Thyroid cytology
September 2019

FNAC in pre-operative evaluation of thyroid disease of :-

- solitary/dominant thyroid nodule
- clinically obvious malignancy
- diffuse goitre

Solitary/dominant thyroid nodule

- prevalence of thyroid nodules 4-8%
- approx. 5% are malignant
- clinical, biochemical and radiological investigations have limitations
- FNAC has higher accuracy in pre-op evaluation of thyroid nodules

Solitary/dominant Thyroid Nodule

Benign

- cysts
- multinodular goitre with hyperplastic nodule
- adenoma

Malignant

- papillary, follicular or medullary carcinoma
- lymphoma

Diagnostic Accuracy of Thyroid FNA

- Sensitivity between 65% and 98%
- Specificity of 76-100%
- False negative rate of 0-5%
- False positive rate of 0-5.7%
- Overall accuracy of 69-97%.

Ref: RCPath guidance on reporting of thyroid cytology specimens 2016

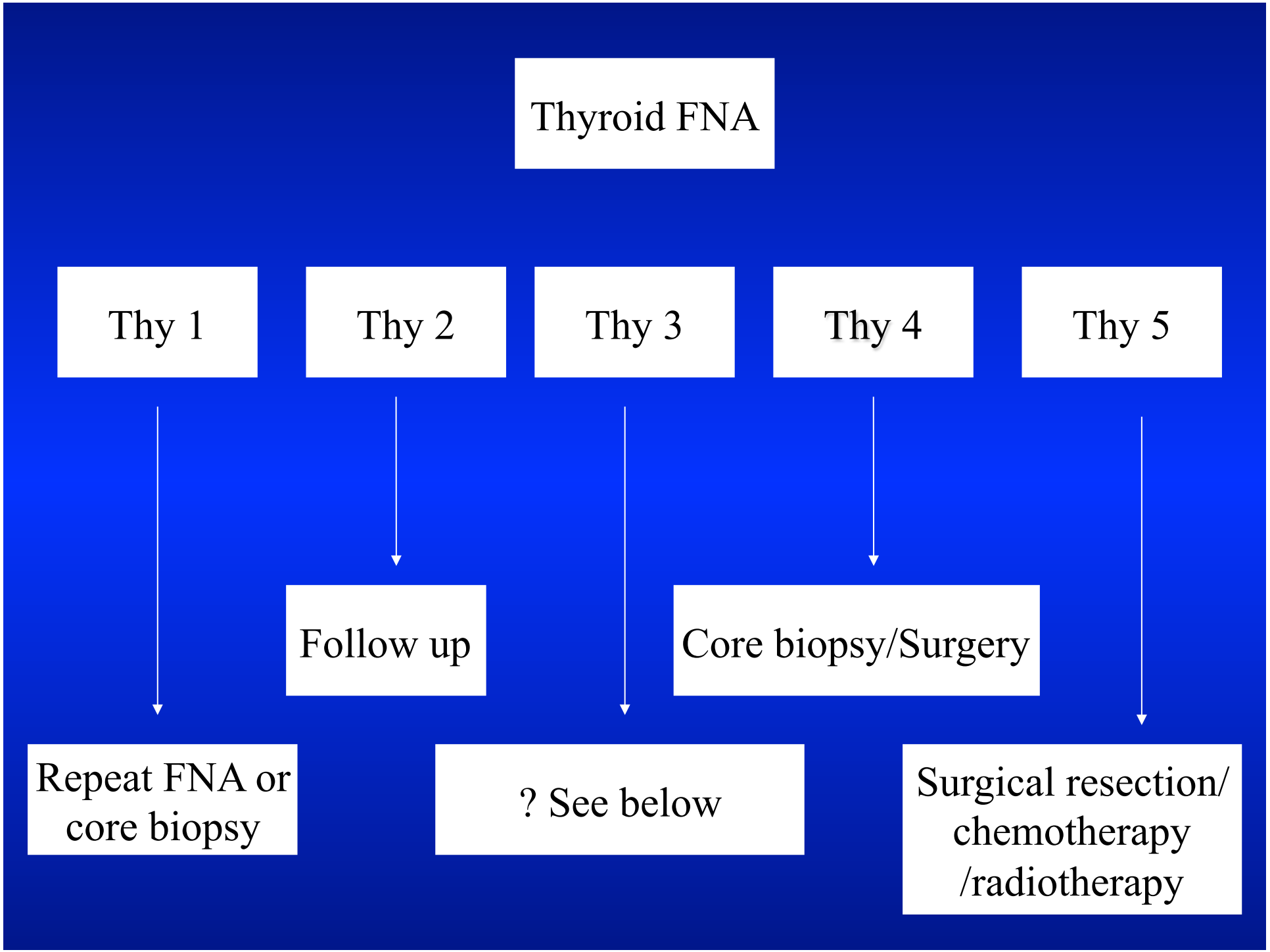
Comparison of Diff-Quick and Papanicolau staining in thyroid smears

Identification of ..	Quick Diff Method	Papanicolau Method
colloid	+++	+
cellular borders	++	+
intracytoplasmic granules in medullary carcinoma	+++	0
oxyphilic cells	+++	+
nuclear details	+/++	+++
nuclear inclusions	++	+++
nuclear grooves	+	+++

Thyroid FNA

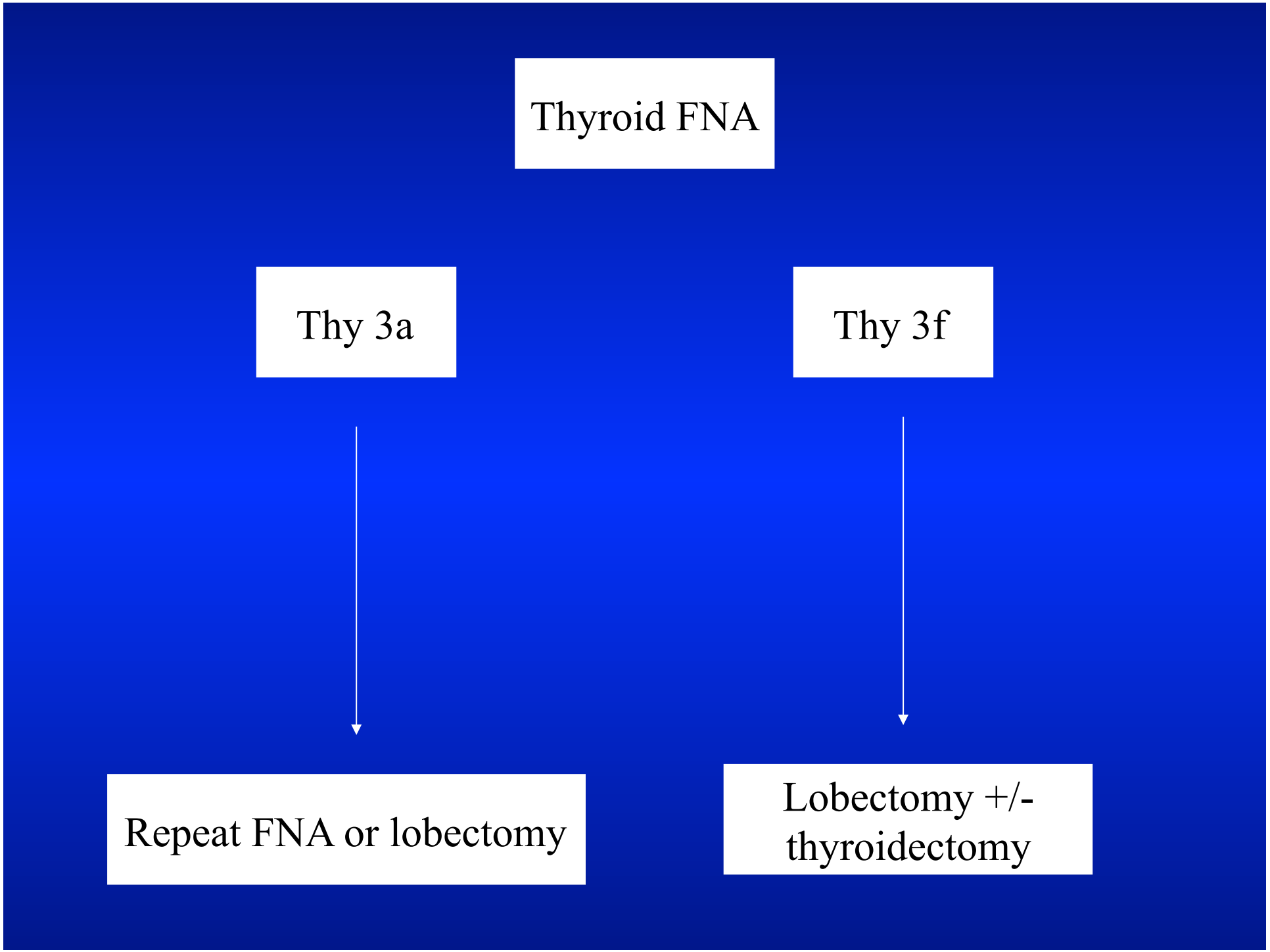
Cell block preparation

- cell blocks
  - preparation
    - plasma/thrombin clot
  - tissue fragments
    - architecture
  - immunohistochemistry


Thyroid FNA
Thy 1
Thy 2
Thy 3
Thy 4
Thy 5
Repeat FNA or core biopsy
Follow up
? See below
Core biopsy/Surgery
Surgical resection/ chemotherapy /radiotherapy

RCPath 2016

- Non diagnostic for cytological diagnosis (Thy 1 or Thy 1c if cystic)
- Non-neoplastic (Thy 2 or Thy 2c if cystic)
- Neoplasm possible (Thy 3)
  - atypia/non-diagnostic (Thy 3a)
  - suggesting follicular neoplasm (Thy 3f)
- Suspicious of malignancy (Thy 4)
- Malignant (Thy 5)


Thyroid FNA
Thy 3a
Thy 3f
Repeat FNA or lobectomy
Lobectomy +/-
thyroidectomy

Risk of malignancy*

Diagnostic Category	Risk of malignancy (%)
Thy1/Thy1c (unsatisfactory)	0-10
Thy2/Thy2c (benign)	0-3
Thy 3a (follicular lesion of uncertain significance or atypia of uncertain significance)	5-15
Thy 3f (follicular neoplasm or suspicious of follicular neoplasm)	15-30
Thy 4 (suspicious)	60-75
Thy 5 (malignant)	97-100

Thyroid FNAC Interpretation

Important

- cellularity
- cell:colloid ratio
  - colloid difficult to interpret in bloodstained material

Not important

- detailed cell morphology (follicular lesions)

