I have no disclosures
Objectives

- Define abnormal uterine bleeding (AUB)
- Describe algorithm for evaluating abnormal vaginal bleeding and abnormal uterine bleeding
- Name indications for hormone replacement therapy
- Describe evaluation of post-menopausal bleeding
Abnormal Vaginal Bleeding (AVB)
What is normal?

Normal parameters:
- Cycle interval: 24 – 35 days
- Menses: 4 – 7 days
- Blood loss: 30 – 45 mL

Onset
- By 15 years old with 2° sex characteristics
- Start evaluation at 13 years of age if no sexual development
Normal Menstrual Cycle

Requires:
Normal Menstrual Cycle

- Regular menses
- Irregular menses
Abnormal Uterine Bleeding

• **Definition:**

  Bleeding that is NOT normal
## Term Definitions

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>normal</td>
<td>24 to 35 days, lasting from 2-7 days, and flowing &lt; 80 mL per cycle (ave. normal amount is 30-40 mL per cycle).</td>
</tr>
<tr>
<td>menorrhagia</td>
<td>Blood loss &gt;80 mL/cycle and menstrual periods lasting &gt;7 days</td>
</tr>
<tr>
<td>amenorrhea</td>
<td>Absence of bleeding for at least three usual cycle lengths</td>
</tr>
<tr>
<td>oligomenorrhea</td>
<td>Bleeding that occurs at an interval &gt; 35 days</td>
</tr>
<tr>
<td>polymenorrhea</td>
<td>Bleeding that occurs at an interval &lt; 24 days</td>
</tr>
<tr>
<td>metrorrhagia</td>
<td>Light bleeding at irregular intervals</td>
</tr>
<tr>
<td>menometrorrhagia</td>
<td>Heavy bleeding at irregular intervals</td>
</tr>
<tr>
<td>intermenstrual bleeding</td>
<td>Bleeding that occurs between menses or between expected hormone withdrawal bleeds if using OCP or HRT</td>
</tr>
<tr>
<td>premenstrual spotting</td>
<td>Light bleeding preceding regular menses</td>
</tr>
<tr>
<td>post-coital bleeding</td>
<td>Vaginal bleeding within 24 hours of vaginal intercourse.</td>
</tr>
</tbody>
</table>

**Older Definitions**

Avoid these definitions.
Initial approach to vaginal bleeding

Is the pt pregnant?

Pregnancy

• If yes—viability, location, dating

Is it uterine?

If no, pelvic exam to evaluate uterine vs non uterine bleeding

• Non uterine includes cervix, vagina, urethra, anus

If uterine, what could be causing the bleeding?

AUB classification

• PALM-COEIN
PALM-COEIN

- **P** polyps
- **A** adenomyosis
- **L** leiomyoma
- **M** malignancy or hyperplasia
- **C** coagulopathy
- **O** ovulatory dysfunction
- **E** endometrial
- **I** iatrogenic
- **N** not yet classified

Munro MG, et al., 2011
AUB-PAL (of PALM-COEIN)

**Polyp**

- Presents with
  - spotting in between periods
  - post-coital spotting

**Adenomyosis**

- Presents with
  - painful periods
  - painful intercourse
  - chronic pelvic pain
  - heavy menstrual bleeding

**Leiomyoma**

- Presents with
  - heavy menstrual bleeding

**Submucosal**

- Presents with
  - heavy menstrual bleeding

**Other**
M: Malignancy and hyperplasia (endometrial)

- Presentation:
  - Post-menopausal bleeding
  - Recurrent perimenopausal irregular bleeding
  - Chronic anovulatory pattern (PCOS) with irregular bleeding
AUB-C (coagulopathy)

- Clotting factor deficiency or defect
  - Liver disease
  - Congenital (Von Willebrands Disease)

- Platelet deficiency (thrombocytopenia) with platelet count <20,000/mm³
  - Idiopathic thrombocytopenic purpura (ITP)
  - Aplastic anemia

- Platelet function defects

- Anticoagulants
  - Supra-therapeutic anticoagulation: heavy menstrual bleeding
    **Therapeutic levels should not cause bleeding problems**
Coagulopathy Screening

