



PITFALLS IN FNA OF THYROID  
AUBMC EXPERIENCE  
2005-17

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# Methods

- All FNAs of thyroid are correlated with surgical pathology: QA
- Discrepancies:
  - Sampling error: (common)
  - Interpretive error: (FNA material is adequate and representative but the pathologist made an error in diagnosis)
- All IEs reviewed blindly Dr Chirine Khaled and myself

# Results

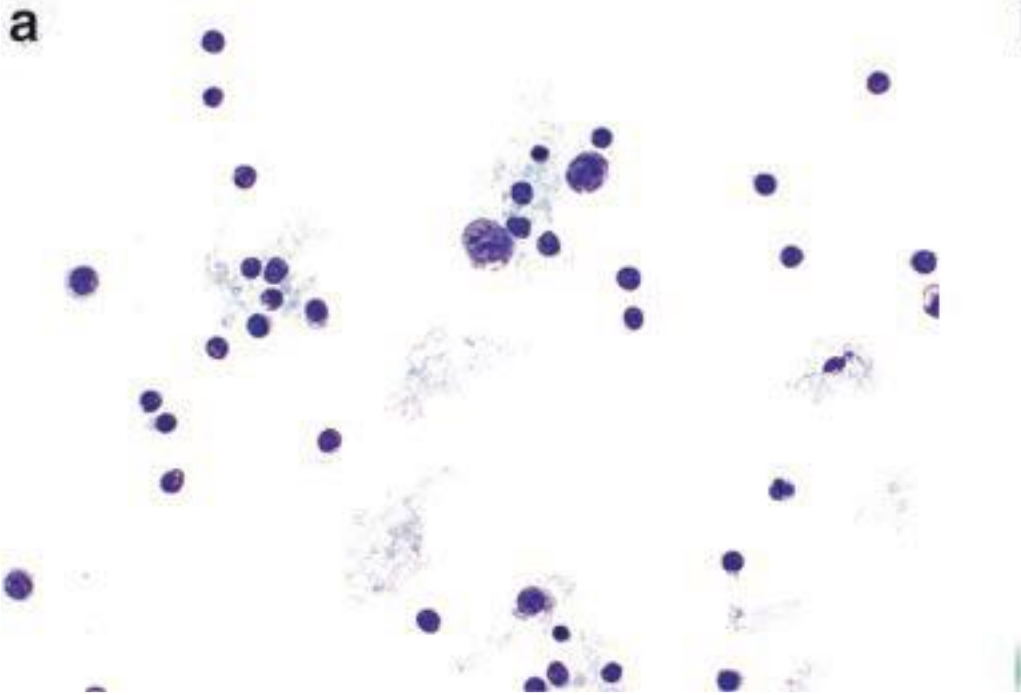
- Total thyroid FNAs: 4926
- IEs: 11
  - Hashimoto's Thyroiditis: 4
  - Multinodular Goiter: 5
  - Miscellaneous: 2
    - Medullary carcinoma: 1
    - Minimally invasive follicular carcinoma: 1

# Hashimoto's Thyroiditis

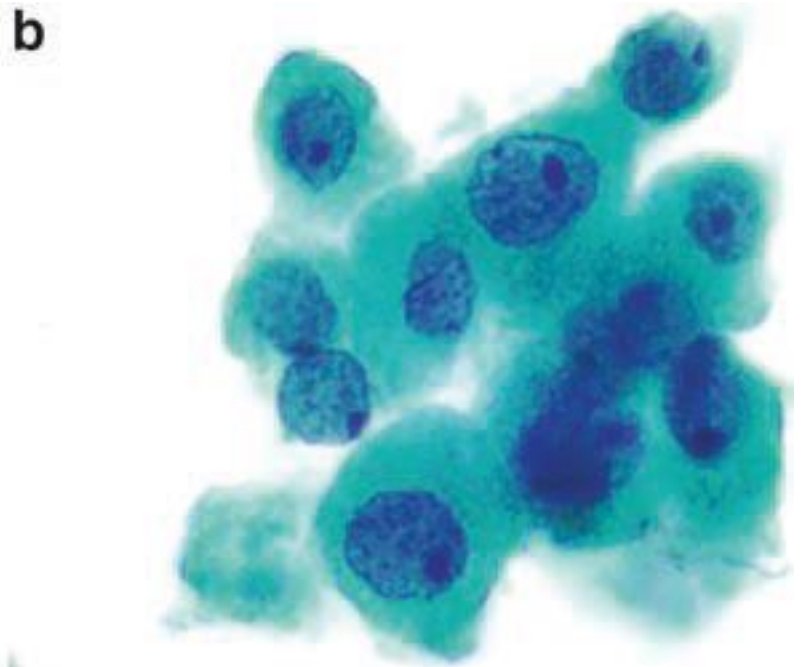
IEs: AUBMC 2005-2017

Final pathology diagnosis	Case #	Original FNA IE	Surgical procedure	Blinded review diagnosis
Hashimoto's thyroiditis	1	Suspicious for malignancy/metastatic lung ca.  <b>Suspicious for Malignancy</b>	Hemi thyroidectomy	Hashimoto's thyroiditis
	2	SFN HCT  <b>Suspicious for Malignancy</b>	Total thyroidectomy	Hashimoto's thyroiditis
	3	Suspicious Large cell lymphoma	Total thyroidectomy + LN dissection	Hashimoto's thyroiditis vs LCL
	4	Suspicious papillary Ca	Total thyroidectomy + LN dissection	FLUS
				<b>Unnecessary surgery</b>

# FNA of Hashi's

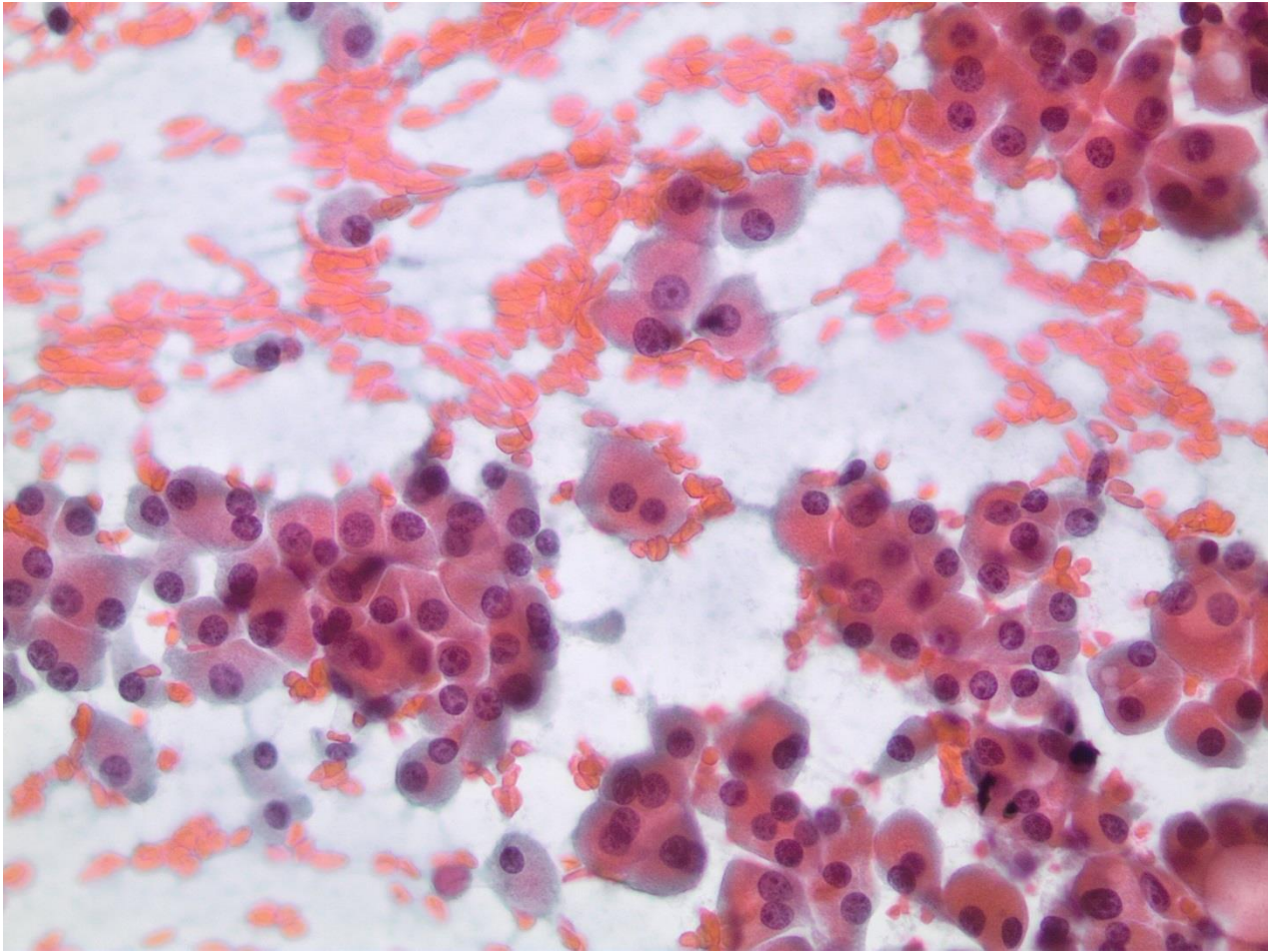


Lymphocytes: Polymorphous

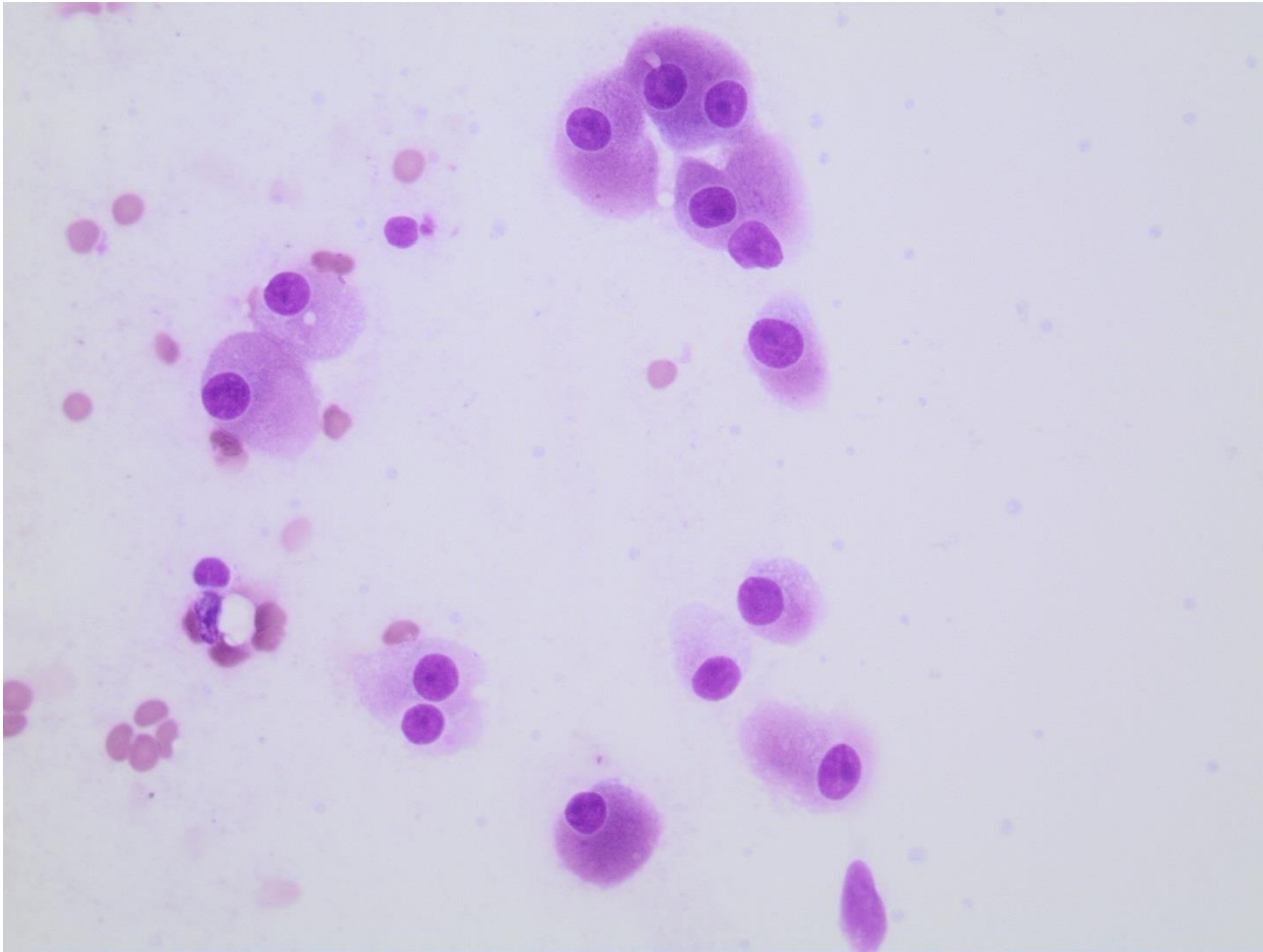


Hurthle cells (HCs)

