NCPTS

The Squamous Spectrum

Predicting squamous lesions of the cervix by cervical cytology

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2017

Bethesda 2001

Atypical Squamous Cells (ASC)

- of undetermined significance (ASC-US)
- cannot exclude HSIL (ASC-H)

LSIL: Low-grade Squamous Intraepithelial Lesion

HSIL: High-grade Squamous Intraepithelial Lesion

- with features suspicious for invasion

Squamous Cell Carcinoma

Squamous abnormalities

Cytology	NZ Samples *
ASC-US	1.9%
LSIL	3.6%
ASC-H	0.6%
HSIL	1.1%

- clinical outcome justifies cytology result categories
- ASC-US + LSIL cytology identifies almost as many HSIL histology cases as ASC-H + HSIL cytology

**% of satisfactory samples Jan-June 2016 NCSP Monitoring Report 45*

HSIL

Cells - small or intermediate size. Usually non-keratinised.

- arranged singly, in sheets or crowded groups.

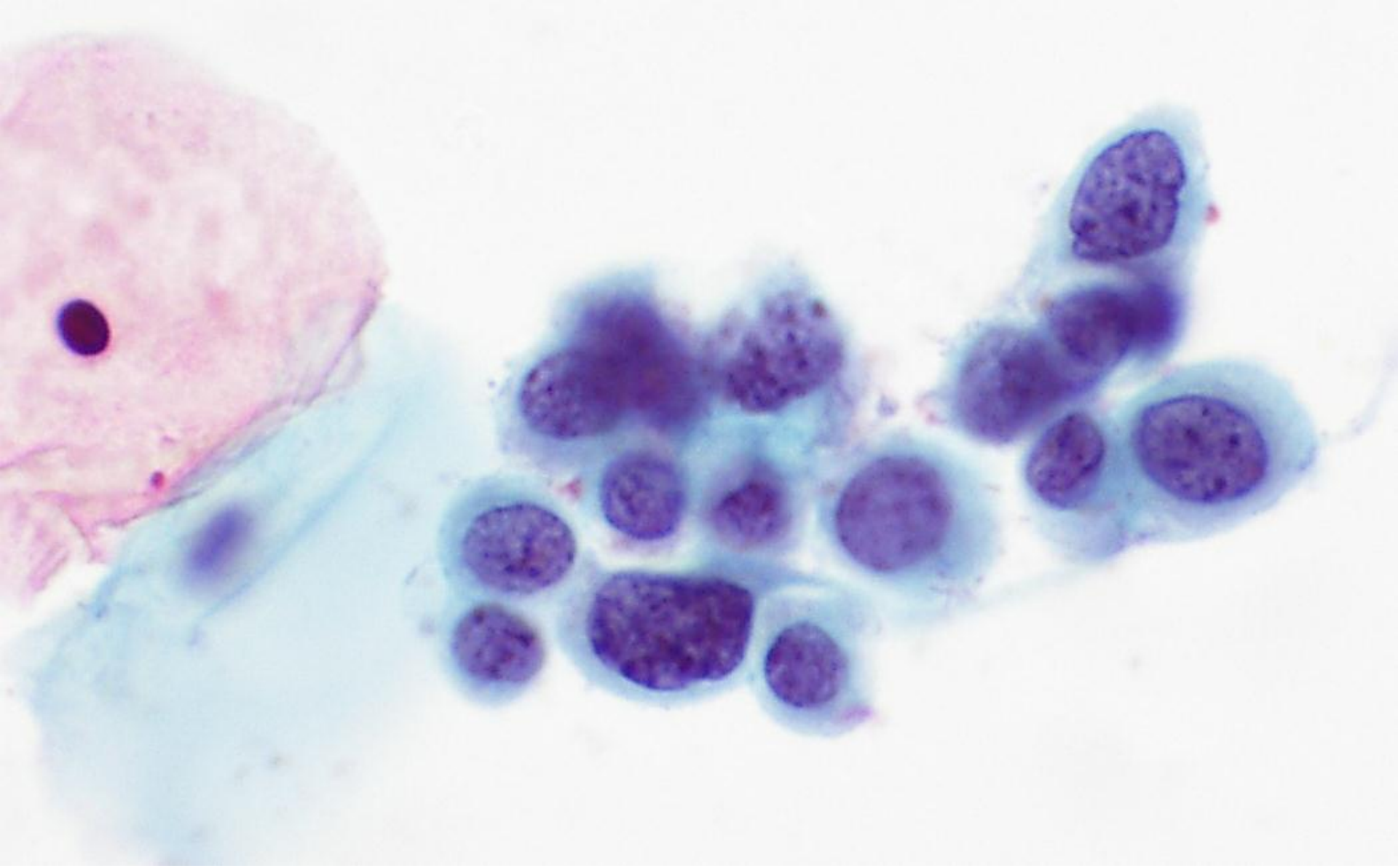
Nucleus High N:C ratio (>50% of the cell is occupied by the nucleus)

Nuclear variability is central to the diagnosis

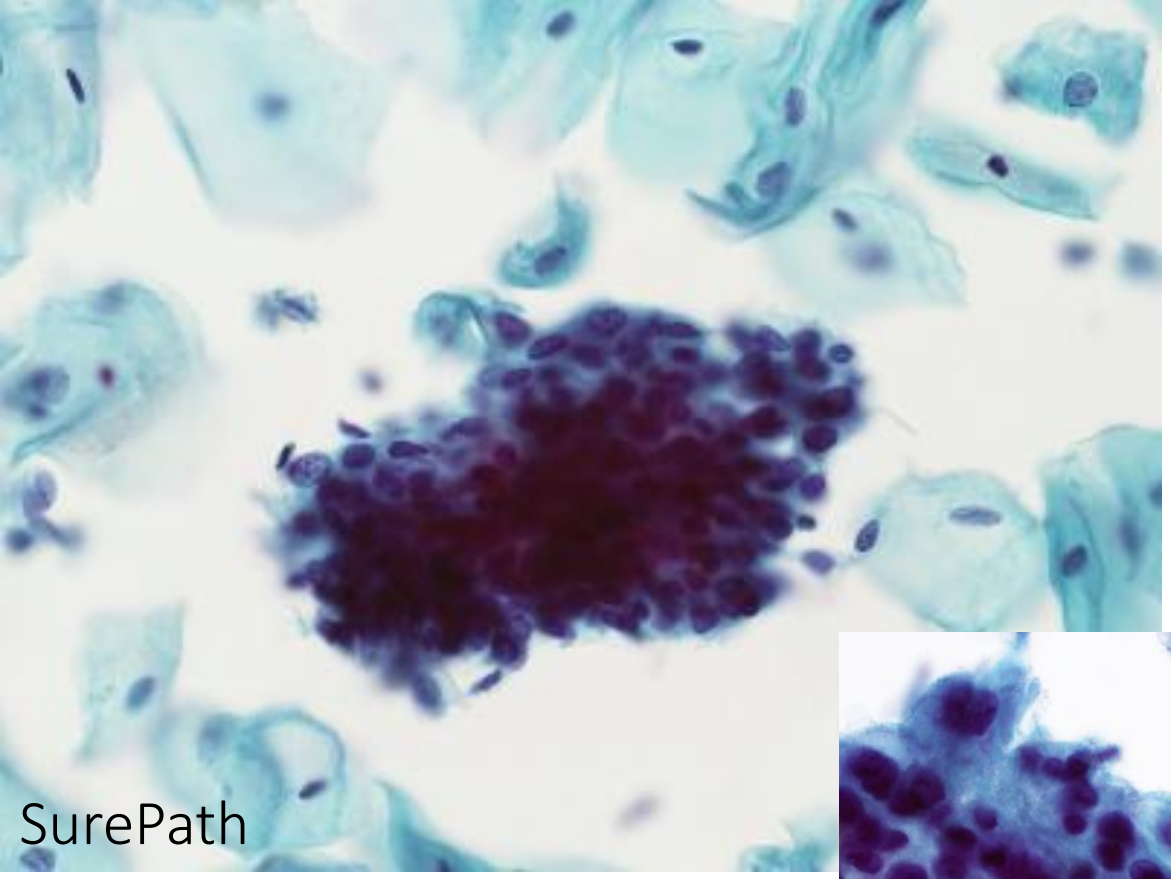
- nuclear size varies
- membrane usually irregular with folds and indentations
- hyperchromatic: fine or coarse evenly distributed chromatin
- nucleoli uncommon
- sticky bare abnormal nuclei may be present

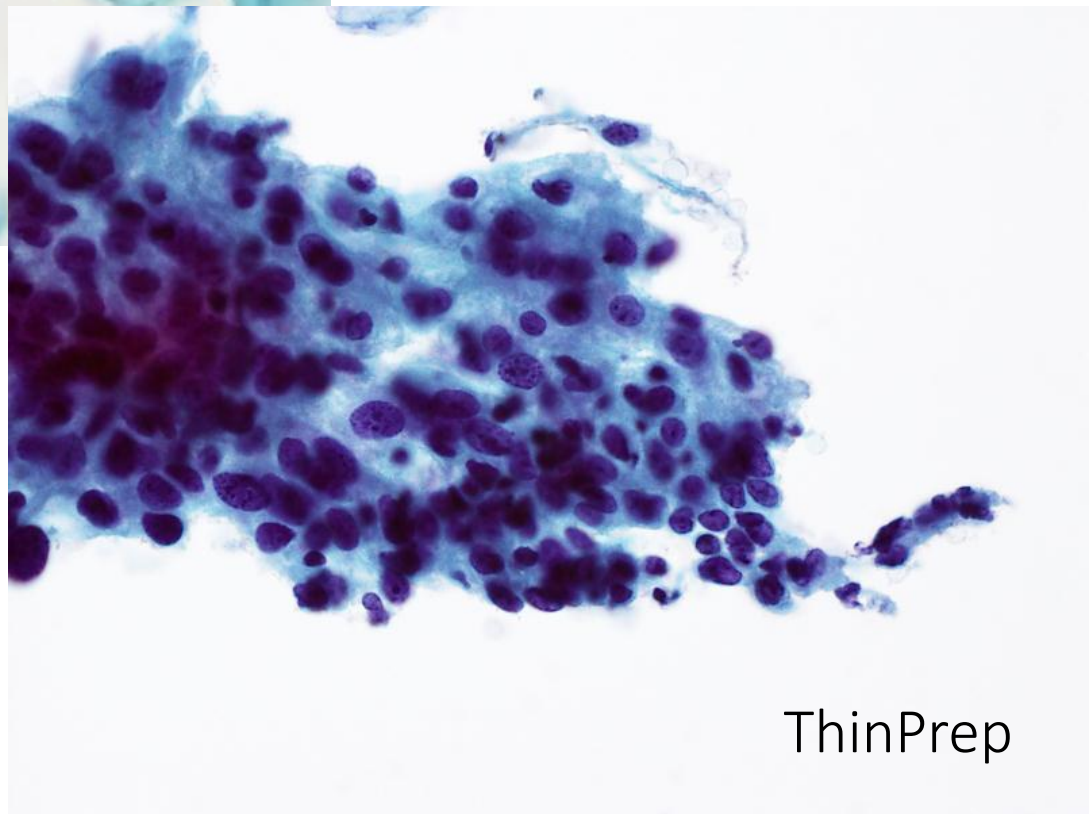
Cytoplasm - variable: squamoid, lacy and delicate, densely metaplastic occasionally keratinised

