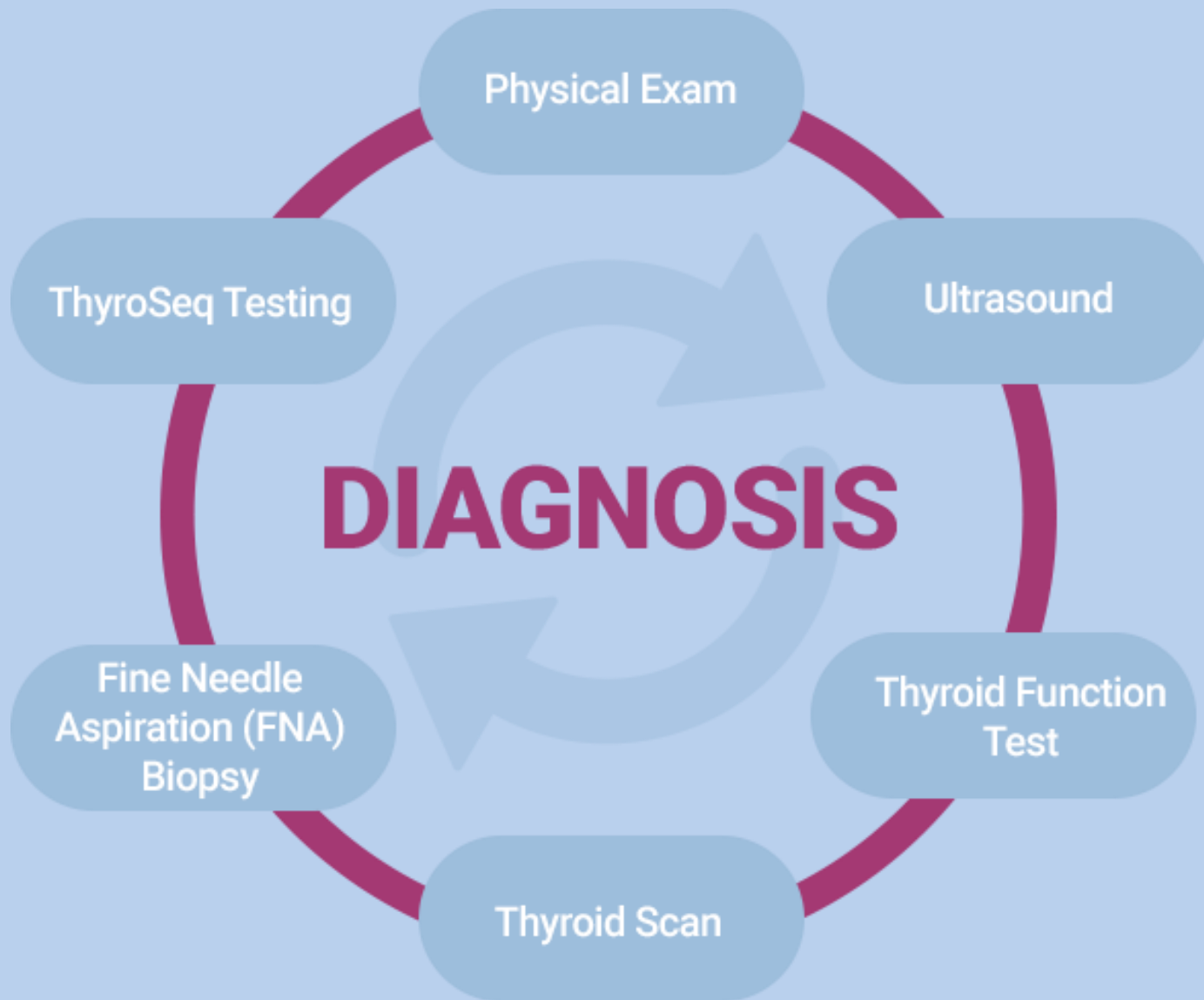


# THYROID FNA

دکتر آذر هوش

دانشیار پاتولوژی دانشگاه علوم پزشکی گلستان



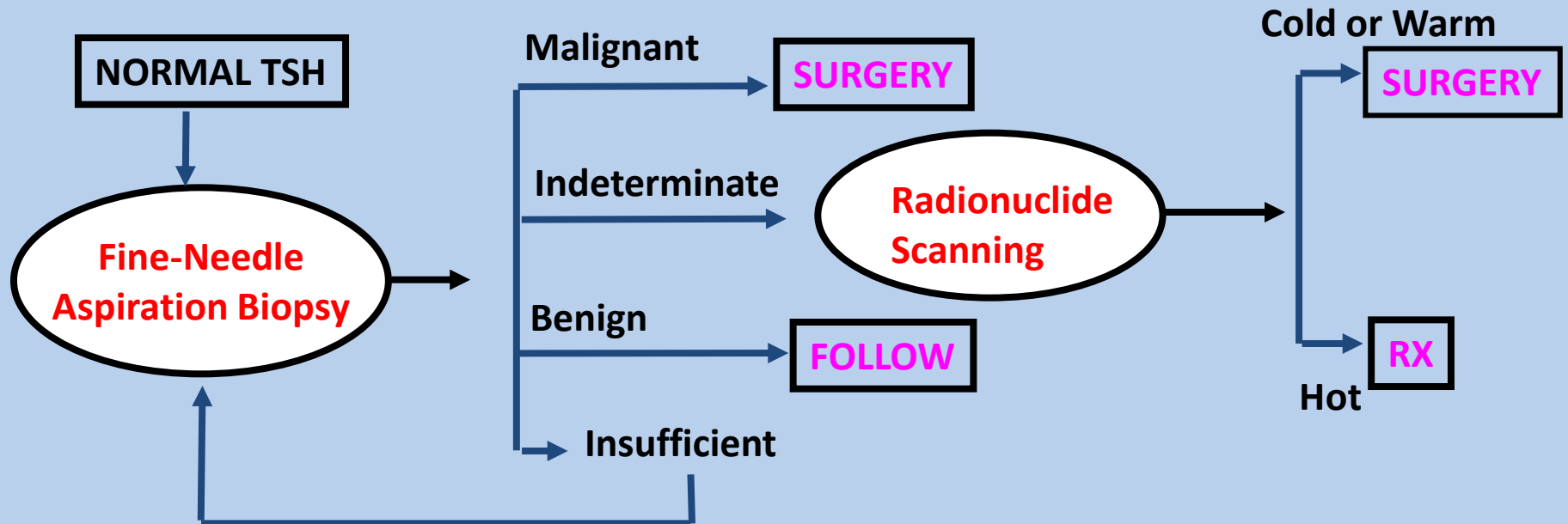
# **FNA : clinical indications**

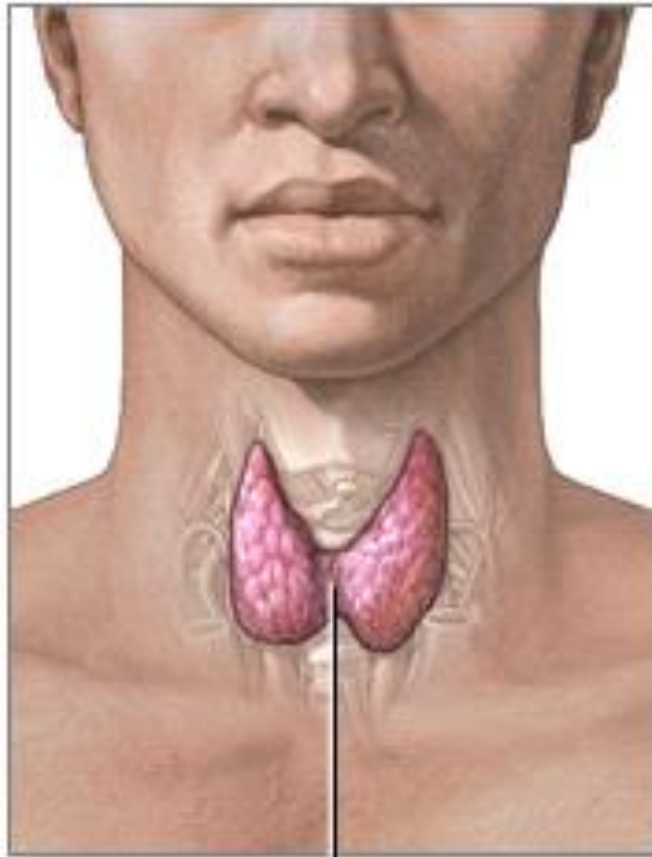
- First-line investigation for a solitary thyroid nodule
- A valuable role in the diagnosis of the diffuse non-toxic goiter

# **FNA :clinical indications**

- To confirm the diagnosis of clinically obvious malignancy
- Separation of treatable lymphomas from poor prognosis anaplastic carcinomas

# Evaluation of Thyroid Nodules





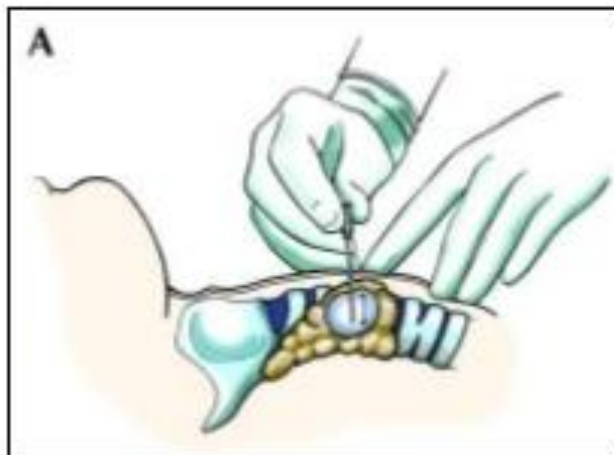
Thyroid gland

Fine needle





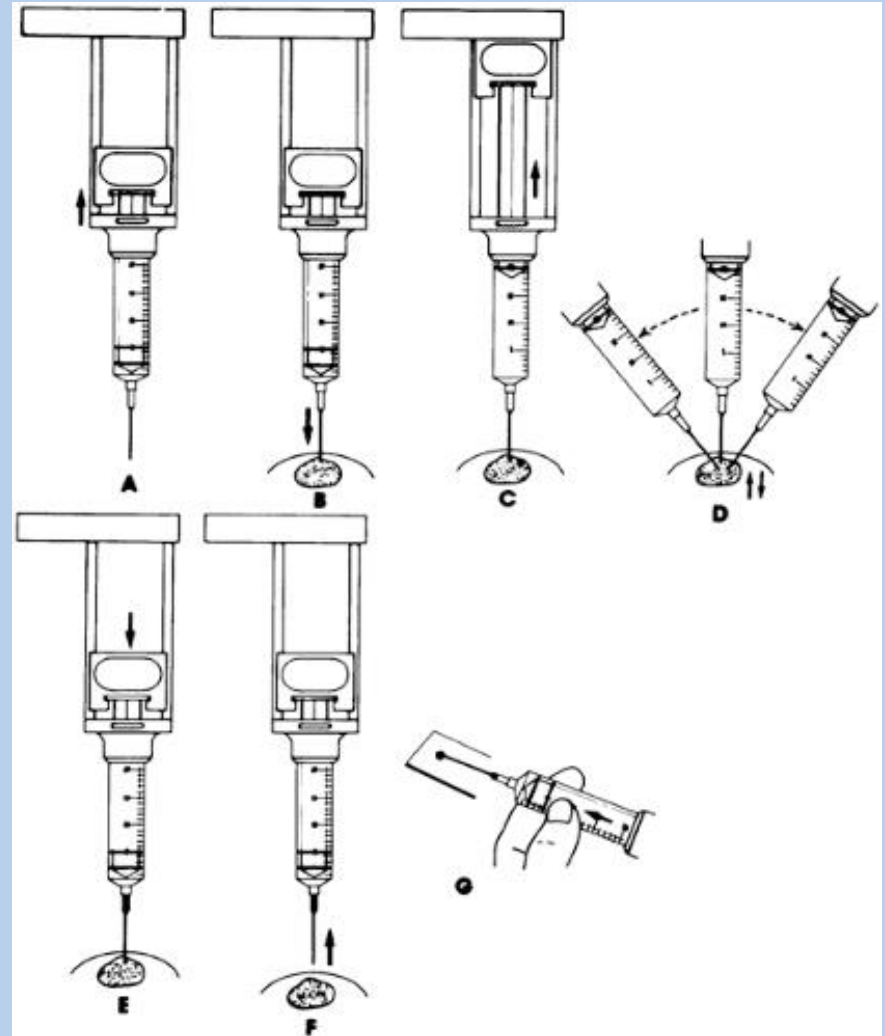
**Fine Needle Non Aspiration (FNNA) biopsy showing needle, position & direction for biopsy.**



**Immediately after FNA, firm pressure is applied to biopsy sites**

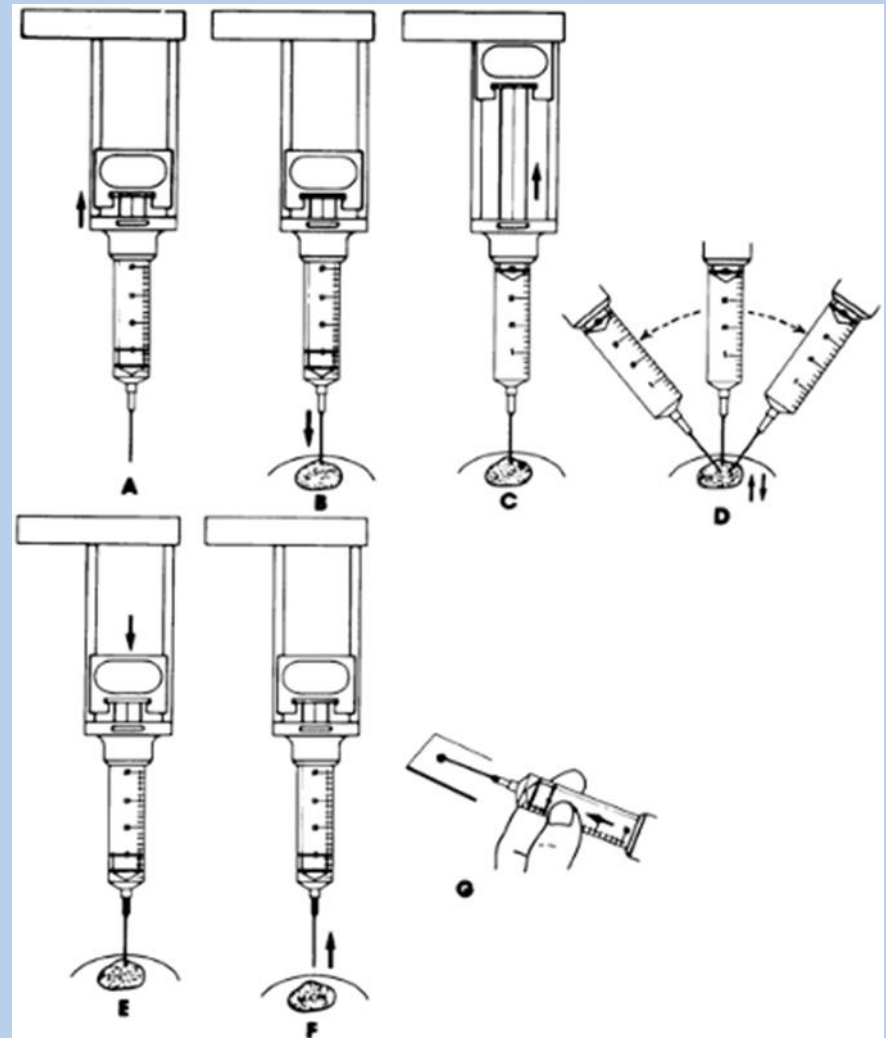
# careful sampling

- The careful sampling necessary in the thyroid because of its vascularity

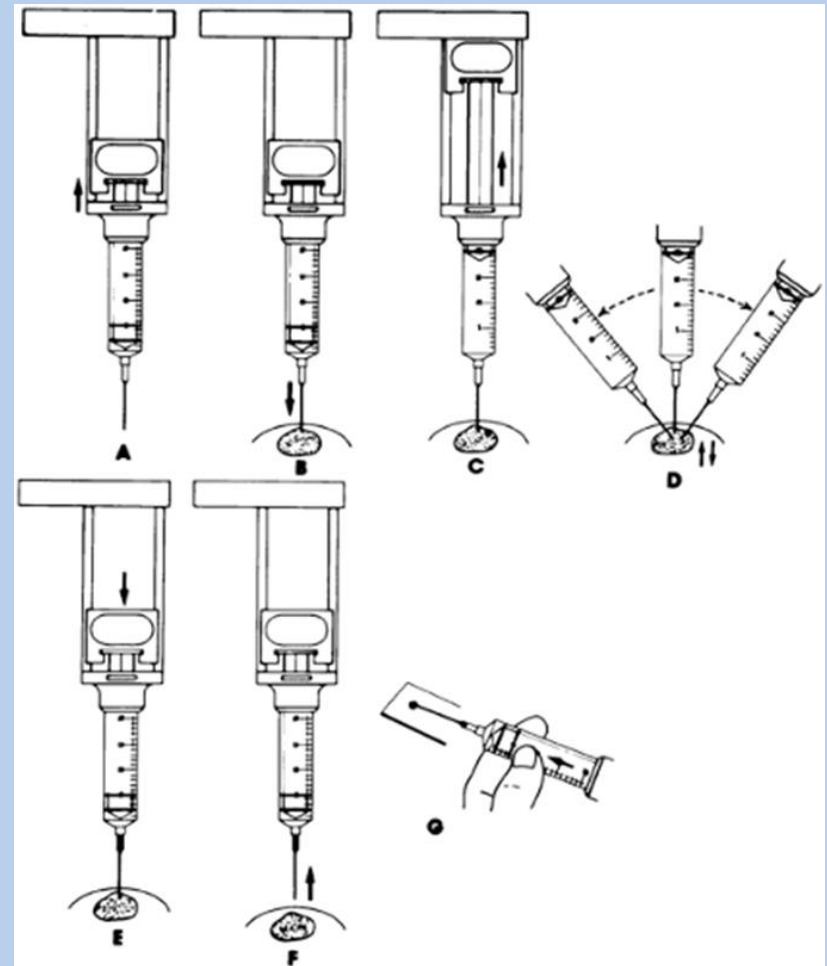




- At least two aspirates should be taken at anyone time from lesions to reduce the risk of false negative diagnosis.



- Blood contamination of the sample lead to **dilution or loss of diagnostic features**





**No absolute contraindications** to  
needle aspiration of the thyroid in  
cooperative patients.

# Complications

- The main risk is **hematoma** formation in those with large goiters or malignant tumours in the neck causing marked tracheal compression.
- Care should be exercised in those who are **anticoagulated** and clotting status checked prior to neck aspiration.

# Complications

- **Puncture of the carotid** requires the aspirator to occlude the puncture site for five minutes.
- **Puncture of the trachea** may lead to transient coughing.

# Complications

- Temporary laryngeal nerve paresis has been recorded post aspiration, as has haemorrhagic necrosis of thyroid tumours, particularly adenomas

# Complications

- Needle track implantation by a thyroid malignancy is extraordinarily rare.
- Infection following FNA is very rare



# Worrisome histological alterations

may occur in approximately 10% of thyroid excisions following FNA such as :

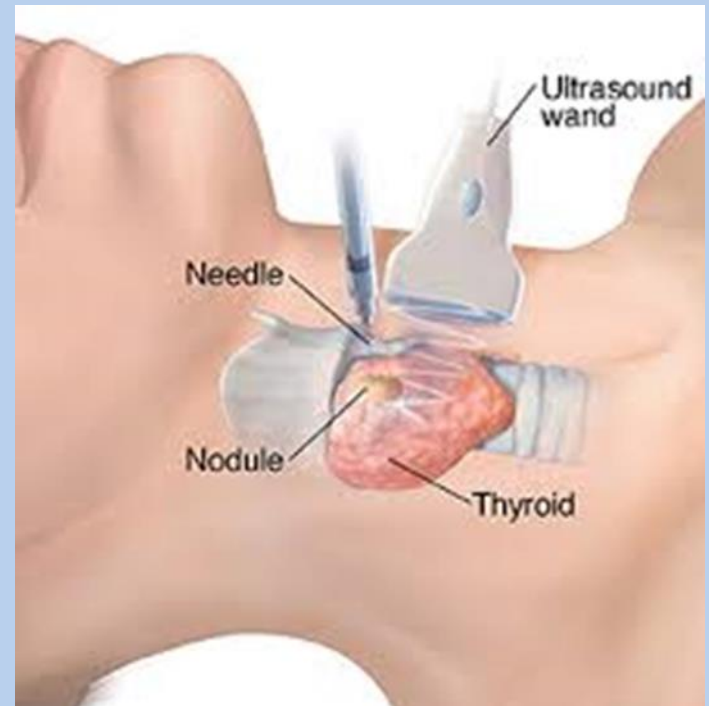
- Regenerative nuclear changes
- Vascular proliferations
- Metaplasias
- Capsular pseudo-invasion

# Worrisome histological alterations

- awareness of artefacts by histopathologists avoids misdiagnosis.

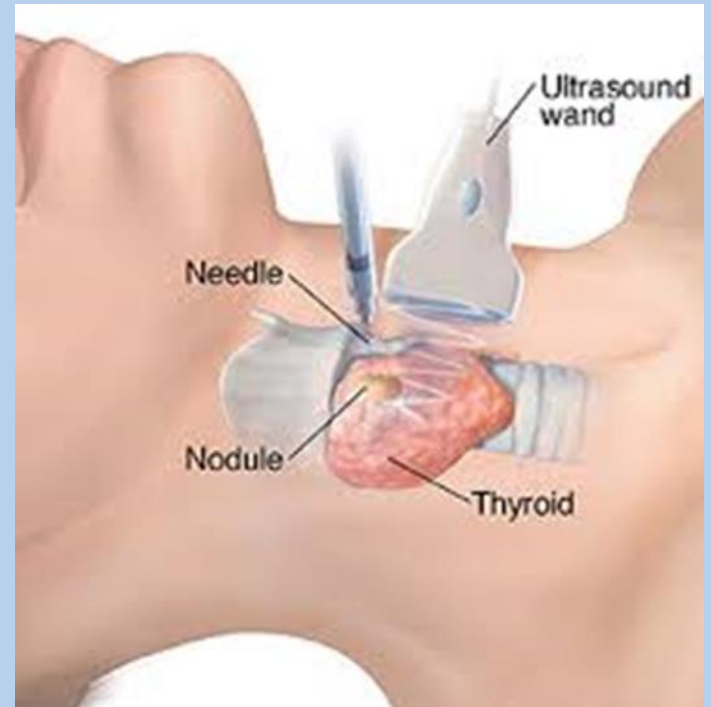
# Ultrasonographic guidance

- Thyroid FNA under ultrasonographic guidance achieved higher rates of adequate cell samples, in the range of 79–99.3% (mean, 91%).



