Pathology of the Endometrium

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Changes in the Uterus

Thoughout life there are marked changes in the size of the uterus
**Endometrium**

*Most common diseases:*

- Abnormal uterine bleeding
- Inflammatory conditions
- Benign neoplasms
- Endometrial cancer

**Anatomical Regions**

*Corpus:* Responsive to hormones
Thickness changes with cycle

*LUS:* Thinner than corpus
Less hormonally responsive
Hybrid between endocervix and endometrium
Changes in the Uterus

Throughout life there are marked changes in the size of the uterus.

Cellular Components

**Epithelium:** Basalis-type cell
- Secretory cells
- Ciliated cells

**Stroma:** Stromal cells
- Stromal granulocytes
Endometrium

Composed of both glandular and stromal elements

Cyclical Changes in the Endometrium
Cyclical Changes in the Endometrium

Early Proliferative Phase

Small circular glands with numerous mitoses are present.
16 Day

Glands are somewhat dilated with secretions
Subnuclear vacuoles
Many mitoses
*Can't tell if ovulation has occurred*

23 Day

Stroma shows prominent spiral arterioles with predecidual change adjacent to them
Glands contain secretions
23 Day

Stroma shows prominent spiral arterioles with predecidual change adjacent to them

Glands contain secretions

26 Day

Stroma shows predecidual change that bridges surface to spiral arterioles

Glands still contain secretions
Cyclical Changes in the Endometrium

Dysfunctional Bleeding

Definition:

Abnormal bleeding - Dx of exclusion
Most patients are anovulatory or short duration cycles
Most common in postpubertal period and perimenopausal period
Can be associated with PCO, stress
**Dysfunctional Bleeding**

**Endometrium:**
- Weakly proliferative endometrium
- Normal proliferative endometrium
- Disordered proliferative
- Endometrial hyperplasia
- Asynchronously developed endometrium

**Persistent Proliferative**
- Dilated proliferative type glands, with pseudostratification
- Focal breakdown common
- *Due to unopposed estrogen*
Irregularly Developed

Secretory type glands co-exist with proliferative glands.
This pattern is sometimes seen in women with dysfunctional bleeding.

Non-neoplastic Disorders

Iatrogenic endometrium
Exogenous hormones
Tamoxifen
IUD's

Endometritis
Metaplasias
Hyperplasia
**Progestational Agents**

Marked pseudo-decididualization of stroma.

Glands are small with secretory exhaustion.

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**Metaplasias**

*Tubal metaplasia* occurs in setting of estrogen excess or postmenopausal.

*Squamous metaplasia* frequently occurs in hyperplasia, neoplasia, CEMI.

*Mucinous, papillary and eosinophic* types are less common.
**Tubal Metaplasia**

The endometrium looks very much like the epithelium of the fallopian tube. Cilia are present.

*Post-menopausal women with estrogen excess*

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**Squamous Metaplasia**

A morule of squamous differentiation is present in the center of a group of glands with atypical hyperplasia.
## Endometritis

**Acute:** Microabcesses - stroma / glands  
Classically postabortal  
Strep., Staphy., GC

**Stroma:** Stromal cells  
Stromal granulocytes

This is a post-abortion septic uterus. Abortion was performed by non-medical personnel.
Chronic Endometritis

Multiple plasma cells are identified. These are not normally seen in the endometrium and when present indicate chronic endometritis.

Tubercular Endometritis

A caseating granuloma is present with giant cells. TB of the endometrium is uncommon in the U.S. but is seen not infrequently in many areas of the world.
**Endometrial Hyperplasia**

Abnormal proliferation of endometrial glandular epithelium (and often stroma) that lacks stromal invasion.

**Endometrial Hyperplasia**

Wide spectrum of patients
Associated with prolonged, unopposed exposure to estrogen
Therapy depends on type / patient / setting
Endometrial Hyperplasia

The endometrium is markedly thickened and is folded into prominent polypoid masses

Current Terminology:

- Simple hyperplasia
- Complex hyperplasia (*adenomatous*)
- Simple atypical hyperplasia
- Complex atypical hyperplasia
**Simple Hyperplasia**

Dilated proliferative type glands, with pseudostratification

Increased gland:stroma ratio and some "budding"

*Due to unopposed estrogen*

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**Complex Hyperplasia**

The volume of glands is increased and the glands are "crowded"

Glands are dilated and have irregular outlines
**Complex Hyperplasia**

Some glands have papillary projections into them
Outlines are complex

**Atypical Hyperplasia**

There is both cytological and architectural atypia present.
The architectural atypia is demonstrated by the cribiforming.
Atypical Hyperplasia

"Glands within glands" are seen. There is squamous metaplasia in the center gland.