HSIL (SurePath): Nuclear features

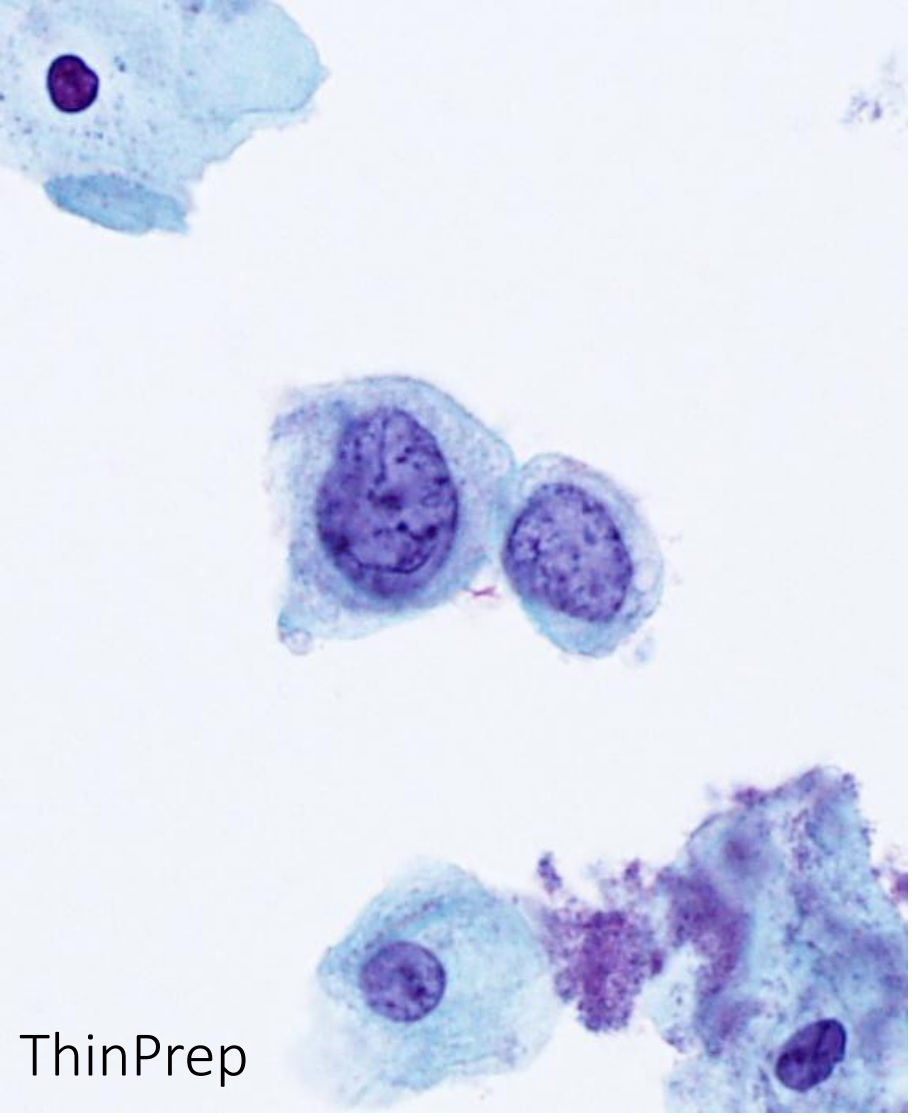


HSIL (ThinPrep): Nuclear features

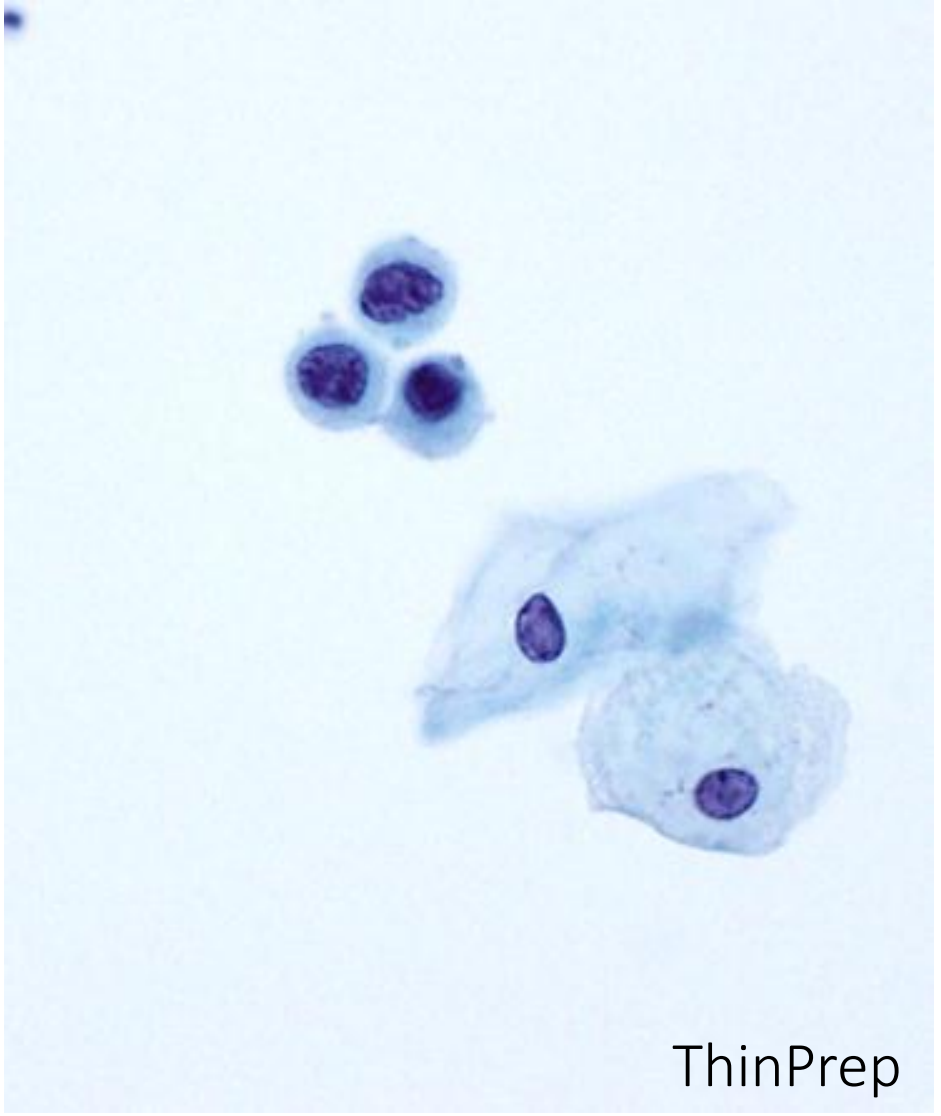




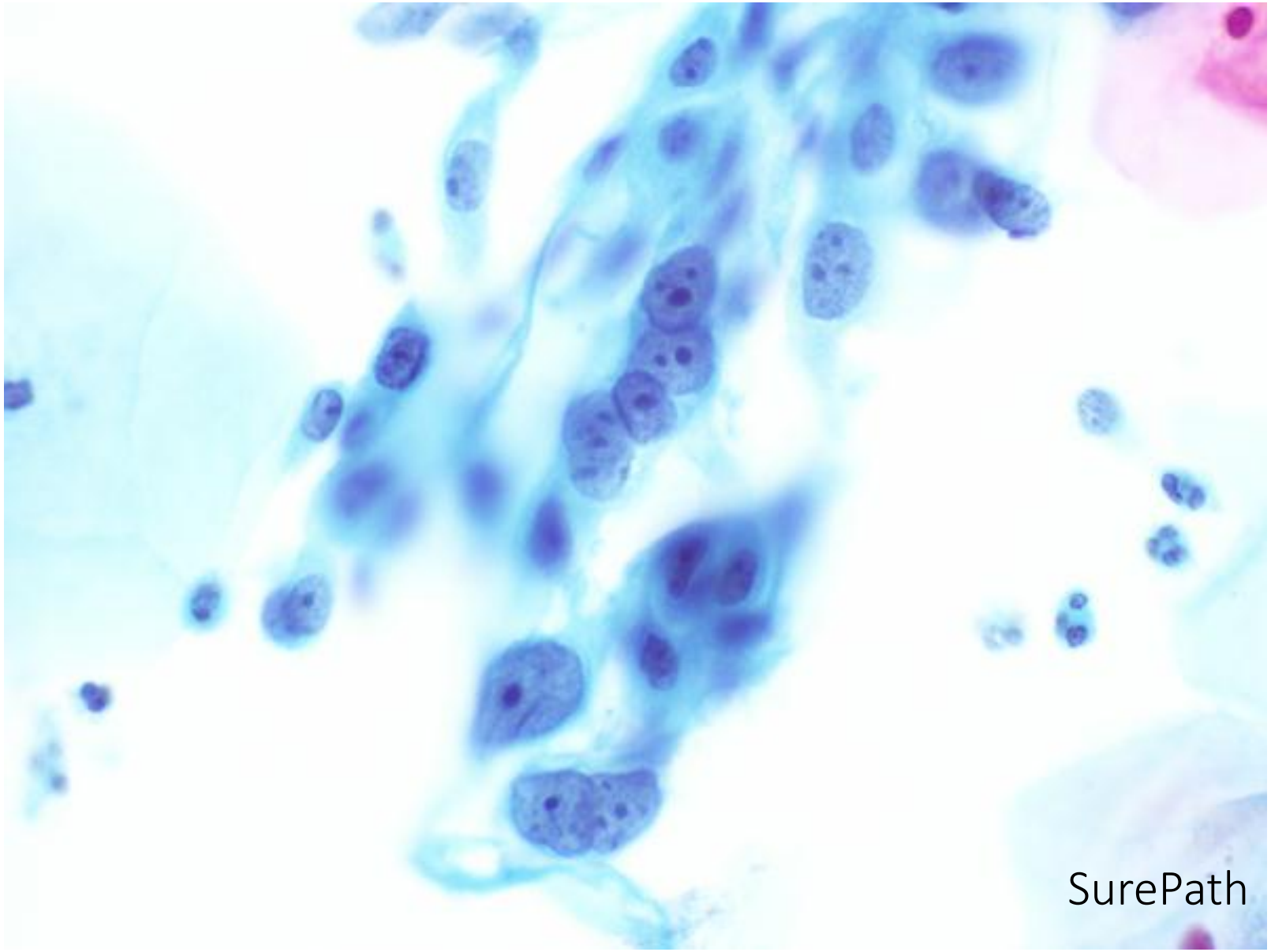
HSIL:
Hyperchromatic crowded groups



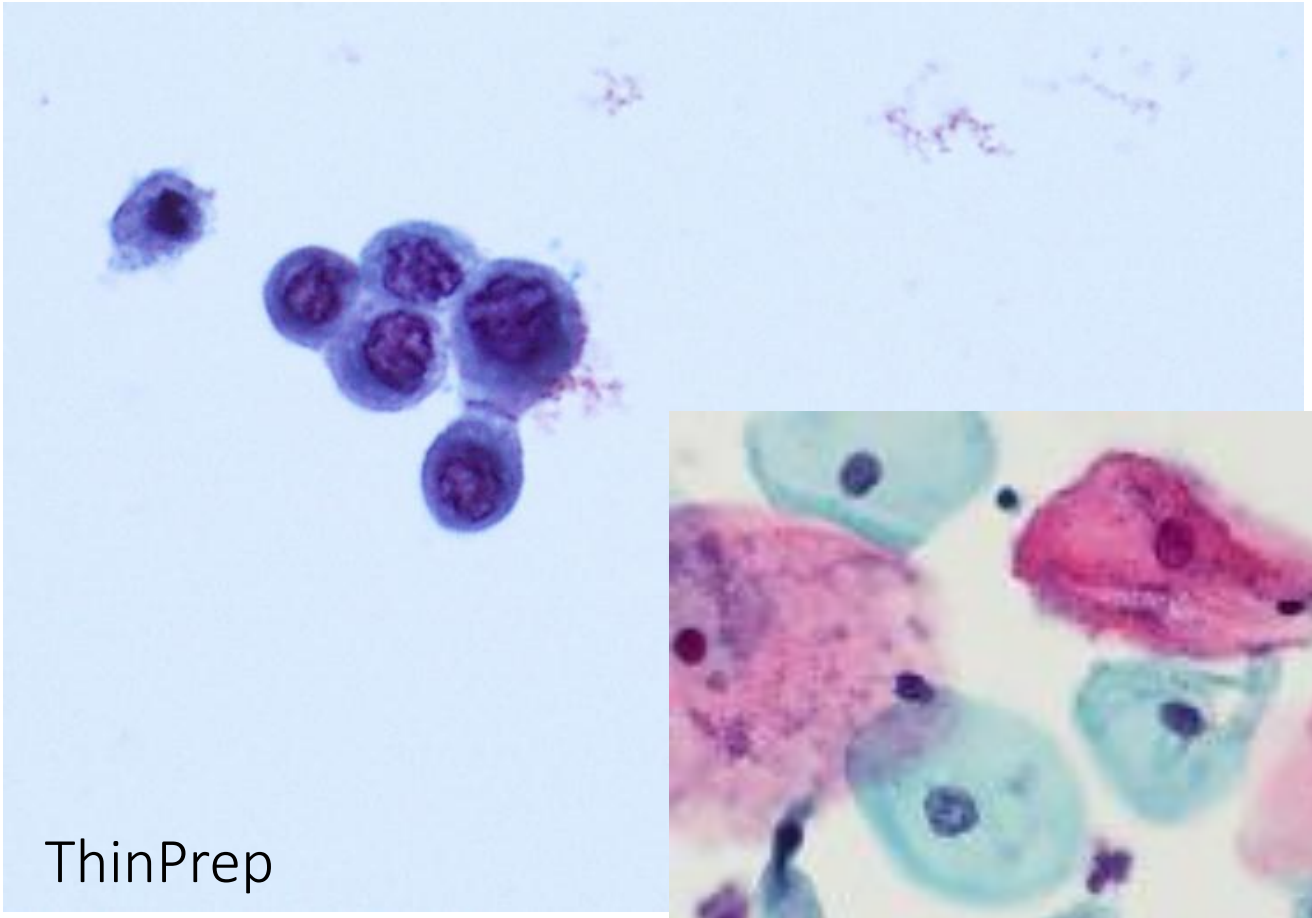
HSIL: Large cells

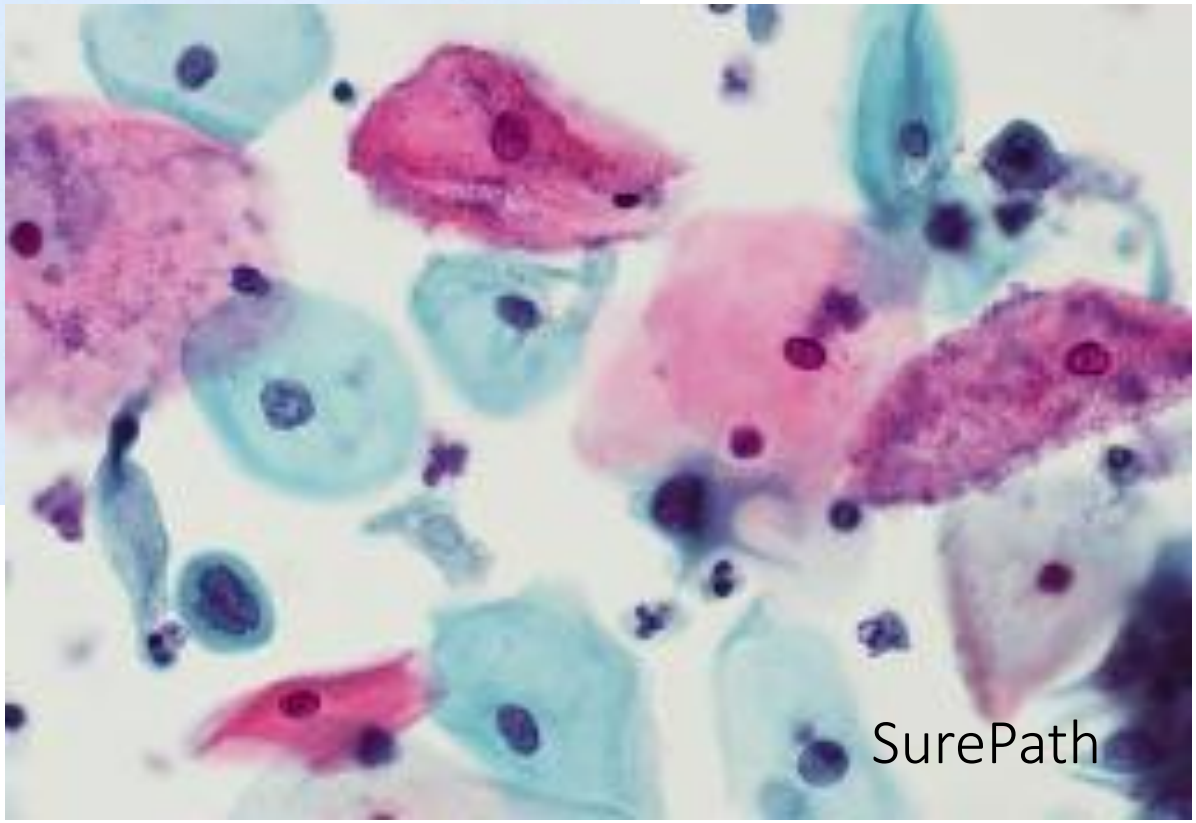


HSIL: Small cells

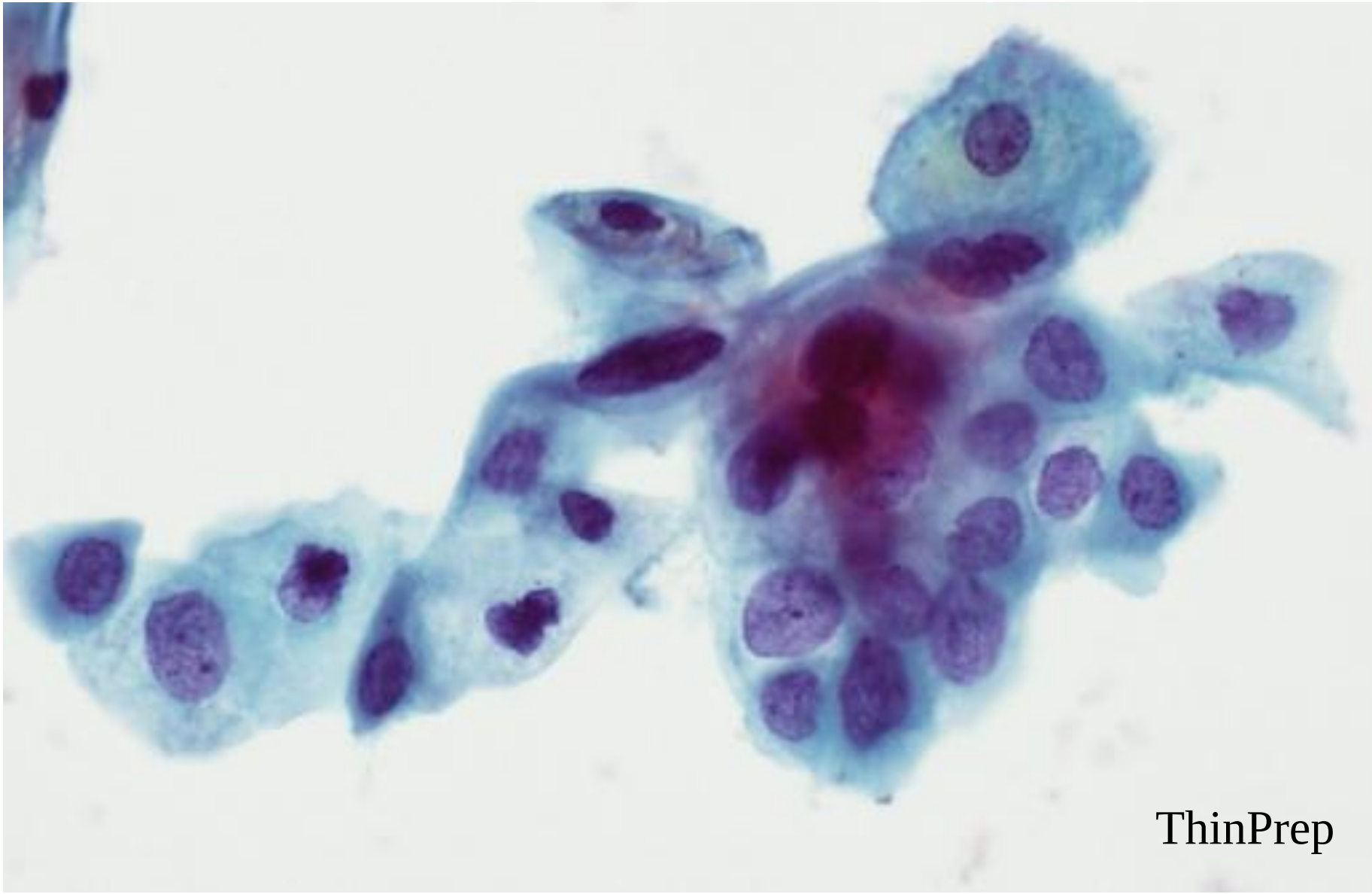


HSIL with nucleoli

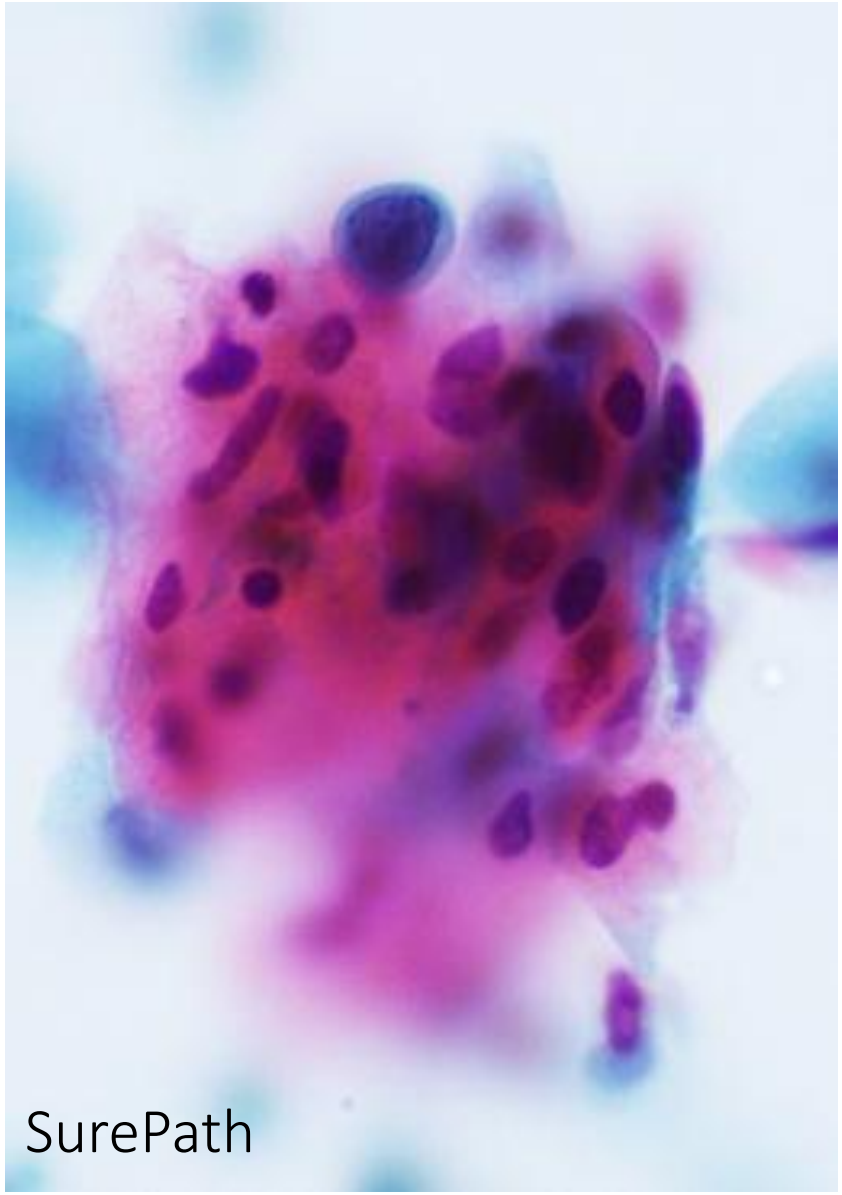


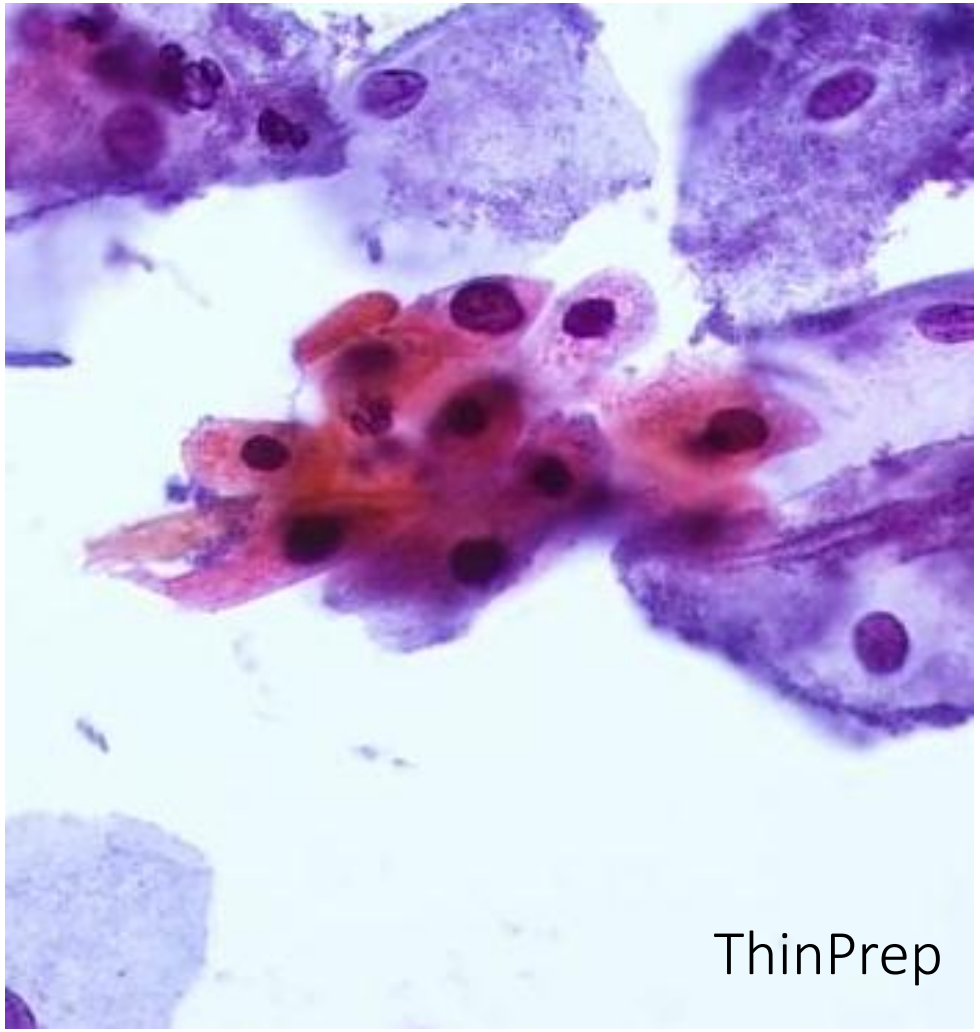


HSIL: Dense metaplastic cytoplasm

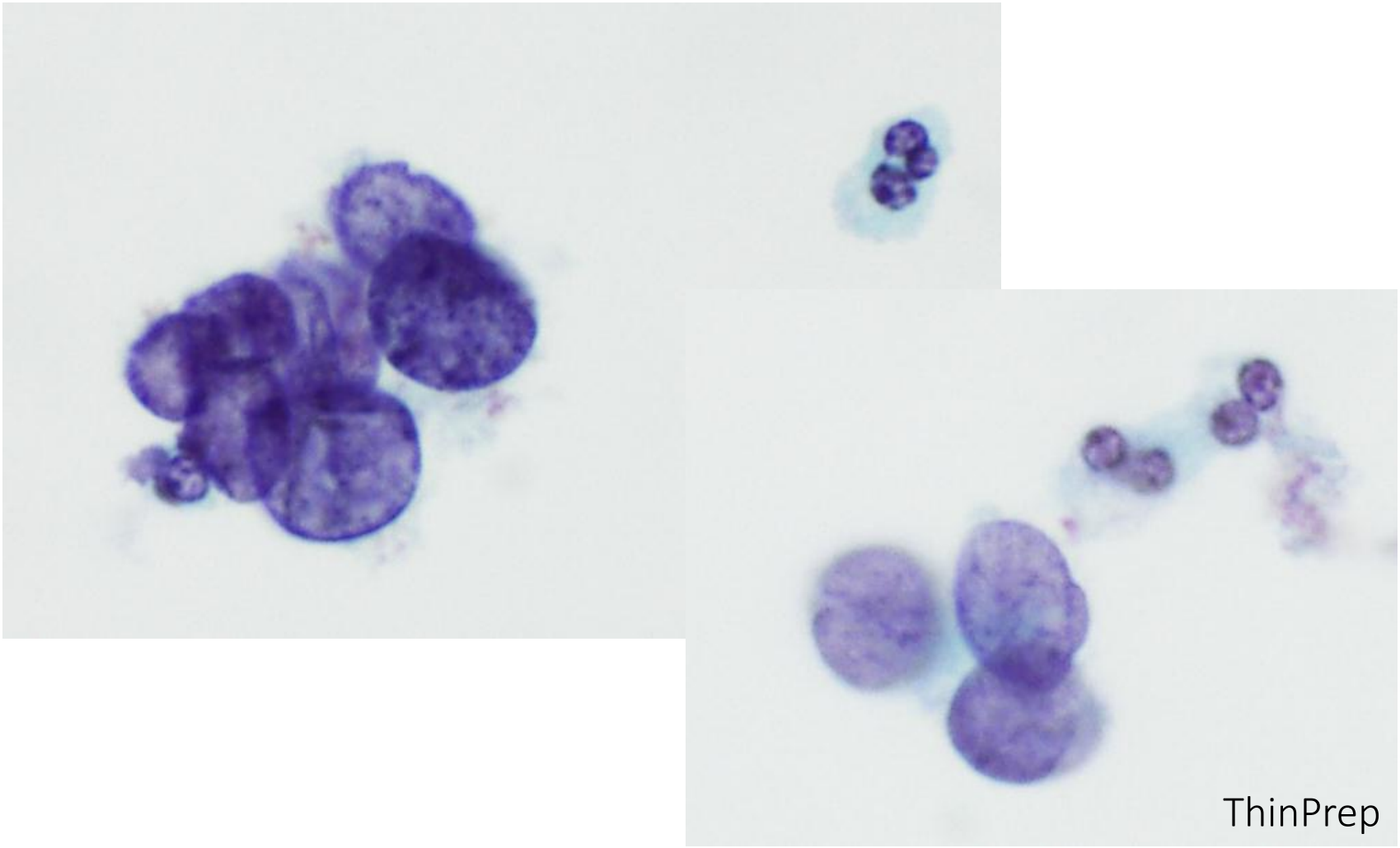