# Ultrasonographic guidance

- Ultrasound-guided thyroid FNA proved to be useful in sampling TNs smaller than 2 cm in greatest dimension, complex or solid-cystic TNs and abnormal thyroid beds.



# thyroid tumour + regional adenopathy

- Where a thyroid tumour coexists with regional adenopathy, both the thyroid and the lymph node should be aspirated to rule out coexisting pathology and to allow preoperative staging in the case of thyroid malignancies.

# Staining of slides

- May-Grunwald-Giemsa (MGG) or a rapid Romanowsky-type stain such as Diff-Quik'o is recommended as this allows the visualization of colloid and can be used alone in thyroid fine needle aspiration.

- Wet fixation and Papanicolaou staining can provide complementary information in a minority of cases.

# Specimen Adequacy

- The range of inadequate or unsatisfactory specimens reported in the literature ranges from 2–21% (means 17%) .



# Specimen Adequacy

- Some investigators require that an adequate sample should contains five to six groups of well-preserved and well-visualized follicular cells with each group containing 10 or more cells.

# adequacy criteria

- One group requires multiple punctures of the TN to be evaluated, with at least six properly prepared smears and a minimum of 8–10 tissue fragments of well-preserved follicular epithelium on each of two slides.
- Another group requires 10 clusters of follicular cells with at least 20 cells in each cluster.

# specimen adequacy

- The Papanicolaou Society of Cytopathology Task Forces on Standard of Practice does not specify any numbers and groups of thyroid follicular epithelial cells for specimen adequacy.

# adequacy criteria

- Two practical exceptions to these adequacy criteria are applied:
- (a) a benign colloid nodule may be suggested if a large amount of thick colloid material is present, regardless of the number of follicular epithelial cell clusters
- (b) if a cell sample contains one or two small clusters of malignant or highly atypical cells, it should be reported as malignant or suspicious for malignancy and not as unsatisfactory or inadequate for cytodiagnosis.

# Cytodiagnostic Groups

- 1. Benign colloid nodule
  - - Solitary colloid nodule
  - - Prominent nodule in MNG
  - - Macrofollicular adenoma
- 2. Cellular microfollicular lesion
  - - Microfollicular adenoma
  - - Low-grade follicular carcinoma
  - - Hyperplastic microfollicular lesions in HT or MNG
- 3. Hurthle cell lesion
  - - Hurthle cell adenoma
  - - Hurthle cell carcinoma
  - - Hyperplastic Hurthle cell nodule in HT or MNG
- 4. Primary malignant tumor
  - - Papillary carcinoma
  - - High-grade microfollicular carcinoma
  - - Insular carcinoma
  - - Medullary carcinoma
  - - Anaplastic carcinoma
  - - Lymphoma
- 5. Cystic lesions
  - - Benign colloid nodule
  - - Papillary carcinoma
  - - Other thyroid neoplasms
- 6. Thyroiditis
  - - Acute thyroiditis
  - - Hashimoto thyroiditis
  - - Subacute thyroiditis
- 7. Other lesions
  - - Graves disease
  - - Metastatic cancer
- 8. Non-diagnostic category
  - -
  - \* *HT, Hashimoto thyroiditis; MNG, multinodular colloid goiter*

# 1. Benign Colloid Nodule

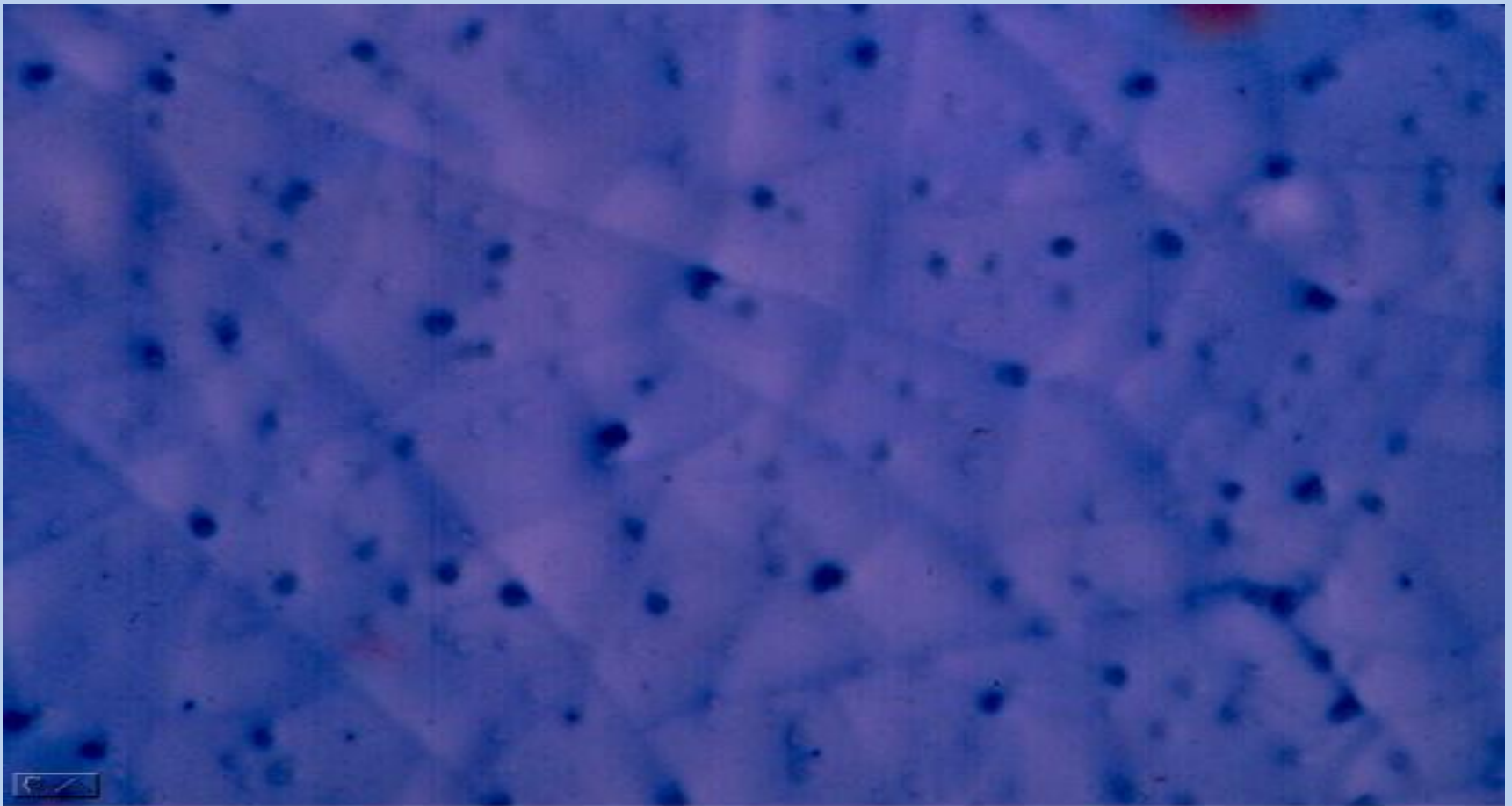
- This group includes

*1-solitary benign colloid nodules and*

*2-prominent benign colloid nodules in a multinodular colloid goiter.*

# Benign Colloid Nodule

- abundant, thick colloid material with cracking or bubble pattern
- sheets of benign follicular epithelial cells in honeycomb arrangement .
- Clusters of slightly hyperplastic Hurthle cells



Thick, deep blue colloid material with cracking pattern in FNA of a benign colloid nodule



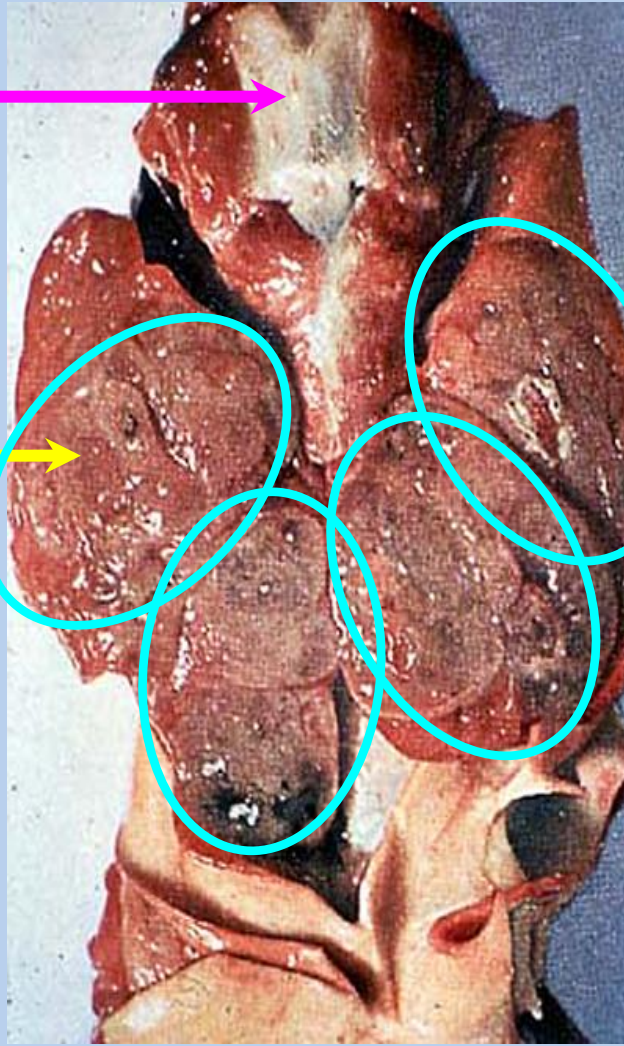
# Later Stage Adenomatous Goiter

Multiple Soft Large Nodules

Thyroid Cartilage



Thyroid



# Adenomatous Goiter

Many nodules

Capsule incomplete, irregular

Follicles variable

No compression of  
surrounding follicles

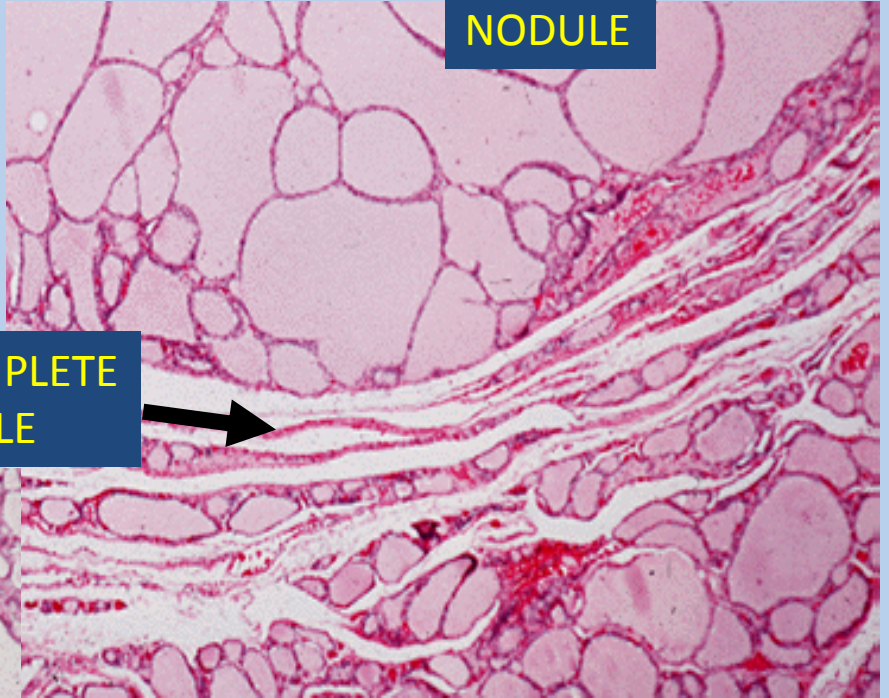
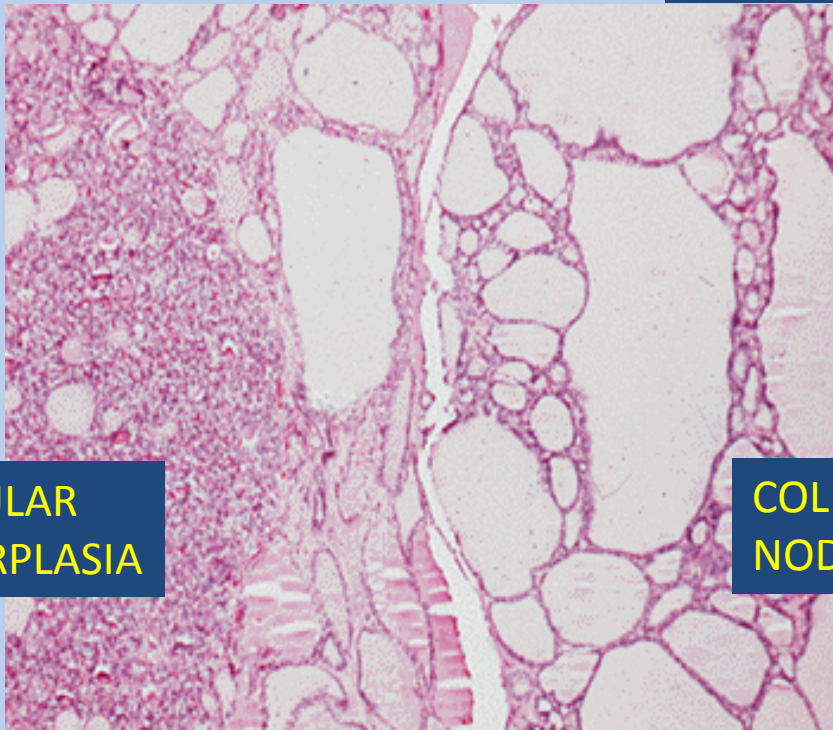
COLLOID  
NODULE

INCOMPLETE  
CAPSULE



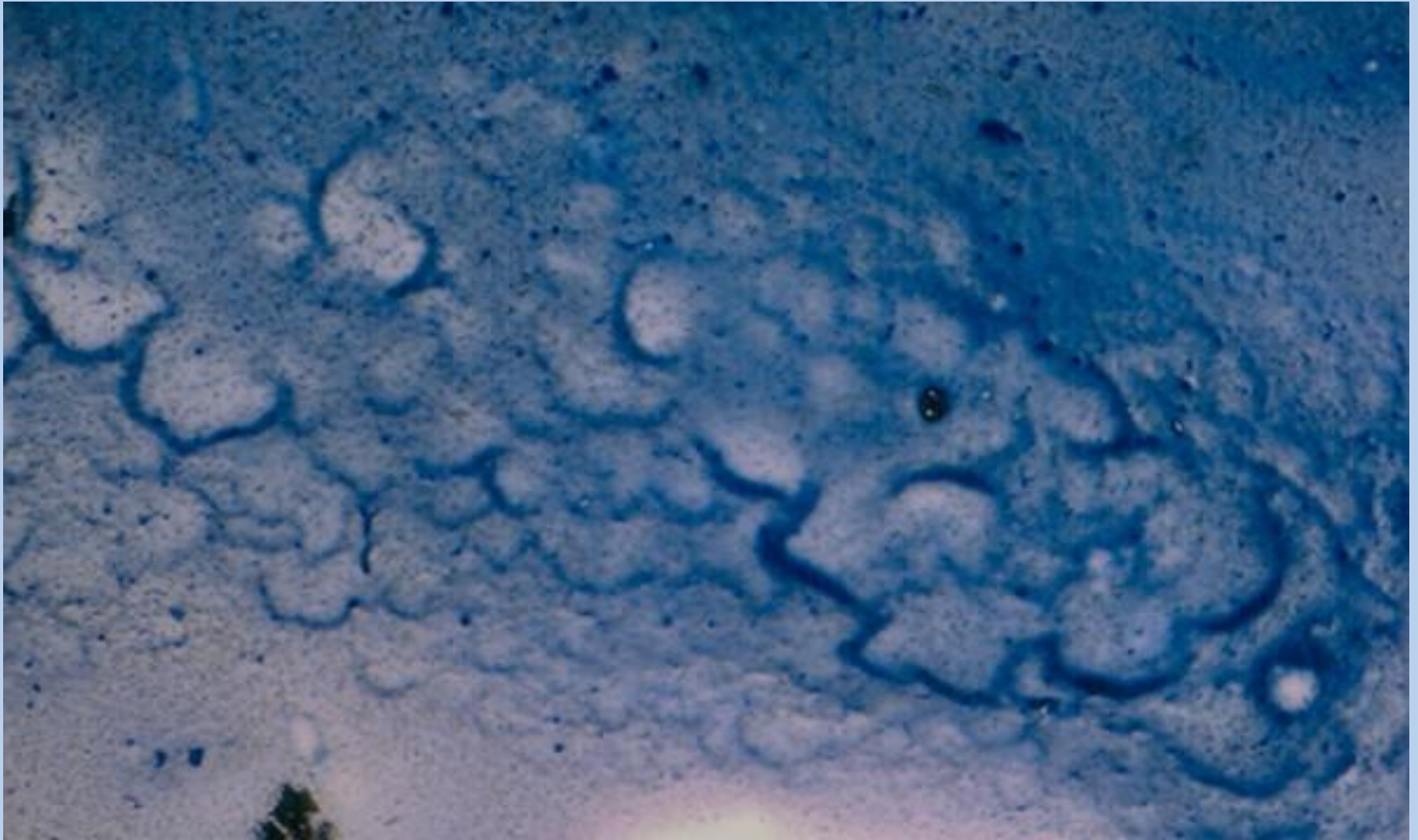
NODULAR  
HYPERPLASIA

COLLOID  
NODULE

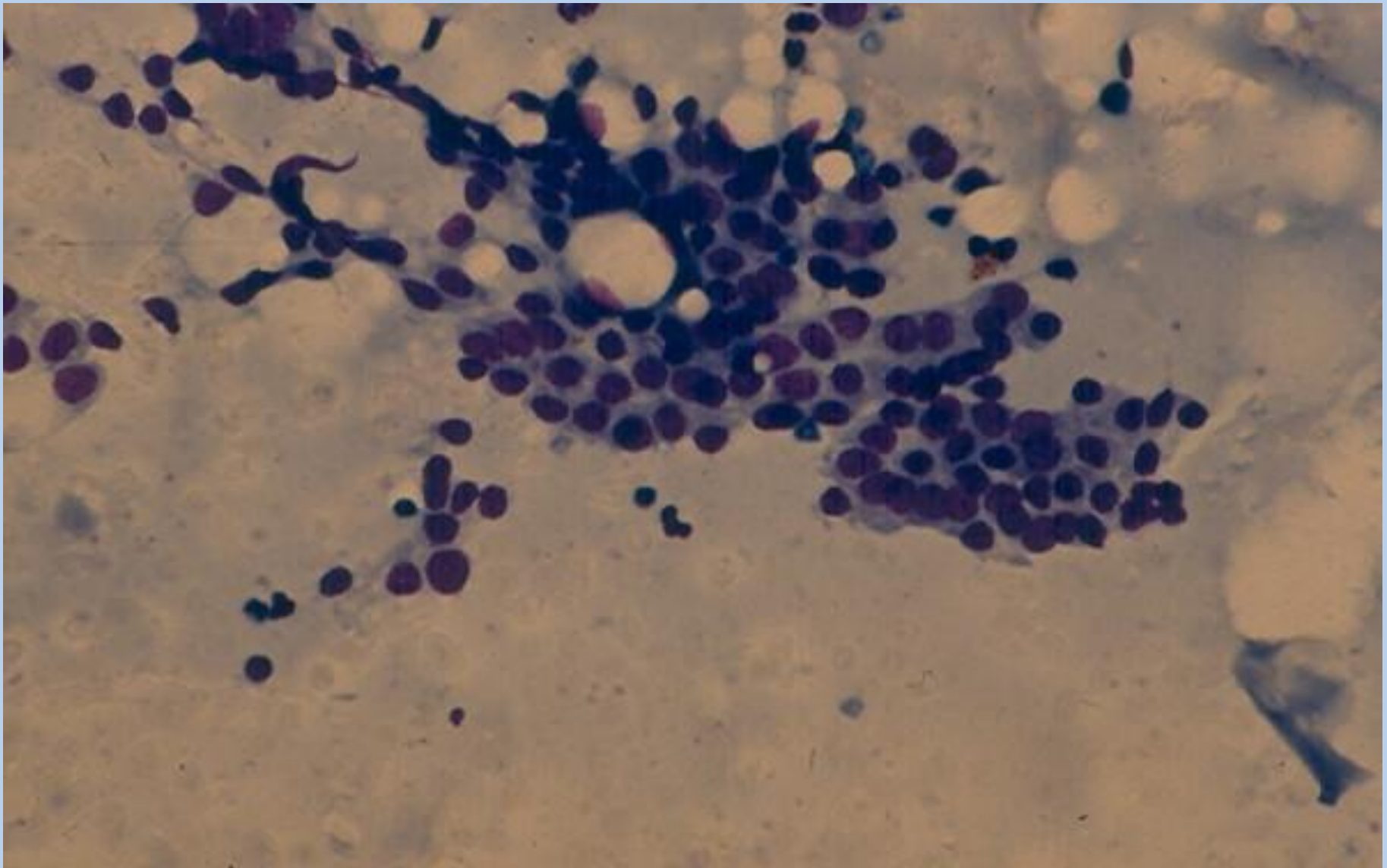


- The cytological differential diagnosis between a benign colloid nodule and a *macrofollicular adenoma* of the thyroid is extremely difficult if not impossible.
- The two lesions usually show abundant, thick colloid and similar follicular cells.