Endometrial Hyperplasia

Understanding its impact:

Early studies had lots of problems
Endometrium is histologically complex
Cytologic changes are difficult to judge
Can't follow without biopsy
### Progression of Hyperplasia*

<table>
<thead>
<tr>
<th>Type of Hyperplasia</th>
<th>% to CA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple (&quot;Cystic&quot;)</td>
<td>13%</td>
</tr>
<tr>
<td>Complex (&quot;Adenomatous&quot;)</td>
<td>27%</td>
</tr>
<tr>
<td>Atypical</td>
<td>75%</td>
</tr>
<tr>
<td>AdenoCA in situ</td>
<td>100%</td>
</tr>
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</table>

*Wentz, AJOG, 1984*

### Progression of Hyperplasia

<table>
<thead>
<tr>
<th>Type</th>
<th>Regress</th>
<th>Persist</th>
<th>CA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple</td>
<td>80%</td>
<td>19%</td>
<td>1%</td>
</tr>
<tr>
<td>Complex</td>
<td>80%</td>
<td>17%</td>
<td>3%</td>
</tr>
<tr>
<td>Simple atypical</td>
<td>69%</td>
<td>23%</td>
<td>8%</td>
</tr>
<tr>
<td>Complex atyp.</td>
<td>57%</td>
<td>14%</td>
<td>29%</td>
</tr>
</tbody>
</table>
Progression of Hyperplasia

Endometrium

Constant estrogen

Hyperplasia

Simple Hyperplasia
Atypical Hyperplasia
Adenocarcinoma

Other factors

Neoplastic Disorders

Endometrial polyps
Endometrial stromal lesions
Endometrial carcinomas
Mesenchymal tumors
Mixed tumors
Endometrial Polyps

Are quite common, especially 40 - 50 yrs.
Develop as focal hyperplasia of basalis.
Four classic features:

- Fibrotic stroma
- Prominent vascularity
- Glands out of phase
- Irregular gland architecture

Endometrial Polyp

Small soft polyp arises from the fundus of the uterus
**Endometrial Polyp**

![Image of Endometrial Polyp](image1)

**Endometrial Polyp**

![Image of Endometrial Polyp](image2)
**Uterine Leiomyoma**

Proliferation of smooth muscle cells
Lesion of reproductive years
20 - 30% of women 30 years and older
More common in blacks
Present with bleeding, pain, pressure

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**Uterine Leiomyomas**

*Pathogenesis:*

In reproductive yrs - rare after menopause
Contain estrogen / progesterone receptors
Hormones thought to play a role
Gonadotropin releasing hormone agonists cause regression
Uterine Leiomyomas

Pathogenesis:

Lesions are monoclonal - G6PD or PCR
Non-random chromosomal abnormalities quite common (40% of cases)
30% of abnormal karotypes involve region 12q14-15 (same area as involved in lipomas and rhabdiosarcomas)

Fibroid Uterus

The uterus is distorted by multiple intramural leiomyomas.
Cut section through this leiomyoma shows a well-demarcated firm mass with a whorled appearance.
**Endometrial Carcinomas**

**Clinical features:**

Most common genital tract cancer  
High incidence in North America / Europe  
Associated with ERT, obesity, diabetes, hypertension, nulliparity, tamoxifen  
Two clinico-pathologic forms

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**Endometrial Adenocarcinoma**

A necrotic mass arises from the posterior wall of the uterus and protudes into the endometrial cavity.
Extensive and Deeply Invasive Cancer

WHO Classification

- Endometrioid carcinoma
- Serous carcinoma
- Clear cell adenocarcinoma
- Mucinous adenocarcinoma
- Squamous cell carcinoma
- Mixed carcinoma
- Undifferentiated carcinoma
### Endometrial Cancer - Types

<table>
<thead>
<tr>
<th></th>
<th>Type I</th>
<th>Type II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Young</td>
<td>Old</td>
</tr>
<tr>
<td>Unopposed estrogen</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Diabetes / obesity</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Grade / stage</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Survival</td>
<td>Good</td>
<td>Poor</td>
</tr>
</tbody>
</table>

**Endometrioid Adenocarcinoma**

This is a well-differentiated lesion
Back-to-back glands with little intervening stroma
No solid areas
Difficult to identify "stromal invasion"
**Endometrioid Adenocarcinoma**

Glands are pseudo-stratified with multiple layers
Enlarged, round nuclei
Coarse chromatin
Prominent nucleoli

**Uterine Serous Carcinoma**

Usually papillary
Looks like ovarian CA
High nuclear grade
*Poor prognosis*
**Uterine Serous Carcinoma**

- Very high nuclear grade tumor
- Histology resembles that of ovarian papillary serous CA

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**Endometrial Cancer**

**Histological grading:**

Based predominantly on architecture:

- $< 5\%$ solid $\rightarrow$ well-differentiated
- $5 - 50\%$ solid $\rightarrow$ moderately diff
- $> 50\%$ solid $\rightarrow$ poorly differentiated

High nuclear grade can increase the grade
**Endometrial Cancer**

**Prognostic features:**

- Age
- Stage
- Race
- Grade
- Depth of invasion
- Peritoneal cytology
- Vascular invasion

**FIGO Staging - Corpus Cancer**

- **IA** Tumor limited to endometrium
- **IB** Invasion to <1/2 of myometrium
- **IC** Invasion to > 1/2 myometrium
- **II** Involvement of corpus and cervix
- **III** Extension outside of uterus, but not outside of true pelvis
- **IV** Extends outside true pelvis or involves mucosa of bladder or rectum
### FIGO Stage: 5 Year Survival

<table>
<thead>
<tr>
<th>Stage</th>
<th>No.</th>
<th>% Survival</th>
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</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>11,035</td>
<td>73%</td>
</tr>
<tr>
<td>Stage 2</td>
<td>2,014</td>
<td>56%</td>
</tr>
<tr>
<td>Stage 3</td>
<td>921</td>
<td>32%</td>
</tr>
<tr>
<td>Stage 4</td>
<td>409</td>
<td>11%</td>
</tr>
</tbody>
</table>