HSIL: Delicate cytoplasm



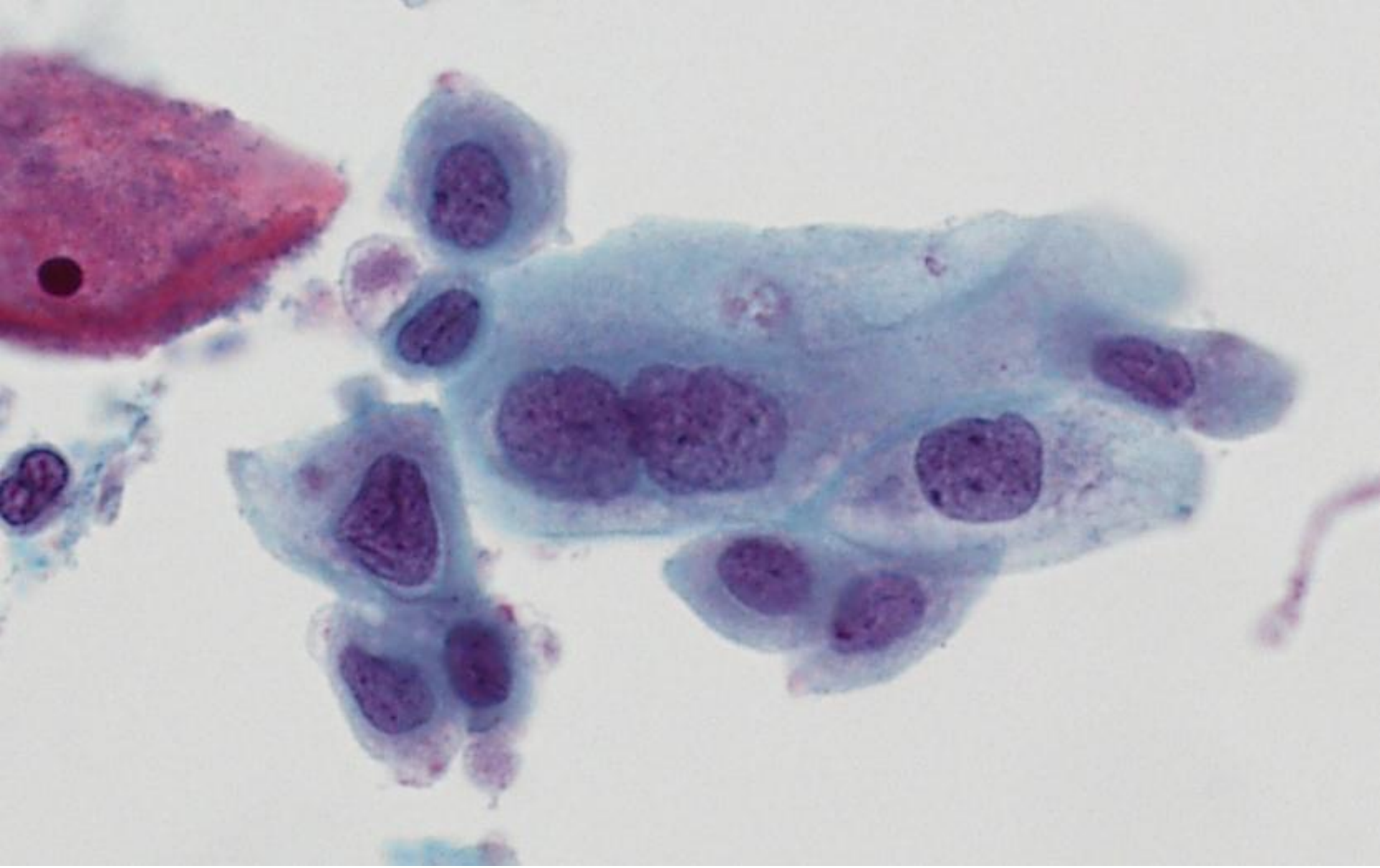


HSIL: Keratinised cytoplasm



HSIL: Sticky bare nuclei

HSIL CIN 2



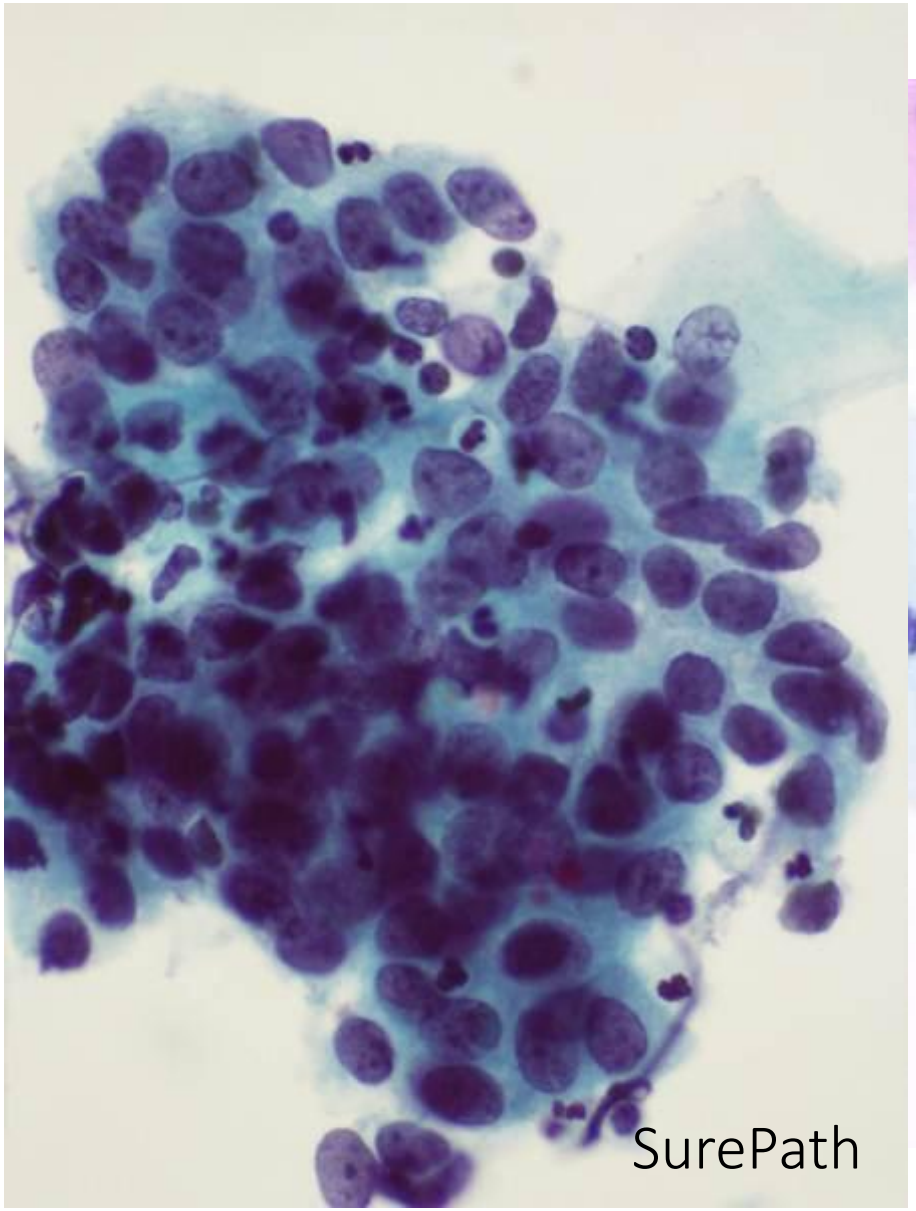
Range of LSIL and HSIL

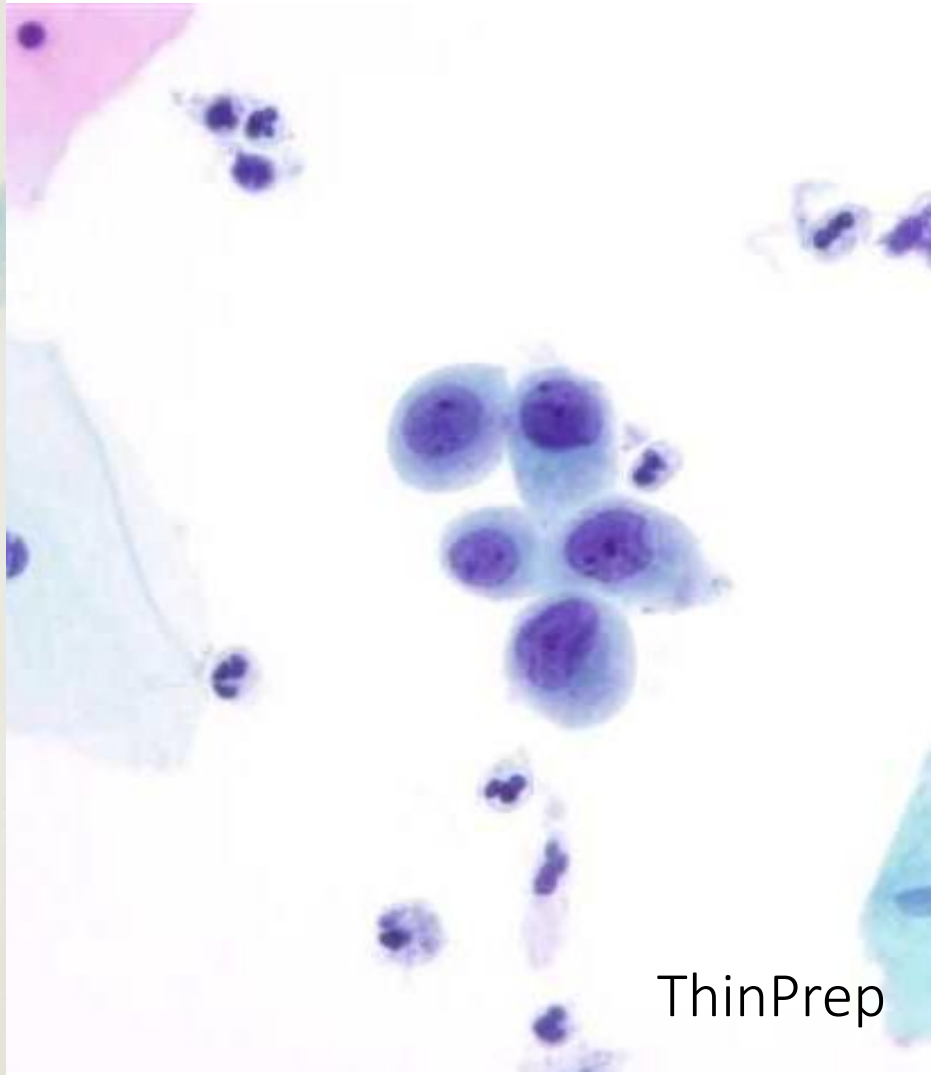
Atypical Squamous Cells, cannot exclude HSIL (ASC-H)

- a report category: suspicious but not diagnostic of HSIL
- differential often HSIL *vs.* normal/benign mimic

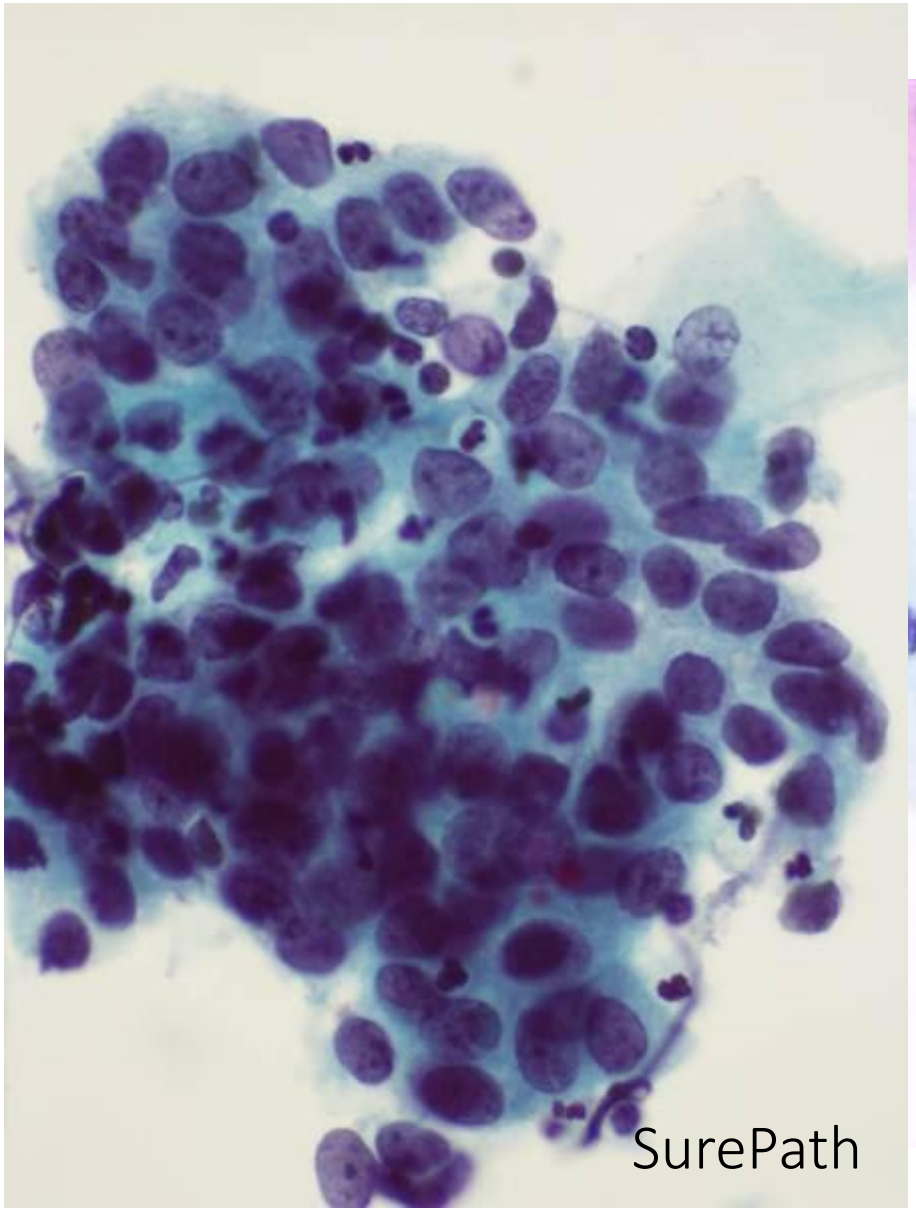
  e.g. immature metaplasia, cervicitis, atrophy
- technical limitations may also mean sample is not diagnostic

