

# Difficult High-Grade Squamous Lesions

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NCPTS 2015

# 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

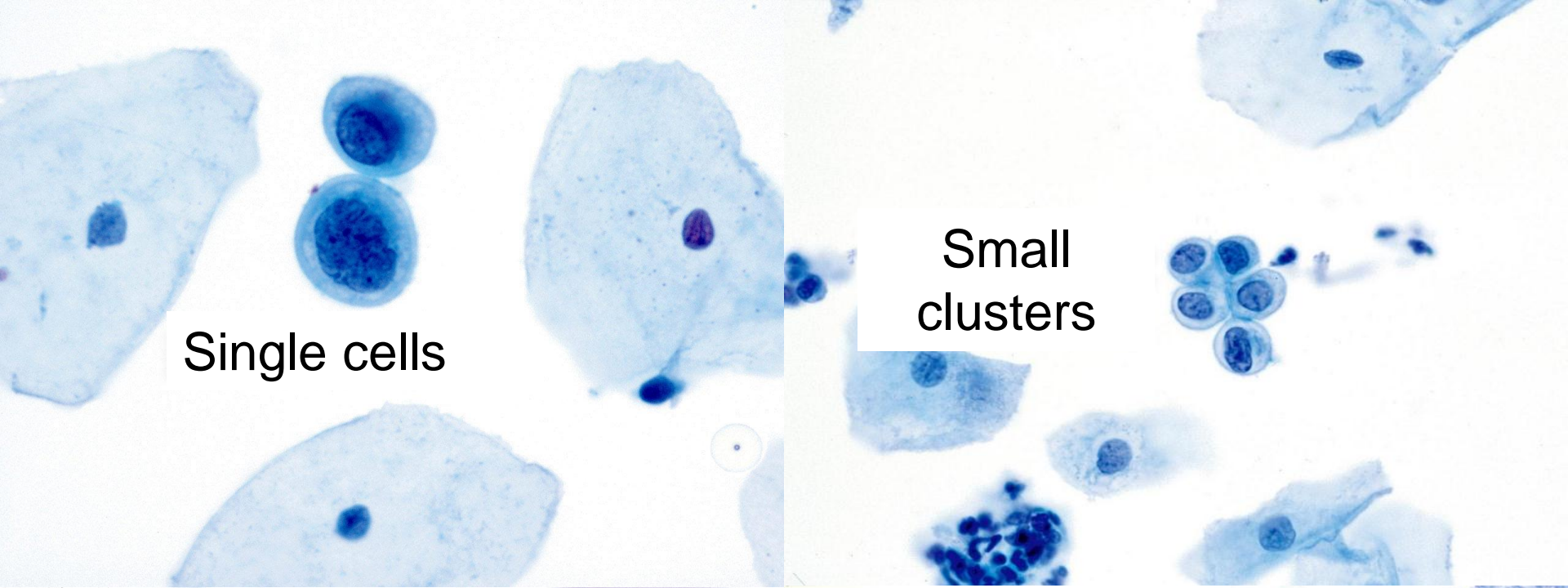
**HSIL: High N:C ratios  
and nuclear variability**

Size variation and  
membrane irregularity

Chromatin abnormal and  
variable

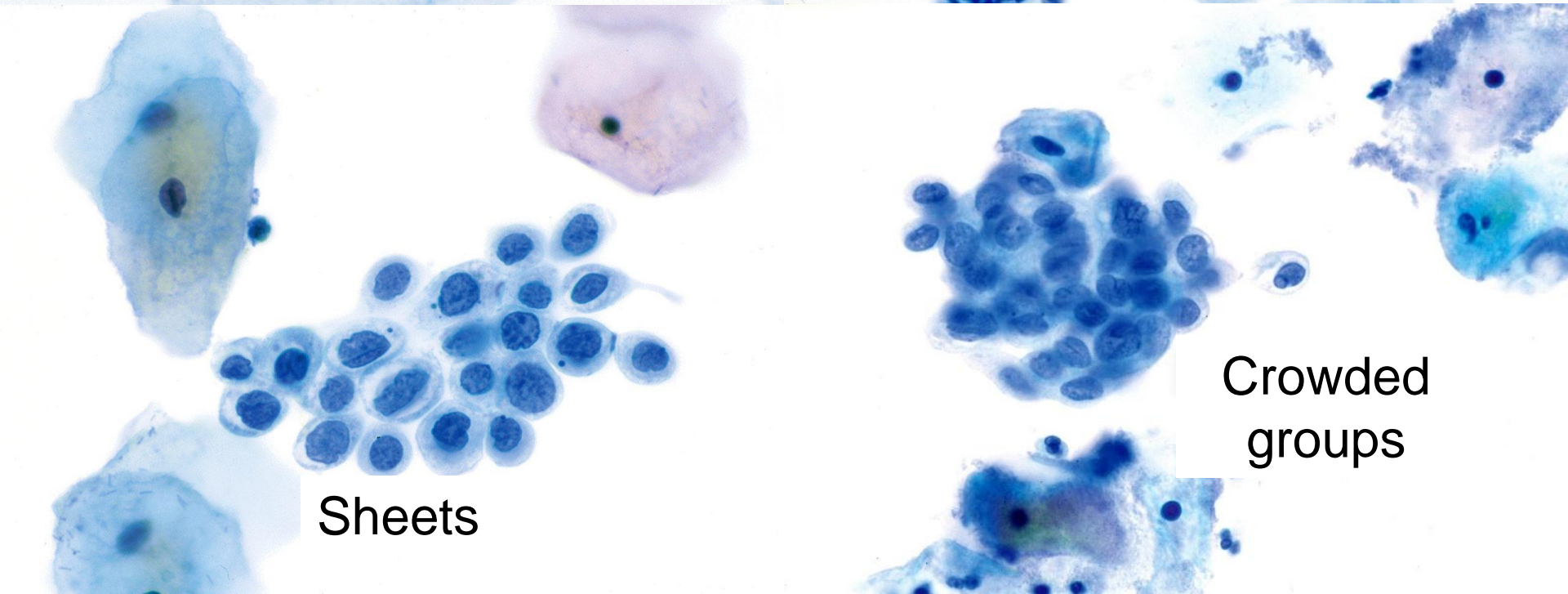
Nucleoli  
sometimes

HOLOGIC



Single cells

Small clusters



Sheets

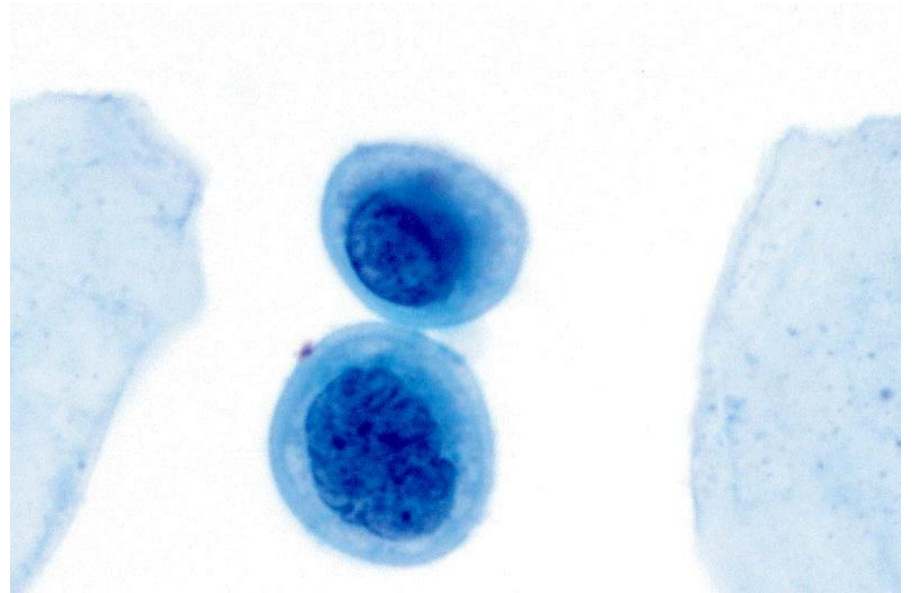
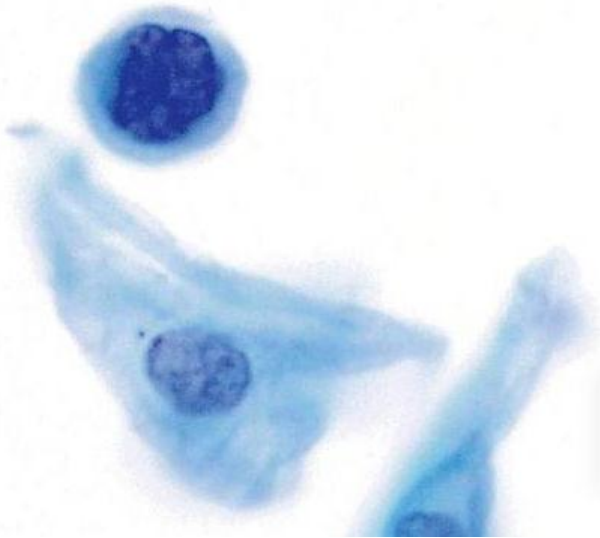
Crowded groups

# 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

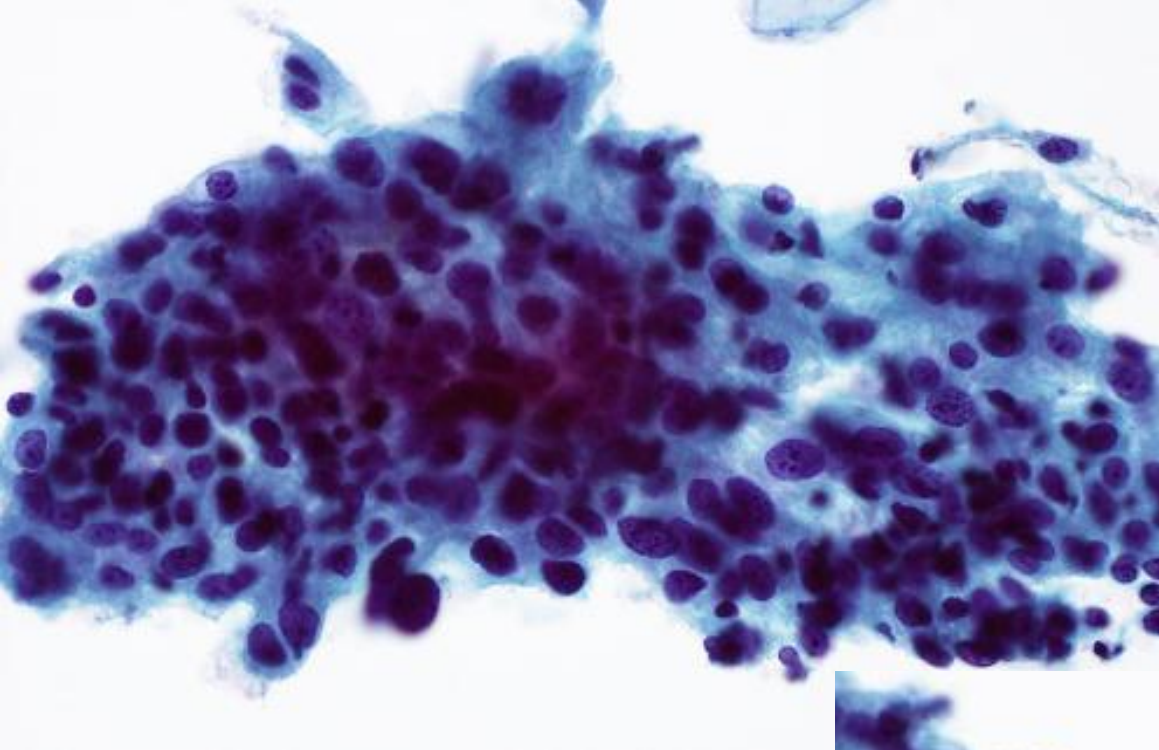
### Cellular features:

- **Nuclei vary significantly and unpredictably**
  - Size, chromasia, chromatin, nuclear border, shape

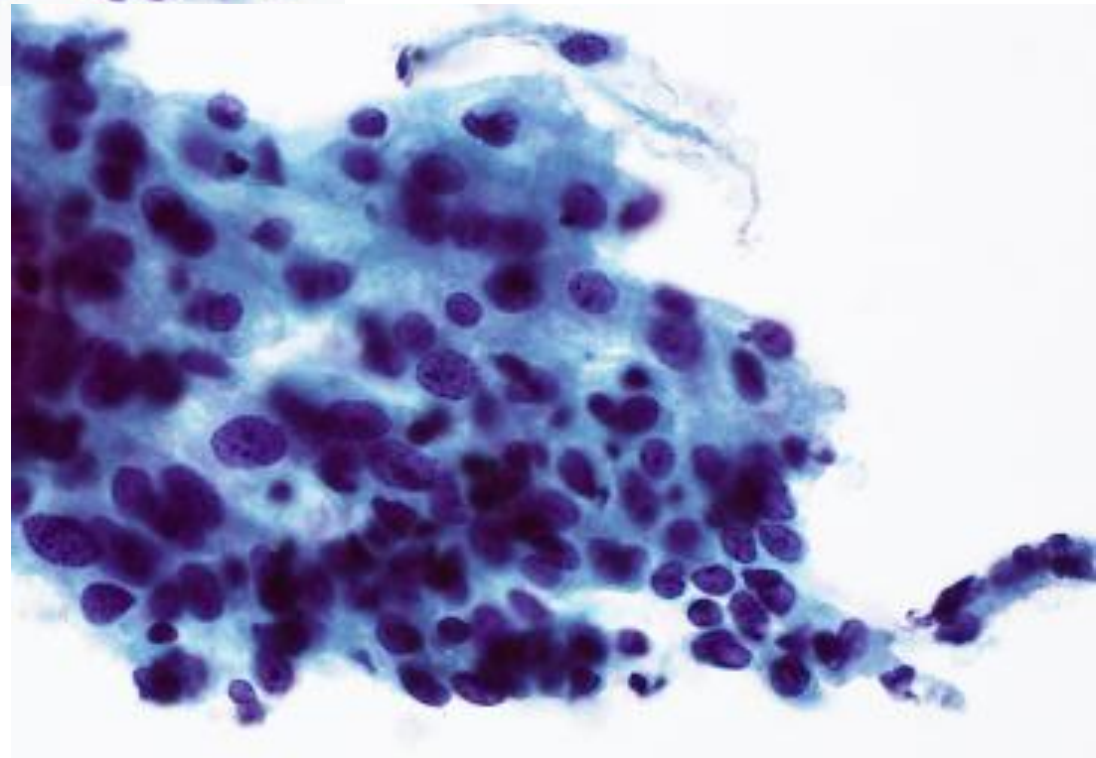
Note: May be little or no nuclear shape irregularity
- May see mitoses (embedded), apoptosis, sticky bare nuclei

