Glandular Lesions of the Cervix

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Normal Glandular Cells In Cervical Smears

- Endocervical
- Endometrial
Sources of Abnormal Glandular Cells In Cervical Smear

**Uterine**
- Cervix
- Endometrium
- Isthmus
- Vagina
- Fallopian tubes
- Vulva

**Extra-uterine**
*Metastaic to genital tract:*
- Ovary
- Primary peritoneal
- Secondary distant sites

*Trans uterine*
- Ovary
- Primary peritoneal

*Direct Invasion*
- Colon, rectum bladder
Endocervical Cells

Endocervix

- Endocervix has no true tubules, acini or gland
  (no body, neck and fundus unit)
- Contain series of clefts which tunnel into stroma forming crypts
- Crypt is lined by a single layer of columns cells
Endocervical Cells

• Tall, columnar, secretory or ciliated cells, size 15 to 20 um
• Intercalated cells can occur but rare in Pap. Smear
• Secretory Cells
  – Abundant cytoplasm
  – Multiple fine or single large vacuoles
  – “Plump and juicy” in
    * Pregnancy
    * Some contraceptive pills
    * Endocervical polyp
Ciliated Cells
* Few in number
* Cytoplasm wispy, basophilic
* Cilia stains pink-red
* Terminal bar
* Detached group of cilia are called ciliocytophthoria
* More common in first half (oesterogenetic) part of cycle and in post-menopausal women
Endocervical Cells (Continued)

Architecture

• Single cells
  * Columnar with basal nuclei and apical cytoplasm

• Strips
  * Picket fence or palisade arrangement of uniform orderly cells

• Sheets
  * Two dimensional
  * Regularly arranged uniform cells
  * Honeycomb pattern with slight prominence of cell membrane
Endocervical Cells (Continued)

Hormonal Influences

- Length of cells varies
  - Longest at mid-cycle
  - Shorter in post-menopausal
Endocervical Cells (Continued)

Nucleus
• Round to oval shape basal nuclei
• Fine vesicular evenly distributed chromatin
• Size is about the size of a parabasal cell nucleus area 54cm²
Bi or multinucleation can occur
Nucleoli ±
Nuclear size vary but shape remains the same (c/f to endometrial cells)
Occasional nipple-like protrusion – smearing artefact
Cytoplasm

- Finely vacuolated or granular
- Vacuole with clean or light purple-pink colour
- Often lyses with naked nuclei lying in finely granular or wispy blue clouds of degenerate cytoplasm and mucus
Endocervical Cells
Normal Variation

- Arias – stella reaction in pregnancy
- Pencil thin cells due to application of Lugol’s iodine before taking smear at colposcopy
- Curshmann’s spirals
- Inspissated mucus
- Mucus Ferning in peri-ovulatory period
- Goblet cells
Endometrial Cells

- Round to oval, smaller than endocervical cells
- Size $<15 \mu m$ - size of a polymorph
- Resemble degenerate lymphocyte or histiocyte
- Cytoplasm scanty, basophilic or amphophilic, may be vacuolated
Endometrial Cells (Continued)

- Bi or multinucleation rare
- Chromatin dense, vesicular, evenly distributed
- Condensation of chromatin underneath nuclear membrane
- Nucleoli small
- Cells usually degenerate due to ischaemia of menstrual shedding and time taken to travel through endocervix
Endometrial Cells (Continued)

Architecture

- Double-contour cell balls (Top hat)
  * Darkly staining stroma inside
  * Lighter staining epithelium outside
- Crowded, three dimensional group without stroma (D/D HCG)
  * Nuclei degenerate
  * Endometrial stroma nearby
Endometrial Stromal Cells (continued)

• Deep stromal cells
  * Spindle or stellate shape
  * Longitudinal groove in nuclear membrane
  * Chromatin similar to histiocyte
Endometrial Cells
(Continued)

Time of Cycle When Endometrial Cells Are Present

• First half of cycle (up to day 12)
• Anytime when endocervical brush is used
• After day 25 of the cycle.
• Up to age 40 in 2% of women between 14-25 days of cycle

• Exodus = 6th to 10th day of cycle contain
  * Endometrial cell balls
  * Histiocytes
  * Stromal cells
Inappropriate Shedding of normal Endometrial Cells

- 2nd half of cycle (day 14-25) in 40+ age group
- In postmenopausal women (not on HRT)

Causes:
* Endometriosis
* Endometritis
* Submucosal fibroid
* Early pregnancy
* Postpartum
* Abortion
* Instrumentation
* HRT
* Abnormal dysfunctional uterine bleeding
* IUD
* Endometrial hyperplasia
* Endometrial neoplasia
Differential Diagnosis of Endocervical and Endometrial Cells

Endocervical

- Larger
- More variable size
- Loose two-dimensional arrangement
- Honeycomb sheets
- Multinucleation, common
- Finer, pale chromatin
- Abundant cytoplasm
- Better preservation
Differential Diagnosis of Endocervical and Endometrial Cells

Endometrial

- Smaller
- More uniform
- Crowded three-dimensional clusters
- Double contoured balls (Top hat)
- Multinucleation rare
- Coarse dark chromatin
- Scanty cytoplasm
- Degeneration
QUIZ TIME
QUIZ TIME

Endocervical

Endometrial
Glandular cells
special features in LBC

Endocervical cells

- Artefact associated with cervex broom
  - Individual cells, smaller groups or in sheets – may be honeycomb
  - Starburst or cartwheel arrangements common
  - Cilia often seen

