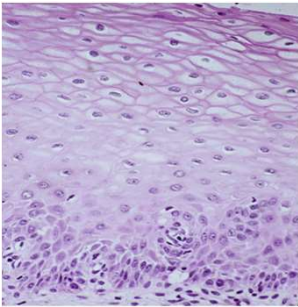


GYN cytology: Squamous Cell Abnormalities-
Atypical squamous cell

Fadi W. Abdul-Karim MD MEd

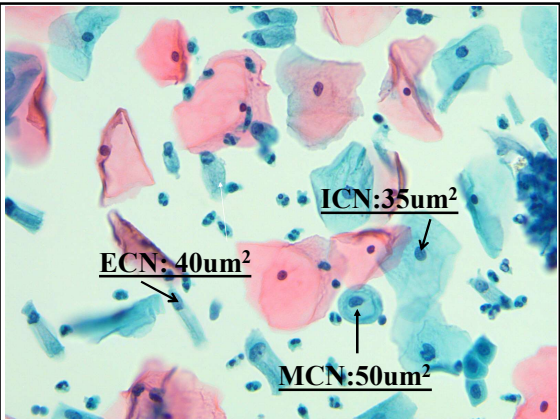
1

Maturation of Squamous Epithelium



- Cells become bigger
- Cells change from round to oval to polygonal
- Cytoplasm volume increases
- Long axis of nucleus changes from perpendicular to parallel
- Nuclear size decreases
- Nuclear size decreases, cytoplasm increases, N/C ratio decreases
- Mitotic activity only in parabasal cells
- Cyanophilic basal cells mature to pink/orange staining cells

2

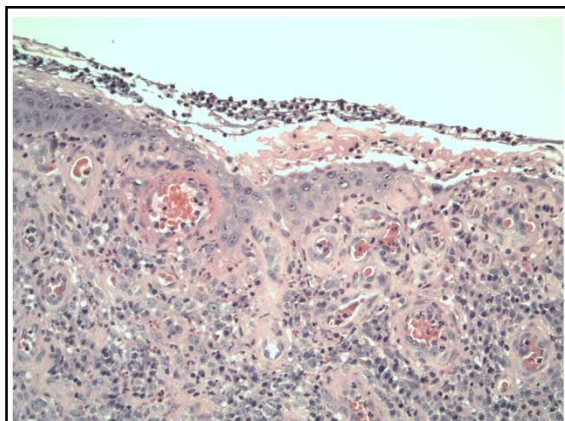


ECN: 40um²

ICN: 35um²

MCN: 50um²

3



4

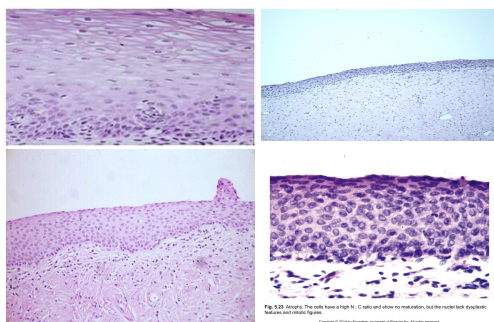
Immature Squamous Epithelium

Composed throughout the entire thickness of basal and/or parabasal cells.

- Squamous epithelial **atrophy** due to low estrogen state
- At the transformation zone where it is called **squamous metaplasia**

5

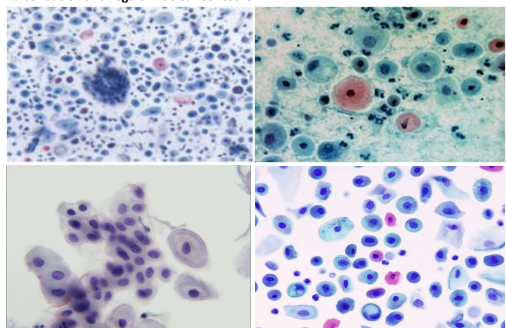
Atrophic Squamous Epithelium



6

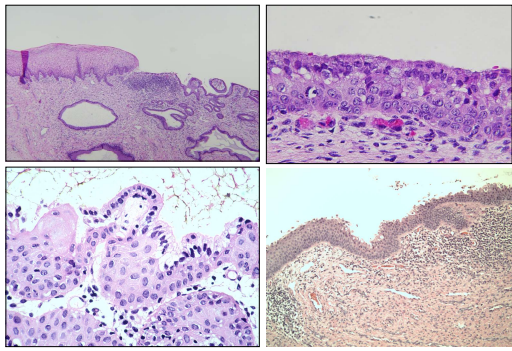
Atrophy: Dispersed parabasal-type cells and small clusters

Mild hyperchromasia and tend to have more elongated nuclei. Uniform chromatin distribution and regular nuclear contours



7

Squamous Metaplasia at TZ



8

TBS: Non-neoplastic Cellular Variations

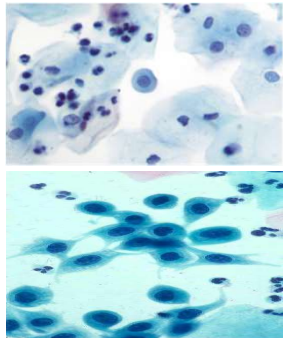
Squamous Metaplasia

Criteria:

- Squamous metaplastic cells which show a range of cytoplasmic differentiation.
- From **immature parabasal-like cells** to those that approximate the appearance of differentiated intermediate/superficial cells . The mean nuclear area is larger than that of the intermediate cell and similar to the parabasal cell at 50 μm^2 .

9

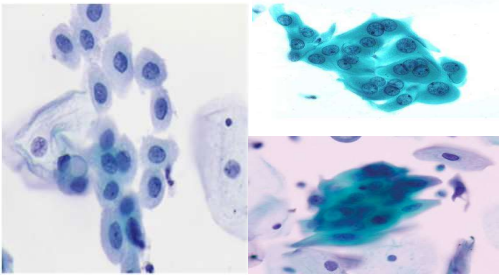
Immature Squamous Metaplasia



- The Cytoplasm**
 - Parabasal shaped
 - Homogeneous/Muddy consistency
 - Amphiphilic color
 - Sharp cytoplasmic borders
 - Punched out vacuoles
 - Cobblestone pattern
- Spider cells can be seen especially in CP:
 - Strange pulled out shapes
 - Most commonly seen in conventional smears

10

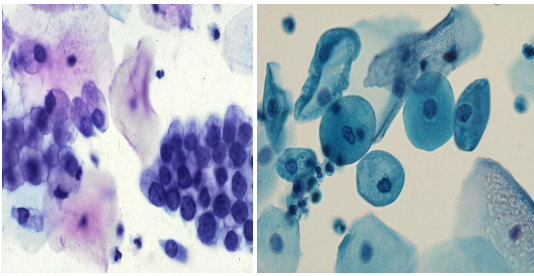
Maturing Squamous Metaplasia



Lower N/C ratio, with finely granular chromatin +/- small nucleoli. With maturation lose muddy cytoplasm and nuclei begin to look more like IC.

