Management of Abnormal Uterine Bleeding
**AUB vs. Anovulatory Uterine Bleeding**

- Abnormal uterine bleeding (AUB): fairly broad term referring to bleeding that occurs outside of normal cyclic menstruation
- Anovulatory uterine bleeding: abnormal bleeding that cannot be attributed to an anatomic, organic, or systemic lesion or disease
- The term “dysfunctional uterine bleeding” is no longer in favor and has been replaced by AUB
AUB Affects . . .

- >10 million women in the U.S.
- Impacts daily activities and quality of life
- May cause anxiety
- May lead to iron-deficiency anemia/fatigue
AUB Affects...

- Adolescents
- Women of reproductive age
- Peri- and postmenopausal women
# Characteristics of Normal Menstruation

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Normal</th>
<th>Abnormal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of flow</td>
<td>4-6 days</td>
<td>&lt;2 days or &gt;7 days</td>
</tr>
<tr>
<td>Volume of flow</td>
<td>30 mL</td>
<td>&gt;80 mL</td>
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<tr>
<td>Length of cycle</td>
<td>24-35 days</td>
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</table>
Definitions

- Amenorrhea: absence of menstruation for at least three usual cyclic lengths
- Oligomenorrhea: cyclic length >35 days
- Polymenorrhea: cyclic length <24 days
- Menorrhagia: regular, normal intervals with excessive volume and durations of flow
- Metrorrhagia: irregular intervals with normal or reduced volume and duration of flow
- Menometrorrhagia: irregular interval and excessive volume and duration of flow
Regulation of Normal Menstruation

- Hypothalamic-pituitary-ovarian (HPO) axis
- GnRH pulses stimulate FSH and LH
- Dominant follicle matures to ovulation and provides negative feedback to stop recruitment
- Estradiol initiates ovulation via LH surge through a positive feedback
- Proliferative phase of the endometrium
- Corpus luteum and progesterone influences the secretory phase of the endometrium
- If implantation fails: progesterone withdrawal, endometrial collapse, and menstruation
Regulation of Normal Menstruation
Etiologic Basis of Anovulatory Uterine Bleeding

- Estrogen-withdrawal bleeding (e.g. iatrogenic with cessation of therapy)
- Estrogen-breakthrough bleeding (e.g. anovulation)
- Progesterone-breakthrough bleeding (e.g. OCP administration)
Ovulatory AUB

- AUB without any attributable anatomic, organic, or systemic cause but associated with regular ovulation
- Uncommon
- Regular progesterone-withdrawal menses every 24-35 days— but excessive blood loss
- Loss of local endometrial hemostasis
- ↑ Ratio of PGE$_{2\alpha}$ : PGF$_{2\alpha}$
- ↑ Level of PGI$_2$
- ↑ Fibrinolytic activity
Anovulatory Uterine Bleeding

- Noncyclic menstrual blood loss due to anovulatory productions of sex steroids
- Estrogen-withdrawal or estrogen-breakthrough bleeding in the absence of cyclic progesterone
- Characterized by a hyperplastic, fragile endometrium prone to localized breakage and bleeding
- Erratic in both timing and volume
Usual Causes of AUB Throughout a Woman’s Lifetime

1. Estrogen withdrawal
2. Foreign body
   - Infection
   - Sarcoma botryoides
   - Ovarian tumor
   - Trauma
3. Blood dyscrasia
   - Hypothalamic immaturity
   - Inadequate luteal function
   - Psychogenic (including anorexia and bulimia)
4. Anovulation
   - Central, intermediate, gonadal
   - Functional
   - Blood dyscrasia, hypothyroidism, luteal dysfunction
   - Iatrogenic
   - Anticoagulation, contraception (hormonal intrauterine), hemodialysis
   - Pregnancy
   - Abortion, ectopic, placental polyp, retained products, trophoblastic disease
   - Uterine
   - Infection, structural (fibroids, hyperplasia, neoplasia, polyps)
5. Carcinoma
   - (cervical, uterine)
   - Climacteric
   - Polyps
6. Atrophic vaginitis
   - Carcinoma (uterine, ovarian)
   - Estrogen replacement
Differential Diagnosis of AUB In Reproductive Age Women

- Complications from pregnancy
- Infection
- Trauma
- Cancer
- Pelvic pathology (benign)
- Systemic disease
- Medications/iatrogenic causes
Submucosal Fibroid

Uterine myometrium

Endometrial cavity

Submucosal fibroid

Slide courtesy of Raymond W. Ke, MD.
Endometrial Polyps

Slide courtesy of Linda Darlene Bradley, MD.
Evaluation of AUB in Premenopausal Women

1. **History and Physical Examination**
   - PREGNANT?
     - YES
     - NO

2. **Evaluate for Complications**
   - Intrauterine pregnancy
   - Ectopic pregnancy
   - Spontaneous abortion
   - Etc.