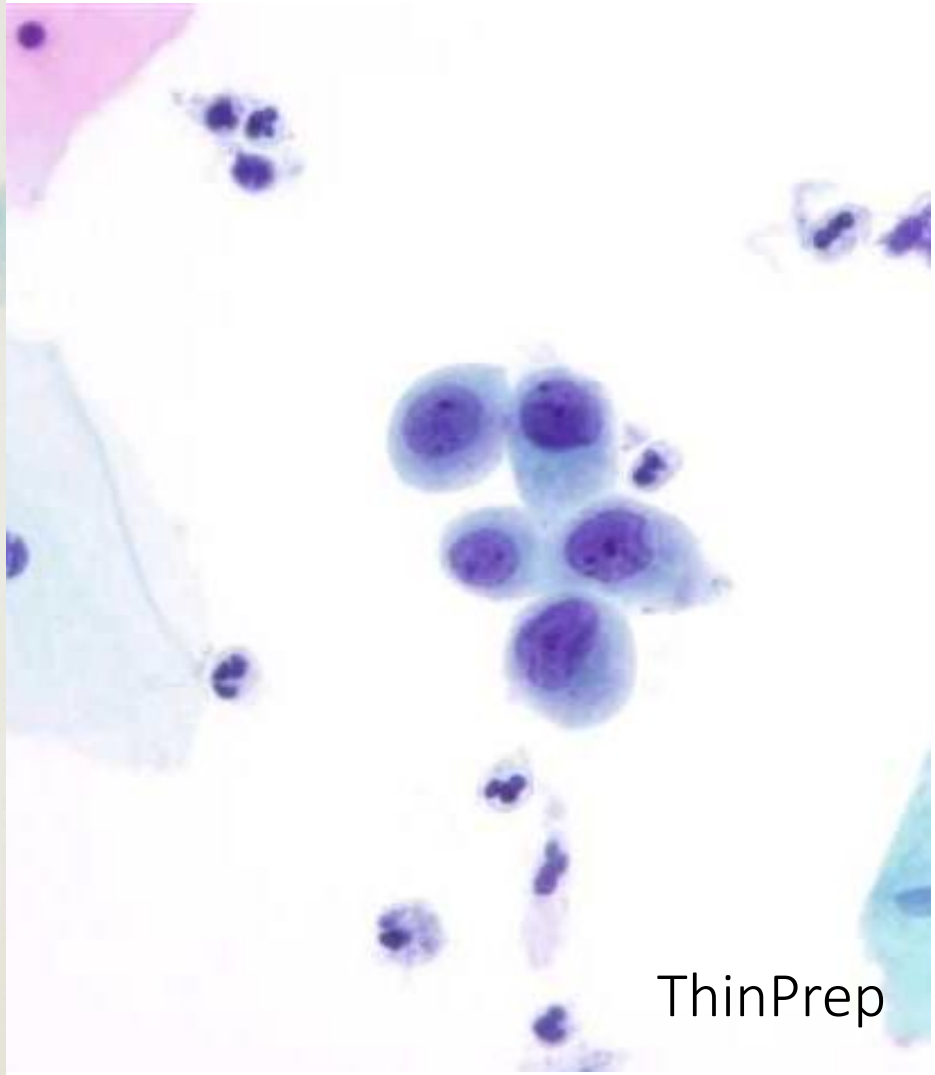
- ASC-H can be used in conjunction with a definite report of LSIL.





