



Cervical Slide Seminar

6th Cytopathology Congress

Bursa, Turkey

October 14, 2015

David C. Wilbur, M.D.

Dept. of Pathology

Massachusetts General Hospital



25 Ulusal Patoloji Kongresi
6. Sitopatoloji Kongresi

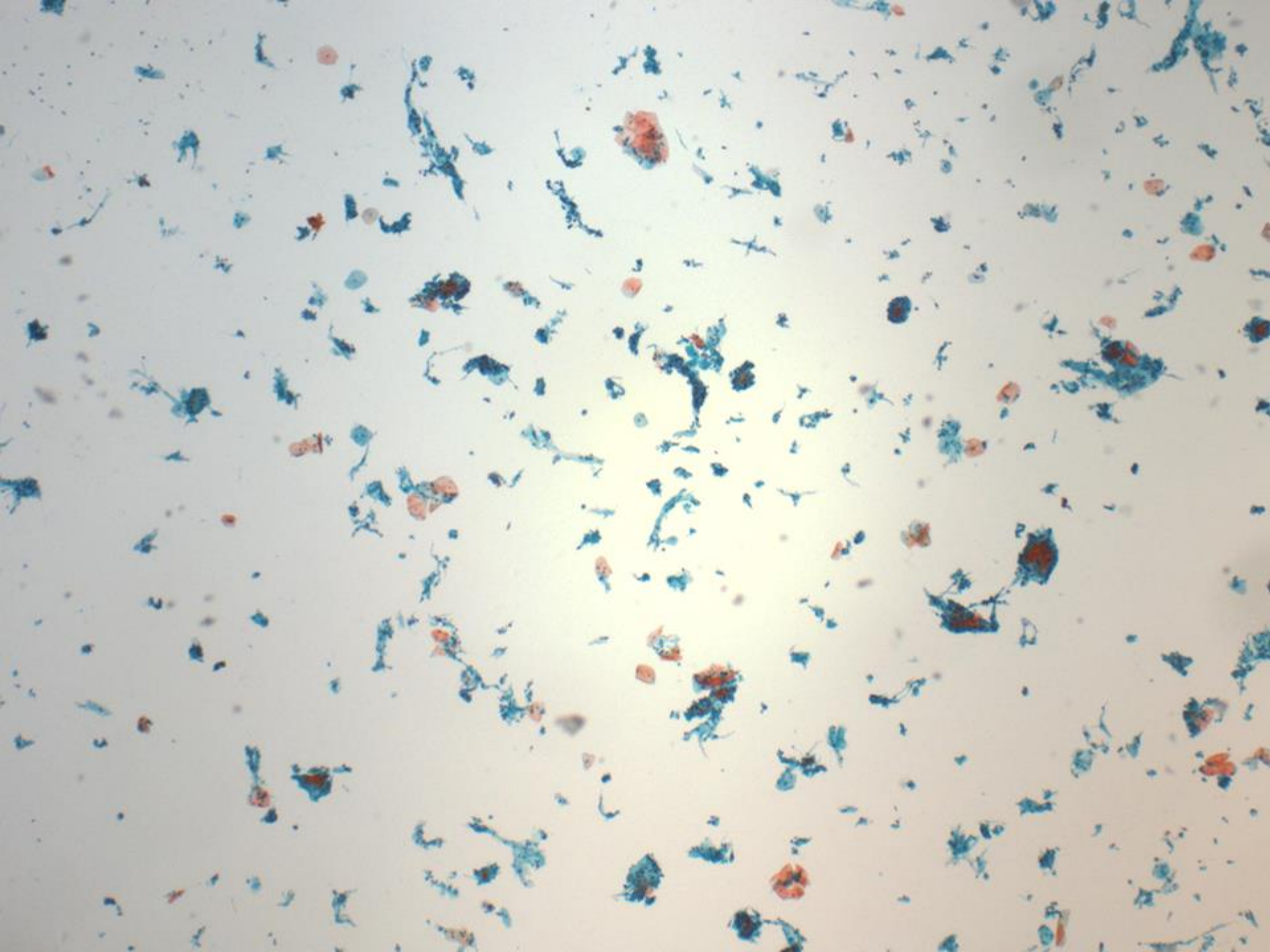
14 - 17 Ekim 2015 / Merinos AKKM - BURSA

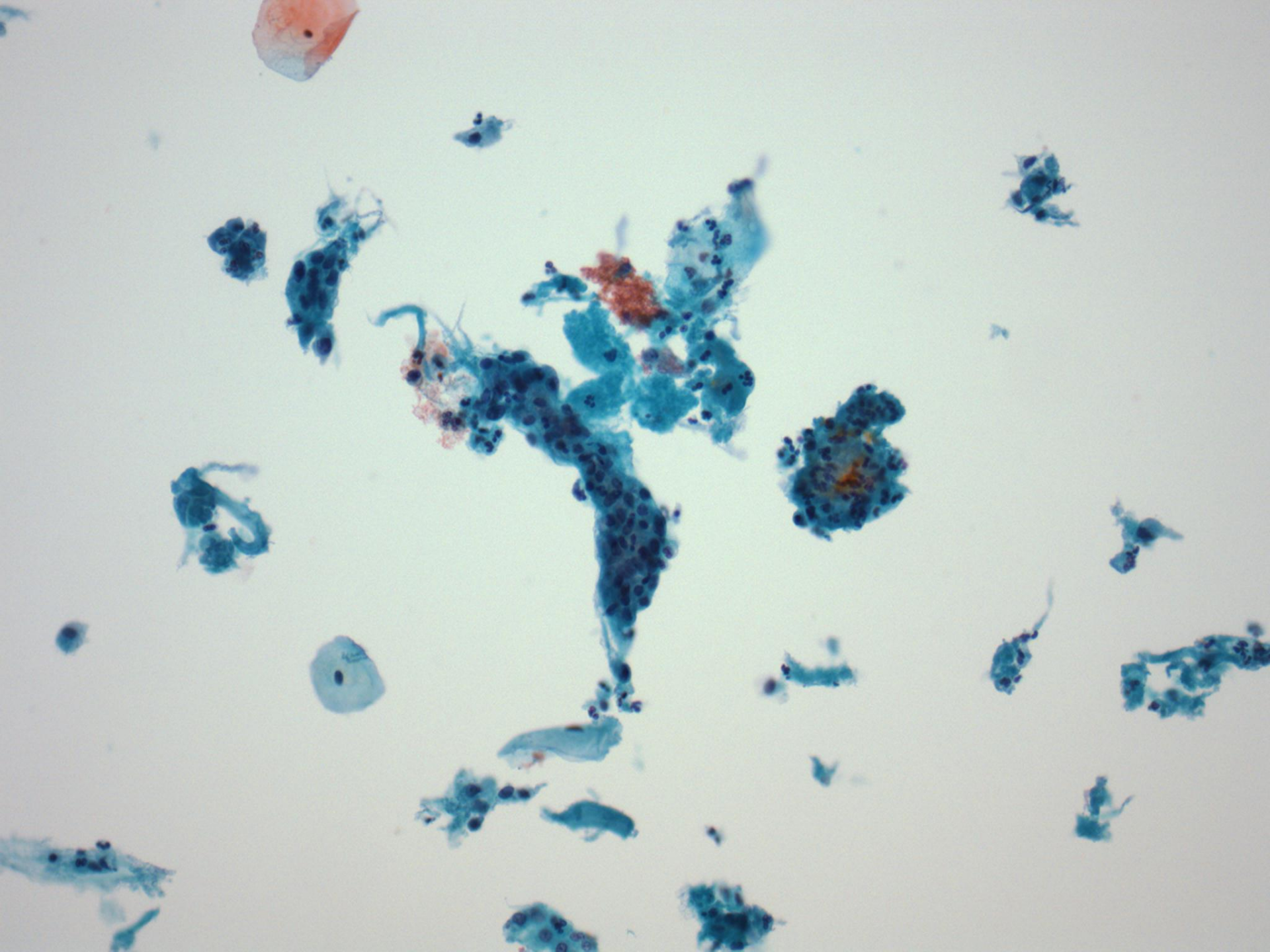


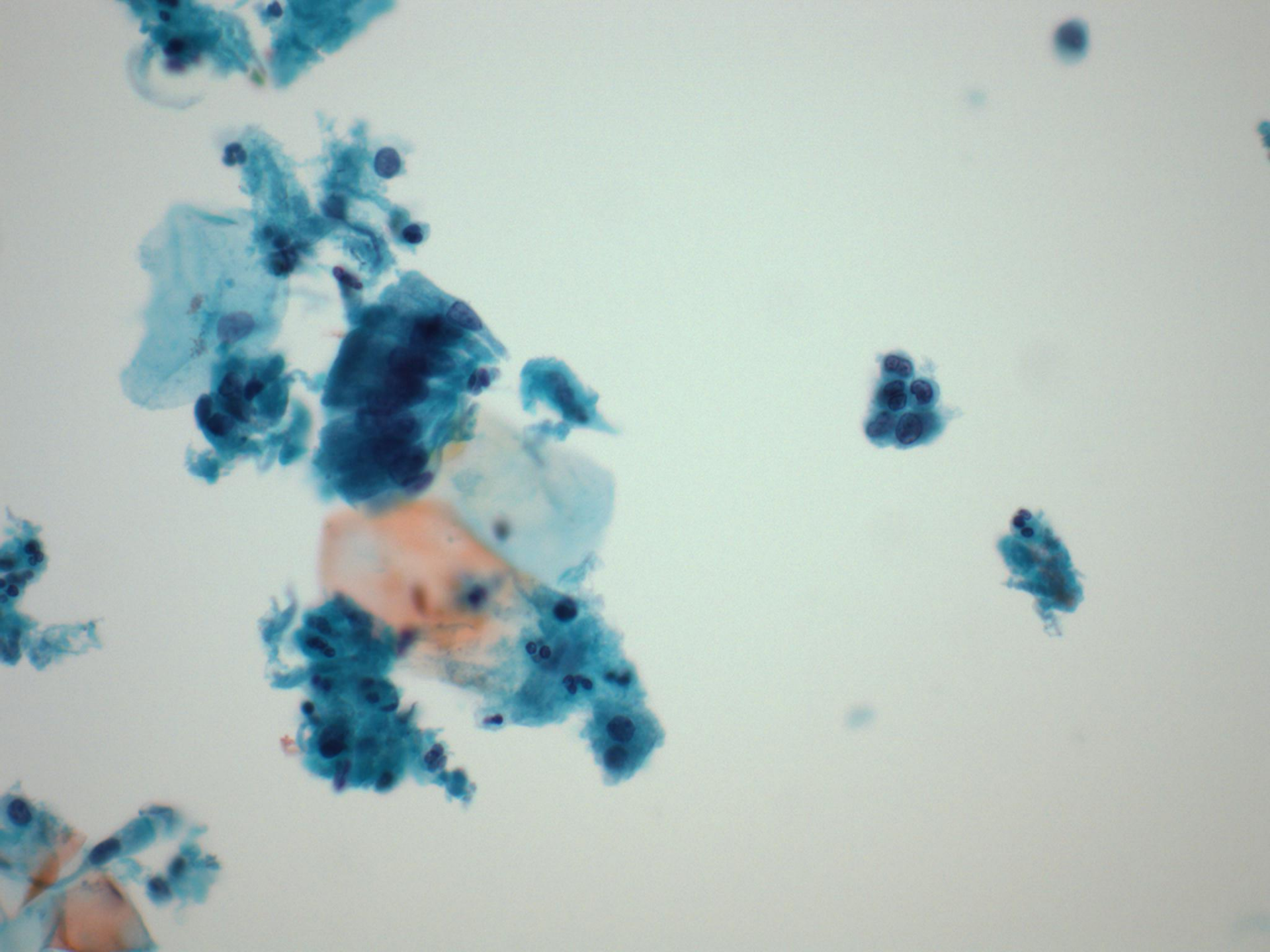
Case 1

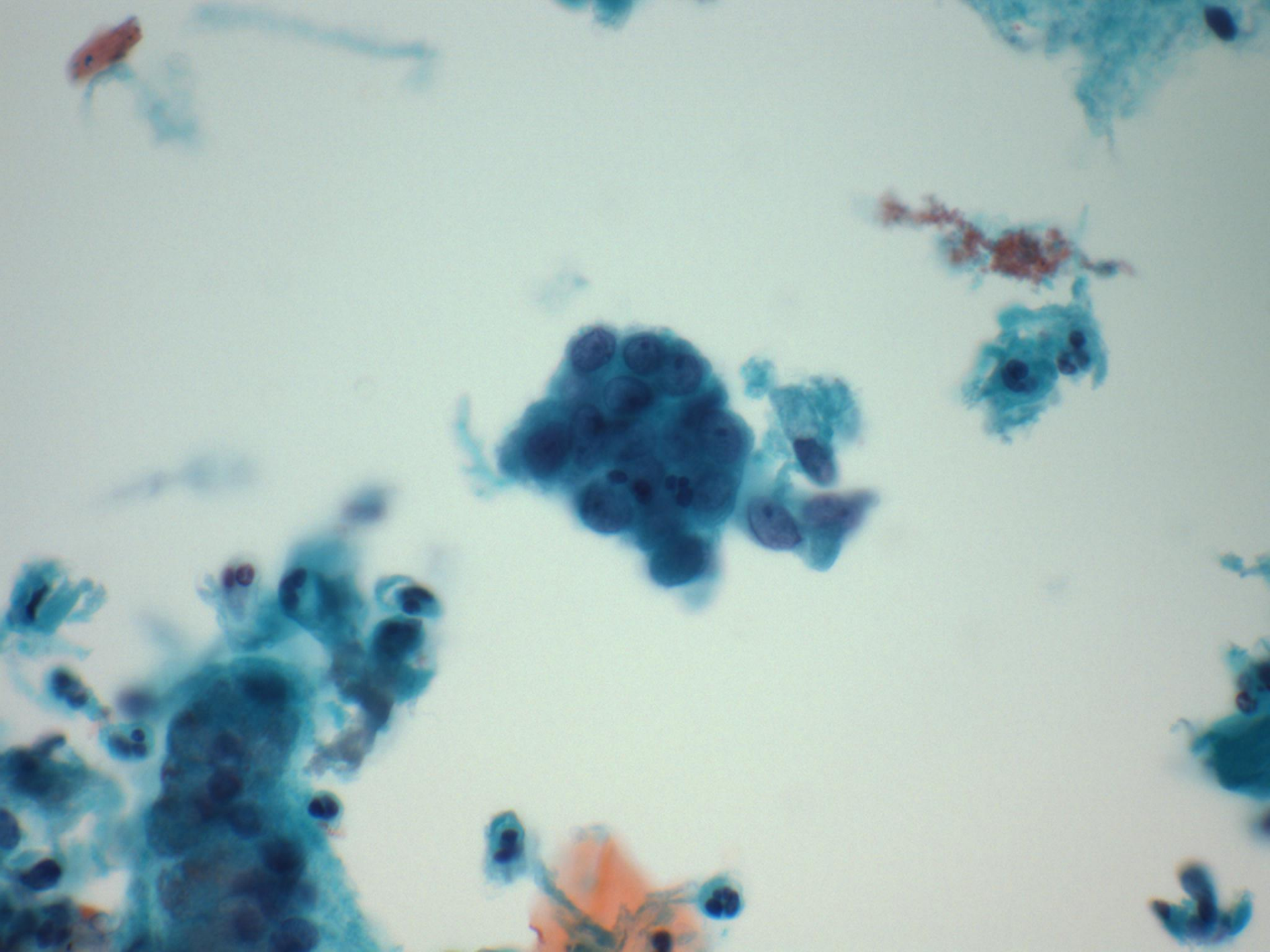
32 year old

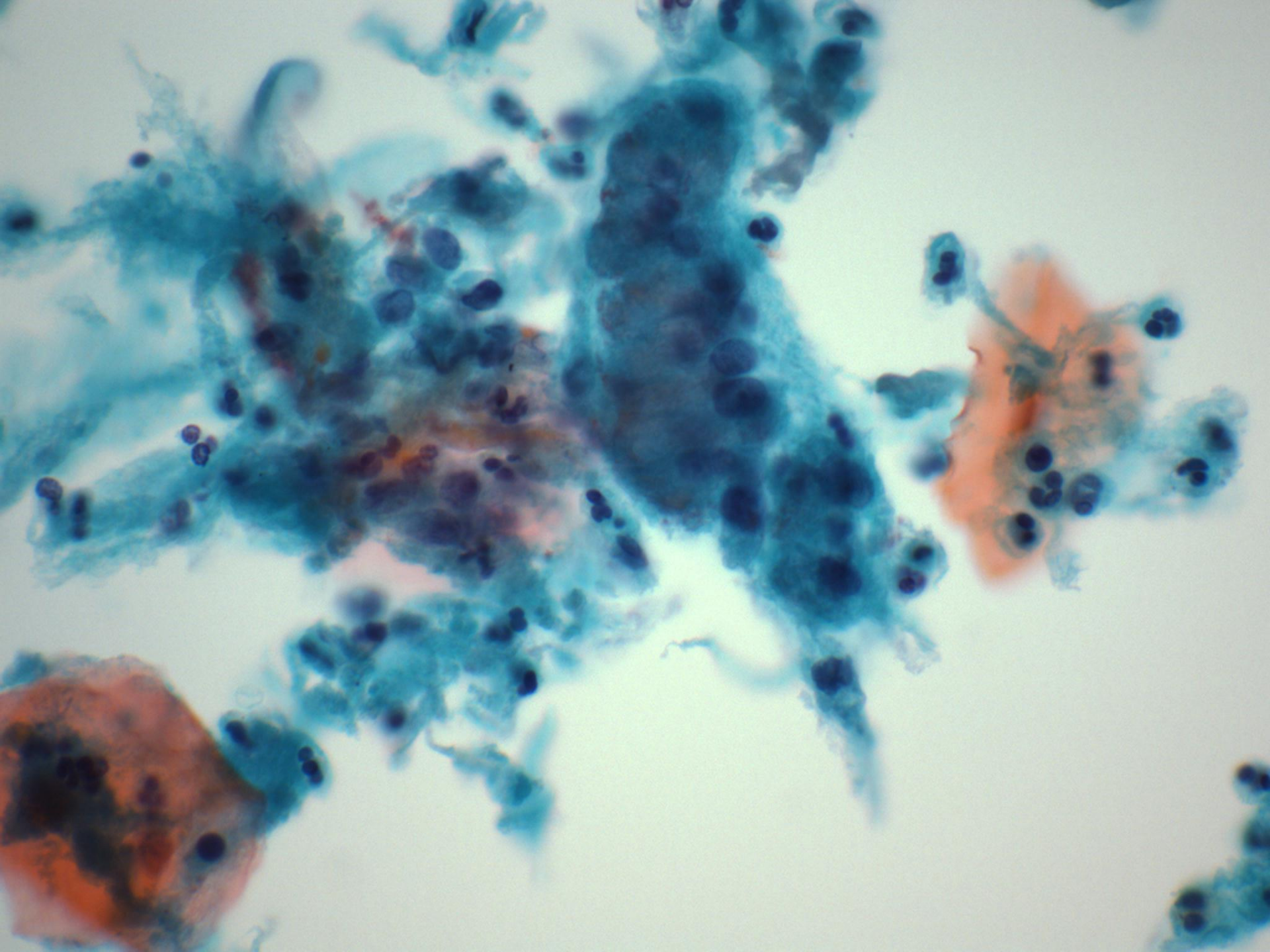
History of prior ASC-US, HPV+

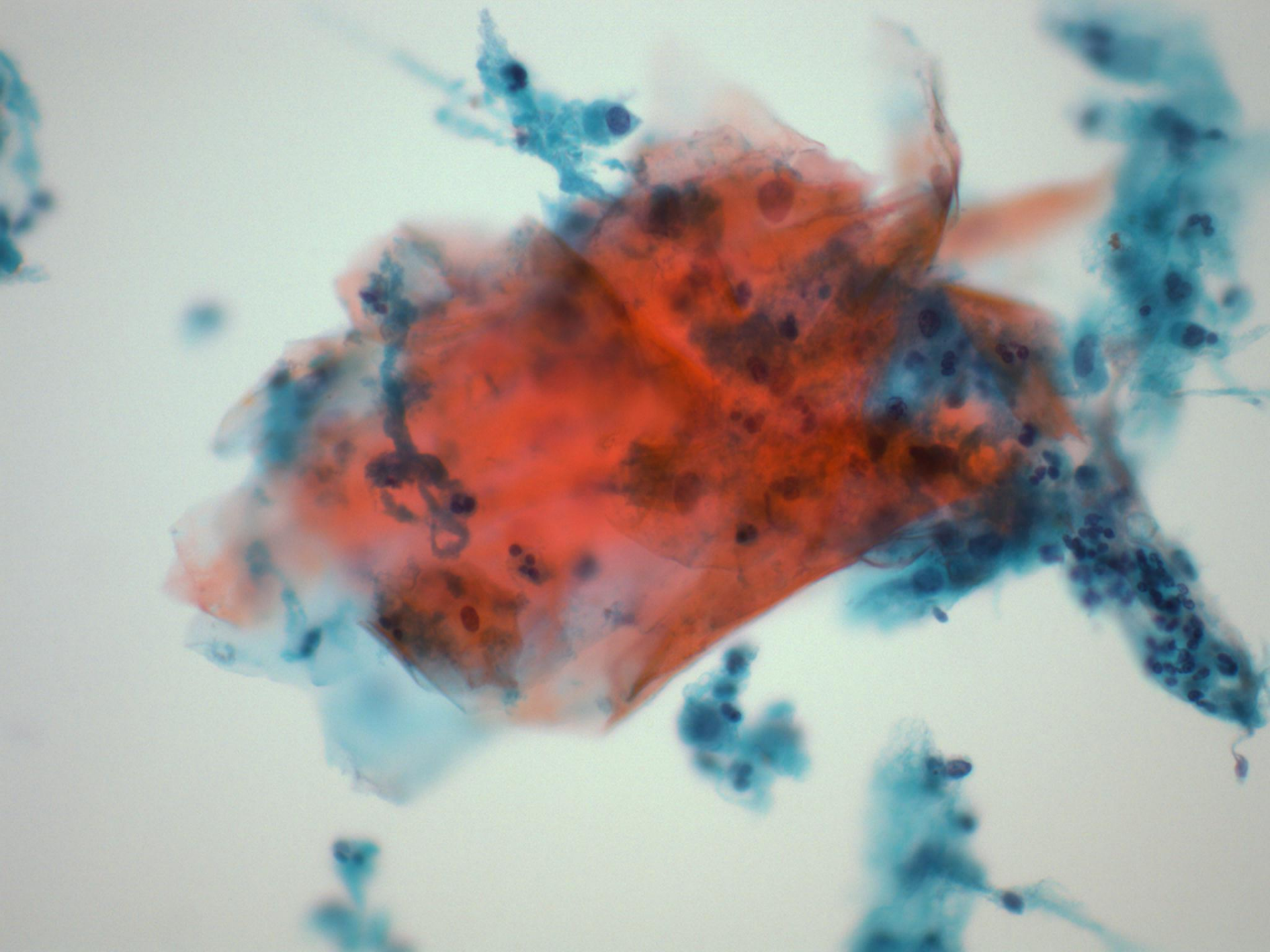


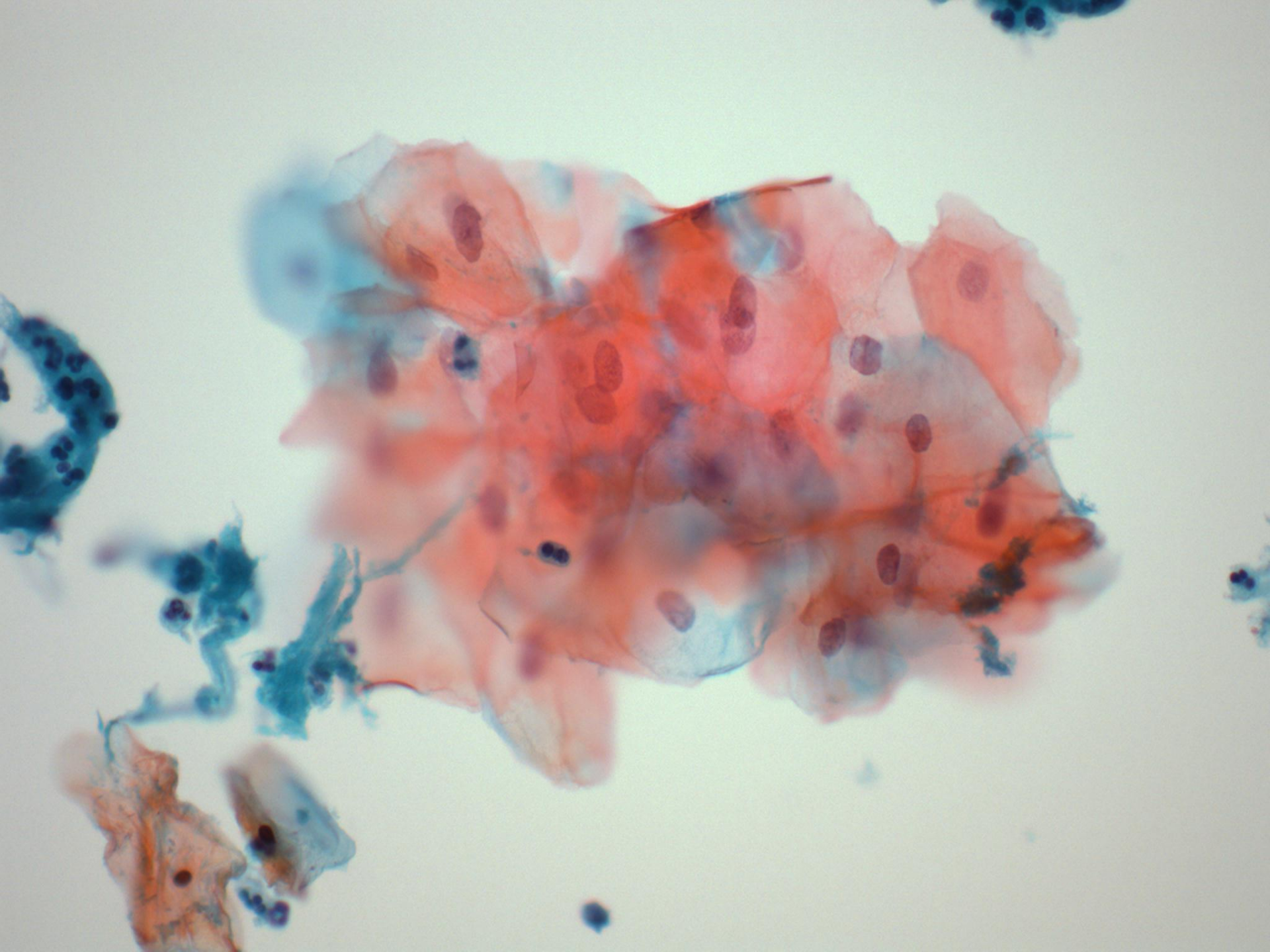


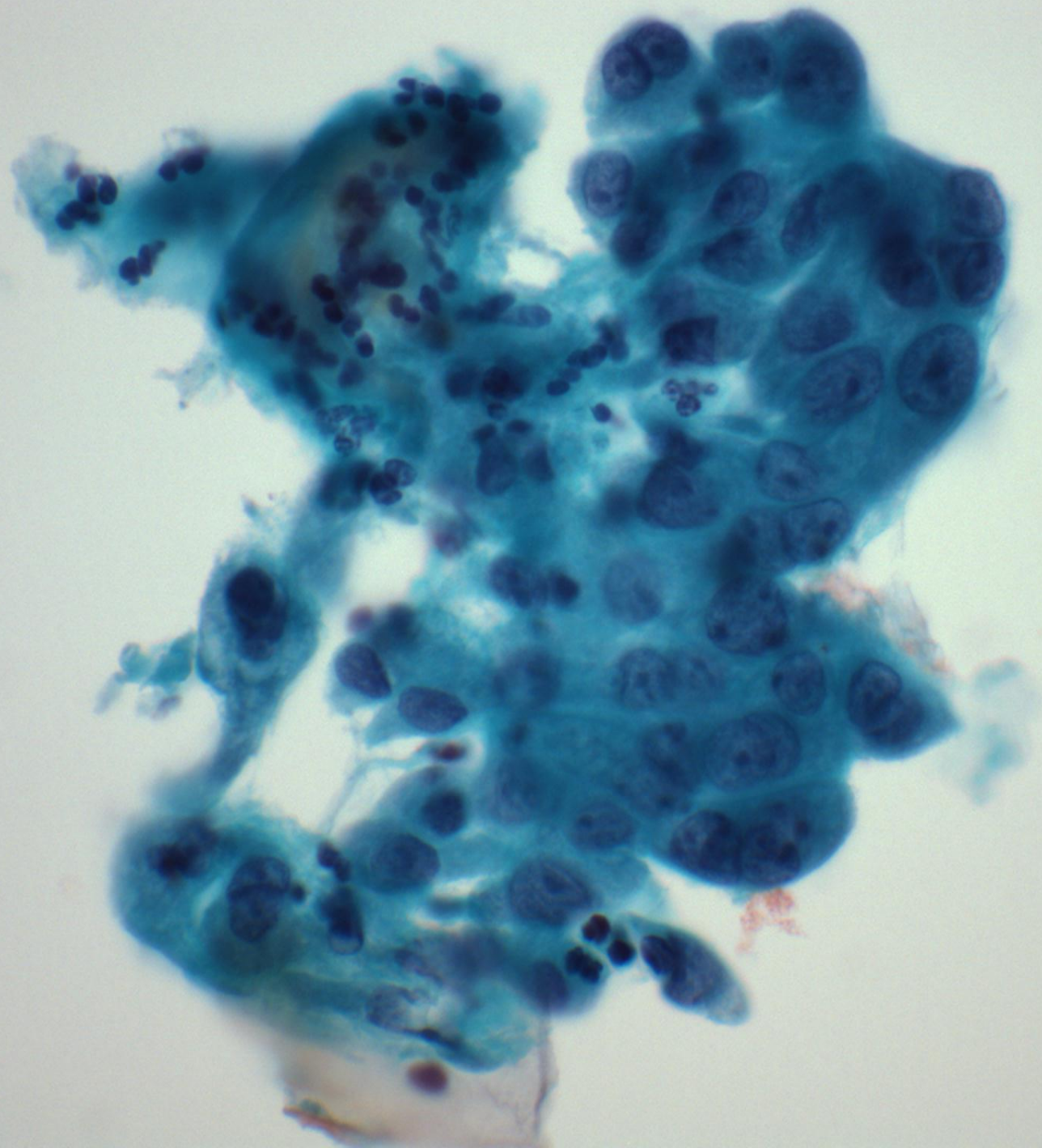


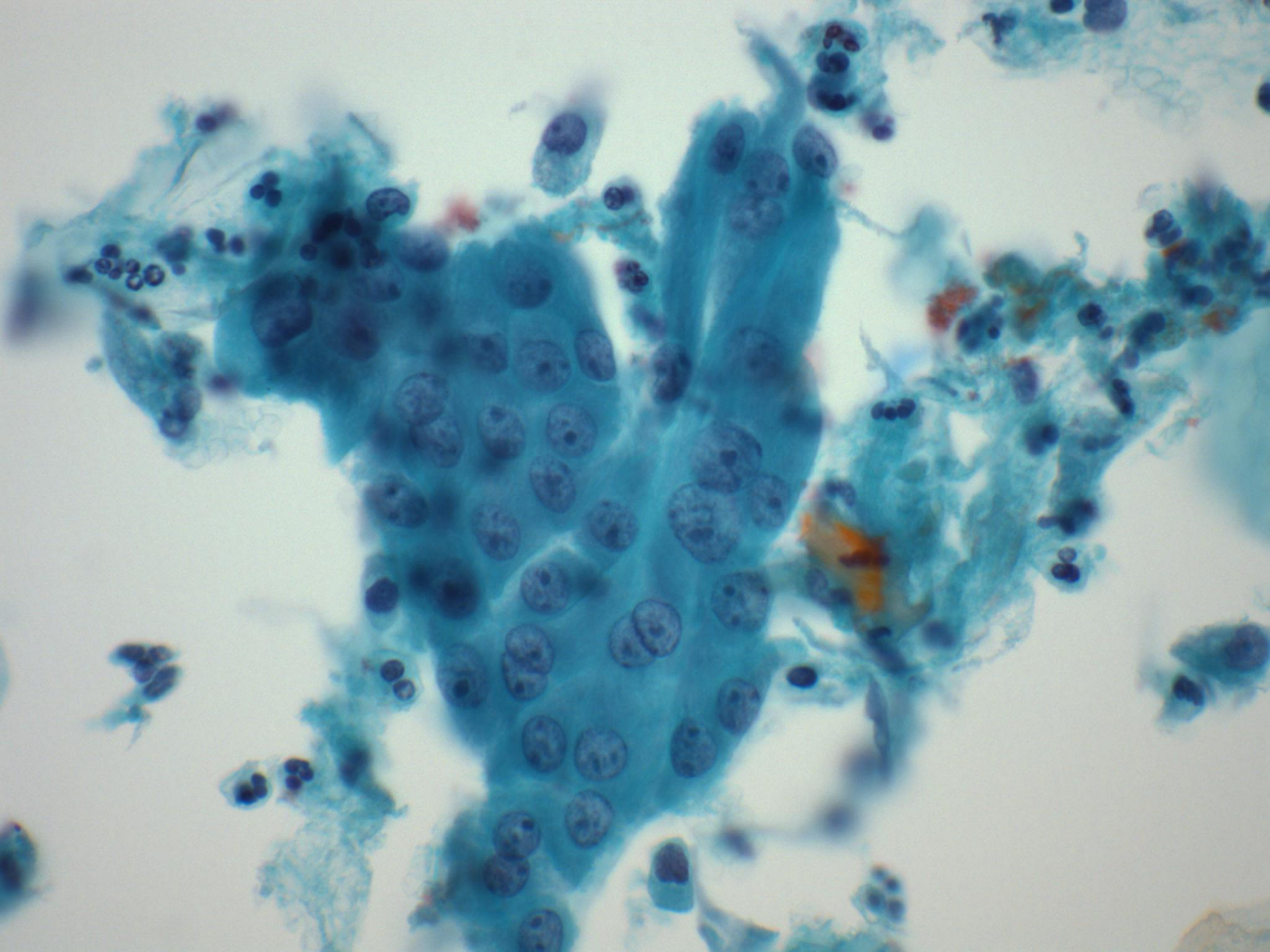


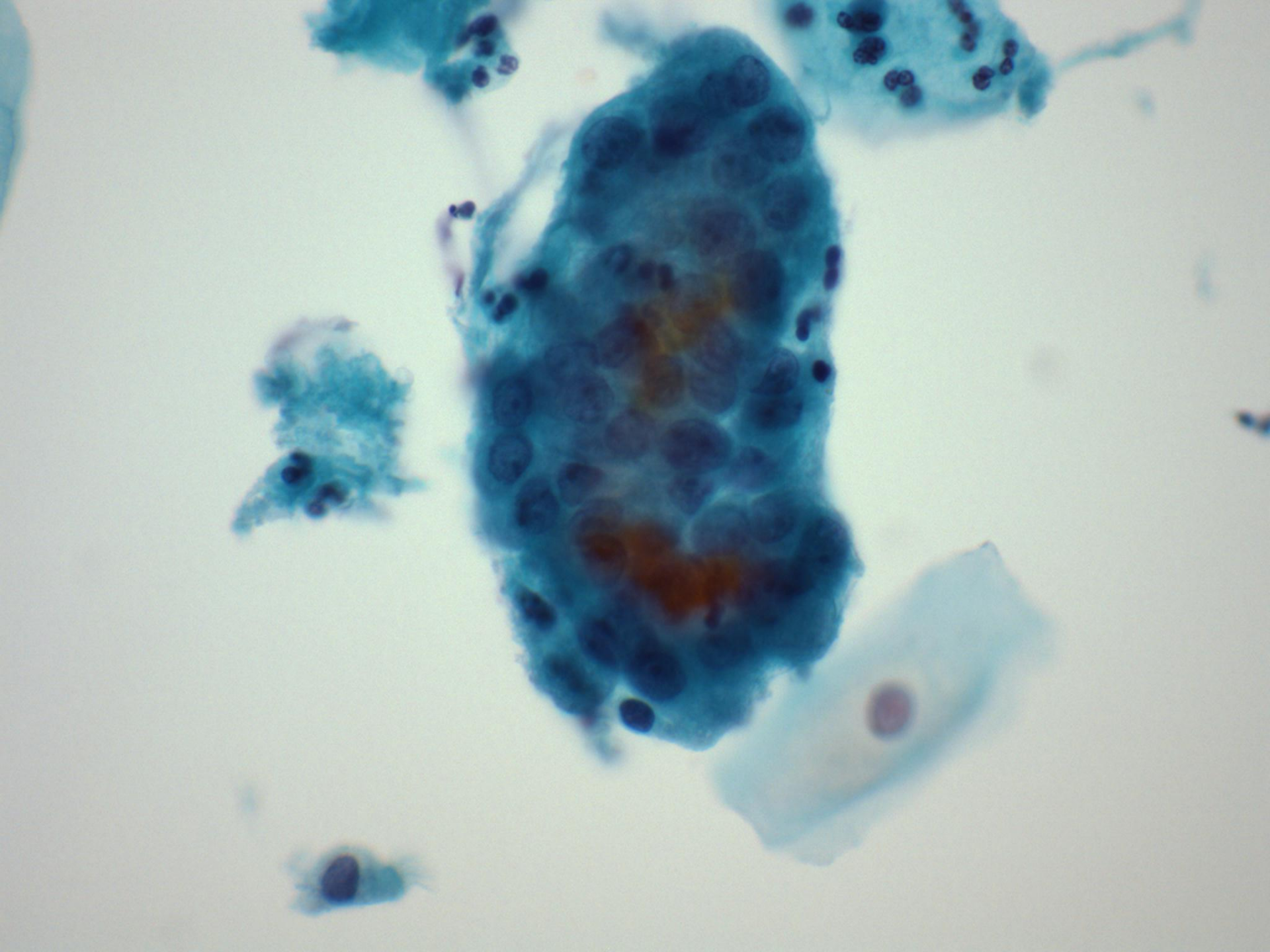












Summary of Key Cytologic Features

- Mature squamous background
- Flat sheets of epithelium with:
 - Inflammation
 - Well-defined cytoplasmic boundaries
 - Prominent nucleoli
 - Abundant granular cytoplasm with elongation
- Hyperkeratotic squamous cells

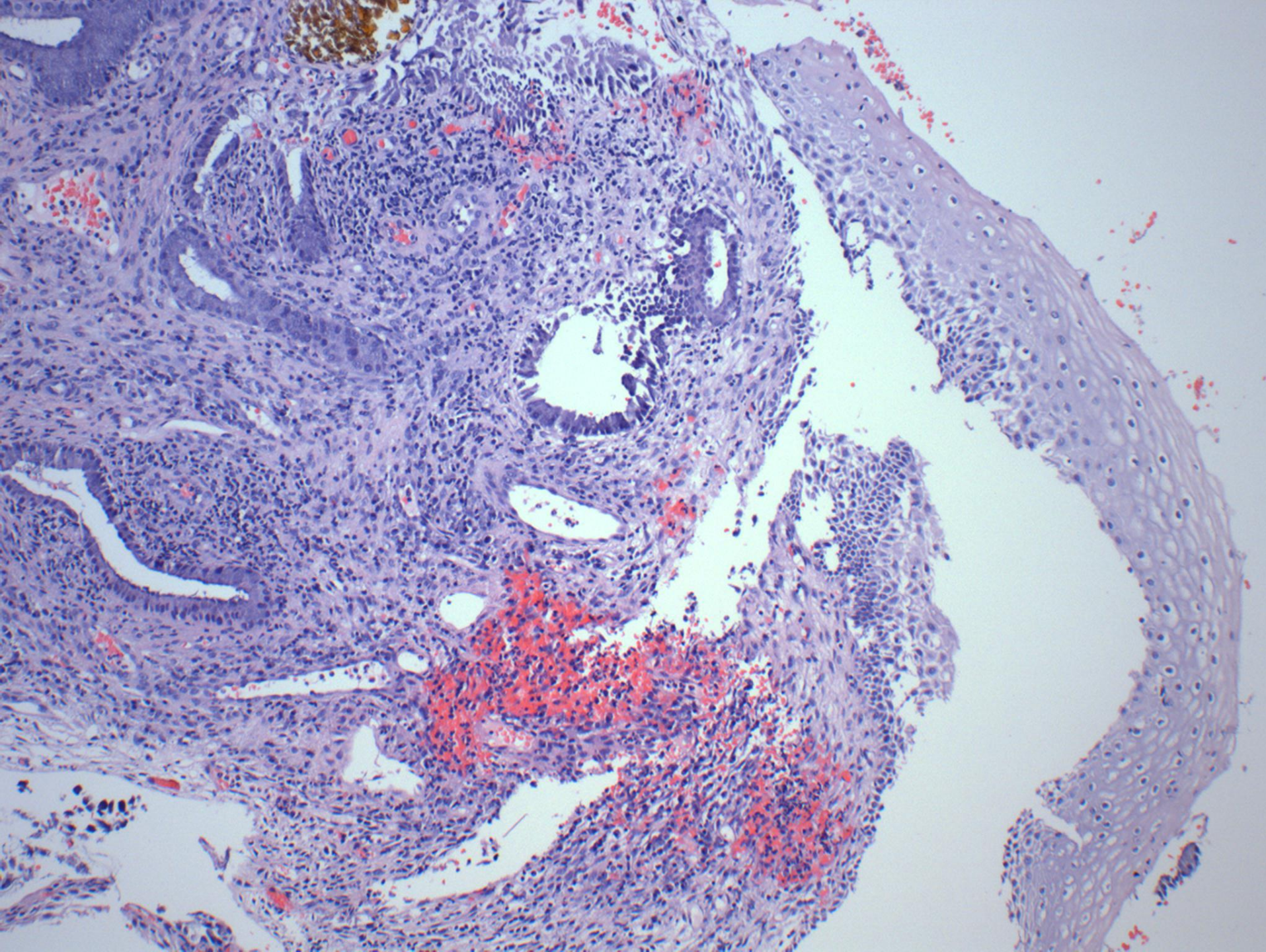
Benign

Malignant

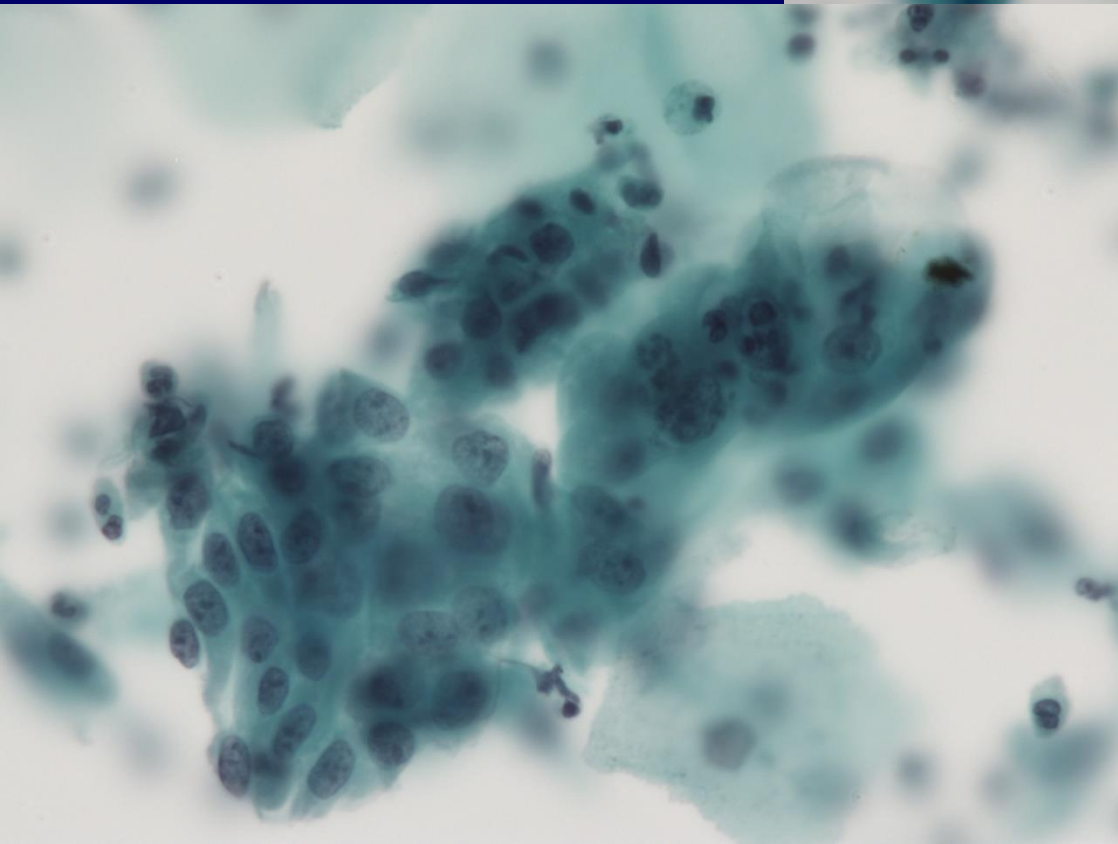
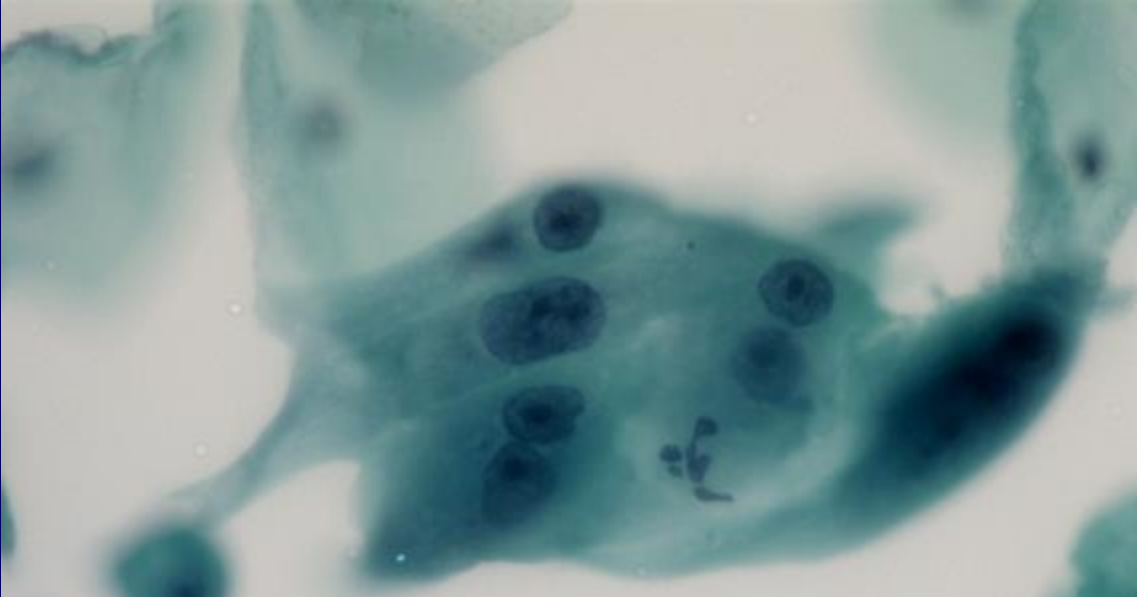
Atypical

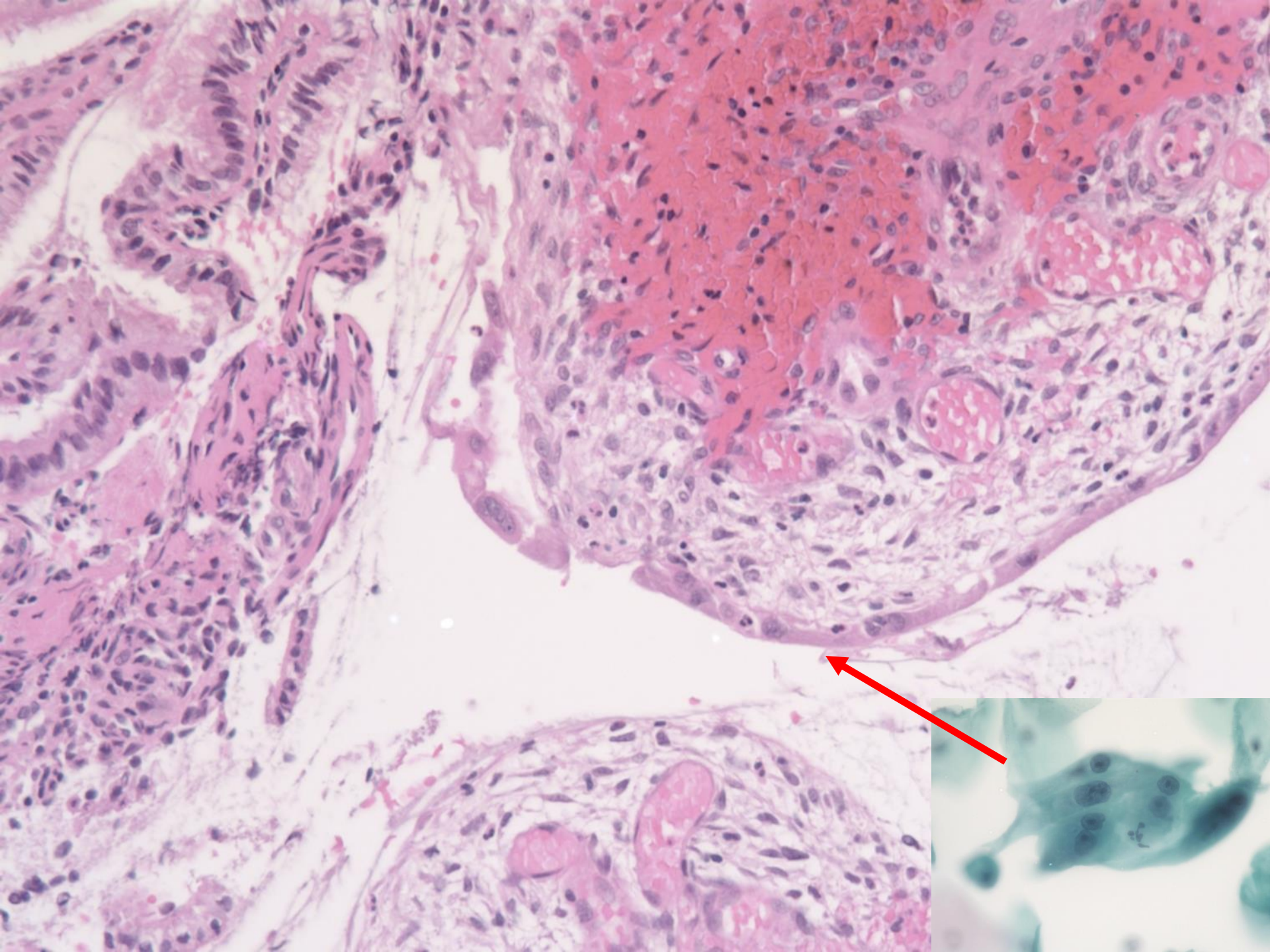
Diagnosis:

