Cytology and Histology of Benign Glandular Lesions of the Uterine Cervix

Máire A. Duggan MD, FRCPC,
9th Annual Meeting,
Hong Kong Society of Cytology,
Hong Kong,
December 5, 2008
Goal

- Know the key cytopathologic and histopathologic features of usual and unusual benign glandular lesions of the uterine cervix
Classification

• **Benign Lesions**
  – Physiologic
  – Iatrogenic
  – Inflammatory
  – Neoplastic
  – Metaplastic
  – Hyperplastic
Cytopathology of Glandular Lesions

- Variable
- Confounded if more than one pathology
- Diagnoses include
  - NILM
    - Other: BEC; age>=40 years
  - Atypical glandular cells
  - Adenocarcinoma in situ
  - Invasive adenocarcinoma

### Cell Features

<table>
<thead>
<tr>
<th></th>
<th>Endocervical</th>
<th>Endometrial</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cell size</strong></td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td><strong>Cytoplasm</strong></td>
<td>Abundant ++</td>
<td>Variable</td>
</tr>
<tr>
<td><strong>Nucleus</strong></td>
<td>Oval /elongated</td>
<td>Round</td>
</tr>
</tbody>
</table>

Benign Endometrial Cells (BEC) in a Pap test

• **NILM**
  – Menstrual
    • Highest frequency: day 1-4
    • Infrequent after day 14
  – Brush artifact of LUS
  – BEC in Women <40 years

• **NILM-OTHER**: predictive of pathology
  – BEC in women >/=40

Menstrual Endometrium

Key features

- Bloody background
- Groups with central stroma and peripheral glandular cells
- Hyperchromatic spindle cells

Abraded Endometrium

Key features

- Biphasic tissue fragments
- Packed spindle cells
- Branching tubular glands
Benign Endometrial Cells in a woman $\geq 40$ years

- **Rationale**
  - Post menopausal: 1.7% endometrial carcinoma
  - Symptomatic: 17% endometrial adenocarcinoma
- **Currently controversial**
  - 2-5 fold increase in reporting
  - 30% increase in endometrial sampling
  - 1% endometrial pathology (0.8% malignant)
  - Not cost effective for asymptomatic women
  - Post menopausal status and symptoms more predictive

AGUS: Atypical Glandular cells of Undetermined Significance

- Nuclear atypia > benign < malignant

AGC: 94 follow up studies

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Terminological Evolution

- Adenocarcinoma in situ (AIS)
  - Precursor lesion of invasive adenocarcinoma
- Cytologic criteria
  - High PPV
  - Excellent reproducibility
- Separate category in TBS 2001
- All other AGUS: atypical glandular cells

AIS: cytologic criteria

- **Arrangements**
  - 3D crowded aggregates
    - Feathering
  - Single cells

- **Nuclear features**
  - Altered polarity
  - Oval/elongated shape
  - Hyperchromasia
  - Apoptosis
  - Mitoses
Adenocarcinoma In Situ:
3 D aggregates, hyperchromasia

Endocervical cells
Adenocarcinoma In Situ: rosette, feathering, ↑n:c, apoptosis
Adenocarcinoma In Situ:
altered polarity, mitoses, strip
AGC: Atypical Glandular Cells

- Classified
  - Not otherwise specified (NOS)
    - Endocervical, endometrial, glandular
  - Favor neoplastic
    - Endocervical, endometrial

**AGC: cytologic features**

- Some but not all features present

<table>
<thead>
<tr>
<th>Cell</th>
<th>Feature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrangements</td>
<td>3D Aggregates</td>
</tr>
<tr>
<td></td>
<td>Rosettes</td>
</tr>
<tr>
<td></td>
<td>Strips</td>
</tr>
<tr>
<td>Borders</td>
<td>Indistinct</td>
</tr>
<tr>
<td>Cytoplasm</td>
<td>Reduced</td>
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</table>

### AGC: cytologic features

- Some but not all features present

<table>
<thead>
<tr>
<th>Nucleus</th>
<th>Feature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrangement</td>
<td>Crowded</td>
</tr>
<tr>
<td></td>
<td>Feathering</td>
</tr>
<tr>
<td></td>
<td>Palisading</td>
</tr>
<tr>
<td>Size and shape</td>
<td>Increased and Variable</td>
</tr>
<tr>
<td>Chromatin</td>
<td>Dark</td>
</tr>
<tr>
<td></td>
<td>Coarsely granular</td>
</tr>
<tr>
<td>Nucleoli</td>
<td>Absent or inconspicuous</td>
</tr>
<tr>
<td>Mitosis</td>
<td>Present</td>
</tr>
</tbody>
</table>

