Temadag og årsmødet 7th – 8th of March 2014
Department of Clinical Pathology, Large auditorium
Windsløwparken 15 1. floor, Odense University Hospital

Squamous Lesions: Diagnostic Pitfalls and Look a Likes (net cases)

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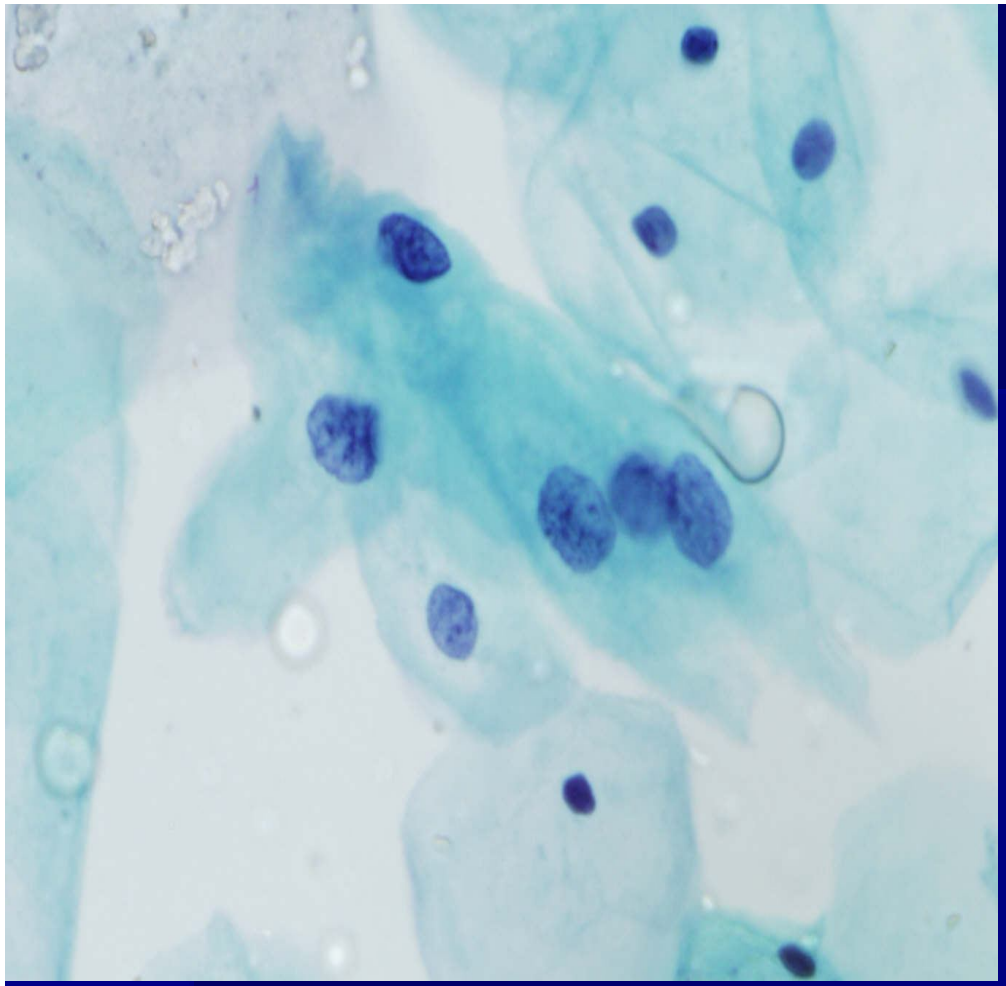
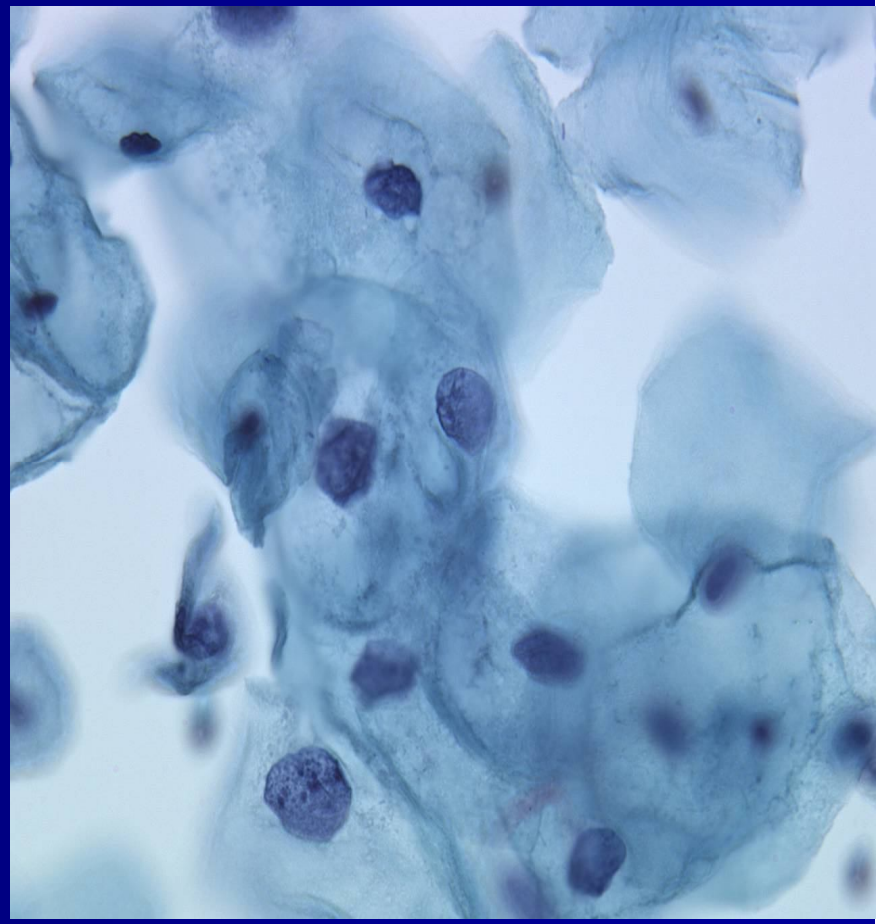
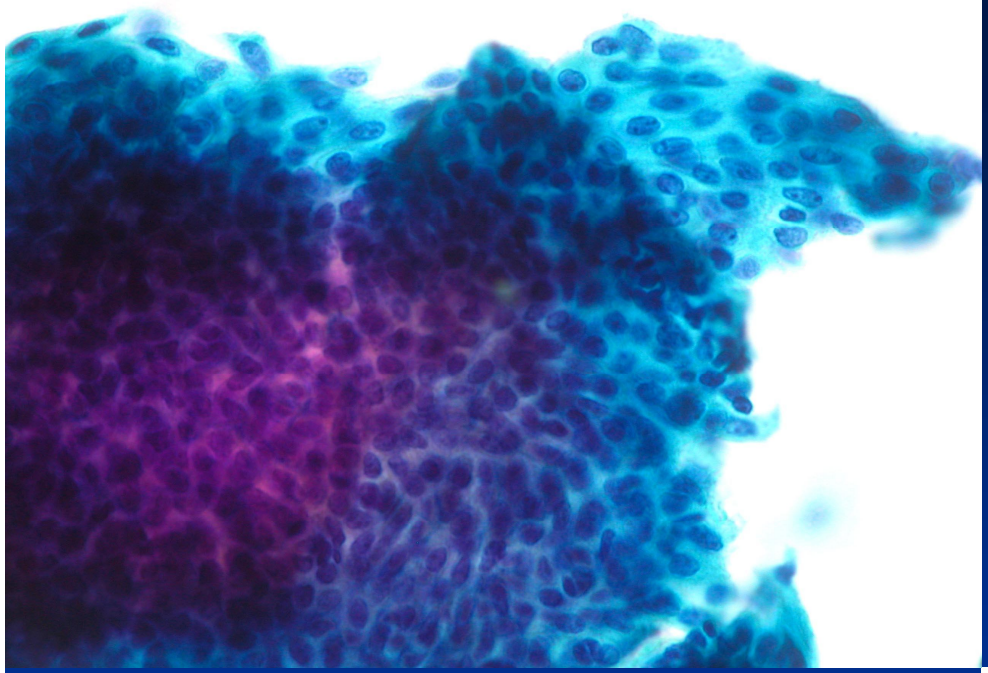
Director/ Manchester & Northwest Cytology Training Centre (2001-2013)
Past Chairman and President/ British Society For Clinical Cytology U.K.

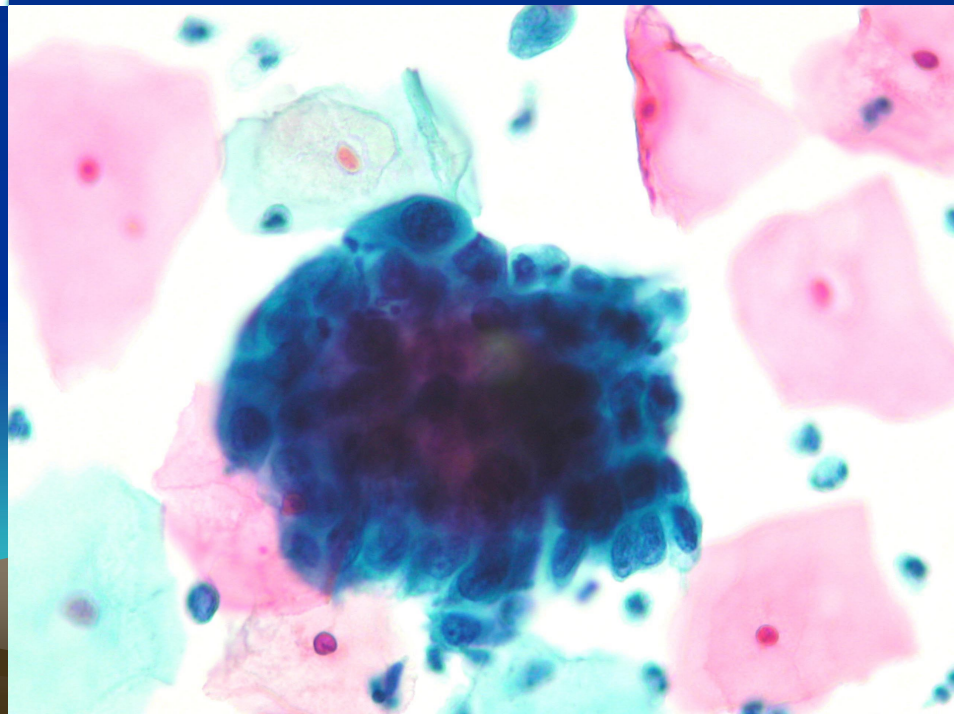
Spot The Difference Neg, ASCUS or LSIL?



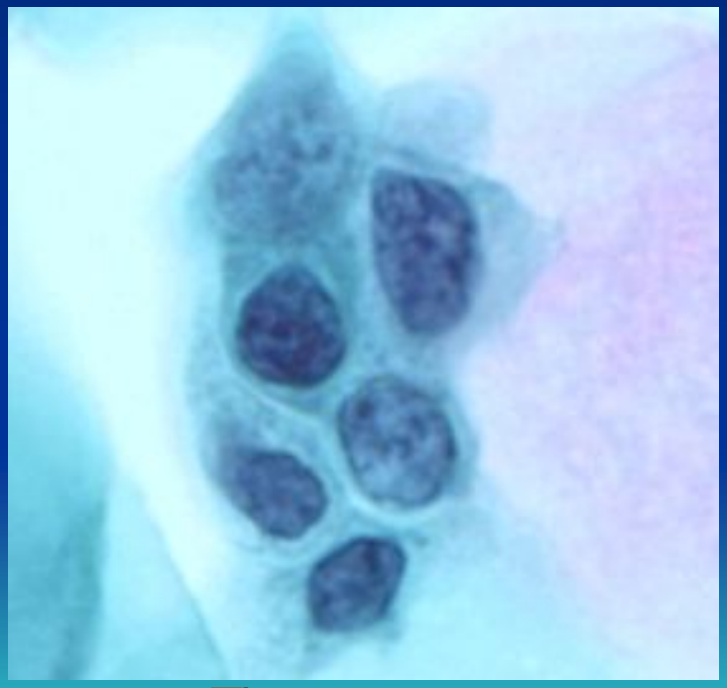


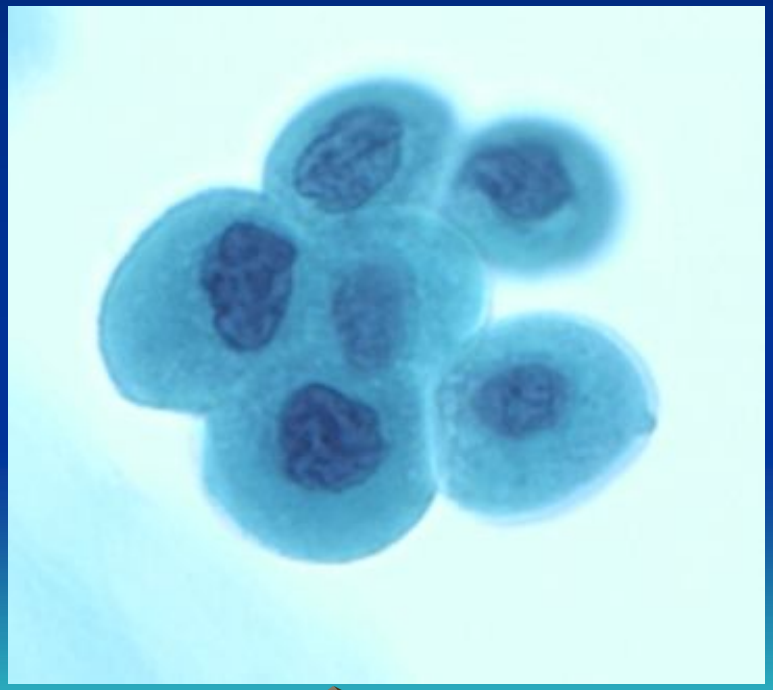


HCG Pitfall
Spot the Difference:
Negative or HSIL

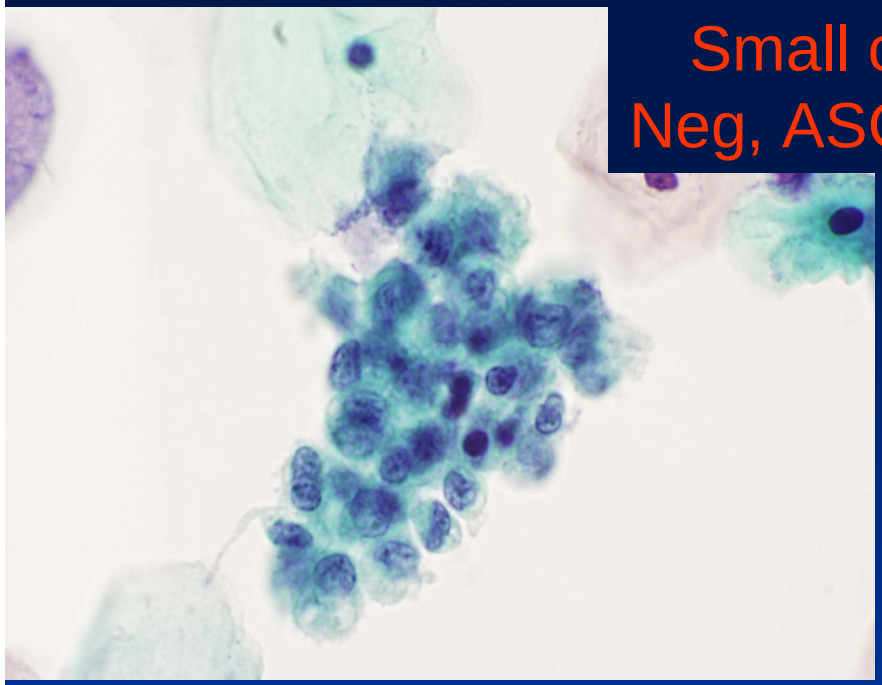


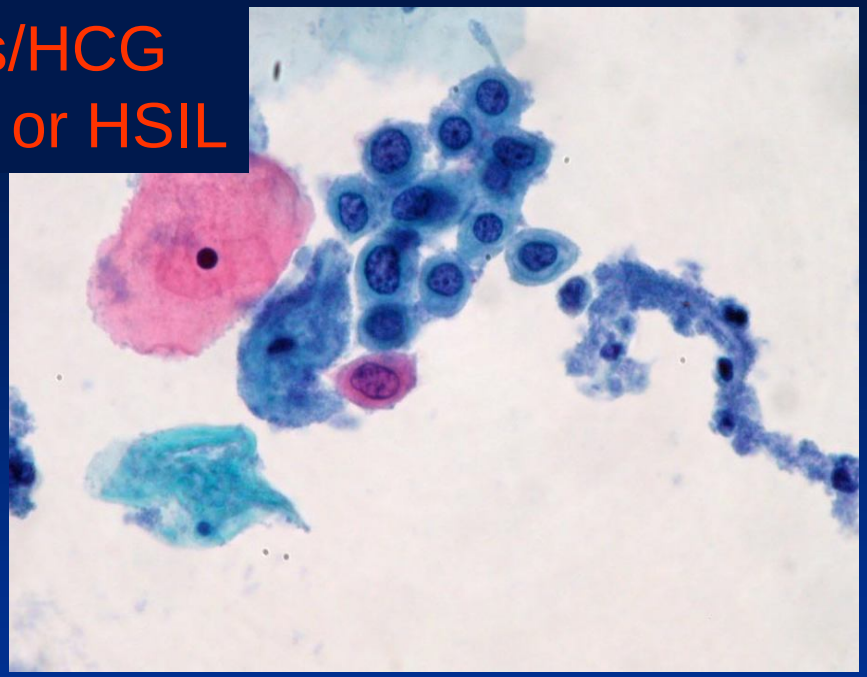
Spot The Difference
Metaplastic Cells
Neg, ASCUS or SIL?

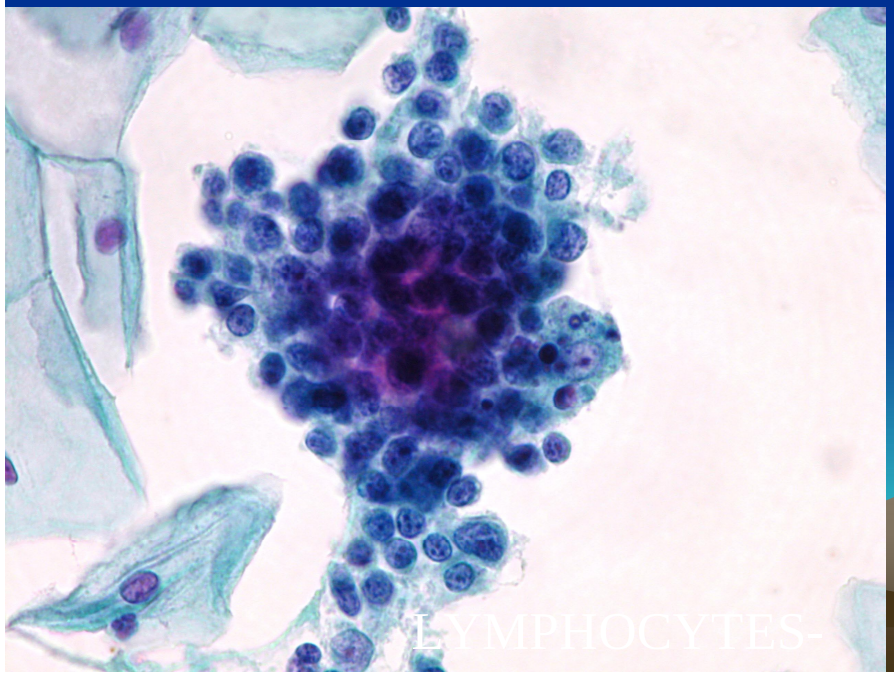


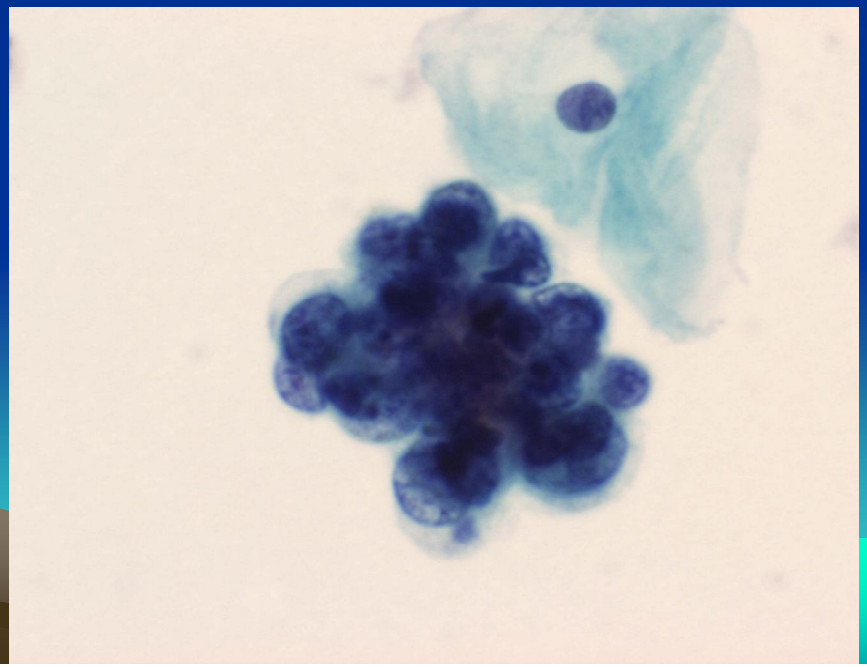


Small cells/HCG
Neg, ASC-H or HSIL



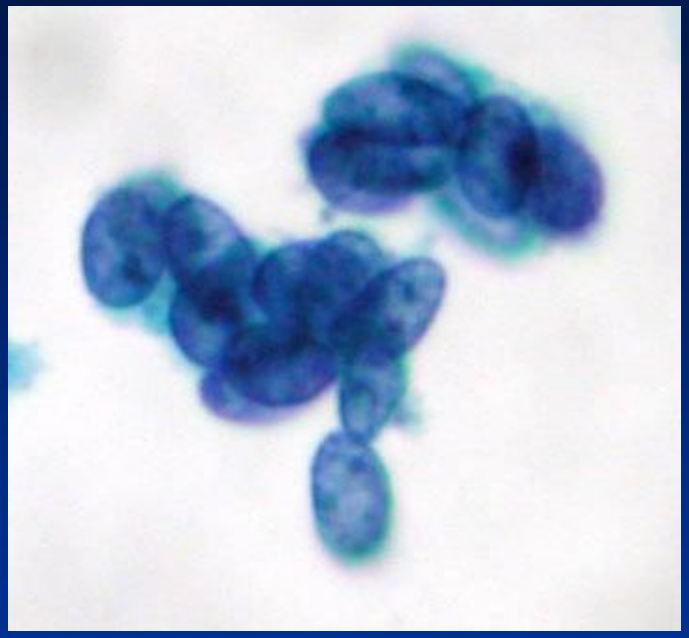


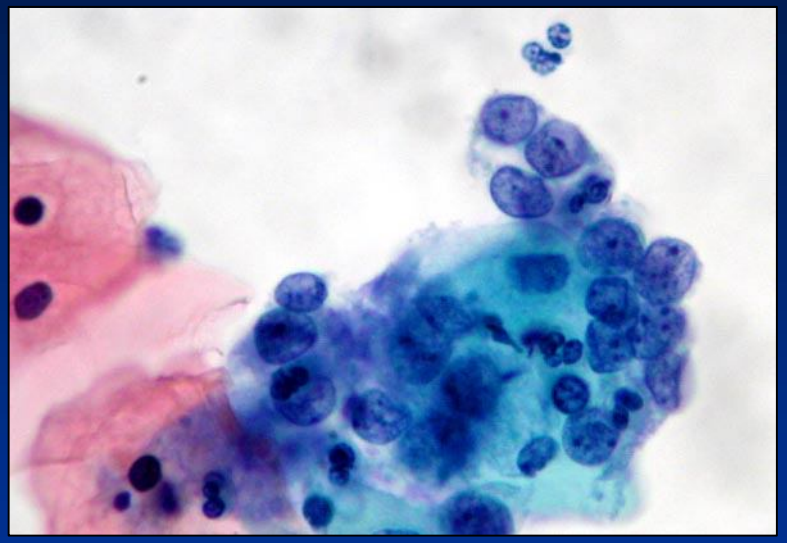


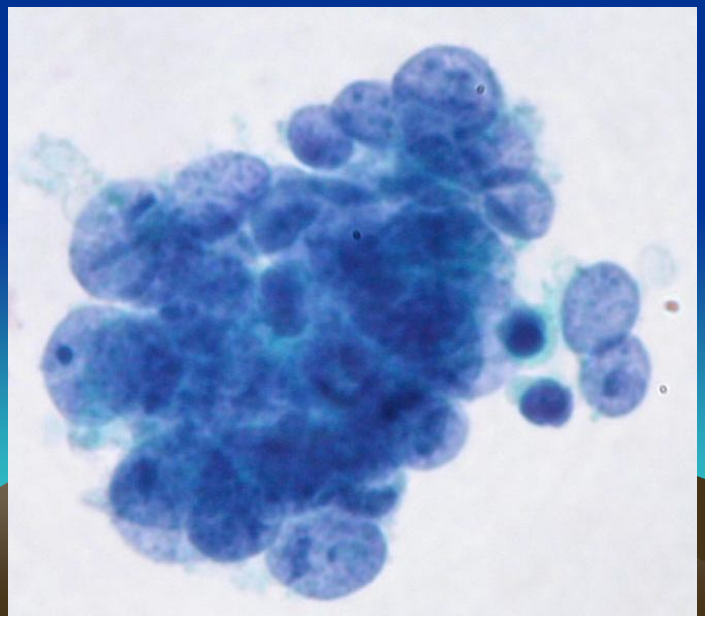


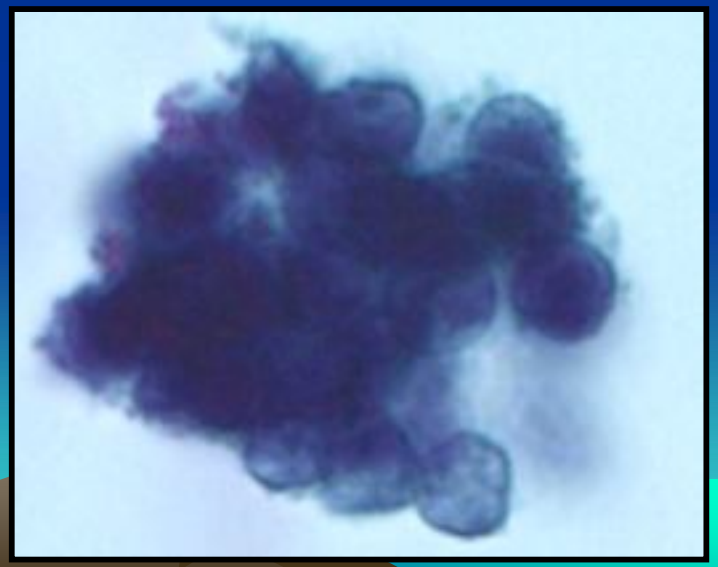
LYMPHOCYTES-

Spot the Difference In Bare nuclei
Neg, ASCUS, ASC-H or SIL

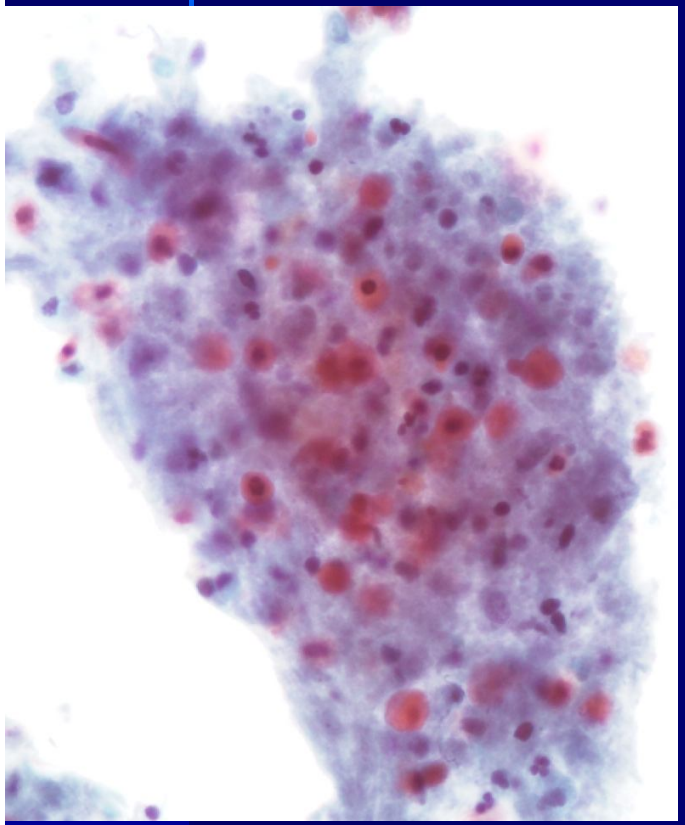


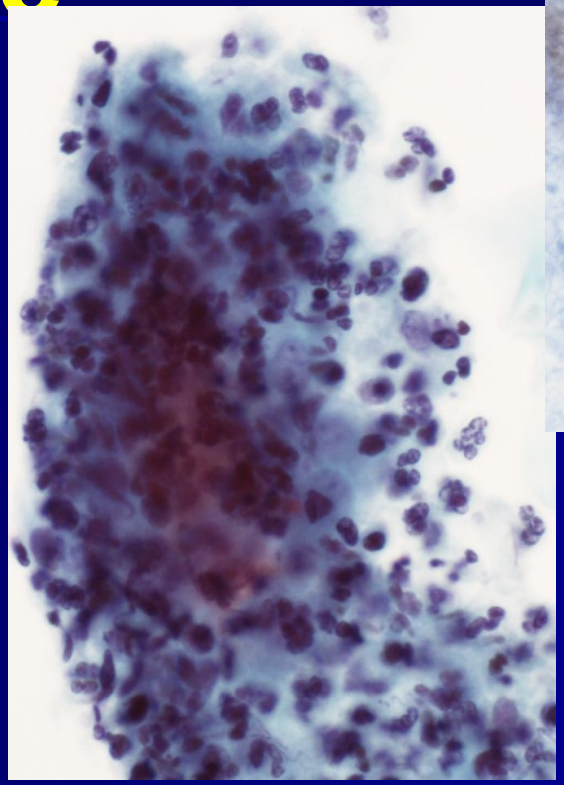


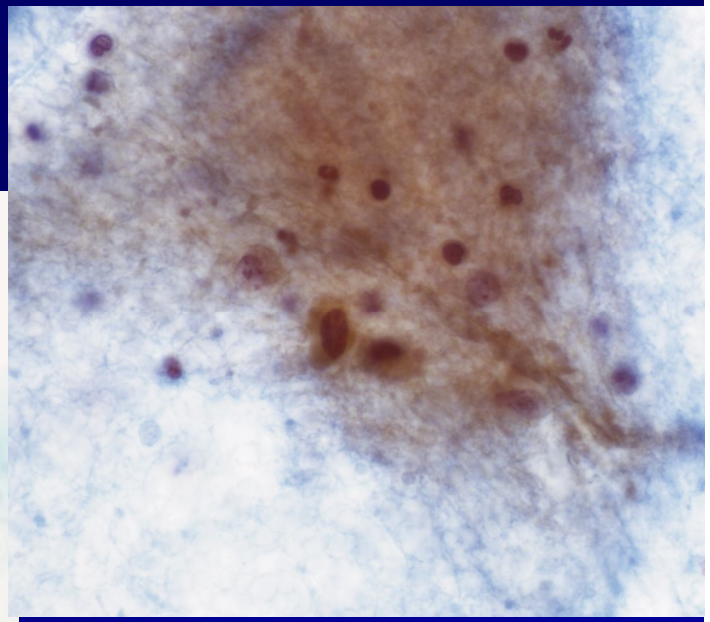


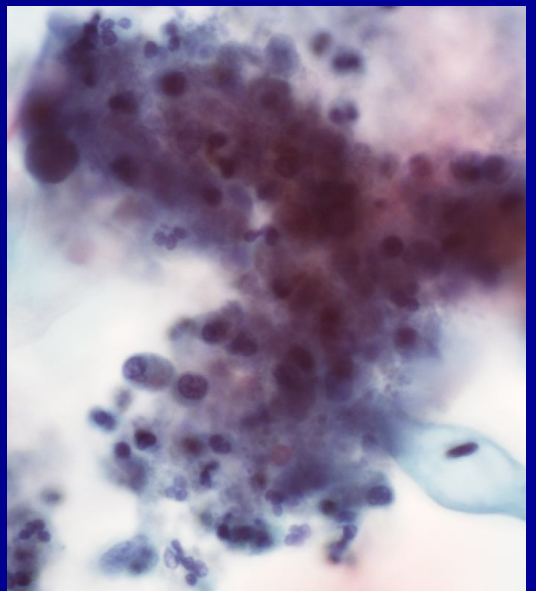


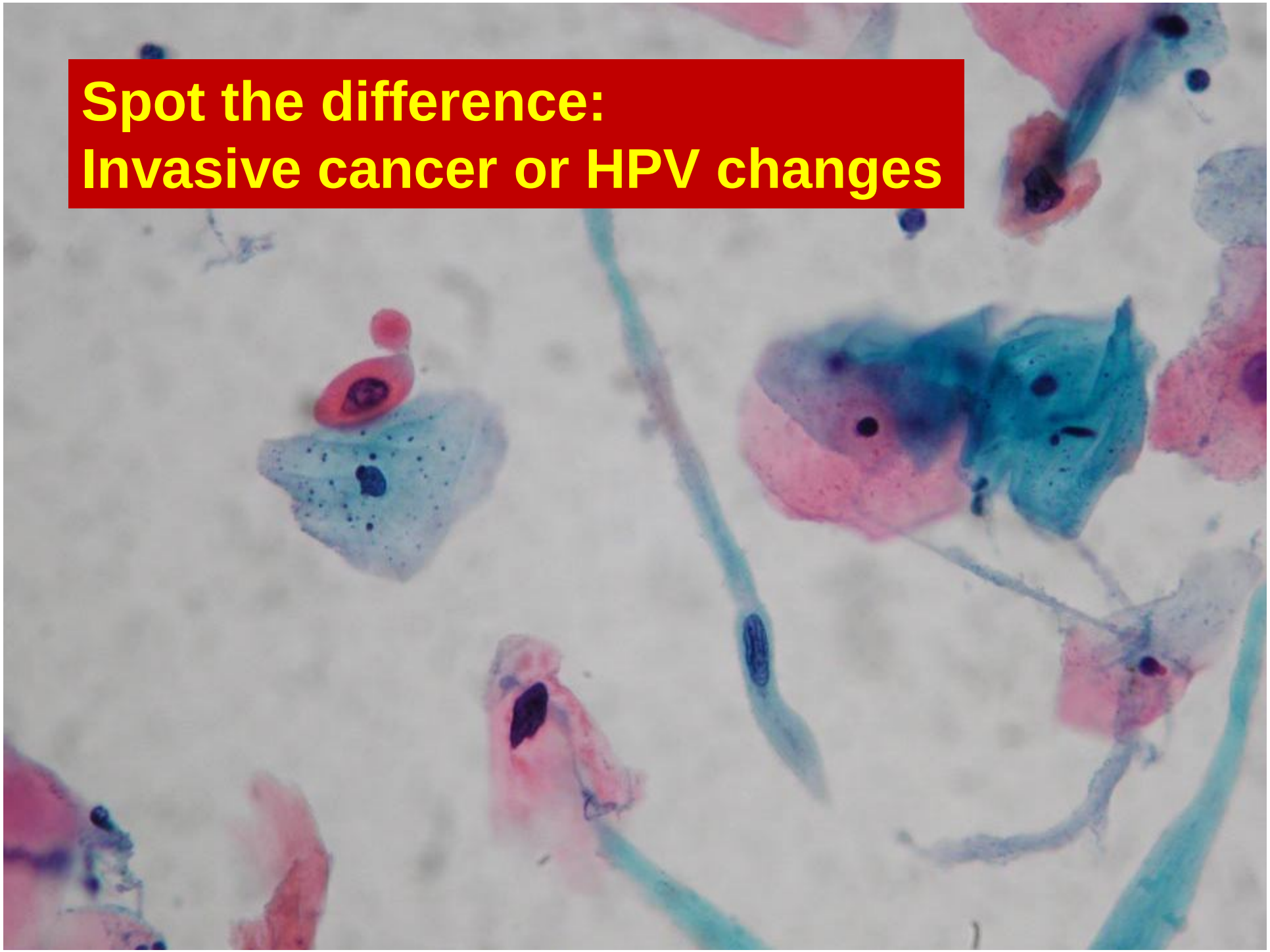
Diathesis Spot The Difference

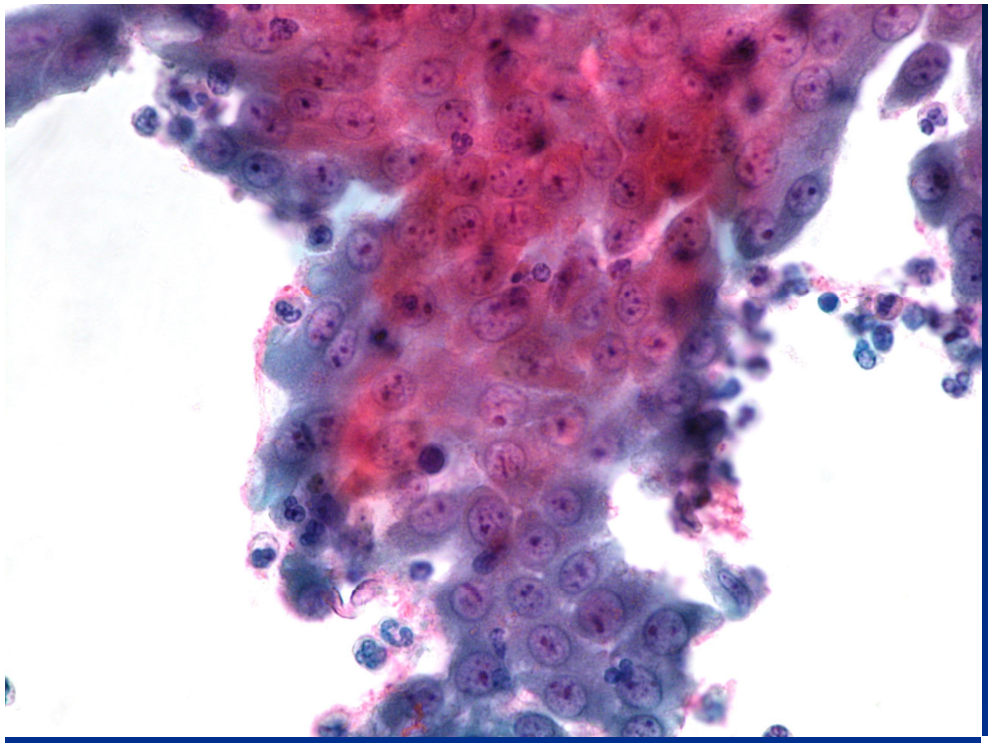




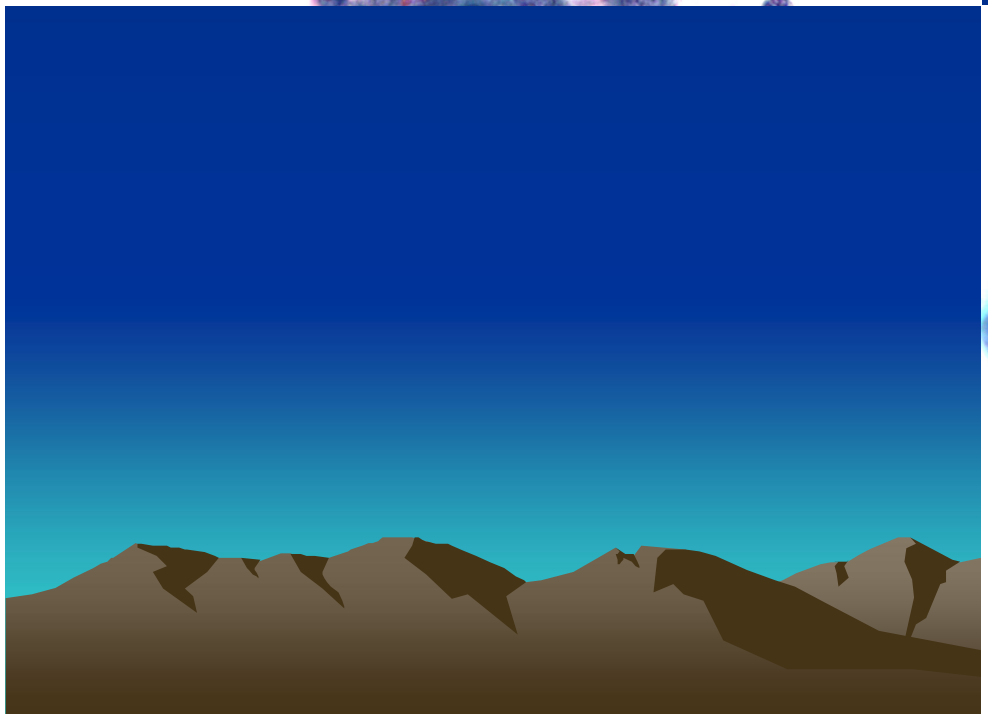


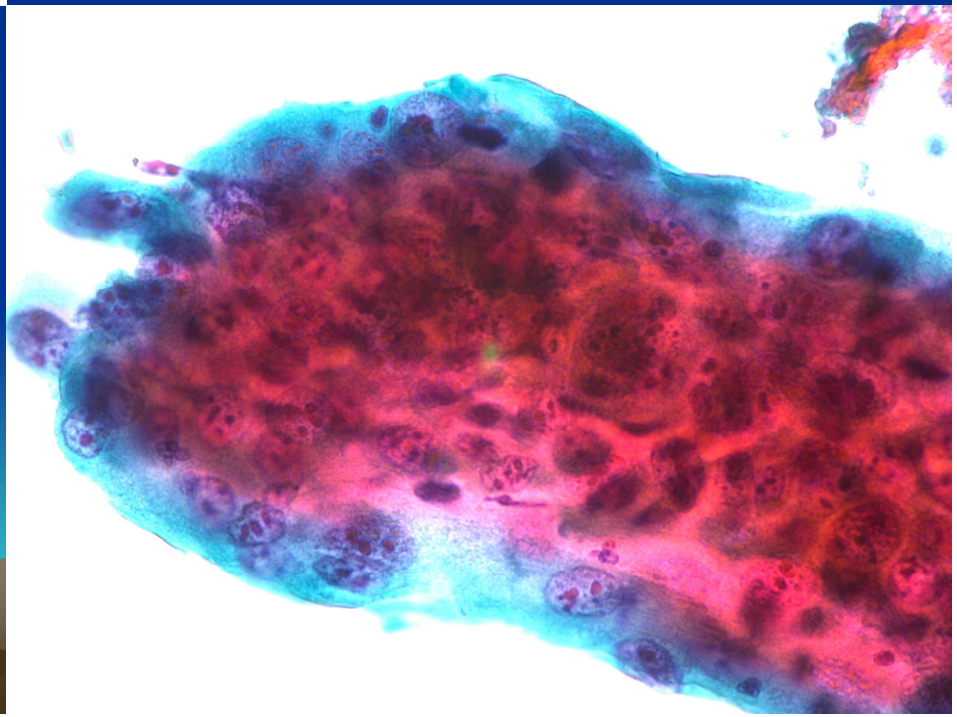



Spot the difference:
Invasive cancer or HPV changes



Spot the Difference: Repair or Invasive Cancer?

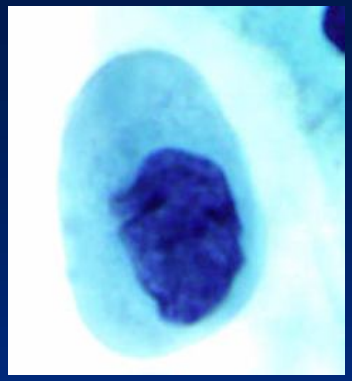




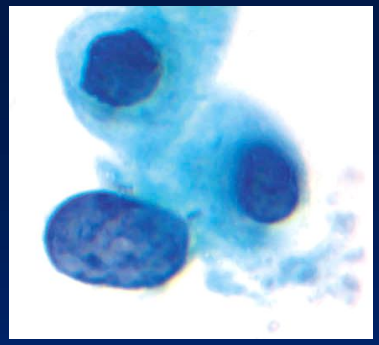
Back to Basics

Definition of ASCUS

ASC - US

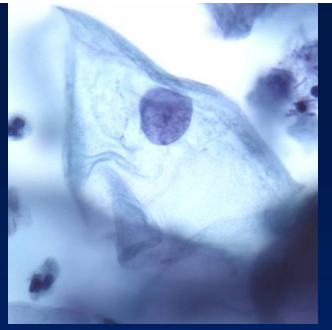


ASCUS
SIL of Indeterminate Grade



ASCUS
SIL in bare nuclei

ASCUS
Quantitatively
insufficient for LSIL



ASCUS
Qualitatively
insufficient
for LSIL

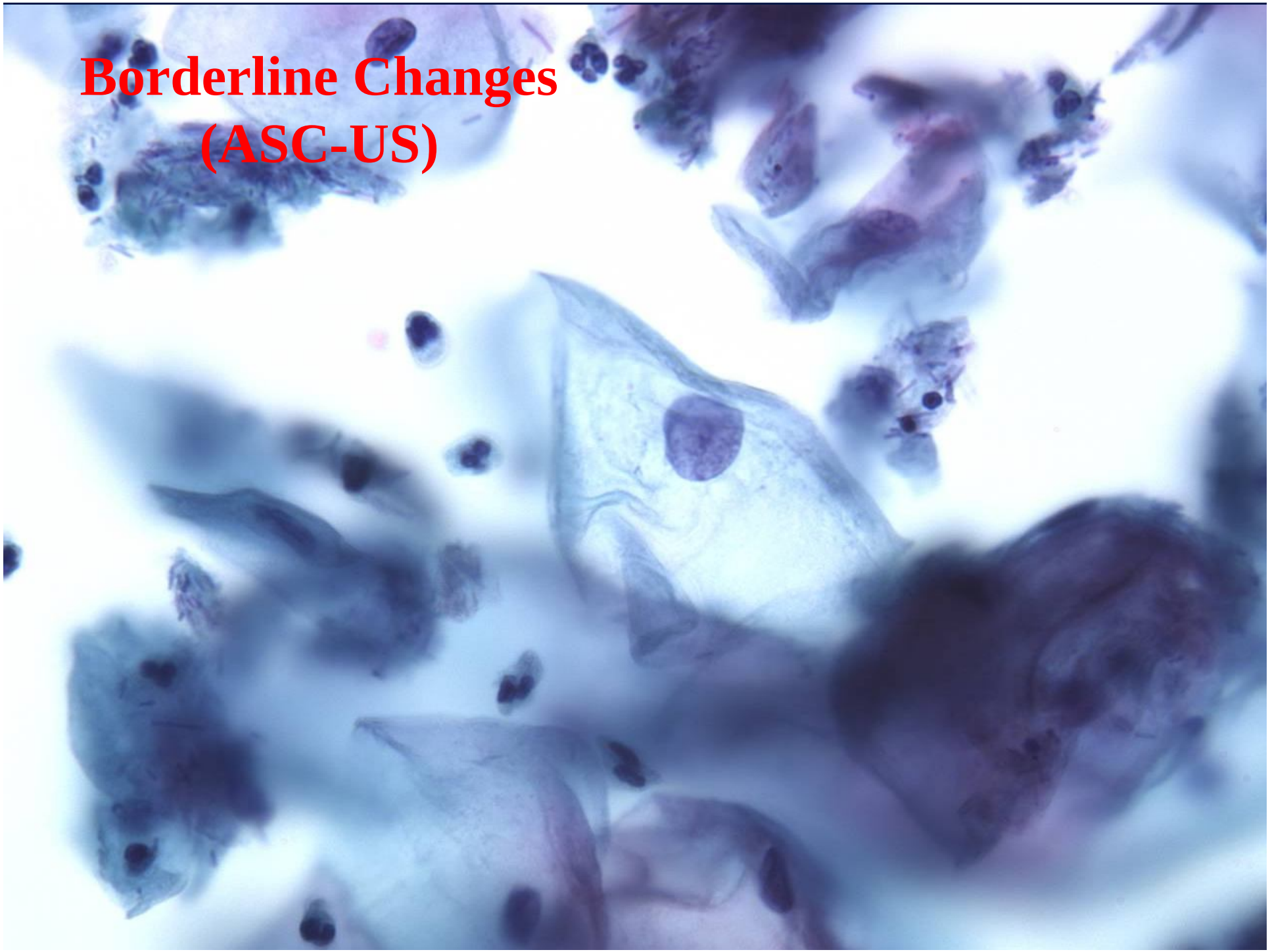
Bethesda definition: Atypical cells of Indetermied significance (ASC-US)

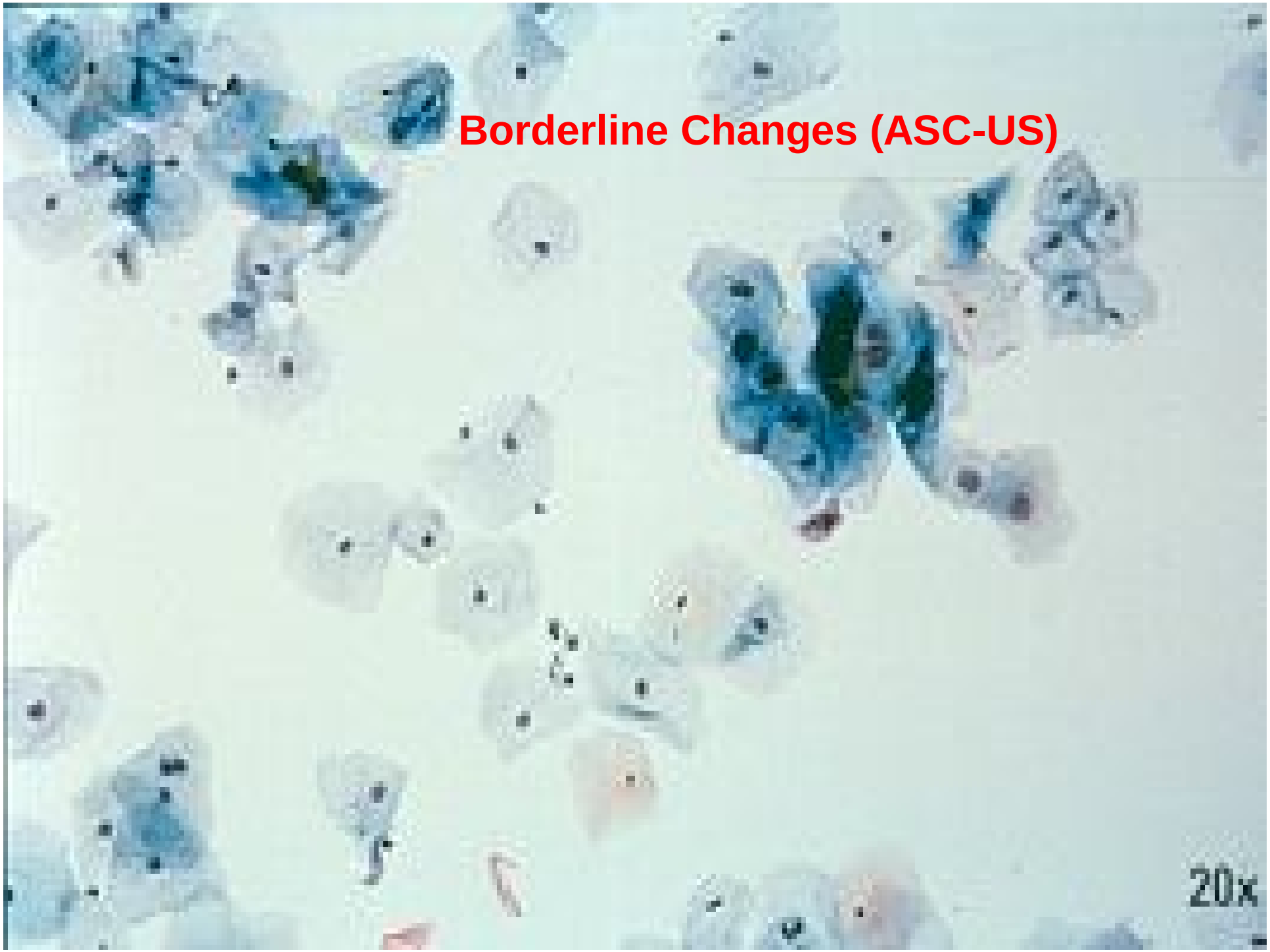
- **Most ASCUS reflects difficulties in the distinction between reactive changes and LSIL**
- **ASCUS refers to changes that are suggestive of LSIL but are quantitatively or qualitatively insufficient for definitive interpretation.**
- **SIL of indeterminate grade or SIL in bare nuclei can also be reported as ASCUS**

(ASC-US)
Morphological Criteria

- **Nuclear enlargement 2½ to 3 times the size of intermediate nuclei (Inflamm. up to 2 times)** or **1½ to 2 times size of metaplastic nuclei**
- **Nuclear envelope usually smooth**
- **Nuclear Hyperchromasia with even chromatin distribution**
- **Minimal chromatin abnormality between fine (ground salt) and speckled (salt and paper)**
- **Occurs in sheets or singly**

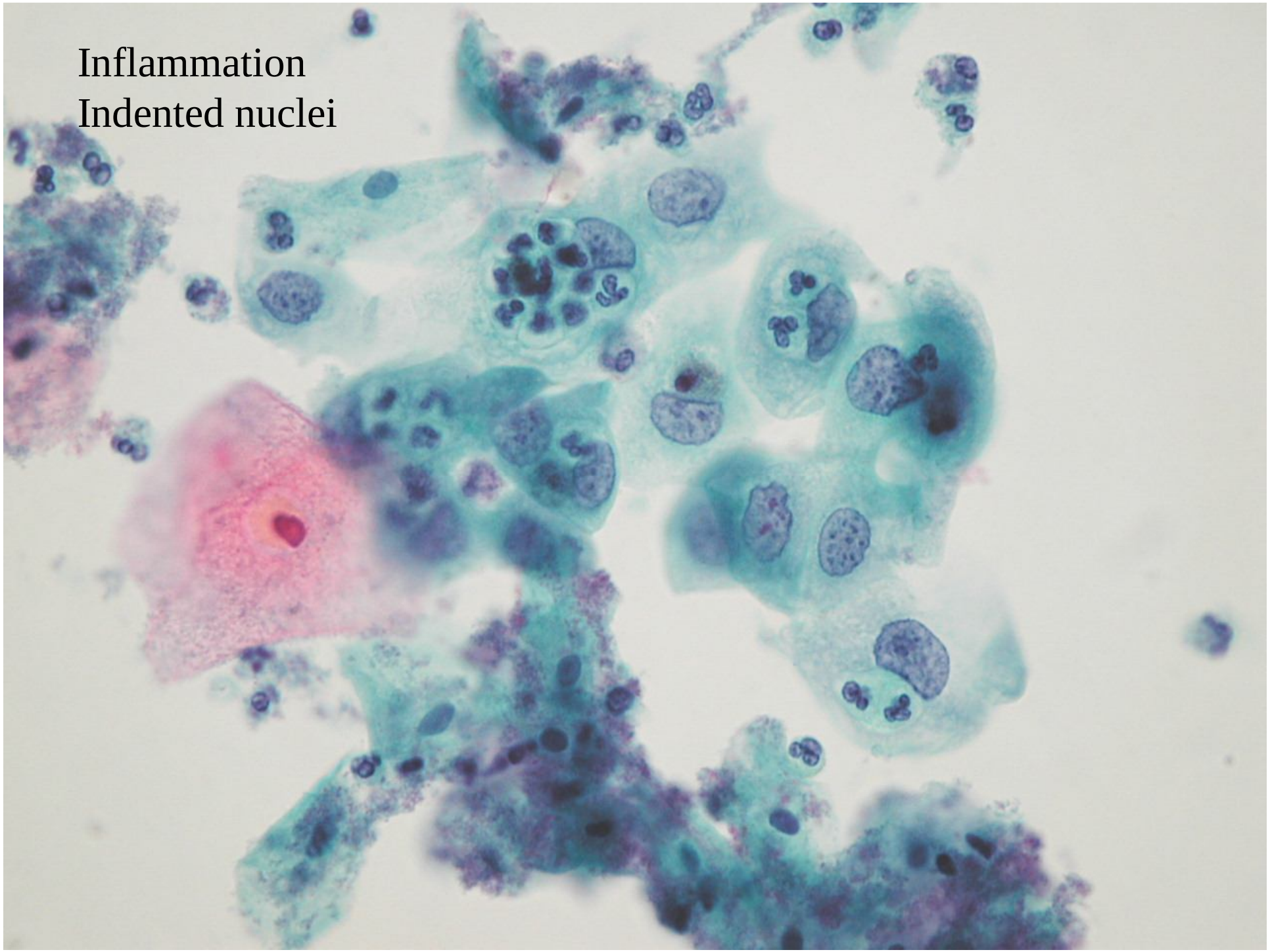
Borderline Changes (ASC-US)



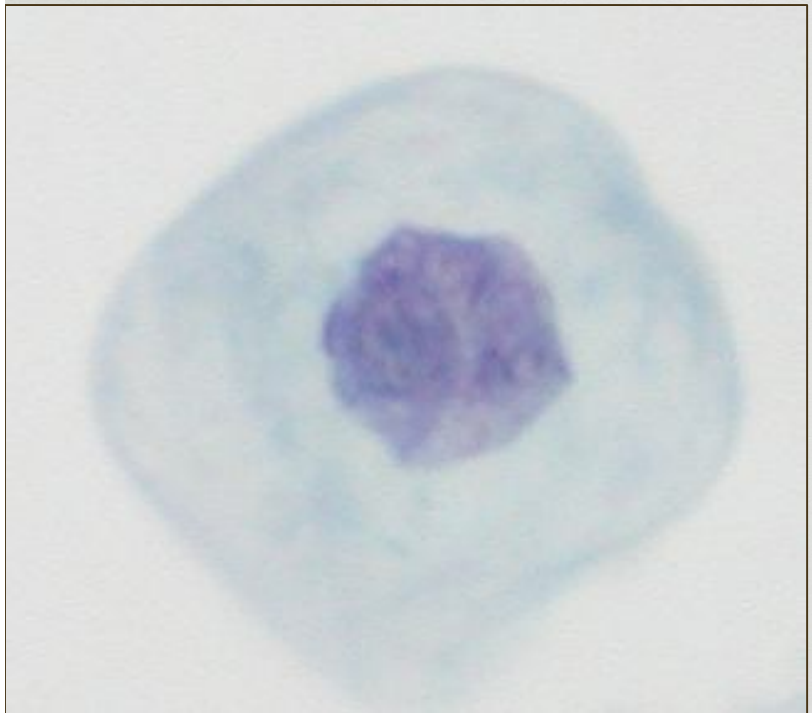

Borderline Changes (ASC-US)
20x

Inappropriate use of the borderline/ASCUS category

Following cases are
NOT SHOWING
Low Grade Abnormality
(NOT ASCUS OR LSIL)