3. **EVALUATE FOR ANOVULATION**
   - ANOVULATORY?
     - NO
     - YES

4. **Perform Endometrium Evaluation**
   - Endometrial biopsy
   - TVS
   - SIS
   - Hysteroscopy

5. **Perform Uterine Evaluation**
   - Uterine evaluation normal?
     - NO
     - YES

6. **TREAT CONDITION**
   - Adenocarcinoma?
   - Endometrial hyperplasia?
   - Polyp?
   - Fibroids?

7. **Ovulatory AUB**
   - NO

8. **Anovulatory AUB**
   - NO
   - YES
Evaluation of AUB in Perimenopausal Women

1. History and Physical Examination
   - PREGNANT?
     - YES
       - Evaluate for complications:
         - Intrauterine pregnancy
         - Ectopic pregnancy
         - Spontaneous abortion
         - Etc.
   - NO
     - Infection?
     - Trauma?
     - Coagulopathy?
     - Systemic disease?
     - Iatrogenic causes?
     - Medications?
     - YES
       - Treat condition
     - NO
       - Perform thorough endometrium evaluation:
         - Endometrial biopsy
         - TVS
         - SIS
         - Hysteroscopy
       - ENDOMETRIUM EVALUATION NORMAL?
         - NO
           - Endometrial carcinoma?
           - Endometrial hyperplasia?
           - Polyps?
           - Fibroids?
         - YES
           - PERIMENOPAUSAL ANOVULATORY AUB
Evaluation of AUB in Postmenopausal Women

- **HISTORY AND PHYSICAL EXAMINATION**

- **ON HRT?**
  - **YES**
  - ON HRT FOR > 6 MONTHS?
    - **NO**
      - CONSIDER WAITING up to 9 months for resolution
    - **YES**
      - **NO**
        - PERFORM ENDOMETRIUM EVALUATION
          - Endometrial biopsy
          - TVS
          - Hysteroscopy

- **ENDOMETRIUM EVALUATION NORMAL?**
  - **NO**
    - **YES**
      - NEOPLASIA IN
        - Vagina?
        - Cervix?
        - Fallopian tube?
        - Bladder/urethra?
        - Rectum?
    - **NO**
      - POST-MENOPAUSAL AUB
        - Re-evaluate in 6 months
        - Consider hysterectomy
  - **YES**
    - TREAT CONDITION

- **TREAT CONDITION**
  - **YES**
  - **NO**
    - Adenocarcinoma?
    - Endometrial hyperplasia?
    - Polyps?
    - Fibroids?
Diagnostic Techniques in AUB

- Endometrial biopsy
- Transvaginal ultrasonography (TVS)
- Hysteroscopy
- Saline infusion sonography (SIS)
- Magnetic resonance imaging (MRI)
Endometrial Biopsy

- Safe, relatively simple procedure useful in perimenopausal or high risk women
- Not sensitive for detecting structural abnormalities (eg, polyps or fibroids)
- Office-based techniques (gold standard replacing D&C
  - Disposable devices (eg, Pipelle, Tis-u-Trap, Accurette, Z-sampler)
  - Reusable instruments (eg, Novak Curette, Randall Curette, Vabra Aspirator)
Possible Endometrial Biopsy Findings

- Proliferative, secretory, benign, or atrophic endometrium
- Inactive endometrium
- Tissue insufficient for analysis
- No endometrial tissue seen
- Simple or complex (adenomatous) hyperplasia without atypia
- Simple or complex (adenomatous) hyperplasia with atypia
- Endometrial adenocarcinoma
Transvaginal Ultrasonography (TVS)

- Inexpensive, noninvasive, and convenient
- Indirect visualization of the endometrial cavity, myometrium, and adnexa
- Measurement of endometrial thickness (<5 mm vs. >5 mm)
- May be used to increase index of suspicion for endometrial atrophy, hyperplasia, cancer, leiomyomas, and polyps
- May not always distinguish among submucosal fibroid, polyp, or adenomyosis
Posterior Fibroid

Slide courtesy of Linda Darlene Bradley, MD.
Hysteroscopy

- Hysteroscopy + biopsy = “gold standard”
- Most are performed to evaluate AUB
- Diagnostic hysteroscopy easily performed in the office setting—although it requires skill
- Particularly useful in the diagnosis of intrauterine lesions in women of reproductive age with ovulatory AUB
- Complications (<1%) may include uterine perforation, infections, excessive bleeding, and those related to distending medium
Flexible hysteroscope
Endometrial Polyps

Slide courtesy of Linda Darlene Bradley, MD.
Endometrial Polyps

Slide courtesy of Linda Darlene Bradley, MD.
Endometrial Hyperplasia
Saline Infusion Sonography (SIS)

- Relatively new technique
- Very useful for evaluation of AUB in pre-, peri-, and postmenopausal women
- May be superior to TVS alone (94.1% vs. 23.5% for detection of focal intrauterine pathology)
- SIS + biopsy: 96.2% sensitivity and 98% specificity
- Disadvantage: small irregularities may be misinterpreted as polyps
- Able to determine penetration depth of uterine fibroids
Posterior Class 3 Fibroid

Slide courtesy of Linda Darlene Bradley, MD.
Saline Infusion Sonography

TVS

SIS
Magnetic Resonance Imaging (MRI)

