Pathology of the Endometrium

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Endometrium

Most common diseases:

- Abnormal uterine bleeding
- Inflammatory conditions
- Benign neoplasms
- Endometrial cancer
**Anatomical Regions**

<table>
<thead>
<tr>
<th>Region</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corpus</td>
<td>Responsive to hormones. Thickness changes with cycle.</td>
</tr>
<tr>
<td>LUS</td>
<td>Thinner than corpus. Less hormonally responsive. Hybrid between endocervix and endometrium.</td>
</tr>
</tbody>
</table>

**Cellular Components**

<table>
<thead>
<tr>
<th>Component</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epithelium</td>
<td>Basalis-type cell, Secretory cells, Ciliated cells</td>
</tr>
<tr>
<td>Stroma</td>
<td>Stromal cells, Stromal granulocytes</td>
</tr>
</tbody>
</table>
Cyclical Changes in the Endometrium

Maturation of follicle
Ovulation
Corpus luteum
Corpus luteum of pregnancy
Implantation begins
Compact layer
Gland
Spongy layer
Basal layer

0 4 14 28
Menstrual phase Follicular or proliferative phase Progestational or secretory phase Gravid phase

Cyclical Changes in the Endometrium

[Image of histological sections of the endometrium at different stages of the menstrual cycle]
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

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

Progestational Agents
Marked pseudo-decidualization of stroma.
Glands are small with secretory exhaustion

Non-neoplastic Disorders

Iatrogenic endometrium
Exogenous hormones
Tamoxifen
IUD's

Endometritis
Metaplasias
Hyperplasia
**Metaplasias**

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

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

*Mucinous, papillary and eosinophilic* types are less common.

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**Tubal Metaplasia**

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

*Post-menopausal women with estrogen excess*

**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

**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

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

Complex Hyperplasia
- The volume of glands is increased and the glands are "crowded"
- Glands are dilated and have irregular outlines

Atypical Hyperplasia
- There is both cytological and architectural atypia present.
- The architectural atypia is demonstrated by the cribiforming.
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>
</tbody>
</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>

**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
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

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 karyotypes involve region 12q14-15 (same area as involved in lipomas and rhabdosarcomas)

Endometrial Carcinomas

Clinical features:
Most common genital tract cancer
High incidence in North America / Europe
Associated with ERT, obesity, diabetes, hypertension, nulliparity, tamoxifin
Two clinico-pathologic forms
**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>
Endometrial Cancer

Histological grading:

Based predominantly on architecture:
- < 5% solid    well-differentiated
- 5 - 50% solid  moderately diff
- > 50% solid  poorly differentiated

High nuclear grade can increase the grade

Endometrial Cancer

Prognostic features:

Age            Depth of invasion
Stage          Peritoneal cytology
Race           Vascular invasion
Grade
**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>
</tr>
</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>
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