ThinPrep® Pap Test Diagnostic Challenges and Differential Diagnoses
ThinPrep® Characteristics

- **Wet Fixation**
  - enhanced cytoplasmic and nuclear detail
  - variability in nuclear staining
- **Cell Size**
  - proportionately smaller
  - single cells more prominent
  - cells may round up in solution e.g.. adenocarcinoma
- **Smear Pattern**
  - Cellular material not pulled out in mucous
  - Mechanical artifacts eliminated
- **Specimen Background**
  - Cellular debris may appear clumped
Differential Diagnoses

- Endocervical Adenocarcinoma vs. Poorly Differentiated Squamous Cell Carcinoma (SCC)
- Endocervical Adenocarcinoma vs. Endometrial Adenocarcinoma
- Endometrial Adenocarcinoma vs. Small Cell Squamous Carcinoma
- Adenocarcinoma-in-situ vs. Tubal Metaplasia
- HSIL vs. Single Endometrial Cells
- HSIL vs. Immature Squamous Metaplasia
- Poorly Differentiated Squamous Cell Carcinoma vs. Repair
Poorly Differentiated Squamous Cell Carcinoma vs. Endocervical Adenocarcinoma

Poorly Differentiated SCC
- 2D sheets and single cells
- Ragged group edges
- Dense, homogenous cytoplasm
- Pleomorphism, irregular nuclear shapes and sizes
- Irregular chromatin clumping
- Nucleoli variable in shape, size, number and position

Endocervical Adenocarcinoma
- 3D cell groupings
- Common group borders
- Delicate, foamy cytoplasm
- Enlarged nuclei, commonly round/oval
- Parachromatin clearing
- Round, central, single or multiple macronucleoli
Endocervical Adenocarcinoma vs. Endometrial Adenocarcinoma

Endocervical Adenocarcinoma

- Abundant abnormal material
  - directly scraped
- Well preserved material
- Cells and cell groupings generally larger in size
- Abundant, foamy cytoplasm, occasionally columnar shaped
- AIS precursor with endocervical architecture may be seen

Endometrial Adenocarcinoma

- Isolated abnormal groups
  - cell shedding
- Variable preservation of cells
- Cells and cell groupings generally smaller in size
- Scant, cyanophilic cytoplasm with occasional conspicuous vacuoles
- Mature hormonal pattern, watery transudate may be seen
<table>
<thead>
<tr>
<th>Endometrial Adenocarcinoma</th>
<th>Small Cell SCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Isolated abnormal groups</td>
<td>• Abundant abnormal material</td>
</tr>
<tr>
<td>• cell shedding</td>
<td>• directly scraped</td>
</tr>
<tr>
<td>• Occasional clusters, fewer single cells</td>
<td>• ++ Single cells, clusters</td>
</tr>
<tr>
<td>• Scant, vacuolated cytoplasm</td>
<td>• Dense, homogenous cytoplasm</td>
</tr>
<tr>
<td>• Eccentrically located nuclei</td>
<td>Centrally located nuclei</td>
</tr>
<tr>
<td>• Parachromatin clearing</td>
<td>• Irregular chromatin clumping</td>
</tr>
<tr>
<td>• Round, central, single or multiple macronucleoli</td>
<td>• Prominent, irregular nucleoli</td>
</tr>
</tbody>
</table>

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## Adenocarcinoma In Situ vs. Tubal Metaplasia

<table>
<thead>
<tr>
<th>Adenocarcinoma In Situ</th>
<th>Tubal Metaplasia</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Crowded sheets &amp; strips</td>
<td>• Cilia and/or terminal bars reliably identified</td>
</tr>
<tr>
<td>• Feathering &amp; pseudostratification</td>
<td>• Crowding without overlap, lacking depth of focus</td>
</tr>
<tr>
<td>• Relative hyperchromasia</td>
<td>• Evenly distributed chromatin</td>
</tr>
<tr>
<td>• Uniformly stippled chromatin</td>
<td>• Cytoplasm dense and cuboidal</td>
</tr>
<tr>
<td>• Nuclear size and shape variation</td>
<td>• Nucleoli absent</td>
</tr>
<tr>
<td>• Block-like nucleoli</td>
<td>• Nuclear membrane irregularities and thickening absent</td>
</tr>
<tr>
<td>• Mitoses and apoptotic bodies</td>
<td>• Occasional elongate nuclear forms</td>
</tr>
</tbody>
</table>

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HSIL vs. Endometrial Cells

**HSIL**
- Sheets, syncitia; thick plaques rather than 3D ball-like clusters
- Hyperchromasia
- Irregular nuclear membranes
- Single cells have centrally located nuclei
- Dense homogenous cytoplasm

**Endometrial Cells**
- 3D ball-like clusters and small, single cells
- Relative hyperchromasia
- Regular nuclear membranes
- Single cells with eccentrically located nuclei
- Scant basophilic cytoplasm with cytoplasmic “blebs”
HSIL vs. Immature Squamous Metaplasia

HSIL
- Single cells, clusters, and thickened plaques
- Variable hyperchromasia
- Irregular nuclear membranes
- Coarse clumped chromatin
- Variation in nuclear size within a cluster

Immature Squamous Metaplasia
- Single cells & cobblestone sheets
- Normochromatic
- Regular nuclear membranes
- Evenly distributed chromatin with pinpoint chromocenters
- Nuclear size & shape consistent
Repair vs. Poorly Differentiated SCC

**Repair (typical)**
- Cohesive sheets
- Significant nuclear size variation but typically round/oval in shape
- Thin, well defined nuclear membranes
- More open chromatin pattern with minimal variability
- Centrally located macronucleoli with smooth, round contours
- Virtually all nuclei display nucleoli

**Poorly Differentiated SCC**
- Poorly cohesive sheets and single cells
- Irregular nuclear shapes & sizes
- Thickened nuclear membranes
- Irregular chromatin clumping
- Nucleoli variable in shape, size, number and position
- Some nuclei display nucleoli, some nuclei do not
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Any Questions?