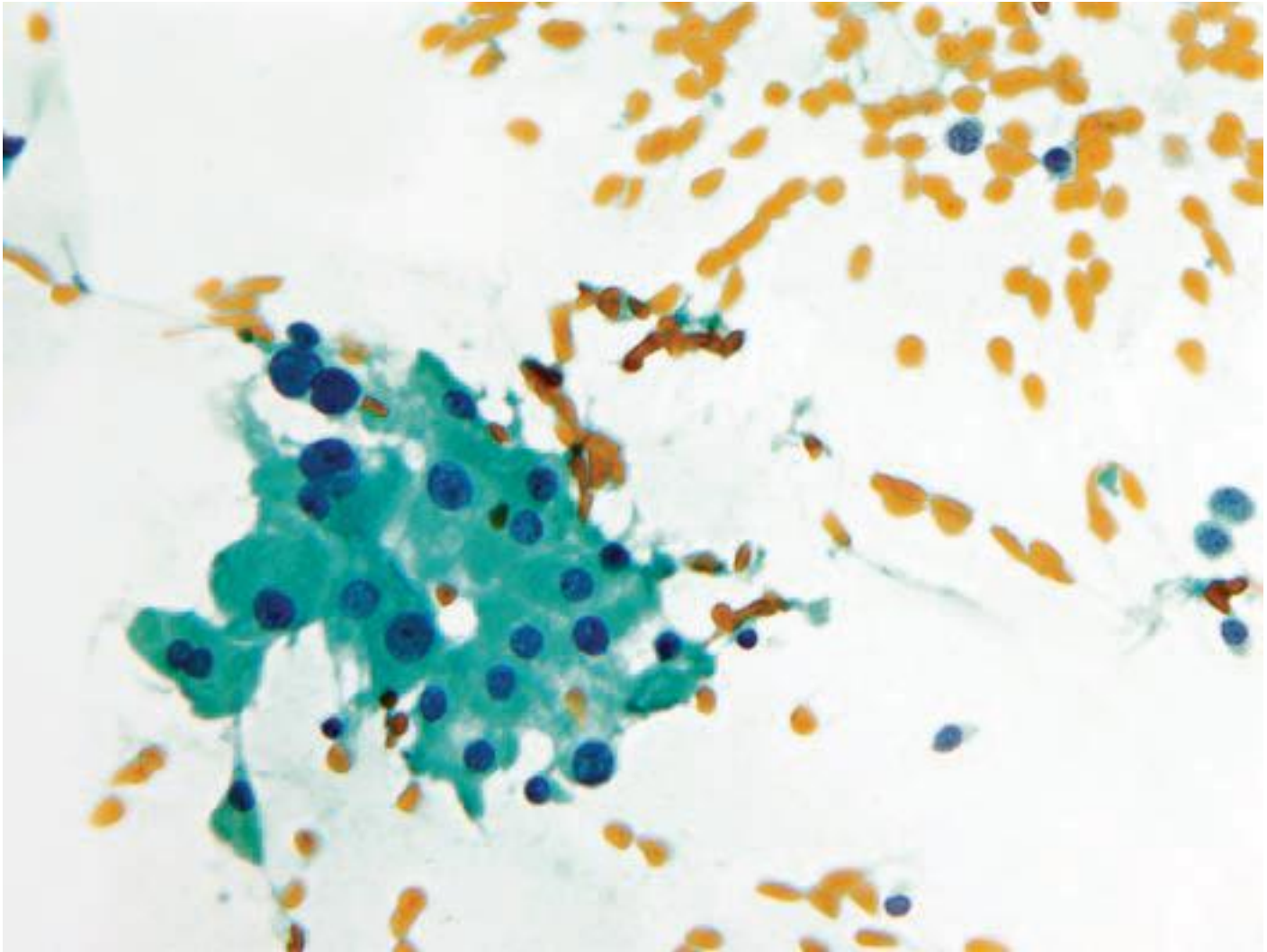
# HCs



# HCs



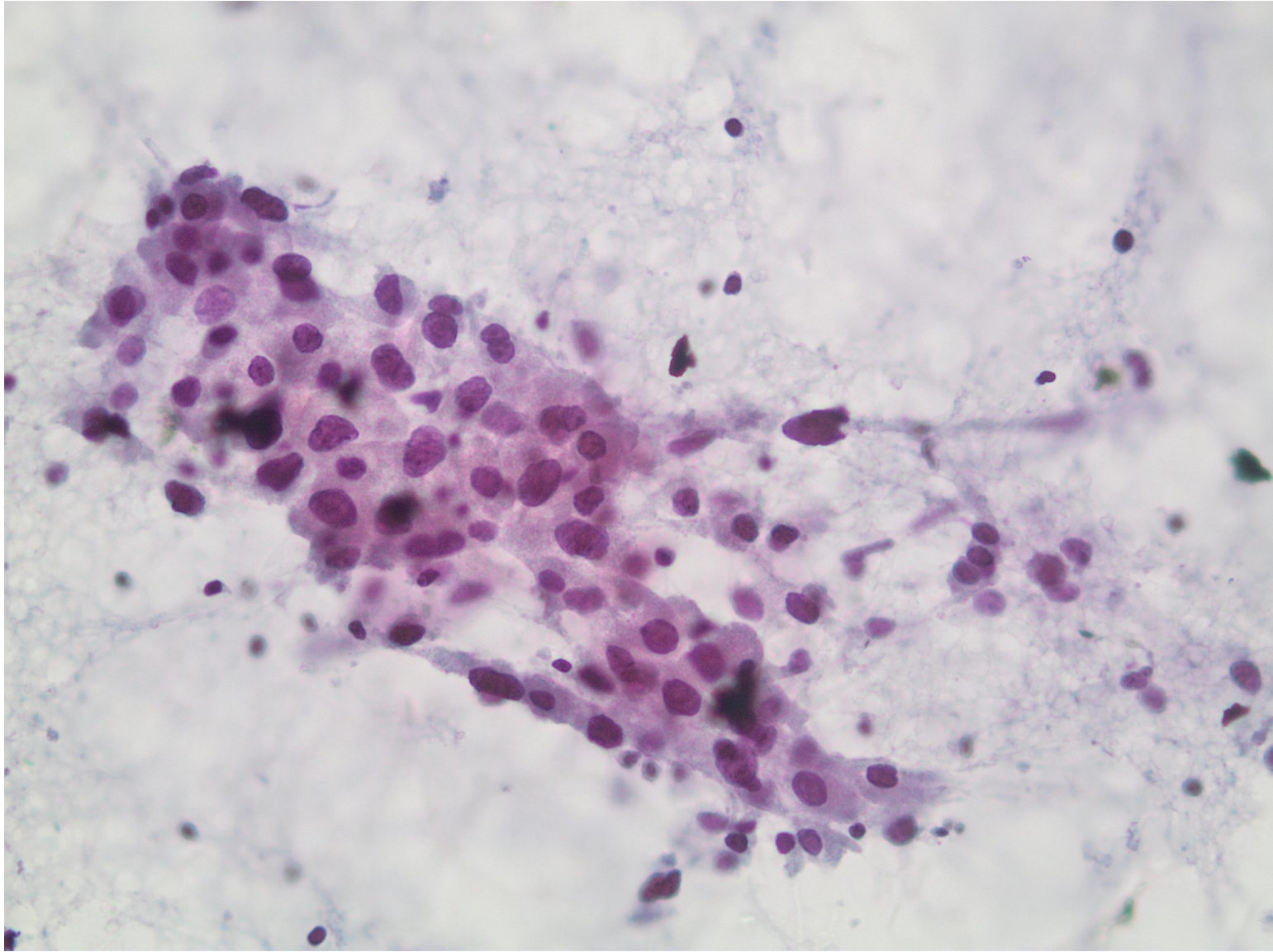
# Hashi's



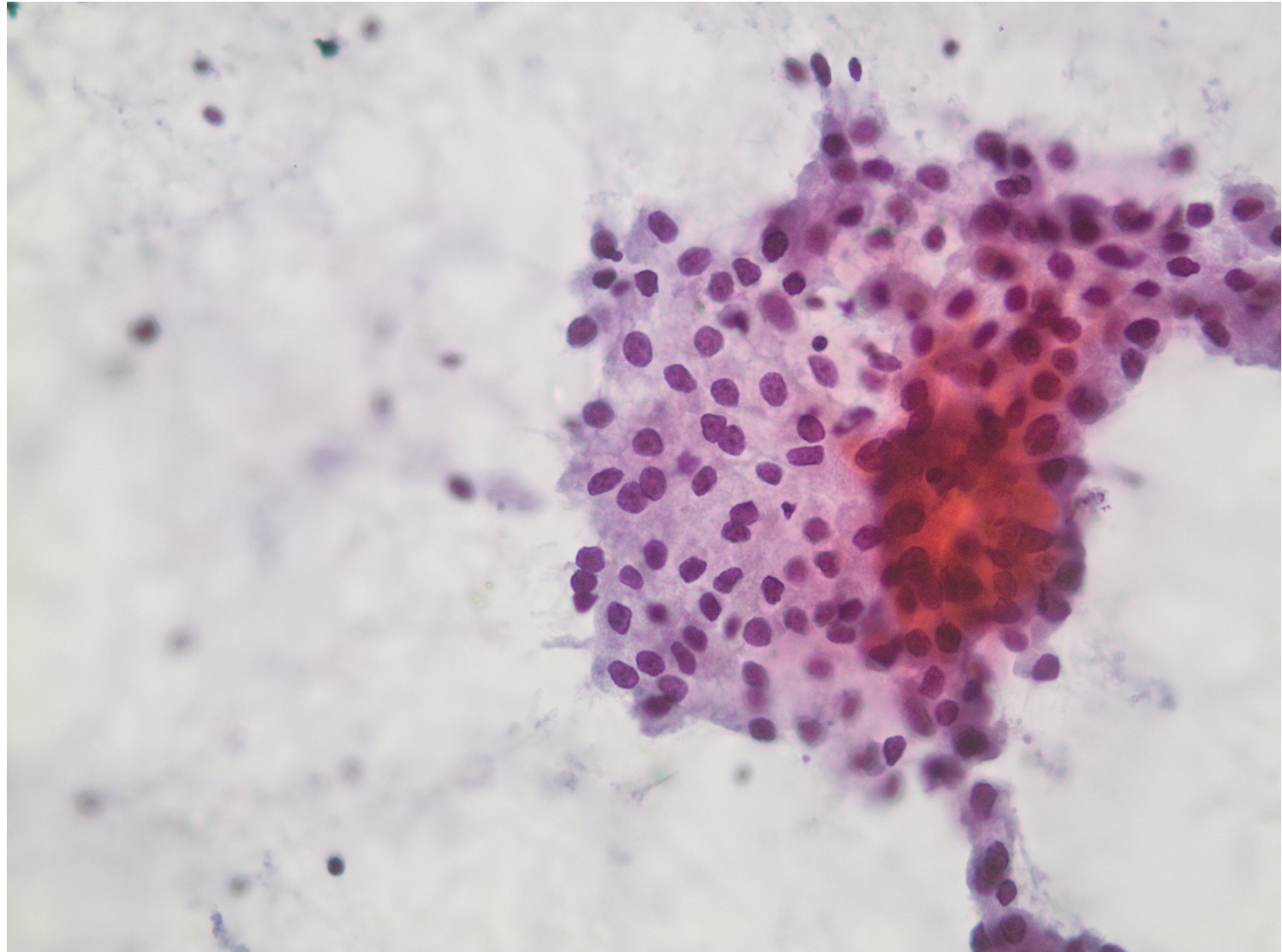
# Reported difficulties in Hashi's

- HC can be quite atypical: Mistaken for malignancy.
- HCs with focal nuclear enlargement, grooves, chromatin clearing → Susp papillary ca? The diagnostic threshold should be raised
- Predominance of HC → SFNHC type.
- Predominance of lymphocytes → Lymphoma?

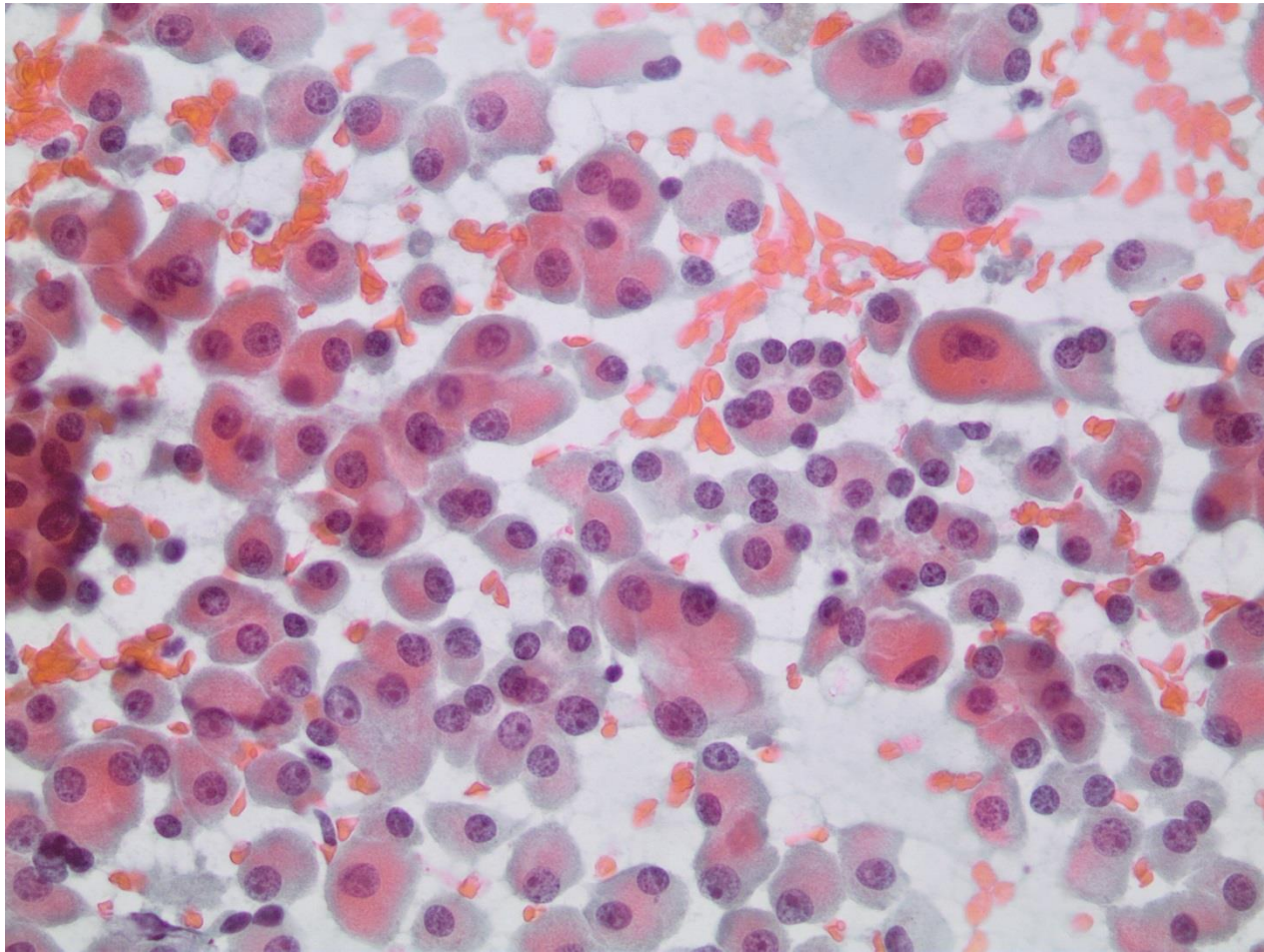
# Hashimoto: IE susp met lung ca



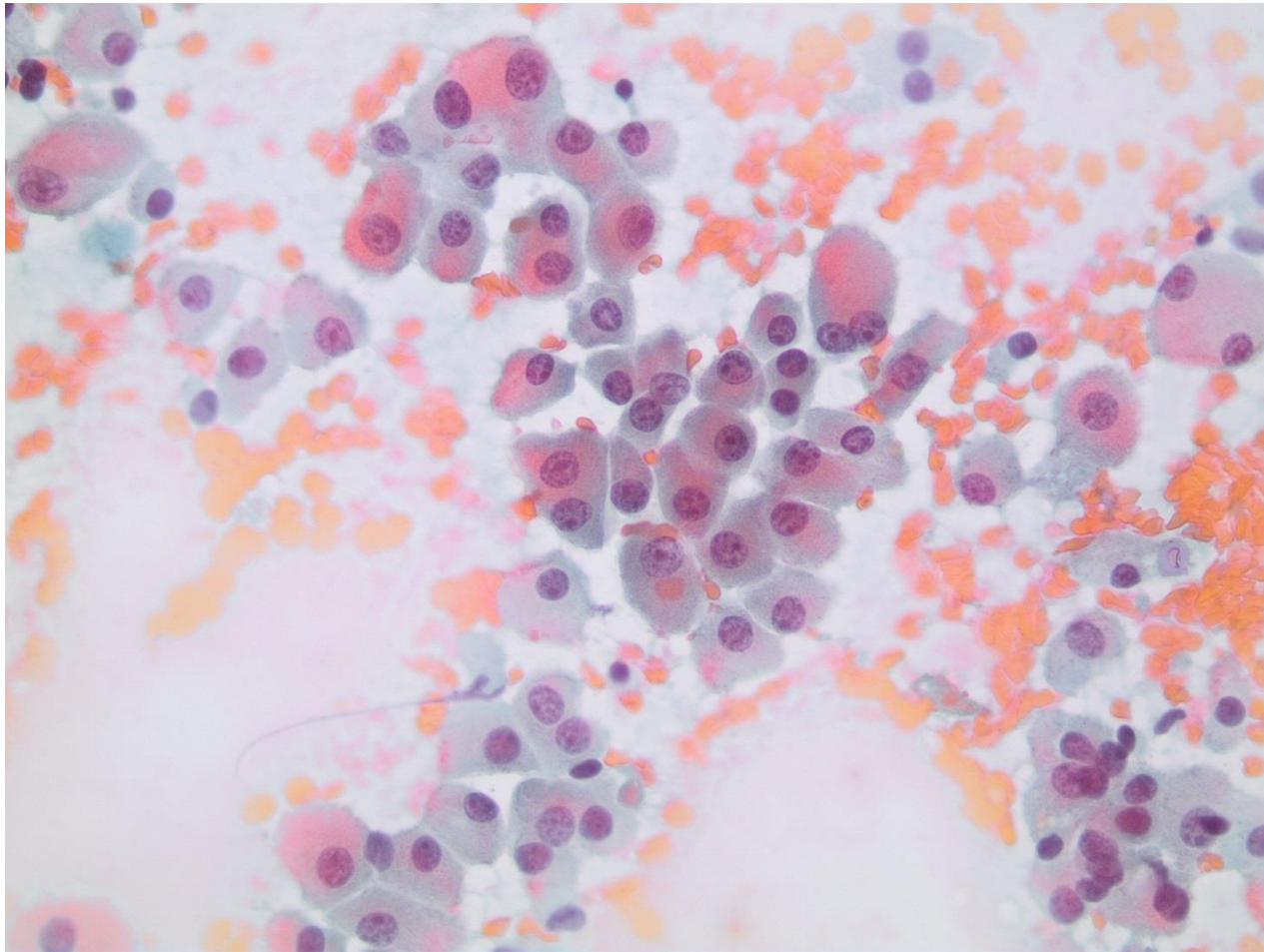
# Hashimoto: IE susp met lung ca



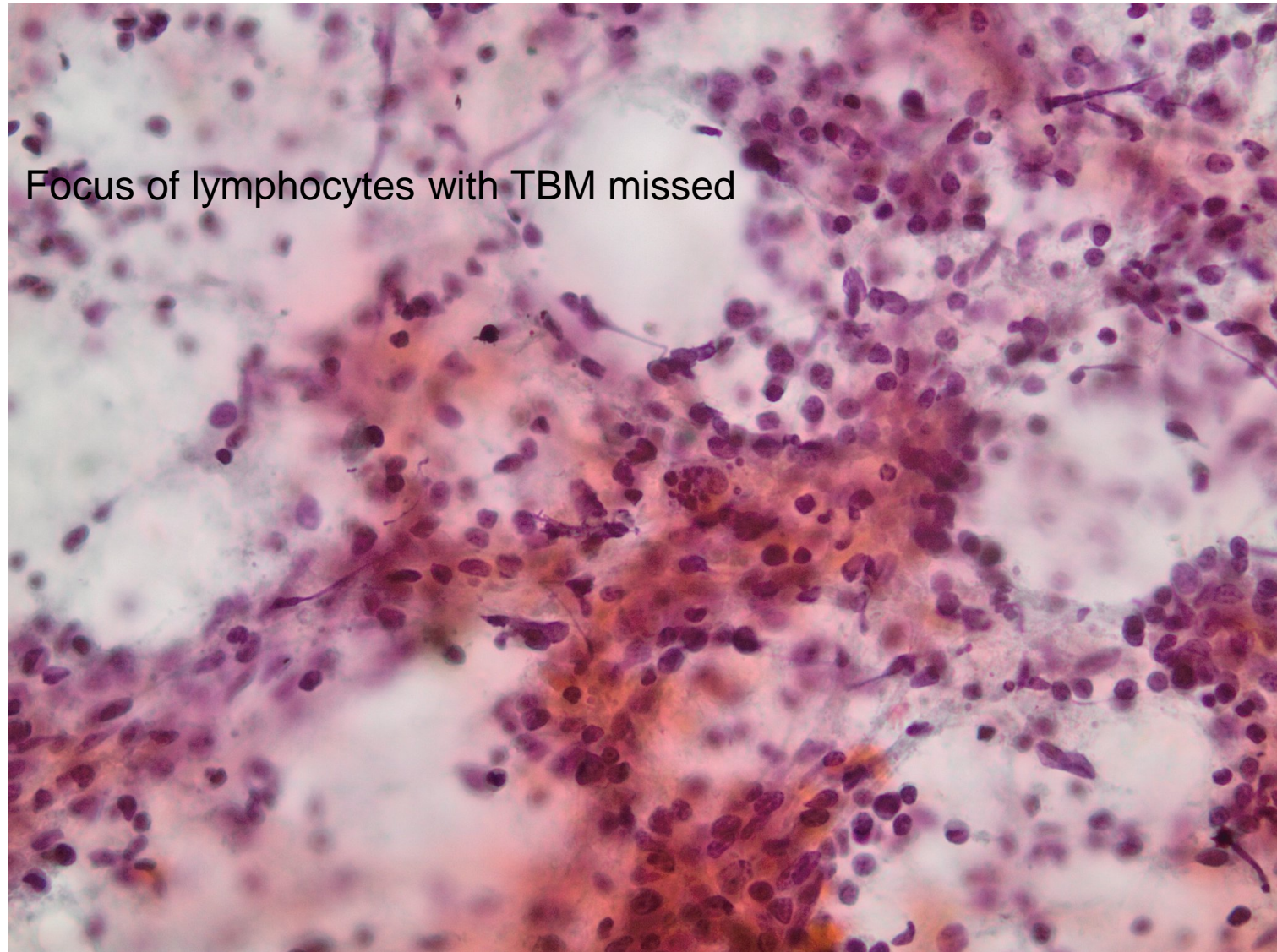
# Hashimoto: IE as SFNHC type



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# Hashimoto: IE as SFNHC type



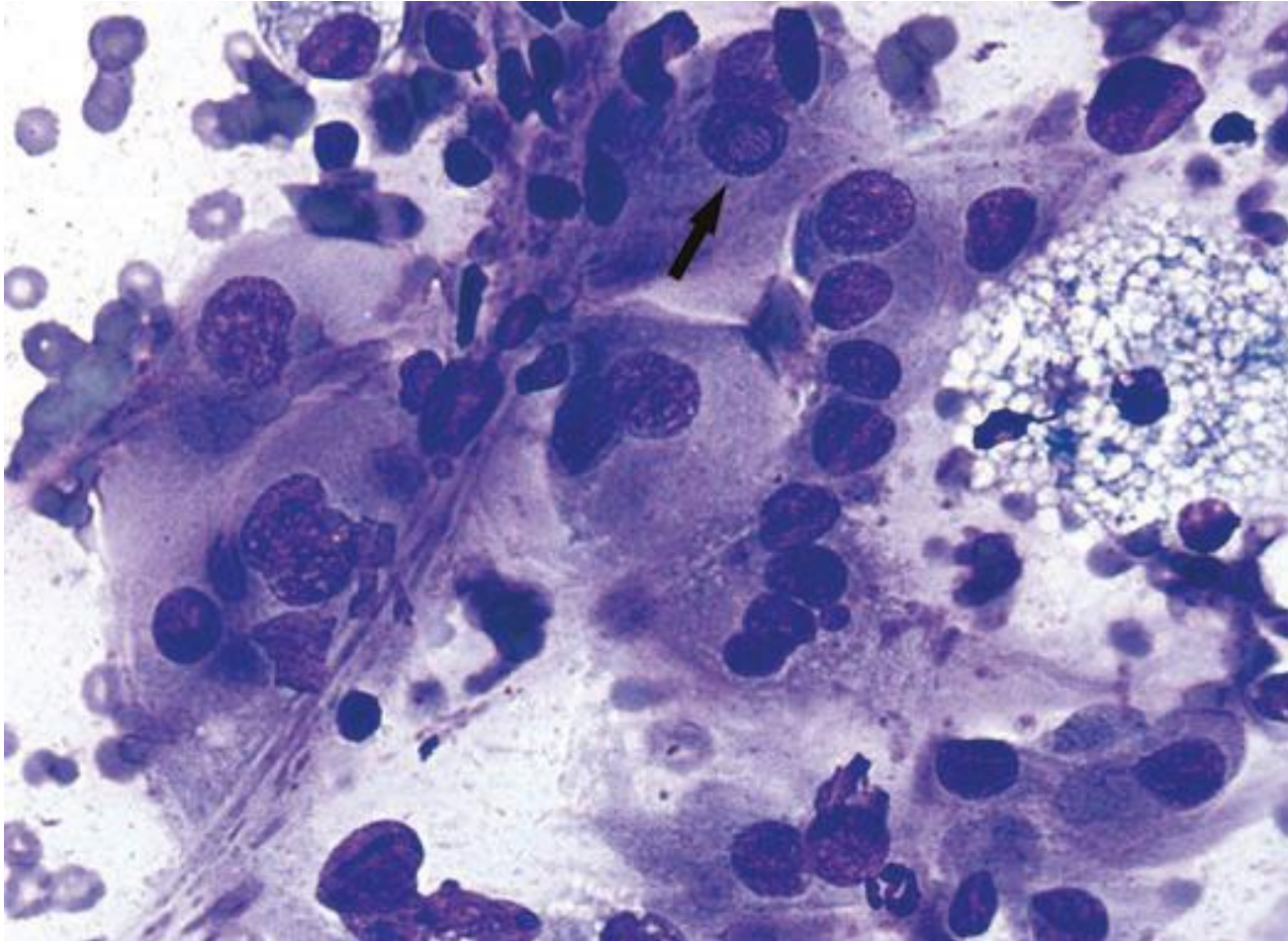
# Hashimotos: IE as susp LCL

- Marginal sample
- Predominance of lymphocytes
- Numerous large lymphocytes from germinal centers.
- Small lymphocytes also present
- Rare HCs not noted.

