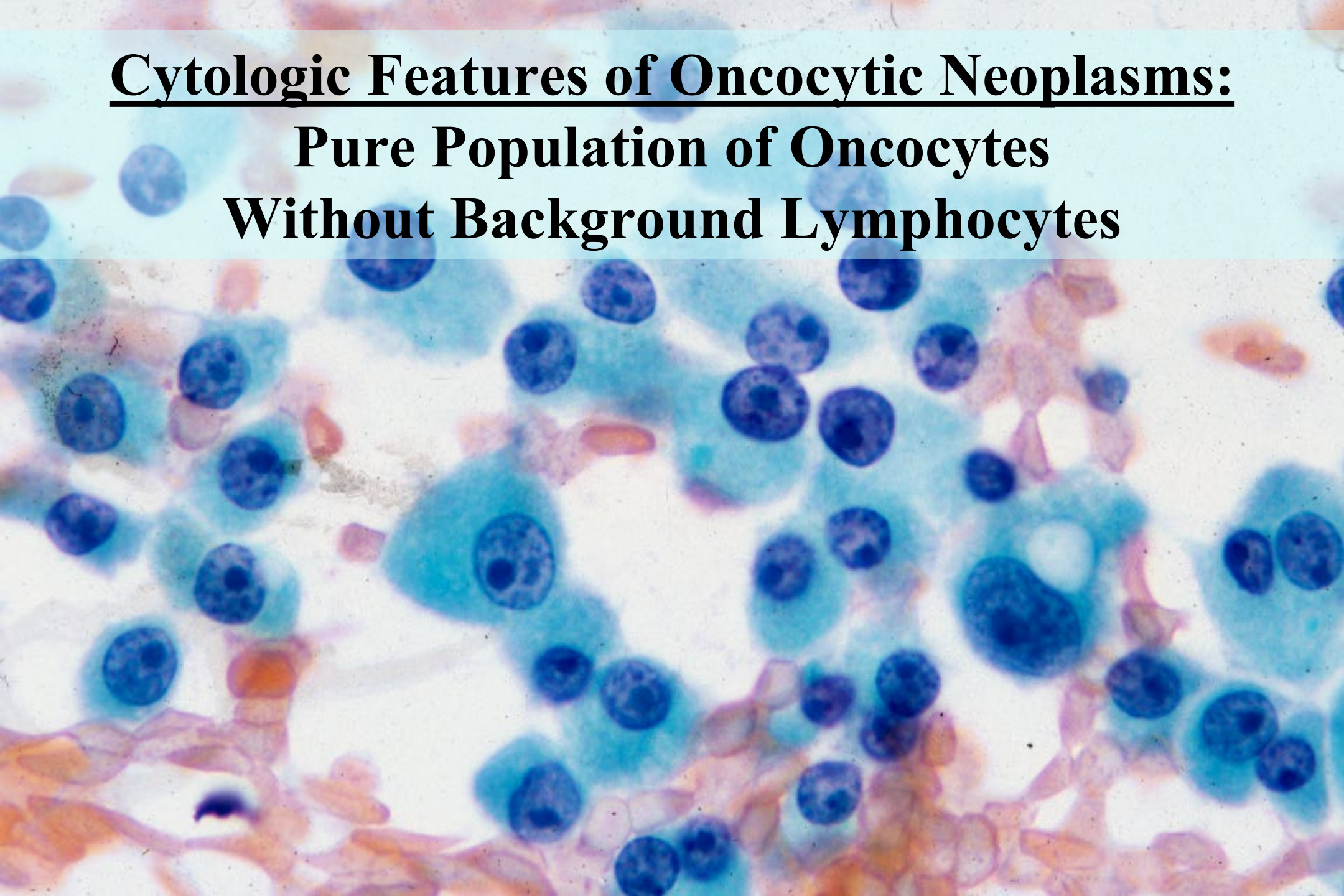
Both oncocytic adenomas and carcinomas are diagnosed by FNA as "Oncocytic Follicular Neoplasm."



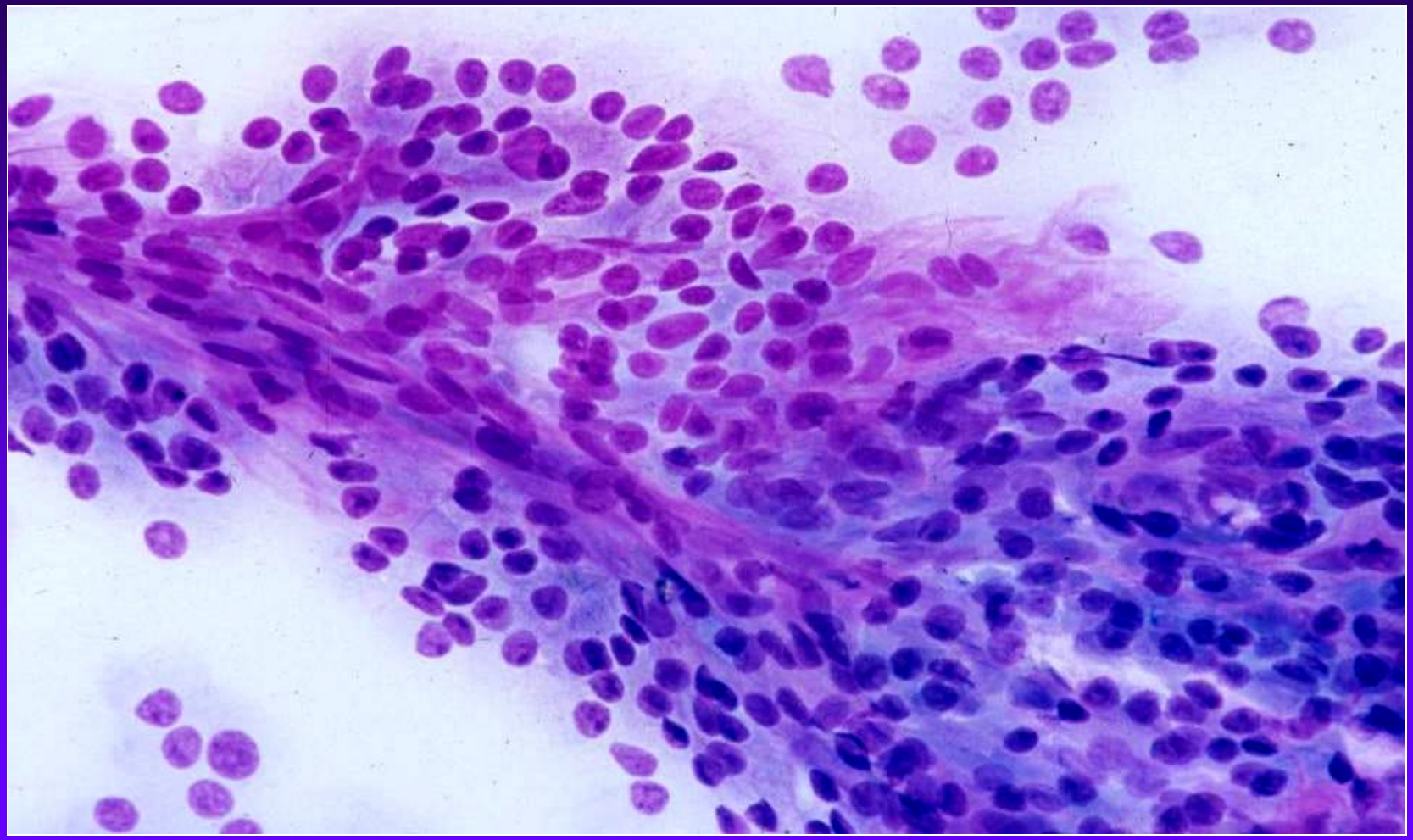


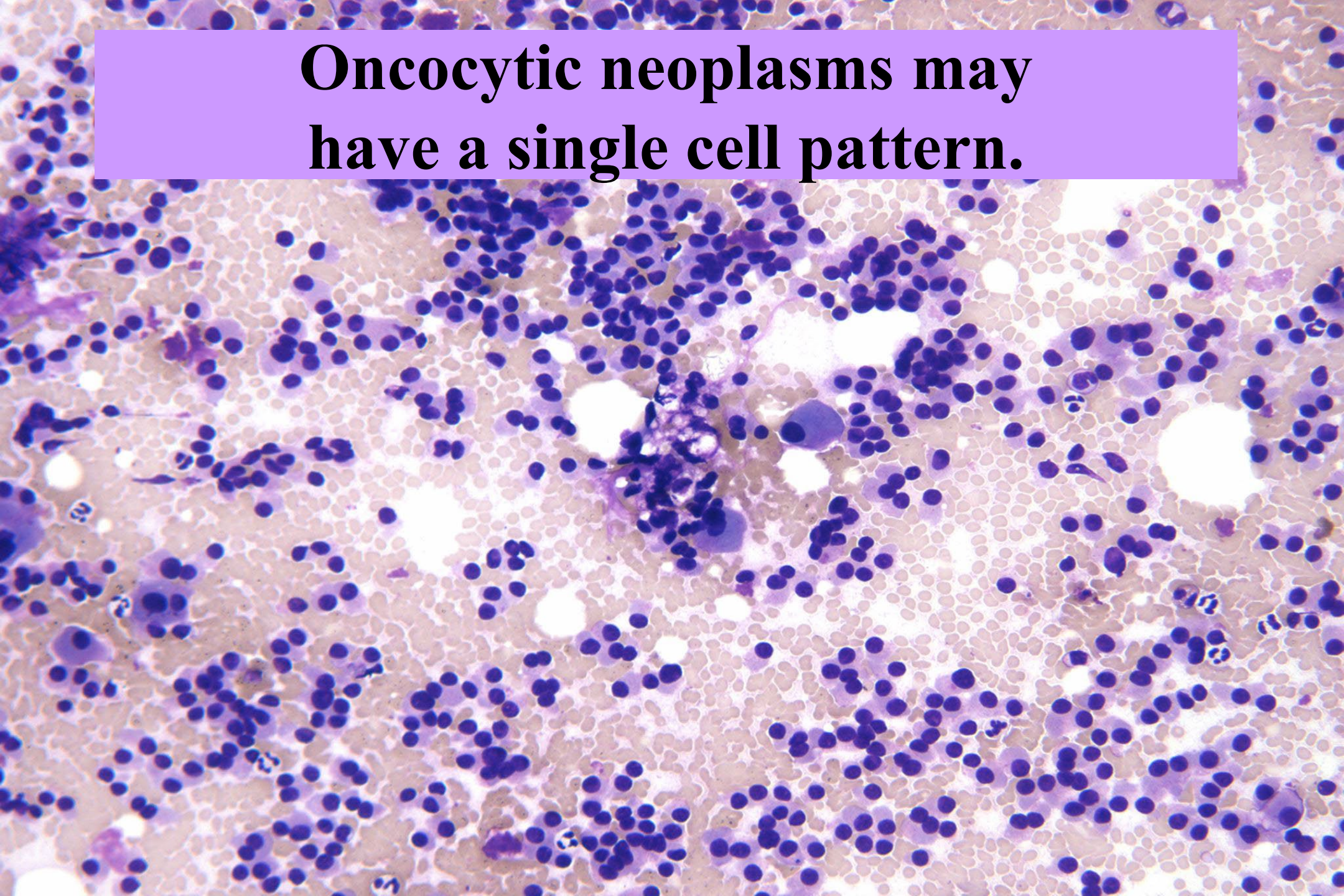
Cytologic Features of Oncocytic Neoplasms:

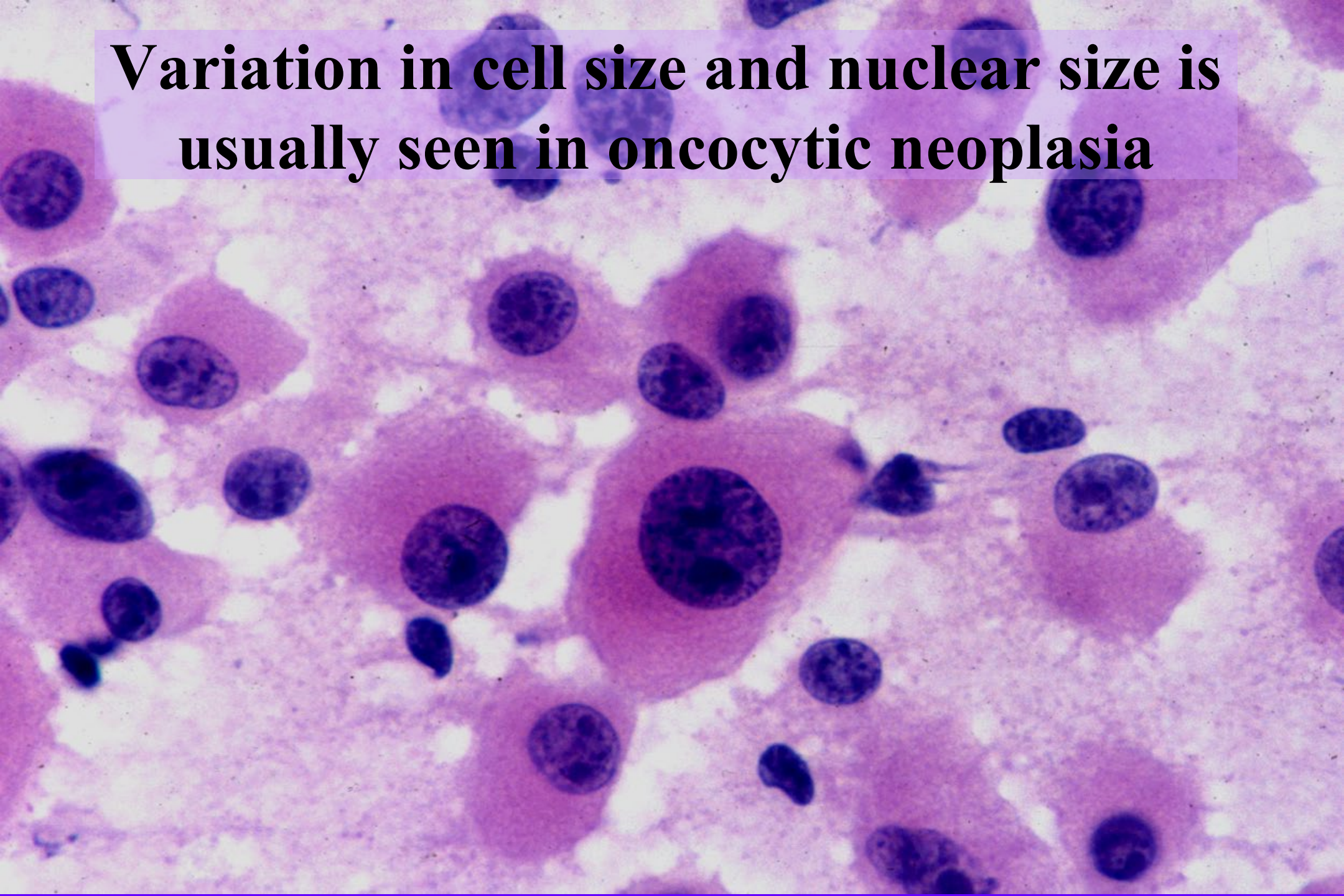
Pure Population of Oncocytes Without Background Lymphocytes



Cytologic Features of Oncocytic Neoplasms: Blood Vessels Traversing Groups are Common




Oncocytic neoplasms may
have a single cell pattern.


Variation in cell size and nuclear size is usually seen in oncocytic neoplasia

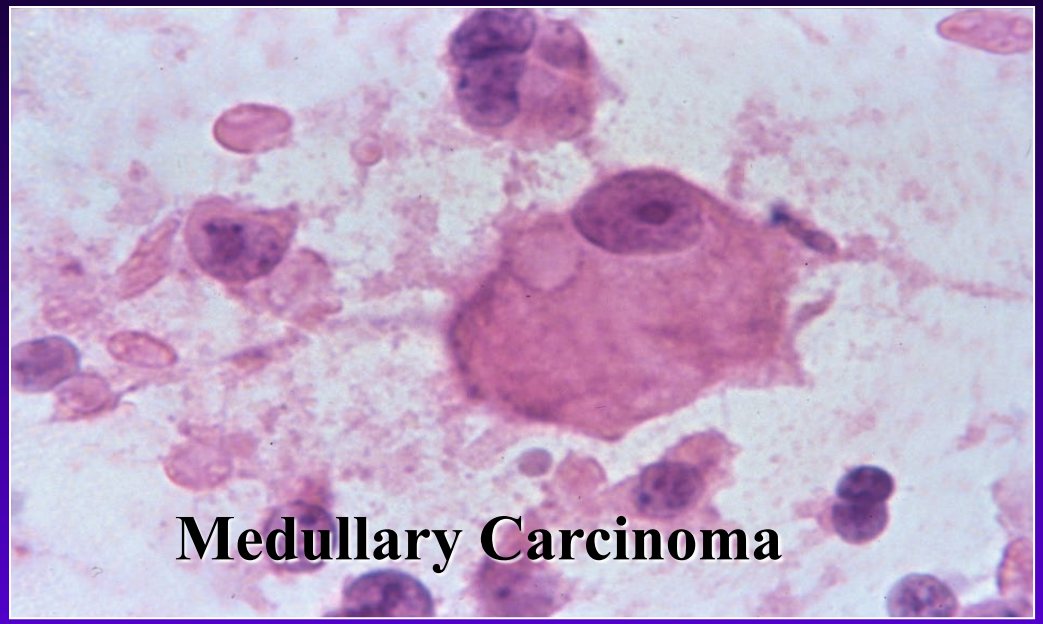
KEY POINT

- **Oncocytic Neoplasm =**
  - **Pure oncocytes**
  - **Absent colloid**
  - **Absent chronic inflammation**

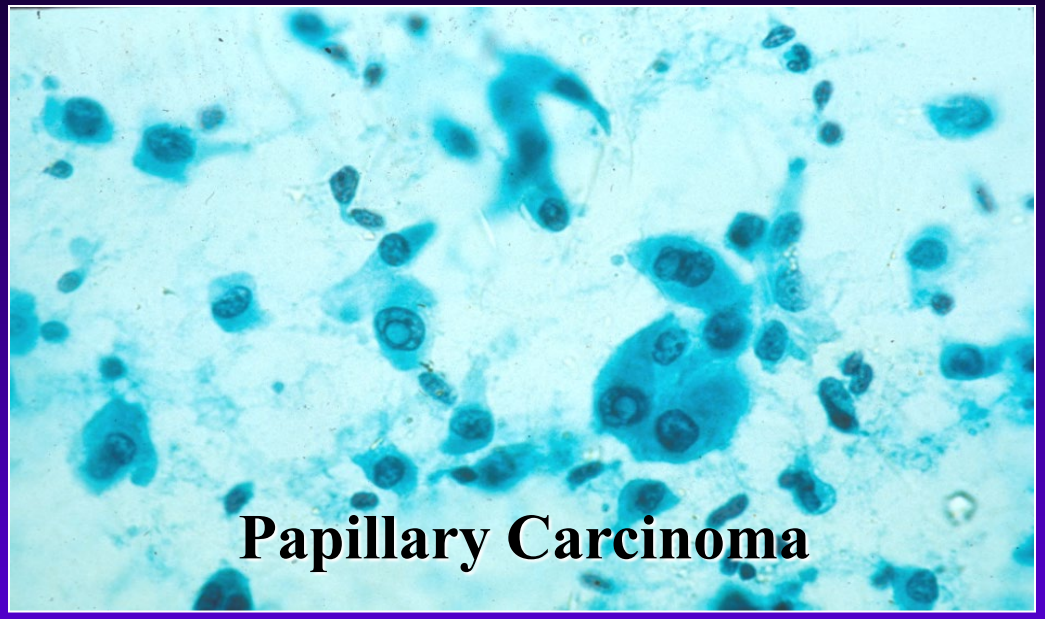
Why is it important to classify a thyroid lesion as "oncocytic?"