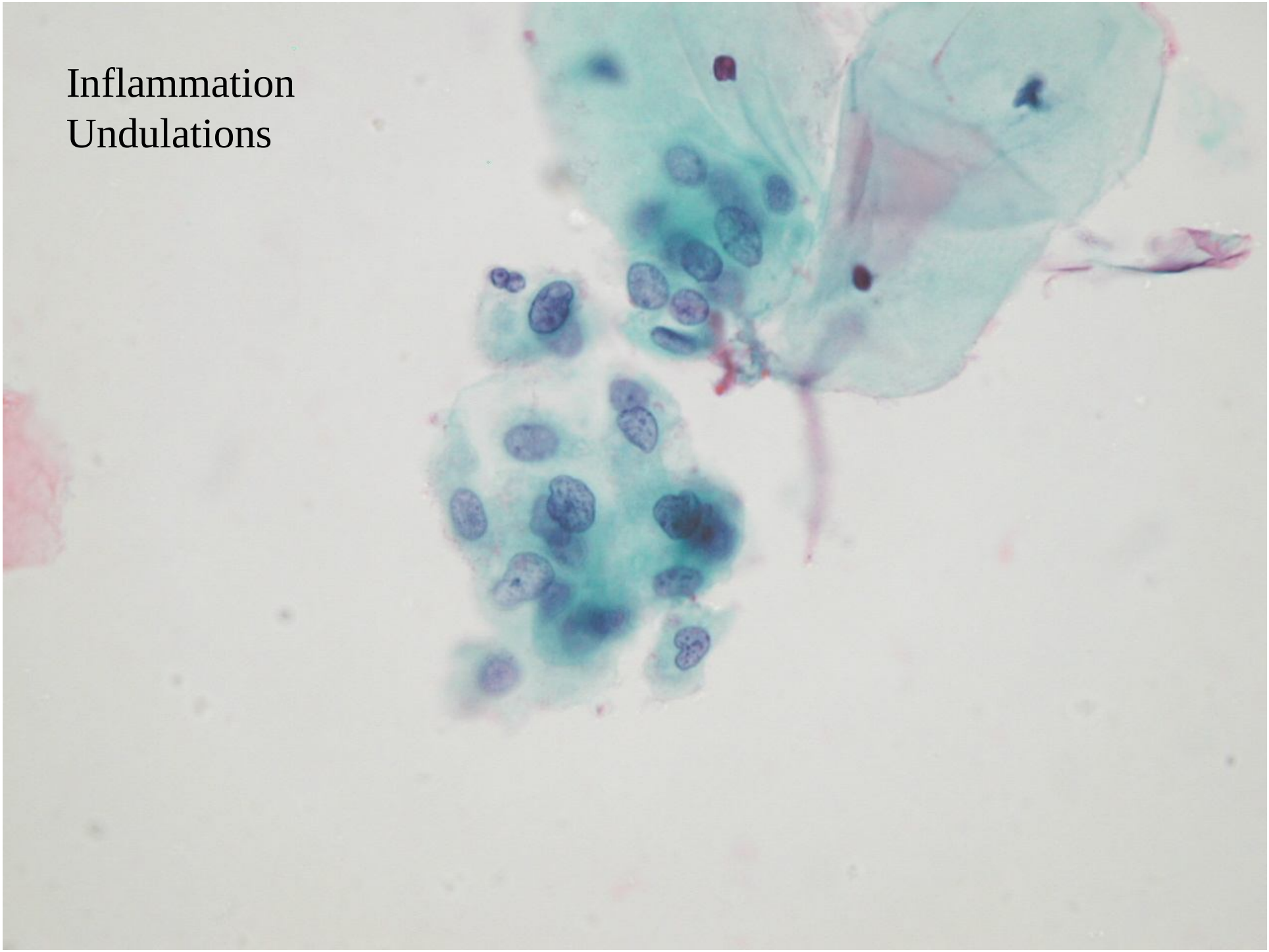

Inflammation
Indented nuclei

Inflammation:
Crenation of nuclear membrane

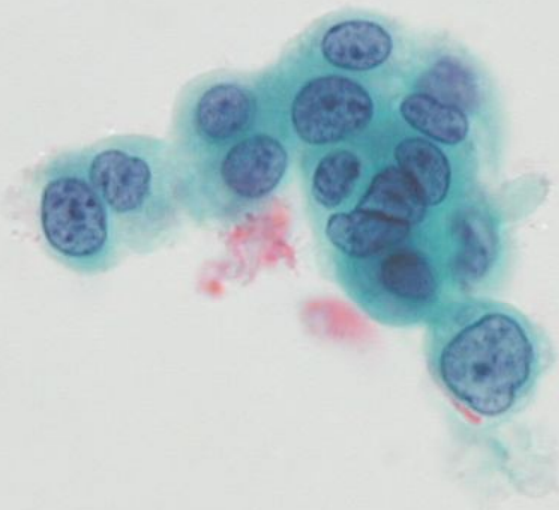


Cell degeneration associated with Herpes infection

Inflammation
Undulations



Reactive changes
Thickened membrane and nucleoli



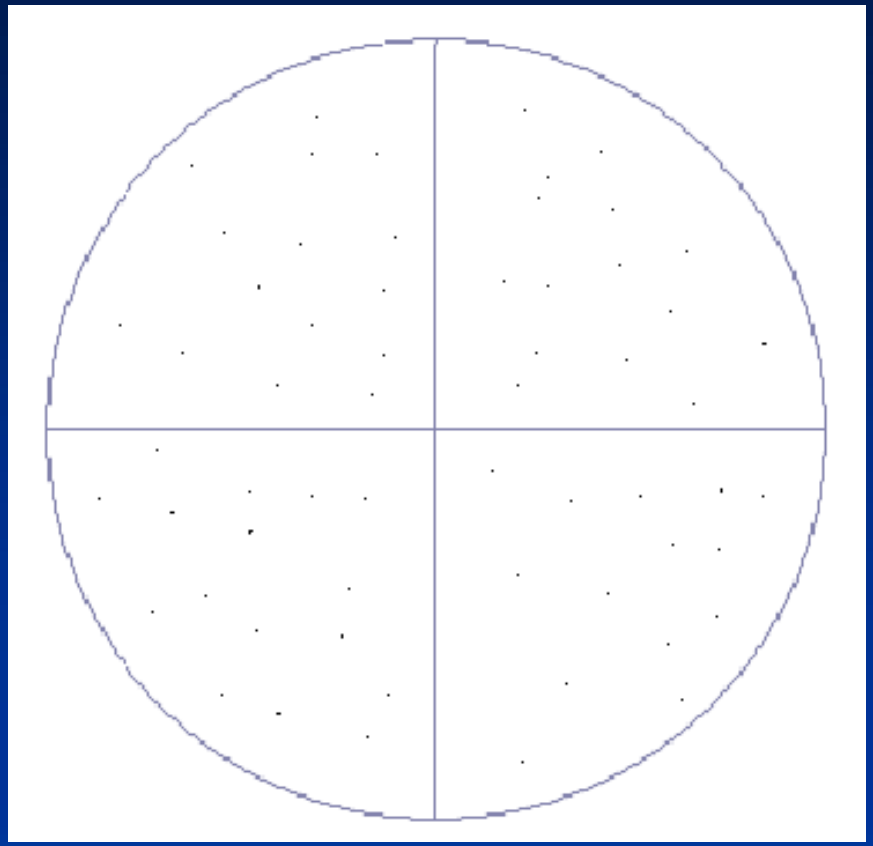
Back to Basics

Definition of SIL

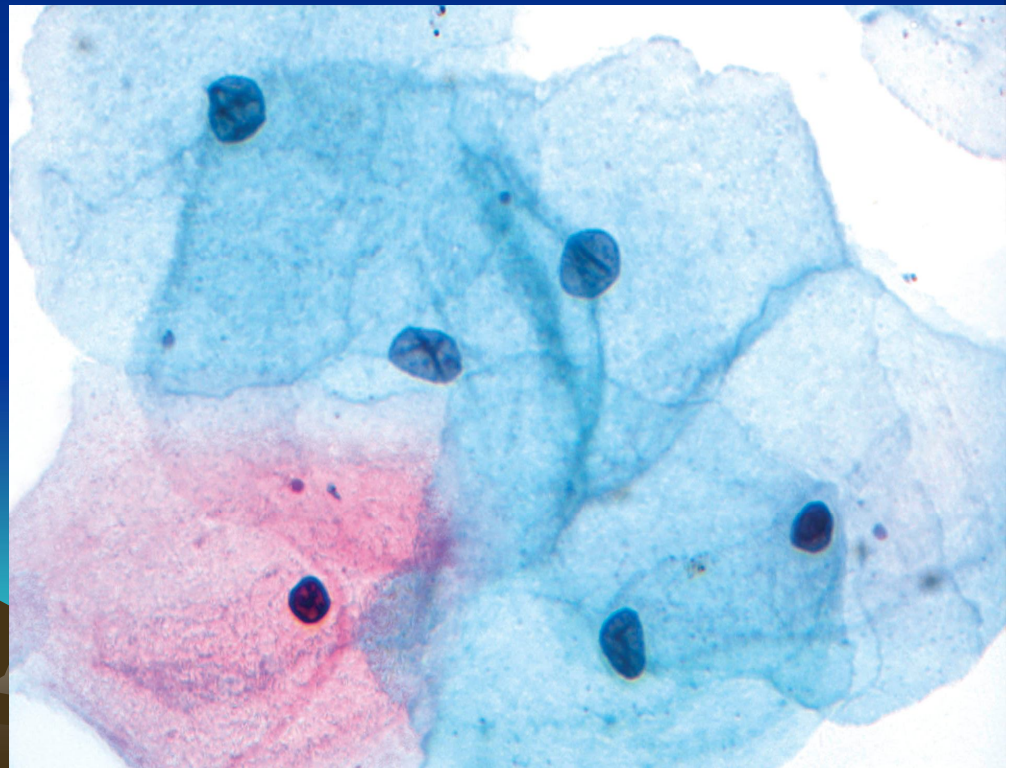
SIL
Definition

- Abnormal chromatin pattern is the essential requirement.
- Finely speckled, punctate or coarsely clumped chromatin
- Abnormal size, spacing and distribution of chromatin granules
- Hyper or Hypochromasia
- Irregular nuclear outline + or –
- Minor changes in nuclear outline e.g.single or multiple folds,wrinkling or serration occur with inflammation and degeneration.
- Large bulbous protrusions,scalloping or deep notches not associated with linear folds occur in dyskaryosis.
- Raised nuclear : cytoplasmic ratio

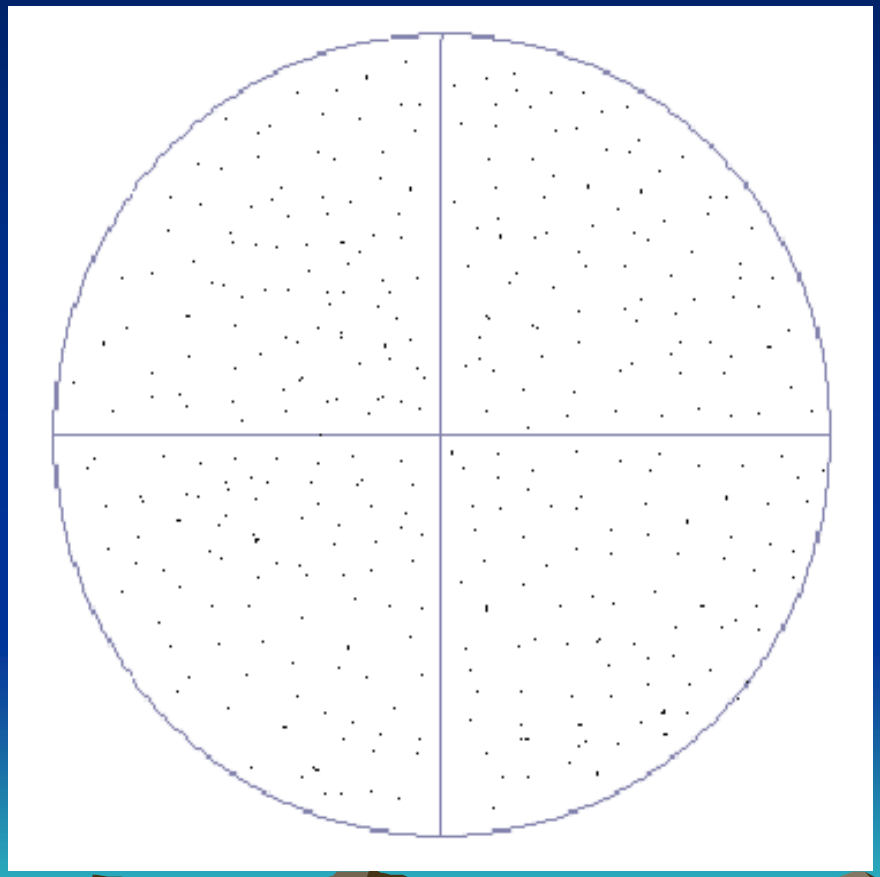
Normal Chromatin Pattern

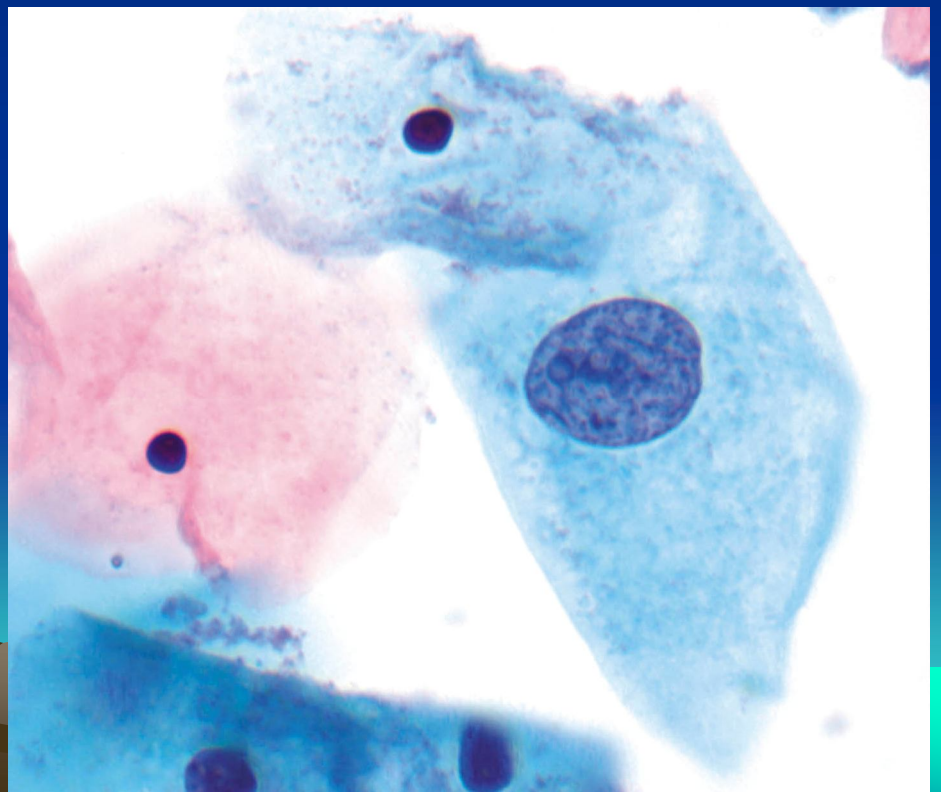


smooth with equal
distribution of nuclear chromatin

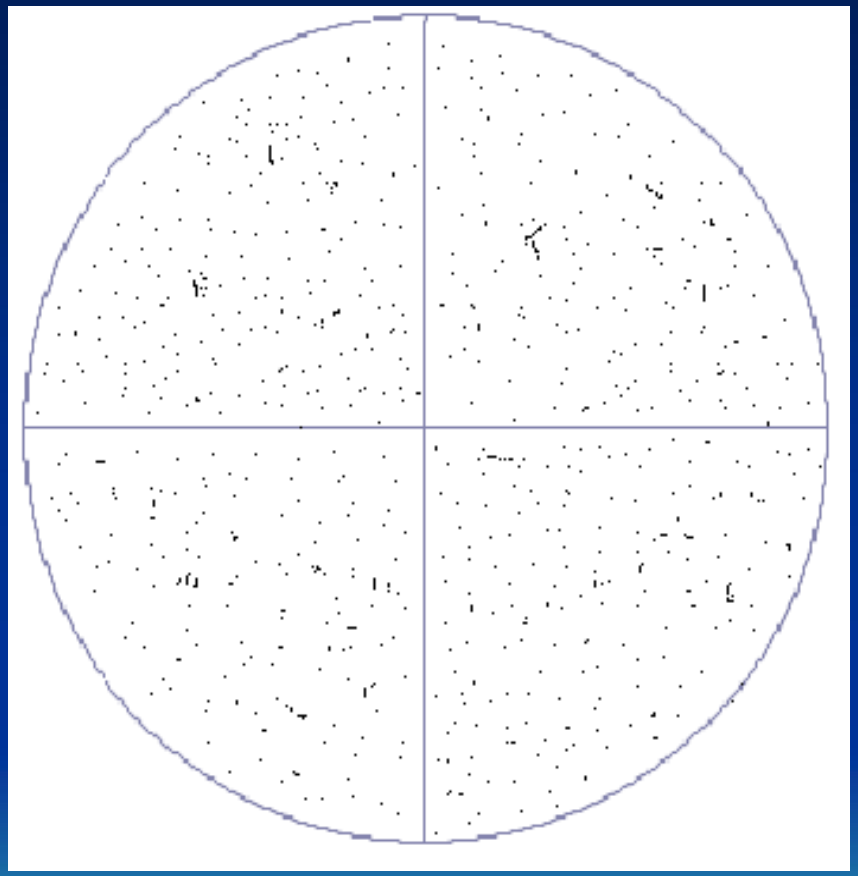


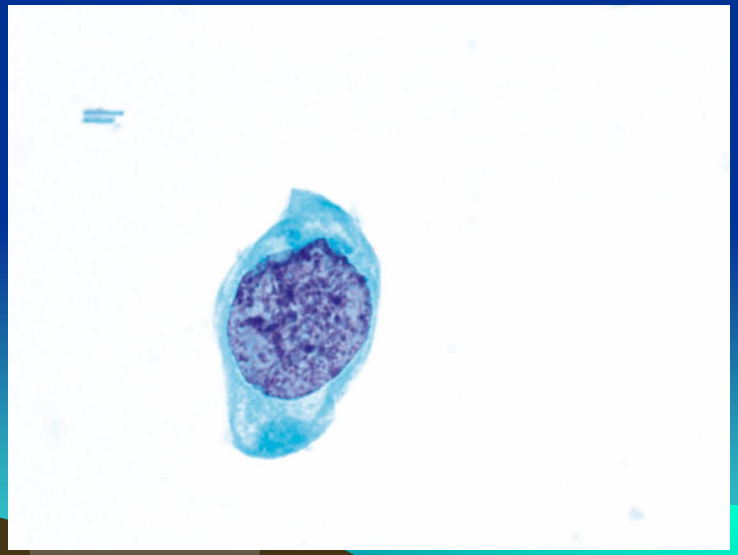
Abnormal Chromatin Pattern - Finely Speckled



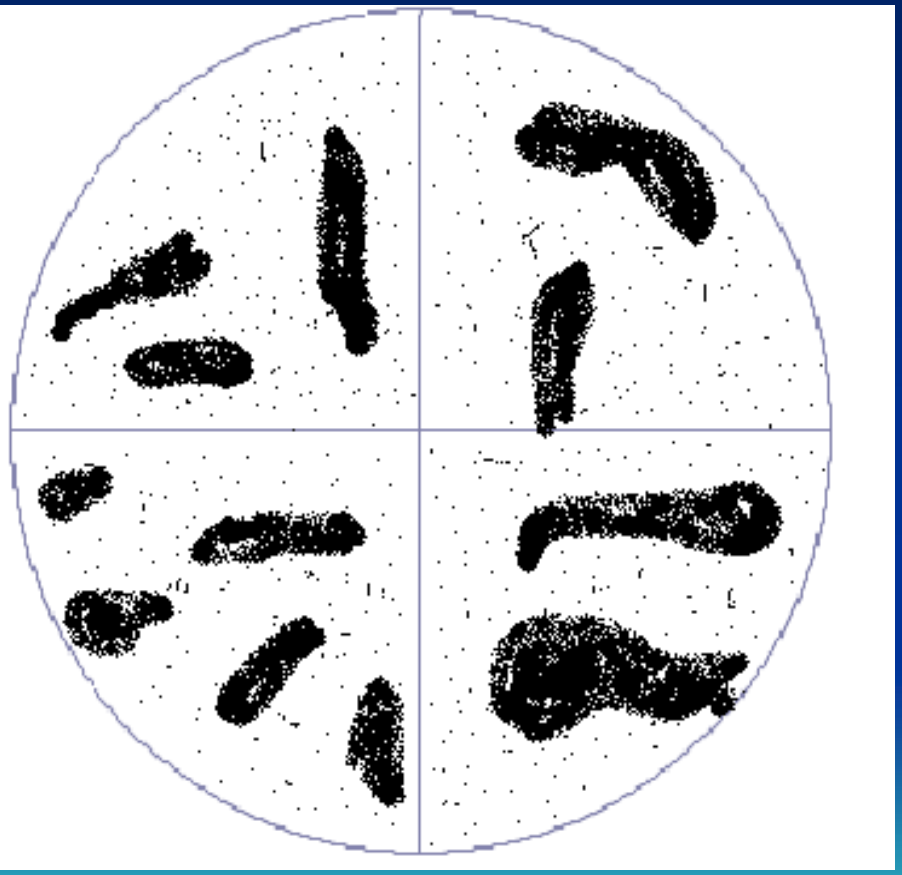


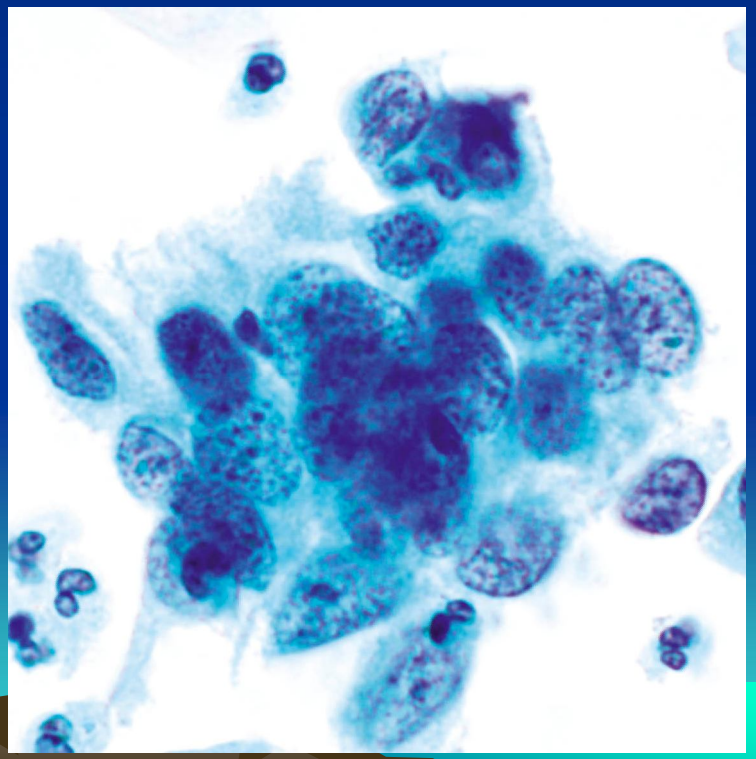
Abnormal Chromatin Pattern - Finely Speckled and Punctate Chromatin





Abnormal Chromatin Pattern - Densely Hyperchromatic with Clumped Chromatin

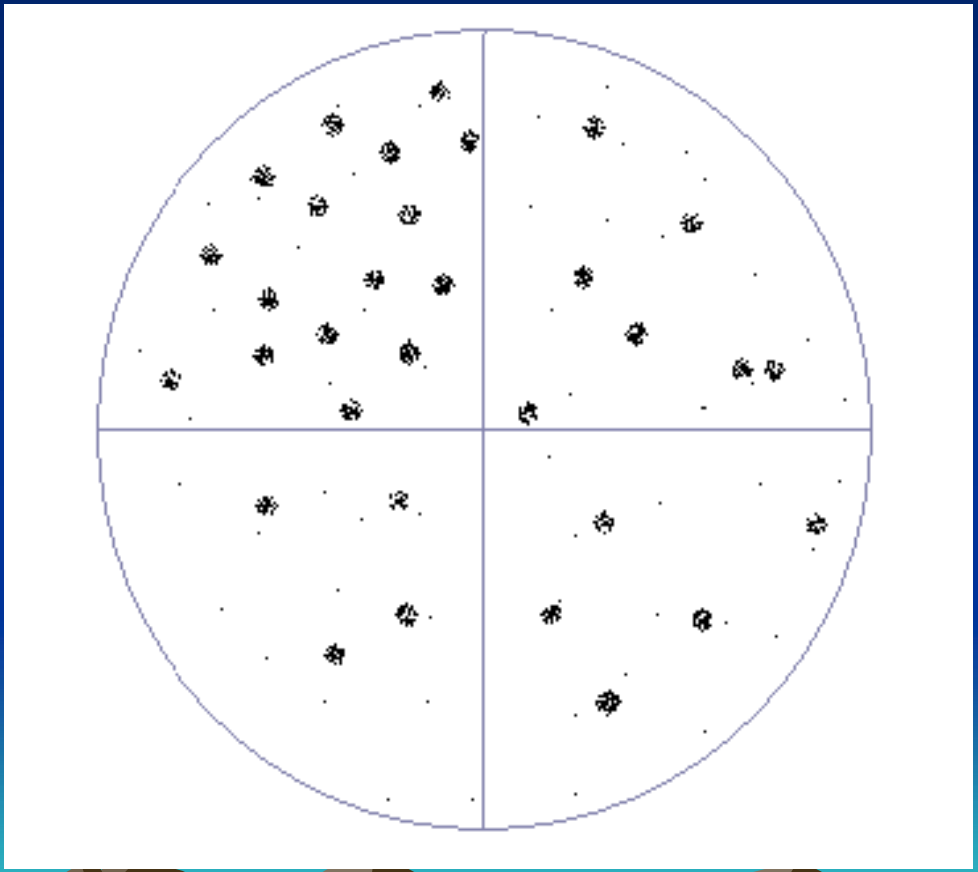




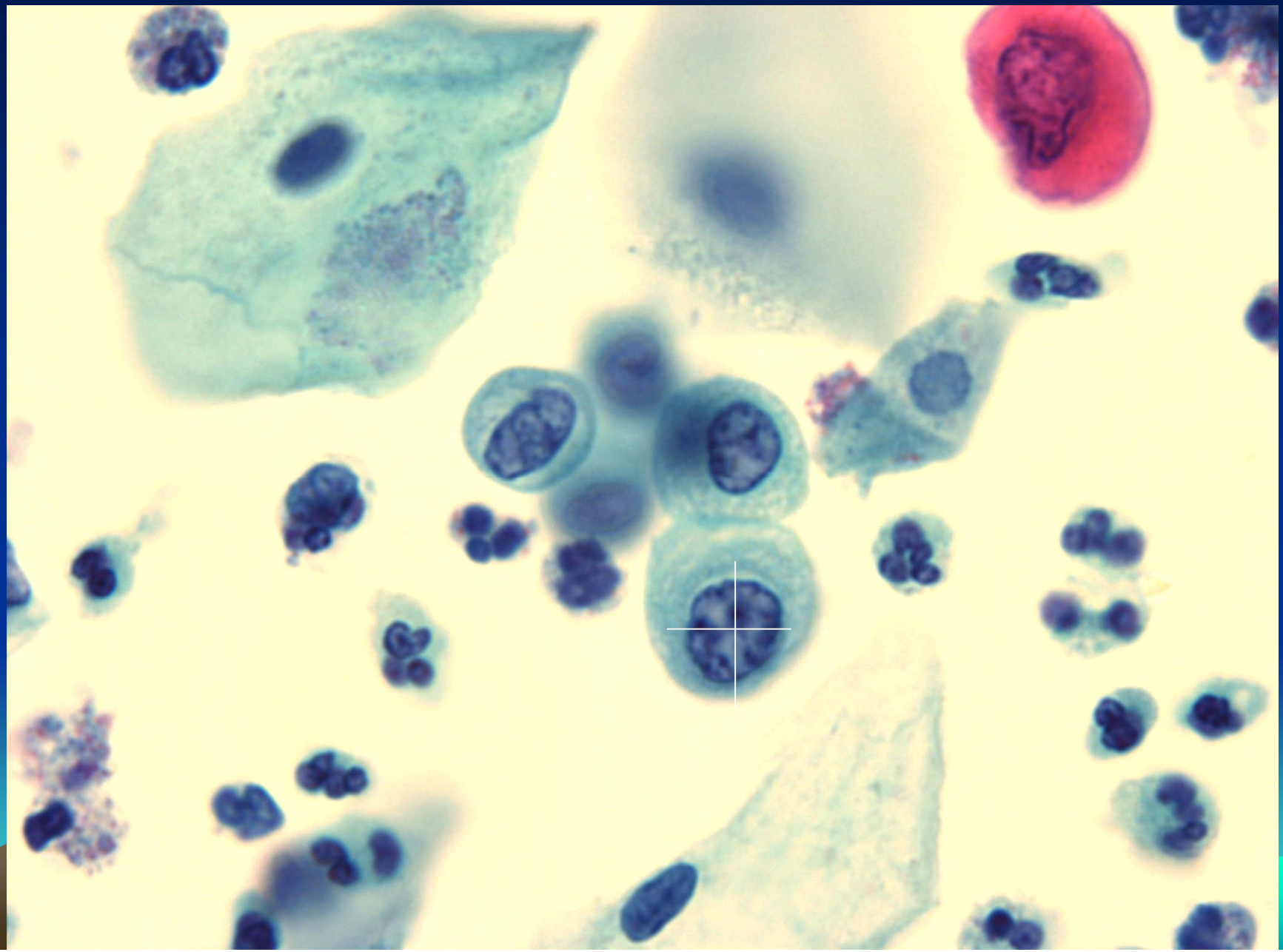
Definition of Dyskaryosis (SIL)

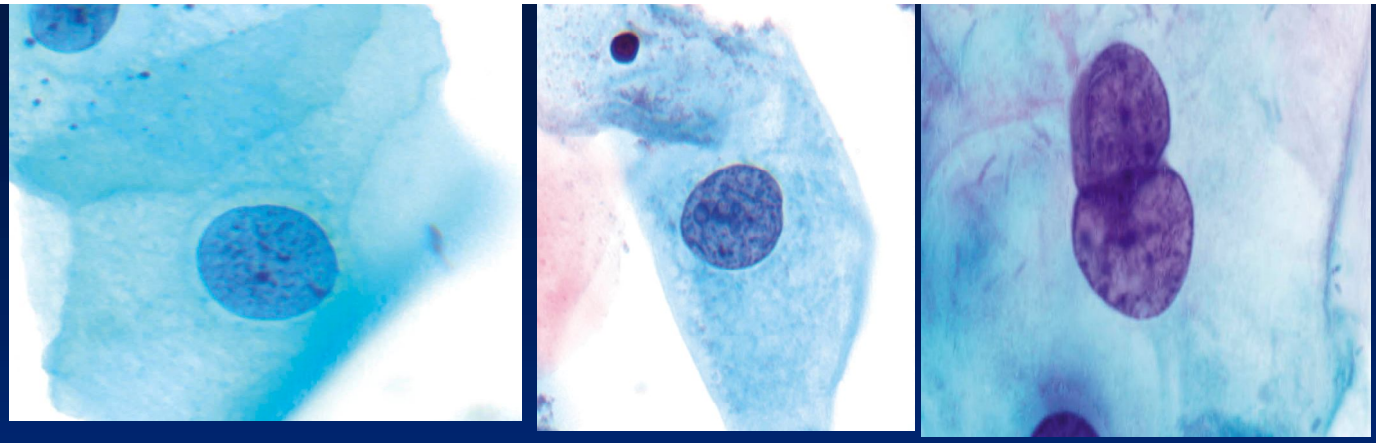
- Abnormal chromatin pattern is the essential requirement.
- Finely speckled, punctate or coarsely clumped chromatin
- Abnormal size,spacing and distribution of chromatin granules
- Hyper or Hypochromasia
- Irregular nuclear outline + or –
- Minor changes in nuclear outline e.g.single or multiple folds,wrinkling or serration occur with inflammation and degeneration.
- Large bulbous protrusions,scalloping or deep notches not associated with linear folds occur in dyskaryosis.
- raised nuclear : cytoplasmic ratio

DYSKARYOTIC CELL (SIL)
Coarse chromatin with unequal distribution

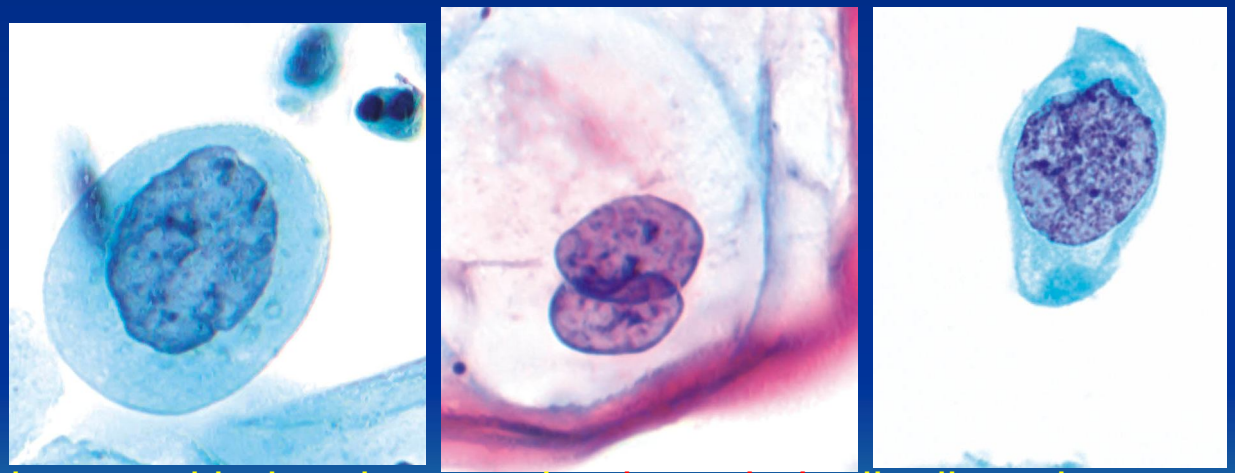


Abnormal Chromatin distribution





Fine,Speckled and coarse granularity but even distribution of chromatin in NON-DYSKARYOTIC nuclei



Fine,speckled and coarse but irregularly distributed chromatin of DYSKARYOTIC (SIL) nuclei

From NHSCSP Atlas

Spot the Difference

Definition of Dyskaryosis

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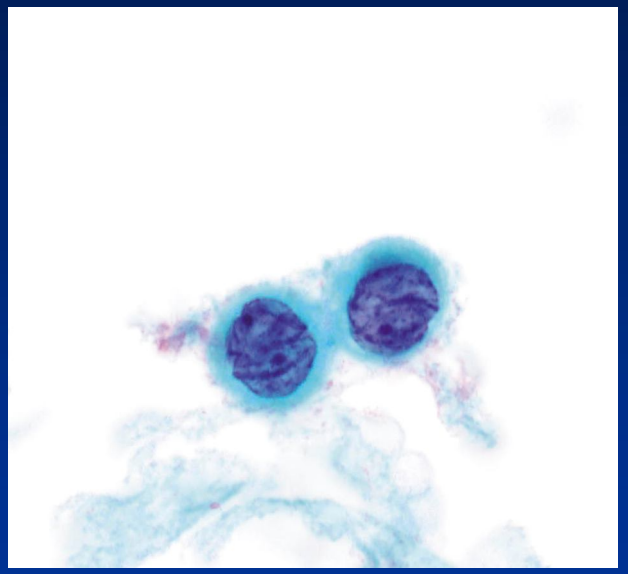
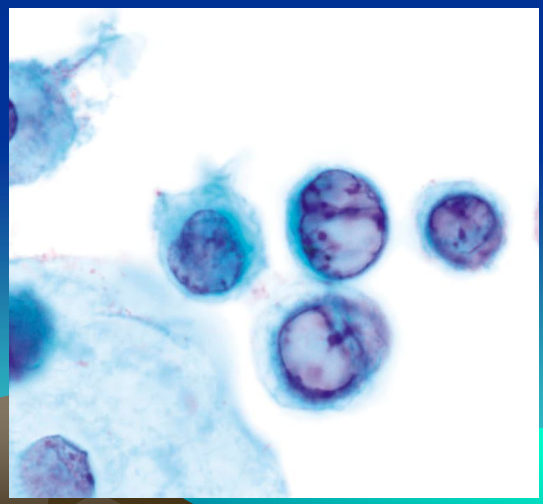
- Large bulbous protrusions,scalloping or deep notches not associated with linear folds occur in dyskaryosis.
- Raised nuclear : cytoplasmic ratio

Chromasia

- **Hyperchromasia**



- **Hypochromasia**



Definition of Dyskaryosis (SIL)

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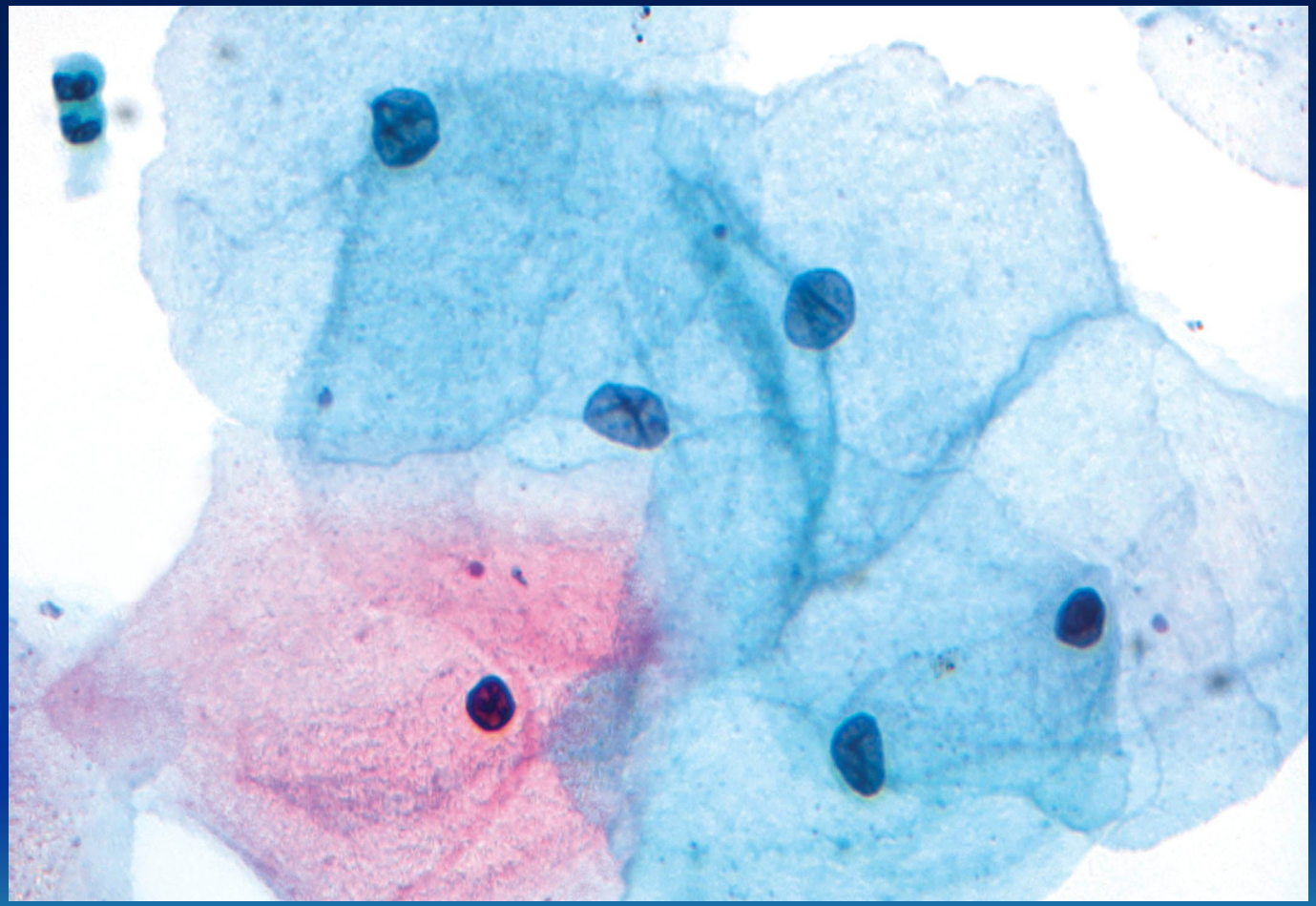
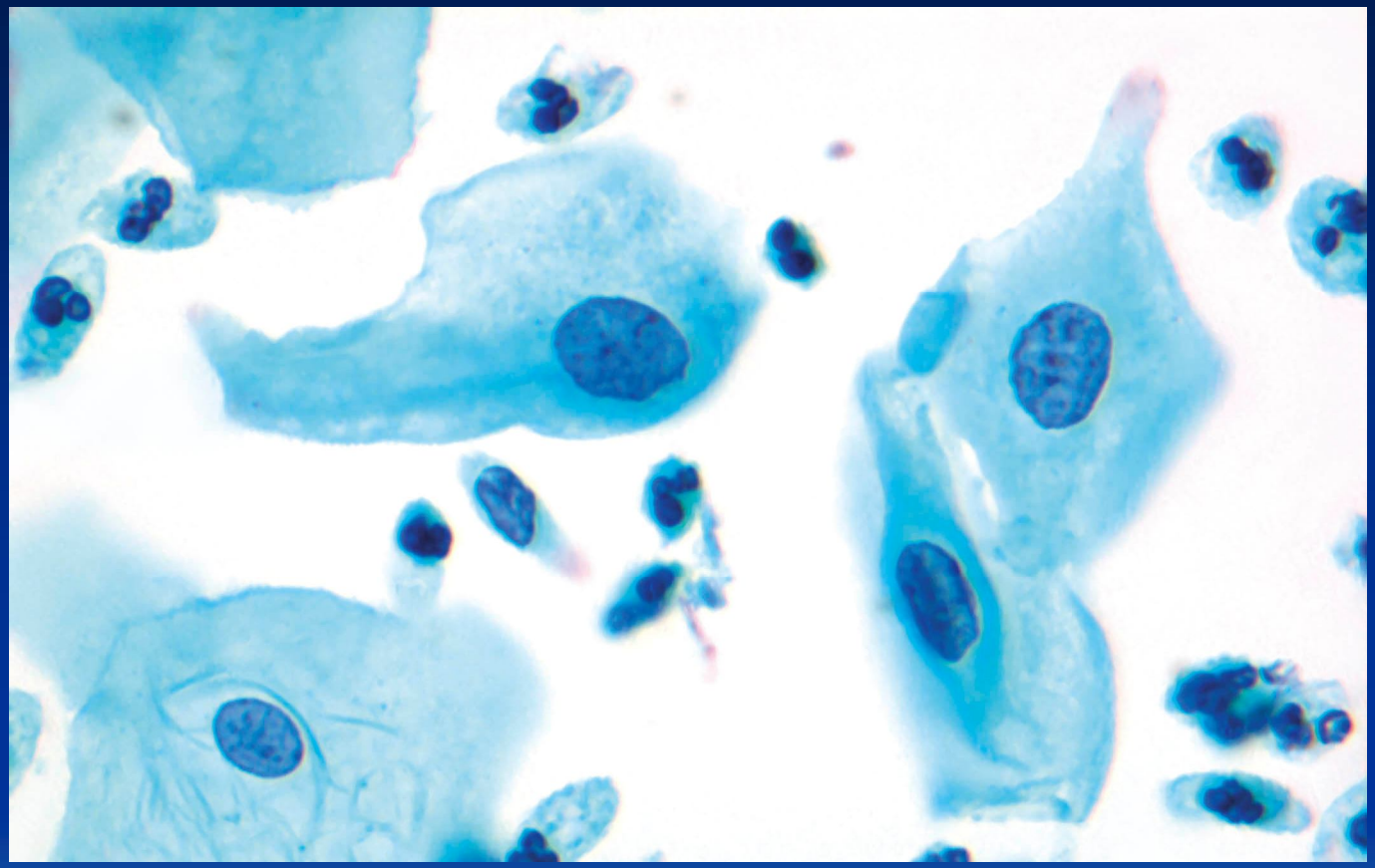
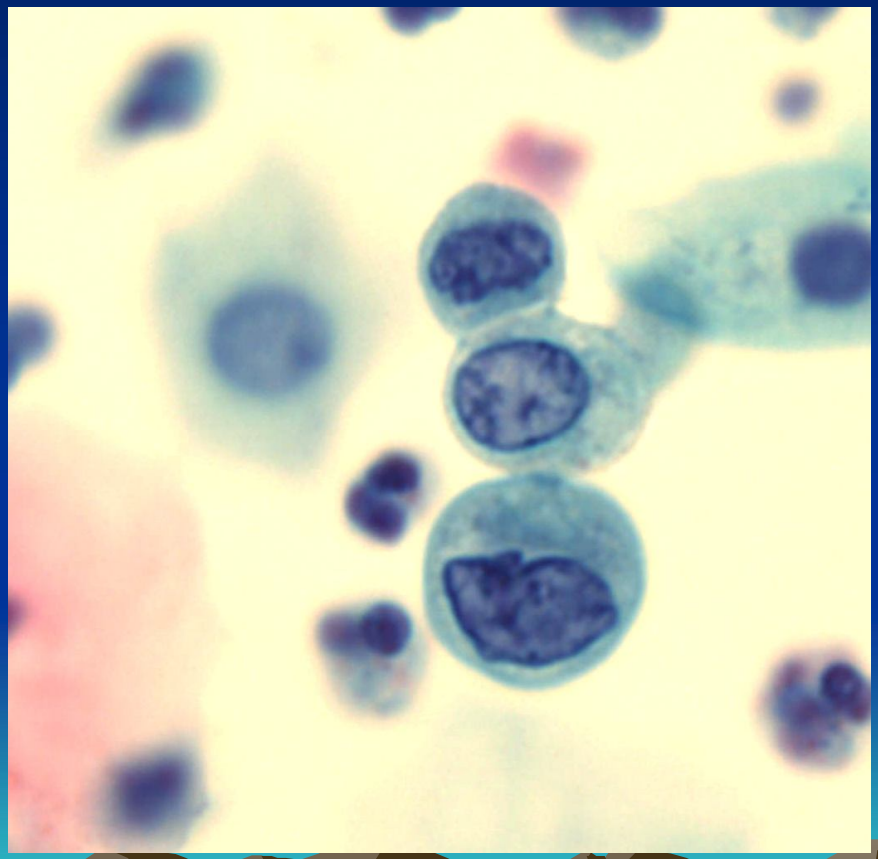


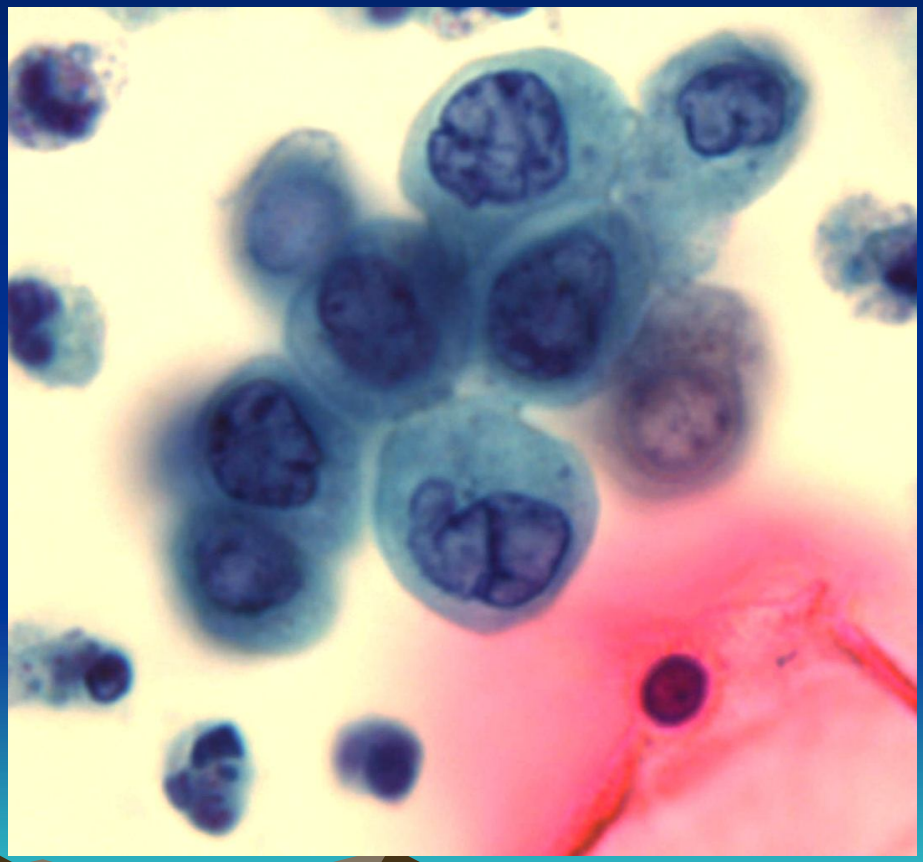
Nuclear folds in
normal cell

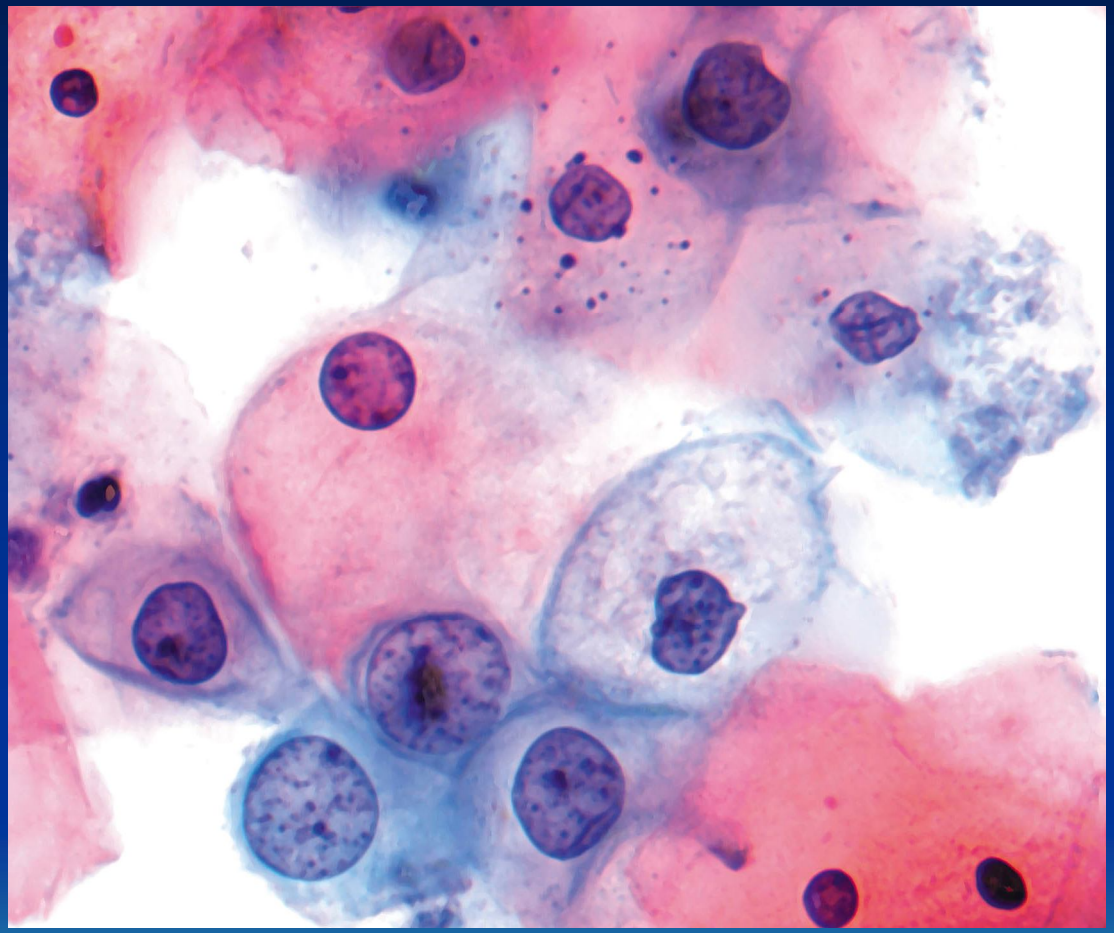


Minor changes in nuclear outline in Inflammation

Abnormal Nuclear membrane In Dyskaryosis (SIL) (Bulbous Protrusion)

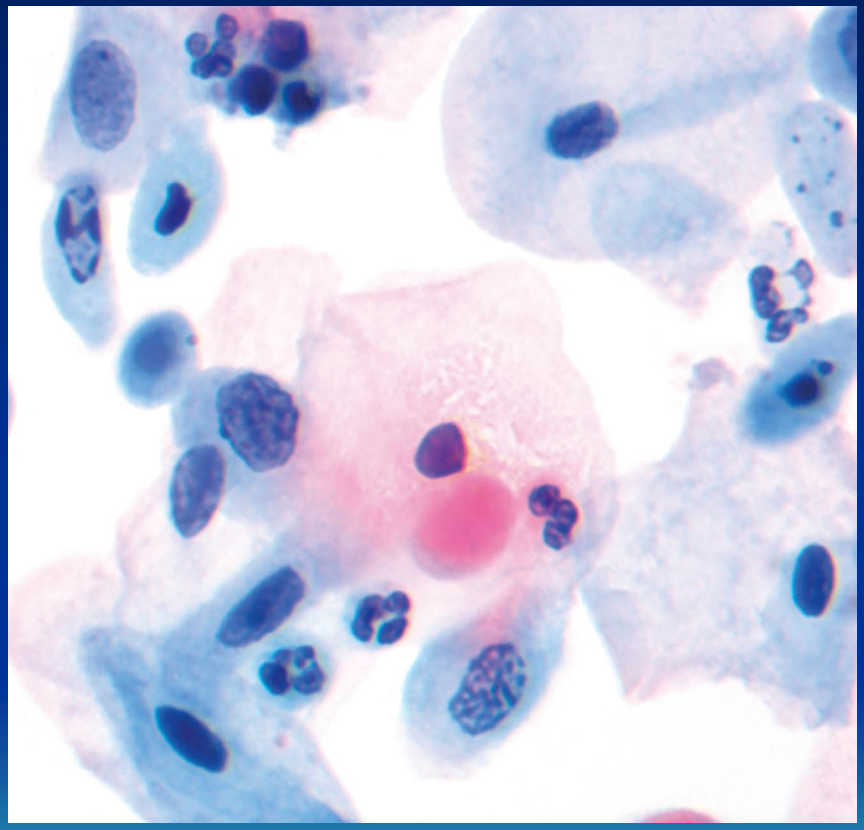


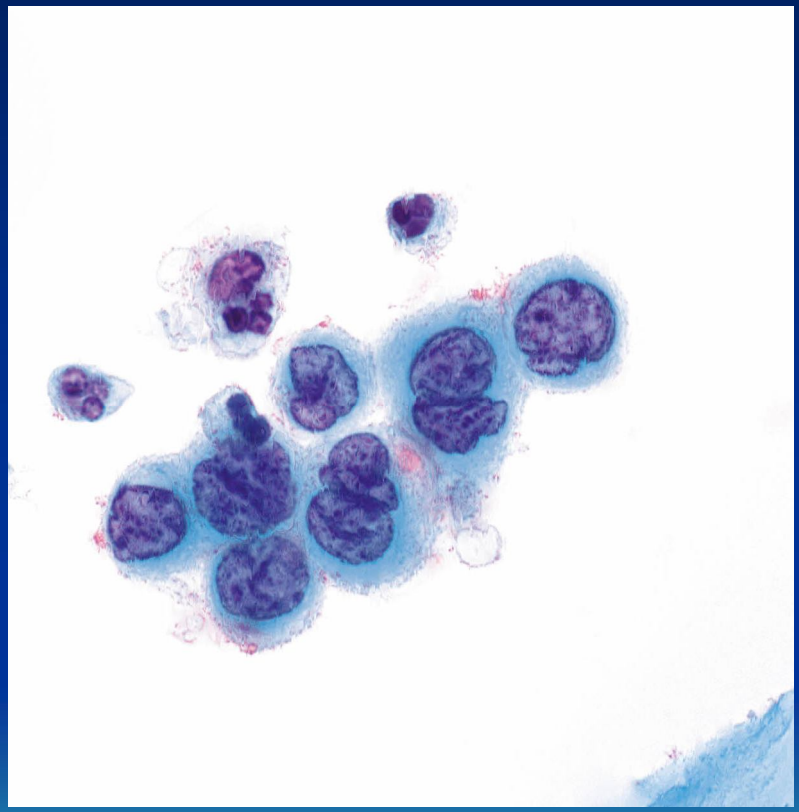




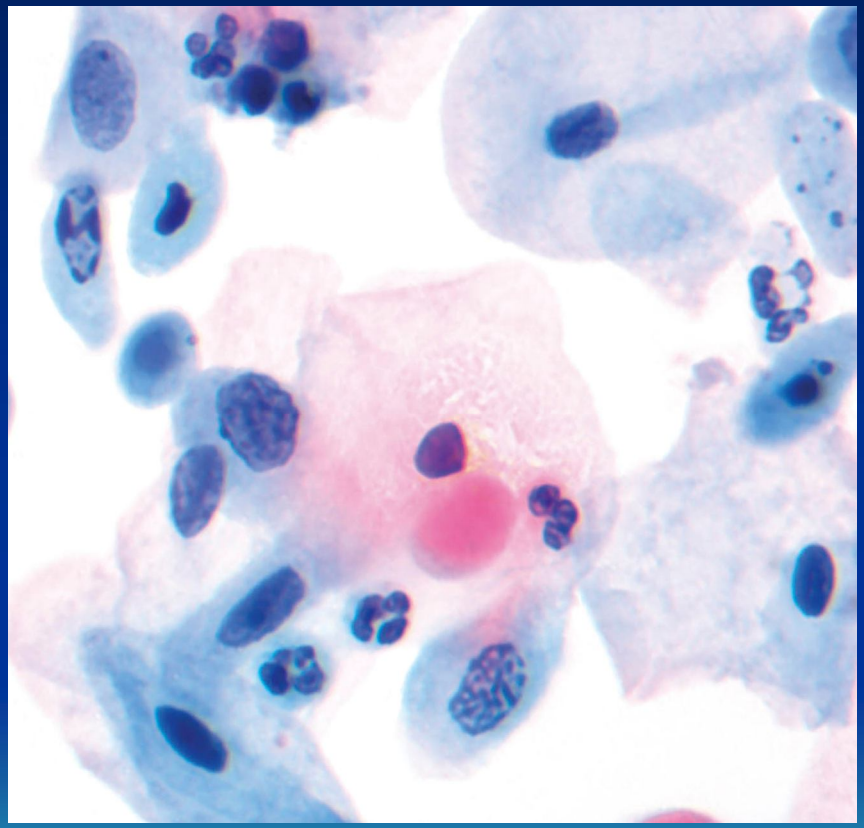
Smooth nuclear membrane In Dyskaryosis (SIL)

Spot the Difference



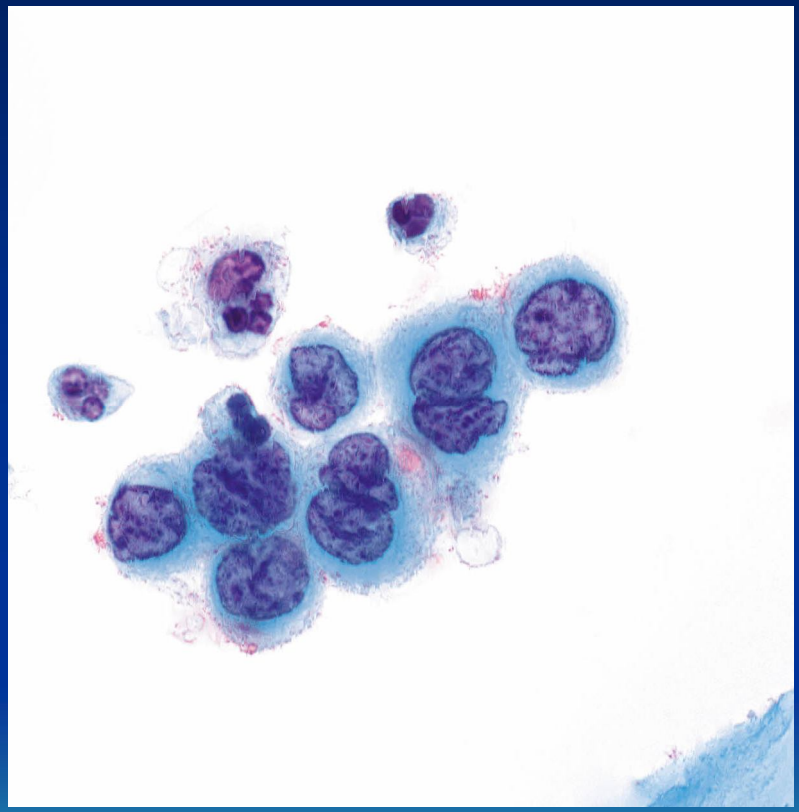


Spot the Difference



Nuclear wrinkling and folding of

NON DYSKARYOTIC cell



Nuclear membrane protrusion and deep notches in

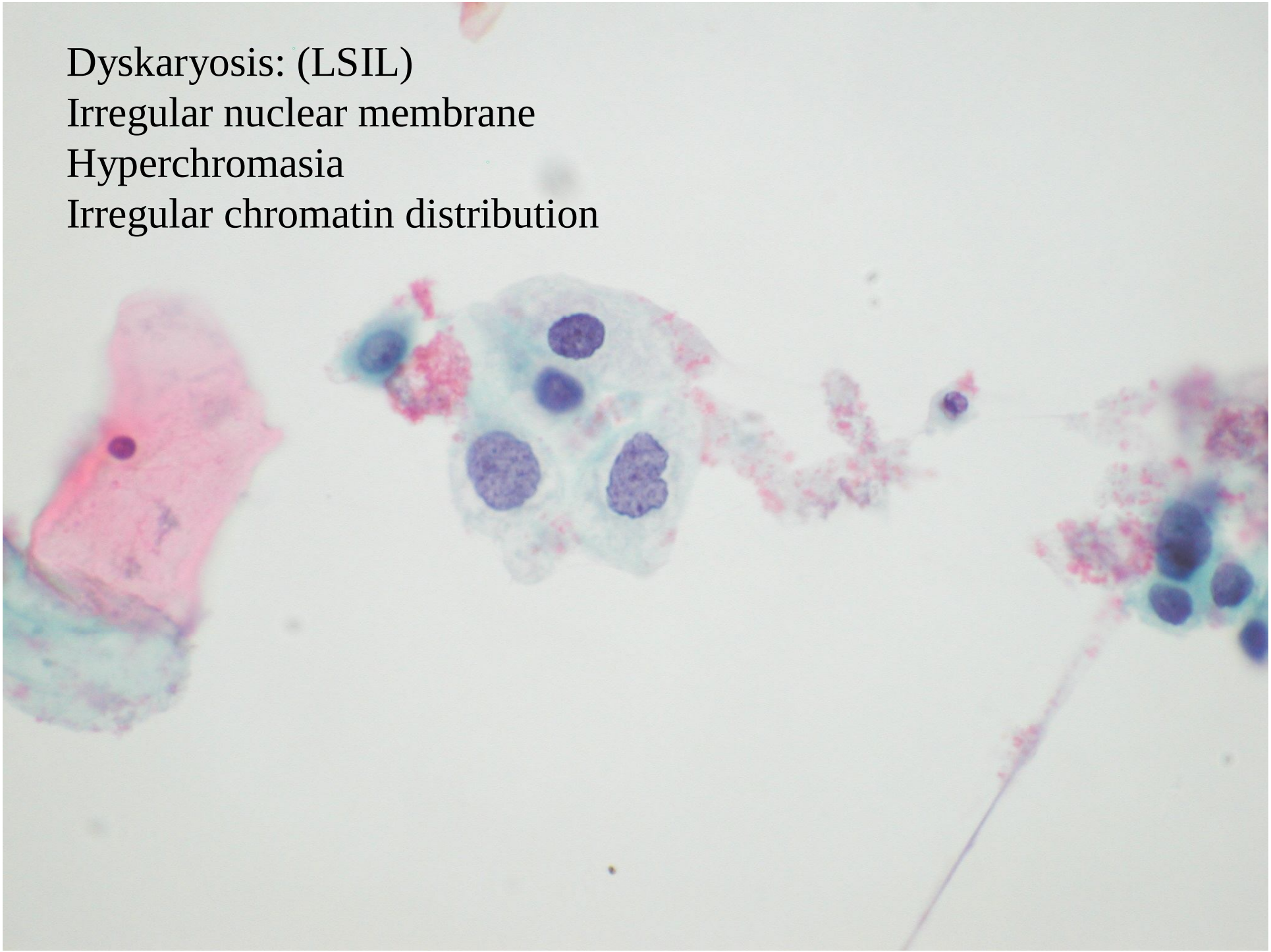
DYSKARYOTIC (SIL) cell

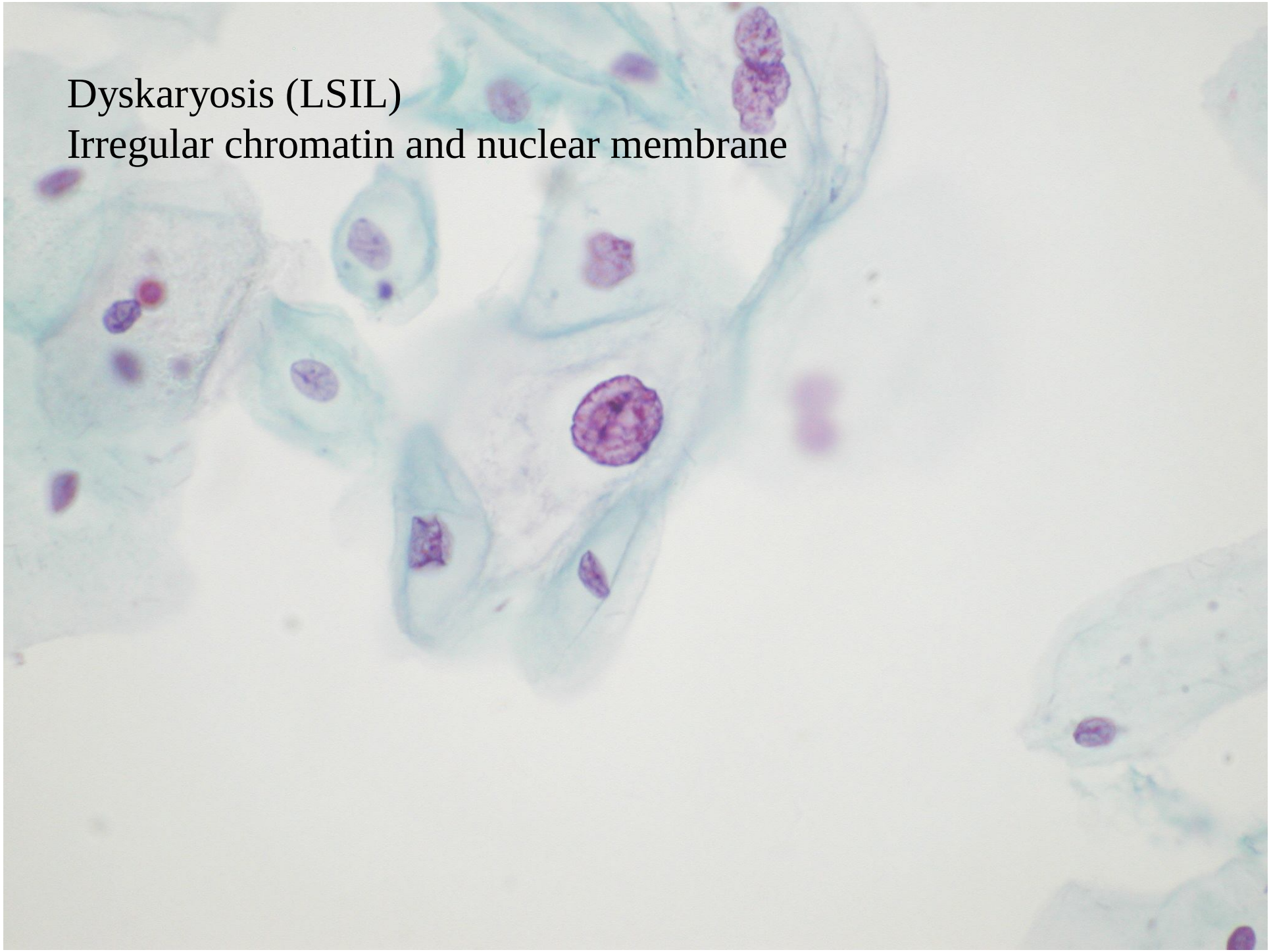
Definition of Dyskaryosis (SIL)