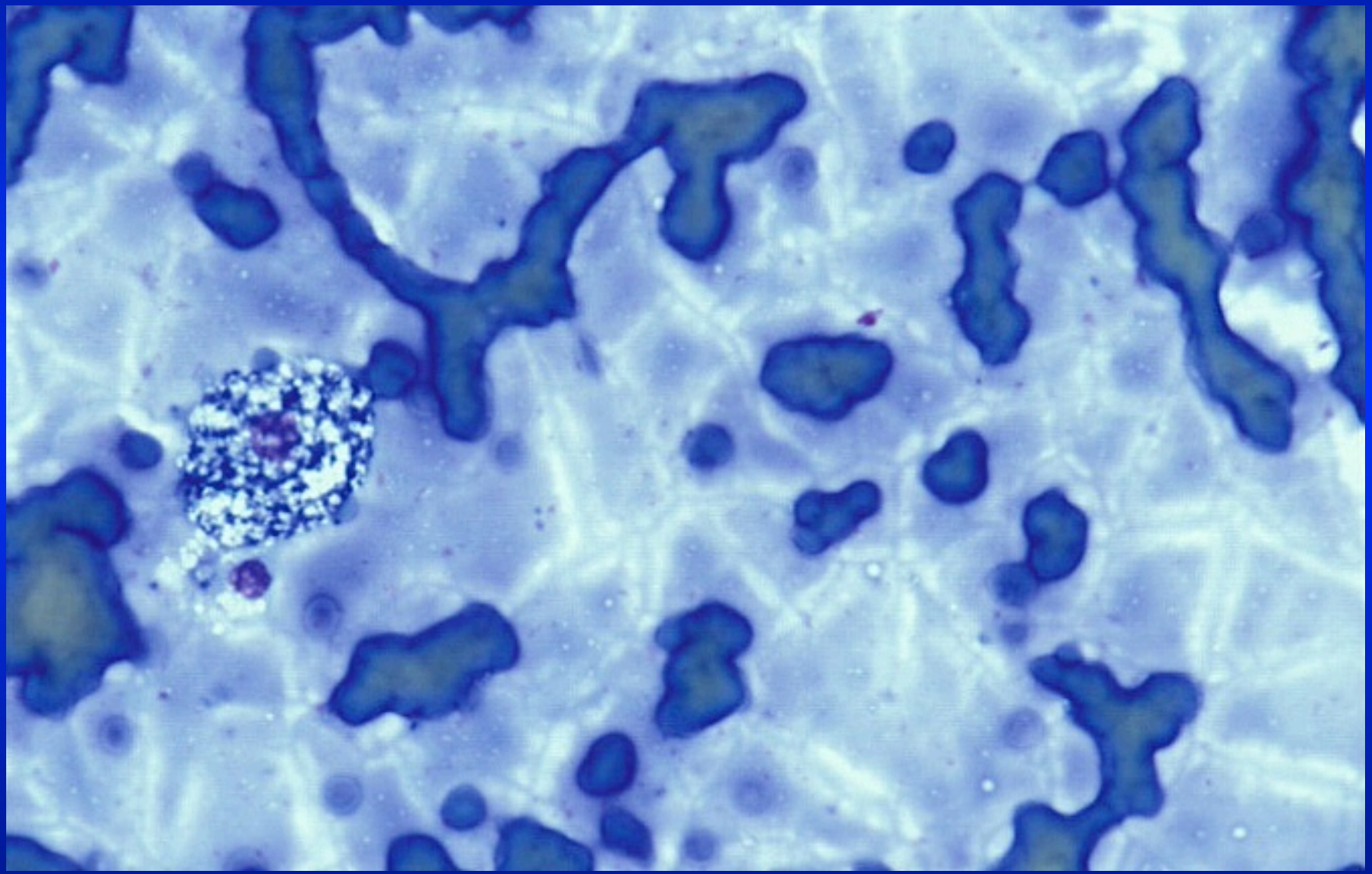
Limitations

- adequacy of material
- overlapping morphological features

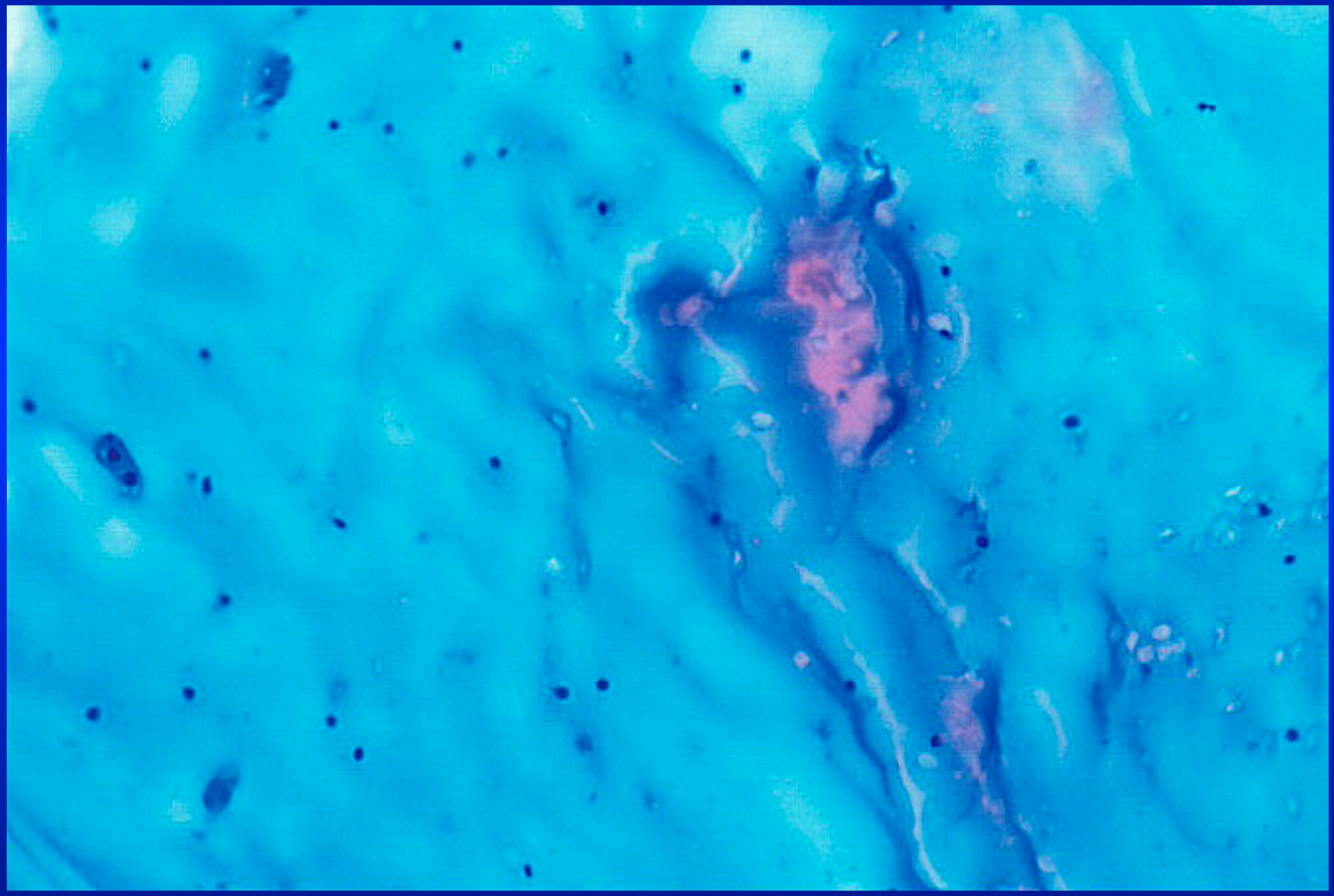
Thyroid FNAC Interpretation

- Colloid
- Cystic lesions
- Follicular pattern
- Papillary pattern
- Oncocytic/Hürthle cells
- Lymphocyte rich pattern
- Spindle cell pattern

