



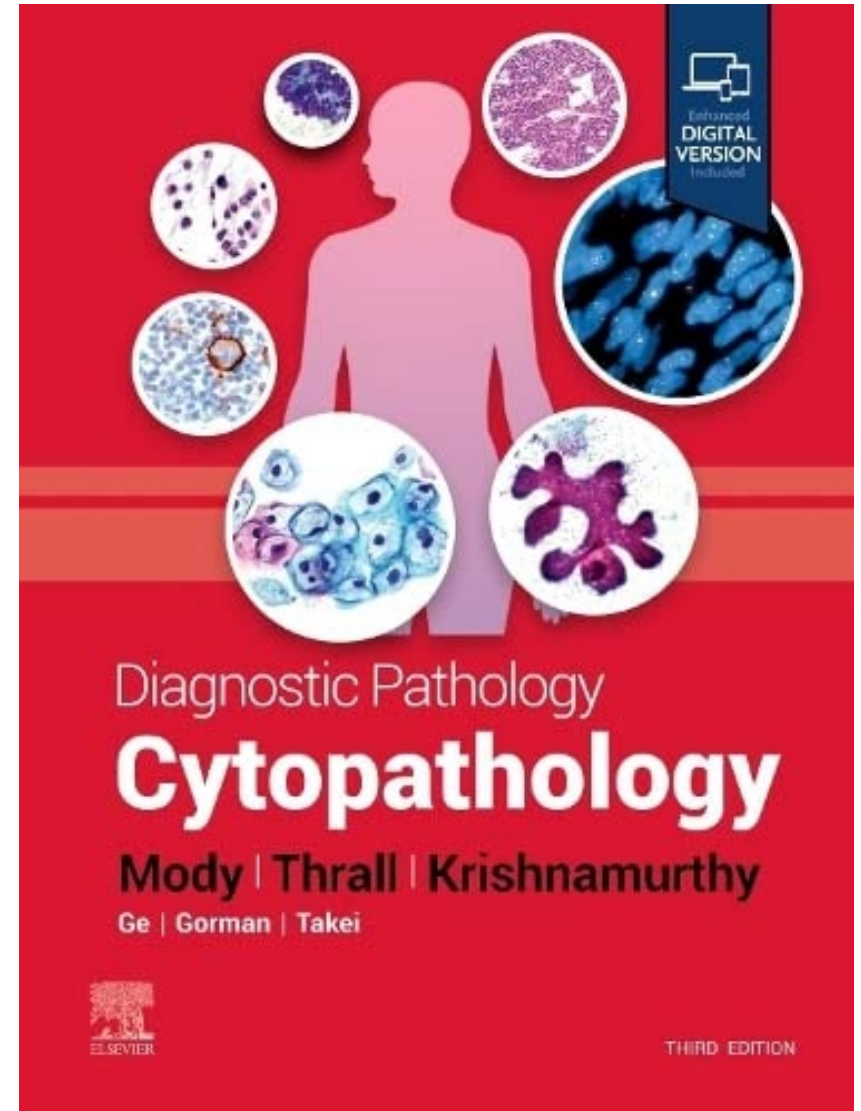
Essentials in Gynecologic Cytology

HOUSTON
Methodist[®]
LEADING MEDICINE

- Michael J. Thrall M.D.
- Director of Cytopathology Fellowship and Digital Pathology
 - Department of Pathology and Genomic Medicine
 - Houston Methodist Hospital in Houston, TX, USA
- Professor, Houston Methodist Hospital Academic Institute and Weill-Cornell College of Medicine



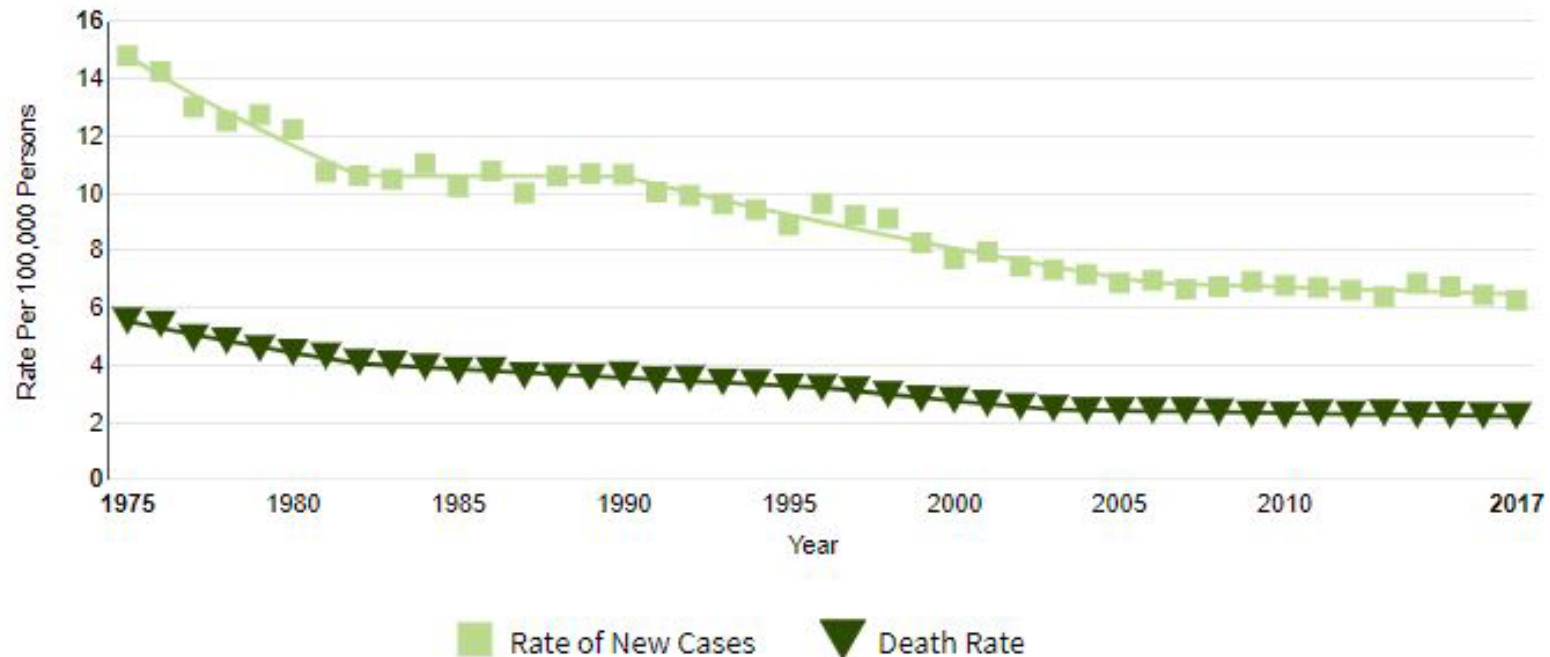
- Co-editor of 2022 textbook Diagnostic Pathology: Cytopathology, 3rd Edition
Publisher: Amirsys/Elsevier



Squamous Lesions

Cervical Cancer Incidence and Mortality

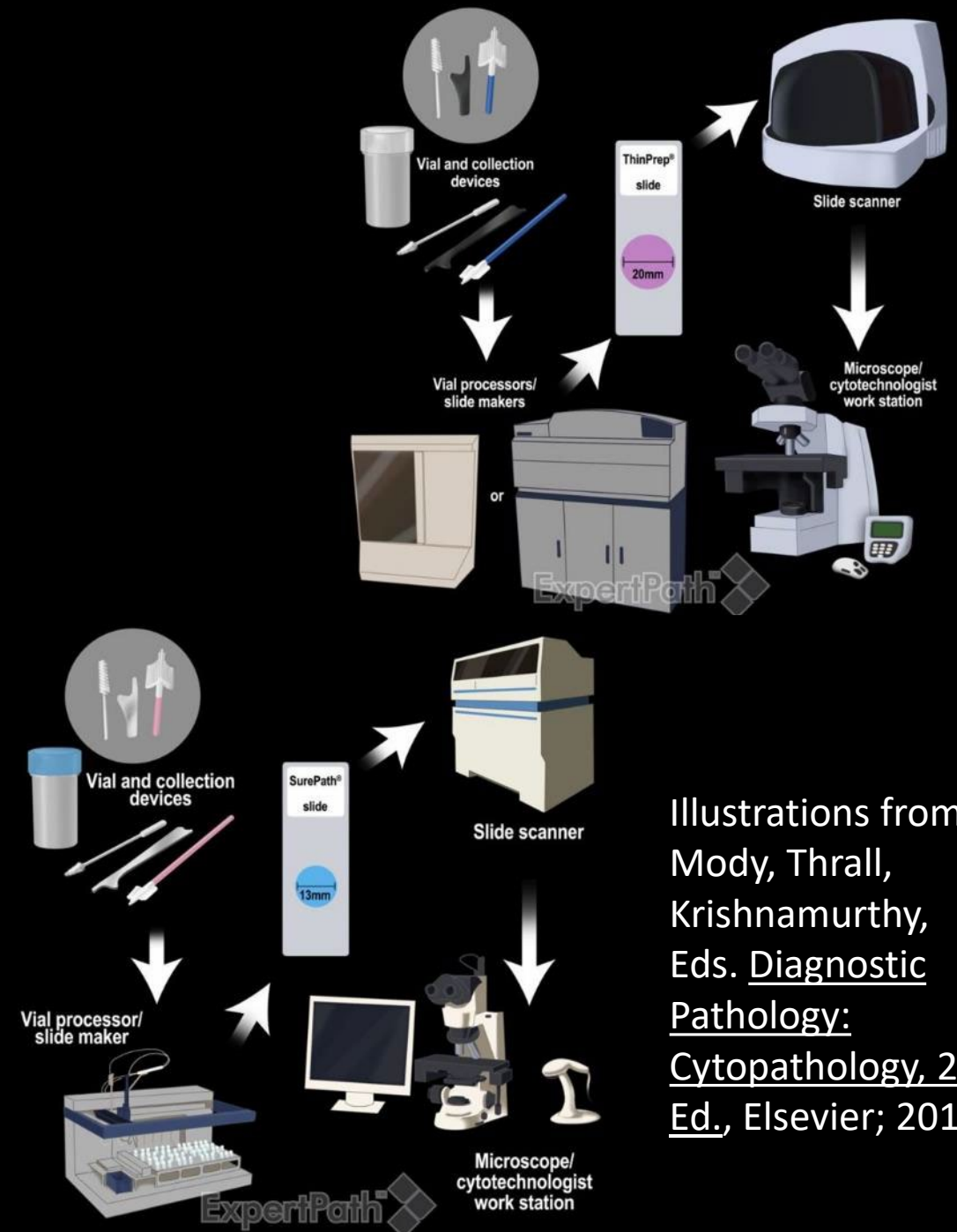
New Cases, Deaths and 5-Year Relative Survival



New cases come from SEER 9. Deaths come from U.S. Mortality.
All Races, Females. Rates are Age-Adjusted.
Modeled trend lines were calculated from the underlying rates using the [Joinpoint Trend Analysis Software](#).
National Cancer Institute: seer.cancer.gov/statfacts/html/cervix.html

Liquid-Based Papanicolaou Testing

- Two major brands:
 - SurePath: 13 mm diameter, gravity sedimentation
 - ThinPrep: 20 mm diameter, filtered
- Remove blood and inflammatory cells
- Allow for automated screening
- Ancillary testing from the same vial including HPV
- Lower unsatisfactory rates



Illustrations from:
Mody, Thrall,
Krishnamurthy,
Eds. Diagnostic
Pathology:
Cytopathology, 2nd
Ed., Elsevier; 2018.

Unsatisfactory Slides

- Liquid-based Pap tests: 5,000 cells
- Conventional Pap smears: 8-12,000 cells
- How do you estimate these?
 - Liquid-based: Count squamous cells in 10 consecutive 40x fields through the center of the slide (TP: 3.8 per HPF; SP: 9 per HPF)
 - Conventional: Birdsong diagrams
- 2,000 cells for vaginal or post-menopausal specimens*

*Lu *et al.* Cancer Cytopathol 2010; 118: 474.

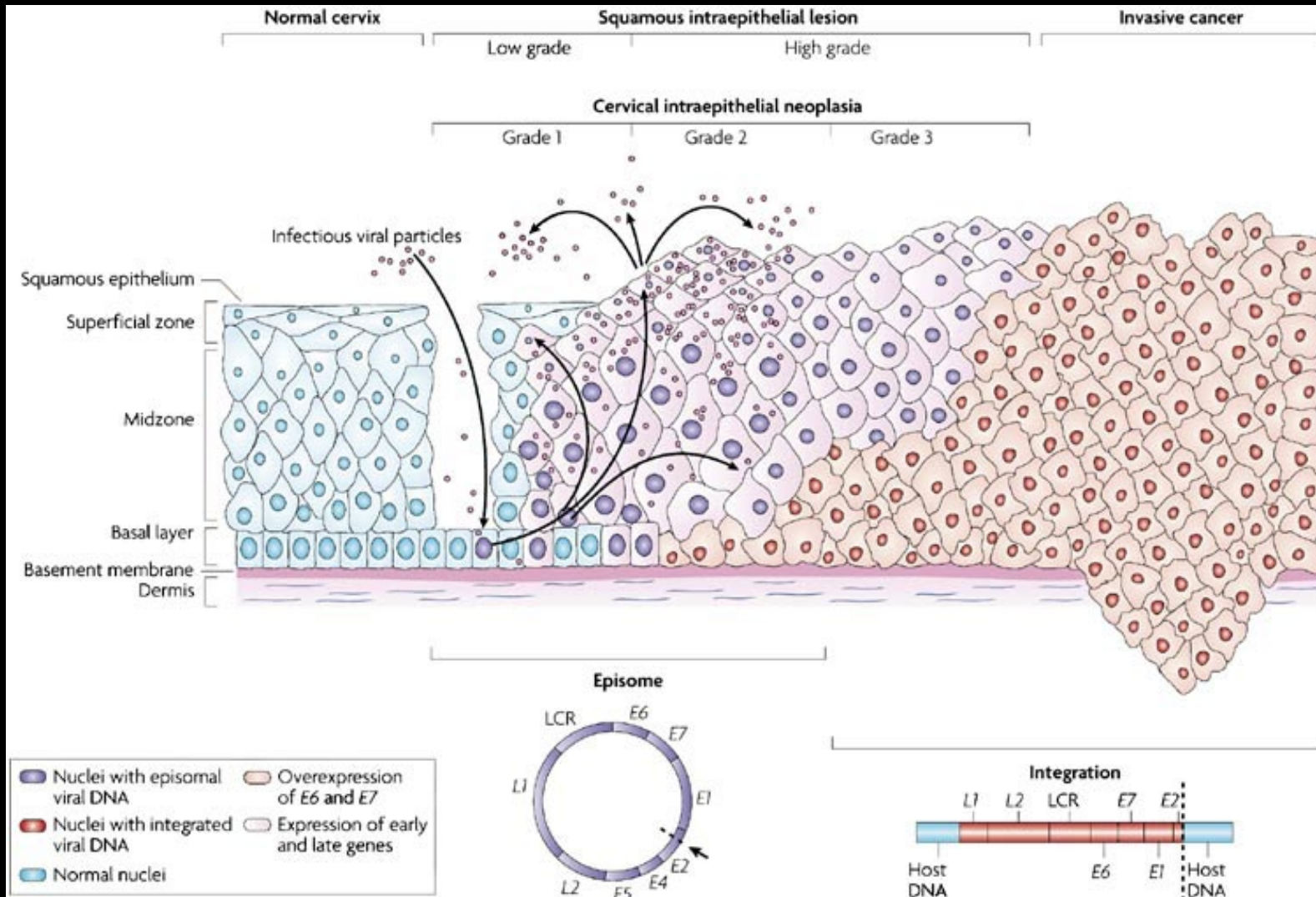
Bethesda 2014

- In the United States cervicovaginal cytology is reported according to the Bethesda System
- The latest version was formulated in 2014
- Many countries around the world have adopted the Bethesda terminology and criteria, sometimes with small variations

Bethesda 2014 Squamous Categories

- Negative for Intraepithelial Lesion or Malignancy (NILM)
- Atypical Squamous Cells of Undetermined Significance (ASC-US)
- Low Grade Squamous Intraepithelial Lesion (LSIL)
- Atypical Squamous Cells, Cannot Rule out High Grade (ASC-H)
- High Grade Squamous Intraepithelial Lesion (HSIL)
 - With Features Suspicious for Invasion
- Squamous Cell Carcinoma

HPV and Progression to Cancer



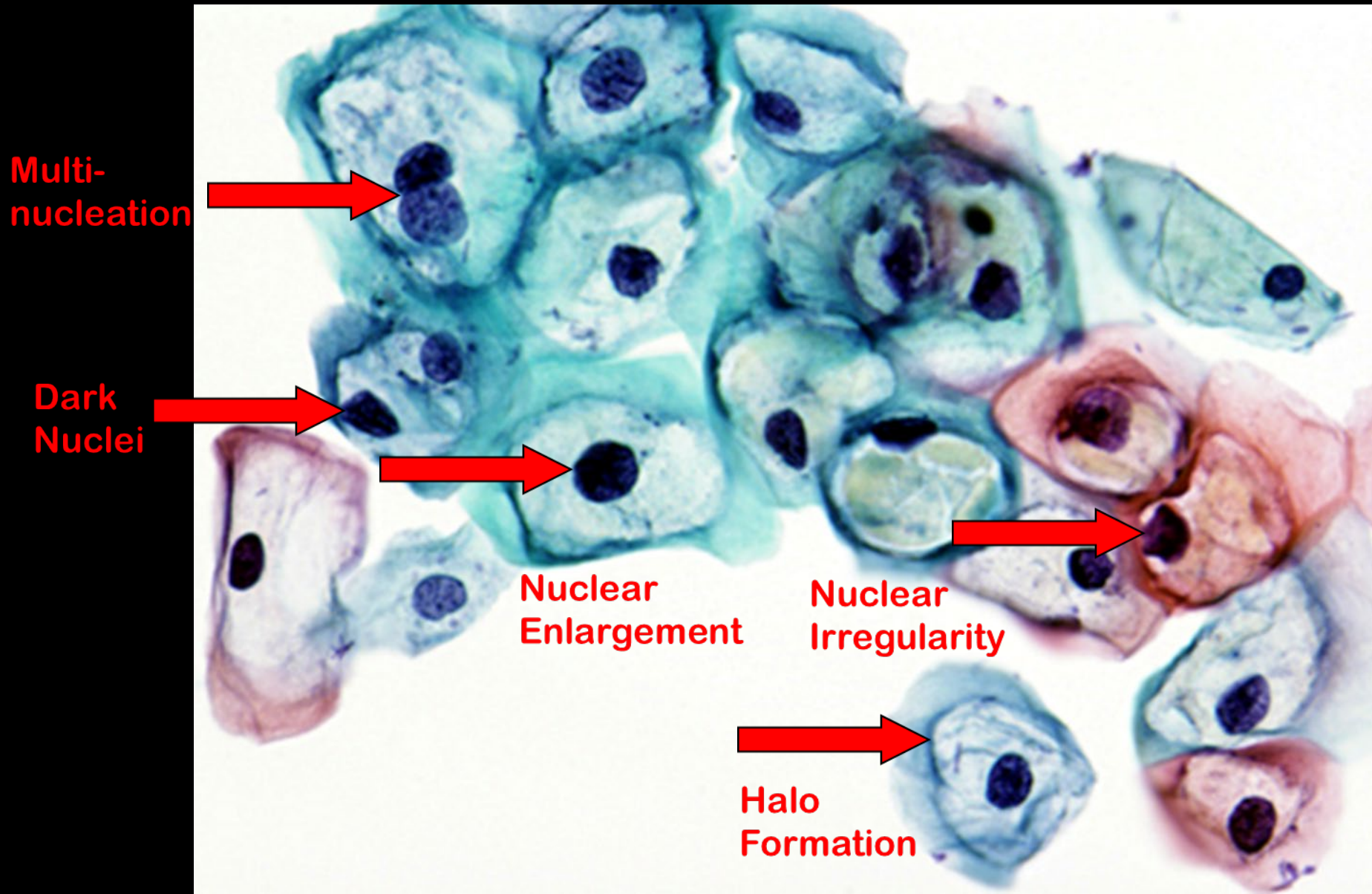
Orange indicates integrated DNA, E6 and E7 over-expression

Low-Grade Squamous Intraepithelial Lesion (LSIL)

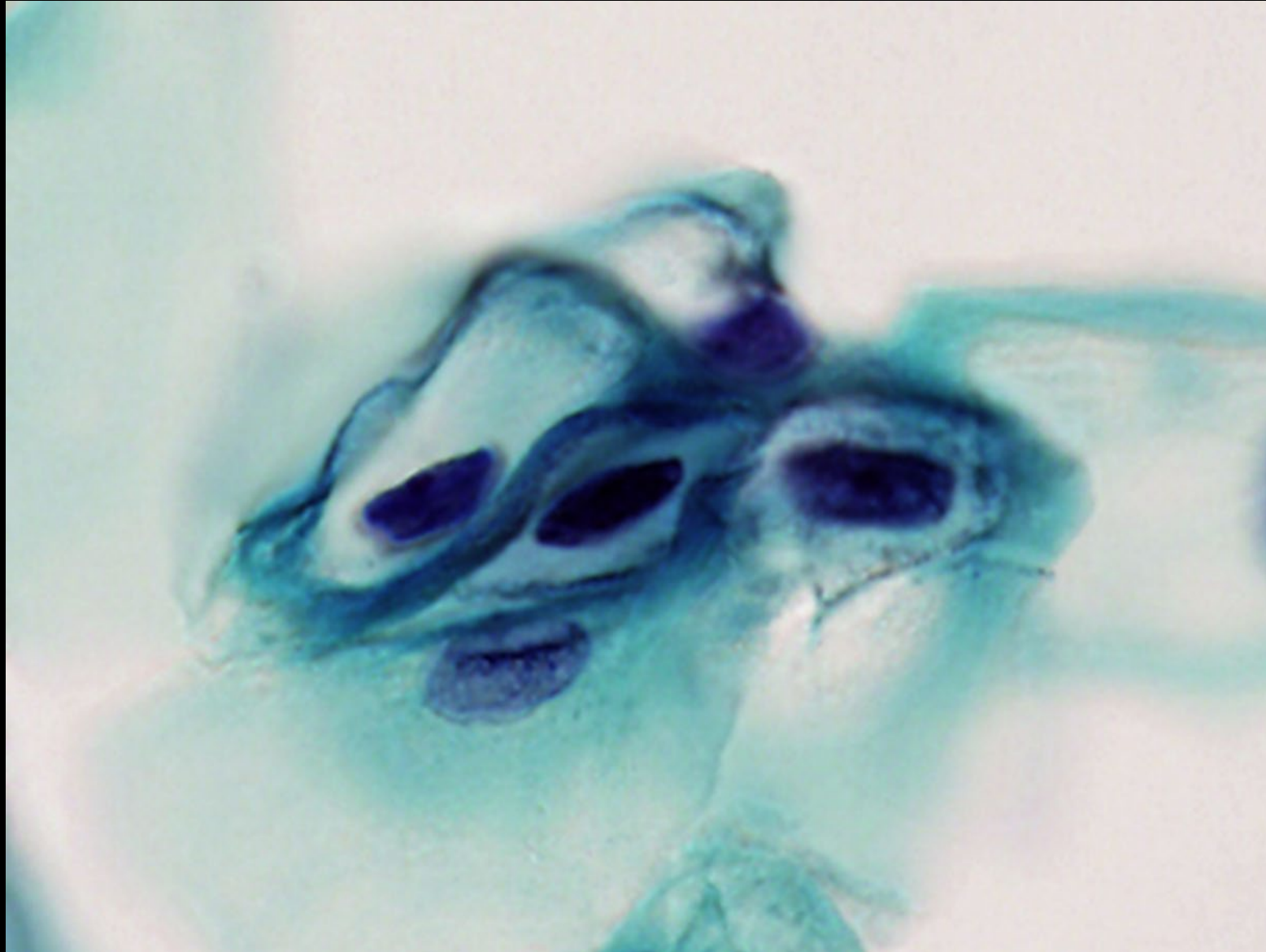
LSIL

- The most reproducible category
- “Koilocytosis” = “Cave cell”
- So-called because the nucleus appears to live “in a cave”

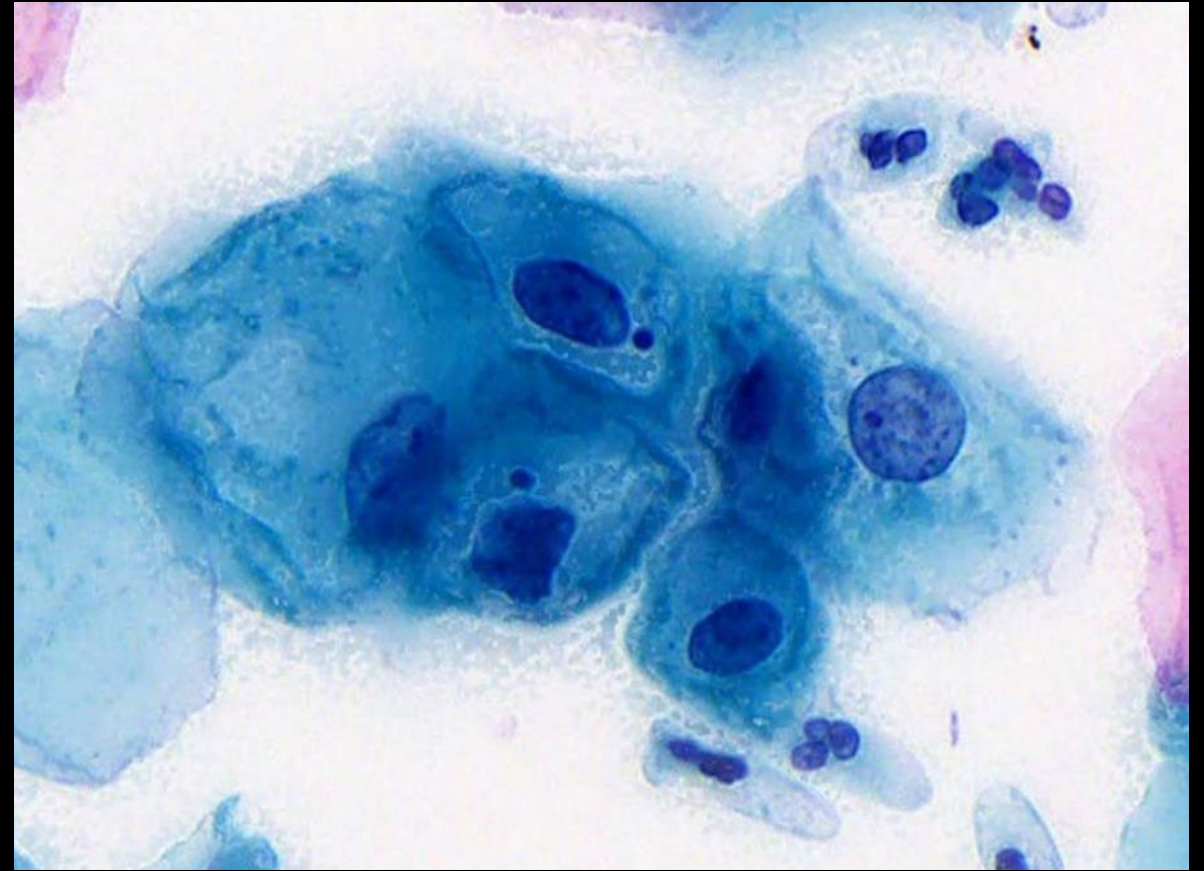
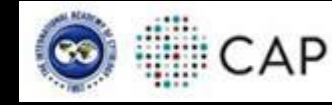
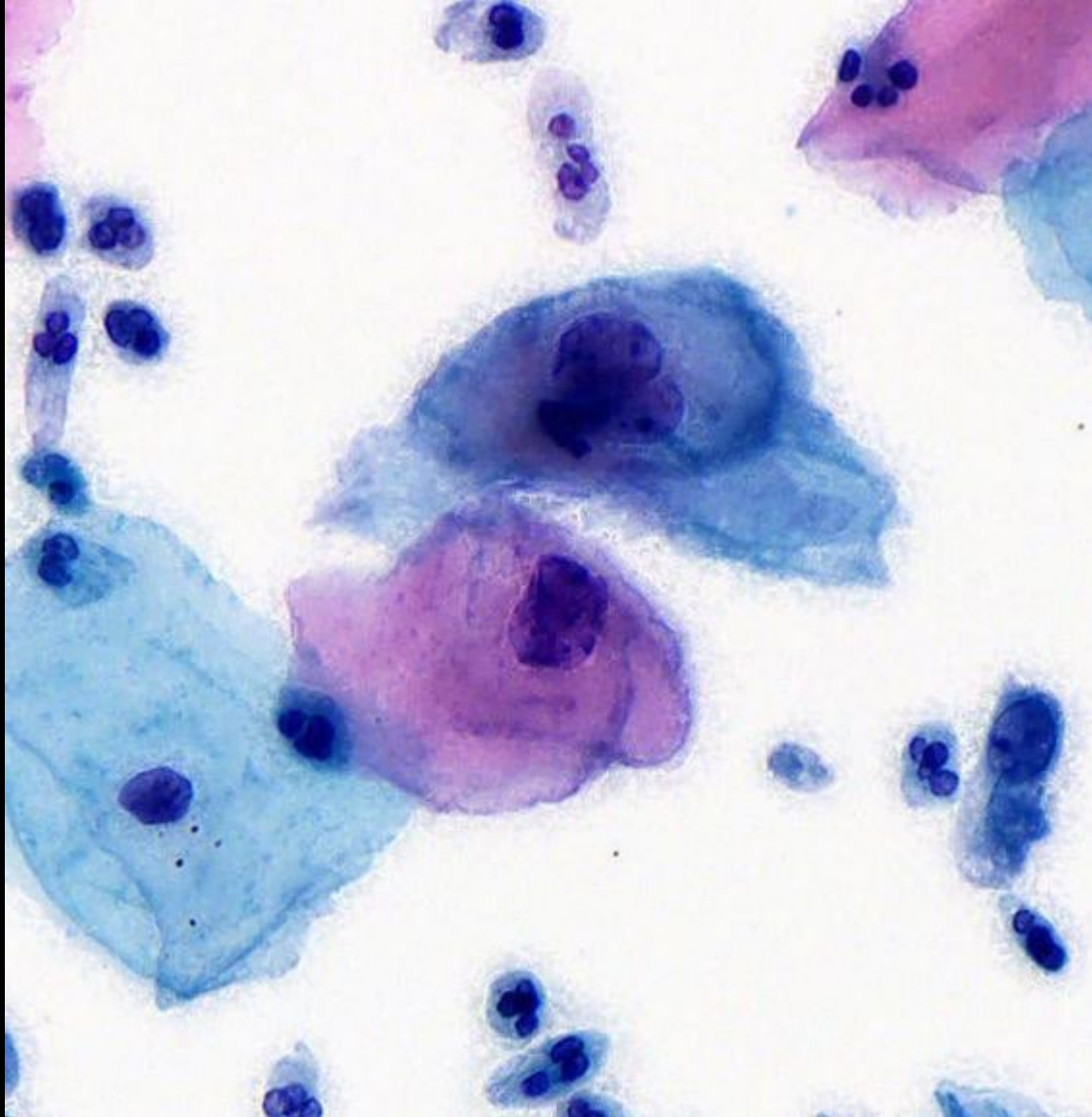
LSIL on ThinPrep



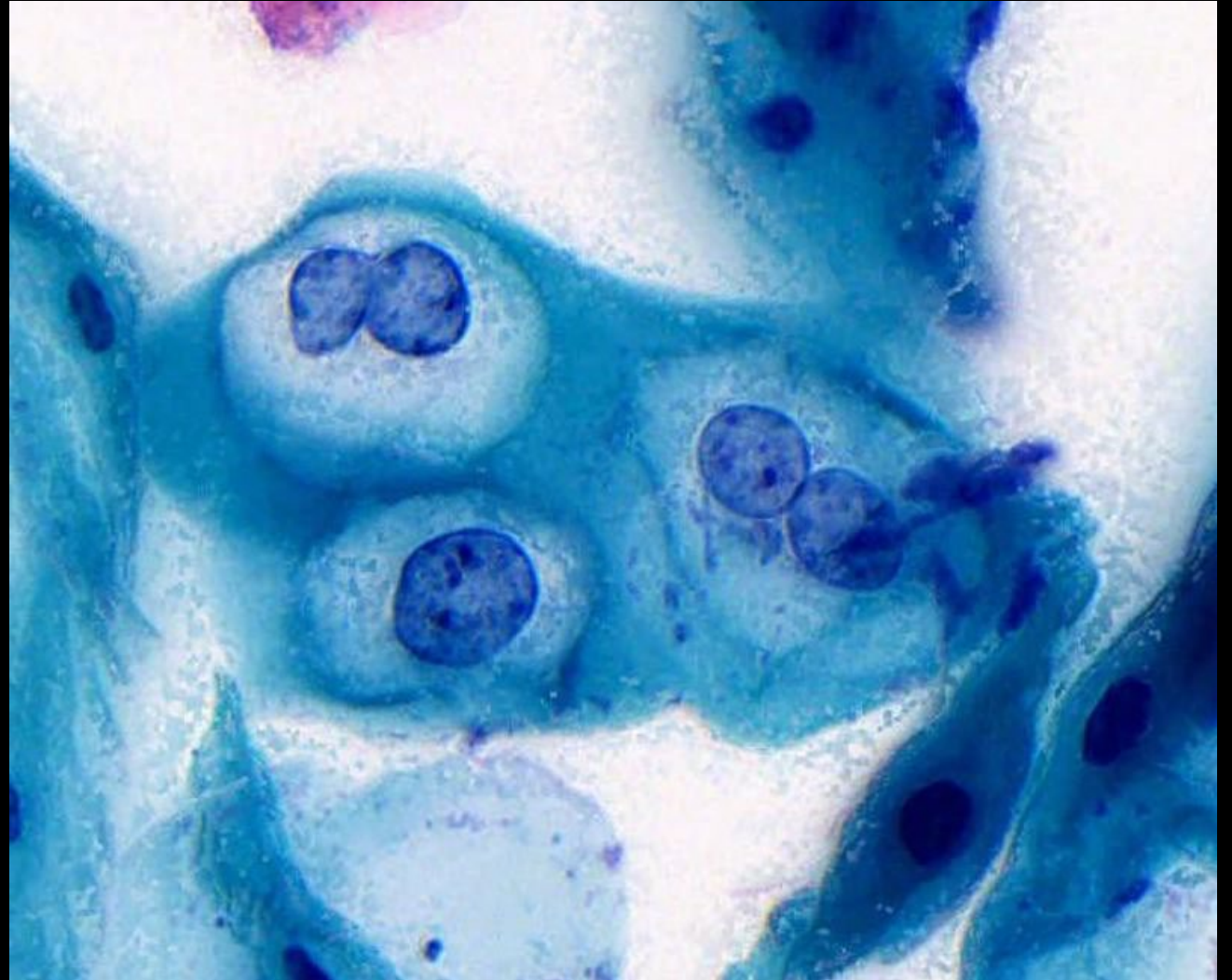
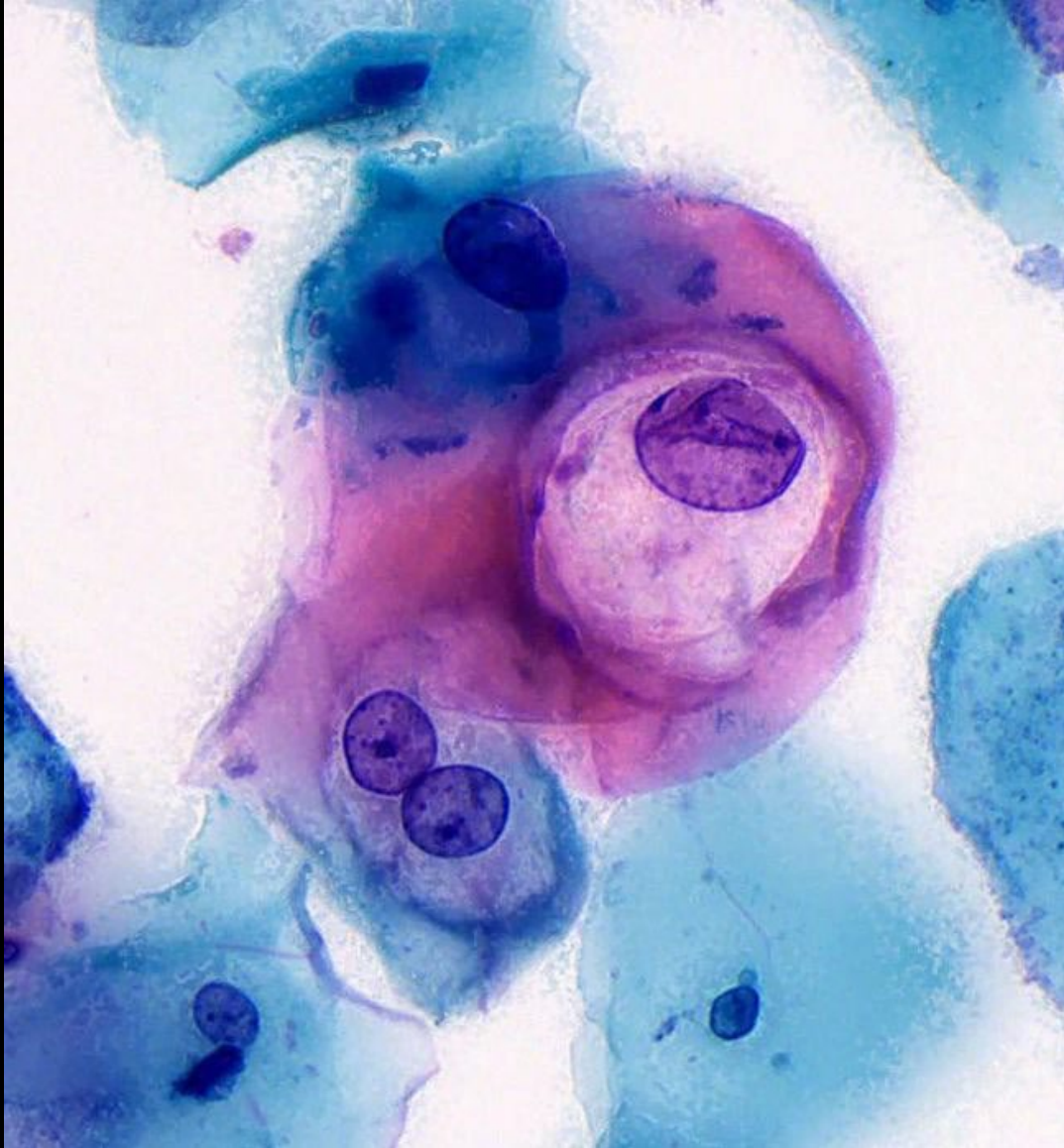
LSIL on SurePath



IAC-CAP Digital Atlas (<https://www.cytology-iac.org/educational-resources/digital-atlas-of-gyn-cytopathology>)



IAC-CAP Digital Atlas



HPV Effect

- Koilocytosis is a form of viral cytopathic effect (like Herpes, CMV, etc.)
- Nuclear changes are due to viral replication and virus-induced suppression of cell-cycle controls
- Halo formation is hard to explain since HPV replicates entirely in the nucleus – but appears to depend on the combination of HPV proteins E5 and E6*

*Krawczyk *et al.* Am J Pathol 2008; 173: 682.

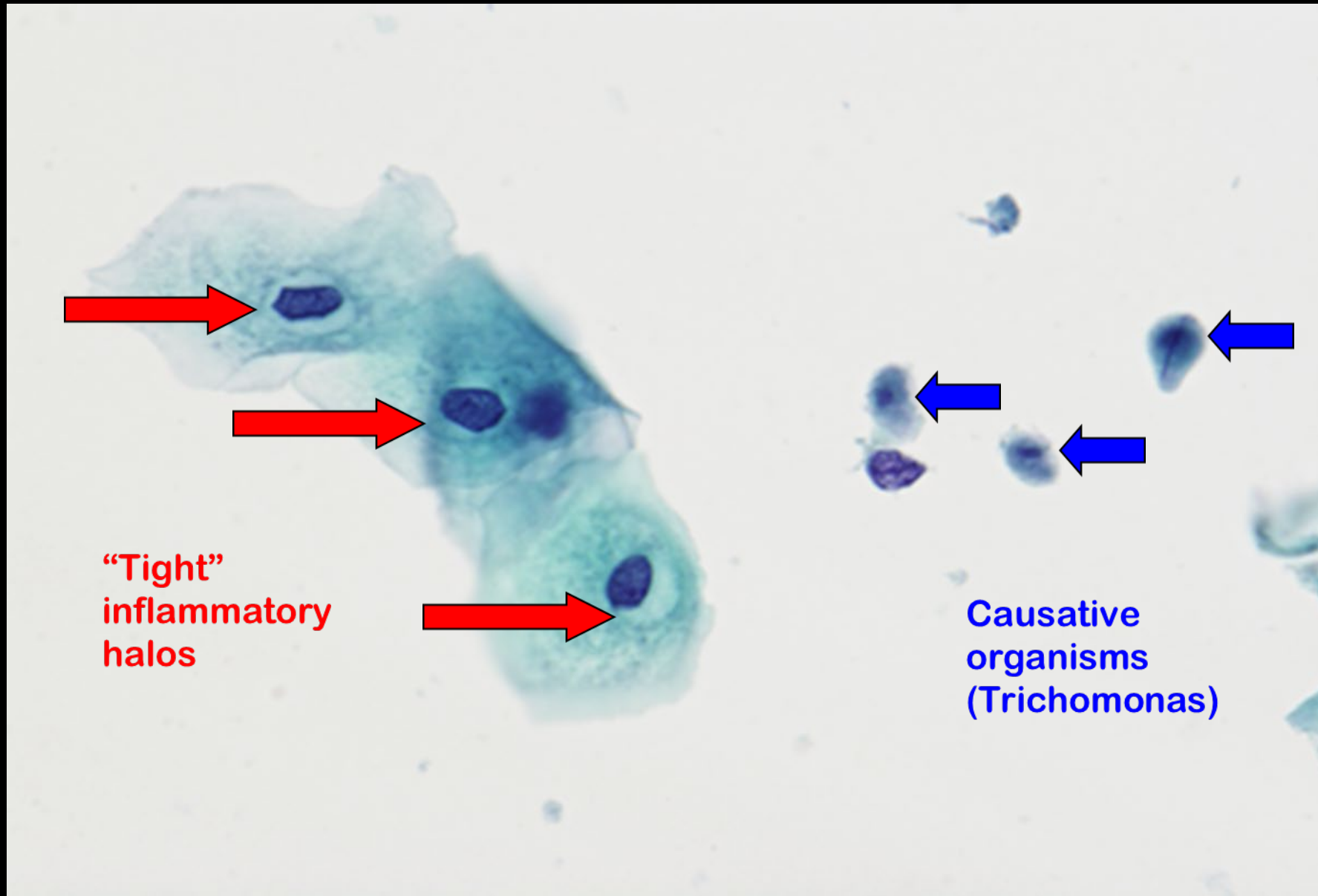
Koilocytosis Mimics

- Many other processes mimic viral halos
- Although halos are the most distinctive feature of HPV effect, they are not sensitive or sufficient
- Nuclear enlargement (>3 times intermediate nucleus), hyperchromasia, and irregular nuclear membranes are more reliable features of LSIL

Pseudohalos – Navicular Cells



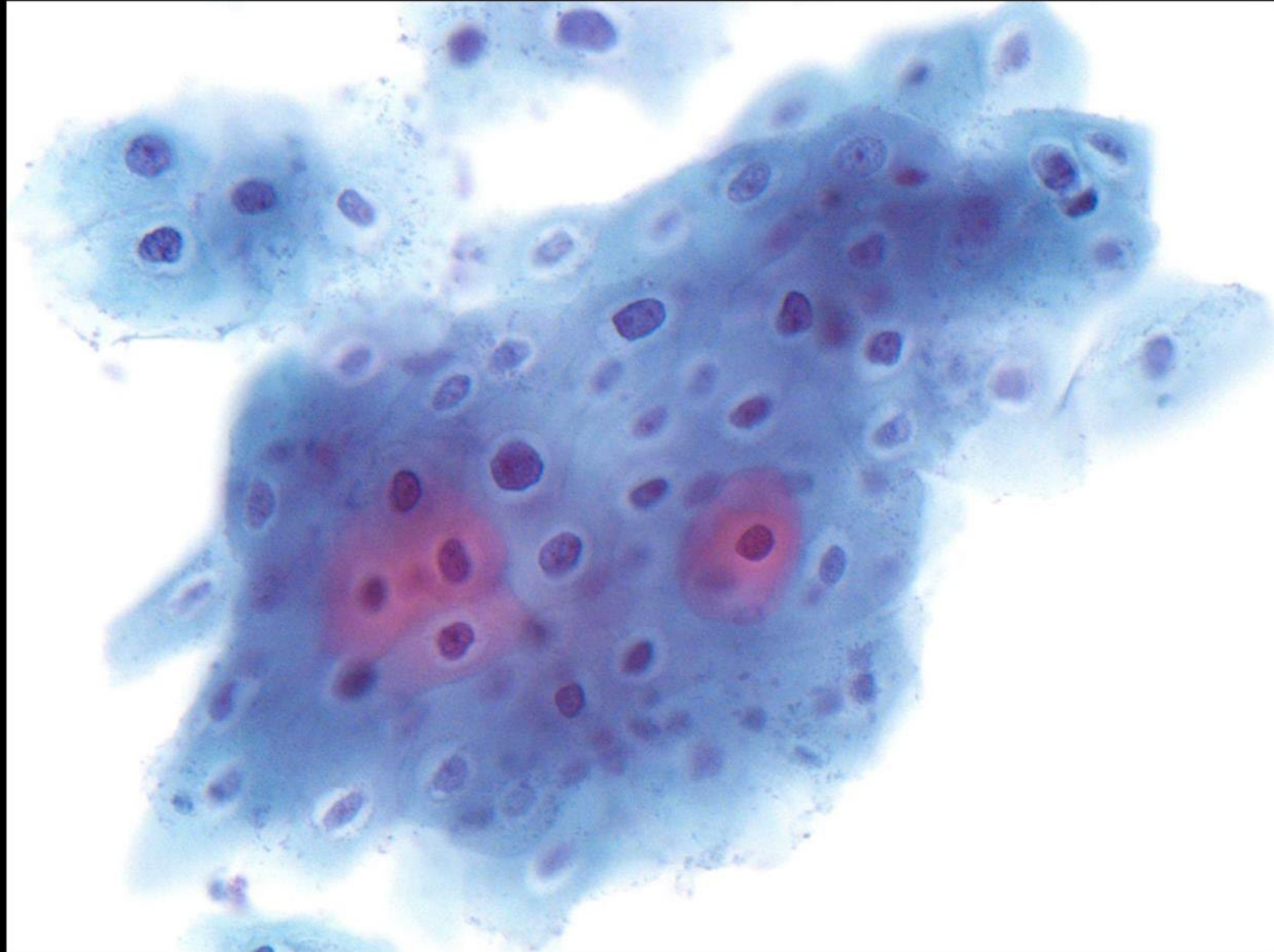
Inflammatory Halos



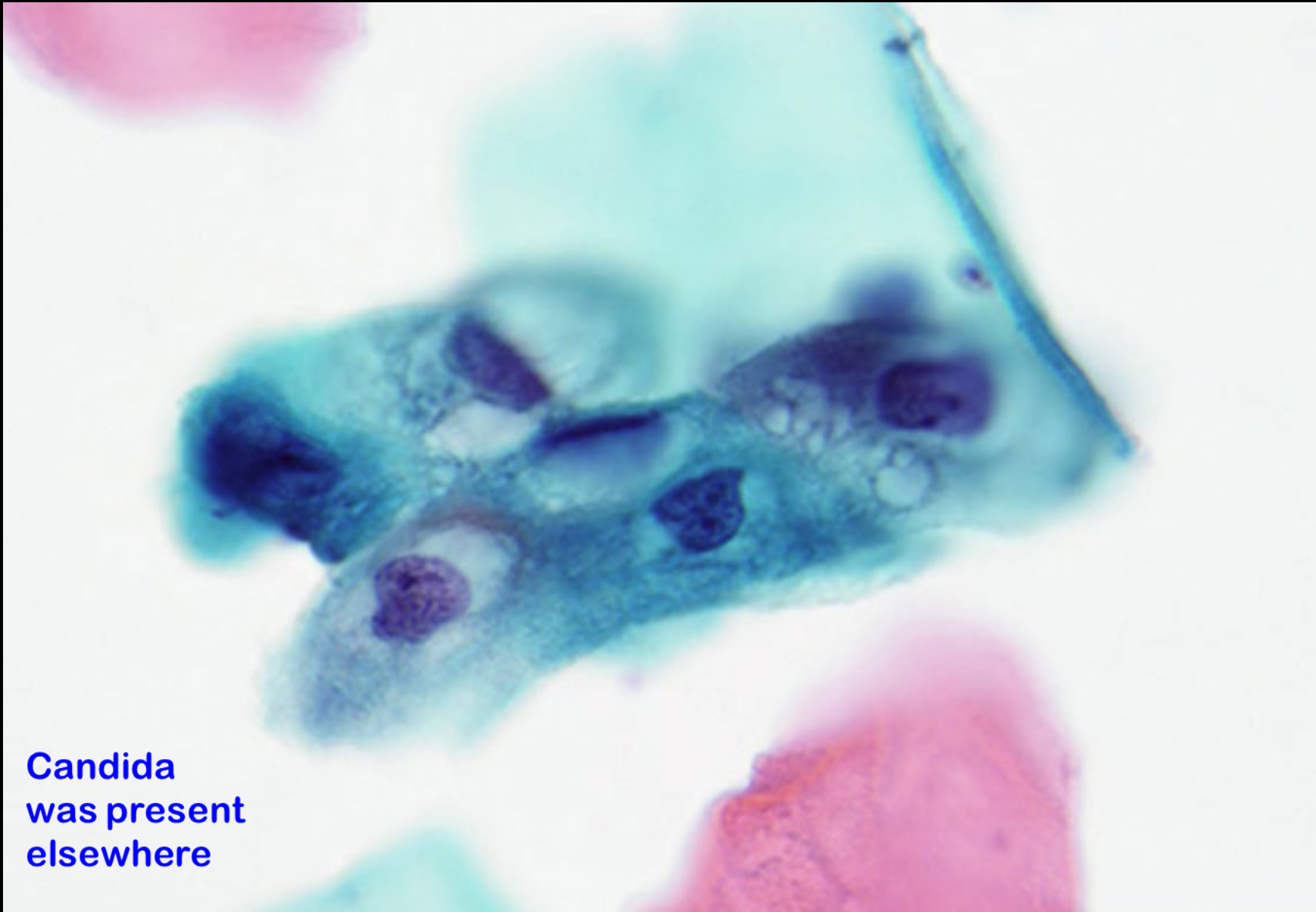
**"Tight"
inflammatory
halos**

**Causative
organisms
(Trichomonas)**

Inflammatory-Type Halos

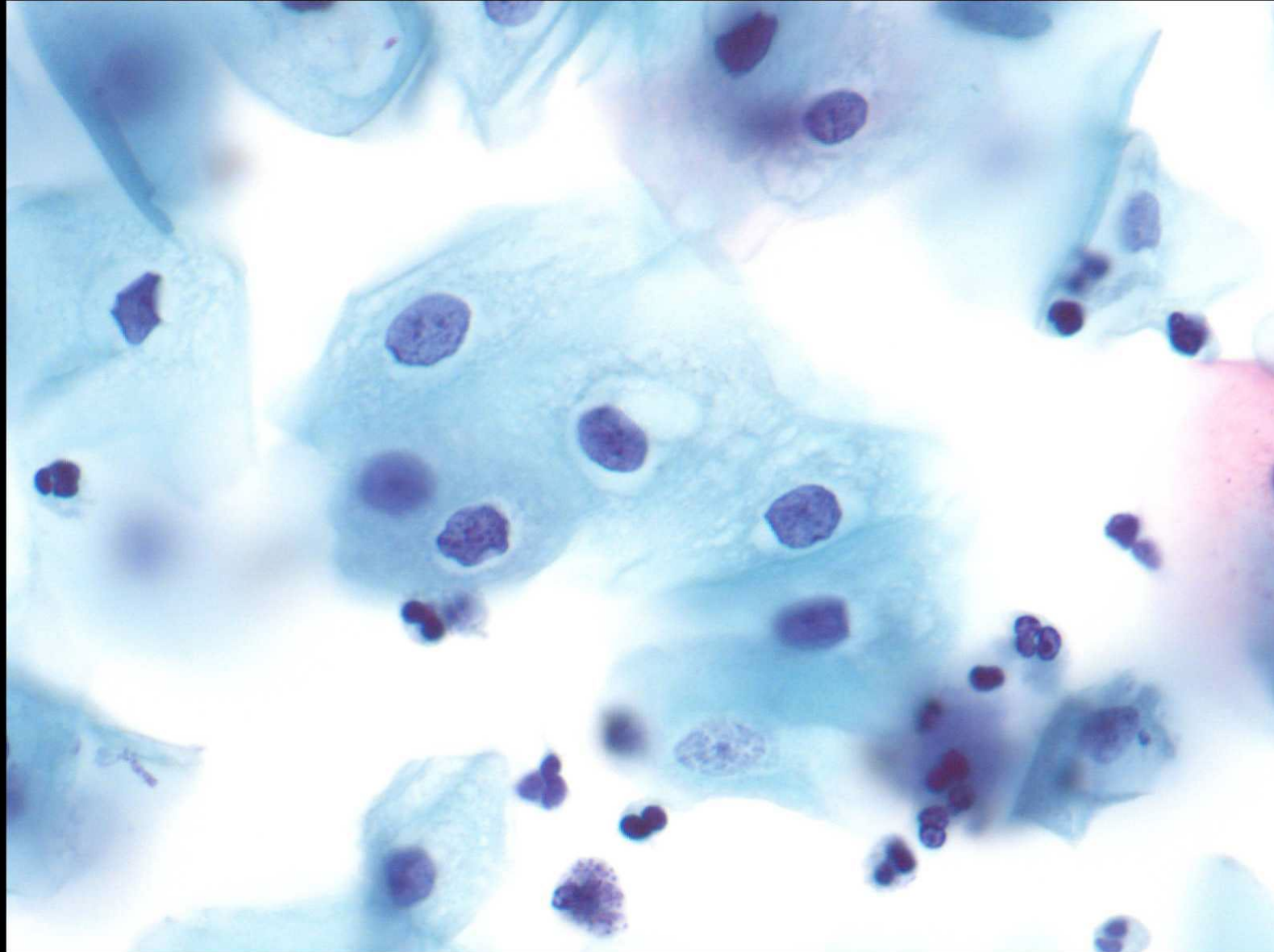


Moth-Eaten Cytoplasm



**Candida
was present
elsewhere**

Moth-Eaten Cytoplasm



Atypical Squamous Cells of Undetermined Significance (ASC-US)

Where is the bottom of LSIL?

- Reactive changes often simulate HPV viral cytopathic effect / LSIL
- If every reactive change was called LSIL the Pap test would produce far too many “positive” results
- If cytologists waited for perfect abnormal cells, Pap test sensitivity would dramatically drop

ASC-US

- An equivocal category designed to maximize sensitivity and specificity
- Primarily defined negatively: not normal (NILM) but also not definitely abnormal (LSIL/HSIL)
- An “objective” criterion: ASC-US cells should have nuclei 2½-3 times the size of an intermediate cell nucleus
- “Eyeballing” nuclear size is not very accurate compared with computer analysis*

*Schmidt *et al.* Cancer Cytopathol 2008; 114: 287.

ASC-US

- There is relatively low inter-observer agreement on ASC-US
- ASC-US rates vary widely among pathologists and laboratories
- Monitoring of ASC:SIL ratio and HPV positive rates in ASC-US have been proposed as means to make the category more uniform*
- CAP periodically publishes survey data that provides normative data for intra-laboratory comparisons

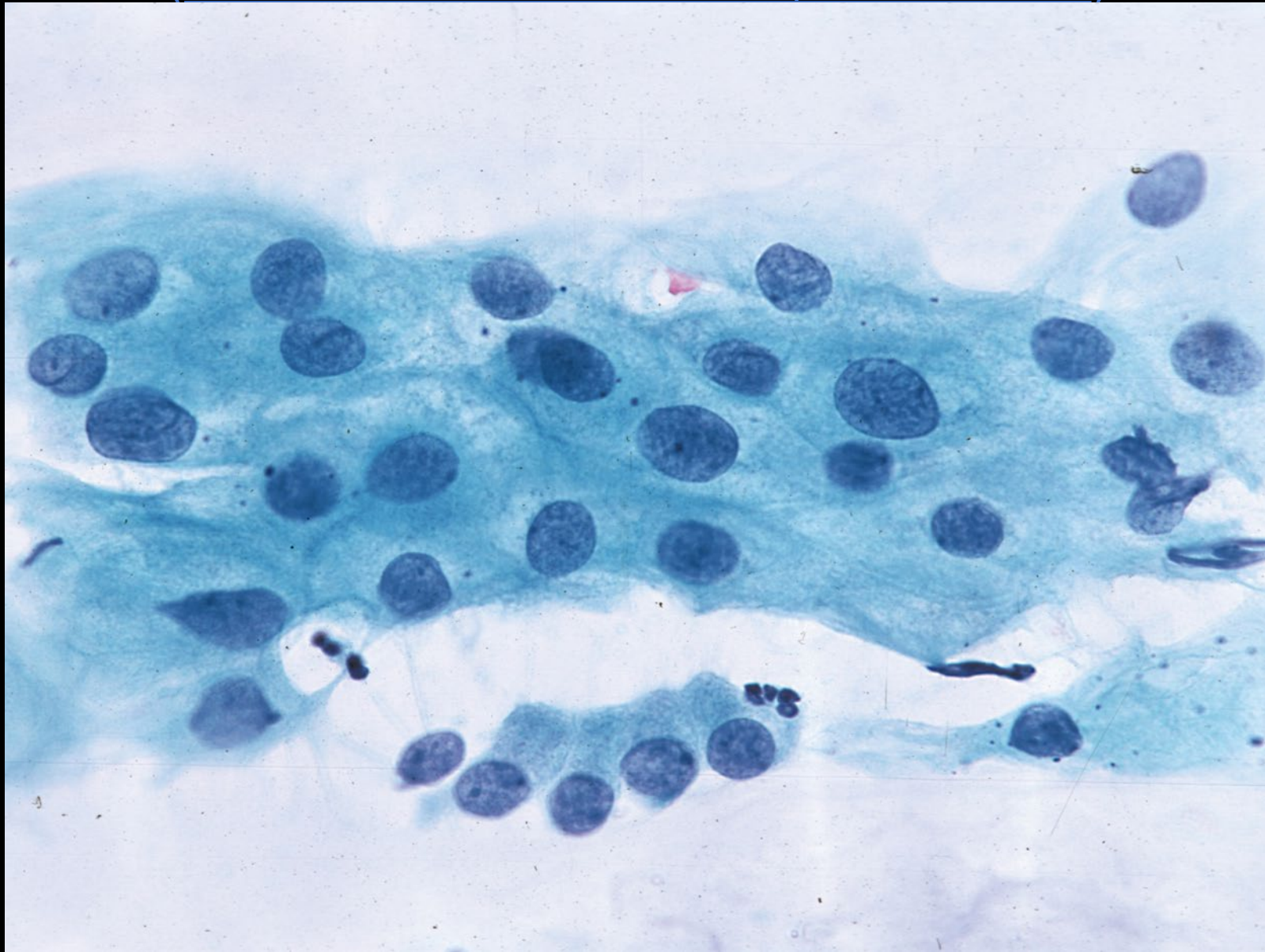
*Cibas *et al.* Am J Clin Pathol 2008; 129: 97.

Can we make ASC-US go away?