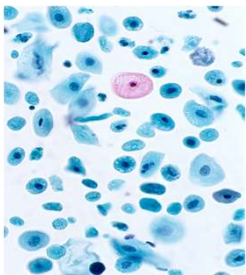
11

Endocervical/TZ component: 10 well-preserved endocervical or squamous metaplastic cells singly or in clusters



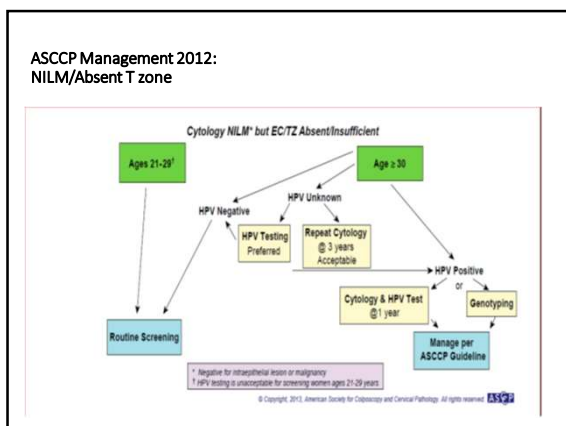
12

Endocervical Component: Atrophy

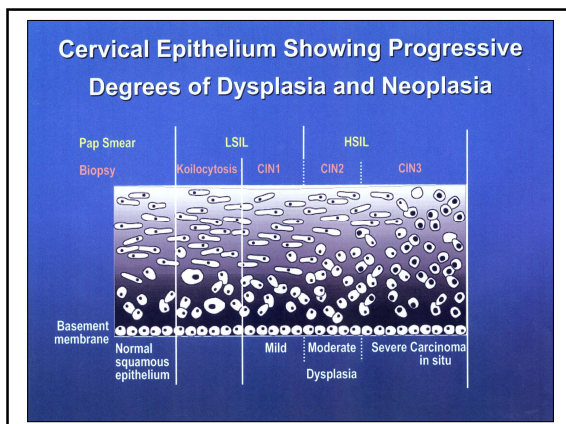


- Parabasal type cells may mimic squamous metaplasia and small columnar cells
- Post partum and progesterone may produce similar patterns as atrophy
- Only use squamous metaplasia as an ECC indicator if they can be definitively identified
- Comment on hormonal pattern inhibiting the ability to determine the presence of an ECC

13

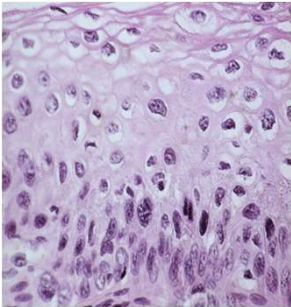


14



15

SIL/CIN/Dysplasia

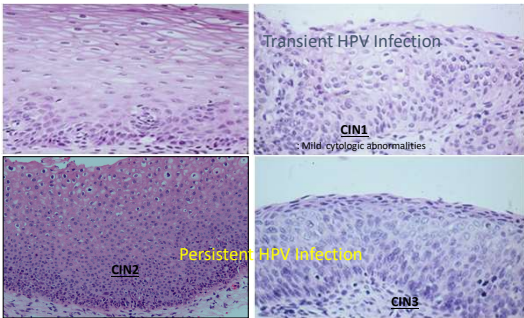


Abnormal partial arrest in differentiation resulting in:

- Increased thickness of "parabasal" layer.
- With increasing severity of SIL, the nuclear-to-cytoplasmic ratios increase, mitotic activity increases, and, in most cases, the cells appear more immature.
- Nuclear changes present throughout the full thickness of the epithelium, irrespective of the severity of the lesion.
- **Cytologic sampling of the superficial layers can detect both low- and high-grade lesions.** In general, it is the relative maturation or lack of maturation of the cytoplasm in the superficial layers, coupled with persistent mitotic activity, that defines the severity of the process.

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Dysplasia/CIN/ SIL: An abnormal cellular proliferation with nuclear atypia that includes enlargement, pleomorphism, change in chromatin texture, and irregular nuclear borders.



Transient HPV infection
CIN1
Mild cytologic abnormalities

CIN2 Persistent HPV infection

CIN3

17

LAST: SIL/CIN

- An abnormal cellular proliferation with nuclear atypia that includes enlargement, pleomorphism, change in chromatin texture, and irregular nuclear borders.
- With increasing severity of SIL, the nuclear-to-cytoplasmic ratios increase, mitotic activity increases, and, in most cases, the cells appear more immature.
- The nuclear changes are usually present throughout the full thickness of the epithelium, irrespective of the severity of the lesion. **For that reason, cytologic sampling of the superficial layers can detect both low- and high-grade lesions.** In general, it is the relative maturation or lack of maturation of the cytoplasm in the superficial layers, coupled with persistent mitotic activity, that defines the severity of the process.

18

Size relationships (benchmarks)

- Intermediate cell
- Squamous metaplasia
- Reactive/ASC
- ASC-US
- SIL

DeMay: The Pap Test

19

The Bethesda System 1988

- TBS should serve as a guideline for cytopathology reports of cervical /vaginal specimens;
- Two tiered reporting: LSIL and HSIL
- **“Atypia”** should not be used as a diagnosis for otherwise defined inflammatory, preneoplastic or neoplastic cellular lesions. ASC-US should include a recommendation for follow-up and /or, type of further investigation.

20

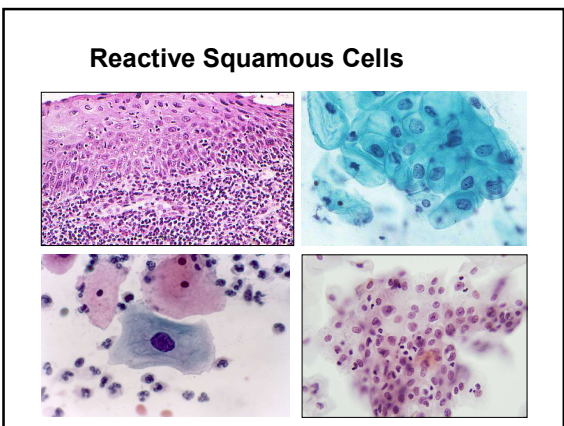
Inflammatory Changes

21

The Bethesda System 1991

- **ASCUS:** An ill-defined category created to address the inherent limitations of cytologic examination in the distinction of subtle cytologic changes.
- Bethesda 1991, **ASCUS:** Cellular abnormalities that are more marked than those attributable to reactive changes but that quantitatively or qualitatively fall short of a definitive diagnosis of squamous intraepithelial lesion.
- ASCUS: Favor reactive, NOS, favor SIL

22




23

TBS: 2014

- 370 atlas illustrations, complemented by robust legends, illustrate a spectrum of morphologic variations observed on both conventional smears and liquid based cytologic preparations;
- 58% of the images are new.
- 42% are from the second edition;
- 60% LBC, 40 % CP
- 40% are from conventional and interpretive dilemmas or “borderline” morphologic features that may not be interpreted in the same way by all cytologists.
- Increase in composite, cell block, IHC, histopathology correlates
- <https://bethesda.soc.wisc.edu/>

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SELF TEST MODULE



32 year old woman, screening Pap test
SurePath

Negative for intraepithelial lesion or malignancy (NILM)
 Endometrial cells shed by a woman aged 45 or older
 Atypical squamous cells of uncertain significance (ASC-US)
 Atypical squamous cells, cannot exclude a high-grade squamous intraepithelial lesion (ASC-H)
 Low-grade squamous intraepithelial lesion (LSIL)
 High-grade squamous intraepithelial lesion (HSIL)
 Squamous cell carcinoma (SCC)
 Atypical endocervical cells (AEC)
 Atypical endometrial cells (AEMC)
 Endocervical adenocarcinoma in situ (AIS)
 Adenocarcinoma (ADC)
 Other malignant neoplasm

25

SELF TEST MODULE

- Type of Preparation:** SurePath
- Clinical History:** 32 year old woman, screening Pap test
- Interpretation:** Negative for intraepithelial lesion or malignancy (NILM)
- Explanatory Notes:** Note the streaming appearance of the squamous cells (so-called school of fish pattern) and the enlarged nuclei with vesicular chromatin and prominent nucleoli; the background shows numerous acute inflammatory cells - these reactive features together are consistent with cellular repair, and should be interpreted as negative for intraepithelial lesion or malignancy (NILM).