Atypical Endometrial Cells

Additional features

- Cells in small 3D groups
  - Hyperchromatic crowded groups (HCG)
- Vacuolated cytoplasm
- Hyperchromatic nuclei
- Small nucleoli

AGC: Atypical Glandular Cells

- Follow up
  - colposcopy, endocervical curettage and endometrial biopsy
  - HPV testing
- Reproducibility
  - poor for cell type and diagnosis
- LBC diagnoses more sensitive and higher PPV
AGC: Psammoma Bodies without Atypia

• Rare occurrence
• Cytology features
  • Psammoma body
  • No cells/single layer of benign cells
• Etiology
  – 50% benign-50% malignant

Benign Lesions: classification

- Physiologic
  - Arias Stella reaction
- Iatrogenic
  - Fallopian tube prolapse
  - Drug/procedure associated
- Inflammatory
  - IUD
Physiologic: Arias Stella Reaction

• Hormonally associated proliferative atypia of glandular epithelium
• Endometrial glands typically involved
• Endocervical glands rarely involved
  – 9% hysterectomies from pregnant women
• Rarely presents as an abnormal Pap test

Histology: Arias Stella Reaction

Key pathology
- Cytoplasmic clearing
- Nuclear enlargement
- Hobnailed nuclei
- Hyperchromasia
Cytology: Arias Stella Reaction

Key features

• Cells: single/aggregates
• Clear cytoplasm
• Nuclei: round/oval
• Variable n:c ratio
• Chromatin: smudgy, granular
• Background: inflammatory

Arias Stella Reaction: differential diagnosis

- Clear cell adenocarcinoma, HSIL
- Clues
  - History of current or recent pregnancy
  - Histology
    - Focal lesion, confined to endocervical glands
    - Absent stromal invasion
  - Cytology
    - Absent diathesis and mitoses
    - Single cells, groups rare
    - Navicular cells may be present
Iatrogenic: Fallopian Tube Prolapse

- Rare complication of vaginal hysterectomy
- Symptoms
  - Dyspareunia
  - Vaginal bleeding and discharge
- Rarely presents as an abnormal Pap test
- Complications: none

Silverberg. Arch Pathol 1974; 97:100.
Fallopian Tube Prolapse

**Key pathology**

- Inflamed Tubal mucosa
- Regenerative changes
Fallopian Tube Prolapse

**Key features**

- Hypercellular smear
- Inflammatory background
- Sheets and groups of small glandular cells
- Uniform nuclei.
- Mitoses infrequent
Prolapsed Fallopian Tube: differential diagnosis

- Well differentiated adenocarcinoma
- Clues
  - Previous hysterectomy for benign disease
  - Histology
    - Absent stromal invasion
    - Absent cell stratification
  - Cytology
    - Absent blood and diathesis
    - Absent nuclear variability and mitoses
Iatrogenic: Tamoxifen Therapy

- **Small blue cells**
  - Post menopausal women/Tamoxifen
  - Origin: parabasal or reserve cell
- **Differential diagnosis**
  - Metastatic breast carcinoma
  - Endometrial carcinoma
- **Clues**
  - History
  - Absent diathesis, nuclear variability, mitoses
Small Blue Cell of Tamoxifen Therapy

Key features

• Loose clusters of naked nuclei
• Smooth nuclear outlines
• Uniform hyperchromasia

Inflammatory: IUD Changes

• Variable changes
  – Type and duration of use

• Endometrium
  – Chronic endometritis
  – Regenerative atypia
  – Squamous and hobnail metaplasia
  – Gland atrophy and decidualization

Cytology: IUD changes

**IUD cells**
- Possibly endometrial
- High N:C
- Multinucleated
- Nucleoli

**Actinomyces**

**Psammoma body**

**Hypermucinated endocervical cells**

Benign Lesions: classification

- **Neoplastic**
  - Endocervical polyp
  - Adenomyoma
  - Papillary adenofibroma
  - Villus adenoma

- **Metaplastic**
  - Tubal
  - Tubo-endometrioid
  - Oxyphilic
  - Prostatic
Neoplastic: Endocervical Polyp