Initial screening for an underlying disorder of hemostasis in patients with excessive menstrual bleeding

Screen for bleeding disorders in women with HMB:

- Heavy menstrual bleeding since *menarche*
- *One* of the following
  - Post-partum hemorrhage
  - Bleeding associated with surgery
  - Bleeding associated with dental work
- *Two or more* of the following symptoms:
  - Bruising 1-2 times per month
  - Epistaxis 1-2 times per month
  - Frequent gum bleeding
  - Family history of bleeding symptoms

Positive screen comprises have 1 of the criteria

- CBC
- PTT/PT
- Fibrinogen
- vWF:Ag, vWF: rCO, FVIII

Kouides PA et Al. Fertil Steril 2005
### AUB – O (ovulatory dysfunction)

**Physiologic**
- Adolescence
- Peri-menopause
- Lactation
- Pregnancy

**Pathologic**
- Hyper-androgenic anovulation (PCOS, CAH)
- Hypothalamic dysfunction
- Hyper-prolactinemia
- Thyroid disease
- Primary pituitary disease
- Premature ovarian failure
- Iatrogenic (eg secondary to XRT or chemo)
- Medications

ACOG Practice Bulletin: Mgmt of Abnl Uterine Bleeding Associated with Ovulatory Dysfunction. 2013
**Interlude: Thyroid disorders**

<table>
<thead>
<tr>
<th></th>
<th>HYPERthyroid</th>
<th>HYPOthyroid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency of abnormal cycles</td>
<td>21%</td>
<td>23%</td>
</tr>
<tr>
<td>Oligo/amenorrhea</td>
<td>63%</td>
<td>55%</td>
</tr>
<tr>
<td>Heavy bleeding</td>
<td>37%</td>
<td>30%</td>
</tr>
</tbody>
</table>


- Consider checking TSH in women with any type of AUB
- Only severe, uncorrected thyroid disease causes abnormal bleeding patterns
AUB – E (endometrial)

- **Idiopathic**
  - Unexplained heavy menstrual bleeding

- **Endometritis**
  - Post-partum
  - Post-abortal endometritis
  - Endometritis component of PID
    - Note: In teens, PID commonly presents with abnormal bleeding (menorrhagia, IMB), not pelvic pain
    - Any teen with abnormal bleeding + pelvic pain requires bimanual exam to evaluate for PID
AUB – I (iatrogenic)

- Chronic steroids
- Progestin-containing contraceptives
- Intrauterine Contraception (IUC)
  - "Normal" side effect – breakthrough bleeding
  - Pregnancy (IUP or ectopic), perforation, expulsion
AUB – N (not yet classified)

- Chronic endometritis
- AVM
- Myometrial hypertrophy
MY PERIOD COMES EVERY MONTH AROUND THE SAME TIME. IT IS SO HEAVY. ON FIRST 2 DAYS, I SOAK BOTH A SUPERABSORBENT PAD AND SUPER-TAMPON EVERY 30 MINUTES. AND AT NIGHT, I HAVE TO GET UP AND CHANGE MY PAD.

CASE 1: “TOO MUCH”
Question: “TOO MUCH”

In addition to a urine pregnancy test and a TSH, which of the following is the most appropriate test to order at this time?

1) FSH
2) Serum beta-HCG
3) Endometrial biopsy
4) Pelvic ultrasound
5) Coagulation tests
6) Testosterone & DHEAS
Initial approach to vaginal bleeding

- Is the pt pregnant?
  - Pregnancy
    - If yes—viability, location, dating
  - If no, pelvic exam to evaluate uterine vs non uterine bleeding
    - Non uterine includes cervix, vagina, urethra, anus
- Is it uterine?
  - If uterine, what could be causing the bleeding?
    - Is the bleeding pattern regular?
Normal Menstrual Cycle

- Regular menses (ovulatory)
  - Heavy menses bleeding
  - Intermenstrual bleeding
  - Post-coital bleeding

- Irregular menses
  - Not functioning
Regular, Heavy Menses

Differential Diagnosis

**Anatomic**
- Leiomyoma
- Polyp
- Adenomyosis

**Coagulopathy**
- VWD
- ITP
- Coumadin use

**Idiopathic**

(aka heavy menstrual bleeding)

Thyroid Disease
PALM-COEIN

- P polyps
- A adenomyosis
- L leiomyoma
- M malignancy or hyperplasia
- C coagulopathy
- O ovulatory dysfunction
- E endometrial
- I iatrogenic
- N not yet classified

Regular, heavy menses
(aka heavy menstrual bleeding)

- C coagulopathy
- L leiomyoma
- A adenomyosis
- P polyps
Regular, Heavy Menses

Coagulopathy
- VWD
- ITP
- Coumadin use

If indicated….