Negative for intraepithelial lesion or malignancy (NILM)	11	72.86%
Atypical endocervical cells (AEC)	4	4.77%
Atypical squamous cells, cannot exclude a high-grade squamous intraepithelial lesion (ASC-H)	4	5.71%
Atypical squamous cells of uncertain significance (ASC-US)	3	4.29%
High-grade squamous intraepithelial lesion (HSIL)	2	2.86%
Squamous cell carcinoma (SCC)	2	2.86%
Endometrial cells shed by a woman aged 45 or older	1	1.43%
Atypical endometrial cells (AEMC)	1	1.43%
Low-grade squamous intraepithelial lesion (LSIL)	0	0.00%
Endocervical adenocarcinoma in situ (AIS)	0	0.00%
Adenocarcinoma (ADC)	0	0.00%
Other malignant neoplasm	0	0.00%

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TBS 2001: Atypical Squamous Cells (ASC)

Cytologic changes suggestive of a squamous intraepithelial lesion that are quantitatively or qualitatively insufficient for a definitive interpretation (ASC ...of LSIL- ASCUS ...or HSIL-ASC-H)

27

TBS: Epithelial Cell Abnormalities - Squamous Cells

- **Atypical squamous cells (ASC)**
- **Undetermined significance (ASC-US)**
- **Cannot exclude HSIL (ASC-H)**

- Low-grade squamous intraepithelial lesion (LSIL) encompassing: human papillomavirus/mild dysplasia/cervical intraepithelial neoplasia (CIN) 1
- High-grade squamous intraepithelial lesion (HSIL) encompassing: moderate and severe dysplasia, carcinoma in situ; CIN 2 and CIN 3
- Squamous cell carcinoma

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TBS: Atypical Squamous Cells (ASC)

- ASC is the least reproducible of all cytological categories.
- The median reporting rate of ASC-US in US laboratories is 4.7%, and the median rate of ASC-H is 0.4%.
- Prevalence of invasive cancer is low in women with ASC (approximately 0.1%-0.2%).

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ASC-US: Not a Single Entity

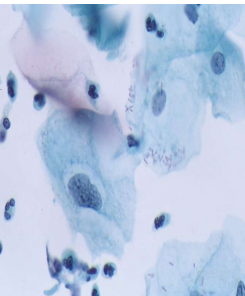
- Atypical cells with "mature" intermediate type cytoplasm (**NOS**)
- **Metaplastic cells** with atypia
- Nuclear abnormalities associated with dense orangeophilic cytoplasm ("**atypical parakeratosis**" /APK).
- **Atypical repair**
- Atypical cells in the setting of **atrophy**
- Cytoplasmic changes that **suggest HPV** cytopathic effect (incomplete koilocytosis) – including poorly defined cytoplasmic halos or cytoplasmic vacuoles resembling koilocytes but with absent or minimal concurrent nuclear changes.
- Atypical cells due to **compromised specimen**
- Other

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ASC-US: Cytologic Features

GENERAL:

- Cells are usually isolated
- Number of affected cells low (3-5)
- Cytoplasmic area approximate superficial or intermediate squamous cells in most instances and less often squamous metaplastic cells.
- Slightly increased ratio of nuclear to cytoplasmic area (N/C).
- Absence of Human Papillomavirus (HPV) cytopathic effect

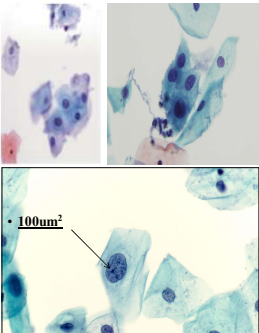


31

ASC-US: Cytologic Features

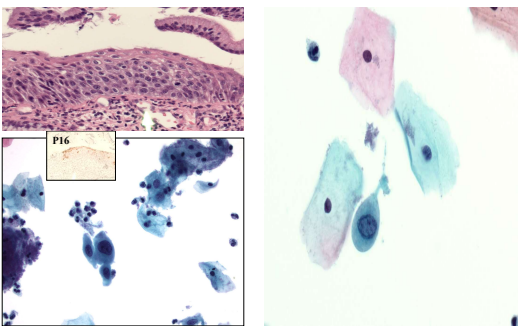
NUCLEAR:

- Nuclei are approximately two and one half to three times the area of the nucleus of a normal intermediate squamous cell (approximately 35 μm^2) or twice the size of a squamous metaplastic cell nucleus (approximately 50 μm^2).
- Limited variation in nuclear size and shape
- Minimal nuclear hyperchromasia and irregularity in chromatin distribution or nuclear shape.

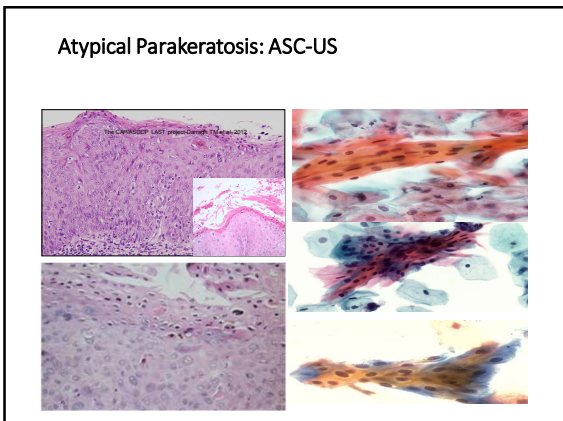


32

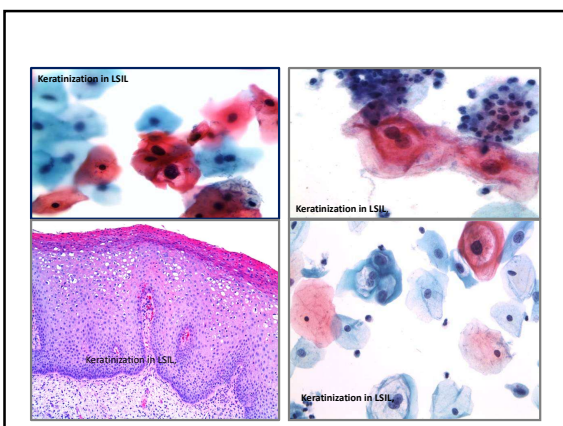
ASC-US: Metaplastic cells with atypia



33



34



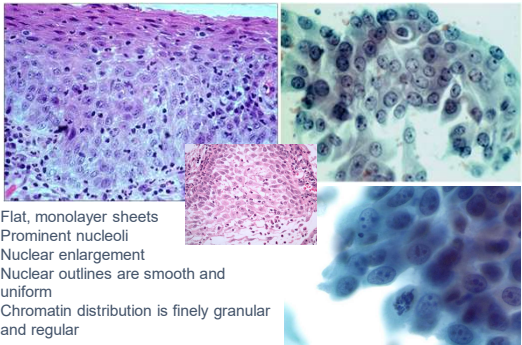
35

TBS: 2014 How to Report Equivocal SIL: Keratinizing Features

- Cellular pleomorphism with marked anisonucleosis
- Caudate, spindle, elongated, tadpole, or bizarre forms
- Dyskeratotic cells: Coarsely granular or smudged chromatin
- Dense orangeophilic cytoplasm with distinct borders
- Refers to the pleomorphic appearance of cells rather than cytoplasmic staining
- Severity determined by degree of pleomorphism rather than cytologic atypia but difficult to predict
- May be difficult to distinguish from keratinizing squamous cell carcinoma
- **REPORT: SIL of undetermined grade (comment as to why?)**