- Some experts have recommended elimination of the ASC-US “wastebasket”
- Unfortunately, every attempt to move the threshold for ASC-US higher comes at the cost of missed cancer and pre-cancer
- Most high grade intraepithelial lesions found by colposcopy follow ASC-US Pap tests

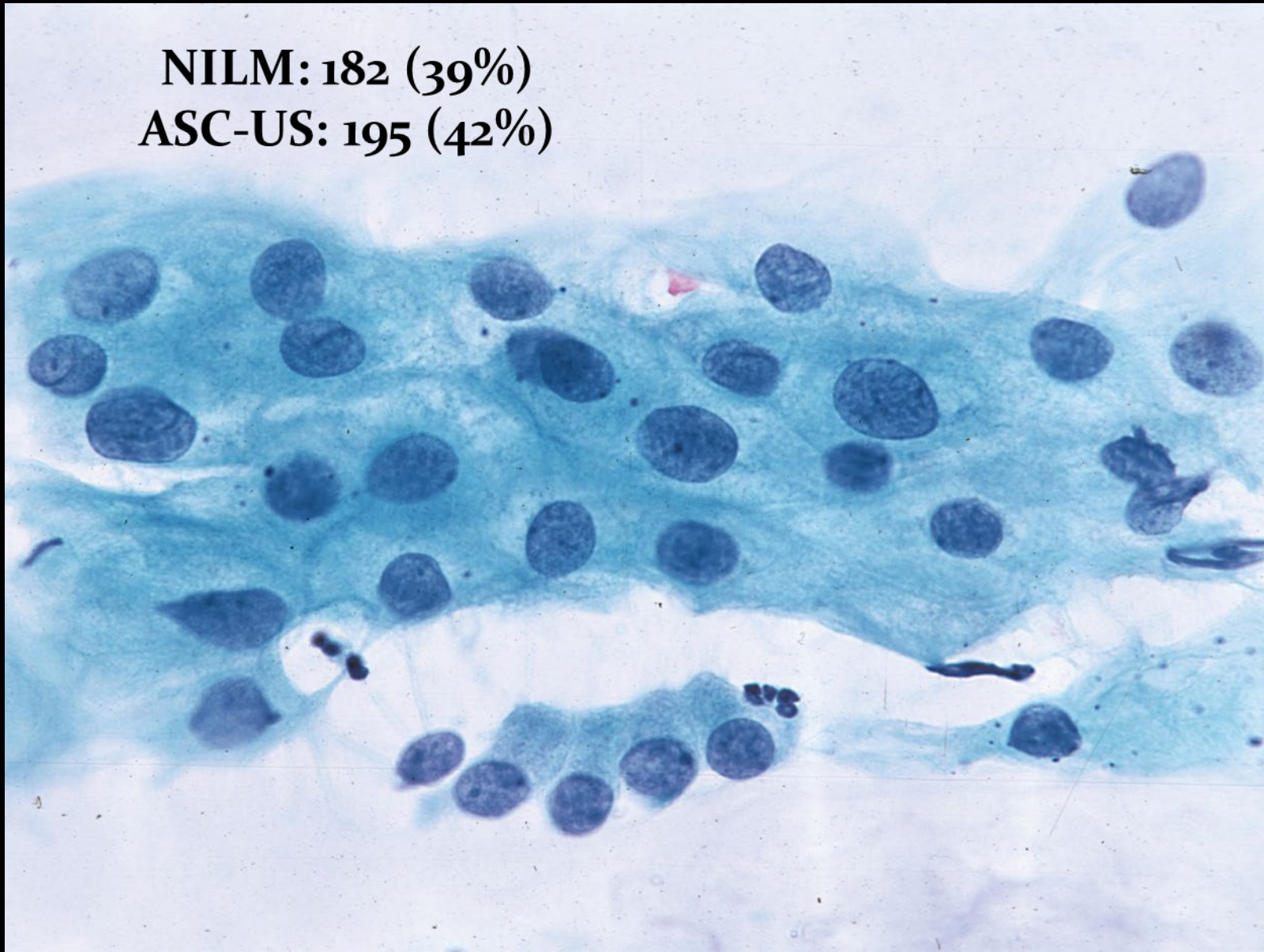
Bethesda Online Atlas

(bethesda.soc.wisc.edu/index.htm)

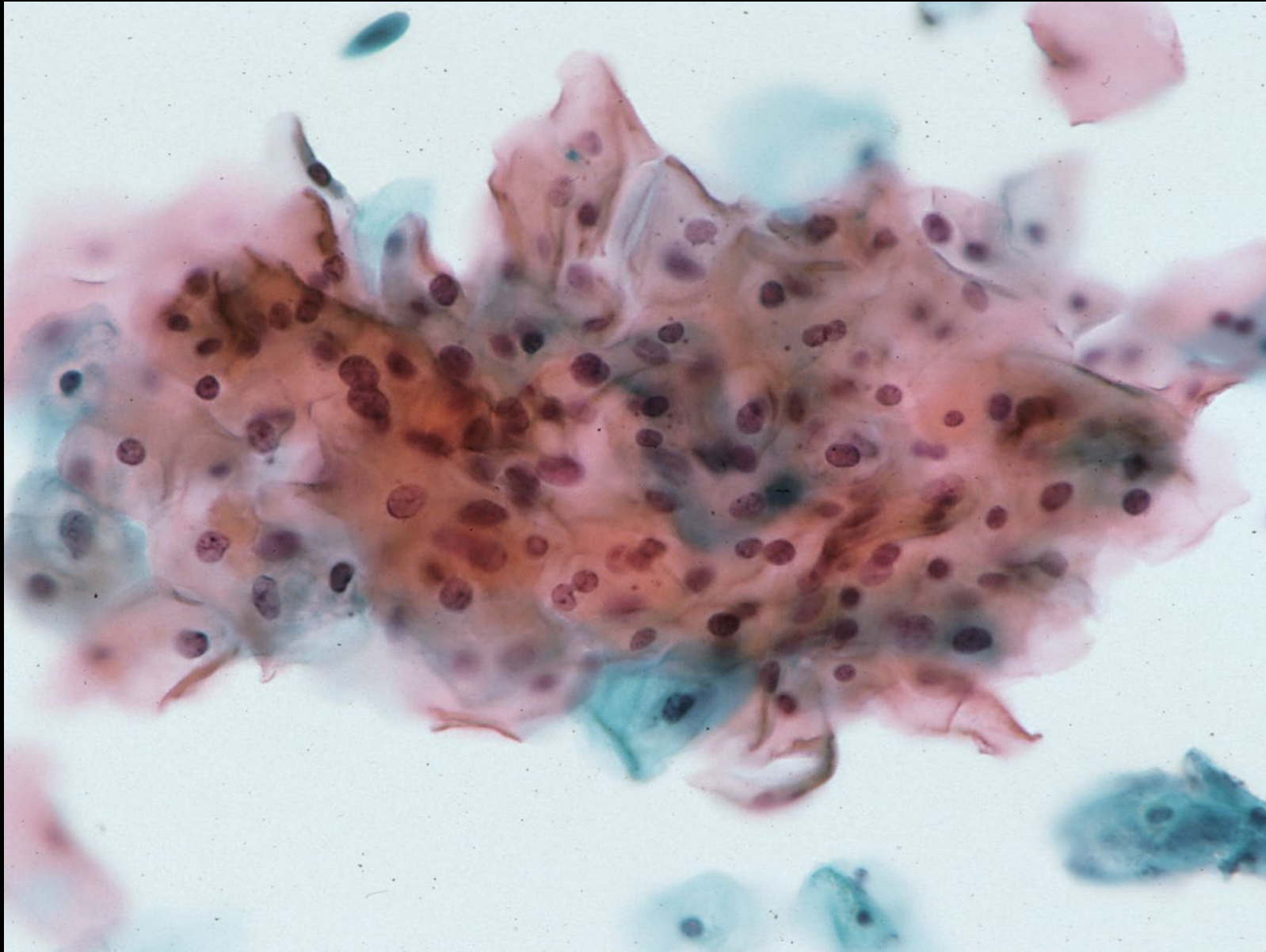


Bethesda Online Atlas

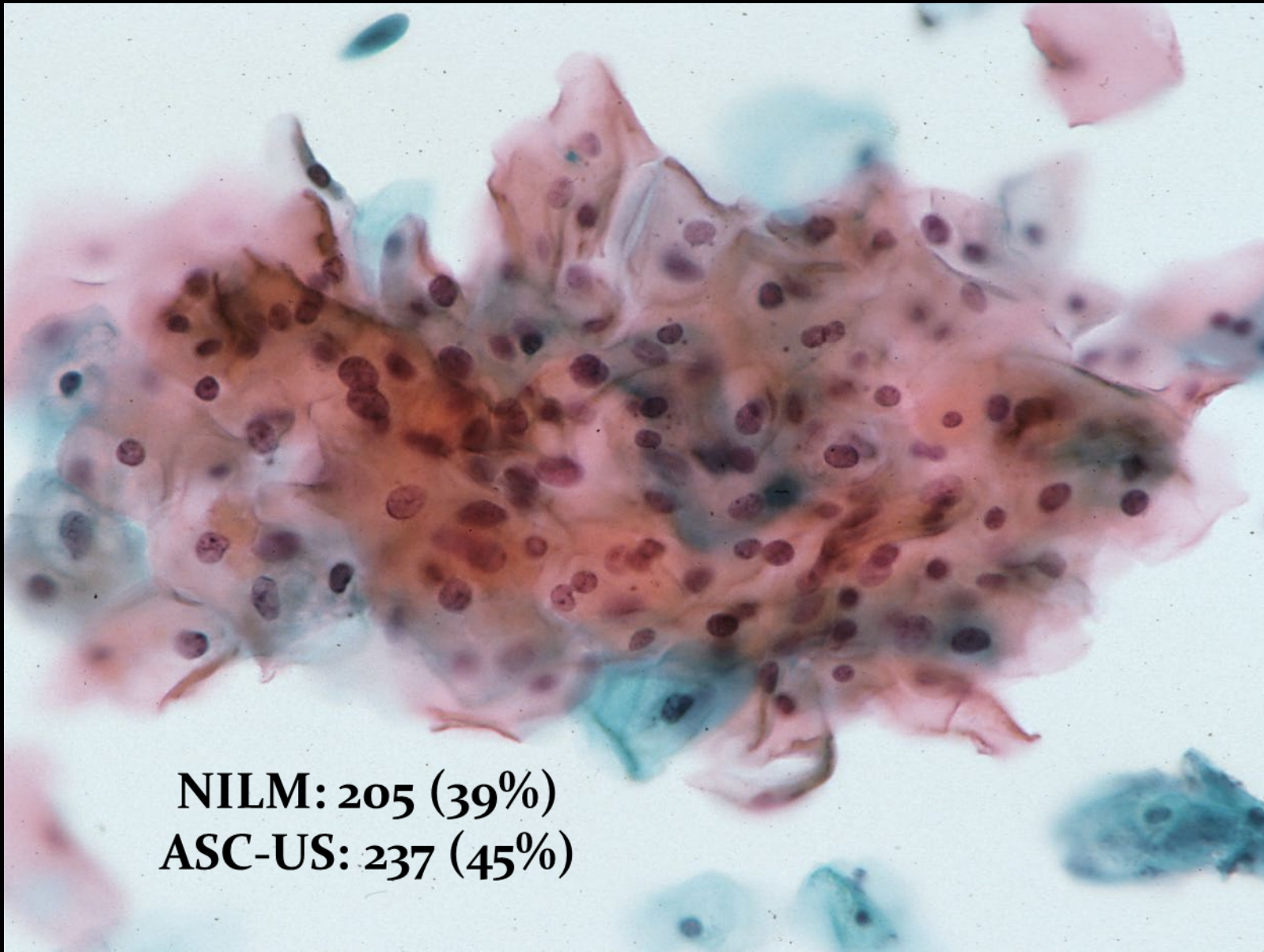
NILM: 182 (39%)
ASC-US: 195 (42%)



Bethesda Online Atlas

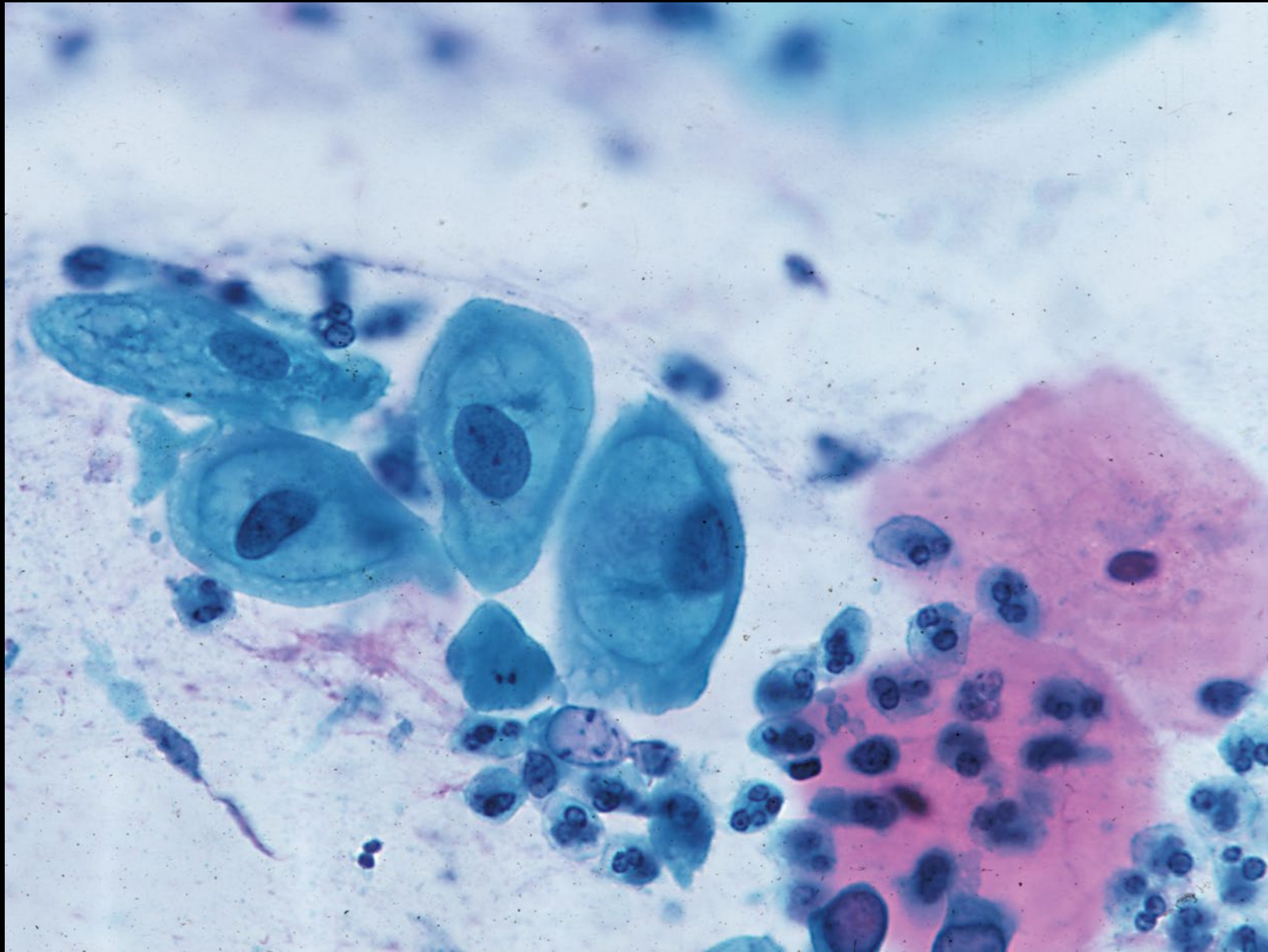


Bethesda Online Atlas

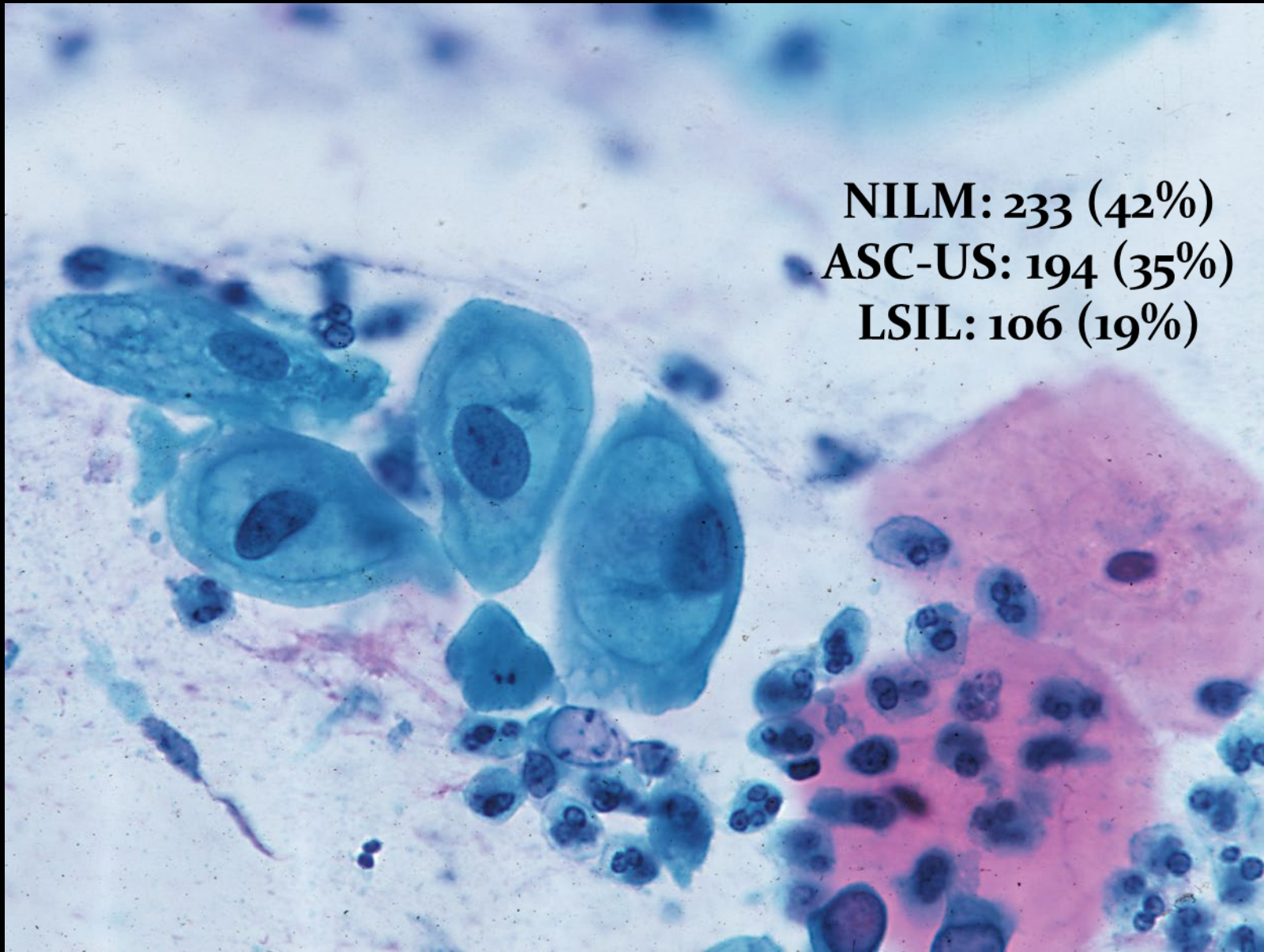


NILM: 205 (39%)
ASC-US: 237 (45%)

Bethesda Online Atlas

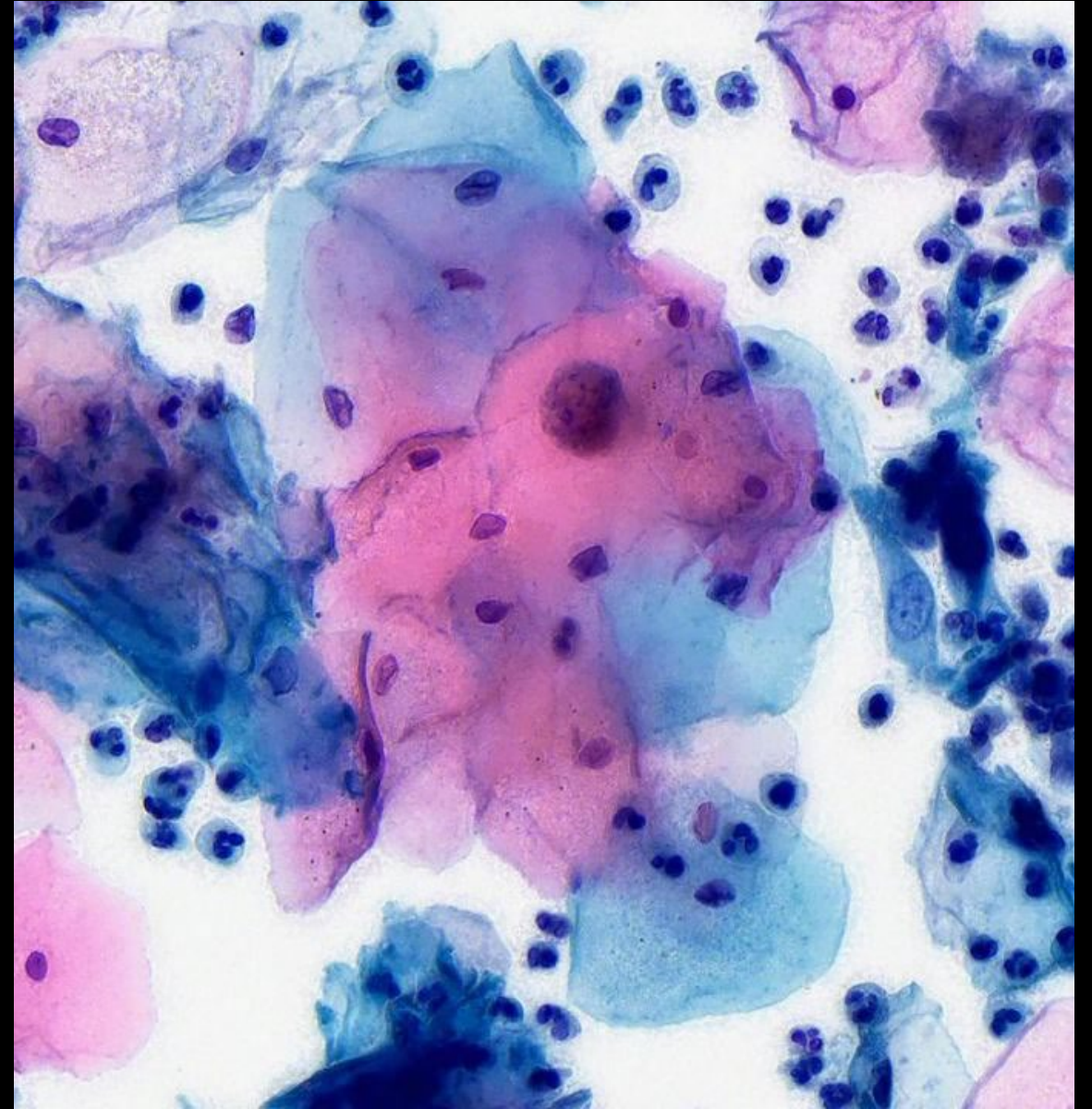
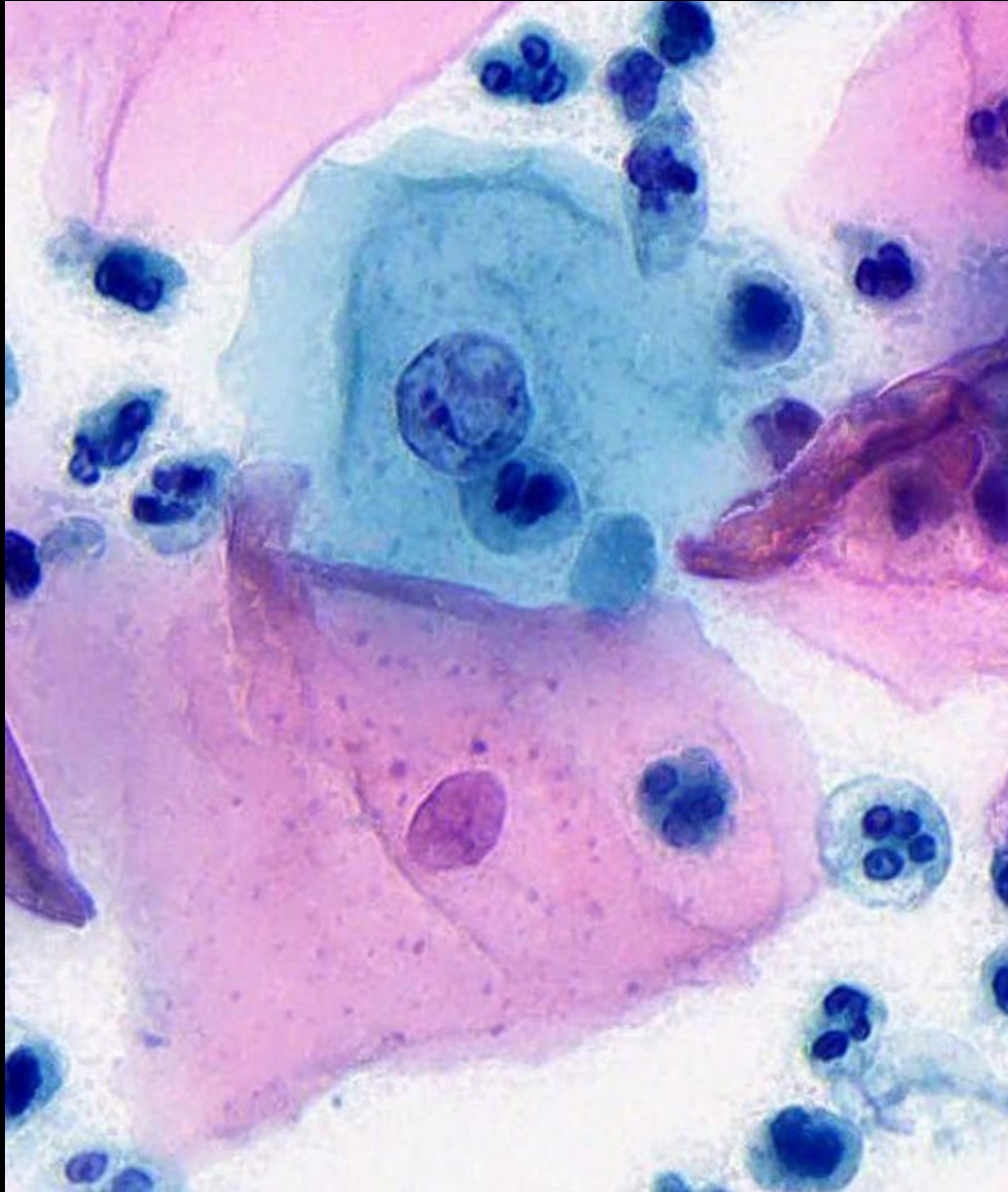


Bethesda Online Atlas

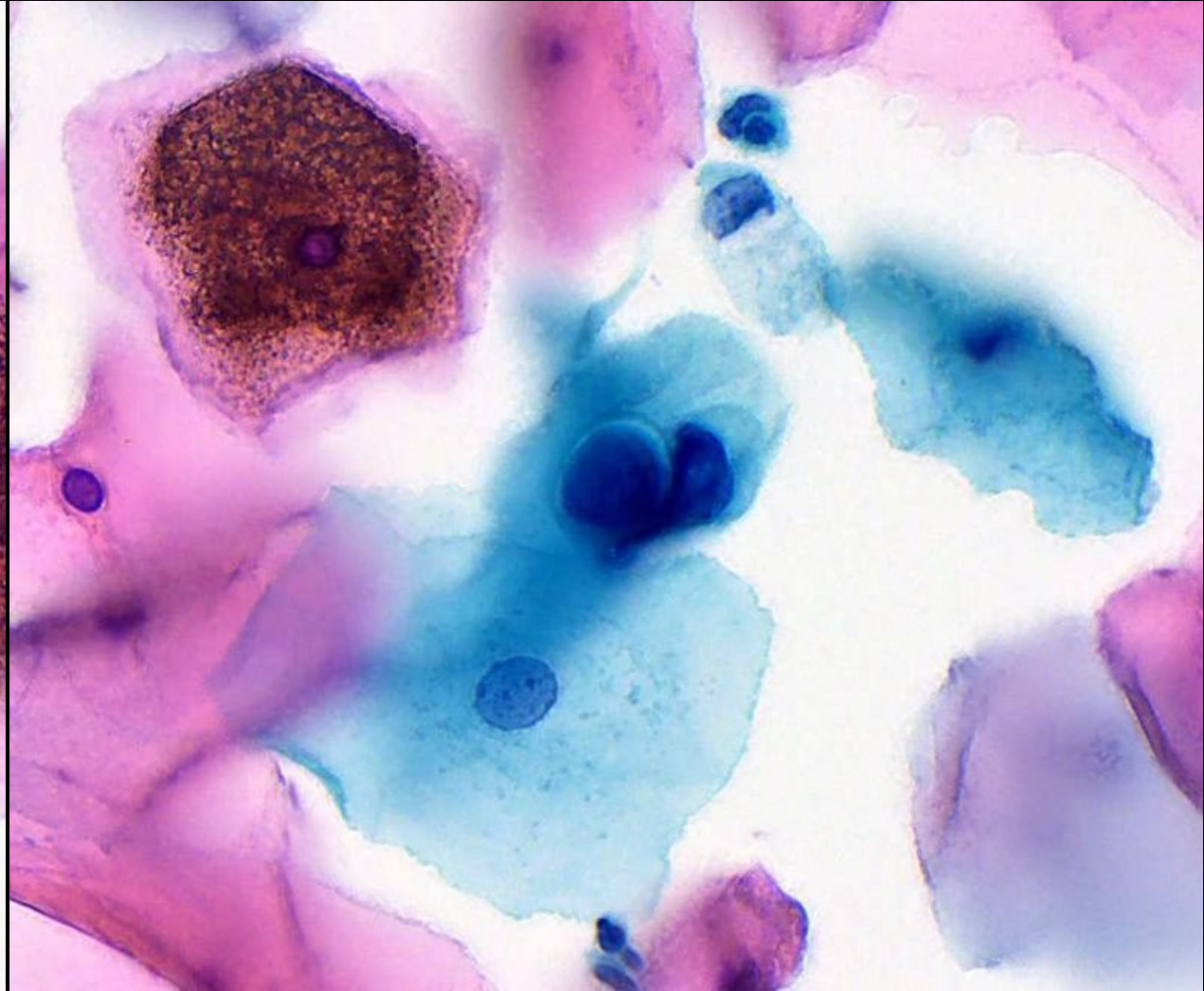
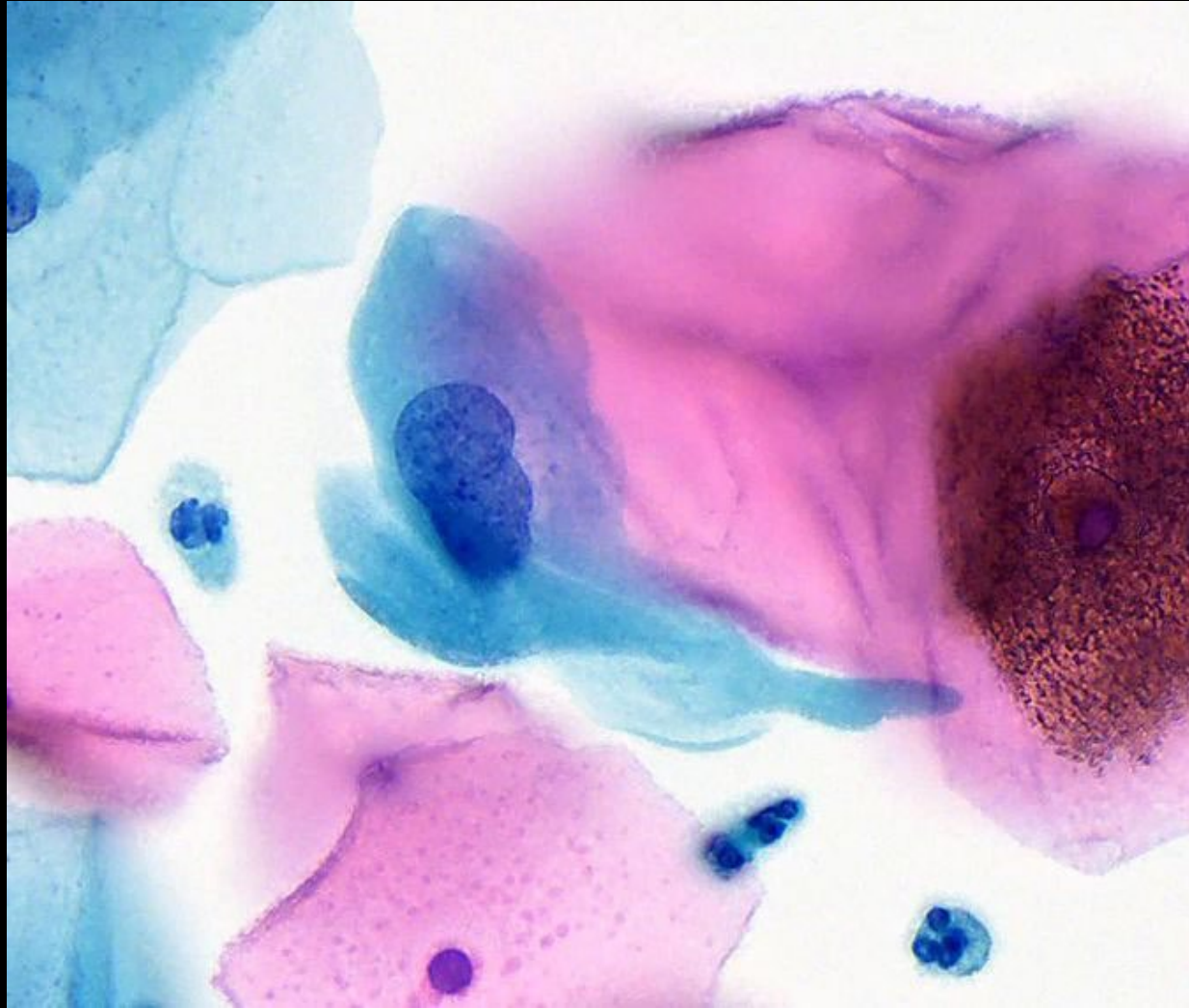


NILM: 233 (42%)
ASC-US: 194 (35%)
LSIL: 106 (19%)

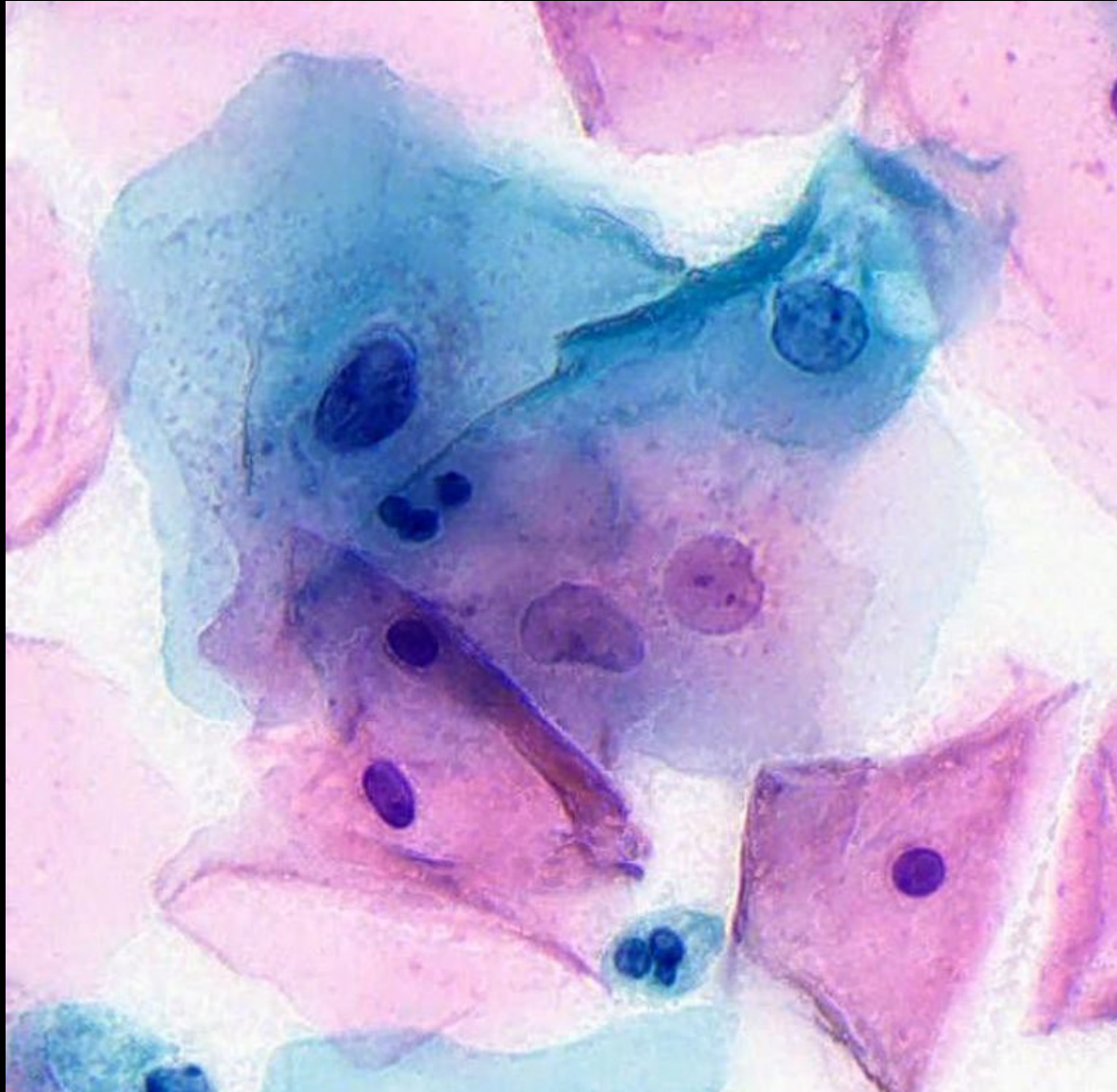
IAC-CAP Digital Atlas



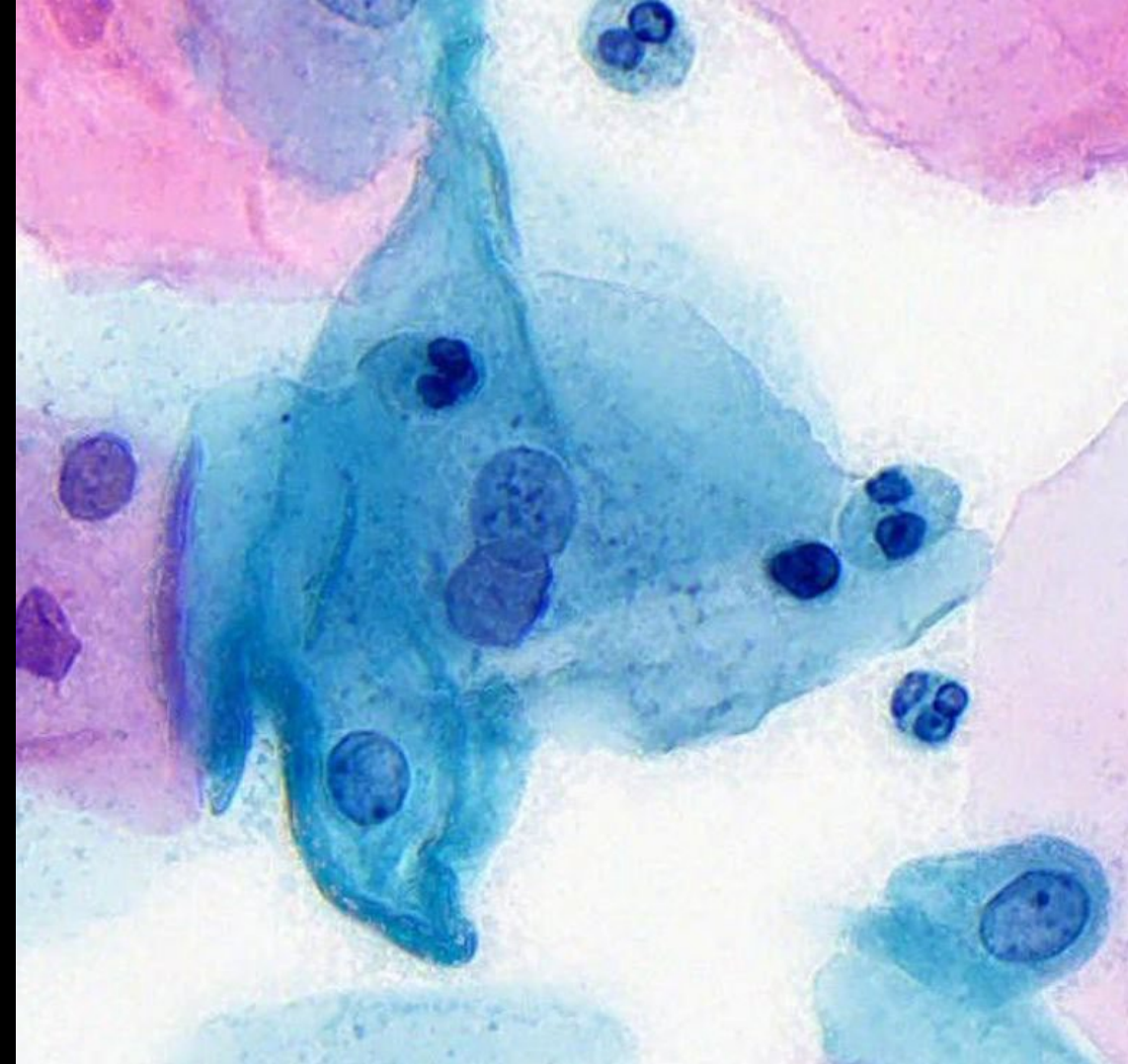
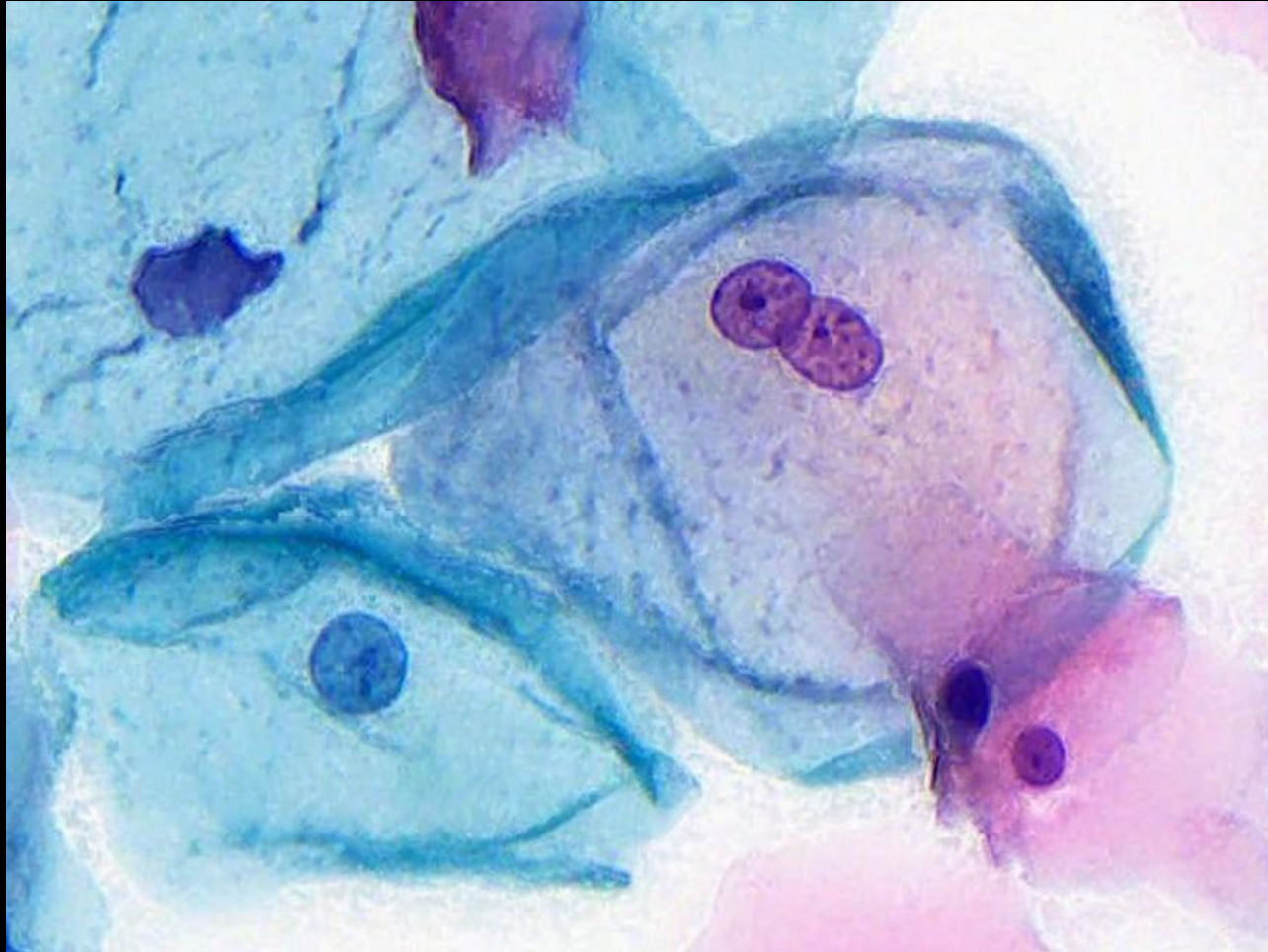
IAC-CAP Digital Atlas



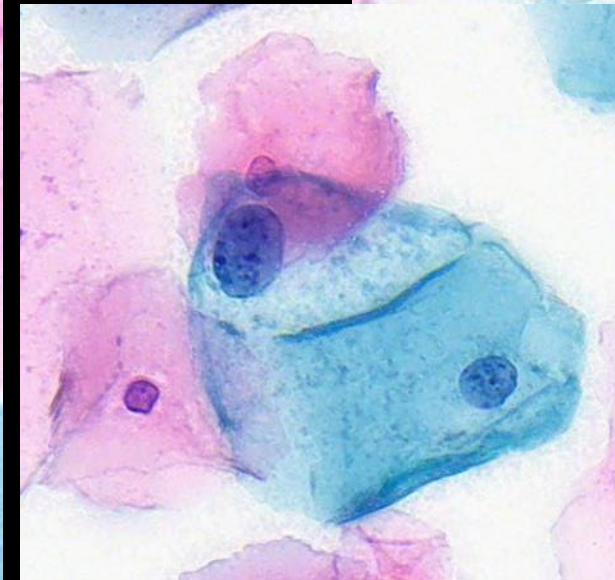
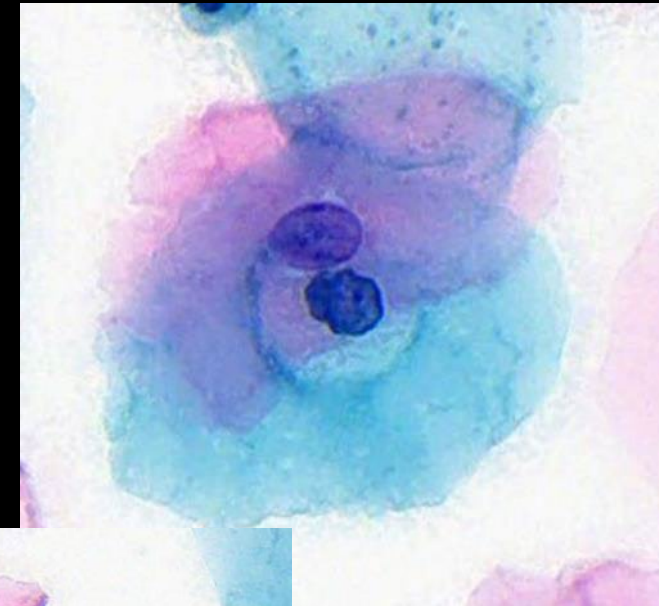
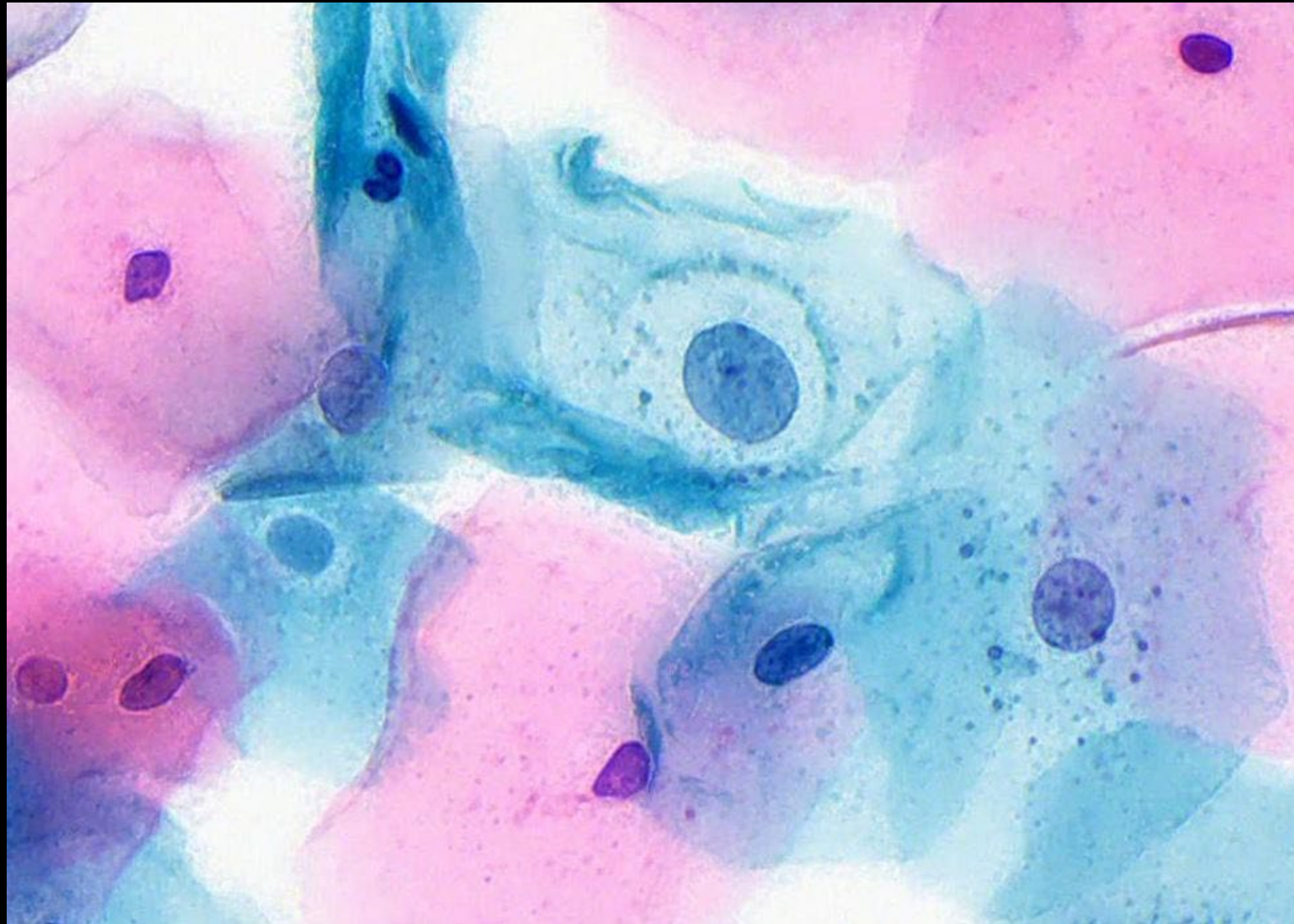
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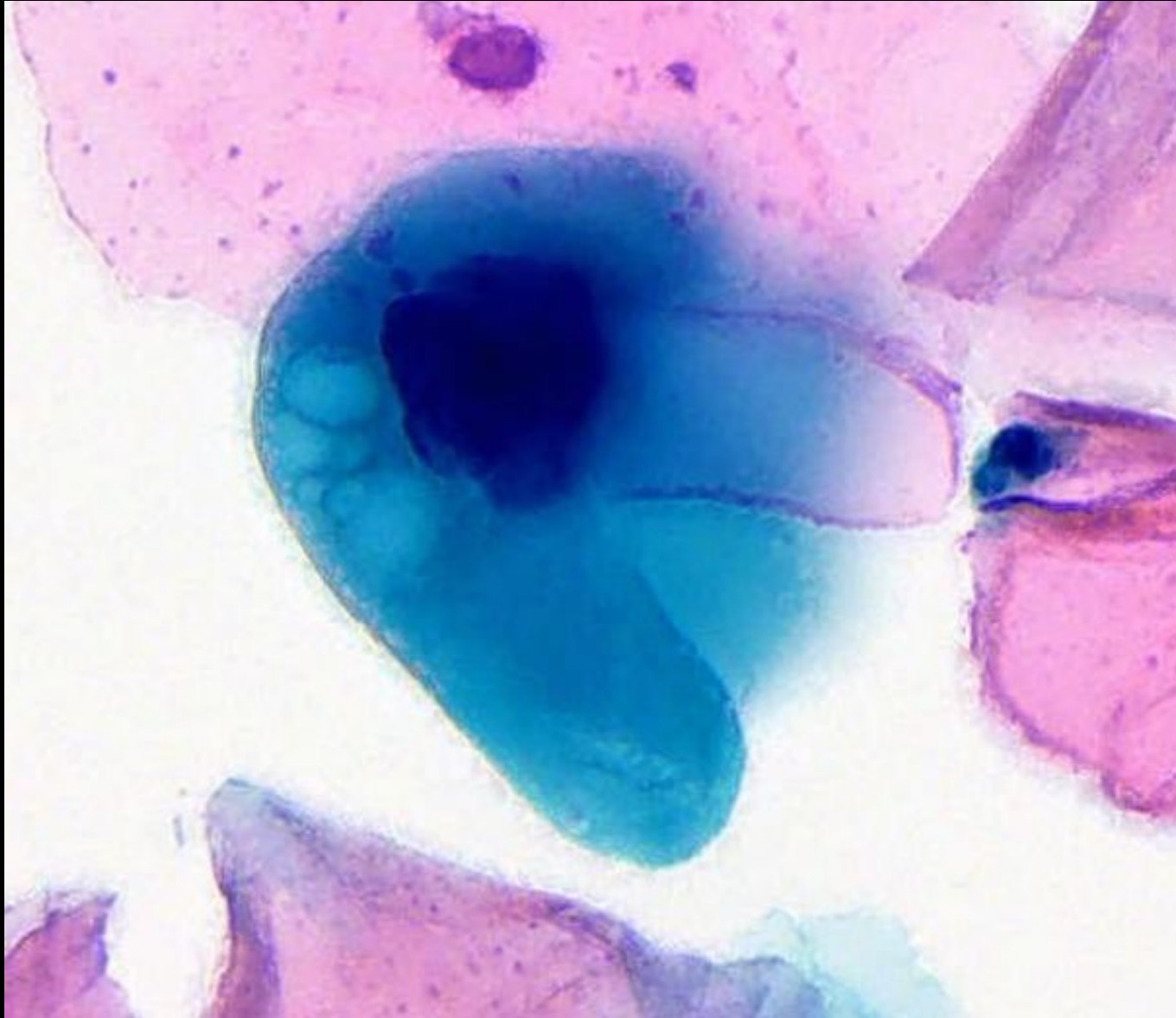
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IAC-CAP Digital Atlas



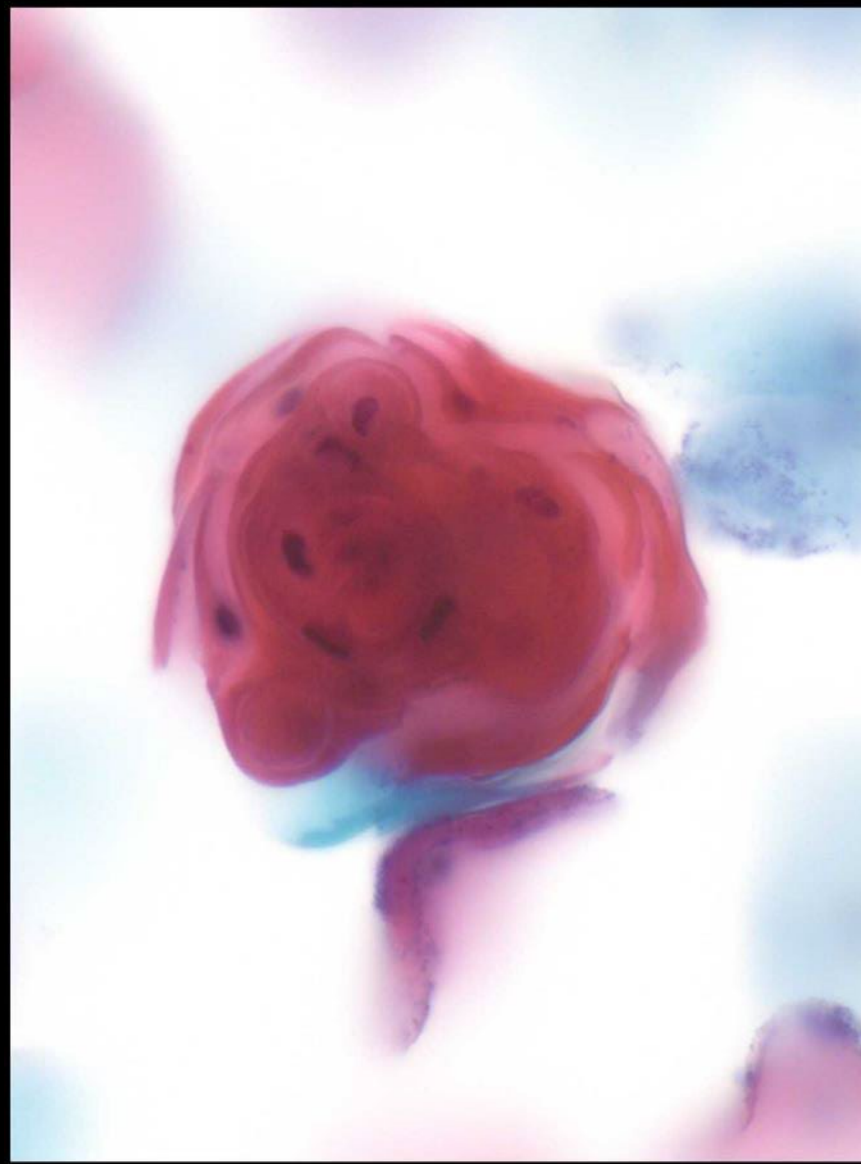
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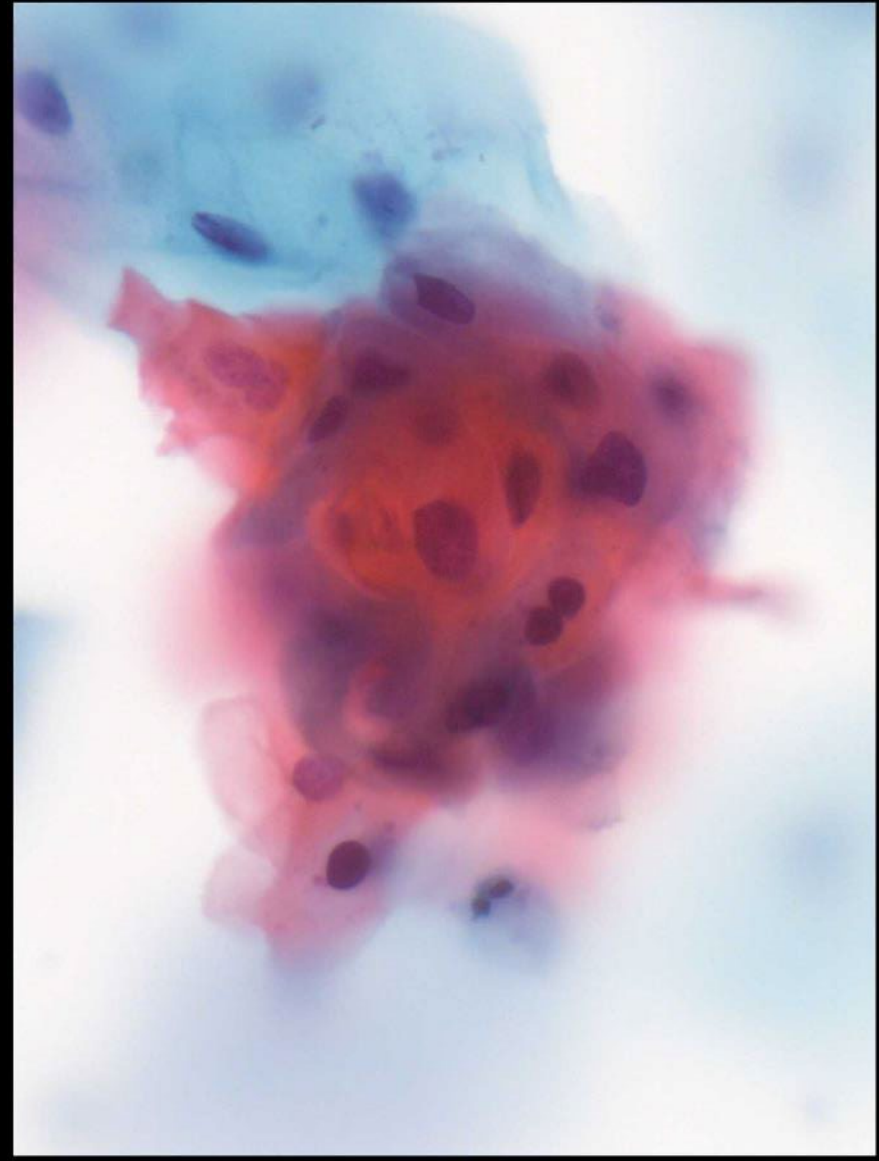
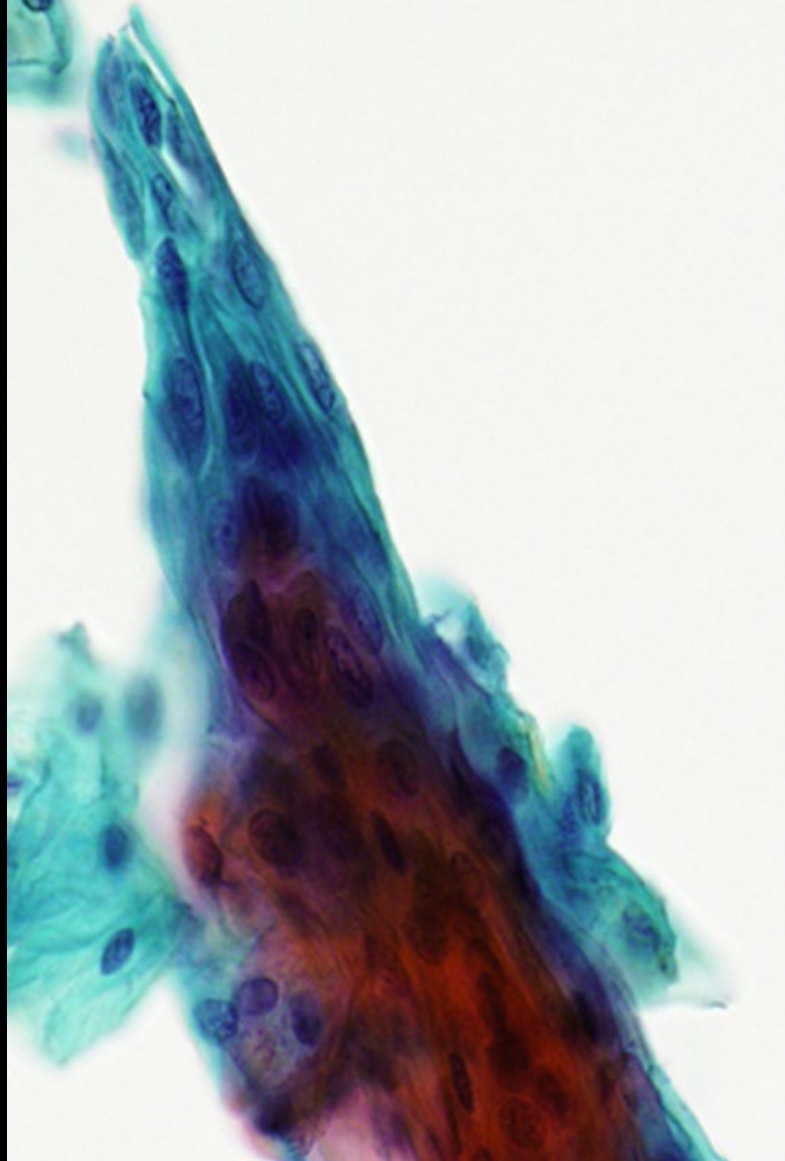
Special Types of ASC-US

- Some problems happen over and over:
 - Atypical parakeratosis
 - Usually reactive to acute inflammation/organisms
 - Cannot rule out the top of a condyloma
 - Atypical repair
 - Atypical nuclear enlargement
 - Could be due to atrophy, inflammation, radiation, chemotherapy, folate/B12 deficiency, etc.
 - Cannot rule out HPV as a contributing factor

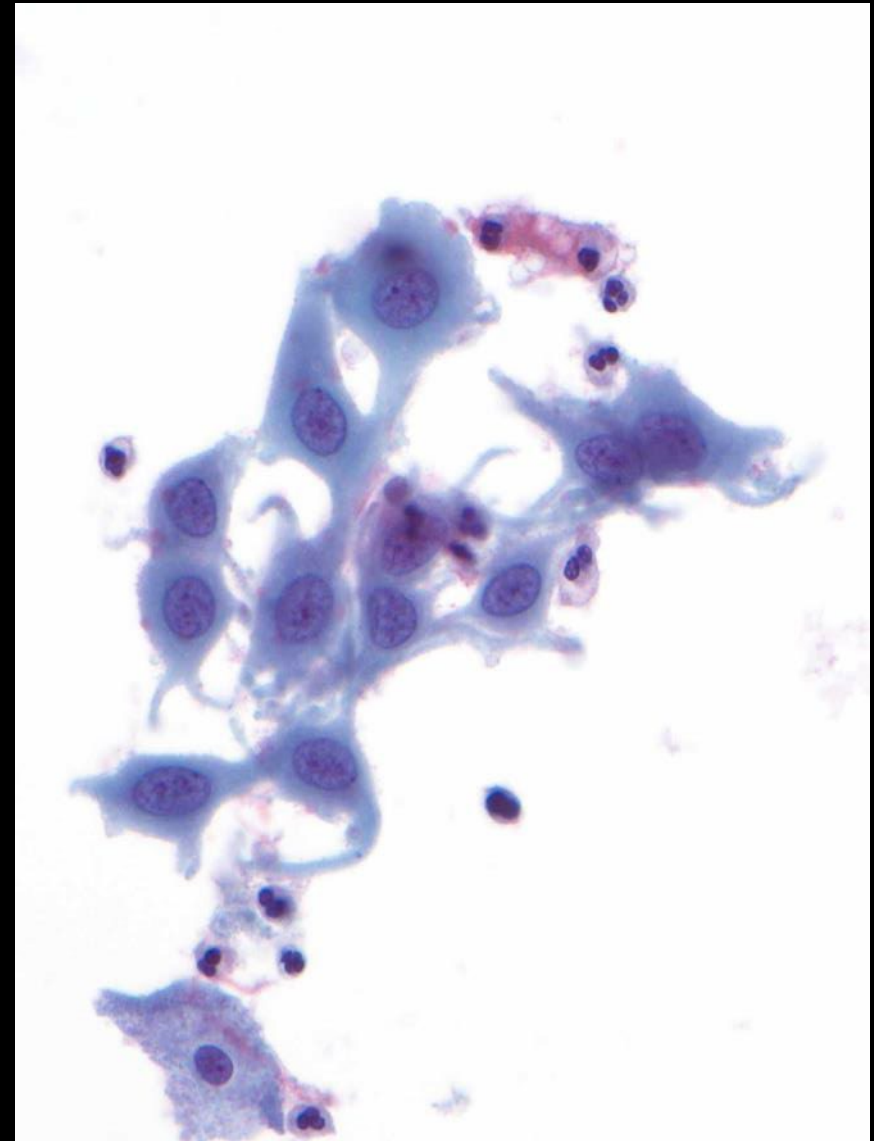
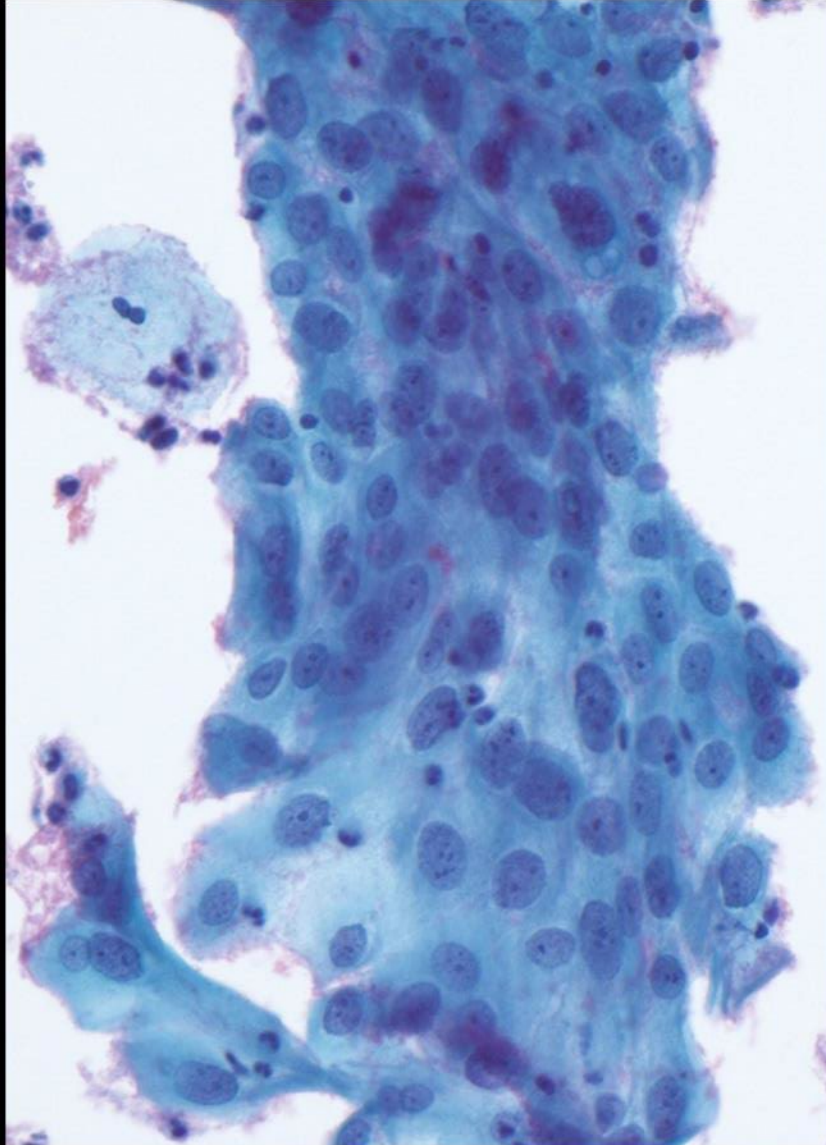
Parakeratosis