- Abnormal chromatin pattern is the essential requirement.
- Finely speckled, punctate or coarsely clumped chromatin
- Abnormal size,spacing and distribution of chromatin granules
- Pale vs. Hyperchromatic
- Irregular nuclear outline + or –
- Minor changes in nuclear outline e.g.single or multiple folds,wrinkling or serration occur with inflammation and degeneration.
- Large bulbous protrusions,scalloping or deep notches not associated with linear folds occur in dyskaryosis.
- Raised nuclear : cytoplasmic ratio

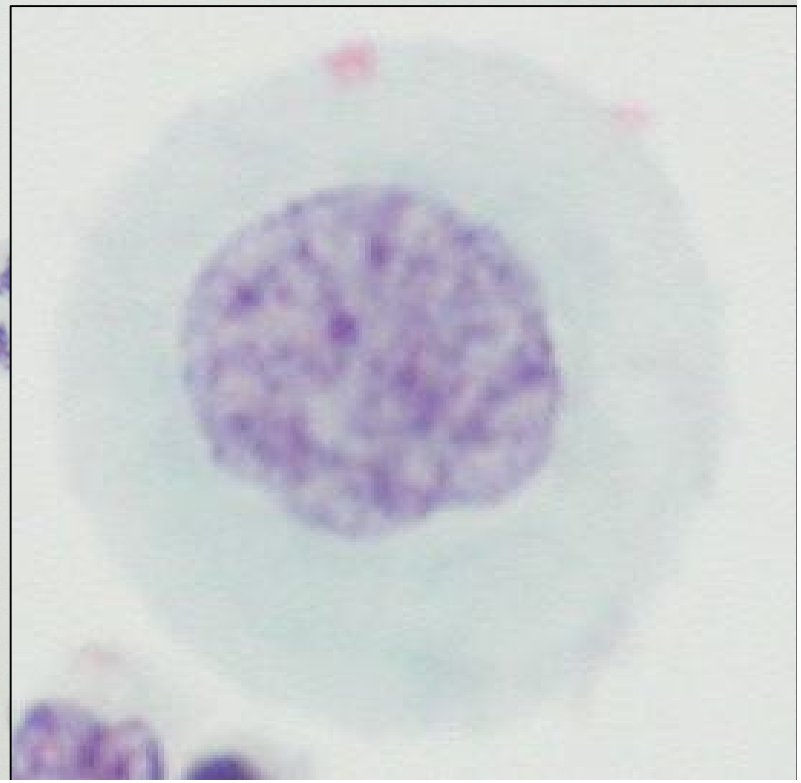
Following cases
are showing
Inappropriate use of the
borderline/ASCUS category
In Dykaryotic (LSIL) smears

Dyskaryosis: (LSIL)
Irregular nuclear membrane
Hyperchromasia
Irregular chromatin distribution

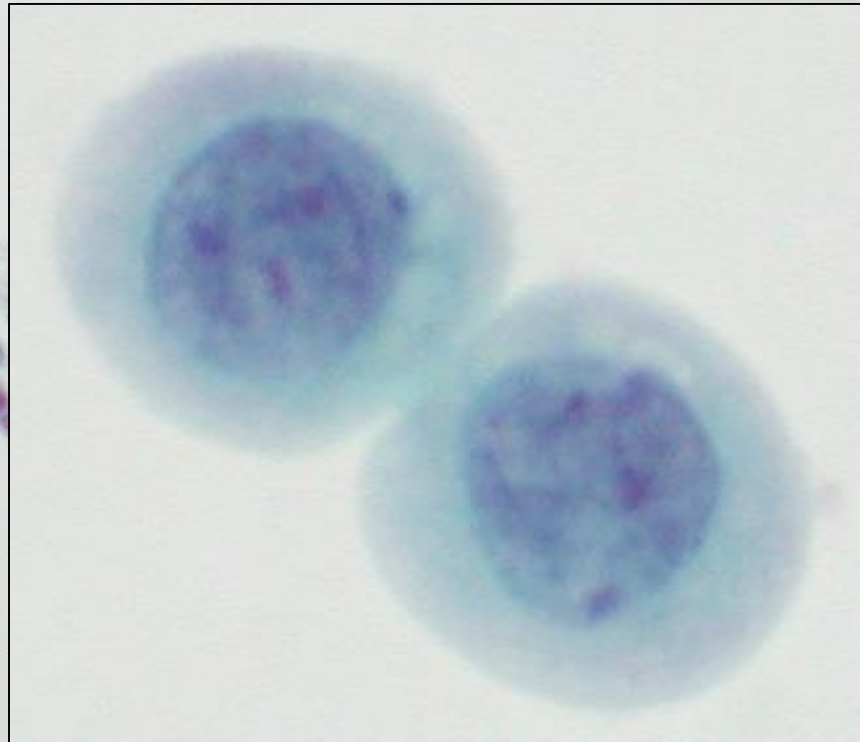



Dyskaryosis (LSIL)
Irregular chromatin and nuclear membrane

Dyskaryosis (LSIL)
Irregular chromatin and nuclear membrane



Dyskaryosis (HSIL)
Irregular chromatin and smooth nuclear membrane



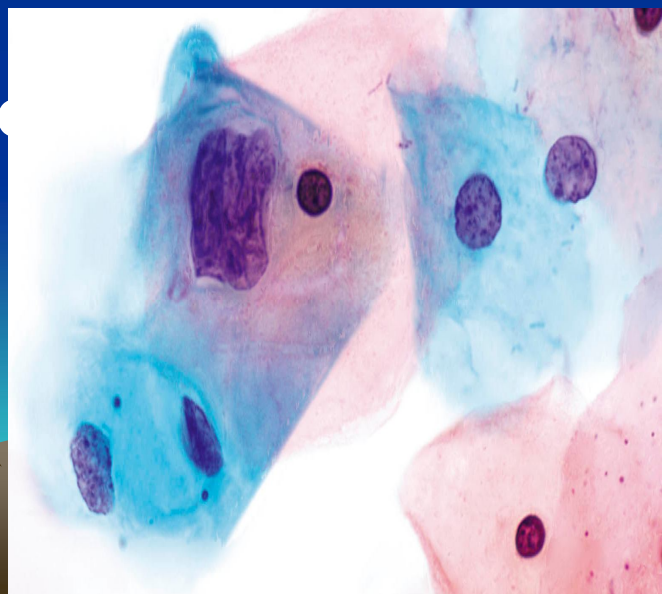
Grading of SIL
Raised Nuclear:Cytoplasmic Ratio

- Used for grading of SIL
- In Low Grade Squamous Lesions, (LSIL), nucleus occupies less than 50% of area of cytoplasm in mature cells
- In High Grade Squamous Lesions (HSIL) ,nucleus occupies more than 50% of area of cytoplasm in less mature cells
- LSIL is seen in superficial or intermediate squamous cells
- HSIL is seen in large, intermediate and small size parabasal and basal squamous cells

Mild Dyskaryosis (LSIL)

Back to Basics

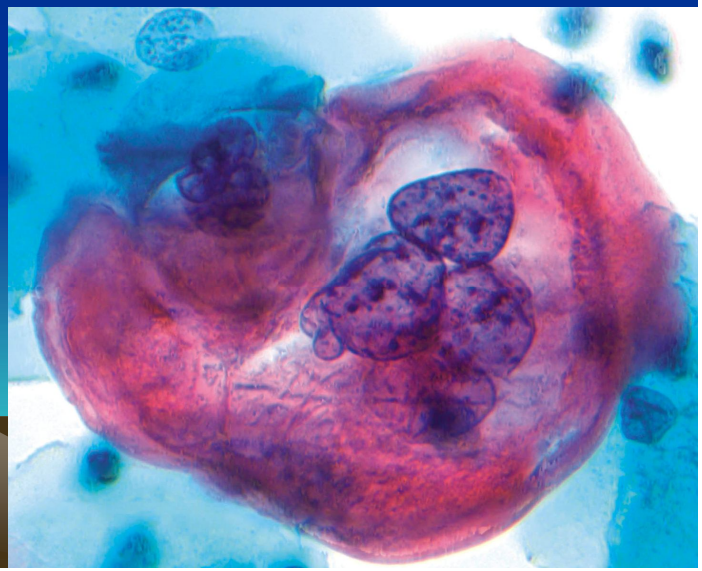
- Cells occur singly and in sheets
- Nuclear changes in mature superficial or intermediate cells
- Nuclear enlargement
- mild dyskaryotic (LSIL) nuclei at least x3 size of intermediate nucleus
- Chromatin irregularity
- Irregularity of nuclear membrane +
  - Notches
  - Protrusions
  - Spurs
  - Not just folds or wavy outline

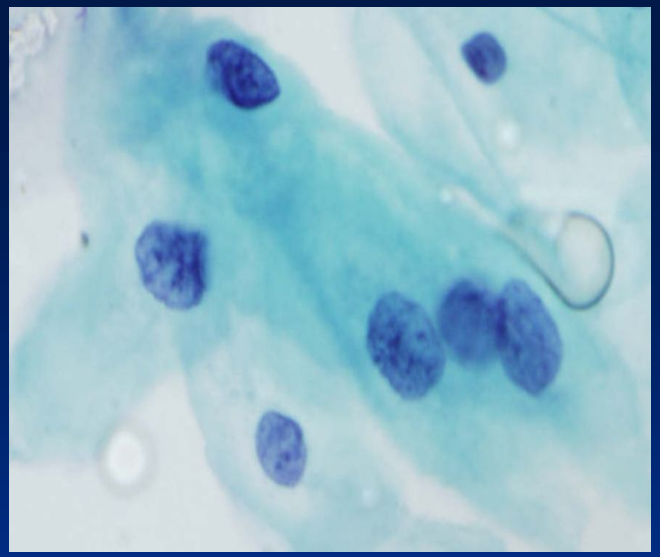


Mild Dyskaryosis (LSIL)

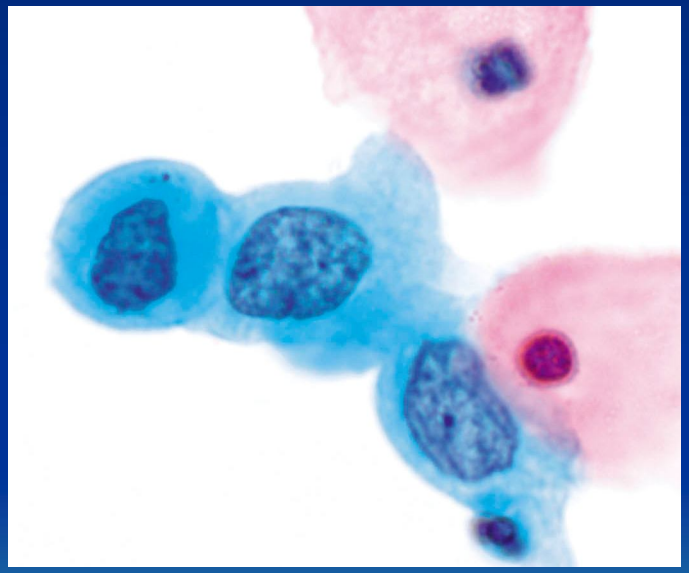
Back To Basics

- **Dyskaryotic nucleus**
- **Enlarged nucleus <50% of cell area**
- **Bi and multinucleation often seen**
- **Polygonal cytoplasm of mature squamous cells, individual cell borders**
- **Strong association with koilocytosis**

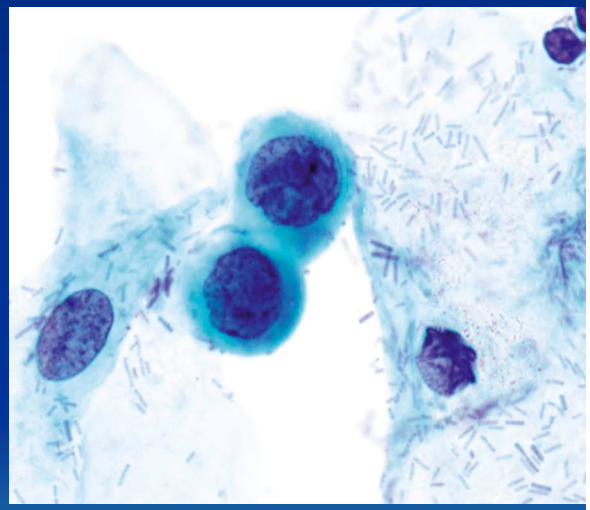




Mild Dyskaryosis
LSIL

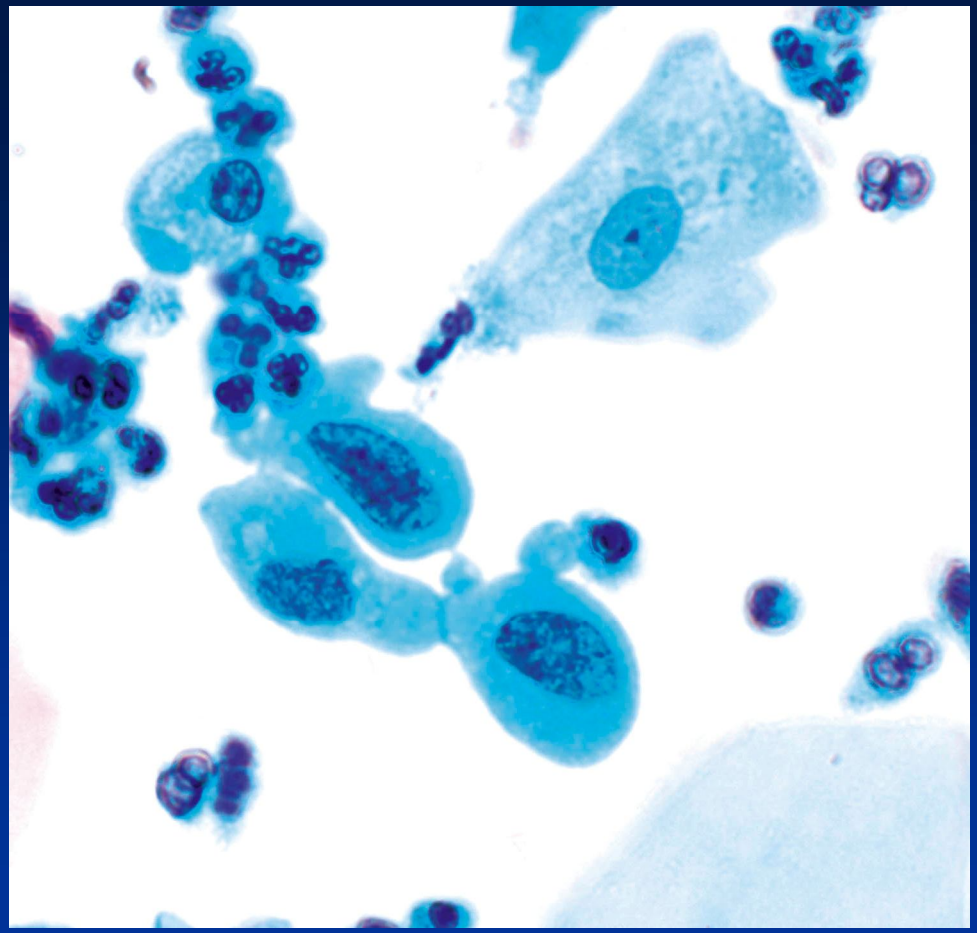


Moderate Dyskaryosis
HSIL

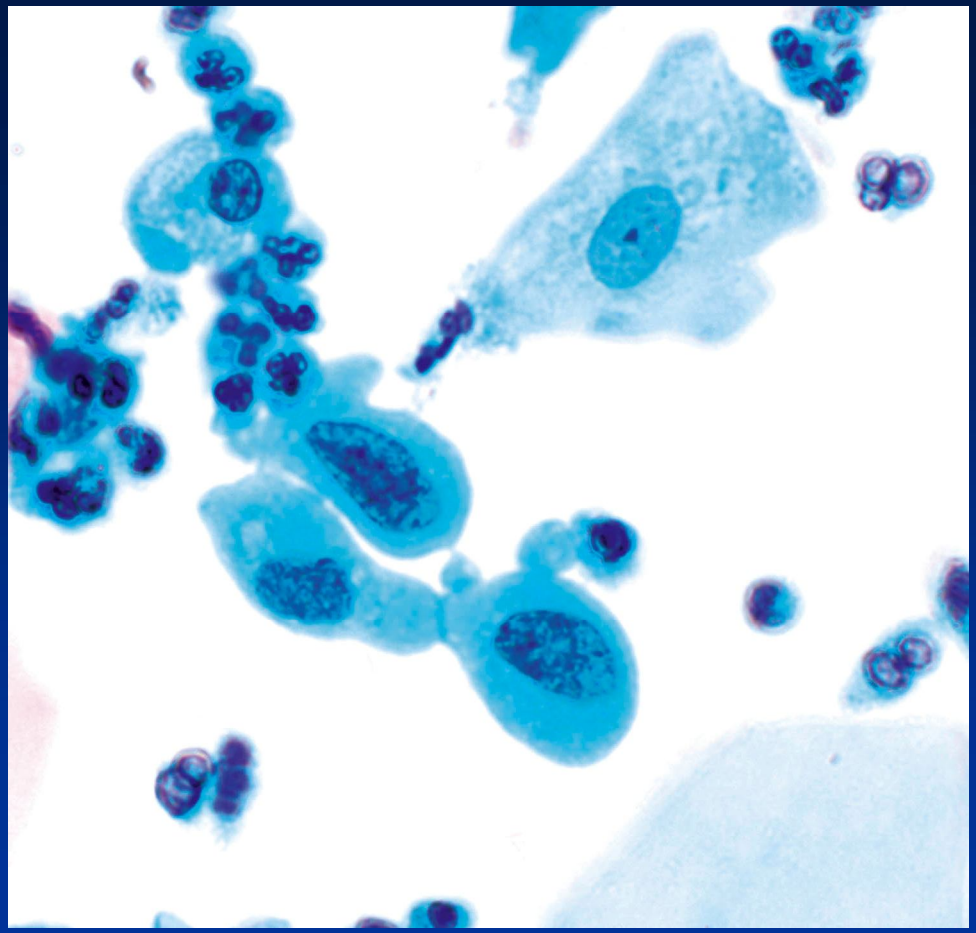


Severe Dyskaryosis
HSIL

Following cases are difficult to grade



LSIL or HSIL?



Mild to Moderate Dyskaryosis

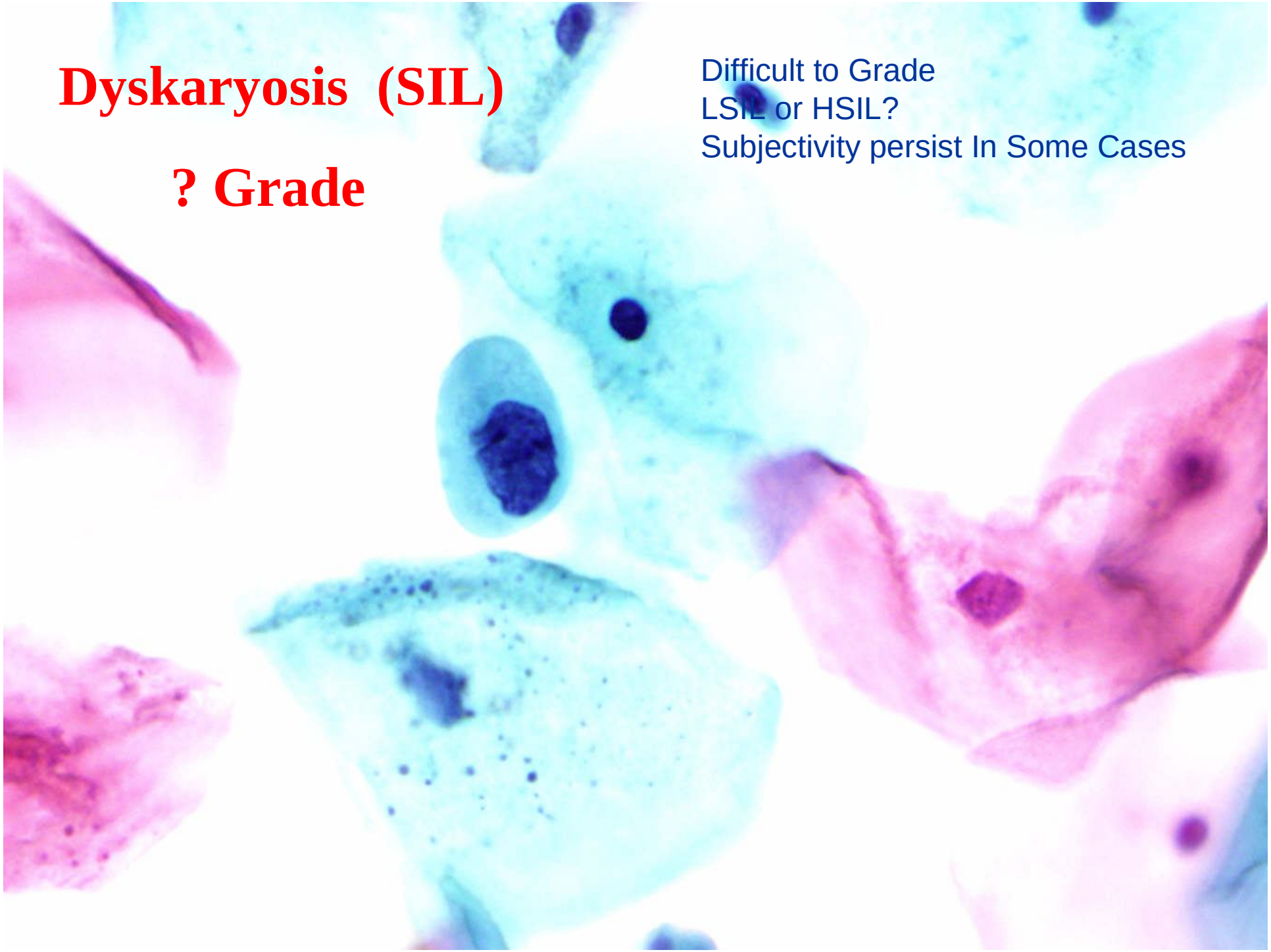
(LSIL TO HSIL)

Subjectivity Still Persist : Not a full proof Science

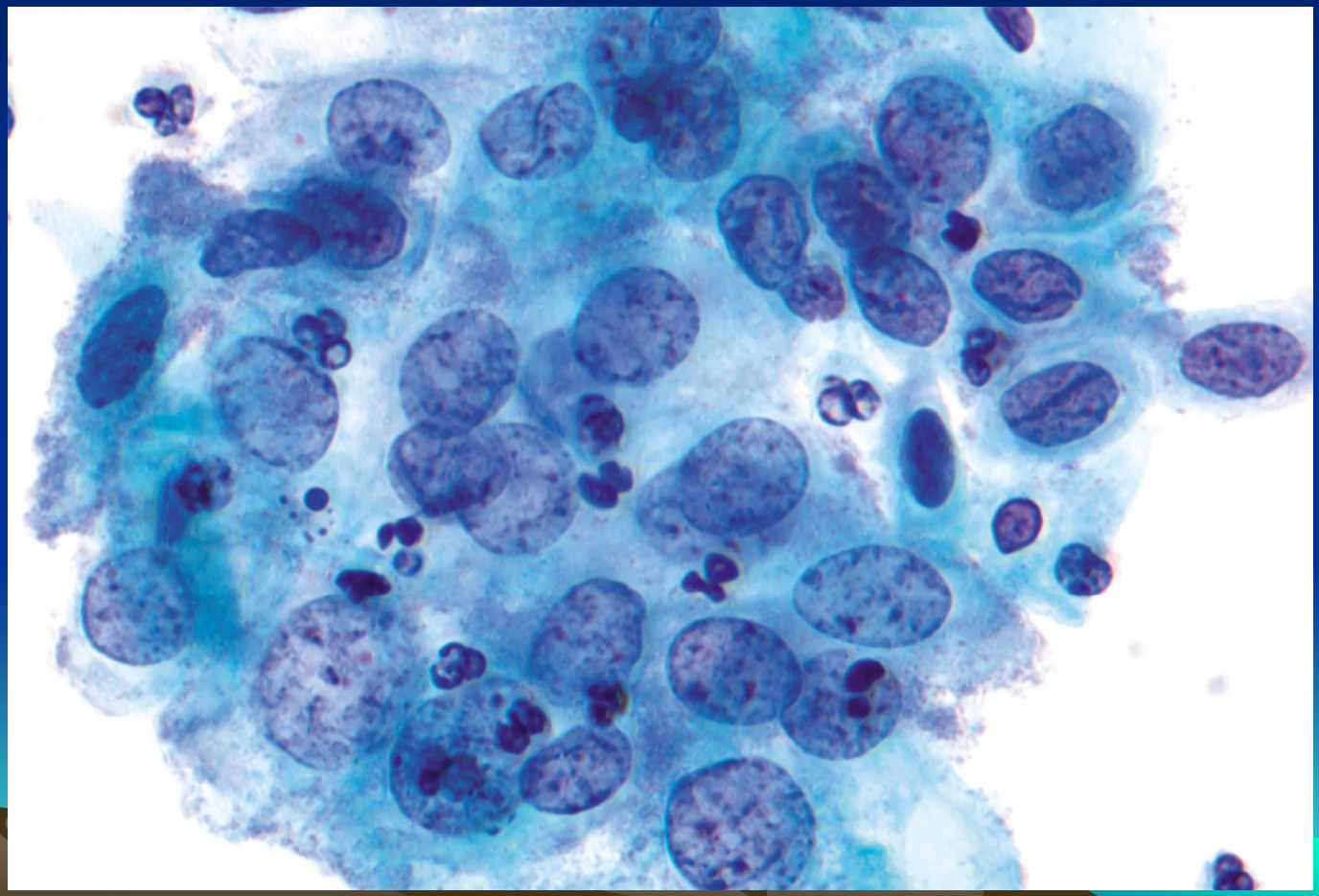
Dyskaryosis (SIL)

? Grade

Difficult to Grade
LSIL or HSIL?
Subjectivity persist In Some Cases

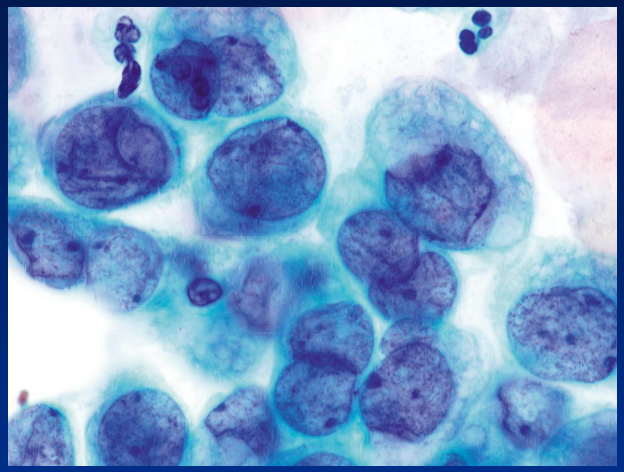


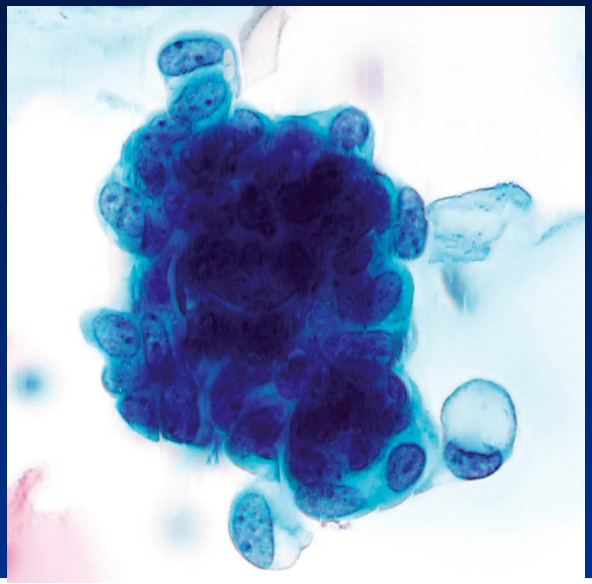
Syncitial Group
LSIL or HSIL?

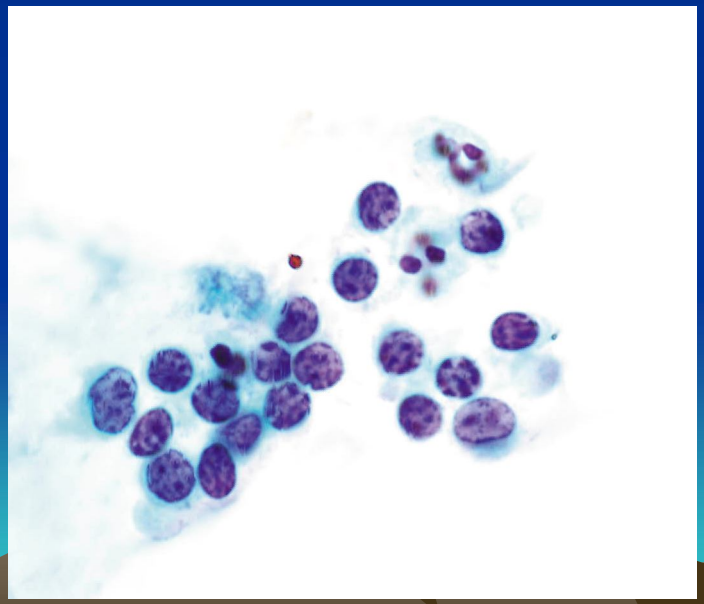


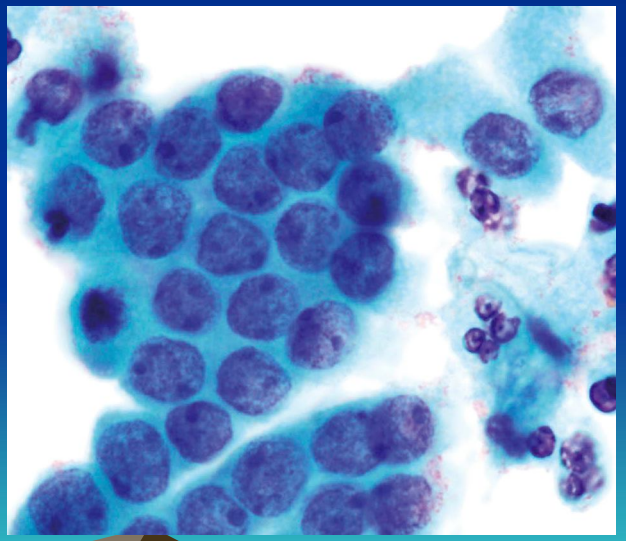
Pitfalls (false positive) - high nuclear:cytoplasmic ratio with:

- **Endocervical cells**
- **Immature squamous metaplastic cells**
- **Endometrial cells**
- **Lymphocytes**

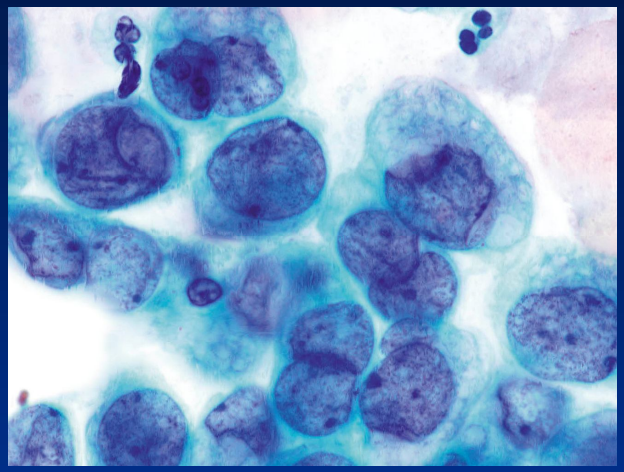




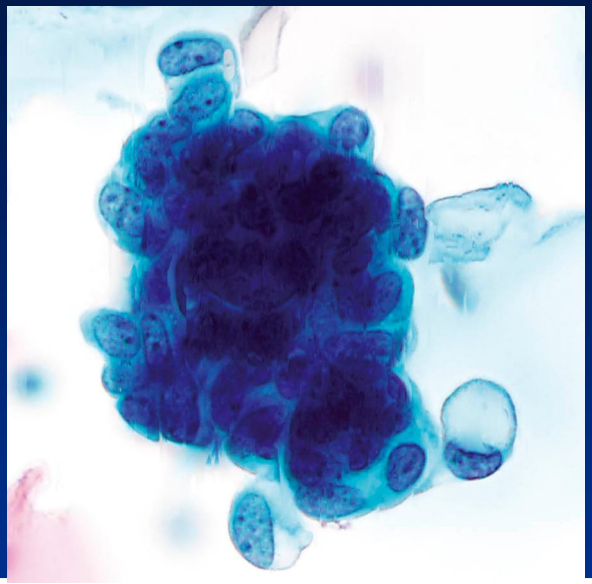


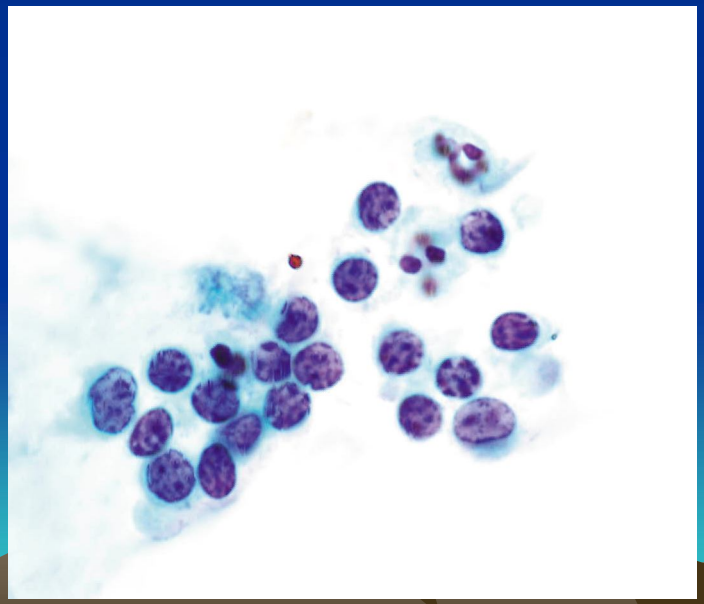


Immature metaplastics

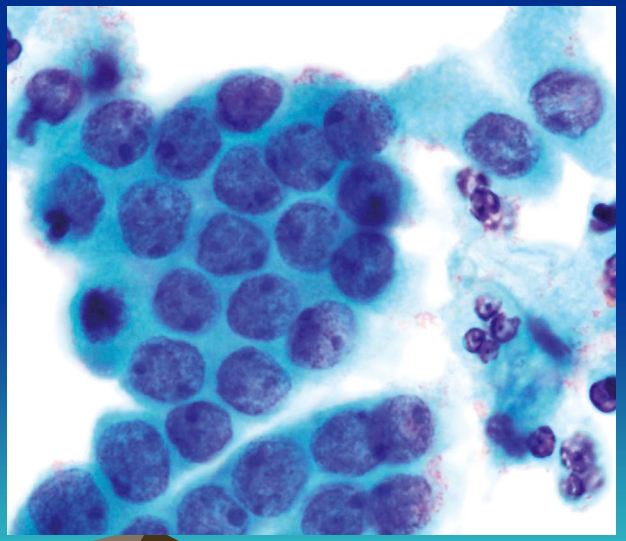


Endometrials





Follicular cervicitis



Endocervicals

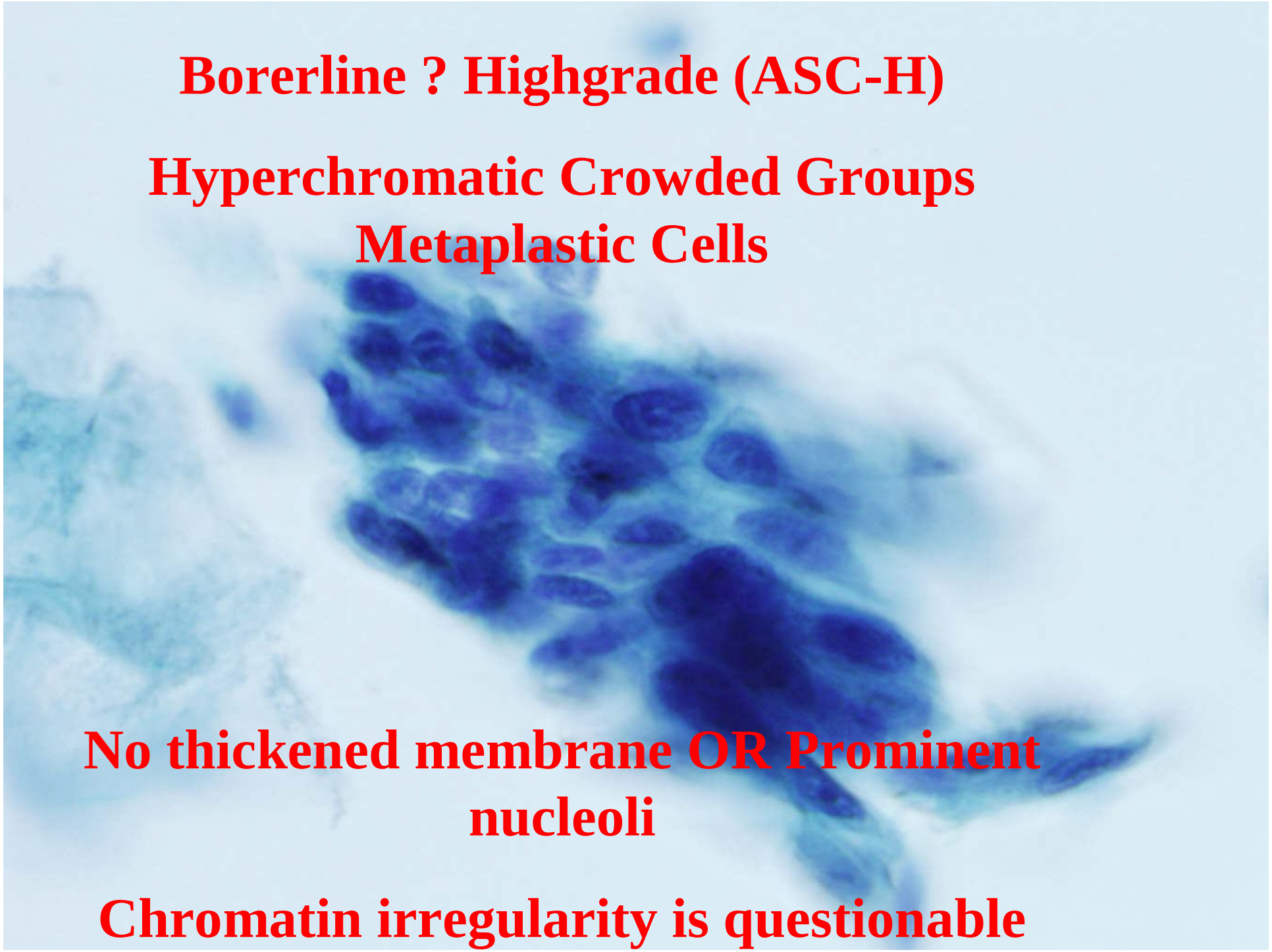
Back to Basics

Definition of ASC-H

Borderline Nuclear Changes High Grade Cannot Be Excluded (ASC-H)

Morphological Subgroups

- Hyperchromatic Crowded Groups
- Atypical immature Metaplasia
- Prominent Nucleoli
- Degenerate and/or poorly preserved cells

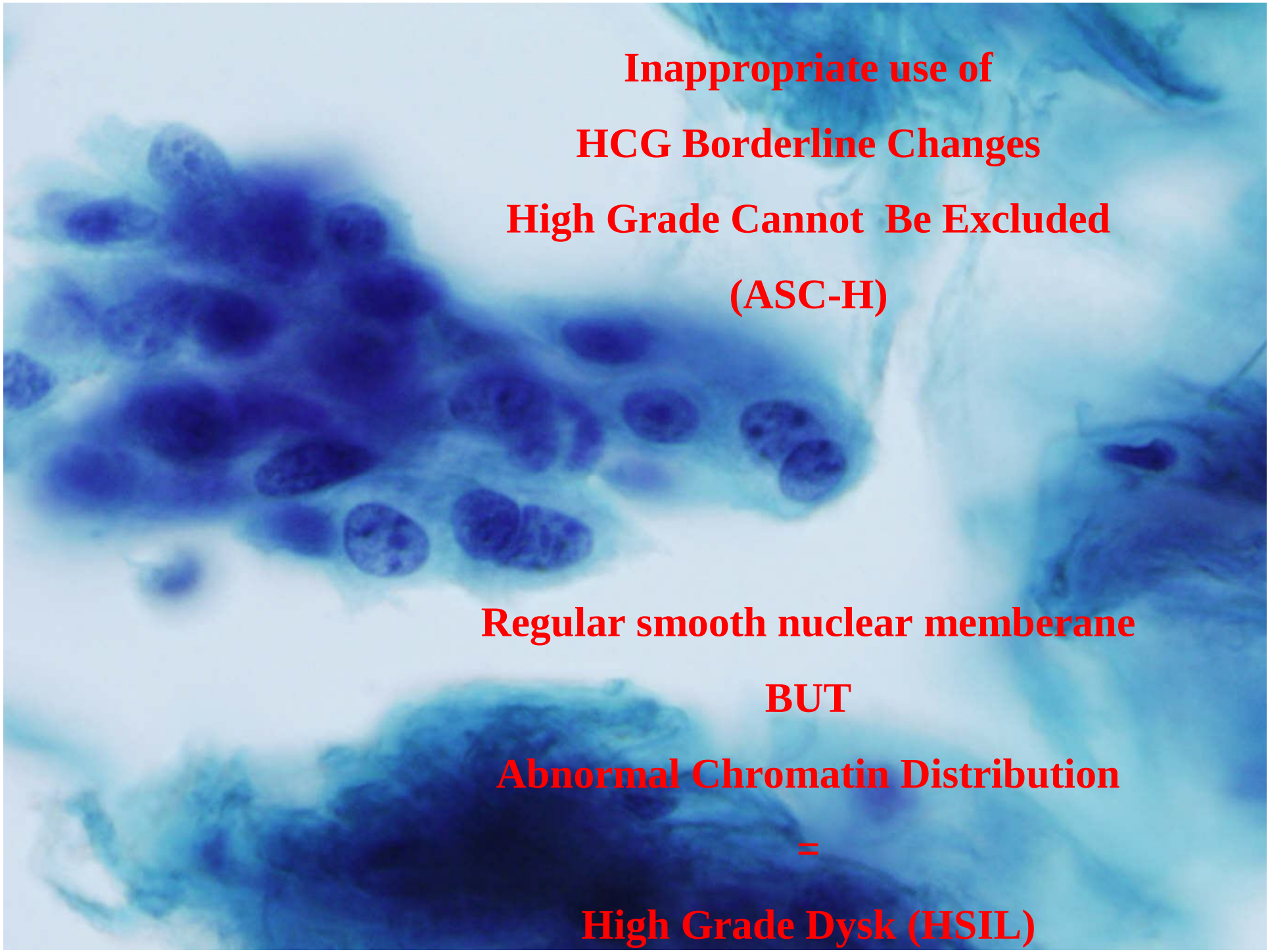


Borerline ? Highgrade (ASC-H)

Hyperchromatic Crowded Groups
Metaplastic Cells

No thickened membrane OR Prominent nucleoli

Chromatin irregularity is questionable

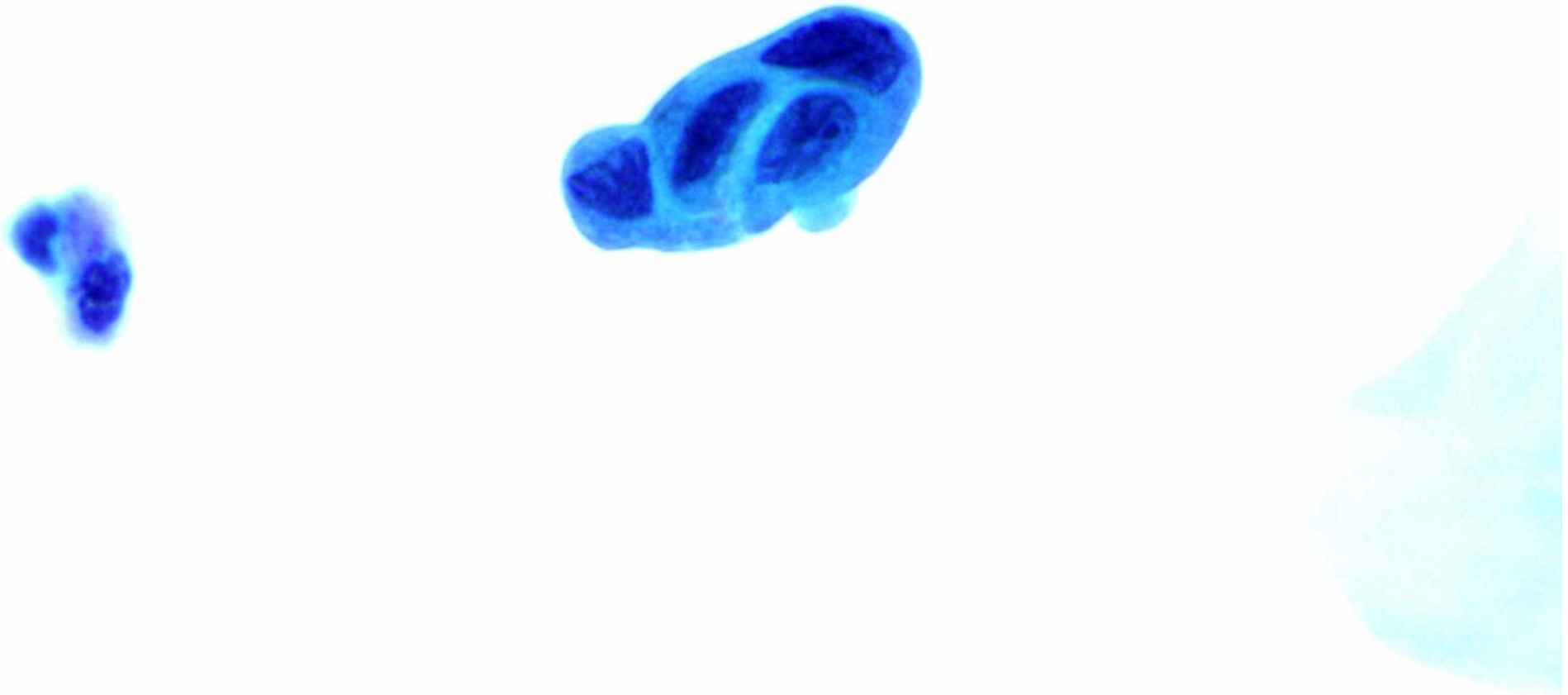

Inappropriate use of
HCG Borderline Changes
High Grade Cannot Be Excluded
(ASC-H)
Regular smooth nuclear memberane
BUT
Abnormal Chromatin Distribution
=
High Grade Dysk (HSIL)

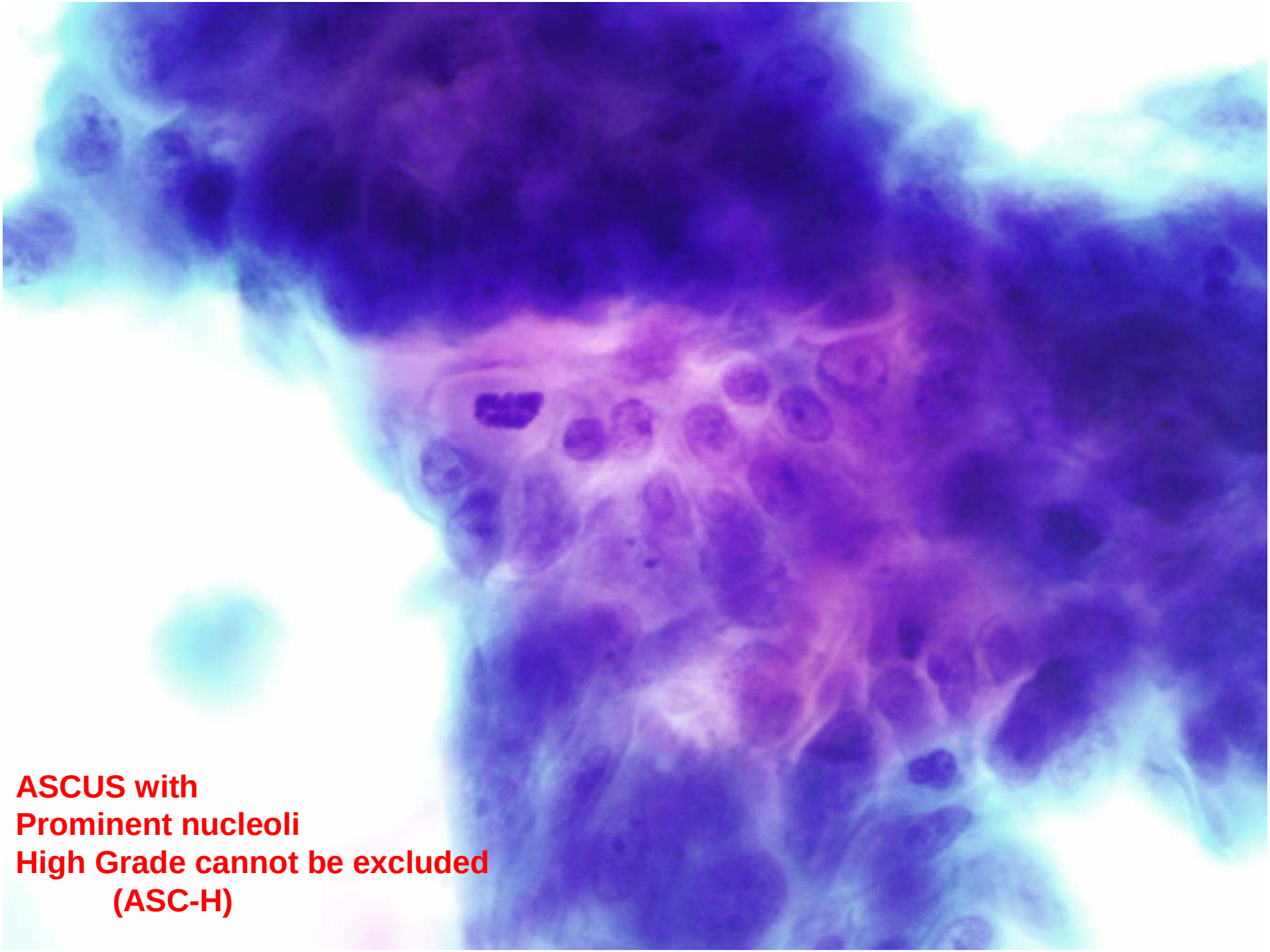
Borderline Changes

High Grade cannot be excluded

(ASC-H)

Atypical, Degenerate, poorly preserved cells

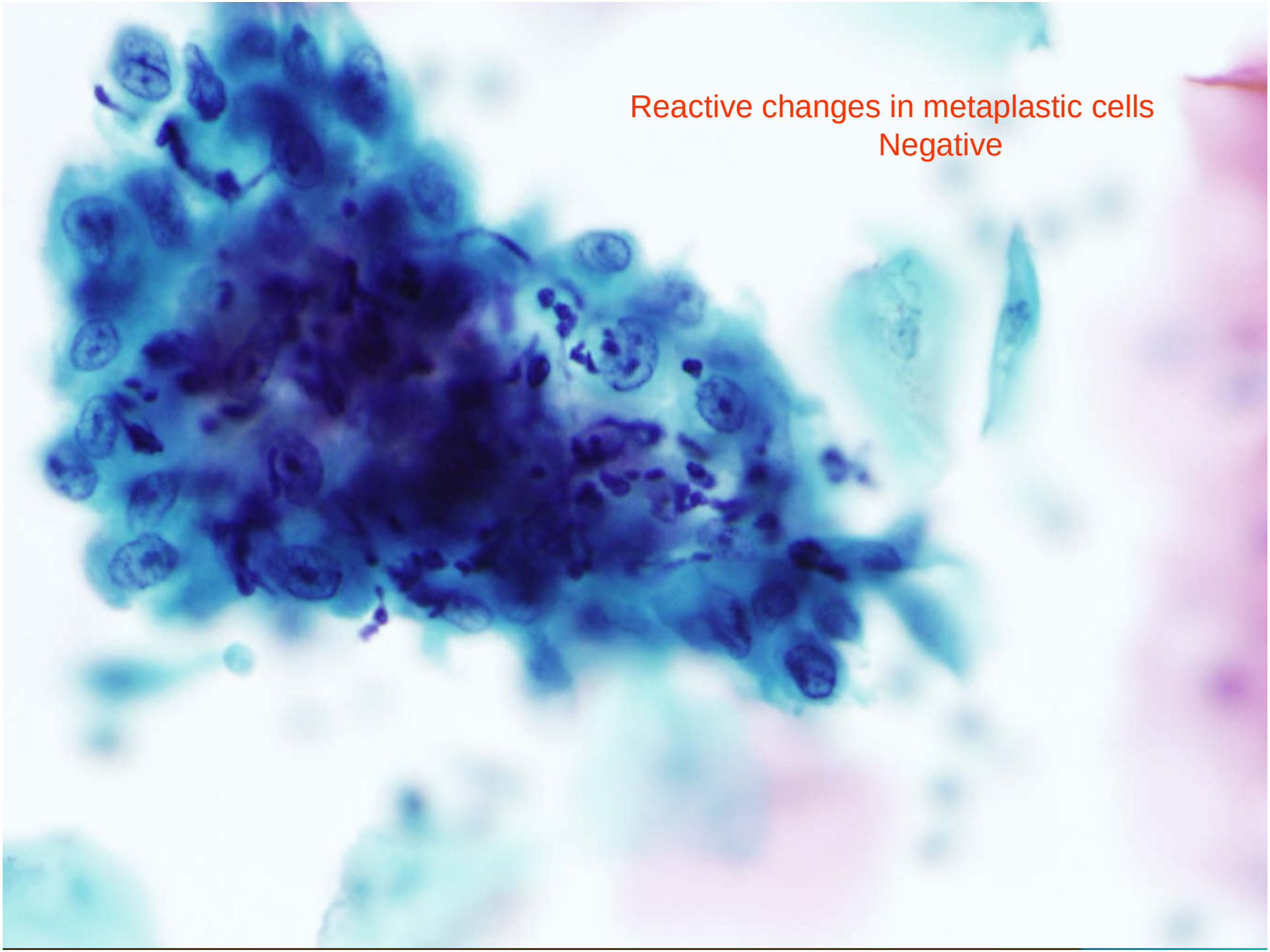




ASCUS with
Prominent nucleoli
High Grade cannot be excluded
(ASC-H)

Word Of Caution

- Mitosis often seen in reactive sheets
- Consider alternative diagnosis if nuclear membrane is very well defined or thickened


Reactive changes in metaplastic cells
Negative

Diagnostic Difficulties and Look-alikes

Diagnostic difficulties and Look alikes

- Inflammatory/**Reactive vs. Borderline (ASC-US)**
- **Borderline (ASC-US) vs. Mild Dyskaryosis (LSIL)**
- **Koilocyte vs. pseudokoilocyte**
- **Metaplasia vs. Borderline (ASC-US)**
- **Assessment of Hyperchromatic Crowded Groups:**

Reactive vs. Borderline (ASC-US)

Borderline (ASC-US) vs. Highgrade Dyskaryosis (HSIL)

- **Prominent Nucleoli**

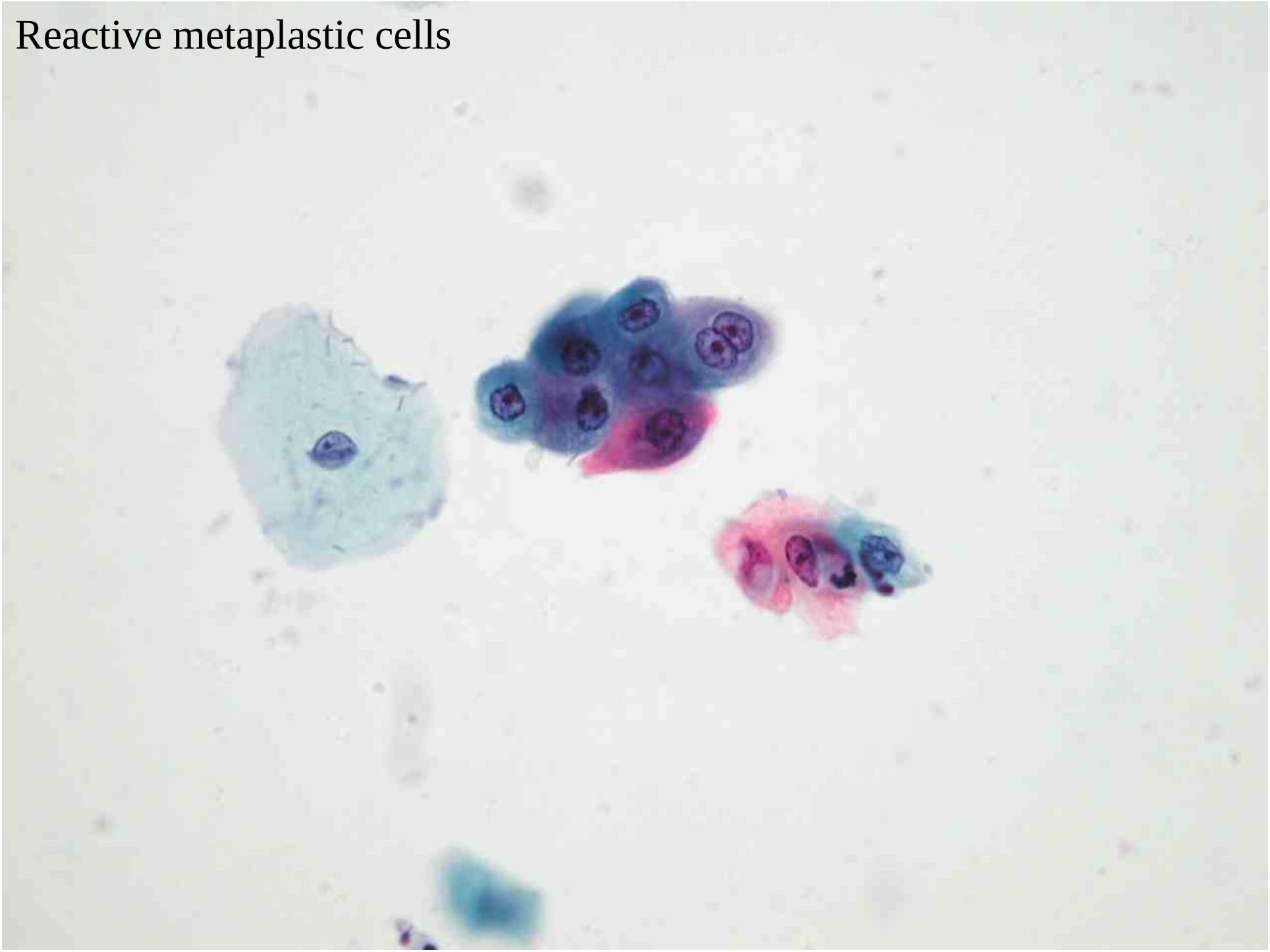
Borderline (ASC-US) vs. Glandular vs. Invasive

Inflammation

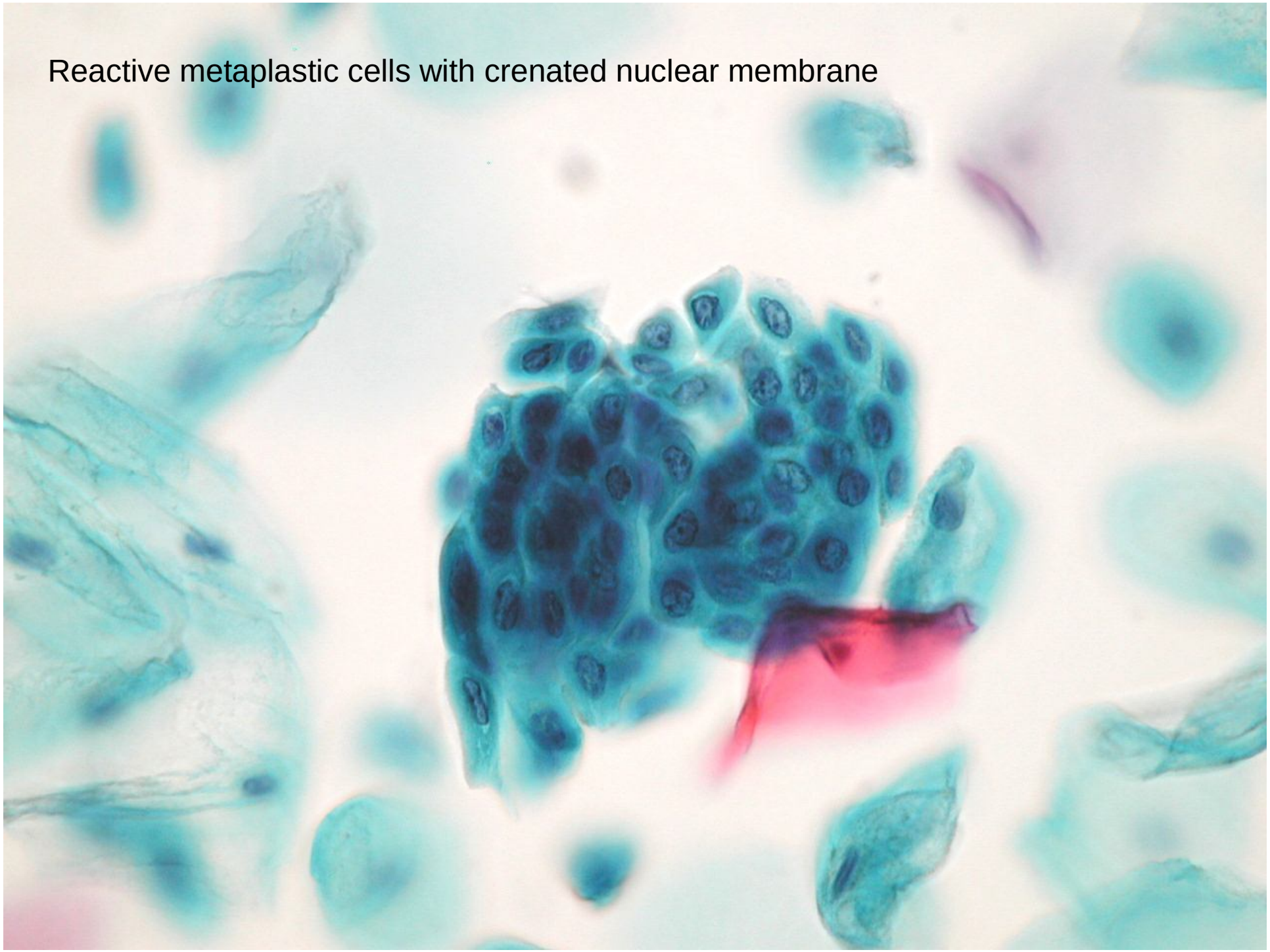
- Chromatin stares at you
- Increase threshold of normality, otherwise increase rate of ASCUS/Borderline diagnoses
- Thickened nuclear membrane is a good indicator of normality

