Detecting endocervical glandular lesions by cervical cytology

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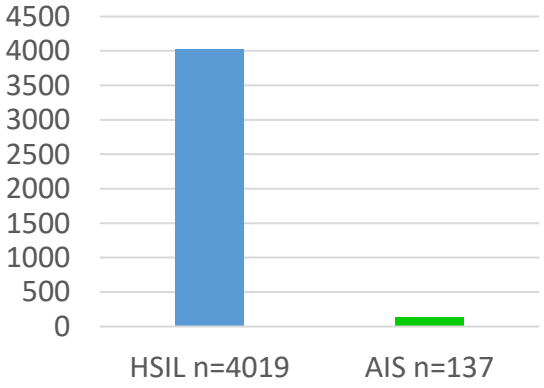
Frequency of endocervical lesions compared with squamous lesions

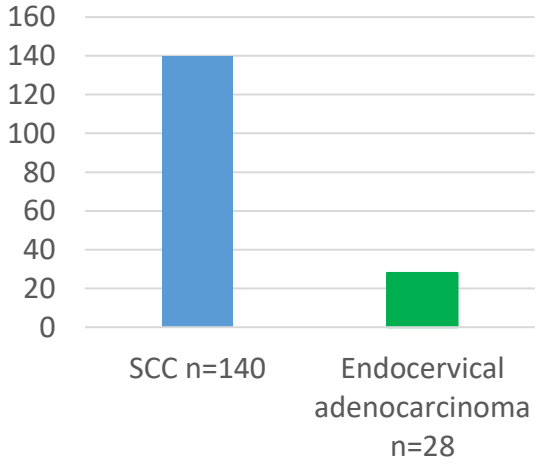
In-situ high-grade lesions

HSIL was reported in histology samples 30 times more often than AIS was reported



Invasive cancers

SCC was reported 4.5 times more often than endocervical adenocarcinoma



The sensitivity for detecting high-grade glandular lesions with cytology is about 50% compared with 80-90% for high-grade squamous lesions

New Zealand NCSP Monitoring Data Jan- Dec 2019

Overview of glandular cell cytology

Endocervical cells

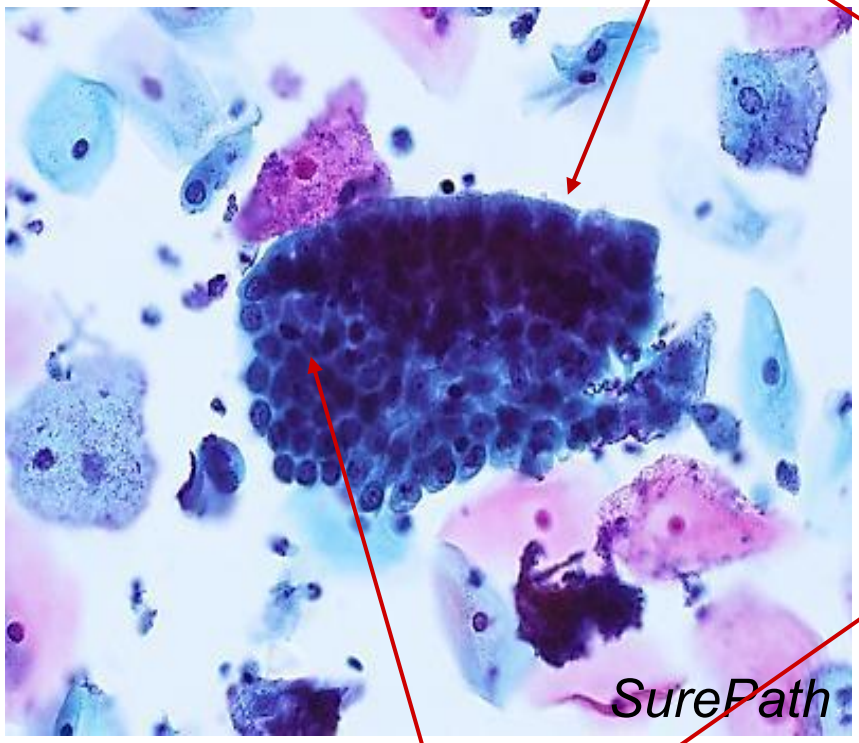
1. Normal and reactive endocervical cells
2. Atypical endocervical cells
3. Adenocarcinoma in situ (AIS)
4. Invasive endocervical adenocarcinoma

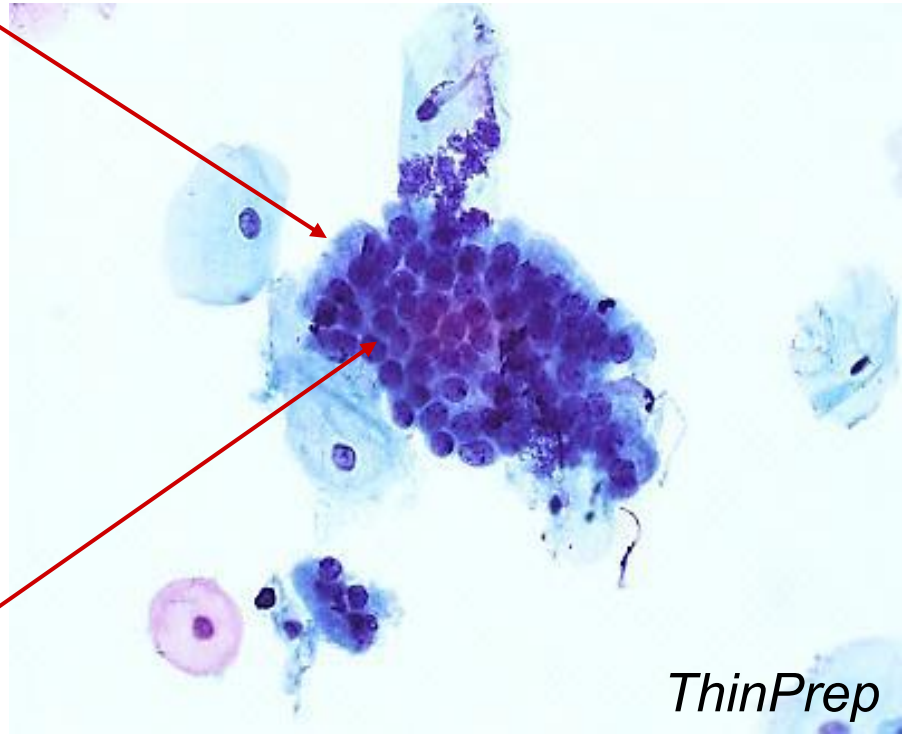
Endometrial cells

1. Normal endometrial cells
2. Atypical endometrial cells
3. Endometrial adenocarcinoma

Other abnormal glandular cells

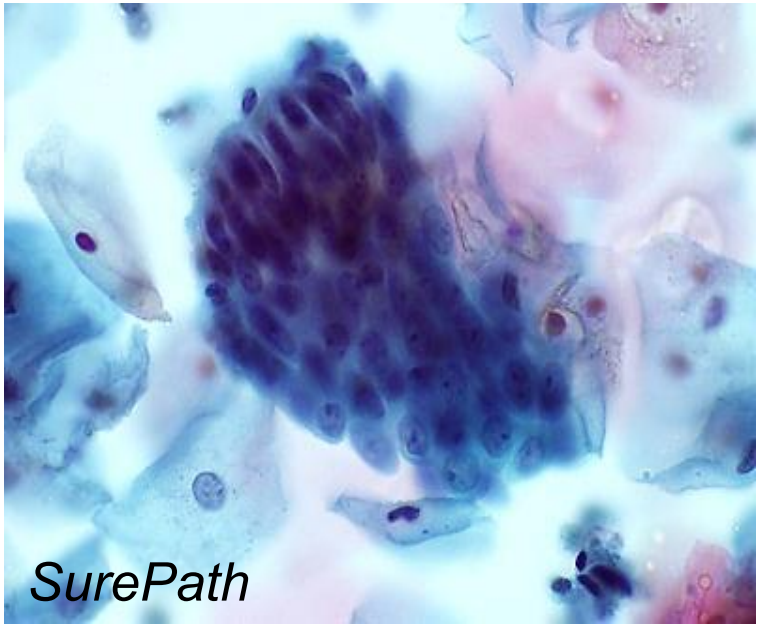
“Picket-fence” appearance when seen side on

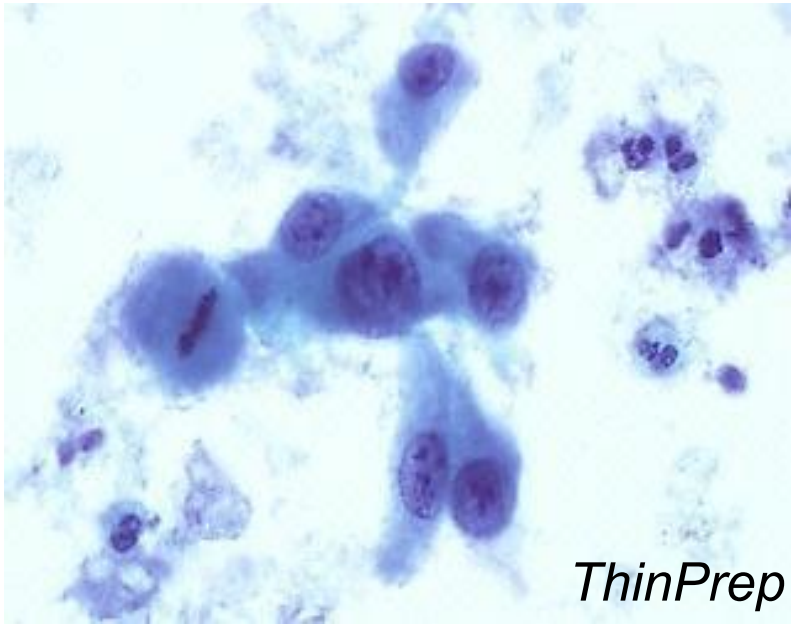




“Honey-comb” appearance when viewed from above (or below)