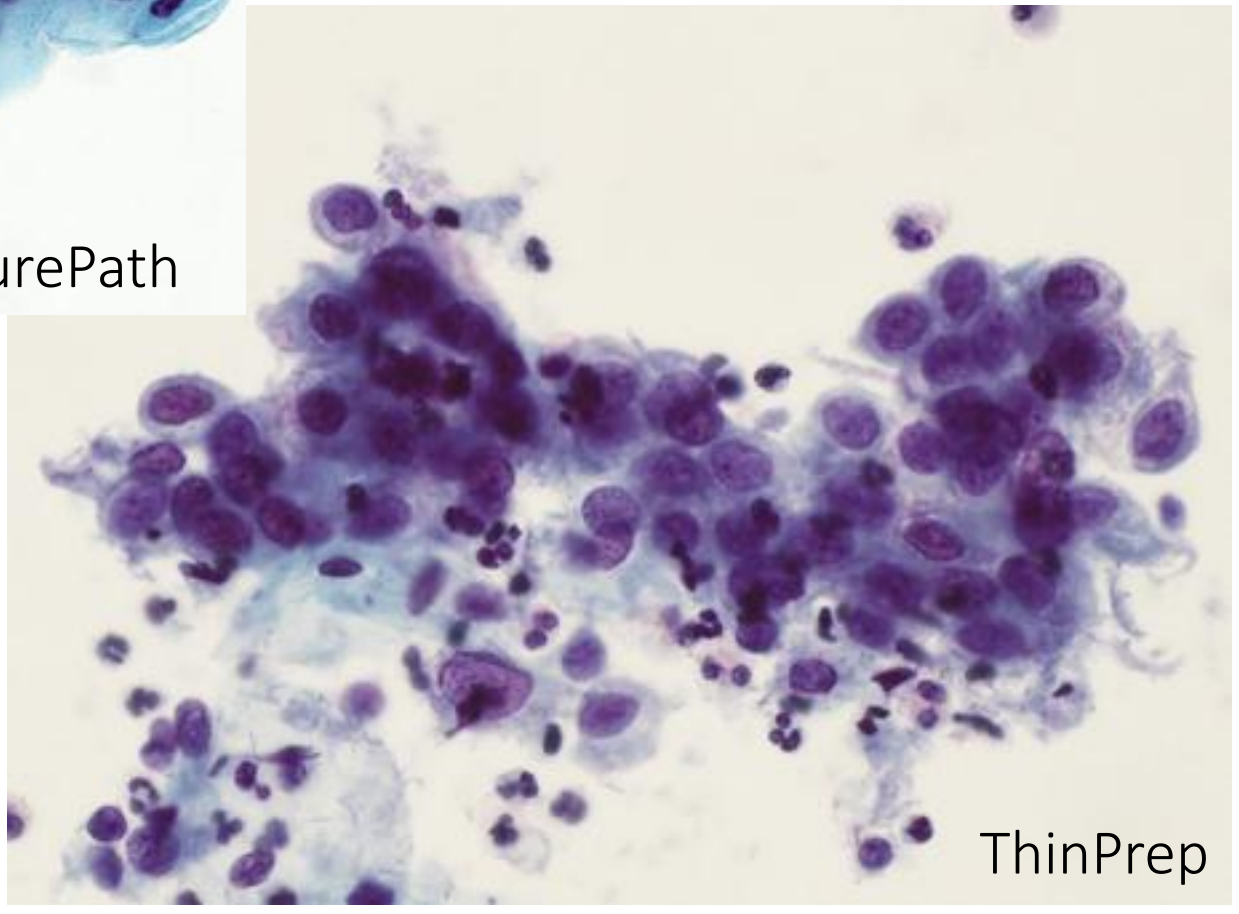
ASC-H Metaplasia *vs* HSIL





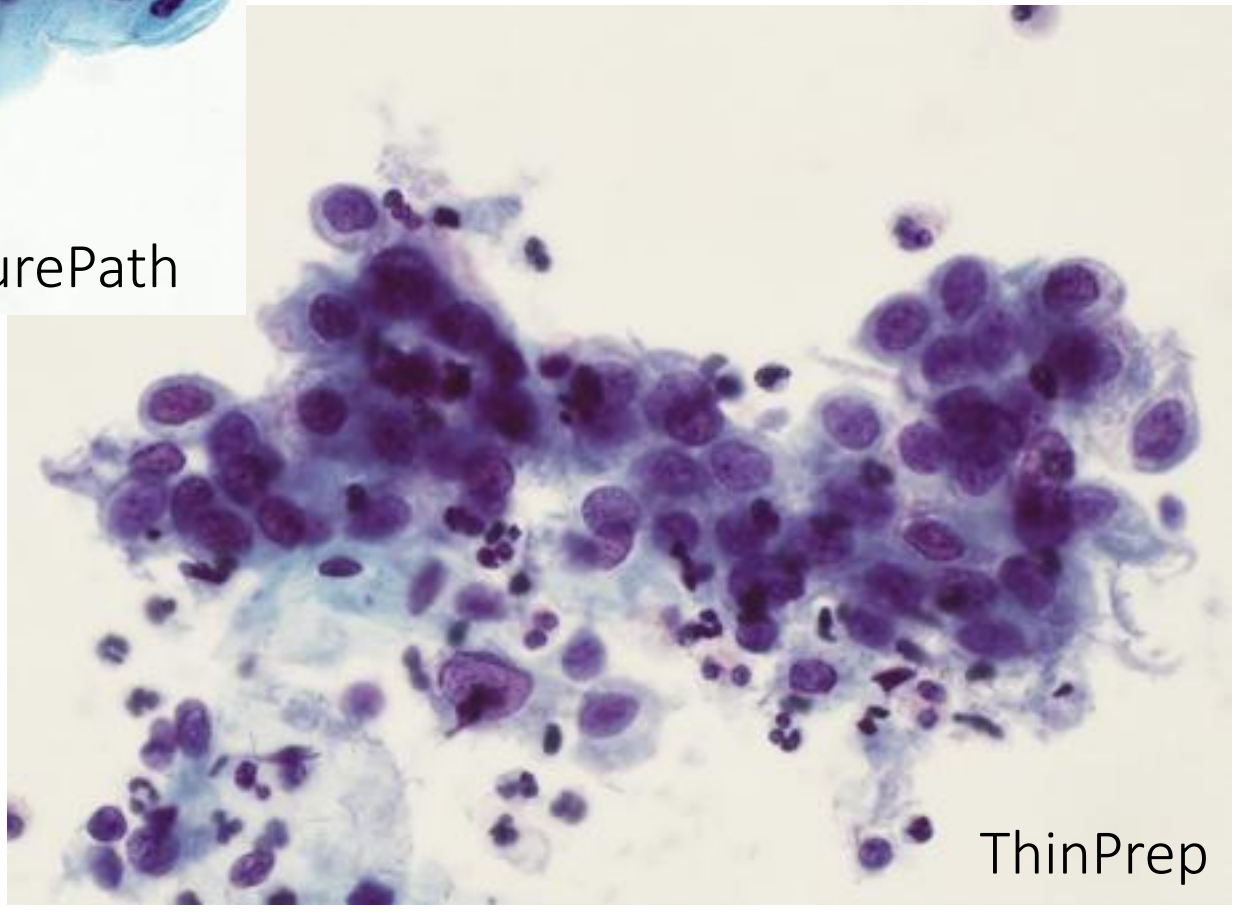
ASC-H Metaplasia *vs* HSIL FU: CIN 2

ASC-H: Cervicitis
vs HSIL

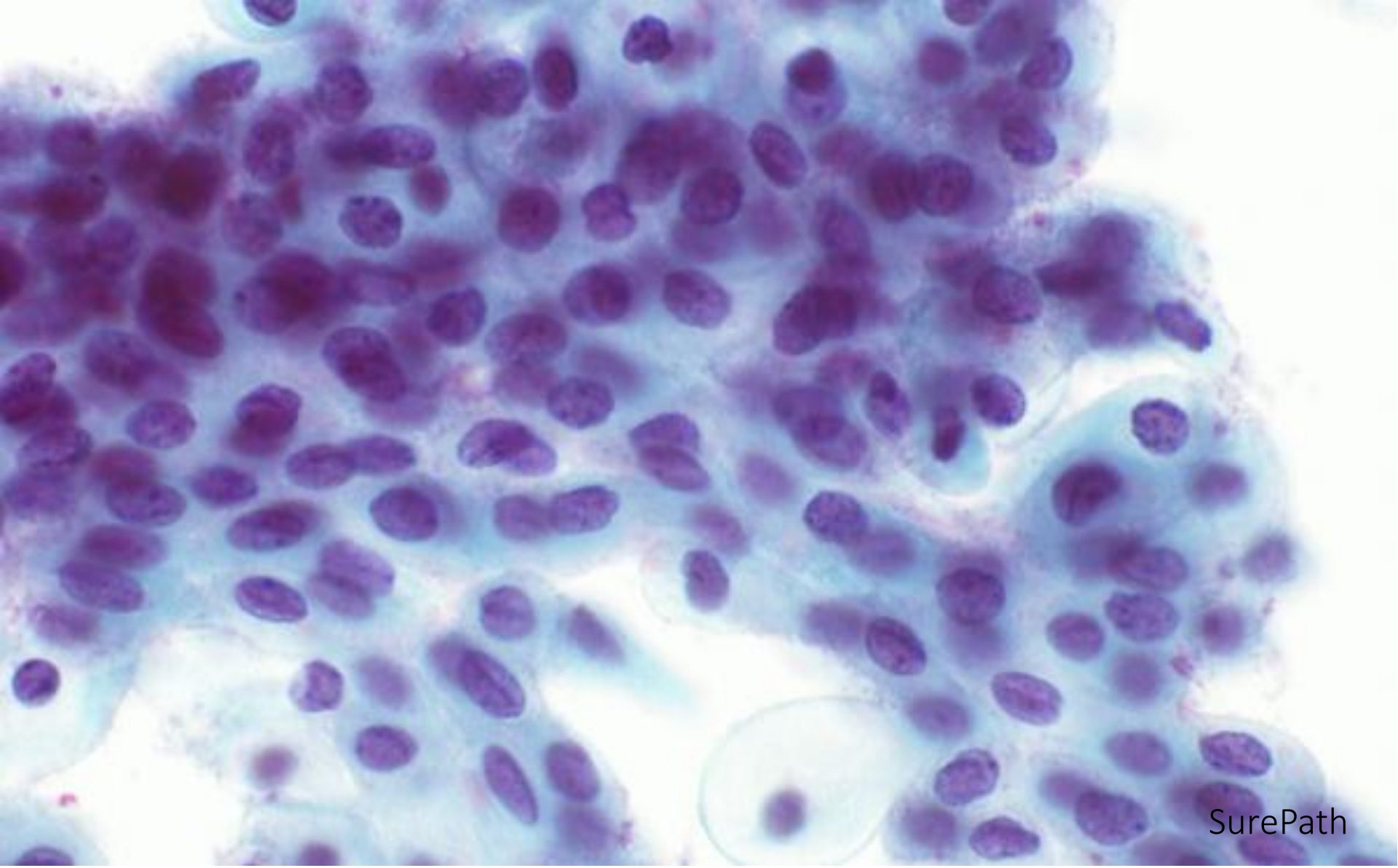


SurePath

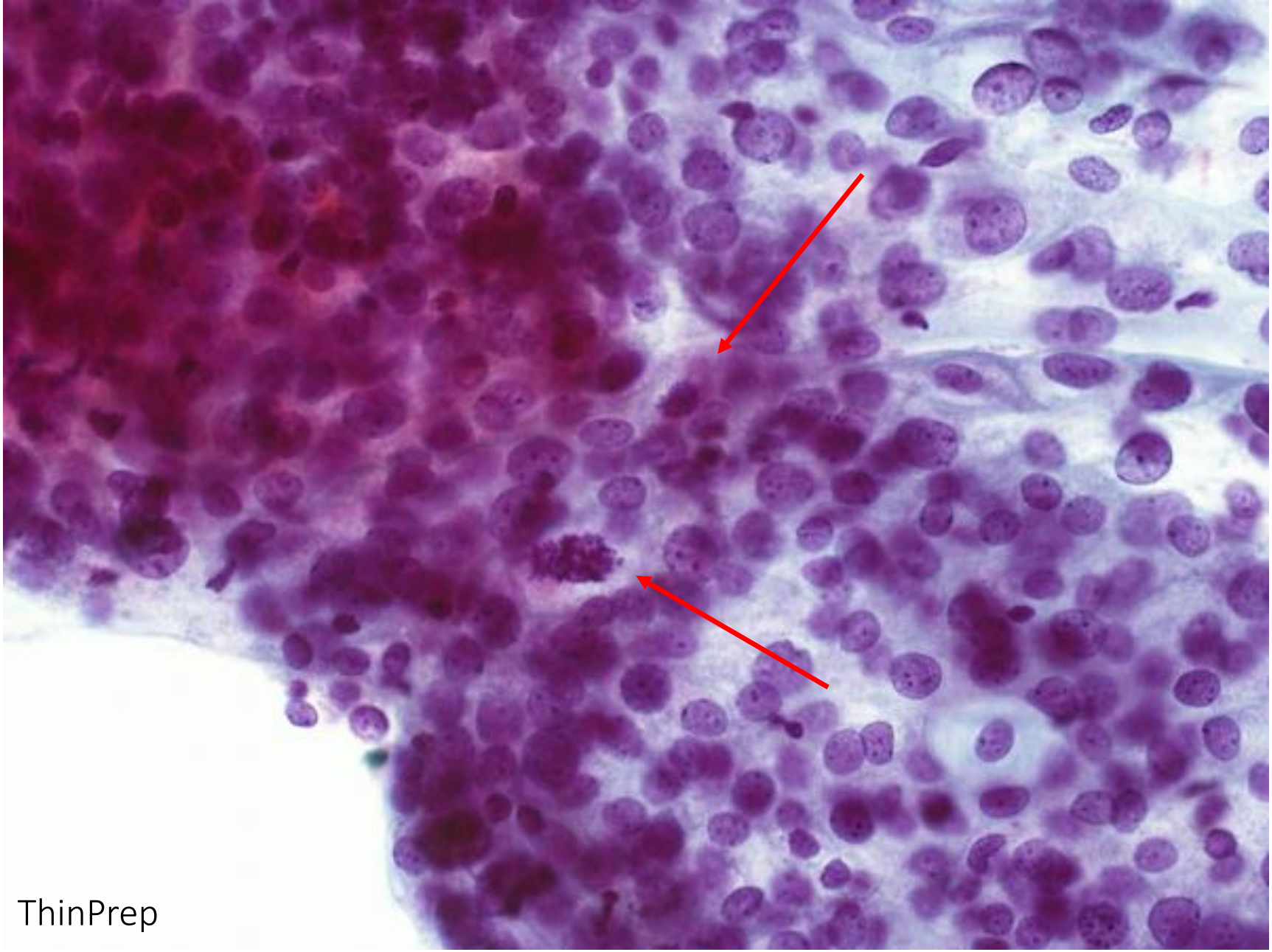
ASC-H: Cervicitis
vs HSIL
FU Cervicitis



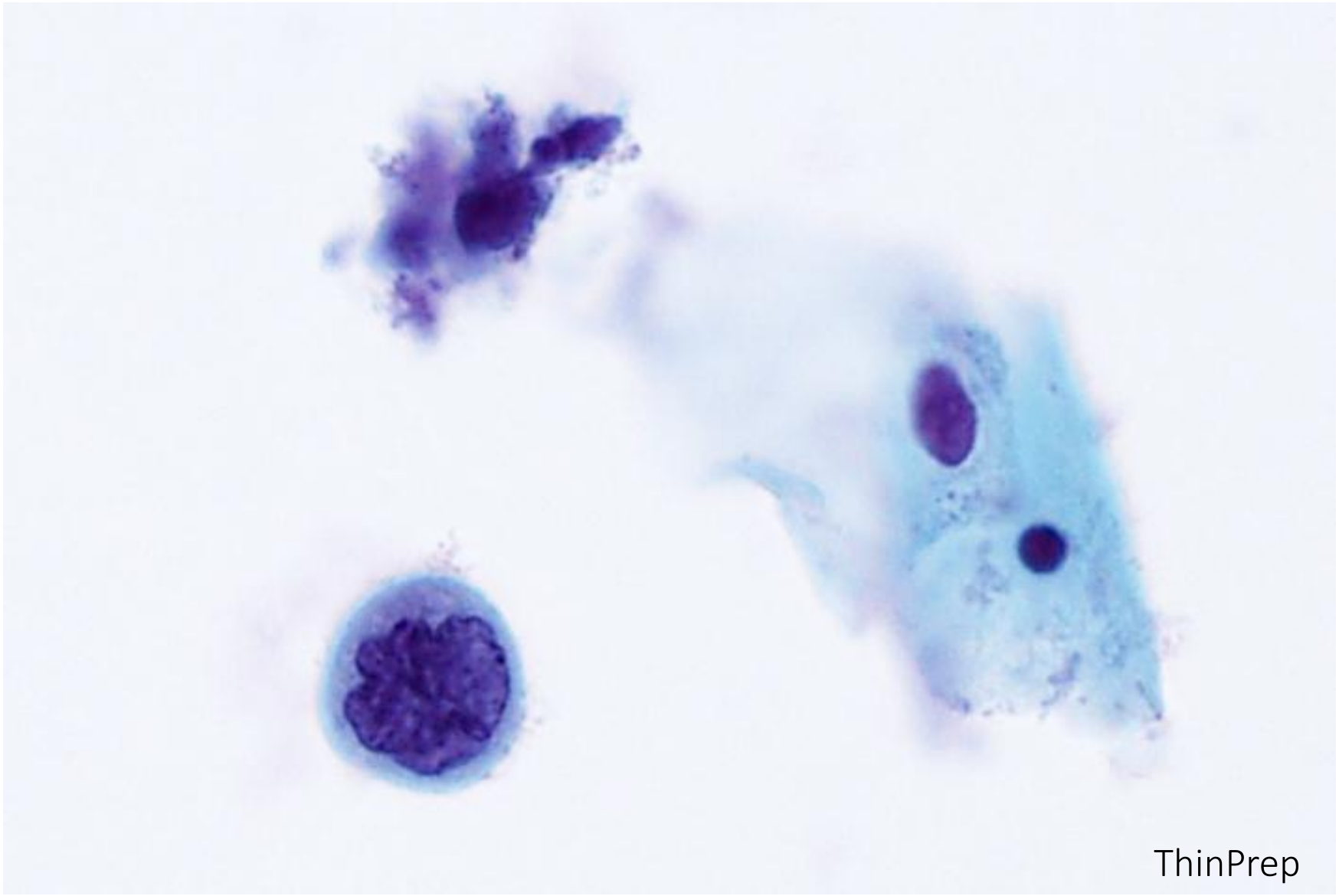
ThinPrep



Parabasal cells in atrophy



HSIL in atrophy: two mitoses



HSIL: Single cell

Invasive Squamous Cell Carcinoma

General - number of cells varies greatly

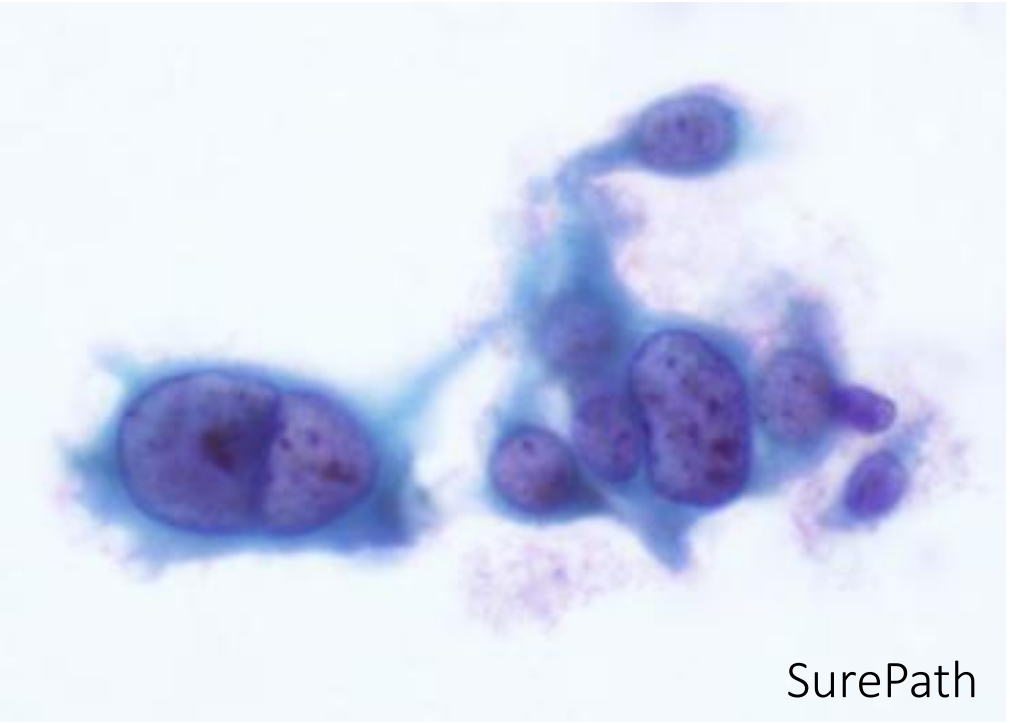
- single cells, sheets or crowded groups
- background blood/inflammation/tumour diathesis

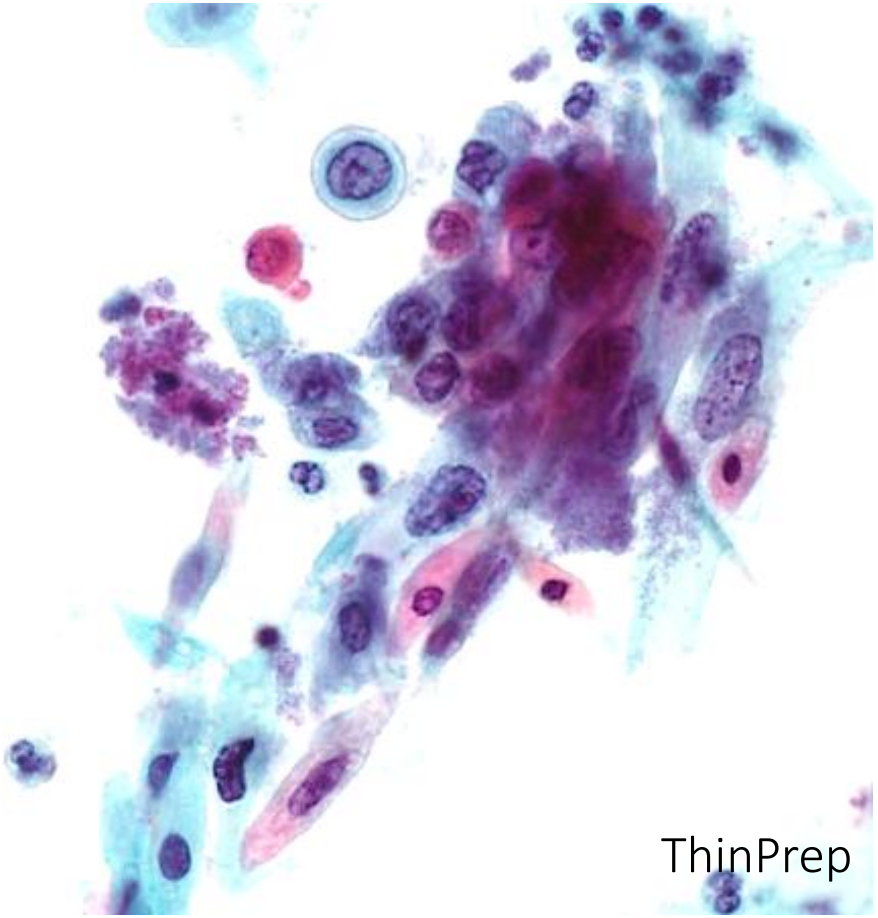
Nucleus - size varies from very small to large

- shape usually irregular with folds and indentations
- chromatin usually coarse and irregularly distributed
- nucleoli large/irregular/multiple
- N:C ratio varies
- sticky bare abnormal nuclei may be present

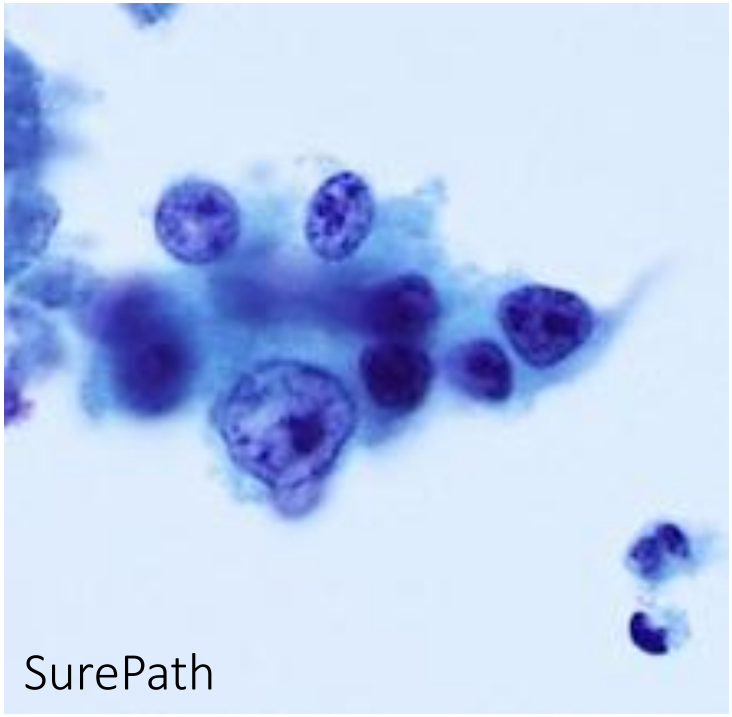
Cytoplasm - cell size varies from very small to very large

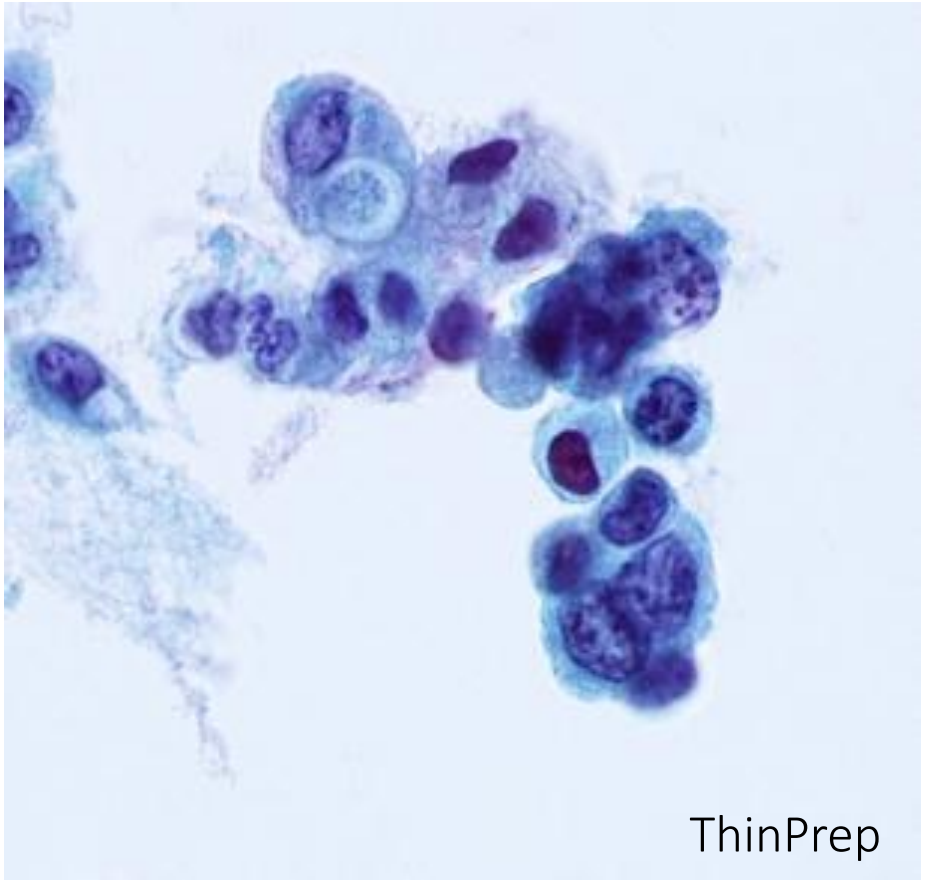
- shape very variable
- can be keratinised or non-keratinised



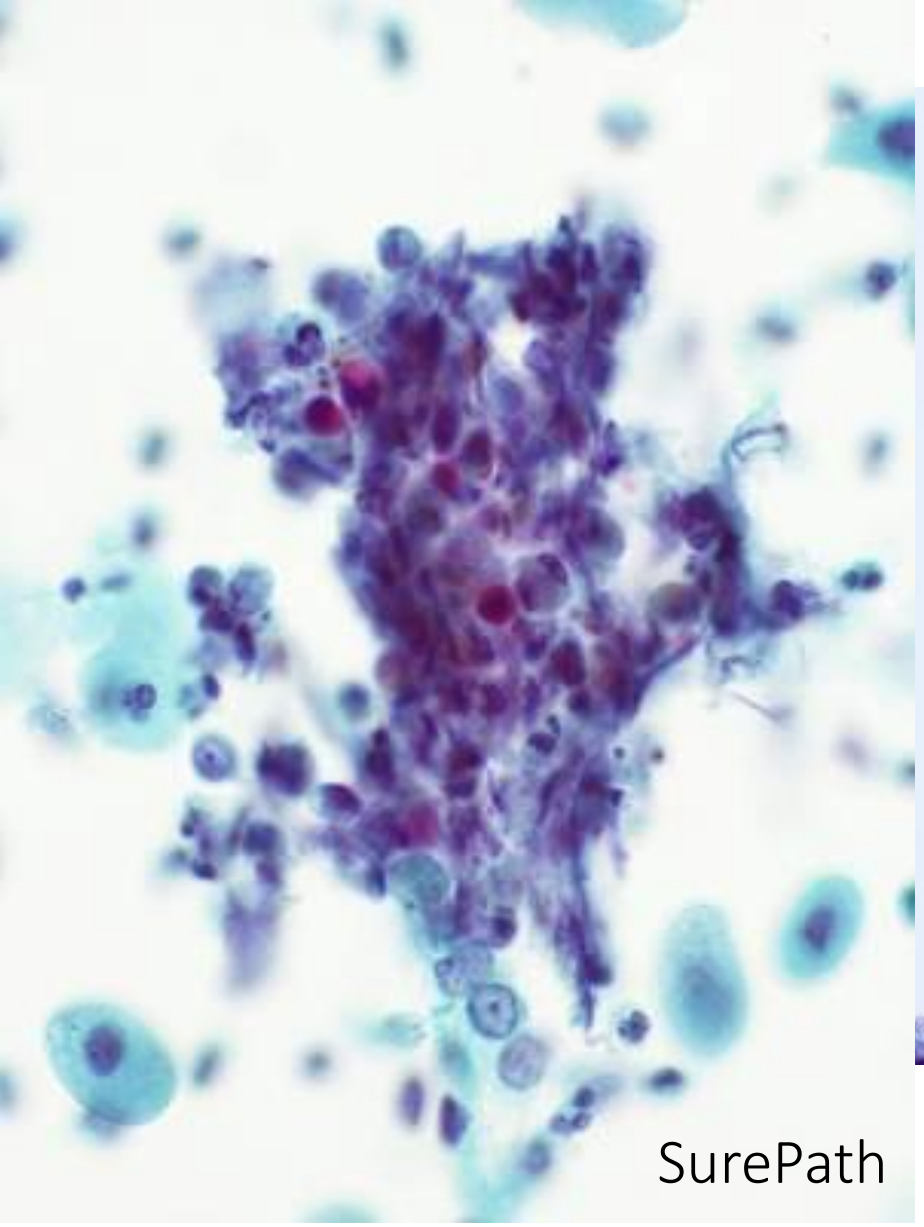


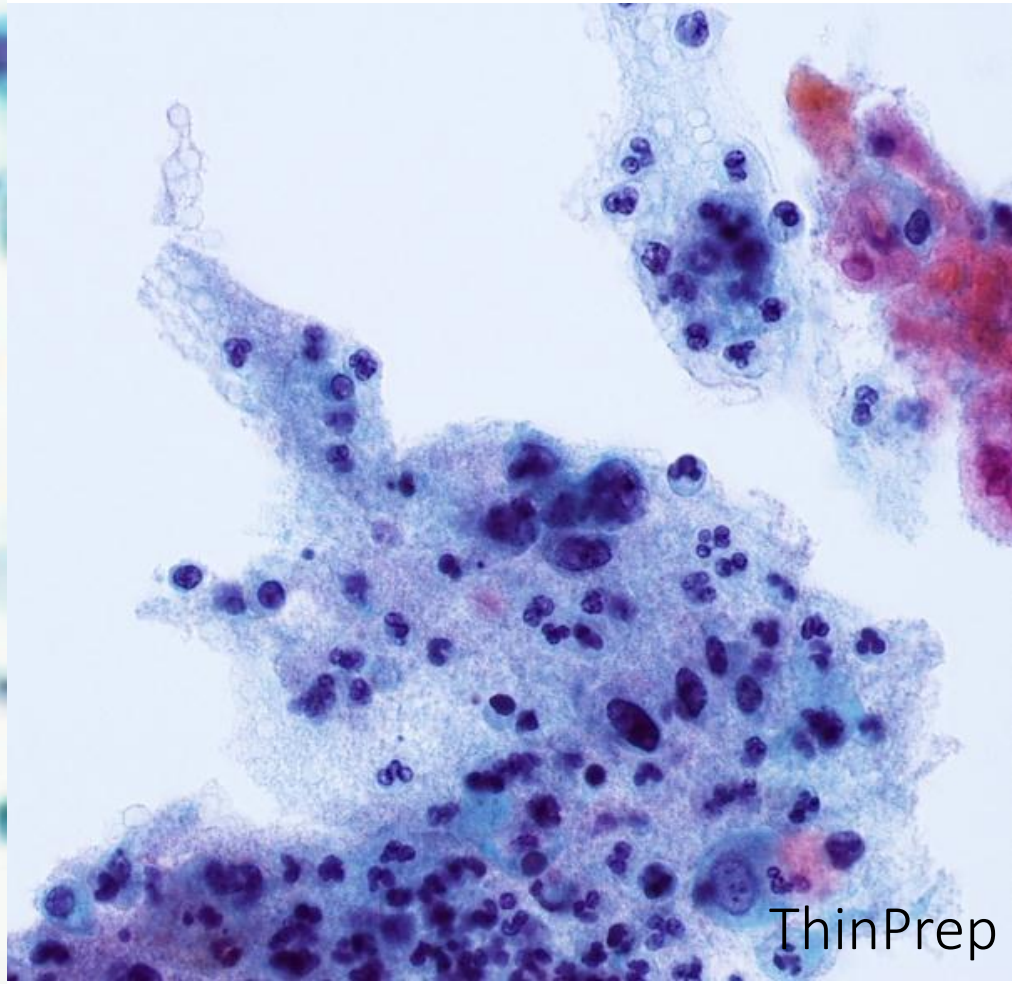
SCC: Cell features





SCC: Clumping and clearing of chromatin





SCC: Tumour diathesis

Keratinising SCC

Background: clean or diathesis

Abnormal cells: number very variable. May be few.