Thick, deep blue colloid material with bubble pattern in FNA of a benign colloid nodule



A monolayered sheet of benign follicular epithelial cells with honeycomb pattern in FNA of a benign colloid nodule

## 2. Cellular Microfollicular Lesion

- This group includes :
  - hyperplastic microfollicular nodules*** in a multinodular colloid goiter or Hashimoto thyroiditis
  - a ***microfollicular adenoma***
  - a ***well-differentiated follicular carcinoma***

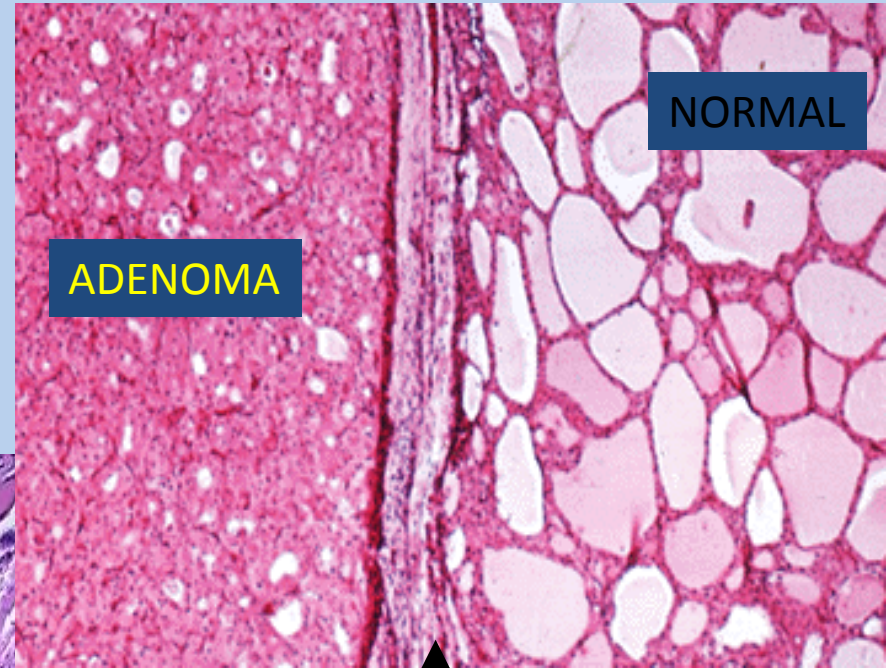
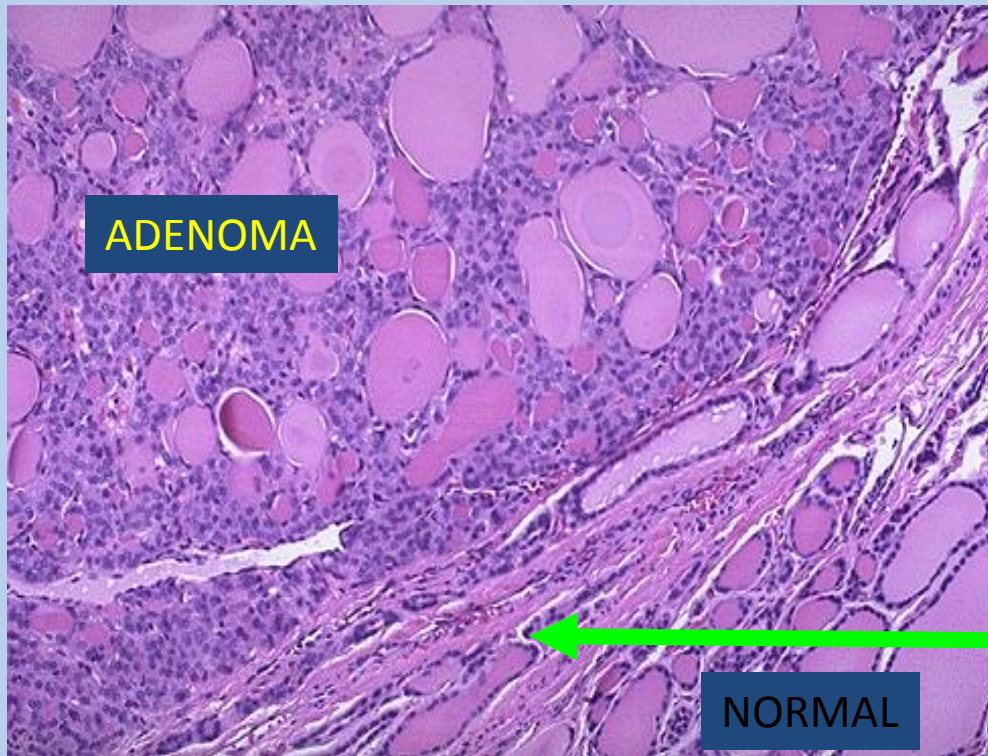
# Cellular Microfollicular Lesion

- These lesions are the most challenging ones to diagnose cytologically.
- They are commonly reported as a microfollicular lesion or tumor with a recommendation for surgical excision.



Solitary  
Monoclonal  
Follicles uniform  
Complete capsule  
No invasion through capsule  
Different morphology  
Compression of surrounding capsule

# Adenoma



COMPLETE CAPSULE

Compression normal  
follicles

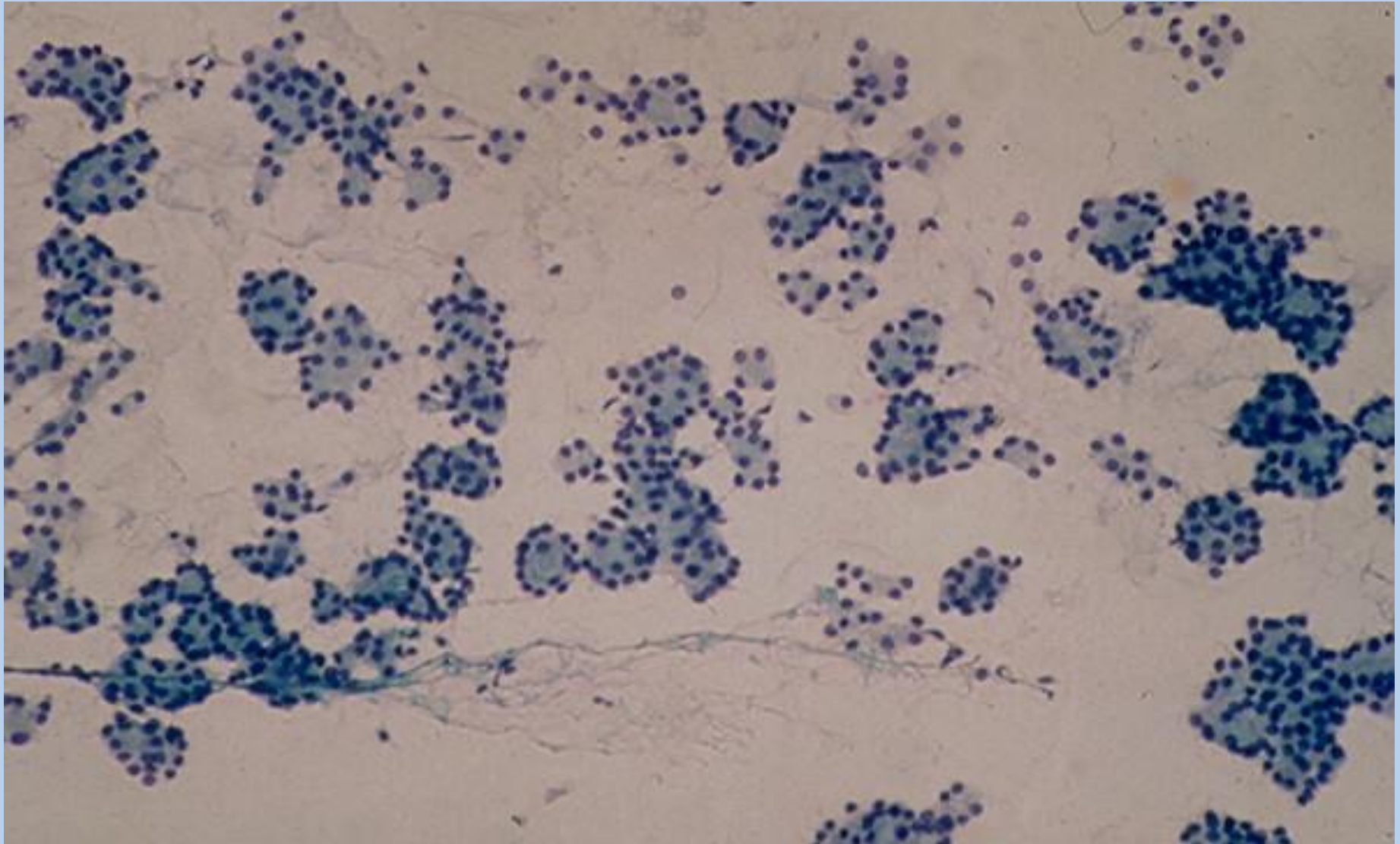


# microfollicular lesion

- Abundant follicular cells in clusters, acini and small monolayered sheets.
- The individual cells show scanty, ill-defined cytoplasm and oval nuclei with regular nuclear contours and inconspicuous or prominent nucleoli.

# microfollicular lesions

- fall into the diagnostic category of **indeterminate or suspicious lesions**
- In one large series 14% of microfollicular lesions were malignant.

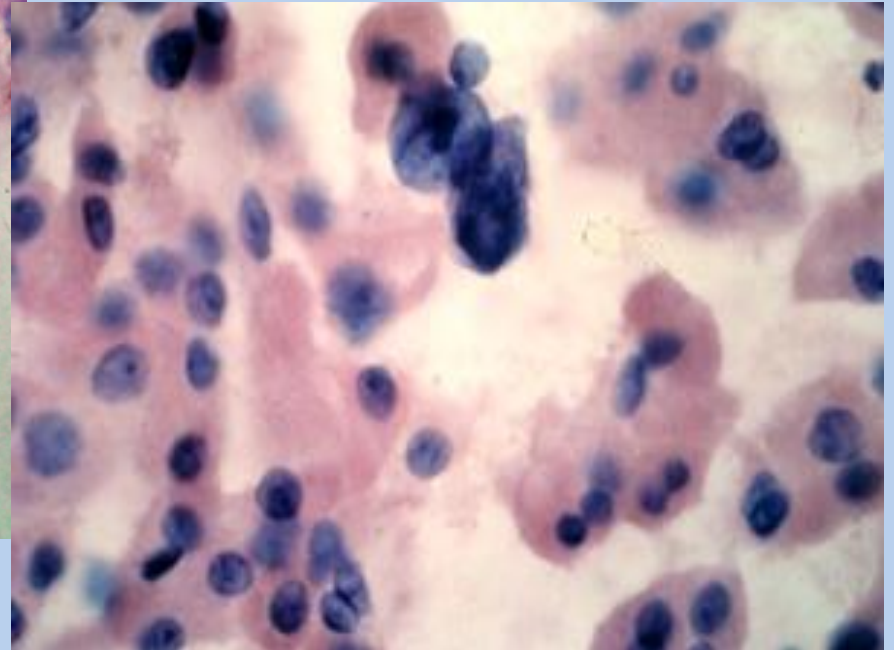
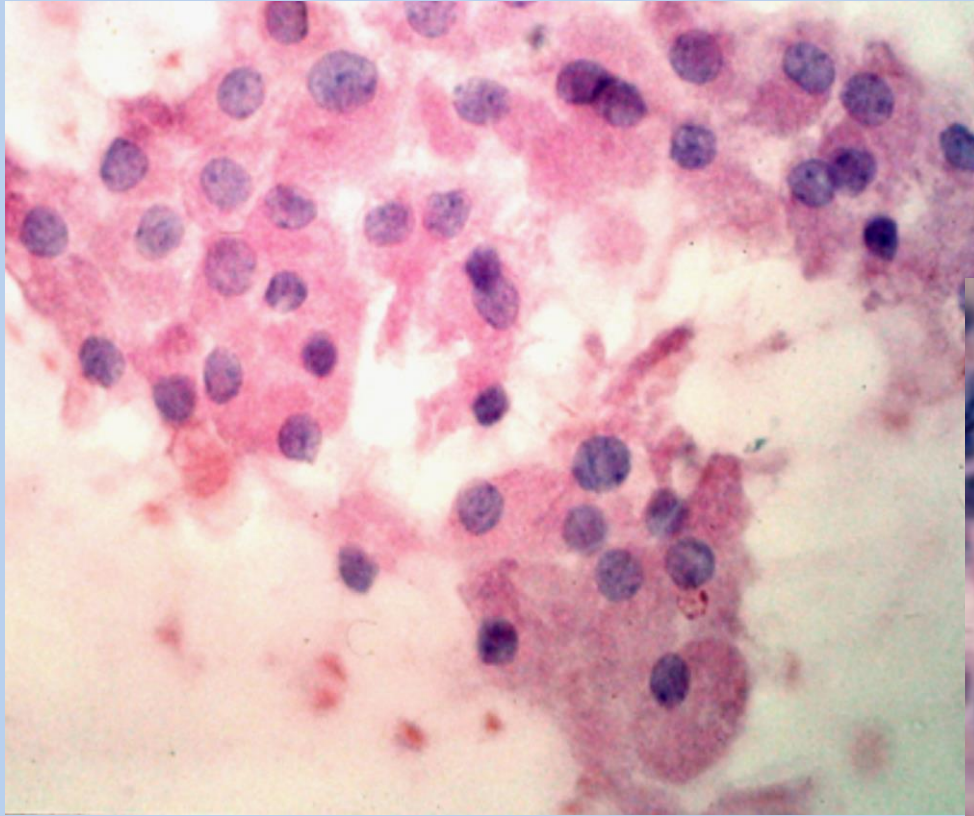


Cellular microfollicular lesion showing in FNA cells with round nuclei arranged in acini and small monolayered sheet

### 3. Hurthle Cell Lesion

- Diagnosis of Hurthle cell lesions is a challenge in thyroid cytology.
- A hyperplastic Hurthle cell nodule in a Hashimoto thyroiditis or in a multinodular colloid goiter and a Hurthle cell neoplasm display similar cytologic findings .
- The presence of numerous lymphocytes or a large amount of thick colloid material in the needle aspirate may indicate a hyperplastic Hurthle cell nodule in Hashimoto disease or a multinodular colloid goiter, respectively.

# Hurthle Cell Thyroid Adenoma

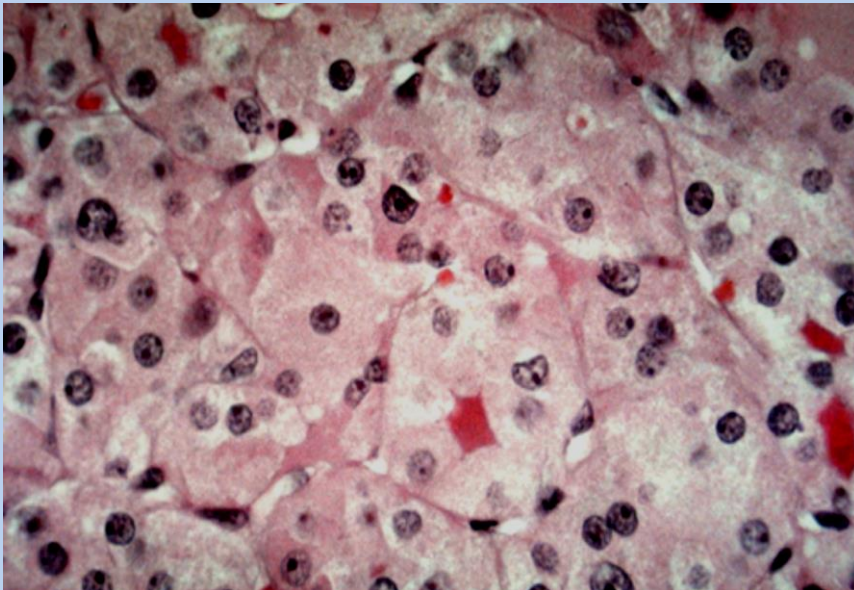


If  $> 90\%$  cells have hurthle changes and no inflammatory cells, the FNA biopsy is considered indeterminate.



# Hurthle Cells

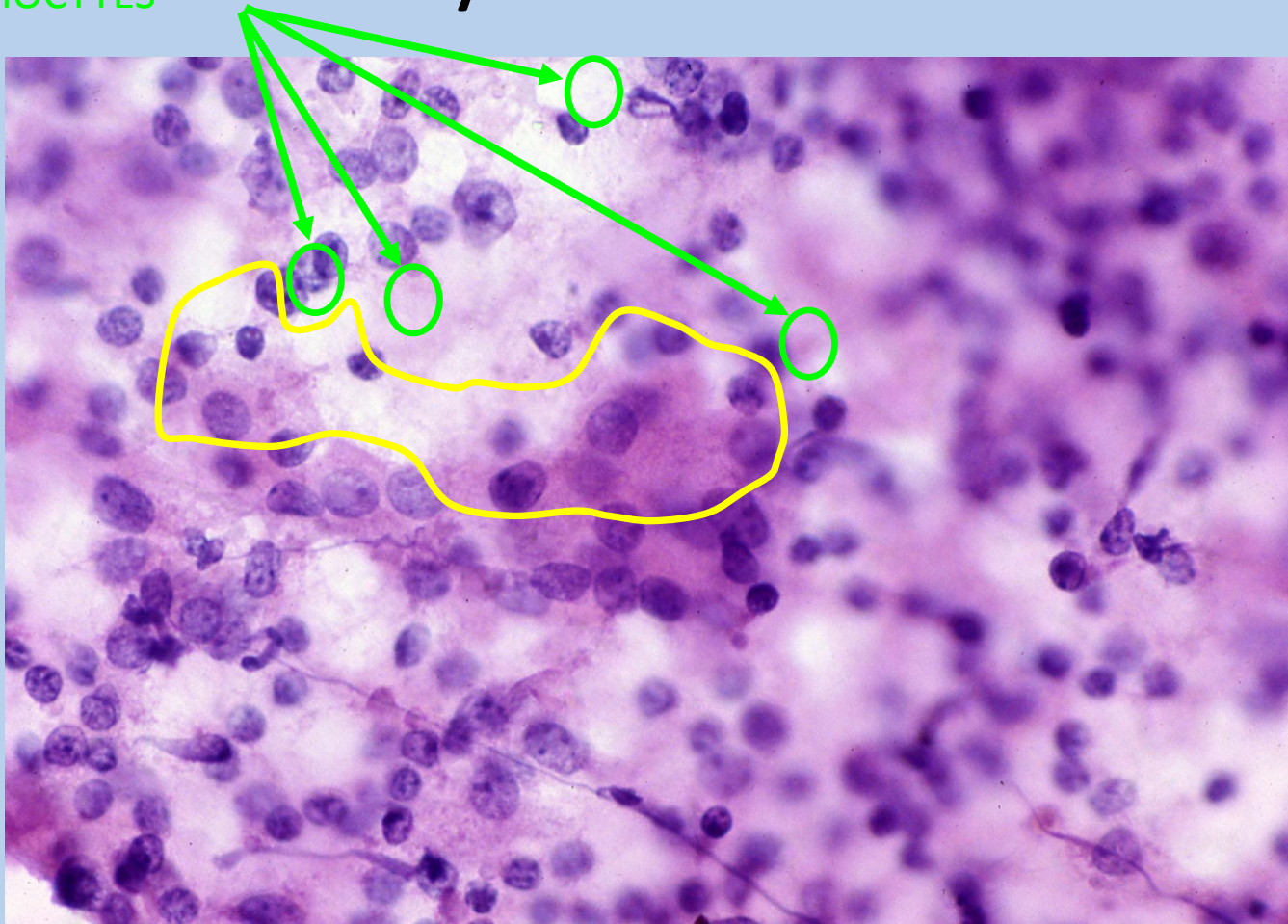
- Histological characteristics
  - Voluminous, pink, granular cytoplasm (mitochondria)
  - Striking Nuclear Atypia
    - Not an indication of malignancy
  - Prominent nucleoli



- May occur in many types of thyroid pathology
  - Hurthle Adenoma
  - Hurthle Carcinoma
    - **Separate WHO classification from Follicular Thyroid CA**
  - Hashimoto's thyroiditis
    - Askanazy cell
    - Lymphocytes
    - Fibrosis
  - Nodular goiter
    - Focal

# Hurthle Cells and Hashimoto Thyroiditis FNA

LYMPHOCYTES



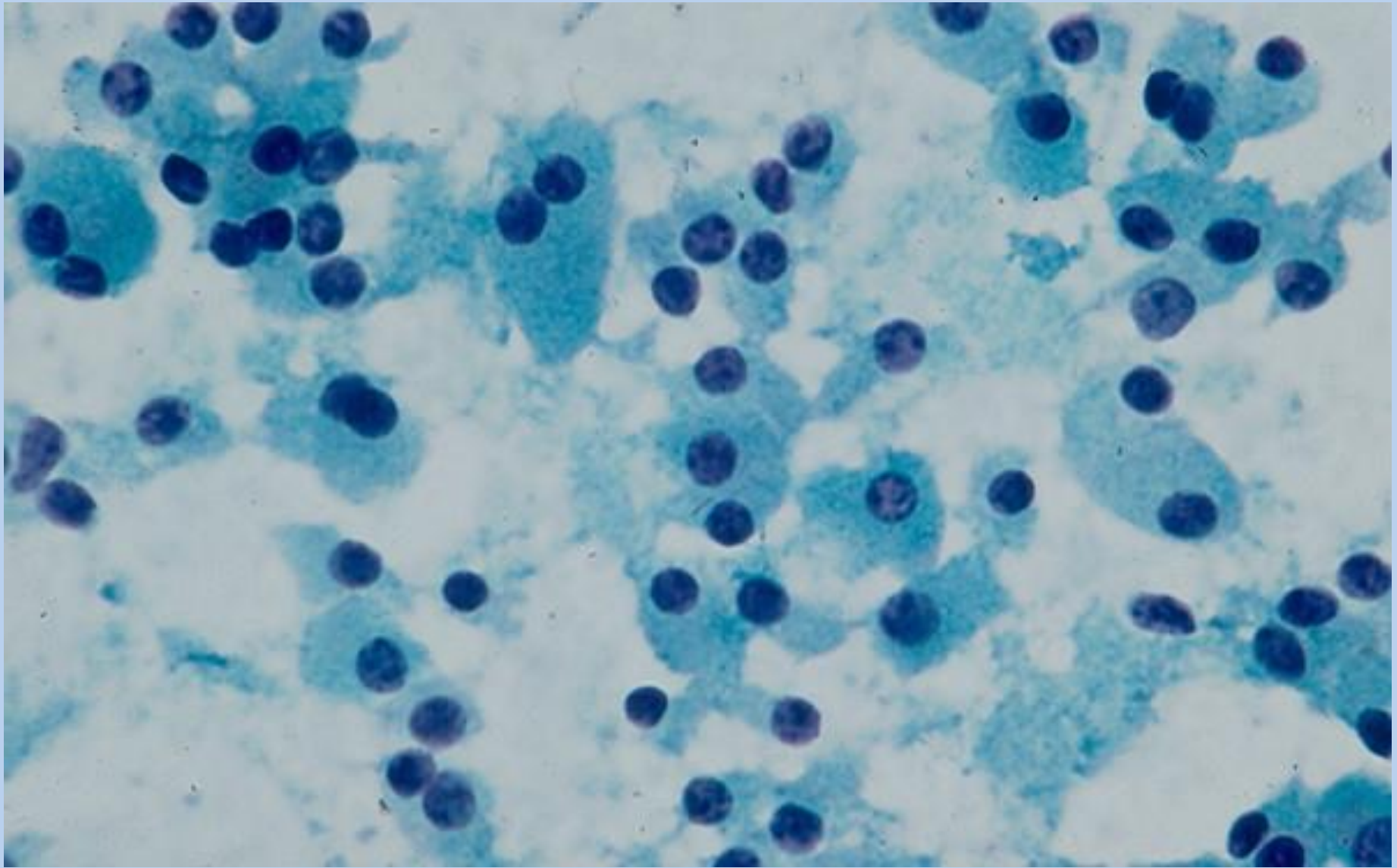
# Hurthle cell lesion

- When a Hurthle cell lesion is detected by FNA, surgical excision is usually indicated for further histologic study .