Normal endocervical cells





Mild reaction:

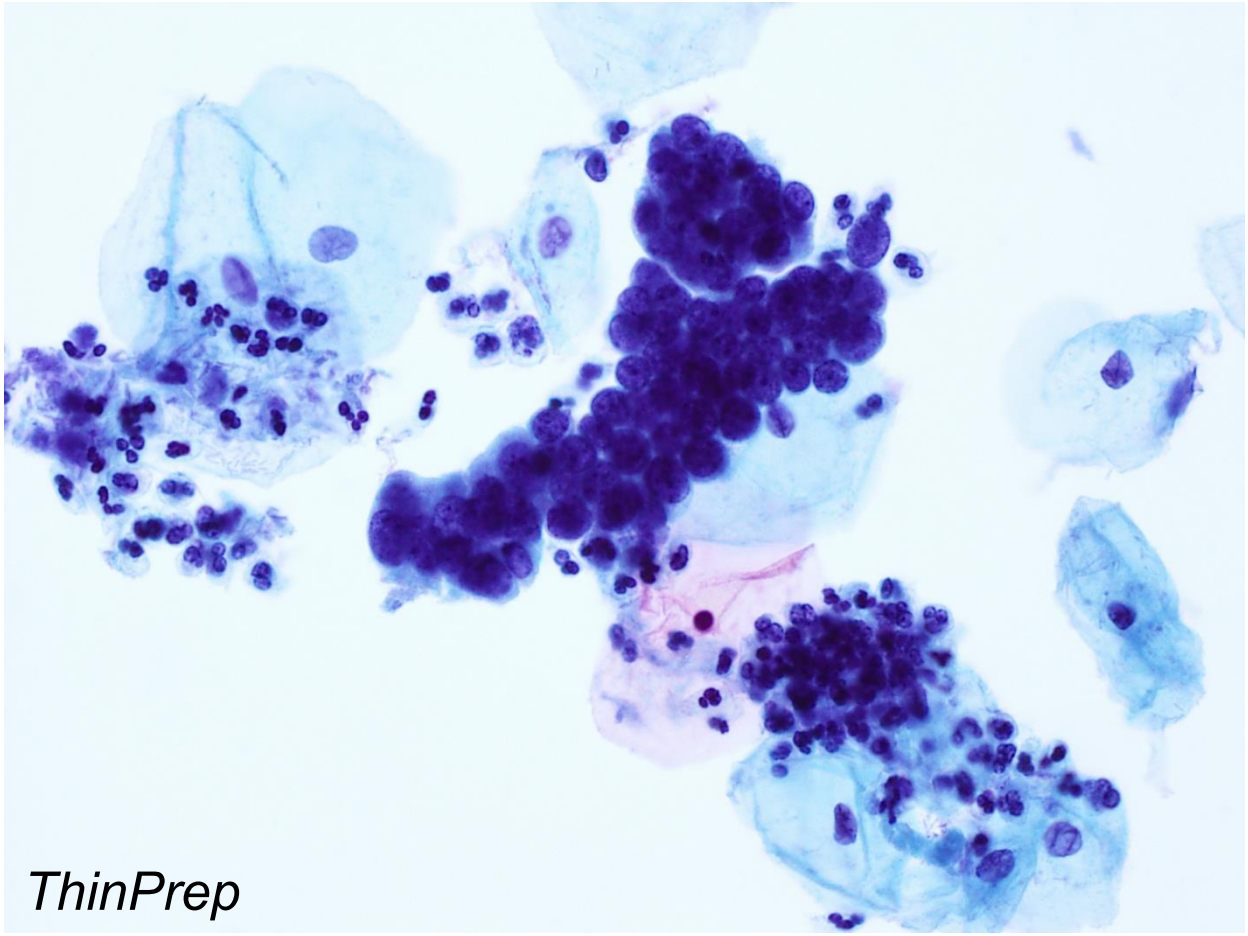
- nuclei larger, have nucleoli
- retain good polarity

Marked reaction:

- marked and variable nuclear enlargement, nucleoli, mitoses
- need to see context to assess this worrying appearance

Reactive endocervical cells

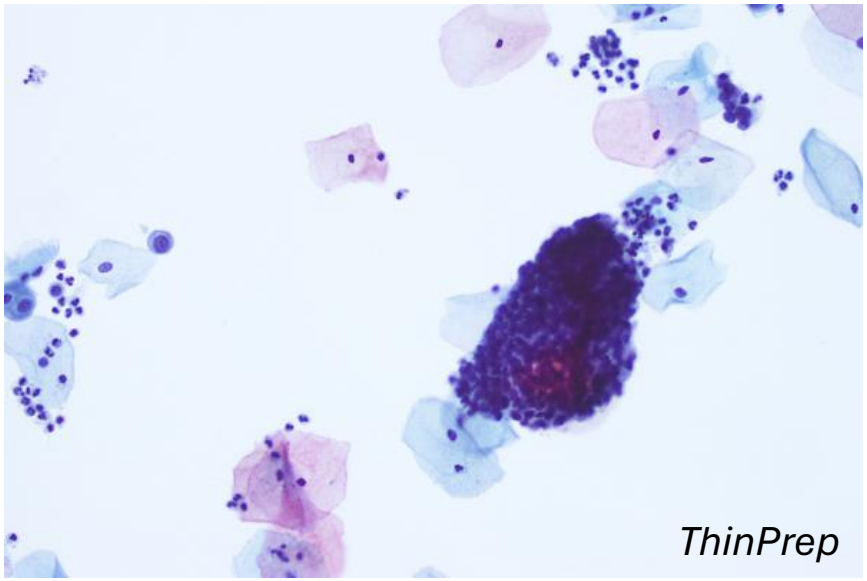
Atypical glandular cells are reported when there is a suspicion of a glandular lesion but the appearances are not diagnostic



Atypical glandular cells: AIS on follow-up

Principles of AIS diagnosis

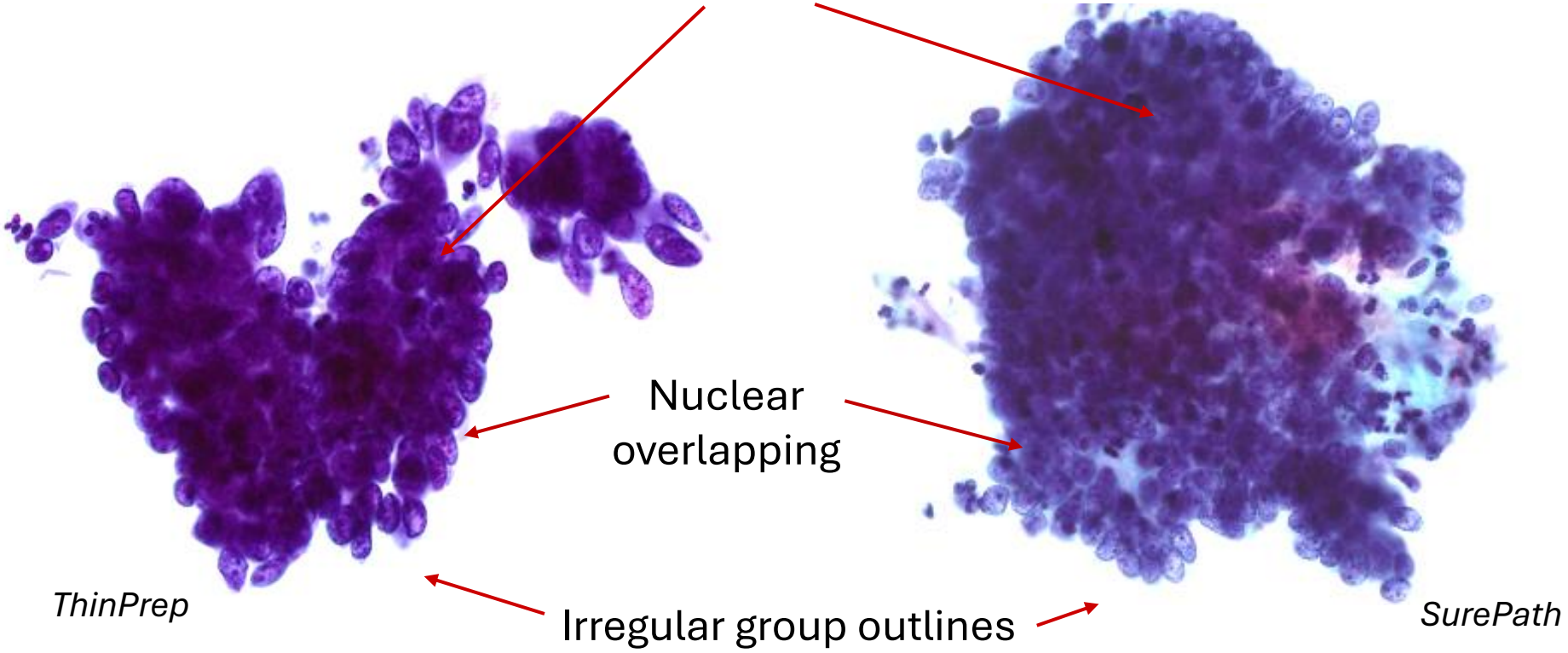
1. Architecture matters most
2. Cell morphology must also be consistent