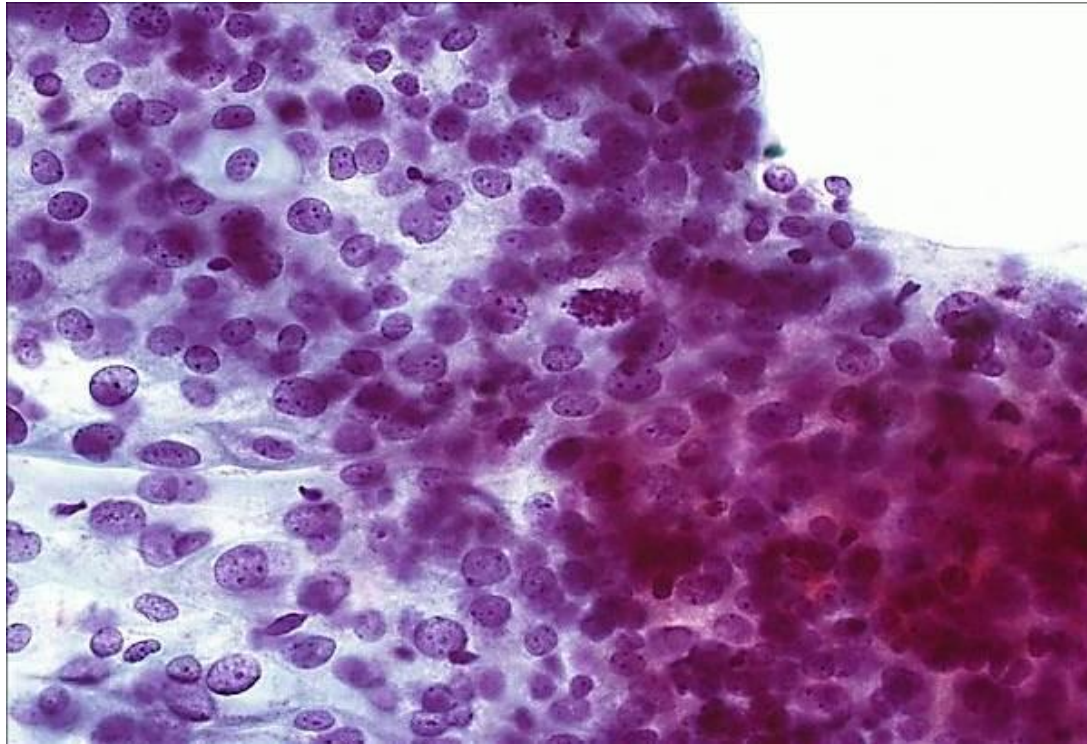
*Acknowledgement: Ron Bowditch*



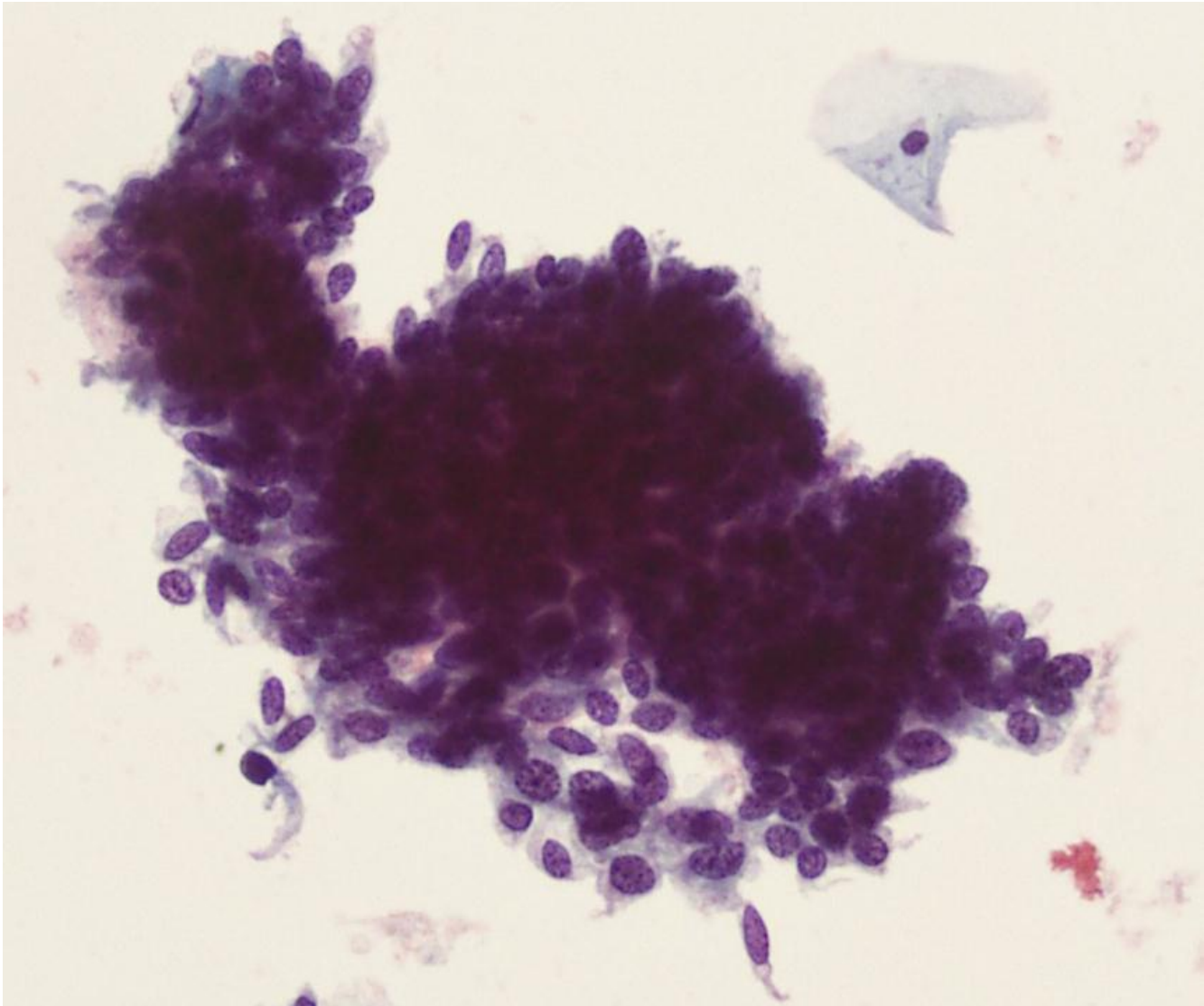


HSIL: Hyperchromatic  
crowded group





Embedded mitoses in HSIL



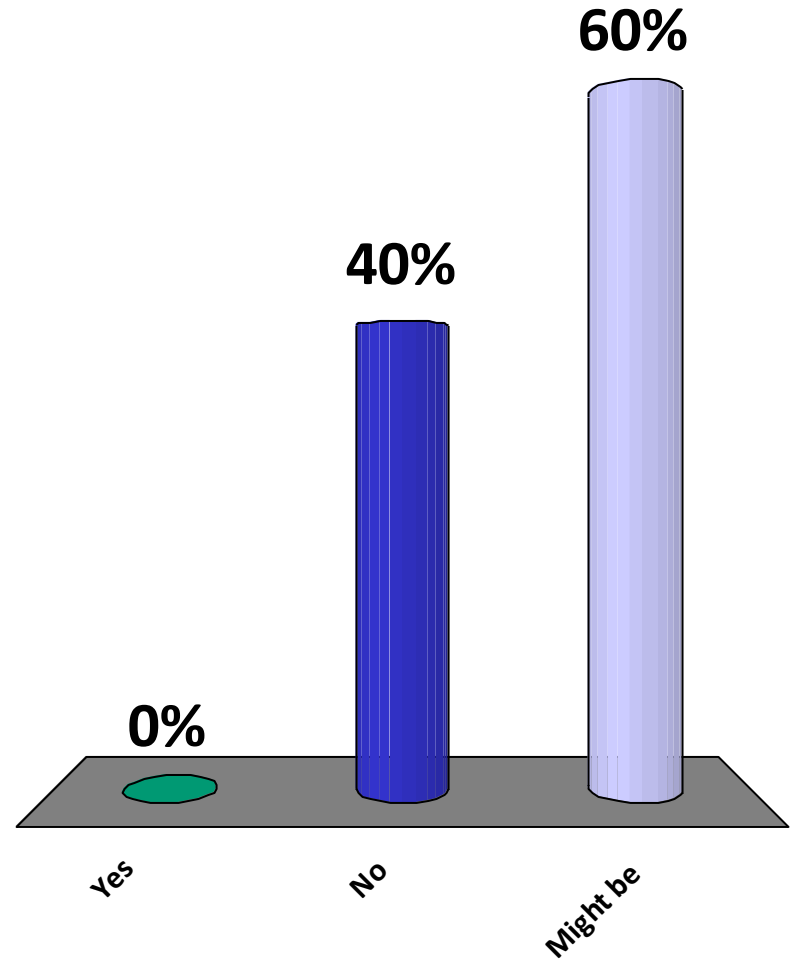
Is this HSIL?

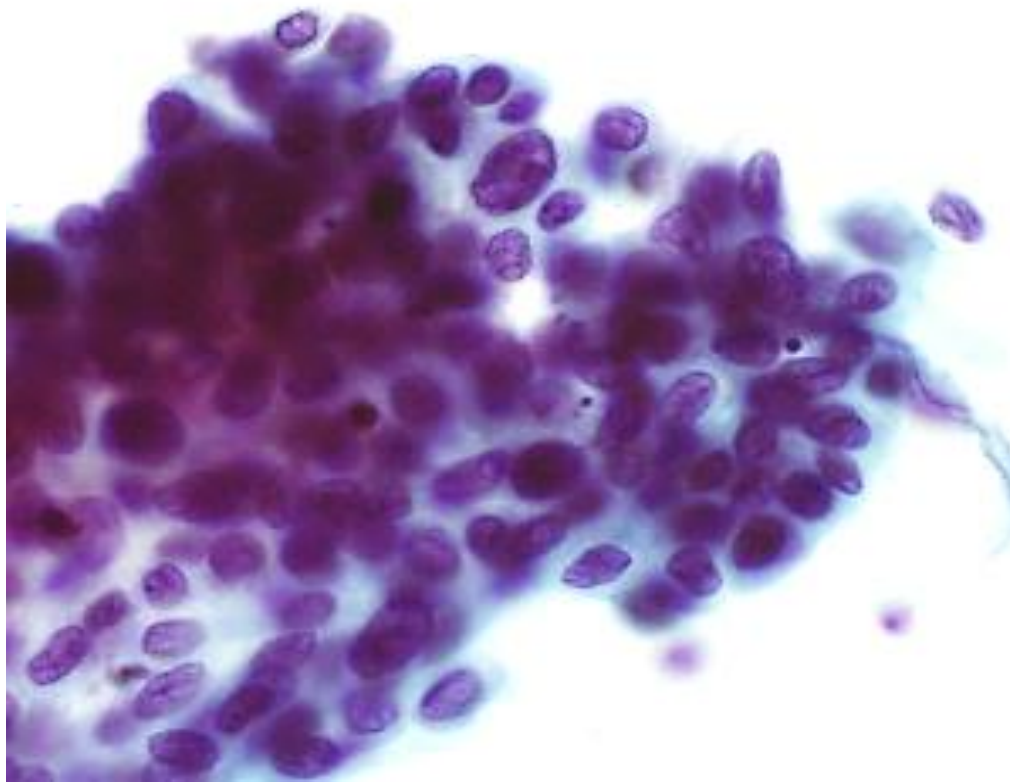
# Is this HSIL?

A. Yes

B. No

C. Might be

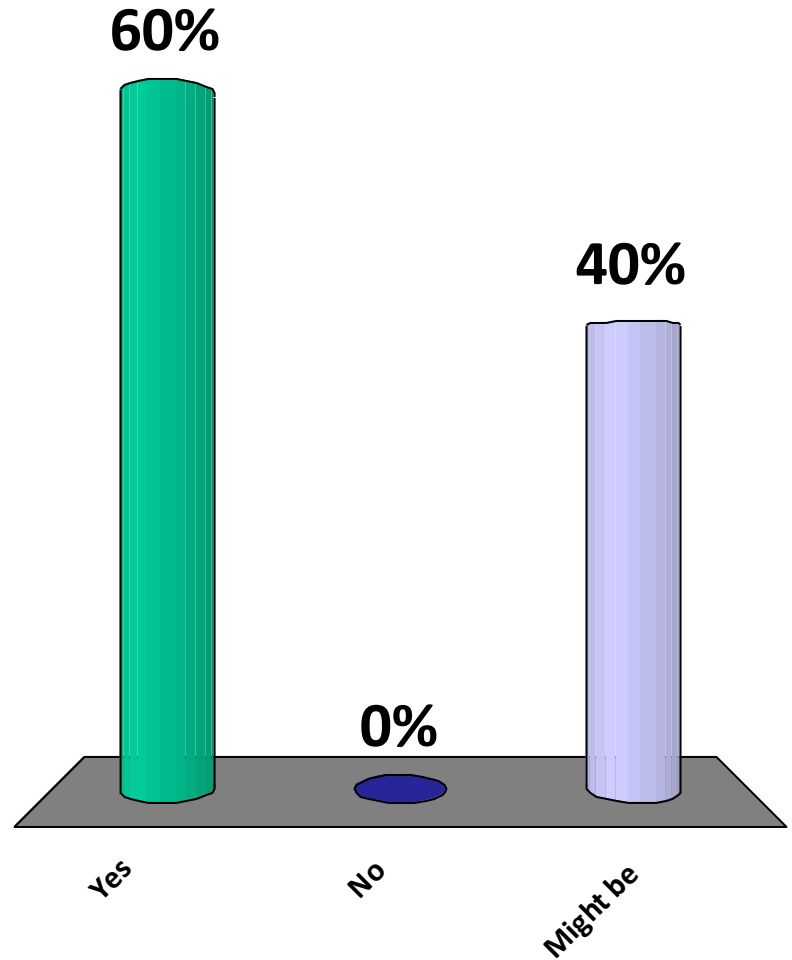




Is this HSIL?

