Presentation Plan
- Bethesda 2001
- Bethesda 2015
- Questions and answers
- Earrings to your ear ..😊
- Look a-like cases

Bethesda System- 2001
- SPECIMEN TYPE
  - Conventional (pap smear) or liquid base preparation
- ADEQUACY
  - Satisfactory for evaluation
    - (describe presence or absence of endocervical/transformation zone component and any other quality indicators, e.g., partially obscuring blood, inflammation, etc)
  - Unsatisfactory for evaluation (specify reason)
    - Specimen rejected/not processed (specify reason)
    - Specimen processed and examined, but unsatisfactory for evaluation of epithelial abnormality because of (specify reason)

BETHESDA 2014
- 5000 cell threshold (8-12000 for CP) should not be rigidly applied in vaginal and post-therapy specimens
- Still recommends the presence or absence of EC/TZ component as a quality indicator
- Their absence should not lead to early repeat screening
Bethesda System- 2001

**INTERPRETATION/RESULT**

- **NEGATIVE FOR INTRAEPITHELIAL LESION OR MALIGNANCY**
  (when there is no cellular evidence of neoplasia, state this in the General Categorization above and/or in the Interpretation/Result section of the report, whether or not there are organisms or other non-neoplastic findings)

**Organisms**
- *Trichomonas vaginalis*
- Fungal organisms morphologically consistent with *Candida* spp
- Shift in flora suggestive of bacterial vaginosis
- Bacteria morphologically consistent with *Actinomyces* spp
- Cellular changes consistent with Herpes simplex virus

**Other non-neoplastic findings** (Optional to report; list not inclusive)
- Reactive cellular changes associated with:
  - Inflammation (includes typical repair)
  - Radiation
  - Intrauterine contraceptive device (IUD)
  - Glandular cells status post hysterectomy
  - Atrophy

**OTHER**
- Endometrial cells (in a woman >= 40 years of age)
  (Specify if negative for squamous intraepithelial lesion)

Endometrial Cells: The How and When of Reporting (Bethesda 2014)

- Increased reporting of benign-appearing endometrial cells: 0.17% to 0.49% of Paps (3x).
- Decreased predictive value for hyperplasia/cancer.

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From D Wilbur 2015

It is now recommended that benign-appearing endometrial cells be reported in women 45 years of age or older

- 2012 ASCCP management guidelines recommends that histologic endometrial assessment only be performed in postmenopausal women.
**Example 1**
- Interpretation/Result
- Endometrial cells are present in a woman ≥ 45 years of age.
- Negative for squamous intraepithelial lesion.

**Example 2**
- NOTE (Optional): Endometrial cells in women 45 years or older may be associated with benign endometrium, hormonal alterations, and, less commonly, endometrial or uterine abnormalities. Endometrial evaluation is recommended in postmenopausal women.

**Example 3**
- Endometrial cells correlate with the menstrual history provided

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**Bethesda System- 2001**

**EPITHELIAL CELL ABNORMALITIES**
- Squamous cell
- Atypical squamous cells
  - Of undetermined significance (ASC-US)
  - Cannot exclude HSIL (ASC-H)
- Low grade squamous intraepithelial lesion (LSIL)
  - Encompassing: HPV/mild dysplasia/CIN 1

**Bethesda System- 2014**

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**QUALITY ASSURANCE in ASC**
- Monitoring the relative frequency of ASC and SIL interpretations by using:
  - ASC/SIL ratio
  - ASC-hrHPV positivity rates

- hrHPV positivity in ASC-US:
  - Experienced pathologists: 50.6%
  - General practice: Lower

**Bethesda System- 2001**

**Glandular cell**
- Atypical
  - Endocervical cells, NOS or specify in comments
  - Endometrial cells, NOS or specify in comments
  - Glandular cells, NOS or specify in comments
- Atypical
  - Endocervical cells, favor neoplastic
  - Glandular cells, favor neoplastic

**Bethesda System- 2014**

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**Endocervical adenocarcinoma in situ**
- Not otherwise specified (NOS)
Please be slowly when you examine the smears and never skip the area.

Case 1

- 36 y GIPI
- She has no abnormal smear before
- No history of sexual transmitted disease
- She uses oral contraceptives
What is your diagnosis?