Cell type: large highly pleomorphic squamous cells, spindle and tadpole forms. Small highly keratinised cells, dense pyknotic nuclei.

Nuclei: large for cytoplasmic maturation. Often dense and opaque

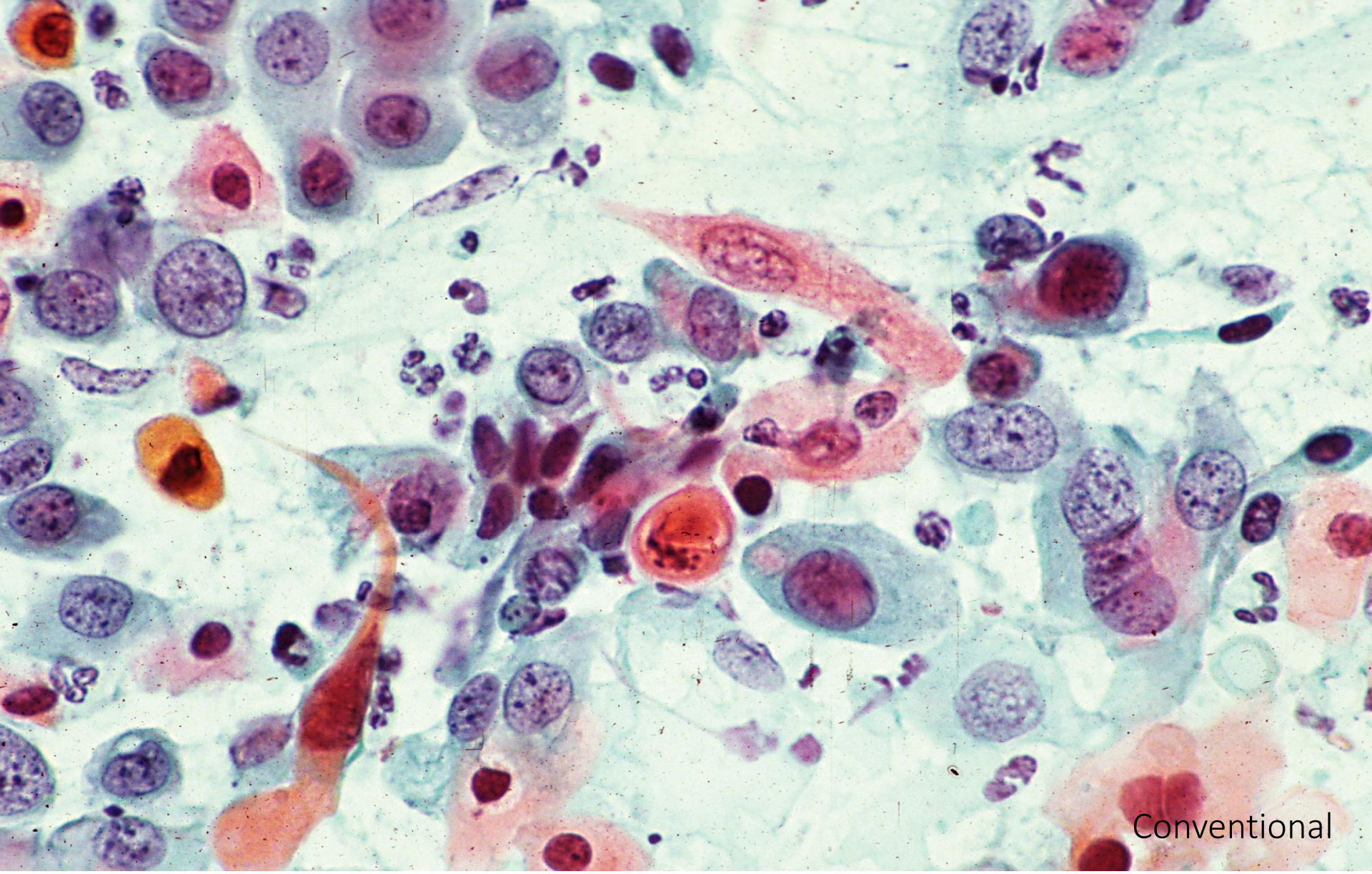
Chromatin: coarsely granular, irregularly distributed

Nucleoli: often prominent.

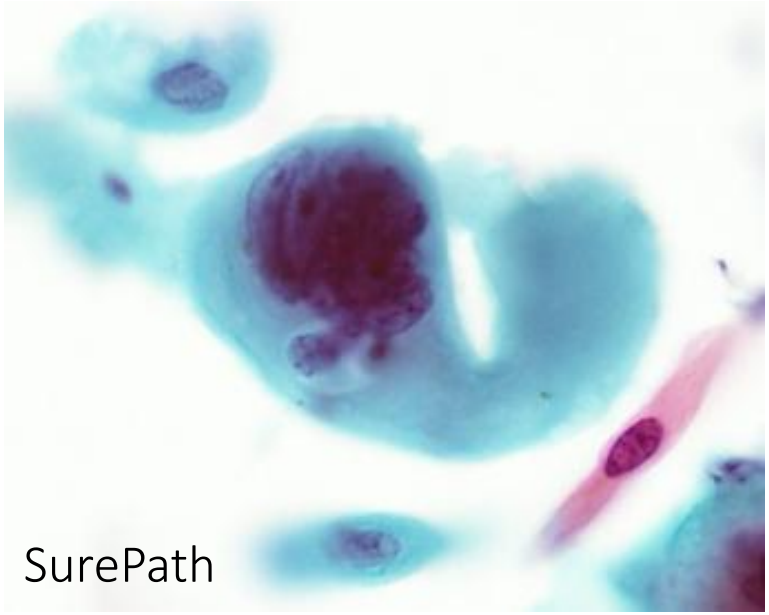
Cytoplasm: dense glassy bright orange (keratinisation)

DD: Keratinising HSIL

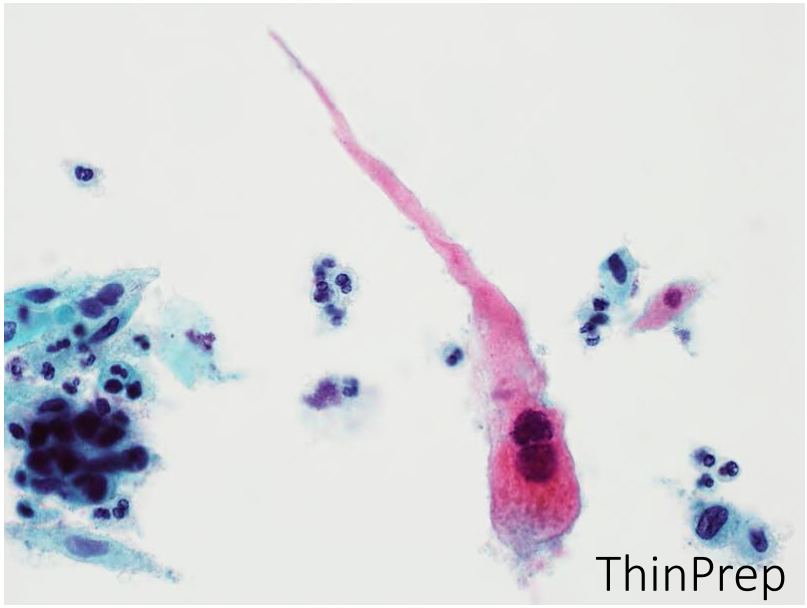
Cervicitis



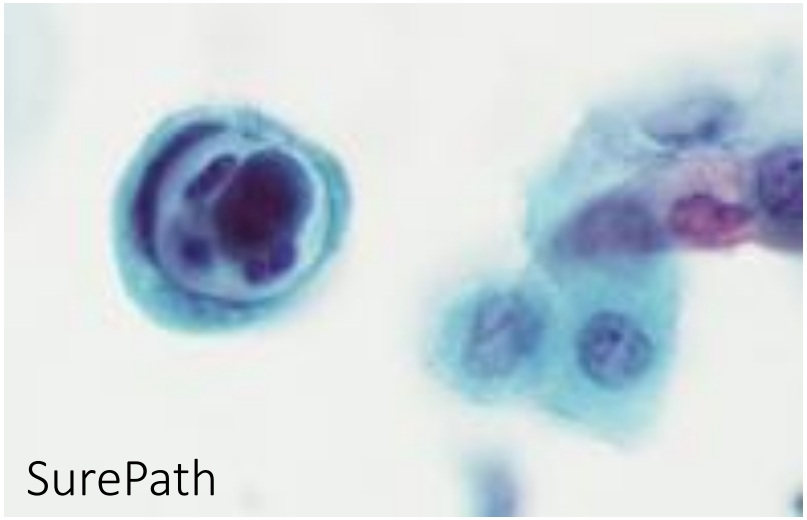
Keratinising SCC



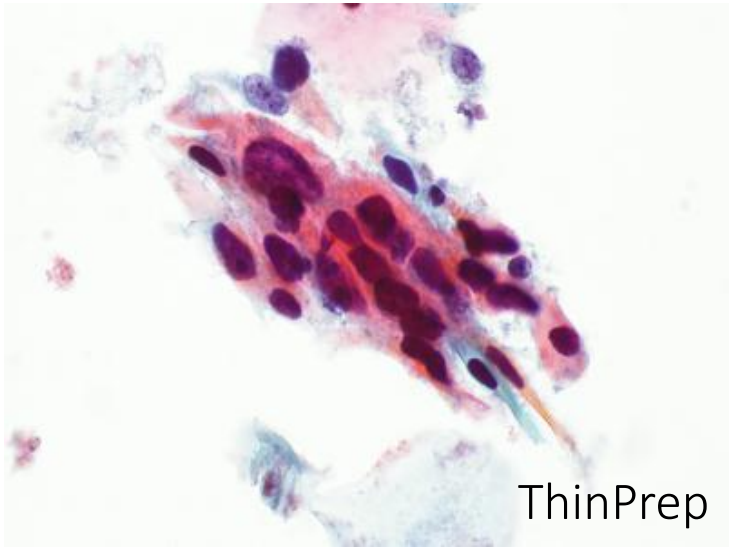
SCC: Marked pleomorphism



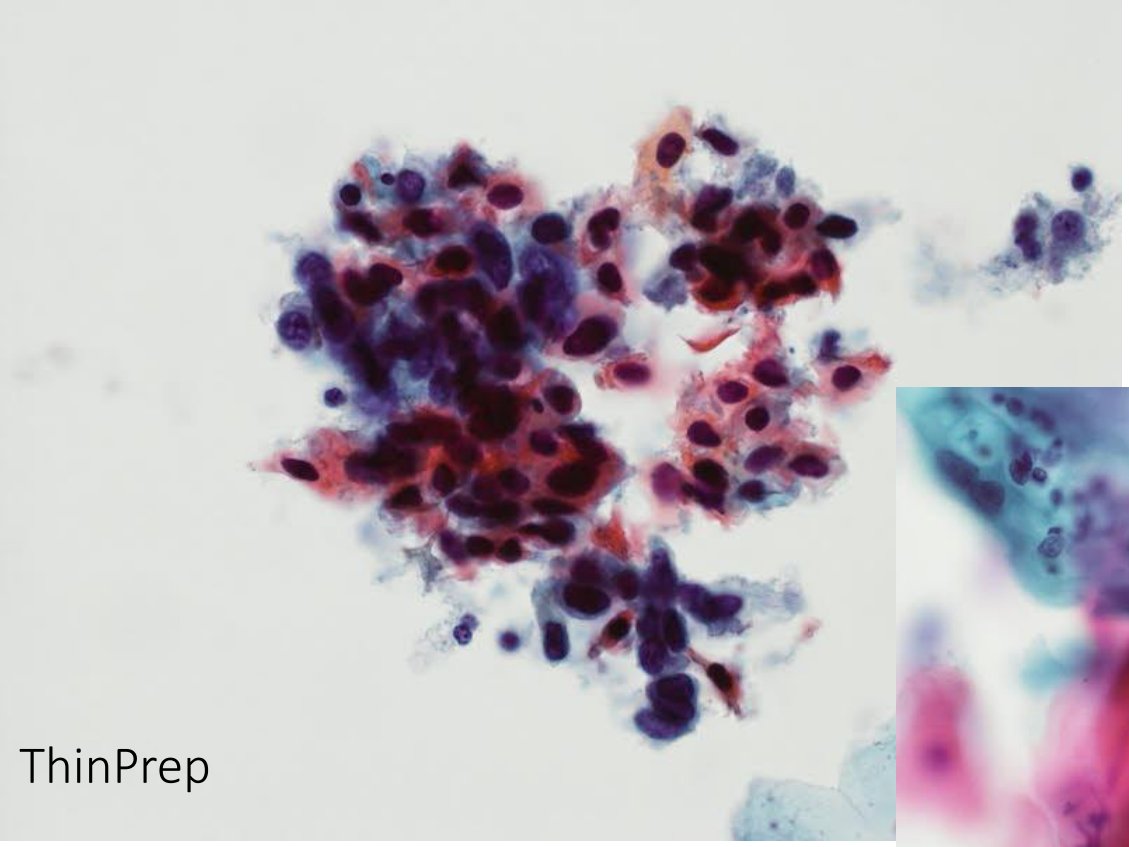
SCC: Tadpole cell

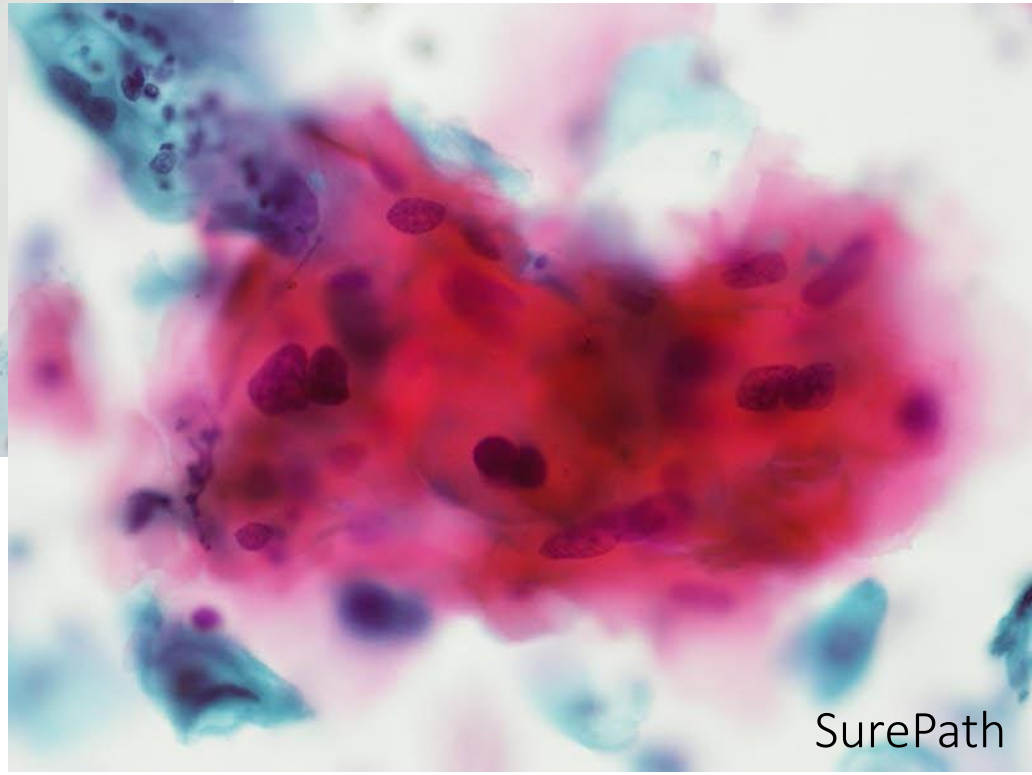


SCC: Cell-in-cell engulfment



SCC: Spindled cells





Keratinising SCC

Non-keratinising SCC

Background: fresh blood common

Abnormal cells: usually many. Single cells or sheets

Cell type: uniform cells resembling HSIL. Intermediate size usually
Large cell and small cell variants.

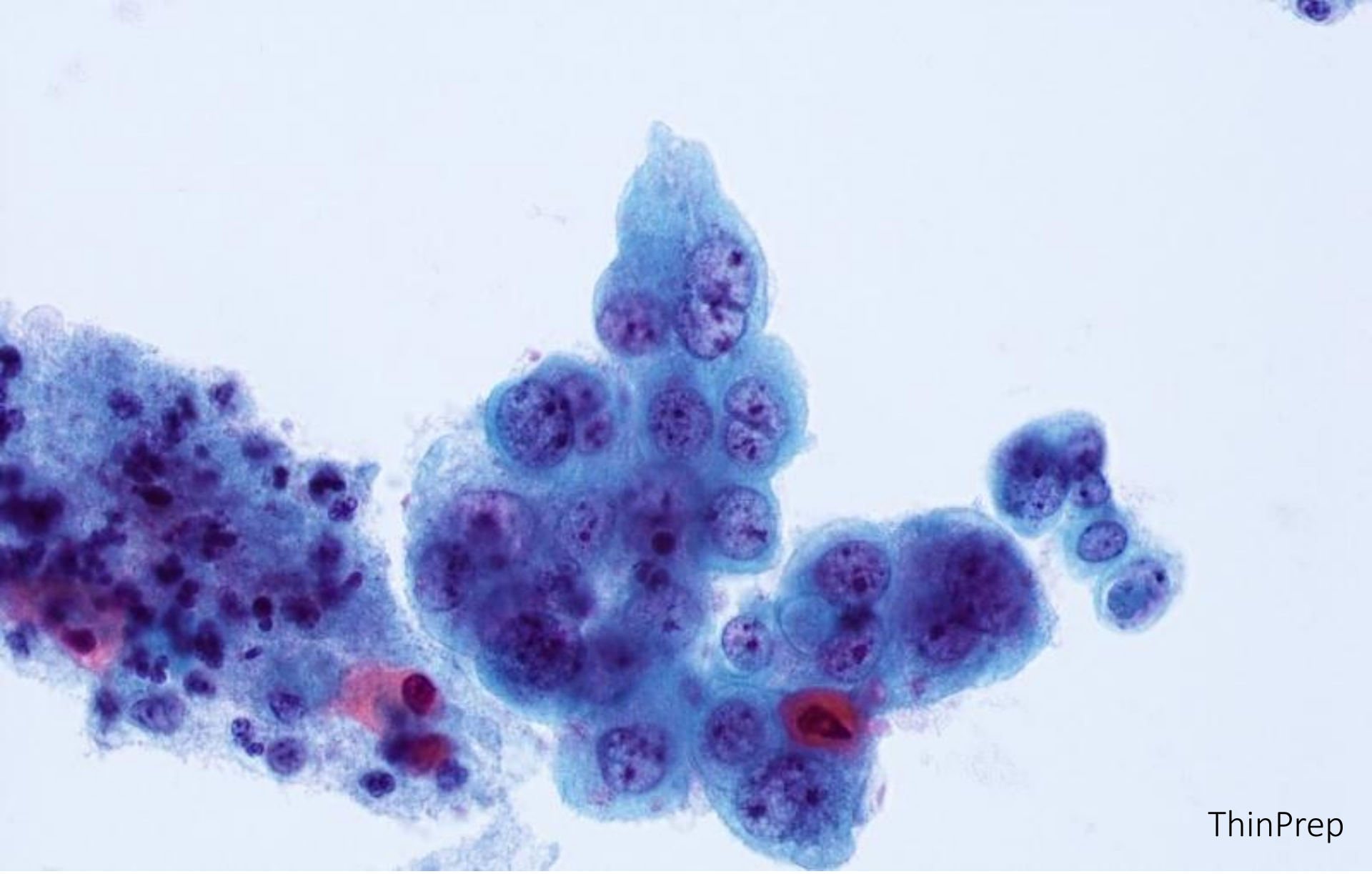
Nuclei: size varies. High N:C ratios.

