Abnormal Uterine Bleeding:
Evaluation of Premenopausal Women

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Objectives

- Define normal and abnormal menstrual bleeding
- Review differential diagnosis and evaluation for abnormal bleeding in premenopausal women
- Recommend guidelines for the use of endometrial biopsy
Normal Uterine Bleeding

Classically…

• Cycle length 24 to 35 days
• Menses 2-7 days
• Less than 80 cc per cycle
The Menstrual Cycle

![Graph showing levels of Estrogen, LH, Progesterone, and FSH during the menstrual cycle.](image-url)
A 24 year old G0 presents with heavy irregular bleeding for 6 months. Her bleeding is every 15-35 days, lasts 4-15 days. She has...

1. Menorrhagia
2. Dysfunctional uterine bleeding (DUB)
3. Menometrorrhagia
Classic Definitions

Excess Bleeding
• Menorrhagia: heavy, regular timing
• Metrorrhagia: light, frequent intervals
• Menometrorrhagia: heavy, frequent, irregular
• Polymenorrhoea: regular, <24 days apart
• Intermenstrual spotting: bleeding between menses

Decreased bleeding
• Oligomenorrhoea: bleeding >35 days apart
Dysfunctional Uterine Bleeding

- Excessive noncyclic bleeding not caused by anatomic lesion, medications, pregnancy or systemic disease
- Primarily due to anovulation
- Most common cause of AUB
- Diagnosis of exclusion
Challenges with Classic Definitions

• Data is from women in Minnesota, 1930s
• Lack of uniformity across clinical settings
• Difficulty in tools for bleeding assessment

Treloar EA, Boynton, Int J Fertil 1967
# Pictorial Blood Loss Assessment Chart

**Name:** Sabine Mustermann

<table>
<thead>
<tr>
<th>Date: Week</th>
<th>Days of bleeding</th>
<th>Sanitary towel</th>
<th>Number of used sanitary towel</th>
</tr>
</thead>
<tbody>
<tr>
<td>5/11</td>
<td>5/18</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Intensity of bleeding per sanitary towel</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>x 1</td>
<td>1</td>
<td>//</td>
<td></td>
</tr>
<tr>
<td>x 5</td>
<td>2</td>
<td>///</td>
<td></td>
</tr>
<tr>
<td>x 20</td>
<td>3</td>
<td>//</td>
<td></td>
</tr>
<tr>
<td><strong>Factor:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>and/or Tampons</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Intensity of bleeding per tampon</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>x 1</td>
<td>4</td>
<td>/</td>
<td></td>
</tr>
<tr>
<td>x 5</td>
<td>5</td>
<td>///</td>
<td></td>
</tr>
<tr>
<td>x 15</td>
<td>6</td>
<td>##/</td>
<td></td>
</tr>
<tr>
<td><strong>Factor:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Daily points:** 2 137 101 21 3 1
- **Total:** 265

Challenges with Classic Definitions

• International meeting of experts 2007 (Menstrual Agreement Process)

• Recommendations:
  – Discontinue use of classic terms
  – Use descriptive terms that patients understand
  – Create uniformity for research

## New Descriptive Terms for AUB

<table>
<thead>
<tr>
<th>Clinical Dimensions</th>
<th>Descriptive Terms</th>
<th>Normal limits (5th to 95th percentiles)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FREQUENCY (days)</td>
<td>Frequent</td>
<td>&lt;24</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>24-38</td>
</tr>
<tr>
<td></td>
<td>Infrequent</td>
<td>&gt;38</td>
</tr>
<tr>
<td>REGULARITY</td>
<td>Absent</td>
<td>-</td>
</tr>
<tr>
<td>Cycle to cycle variation over 1 year</td>
<td>Regular</td>
<td>Variation +2-20 days</td>
</tr>
<tr>
<td></td>
<td>Irregular</td>
<td>Variation &gt;20 days</td>
</tr>
<tr>
<td>DURATION (days)</td>
<td>Prolonged</td>
<td>&gt;8</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>4.5-8</td>
</tr>
<tr>
<td></td>
<td>Shortened</td>
<td>&lt;4.5</td>
</tr>
<tr>
<td>VOLUME (monthly mL)</td>
<td>Heavy</td>
<td>&gt;80</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>5-80</td>
</tr>
<tr>
<td></td>
<td>Light</td>
<td>&lt;5</td>
</tr>
</tbody>
</table>

Case 2

A 33 yo G1P1 with regular, normal periods but three months of light spotting in between periods. Spotting is 5-9 days a month, randomly distributed between cycles. She uses a copper IUD for contraception.

