Difficult High-Grade Squamous Lesions

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NCPTS 2021

Bethesda 2001
High-Grade Squamous Reports

- Atypical Squamous Cells, possible high-grade lesion
- High-grade Squamous Intra-epithelial lesion (HSIL)
- HSIL, possible invasion
- Invasive Squamous Cell Carcinoma

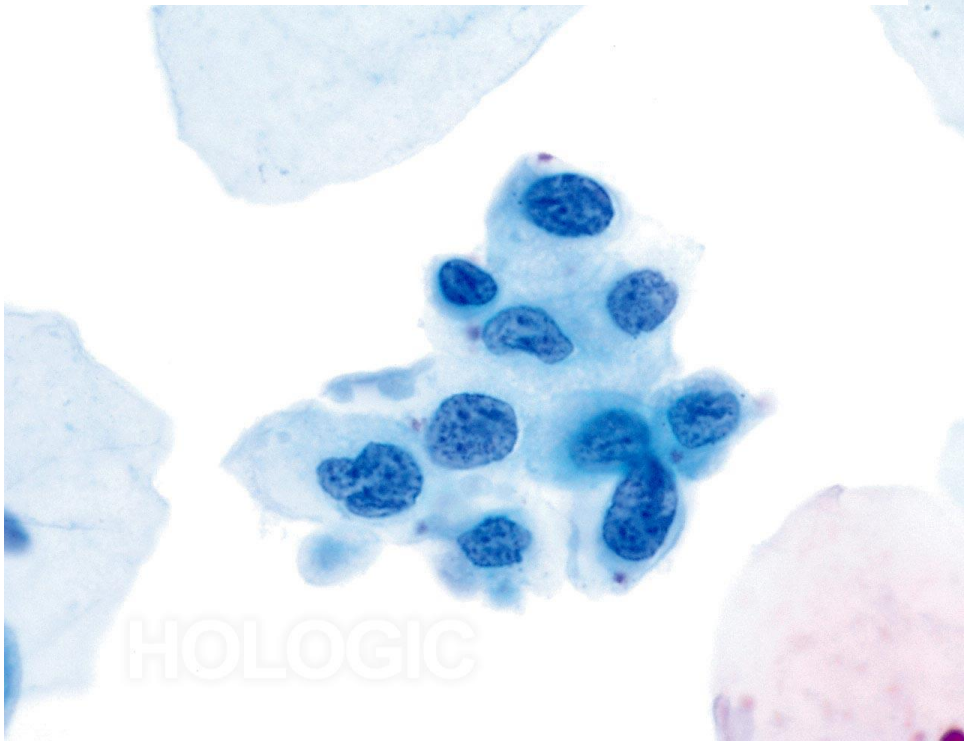
HSIL: Criteria

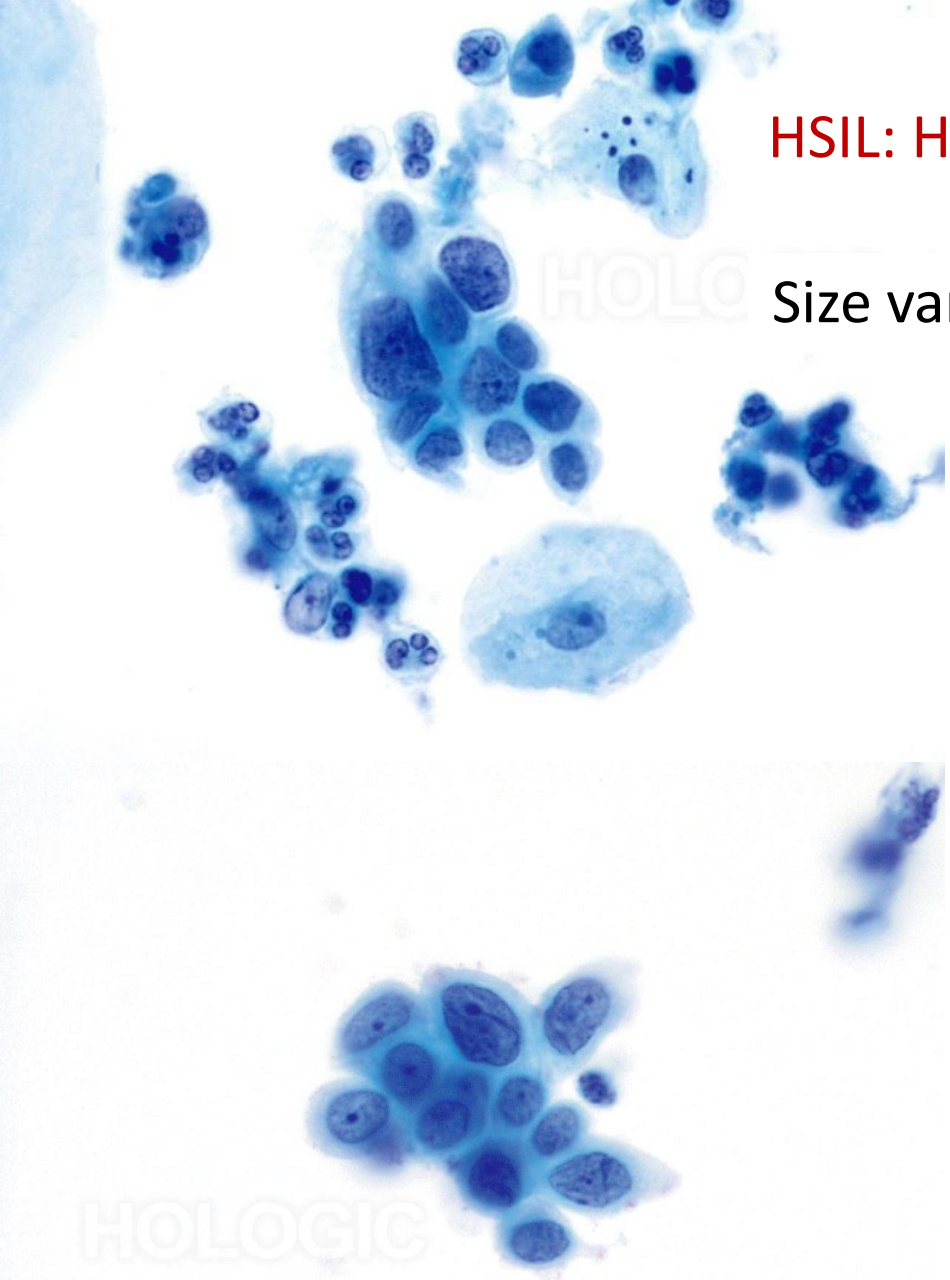
- Markedly increased N:C ratios
  - single, clustered, in crowded groups or sheets
  - cell size can vary
- Nuclear variability is central to the diagnosis
  - nuclear size varies
  - nuclear membrane irregular with variations in border
  - hyperchromasia usual: chromatin variably fine or coarsely granular and evenly distributed
  - nucleoli uncommon
  - sticky bare abnormal nuclei may be present
- Cytoplasm: can be squamoid, delicate, metaplastic or keratinised

HSIL: High N:C ratios and nuclear variability

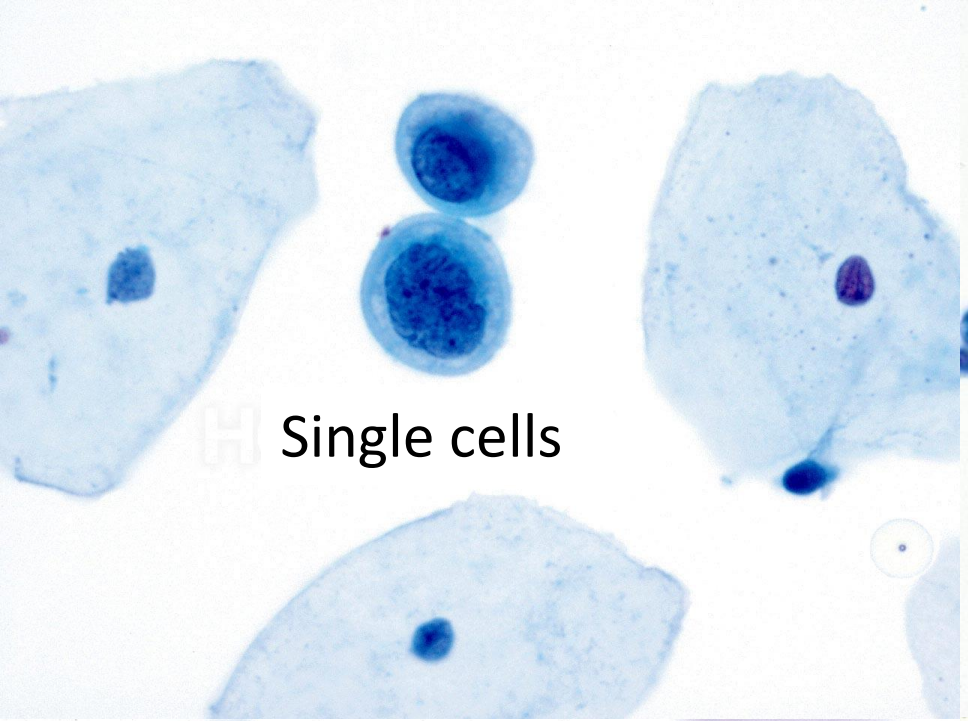
Size variation and membrane irregularity