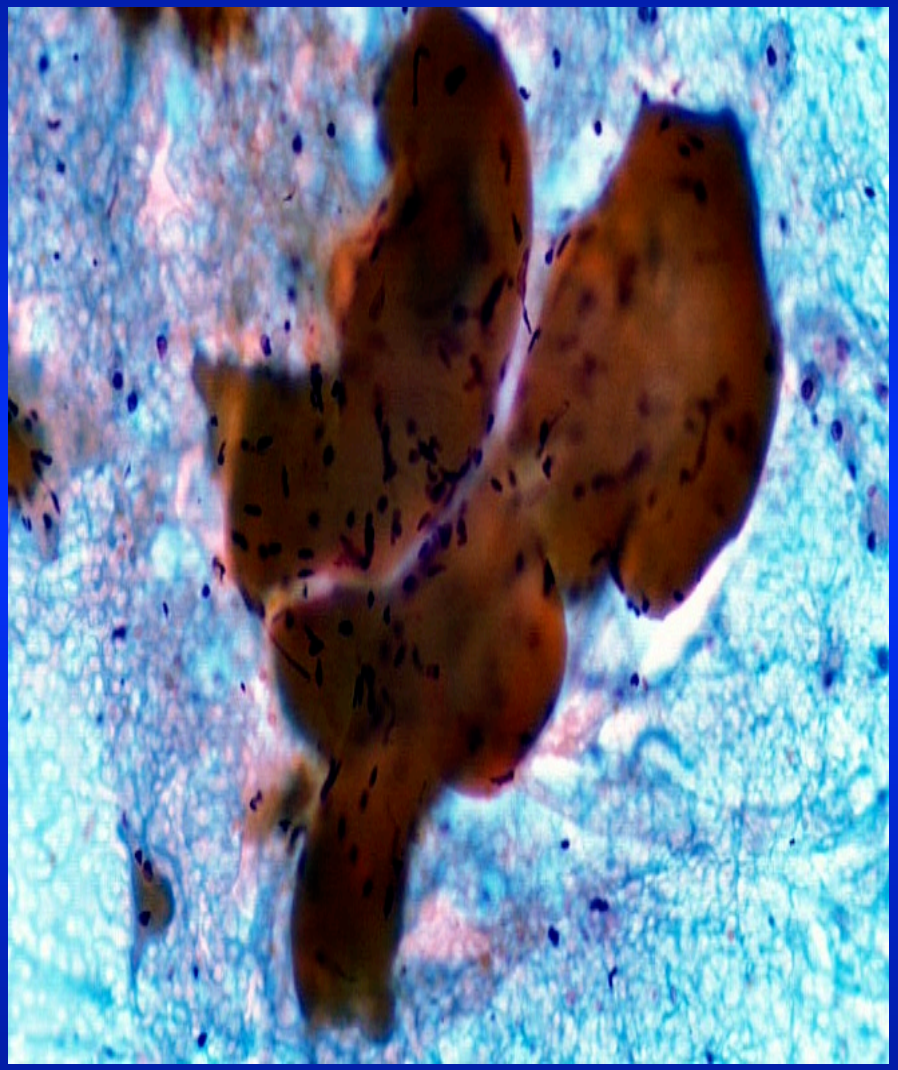
Colloid-HG stain



Colloid Pap stain

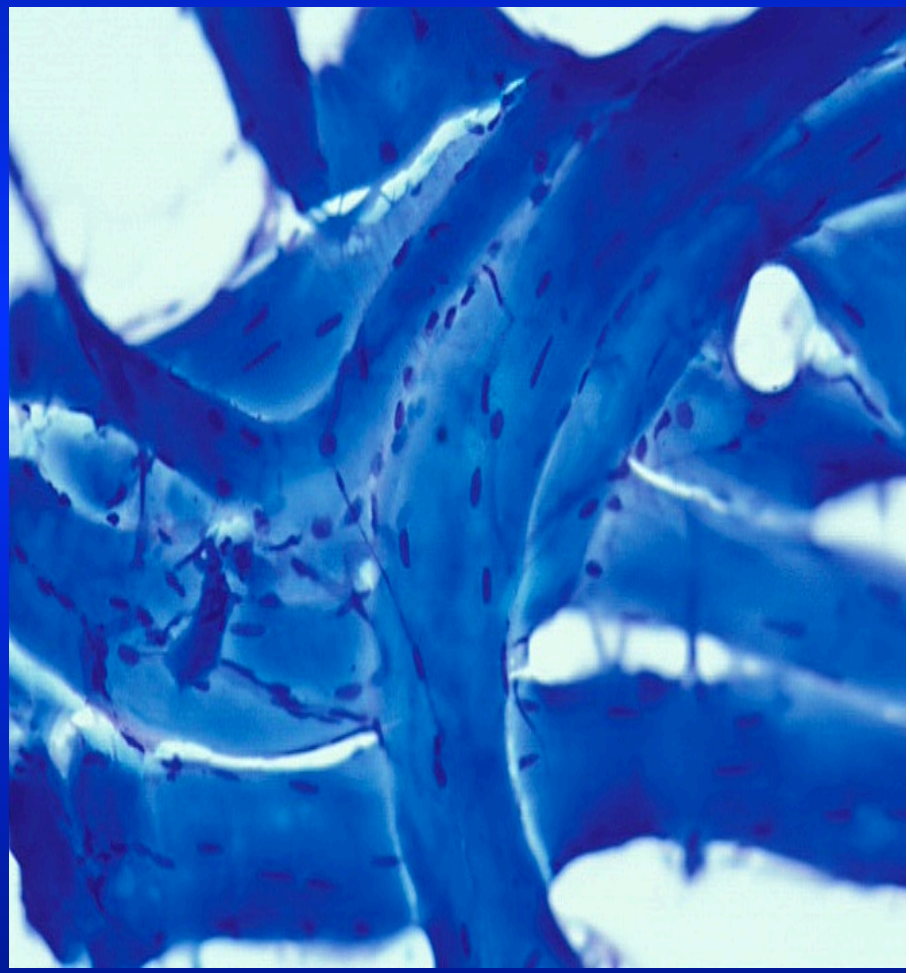


Skeletal muscle

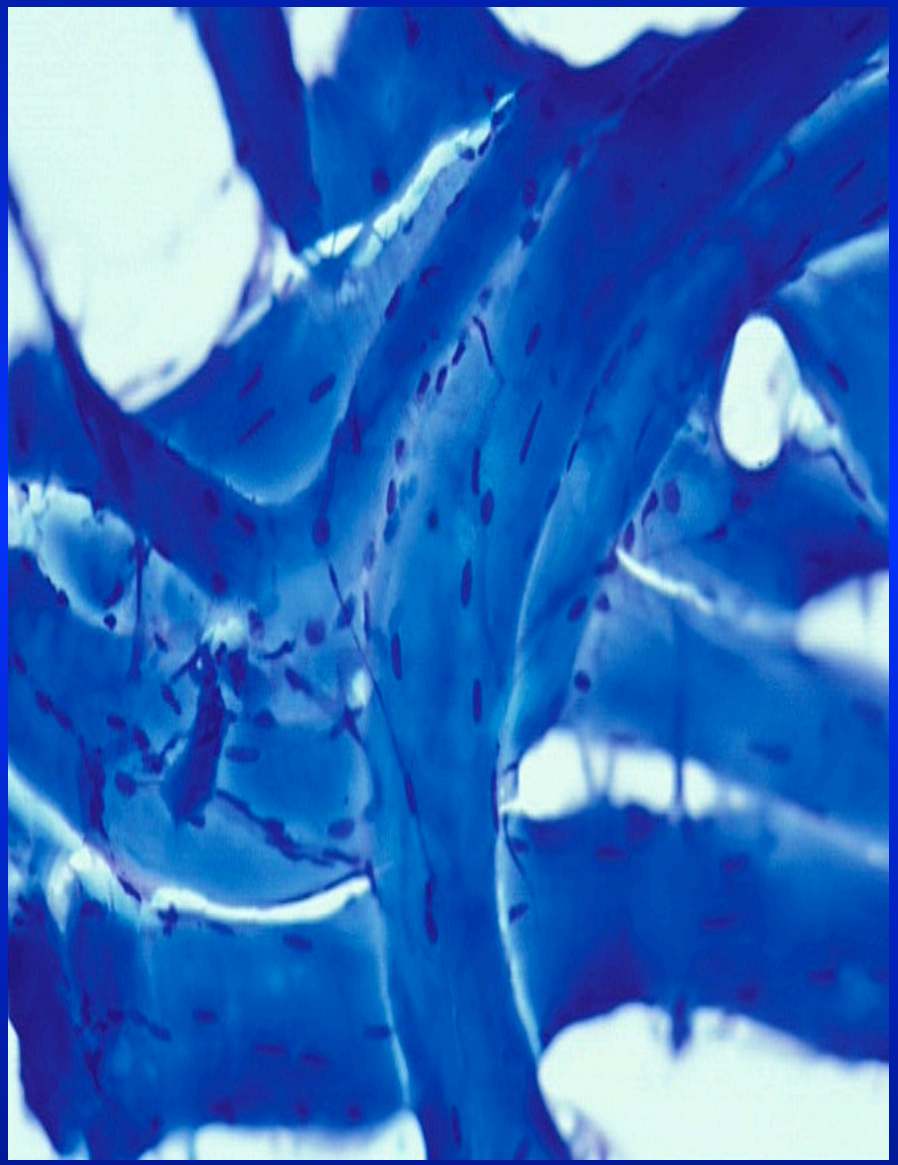


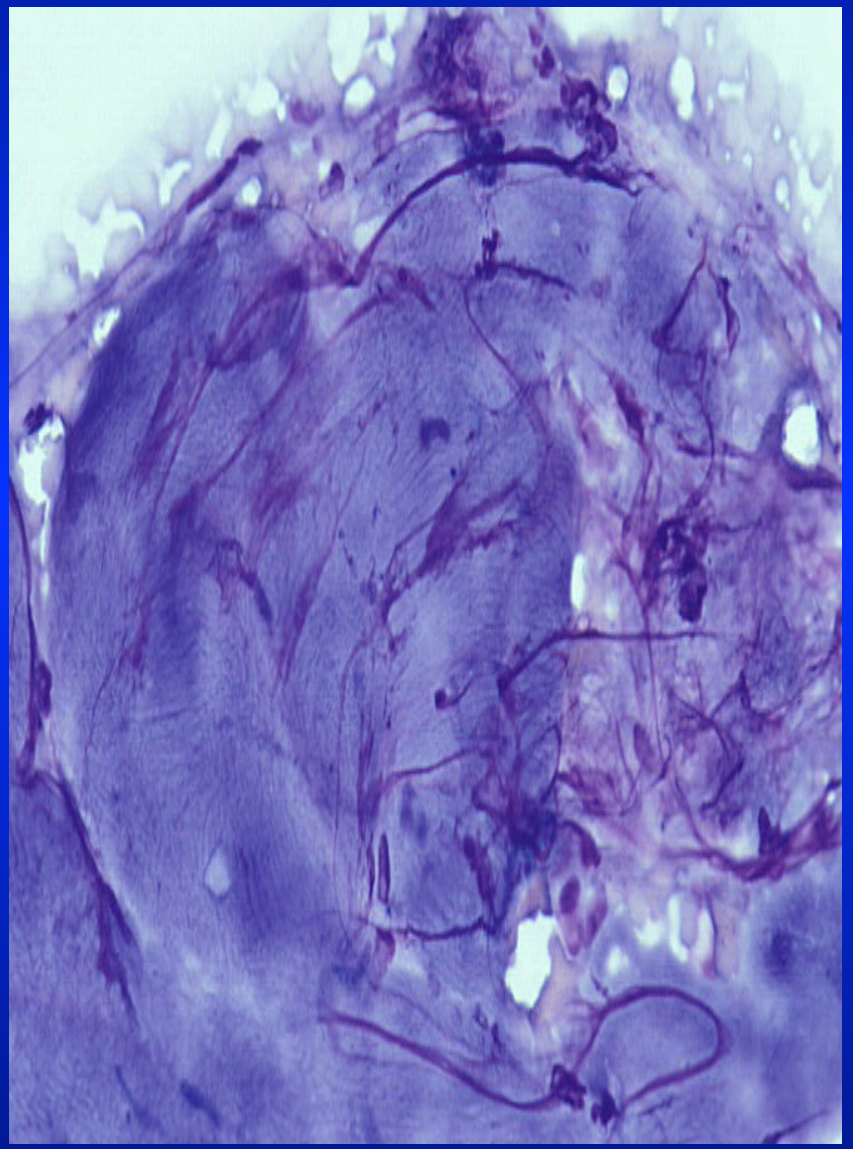
Pap stain

HG stain

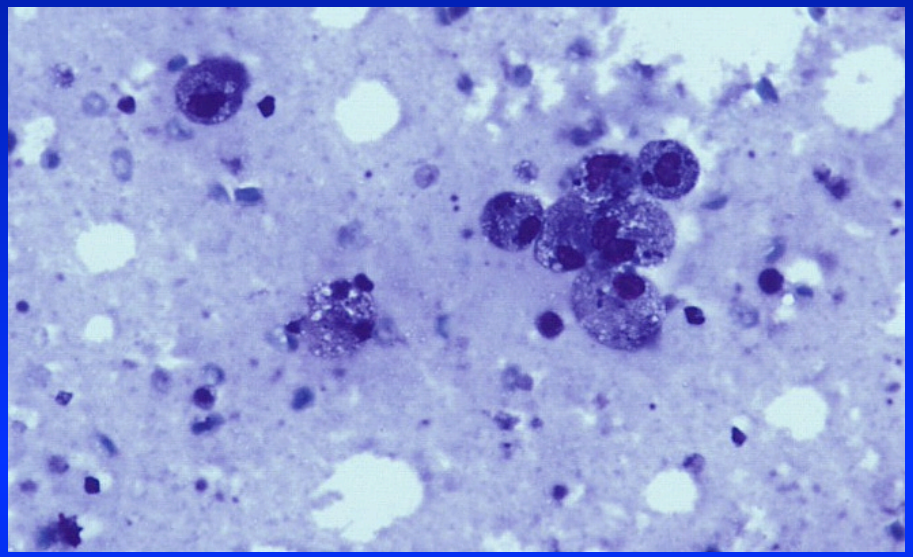


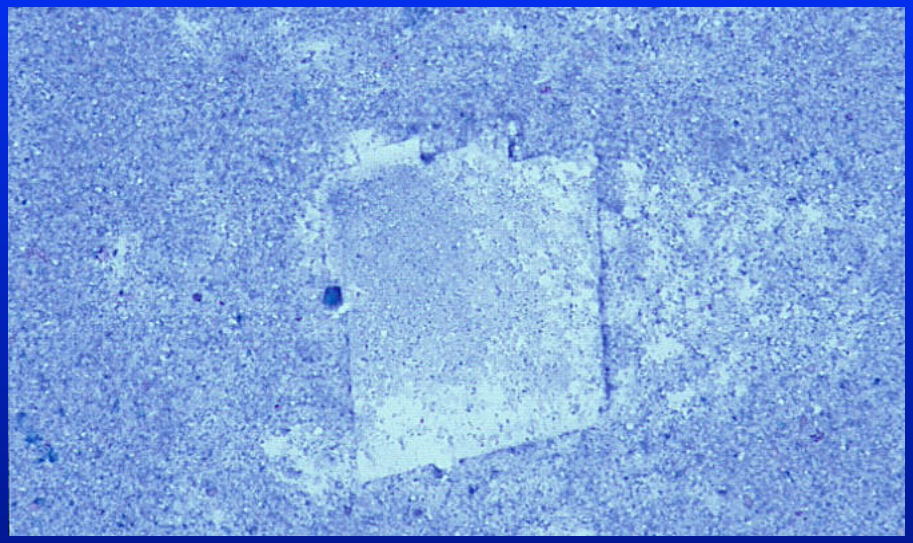
Skeletal muscle

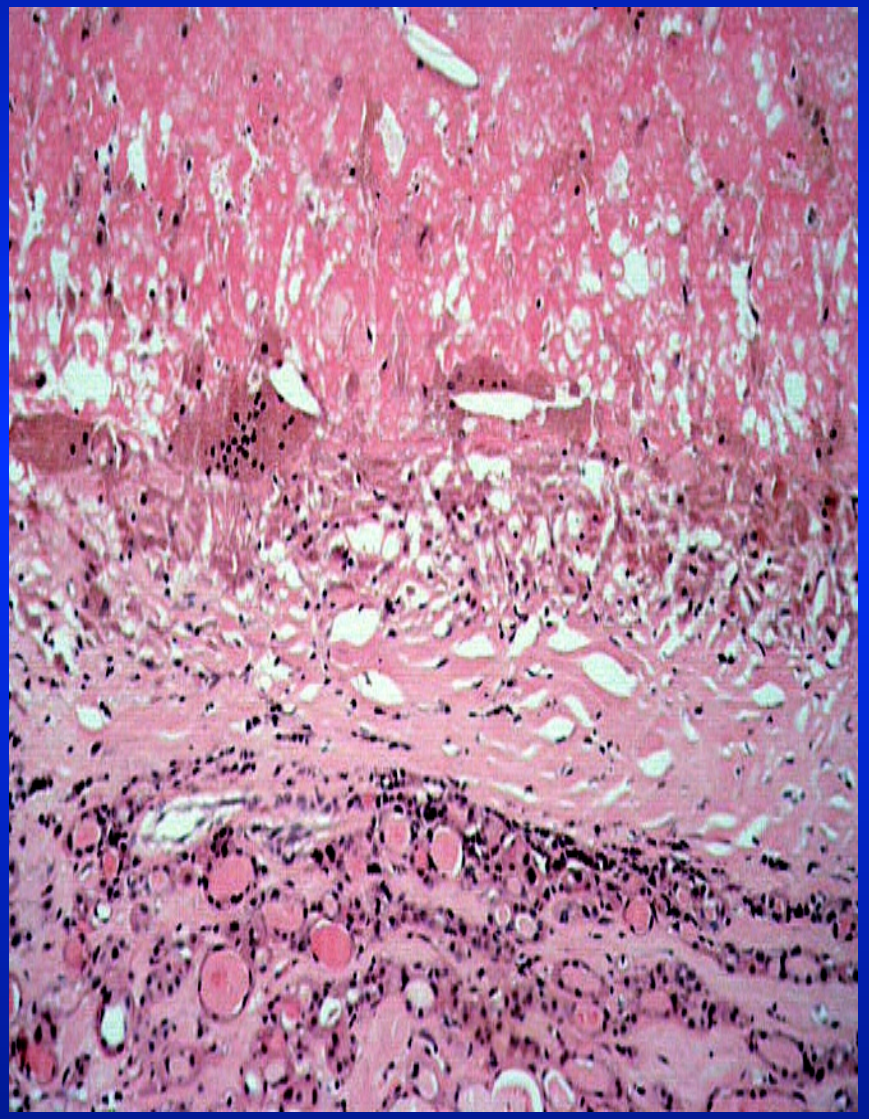




Cystic lesions





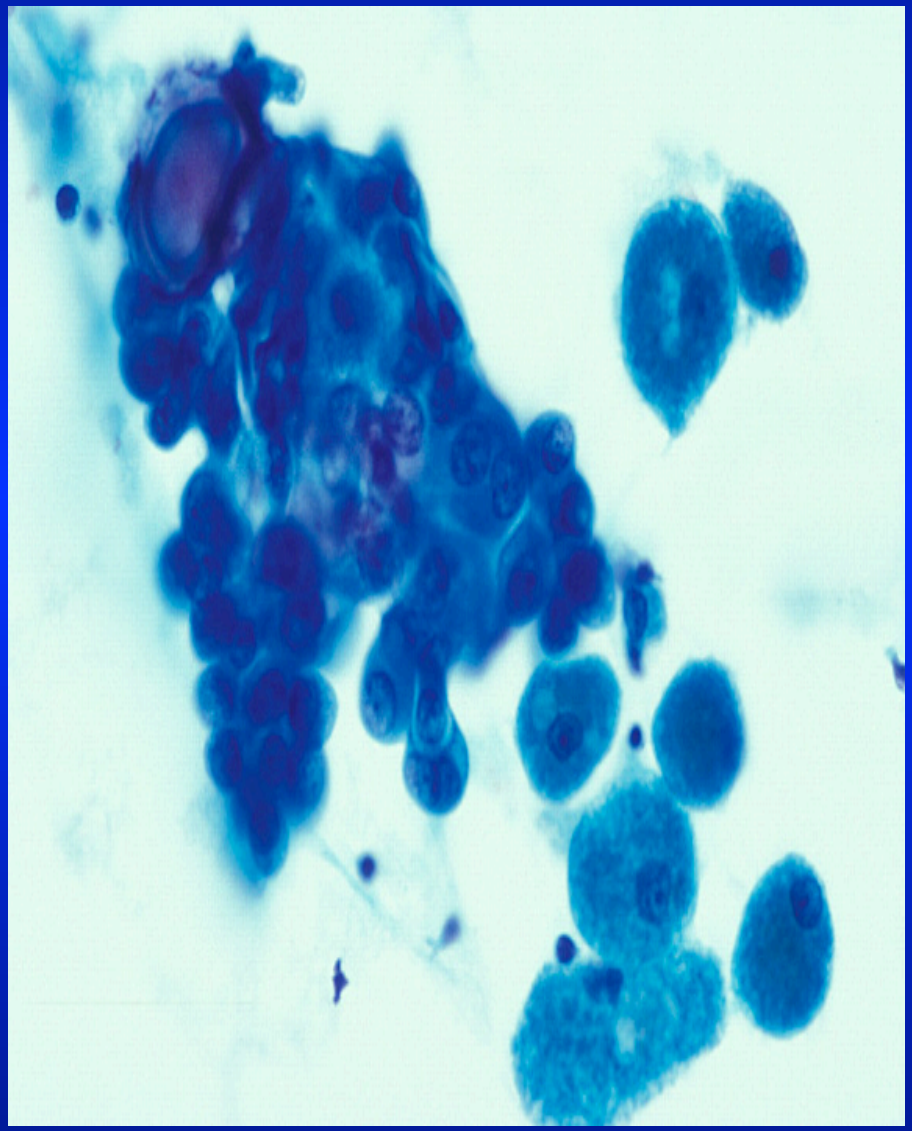


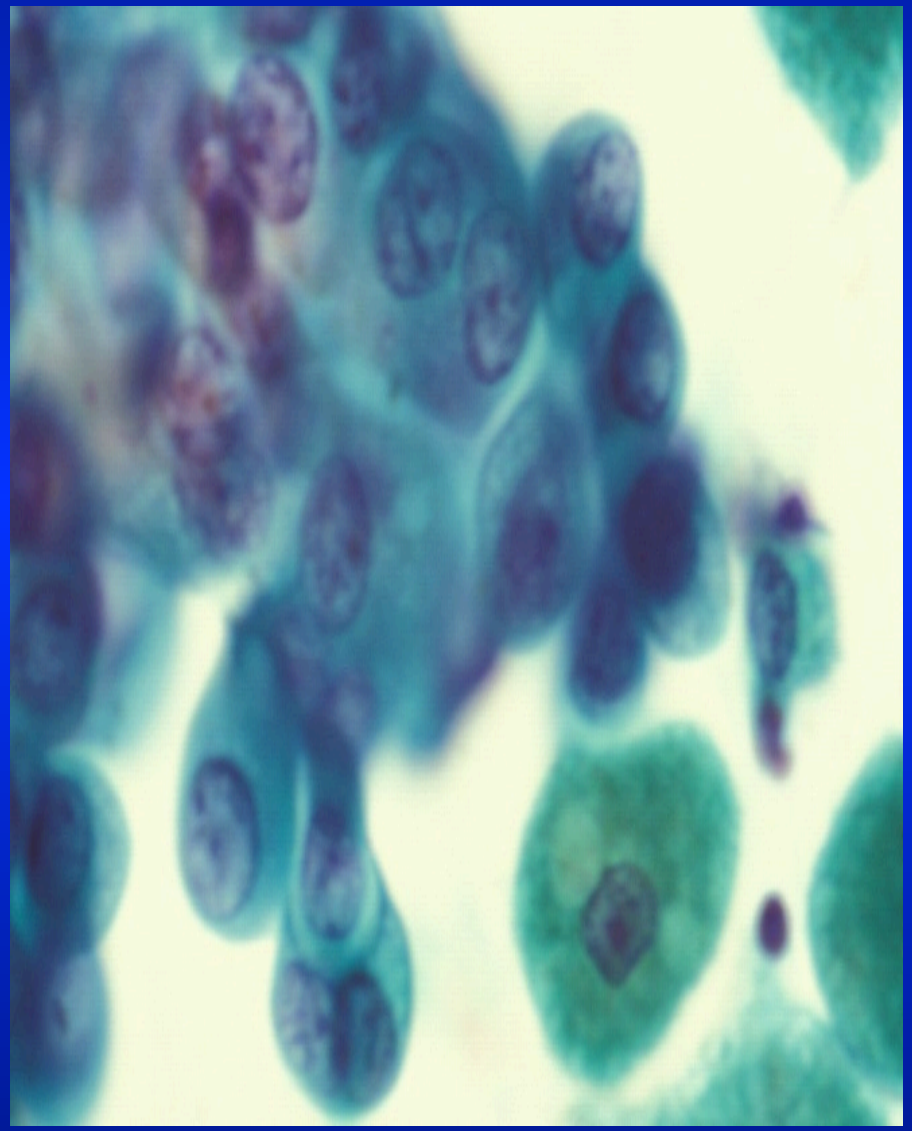
Cyst Appearances

- Colloid rich and few or no epithelial cells
- Little or no colloid & macrophages *
- Haemorrhagic cyst **

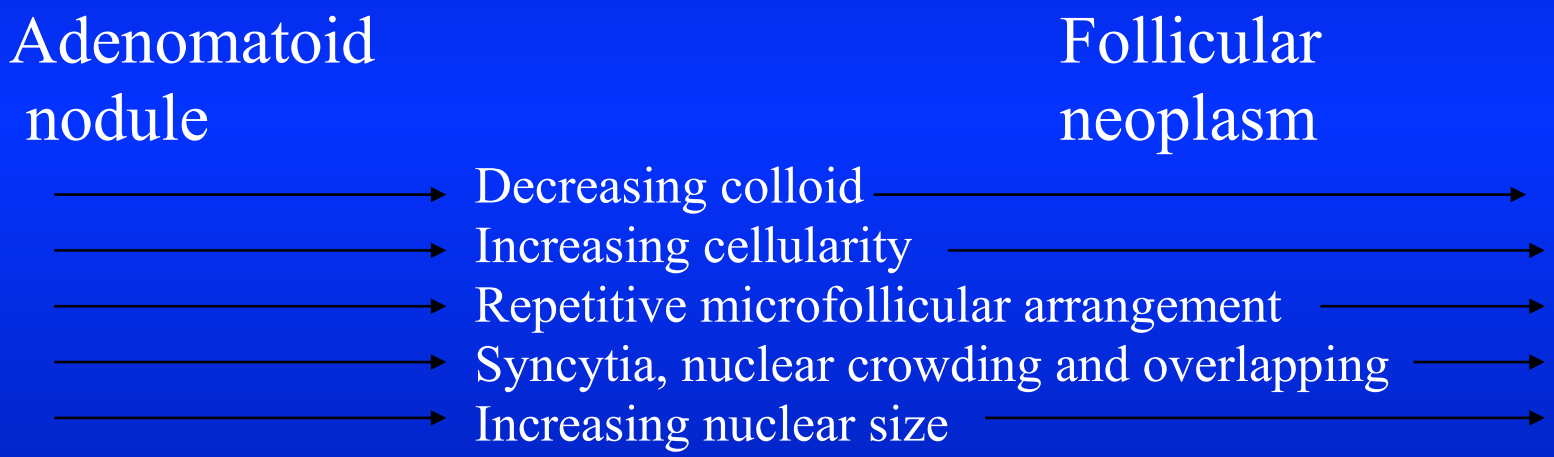
- */** RISK OF PAPILLARY CARCINOMA c. 4%

Cystic papillary carcinoma





Follicular lesions (Thy 3a and f) overlapping smear patterns



Neoplasm possible (Thy 3)