- Most frequent tumor of the cervix
- Gross
  - Single lesion
  - Round with a smooth surface
  - 2-3cm
- Histological Types
  - Mucosal
  - Stromal
  - Vascular

Endocervical Polyp

Key pathology
- Fibrovascular core
- Feeder vessel
- Mucinous epithelium
- Squamous metaplasia
Endocervical Polyp: Cytology

- Not diagnostic
- Benign or atypical cells
  - Enlarged cells and nuclei
  - Multinucleation
  - Hyperchromasia
  - Prominent nucleoli
- Inflammation
  - Pus and blood
- Squamous metaplasia

Metaplasia: Tubo-endometrioid

• Frequent incidental finding
  – 31% cone/hysterectomy specimens

• Etiology
  – Idiopathic
  – Glandular ectopia
  – Repair reaction: laser, 5fu, xrt
  – Adenosis: DES

**Tubo/endometrioid metaplasia**

**Key pathology**
- Usually confined to inner 1/3 of cervix
- Tubal - ciliated, non ciliated, and peg cells
- Endometrioid - non ciliated cells, apical snouts, no peg cells
- Bcl2 positive, p16 focally positive, Ki67＜10%

Tubal Metaplasia: cytology

Key pathology

- Sheets or single cells
- Terminal bars/cilia
- Enlarged, polarized nuclei
- Fine chromatin
- Small nucleoli
- Rare mitosis
- Clean background

Hyperplastic: pseudoneoplastic

- Microglandular hyperplasia
- Endometriosis
- Endocervical hyperplasia
- Mesonephric hyperplasia
- Nabothian cysts and deep glands
- Tunnel Clusters
- Endosalpingiosis
Hyperplasia: Microglandular

- Presentation: incidental or polyp
- Frequency: 27% cone/hysterectomy
- Progestin relationship unclear
- Complications
  - Atypical/florid

Microglandular Hyperplasia

Key pathology
- Focal/diffuse, superficial/deep proliferation
- Closely packed small tubular glands
- Mucinous epithelium, reserve cells, squamous metaplasia
- Mitosis: \( \leq 1/10\text{hpf} \)
- Ki67<10\%, Negative p16
**Microglandular Hyperplasia**

**Cytology features**
- Sheets of enlarged glandular cells
- Vacuolated cytoplasm
- Mild nuclear enlargement
- Fine chromatin
- Small nucleoli

Yahr. Diagn Cytopathol 1991: 7; 248
Hyperplasia: Endometriosis

- **Uncommon**
- **Etiology**
  - Post conization/implantation
- **Pap test presentation: rare**
  - Variable: NILM – HSIL – AIS
  - Absolute diagnosis very difficult

Cervical Endometriosis

Key pathology

- Endometrial glands
- Endometrial stroma
- No atypia
Endometriosis

Cytology features
• Cell spindling
• Cell uniformity
• Absent diathesis

Hyperplasia: Endocervical

- Rare: incidental finding, mucus discharge, mass lesion
- Proliferation confined to inner half of cervix
- Pap test presentation: not reported
- 2 Histological types:
  - Lobular-pyloric gland metaplasia (PGM)
  - Diffuse laminar hyperplasia (DLEH)

Lobular Hyperplasia

Key pathology
- Rounded proliferation of small glands
- Duct centred
- Pseudocribriform pattern
- Bland mucinous epithelium

Immunoprofile
- PAS positive
- p16 positive
- HIK1083 positive
- HPV DNA negative
- CEA negative

Diffuse Laminar Endocervical Hyperplasia

Key Pathology
- Circumscribe glandular proliferation
- Chronic inflammatory infiltrate
- Benign endocervical glands
Mesonephric Remnants

- **Wolffian duct remnants: lateral wall**
  - 22% adults

- **Pap test presentation: rare**
  - Clusters of cuboidal cells

- **Complications**
  - **Hyperplasia**
    - Proliferation > 6mm: diffuse/lobular/ductal
      - Occasionally transmural
  - **Carcinoma**

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Mesonephric Hyperplasia

Key pathology
- Small tubular glands
- No intracellular mucin or glycogen
- PAS positive luminal, colloid like secretion
The End
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Classification