Chromatin abnormal and variable

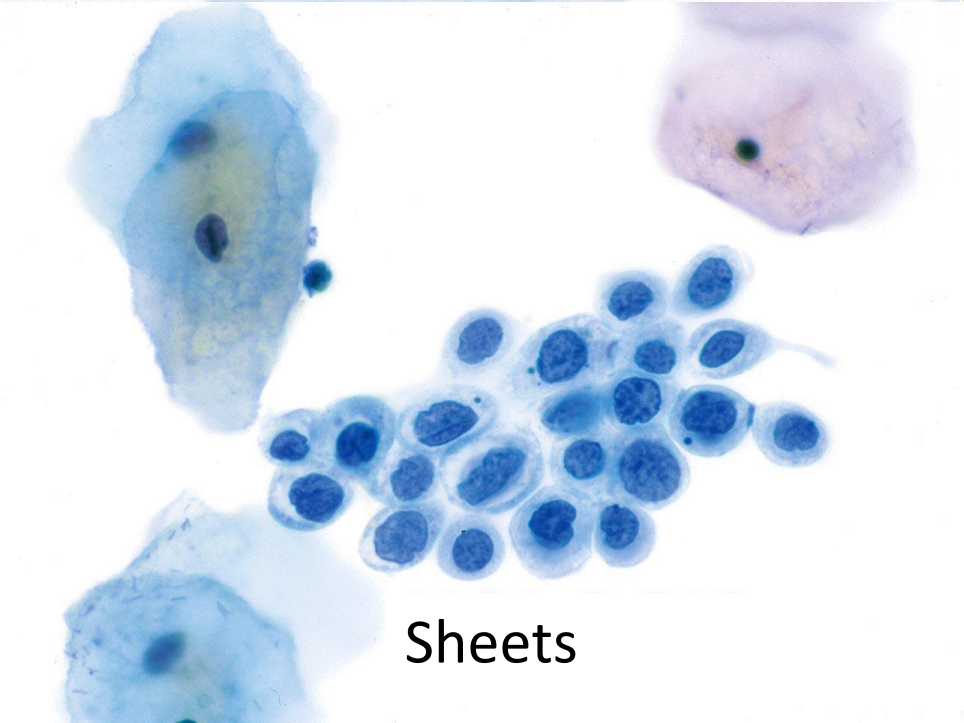


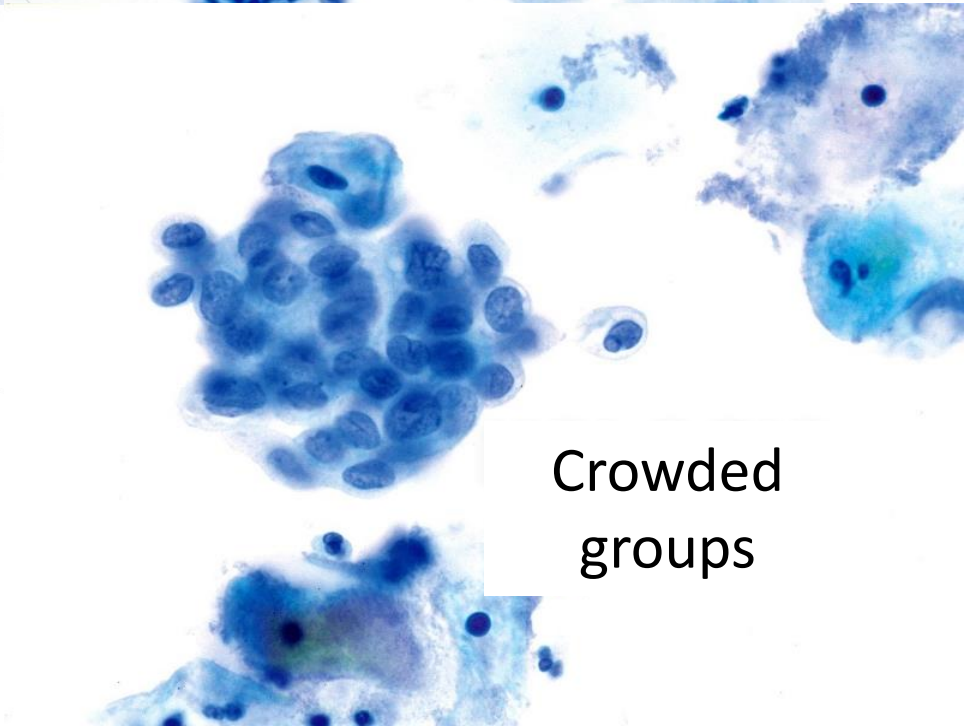


Nucleoli sometimes seen


Single cells


Small
clusters


Sheets


Crowded
groups

Presentations of HSIL

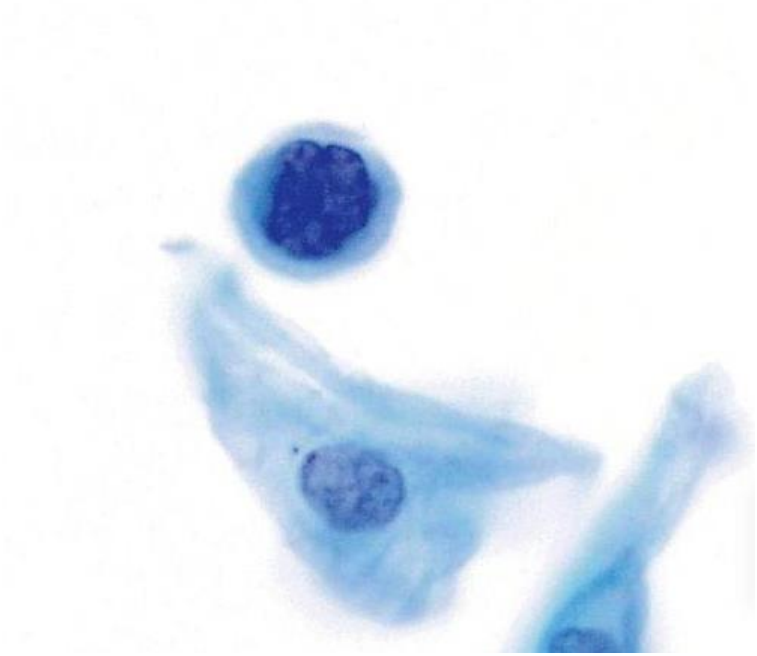
1. Metaplastic HSIL

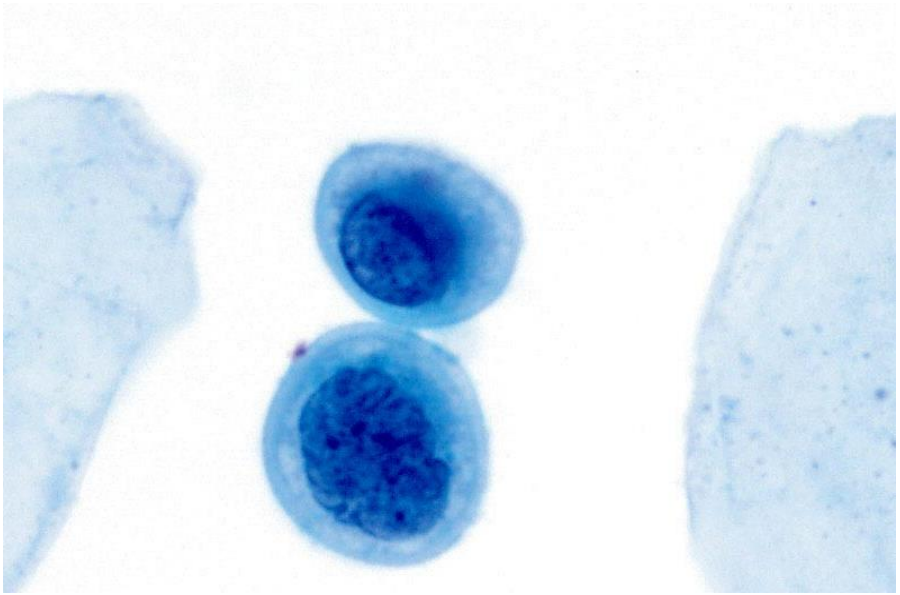
2. Crowded sheets

3. Parakeratotic HSIL

Acknowledgement: Ron Bowditch

Metaplastic HSIL





Assessing Hyperchromatic Crowded Groups
Features of CIN 3

Architecture:

- Sheets usually more than 3 cells thick
- Polarity jumbled
- Nuclei crowded and many overlap

Cellular features:

- Nuclei vary significantly and unpredictably
  - Size, chromasia, chromatin, nuclear border, shape
  - Note: May be little or no nuclear shape irregularity
- May see mitoses (embedded), apoptosis, sticky bare nuclei

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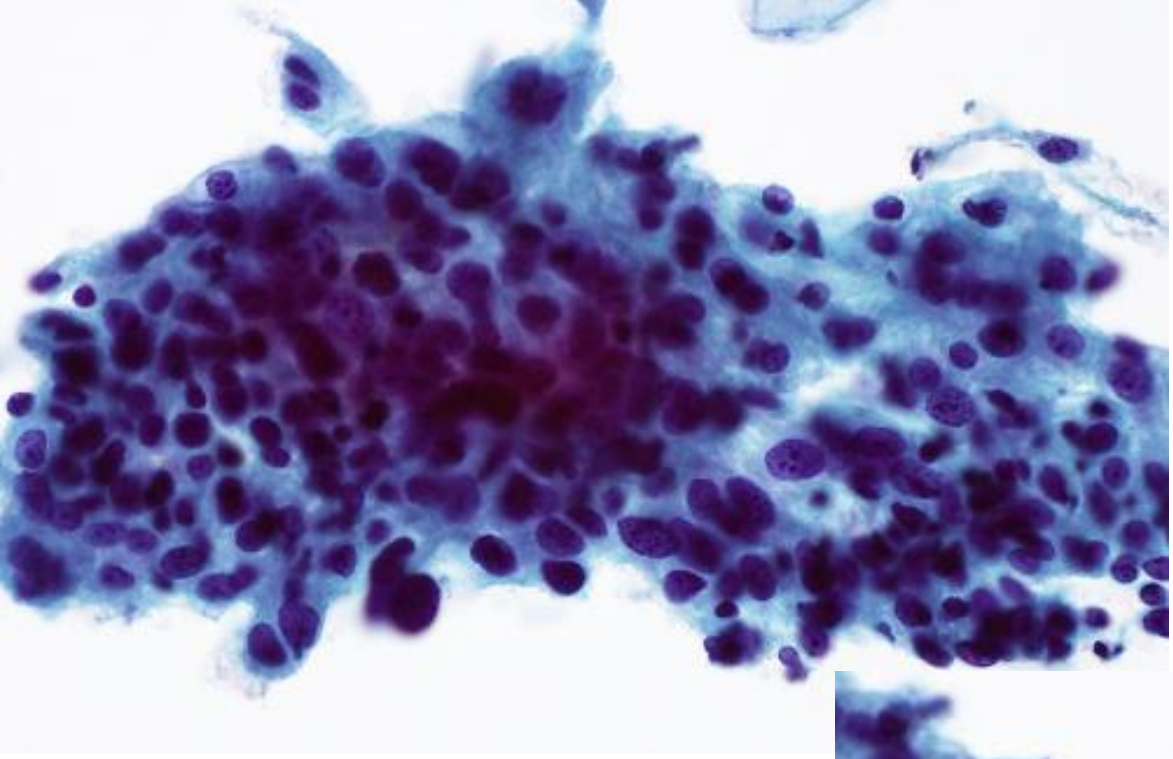
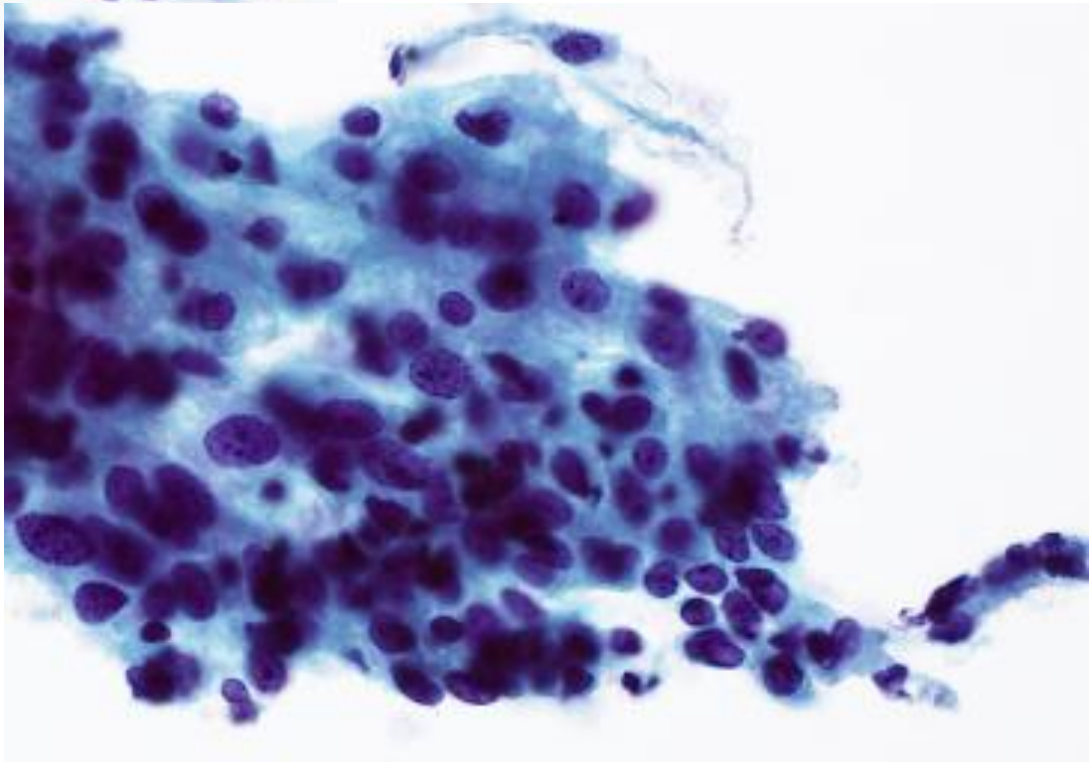
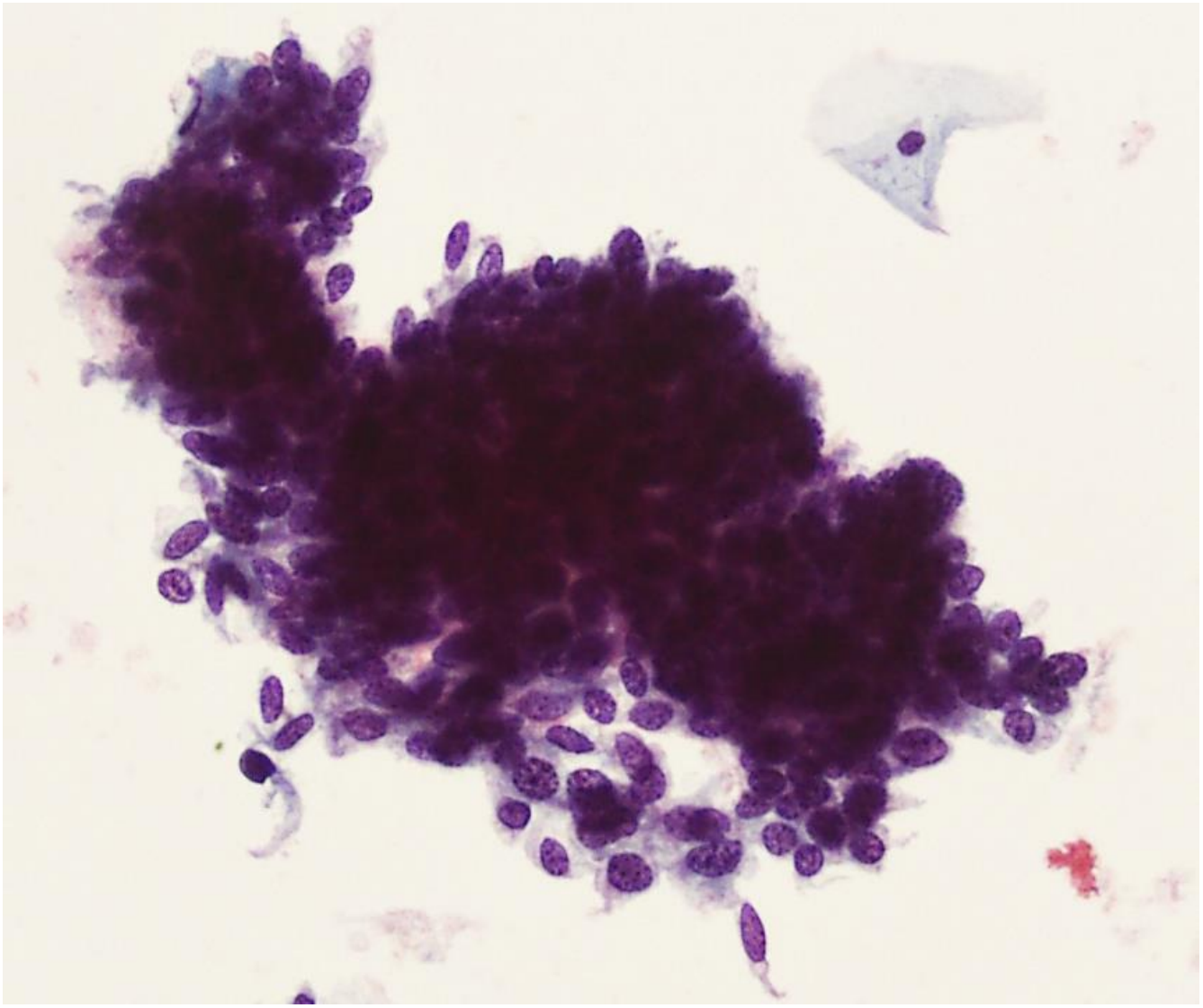


