

The background of the slide features a complex, three-dimensional molecular structure rendered in a dark blue, semi-transparent style. It consists of numerous spherical atoms connected by cylindrical bonds, creating a lattice-like pattern that recedes into the background. The overall color scheme is a deep, uniform blue.

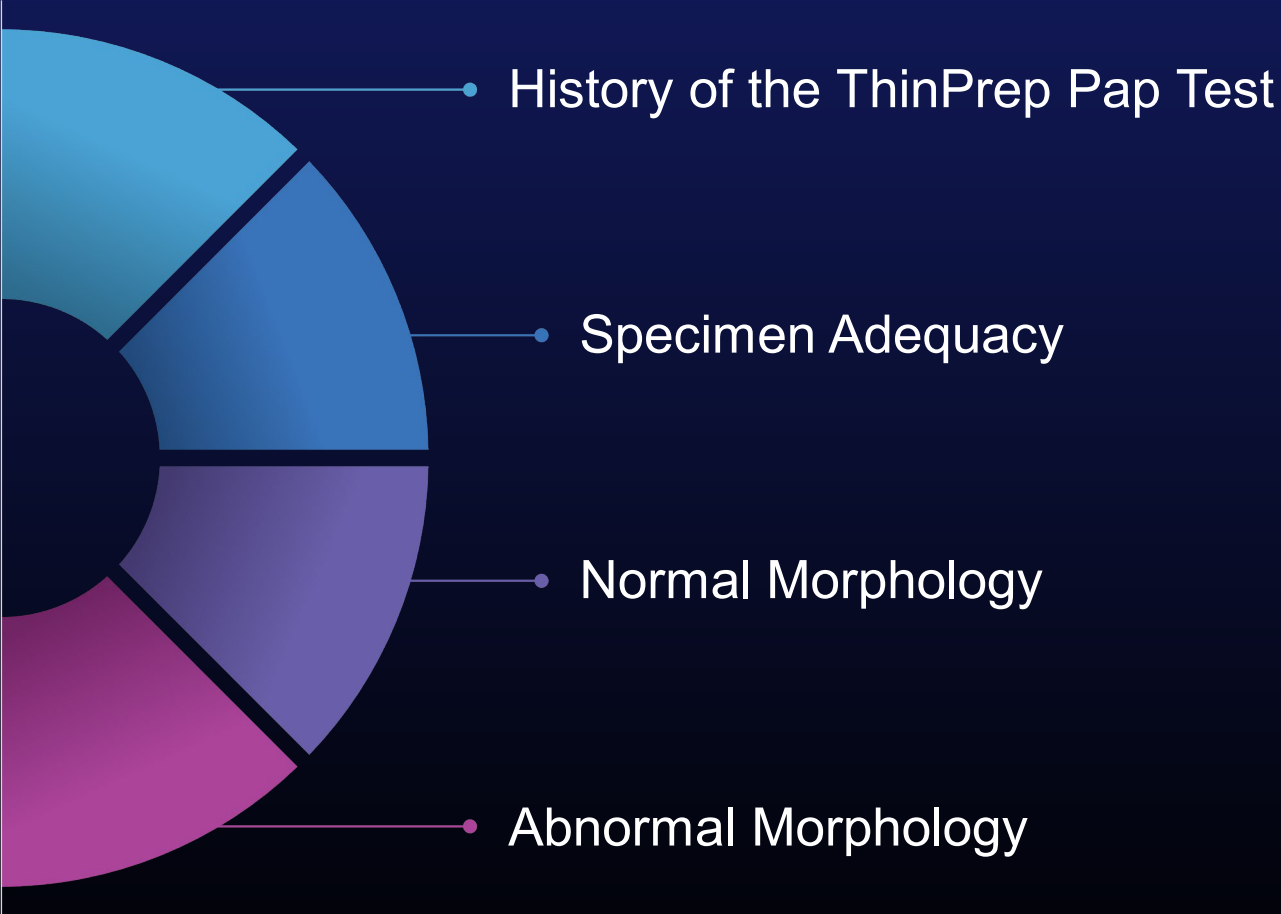
# HOLOGIC<sup>®</sup>



The Science of Sure

## ThinPrep<sup>®</sup> Pap Test Morphology

# ThinPrep Pap Test Morphology Overview



# History of the ThinPrep Pap Test

## Where it all began

- Cytyc's initial development efforts focused on Imaging (1988)
- ThinPrep Pap Test FDA approved 1996
- Sample/Preparation Limitations Addressed



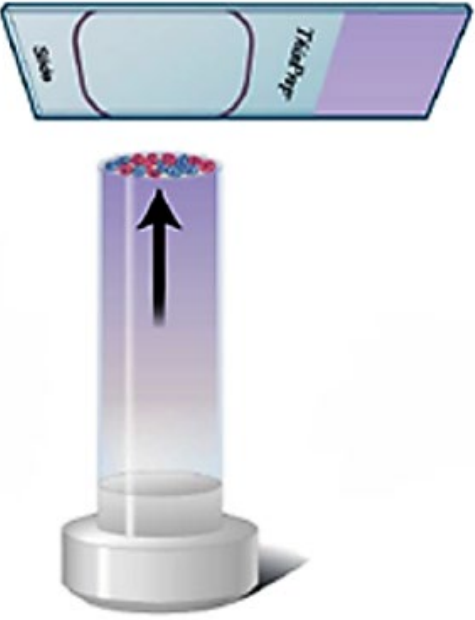
# ThinPrep® Process



Dispersion

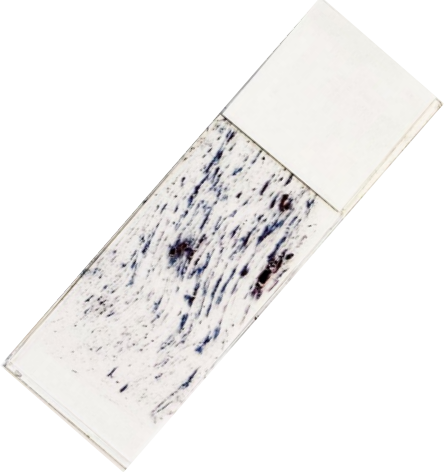
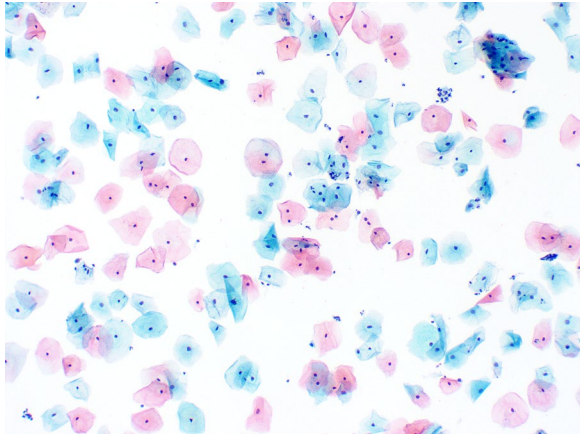
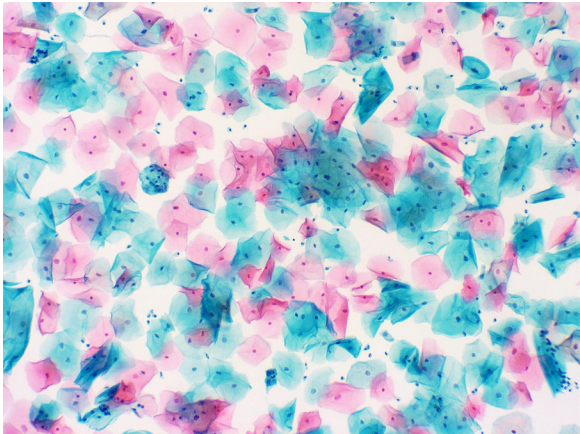
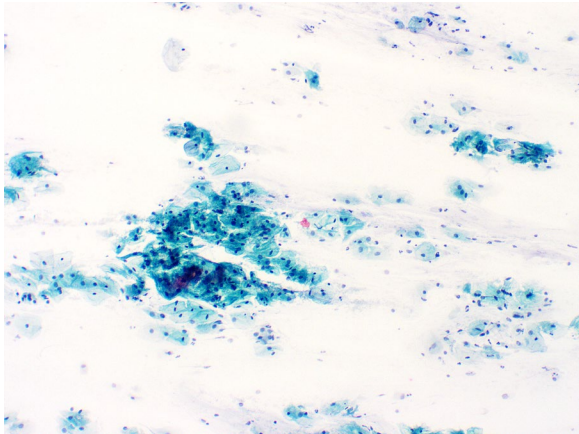


Collection



Transfer

# Pap Test Methods



Conventional Smear



SurePath



ThinPrep Pap

# Pap Test Methods

## ThinPrep vs Conventional

### Similarities

- Classic Cell Morphology
- Assessment of Cellularity
- Slow, Systematic Screening

### Differences

- Collection
- Immediate Fixation
- Thin Layer

# Pap Test Methods

## ThinPrep vs SurePath

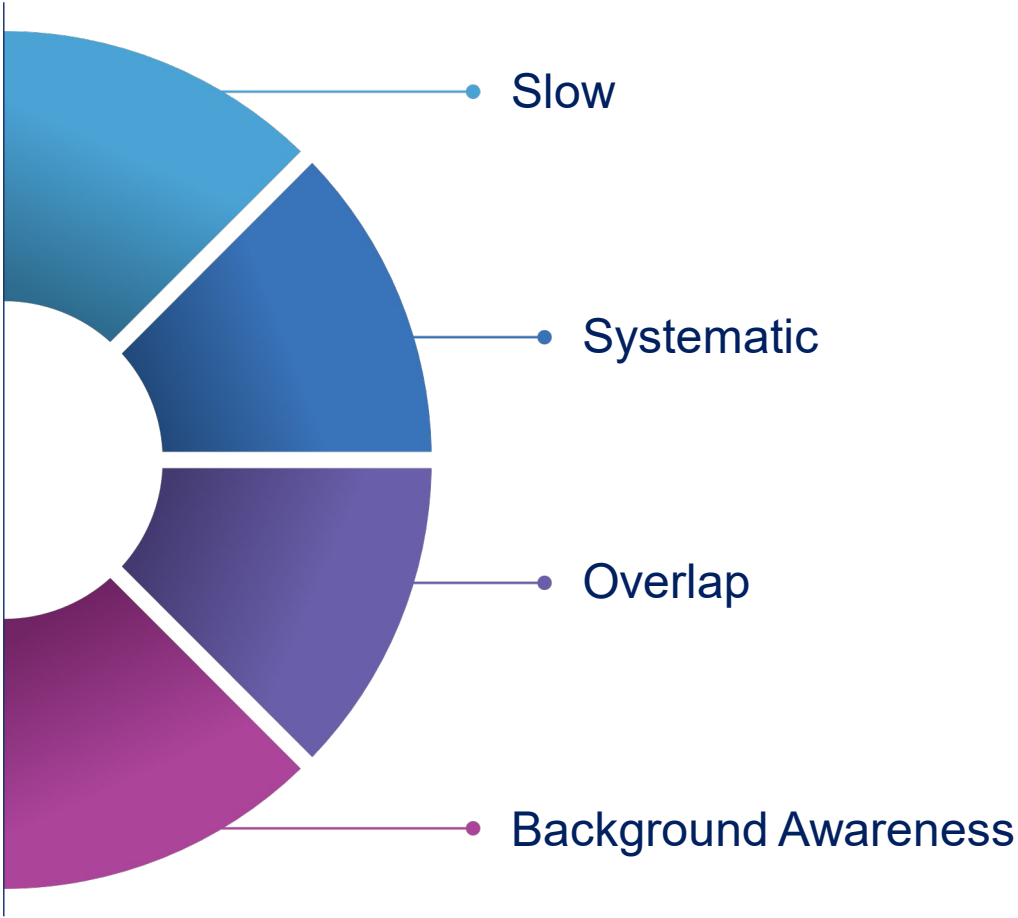
### Similarities

- Liquid based
- Thin layer

### Differences

- Collection
- Fixative
- Sample Transfer

# ThinPrep Screening Tips





# The Bethesda System for Reporting Cervical Cytology

## Adequacy

### 5,000 Well Preserved, Visualized Squamous Cells

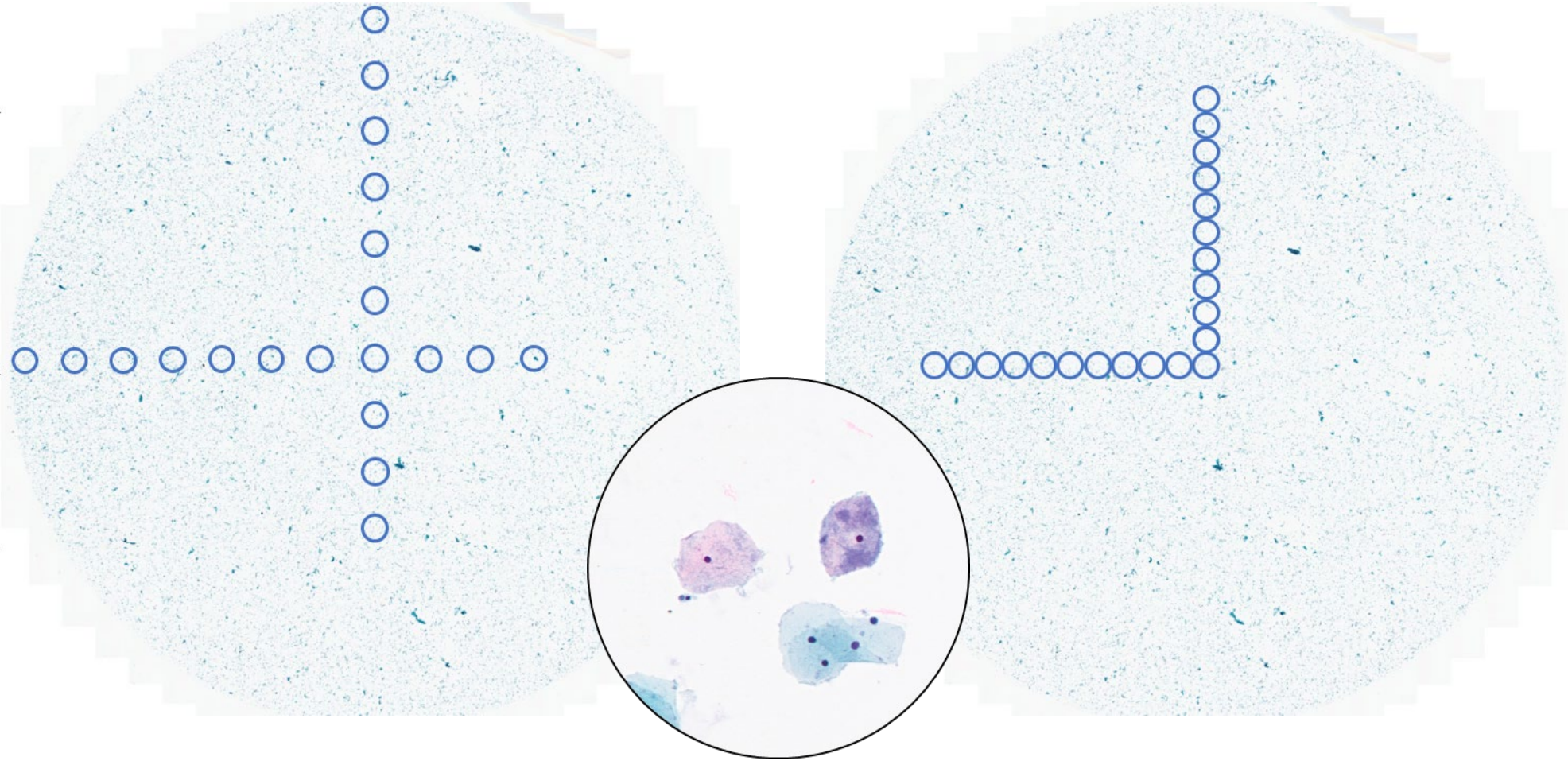
FN20 Eyepiece/ 10x Objective	FN20 Eyepiece/ 40x Objective	FN22 Eyepiece/ 10x Objective	FN22 Eyepiece/ 40x Objective
50.0	3.1	60.5	3.8

1. Nayar, R., & Wilbur, D. C. (2015). Specimen Adequacy. In *The Bethesda System for Reporting Cervical Cytology: Definitions, Criteria, and Explanatory Notes* (3rd ed., 2015 ed., pp. 3–5). Springer.

# The Bethesda System for Reporting Cervical Cytology

Adequacy- Suggested Counting Method #1

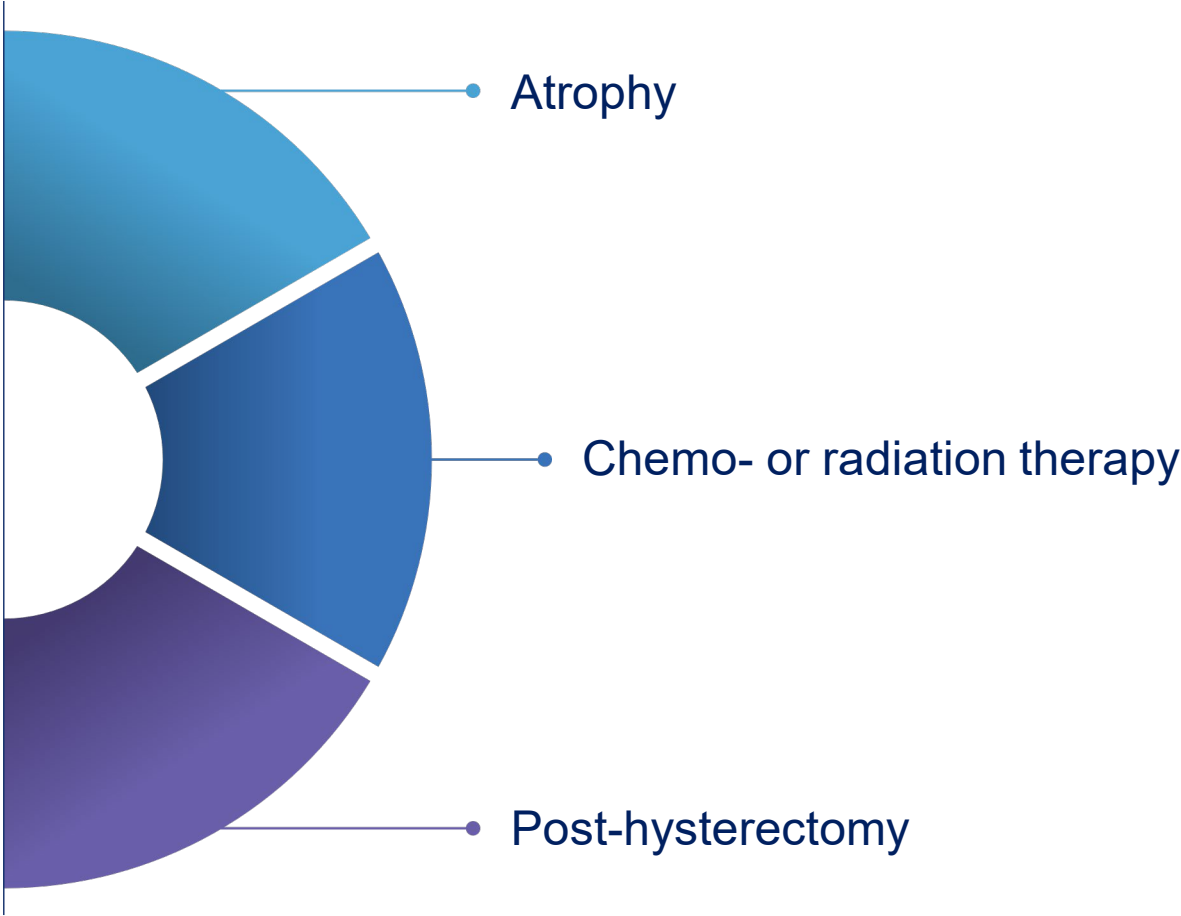
Adequacy- Suggested Counting Method #2



1. Nayar, R., & Wilbur, D. C. (2015). Specimen Adequacy. In *The Bethesda System for Reporting Cervical Cytology: Definitions, Criteria, and Explanatory Notes* (3rd ed. 2015 ed., pp. 4). Springer.

# The Bethesda System for Reporting Cervical Cytology

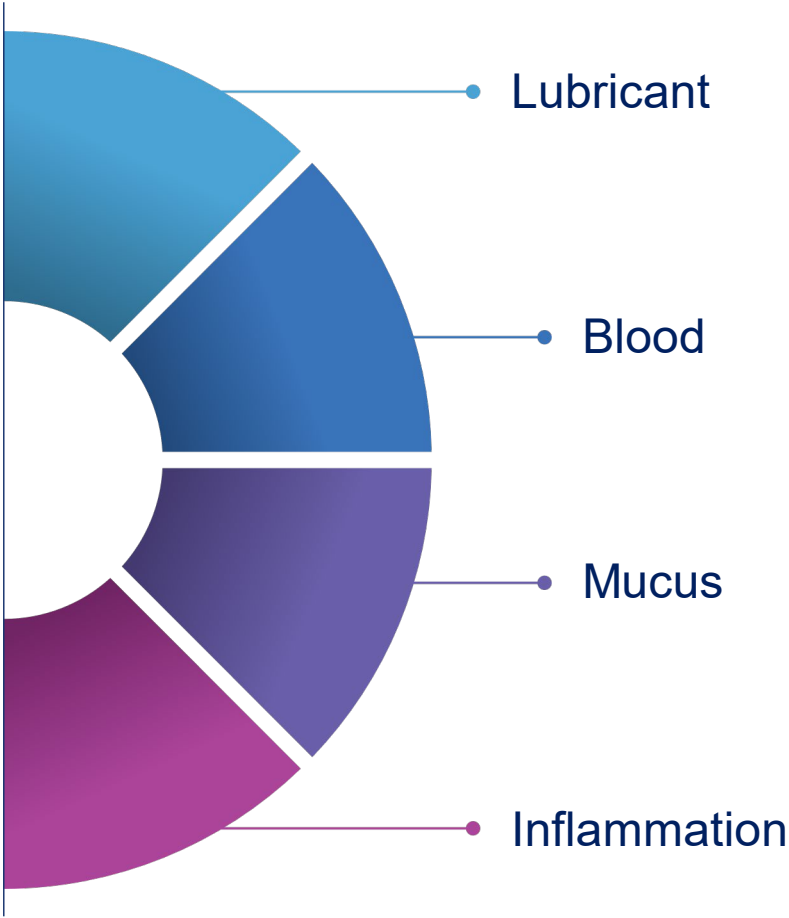
## Adequacy- Other Considerations



1. Nayar, R., & Wilbur, D. C. (2015). Specimen Adequacy. In *The Bethesda System for Reporting Cervical Cytology: Definitions, Criteria, and Explanatory Notes* (3rd ed. 2015 ed., pp. 3,11-12). Springer.

# The Bethesda System for Reporting Cervical Cytology

## Adequacy- Obscuring Factors and Interfering Substances



1.Nayar, R., & Wilbur, D. C. (2015). Specimen Adequacy. In *The Bethesda System for Reporting Cervical Cytology: Definitions, Criteria, and Explanatory Notes* (3rd ed. 2015 ed., pp. 19-22). Springer.

# The Bethesda System for Reporting Cervical Cytology

## Adequacy- Obscuring Factors and Interfering Substances

### Unsatisfactory

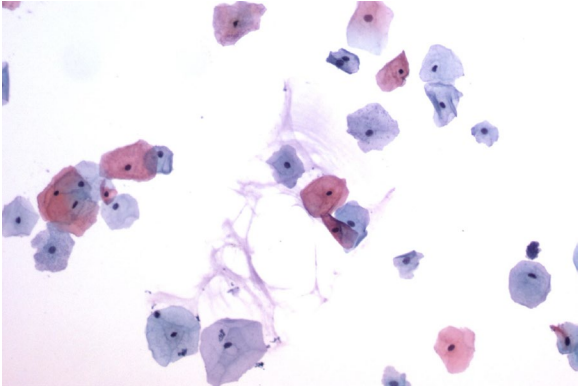
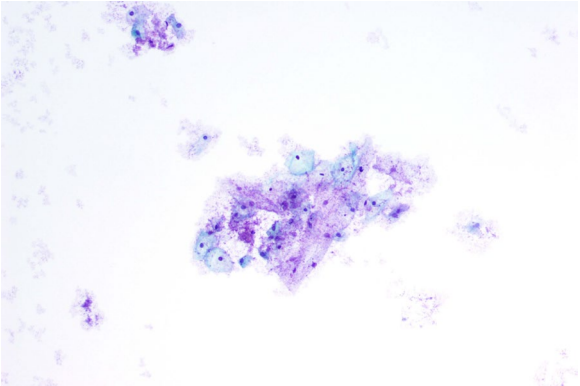
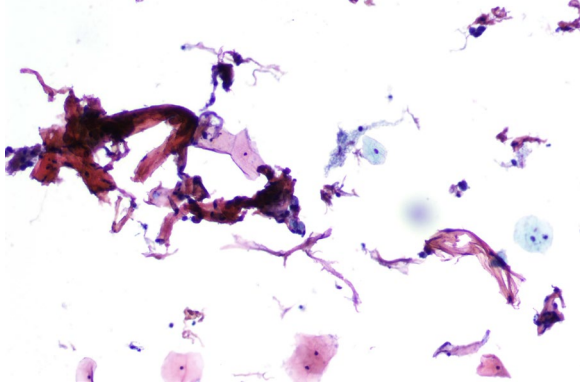
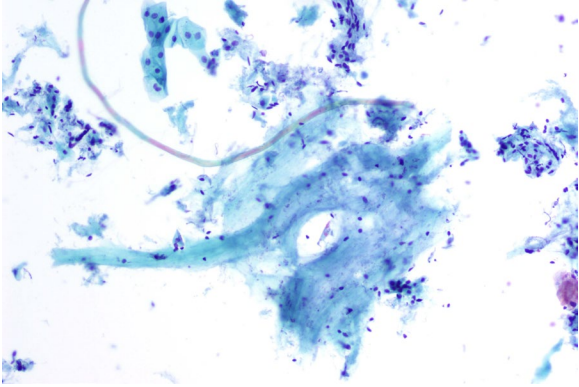
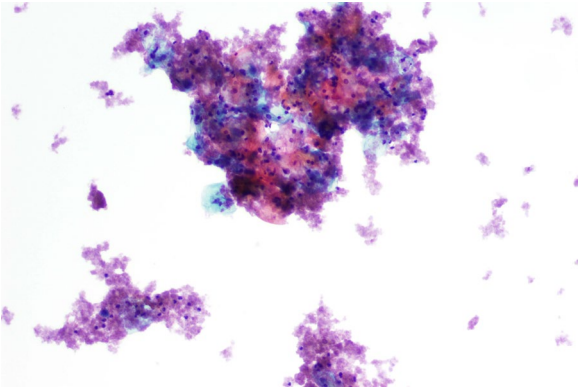
- Greater than 75% squamous cells obscured AND no abnormal cells

### Satisfactory

- 50-75% squamous cells obscured
- Include statement describing the specimen as partially obscured

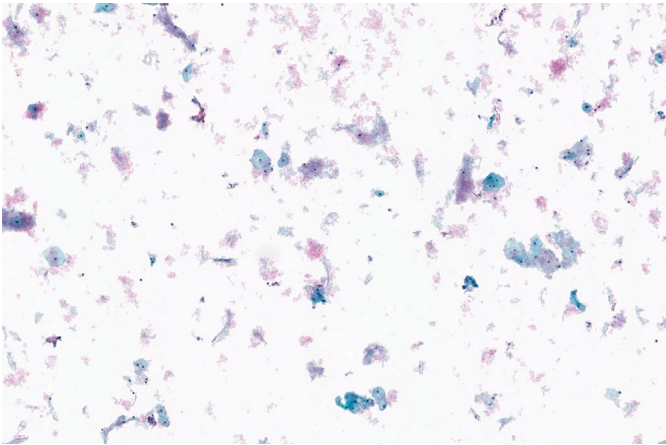
# The Bethesda System for Reporting Cervical Cytology

Adequacy- Obscuring Factors and Interfering Substances: Examples of Lubricant

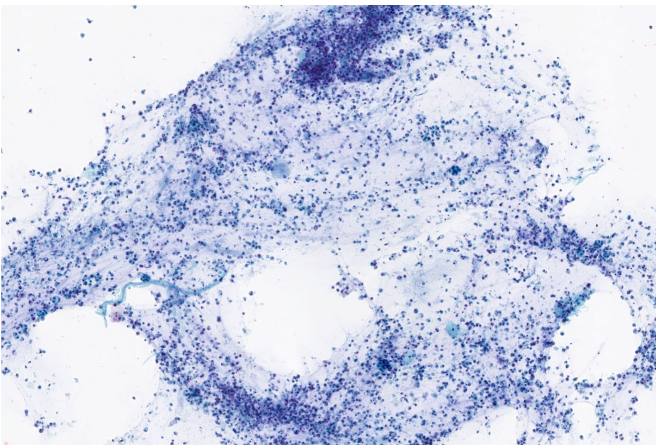


# The Bethesda System for Reporting Cervical Cytology

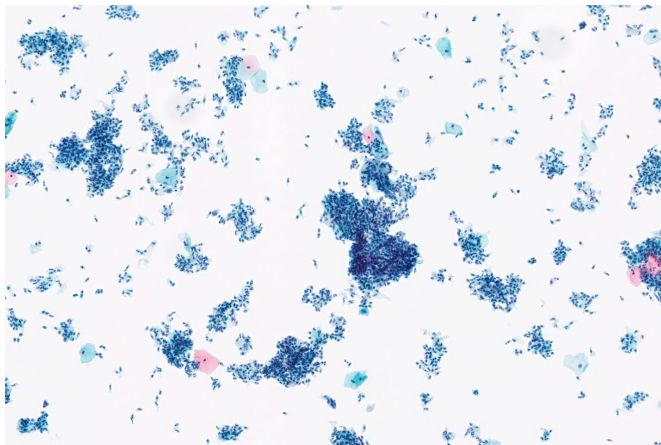
Adequacy- Obscuring Factors and Interfering Substances: Examples of Blood, Mucus, Inflammation



Blood



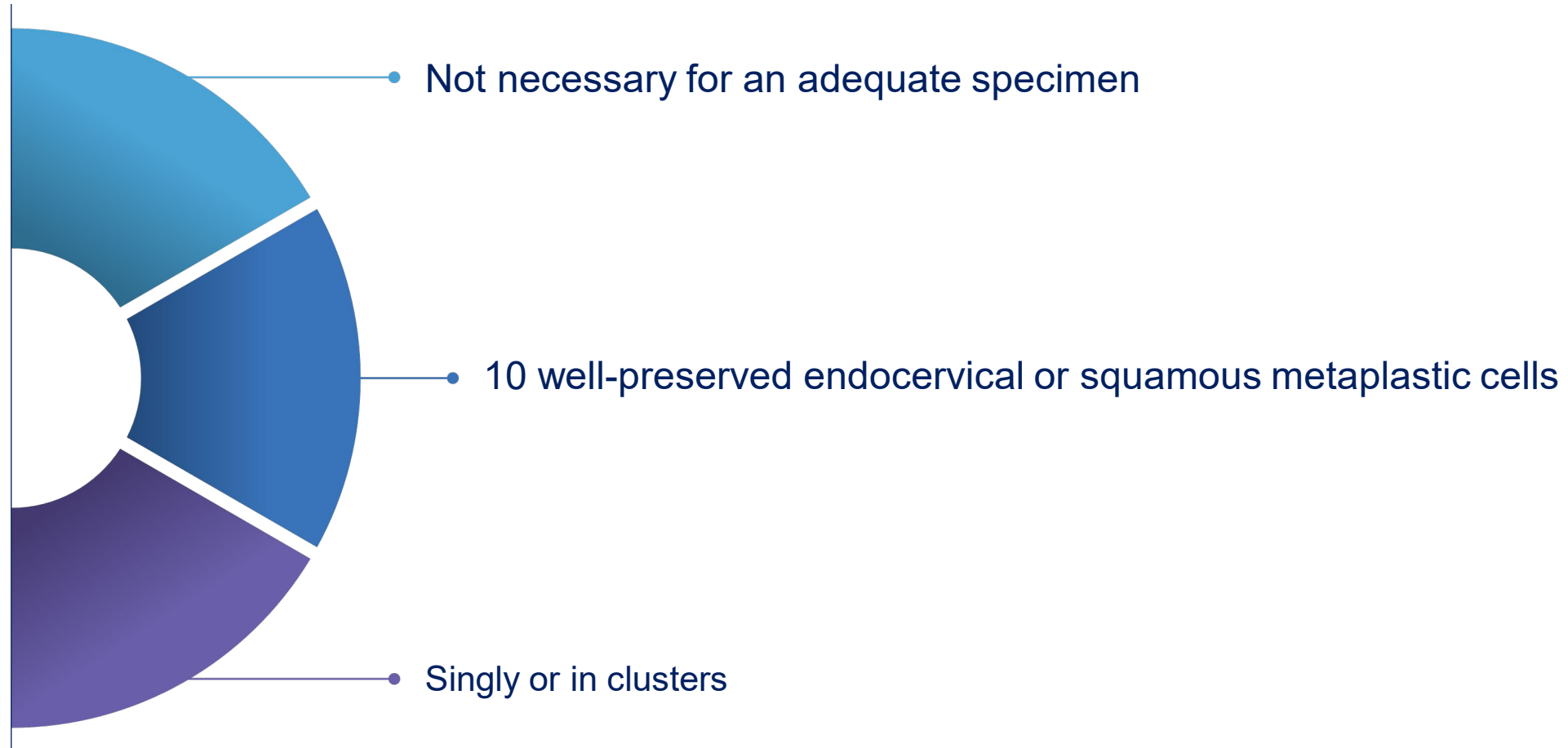
Mucus



Inflammation

# The Bethesda System for Reporting Cervical Cytology

## Endocervical/Transformation Zone Component



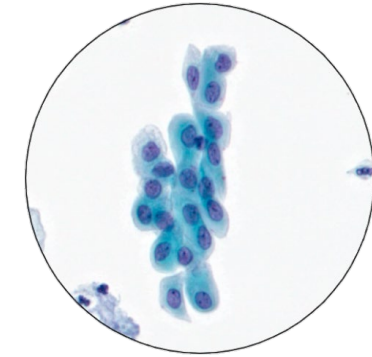


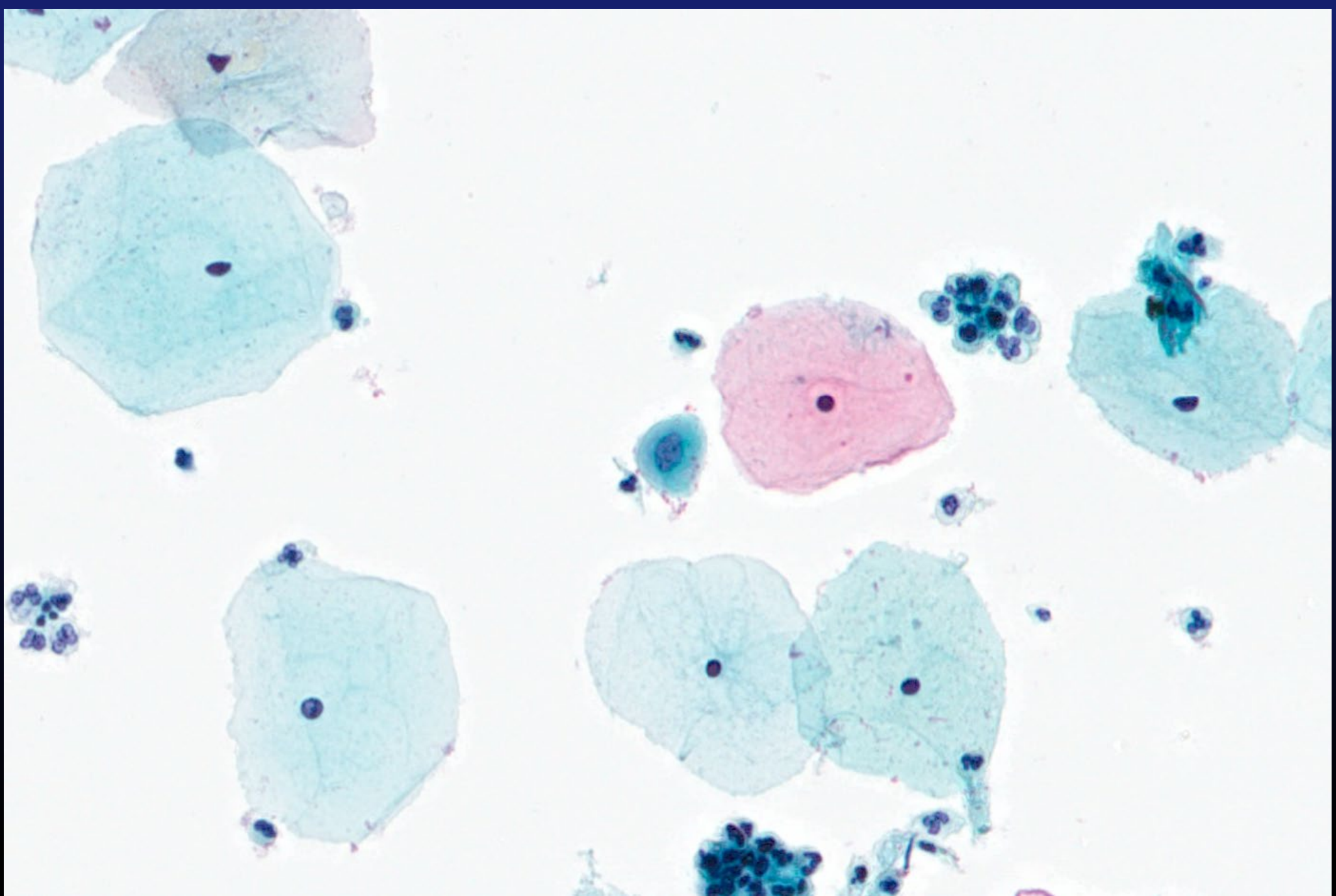
ThinPrep Pap Test:  
**Normal Morphology**

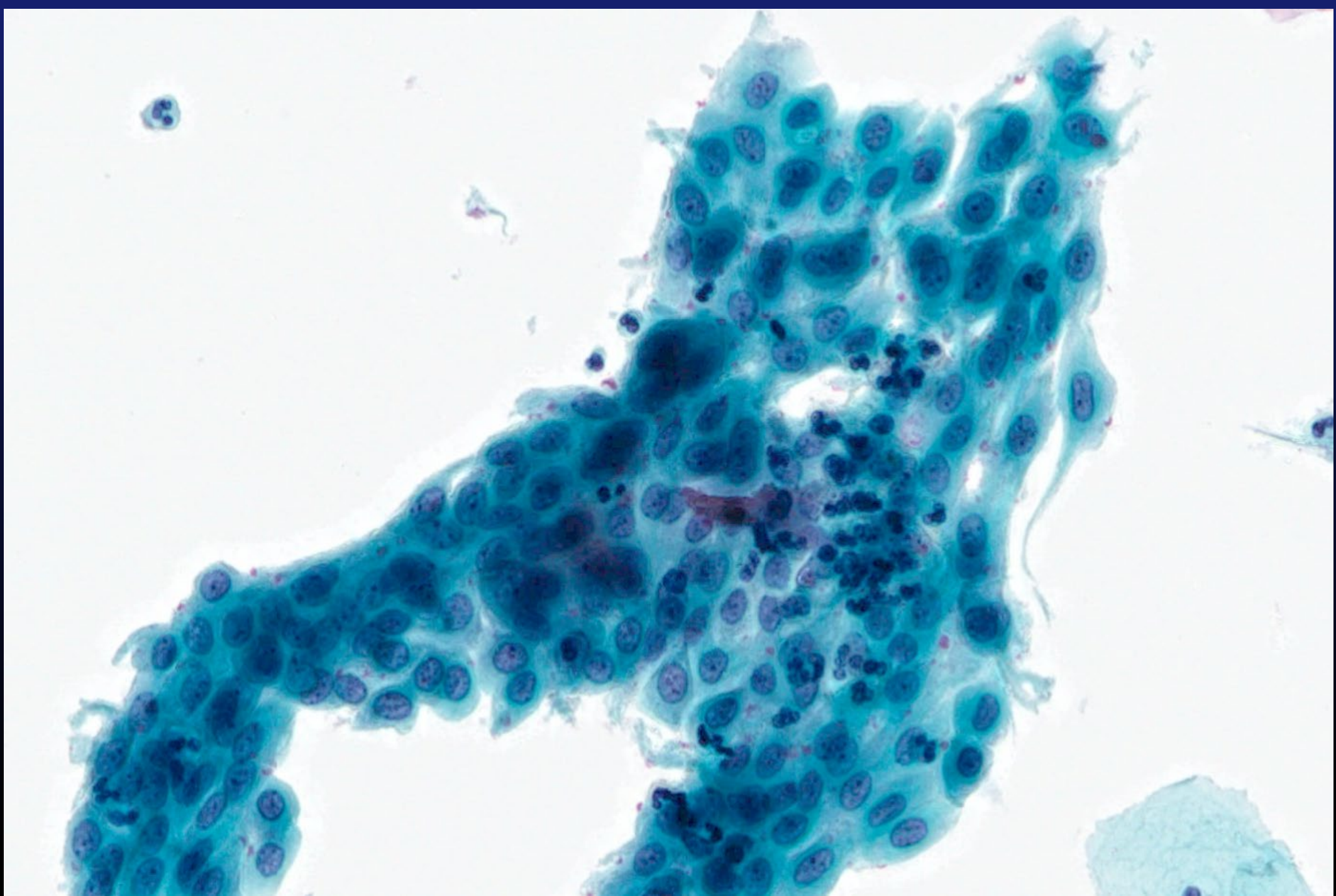
# The Bethesda System for Reporting Cervical Cytology

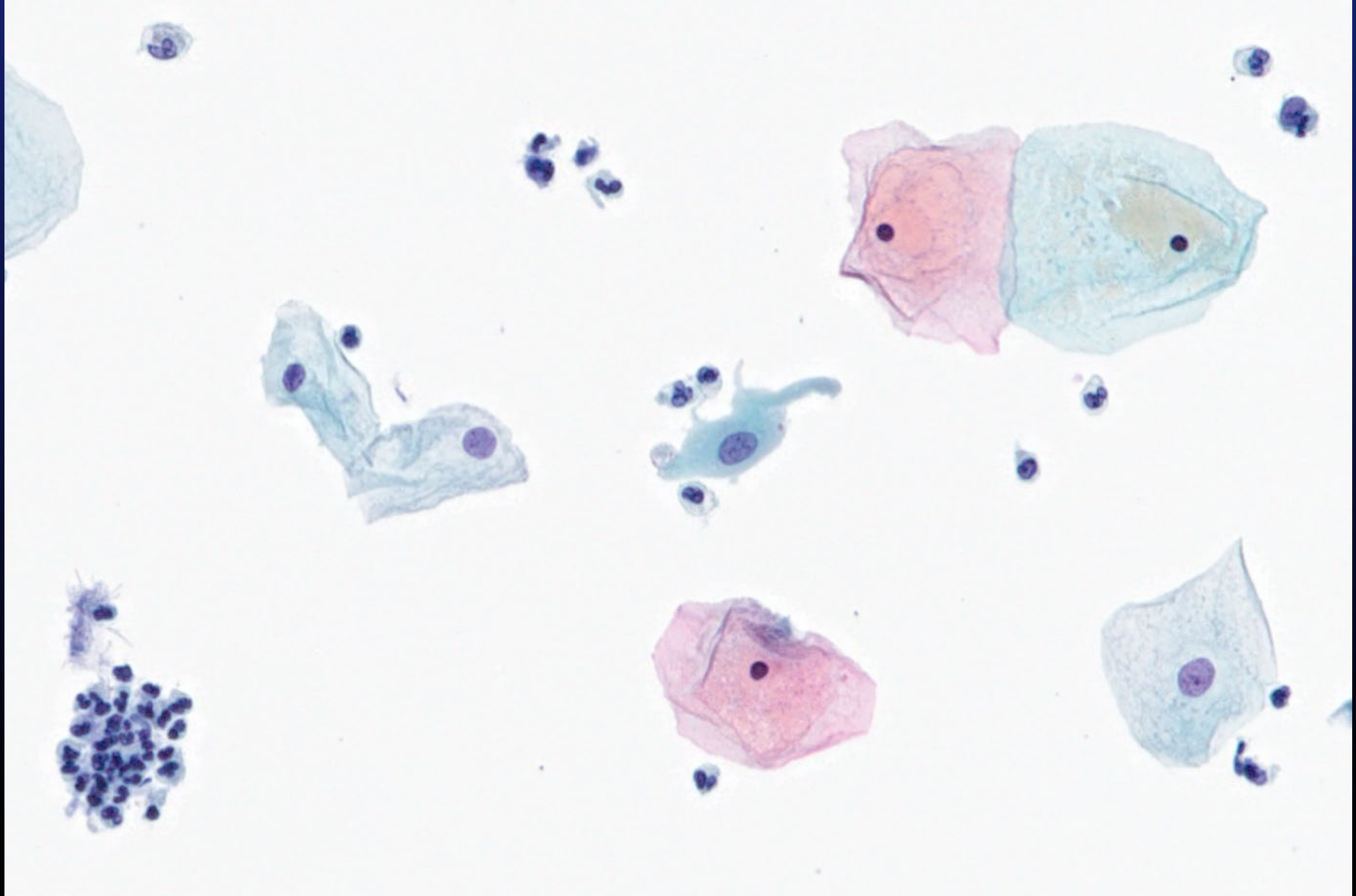
## Normal Morphology – Squamous Metaplasia

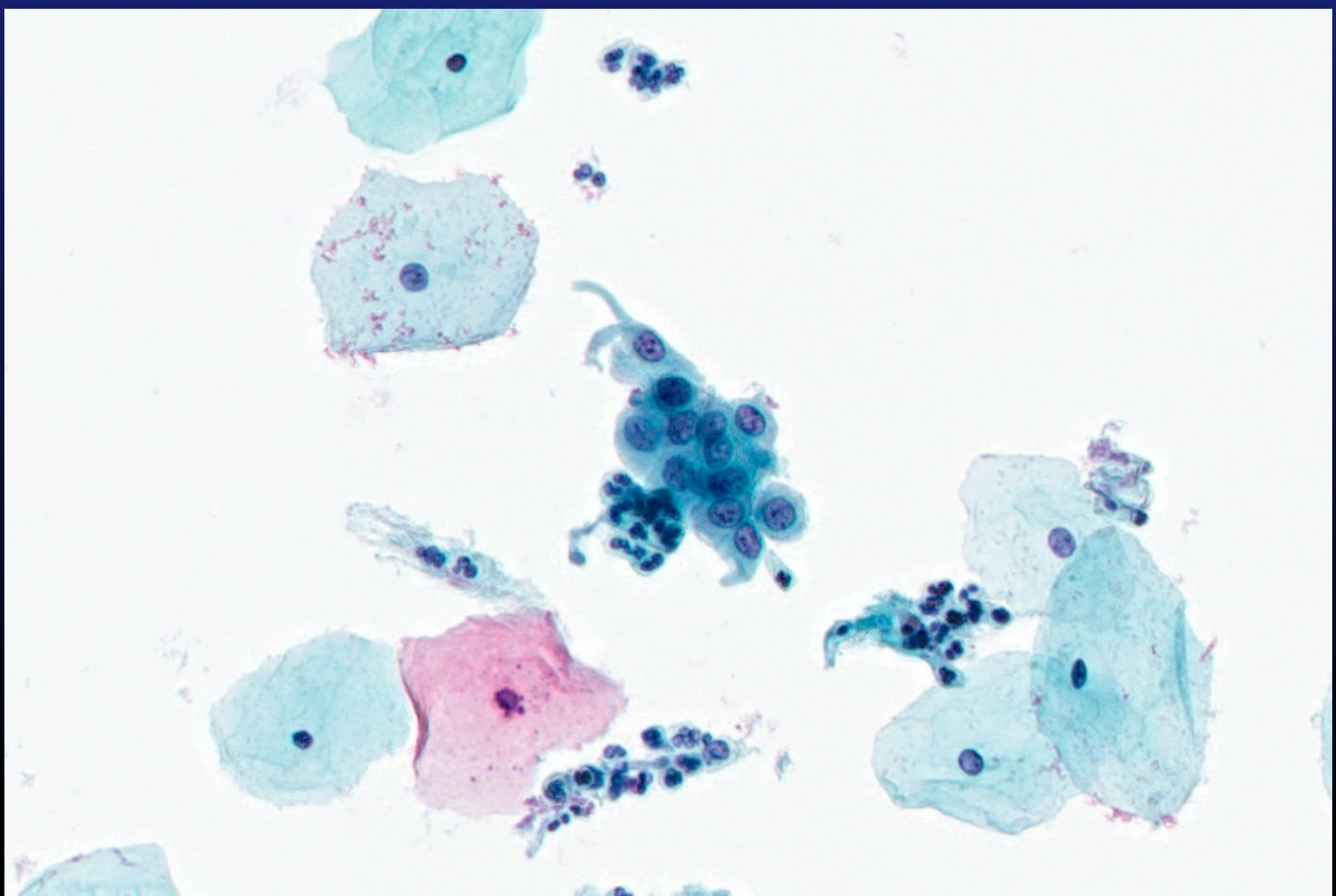
- Singly or in groups (Sheets/cobblestone arrangement)
- Nuclei 1-2x size of intermediate cell nucleus ~50 microns
- N/C ratio may be variable
- Smooth nuclear membranes
- Finely granular and evenly distributed chromatin
- Dense, homogenous cytoplasm may be vacuolated