Assessing hyperchromatic crowded groups

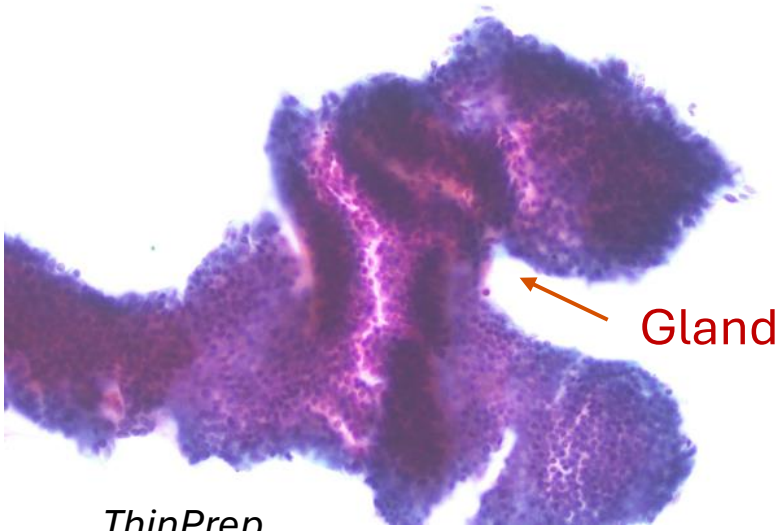
- are easy to see at low-power
- interpretation requires close examination at high-power

AIS ARCHITECTURE



Large irregularly shaped groups

AIS architecture



Gland openings

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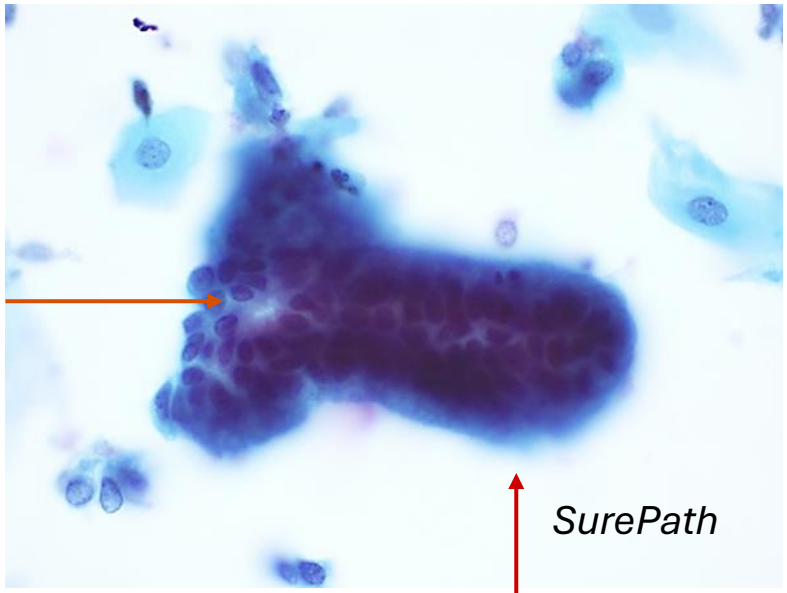

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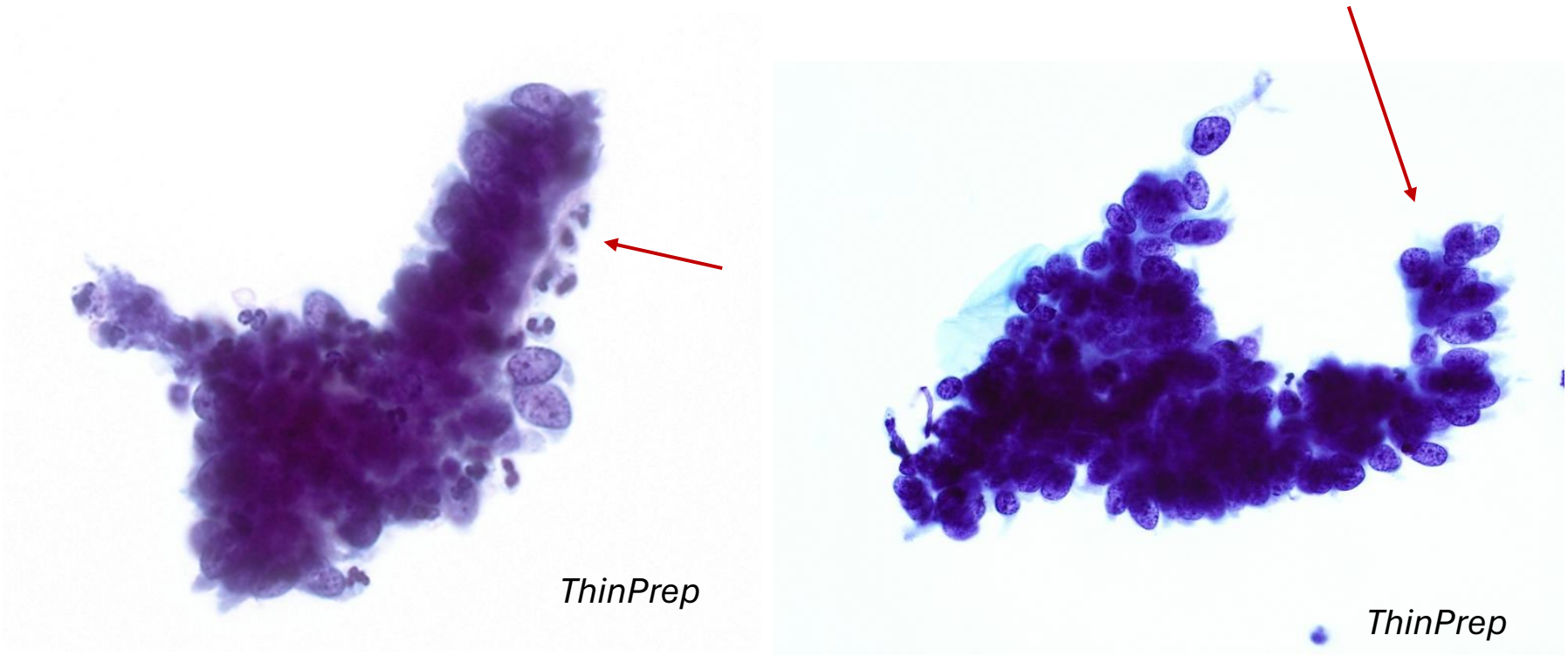
Papillary structures

Glandular architecture: gland openings and papillary structures

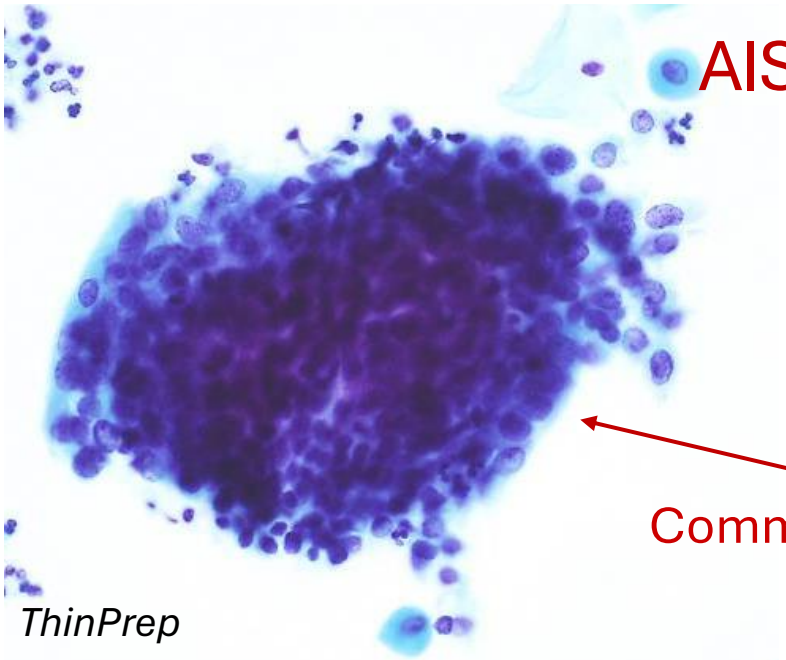
AIS architecture



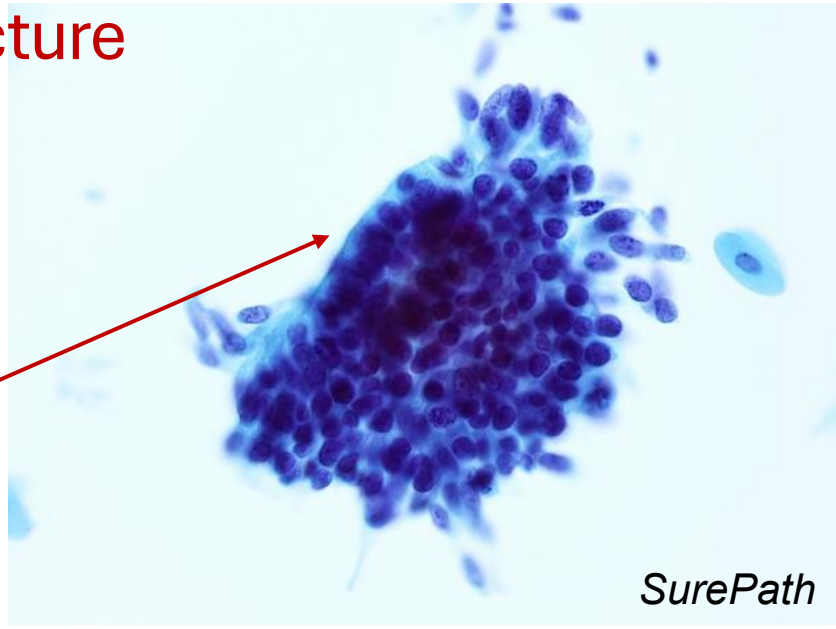
Crowded strips of columnar cells coming off the edge of a crowded sheet