36

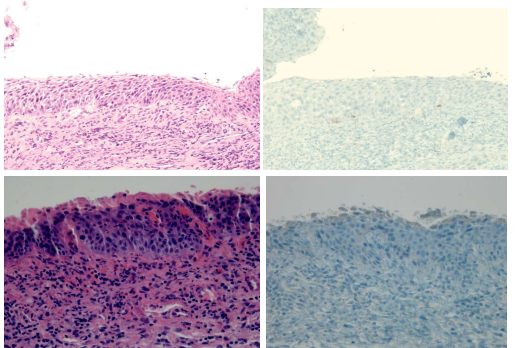
Repair (Typical): NILM



Flat, monolayer sheets
Prominent nucleoli
Nuclear enlargement
Nuclear outlines are smooth and uniform
Chromatin distribution is finely granular and regular

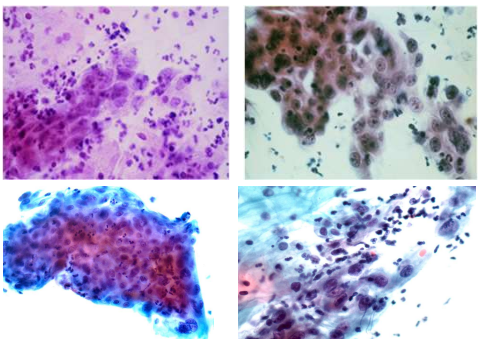
37

"Atypical Repair" (P16 negative)



38

Atypical Repair: ASC-US



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ASC-US: Atypical Repair (AR)

- Reparative changes that manifest some degrees of cellular overlap, dyscohesion, anisonucleosis, and/or loss of nuclear polarity.
- The incidence of subsequent SIL among women with AR:
 - 25 to 43% in high-risk population groups.
 - In a more diverse population much lower (5.2%).
- **ASC-US:** Changes that are at the lower end of the spectrum of atypia.
- **ASC-H:** Those that are concerning for the possibility of invasive carcinoma, especially in high-risk patients.

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Atrophic Squamous Epithelium

Fig. 8.22 Atrophy. The cells have a high N:C ratio and show no maturation, but the nuclei lack abnormality and pleomorphism.

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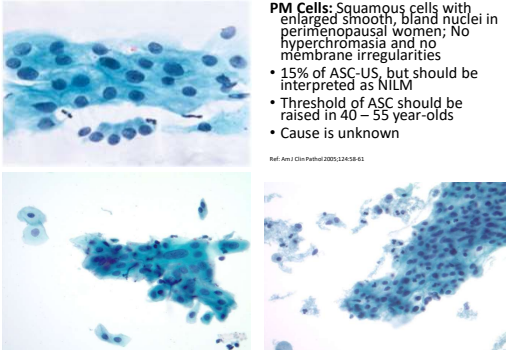
41

Squamous atrophy: Clinical setting associated with low estrogen state/decrease of hormonal support

- **Pre-menarche:** Newborn female will initially have a cellular profile of maternal hormones. Maternal hormones wane, to an to an atrophic pattern. The atrophic pattern is gradually replaced by an IC pattern several years before menarche. Cyclic changes about 18 mo. before menstruation.
- **Post-partum:** 75% of lactating women and one out of three non-lactating women had atrophic smears at six weeks postpartum
- **Post-menopause**
- **Premature ovarian failure**
- **Turner syndrome**
- **Status post bilateral oophorectomy.**
- **High dose progestin therapy**
- **Radiation therapy, chemotherapy, hysterectomy or trachelectomy for invasive cervical cancer**

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Atrophy: Generalized Nuclear Enlargement



PM Cells: Squamous cells with enlarged smooth, bland nuclei in perimenopausal women; No hyperchromasia and no membrane irregularities

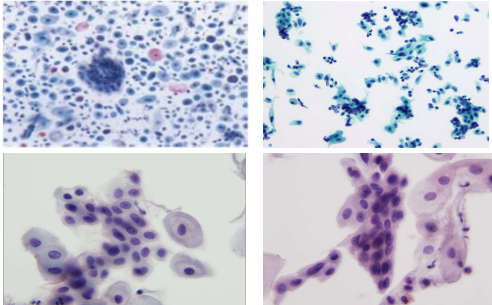
- 15% of ASC-US, but should be interpreted as NILM
- Threshold of ASC should be raised in 40 – 55 year-olds
- Cause is unknown

Ref: Am J Clin Pathol 2005;124:516-61

43

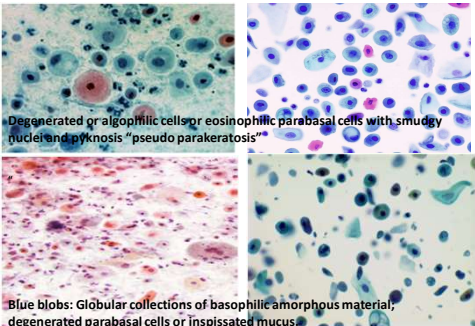
Atrophy: Dispersed parabasal-type cells and small clusters

Mild hyperchromasia and tend to have more elongated nuclei. Uniform chromatin distribution and regular nuclear contours



44

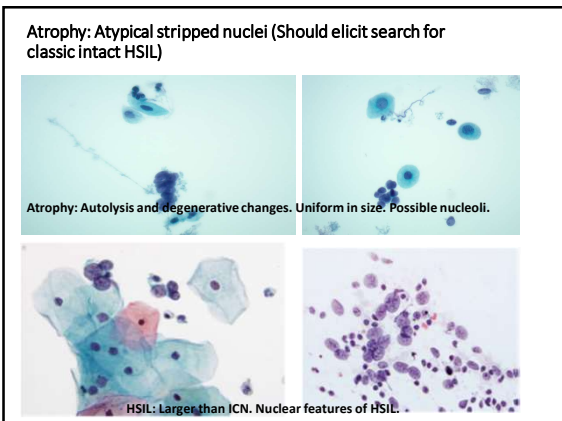
Atrophy: Degenerated parabasal cells: Blue blobs



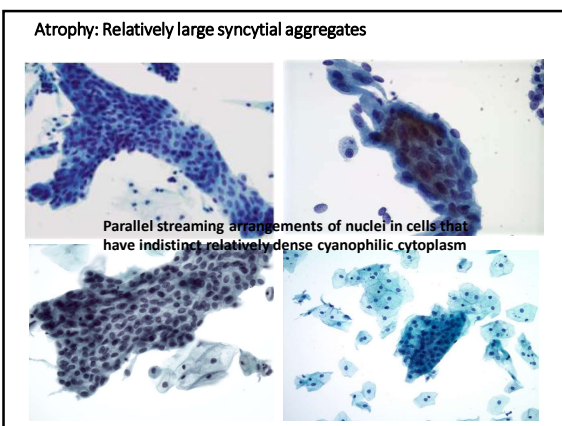
Degenerated or atrophic cells or eosinophilic parabasal cells with smudgy nuclei and pyknosis "pseudo parakeratosis"

Blue blobs: Globular collections of basophilic amorphous material, degenerated parabasal cells or inspissated mucus.