Reparative Change



Repair vs. Carcinoma

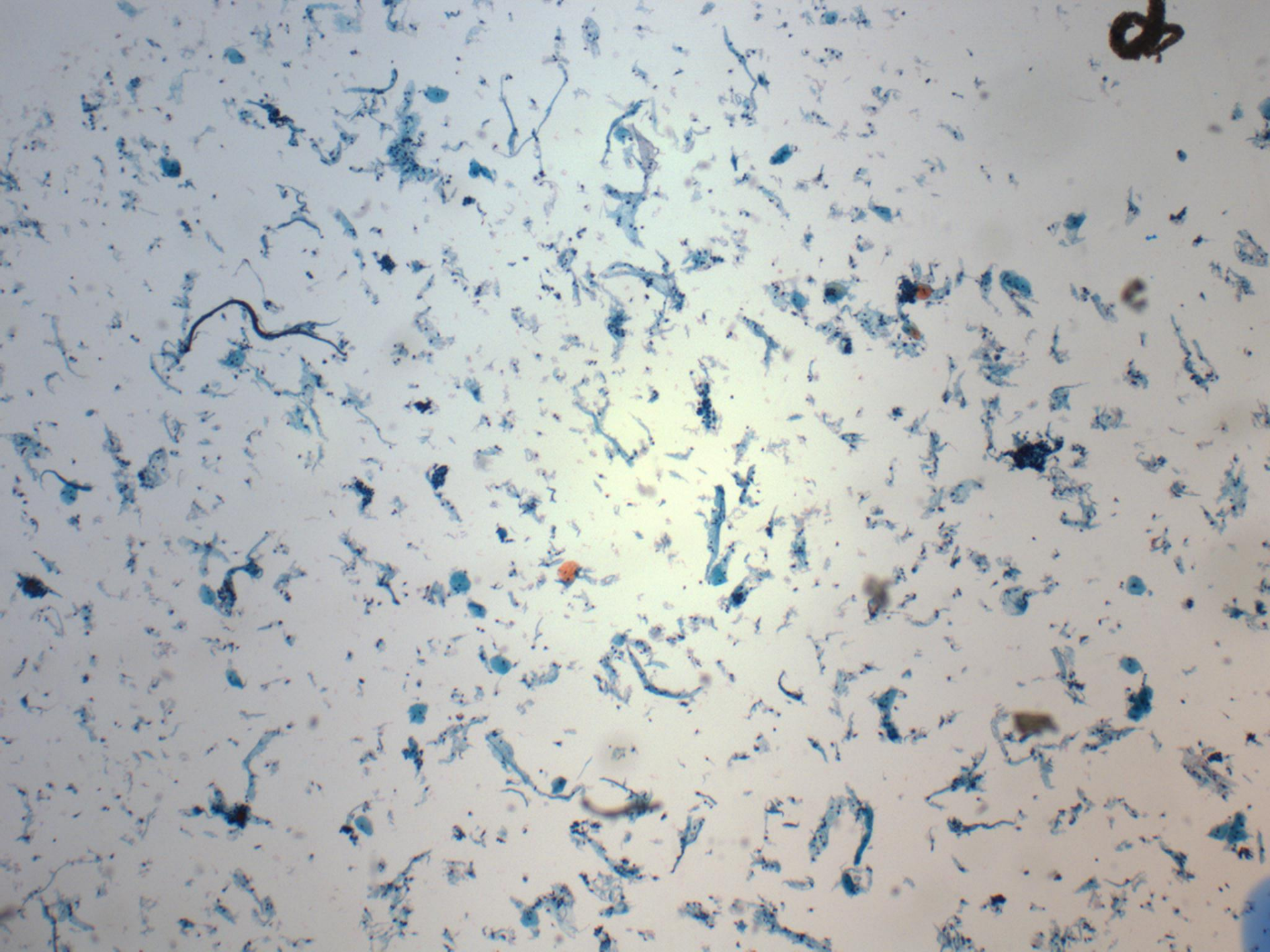


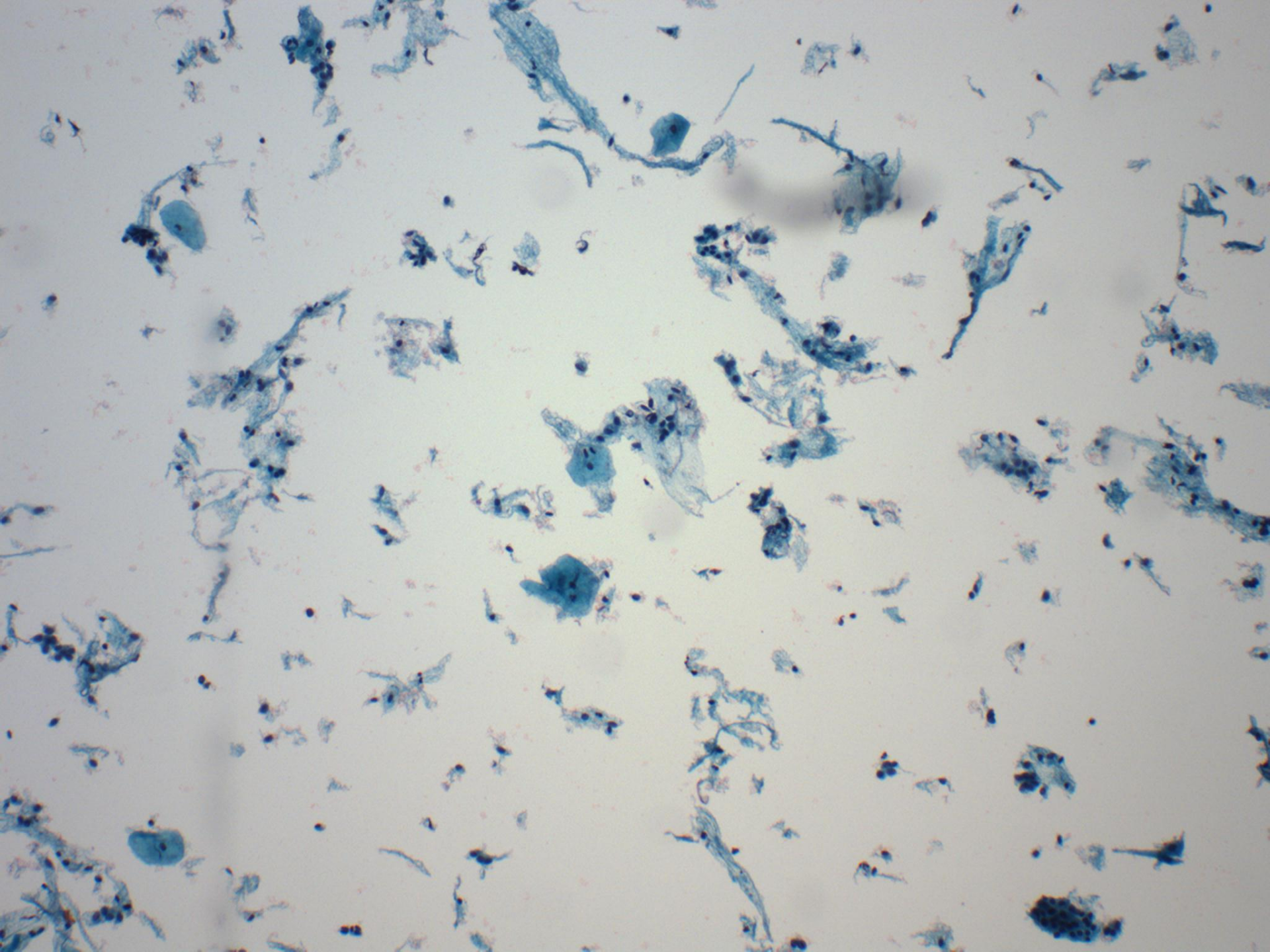


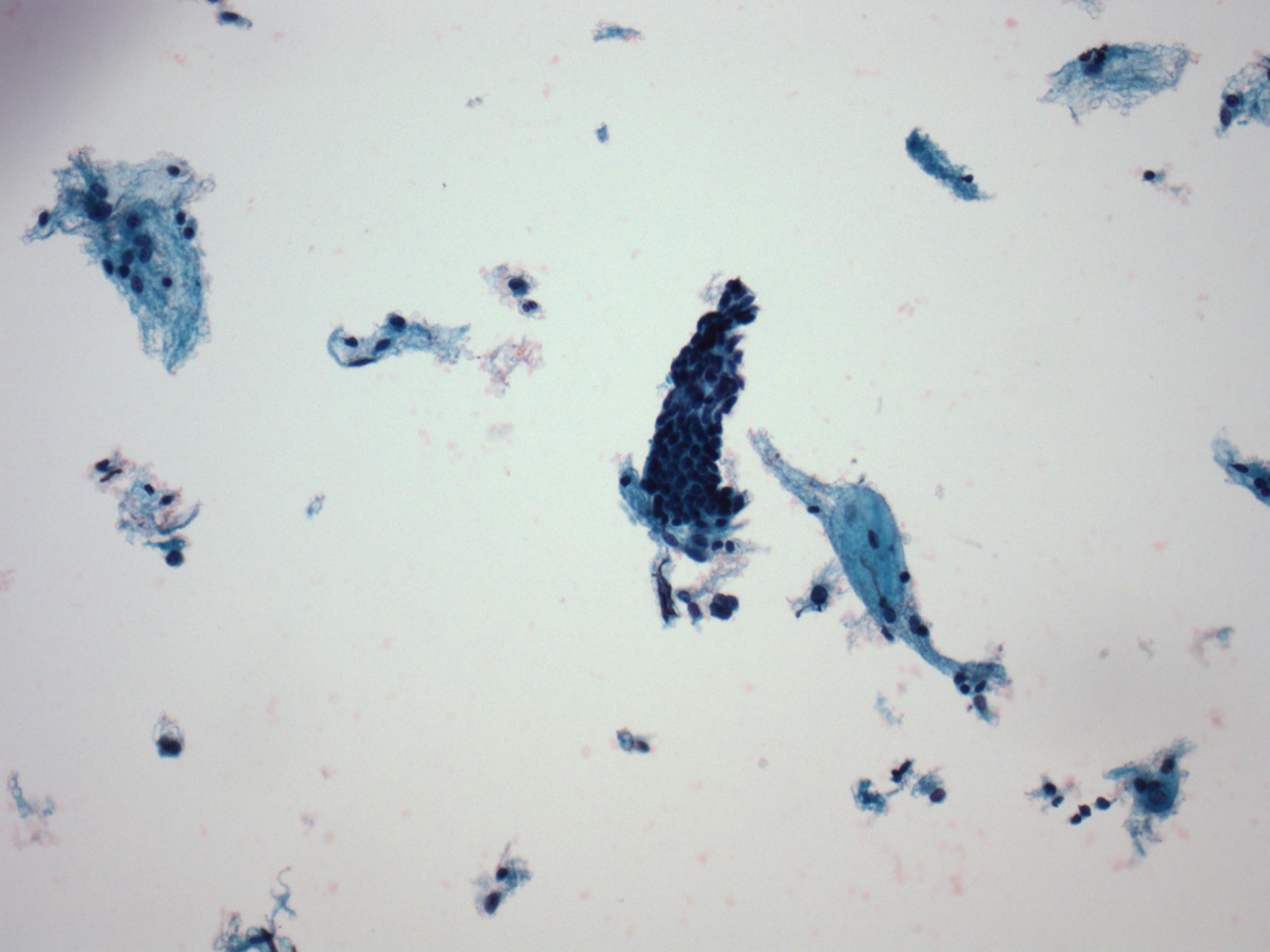
Case 2

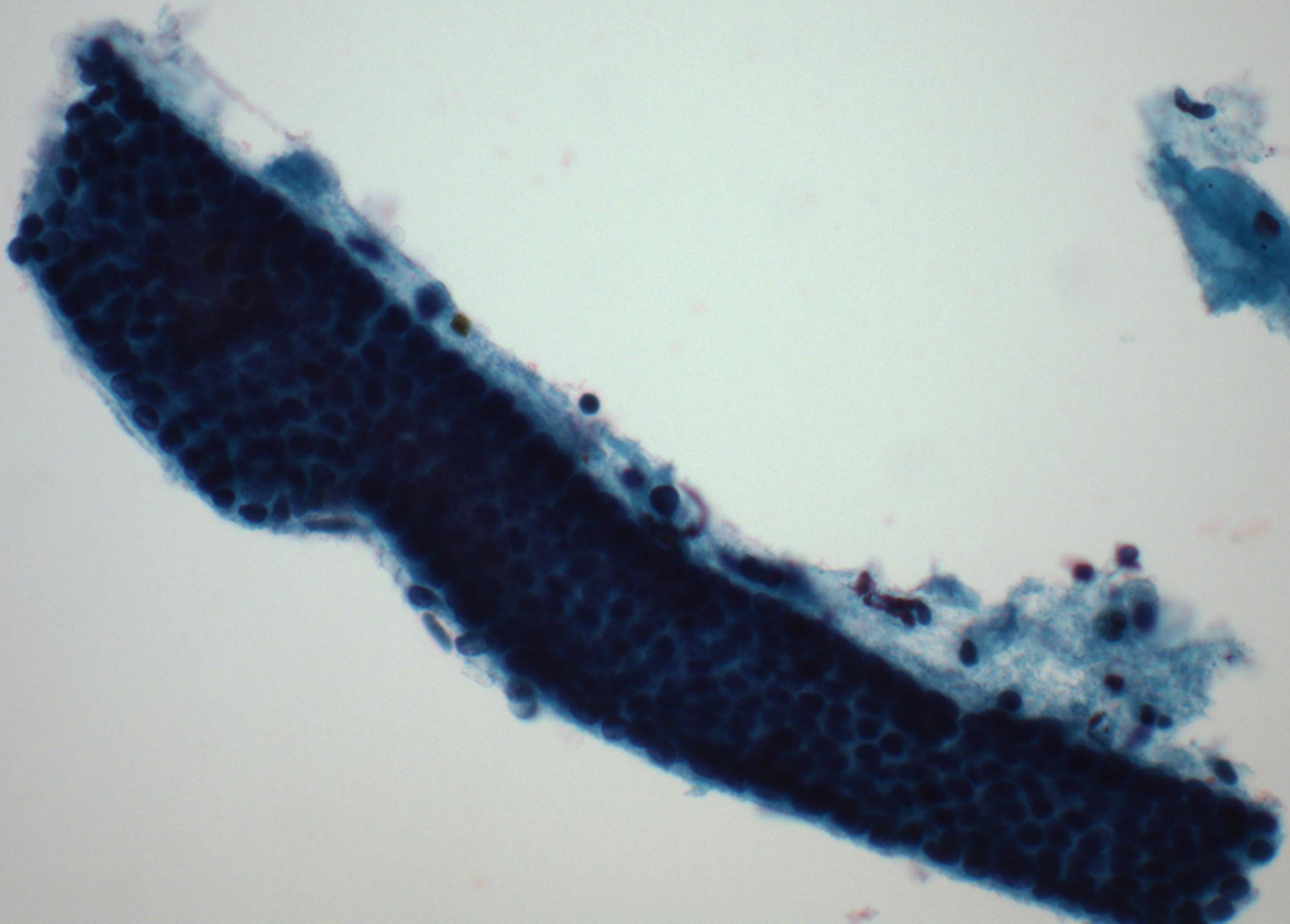
32 year old

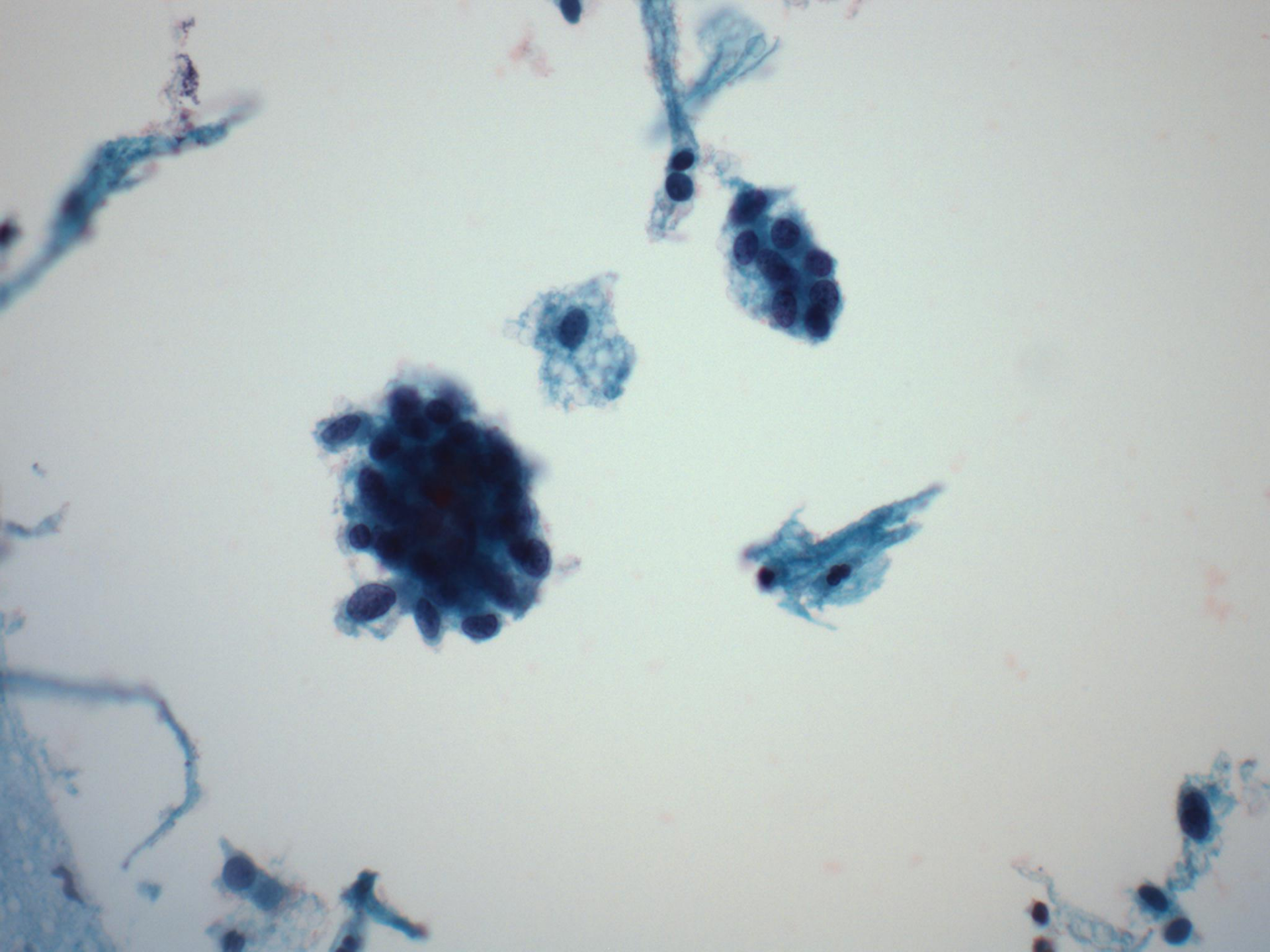
Prior history of CIN 3

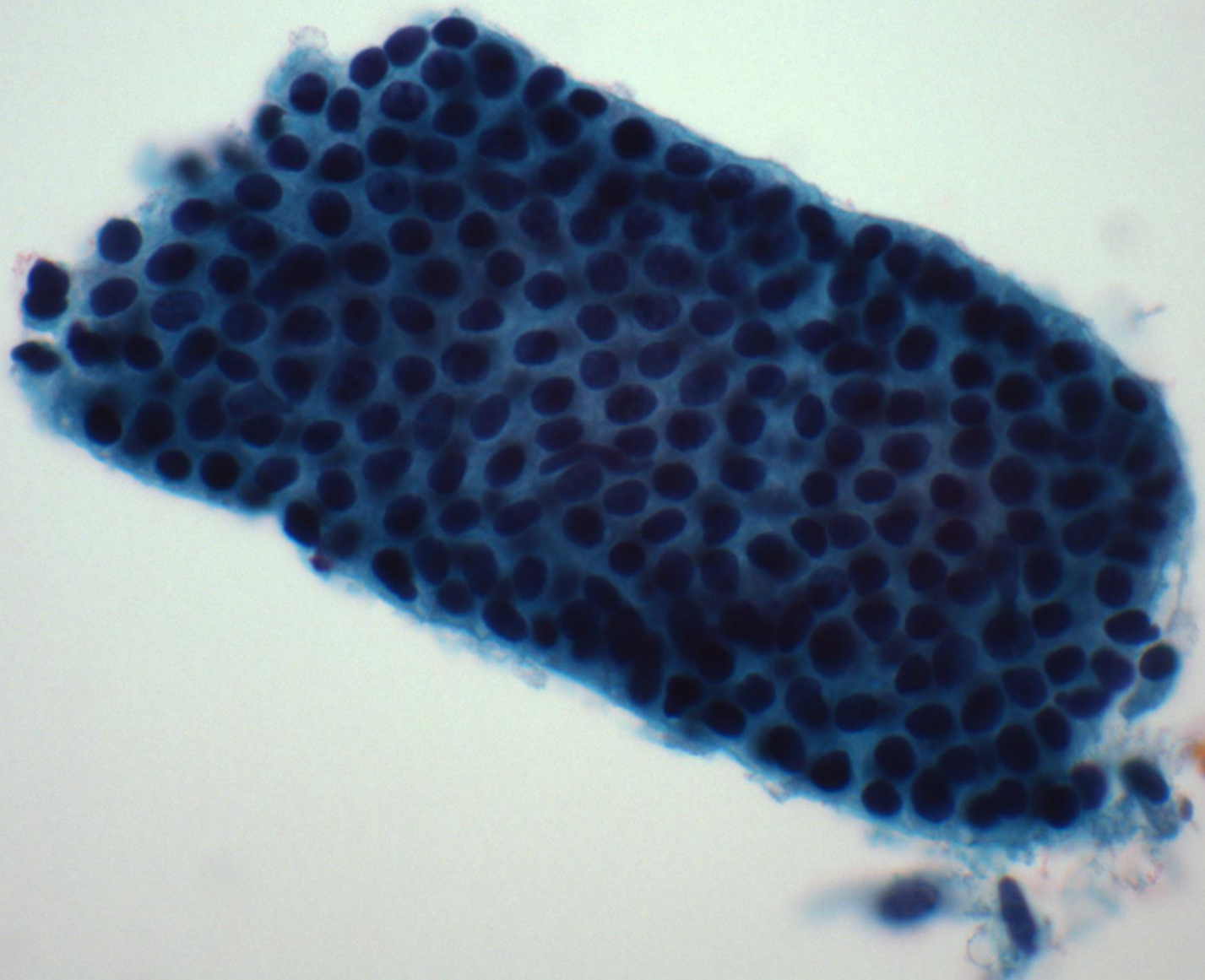


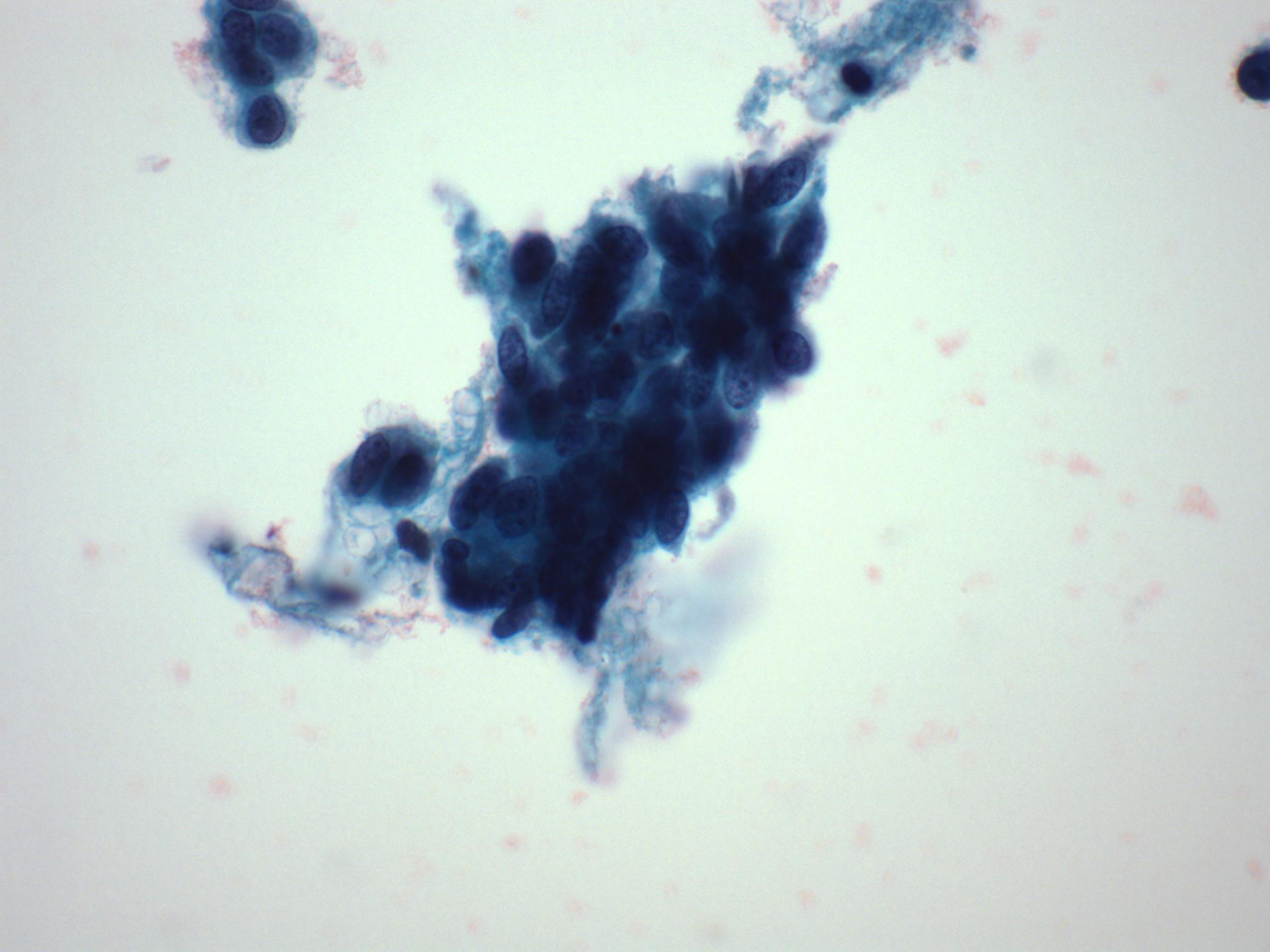


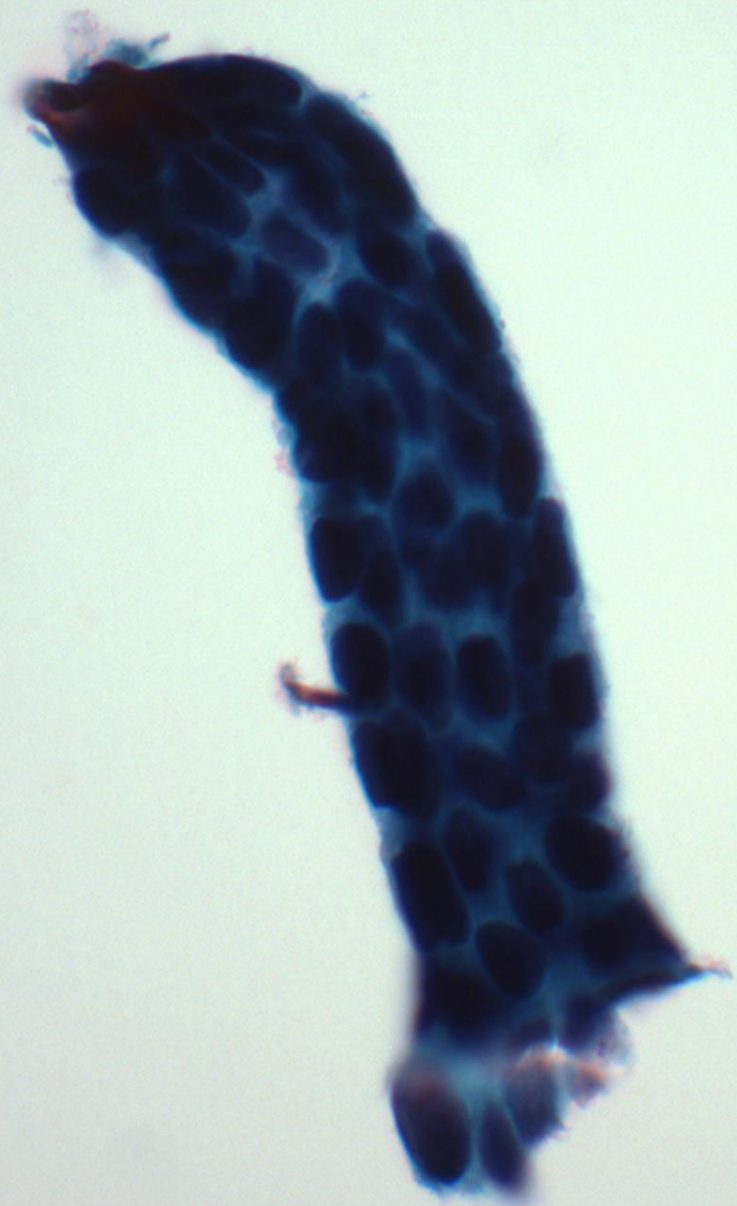












Summary of Key Cytologic Features

- Scantly cellular specimen
- Wispy background material
- Dense groups with organized epithelium and sharply defined margins
- Dense groups of spindle-type cells
 - Isolated and attached to groups

Benign

Malignant

Atypical

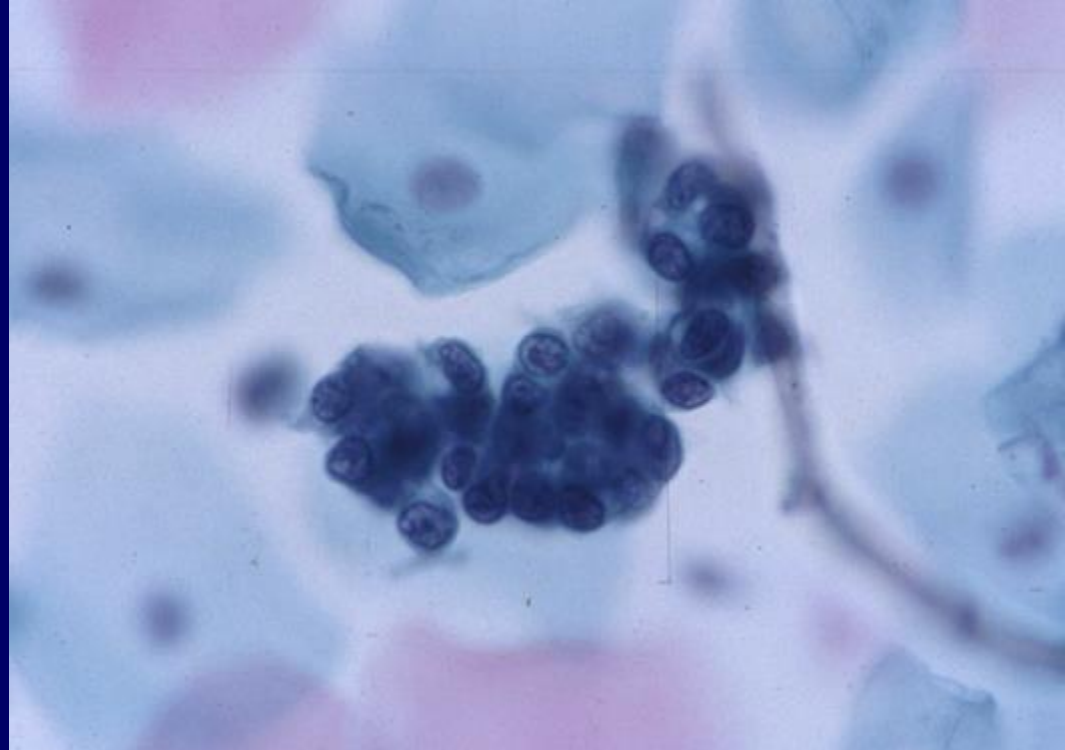
Diagnosis:

Directly Sampled Endometrium

Directly Sampled Endometrium

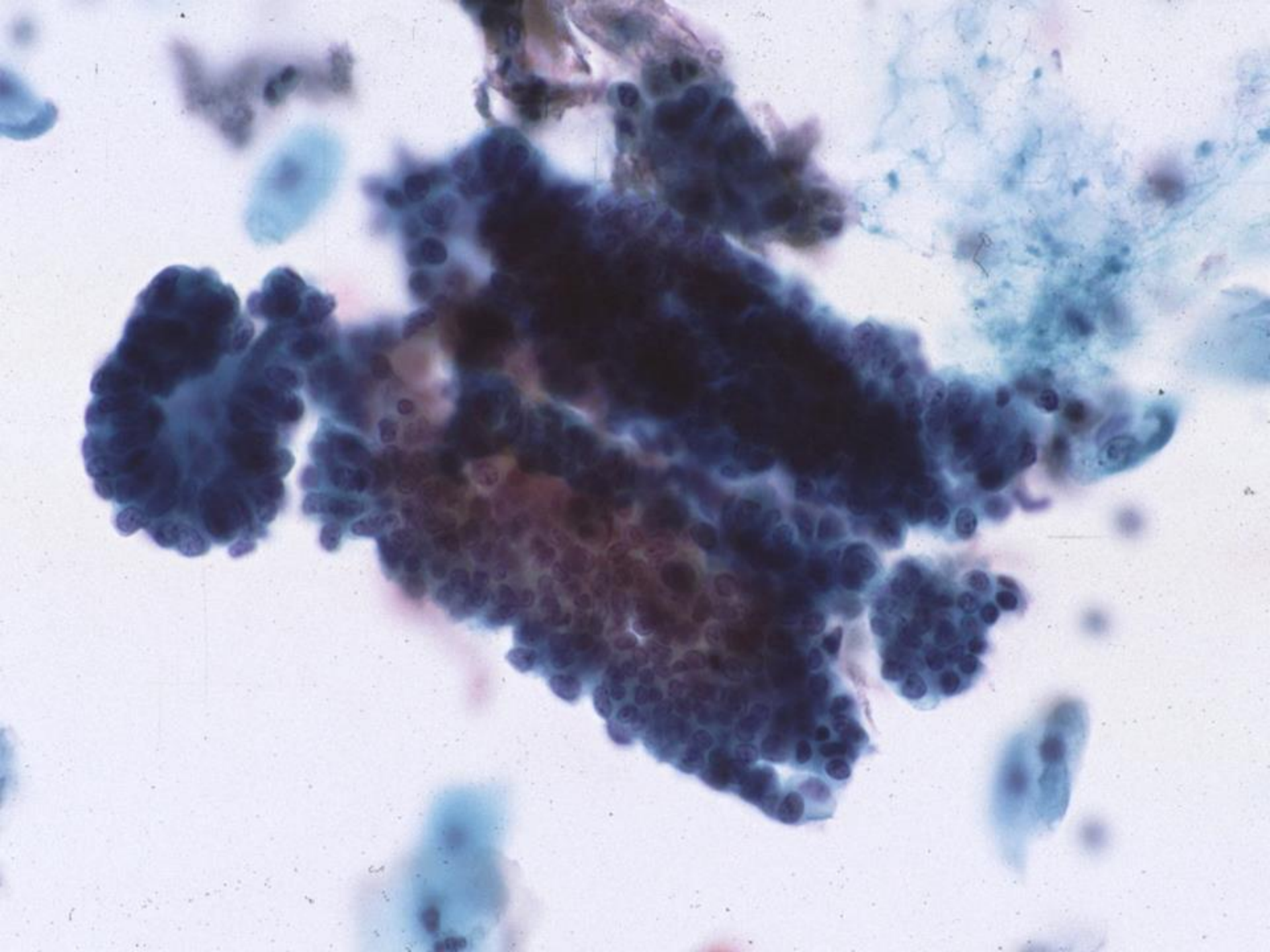
- Present as pseudostratified strips of cells
- Nuclei are generally coarsely granular
- Good look-alike for AIS
- Stromal fragments can be HCG's
- Stromal fragments attached to EM epithelium
- Caveat – small cells with small nuclei
- Post-cone biopsy is common clinical

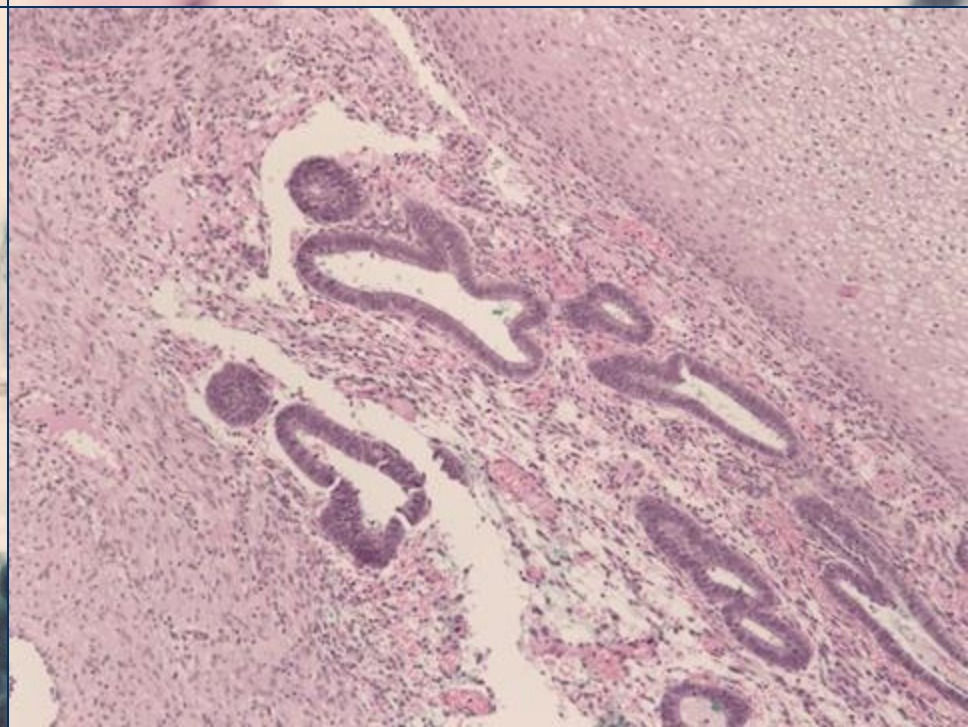
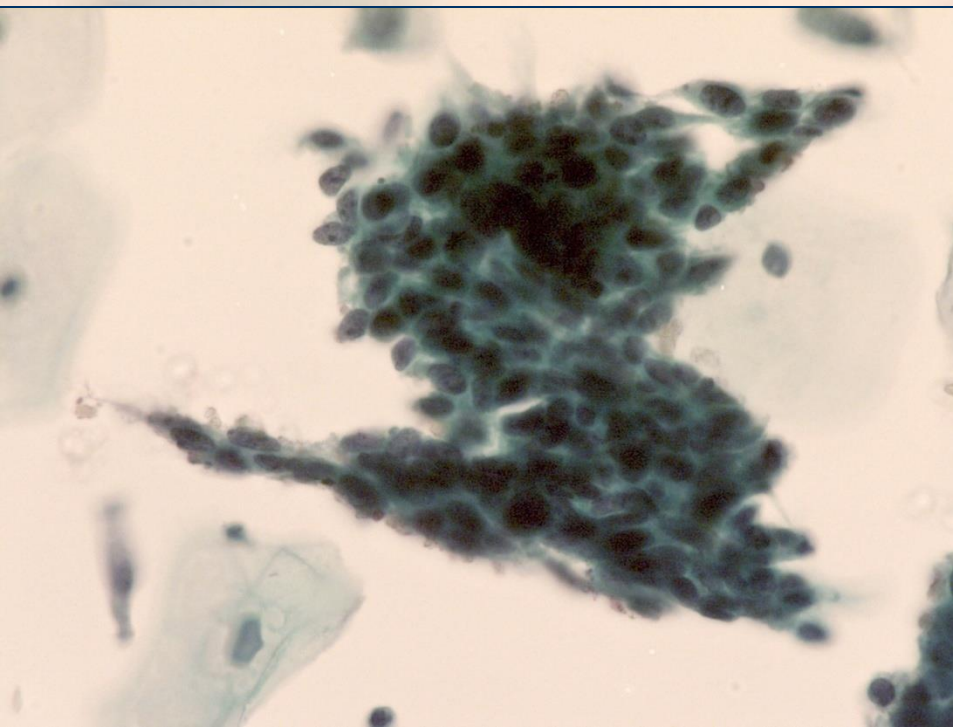
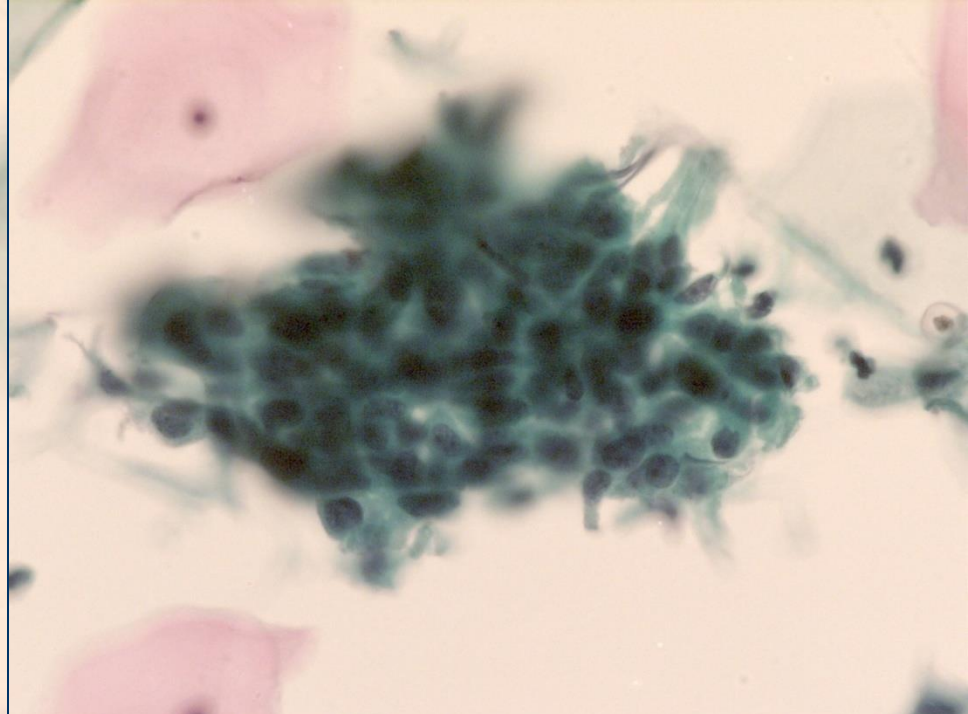
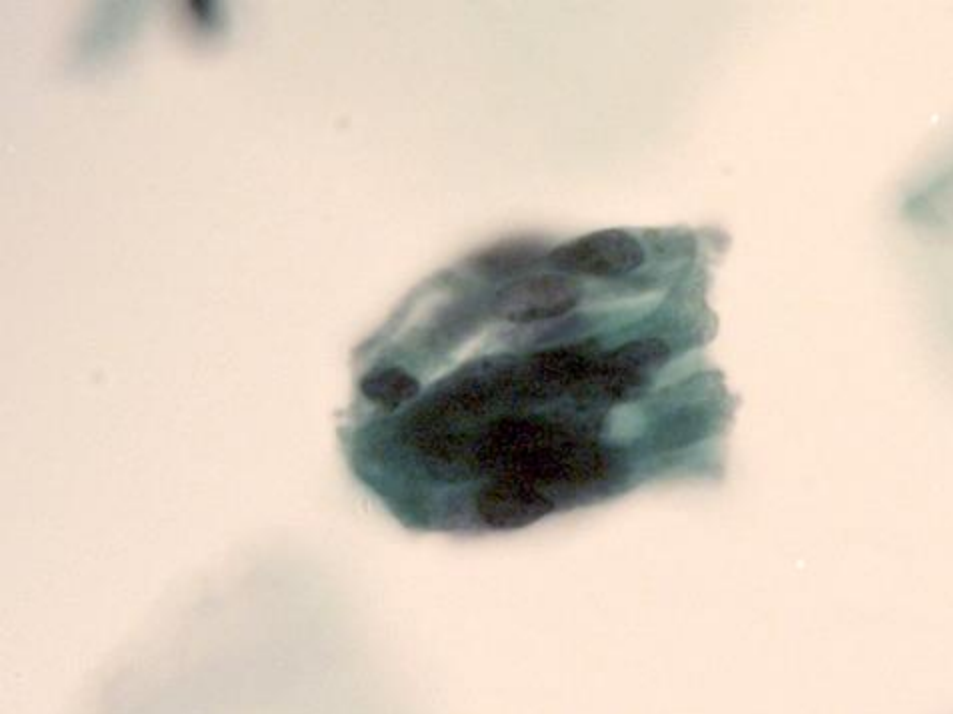
Direct Sampling

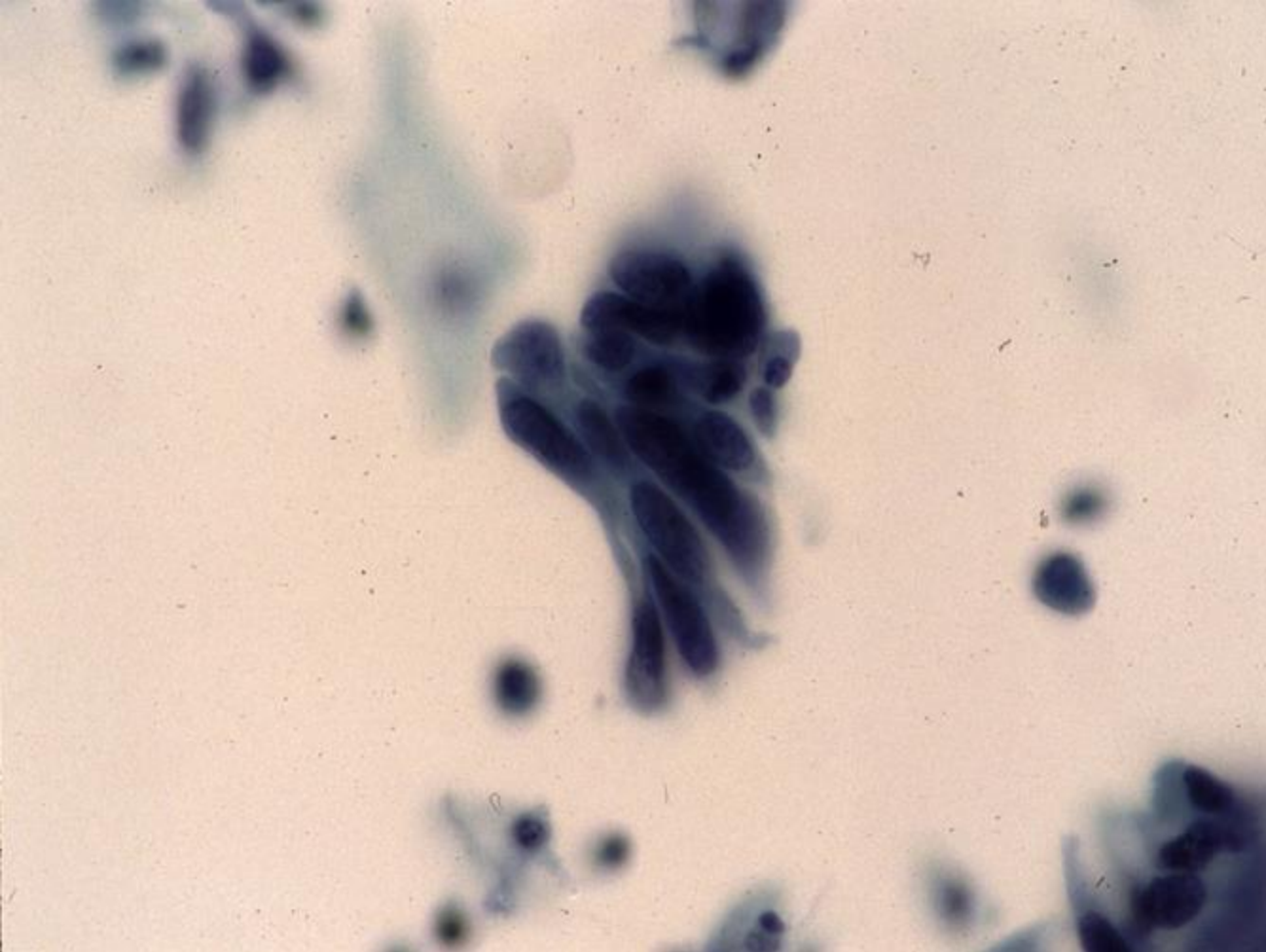


Exfoliated





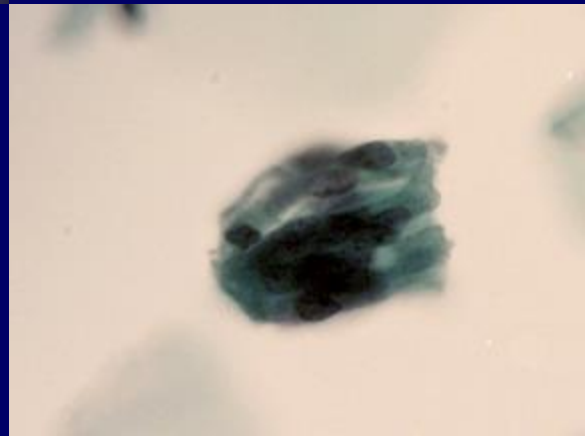




AIS

Direct-sampled
EM

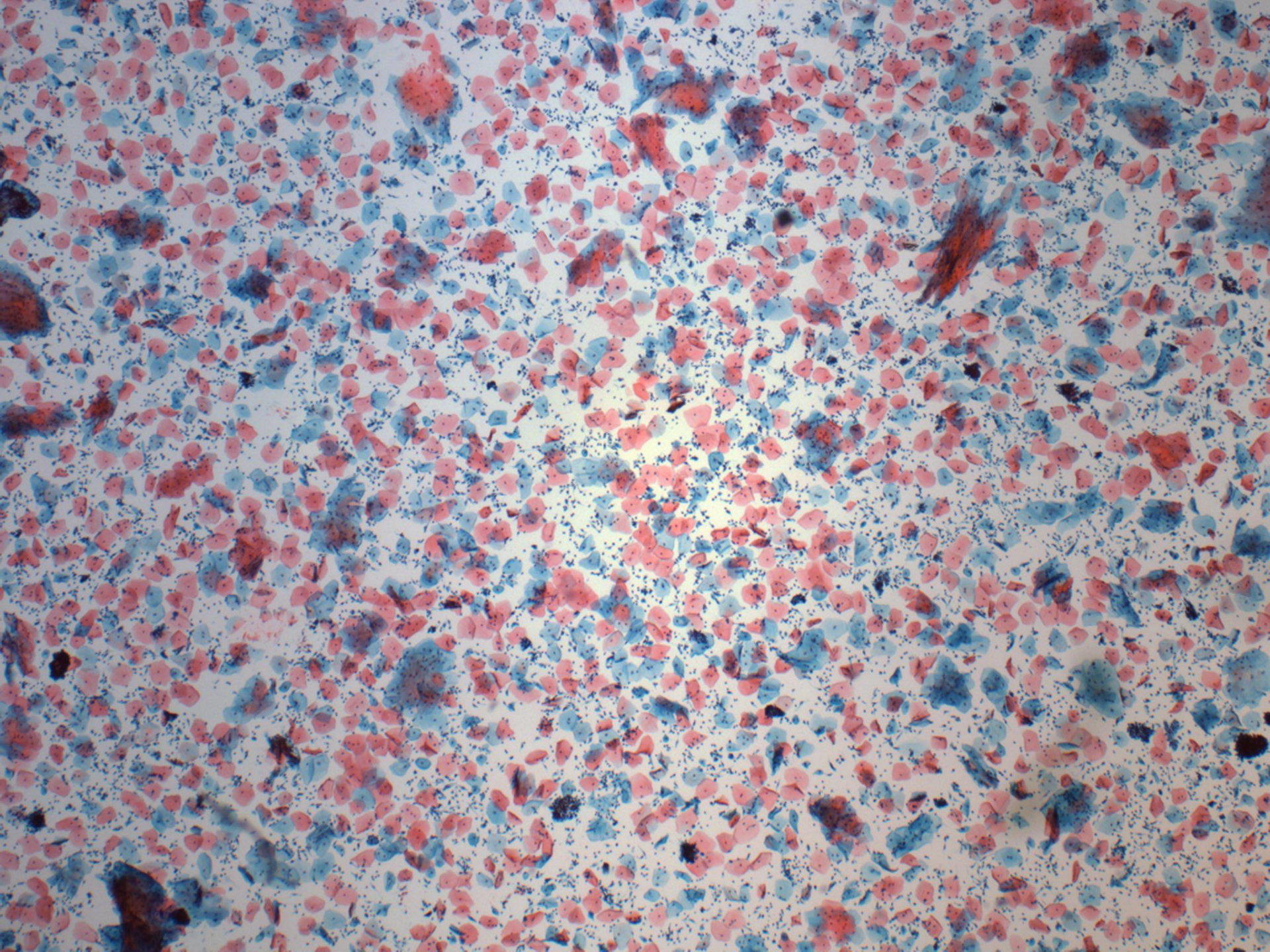
Size Matters!!