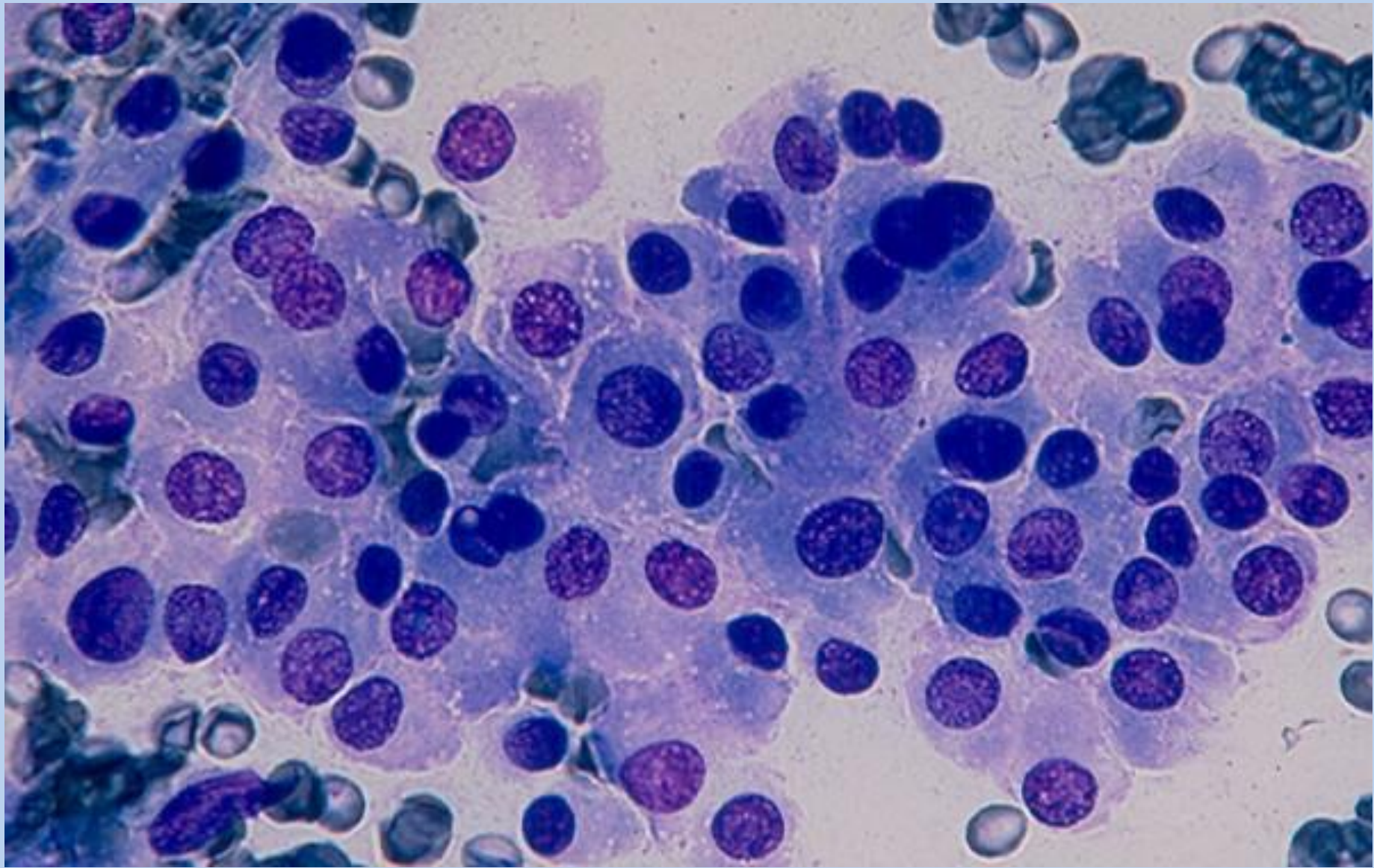


# Hurthle cell lesion

- fall into the cytodiagnostic category of **indeterminate lesions or suspected malignant lesions** , and 13% of Hurthle cell lesions were malignant in one large series .



Hurthle cells with abundant, granular cytoplasm and round, central or eccentrically located nuclei in FNA of a Hurthle cell lesion



Hurthle cells in loose, monolayered sheet and singly in FNA of a Hurthle cell lesion

## 4. Primary Malignant Lesions

- This group includes:
  - Papillary carcinoma
  - high-grade follicular carcinoma
  - Insular carcinoma
  - medullary carcinoma
  - anaplastic carcinoma
  - Lymphoma
- These lesions commonly show distinctive cytologic features that permit a correct identification in the majority of cases .

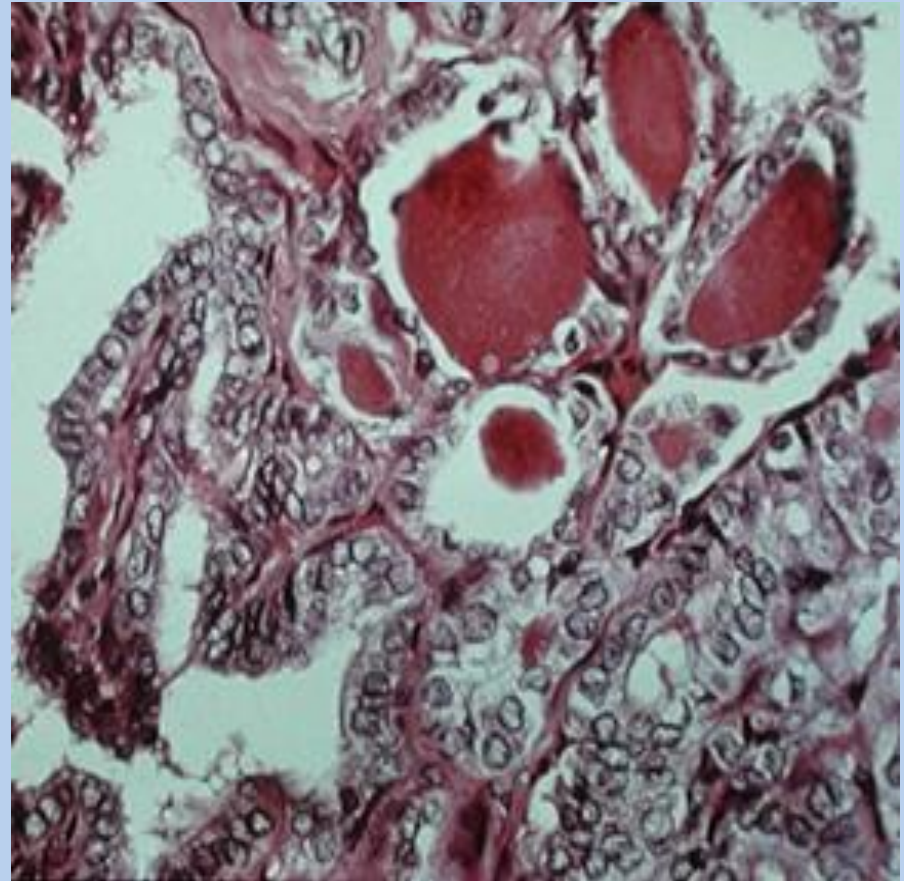


# Papillary carcinoma (PC)

- Thick or thin papillary tissue fragments with fibrovascular cores, sheets of tumor cells showing focal nuclear crowding and overlapping, irregular nuclear contours, intranuclear cytoplasmic inclusions (INCI) and nuclear grooves (NG).
- Psammoma bodies and metaplastic squamous cells may also be present .
- These nuclear changes are recognized with less difficulty in Papanicolaou-stained cell samples, but they may be difficult to identify in cell samples stained with the Romanowsky staining method

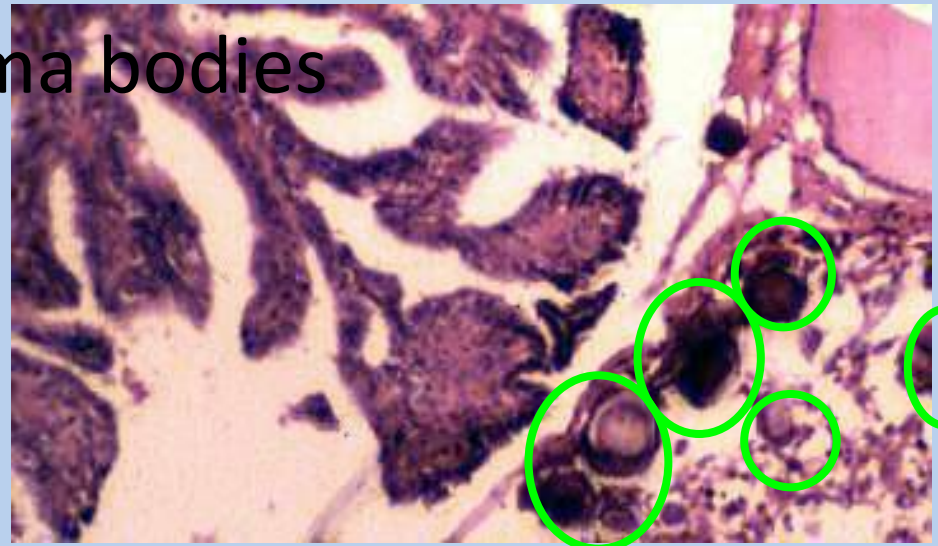
# Papillary Thyroid Carcinoma

- Most common thyroid cancer
- Variable size - average 2 cm
- 25-30 % micrometastases in contralateral lobe
- Often undergoes cystic degeneration
- Frequently has local lymph node metastases - not important for prognosis
- Less commonly has local and distant invasion important for prognosis



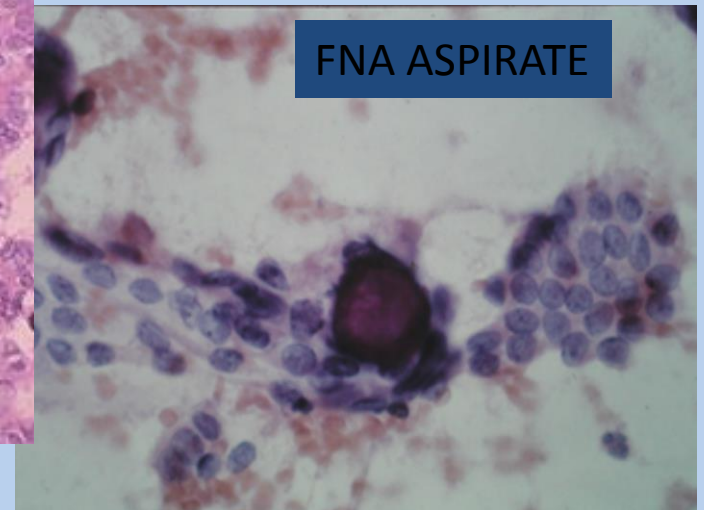
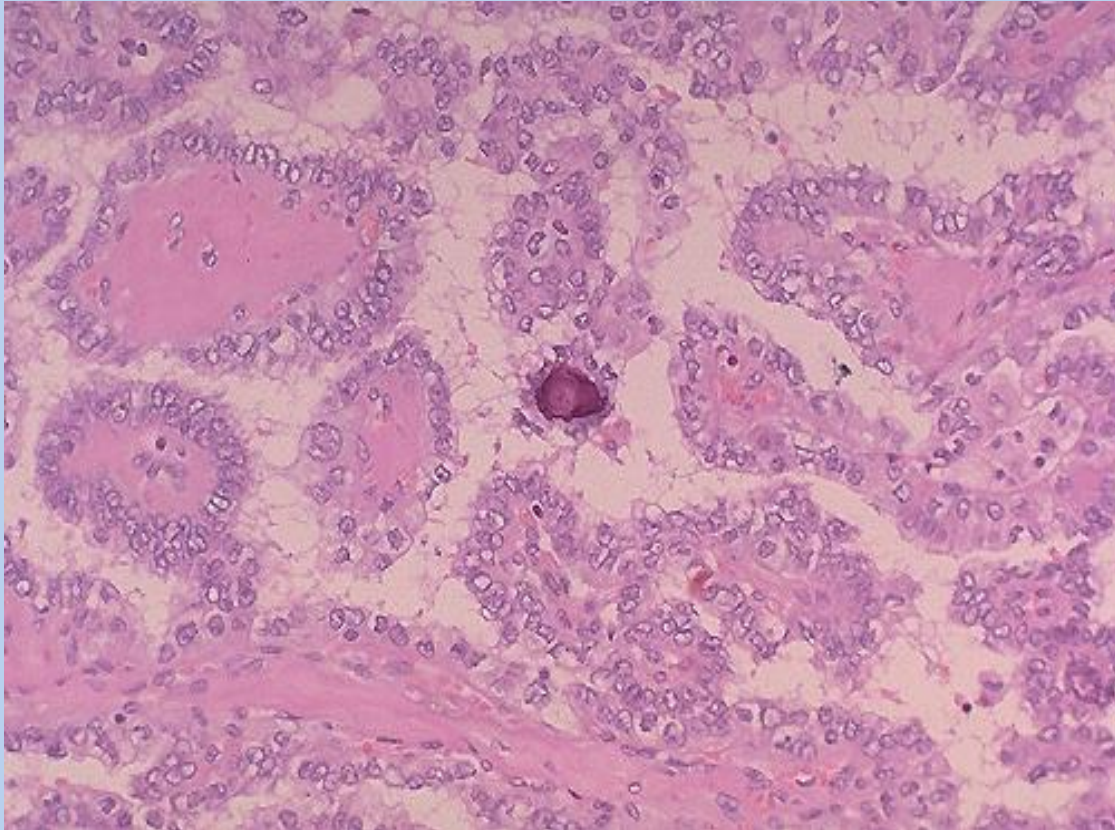
# Papillary Thyroid Carcinoma

- Complex branching structures
- Monolayer sheets of crowded, overlapping, vesicular nuclei
- Fibrovascular core
- Calcifications with concentric lamination: psammoma bodies
- Little colloid



Psammoma bodies

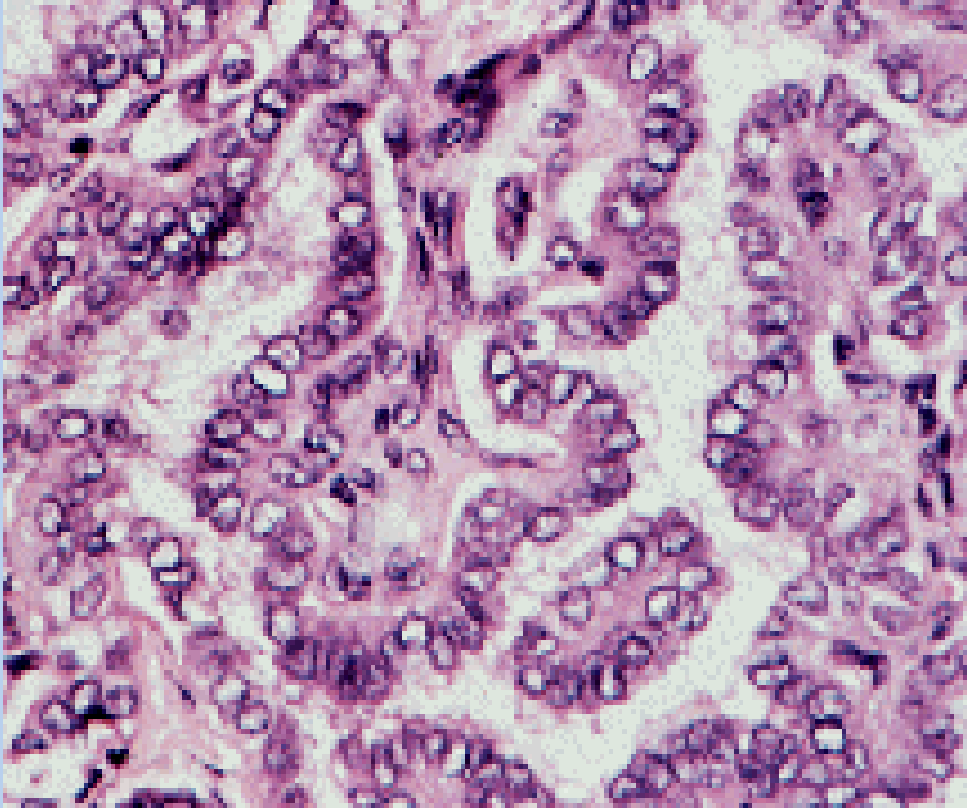
# Psammoma Bodies and Papillary Thyroid CA



Lamellated or layered calcification  
microscopic calcium deposits

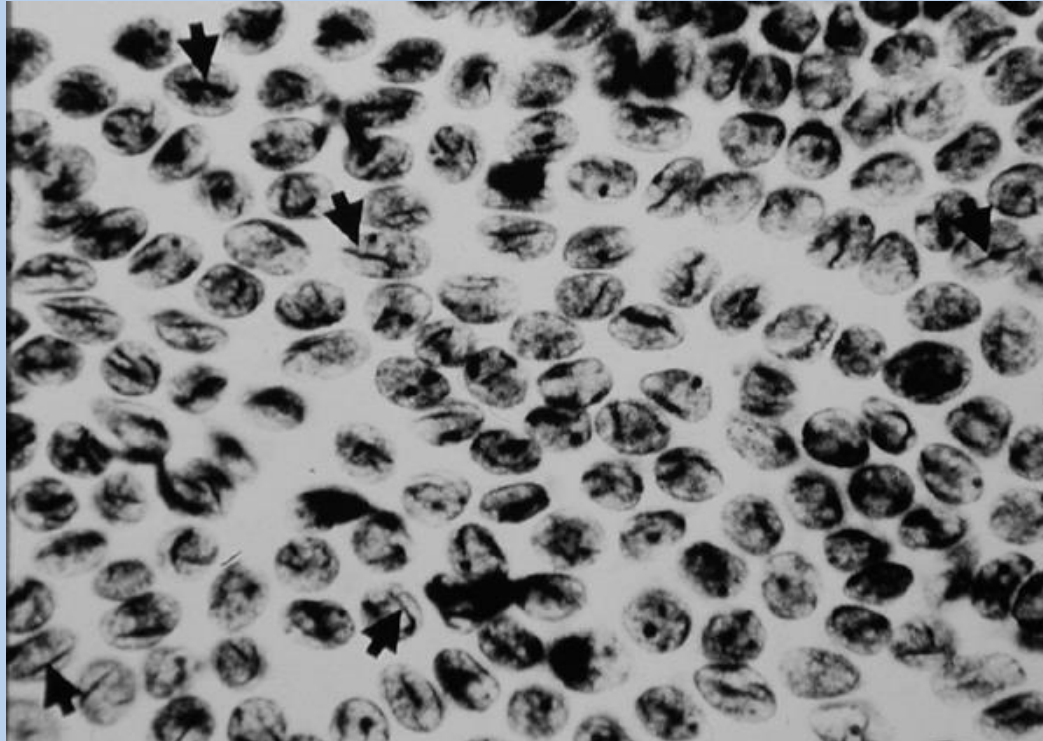


# Papillary Thyroid CA DX Depends on Nuclear Characteristics :Vesicular Nuclei



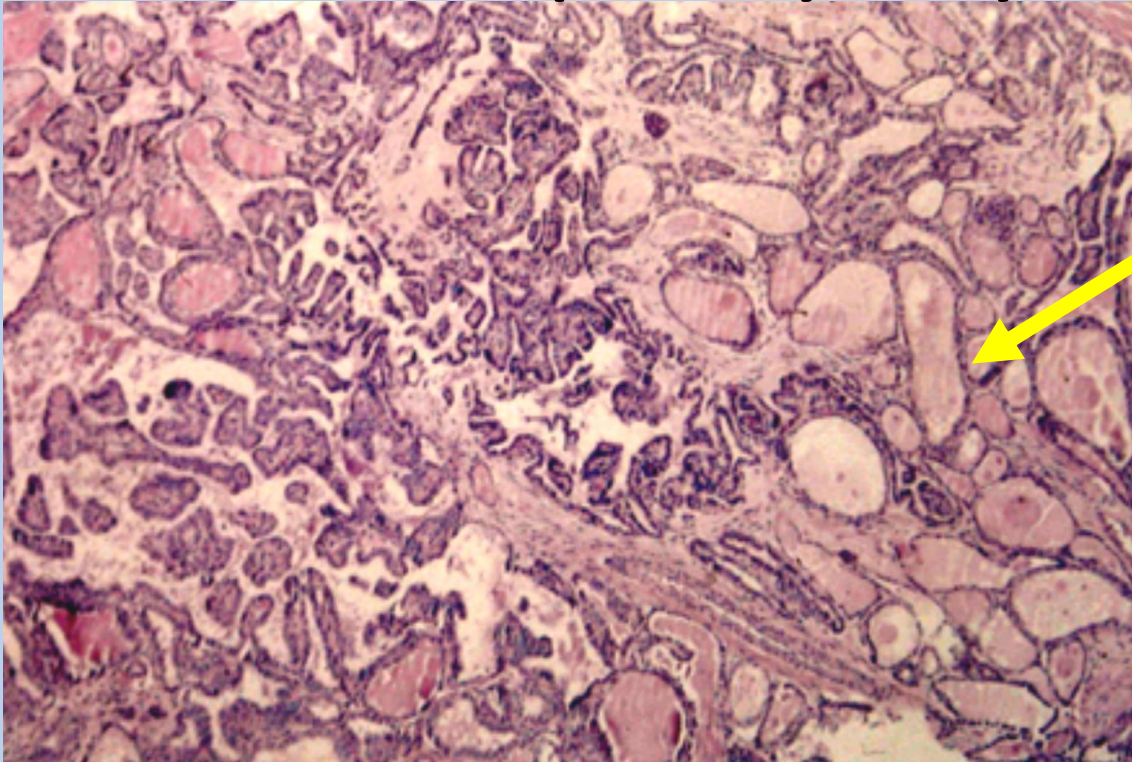
**“Orphan Annie Eyes” is an artifact from formalin fixation  
of FINELY DISPERSED NUCLEAR CHROMATIN**