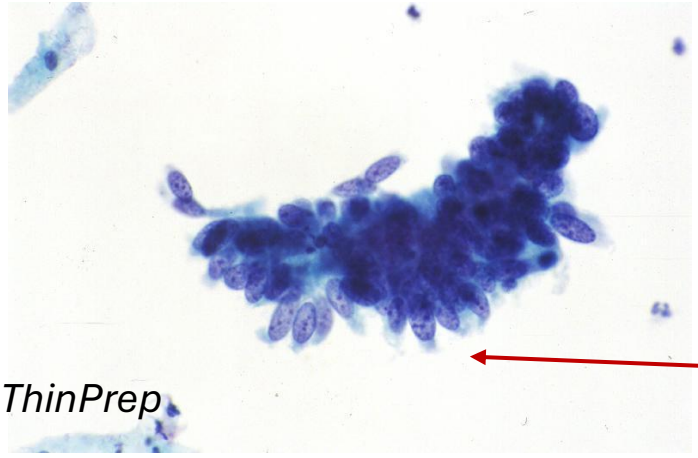
Glandular architecture: strips off sheet edges

AIS architecture

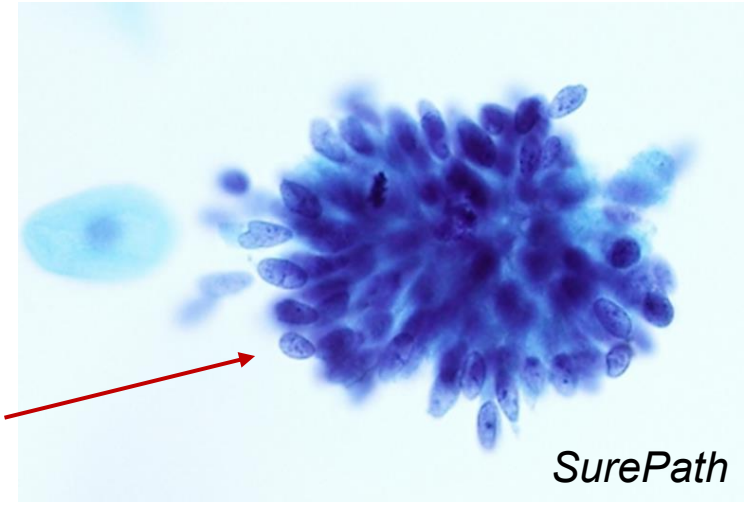


Common border

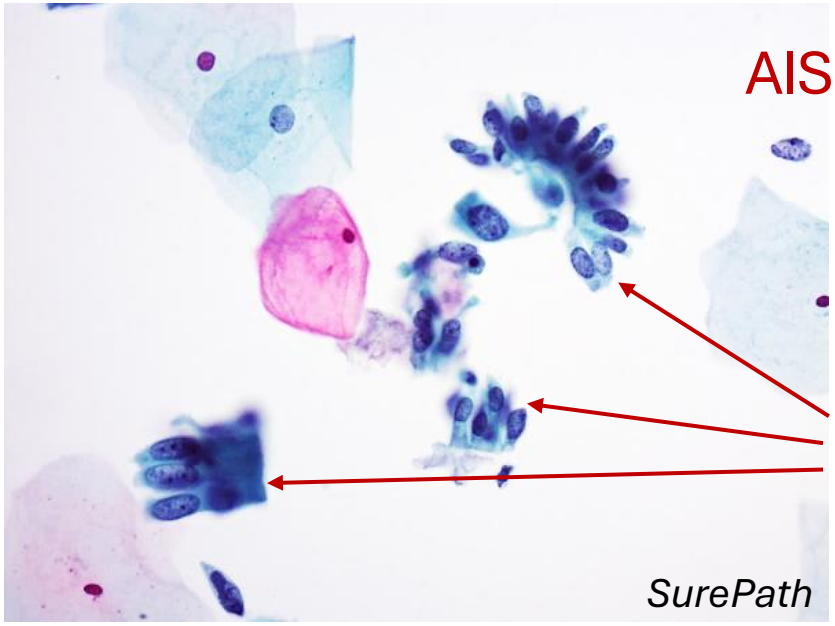


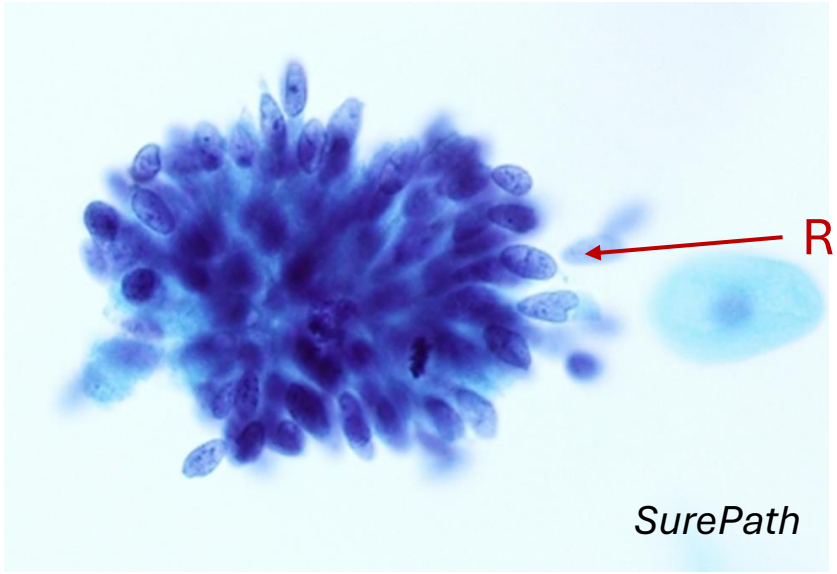


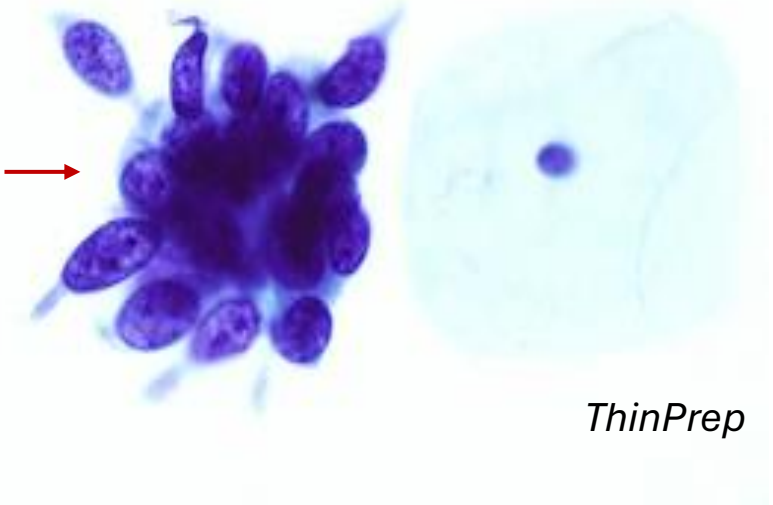
Feathering



Sheet edges: Common borders and feathering

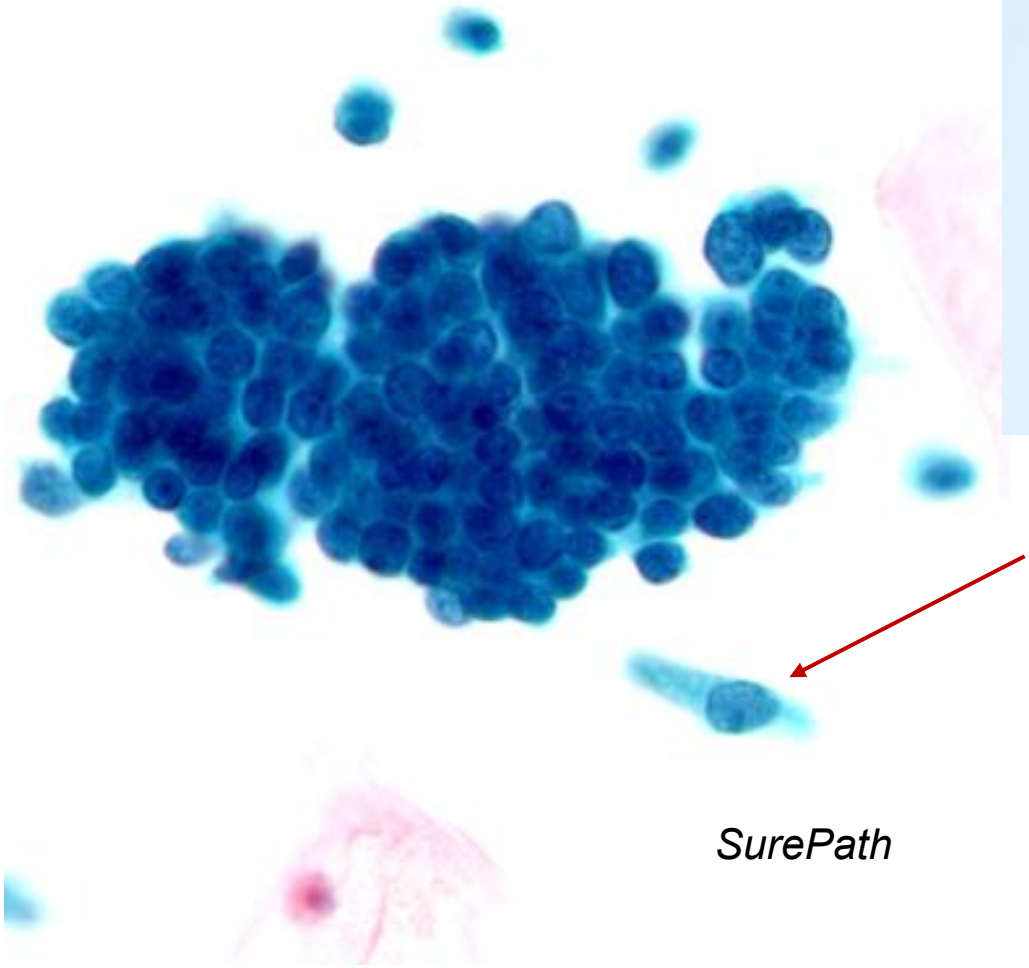






Strips and rosettes

AIS: CELL MORPHOLOGY



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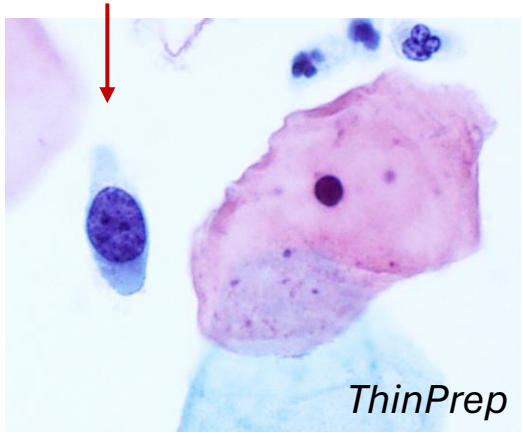
"Frying-pan" cells: The nucleus is wider in diameter than the diameter at both ends of the cell