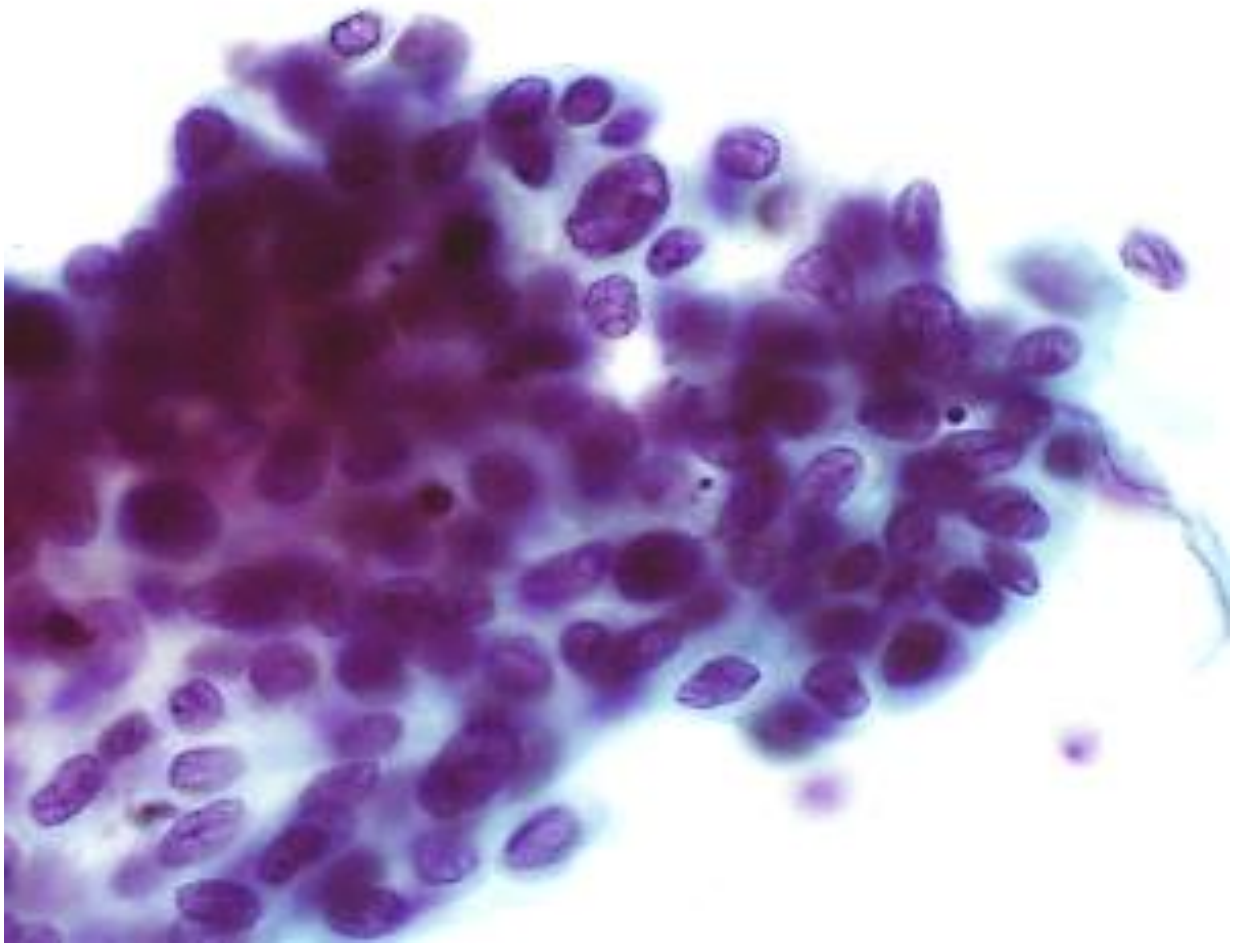


HSIL: Hyperchromatic crowded group

Embedded mitoses in HSIL



Is this HSIL?



Is this HSIL?

Hyperchromatic Crowded Groups
Distinquishing squamous from glandular lesions

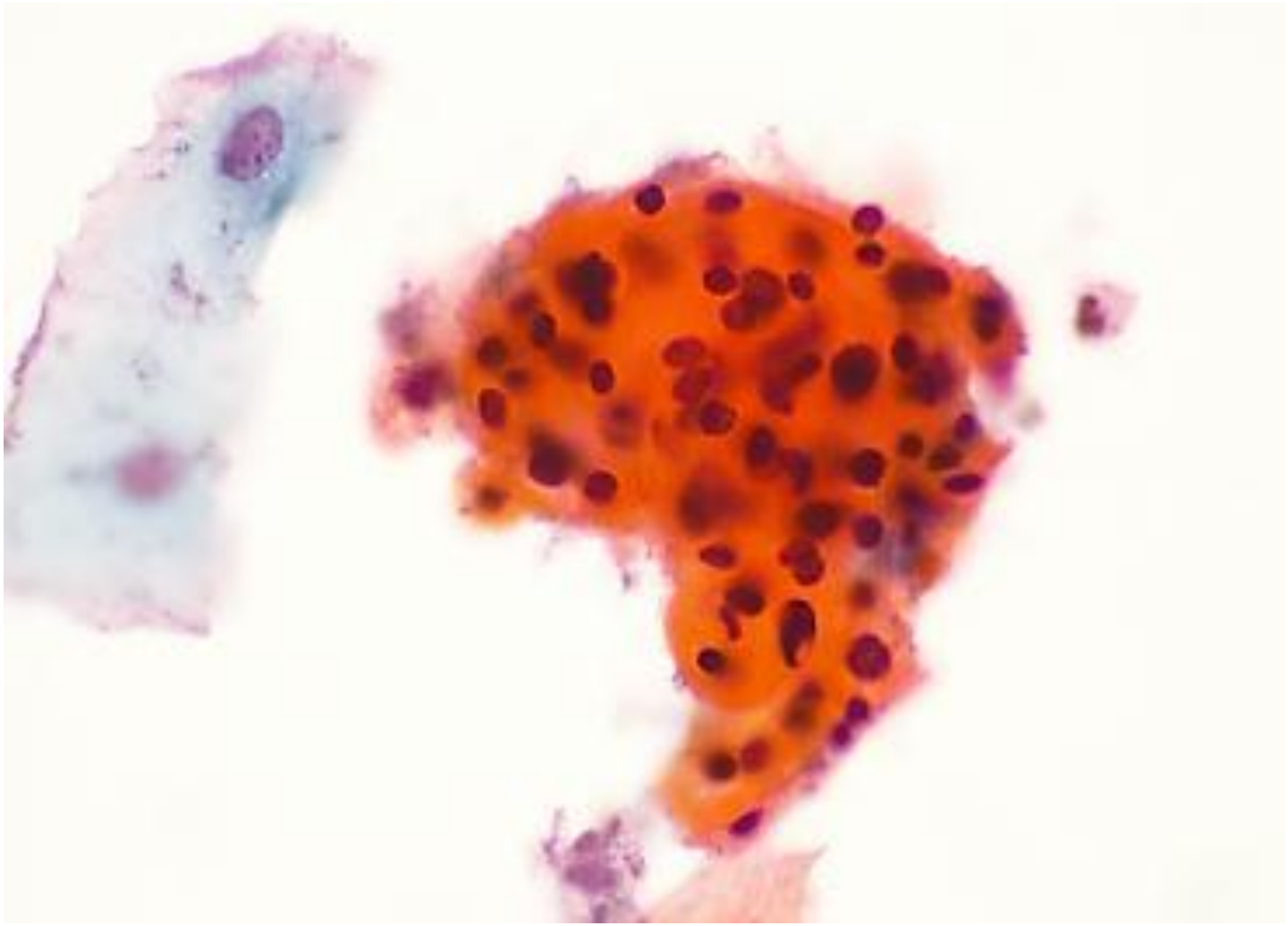
1. Look for architectural and cellular features of a high-grade lesion. Consider benign mimics and the clinical context
2. Look for glandular architectural features such as

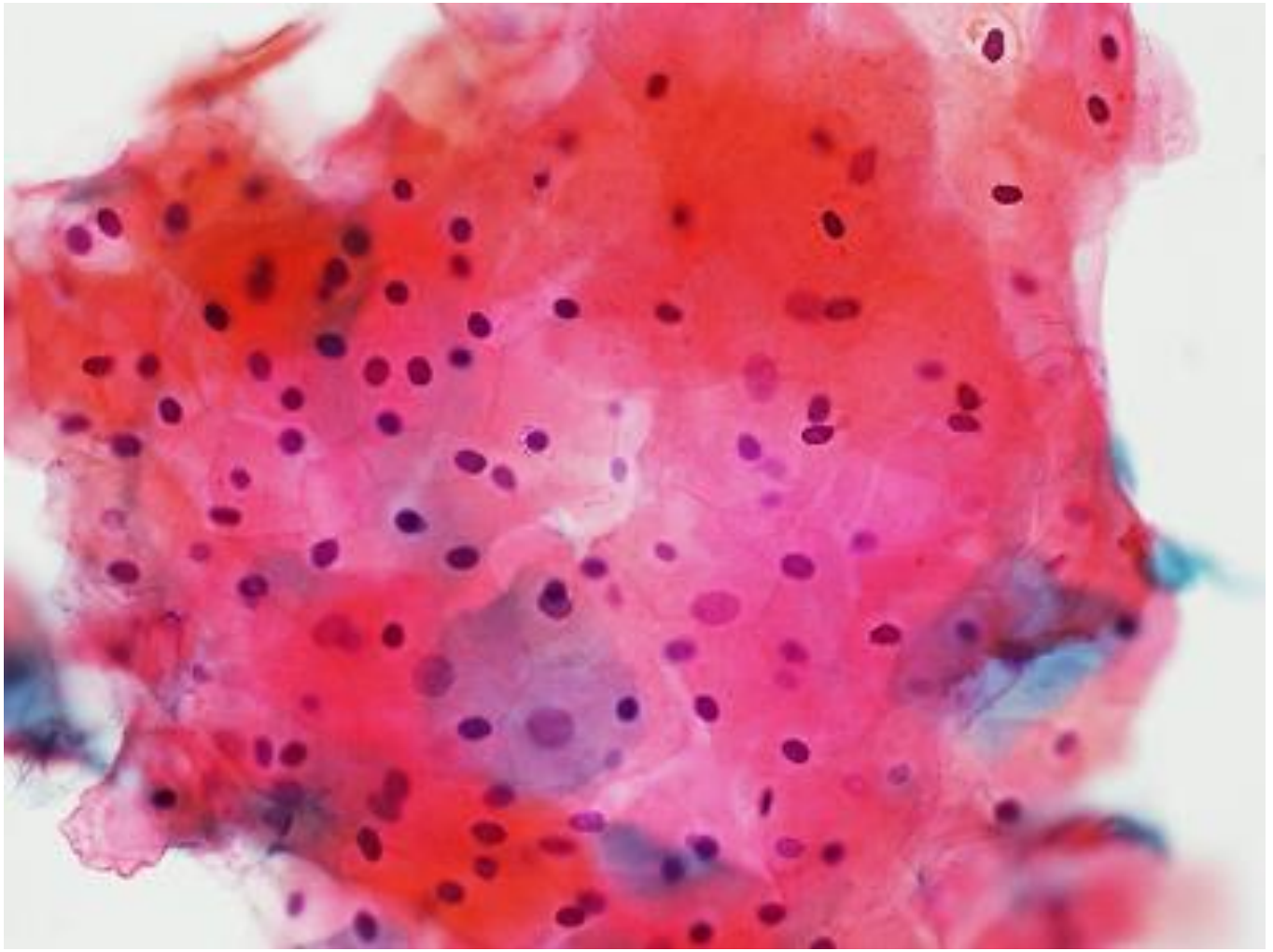
Endocervical: Common border at edge, gland openings, feathering, cytoplasmic tags, strips, rosettes