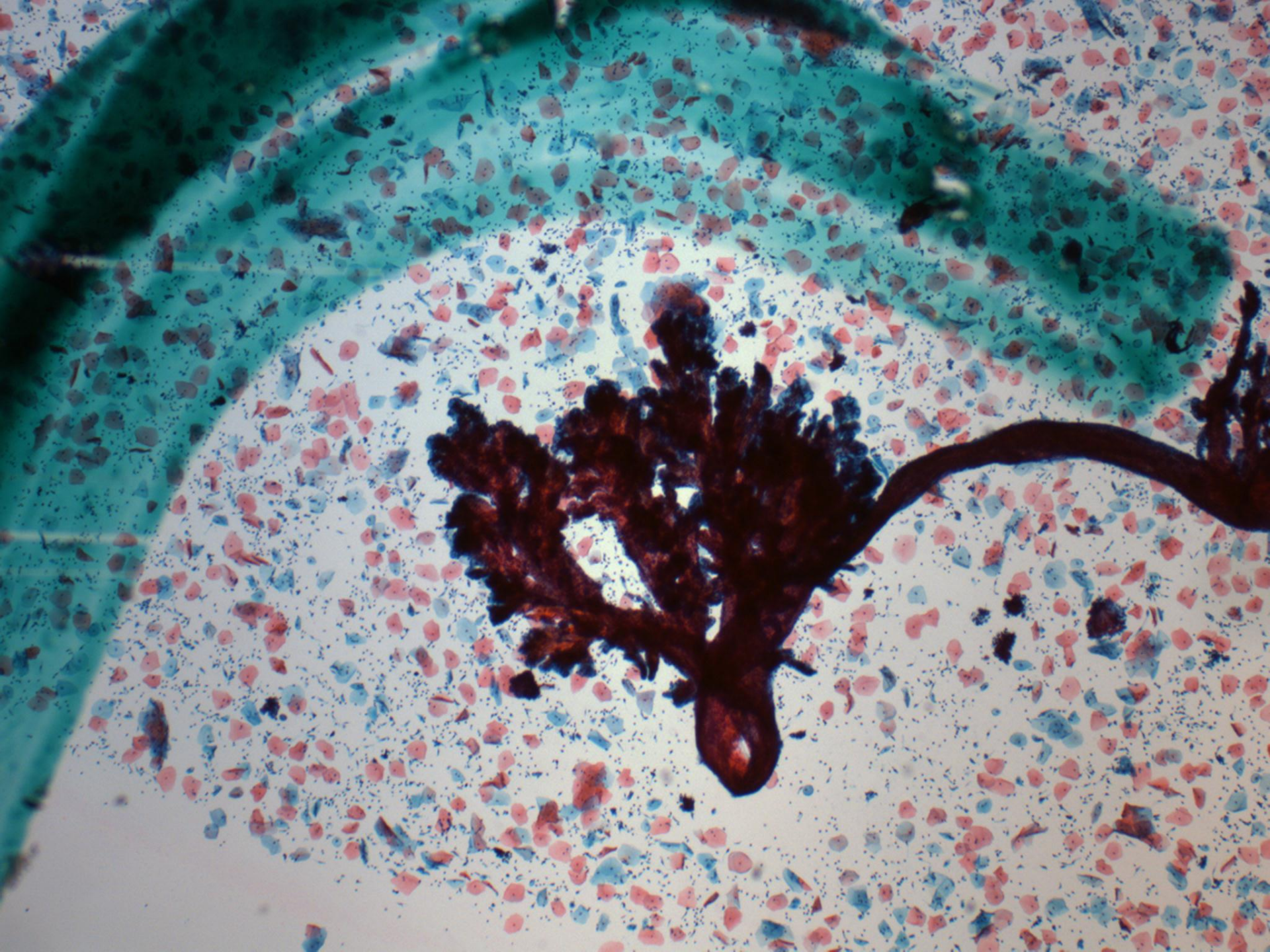


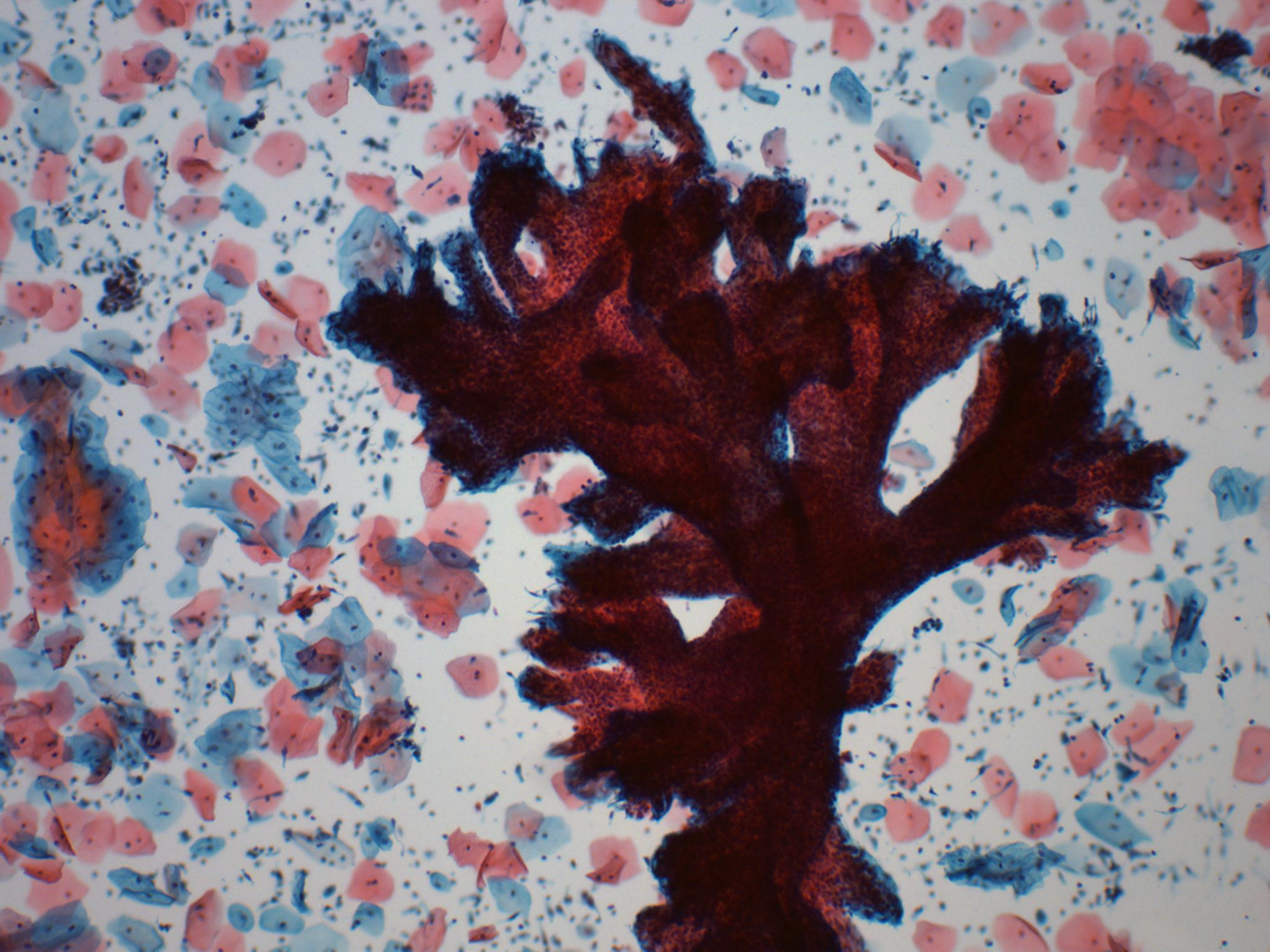
Case 3

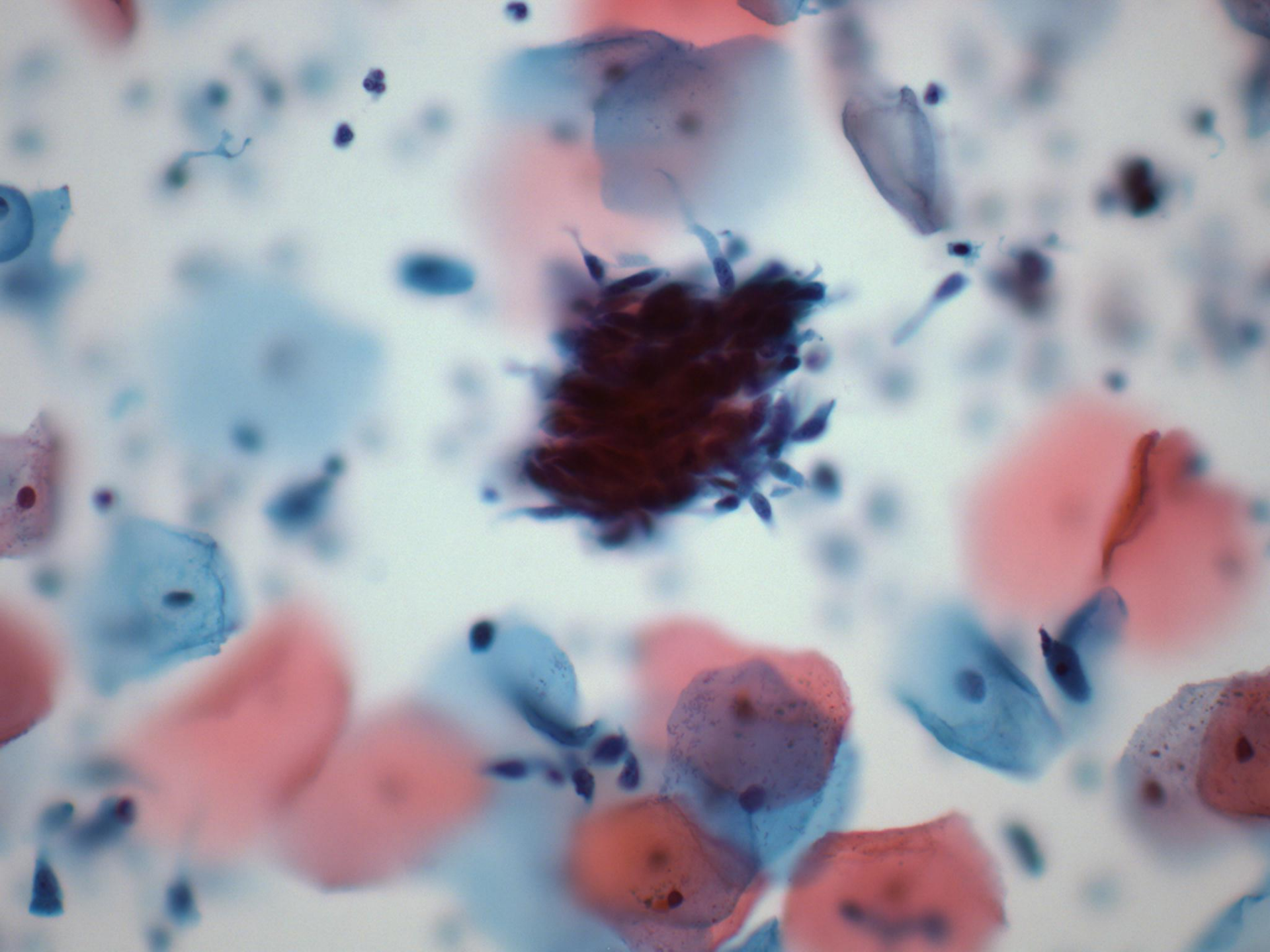
55 year old

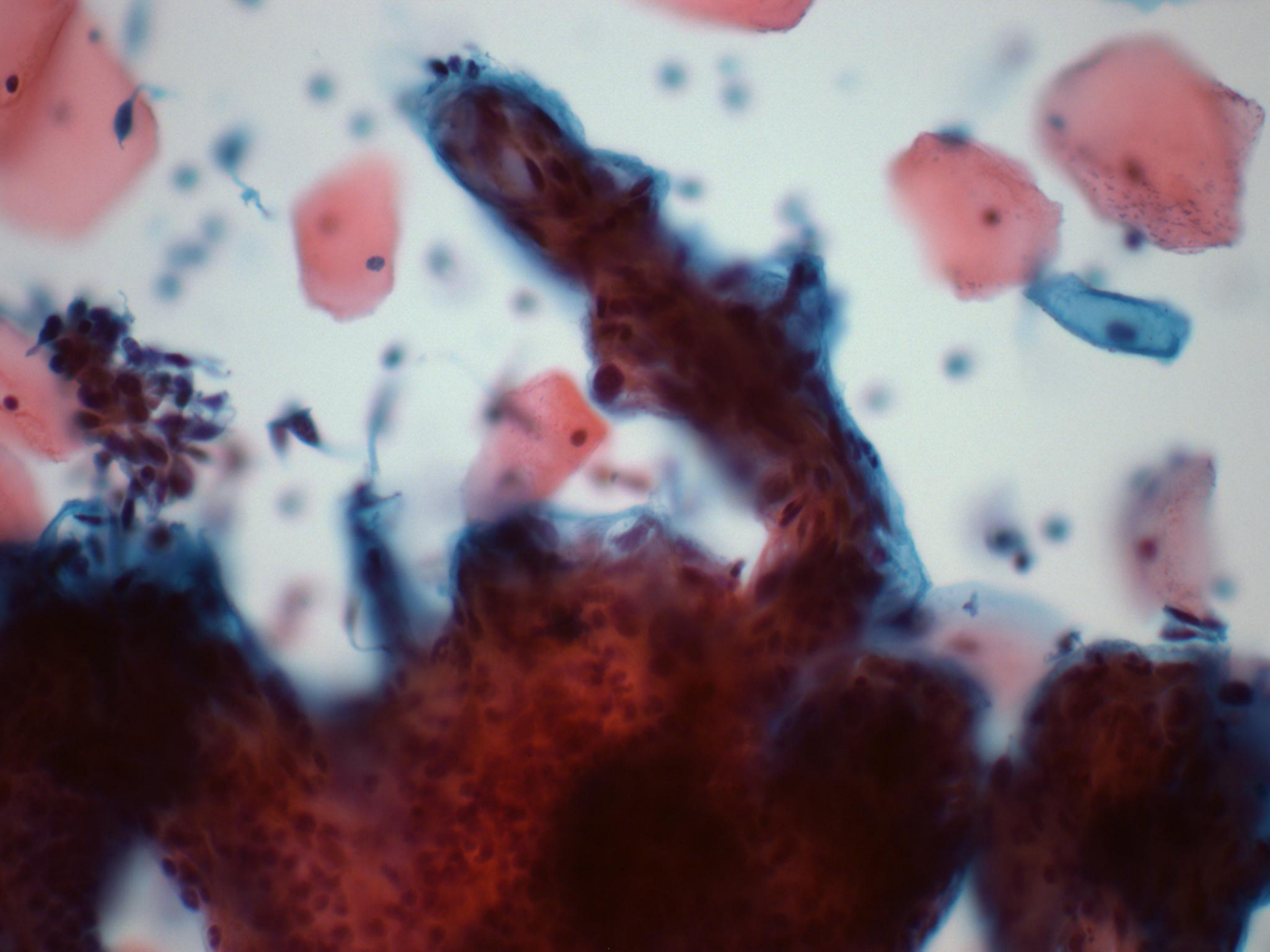
History of post menopausal bleeding

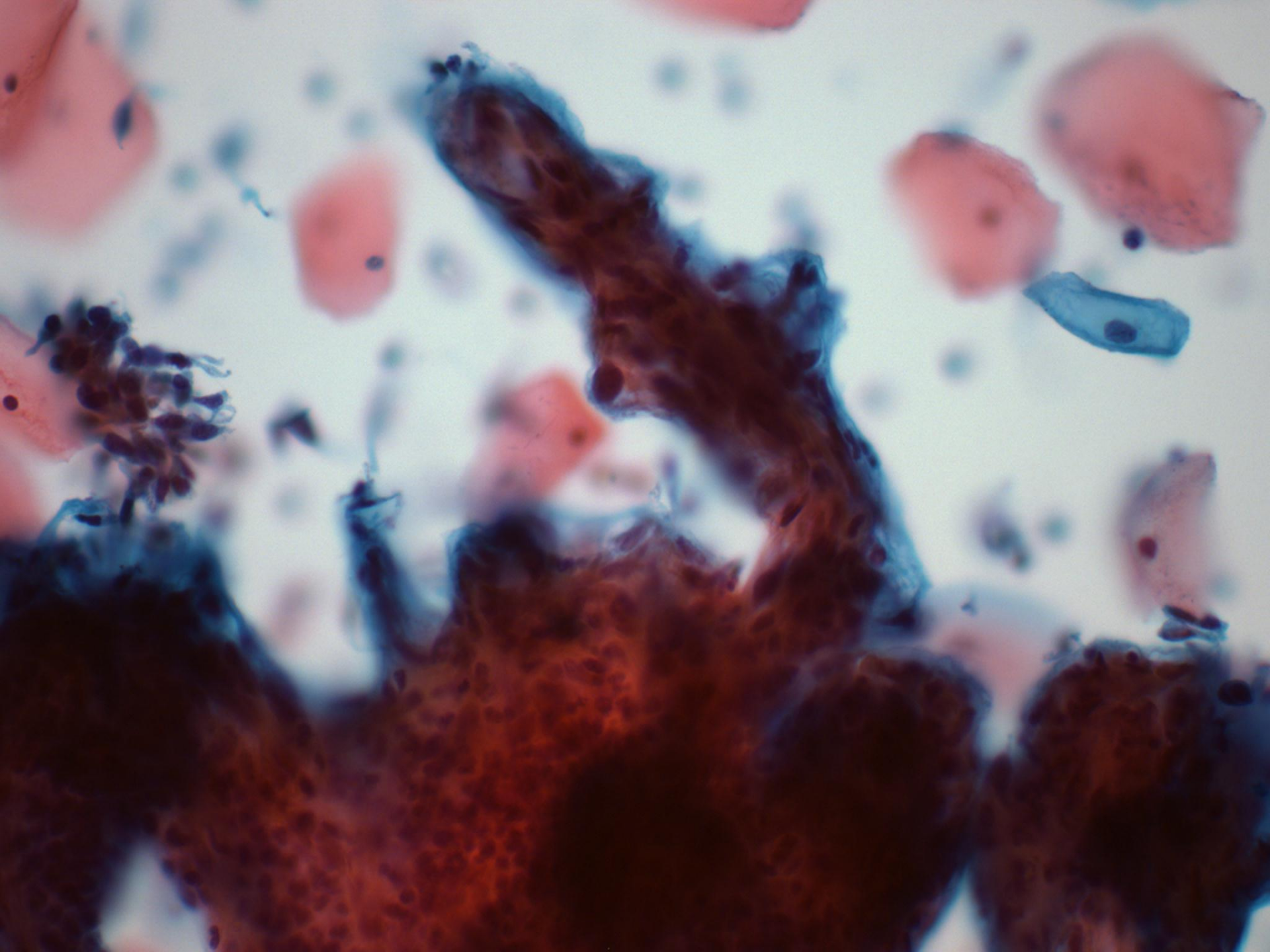


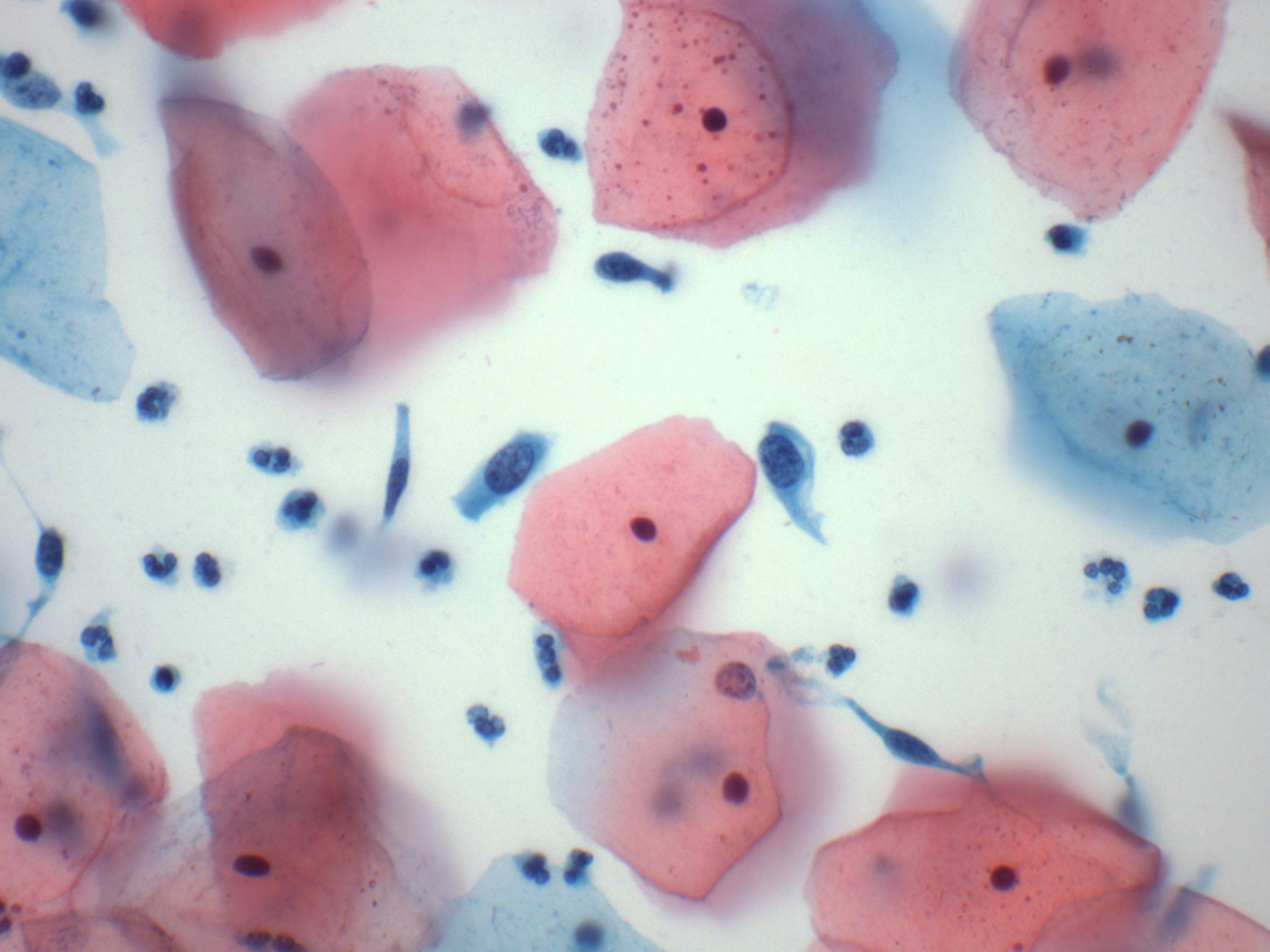


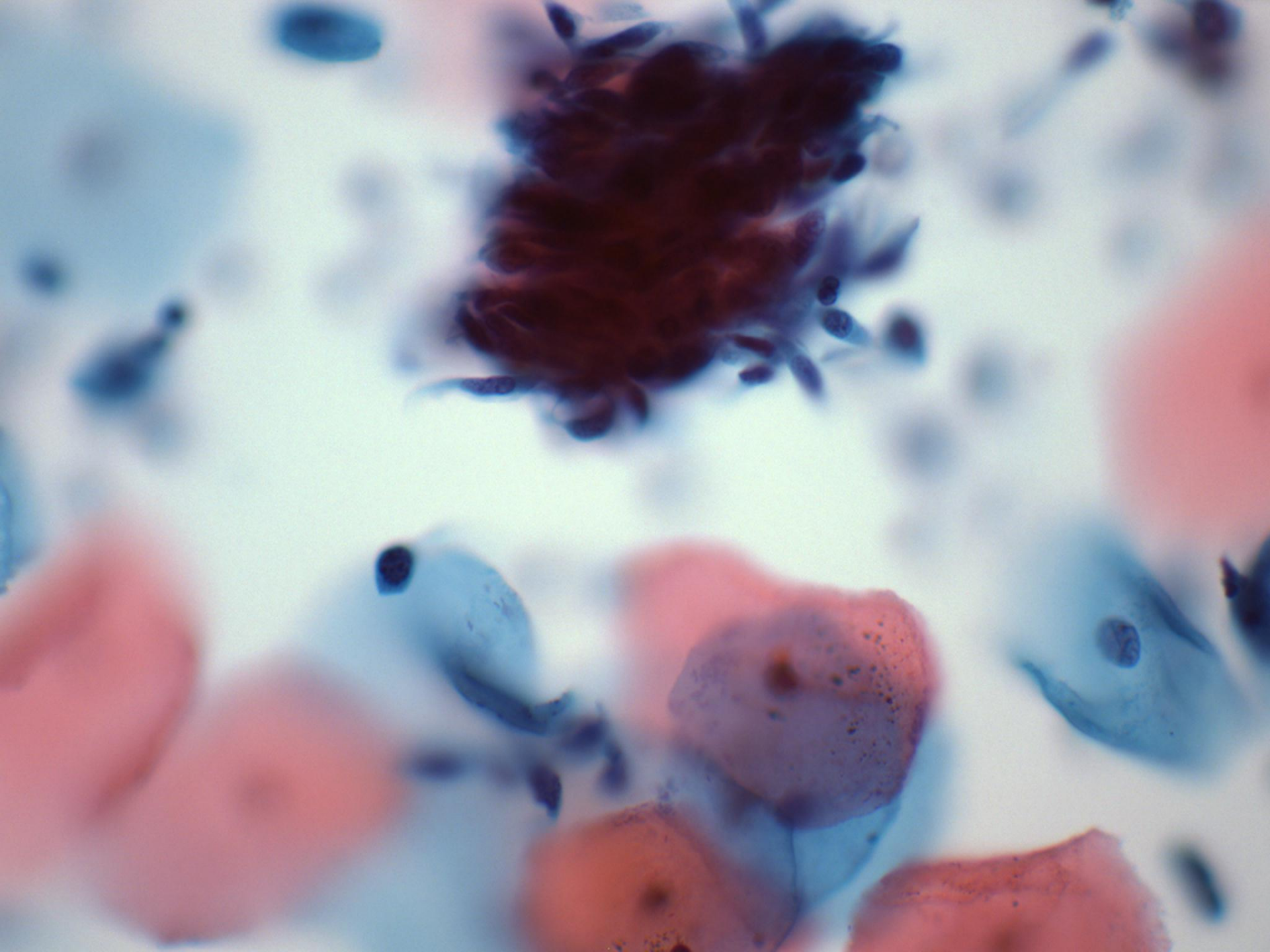


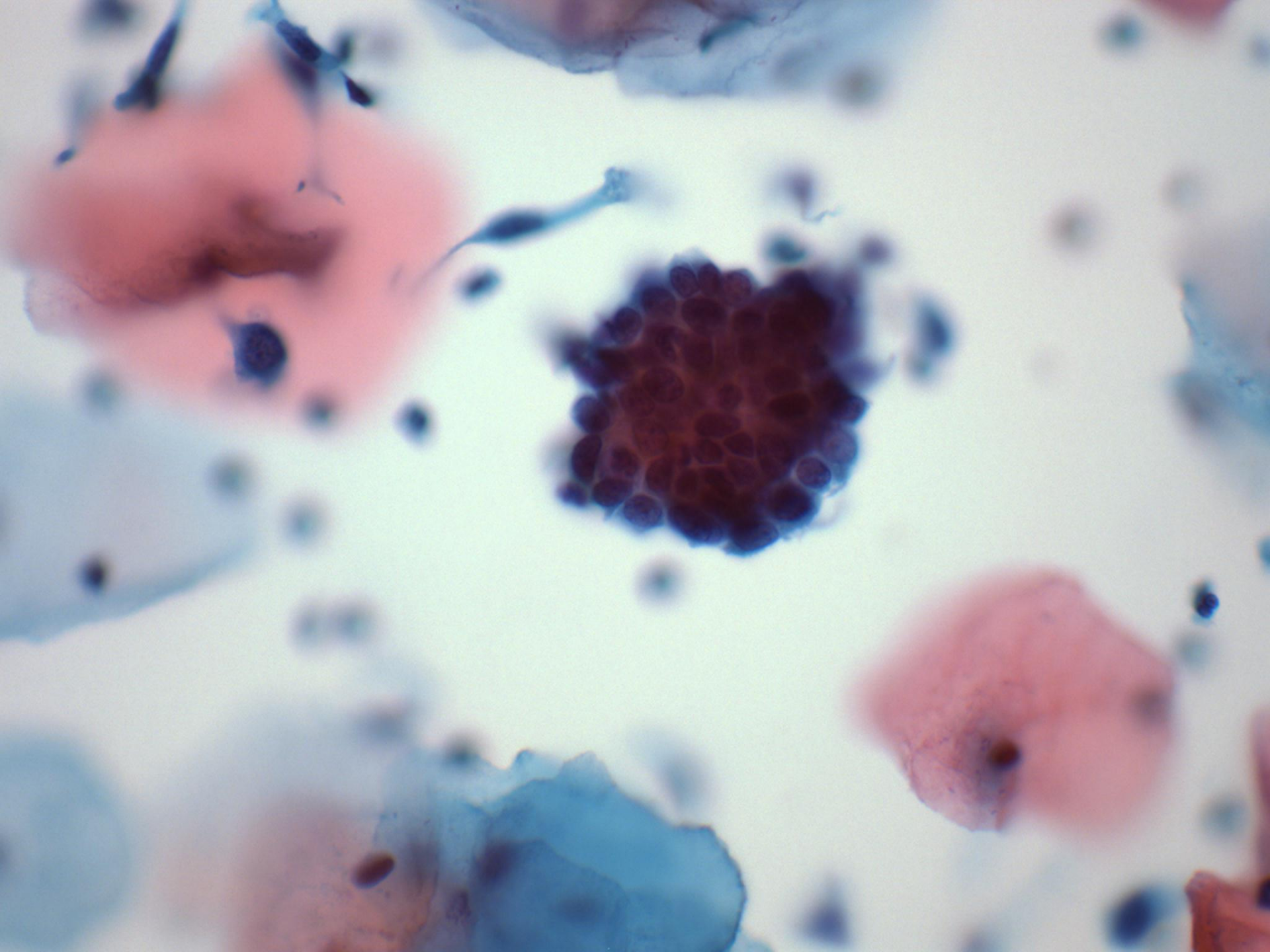


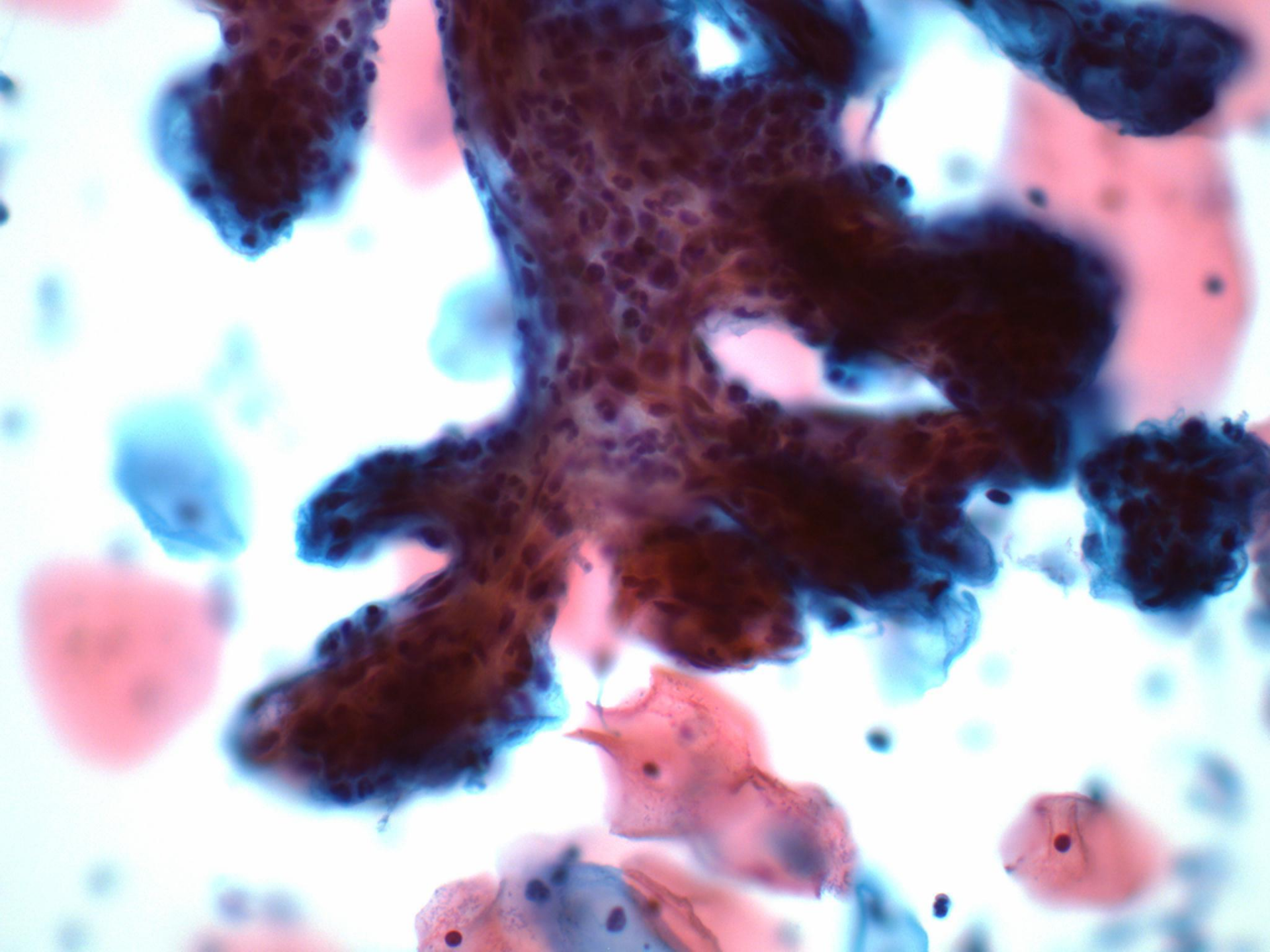


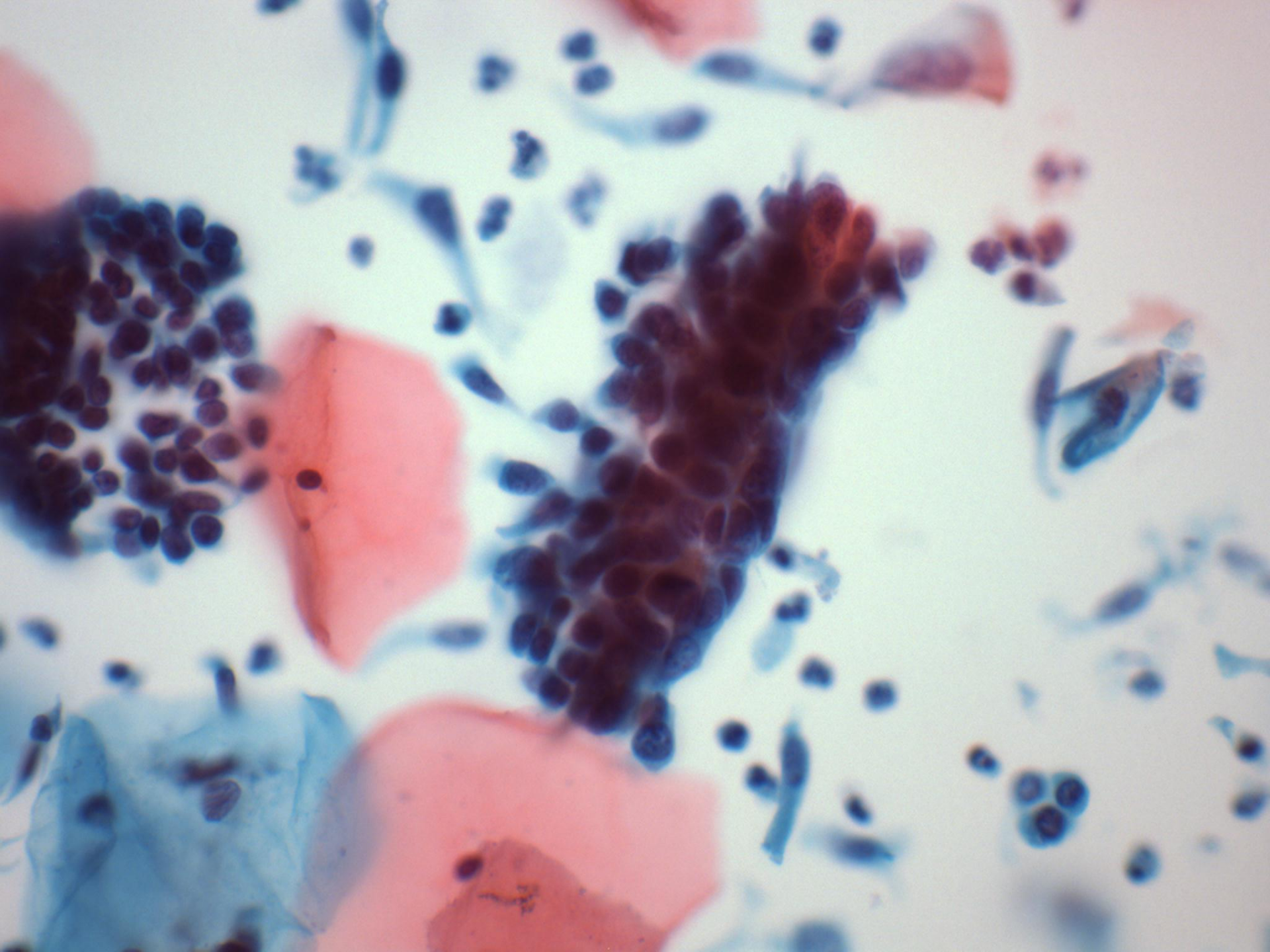












Summary of Key Cytologic Features

- Large numbers of endocervical cells in background
- Large multi-papillary groups with fibrovascular cores – devoid of surface epithelium
- Clusters and strips of pseudostratified columnar epithelium
- Central cores with aggregates of inflammatory cells

Benign

Malignant

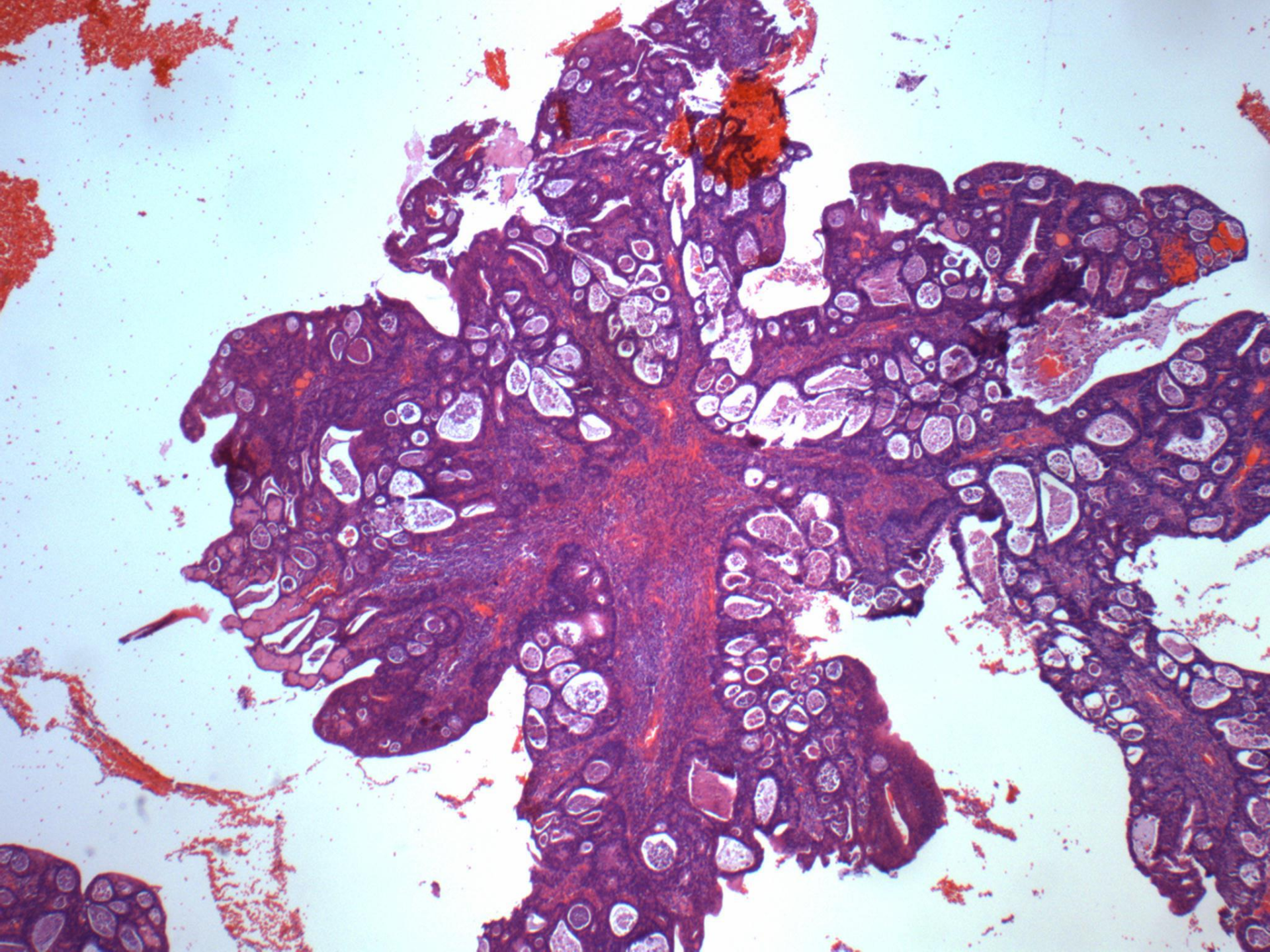
Atypical

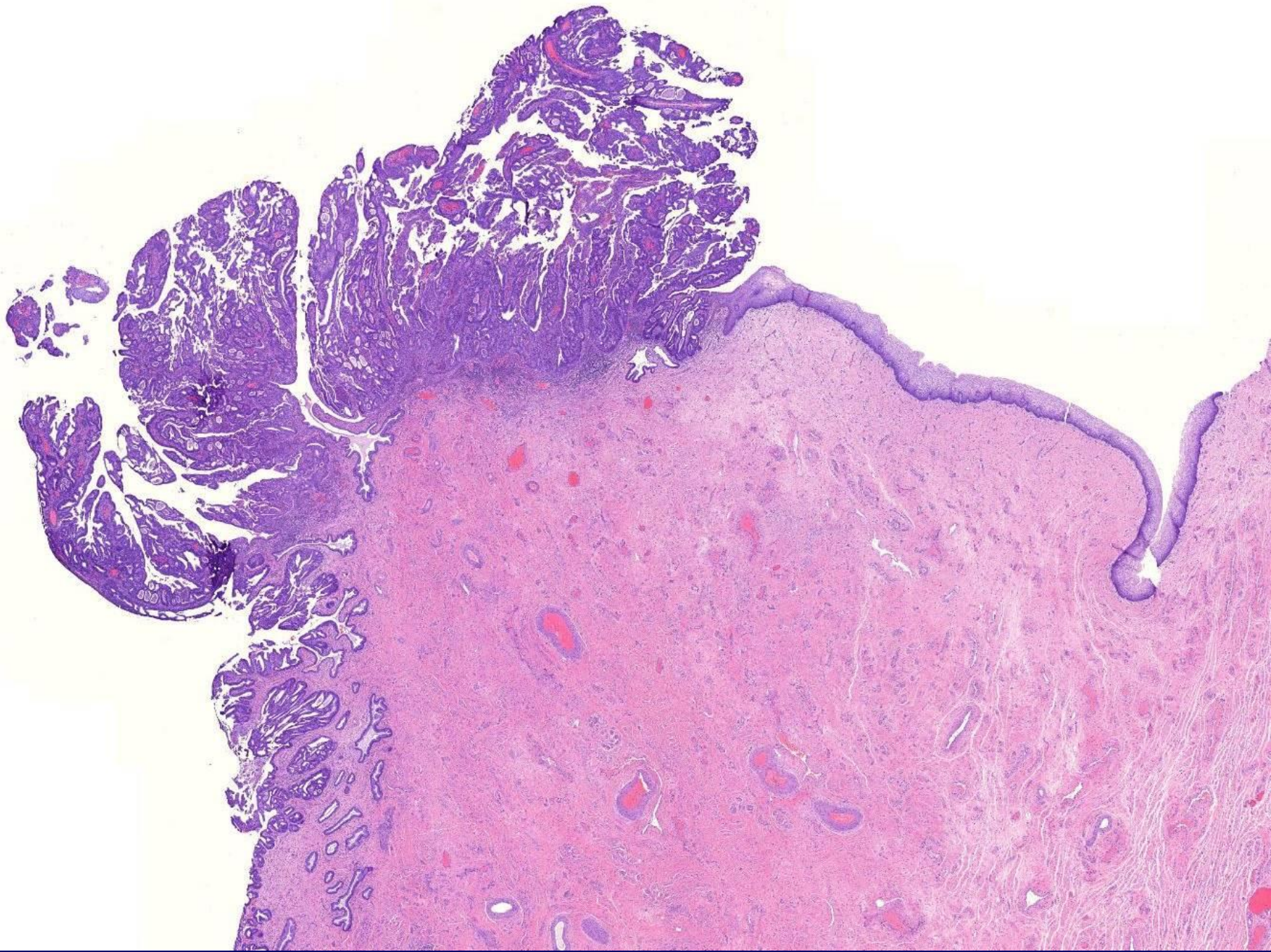
Diagnosis:

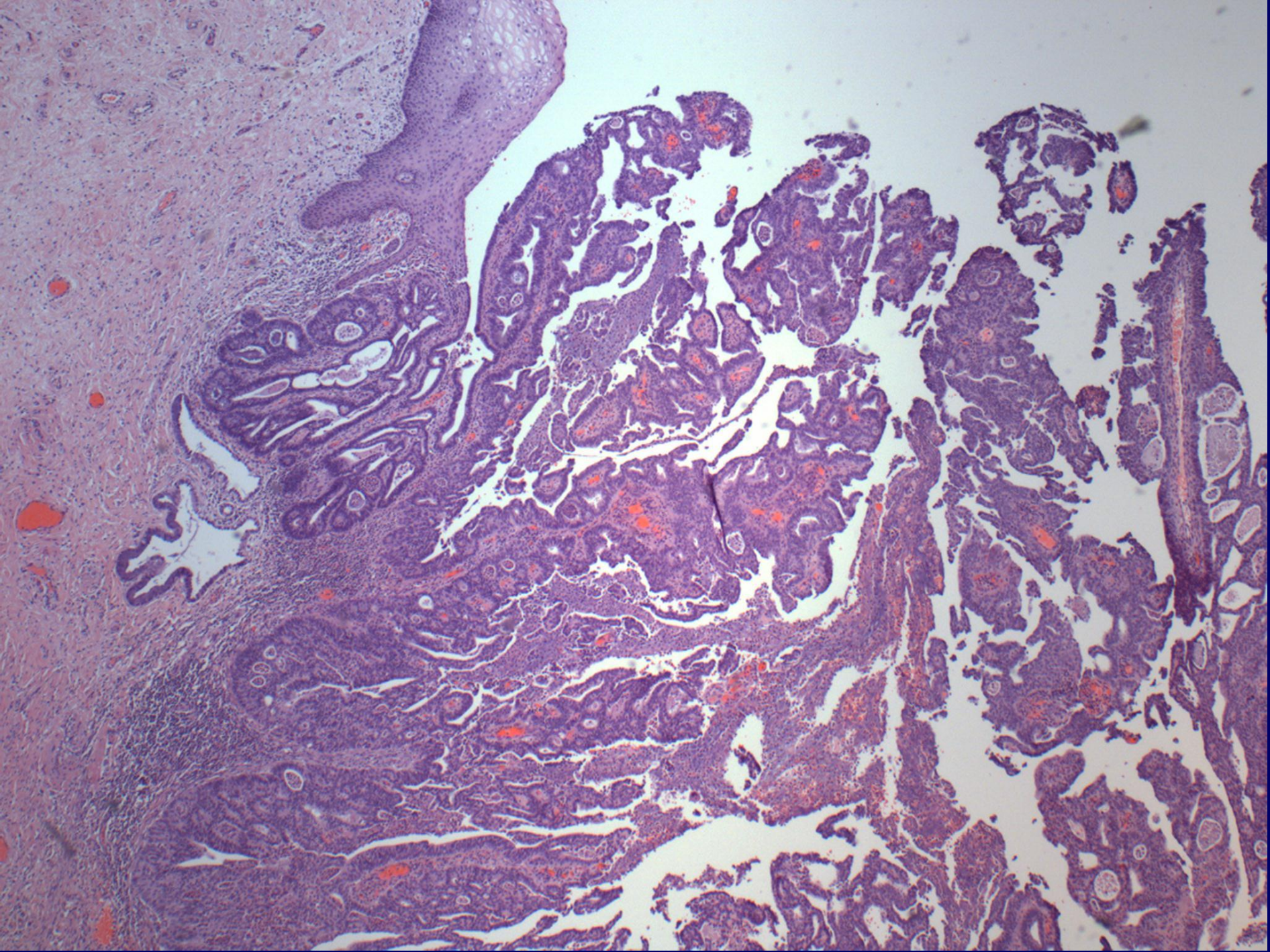
Endocervical Adenocarcinoma

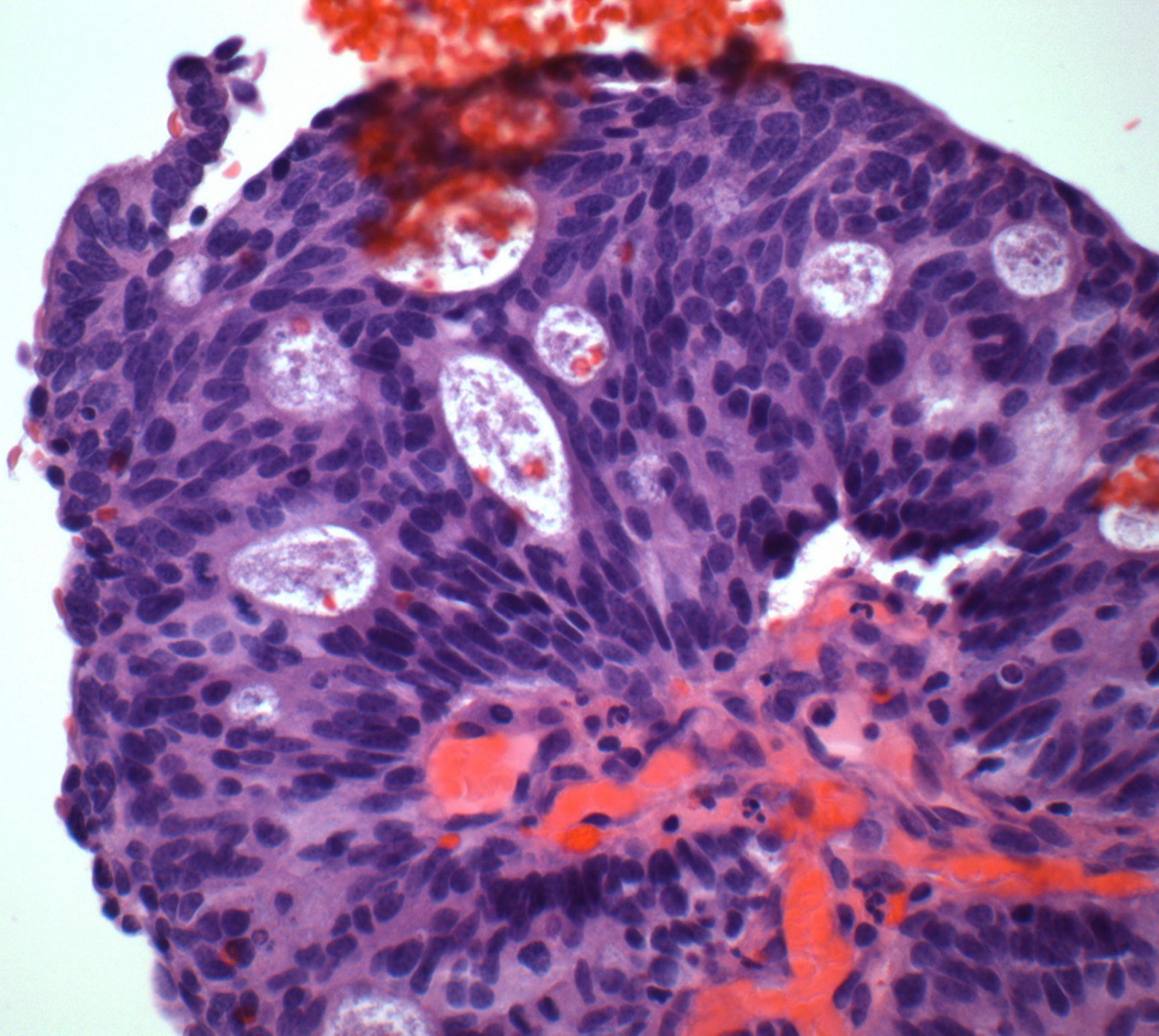
Usual Type

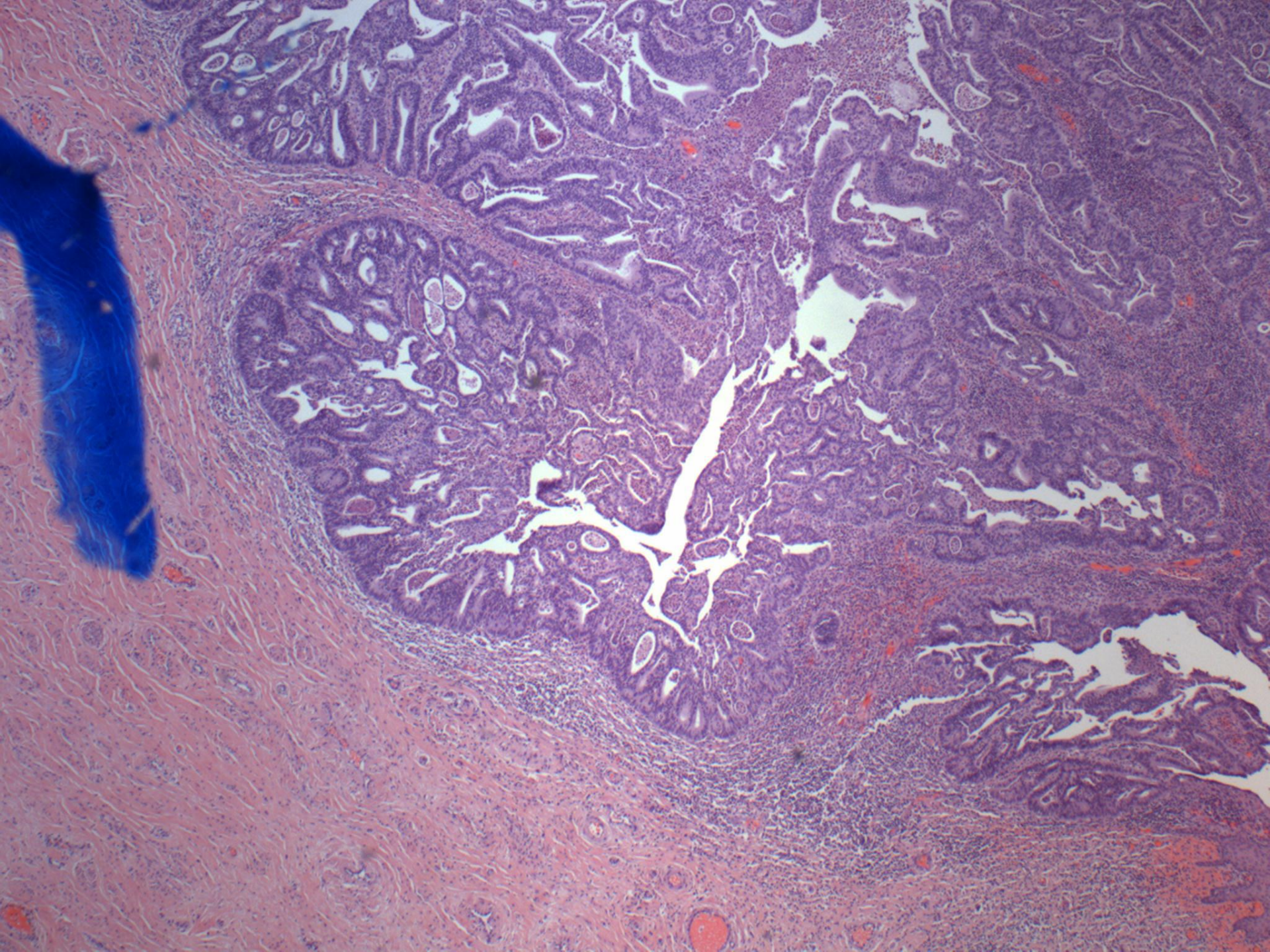
With Villous Growth Pattern

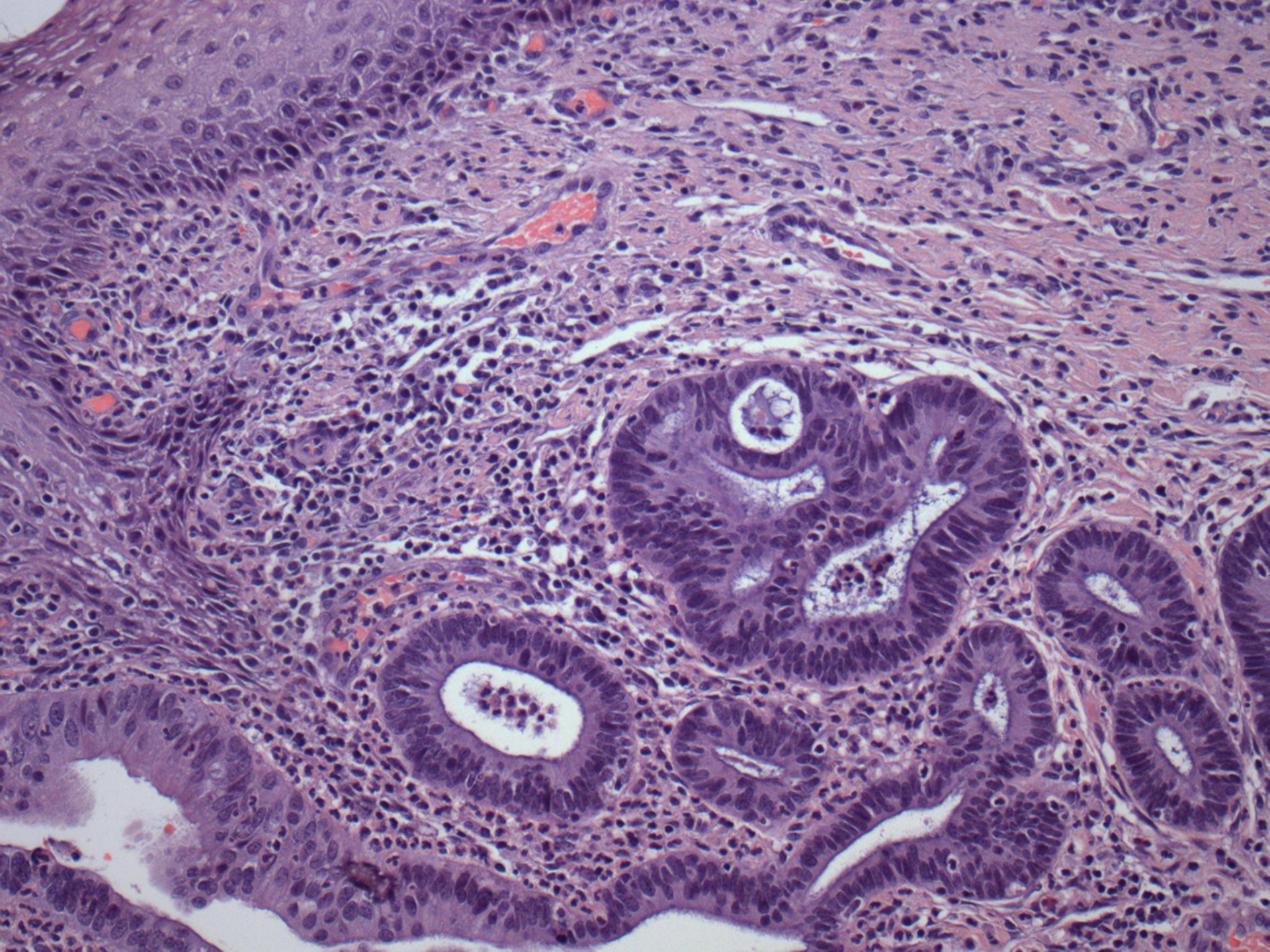












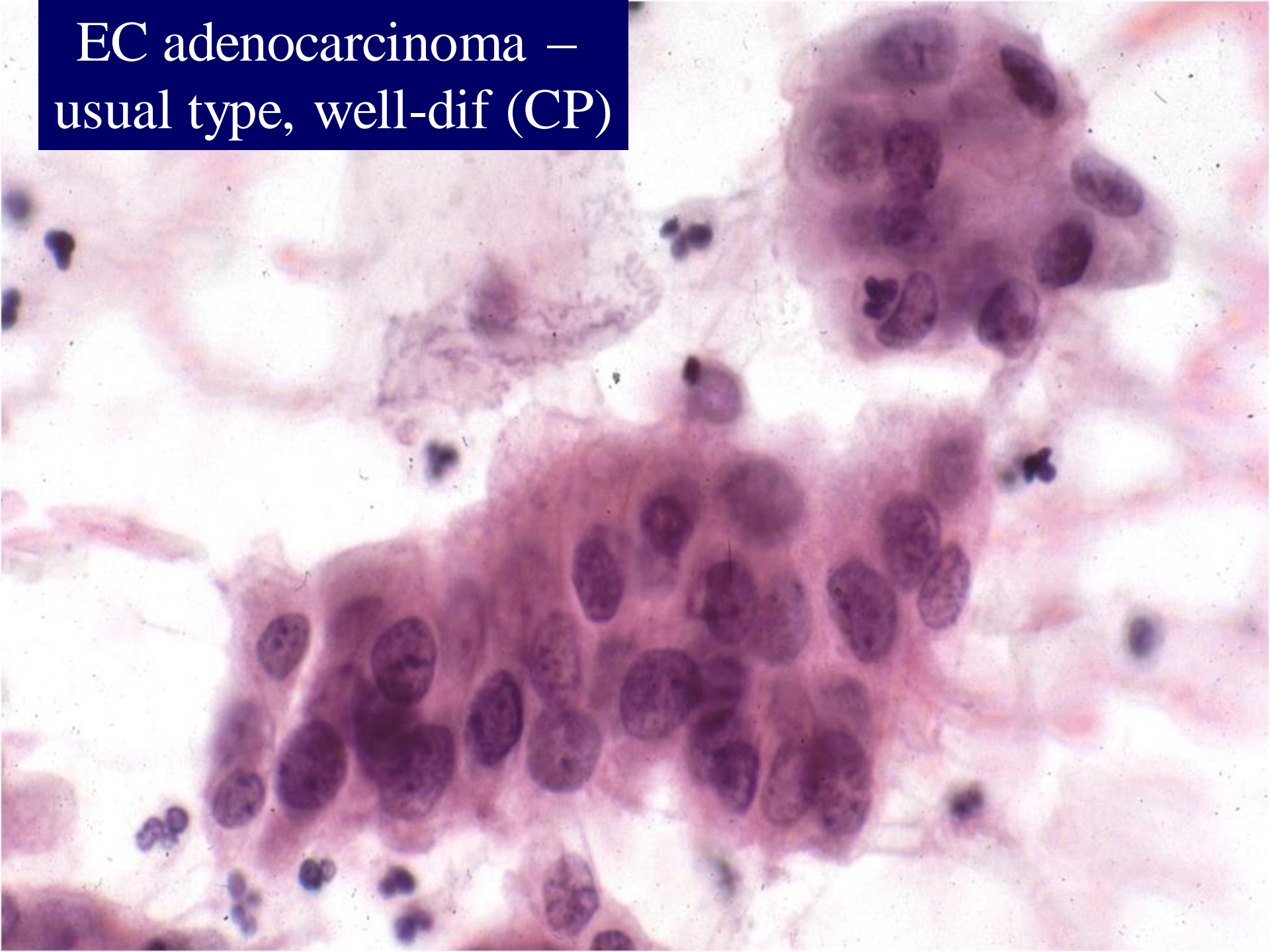
Invasive Endocervical Adenocarcinoma Subtypes (WHO 2014)

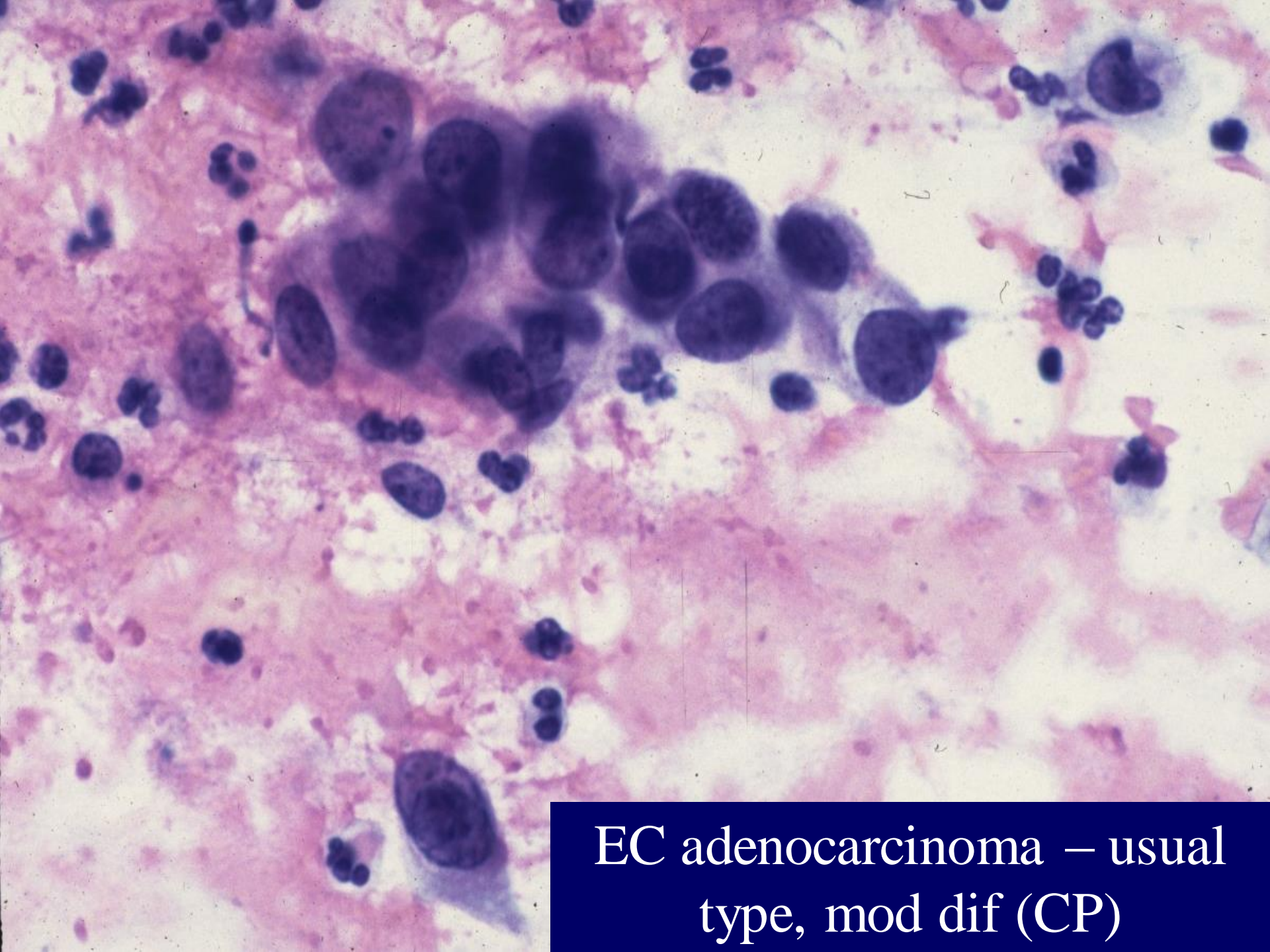
- Usual type
- Mucinous
 - Gastric
 - Intestinal
 - Signet ring cell
- Villoglandular
- Endometrioid
- Clear cell
- Serous
- Mesonephric
- ACA with NE

Invasive Endocervical Adenocarcinoma, Usual Type - Cytology

- Abundant cellularity
- Two dimensional sheets without cohesion
- Architectural features of AIS (WD variants)
- Macronucleoli
- Increased nuclear to cytoplasmic ratio and nuclear size
- Hyperchromasia and irregular chromatin (clearing)
- Tumor diathesis

EC adenocarcinoma –
usual type, well-dif (CP)

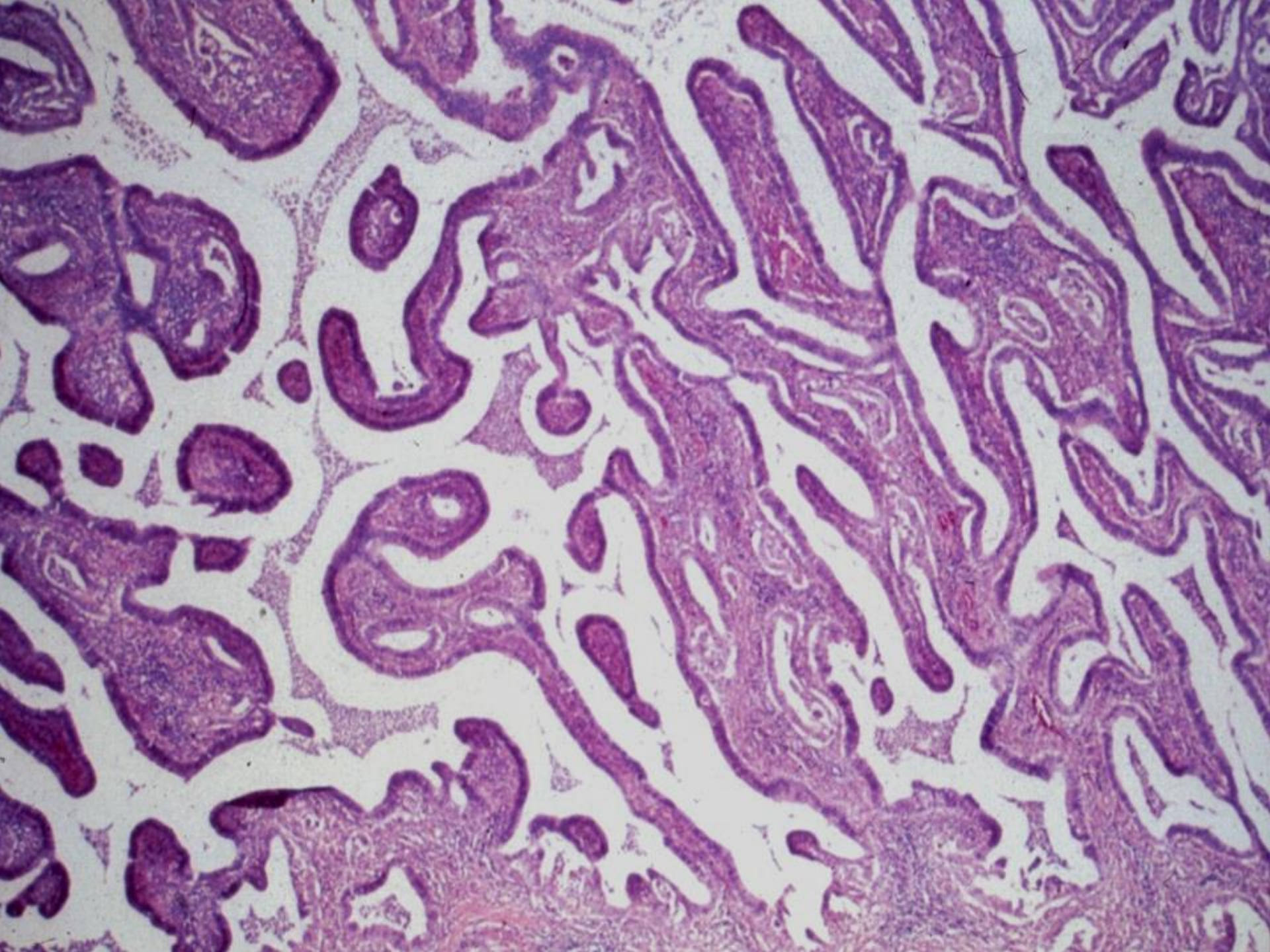


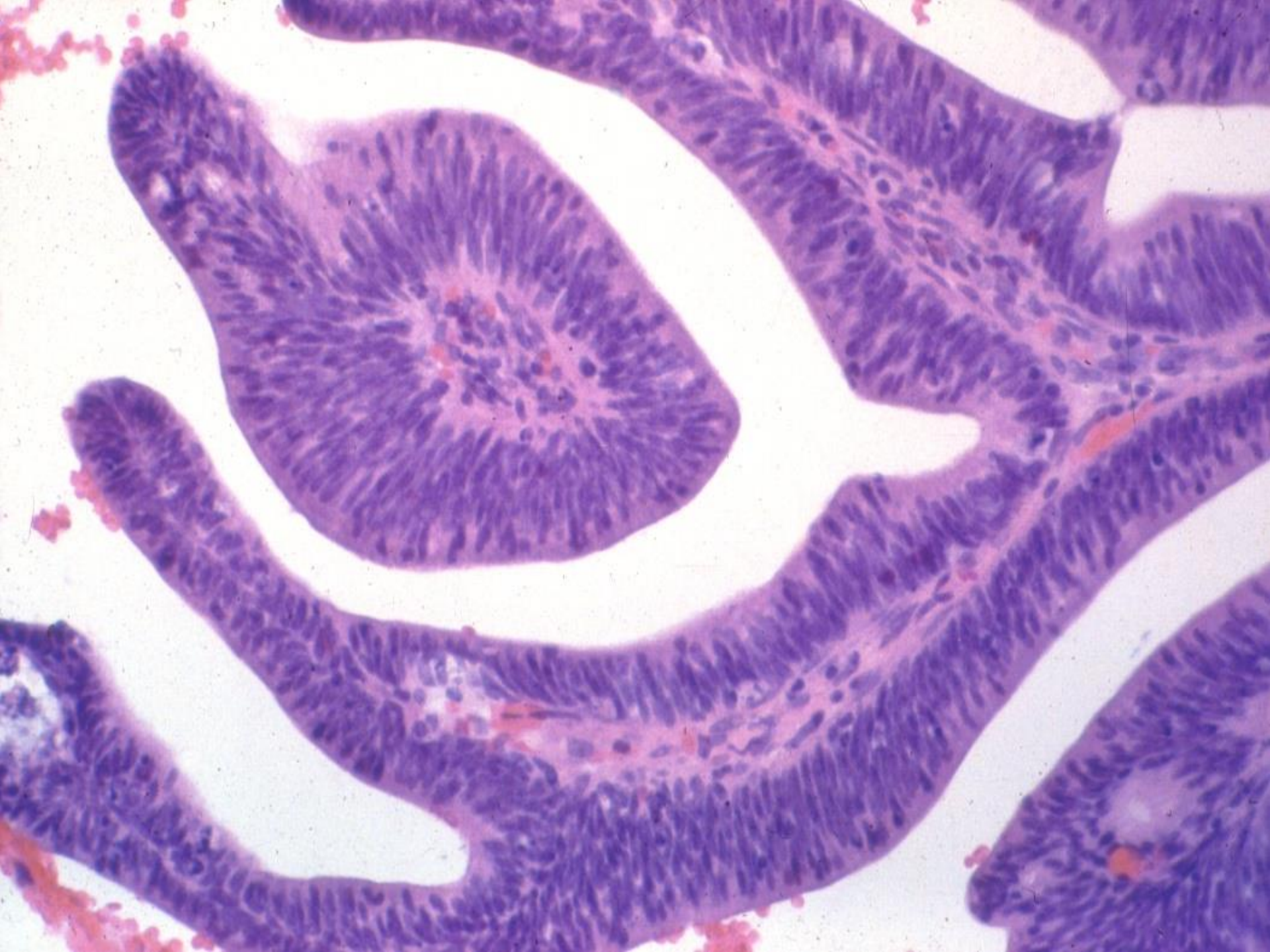


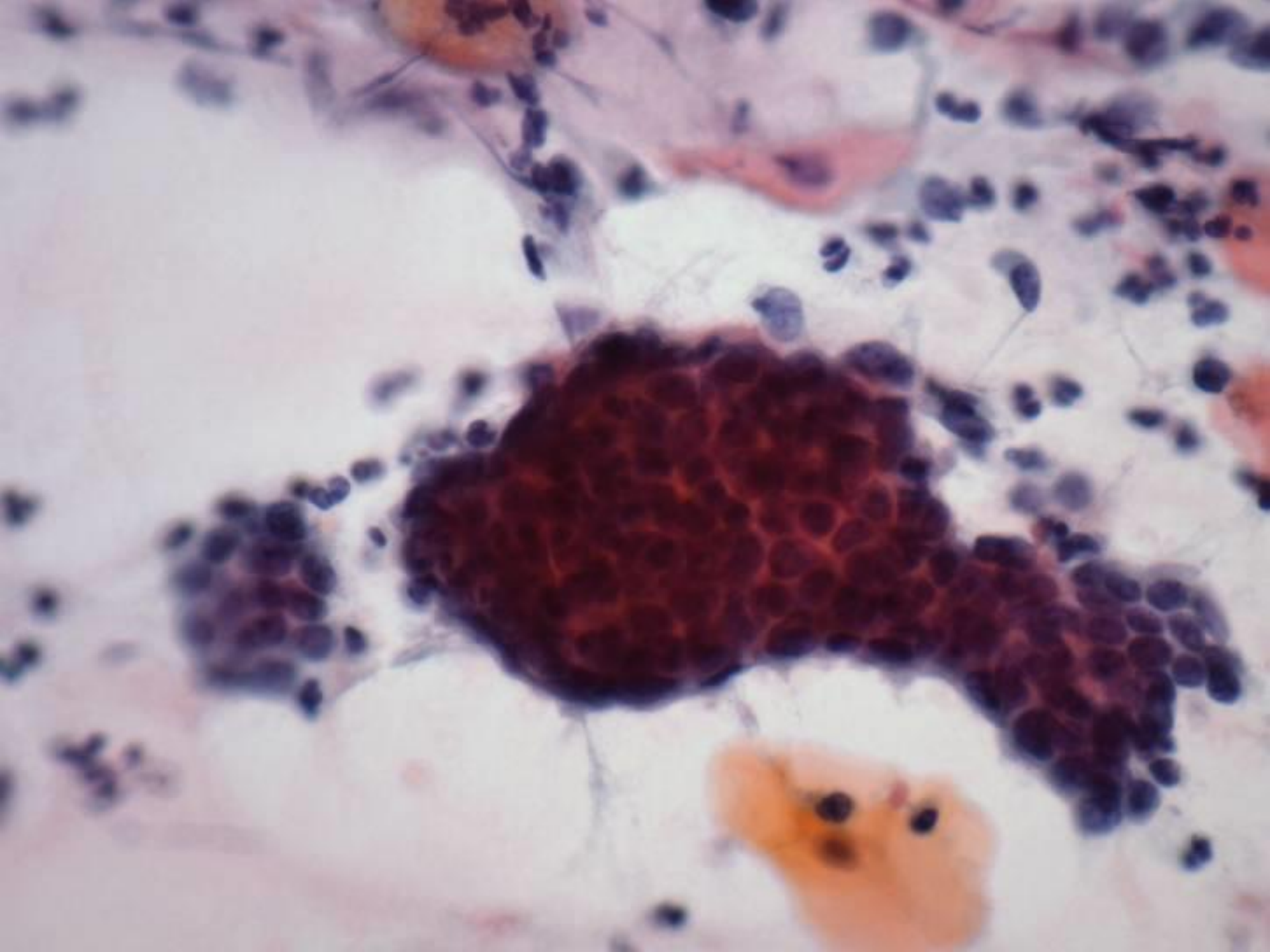
EC adenocarcinoma – usual
type, mod dif (CP)

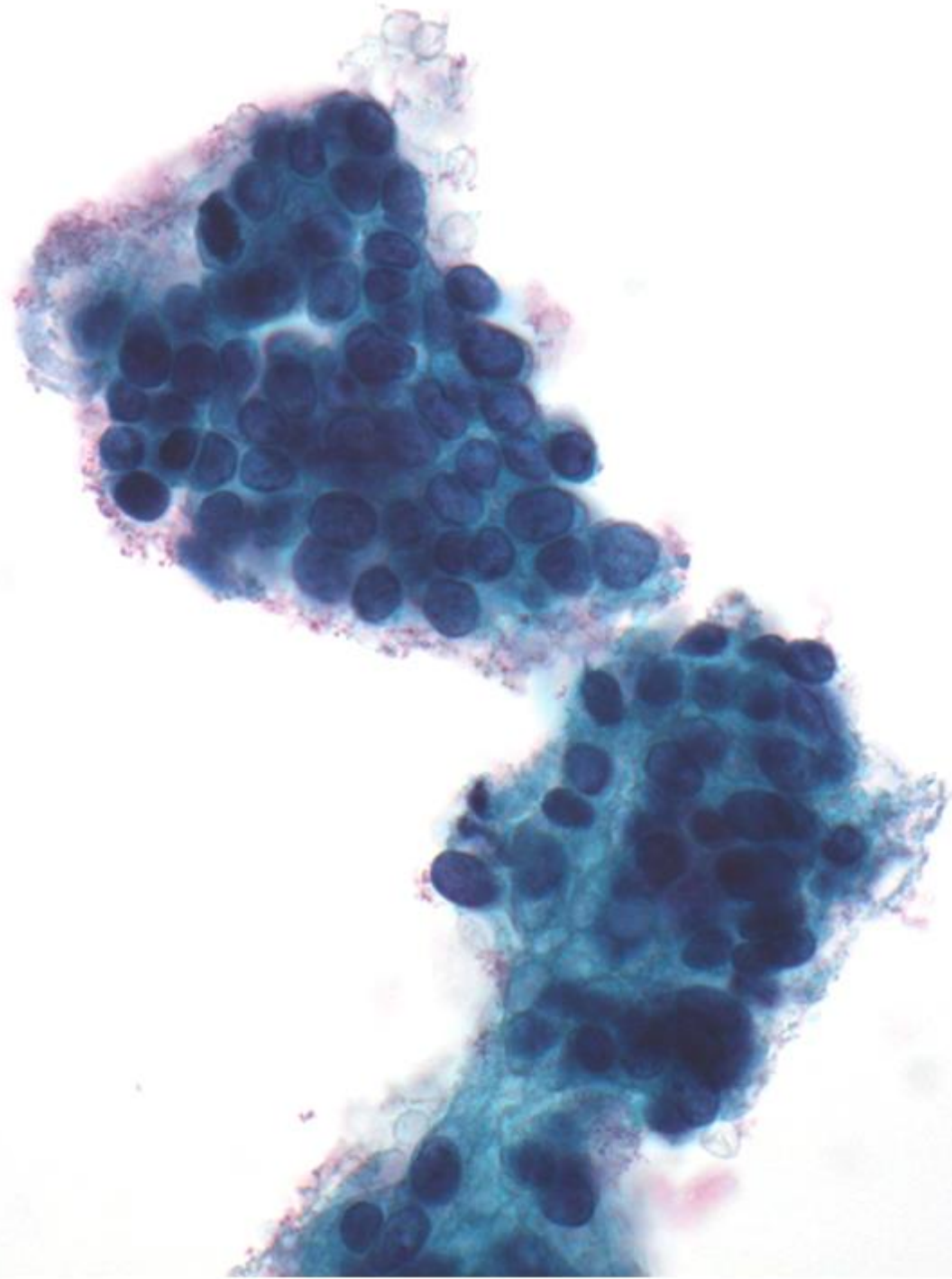
Villoglandular Adenocarcinoma

- Usually occur in younger population (35 y mean)
- 62% history of oral contraceptive use
- Usually well-circumscribed, minimally invasive, exophytic
- Behavior favorable
- LN metastases rare
- Conservative management (cone only) for pure Gr1 lesions with minimal invasion, LVI-, margins-