# Papillary Thyroid CA DX Depends on Nuclear



**Silver stain of pseudo“nuclear grooves” of “coffee bean” nuclei caused by in-folding of redundant nuclear membrane**

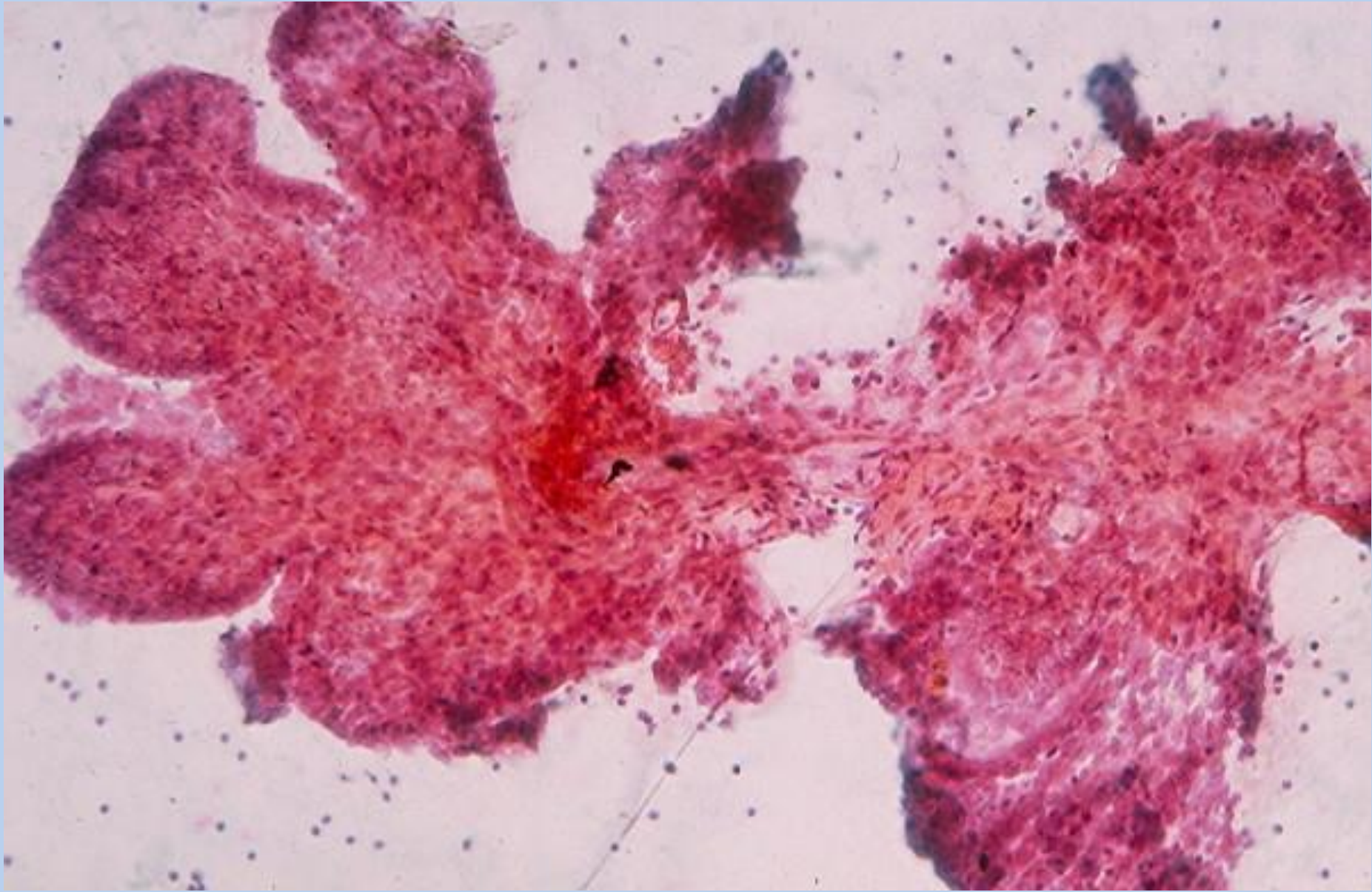
# Papillary Thyroid CA



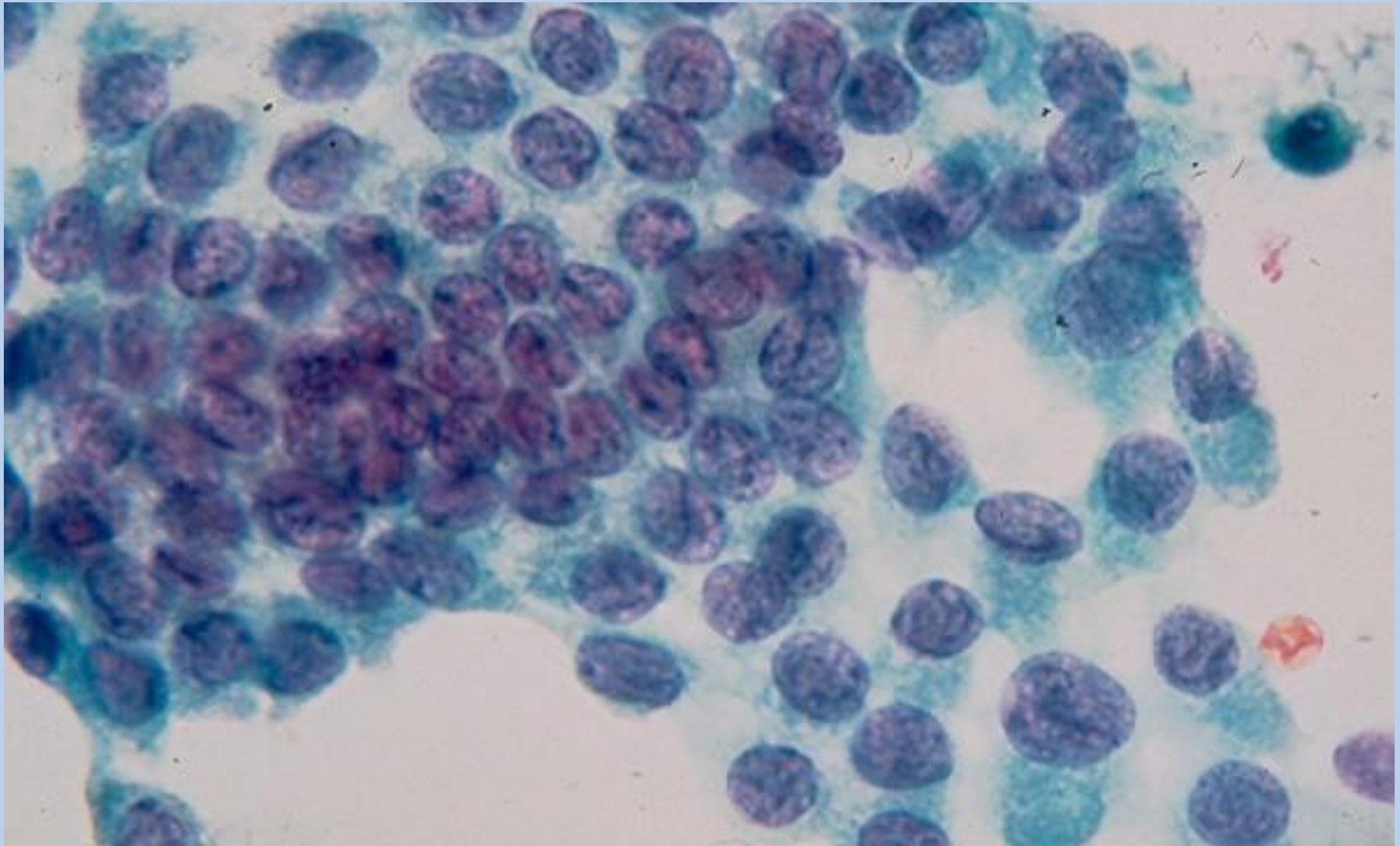
**Follicular variant of PTC:  
Nuclear characteristics of PTC but in solid micro-follicular pattern**

Follicular variant of PTC acts biologically like classic PTC and NOT follicular thyroid CA



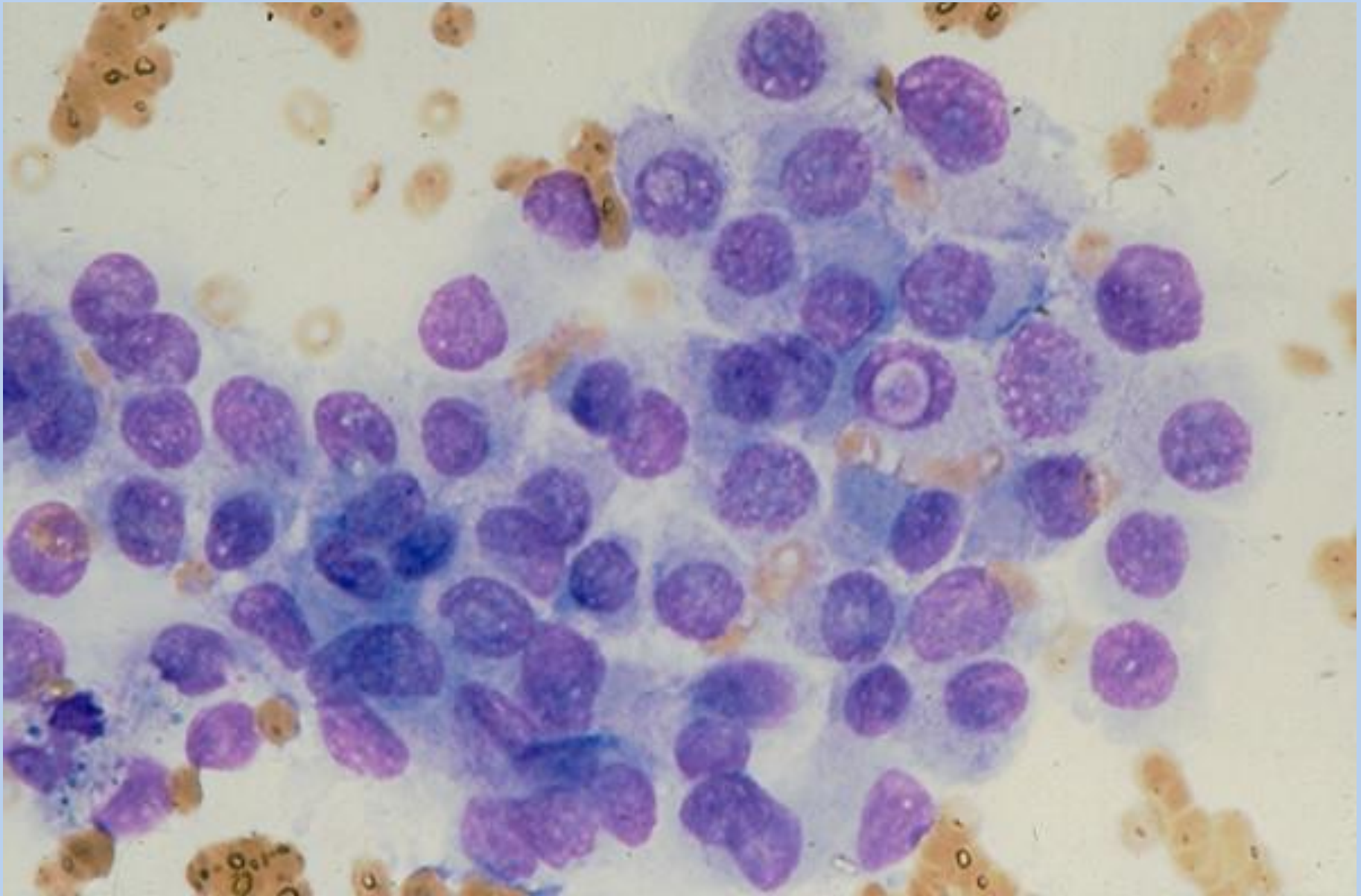


Thick branching papillary tissue fragment with fibrovascular core in FNA of a conventional papillary carcinoma (Papanicolaou stain,  $\times 100$ ).

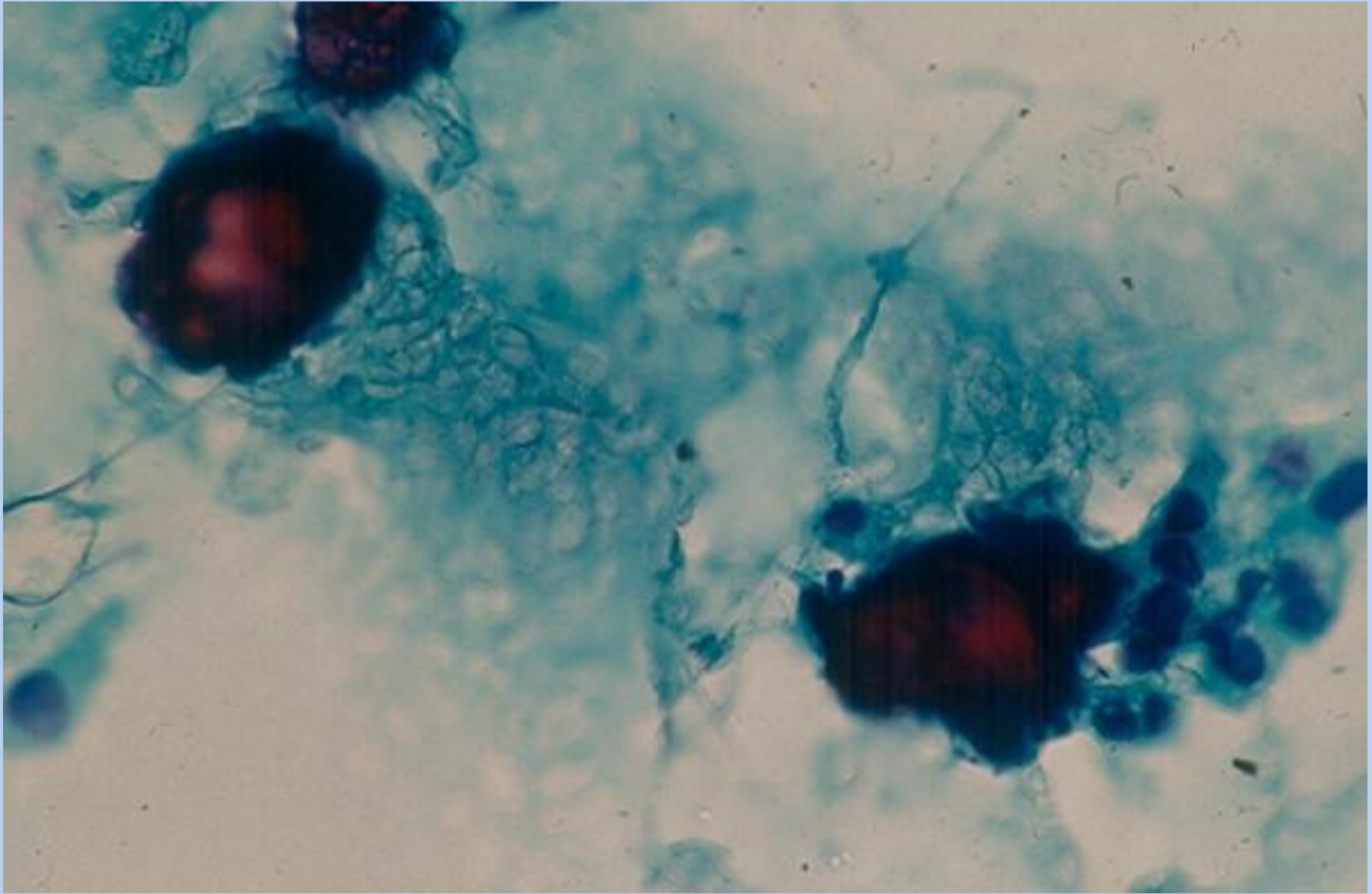


A sheet of tumor cells showing focal nuclear crowding with several cells displaying nuclear grooves in FNA of a conventional papillary carcinoma (Papanicolaou stain,  $\times 400$ ).





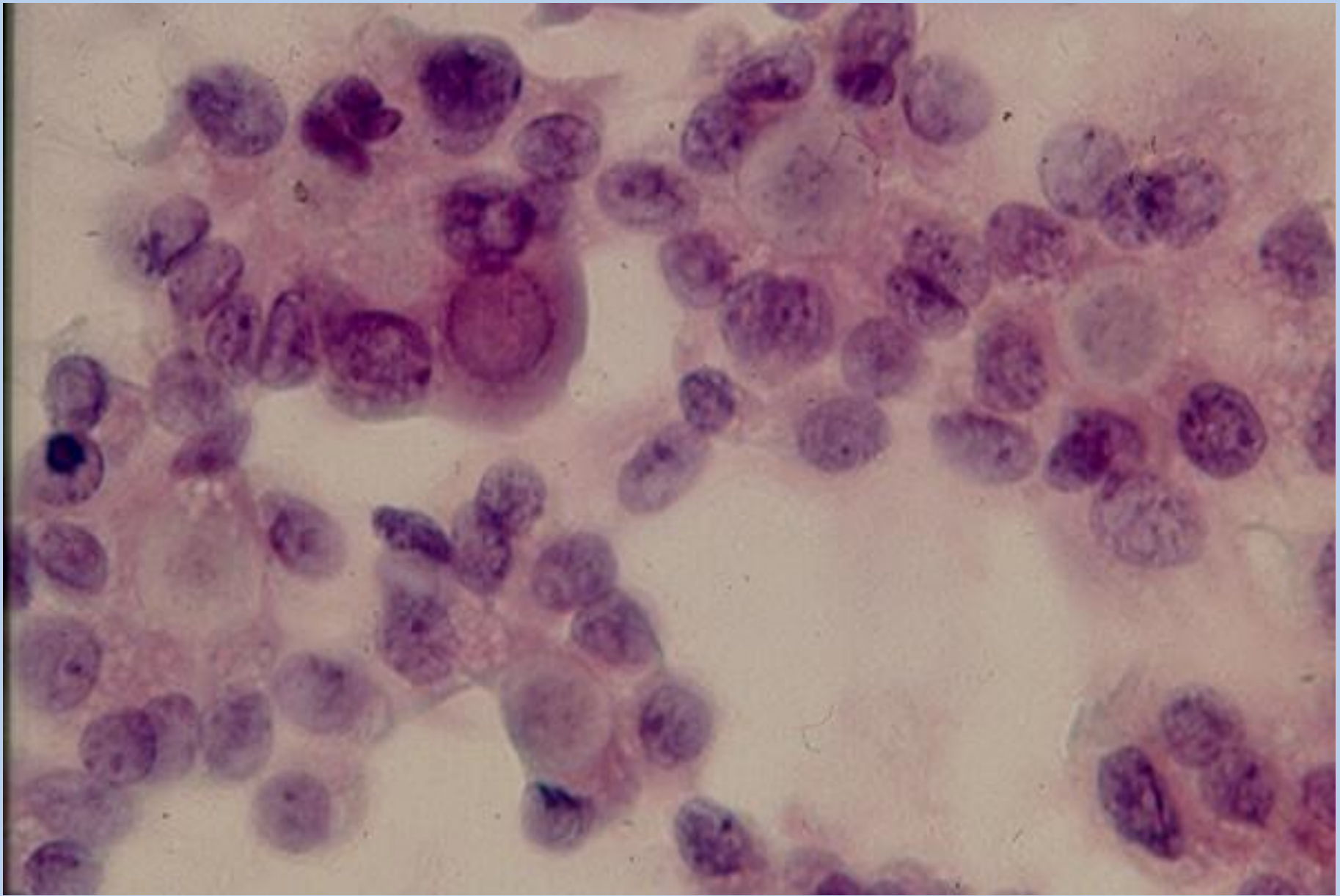
A loose sheet of tumor cells showing minimal nuclear crowding and two cells with intranuclear cytoplasmic inclusions in FNA of a conventional papillary carcinoma (Diff-Quik stain,  $\times 400$ ).



Two psammoma bodies in a smear showing a small amount of colloid material. A small aggregate of poorly preserved follicular cells is seen beside one psammoma body (Papanicolaou stain,  $\times 400$ ).