- CBC with platelets
- INR/PT, PTT
- vWD assays

Structural
- Leiomyoma
- Adenomyosis
- Polyp

- Pelvic ultrasound

Idiopathic

- TSH

Thyroid Disease
MY PERIOD COMES EVERY MONTH AROUND THE SAME TIME. IT IS SO HEAVY. ON FIRST 2 DAYS, I SOAK BOTH A SUPERABSORBENT PAD AND SUPER-TAMPON EVERY 30 MINUTES. AND AT NIGHT, I HAVE TO GET UP AND CHANGE MY PAD.

CASE 1: “TOO MUCH”
CASE 1: “TOO MUCH”

Is the pt pregnant?

If no, pelvic exam to evaluate uterine vs non uterine bleeding

Is it uterine?

If uterine, is the pattern regular or irregular?

Regular bleeding pattern?

UTERINE

NO

YES
In addition to a urine pregnancy test and a TSH, which of the following is the most appropriate test to order at this time?

1) FSH
2) Serum beta-HCG
3) Endometrial biopsy
4) Pelvic ultrasound
5) Coagulation tests
6) Testosterone & DHEAS
Case 1: Treatment

- Treat the underlying problem
  - If structural lesion causing AUB, remove it
  - If evidence of coagulopathy, correct it
  - If thyroid function is abnormal, address it

- Utilize therapies known to decrease bleeding
  - Hormonal treatment (combined hormonal contraception or progestin-only methods including levonorgestrel IUS)
  - Non-hormonal treatment (NSAIDs or tranexamic acid)
  - Specialized GYN procedures (uterine artery embolization, endometrial ablation, or hysterectomy)
CASE OF “TOO MUCH, TOO LATE”

I NEVER KNOW WHEN MY PERIOD IS GOING TO COME. AND I ALWAYS HAVE TO BE READY BECAUSE WHEN IT COMES IT IS HEAVY, LIKE A FLOOD FOR DAYS AND...
Approach to vaginal bleeding

- Is the pt pregnant?
  - No
  - Pregnancy
    - Is it uterine?
      - No
      - UTERINE
      - If no, pelvic exam to evaluate uterine vs non-uterine bleeding
        - If uterine, is the pattern regular or irregular?
          - No
          - Regular bleeding pattern?
Normal Menstrual Cycle

- Regular menses
- Irregular menses

- Irregular bleeding
- Oligomenorrhea
- Amenorrhea

- Not functioning (anovulatory)
<table>
<thead>
<tr>
<th>PALM-COEIN</th>
<th>Irregular menses</th>
</tr>
</thead>
<tbody>
<tr>
<td>P</td>
<td>Ovulatory dysfunction</td>
</tr>
<tr>
<td>A</td>
<td>Iatrogenic</td>
</tr>
<tr>
<td>L</td>
<td>Malignancy or hyperplasia</td>
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<td>M</td>
<td>Iatrogenic</td>
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<tr>
<td>N</td>
<td>Ovulatory dysfunction</td>
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</tbody>
</table>

- P = polyps
- A = adenomyosis
- L = leiomyoma
- M = malignancy or hyperplasia
- C = coagulopathy
- O = ovulatory dysfunction
- E = endometrial
- I = iatrogenic
- N = not yet classified

O! I'M bleeding…
AUB – O (ovulatory dysfunction)

**Physiologic**
- Adolescence
- Peri-menopause
- Lactation
- Pregnancy

**Pathologic**
- Hyper-androgenic anovulation (PCOS)
- Hypothalamic dysfunction
- Hyper-prolactinemia
- Thyroid disease
- Primary pituitary disease
- Primary ovarian insufficiency
- Iatrogenic (eg secondary to XRT or chemo)
- Medications