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Nuclear size is increased

AIS: Cell morphology

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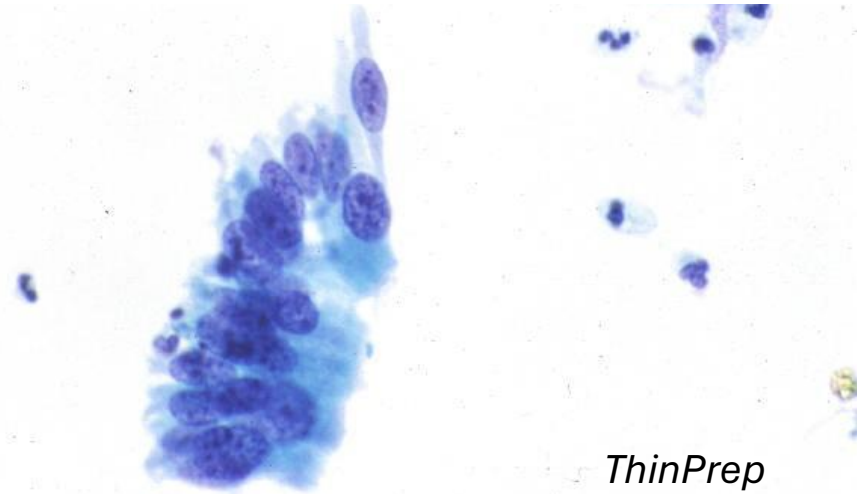

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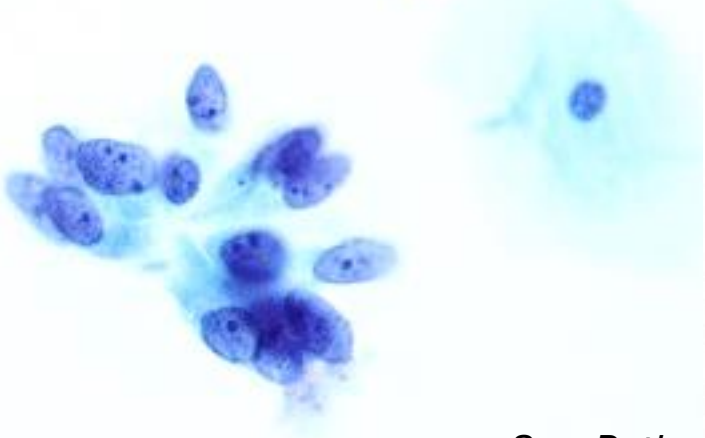

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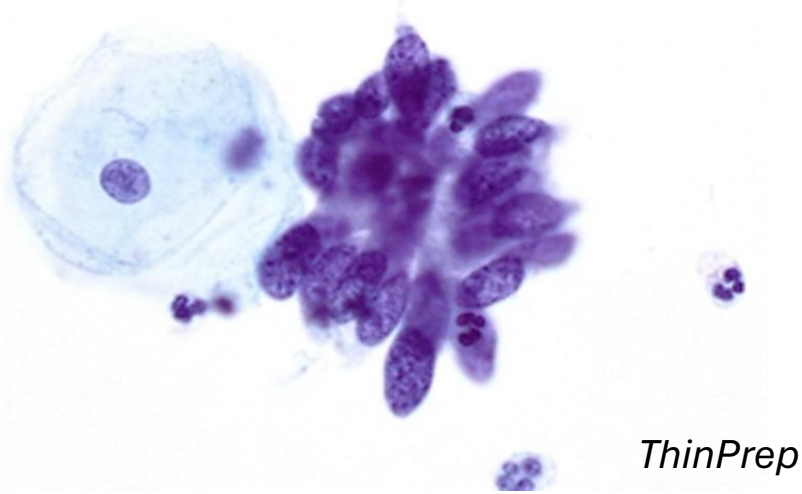

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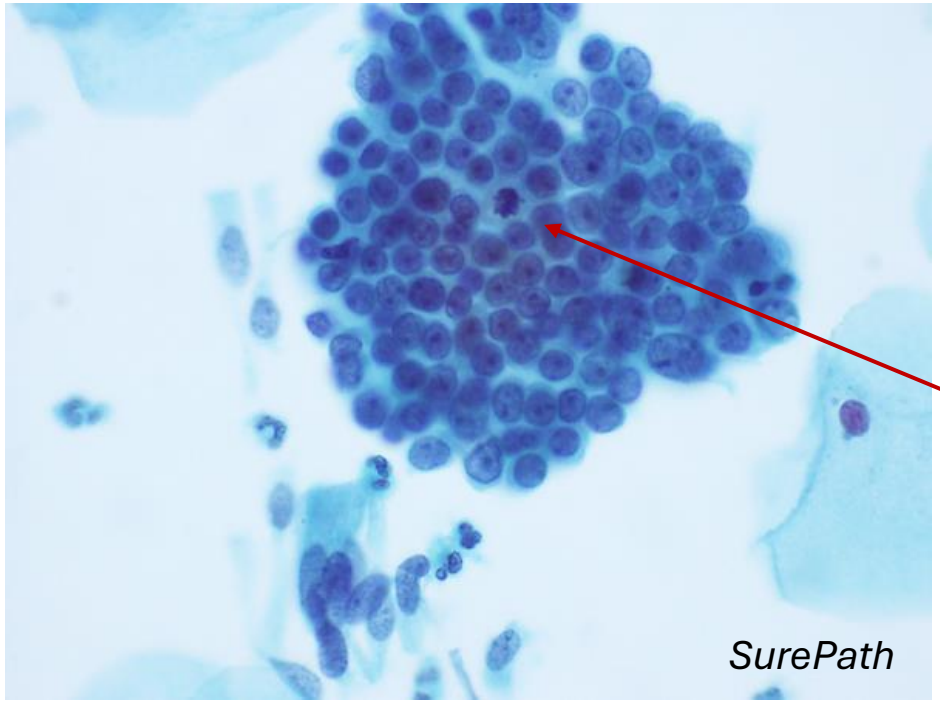
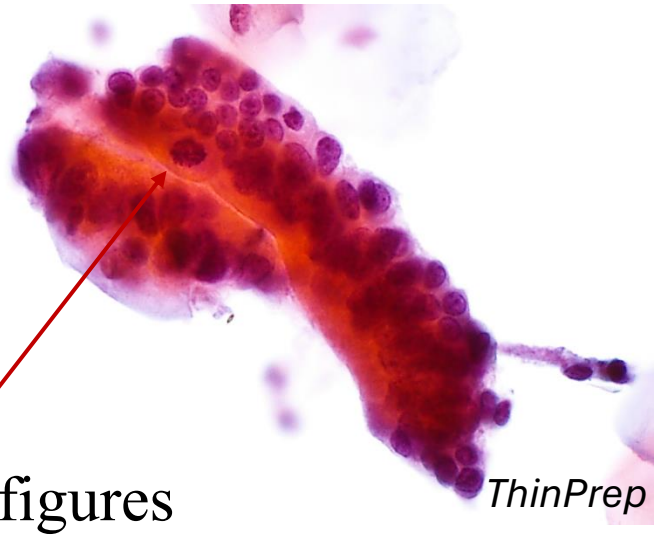
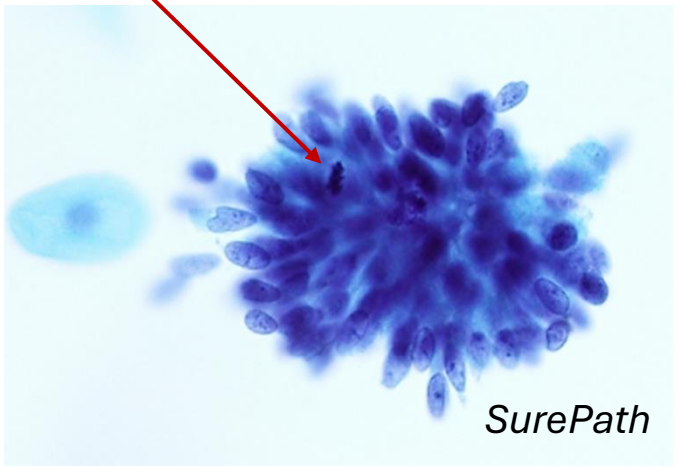
Hyperchromasia with stippled chromatin