- - Micro- and macrofollicular PCs constitute a diagnostic challenge.
- A microfollicular PC may show in FNA follicular cells forming acini similar to those seen in the aforementioned cellular microfollicular lesions
- A macrofollicular PC may be easily mistaken for a macrofollicular adenoma or a benign colloid nodule cytologically, as nuclear changes characteristic for a thyroid PC may not be seen .



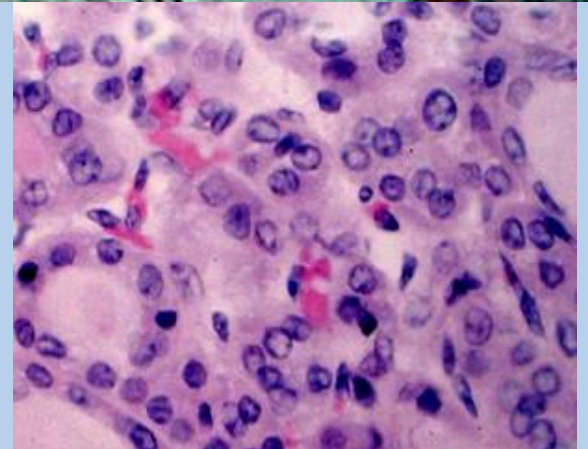
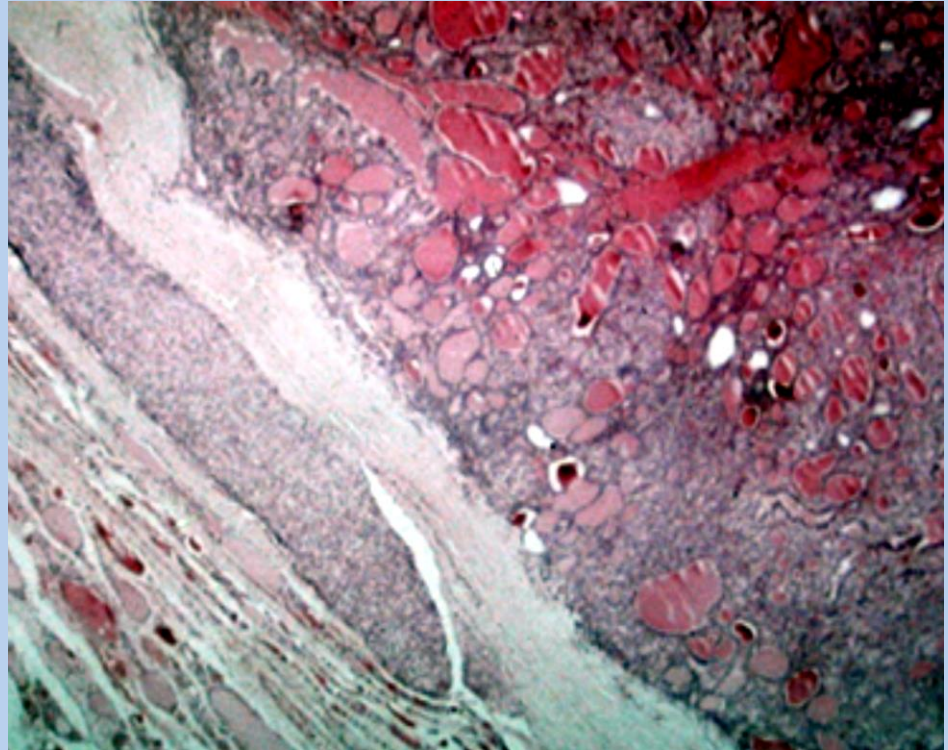


Papillary carcinoma, microfollicular variant showing in FNA cells in acinar arrangement. A tumor cell with an intranuclear cytoplasmic inclusion is noted (Papanicolaou stain,  $\times 400$ ).

# Follicular Carcinoma

Require capsular and vascular invasion otherwise looks like adenoma

- Low risk:
  - Encapsulated
  - Hypercellular with follicles
  - Focal capsular or vascular invasion
  - Rarely metastatic
- High risk:
  - Partially or non-encapsulated
  - Ranges from follicles to solid growth
  - Prominent capsular and/or vascular invasion
  - Frequently metastatic, often distant spread

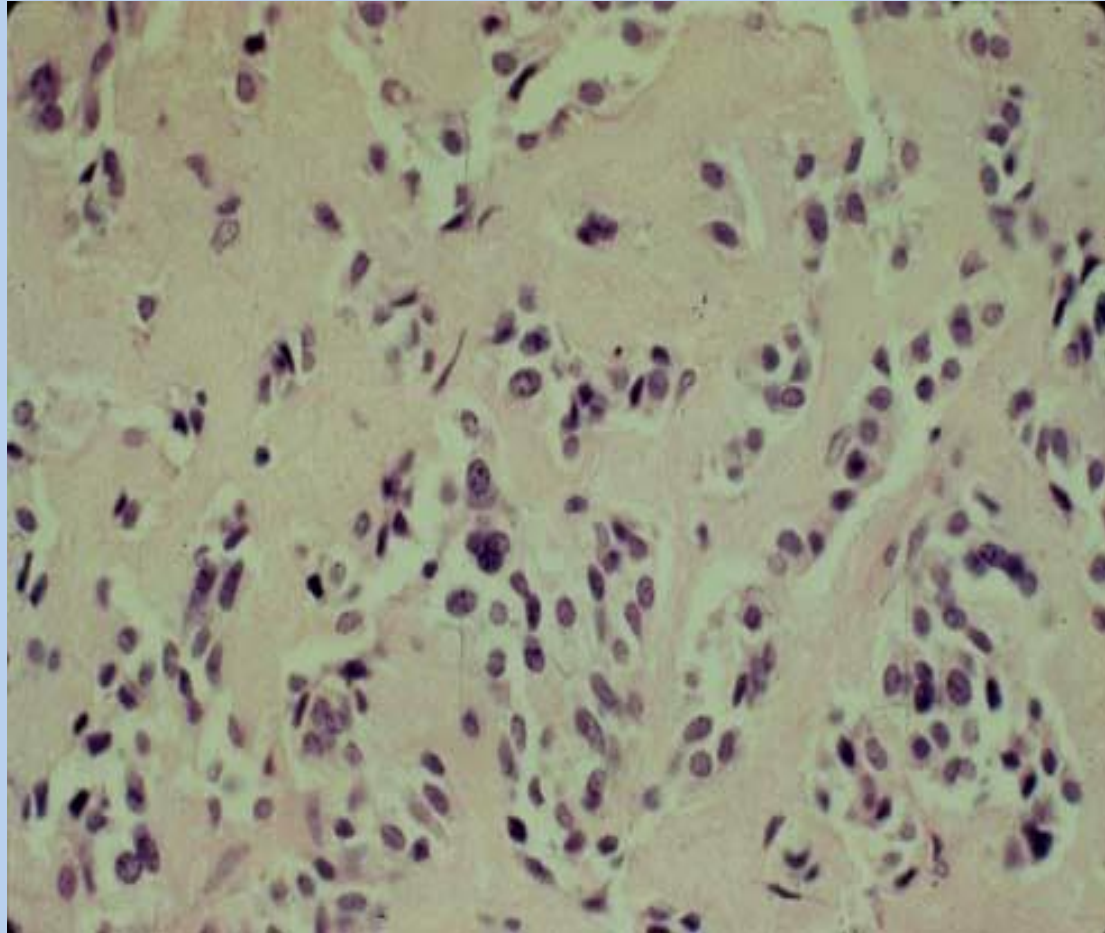


# medullary carcinoma

- shows in FNA a mixture of single and clustered polygonal cells and spindle tumor cells that may display INCI's .
- The tumor cells cytoplasm may show intracytoplasmic pink azurophil granules that are well-visualized by MGG or Diff-Quik stain and stain positively with calcitonin antibody.
- Amyloid material that stains positively with Congo red may be seen .