Because the DDX includes other important entities....

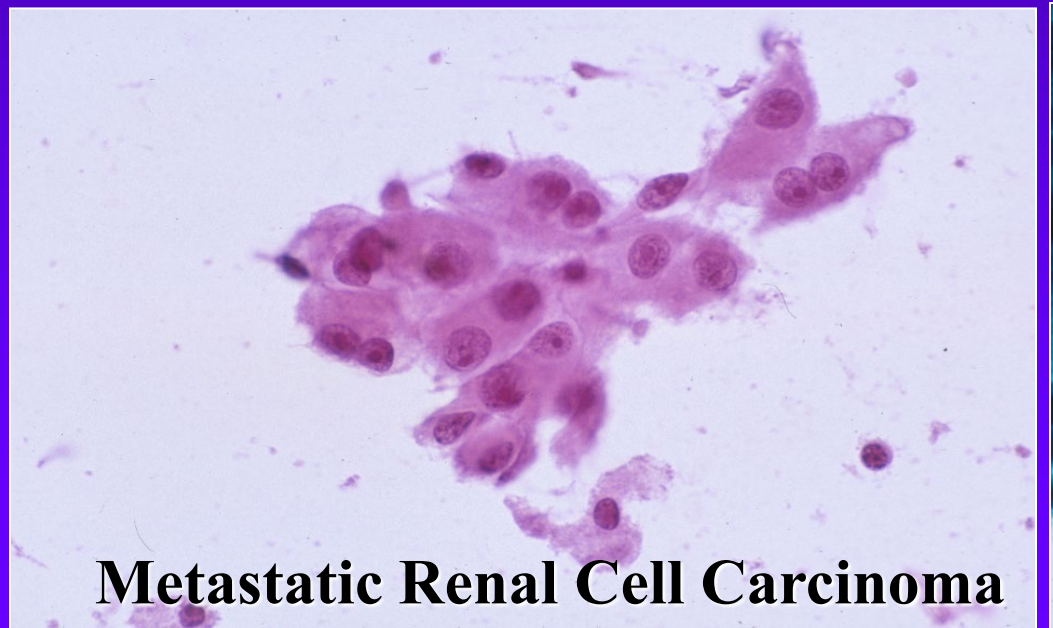
Oncocytic Neoplasms in the DDX



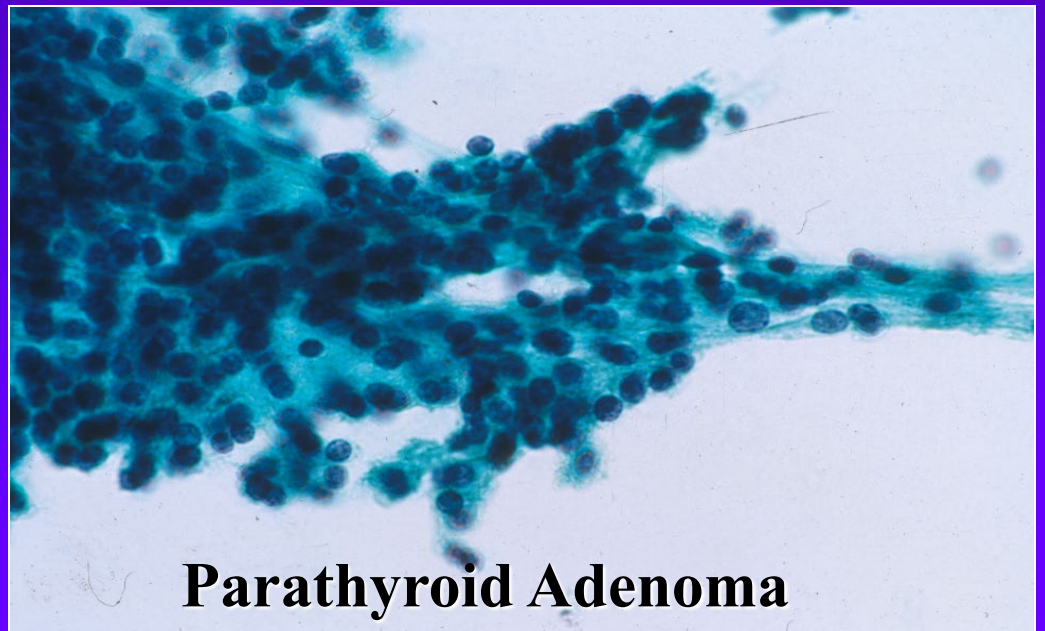
Medullary Carcinoma



Papillary Carcinoma



Metastatic Renal Cell Carcinoma

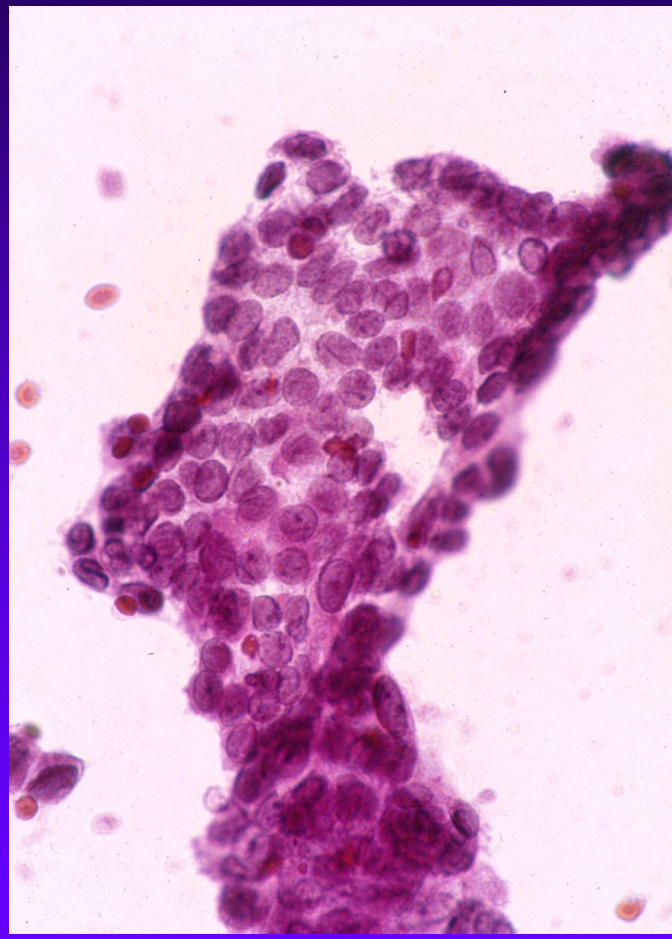


Parathyroid Adenoma


When do we diagnose an FNA as
“Suspicious for malignancy” or
“Malignant” in the Bethesda System?

Papillary Thyroid Carcinoma is the Most Common Cause of a "Suspicious/Malignant" Dx

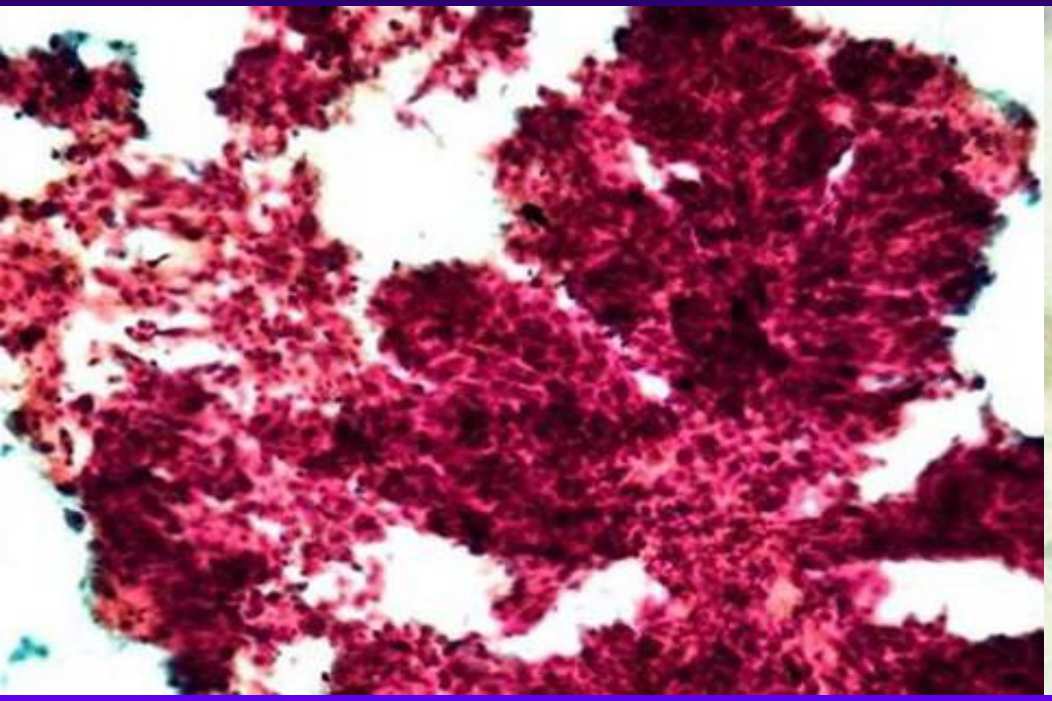
- **FNA is highly accurate:**
  - **>90% are diagnosed as positive or suspicious by FNA**

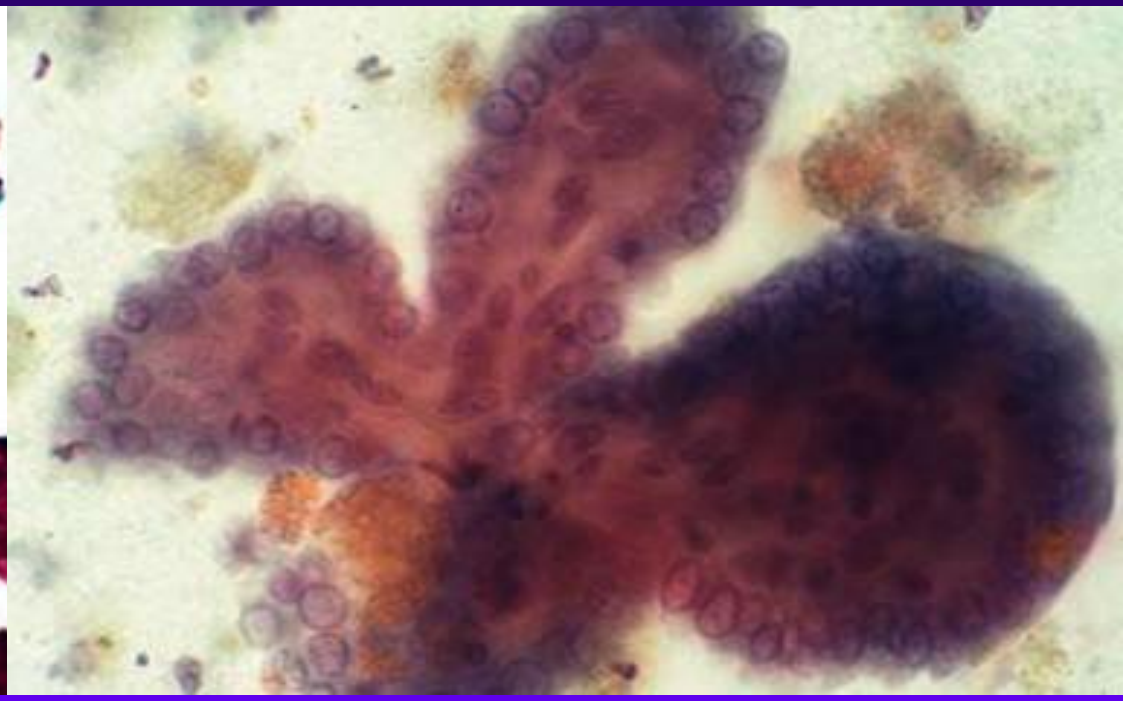


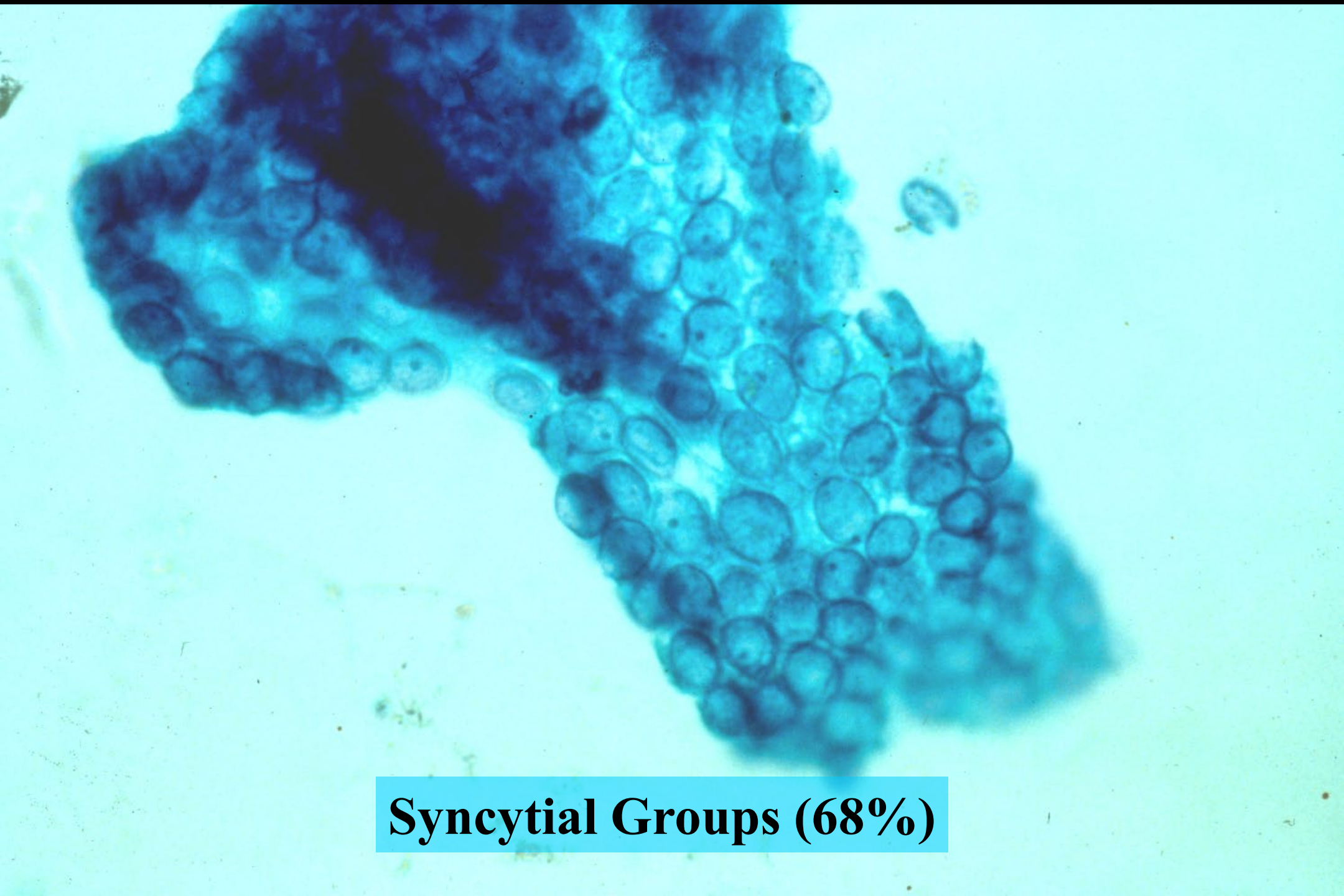
What are the BASIC features that we use to diagnose PTC by FNA?