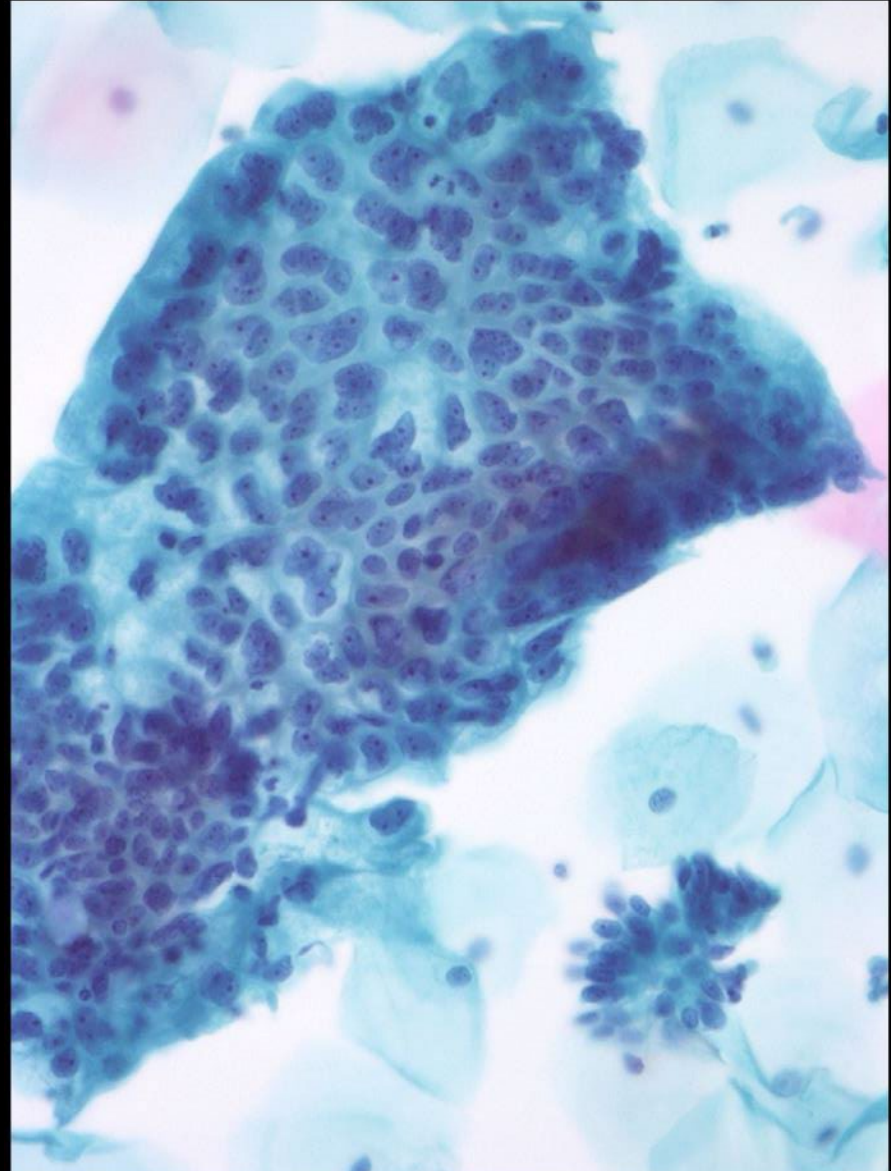
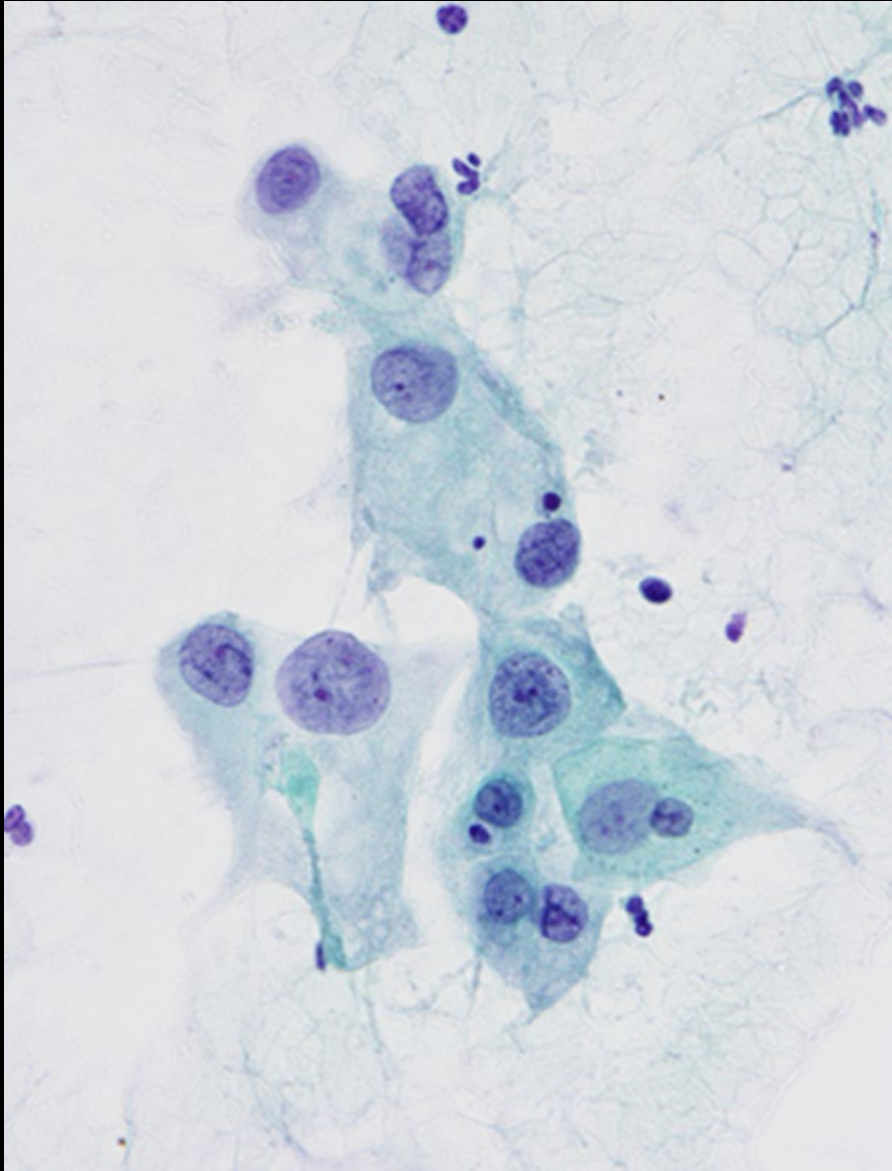
Atypical Parakeratosis



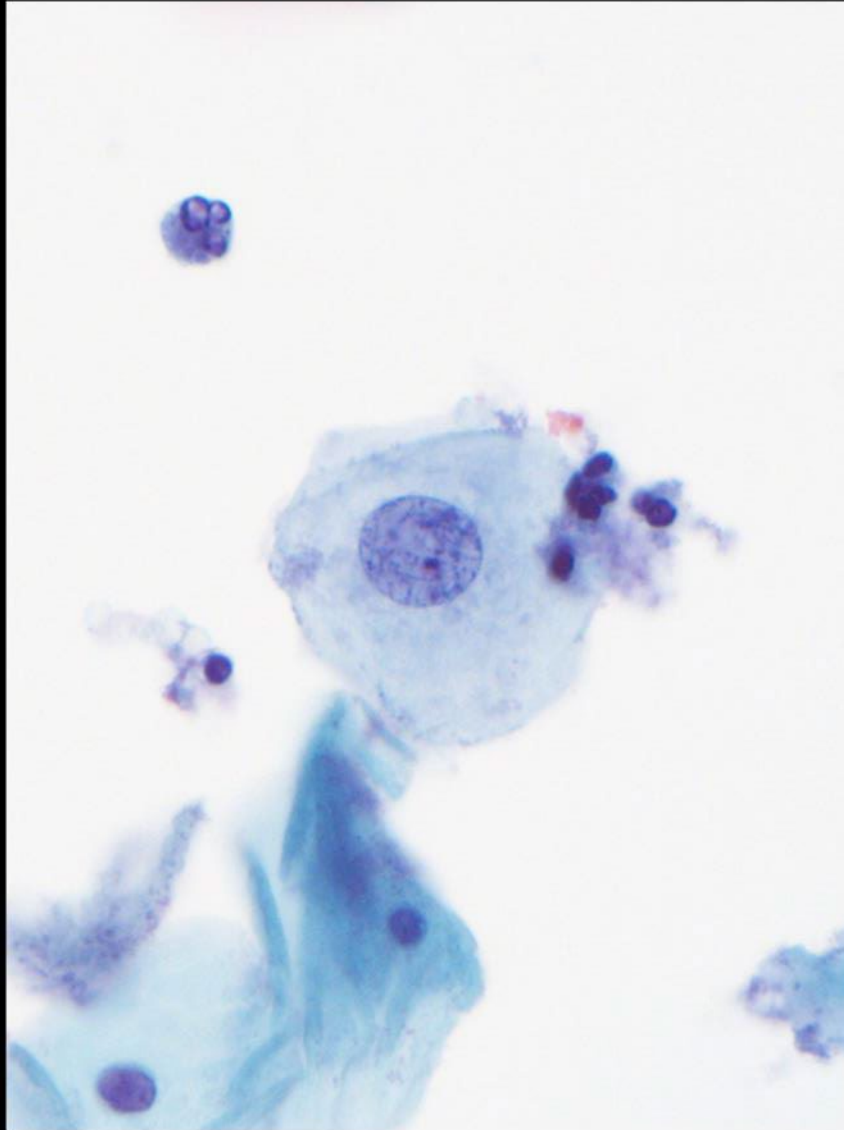
Repair



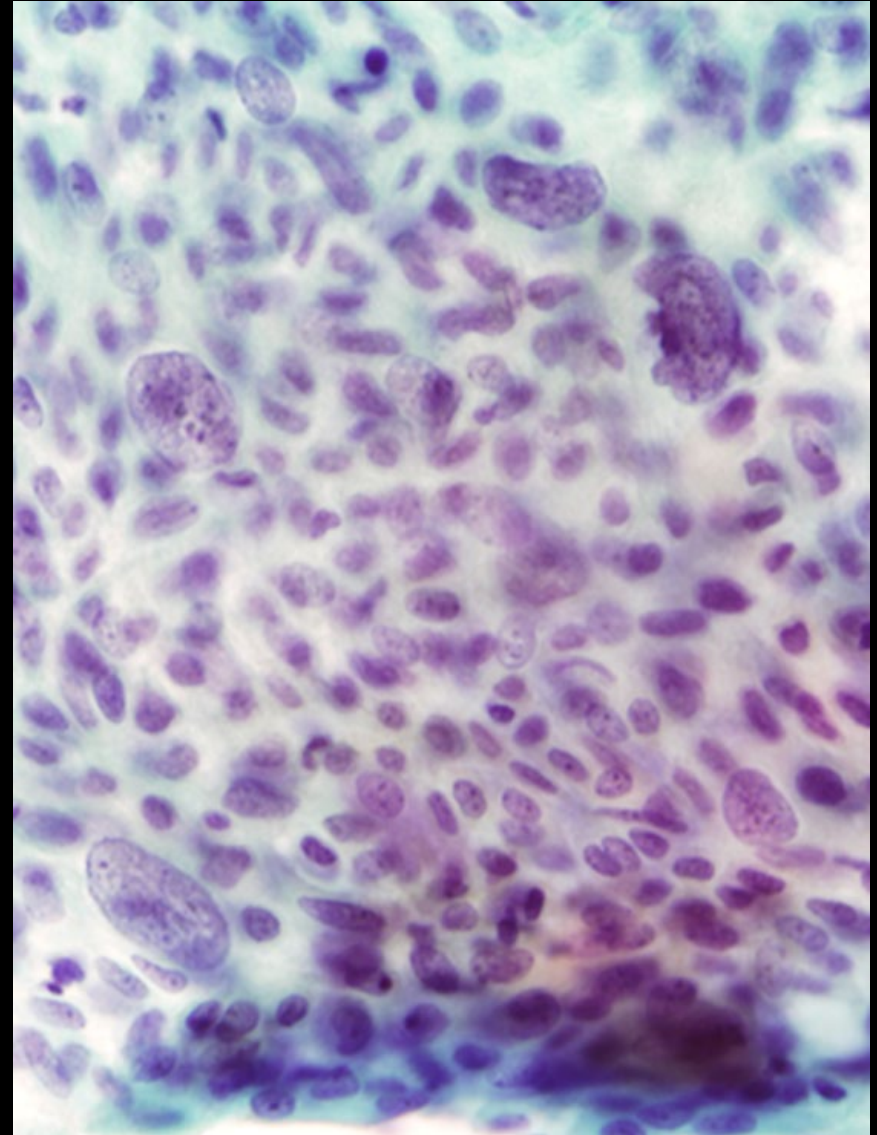
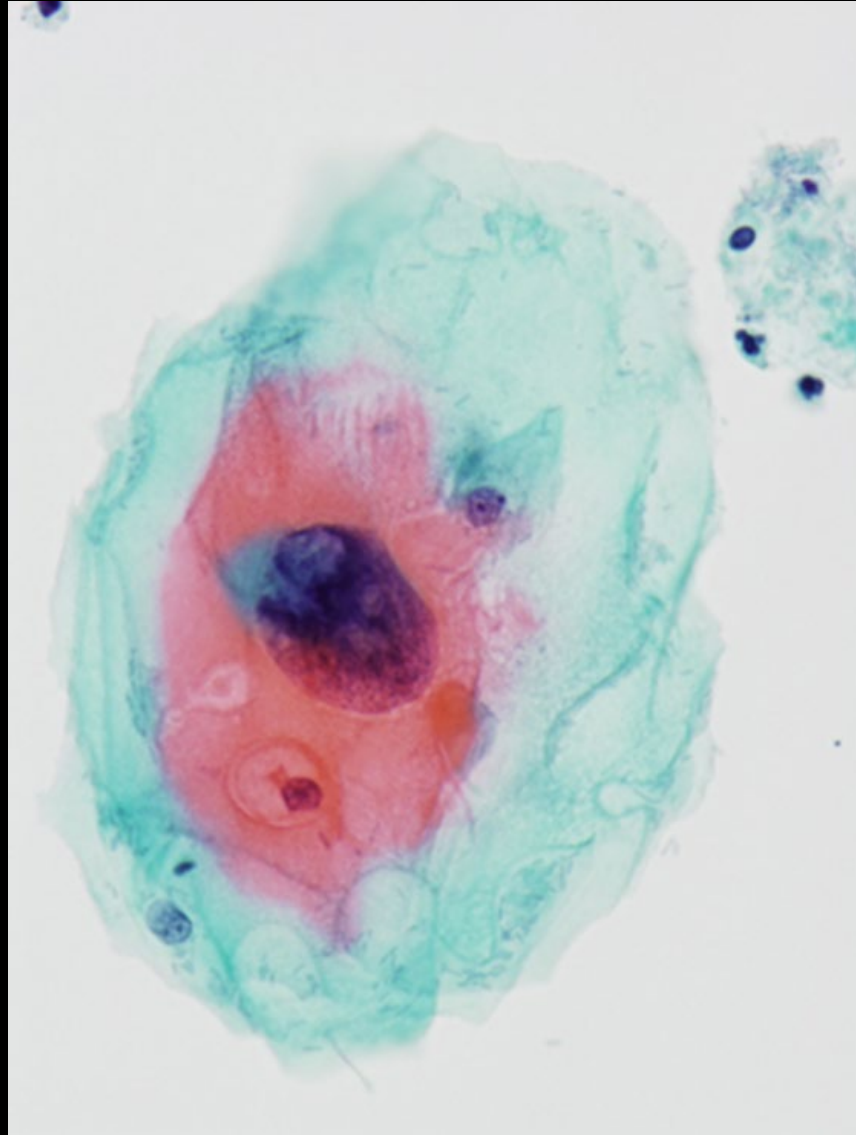
Atypical Repair



Nuclear Enlargement



Atypical Nuclear Enlargement



High-Grade Squamous Intraepithelial Lesion (HSIL)

HSIL

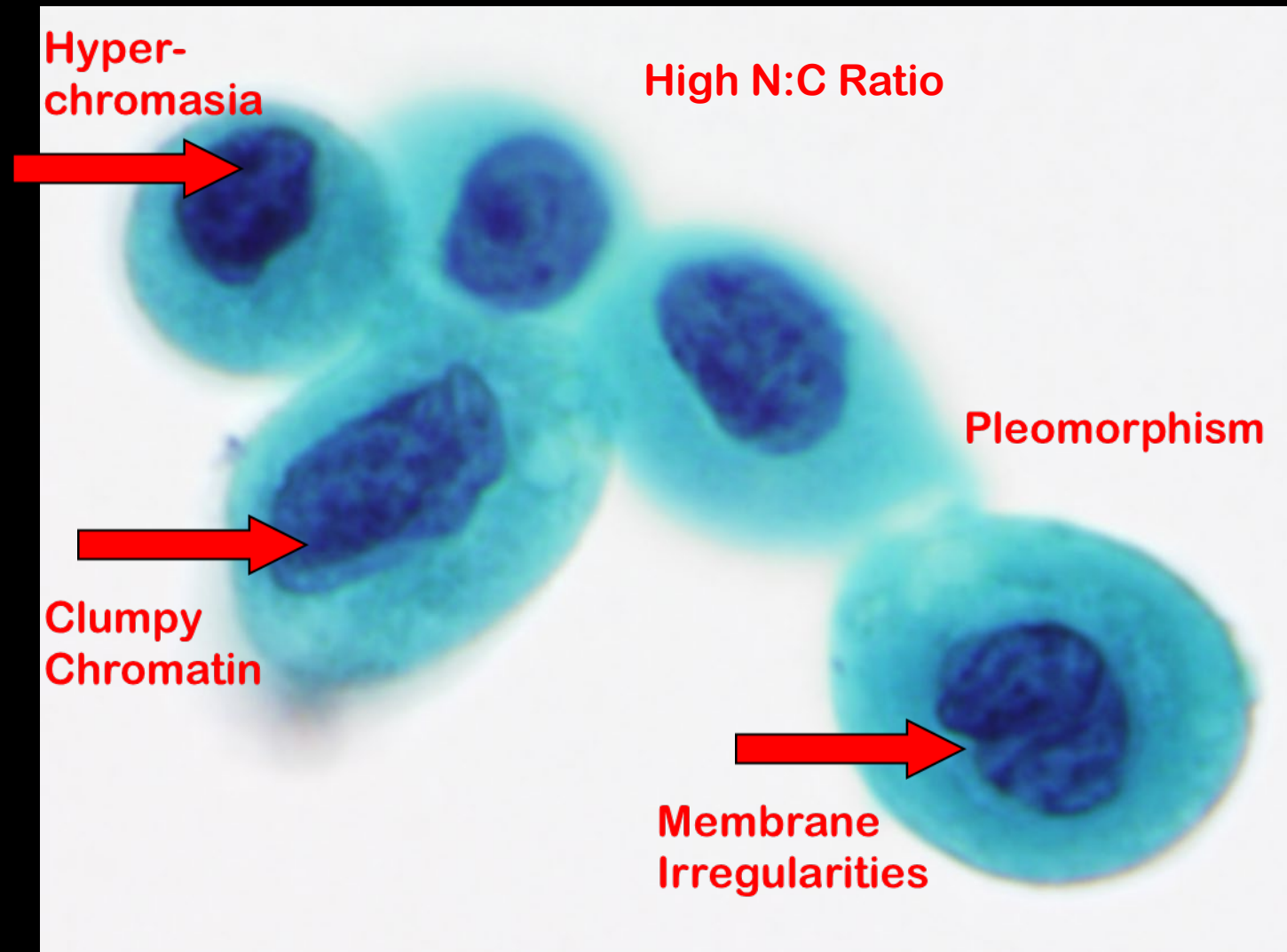
- This is what we are really looking for
 - LSIL is easier to recognize but less important
 - Even after LSIL is found, the rest of the slide must still be screened for HSIL
- HSIL is puzzling to many trainees because it “breaks the rules”
 - The nuclear size of HSIL is usually smaller than LSIL
 - HSIL is “squamous” but often displays glandular-type features due its location at the transformation zone

HSIL

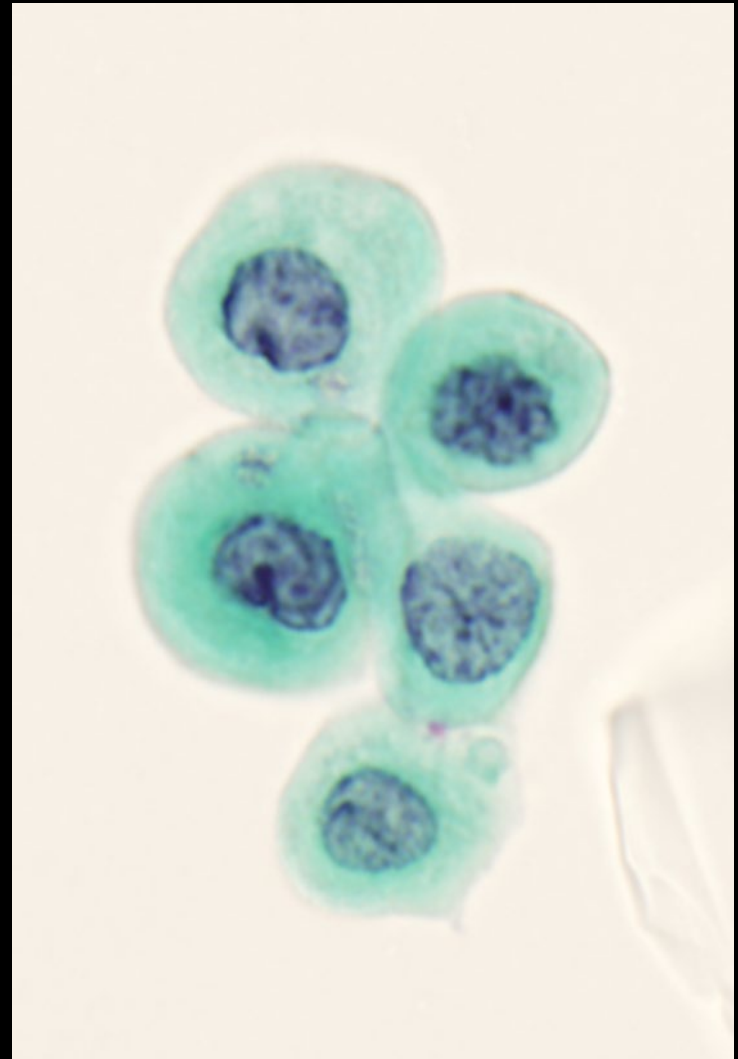
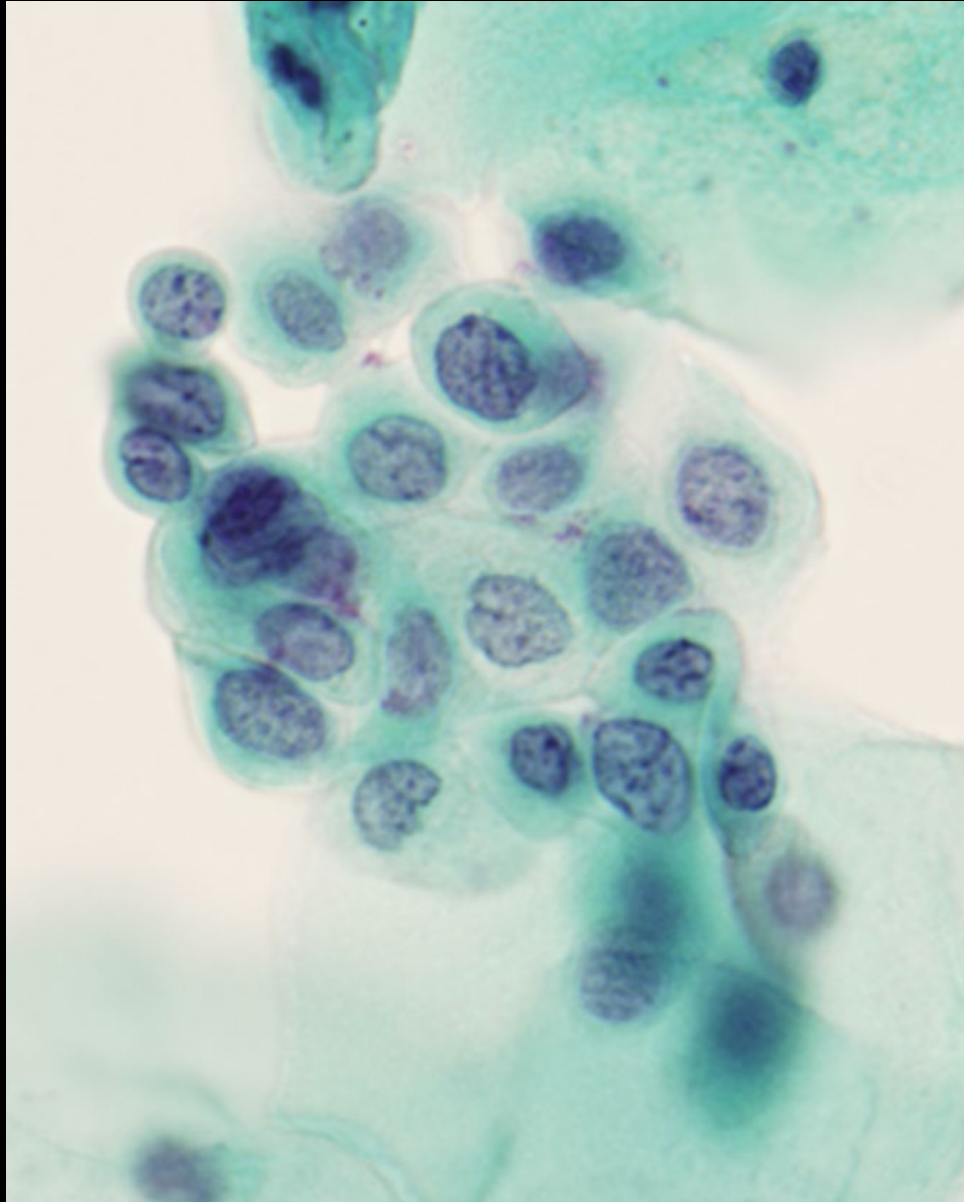
- LSIL is viral cytopathic effect
 - The virus is replicating itself with the goal of shedding infectious virions
- HSIL follows integration of HPV into the host genome
 - HPV tries to sustain the cells it lives in, triggering carcinogenesis via the p16/RB pathway
- Nuclear changes (darkness, enlargement) correspond to increased numbers of chromosomes*

*Olaharsky *et al.* Carcinogenesis 2006; 27: 337.

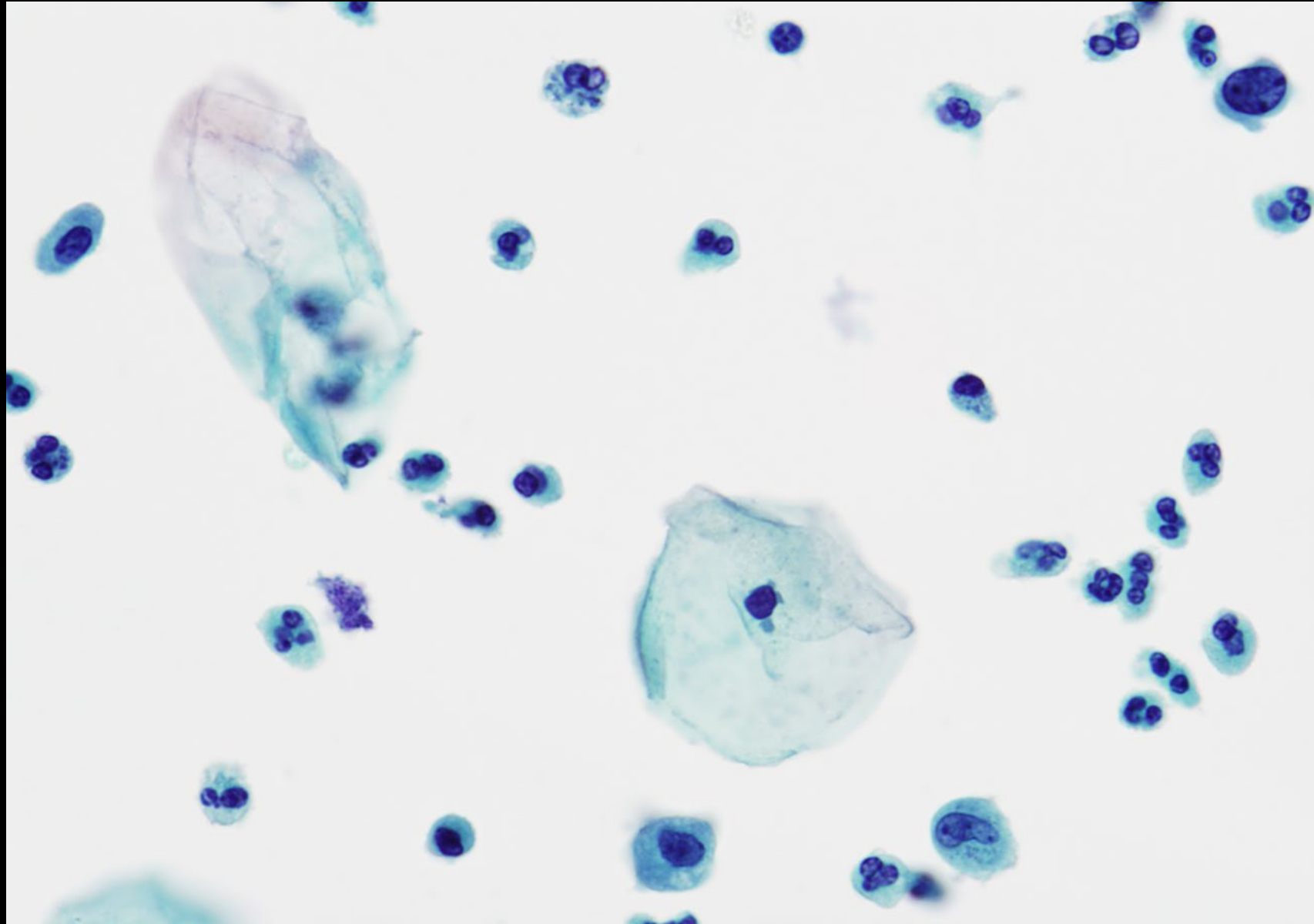
HSIL Features (SurePath)



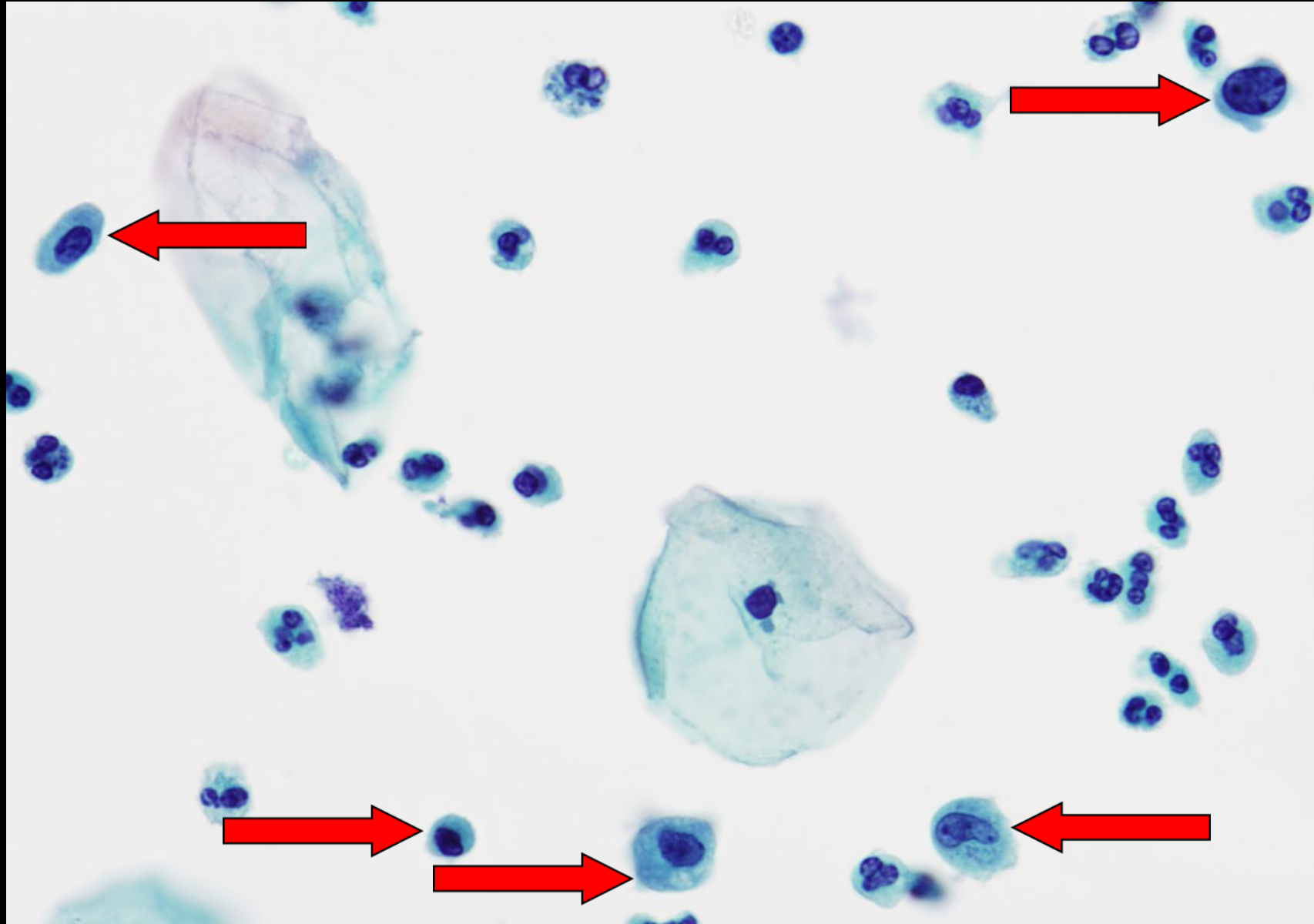
HSIL on ThinPrep



“Litigation Cells”



Individual cells may be subtle

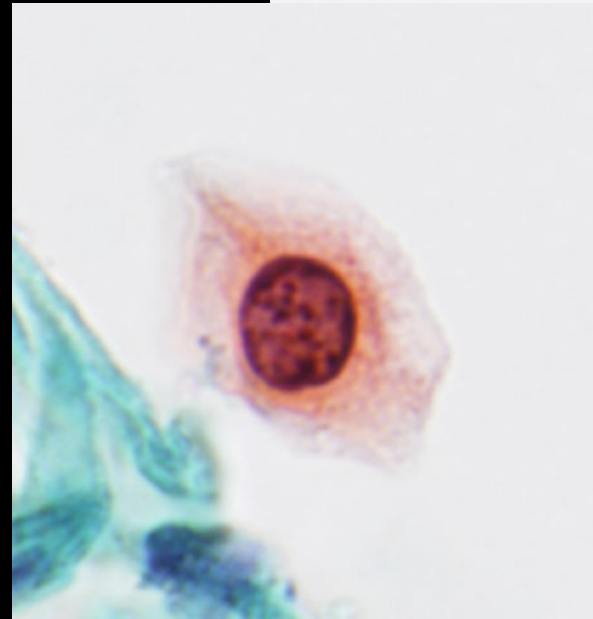
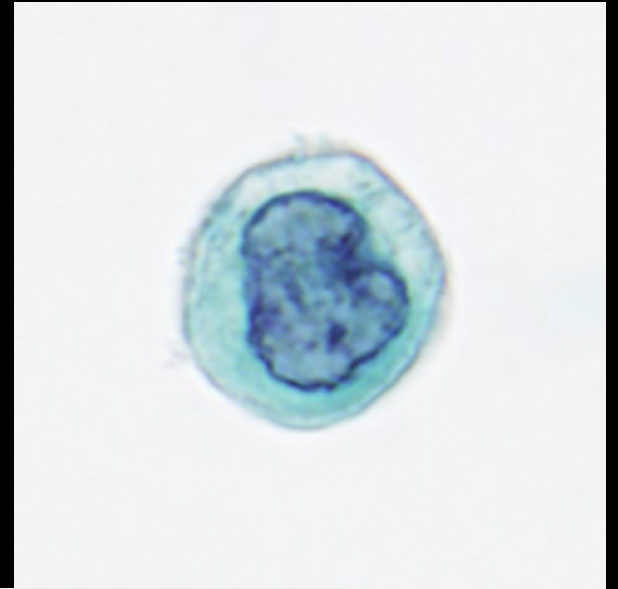
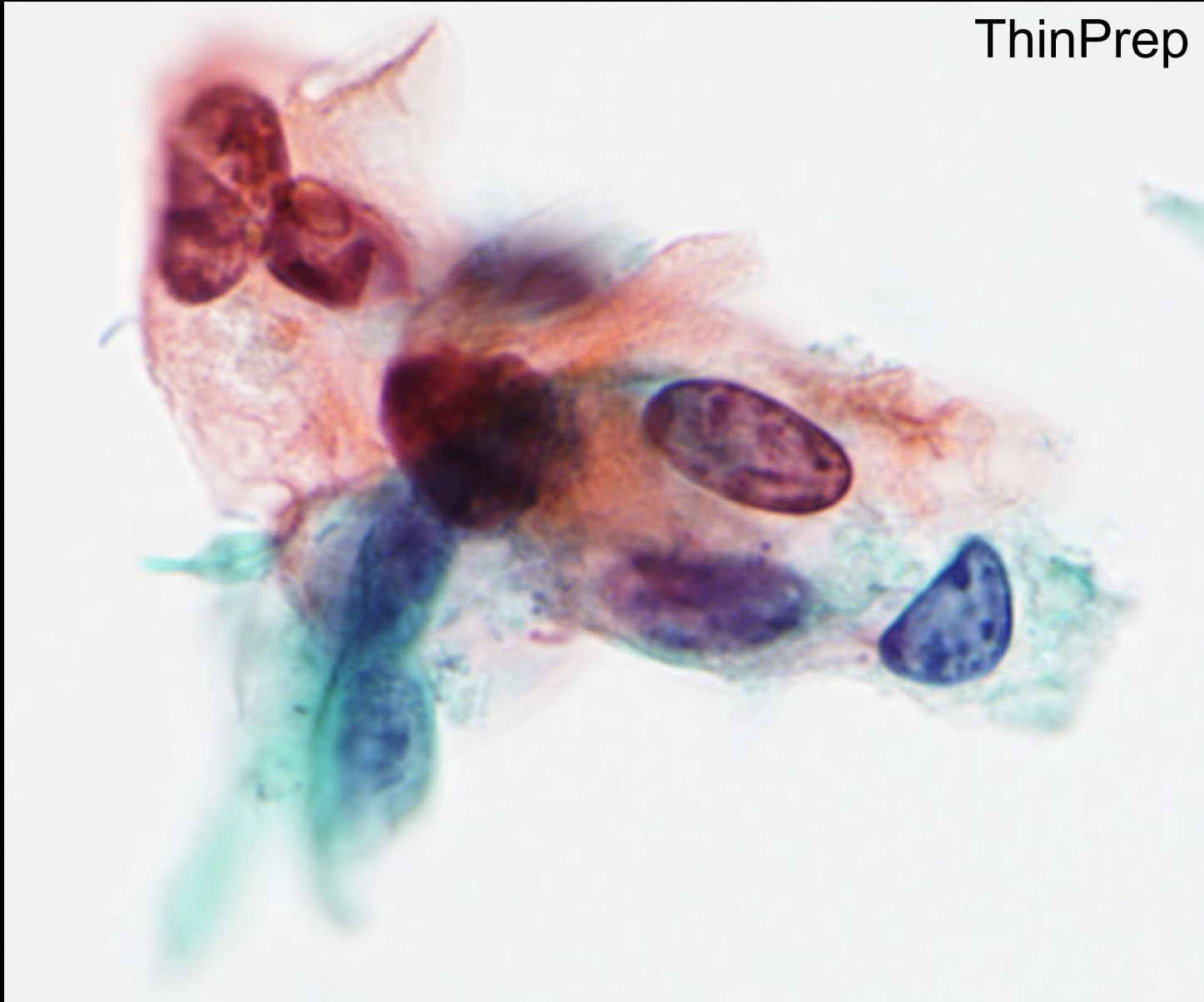


Keratinizing Dysplasia

- Not all HSIL cells are of squamous metaplastic / parabasal type
- Sometimes high grade changes can be found in keratinizing cells
- Usually metaplastic-type cells predominate
- Keratinizing dysplasia alone can be easily missed

Keratinizing Dysplasia

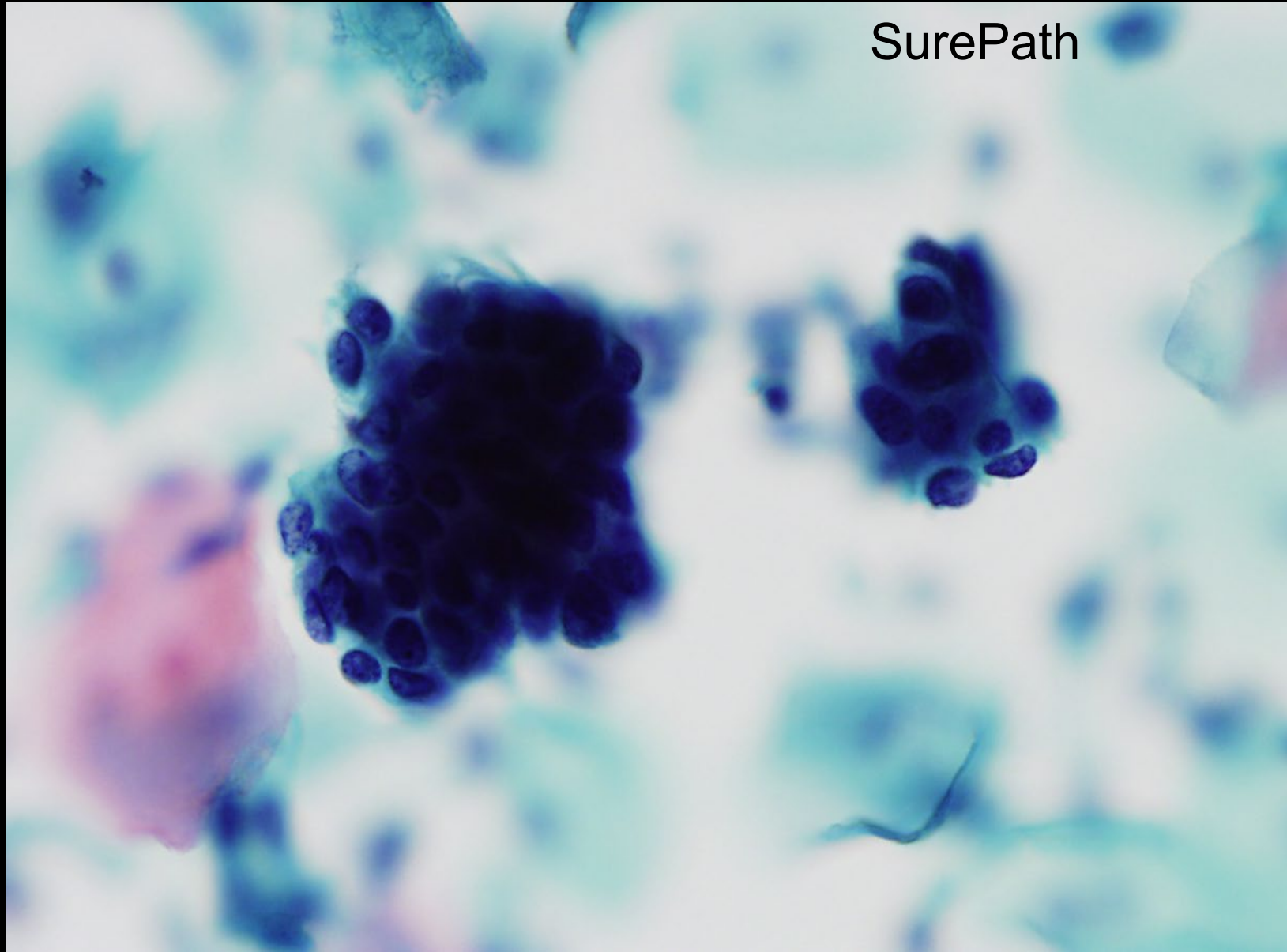
ThinPrep



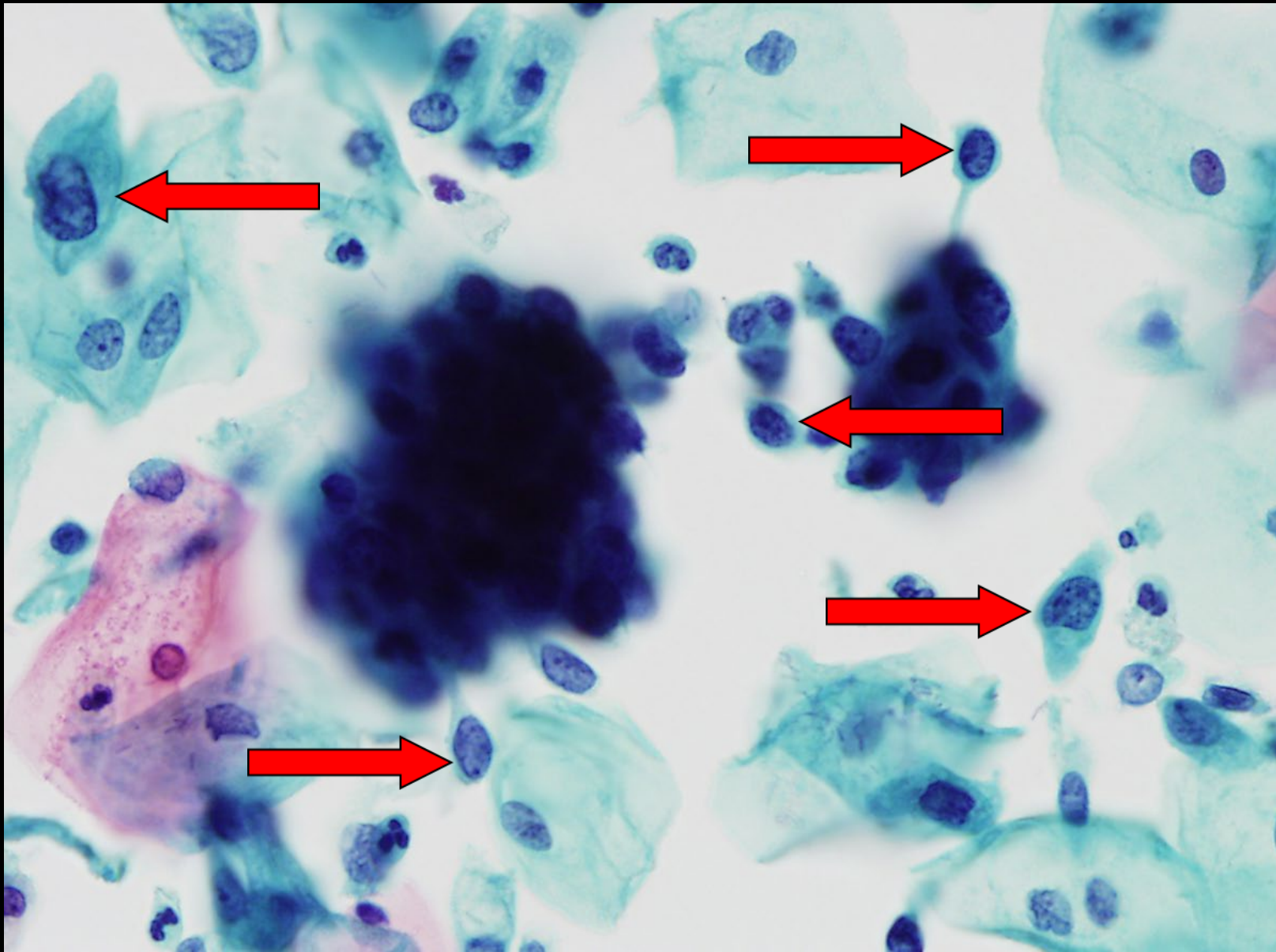
Hyperchromatic Crowded Groups

- Glandular cells tend to “round up” in fluids, forming balls of cells
- These balls obscure the cytologic features of the individual cells
- Looking at the edges of cell balls and the background is key to correct identification
- Hyperchromatic crowded groups differential: HSIL, endocervical cells, endometrial cells, carcinoma

Hyperchromatic Crowded Groups



Change of focus

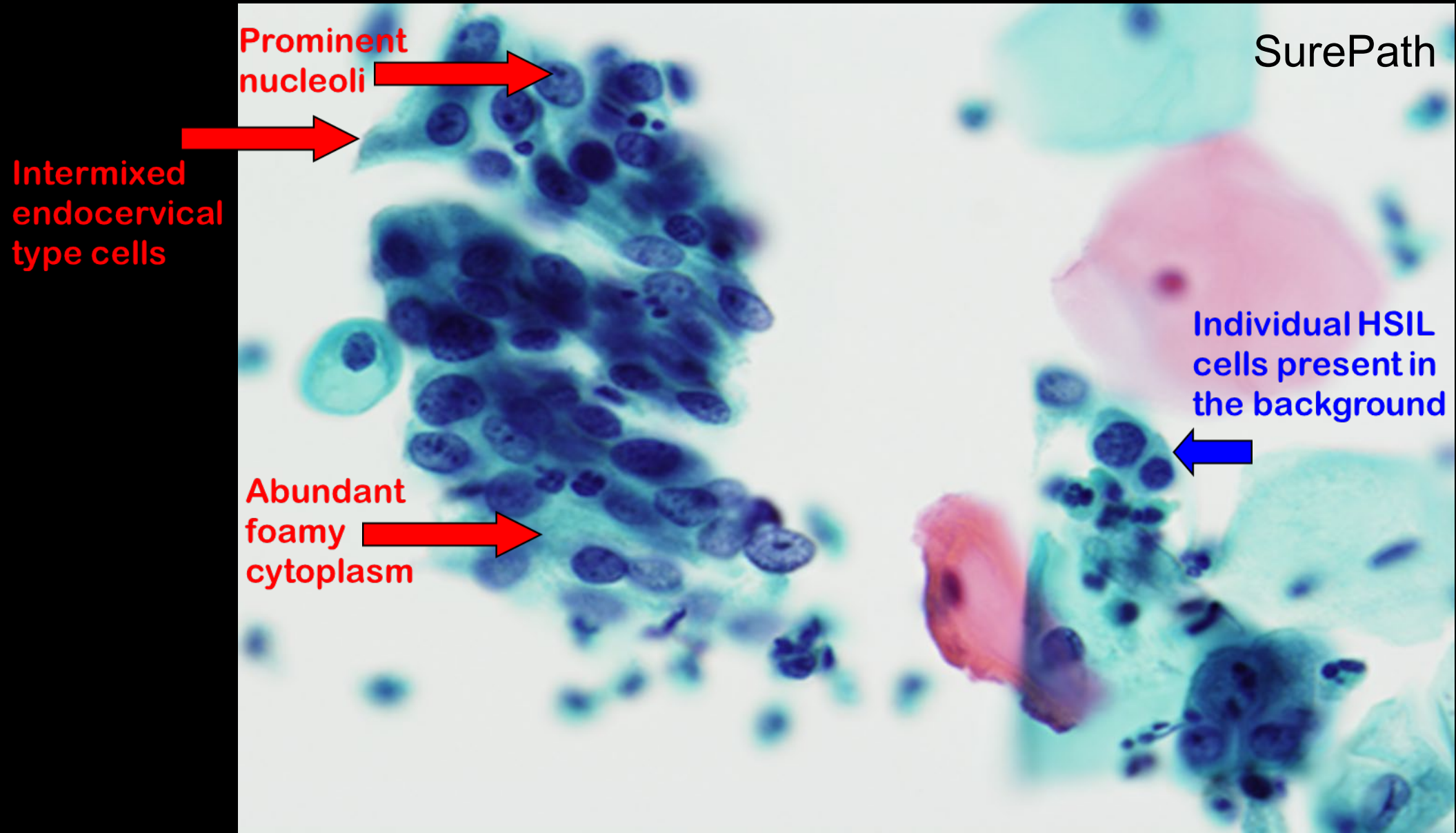


High Grade in a Gland

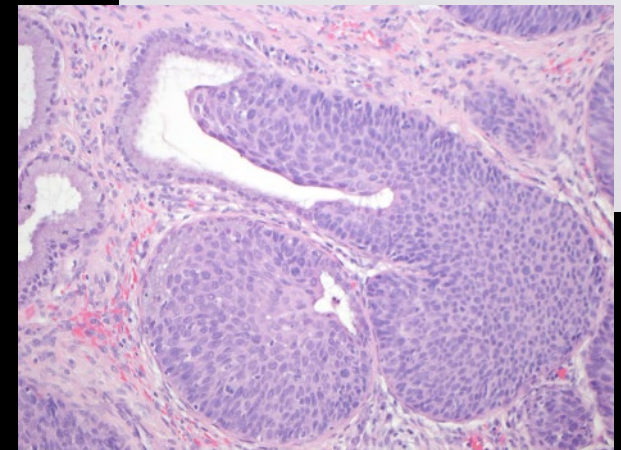
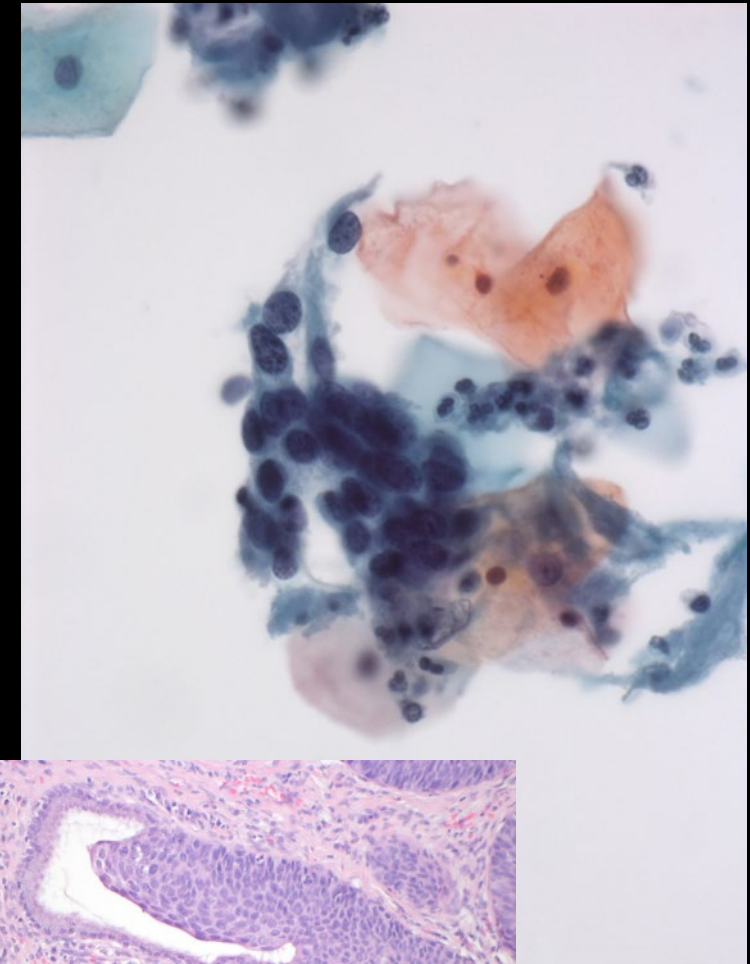
- HSIL often involves glands by direct extension from surface mucosa
- These often take the form of “hyperchromatic crowded groups” because they stay in rounded-up gland-like formations
- “Atypical Glandular Cells” more often corresponds to CIN 2-3 than Adenocarcinoma In Situ*

*Schnatz *et al.* Obstet Gynecol 2006; 107: 701.

High Grade in a Gland



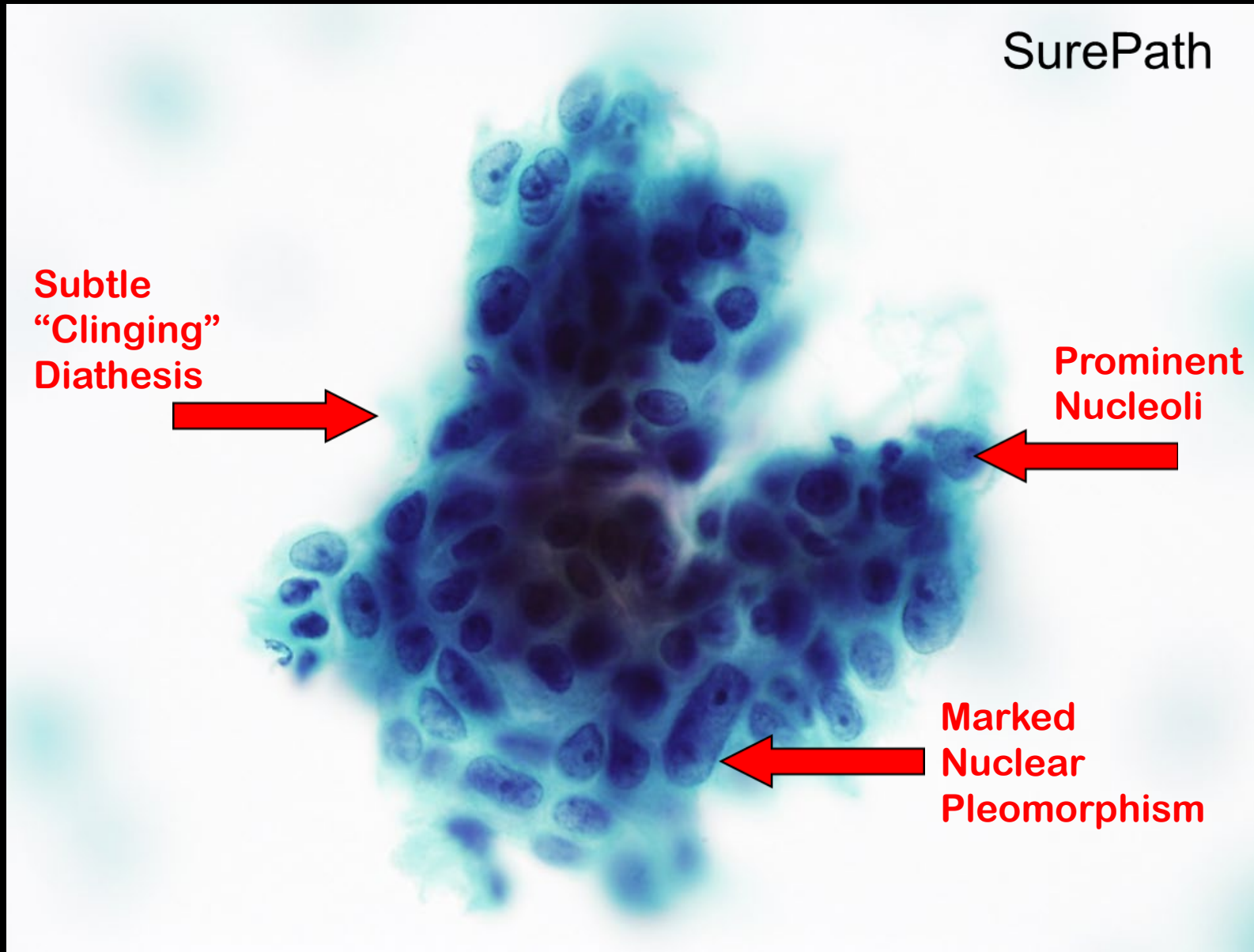
High Grade in a Gland



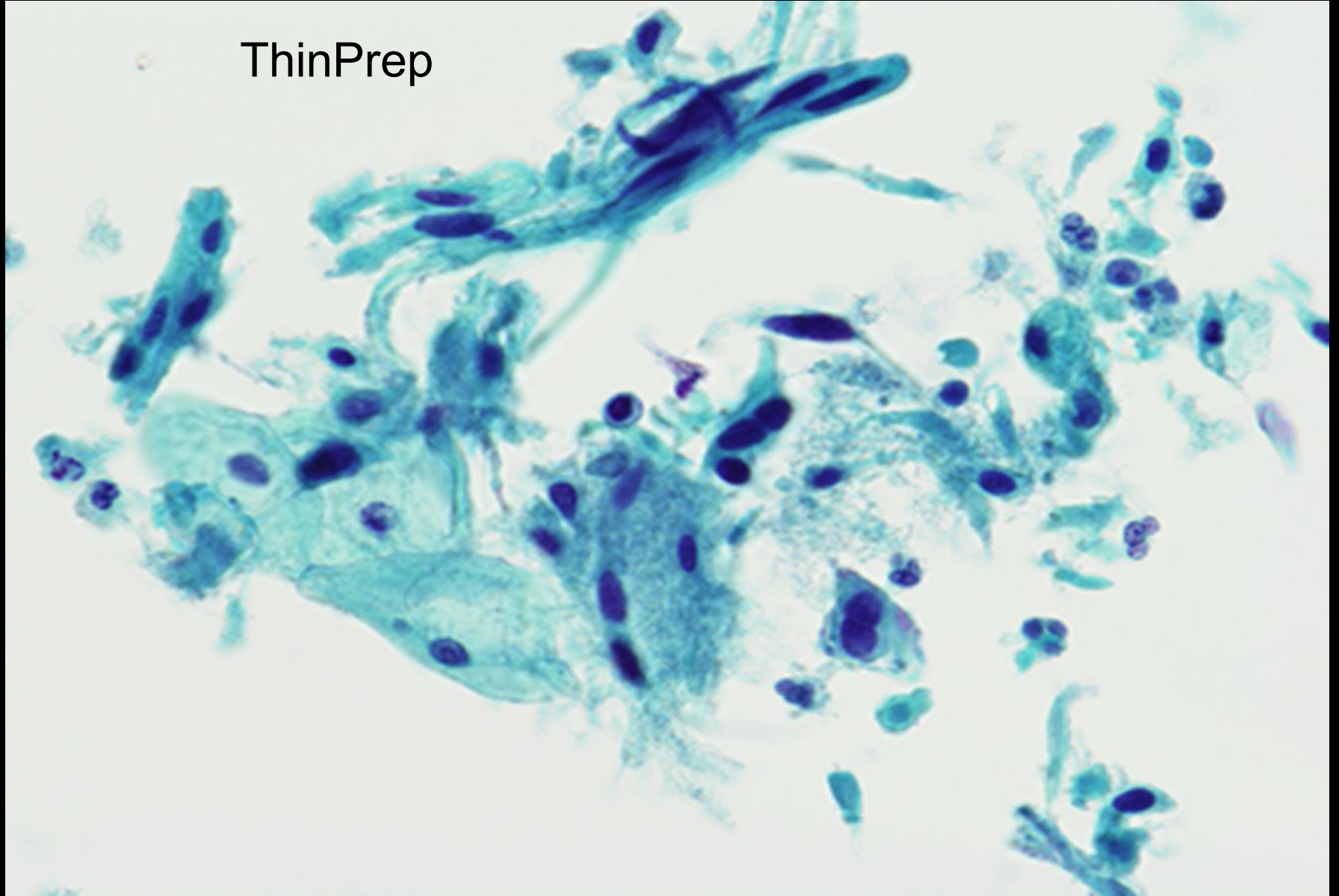
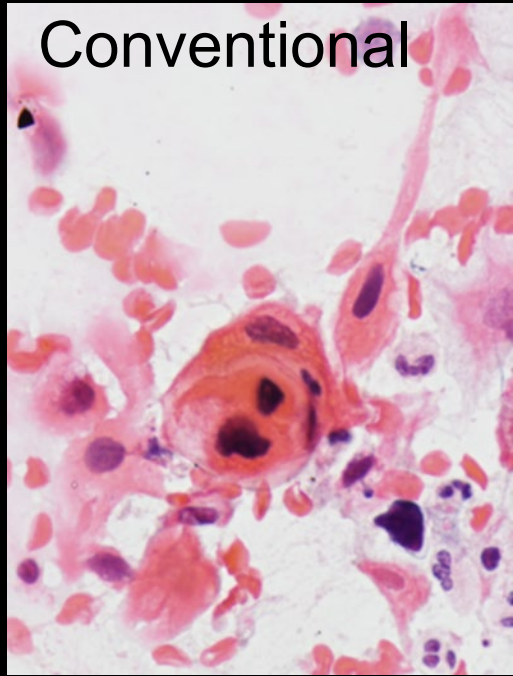
HSIL vs. Invasive Carcinoma

- This can be a difficult distinction
- Marked pleomorphism, prominent nucleoli, keratinization, and diathesis favor invasion
- High cellularity is often the best indicator
- Can call it HSIL, with features suspicious for invasion

Invasive Squamous Cell Carcinoma



Invasive Squamous Cell Carcinoma



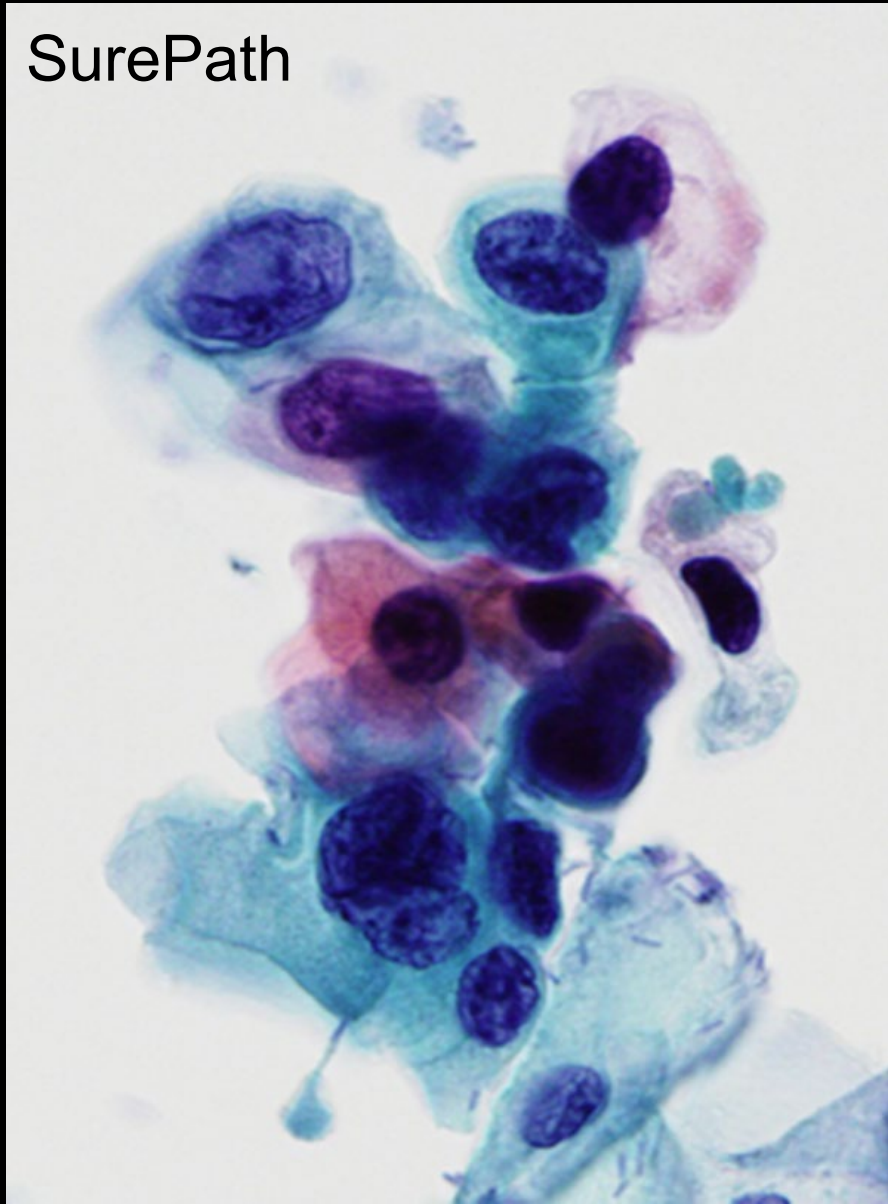
Atypical Squamous Cells,
Cannot Exclude HSIL (ASC-H)