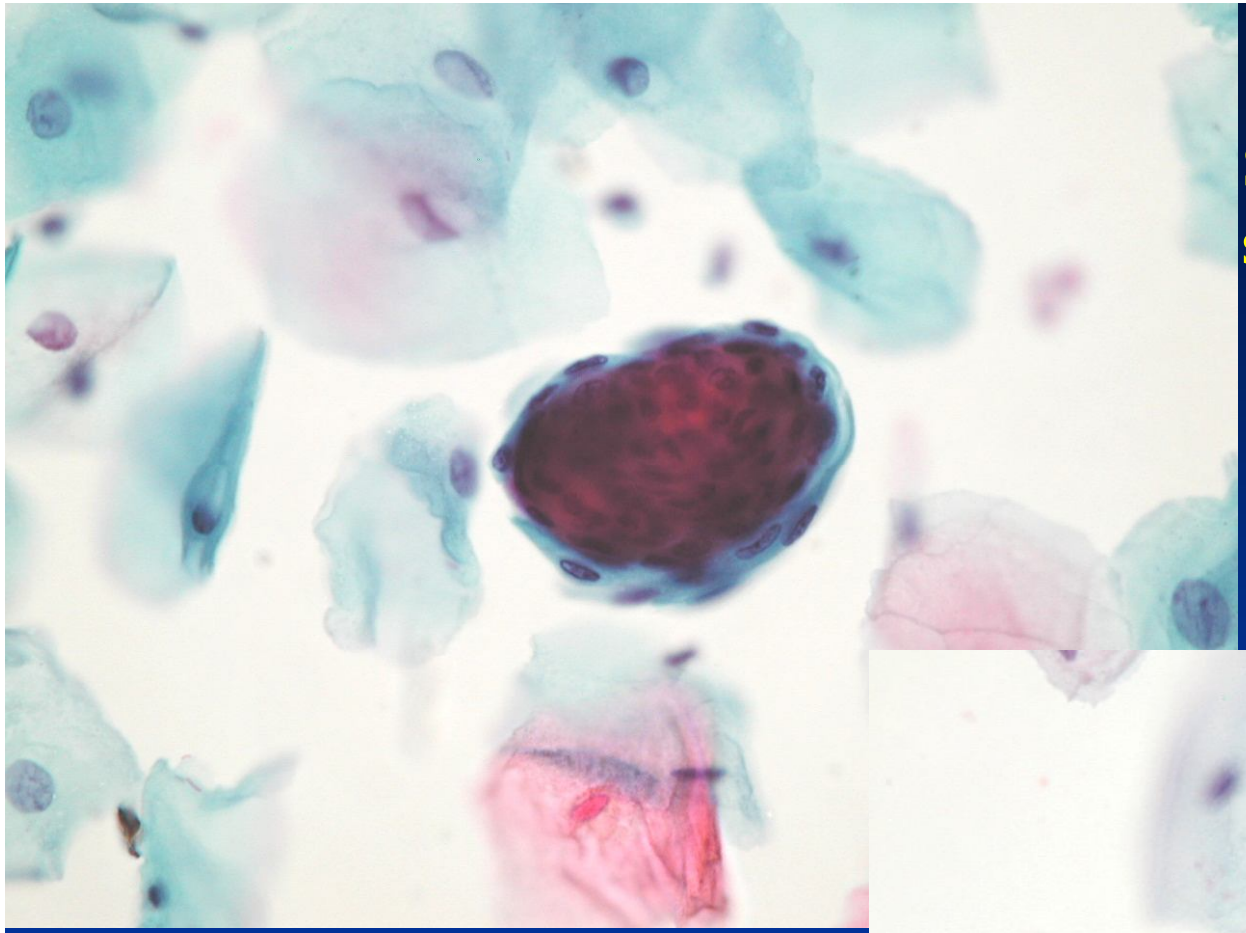
Following cases were wrongly called as Borderline/ASCUS during learning curve

Reactive metaplastic cells

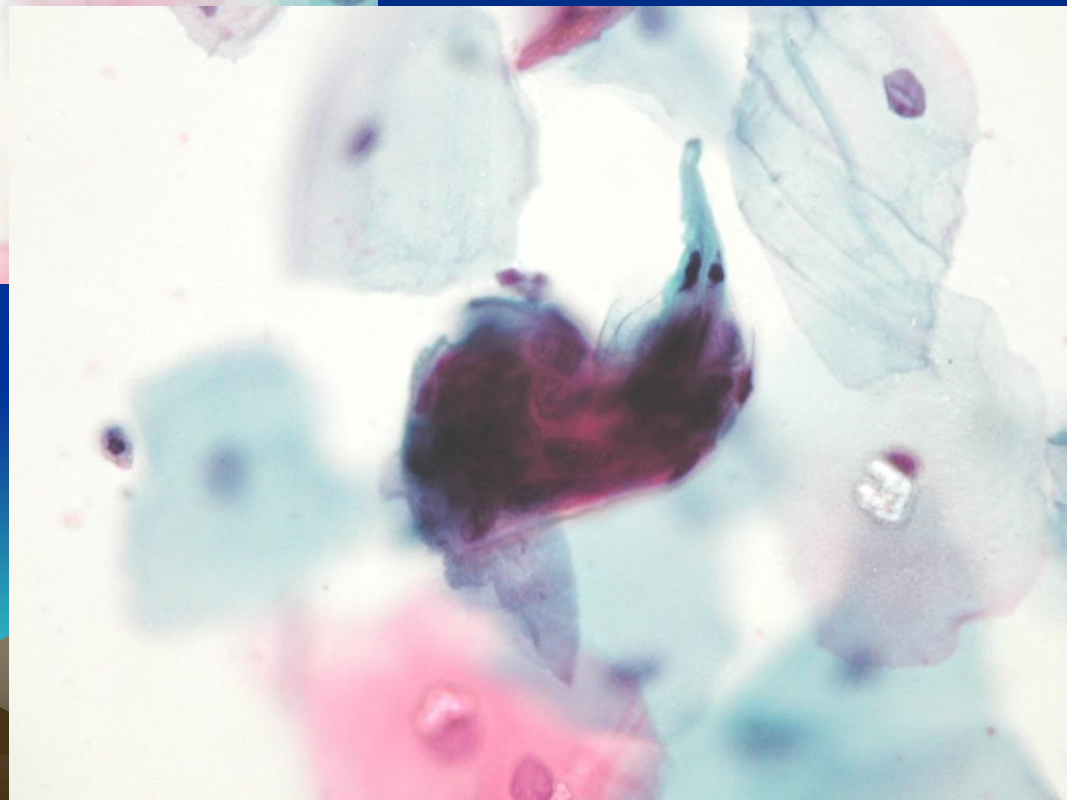


Reactive metaplastic cells with crenated nuclear membrane



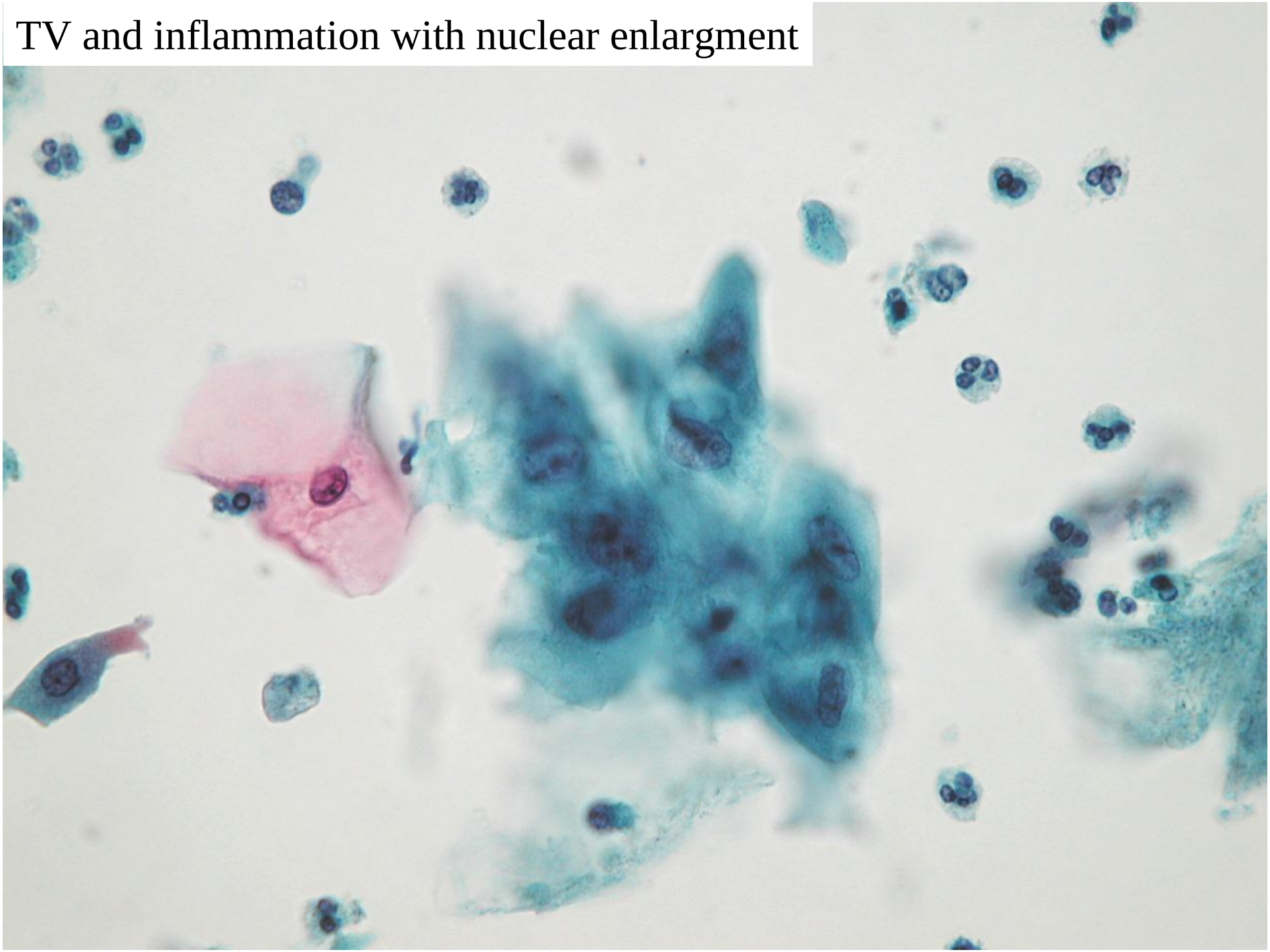


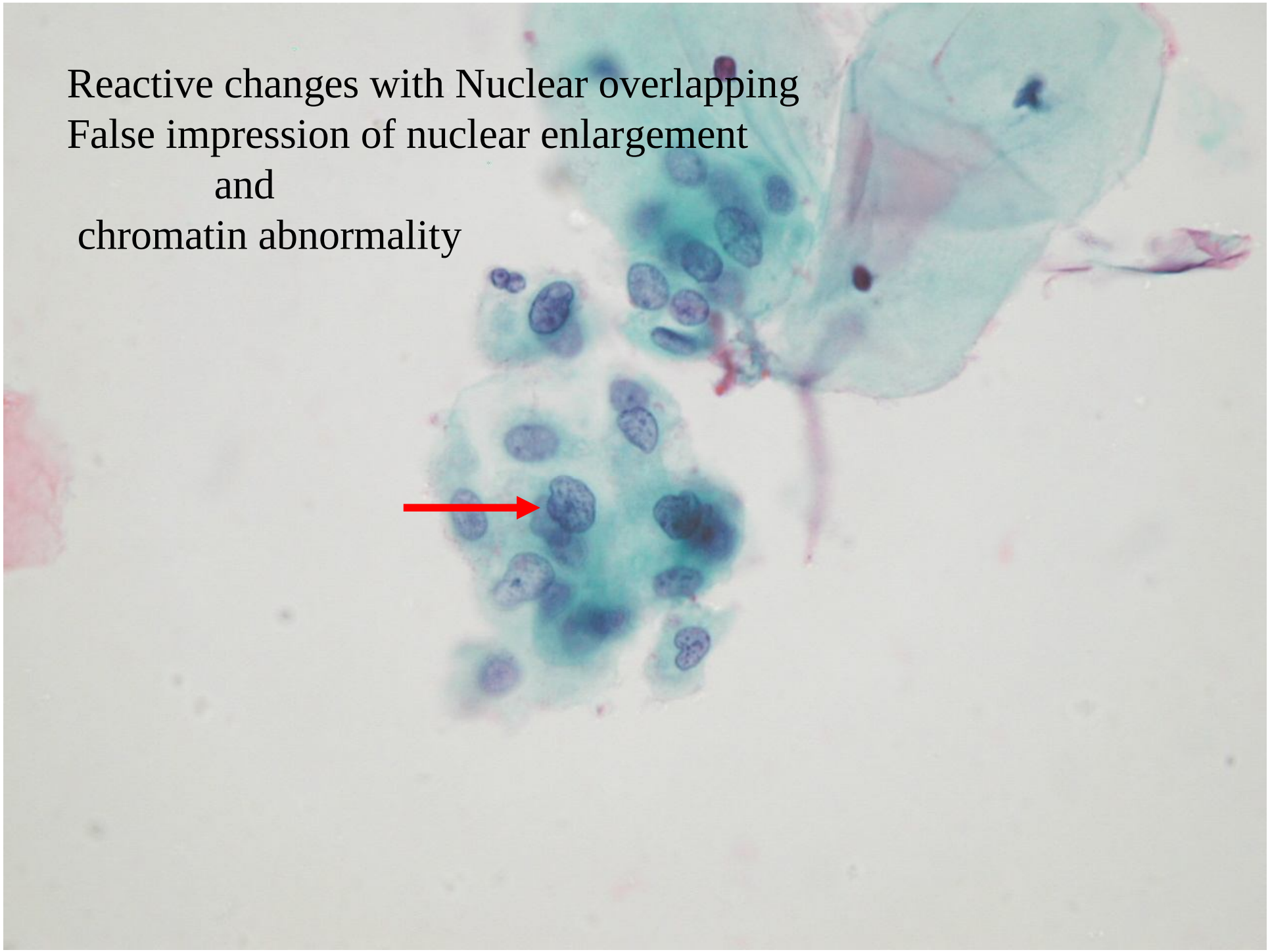
Squamous pearl with
slight nuclear enlargement



Dyskeratosis without
Nuclear abnormality

TV and inflammation with nuclear enlargment




Reactive changes with Nuclear overlapping
False impression of nuclear enlargement
and
chromatin abnormality

Look a likes of Cytology of HPV

Two Pathognomic cell pattern

- Koilocyte
- Dyskeratocyte

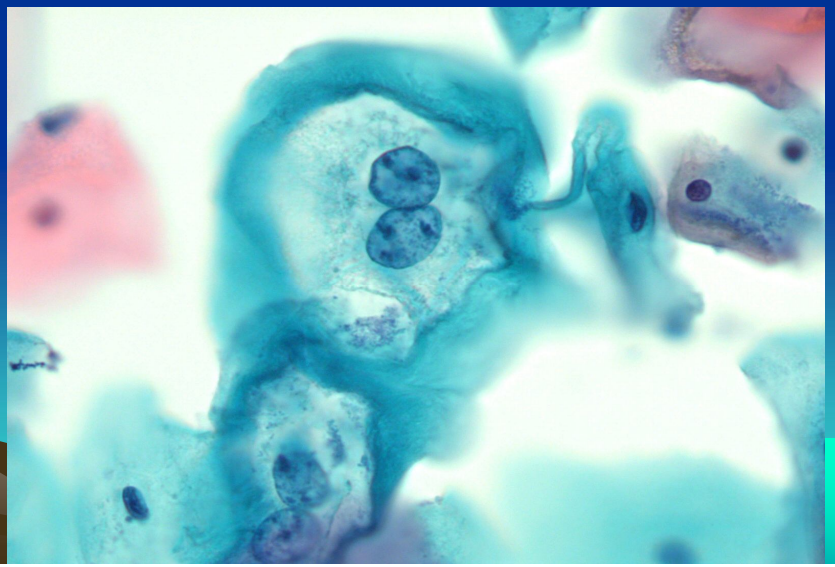
Other Non- specific cell patterns

- Cells – Macrocytes , Kites, balloons
- Cytoplasm – Polka dots, cracks
- Nuclei – Bi and multinucleation, spindling, smudging

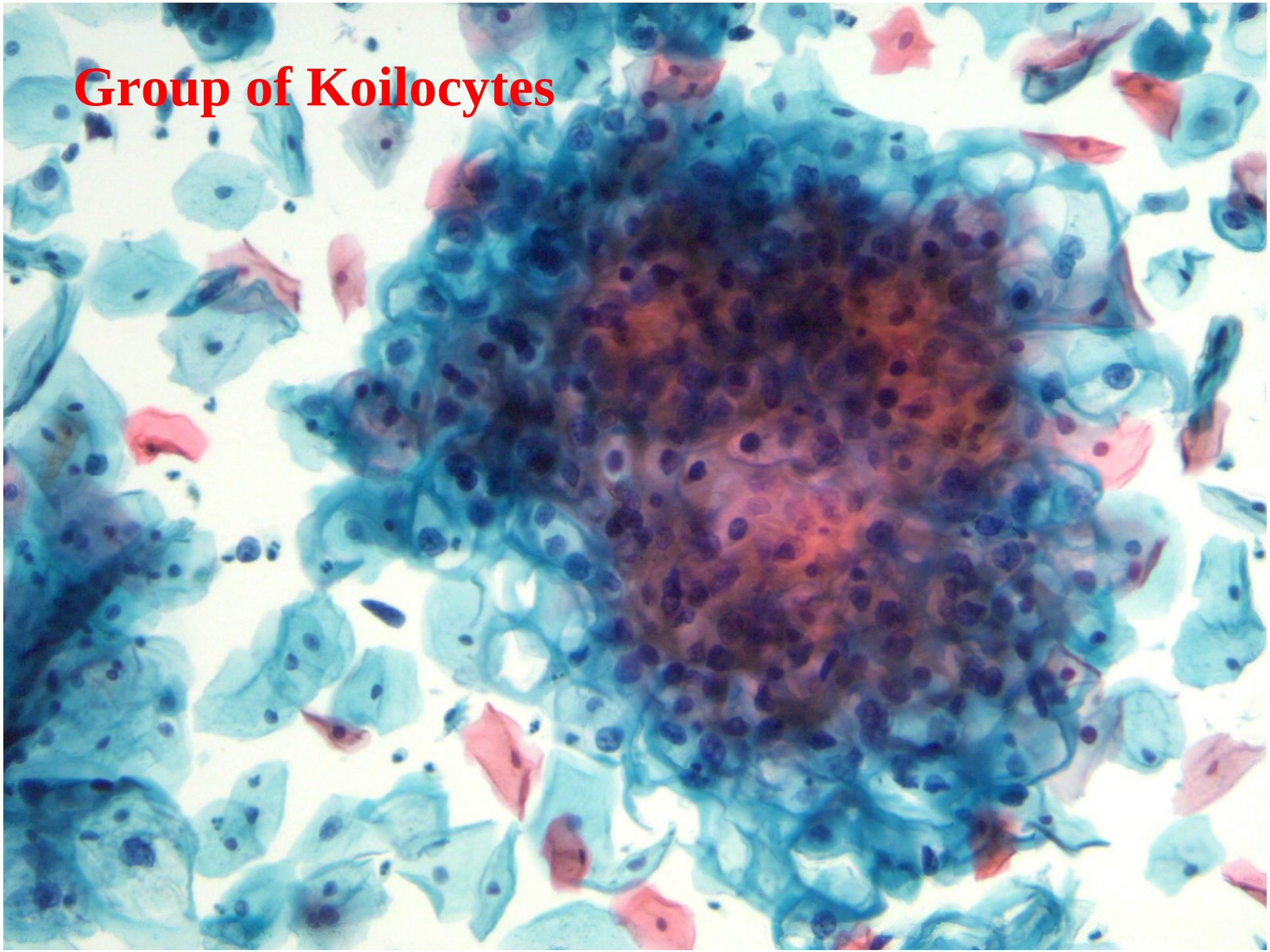
Koilocytotic Atypia

Back To Basics

- **Clear well defined area around nucleus**
- **Thickened edge, sharply demarcated border**
- **Look for the pencil drawn line**
- **Some nuclear atypia**



Group of Koilocytes



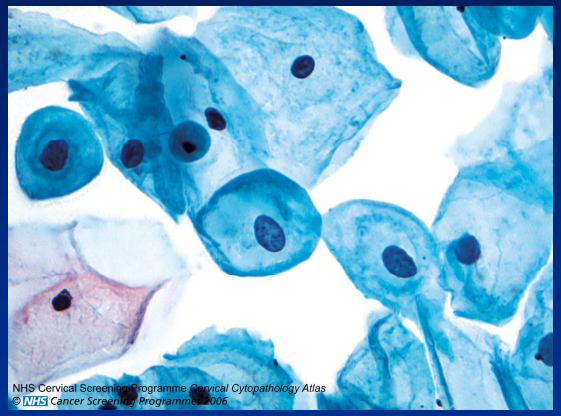
Diagnostic Dilemmas

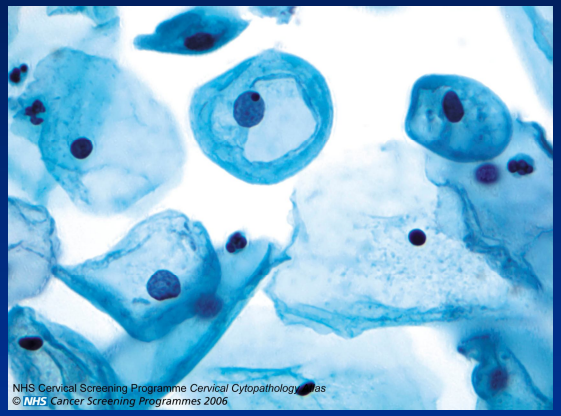
Koilocyte Simulation (Pseudokoilocyte)

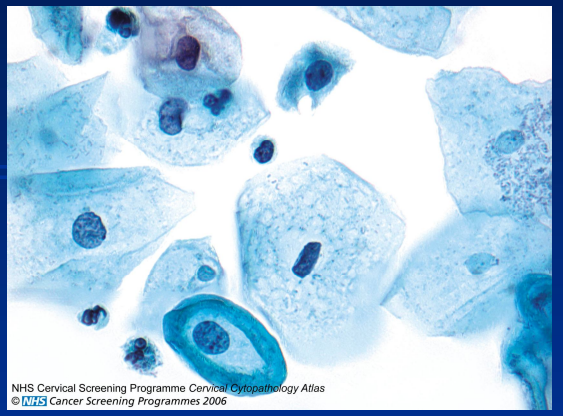
- Non HPV changes
- Rolling edge of cytoplasm (common with LBC)
- Intracytoplasmic glycogen lacking yellow-brown staining
- Non HPV inflammation

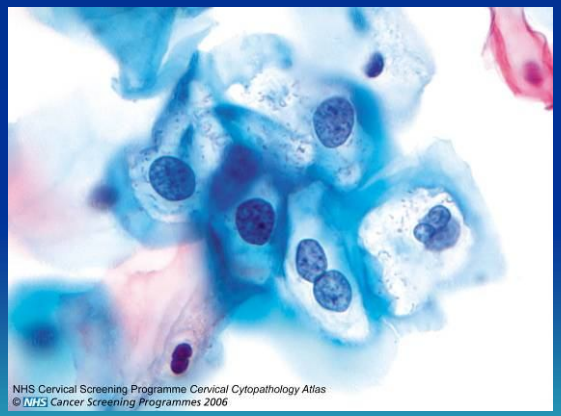
Koilocyte Simulation

From NHSCSP Atlas

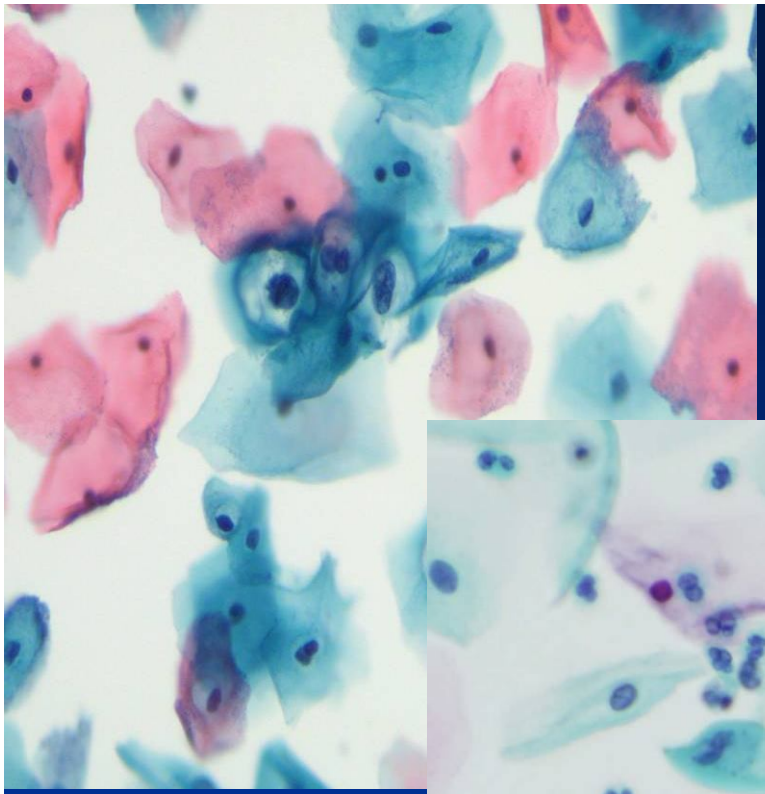


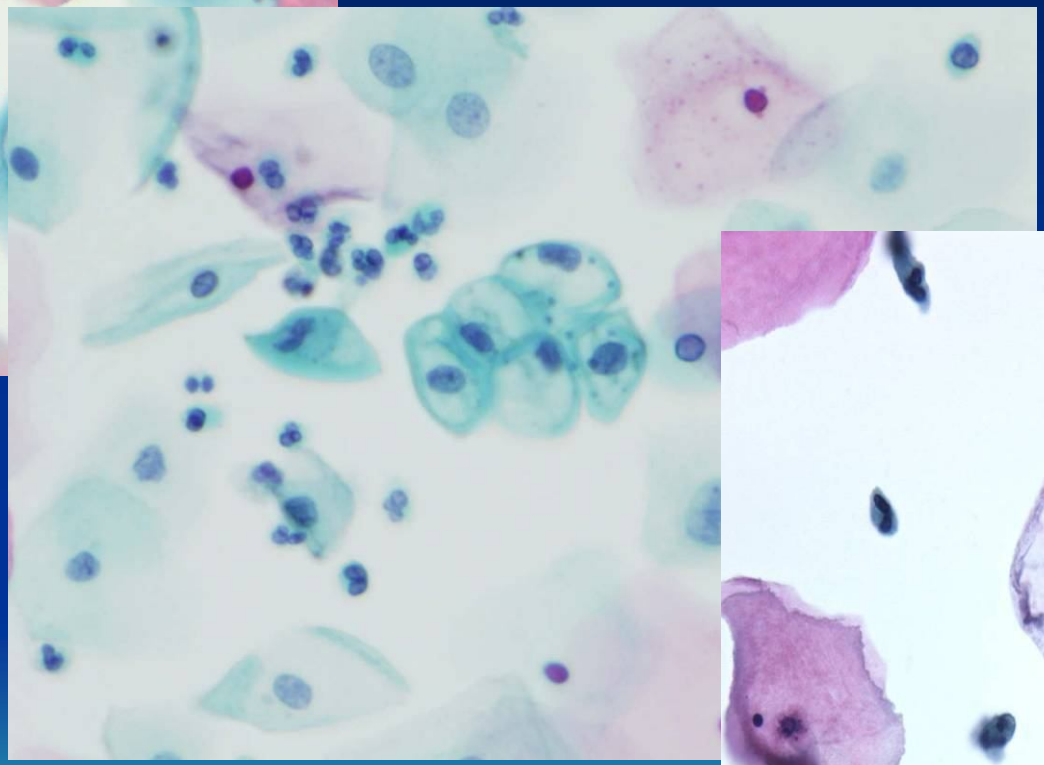


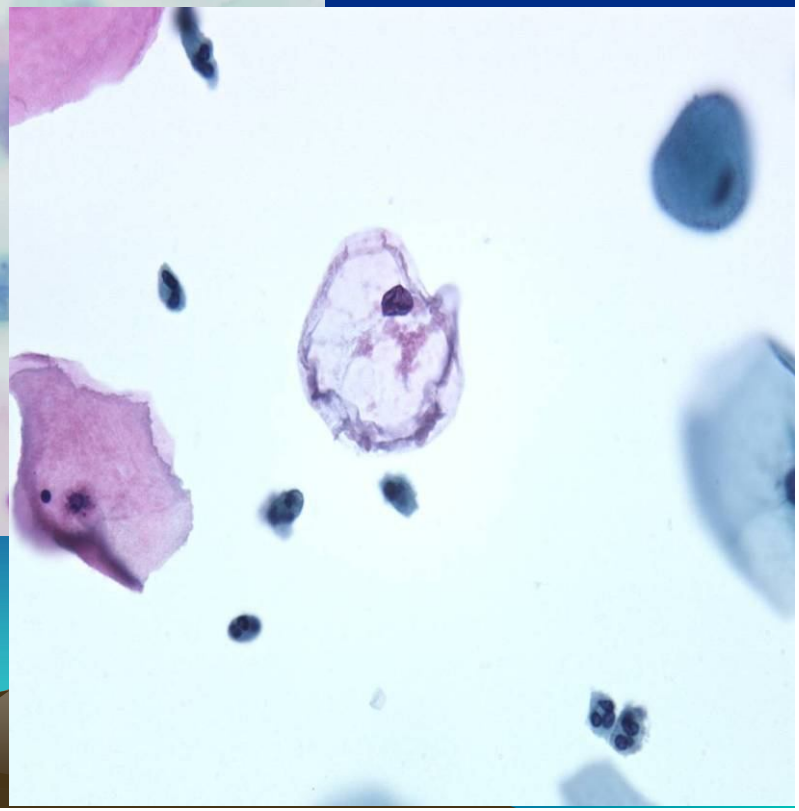


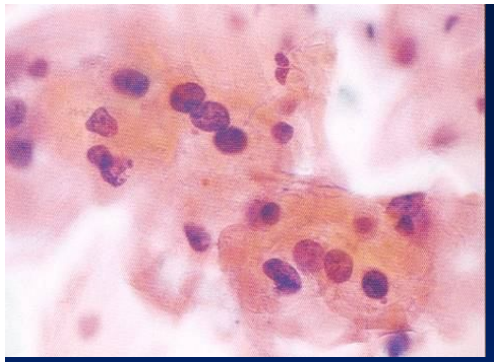


Spot The Difference

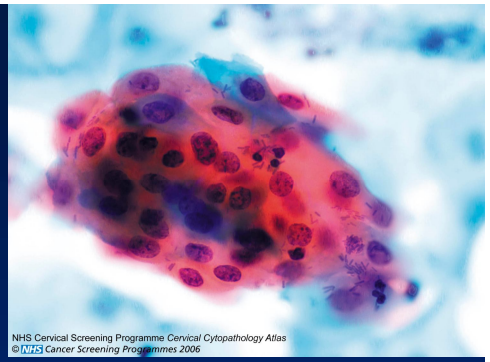








HPV Cytology Dyskeratocytes

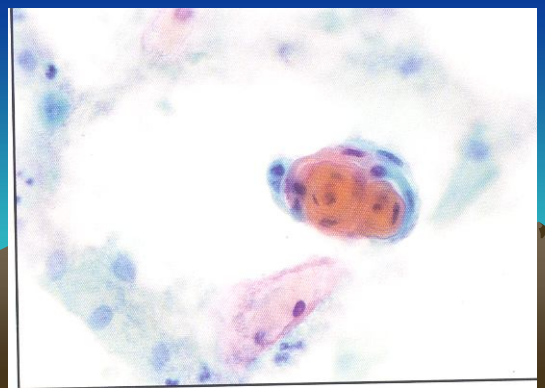


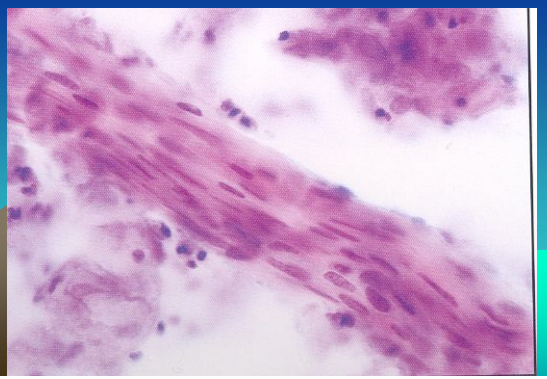
- Abnormal Keratinization
- Keratinized squamous cells staining brilliant orange with OG-6 of pap stain

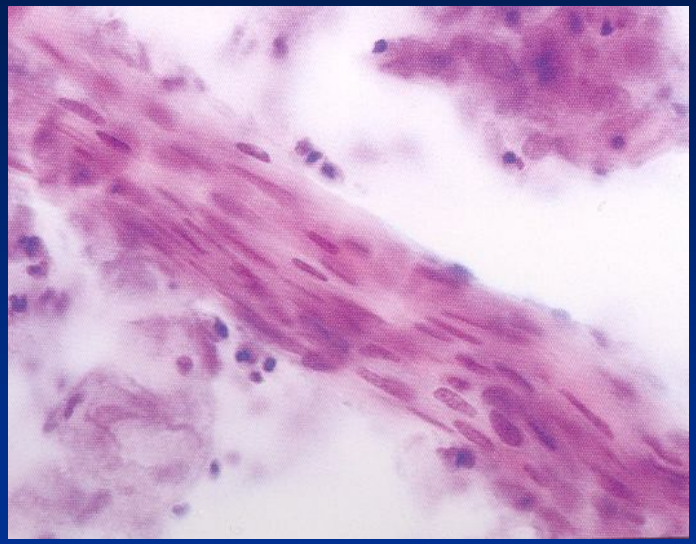
  (Pink with Surepath LBC)
- Single or in thick, 3D clusters
- Clusters without discernible polarity
- Nuclear enlargement with condensed or granular chromatin details

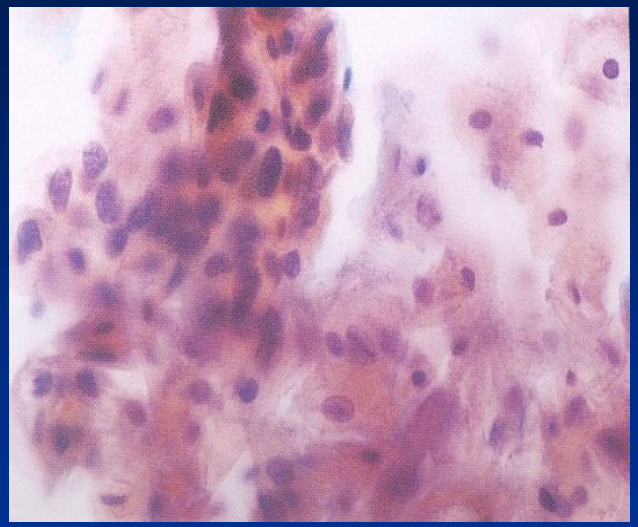
Dyskeratocytes In The Absence Of HPV Infection

- Small keratinized pearls, rafts or spikes
- Cells arranged in orderly pattern
- Small,uniform,widely spaced nuclei that flattens towards the edge to lie along the long axis of the group
- No nuclear abnormality









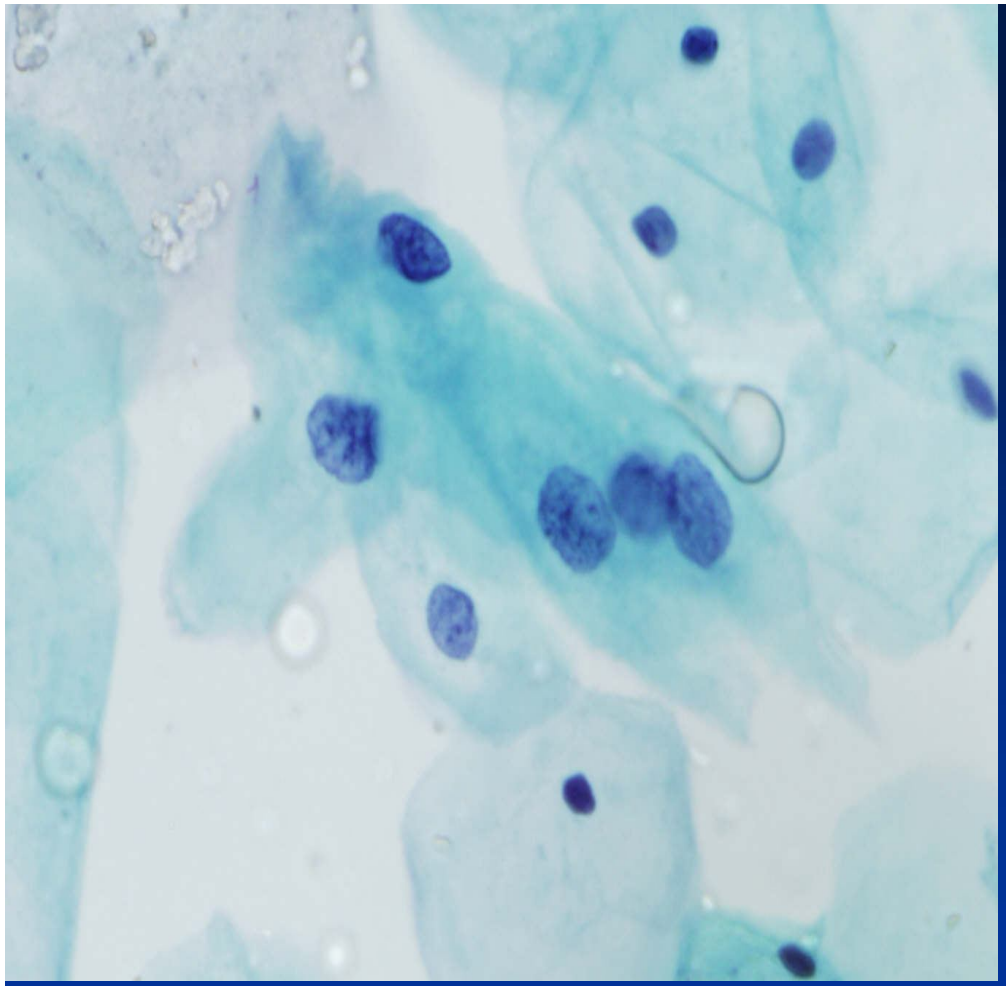
Dyskeratotic cells

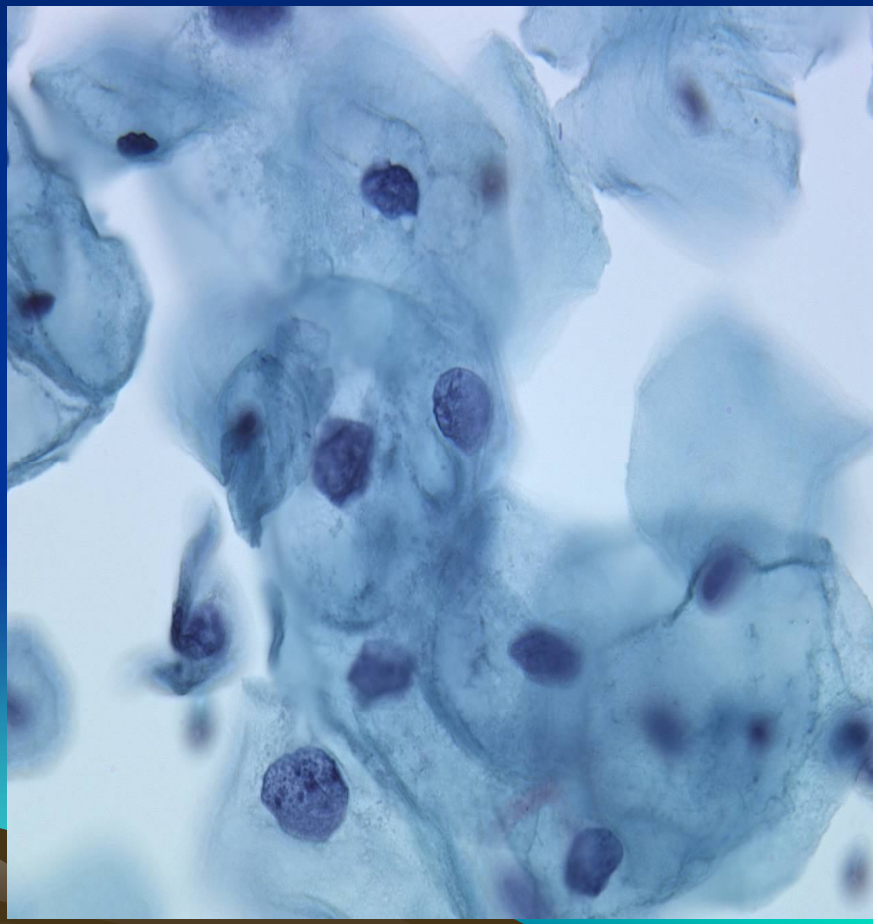
Without HPV

Dyskeratotic cells

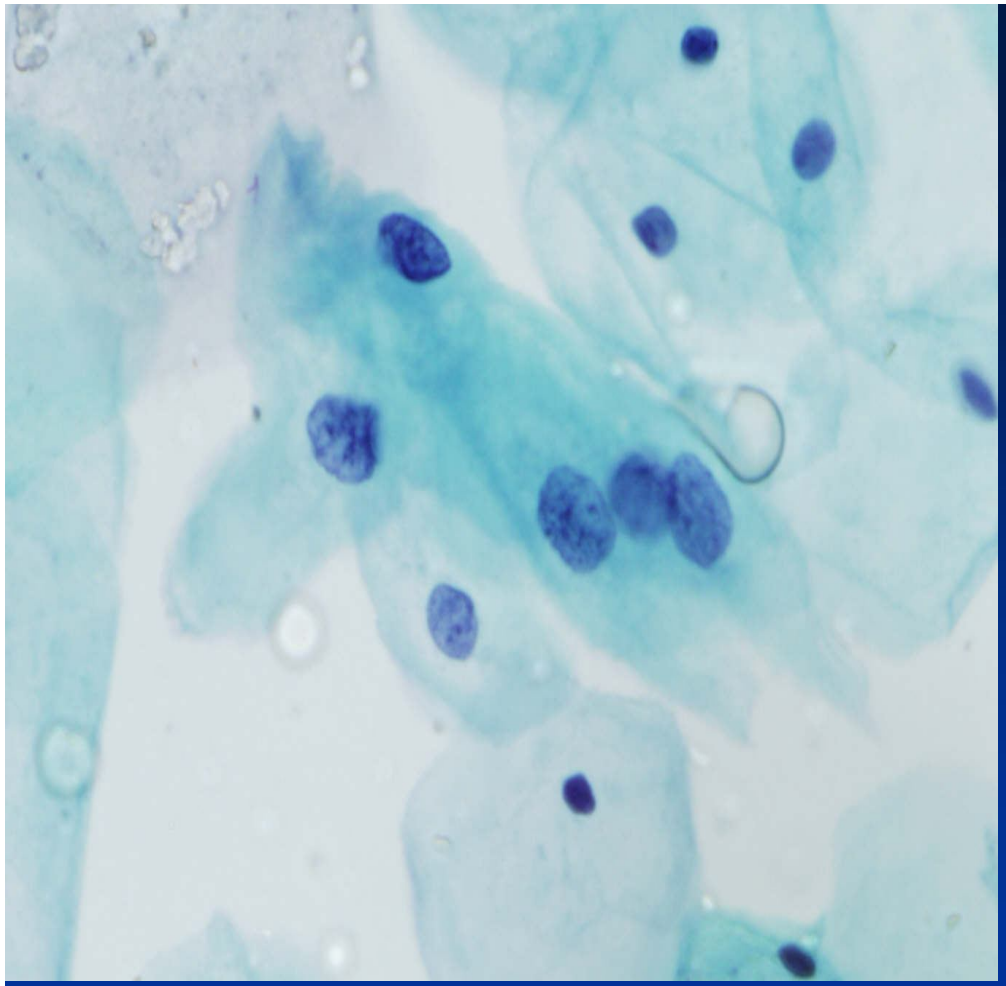
With HPV

Net case1
Spot The Difference
Neg, ASCUS or LSIL?

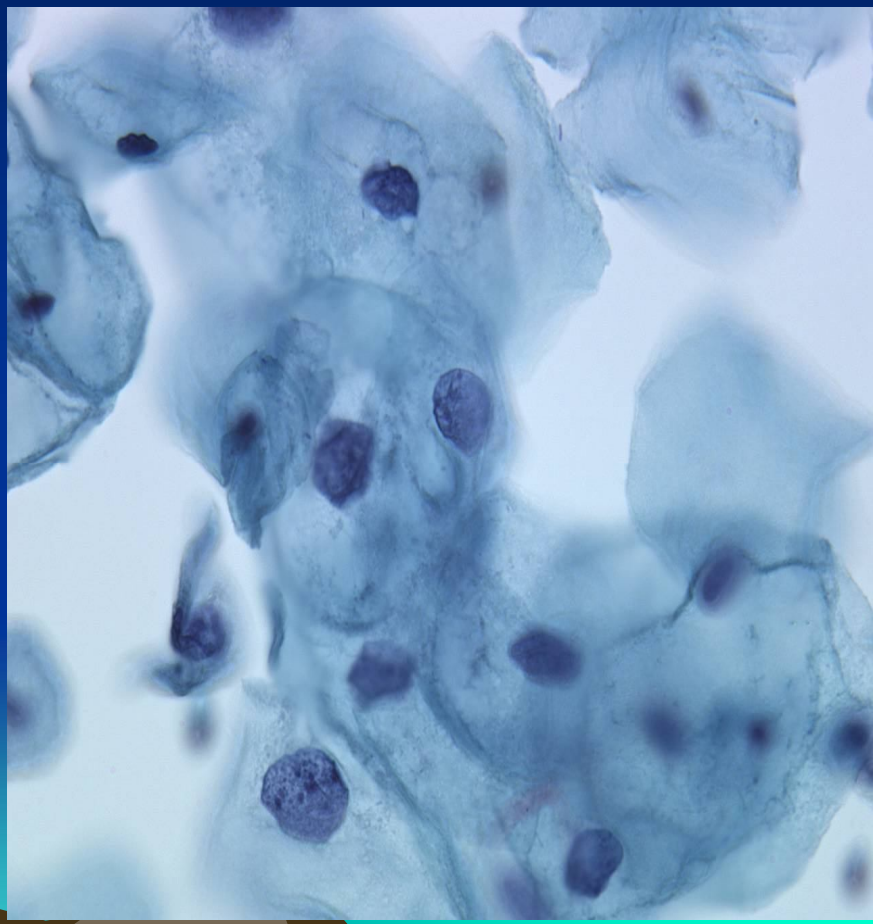




Net case1
Spot The Difference
Neg, ASCUS or LSIL?



Mild Dyskaryosis (LSIL)



Borderline changes (ASCUS)

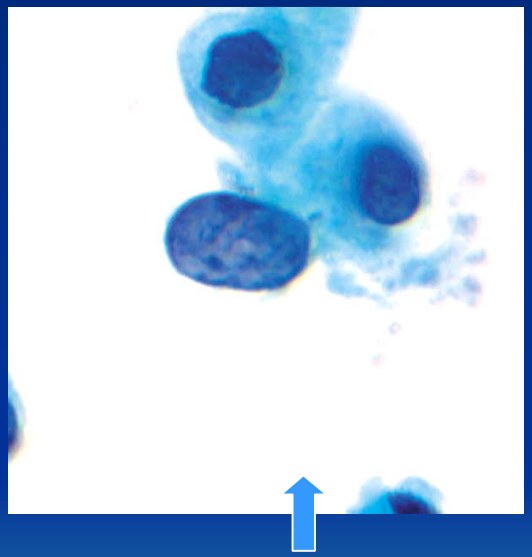
Pitfalls and Look a likes of different Patterns of Dyskaryosis (SIL)
Pattern recognition and experience

Patterns of dyskaryosis (SIL)

- **Ungraded Dyskaryosis (SIL)**
- **Large cell non-keratinising (Syncitial)**
- **Keratinising**
- **Mixed**
- **Scanty dyskaryosis (SIL)**
- **Small cell dyskaryosis (SIL)**
- **CIN microbiopsies (HCGs)**
- **Flag cells**
- **Pale cell dyskaryosis (SIL)**
- **Bland cell dyskaryosis (SIL) In Thinprep**

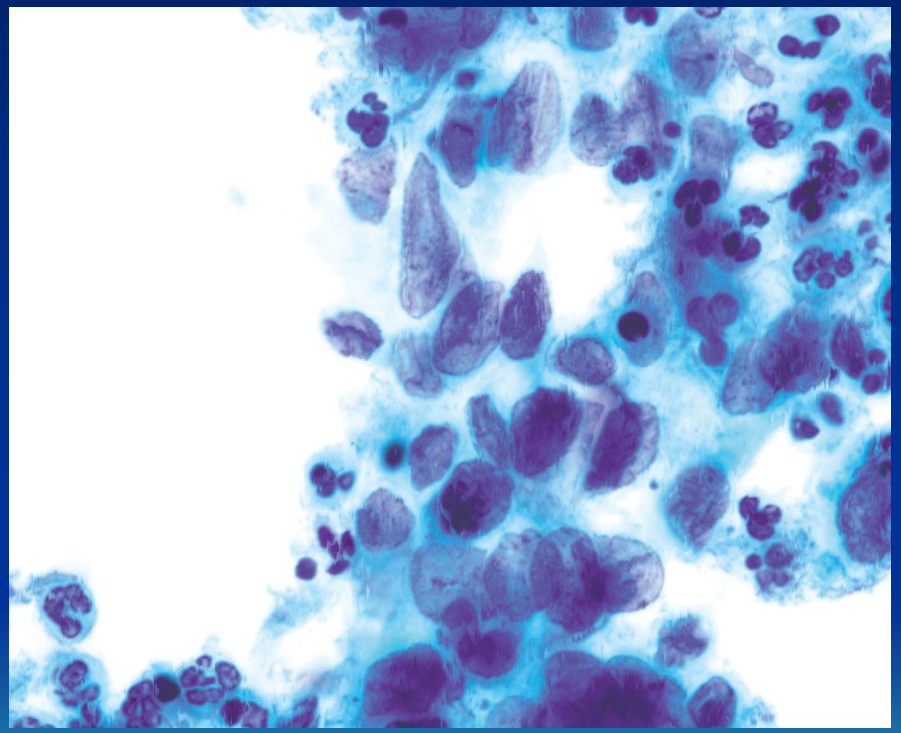
Ungraded Dyskaryosis (SIL)

- Dyskaryotic bare nuclei
- Loss of cytoplasm due to cytolysis or atrophy
- Loss of cell boundaries



- Grade as High grade dyskaryosis (HSIL)

High Grade Dyskaryosis with bare nulcei

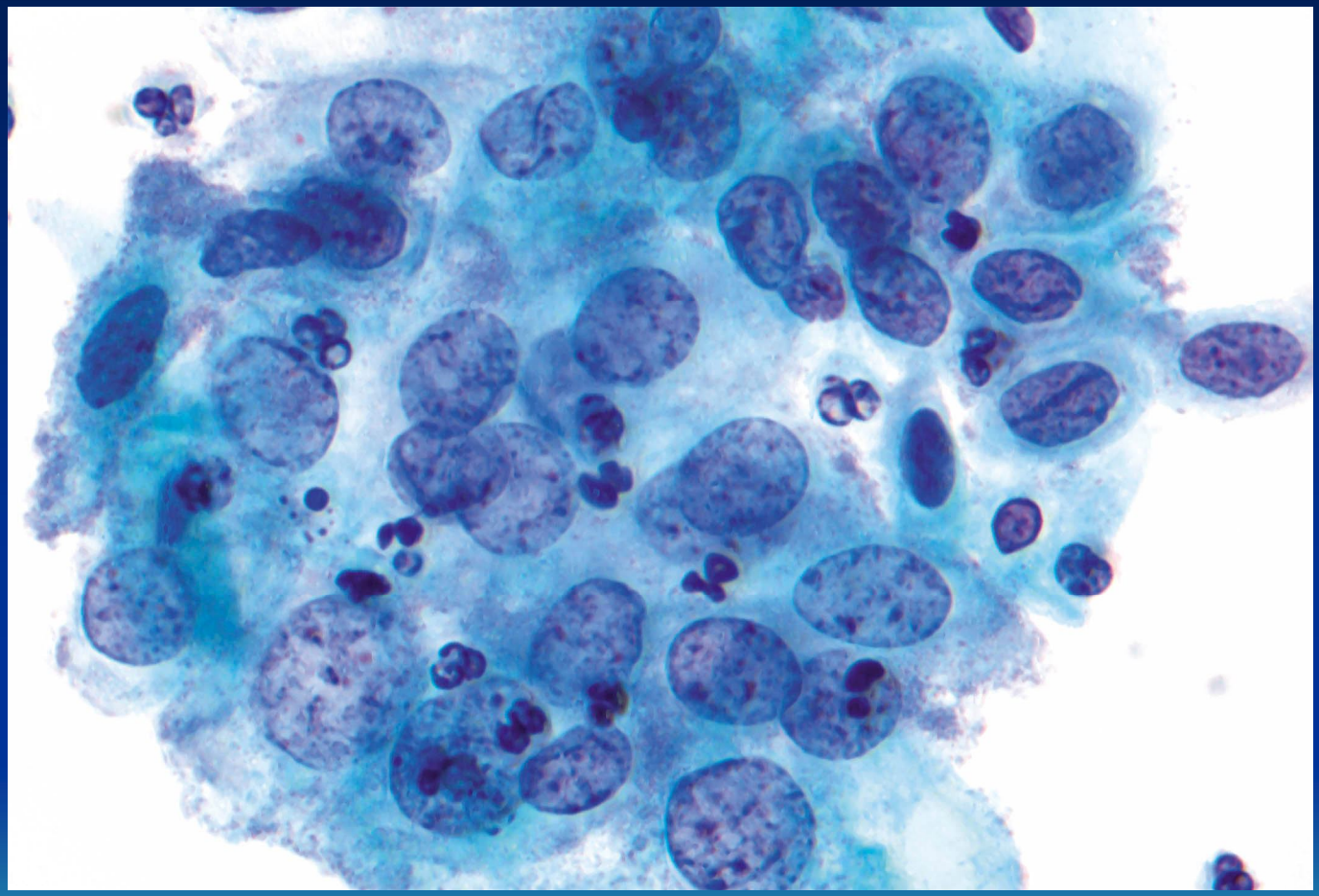


Ungraded Dyskaryosis

Large cell non-keratinising (syncitial) High gradeDyskaryosis (HSIL)

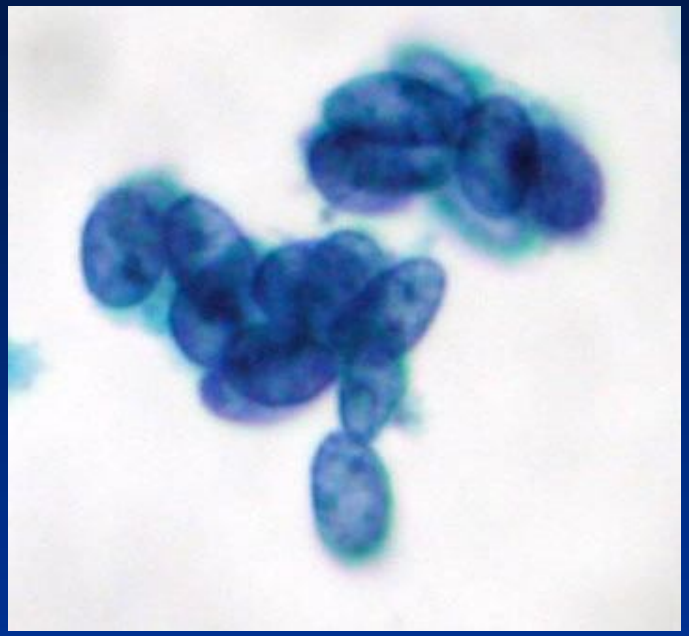
- Loose syncytial groupings
- Nuclei four to six times diameter of polymorphs
- Nuclei rounded and pale staining
- Finely speckled chromatin
- Cytoplasm relatively abundant, delicate and indistinct
- N/C ratio difficult to assess, usually less than half, misinterpreted as mild diskaryosis (LSIL)
- Misinterpreted as CGIN when in continuity with endocervical cells

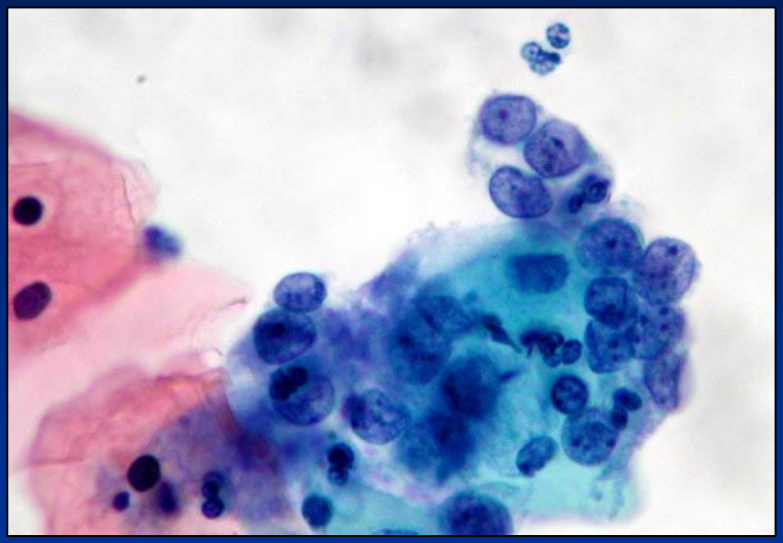
Large cell non-keratinising HSIL

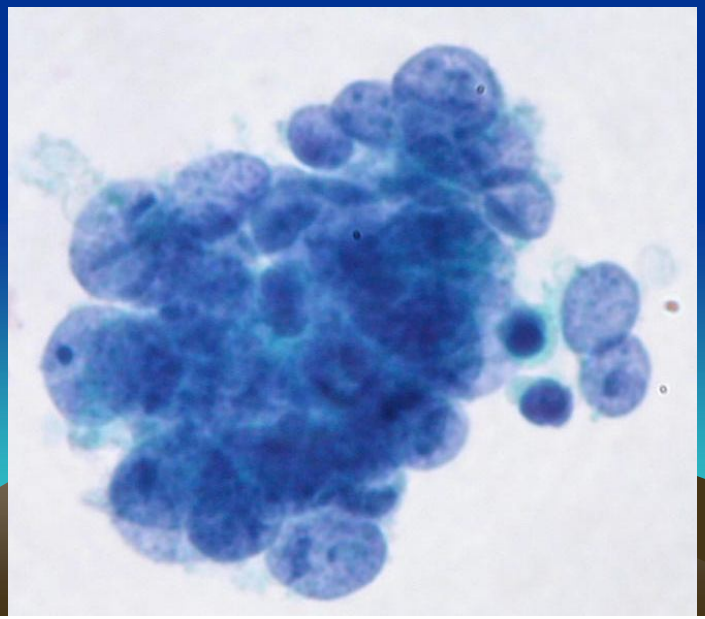


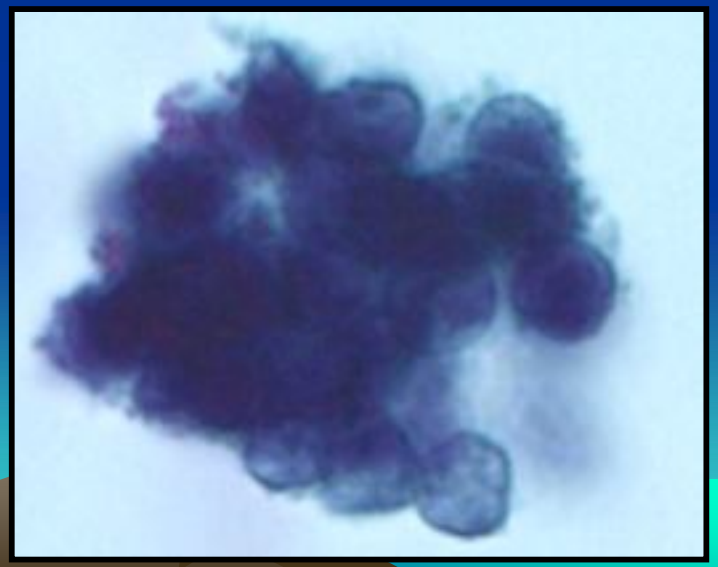
Syncytial variety

Net case 5
Spot the Difference In Bare nuclei
Neg, ASCUS, ASC-H or SIL



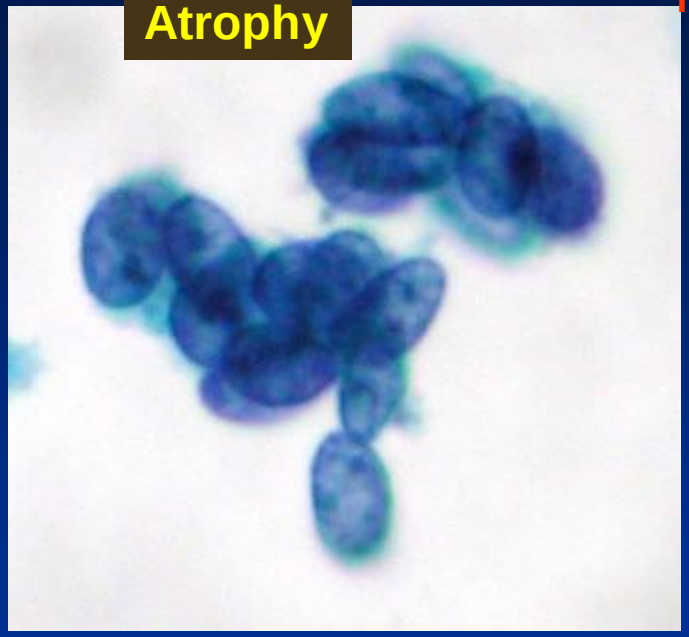




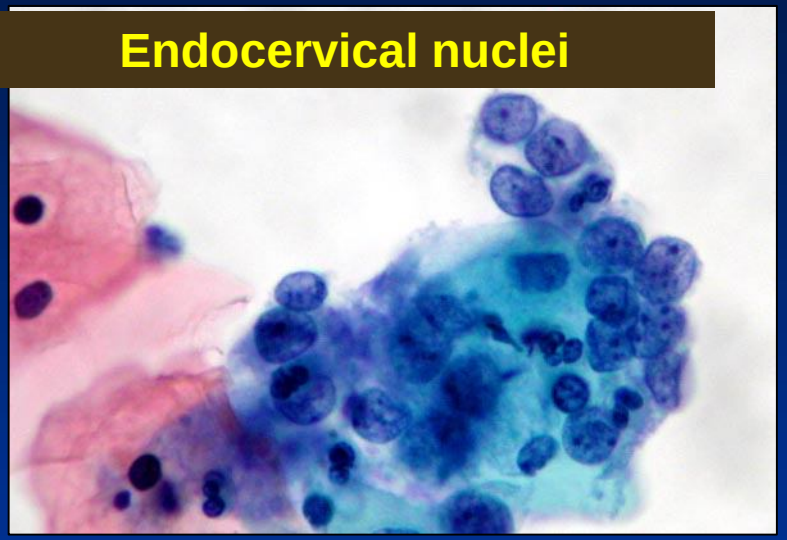


Net case 5
Spot the Difference In Bare nuclei
Neg, ASCUS, ASC-H or SIL

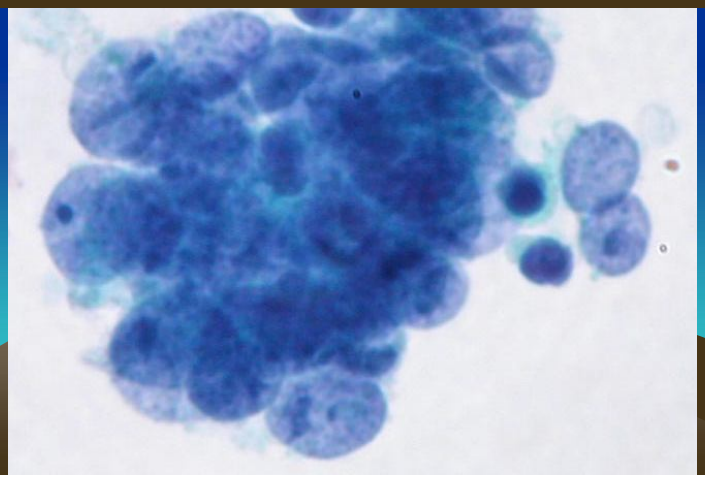
Atrophy



Endocervical nuclei



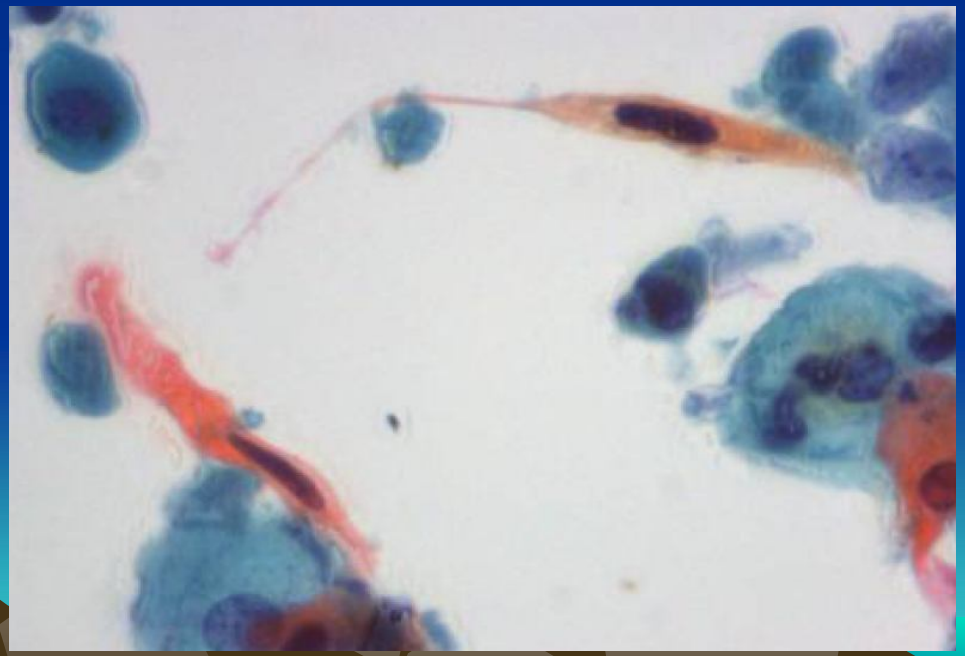
HSIL/High Grade Dyskaryosis



Tamoxifen changes

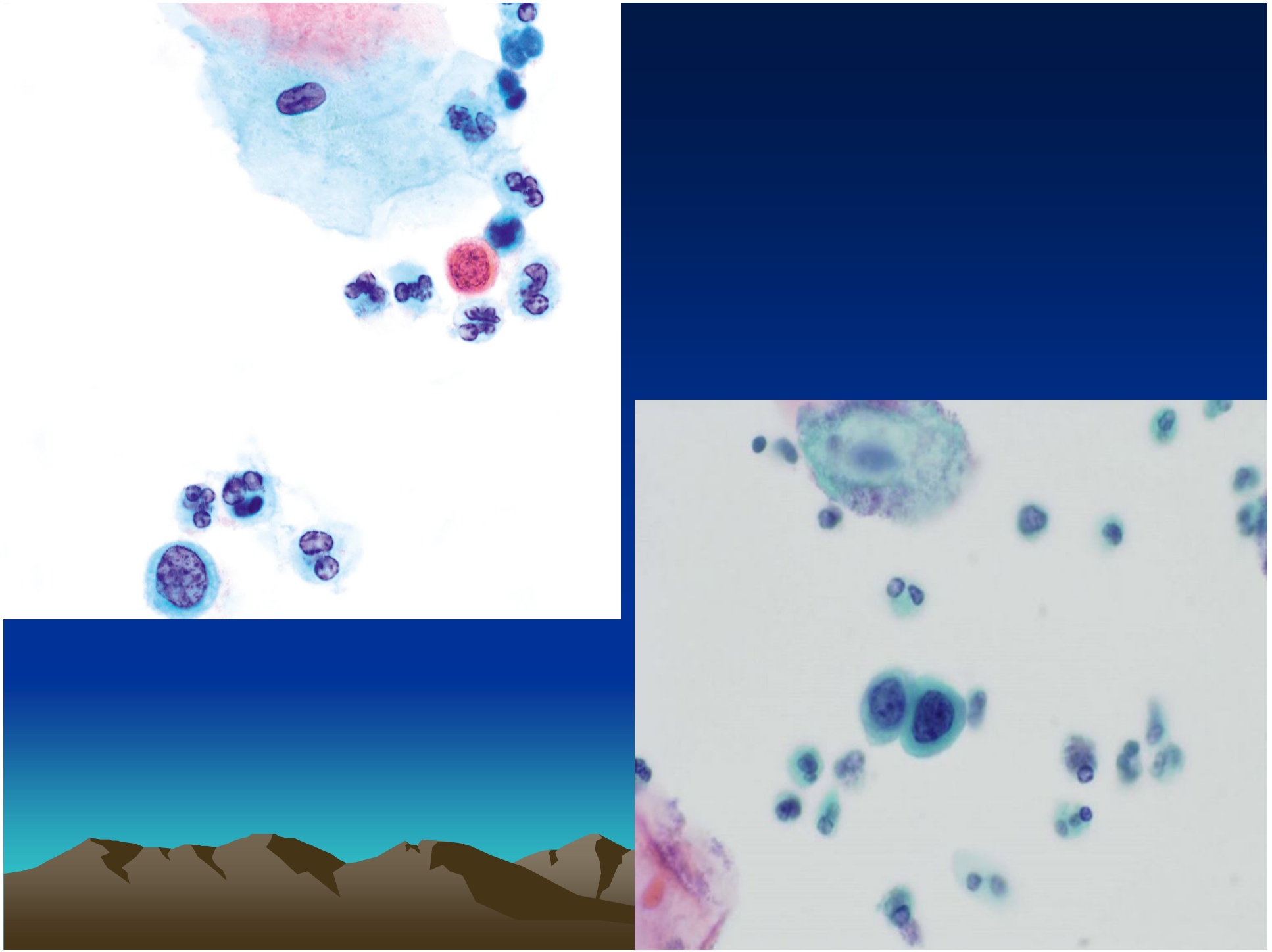
Keratinising High grade Dyskaryosis (HSIL)