Papillary Cytoarchitecture (88%)

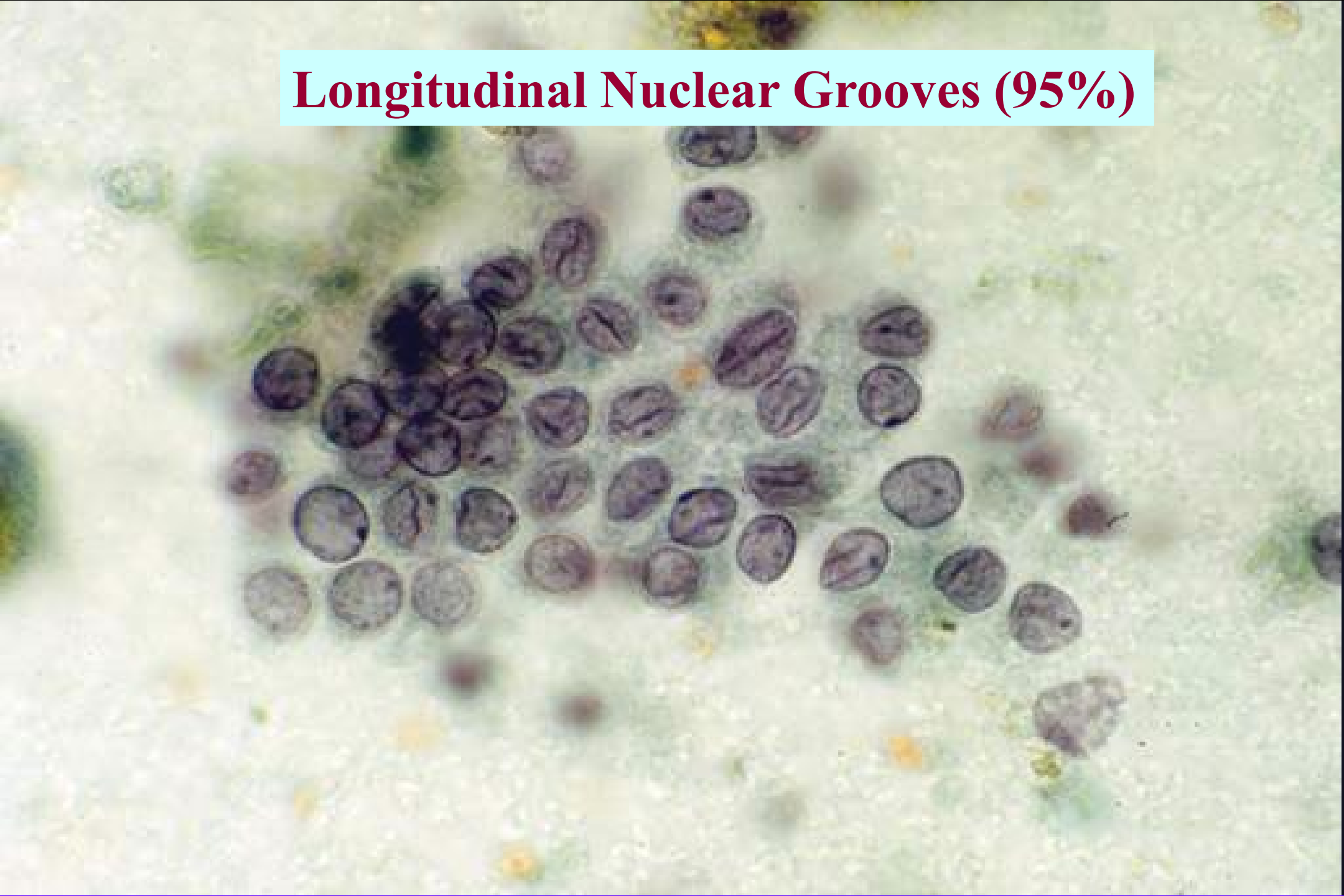
Essential to Exclude NIFTP

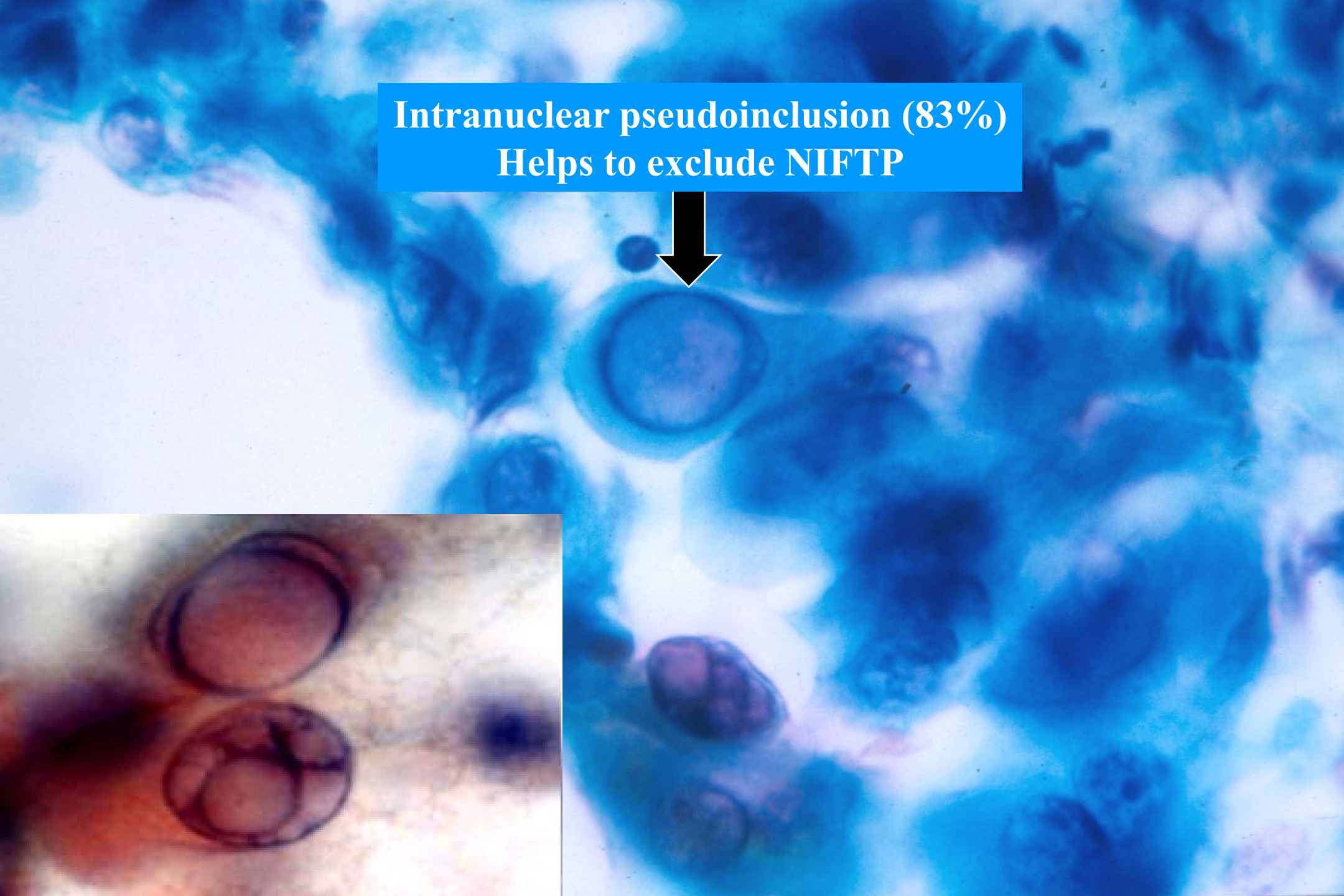


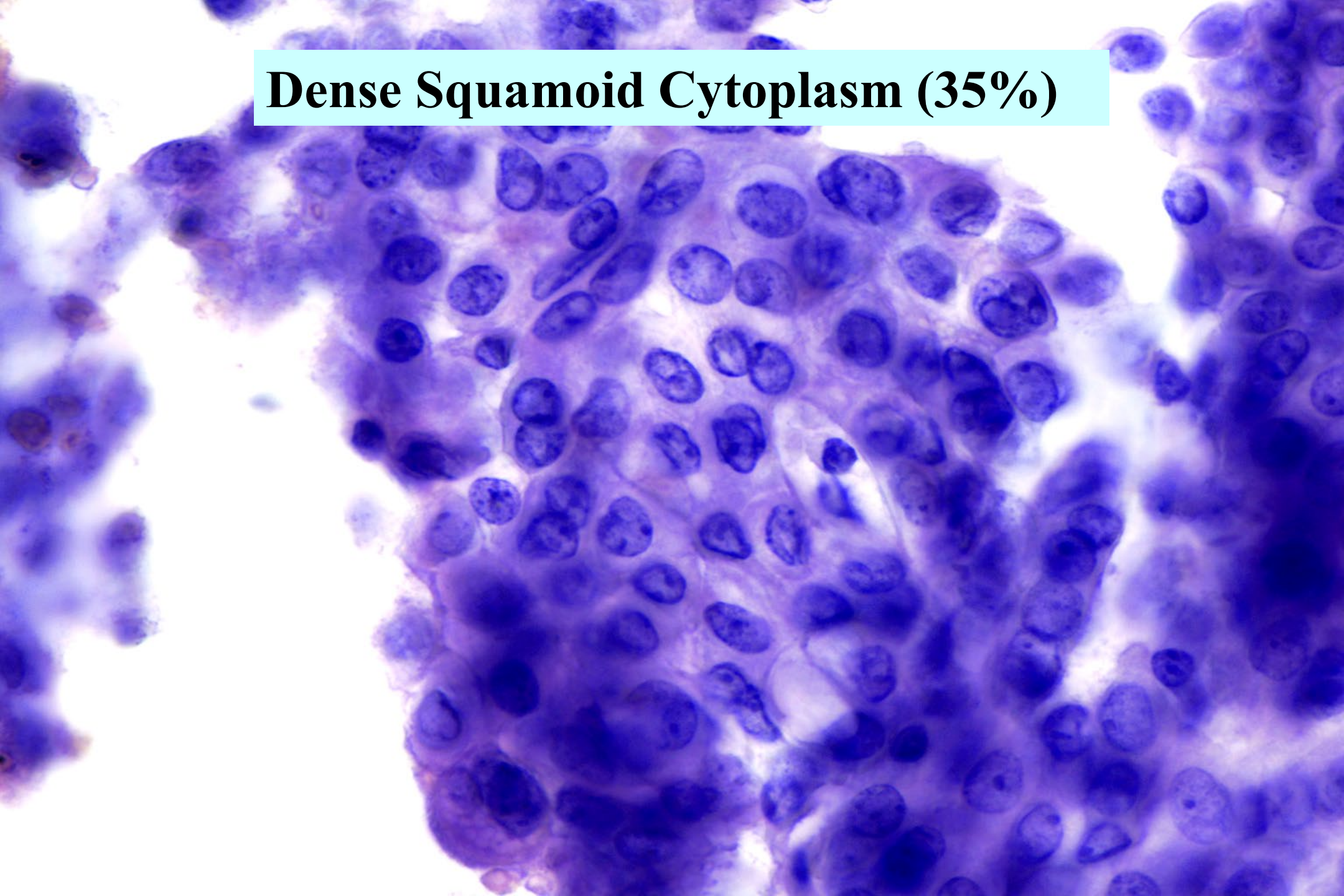


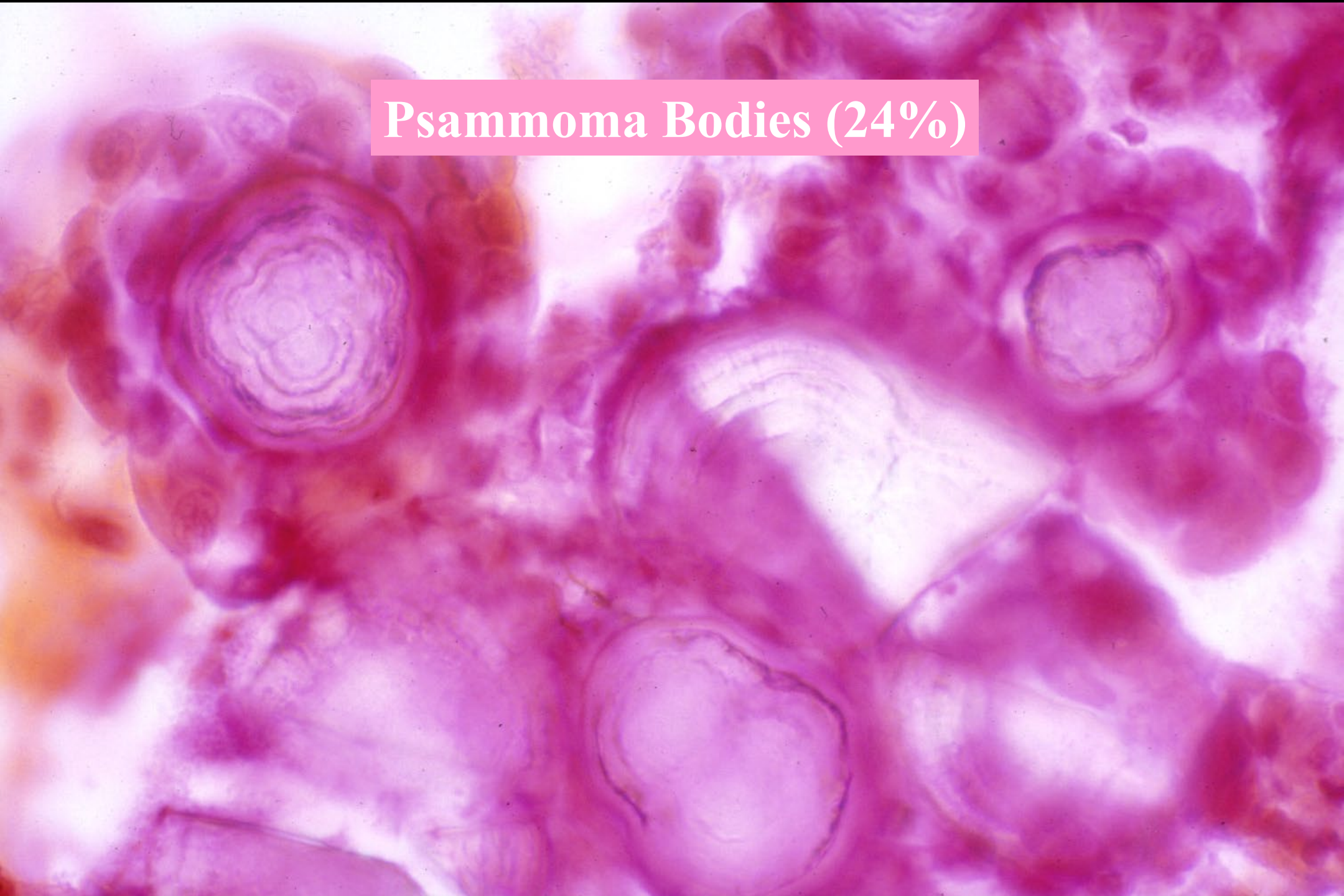

Syncytial Groups (68%)

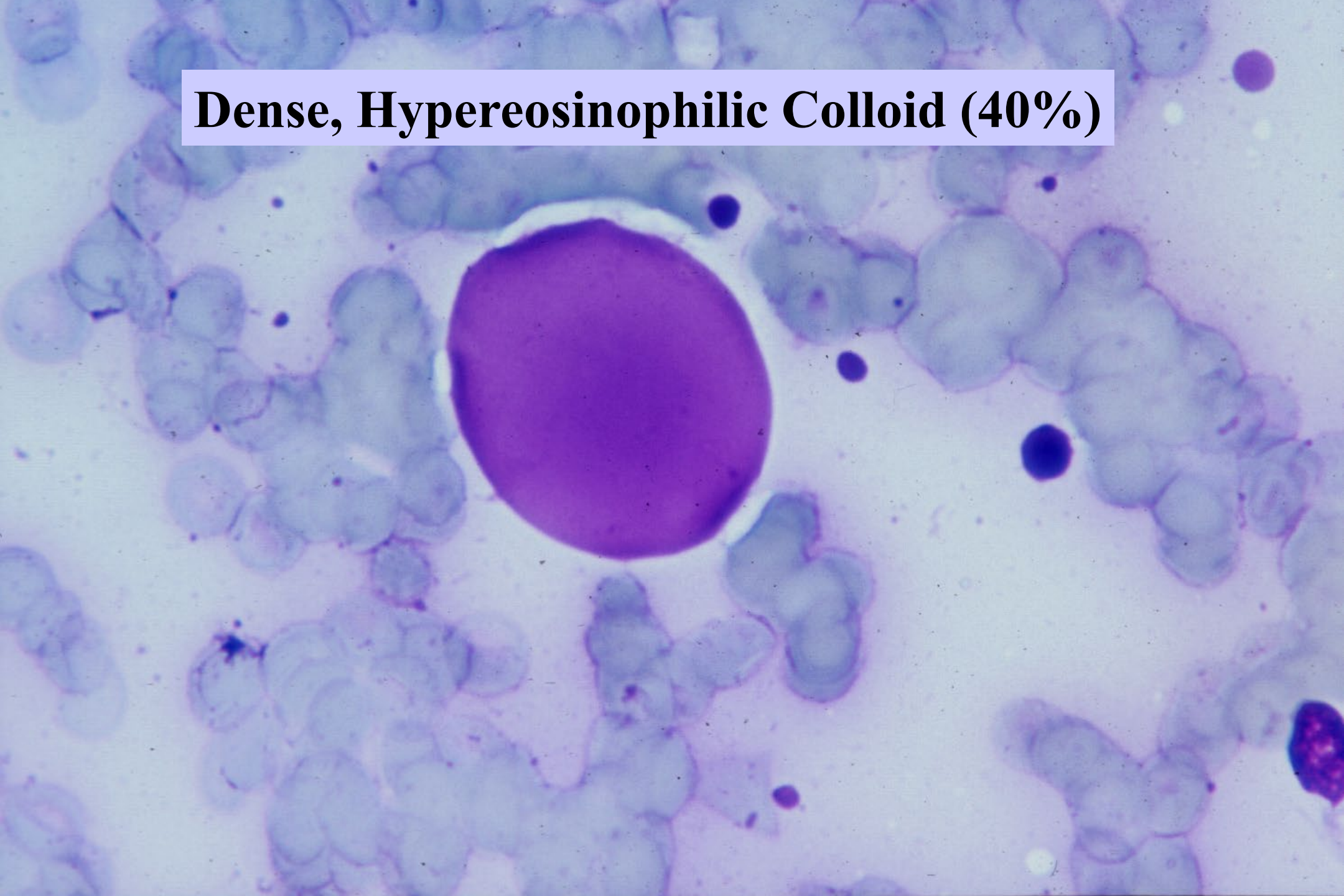
Longitudinal Nuclear Grooves (95%)