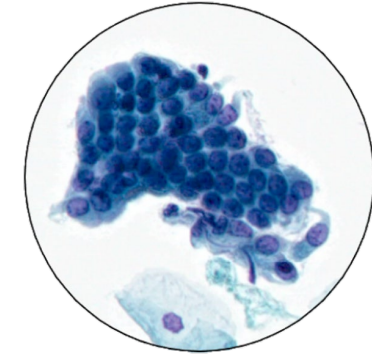


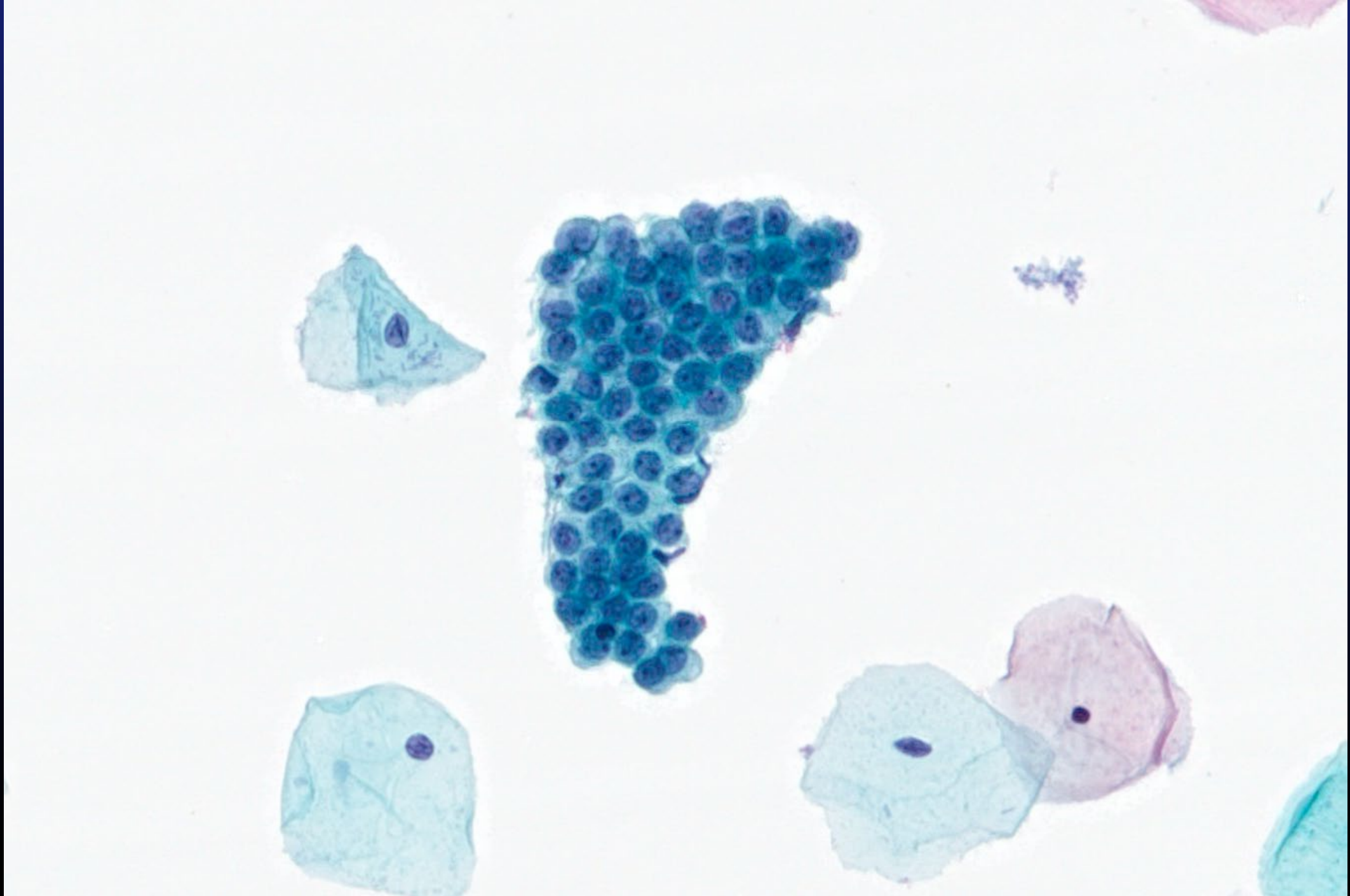


# The Bethesda System for Reporting Cervical Cytology

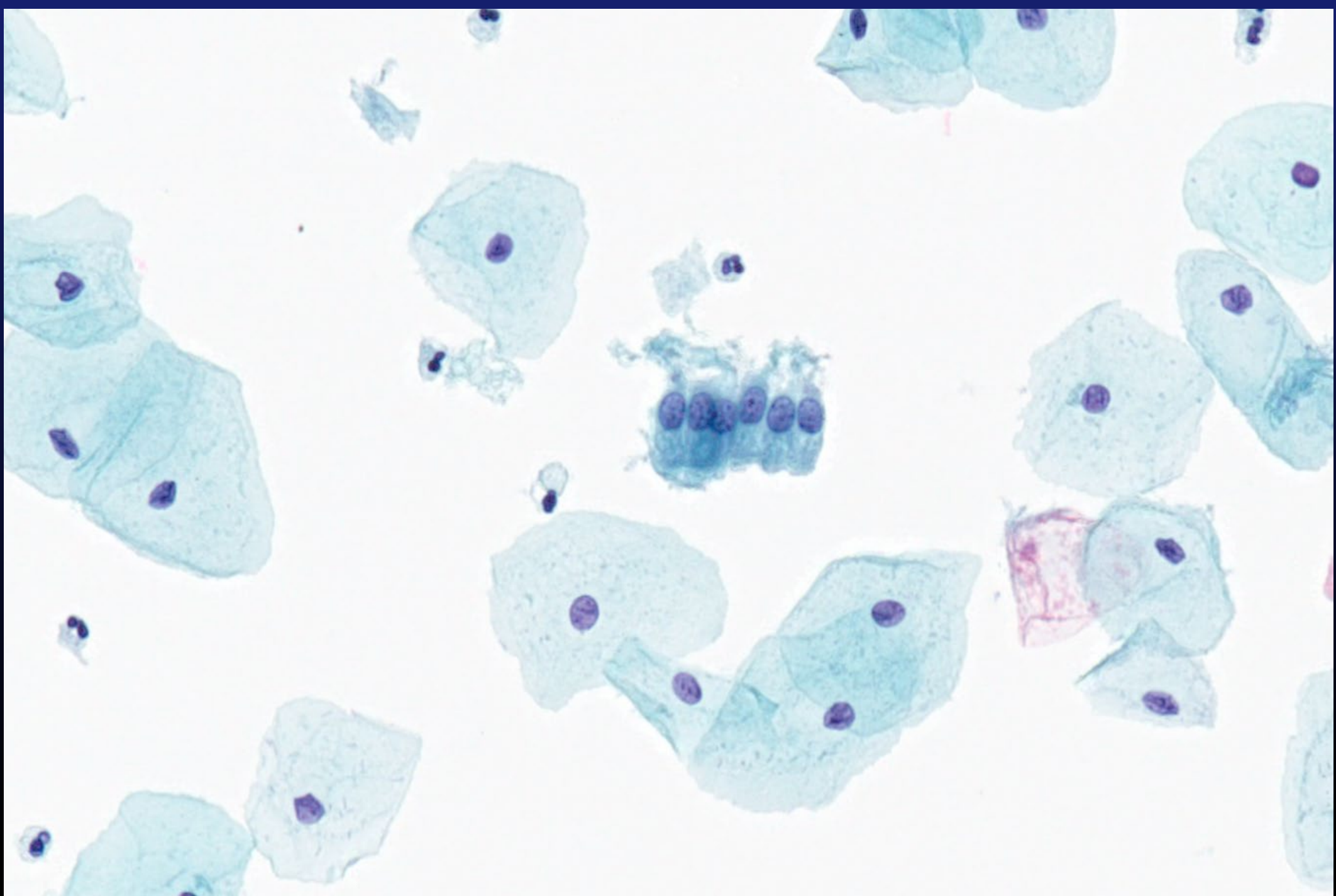
## Normal Morphology – Endocervical Cells

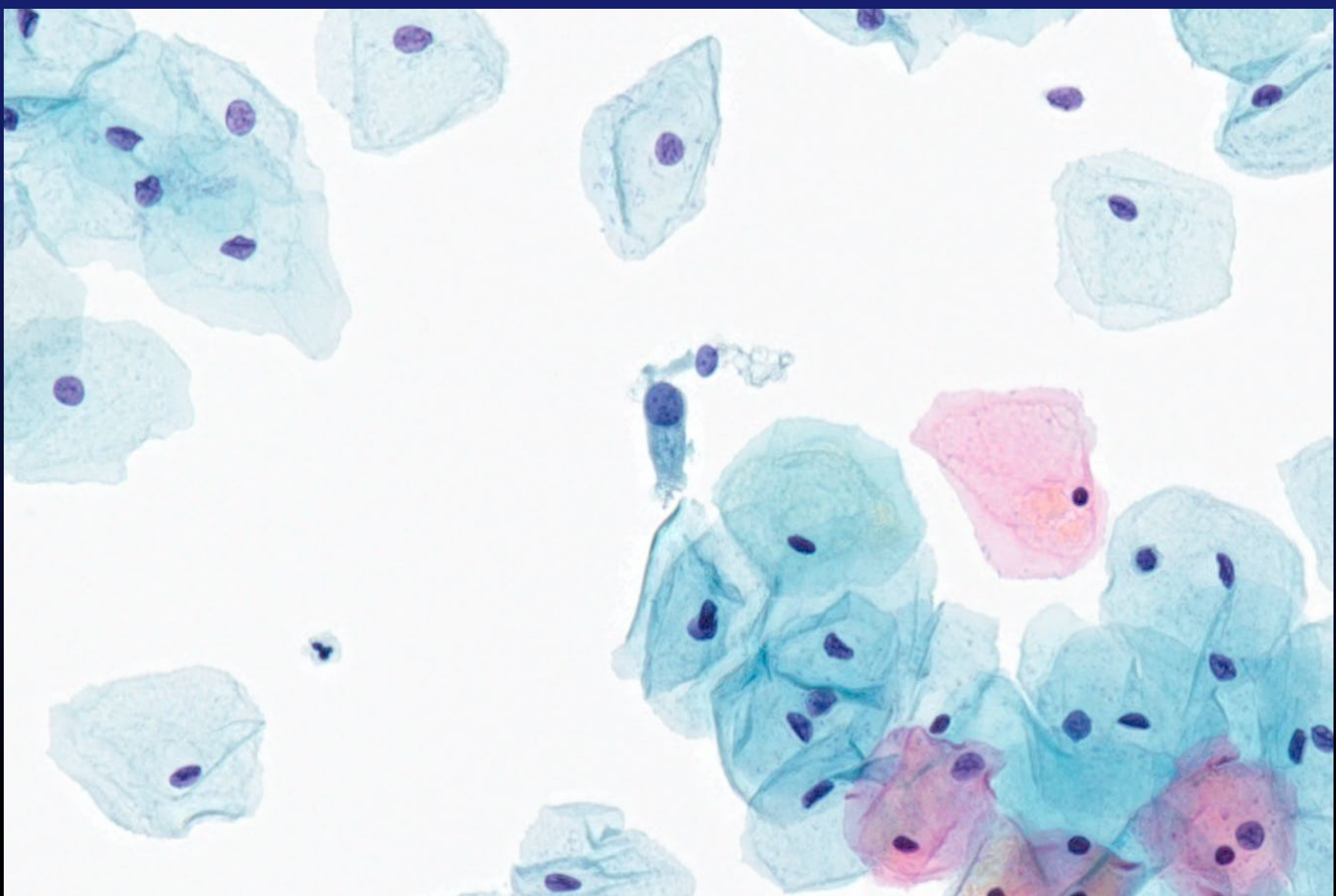
- Singly or in groups
- “Honeycomb” or “picket-fence” arrangements
- Nuclear size is highly variable
- Smooth nuclear membranes
- Finely granular and evenly distributed chromatin
- Cytoplasm is diffusely vacuolated or granular
- Small nucleoli may be present

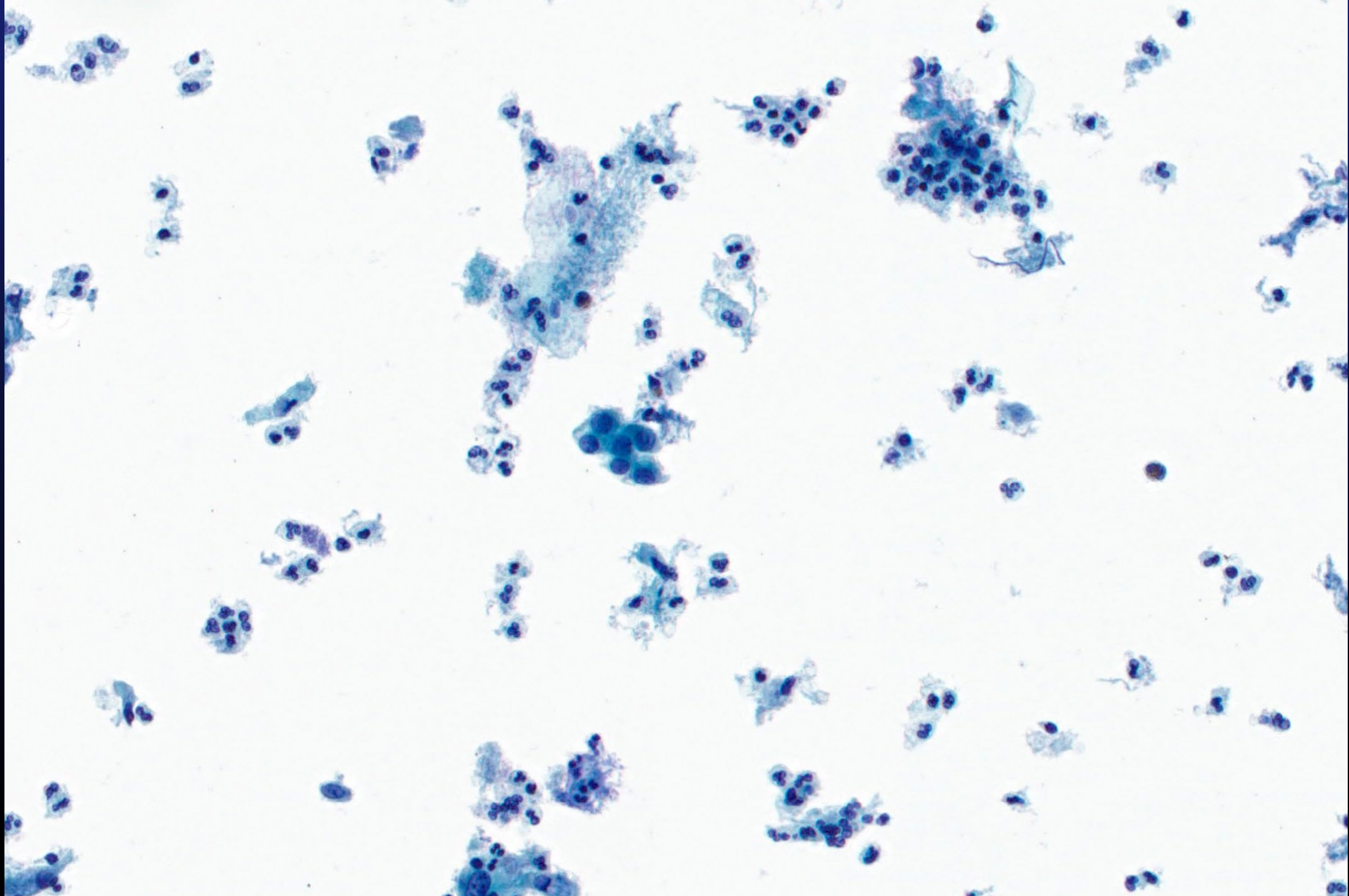


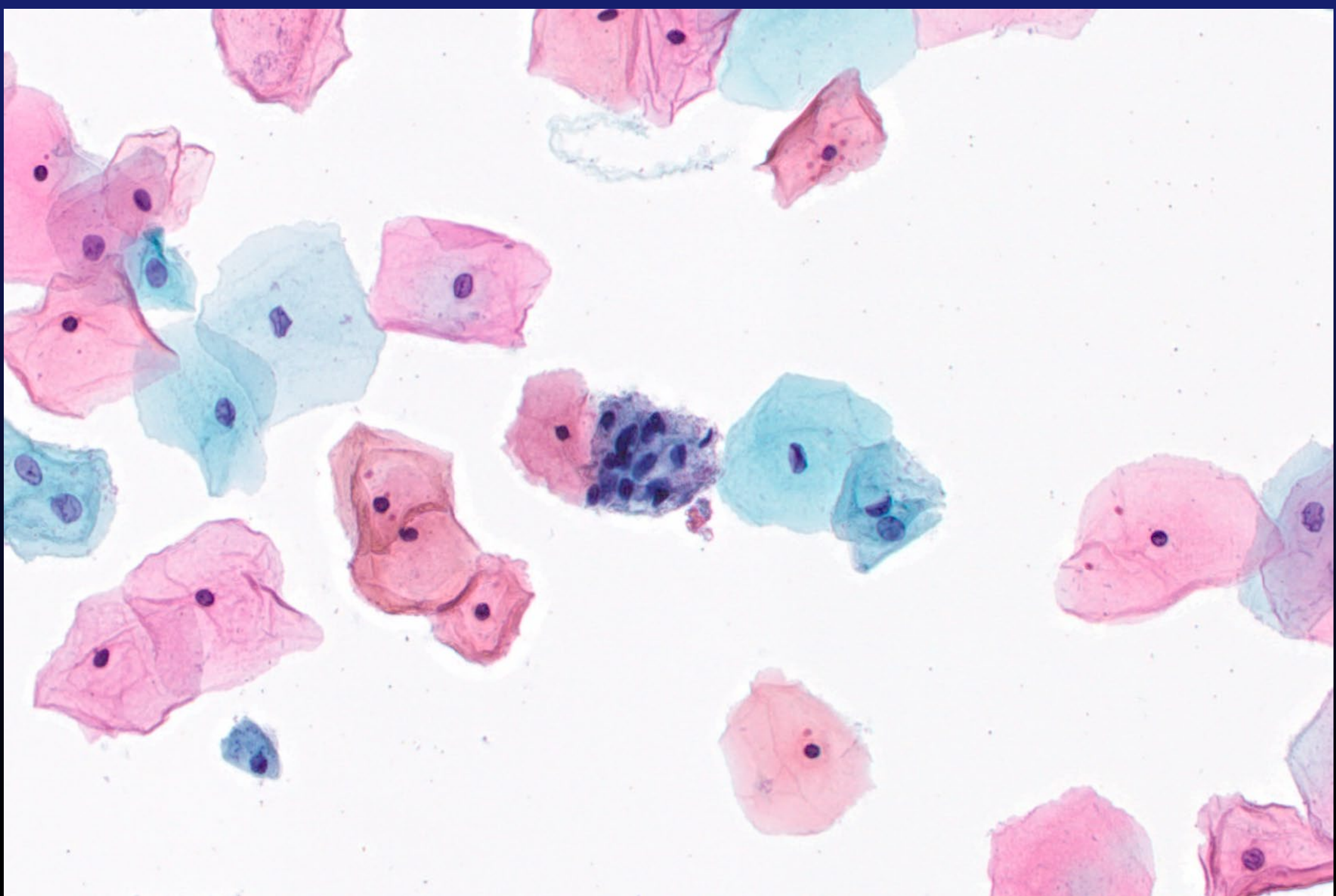








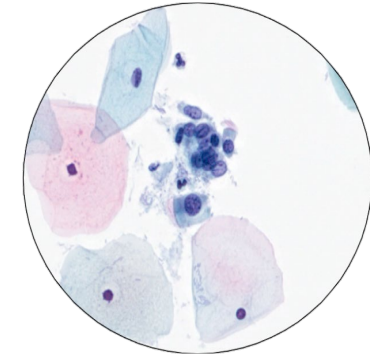


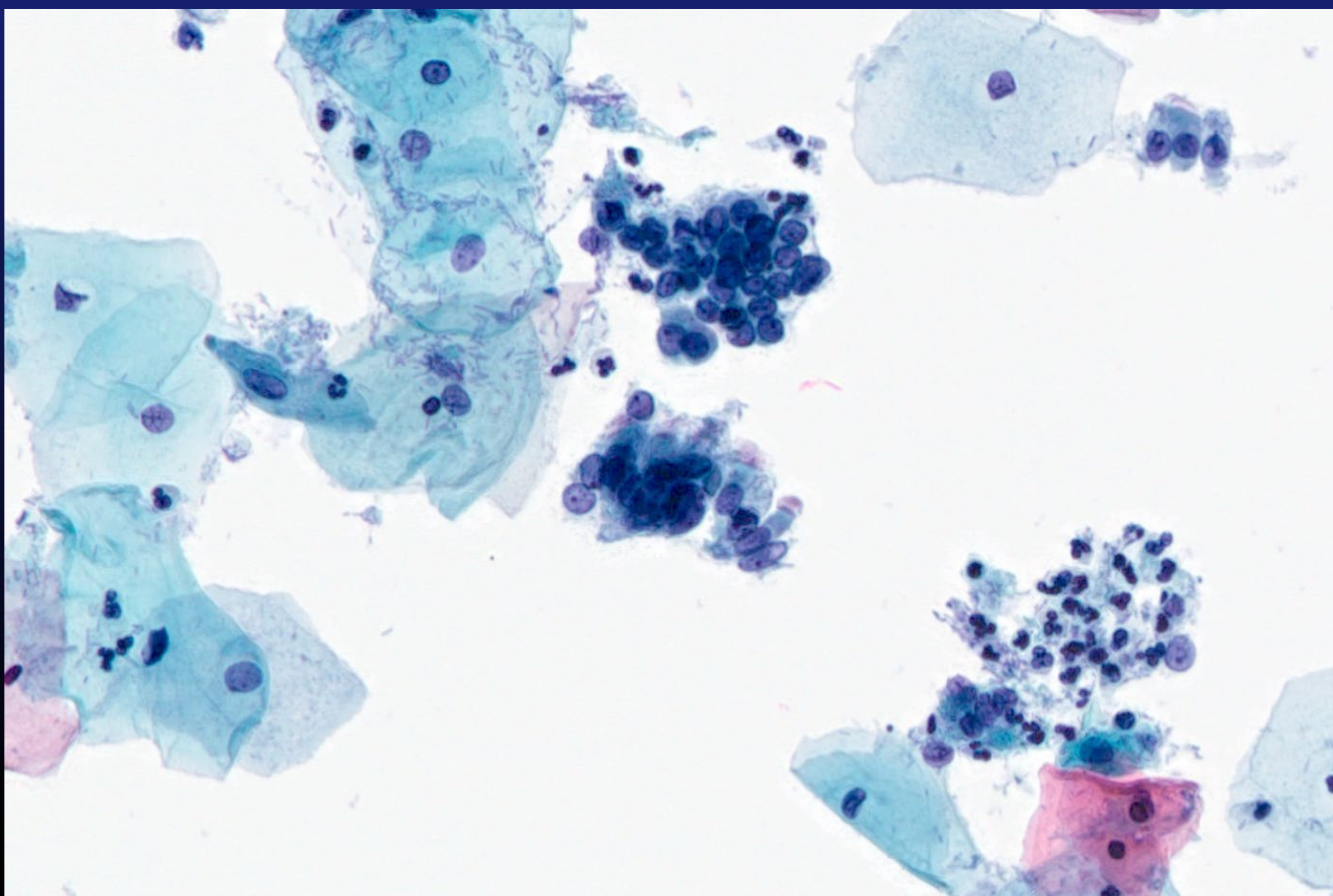


# The Bethesda System for Reporting Cervical Cytology

## Normal Morphology – Tubal Metaplasia

- Pseudostratified crowded groups with maintained polarity
- Terminal bars and cilia
- Nuclei are round to oval and may be enlarged, pleomorphic, and often hyperchromatic
- N/C ratio can be high
- Cytoplasm may show discrete vacuoles or goblet cell change
- Nucleoli are not usually seen

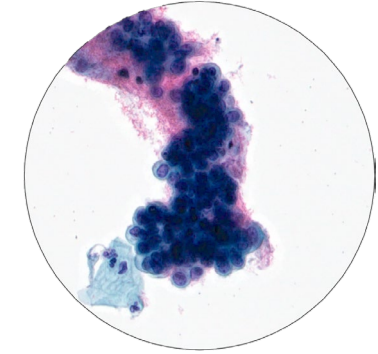


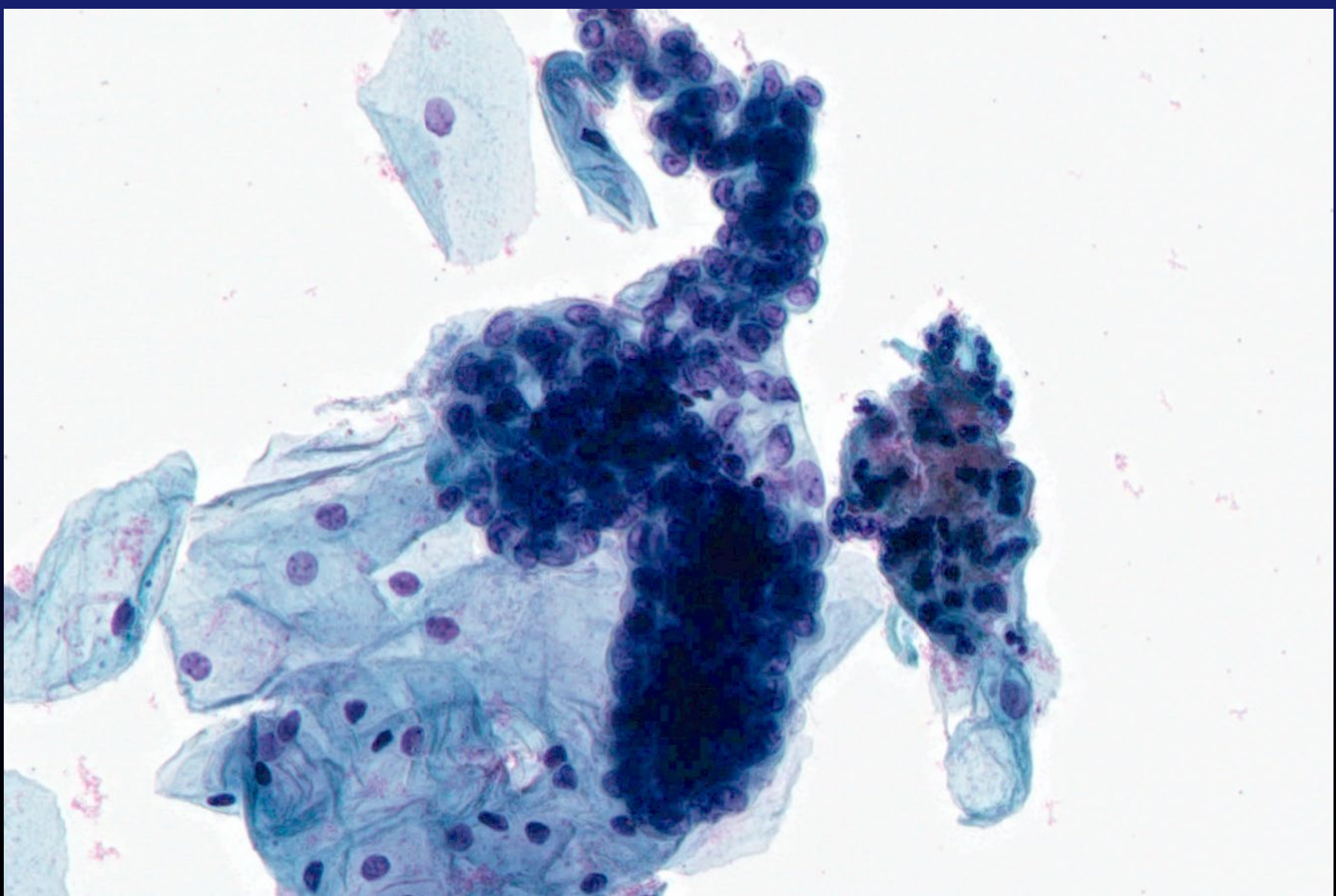


# The Bethesda System for Reporting Cervical Cytology

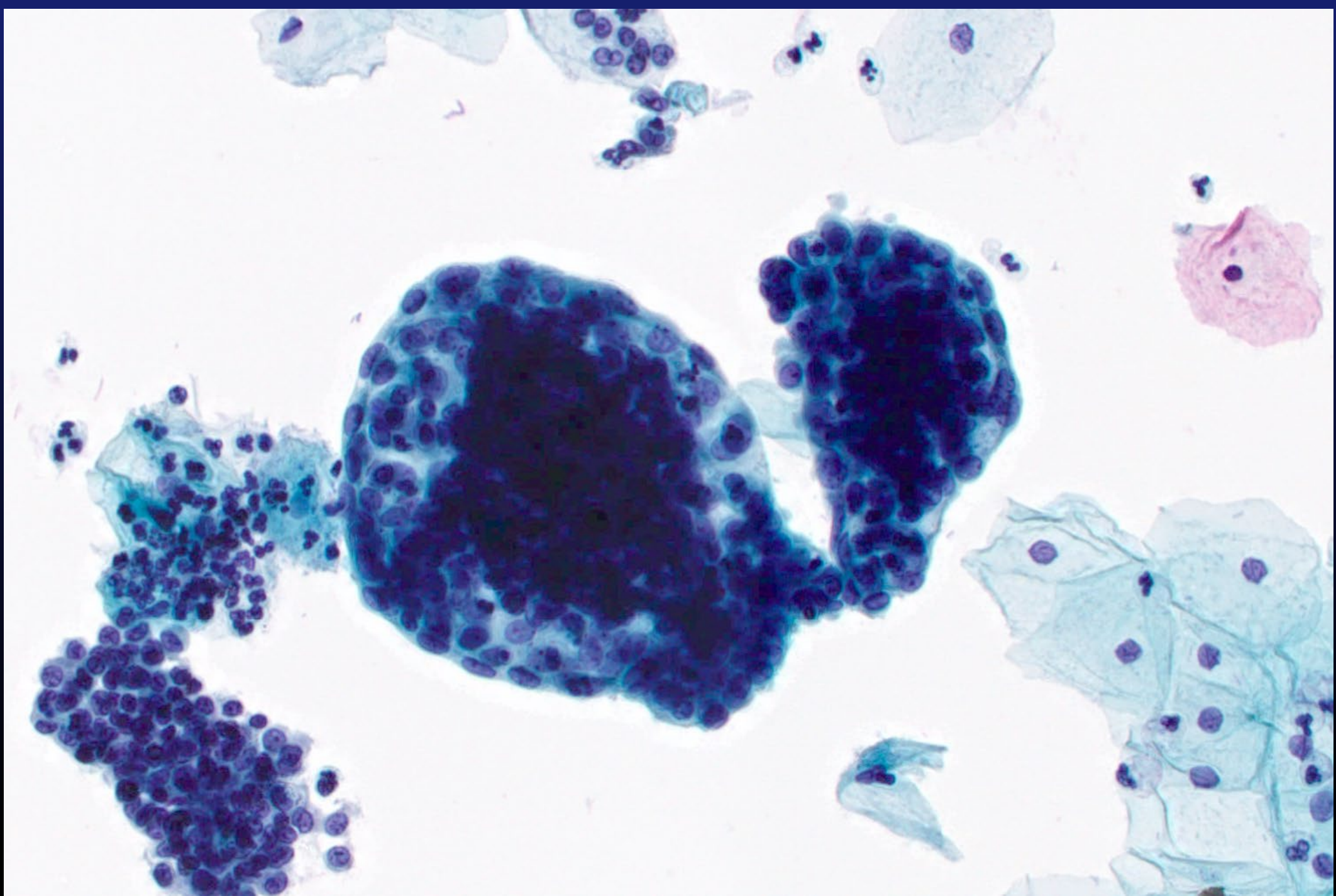
## Normal Morphology – Endometrial Cells

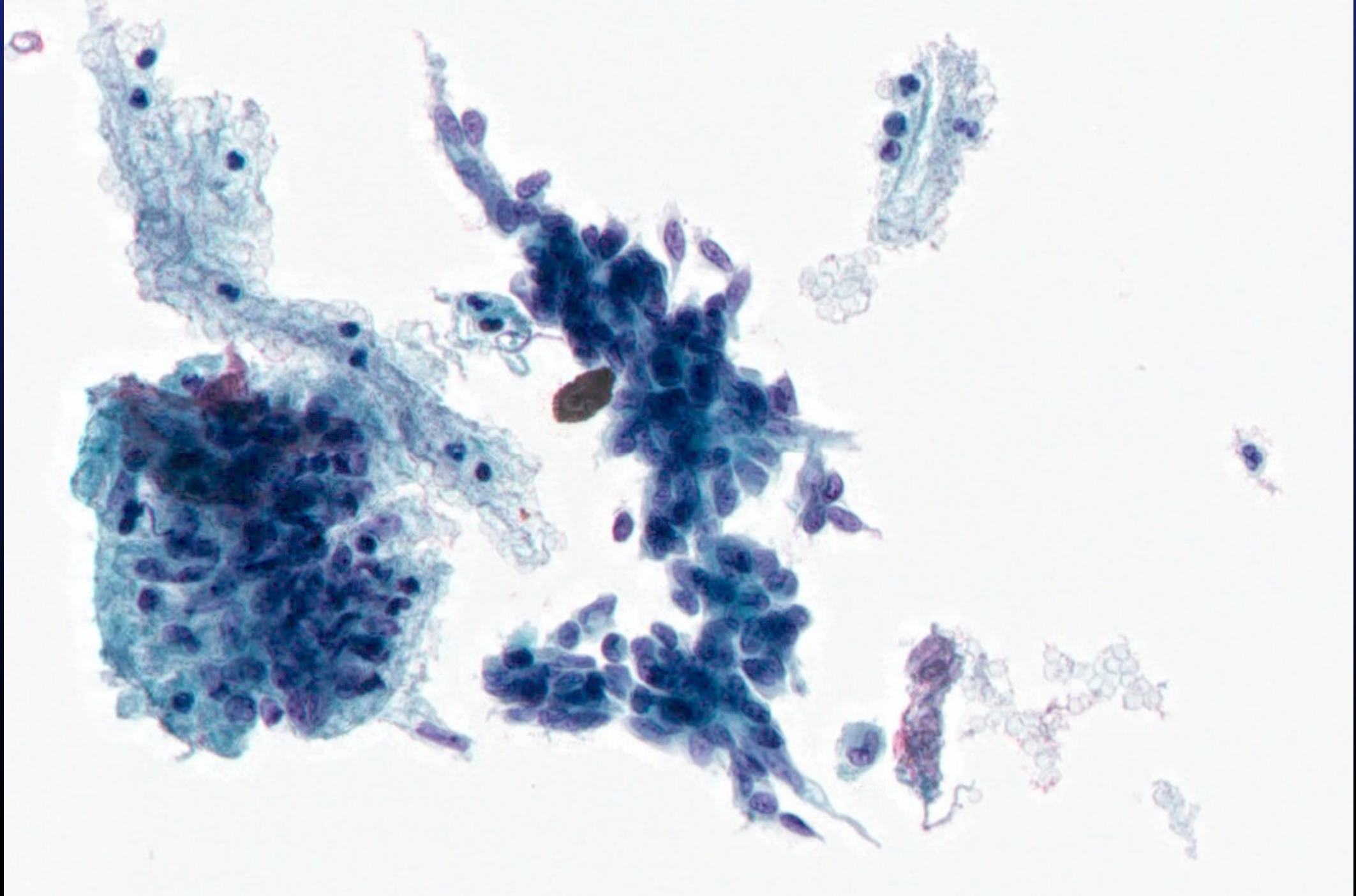
- Dense 3-dimensional groups, exodus ball, or loose aggregates
- Nuclei with dense, heterogenous chromatin
- Nuclear size slightly smaller than benign intermediate cell nucleus ( $\sim 35 \mu\text{m}^2$  )
- Nuclear membranes may be irregular
- Cytoplasm is scant, dense, or vacuolated

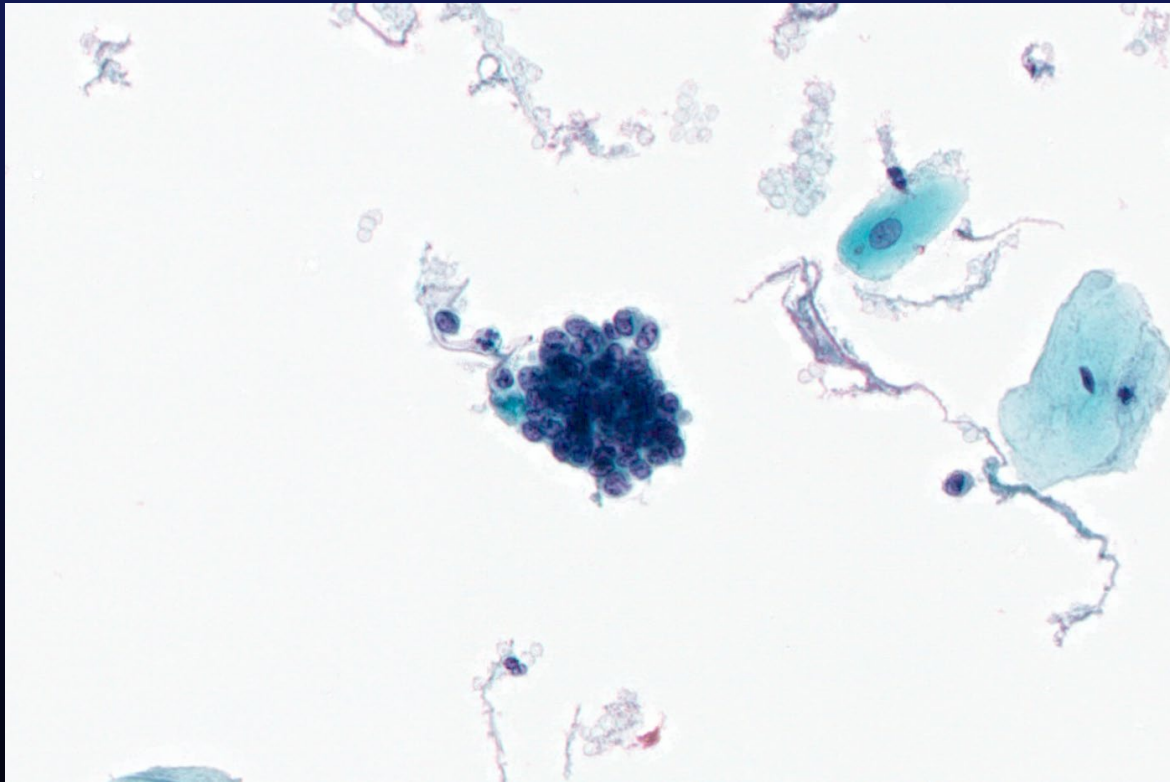




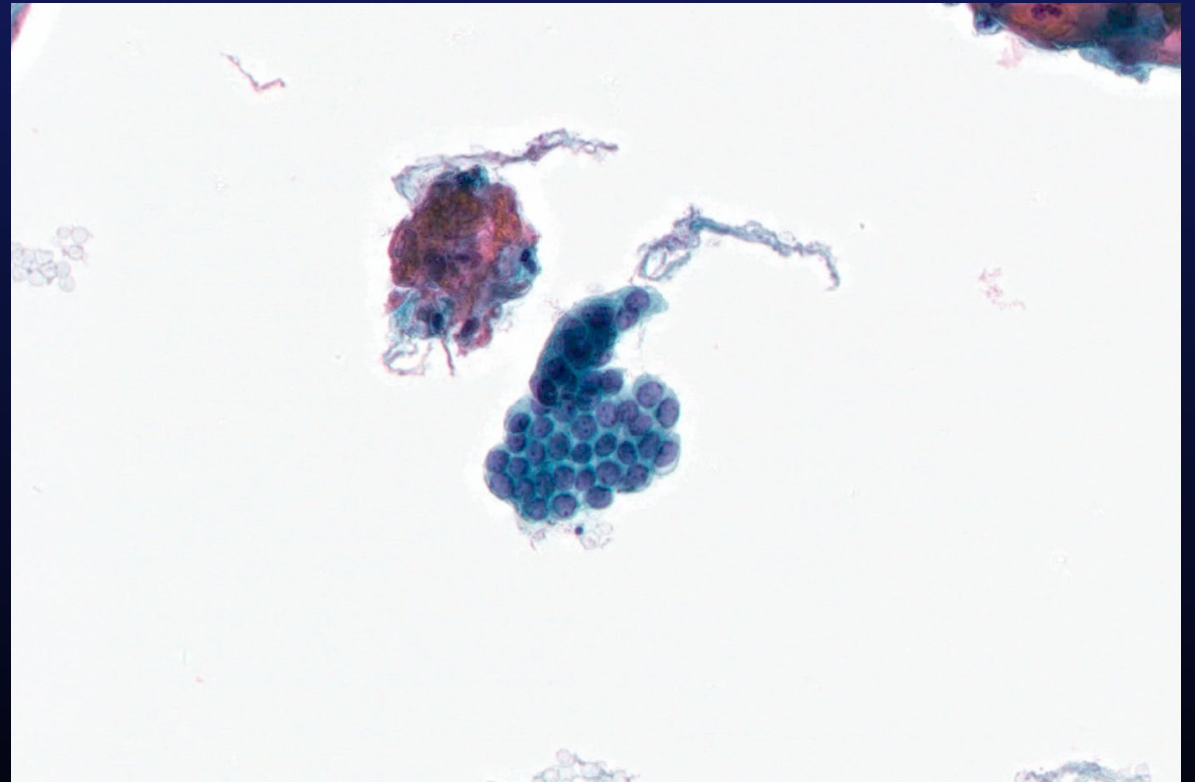








Endometrial Cells

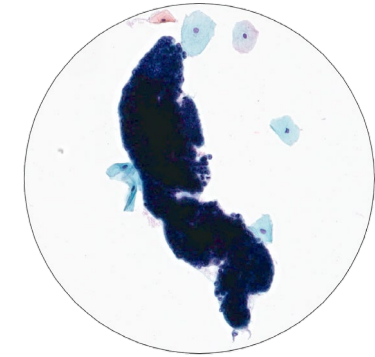


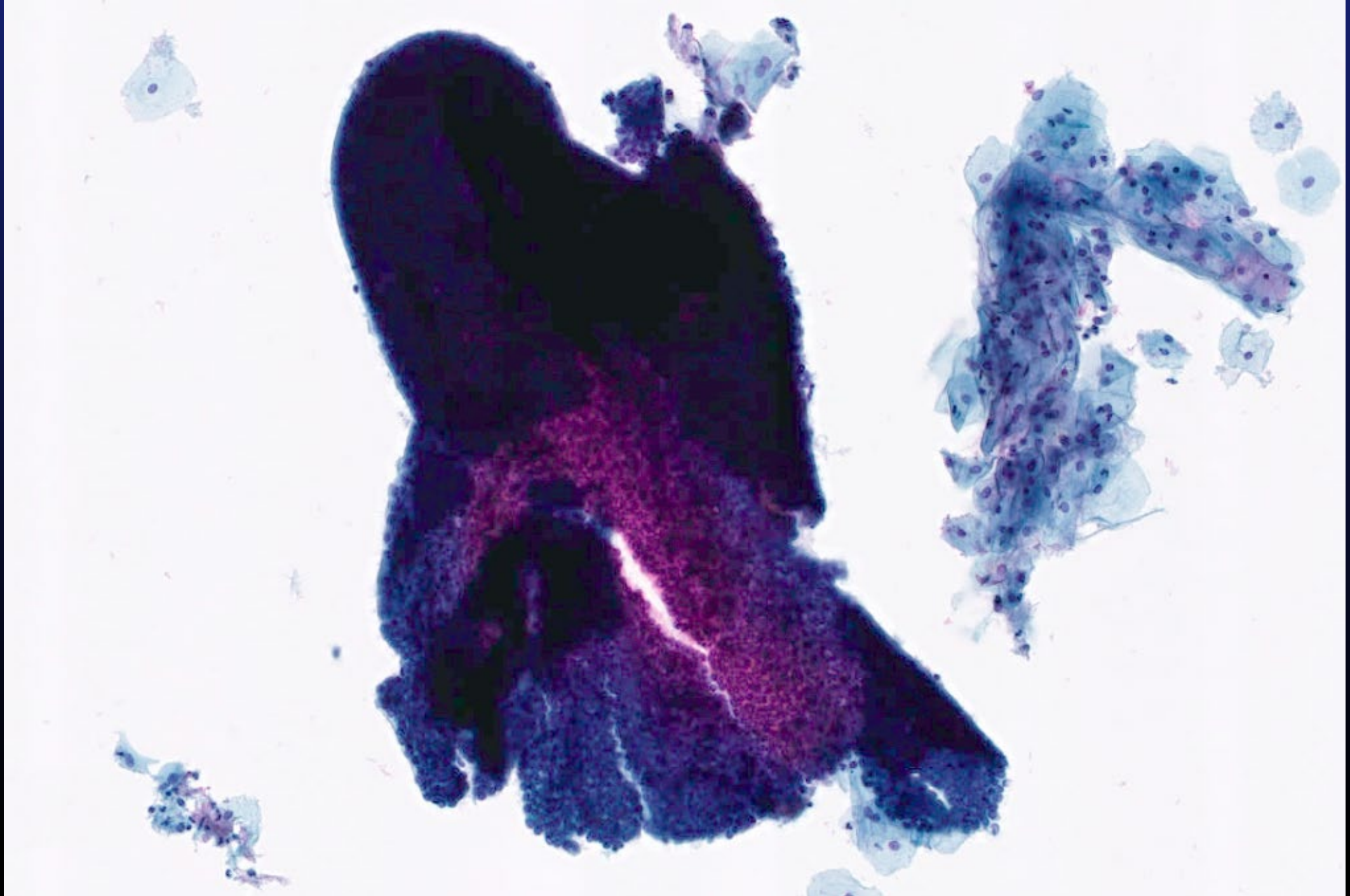
Cuboidal Endocervical Cells

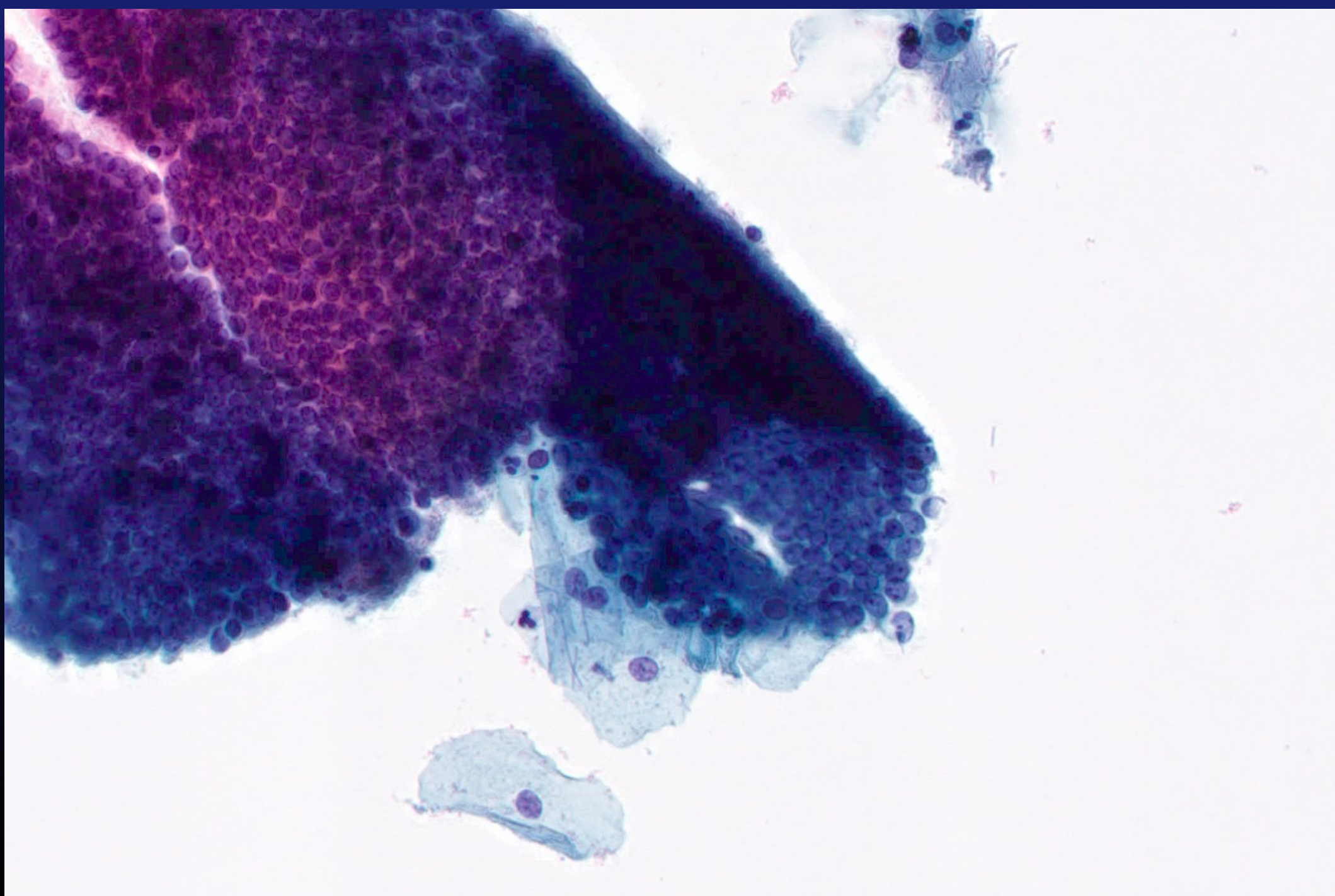
# The Bethesda System for Reporting Cervical Cytology

## Normal Morphology – Lower Uterine Segment (LUS)

- Columnar in shape and may present in tubular formation
- Nuclear crowding and overlapping with polarity maintained
- Nuclei are small, round to oval, and variably hyperchromatic
- Smooth nuclear membrane
- Moderately coarse, evenly distributed chromatin
- Scant, spindled cytoplasm
- Inconspicuous nucleoli may be present



