Endometrial Hyperplasia & Carcinoma *

David Engle, MD, MS, FACOG
Associate Professor, Dept. of OB/GYN
University of Alabama

Division of Gynecologic Oncology
Huntsville Hospital

*Based on APGO Student objectives 10th Ed
Learning Objectives
Endometrial Hyperplasia & Endometrial Cancer

- Risk factors
- Describe symptoms and physical findings
- Causes, diagnosis, and management of postmenopausal bleeding
Signs & Symptoms

Vaginal Bleeding

- Post menopausal bleeding
  - Even a drop should be worked up
  - Approximately 10% caused by cancer

- Abnormal Uterine Bleeding (pre & peri-menopausal)
  - Especially with risk factors
# Postmenopausal Bleeding

## Causes

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrophy</td>
<td>(60-80%)</td>
</tr>
<tr>
<td>Hormone Therapy</td>
<td>(15-25%)</td>
</tr>
<tr>
<td>Endometrial Cancer</td>
<td>(10-15%)</td>
</tr>
<tr>
<td>Hyperplasia</td>
<td>(5-10%)</td>
</tr>
<tr>
<td>Polyps</td>
<td>(2-12%)</td>
</tr>
</tbody>
</table>
Postmenopausal Bleeding

- 80-90% of Endometrial Cancer present with postmenopausal bleeding or discharge
Postmenopausal Bleeding

**Work-Up**
- **History**
- **Physical-exam**
- **Assessment of endometrium**
  - Trans-vaginal Ultrasound (saline infused may help)
  - Endometrial sampling (biopsy, D&C)
Postmenopausal Bleeding

**Evaluation Recommendations**

- Any vaginal bleeding in a postmenopausal woman requires assessment to exclude malignancy.
- Women with postmenopausal uterine bleeding may be assessed initially with either endometrial biopsy or transvaginal ultrasonography; this initial evaluation does not require performance of both tests.
- When endometrial biopsy is performed and tissue is reported as insufficient for diagnosis, some further investigation is necessary and transvaginal ultrasonography may be performed.
- When transvaginal ultrasonography is performed for patients with postmenopausal bleeding and an endometrial thickness of less than or equal to 4 mm is found, endometrial sampling is not required.
Evaluation

Recommendations (ACOG-C.O. #440 9/09)

- Endometrial thickness of greater than 4 mm in a patient with postmenopausal bleeding should trigger alternative evaluation (such as sonohysterography, office hysteroscopy, or endometrial biopsy), as should an inability to adequately visualize thickness.

- Meaningful assessment of the endometrium by ultrasonography is not possible in all patients. In such cases, alternative assessment should be completed.

- When bleeding persists despite negative initial evaluations, additional assessment usually is indicated.

- The significance of an endometrial thickness of greater than 4 mm in an asymptomatic, postmenopausal patient has not been established, and this finding need not routinely trigger evaluation.
Postmenopausal Bleeding

- Endometrial sampling
  - In office biopsy
    - Done with Endometrial Pipelle
  - Operative biopsy
    - D&C
    - For patients unable to tolerate or undergo an in office biopsy
    - Gold standard
Risk Factors
Endometrial Hyperplasia/Malignancy

- Obesity
- Nulliparity
- Late age at menopause, early menarche, history of irregular bleeding (anovulatory cycles)
- Metabolic Syndrome (diabetes, hypertension, gallbladder disease…)
- Tamoxifen exposure
- Hereditary
Risk Factors
Endometrial Cancer

- Obesity
  - Up to 10x increased risk
  - Androstenedione produced by adrenal is converted to estrone via aromatization in adipose tissue
  - Especially increases risk in younger women (even in 20’s and 30’s)
Risk Factors

- Tamoxifen
  - Increases risk 2.5-7.5

- Unopposed postmenopausal estrogen replacement therapy
  - Increases 4.5

- Late menopause
  - Increases risk 2.5

- Early menarche
  - Increases risk 1.5
Risk Factors

- Nulliparity
  - Increases risk 2x compared to woman with 1 child
  - Increases risk 3x compared to woman with 5 children

- Diabetes
  - Increases risk 2x
Risk Factors

- Polycystic ovarian disease
  - Increases risk but amount unknown

- Hypertension
  - Does not increase risk when controlled for other factors
Protective Factors

- Current types of oral contraceptives
  - Decrease risk up to 50%
Endometrial Hyperplasia

- Precursor lesion for endometrial adenocarcinoma
- Types of hyperplasia
  - Simple hyperplasia
  - Complex hyperplasia
  - Nuclear Atypia (+/-)
- Atypical Complex Hyperplasia has a >40% of having a synchronous endometrial adenocarcinoma
Endometrial Hyperplasia

Treatment

Based on patients age, future fertility desire, co-morbidities...