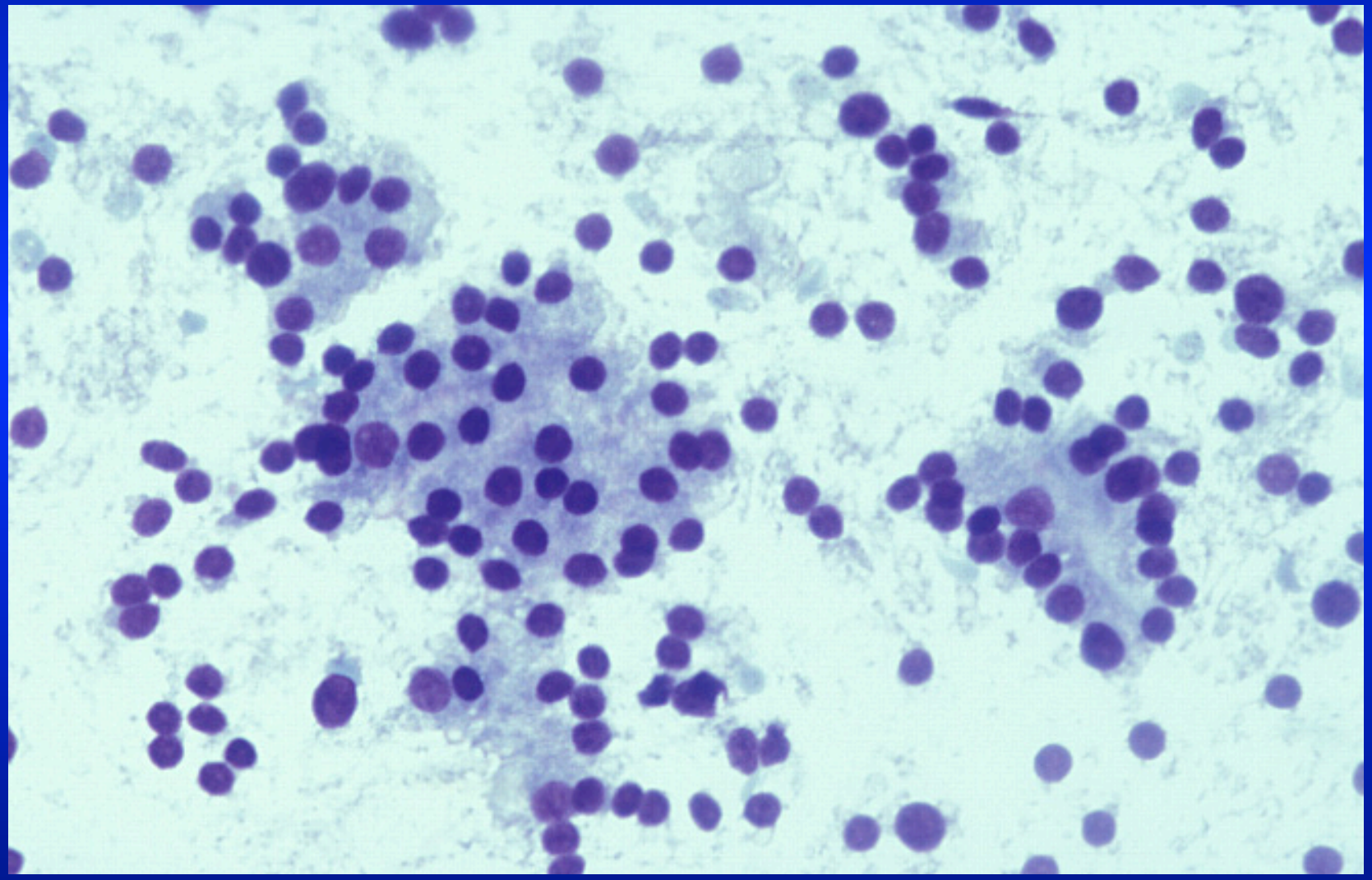
Thy 3:

- Atypia
  - cytological/nuclear or architectural
- Other features raising possibility of neoplasia
- Subdivided into Thy 3a and Thy 3f categories

Neoplasm possible (Thy 3a)

- Sparsely cellular sample, predominantly microfollicular
- Architectural atypia
  - Mixed micro- and macrofollicular pattern (approx. equal proportions) and/or little colloid
- Cytological/nuclear atypia such that papillary thyroid carcinoma cannot be confidently excluded
- Compromised specimen
  - XS blood or thickly spread containing some atypical cells
- Atypical cyst lining cells
- Predominance of lymphoid cells with very scanty epithelium

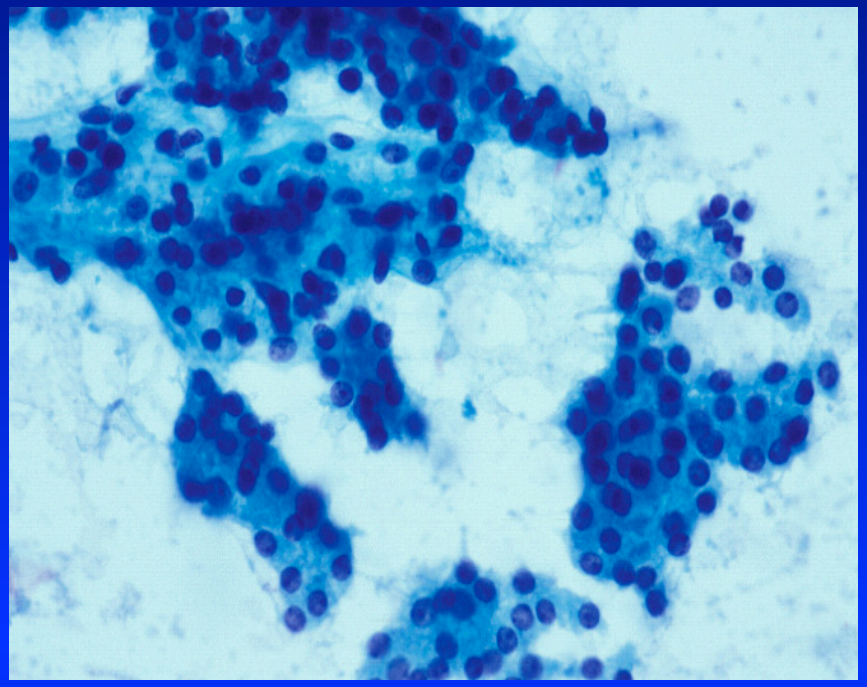
Follicular pattern
THY3a

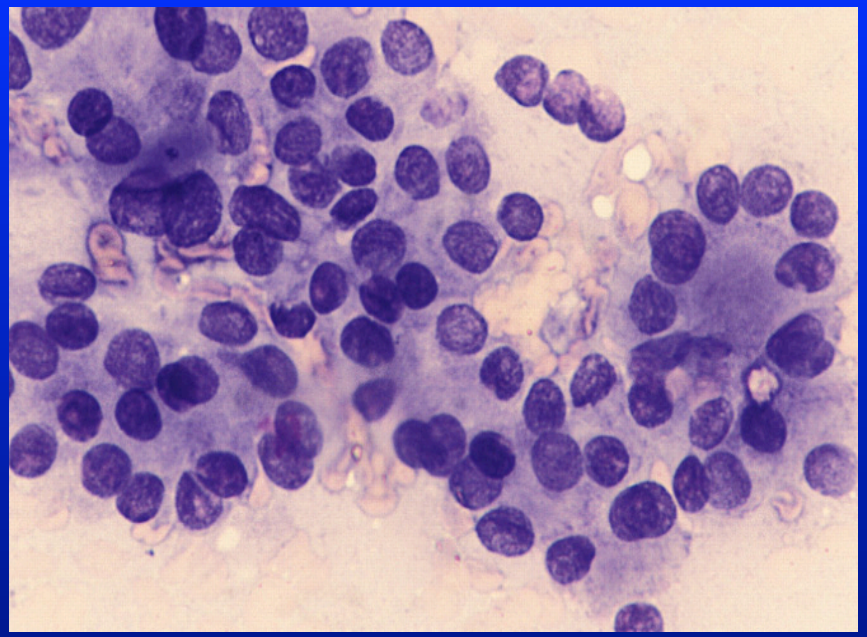


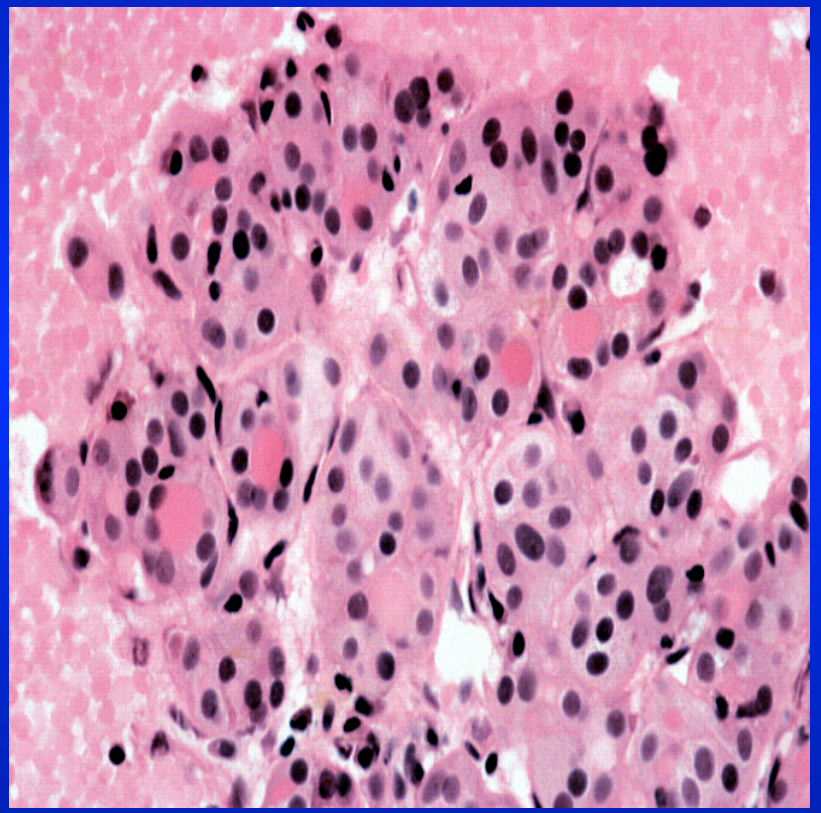
Neoplasm possible (Thy 3f)

- Sample suggests follicular neoplasm
  - Cellular sample
  - Microfollicles predominate
  - High cell to colloid ratio
- Includes
  - Follicular variant PTC
  - Samples consisting exclusively/almost exclusively of oncocytic cells (>75% cell content)

Follicular pattern
Thy 3f

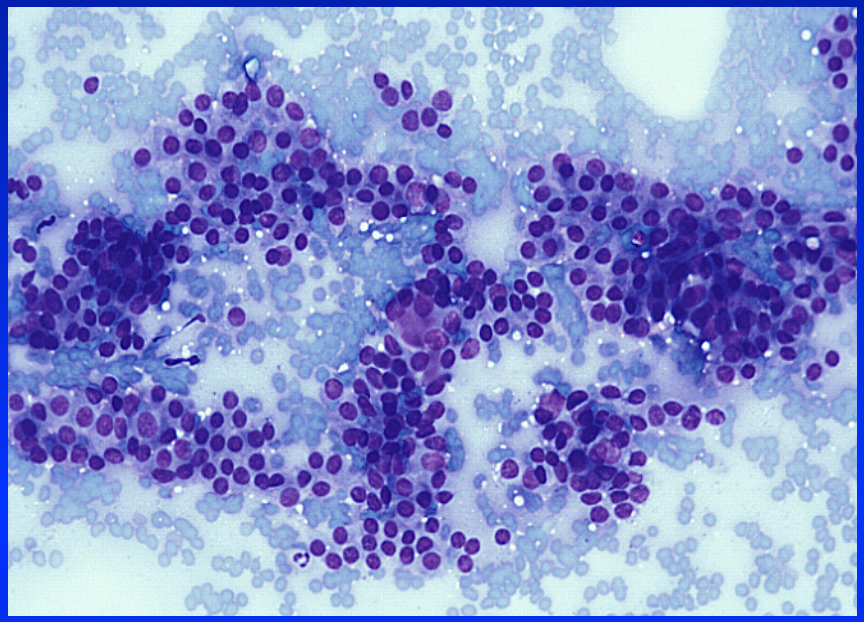


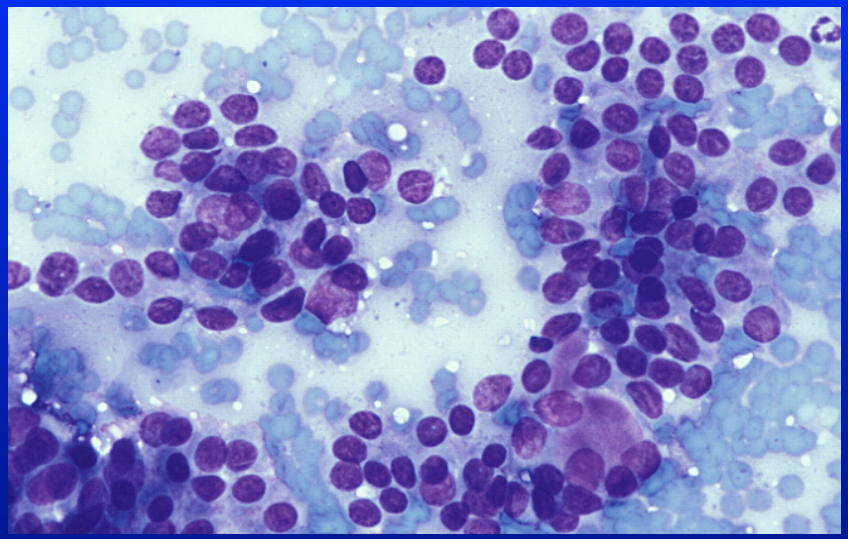


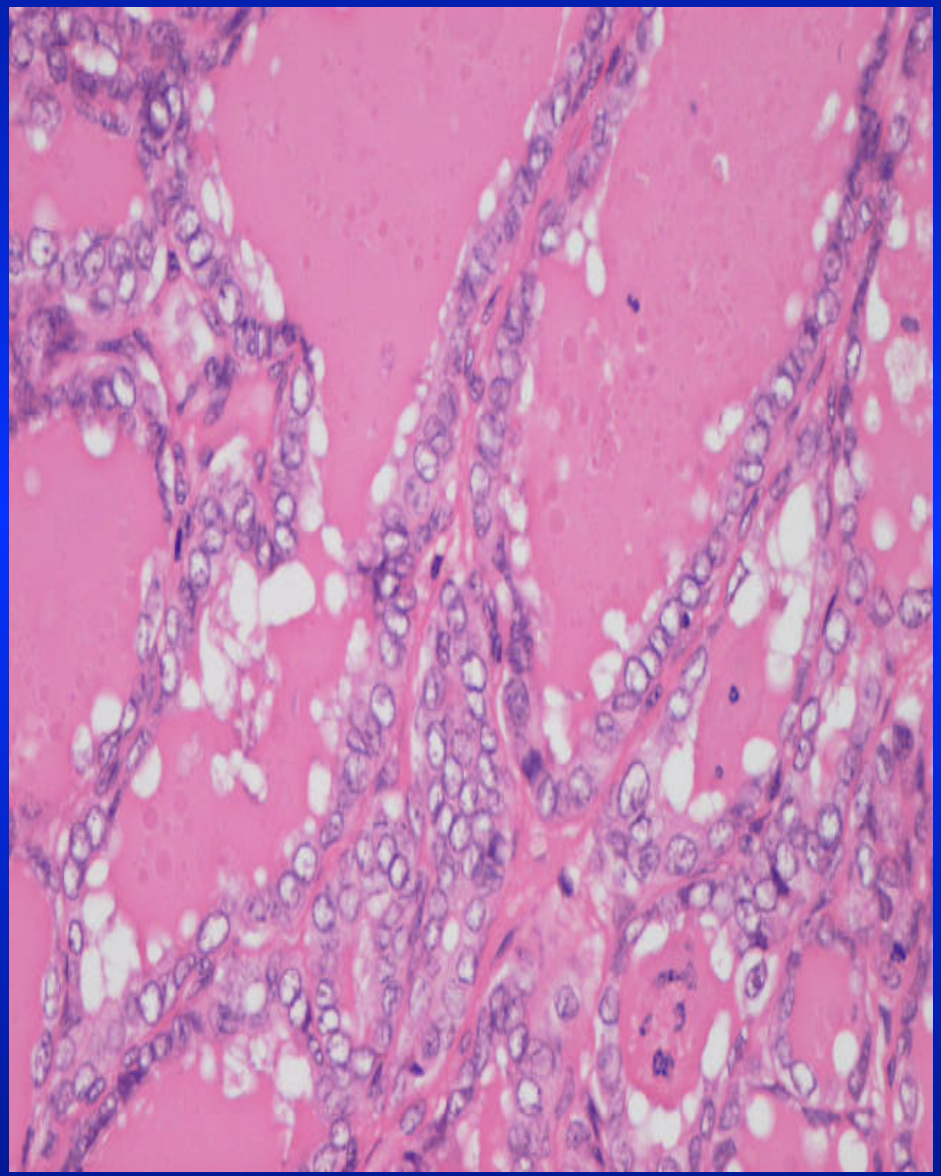


Clot preparation

Follicular pattern: papillary carcinoma







Follicular pattern Thy 3f

- Follicular variant of papillary carcinoma
  - cellular with clusters, syncitia and follicles
  - colloid balls
  - cytological features of papillary carcinoma
  - giant cells