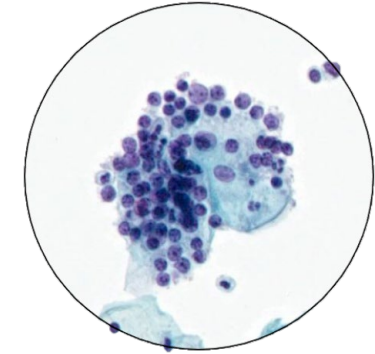


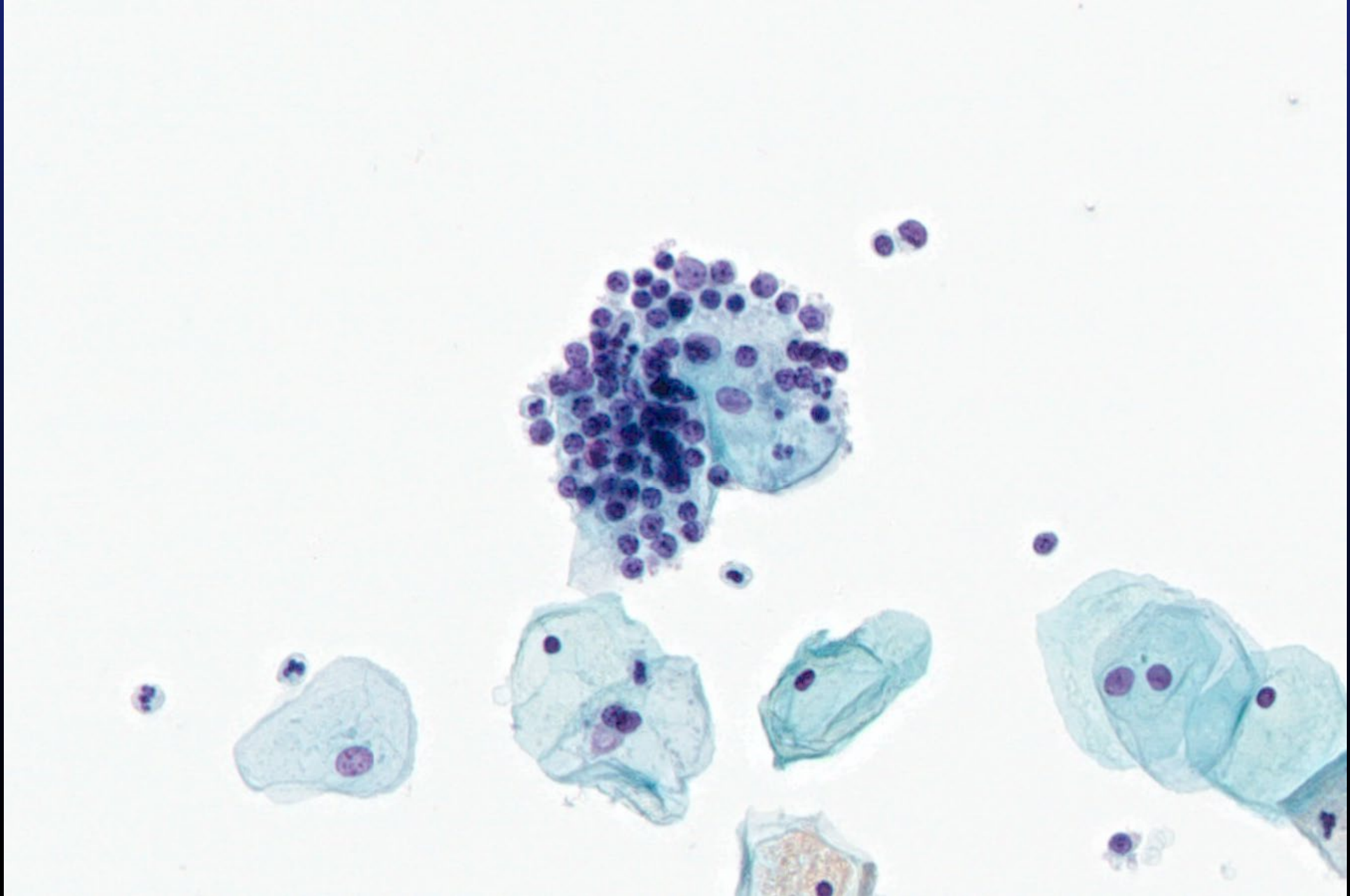


# The Bethesda System for Reporting Cervical Cytology

## Normal Morphology – Lymphocytic (Follicular) Cervicitis

- Polymorphous population of lymphocytes
- Loose aggregates or scattered single cells in the background
- Tingible body macrophages may be present



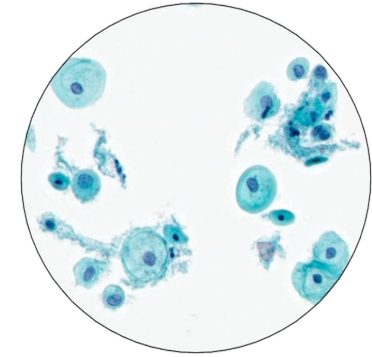


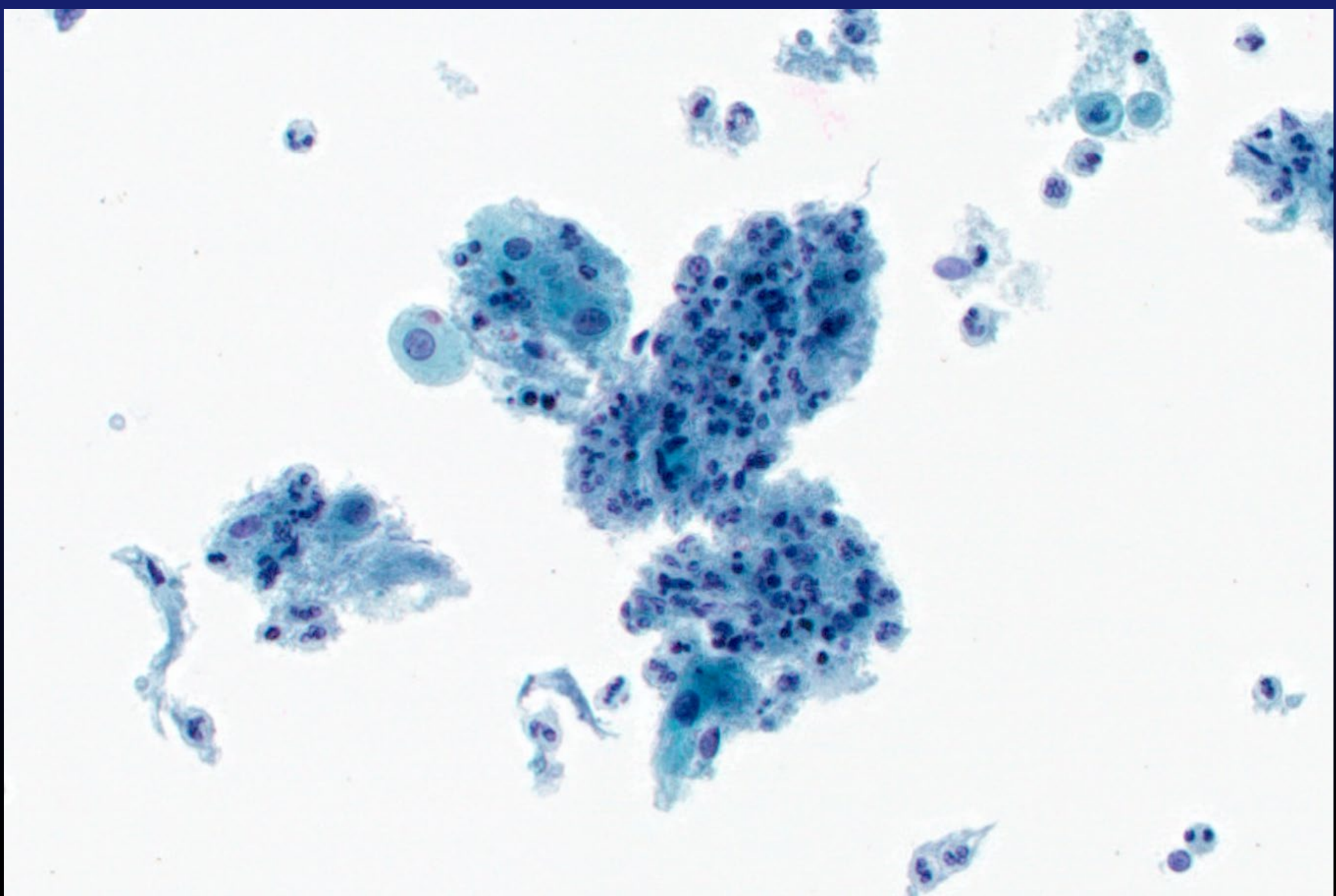


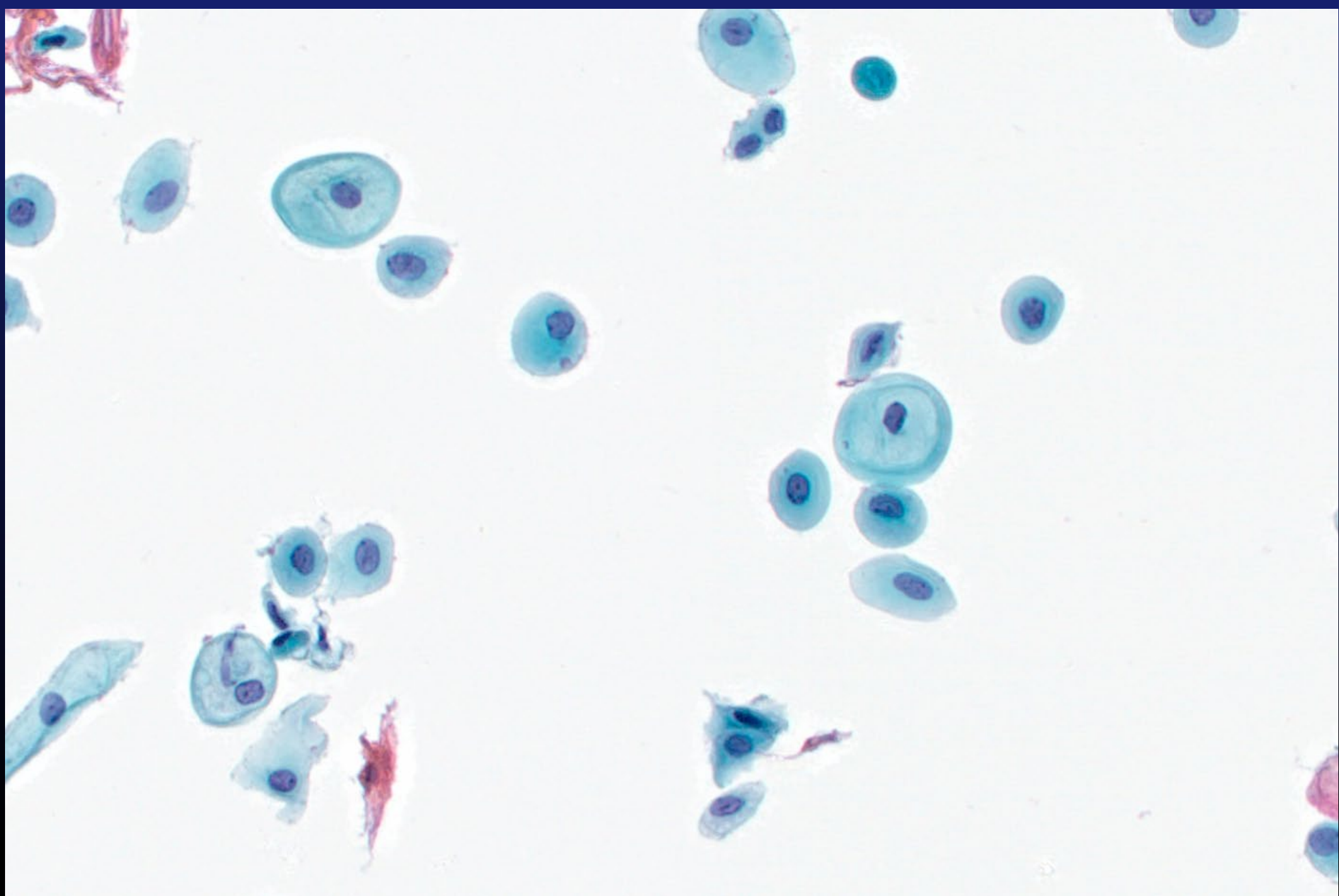
# The Bethesda System for Reporting Cervical Cytology

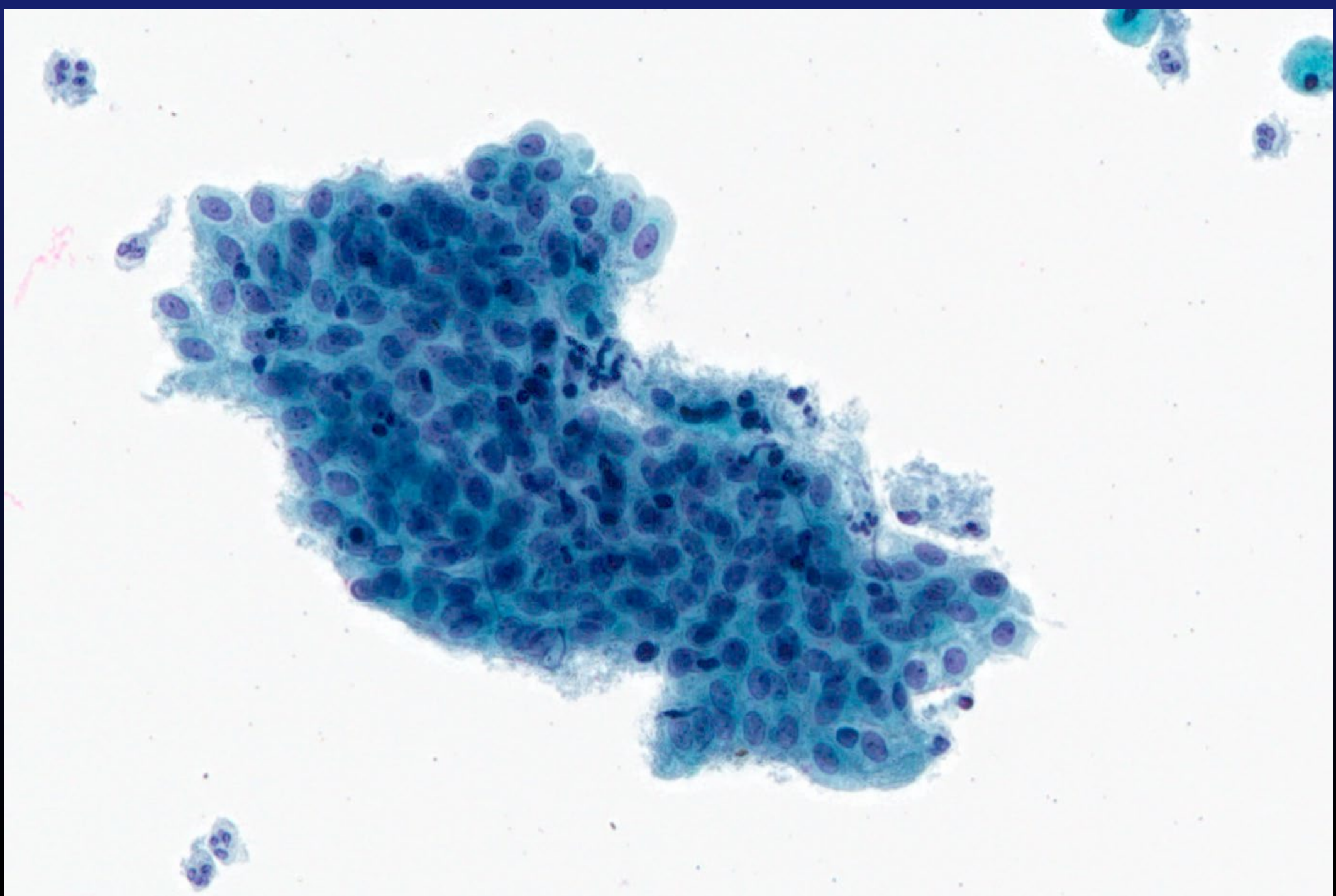
## Normal Morphology – Parabasal Cells (Atrophy)

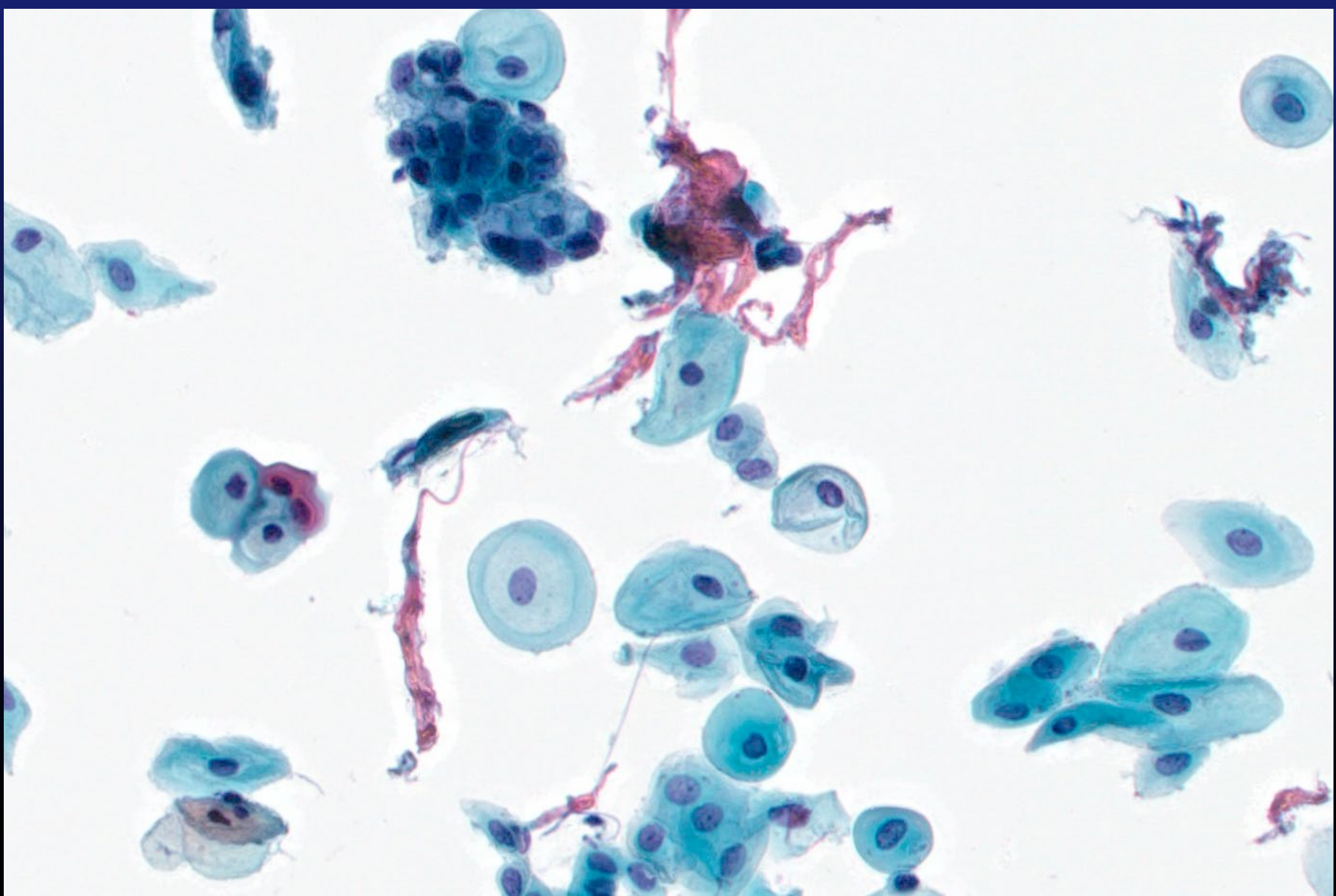
- Single cells and/or flat monolayer sheets with preserved nuclear polarity
- Oval nuclei with finely granular evenly distributed chromatin
- Smooth nuclear membranes
- Nuclear size approximately  $50 \mu\text{m}^2$
- N/C ratio increased compared to intermediate/superficial cells
- Cytoplasm is more granular and dense
- Naked nuclei may be present







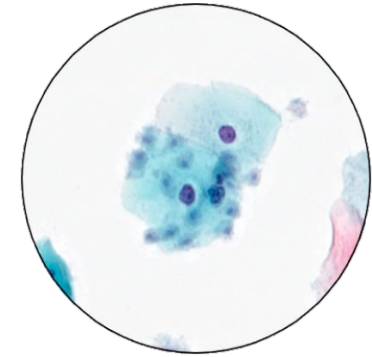


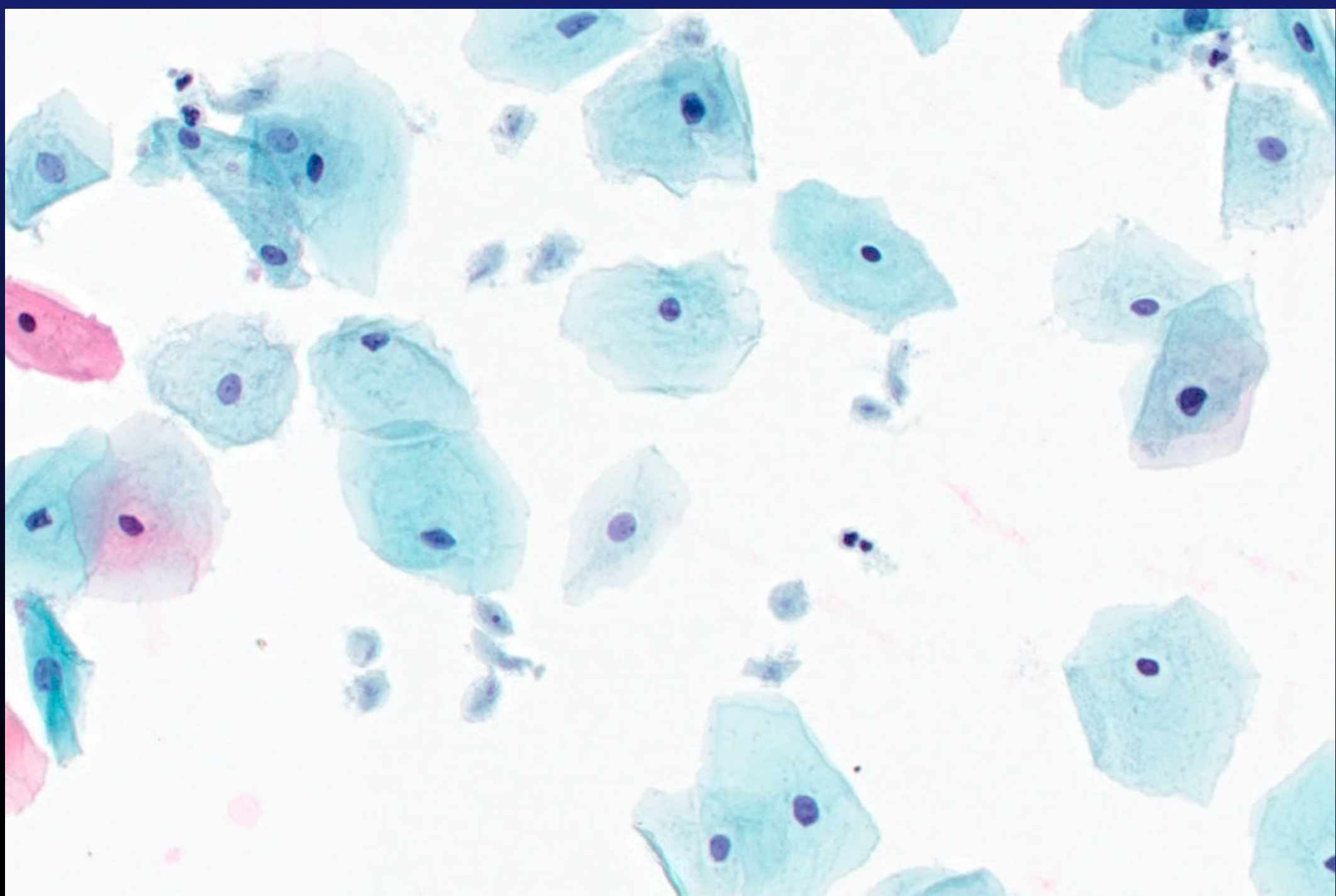


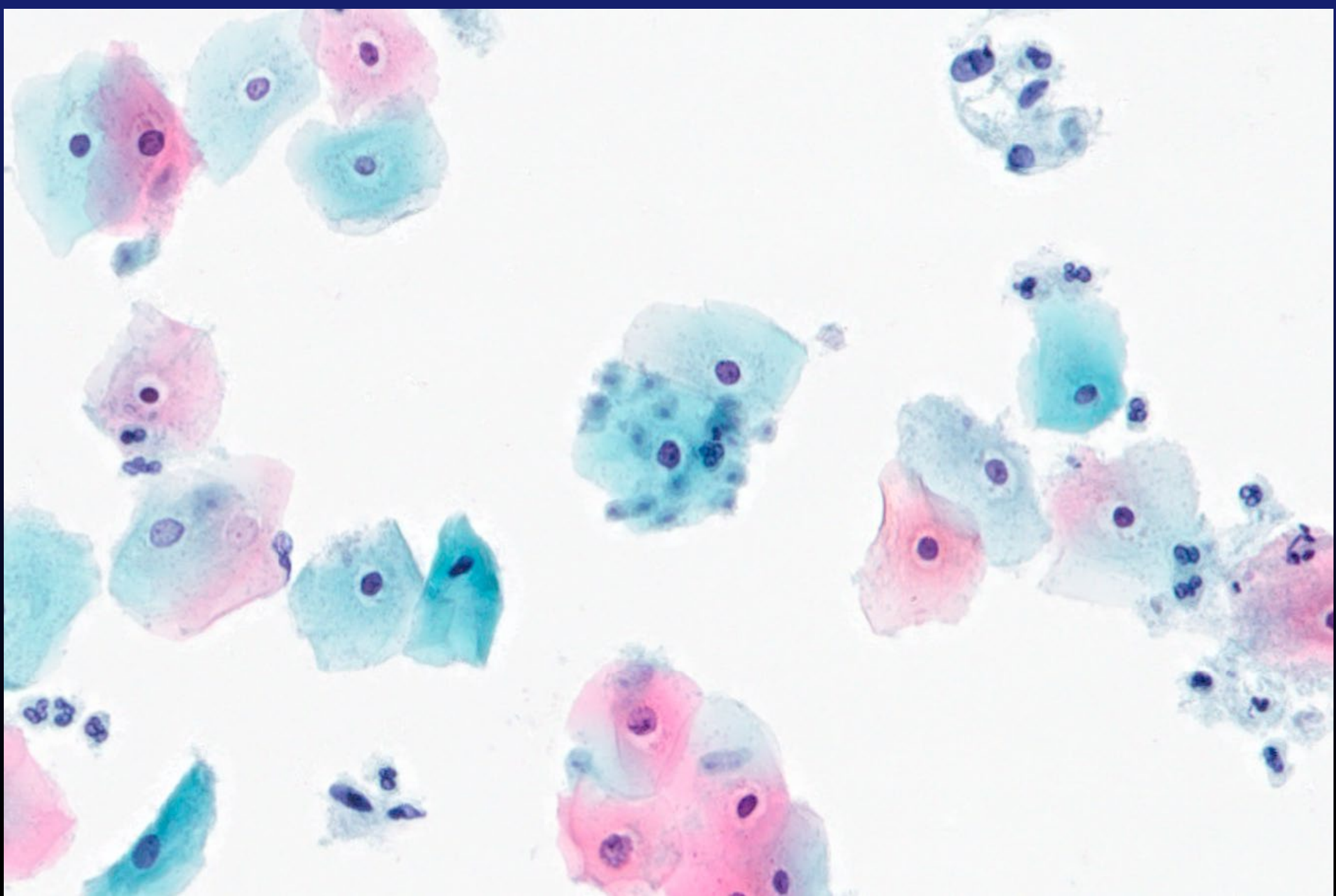
# The Bethesda System for Reporting Cervical Cytology

## Normal Morphology – Trichomonas

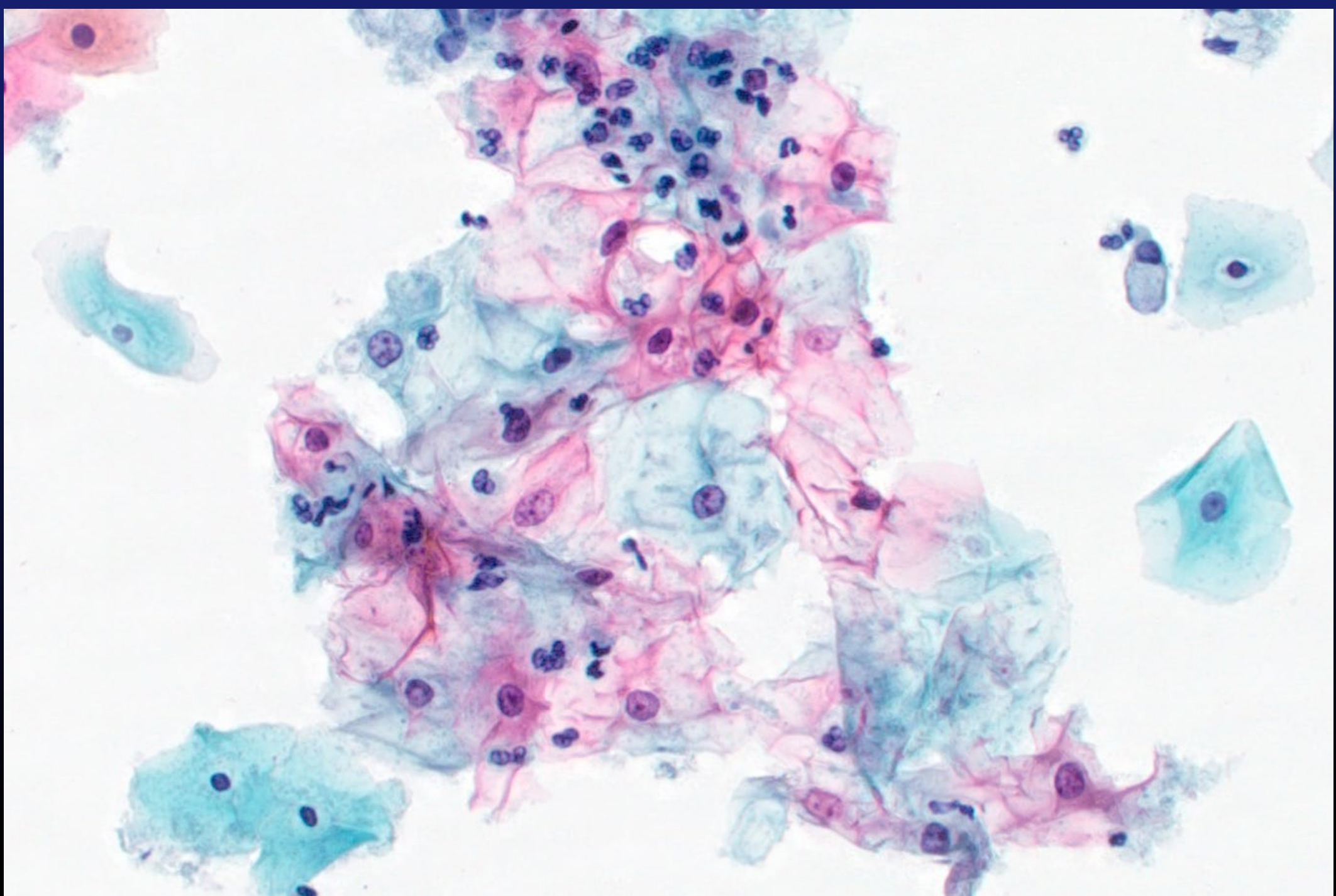
- Pear-shaped, oval and/or round organisms from 15 to 30  $\mu\text{m}^2$
- Eccentrically located pale, vesicular nuclei
- Eosinophilic cytoplasmic granules
- Squamous cells with perinuclear halos

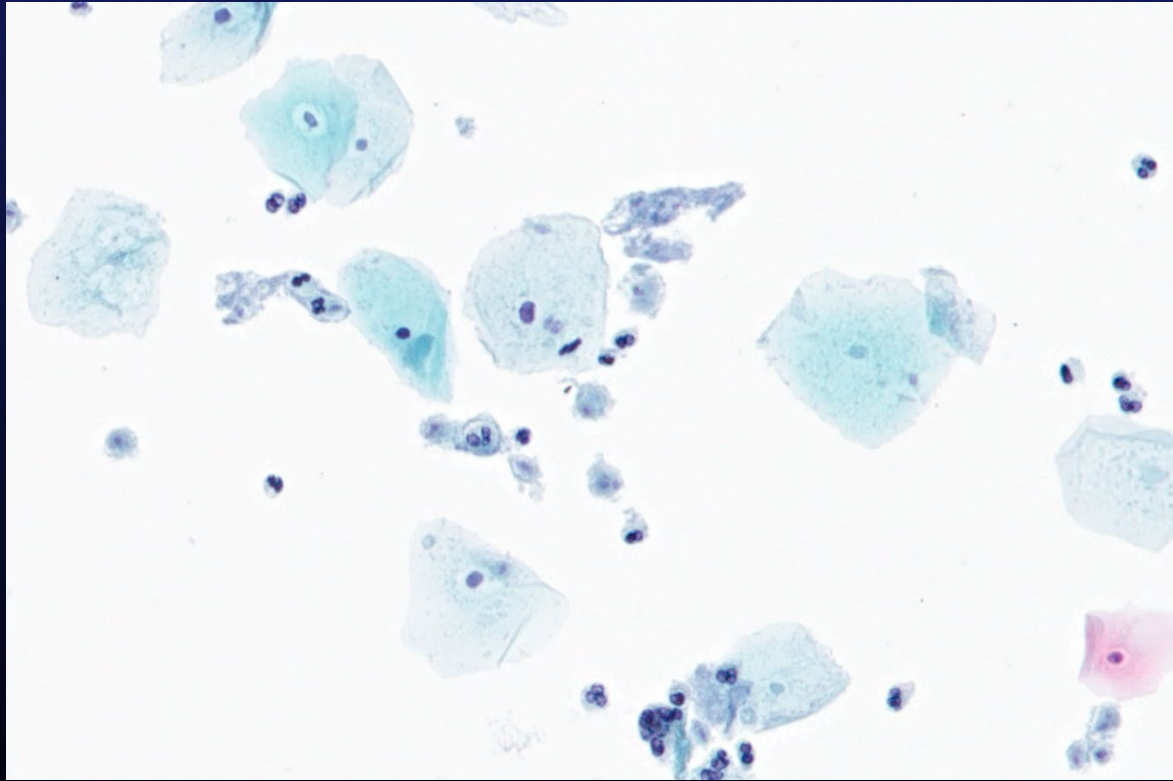




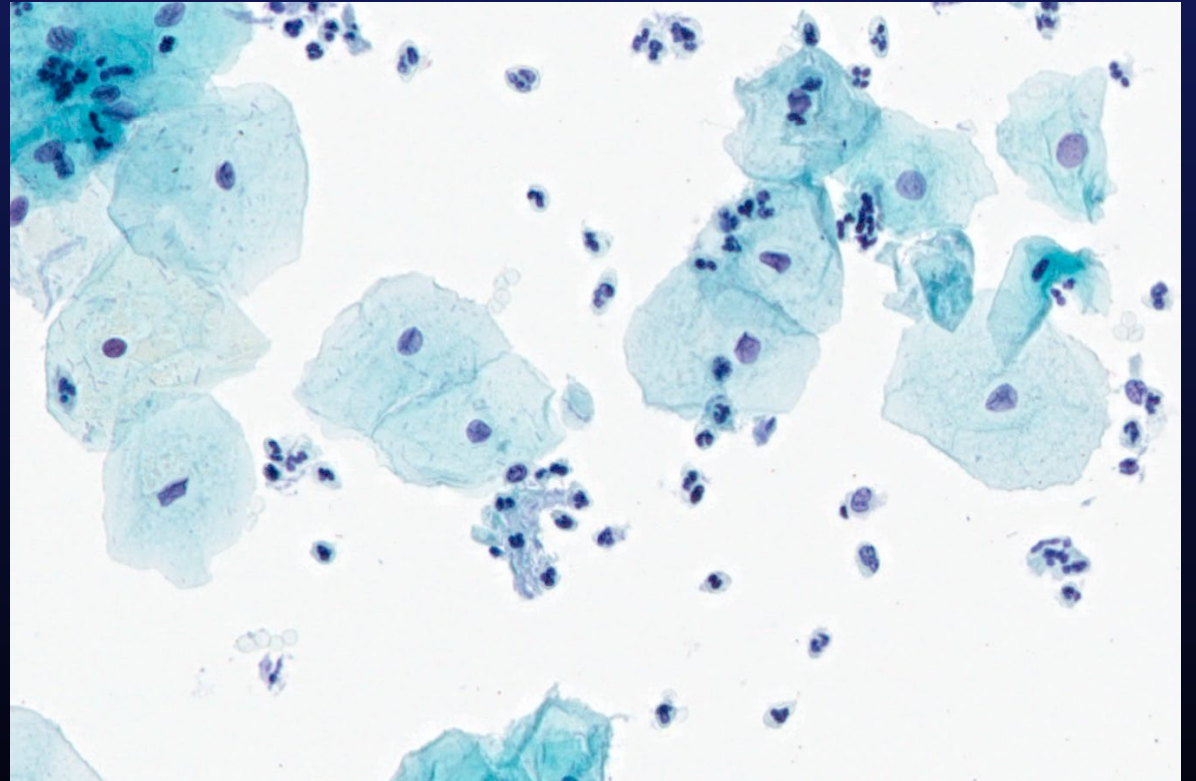








Trichomonas

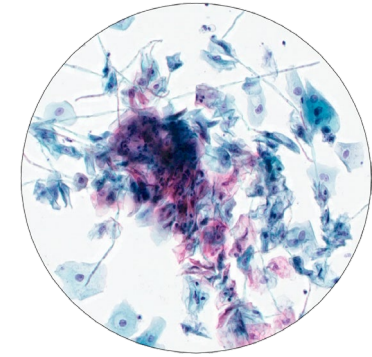


Cytoplasmic Blob

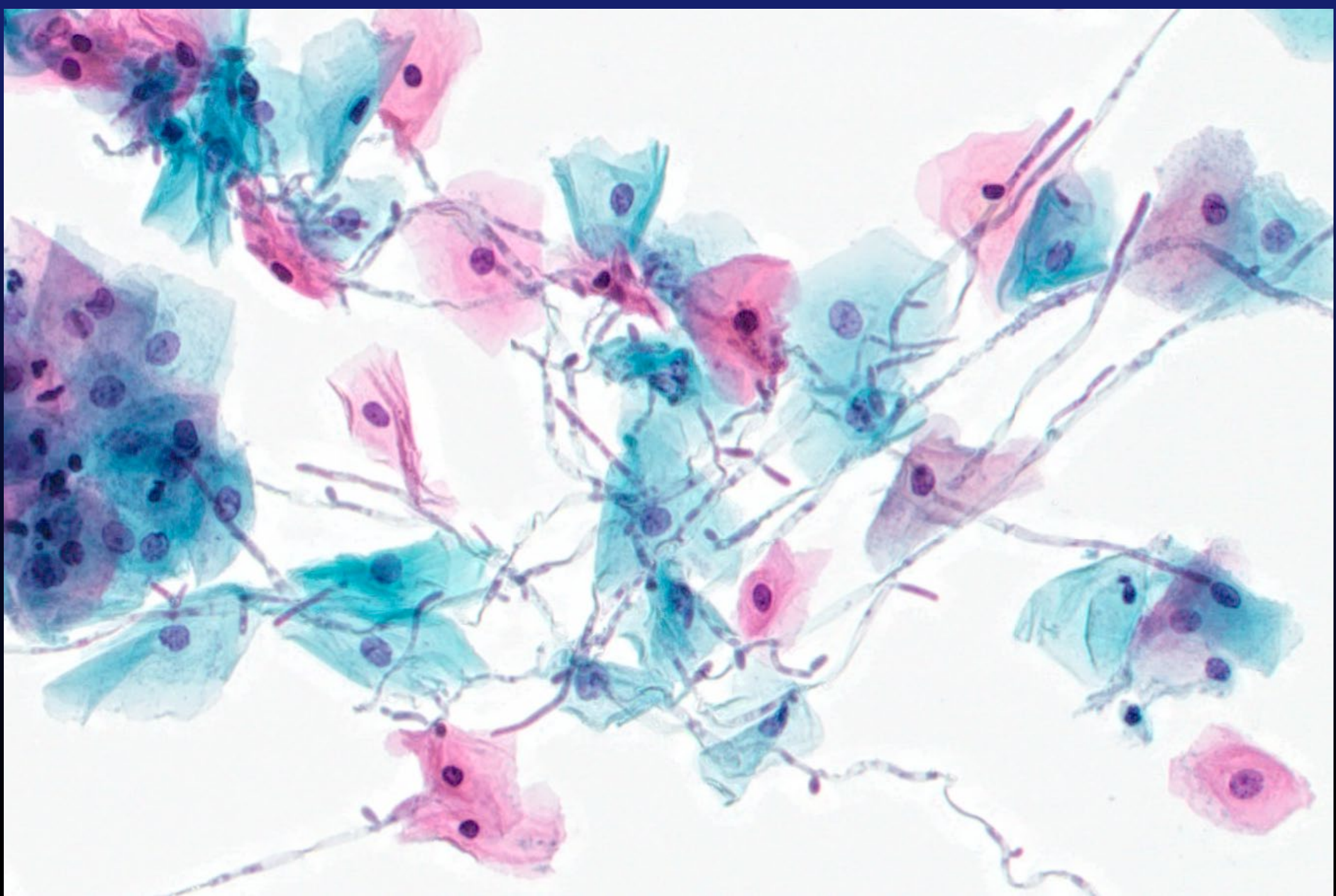
# The Bethesda System for Reporting Cervical Cytology

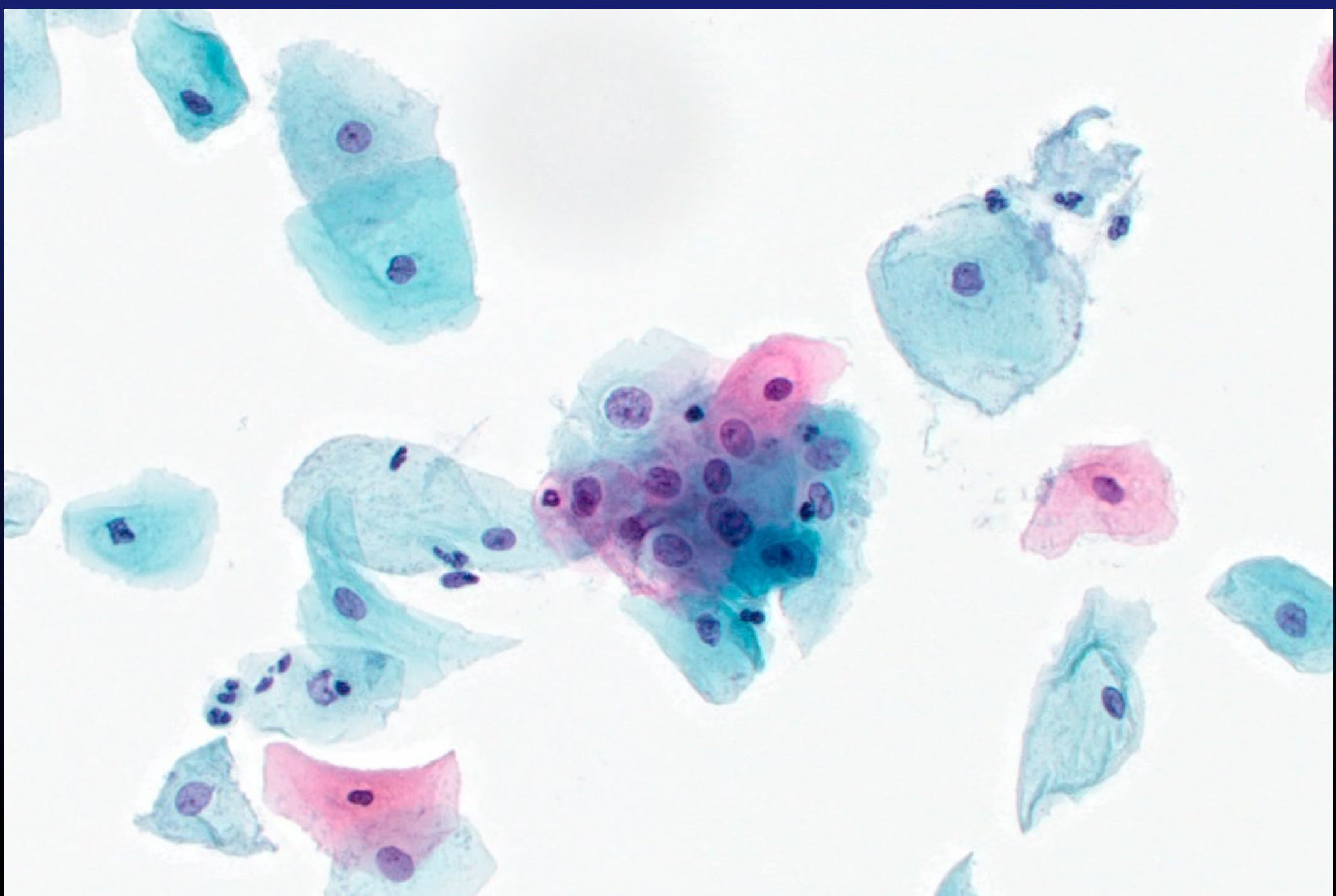
## Normal Morphology – Candida

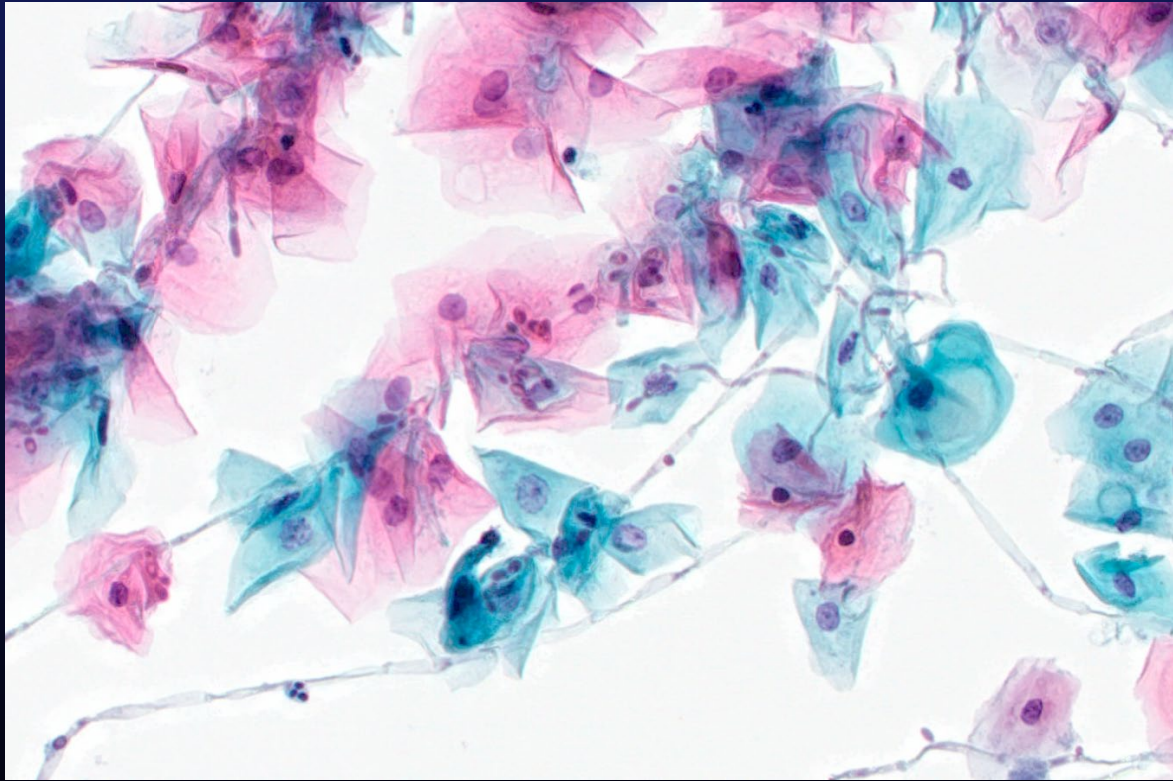
- Pseudohyphae of various lengths
- Budding yeast (3-7  $\mu\text{m}^2$ )
- “Spearing” of epithelial cells, often seen on low power
- Reactive squamous cells with mild nuclear enlargement may be seen