ASC-H

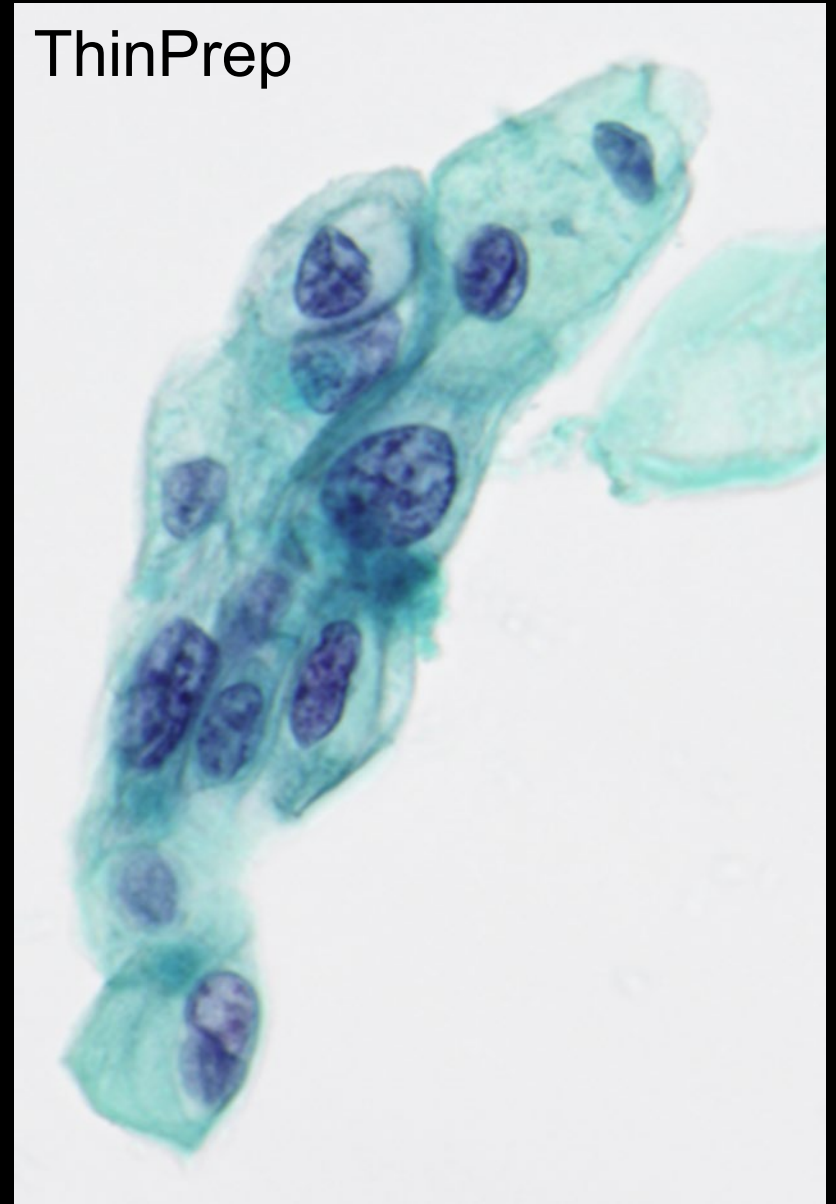
- Atypical squamous cells, cannot exclude HSIL is meant to be used when few cells suggest the possibility of HSIL but are not definitive
- This category has a higher likelihood of corresponding to HSIL on follow-up biopsy than ASC-US or LSIL
- In fact, if both ASC-H and LSIL are included in the same report, the ASC-H is more important despite being just “atypical”

ASC-H and LSIL

SurePath



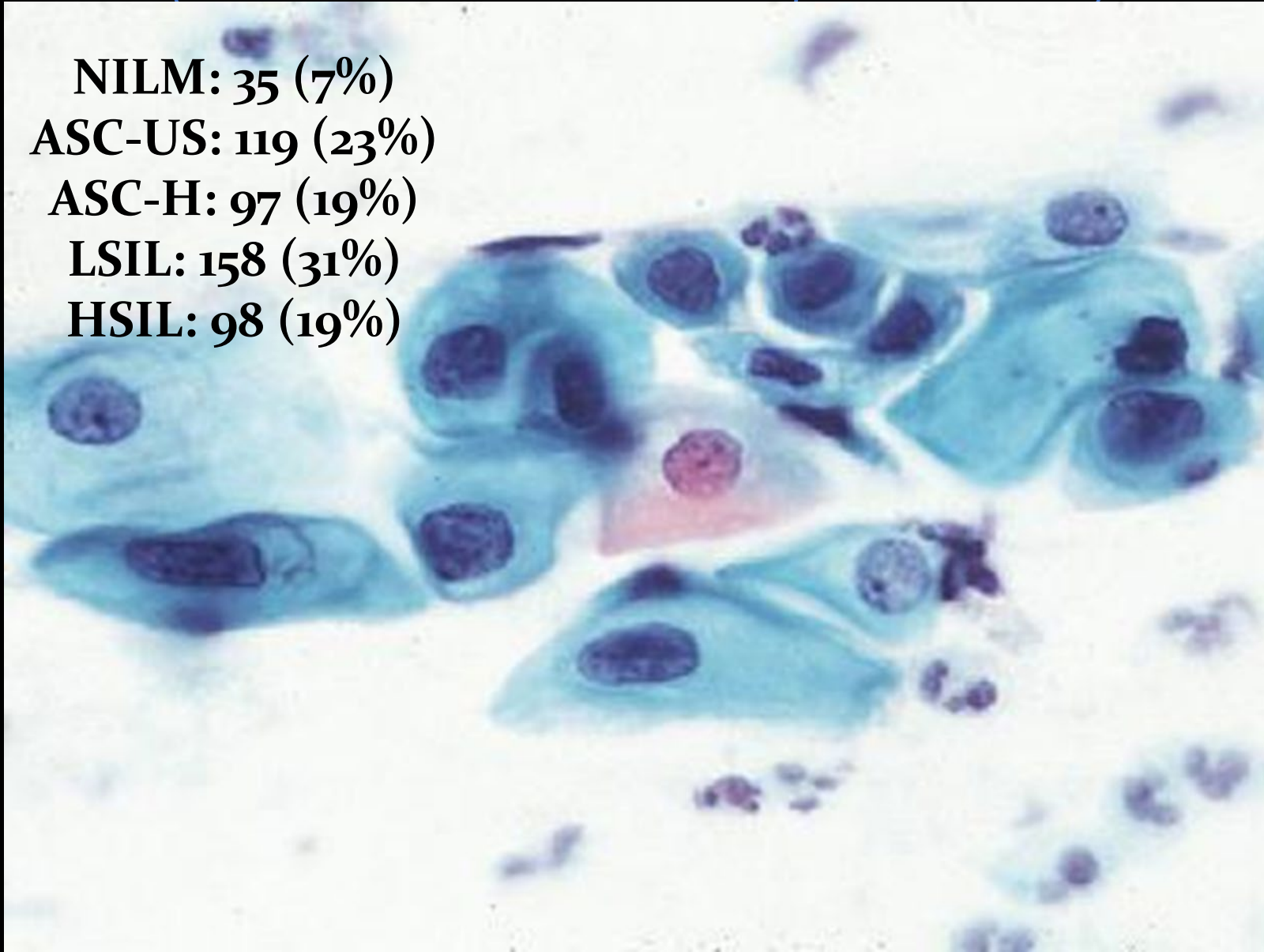
ThinPrep



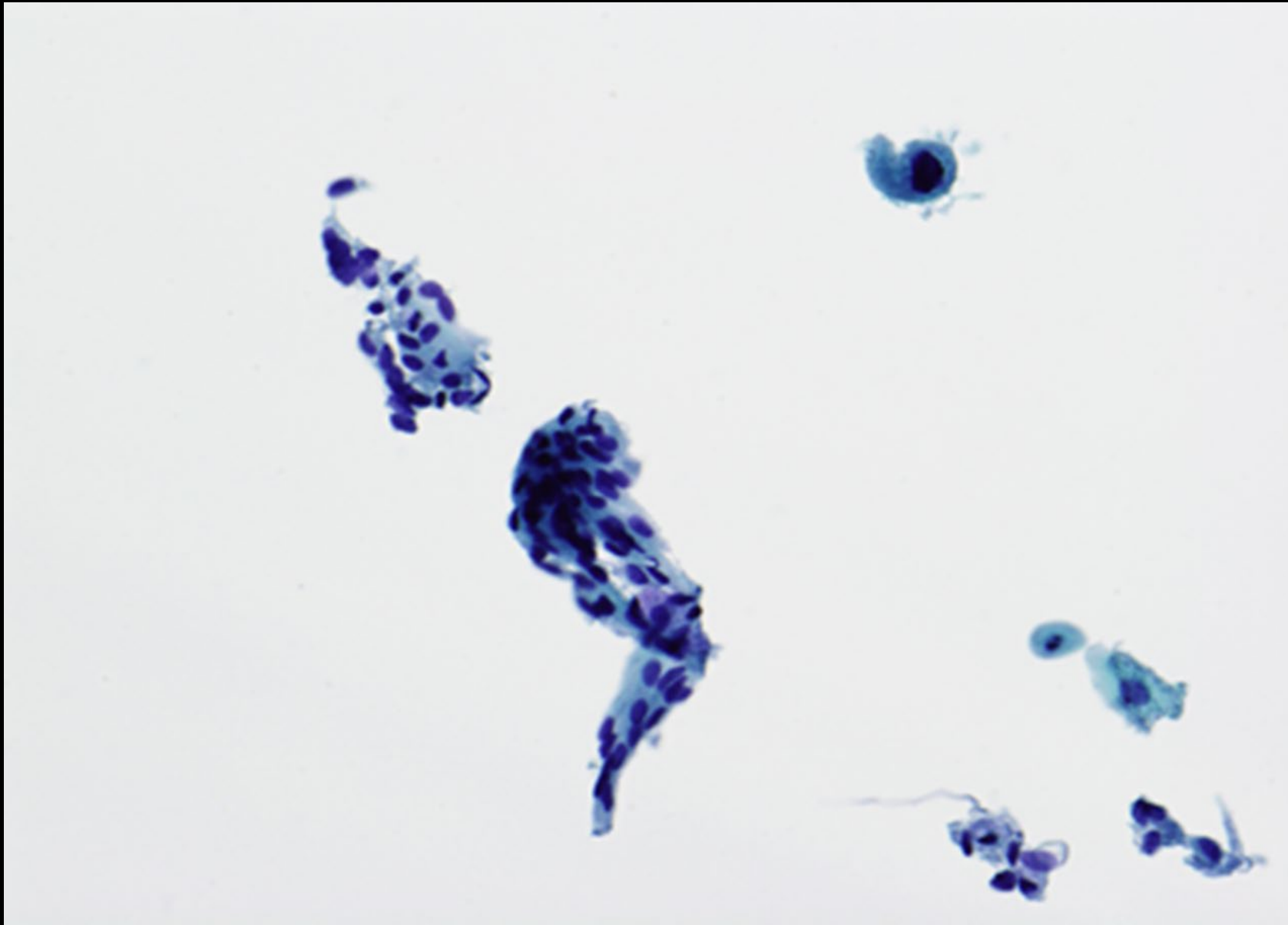
Bethesda Online Atlas

(bethesda.soc.wisc.edu/index.htm)

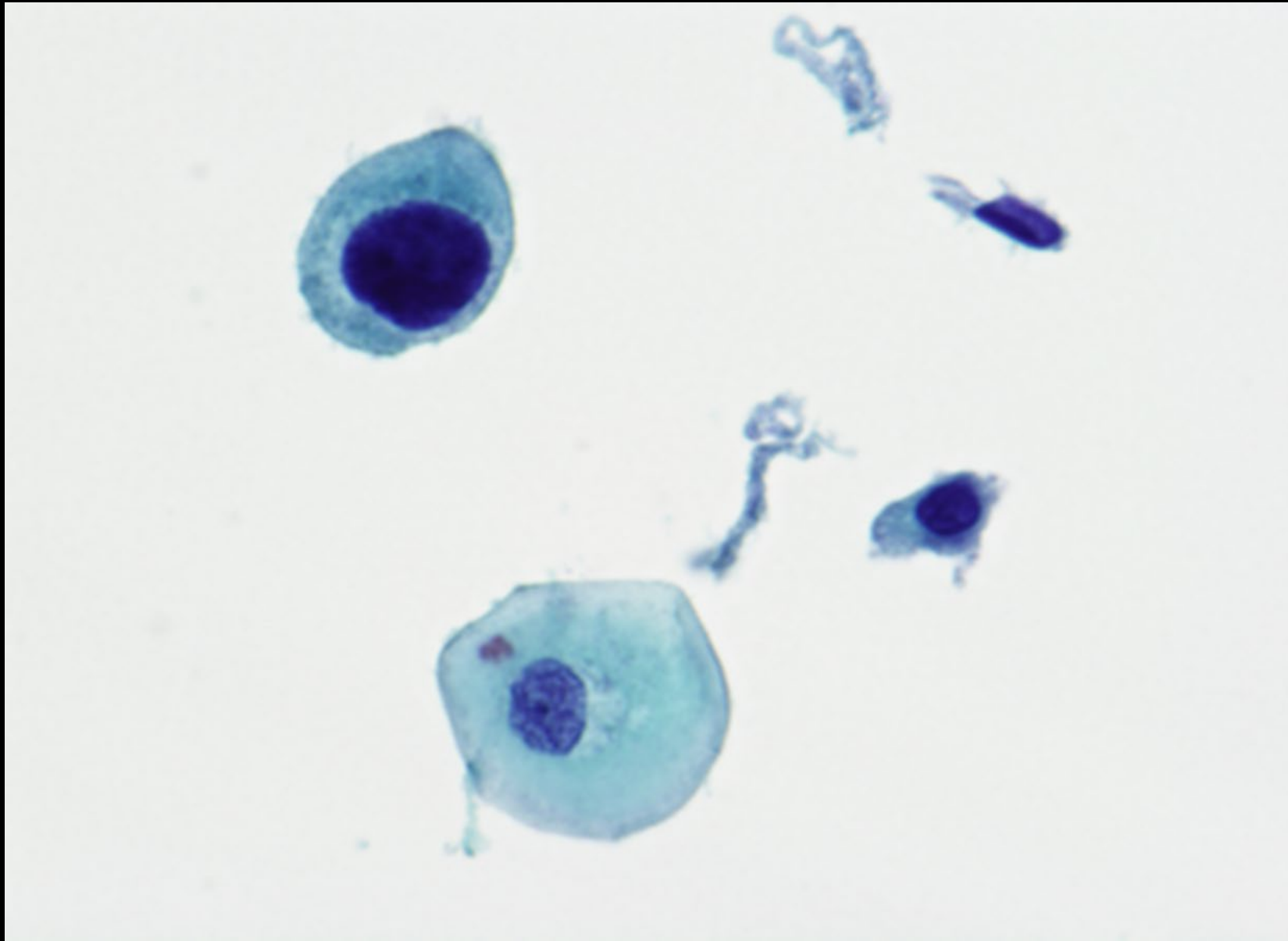
NILM: 35 (7%)
ASC-US: 119 (23%)
ASC-H: 97 (19%)
LSIL: 158 (31%)
HSIL: 98 (19%)



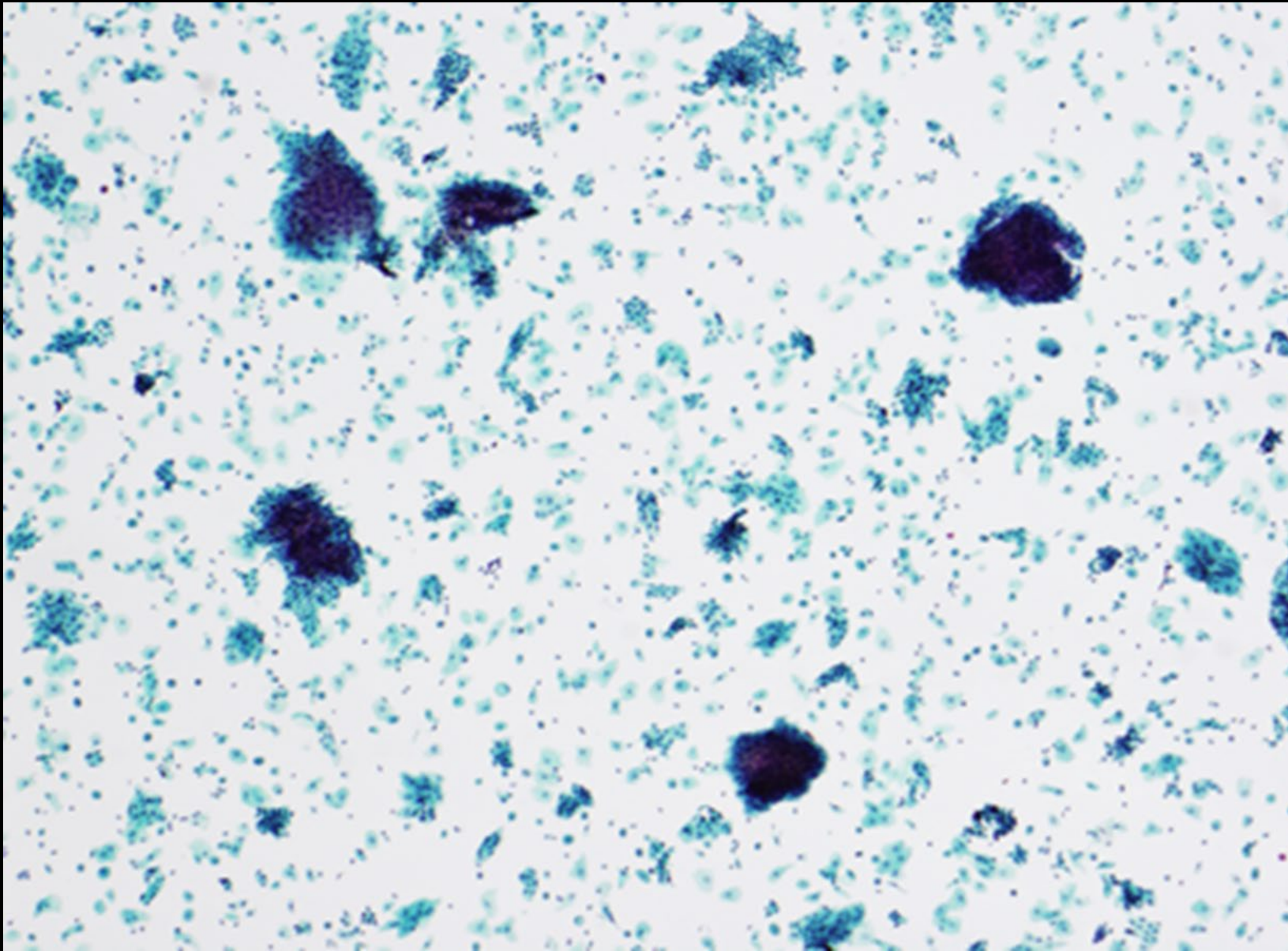
Atrophy and ASC-H: Few Cells



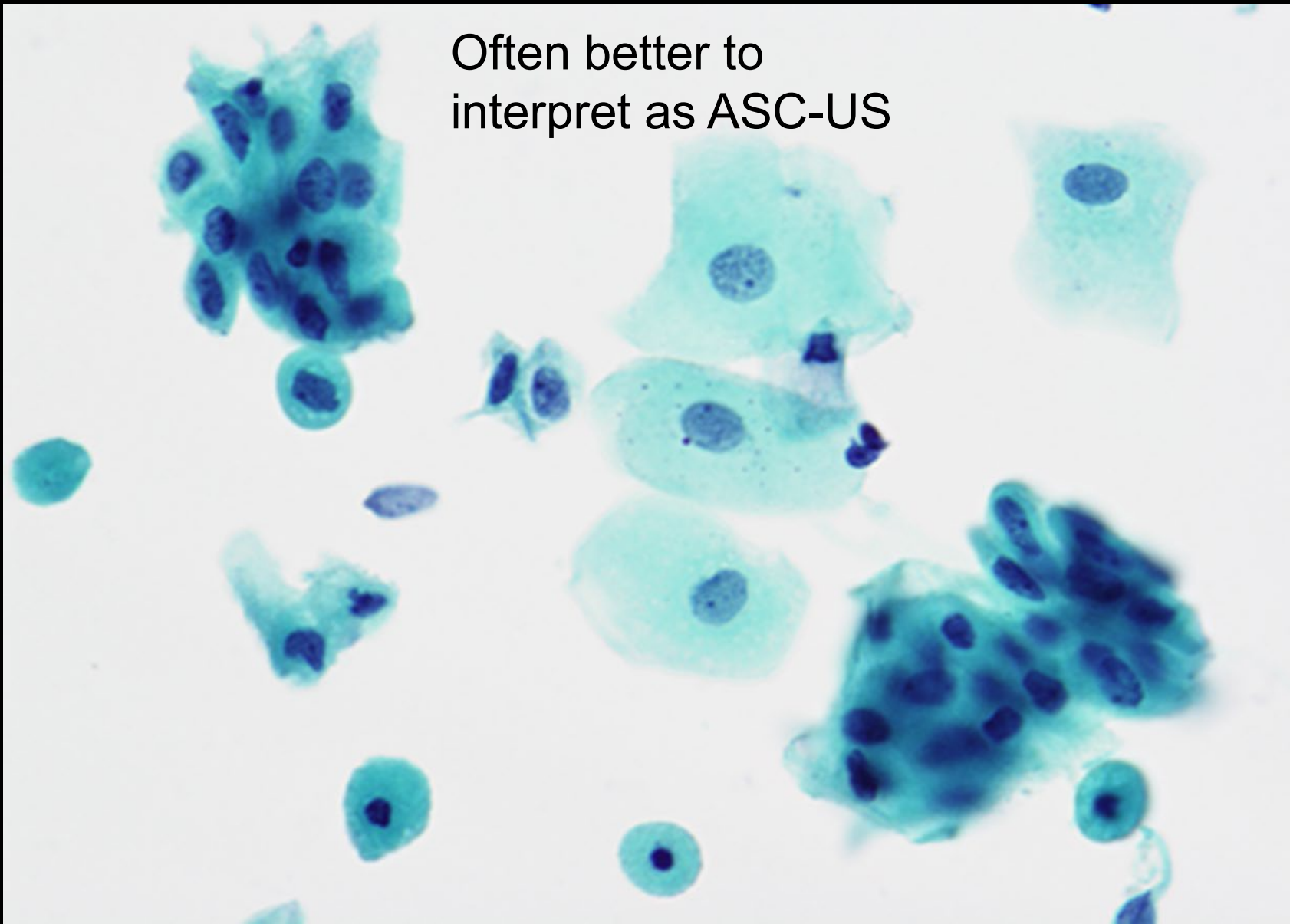
Higher power of the same case



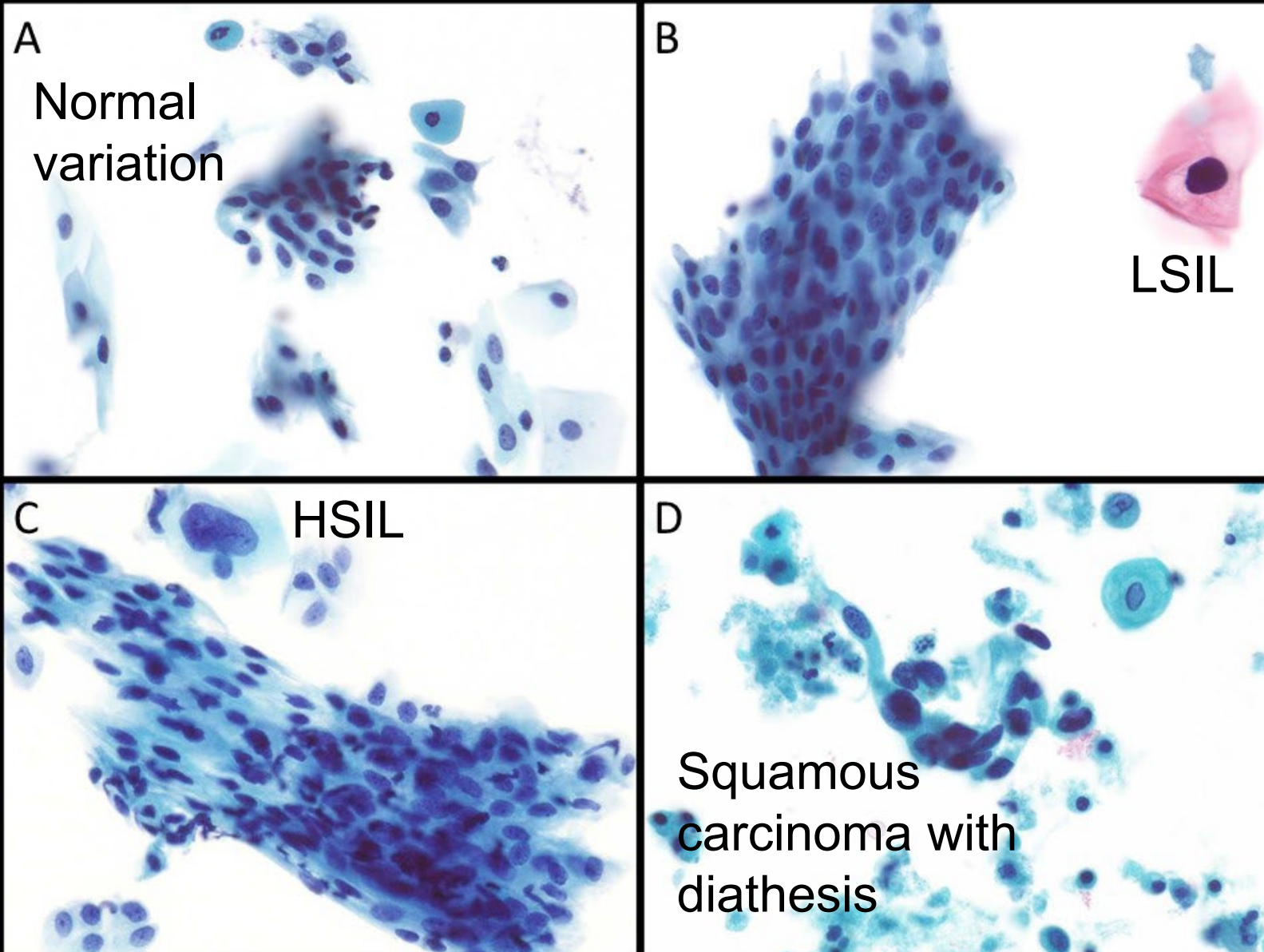
Atrophy and ASC-H: Many Cells



Higher power of the same case

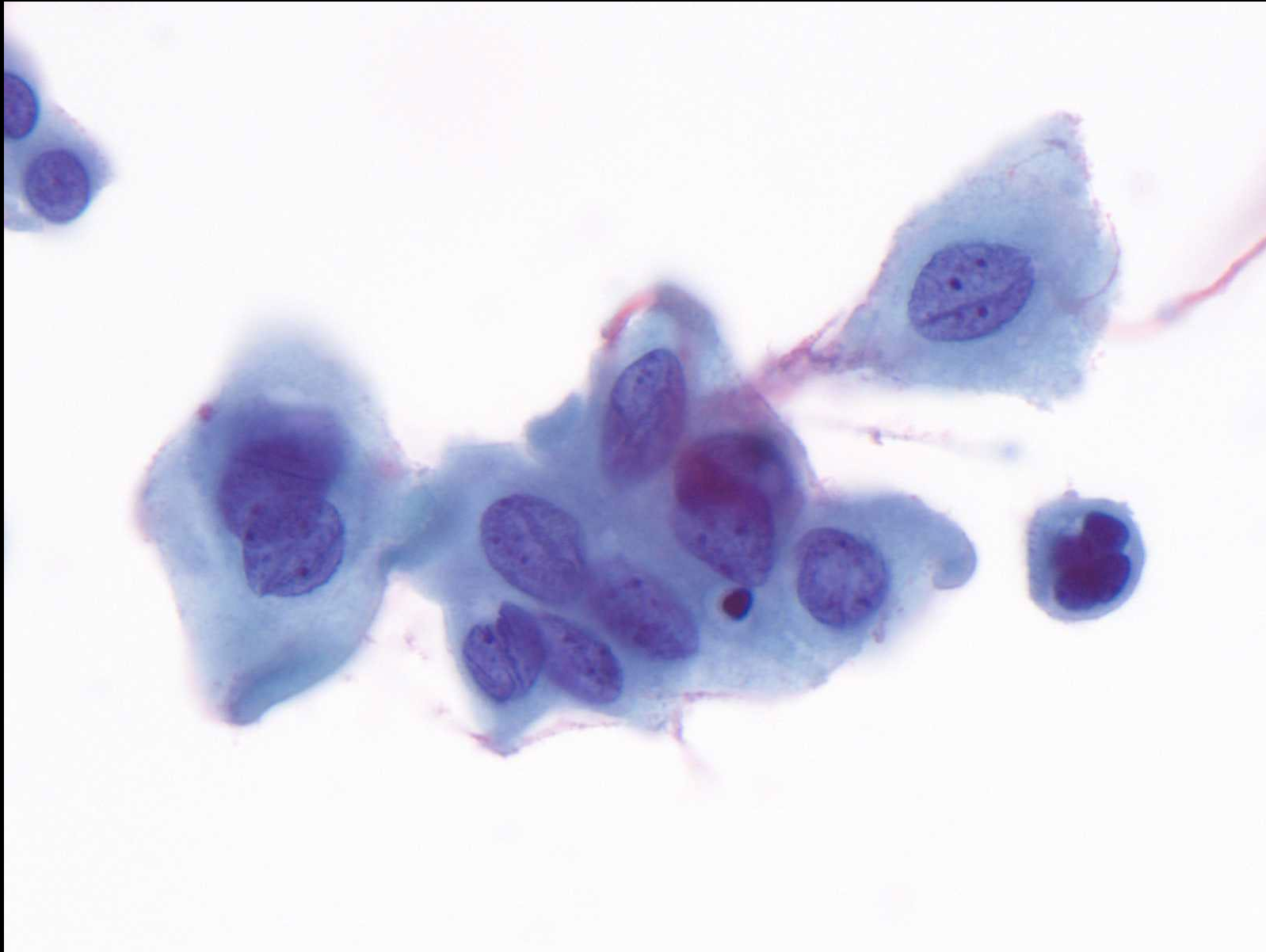


Atrophy



From: Thrall. Acta Cytol
2023; 67: 129.

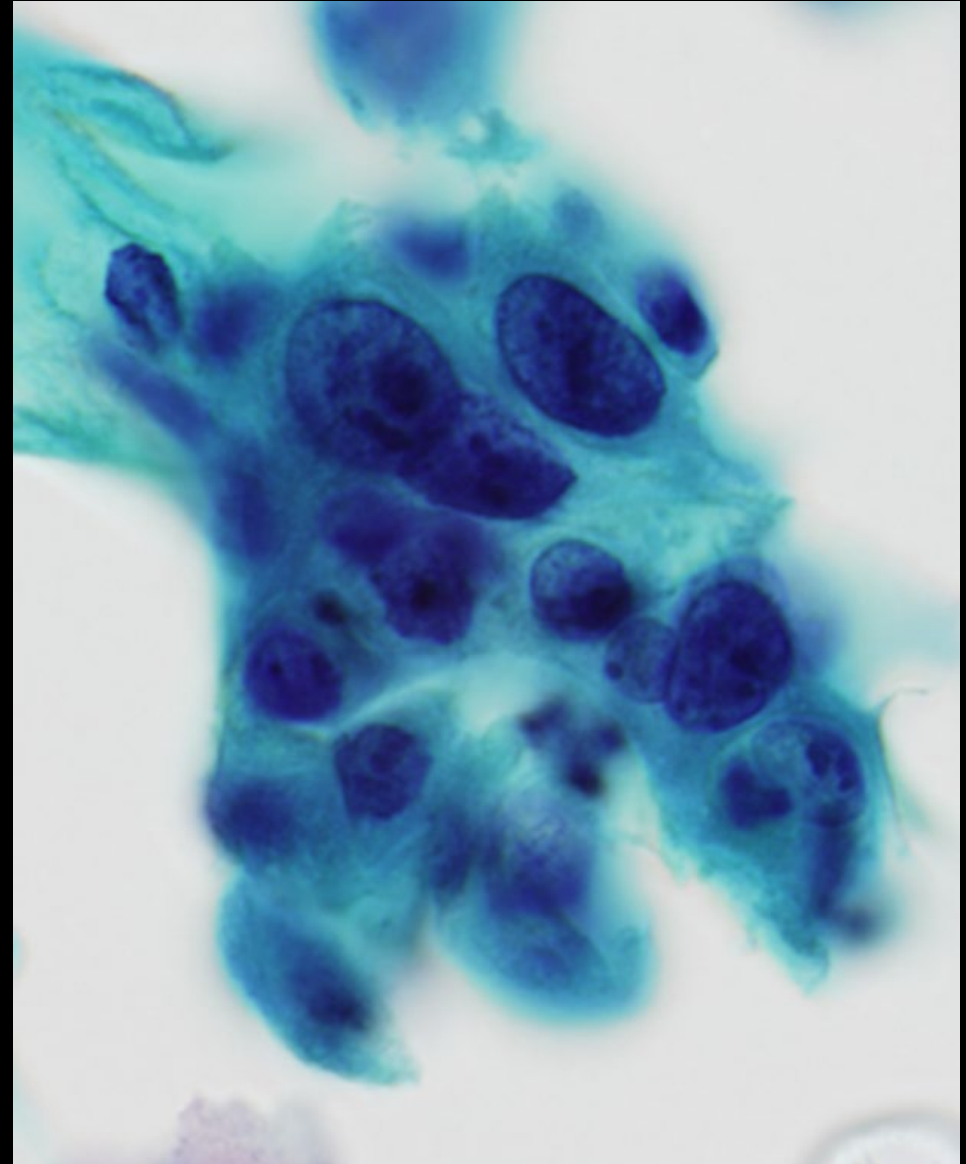
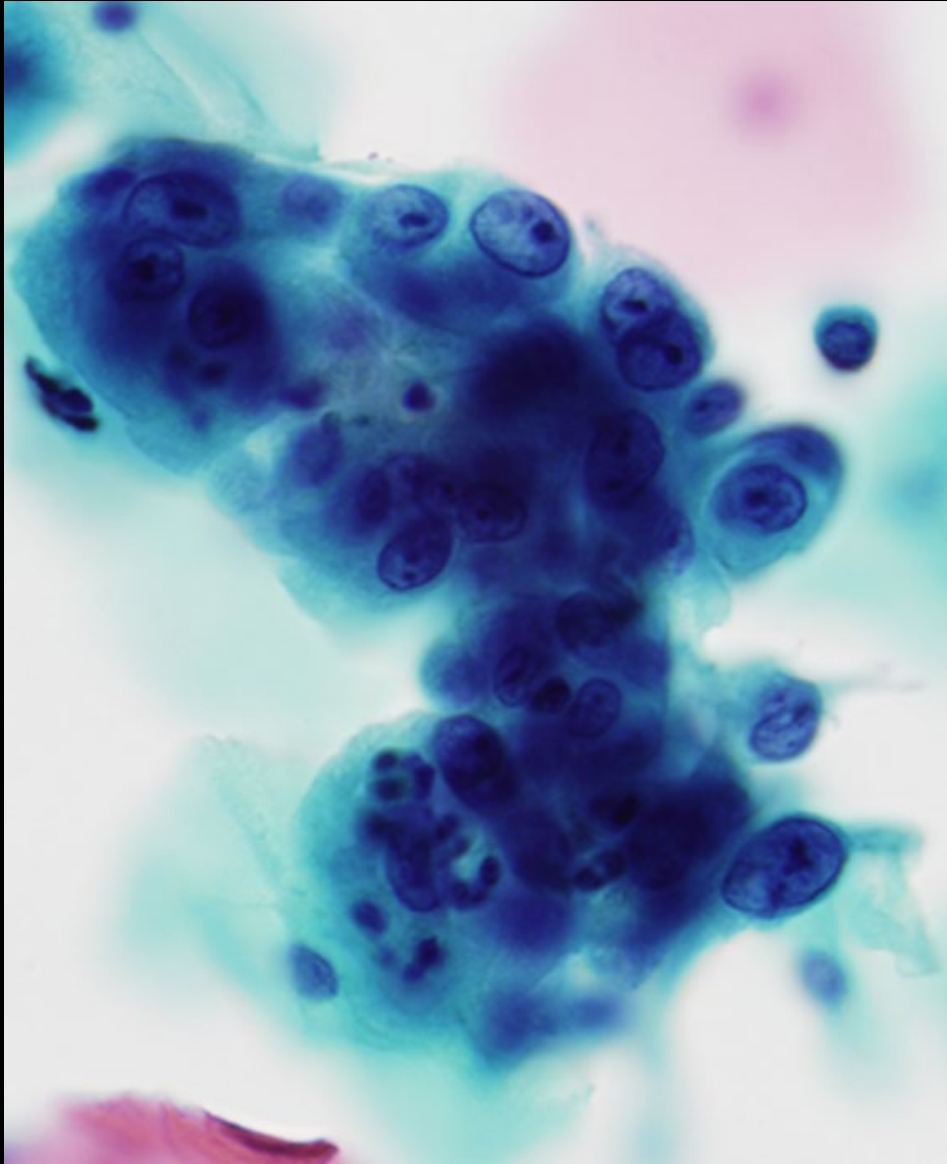
Transitional Cell Metaplasia



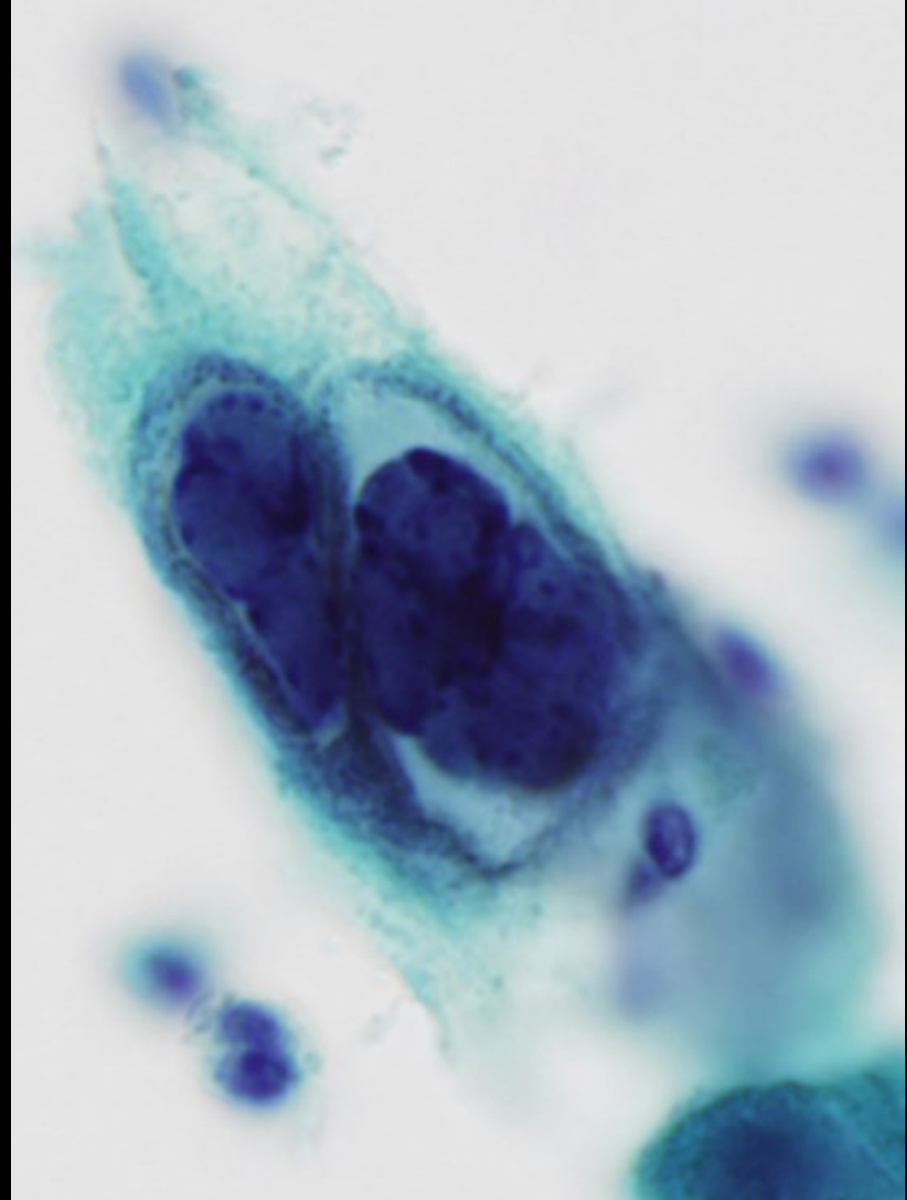
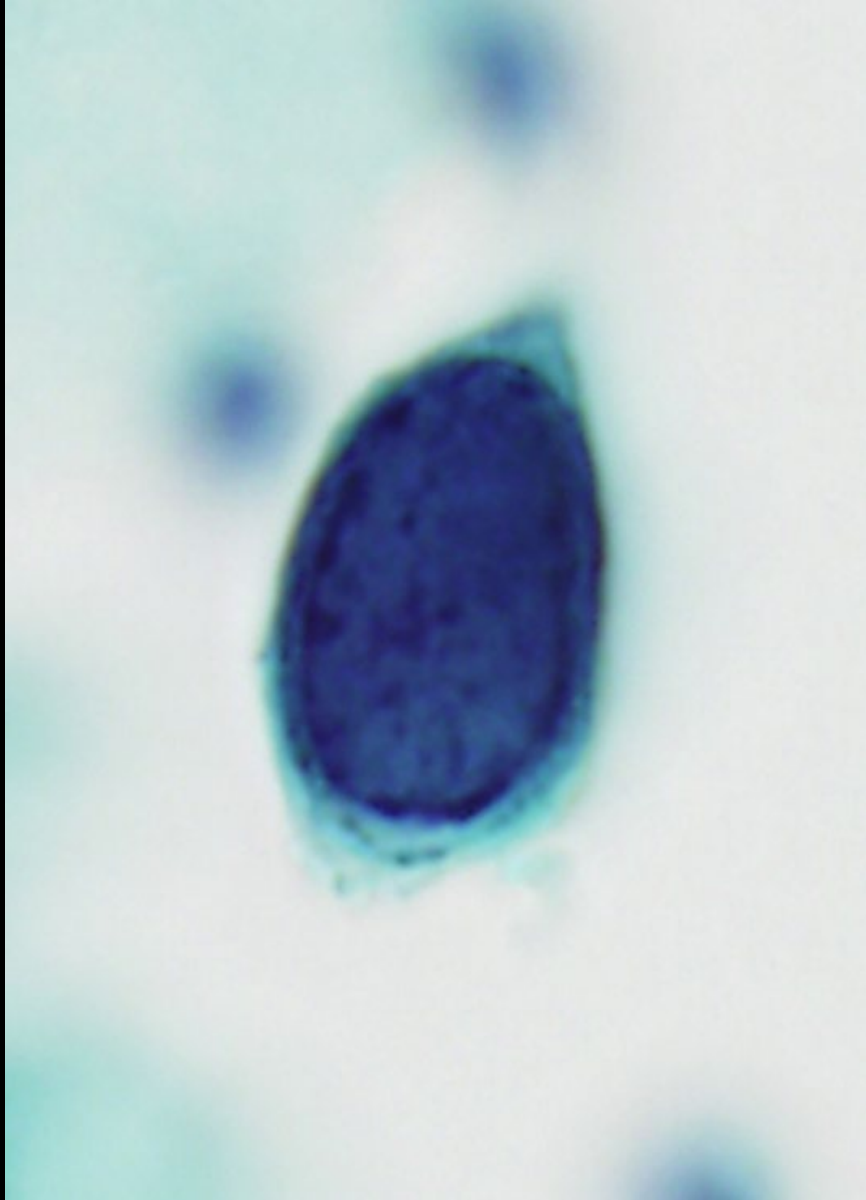
Other HSIL Mimics

- HSIL mimics are less frequent than koilocyte mimics
- Most reactive processes have abundant cytoplasm
 - Some exceptions to follow
- Degenerative changes probably account for a large percentage of false-positive ASC-H
 - It may be better to classify high N:C ratio cells that are atypical and degenerated as ASC-US instead

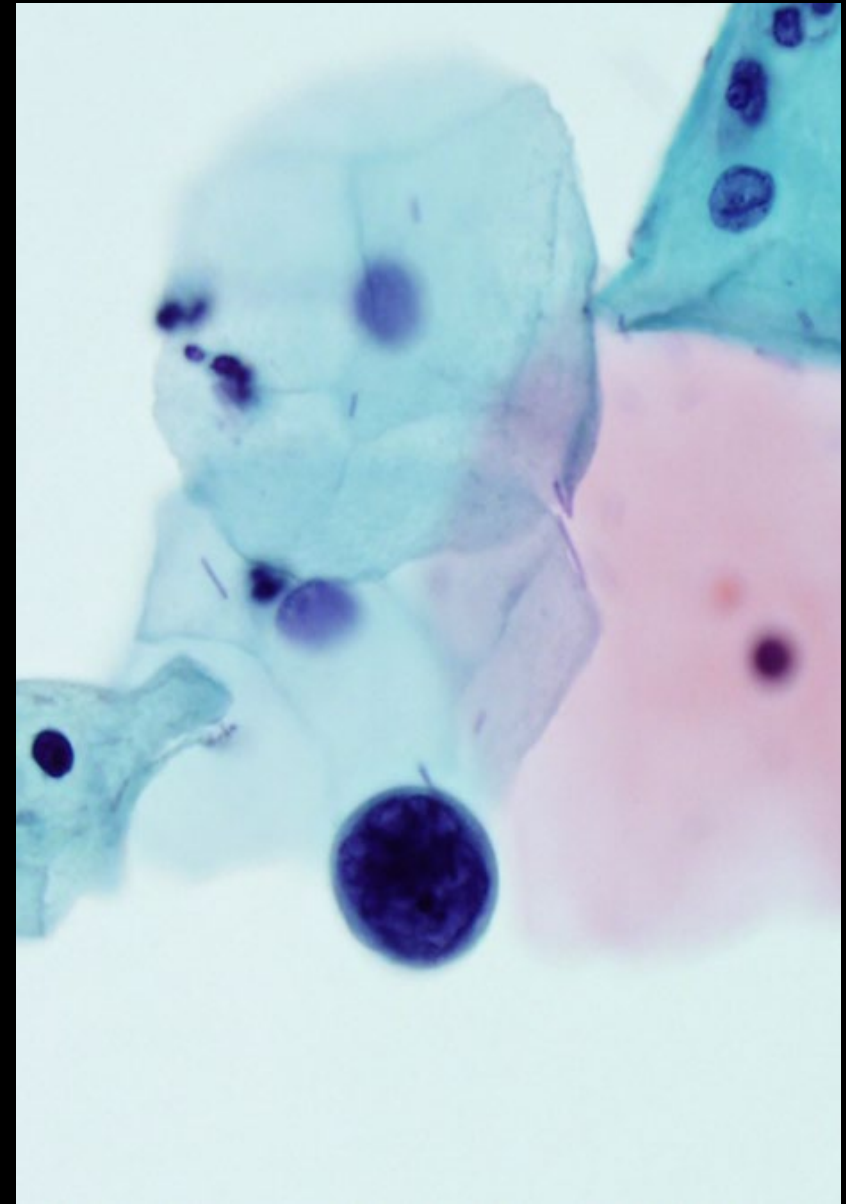
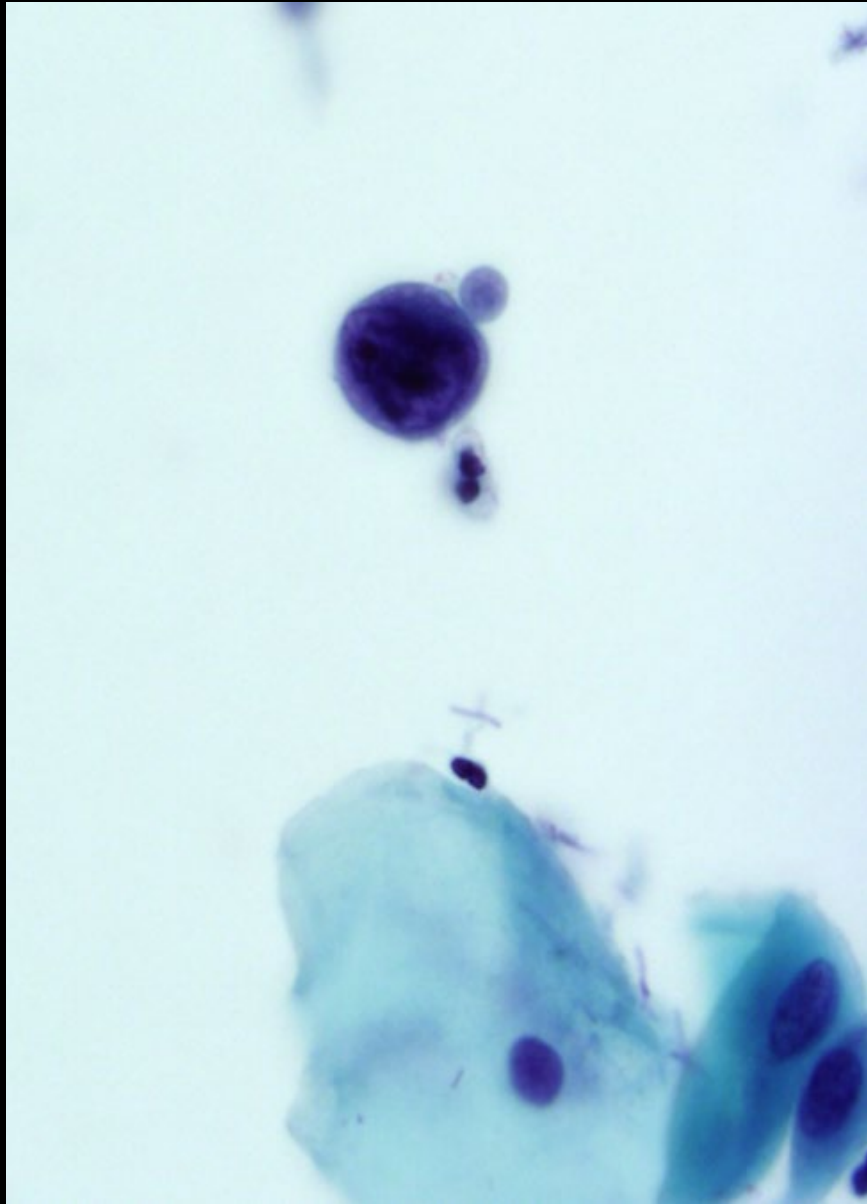
Atypical Repair Mimicking HSIL



Herpes Mimicking HSIL



IUD Effect Mimicking HSIL



Summary

- Identification of HSIL is the primary objective of Pap test screening
- LSIL is viral cytopathic effect and only a marker of risk
- The ASC-US and ASC-H categories are critical to improve the sensitivity of Pap testing
- HPV testing can be of great help in screening algorithms

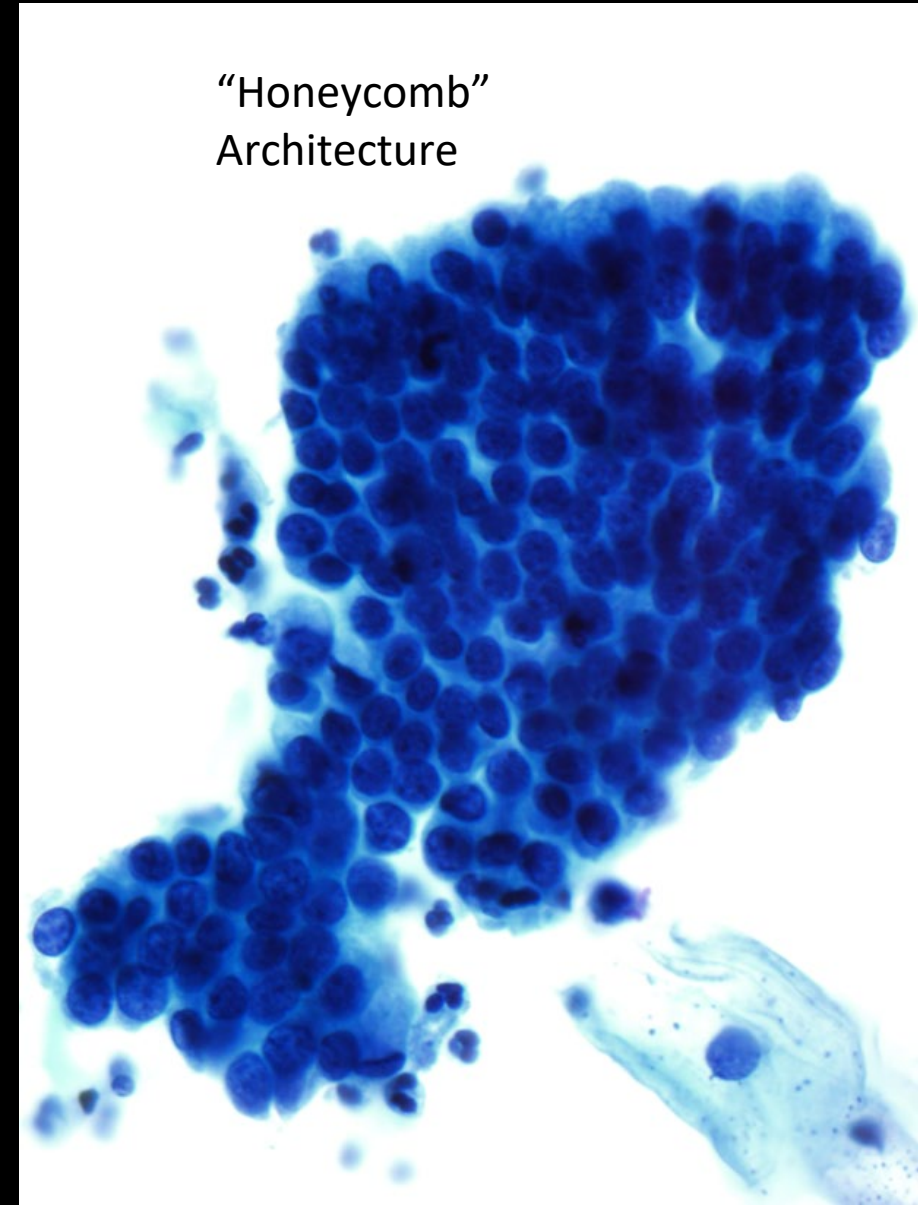
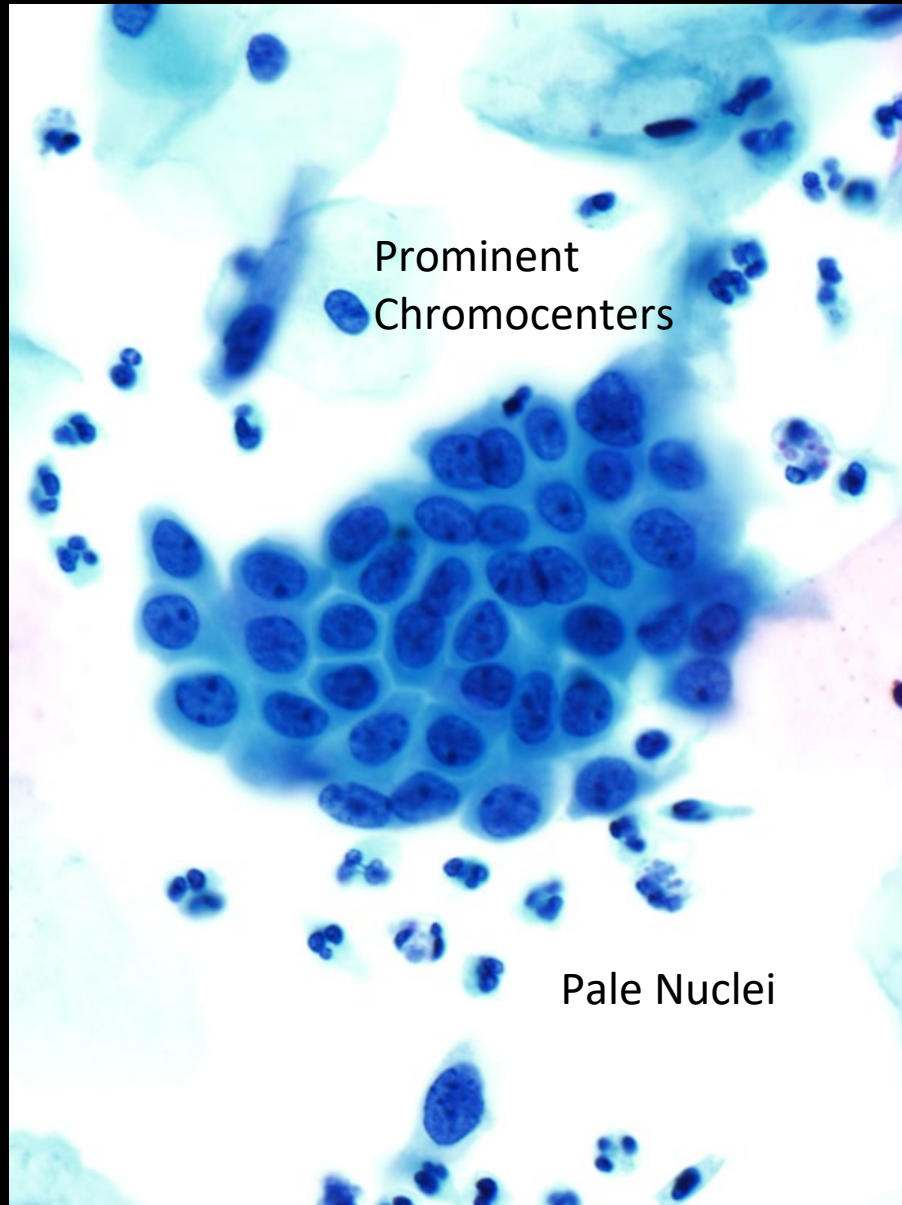
Glandular Lesions

Glandular Cells

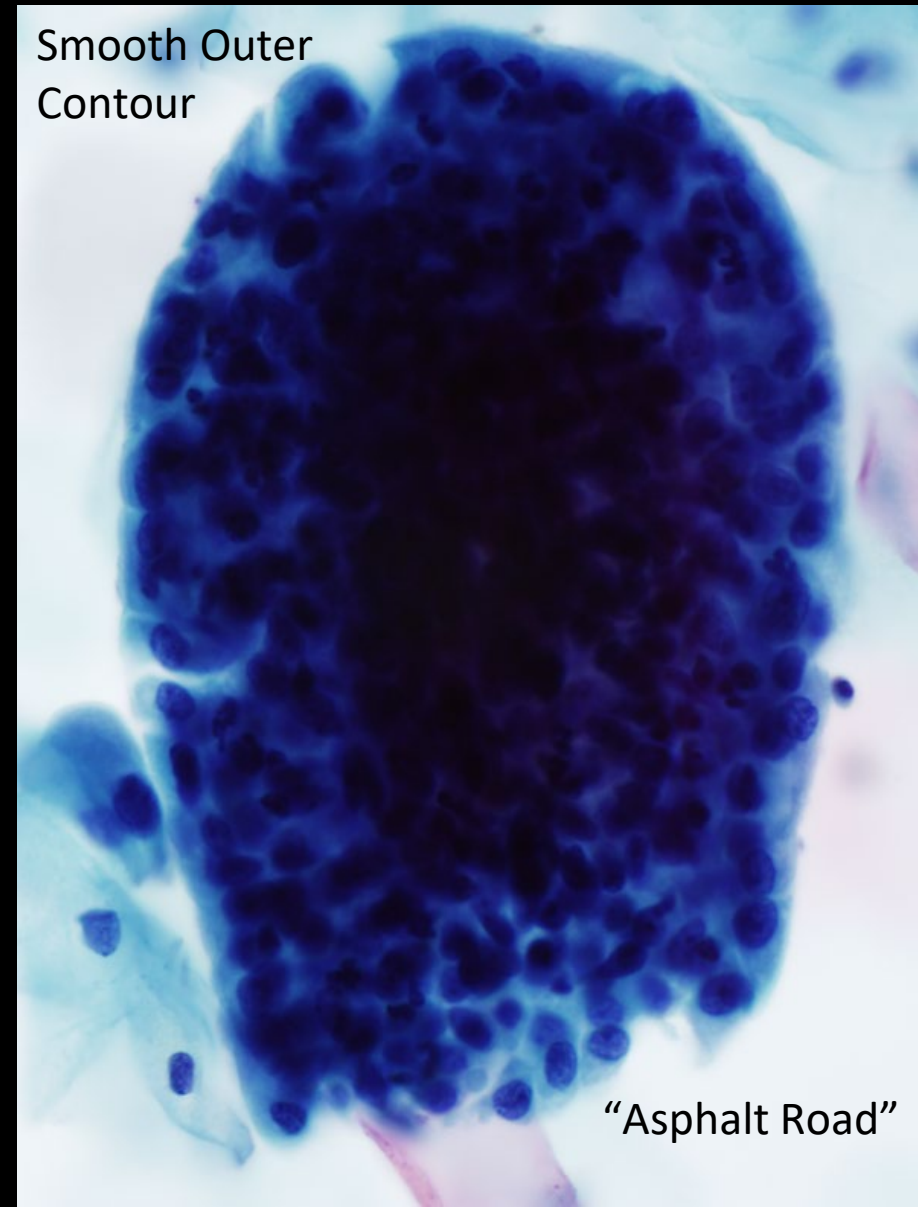
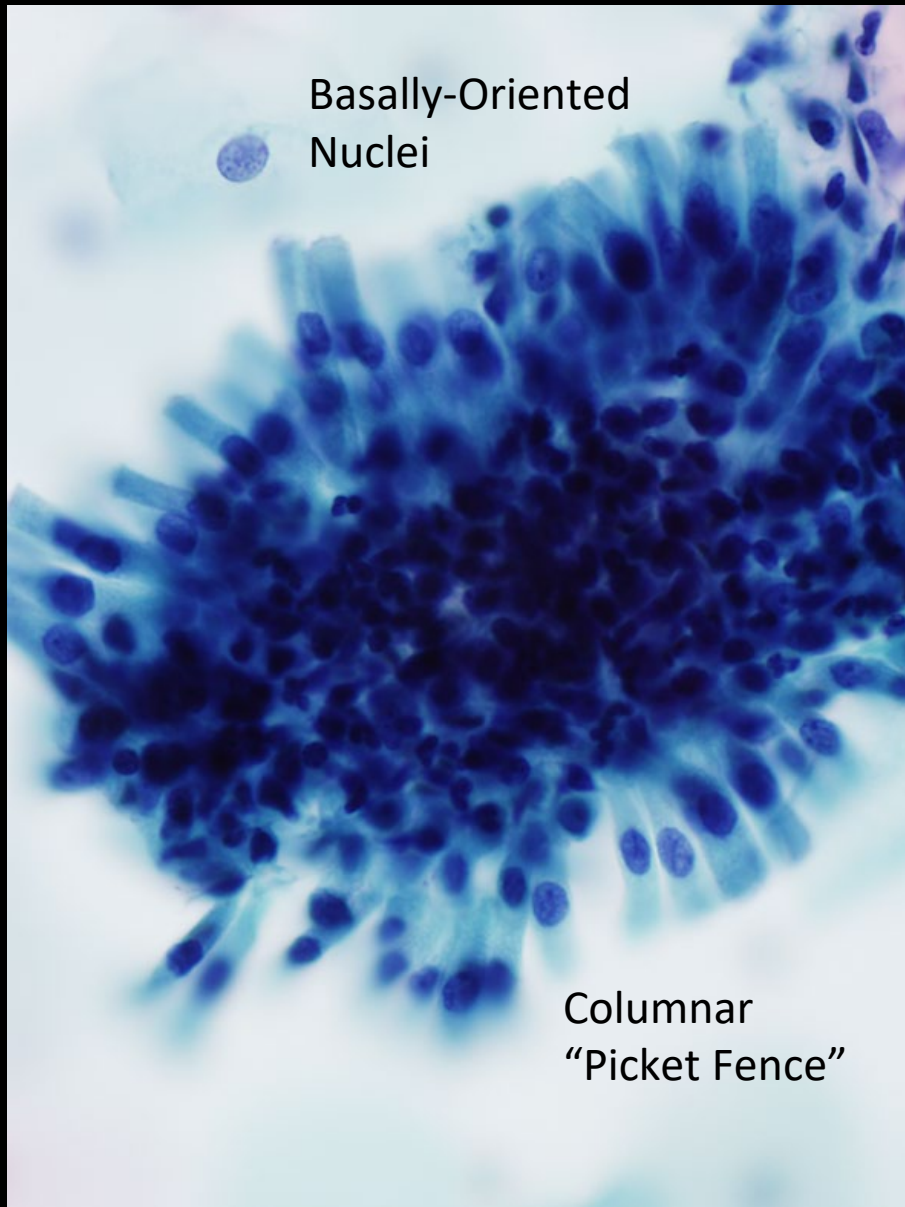
- Glandular cells are a perennial problem in Papanicolaou tests
- The Pap test is designed to find squamous dysplasia and carcinoma
- Glandular lesions are a “bonus”
- The sensitivity of Pap tests for adenocarcinoma is much less than for squamous dysplasia
- Liquid-based Pap tests appear to perform slightly better than conventional smears*

*Burnley *et al.* Diagn Cytopathol 2011; 39: 869.