Endometrial: open tubules, fraying at sheet edges, stromal component present

Bottom line: Hyperchromatic crowded groups without glandular (or squamous) features are much more likely to be HSIL than a high-grade glandular lesion

Parakeratotic HSIL





Normal maturing parakeratotic squamous epithelium

Atypical Squamous Cells, possible High-Grade lesion (ASC-H)

- A report category: suspicious but not diagnostic of a high-grade lesion (HSIL or Invasive SCC)
  - "?high-grade lesion *or* normal/benign mimic" is often the issue
  - technical limitations may also mean a sample is suspicious of high-grade disease but is not diagnostic
  - can be used in conjunction with a report of LSIL.
- All cases referred for colposcopy

ASC-H

Mimics of HSIL

- Immature squamous metaplasia
- Active cervicitis (crowded sheets)
- Post-partum effect
- Atrophy
- High-sampling
- Acute florid HPV infection

Mimics of SCC

- Atypical repair
- Radiation-induced change

Technically difficult to interpret

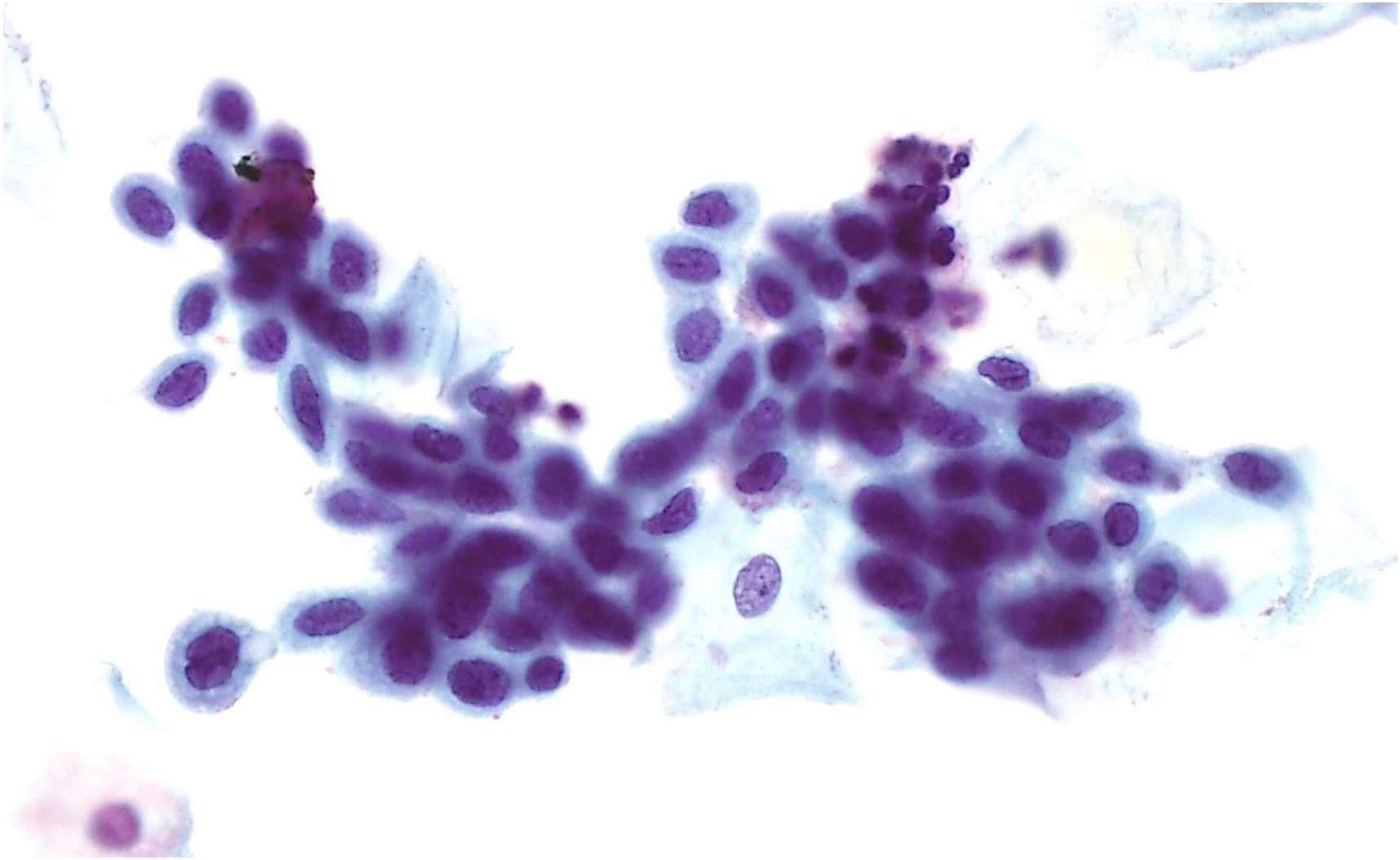
- “unsatisfactory” smears with suspicious cells/groups
- scanty abnormal cells/groups
- degenerate cells

Atypical Squamous Cells, possible HSIL (ASC-H)
Bethesda 2001

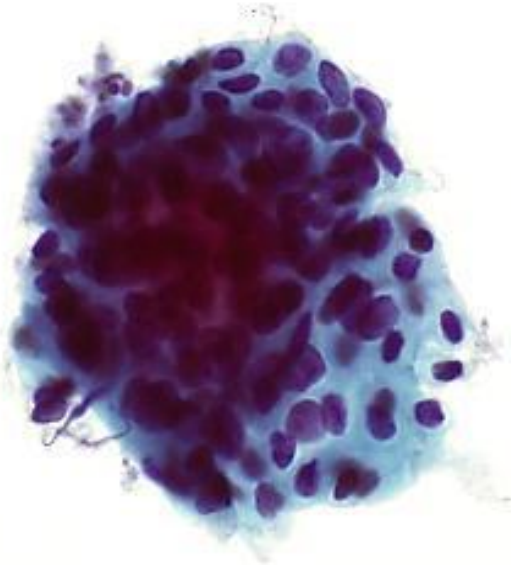
- 5 - 10% of Atypical Squamous Cells category
- 70-85% HrHPV positive *c.f.* 50% for ASC-US

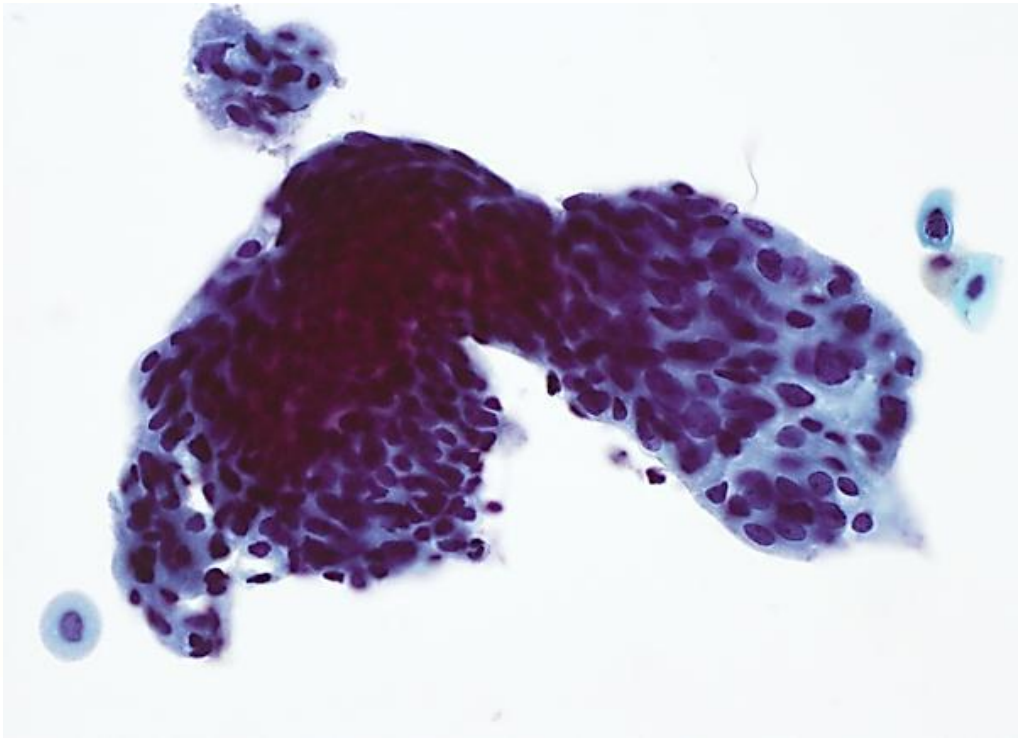
- PPV for HSIL (% confirmed HSIL at colposcopy):
  ASC-H 44% *c.f.* ASC-US 10-15% and HSIL 84%

- Manage as for HSIL but if biopsies fail to confirm CIN2+, then correlate colposcopic findings, biopsies and smear appearances to determine management.



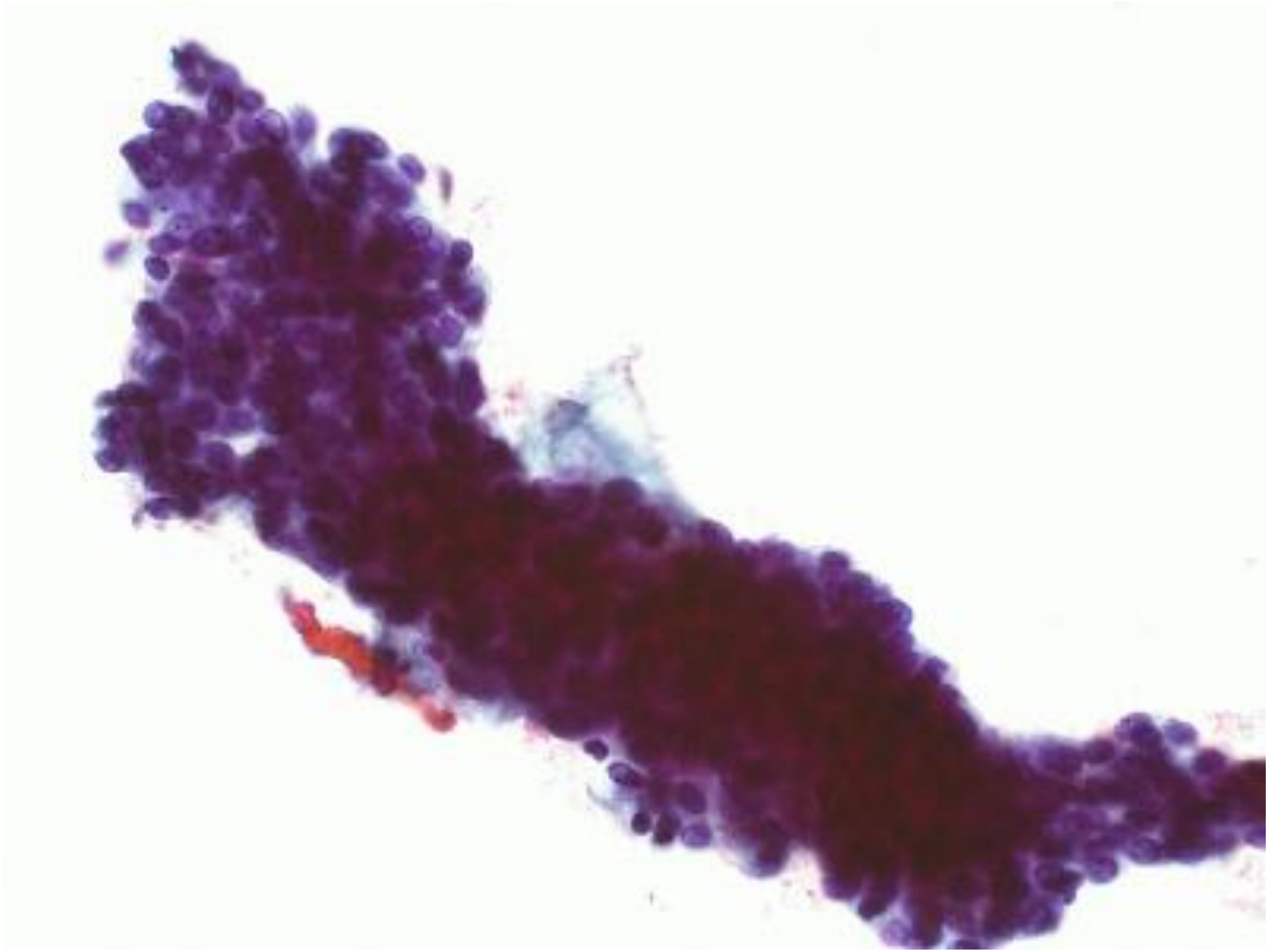
Post-partum 34 yrs: Reported as ASC-H
HSIL or benign/reactive metaplasia?