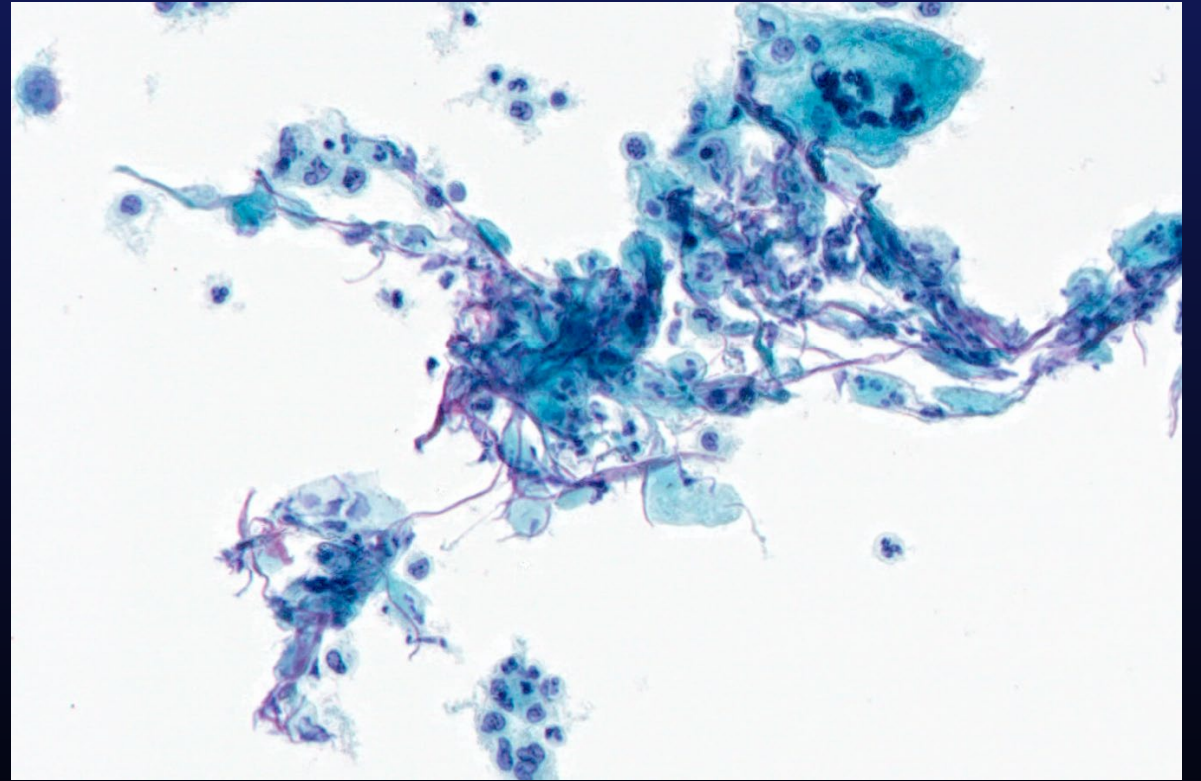








Candida Hyphae

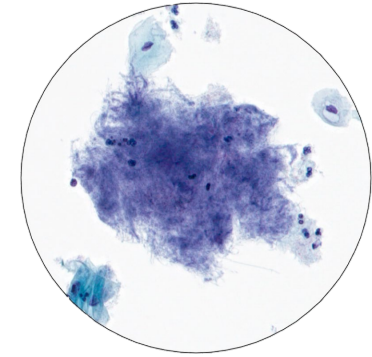


Mucous Strands

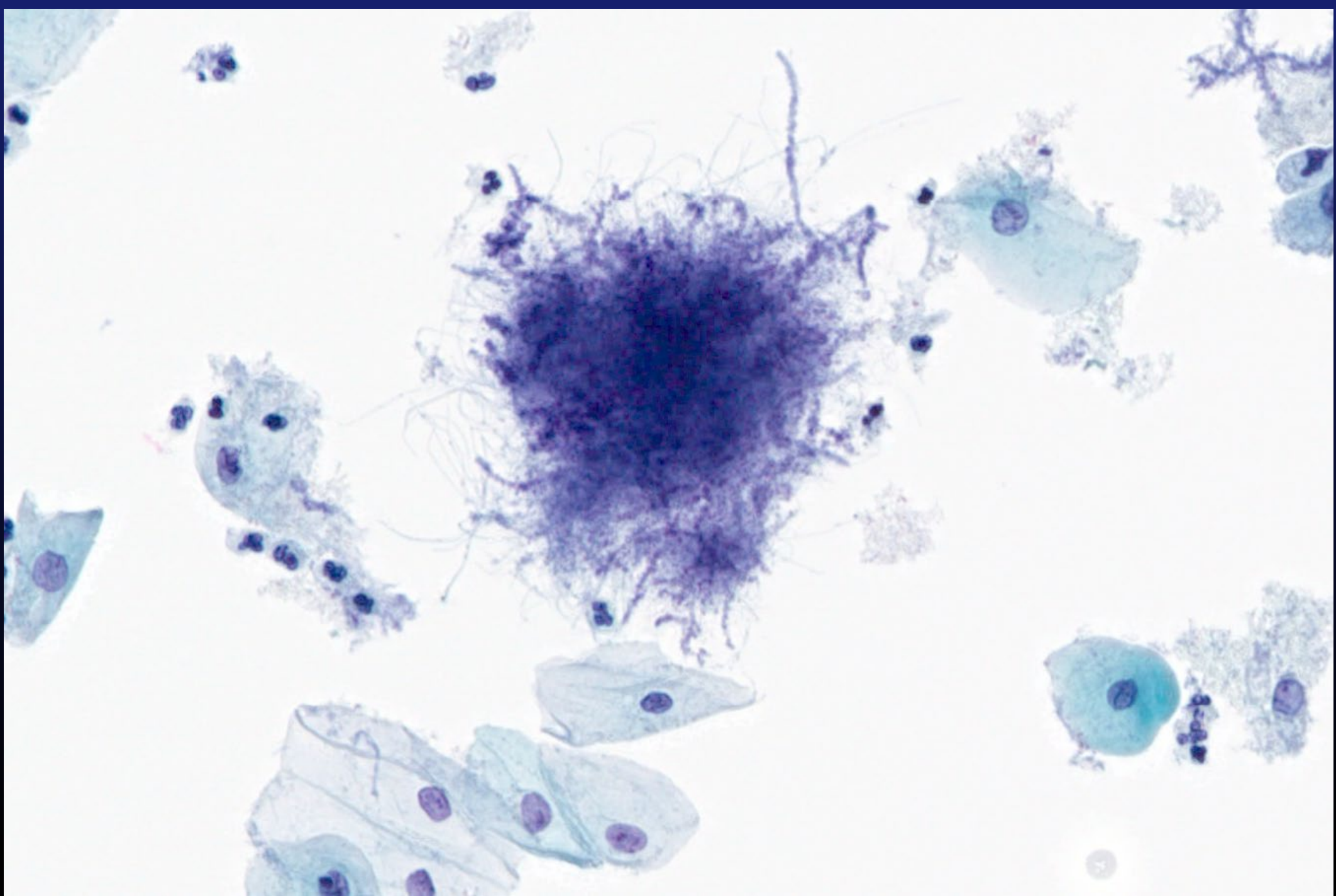
# The Bethesda System for Reporting Cervical Cytology

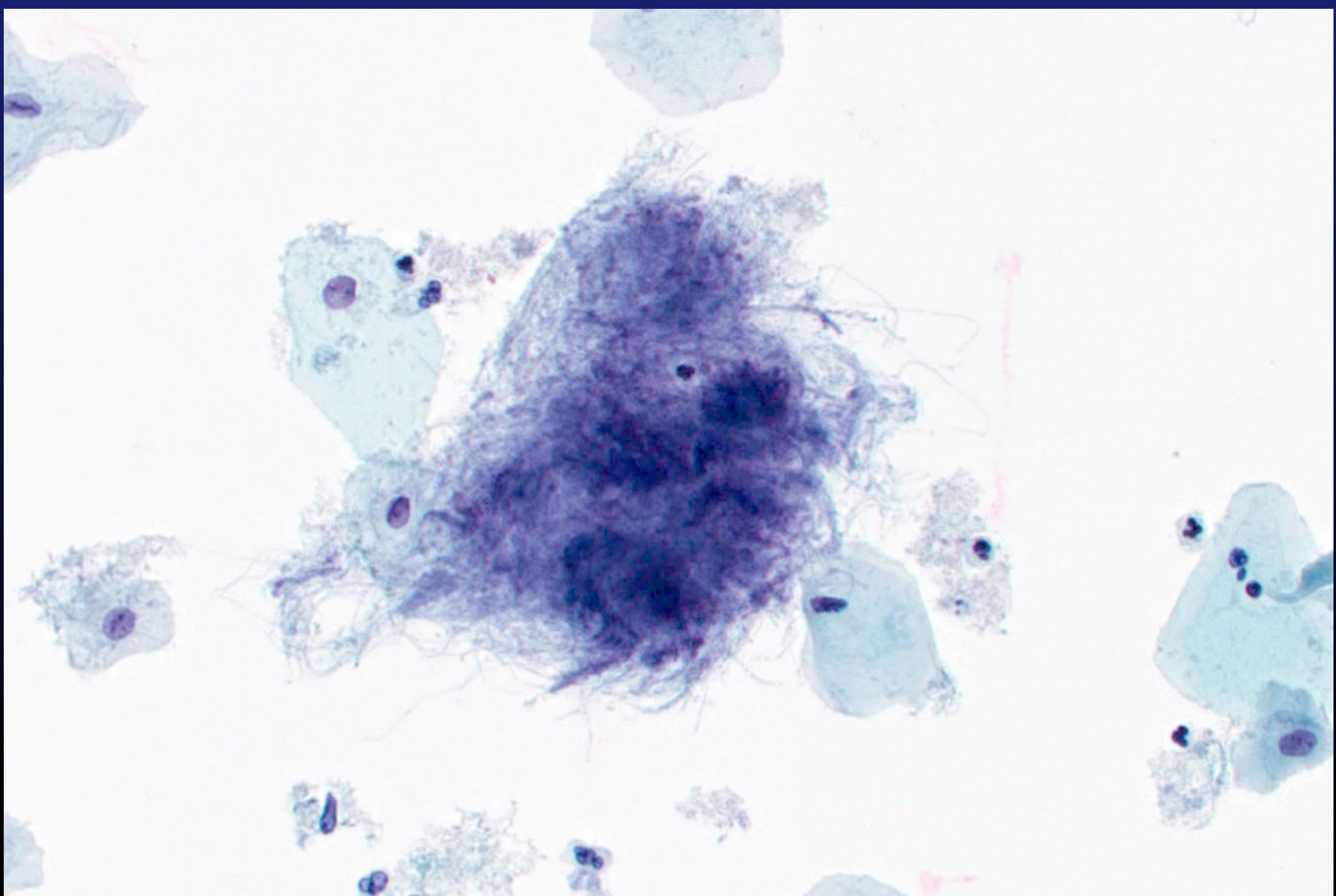
## Normal Morphology – Actinomyces

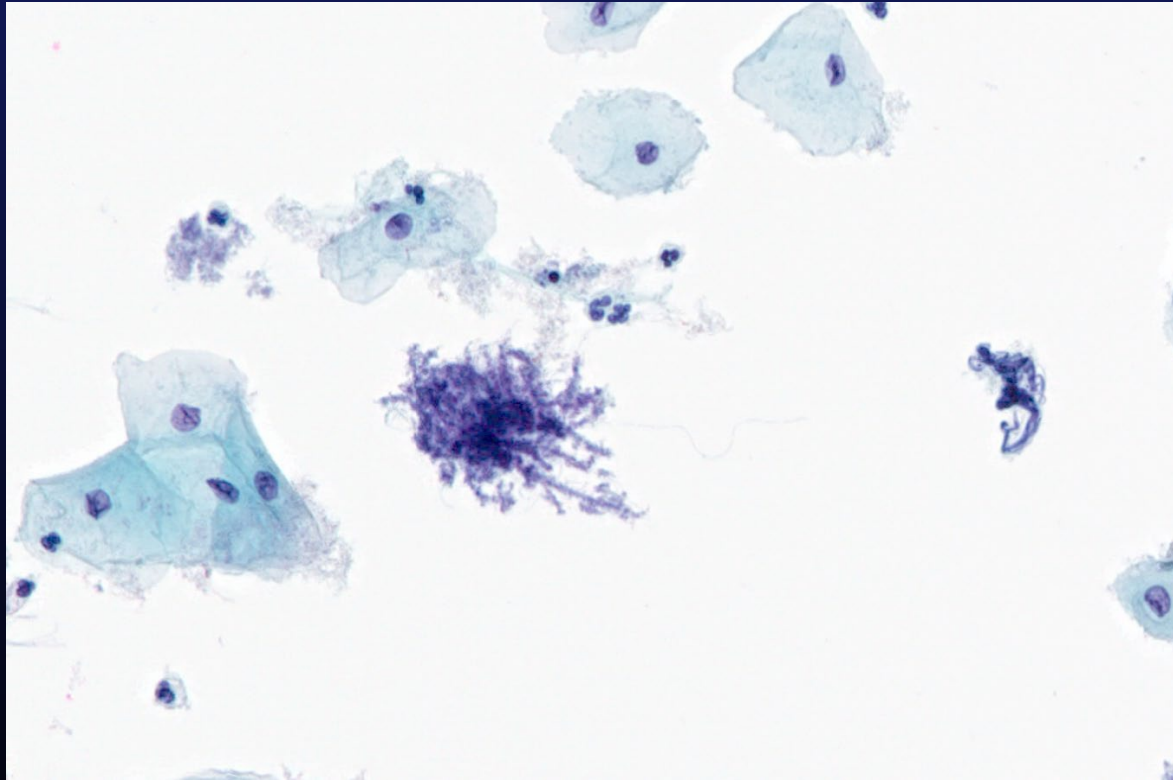
- Thin and thick filaments with radial distribution
- Tangled clumps of filamentous organisms



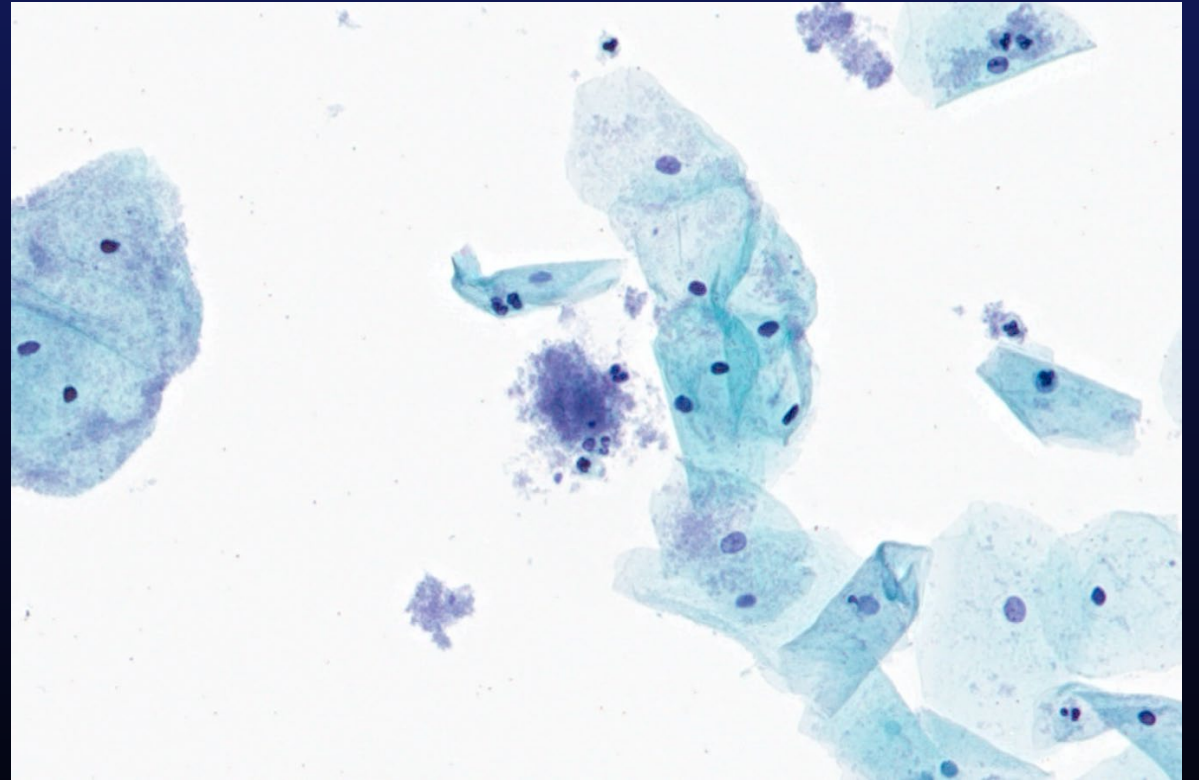








Actinomyces

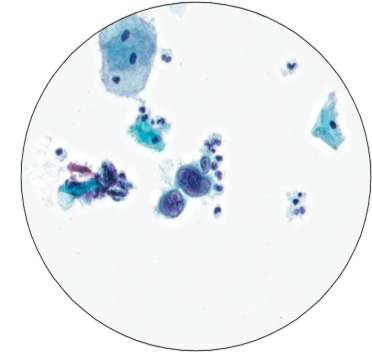


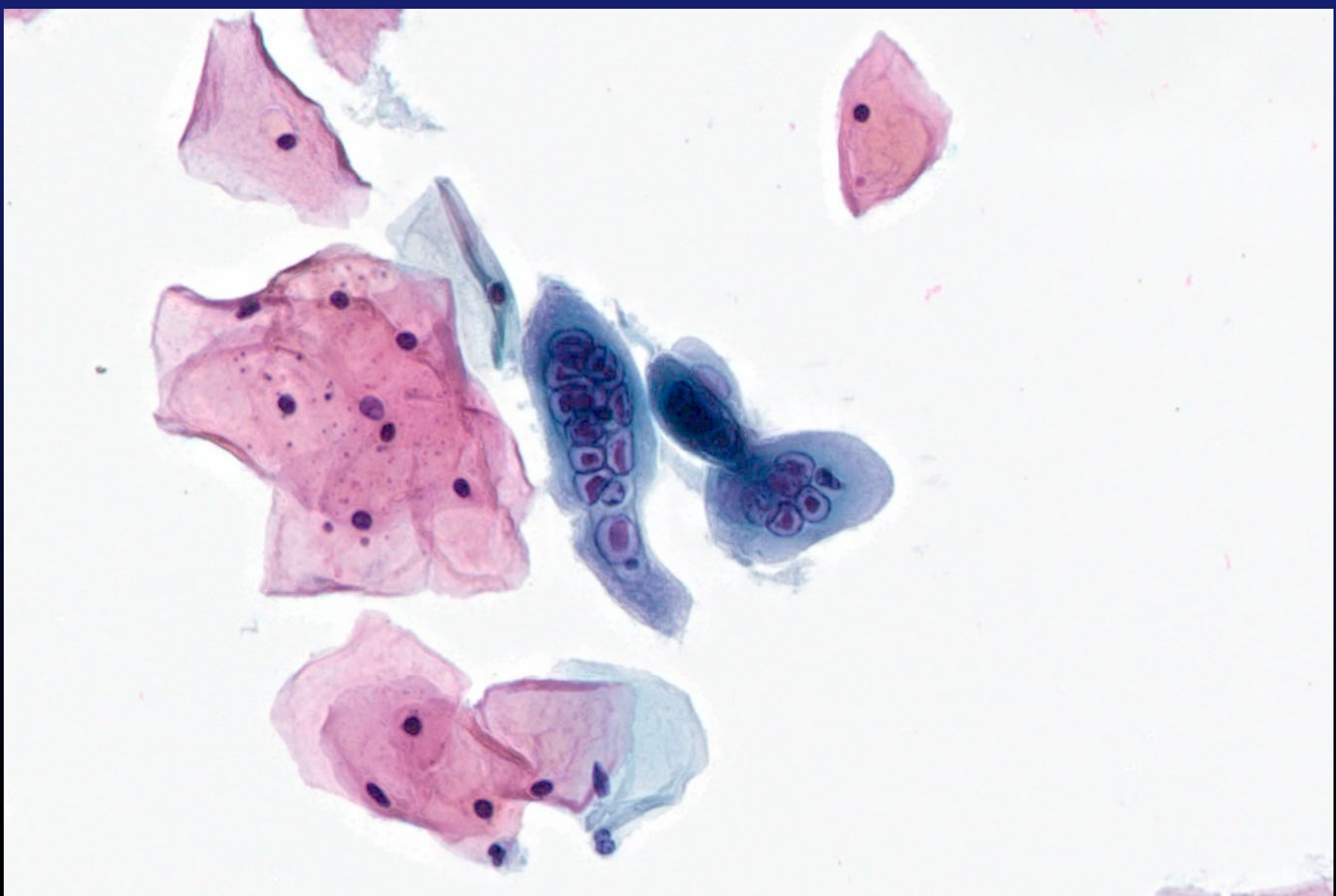
Bacterial Ball

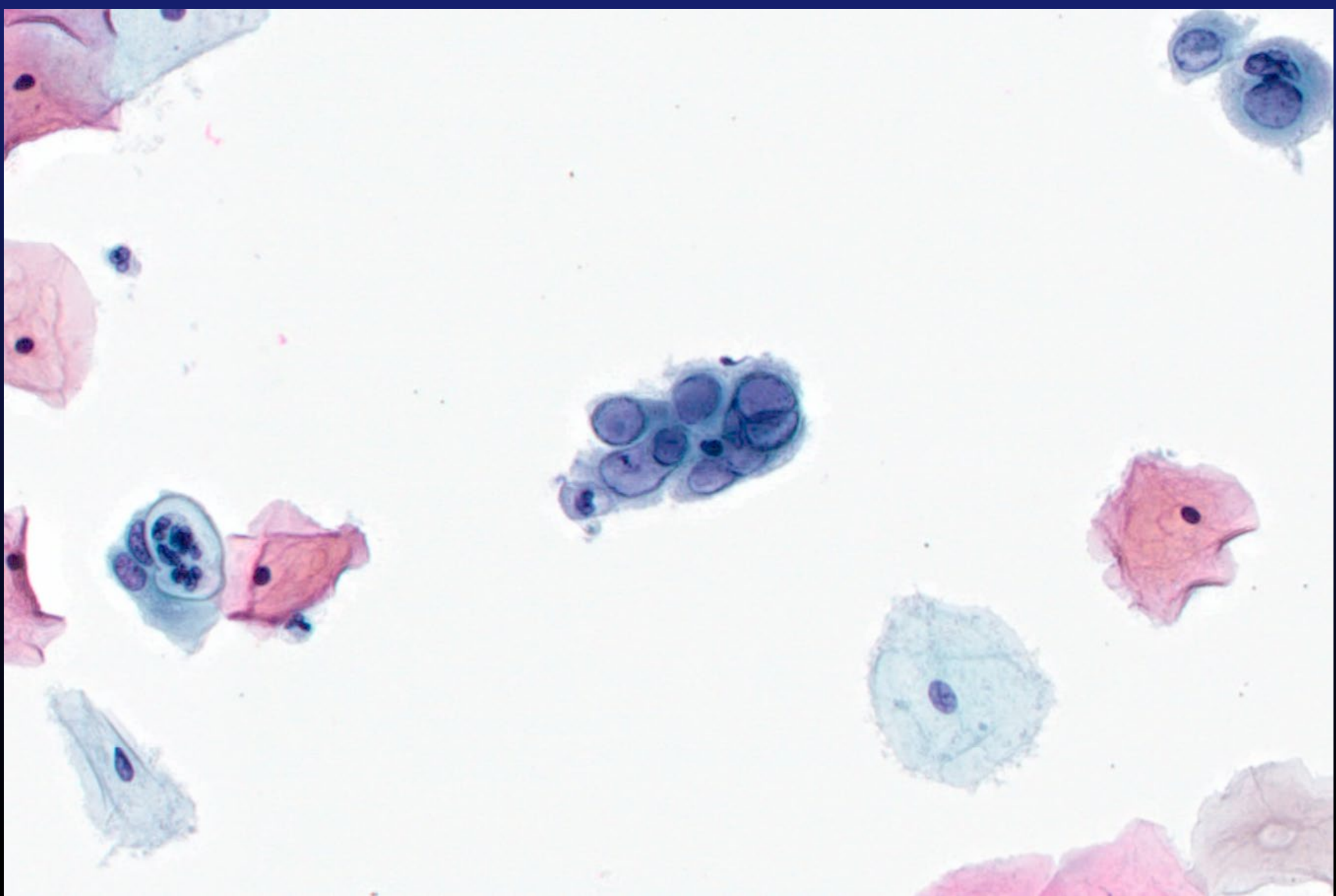
# The Bethesda System for Reporting Cervical Cytology

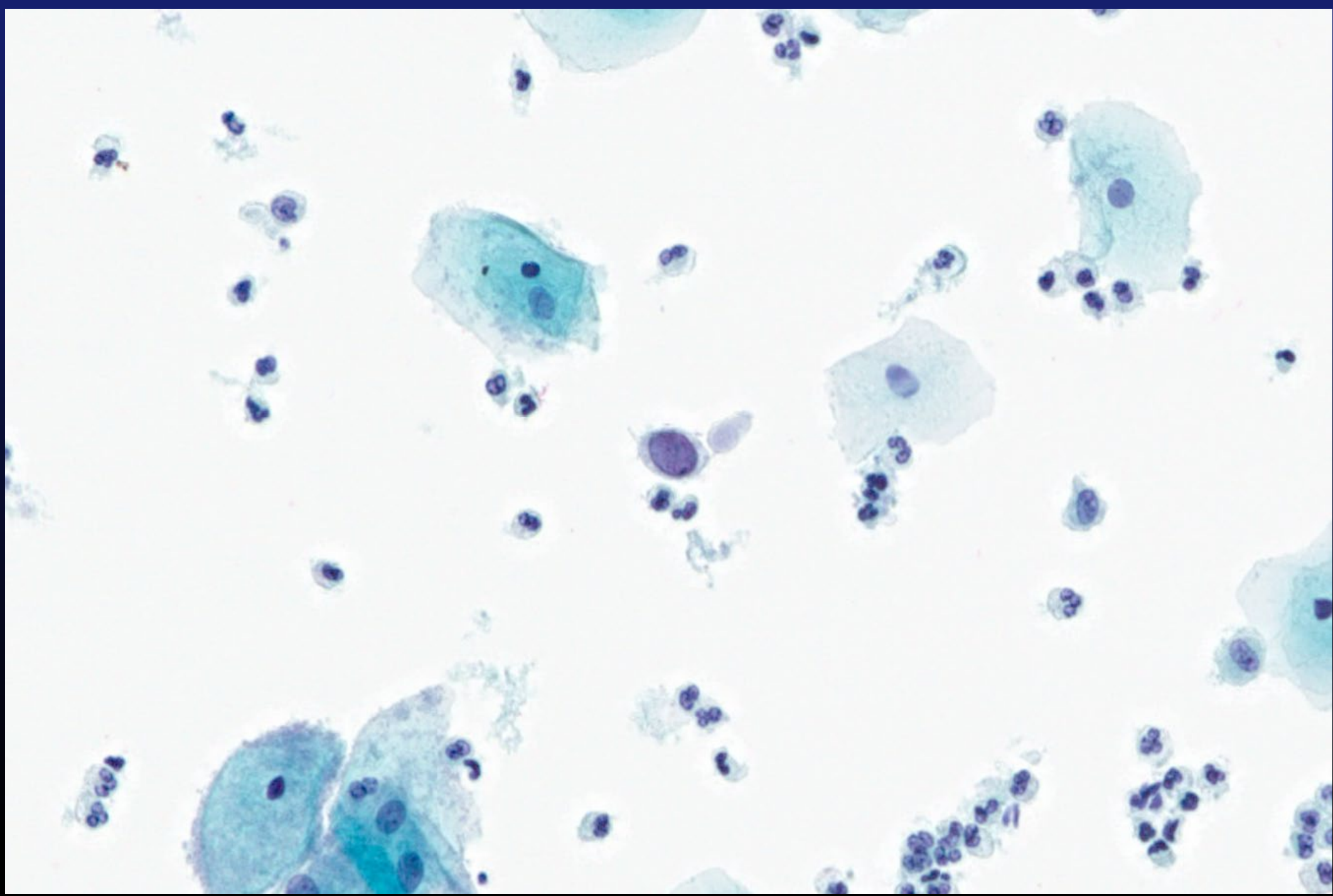
## Normal Morphology – Herpes

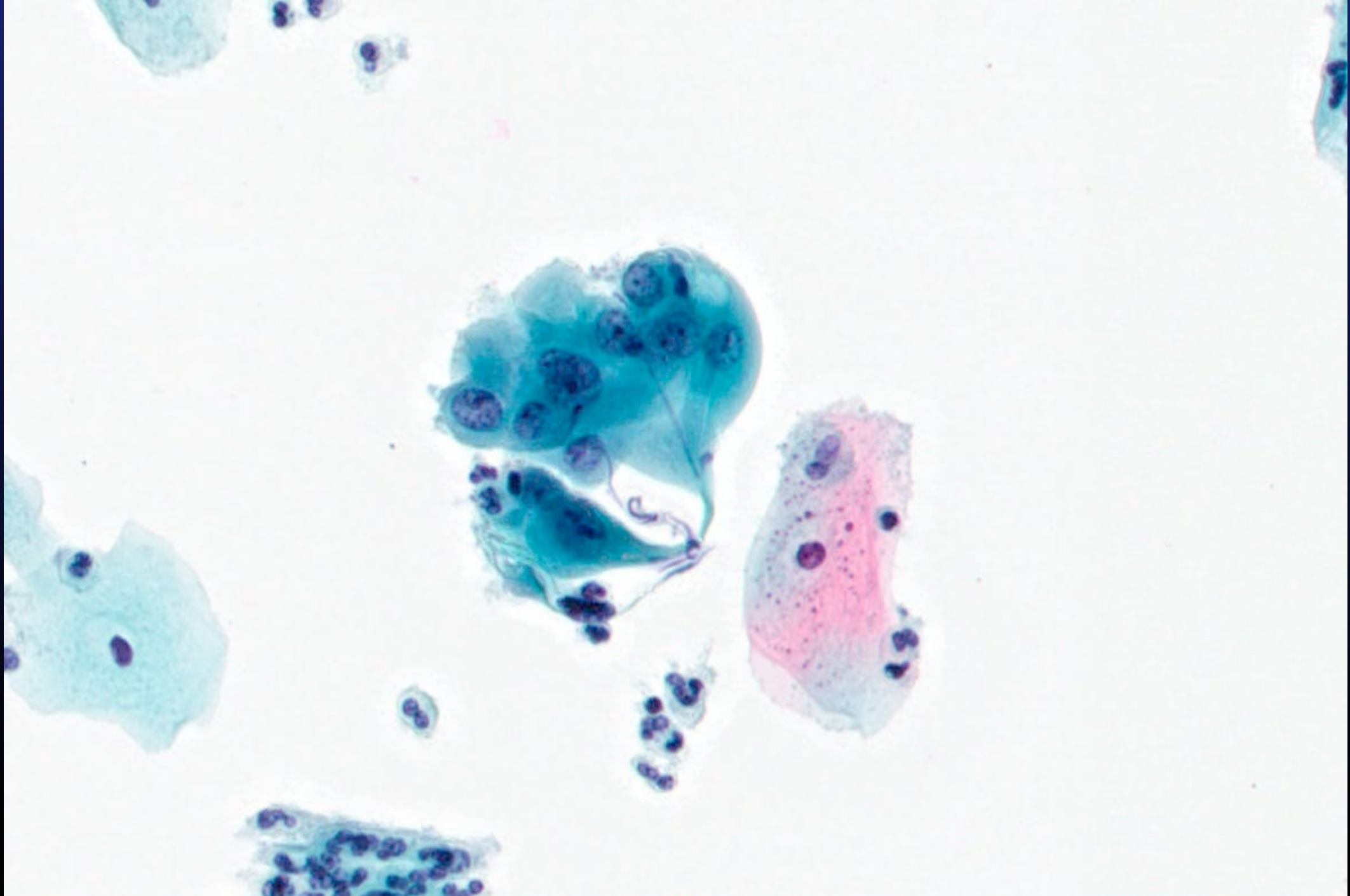
- Nuclei with “ground-glass” appearance
- Multinucleation
- Margination of chromatin
- Nuclear molding
- Eosinophilic nuclear inclusions









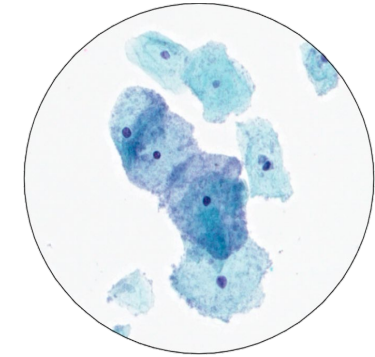


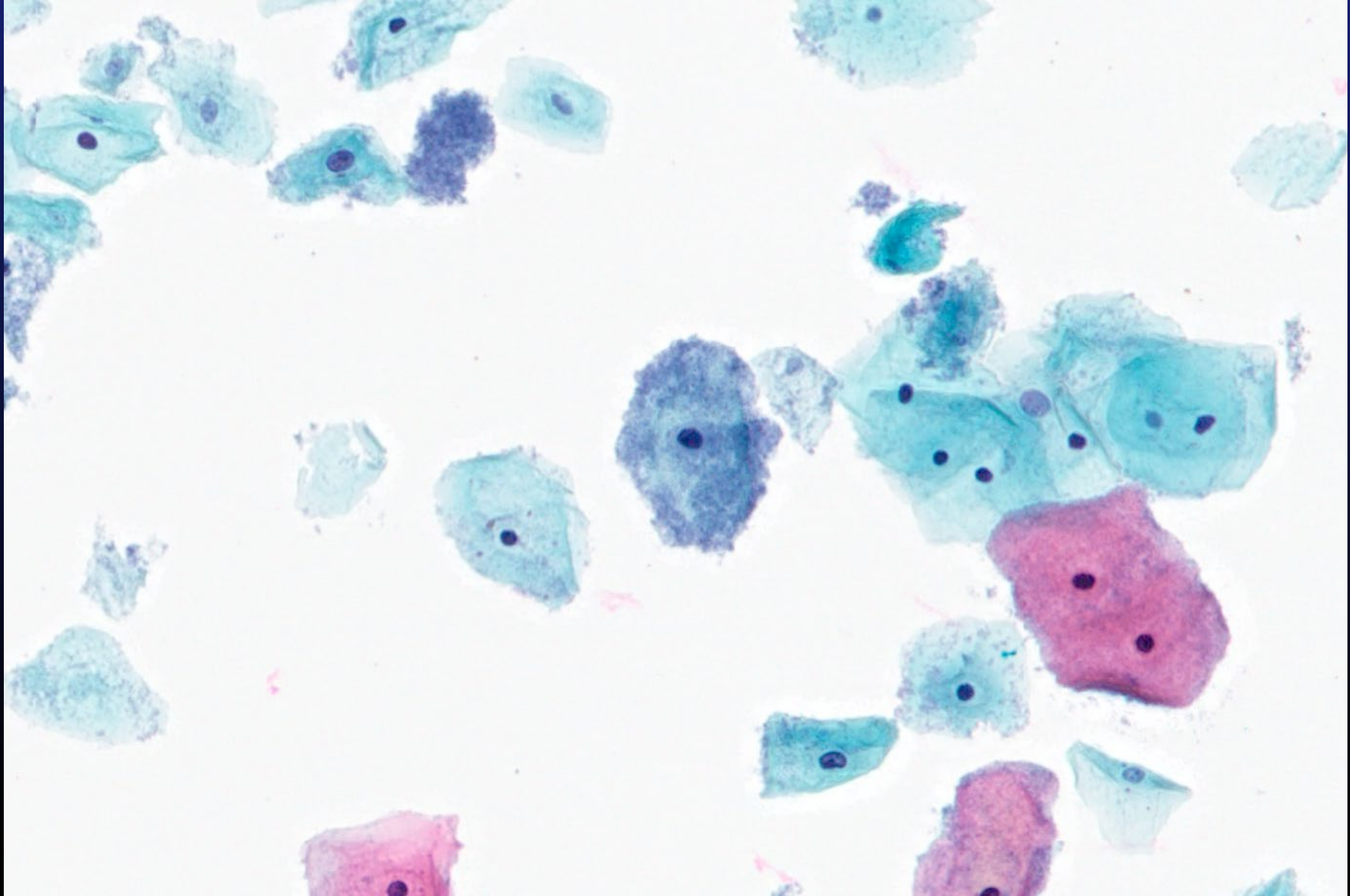


# The Bethesda System for Reporting Cervical Cytology

## Normal Morphology – Shift in Flora (Bacterial Vaginosis - BV)

- Squamous cells covered with coccobacilli - “clue cells”
- Cloudy, filmy appearance

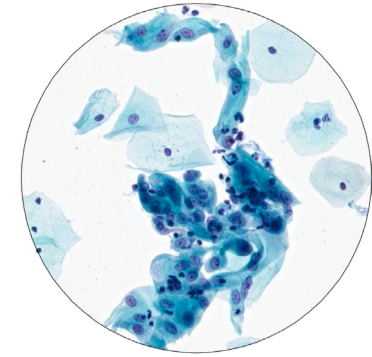


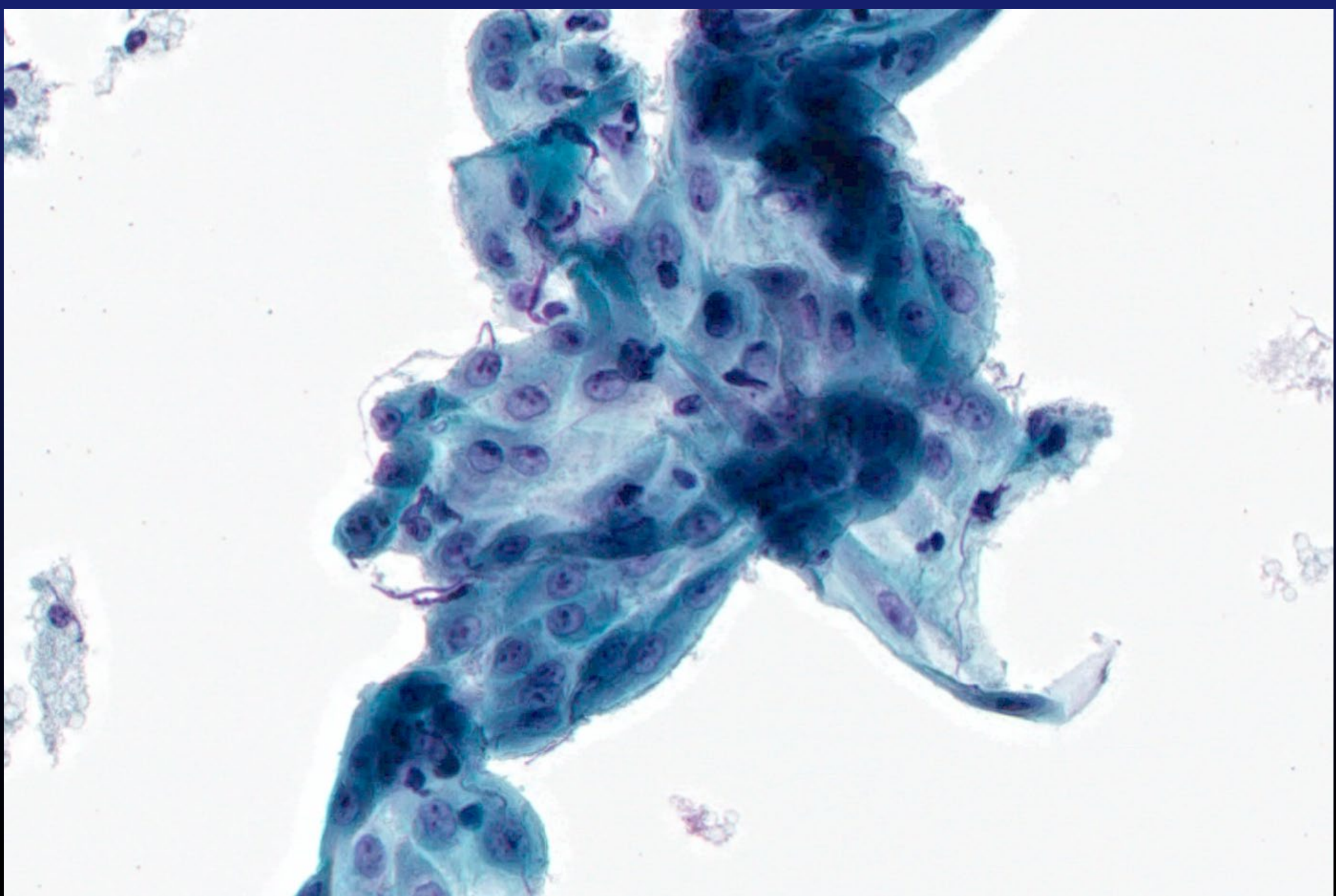


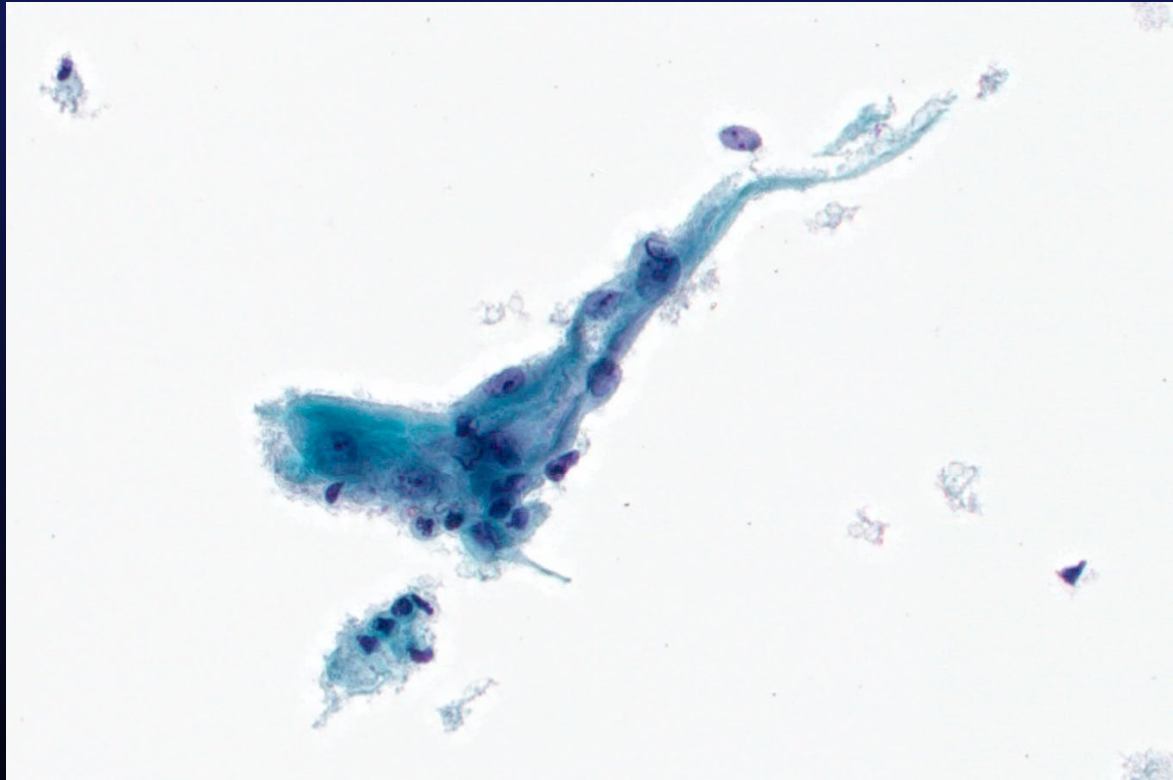
# The Bethesda System for Reporting Cervical Cytology

## Normal Morphology – Reactive/Repair

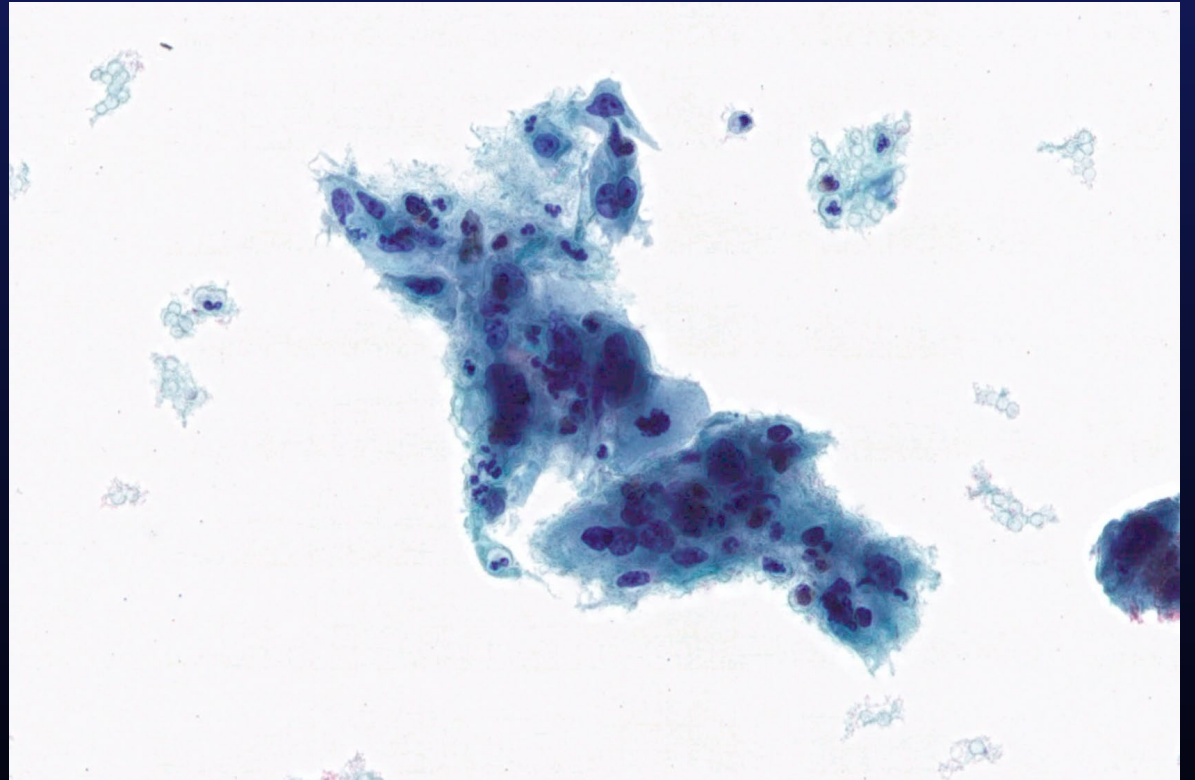
- Cells present in cohesive sheets with maintained polarity (“school of fish”)
- Nuclear size variable
- Nuclear membranes are smooth, round, and uniform
- Chromatin is finely granular and evenly distributed
- Prominent single or multiple nucleoli may be seen
- Cytoplasmic boundaries are well defined







Repair

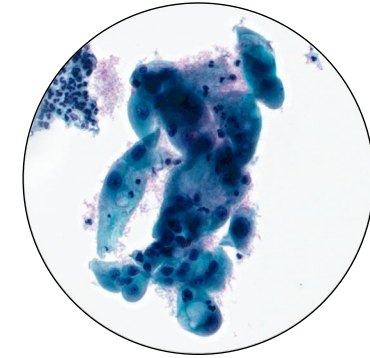


Non-Keratinizing Squamous Cell Carcinoma

# The Bethesda System for Reporting Cervical Cytology

## Normal Morphology – Radiation Changes

- Cell size markedly increased without substantial increase in N/C Ratio
- Bizarre cell shapes
- Binucleation and multinucleation
- Enlarged nuclei with degenerative/smudgy chromatin or mild hyperchromasia
- Prominent single or multiple nucleoli may be seen
- Cytoplasmic vacuoles and/or polychromasia may be seen



**PATIENT HISTORY IS KEY**





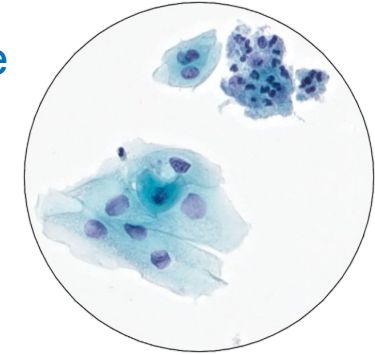


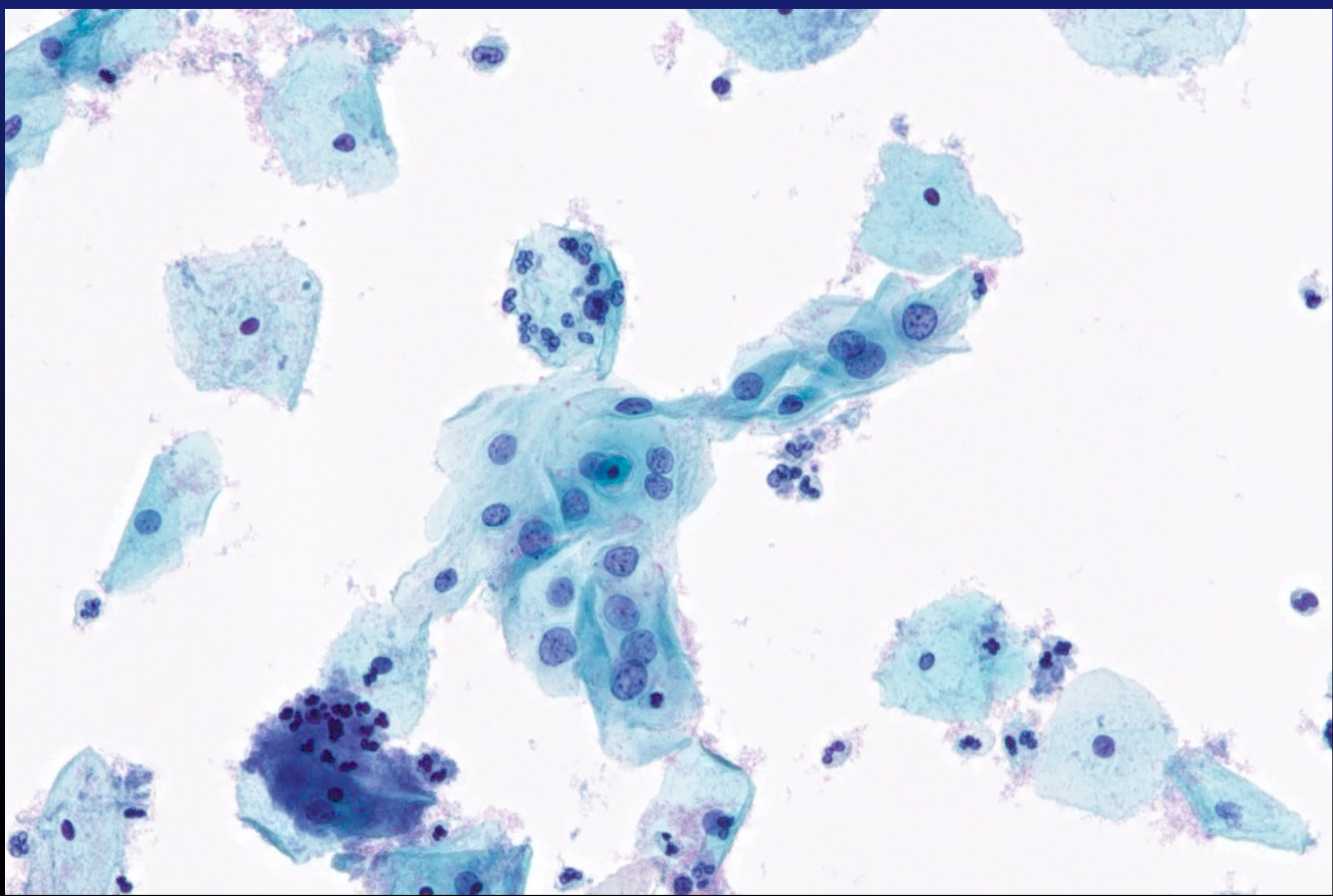
# ThinPrep Pap Test: Abnormal Morphology