# Hashimoto: IE susp papillary ca

- Borderline sample
- Scant and air dried cells
- Few HCs with pseudo-inclusions and grooves.
- Maybe FLUS would be a better interpretation.
- Prior to Bethesda. No good criteria and/or recommendations

# AUS



Oncocytic follicular cells show nuclear enlargement and rare nuclear pseudoinclusions (arrow)

# Multinodular Goiter

IEs: AUBMC 2005-2017

Final pathology diagnosis	Case #	Original FNA IE	Surgical procedure	Blinded review diagnosis
MNG/BFN	1	SFN HCT	Hemi thyroidectomy	Inadequate: Macrophages, benign cyst content
	2	Susp papillary Ca	Hemi thyroidectomy	BFN, hemorrhagic, cystic
	3	Susp papillary Ca	Total thyroidectomy + LN dissection	Susp for Ca medullary? Papillary?
	4	Susp papillary Ca	Total thyroidectomy + LN dissection	FLUS
	5	Susp papillary Ca	Total thyroidectomy + LN dissection	FLUS, favor BFN

Unnecessary surgery

Susp malignancy

Non-surgical dx 4/5

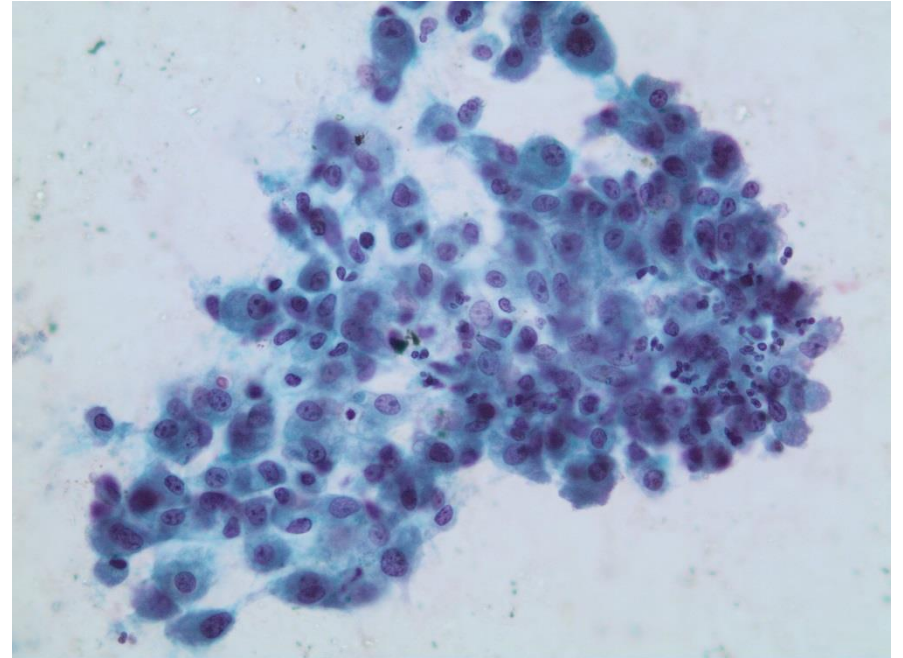
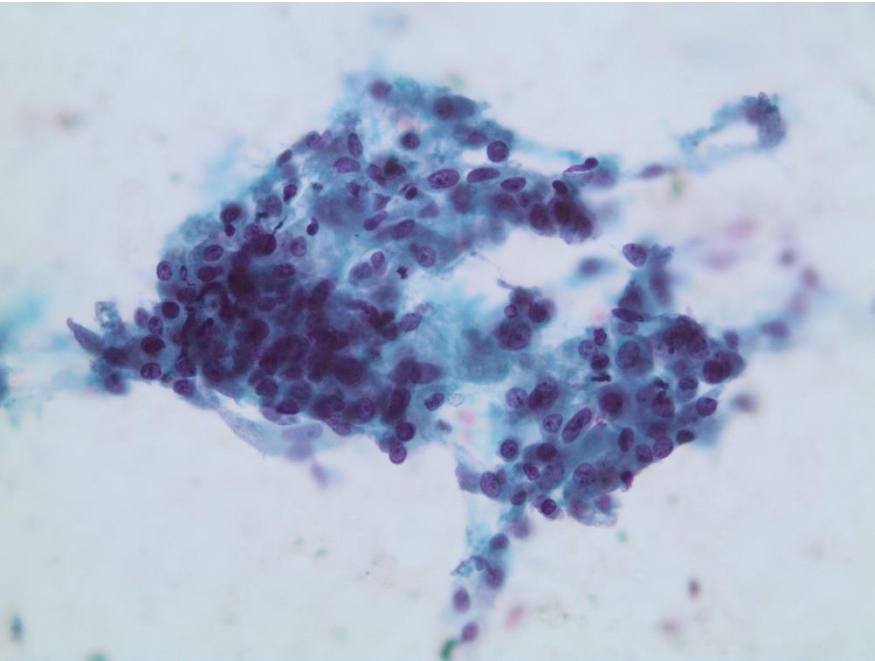
# Multinodular Goiter

IEs: AUBMC 2005-2017

Final pathology diagnosis	Case #	Original FNA IE	Comment/Problem	Surgical procedure	Blinded review diagnosis
MNG/BFN	1	SFN HCT	Macrophages misinterpreted as HCs	Hemithyroidectomy	Inadequate: Macrophages, benign cyst content
	2	Susp papillary Ca	WARD: Reactive cyst lining cells: Enlarged spindle nuclei with pseudoinclusions and rare grooves	Hemithyroidectomy	BFN, hemorrhagic, cystic
	3	Susp papillary Ca	WARD: Reactive cyst lining cells. Spindled nuclei, salt and pepper chromatin. Few MNGCs and psammoma bodies	Total thyroidectomy and central LN dissection	Susp for Ca, medullary? Papillary?
	4	Susp papillary Ca	Rare follicular cells with nuclear enlargement, pseudoinclusions and grooves Borderline cellularity.	Total thyroidectomy and central LN dissection	FLUS
	5	Susp papillary Ca	Rare follicular cells with nuclear enlargement, pseudoinclusions and grooves	Total thyroidectomy and central LN dissection	Adequate, FLUS, favor BFN

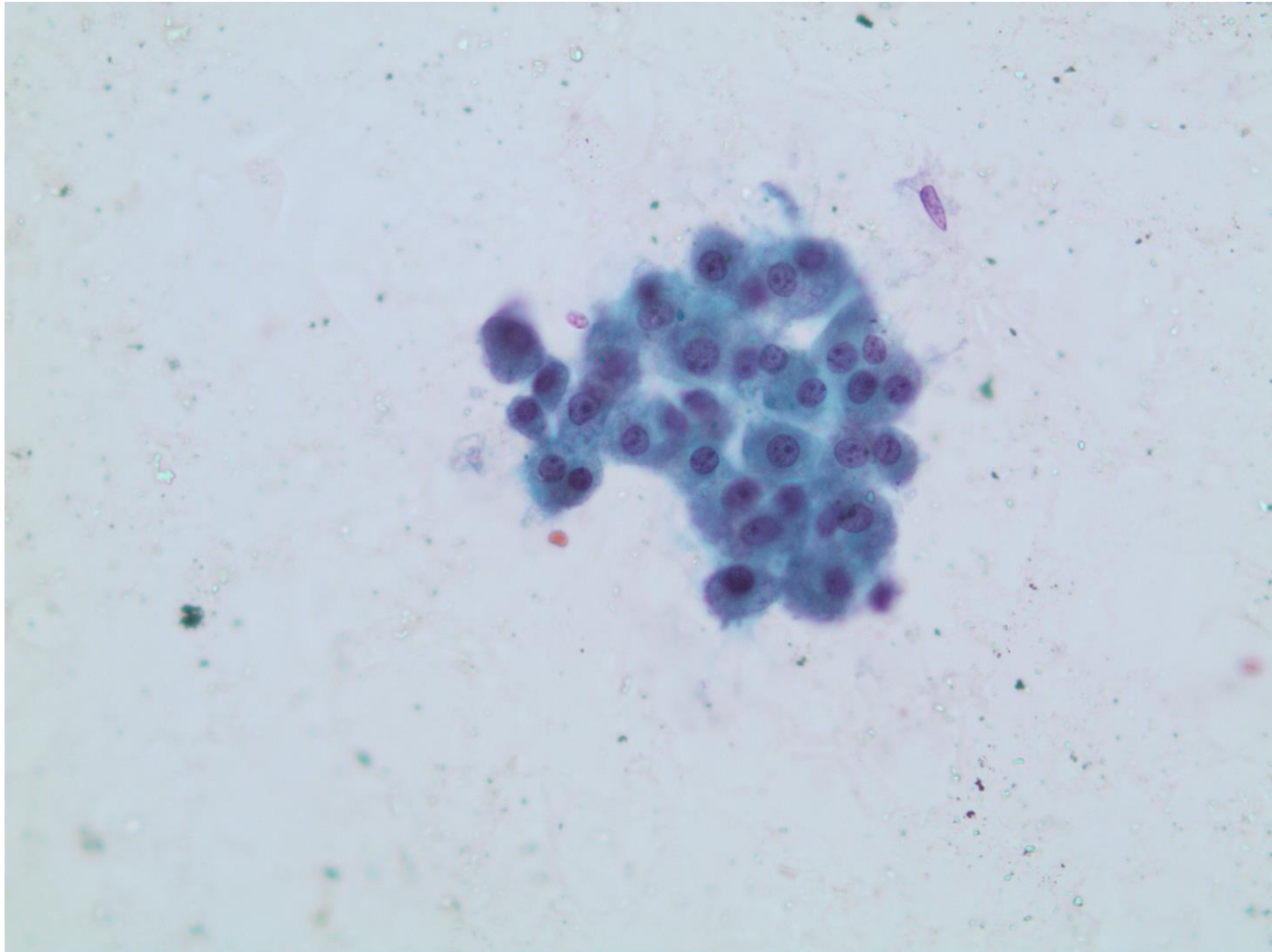
# MNG

## IE: SFNHC type

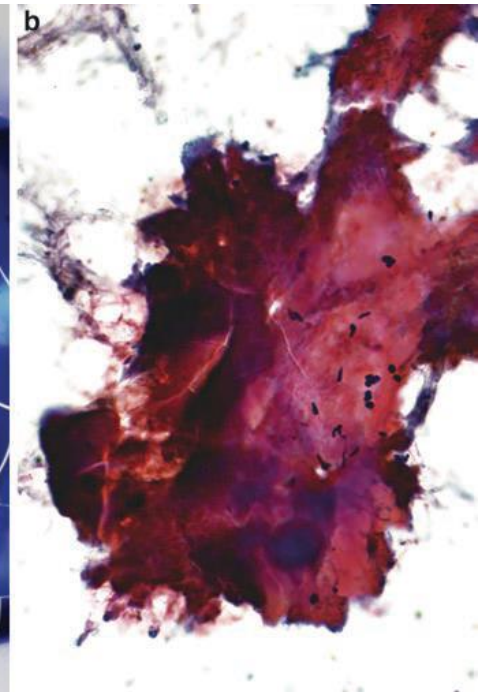
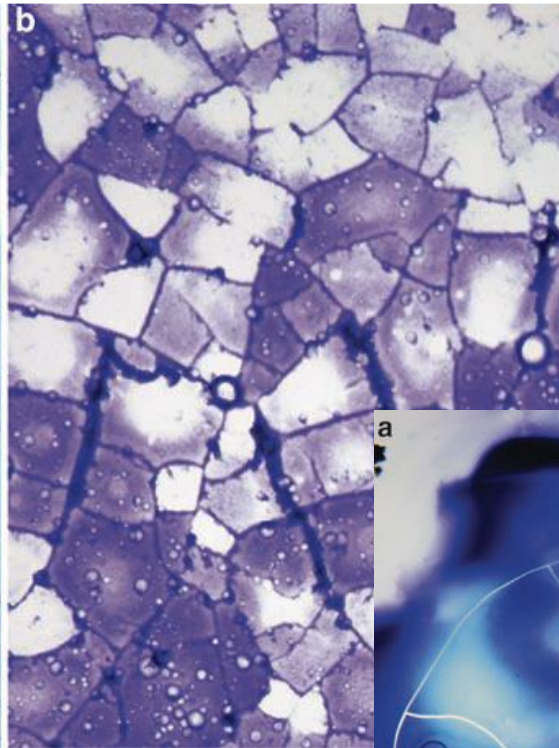
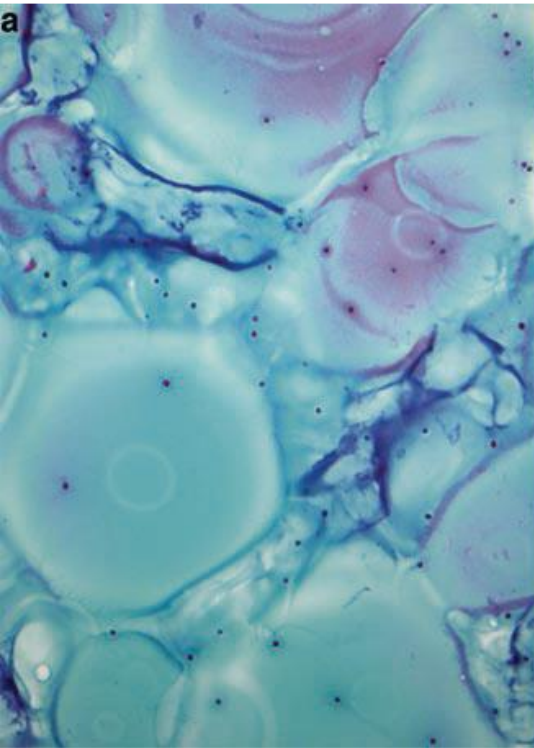


Macrophages misinterpreted as HCs

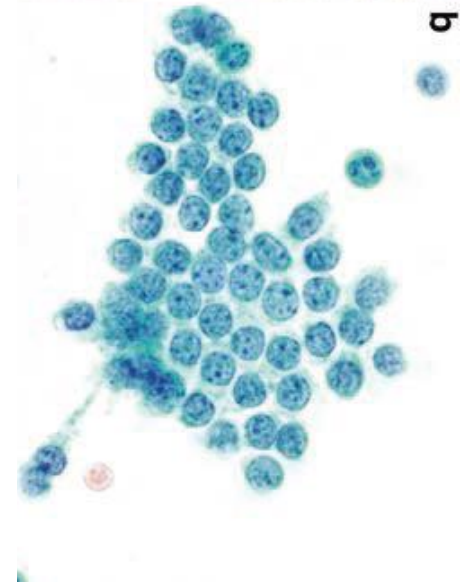
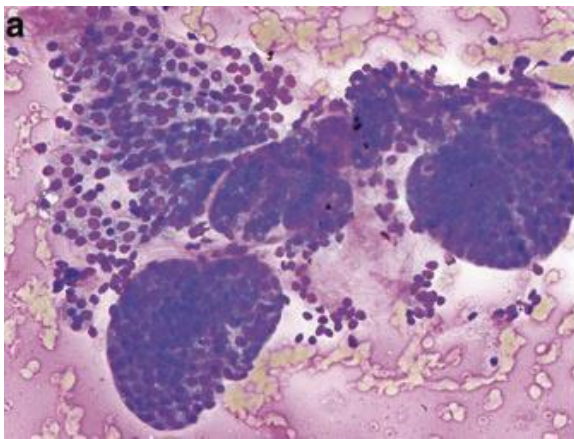
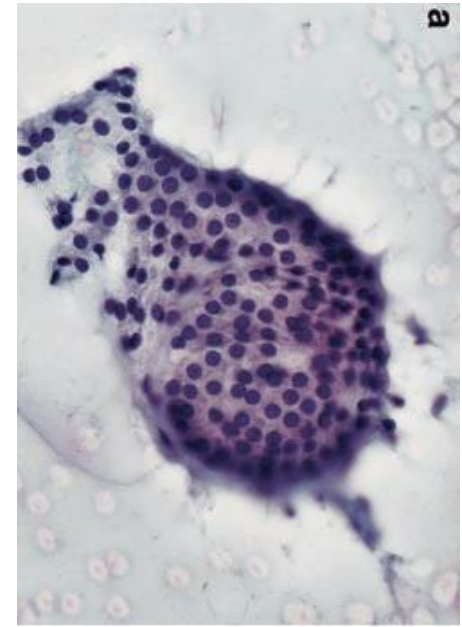
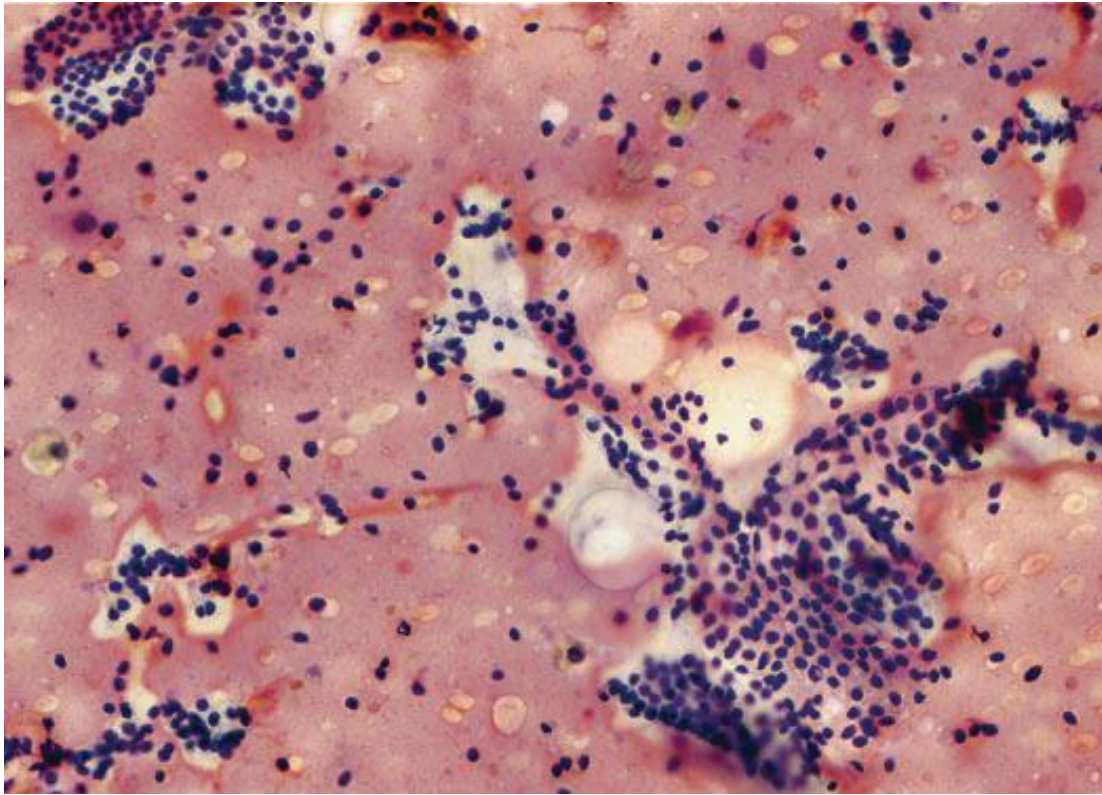
# Macrophages misinterpreted as HCs