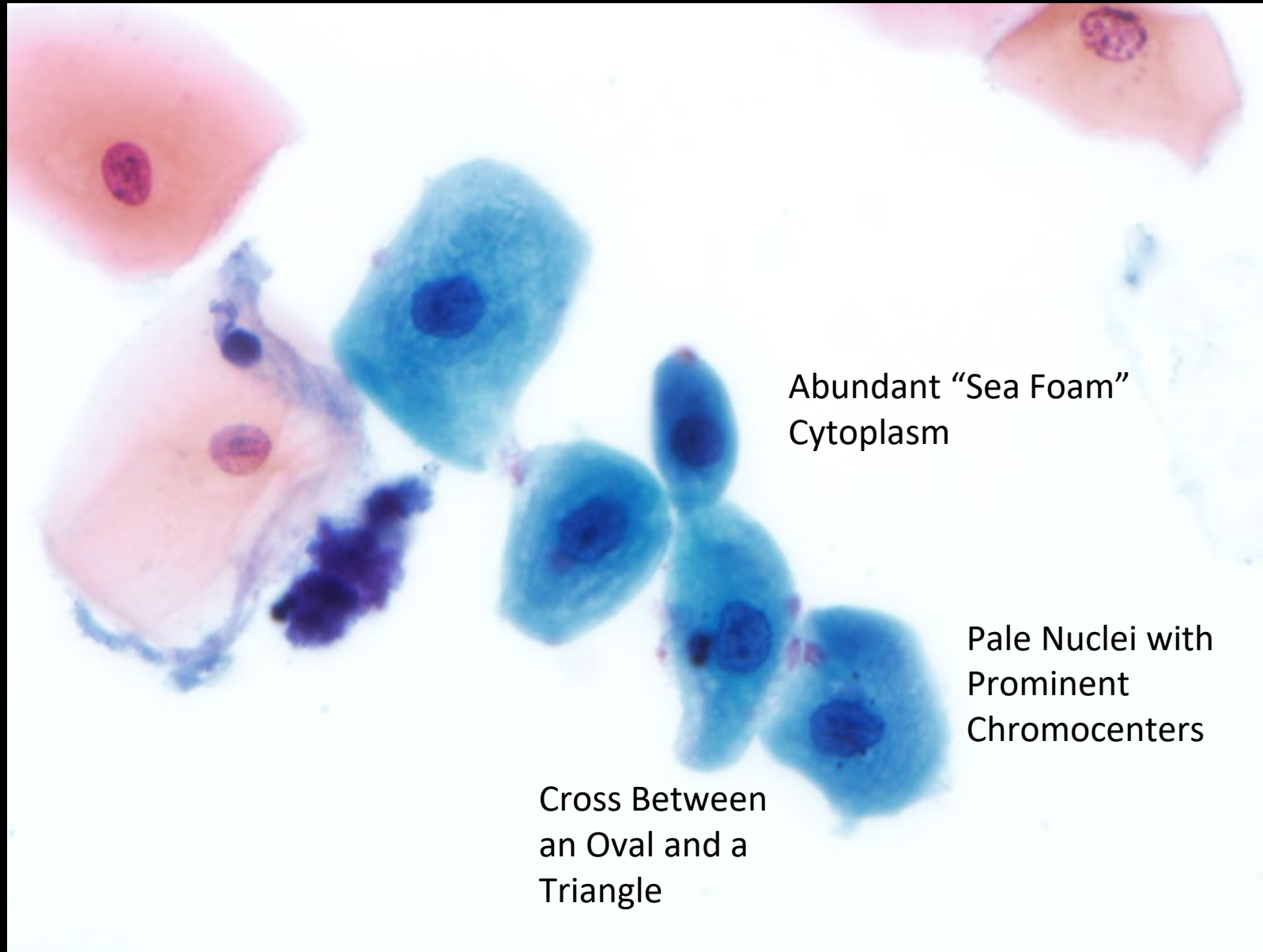
Endocervical cells



Columnar Cells, Smooth Contour



Squamous Metaplastic Cells



Adequacy

- The Bethesda System includes the presence or absence of endocervical cells in the adequacy assessment
- These cells are more likely to be absent in older women
- Counterintuitively, Pap tests without endocervical cells are not more likely to be false negative*

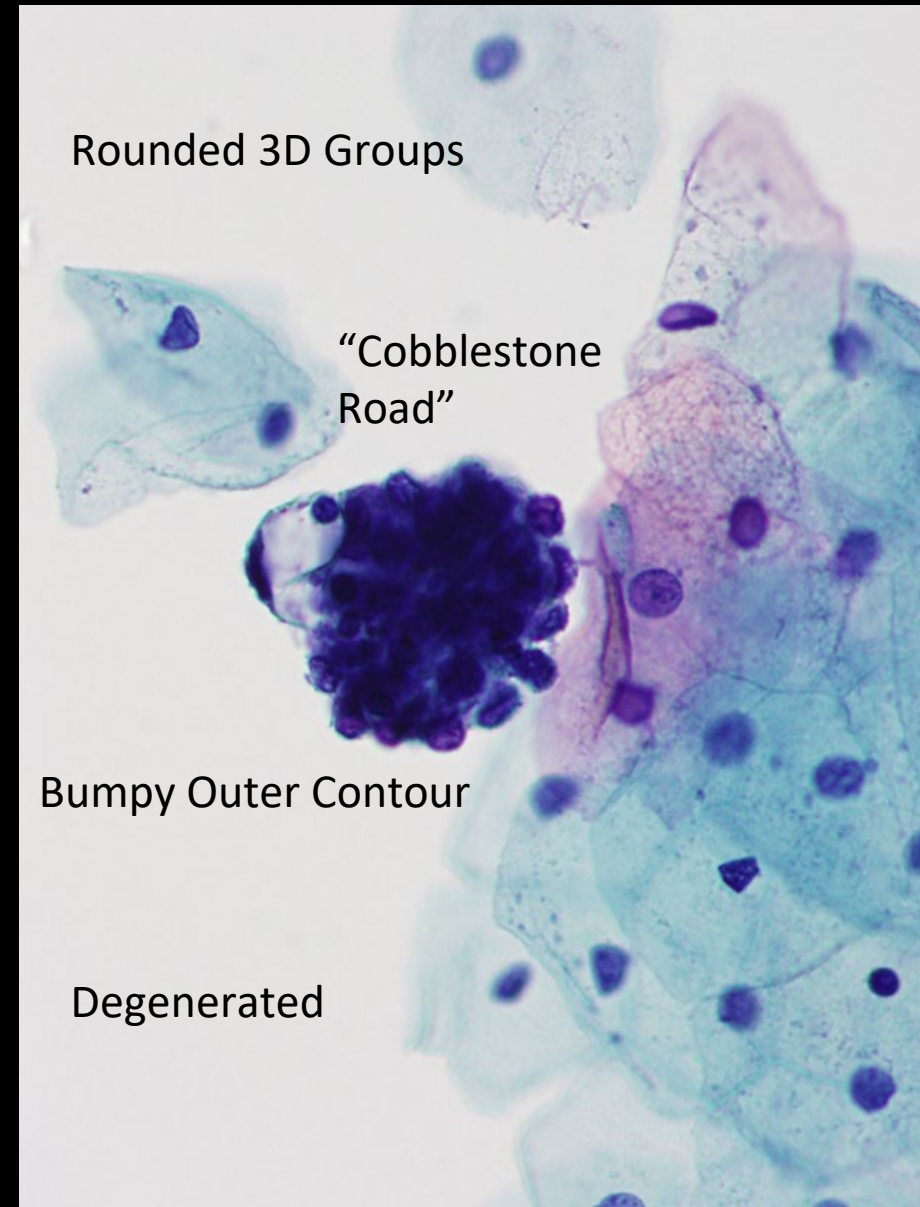
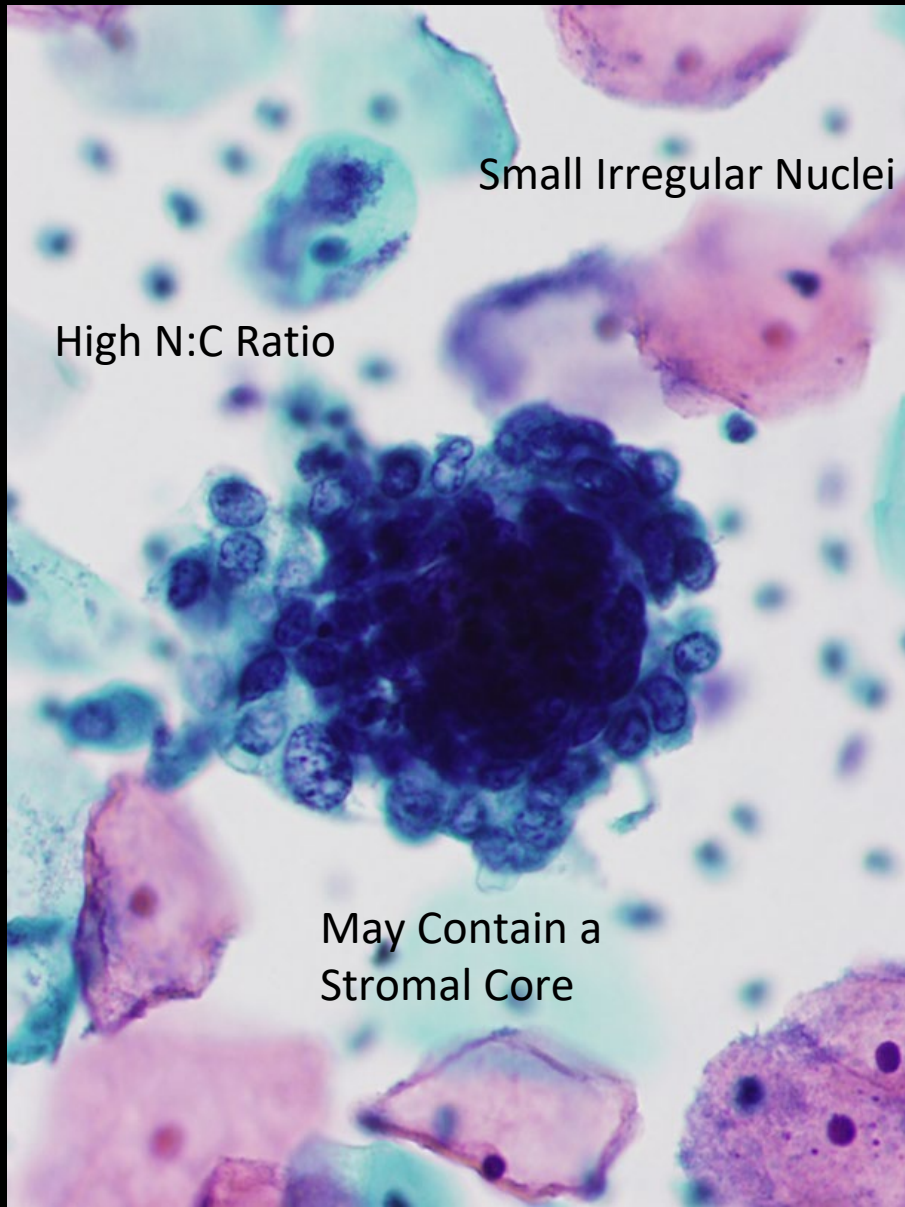
* Zhao and Austin Obstet Gynecol 2007; 107: 231.

Benign-Appearing Glandular Cells Post-Hysterectomy

- Reporting the presence of glandular cells after a hysterectomy is optional if the cells appear benign
- Benign-appearing glandular cells do not imply recurrence after hysterectomy for an adenocarcinoma*
- The cells are probably of vaginal or paravaginal origin
- Sometimes there is an unreported history of supracervical hysterectomy

* Tambouret *et al.* Acta Cytol 1998; 42: 1403.

Endometrial Cells



Endometrial Cells Over Age 45

- There is a special Bethesda System category of “Other” for endometrial cells in women aged 45 years or more
- These cells have low positive predictive value for endometrial hyperplasia or malignancy
- Biopsy follow-up is only recommended for post-menopausal or symptomatic women*

*Fadare et al. Adv Anat Pathol 2005; 12: 274.

Bathesda Categories

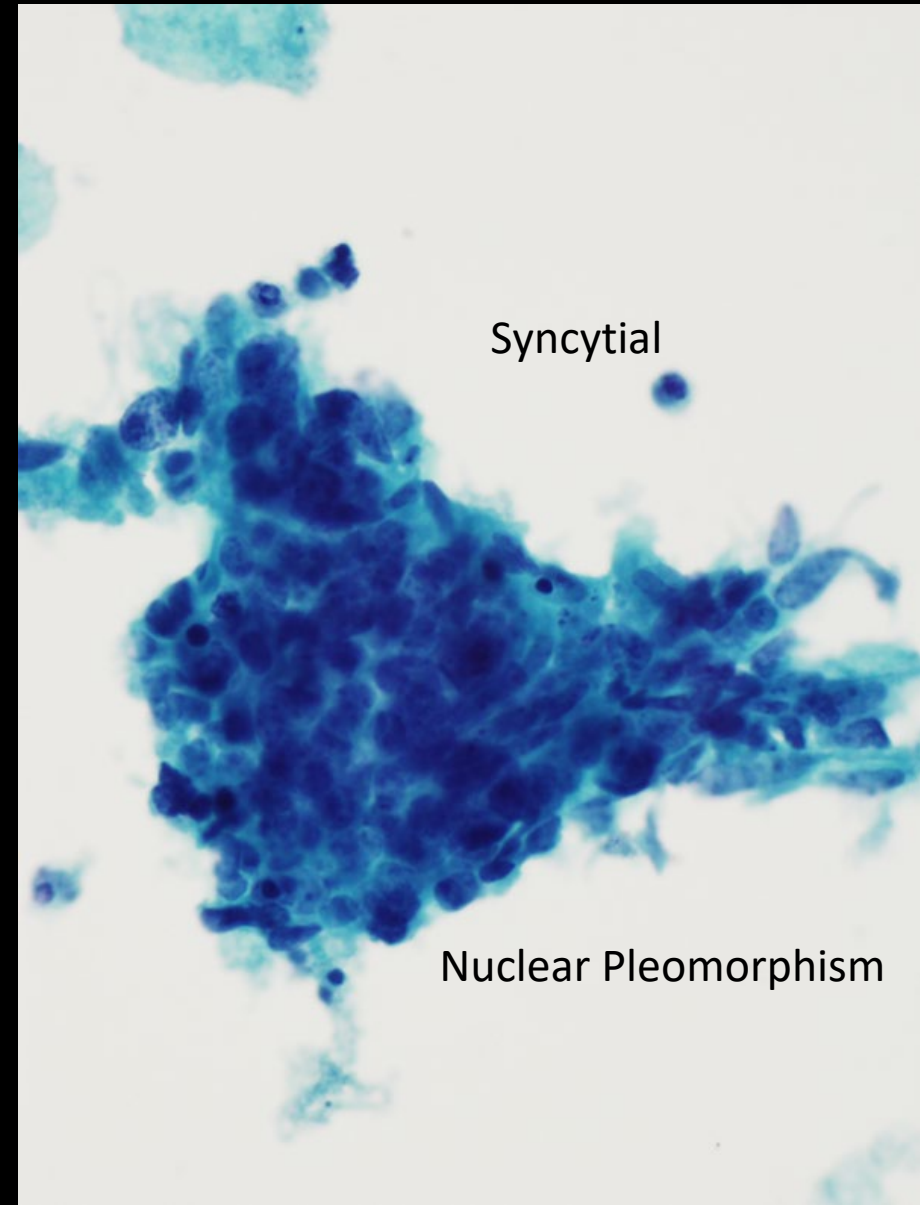
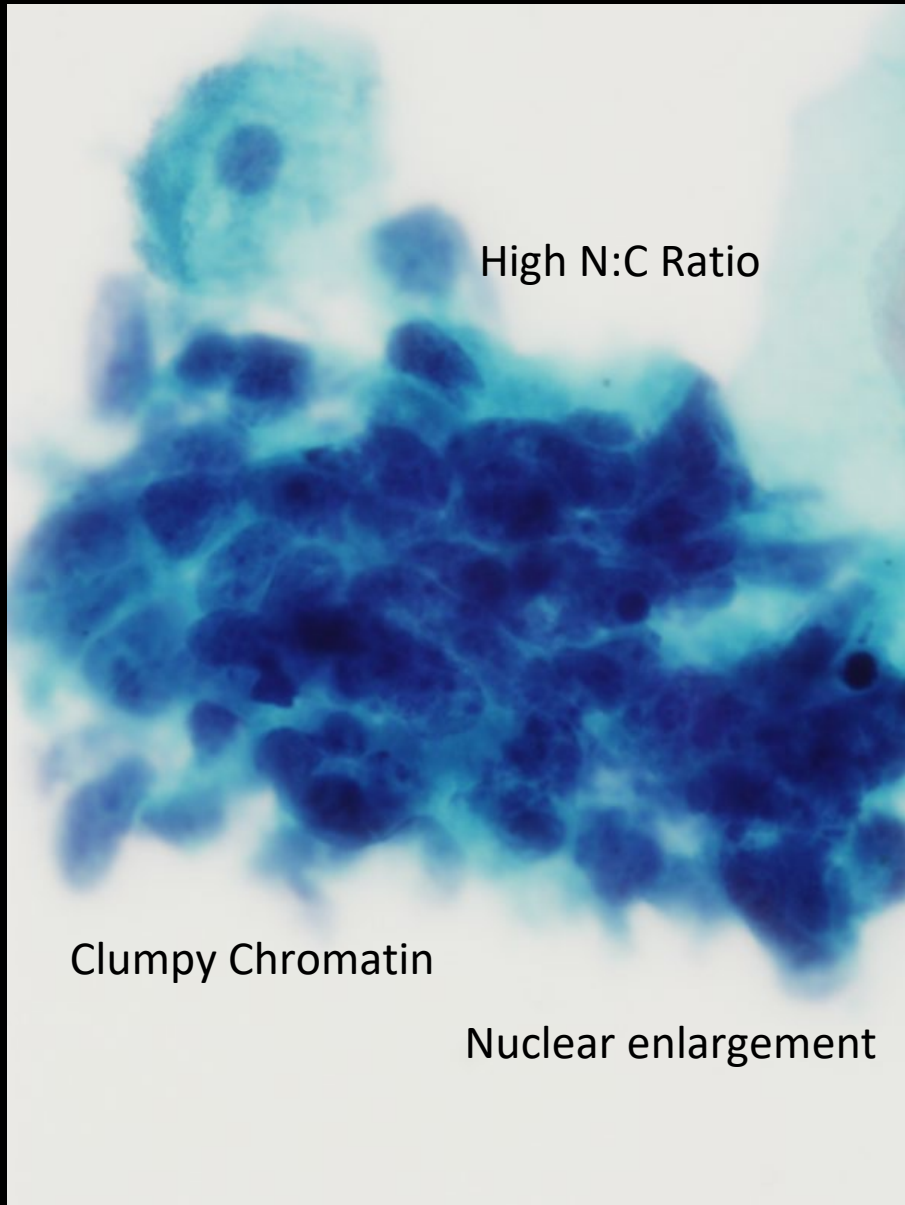
- The classification of glandular abnormalities is very complex:
- Atypical glandular cells (AGC)
 - Multiple sub-categories
- Endocervical adenocarcinoma in situ (AIS)
- Adenocarcinoma
 - Multiple sub-categories
- “Reversing the order” makes the system easier to understand
 - Once you recognize malignancy, “atypical” is more meaningful

Adenocarcinoma

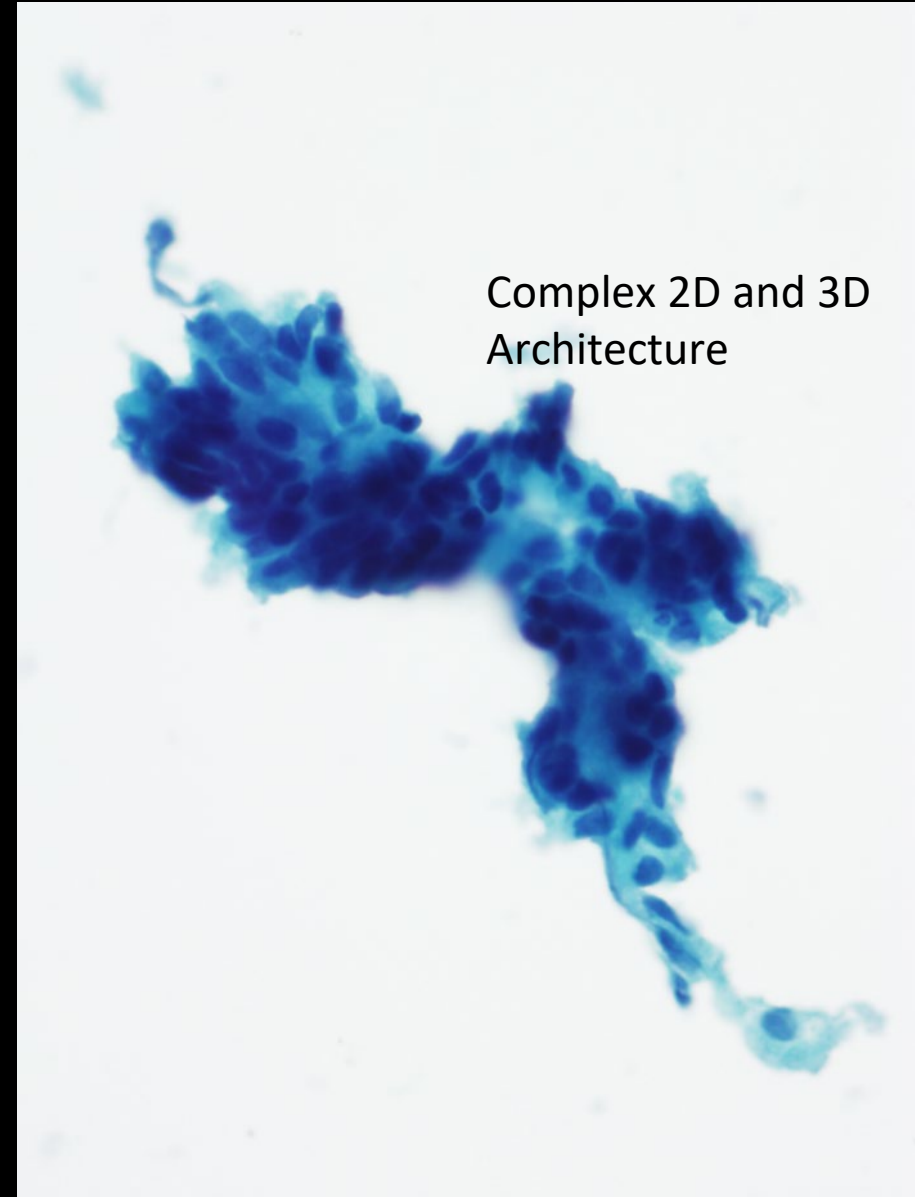
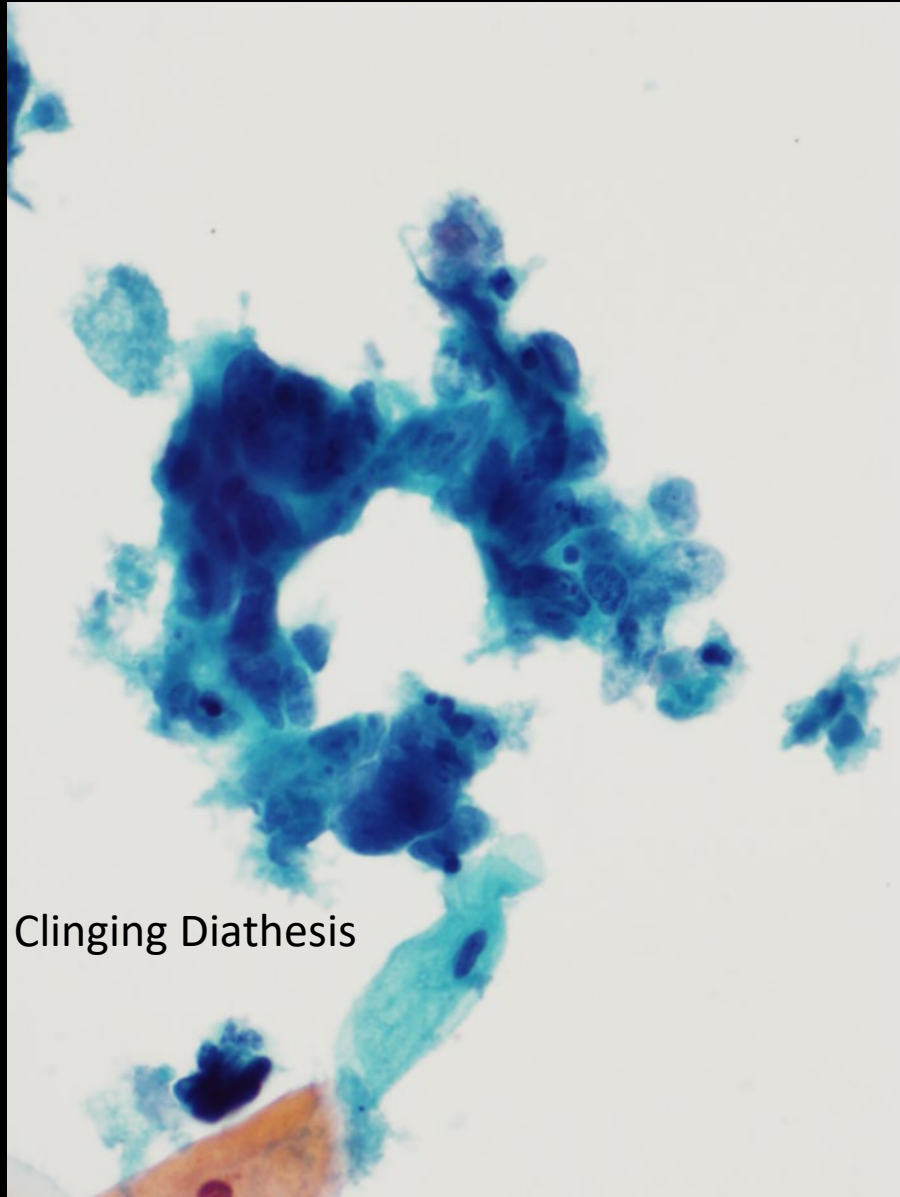
Adenocarcinoma

- Adenocarcinoma:
 - Endocervical
 - Endometrial
 - Extra-uterine
 - Not otherwise specified (NOS)

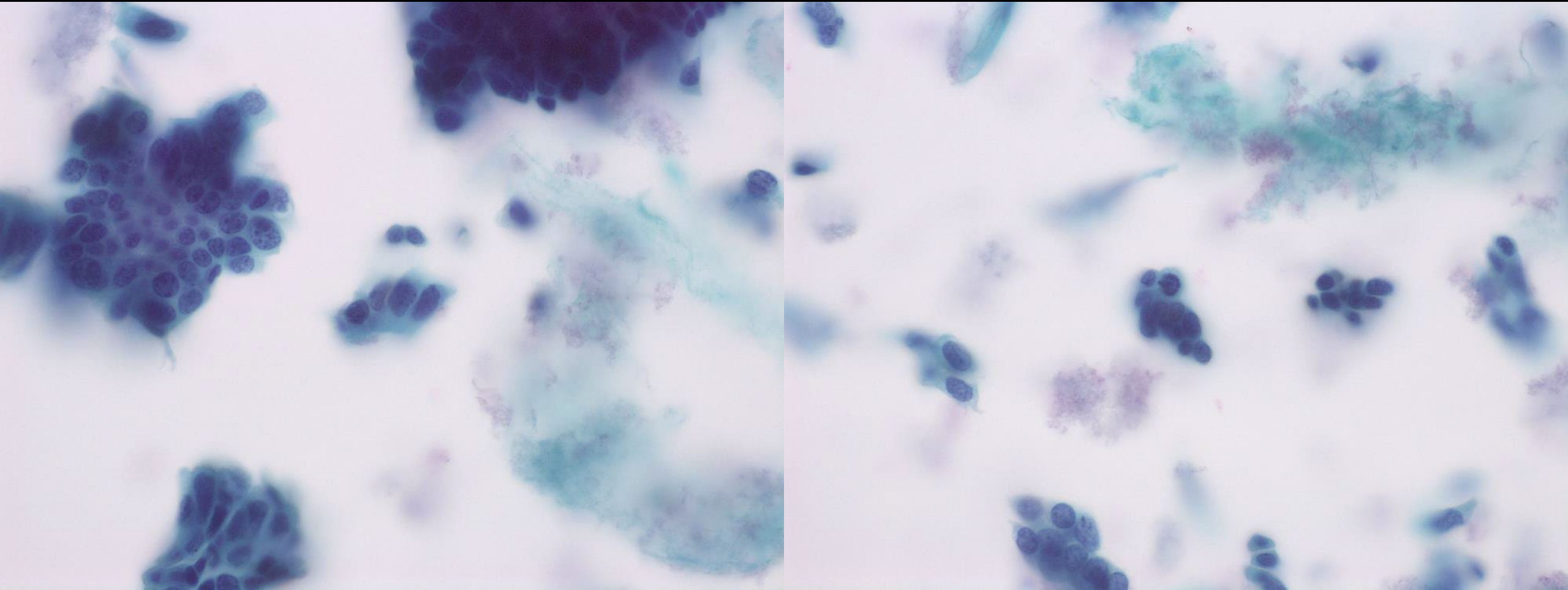
Endocervical Adenocarcinoma



Endocervical Adenocarcinoma



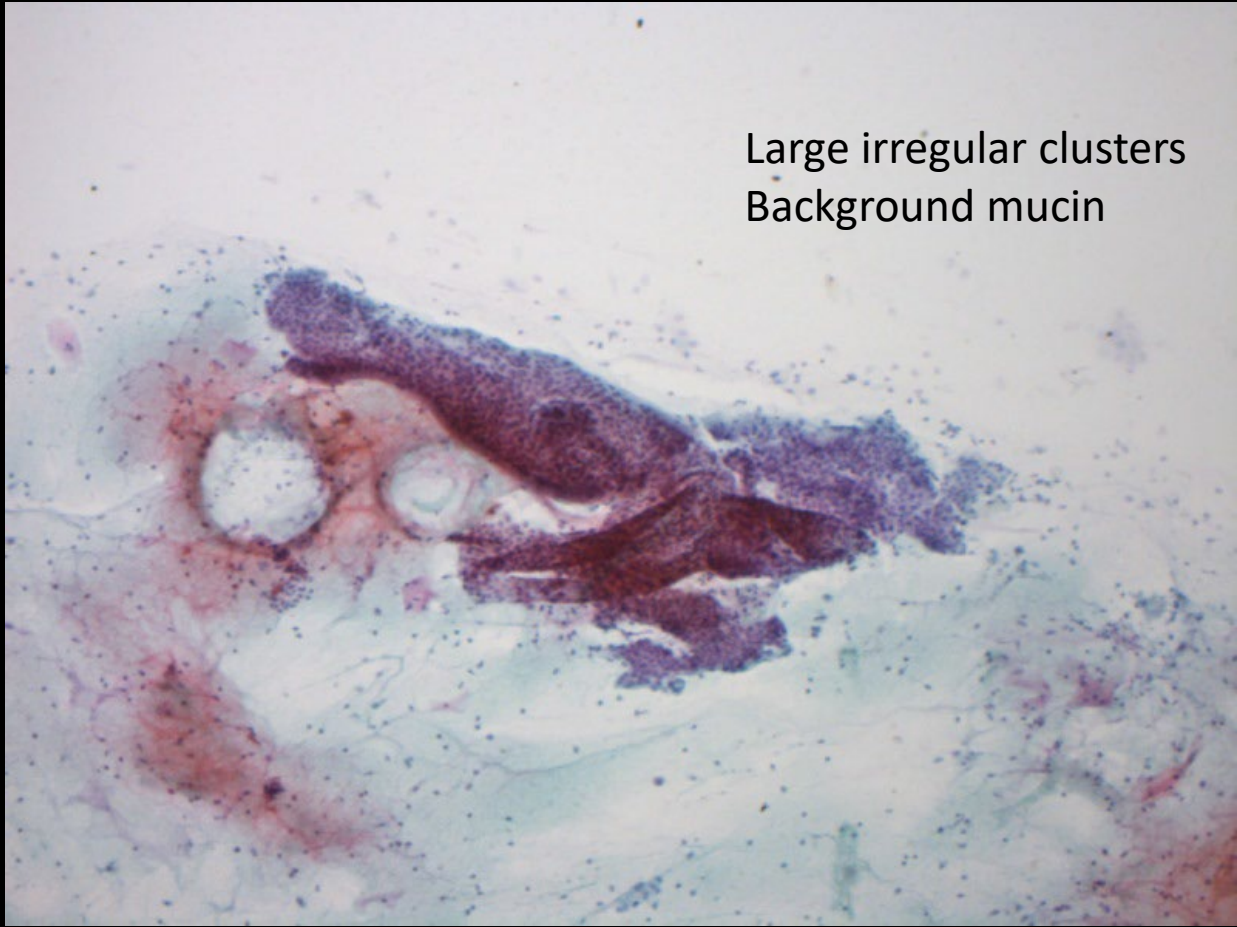
Endocervical Adenocarcinoma Diathesis



Endocervical Adenocarcinoma

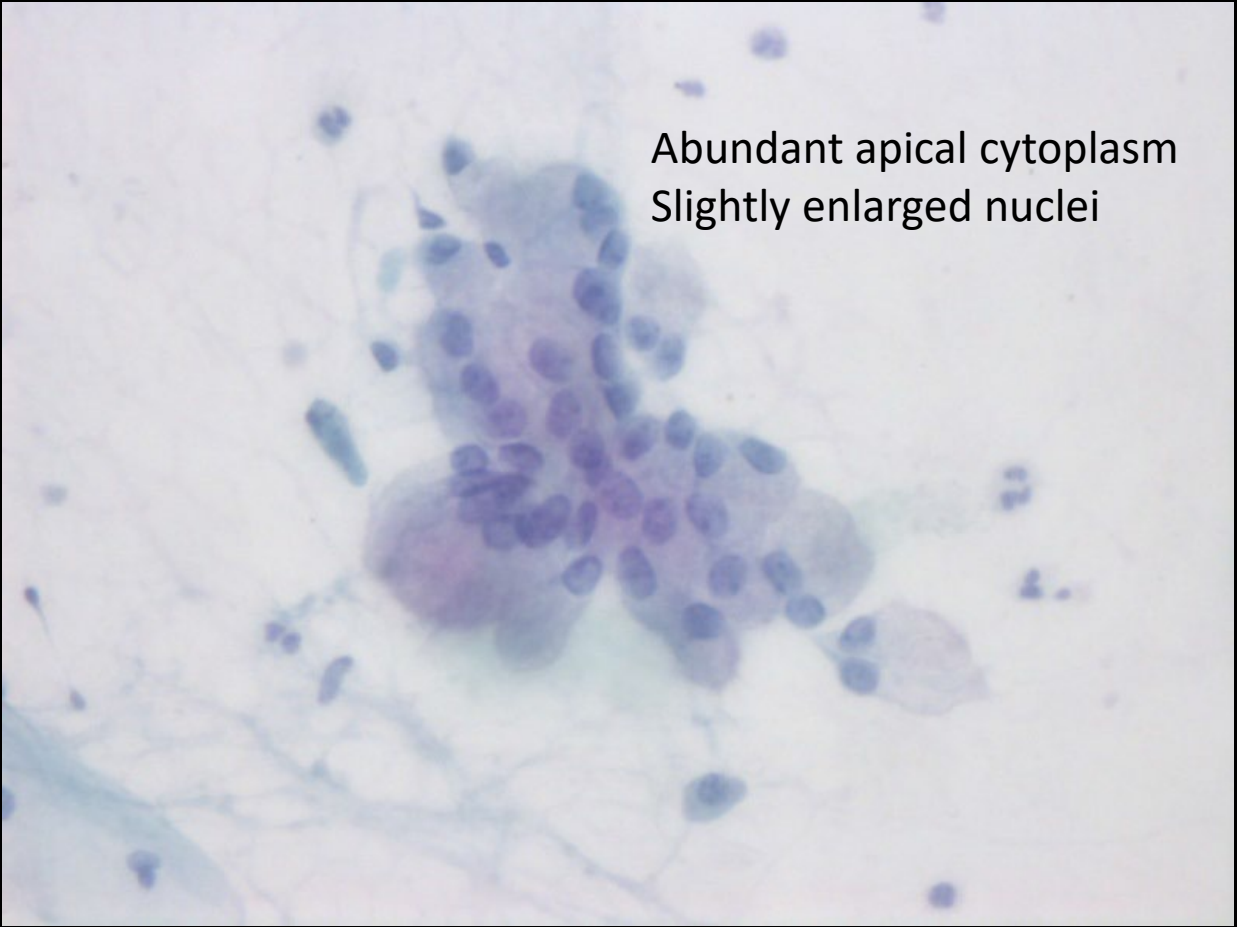
- Abundant abnormal cells, typically columnar
- Enlarged, pleomorphic nuclei with irregular chromatin, parachromatin clearing, and nuclear membrane irregularities
- Single cells, 2D sheets, 3D clusters, and syncytial aggregates are commonly seen
- Macronuclei may be present
- Cytoplasm is usually finely vacuolated
- Tumor diathesis may be present
- Abnormal squamous cells may be present

Gastric-Type Endocervical Adenocarcinoma



Large irregular clusters
Background mucin

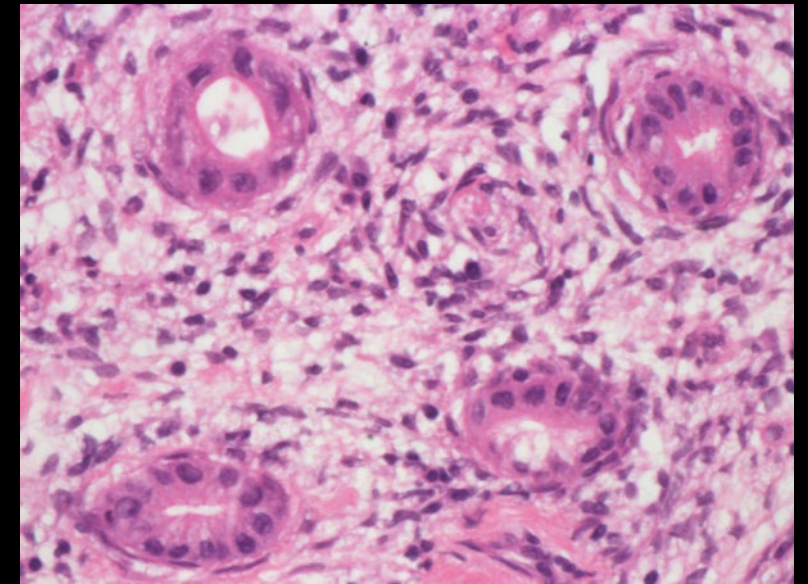
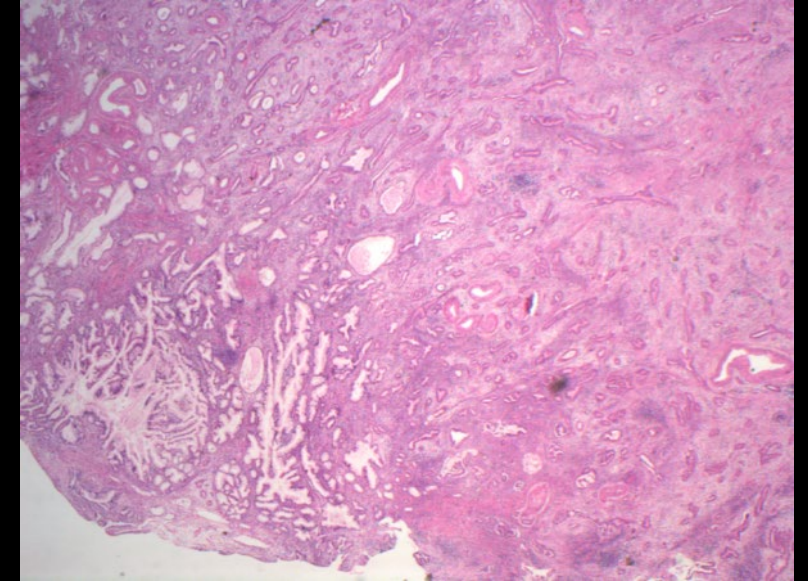
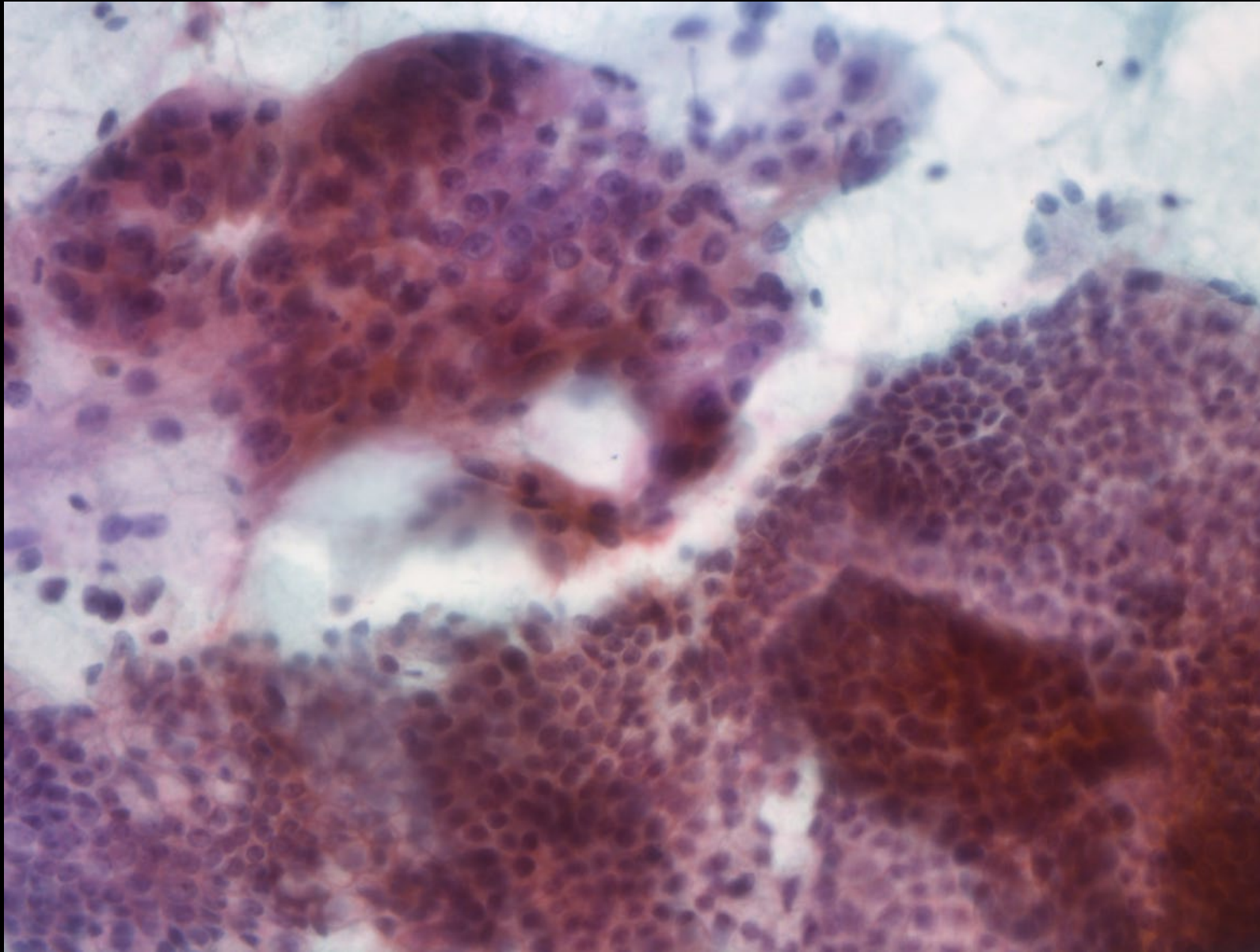
This micrograph shows a large, irregular cluster of cells with a dark purple hue, characteristic of adenocarcinoma. The cluster is surrounded by a light blue, mucinous background. The cells within the cluster are densely packed and show some architectural disorganization.



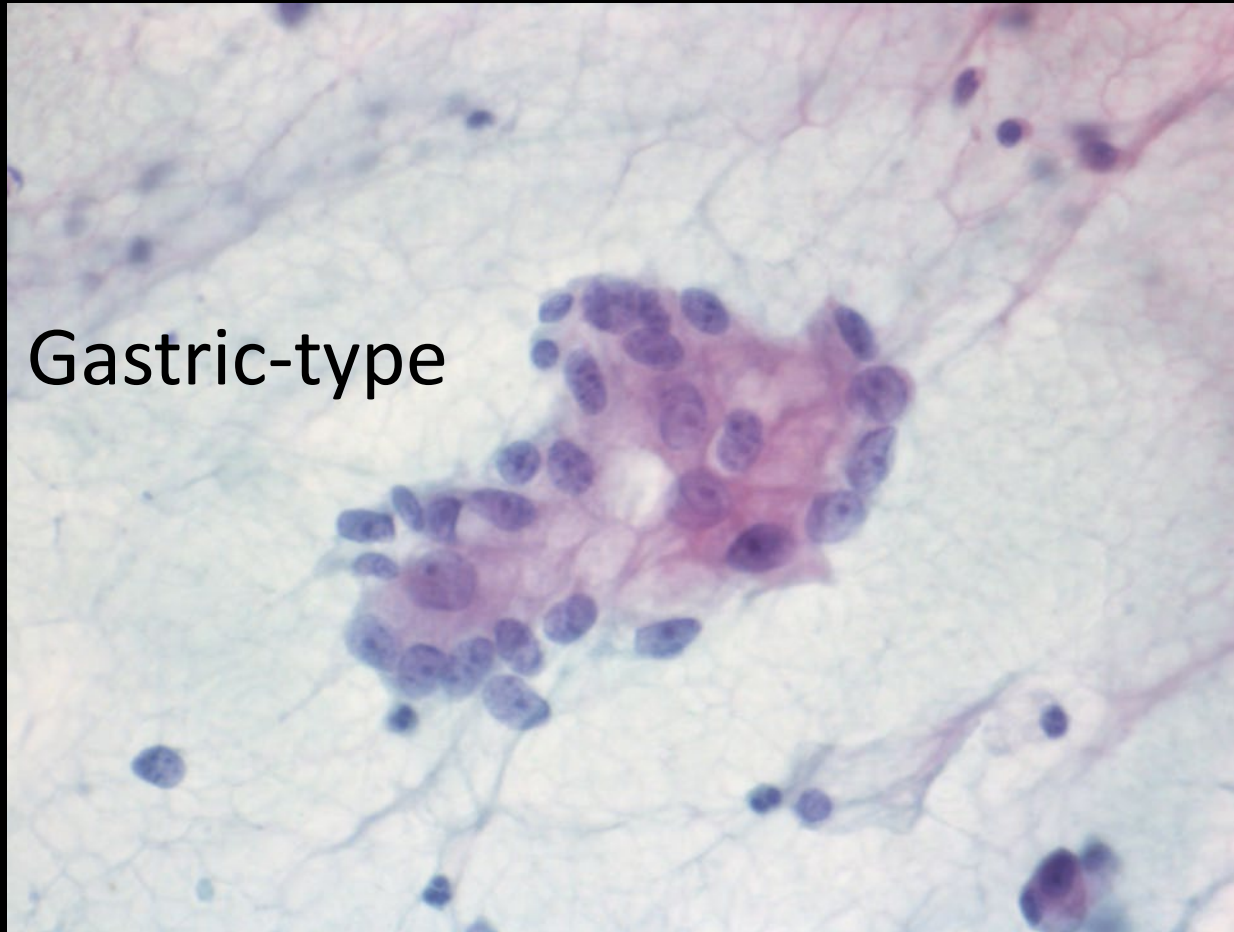
Abundant apical cytoplasm
Slightly enlarged nuclei

This micrograph provides a closer view of the adenocarcinoma cells. The cells are arranged in a cluster and exhibit abundant apical cytoplasm, which is a characteristic feature of this type of cancer. The nuclei are slightly enlarged and hyperchromatic, indicating malignancy.

Endocervical Gastric-Type Adenocarcinoma



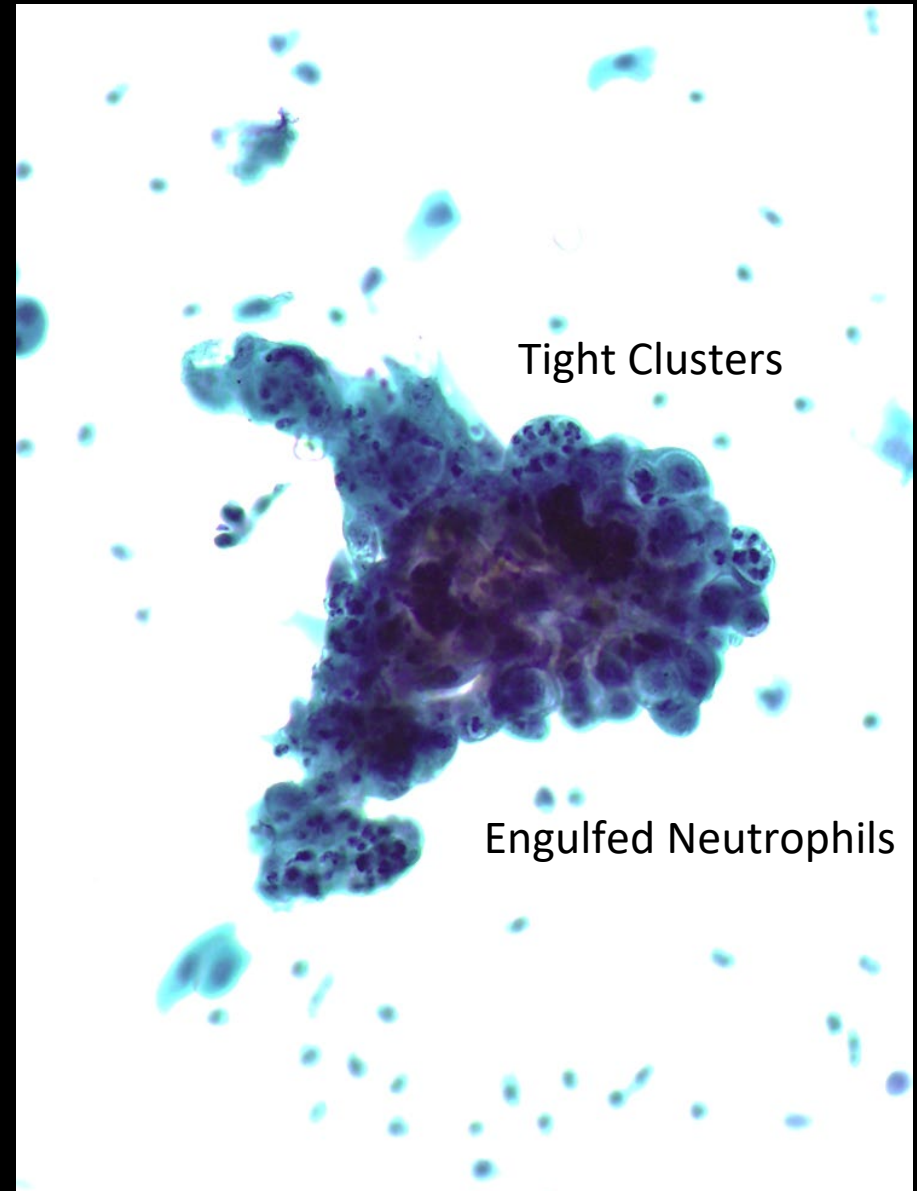
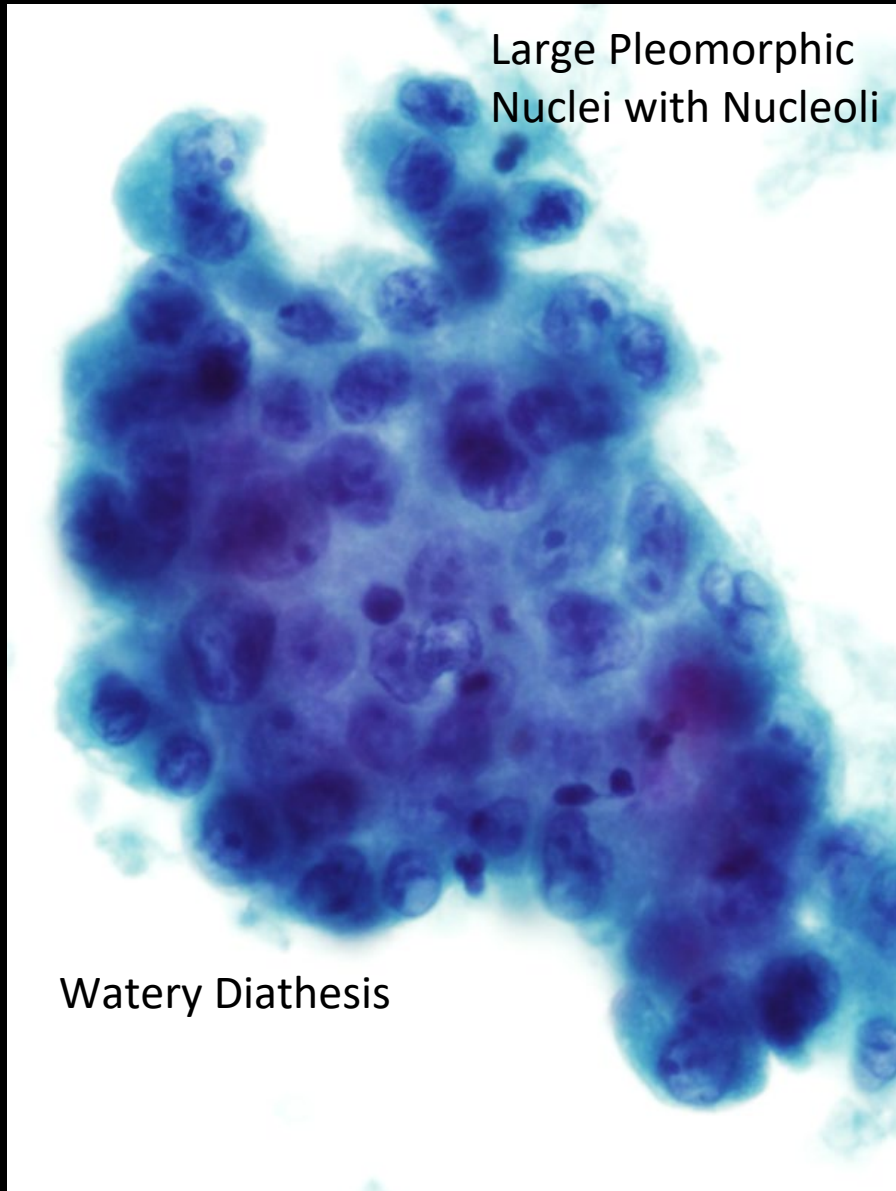
Comparison With HPV-Driven AIS



Gastric-Type Neoplasia

- Arises from gastric (or pyloric) metaplasia that is usually not discernable by H&E (yellow-tinged mucus may be seen on Pap tests)
- HIK 1083 stain can identify as a research tool
- Spectrum includes lobular endocervical glandular hyperplasia (LEGH) and adenoma malignum/minimal deviation adenocarcinoma as well as high-grade adenocarcinoma
- This process is not HPV-driven; negative for p16 and HR-HPV testing
- *STK11* mutations and Peutz-Jeghers association
- Significant minority of adenocarcinomas, up to 25% in Japan

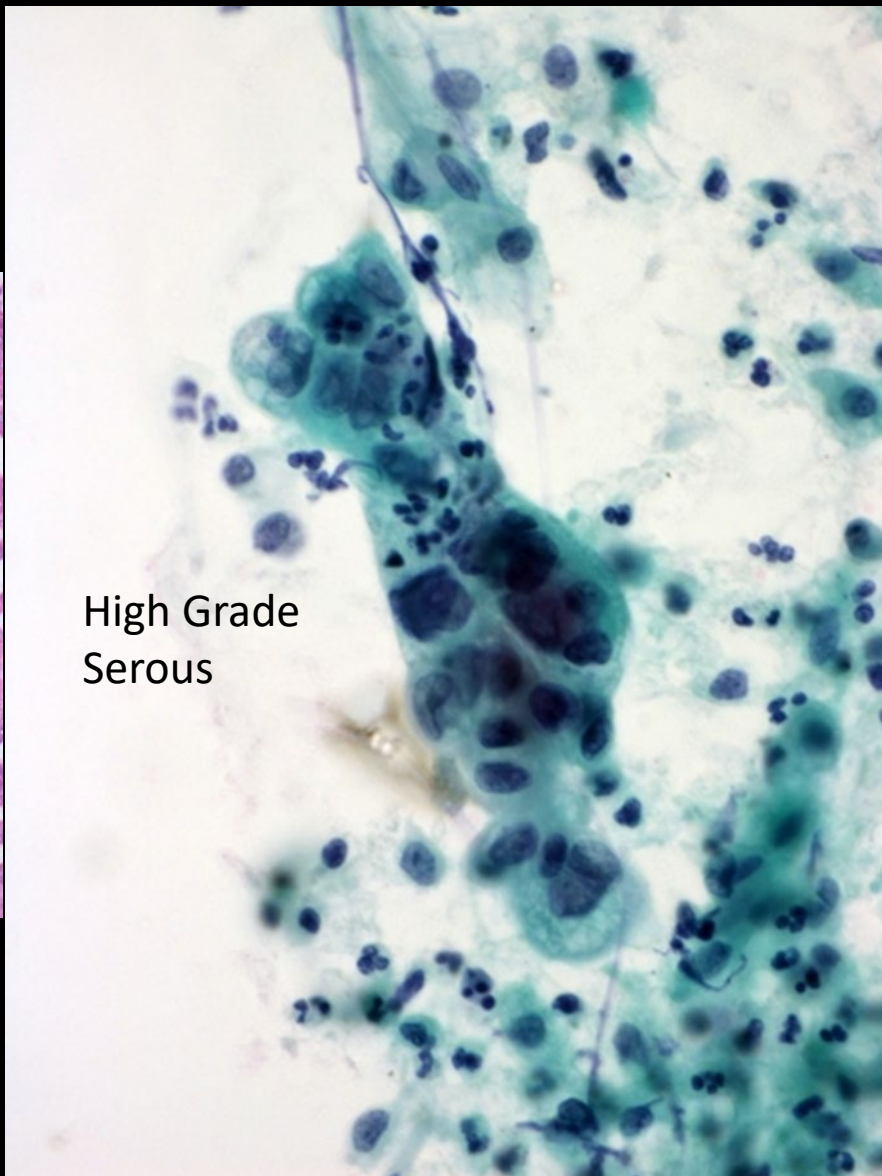
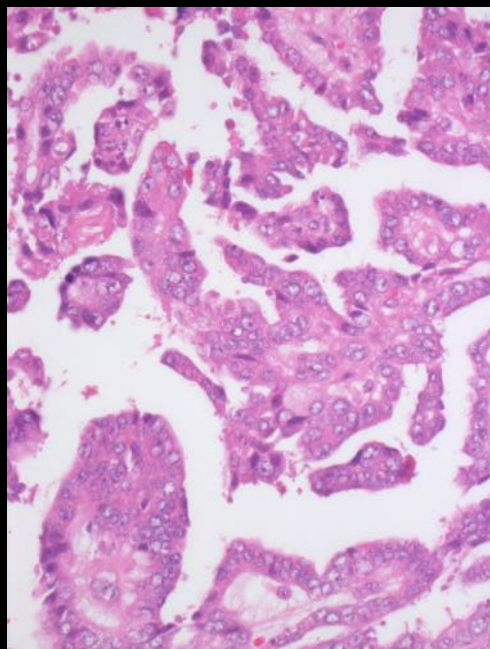
Endometrial Adenocarcinoma



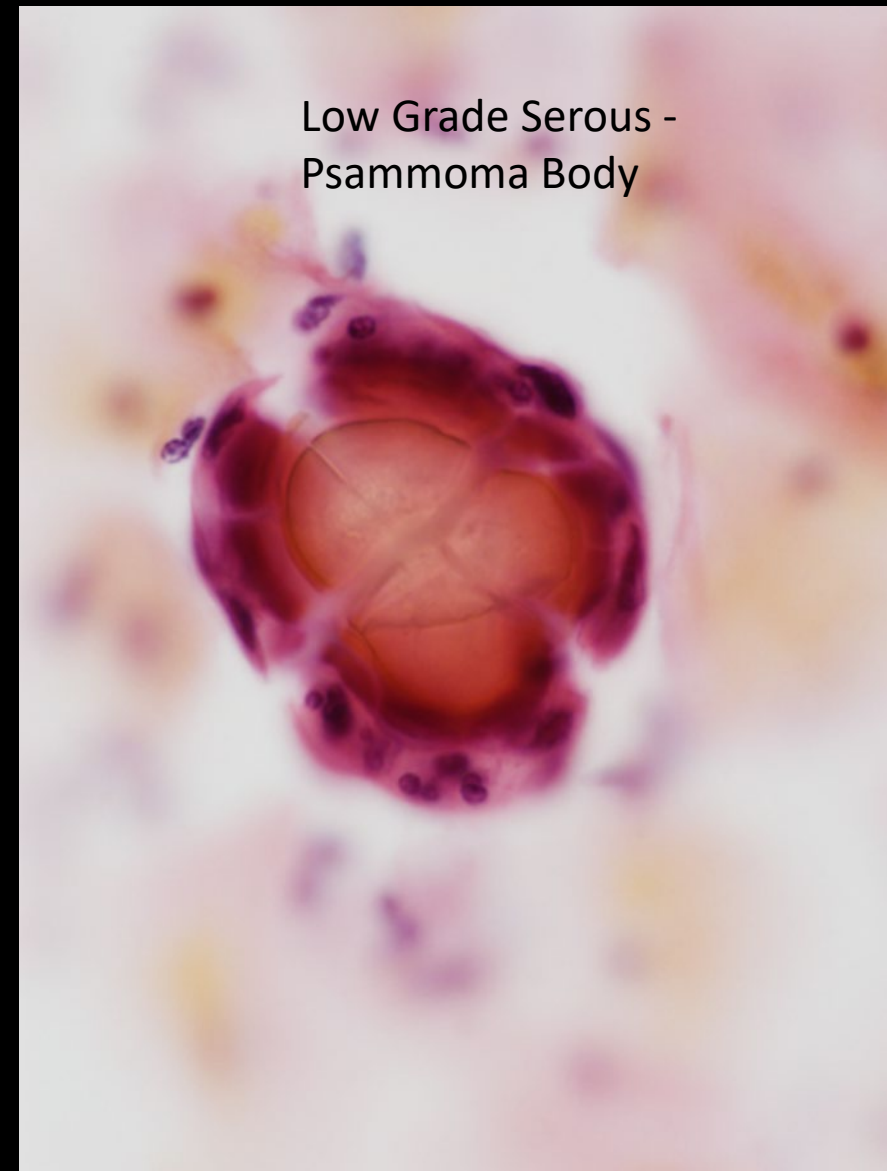
Endometrial Adenocarcinoma

- Cells occur singly or in small, tight clusters
- Nuclear enlargement (varies by grade)
- Variation in nuclear size and loss of polarity
- Nuclear hyperchromasia with irregular chromatin and parachromatin clearing
- Nucleoli
- Scant cytoplasm that may be vacuolated or contain engulfed neutrophils
- Watery (finely granular) diathesis may be present

Serous Carcinoma

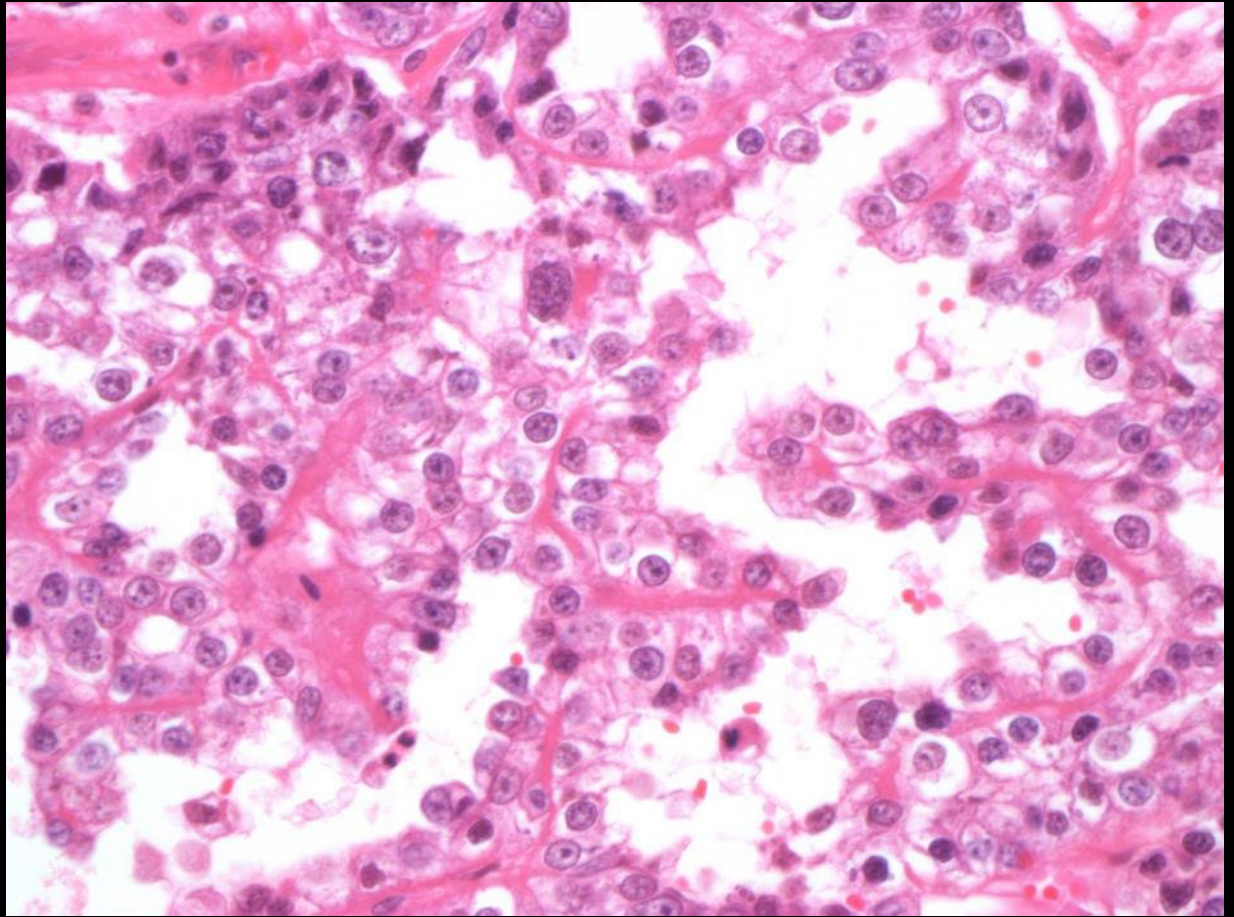
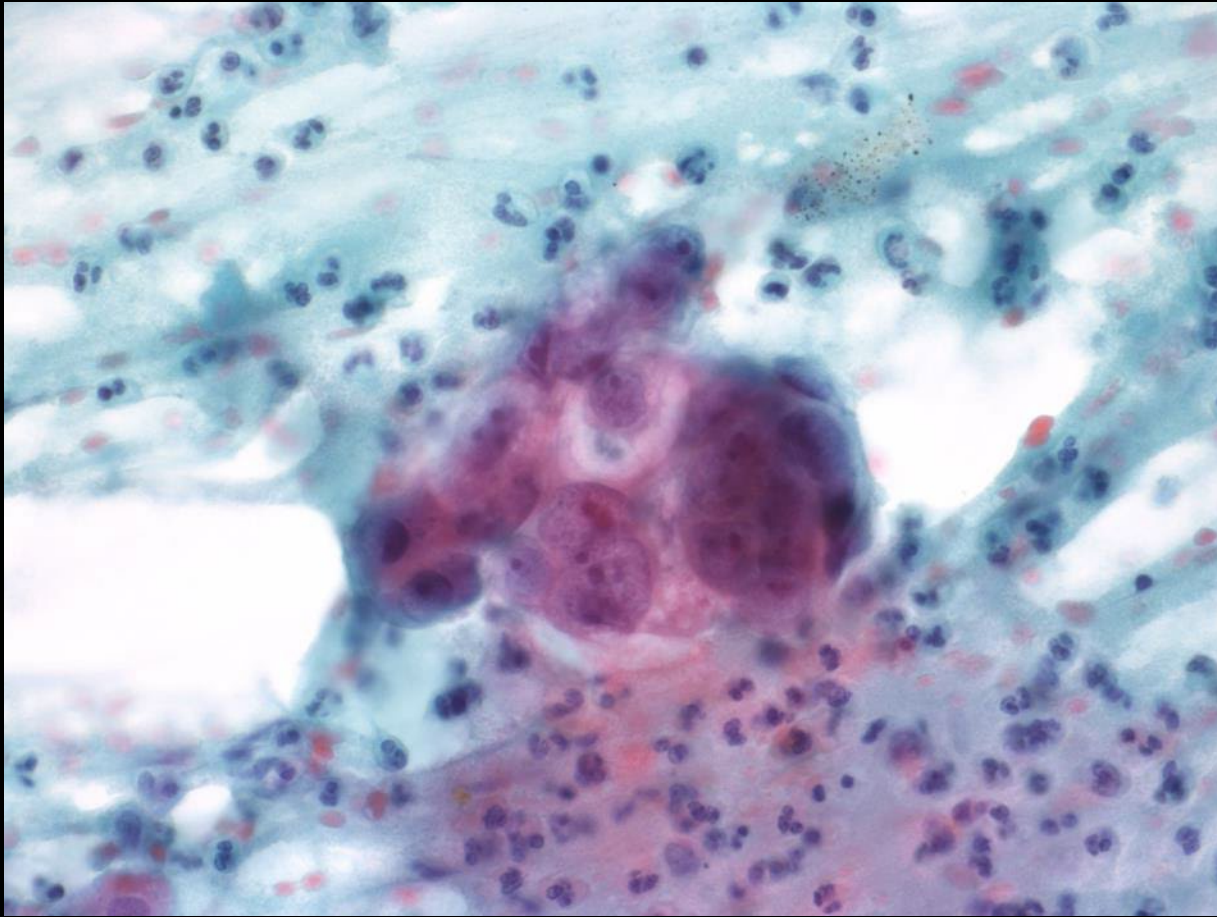