# Is this HSIL?

- A. Yes
- B. No
- C. Might be



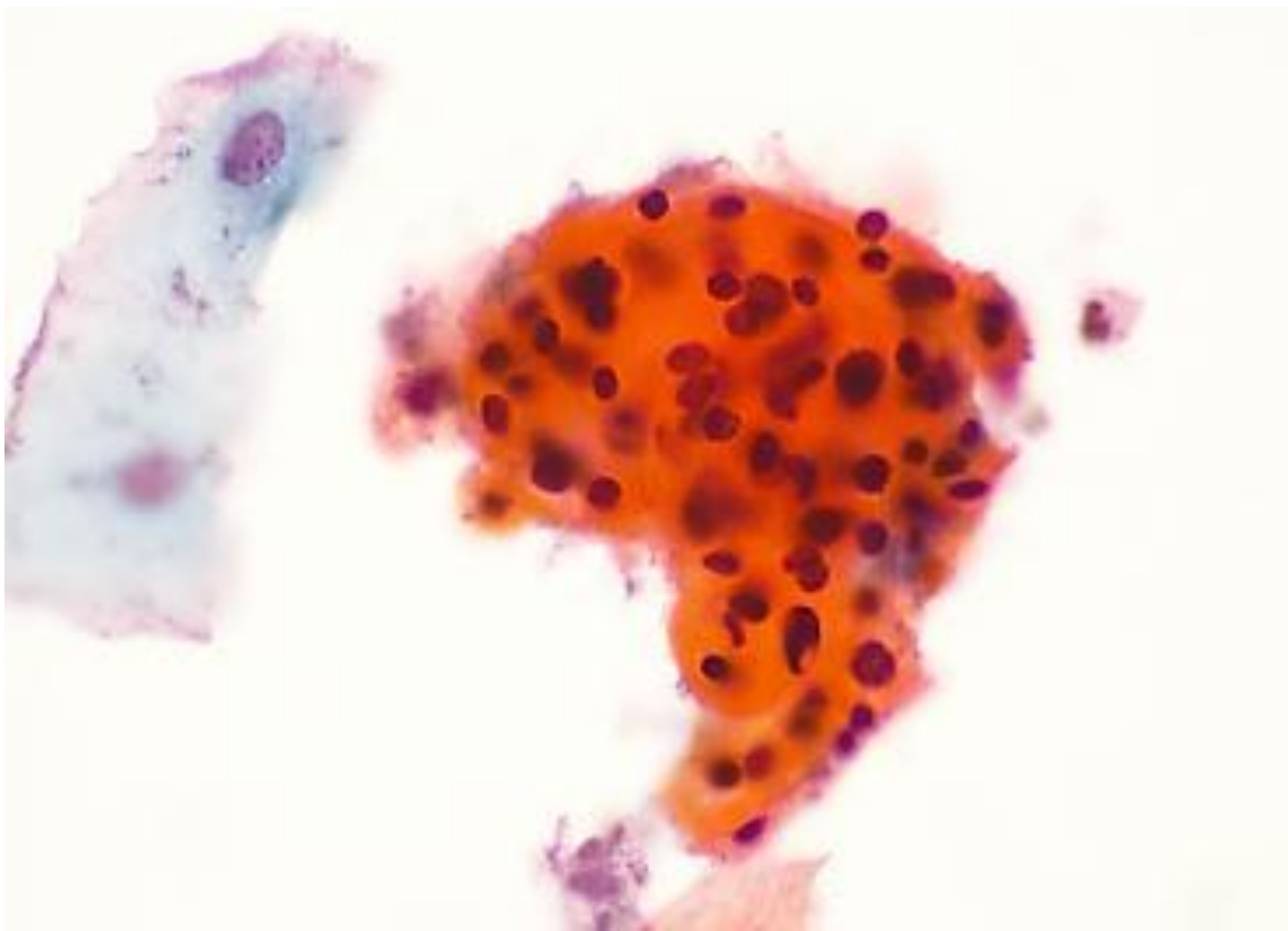
# Hyperchromatic Crowded Groups

## Distinguishing squamous from glandular lesions

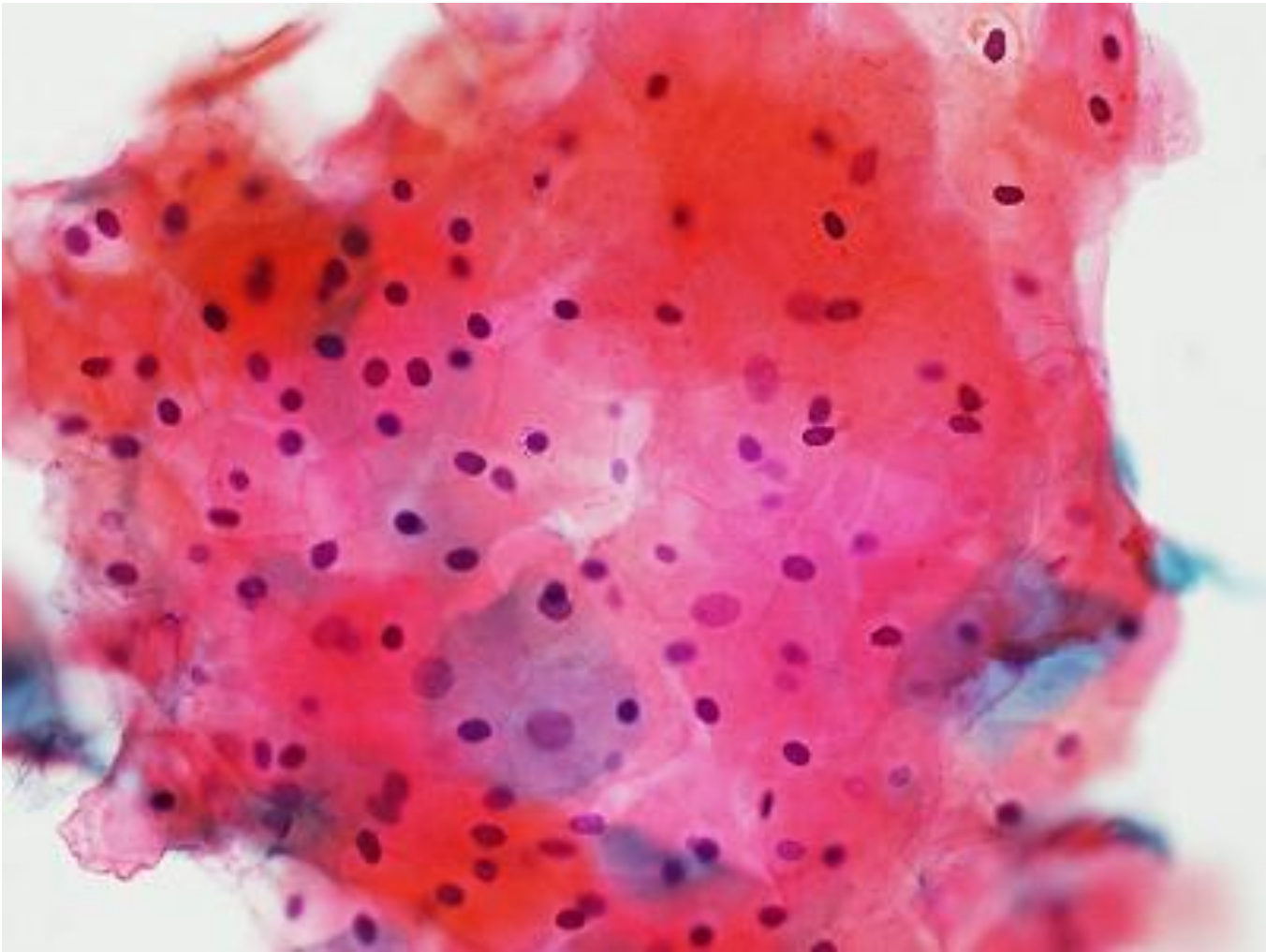
1. Look for architectural and cellular **features of a high-grade lesion**. Consider benign mimics and the clinical context
2. Look for **glandular architectural features** such as
  - Endocervical*: Common border at edge, gland openings, feathering, cytoplasmic tags, strips, rosettes
  - Endometrial*: 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

# 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.

# ASC-H

## Mimics of HSIL

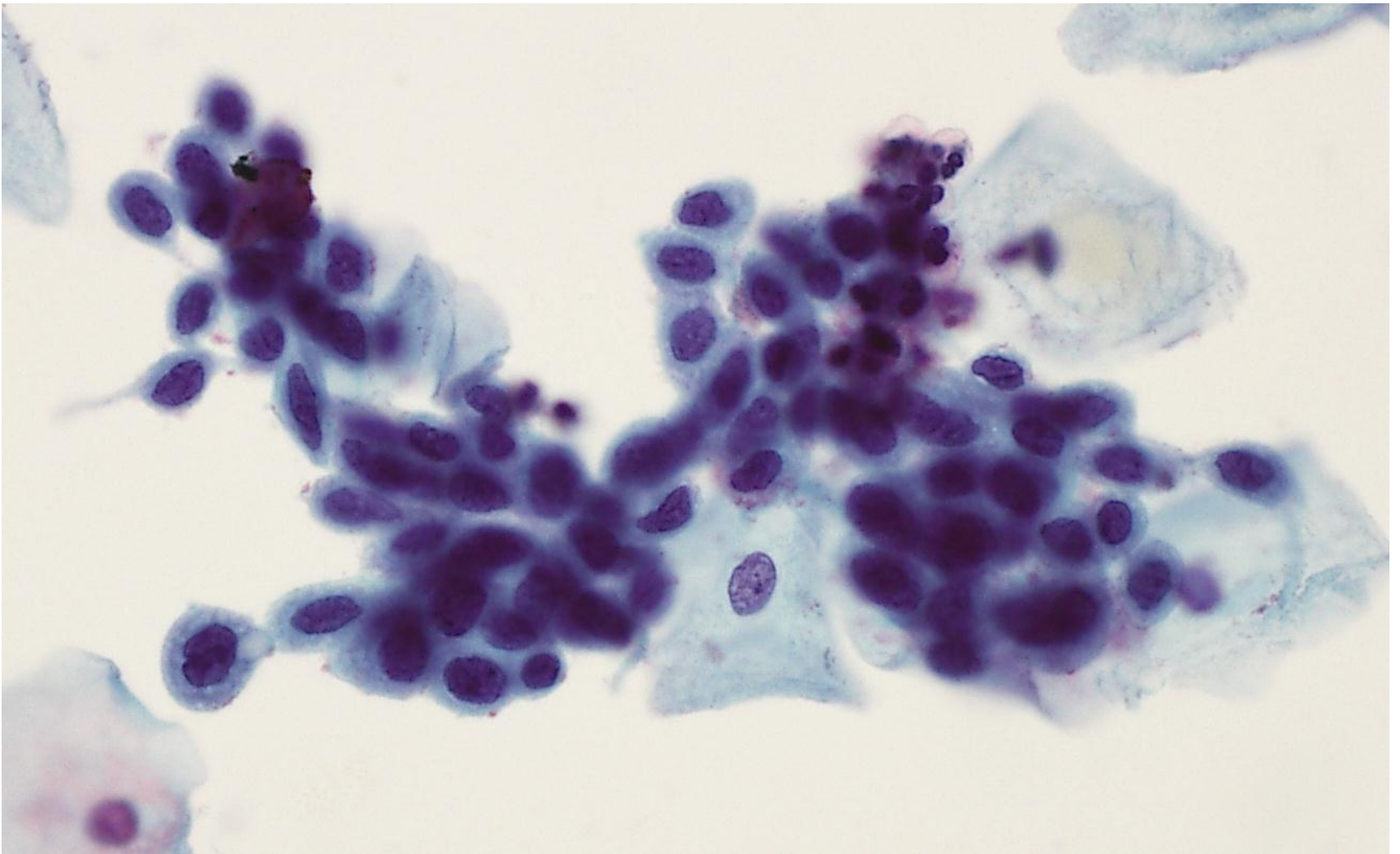
- Immature squamous metaplasia
- Active cervicitis (crowded sheets)
- Post-partum effect
- Atrophy
- High-sampling
- Acute florid HPV infection