- **Malignant Lesions**
  - Premalignant lesions
    - Adenocarcinoma in situ: AIS
    - Endocervical glandular dysplasia: EGD
    - Stratified mucin producing intraepithelial lesion: SMILE
  - Adenocarcinoma
Glandular Premalignancy

• Precursor lesions of adenocarcinoma
  – AIS: good evidence
  – Dysplasia: poor evidence
• AIS incidence: 0.6/100,000
  – CIN III: x50 more frequent
• AIS prevalence: increasing
AIS: risk factors

- 50% AIS: concomitant SIL
- Risk factors similar to SIL
- HPV 16 and 18
- Multiple sexual partners
- OCP
- Early onset sexual activity
- Low socio-economic status

AIS: clinical features

- Mean age: 29 years
- Symptoms
  - None, discharge, abnormal Pap test
- Location: 65% T zone
- Mostly unifocal
- Colposcopy: no specific pattern
AIS

- Frequency: 10% of glandular malignancies
- Histological types: not clinically significant
  - Mucinous
  - Intestinal
  - Adenosquamous
  - Clear cell
  - Endometrioid
  - Ciliated

AIS

Key pathology

- Normal glandular architecture
- Decreased mucin
- Stratified columnar cells
- Hyperchromatic nuclei
- Mitoses
- Absent stromal invasion
AIS: HPV status and IHC

• HPV DNA
  – 66% (40-90%) positive
  – HPV 16 and 18
  – Predominance of HPV 18

• Antibody positive
  – CEA (70%) and Steroid receptors
  – P16 and p53
  – Ki67: high index (>30%)

• Antibody negative
  – Vimentin and bcl2

AGC and HSIL

• Approximately 16% of AGC in follow up = HSIL

• Reasons
  – Co- incidental lesions
    • AIS and HSIL: 50%
  – Glandular mimics
    • HSIL in endocervical glands
AIS and HSIL: 2 cell types
HSIL involving endocervical glands

SMILE

- Uncommon lesion
- Resembles SIL with full thickness cytoplasmic vacuolization
- Described in association with cervical adenocarcinoma
- Also associated with HSIL, AIS or squamous cell carcinoma

**Key pathology**
- Dysplastic nuclei
- Mucin vacuoles
- Mitoses

**Cytology features**
- Not reported
Endocervical Dysplasia

• Controversial lesion
  – No outcome studies

• Alternate terminologies
  – Low CGIN: UK
  – Superficial (early) AIS

• Investigation
  – HPV testing
  – P16 positive
  – Steroid receptor positive

Endocervical dysplasia: criteria

- Hyperchromatic nuclei
- Occasional mitoses
- Minimal stratification
- AIS in one gland
- Other criteria

- Management
  - controversial

Adenocarcinoma: epidemiology

- 20-25% cervical carcinomas
- Mean age at presentation
  - Microinvasive adenocarcinoma: 39-44 years
  - Invasive adenocarcinoma: 44-54 years
- Incidence increasing in Canada and elsewhere
  - 1994-96: 1.83/100,000
    - 41% relative increase in 22 years
    - Higher Pap test false negative rate due to sampling error

Adenocarcinoma: risk factors

- Sexual behavior
  - Early age of onset of sexual activity
  - Lifetime number of sexual partners
  - Early age of first birth and increasing parity
- Oral contraceptives
- Obesity and body fat distribution
- No association with cigarette smoking

Adenocarcinoma: risk factors

• Human Papilloma Virus (odds ratio=81)
  – 88% HPV DNA positive
  – Types 16/18 in 82%
    • Type 16 predominant in endometrioid and VGA
    • Type 18=16 or slight predominance in others

• Genetic
  – Ovarian carcinoma
  – Peutz Jegher’s syndrome

Adenocarcinoma: classification

- 57% Mucinous
- 30% Endometrioid
- 11% Clear cell
- 2% Rare types
  - Minimal deviation
  - Serous
  - Mesonephric
  - Well differentiated villoglandular

Wright. Springer Verlag, 2002.
Classification System

Deficiencies

- Variable frequency of endometrioid
  - 7-50%

- Interobserver agreement
  - Endocervical, endometrioid, clear cell, serous: moderate-good
  - Mixed carcinomas: fair-poor
  - Villoglandular, adenosquamous: poor

Mucinous Adenocarcinoma

• Synchronous premalignancy
  – 66% AIS
  – 16% HSIL

• Synchronous mucinous tumors of ovary and fallopian tube
  – Primary or metastatic