- Hormonal (progesterone)
- Surgical (hysterectomy)
Endometrial Cancer

- Most common gynecologic malignancy
- Lifetime risk 1:40
- 1.8 times more common in African American than Caucasians
- Approximately 46,470 new cases and 8,120 deaths in 2011
Endometrial Cancer

- 80% are believed to be early stage
  (however, only 20% receive proper staging)
- Median age is 60
- 75% occur in postmenopausal women
- 25% occur in premenopausal women
- 5% occur in women < 40 years old
Types of Endometrial Cancer

- **Epithelial Tumors**
  - Type I (estrogen dependent)
    - 70-80% all cases
    - Example: endometrioid
  - Type II (estrogen independent)
    - 10-20% all cases
    - Example: papillary serous (UPSC)

- **Mesenchymal Tumors**
  - Sarcoma (rare)
Treatment Options

- Endometrial cancer is best managed by a Gynecologic Oncologist
- Surgical Option
  - Include total hysterectomy, bilateral salpingoophorectomy, +/- staging
- Non-surgical
  - Radiation
  - Hormonal
- Based on patients desire for future fertility and medical co-morbidities (poor surgical candidates)
Endometrial Cancer Staging

- Staging is surgical
  - Pelvic and para-aortic lymphadenectomy
- May be able to omit staging and avoid increased post operative morbidity in a selection of low grade minimally invasive tumor
  - This decision is best made by a Gynecologic Oncologist
Tissue Diagnosis

- Histologic grade and depth of invasion two most sensitive indicators of spread to pelvic lymph nodes

<table>
<thead>
<tr>
<th>Depth</th>
<th>Grade I</th>
<th>Grade II</th>
<th>Grade III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endometrium</td>
<td>0%</td>
<td>3%</td>
<td>0%</td>
</tr>
<tr>
<td>Inner</td>
<td>3%</td>
<td>5%</td>
<td>9%</td>
</tr>
<tr>
<td>Middle</td>
<td>0%</td>
<td>9%</td>
<td>4%</td>
</tr>
<tr>
<td>Outer</td>
<td>11%</td>
<td>19%</td>
<td>34%</td>
</tr>
</tbody>
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GOG #33
## Tissue Diagnosis

<table>
<thead>
<tr>
<th>FIGO Stage</th>
<th>Carcinoma of the Endometrium -- 2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>Tumor limited to endometrium or invades less than one-half of the myometrium</td>
</tr>
<tr>
<td>IB</td>
<td>Tumor invades one-half or more of the myometrium</td>
</tr>
<tr>
<td>II</td>
<td>Tumor invades stromal connective tissue of the cervix but does not extend beyond uterus**</td>
</tr>
<tr>
<td>IIIA</td>
<td>Tumor involves serosa and/or adnexa (direct extension or metastasis)</td>
</tr>
<tr>
<td>IIIB</td>
<td>Vaginal involvement (direct extension or metastasis) or parametrial involvement</td>
</tr>
<tr>
<td>IIIC-1</td>
<td>Regional lymph node metastasis to pelvic lymph nodes</td>
</tr>
<tr>
<td>IIIC-2</td>
<td>Regional lymph node metastasis to para-aortic lymph nodes, with or without positive pelvic lymph nodes</td>
</tr>
<tr>
<td>IVA</td>
<td>Tumor invades bladder mucosa and/or bowel mucosa (bullous edema is not sufficient to classify a tumor as T4)</td>
</tr>
<tr>
<td>IVB</td>
<td>Distant metastasis (includes metastasis to inguinal lymph nodes intraperitoneal disease, or lung, liver, or bone.</td>
</tr>
</tbody>
</table>

** Endocervical glandular involvement only should be considered as stage I and not Stage II