## Mimics of SCC

- Atypical repair
- Radiation-induced change

## Technically difficult to interpret

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

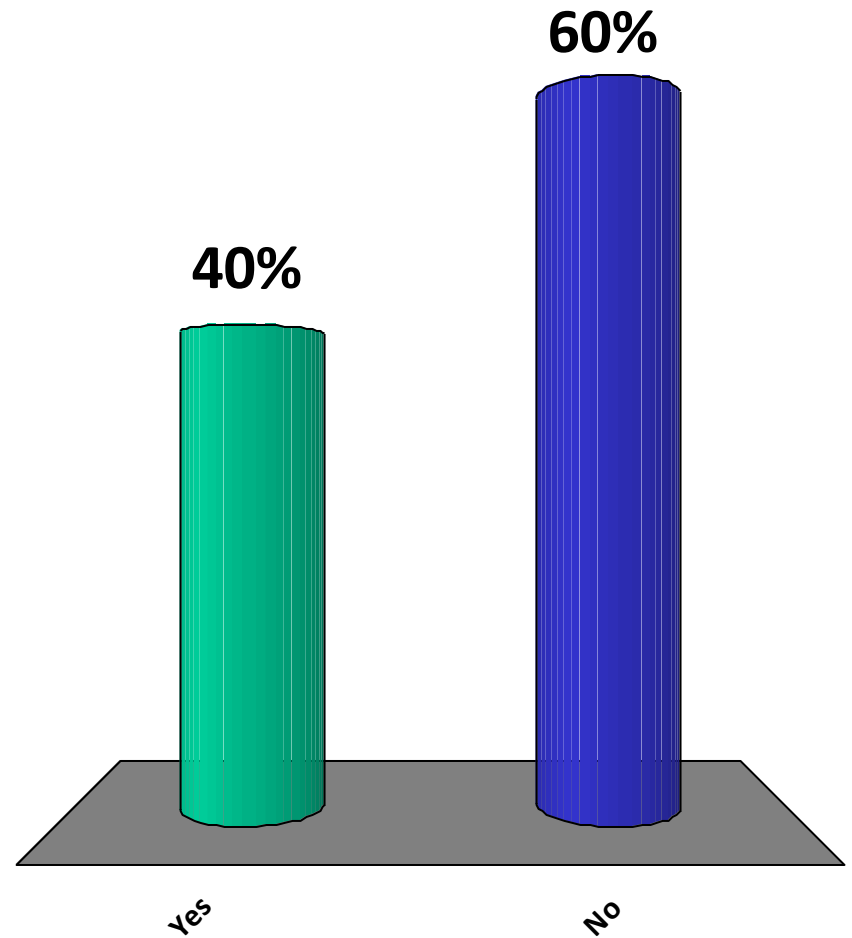


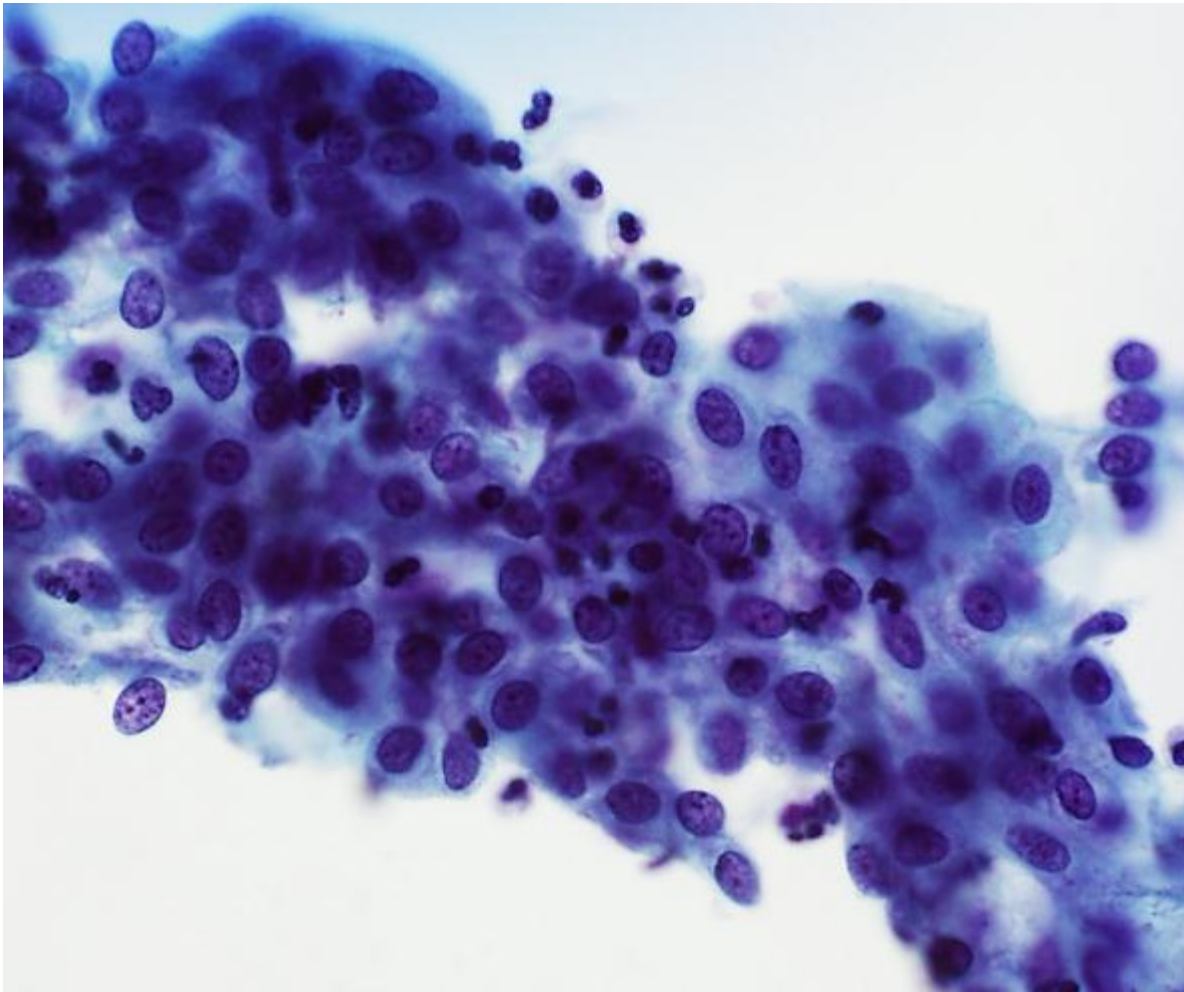
Post-partum 34 yrs: Reported as ASC-H  
HSIL or benign/reactive metaplasia?

# Is this HSIL?

A. Yes

B. No



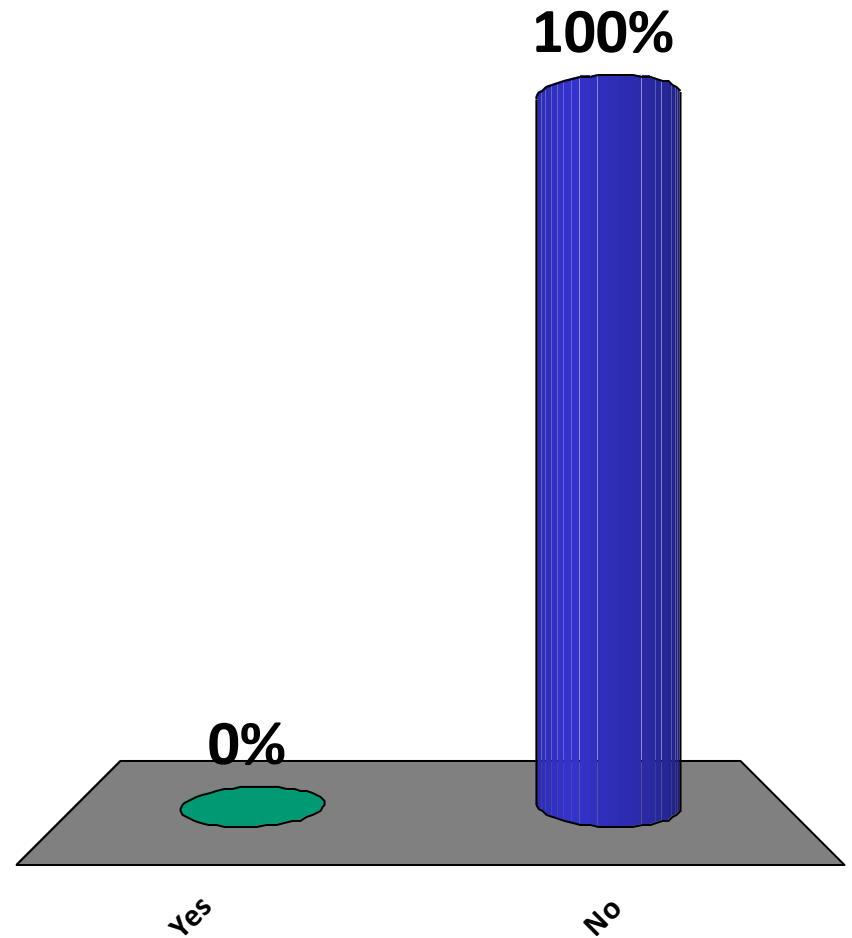


35 years. Reported as ASC-H  
Is this HSIL?

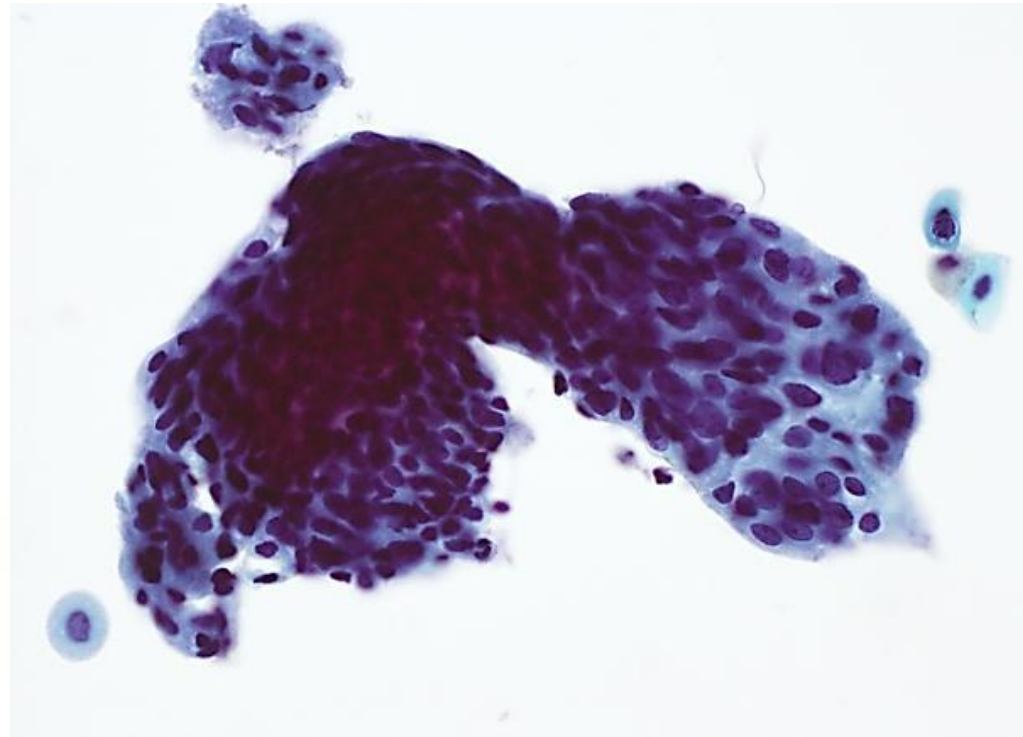
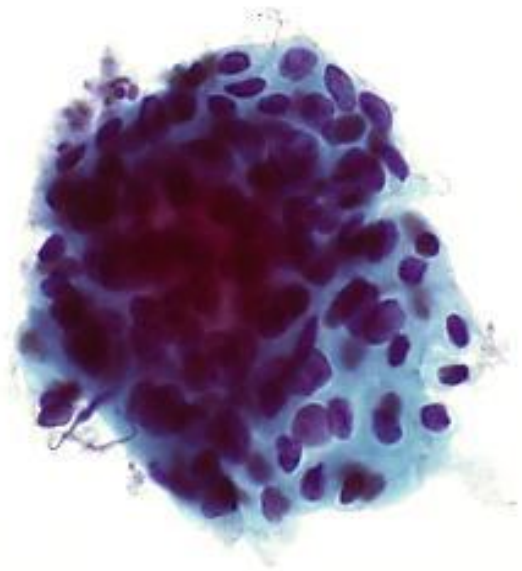
# Is this HSIL?

A. Yes

B. No



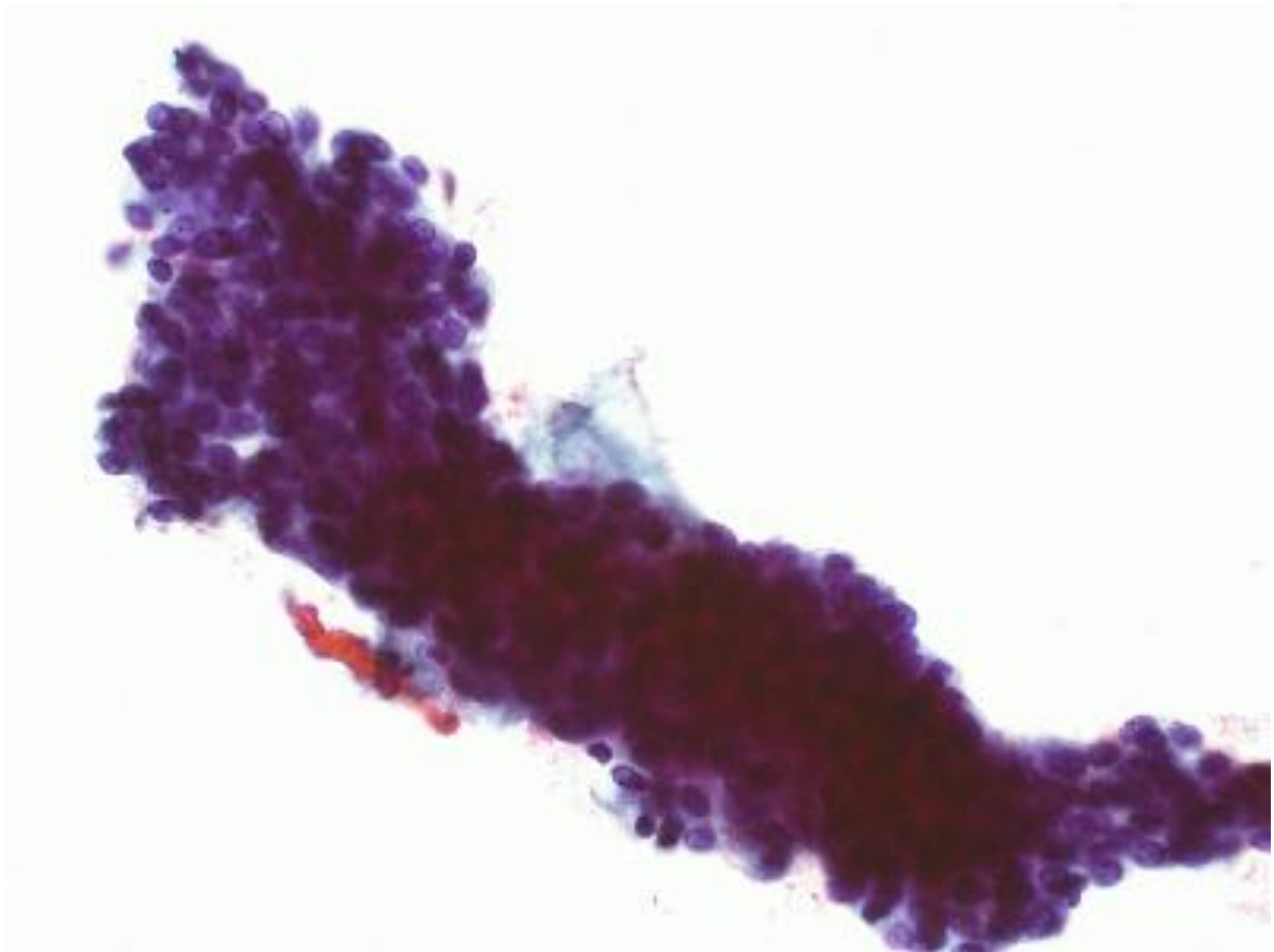




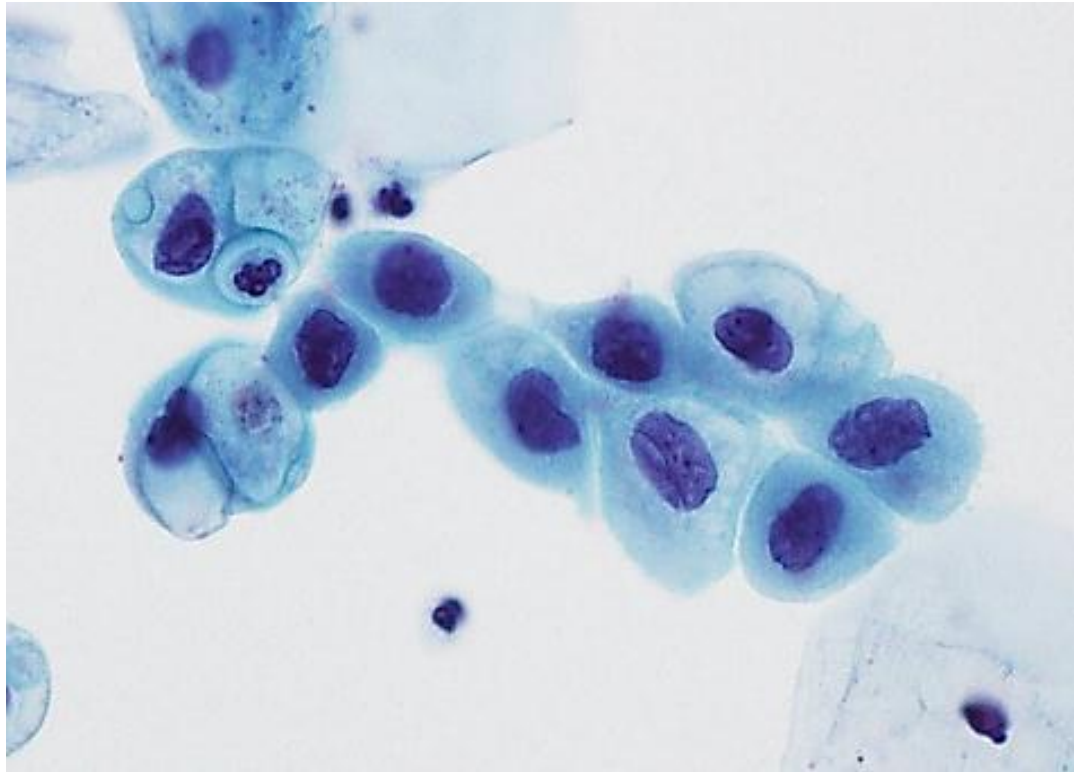
ASC-H in atrophy

FU: Left = CIN 3

Right = atrophy only



High Sampling



What would you report this as?