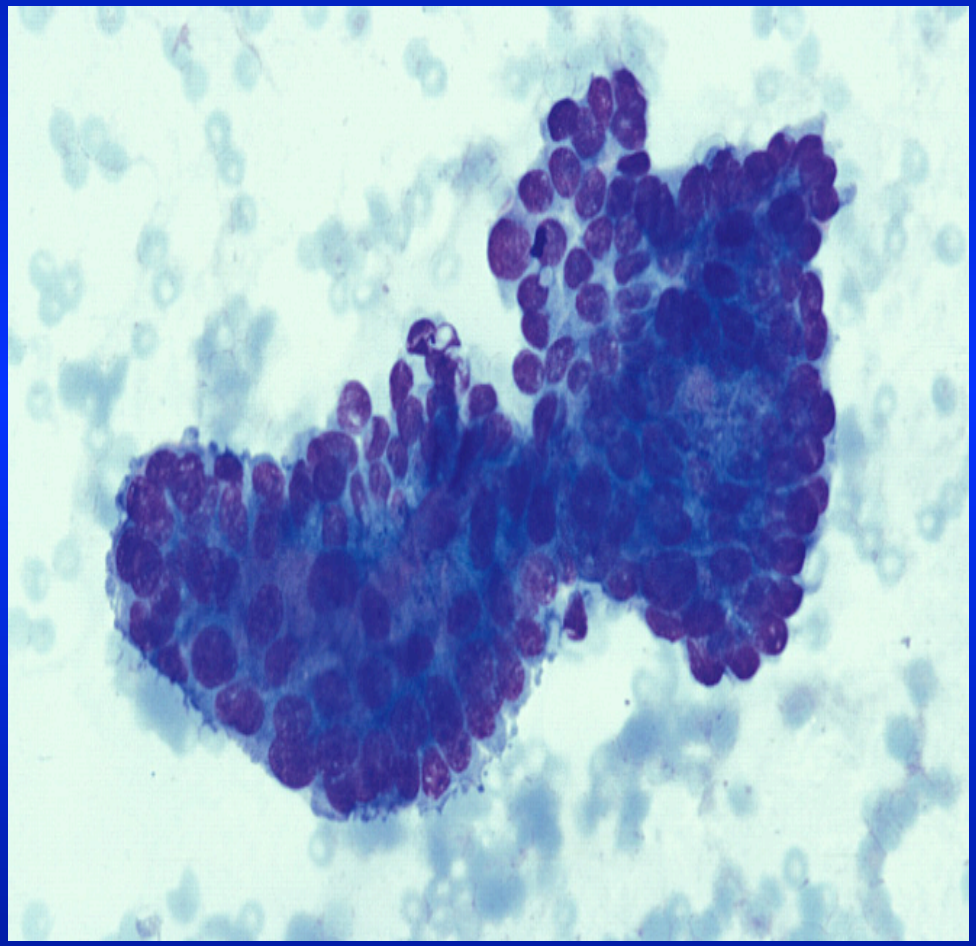
Follicular pattern

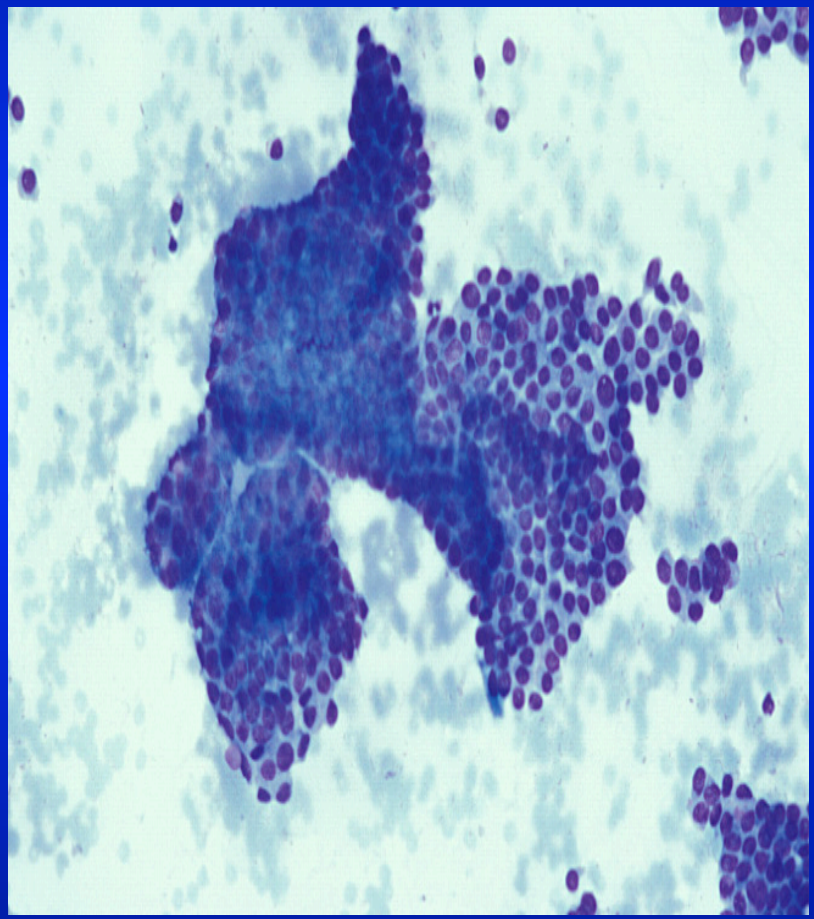
- Parathyroid adenoma
  - resembles follicular or oxyphilic adenoma of thyroid
  - cellular smears, high proportion of naked nuclei
  - nuclei uniform, small, round

Papillary pattern

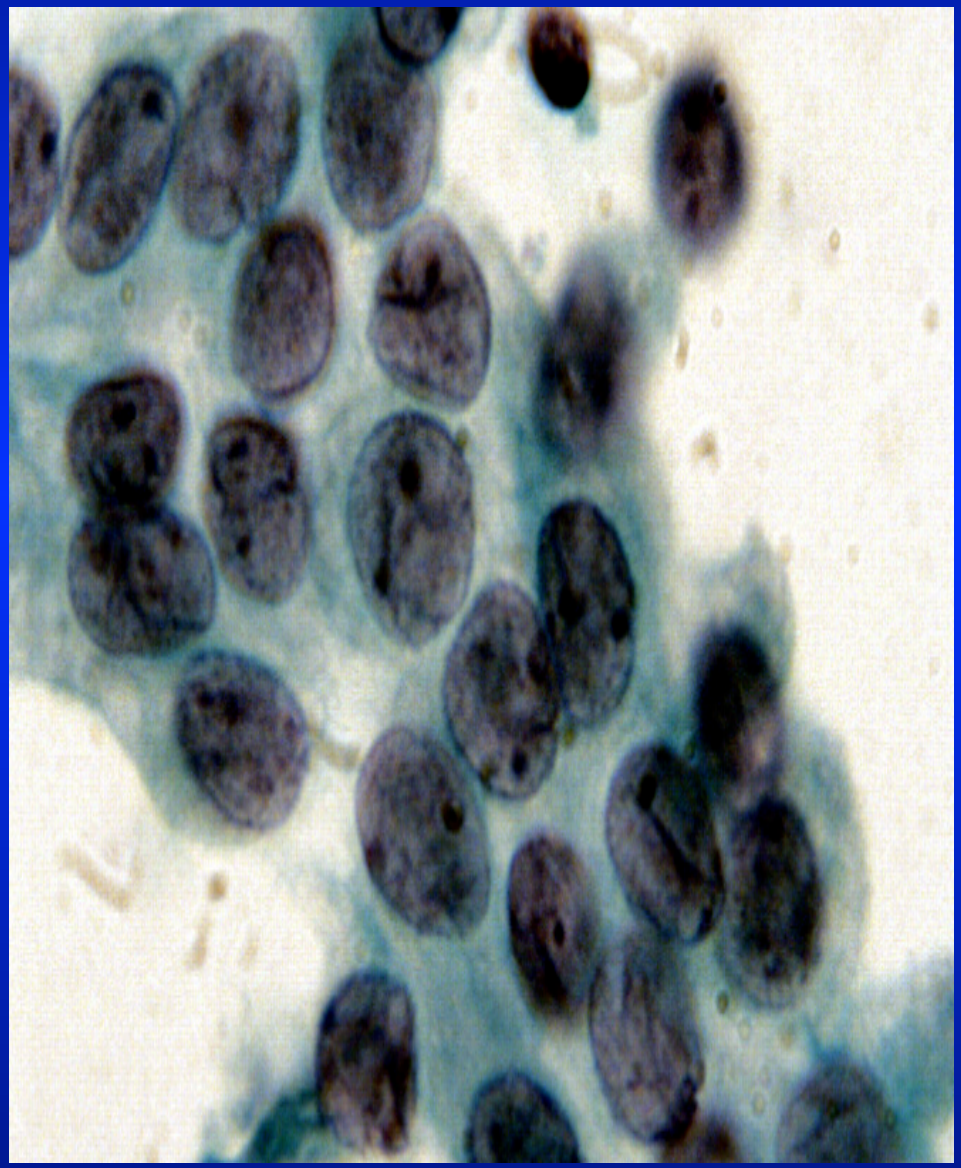
- Papillary carcinoma
  - inclusions and grooves
  - strongly associated with thyroid malignancy therefore histological confirmation mandatory
- Multinodular goitre
  - papillary hyperplasia
  - pale nuclei with powdery chromatin in hyperplasia
- Follicular adenoma
  - cohesive branching epithelial tissue fragments but lack anatomical edge