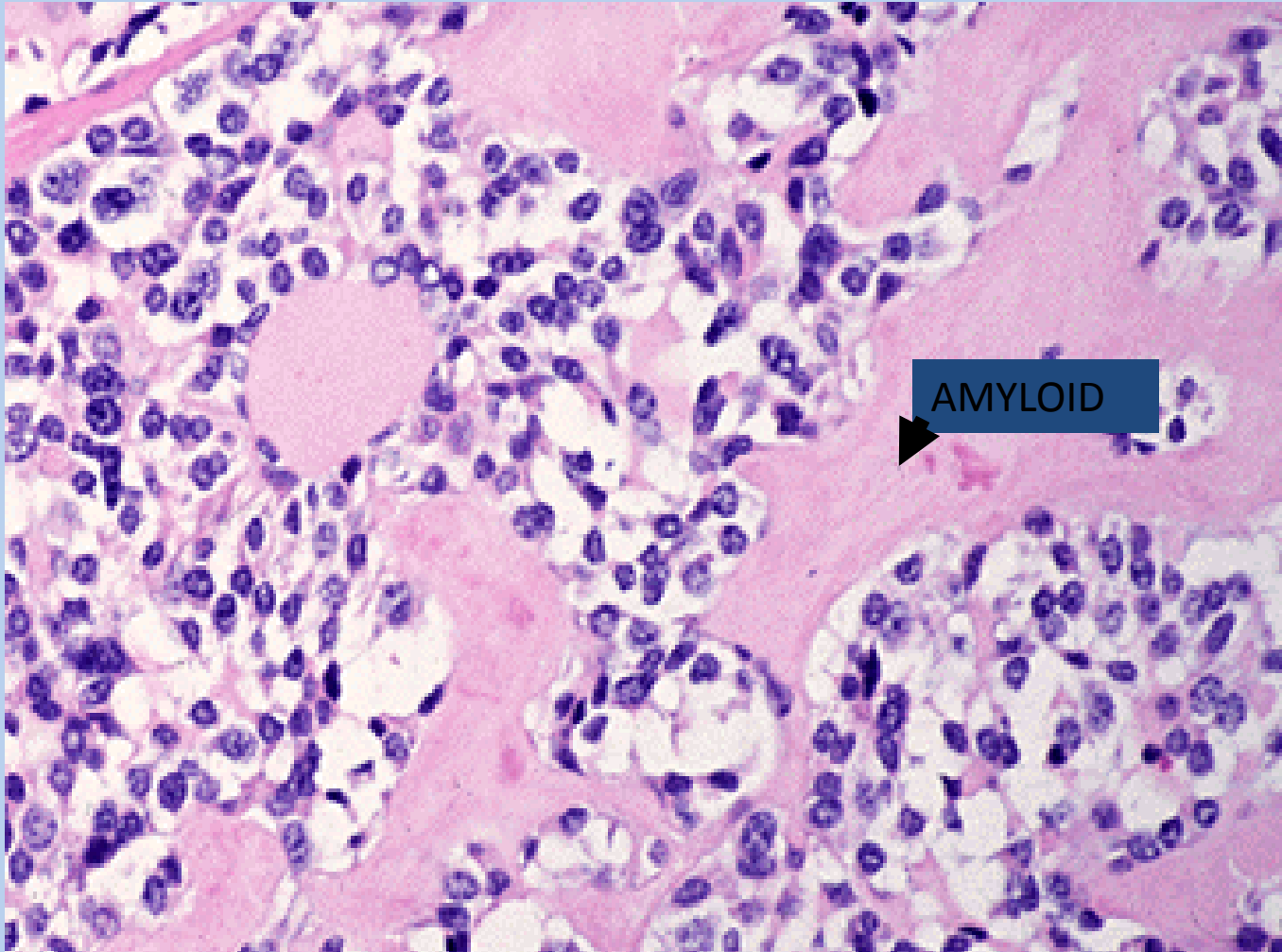


# Medullary Thyroid Carcinoma

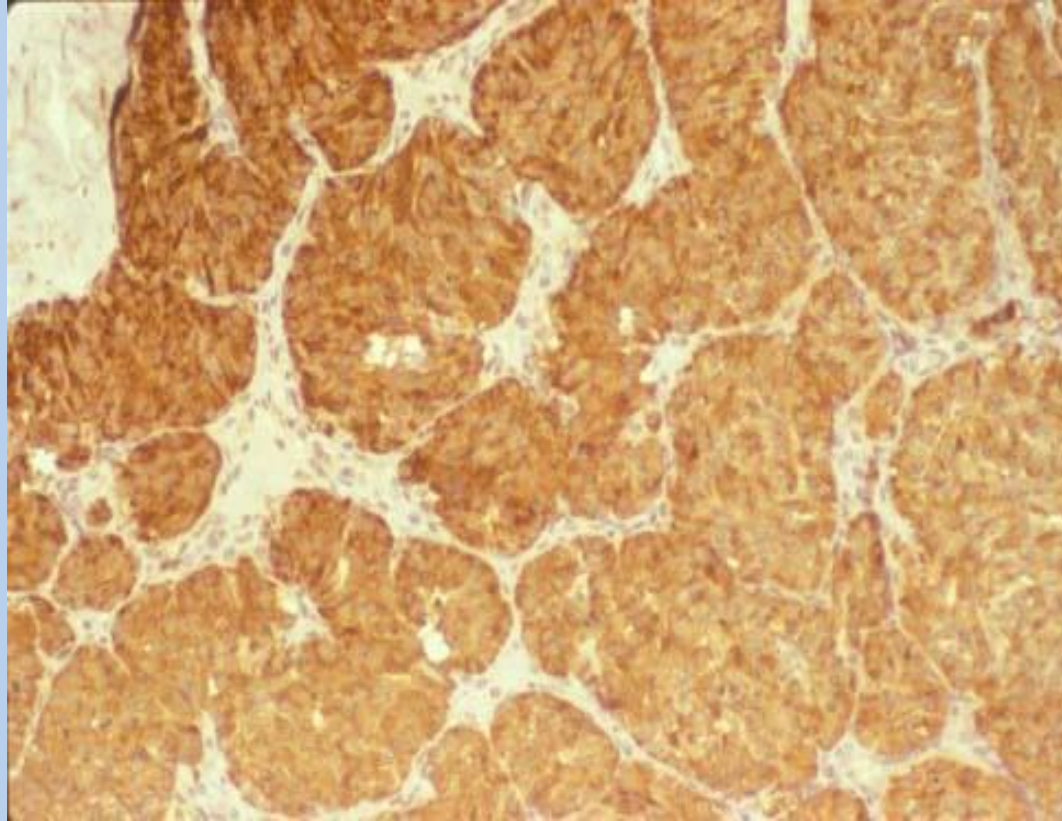


- Solid growth pattern with amyloid

# Medullary Thyroid Carcinoma



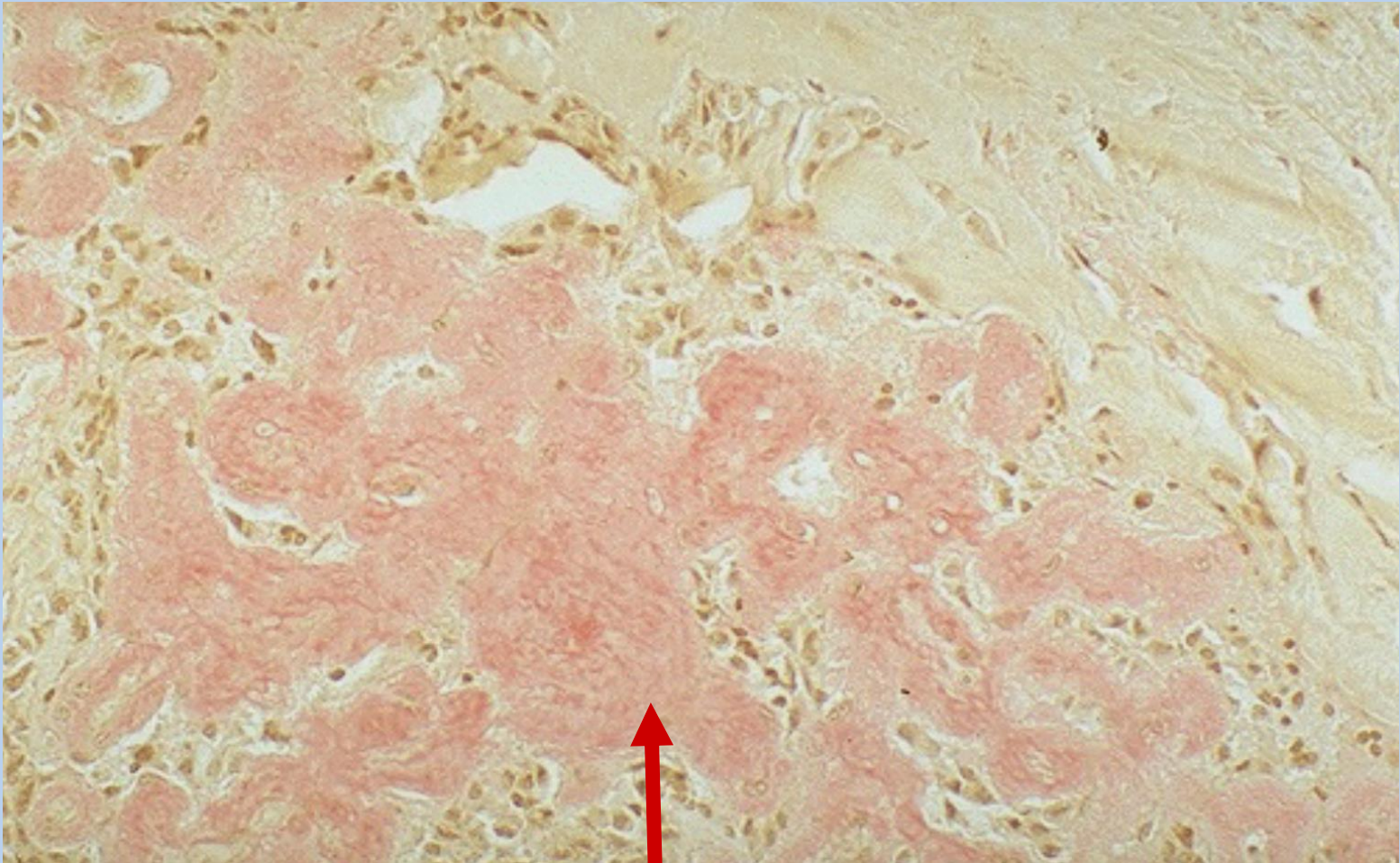
# Medullary Thyroid Carcinoma



IMMUNOSTAIN FOR CALCITONIN

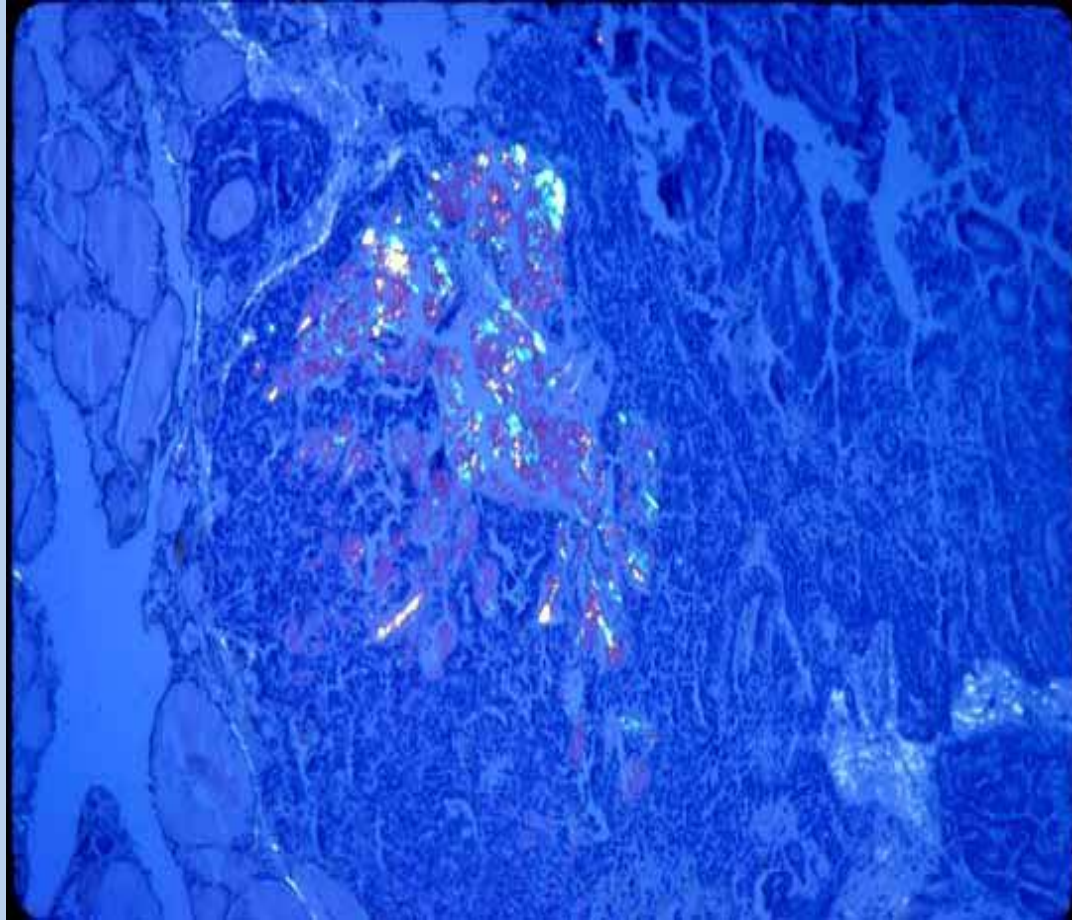


# Medullary Thyroid Carcinoma



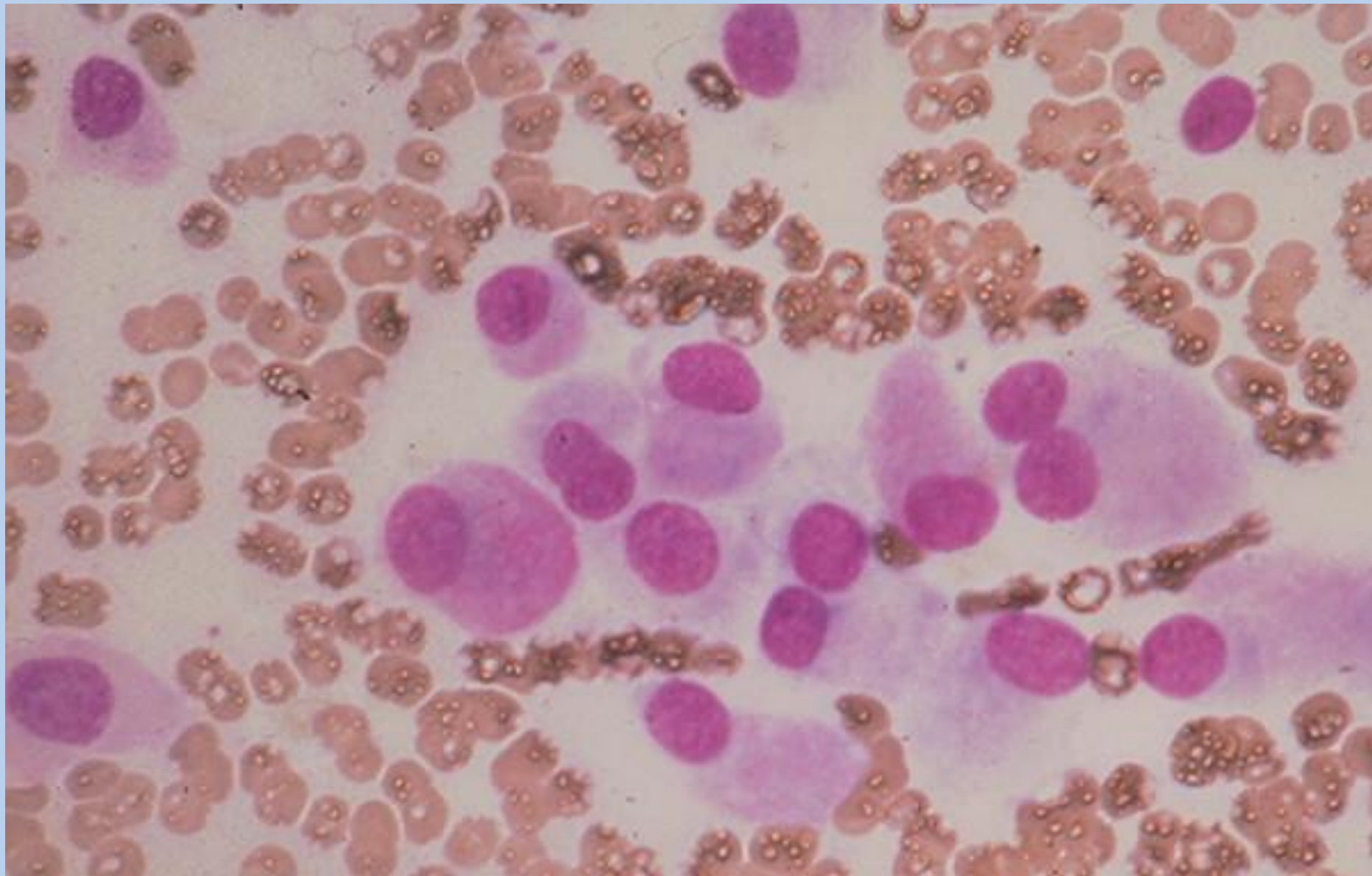
AMYLOID - CONGO RED STAIN

# Medullary Thyroid Carcinoma

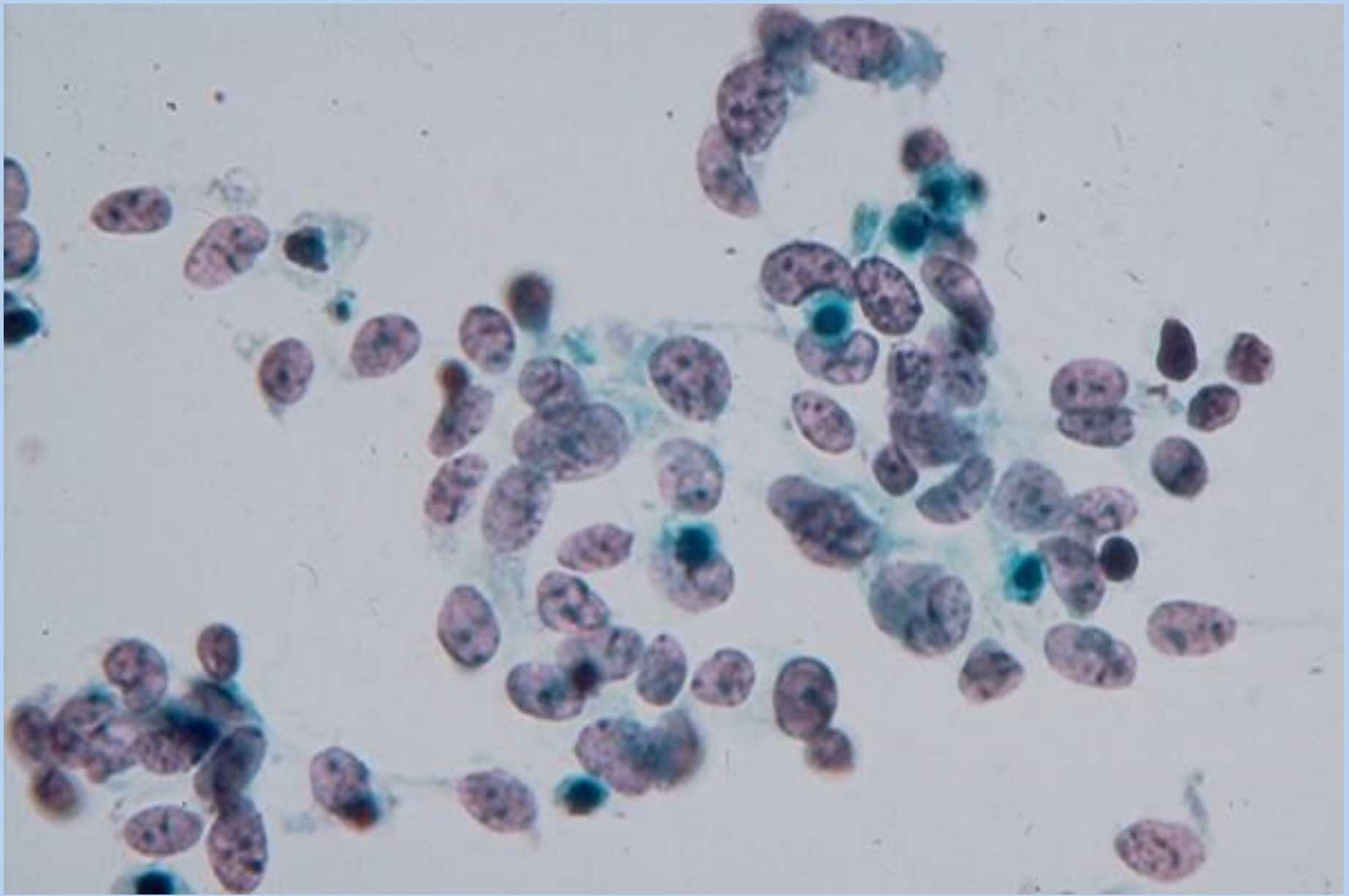


AMYLOID - CONGO RED STAIN

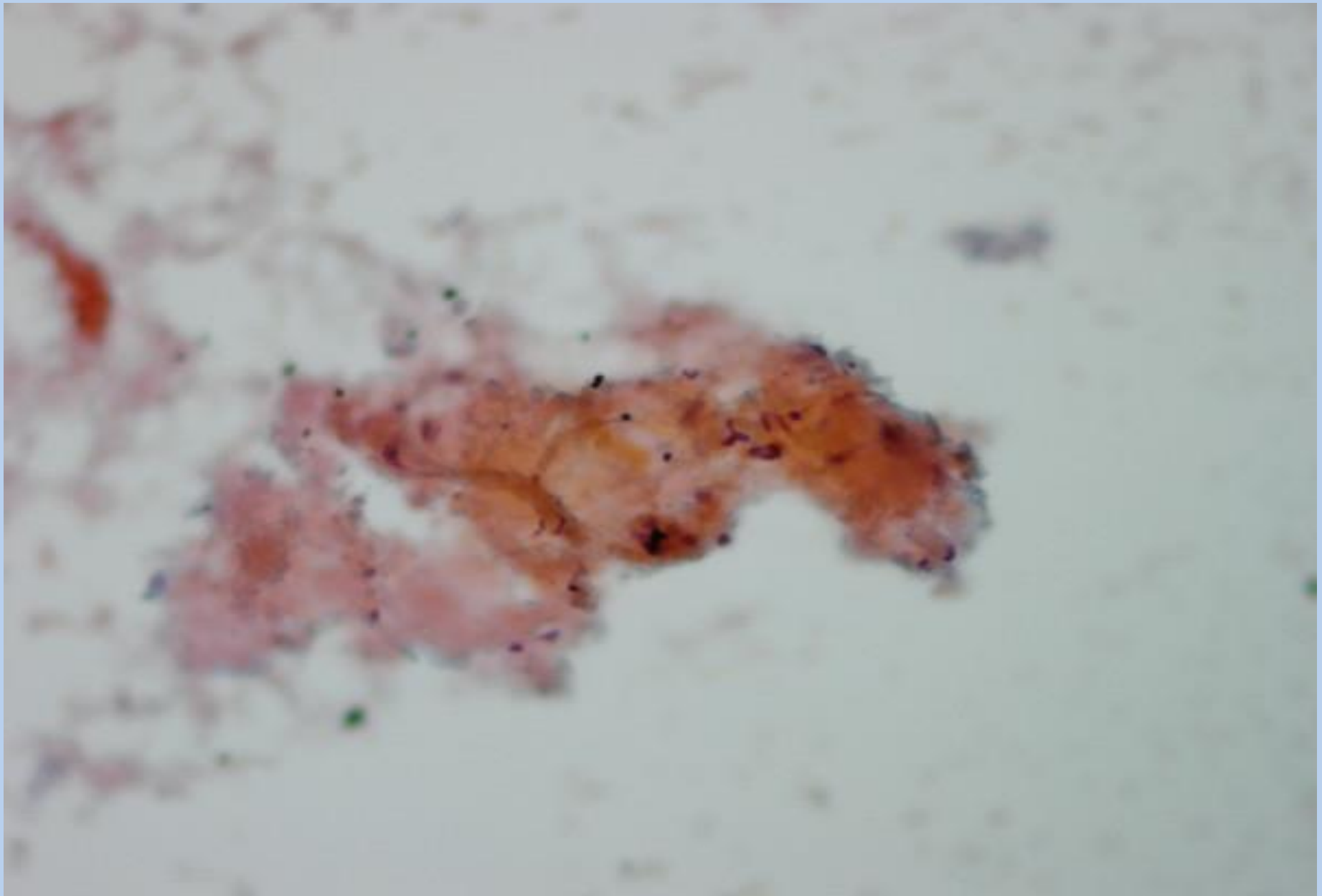




Medullary carcinoma showing in FNA dyshesive plasmacytoid tumor cells with eccentrically located round nuclei and intracytoplasmic azurophil granules (Diff-Quik stain,  $\times 400$ ).



Medullary carcinoma showing in FNA loosely clustered spindle-shaped tumor cells with scanty, ill-defined cytoplasm (Papanicolaou stain,  $\times 400$ ).



A fragment of orange and granular amyloid material seen in FNA of a thyroid medullary carcinoma (Papanicolaou stain,  $\times 400$ ).

# Anaplastic thyroid carcinoma

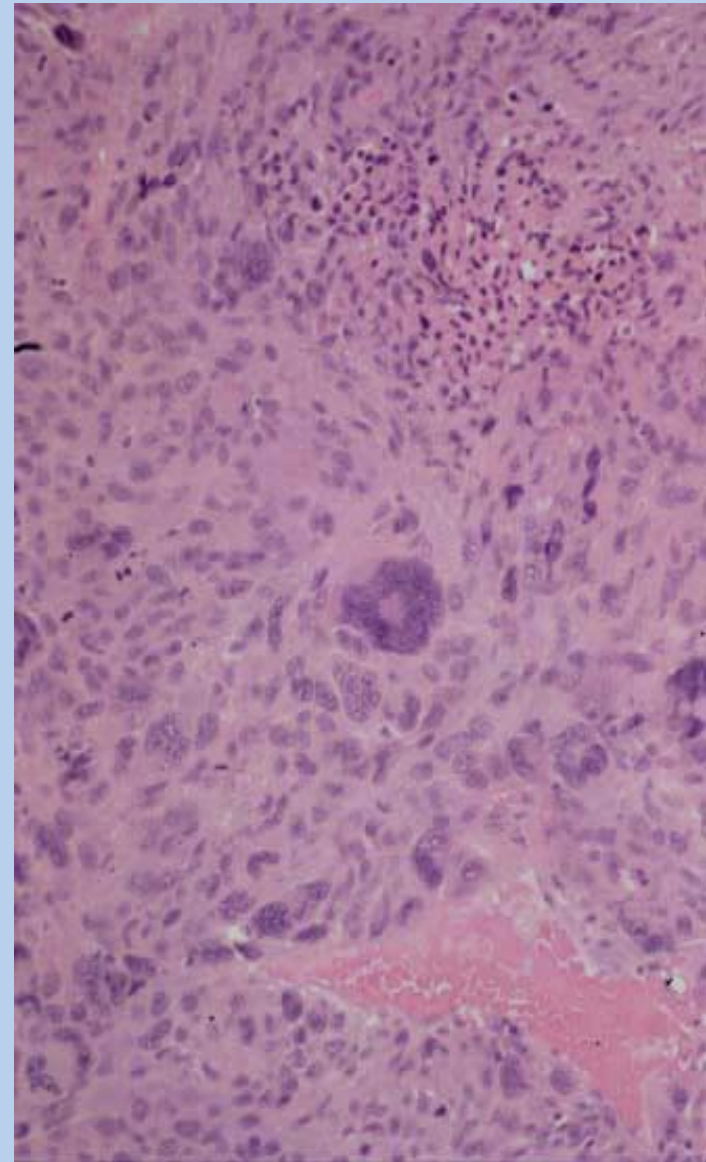
- Consists of two main histologic variants:
  - Giant cell
  - Spindle cell
- Depending on the histologic subtype, an anaplastic thyroid carcinoma may display in FNA pleomorphic large, bizarre cancer cells with prominent nucleoli or spindle cancer cells admixed with a variable amount of necrotic debris .

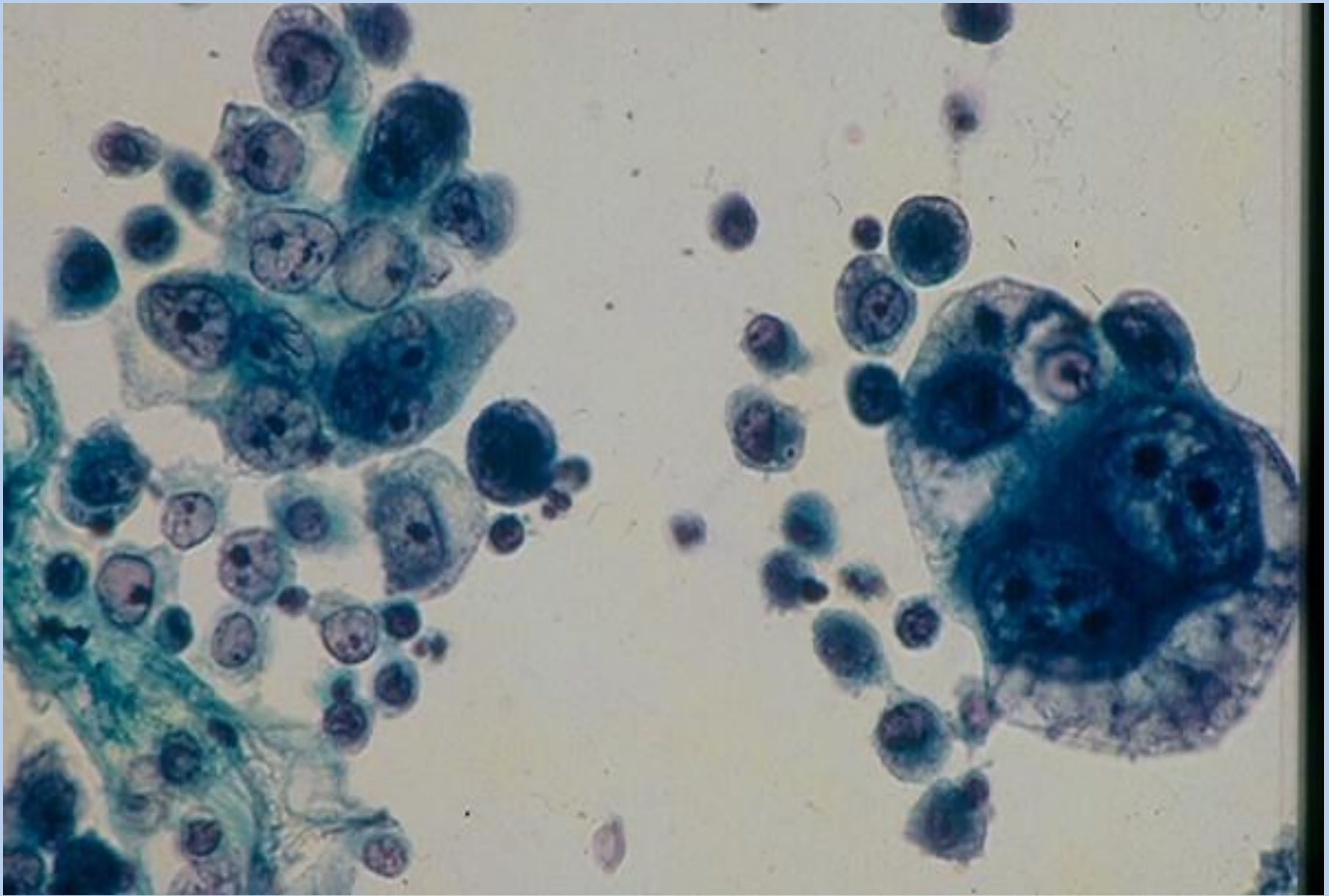


# Anaplastic Thyroid Carcinoma:

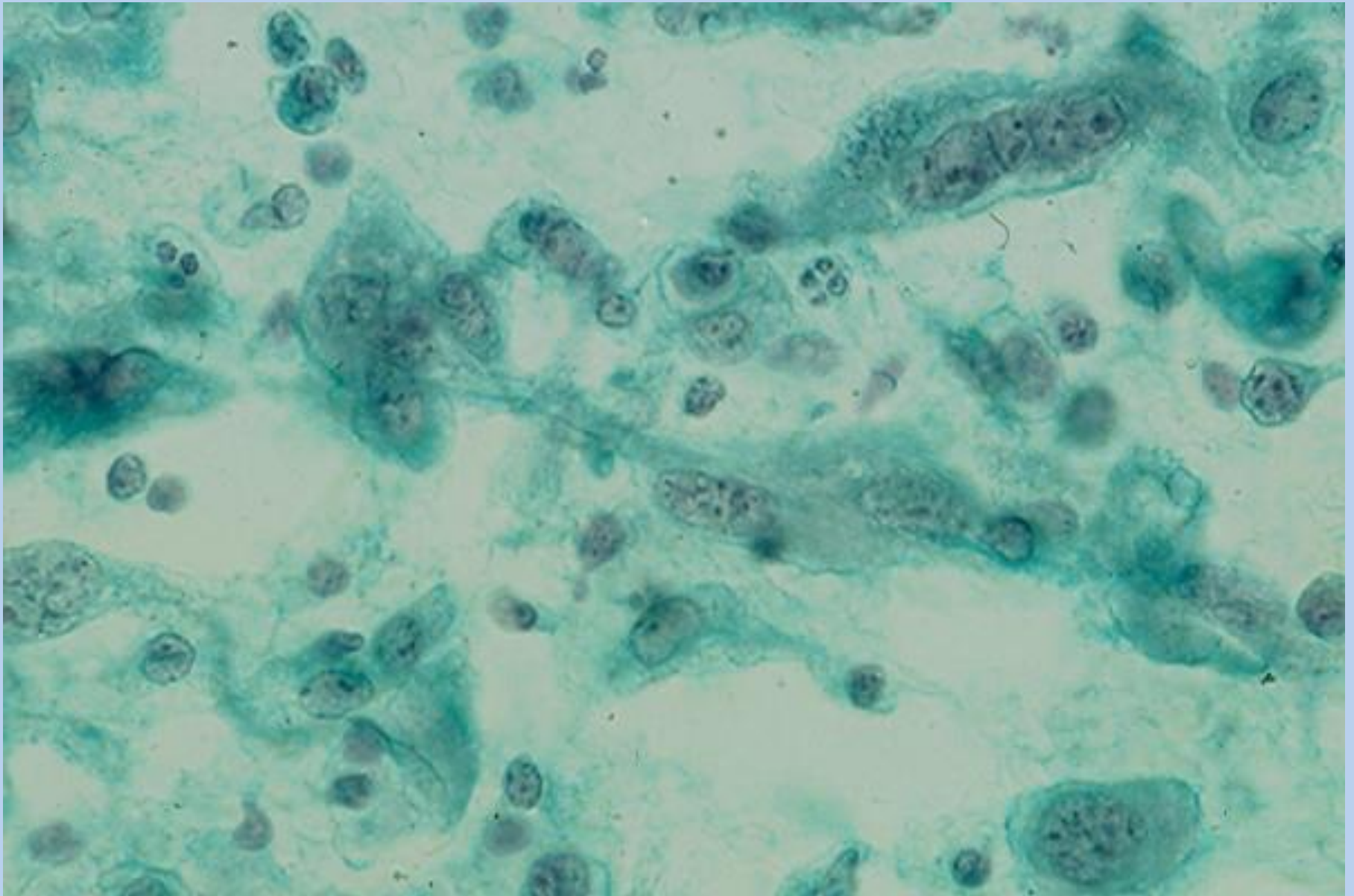
## Giant and Spindle Cells

- Hard, fixed irregular mass
- Frequently invasive with distant metastases
- Solid growth pattern
- Giant and spindle cells
- Subclassified as spindle, giant and small cell types
- Does not take up radioactive iodine





Anaplastic carcinoma, giant-cell type showing in FNA single and clustered large, bizarre malignant cells with pleomorphic nuclei and prominent nucleoli (Papanicolaou stain,  $\times 400$ ).