What is the differential diagnosis?
Evaluation: premenopausal women

Four steps:
1) Is it uterine?
2) Is she pregnant?
3) Describe the bleeding.
4) Is it ovulatory?
Evaluation: premenopausal women

Four steps:

1) Is it uterine?
   • Detailed history to r/o GI/GU sources
   • Exam to r/o obvious vulvar, vaginal, cervical lesions
   • Up to date Pap smear
Case 2

During the pelvic exam, the patient is noted to have a 2cm cervical polyp which is removed in the office. She has full resolution of her bleeding at 6 week follow-up.
Evaluation: premenopausal women

Four steps:
1) Is it uterine?
2) Is she pregnant?
   Check pregnancy test in at-risk women
Case 3

A 41 yo G3P2 with 4 months of abnormal bleeding. Regular cycle length every 29-32 days, lasts 7 days, but bleeding is heavy. She changes a tampon every hour for the first 3 days and has to get up at night to change tampons/pads.
Evaluation: premenopausal women

Four steps:
1) Is it uterine?
2) Is she pregnant?
3) Describe the bleeding.
   • Detailed history will guide w/u and treatment
   • Consider menstrual calendar X 2-3 cycles
Tips to assess bleeding history

Factors associated with heavy bleeding:

1. Bleeding history (but only 34% with “heavy bleeding” had EBL >80cc)
2. Change pads/tampons ≤3 hour intervals
3. High number of pads/tampons per cycle (>21)
4. Require change of tampon/pad during night
5. Have clots >1 inch

Warner, Critchley et al, Am Jo Obstet Gynecol, 2004
Case 3

A 41 yo G3P2 with 4 months of abnormal bleeding. Regular cycle length every 29-32 days, lasts 7 days, but bleeding is heavy. She changes a tampon every hour for the first 3 days and has to get up at night to change tampons/pads.

Bleeding is **REGULAR** in timing and duration but **HEAVY** volume (menorrhagia).
Evaluation: premenopausal women

Four steps:
1) Is it uterine?
2) Is she pregnant?
3) Describe the bleeding.
4) Is it ovulatory?
   – Regular intervals
   • Moliminal symptoms
Classic Definitions

Ovulatory
- Menorrhagia: heavy, **regular** timing
- Polymenorrhea: **regular**, <24 days apart
- Intermenstrual spotting: bleeding between regular menses

Anovulatory
- Metrorrhagia: light, frequent intervals
- Menometrorrhagia: heavy, frequent, irregular
- Oligomenorrhea: bleeding >35 days apart
- Intermenstrual spotting: bleeding between menses
Ovulatory AUB

Hypothalamic-pituitary-ovarian axis intact
Ovulatory AUB: Differential Diagnosis

OVULATORY AUB

- Anatomic
  - Fibroids
  - Adenomyosis
  - Polyps

- Bleeding disorder/Medication
  - VonWillebrand's
  - ITP
  - Coumadin

- Idiopathic
Ovulatory AUB: History

- Medical comorbidities
- Medications
- Thyroid symptoms
- Disorder of hemostasis
  - Heavy menses since menarche OR
  - History of postpartum hemorrhage, bleeding with surgery/dental work OR
  - 2 or more of the following—bruising >5cm or epistaxis 1-2/month, frequent gum bleeding, family history of bleeding

Ovulatory AUB: Physical exam

**UTERINE FIBROIDS**

- Intramural
- Pedunculated
- Subserosal
- Submucosal

**Fibroids**

**Adenomyosis**
Ovulatory AUB: Blood tests

- CBC
- Screen for disorders of hemostasis according to history or if pt plans major surgery
  - PT, APTT
  - VWF antigen, ristocetin cofactor, factor VIII

Ovulatory AUB: Ultrasound

- Perform on day 4-6 of cycle
- TVUS polyps and fibroids: sensitivity 80%, specificity 69%
- Not useful to rule out hyperplasia and cancer
- Consider saline sono, office hysteroscopy, or MRI
Case 3

A 41 yo G3P2 with 4 months of abnormal bleeding. Regular cycle length every 29-32 days, lasts 7 days, but bleeding is heavy. She changes a tampon every hour for the first 3 days and has to get up at night to change tampons/pads.

Bleeding is **REGULAR** in timing and duration but **HEAVY** volume (**menorrhagia**).

- No PMH
- No medications
- Hct 29
- Pelvic ultrasound: 3cm submucosal fibroid, 80% in the endometrial cavity
Case 3

Submucosal fibroid, ultrasound image

Treatment
- Hysteroscopic myomectomy
- Hysterectomy
49 yo G2P2 with 5 months of heavy bleeding. Regular cycle length and duration, but heavy bleeding resulting in significant anemia. Does she need an endometrial biopsy?