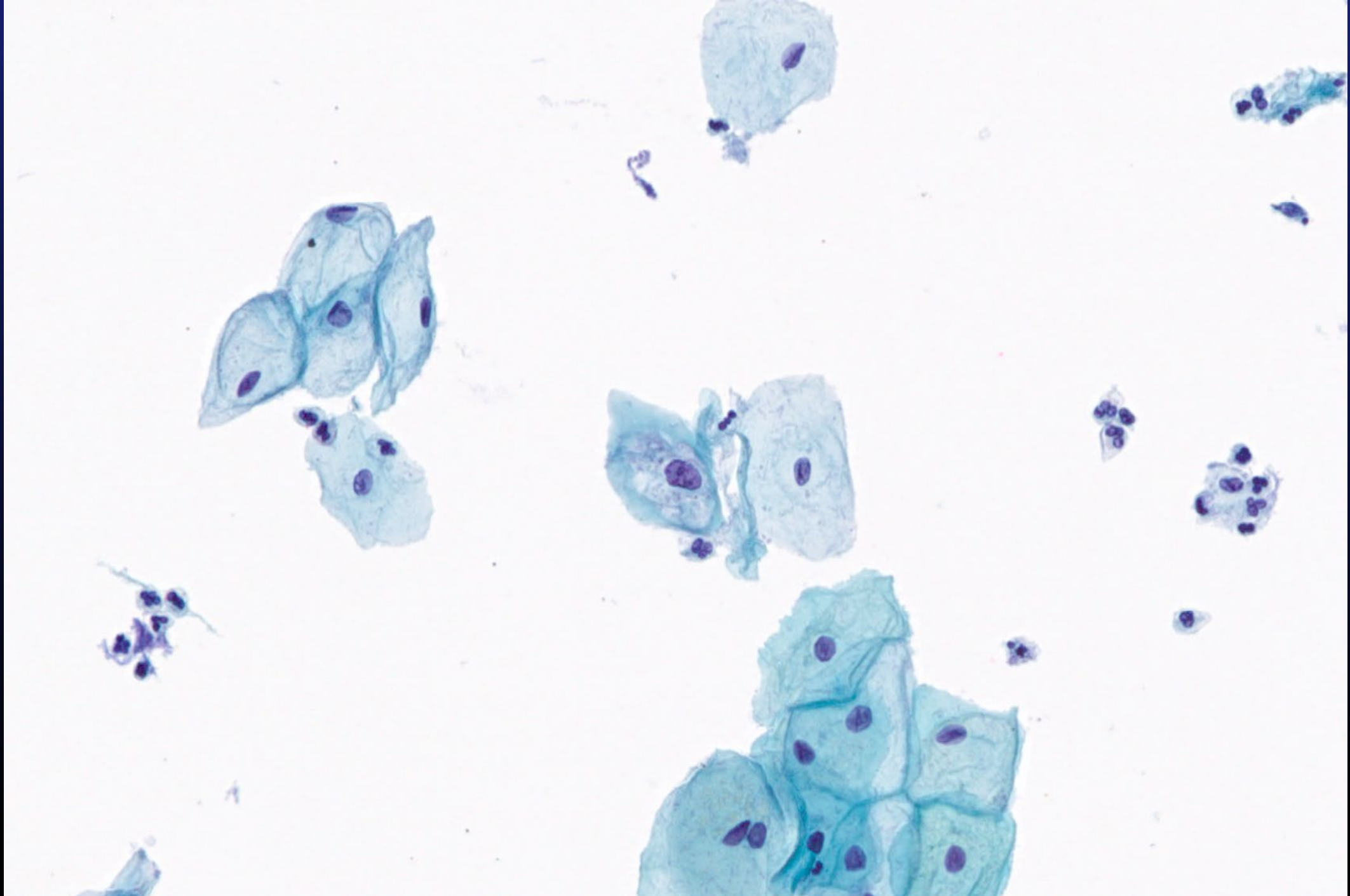
# The Bethesda System for Reporting Cervical Cytology

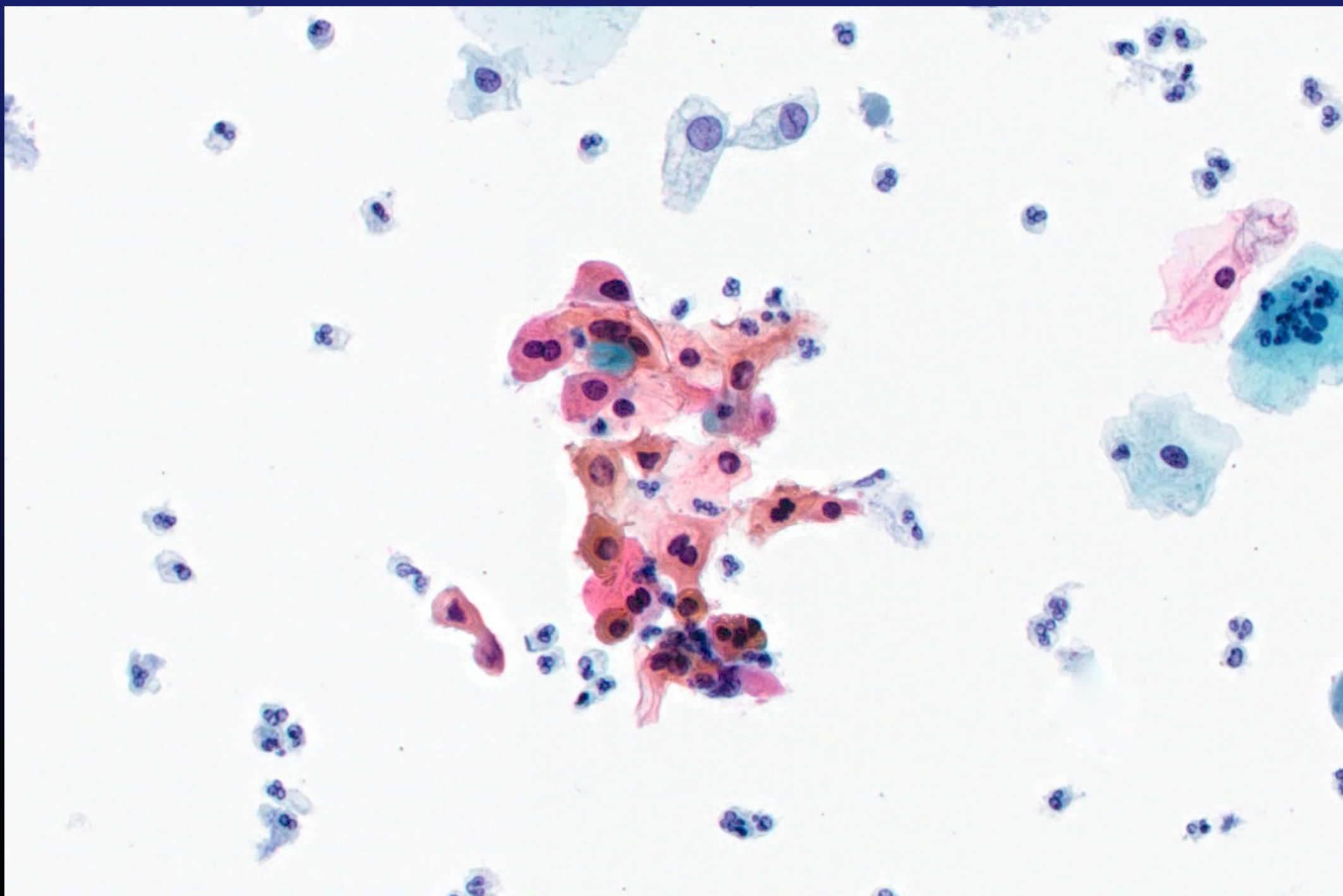
## Abnormal Morphology – Atypical Squamous Cells of Undetermined Significance (ASCUS)

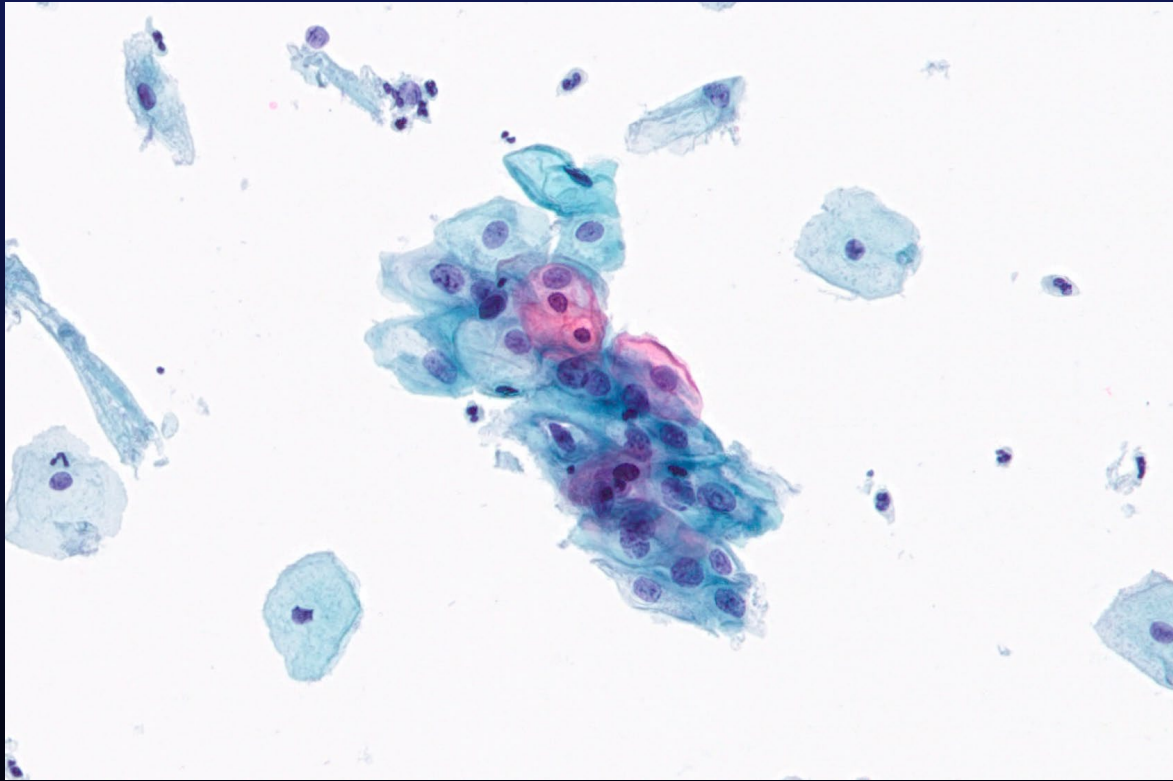
- Singly or sheets
- Nuclei 2 ½ to 3 times the area of an intermediate nucleus
- Slight increase in N/C ratio
- Mild irregular nuclear membranes
- Minimal hyperchromasia
- Mild irregular chromatin distribution
- Cytoplasm can be keratinized and/or exhibit poorly defined cytoplasmic halos or vacuoles



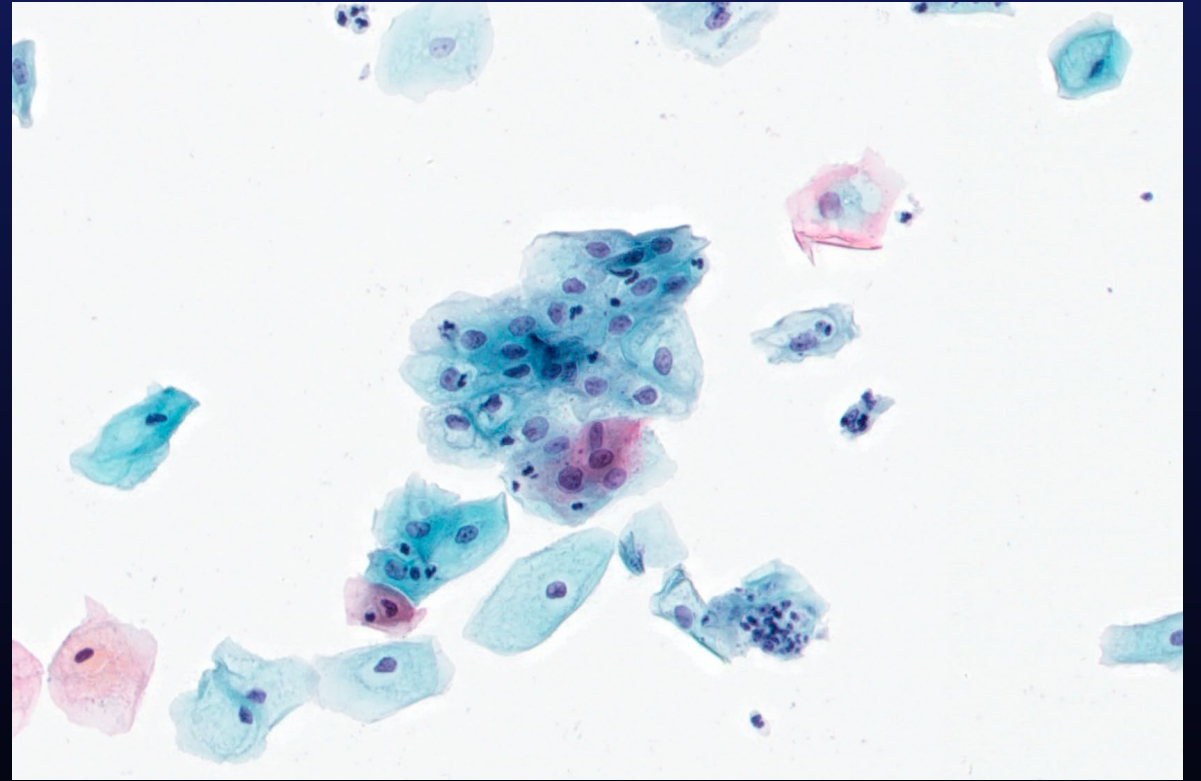








ASCUS

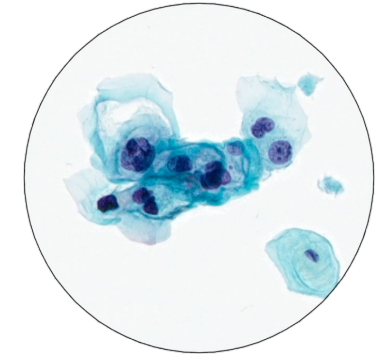


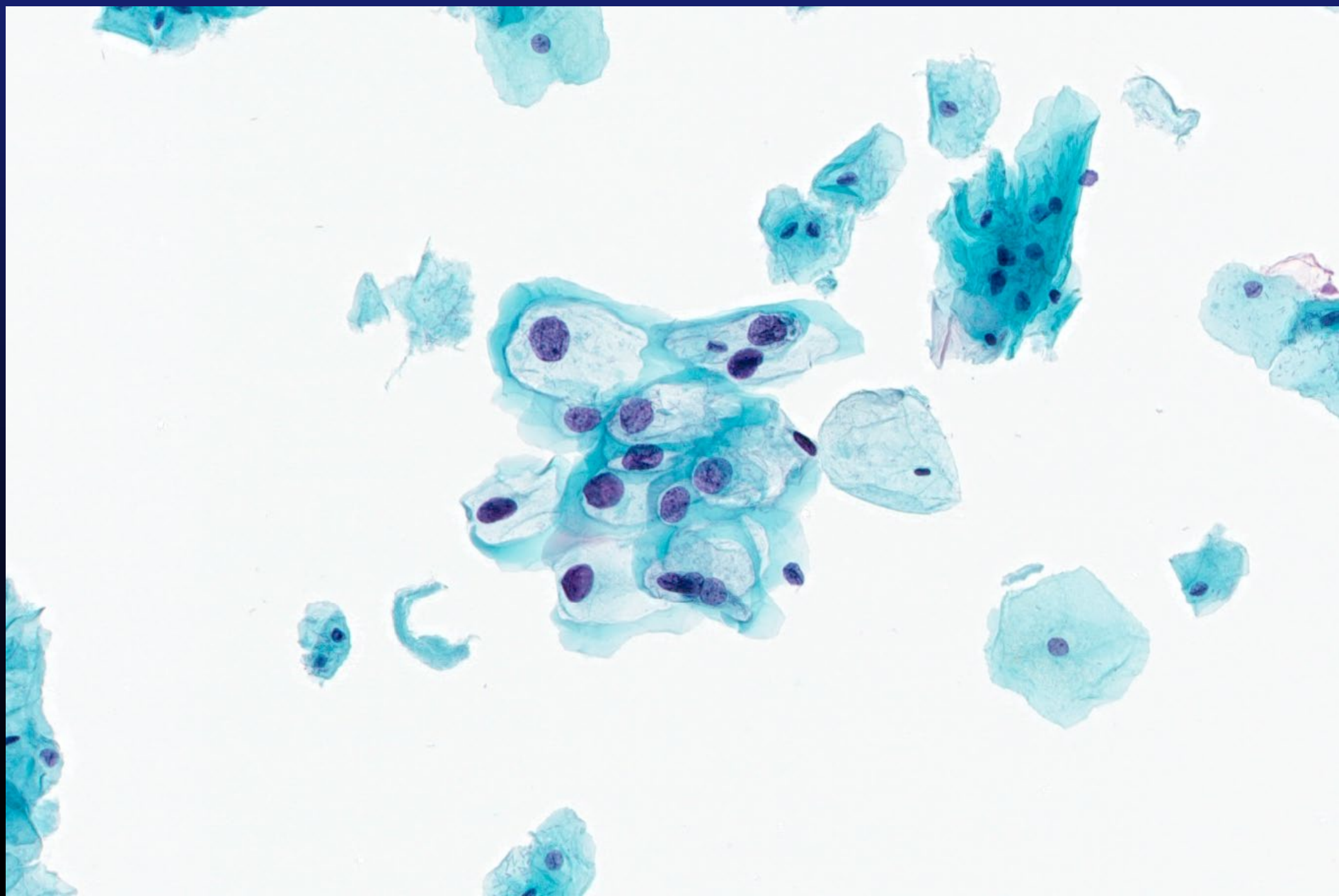
Reactive Squamous Cells

# The Bethesda System for Reporting Cervical Cytology

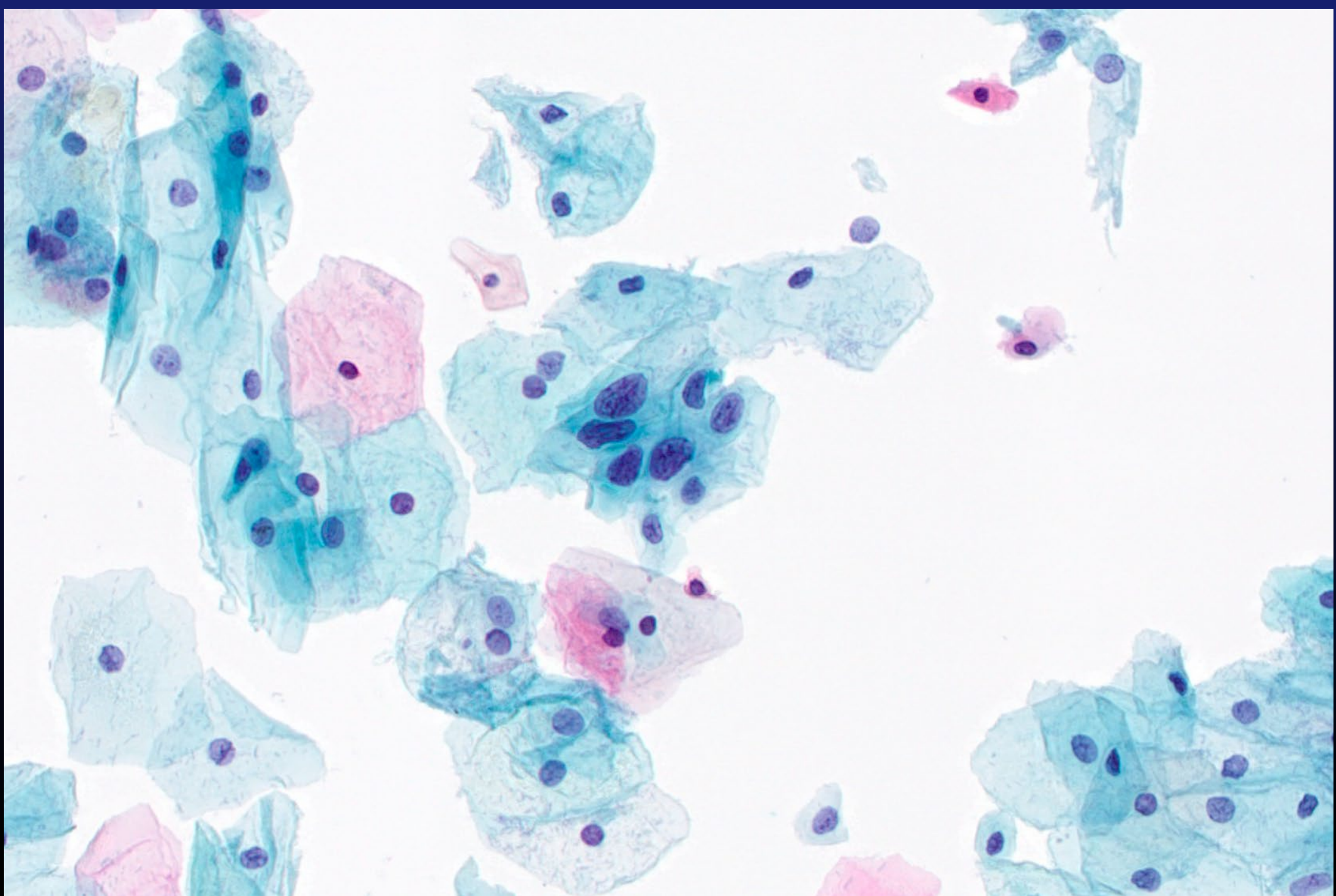
## Abnormal Morphology – Low Grade Squamous Intraepithelial Lesion (LSIL)

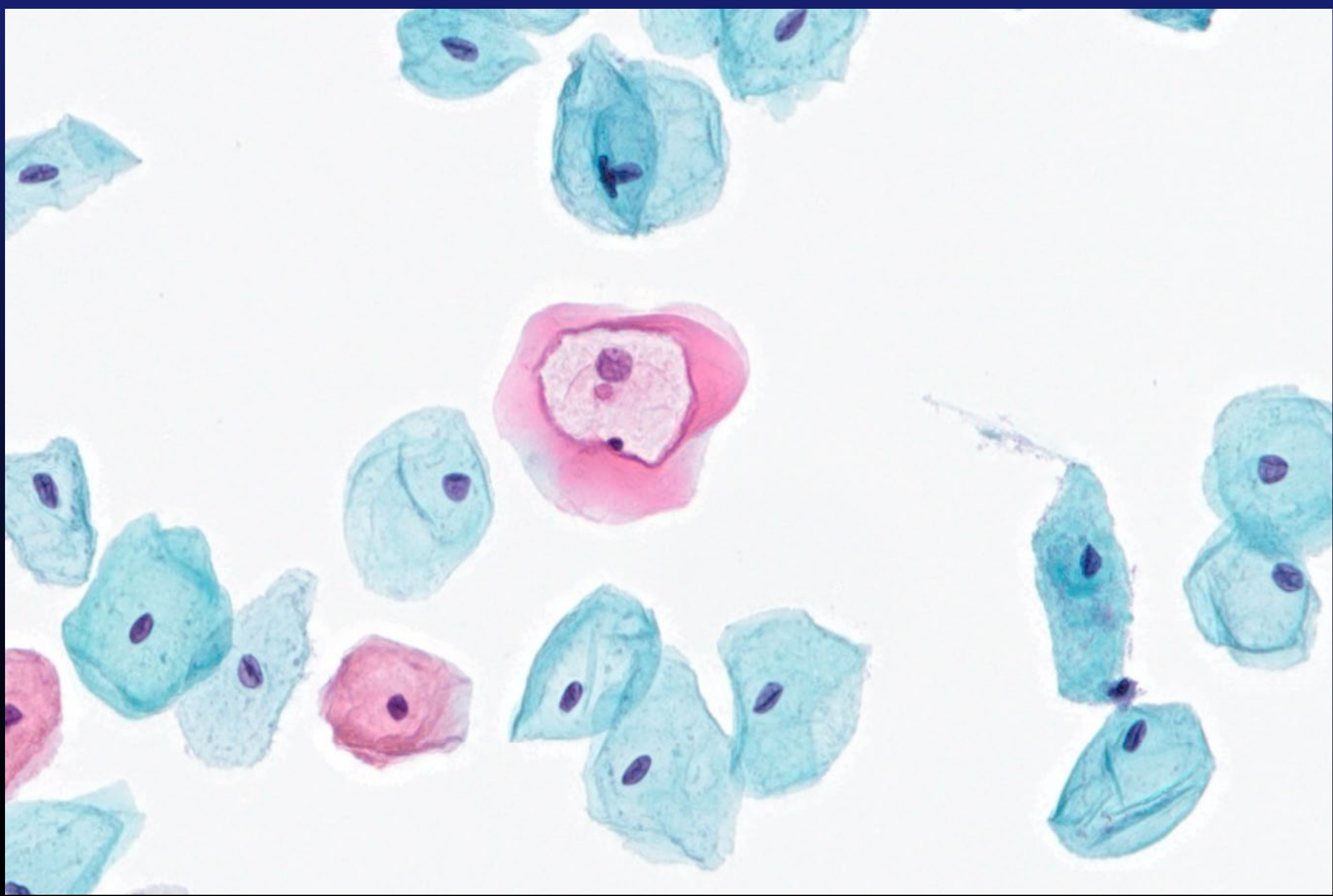
- Cells occur singly, in clusters, and in sheets
- Low but slightly increased N/C ratio
- Nuclei more than 3 times the area of an intermediate nucleus
- May be hyperchromatic
- Chromatin is uniform and coarsely granular, smudgy and/or opaque
- Variable nuclear membranes
- Koilocytosis/perinuclear cavitation
- Binucleation and/or multinucleation
- Nucleoli absent or inconspicuous if present

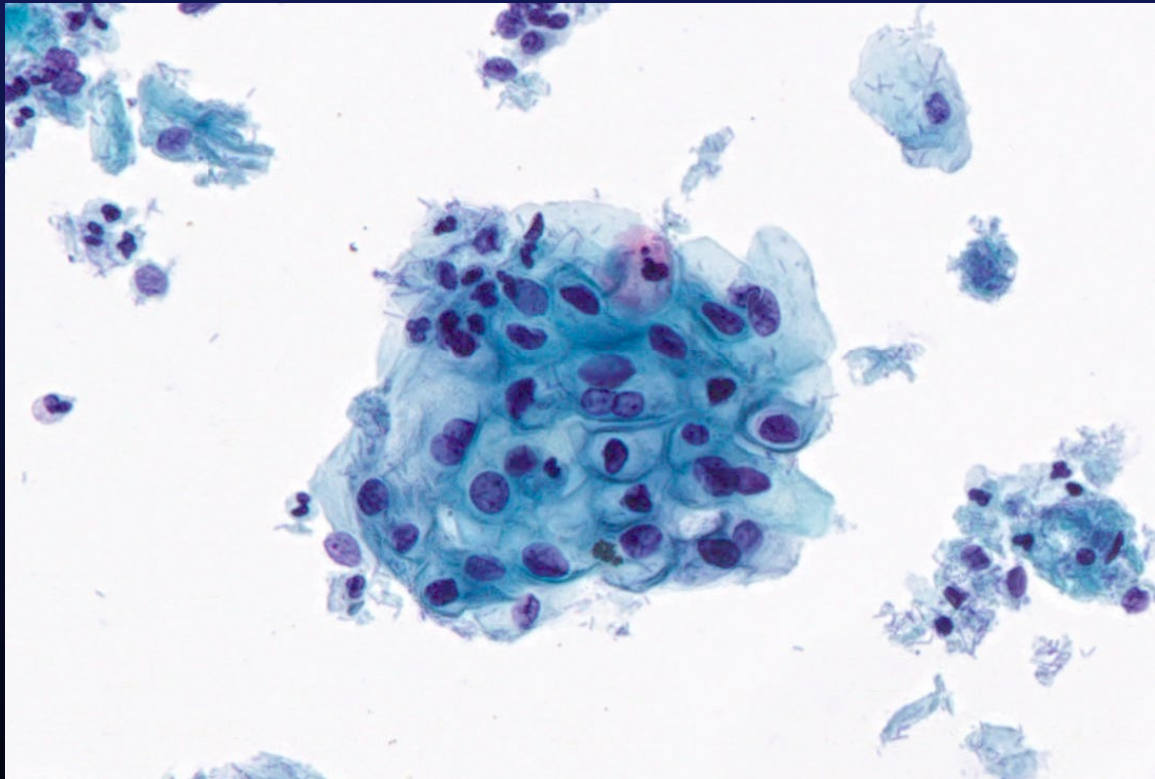




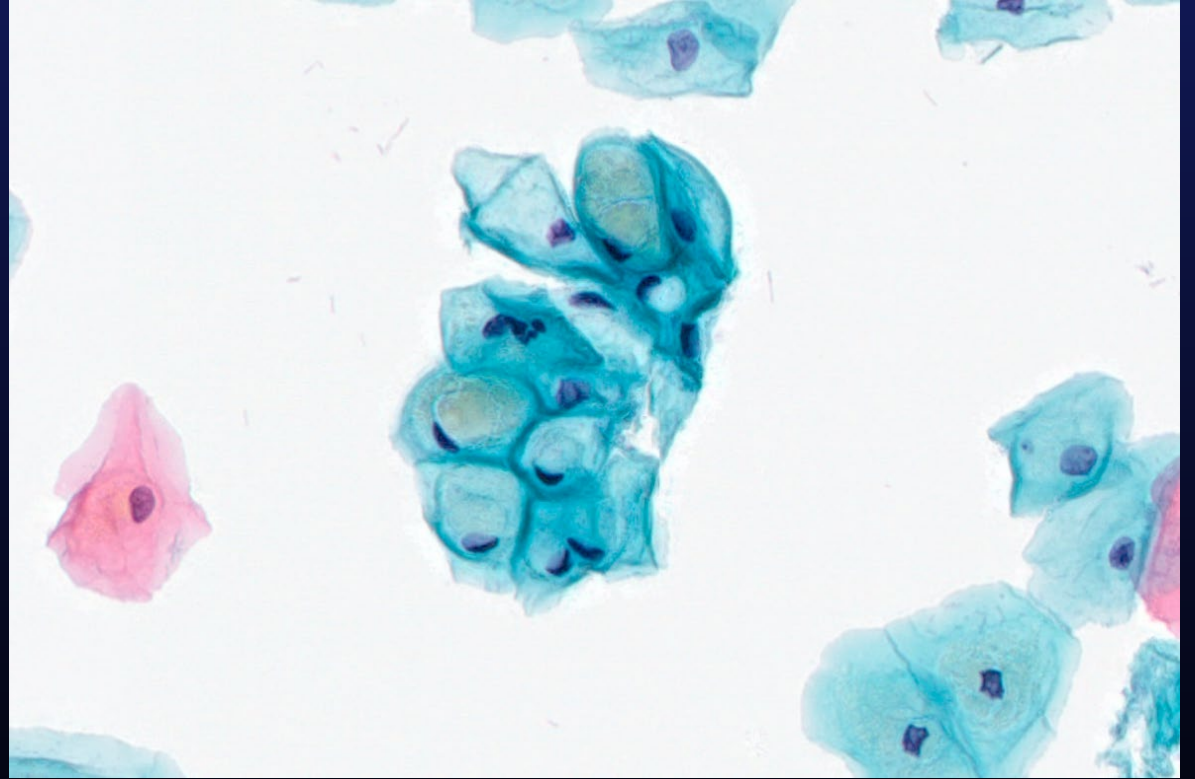








LSIL

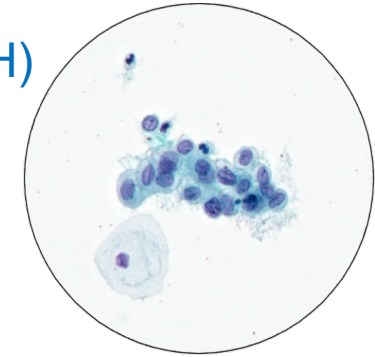


Navicular Cells

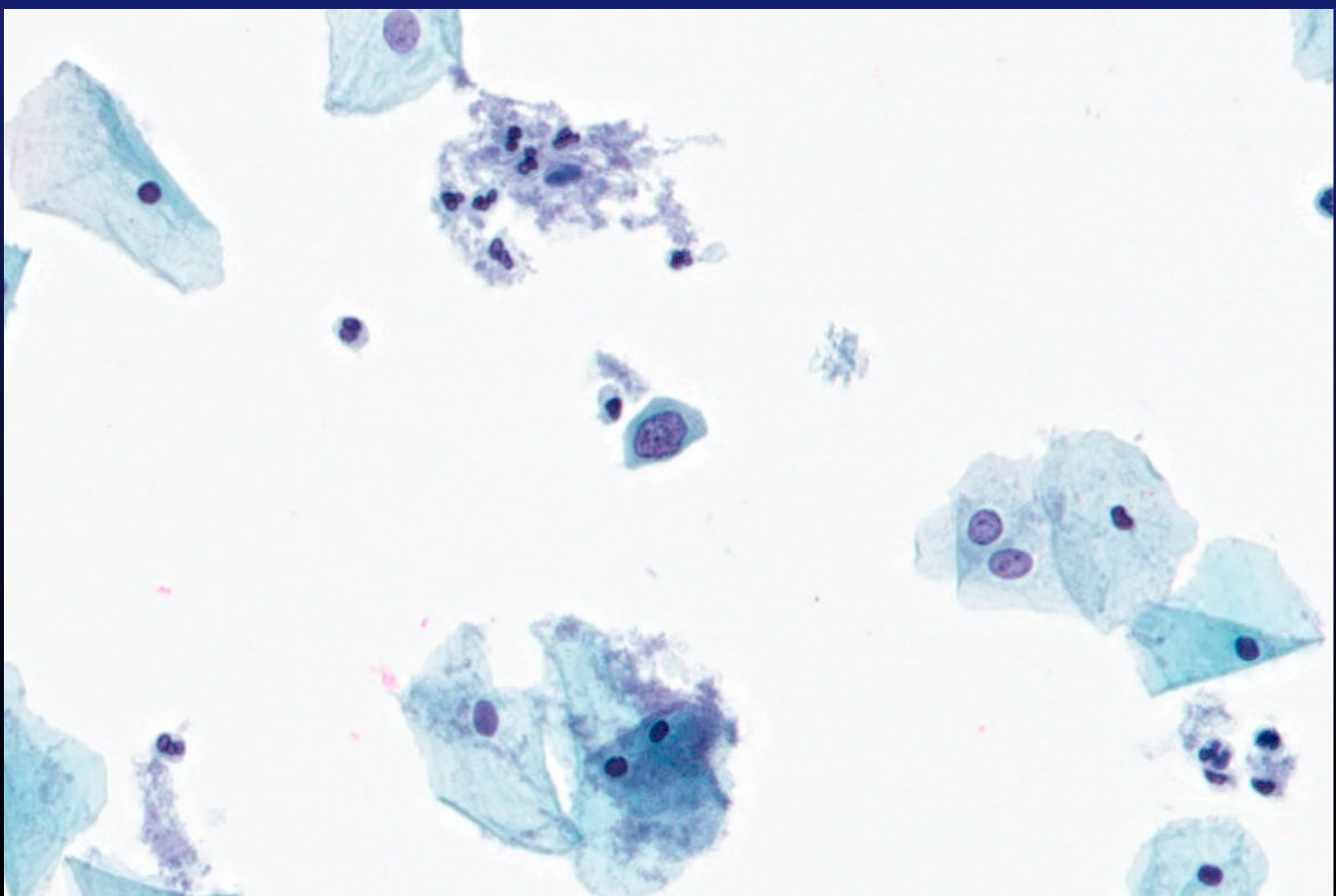
# The Bethesda System for Reporting Cervical Cytology

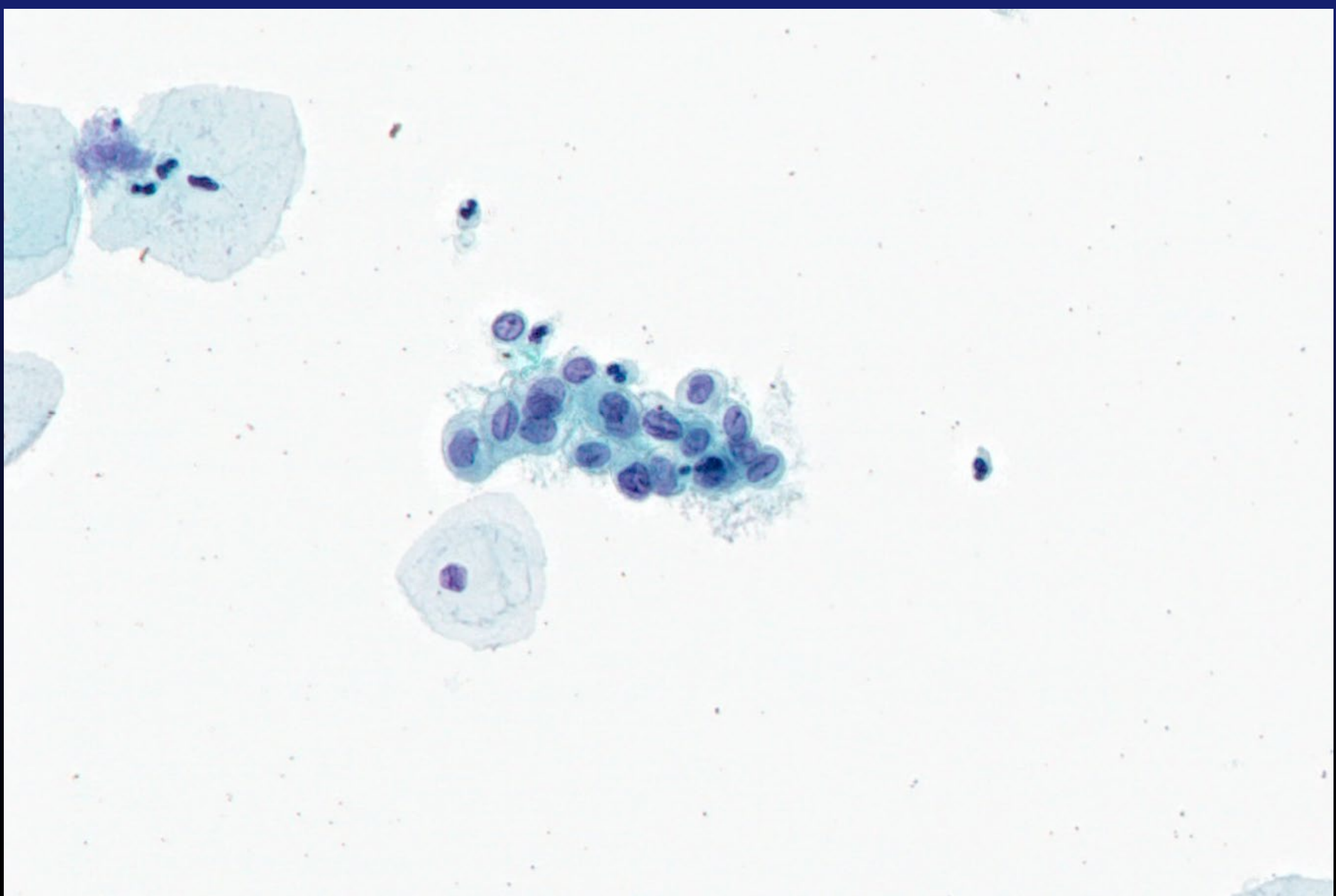
## Abnormal Morphology – Atypical Squamous Cells- Cannot Exclude HSIL (ASC-H)

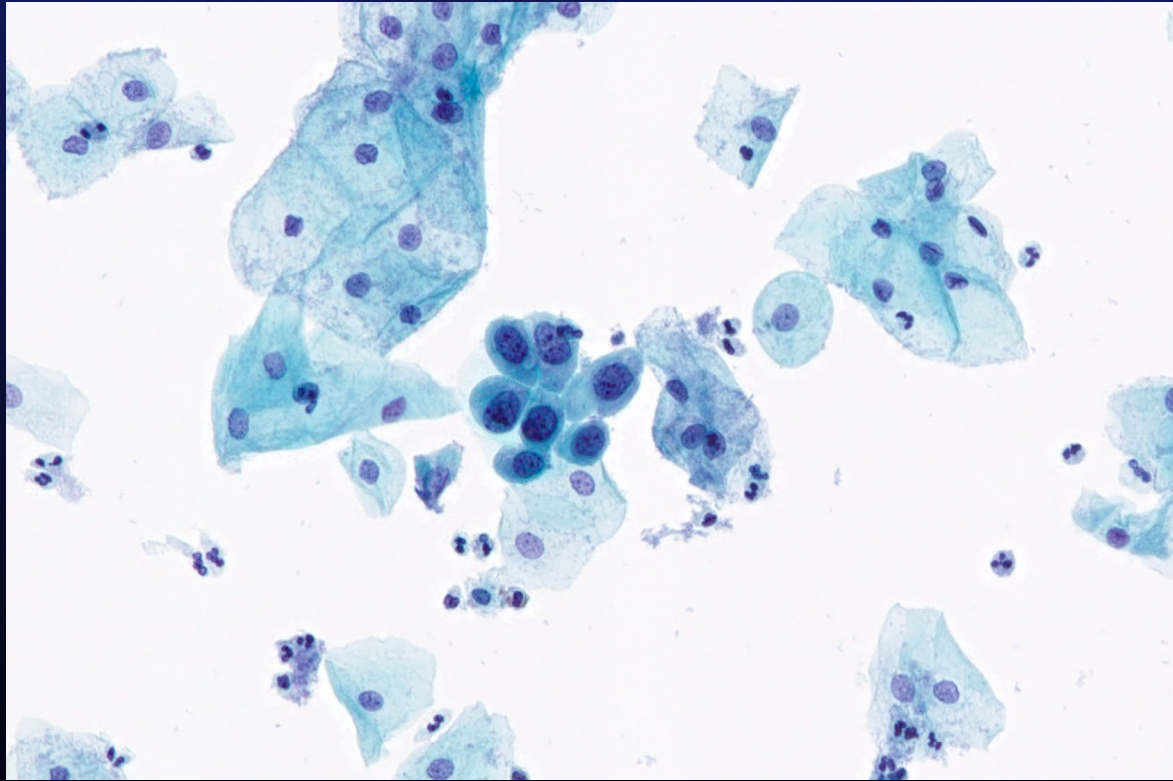
- Occurs singly or in small groups of less than 10 cells
- Nuclei 1 ½ to 2 ½ times the area of a normal metaplastic nucleus
- N/C ratio similar to that of HSIL
- Chromatin irregularity
- Hyperchromasia
- Irregular nuclear membranes



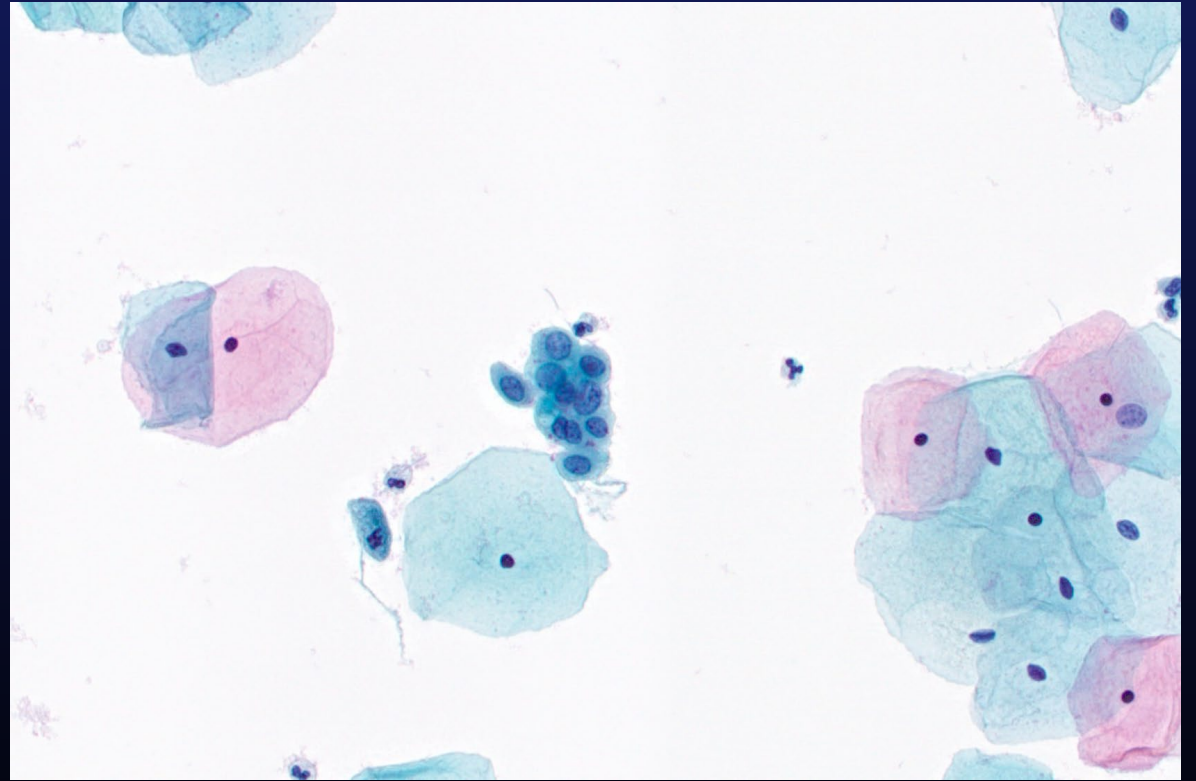
## CRITERIA INSUFFICIENT FOR HSIL DIAGNOSIS