- Cytologically indistinguishable from keratinising squamous cell carcinoma



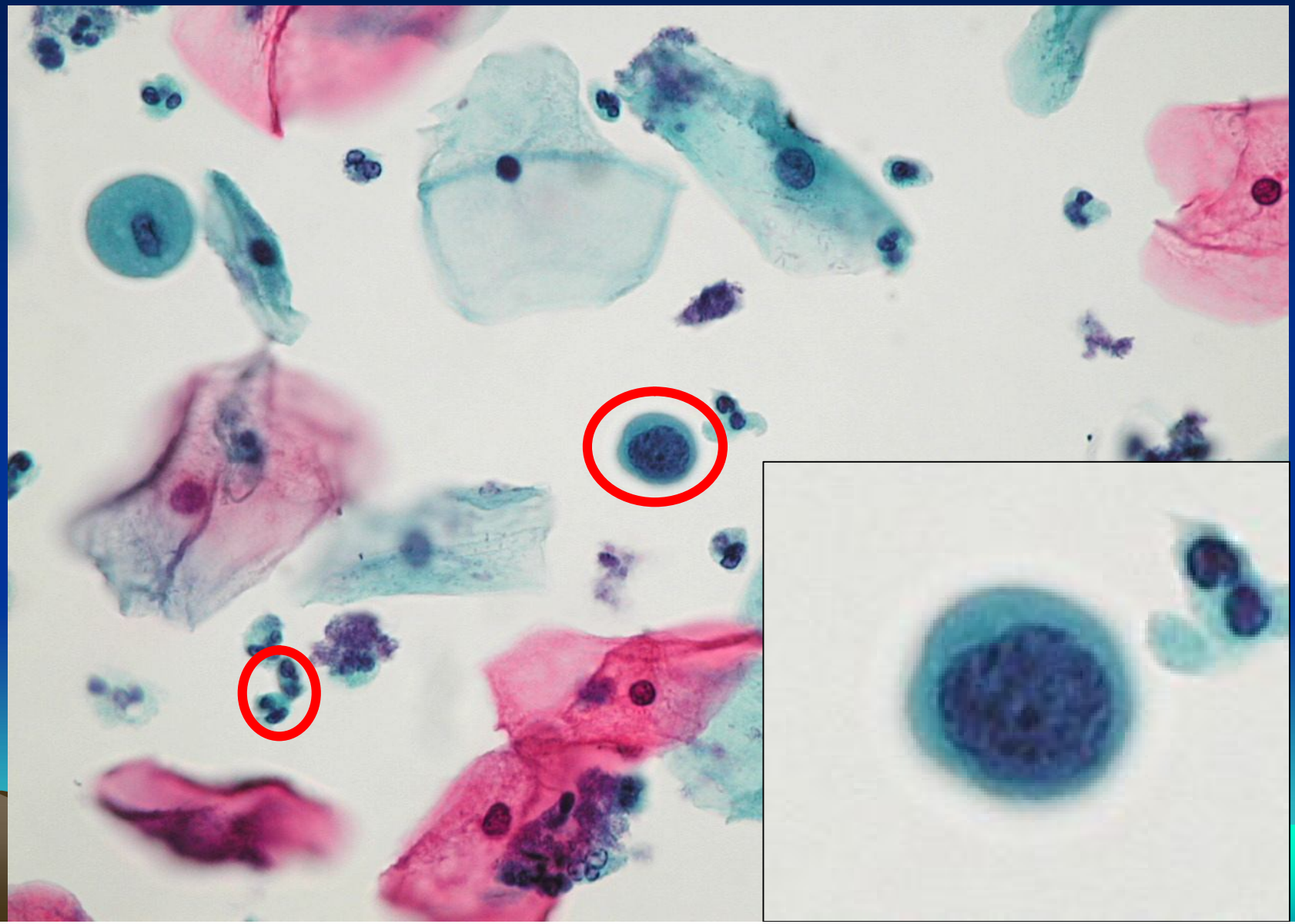
Small Cell Dyskaryosis (HSIL)

- Monotonous cell population
- Abnormal chromatin pattern
- Nuclear diameter less than twice of polymorphs or lymphocyte
- High nuclear:cytoplasmic ratio
- Can have regular nuclear membrane
- D/D immature metaplastic cell,EM,Histiocyte,Follicular cervicitis,atrophic EC and atrophic parabasal squamous cells



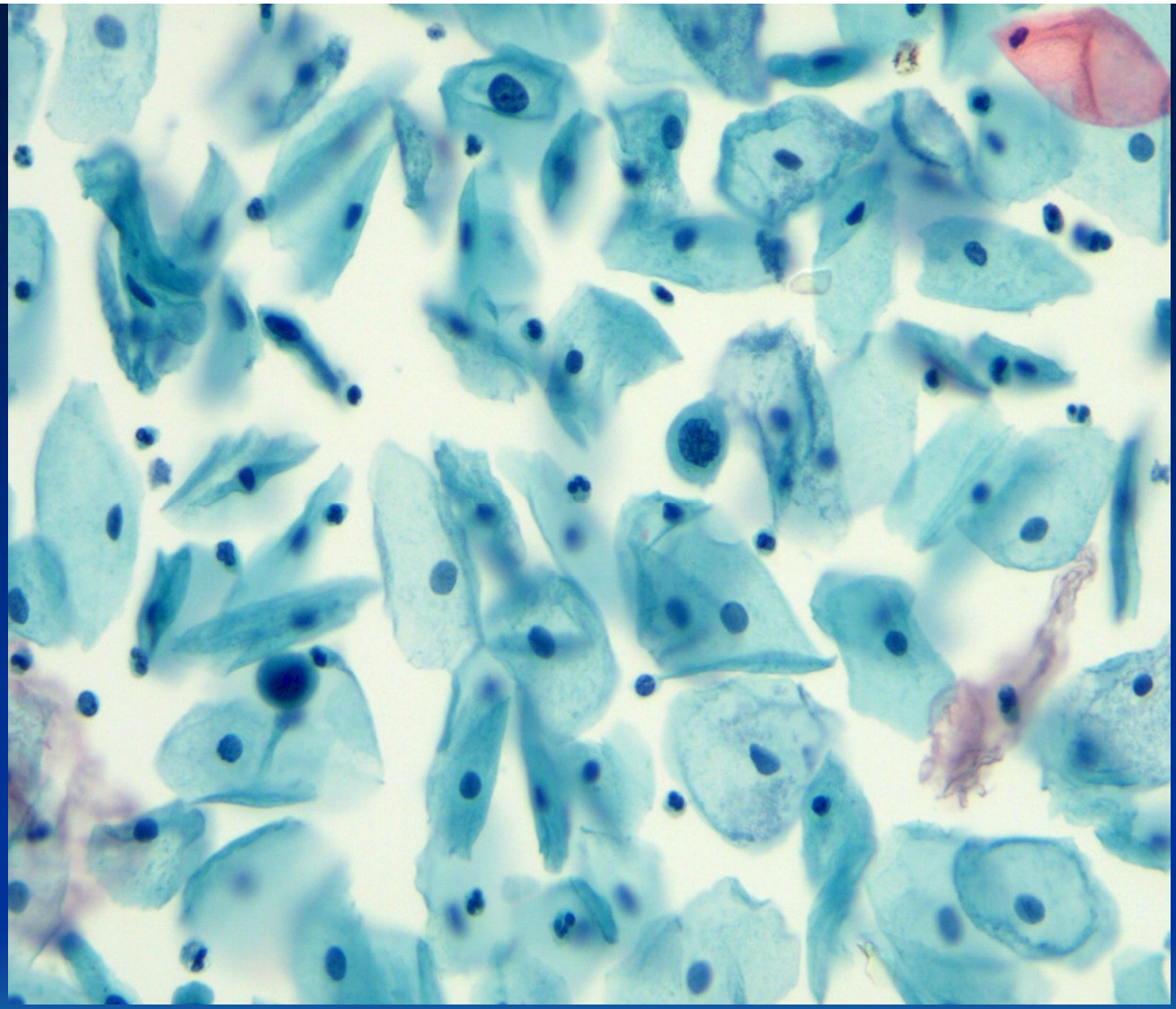
Small cell dyskaryosis

Screening and Interpretation Error



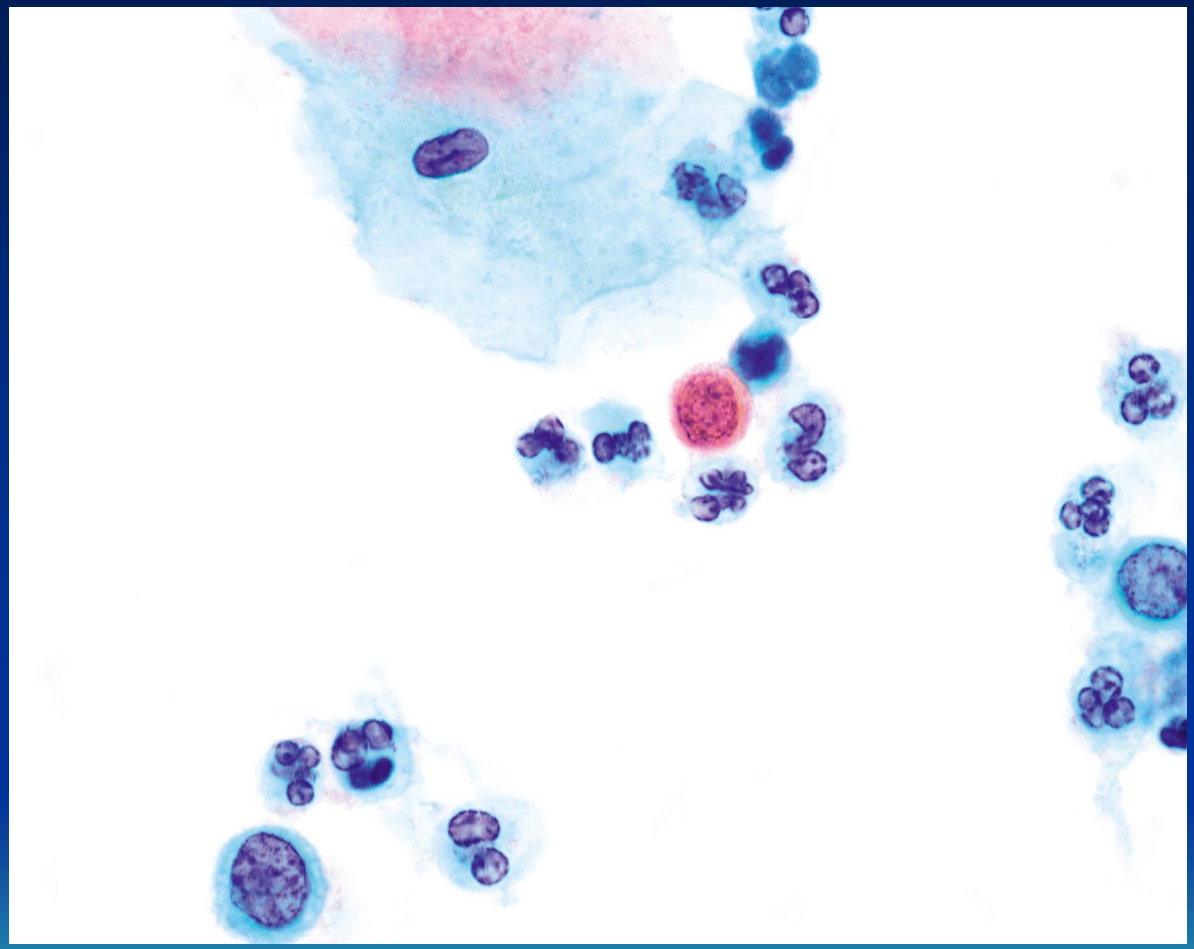
Sparse (Scanty) dyskaryosis (SIL)

- **Litigation cell**
- **Easily overlooked in routine screening**
- **More difficult to recognise if pale,small and single**

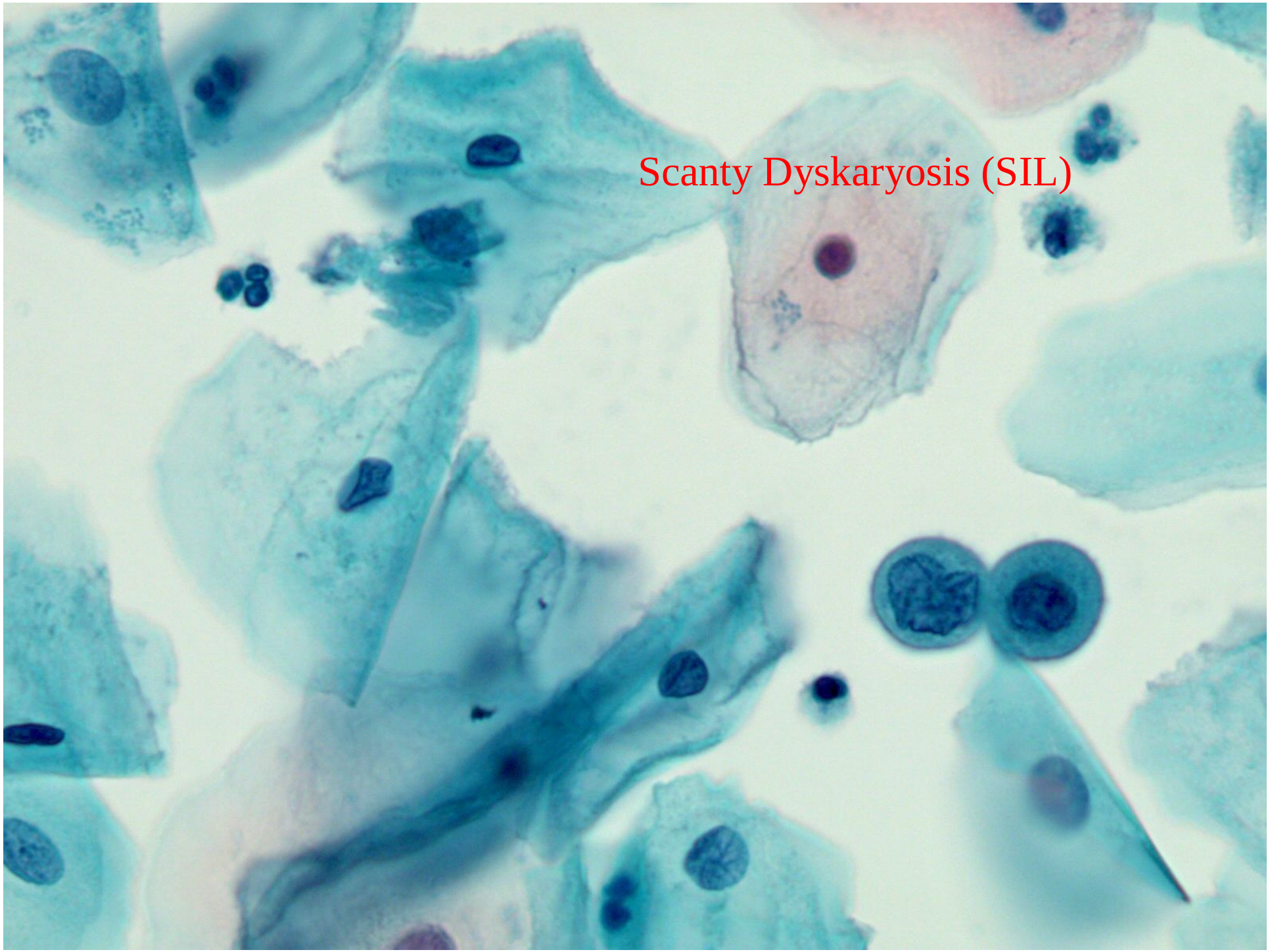


Scanty Dyskaryosis (SIL): overlapping of the fields is essential in screening

Scanty dyskaryosis (SIL)

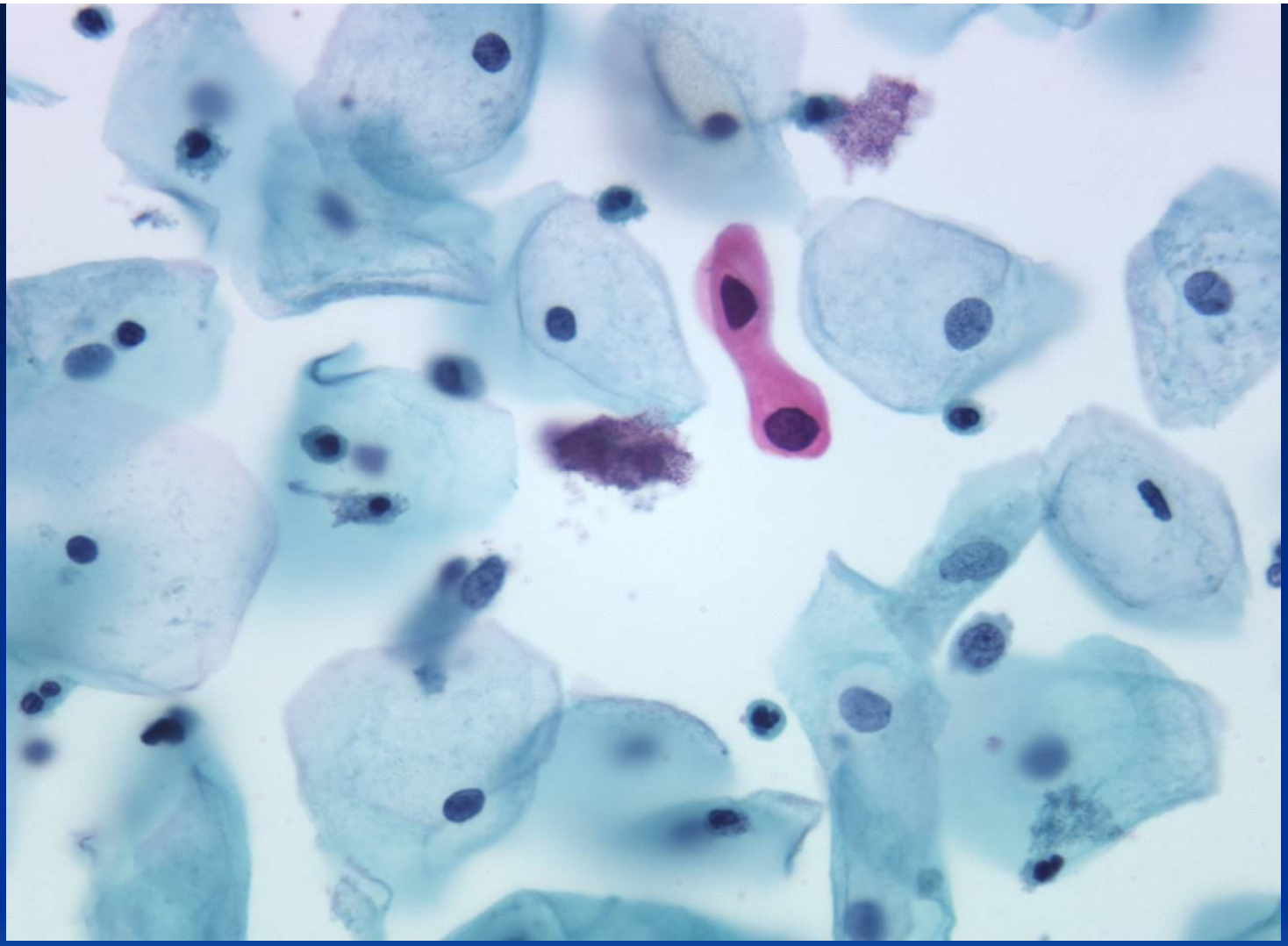


Litigation cell

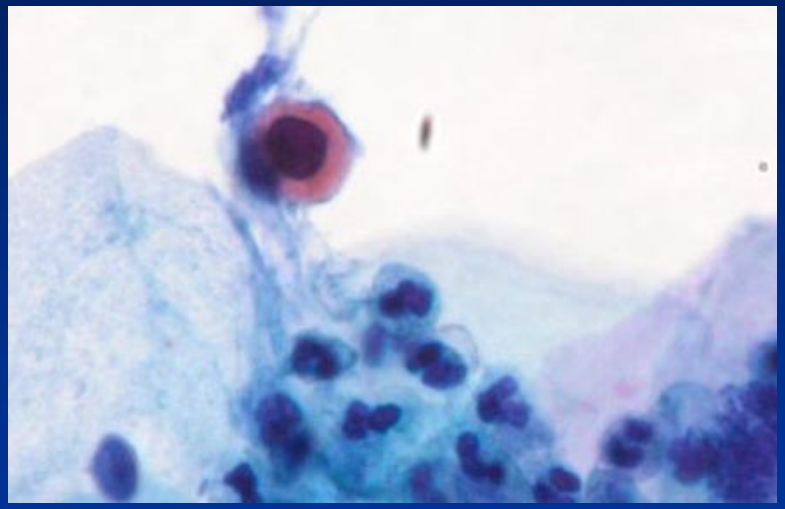

Scanty Dyskaryosis (SIL)

Flag Cell

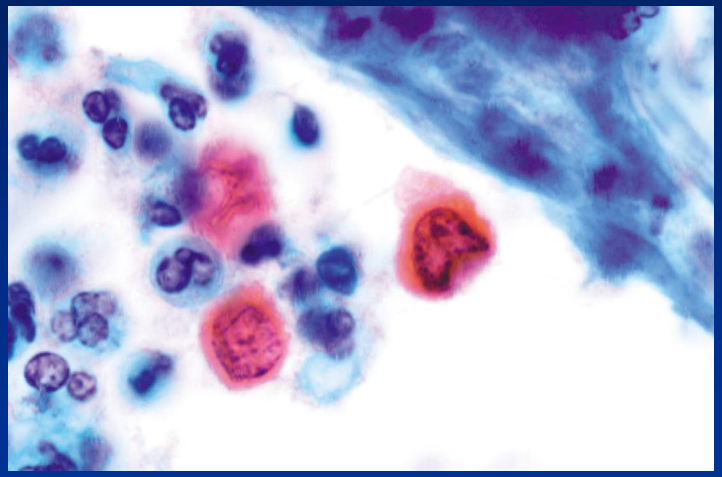
- Small keratinised cell with pyknotic, India ink nucleus
- On its own should not be reported as High grade dyskaryosis
- Search for High grade dyskaryosis in other areas



Flag cells : Search for High grade dyskaryosis (HSIL) or invasive features



Flag cell

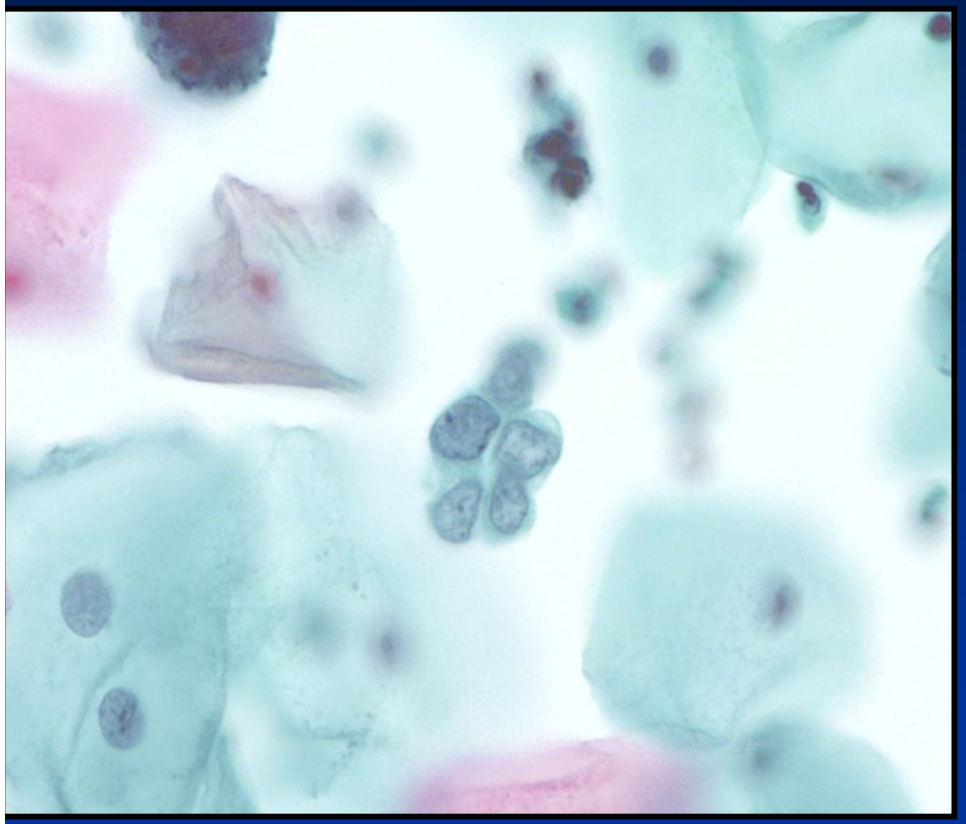


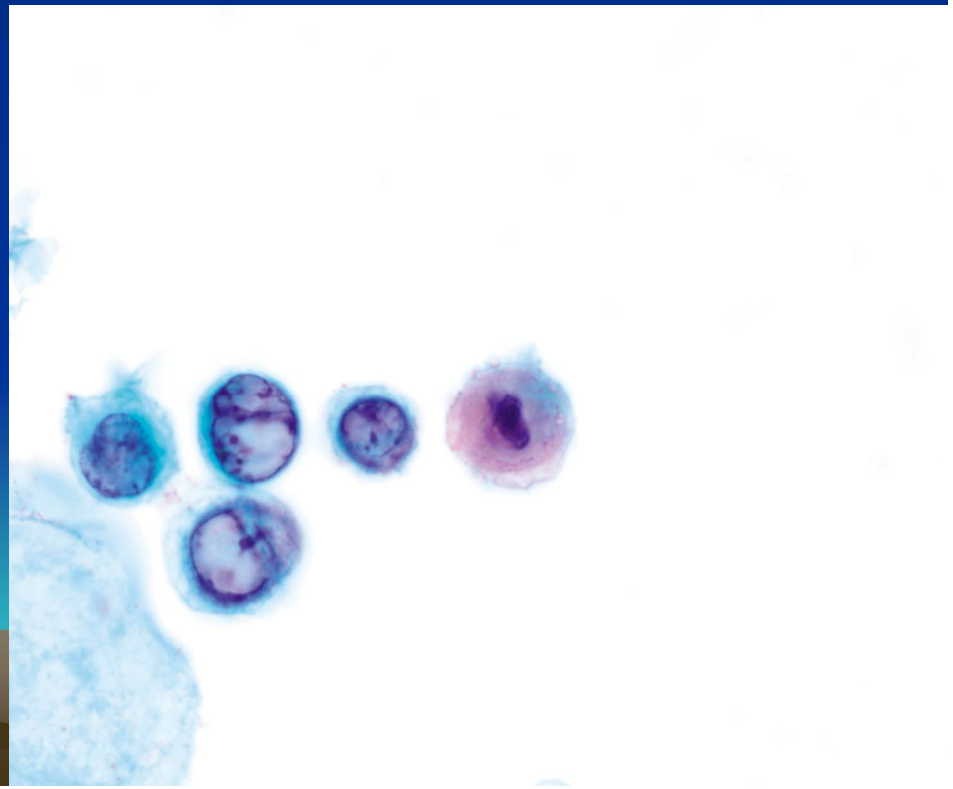
Associated High grade dyskaryosis

Pale cell Dyskaryosis (SIL)

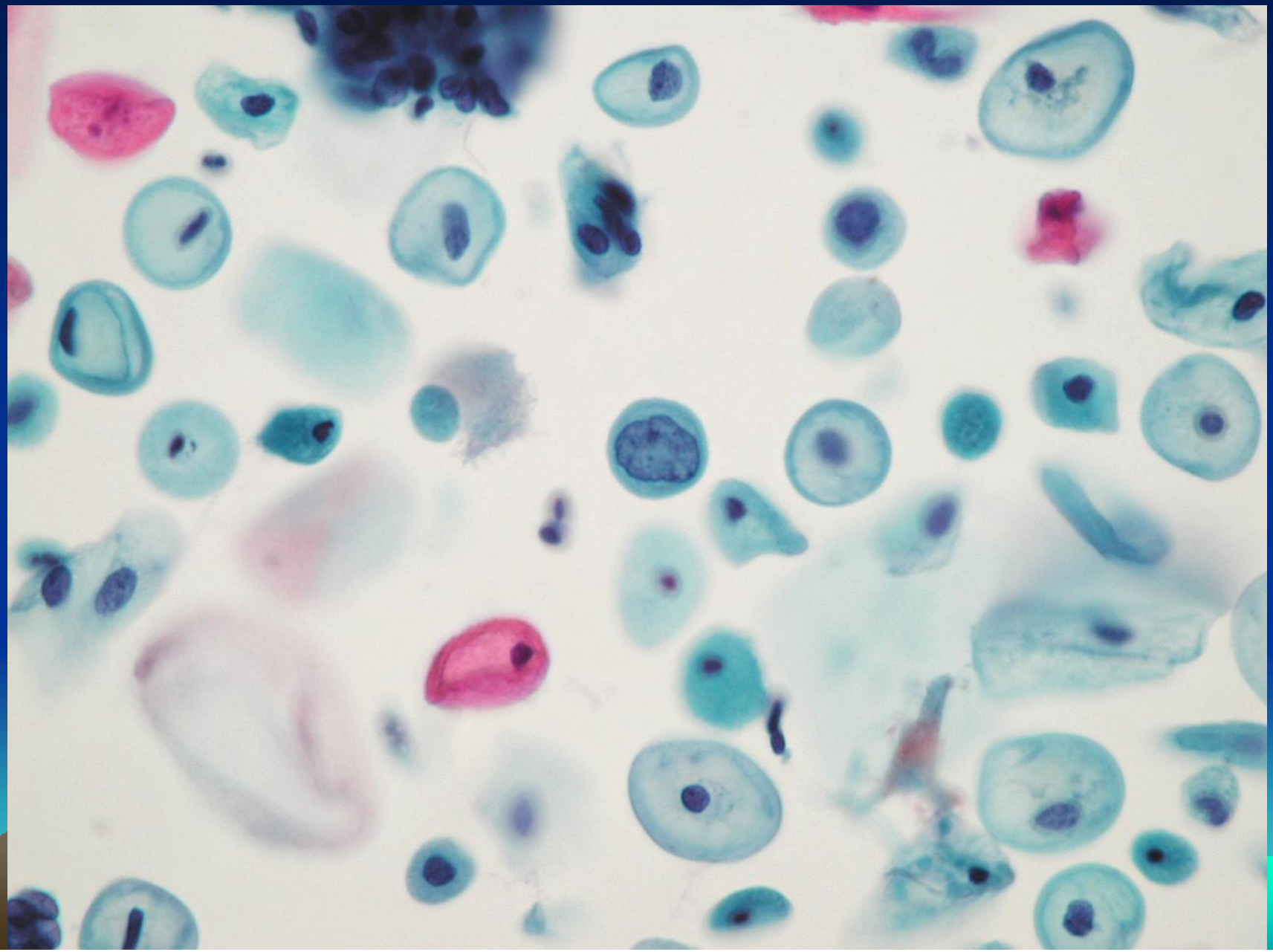
- Hypo chromatic nuclei
- May be a staining artefact
- Identified by abnormal chromatin pattern
- Can be seen in all grades of dyskaryosis (SIL) and types of cells
- Often present mixed with some “normal” staining cells
- Nuclear membrane irregularity + or -

Pale cell Dyskaryosis (SIL)

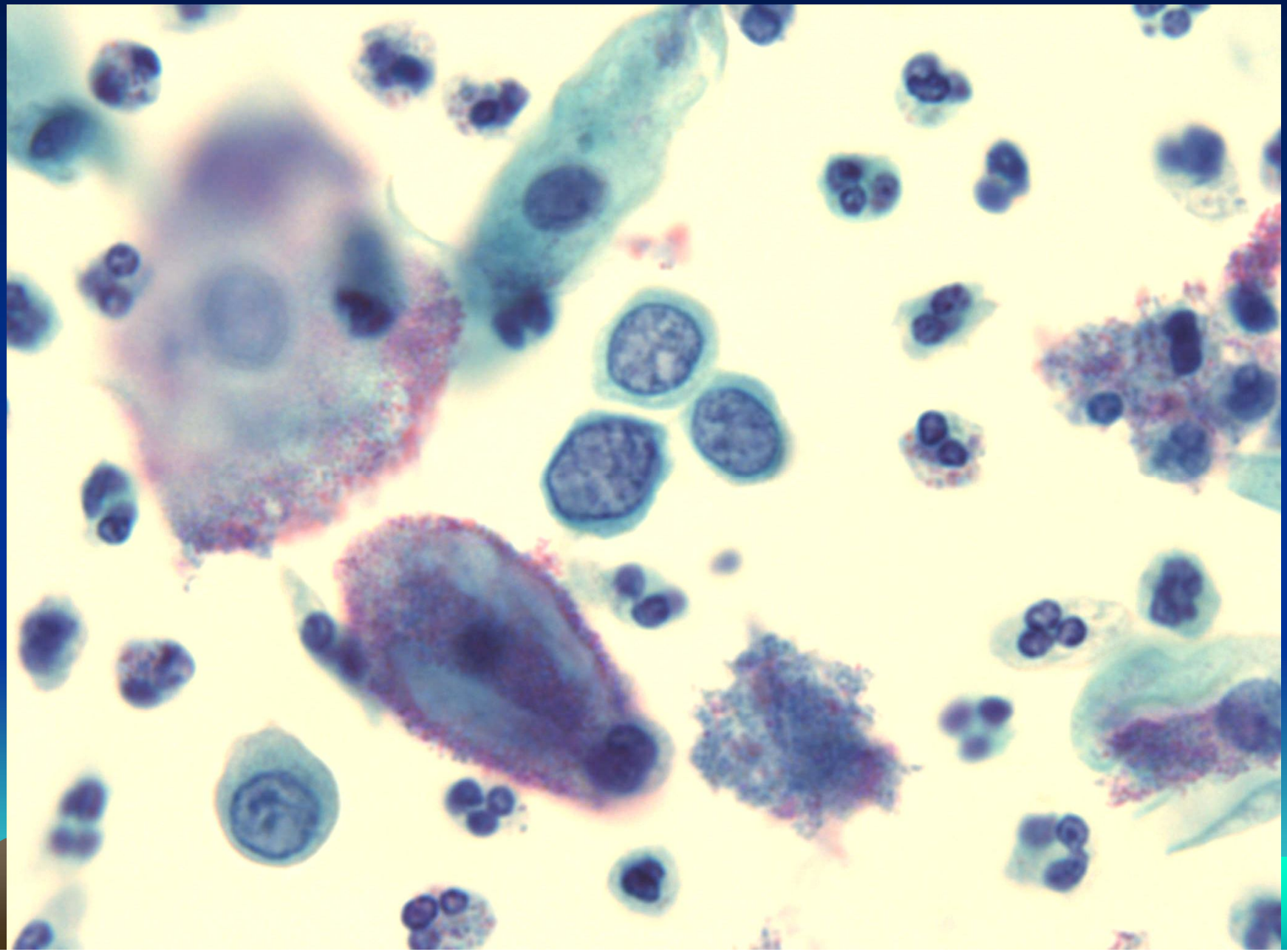




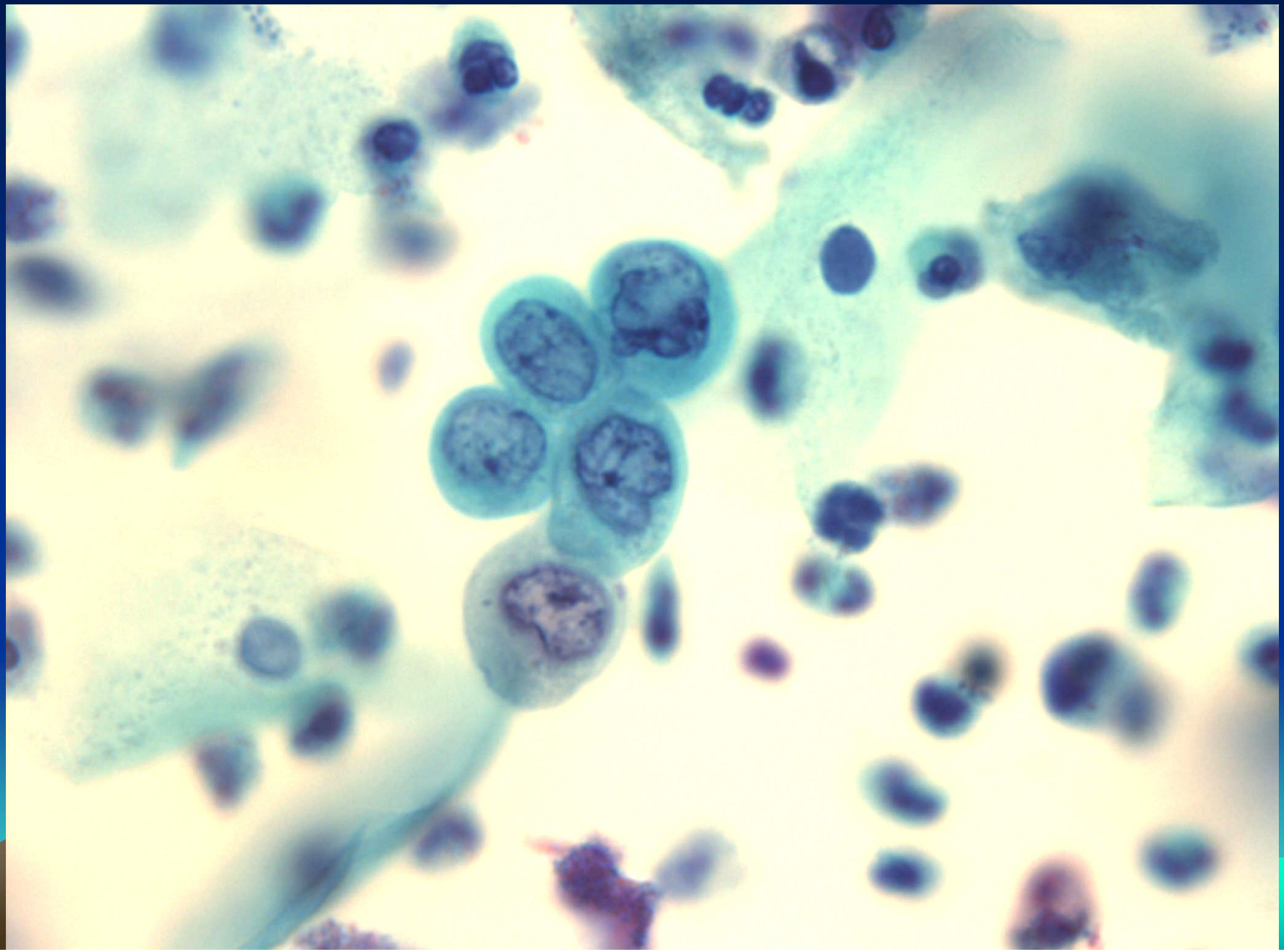
Pale dyskaryosis /SIL



Pale dyskaryosis/SIL



Pale dyskaryosis/SIL



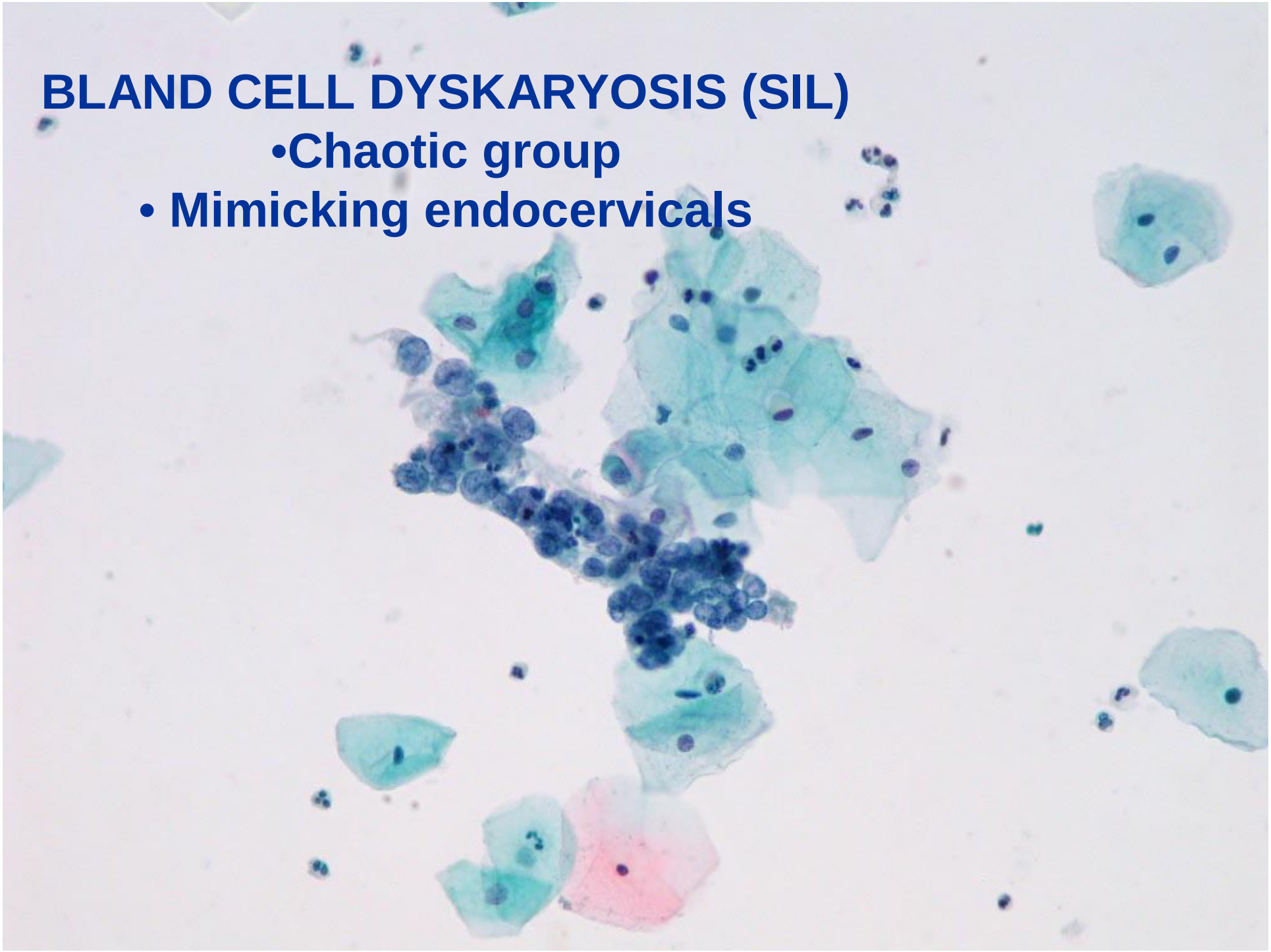
Bland Dyskaryosis/SIL: A New Pitfall in Liquid Based Cytology (ThinPrep)

Dr. D.N.Rana,Dr.K.Denton,
Dr. M. Desai & Dr. M. Lynch

Cytopathology May-June 2008,
19(3) P162-166

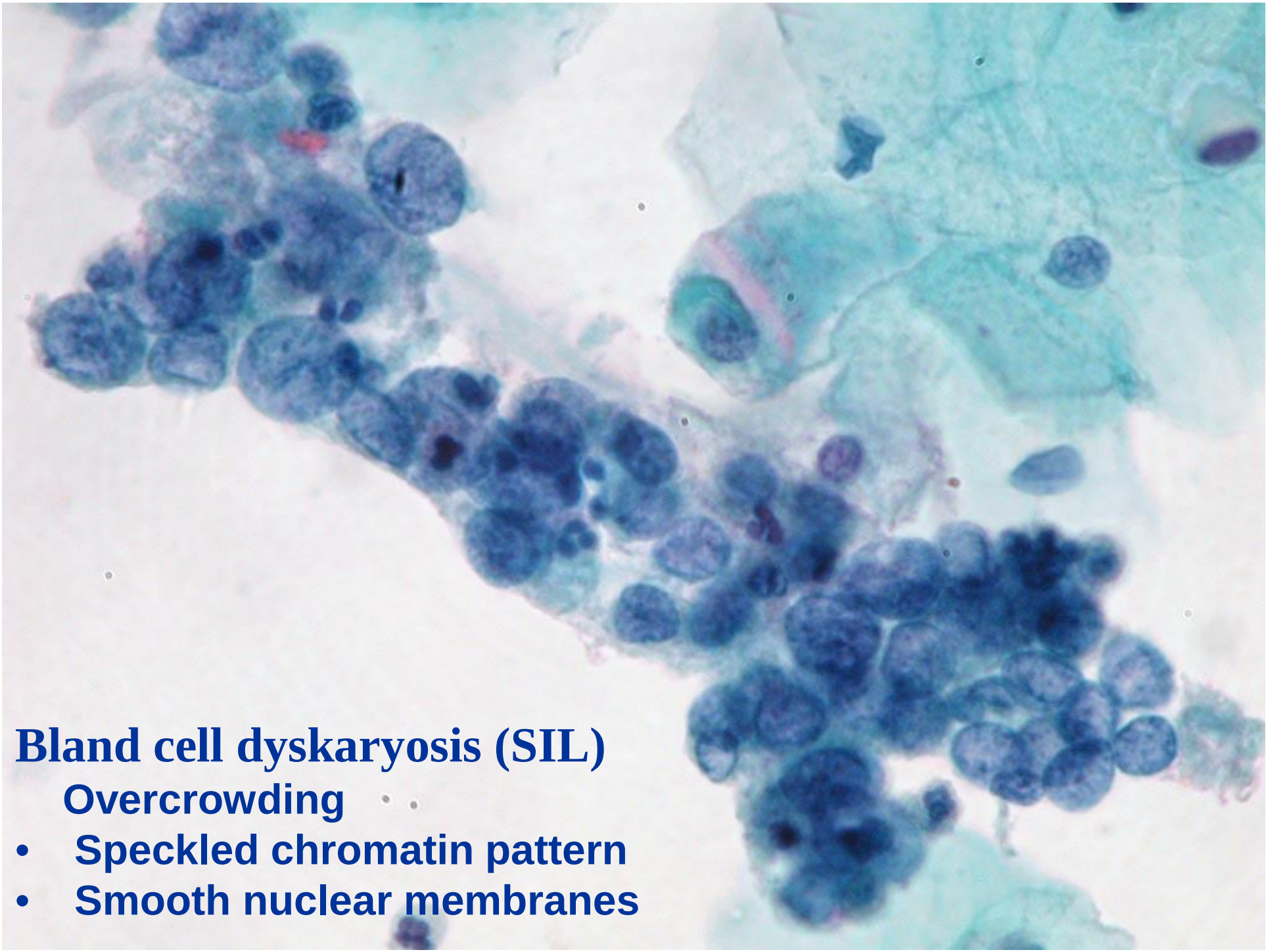
Bland Dyskaryosis (SIL)

- Dyskaryotic/SIL cells appear deceptively bland on low - power examination
- Misinterpreted as squamous metaplastic cells or endocervical cells
- Seen in groups
- Disorganised architecture within the group


BLAND CELL DYSKARYOSIS (SIL)
•Chaotic group
• Mimicking endocervicals

Bland Dyskaryosis (SIL)

- Variation in cell size
- Raised nuclear:cytoplasmic ratio
- Speckled / punctate chromatin pattern
- Chromatin may be evenly distributed
- Smooth nuclear outlines



Bland cell dyskaryosis (SIL)

Overcrowding

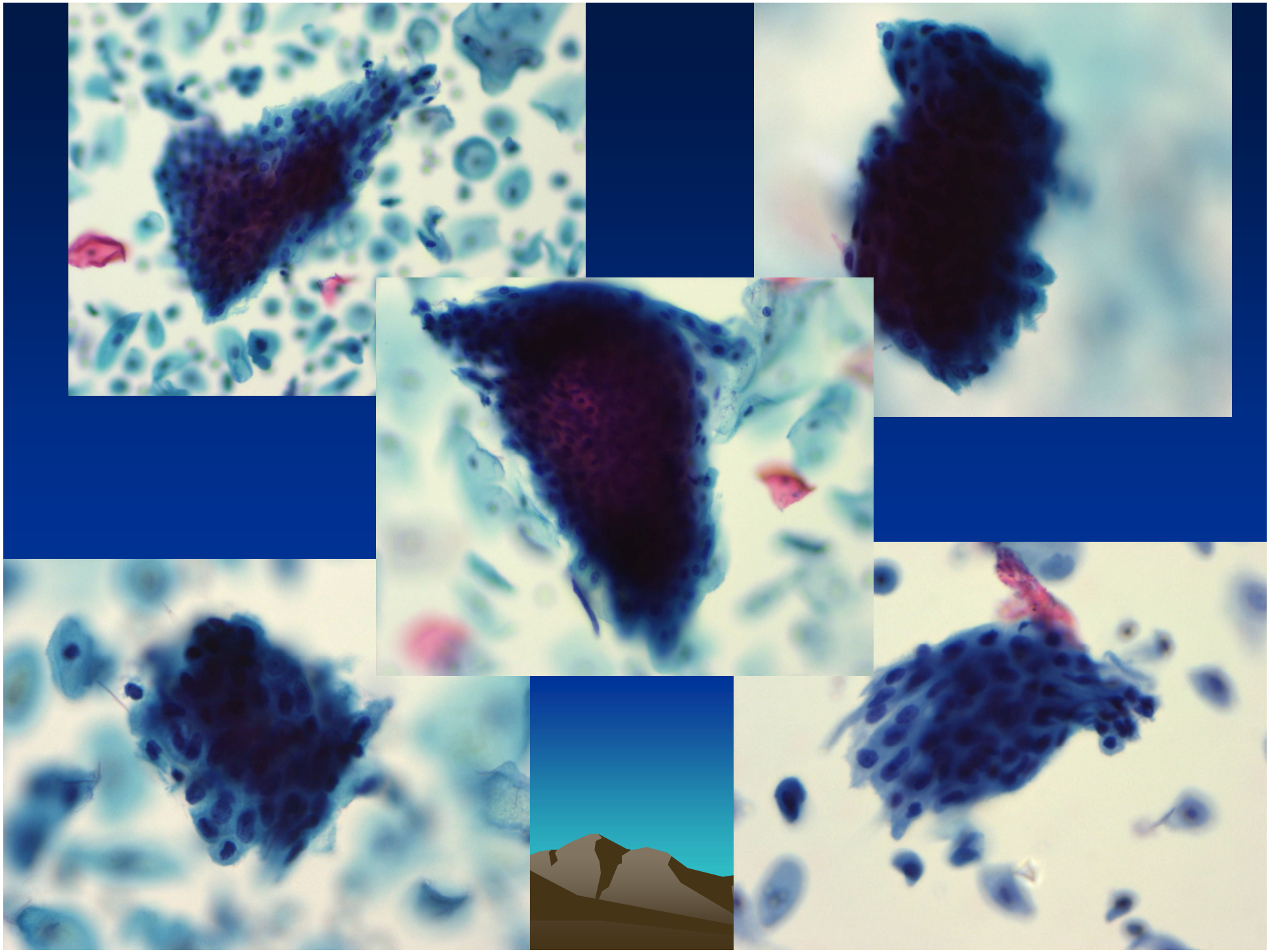
- **Speckled chromatin pattern**
- **Smooth nuclear membranes**

HCCG
Major Pitfall in Surepath LBC

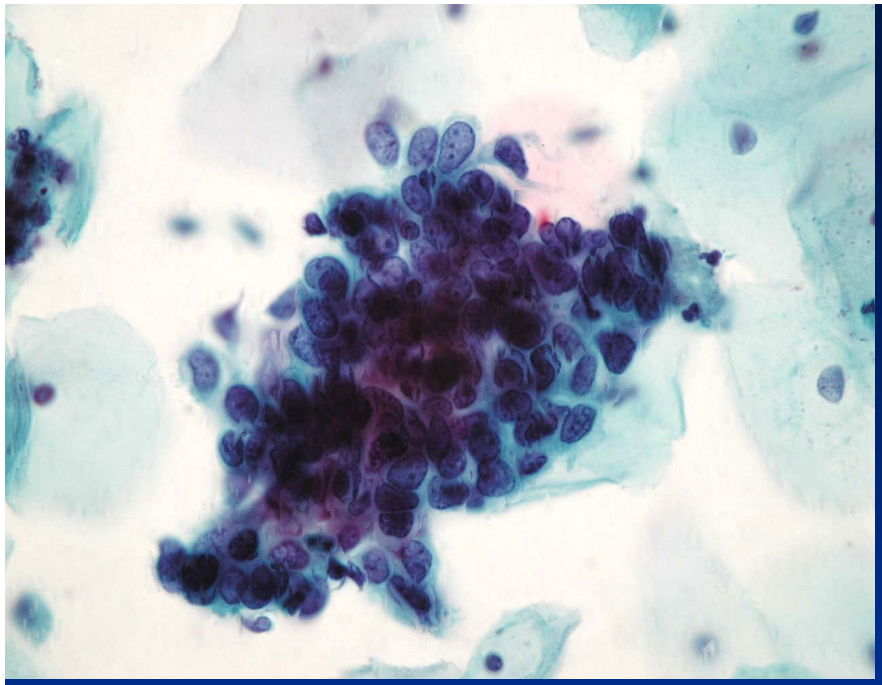
HCGs

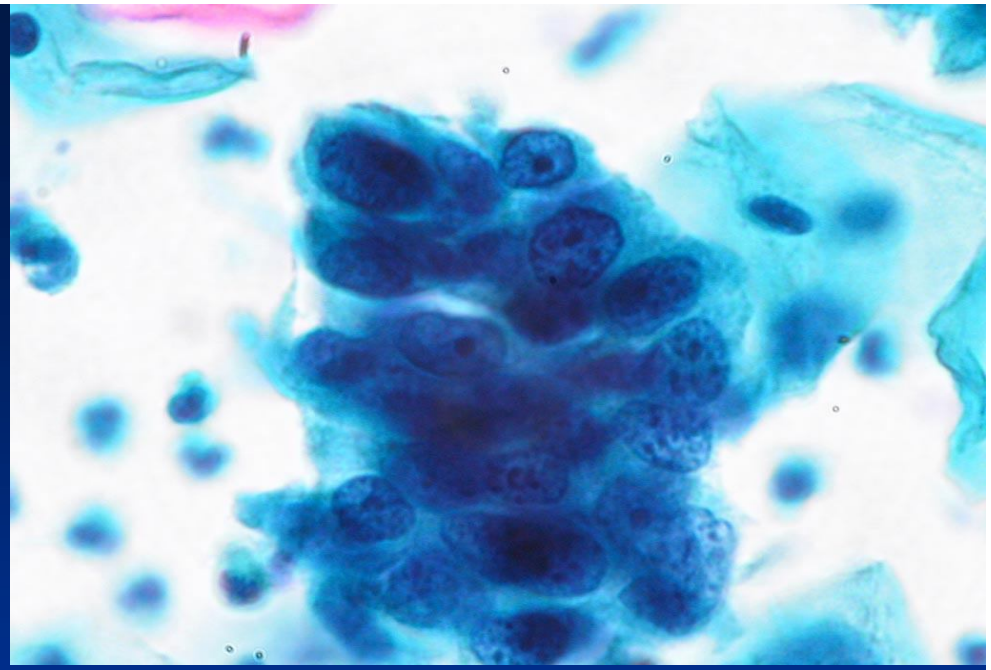
- Microbiopsies or tissue fragments
- 3-dimensional aggregates of crowded cells with hyperchromatic nuclei
- Normal or abnormal cells
- When abnormal, may be the only abnormality present
- Most common cause of interpretative error

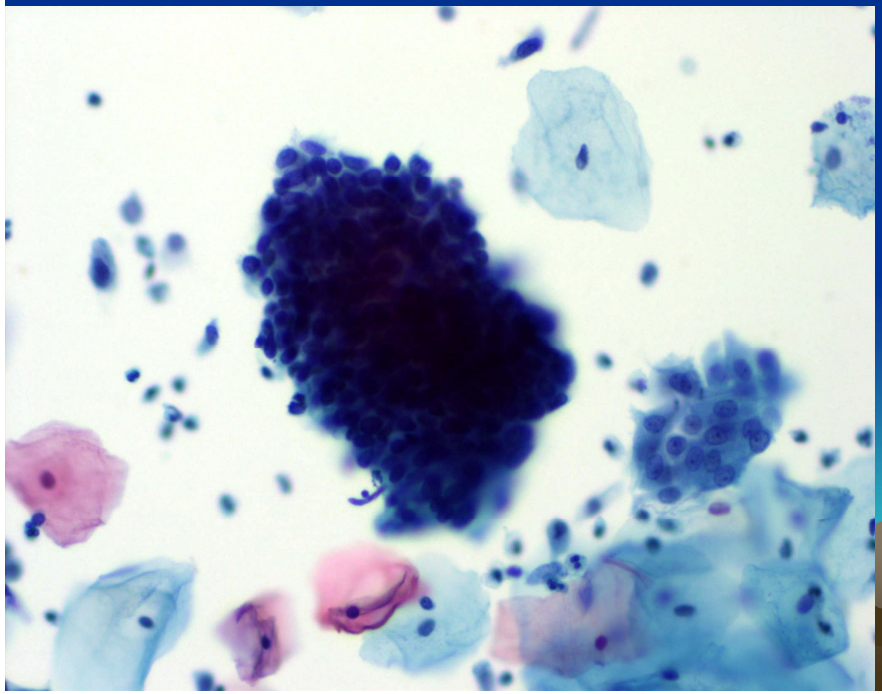
ALL of the following cells are normal !