Chromatin: coarsely granular, hyperchromatic, markedly irregular

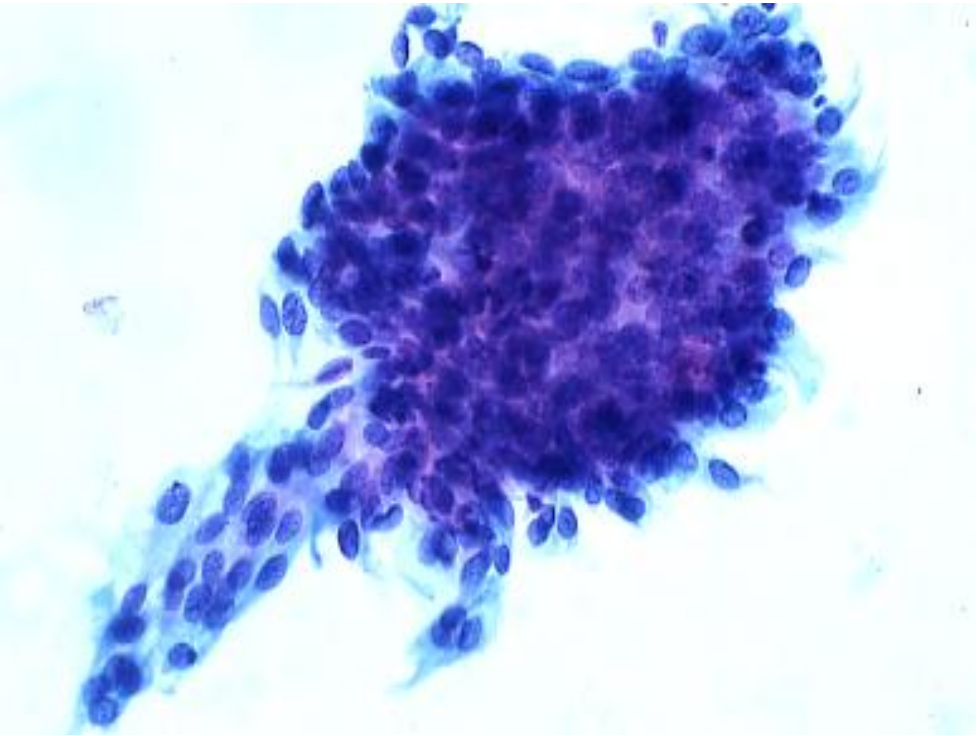
Nucleoli: often multiple and irregular.

Cytoplasm: poorly defined cell borders.
May be individual cell keratinisation

DD: HSIL
Reactive cells
Endometrial cells, lymphoma

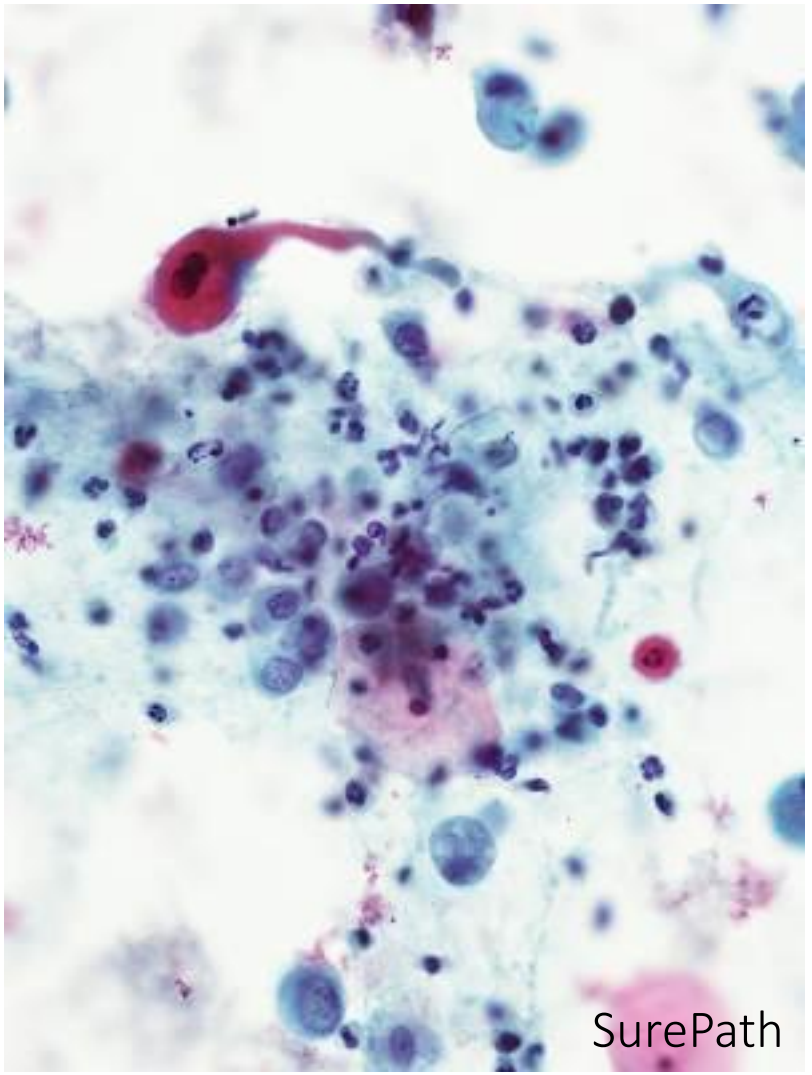


Non-keratinising SCC: large cell type

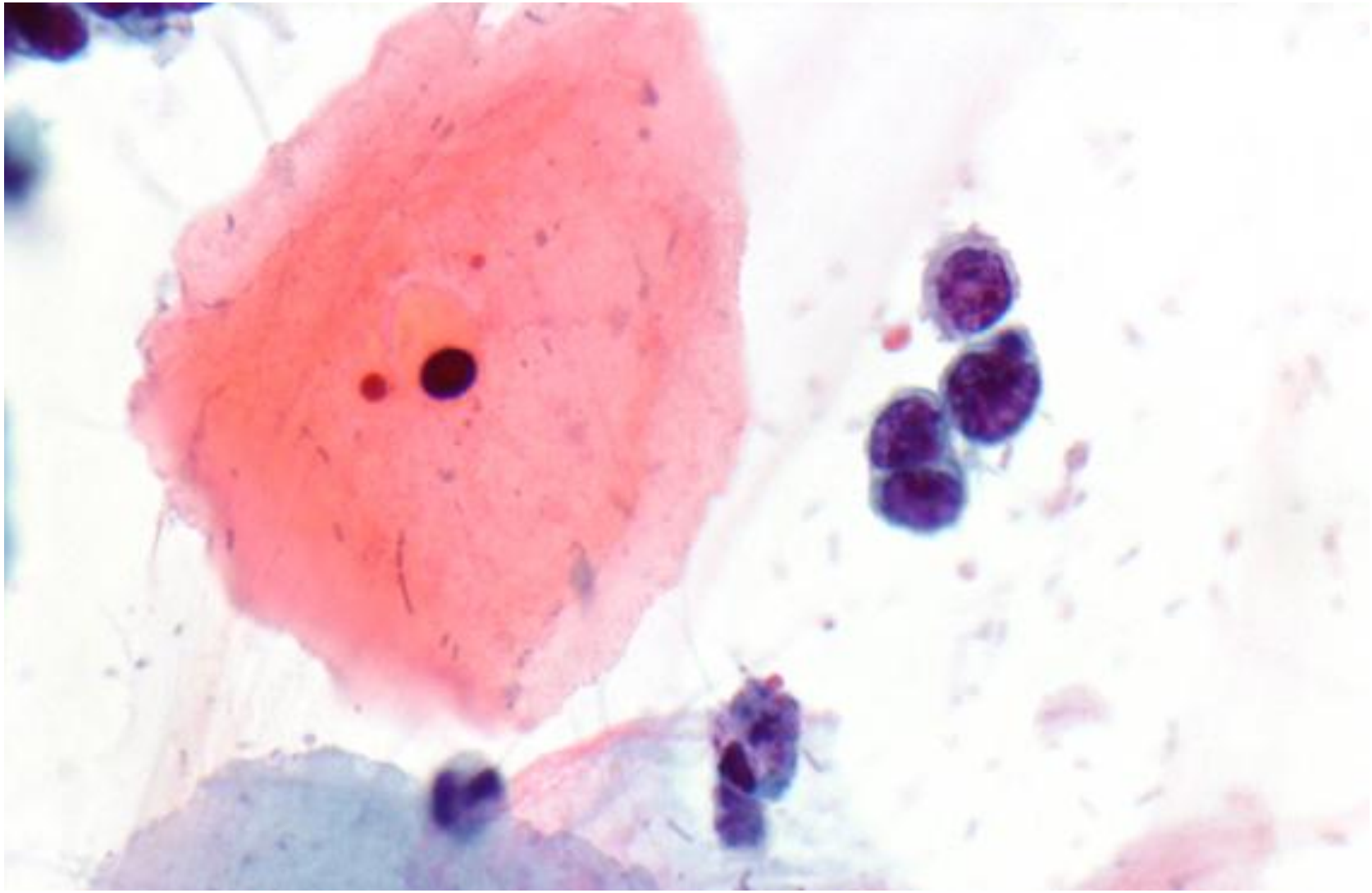


ThinPrep

SCC: Crowded sheet



SCC: Apoptotic debris



Non-keratinising SCC: small cell type

LSIL

Koilocytes: sharply defined perinuclear clearing

condensed outer rim of cytoplasm

abnormal nucleus: enlarged, multinucleated, irregular nuclear membrane, smudged or granular chromatin

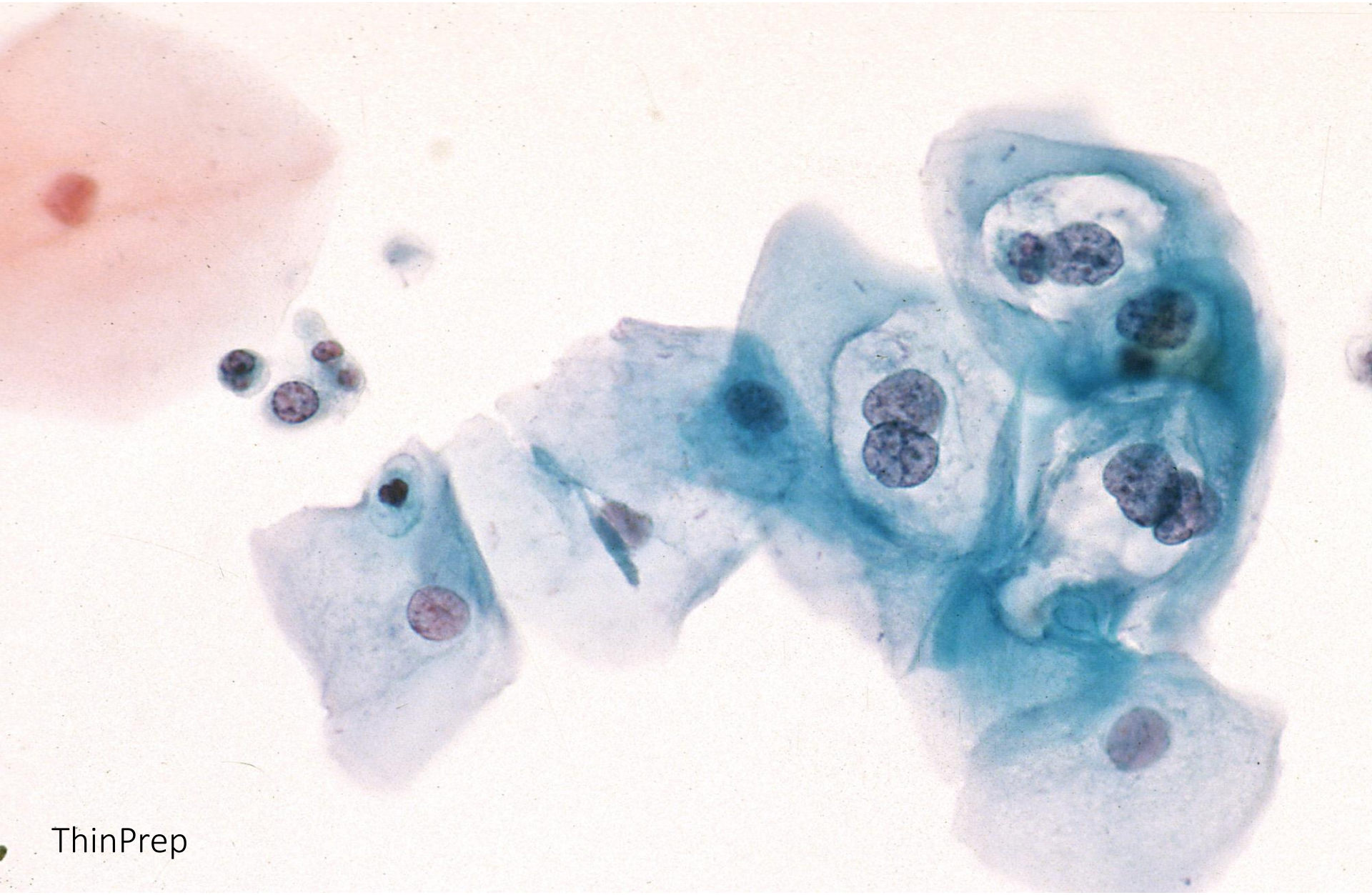
"Classical CIN 1": mild nuclear enlargement, size variation, mild nuclear membrane irregularity

increased N:C ratio but cytoplasm still abundant

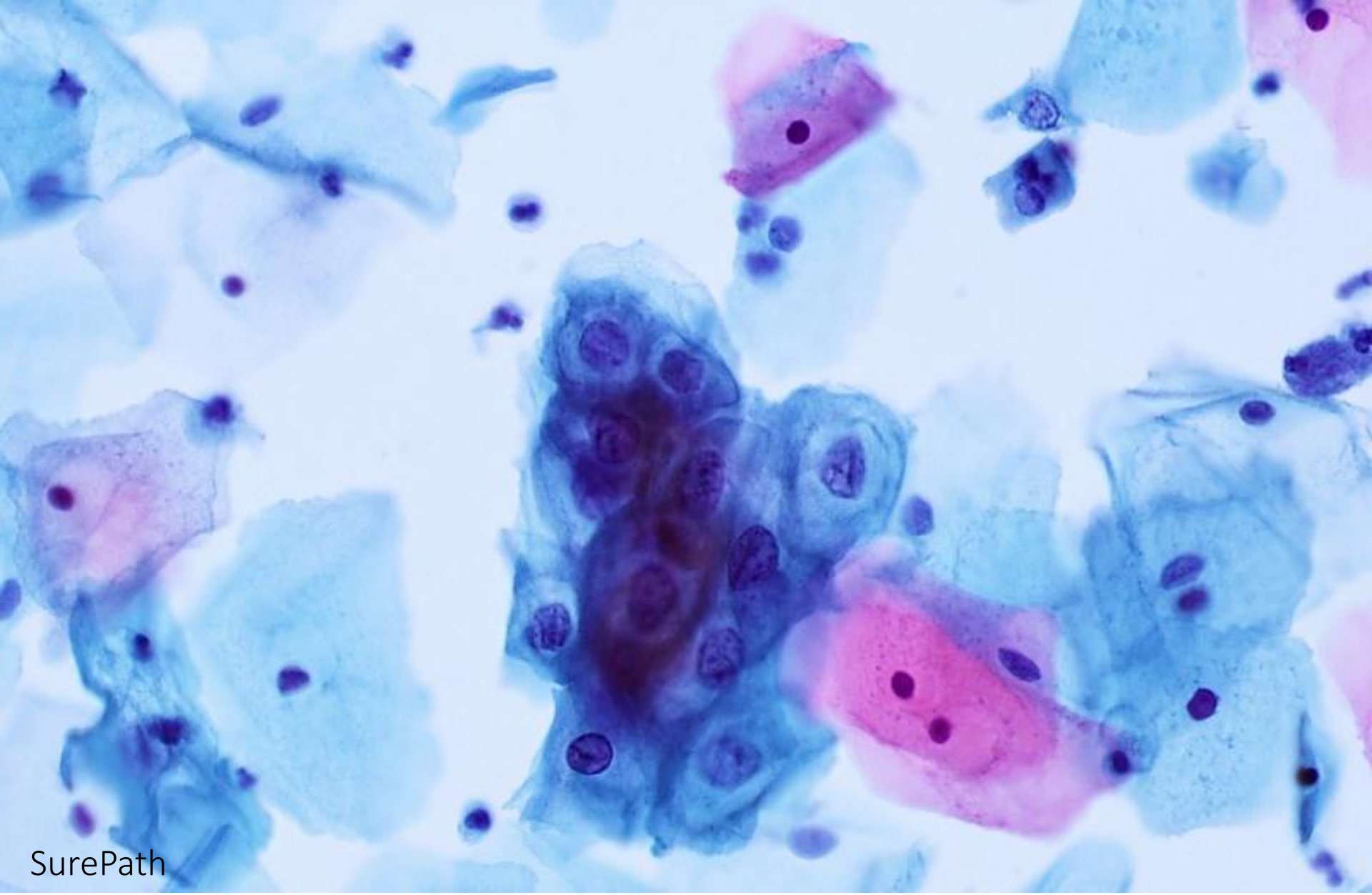
chromatin uniform and finely granular or smudged

Dyskeratotic cells: dense intensely orange cytoplasm (keratinisation)