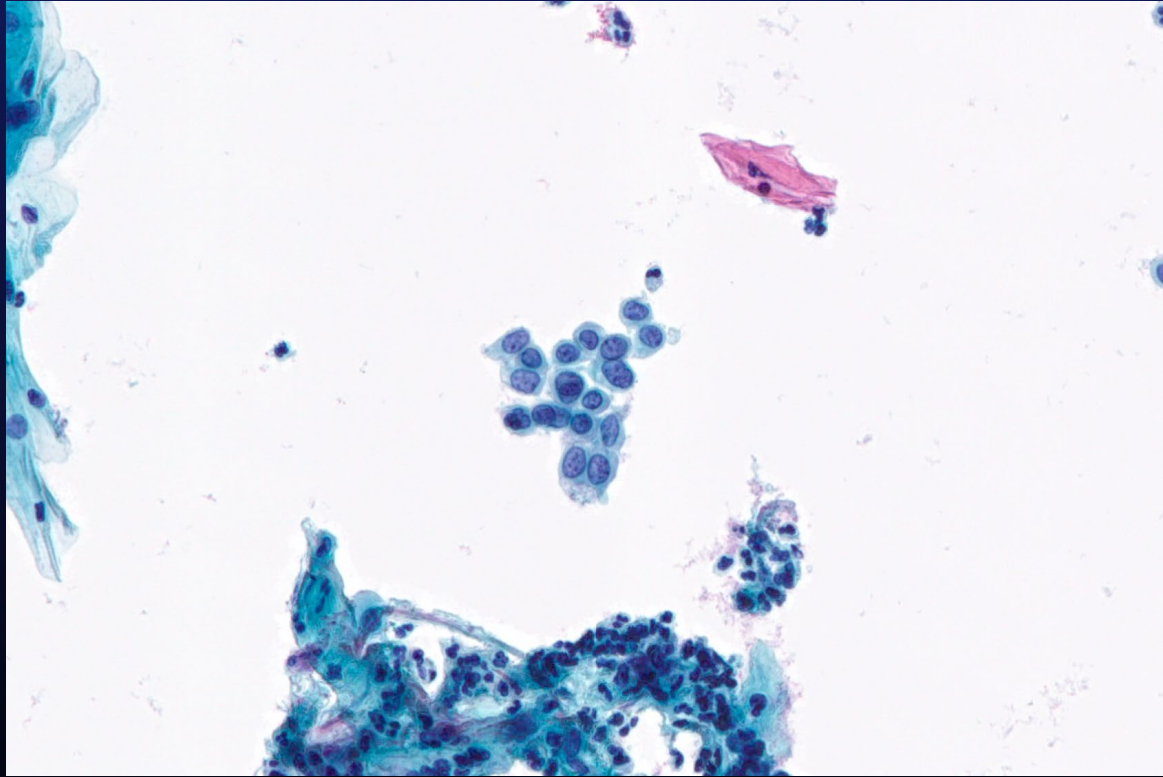




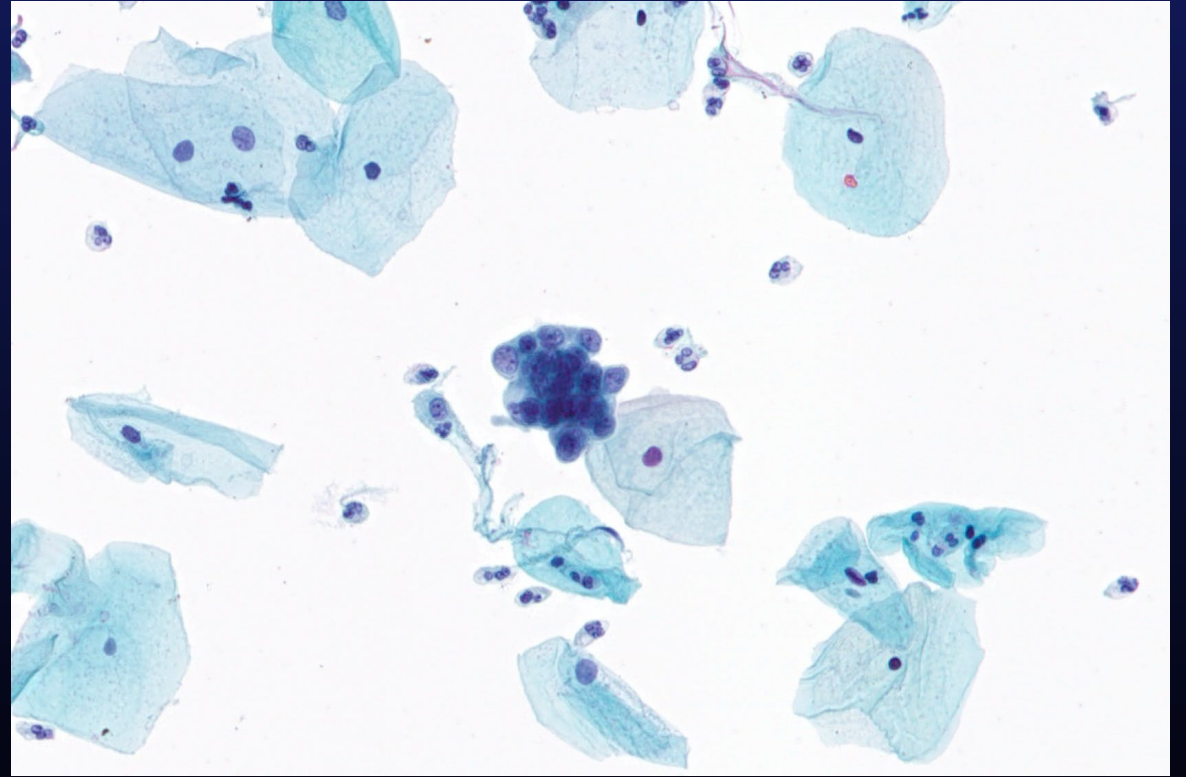
ASC-H



Reactive Squamous Metaplasia



ASC-H



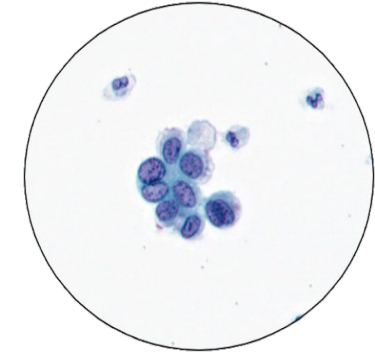
Endometrial Cells

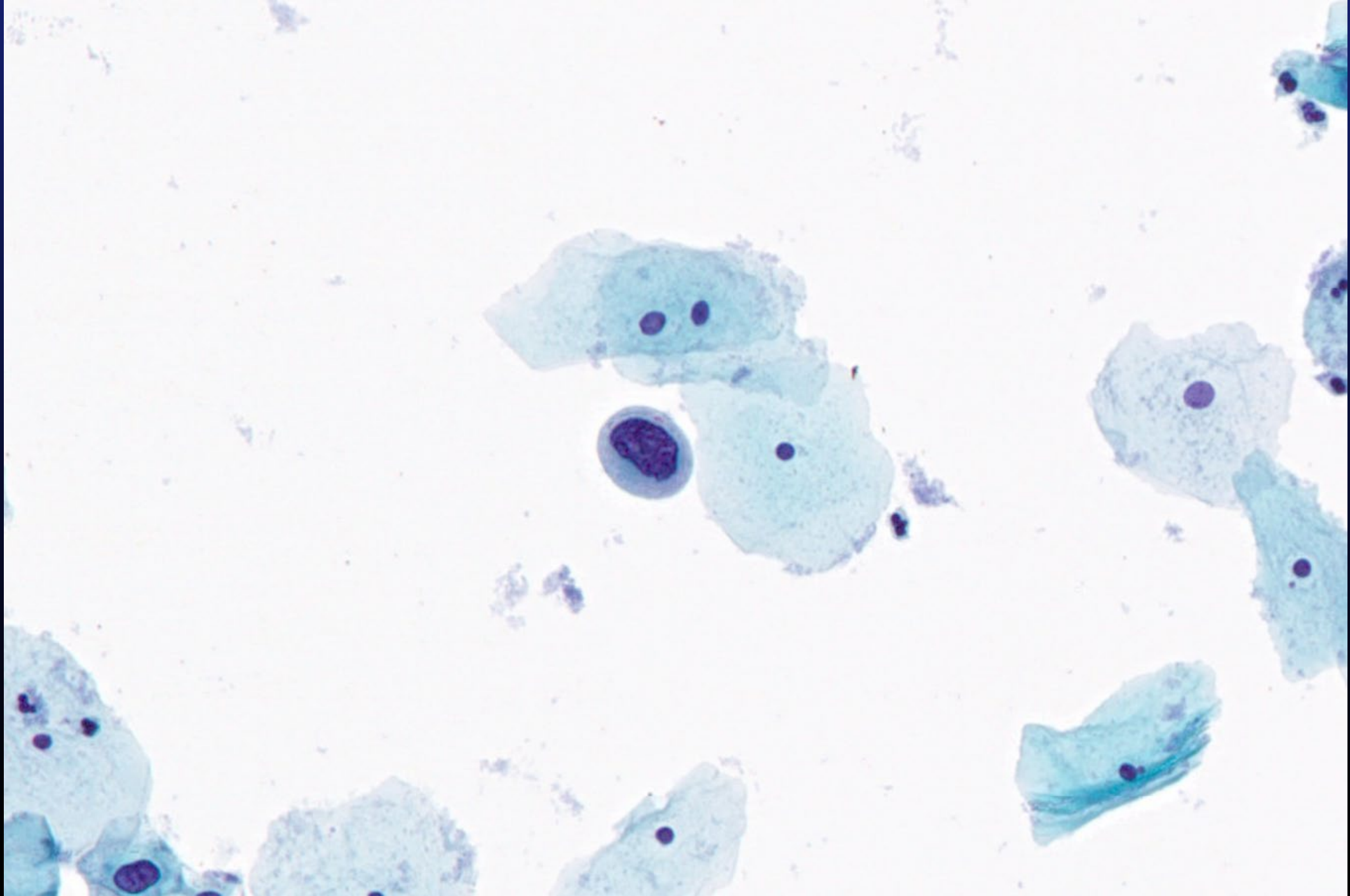


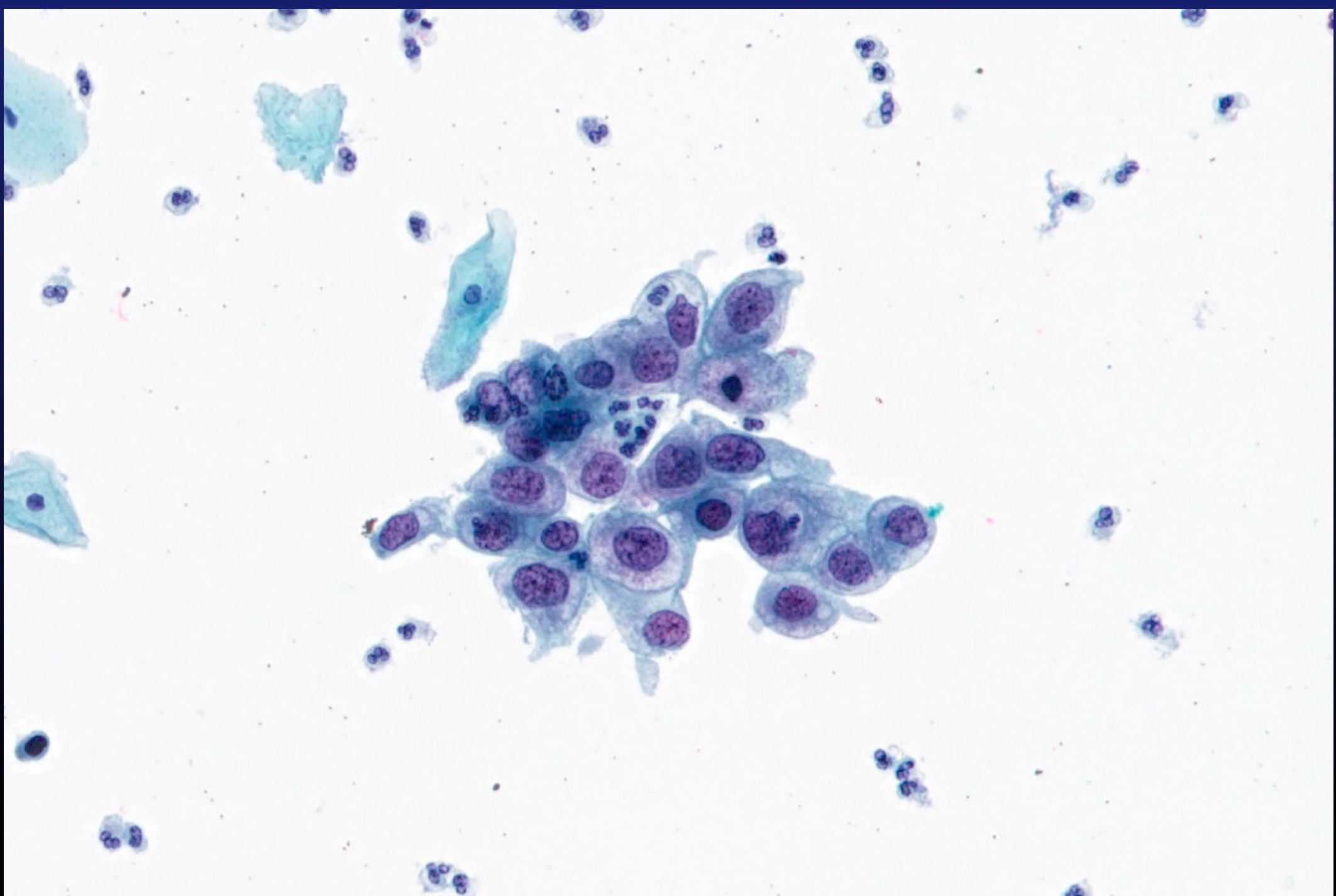
# The Bethesda System for Reporting Cervical Cytology

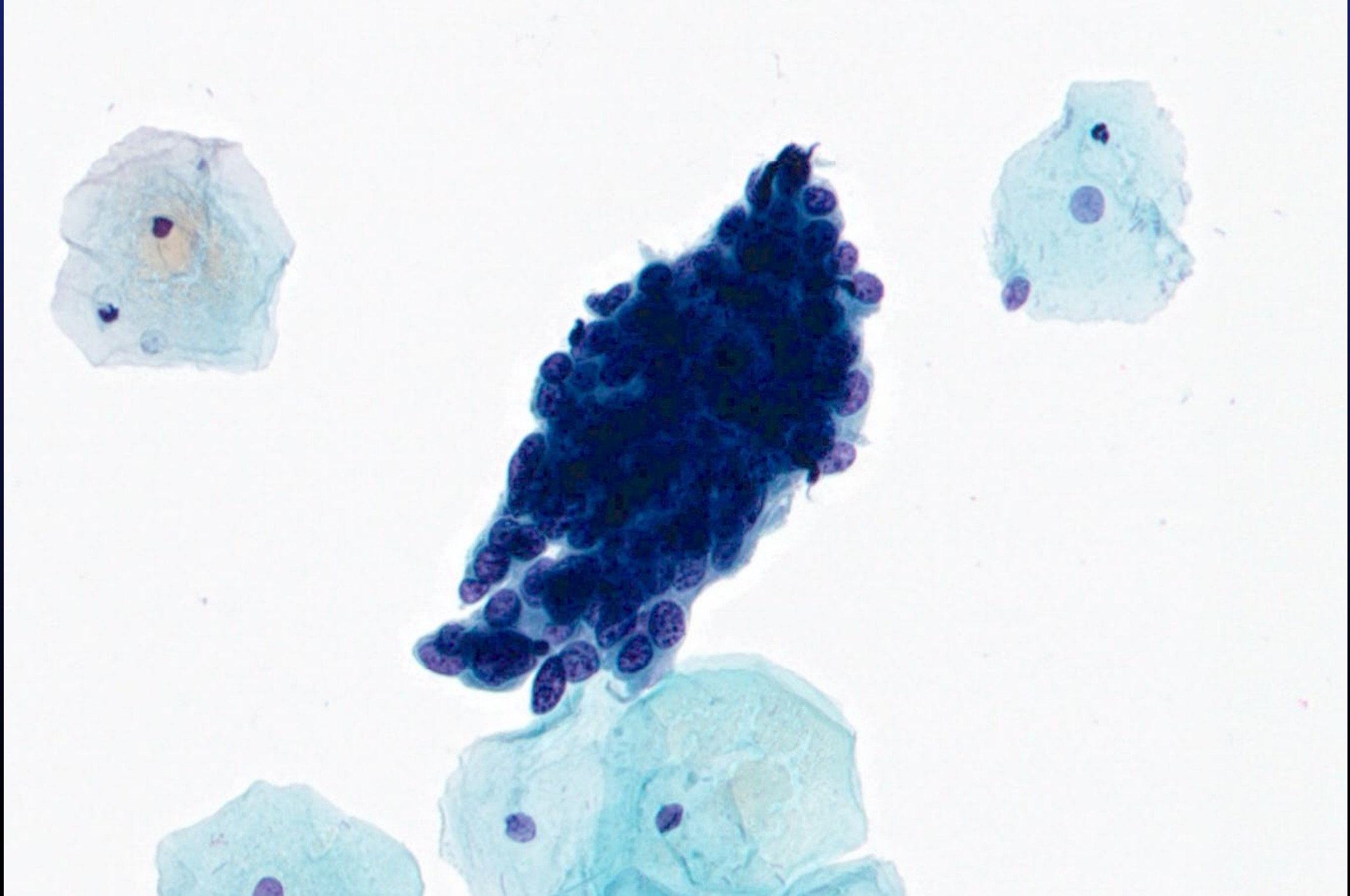
## Abnormal Morphology – High Grade Squamous Intraepithelial Lesion (HSIL)

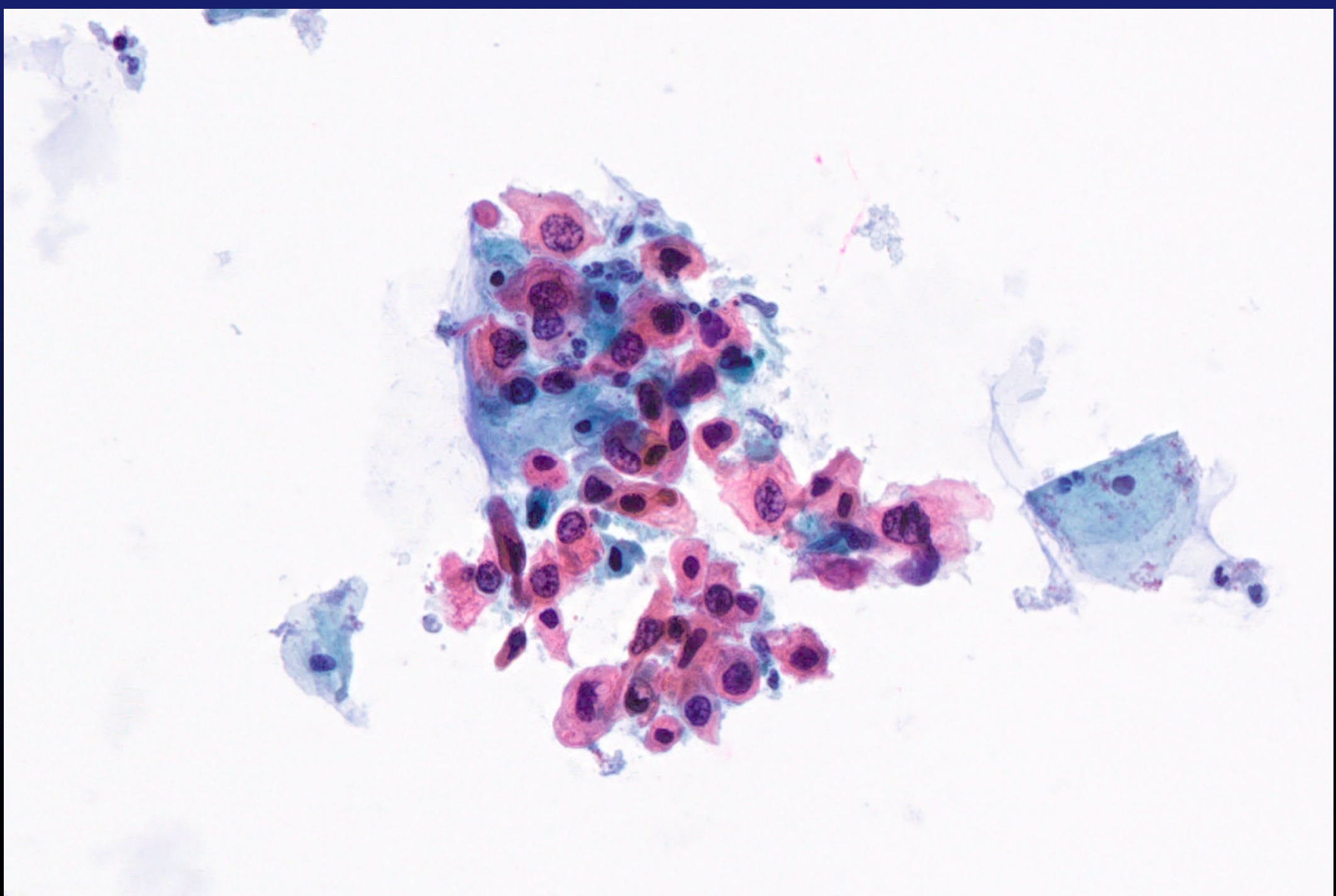
- Appear singly, in sheets, or in syncytial-like aggregates
- High N/C ratio
- Variable nuclear size
- Chromatin can be fine or coarse and evenly distributed
- May appear hyper- or hypochromatic
- Irregular nuclear membrane with frequent indentations/grooves
- Cytoplasm can appear “immature”, lacy, and delicate, densely metaplastic, or keratinized
- Nucleoli generally absent but may occasionally be seen

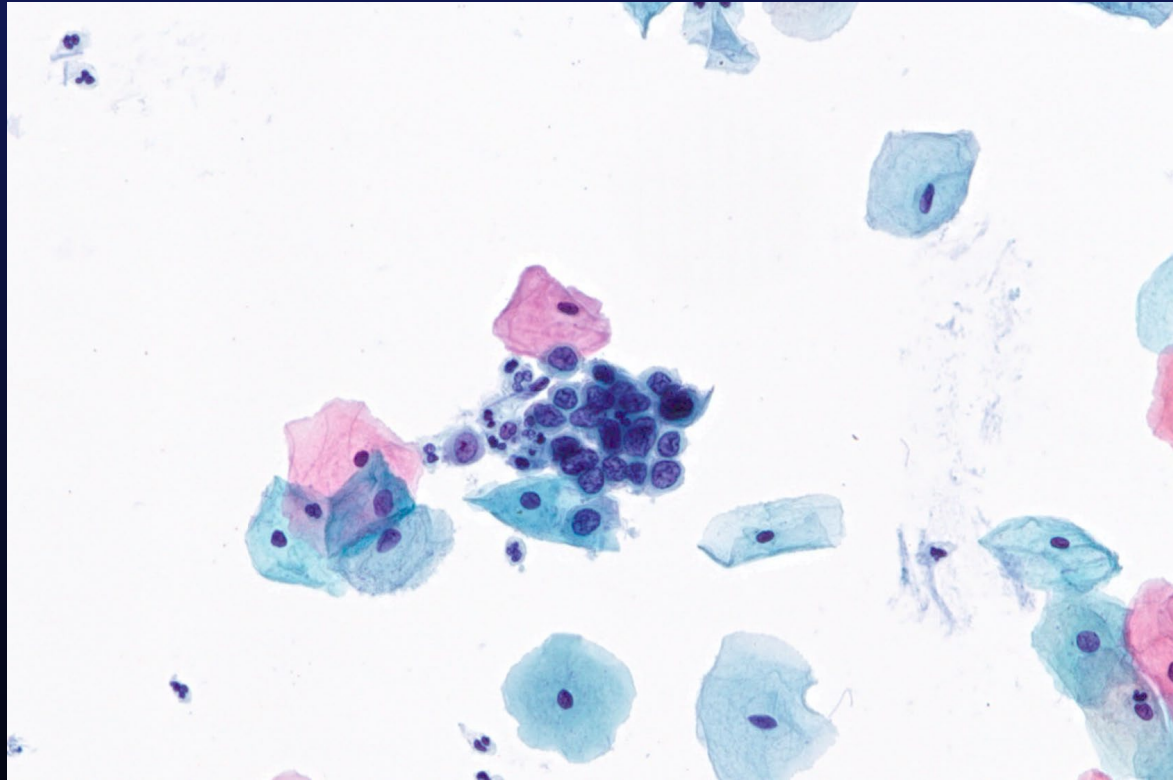




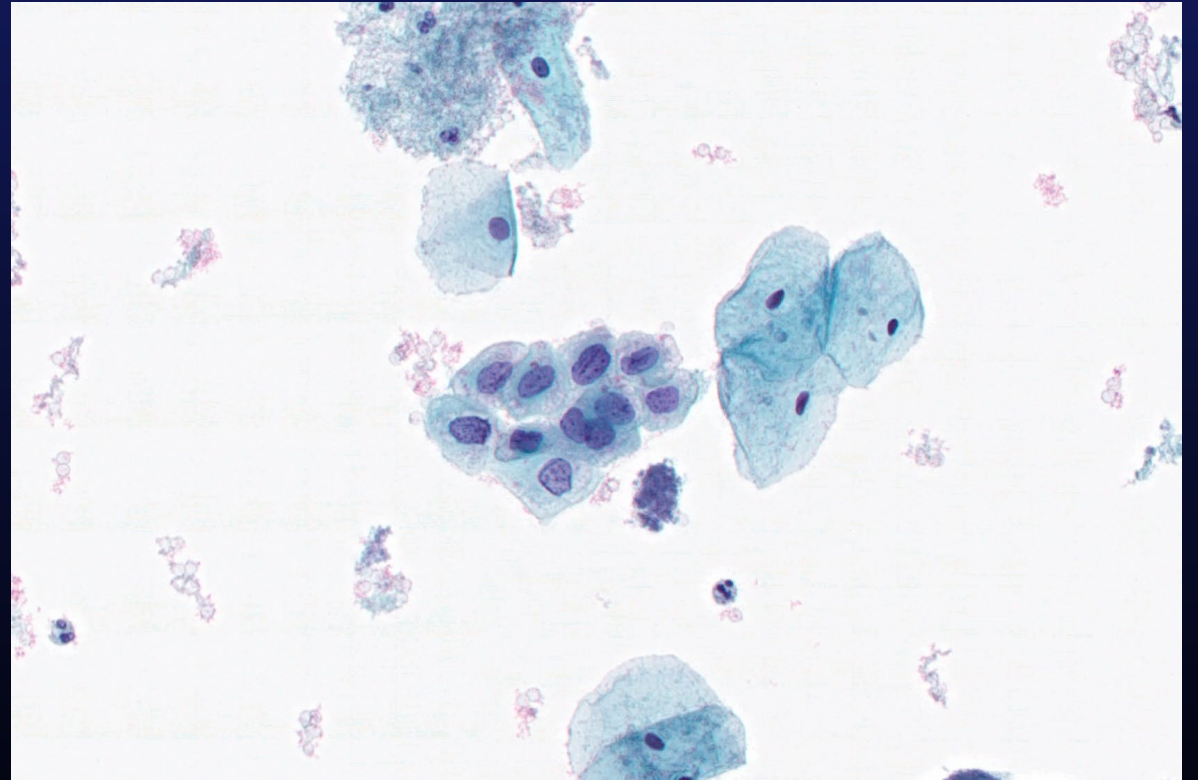




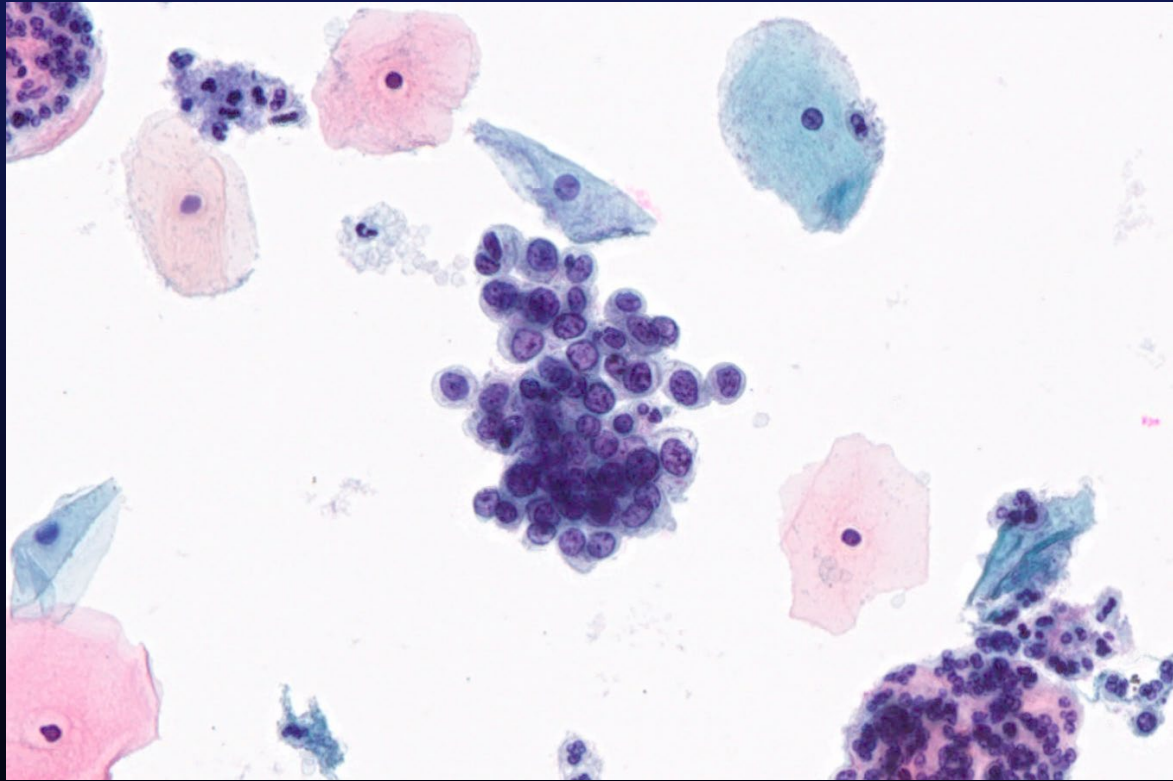




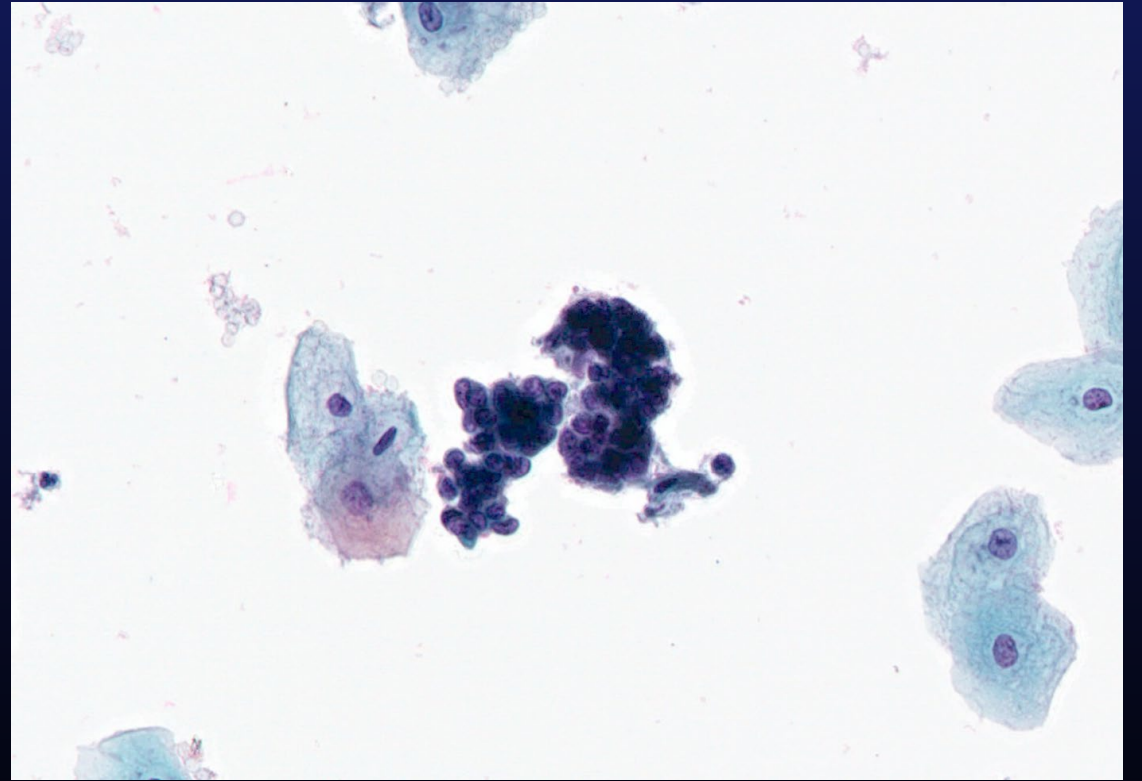
Hyperchromatic HSIL



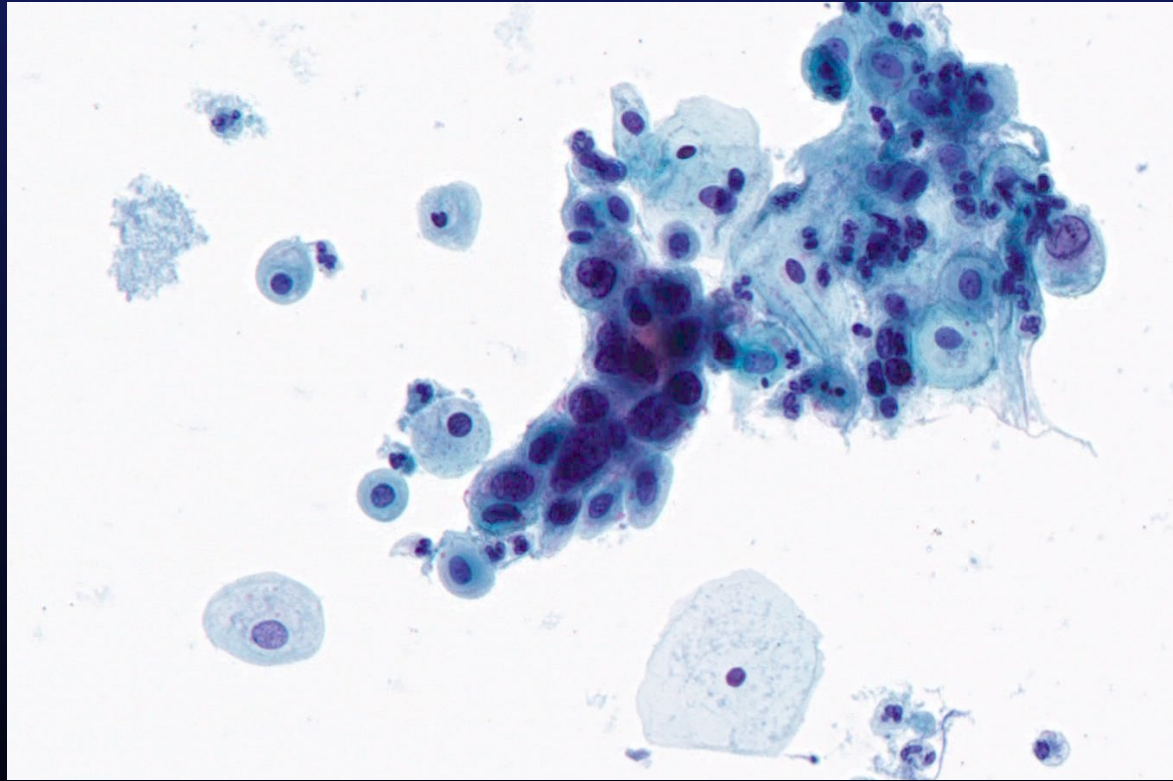
Hypochromatic HSIL



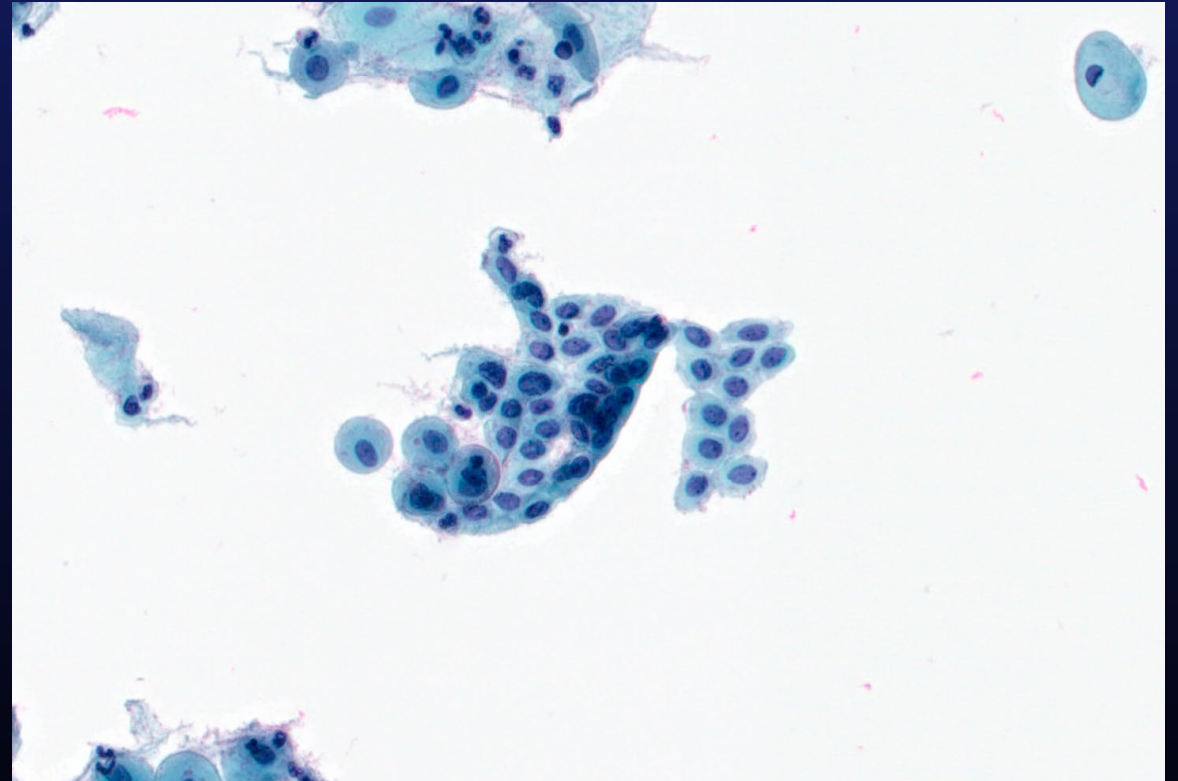
HSIL



Endometrial Cells



HSIL



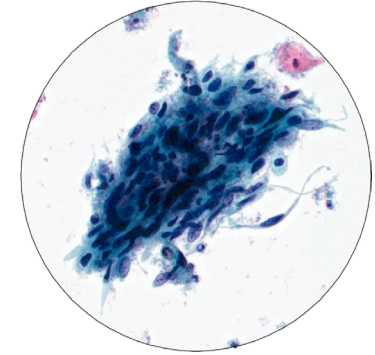
Parabasal Cells

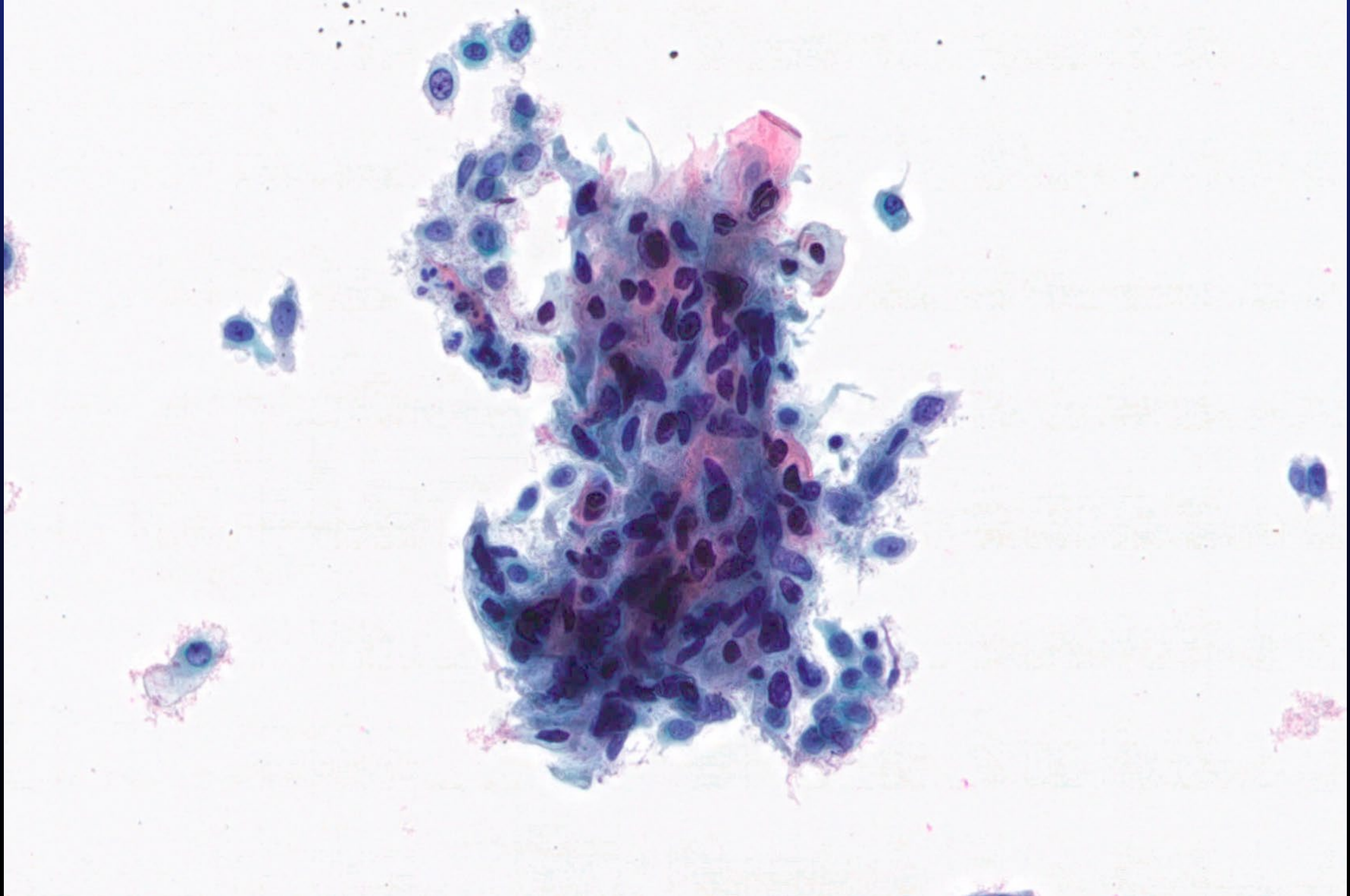


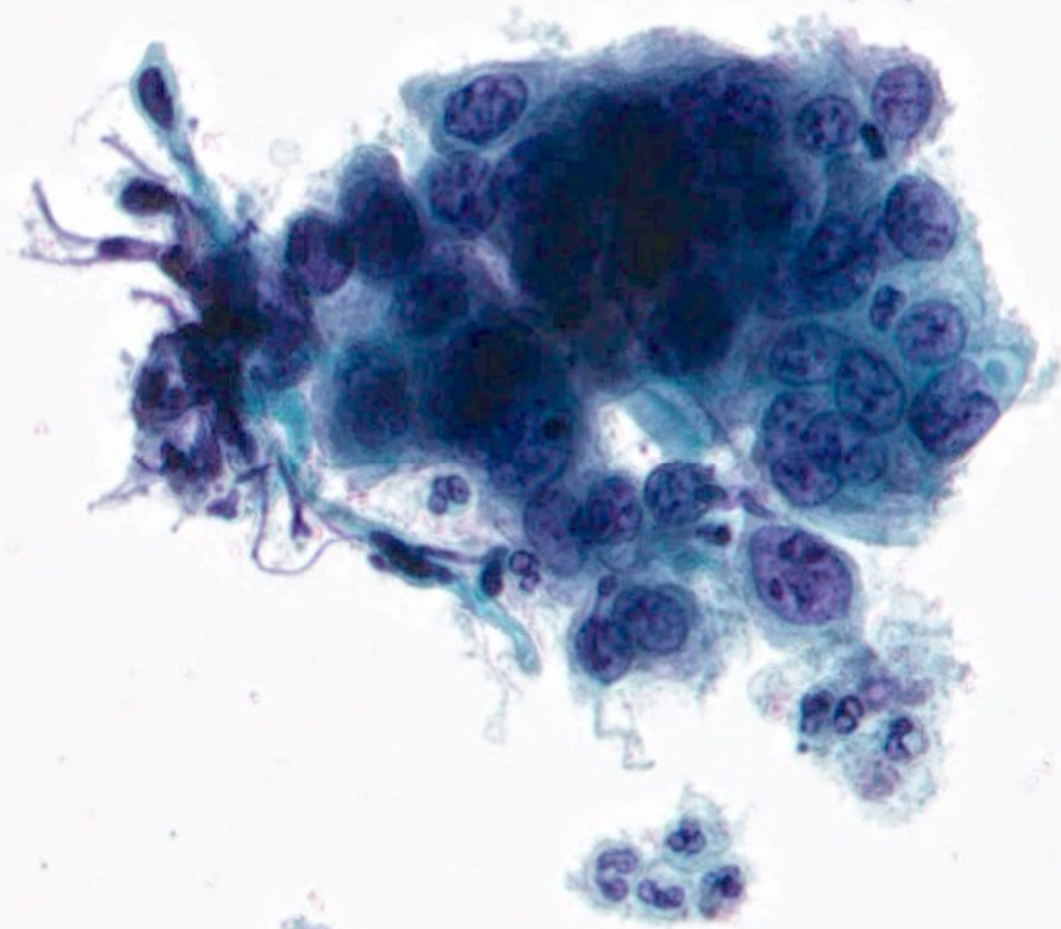
# The Bethesda System for Reporting Cervical Cytology

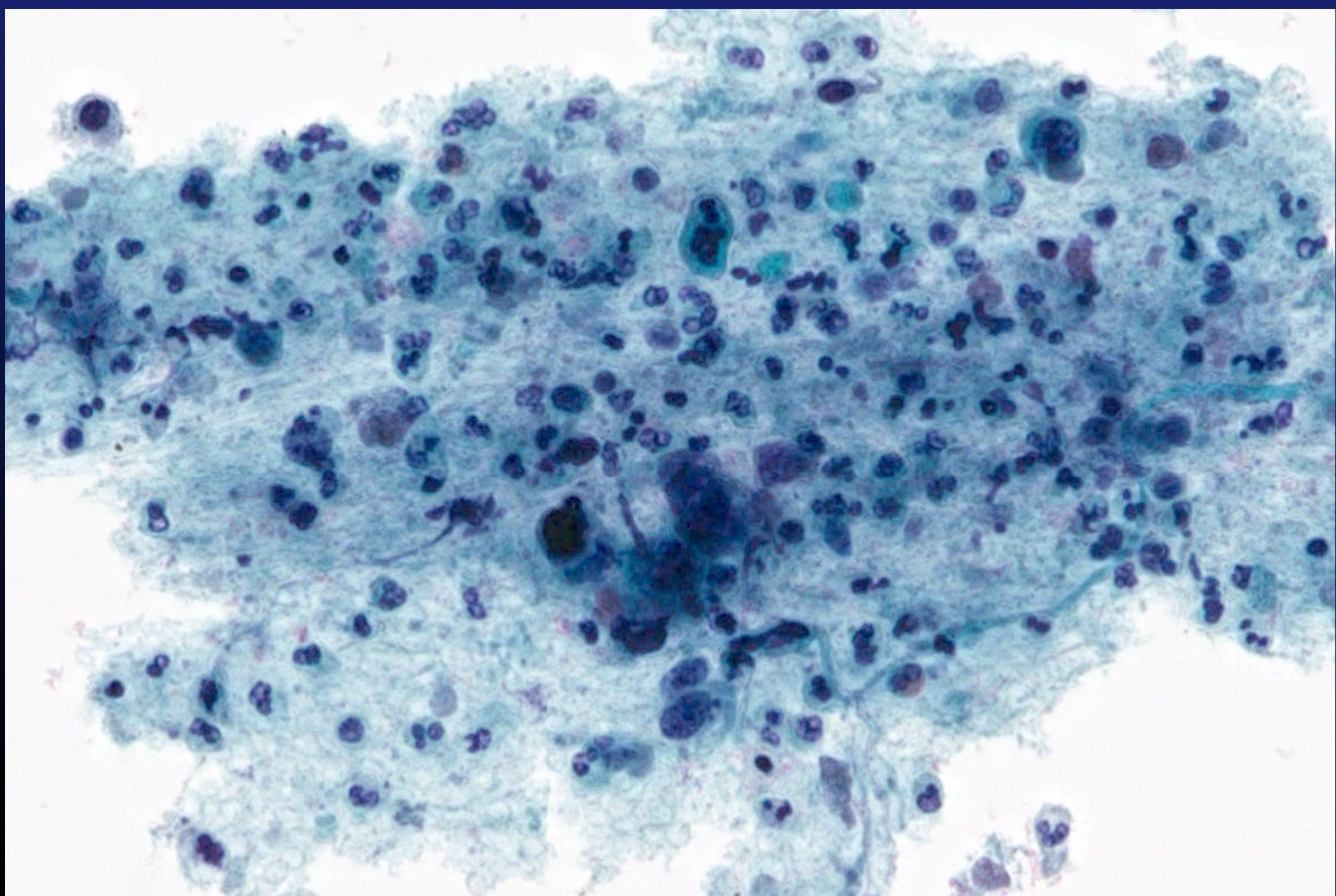
## Abnormal Morphology – Squamous Cell Carcinoma

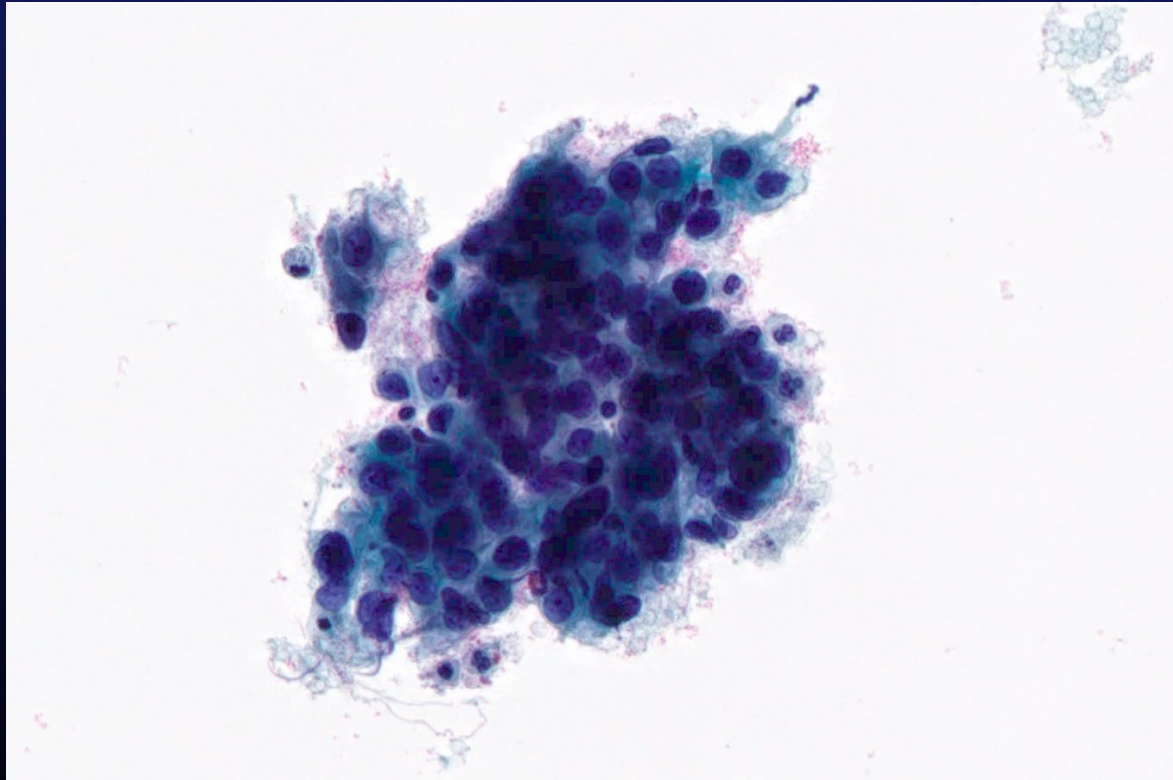
- Isolated single cells or syncytial aggregates with poorly defined cell borders
- Nuclei vary markedly in size and shape and may be densely opaque
- Irregular nuclear membranes
- Chromatin may appear coarsely granular, irregularly distributed with chromatin clearing
- Nucleoli may be prominent, but less common in Keratinizing Squamous Cell Carcinoma
- Caudate/spindle cells
- May be keratinized
- Tumor diathesis