45



46



47

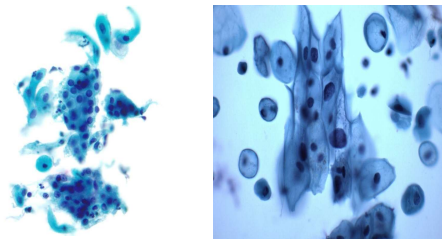
ASC in Atrophy

- Reporting of atrophic changes is variable and poorly reproducible:
- A patient is more likely to have significant disease:
 - In face of a history of previous cervical abnormality
 - Prior positive high-risk HPV test.

Atrophy may coexist with dysplasia or neoplasia, and the diffusely increased nuclear to cytoplasmic ratio of background parabasal/basal squamous cells can make identification of true abnormalities more challenging. As such, these cases should be reviewed with care.

48

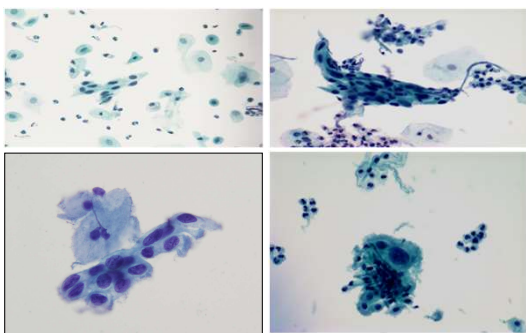
ASC in PM: Nuclear enlargement, hyper-chromasia, irregularities in nuclear contour or chromatin or marked cellular pleomorphism (tadpole or spindle cells)



Nuclear enlargement 2.5-3x size of 1 cell (in Atrophy ? 3-4 times).
Slight increase N:C
+/- variation in nuclear size and shape
+/- binucleation, mild hyperchromasia
Even chromatin, smooth nuclear contour
Features suggestive of SIL

49

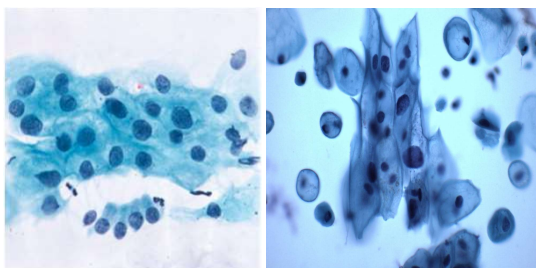
ASC in Atrophy: ASC-US



50

Atrophy: NILM

ASC-US



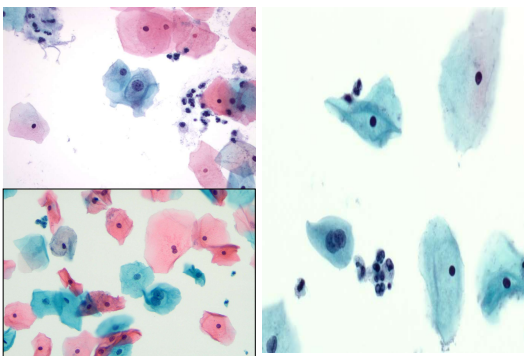
51

ASC-US: Atypia in Postmenopausal Women and in Atrophy

- **NILM-PM:** Mild bland nuclear enlargement is a common cause for ASC over utilization. Mild nuclear enlargement without significant hyperchromasia or nuclear irregularity "postmenopausal atypia" and are usually HPV-neg. NILM: In the absence of definitive abnormalities, especially if there is no prior history of squamous cell abnormalities or do not have a HPV +ve.
- **ASC-US:** Nuclear enlargement with hyperchromasia that fall short of SIL.
- **ASC-H:** Occasionally and especially in high risk population, if it raises concern for HSIL
 - The interpretation of HSIL may be difficult to make in an atrophic background because of the lack of maturity (and hence high nuclear to cytoplasmic ratio) of the parabasal cells.
 - **In low-risk scenarios, it may be prudent to categorize such atypias as ASC-US rather than ASC-H and allow adjunctive hrHPV testing to determine downstream management which may avoid overtreatment.**

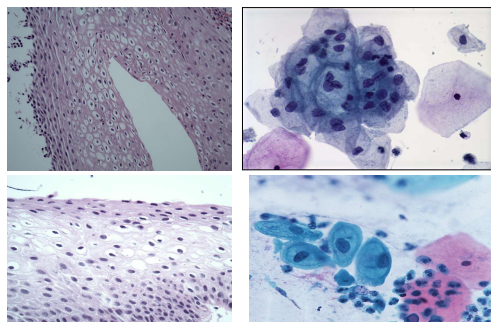
52

Atypical Squamous Cells with features suggestive of HPV: ASC-US

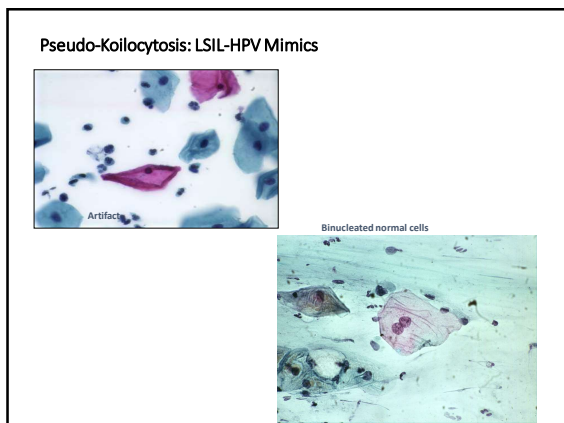


53

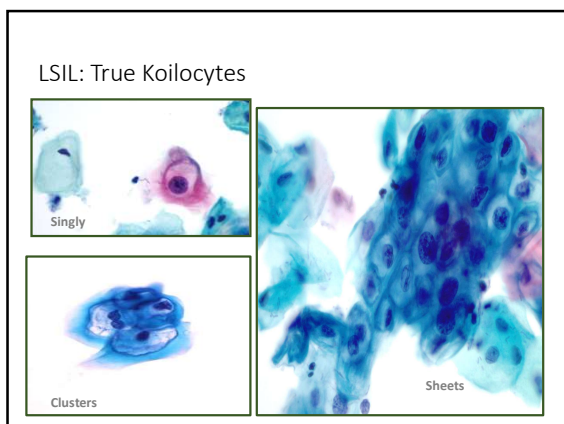
**Pseudo-Koilocytosis: LSIL-HPV Mimics
Glycogenated Squamous Epithelium**



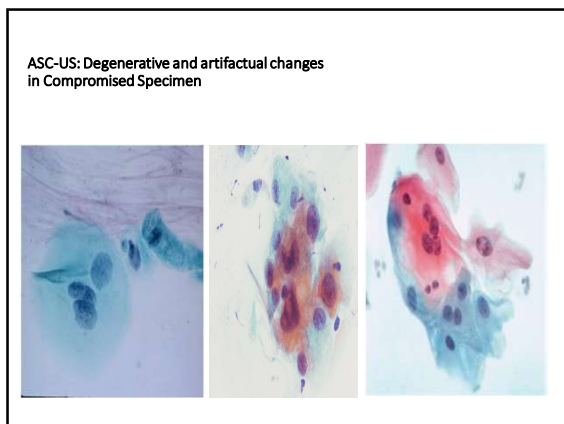
54



55



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ASC-US: HPV Status

- Prevalence of ASC-US declines with increasing age, as does the prevalence of hrHPV DNA (including genotypes 16 and 18)
- ASC-US cytology in younger women is more prevalent and more indicative of HPV-related etiology than in older women .
- Regardless of age, knowledge of a patient’s concurrent HPV result could potentially bias the perspective of the cytotechnologist or cytopathologist when making an interpretation of NILM vs. ASC-US, especially for cases with minimal cytologic changes. Hence, care should be taken when reviewing cases with this a priori knowledge of HPV status.

