Uterine Malignancy

Notes by: Roa Alsajjan

Post-Menopausal Bleeding

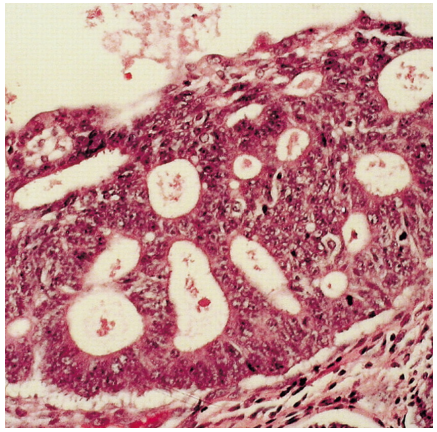
Source: Sakala, and Hacker & Moore

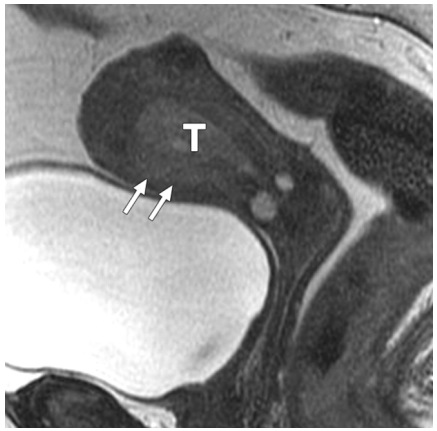
Causes of Postmenopausal Bleeding

Exogenous Estrogens	**30%**
Atrophic endometritis/vaginits	**30%**
Endometrial cancer	**15%**
Endometrial/Endocervical polyps	**10%**
Endometrial hyperplasia	**5%**
Other: cervical cancer, uterine sarcoma, urethral caruncle, trauma	**10%**

Endometrial Cancer

- The most common **SYMPTOM** of endometrial cancer is abnormal vaginal bleeding, which is present in 90% of patients.
- **Postmenopausal bleeding is always abnormal and must be investigated!**
- **Any woman who presents with postmenopausal bleeding should have a transvaginal ultrasound!**
- **If the endometrial biopsy is negative for cancer or reveals endometrial hyperplasia, a fractional dilatation and curettage (D&C) should be performed under general anesthesia**
- In the *premenopausal* patient, especially after age 35 years, menorrhagia or intermenstrual bleeding may signal an endometrial malignancy.