A. LSIL

B. Benign reactive change

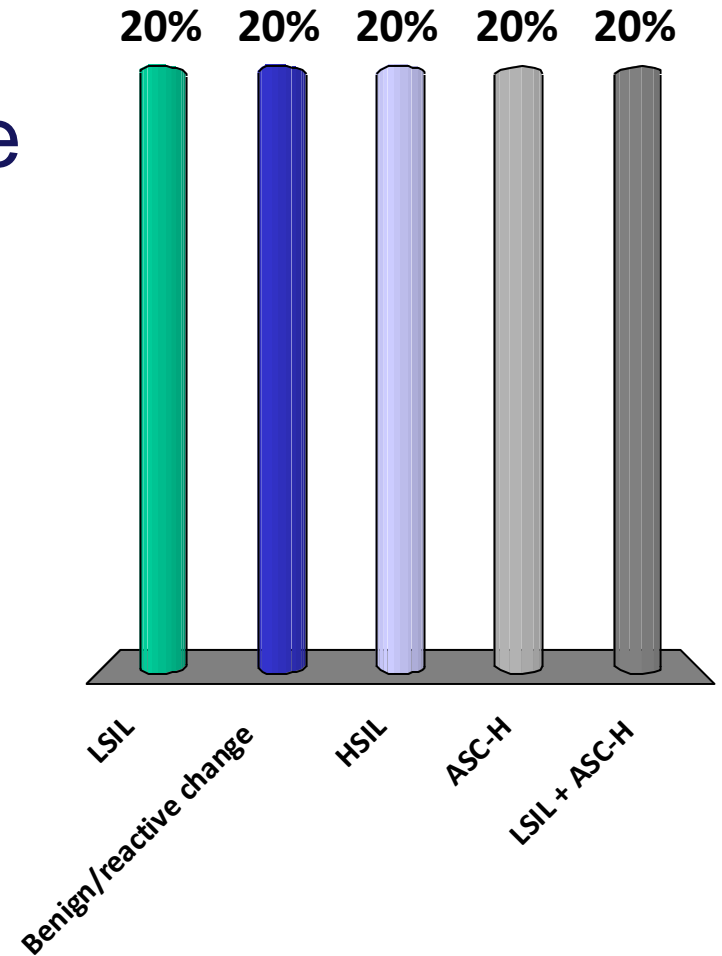
C. HSIL

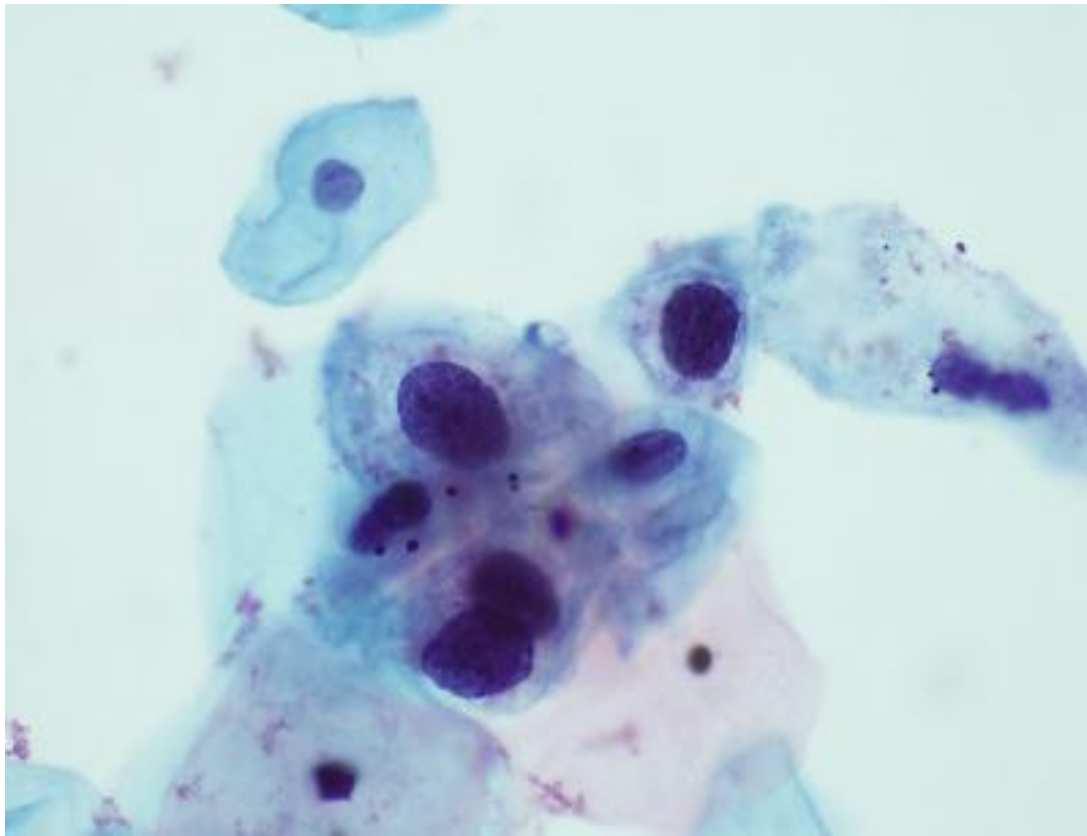
D. ASC-H

E. LSIL + ASC-H

# What would you report this as?

- A. LSIL
- B. Benign/reactive change
- C. HSIL
- D. ASC-H
- E. LSIL + ASC-H



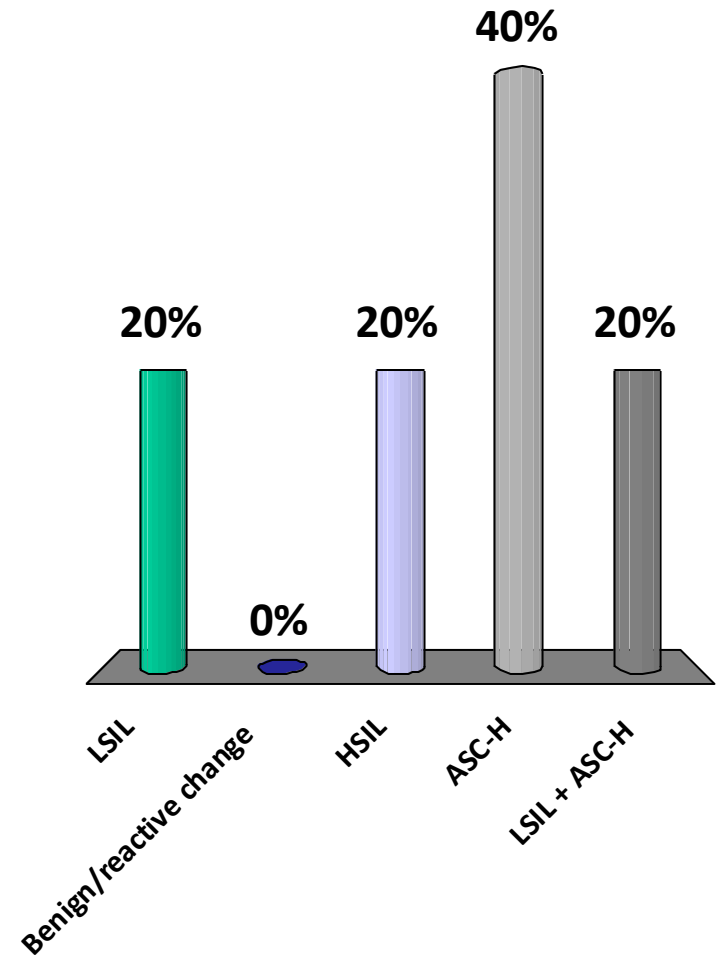


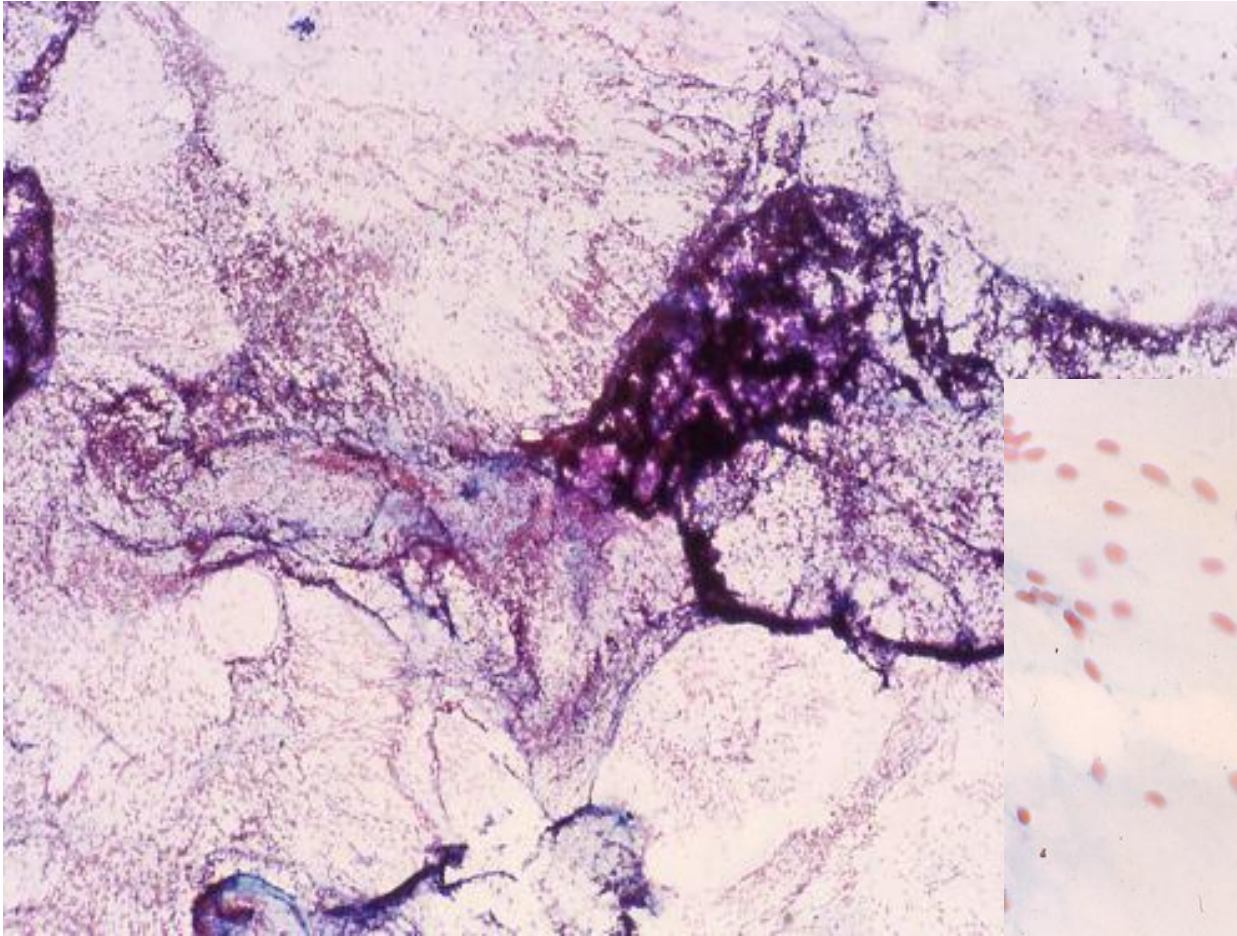
**What would you report this as?**

- A. LSIL
- B. Benign reactive change
- C. HSIL