• 3 morphologic types
  – Endocervical, intestinal, signet ring
    • Pure
    • Mixed

Endocervical adenocarcinoma

Key pathology

- Complex racemose glands
- Surface and intraluminal papillae
- Pale granular cytoplasm
- Brisk mitotic activity
- Apoptotic bodies

Young. Histopathol 2002; 41: 185.
Endocervical adenocarcinoma

• Mostly neutral mucin: content variable
  – Pas/al blue: red/purple mixed cytoplasmic stain
  – Mucicarmine: cytoplasmic positivity

• Antibody positive
  – CEA: cytoplasmic
  – P16 positive: diffuse and strong

• Antibody negative
  – Vimentin
  – Estrogen receptor

Endocervical adenocarcinoma

- Pas/al blue
- CEA
- Vimentin
- p16
Cytology: endocervical adenocarcinoma

- Hypercellular smears
- Cells
  - Single
  - Sheets
  - Clusters
- Cell features of AIS
- Additional features
  - Perinuclear clearing
  - Macronucleoli
  - Tumor Diathesis

Intestinal adenocarcinoma

Key pathology
• Glands and papillae
• Pseudostratified mucin poor cells
• Goblet cells

Signet ring carcinoma

Key pathology
- Signet ring cells
- Pure form is rare
- Usually mixed with other types

Young. Histopathol 2002; 41: 185.
Endometrioid Adenocarcinoma

• Resembles endometrial counterpart

• Synchronous premalignancy
  – Higher compared to non endometrioid carcinomas
    • 81% AIS
    • 54% HSIL

• Difficult to distinguish from mucin poor mucinous carcinomas

• Lower frequency of squamous differentiation

• Better prognosis than mucinous carcinoma

Endometrioid adenocarcinoma

Key pathology
- Glandular architecture
- Benign squamous differentiation
- Stratified, oval nuclei
- No cytoplasmic mucin

Young. Histopathol 2002; 41: 185.
Endometrioid carcinoma

Cytology features

- Similar to mucinous carcinoma
Clear cell Carcinoma

- **DES exposed**
  - Young women
  - Location
    - Ectocervical
  - HPV status
    - Usually negative
    - Rare cases HPV 31 positive

- **Sporadic**
  - Post menopausal women
  - Location
    - Endo or ectocervical

Clear cell Carcinoma

Key pathology
- Solid, tubulocystic, papillary
- Glycogenated clear cytoplasm
- Intracystic mucin
- Hobnail cells

Young. Histopathol 2002; 41: 185.
Clear cell Carcinoma

Cytology features
• Large cells
• Abundant cytoplasm
• Round nucleus
• Prominent nucleolus
Minimal Deviation
Adenocarcinoma

• Rare tumor
  – 3 types
• Associations
  – Not HPV related: 1 report of type 16 and 18+
  – Lobular endocervical hyperplasia (PGM)
  – AIS with a gastric immunophenotype
  – Adenoma malignum (AM)
    • Mucinous ovarian tumors
    • SCTAT
    • Peutz Jeghers Syndrome

Adenoma Malignum

• Symptoms
  – Profuse watery discharge/bleeding
• Difficult on cytology and small biopsies
• Cytology features
  – Irregular sheets of benign glandular cells
  – Rare malignant cells with large nucleoli
• Prognosis
  – Worse than mucinous carcinoma

Adenoma malignum

**Key pathology**
- Atypical glands: shape, size, location
- Desmoplasia near outpouchings
- Single layer of low grade mucinous cells
- Rare gland with malignant cells
### Adenoma Malignum versus Normal or Benign Endocervix

<table>
<thead>
<tr>
<th>Stain</th>
<th>Adenoma Malignum</th>
<th>Normal or Benign</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAS/Al Blue</td>
<td>Mostly red</td>
<td>Purple/ violet</td>
</tr>
<tr>
<td>HIK1083-PGM</td>
<td>+</td>
<td>-*</td>
</tr>
<tr>
<td>CEA</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>P16</td>
<td>30% +</td>
<td>-</td>
</tr>
<tr>
<td>Alpha SMA</td>
<td>Increased + stroma</td>
<td>- stroma</td>
</tr>
<tr>
<td>ER</td>
<td>- stroma</td>
<td>+ stroma</td>
</tr>
</tbody>
</table>