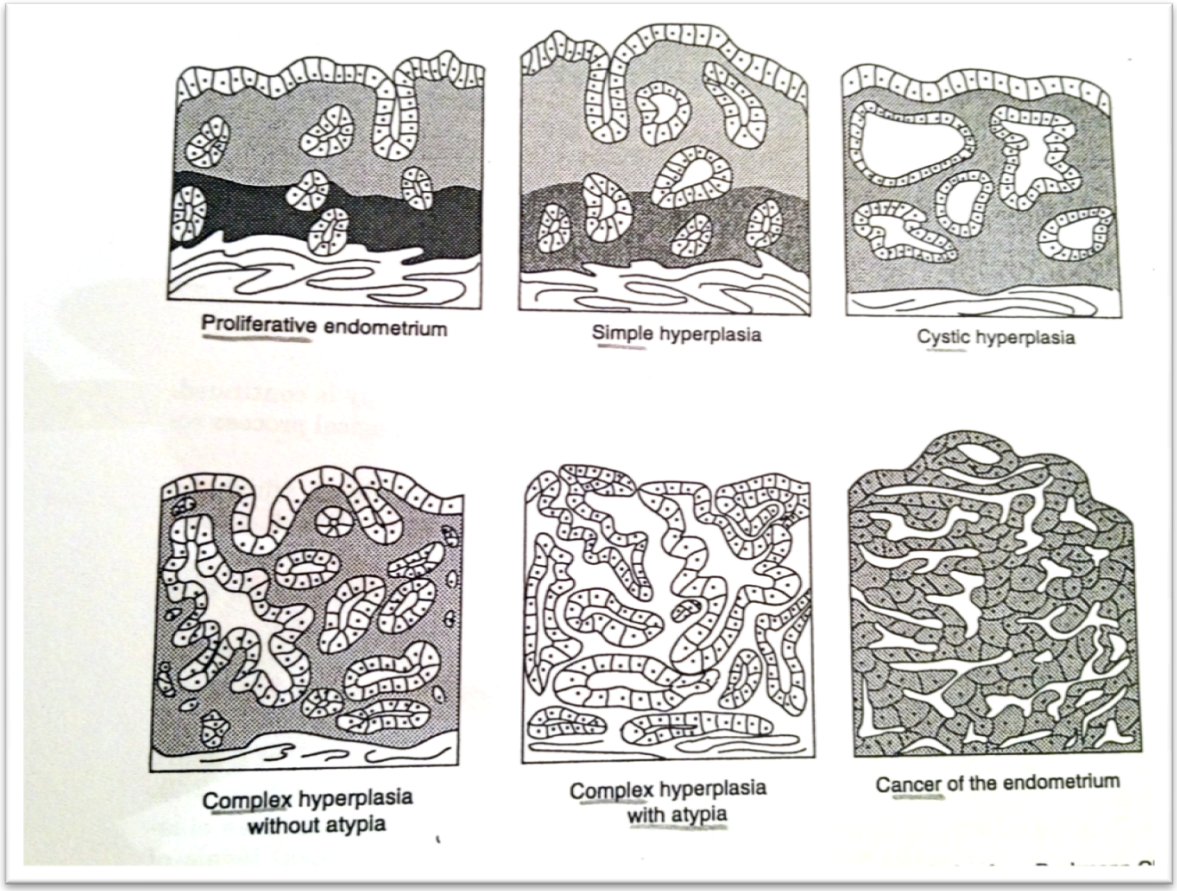




Endometrial Cancer

- Primary concern when bleeding occurs after 12 months of amenorrhea, in middle-aged women not receiving HRT
- It is the **most common gynecological malignancy**
- 75% are pure adenocarcinomas (better prognosis than clear cell, squamous or serous carcinomas)
- It can progress from simple hyperplasia to invasive cancer
- Mechanism: prolonged estrogen stimulation unopposed by progesterone)
  - ERT
  - Peripheral aromatization of androstenedione to esterone
  - Estrogen-producing tumor
  - Tamoxifen

Histology: Hyperplasia to Carcinoma



Histology: Hyperplasia to Carcinoma

Type	Findings	Progress to Cancer
Simple hyperplasia	Crowding of normal glands w/normal stroma	**<1%**
Complex hyperplasia w/o atypia	Complex crowded glands w/little stroma	**5%**
Simple hyperplasia w/atypia	Glands lined by enlarged cells w/↑ nuclear:cytoplasmic ratio	**10%**
Complex hyperplasia w/ atypia	Glands lined by enlarged cells w/↑ nuclear:cytoplasmic ratio	**30%**
Carcinoma	Obvious glandular anaplasia, w/stromal, myometrial or vascular invasion	**100%**

Risk Factors

Any factor that increases the exposure to unopposed estrogen increases the risk of endometrial cancer.

Risk Factor	Consequence
Nulliparity	Prolonged estrogen stimulation
Ovarian cancer	Estrogen production
Late menopause, PCOS	**Unopposed estrogenic stimulation from anovulatory cycles**
Tamoxifen for breast cancer	**2-3 fold increased risk**
Obesity	**Increased extraovarian aromatization of androstenedione to estrone**
Hypertension	
Breast or colon cancer	
Diabetes mellitus	

Differential & Diagnosis

Differential

1. GI tract causes: hemorrhoids, fissures, colorectal cancer
2. Lower reproductive tract: atrophic vaginitis, vaginal/ cervical/vulvar fissures/ lesions/tumors
3. Upper reproductive tract: atrophic endometritis, endometrial polyps/ hyperplasia/carcinoma

Screening:
- Pap smear identifies only 50% of cases
- U/S endometrial stripe thickness >5 mm
  - Tamoxifen gives false +ve

Work Up

1. GI: Physical, PR exam, stool guaiac (detect blood), proctosigmoidoscopy
2. LRT: Pelvic exam, pap smear & biopsy
3. URT:
   a) Endometrial biopsy (↓ sensitivity) – misses polyps
   b) U/S: thickness >5mm
   c) D&C: gold standard → cervical & endometrial specimens
   d) Hysteroscopy: usually w/D&C; useful for polyps → immediate resection
   e) Pap smear (↓ sensitivity)

Patterns of Spread

Route	To
Direct extension (MOST COMMON)	Myometrium, cervix, and rarely, vagina, rectum & bladder
Transtubal migration	Ovaries, peritoneum & omentum
Lymphatic (depends on grade & depth of myometrial invasion)	Pelvic nodes; progression to periaortic nodes
Hematogenous (UNCOMMON)	Lungs and liver

FIGO Surgical Staging (1988)

Stage	Grade	
I	Limited to the uterus (Grades 1,2, and 3)	Ia: Limited to endometrium Ib: <1/2 of myometrium Ic: >1/2 of myometrium
II	Limited extension beyond uterus (Grades 1,2, and 3)	IIa: **Endocervical** glands IIb: **Cervical** stroma
III	Extension within pelvis (Grades 1,2, and 3)	III: Invasion of **serosa**/**adnexa** or +ve **peritoneal** cytology IIIb: **Vaginal** metastases IIIc: Pelvic/paraaortic nodes
IV	Distant metastases	IVa: Invasion of **bladder/bowel** mucosa IVb: **Distant** metastases/ extra-abdominal or inguinal nodes

Management

Endometrial Hyperplasia

Management is influenced by patient's age, tumor histopathology and future desire for fertility.