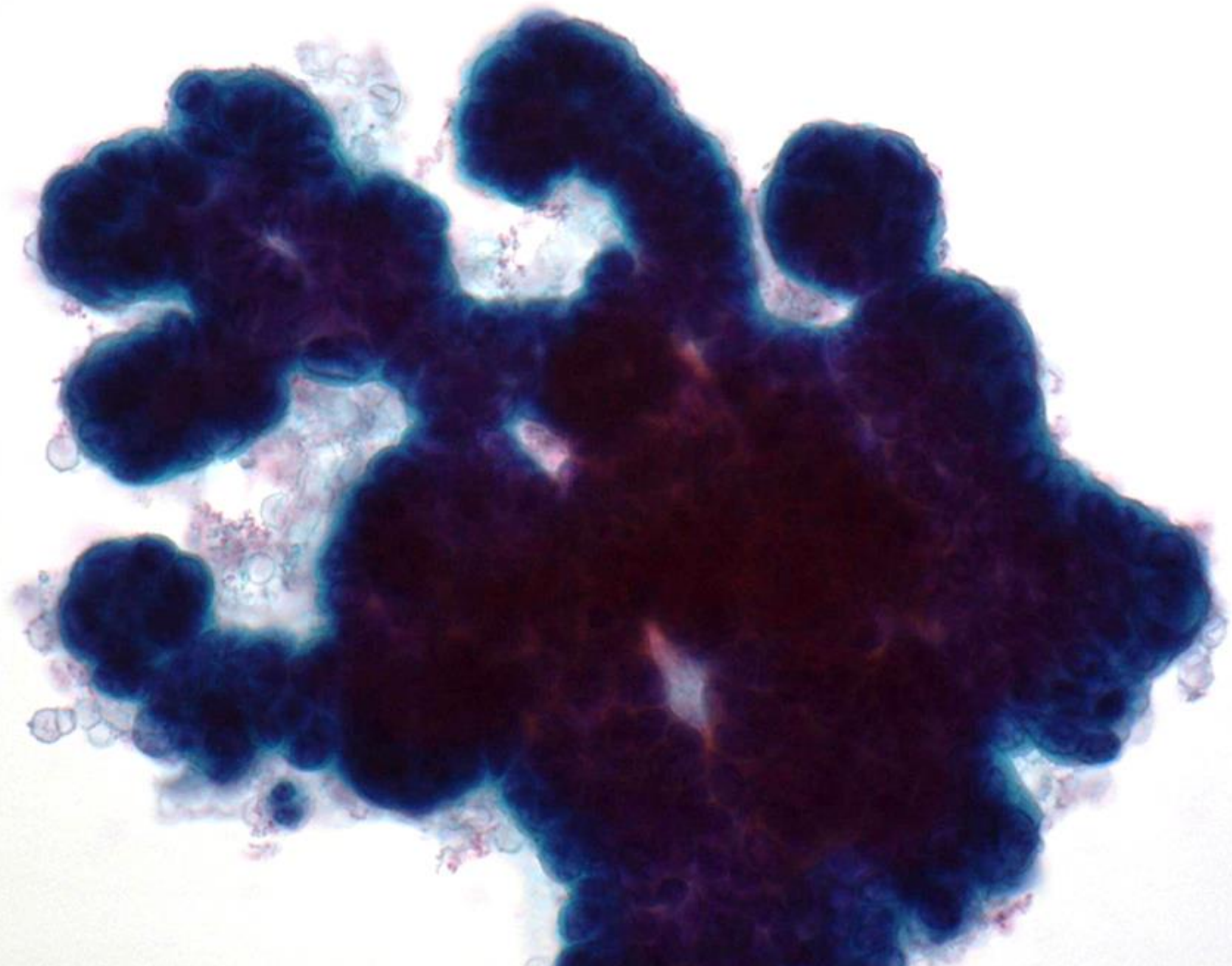








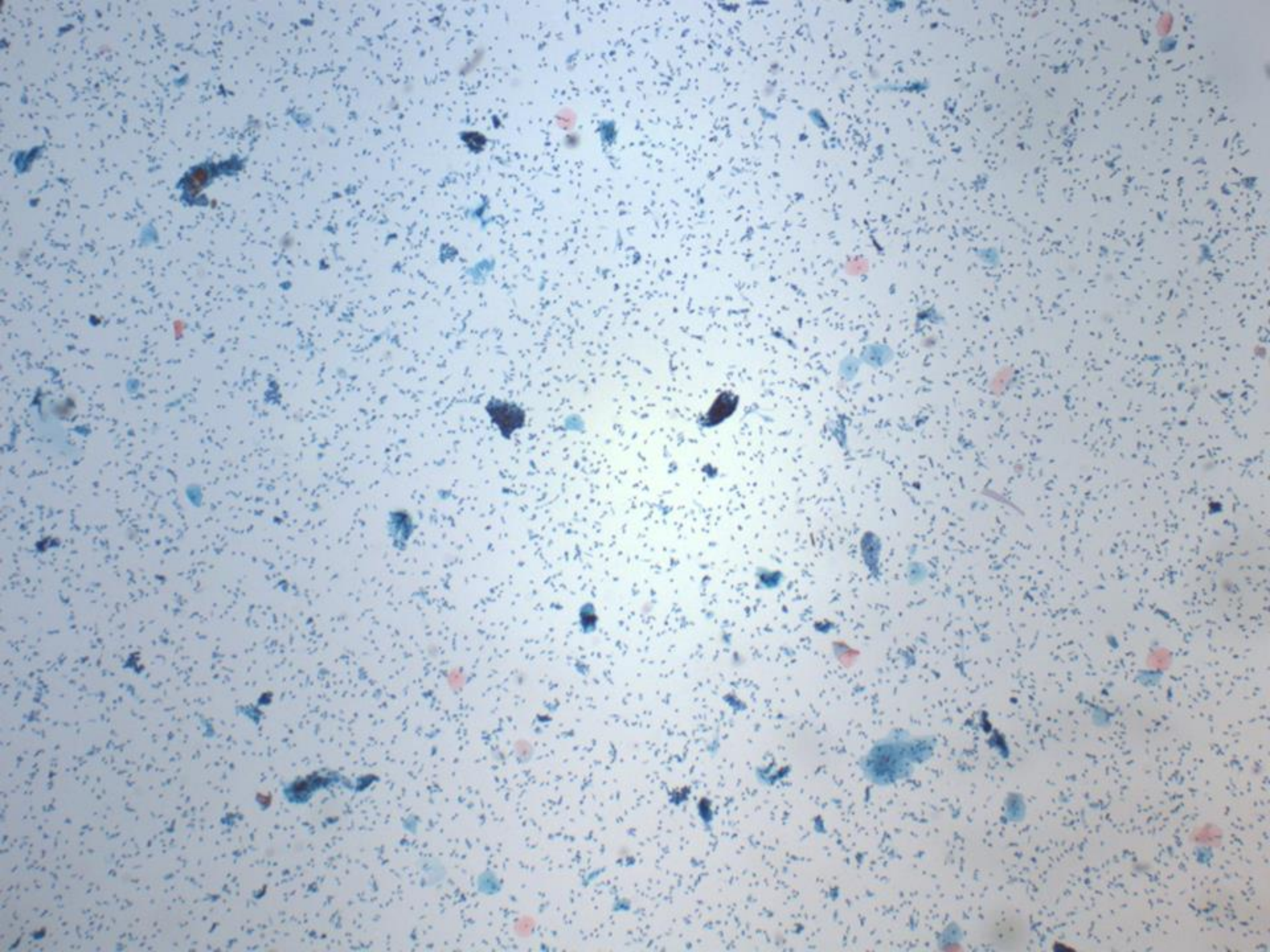
EC Adenoc
VG variant

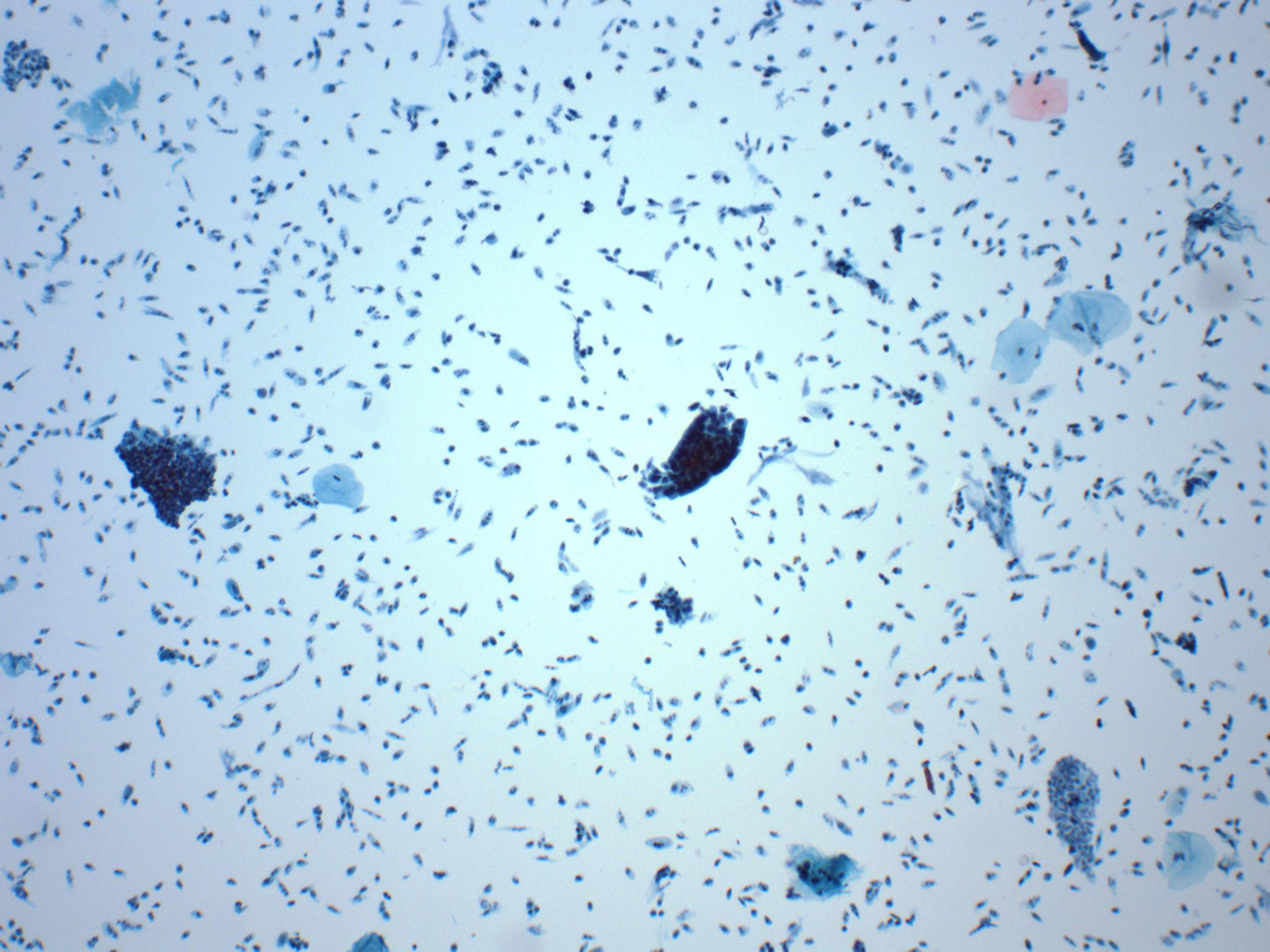


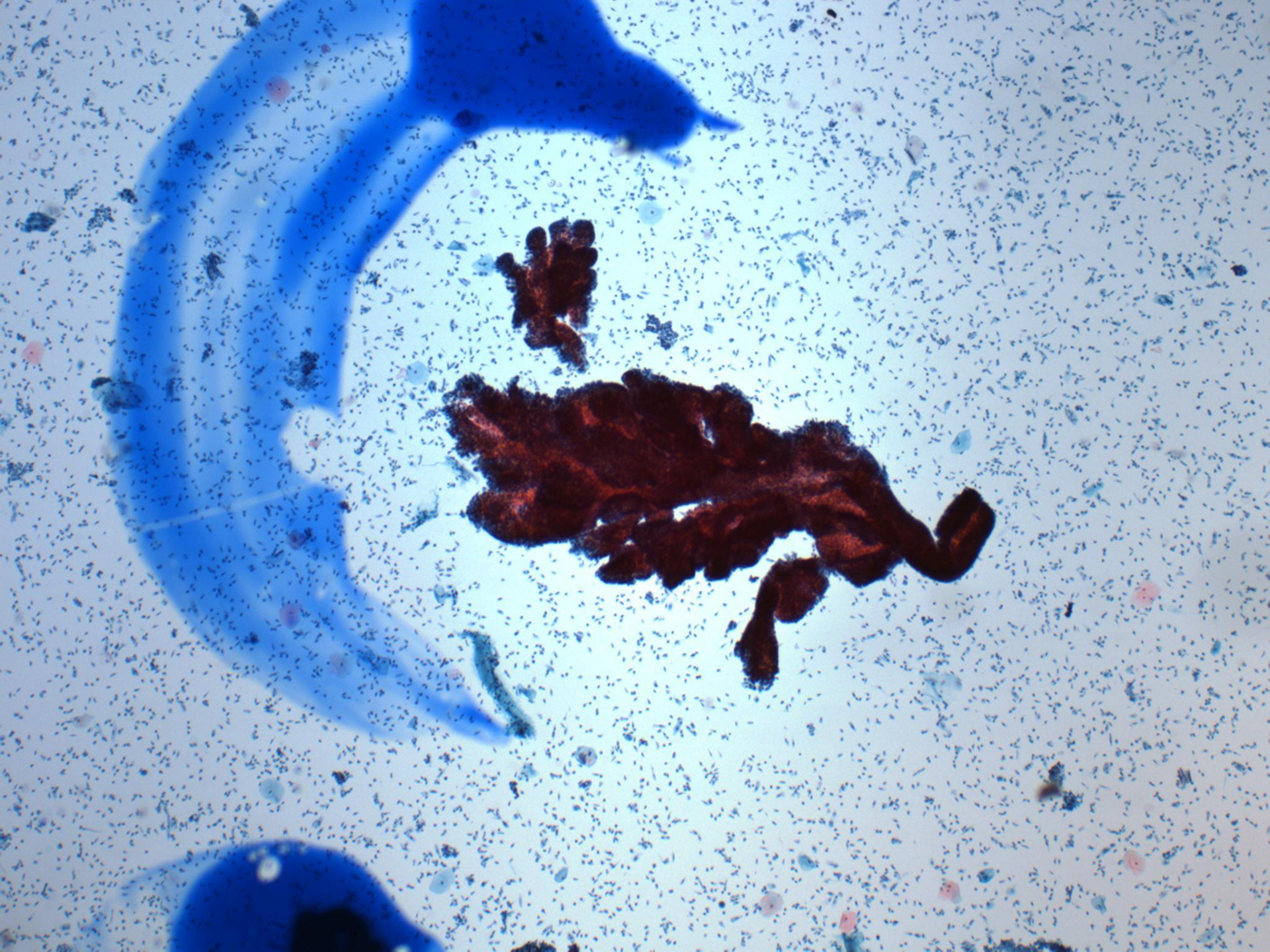
Case 4

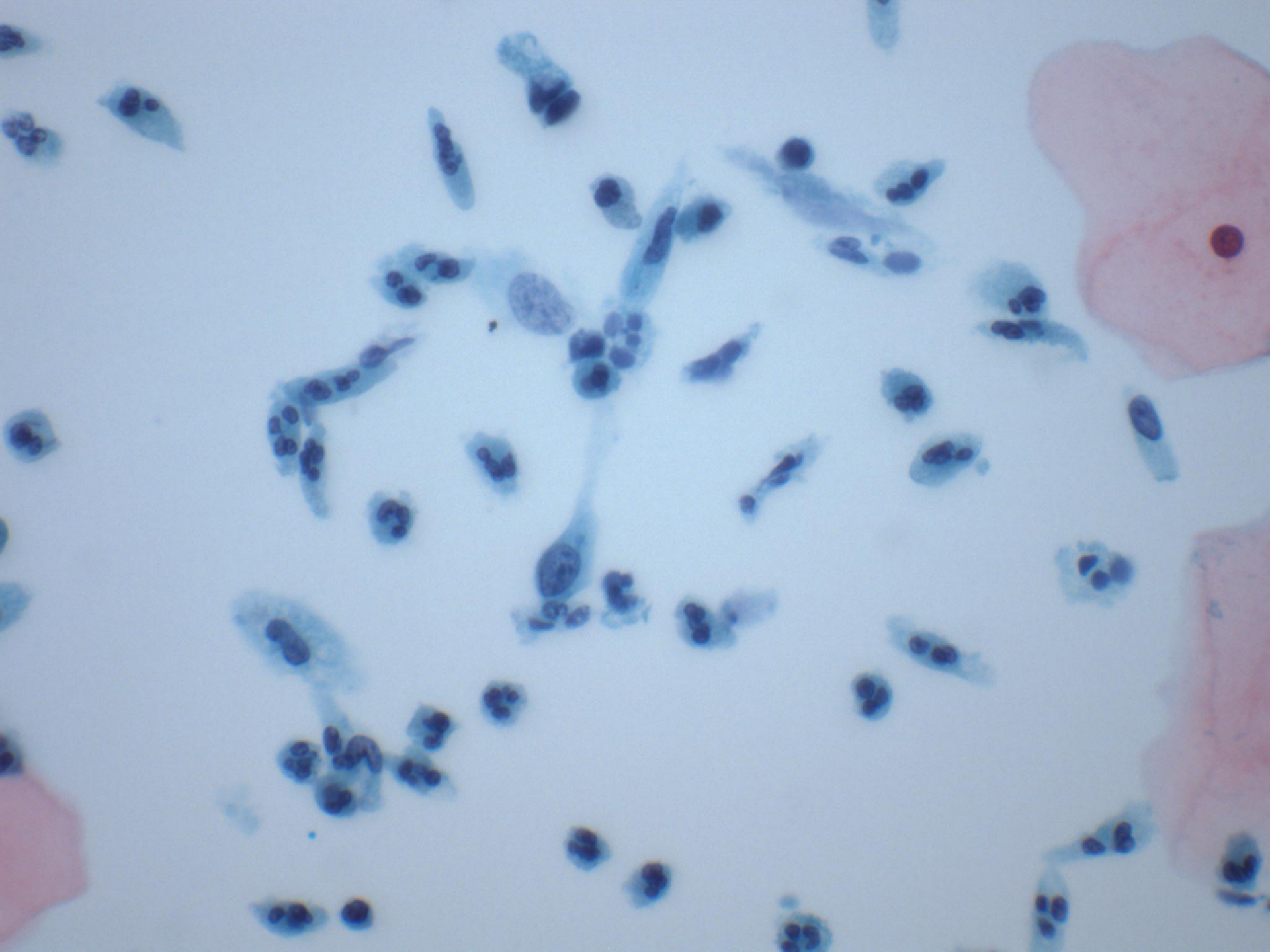
42 year old

History of vaginal watery discharge

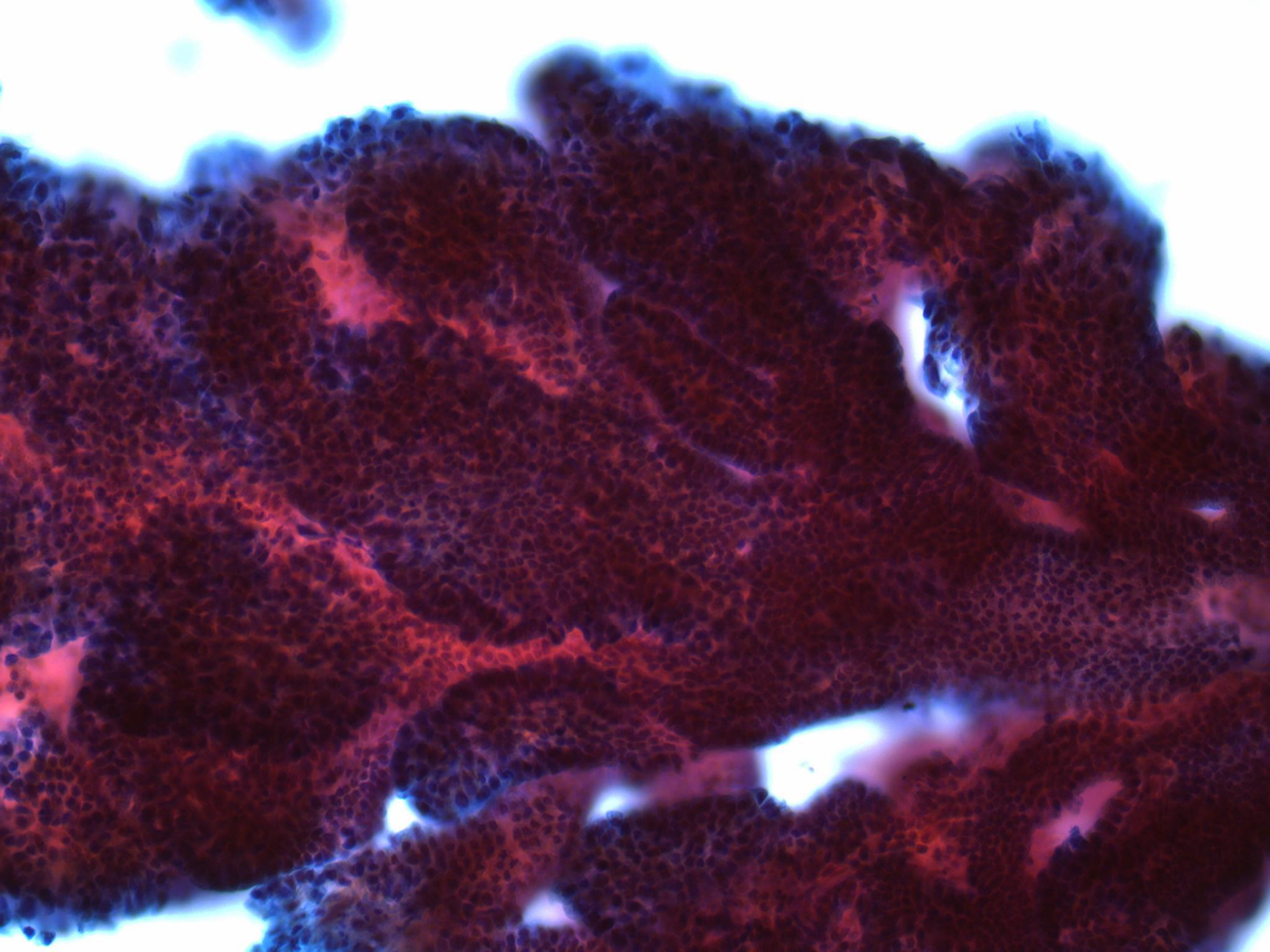


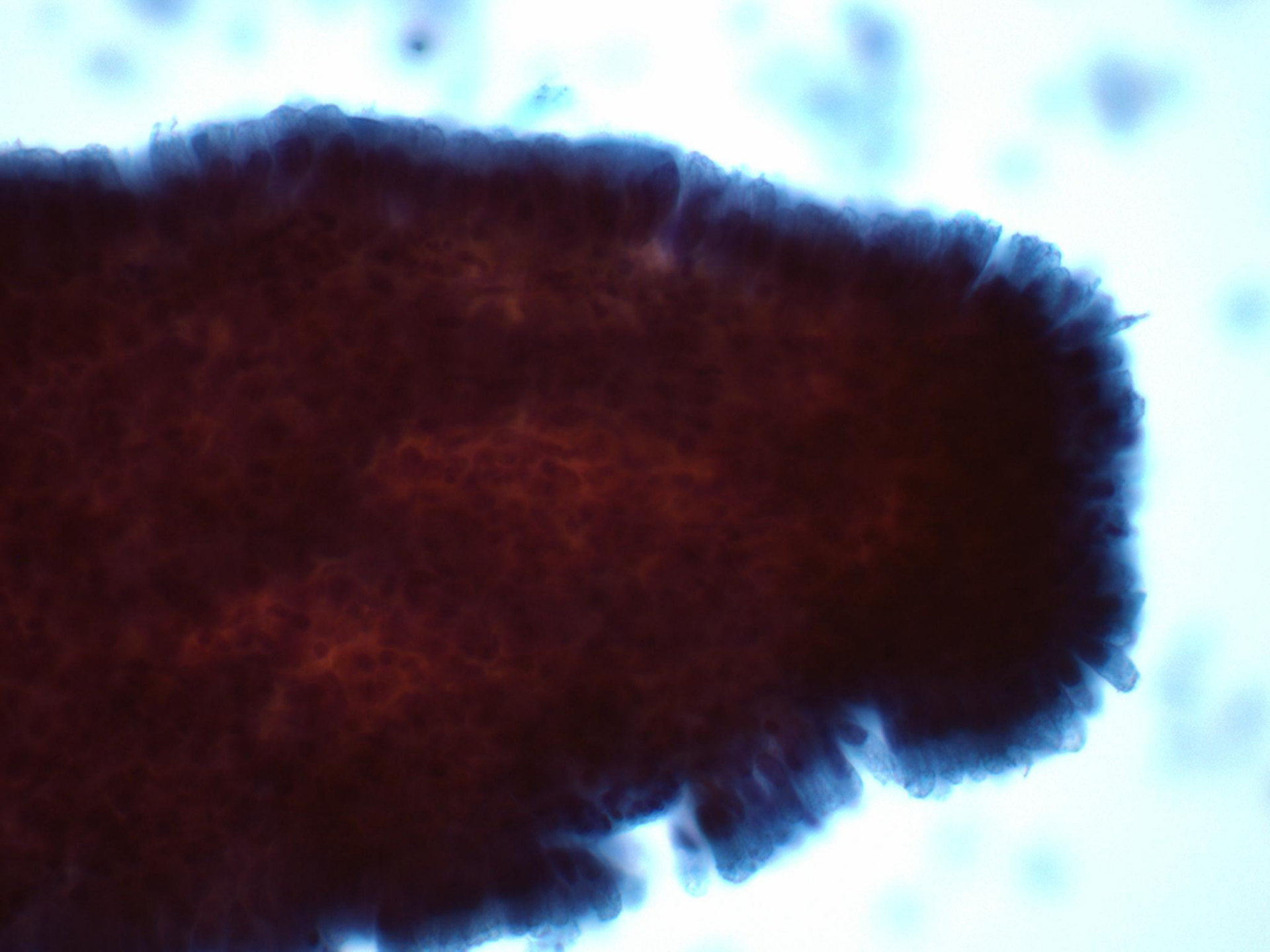


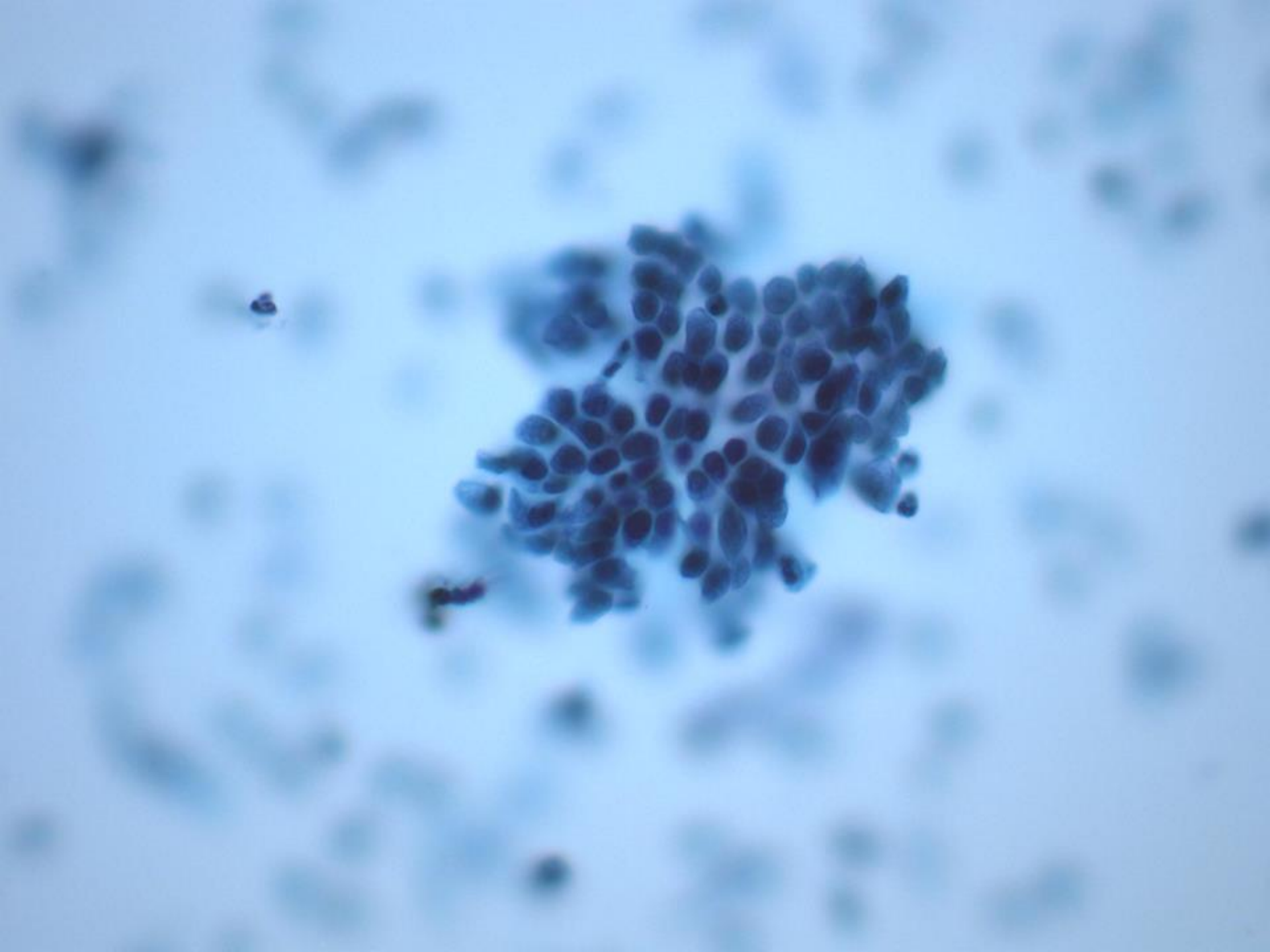


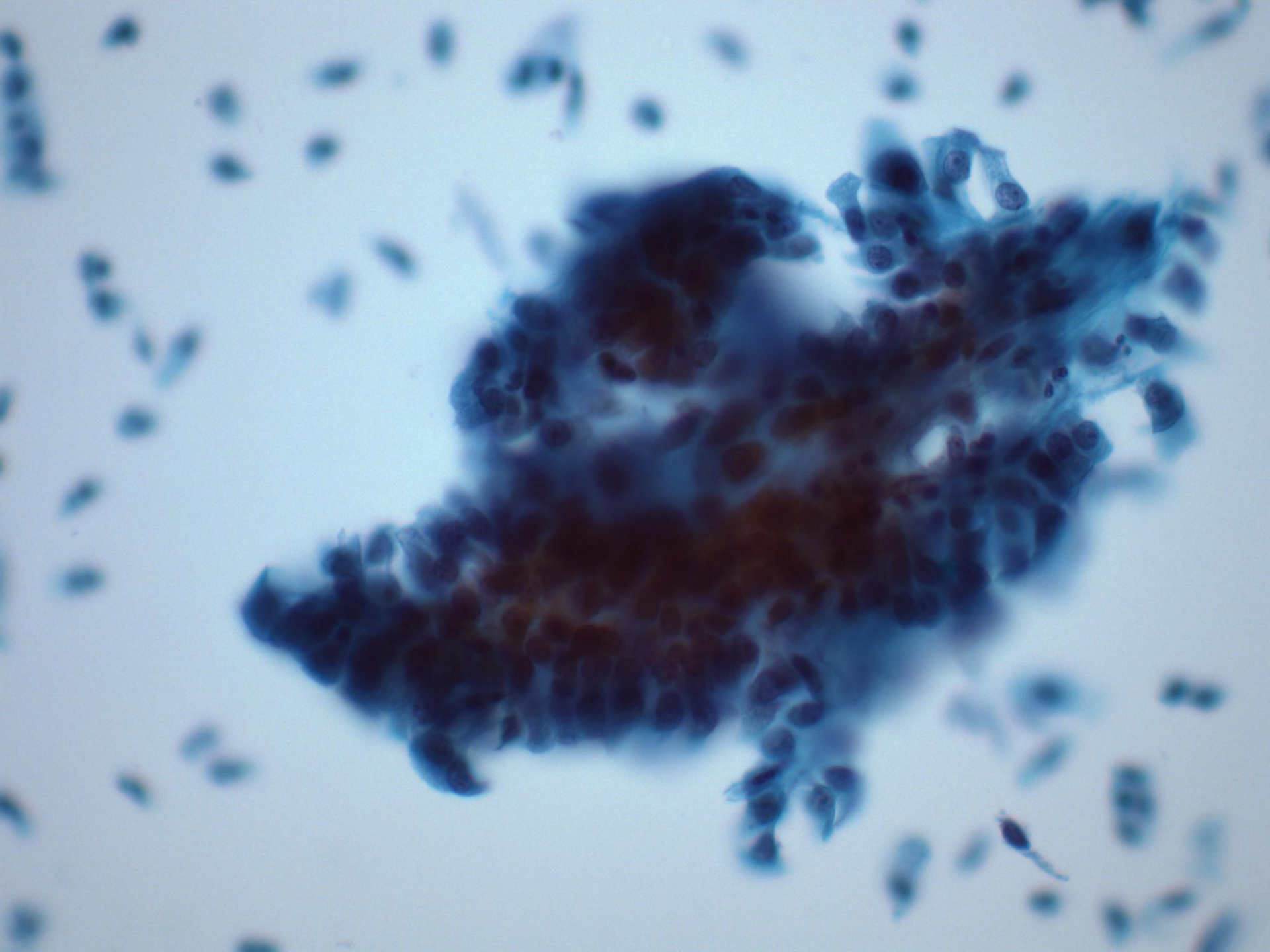


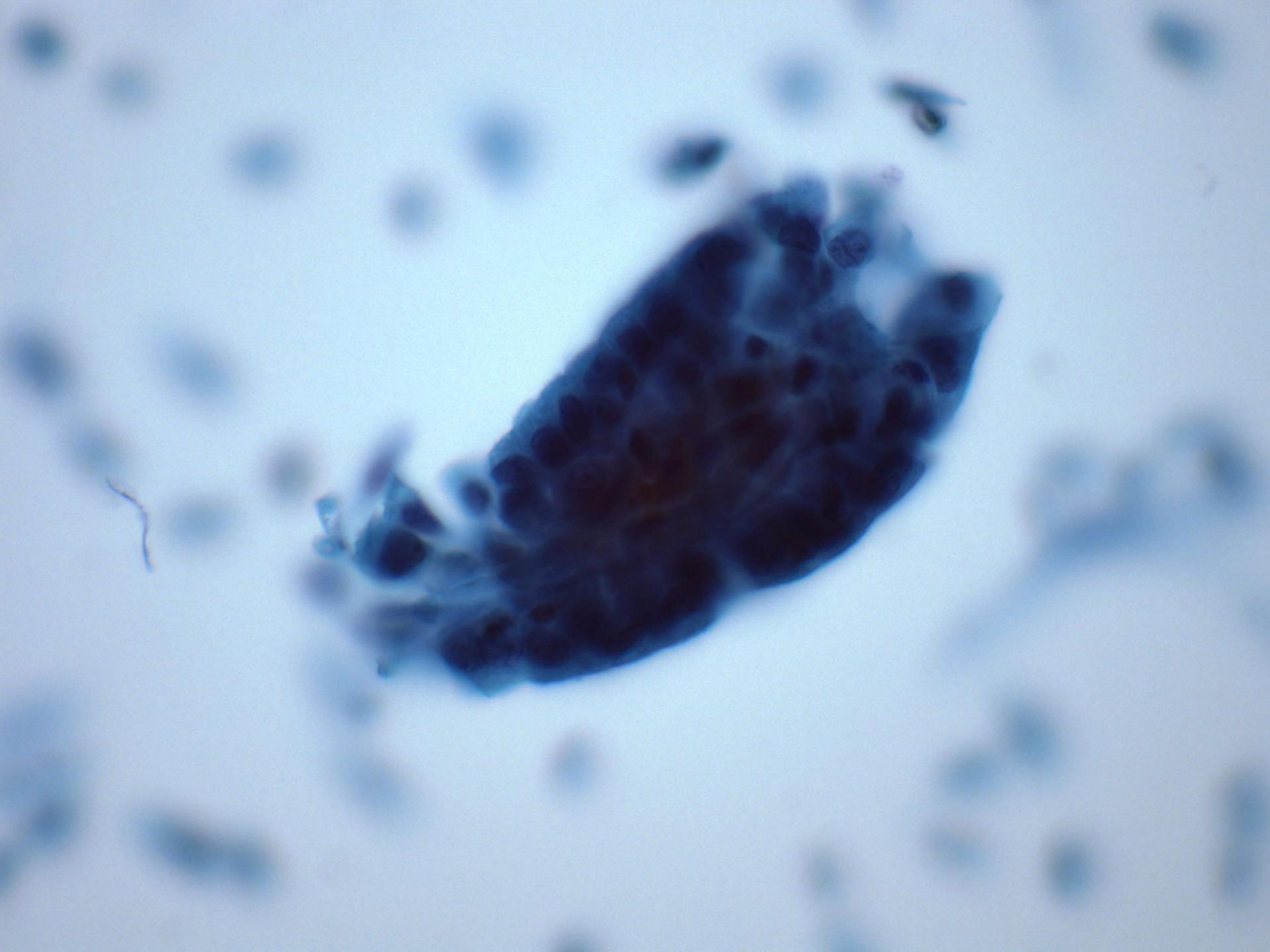












Summary of Key Cytologic Features

- Scantly cellular specimen
- Marked inflammation
- Large tufted papillary cell groupings
- Consisting of densely-packed columnar cells
- Benign-appearing isolated EC cells in background

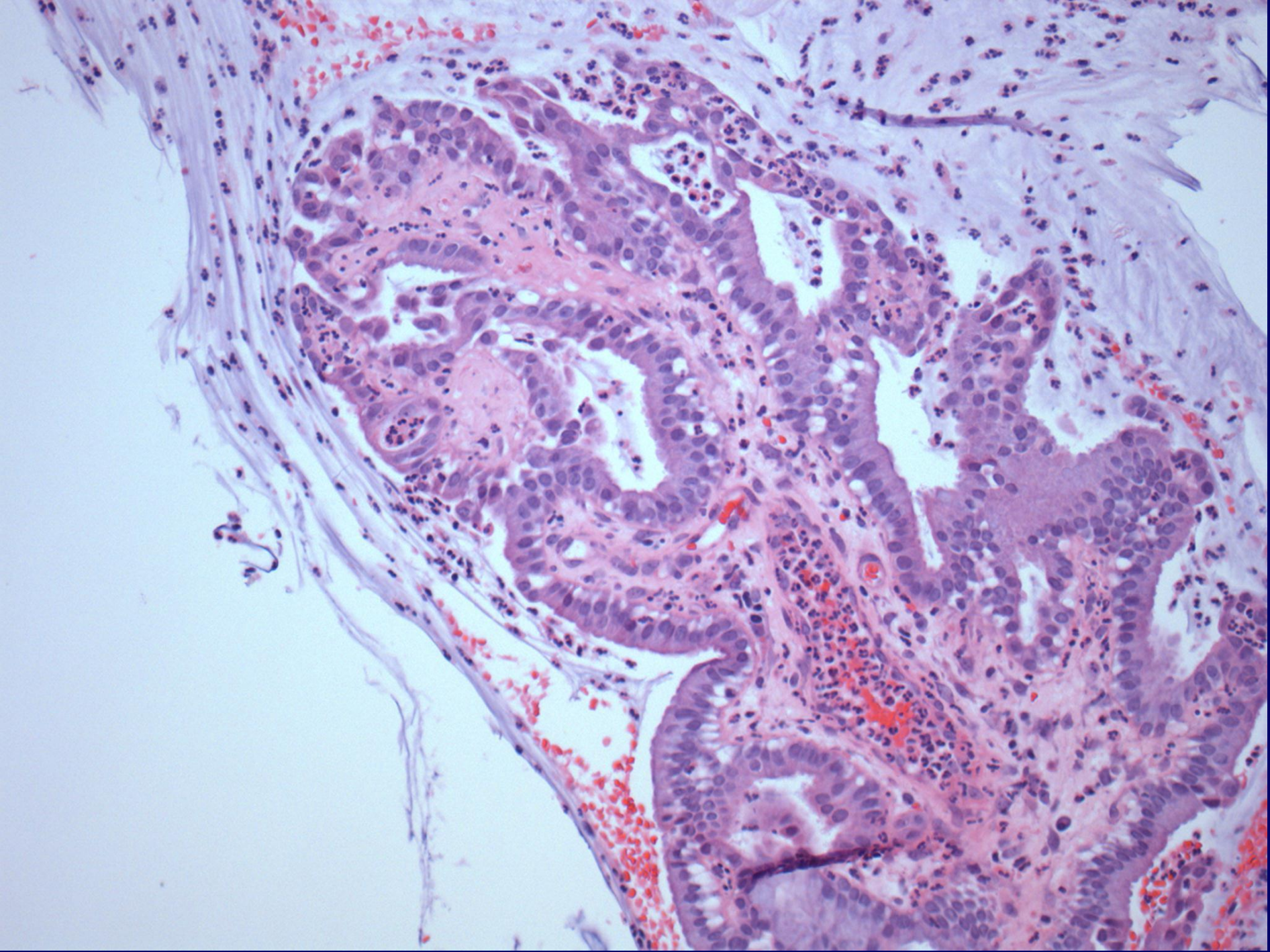
Benign

Malignant

Atypical

Diagnosis:

Endocervical polyp with
Microglandular hyperplasia

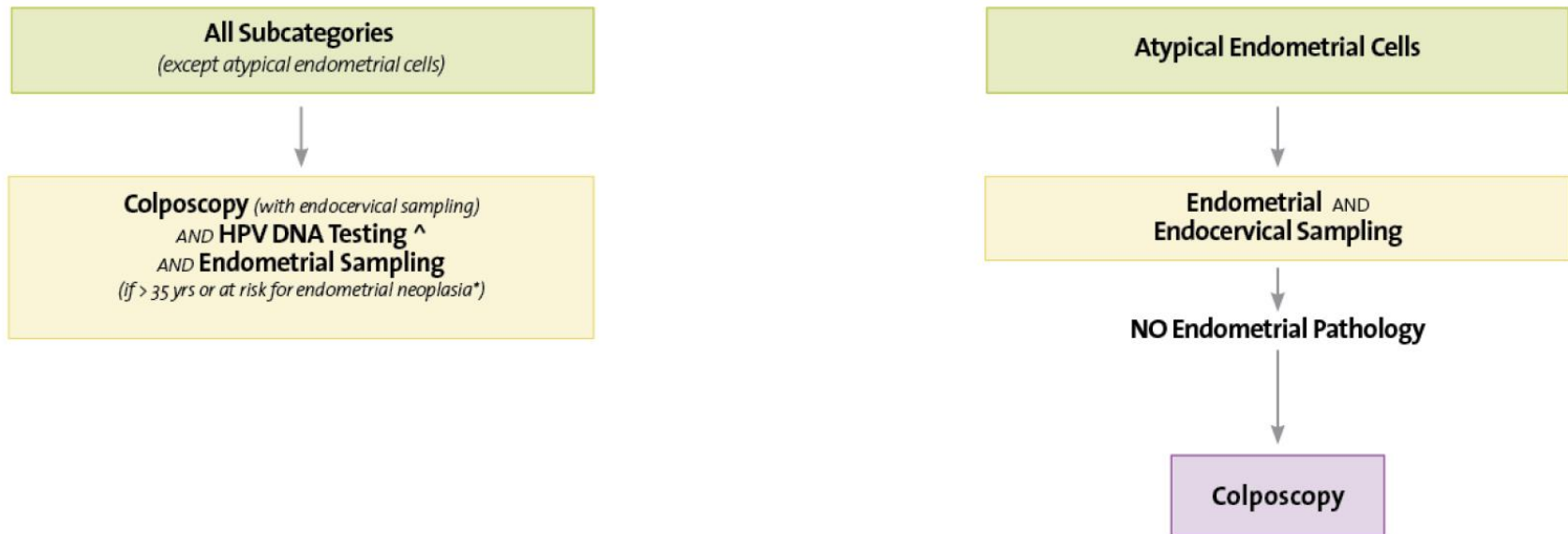


MGH vs. Clear Cell Adenocarcinoma

- In Common
 - Closely packed glands
 - Cystic glands
 - Inflammatory cells
- Different – MGH
 - Reproductive age pts
 - No symptoms/mass
 - Endocervical polyp
 - Bland nuclei
 - Subnuclear vacuoles
 - Hyalinized or myxoid stroma
 - p16 negative or patchy
- Different – CC ACA
 - Older patients
 - Symptoms/mass
 - High-grade atypia/mitoses
 - Papillae
 - Abundant clear cytoplasm
 - p16 + patchy or diffuse

ASCCP Flowchart

Initial Workup of Women with Atypical Glandular Cells (AGC)



^ If not already obtained. Test only for high-risk (oncogenic) types.

* Includes unexplained vaginal bleeding or conditions suggesting chronic anovulation.

Atypical Glandular Cells

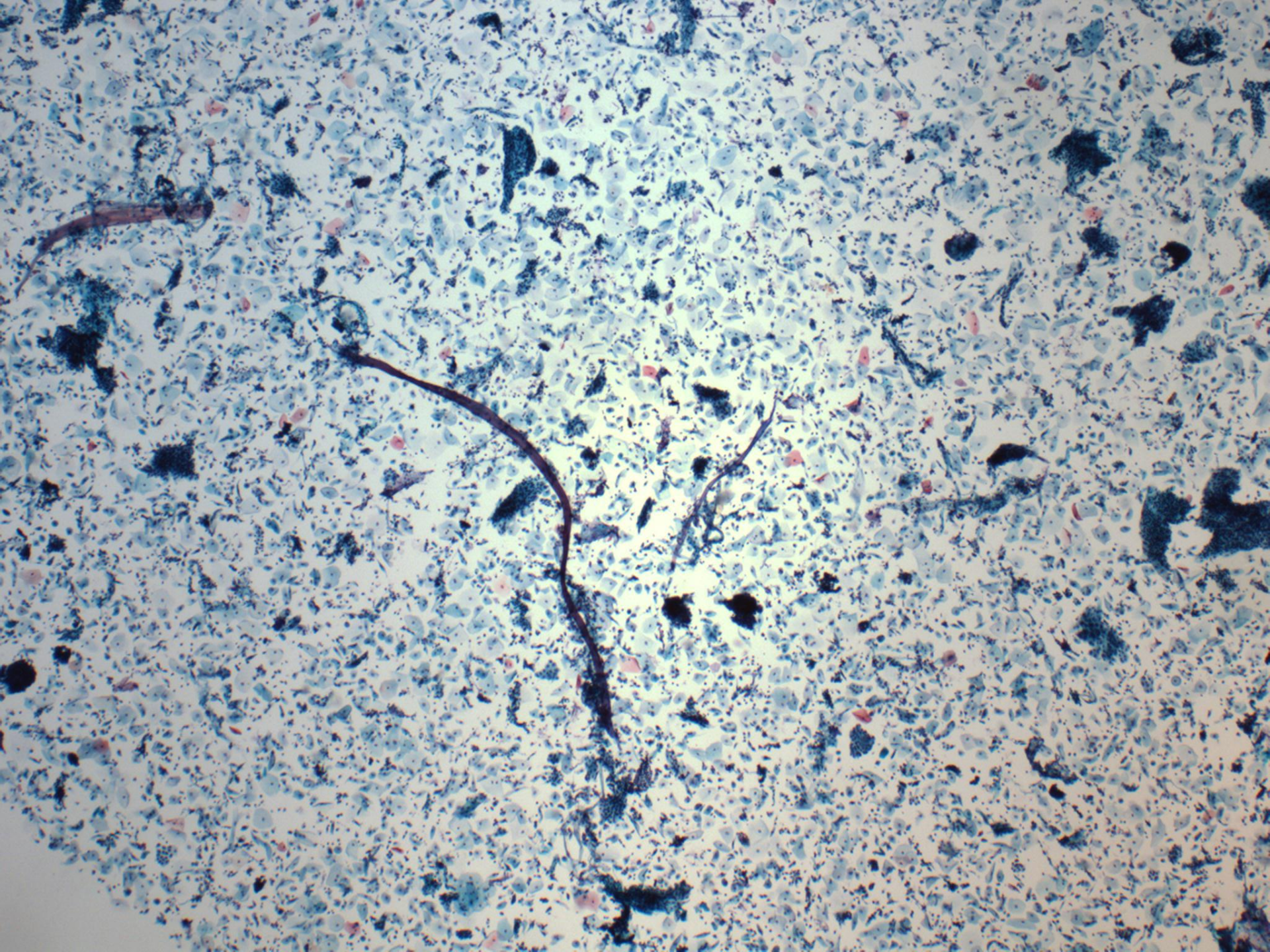
Quality Control/Quality Assurance

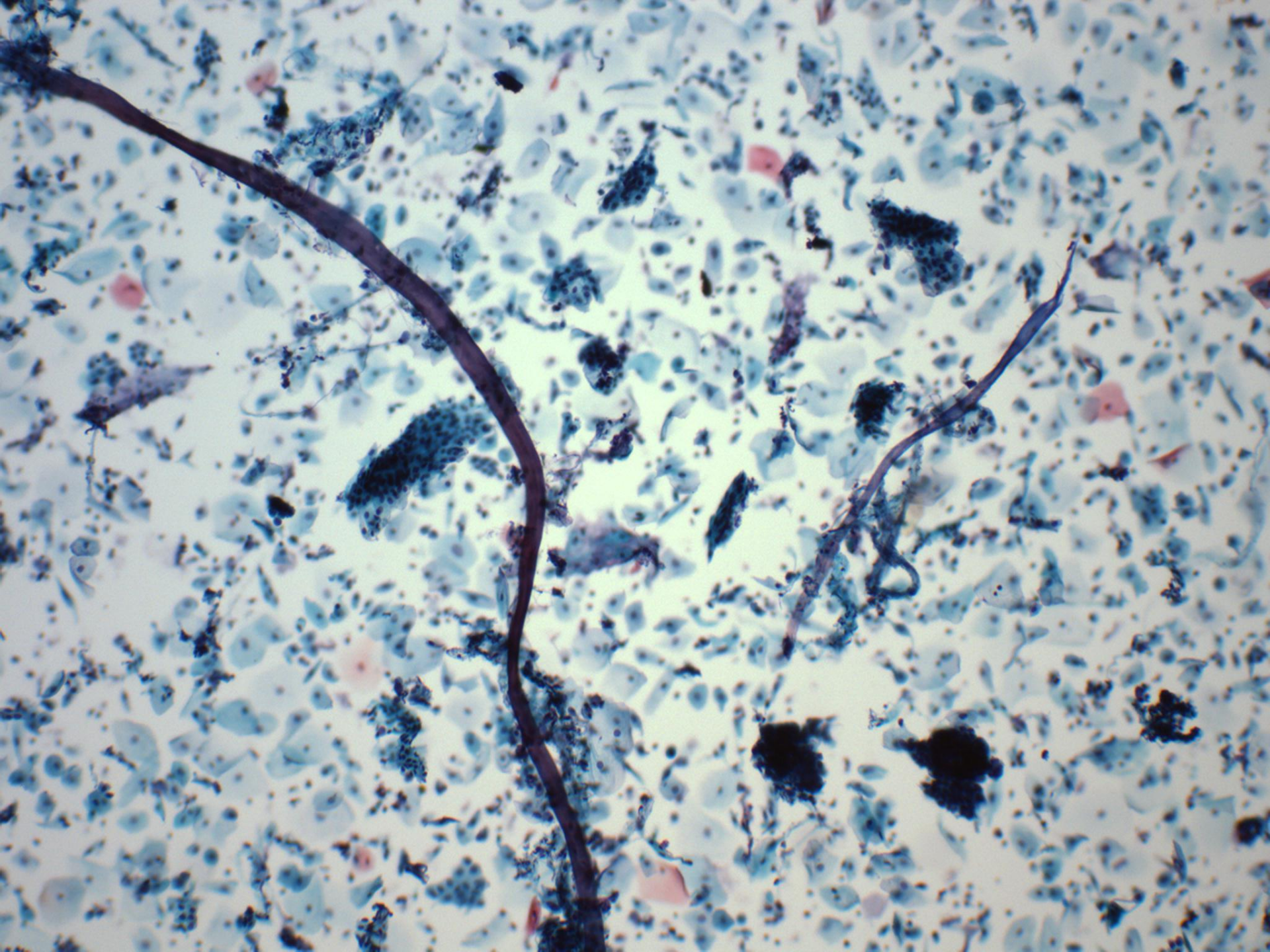
- 1) Prevalence of AGC (<1%)
- 2) Clinical history
- 3) Communication
- 4) Criteria Application
- 5) Retrospective Review
- 6) Cytology/Histology Correlation