# BFN/ Colloid



# BFN/Follicular cells



# Reported difficulties in MNG

- Focal and subtle nuclear features of papillary Ca
  - Follicular cells
  - Reactive cyst lining cells (WARDs)

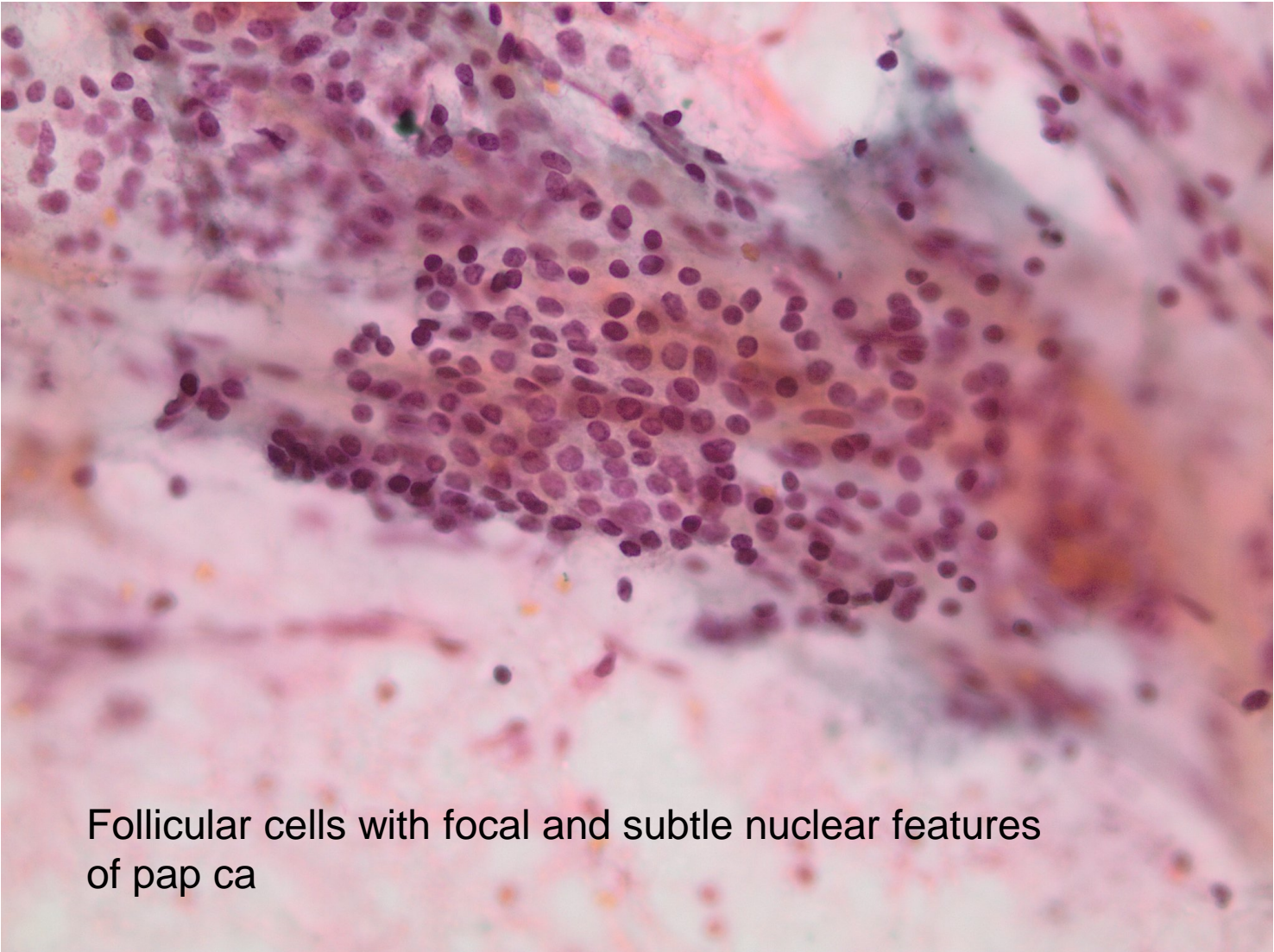
# FLUS

- There are follicular cells with focal features suggestive of papillary carcinoma, including nuclear grooves, enlarged nuclei with pale chromatin, and alterations in nuclear contour and shape in an otherwise predominantly benign-appearing sample (especially in patients with Hashimoto thyroiditis or those with abundant colloid and other benign-appearing follicular cells).

# FLUS

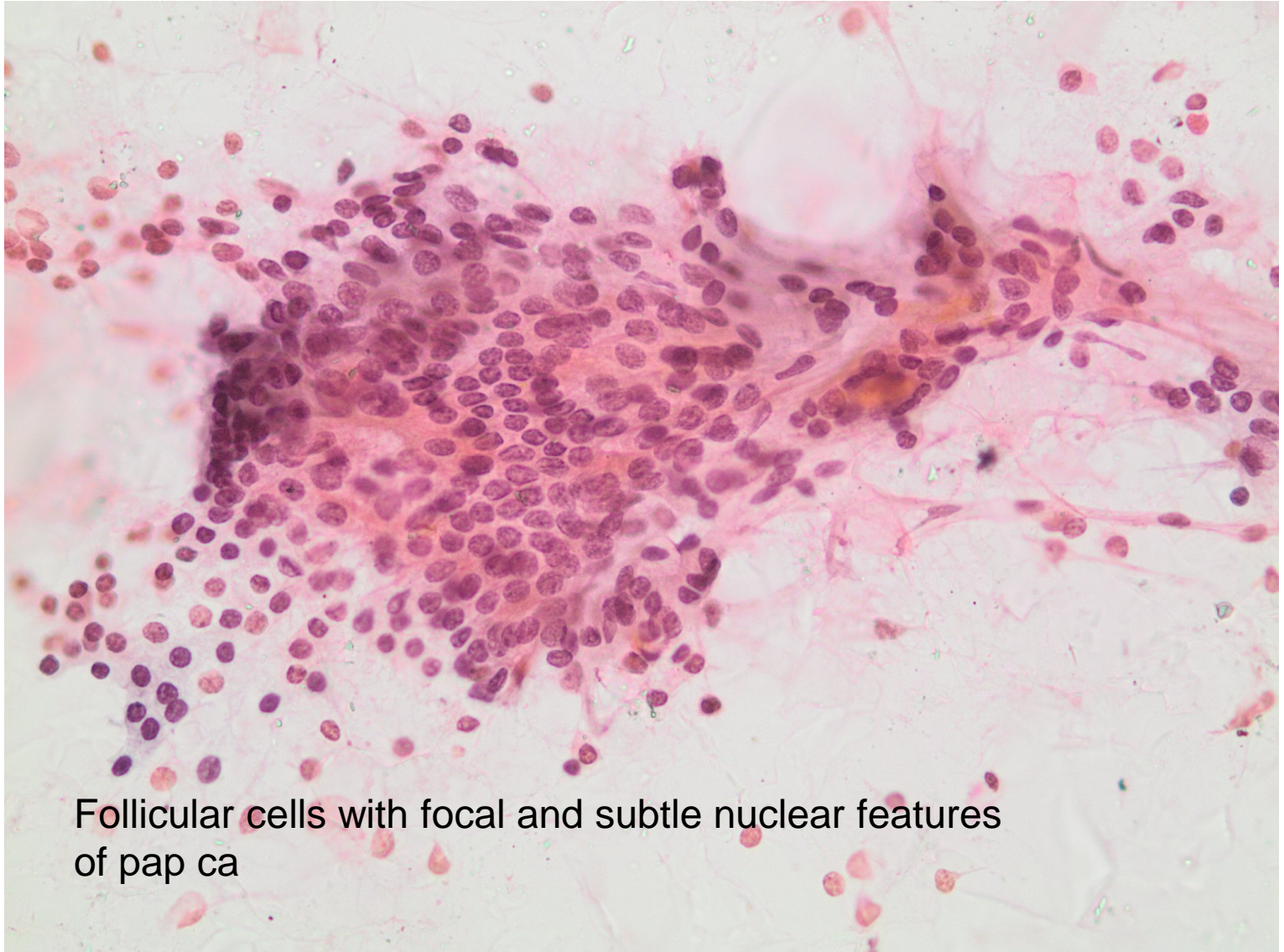
- Background benign
- Focal “soft nuclear features”
  - No good intranuclear inclusions.
  - No widespread grooves
  - No psammoma bodies.

# MNG: IE Susp pap ca



Follicular cells with focal and subtle nuclear features of pap ca

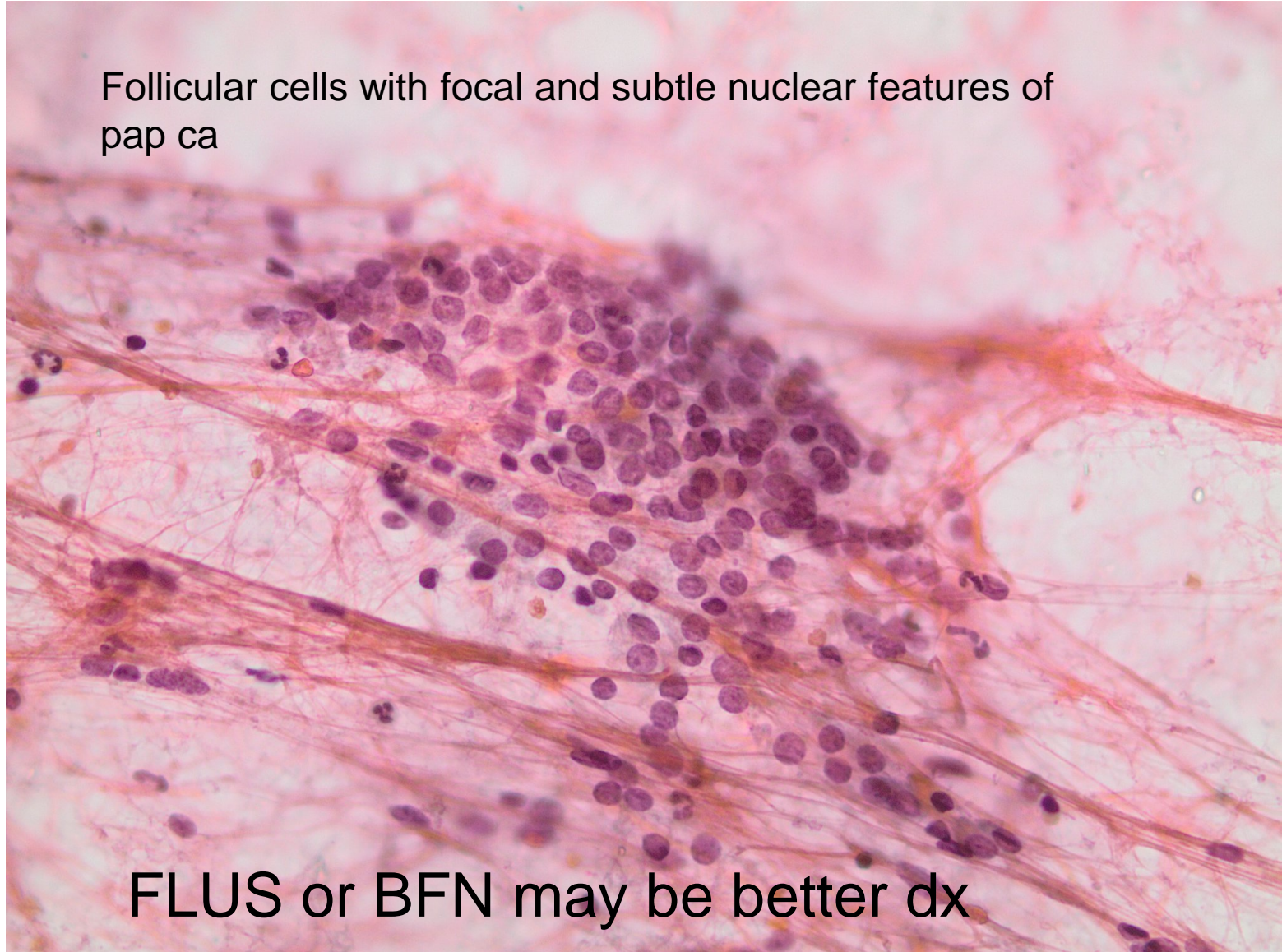
# MNG: IE Susp pap ca



Follicular cells with focal and subtle nuclear features of pap ca

# MNG: IE Susp pap ca

Follicular cells with focal and subtle nuclear features of pap ca



FLUS or BFN may be better dx

**WARD**

**Cyst lining cells**

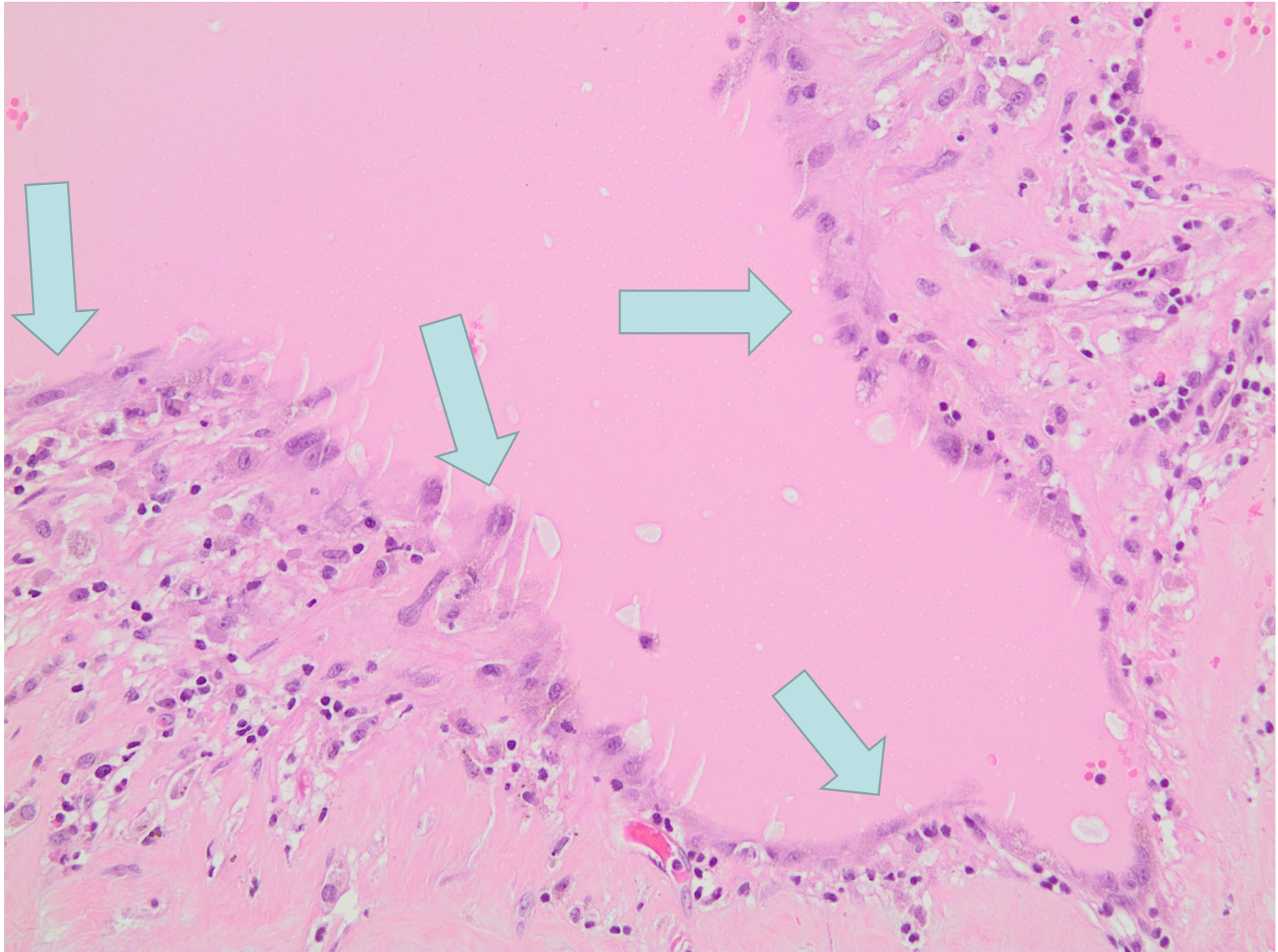
**Wispy cells**

# WARDs:

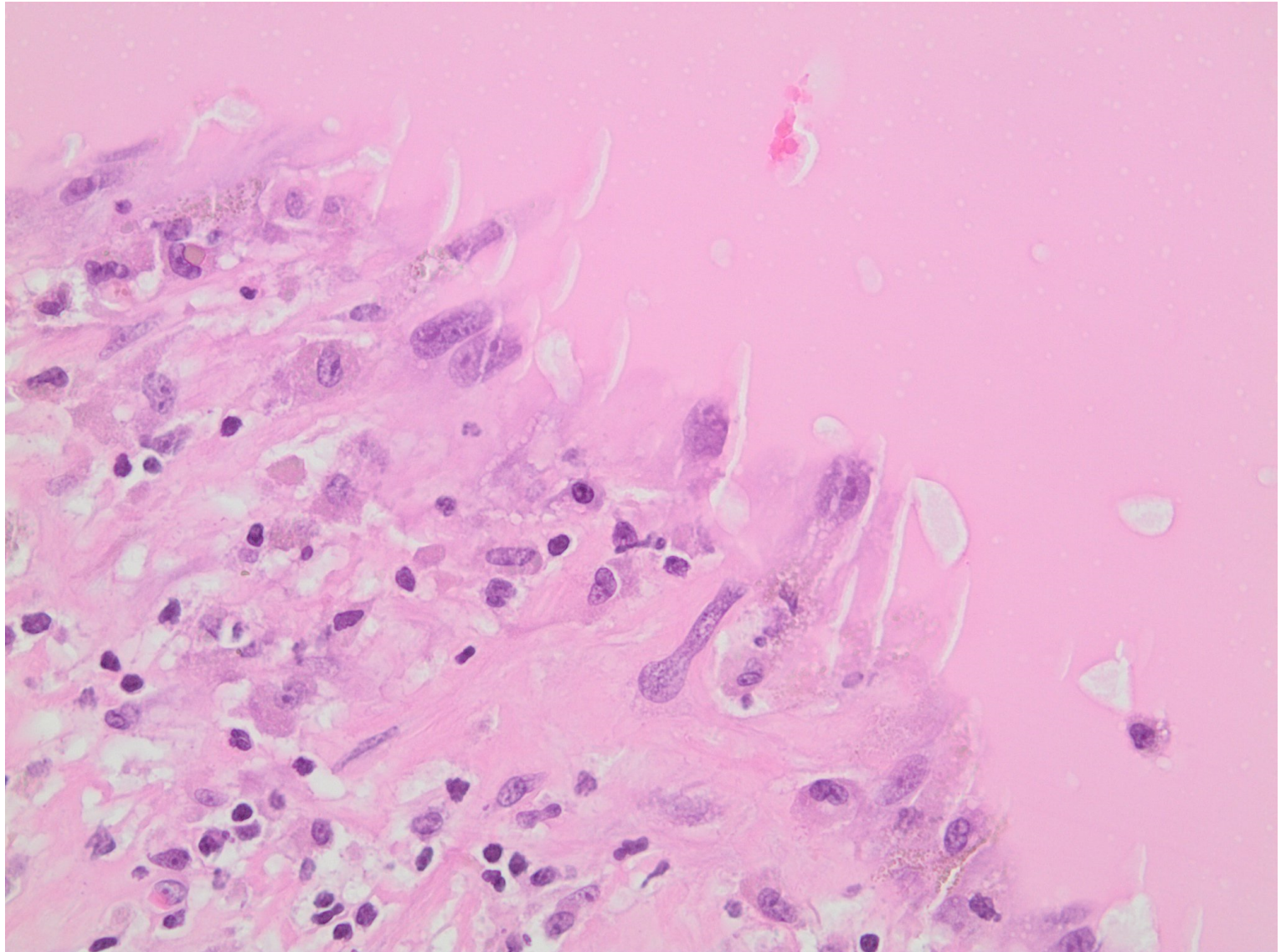
Worrisome atypical cells of regenerative –  
degenerative processes (De May, 2012)

- Reactive cyst lining cells.
- Wispy/whispy cells
- Cause False + diagnosis
- Most often papillary
- Rarely medullary, anaplastic, HC neoplasm

# WARDs: Reactive cyst lining cells



# MNG: Reactive cyst lining cells



[Cancer](#). 2005 Apr 25;105(2):71-9.