Endometrial cell

- Tight cell ball (top hat) or
  - Well preserved loose cell groupings with depth of focus and disordered arrangement (3D clusters)
  - Major pitfall of HCCG with false +ve diagnosis of HSIL/Severe dyskaryosis
Benign Variants Of Normal Glandular Cells

- Reactive endocervical cells
- Tubo-endometrioid Metaplasia
- Lower Uterine Segment Sampling
- IUCD changes (bubblegum cells)
- Endometriosis
- Microglandular hyperplasia
- Proplapse fimbrial remnants (In vault smear)
Reactive Endocervical Cells

- Nuclear enlargement and hyperchromasia
- Smooth nuclear membrane and bland chromatin
- Prominent Nucleoli
- Mitotic figure + or _
- Minimal nuclear crowding or overlap
- Multinucleation common
- Cells lie flat (No 3D effect)
- Moderate amount of cytoplasm
- Well defined cell borders
- Fine cytoplasmic vacuolation
### ATYPICAL Glandular cells

**Comparison of BSCC (UK), Bethesda (USA) and ECTP (European) Terminology**

<table>
<thead>
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<tbody>
<tr>
<td>Borderline nuclear change</td>
<td>Borderline change in endocervical cells.</td>
<td>Atypical endocervical / endometrial / glandular cells: NOS or favour neoplastic.</td>
<td>Atypical glandular cells (qualify).</td>
</tr>
</tbody>
</table>
Borderline Endocervical Cells (Atypical endocervical cells/NOS)

• Nuclear or architectural abnormality more marked than reactive changes but fall short of glandular neoplasia

Architectural abnormality
• Slight crowding of cells
• Strips with multi layering of nuclei in basal part of cells

Nuclear abnormality
• Increase N/C ratio
• Moderately granular chromatin
Borderline Endocervical Cells

(Atypical endocervical cells/ Favour Neoplastic)

- Cell morphology fall short of endocervical neoplasia
  
  **Architectural abnormality**
  - Sheets and strips with nuclear crowding and overlap
  - Occasional rosette and feathering
  
  **Nuclear abnormality**
  - Nuclear enlargement with hyperchromasia
  - Cell border ill defined but no snake-egg appearance
  - Round to oval nuclei
  - Inconspicuous nucleoli
  - Stratification of nuclei reaching in the upper half of cells
  - Chromatin granular but evenly distributed
  - Mitosis +/-
  - Clear or slightly bloody background
Neoplastic Glandular cells

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From: Revised BSCC terminology : Cytopathology Vol19 no.3 June 2008 P.137-157
Features of cervical glandular neoplasia (AIS)

Architectural features-
- Increased cellularity
- Overcrowding
- Clusters, sheets, pseudostratification/
  Community border- (dense common border, bird tail pattern)
- Rosettes and feathering
- Shallow bare-edged microbiopsies
- Central cell polarity maintained in clusters/sheets
- Discrete abnormal cells in background
Nuclear features-
- Smooth round to oval nuclei
- Cigar shaped nuclei
- Normal/hypo/hyperchromasia
- Granular stippled but even nuclear chromatin
- Nucleoli inconspicuous
- Irregular nuclear membrane thickness
- Mitosis and apoptosis
- Snake and egg pattern (nuclei bulging out of the cytoplasm)
- Raised N:C ratio- not necessarily increased nuclear size

Cytoplasm-
- Vacuolated
- Dense

Background
- Clear
Features of Endocervical Adenocarcinoma

- Features of AIS but with cellular enlargement and pleomorphism
- 3D groups, syncitia and single cells
- Nuclear membrane irregularity
- Irregular chromatin
- Macronucleoli
- Tumour diathesis
Atypical endometrial cells

- Small groups of 5-10 cells
- Slight enlargement of nuclei
- Small nucleoli
- Slight hyperchromasia
- Ill defined cell border
- Scanty cytoplasm
- Vacuoles +/-
Endometrial Adenocarcinoma

- In peri and post menopausal age
- 3D berry cluster or papillary fragment of cuboidal cells
- Nuclei at the outside margin of the cluster
- Prominent nucleoli
- Polymorphs ingestion in the cytoplasm
QUIZ TIME
QUIZ TIME

Normal endocervical

Endocervical Glandular Neoplasia/AIS
QUIZ TIME
QUIZ TIME

Normal Endometrial

Endometrial Adenocarcinoma
Glandular cells
Pitfalls
Features of Tuboendometrioid metaplasia

Architectural features-

- Crowded clusters of glandular cells
- Pseudostratified strips of cuboidal cells
- Well formed cytoplasmic border and terminal bar with cilia
Features of Tuboendometrioid metaplasia

**Architecture**
Square edges with box like arrangement

**Nuclear features**-
- Round to oval nuclei
- Finely granular dark nuclear chromatin
- Nucleoli inconspicuous or absent
- Apoptosis rare

**Cytoplasm features**-
- Dense, blunted margin
- Terminal bars (well-defined cytoplasmic borders)
- cilia+-
- +/- discrete vacuoles
Lower-uterine Segment Sampling

- Biphasic pattern
- Crowded clusters of glandular cells with peripheral palisading
- Disorganised stromal tissue containing blood vessels with spindle shape cells
- Histiocytes with kidney bean shape nuclei
- H/O treatment for CIN/CGIN
Peripheral palisading of cuboidal cells

Elongated spindle shaped stromal cells
Endometrials

Ding cell – IUCD related
The End