A. ASC-US
B. ASC-H
C. LSIL
D. HSIL
E. AGC-NOS

EPITHELIAL CELL ABNORMALITIES

- Deciding to abnormalities of a squamous cell should be done due to classical atypia features
- The reference cell is intermediate cell:
  - Size
  - Hyperchromasia
  - Chromatine pattern

ASC

- Diagnostic uncertainty
- Gray zone...
- There is no definitive histologic ...
- 95% of them ASC-US
- >5% are ASC-H
**ASC-US: Atypical squamous cells of undetermined significance**

- Between reactive cellular changes and LSIL
- Not reactive but no sufficient evidence for LSIL
- Nucleus: 2.5-3 times larger than normal intermedier cell nucleus (Average diameter: 35µm)

**ASC-US**

- large cytoplasm,
- orangeophili (parakeratosis),
- perinuclear halo (pseudo-coilosytosis)
- minimal nuclear hyperchromasia,
- chromatin clumping,
- nuclear membran irregularity,
- bi or multinucleation

**Reporting rate of ASC-US is 4.5% according to ASC**

**LSIL: 1.6%**


Steinocyte like changes HPV DNA positive ASC-US (ThinPrep, Papanicolaou, 400).
ASC-US

- If the miniature polygonal squamous cells which have densely orageophlic cytoplasm and small picnotic nuclei are appeared like normal squamous cells, you should classify as "benign" (NILM).
- Be careful!
  - Decidual cells and trophoblasts also can be reported as ASC-US!
- Bin syndrome

Case 2

- 48y G3P2
- Diabetes M. (+)
- She has only one smear test (at 40y old): (-)
- No history of sexual transmitted disease
**Tanınız:**

A. ASC-US
B. ASC-H
C. LSIL
D. HSIL
E. Skuamöz hücreli karsinom

**ASC-H: Atypical Squamous cells- can not be excluded HSIL**

- Suspicious for HSIL but diagnostic criterias are not clear.
- Two patterns are mentioned in Bethesda system
  - **Atypical (Immature) Metaplasia**: Small cells with high N/C ratio
  - **Crowded Sheet Pattern**

**Atypical (Immature) Metaplasia Pattern**

- Cells usually occur singly or in small fragments of less than 10 cells
- In conventional smears, cells may “stream” in mucus
- Cells are the size of metaplastic cells with nuclei that are about 1.5 to 2.5 times larger than normal
- N/C ratio may approximate that of HSIL
- Nuclear abnormalities are similar with HSIL
Crowded Sheet Pattern

- Crowded cells containing nuclei that may show loss of polarity or are difficult to visualize
- Dense cytoplasm, polygonal cell shapes and fragments with sharp linear edges generally favor squamous over glandular differentiation

LBP

- ASC-H cells are quite small
- Nuclei are only 2 to 3 times the size of neutrophil nuclei.

ASC-H

- ASC-H cells have higher PPV than ASC-US for predicting the high grade lesions.
- In different studies to detect the high grade dysplasia ratio in following biopsy of ASC-H cases are reported as: 68%*, 48%** and 26%***
- Because there is no sharply criteria for ASC-H diagnosis.

When reporting an ASC-H case...

- You should be sure that the cell is SQUAMOUS.
- Beware that not be lymphoid cell or histiocyte!
- Specially in LBP beware that “shrinkage” artifact!
- Turn to foci of microscope to be sure does it really single nucleus??
- Don’t forget: The metaplastic cells never have coarse chromatine

CASE 3

- 28 y, G0P0
- She has no complaint, only routine control
- This is the first time for taking a cervical smear in her life
Diagnosis

A. ASC-US
B. ASC-H
C. LSIL
D. HSIL
E. Squamous cell carcinoma

Low Grade Squamous Intraepithelial Lesion - LSIL

- Cells occur singly and in sheets
- The cells have large cytoplasm similar to mature or superficial cell
- Overall cell size is large
- Nuclear enlargement more than three times the area of normal intermediate nuclei results in a slightly increased N/C ratio.
- Variable degrees of hyperchromasia
- Binucleation or multinucleation are common
- Chromatin is often uniformly distributed, but coarsely granular; alternatively, chromatin may appear smudged or densely opaque.