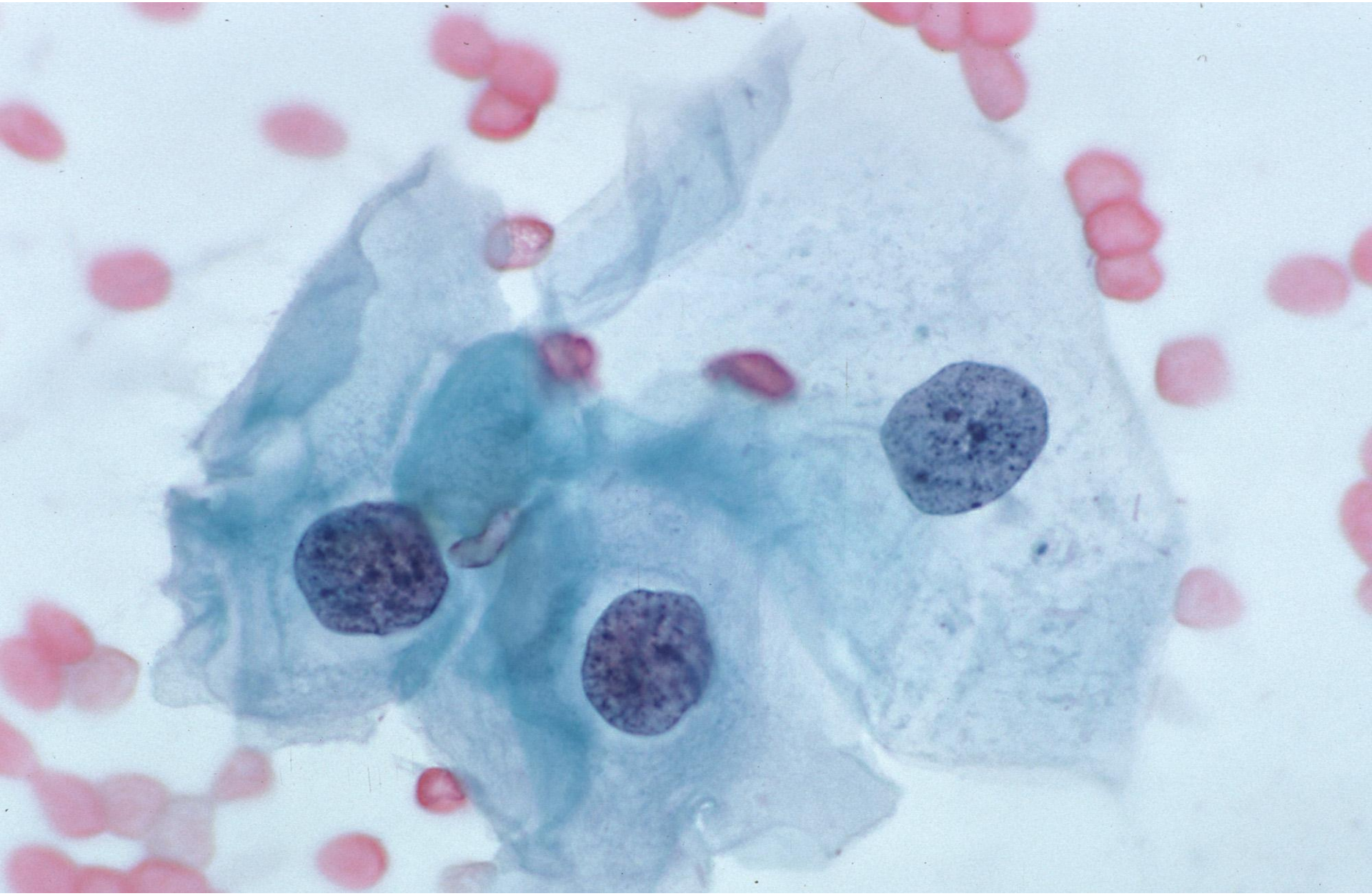
nuclei atypical (pyknotic, hyperchromatic, smudged) with nuclear membrane irregularity



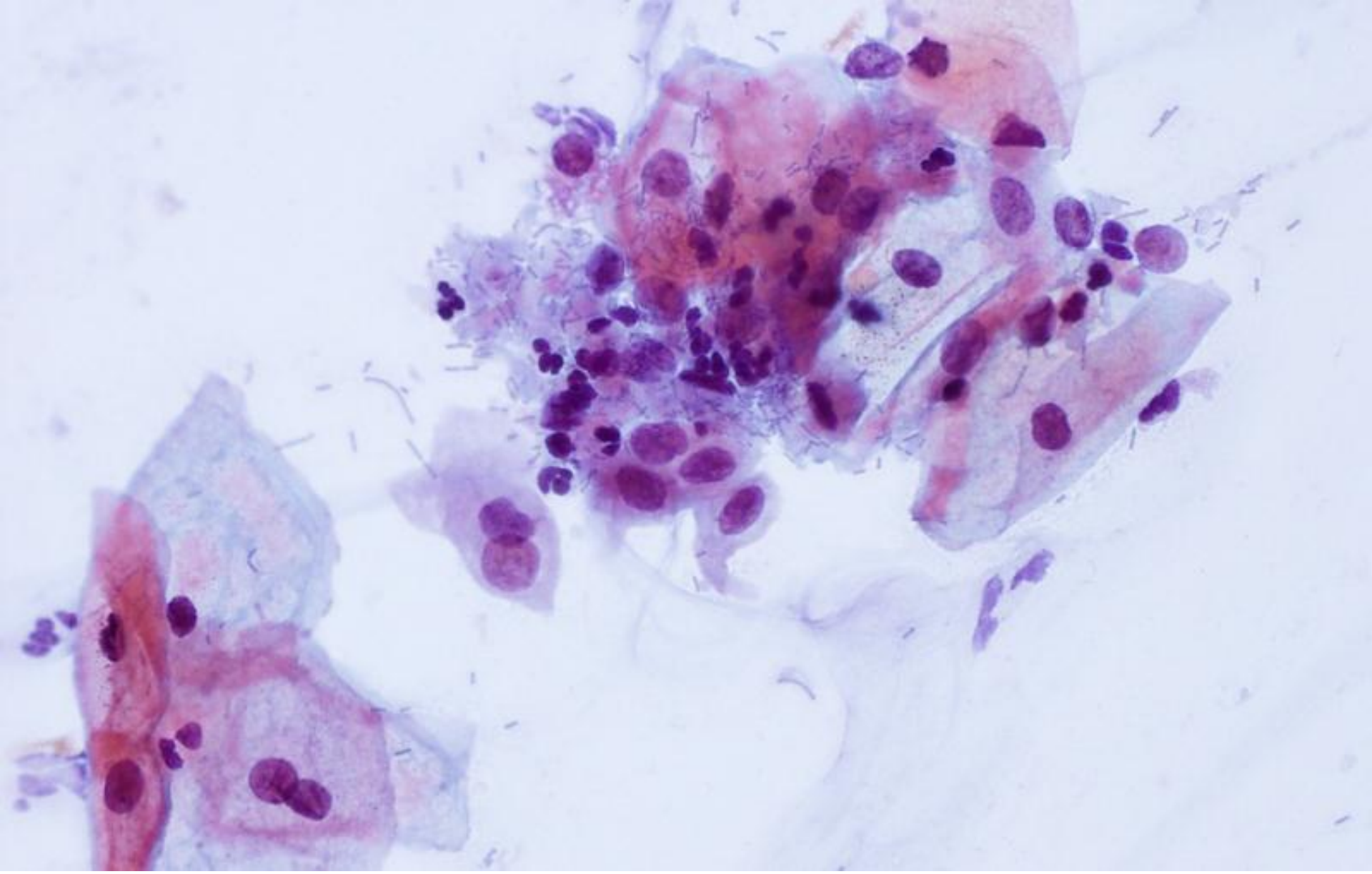
LSIL: koilocytes



LSIL: koilocytes



LSIL: no koilocytes

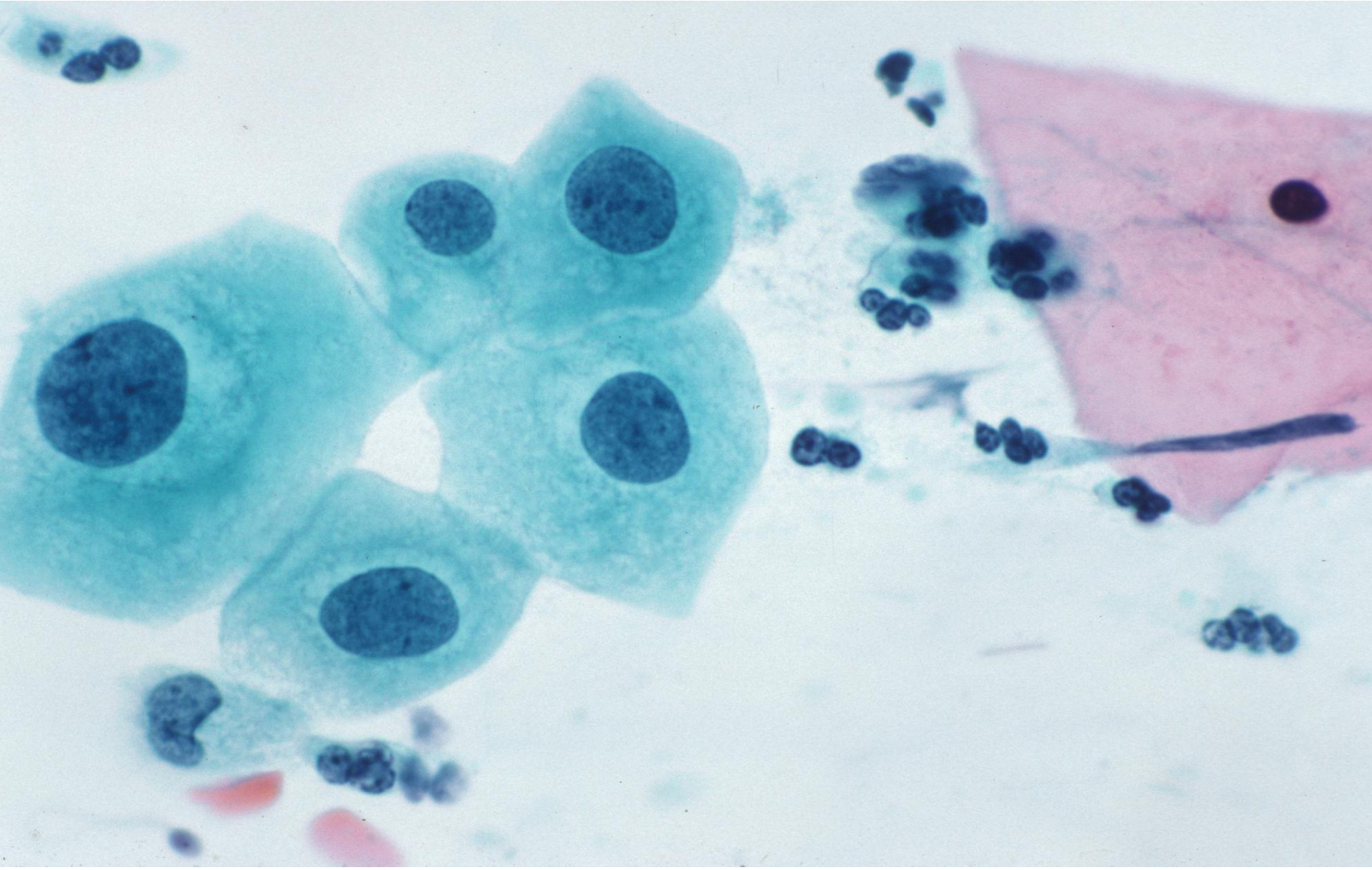


LSIL and missed HSIL (CIN 2)

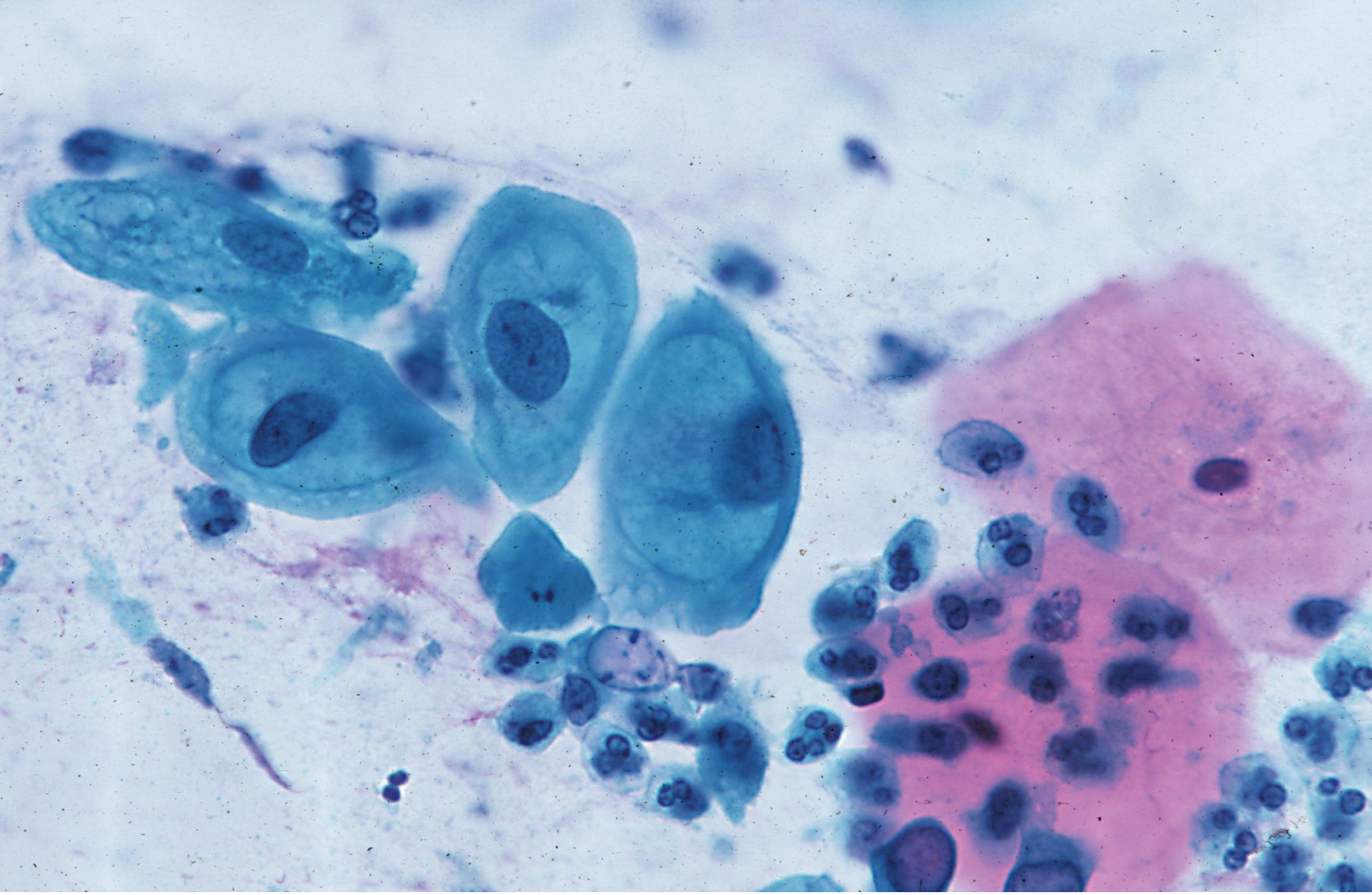
ASC-US

Criteria

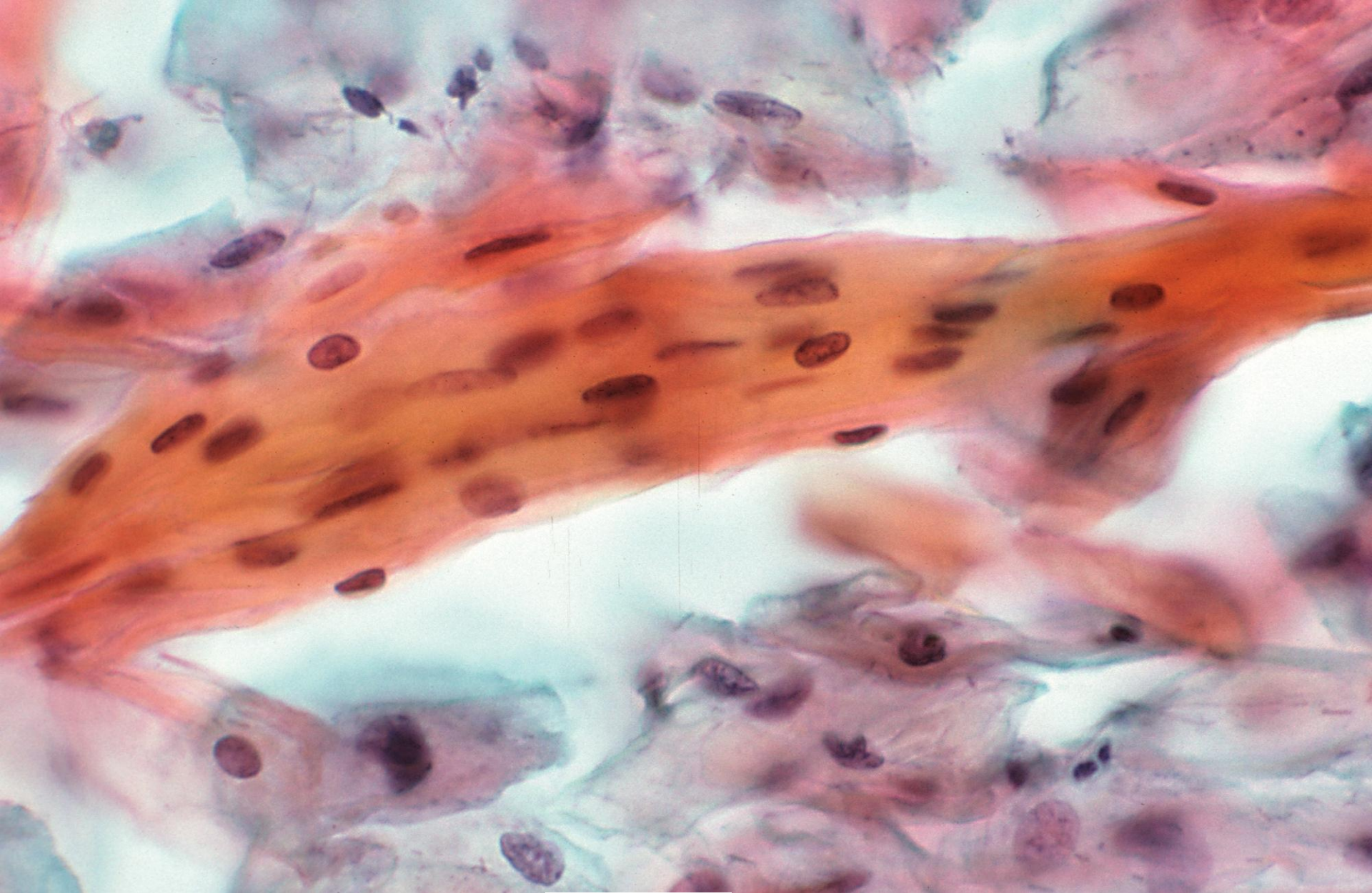
- Nuclei enlarged
- Slight increase in N:C ratio
- Minimal nuclear hyperchromasia, irregularity in chromatin distribution or nuclear shape
- Minimal nuclear abnormalities associated with dense orangeophilic cytoplasm



ASC-US



ASC-US



ASC-US

Concluding Comments

- A variety of appearances are seen with high-grade squamous lesions and some are difficult patterns to recognize: See as many abnormal cases as you can.

- Different lesions can coexist.
  - LSIL and HSIL
  - HSIL and glandular lesions