Amenorrhea and Abnormal Uterine Bleeding: You Will Never Be Confused Again

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Goals

Understand normal cycles
Know how to evaluate secondary amenorrhea
Know how to evaluate “abnormal uterine bleeding”
Know when an endometrial biopsy is indicated

The Menstrual Cycle:

- **ovulation**
- **menstrual period**

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- **follicular**
- **luteal**

- **FSH**
- **LH**

- **developing follicle**
- **corpus luteum**

- **estrogen**
- **progestin**

- **endometrial proliferation**
- **endometrial stabilization**

"bricks" "mortar"

Normal, ordered endometrial lining: bricks and mortar
Unstable, thick endometrial lining: all bricks, no mortar

Unstable, thin endometrial lining: all mortar, no bricks

Endometrial lining on OCPs (containing estrogen and progestins): Lots of mortar with just a few stabilizing bricks

Definition: amenorrhea

Primary - the absence of menarche by age 16 years
Secondary - the absence of menstruation for 3 or more months in women with past menses
**Secondary amenorrhea: differential diagnosis**

1. Pregnancy  
2. Menopause (premature ovarian failure)  
3. Chronic anovulation / polycystic ovarian syndrome (PCOS)  
4. Hyperprolactinemia (breastfeeding, prolactinoma)  
5. Hypothyroidism  
6. Hypothalamic amenorrhea (weight loss / exercise)  
7. Medications (e.g., neuroleptics)  
8. Asherman's syndrome

**Work-up**

- History  
- Physical  
- Laboratory tests  
- Diagnostic in vivo tests

**History**

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<tbody>
<tr>
<td>1. Pregnancy</td>
<td>Exposure to pregnancy</td>
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<td>2. Menopause</td>
<td>Hot flashes, night sweats</td>
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<td>3. Chronic anovulation (PCOS)</td>
<td>H/o irregular cycles</td>
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<td>4. Hyperprolactinemia</td>
<td>Galactorrhea</td>
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<tr>
<td>5. Medications</td>
<td>OCPs, neuroleptics, metaclopramide</td>
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<td>6. Hypothalamic</td>
<td>Weight loss</td>
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<tr>
<td>7. Asherman's syndrome</td>
<td>Recent uterine surgery (D&amp;C)</td>
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<td>8. Hypothyroidism</td>
<td>Constipation, fatigue</td>
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**Physical Examination**

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<tr>
<td>1. Pregnancy</td>
<td>Uterine size</td>
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<tr>
<td>2. Menopause</td>
<td>Urogenital atrophy</td>
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<tr>
<td>3. Chronic anovulation (PCOS)</td>
<td>Hirsutism</td>
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<tr>
<td>4. Hyperprolactinemia</td>
<td>Galactorrhea</td>
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<td>5. Medications</td>
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<td>6. Hypothalamic</td>
<td>Urogenital atrophy</td>
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<td>7. Asherman's syndrome</td>
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**Laboratory Examination**

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<tr>
<td>1. Pregnancy</td>
<td>B HCG</td>
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<tr>
<td>2. Menopause</td>
<td>FSH</td>
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<tr>
<td>3. Chronic anovulation (PCOS)</td>
<td>-</td>
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<tr>
<td>4. Hyperprolactinemia</td>
<td>Prolactin</td>
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<tr>
<td>5. Medications</td>
<td>-</td>
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<tr>
<td>6. Hypothalamic</td>
<td>FSH/LH</td>
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<tr>
<td>7. Asherman’s syndrome</td>
<td>-</td>
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<tr>
<td>8. Hypothyroidism</td>
<td>TSH</td>
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**What’s left?**

- Chronic anovulation / (PCOS); a hyperestrogenic state (many bricks, no mortar)
- Menopause, hypothalamic amenorrhea and hypothyroidism; all are hypoestrogenic states (no bricks, no mortar)
- Does the patient have “bricks”?

**Progestin challenge test**

- Add mortar and take it away
- Mimics ovulation and the function of the corpus luteum (you are providing progesterone instead)
- Provera® 10 mg po QD X 10 days
- Return in 2 weeks
- Did patient bleed?

**At first visit**

- 3/8 ruled out (pregnancy, Asherman’s and medications)
- Send patient for prolactin, TSH
- Do progestin challenge test
At second visit

- Results of progestin challenge known
- 6/8 ruled out (hyperprolactenemia and hypothyroidism)
- Hypothalamic amenorrhea and menopause are left
- Get an FSH (if high, menopause; if low, hypothalamic amenorrhea)

Can we be even briefer?