- D. ASC-H
- E. LSIL + ASC-H

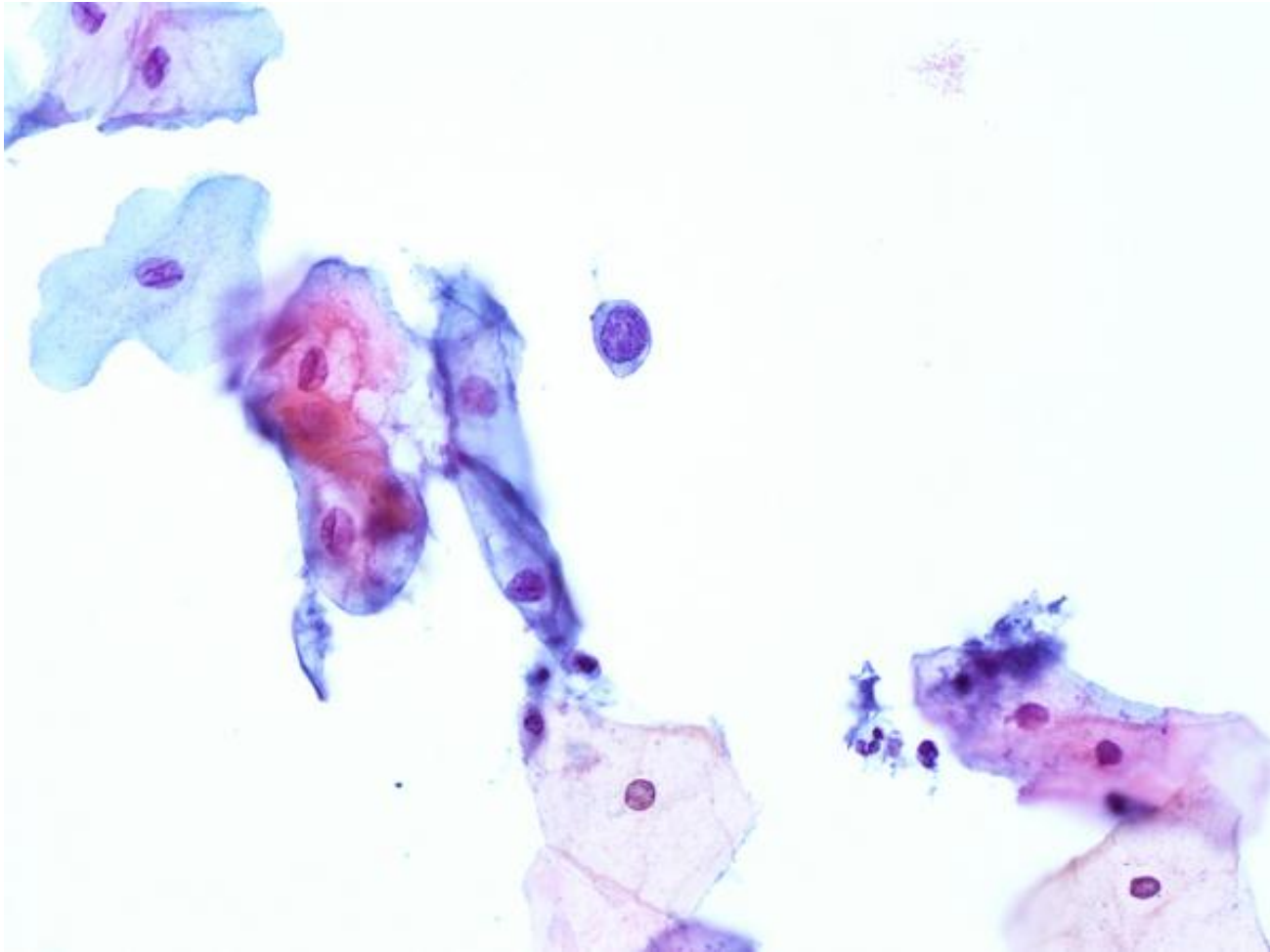
# What would you report this as?

- A. LSIL
- B. Benign/reactive change
- C. HSIL
- D. ASC-H
- E. LSIL + ASC-H



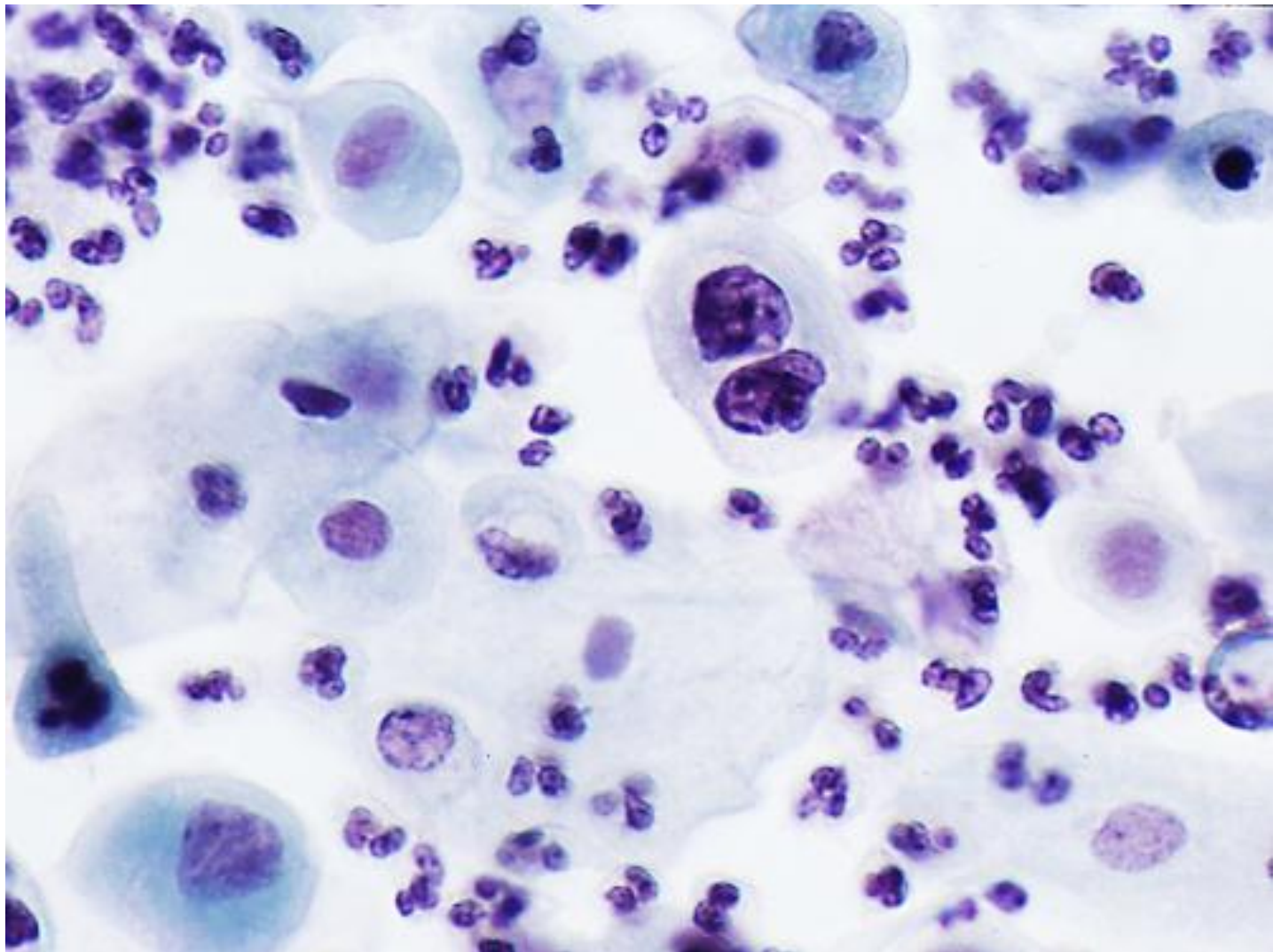


Reported as Unsatisfactory  
Missed adeno-squamous carcinoma

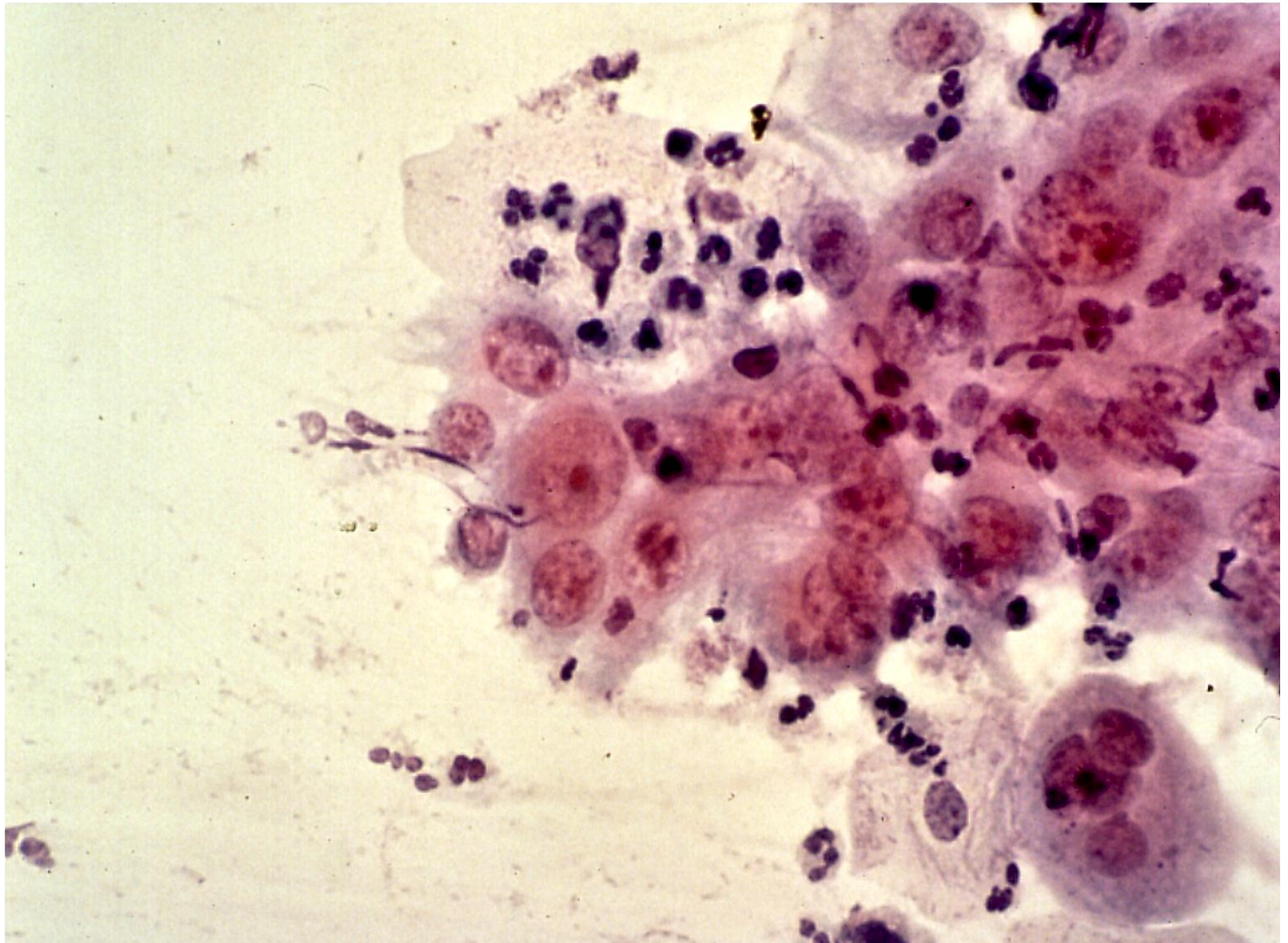


HSIL: Single cell

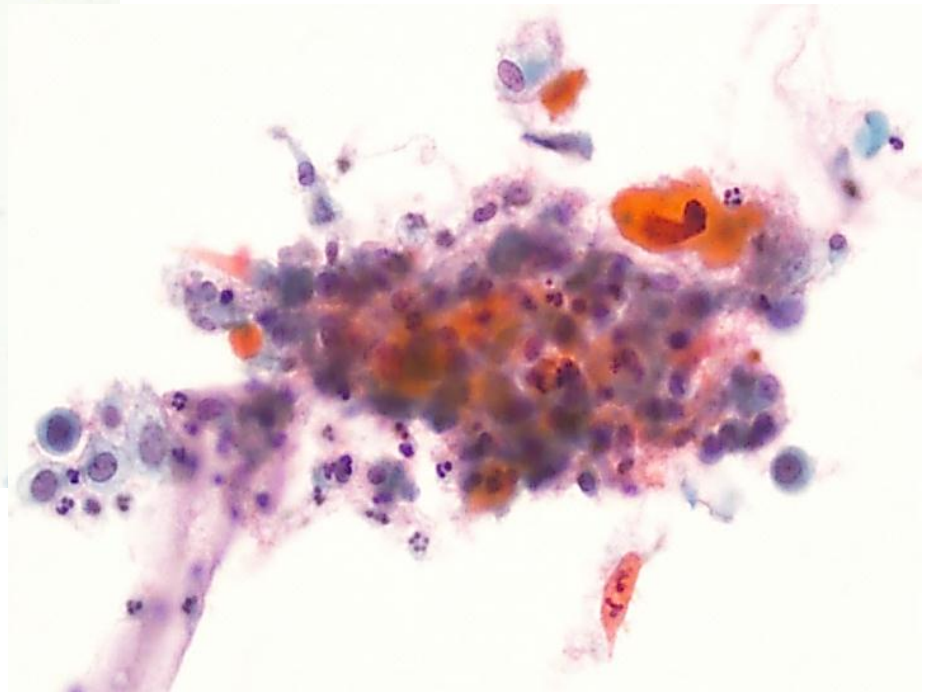
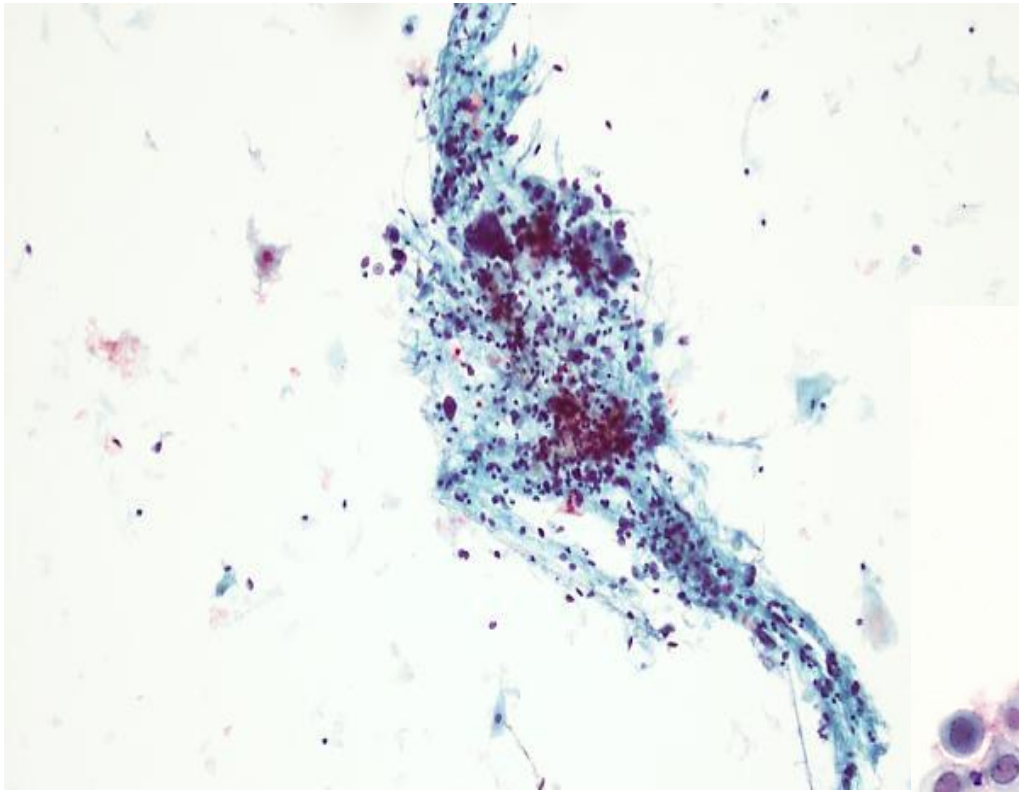