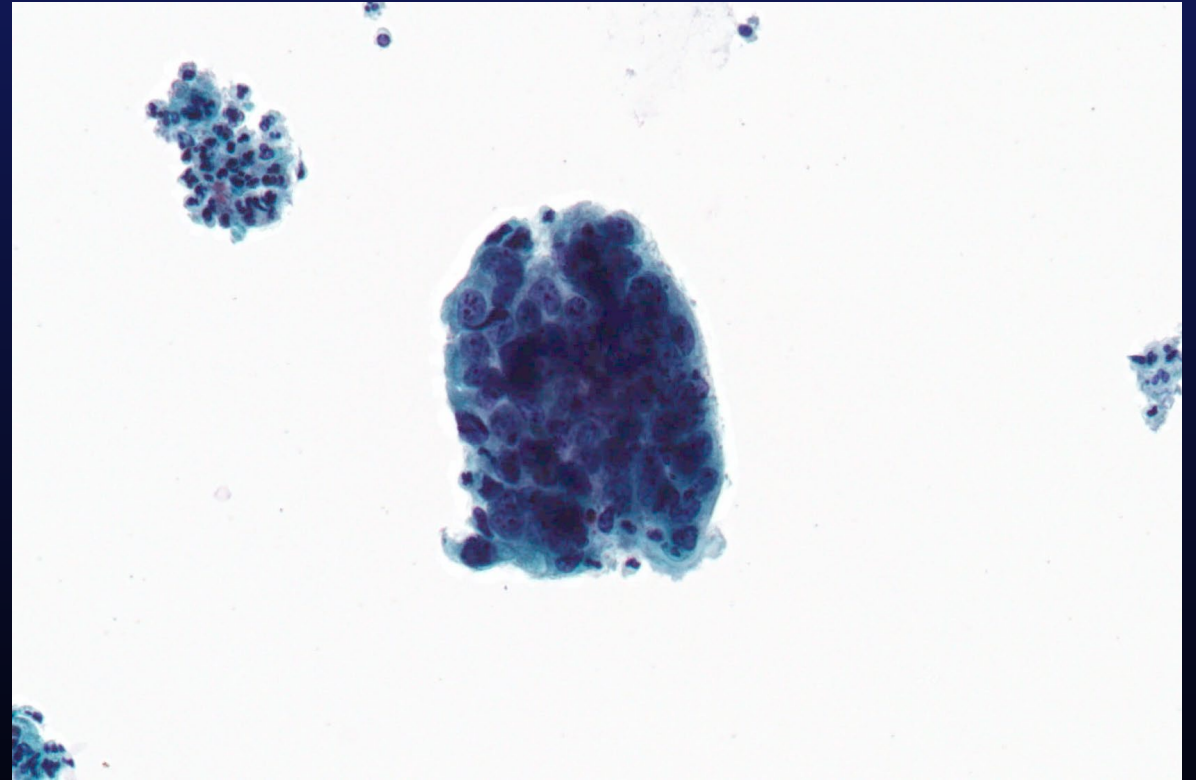








Non-Keratinizing Squamous Cell Carcinoma

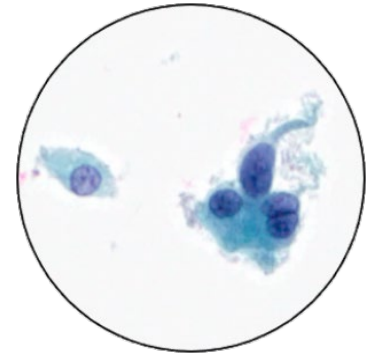


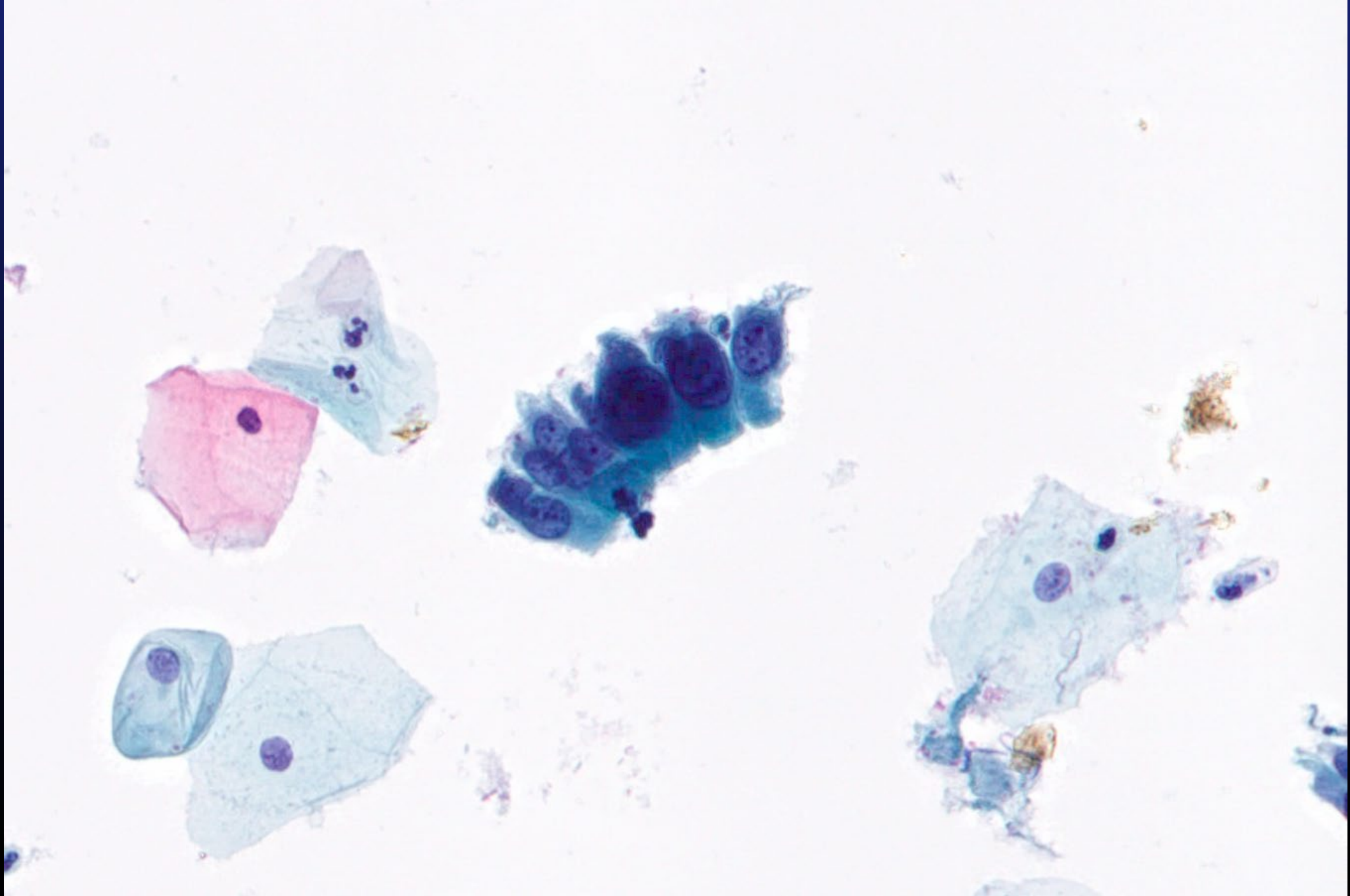
Endocervical Adenocarcinoma

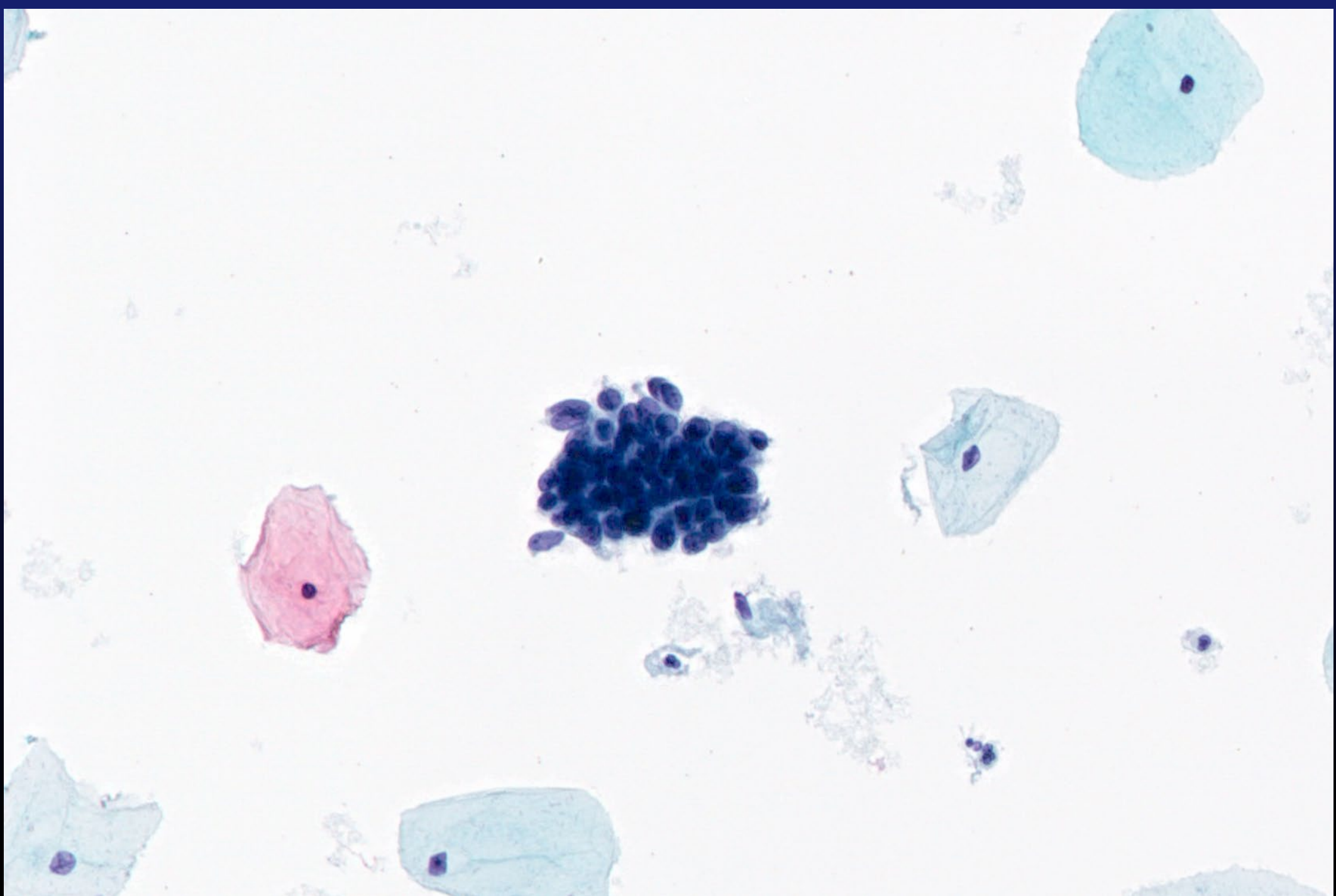
# The Bethesda System for Reporting Cervical Cytology

## Abnormal Morphology – Atypical Endocervical Cells, NOS

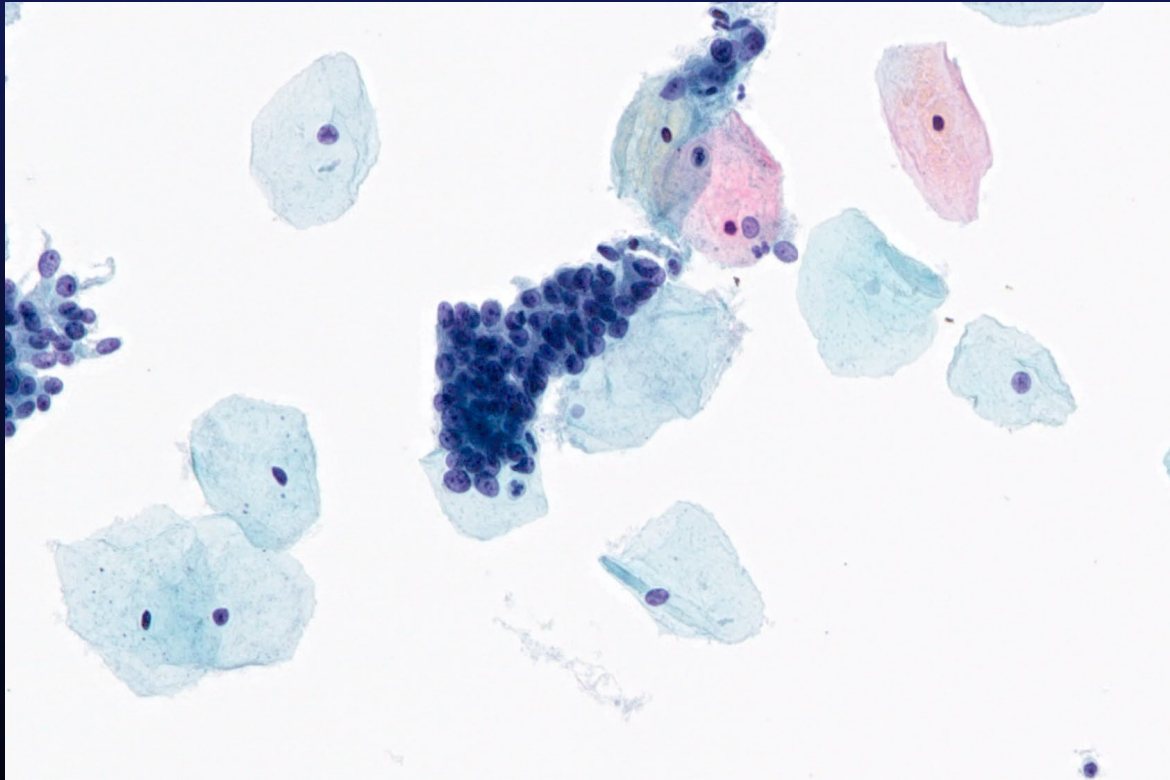
- Sheets, strips and/or 3-dimensional clusters with cell crowding, nuclear overlap and/or pseudostratification
- Slight variation in nuclear size and shape
- Nuclear enlargement, up to 3 to 5 times normal
- Mild nuclear hyperchromasia and chromatin irregularity
- Occasional nucleoli
- Cytoplasm may be abundant with distinct cell borders



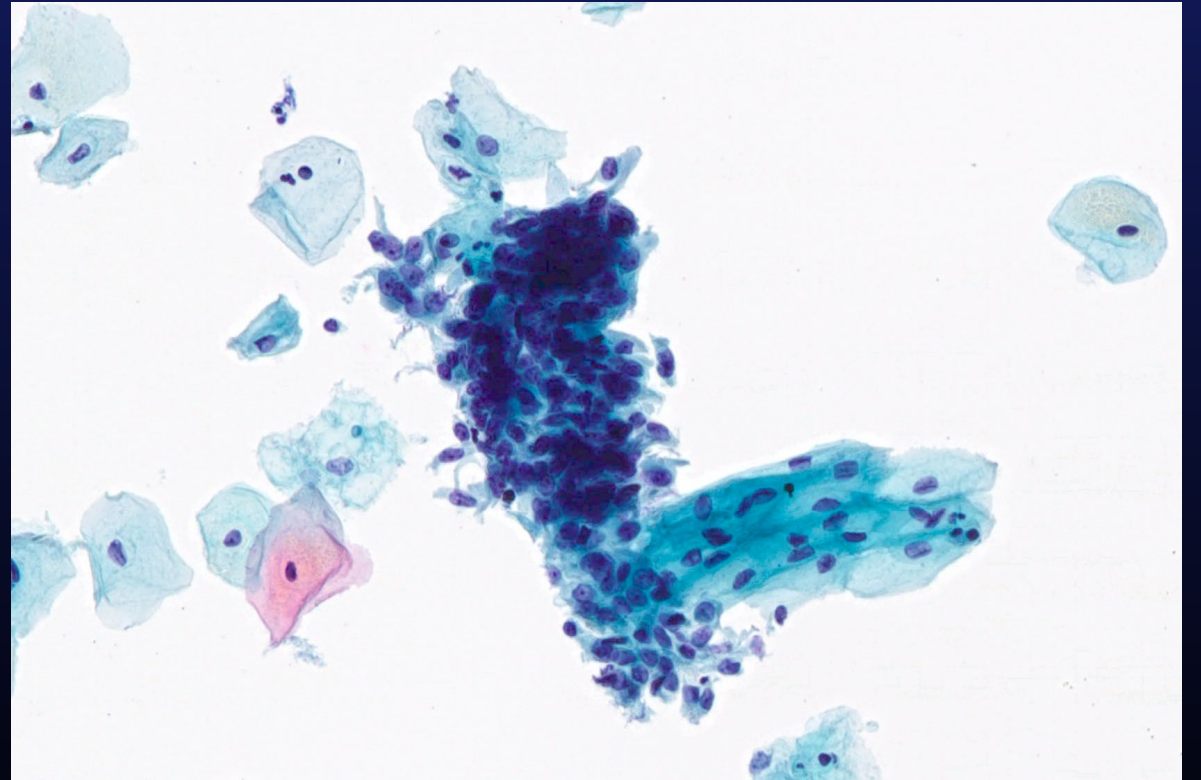




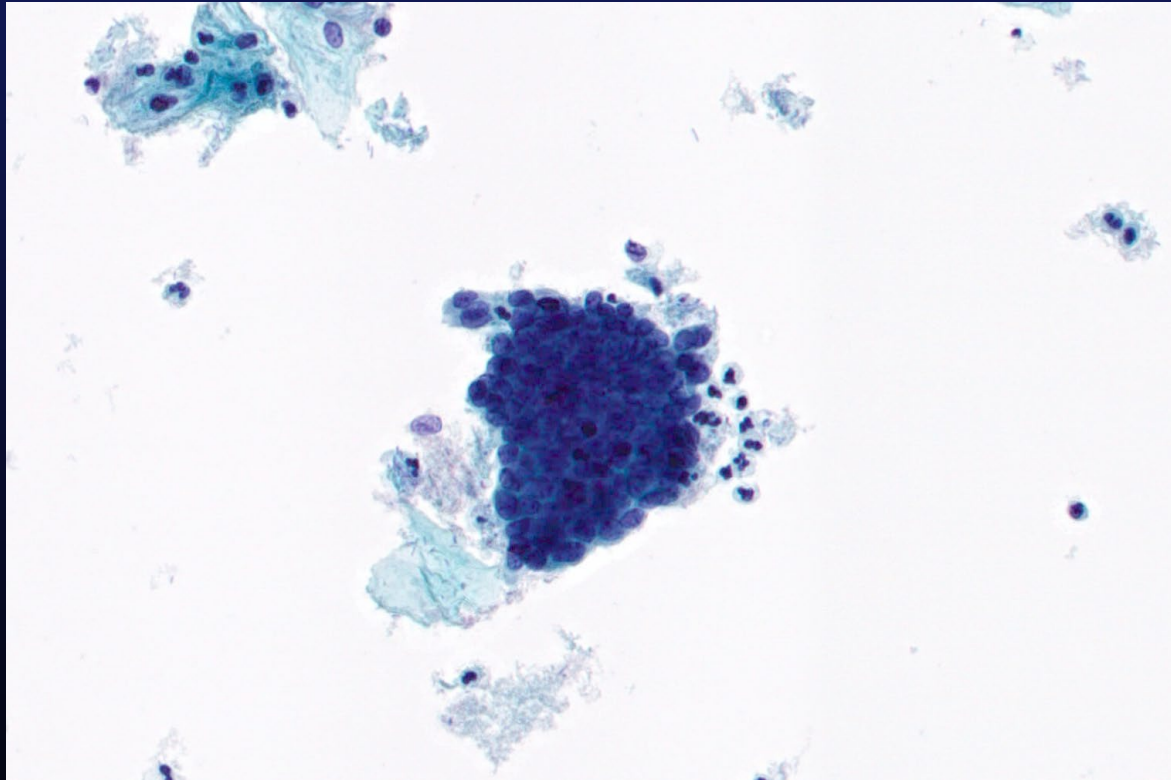




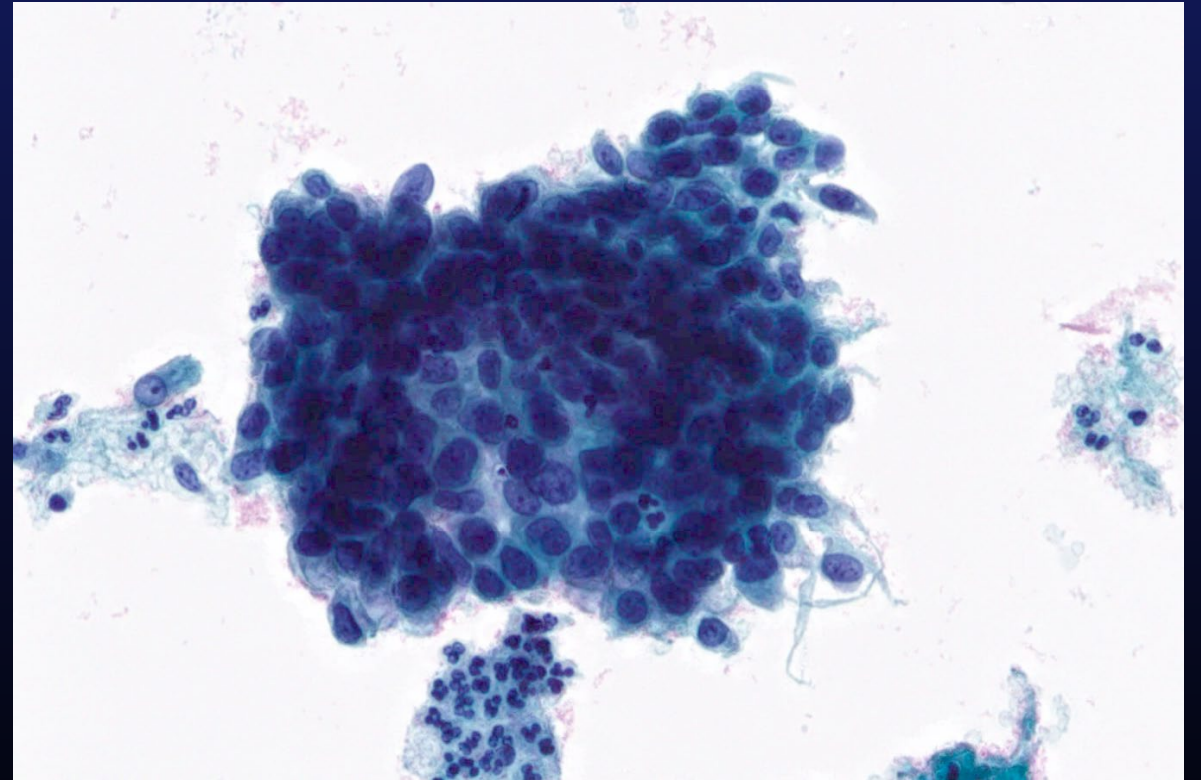
AGC Endocervical, NOS



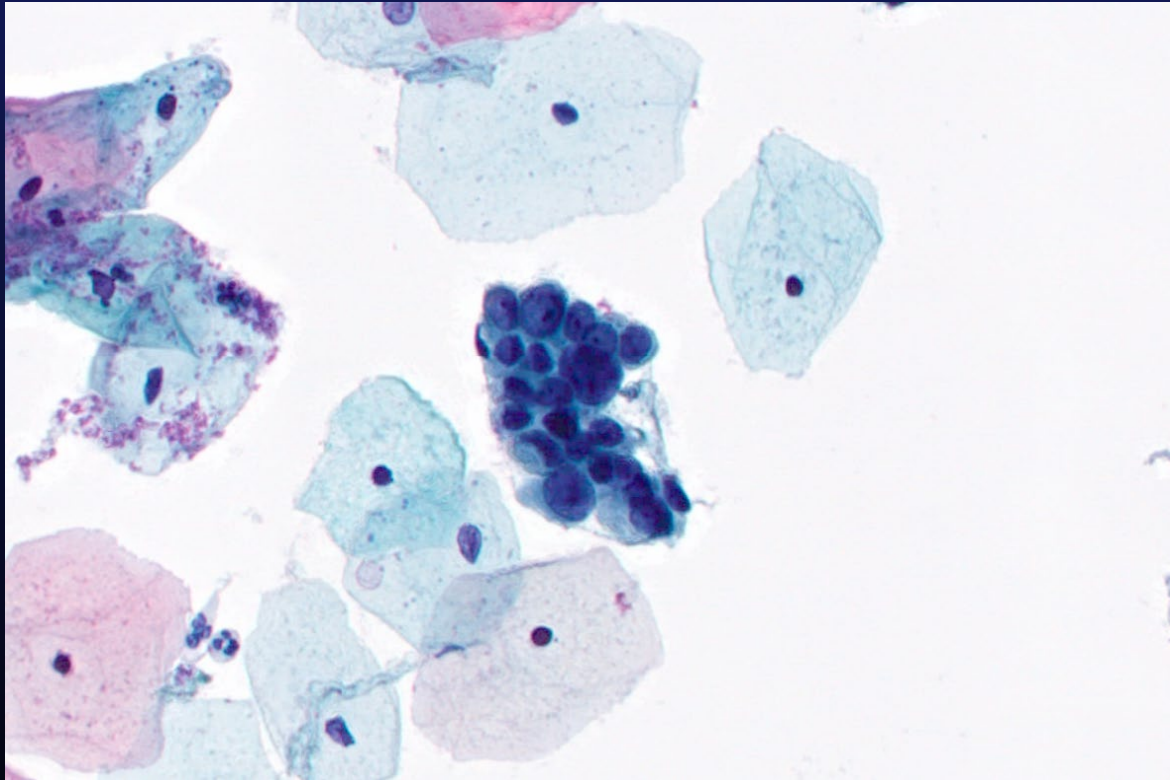
Reactive Endocervical Cells



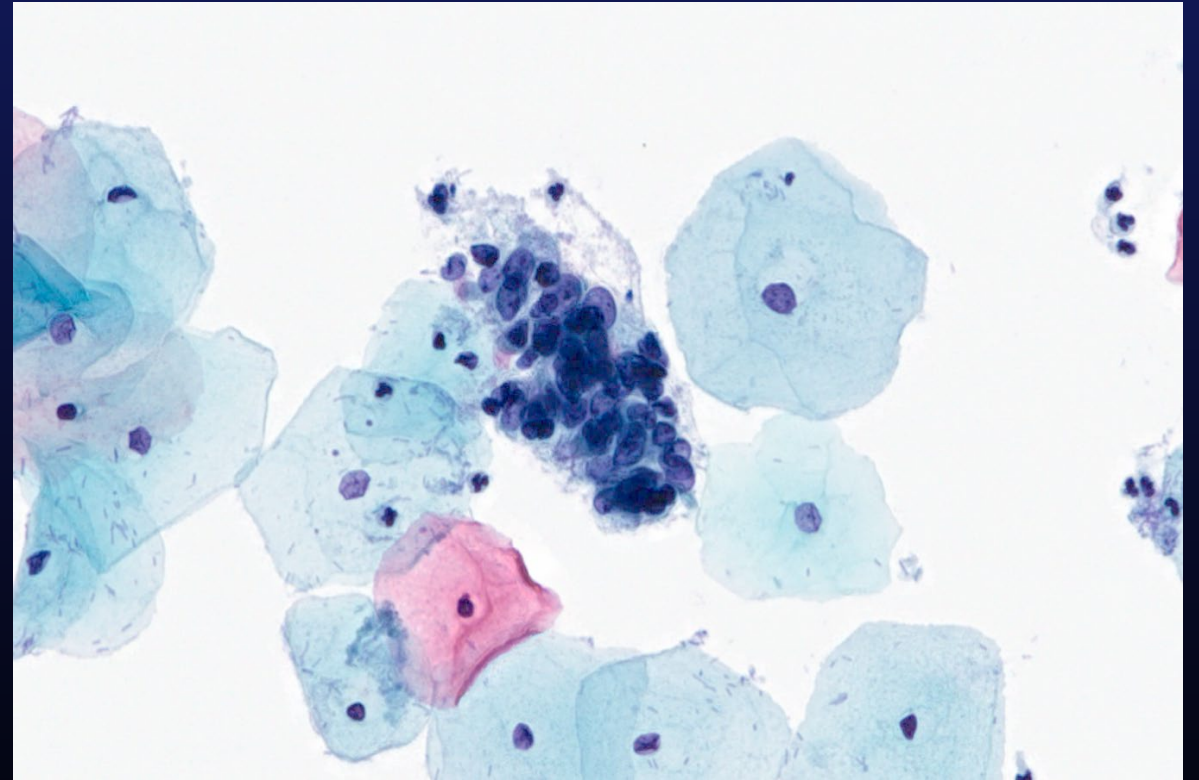
AGC Endocervical, NOS



HSIL with Glandular Involvement



AGC Endocervical, NOS

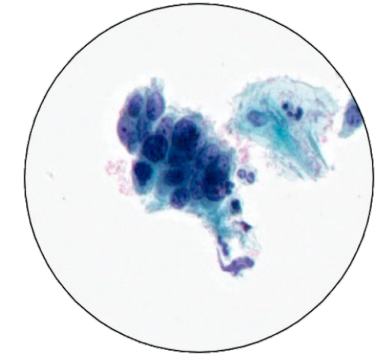


Tubal Metaplasia

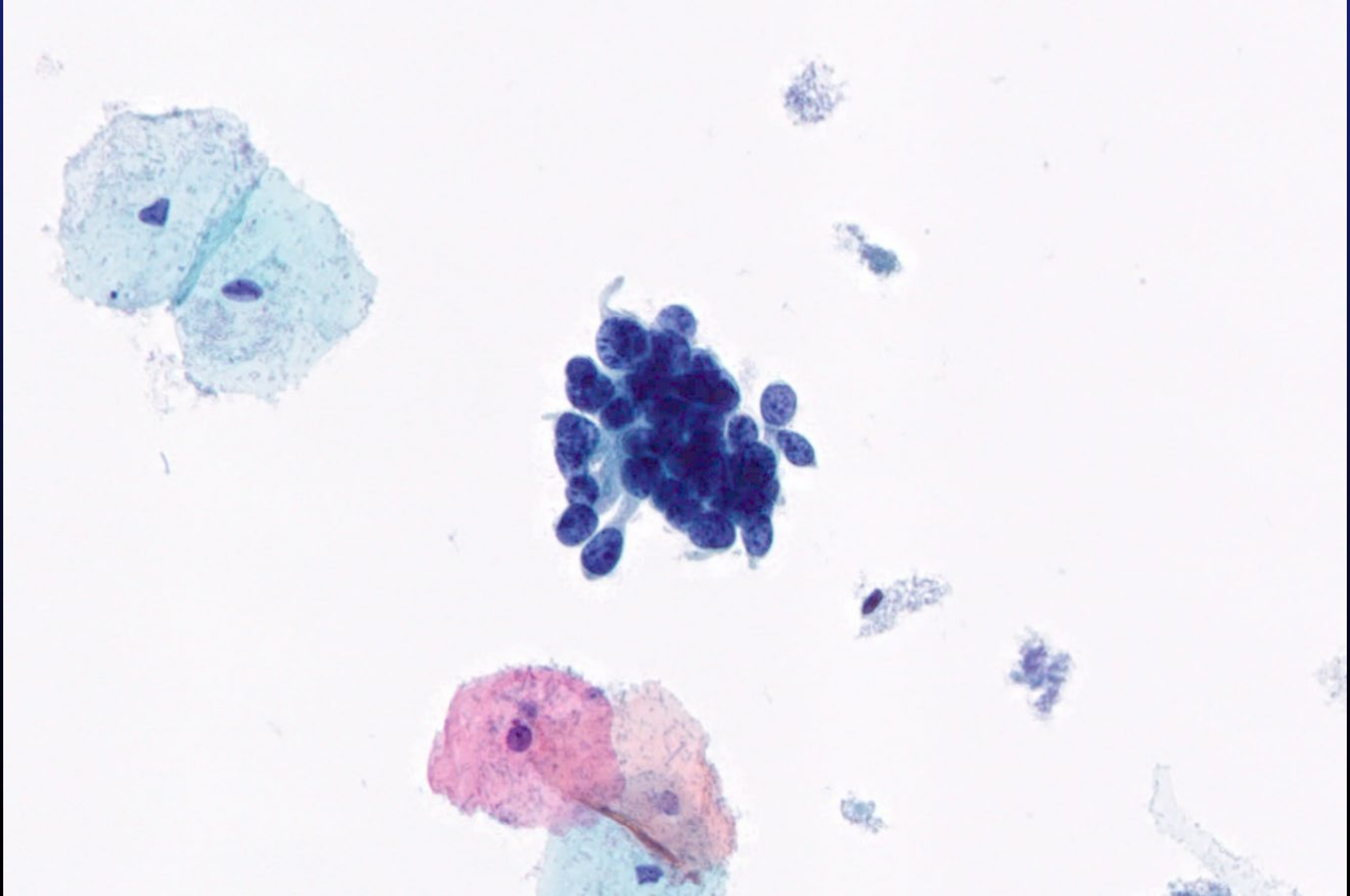
# The Bethesda System for Reporting Cervical Cytology

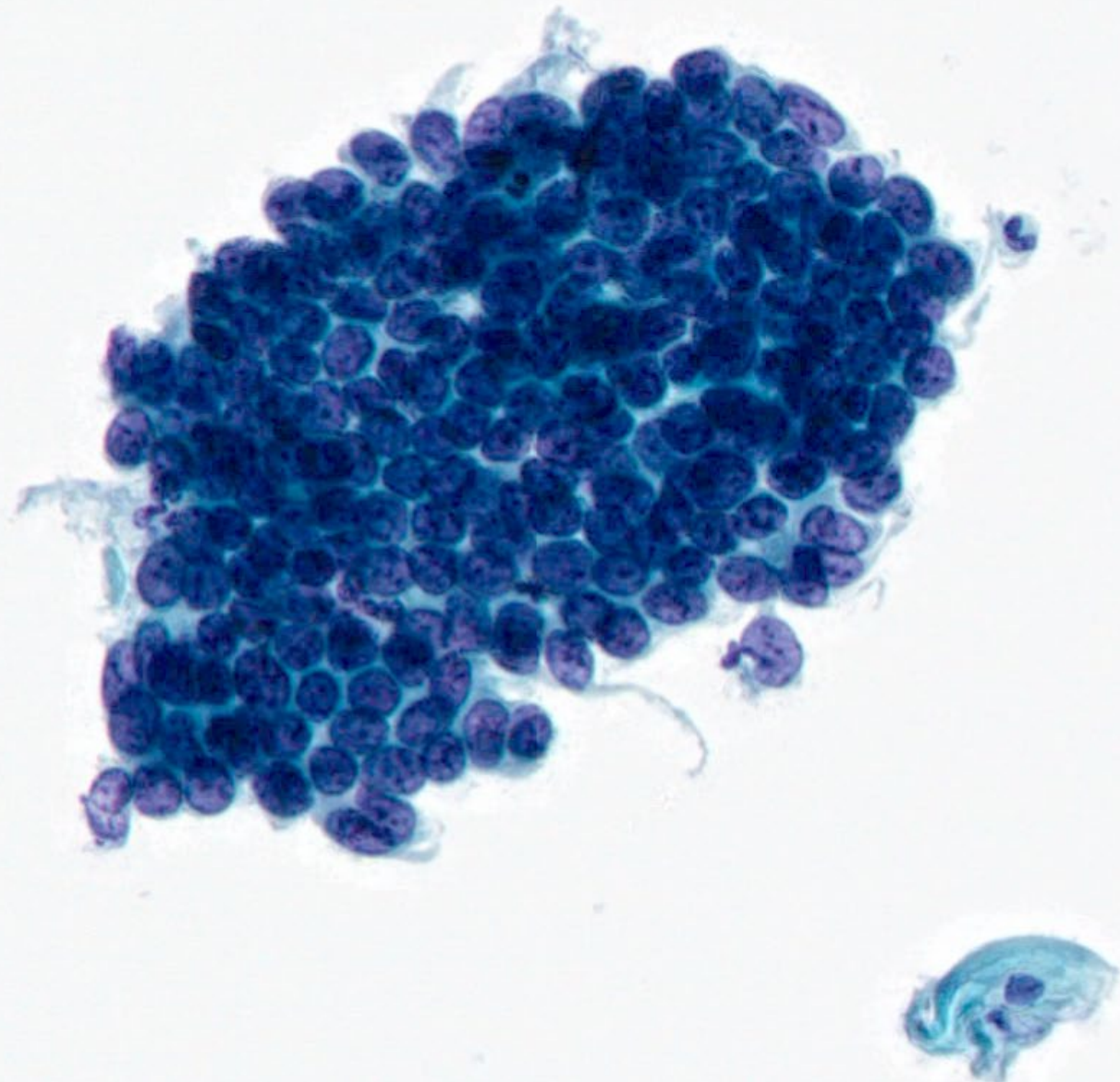
## Abnormal Morphology – Atypical Endocervical Cells, Favor Neoplastic

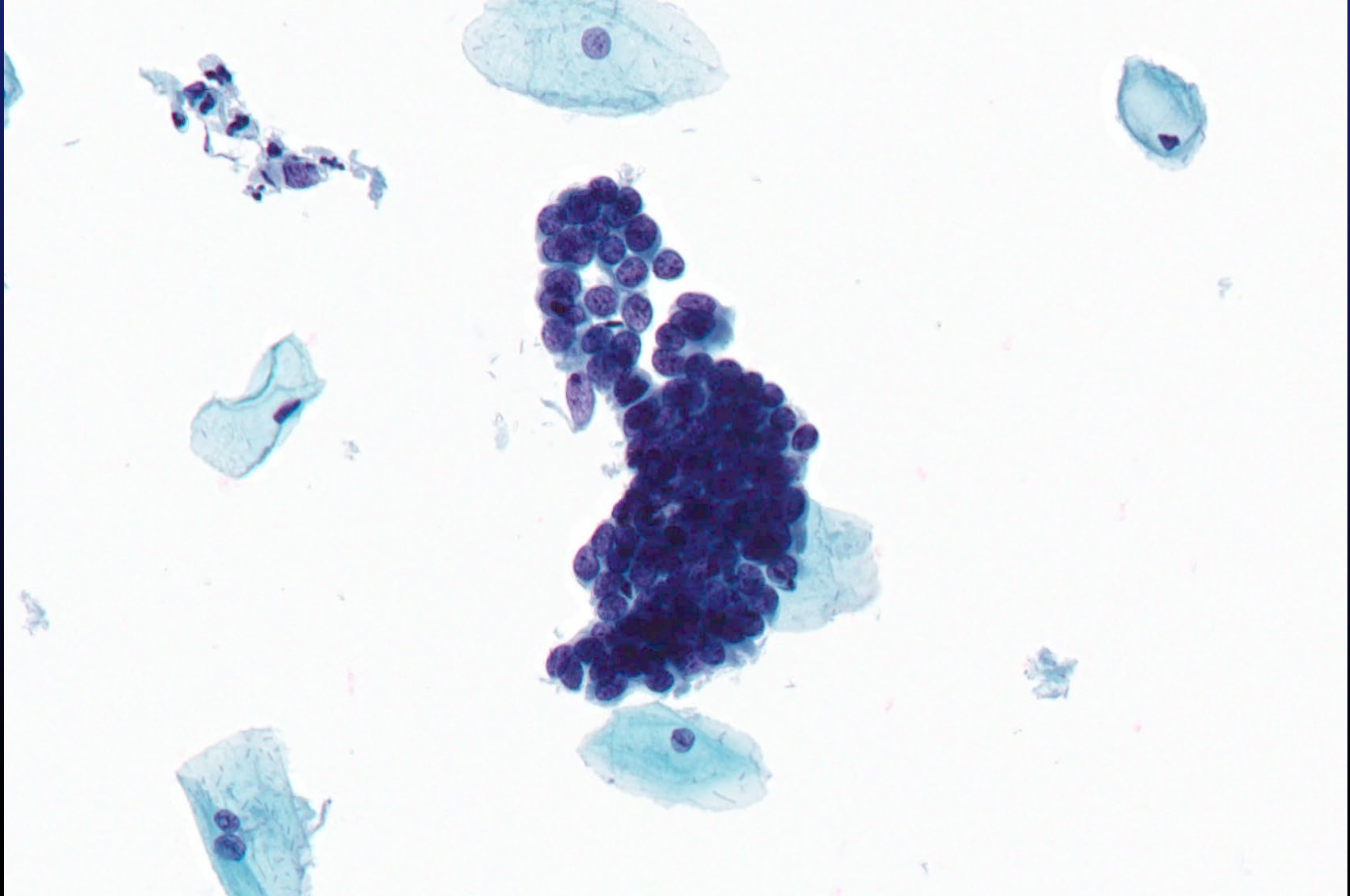
- Appear in sheets and strips with nuclear crowding, overlap, and/or pseudostratification
- Rare cell groups with rosettes or feathering
- Nuclei are enlarged and often elongated with some hyperchromasia
- Variable coarse chromatin
- Increased N/C ratio
- Poorly defined cell borders

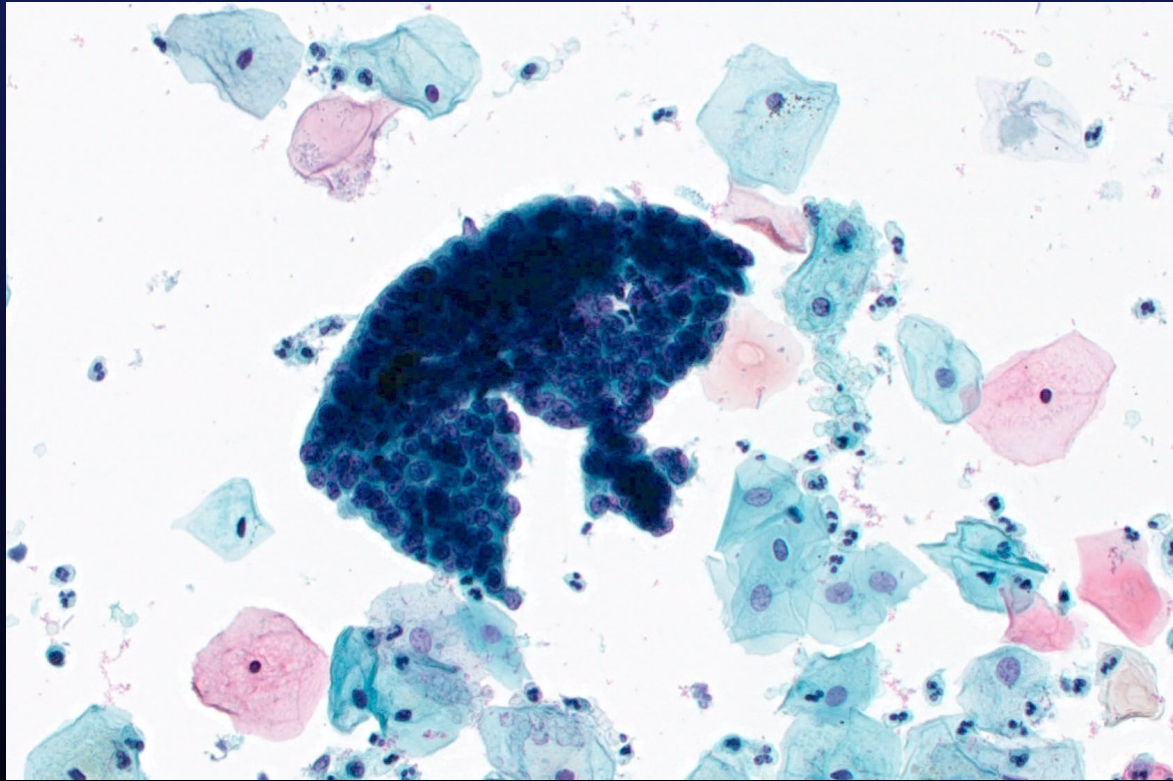


**CRITERIA INSUFFICIENT FOR AIS OR INVASIVE ADENOCARCINOMA**

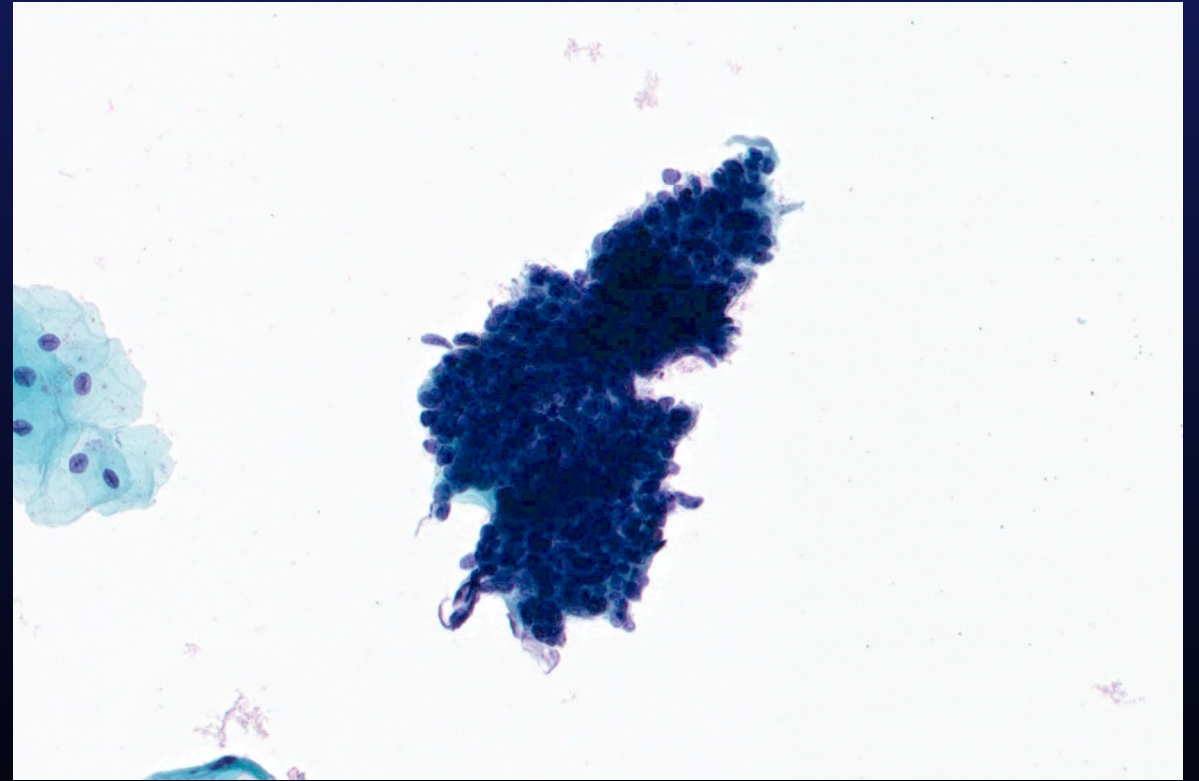








AGC Endocervical, Favor Neoplasia



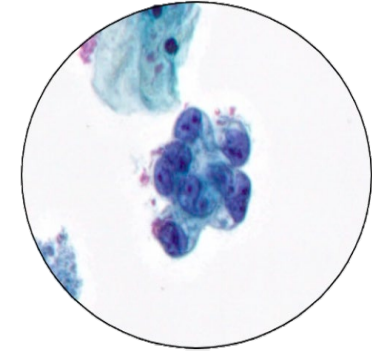
Lower Uterine Segment (LUS)



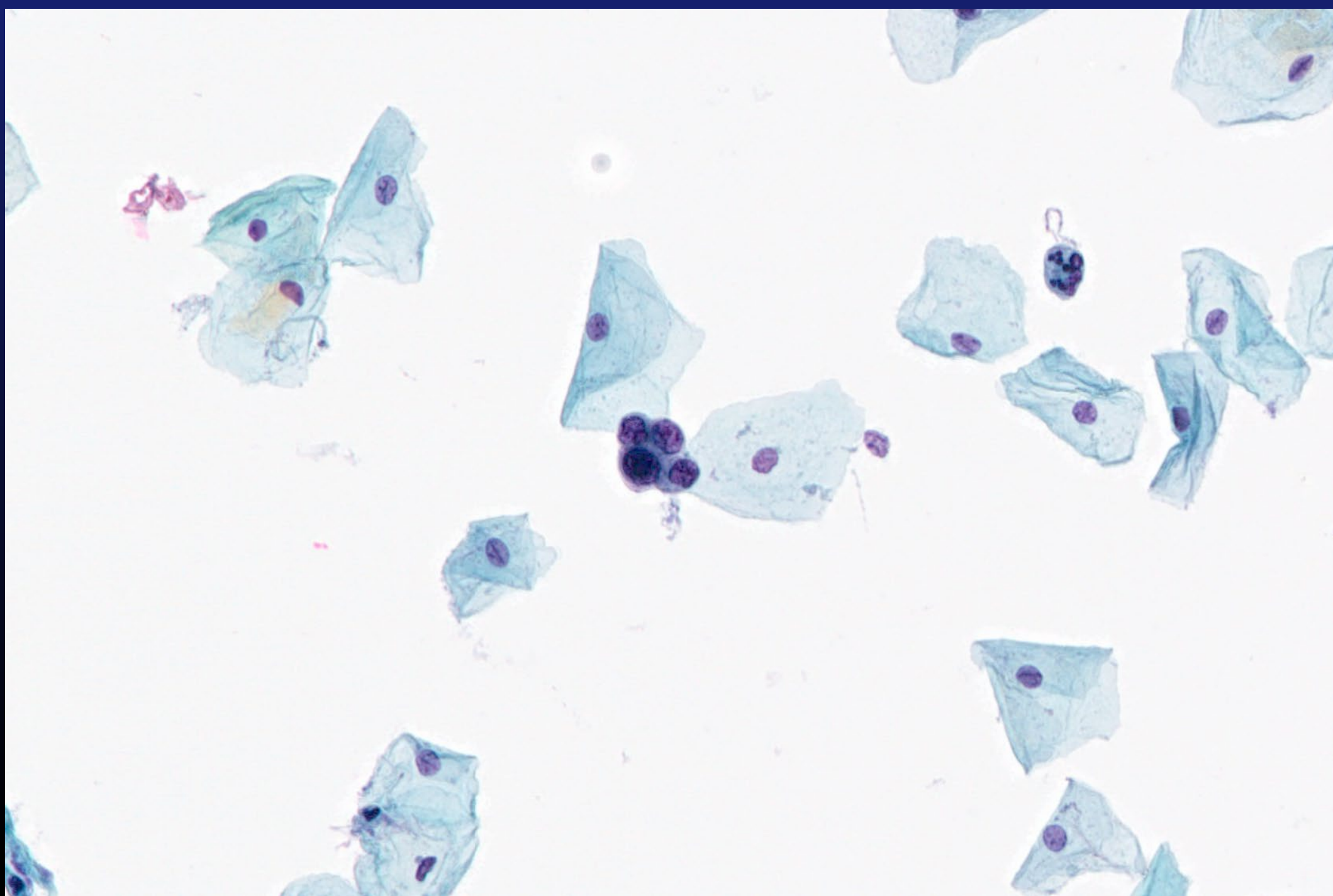
# The Bethesda System for Reporting Cervical Cytology

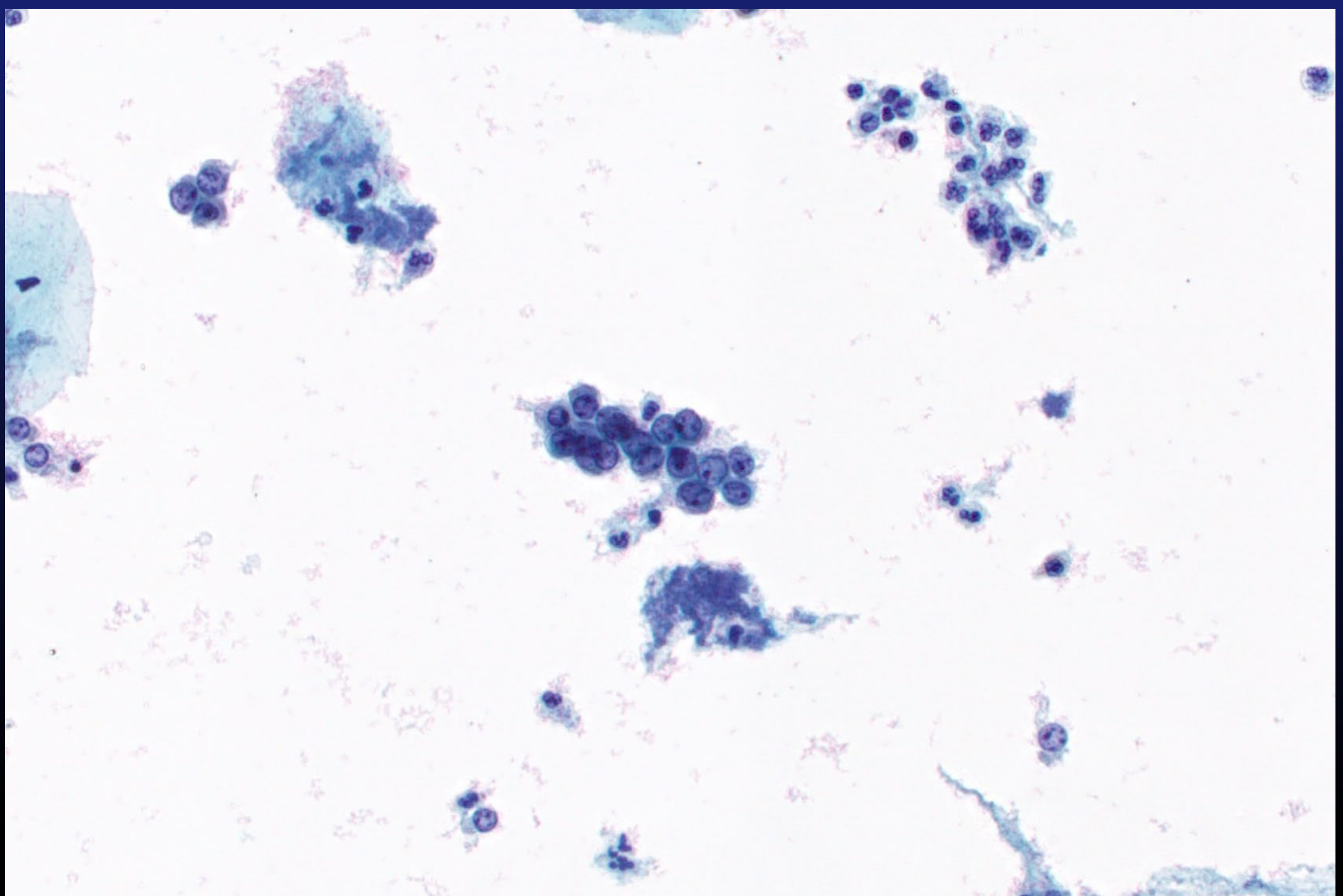
## Abnormal Morphology – Atypical Endometrial Cells