58

The Tahoe Study: Bias in the Interpretation of Papanicolaou Test Results When Human Papillomavirus Status Is Known

- Results—Without knowledge of the HPV status, slides were more often categorized as NILM and less likely identified as an ECA . There was an increase across all categories of ECAs in the biased responses compared with the unbiased responses .
- Conclusions—Knowledge of positive HPV status biases morphologic Pap test result interpretation. If the HPV status is positive, observers are more likely to report a Pap test result as abnormal across all categories of ECAs.

Moriarty A et al. Arch Pathol Lab Med. 2014;138:1182–1185

59

ASC-US bias: Reflex vs. contesting

- *ASCUS in the reflex group (41.5%) was significantly higher than the cotesting group (33.0%). There was no difference in HPV-HR positivity or ASCUS/squamous intraepithelial lesion (SIL) ratios between the two groups.*
- *HPV-HR reflex testing may introduce bias in cytologic diagnosis, making it more likely that an ASCUS diagnosis is rendered.*

Increased Rate of ASCUS Diagnosis With Concomitant Request for High-Risk Human Papillomavirus Reflex Testing May Be Due to Cognitive Bias. Pender JA. Am J Clin Pathol May 2015;145:423–433

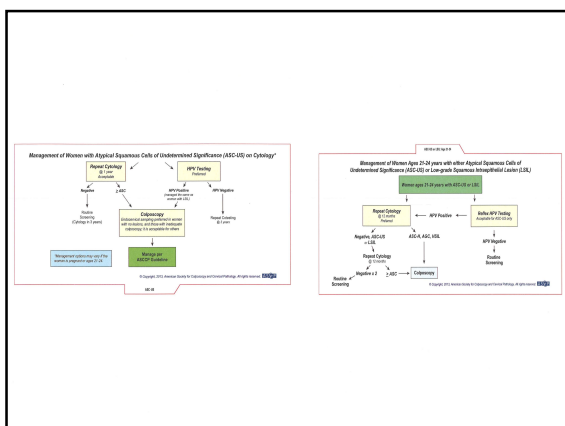
60

ASC-US HPV+/LSIL

- ALTS: 85% of ASC-US/HPV +ve or LSIL have at colposcopy/biopsy CIN
 - 67% CIN 1,
 - 18% CIN 2,3
 - 0.3% invasive cancer (14% no lesion).
- **Cumulative probability of HSIL/CIN 2+ in 2 years ASC-US/HPV positive is 25-30% (12-17% at incident colposcopy) and is similar to LSIL.**
- Recent Studies/Co-tested women 30-64 years: CIN 2/3: 16% of ASC-US/HPV +, 15% of LSIL/HPV +, 9% of LSIL/HPV -

LSIL /HPV + or HPV unknown AND ASC-US/HPV POSITIVE SHOULD BE TREATED SIMILAR

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ATHENA Trial: ASC-US and HPV Genotyping

- ASC-US/HPV-16 or HPV-18 detected had approximately twice the risk of CIN 3+ as women with ASC-US and high-risk HPV types other than 16 or 18. Nevertheless, the risk for CIN 3+ in both groups exceeded the threshold for colposcopy.
- **HPV-16/18 genotyping of HPV positive women with ASC-US did not appear to lead to different management.**
- **Genotyping is a determinant of management For NILM- HPV + Pap tests**

63

ASC: Quality assurance measures

- **ASC-HPV positive rates:**
ALTS trial: Adjudicated by experienced pathologists to be 50.6%; however, in general practice this rate has been found to be lower generally ranging between 40 and 50%, most likely due to conservatism and the bias that provides an objective test in equivocal cases.
- **ASC/SIL median ratio is 1.5**
For laboratories that serve high-risk populations, the ASC/SIL ratio should not exceed 3:1. A higher ratio suggests over use of ASC; however, over interpretation of both ASC and SIL can keep this ratio within accepted guidelines.

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ASC: Quality assurance measures

- Neither is a measure of diagnostic accuracy: Useful in spotting trends related to interpretation thresholds.
- Cyto-Histologic Correlation: Neither cytology, colposcopy, nor biopsy represents a diagnostic "gold" standard.

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TBS: ASC-H

Definition: Cytologic changes that are suggestive of HSIL but lack criteria required for a definitive interpretation

Incidence and association:

- Uncommon diagnosis; 5-10% Of ASC (Majority are ASC-US)
- 50-85% have an underlying CIN2 +
- Incidence of CIN on follow-up higher in patients 40 years or younger

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ASC-H: Not Synonymous with HSIL

- Not a “biologic” or “morphologic” entity.
- PPV for high grade lesion (CIN2+) is > than ASC-US, but < than HSIL. In general practice, CIN2+ is likely to be slightly lower than reported.
- Should be investigated like HSIL, but if CIN2,3 is not confirmed by histology, may be spared aggressive treatment.
- Encourage pathologists to correlate cytology and histology if CIN2 + is not confirmed.

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ASC-H

- ASC-H cells are sparse
- Singly or in tight small clusters (<10 cells).
- Resemble metaplastic cells “atypical immature metaplastic cells”
- Nuclei about 1.5-2.5 times larger than normal.
- Mild irregular nuclear contours, mild hyperchromasia (more likely to be euchromatic in LBP)
- Slight increase in N/C ratio (usually $\geq 50\%$)- N/C ratio similar to HSIL.
- Can be subtle

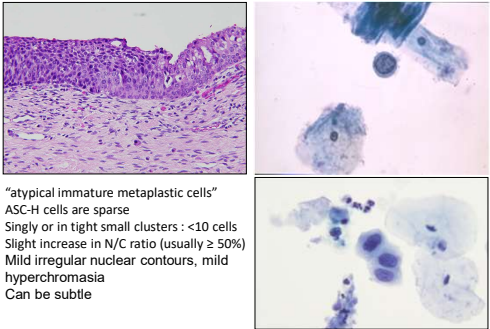
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ASC-H Patterns: “Atypical Immature Metaplasia”:

- Small Cells with High N/C Ratio.
- Singly or in small fragments < 10 cells; occasionally, in
- Cells are the size of metaplastic cells with nuclei that are about 1.5–2.5 times larger than normal (Nuclear to cytoplasmic ratio may approximate that of HSIL).
- Nuclear abnormalities such as hyperchromasia, chromatin irregularity, and abnormal nuclear shapes with focal irregularity favor an interpretation of HSIL.