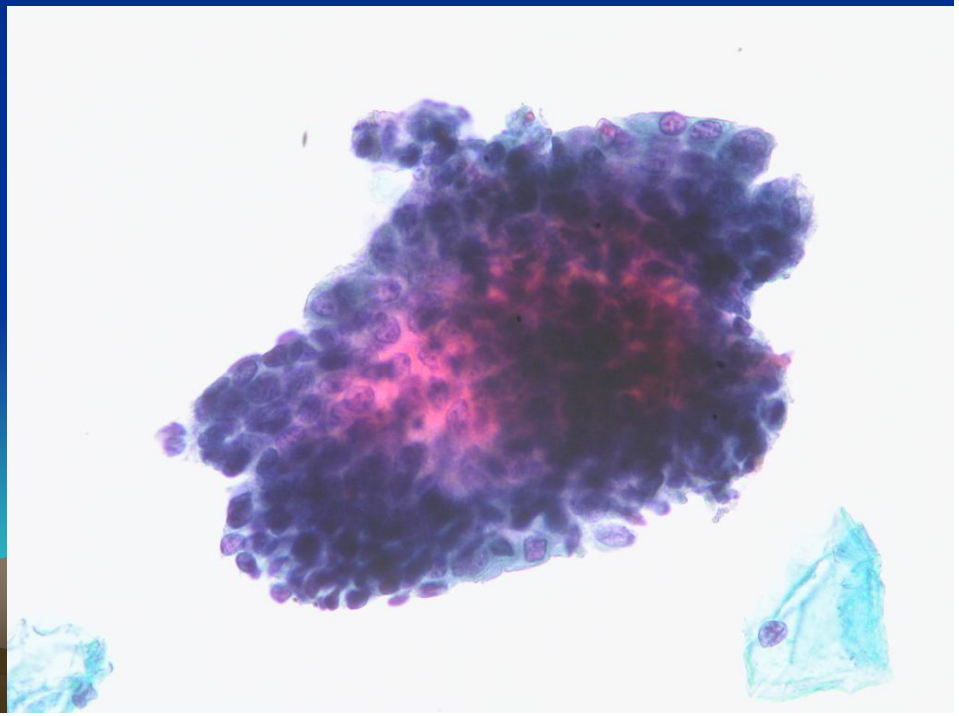


ALL of the following cells are abnormal !









HCGs

Normal and Reactive

- Endometrial cells
- Atrophy
- Endocervical cells
- Reactive endocervical cells
- Tubal metaplasia
- Lower-uterine segment
- Repair
- Atypical repair

Abnormal

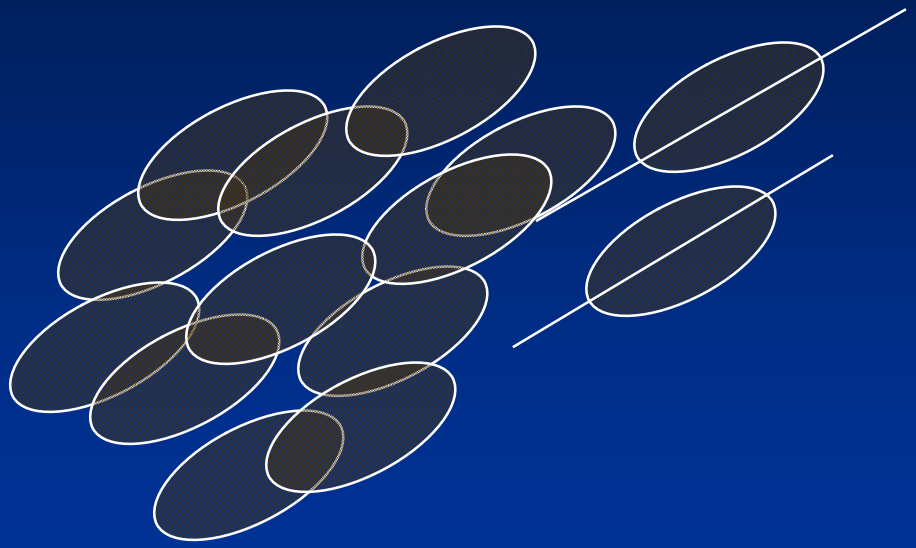
- High-grade CIN
- Squamous cell carcinoma
- Glandular neoplasia
  - cervical
  - non-cervical
- Metastatic carcinoma

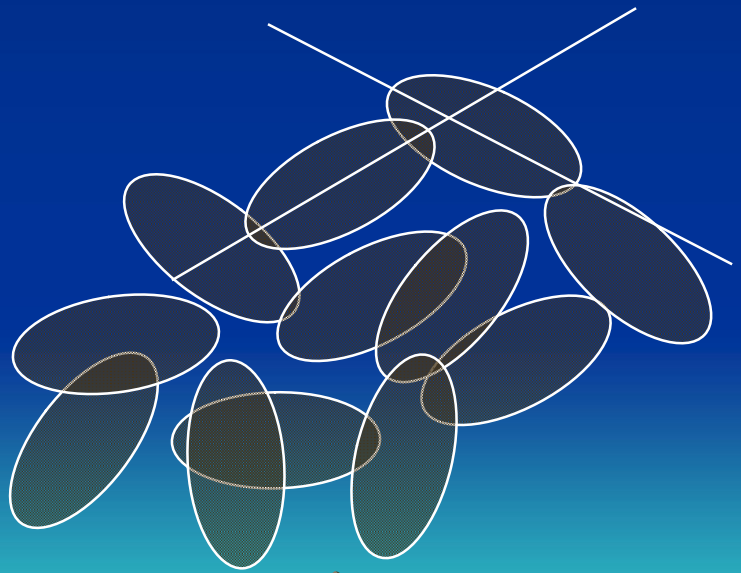
Interpretation of HCGs

- Detect at Low power
- Assess architecture and nuclear polarity
- Examine periphery for nuclear detail i.e. Chromatin distribution and nuclear membrane
- Examine periphery for surface differentiation
- Look for mitotic figures
- Try to find diagnostic isolated cells away from HCGs

The interpretation of microbiopsies

Maintenance of polarity = probably benign





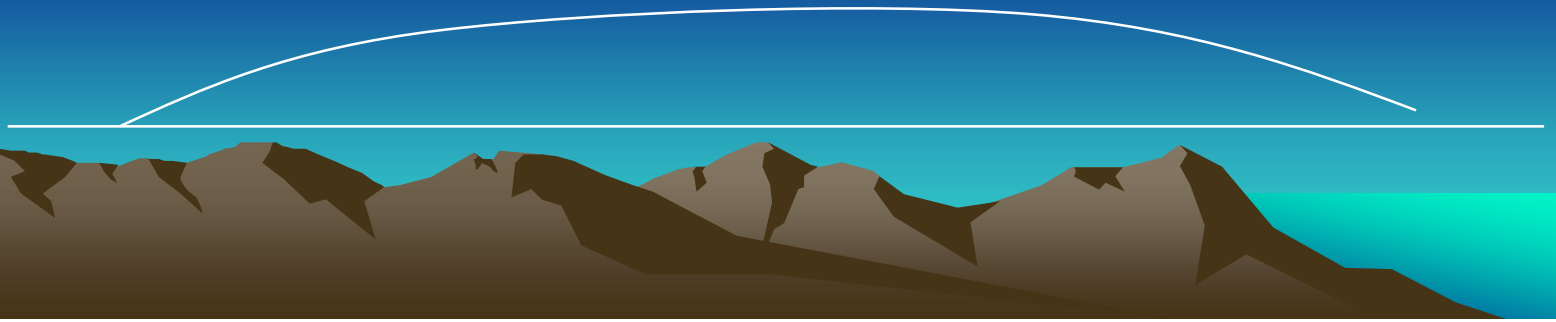
Loss of polarity = probably neoplastic

The interpretation of microbiopsies

Periphery

Steep relief = probably neoplastic

Shallow relief = probably benign

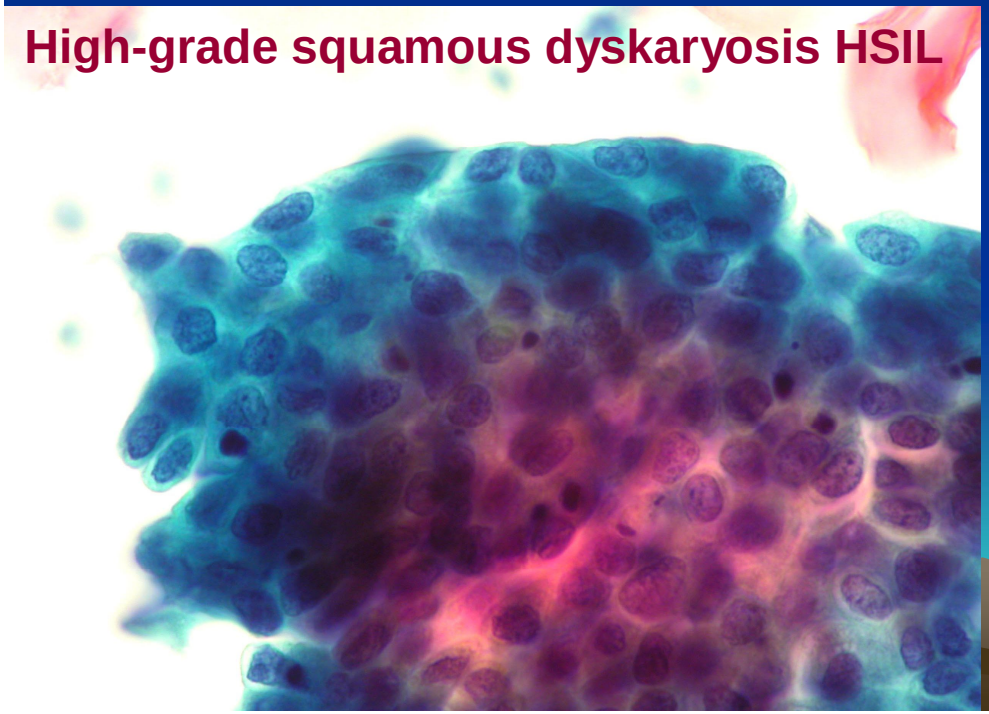


HCGs: Further Diagnostic Clues at the Periphery

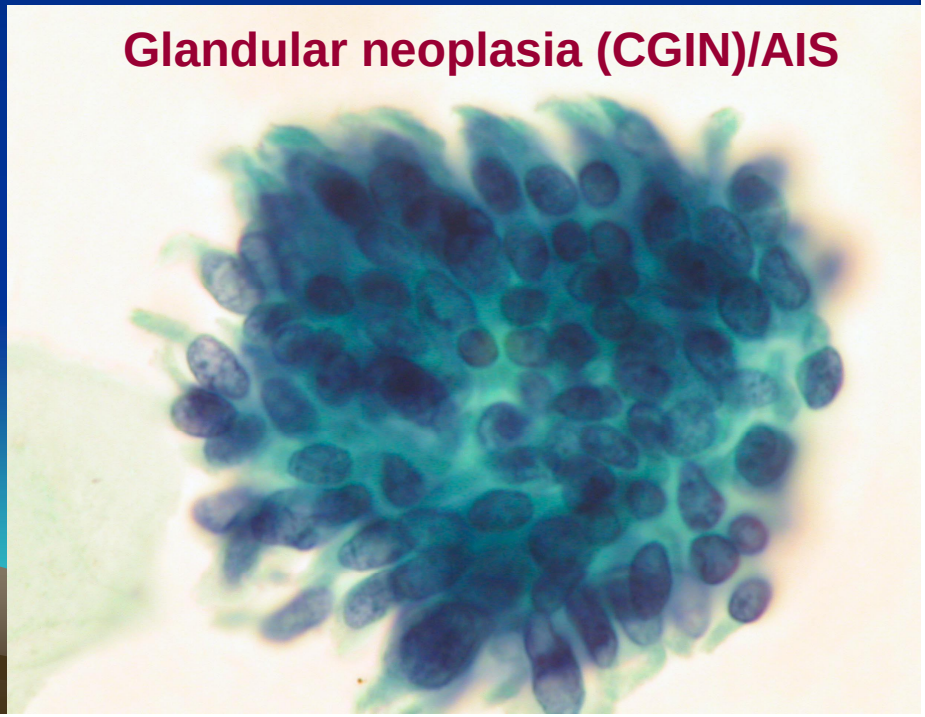
More Clues

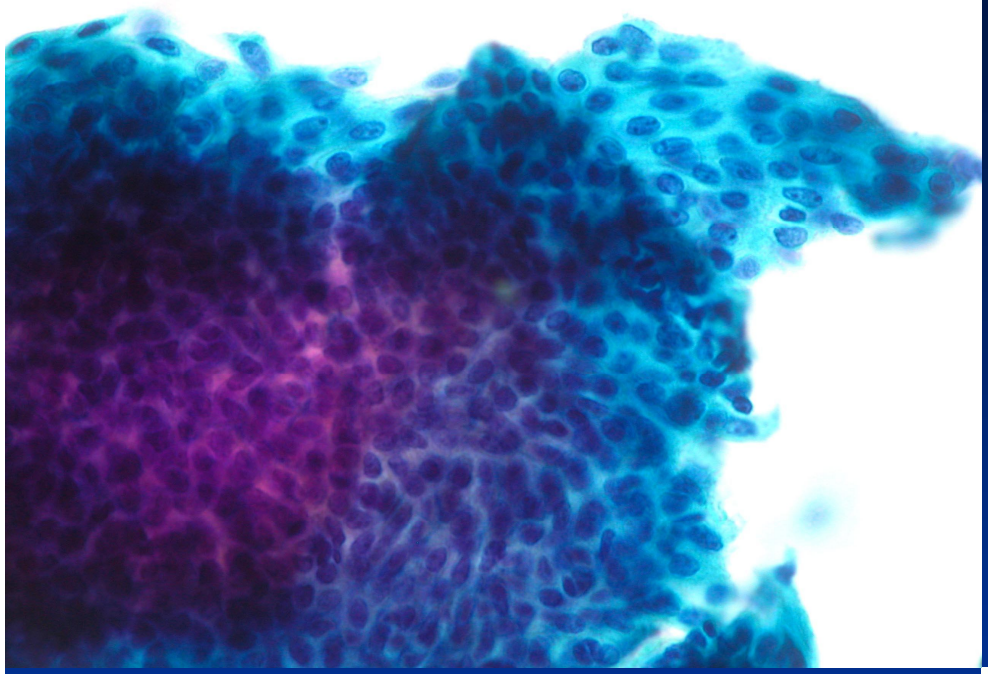
- **CIN infiltrating into crypts (Flat edge with horizontal nuclei)**
- **Glandular neoplasia (Glandular border with vertical nuclei)**

High-grade squamous dyskaryosis HSIL

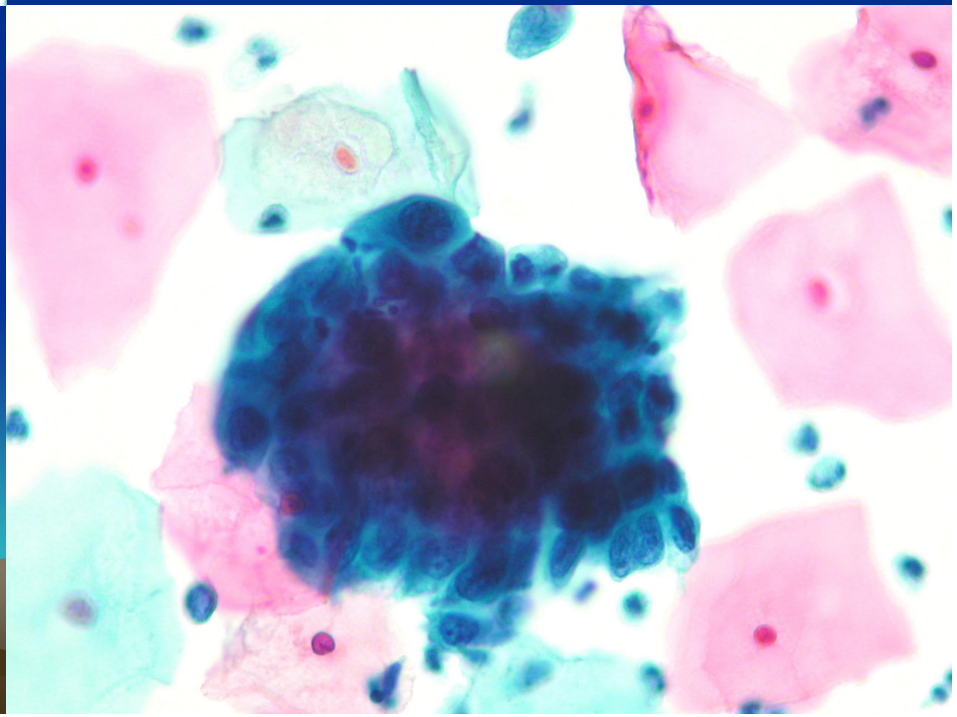


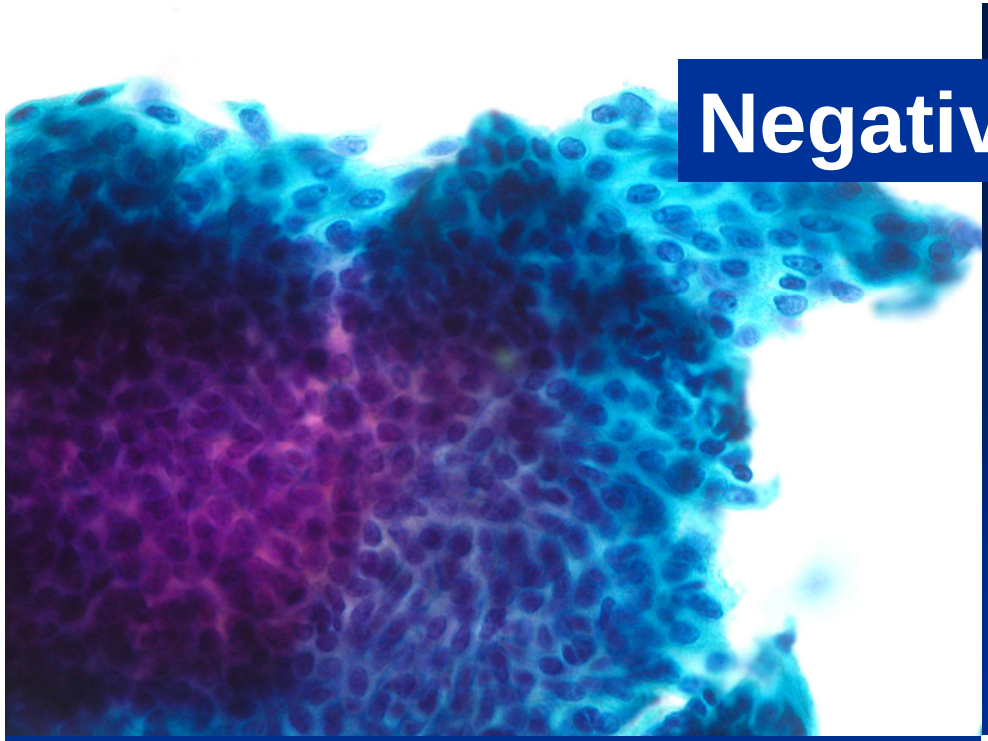
Glandular neoplasia (CGIN)/AIS





Net case 2
HCG Pitfall
Spot the Difference:
Negative or HSIL

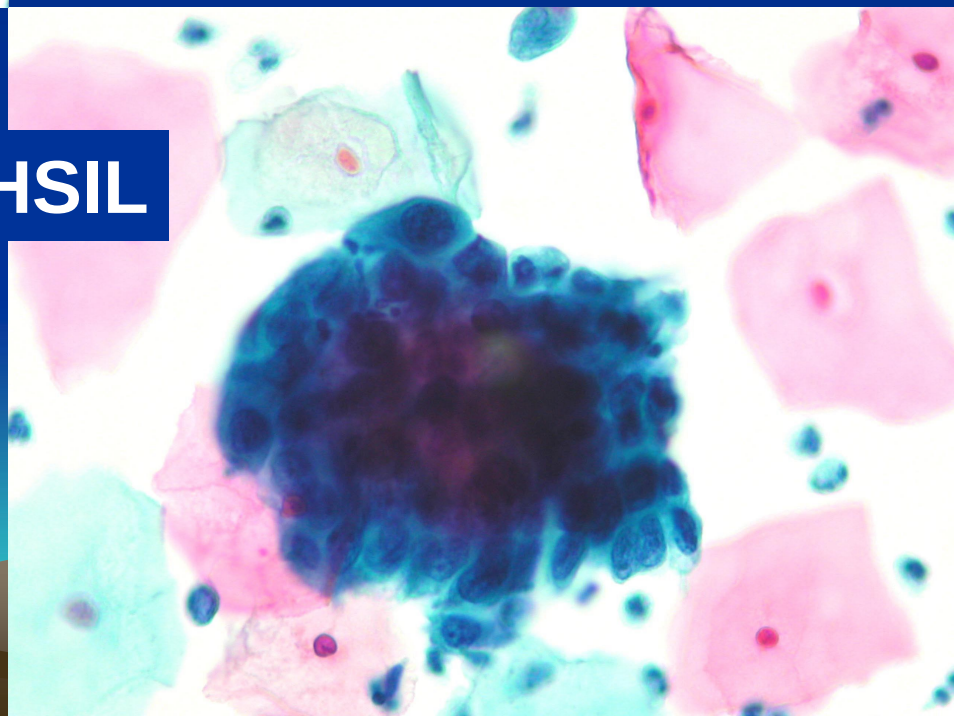




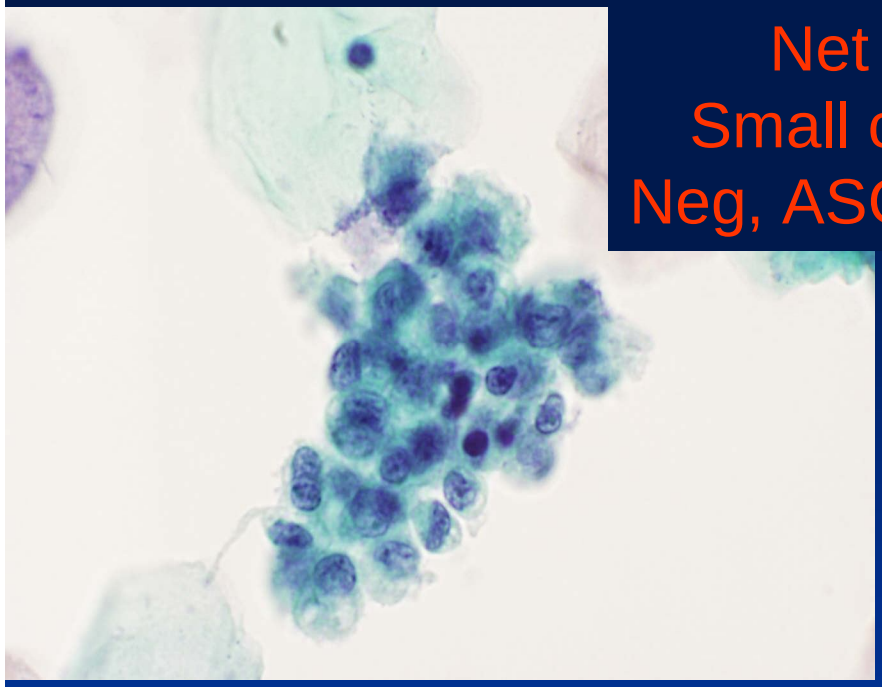
Negative atrophy

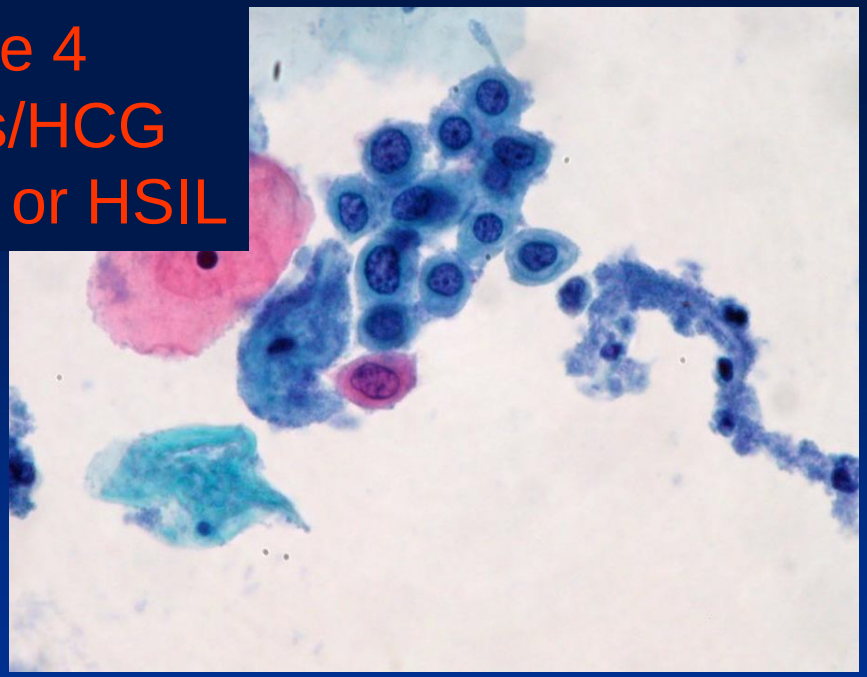
Net case 2
HCG Pitfall
Spot the Difference:
Negative or HSIL

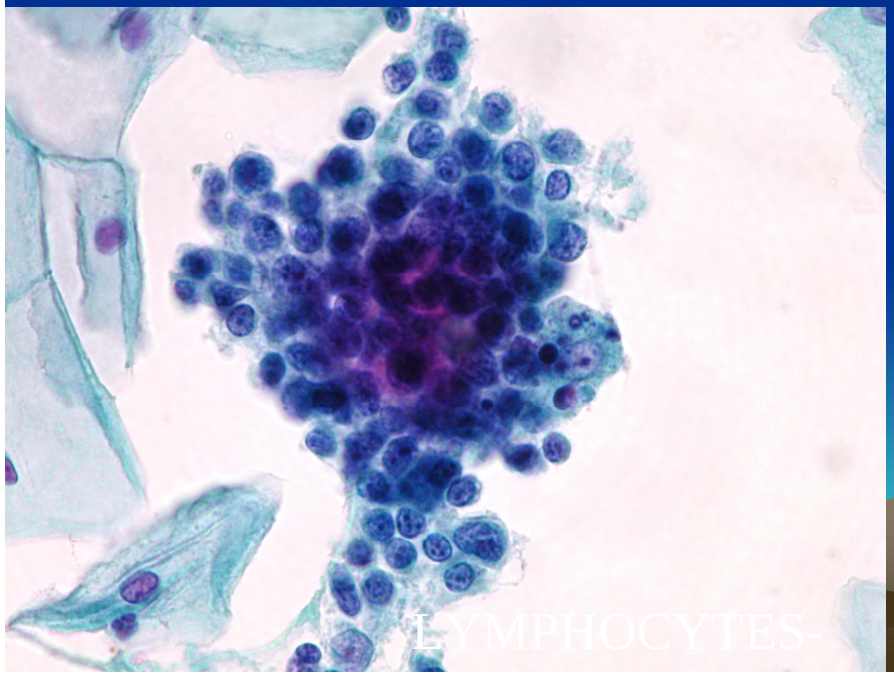
HSIL

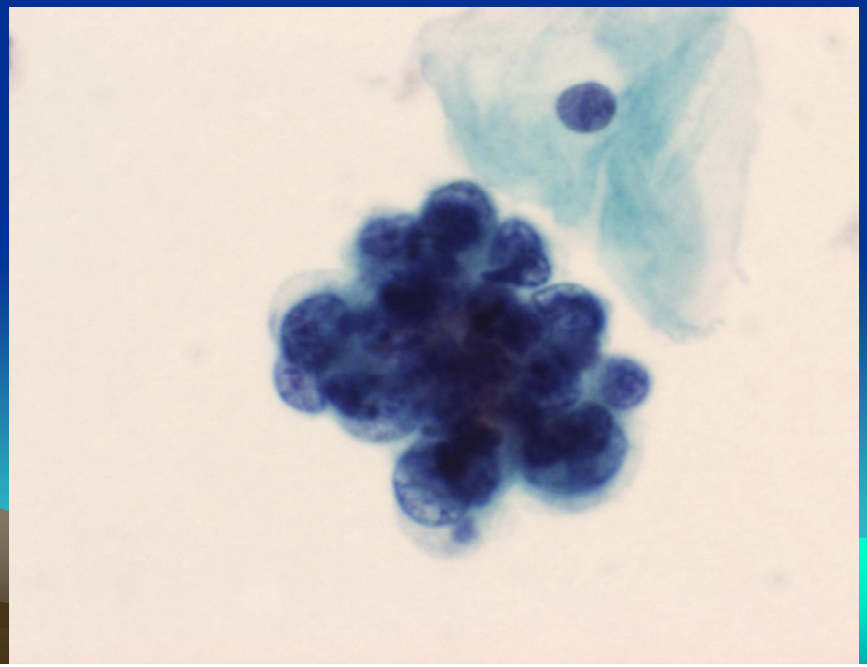


Net case 4
Small cells/HCG
Neg, ASC-H or HSIL





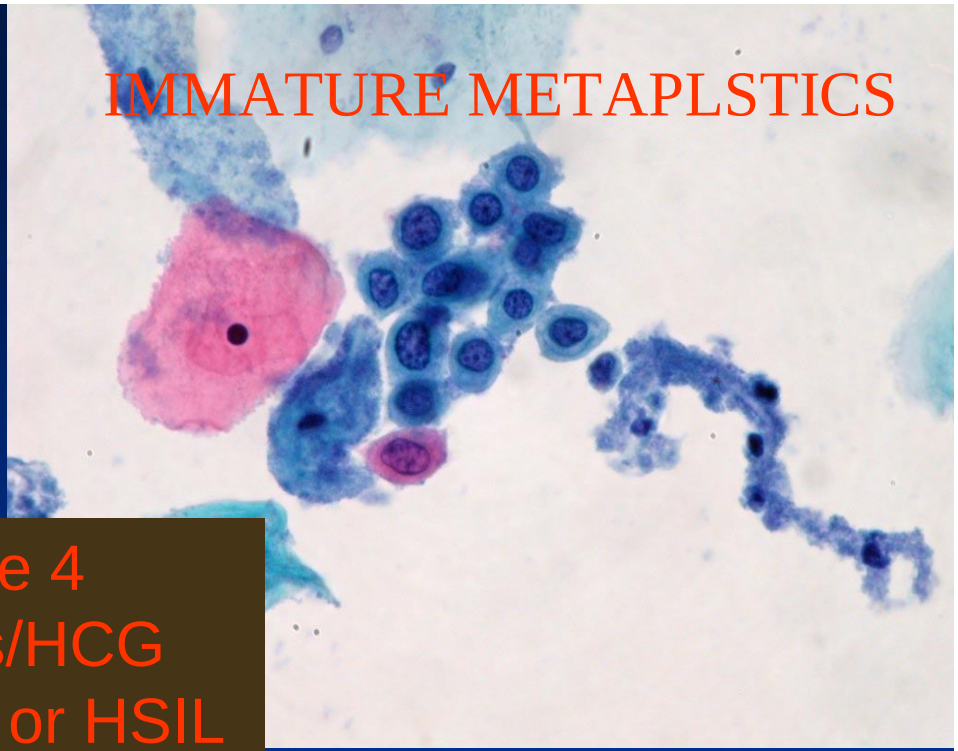




LYMPHOCYTES-

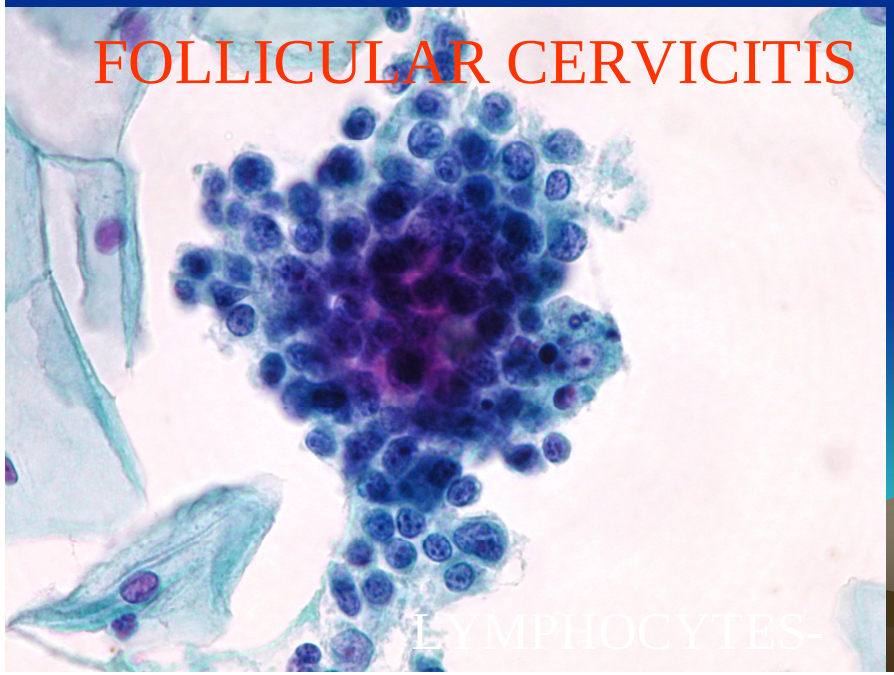
HISTIOCYTES,

IMMATURE METAPLSTICS

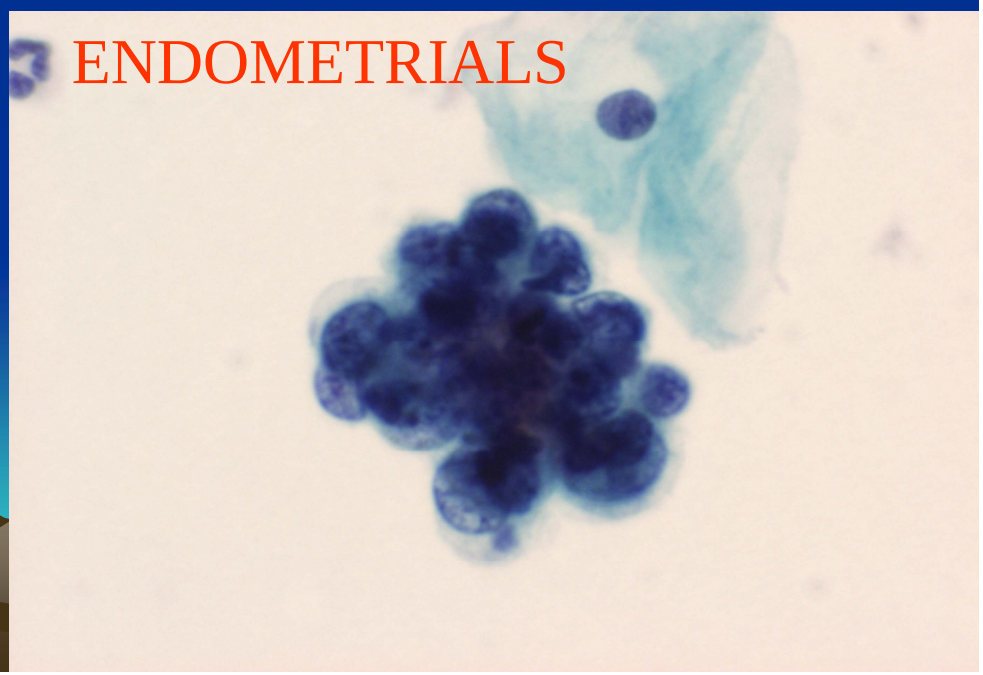


Net case 4
Small cells/HCG
Neg, ASC-H or HSIL

FOLLICULAR CERVICITIS



ENDOMETRIALS



LYMPHOCYTES-

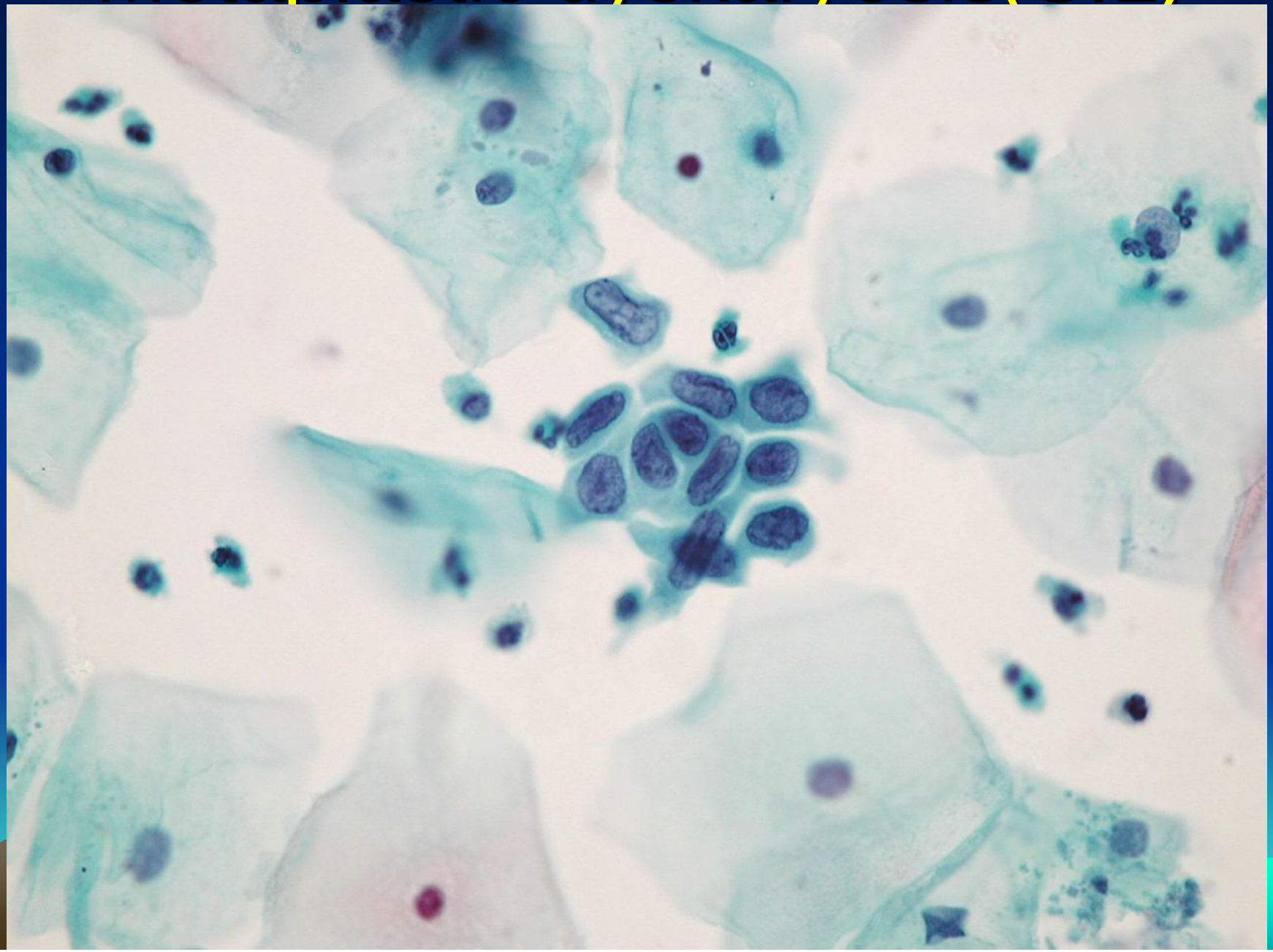
Metaplastic Cells
Major Pitfall in Thinprep LBC

Differential diagnosis is often between normal reactive or moderate (HSIL) dyskaryosis

Metaplastic Cells
Major Pitfall in Thinprep LBC

- Can cause diagnostic difficulty, especially when the N/C ratio is high
- Some nuclear membrane irregularity is common
- Nuclear pleomorphism
- Immature sheets
- Differential diagnosis is often between normal reactive or moderate (High grade) dyskaryosis

Metaplastic dyskaryosis(SIL)

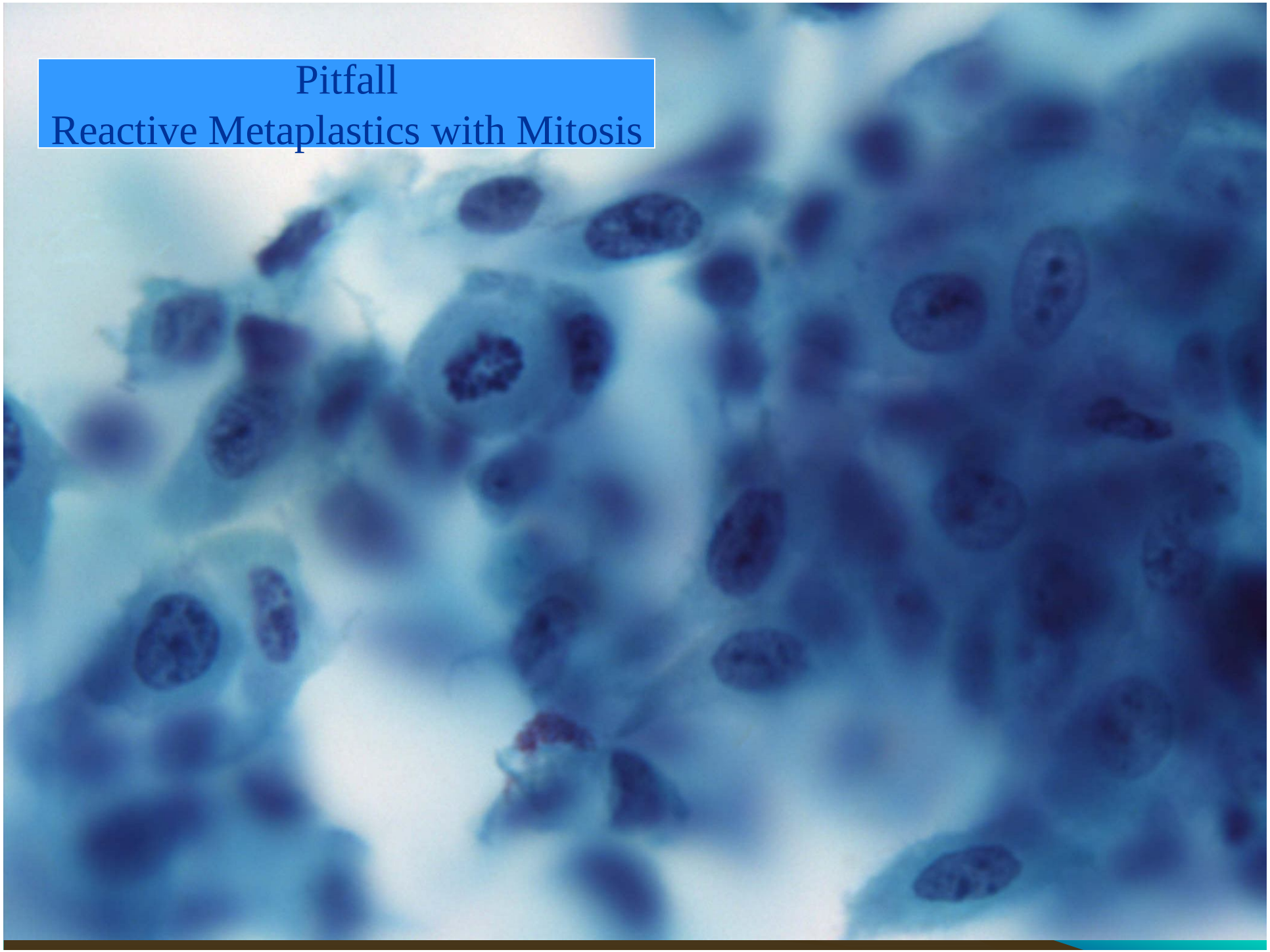


Useful pointers for immature squamous metaplasia

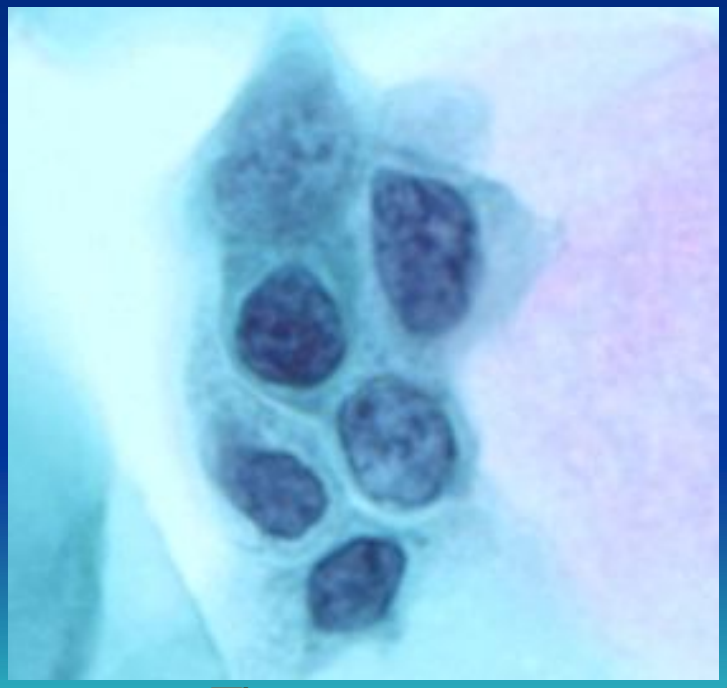
- Always keep it in mind when considering whether a cluster of cells is HG dyskaryosis
- A thick even nuclear membrane is a major clue for benign nature
- The membrane is only focally wavy rather than highly irregular
- The chromatin is moderately coarse but even when comparing quadrants

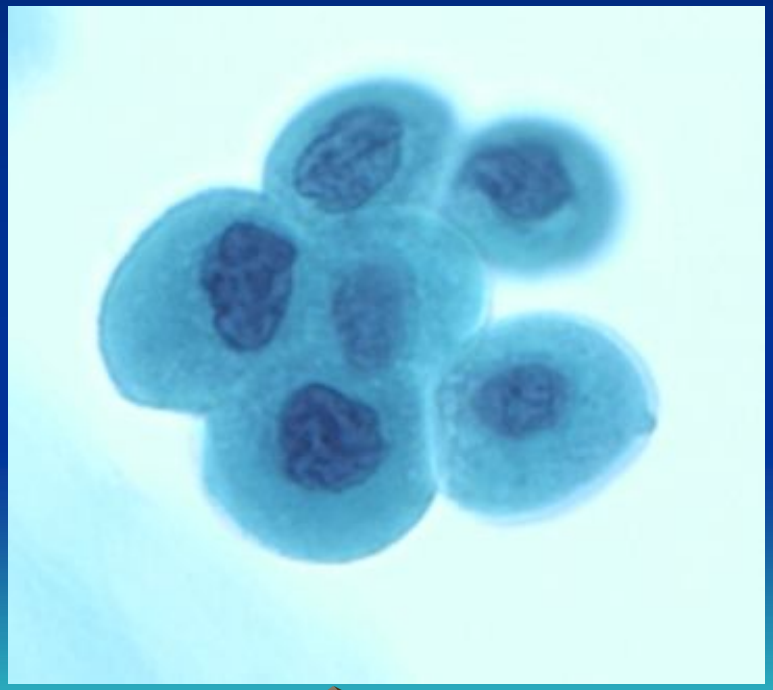
Features	Metaplastic cells	High-grade dyskaryosis cells
Nuclear size	Small to moderately sized N:C ratio varies depending on maturity	Large High N:C ratio in high-grade dyskaryosis
Nuclear shape	Some mild waviness, otherwise smooth	May be any shape (smooth or irregular)
Nuclear chromatin	Fine to moderately coarse even distribution	Fine to coarse Uneven distribution
Nucleoli	+	+/-
Nuclear grooves	+	-
Nuclear membrane	Thick and prominent in reactive metaplastics	Smooth or walnut like

Pitfall
Reactive Metaplastics with Mitosis



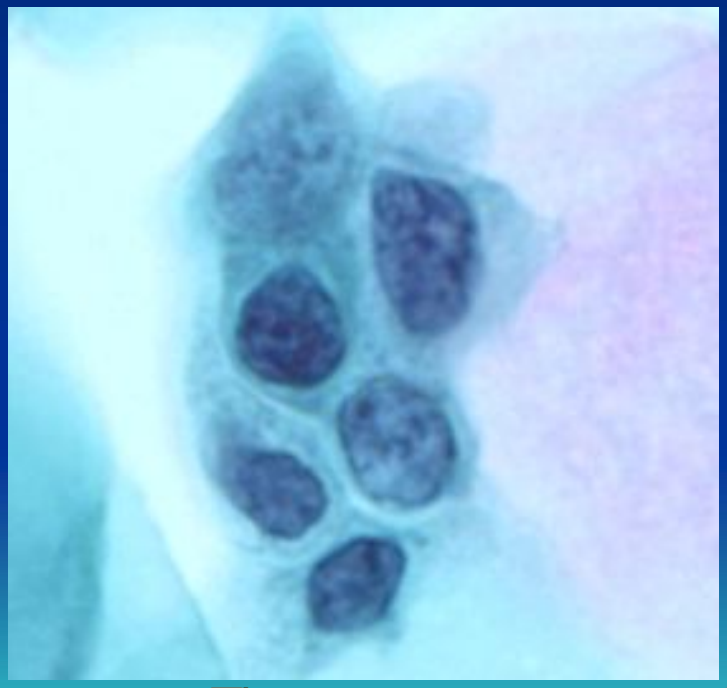
Net case 3
Spot The Difference
Metaplastic Cells
Neg, ASCUS or SIL?



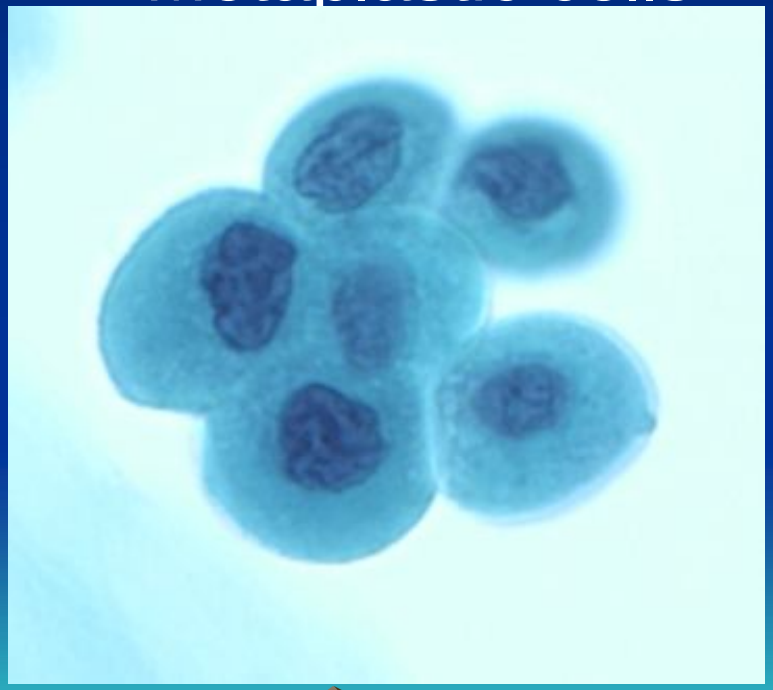


Net case 3
Spot The Difference
Metaplastic Cells
Neg, ASCUS or SIL?

- Dyskaryosis (HSIL)



- Neg.
- Metaplastic cells



Invasive Squamous Carcinoma

Different types of Invasive Squamous Cell Carcinoma

- Micro invasive
- Keratinising
- Non keratinising large cell
- Non keratinising small cell
- Verrucous carcinoma

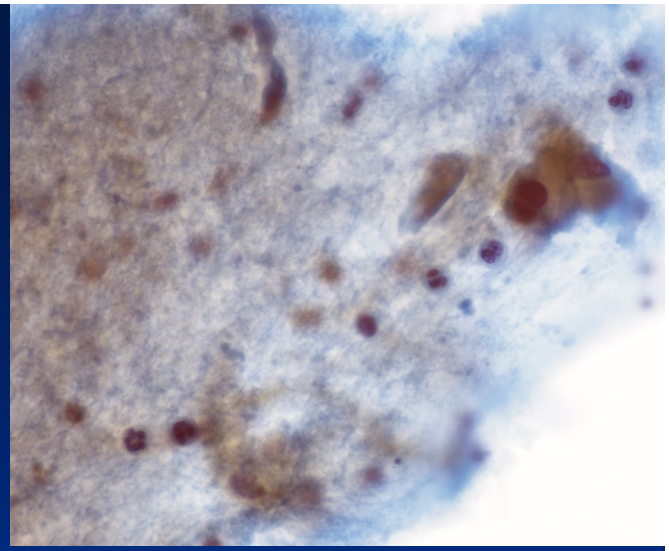
Microinvasive

* Can not be diagnosed reliably
* Indistinguishable from severe dyskaryosis
* Macronucleoli in syncitial aggregates of severe dyskaryosis
* Irregular chromatin distribution

Invasive Squamous cell Carcinoma: Architectural features

* Tumour diathesis
* Large numbers of dyskaryotic (HSIL) cells
* Single cells, loose aggregate
* Sheets of undifferentiated cells HCCG

Tumour Diathesis
Of Invasive Carcinoma in LBC



*Grey/blue granular or fibrillar material with "ratty" appearance

Or "tissue paper like" sheet of proteinaceous material

- clinging to malignant cells

(Clinging Diathesis)

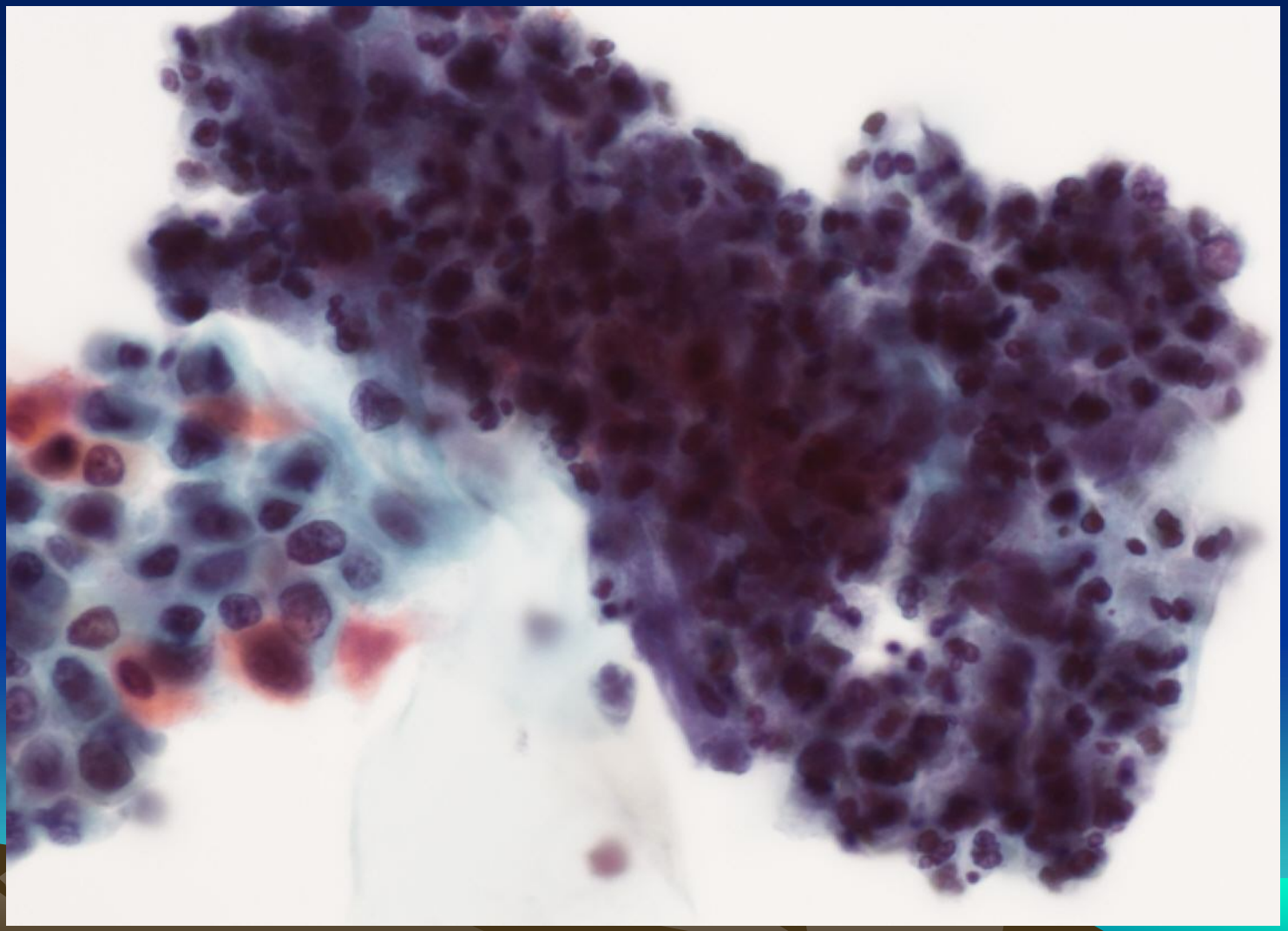
* Blood fresh and old (haemosiderine)
* Fibrin and protein
* Cell necrosis and debris
* Nuclear and cytoplasmic fragment of malignant cells

•polys ,inflammatory dirty background

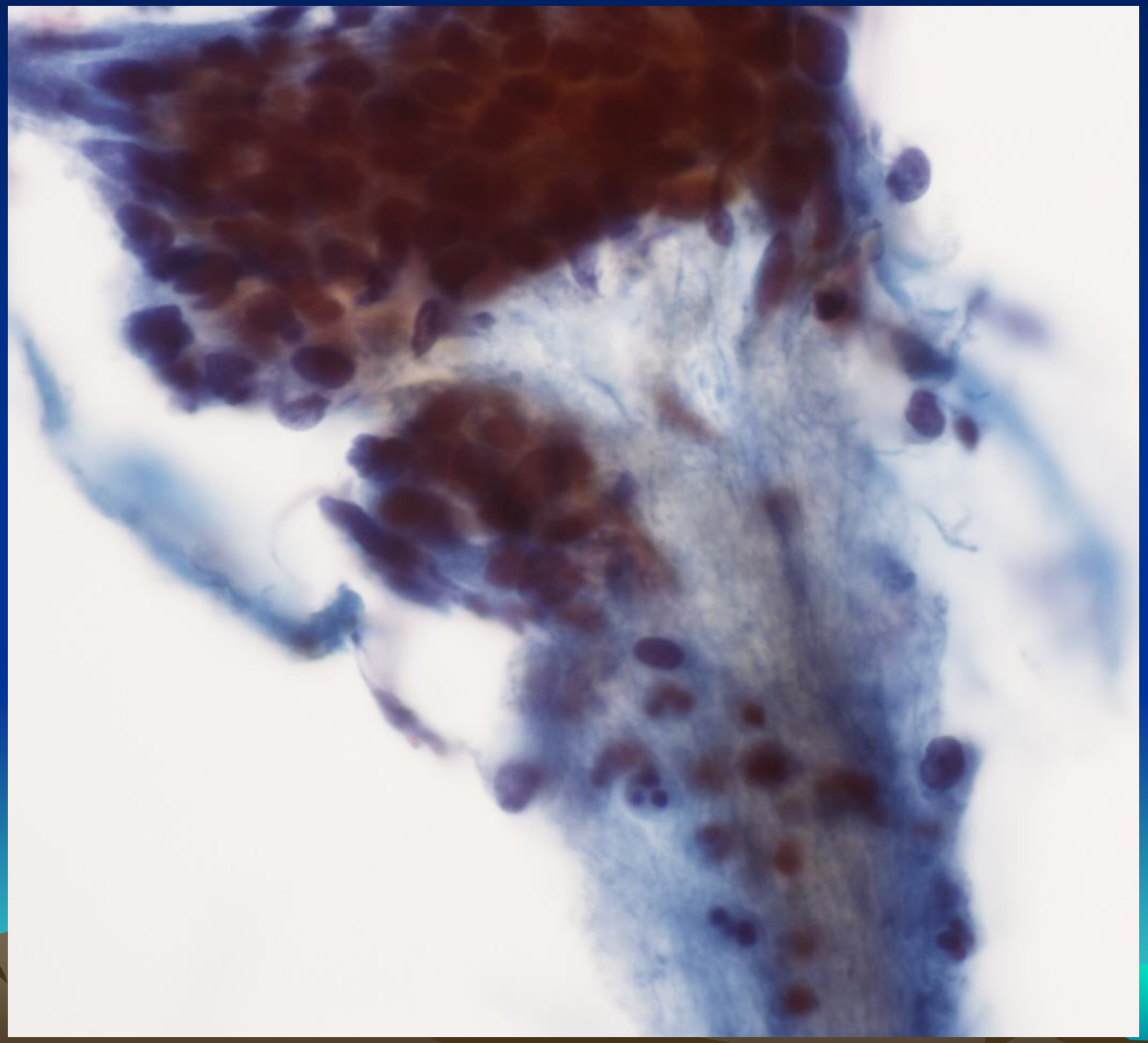
Diathesis is rare, reflects ulceration of surface mucosa and associated with late stage disease