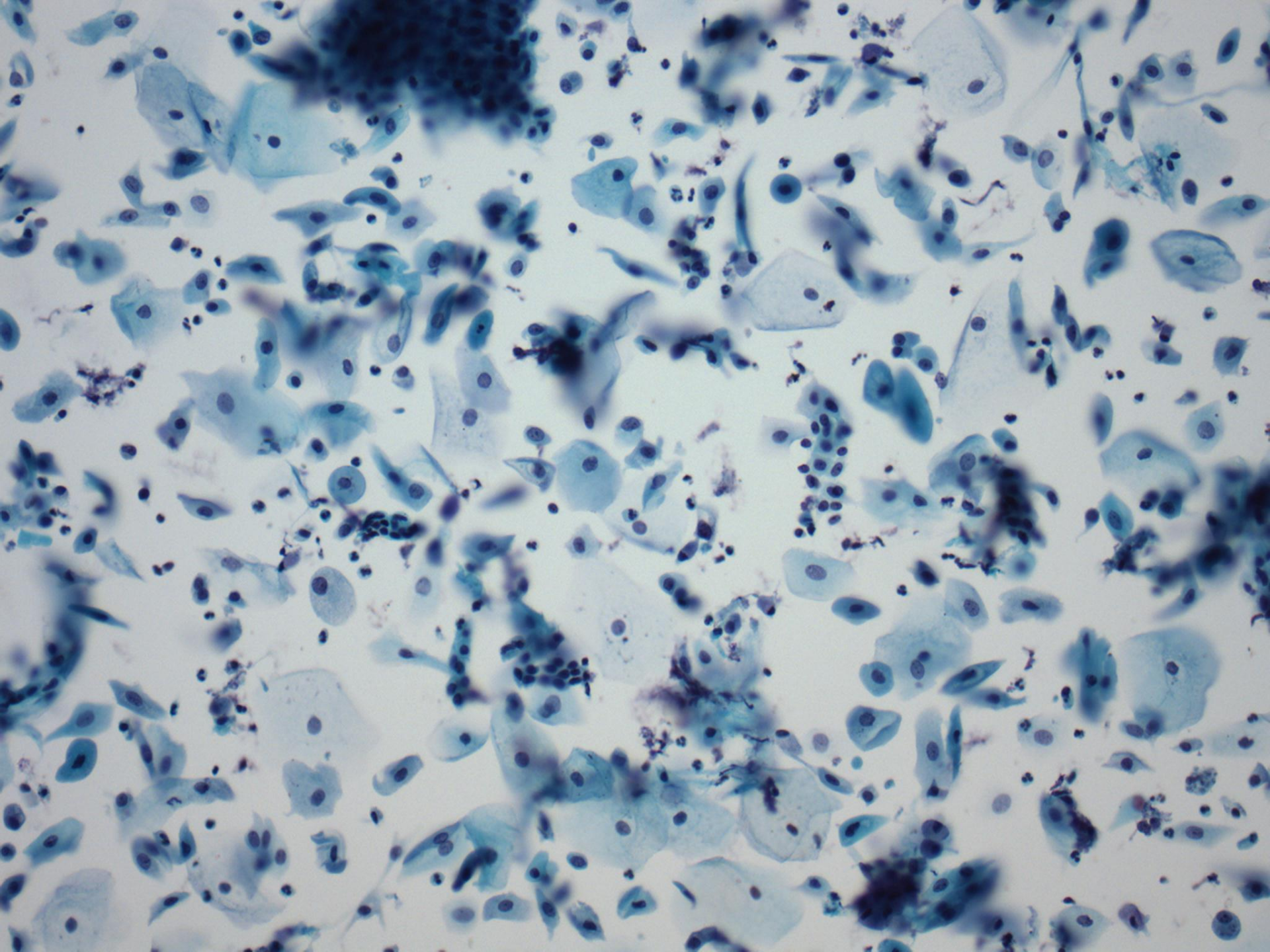
Case 5

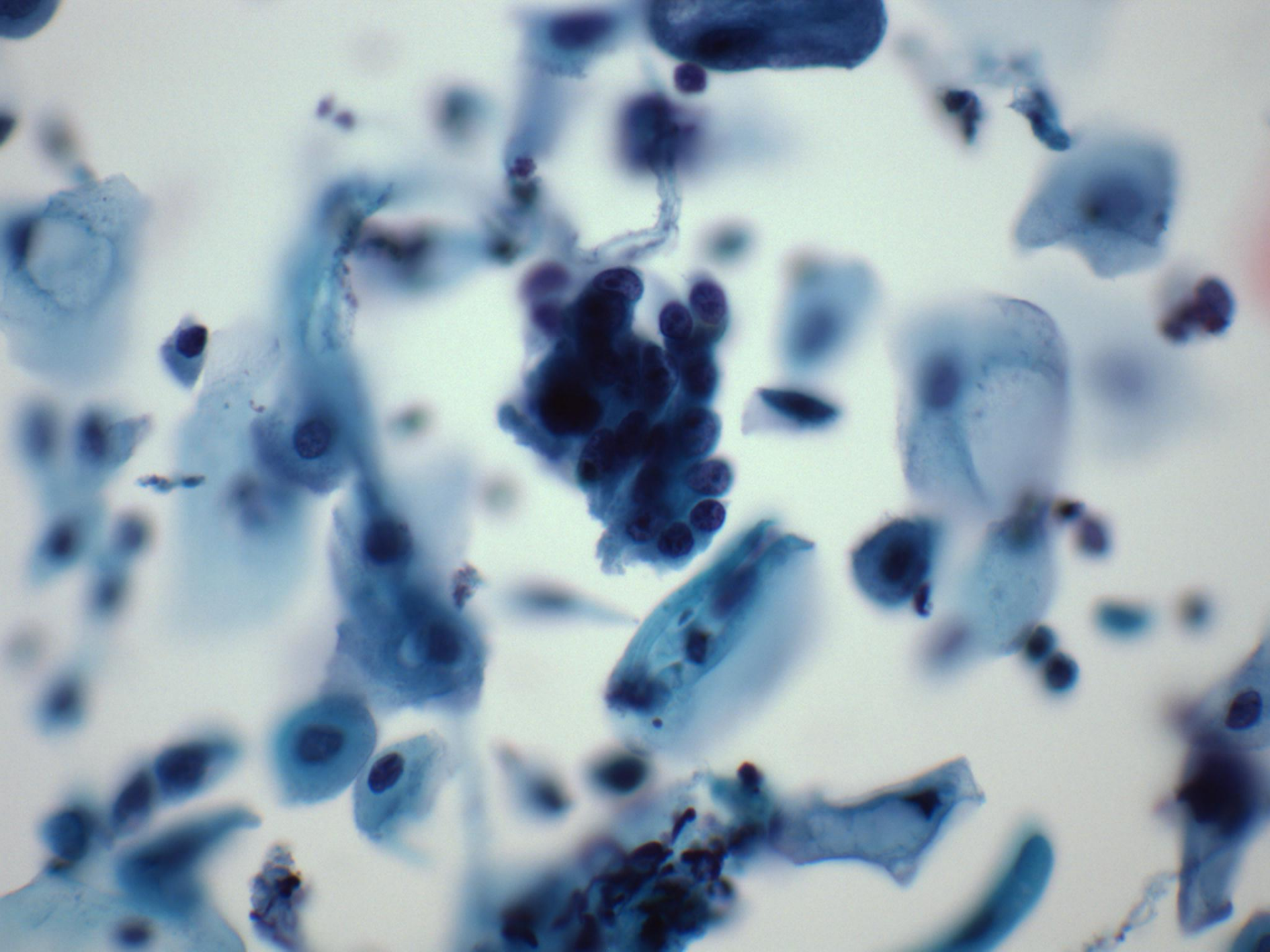
65 year old

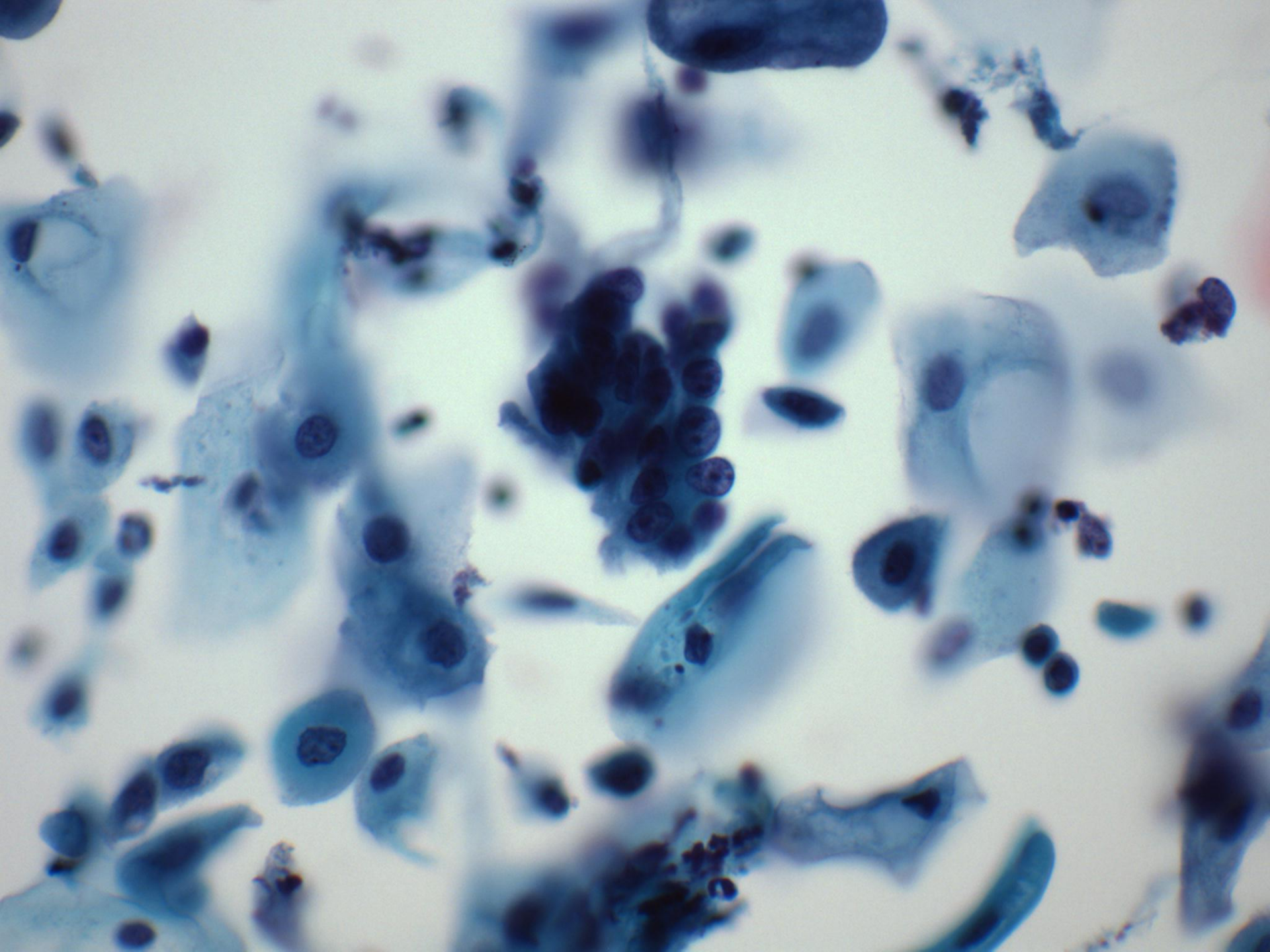
No history given

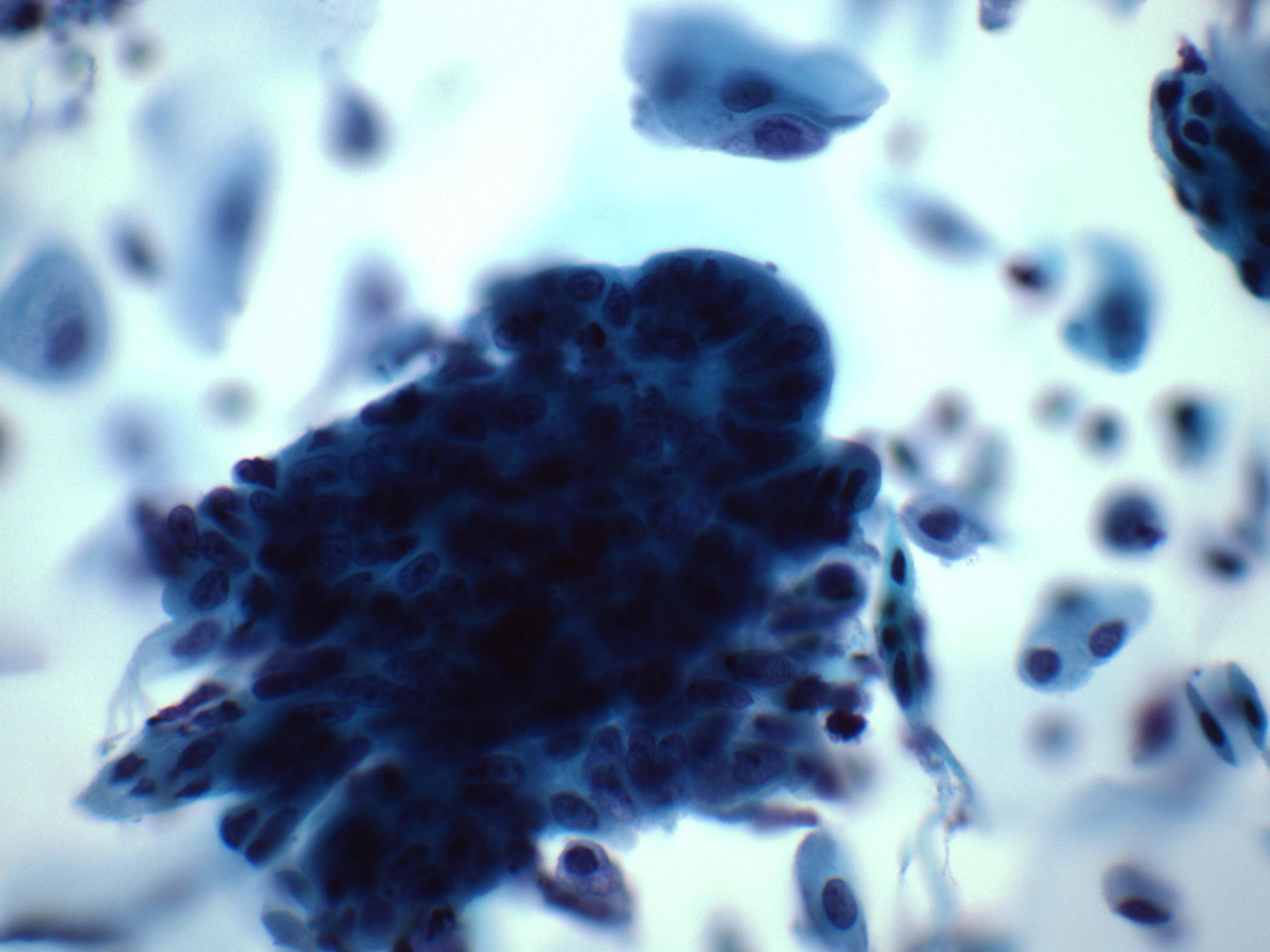


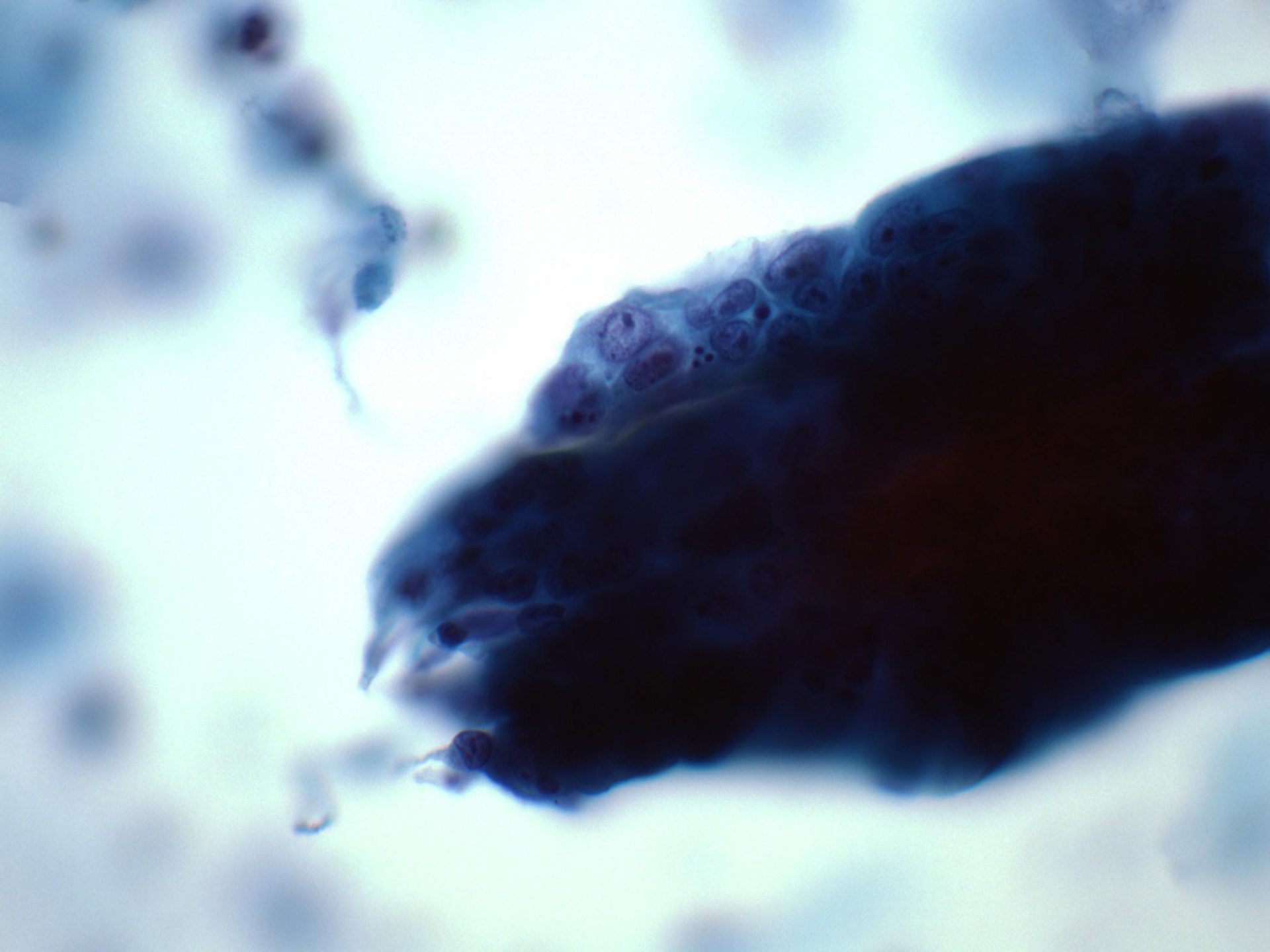


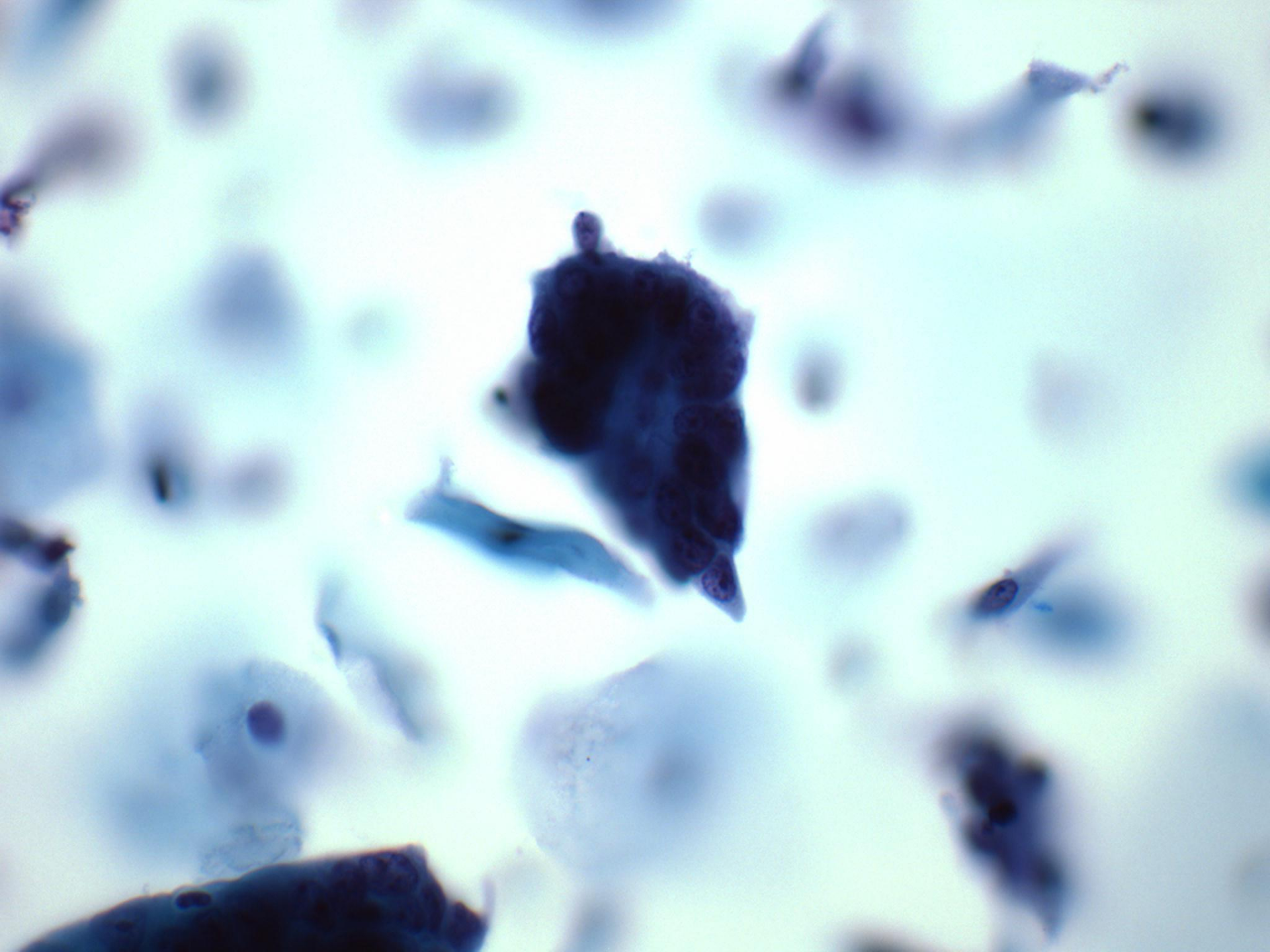


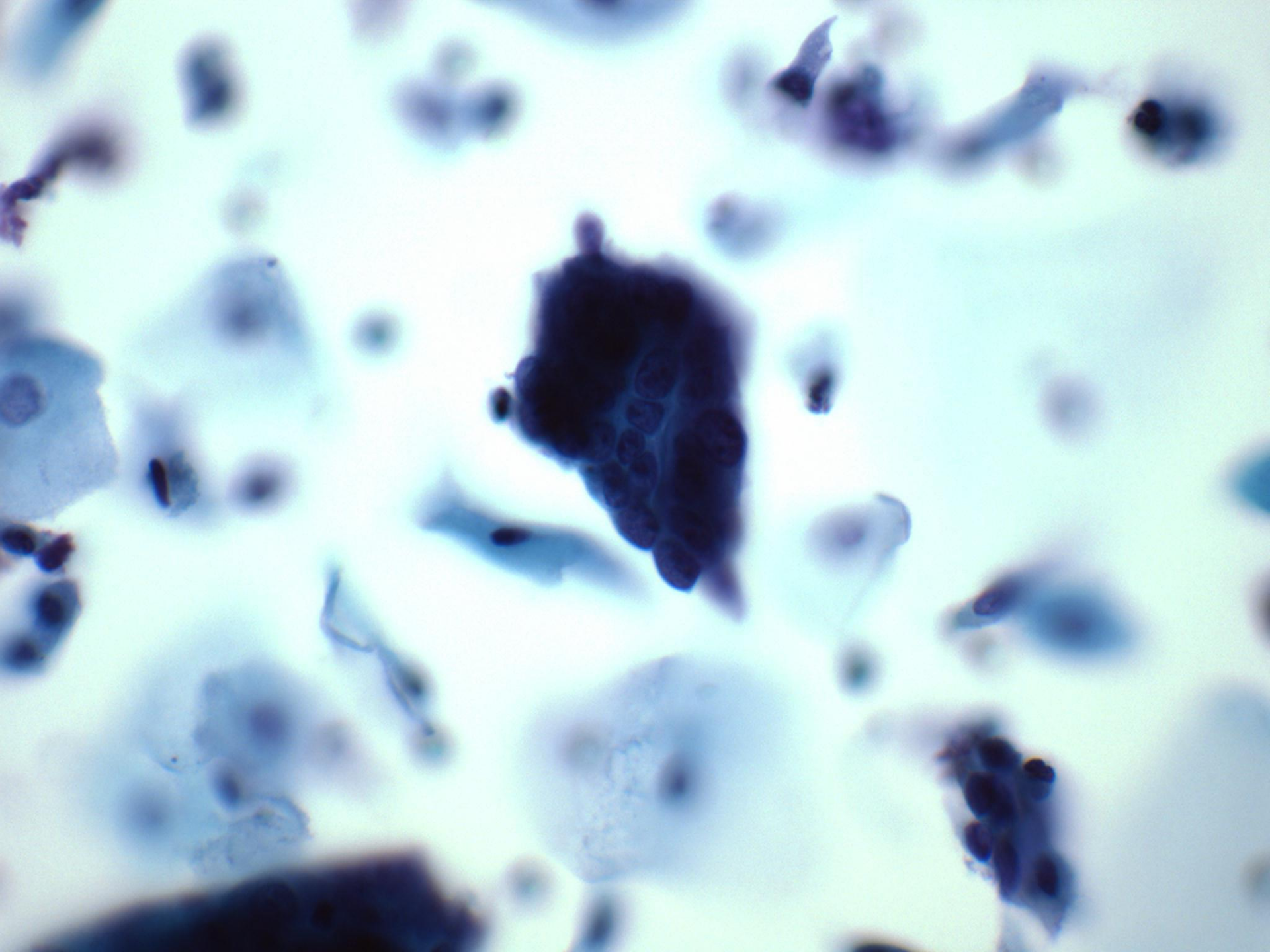












Summary of Key Cytologic Features

- Atrophic background
- Mild inflammation
- Some amorphous debris
- Non-cellular material
- Large dense groups – HCGs
- Pseudostratified strips and gland formations
- Columnar cells with atypical nuclei
- Apoptotic debris

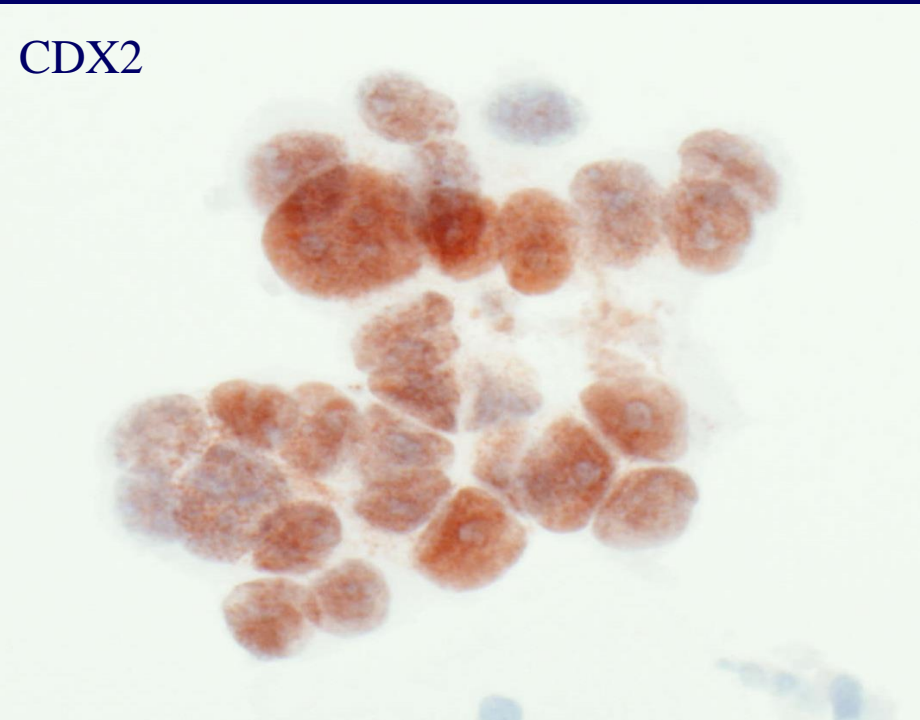
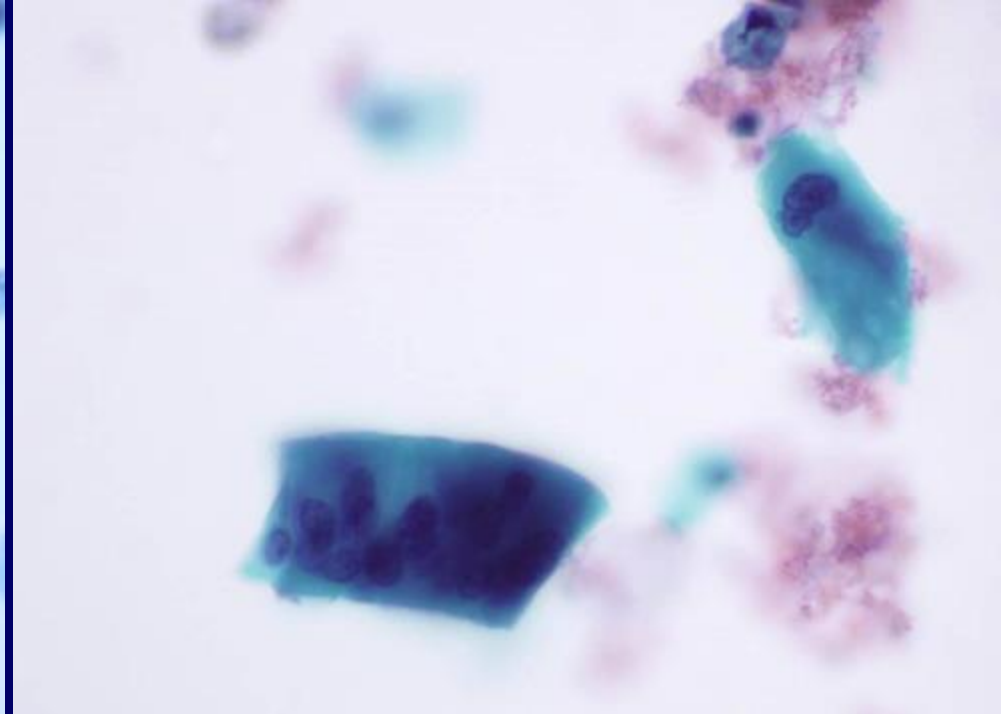
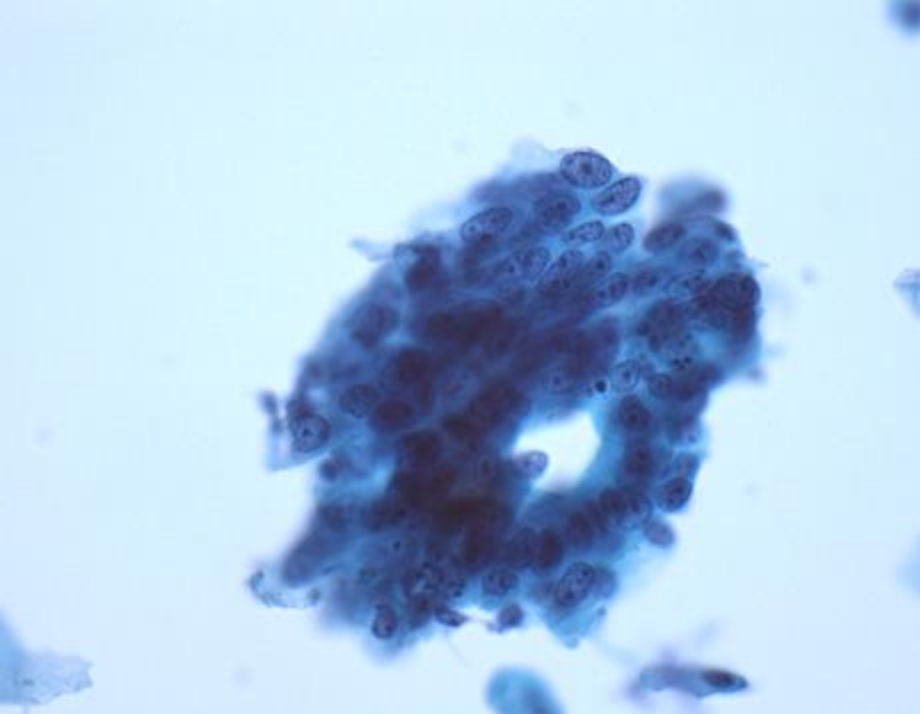
Benign

Malignant

Atypical

Diagnosis:

Colonic Adenocarcinoma
Recto-vaginal Fistula



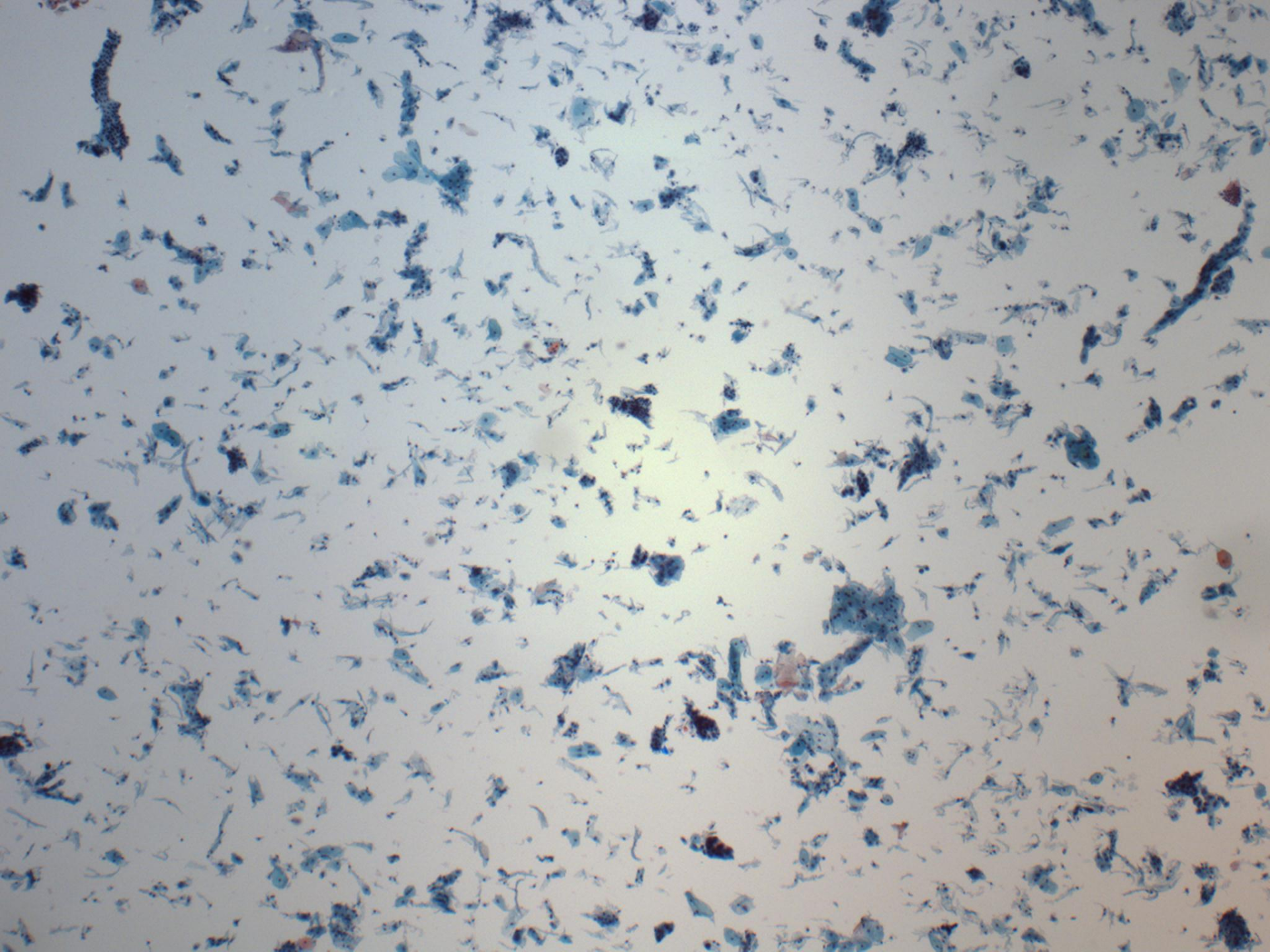
“Clues to Primary Sites”

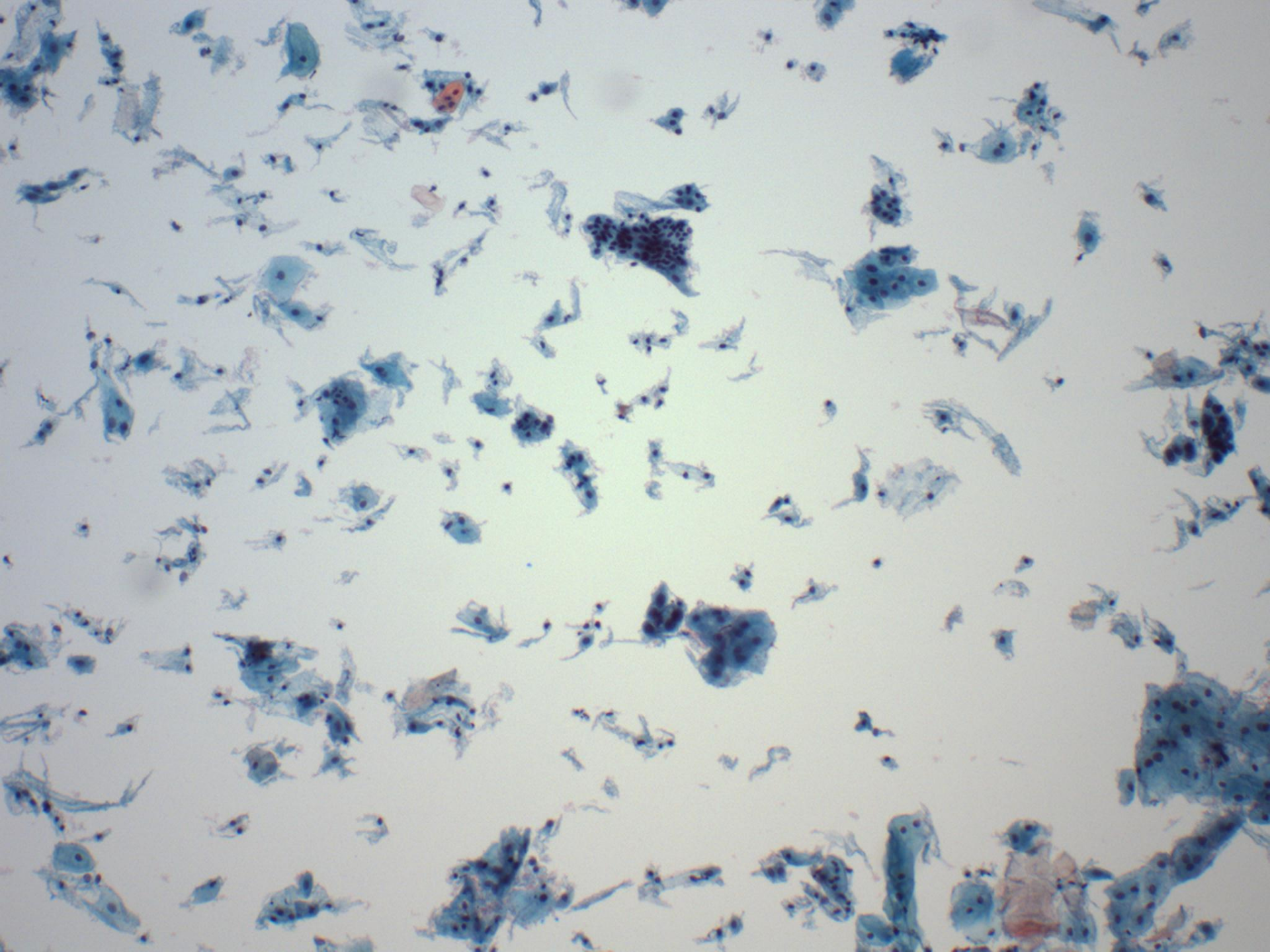
| Clue | Possible Site |
|-------------------------------|--------------------------|
| Papillary arrangements | Ovary, renal |
| Psammoma bodies | Ovary, benign conditions |
| Single file chains | Breast, Stomach |
| Intracytoplasmic lumens | Breast |
| Clear cells | Renal |
| Signet ring cells | Stomach, breast |
| Pollywogs (cercariform) | Urothelial |
| Neuroendocrine | Lung vs cx primary |
| Tall, cigar, goblet, necrosis | Colorectal |

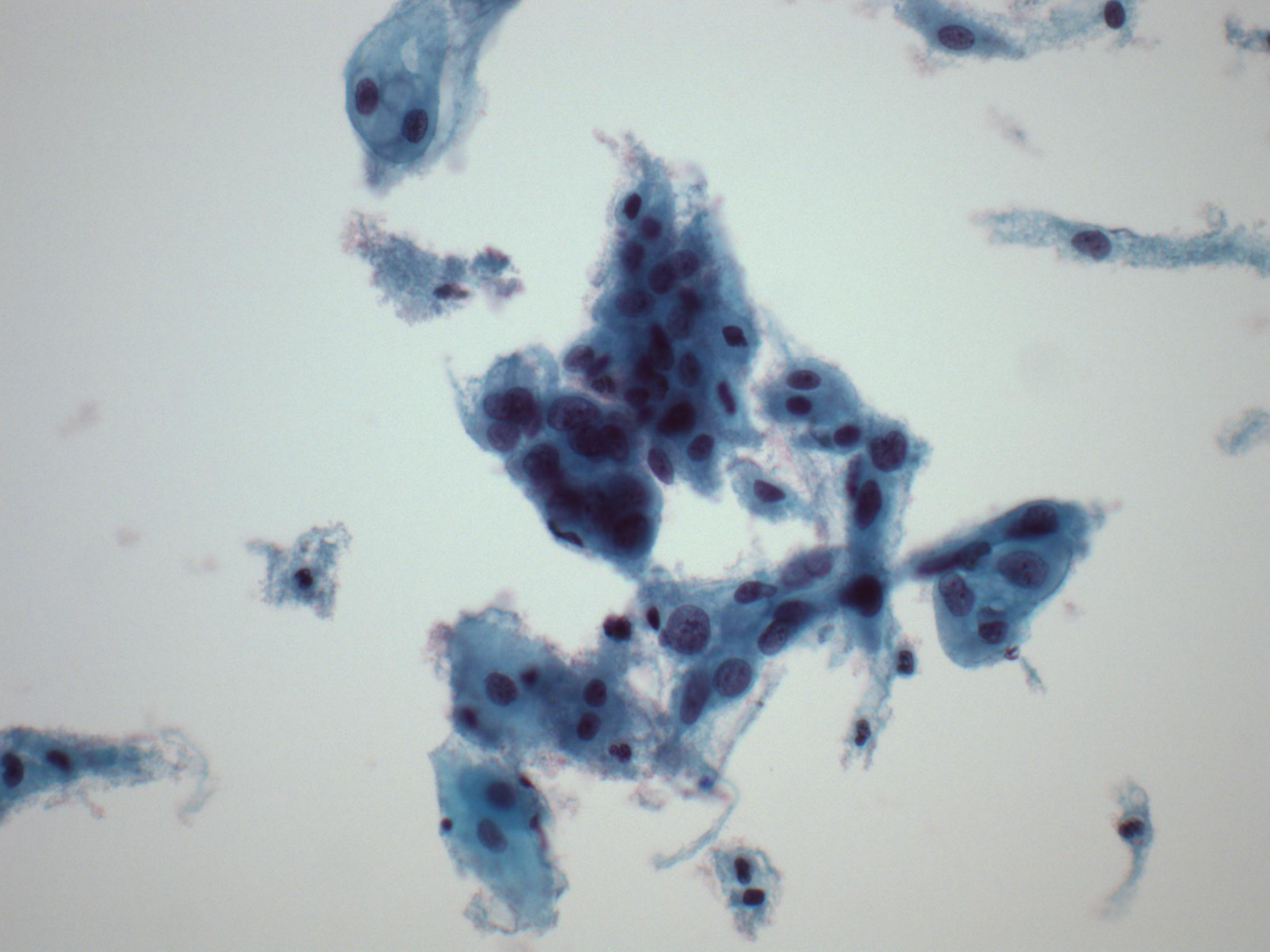
Case 6

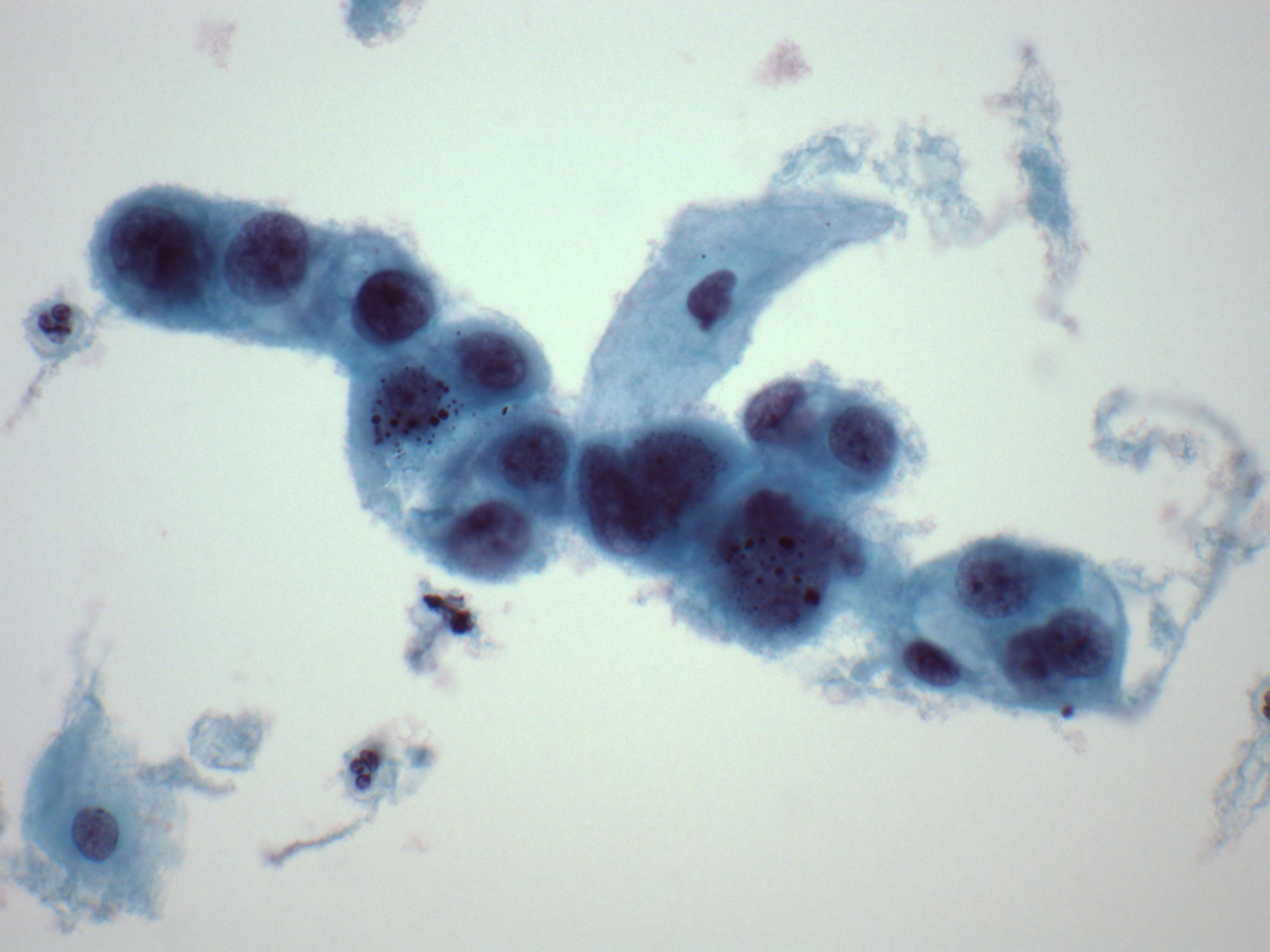
48 year old

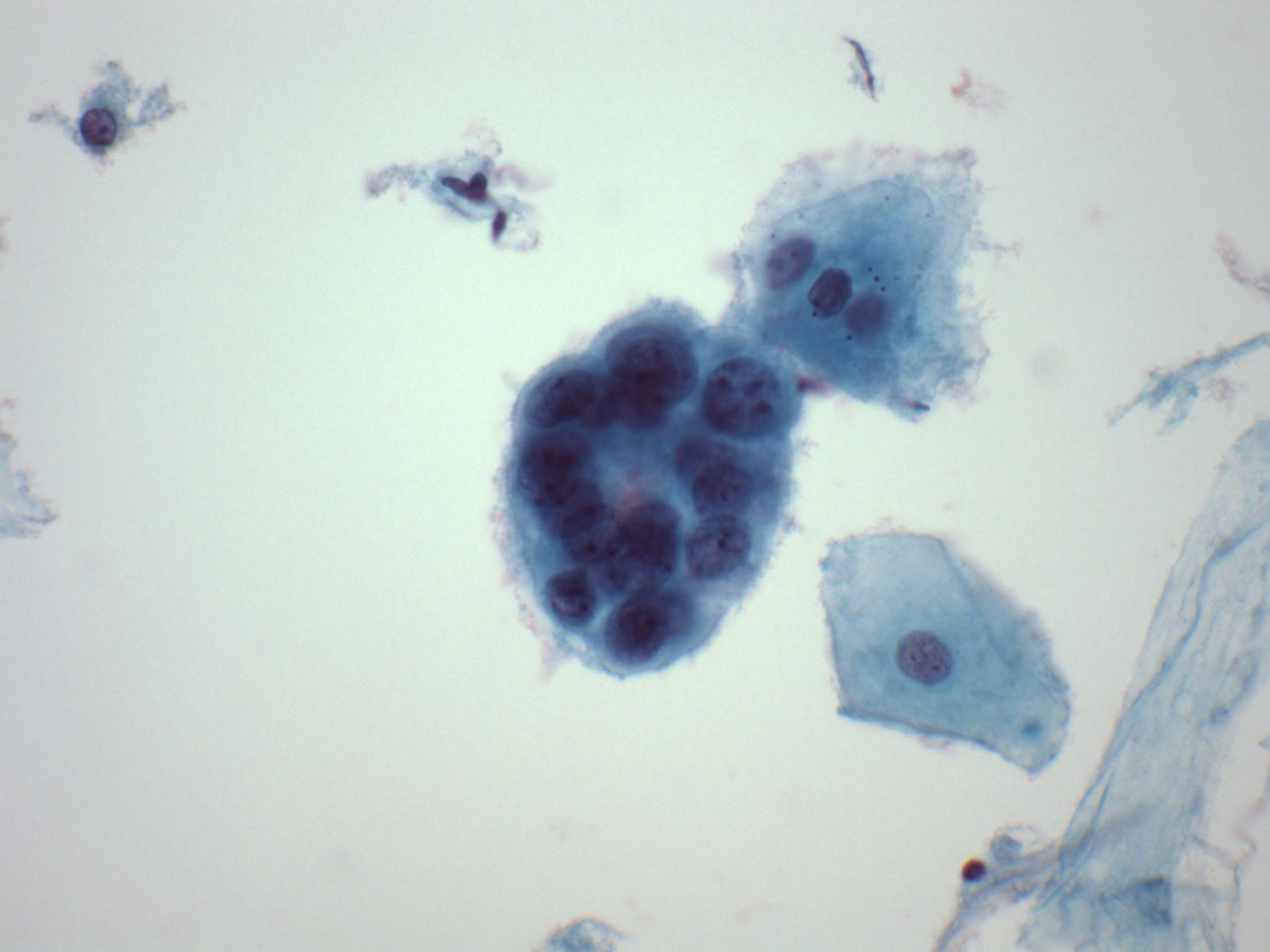
No significant Pap history

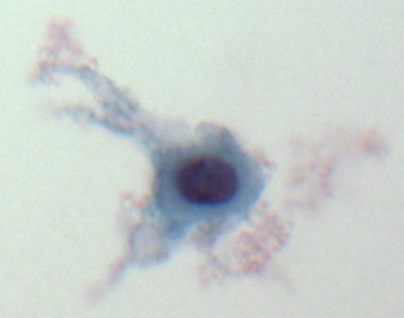
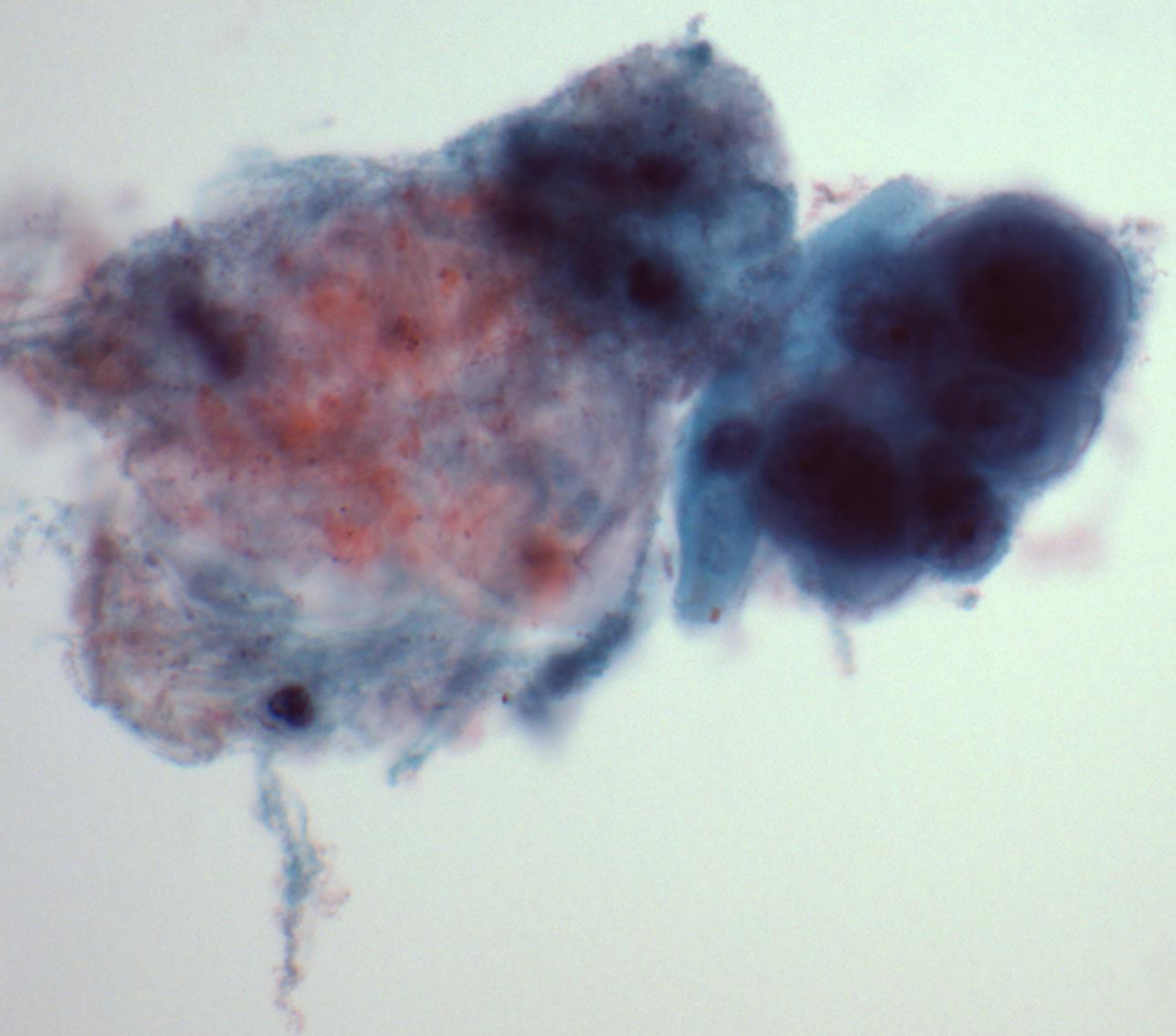


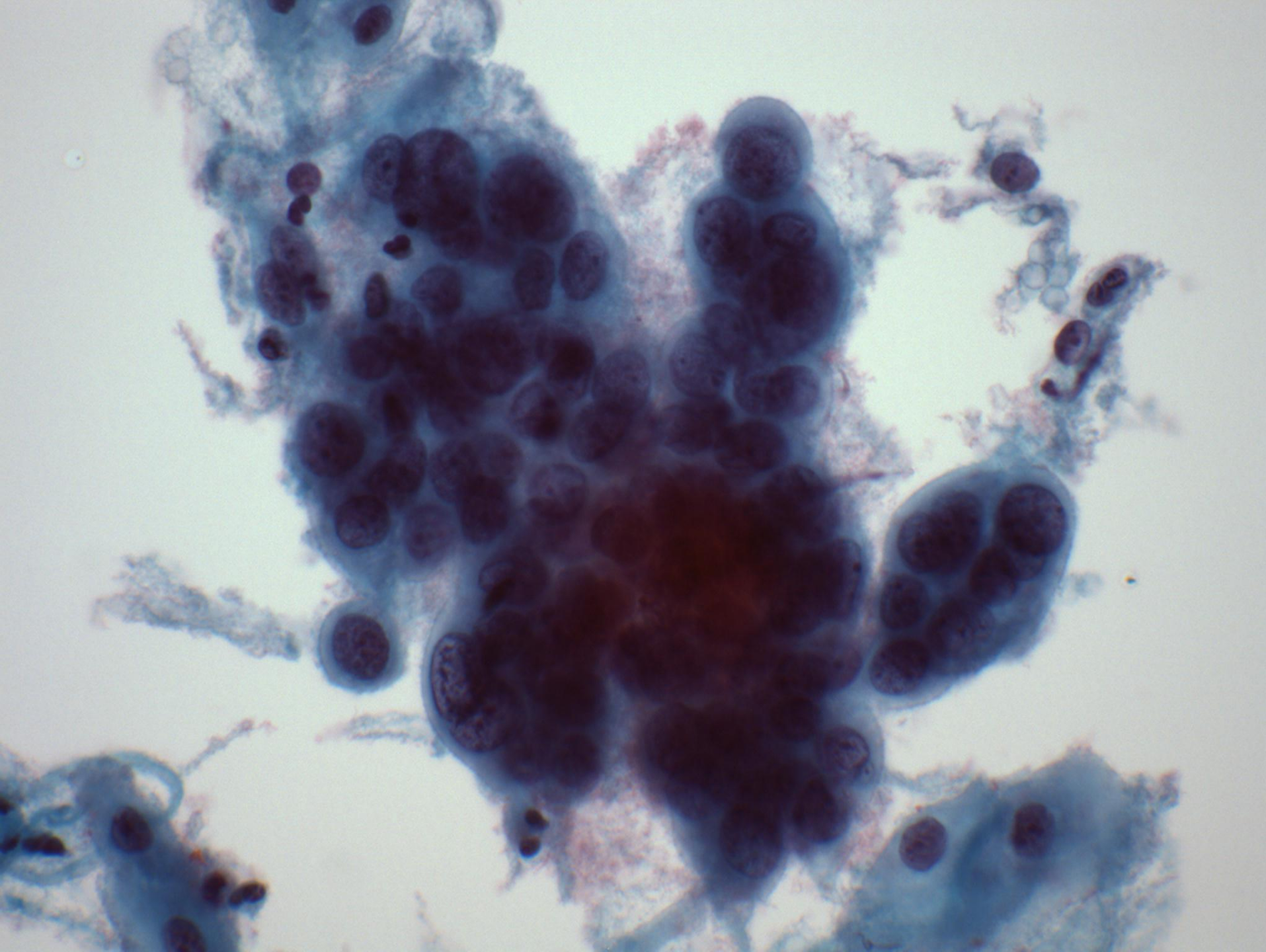


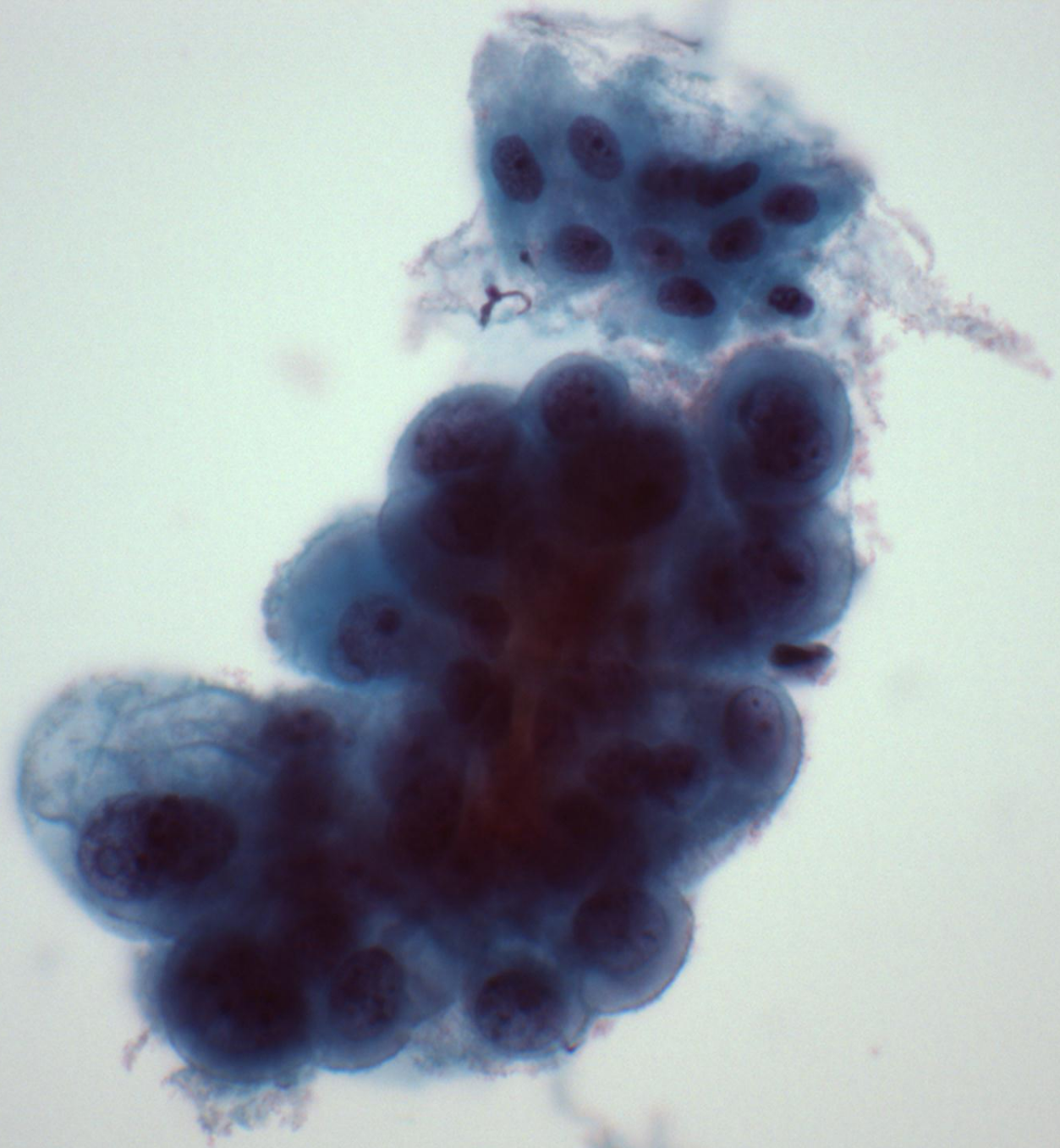












Summary of Key Cytologic Features

- Low cellularity specimen
- Atrophic background
- Abundant wispy background material
- 3-dimensional cell clusters
- Nuclear atypia
- Apoptotic debris

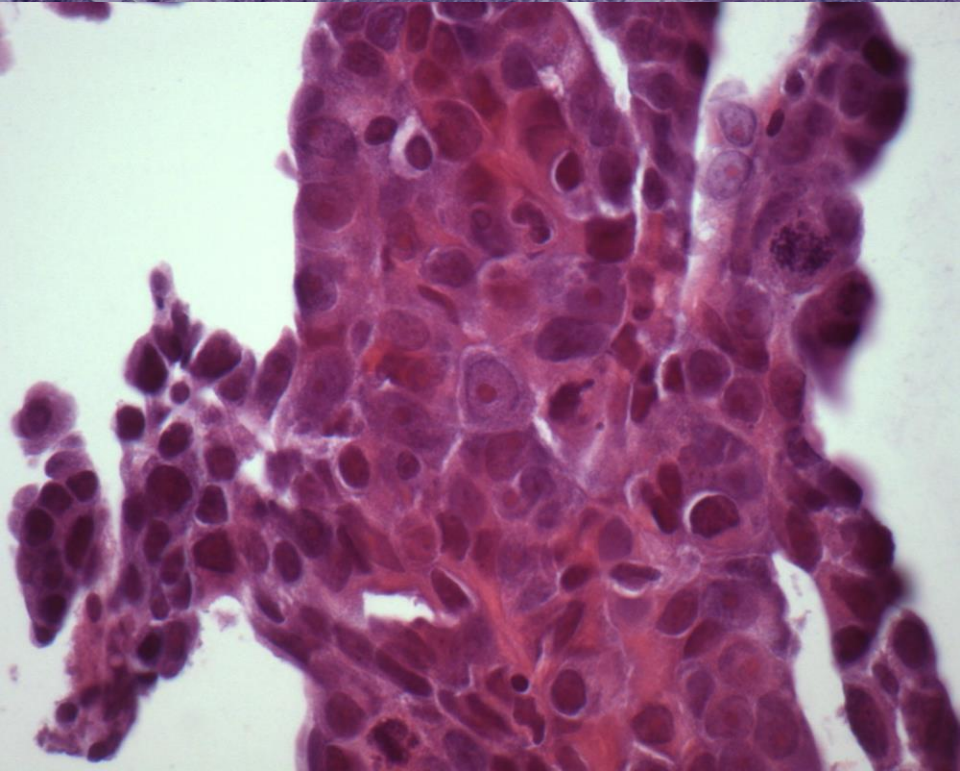
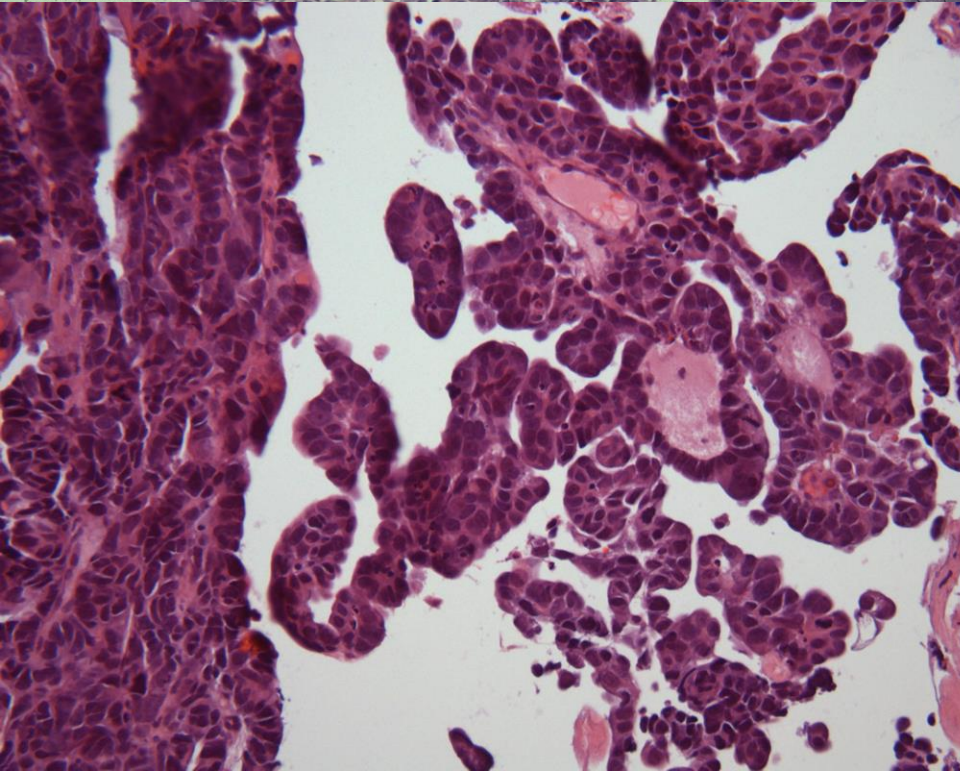
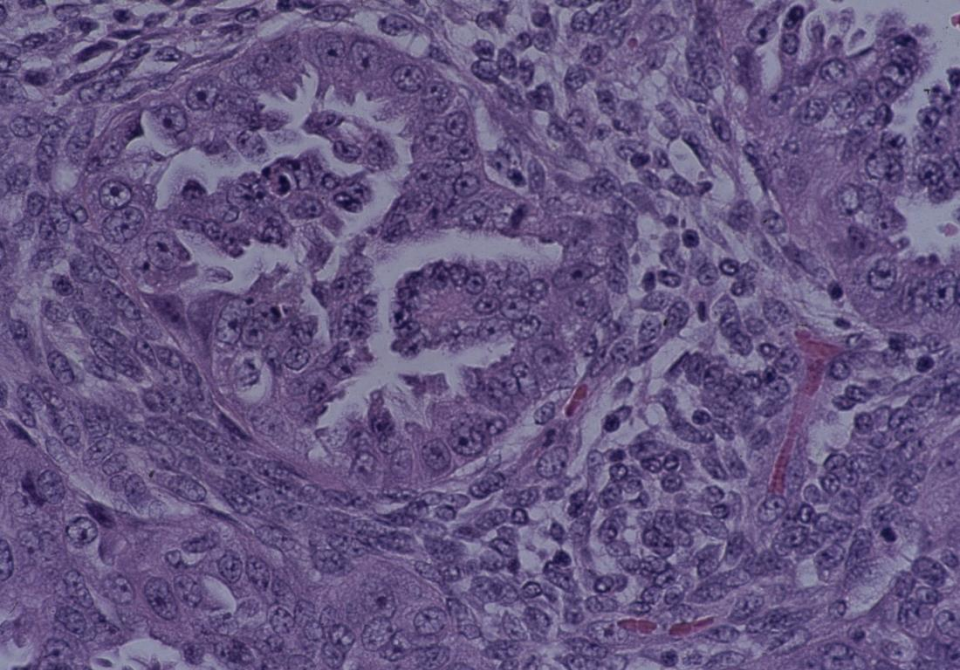
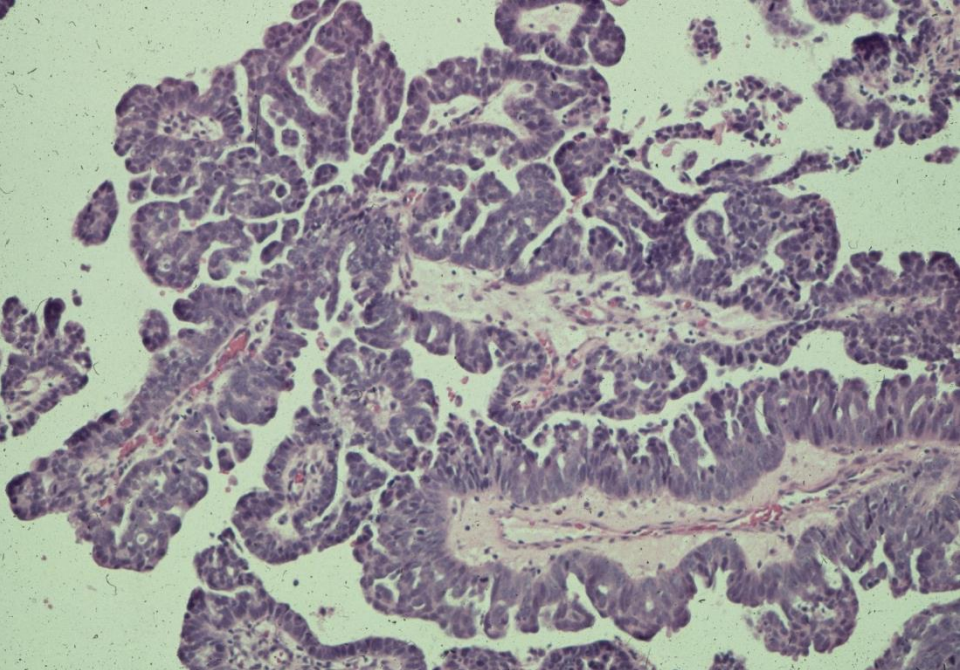
Benign

Malignant

Atypical

Diagnosis:

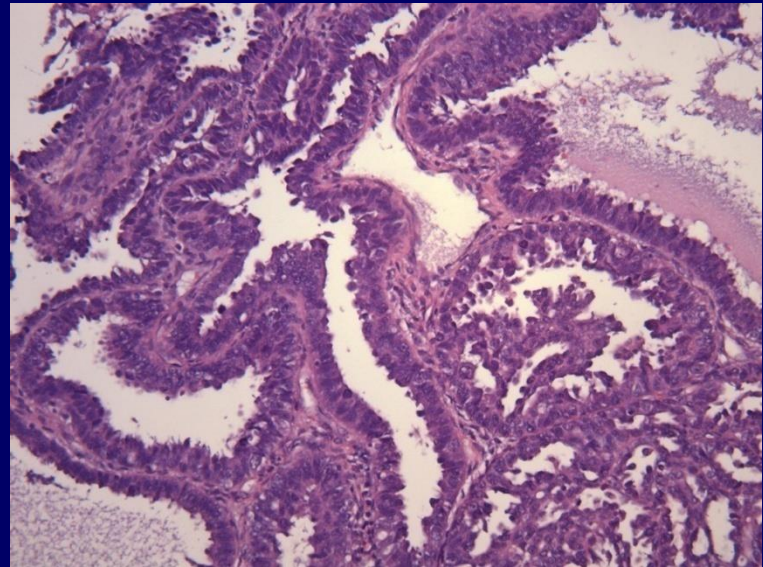
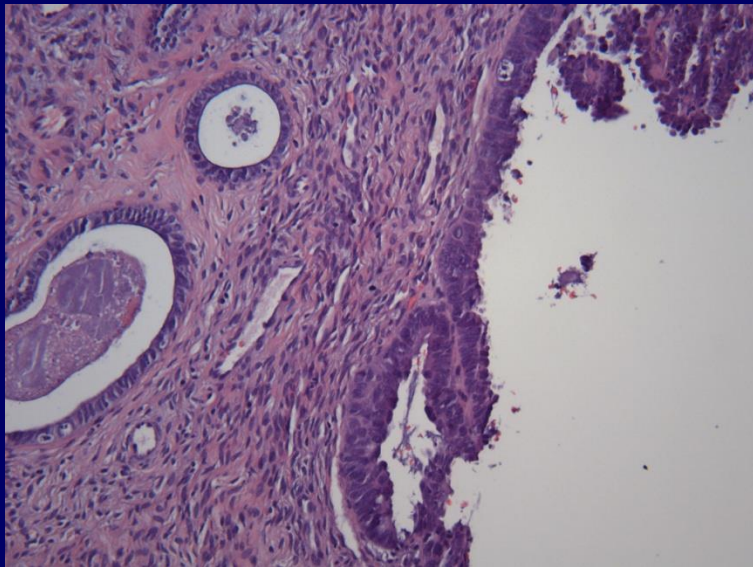
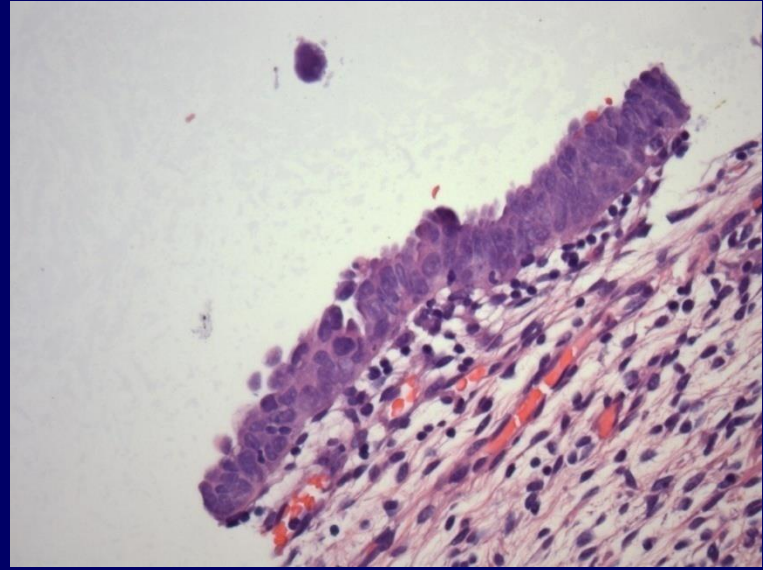
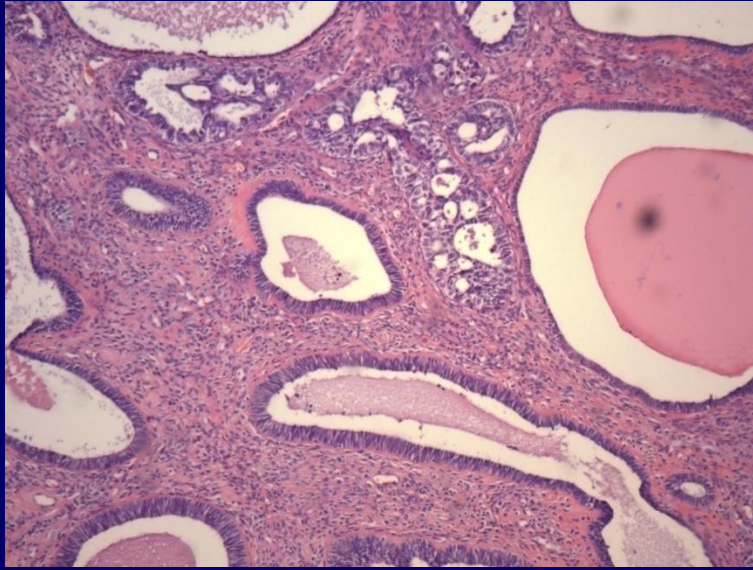
Endometrial Carcinoma
Papillary Serous Type