- Yes
- First visit: rule out Asherman’s and medications by history; rule out pregnancy by βHCG
- Order a TSH, prolactin and FSH
- Assume chronic anovulation and prescribe OCPs
- If prolactin, FSH or TSH abnormal, treat accordingly

Treatments

Contemporary practice focused on treatment of the primary problem

- Hyperprolactinemia
- Hypothyroidism
- Hypothalamic amenorrhea: OCPs, ERT
- Medication-induced amenorrhea: if medication is needed, consider OCPs, ERT

Treatments: chronic anovulation

- If pregnancy not desired, OCPs or cyclic Provera
- If pregnancy desired, ovulation induction e.g., clomiphene citrate
**Case 1**

28 y.o. on OCPs for 11 months now with spotting for 4 months

- r/o pregnancy
- May d/c OCPs for one week (use back-up method of birth control)
- May prescribe estrogen (0.625 BID for one week)

**Abnormal uterine bleeding**

- Heavy, regular periods (menorrhagia)
- Heavy, irregular periods (menometrorrhagia)
- Spotting (intermenstrual bleeding)
- Postmenopausal bleeding
- Whatever the patient says is abnormal for her

**Case 2**

42 y.o. presents with heavy, irregular bleeding for 6 months. She feels more tired than usual.

She is of normal weight, has no medical problems and does not smoke.

Her vital signs and exam are normal.

**Abnormal uterine bleeding**

- Heavy, *regular* periods (menorrhagia)
- think benign causes: fibroids, polyps, adenomyosis
- think medical treatments as a first line: OCPs, non-steroidal, progestins
- think diagnostic evaluation for medical treatment failures: (ultrasonography, hysteroscopy)
Abnormal uterine bleeding

- Heavy, *irregular* periods (menometrorrhagia)
  - think benign *and* malignant causes: (fibroids, polyps, adenomyosis; endometrial cancer)
  - do endometrial biopsy in high-risk women, then think of medical treatments as a first line: OCPs, non-steroidals, progestins
  - think diagnostic evaluation for medical treatment failures: (ultrasonography, hysteroscopy)

Abnormal uterine bleeding

- Spotting (intermenstrual bleeding)
  - think benign *and* malignant causes: cervicitis, polyps, exogenous hormones (OCPs); cervical and endometrial cancer
  - think diagnostic evaluation (cervical exam, cultures, endometrial biopsy in high-risk women)

Abnormal uterine bleeding

- Postmenopausal bleeding
  - think malignant causes (endometrial cancer)
  - think atrophy

Who is at high risk for endometrial cancer?

In whom is an EMB indicated?
Endometrial Cancer: Facts

- 4th most common cancer in women
- Average age 61 but 25% occur pre-menopausally
- 10% of post-menopausal women with bleeding have cancer
- Presents at early stage with bleeding
- Rare in the absence of bleeding
- Major Risk Factors = obesity, increased estrogen, anovulation (too many bricks)
- Protective = smoking, OCPs

ACOG guideline

...based on age alone, endometrial assessment to exclude cancer is indicated in any woman older than 35 years who is suspected of having anovulatory uterine bleeding.

A Rational Approach to EMB

Postmenopausal women: all women with any bleeding (except 4-6 months after starting HRT)
Pre-menopausal women (aged 35+ years): all women with recurrent episodic bleeding less than a month apart
Women with some Pap smear findings (atypical glandular cells in women over 35 or any age with RFs; endometrial cells in post-menopausal women)

A Rational Approach to EMB (cont’d)

Further evaluation needed if:

1. Persistent abnormal bleeding after negative EMB or ultrasound
2. Persistent abnormal bleeding after 3-6 months of medical therapy
**Can I get an ultrasound instead?**

Transvaginal Ultrasound
- Measure endometrial stripe
- \( \geq 5 \text{mm} \) is abnormal
- Non-specific: myomas, polyps and hyperplasia all cause thick EM
- Operator skill mandatory
- NOT USEFUL PRE-MENOPAUSE

**Case 2**

42 y.o. presents with heavy, irregular bleeding for 6 months. She feels more tired than usual. She is of normal weight, has no medical problems and does not smoke. Her vital signs and exam are normal.
The plan:
1) BHCG
2) Endometrial biopsy
3) Hematocrit
4) Iron supplementation
5) Oral contraceptive pills
6) NSAIDs (ibuprofen 600 QID)

**Case 3**

42 y.o. presents with heavy, irregular bleeding for 6 months. She feels more tired than usual. She is of normal weight, has no medical problems but she smokes one pack of cigarettes a day. Her vital signs and exam are normal.
The plan:
1) BHCG
2) Endometrial biopsy
3) Hematocrit
4) Iron supplementation
5) Progestin-only treatments (more mortar): cyclic progestins, Depot MPA, Implanon, progestin IUD (IUS) (Mirena)
6) NSAIDs (ibuprofen 600 QID)

**Perimenopausal Bleeding**

R/o pregnancy

↓ EMB

Treat first as if anovulatory bleeding:
- NSAID’s
- Hormones [OCP’s, Levo IUS]

↓ If persists, proceed to surgical diagnosis and/or treatment
Conclusions

• Persistent abnormal bleeding requires continued work-up even if EMB and/or ultrasound are negative

• Rule out pregnancy first

• Treat all bleeding the same: NSAID’s plus hormones