AIS: Cell morphology



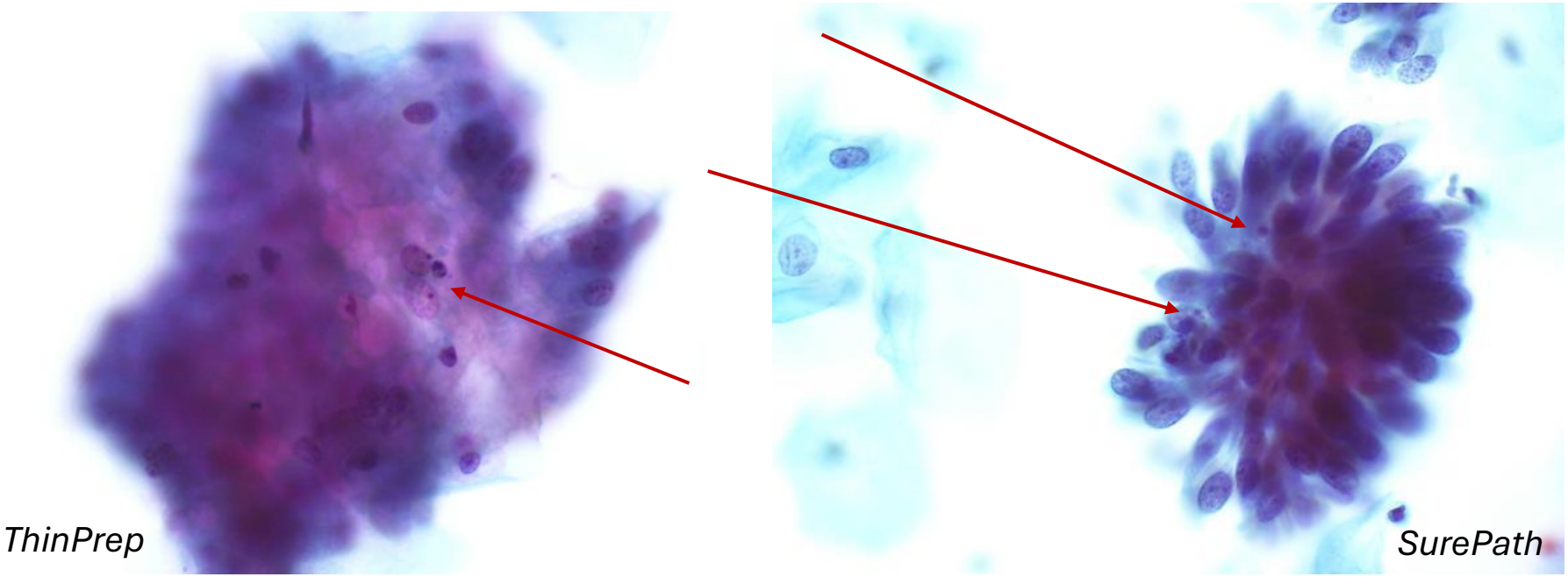


Mitotic figures



Mitoses are seen occasionally

AIS: Cell morphology



Apoptotic debris

Adenocarcinoma in situ (AIS) features

Cell aggregates: ARCHITECTURE matters most

1. Irregularly shaped groups of tightly crowded cells with nuclear overlapping
2. Glandular architecture: strips off sheet edges, papillary groups, gland openings
3. Sheet edges: palisaded nuclei, common borders, feathering
4. Strips and rosettes with pseudo-stratification

Cell morphology needs to be consistent too:

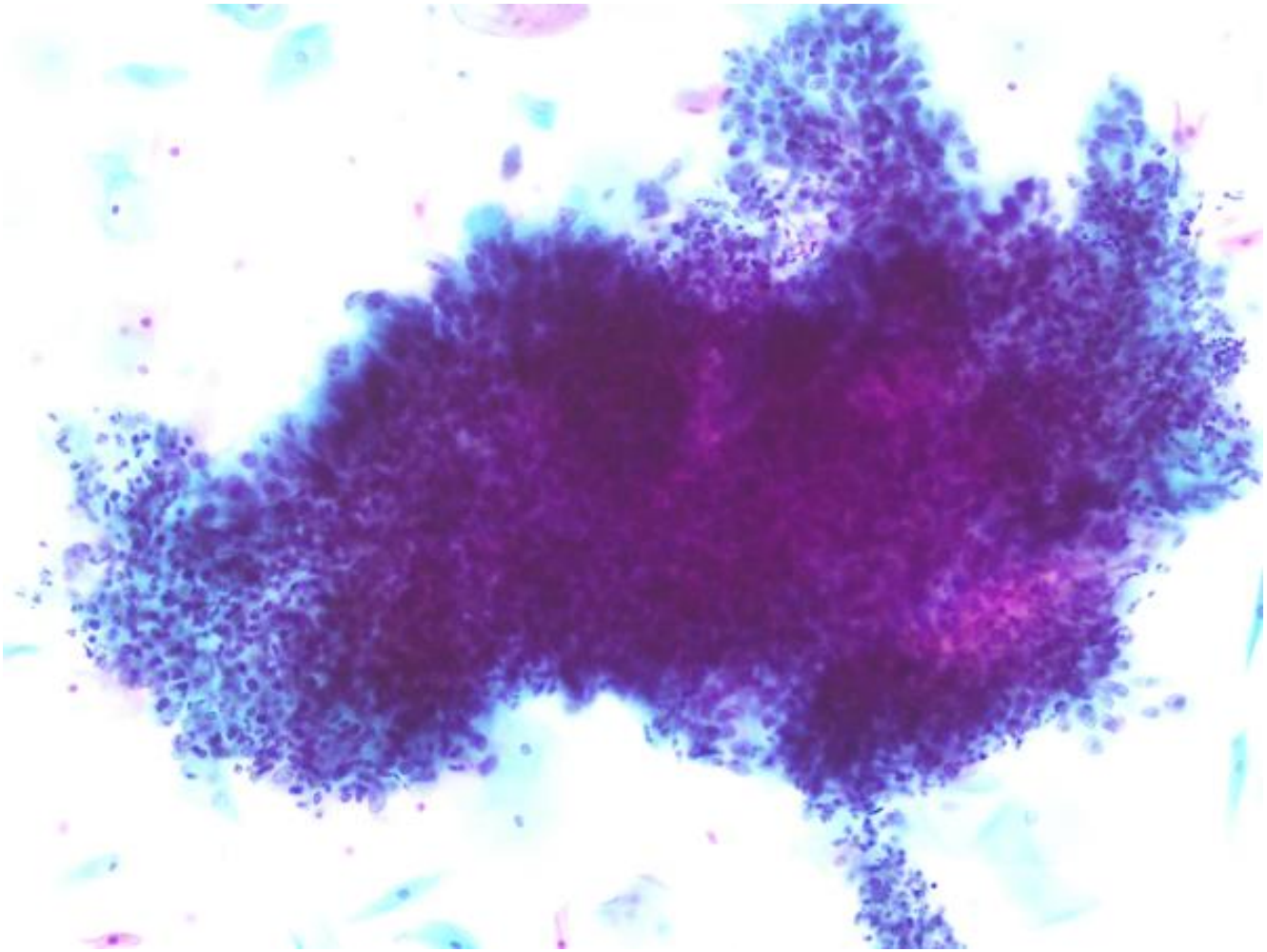
1. Nuclear size mildly increased
2. Hyperchromasia with uniform stippled chromatin
3. Mitoses sometimes present
4. Apoptotic debris may be present

Endocervical adenocarcinoma

1. Features of AIS

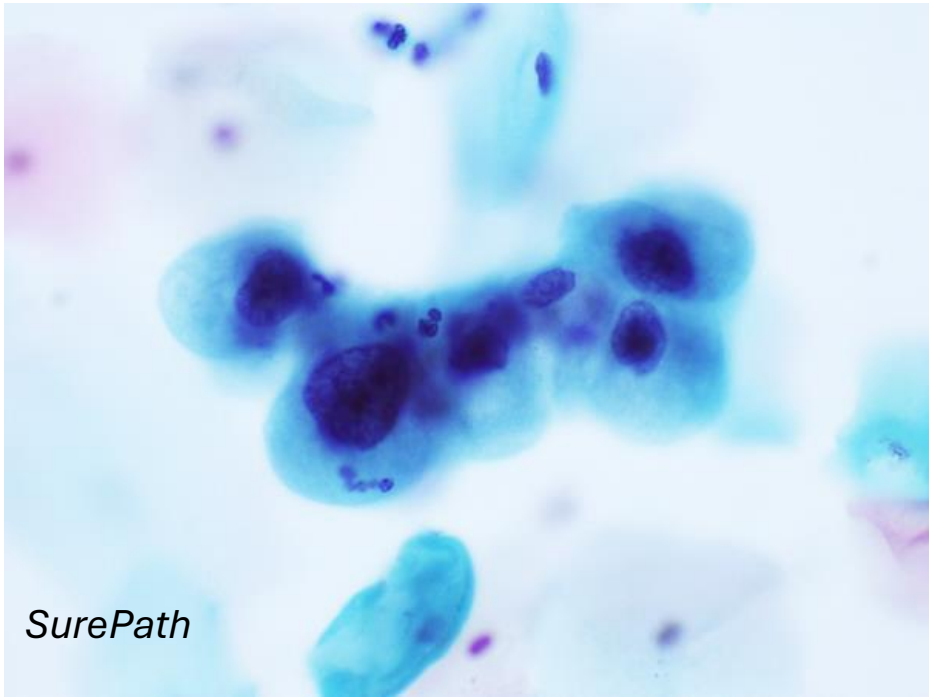
2. Features suggestive of invasion
   - supercrowding with loss of polarity
   - marked pleomorphism
   - nuclei: chromatin clearing, conspicuous nucleoli
   - more single cells, fewer strips and rosettes
   - tumour diathesis and/or blood