Serous Carcinoma

- 1 to 10% of EM Ca
- Morphology similar to ovarian pap serous ca
- Complex papillary pattern with fibrous stalks
- Covering of highly atypical cells (grade 3)
- Bud formation/tufting
- Solid areas or irregular slit-like spaces
- Hobnail cells often noted
- May have mixtures with endometrioid CA
- Psammoma bodies variable

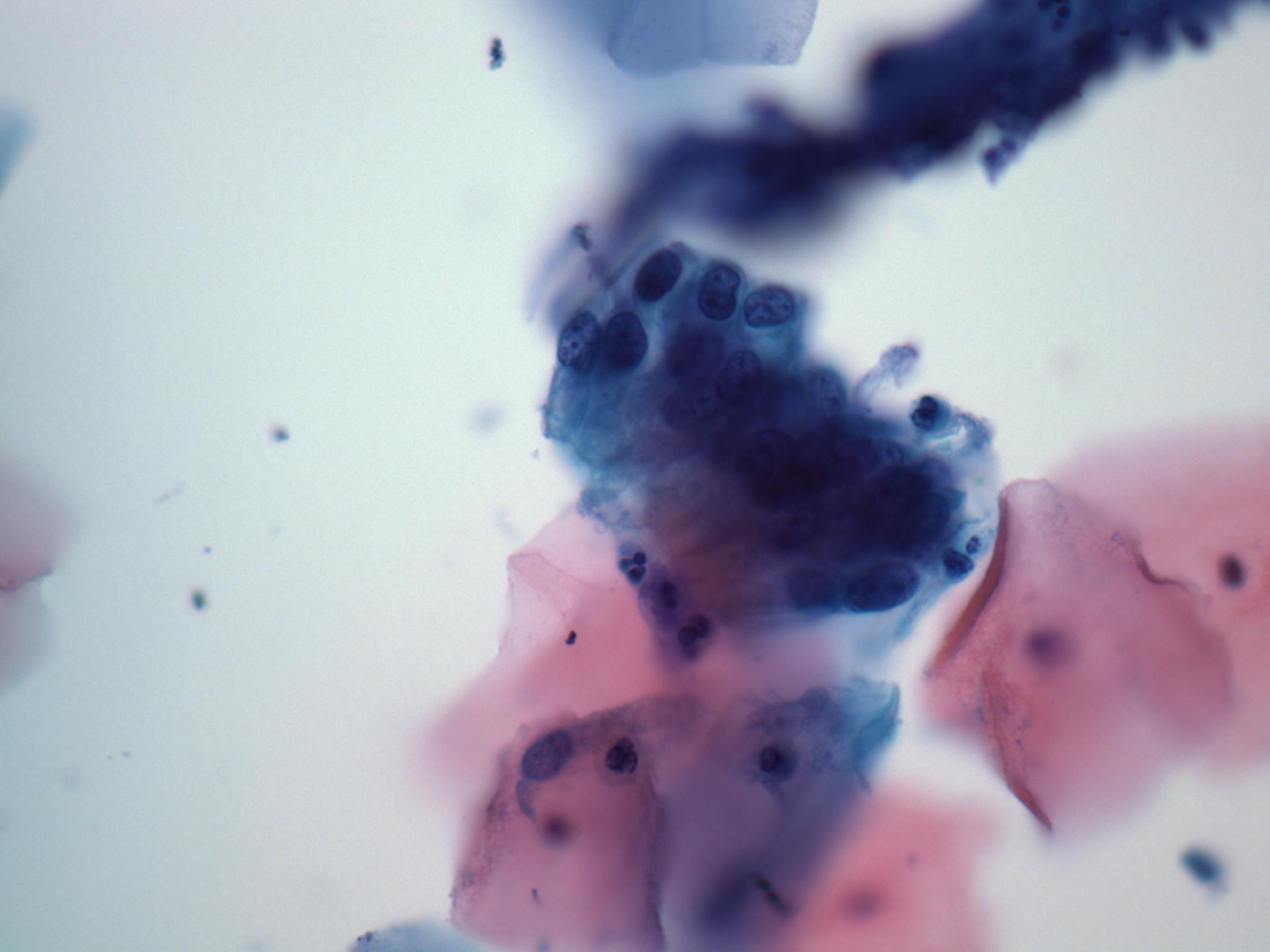
EMP with serous CA

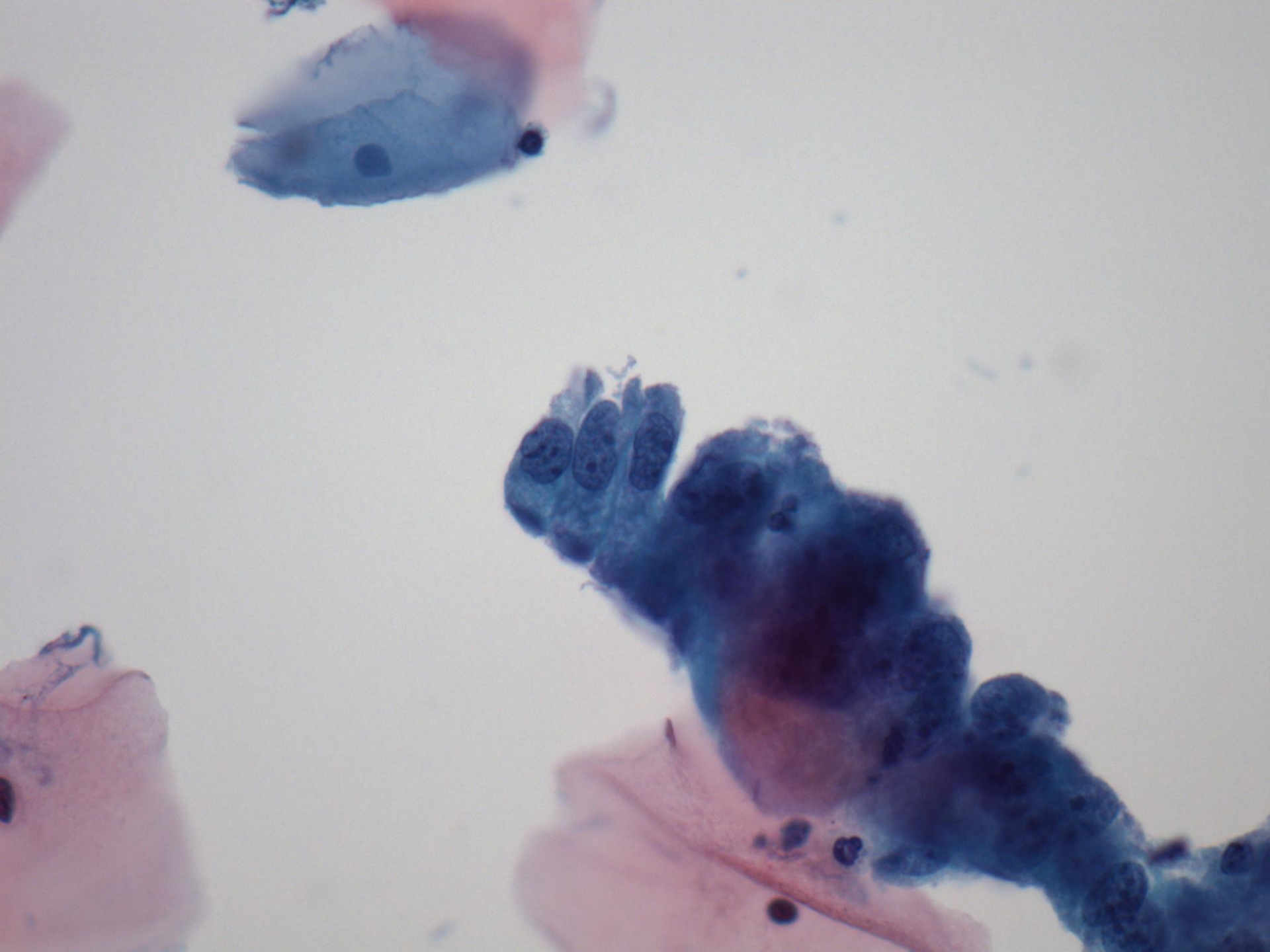


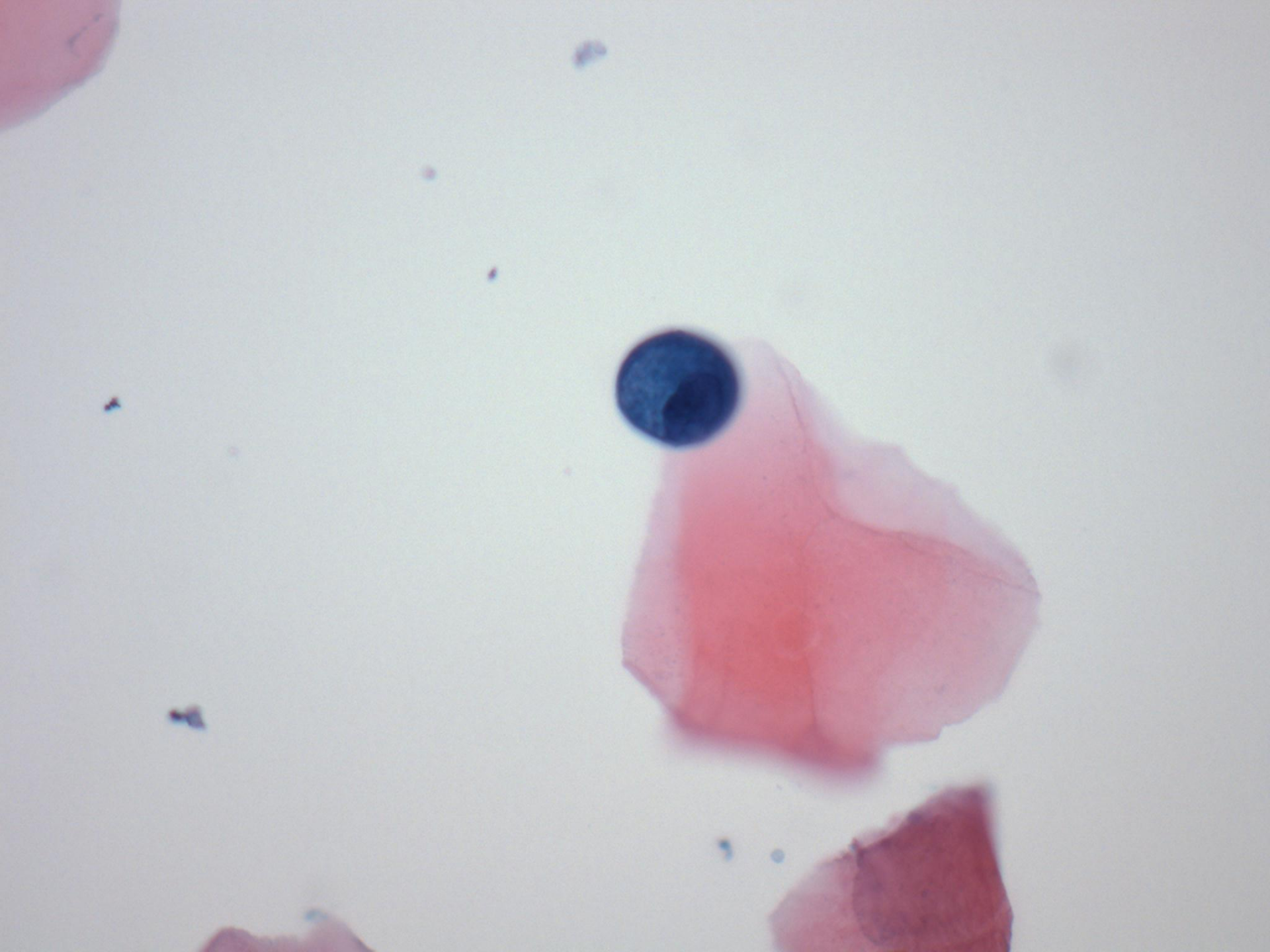
Case 7

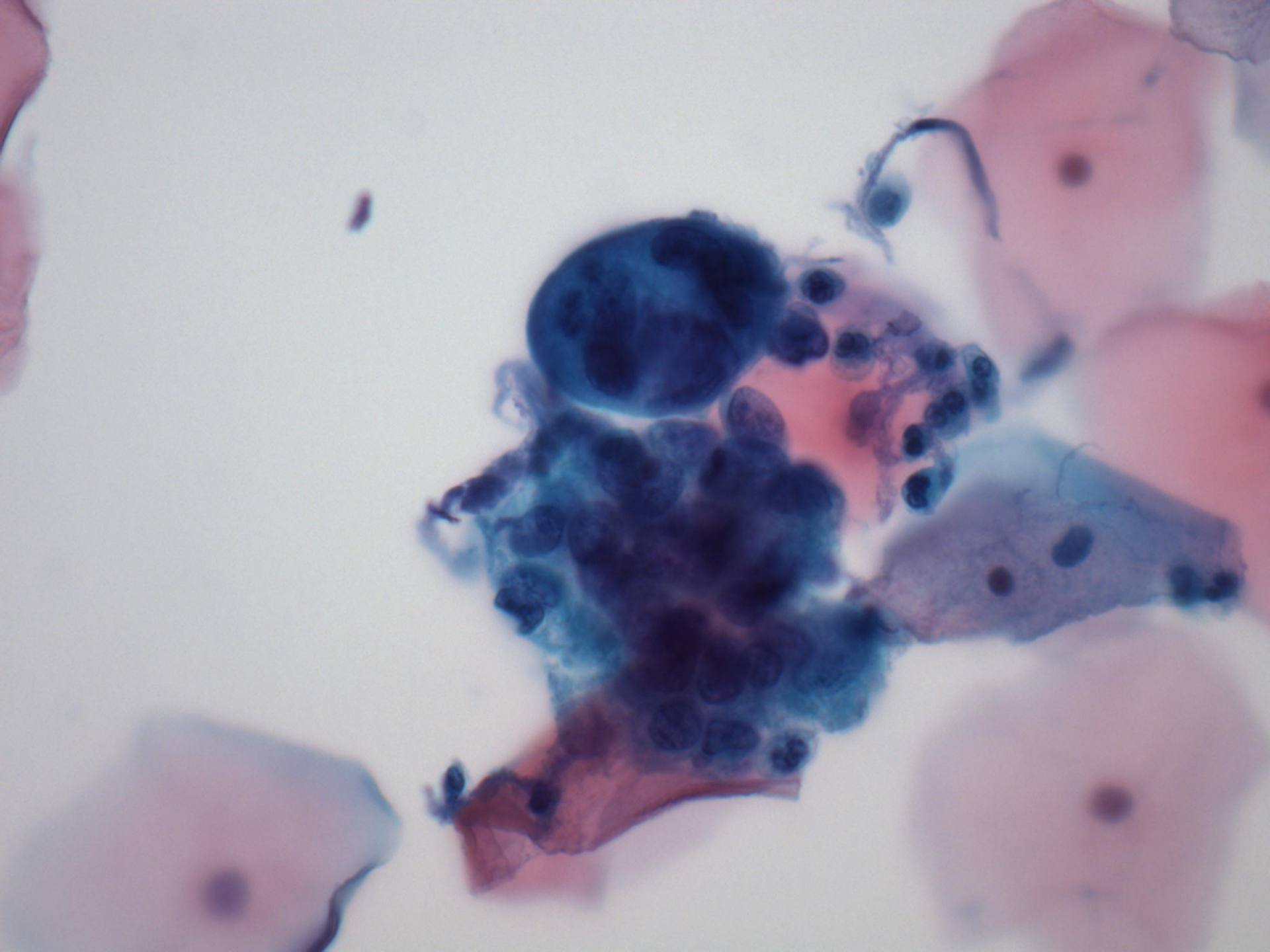
42 year old women

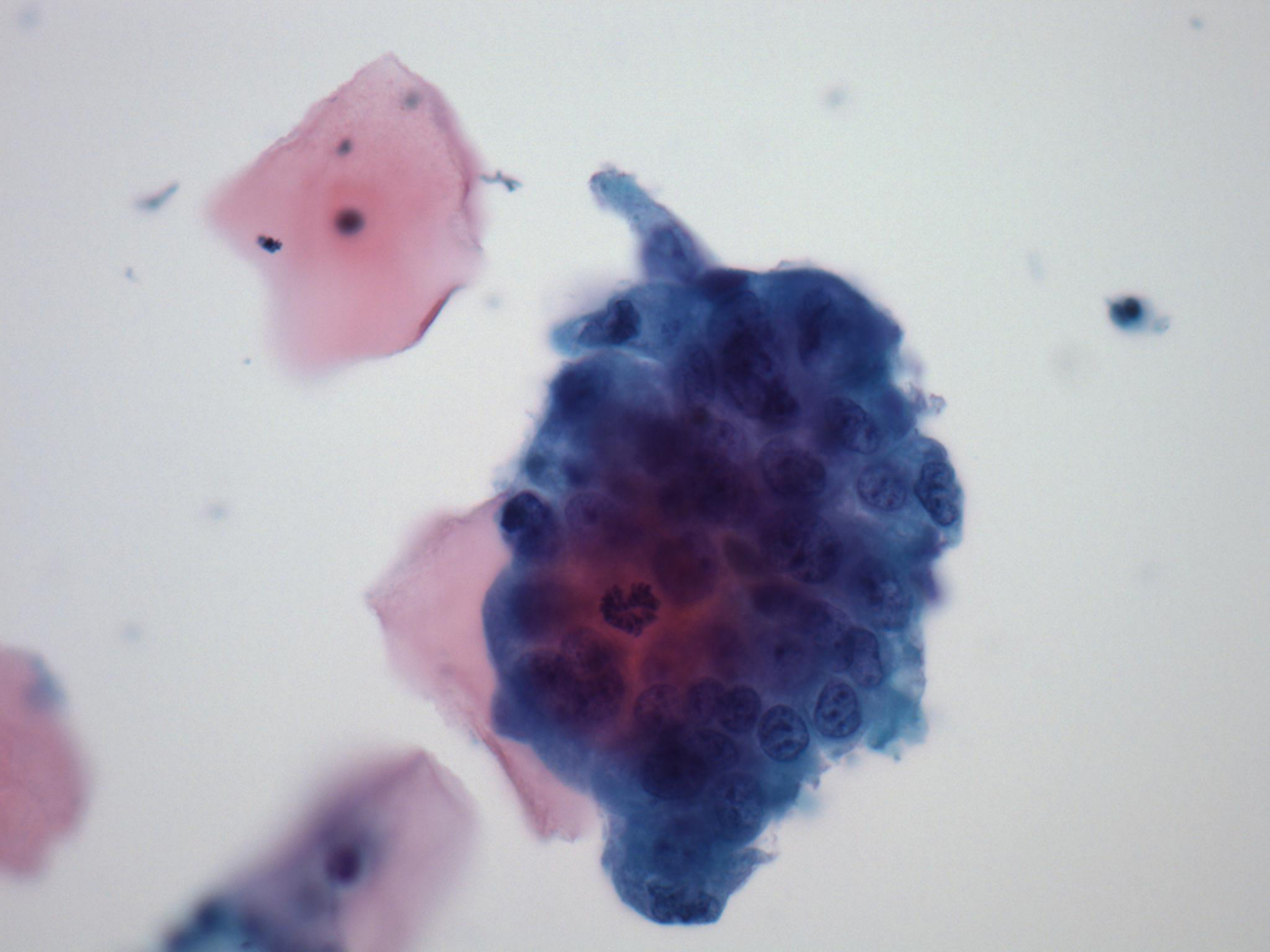
No prior history given











Summary of Key Cytologic Features

- Groups, strips, and isolated columnar cells
- Abundant frothy mucus in columnar cells
- Moderate nuclear atypia
 - Irregularity, nucleoli, bland chromatin
- Scant amorphous debris in background

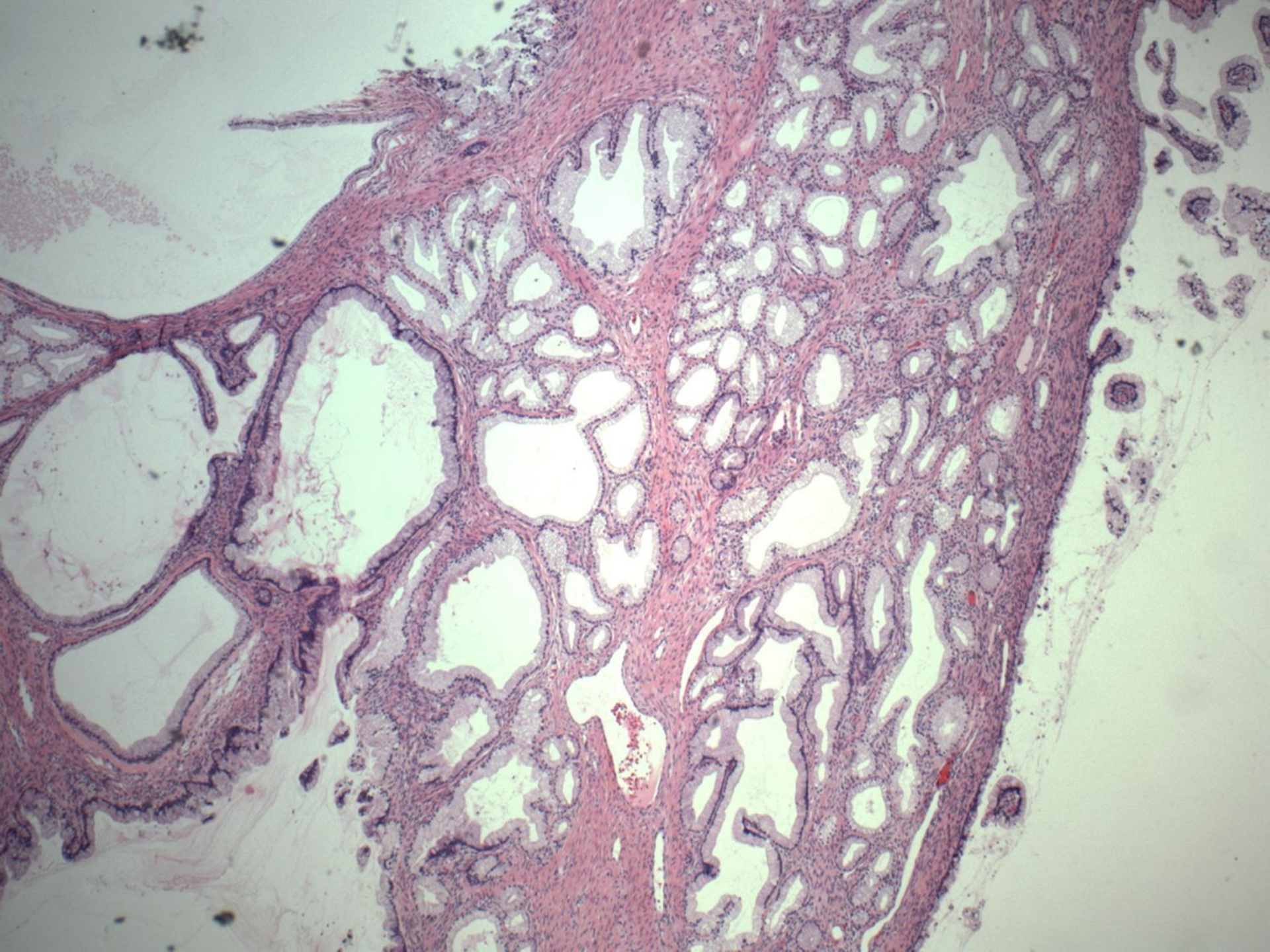
Benign

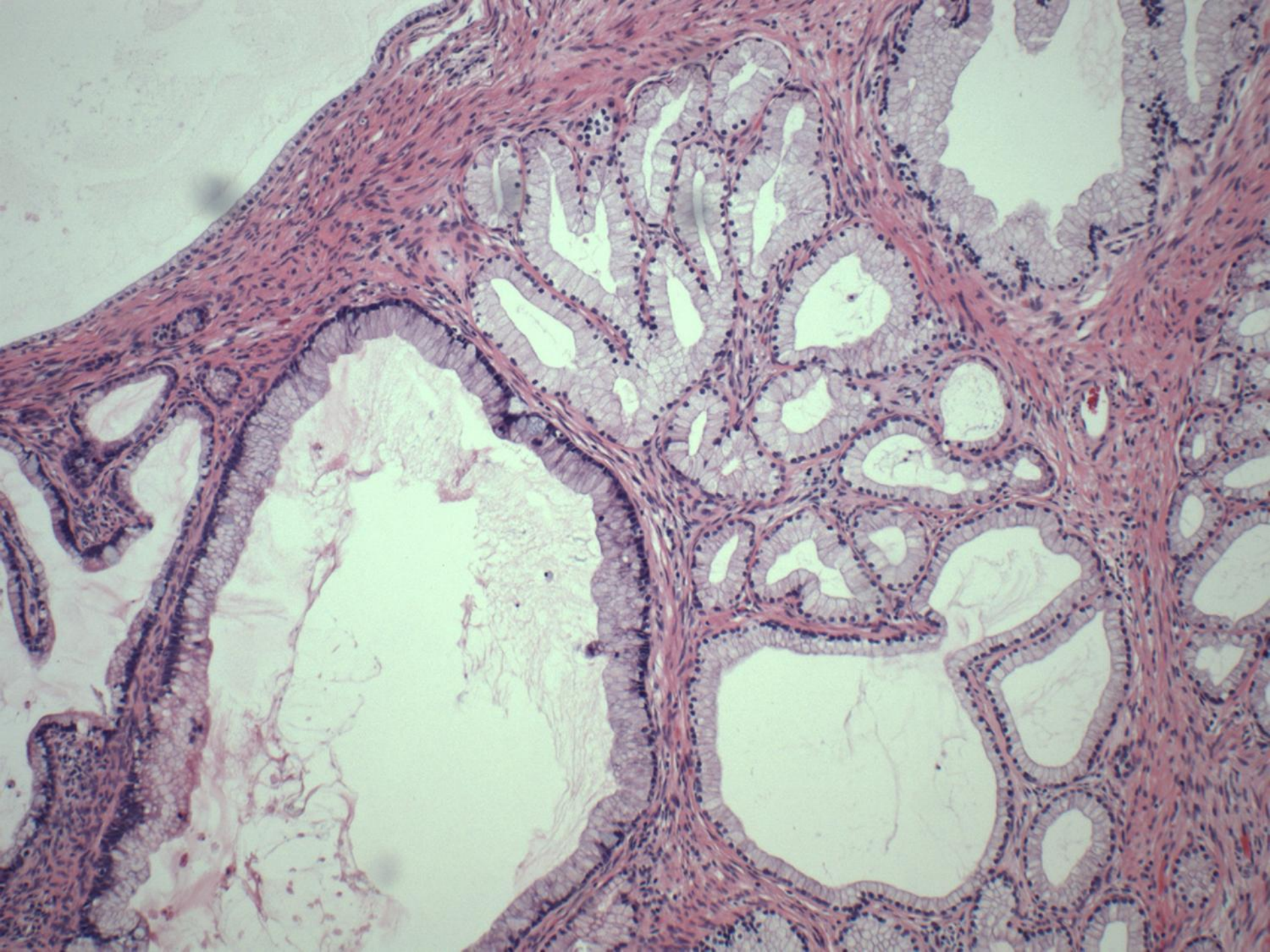
Malignant

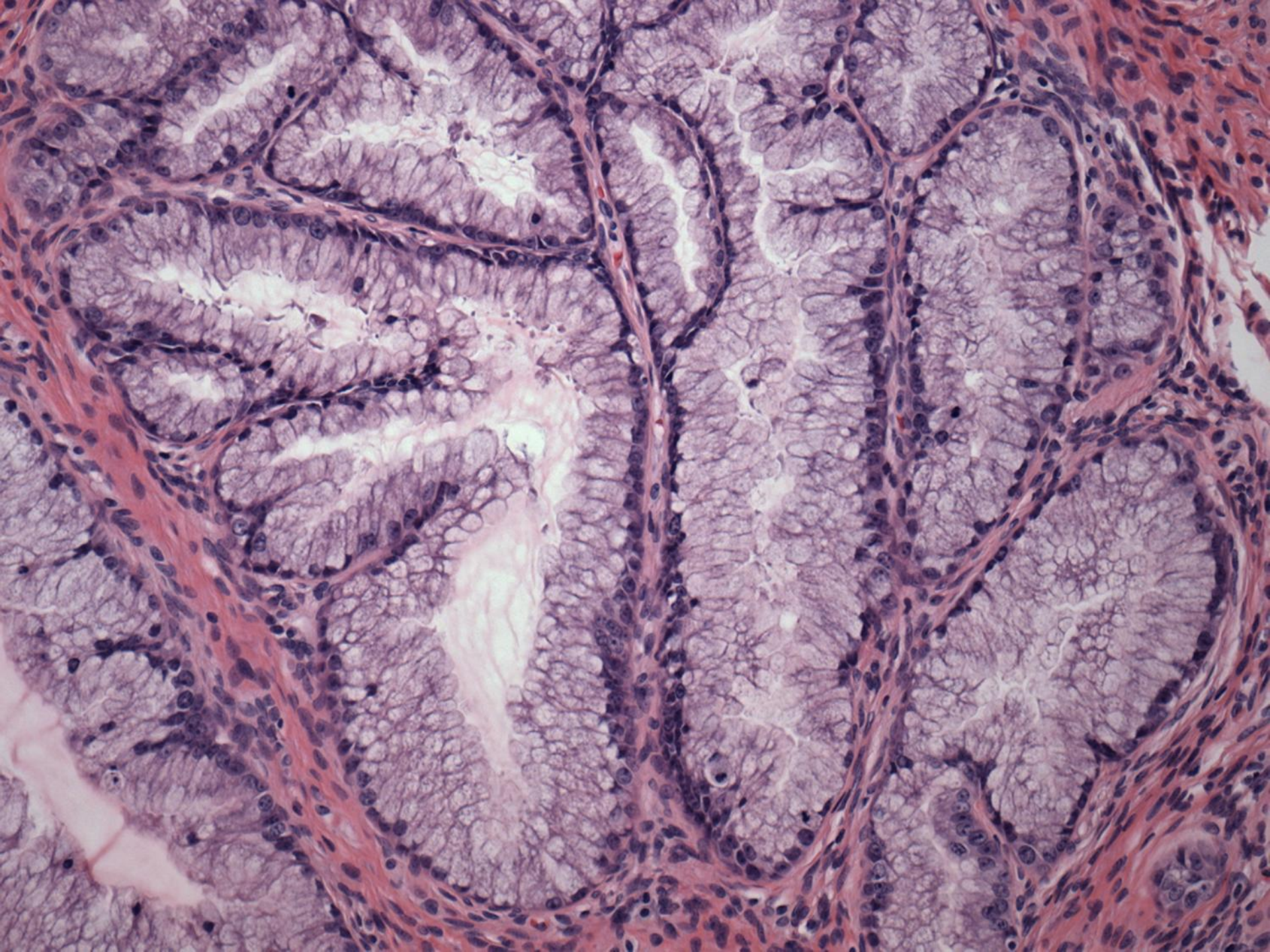
Atypical

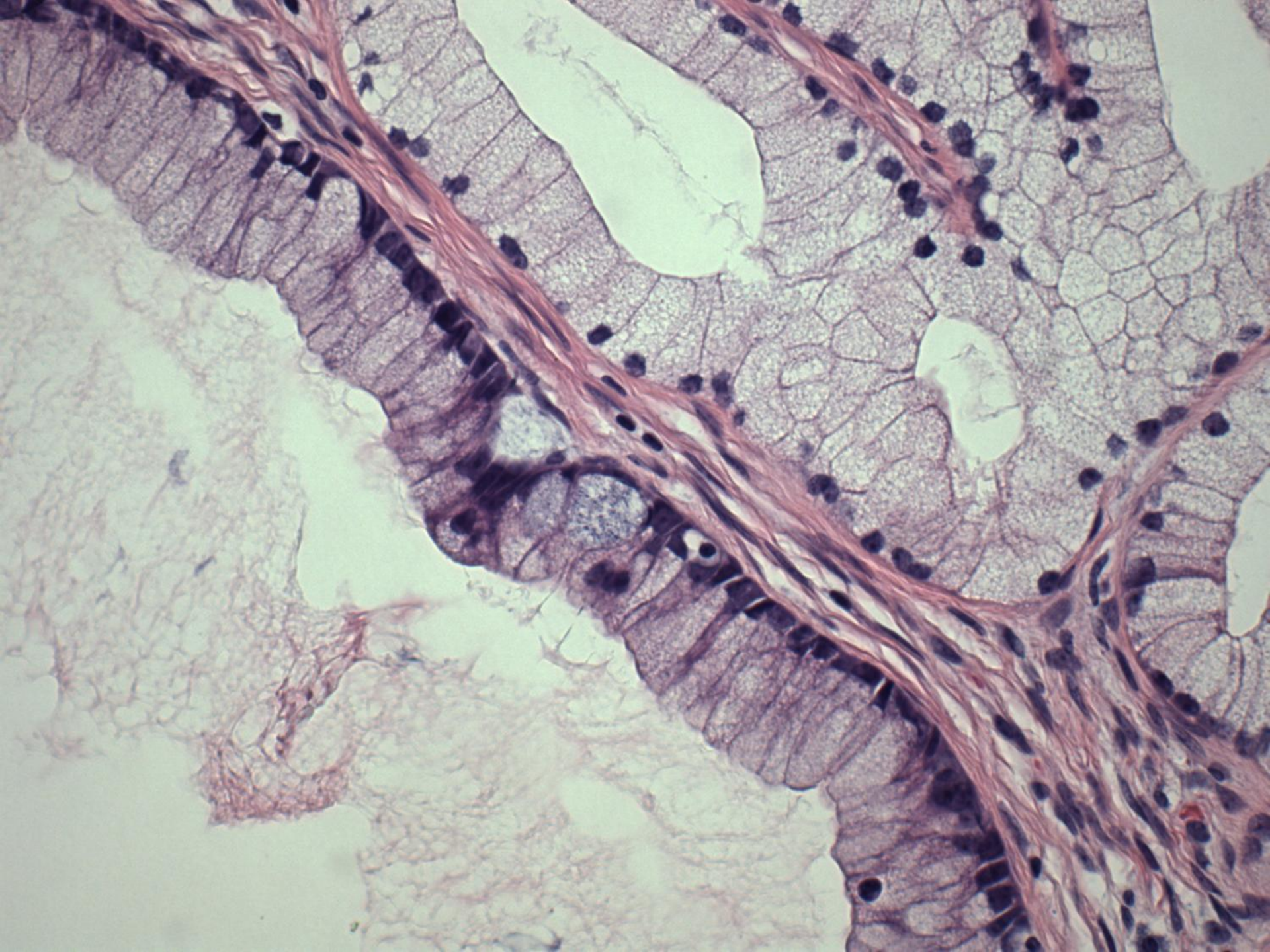
Diagnosis

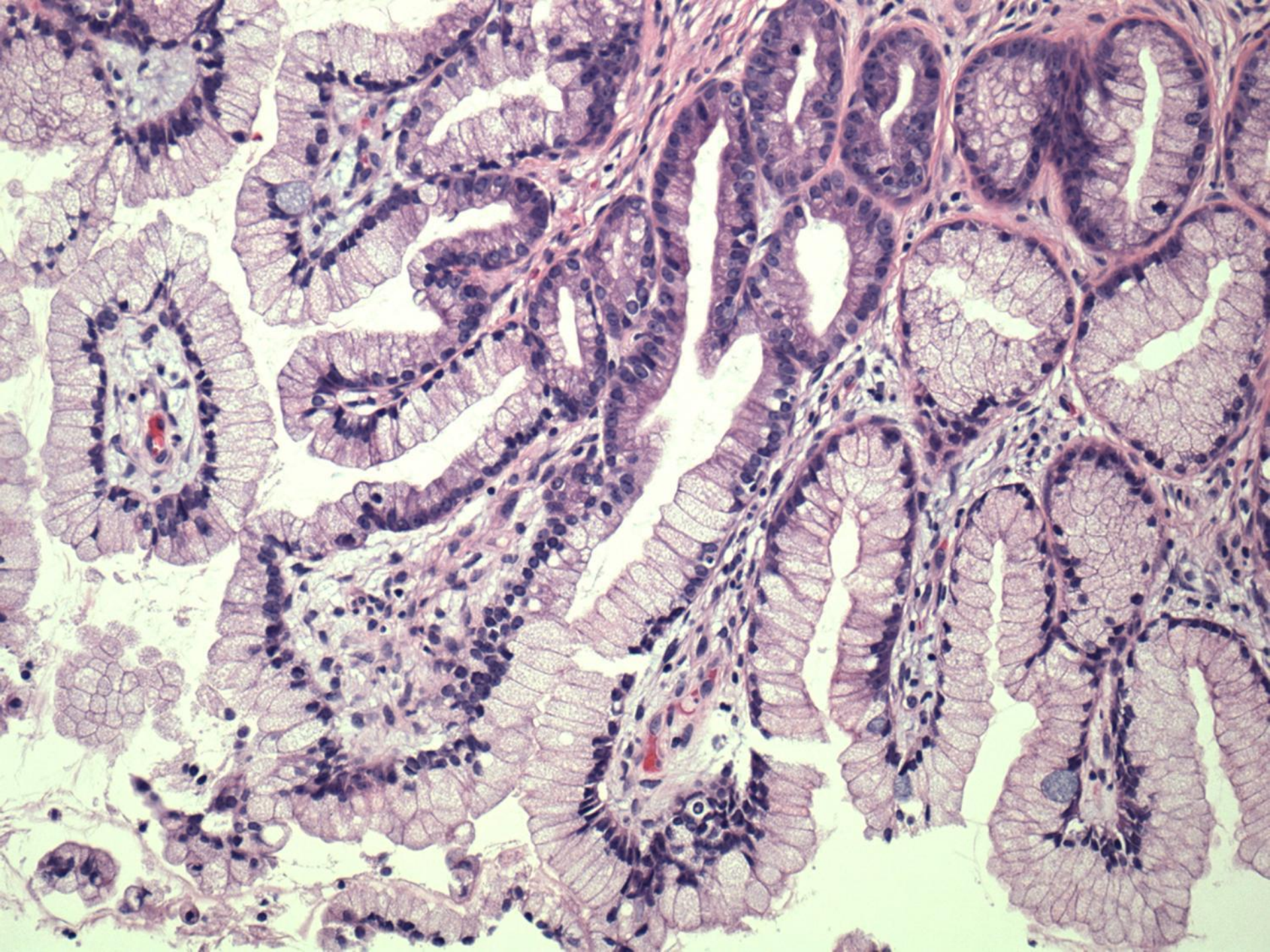
Lobular endocervical hyperplasia
with mucinous AIS

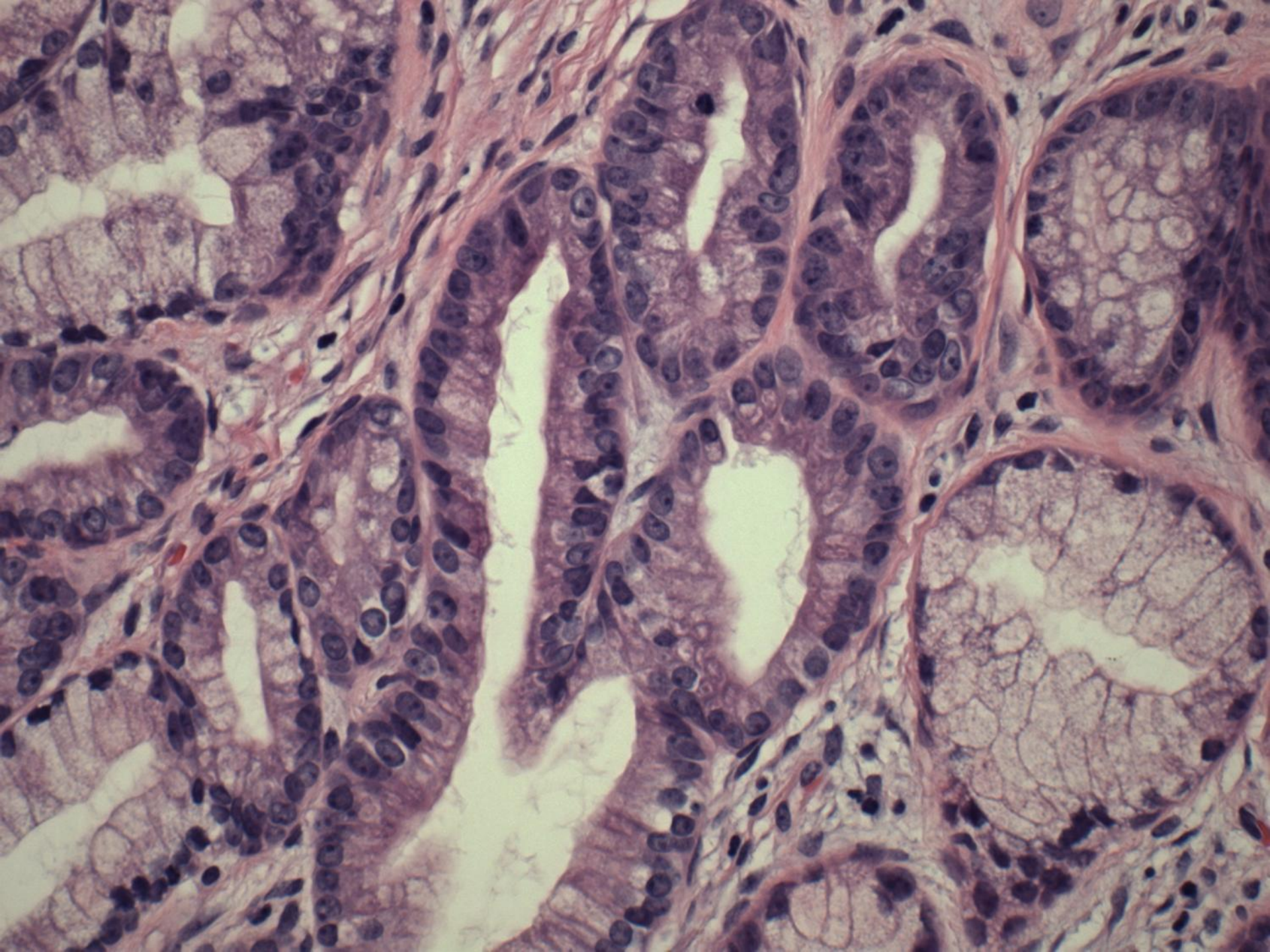


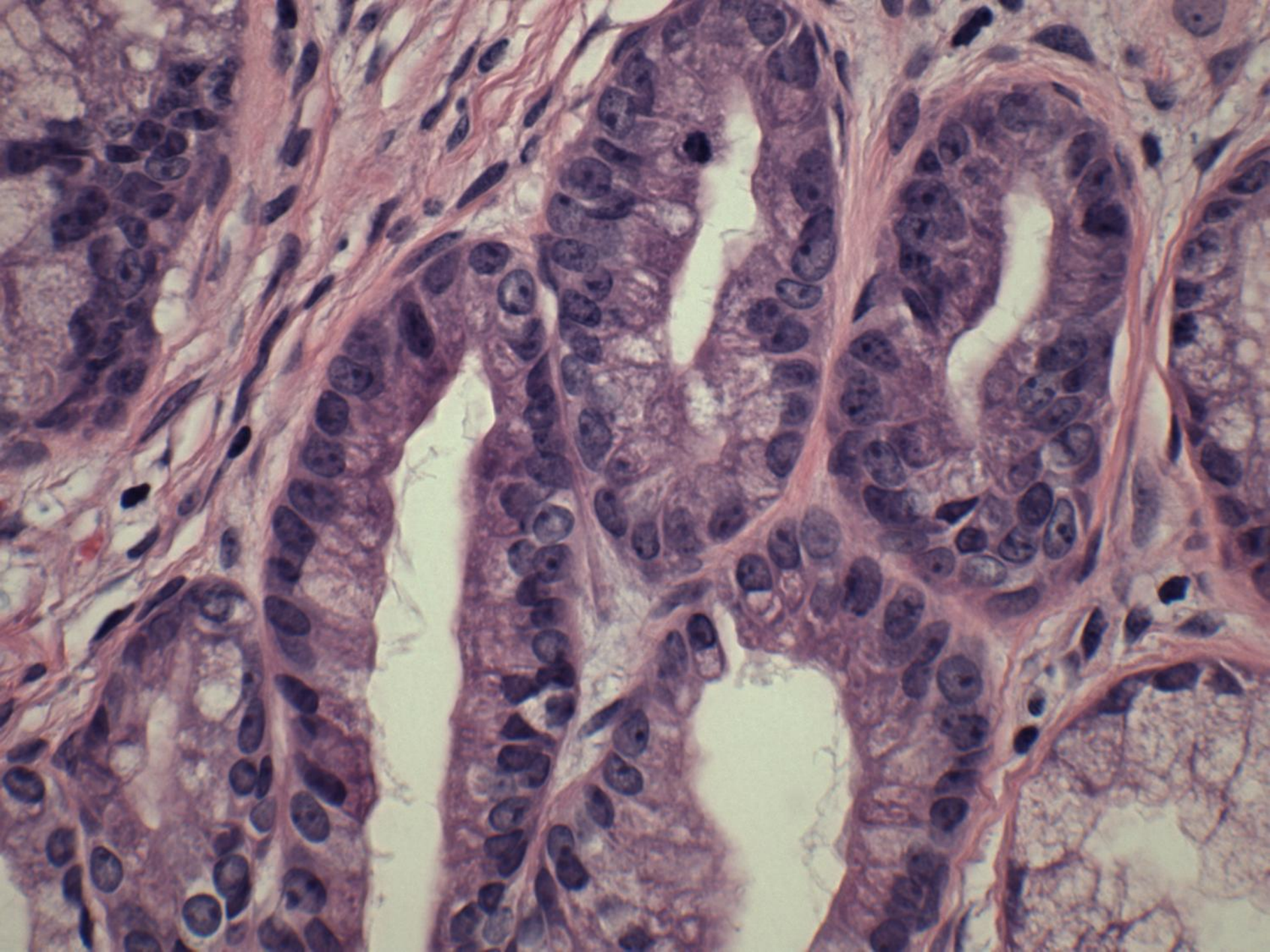


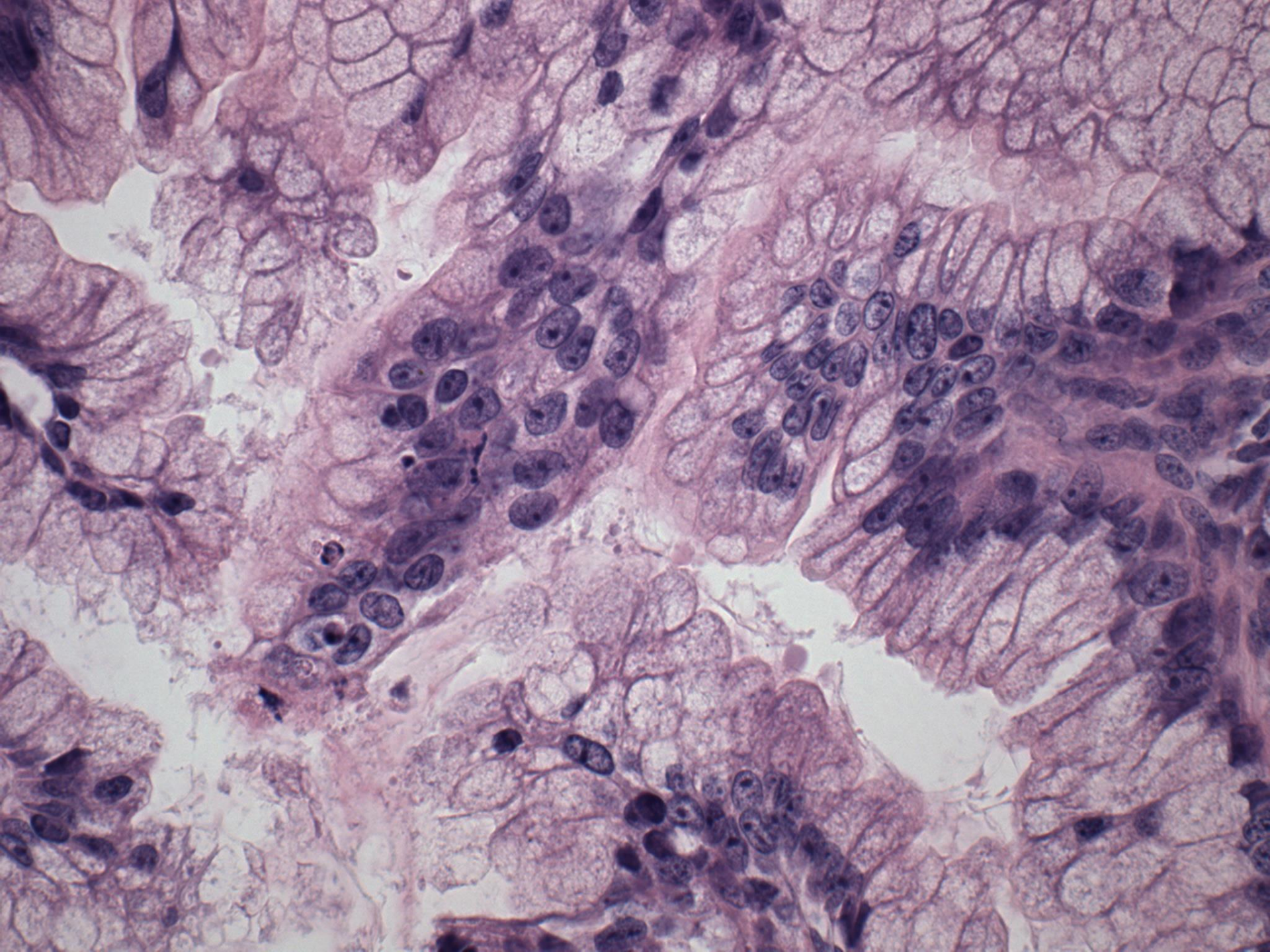


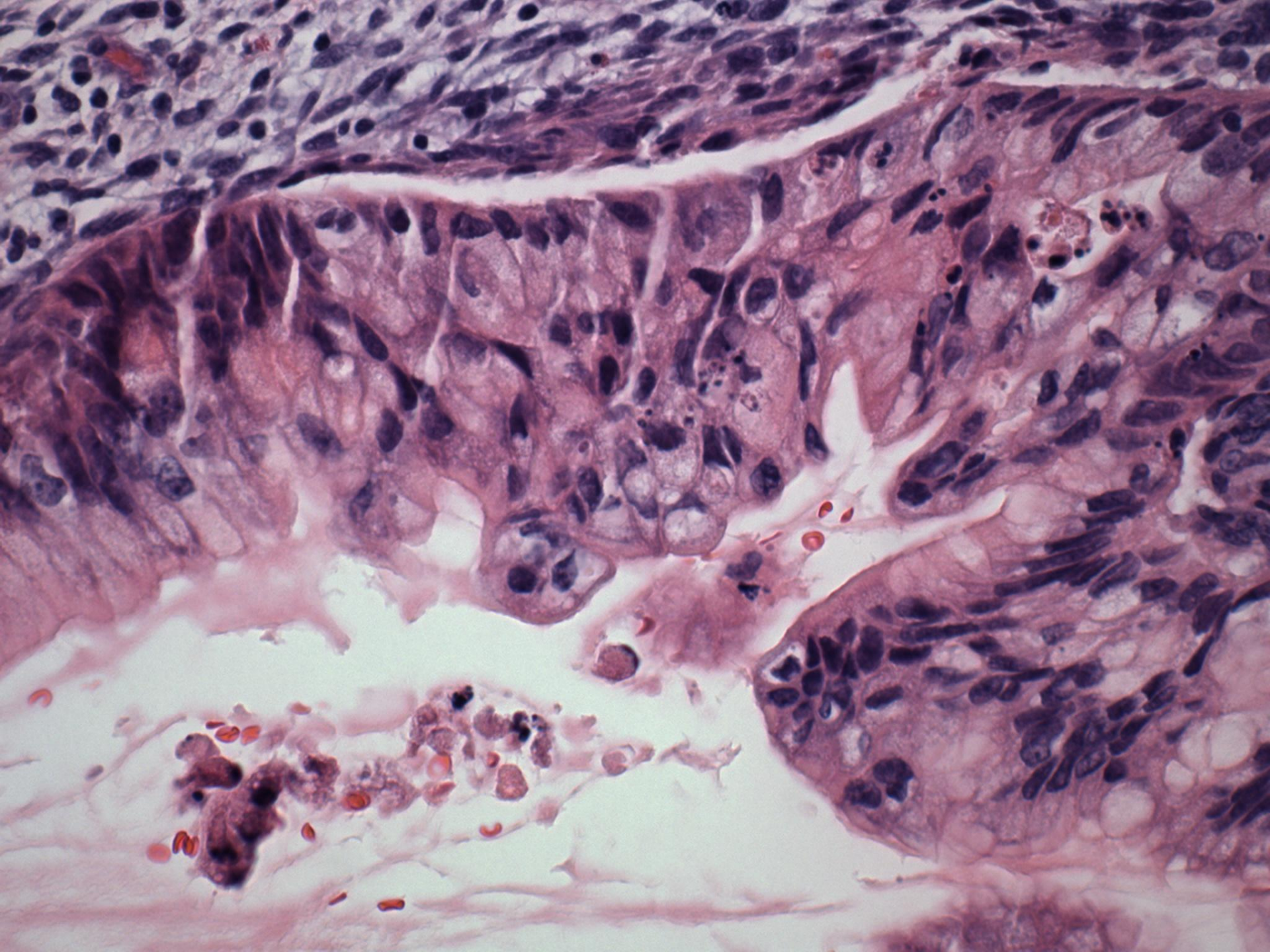






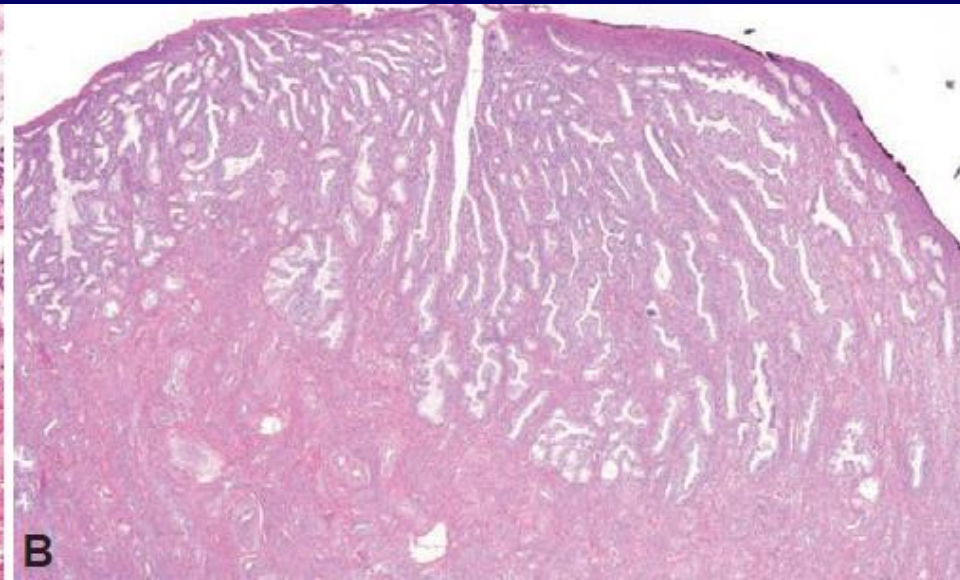
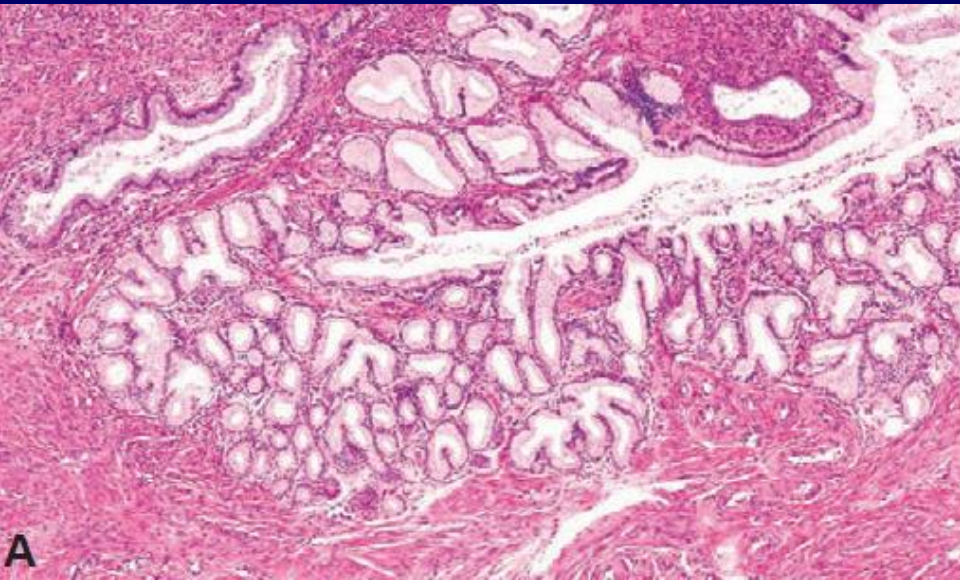






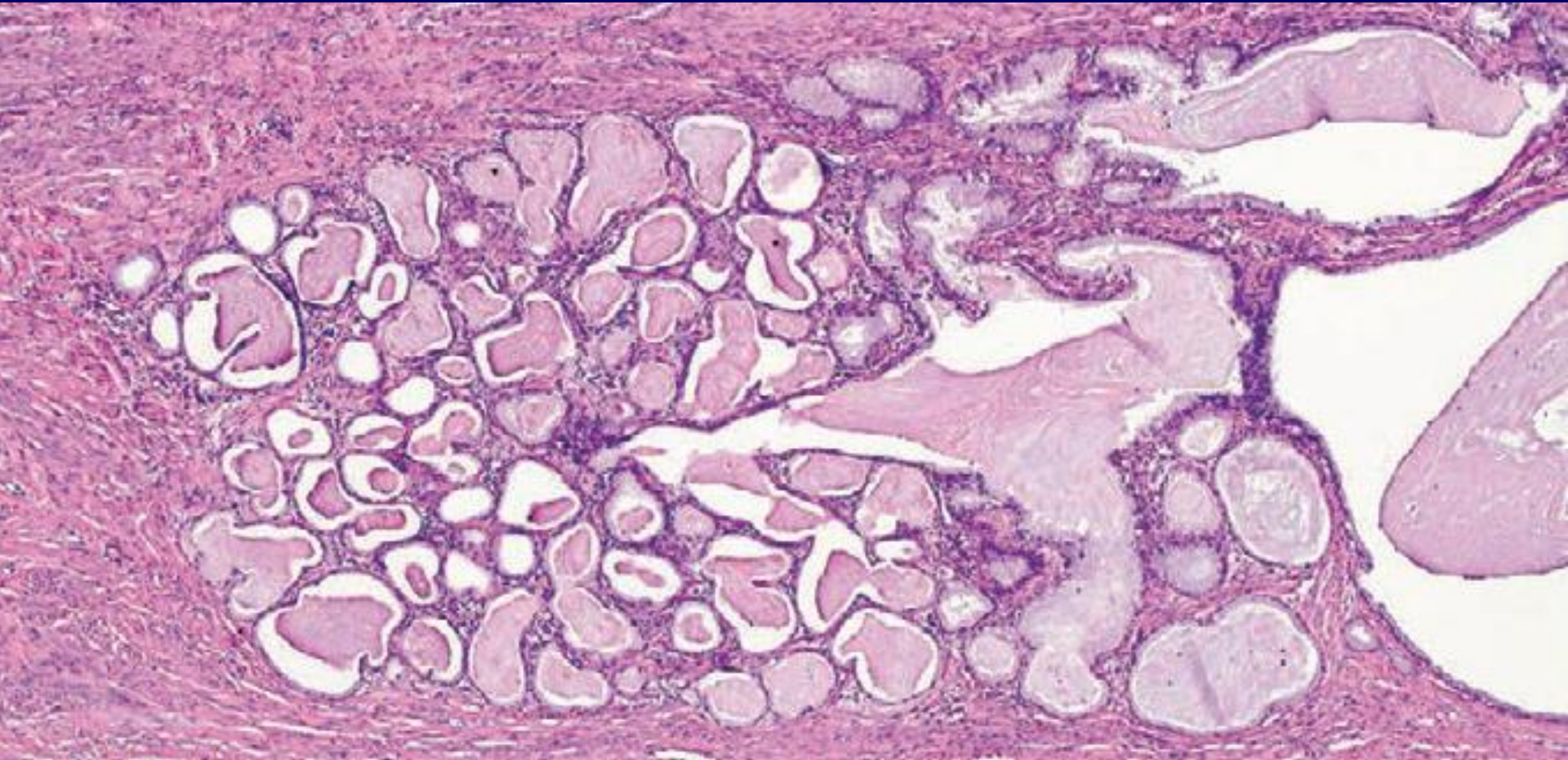
Lobular Endocervical HP

- Thought to be a precursor lesion to gastric type mucinous endocervical carcinoma
- HPV negative – gastric cancer pathway
- In this case – interface of benign and neoplastic
- Marked cytologic atypia, apoptosis, architectural complexity