High Grade
Serous



Low Grade Serous -
Psammoma Body

Clear Cell Carcinoma

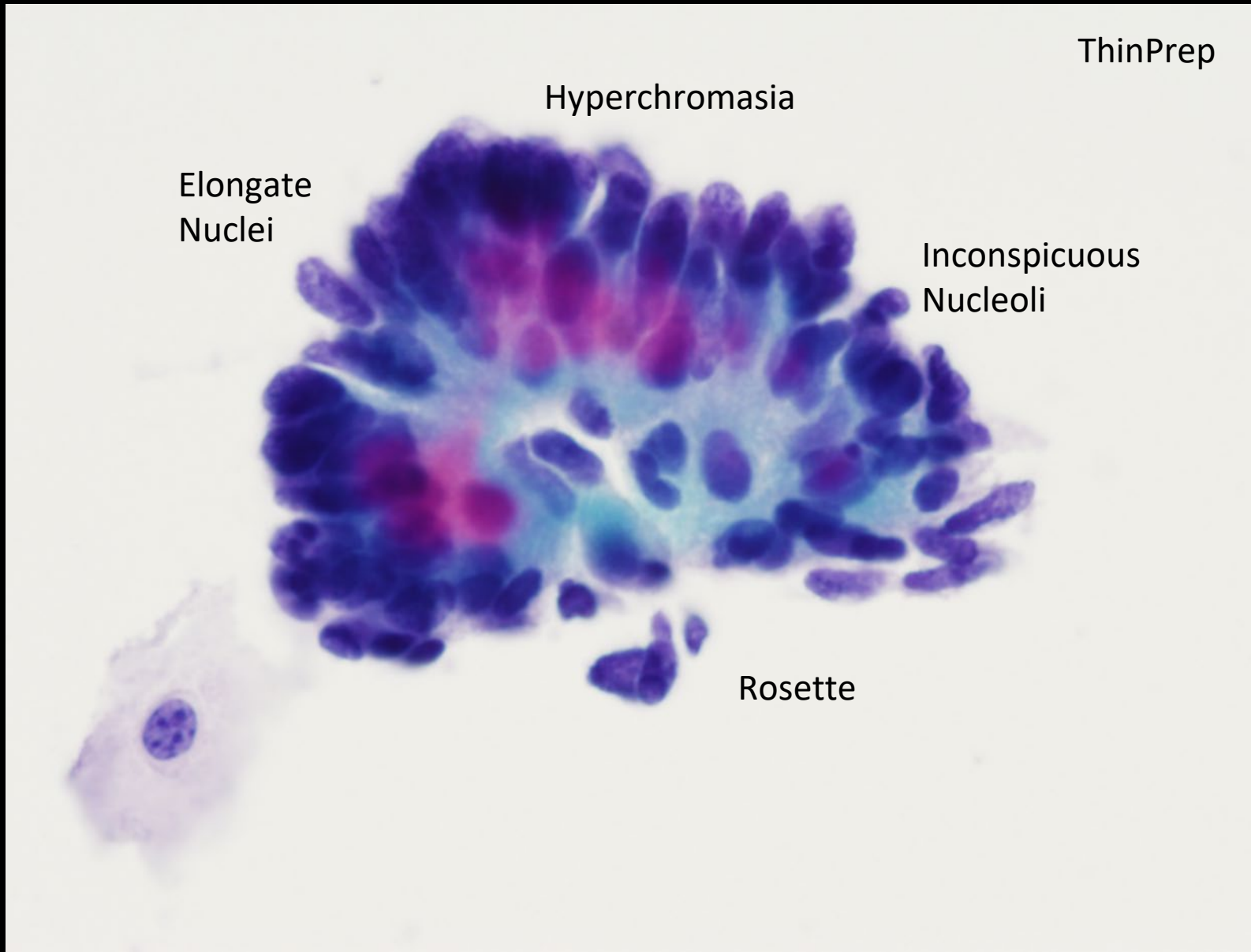


Adenocarcinoma In Situ (AIS)

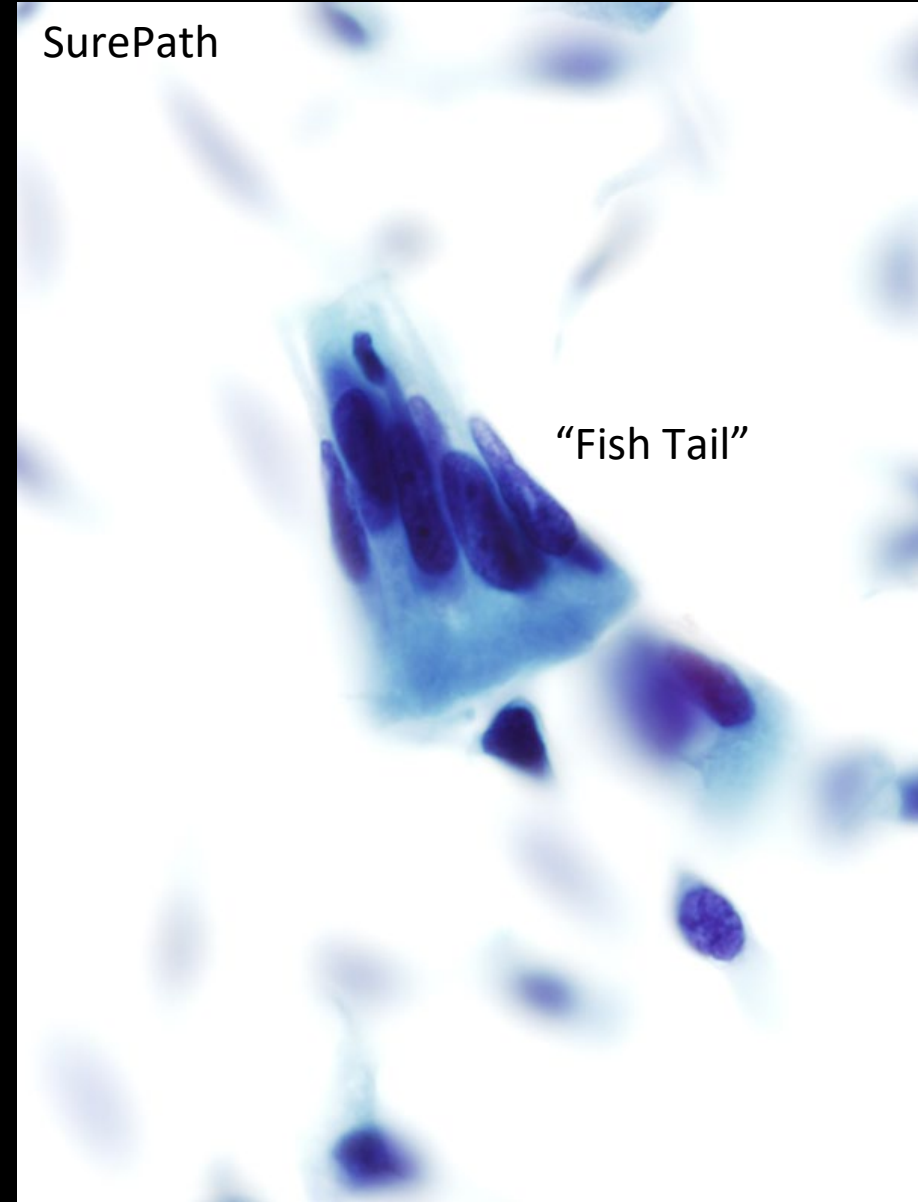
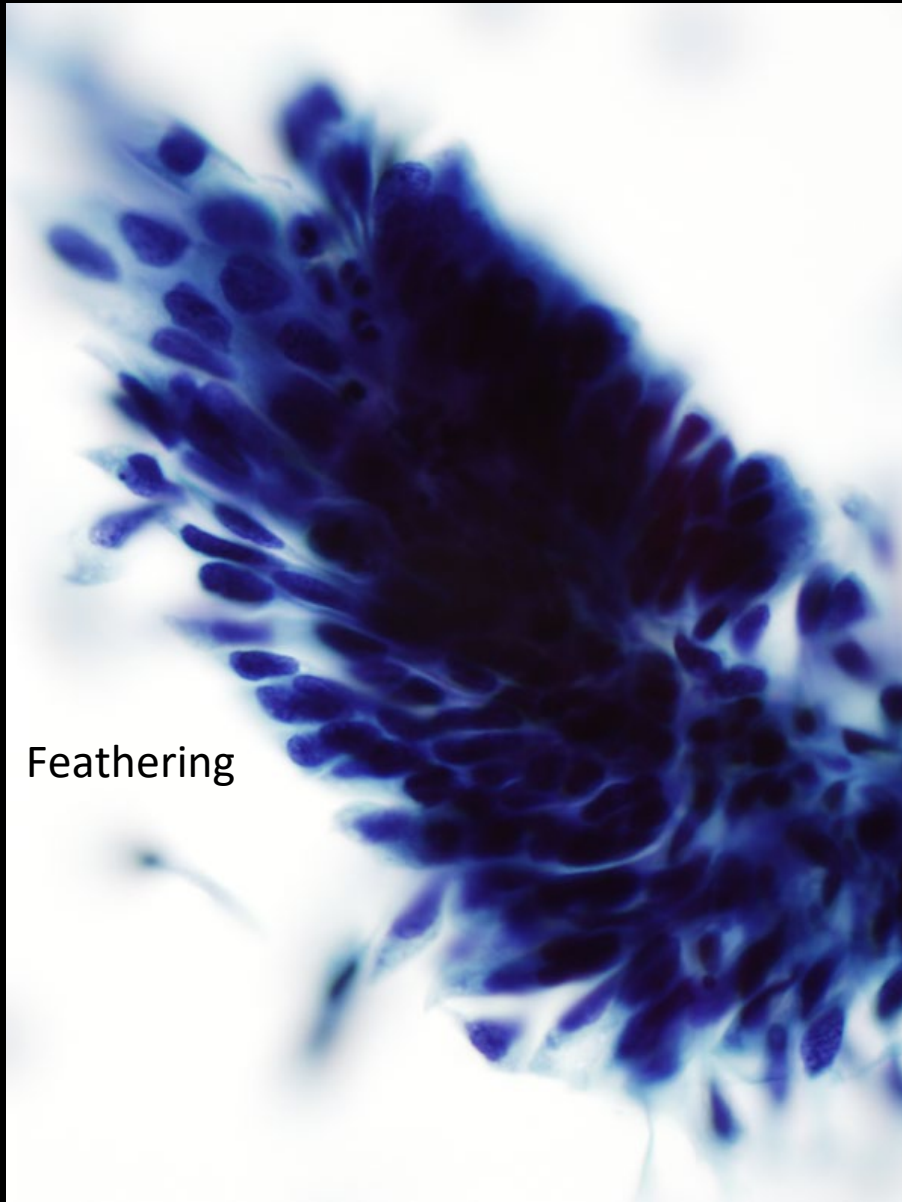
Adenocarcinoma In Situ

- Sheets, clusters, strips, or rosettes with nuclear crowding and overlap
- Feathering
- Nuclear enlargement with anisonucleosis, elongation, and stratification
- Nuclear hyperchromasia with evenly dispersed coarse chromatin
- Mitosis and apoptotic bodies
- Some cells show a definite columnar arrangement
- Inconspicuous or small nucleoli
- Increased N:C with decreased cytoplasm and mucin
- Clean background
- Abnormal squamous cells may also be present

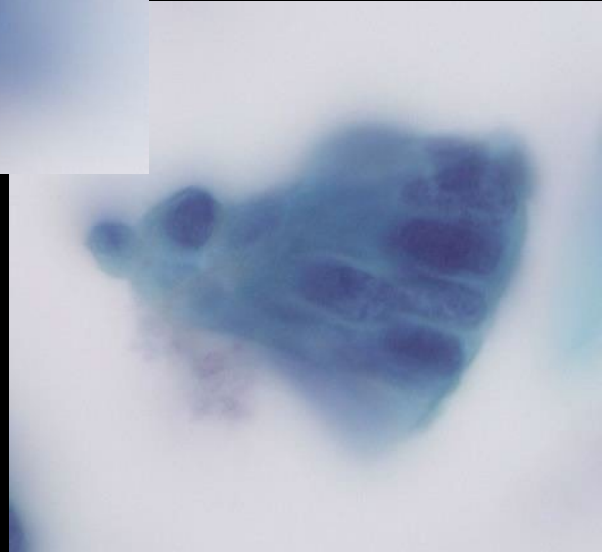
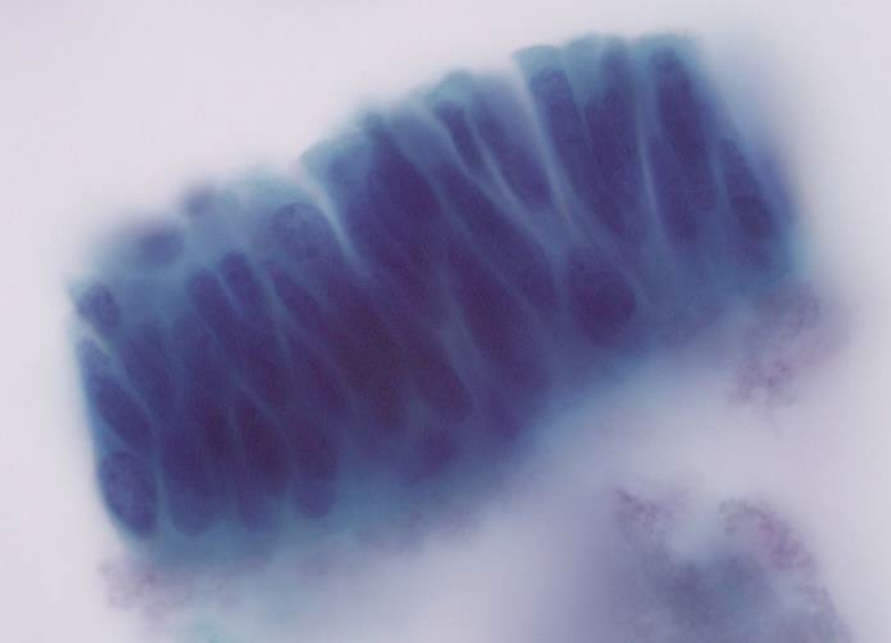
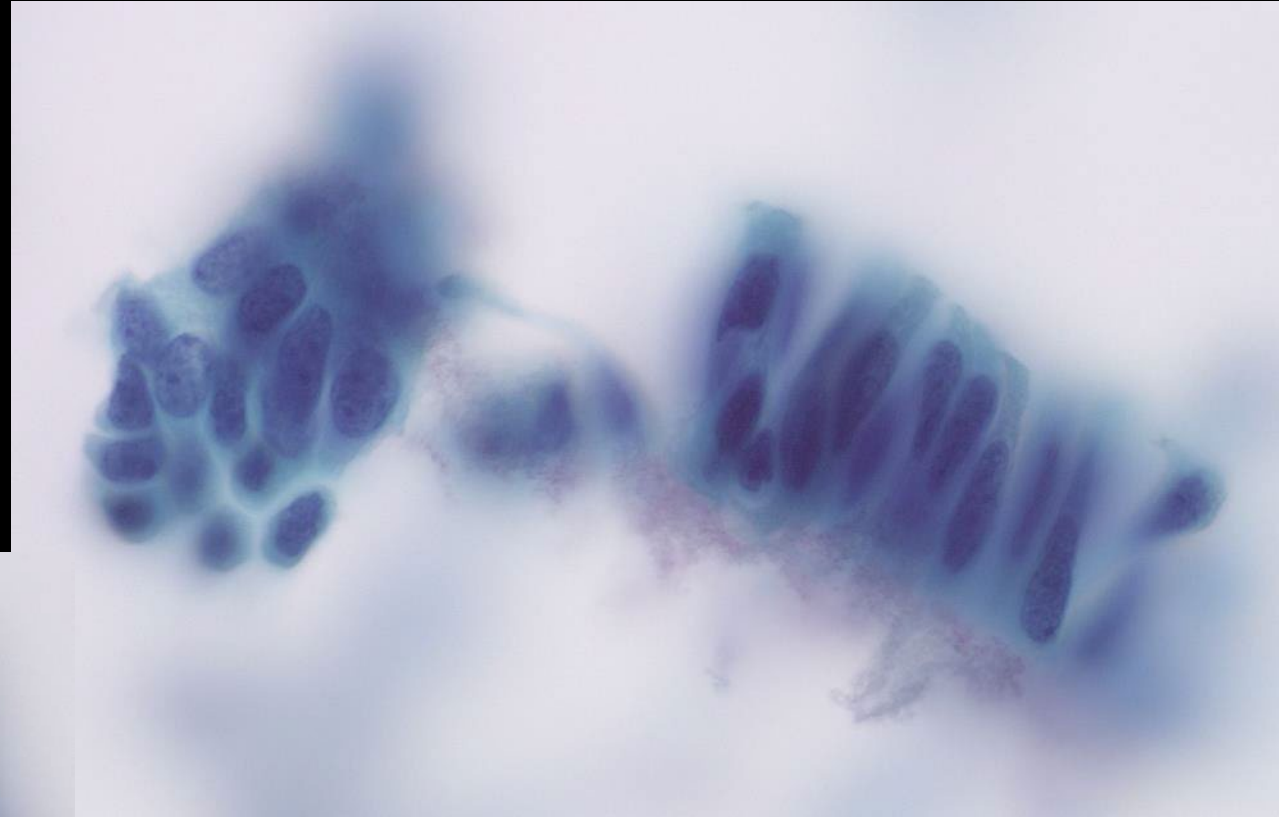
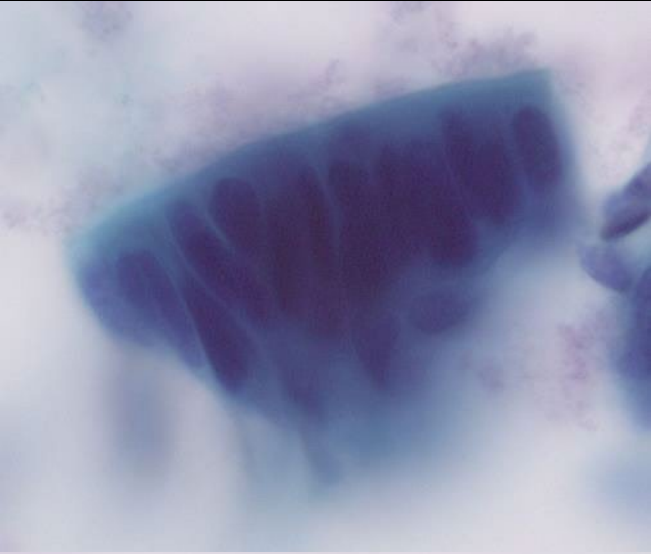
Adenocarcinoma In Situ



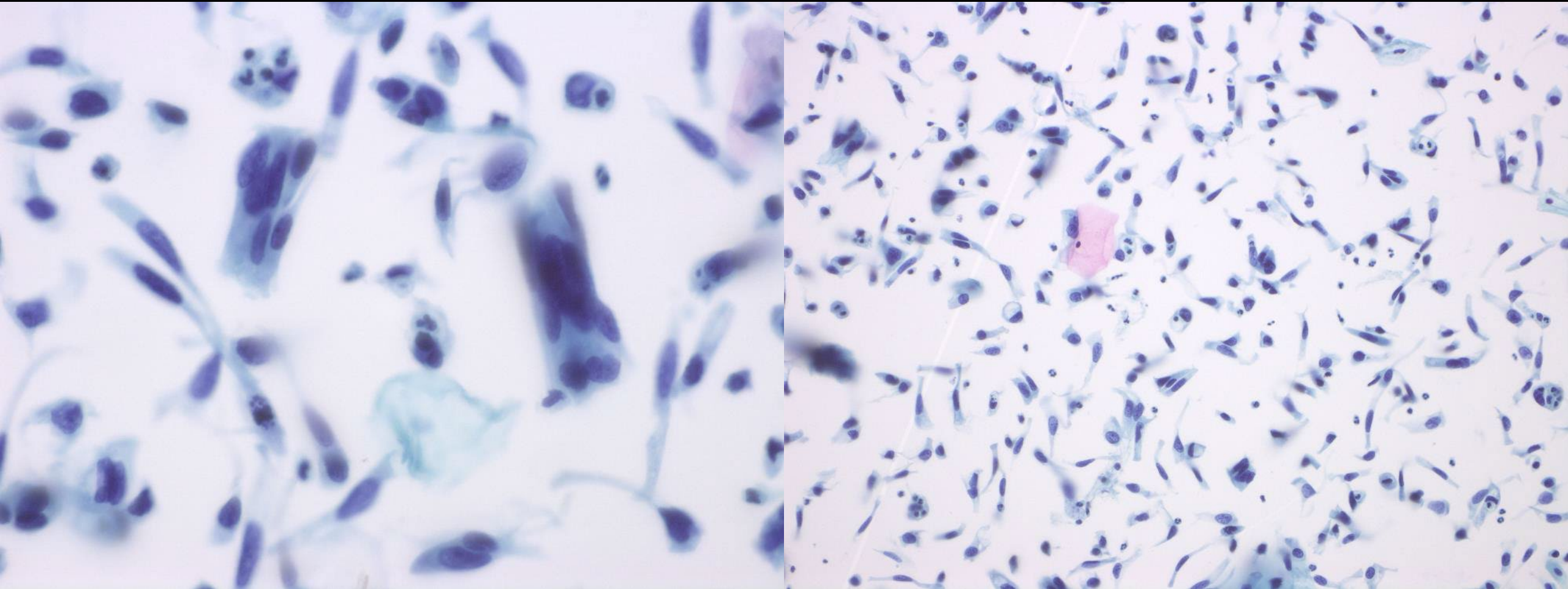
Adenocarcinoma In Situ



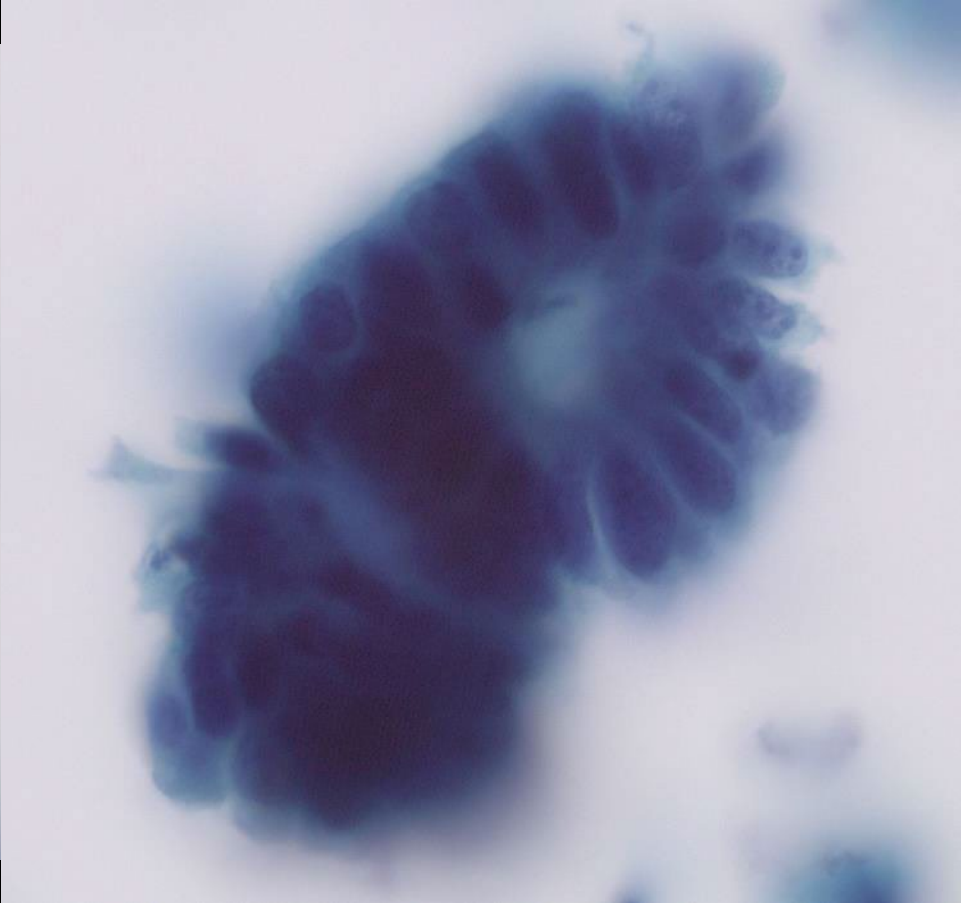
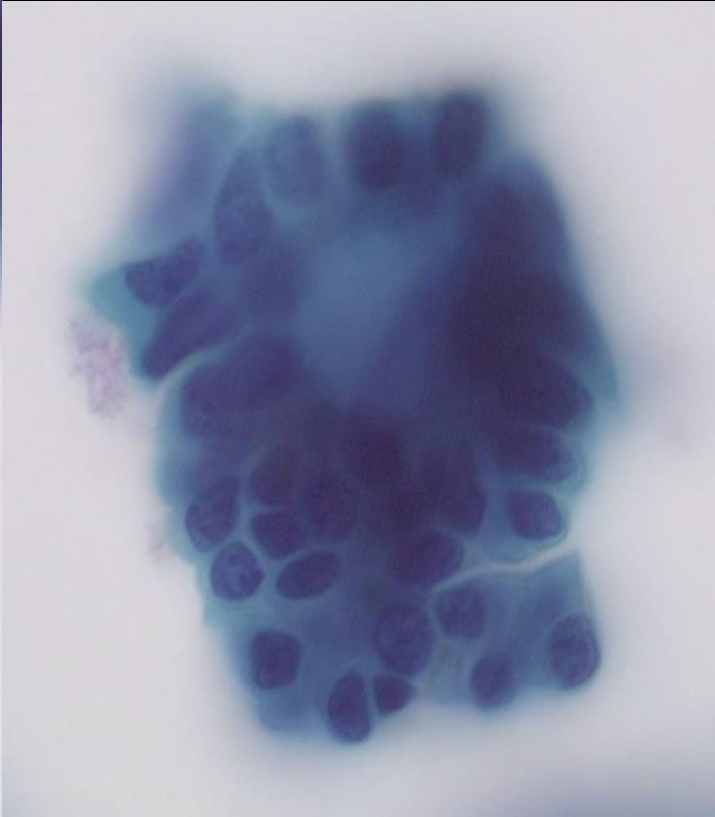
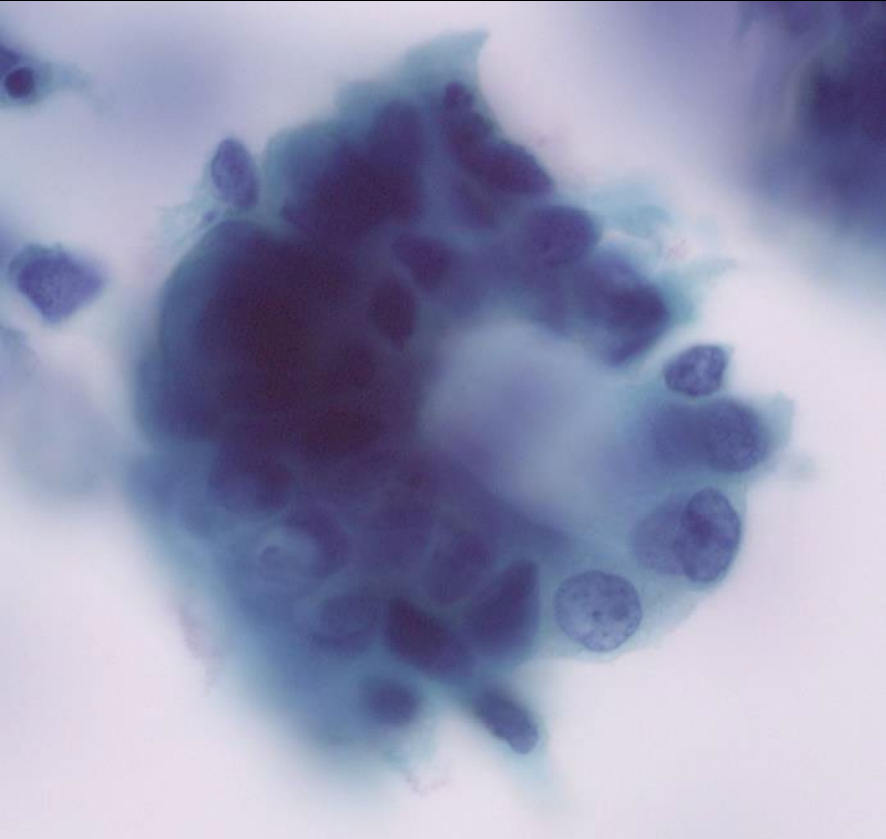
Bird Tails and Strips



Individual Tumor Cells



Rosettes



Atypical Glandular Cells (AGC)

Atypical Glandular Cells (AGC)

- Atypical glandular cells
 - NOS (not otherwise specified)
 - Favor neoplastic
- Atypical endocervical cells
 - NOS (not otherwise specified)
 - Favor neoplastic
- Atypical endometrial cells

AGC in Liquid-Based Pap Tests

- AGC is more frequent in liquid-based Pap tests, but is still uncommon (mean 0.2% of all Paps)
- HPV testing has been proposed for triage because cervical lesions are usually HPV+, especially types 18 and 16
- However, most cancers found in follow-up for AGC are endometrial*

*Zhao *et al.* Gynecol Oncol 2009; 114: 383.

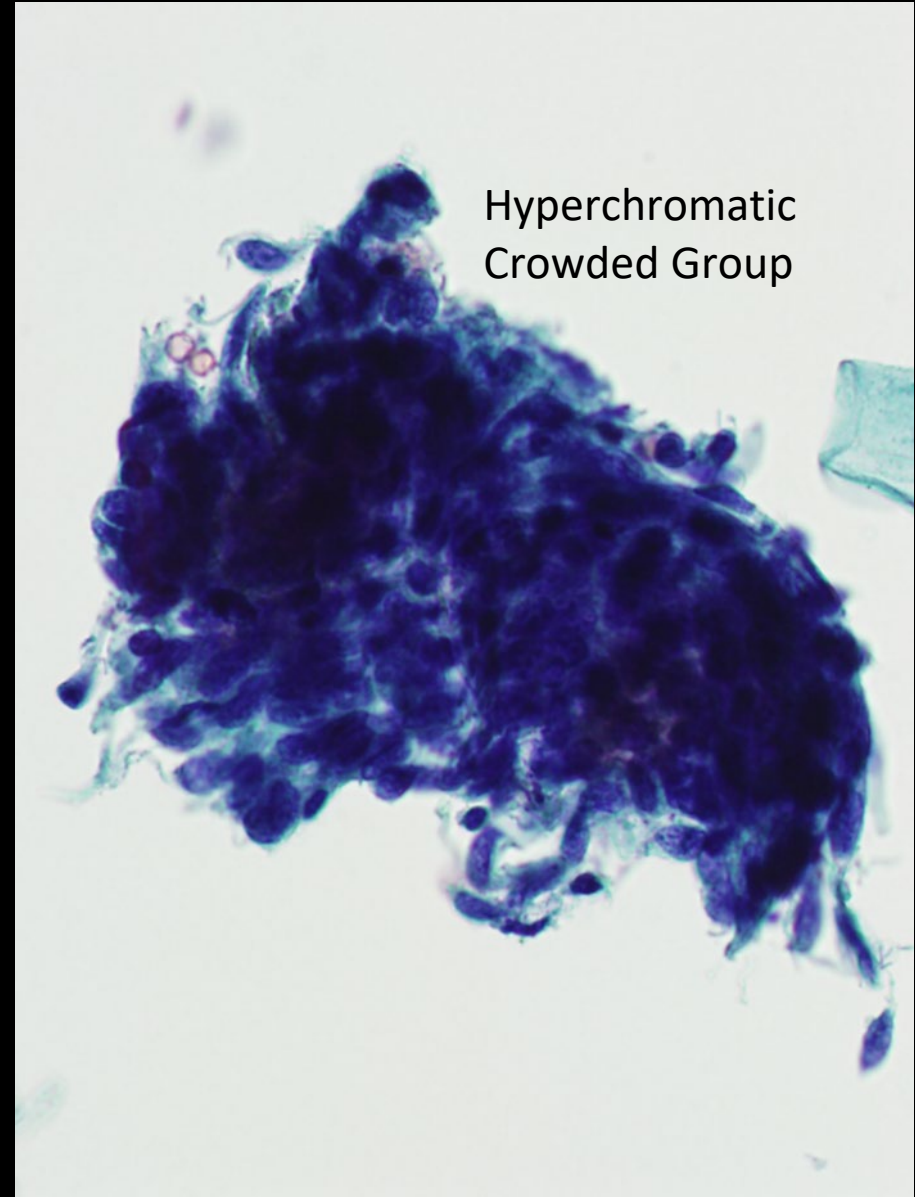
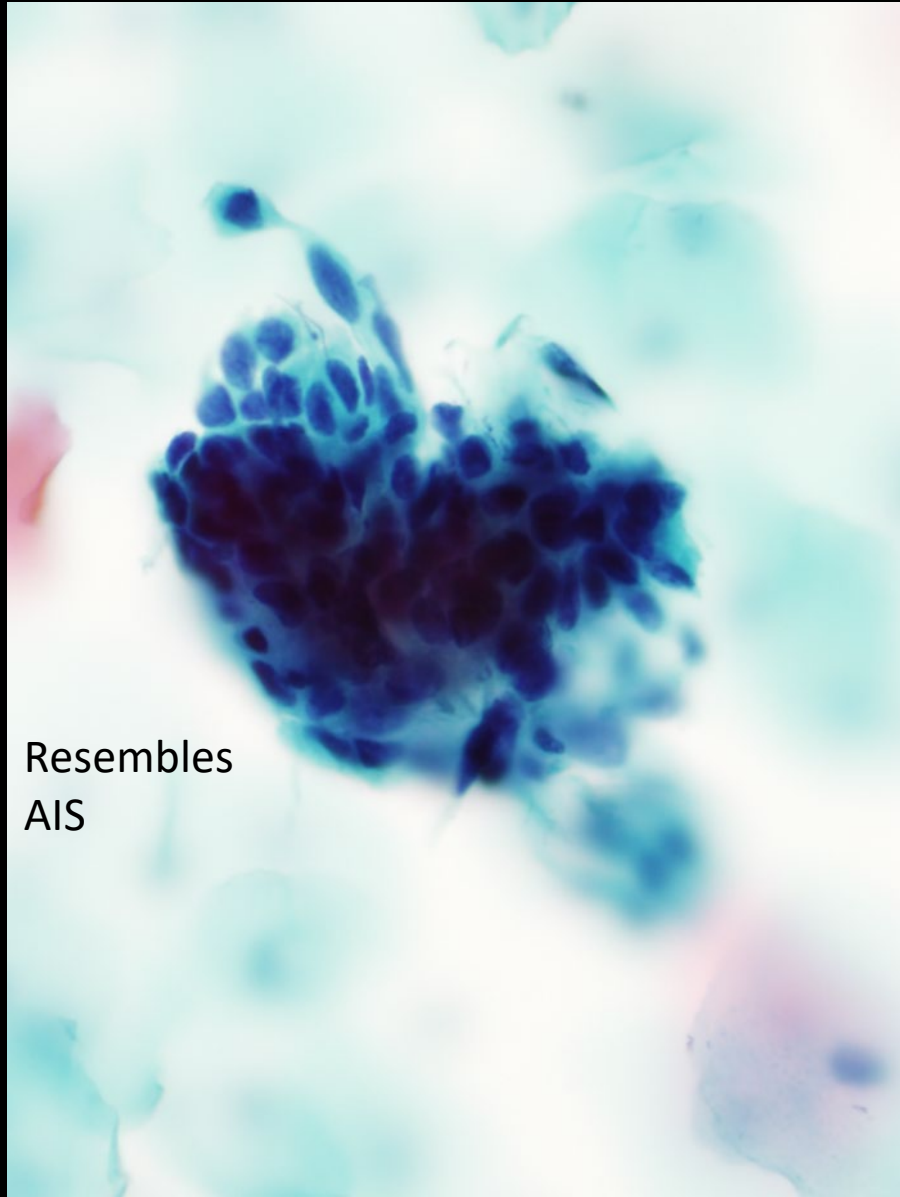
Atypical Endocervical Cells, NOS

- Should be present:
 - Sheets and strips with some cell crowding/overlap and/or pseudostratification
 - Increased N:C ratios
 - Some variation in nuclear size and shape
- May or may not be present:
 - Nuclear enlargement (3-5x normal)
 - Mild hyperchromasia or chromatin irregularity
 - Occasional nucleoli
 - Rare mitoses
 - Distinct cell borders

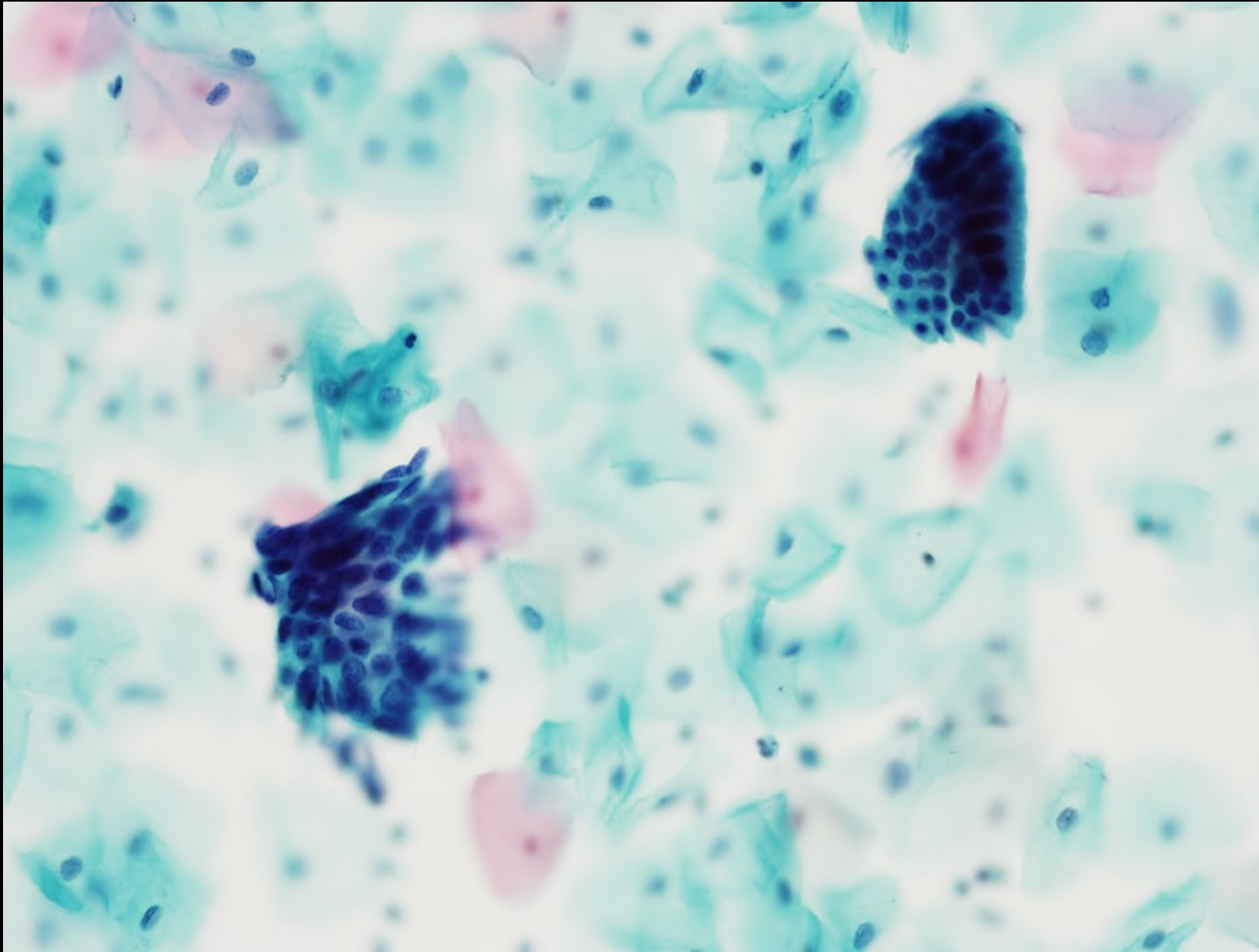
Atypical Endocervical Cells, Favor Neoplastic

- Should be present:
 - Sheets and strips with nuclear crowding/overlap and/or pseudostratification
 - Enlarged hyperchromatic nuclei (often elongated)
 - Increased N:C ratios
- May or may not be present:
 - Rare cell groups with feathering or rosettes
 - Occasional mitoses or apoptotic debris
 - Ill-defined cell borders

Atypical Endocervical Cells



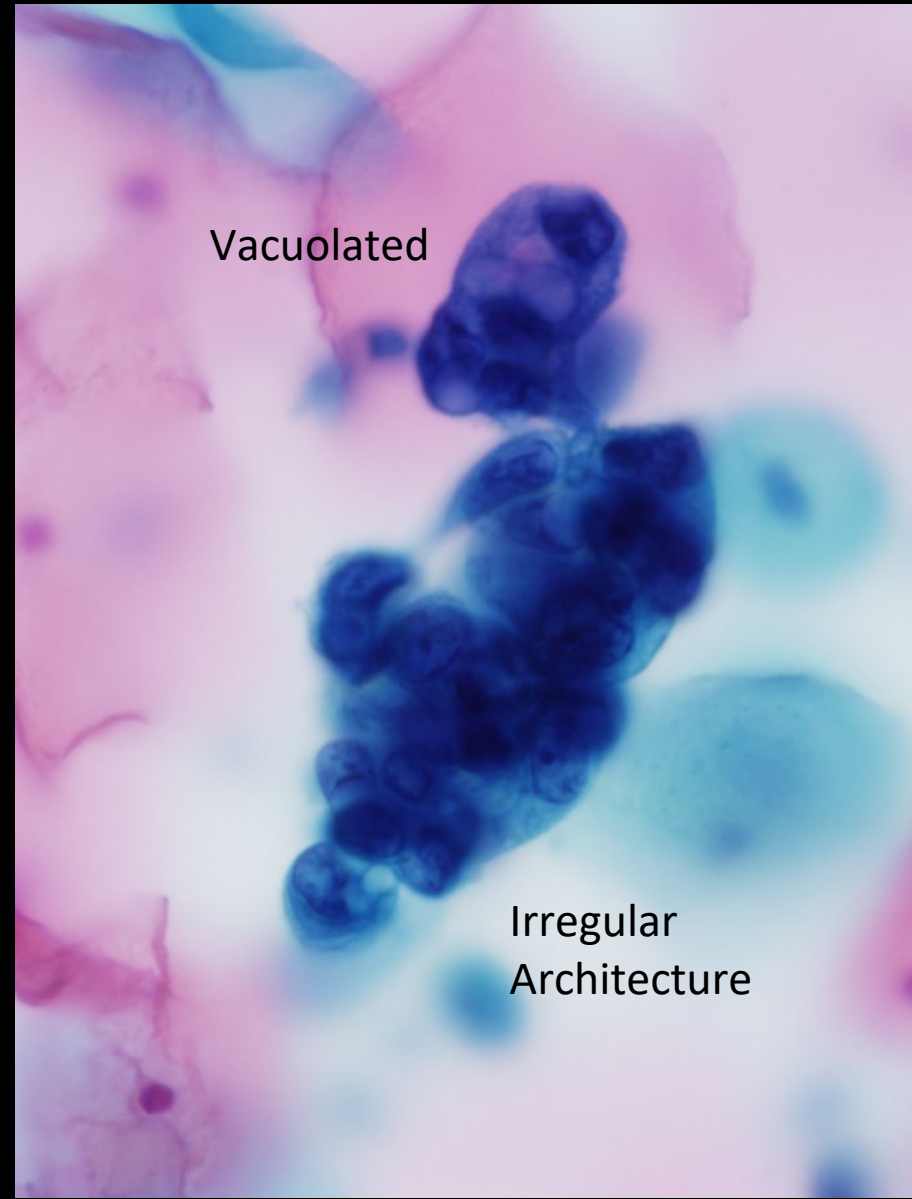
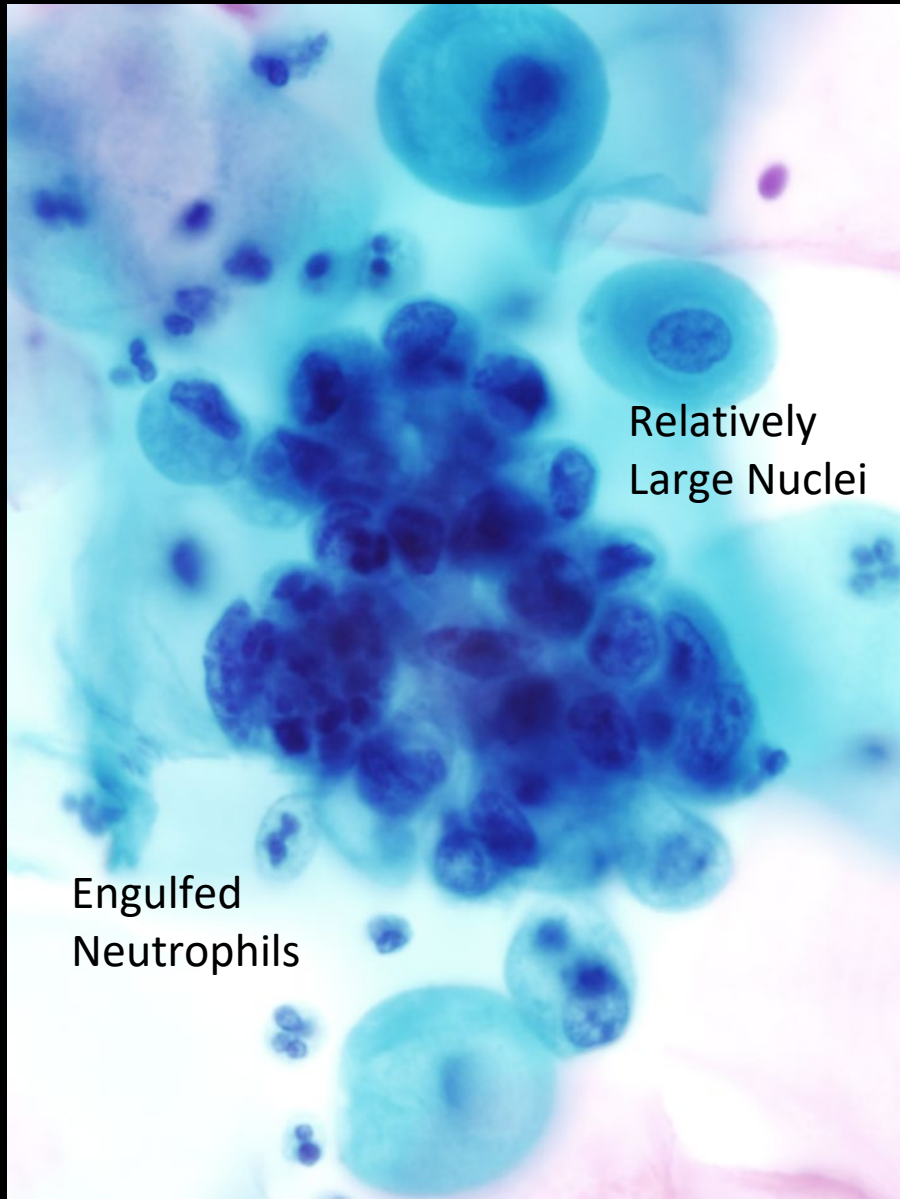
Contrast Atypical Versus Normal



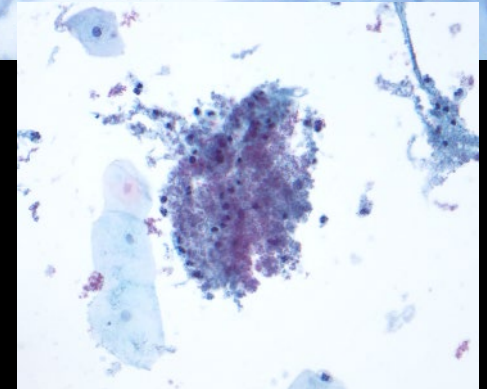
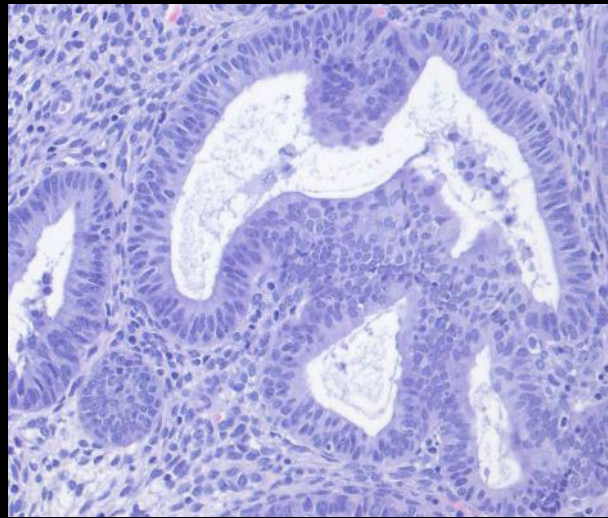
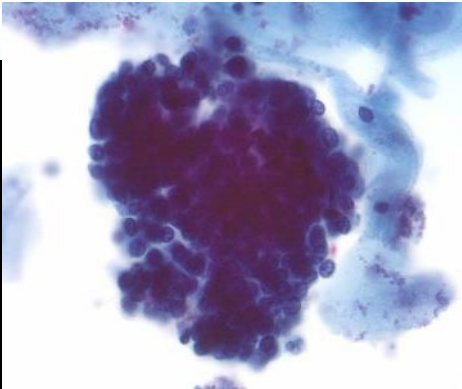
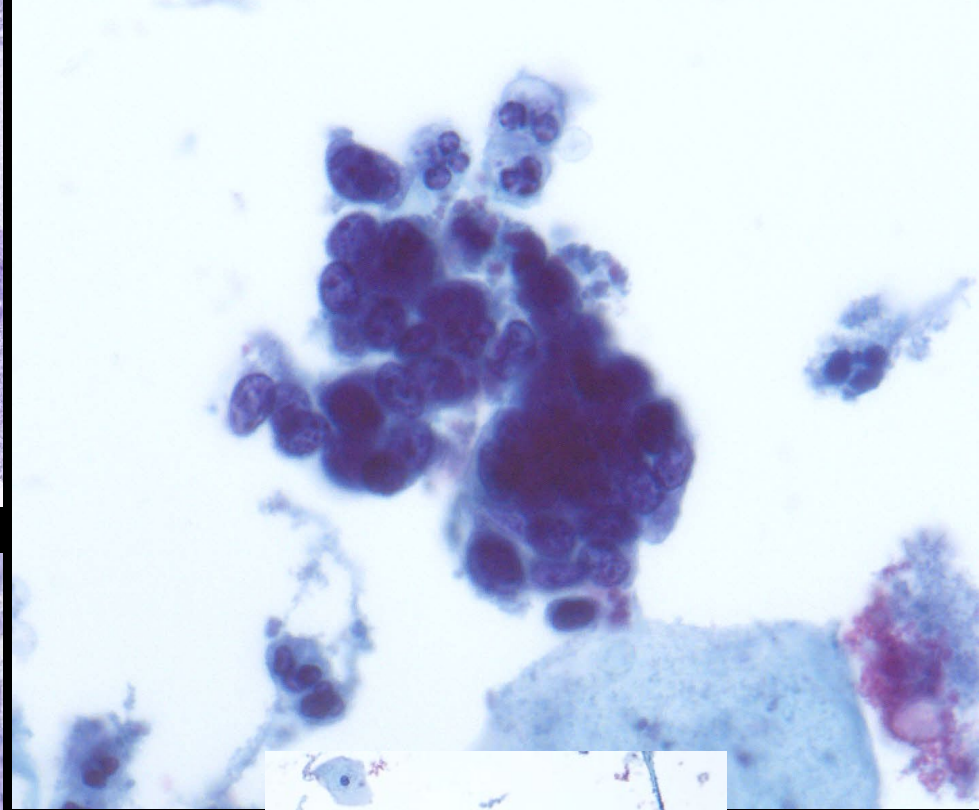
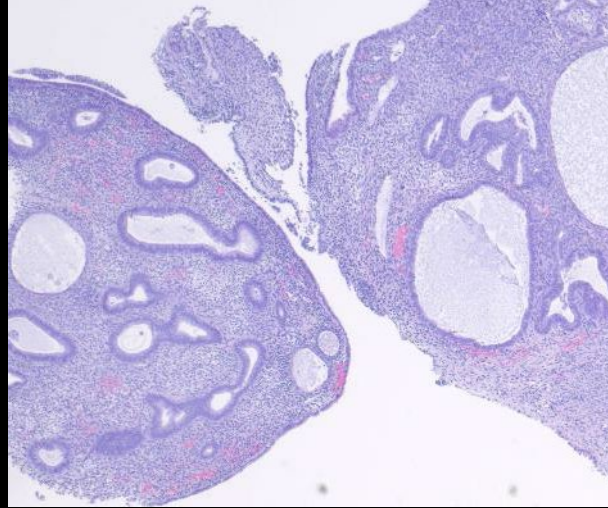
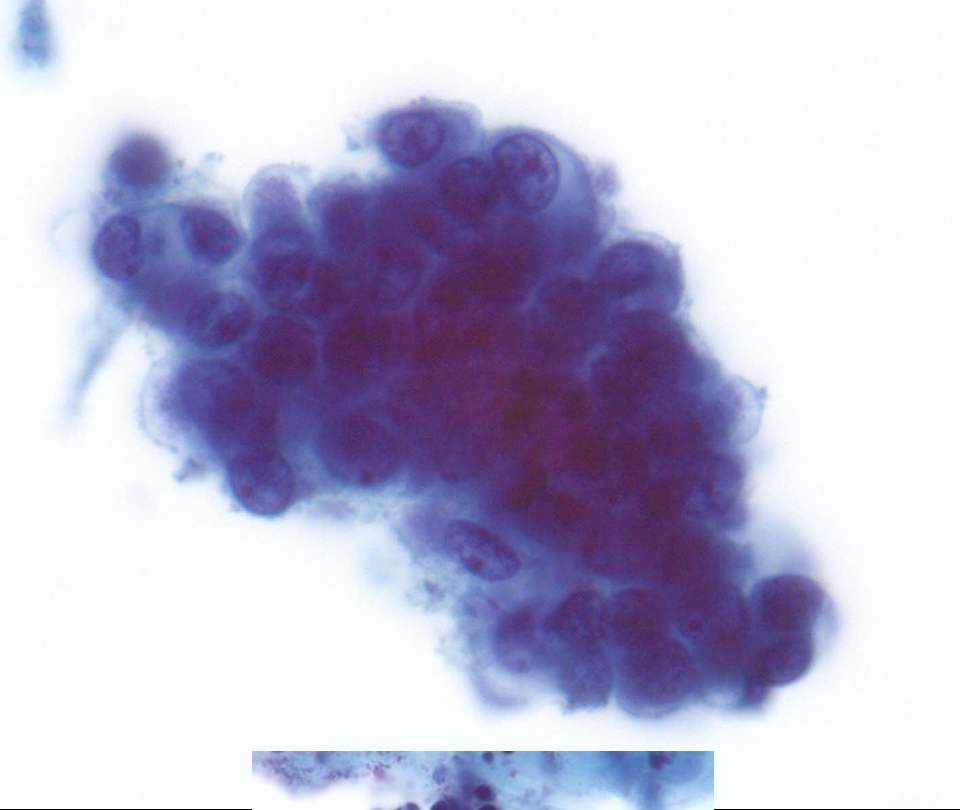
Atypical Endometrial Cells

- No separate criteria for NOS vs. favor neoplastic
- Should be present:
 - Cells occur in small groups (5-10)
 - Nuclear enlargement (often slight)
 - Mild hyperchromasia
 - Chromatin heterogeneity
 - Ill-defined cell borders
- May or may not be present:
 - Small nucleoli
 - Vacuolated cytoplasm

Atypical Endometrial Cells



Endometrial Polyp



Do these distinctions really matter?

- For the most part, the ASCCP guidelines acknowledge that we as cytologists have a difficult time accurately sub-categorizing atypical glandular cells
 - The follow-up guidelines extensively overlap
 - There are a few significant differences to keep in mind, however

ASCCP Algorithm for AGC

All Subcategories (except Atypical Endometrial Cells)

Colposcopy with endocervical sampling and endometrial sampling if ≥ 35 yrs or at risk for endometrial pathology*

*Includes unexplained vaginal bleeding or conditions suggesting chronic anovulation

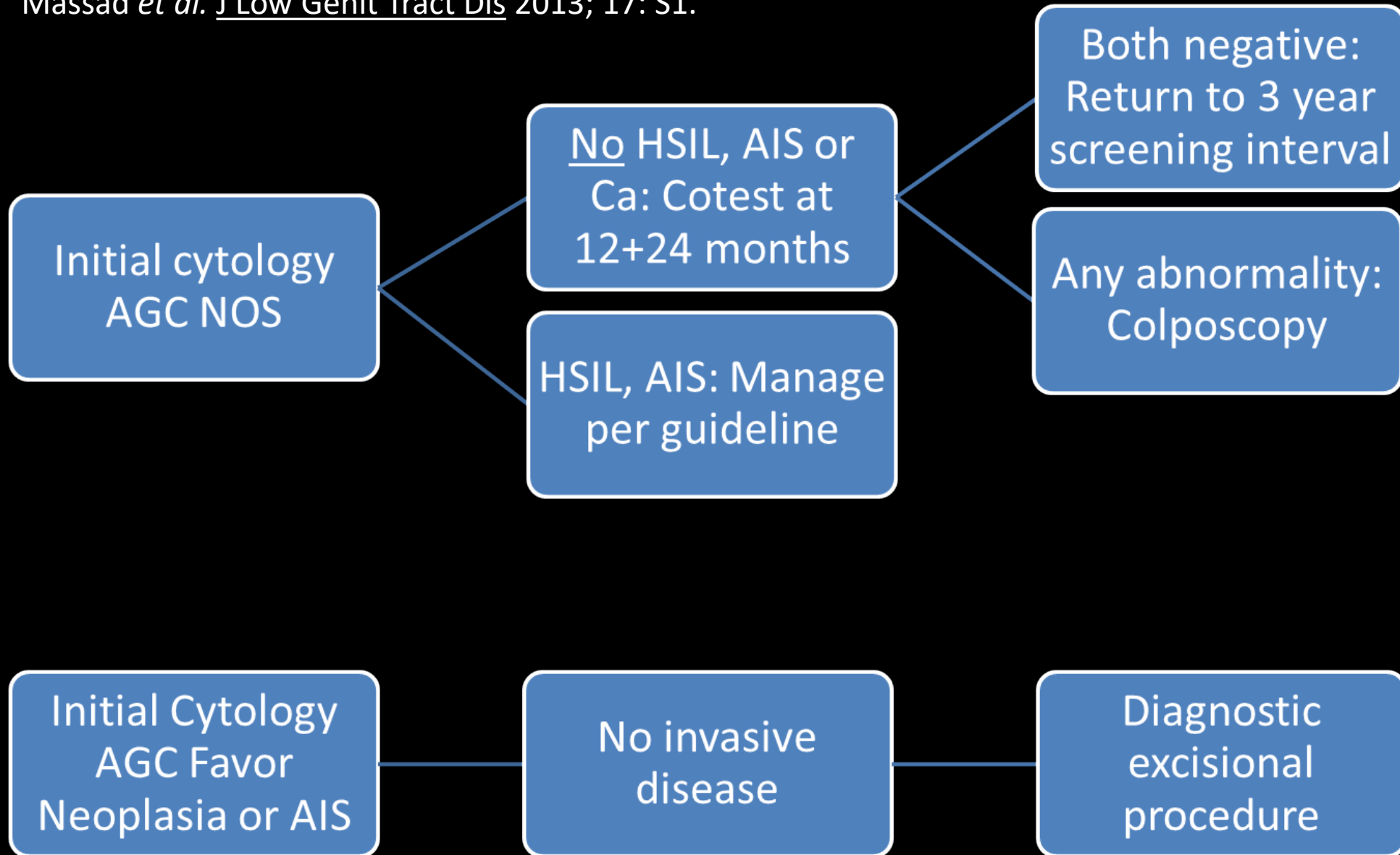
Atypical Endometrial Cells

Endometrial and endocervical sampling*

*Colposcopy if no endometrial pathology

ASCCP Follow-up Guidelines

Massad *et al.* J Low Genit Tract Dis 2013; 17: S1.