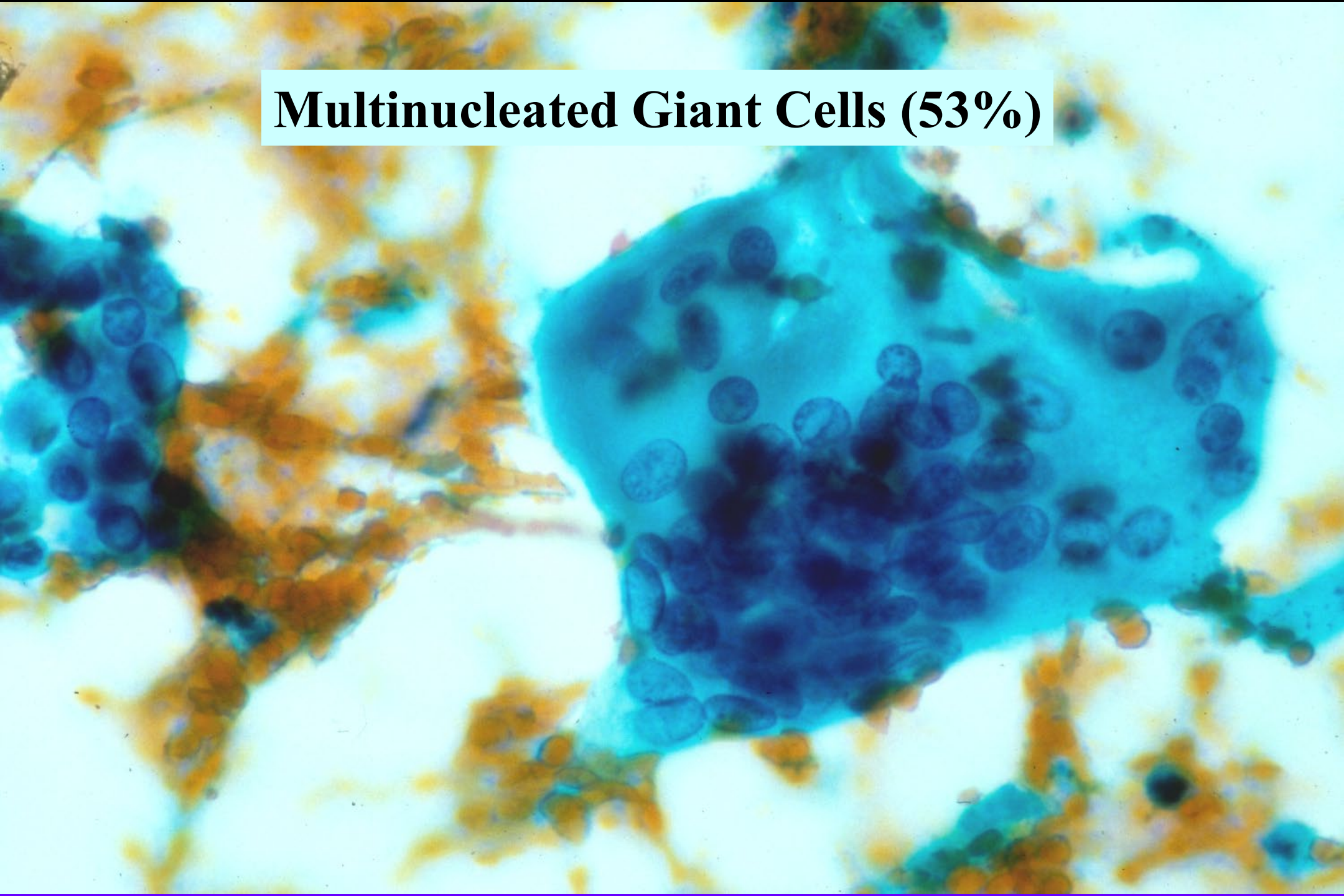



Intranuclear pseudoinclusion (83%)
Helps to exclude NIFTP


Dense Squamoid Cytoplasm (35%)


Psammoma Bodies (24%)


Dense, Hypereosinophilic Colloid (40%)


Multinucleated Giant Cells (53%)

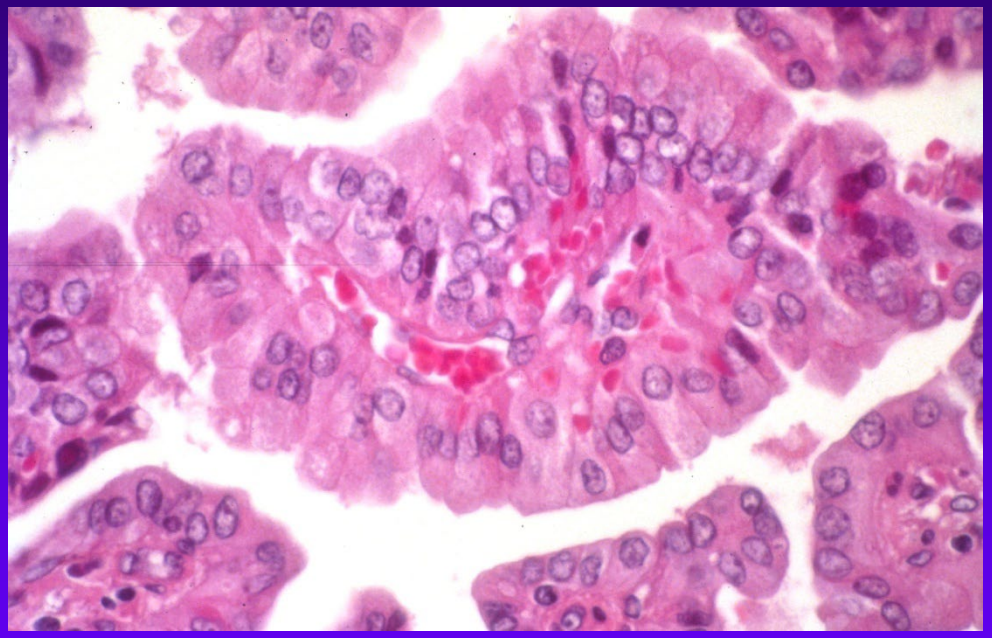
KEY POINT

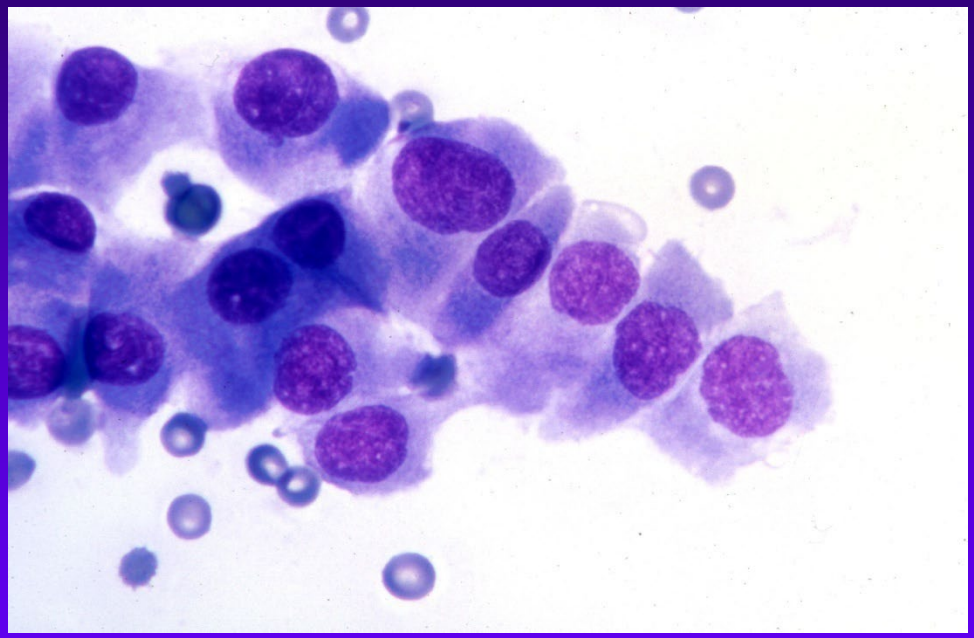
No single cytologic feature is diagnostic of papillary thyroid carcinoma!

You do not need to subtype PTC by FNA, but some features may suggest a subtype

Tall Cell Subtype of Papillary Carcinoma:

≥3x as tall as wide





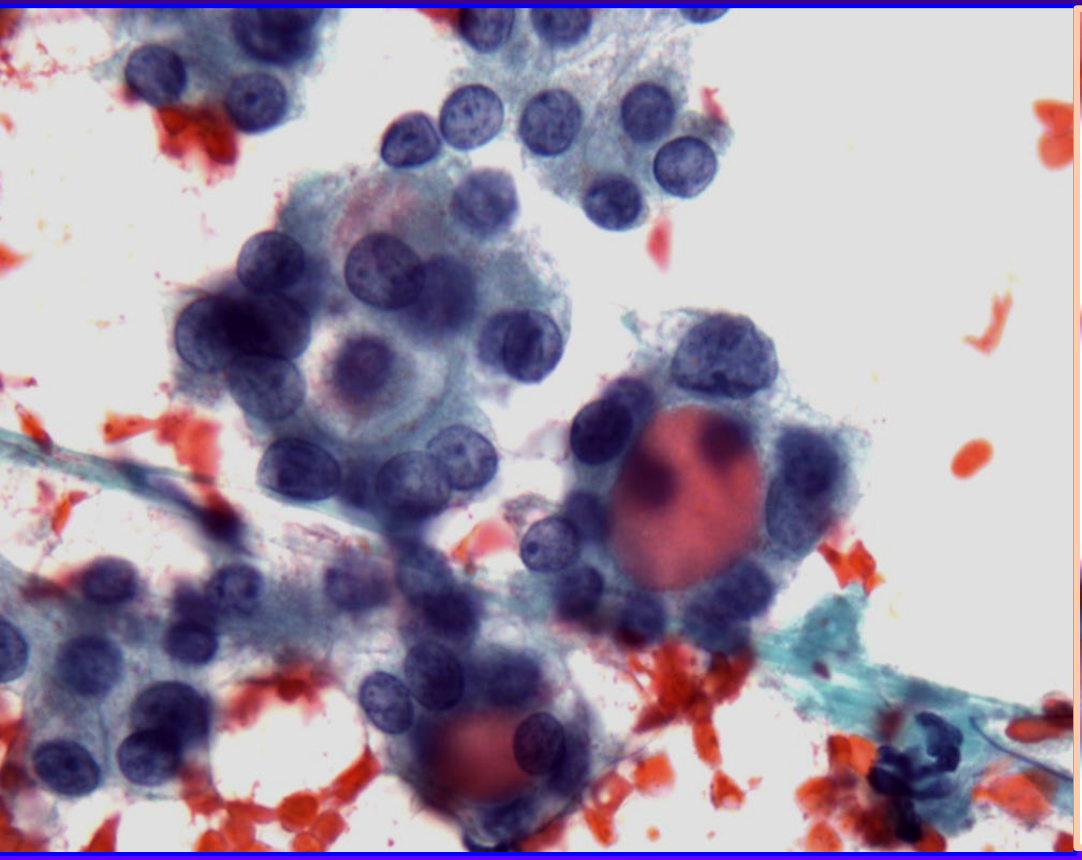
KEY POINT

Avoid diagnosing PTC in the absence of papillary architecture!

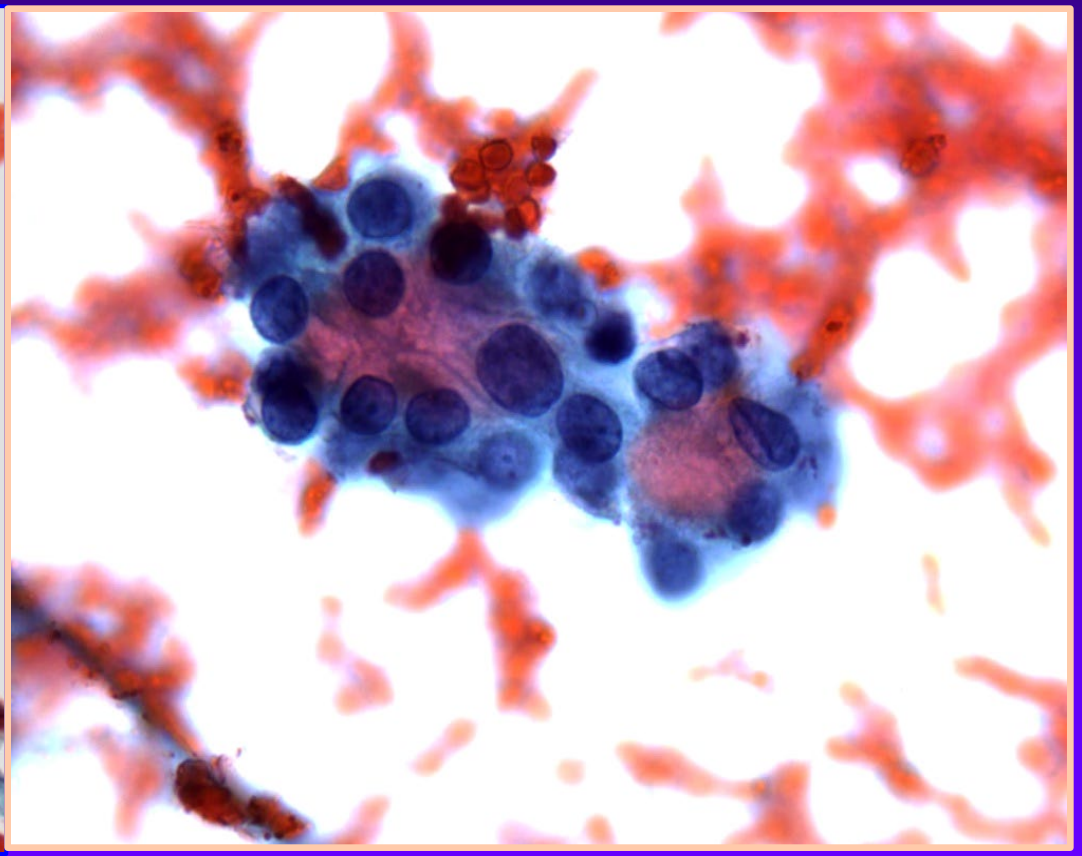
Many of these will be classified in the "Follicular Neoplasm" or "AUS" …
And a large subset will be NIFTP... Some will be FVPTC!

FVPTC vs NIFTP:
Cannot be accurately distinguished by FNA

Invasive FVPTC

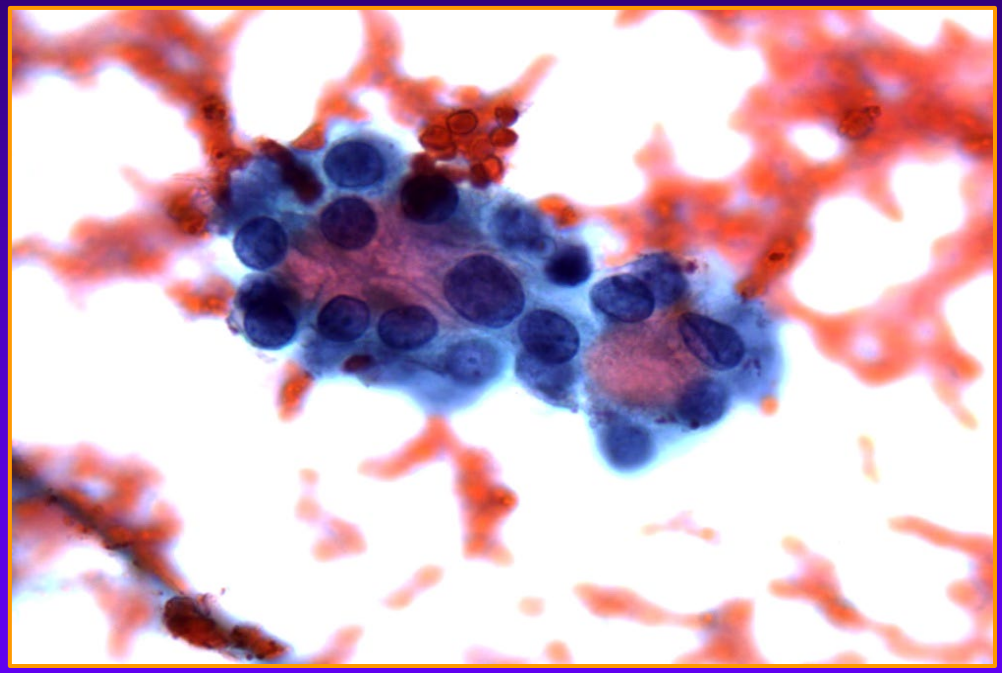


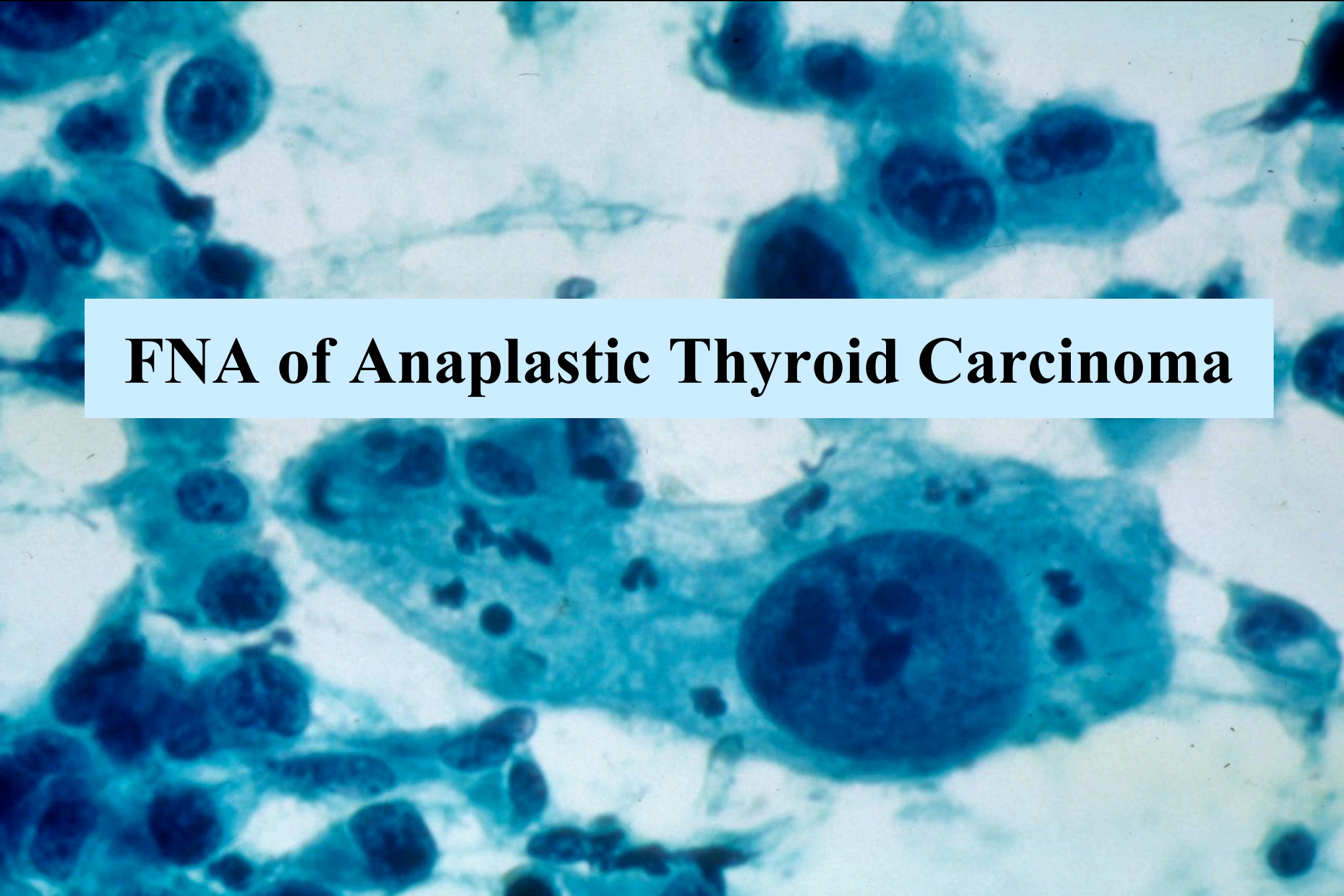
NIFTP



FNA of NIFTP:
Cytologic Features

- Follicular-patterned
- Nuclear:
  - Enlargement
  - Pallor
  - Grooves
  - Overlap
- Usually absent:
  - Pseudoinclusions
- Absent:
  - Papillae
  - Psammoma bodies