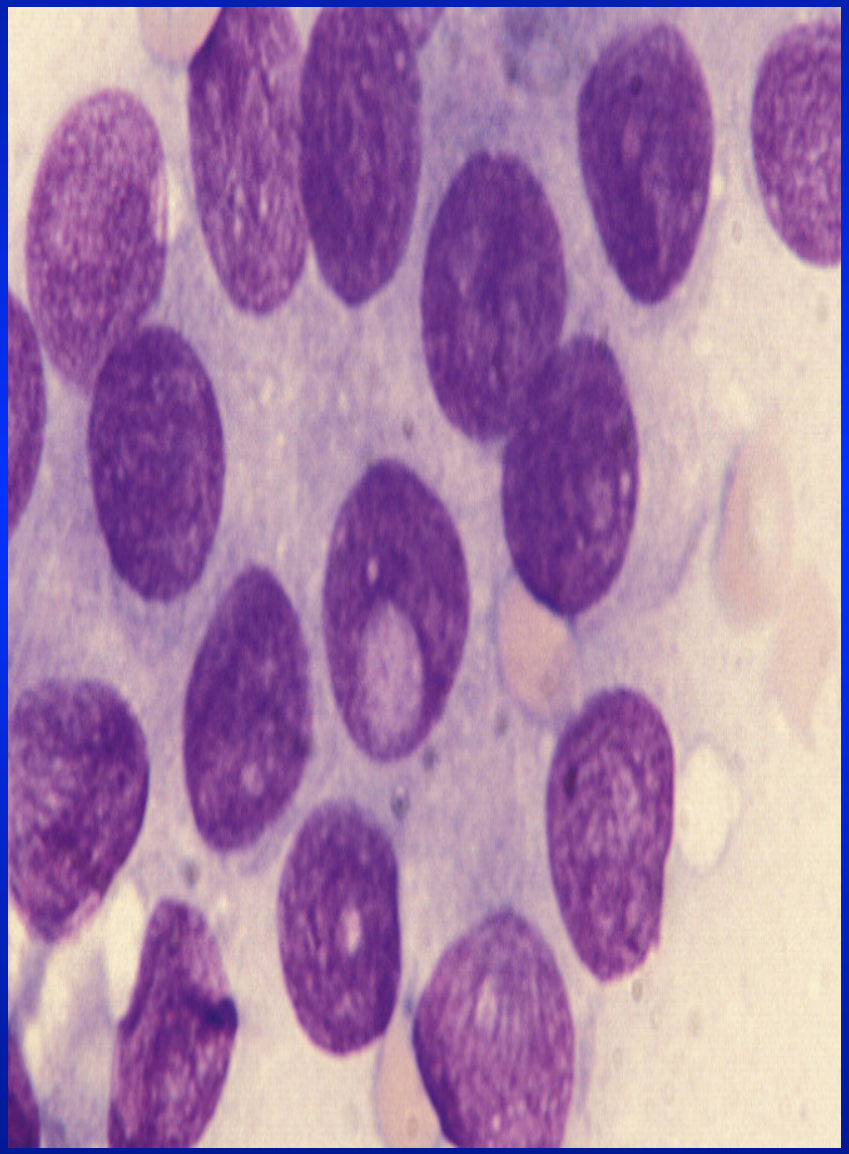
Papillary carcinoma



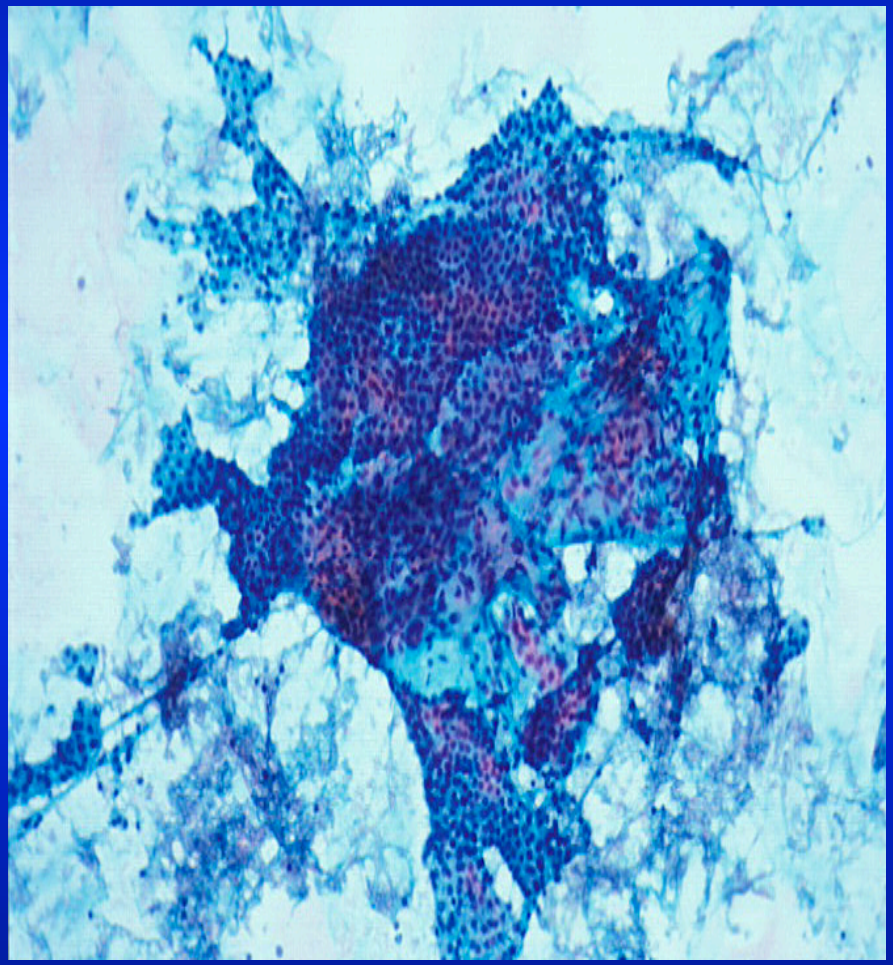


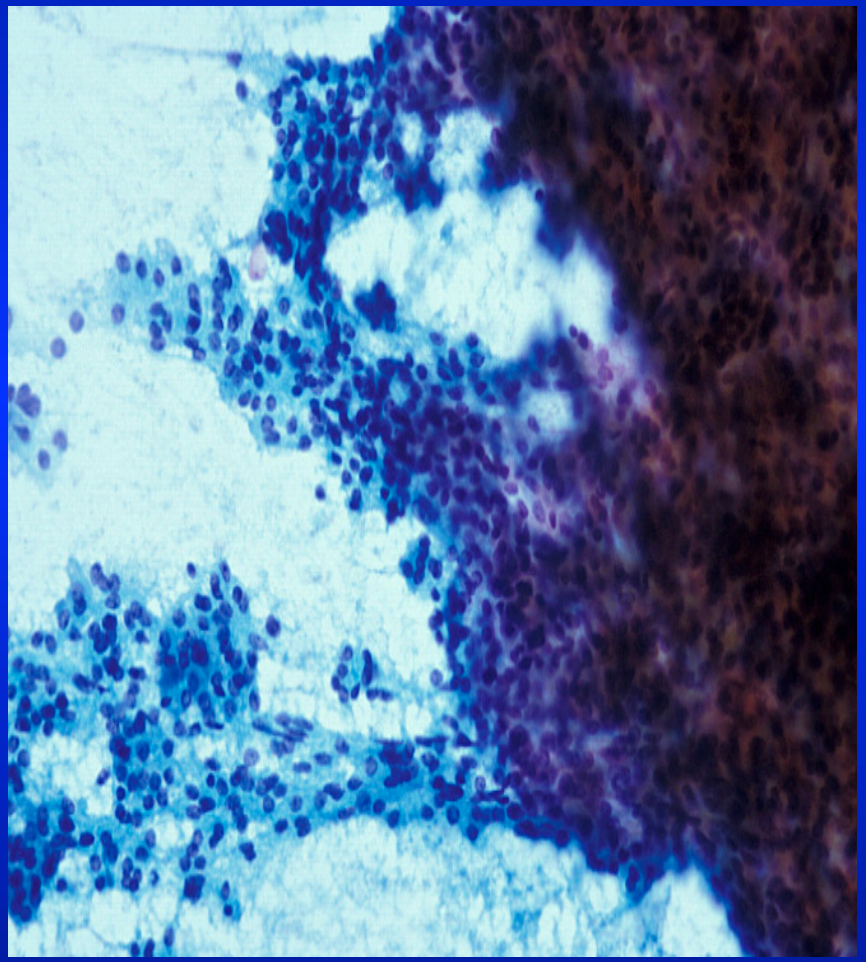
Papillary carcinoma





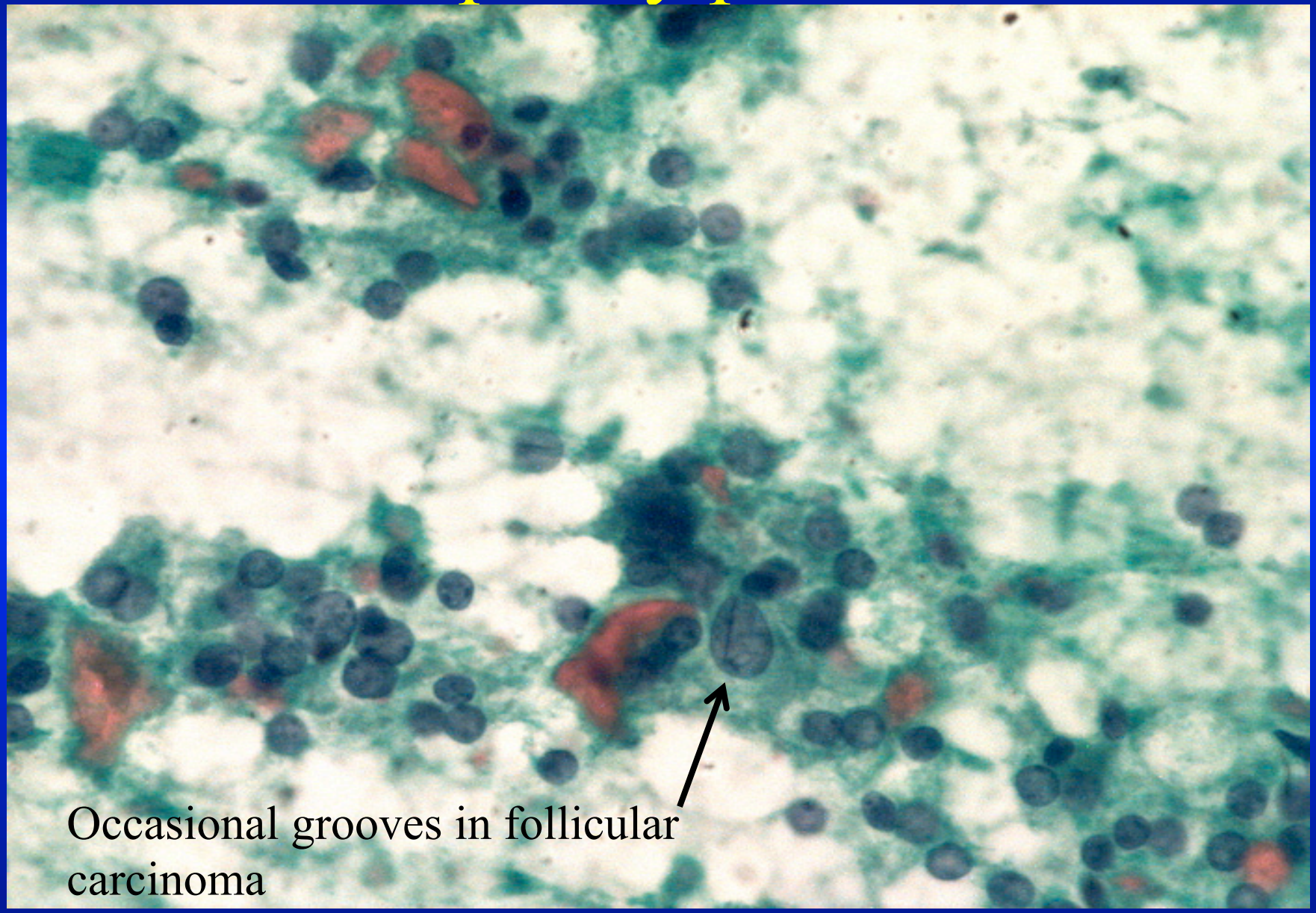
Papillary pattern





Branching fragments in hyperplasia

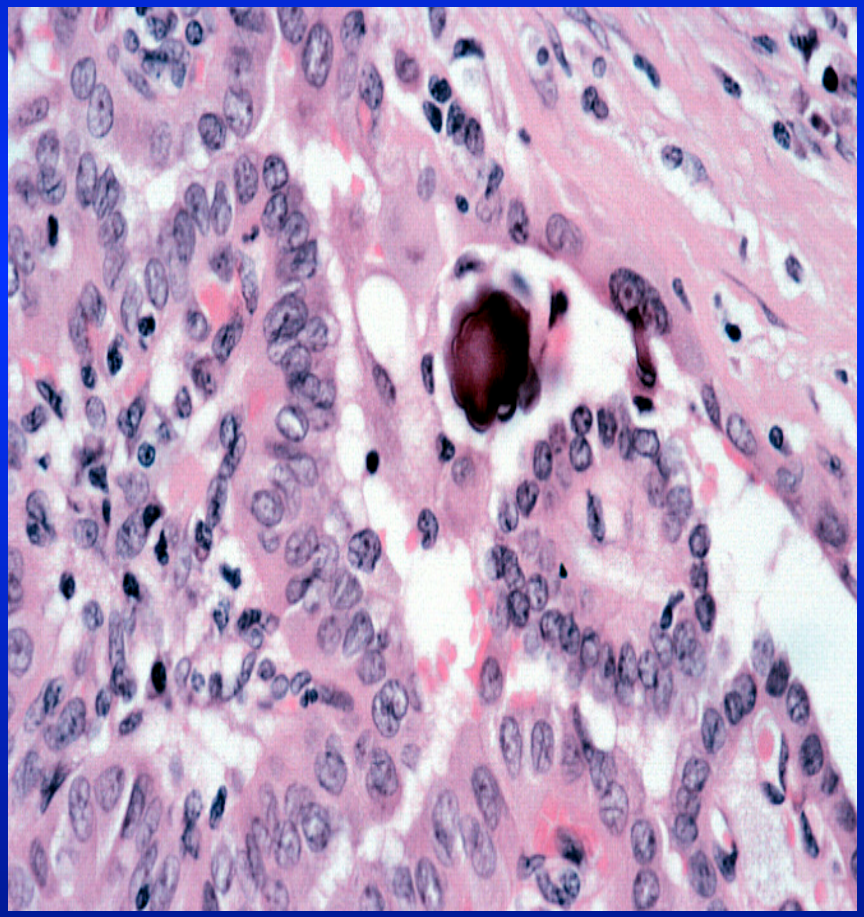
Papillary pattern

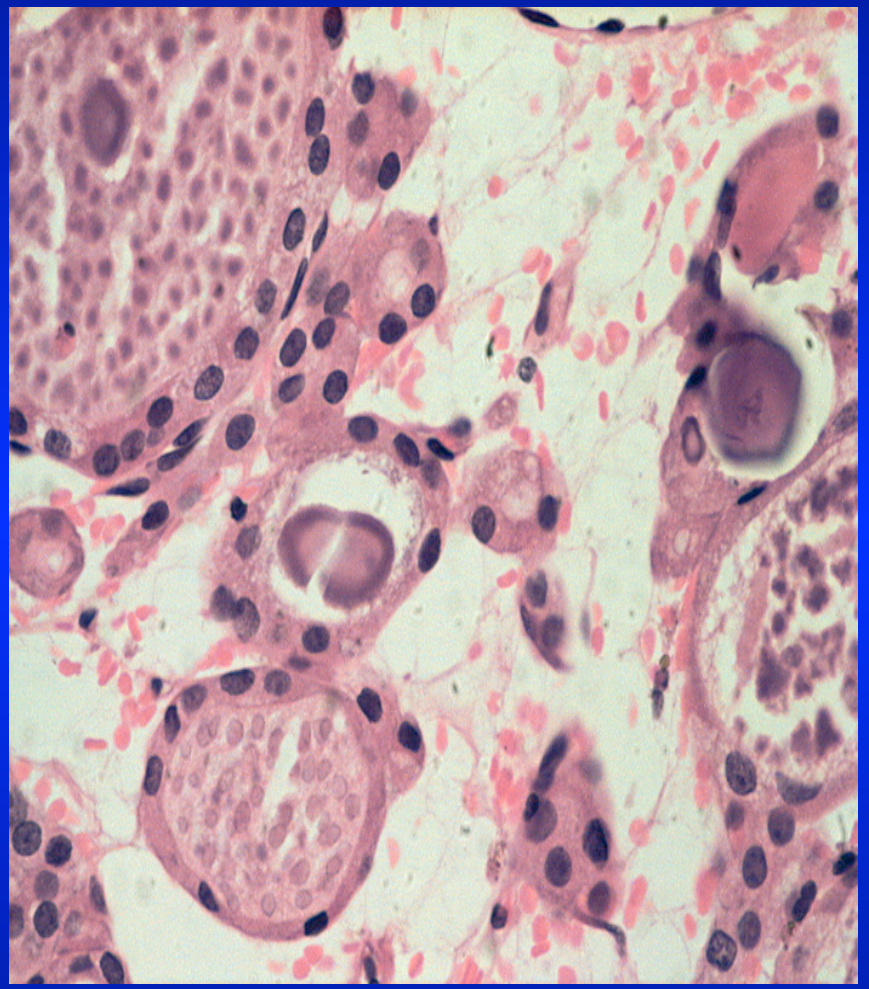


Papillary pattern

- Psammoma bodies

Papillary carcinoma



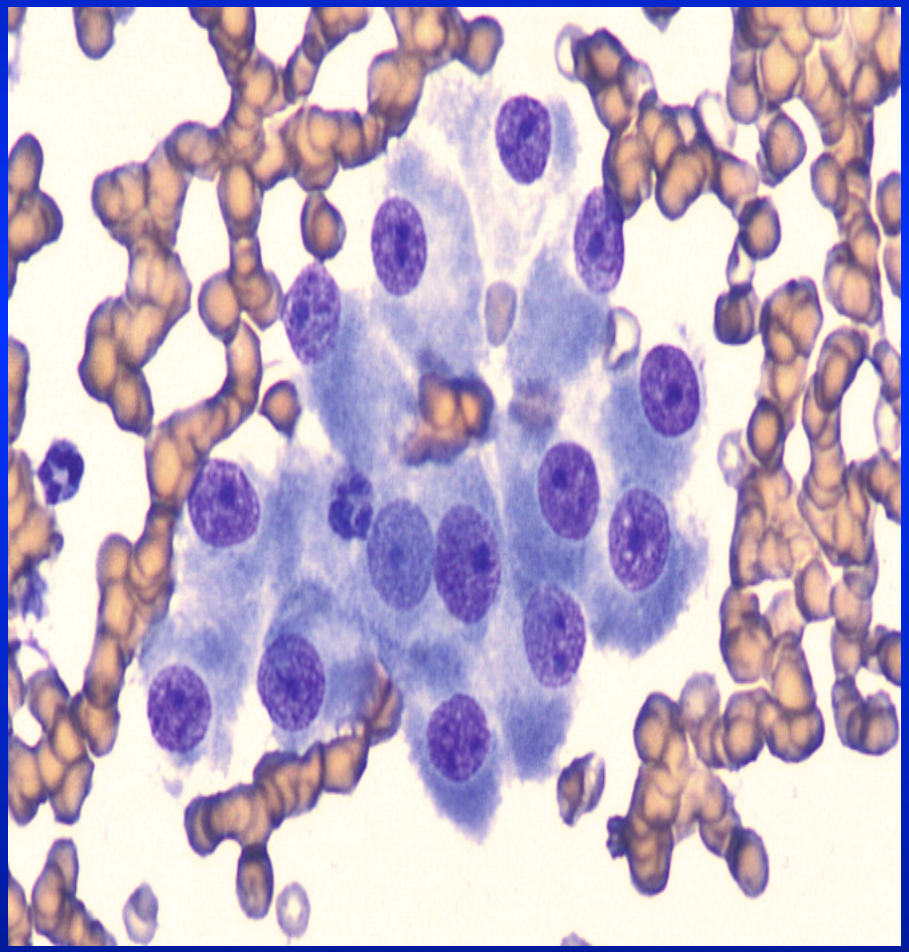


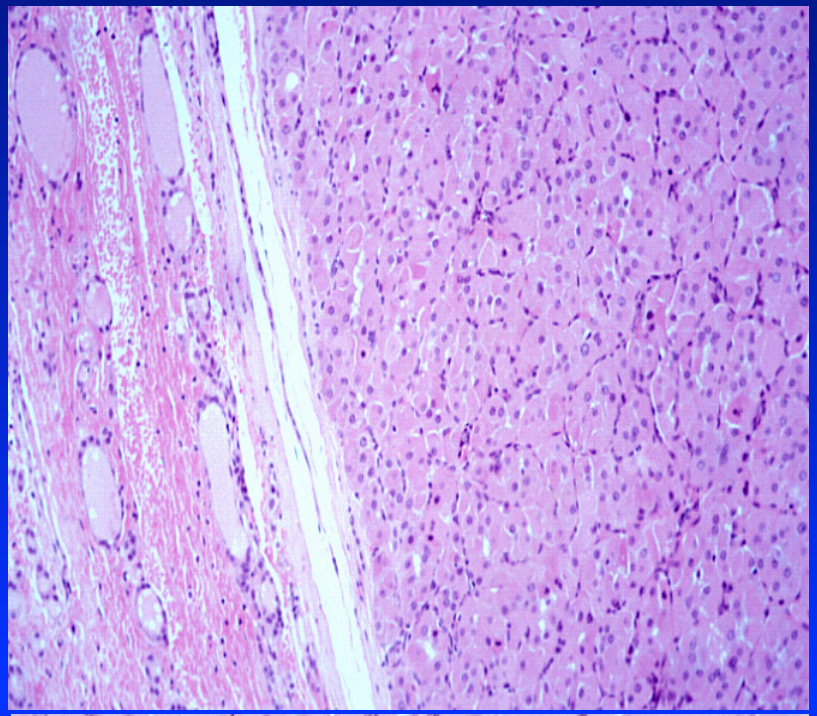
Hurthle cell adenoma

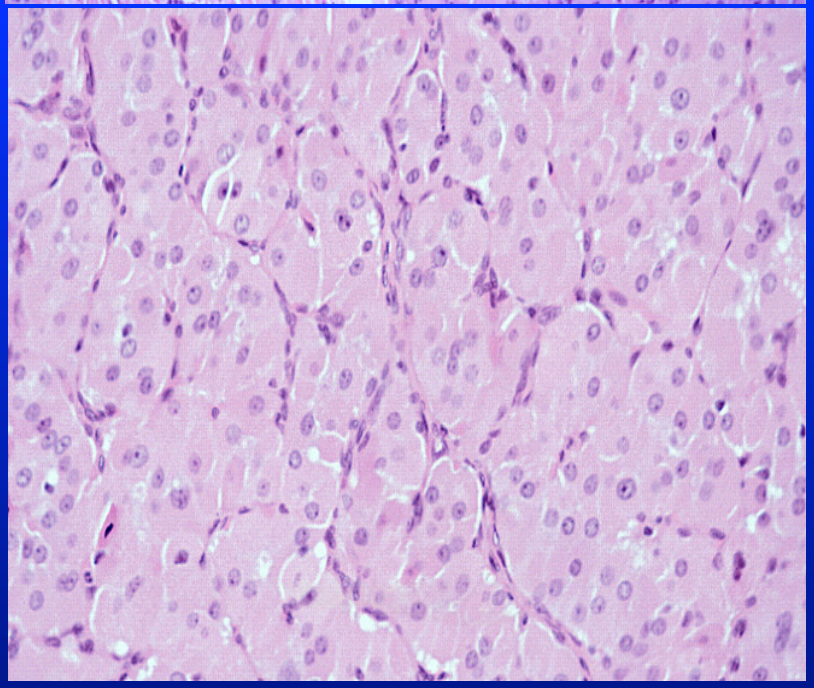
Oncocytic/Hürthle cells

- Related to increasing age
- Multinodular goitre
- Neoplasm
  - Oxyphil/Hürthle cell adenoma/carcinoma or oxyphilic variant of papillary carcinoma