Absent in microinvasive and verrucous carcinoma

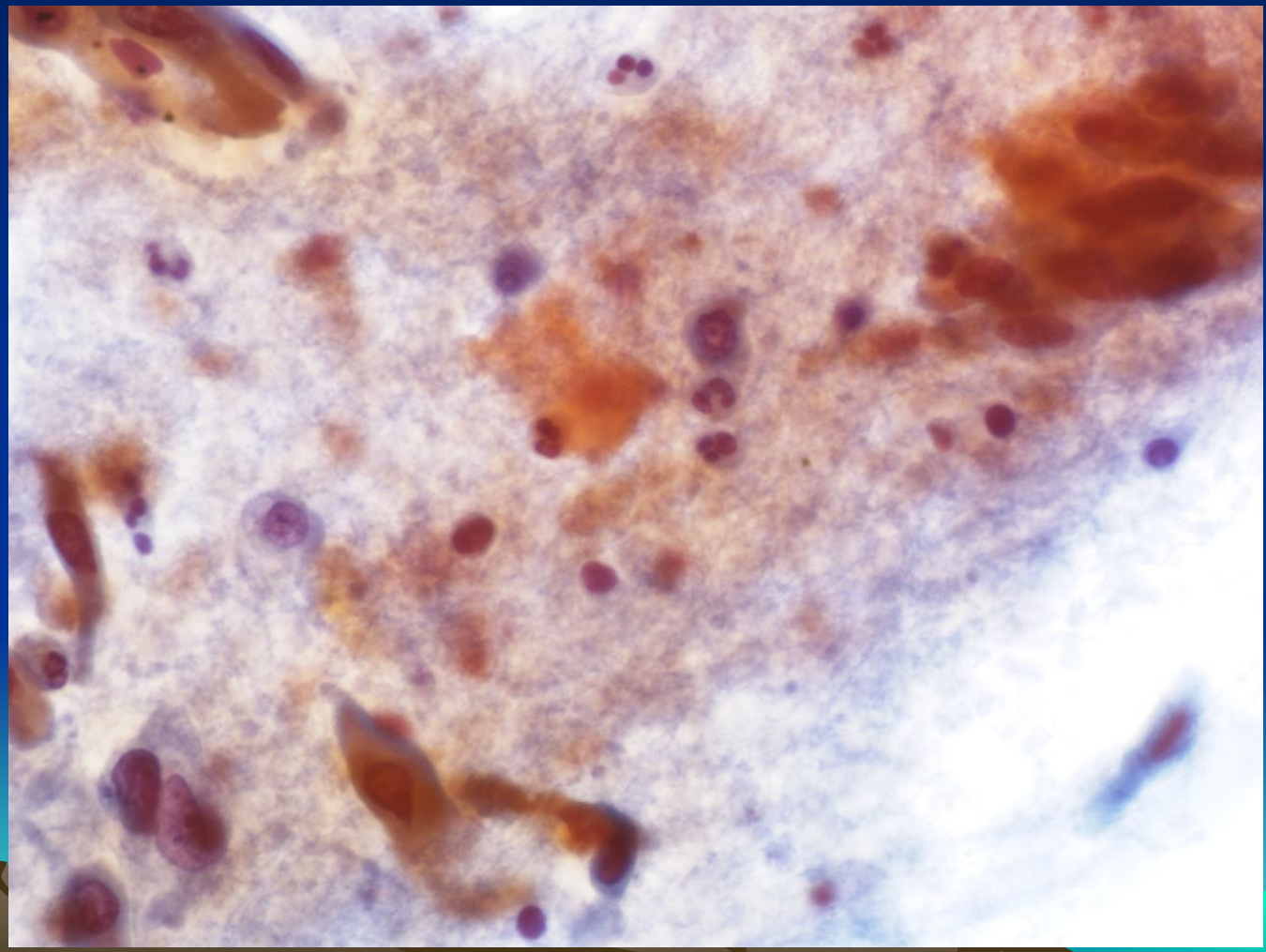
Clinging Diathesis



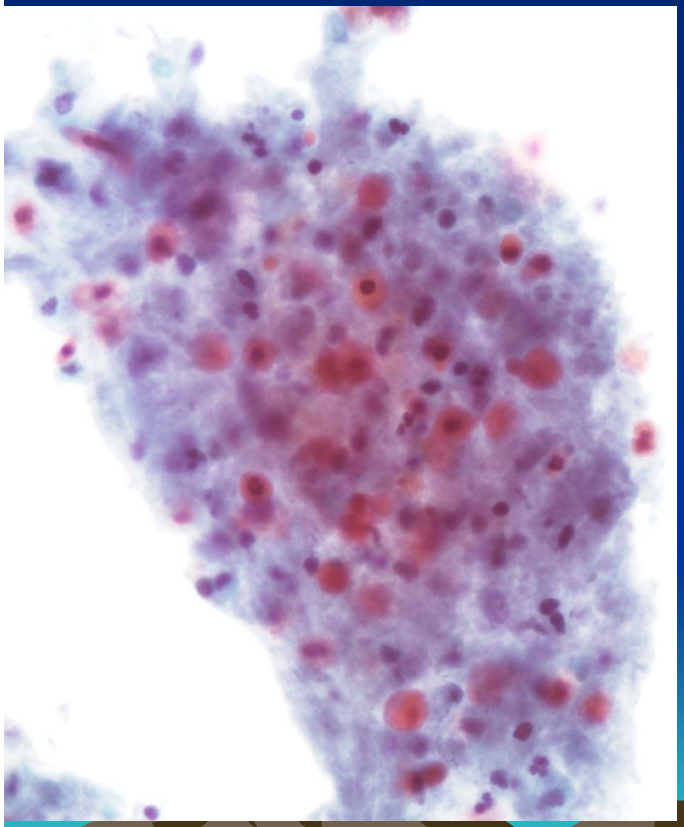
Tissue paper like material
Clinging Diathesis

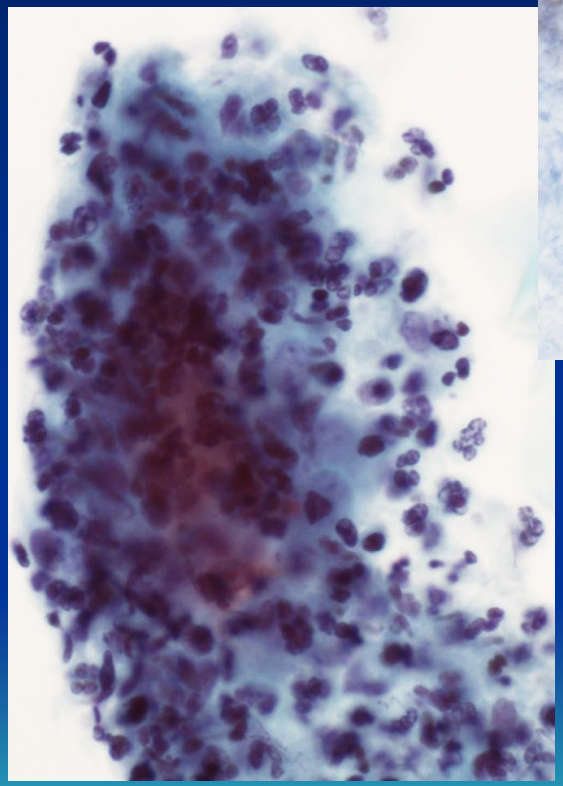


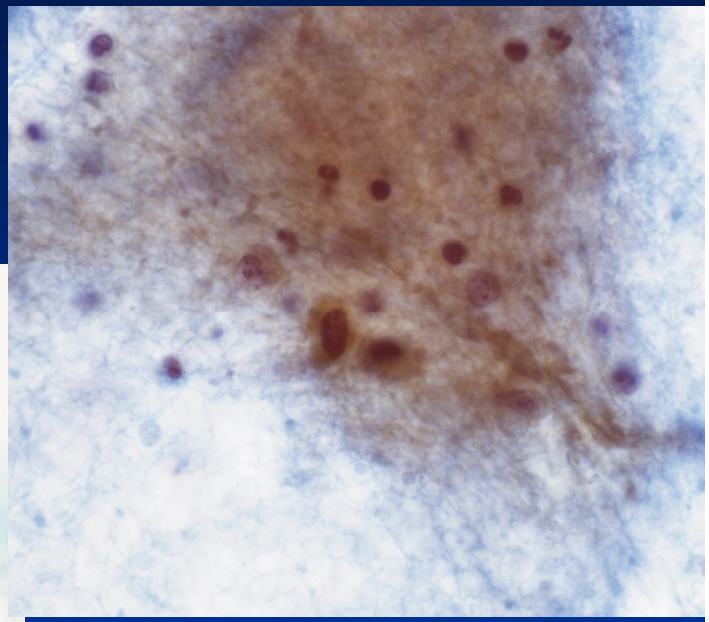
Tumour Diathesis
Granular material
Tumour cell necrosis and Nuclear and Cytoplasmic fragments of malignant cells

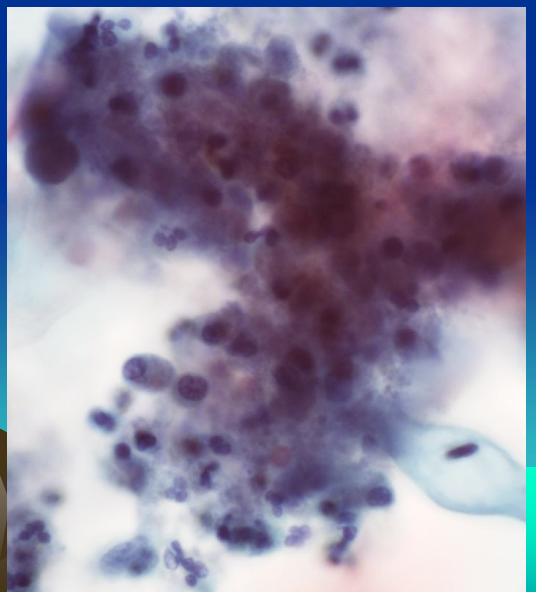


Net case 6
Diathesis
Spot The Difference

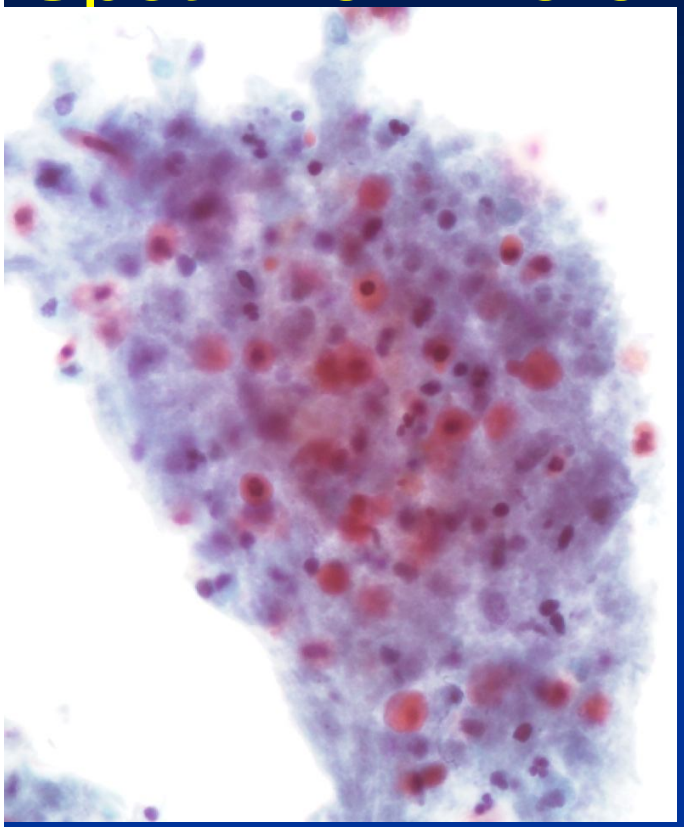




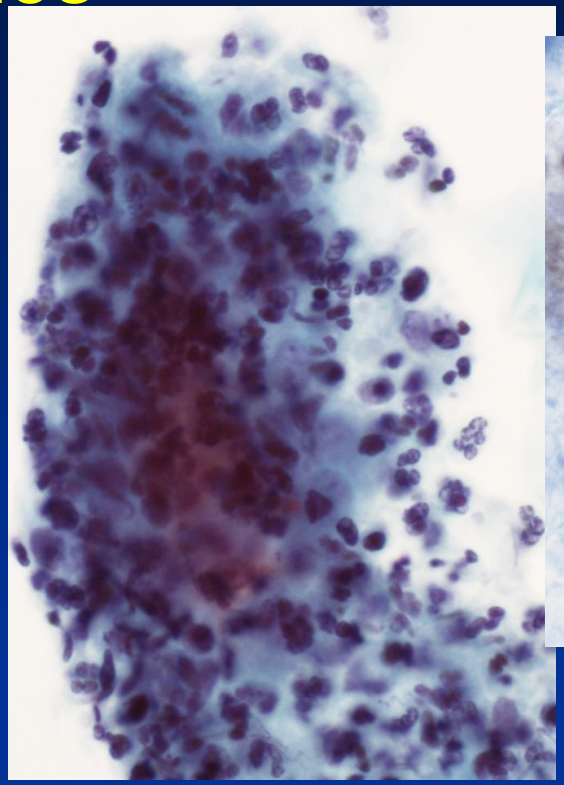




Net case 6
Spot The Difference

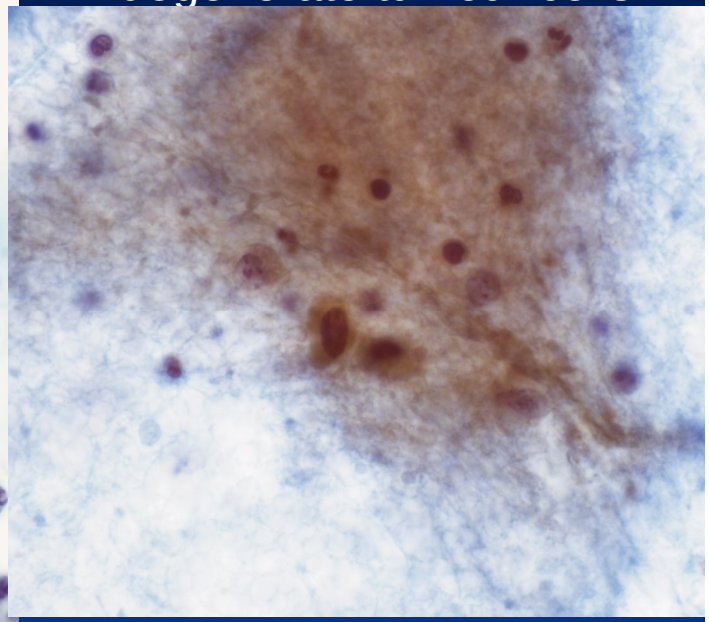


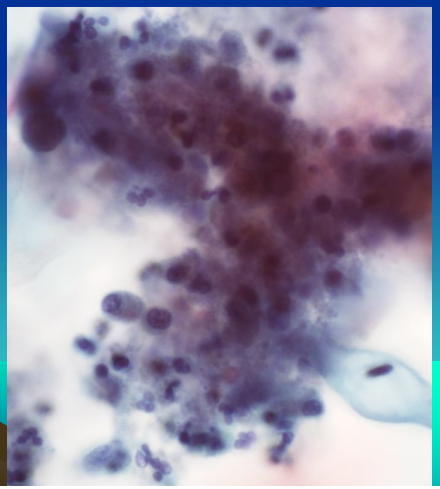
Atrophic vaginitis
Red Atrophy



Benign Diathesis
Trichomonas

Tumour Diathesis
Fibrillar material
with ratty appearance and
degenerate tumour cells





Menstrual Smear
Day 6th of cycle

Invasive squamous cell carcinoma : Cellular features

*** Very bizarre cell shapes**

*** Fibre and tadpole cells**

*** Cell embracement (cell into cell pattern)**

Invasive Squamous cell Carcinoma: Nuclear features

- **Marked pleomorphism**

(Different size & shape)

- Irregular Nuclear Membrane
- Coarse, granular chromatin pattern
- **Hyperchromasia with windowing (parachromatin clearing)**
- Angulated chromatin
- Mitotic figure
- irregular macronucleoli

Abnormal nucleoli

- These can be single or multiple
- If single, they are usually large and abnormal with windowing
- If multiple the nucleoli vary in size and shape
- They may be red staining

Small Cell Non-keratinizing Squamous Carcinoma

* Tumour cells occur singly or in small discohesive syncitial like groups.
* Cells small, cuboidal or round
* Scanty cytoplasm
* High N/C ratio
* No keratinization
* Nuclei large, round to oval
* Hyperchromatic, coarsley granulated chromatin
* Nucleoli small, may be obscured

Differential Diagnosis of Small Cell Squamous cell carcinoma

* Normal and abnormal endometrial cells
* Lymphoid lesions
* Small cell severe dyskaryosis
* Reserve cell hyperplasia

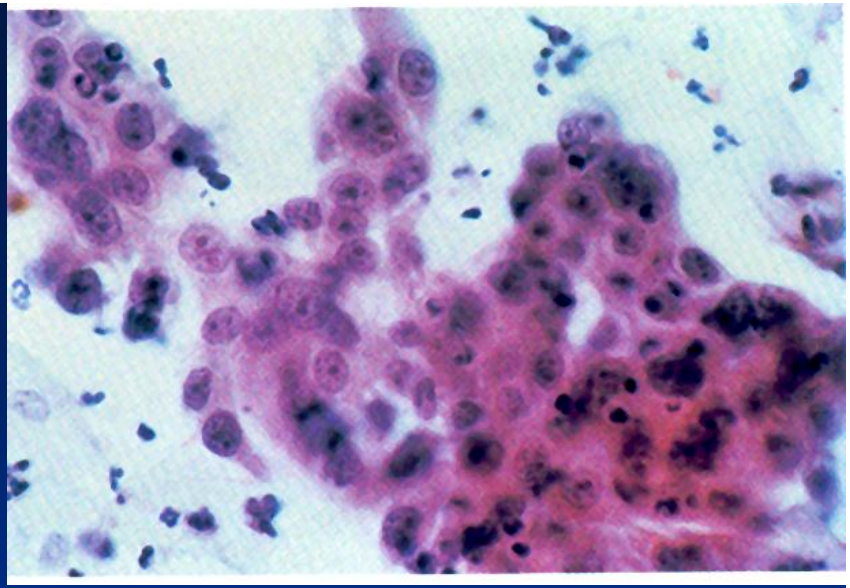
Large Cell Non-Keratinizing Squamous cell carcinoma

* Numerous single cells and discohesive syncitial groups of cells
* Cellular and nuclear pleomorphism is less than keratinizing SCC
* High N/C ratio
- Nuclear overlapping
- Prominent Nucleoli

Differential Diagnosis of Large cell, Non-keratinizing Squamous cell carcinoma

* Repair cells
* Endocervical Adenocarcinoma

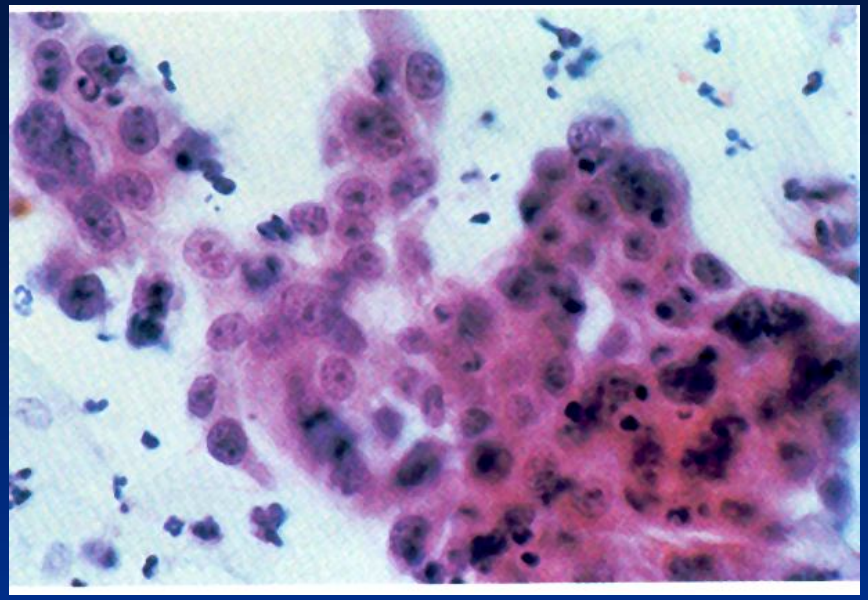
Repair Cells



* Cohesive, flat, monolayered sheets of polygonal squamous cells
* Distinct cytoplasmic boundaries
* Frequent cytoplasmic projectious (pseudopodia)
* Tumour diathesis ABSENT

cont……

Repair Cells

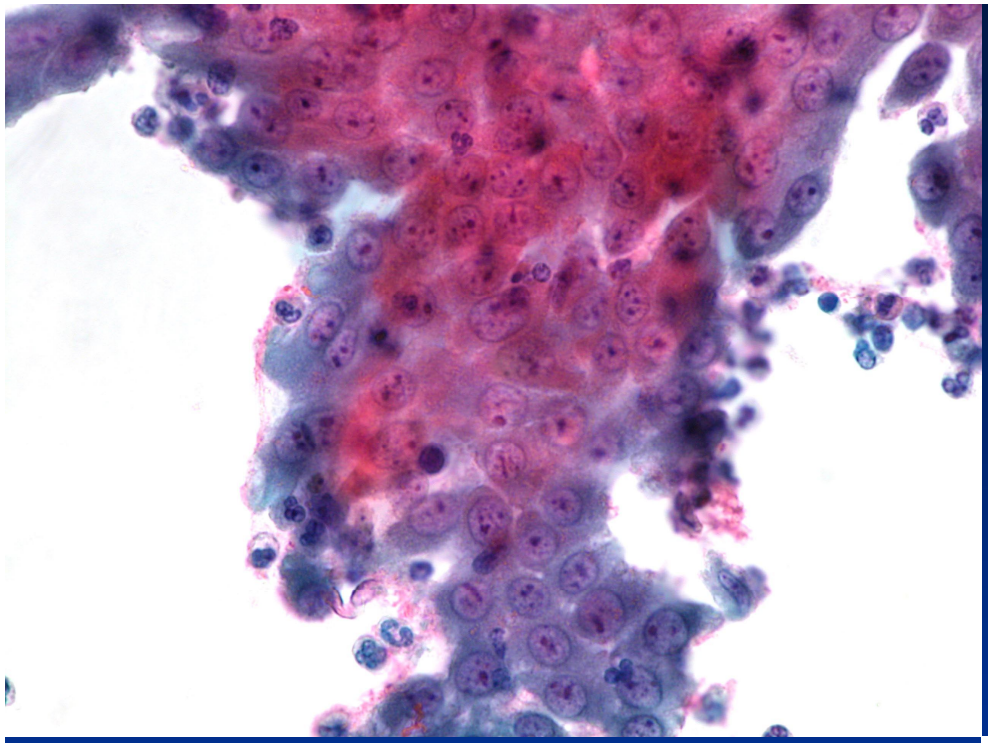


* Inflammatory benign diathesis
* Cytoplasm delicate, cyanophilic, no keratinization
* Cytoplasmic vacuoles containing neutrophils and nuclear debris
* Nuclei enlarged
* N/C ratio is only slightly or moderately Increased
* Nuclear chromatin finely granular and evenly distributed
* One or several prominent eosinophlilic nucleoli
* Mitotic figures may be present

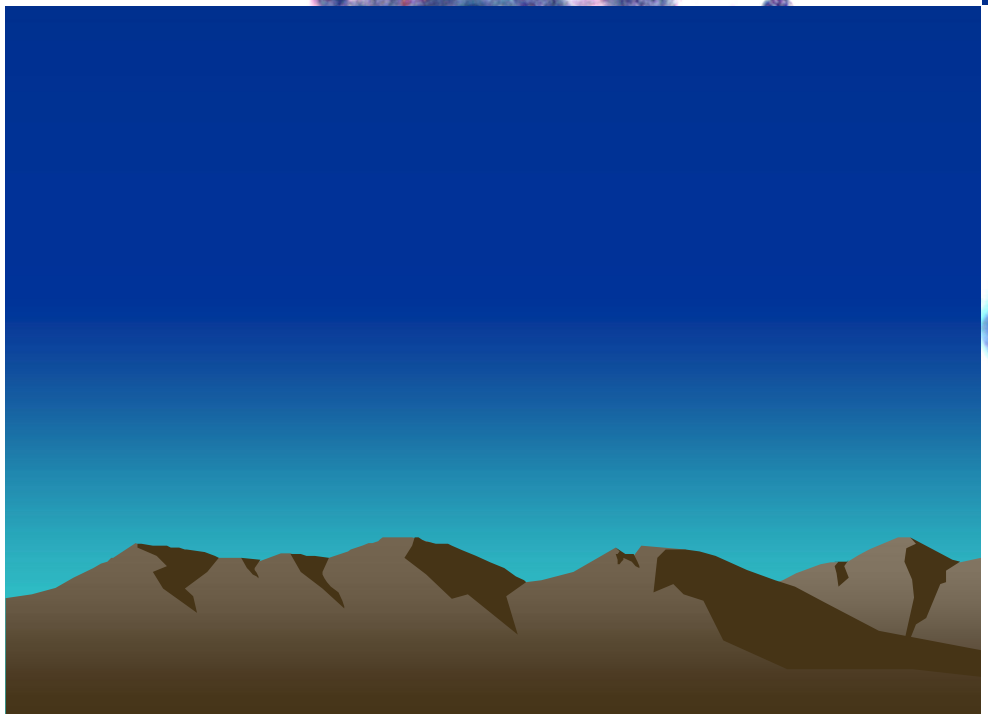
Differential Diagnosis of Repair Cells vs Non-keratinizing SCC

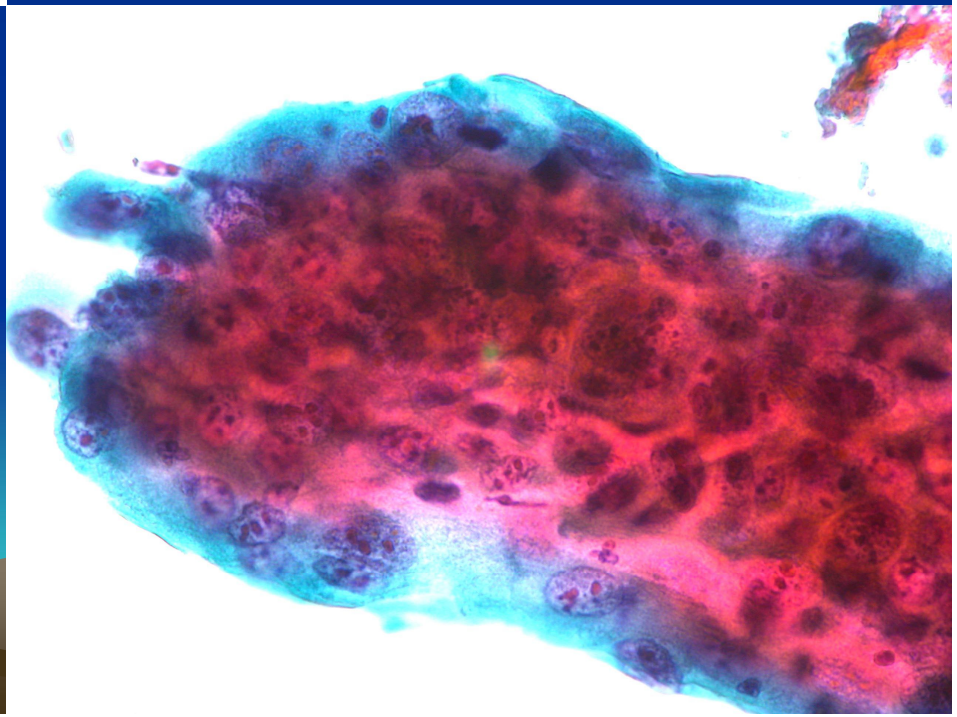
Features Favour Repair

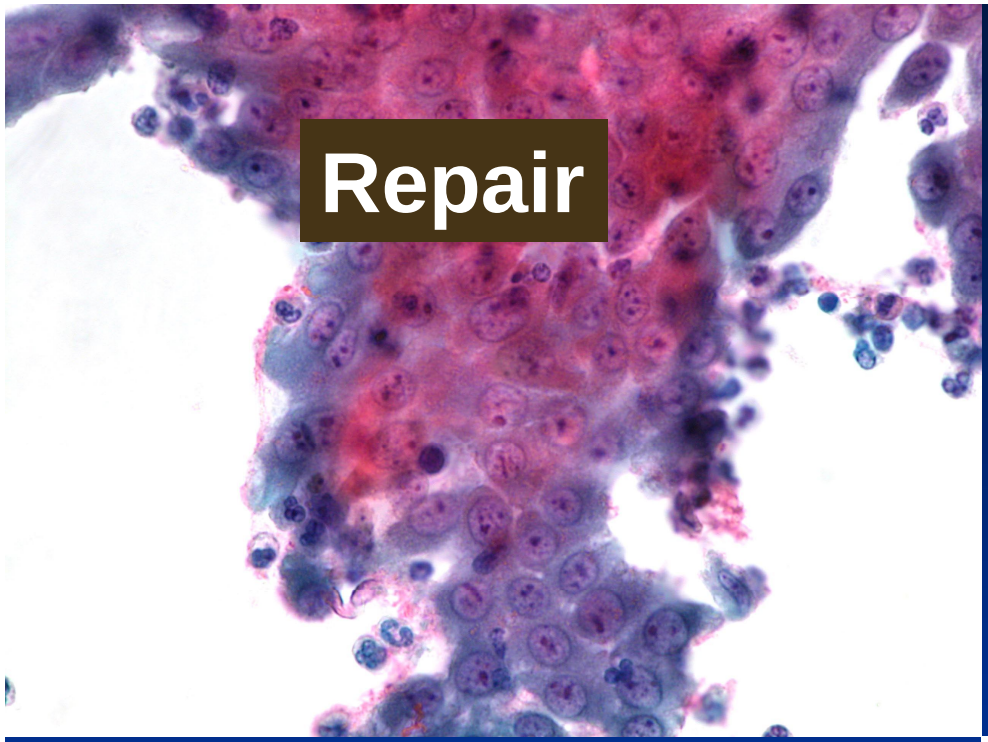
* Flat sheet arrangement of cells rather than syncitia or three dimensional clusters
* Lack of nuclear overlapping
* Lack or rarity of single cells
* Lack of tumour diathesis
* Fine Chromatin



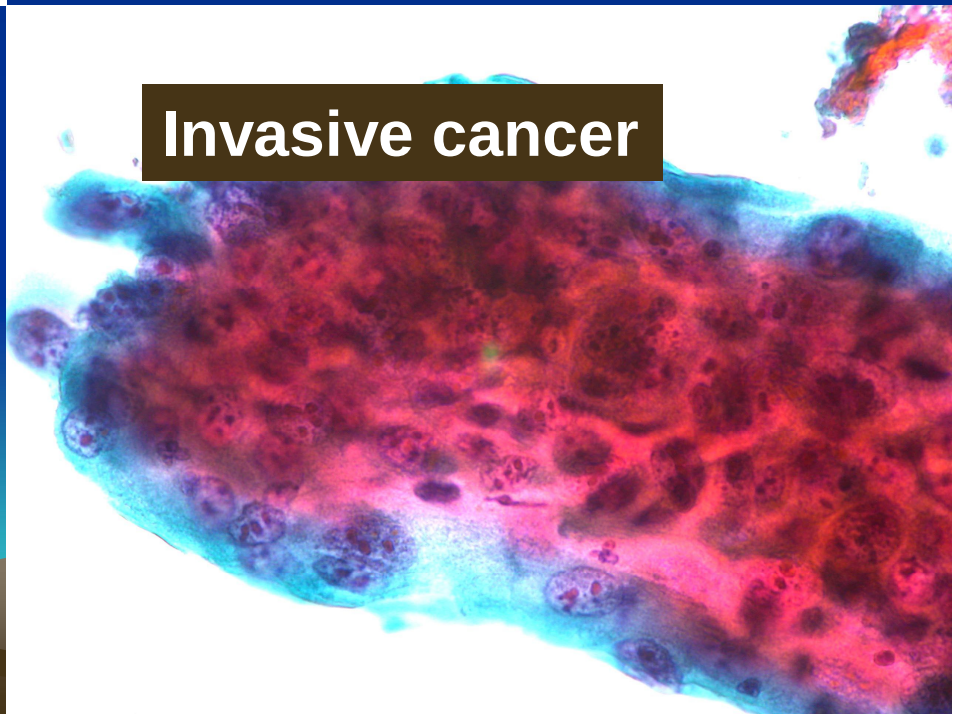
Net case 8
Spot the Difference: Repair or Invasive Cancer?



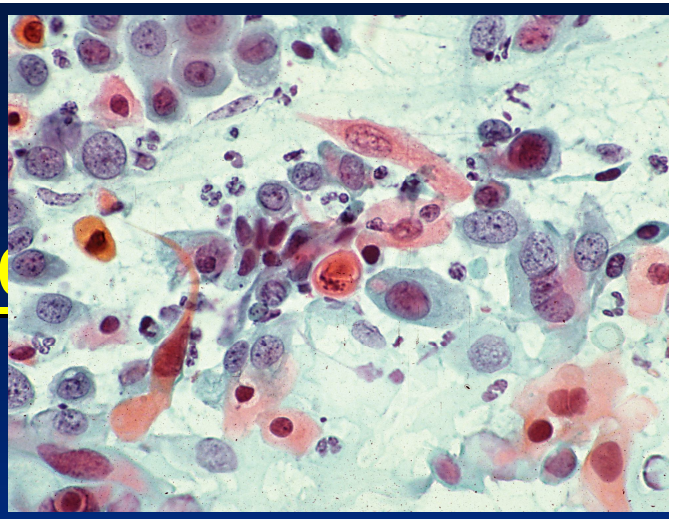




Net case 8 Spot the Difference: Repair or Invasive Cancer?

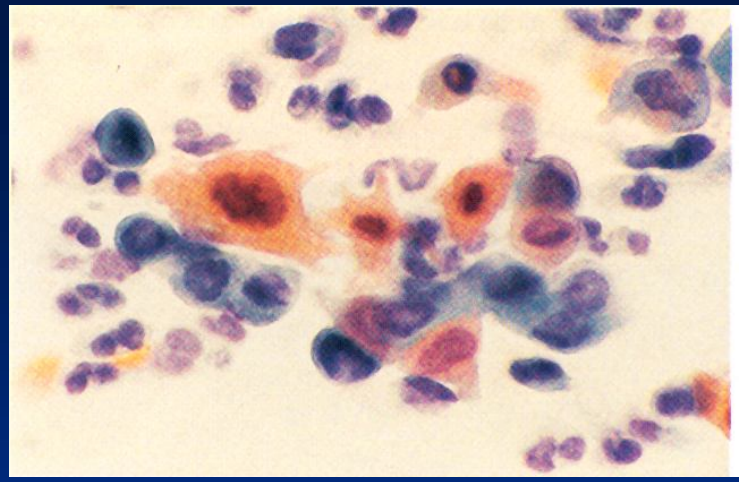


Keratinizing Squamous Cell Carcinoma



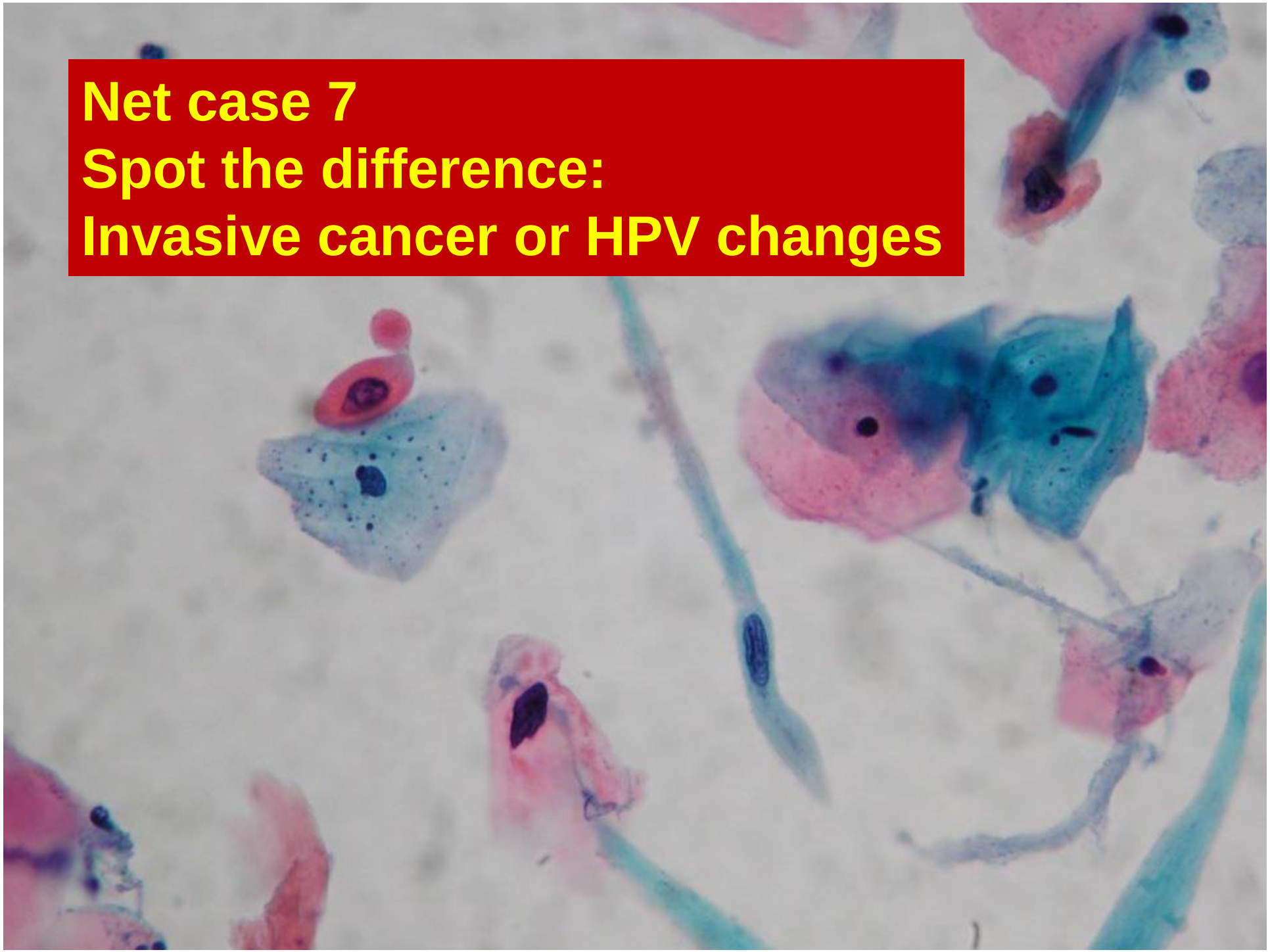
* Highly discohesive cells
* Spindle keratinized cells
* Keratinised cells with bizarre cytoplasmic forms
* Tadpole and caudate Cells
* Nuclei hyperchromatic with coarsely clumped, irregularly distributed chromatin
* Indistinct nucleoli
* Tumour diathesis maybe absent

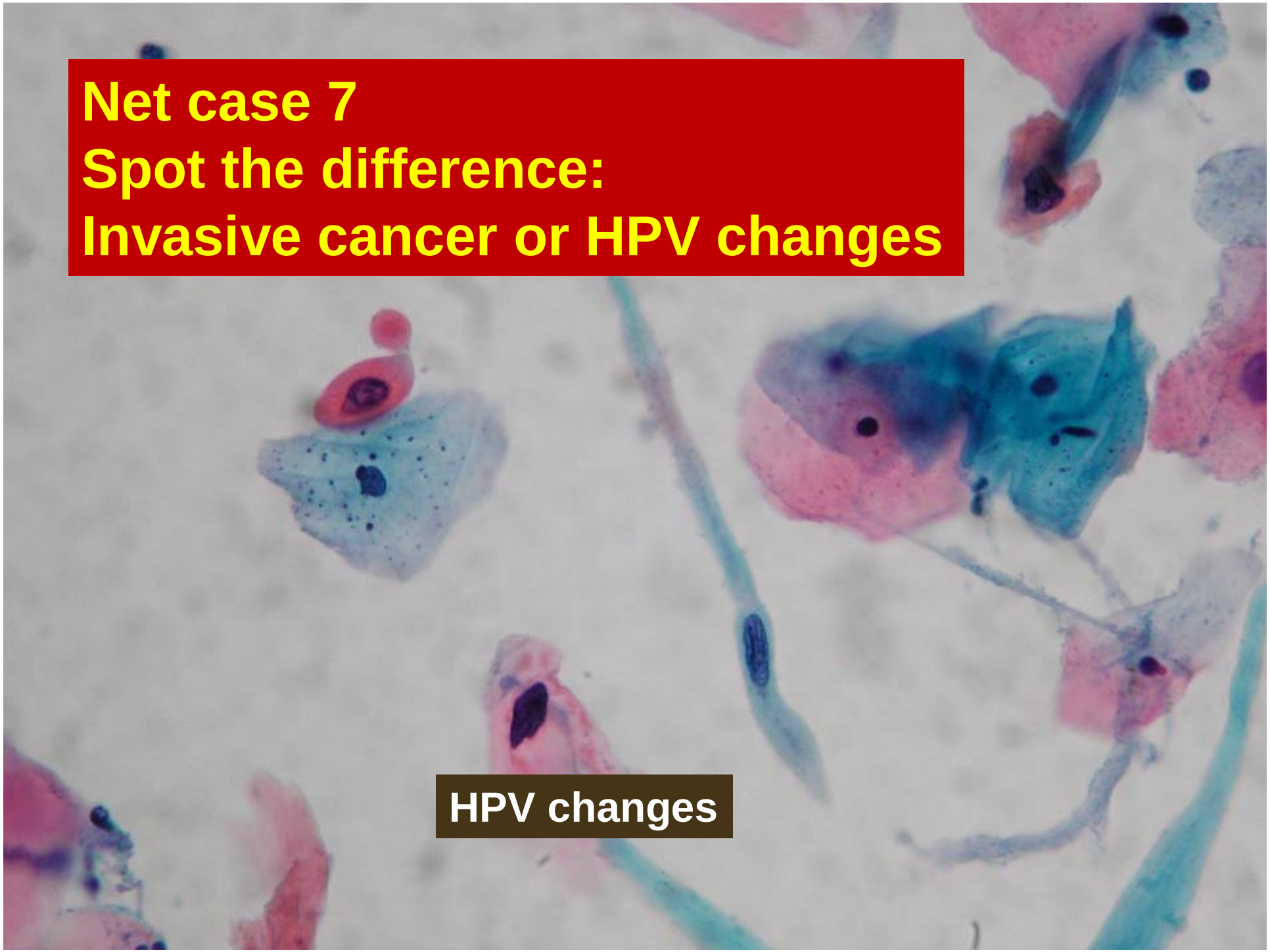
Differential Diagnosis of Keratinizing SCC



Atypical parakeratosis/ dyskeratosis

- individual cell may look malignant but are too small
- can occur in Sq.cell ca, inflammation, condyloma (wart) and keratinizing CIN


Net case 7
Spot the difference:
Invasive cancer or HPV changes


Net case 7
Spot the difference:
Invasive cancer or HPV changes
HPV changes

Keratinizing SCC

False negative result

*Infected,ulcerated tumour

*Scanty malignant cells

*Verrucous carcinoma

Verrucous Carcinoma

*Rare tumour

*Slow growing, exophytic tumour,

*rarely metastasize

*Cytology misleading

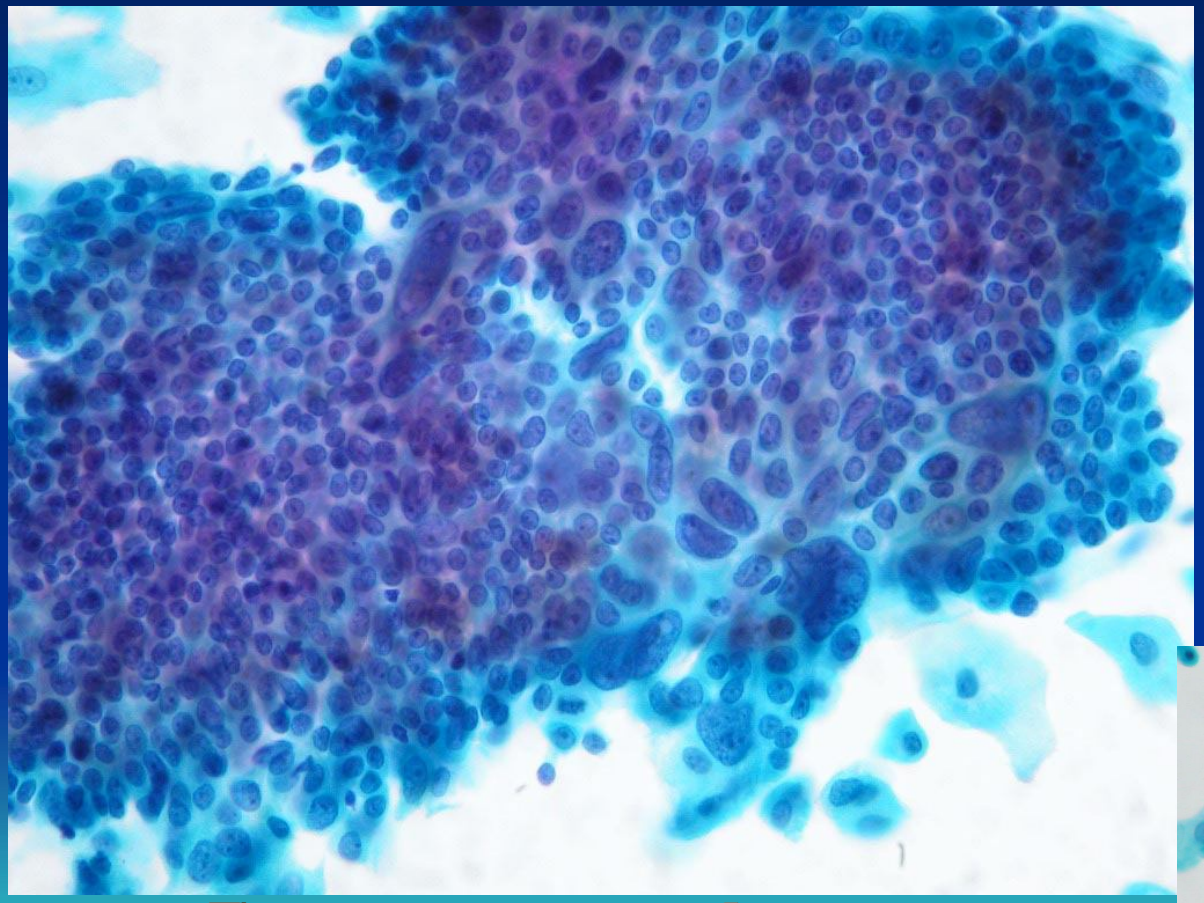
*Hyperkeratosis and parakeratosis

*Scanty dyskaryotic cells

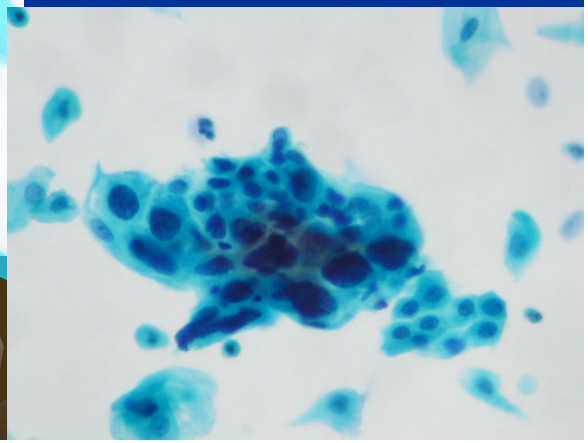
*Absence of Malignant nuclei

Post radiotherapy changes and Atypia of Atrophy

Can mimic recurrent dyskaryosis



Smudgy Chromatin Is the clue For the Diagnosis

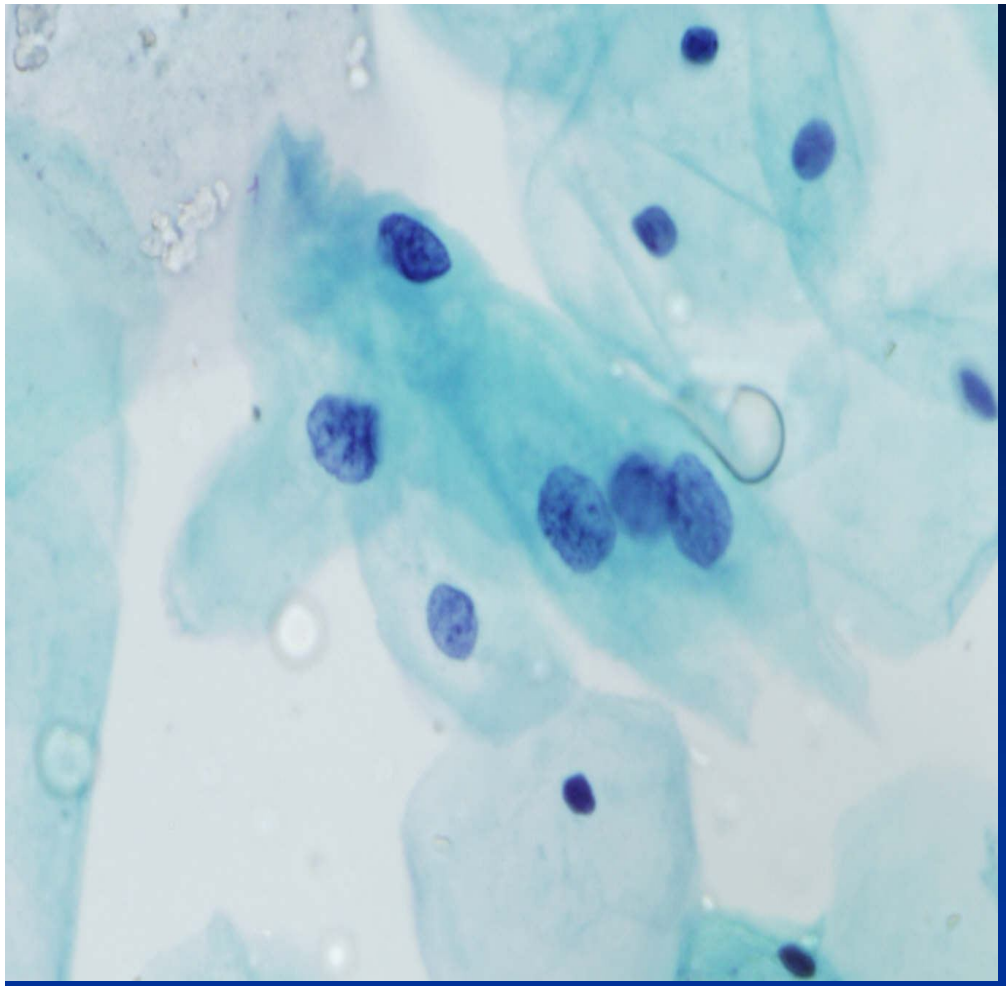


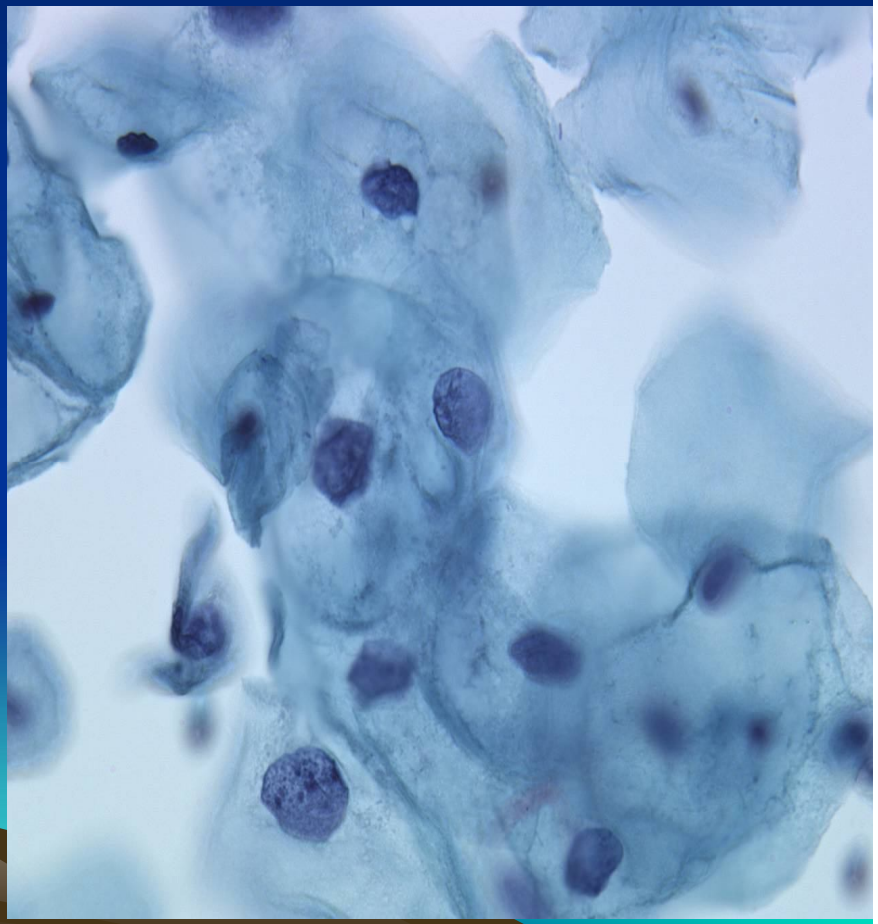
Acknowledgement

My special thanks to
Dr. Rana,Dr. Denton & Dr. Bijal Shah
From UK
&
Mr.Andrew Evered
From Wales Training School
For
Producing images and drawings
and
Writing some of the texts

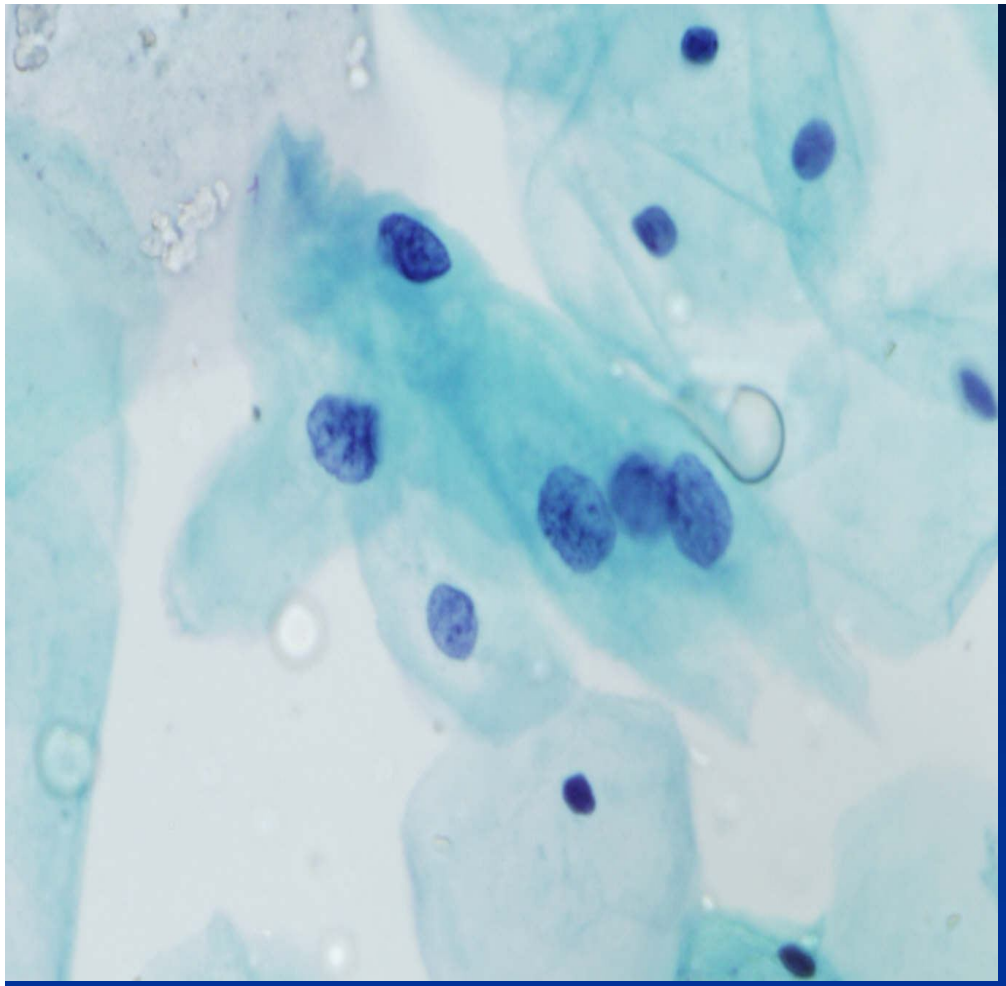
I have also used Hologic Cytyc Thinprep Images, BD Surepath Images Images from NHSCSP atlas and images and the tables from arts and Science of cytology book from Prof. DeMay for this presentation

Net case1
Spot The Difference
Neg, ASCUS or LSIL?

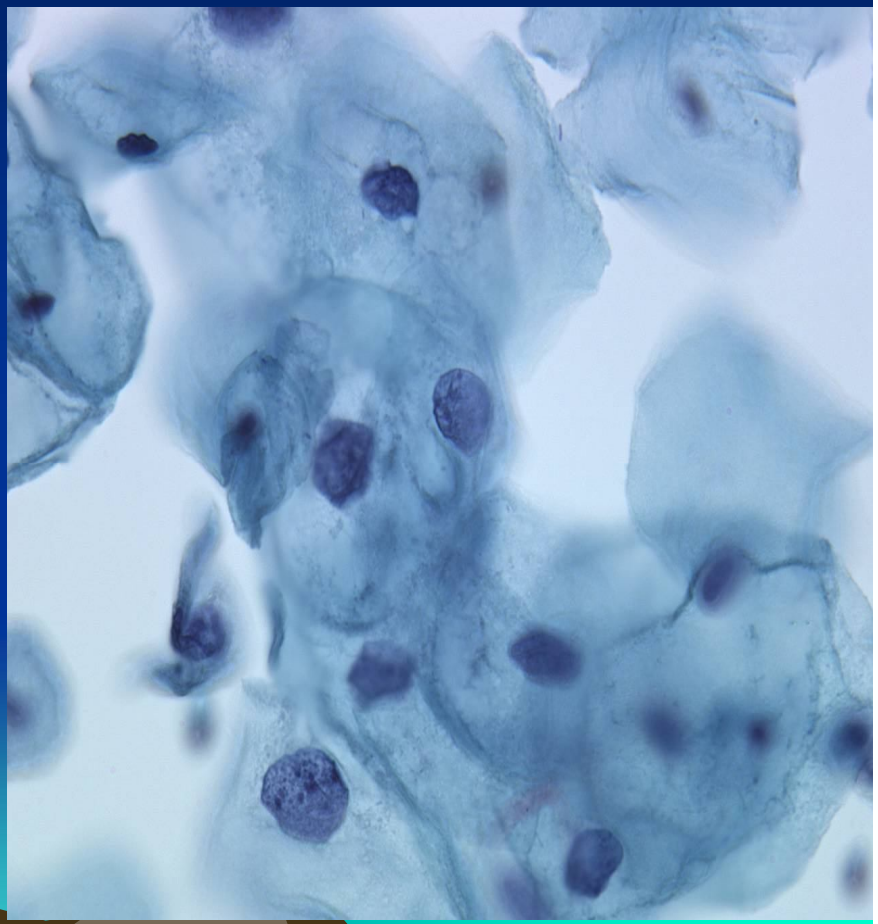




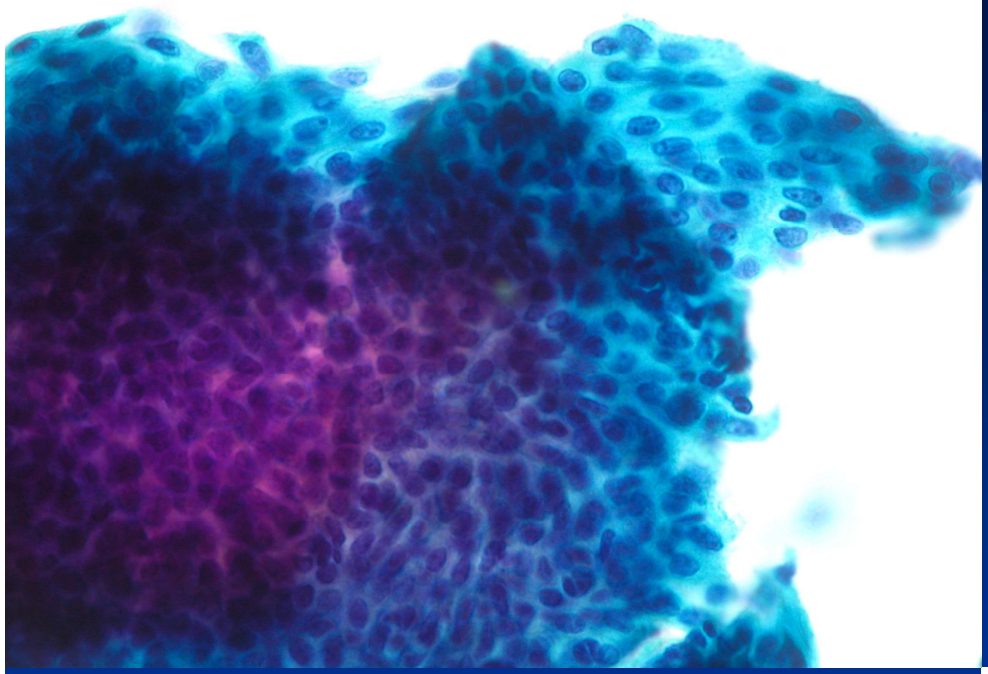
Net case1
Spot The Difference
Neg, ASCUS or LSIL?