ACOG Practice Bulletin: Mgmt of Abnl Uterine Bleeding Associated with Ovulatory Dysfunction. 2013
AUB – O (ovulatory dysfunction)

High Estrogen States

- Physiologic (menarche, perimenopause)
- Hyperandrogenic (PCOS/CAH/Cushing's)
- Systemic Disease (Thyroid, Liver/Renal Disease)

Low Estrogen States

- Hypothalamic (stress, anorexia)
- Pituitary (prolactinemia, Sheehan's syndrome)
- Ovarian failure (POI or perimenopause)

Labs
- CBC
- TSH
- Androgens
- 21-OHP

Labs
- CBC
- TSH
- Prolactin
- FSH
CASE OF “TOO MUCH, TOO LATE”

I NEVER KNOW WHEN MY PERIOD IS GOING TO COME. AND I ALWAYS HAVE TO BE READY BECAUSE WHEN IT COMES IT IS HEAVY, LIKE A FLOOD FOR DAYS AND
Case 2: “TOO MUCH, TOO LATE”

A 35 yo woman reports very heavy periods about every few months since menarche.

- Required letrozole to become pregnant, had 1 child at age 25
- Has had to wax her upper lip and chin for many years for “stubborn hair” and has acne

FOR THIS PATIENT, WHAT ADDITIONAL TESTING IS REQUIRED TO DIAGNOSE PCOS?

a. Ultrasound
b. Total testosterone
c. DHEA-S
d. LH/FSH ratio
e. All of the above
f. None of the above
# PCOS – Diagnostic criteria

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>+ Ovulatory dysfunction</td>
<td>2 of 3 required</td>
<td></td>
</tr>
<tr>
<td>+ Hyperandrogenism</td>
<td>- Ovulatory dysfunction</td>
<td>- Ovulatory dysfunction +/-</td>
</tr>
<tr>
<td>+ Exclusion of other</td>
<td>- Hyperandrogenism</td>
<td>- Hyperandrogenism</td>
</tr>
<tr>
<td>etiologies</td>
<td>- Polycystic ovaries (US)</td>
<td>- Exclusion of other etiologies</td>
</tr>
<tr>
<td></td>
<td>- Exclusion of other etiologies</td>
<td></td>
</tr>
</tbody>
</table>
Hyperandrogenism

Most women have BOTH clinical and biochemical hyperandrogenism

- Clinical: hirsutism, acne, male-pattern hair loss
- Chemical: elevated total testosterone and/or DHEA-S

No signs of virilization:
- rapid onset of hirsutism, increased muscle mass, deepening voice, clitoromegaly
Exclusion of Other ETIOLOGIES

(1) Other causes of ovulatory dysfunction
- Pregnancy ➔ UPT
- Thyroid dysfunction ➔ TSH
- Hyperprolactinemia ➔ prolactin
- Primary ovarian insufficiency ➔ FSH

(2) Other causes of hyperandrogenism
- Non-classic congenital adrenal hyperplasia ➔ 17 hydroxyprogesterone
- Ovarian or adrenal tumor if signs of virilization ➔ total testosterone & DHEA-S*
- Cushing’s syndrome or acromegaly

*Ovarian tumor: testosterone > 200 g/dL
Adrenal tumor: DHEAS > 800 mcg/dL
Ovulatory Dysfunction

Oligo or amenorrhea

Typically begins in the peripubertal period

Periods typically very heavy with spotting between

Chronic anovulation (lack of progesterone)

Chronic unopposed estrogen

Endometrial proliferation

Endometrial hyperplasia and/or cancer (3x increased risk)

Menstrual Irregularity
Anovulatory Bleeding

In the absence of ovulation:

- Ovary does not make progesterone
- Continued endometrial proliferation
- Fragile endometrium bleeds erratically

Irregular bleeding
Polycystic Ovaries (by ultrasound)

- Affect 1 or both ovaries
- Meet one of the following criteria:
  - >12 follicles
  - Increased ovarian volume (>10 cm³)

- NOT SPECIFIC for PCOS
- No need for ultrasound if pt has other 2 criteria
Case 2: “TOO MUCH, TOO LATE”

A 35 yo woman reports very heavy periods about every few months since menarche.