- Hashimoto's thyroiditis
- Parathyroid hyperplasia or adenoma

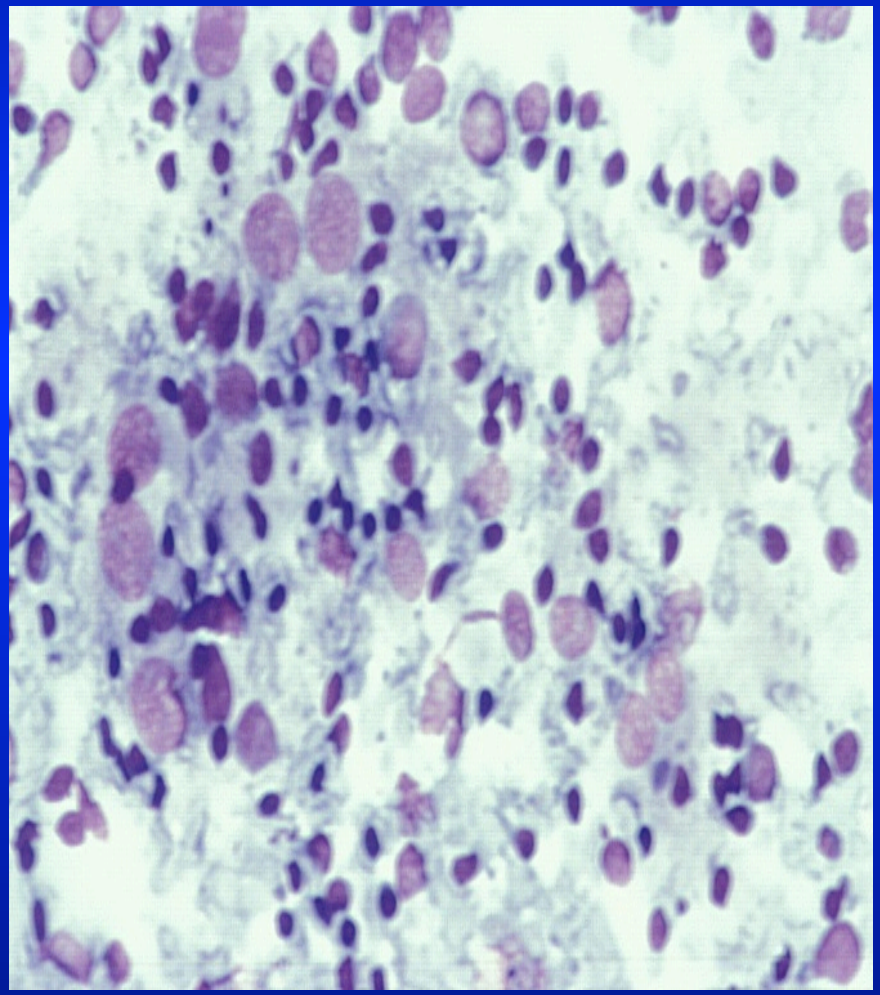
Hurthle cell neoplasm

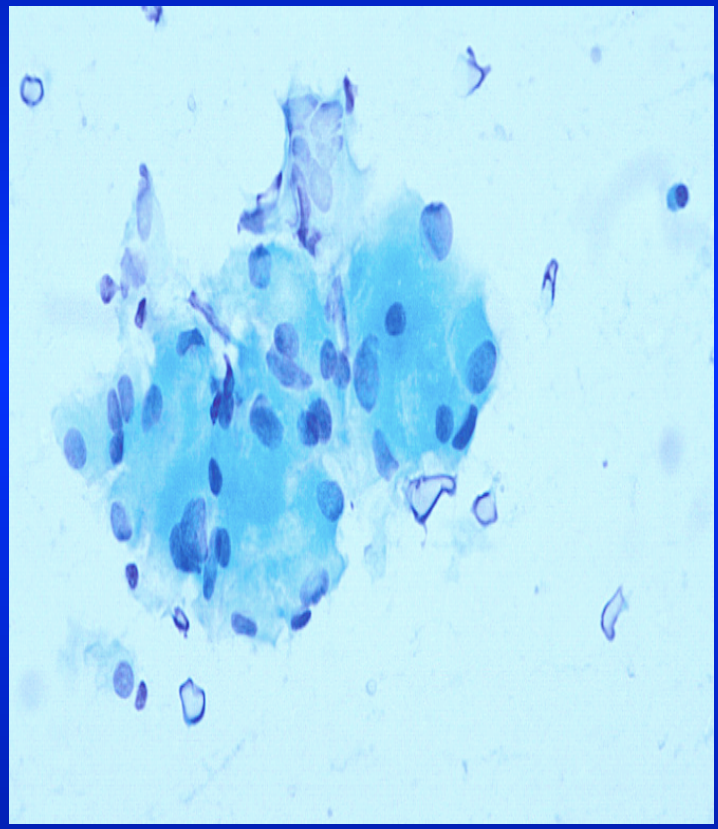






Hashimoto’s thyroiditis





Follicular pattern

Lymphoid infiltrate

- Thyroiditis
- Graves' disease
- PTLD
- Lymphoma
  - Rare, almost always on background of Hashi's
  - Originate from marginal zone of lymphoid follicles

Spindle cell/ pleomorphic cell pattern

Medullary carcinoma

Anaplastic carcinoma

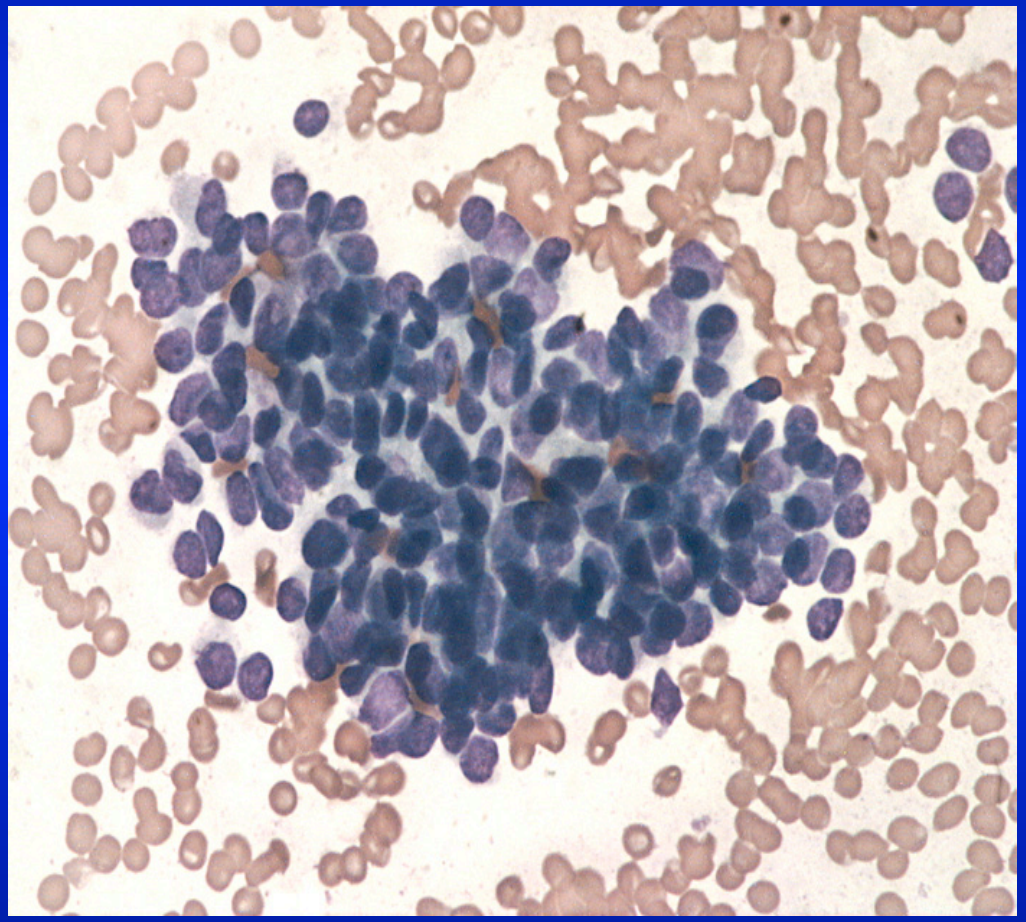
Angiosarcoma

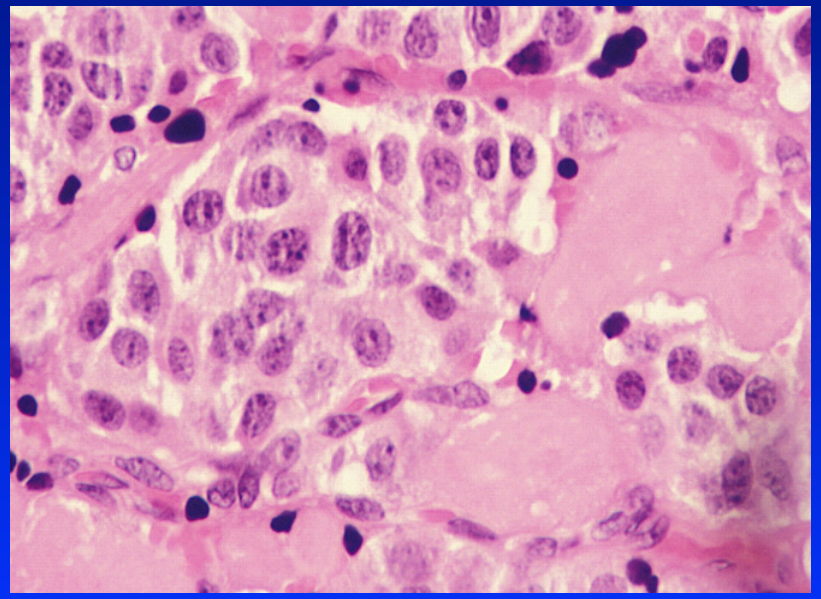
Metastatic carcinoma

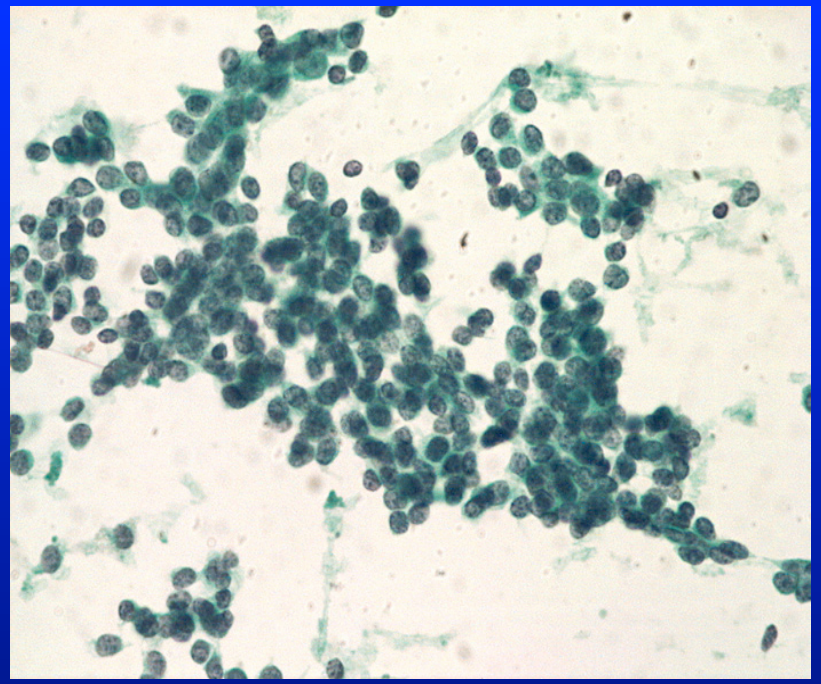
Primary squamous carcinoma

Colloid cyst

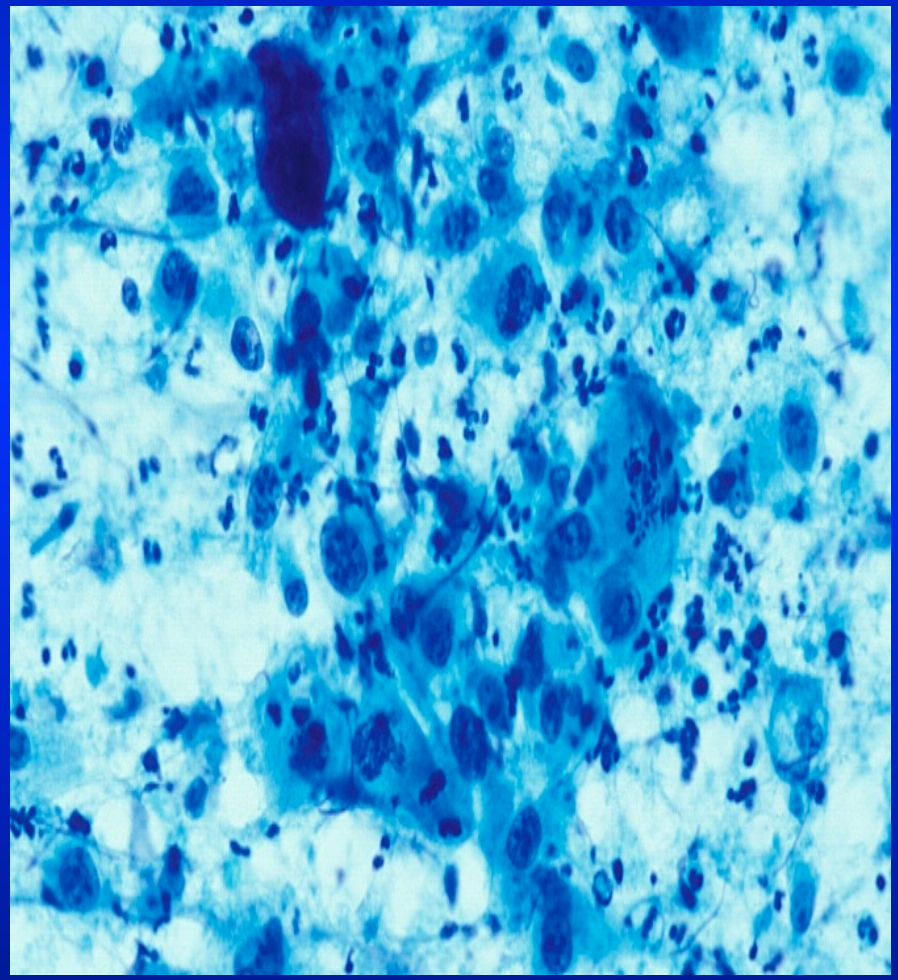
Spindle cell pattern-medullary carcinoma