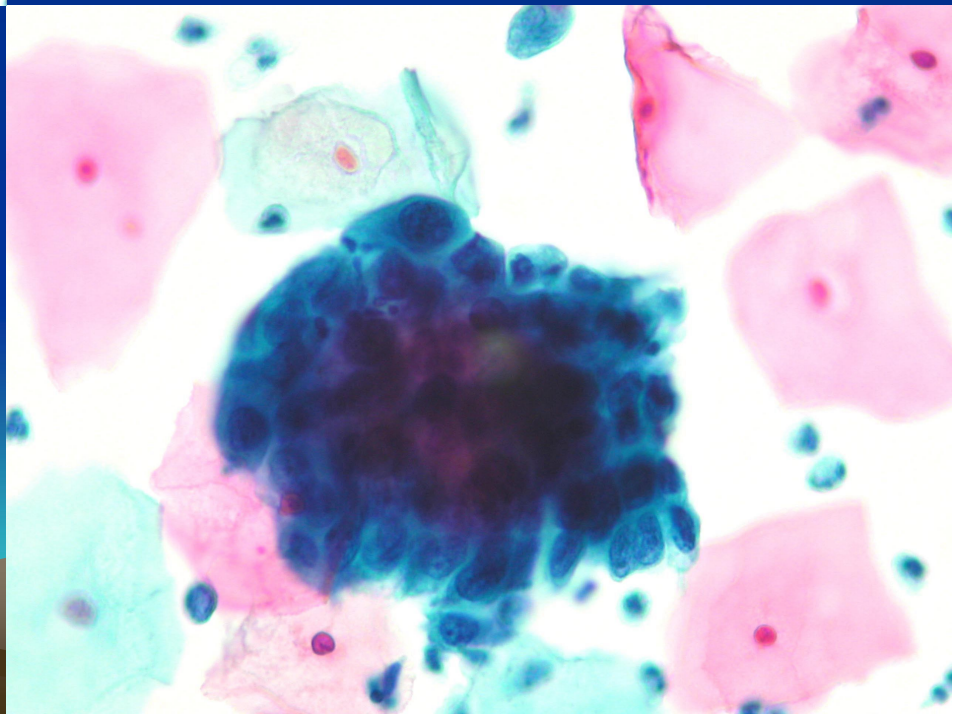
Mild Dyskaryosis (LSIL)

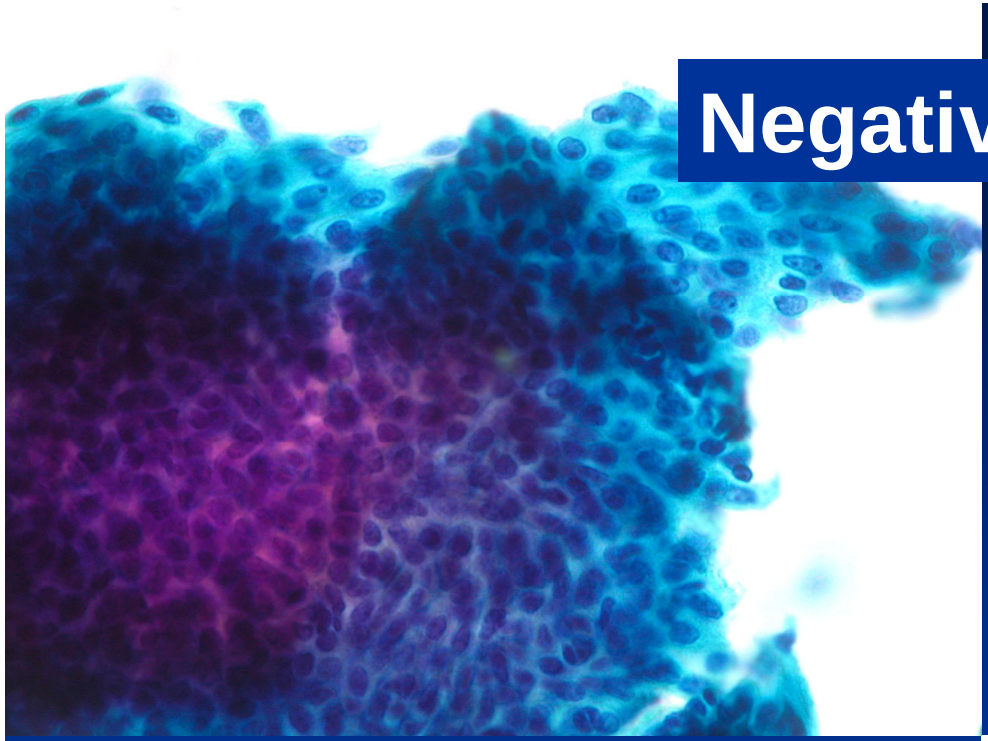


Borderline changes (ASCUS)



Net case 2
HCG Pitfall
Spot the Difference:
Negative or HSIL

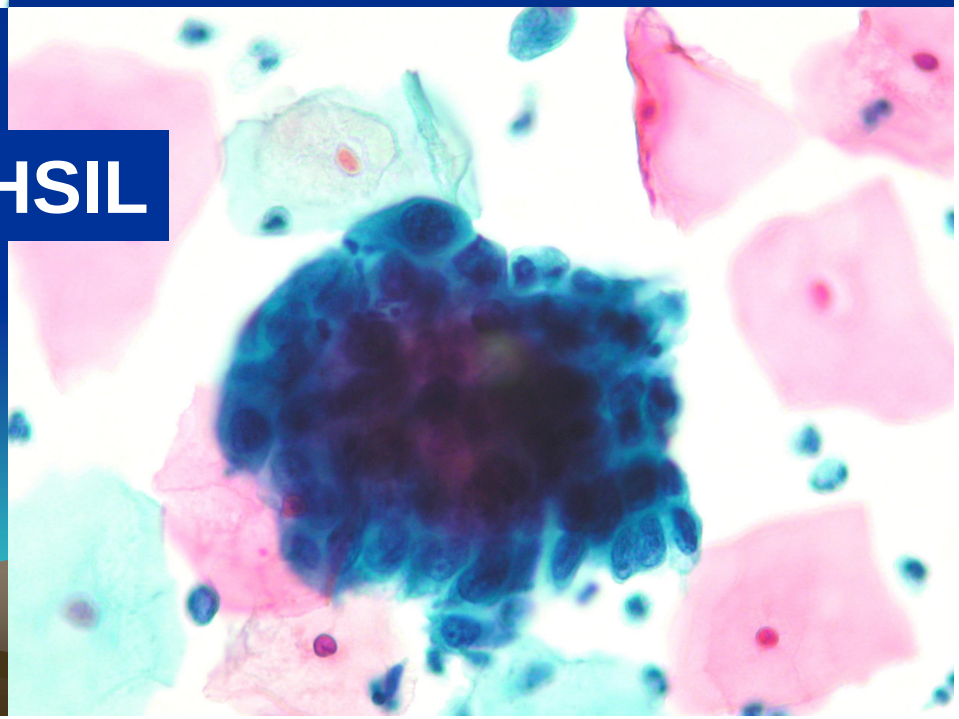




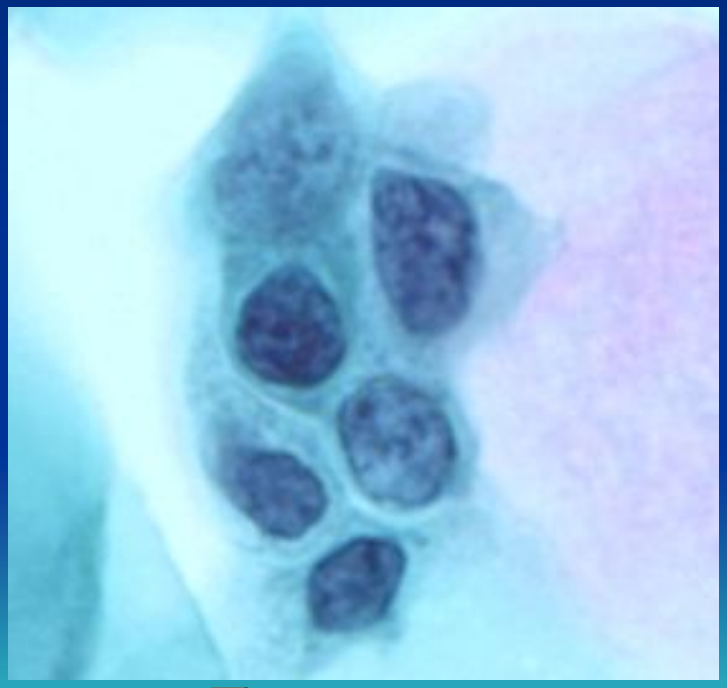
Negative atrophy

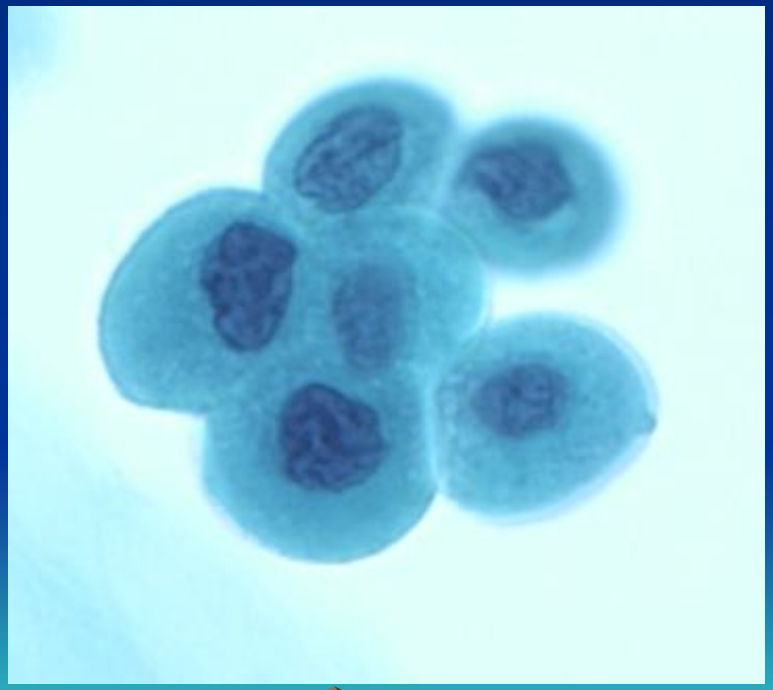
Net case 2
HCG Pitfall
Spot the Difference:
Negative or HSIL

HSIL



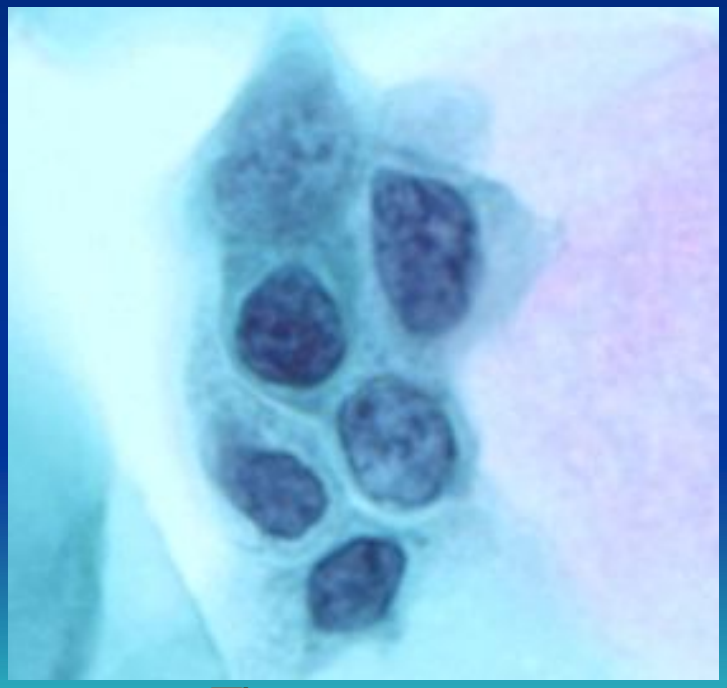
Net case 3
Spot The Difference
Metaplastic Cells
Neg, ASCUS or SIL?



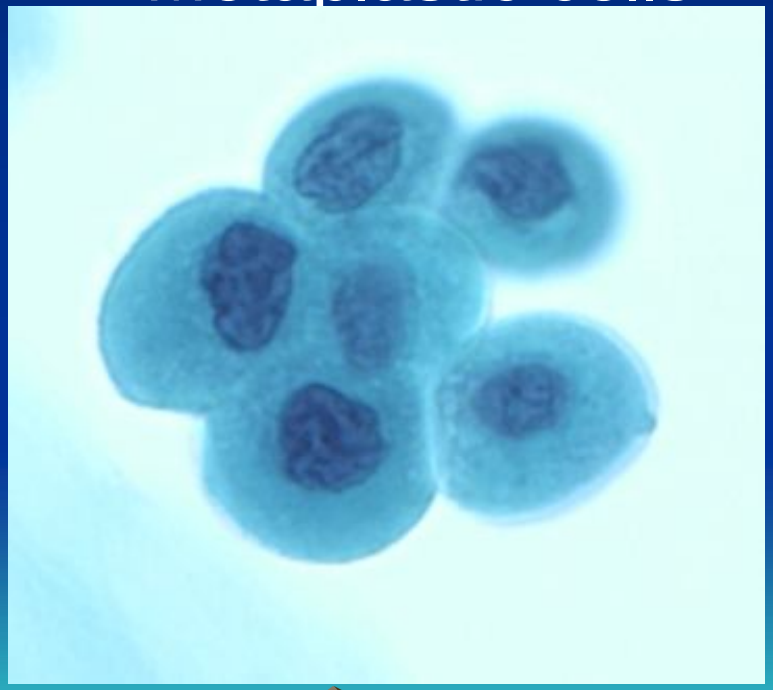


Net case 3
Spot The Difference
Metaplastic Cells
Neg, ASCUS or SIL?

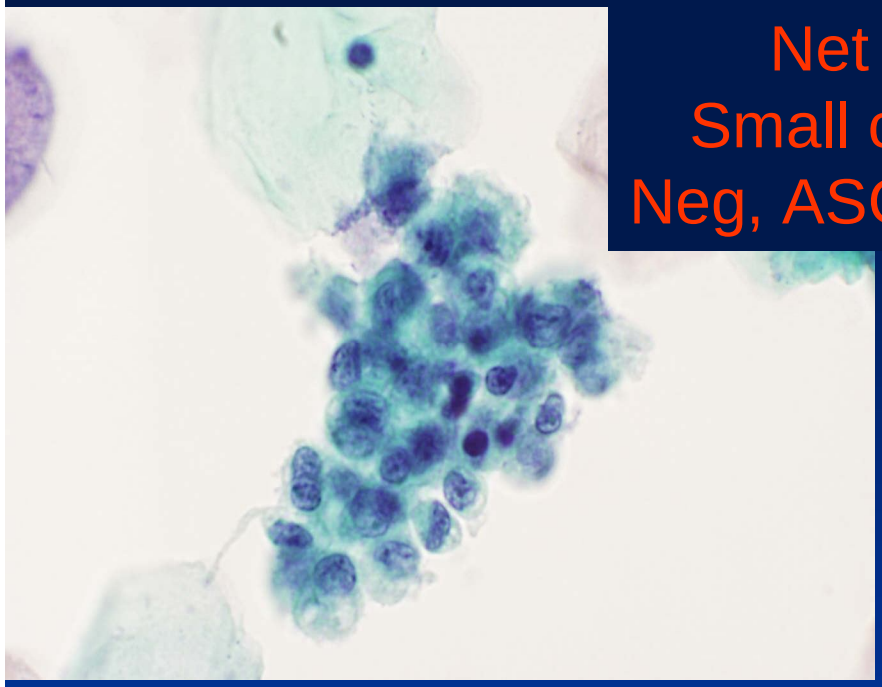
- Dyskaryosis (HSIL)

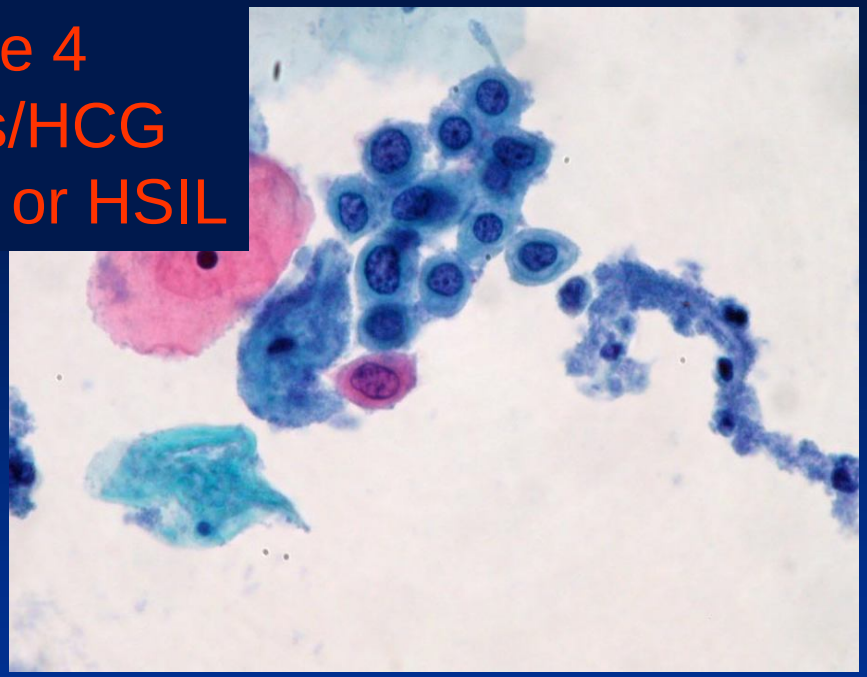


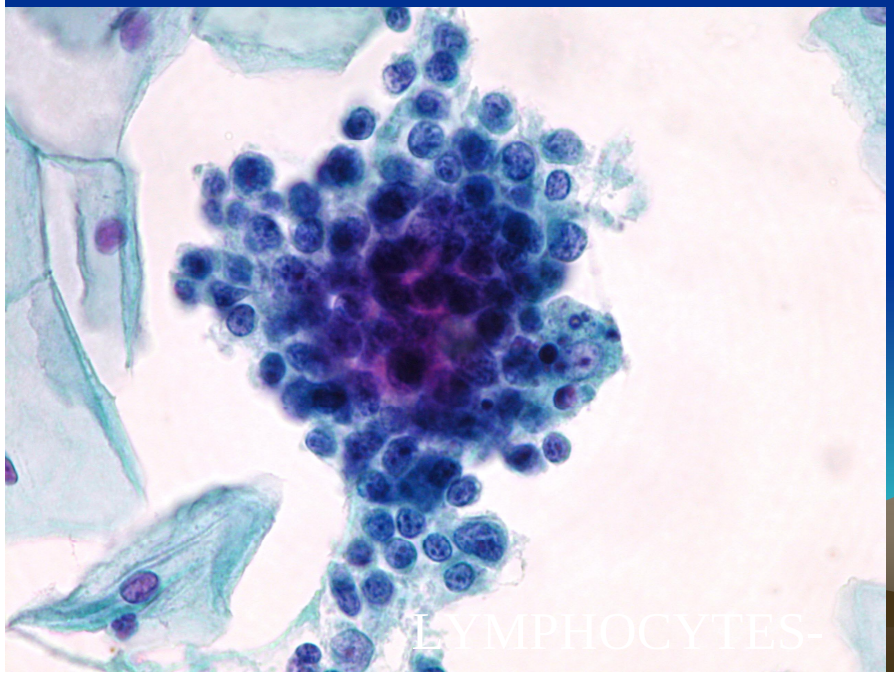
- Neg.
- Metaplastic cells

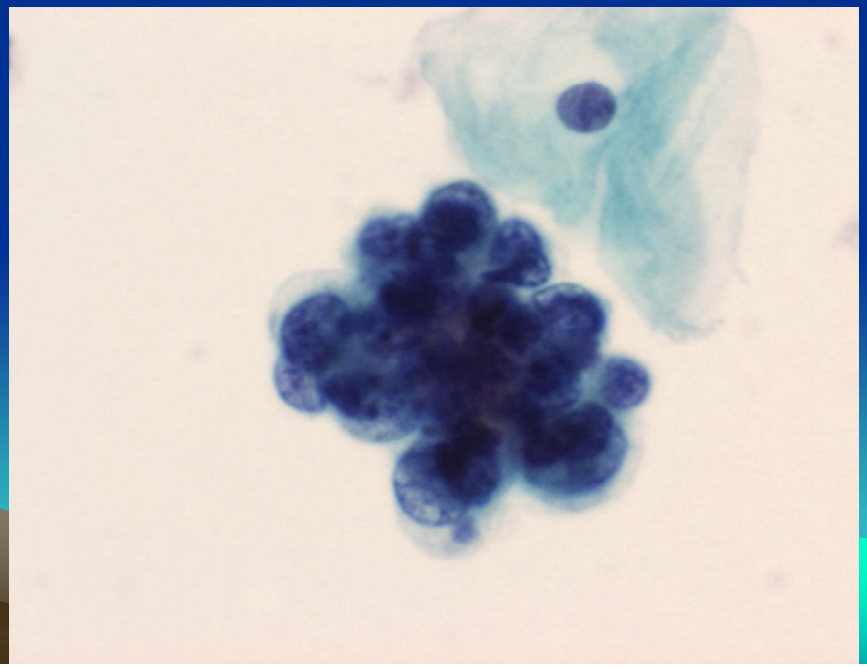


Net case 4
Small cells/HCG
Neg, ASC-H or HSIL





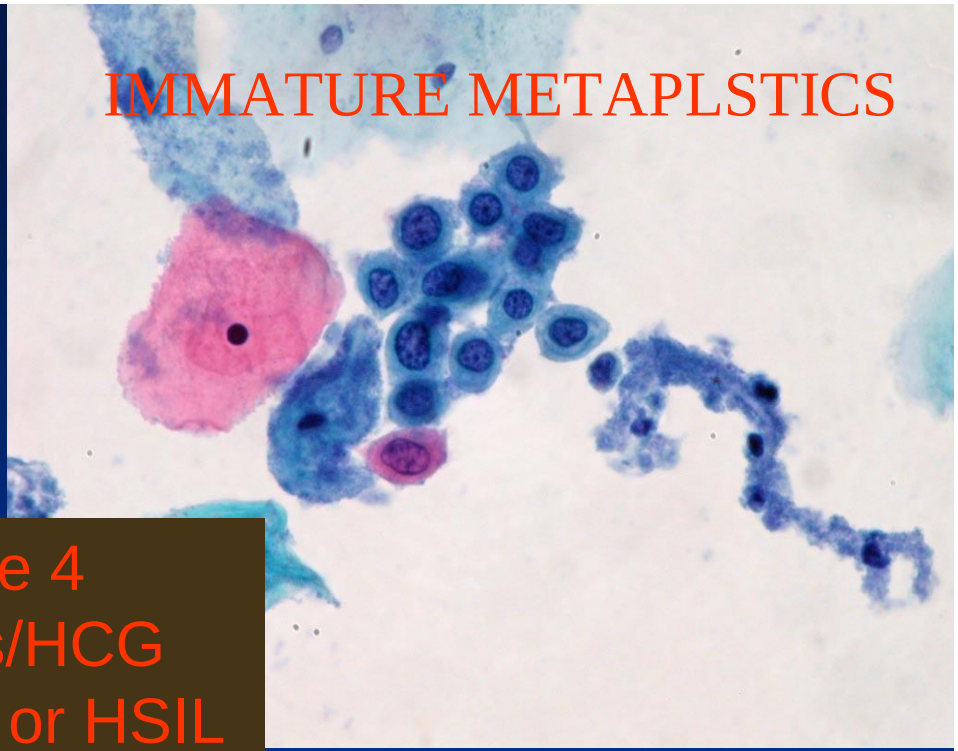




LYMPHOCYTES-

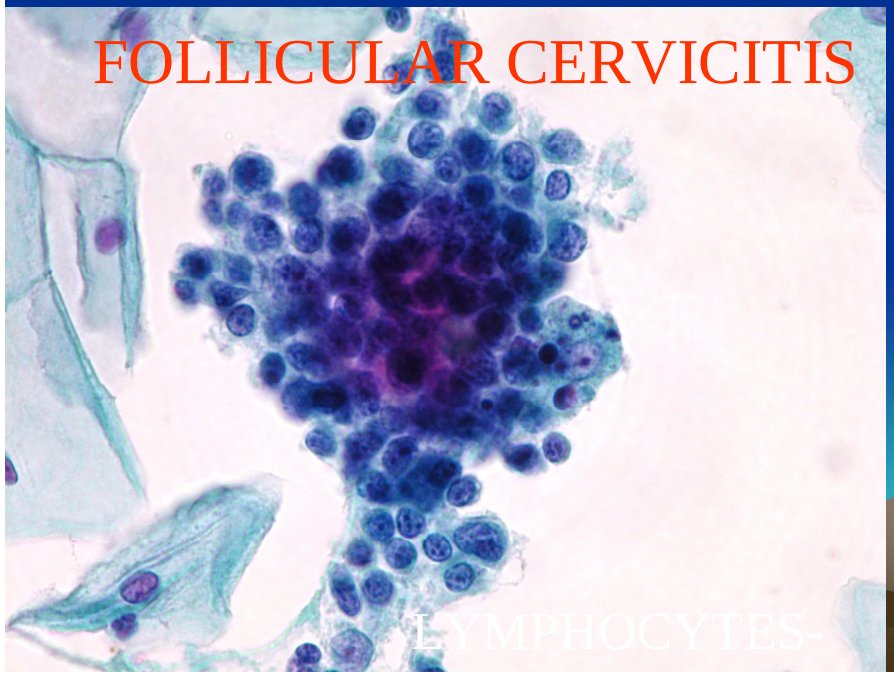
HISTIOCYTES,

IMMATURE METAPLSTICS

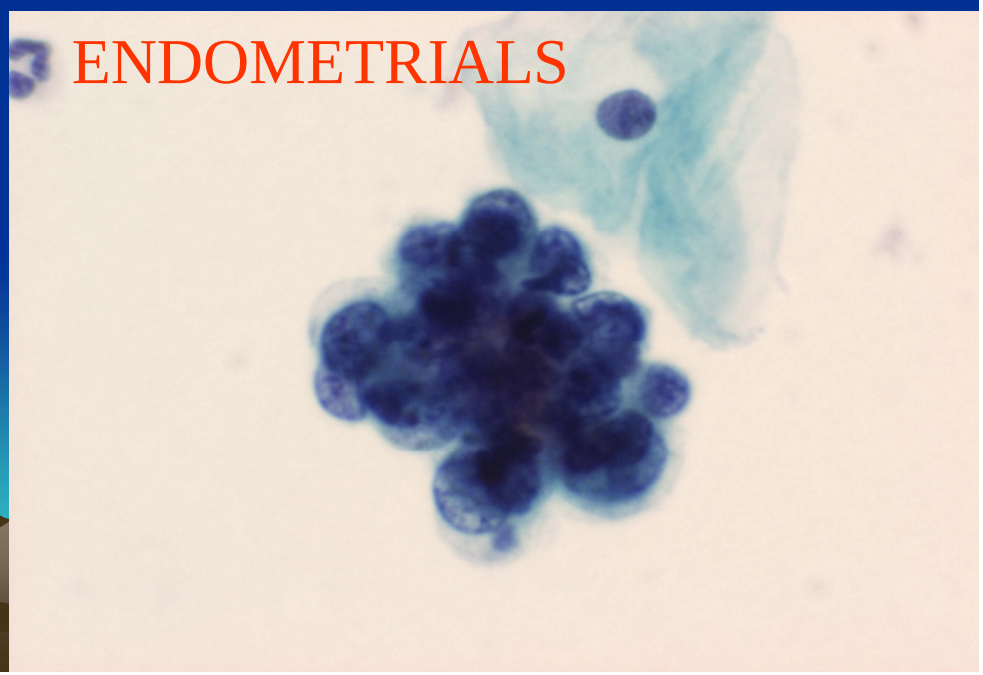


Net case 4
Small cells/HCG
Neg, ASC-H or HSIL

FOLLICULAR CERVICITIS

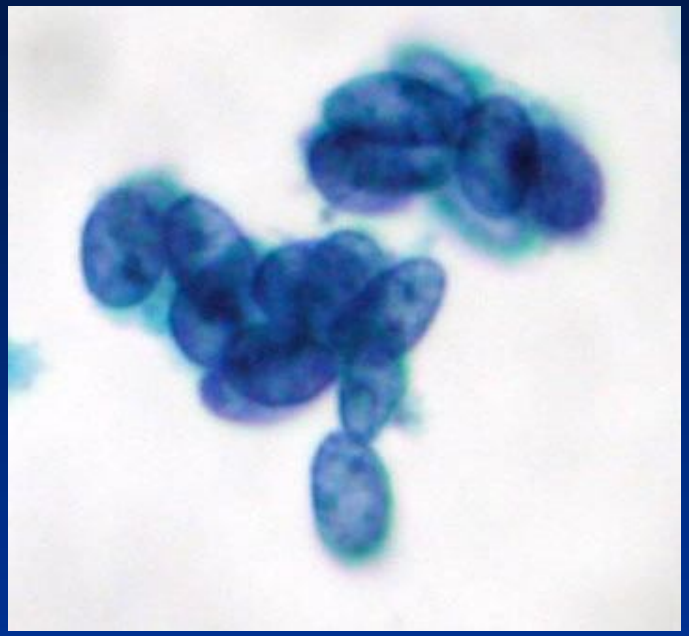


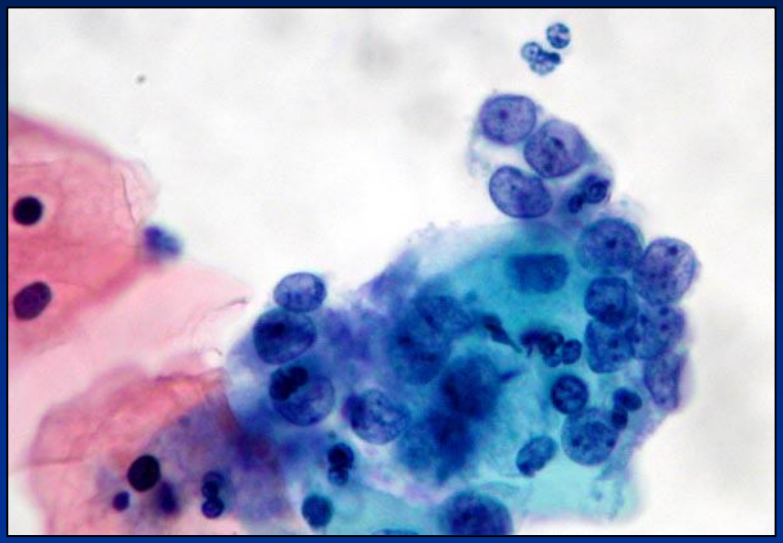
ENDOMETRIALS

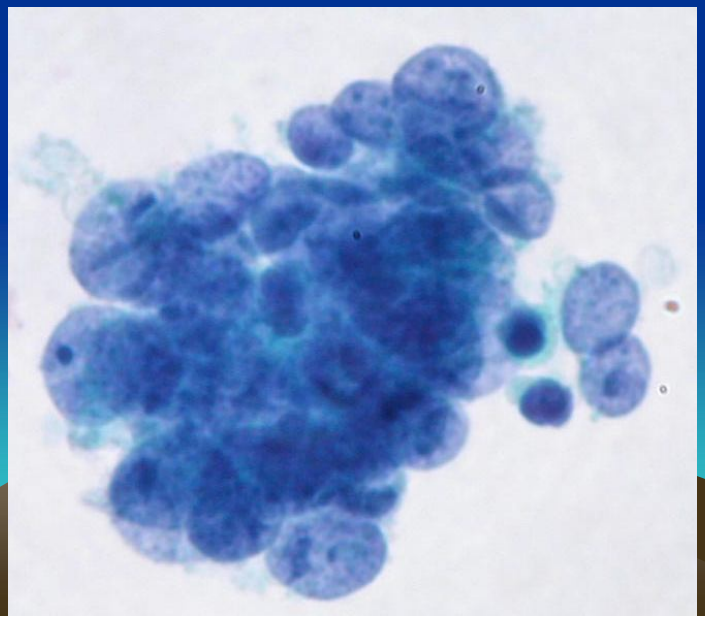


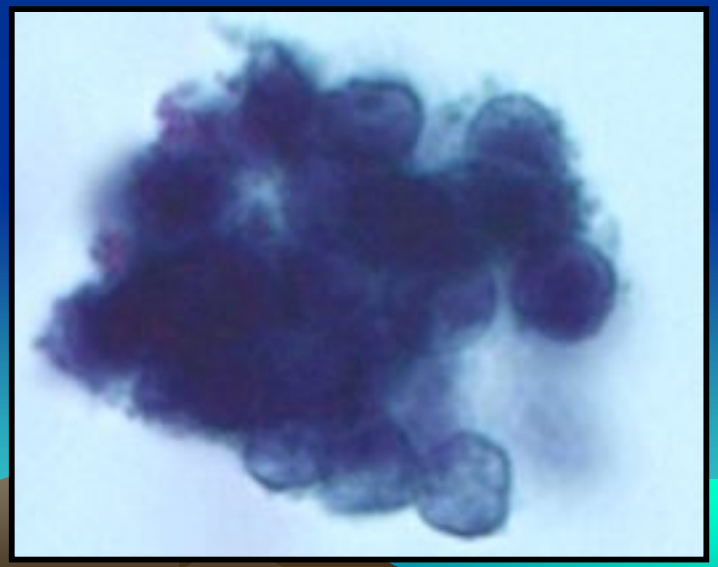
LYMPHOCYTES-

Net case 5
Spot the Difference In Bare nuclei
Neg, ASCUS, ASC-H or SIL



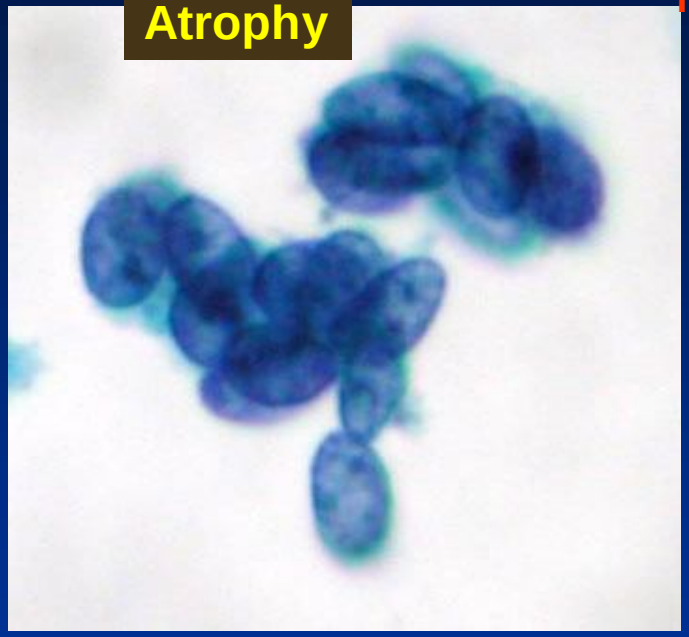




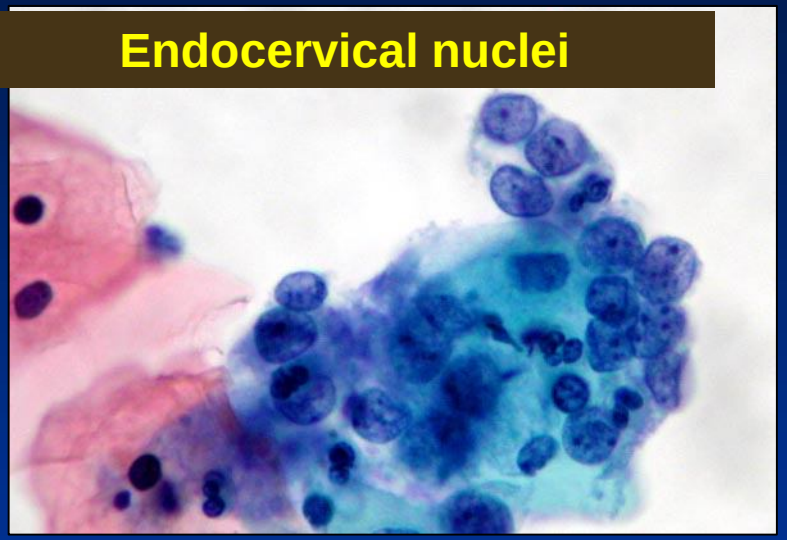


Net case 5
Spot the Difference In Bare nuclei
Neg, ASCUS, ASC-H or SIL

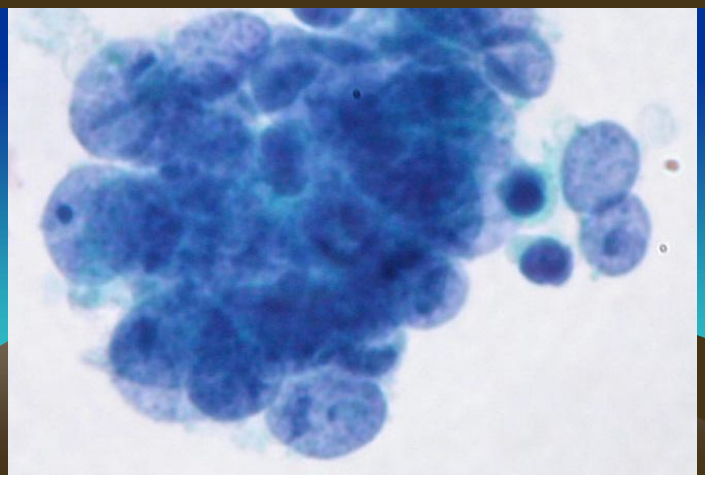
Atrophy



Endocervical nuclei

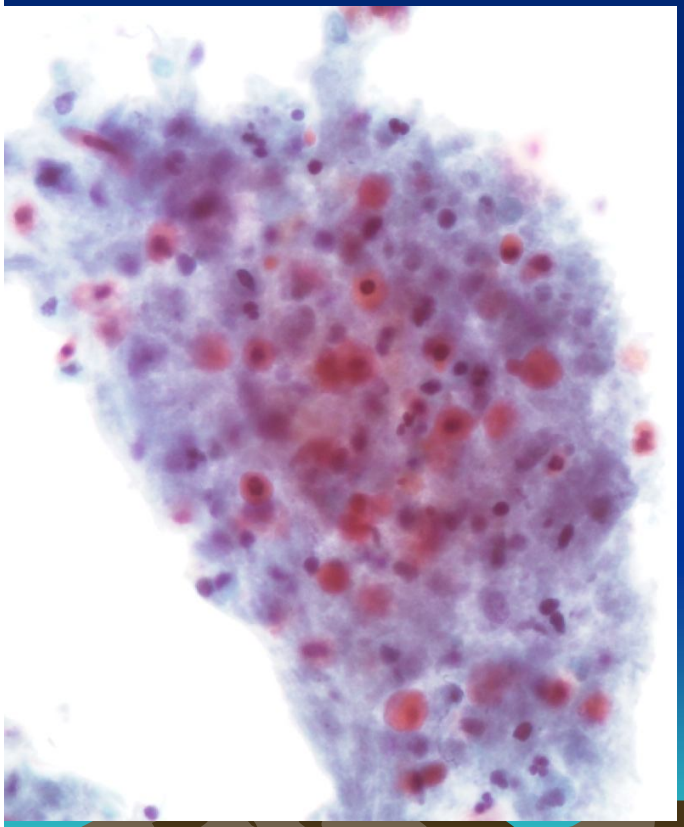


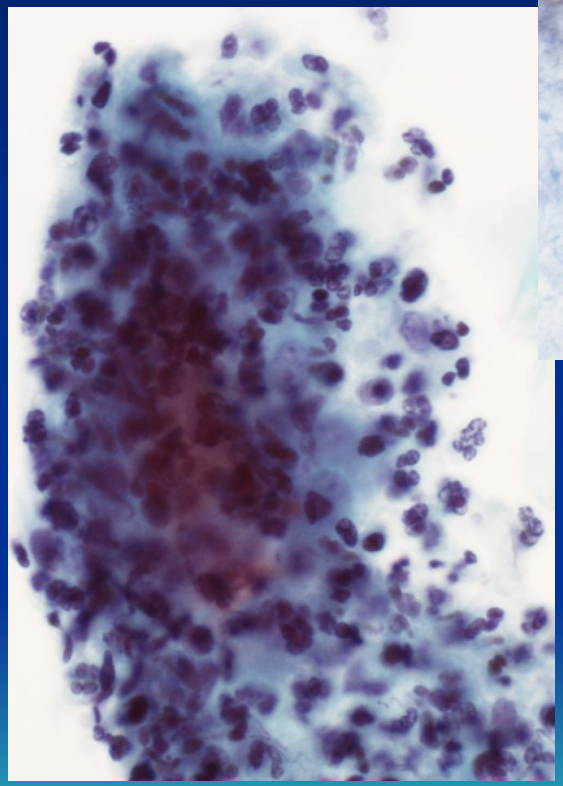
HSIL/High Grade Dyskaryosis

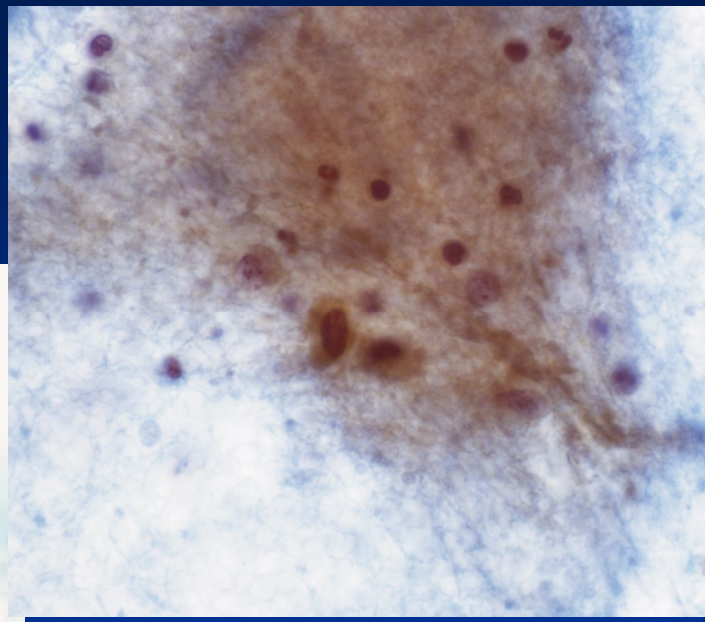


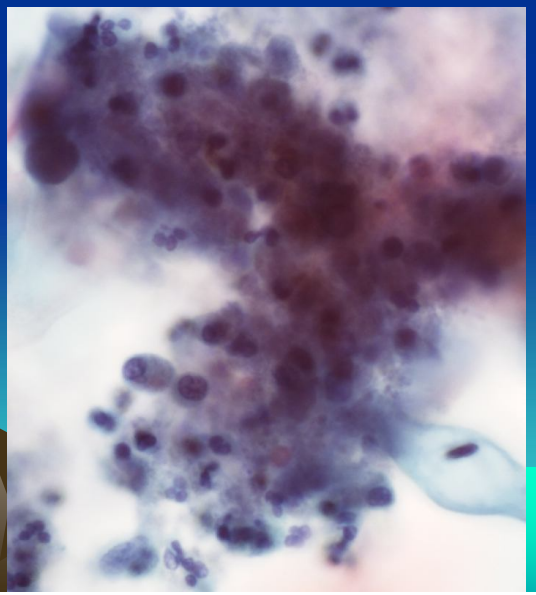
Tamoxifen changes

Net case 6
Diathesis
Spot The Difference

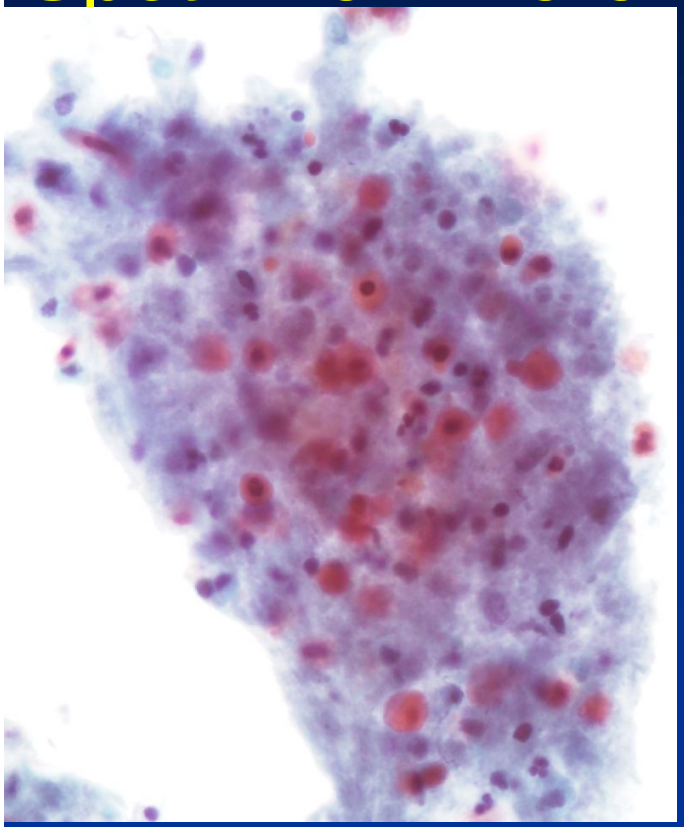




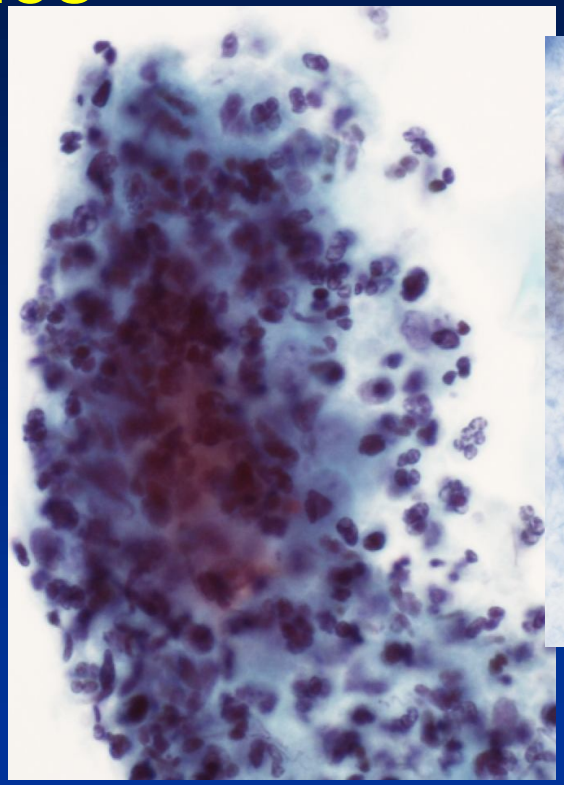




Net case 6
Spot The Difference

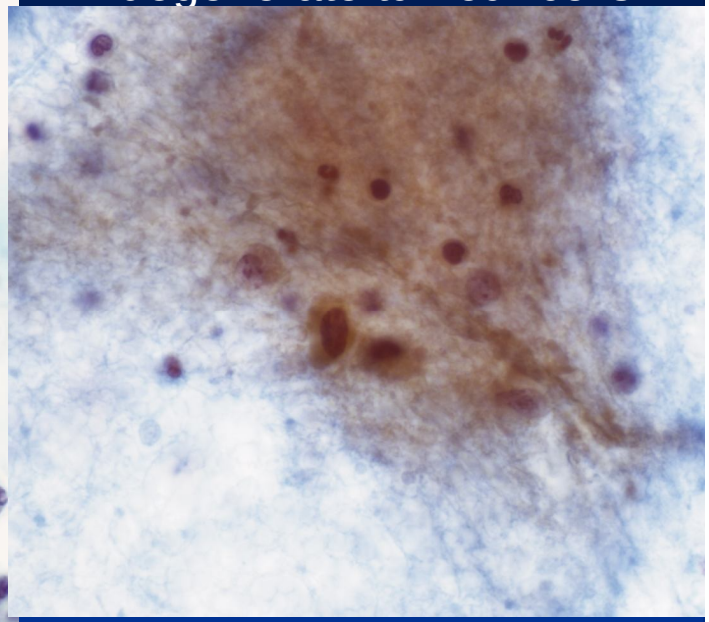


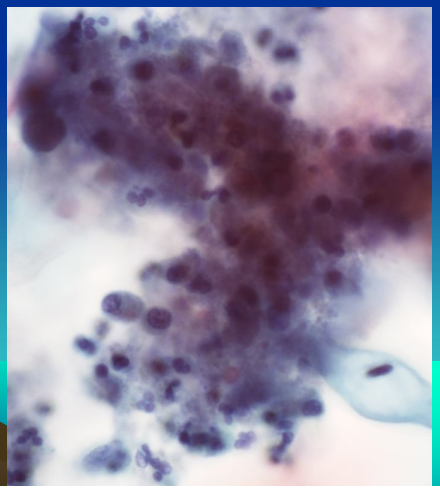
Atrophic vaginitis
Red Atrophy



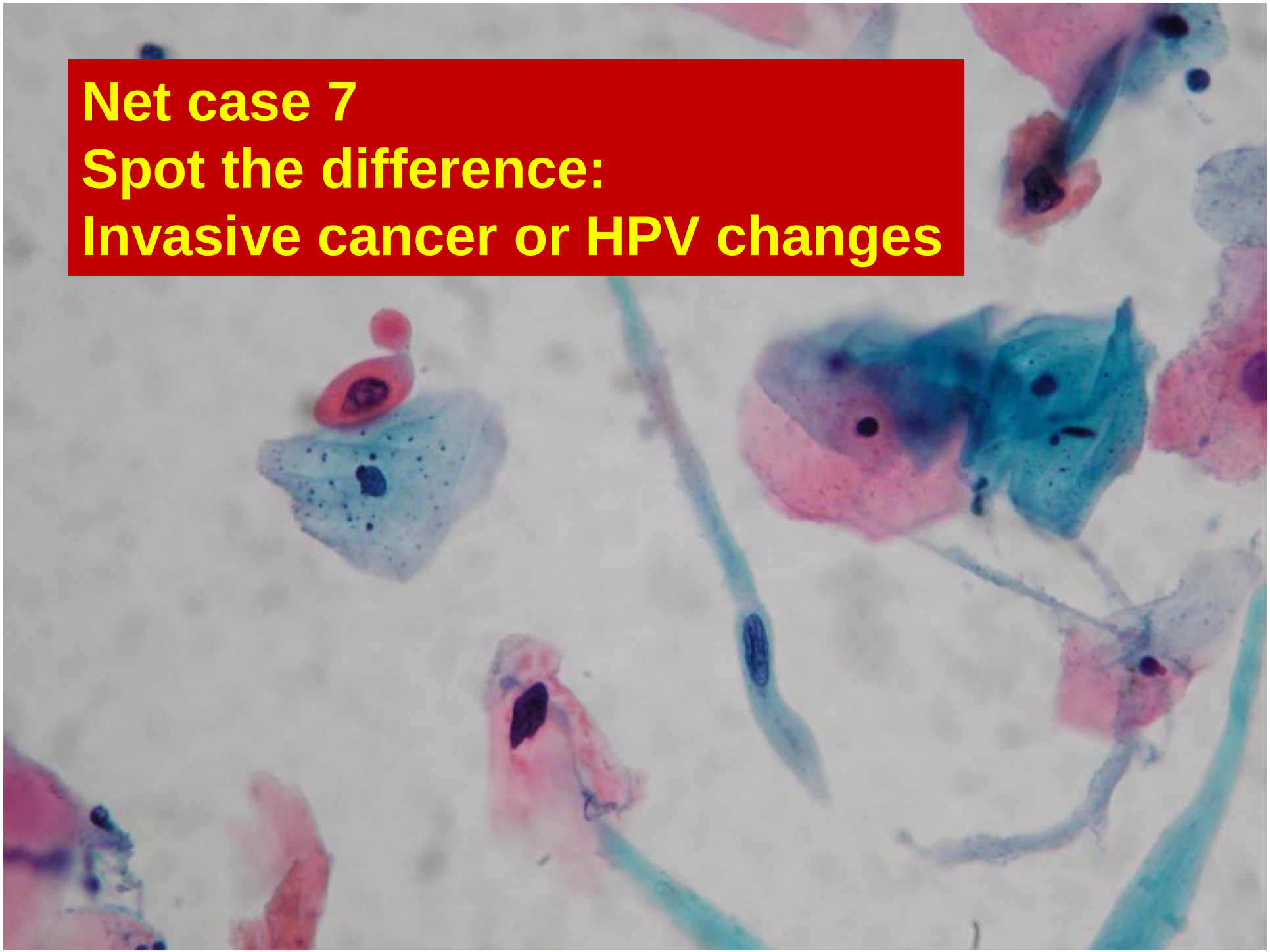
Benign Diathesis
Trichomonas

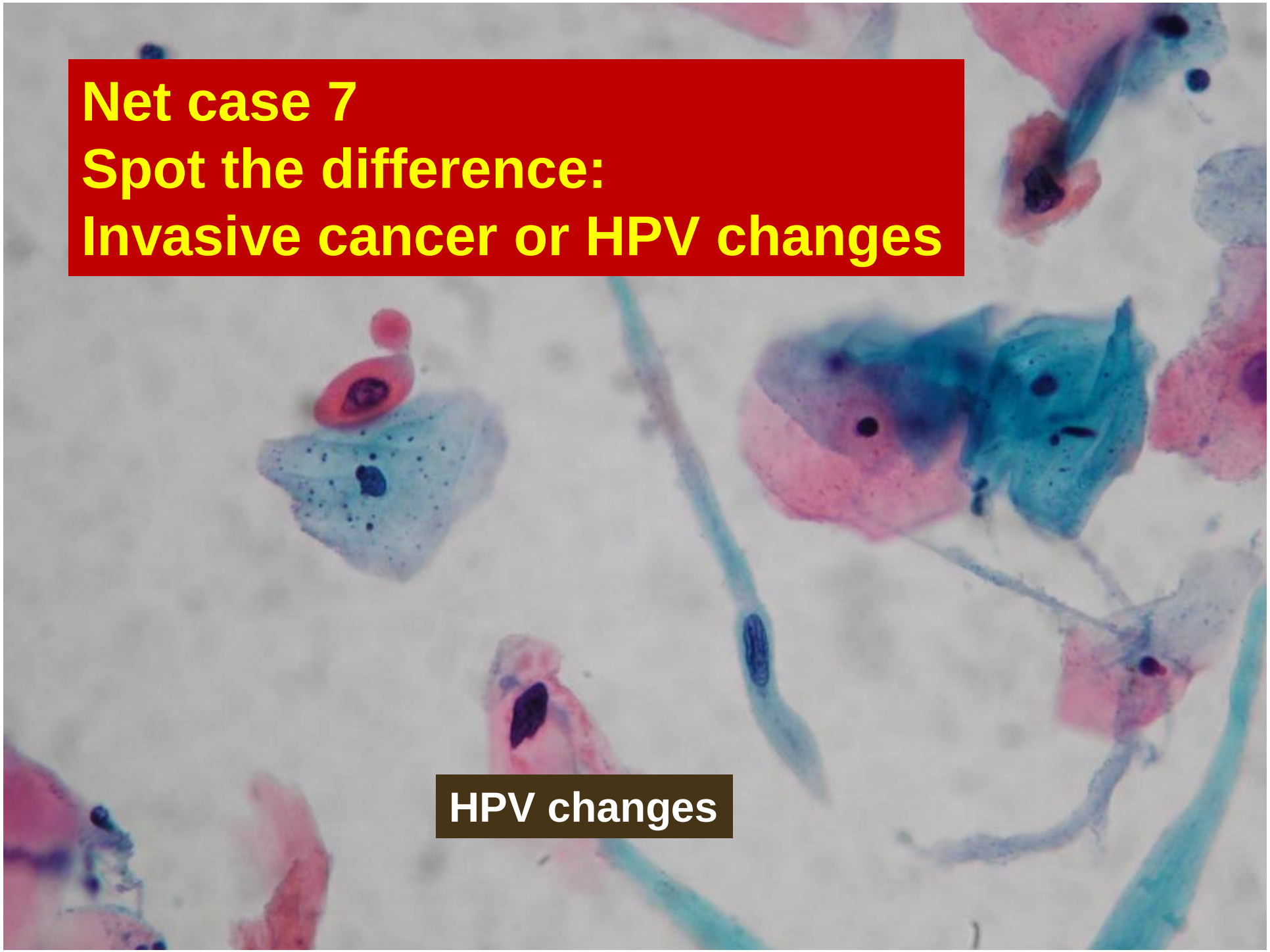
Tumour Diathesis
Fibrillar material
with ratty appearance and
degenerate tumour cells

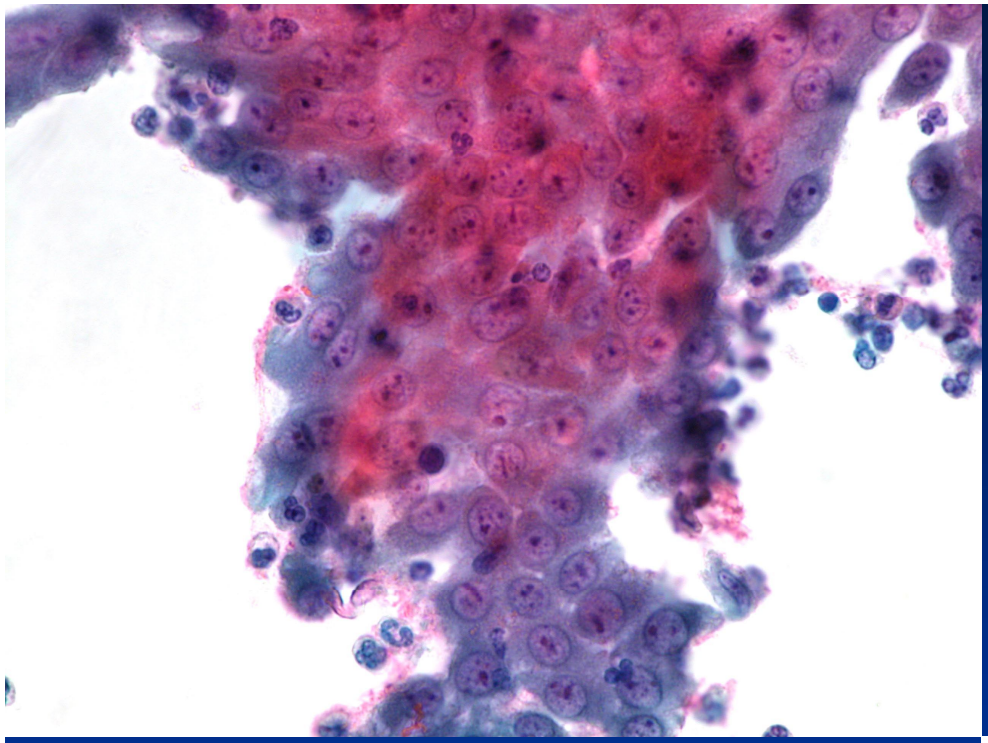




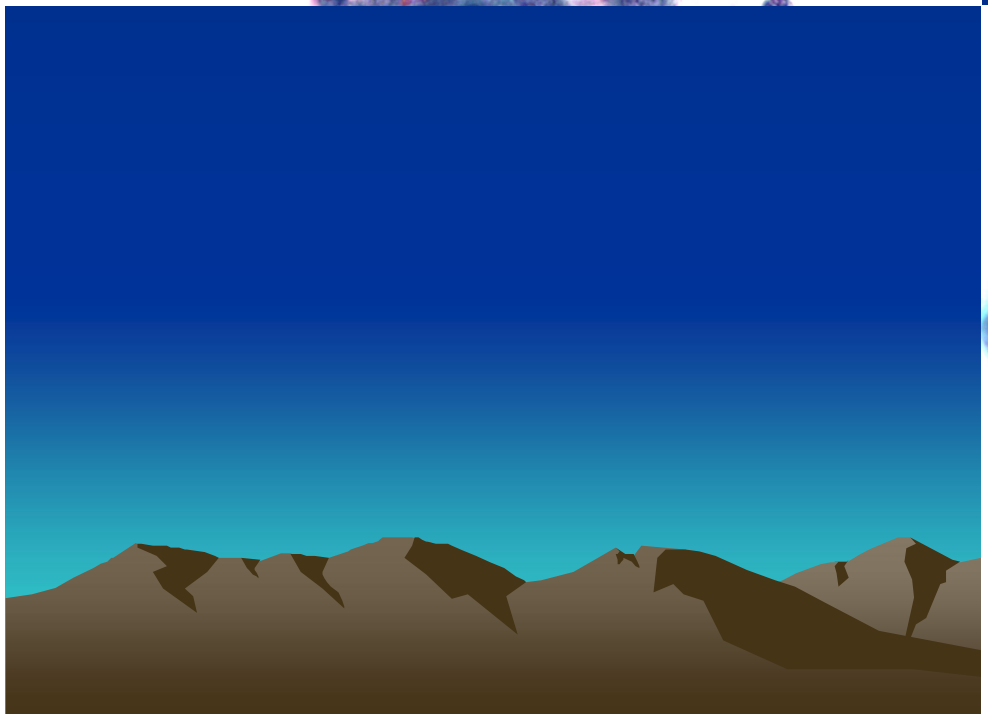
Menstrual Smear
Day 6th of cycle

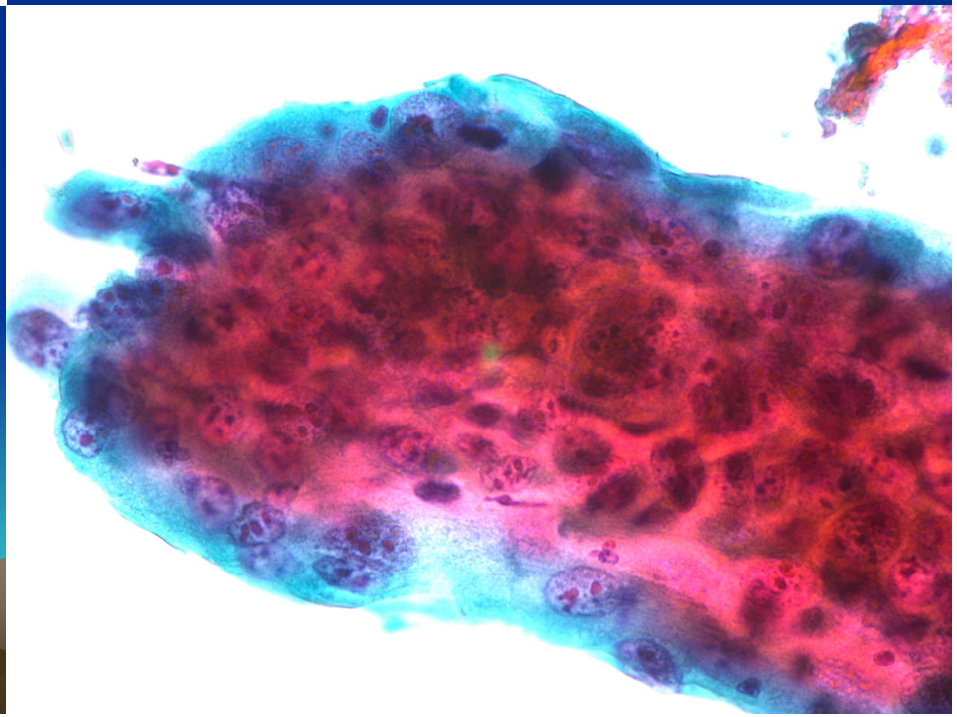

Net case 7
Spot the difference:
Invasive cancer or HPV changes

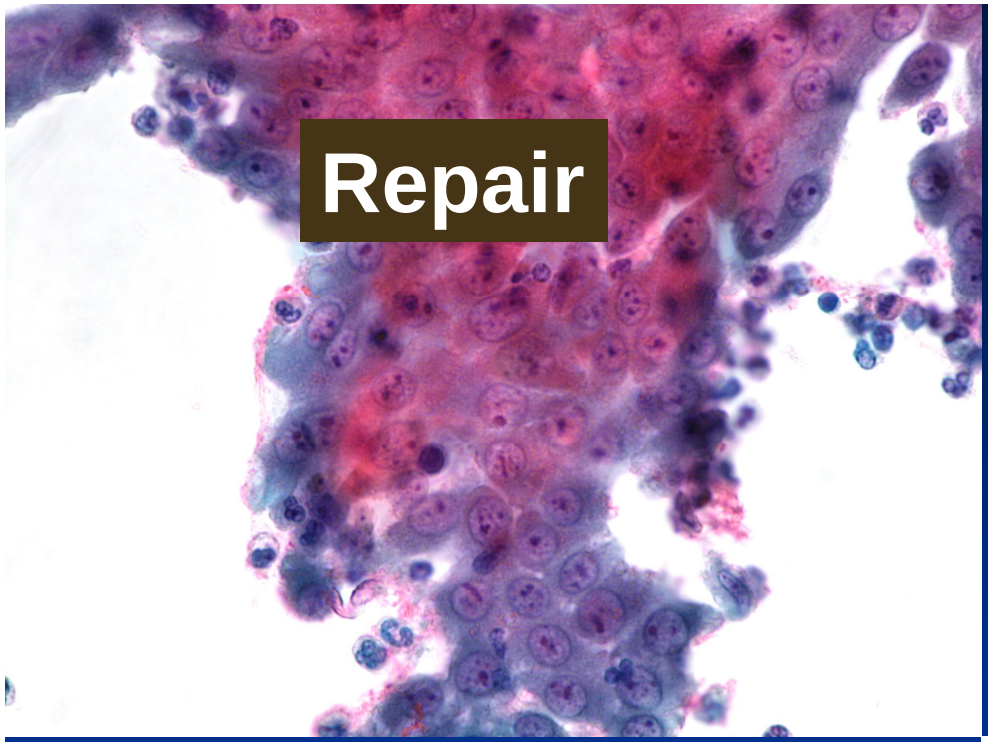

Net case 7
Spot the difference:
Invasive cancer or HPV changes
HPV changes



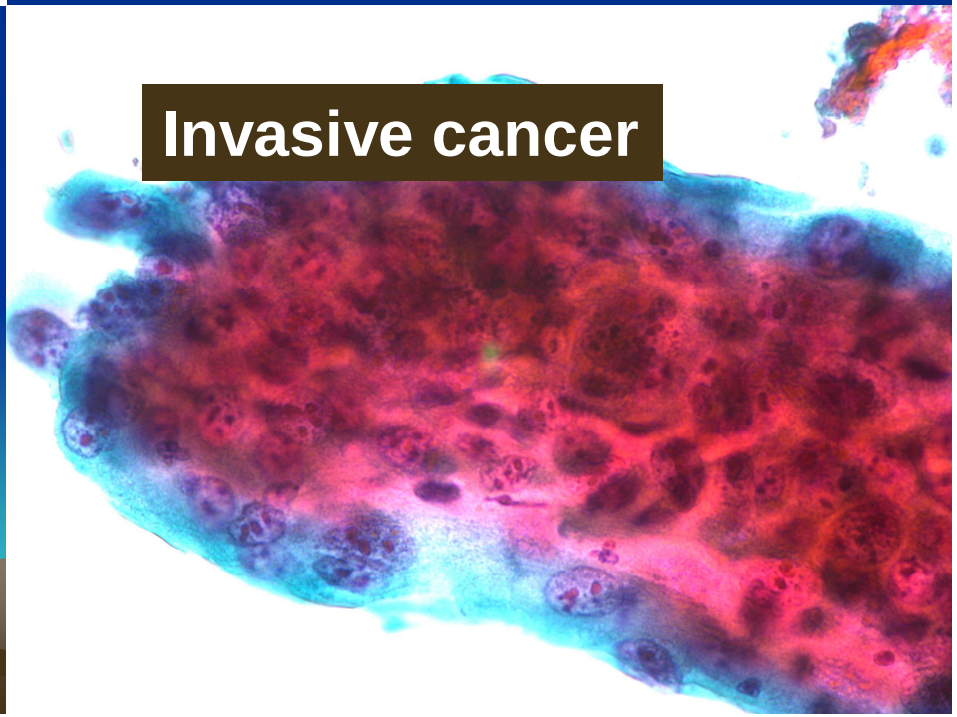
Net case 8
Spot the Difference: Repair or Invasive Cancer?







Net case 8 Spot the Difference: Repair or Invasive Cancer?



The End