**"Atypical" cells in fine-needle aspiration biopsy specimens of benign thyroid cysts.**

[Faquin WC](#)<sup>1</sup>, [Cibas ES](#), [Renshaw AA](#).

# WARDS

- Background:
  - Hypocellular
  - Watery colloid
  - Macrophages
  - Benign macro-follicle fragments

# WARDS

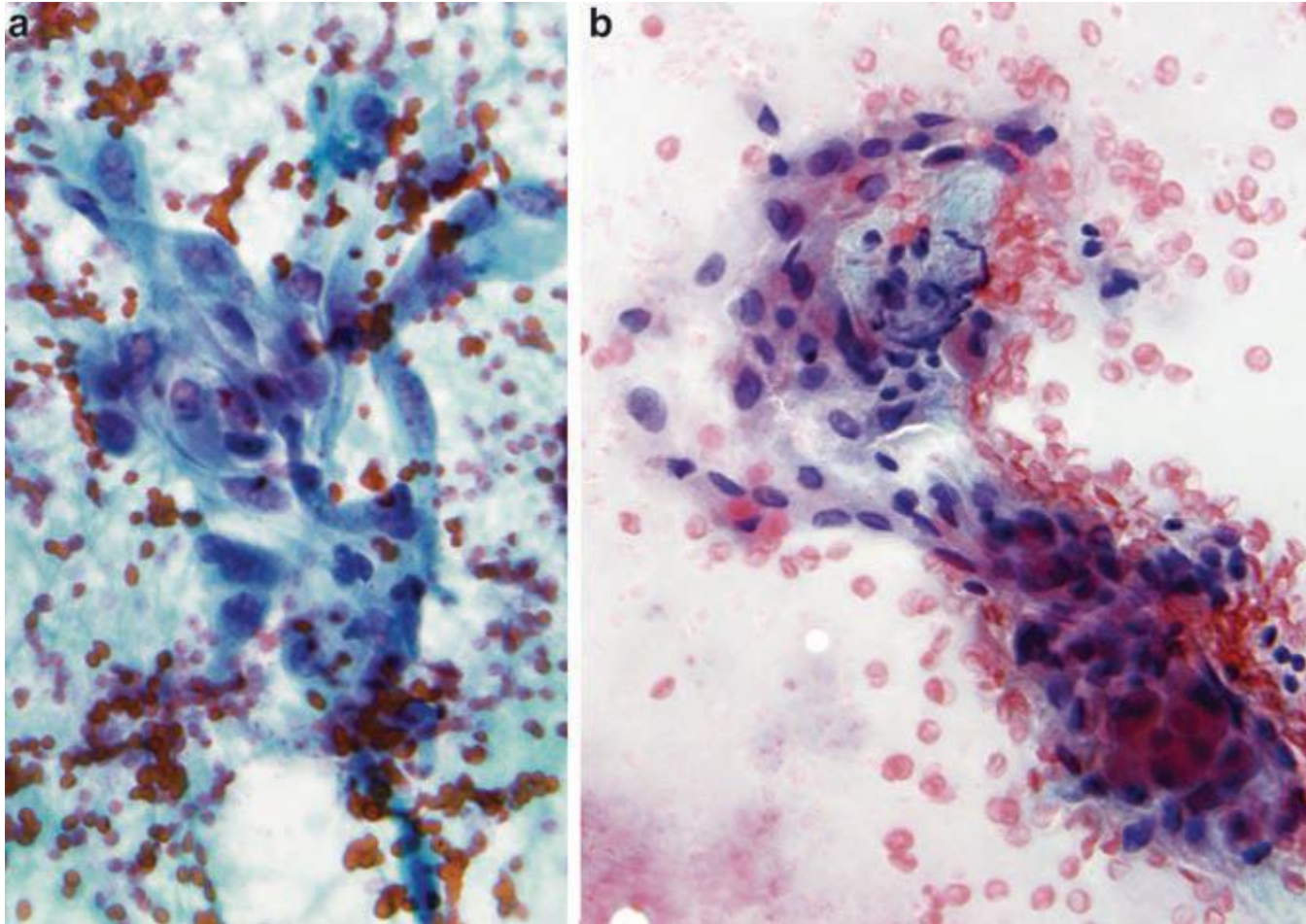
- Resemble reparative epithelial cells (tissue culture)
- Usually elongated/spindled/pulled out look.
- Can be epithelioid resembling HCs
- ↓ N/C ratio
- Small cohesive 2D flat sheets
- Distinct cell borders and windows
- CKAE1/3 and thyroglobulin: +

# WARDS

- Nuclei: slightly enlarged, grooves, pale chromatin, small nucleolus. No crowding or overlapping
- **REGULAR** nuclear borders

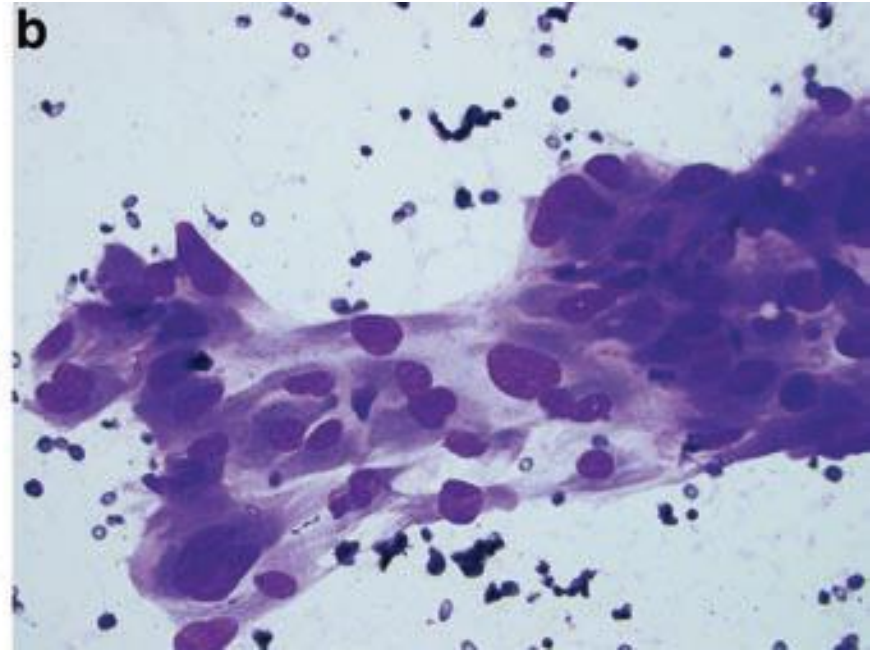
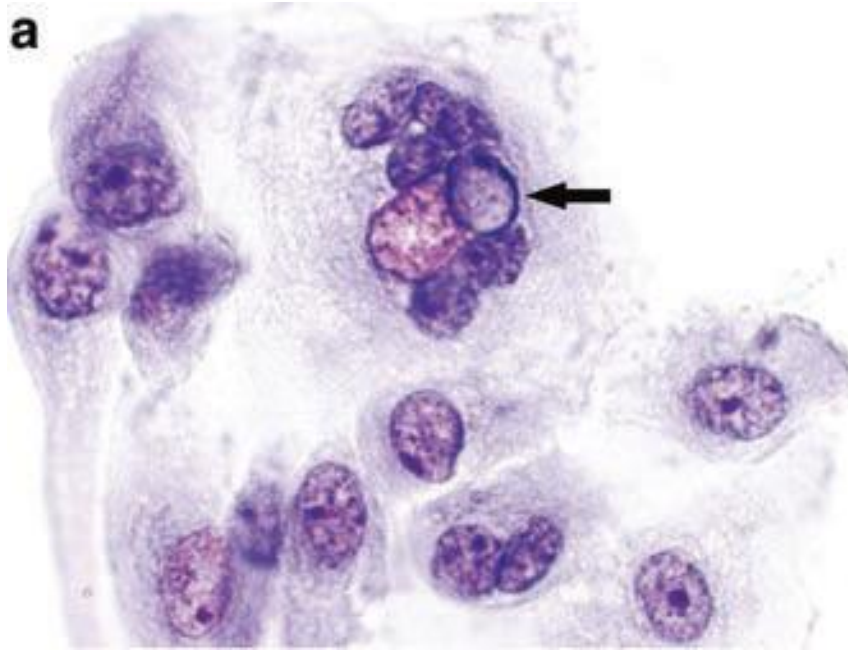
# BFN/Cyst lining cells

Bethesda



Enlarged nuclei, finely granular chromatin, squamoid/spindle shaped  
(tissue culture cell)

# AUS/ Cyst lining cells

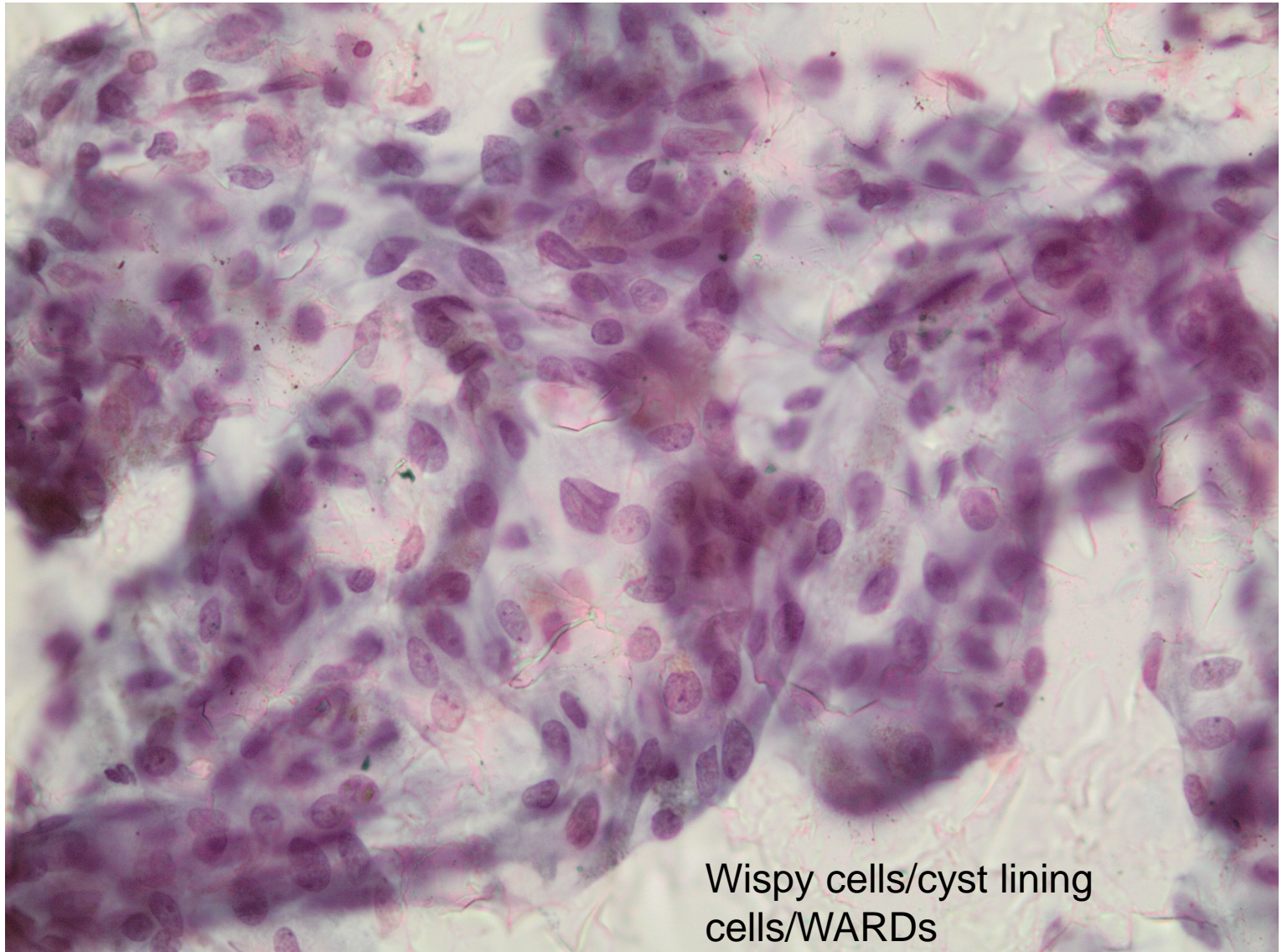


# WARDs: AUS/FLUS (Bethesda)

- There are cyst-lining cells which may appear atypical due to the presence of nuclear grooves, prominent nucleoli, elongated nuclei and cytoplasm, and/or intranuclear cytoplasmic inclusions in an otherwise predominantly benign-appearing sample.

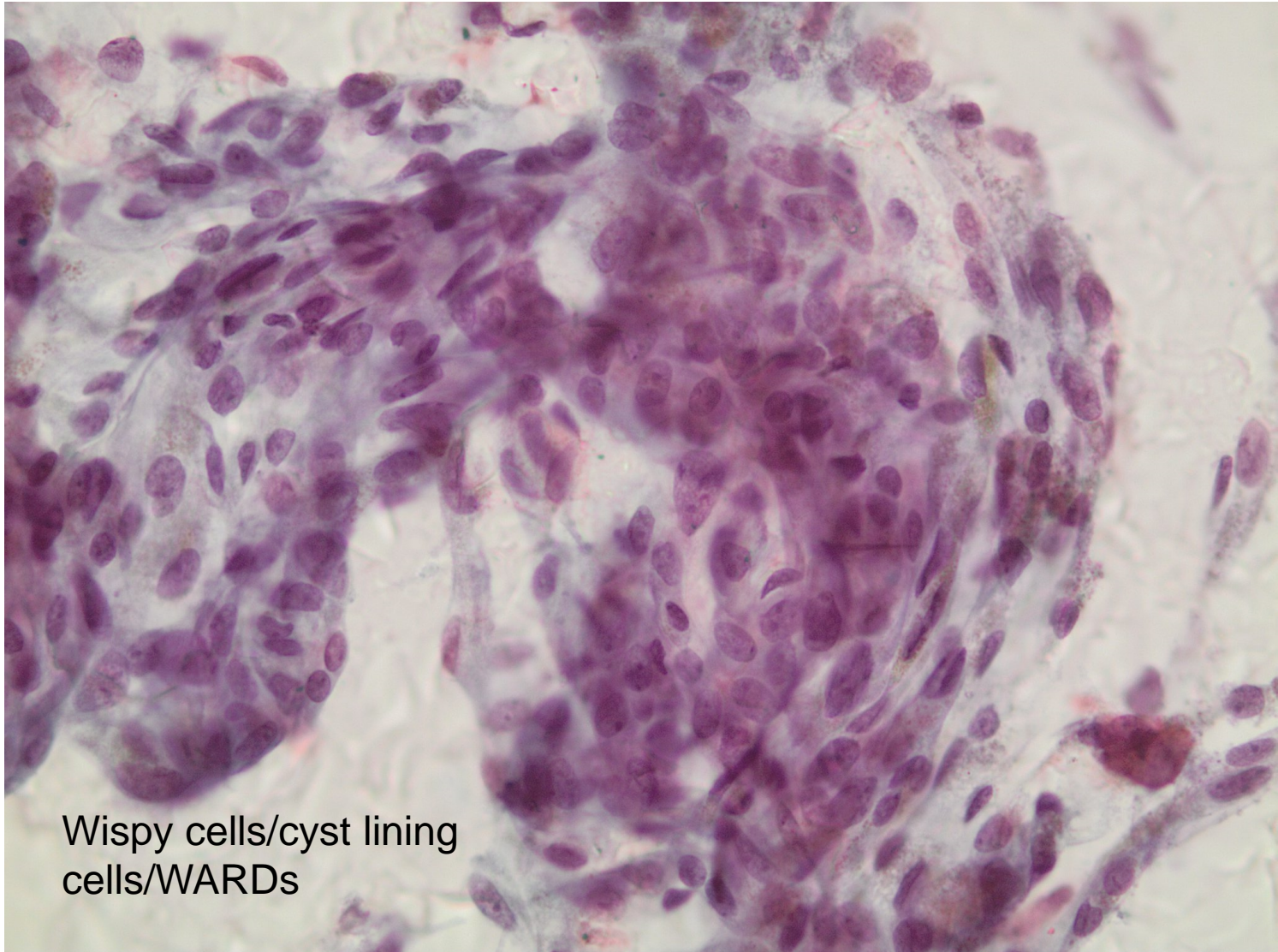
- Our WARDs misdiagnosed as suspicious for papillary or medullary ca