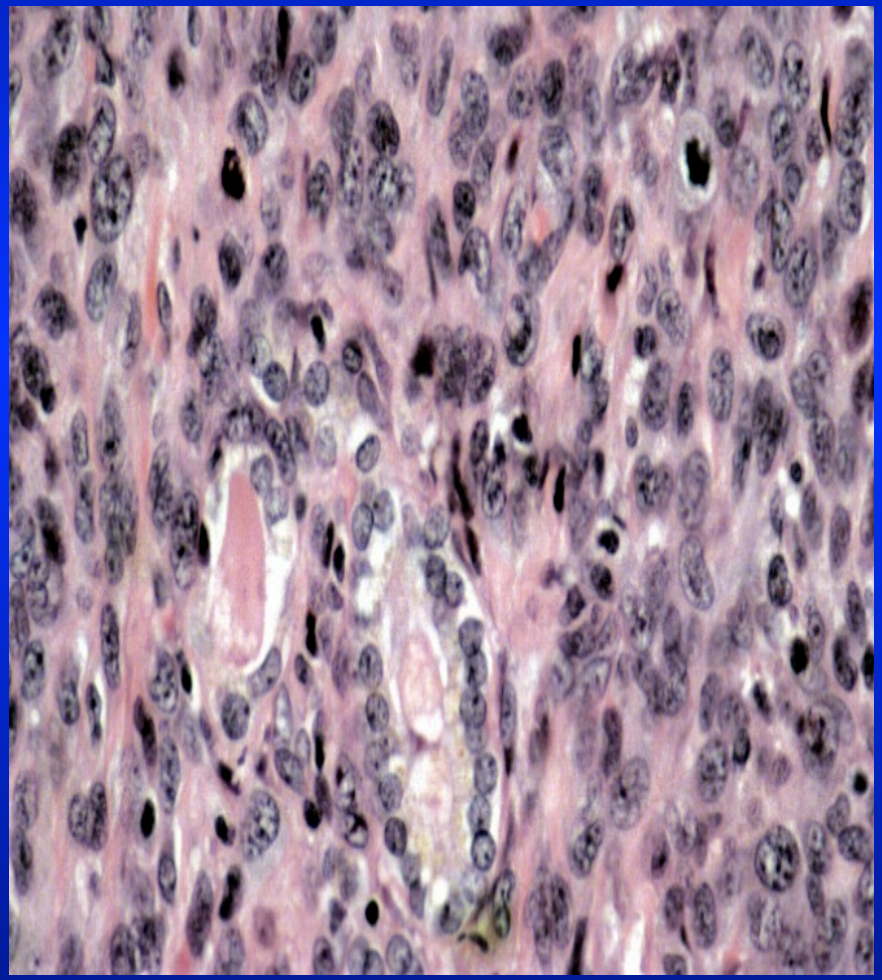




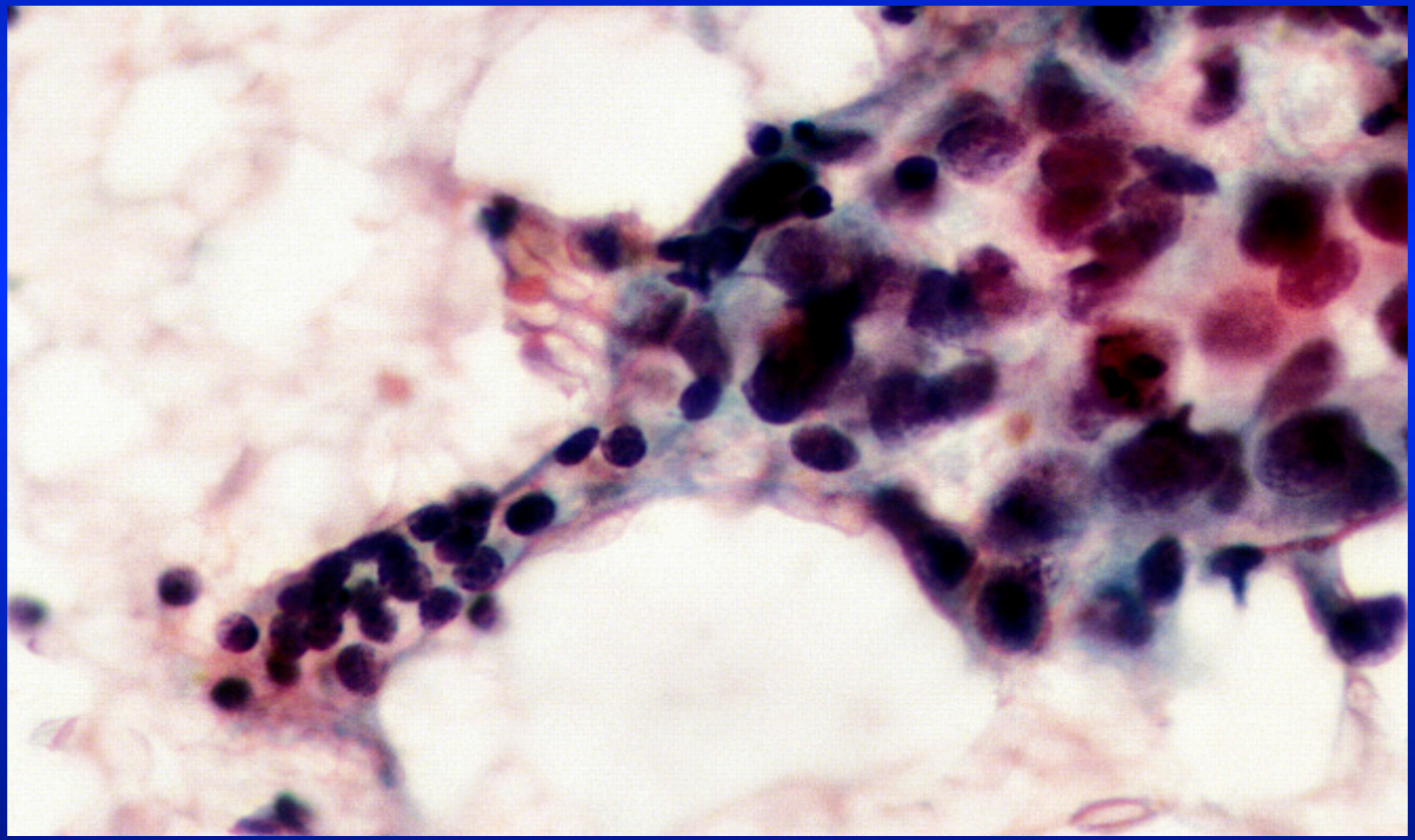


Spindle cell/pleomorphic cell pattern - anaplastic carcinoma

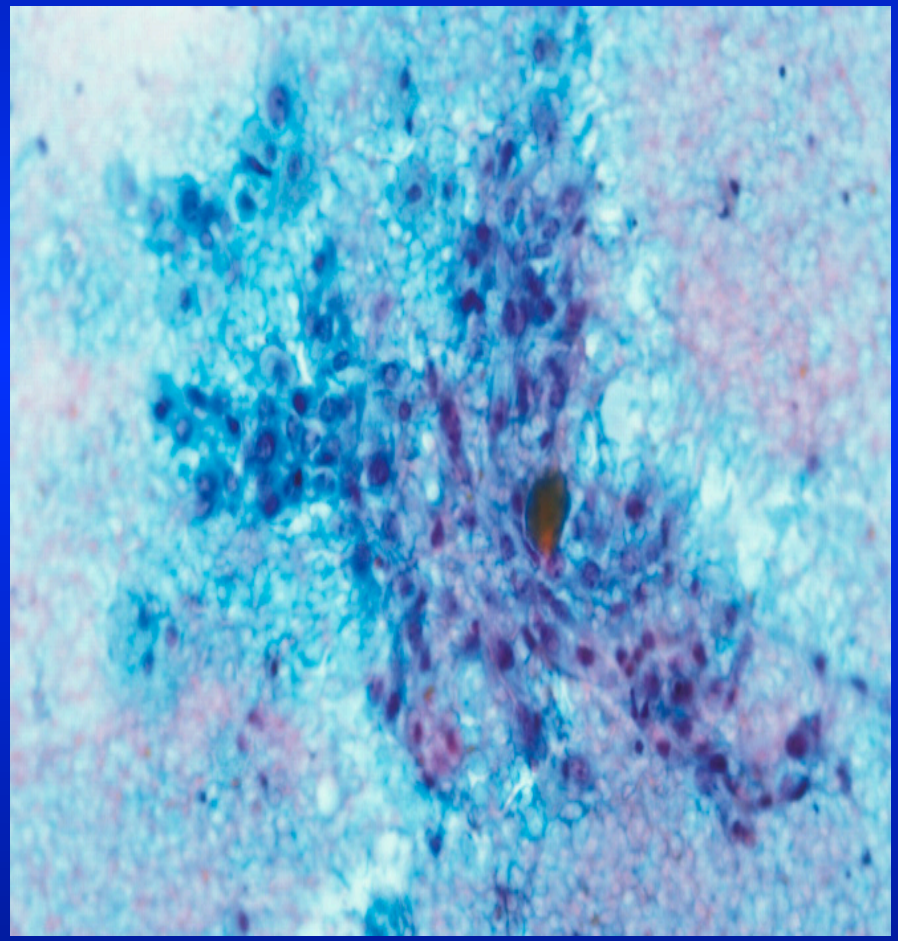


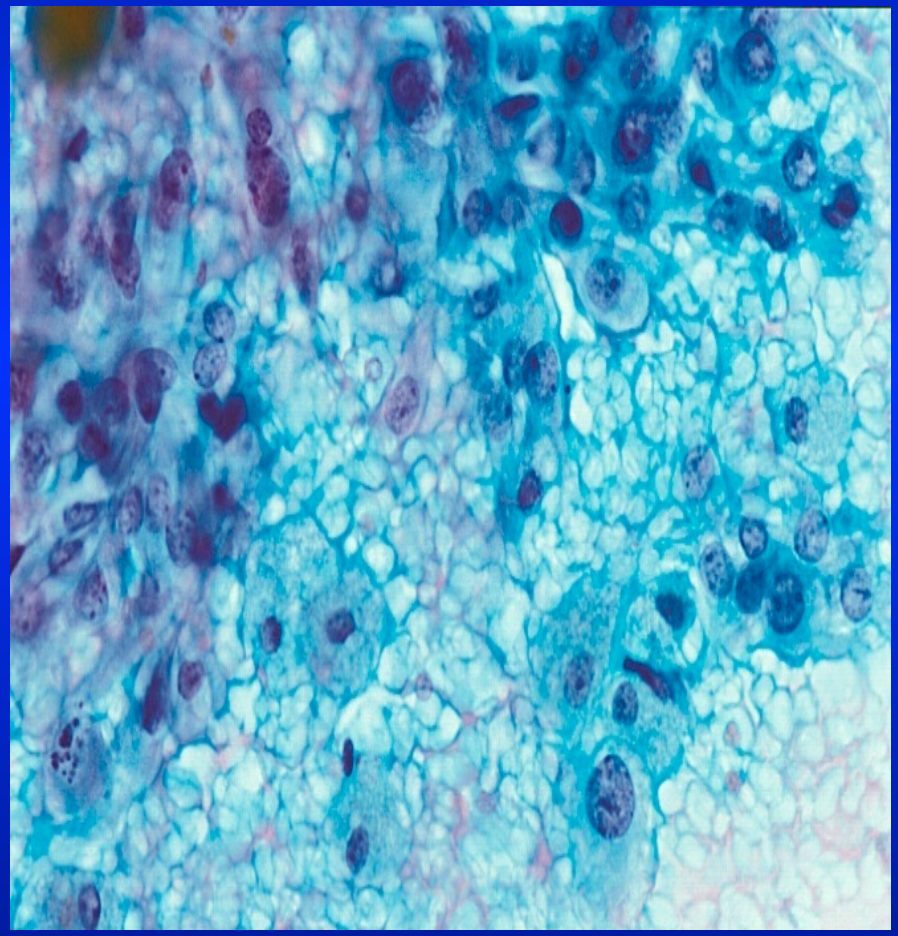


Spindle cell and pleomorphic cell pattern - metastatic carcinoma



Spindle cell and pleomorphic cell pattern - multinodular goitre





Molecular analysis of cytology

- Use of molecular markers to aid in diagnosis and patient stratification for possible further treatment has grown significantly
- Molecular markers, such as BRAF, RAS, RET/PTC, and PAX8/PPARγ, should be considered in the management of patients with indeterminate FNA cytology
- Not in routine use in UK

Immunohistochemistry

Thy 3 or 4 lesions

- Thyroglobulin, TTF1 and CD56
- Gal-3, HBME1, PAX 8 and CK19
    - markers associated with thyroid cancer
    - none are specific
  - BRAF if papillary ca. suspected

Medullary carcinoma

  - Calcitonin, CEA, TTF-1 and general neuroendocrine markers

Anaplastic (undifferentiated) carcinoma

  - Cytokeratin; vimentin; EMA and CEA (focal positivity)

Lymphoma

  - Flow cytometry, lymphoma panel

?Parathyroid lesion

  - PTH, TTF-1

Suggested Reading

- RCPath
  - Tissue pathways for endocrine pathology 2012
  - RCPath guidance on reporting of cytology specimens 2016
  - Dataset for thyroid cancer histopathology reports 2014 and NIFTP addendum 2016
- British Thyroid Association Guidelines for the Management of Thyroid Cancer 2014
- WHO Tumours of Endocrine Organs 2017
- TNM Classification of Malignant Tumours 8th Edn
- Rosai and Ackerman's Surgical Pathology

Sample Answer

Follicular lesion, Thy 3f

Description:

- Cellular sample containing sheets and groups of follicular epithelial cells, many with a microfollicular architecture. Thick colloid is evident within some of the microfollicles. There are no nuclear features to suggest papillary thyroid carcinoma.

Conclusion:

- Follicular lesion with features favouring a follicular neoplasm (Thy 3f)

Comment:

- Discussion at MDT meeting with the clinical and radiological findings is warranted

Sample Answer

Papillary thyroid carcinoma, Thy 5

Description

•Cellular sample containing sheets and groups of cells some with a papillary architecture. The cells have enlarged oval overlapping nuclei showing irregularity of the nuclear membrane, grooving and intranuclear inclusions. Chromatin is pale and powdery. Scanty thick colloid and multinucleate cells are also identified.

Conclusion

•Papillary thyroid carcinoma (Thy 5)

Comment

•Discussion at MDT meeting with the clinical and radiological findings is warranted