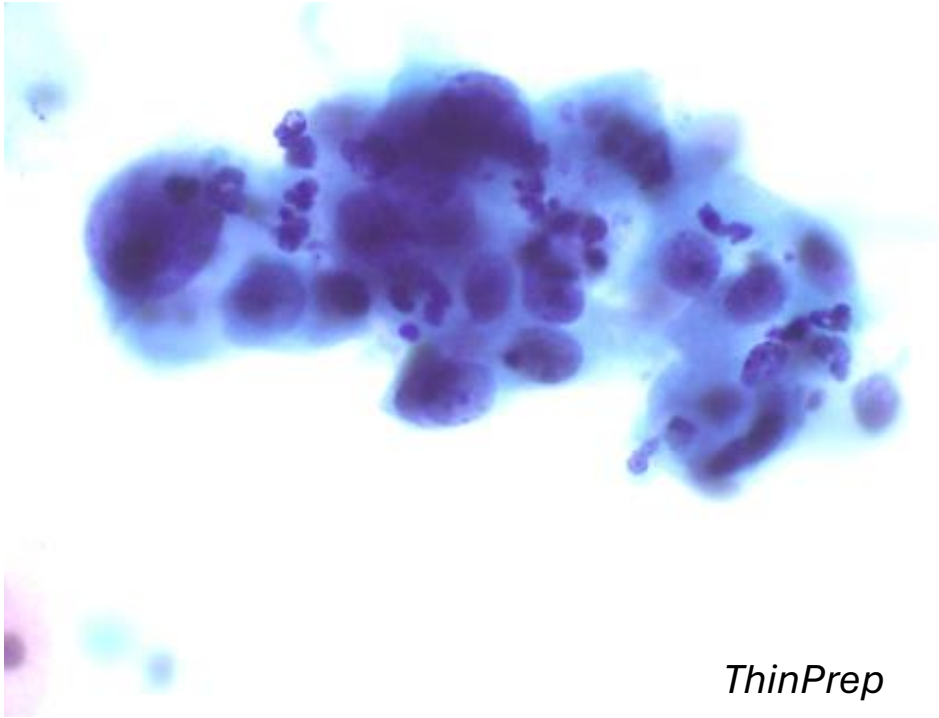
Endocervical adenocarcinoma



Large supercrowded complex microbiopsies

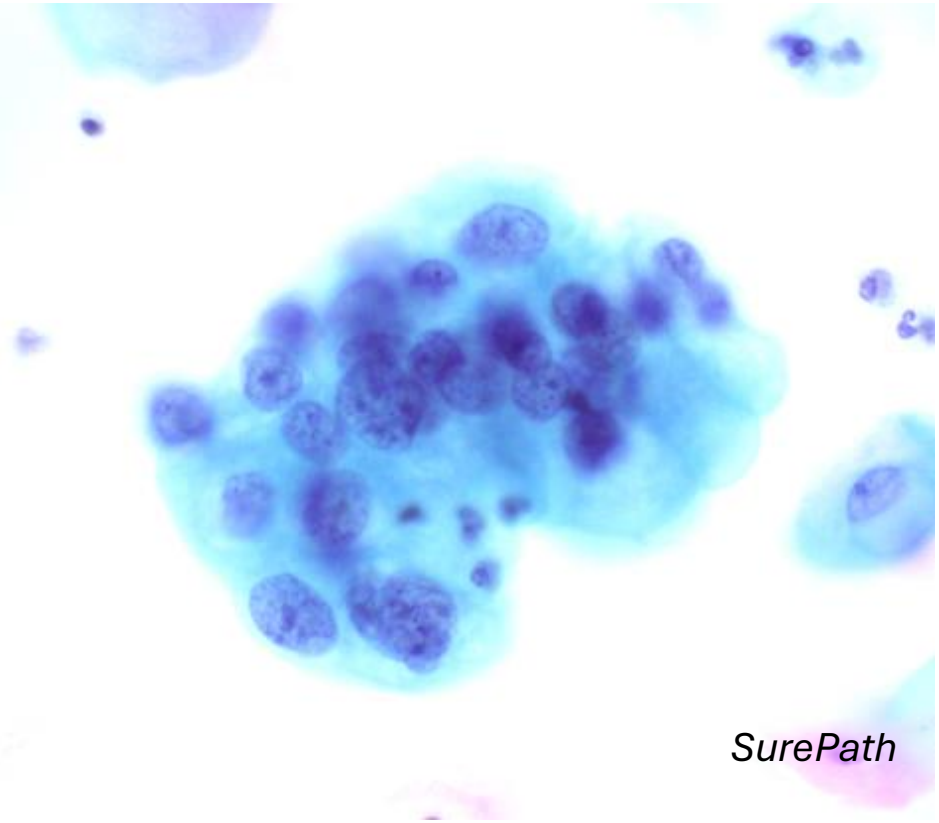
Endocervical adenocarcinoma





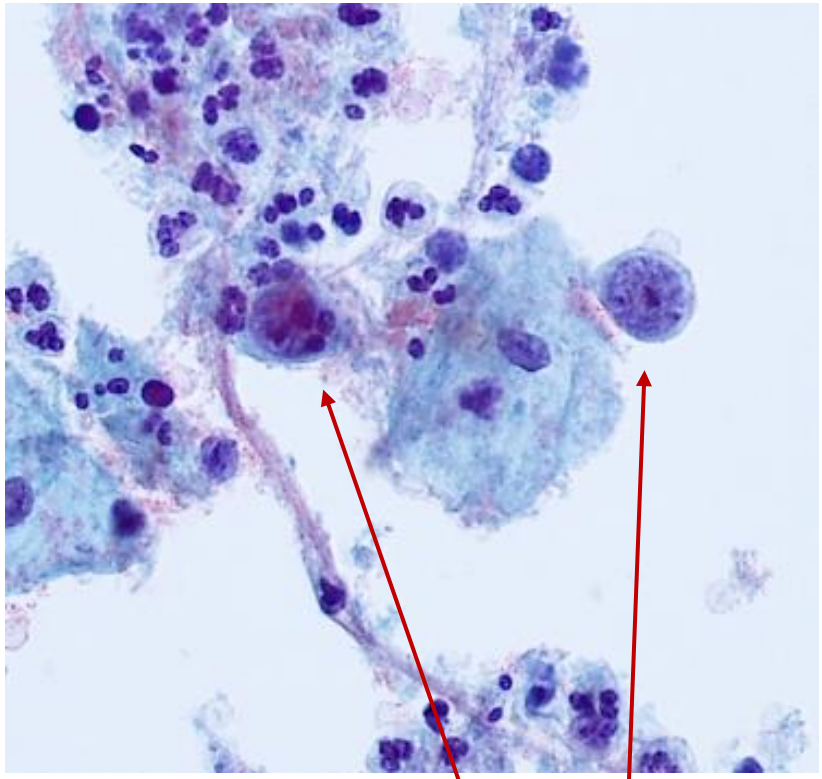
Marked pleomorphism

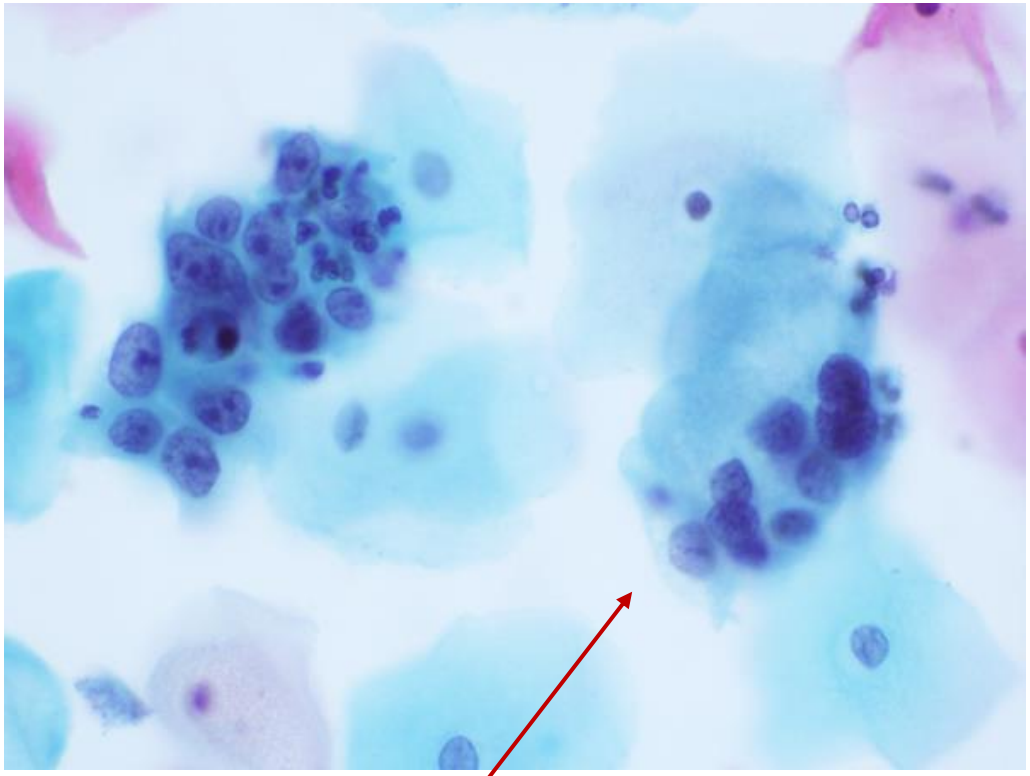
Endocervical adenocarcinoma



Nuclei: chromatin clearing, conspicuous nucleoli

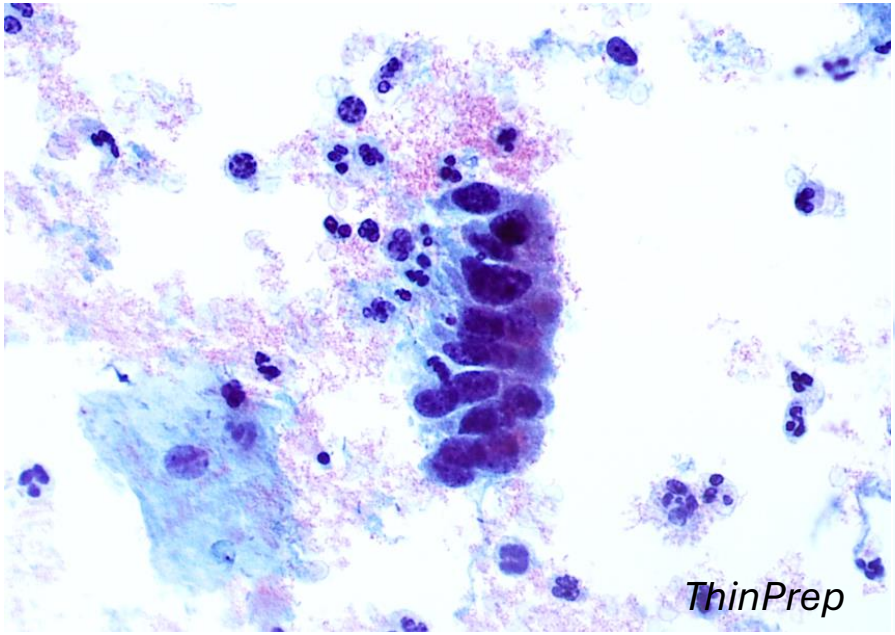
Endocervical adenocarcinoma

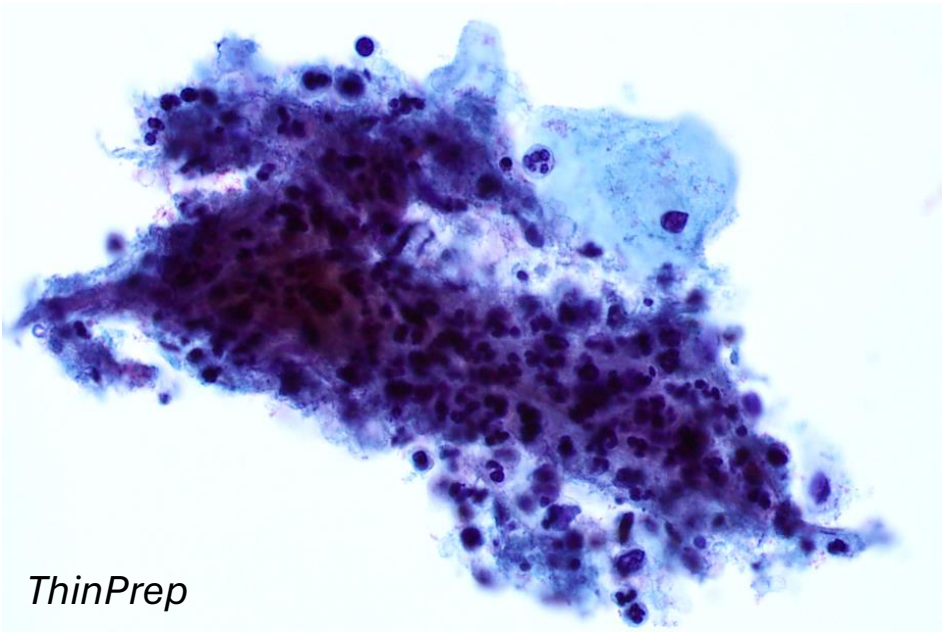




Single cells, occasional AIS strips

Endocervical adenocarcinoma





Background: blood and/or diathesis

Differential diagnoses: mimics of glandular lesions

Glandular lesions can be difficult – there are many mimics and pitfalls

1. Normal mimics
    - High sampling of cells from the lower uterine segment
2. Benign/reactive mimics
    - Tubal metaplasia
    - Cervical endometriosis
3. Dysplasia/other malignant mimics
    - HSIL, particularly if involving glands
    - Endometrial carcinoma, particularly if invading the cervix and directly sampled

Type distribution of human papillomavirus among adult women diagnosed with invasive cervical cancer (stage 1b or higher) in New Zealand

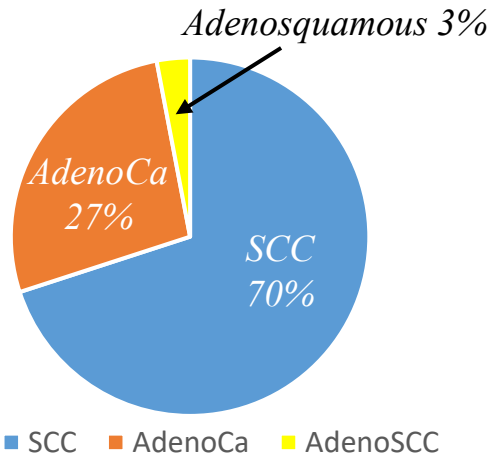
Peter Sykes et al *BMC Infectious Diseases* 2014,14:374

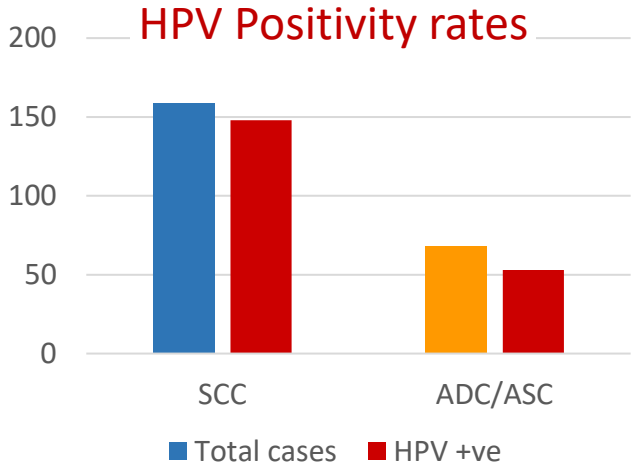
Invasive cancer cases n=227

Squamous cell carcinoma (SCC) = 70% (n=159)

Adenocarcinoma (ADC) = 27% (n=61)