1. Progestin therapy

- For: **POST**menopausal who are unfit for surgery or **PRE**menopausal desiring fertility
- Simple or complex hyperplasia without atypia regresses with monthly cycling. Follow-up biopsy in 3-6 months
- Hyperplasia with atypia has lower rates of response. Follow up biopsy in 3 months

2. Surgical therapy

- For **PRE**menopausal who have hyperplasia with atypia not desiring fertility, or postmenopausal
- Total hysterectomy is Rx of choice
- D&C alone may be theraputic and curative occasionally

Endometrial Carcinoma

Management of carcinoma is primarily surgical.

Stage I: Limited to uterus

- **Total abdominal hysterectomy and bilateral salpingo-oophorectomy is performed on all patients**, unless there are absolute medical contraindications
- Cytological examination of peritoneal washings; +ve in 15% of patients
- For high-risk patients (serous, clear or grade 3 histology, myometrial invasion or cervical extension): pelvic lymphadenectomy (pelvic & para-aortic nodes)
- Radiation

Endometrial Carcinoma

Radiation therapy

Stage/Characteristics	Adjuvant therapy
Stage Ia or Ib, grade 1 or 2 endometrioid carcinomas confined to the inner ½ of the myometrium	No adjuvant therapy
High risk carcinomas with -ve pelvic nodes (any stage Ic; grade 3, clear cell or serous; or any stage II cancer)	Vault brachytherapy (without external beam pelvic radiation)
One +ve pelvic node	External pelvic radiation
Multiple +ve pelvic nodes or proven +ve paraaortic nodes	extended field radiation (i.e. pelvic and paraaortic)
Patients with adnexal or omental metastases completely resected	Whole abdominal radiation

- In patients unfit for surgery, radiation therapy alone may be employed.
- A combination of intracavitary + external beam radiation is used.
- The overall 5-year survival rate is 20% lower than hysterectomy

Endometrial Carcinoma

Stage II: Limited extension beyond uterus

- **If the cervix is grossly normal** and **involvement is detected only on the histologically** → treatment may be the same as for stage I disease (TOH, bilateral salpingo-oophorectomy, surgical staging, and tailored postoperative radiotherapy)
- **If the cervix is grossly enlarged** →
  - **Primary radical hysterectomy**
  - **Bilateral salpingo-oophorectomy**
  - **Surgical staging**
  - **Postoperative external beam therapy for positive lymph nodes**

Endometrial Carcinoma

Stage III & IV: Extension within pelvis and distant metastases

- **For advanced disease, treatment is individualized**
- **The uterus, tubes, and ovaries should be removed → for palliation of bleeding and other pelvic symptoms**
- **If gross disease is present in the upper abdomen, tumor metastases that are readily removable should be destroyed → to improve the patient's quality of life by temporarily decreasing abdominal discomfort and ascites**
- **Preoperative or postoperative radiation**
- **Hormonal therapy, with or without chemotherapy**

Endometrial Carcinoma

Recurrent Disease

- **Seventy-five percent of recurrences develop within 2 years of treatment**
  - 70% to 80% of patients can be salvaged by radiation therapy
- Lesions are palliated by RADIATION for **pelvic** sites, and by PROGESTINS AND CHEMOTHERAPY for **extra-pelvic** sites
- **Metastases in other sites, such as the upper abdomen, lungs, or liver, are treated initially with high-dose progestins or antiestrogens** → 80% of patients with receptor +ve tumors respond
  - **If disease progresses while the patient is receiving progestins, chemotherapy may be offered**

Prognosis & Follow-Up

- Prognosis depends on:
  - Uterine **size**,
  - Histologic **type**
  - **Grade** of tumor
  - Depth of **myometrial** penetration
  - Status of **lymph nodes**
  - Status of **peritoneal cytologic features**
  - Presence or absence of occult adnexal or upper abdominal **metastases**
- *Serous and clear cell endometrial carcinomas have the worst prognosis*
  - *Both of these histologic types are prone to early dissemination*
  - *5-year survival rates for these tumor types are **<50%**, even for patients with stage I*
- ***Follow-Up:*** examinations every 3 months for 2 years, every 6 months for 3 years, and then annually. It is important to take a vault pap smear on patients who have not had radiation therapy.