Anaplastic carcinoma, spindle-cell type showing in FNA dyshesive spindle- shaped malignant cells with scant, ill-defined cytoplasm (Papanicolaou stain,  $\times 400$ ).



# lymphoma

- is usually of large cell type and yields in FNA cells similar to those of a lymph node involved by the same neoplastic process.
- A thyroid Hodgkin disease is characterized by Reed-Sternberg cells admixed with benign lymphoid cells and eosinophils .

# Cystic Lesion

- Benign cysts account for the majority of thyroid cystic lesions.
- They are formed as the result of hemorrhagic degeneration of a benign colloid nodule.
- FNA from a benign colloid cyst may show colloid material admixed with benign follicular epithelial cells and hemosiderin laden macrophages.

# Cystic Lesion

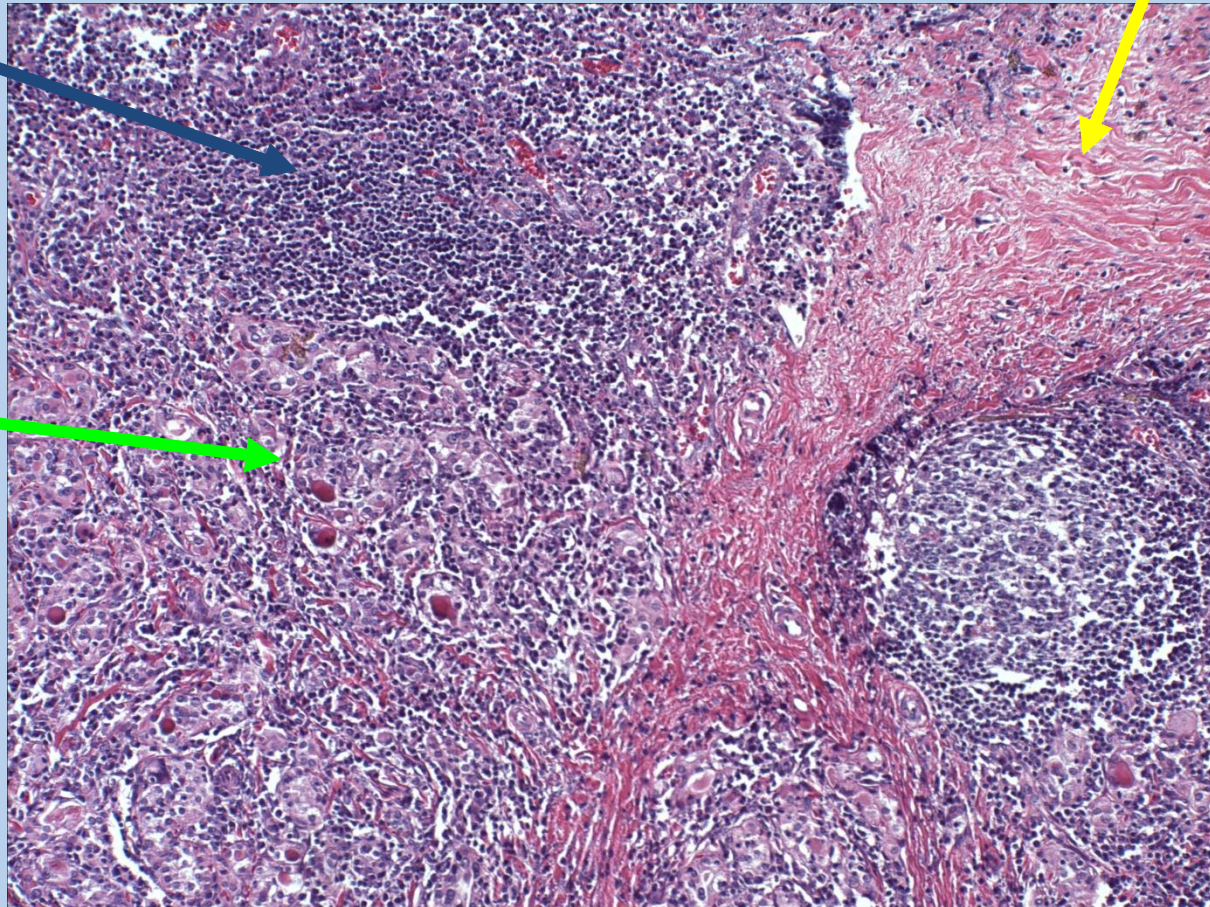
- Any thyroid neoplasm may undergo hemorrhagic necrosis and become a cystic lesion .
- Of the thyroid neoplasms, PC tends to undergo marked hemorrhagic degenerative change.
- FNA from the tumor commonly shows a large amount of blood and the cystic lesion tends to recur rapidly .

## 6. Thyroiditis

- Hashimoto thyroiditis and subacute thyroiditis commonly have fairly distinctive clinical findings.
- Rarely, these lesions may present as a nodular lesion mimicking a thyroid neoplasm.
- Hashimoto thyroiditis is characterized by the presence of numerous benign lymphoid cells admixed with benign follicular cells and Hurthle cells.
- A subacute thyroiditis may yield clustered epithelioid cells, scattered lymphocytes and a few multinucleated giant cells containing up to one hundred nuclei

# Hashimoto Thyroiditis

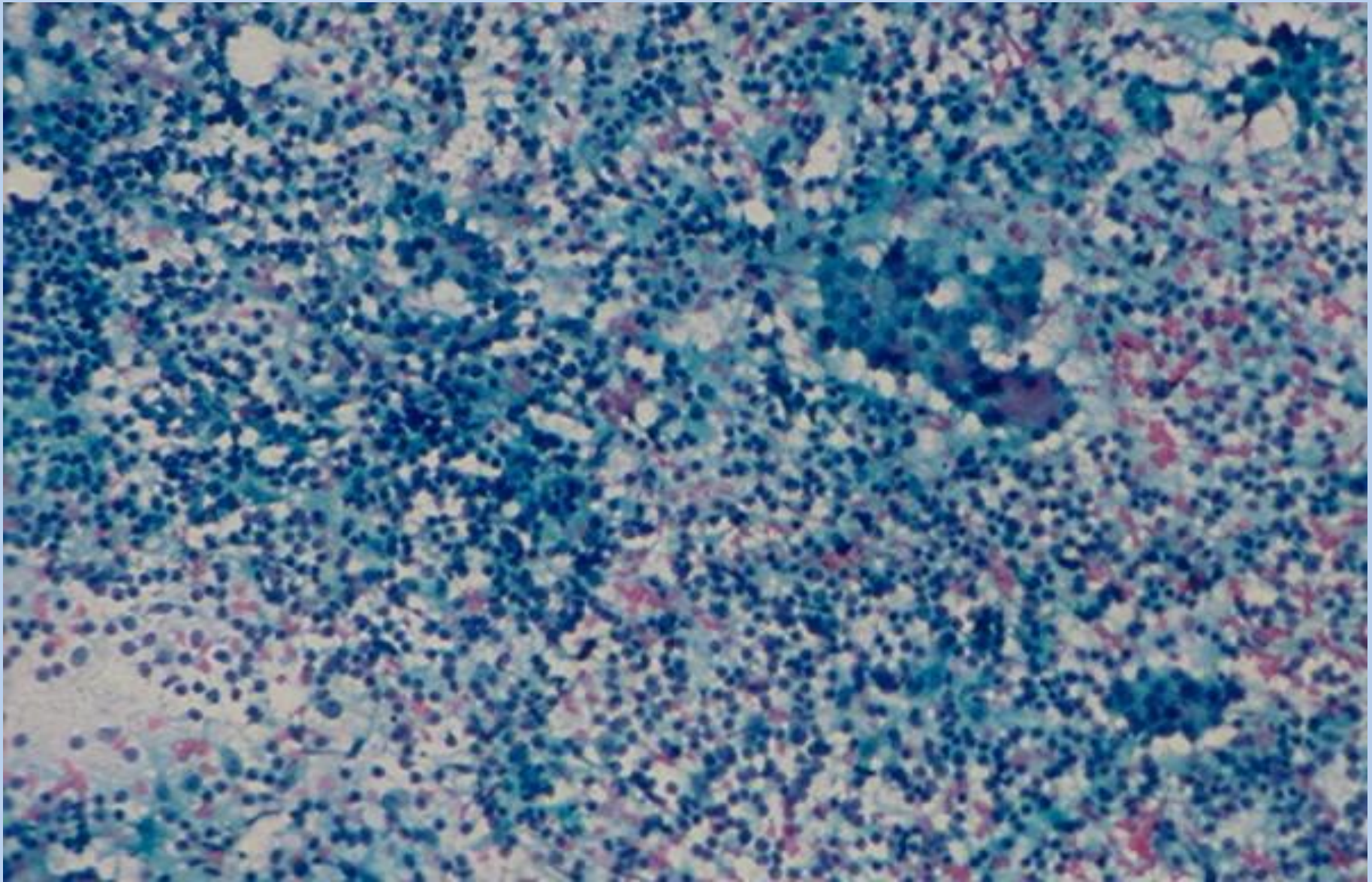
FIBROSIS



LYMPHOCYTES

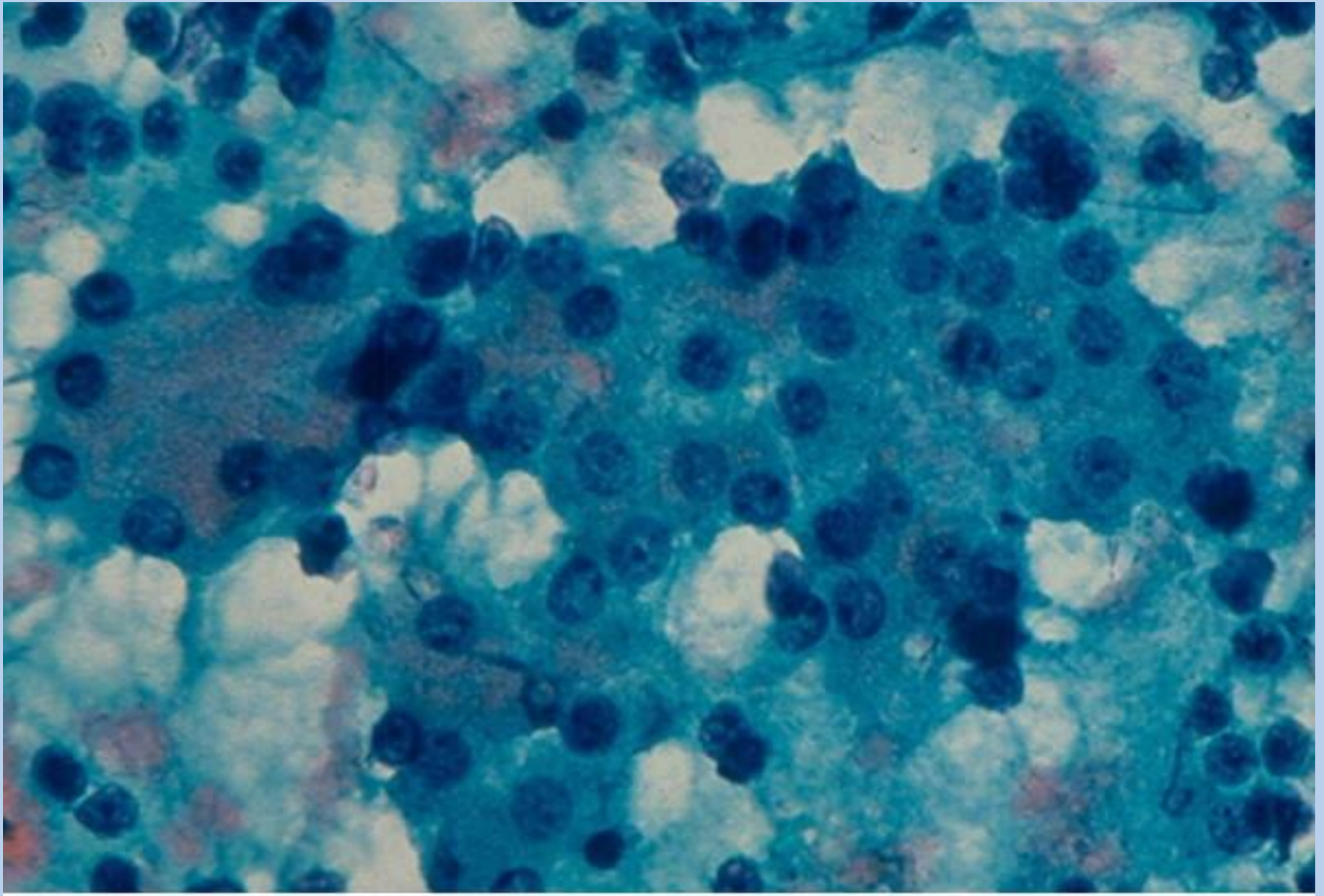
HURTHLE  
CELLS



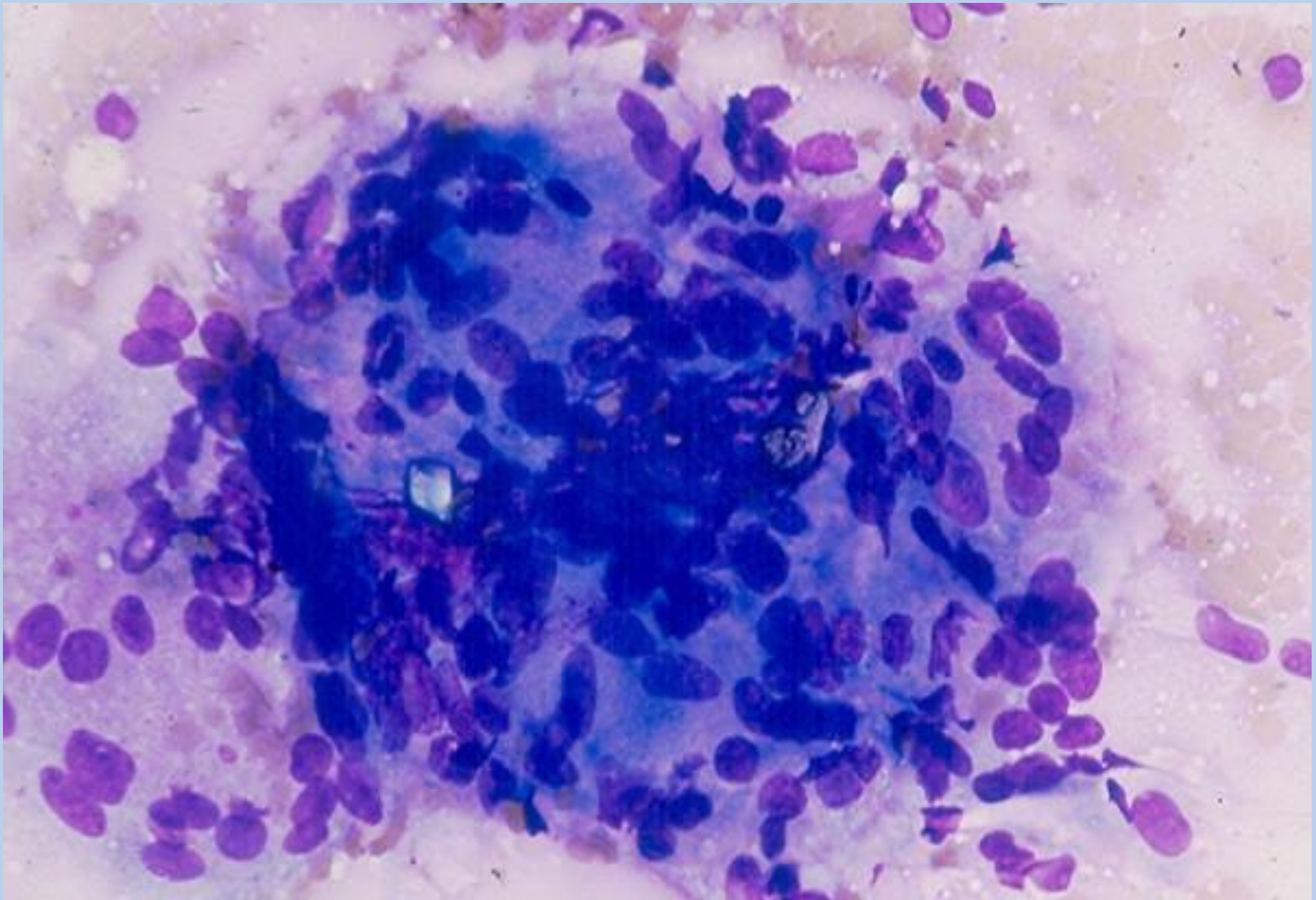


Hashimoto thyroiditis showing in FNA numerous lymphoid cells admixed with a sheet of follicular epithelial cells



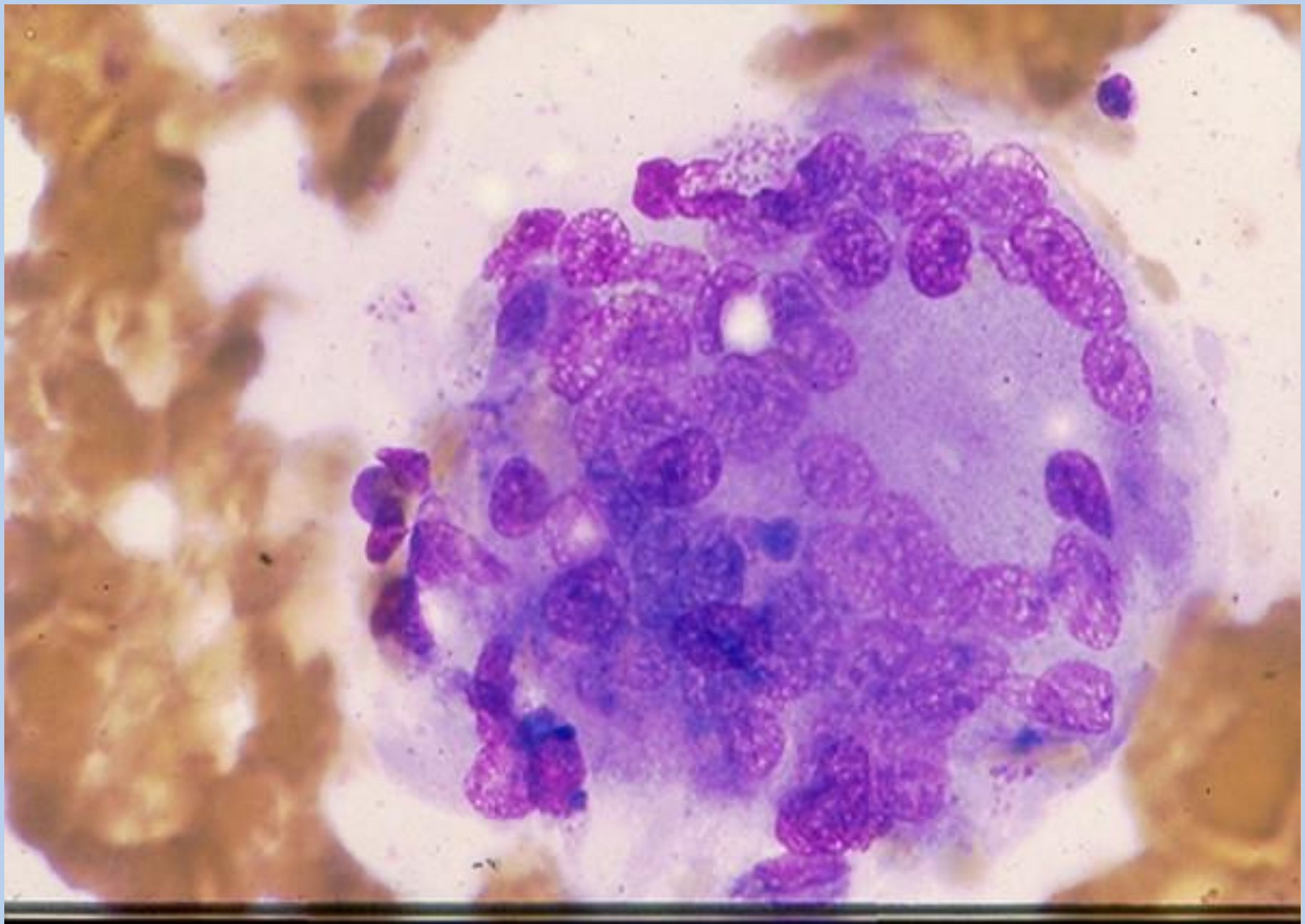


A sheet of follicular epithelial cells with oncocytic change admixed with benign lymphoid cells seen in FNA of a Hashimoto thyroiditis (Papanicolaou stain,  $\times 400$ ).



A syncytial cluster of epithelioid cells with carrot-shaped nuclei seen in FNA of a subacute thyroiditis (Diff-Quik stain,  $\times 400$ ).





A large multinucleate giant cell present in FNA of a subacute thyroiditis (Diff-Quik stain,  $\times 400$ ).

## 7. Other Lesions

- **Graves disease** may rarely present as a nodular thyroid lesion .
- It yields non specific cytologic findings
- **Metastatic cancers** to the thyroid are common in patients with advanced cancers arising from other body sites .
- However, metastatic cancer to the thyroid gland presenting as a palpable TN is uncommon.
- Renal cell carcinoma is the most common metastatic neoplasm to the thyroid, and cases of clinically occult renal cell carcinoma presenting initially as a large thyroid mass have been documented.

## 8. Non-Diagnostic Category

- In this category the FNA yields non-diagnostic or inadequate cellular materials.
- In one study, cystic thyroid lesions yielded non-diagnostic cell samples at initial FNA in about 50% of cases .
- In the Mayo Clinic experience, repeating the FNA in the cases with initial non-diagnostic needle aspirates revealed diagnostic material in 30 to 80% of cases

# Diagnostic Accuracy and Errors

- Gharib and Goellner found that the biopsy technique had a sensitivity rate varying from 65 to 98% (mean 83%), and that its specificity rate varied from 72 to 100% (mean 92%) .



- The false-negative rate varied from 1 to 11.5% (mean, 5.2%), and the false-positive rate varied from 0 to 7.7% (mean, 2.9%) .

- The overall cytodiagnostic accuracy rate of thyroid FNA approached 95% according to some reported series.

با تشکر و تقدیم احترام