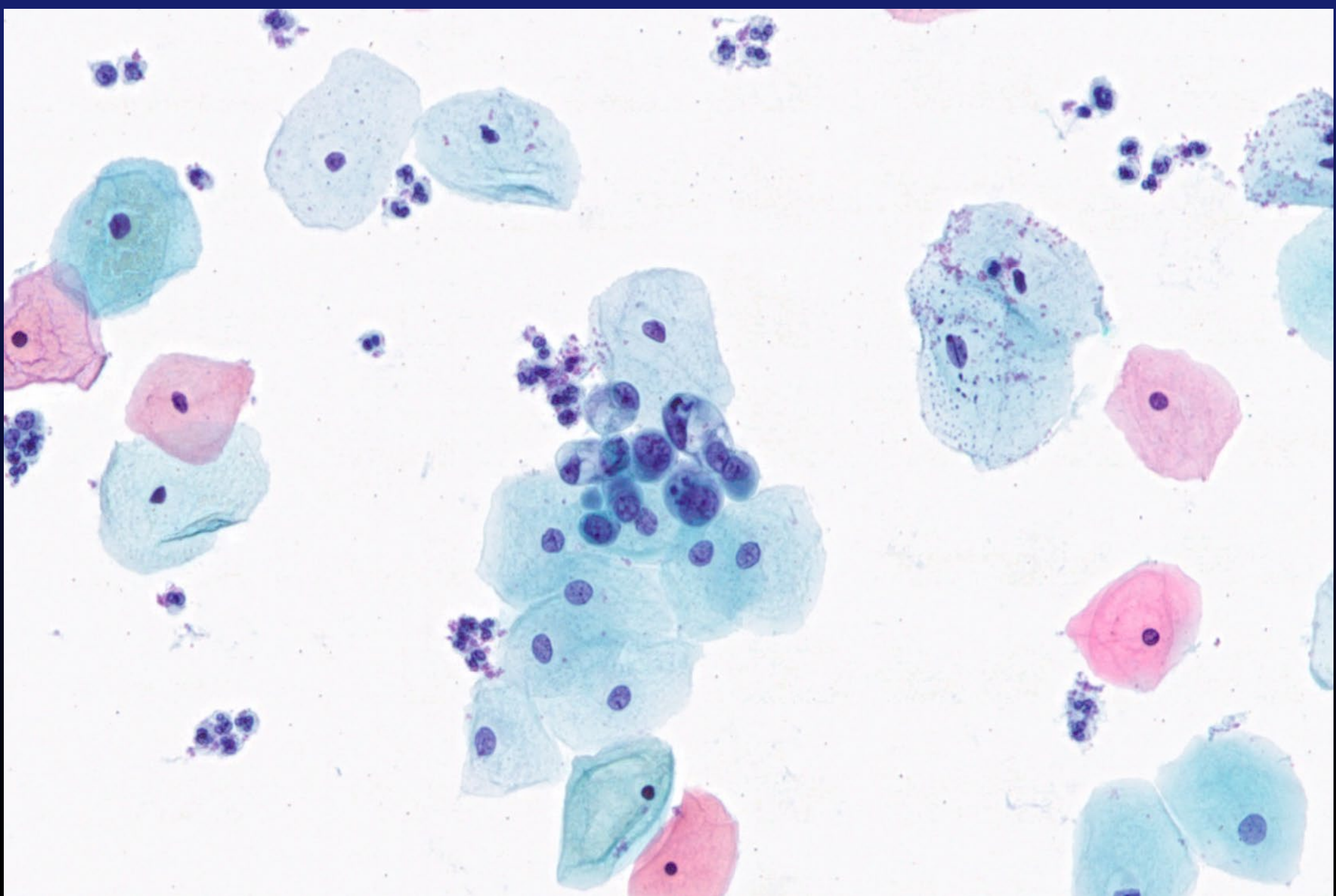
- Small 3-dimensional clusters (usually 5-10 cells per group)
- Nuclei are slightly enlarged compared to normal
- Chromatin variability
- Mild hyperchromasia
- Occasional small nucleoli
- Scant, vacuolated cytoplasm



**ATYPICAL ENDOMETRIAL CELLS ARE NOT FURTHER QUALIFIED**



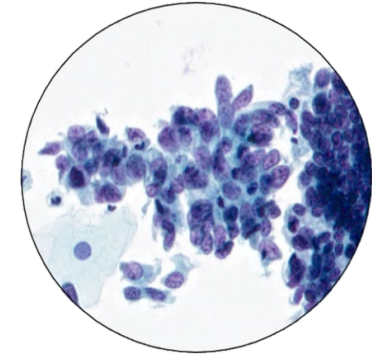


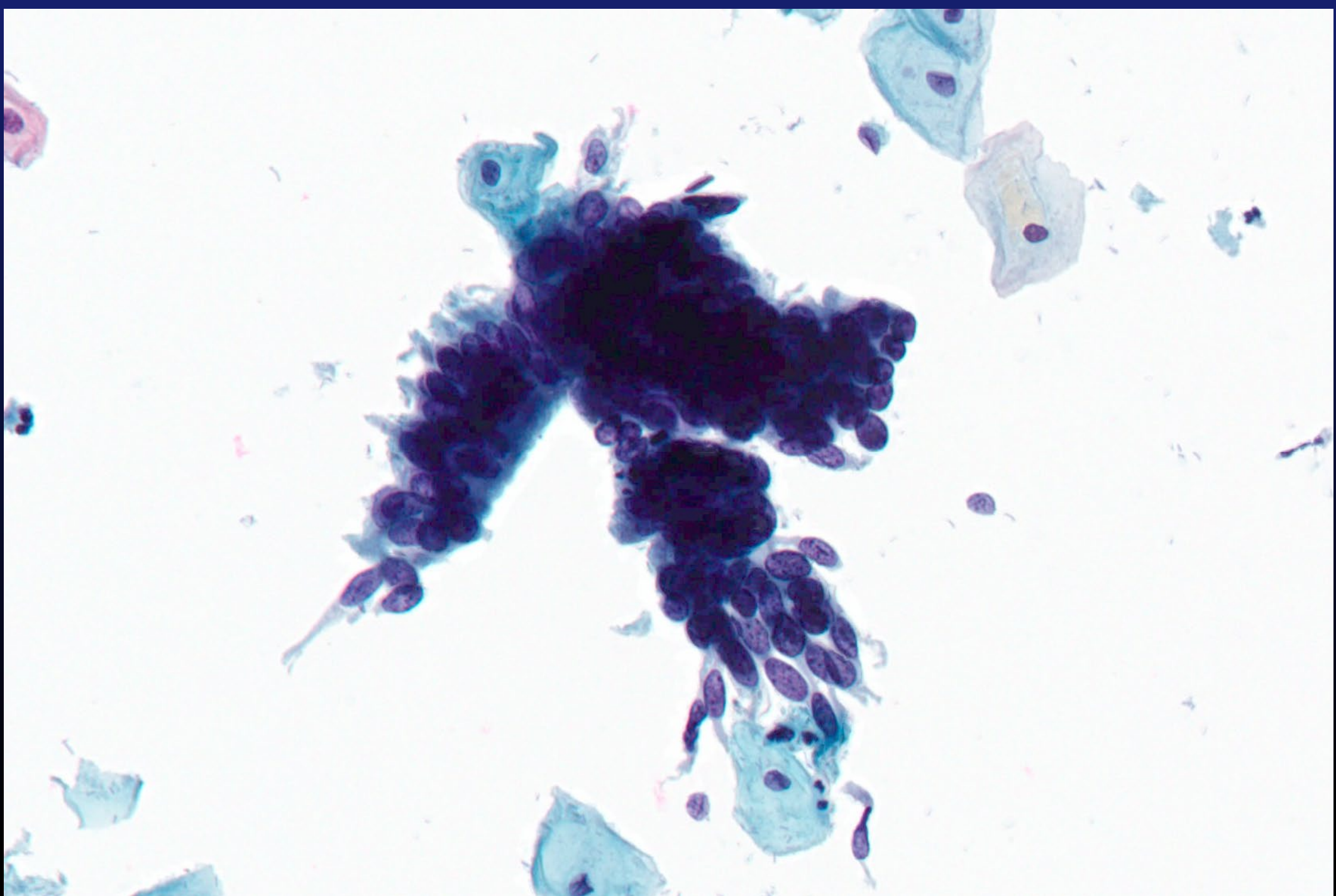


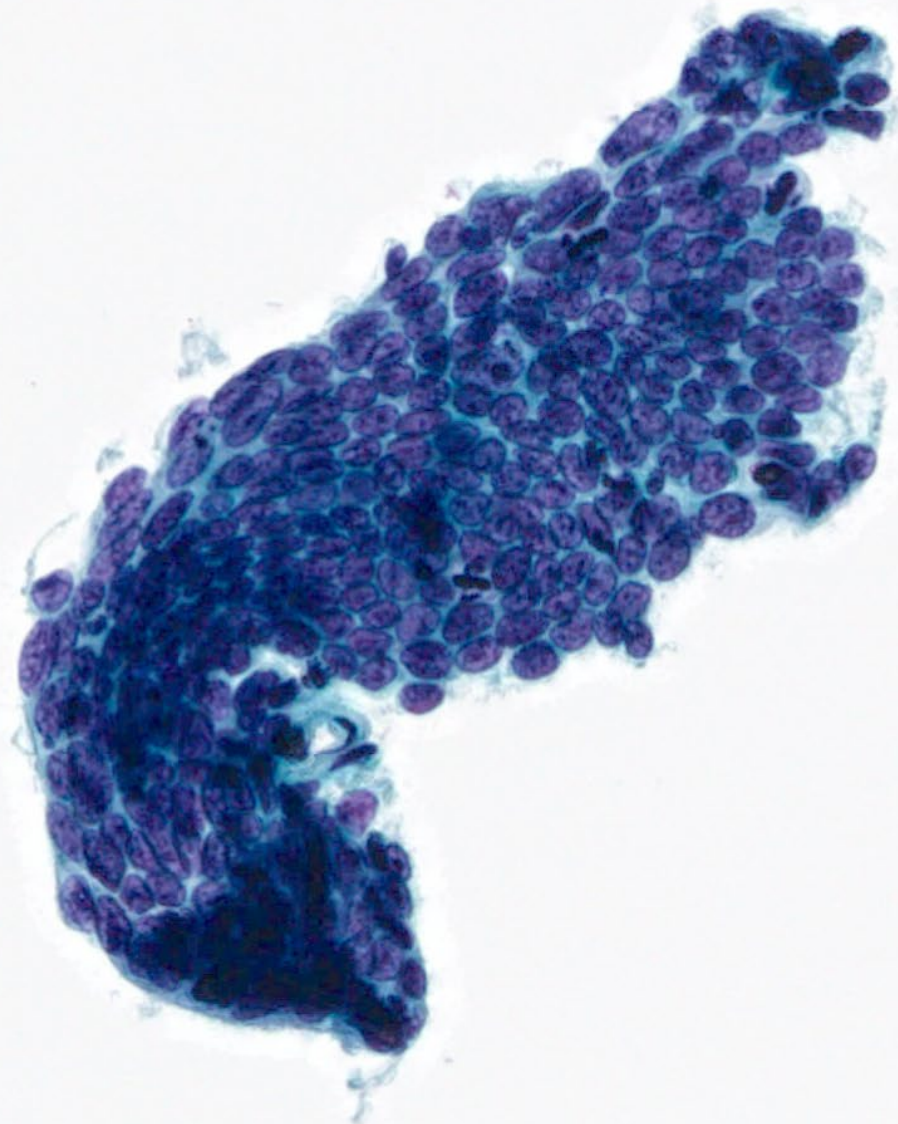
# The Bethesda System for Reporting Cervical Cytology

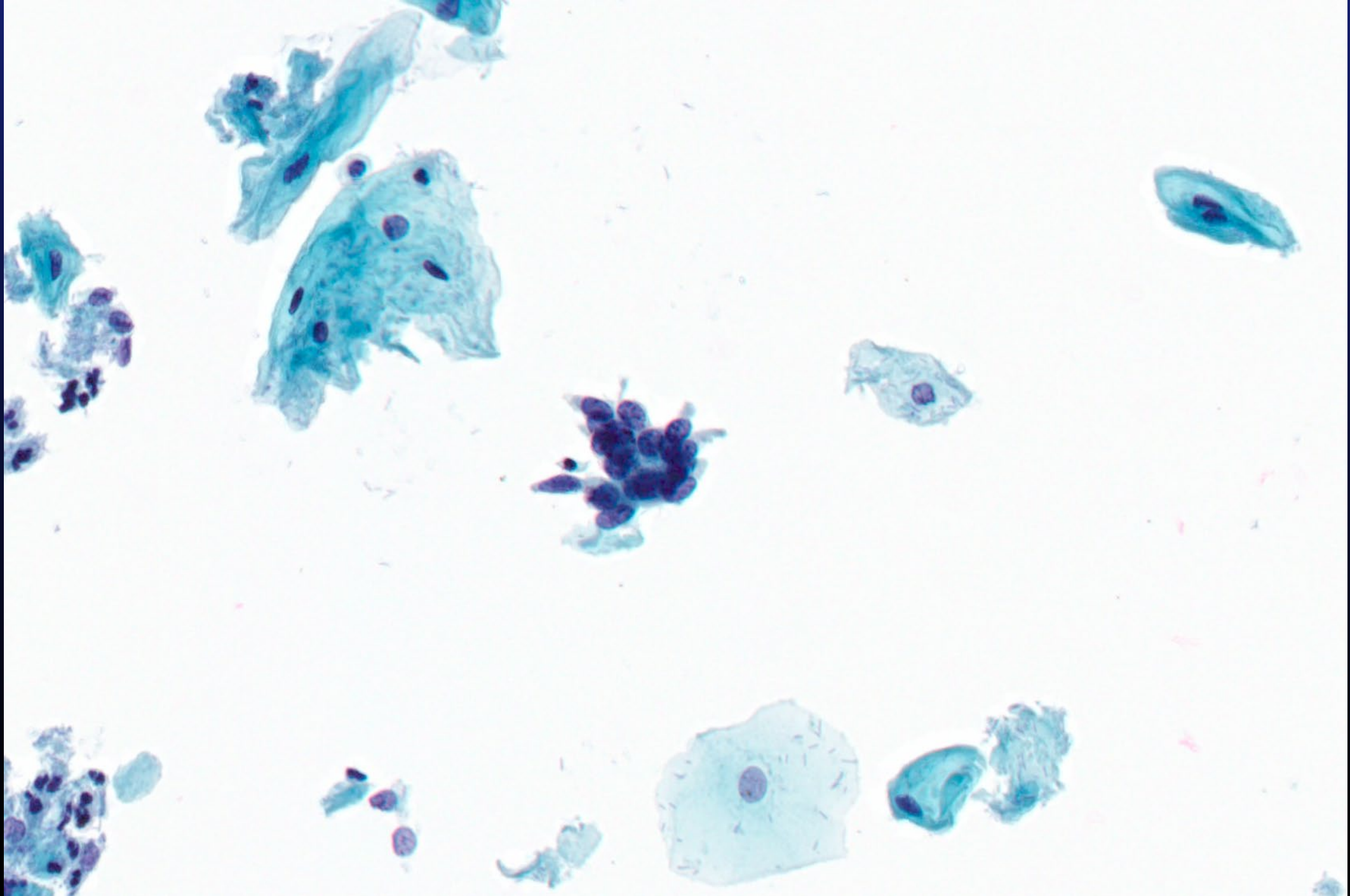
## Abnormal Morphology – Endocervical Adenocarcinoma In Situ (AIS)

- Hyperchromatic crowded groups (HCG)
- Pseudostratified strips and/or rosettes
- Palisading nuclear arrangement- “feathering”
- Nuclear enlargement with crowding and overlap
- Oval or elongated nuclei of variable sizes
- Hyperchromatic nuclei with evenly dispersed, coarsely granular chromatin
- Small or inconspicuous nucleoli
- Mitotic figures common
- Absence of tumor diathesis







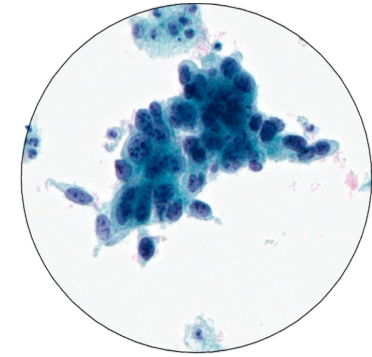


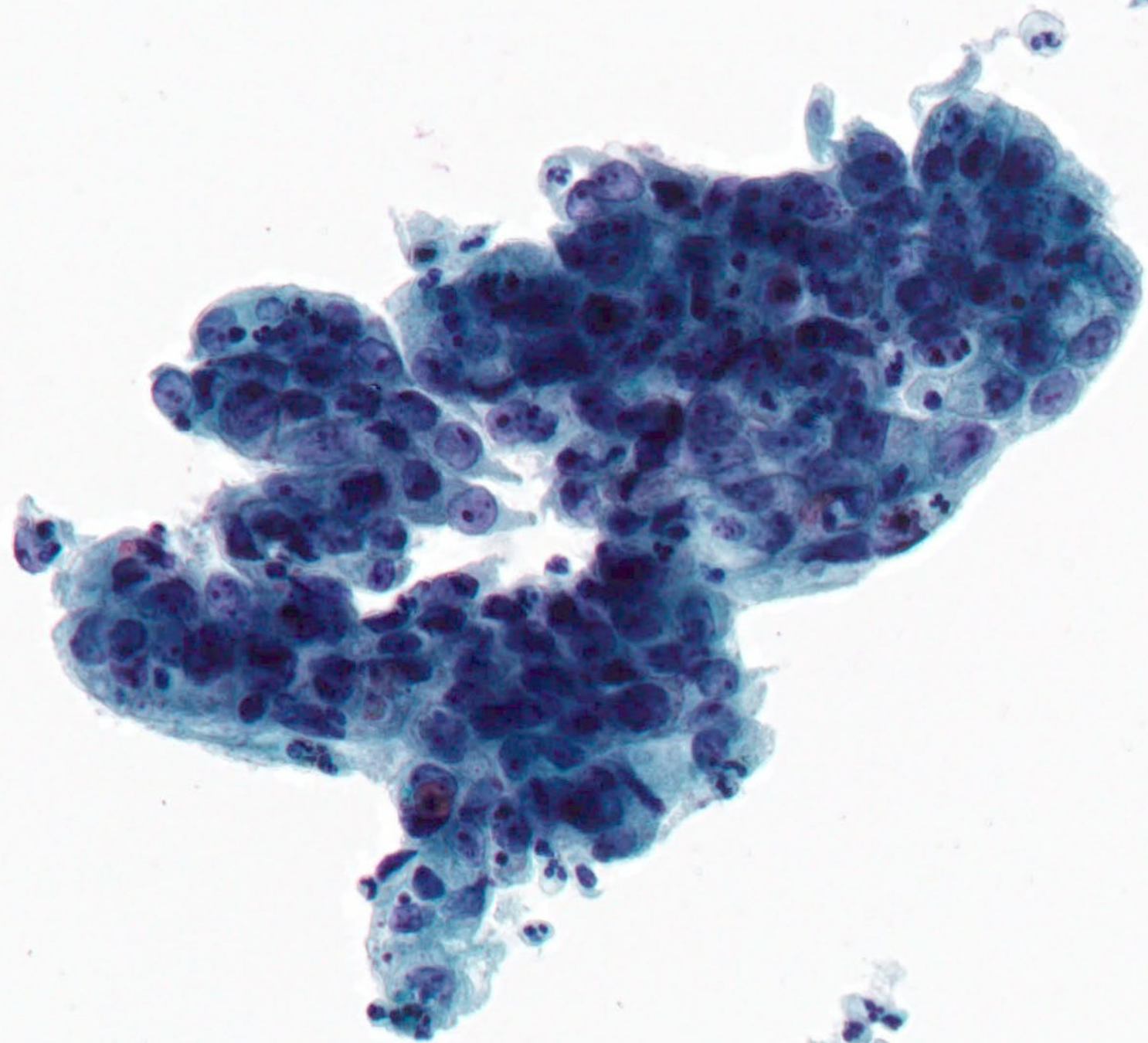


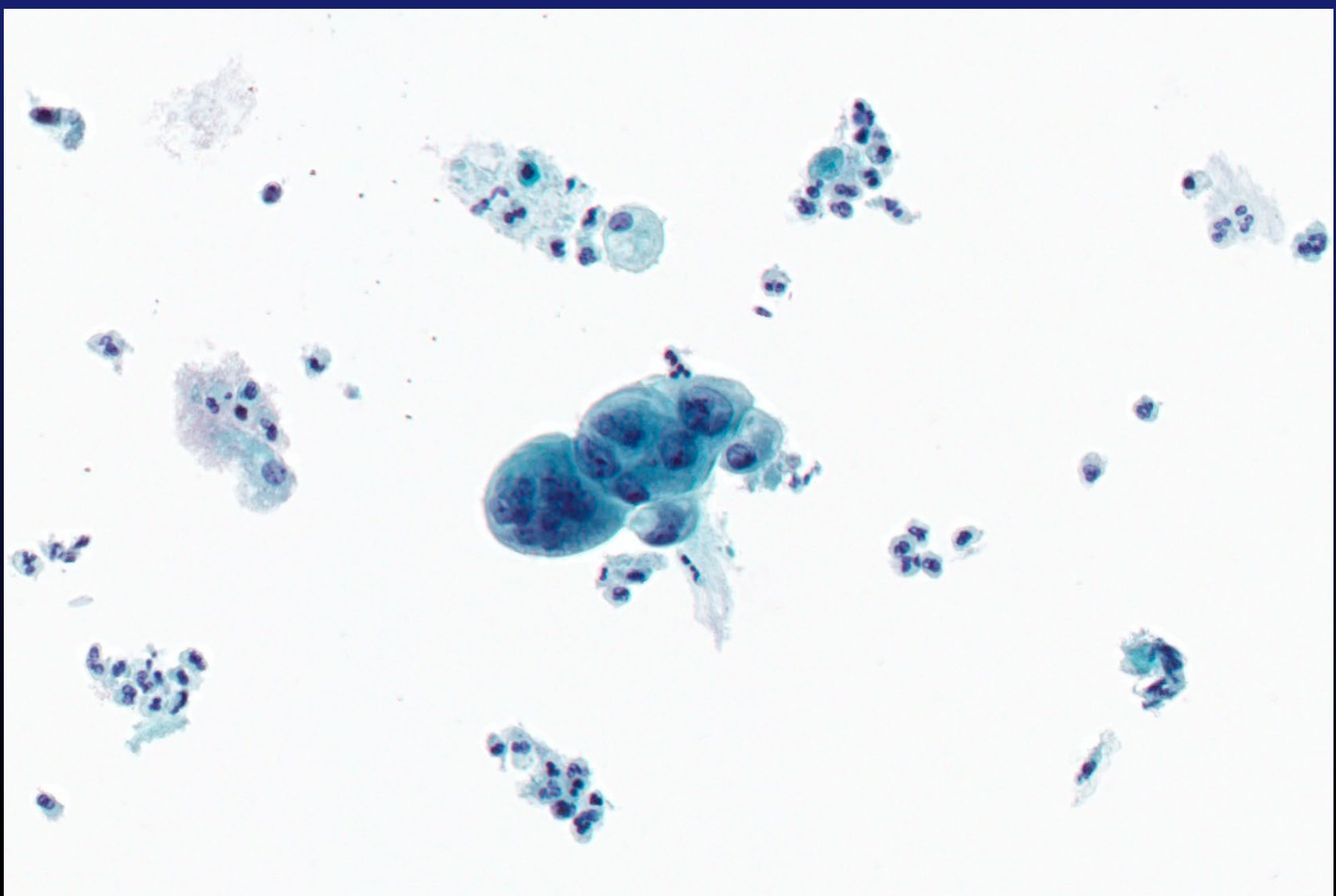
# The Bethesda System for Reporting Cervical Cytology

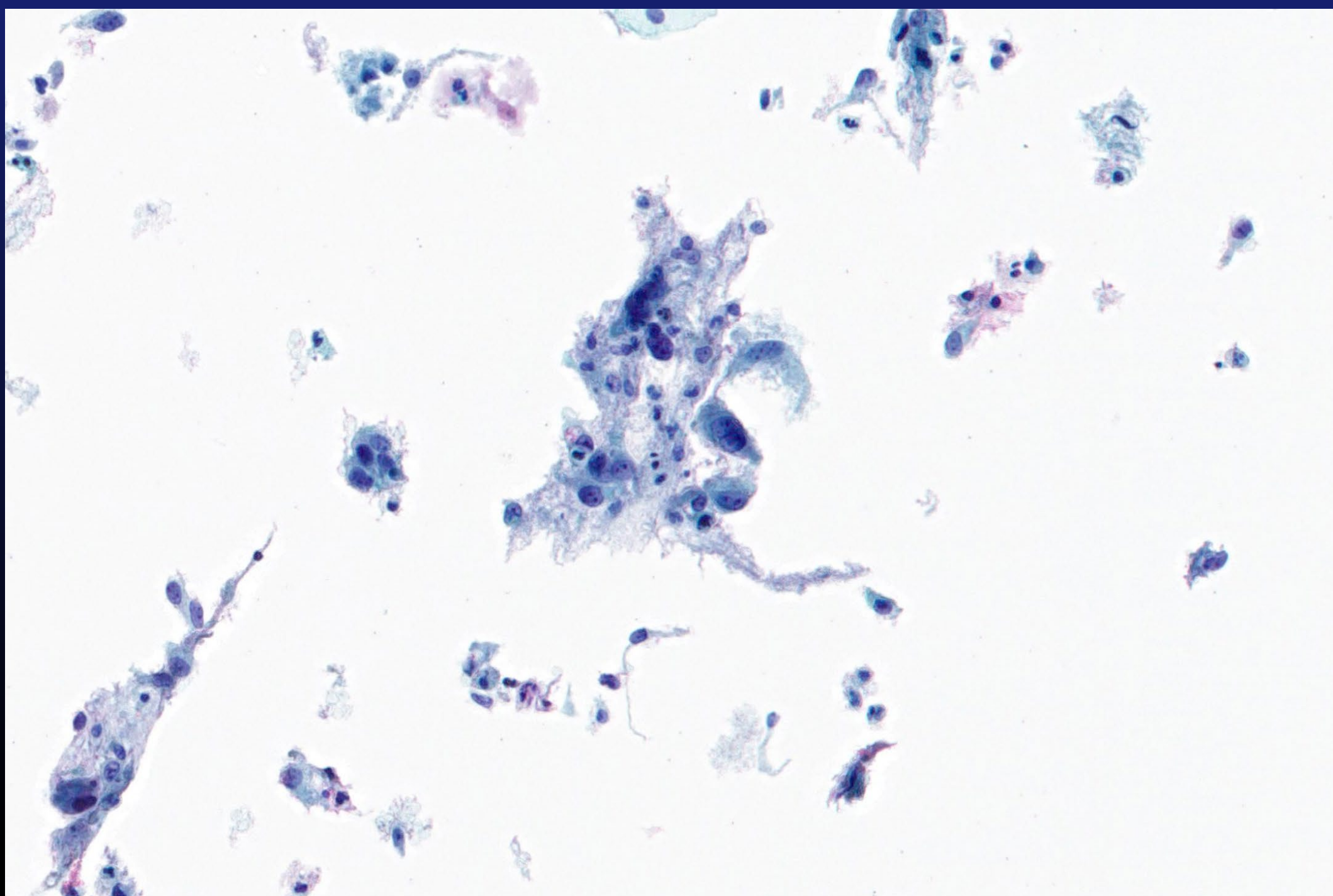
## Abnormal Morphology – Endocervical Adenocarcinoma

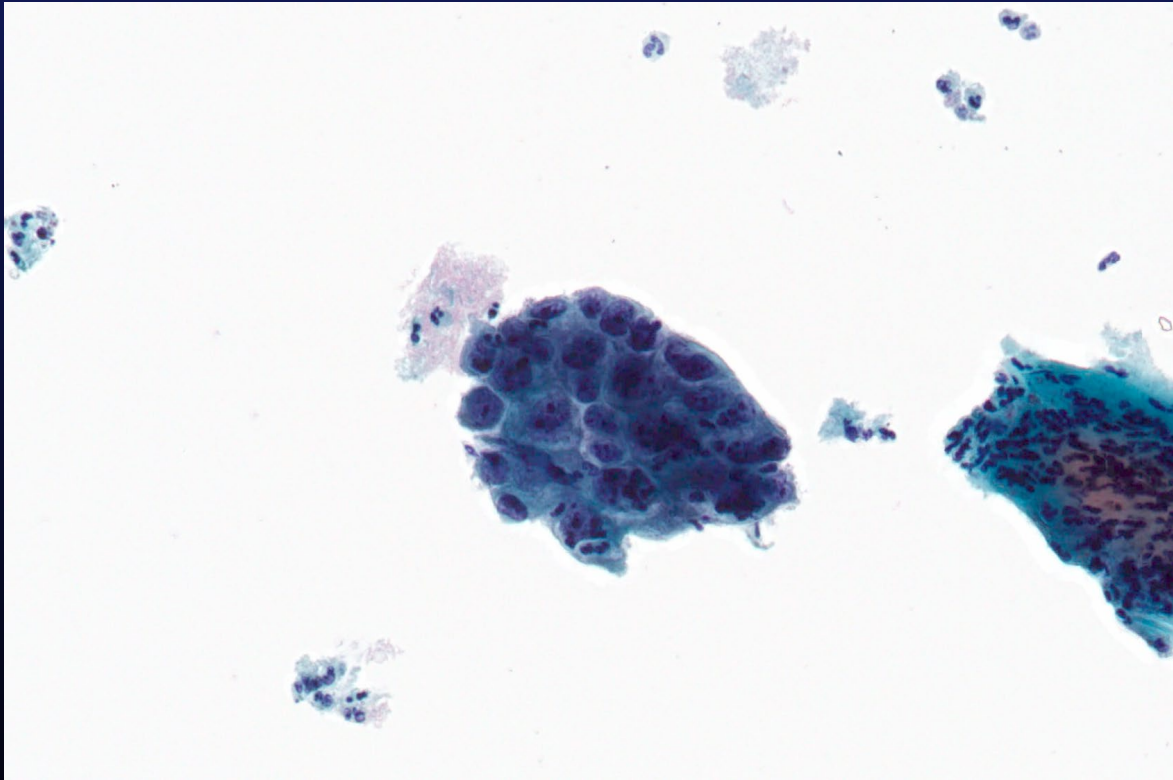
- Single cells, sheets, and/or 3-dimensional clusters with cell crowding
- Nuclear enlargement with pleomorphism
- Fine or coarsely granular but irregularly distributed chromatin
- Irregular nuclear membranes
- Prominent nucleoli
- Vacuolated cytoplasm
- Tumor diathesis



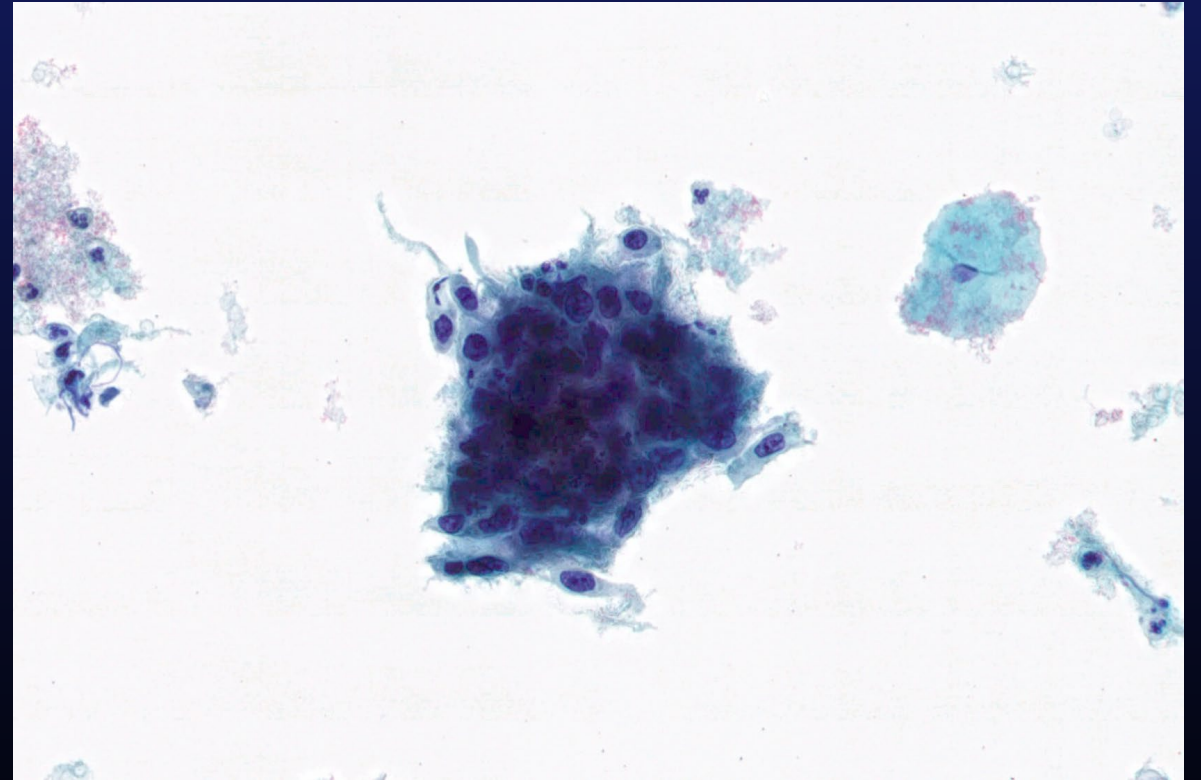








Endocervical Adenocarcinoma

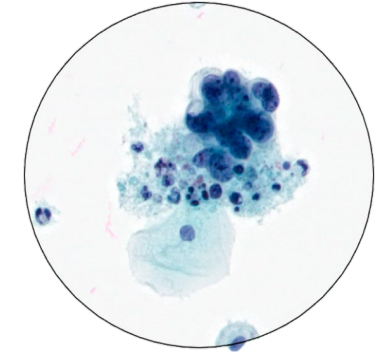


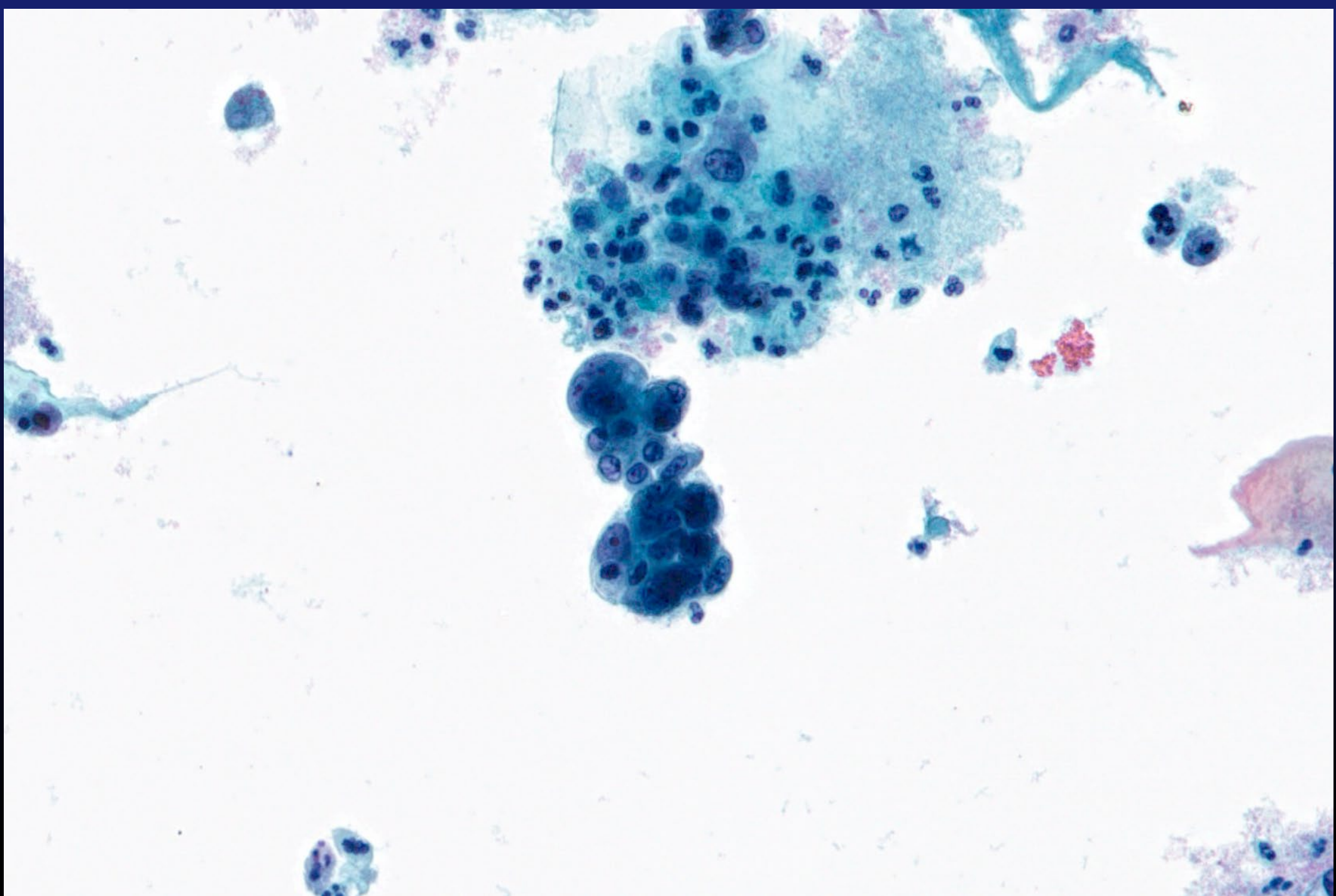
Non-Keratinizing Squamous Cell Carcinoma

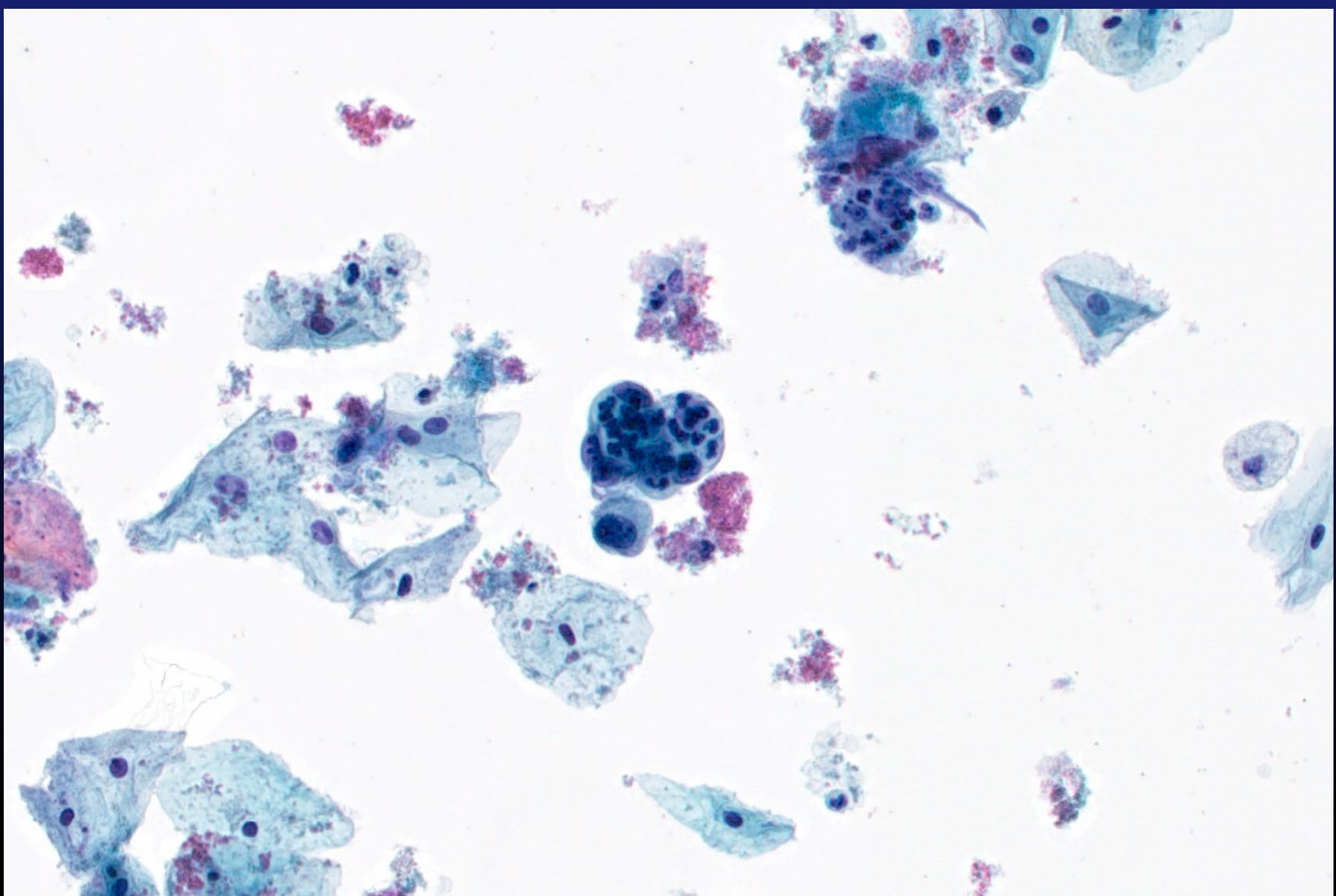
# The Bethesda System for Reporting Cervical Cytology

## Abnormal Morphology – Endometrial Adenocarcinoma

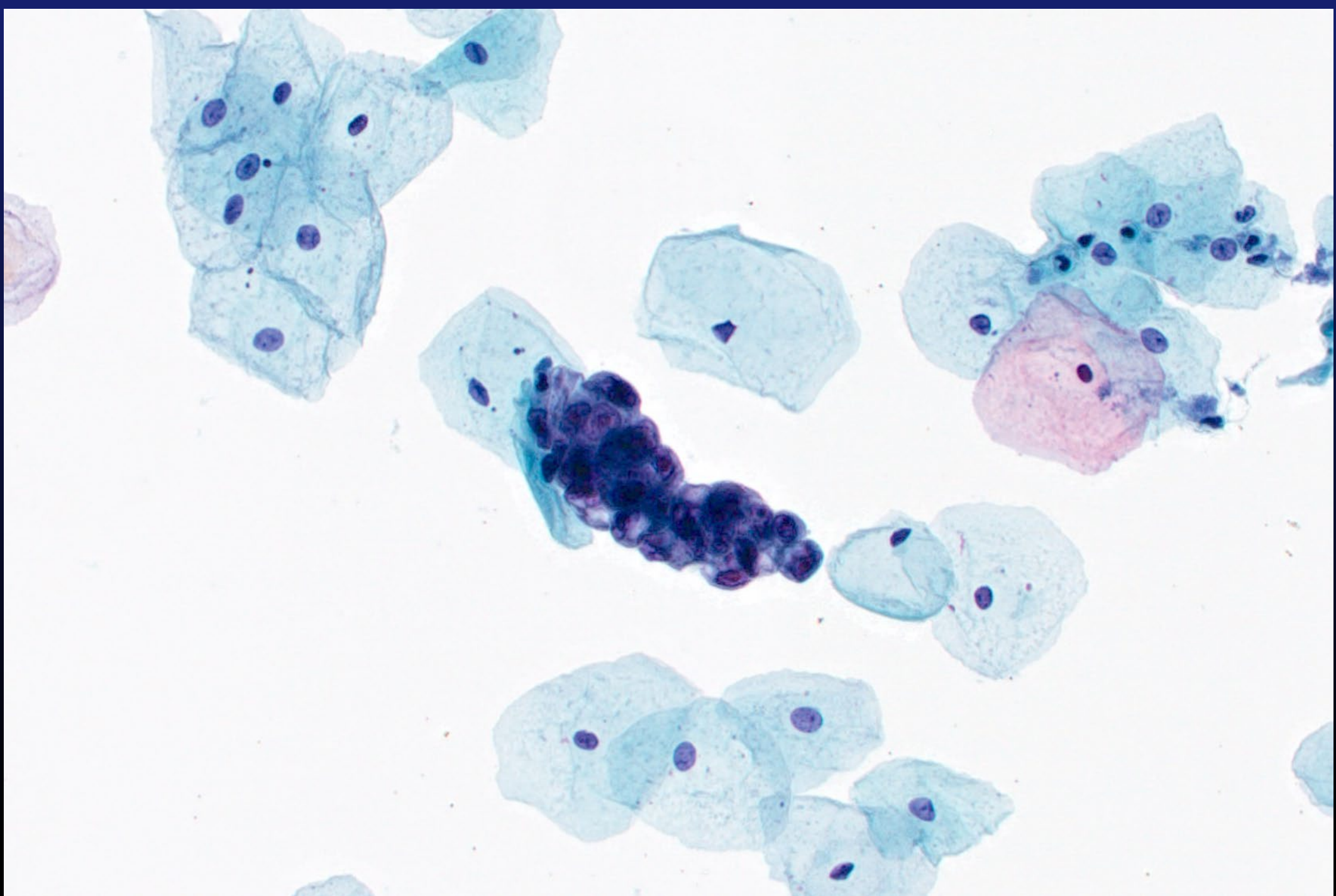
- Single cells and/or small 3-dimensional clusters with cell crowding
- Variable nuclear enlargement
- Fine or coarsely granular, slightly irregular chromatin
- Small to prominent nucleoli
- Vacuolated cytoplasm
- Poly engulfment may be present
- Tumor diathesis – may be finely granular or “watery”

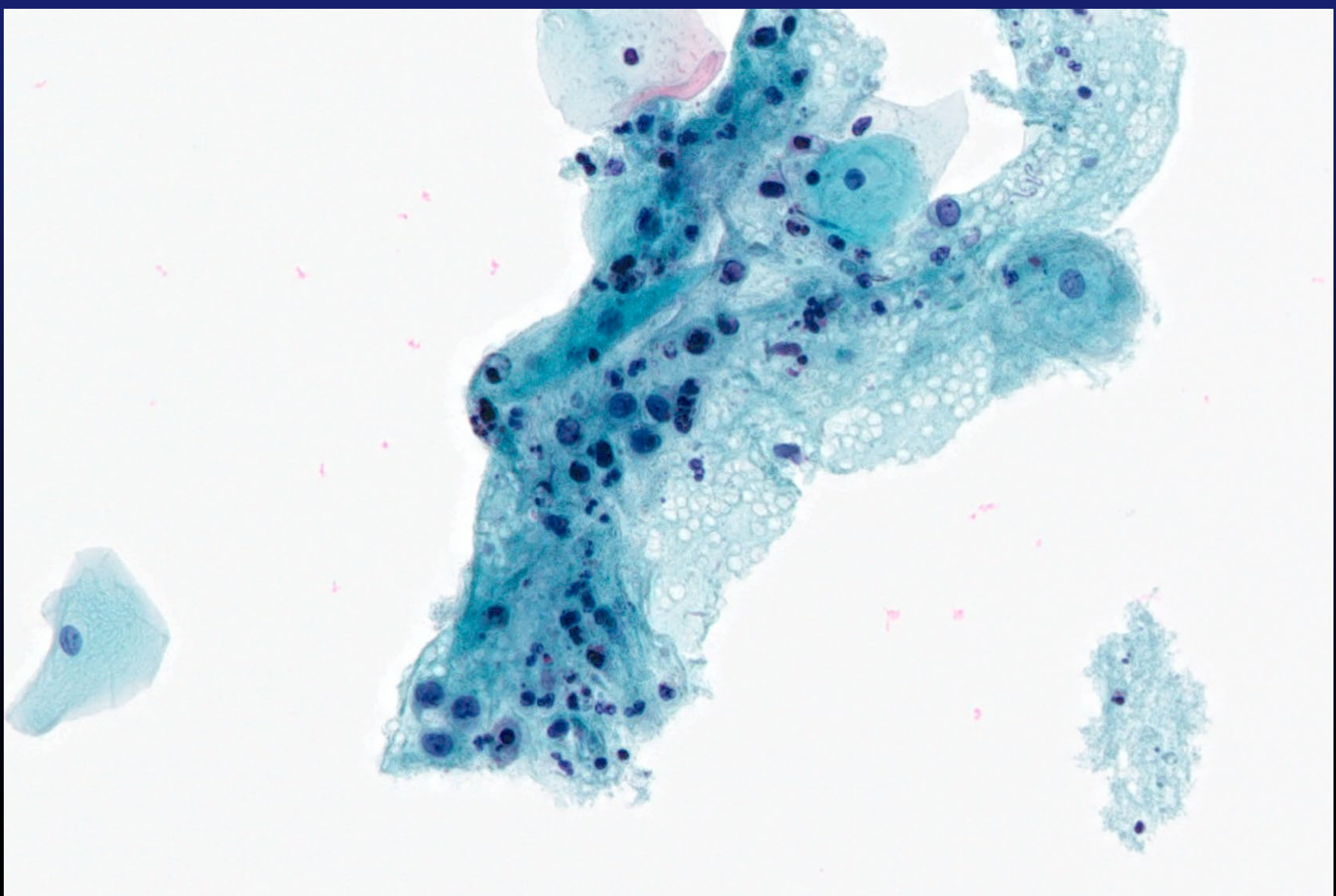












# Thank you for your participation



- **Contact Information**

[Email address – enter presenter information]  
[Phone number – enter presenter information]

- **Additional Resources**

[www.hologic.com](http://www.hologic.com)  
[www.cytologystuff.com](http://www.cytologystuff.com)