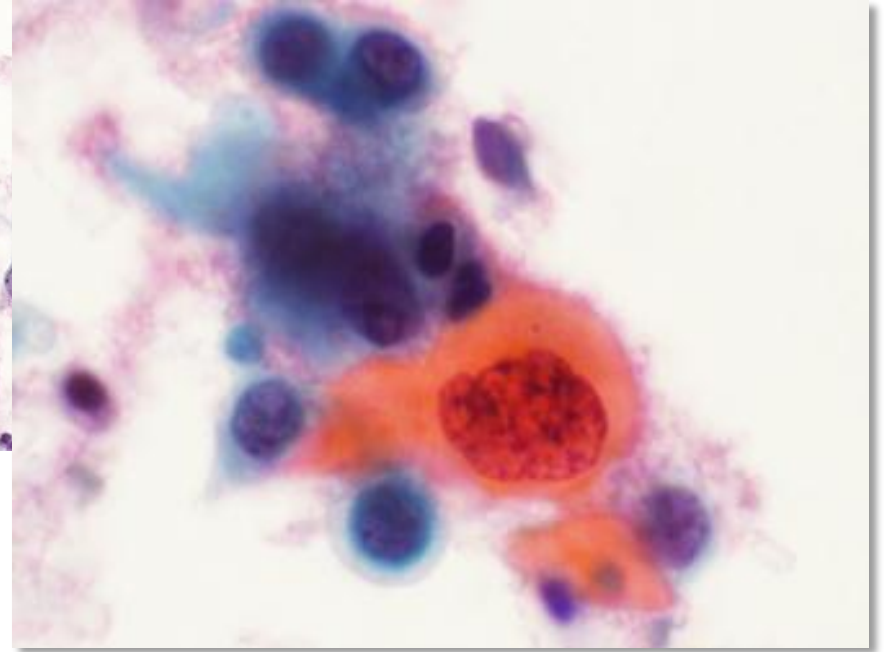
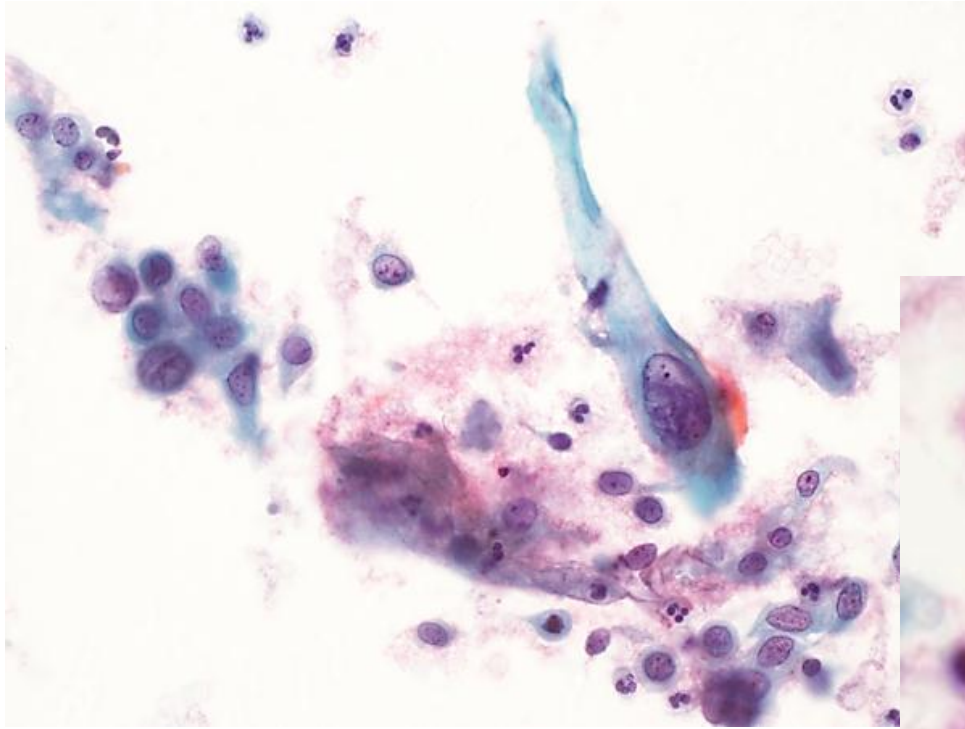
ASC-H: Vaginal smear. Previous VAIN  
Degenerate hyperchromatic suspicious cells  
Follow-up VAIN 3



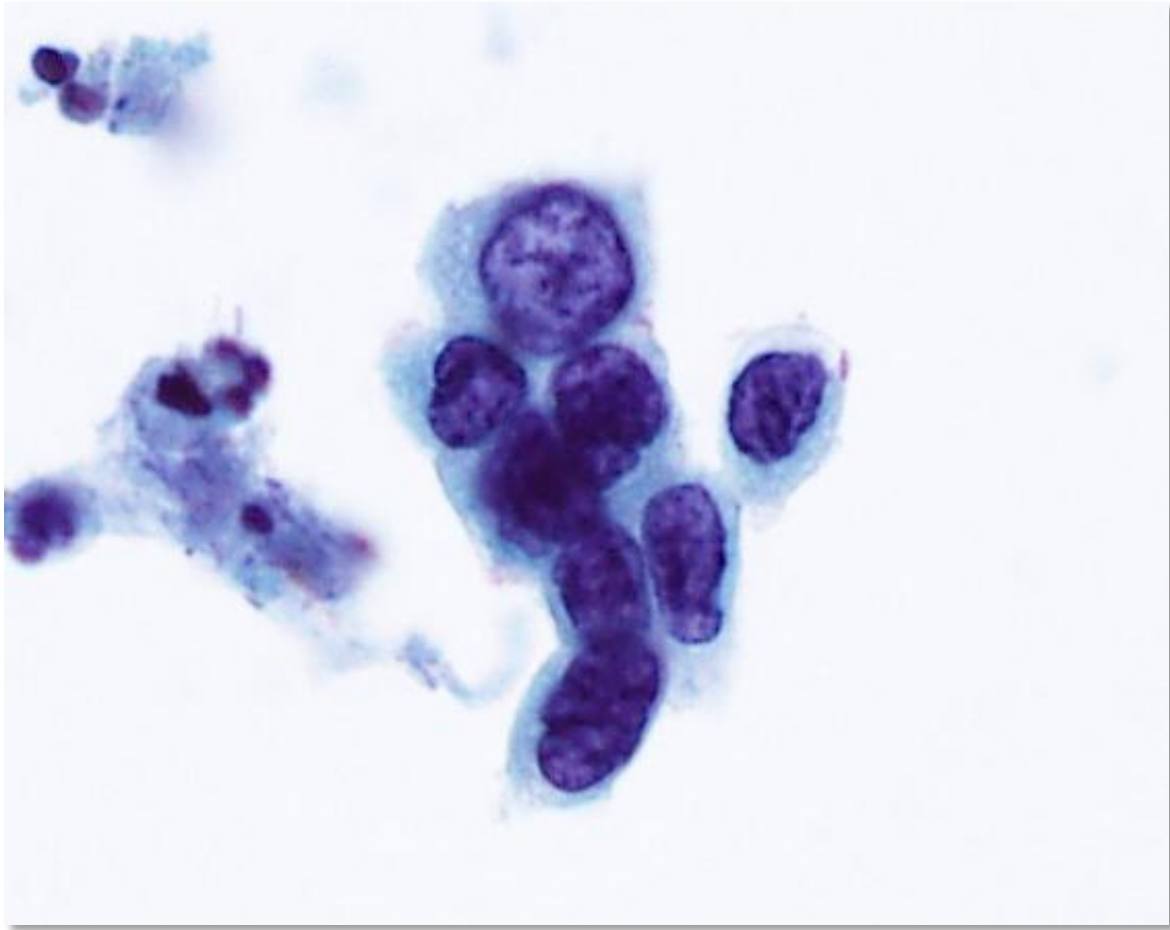
Follow-up: Micro-invasive SCC



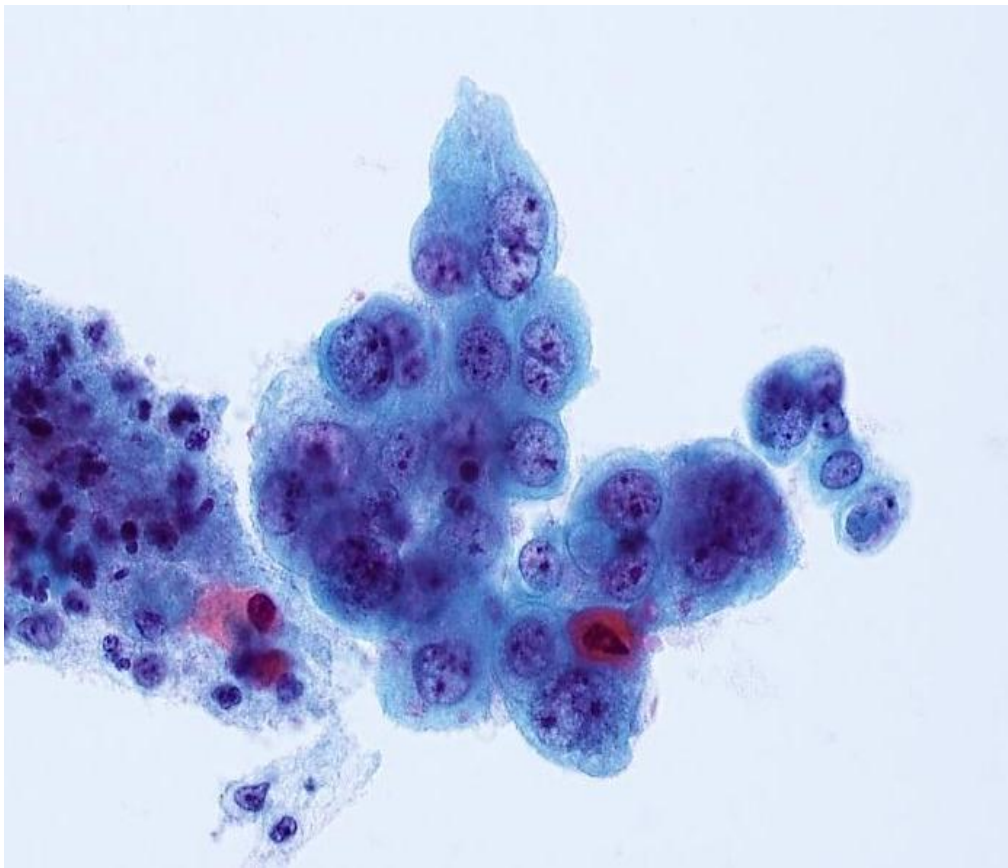
**Squamous cell carcinoma**  
Low-power appearance, diathesis