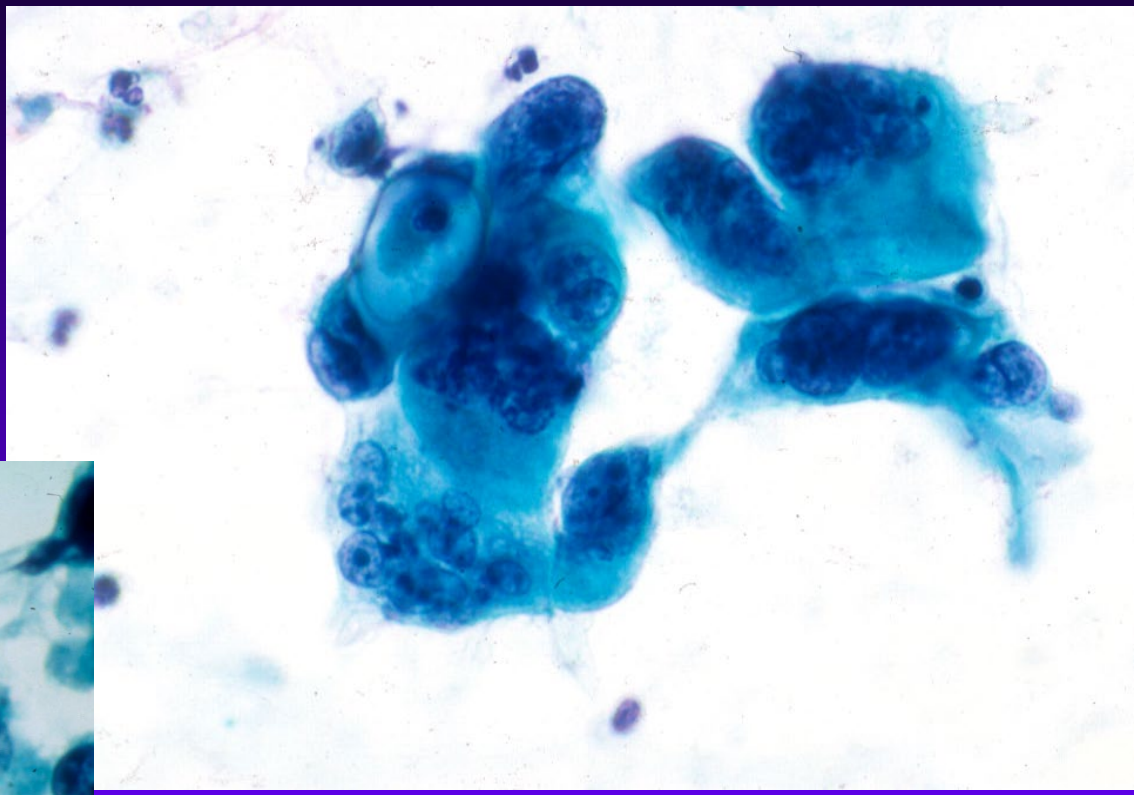
FNA of Anaplastic Thyroid Carcinoma

It is critical to make a diagnosis of anaplastic carcinoma on FNA, since surgery may not be warranted.

Anaplastic Thyroid Carcinoma

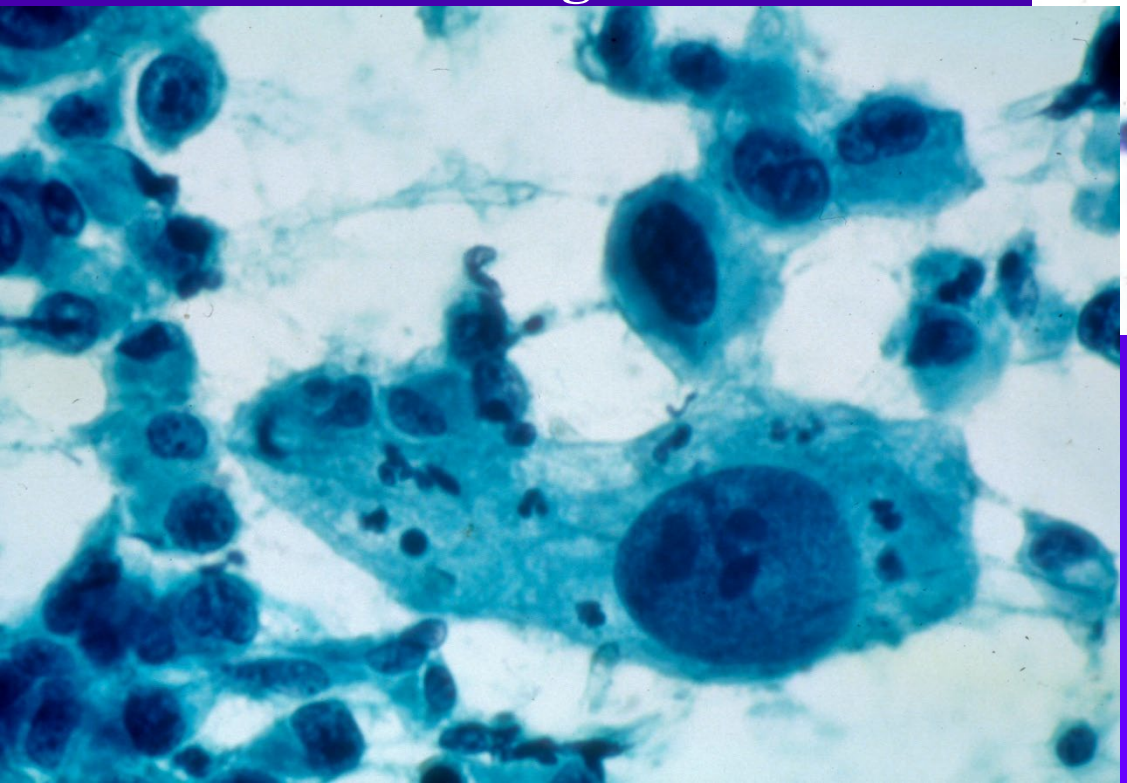
- **Combination of three cellular patterns:**
  - **Spindle cell**
  - **Giant cell**
  - **Squamoid**

Anaplastic Thyroid Carcinoma:
Patterns that are easily recognized

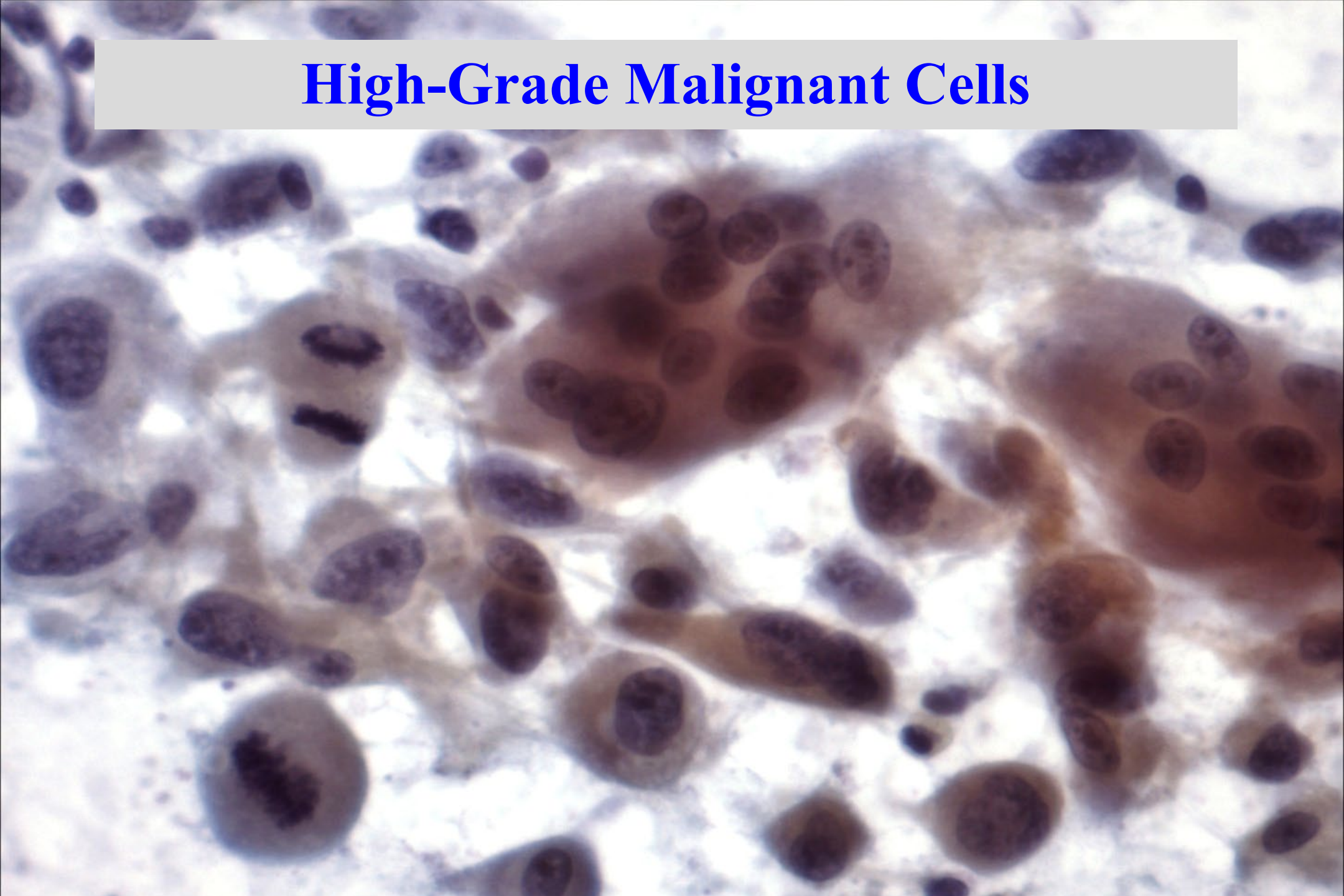


Multinucleated tumor cells

Bizarre tumor giant cells

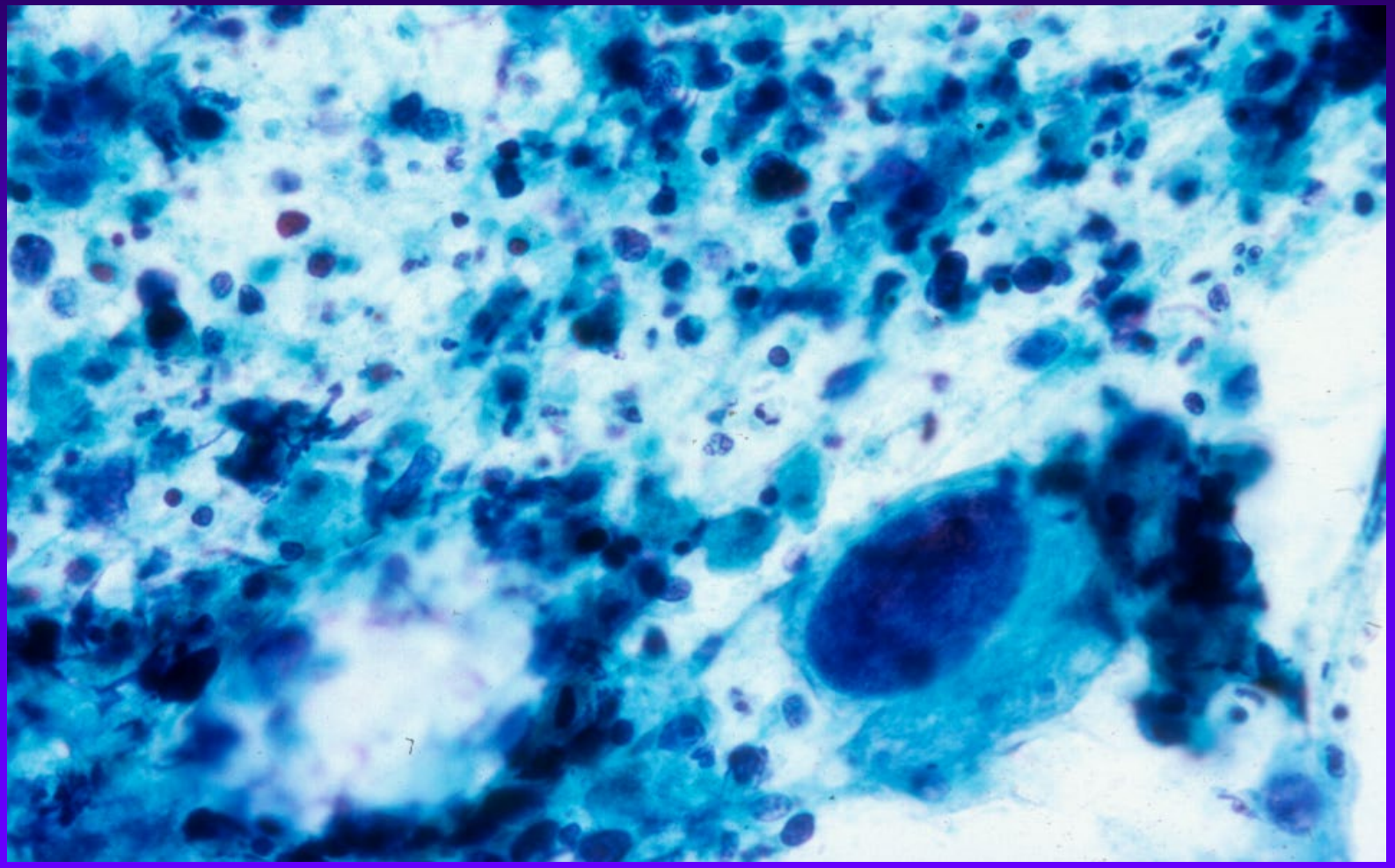


High-Grade Malignant Cells



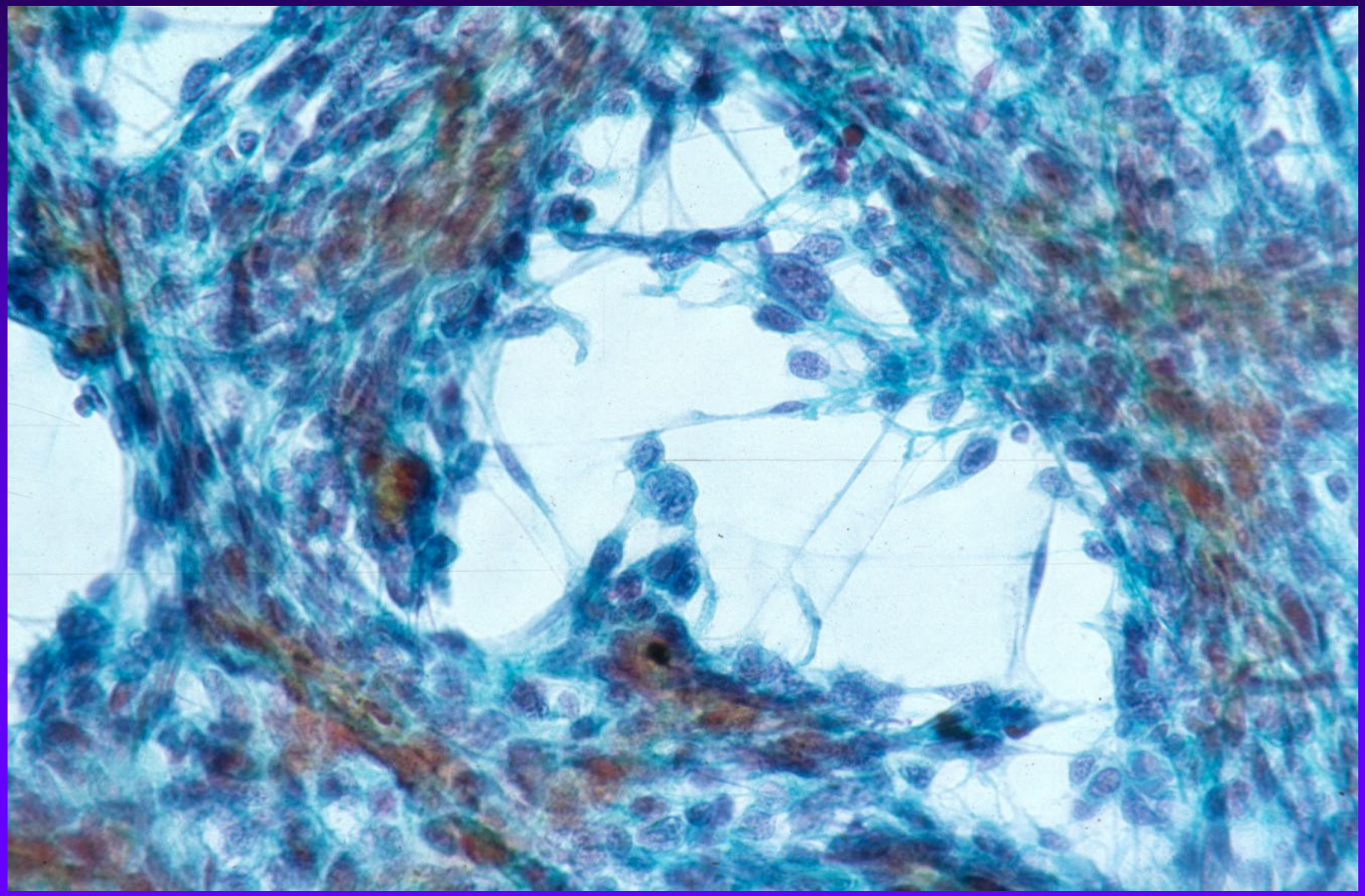
Anaplastic Thyroid Carcinoma:

Prominent tumor diathesis is often present



Anaplastic Thyroid Carcinoma:

Predominance of spindled cells – a subset are keratin negative!