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ASC-H: Atypical Immature Squamous Metaplasia



"atypical immature metaplastic cells"
ASC-H cells are sparse
Singly or in tight small clusters : <10 cells
Slight increase in N/C ratio (usually $\geq 50\%$)
Mild irregular nuclear contours, mild hyperchromasia
Can be subtle

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TBS: ASC-H

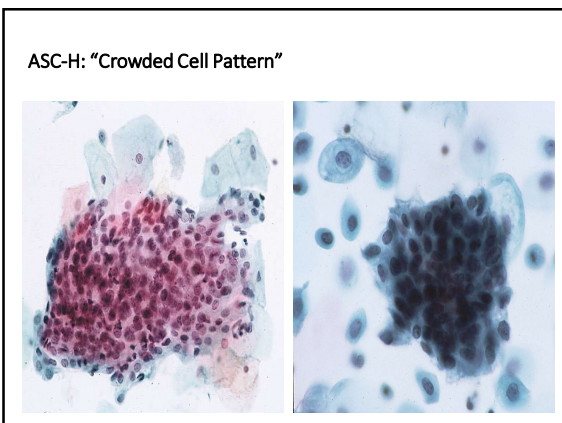


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ASC-H: "Crowded Sheet Pattern"

- A microbiopsy of crowded squamous cells containing nuclei that may show atypical features as noted above:
 - Overlapping nuclei: Difficult to visualize- focus up and down
 - Loss of nuclear polarity.
- Dense cytoplasm, polygonal cell shape, and fragments with sharp linear edges generally favor squamous over glandular (endocervical) differentiation.

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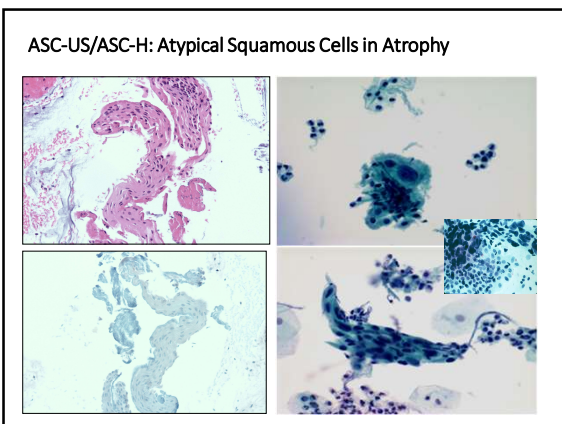


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Hyperchromatic Crowded Groups

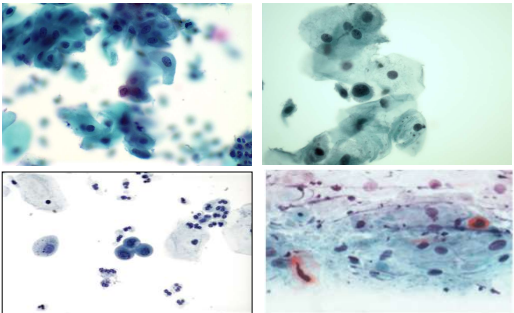
<ul style="list-style-type: none">• Benign <ul style="list-style-type: none">• Reactive endocervical cells: vigorous scraping.• Endometrial cells• LUS• Atrophy• Tubal metaplasia• Microglandular hyperplasia• Clusters of inflammatory cells• IUD changes	<ul style="list-style-type: none">• Neoplastic/Preneoplastic <ul style="list-style-type: none">• HSIL• AGC• AIS• Squamous cell carcinoma• Adenocarcinomas
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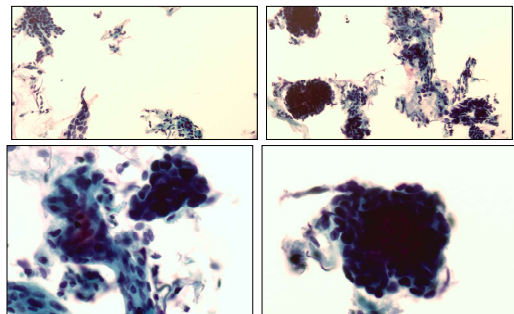
ASC-H in Atrophy



ASC-H in PM is usually associated with NILM or LSIL on follow up. HSIL in 6% while 22% in premenopausal. In low risk patients consider ASC-US to allow for HPV testing.

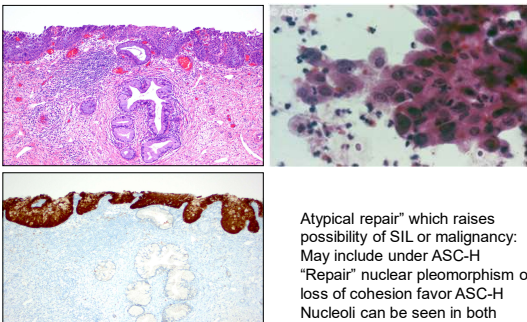
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ASC-H/HSIL in Atrophy



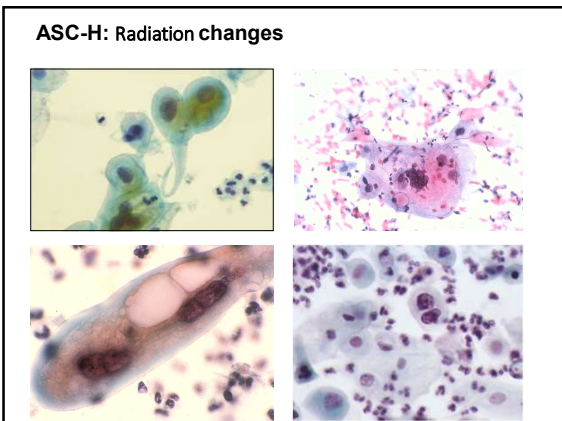
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ASC-H: Markedly Atypical Repair Mimicking HSIL/Carcinoma

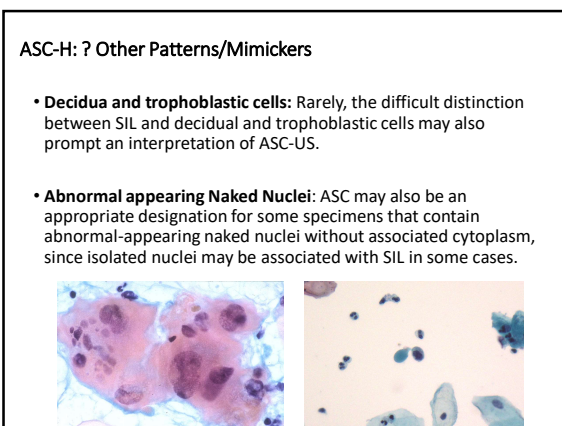


Atypical repair" which raises possibility of SIL or malignancy: May include under ASC-H "Repair" nuclear pleomorphism or loss of cohesion favor ASC-H Nucleoli can be seen in both