- Required letrozole to become pregnant, had 1 child at age 25
- Has had to wax her upper lip and chin for many years for “stubborn hair” and has acne

For this patient, what additional testing is required to diagnose PCOS?

- a. Ultrasound
- b. Total testosterone
- c. DHEA-S
- d. LH/FSH ratio
- e. All of the above
- f. None of the above
Anovulatory Bleeding

In the absence of ovulation:

- Ovary does not make progesterone
- Fragile endometrium bleeds erratically
- Irregular bleeding

- Progestin therapy
Case 2: Treatment Options

- Goals
  1. Stop bleeding
  2. Prevent irregular bleeding
  3. Provide contraception
  4. Protect endometrium

- Treatment options
  1. Progestin-only therapies (IUD, DMPA, oral progestins)
  2. Combined hormonal contraceptives
  3. Correct underlying endocrine abnormality
  4. Surgical management via hysterectomy
Case 2 – Crazy Cycles
Addendum

And in a month SW calls your office, saying that she is bleeding through a supertampon every hour. What treatment options does she have at this time?
# Medical Treatment for Acute Uterine Bleeding

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
<th>Dose Scheduled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conjugated equine estrogen</td>
<td>25mg IV</td>
<td>q4-6h x 24 hours</td>
</tr>
<tr>
<td>Combined oral contraception</td>
<td>Monophasic with at least 35mcg EE</td>
<td>TID x 7 days</td>
</tr>
<tr>
<td>Medroxyprogesterone acetate</td>
<td>20mg PO</td>
<td>TID x 7 days</td>
</tr>
<tr>
<td>Tranexamic acid</td>
<td>1.3g PO or 10mg/kg IV (max dose 600mg)</td>
<td>TID or q8h x 5 days maximum</td>
</tr>
</tbody>
</table>

ACOG Committee Opinion #557: Management of Acute Abnormal Uterine Bleeding in Nonpregnant Reproductive-Aged Women, 20
Surgical Treatment for Acute Uterine Bleeding

- D&C
- Endometrial ablation
- Polypectomy or myomectomy
- Uterine artery embolization
- Hysterectomy
Case 2: Additional thoughts

+ Does SW need an endometrial biopsy?

+ Recommendations for endometrial biopsy (ACOG, 2012)
  + AUB in women ≥ 45yo
    + Includes post-menopausal bleeding
  + History of unopposed estrogen exposure
  + Failed medical management
  + Persistent AUB
Case 2: Additional thoughts

What if her endometrial stripe on ultrasound was 18mm?
Case 2: Additional thoughts

+ If SW were 46yo, would you recommend an endometrial biopsy?

+ If SW were 46yo and had regular but heavy menses, would you recommend an endometrial biopsy?

+ If SW were 46yo and her menses were becoming less frequent and were light, would you recommend an endometrial biopsy?
Perimenopausal bleeding

Trends in perimenopause

12% stop bleeding suddenly
18% have longer, heavier menses
70% have short irregular menses
Who should we biopsy in the perimenopausal period?

- Heavy, irregular bleeding? **YES**
- Risk factors for cancer? **YES**
- Perimenopausal infrequent/scant bleeding? **NO**
- Regular bleeding? **NO**
Case 3: “TOO LATE”

TA is a 54yo G2P2 woman with 2 days of post-menopausal bleeding.

Post-menopausal bleeding is AUB!
Menopause
Menopause

“The final menstrual period, which can be confirmed after 12 consecutive months without a period. This time marks the permanent end of menstruation and fertility. It is a normal, natural event associated with reduced functioning of the ovaries, resulting in lower levels of ovarian hormones (primarily estrogen).”