*positive staining in lobular hyperplasia*

Adenoma Malignum: Pas Al Blue*

*ph=2.5

Serous Carcinoma

- Histology similar to ovarian and endometrial counterparts
- Metastatic spread should be excluded
- Outcome
  - Stage 1 = Stage 1 endocervical adenocarcinoma
  - Advanced stage: rapidly fatal

Serous carcinoma

Key pathology
- Complex papillary proliferation
- Stratification and tufting
- High grade nuclei
  - P53 positive, CEA negative

Serous Carcinoma

Cytology features
- Single cells
- Sheets
- Tight balls
- Malignant features obvious
- Psammoma bodies
Mesonephric carcinoma

- Rare tumor
  - 30 documented cases
- Arise from mesonephric duct remnants
- Gross appearance
  - Cervical mass
- HPV negative
- Outcome
  - More indolent than mucinous carcinoma

Mesonephric carcinoma

**Key pathology**
- Variable pattern: mostly ductal
- Retiform, tubular, sex cord, spindle cell
- Eosinophilic mucinous secretion
- Mesonephric remnants
Mesonephric carcinoma: immunohistochemistry

• Pattern similar to mesonephric remnants
• Negative staining
  – mCEA, CTK 20, ER/PR
• Positive staining
  – EMA, CTK 7, CAM 5.2, CD10, Vimentin, Calretinin, Inhibin, p16
• CEA, CD10, and vimentin pattern is controversial

Well Differentiated Villoglandular Adenocarcinoma

- Rare tumor of young women
  - Average age: 35
- Presentation: vaginal bleeding/exophytic mass
- May be mixed with other types of carcinoma
- HPV status
  - 100% type16/18 positive
  - Mostly type 16
- Prognosis usually excellent

Well differentiated villoglandular adenocarcinoma

Key pathology
- Papillary architecture
- Minimal cytological atypia
- Minimal stromal invasion
- No desmoplasia
Well differentiated villoglandular adenocarcinoma: cytology

- Not specific
- Atypical glandular cells
  - Papillary fragments
  - Nuclear crowding
  - Subtle atypia
- High false negative rate

Secondary Adenocarcinoma

- Genital tract
  - Endometrial carcinoma
  - Ovarian, tubal and peritoneal
- Extragential sites
  - Rare
    - Breast
    - Colorectal
    - Gastric

Endometrial carcinoma

• Stage II tumors
  – IIa: Surface cancerization
  – IIb: Stromal invasion

• Tumor source
  – Direct spread
  – Surface metastases
  – Embolic

Stage II endometrial carcinoma: histology

Stage IIa

Stage IIb
Endometrial endometrioid carcinoma: cytology

Key Pathology
- Watery diathesis
- Crowded groups
- Prominent nucleoli
- Ingested PMNs
### Cervical Primary versus Stage II Endometrial Carcinoma

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Cervix</th>
<th>Endometrium</th>
</tr>
</thead>
<tbody>
<tr>
<td>ER/PR</td>
<td>83% -</td>
<td>70% +</td>
</tr>
<tr>
<td>CEA</td>
<td>86% +</td>
<td>89% -</td>
</tr>
<tr>
<td>Vimentin</td>
<td>86% -</td>
<td>59% +</td>
</tr>
<tr>
<td>P16</td>
<td>100% +</td>
<td>30%+</td>
</tr>
<tr>
<td></td>
<td>strong/diffuse</td>
<td>Moderate/patchy</td>
</tr>
</tbody>
</table>

Stage II Endometrial Carcinoma

PTEN: tumor suppressor gene
- Endometrial carcinoma: somatic mutations
  - Expression is diminished
- Cervical adenocarcinoma
  - Expression retained

Extrauterine genital tract primaries

- Dissemination pathways
- Direct spread
- Embolic spread
- Transtubal migration


Transtubal migration: serous ovarian carcinoma
Metastatic Breast Carcinoma

- Frequency increasing
  - longer survival
- Lobular more frequent than ductal
- Pap test: rare malignant cells
- Histology: isolated metastasis

Metastatic colonic carcinoma

Key cytology features
• Dirty background
• Glandular groups
• Palisading of basal nuclei

The End

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Hong Kong
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References


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8,097 women with squamous cell carcinoma and 1,374 women with adenocarcinoma from 12 epidemiological studies. Int J Cancer 2007; 120: 885-91.


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