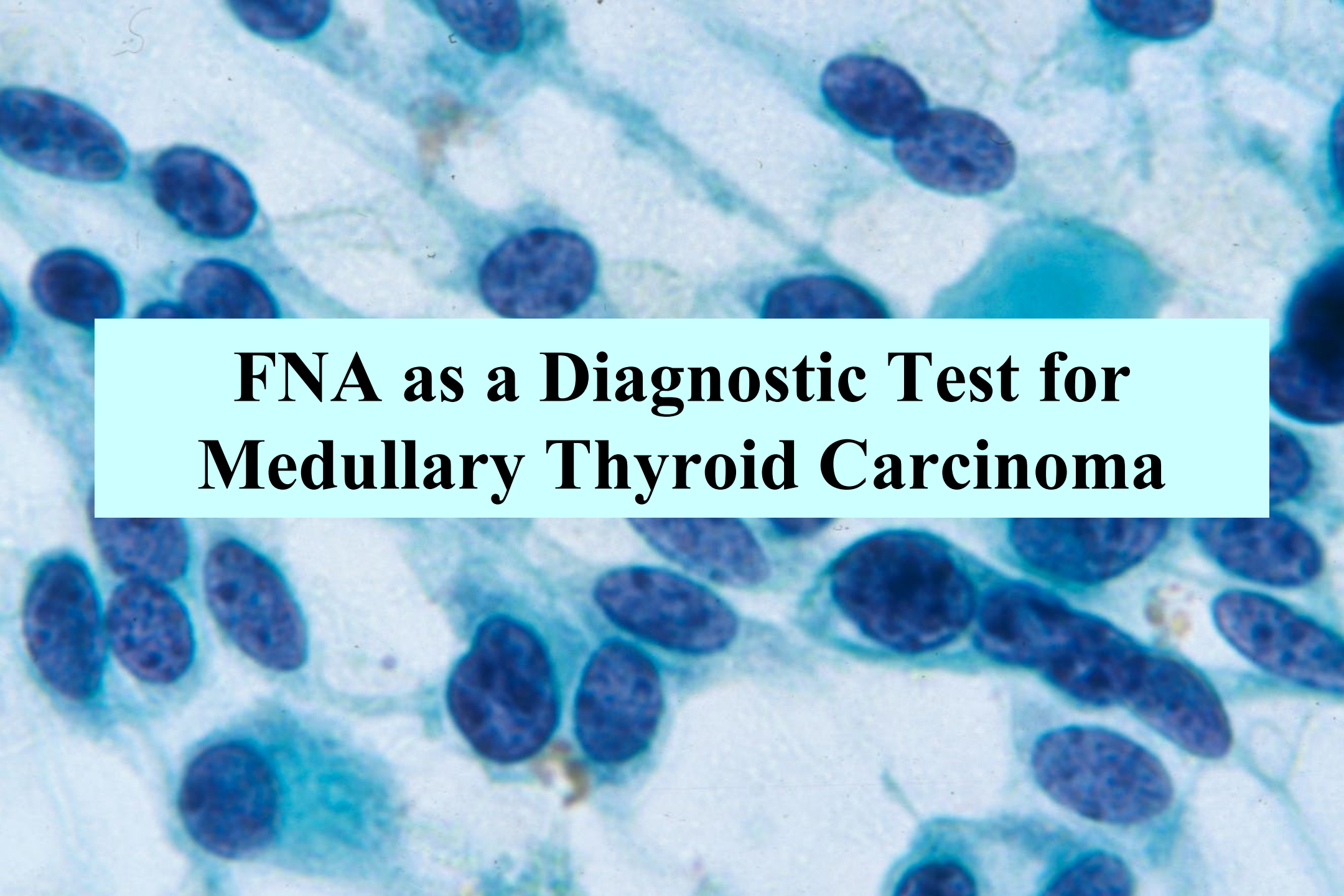
Anaplastic Thyroid Carcinoma

PAX-8 is usually retained

- **Immunocytochemistry –**
  - **LMW keratin +**
  - **PAX8+**
  - **P53 +**
  - **Thyroglobulin – NEGATIVE**
  - **TTF-1 – NEGATIVE**
  - **B-catenin +**
  - **Calcitonin & CEA -**

KEY POINT

- **Anaplastic thyroid carcinoma =**
  - **Overt high-grade features**
  - **Mitotically active**
  - **Tumor diathesis**



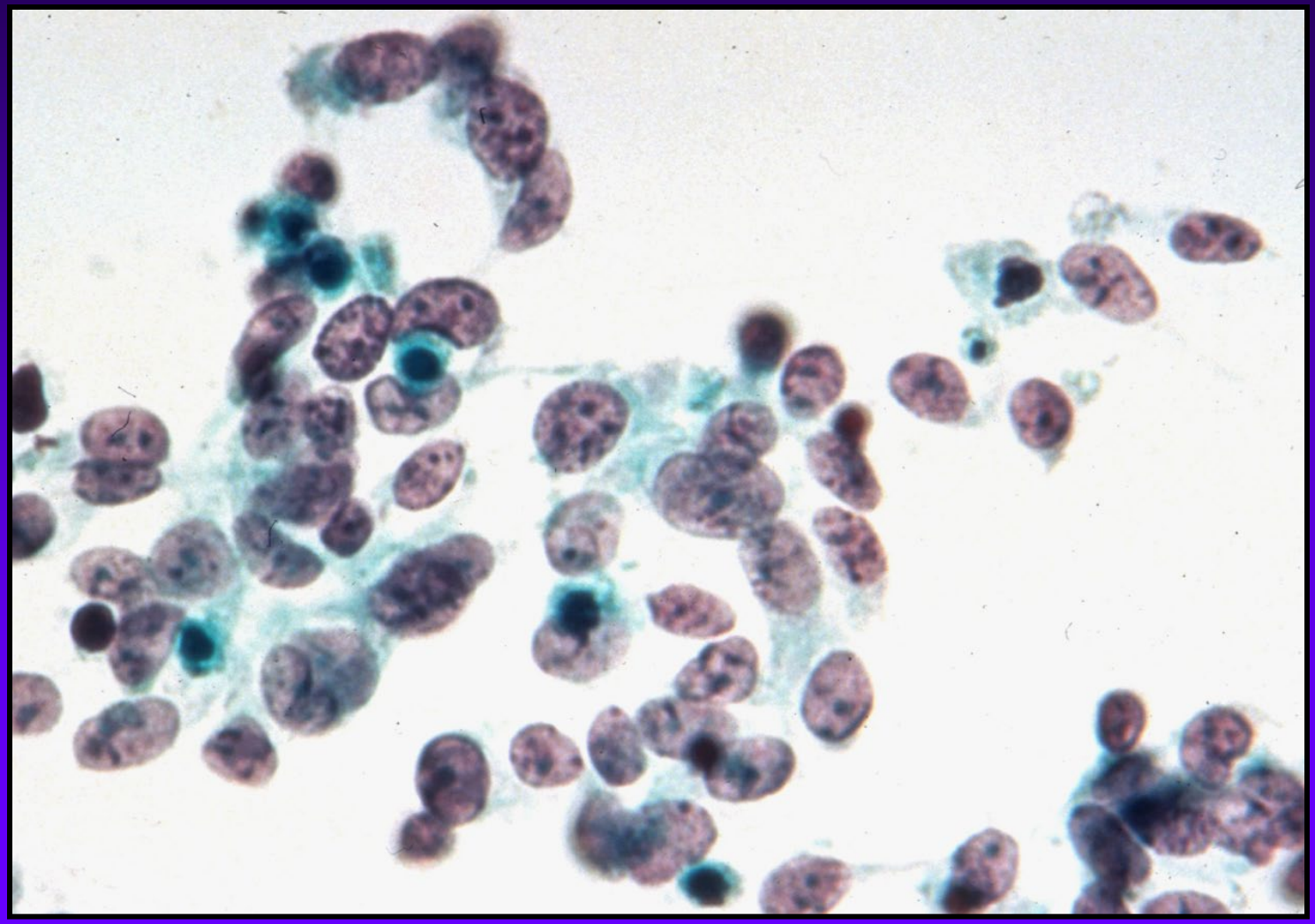
FNA as a Diagnostic Test for Medullary Thyroid Carcinoma

Medullary Thyroid Carcinoma

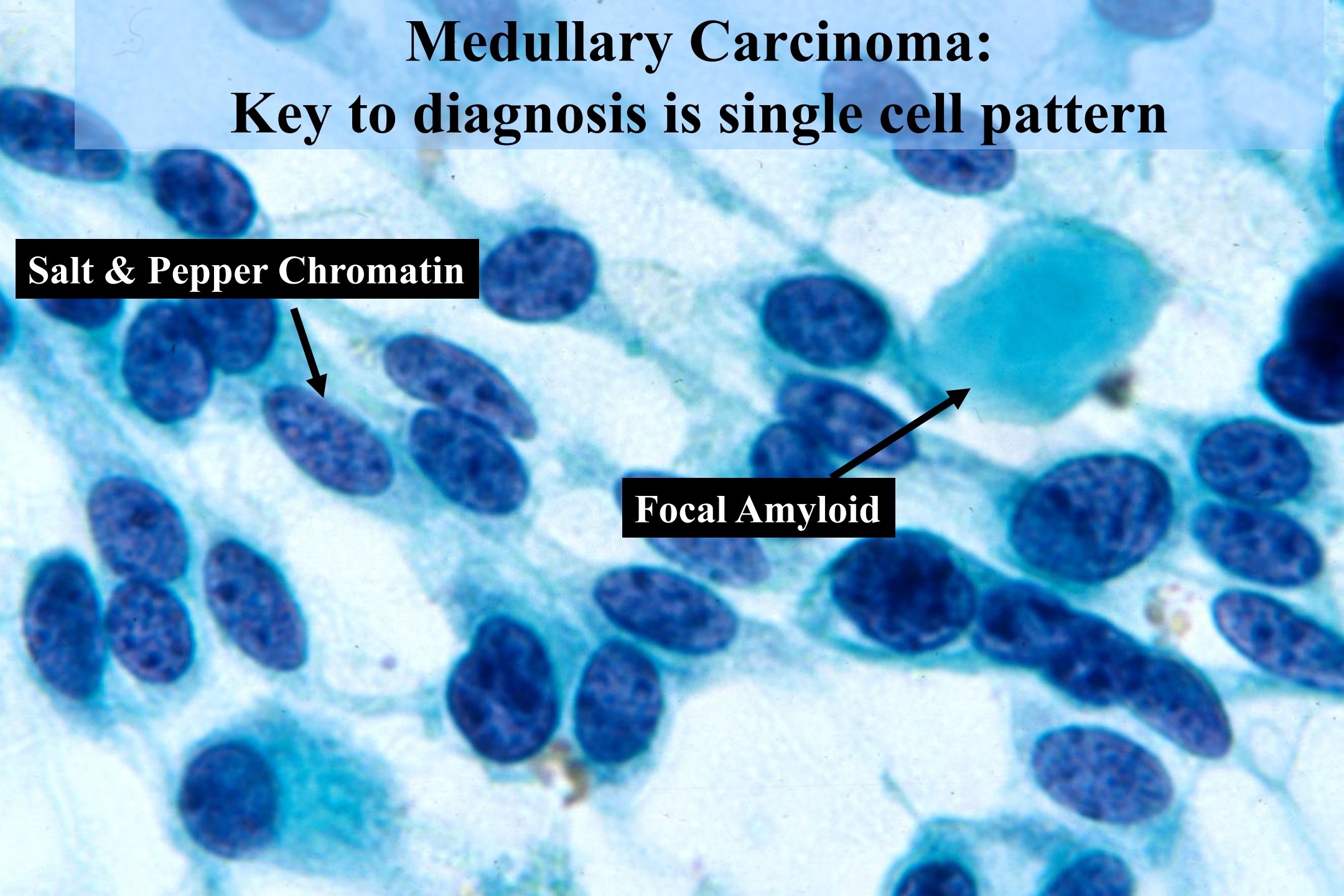
- **Key Cytologic Features:**
  - **Uniform, dispersed single cells:**
    - » **Plasmacytoid**
    - » **Spindled**
    - » **Polygonal**
  - **Granular "salt-and-pepper" chromatin**
  - **Background amyloid (approx. 80% of cases)**

Medullary Thyroid Carcinoma:

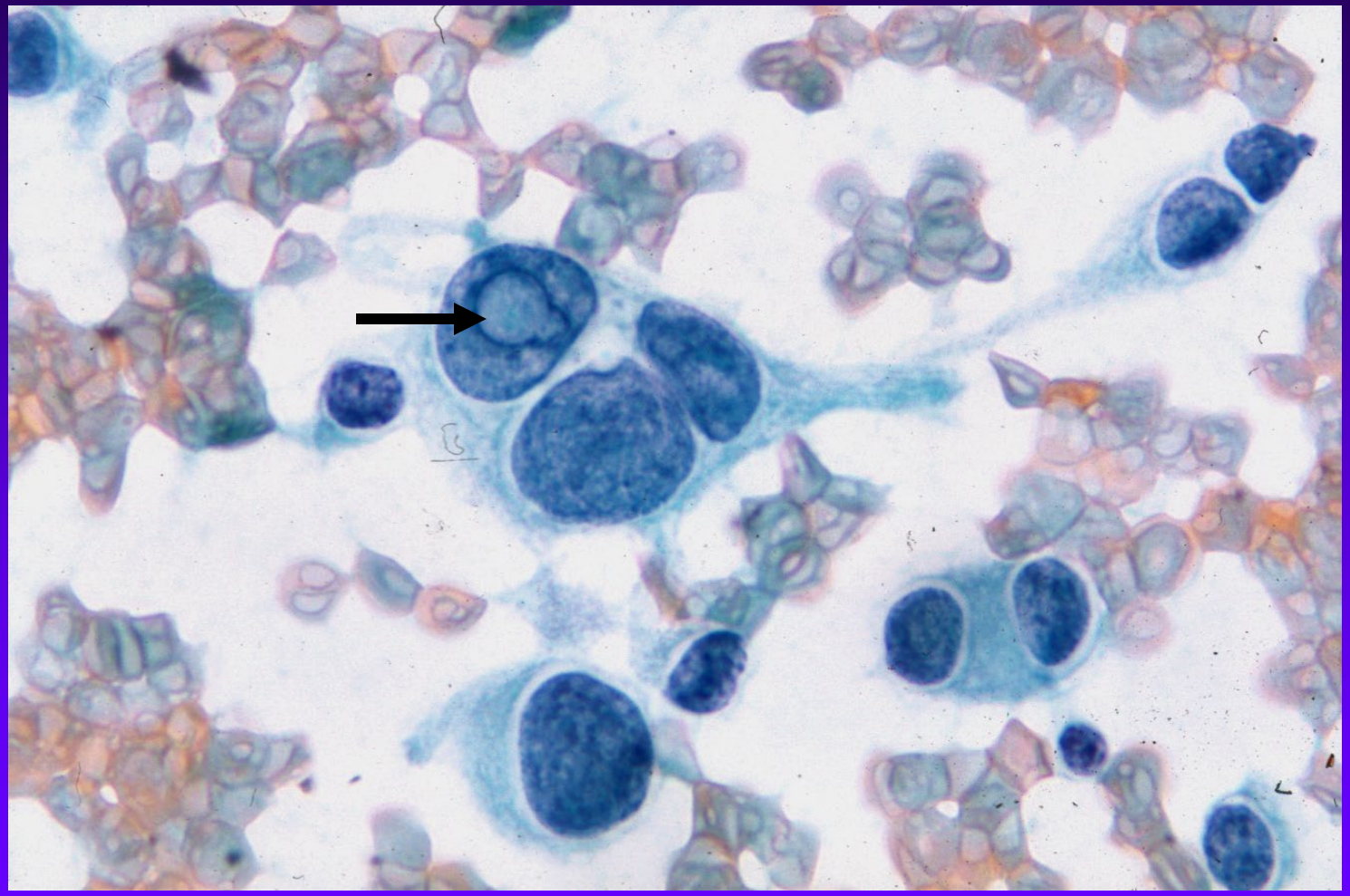
The Classic Pattern!



Medullary Carcinoma: Key to diagnosis is single cell pattern



Medullary Thyroid Carcinoma:
Multinucleation and Inclusions



Medullary Thyroid Carcinoma

Because of its propensity for LN metastasis, the first presentation may be in a cervical LN.

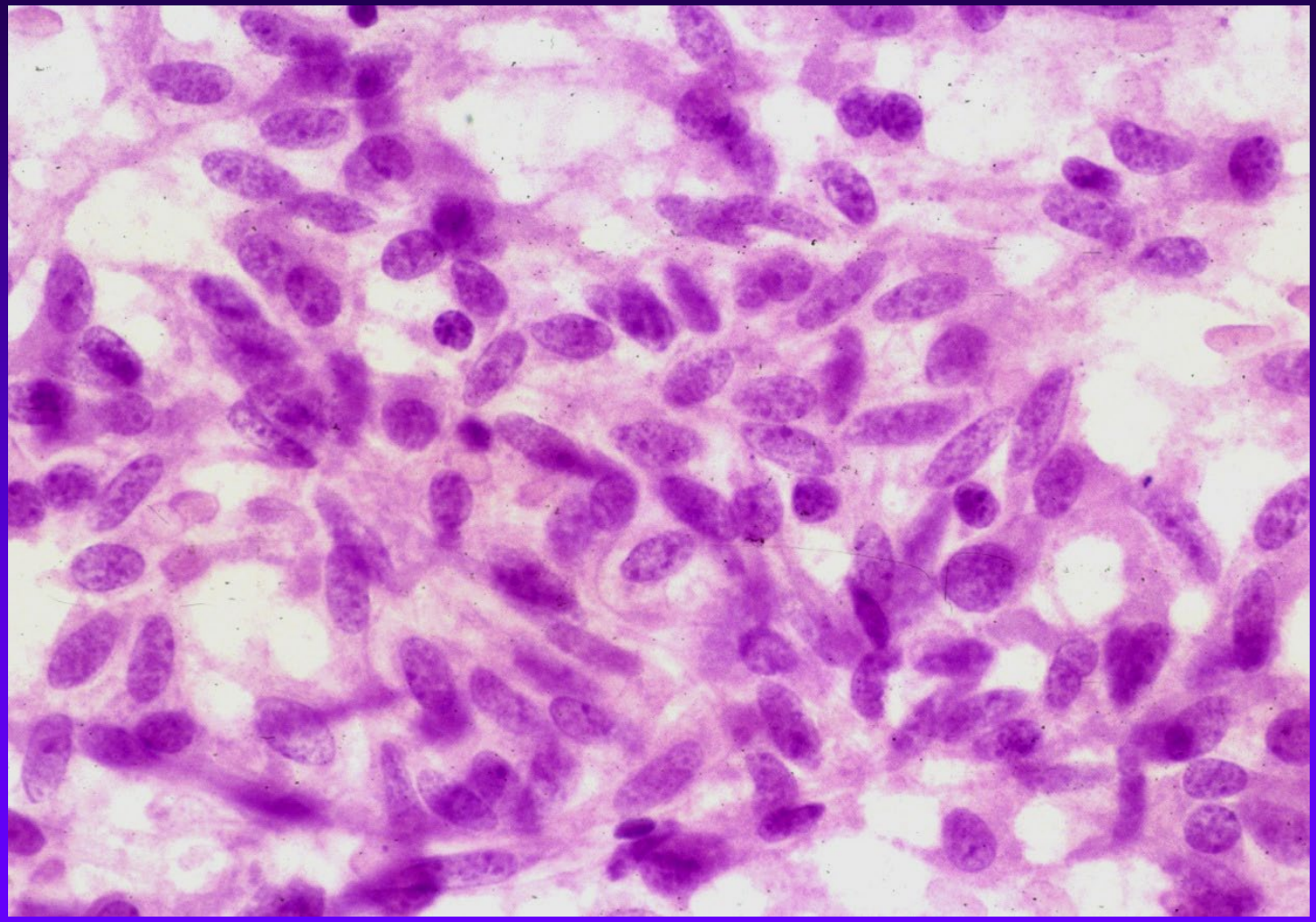
Medullary carcinoma is the "great mimicker"…it can look like anything… BEWARE!