North American Menopause Society, 2015
Stages of Reproductive Aging Workshop (STRAW)- WHO

<table>
<thead>
<tr>
<th>Stages:</th>
<th>-5</th>
<th>-4</th>
<th>-3</th>
<th>-2</th>
<th>-1</th>
<th>+1</th>
<th>+2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Terminology:</td>
<td>Reproductive</td>
<td>Menopausal Transition</td>
<td>Postmenopause</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Early</td>
<td>Peak</td>
<td>Late</td>
<td>Early</td>
<td>Late*</td>
<td>Early*</td>
<td>Late</td>
</tr>
<tr>
<td>Duration of Stage:</td>
<td>variable</td>
<td>variable</td>
<td>a 1 yr</td>
<td>b 4 yrs</td>
<td>until demise</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Menstrual Cycles:</td>
<td>variable to regular</td>
<td>regular</td>
<td>variable cycle length (&gt;7 days different from normal)</td>
<td>≥2 skipped cycles and an interval of amenorrhea (≥60 days)</td>
<td>none</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endocrine:</td>
<td>normal FSH</td>
<td>↑ FSH</td>
<td>↑ FSH</td>
<td>↑ FSH</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Pathophysiology of menopause organ changes

Sources: Lentz: Comprehensive Gynecology, 6E
Williams Textbook of Endocrinology, 12E

↓ Estradiol

CNS/ Vasomotor instability
- ↑ norepinephrine
- ↑ serotonin
- Narrow thermoregulatory setpoint in hypothalamus
- Hot flashes
- Night sweats
- Sleep disturbance
- Depression
- Daytime fatigue

Urogenital mucosa
- ↓ collagen synthesis
- Weakening of vaginal walls
- ↓ blood flow in vaginal epithelium
- ↓ glycogen production
- ↓ energy source for lactobacillus
- ↑ stress incontinence
- ↑ pelvic organ prolapse
- ↑ vaginal pH

Cardiovascular
- ↑ total cholesterol
  - ↑ LDL
  - ↓ HDL
- ↓ prostacyclin
  - ↑ endothelin
  - ↓ NO synthase
  - ↑ ACE → ↑ Ang II
- Vasoconstriction
- Endothelial dysfunction
- ↑ risk of atherosclerosis

Bones
- ↓ osteoclast apoptosis (e.g., via ↓ TGF-β)
- ↓ OPG secretion by osteoblast
- ↑ RANK ligand
- ↑ osteoclast maturation and survival
- Bone resorption > formation

Vasomotor symptoms occur due to narrowing of the hypothalamic thermoneutral zone. A premenopausal woman easily crosses the upper and lower setpoints, leading to vasodilation/sweats (hot flashes) when body is slightly warm and chills/shivers when slightly cool. The symptoms are worst at night, leading to frequent wakeings and poor sleep quality. This effect is due to changes in estrogen level rather than absolute deficiency. Unlike other menopause changes, this will improve over time.

- ↑ dryness
- ↑ irritation
- ↑ infections
- Dyspareunia

- ↑ risk of myocardial infarction

- Estrogen
  - only if before plaque formation (i.e., during perimenopausal years)
  - once atherosclerotic plaques are formed, exogenous estrogen will destabilize plaques and lead to thrombus formation

- Trabecular bone loss > cortical bone in early stages
- Vertebrae: most easily fractured due to high trabecular bone turnover
- ↓ collagen synthesis contributes to osteoporosis as well
- Weight-bearing exercises, vitamin D, and calcium are important lifestyle factors in reducing osteoporosis
Cardinal symptoms of menopause

**Vasomotor symptoms**
- Hot flashes
- Increase during menopausal transition & peak 1 year after menopause
- Related to narrowing of thermoregulatory zone

**Genitourinary syndrome of menopause**
- Vaginal atrophy secondary to hypoestrogenic state
- Physiologic and anatomic changes to genitourinary tract
- Symptoms include vaginal or vulvar dryness, discharge, itching, and dyspareunia
Treatment of vasomotor symptoms

+ Most effective treatment: systemic hormone therapy (HT) with estrogen therapy

If uterus present...

Estrogen + Progestin (EPT)

If uterus absent...