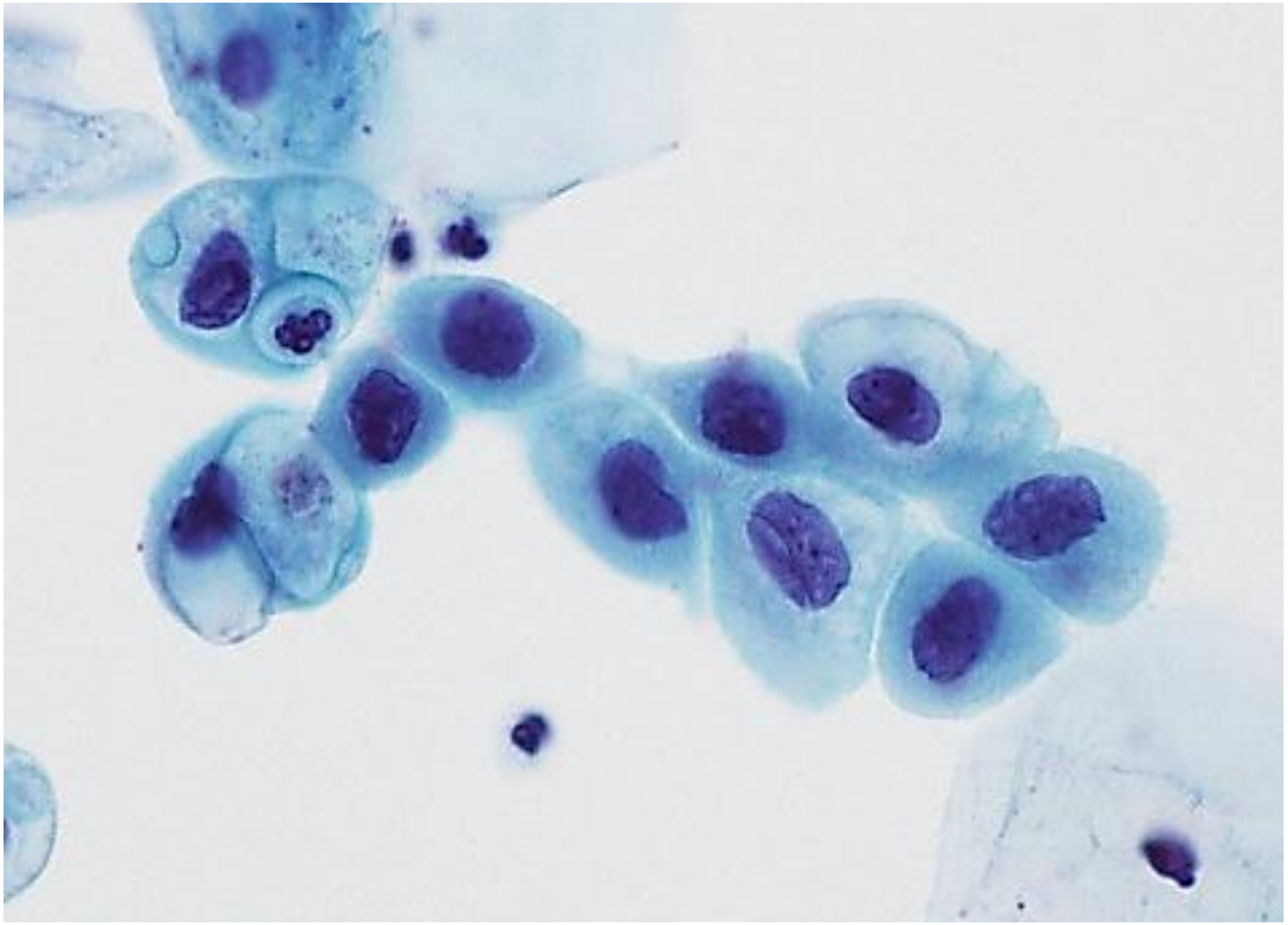


ASC-H in atrophy

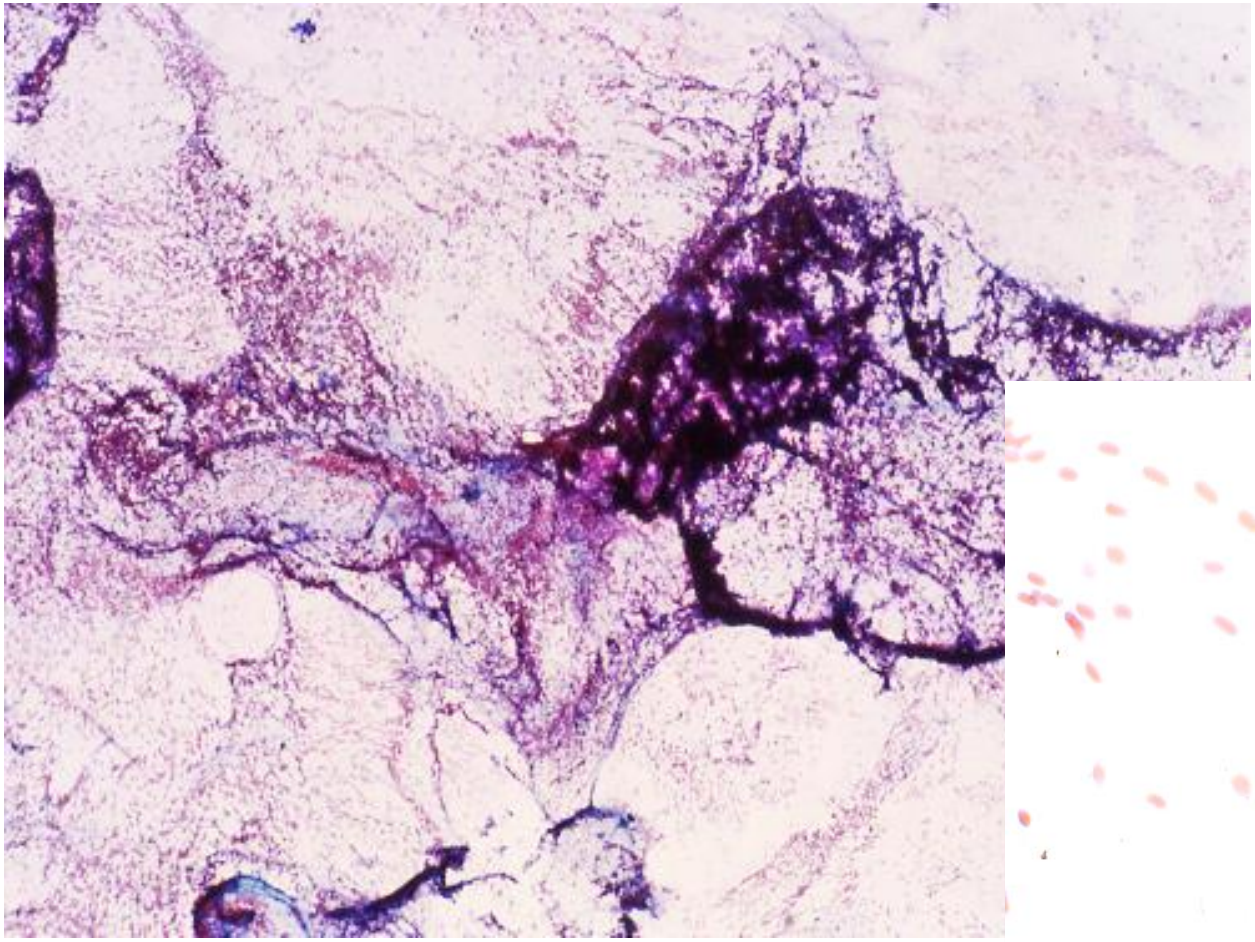
FU: Left = CIN 3 Right= atrophy only

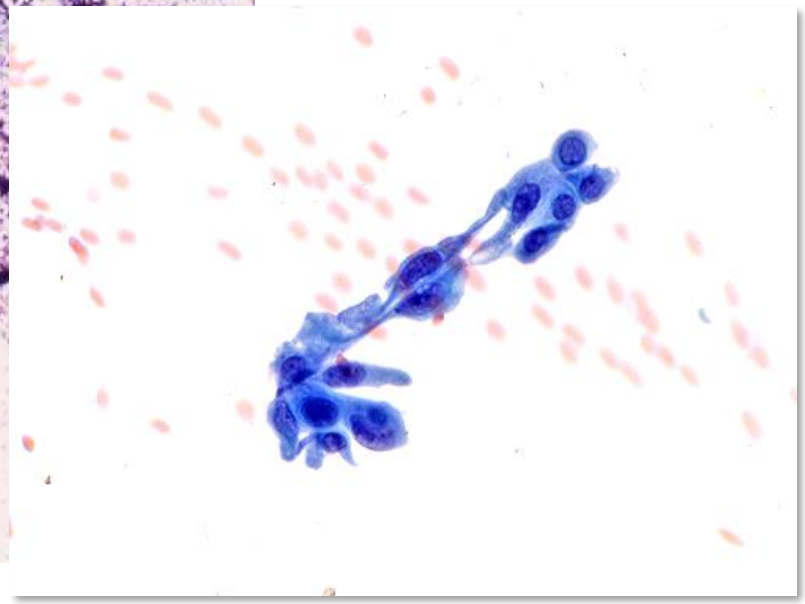


High Sampling

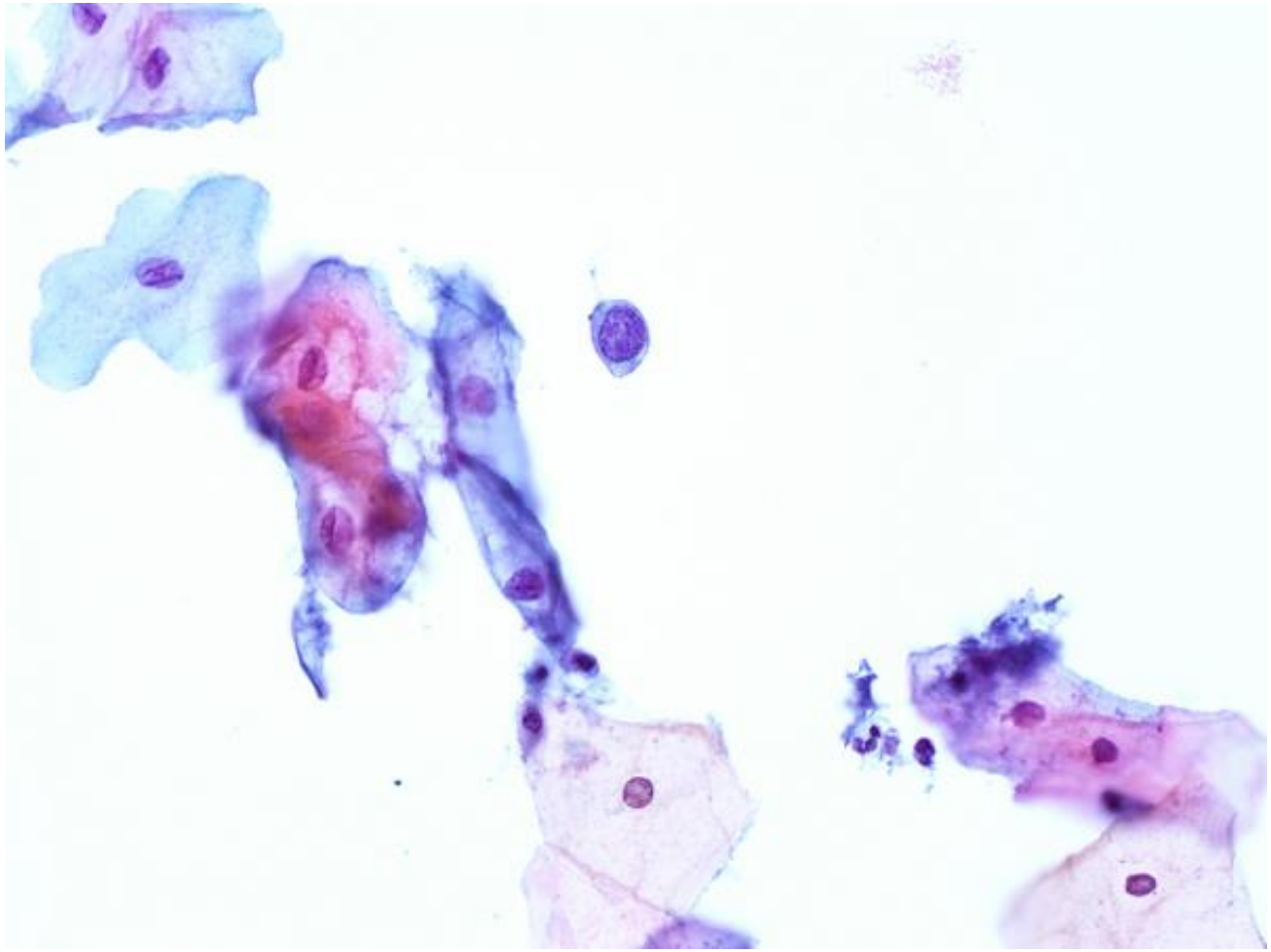


LSIL + ASC-H

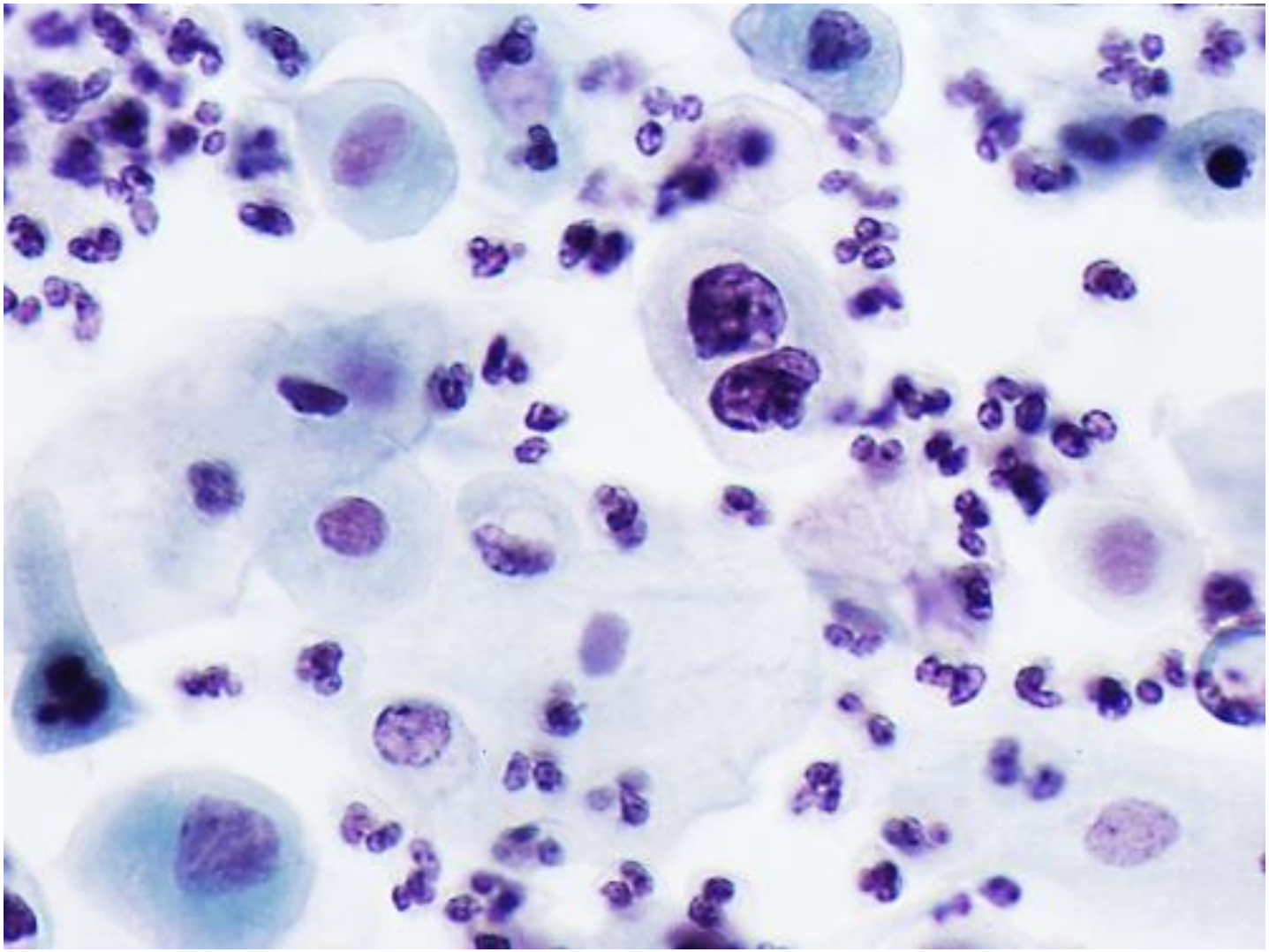