63%  1. Yes
38%  2. No
38 yo G2P2 with 5 months of irregular bleeding. Bleeding is every 2-3 weeks, lasts 5-12 days, and heavy. Has to change tampon every 1-2 hours for the first few days. Does she need an endometrial biopsy?

<p>| | |</p>
<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>61%</td>
<td>1. Yes</td>
</tr>
<tr>
<td>39%</td>
<td>2. No</td>
</tr>
</tbody>
</table>
Endometrial Biopsy

Endometrial Cancer Facts

• 4th most common cancer in women (2.5% lifetime risk)
• Average age 61 but 25% occur pre-menopausally
• Rare to have cancer without abnormal bleeding
• Risk factors: unopposed estrogen (anovulation), obesity, nulliparity, diabetes, hypertension
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.”
Normal Perimenopause

• 12% suddenly stop menstruating
• 18% have longer, heavier menses
• 70% have short, irregular menses

Should we perform EMB on 88% of perimenopausal women?

Treloar EA, Boynton, Int J Fertil 1967
Suggested guidelines for performing endometrial biopsy

Premenopausal, age >35 years:
- Heavy, irregular bleeding: **YES**
- Risk factors for cancer: **YES**
- Perimenopausal infrequent/scant bleeding: **NO**
- Regular bleeding pattern: **NO**
## AUB: 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
- Check TSH/Free T4 if suspect hypothalamic/pituitary lesion to detect central hypothyroidism

Case 6: Anovulatory bleeding

A 24 yo G0 with 8 months abnormal bleeding. Bleeding is every 10-45 days, lasts 5-20 days, heavy for most days of bleeding. BMI 33.
Evaluation: premenopausal women

Four steps:
1) Is it uterine? YES.
2) Is she pregnant? Upreg neg.
3) Describe the bleeding. Heavy, frequent, irregular, prolonged (menometrorragia)
4) Is it ovulatory? NO.
Anovulatory AUB: Differential Diagnosis

ANO Vul TORY AUB

Estrogenic (excess bleeding)

Hypoestrogenic (decreased bleeding)
Anovulatory AUB: Differential Diagnosis

- ANOVULATORY AUB
  - Estrogenic
    - Physiologic
      - Adolescence, Perimenopause
    - Hyperandrogenic
      - PCOS, CAH, Cushings
    - Systemic disease/Medications
      - Renal or liver disease, Chronic steroids
Anovulatory AUB: Differential Diagnosis

ANOVULATORY AUB

Hypoestrogenic

- Hypothalamic (stress, anorexia, mass lesion)
- Hyperprolactinemia
- Ovarian Failure (Premature: POF)
Miscellaneous

Ovulatory, but irregular
  • Infection
    Usually light/frequent bleeding
  • Endometrial hyperplasia/cancer
    Usually heavy/frequent

Anovulatory, iatrogenic
  – Use of hormonal contraception
Anovulatory AUB: History

History (Estrogenic)
• Hirsutism, other androgen excess
• Medications
• Chronic disease

History (Hypoestrogenic)
• Galactorrhea
• Hot flashes, other menopausal symptoms

Physical
• BMI
• Hirsutism
• Acanthosis nigracans
Anovulatory AUB: Tests and Imaging

**Labs**
- CBC
- TSH
- Prolactin
  - for oligomenorrhea only
- FSH
  - For oligomenorrhea in <40 years with menopausal symptoms and/or no other explanation of hypoestrogenism

**Consider EMB**

**Imaging**
- Not necessary unless abnormal exam or does not respond to treatment
Case 6: Anovulatory bleeding

A 24 yo G0 with 8 months abnormal bleeding. Bleeding is every 10-4 days, lasts 5-20 days, heavy for most days of bleeding. BMI 33.

- No PMH. No meds.
- Removes hair from upper lip and chin every 2 weeks.
- Exam: obese, coarse dark hair upper lip, uterus/adnexa not palpable.
- Labs: Hct 30. TSH wnl.
Case 6: Anovulatory bleeding

A 24 yo G0 with 8 months abnormal bleeding. Bleeding is every 10-14 days, lasts 5-20 days, heavy for most days of bleeding. BMI 33.

- No PMH. No meds.
- Removes hair from upper lip and chin every 2 weeks.
- Exam: obese, coarse dark hair upper lip, uterus/adnexa not palpable.
- Labs: Hct 30. TSH wnl.

Diagnosis: Polycystic ovarian syndrome
Treatment: Oral contraceptive pills, screening for DM, lipids
Summary

• Distinguish ovulatory (regular) vs. anovulatory (irregular) bleeding

• If ovulatory, likely anatomic cause  
  – Check pelvic ultrasound

• If anovulatory, likely hormonal dysfunction  
  – Consider endometrial biopsy