Estrogen alone (ET)
Indications for HT (FDA-approved)

1. Vasomotor symptoms
2. Prevention of bone loss
3. Hypoestrogenism (caused by hypogonadism, oophorectomy, or POI)
4. Genitourinary syndrome of menopause (GSM) (or vulvo-vaginal atrophy)
## Risks/benefits of systemic HT for post-menopausal women

<table>
<thead>
<tr>
<th>Possible Risk</th>
<th>Estrogen only</th>
<th>Estrogen/Progest in</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart disease</td>
<td>No effect</td>
<td>↑</td>
</tr>
<tr>
<td>Stroke</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Venous thromboembolism</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>No effect</td>
<td>↑</td>
</tr>
<tr>
<td>Colon cancer</td>
<td>No effect</td>
<td>↓</td>
</tr>
<tr>
<td>Fractures</td>
<td>↓</td>
<td>↓</td>
</tr>
</tbody>
</table>
Risks and benefits of HT in women ages 50-59 or <10 years of menopause

Santen et al. J Clin Endocrinol Metab. 2010
Number of women benefitting from HT vs. number of women experiencing risks and/or benefits

- **Symptoms worse**
  - Fractures
  - Diabetes
  - Breast cancer
  - Colo-rectal cancer
  - Overall mortality
  - Coronary heart disease
  - Endometrial cancer
  - Non-small cell lung cancer
  - Veno-thrombotic episodes
  - Stroke
  - Cholecystitis

- **Symptoms better**

- **Risks**

- **Benefits**

Santen et al. 2010
Systemic hormone therapy (HT) options (ACOG Bulletin 141: Management of menopausal symptoms)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dosage/Regimen</th>
<th>Evidence of Benefit</th>
<th>FDA Approved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hormonal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estrogen-alone or combined with progestin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Standard Dose</td>
<td>Conjugated estrogen 0.625 mg/d</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Micronized estradiol-17β 1 mg/d</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Transdermal estradiol-17β 0.0375–0.05 mg/d</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>• Low Dose</td>
<td>Conjugated estrogen 0.3–0.45 mg/d</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Micronized estradiol-17β 0.5 mg/d</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Transdermal estradiol-17β 0.025 mg/d</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>• Ultra-Low Dose</td>
<td>Micronized estradiol-17β 0.25 mg/d</td>
<td>Mixed</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Transdermal estradiol-17β 0.014 mg/d</td>
<td>Mixed</td>
<td>No</td>
</tr>
<tr>
<td>Estrogen combined with estrogen agonist/antagonist</td>
<td>Conjugated estrogen 0.45 mg/d and bazedoxifene 20 mg/d</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Progestin</td>
<td>Depot medroxyprogesterone acetate</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Testosterone</td>
<td></td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Tibolone</td>
<td>2.5 mg/d</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Compounded bioidentical hormones</td>
<td></td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>
Contraindications to systemic HT

- Unexplained vaginal bleeding
- Severe active liver disease
- Estrogen-sensitive breast or endometrial cancer
- Coronary heart disease
- Stroke
- Personal history or inherited high risk of venous thromboembolism
Non-hormonal treatments for vasomotor symptoms

- **SSRIs and SSNRI s**
  - Data mixed but RCTs support use
  - Paroxetine (7.5mg/day) – only non-hormonal therapy approved by FDA for treatment of vasomotor symptoms

- **Clonidine (0.1 mg/day)**
  - Limited data, small benefit in comparison to placebo

- **Gabapentin**
  - Similar efficacy to SSRIs/SSNRI s, reduce vasomotor symptoms by 50-60%
Treatment for genitourinary syndrome of menopause (GSM)

- Low dose vaginal estrogen preparations are effective and safe
- Progestin therapy is not needed
- Benefits of vaginal estrogen include:
  1. reduction of vaginal dryness, burning, & irritation
  2. improvement in lubrication, blood flow, & sensation
  3. prevention of recurrent UTIs
- Non-estrogen alternatives include: (1) ospemifene and (2) intra-vaginal DHEA
Overall benefit-to-risk ratio

- HT is most effective treatment for vasomotor symptoms and genitourinary syndrome of menopause
- Benefits of HT most likely outweigh the risks for symptomatic women who initiate HT < age 60 or who are < 10 years of menopause
- “Appropriate dose, duration, regimen, and route of administration”
Case 3: “TOO LATE”

TA is a 54yo G2P2 woman with 2 days of post-menopausal bleeding.
Case 3: Differential diagnosis

- Endometrial hyperplasia/cancer
- Vaginal atrophy
- Endometrial atrophy
- Polyps (cervix, endometrium)
- Hormone replacement therapy
- Disease in adjacent organs (GU or GI)
- Post-radiation therapy
- Anticoagulation
- Herbal and dietary supplements
Case 3: Evaluation

- Endometrial biopsy is recommended as initial diagnostic test in post-menopausal bleeding.
Case 3: Need for EMB?