# MNG: IE: Susp pap ca



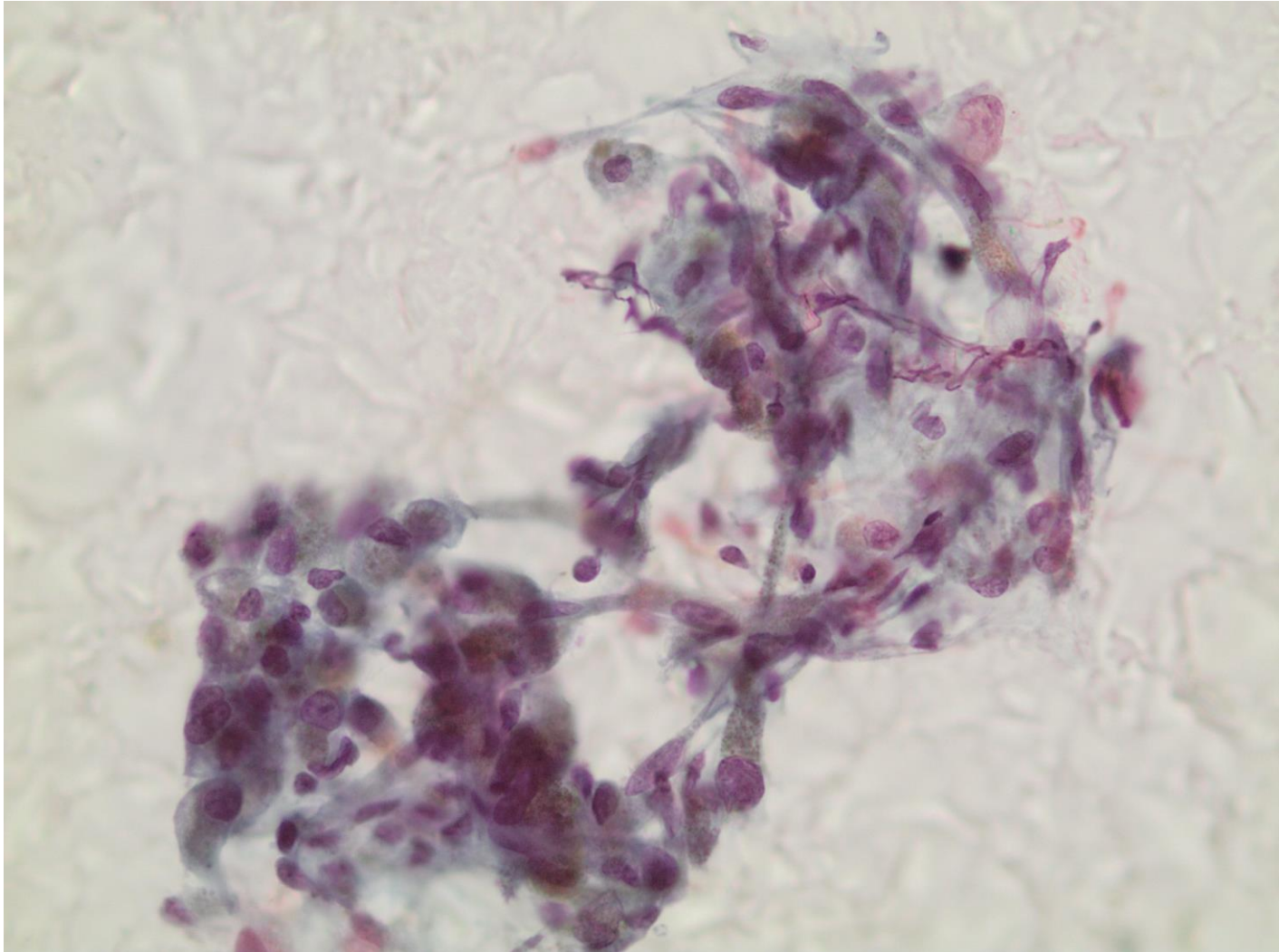
Wispy cells/cyst lining  
cells/WARDS

# MNG: IE: Susp pap ca

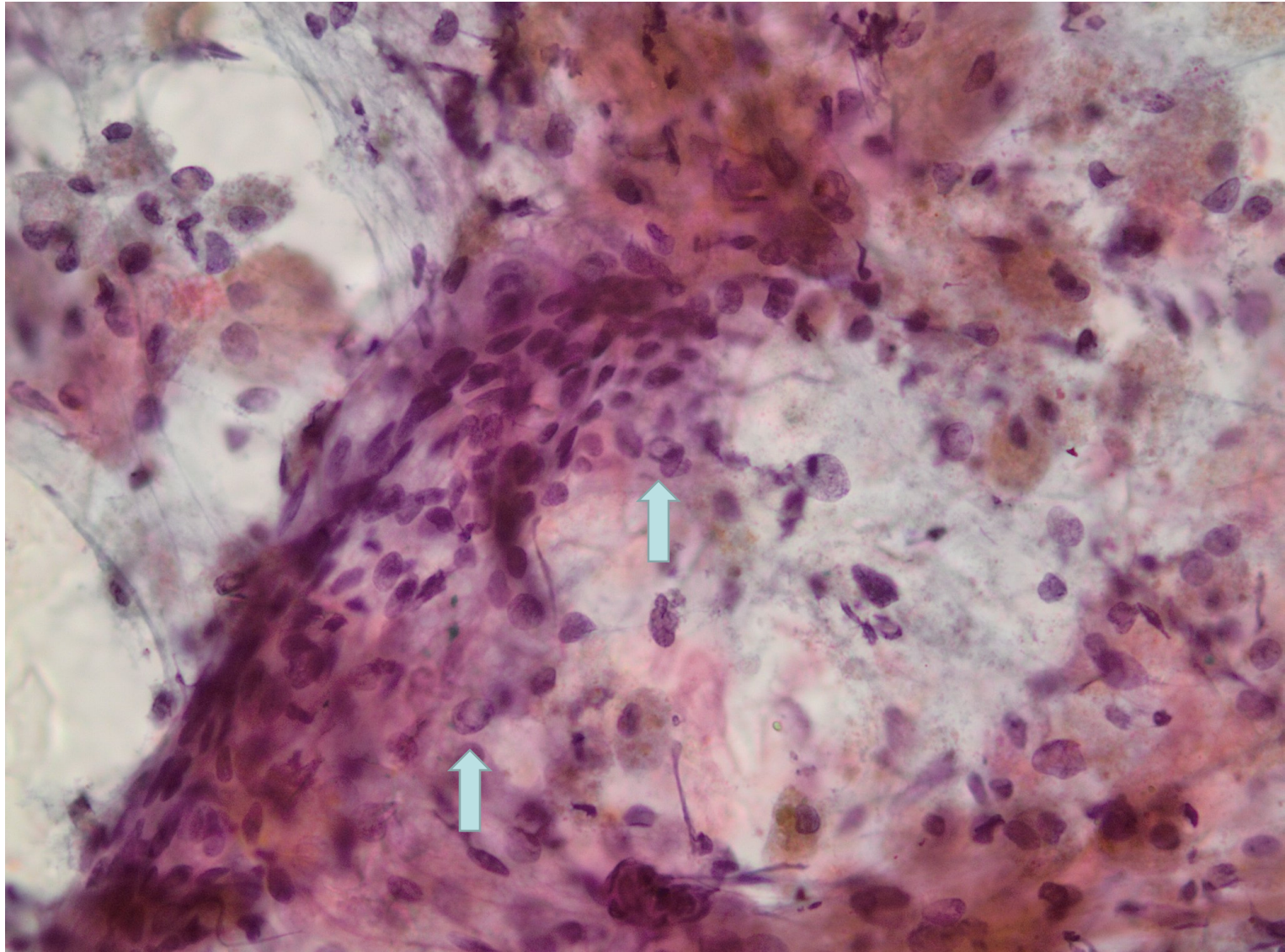


Wispy cells/cyst lining  
cells/WARDS

# WARDs + Macrophages

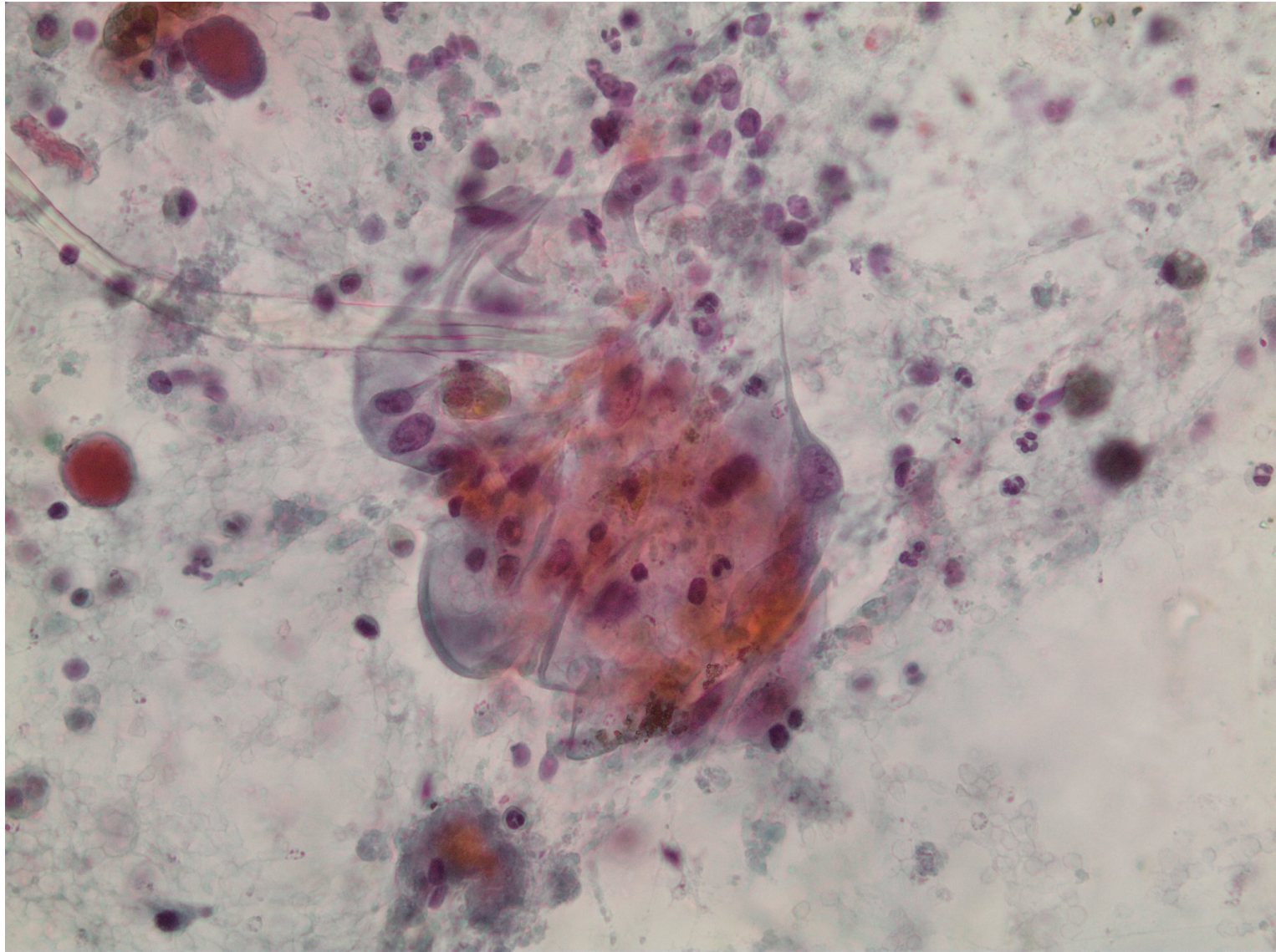


# WARDs focal papillary nuclei



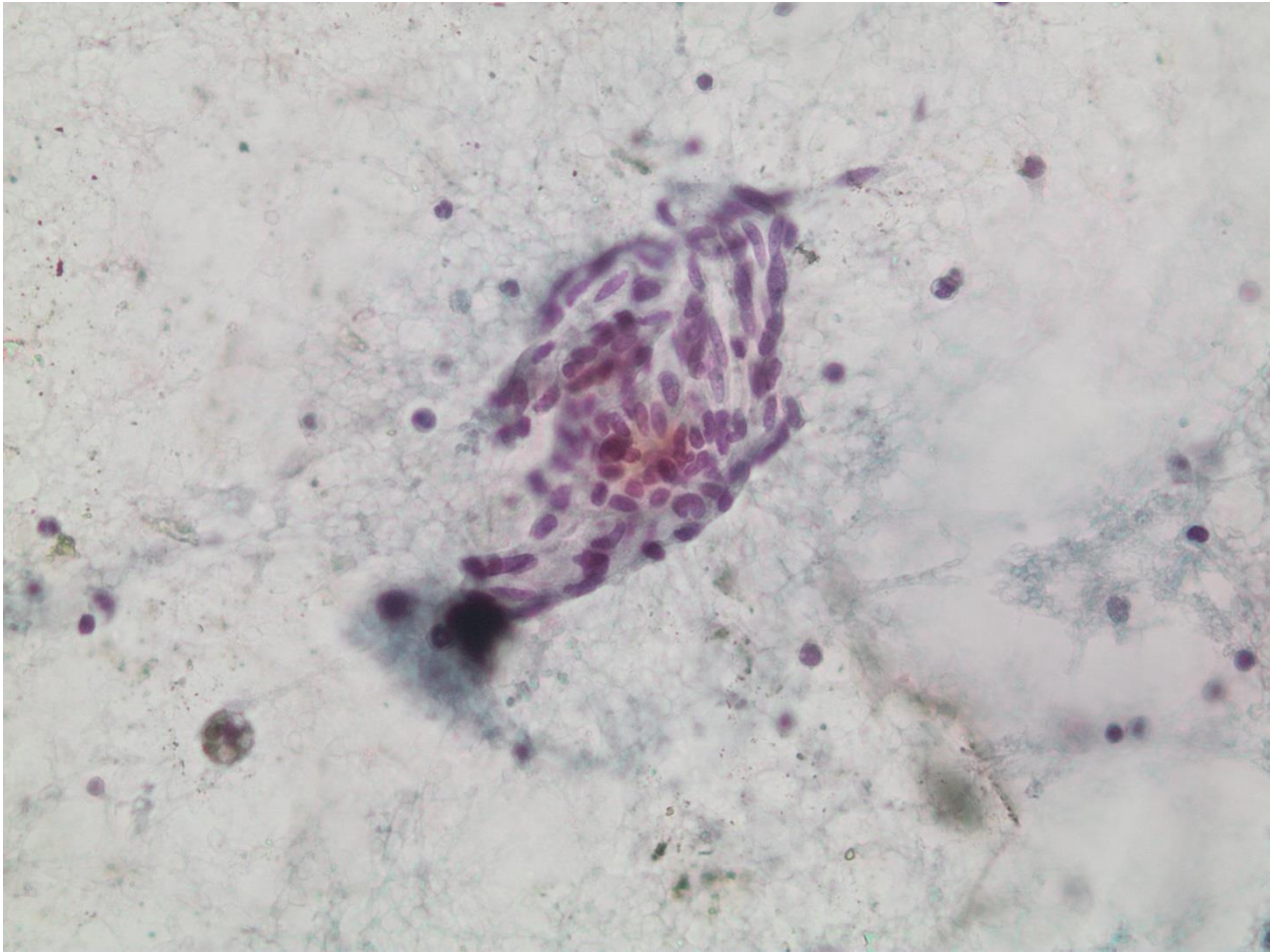
# WARDs:

Tissue culture appearance

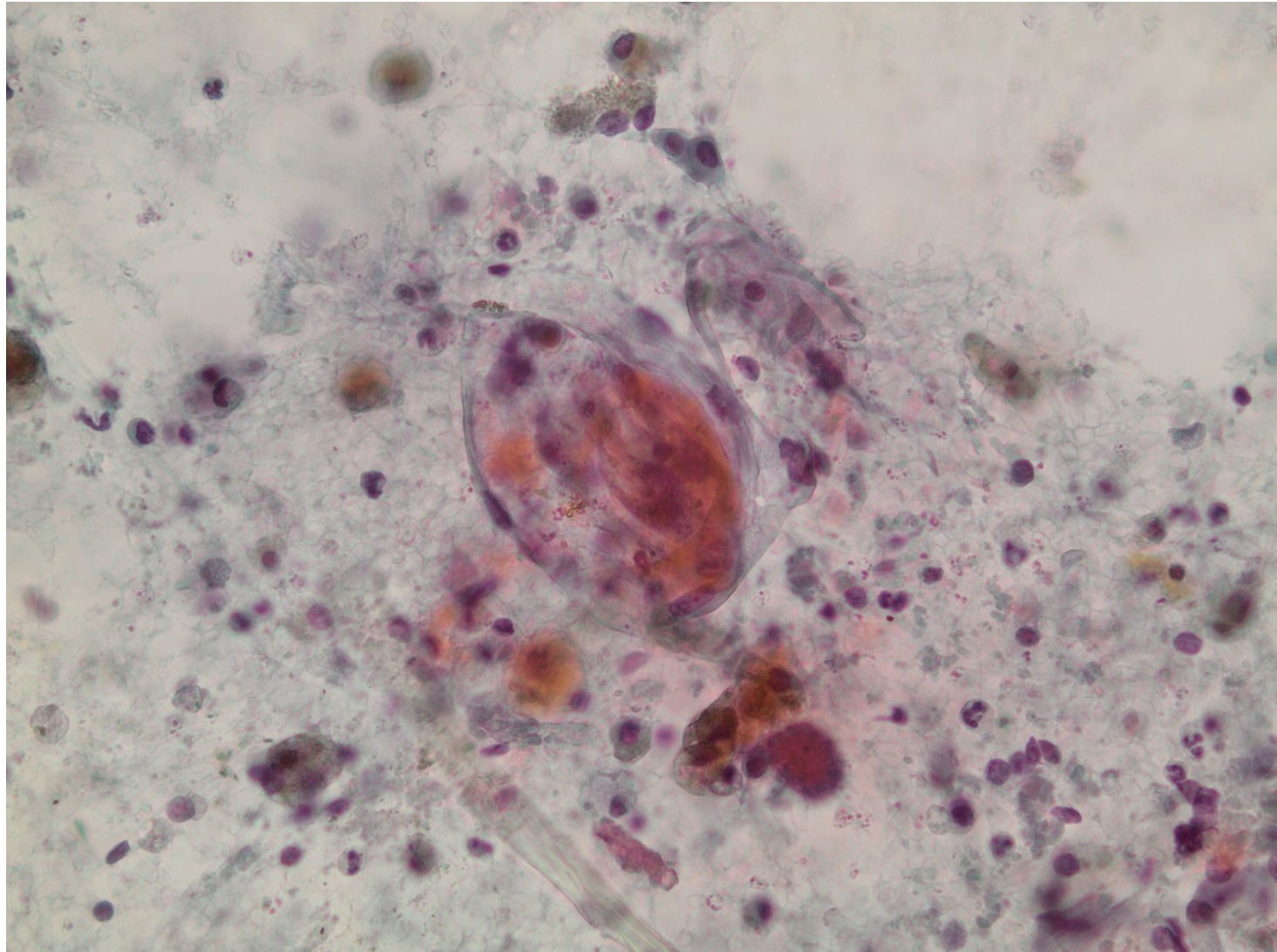


# WARDs:

Spindle cells



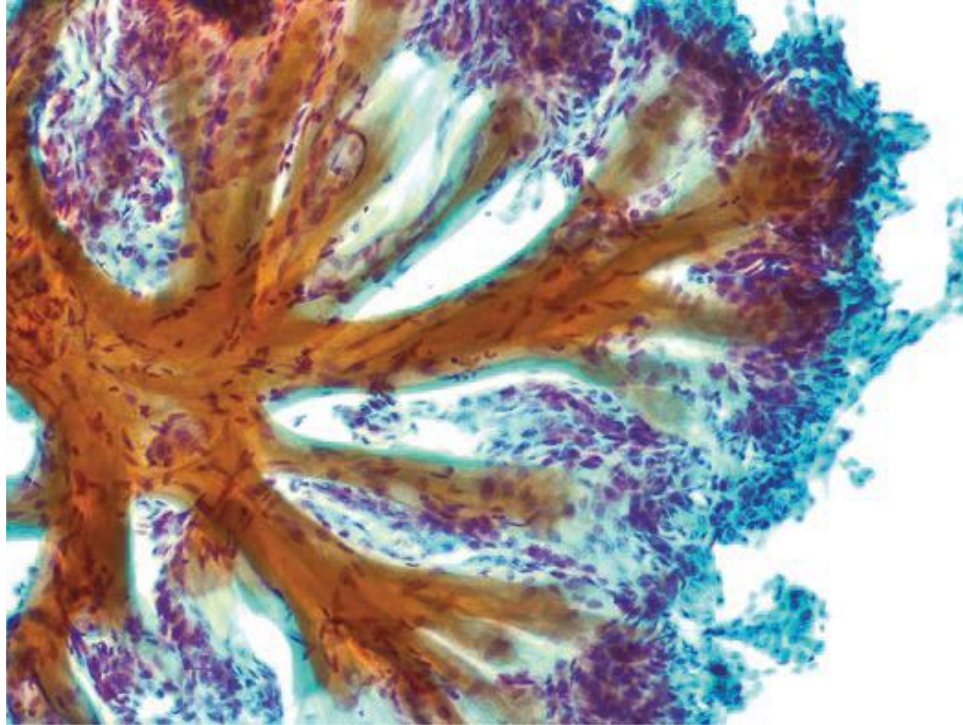
# WARDs/cyst lining cells/Wispy cells



# Papillary Thyroid Carcinoma Criteria:

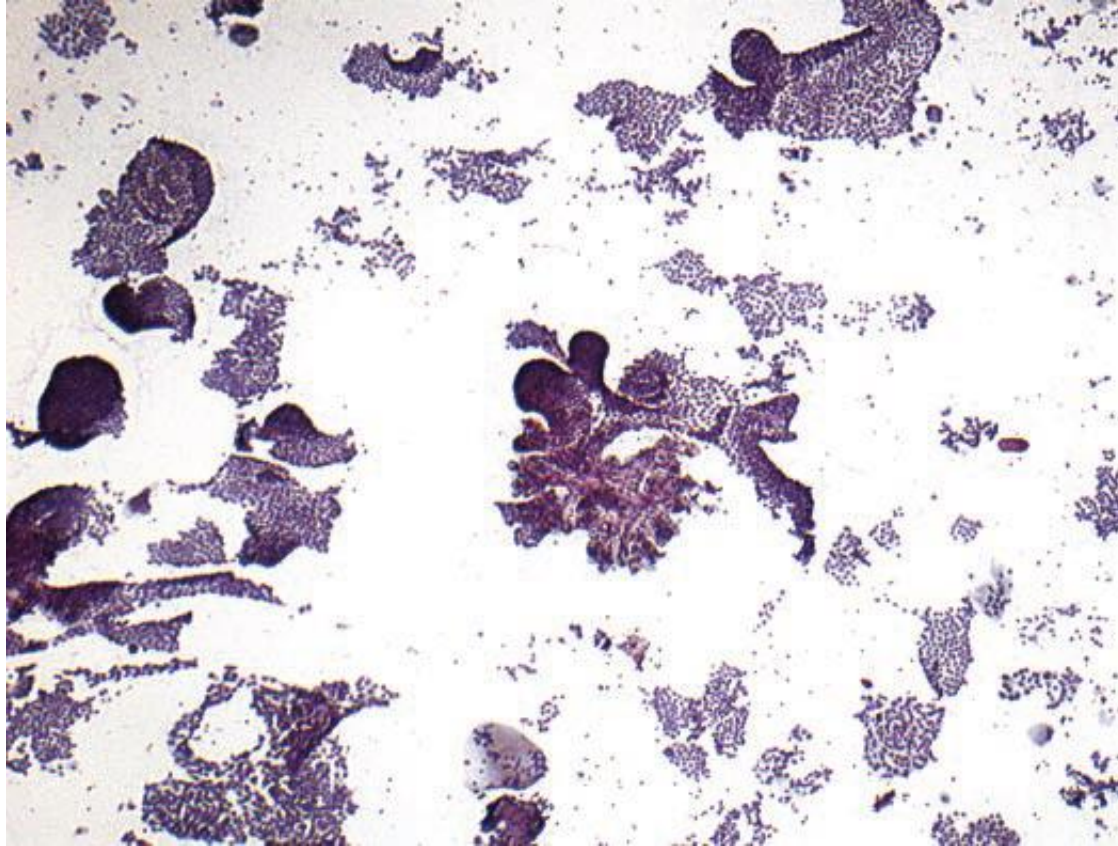
- Architecture: Papillae and/or syncytial-like monolayers.
- Nuclear features:
  - Enlarged
  - Oval or irregularly shaped, sometimes molded nuclei
  - Longitudinal nuclear grooves
  - Intranuclear cytoplasmic pseudoinclusions (INCI)
  - Pale nuclei with powdery chromatin (“Orphan Annie” nuclei)
  - Marginally placed micronucleoli, solitary or multiple
- Psammoma bodies are sometimes present.
- Multinucleated giant cells are common.