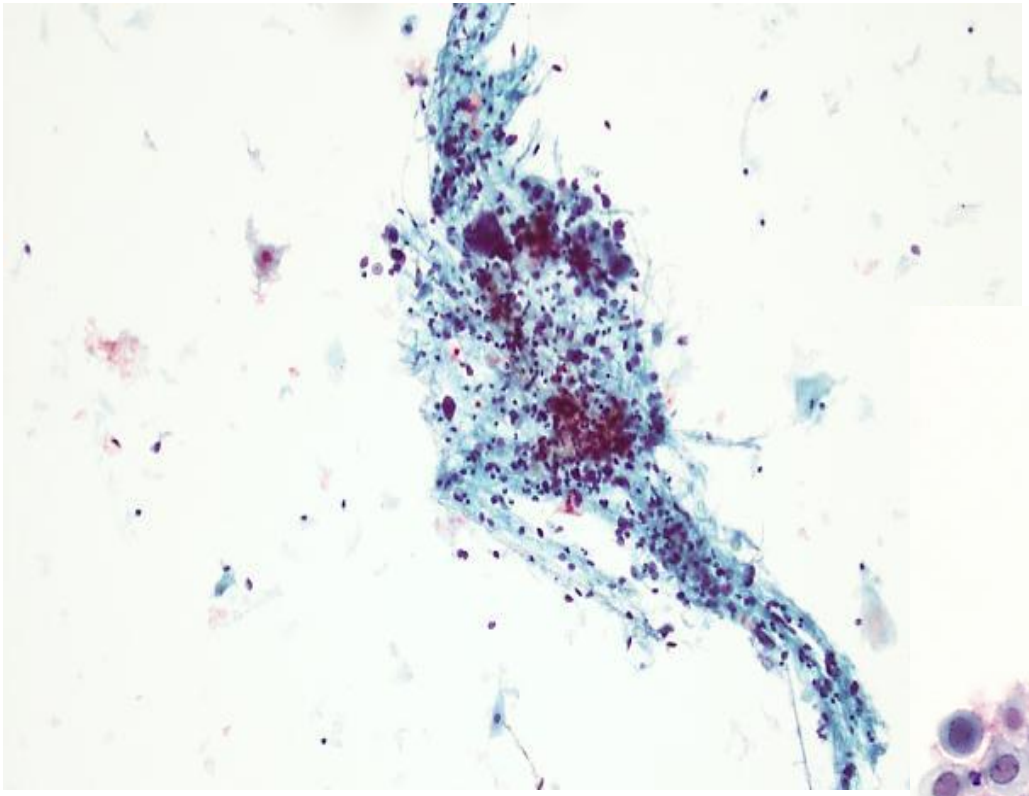
Reported as Unsatisfactory
Missed adenosquamous carcinoma

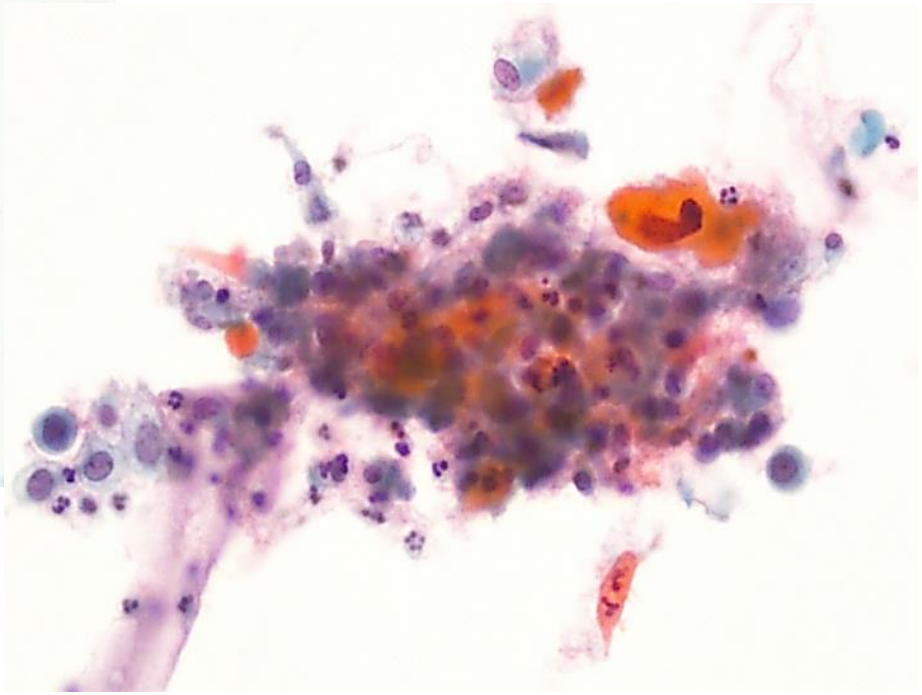


HSIL: Single cell



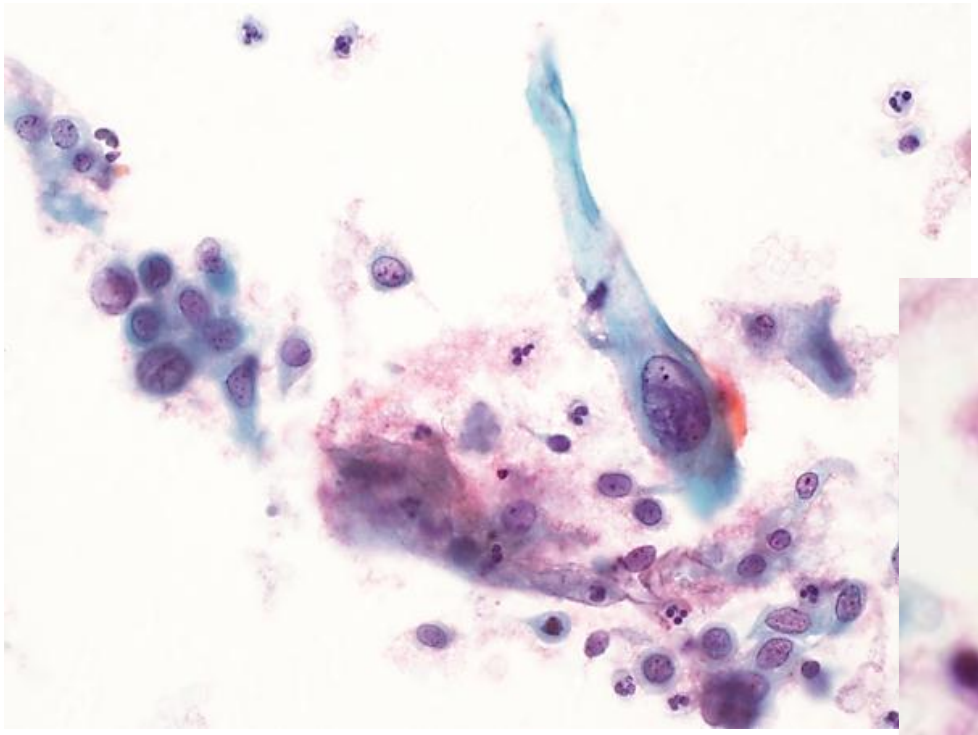
ASC-H: Vaginal smear. Previous VAIN
Degenerate hyperchromatic suspicious cells
Follow-up VAIN 3