For post-menopausal women:

- Women with bleeding & endometrial lining on US ≥ 4mm
- Endometrium not adequately visualized
- Persistent bleeding
- Asymptomatic women with endometrial stripe ≥ 11mm
- Bleeding occurring after 6+ months of HRT
Figure 39. Coronal US image of the uterus after menopause shows a thin (3-mm) endometrial echo complex (arrow).
Have a broad differential for vaginal bleeding – don’t miss non-uterine etiologies of bleeding

Strive to characterize bleeding as regular and irregular

Utilize your refined differential diagnosis to develop a cost-conscious diagnostic plan

Understand indications for hormone therapy and counsel patients about benefits/risks (which are informed by age and years since menopause)

Use evidence-based approach to determine need for endometrial sampling in perimenopausal and post-menopausal women
References


Additional diagrams for evaluation of abnormal vaginal bleeding
Hx, PE, Preg test

Preg test POS

Pregnant
- Location
- Viability
- GA Dating

Preg test NEG

Pelvic Exam

Abnl Uterine bleeding
- Cervix
  - Cervicitis
  - Ectropion
  - Cancer
- Vagina
  - Inflam’n
  - Trauma
  - Neoplasm
- Urethra
- Anus
  - Caruncle
  - Hemorr’d
  - Fissure
  - Cancer

Non-uterine bleeding
Policar, 2017

Hx, PE, Preg test

Preg test POS
- Pregnant

Preg test NEG
- Abnormal Uterine Bleeding
  - Non-structural (COEIN)
  - Structural (PALM)

Abnormal Vaginal Bleeding
- Non-uterine bleeding
  - Cervix
  - Vagina
  - Urethra
  - Anus
AVB: History

- Is the patient pregnant?
  - Pregnancy symptoms, esp. breast tendernessness
  - Intercourse pattern
  - Contraceptive use

- Is it uterine?
  - Coincidence with bowel movement and wiping, during or after urination
  - Pain or irritation of vagina, introitus, vulva, perineum, or anal skin
AVB: History

- Is bleeding ovulatory or anovulatory?
  + Bleeding pattern: regular, irregular, none
  + *Moliminal symptoms*: only in ovulatory cycles
  + Previous history of menstrual disorders
  + Recent onset weight gain or hirsutism
  + Menopausal symptoms
  + History of excess bleeding; coagulation disorders
  + Current and past medications; street drugs
  + Chronic medical illnesses or conditions
  + Nipple discharge from breasts
AVB: Physical Exam

- General: BMI > 30
- Skin: acne, hirsutism, acanthosis nigricans; bruising
- Breasts: galactorrhea
- Abdomen: uterine enlargement, abdominal pain
- Pelvic exam
  - Vulva and perineum
  - Anal and peri-anal skin
  - Speculum: vaginal walls and cervix
  - Bimanual: uterine enlargement, softness, masses
AVB: Laboratory

**Urine pregnancy test**
- Quantitative BhCG is unnecessary

**CBC**
- Find severe anemia; baseline value for observation
- Platelet estimation (detect thrombocytopenia)

**TSH, Prolactin**
- Check TSH for any AUB
- Check PRL for amenorrhea or recurrent anovulatory bleeds *only*

**FSH, LH**
- Levels are usually *unnecessary*
AUB - Imaging

- Mainly for evaluation of **heavy menstrual bleeding** if no response to treatment or suspect anatomic defect

- Not useful for demonstrating or excluding hyperplasia or cancer in premenopausal women

- Types of imaging: (1) pelvic ultrasound, (2) saline sonogram, (3) hysteroscopy