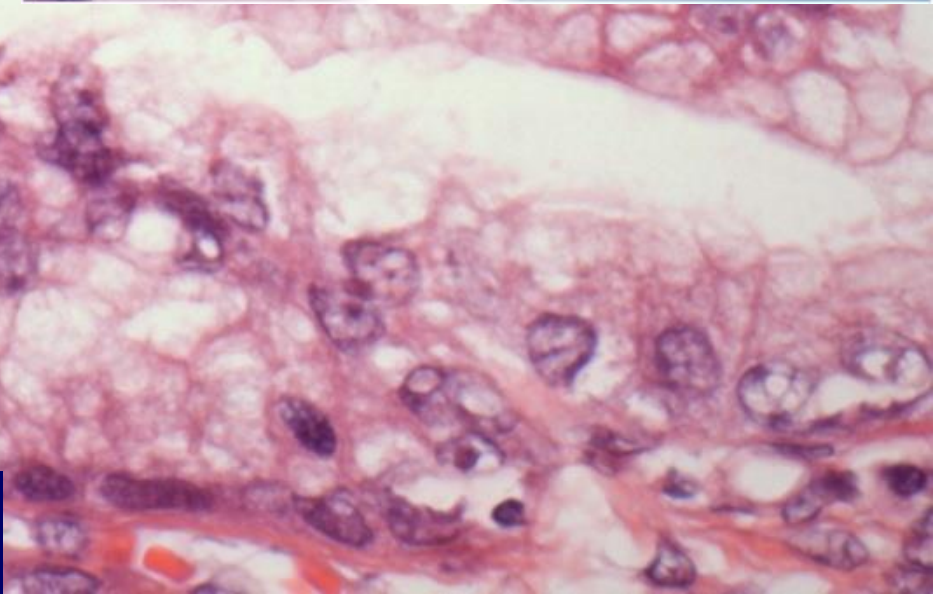
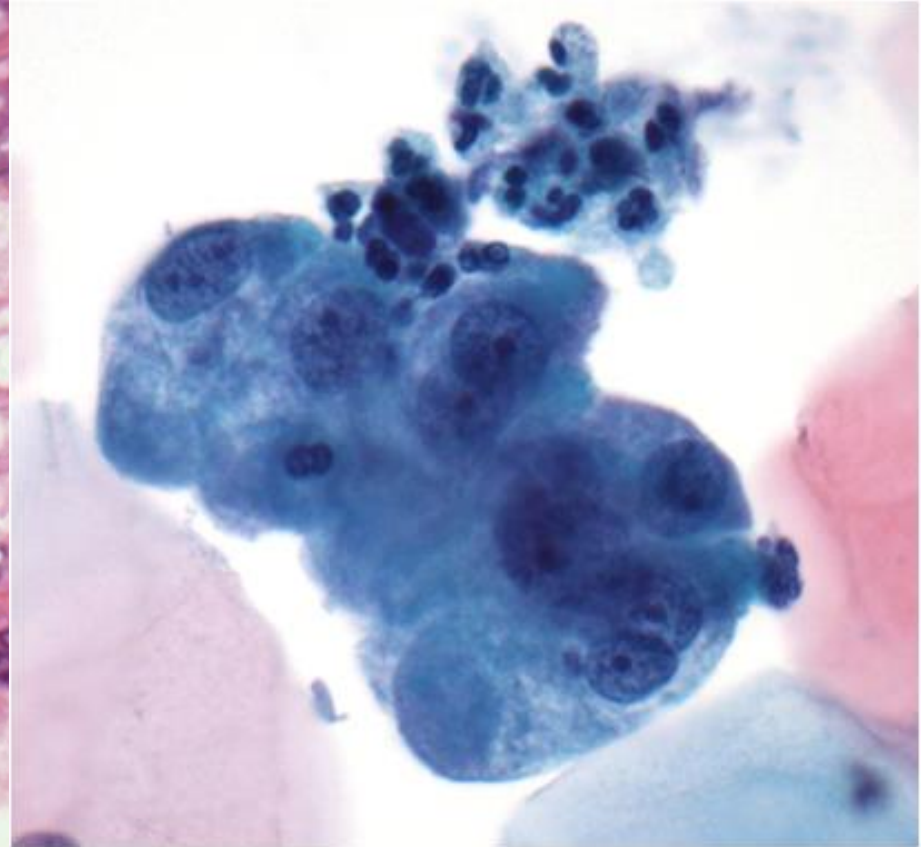
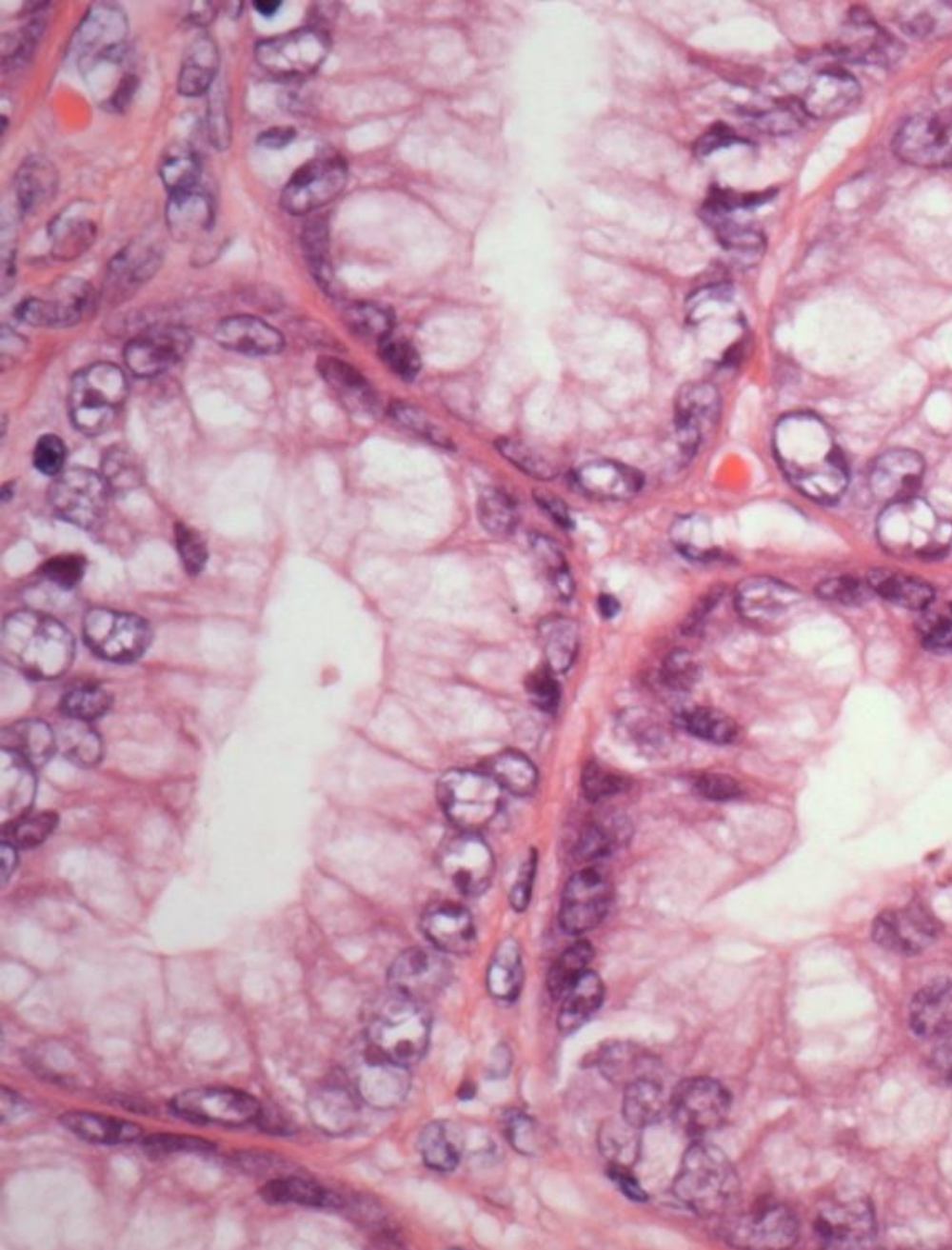


Lobular hyperplasia

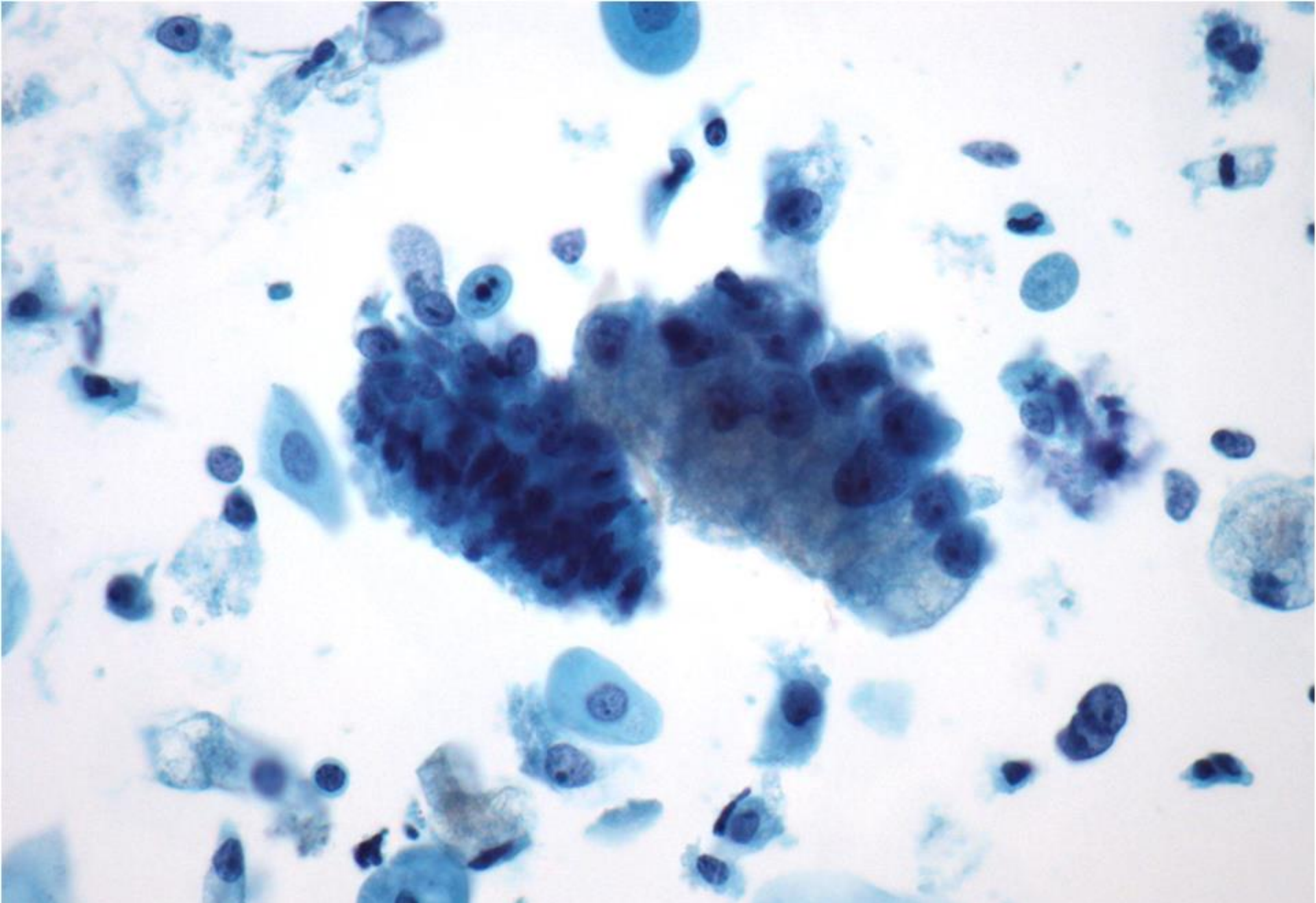
Diffuse Lamellar Hyperplasia



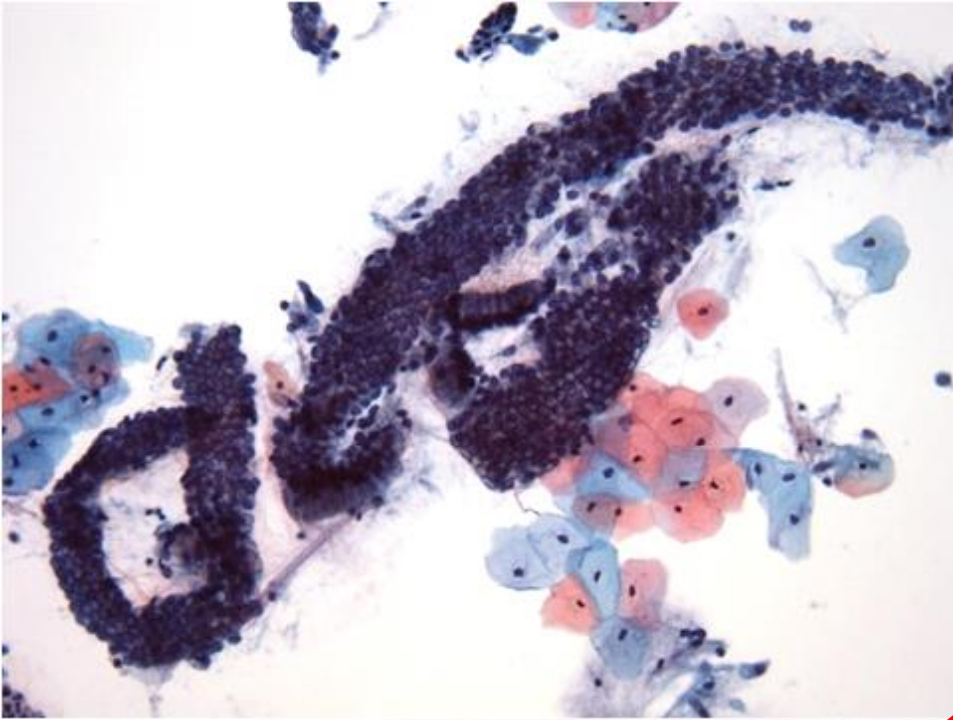
Tunnel Clusters



Mucinous Adenocarcinoma

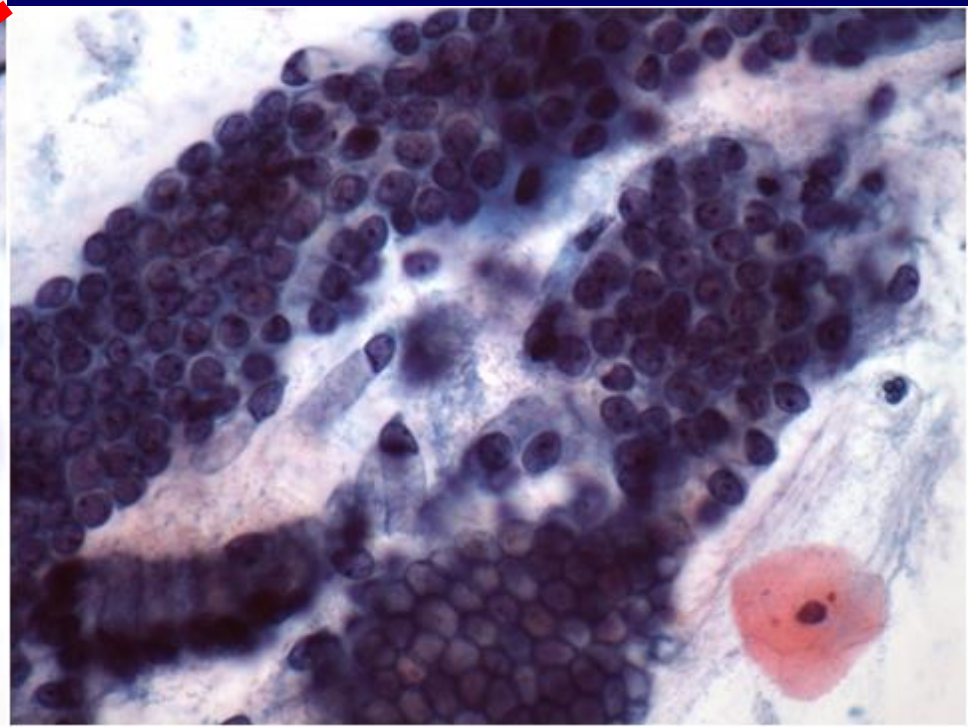


Mucinous Adenocarcinoma - LBP



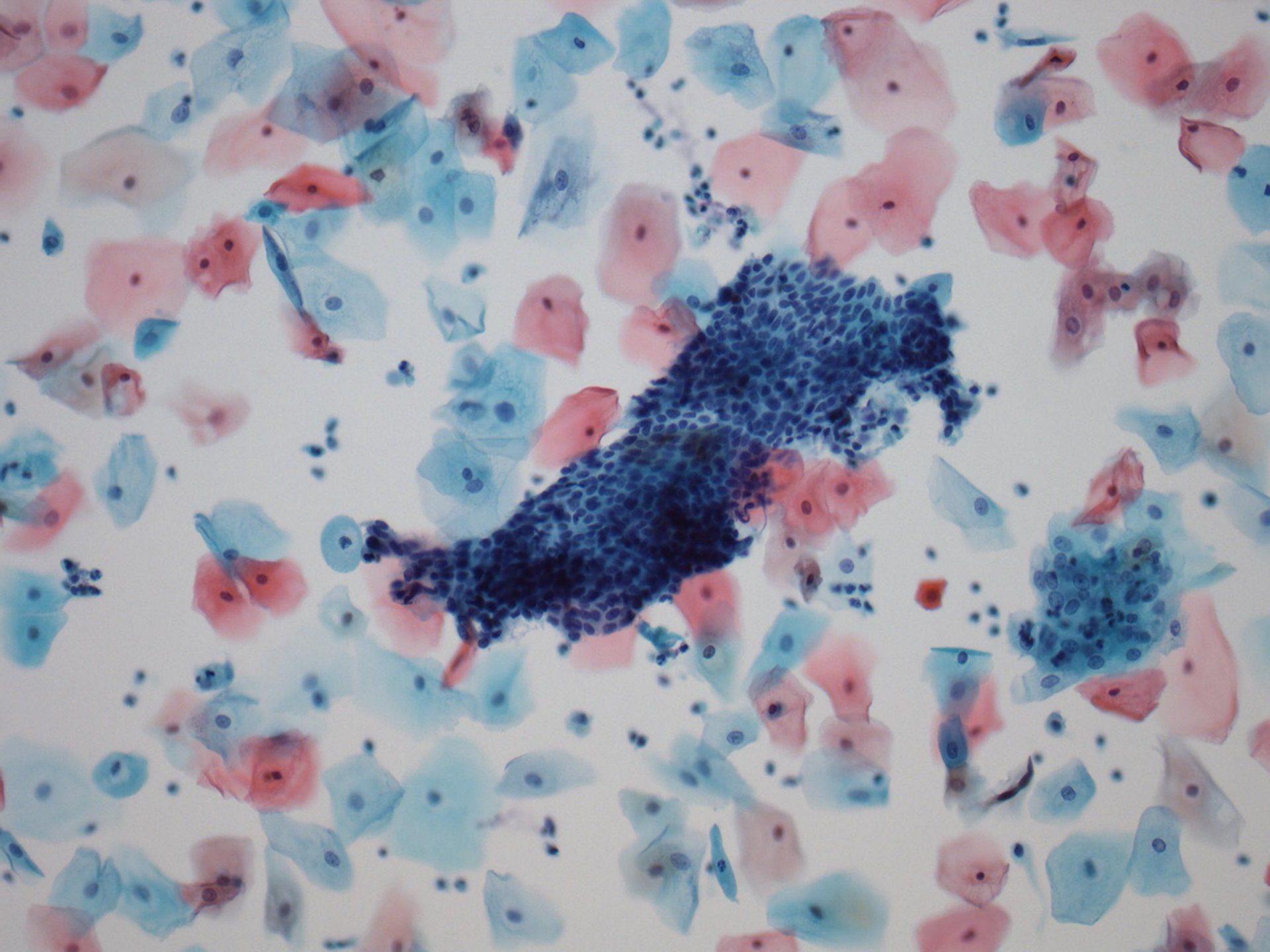
Adenoma Malignum
“too many EC cells”

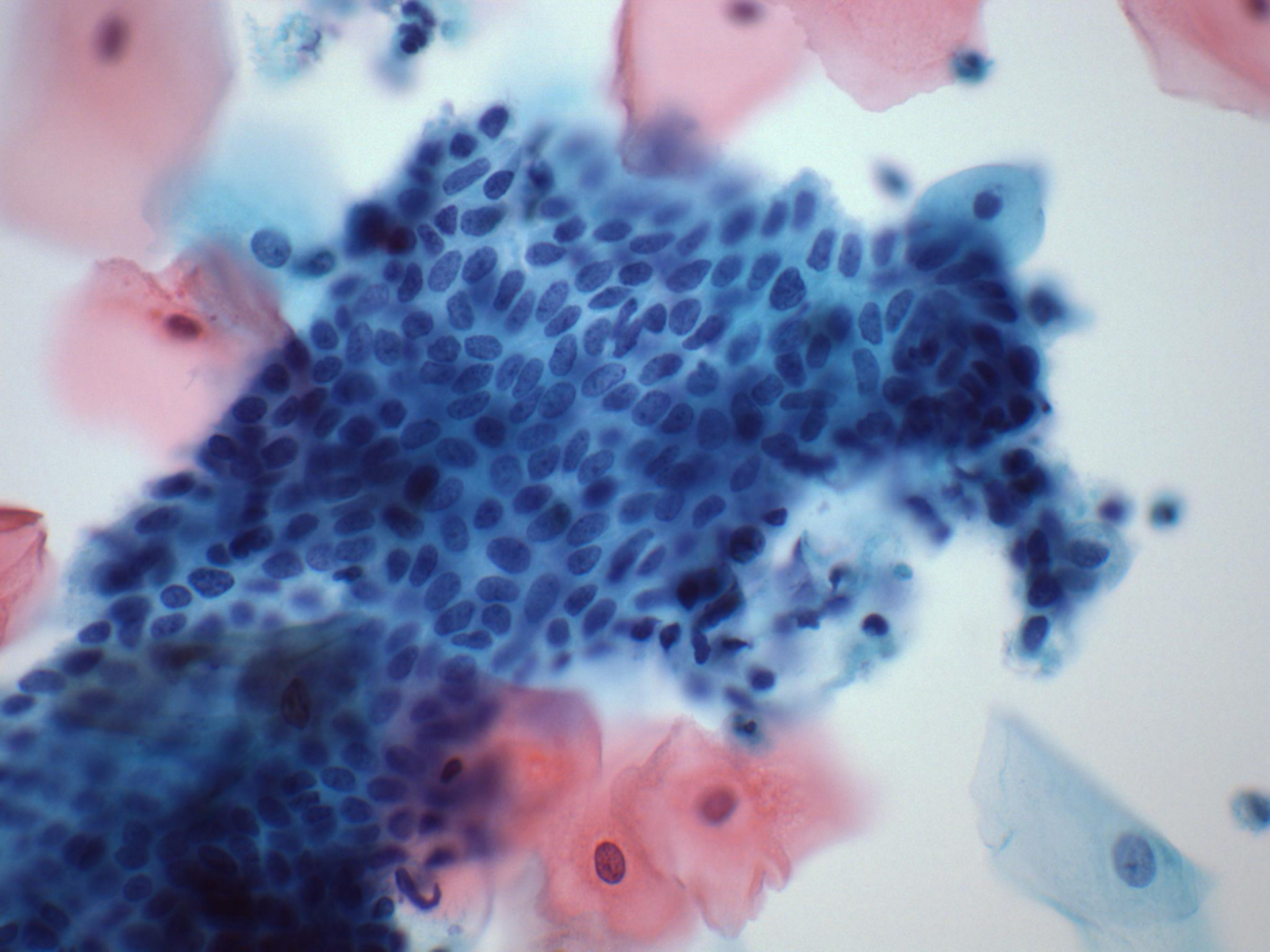
Note mucous caps in
different focal plane

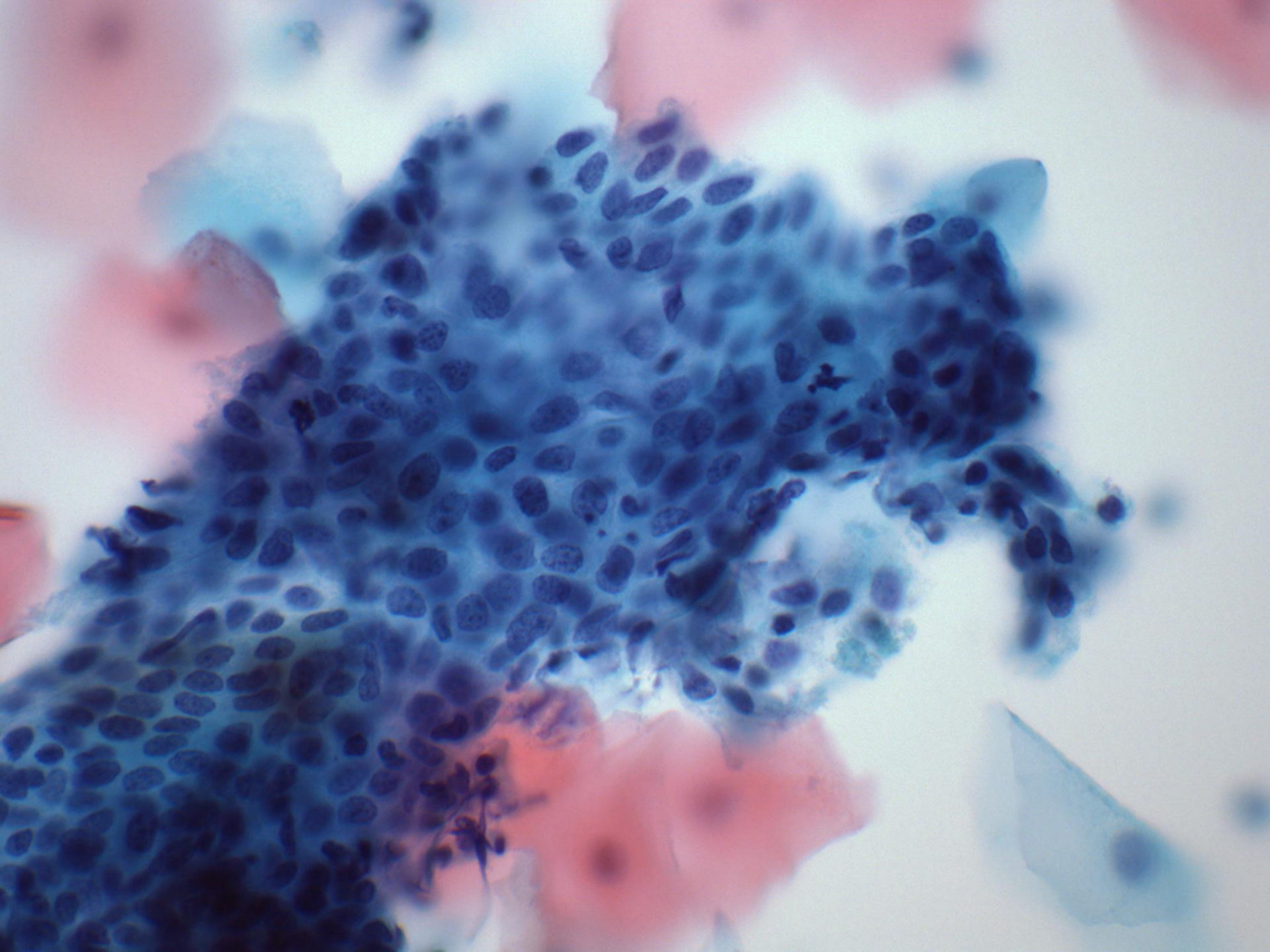


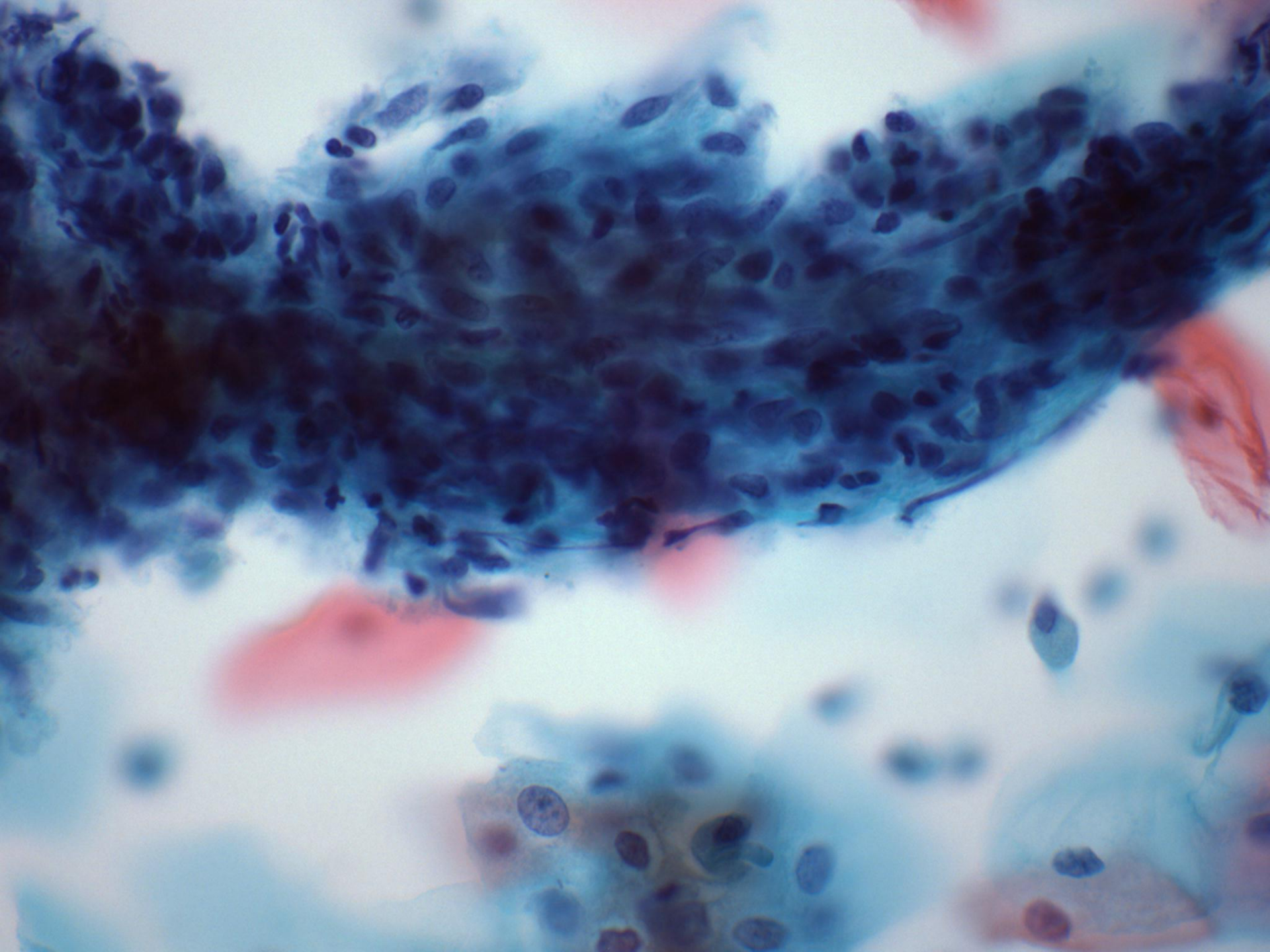
Case 8

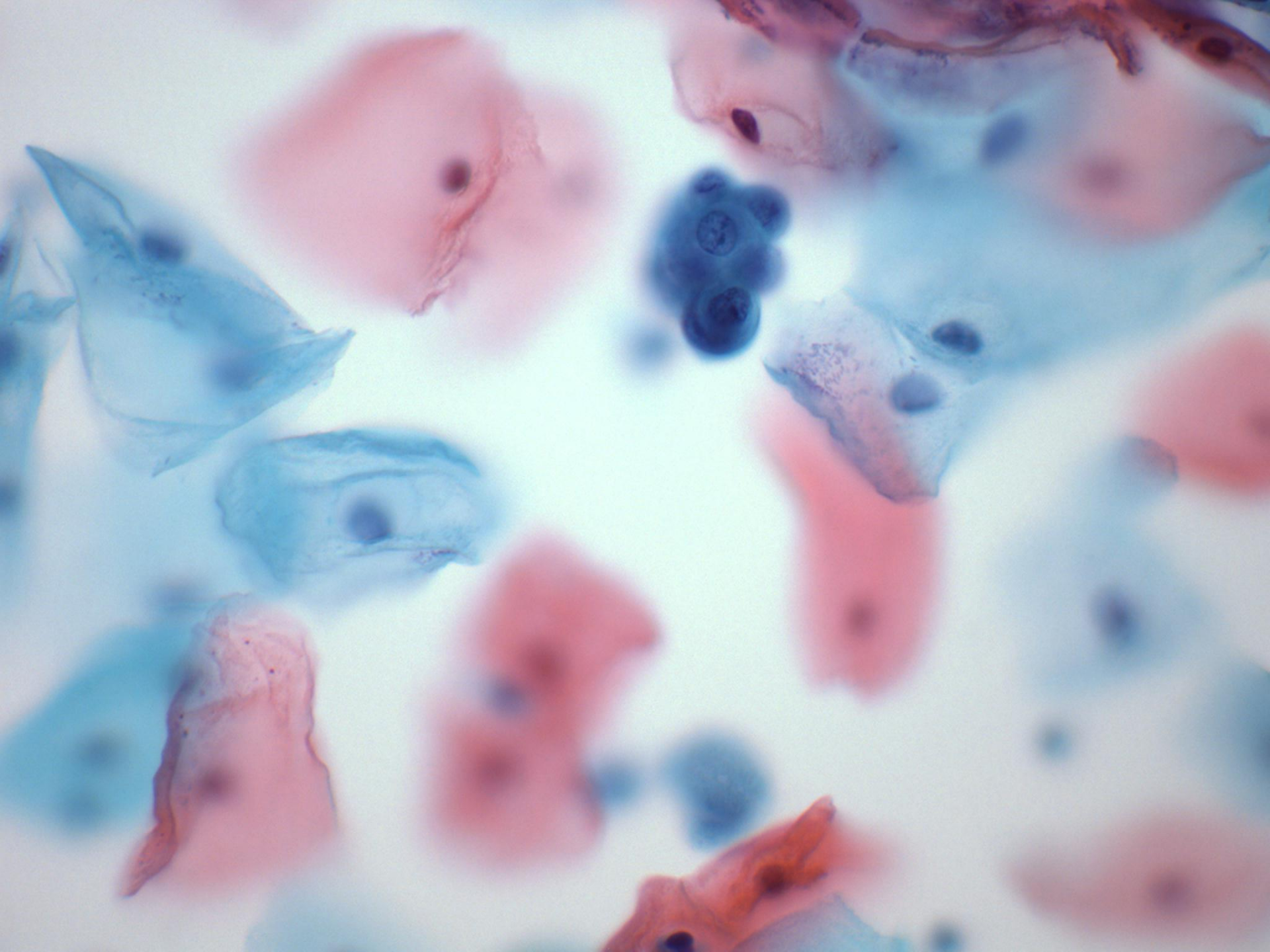
49 year old woman
Routine screening Pap test

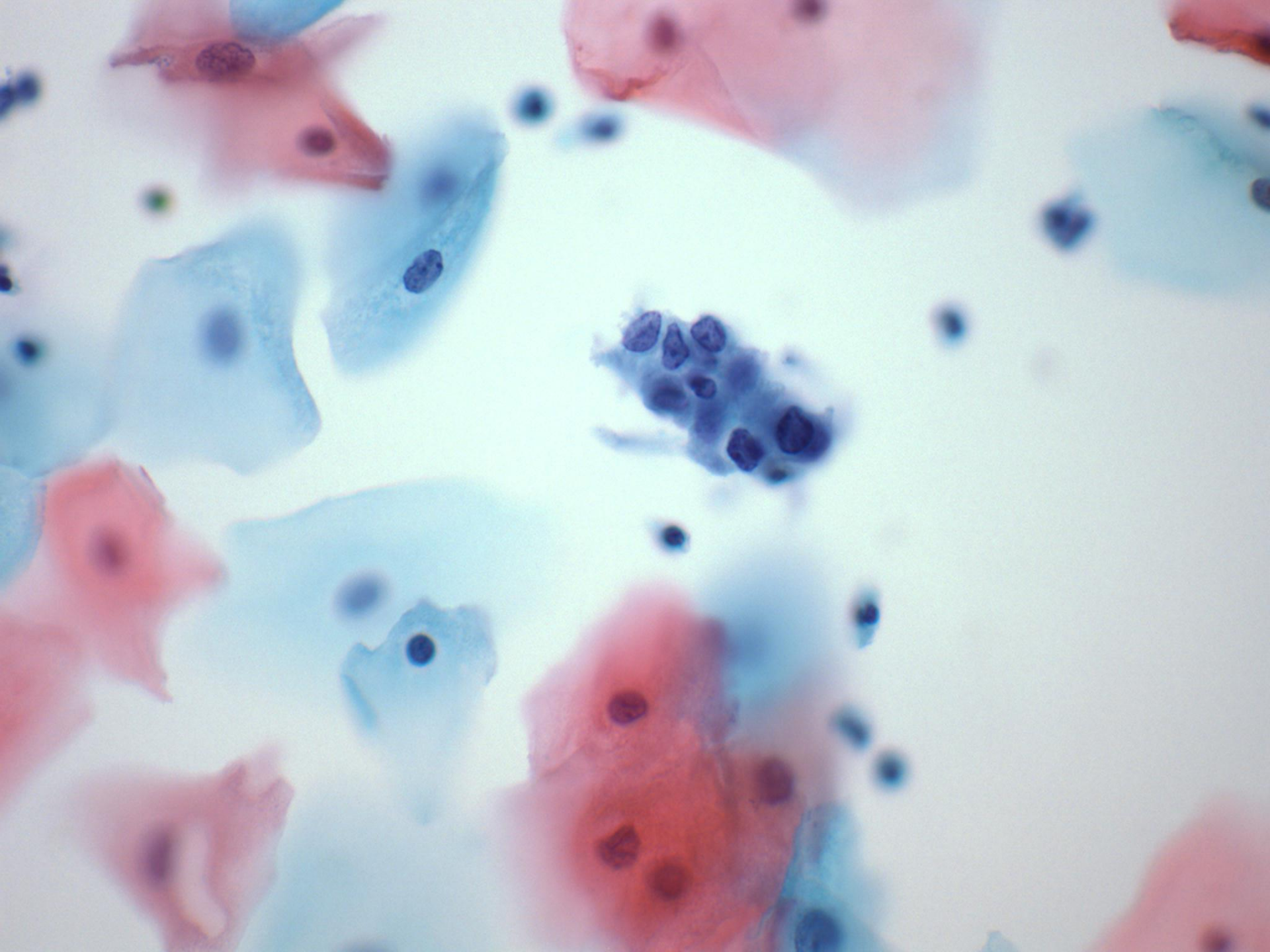


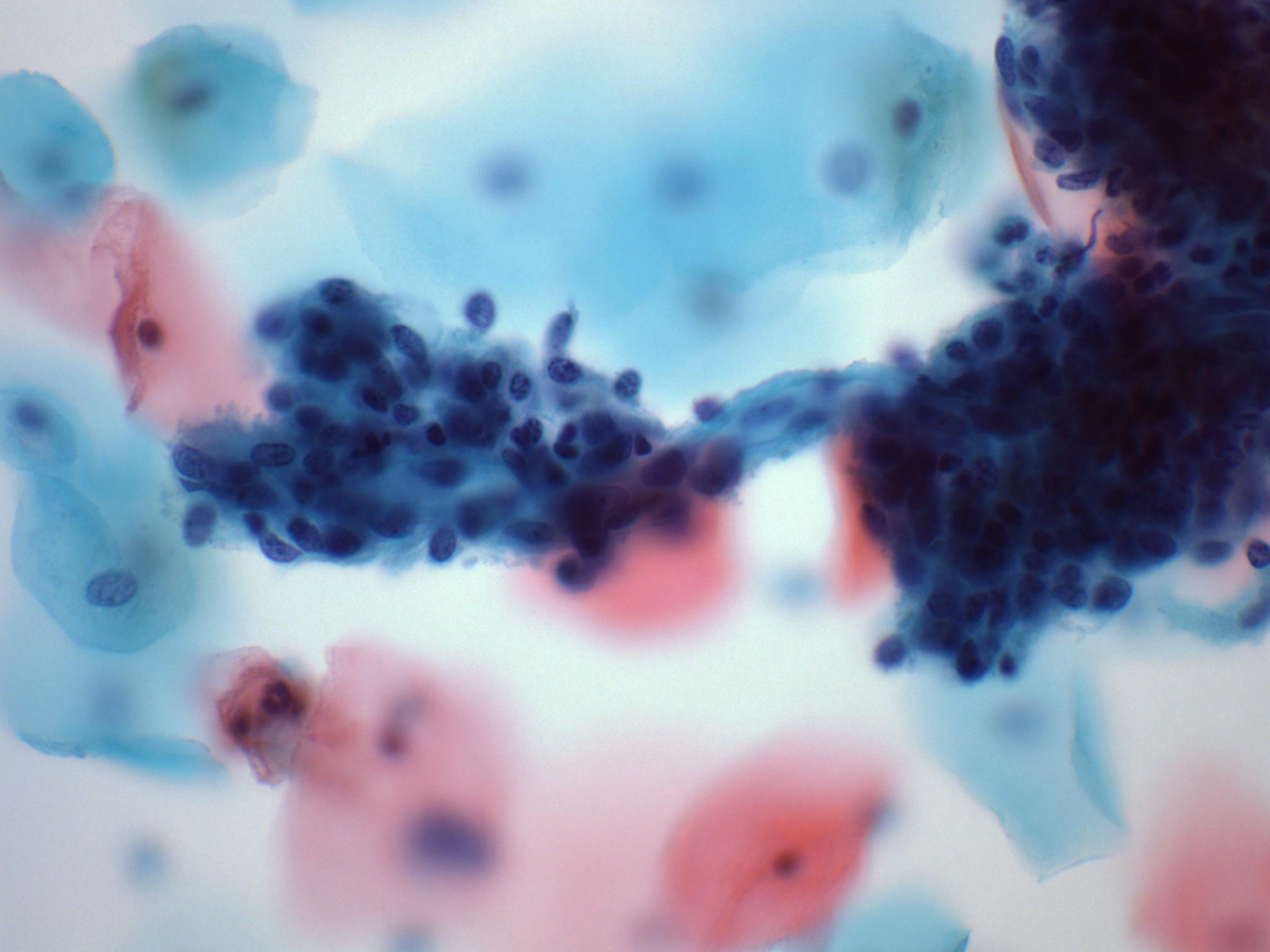


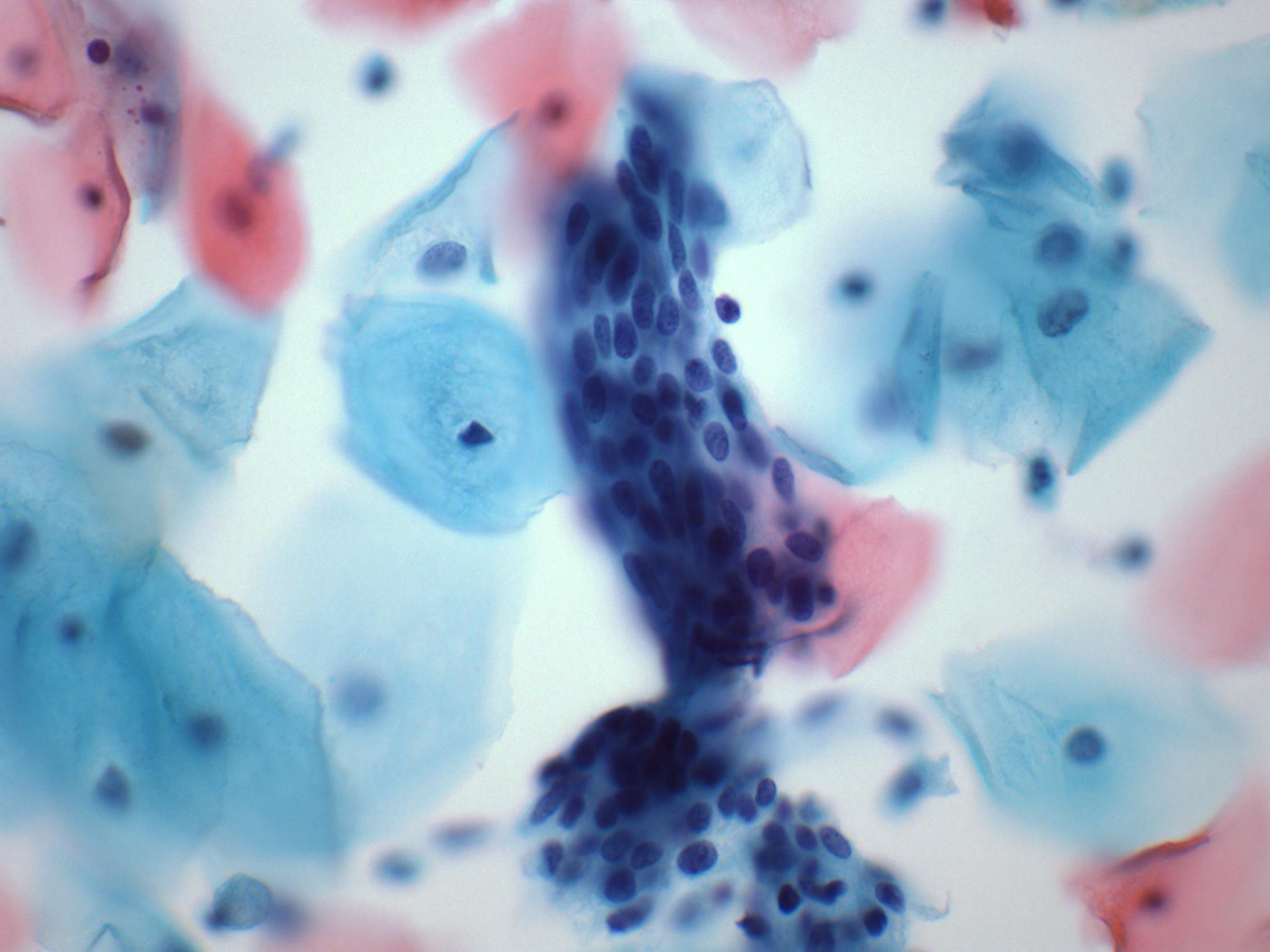


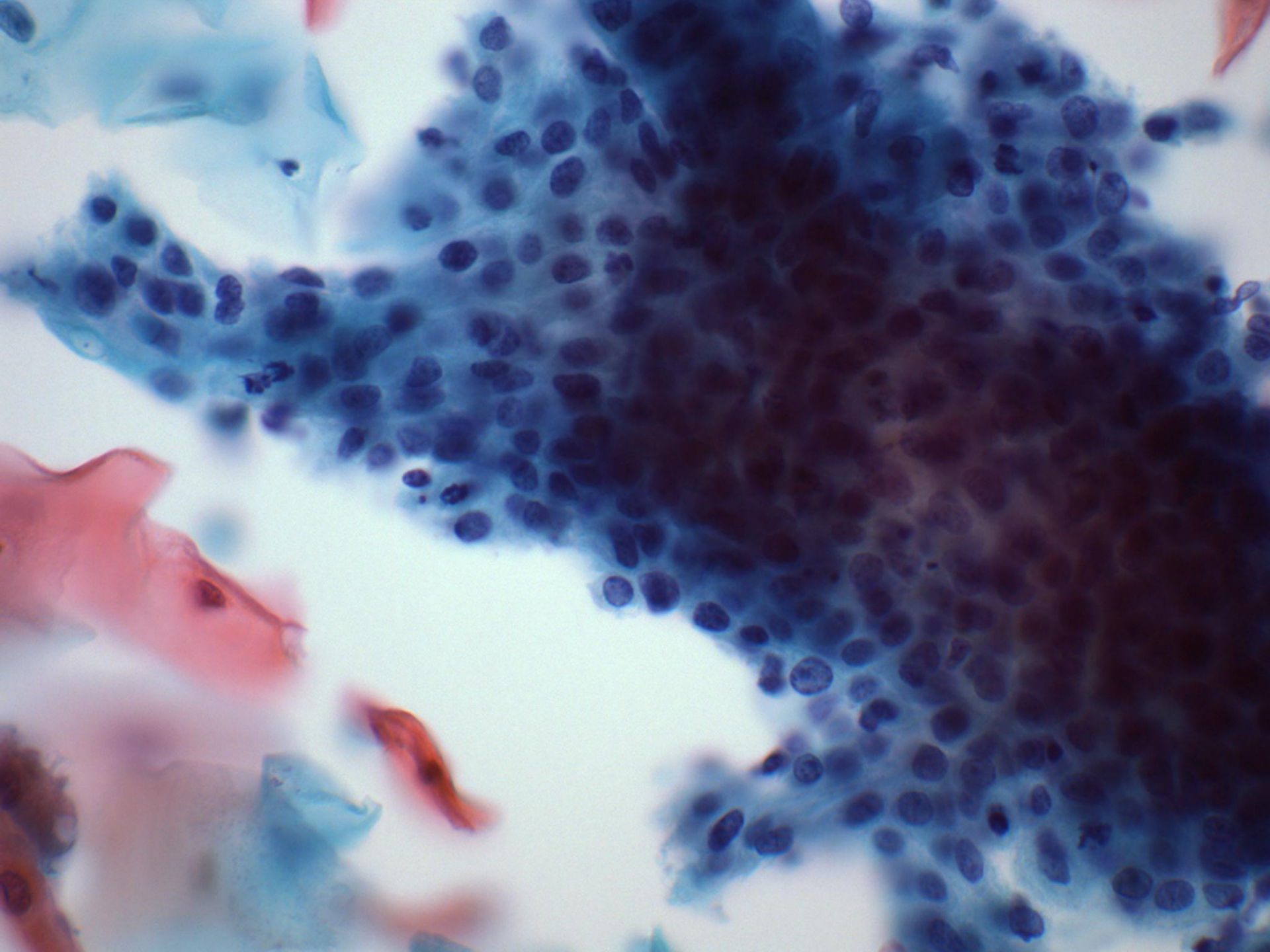


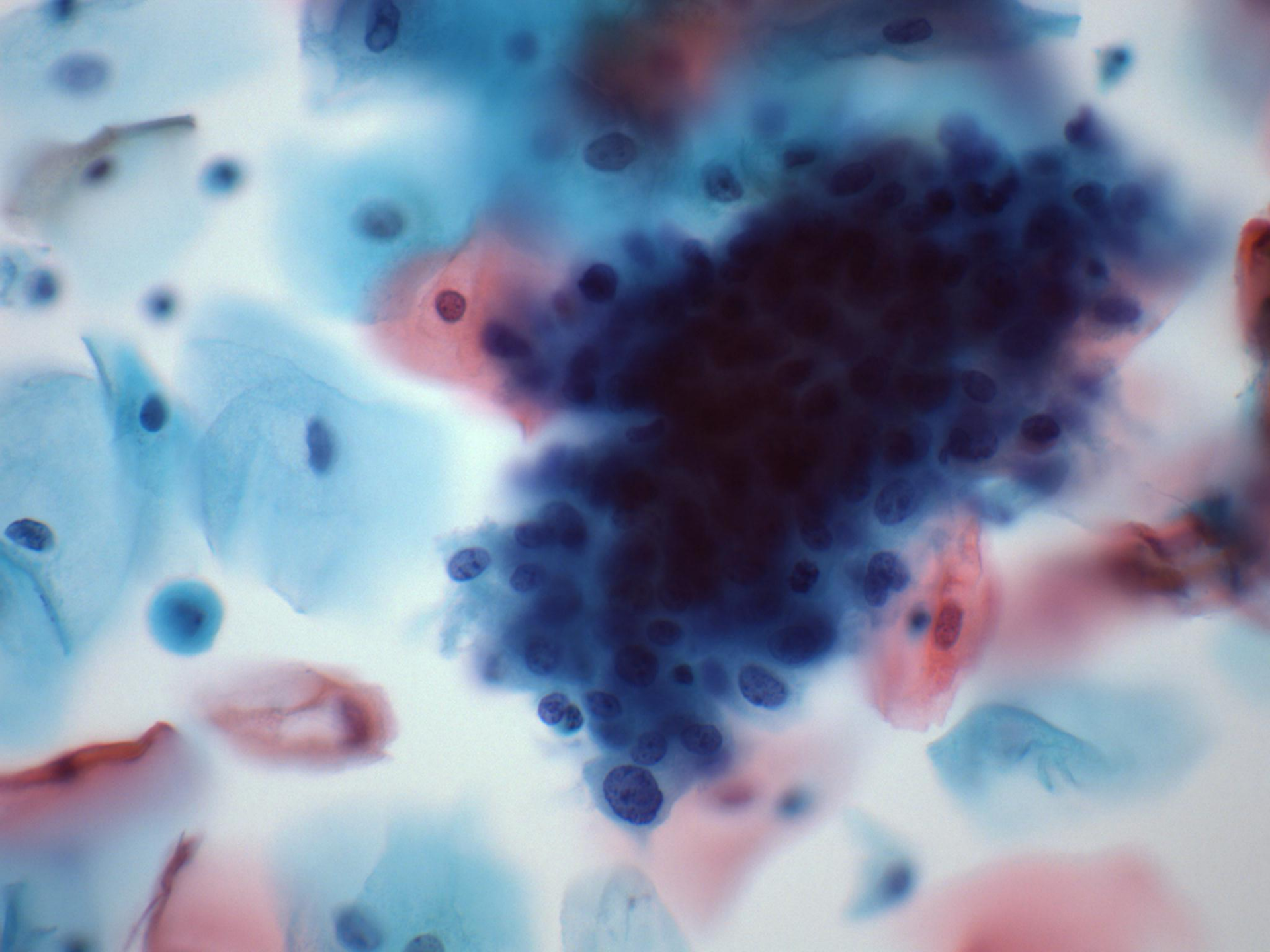


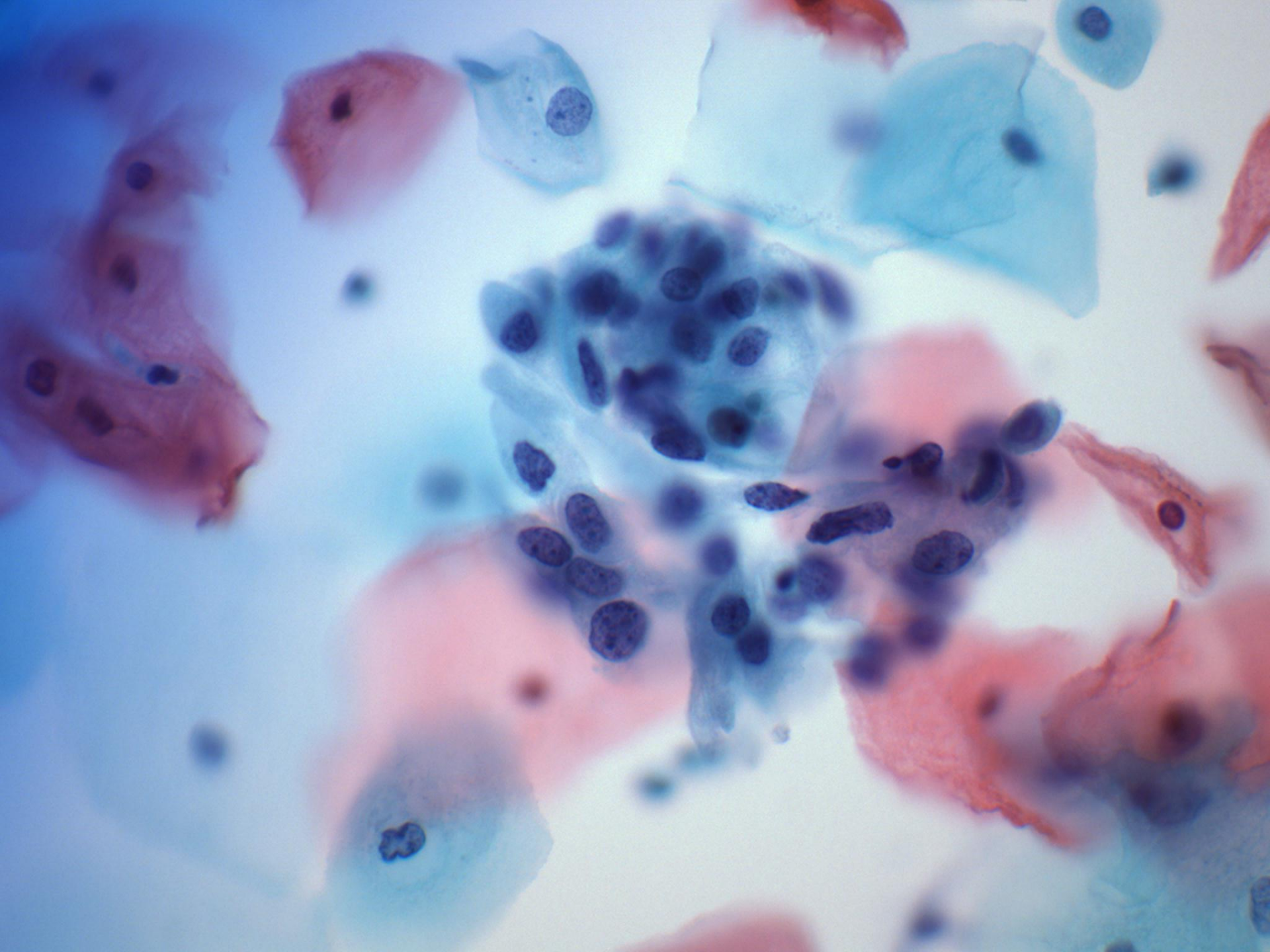


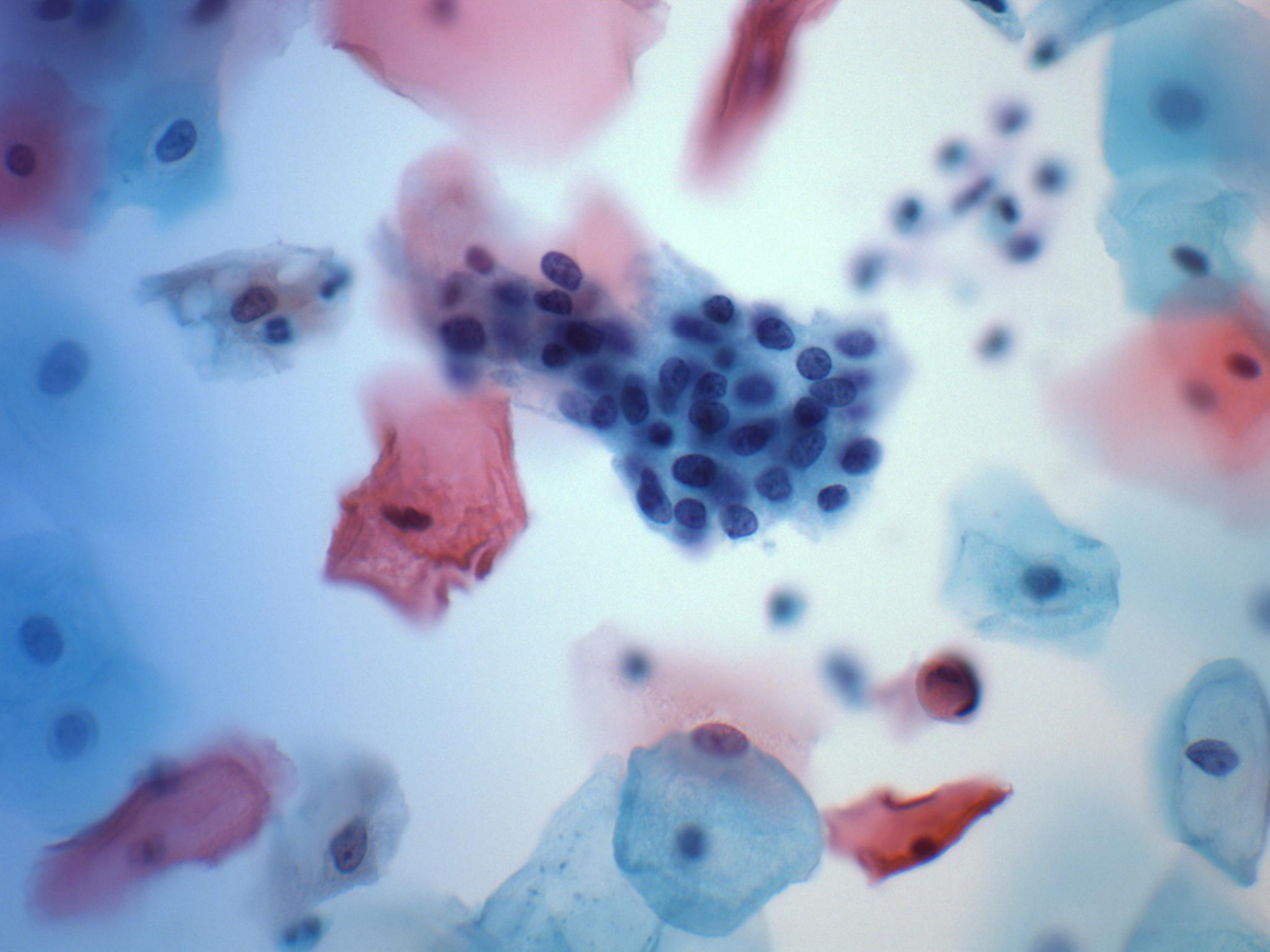












Summary of Key Cytologic Features

- Small tightly packed 2-d groups of cells
 - Vague “honey-combed” appearance
- Small isolated cells with mod to high N:C
- Prominent spindle cell component
- Cytoplasm spindles from group margins
- “Taffypull” cytoplasm
- Marked shape and size pleomorphism
- Hyperchromatic but “bland” chromatin
- Frequent mitoses, apoptotic debris