# Papillary Thyroid Carcinoma

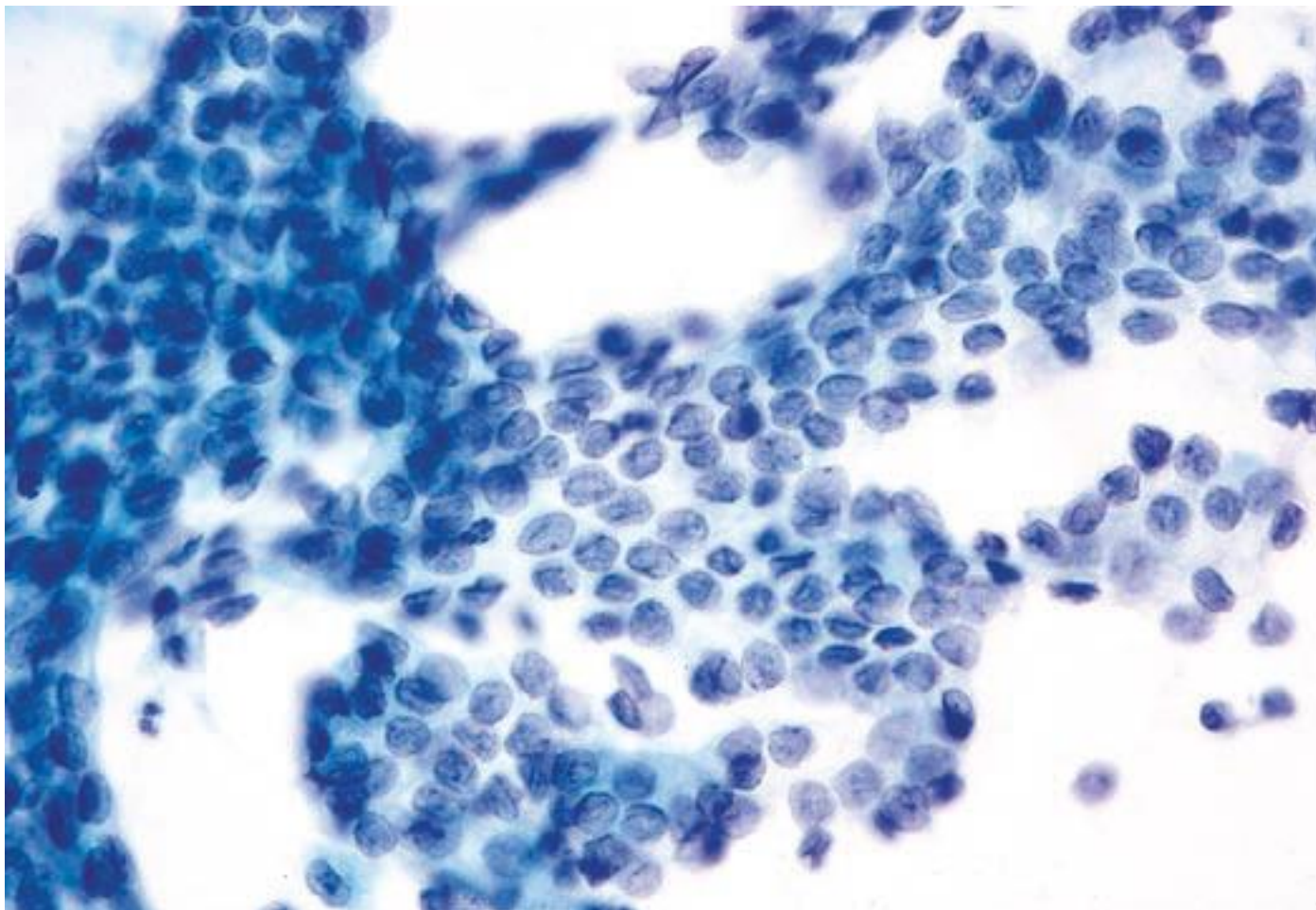


Papillary fibrovascular cores

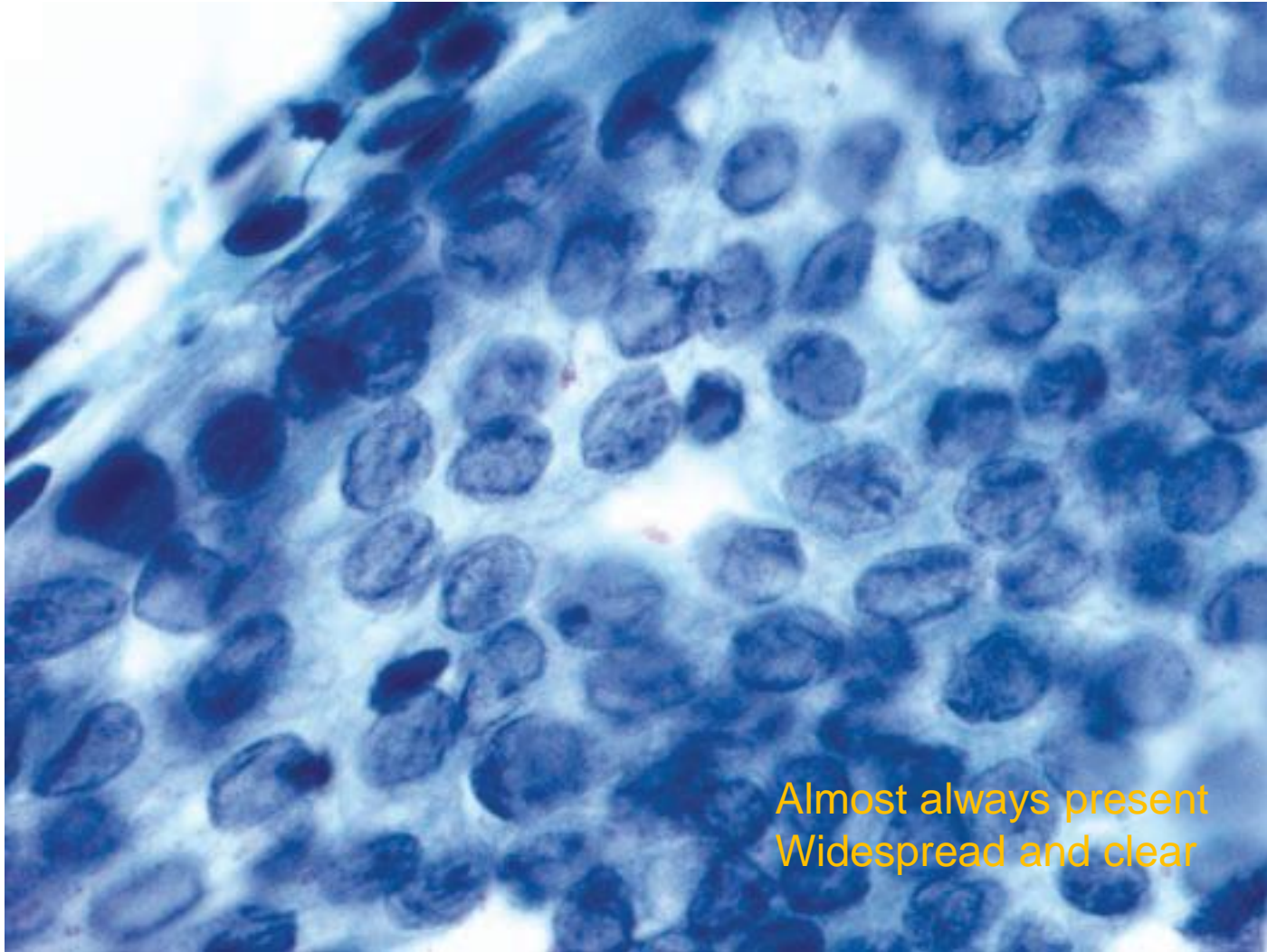
# Cellular smears, papillary or syncytial groups



Overlapping, oval nuclei, nuclear grooves

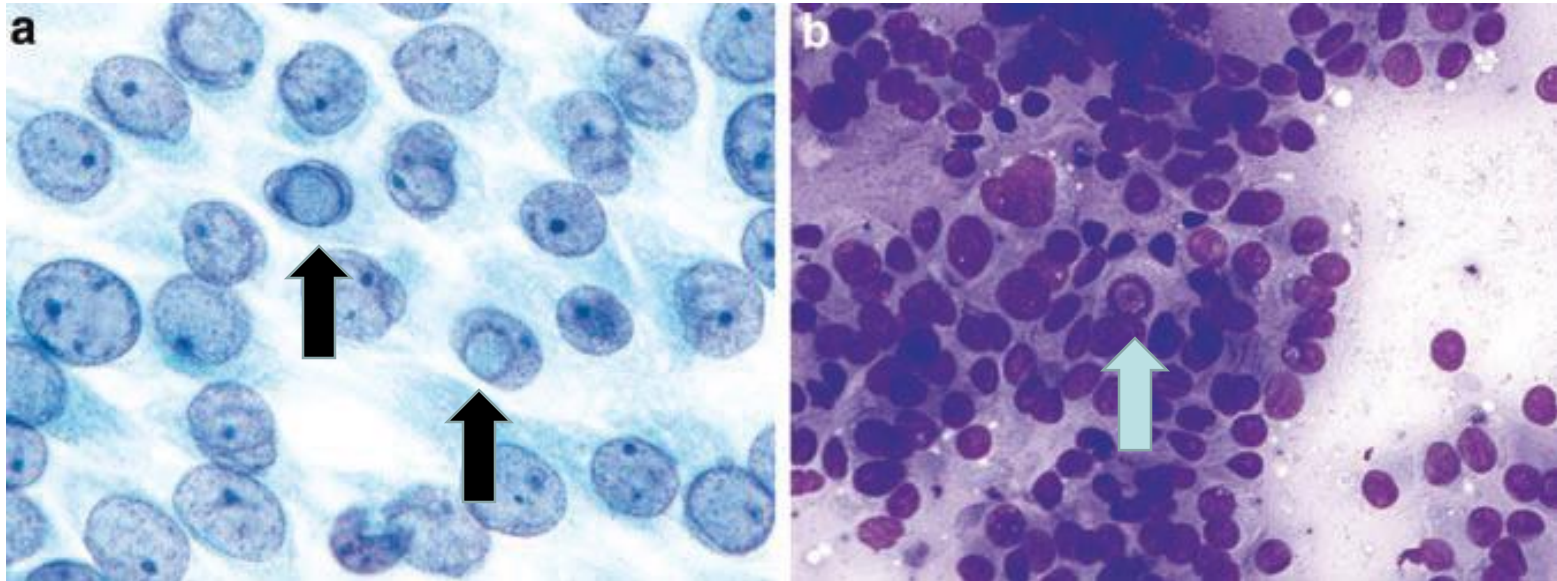


Nuclear grooves, (indented/folded nuclear membranes)



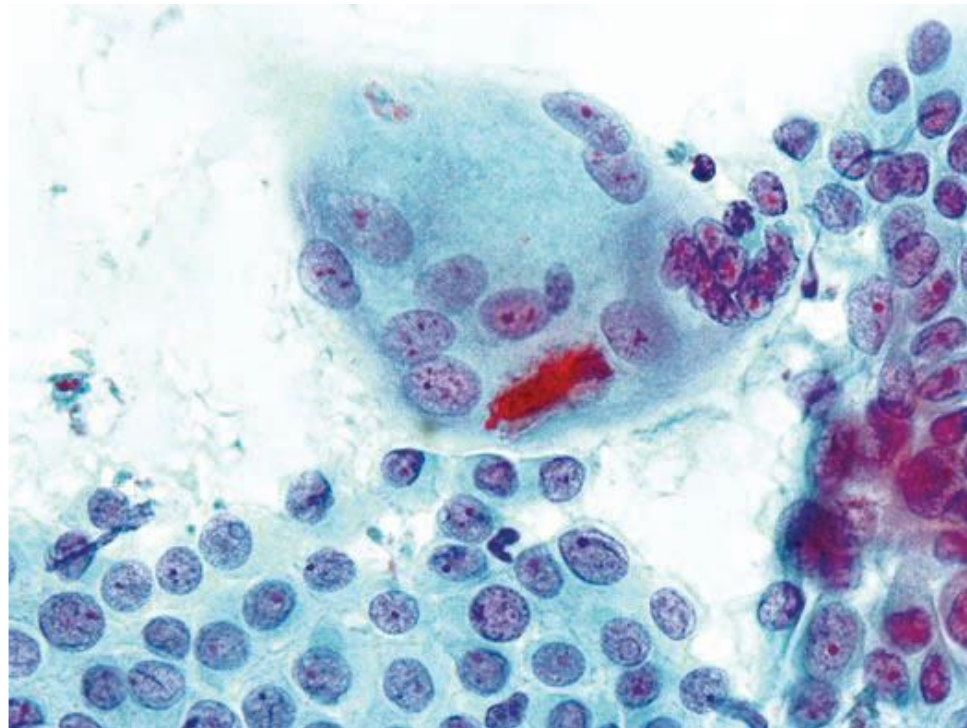
Almost always present  
Widespread and clear

# Intranuclear inclusions

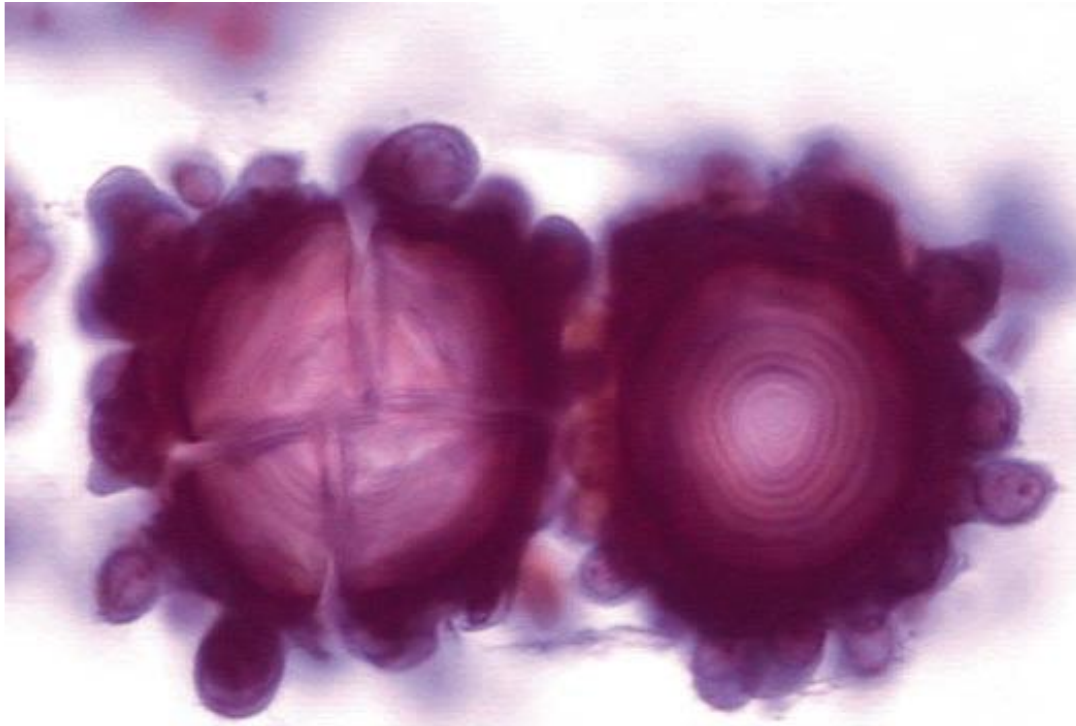


- Most specific.
- Not found in all cases.
- Strict criteria: Large, well delineated, dark outline to be discriminated from superimposed RBCs and artifacts.

# Multinucleated Giant Cells



# Psammoma bodies



Pathognomonic

# AUS/FLUS (Bethesda)

- Specimen preparation artifacts:  
Inadvertent air drying of alcohol-fixed, Papanicolaou may result in follicular cells with enlarged nuclei that have pale but slightly smudgy chromatin and irregular nuclear outlines. These features can raise the possibility of papillary carcinoma.