NOS Versus Favor Neoplastic or AIS

- If you use AGC favor neoplastic or AIS, the patient will always get at least a LEEP according to ASCCP guidelines
- AGC NOS allows for more discretion on the part of gynecologists to avoid LEEP if the initial biopsy is negative, LSIL, or HSIL
- LEEP has long been thought to increase the risk of pregnancy loss, but now this is being challenged on the basis of socioeconomic status adjustment

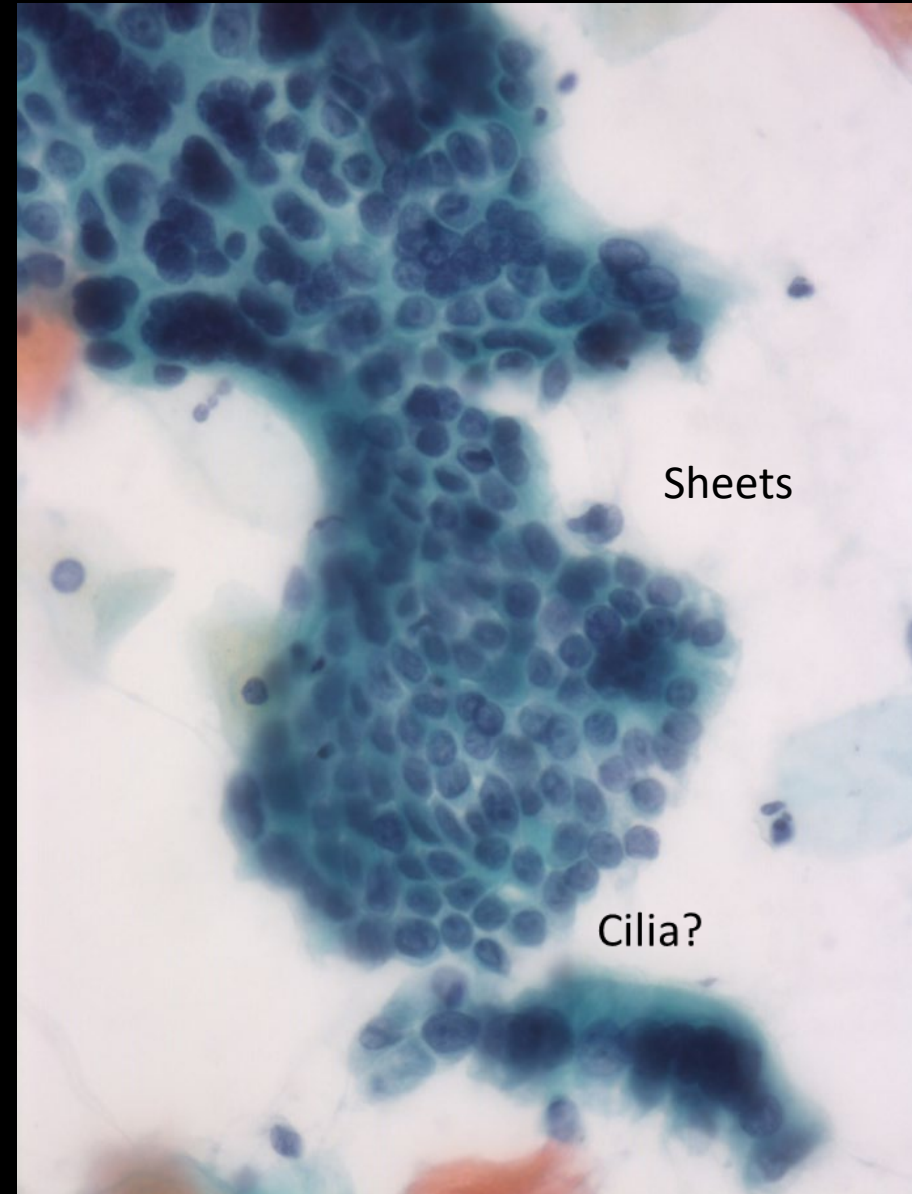
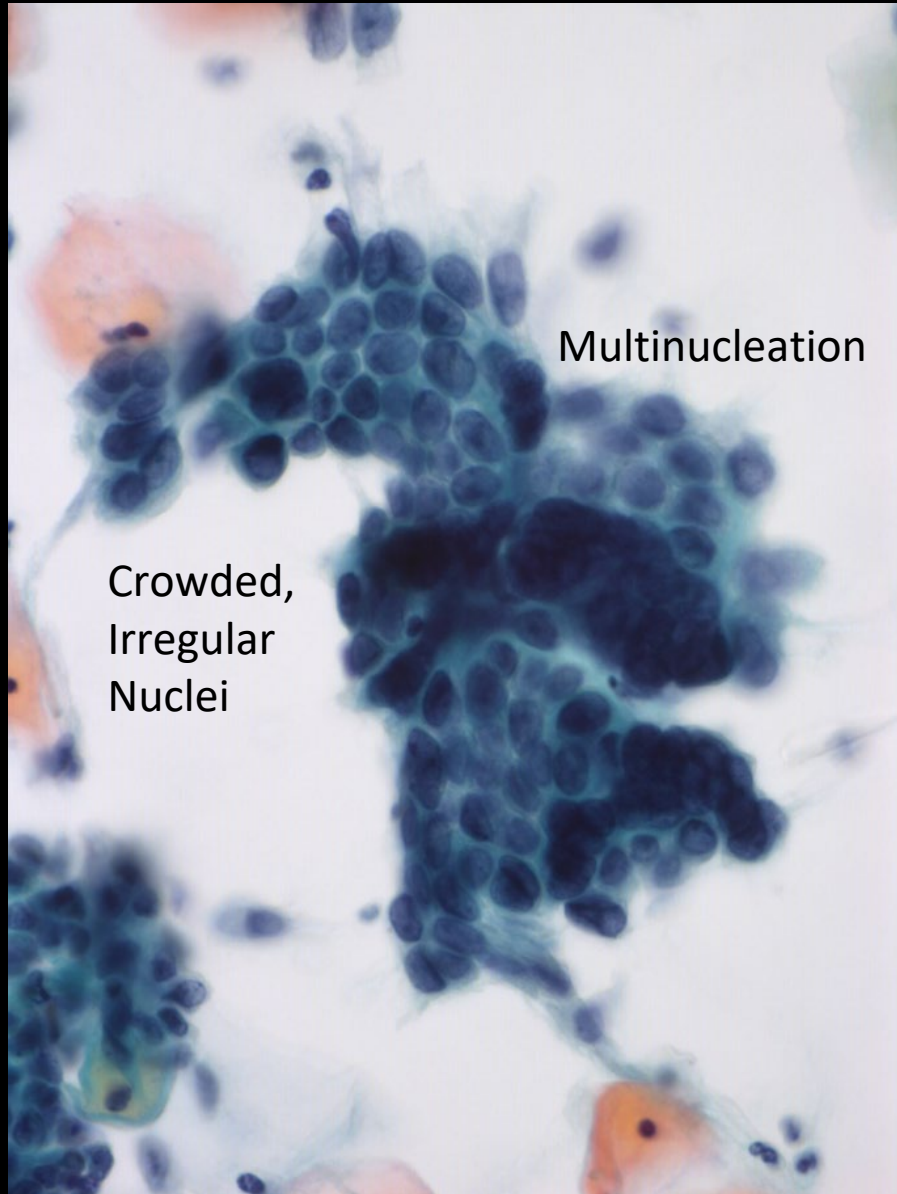
Squamous Intraepithelial Lesions

- Correct categorization of squamous dysplasia can help to keep AGC rates down without losing sensitivity
- HSIL in a gland does not have prominently elongated nuclei or AIS-like architecture
- Lesions that look endocervical but not very AIS-like may be better categorized as ASC-H instead

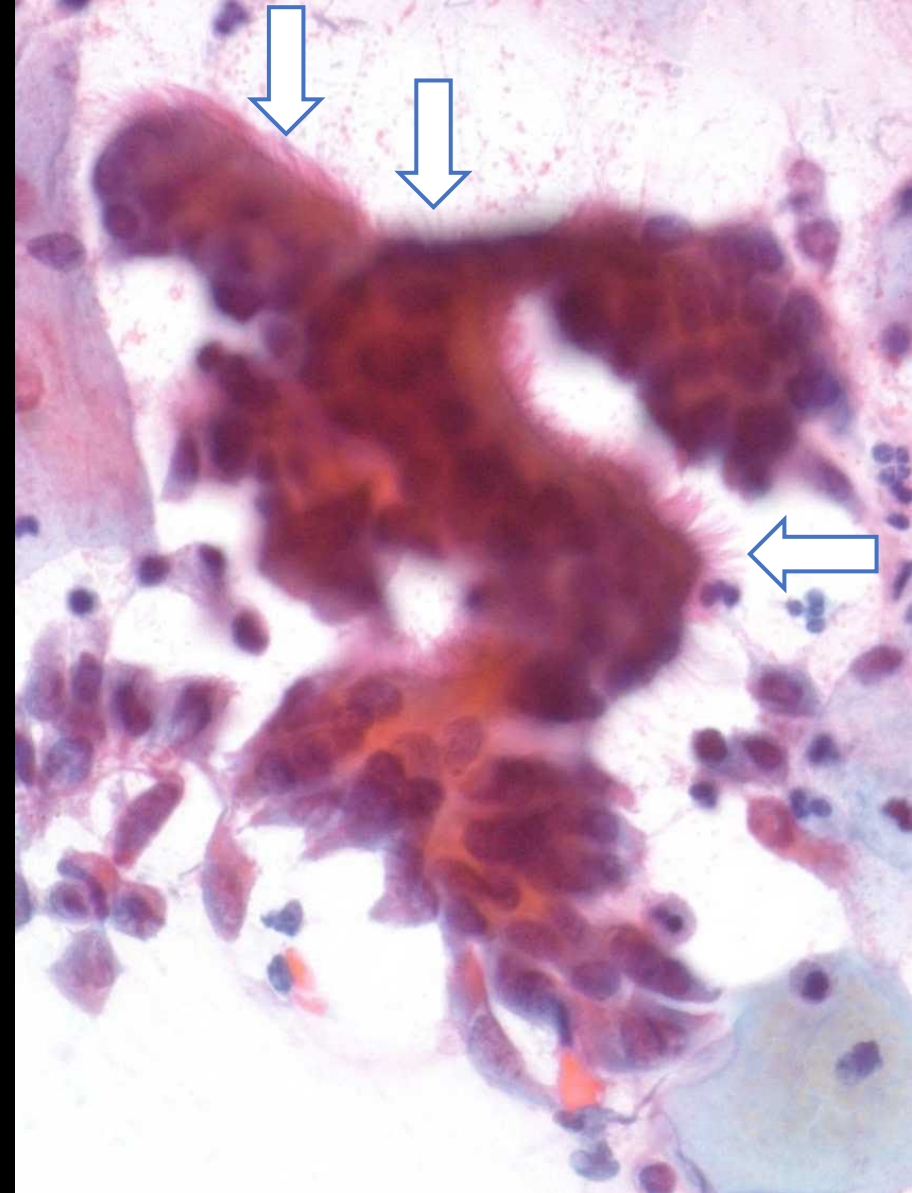
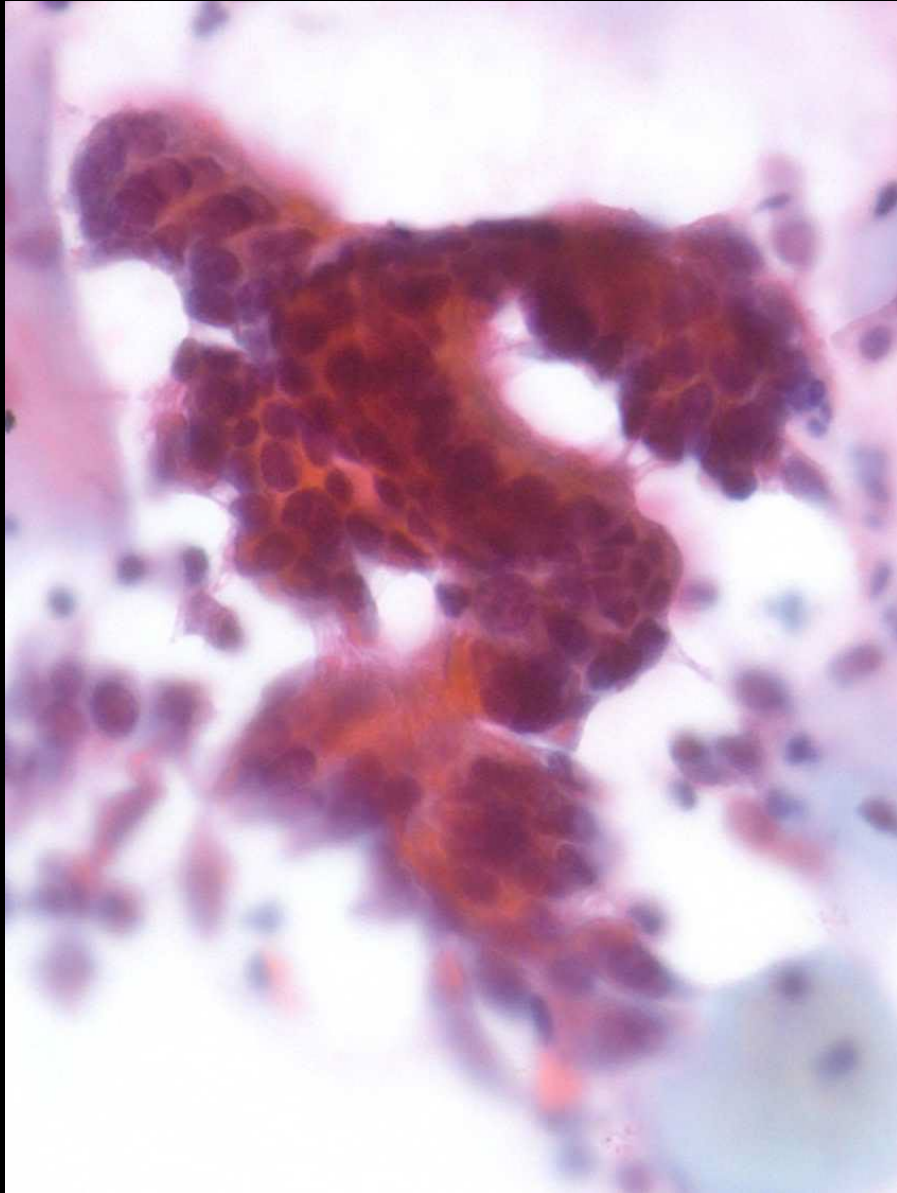
Many AGC cases will be benign

- There are cases that show atypia deserving of an interpretation of AGC that will be benign on biopsy follow-up
- Tubal metaplasia, microglandular hyperplasia, and endocervical polyps can show AGC features, especially if complicated by inflammation or repair
- IUD effects are another well-known mimic
- Menstrual endometrium is an under-appreciated problem

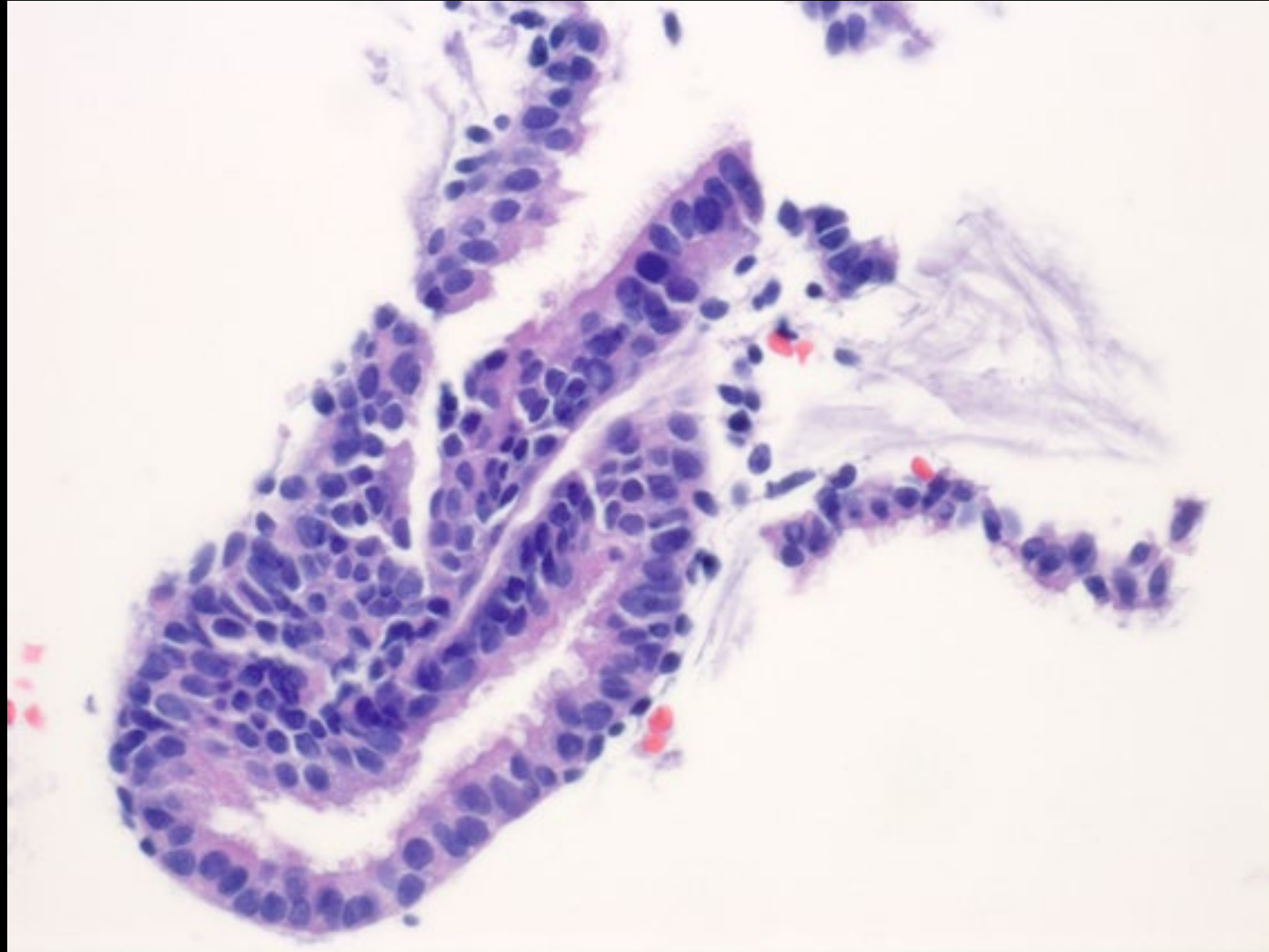
Tubal Metaplasia



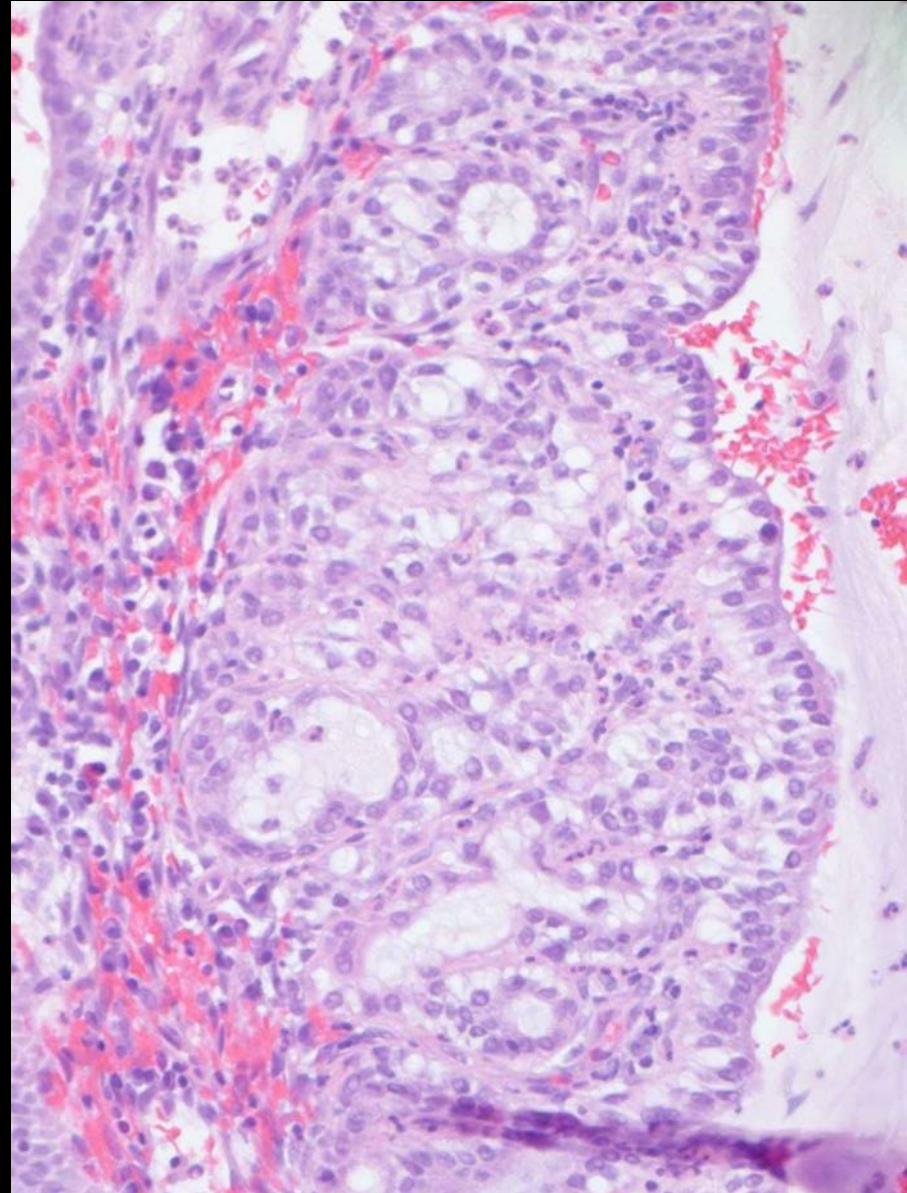
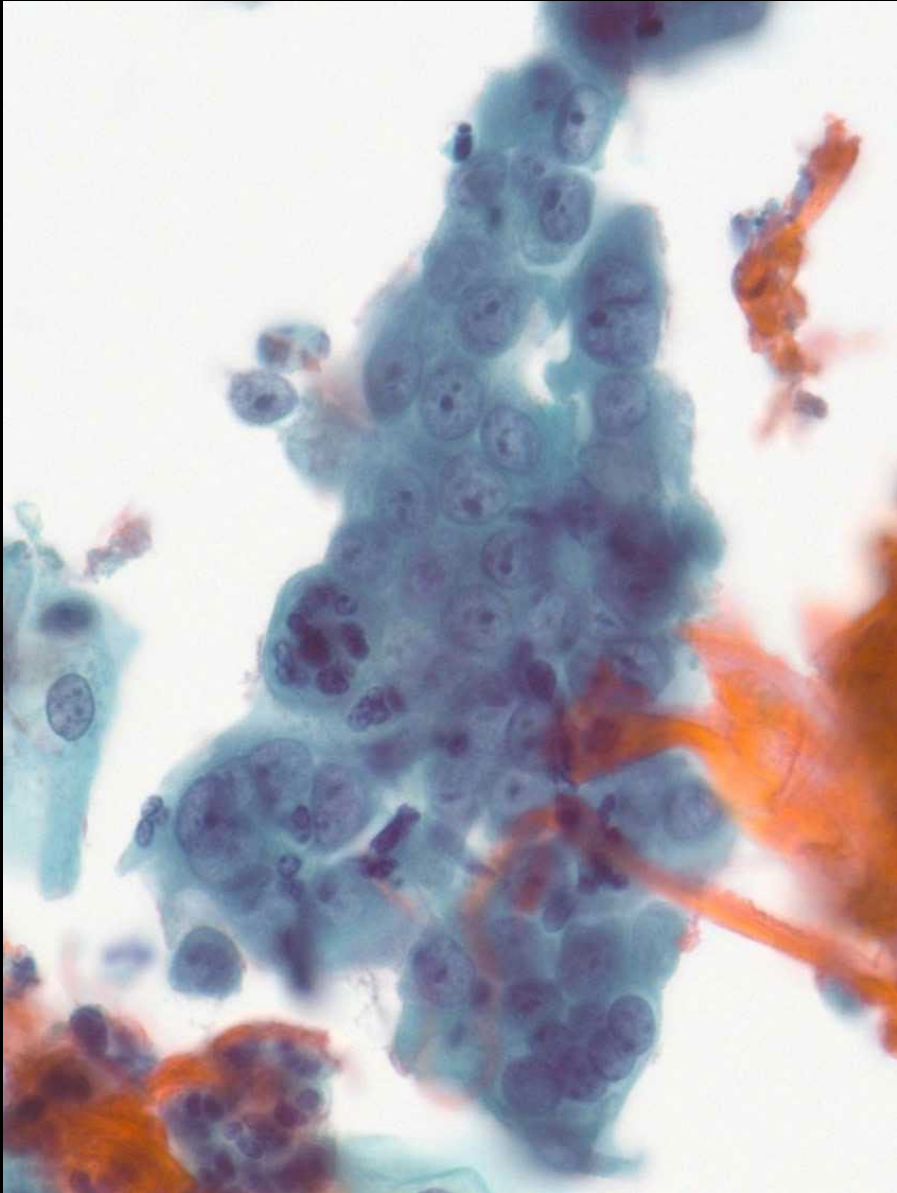
Look for Cilia in Tubal Metaplasia



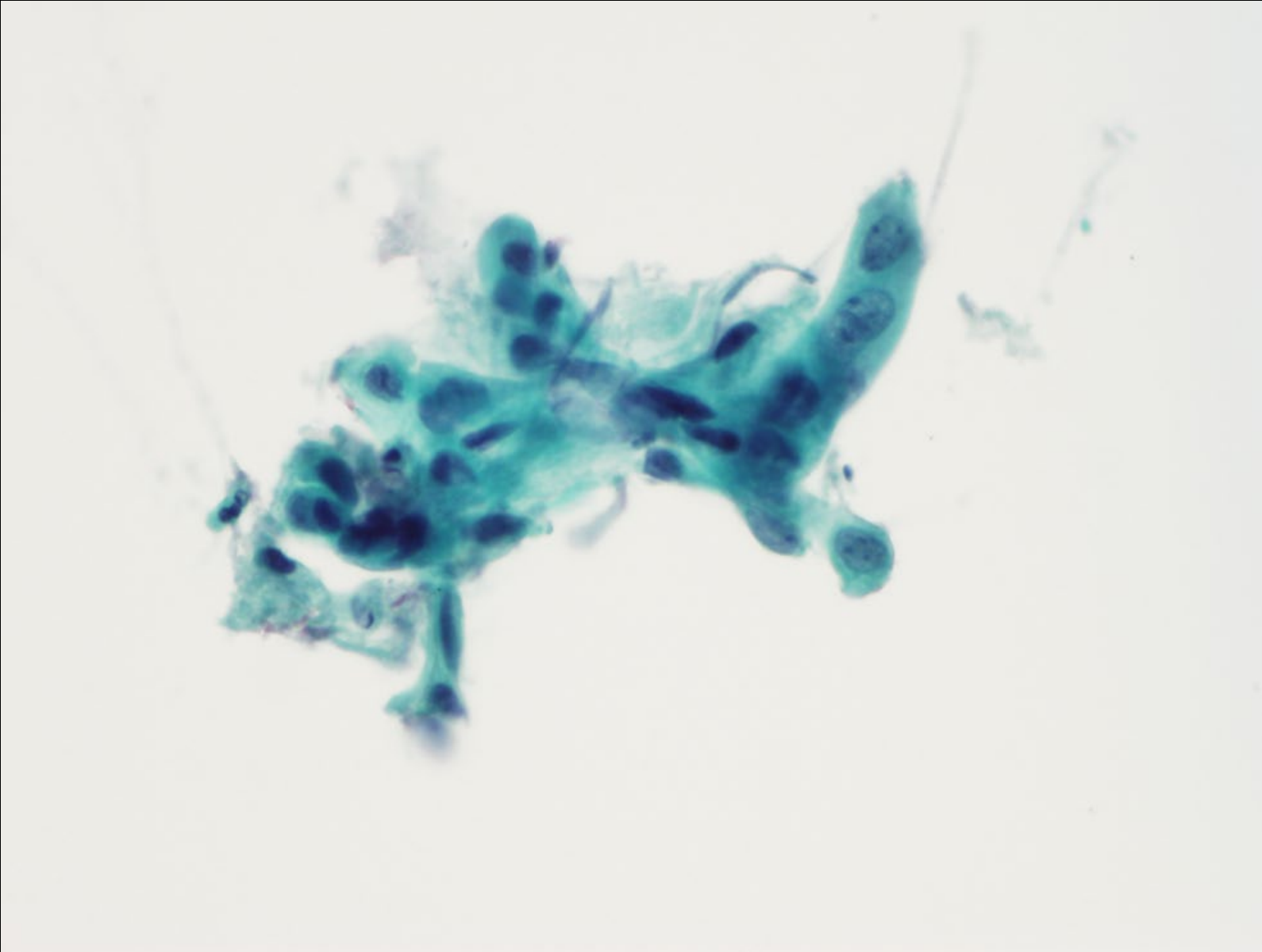
Tubal Metaplasia Curettage Histology



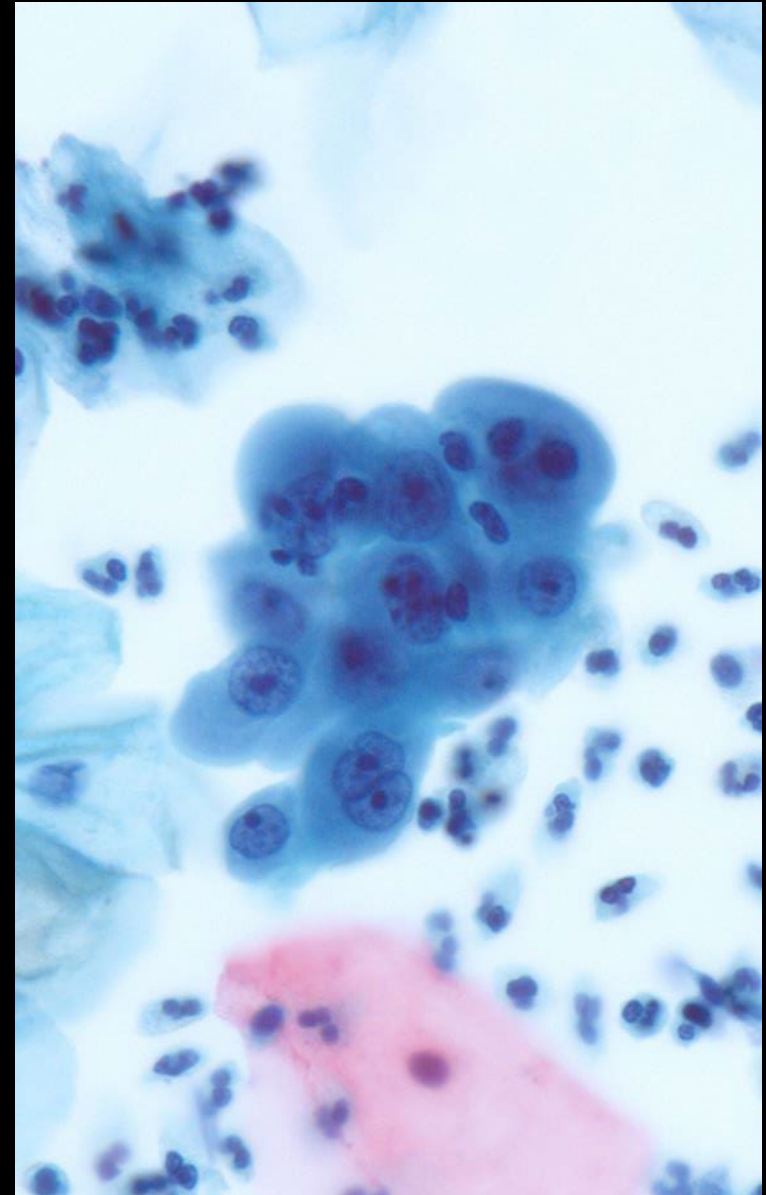
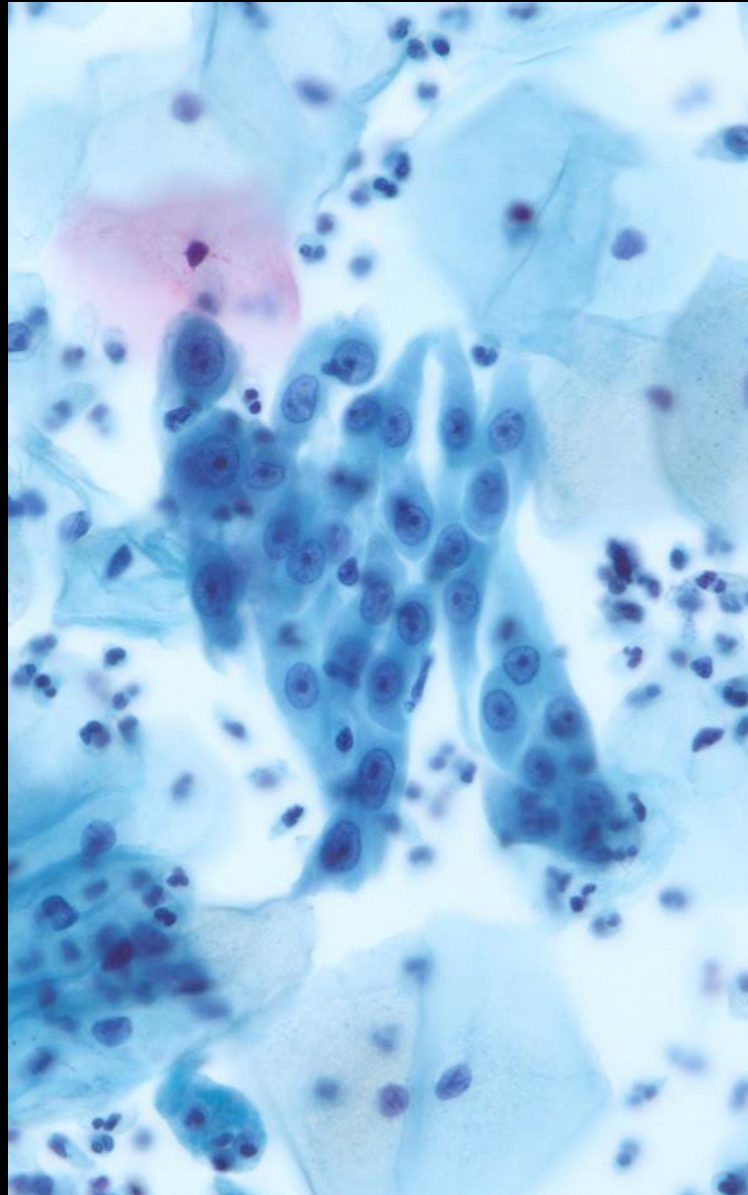
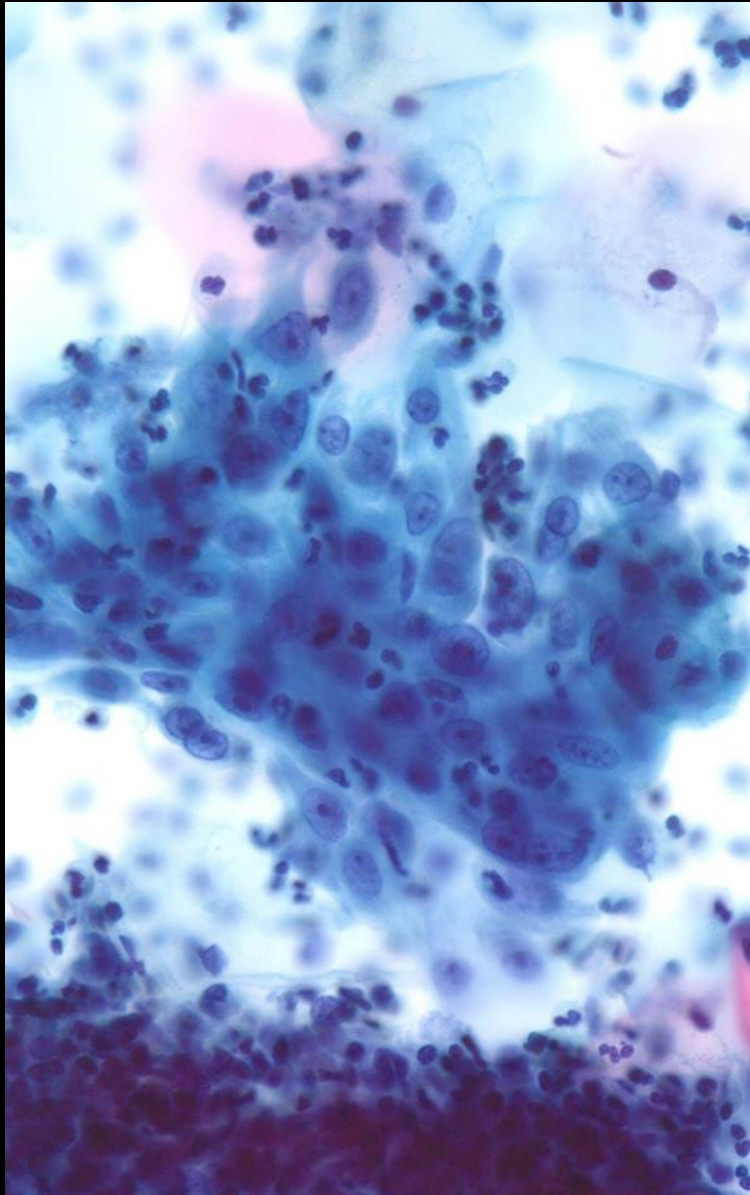
Microglandular Hyperplasia



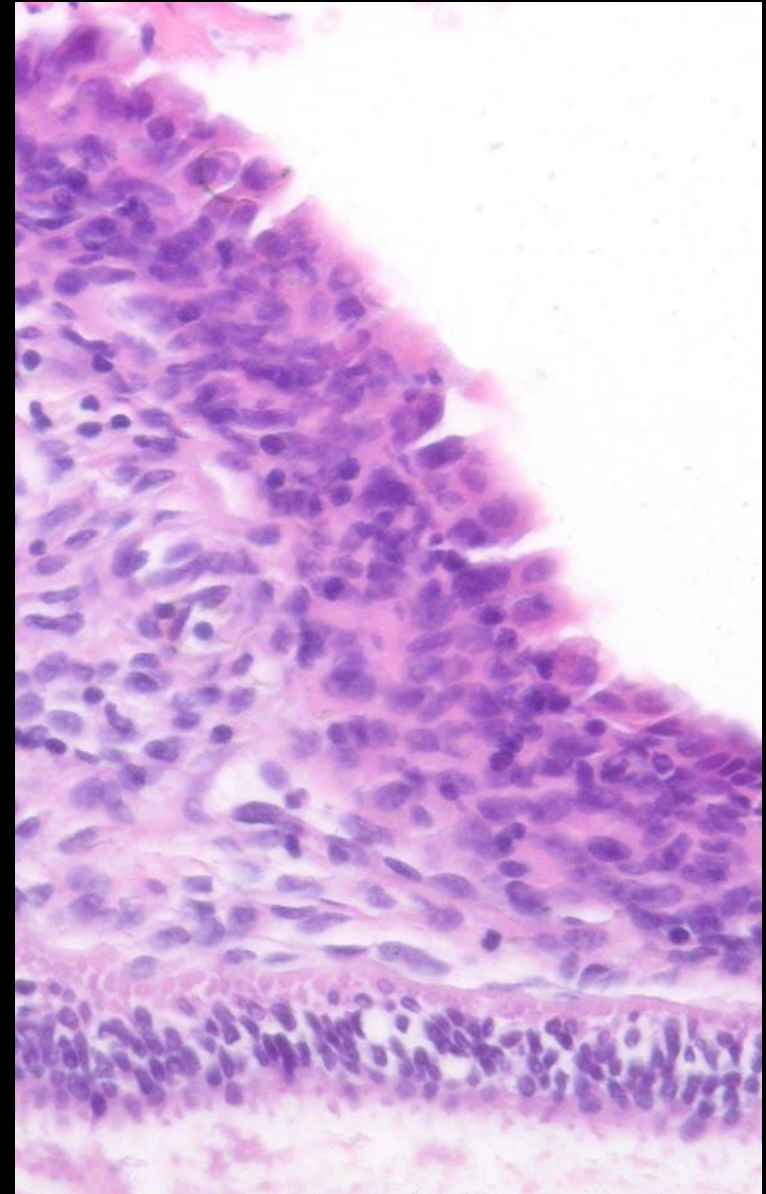
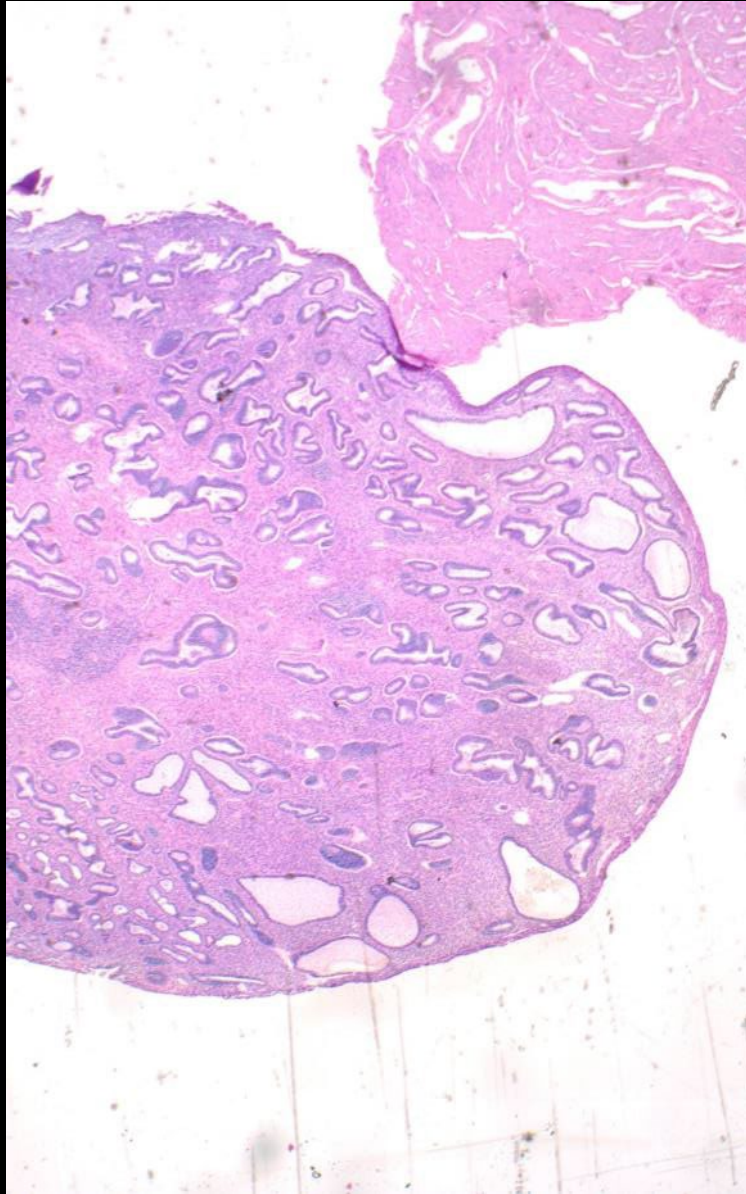
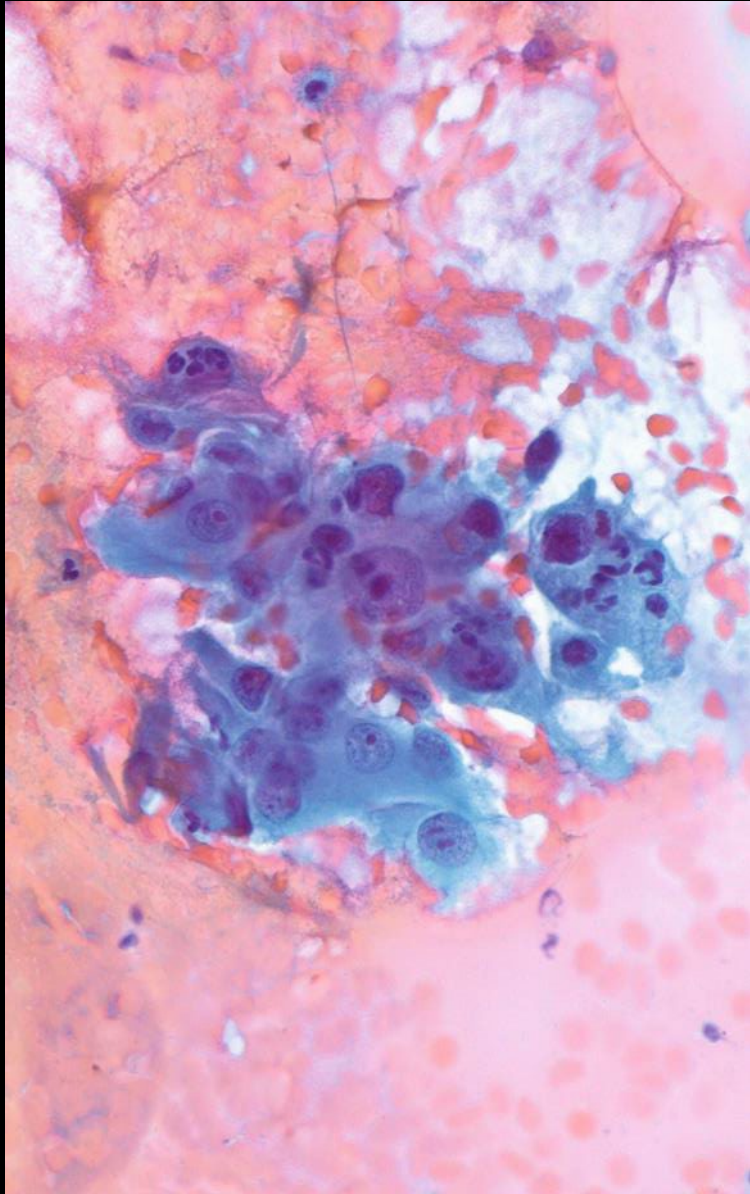
Microglandular Hyperplasia Marked Atypia



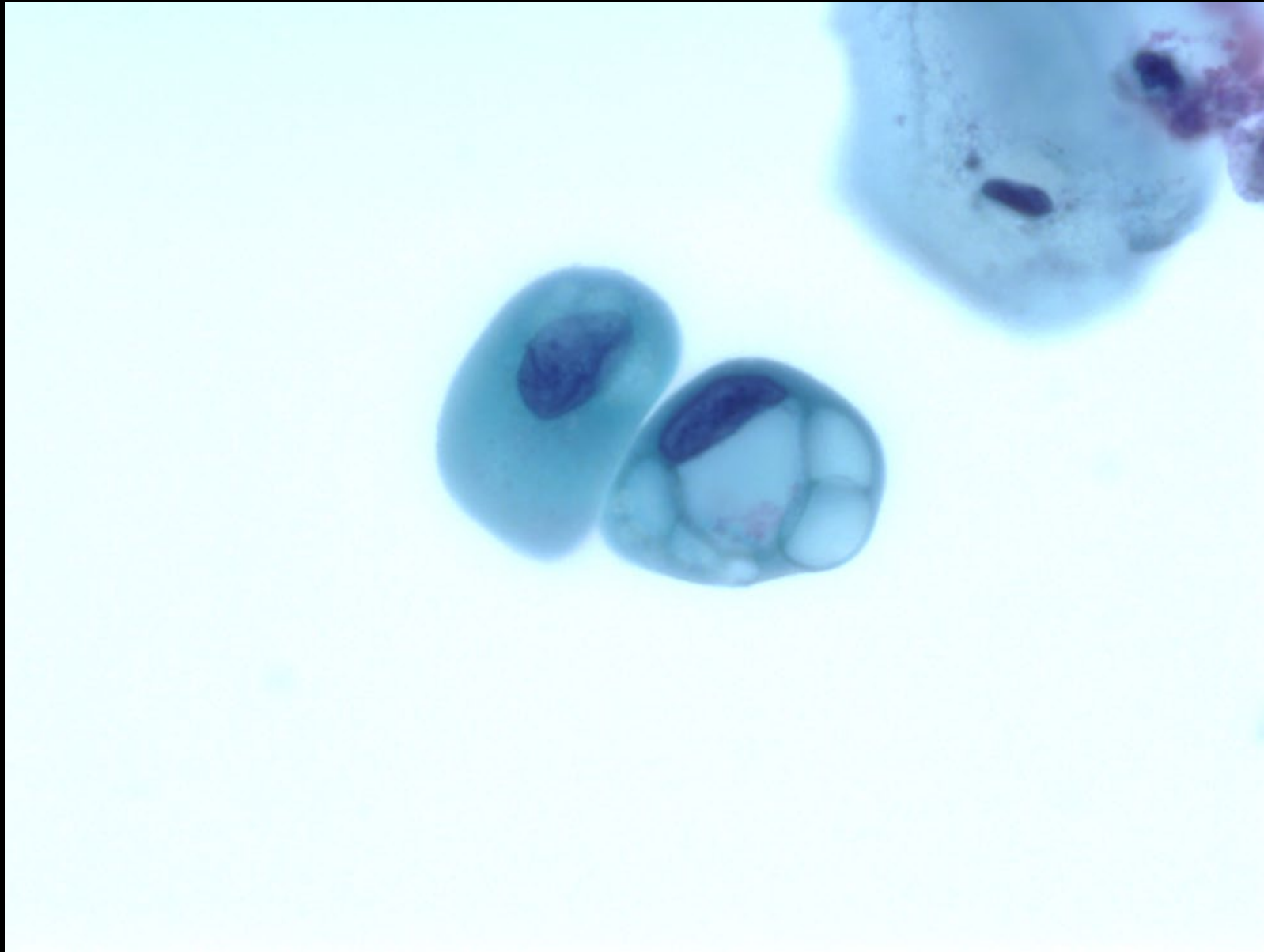
Atypical Repair



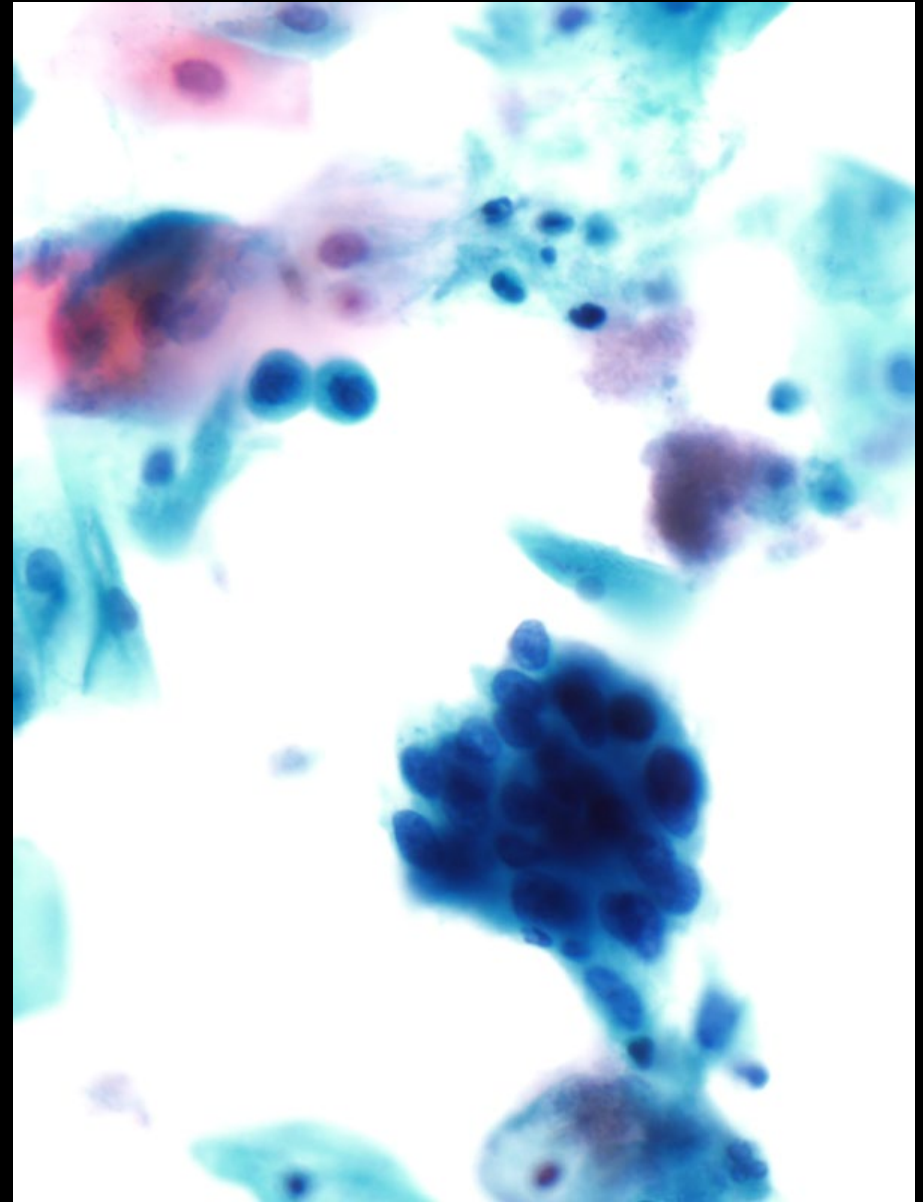
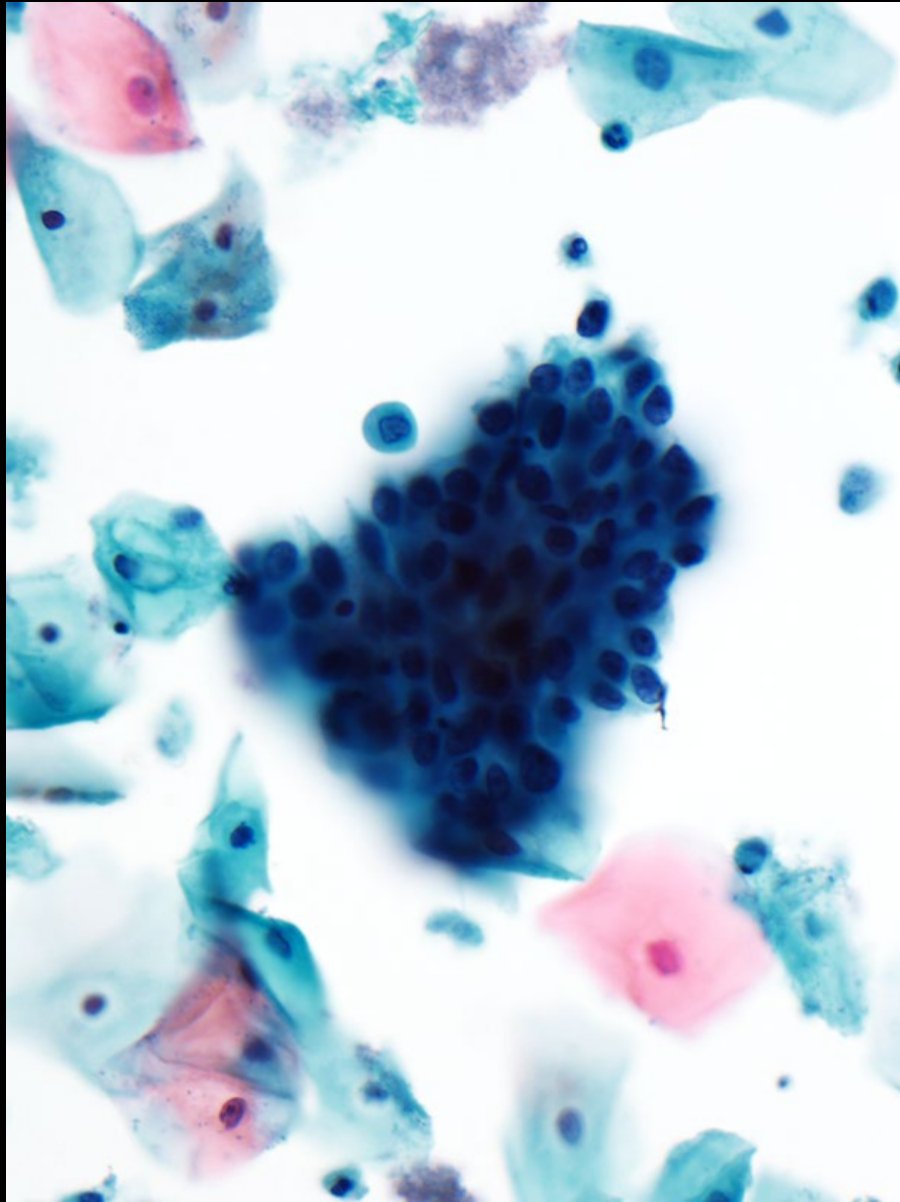
Polyp-Associated Repair



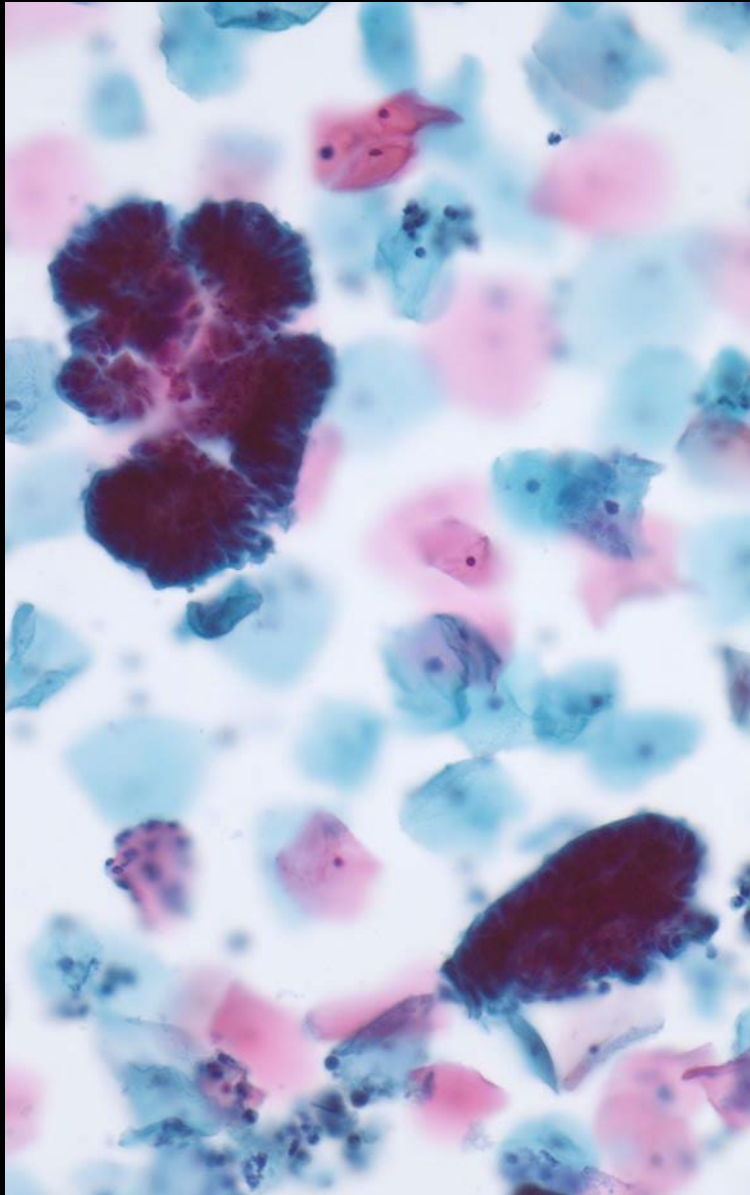
Vacuolated IUD Cell



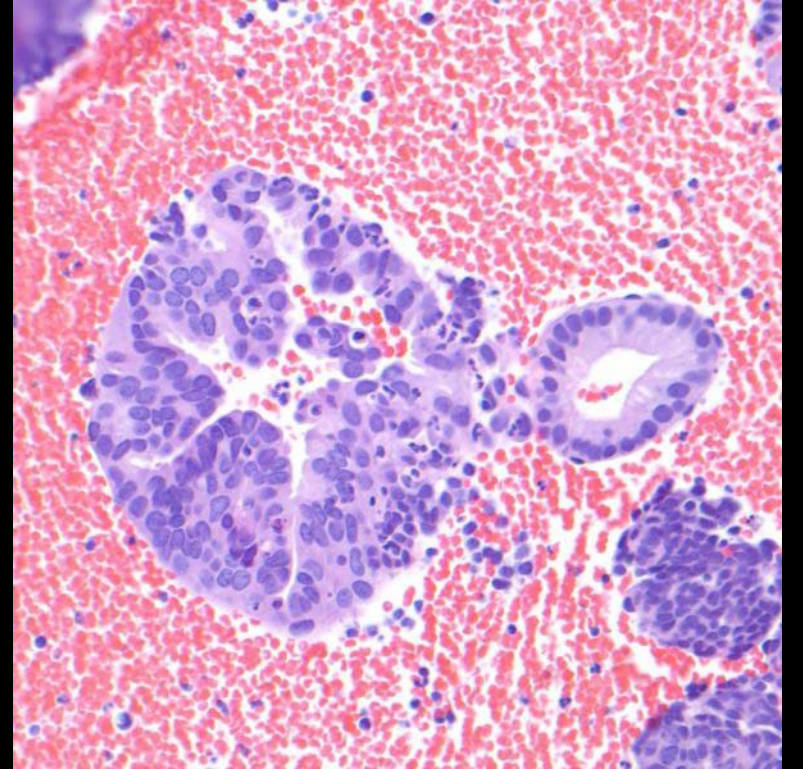
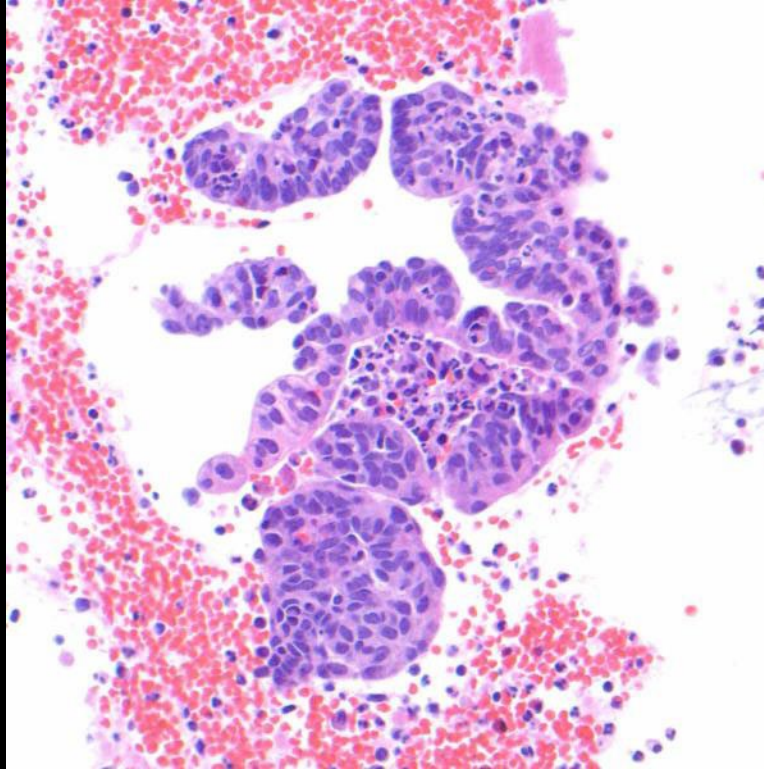
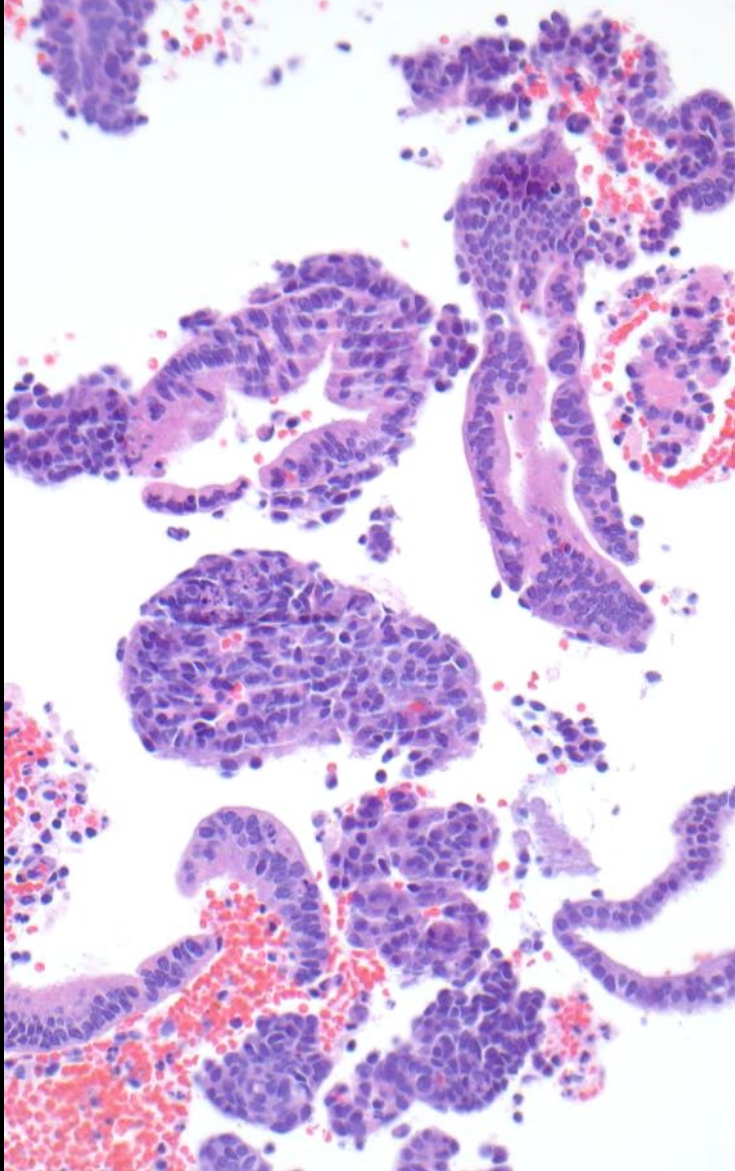
Menstrual Endometrium



Menstrual Endometrium Geometric Clusters



Menstrual Endometrium Biopsy



Menstrual Endometrium

- Menstrual endometrium is “fresh” and looks different from the typical rounded up degenerated groups
- Menstrual endometrium may mimic AIS or even small cell carcinoma
- Pap tests during menstruation should be avoided, but rescheduling is difficult so sometimes it happens
- The LMP is often not given or is about one month earlier

Summary Tips for AGC

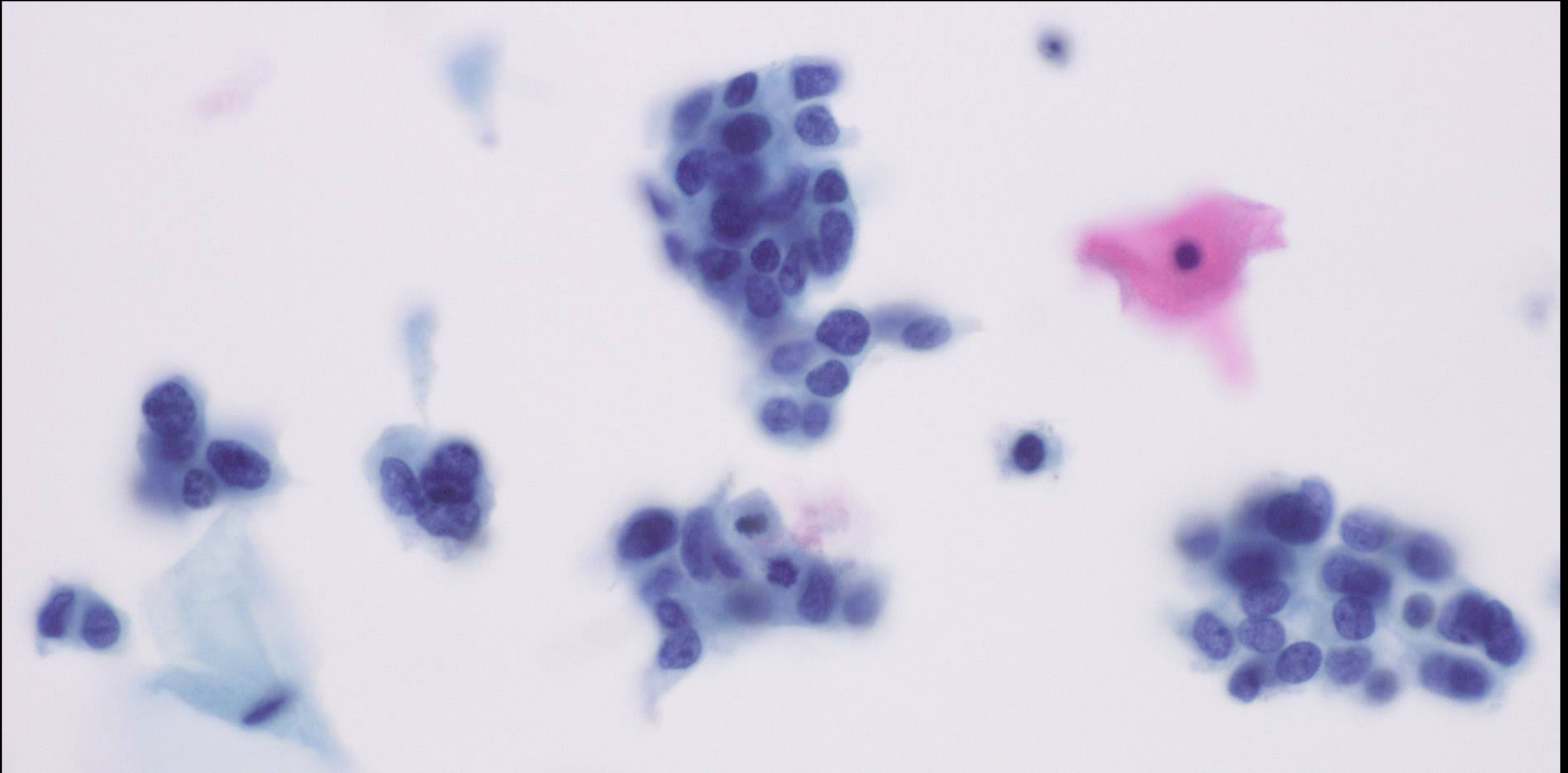
- If it's cervical but doesn't look like AIS or squamous dysplasia, it's probably benign/reactive
- Whenever considering AGC, also think about squamous dysplasia
- Look for features of tubal metaplasia besides cilia and terminal bars as these are frequently absent
- Remember endometrial carcinoma in older women
- Don't be too aggressive about using "favor neoplastic"
- HPV is of limited value for triage