Adenosquamous carcinoma (ASC) = 3% (n=7)





HPV was detected in 88.5% of cases (tumour tissue samples analysed)

SCC = 93.1%

ADC/ASC= 77.9%

- a lower proportion of glandular cancers are HPV positive compared with SCC
- the sensitivity for detecting high-grade glandular lesions using HPV testing is still considerably better than the sensitivity for detection using cytology

HPV genotypes in endocervical adenocarcinoma

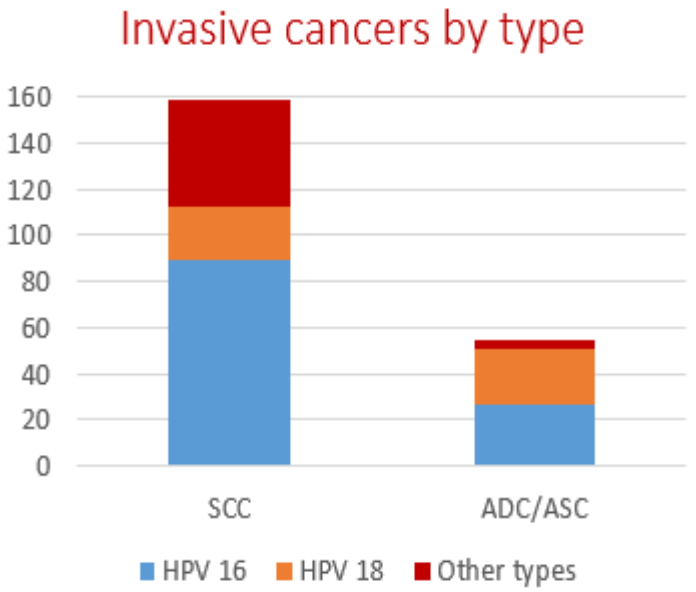
For the 227 cancer cases, HPV 16 and HPV 18 were the most frequent HPV types

51% were HPV 16 +ve:

56% of SCC 40% of ADC/ASC

21% were HPV 18 +ve:

15% of SCC 35% of ADC/ASC



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Detecting endocervical glandular lesions by cervical cytology

- Glandular lesions are difficult to detect and accurately interpret in cytology: AIS is the key diagnostically: learn to identify this first
- The sensitivity for detecting high-grade cervical lesions using cytology is only about 50% but more cases will be detected using HPV primary screening
- Investigation using colposcopy and biopsy is also difficult as the lesions are often in the endocervical canal
    - Cytology still plays a key role in identifying the presence and type of a high-grade glandular lesion so that appropriate investigation and management occurs

It is particularly important to work closely with histopathologists and colposcopists (e.g. at MDM) to achieve the best outcome