# Conclusion

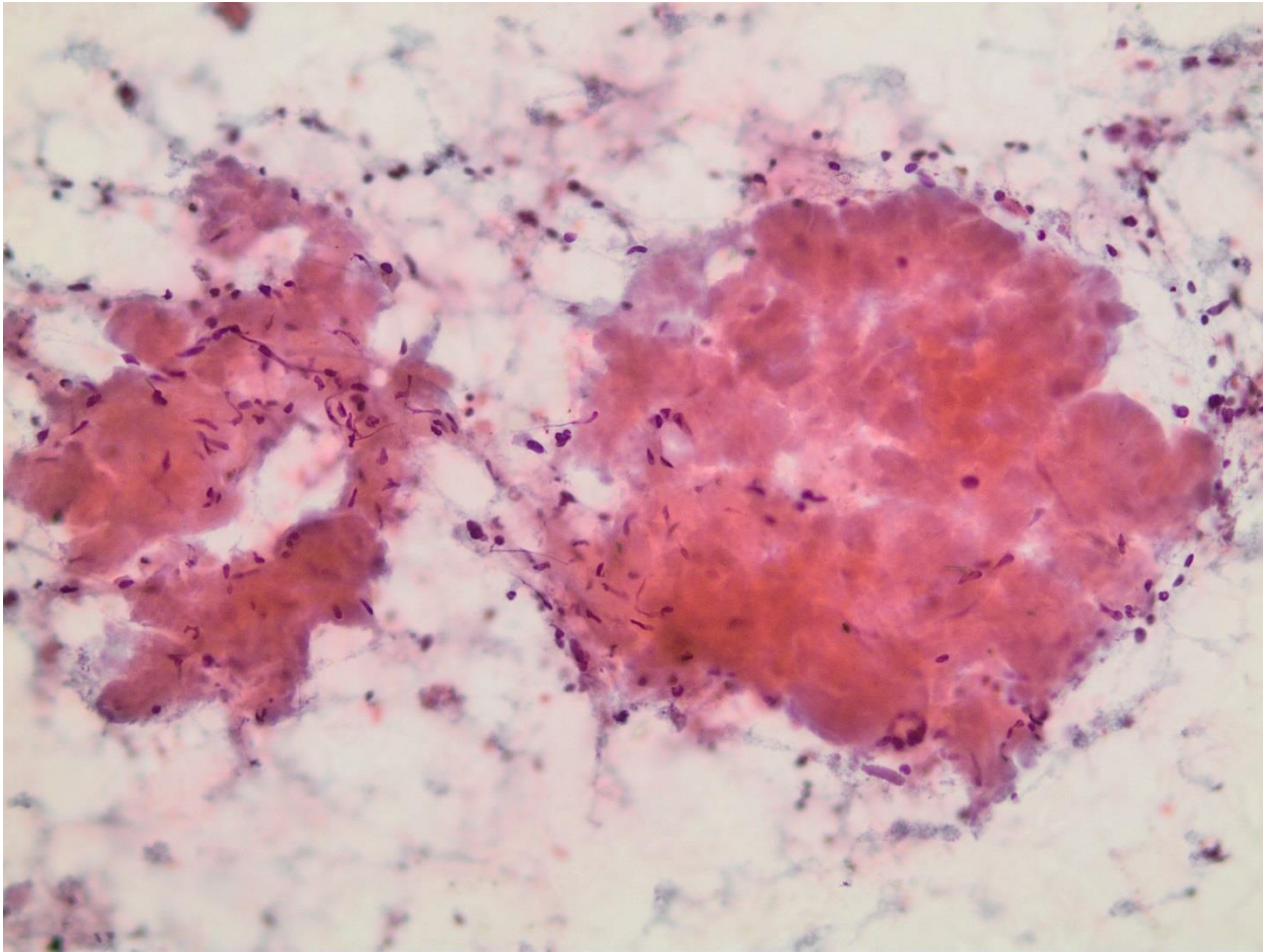
- Focal and subtle nuclear features of papillary ca
  - Follicular cells
  - WARDS
- Better diagnosis as benign MNG or FLUS

# Miscellaneous

IEs: AUBMC 2005-2017

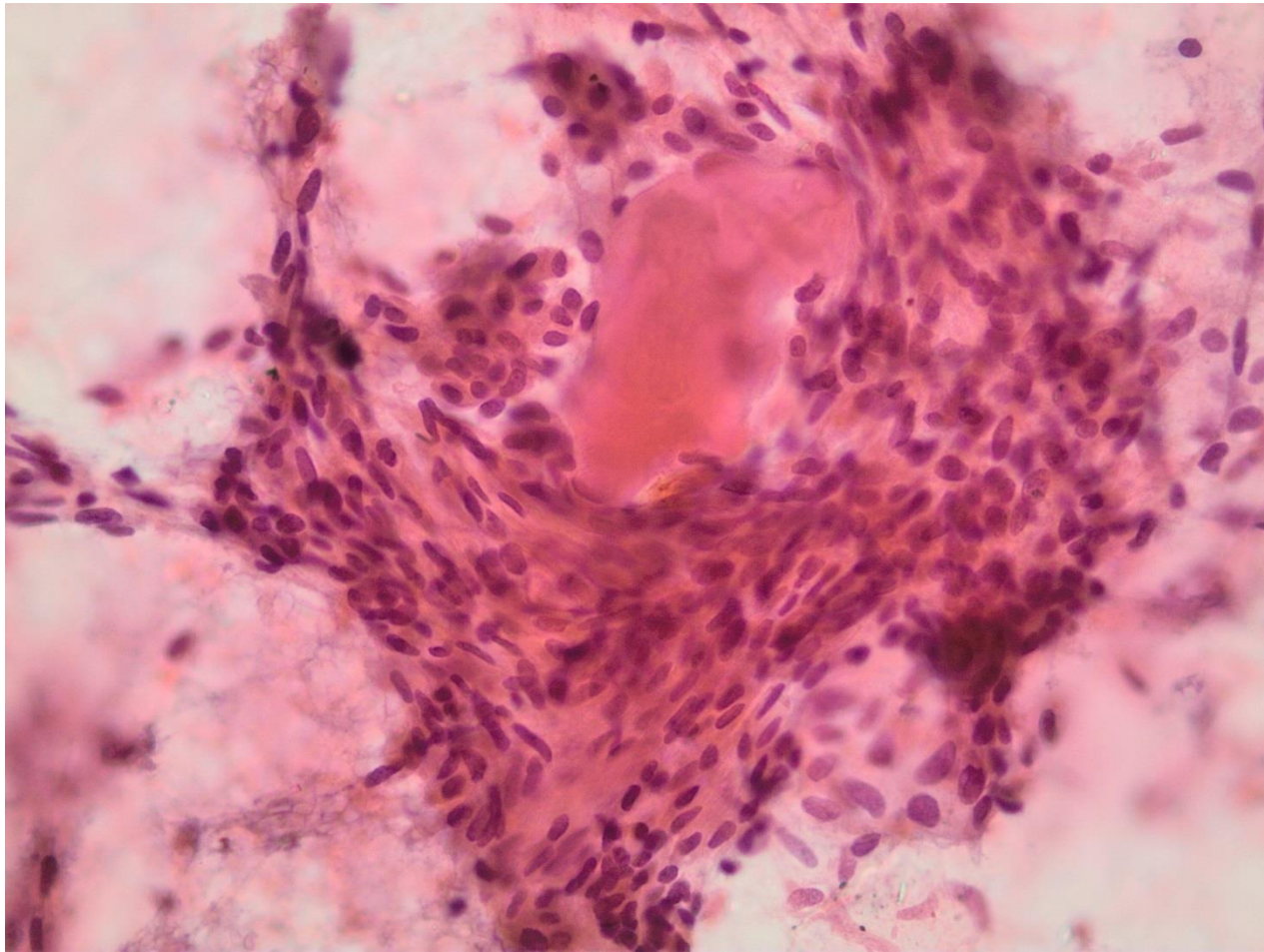
Final pathology diagnosis	Case #	Original FNA IE	Comment/Problem	Surgical procedure	Blinded review diagnosis
Follicular carcinoma, minimally invasive	1	BFN	Minimally invasive follicular carcinoma composed of <b>micro and macrofollicles</b> . Capsular and vascular invasion present.	Total thyroidectomy	SFN favor BFN
Medullary carcinoma	1	SFN	Medullary carcinoma cells misinterpreted as follicular cells. <b>Amyloid mistaken for colloid</b> .	Total thyroidectomy and central LN dissection (high serum calcitonin)	Susp for medullary Ca

# Amyloid



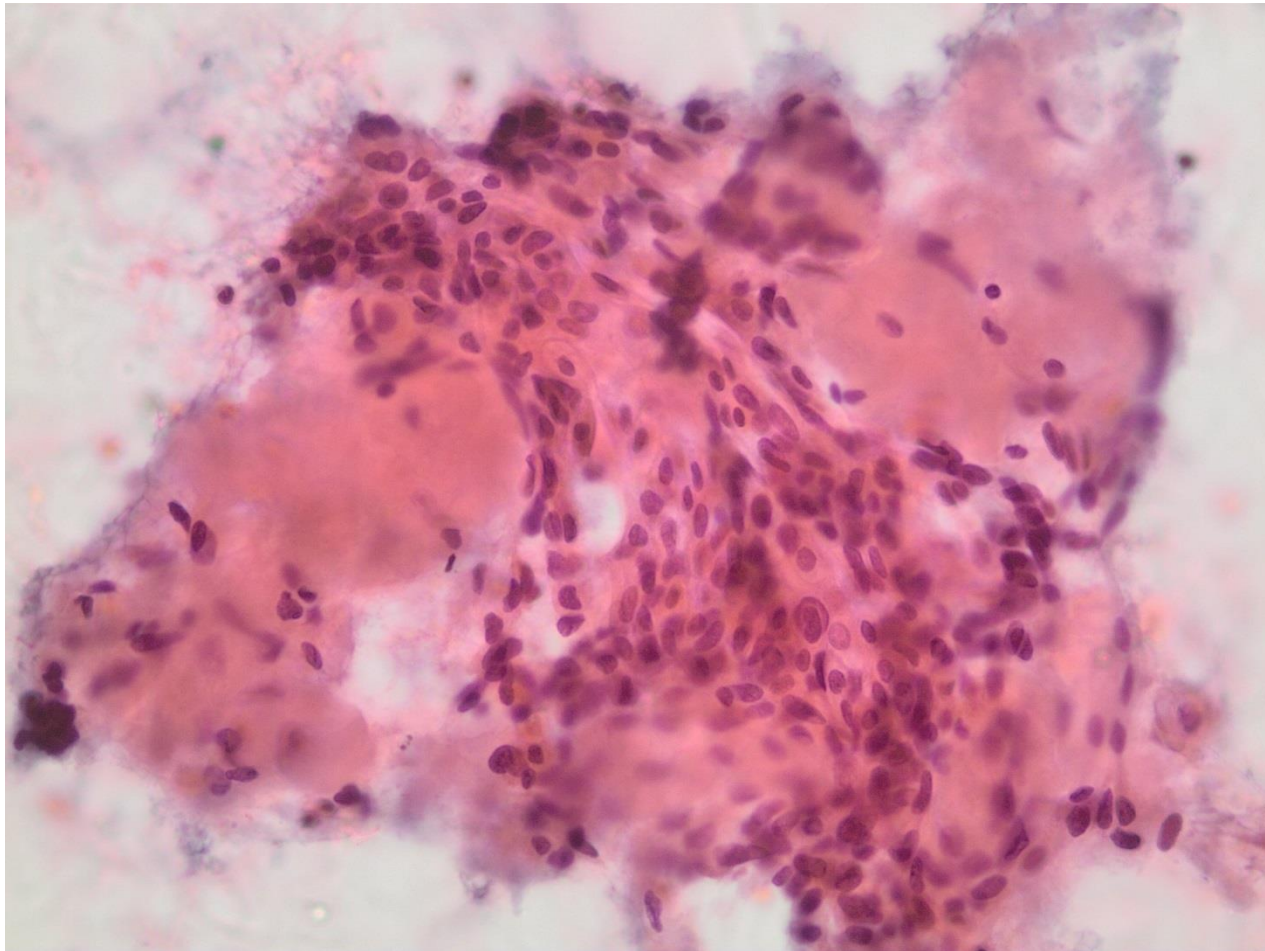
# Amyloid

Misinterpreted as colloid

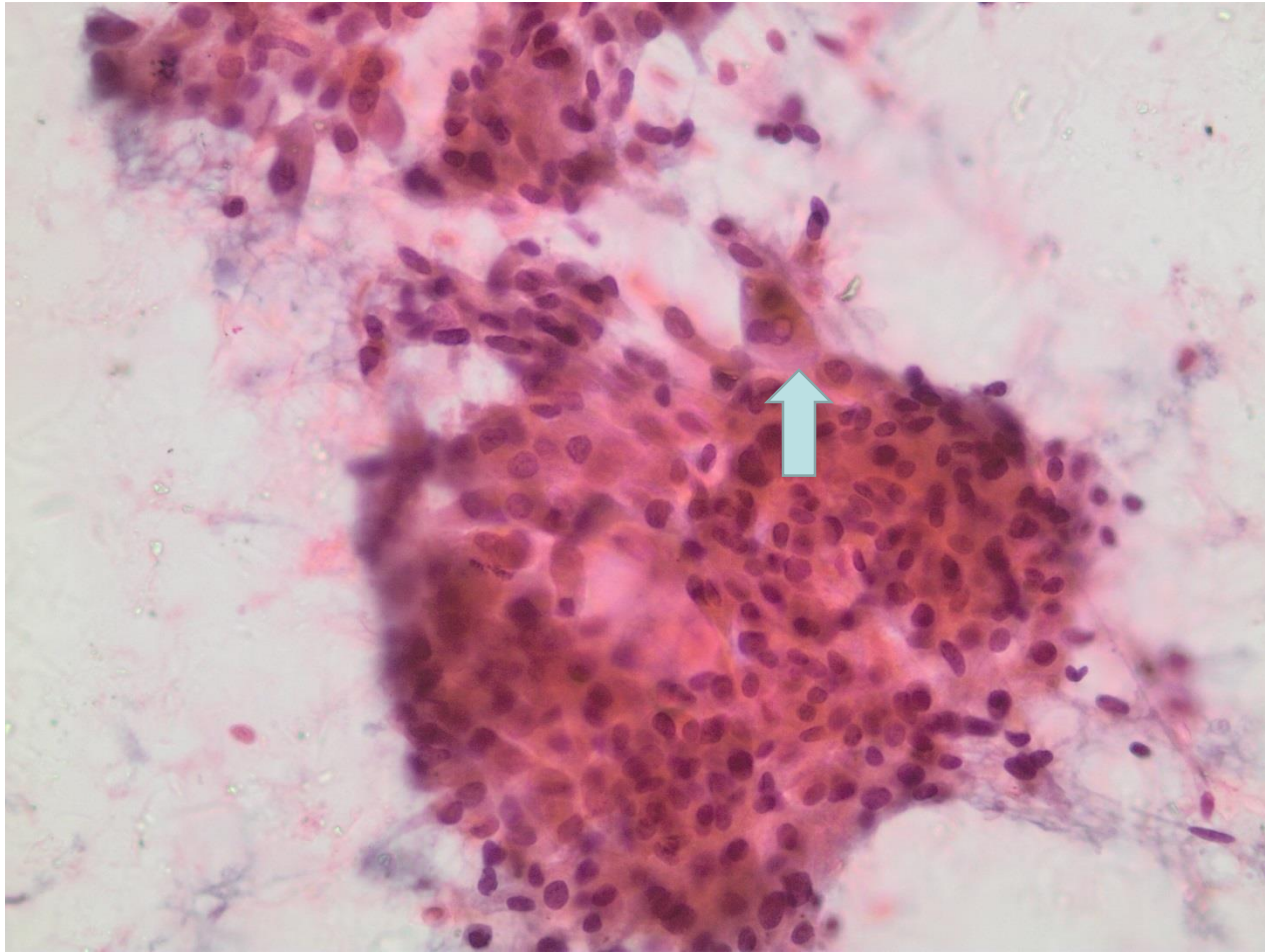


# Amyloid

Misinterpreted as colloid

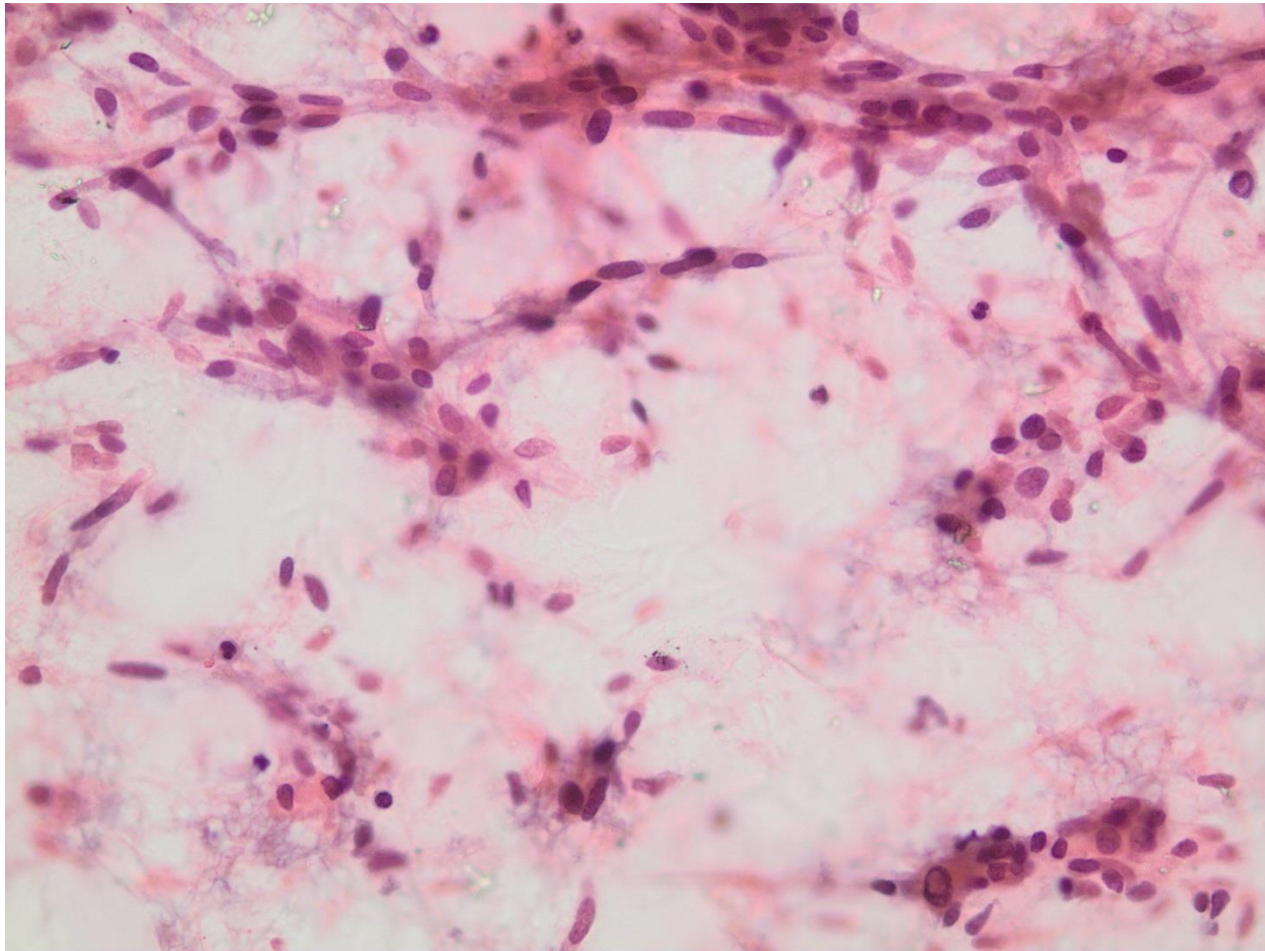


# Intranuclear inclusion



# Spindle cells

S&P chromatin



# Conclusions

# Hashi's

- Learn to identify HCs.
- Recognize their innate atypical cytology; do not misinterpret as metastatic ca.
- Allow for some nuclear abnormalities mimicking papillary ca (enlargement, overlapping, grooves, pseudoinclusions. Increase threshold.
- Screen the slides well for “other cells”: Lymphocytes: Polymorphous (numerous large lymphocytes).
- Recognize suboptimal samples (scant/air dry) and do not over diagnose. Use Bethesda and FLUS in such cases.
- Consult a colleague when in doubt!

# MNG

- Focal and soft nuclear features of papillary ca, whether in follicular cells or WARDs:
  - Can be ignored if the background is benign
  - Can be diagnosed as FLUS if you feel better with a repeat FNA
- Differentiate histiocytes from HCs

# General Recommendations

- Screen slides thoroughly in all cases identifying all components of the lesion
- Consult a colleague.
  - 4 eyes are better than 2