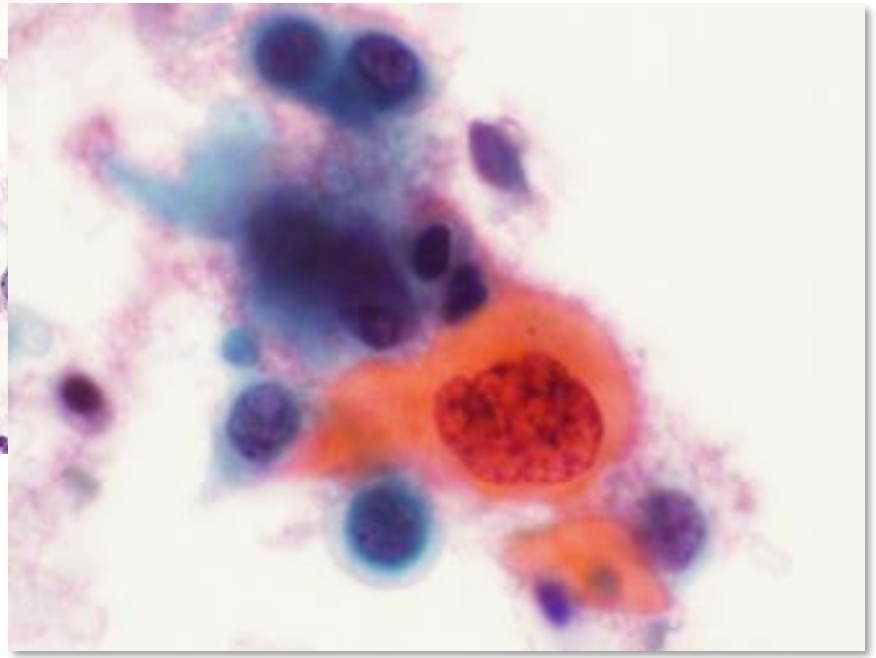




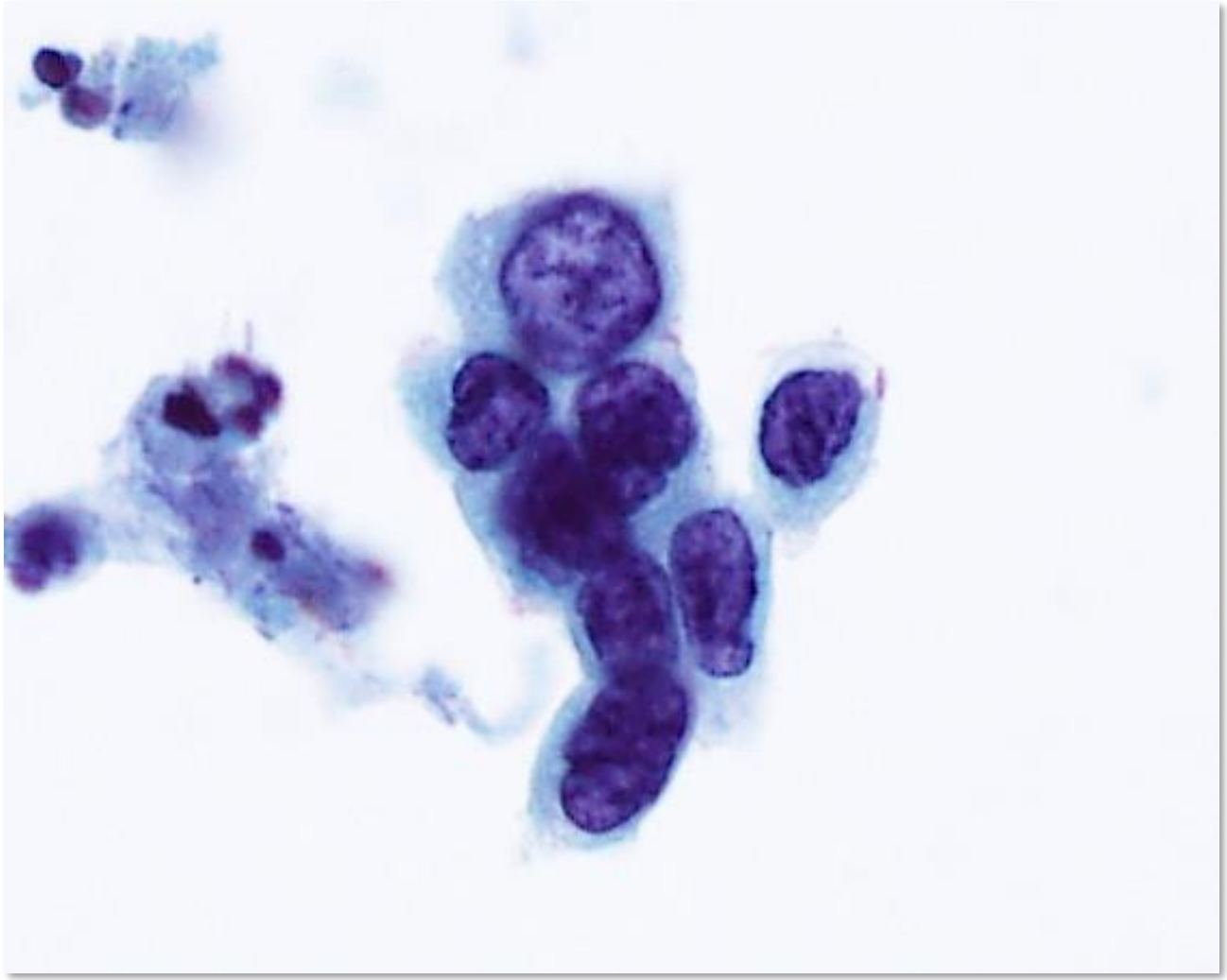
Squamous cell carcinoma

Low-power appearance, diathesis

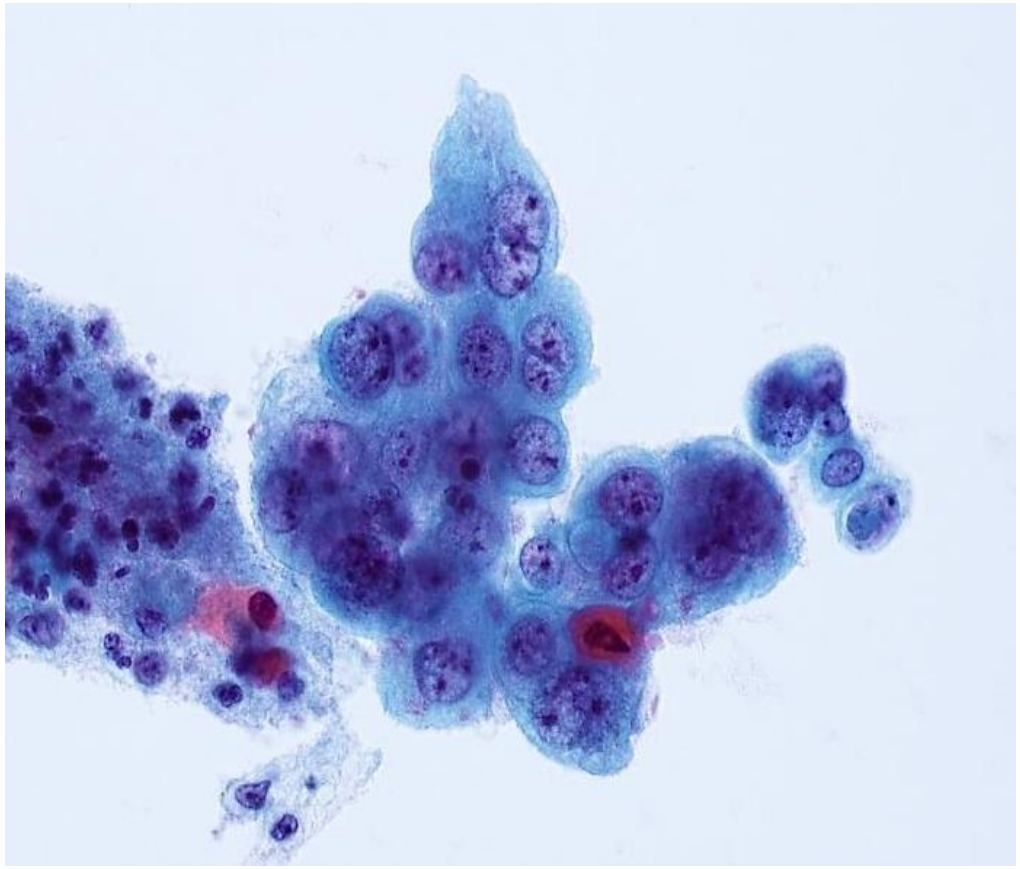




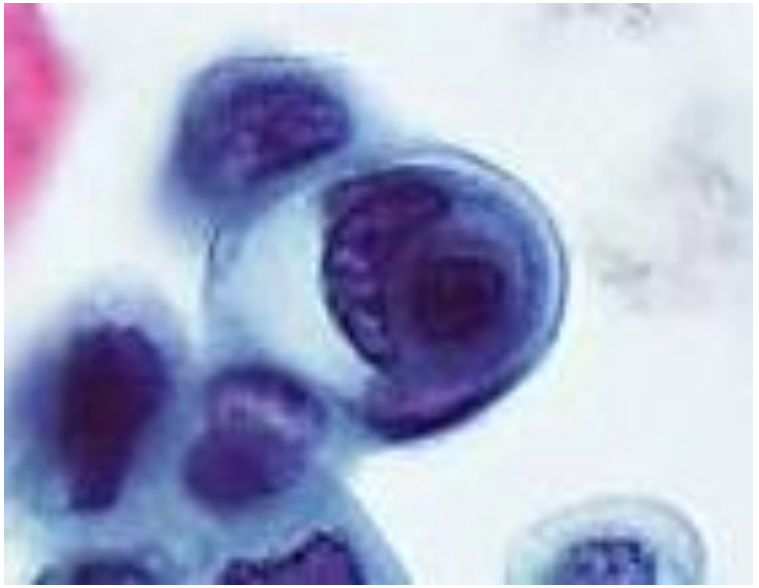
Marked pleomorphism



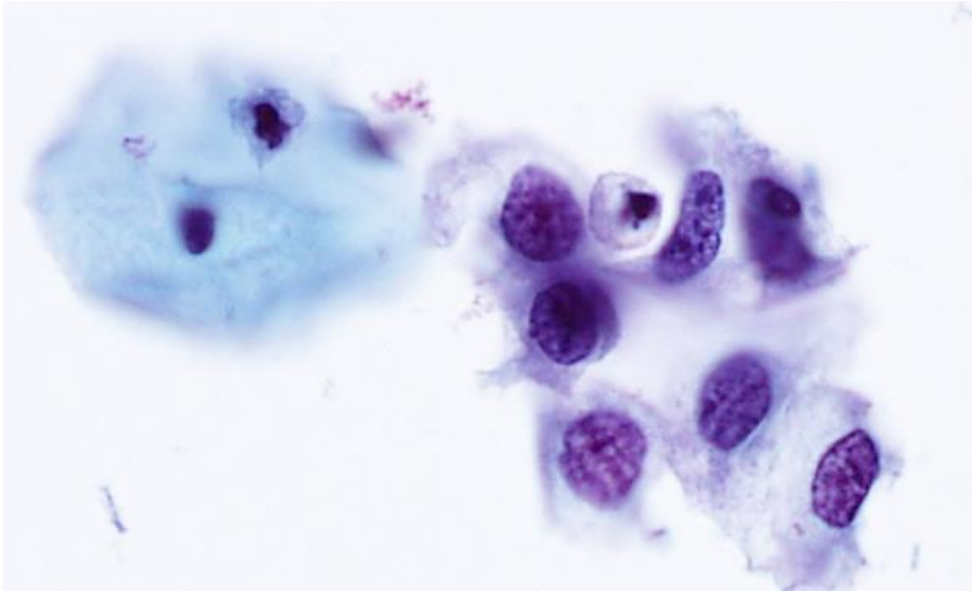
Chromatin clumping and clearing



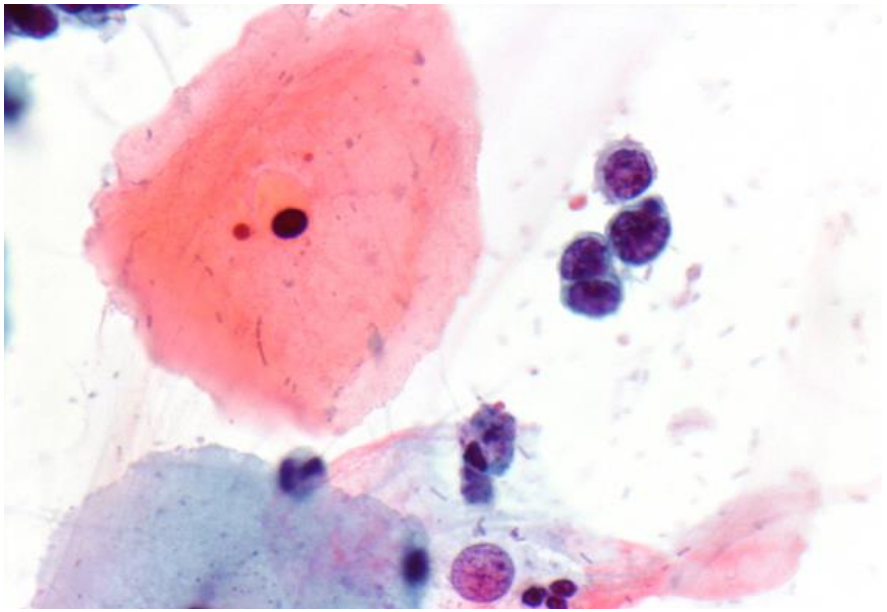
Nucleoli



Cell-in-cell engulfment



SCC: Large cells



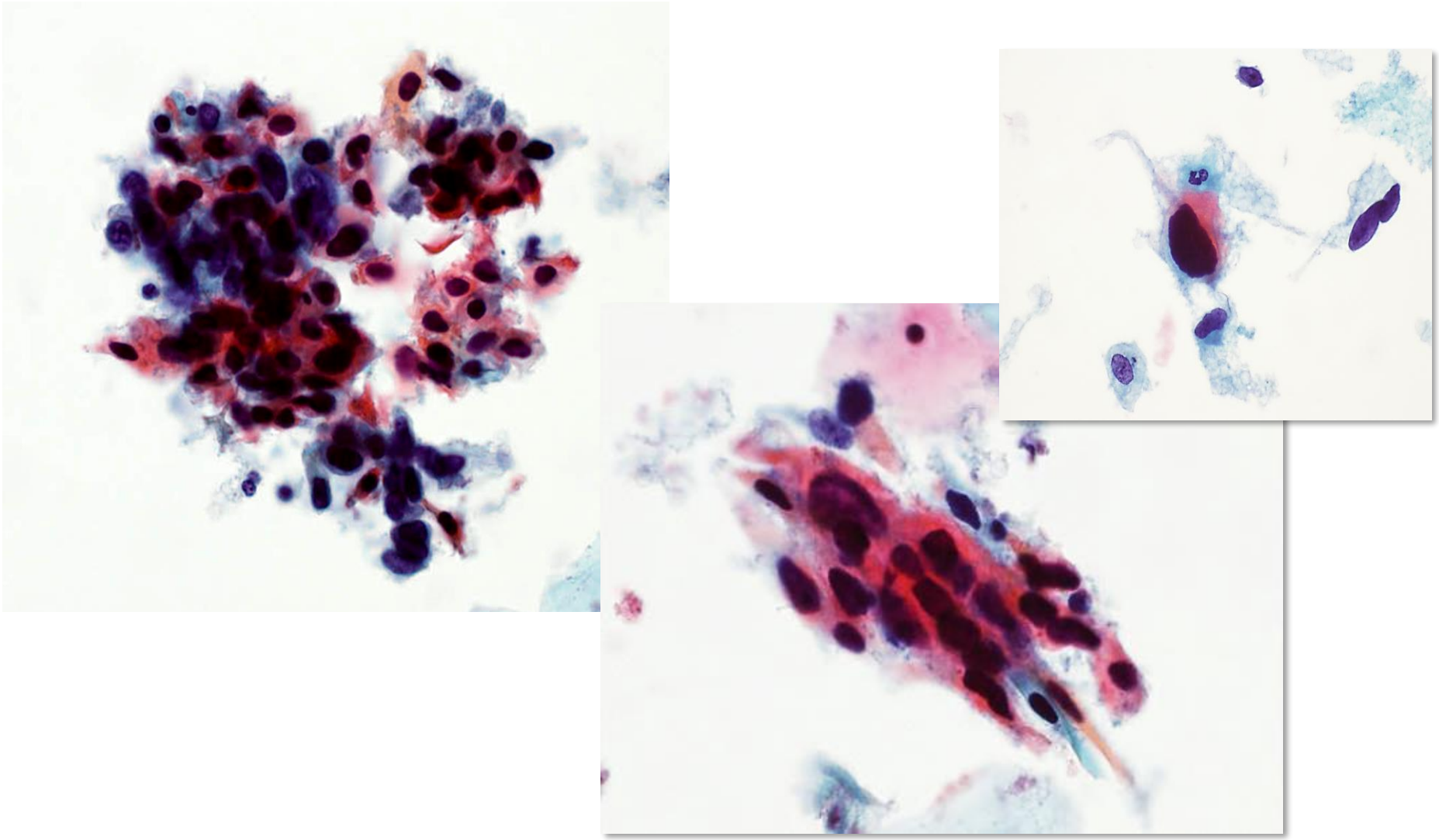
SCC: Small cells

Keratinising SCC

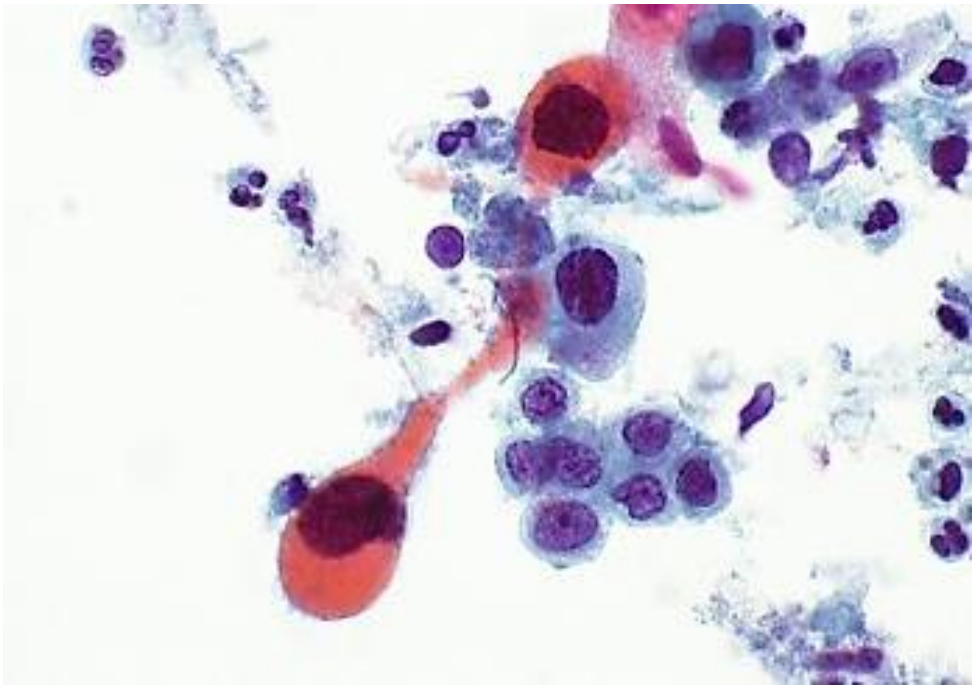
- Clean background or diathesis
- Number of abnormal cells very variable. May be few.
- Large highly pleomorphic squamous cells, spindle and tadpole forms. Can be small highly keratinised cells with dense pyknotic nuclei.
- Coarsely granular chromatin, irregularly distributed