Medullary Thyroid Carcinoma

MTC Patterns:

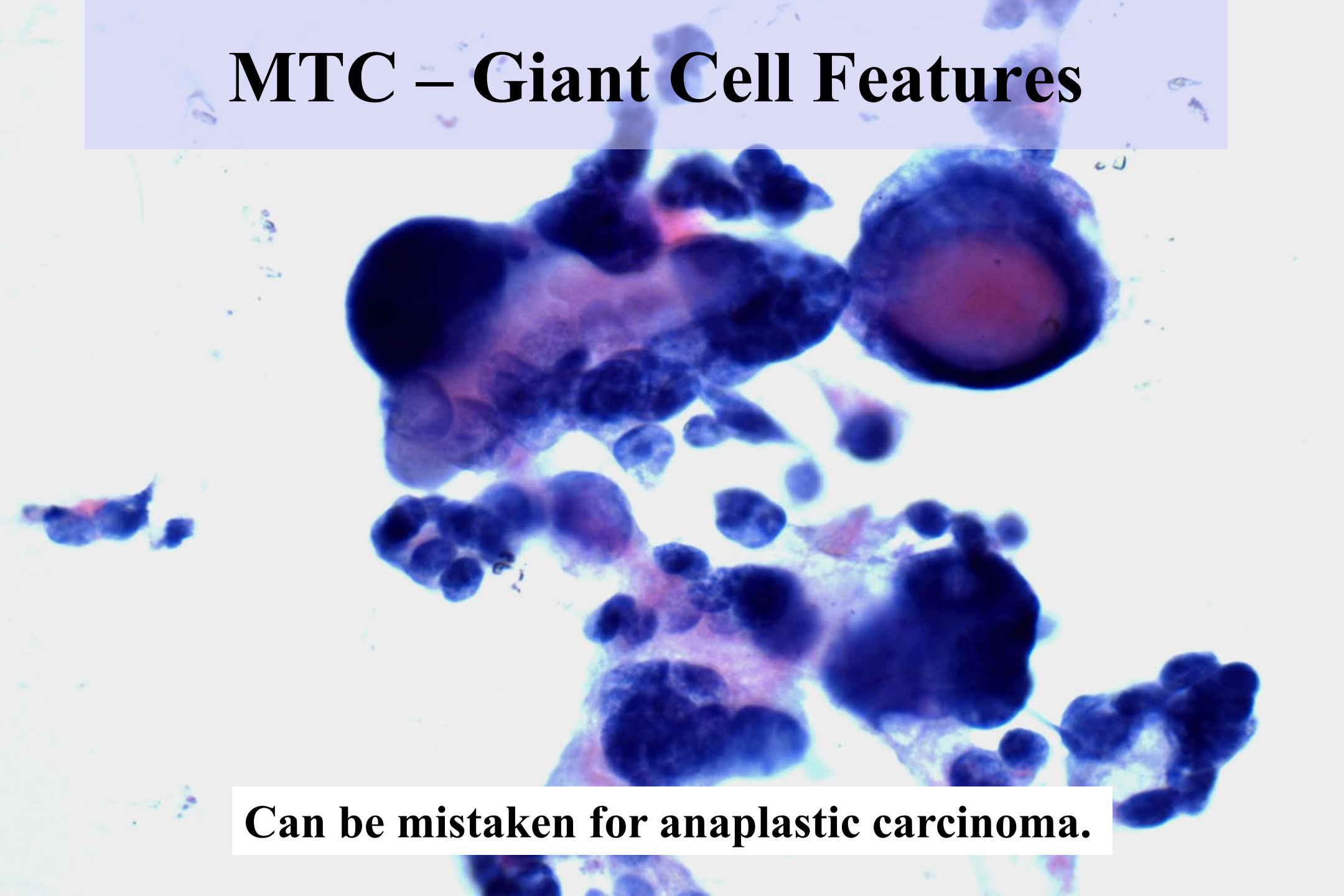
- –Oncocytic
- –Spindle cell
- –Papillary
- –Mixed follicular and MTC
- –Clear cell
- –Small cell
- –Giant cell (anaplastic) MTC

MTC – Spindle Cell Features



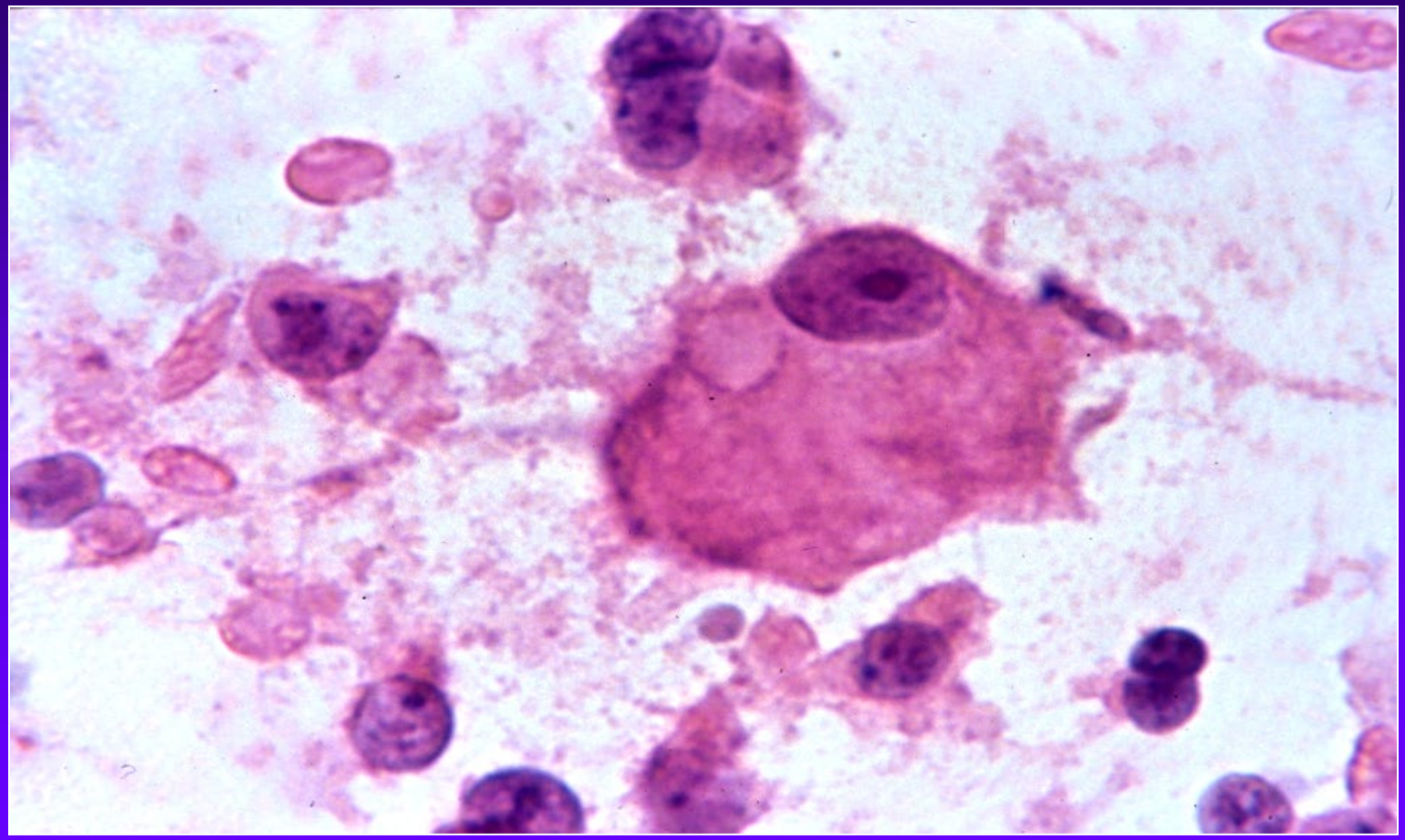
Can be mistaken for sarcoma or anaplastic carcinoma.

MTC – Giant Cell Features

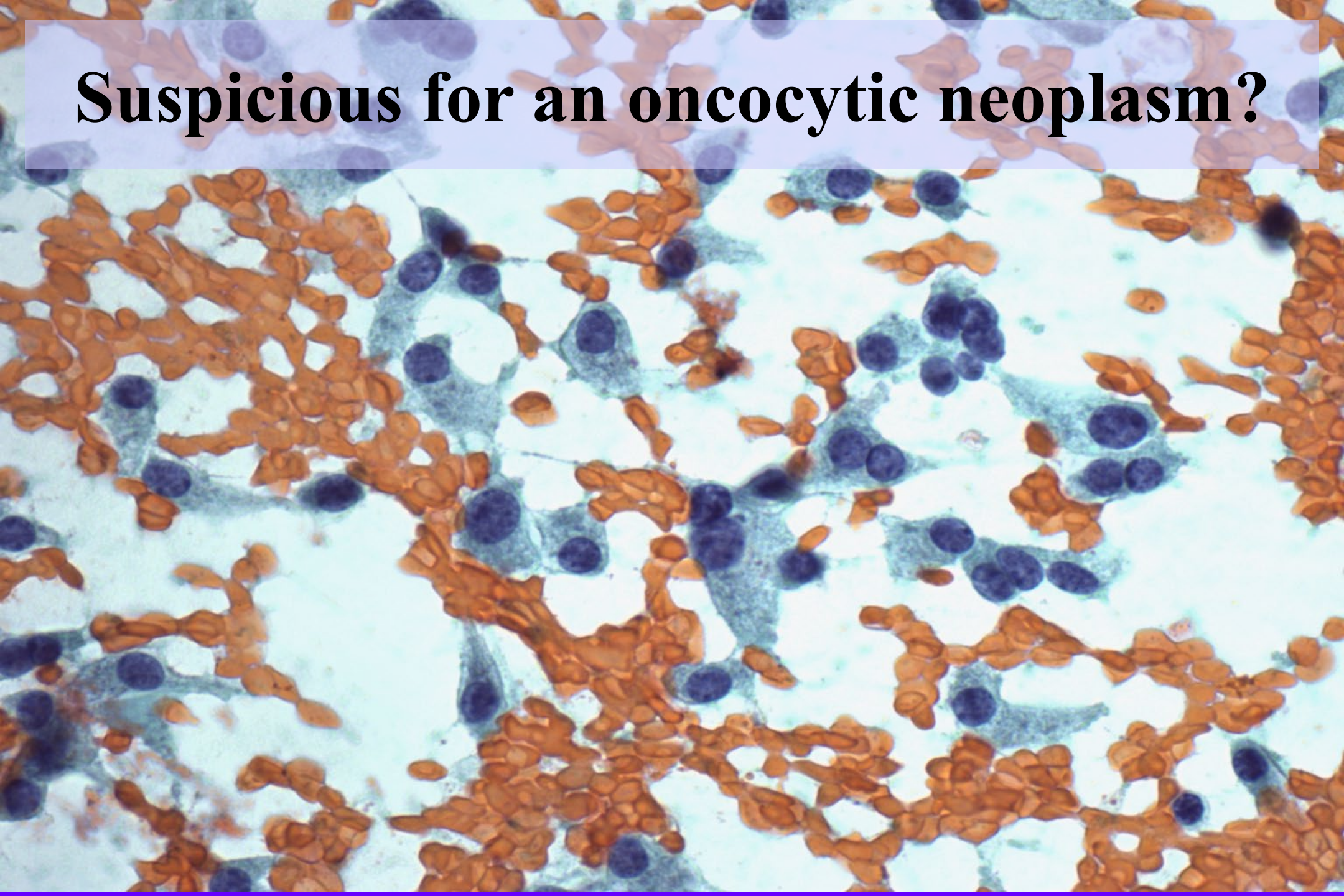


Can be mistaken for anaplastic carcinoma.

MTC – Oncocytic Features
Can be mistaken for an oncocytic tumor



Suspicious for an oncocytic neoplasm?



KEY POINT

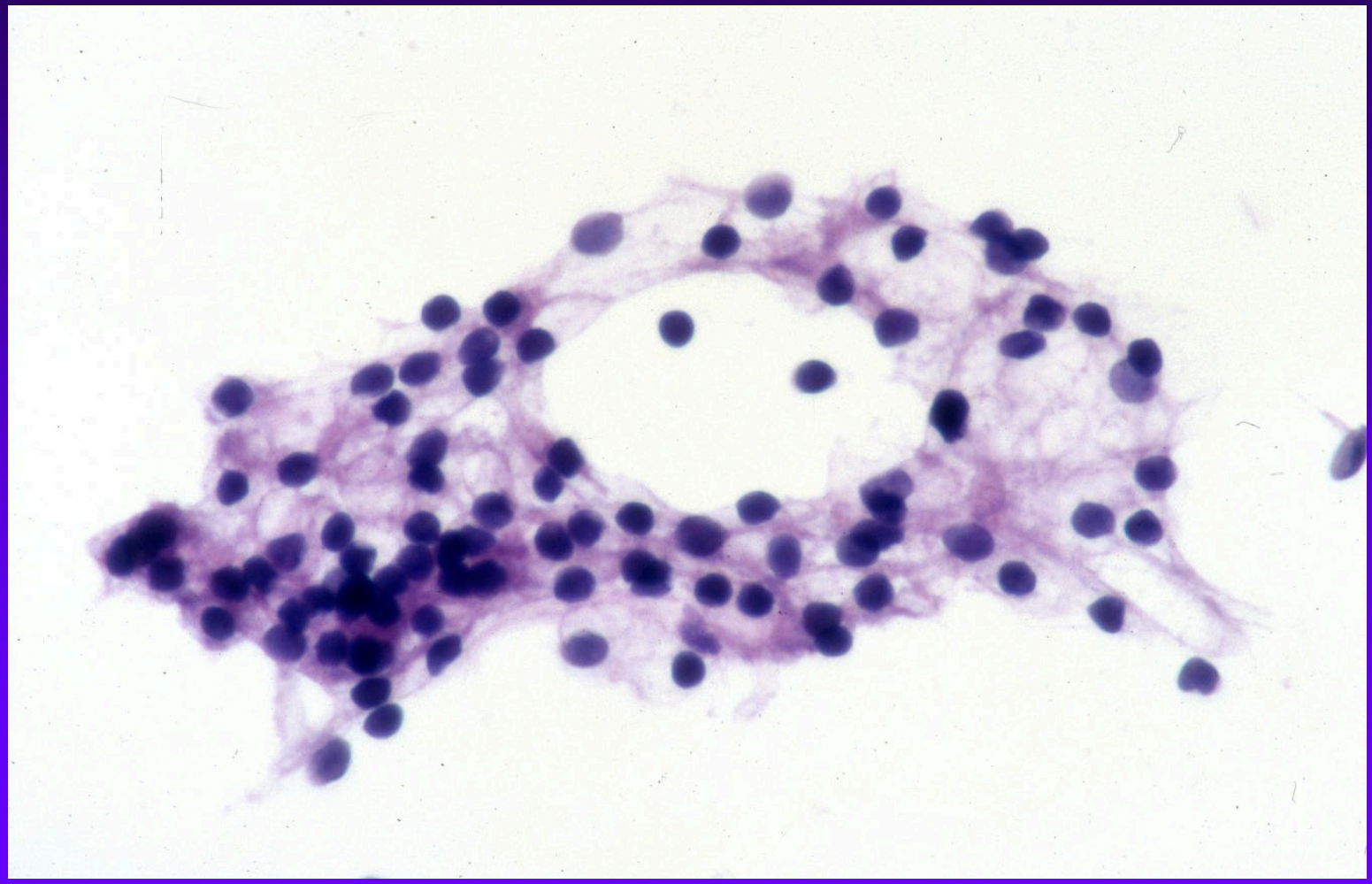
Anytime that the FNA has single cells or an unusual pattern, consider medullary thyroid carcinoma…and consider doing a serum calcitonin.

One last topic, just for fun....