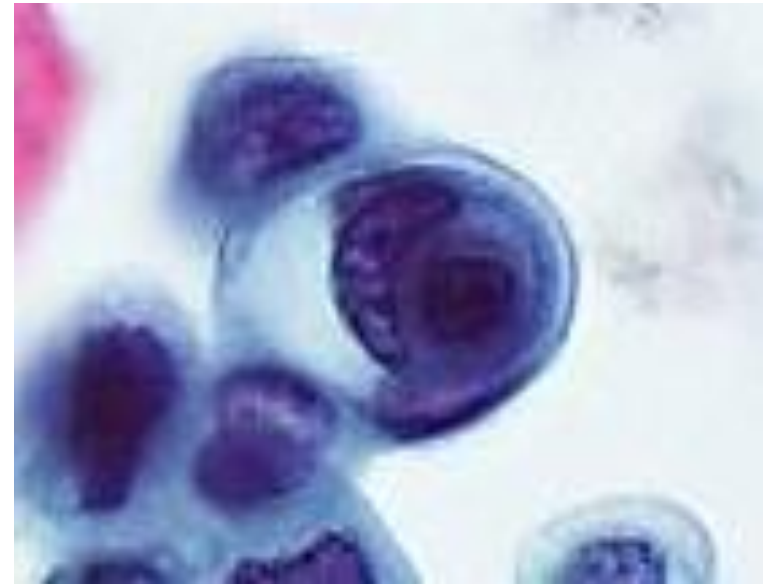
Marked pleomorphism



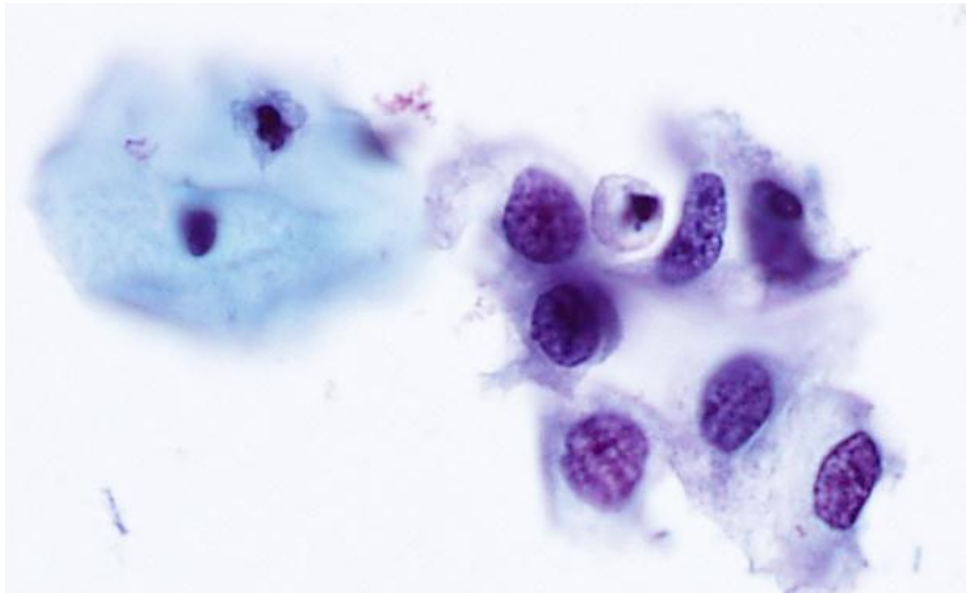
Chromatin clumping and clearing



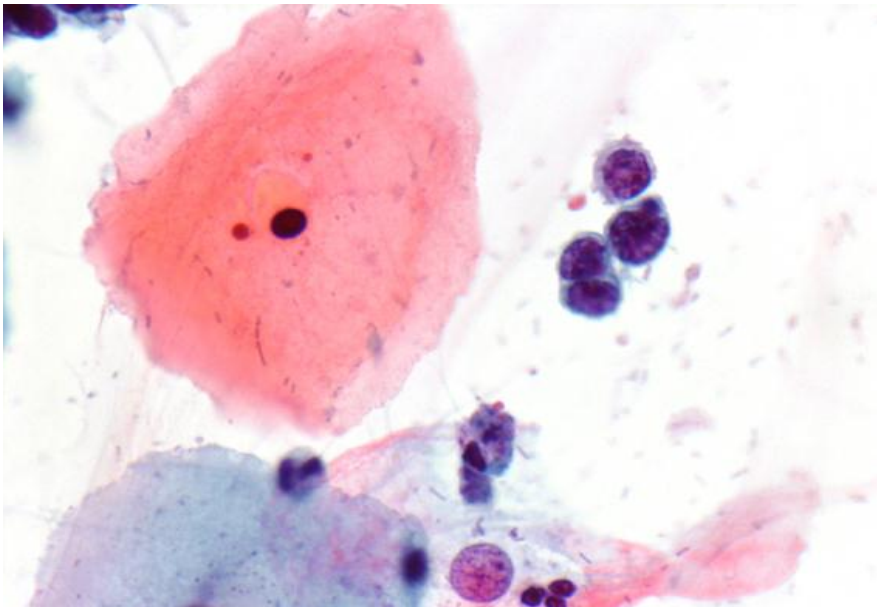
**Nucleoli**



**Cell-in-cell engulfment**



SCC: Large  
cells



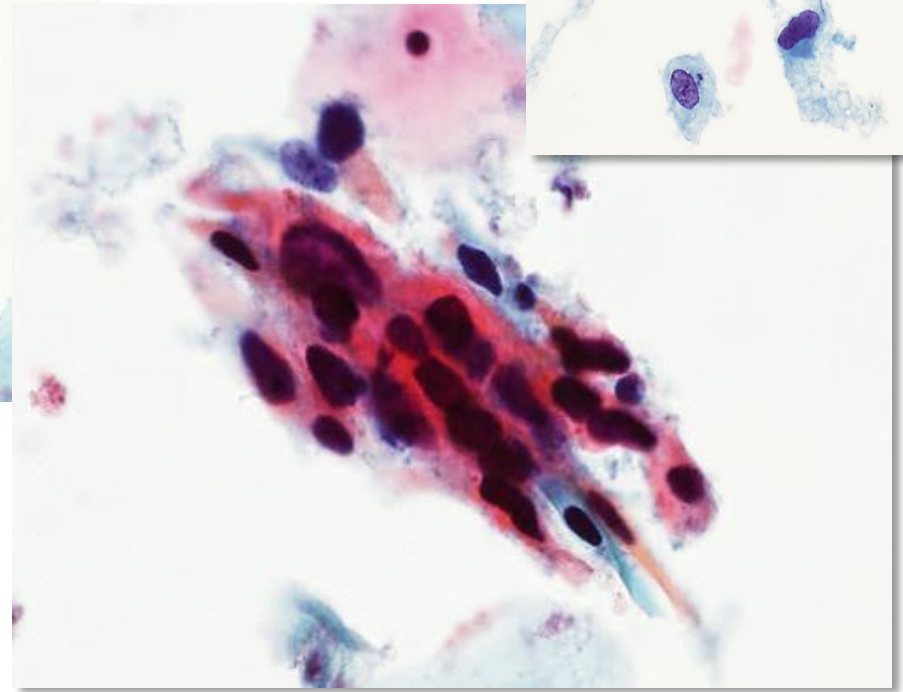
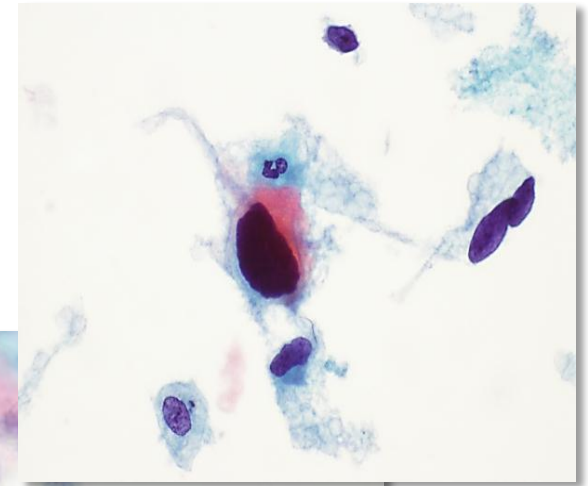
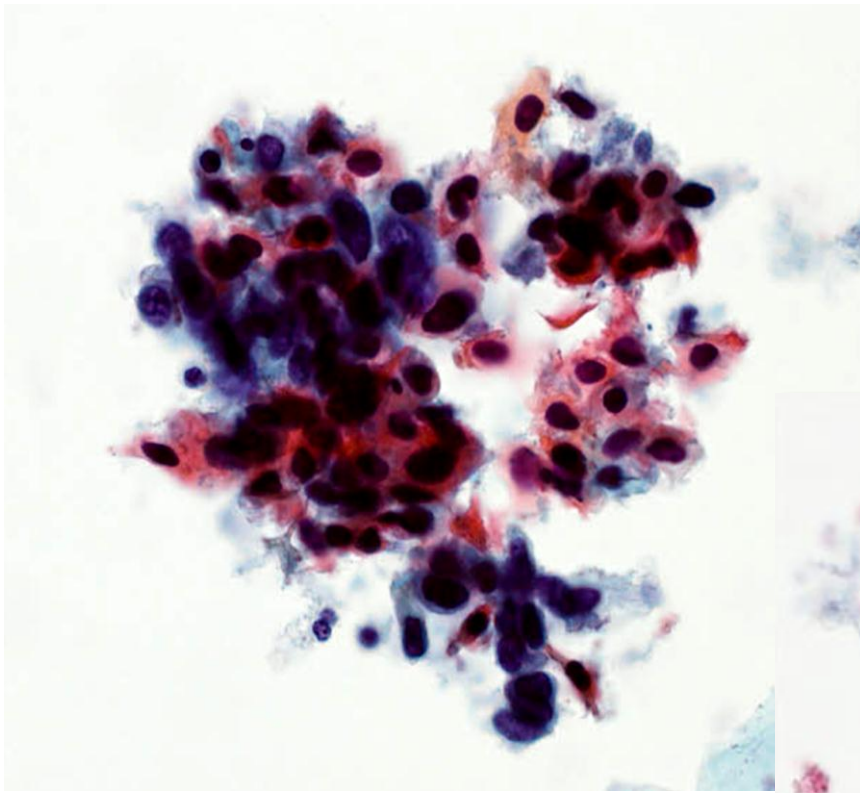
SCC: Small  
cells

# Keratinising SCC

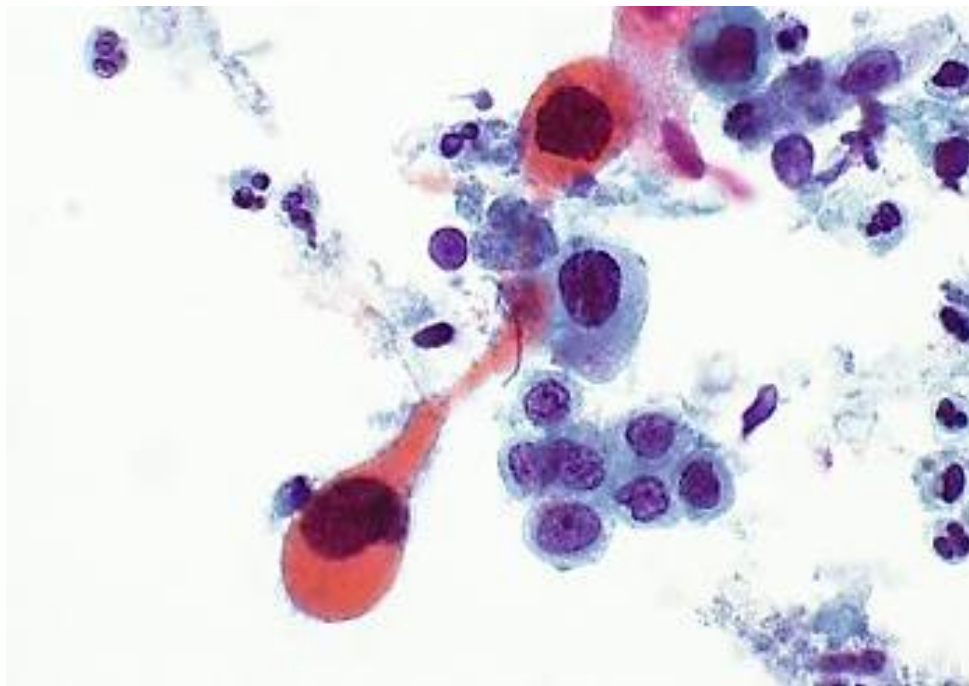
- clean background or diathesis
- number of abnormal cells very variable. May be few.
- large highly pleomorphic squamous cells, spindle and tadpole forms. Can be small highly keratinised cells with dense pyknotic nuclei.
- nuclei are large for cytoplasmic maturation. Often dense and opaque.
- coarsely 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

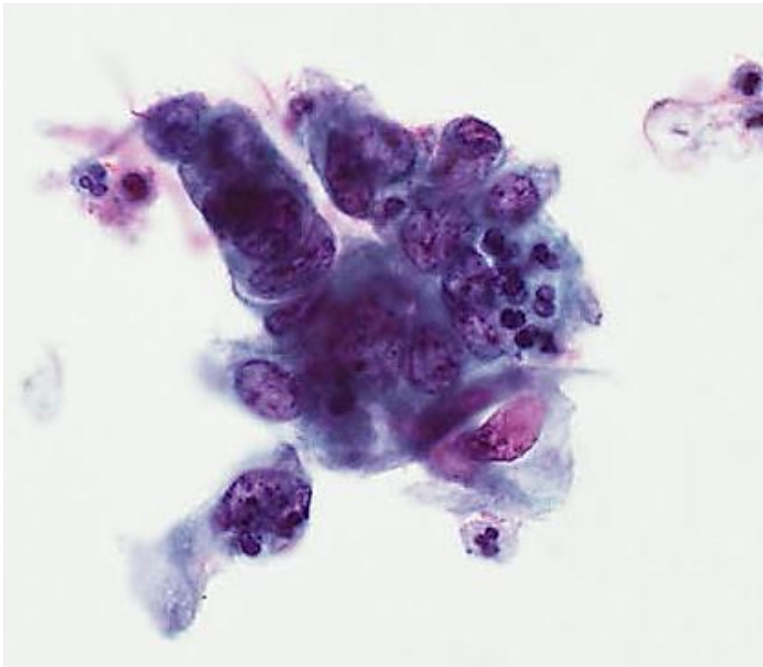
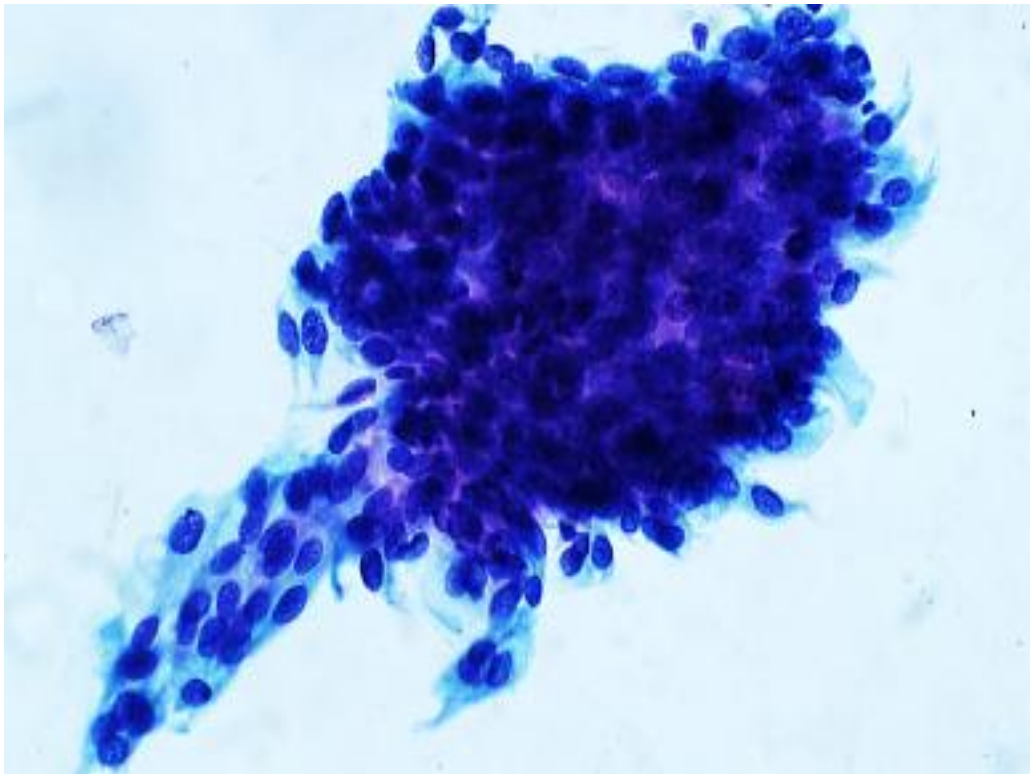
# Non-keratinising SCC

- 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

# The NZ Cervical Cancer Audit 2000 - 2002

- 336 smears from 178 women taken 4 years or less before a histological diagnosis of invasive cervical cancer were rescreened
- Mostly conventional smears, some ThinPrep samples
- for smears preceding SCC which were upgraded to “high-grade”:
  - 50% had less than 50 high-grade cells
  - 33% had single cells only
  - 22% showed bland nuclear chromatin
  - 8% showed small cell size