Small Cell Carcinoma

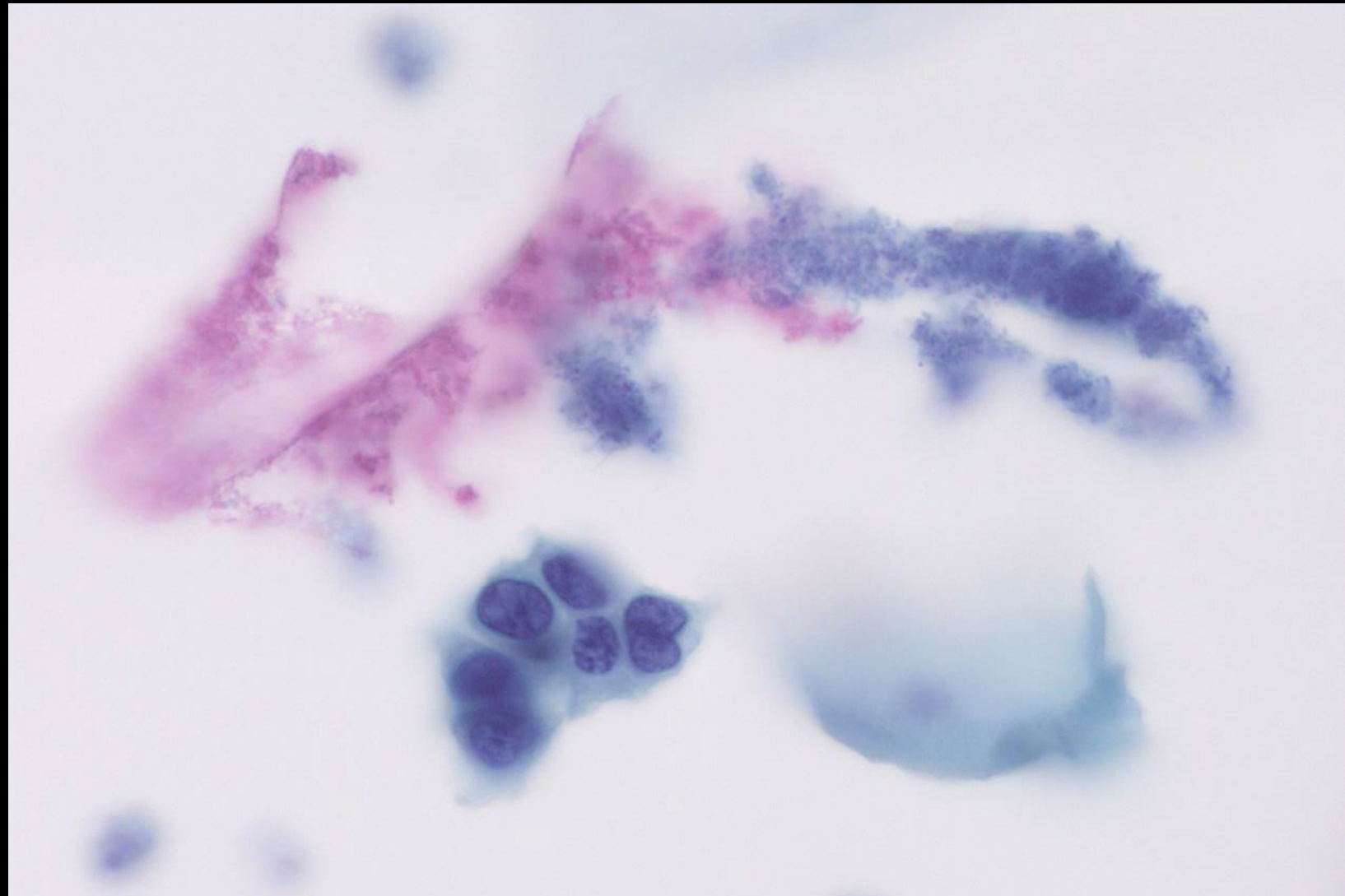
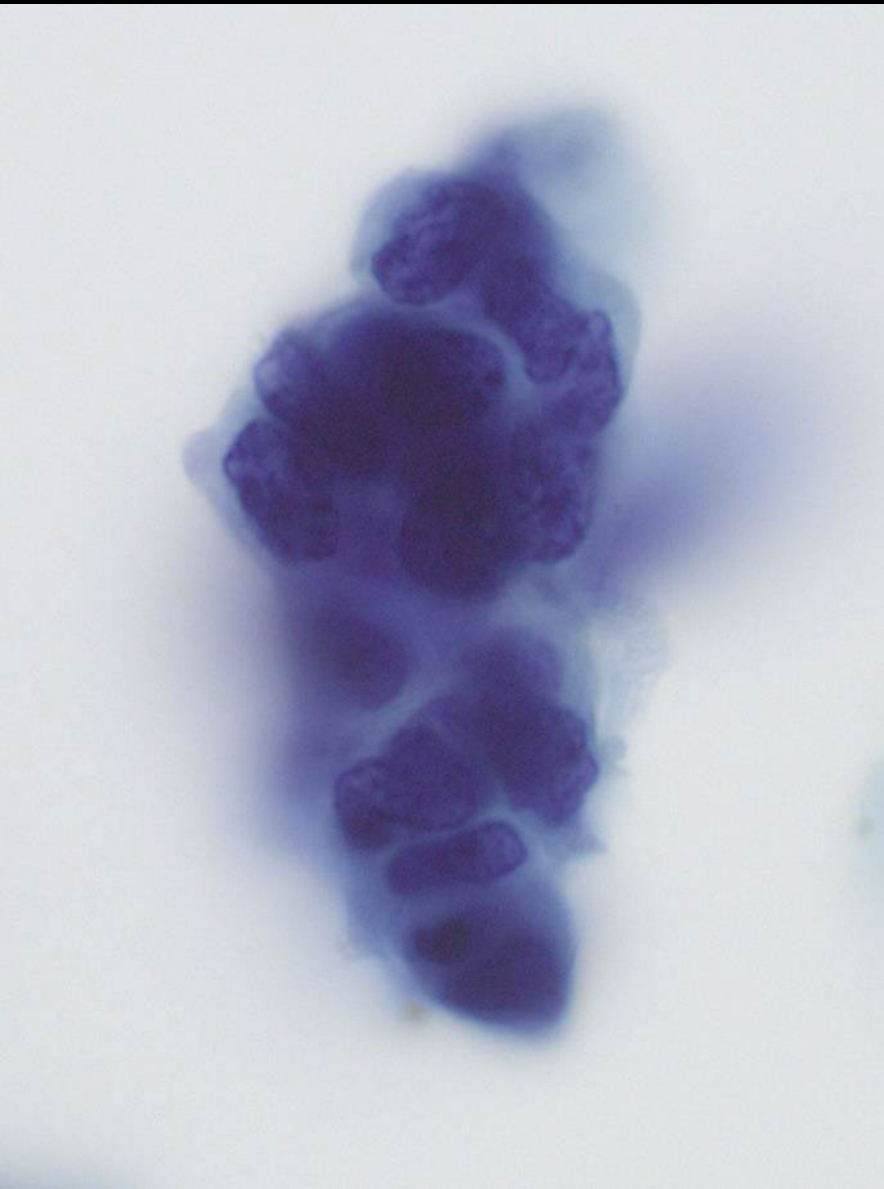
Small Cell Carcinoma

- Small cell carcinoma is rare as a cervical primary
- It is associated with HPV (types 18 and 16)
- May have a previous history of HPV+ or SIL
- Highly aggressive and usually fatal
- May be difficult to distinguish from metastasis
 - Younger age favors cervical primary
 - HPV testing of the tumor may be helpful

Small Cell Carcinoma



Small Cell Carcinoma

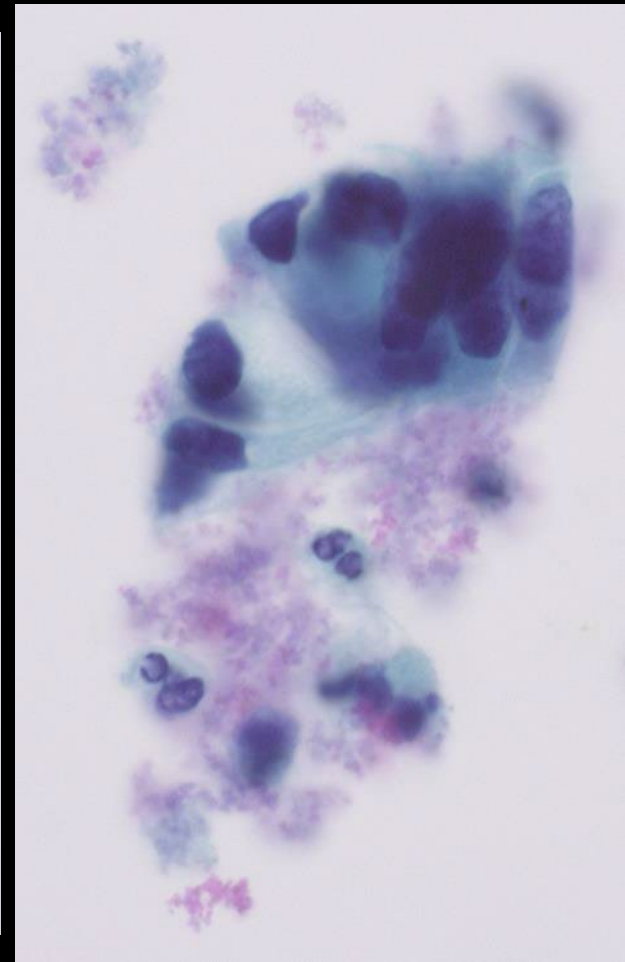
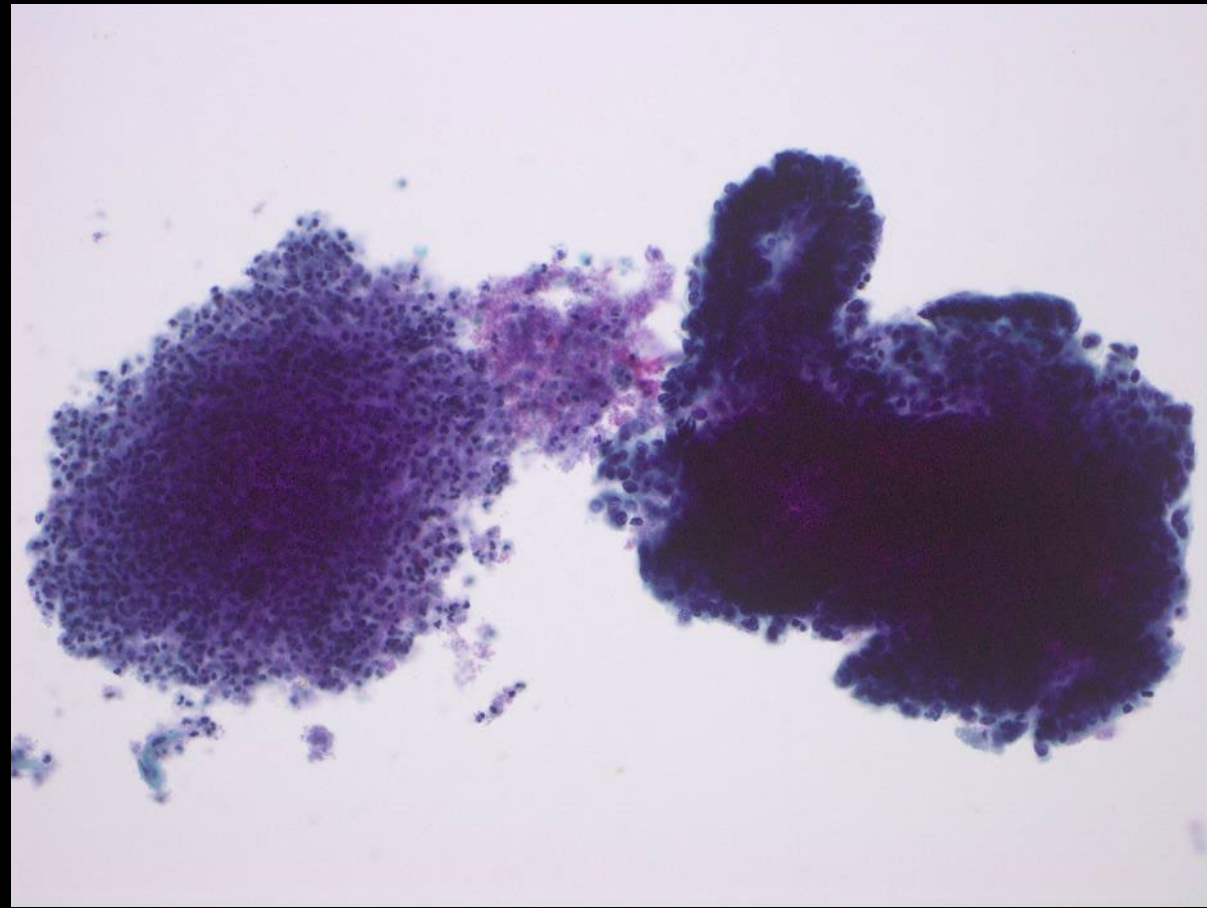
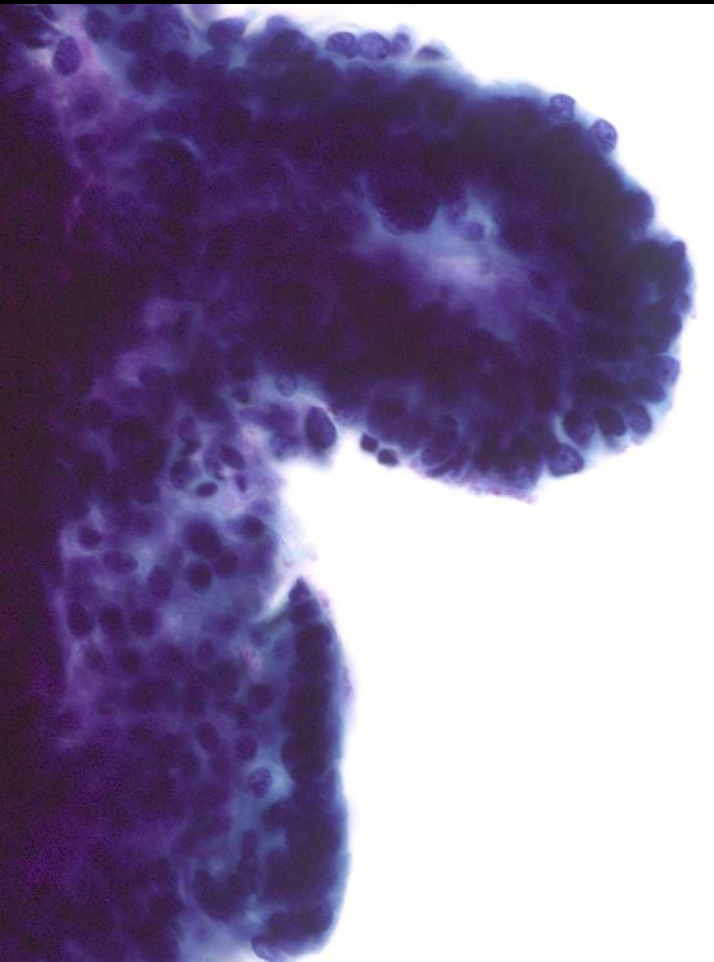


Extrauterine Malignancies

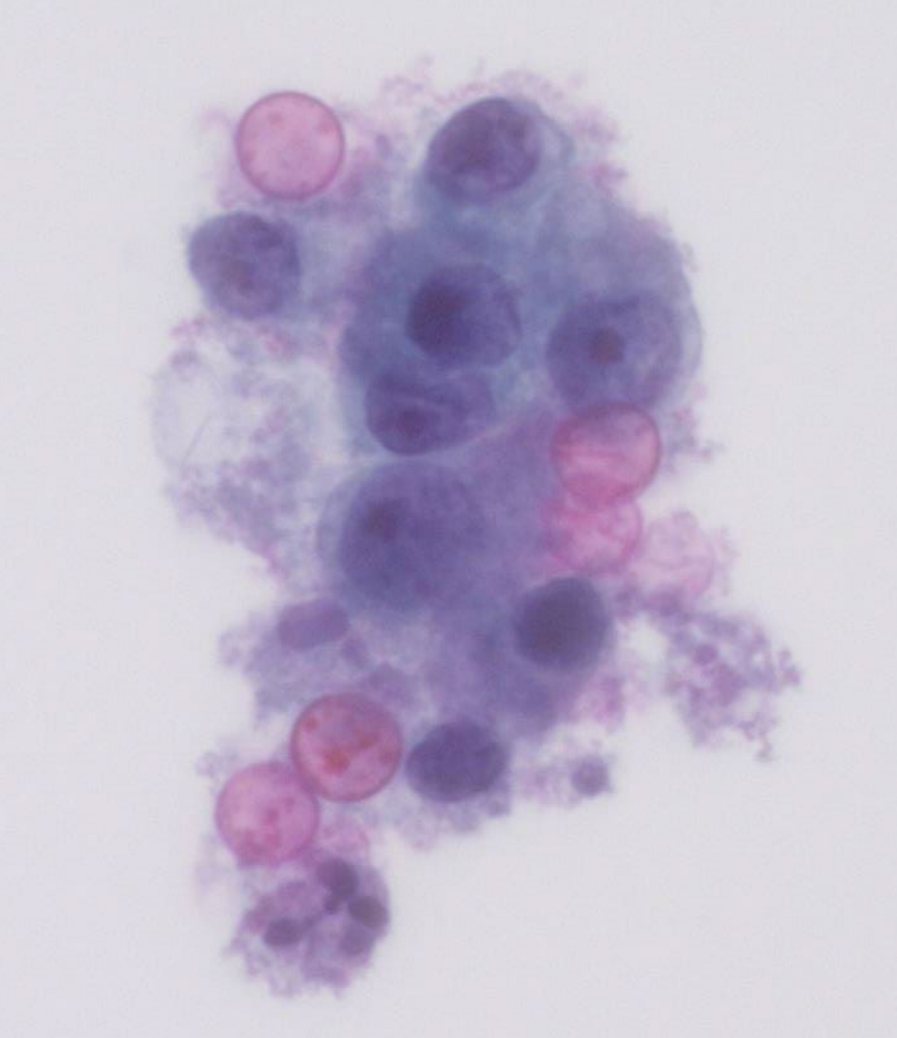
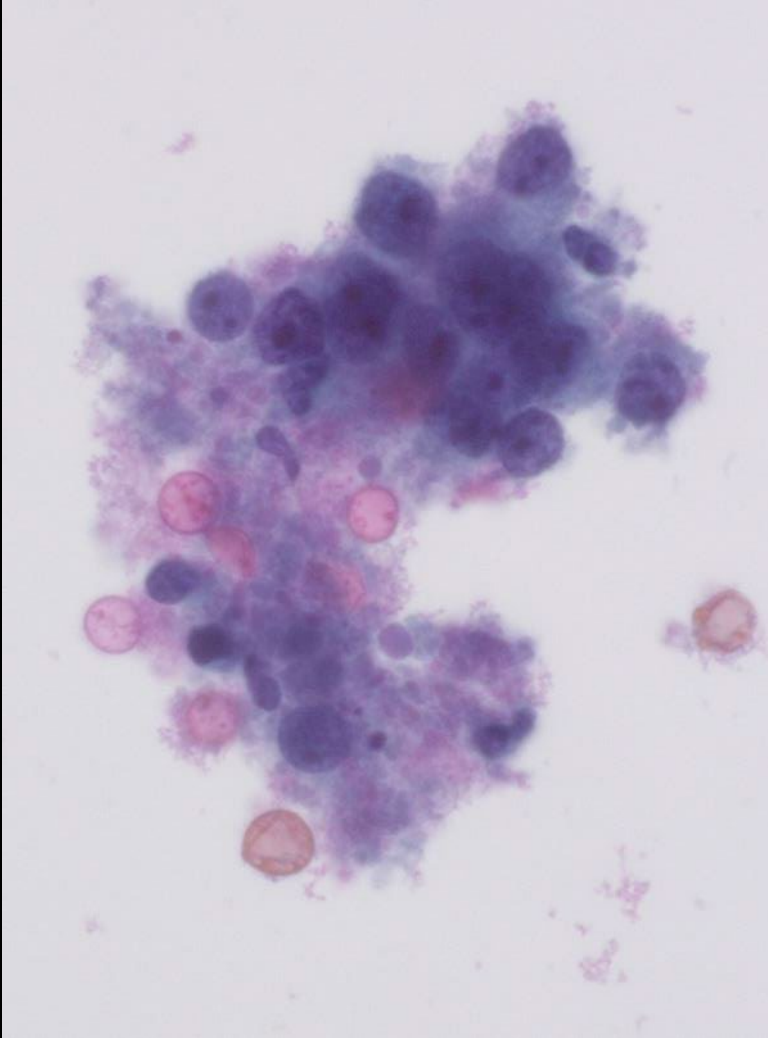
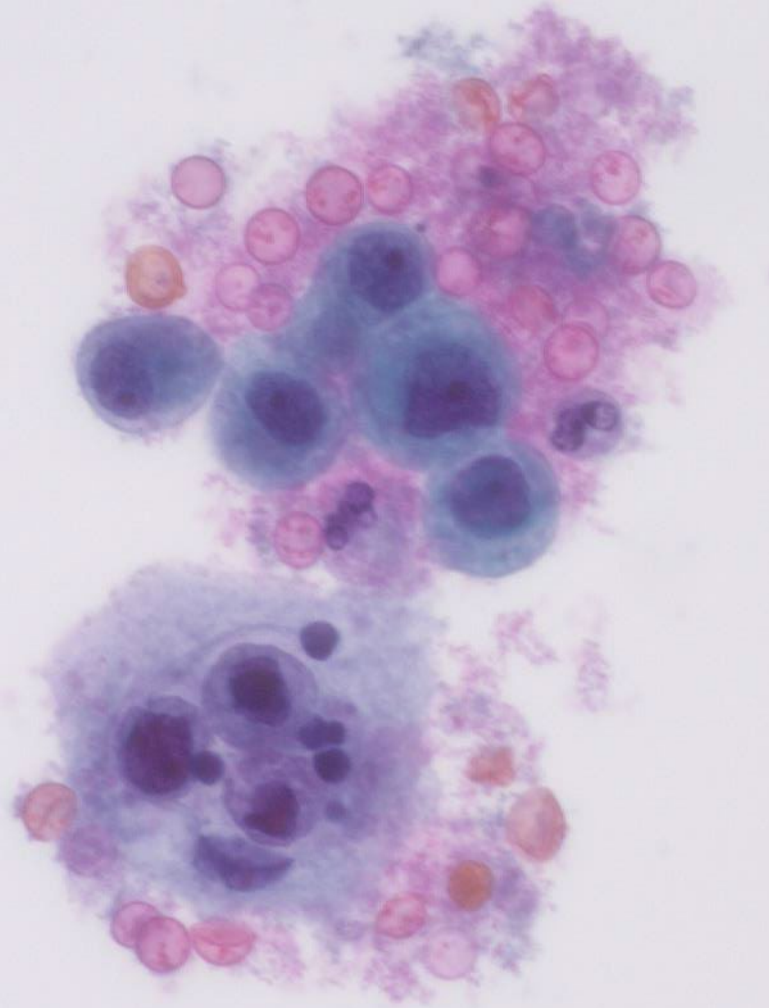
Extra-Uterine Malignancies

- Malignancies from adjacent structures may invade directly into the vagina or cervix and appear in Pap tests
 - Rectum, bladder, and vulva most common
- Metastasis from distant sites may also rarely occur
 - Lobular breast carcinoma may be especially problematic
- These malignancies usually have an obvious prior history
- Cell blocks and immunohistochemistry may be helpful

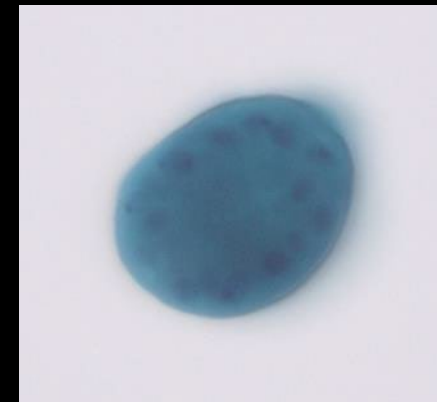
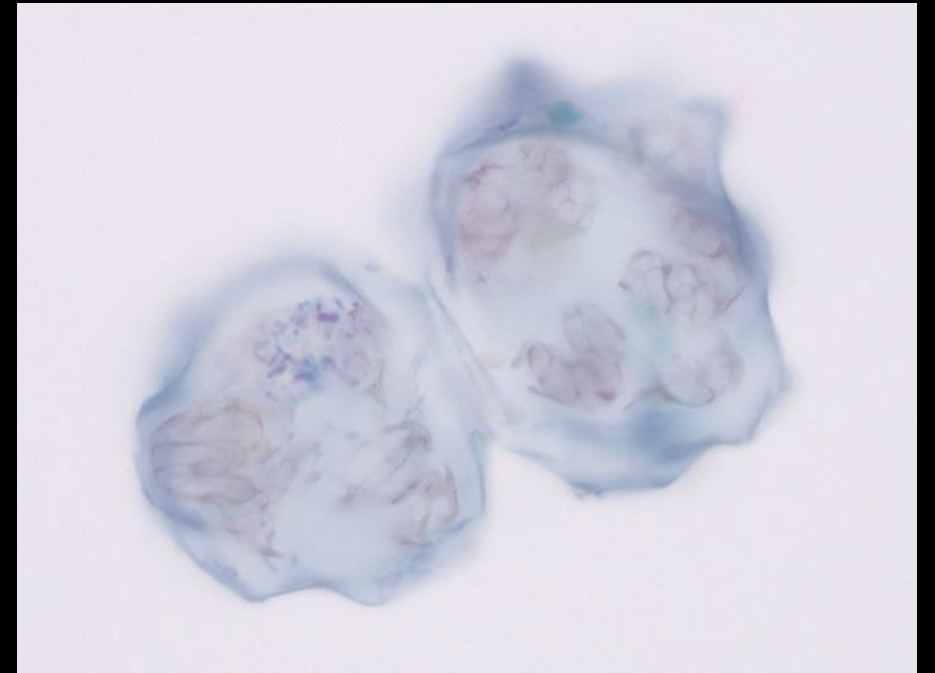
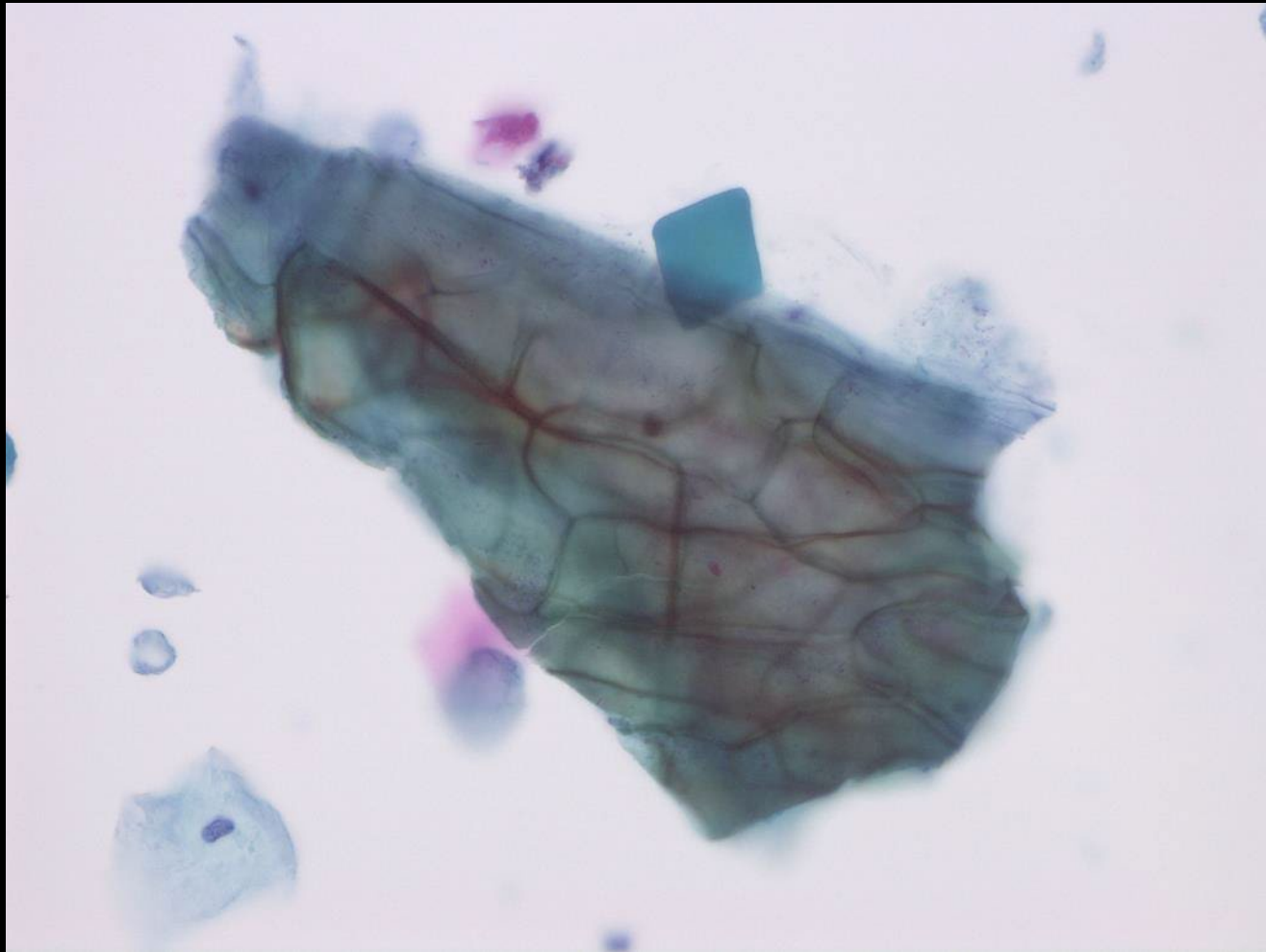
Rectal Adenocarcinoma



Rectal Adenocarcinoma (Signet Ring Type)

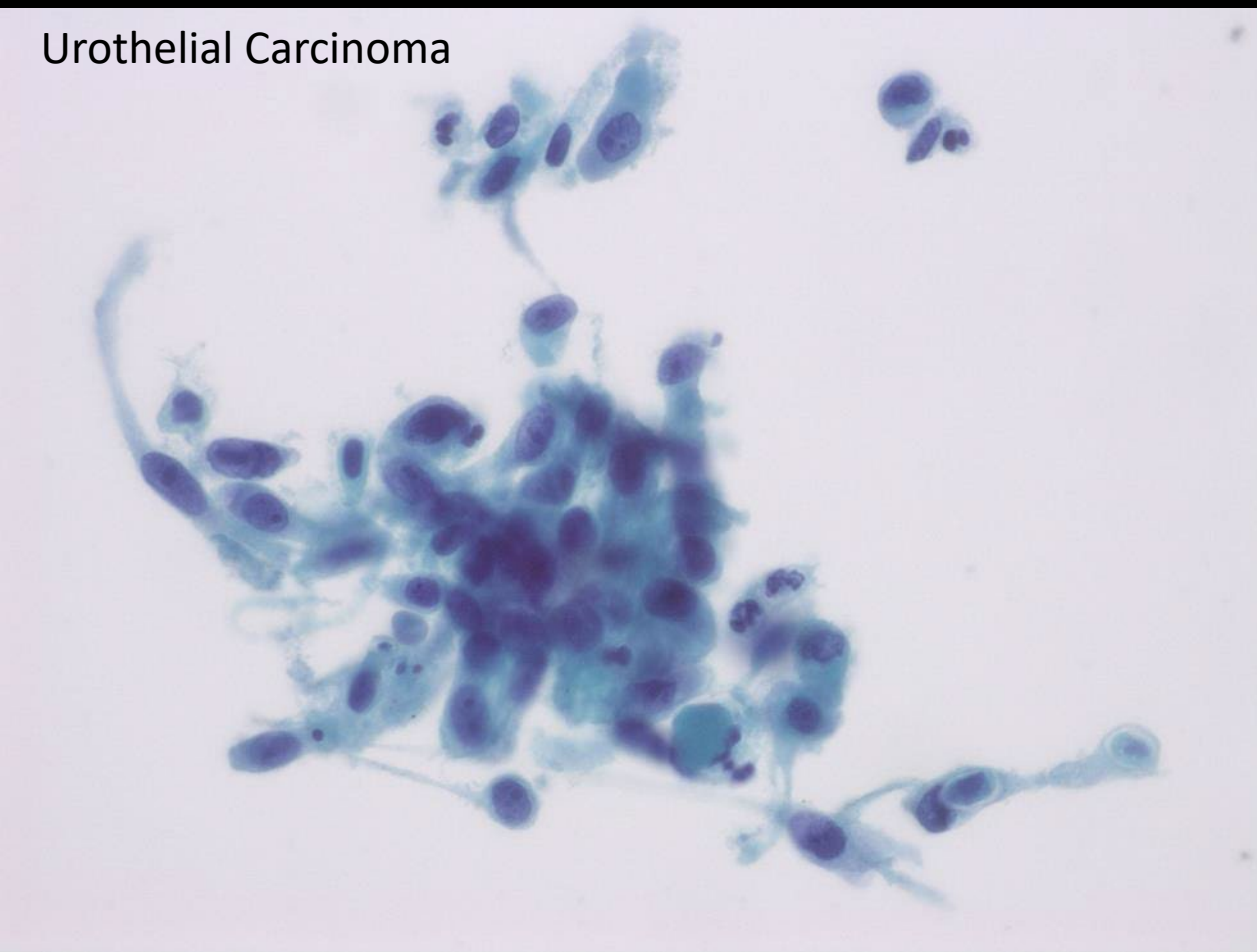


Vegetable Matter Due to Fistula Post-Irradiation

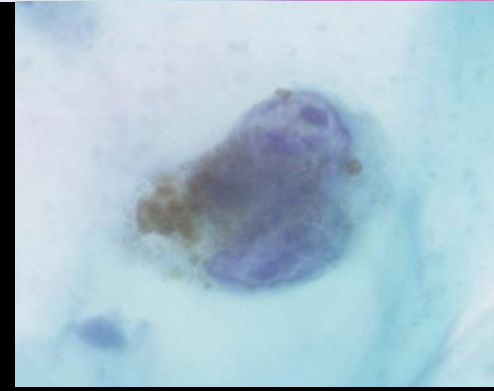
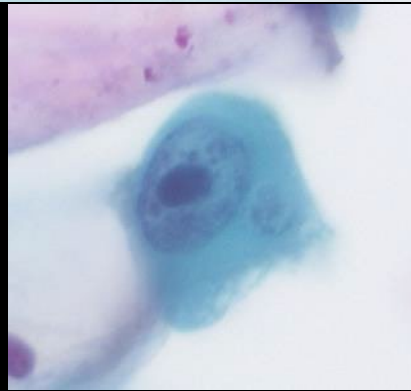
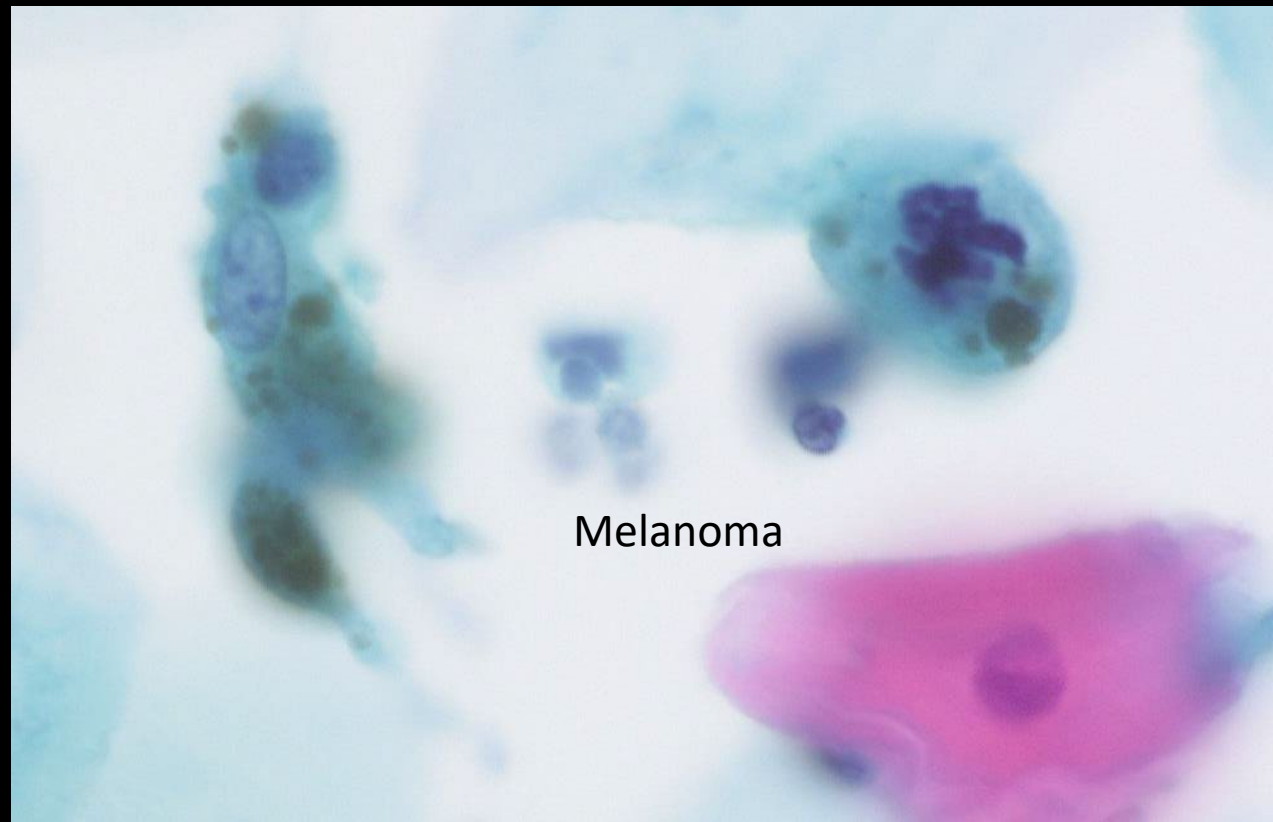


Other Extra-Uterine Malignancies

Urothelial Carcinoma

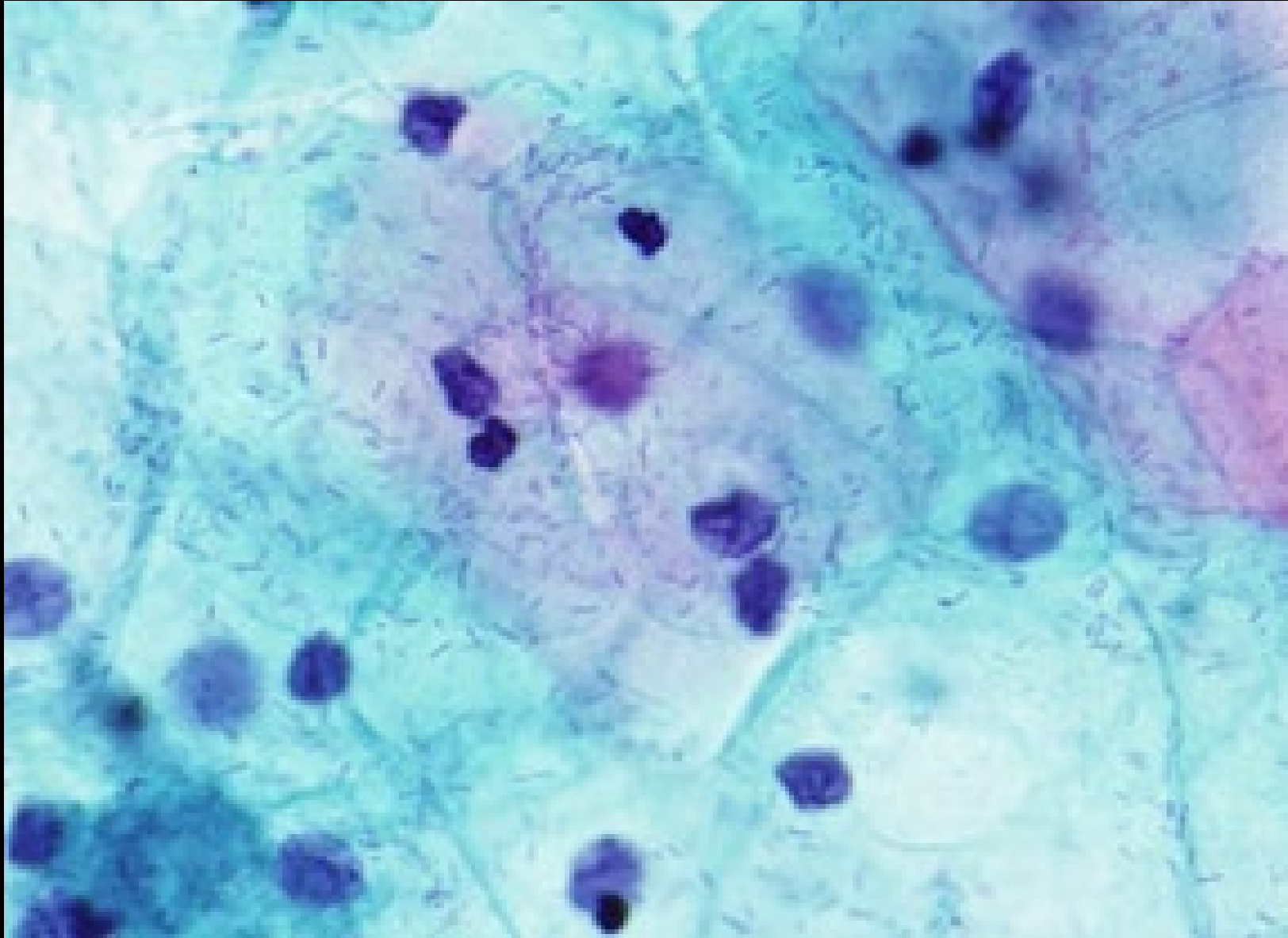


Melanoma

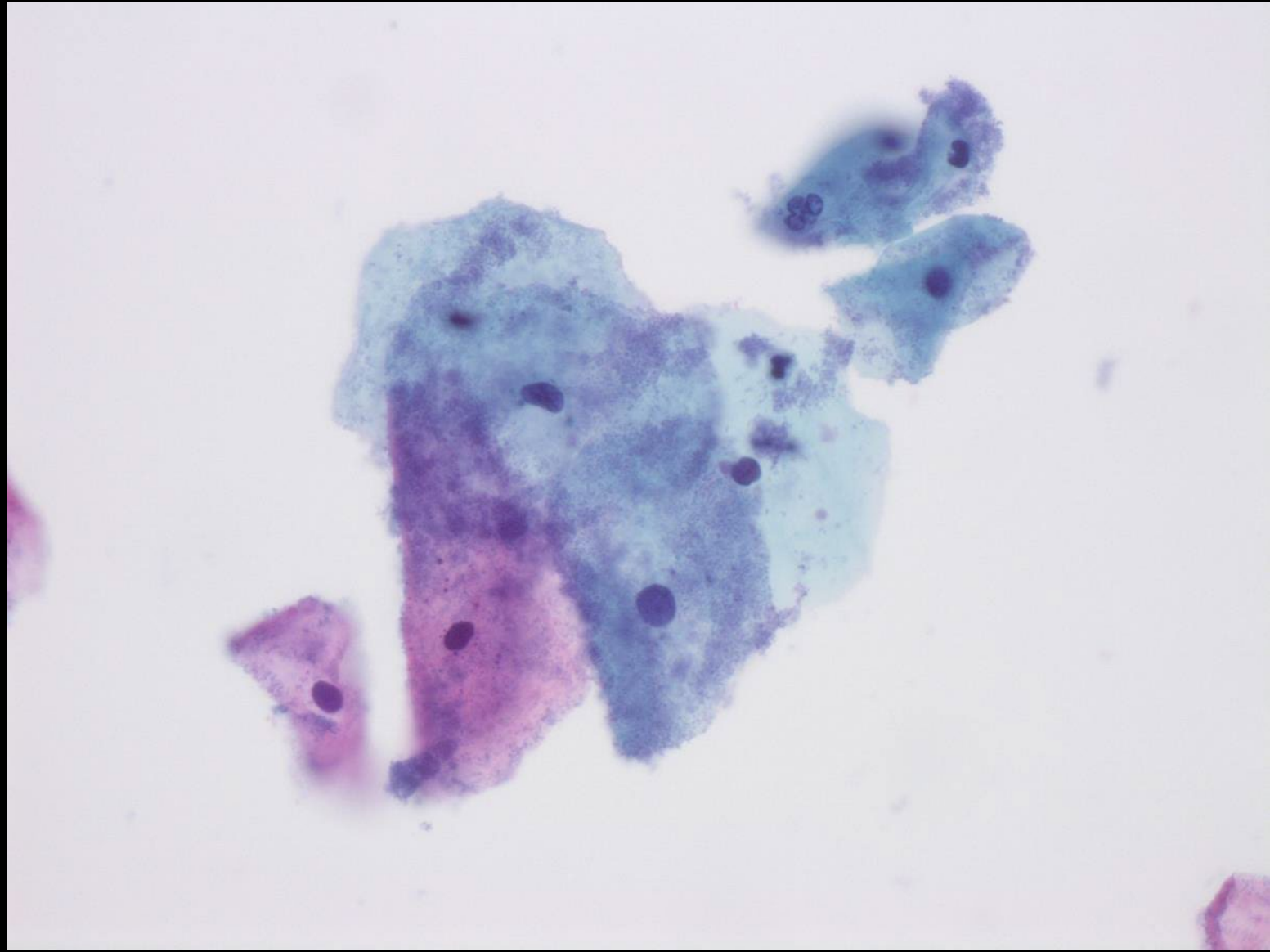
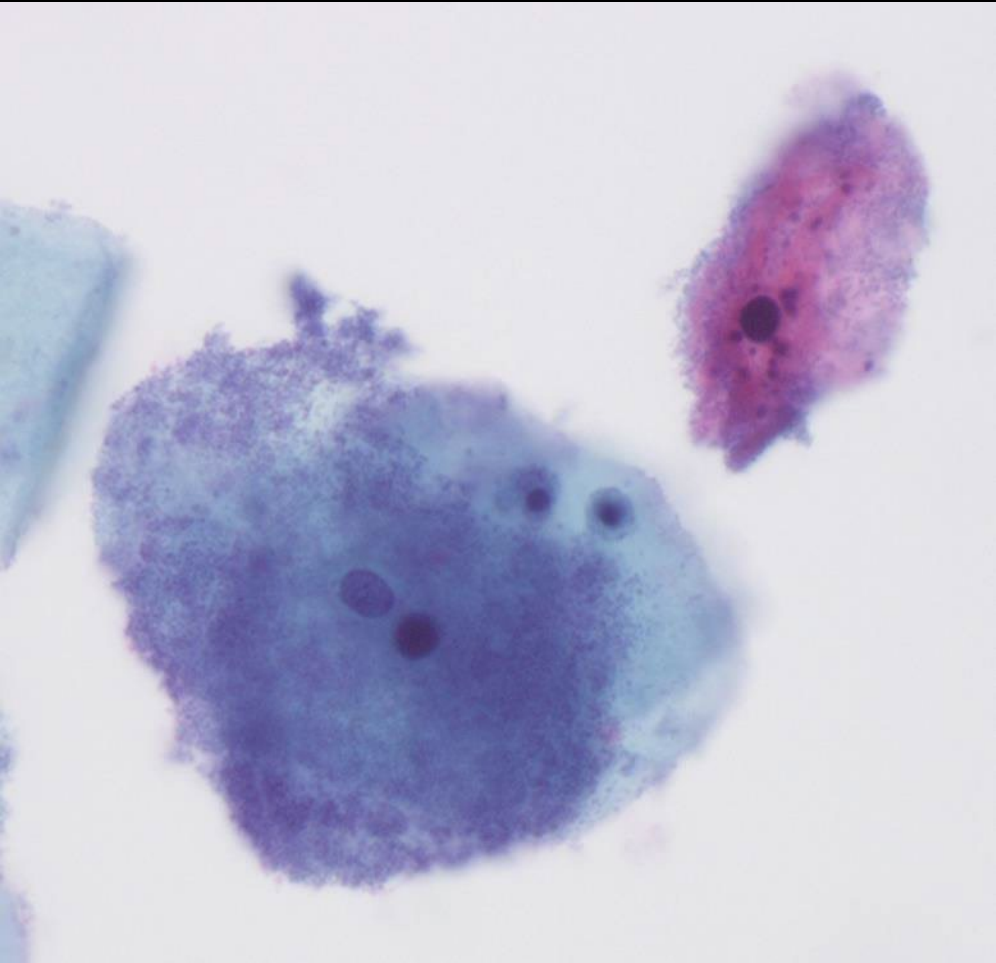


Organisms

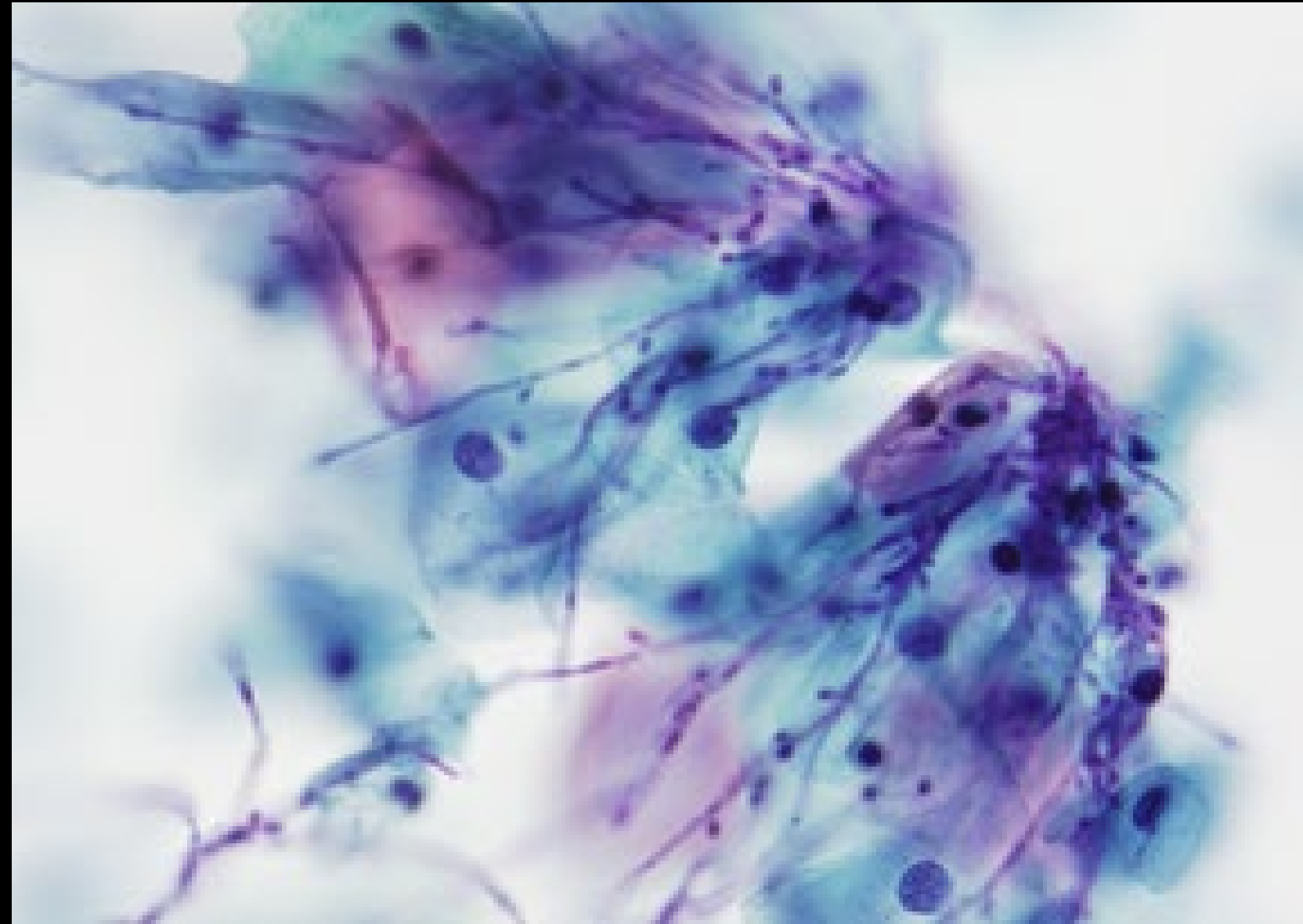
Normal - Lactobacillus (Döderlein Bacillus)



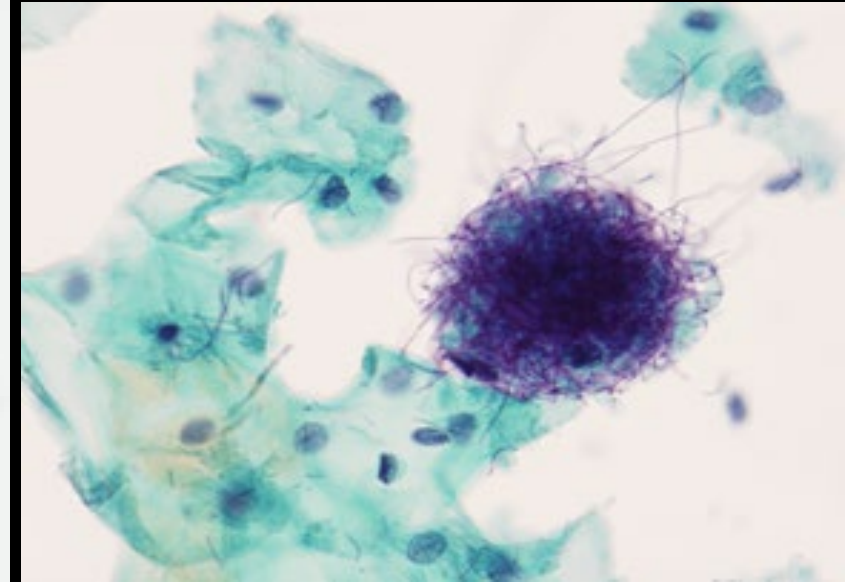
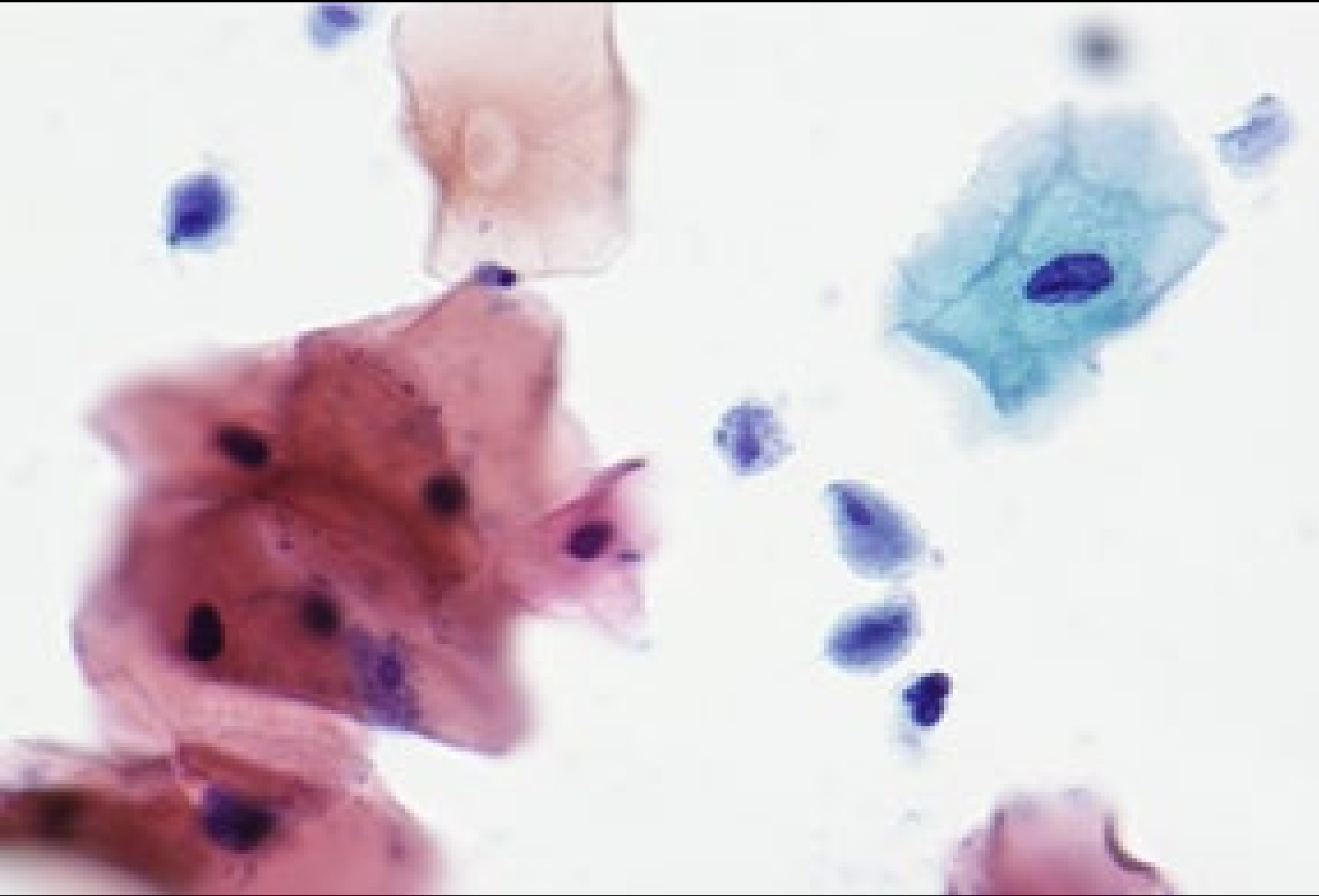
Bacterial Vaginosis - Gardnerella



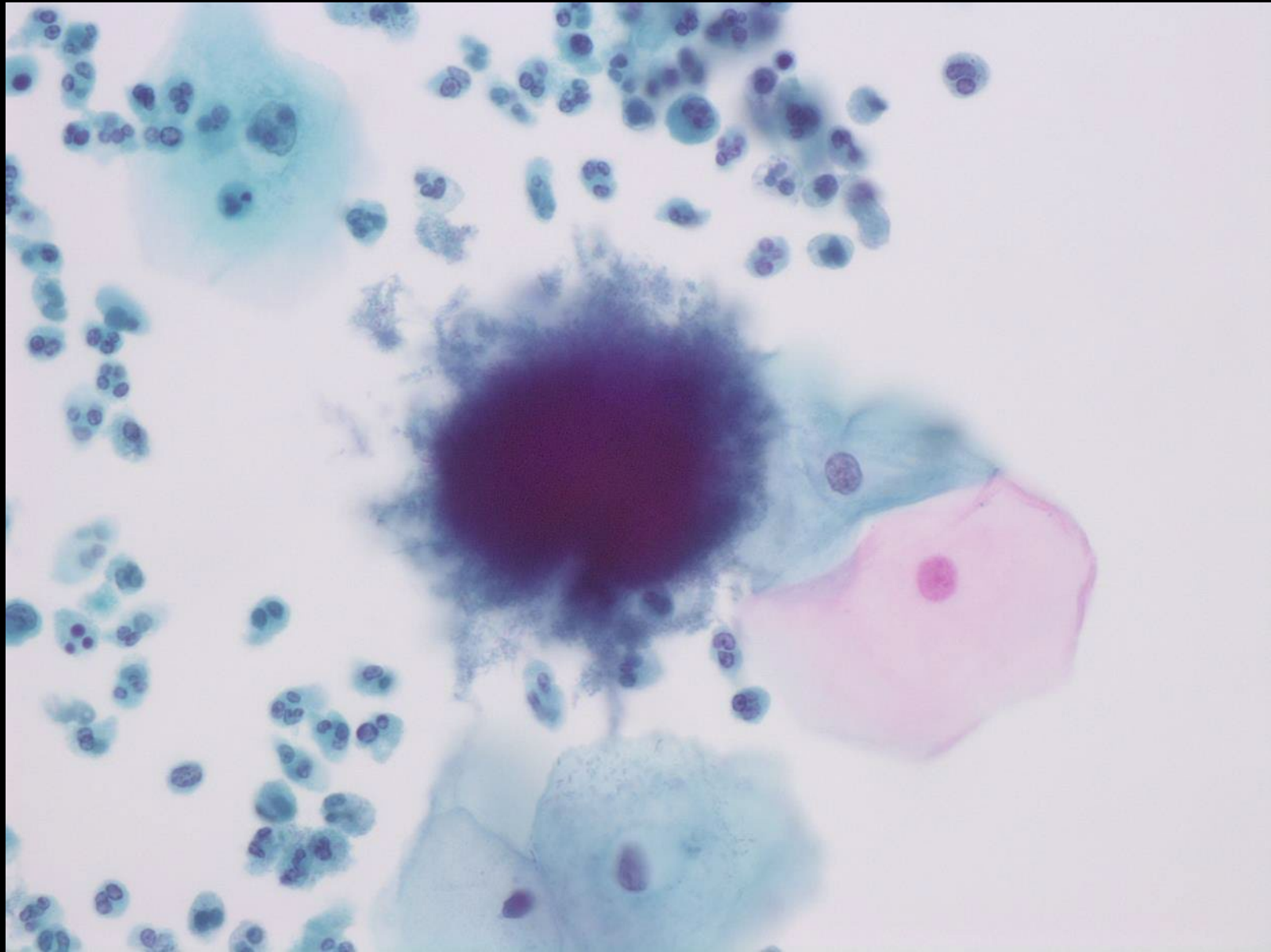
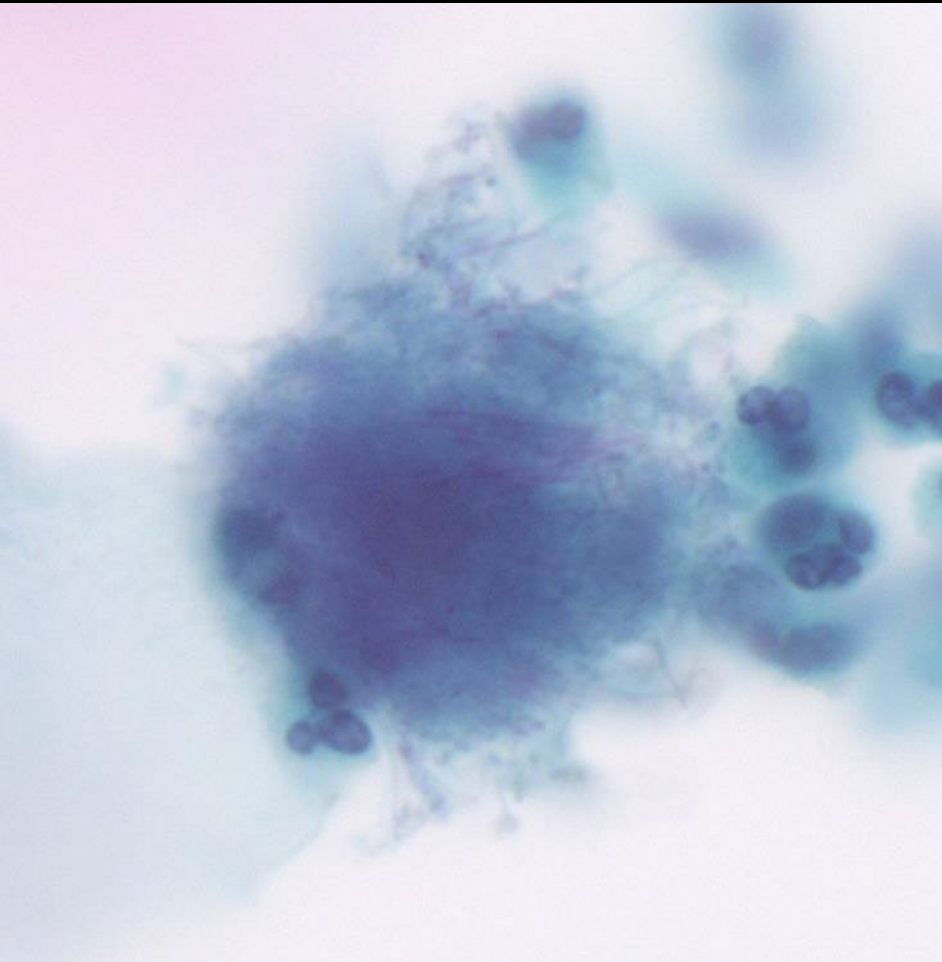
Candida



Trichomonas and Leptothrix



Actinomyces



Herpes