- Nucleoli often prominent.
- Dense glassy bright orange cytoplasm (keratinisation)

DD: Keratinising HSIL

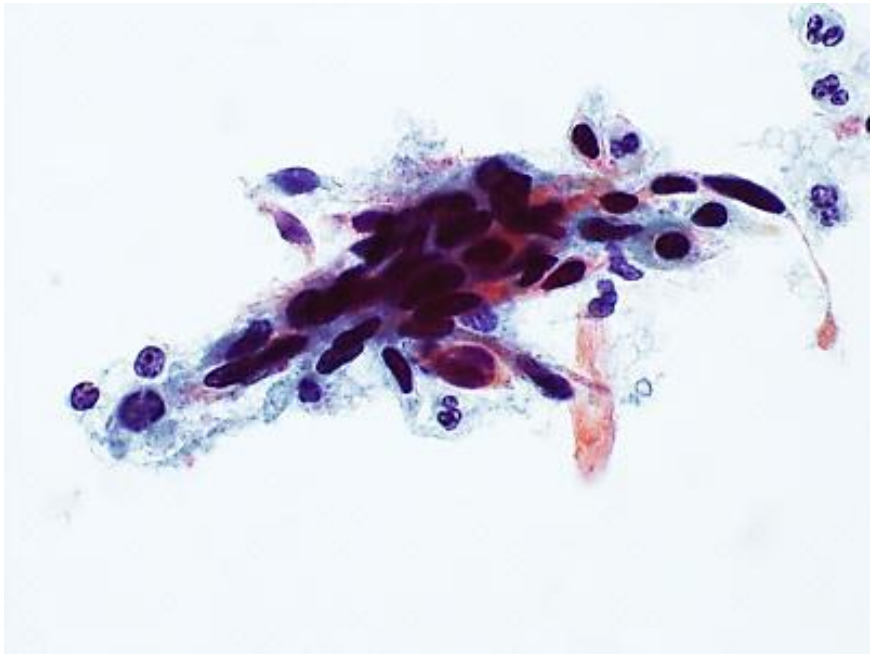
Cervicitis



Highly keratinised SCC



Tadpole (Caudate) cells

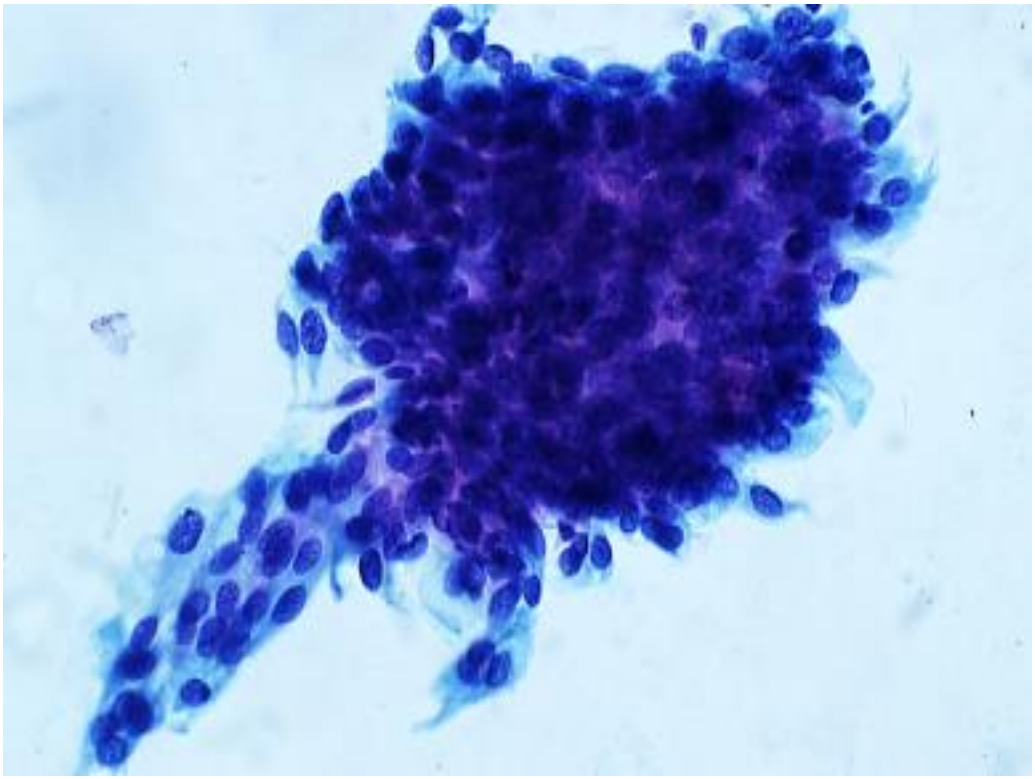


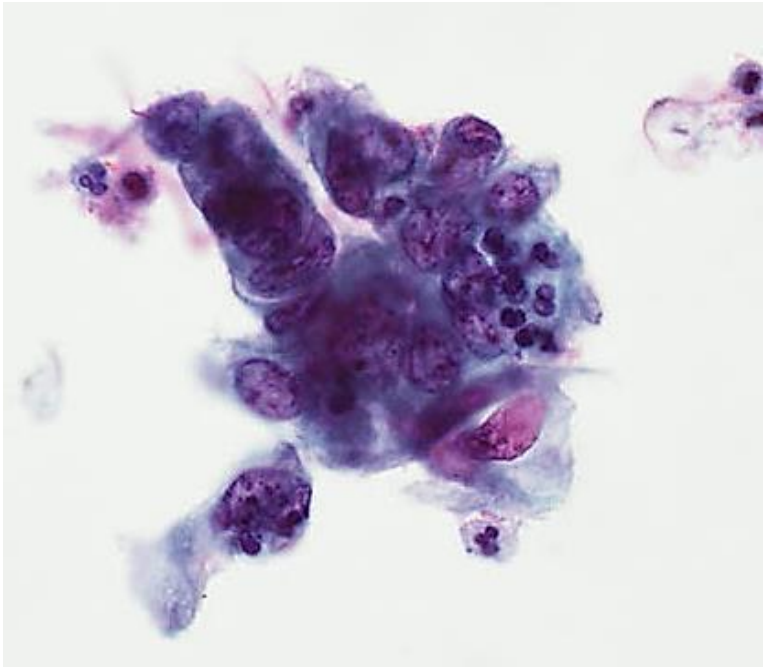
Spindled cells

Non-keratinising SCC

- Background - fresh blood common.
- Usually many abnormal cells. Single cells or sheets.
- More uniform cells, resembling HSIL. Usually intermediate size but may see large and small cell cases.
- Nuclear size varies. High N:C ratios.
- Coarsely granular chromatin, hyperchromatic, markedly irregular
- Nucleoli often multiple and irregular.
- Poorly defined cytoplasmic borders. Individual cells keratinised

DD: HSIL
Reactive cells
Endometrial cells, lymphoma





Non-keratinising SCC