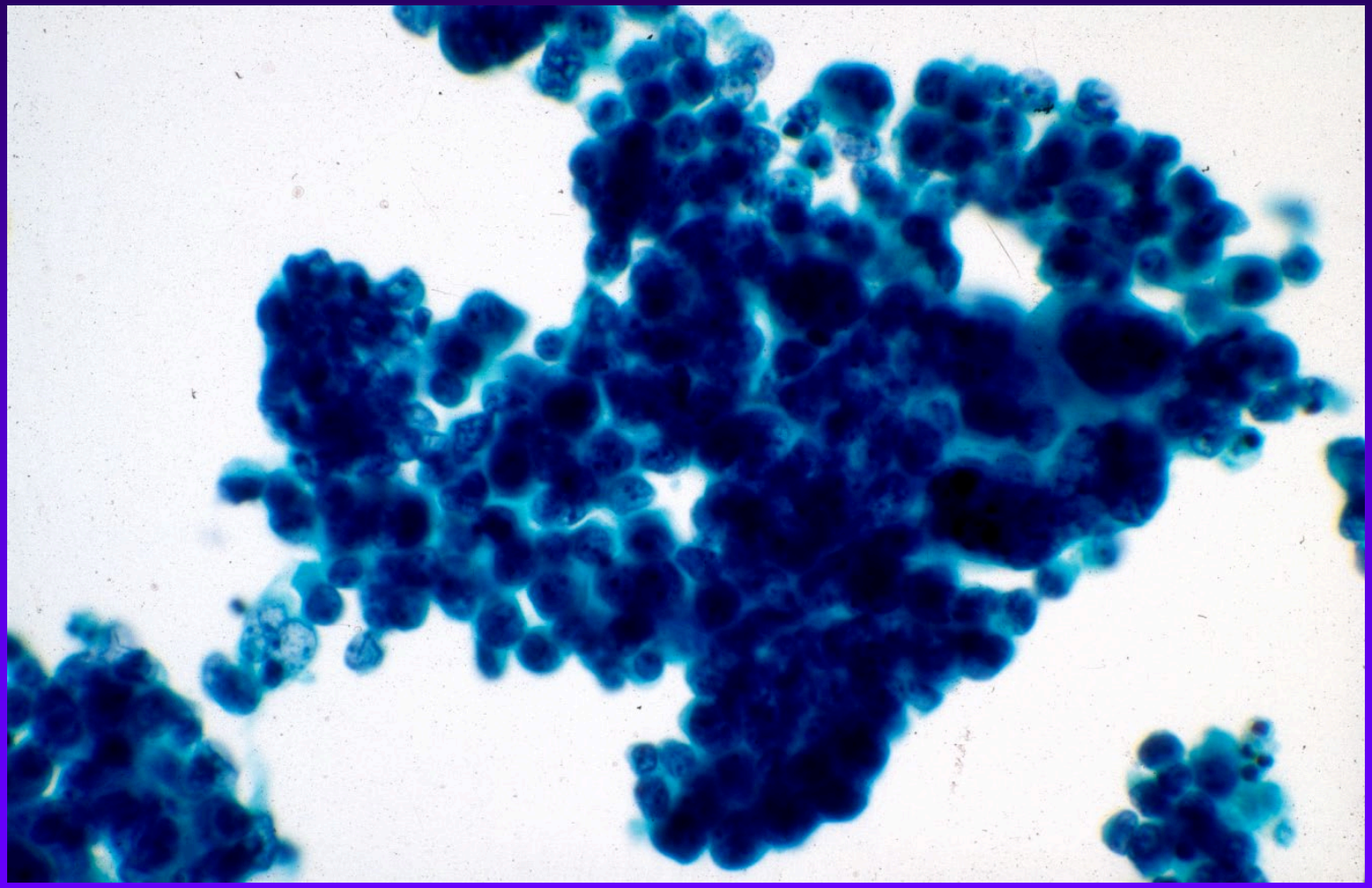
Secondary Tumors of the Thyroid

- Uncommon (0.1% of thyroid FNAs)
- Most frequent include:
  - Renal (among the most difficult to recognize)
  - Lung
  - Breast
  - Malignant melanoma
  - Colorectal
  - Malignant lymphoma
  - Head and neck squamous cell carcinoma

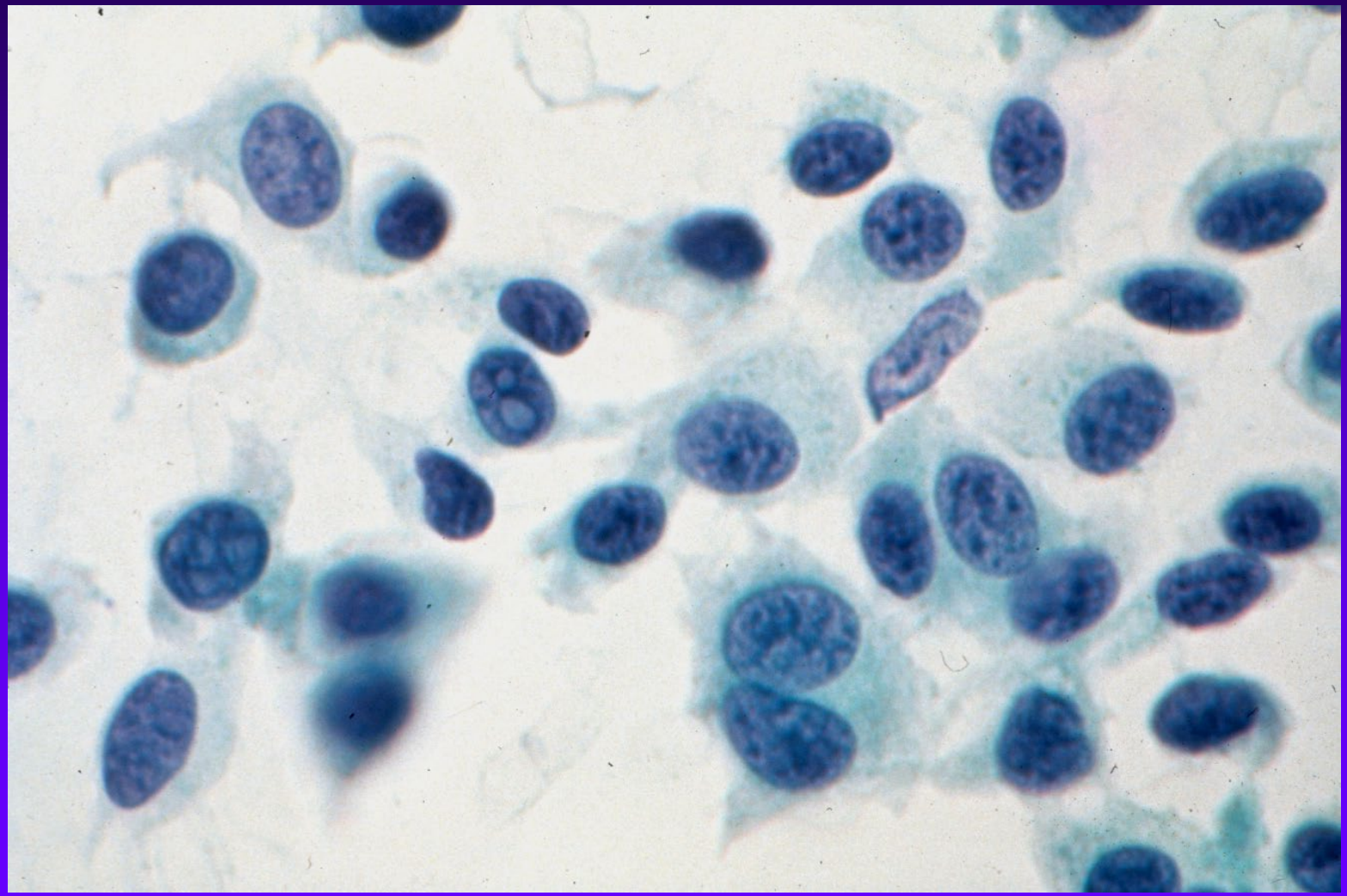
Secondary Tumors of the Thyroid



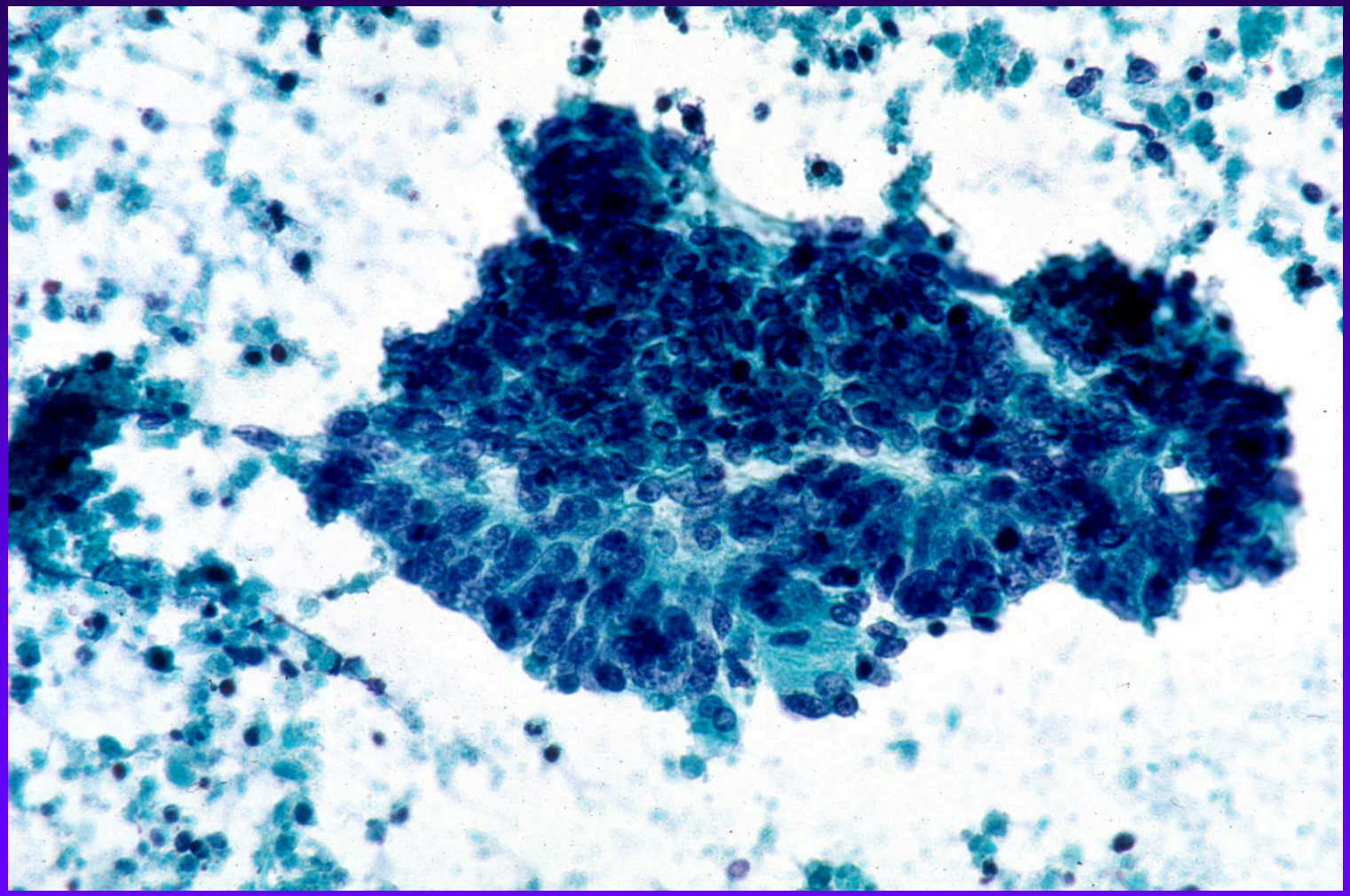
Secondary Tumors of the Thyroid



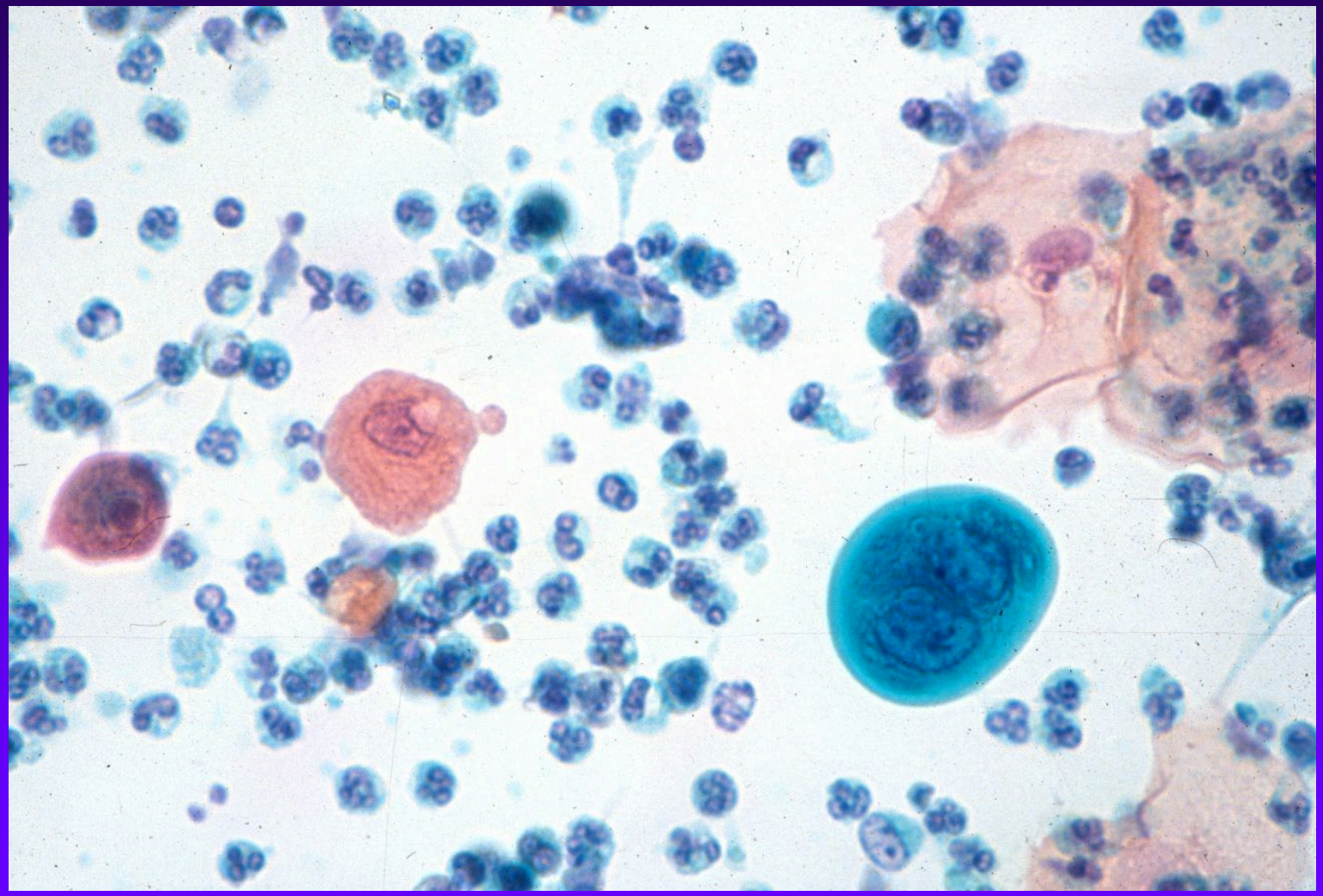
Secondary Tumors of the Thyroid

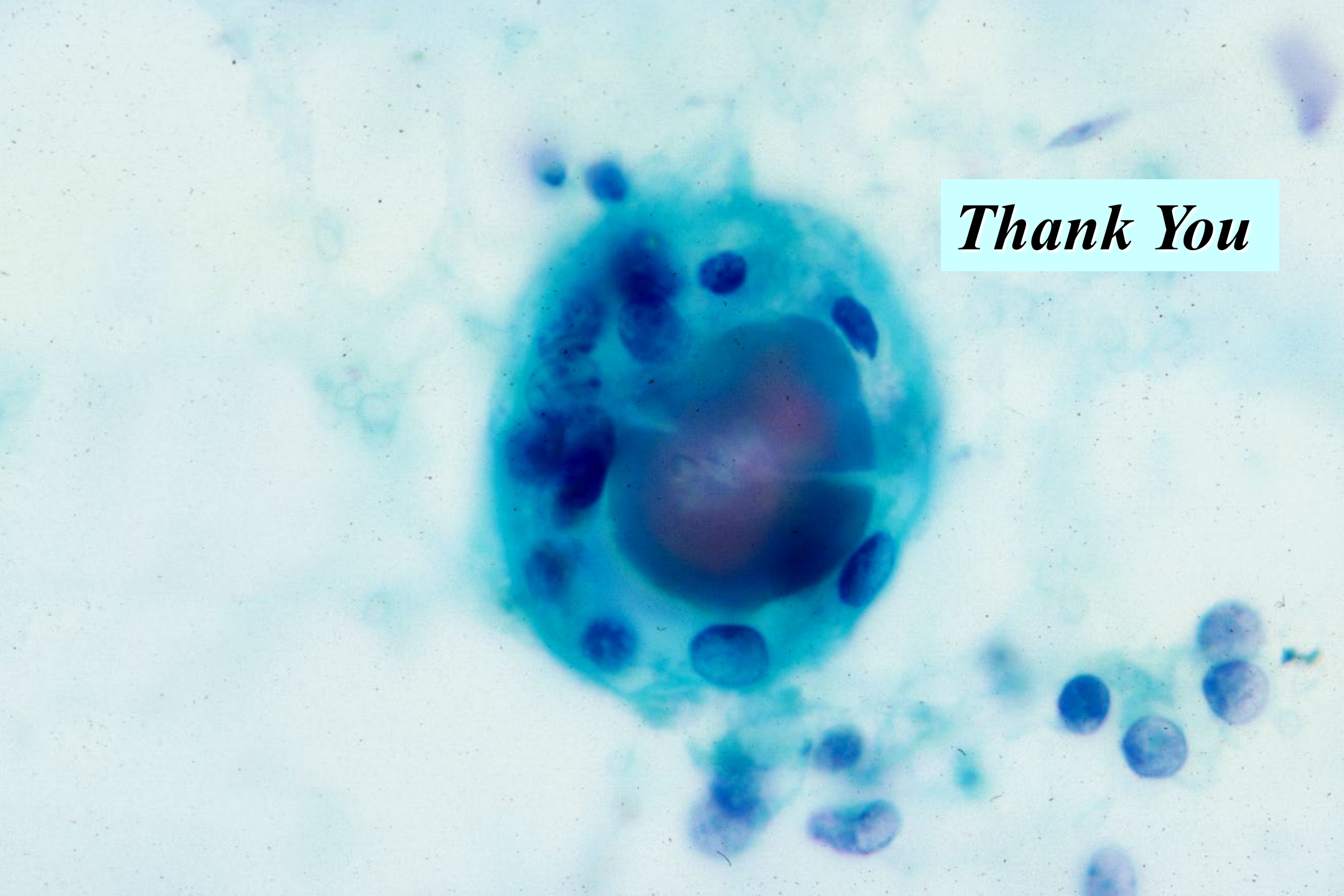


Secondary Tumors of the Thyroid



Secondary Tumors of the Thyroid




Thank You