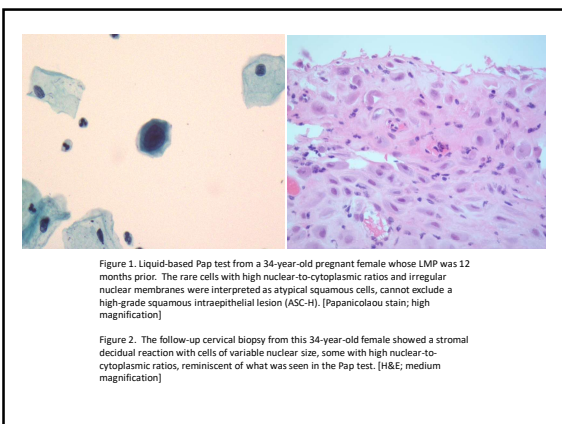
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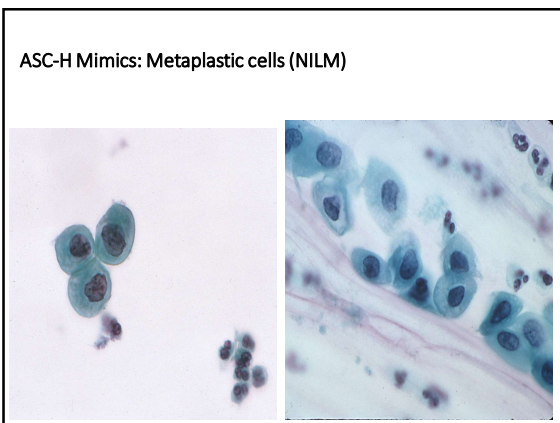
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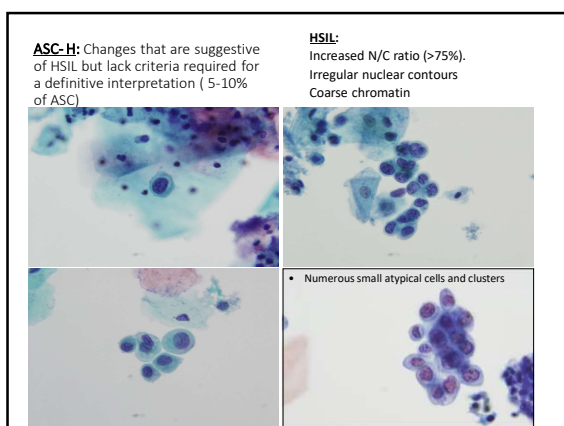
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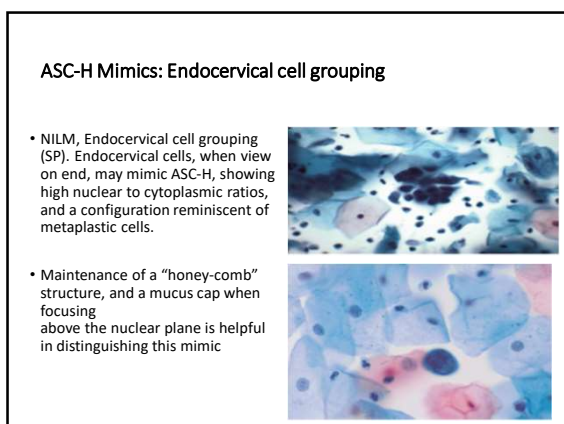
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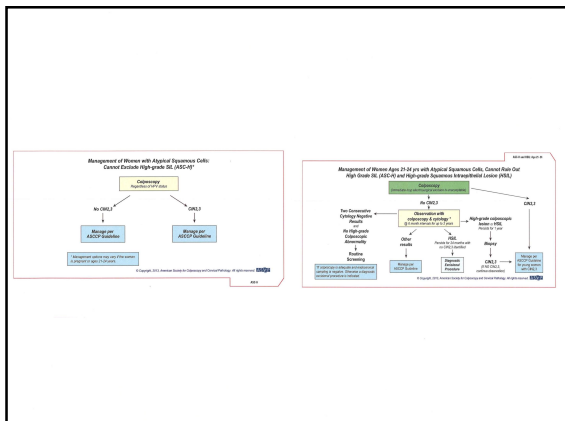
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TBS 2014-Ch 4: ASC

- The category of ASC is by far the most commonly reported abnormal cervical cytology interpretation.
- ASC continues to be defined as the general category with sub-categorization as ASC-US and ASC-H. The dichotomous reporting for ASC mirrors that observed for LSIL and HSIL.
- It must be emphasized that the ASC category was developed to designate the interpretation of an entire specimen, not individual cells, because atypia in individual cells remains a highly subjective and, hence, variable interpretation.
- Common patterns interpreted as ASC-US and ASC-H are reviewed and guidance provided to enable laboratories to use this reporting category along with HPV test results to monitor quality and consistency among practitioners and laboratories.

McN, Nease, A, Wilbur, D. Cytopathol. 2015; 15(4):275-81.

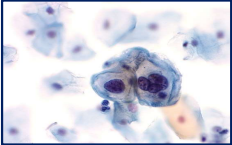
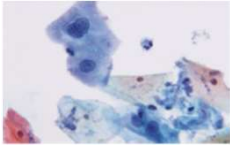
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Gynecologic Cyto- Histo Correlation

Cytology	HPV Testing	5 yr Risk CIN2+	Recommend Management
Negative	Negative	0.27	Repeat testing in 5 yrs
Negative	Positive	10	Repeat testing in 6-12 months
ASC	Negative	1.1	Repeat testing in 3 yrs
ASC	Positive	18	Immediate colposcopy if >25
LSIL	Negative	5.1	Repeat testing in 6-12 months
LSIL	Positive	19	Immediate colposcopy if >25
ASC-H	Negative	12	Immediate colposcopy
ASC-H	Positive	45	Immediate colposcopy
HSIL	Negative	49	Immediate colposcopy
HSIL	Positive	71	Immediate colposcopy
AGC	Negative	2.2	Immediate colposcopy
AGC	Positive	45	Immediate colposcopy

Schiffman M and Solomon D. Cervical Screening with HPV and Cytologic Co-testing. New Engl J Med. 2013; 369:2324-31

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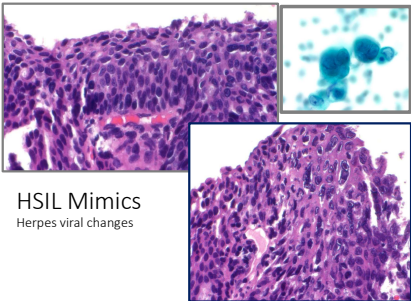
<u>LSIL</u>	<u>ASC-US</u>
<ul style="list-style-type: none">• Multiple cells• Enlarged nucleus (>x3intermediate cell nucleus)• Smudgy or hyperchromatic nuclei• Nuclear membrane irregularities• Koilocytes	<ul style="list-style-type: none">• Few cells• Slight nuclear enlargement (x2-3 intermediate cell nucleus)• Stippled chromatin• Regular nuclear membranes• Most common Pap interpretation that preceded a biopsy on CIN2
	

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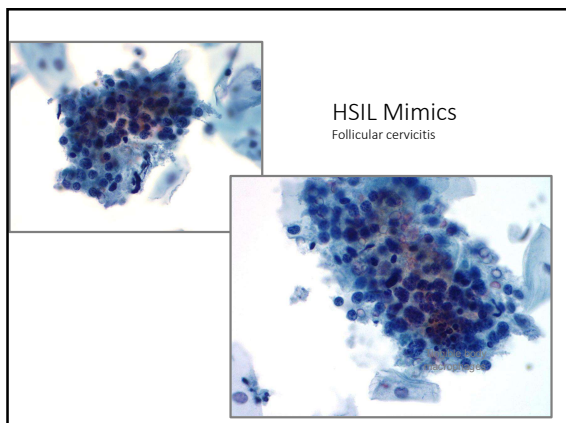


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HSIL Mimics
Herpes viral changes



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