Benign

Malignant

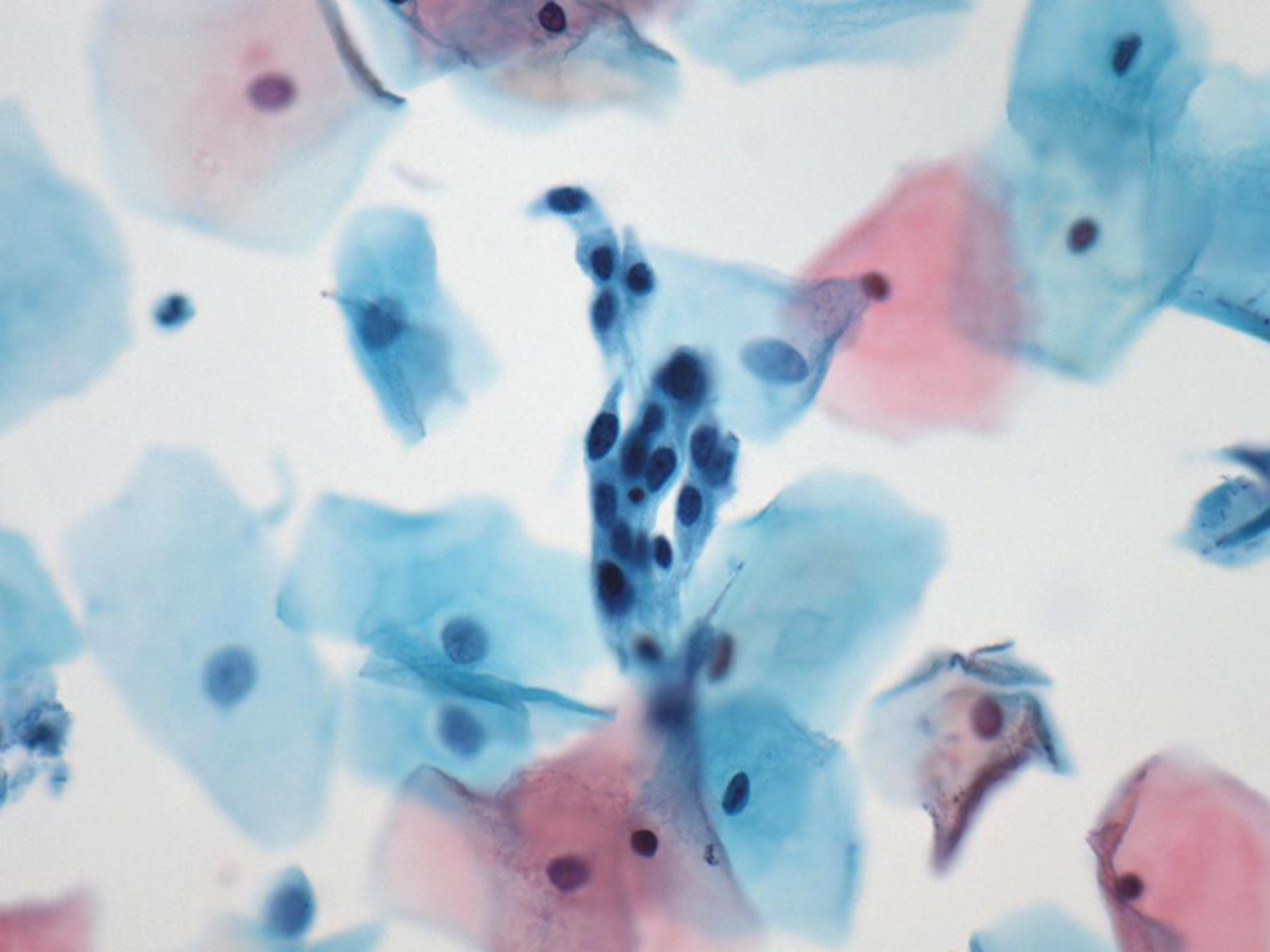
Atypical

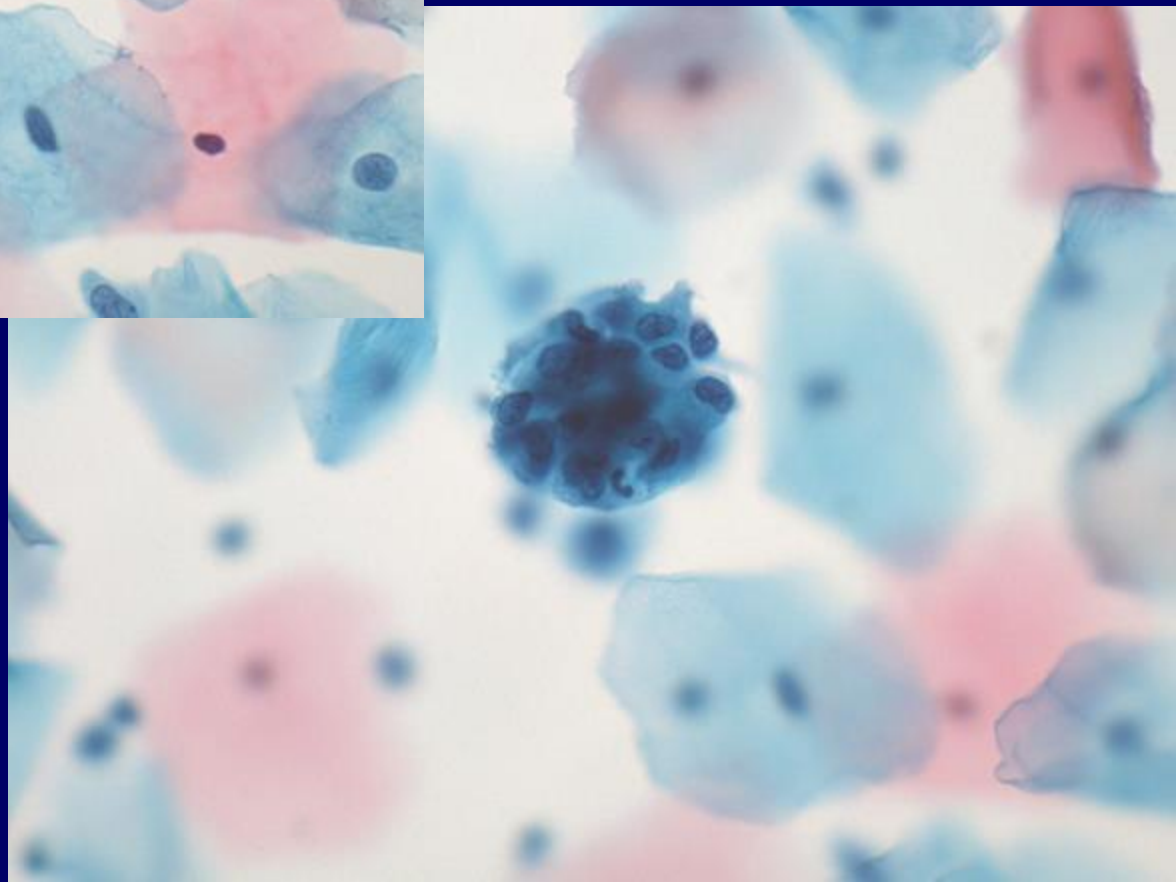
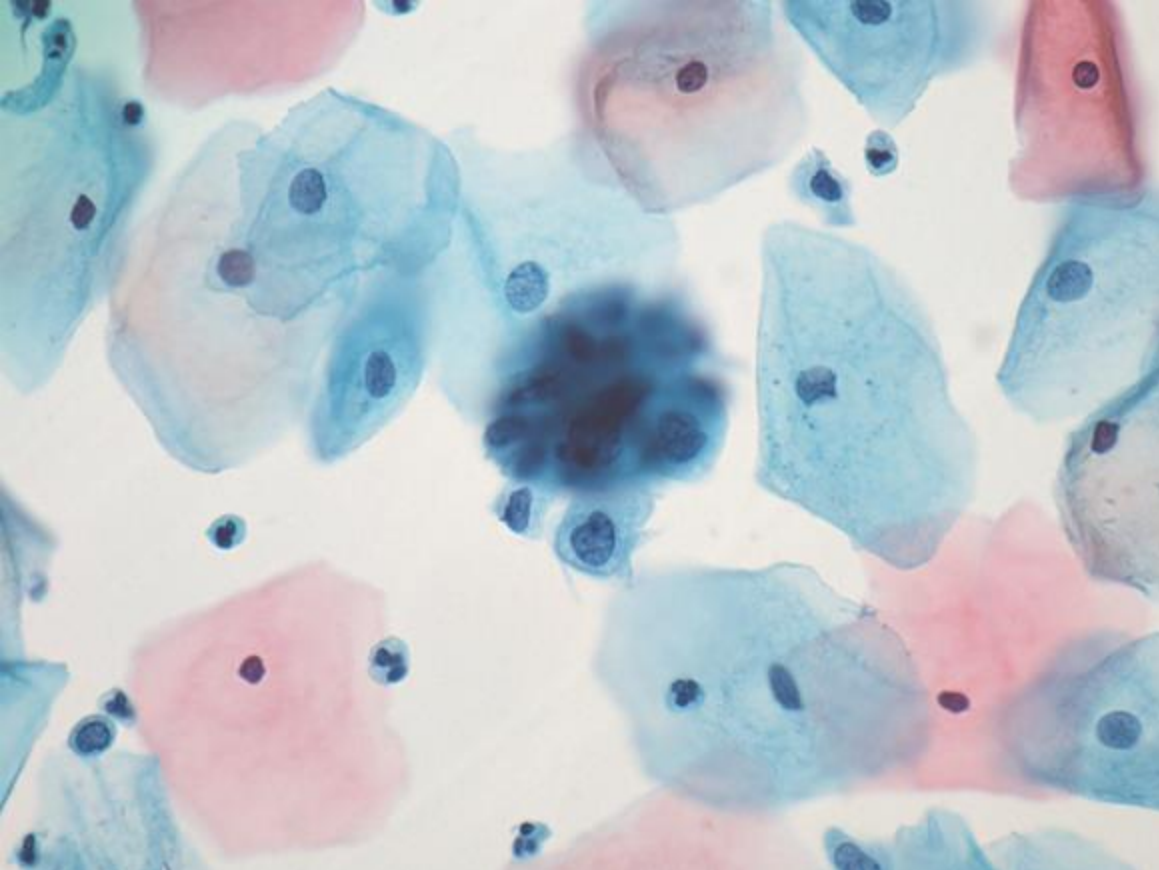
Patterns of HSIL/CA

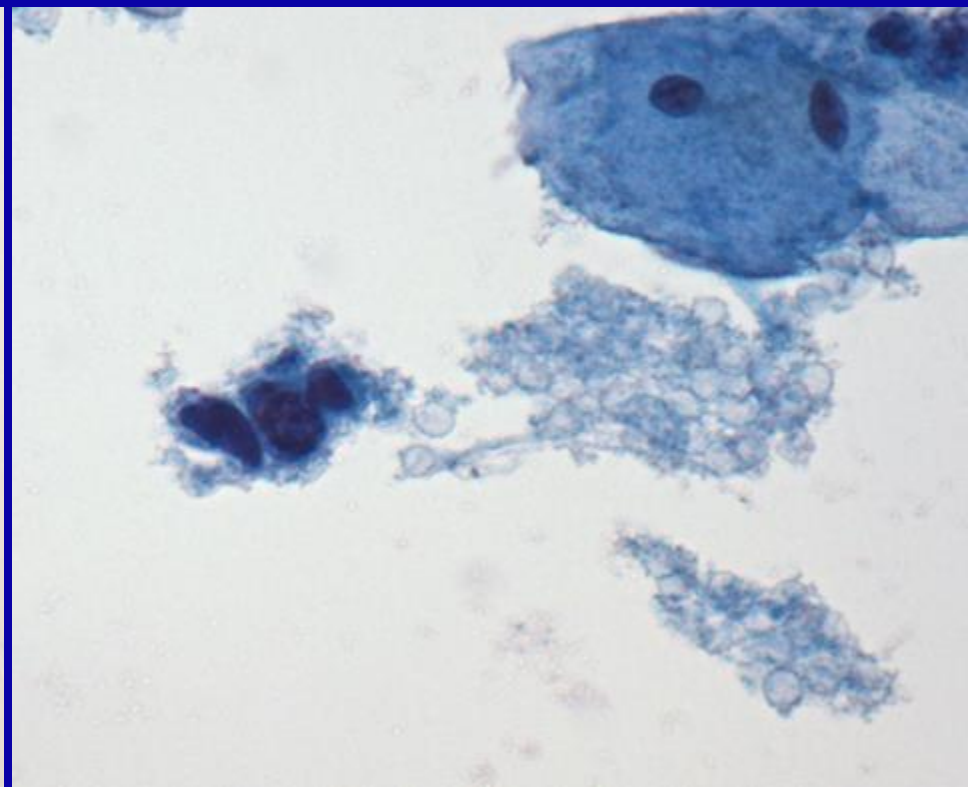
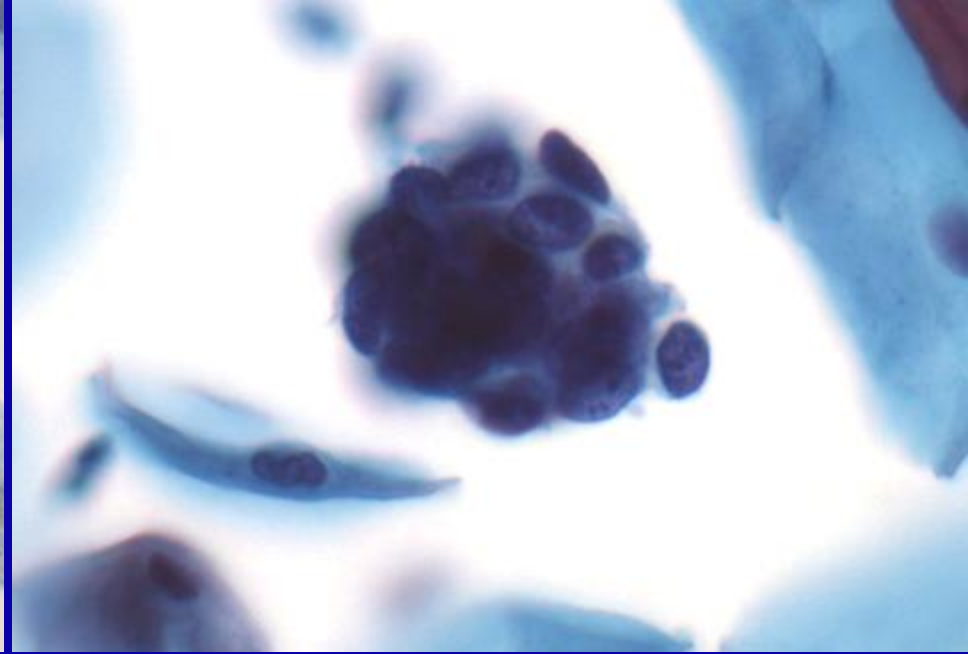
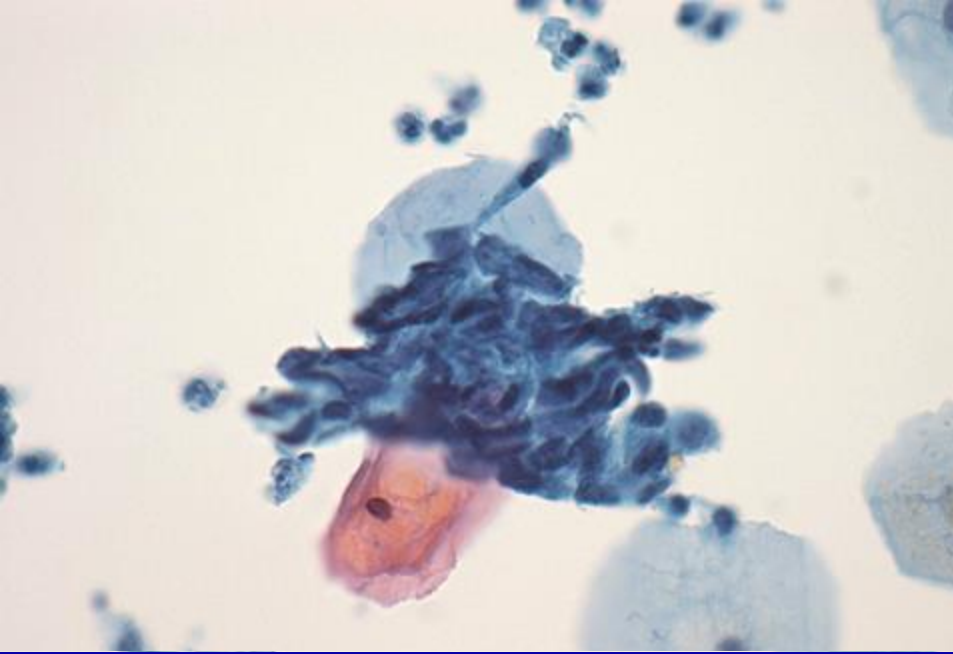
- Classic – single cell, syncytia
- Involving glands
- In atrophy
- Stripped nucleus
- **EM stroma-like/repair-like**
- Hypochromatic
- Keratinizing

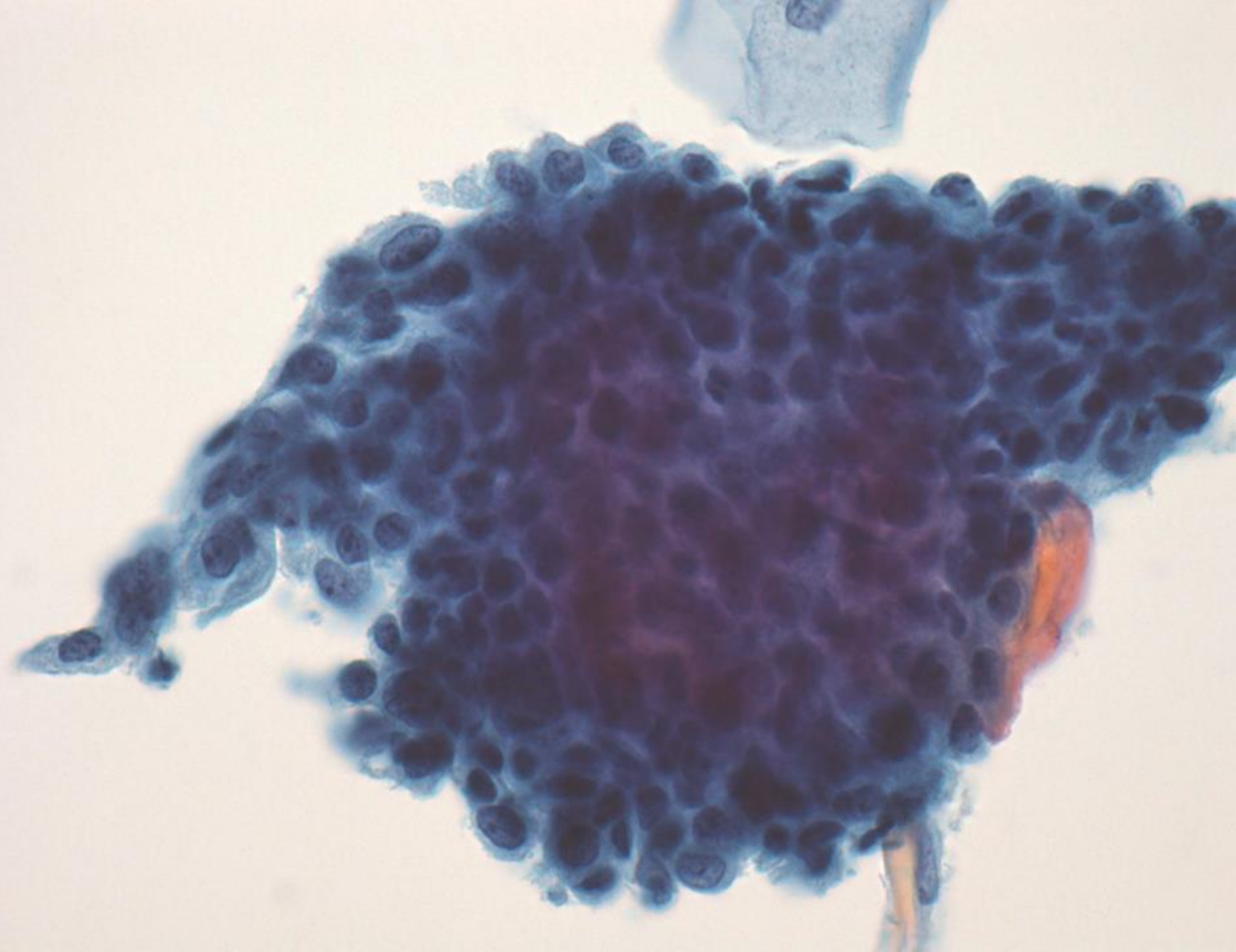
HSIL -- EM-stroma/repair-like

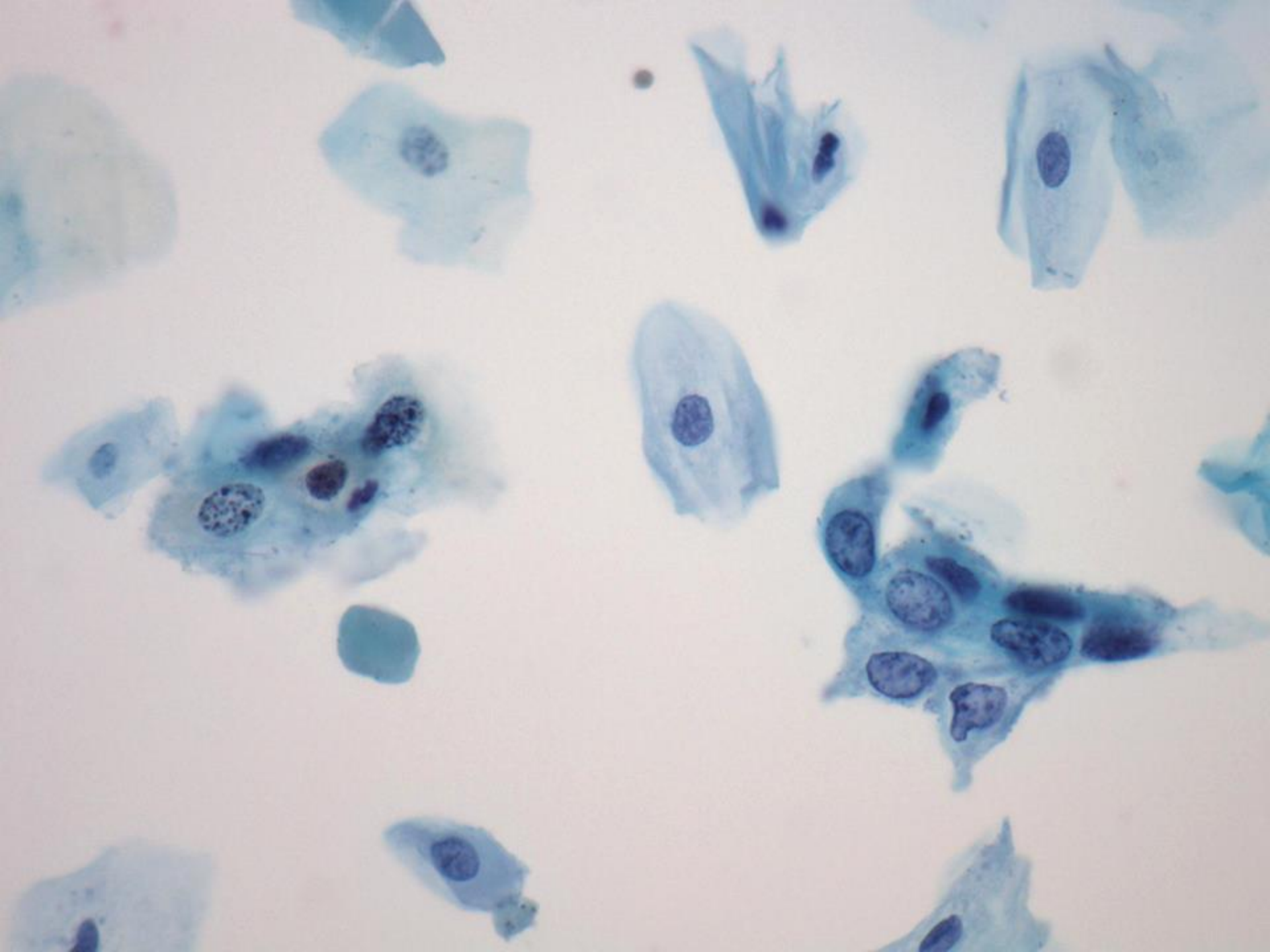
- Bloody background simulating menses
- Small tightly packed groups of cells
- Small isolated cells with high N:C
- Prominent spindle cell component
- Cytoplasm spindles from group margins
- “Taffypull” cytoplasm
- +/- nucleoli
- May be associated with “classic” HSIL
- Commonly missed – called menstrual endometrium







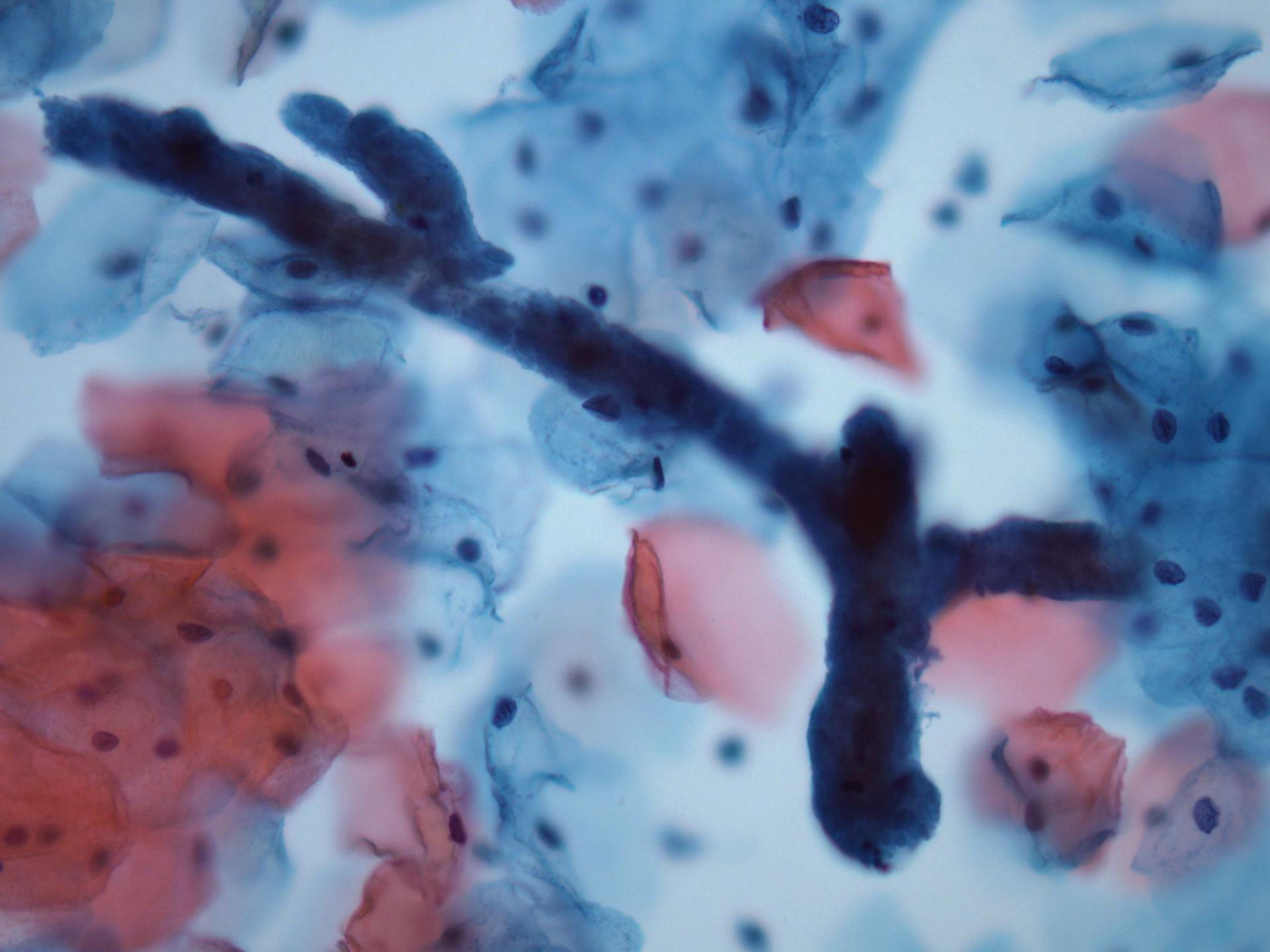


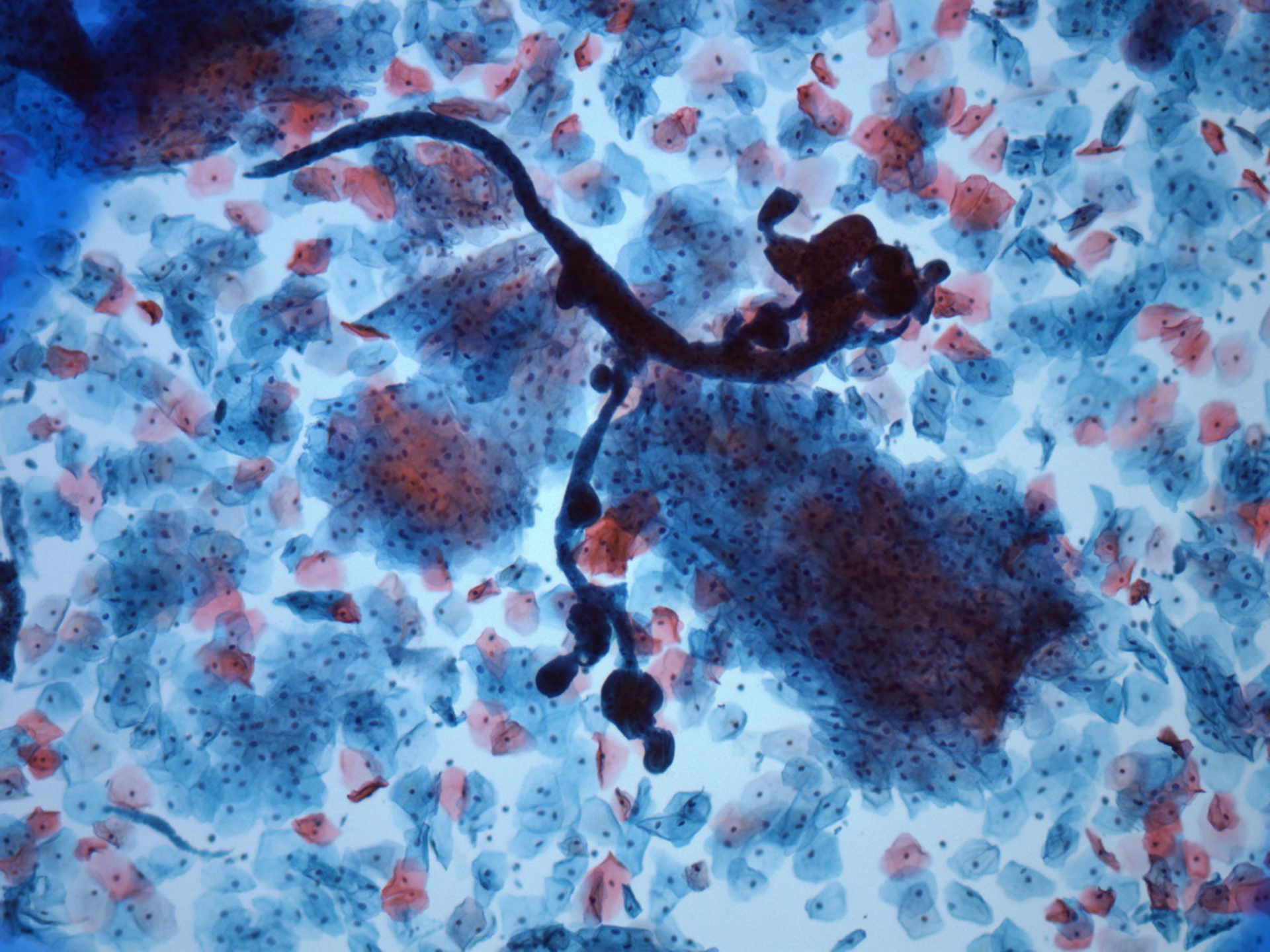


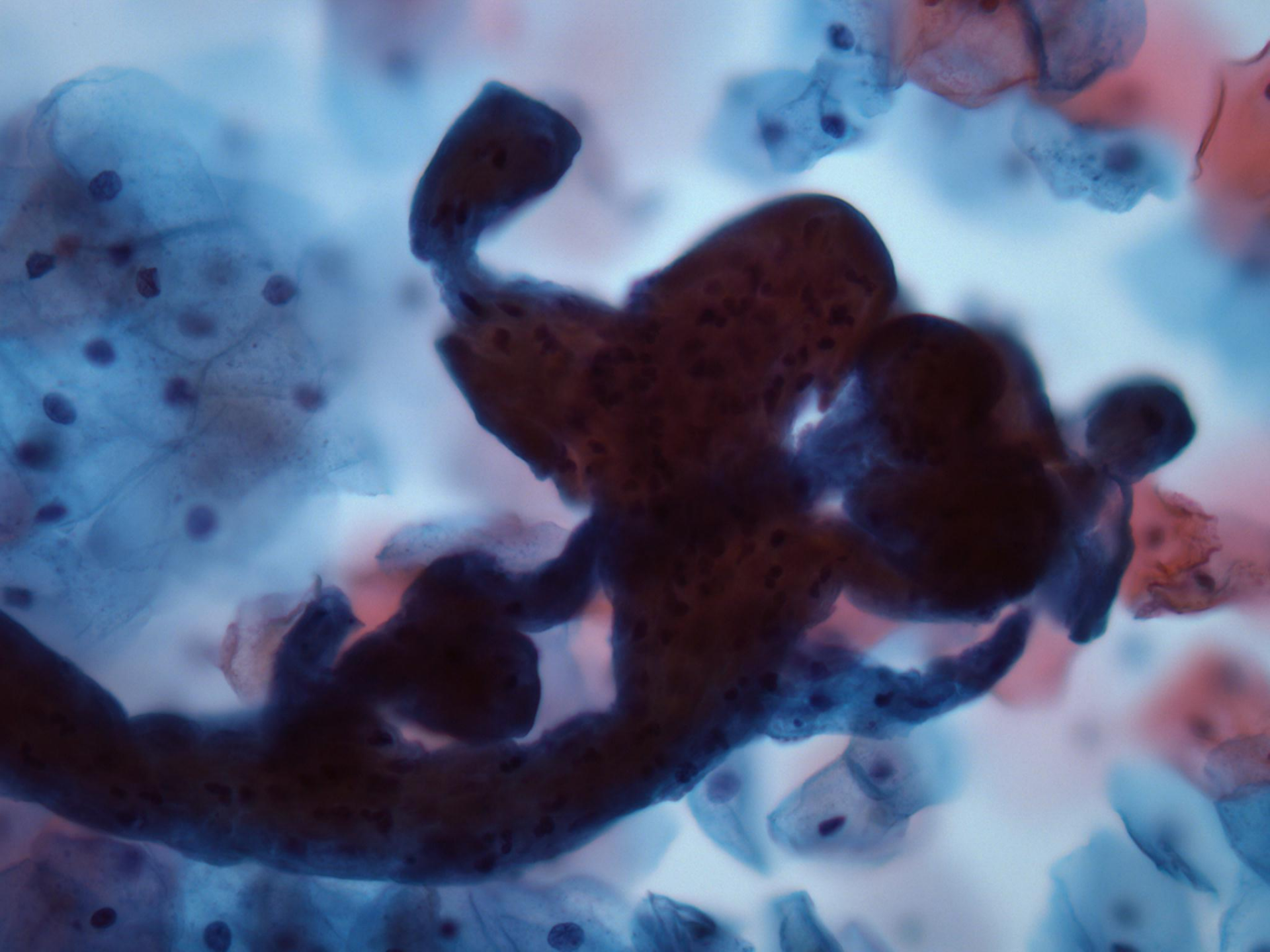
Case 9

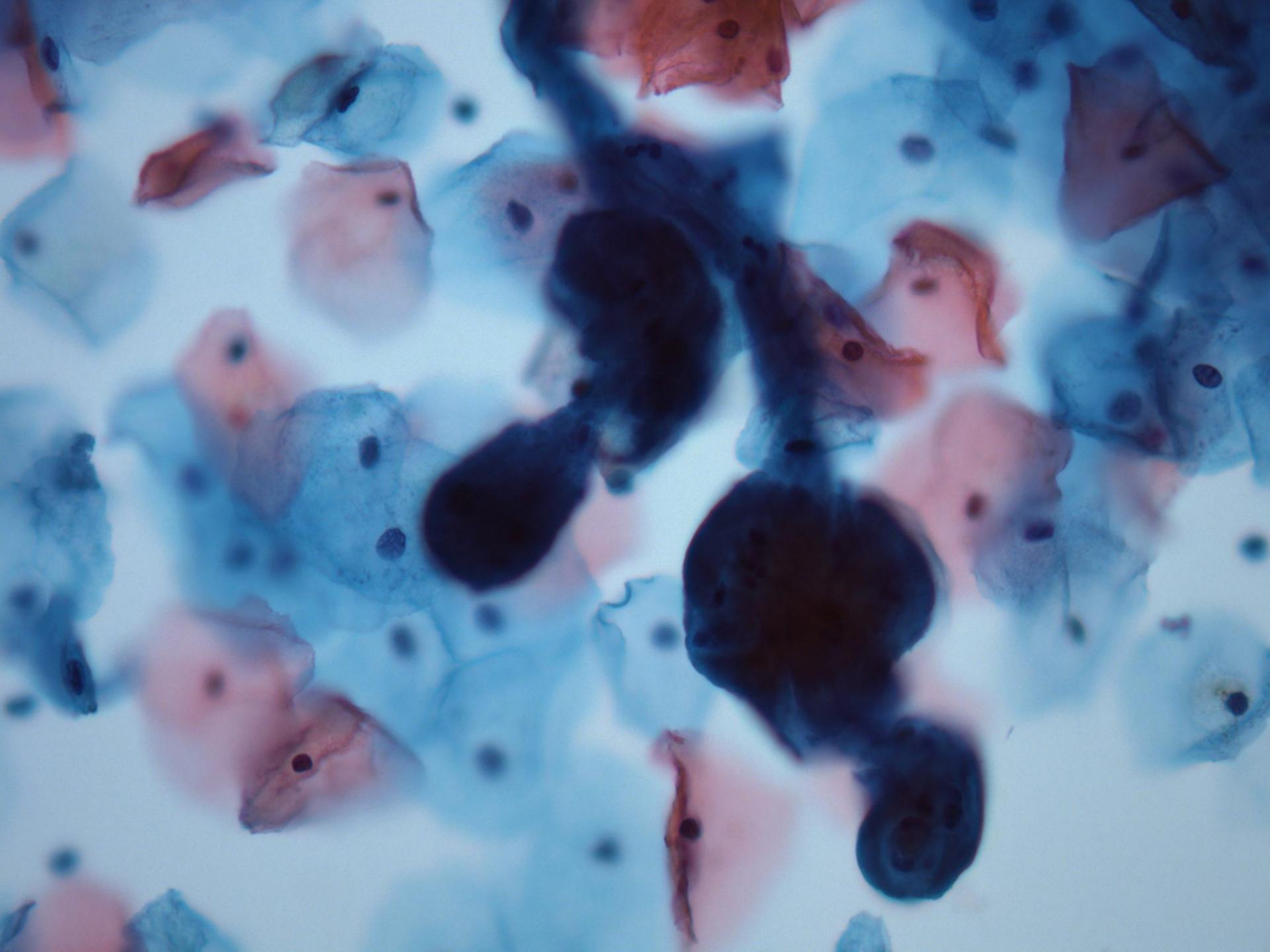
32 year old

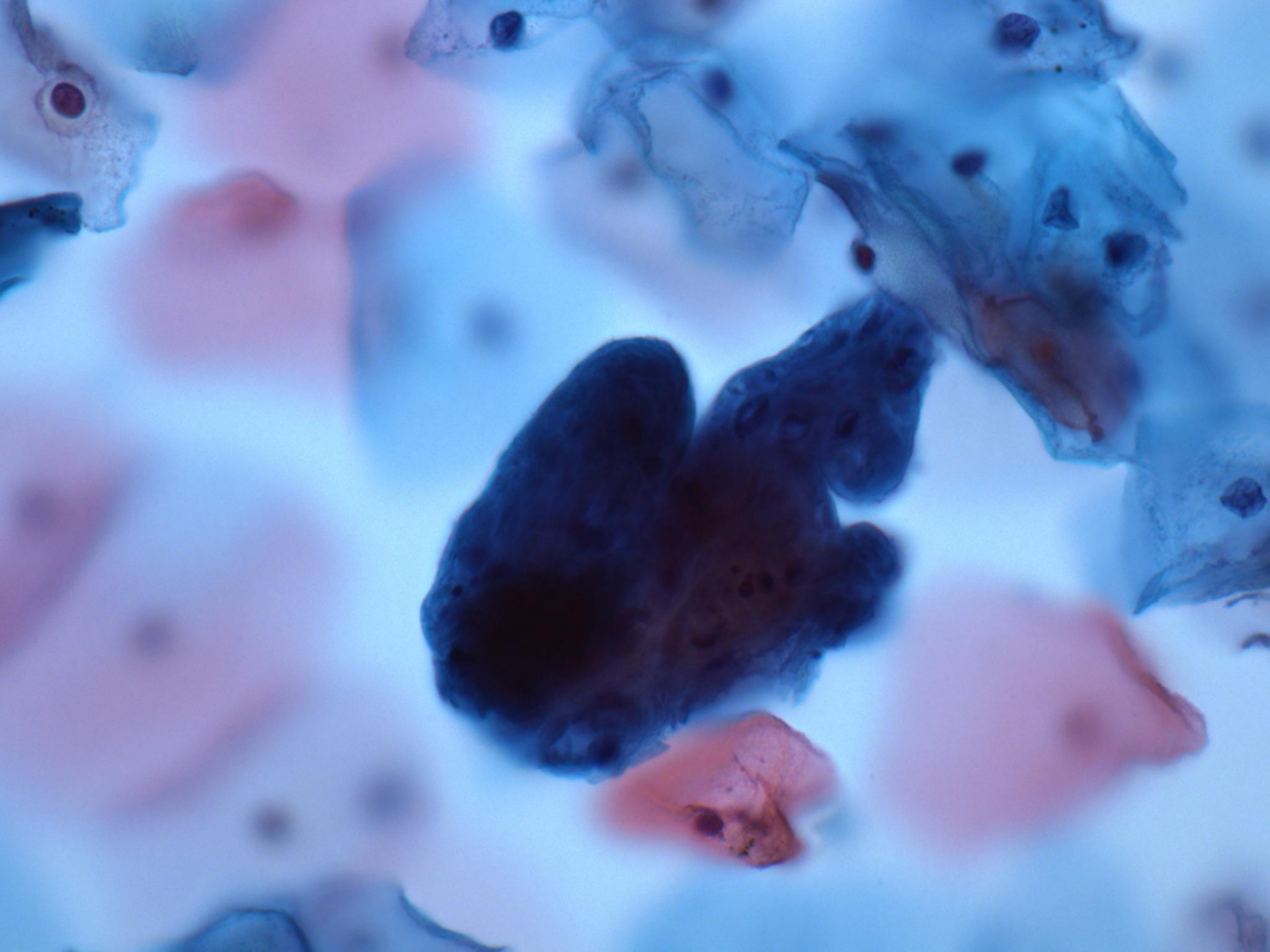
Pap test in follow up of LSIL











Summary of Key Cytologic Features

- 3-dimensional groups with “bulbous” projections
- “Dragon-like” configuration
- Cells all stromal
- No covering epithelium
- Clean, mature background of squamous cells

Benign

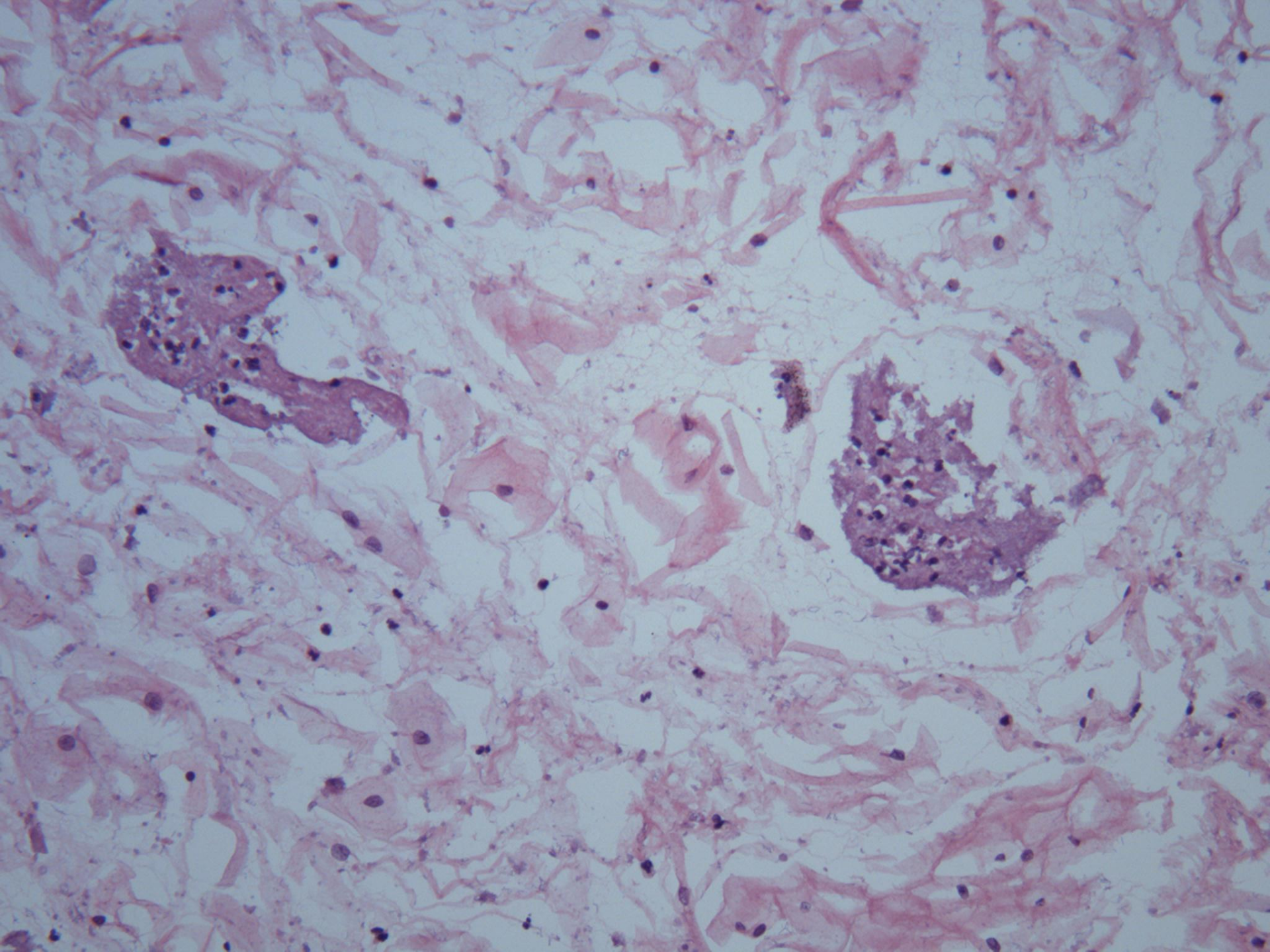
Malignant

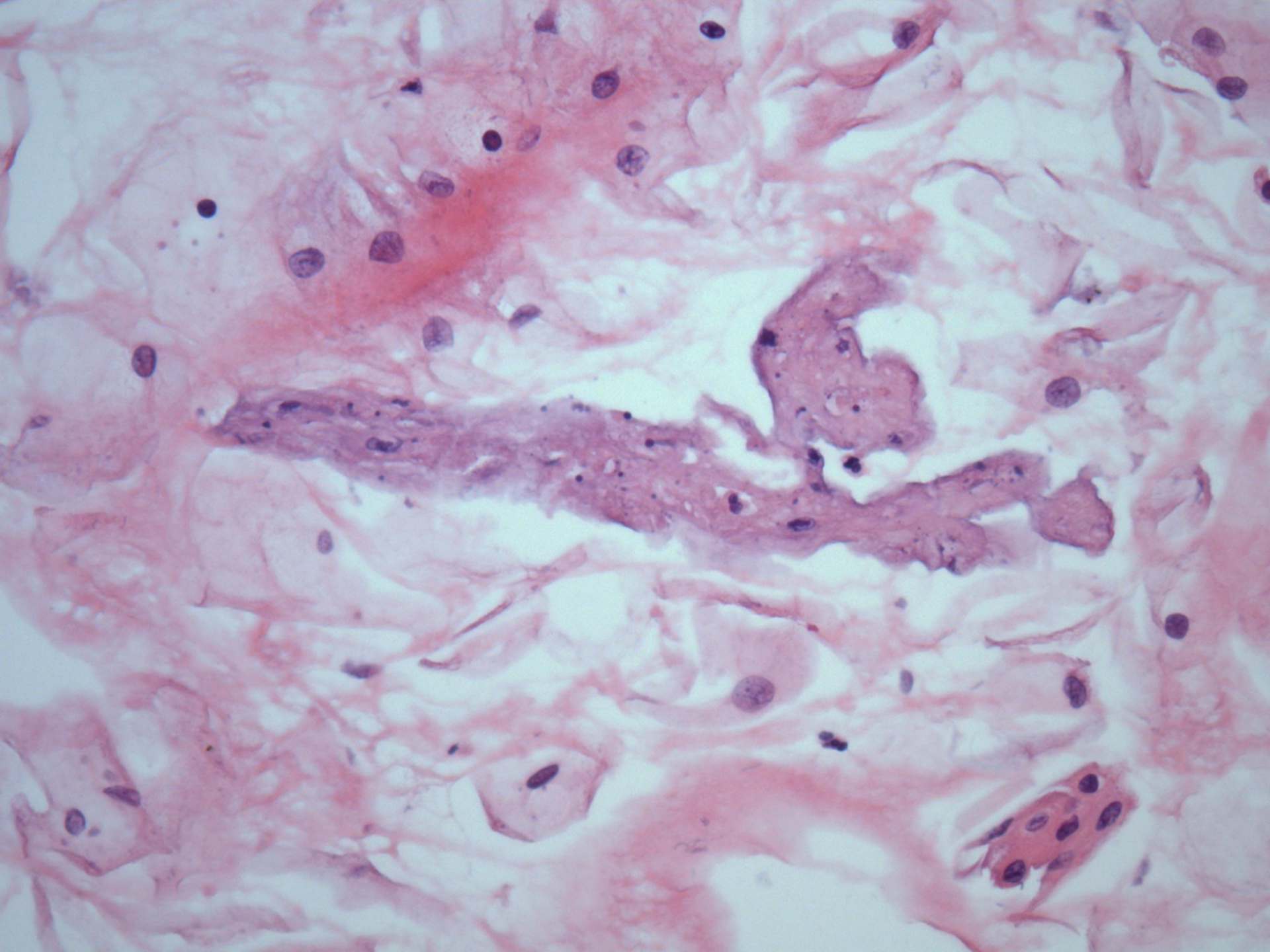
Atypical

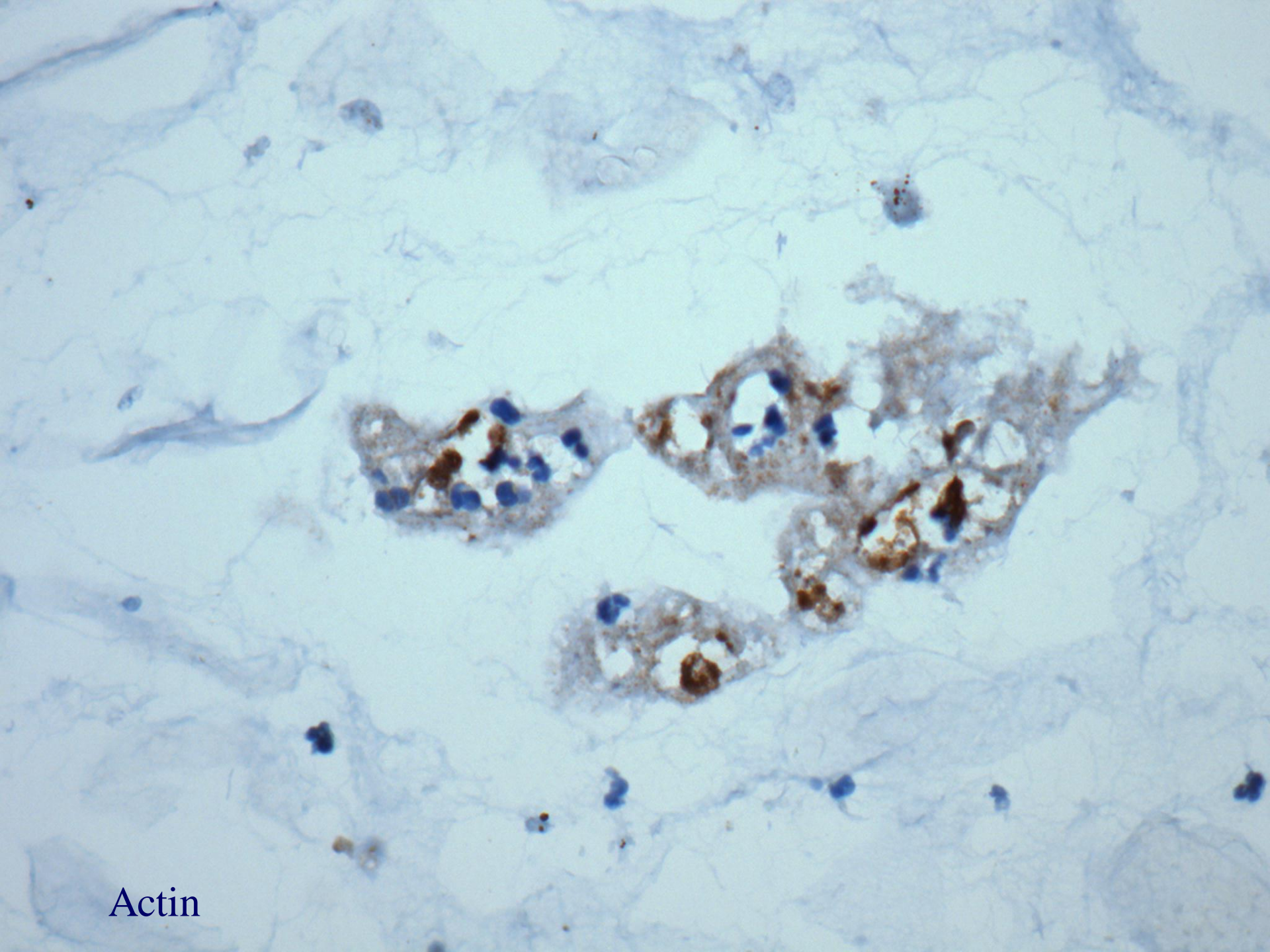
Diagnosis:

Degenerating chorionic villi

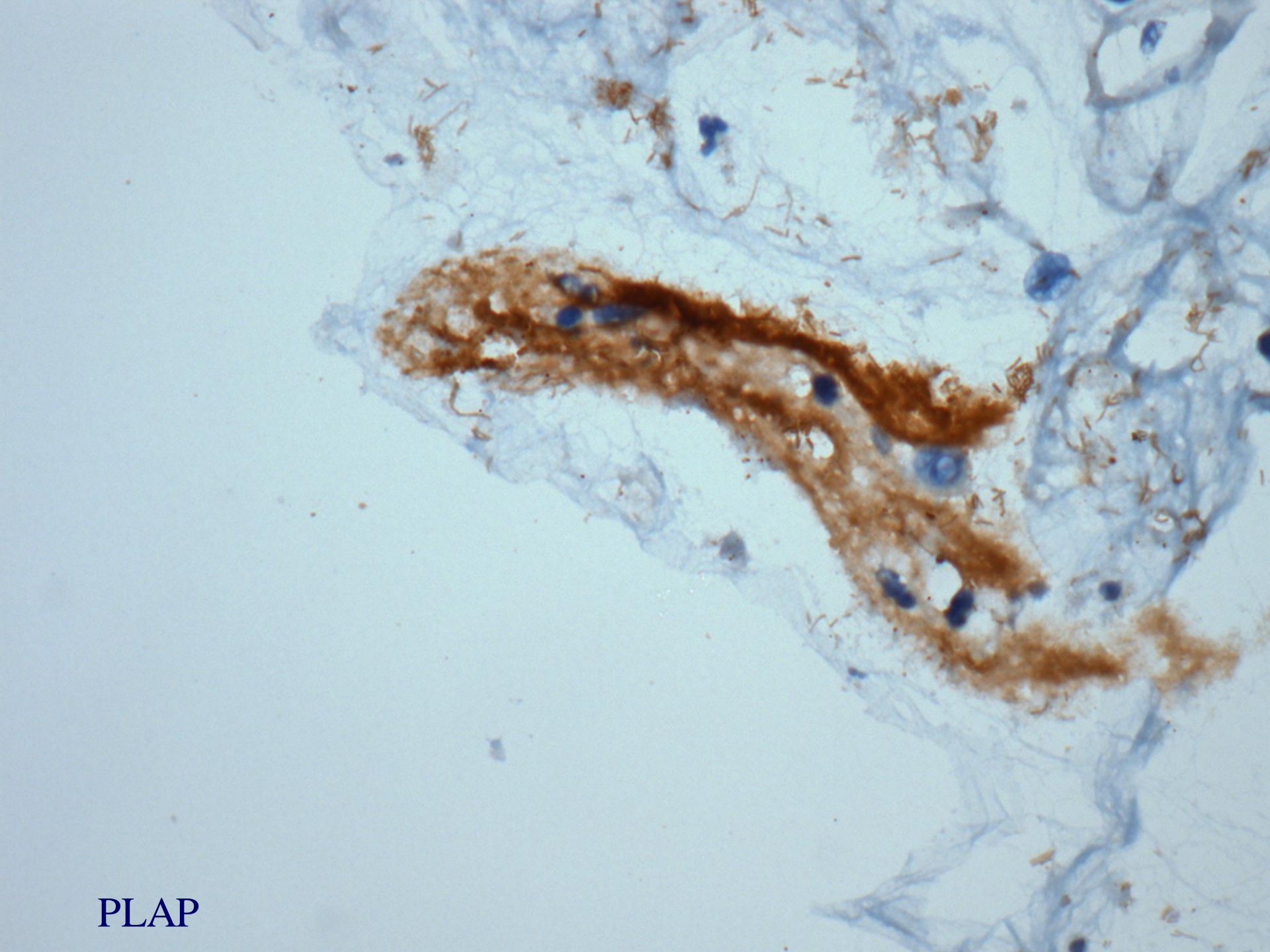
Post-abortion



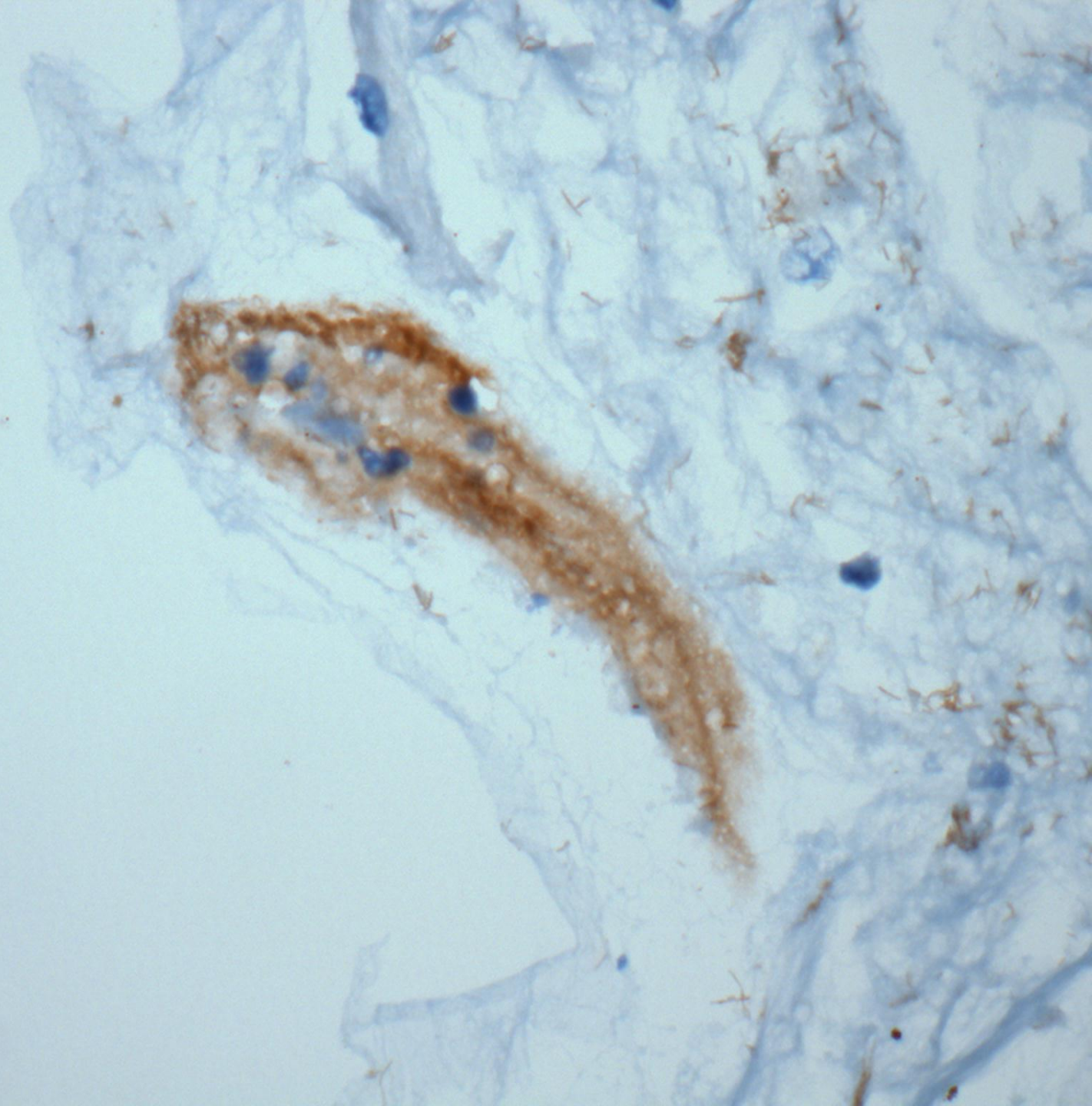




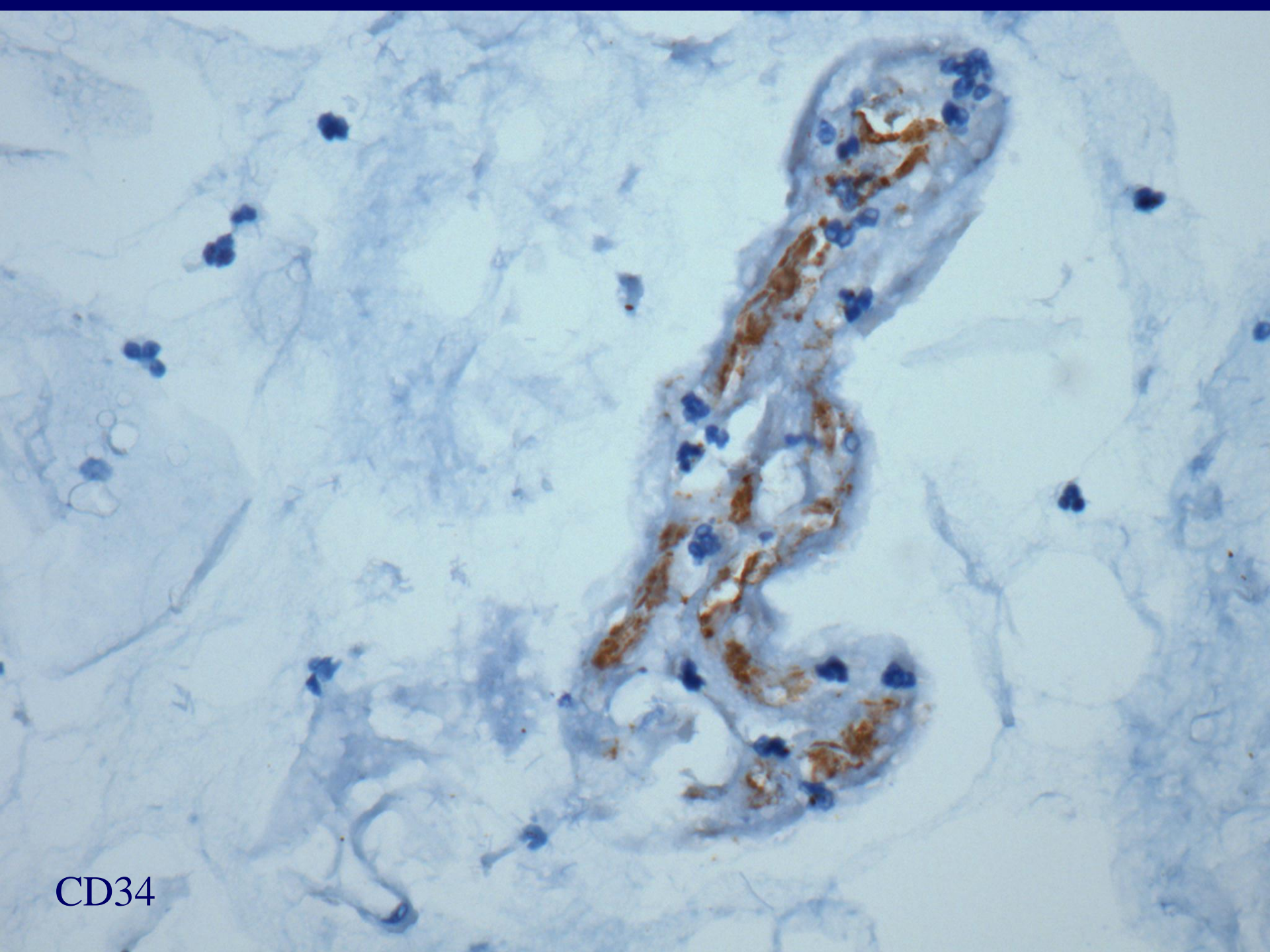
Actin



PLAP



Inhibin



CD34