Low Grade Squamous Intraepithelial Lesion - LSIL

- Nucleoli are generally absent or inconspicuous if present
- Contour of nuclear membranes is often slightly irregular, but may be smooth.
- Cytoplasmic borders are distinct

LSIL

- Perinuclear cavitation (koilocytosis): Sharply delineated clear perinuclear zone and peripheral rim of densely stained cytoplasm, is characteristic feature for LSIL, but it is not required for the interpretation; alternatively, the cytoplasm may appear dense and orangeophilic (keratinized).
- Cytoplasmic perinuclear cavitation or dense orangeophilic nuclear abnormalities = LSIL
- In LBP; nuclei may not show significant hyperchromasia.

3 "nonclassical" cytomorphologic features are described related with HPV infection:
- Partial koilocytosis
- Spindle cells
- Binucleation or multinucleation
Partial koilocytosis

- Cytoplasmic clarity without irregular sharply demarcated borders and large perinuclear cavitation that were seen in classical koilocytosis can be seen in cells.

- Spindle cell: Short spindle nucleus in dyskeratotic squamous epithelial cells. This feature can support presence of any kind of HPV type.

- Bi or multinucleation is detected in HPV DNA.

LOOK-ALIKE ENTITIES

<table>
<thead>
<tr>
<th></th>
<th>Reactive</th>
<th>ASC-US</th>
<th>LSIL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nucleus</td>
<td>Enlarged 1.5-2 times, flat</td>
<td>Enlarged 2-3 times, flat to minimal depth of focus</td>
<td>Enlarged 3-4 times, slight depth of focus</td>
</tr>
<tr>
<td>Nuclear Membrane</td>
<td>Smooth</td>
<td>Smooth to slightly irregular</td>
<td>Smooth to slightly irregular</td>
</tr>
<tr>
<td>Chromatin</td>
<td>Finely granular, evenly distributed</td>
<td>Finely granular, evenly distributed</td>
<td>Slightly more granular, evenly distributed</td>
</tr>
<tr>
<td>Nucleoli/ Chromosomizers</td>
<td>Small to conspicuous, sometimes multiple</td>
<td>Inconspicuous or absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Cytoplasmic Features</td>
<td>Peri-nuclear halos present</td>
<td>Questionable cavitation</td>
<td>Diagnostic HPV cavitations</td>
</tr>
<tr>
<td>Richromasia</td>
<td>Can be present</td>
<td>Not present</td>
<td>Not present</td>
</tr>
</tbody>
</table>

Case 5

- 61 y. 65P3
- She is in menopause for 12 years
- She has one (-) smear in 40 years.
- She has vaginal discharge complaint
- Cigarette smoker for 40 years.
High Grade Squamous Intraepithelial Lesion - HSIL

- Smaller than mature cells or LSIL cells
- Single cells or in sheets, or in syncytial aggregates
- Nuclear hyperchromasia is evident. It can be accompanied by variations in nuclear size and shape.

HSIL

- Overall cell size is variable. Ranges from cells that are similar in size to those observed in LSIL to quite small basal-type cells.
- Nuclear enlargement is more variable than that seen in LSIL.
- Some HSIL cells have the same degree of nuclear enlargement as in LSIL, but the cytoplasmic area is decreased, leading to a marked increase in N/C ratio (>50%).
- Chromatin may be fine or coarsely granular and evenly distributed.
- Contour of the nuclear membrane is quite irregular and frequently demonstrates prominent indentations or grooves.
- Nucleoli are generally absent, but may occasionally be seen, particularly when HSIL extends into endocervical gland spaces.

HSIL

- Appearance of cytoplasm is variable, it can appear "immature", lacy, and delicate or densely metaplastic.
- Occasionally the cytoplasm can be "mature" appearance and densely keratinized.
- In LBP dispersed abnormal single cells are seen more often than sheets and syncytial aggregates.
- Isolated cells may be present in the empty spaces between cell clusters.
- Relatively fewer abnormal cells may be present.
- As in LSIL, some HSIL cells may not show significant hyperchromasia, but other cytologic features of HSIL are present.
Sleeping Beauty

Isolated HSIL cells

Attention to the background

Thank you for your attention...

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