- Powerful, noninvasive technique for visualizing the endometrial cavity and uterine abnormalities
- Reliably differentiates uterine anatomy, localizes pelvic pathologic conditions, and estimates the size of lesions
- Can reliably distinguish between adenomyosis and leiomyomata—more sensitive than TVS and SIS
- May not be superior to SIS and hysteroscopy in overall diagnostic potential
- Able to determine penetration depth of uterine fibroids
Medical Treatment of AUB

- Iron
- Antifibrinolytics
- Cyclooxygenase inhibitors
- Progestins
- Estrogens + progestins (OCs)
- Parenteral estrogens (CEEs)
- Androgens
- GnRH agonists and antagonists
- Antiprogestational agents
Iron

- Menstrual volume >60 mL—iron-deficiency anemia
- Primary symptom is fatigue
- Daily doses of 60-180 mg of iron
- In some cases, may be the only treatment necessary
Antifibrinolytics

- Fibrinolysis—endometrial hemostasis
- Tranexamic acid (TA) and precursors effective in reducing menstrual blood loss
- TA reduced blood loss by up to 54%
- Rarely administered in North America, but a mainstay treatment elsewhere
- Concern about thromboembolic events may be unwarranted based on retrospective data
COX Inhibitors

- Prostaglandins: central role in menstrual hemostasis
- NSAIDs have been shown to be effective in the treatment of menorrhagia. Mefenamic acid, diclofenac, flurbiprofen, ibuprofen, indomethacin, naproxen, meclofenamate sodium, and naproxen sodium
- New COX 2 drugs may have a role in alternate pathways
Progestins

- Medroxyprogesterone acetate: North America
- Norethindrone: worldwide
- Cyclic, continuous, or local administration
- Ovulatory AUB: continuous progestins may be better than cyclic progestins
- Anovulatory uterine bleeding: cyclic progestins more effective
- Local (IUD) progestins: reductions in bleeding volume of 79% to 94%; up to 82% of women elected to cancel hysterectomies
Estrogens + Progestins (OCs)

- Effective for ovulatory AUB and anovulatory uterine bleeding—most commonly prescribed treatment in the U.S.
- Effective in adolescents with excessive bleeding
- For AUB: choose an OC containing 30-35 μg of ethinyl estradiol
- Low-dose OCs may be effective add-back therapy for women taking GnRH agonists
Parenteral Estrogens (CEEs)

- IV or IM conjugated equine estrogens (CEEs): most widely prescribed emergent treatment for acute, rapid, and excessive uterine bleeding
- May be effective for both ovulatory AUB and anovulatory uterine bleeding: 71% bleeding cessation vs. 38% for placebo
- High-dose CEEs (25 mg IV every 4 hrs) effective in adolescents with acute bleeding
Androgens

- Danazol (synthetic testosterone derivative) has reduced bleeding volume in 50% of women with ovulatory AUB
- More effective than cyclic progestins and NSAIDs for women with ovulatory AUB
- Adverse effects associated with androgen therapy may make long-term treatment undesirable for many women
GnRH Agonists/Antagonists

- May be effective for the treatment of both ovulatory AUB and anovulatory uterine bleeding
- Agonists induce amenorrhea by shrinking total uterine volume by 40% to 60%
- Gonadotropin “flare” associated with agonists may induce bleeding in 2\textsuperscript{nd} week of treatment (not associated with antagonists)
- Cost and adverse effects (eg, osteopenia) may limit utility in women with AUB, and physicians in the U.S often regard GnRH agonists as a treatment of last resort
Antiprogestational Agents

- Mifepristone 50 mg/day reported to induce amenorrhea in women with leiomyomas
- Reduces the number of progesterone-receptors in the myometrium, but not the number of estrogen-receptors
- May reduce uterine size in leiomyoma patients (Obstet Gynecol 2/03)
Ovulatory AUB

- If contraception desired: combination OCs or progestin IUDs are good initial treatment
- If fertility desired: NSAIDs or tranexamic acid (rarely used in the U.S.) would reduce bleeding volume
- GnRH agonists may be effective as second-line treatment
Medical Therapy: Anovulatory Uterine Bleeding

- Cause of anovulation should be identified and treated
- Cyclic progestins and combination OCs are usually effective—cyclic progestins may be ideal for women with contraindications to OCs (eg, smokers >35, hypertension)
- GnRH agonists are effective, but expensive
- Less likely to benefit from antifibrinolytics, NSAIDs, progestin IUDs, or continuous progestins
Surgical Treatment of AUB

- Hysterectomy
- Hysteroscopic endometrial ablation
- Nonhysteroscopic endometrial ablation
Hysterectomy

- Abdominal hysterectomy (AH)
- Vaginal hysterectomy (VH)
- Laparoscopically-assisted vaginal hysterectomy (LAVH)
Hysteroscopic Endometrial Ablation

- Nd:YAG laser
- Electrosurgical techniques (e.g., rollerball, loop electrode, vaporization)
- Hydrothermablation: heated free fluid (Hydro ThermAblator® Endometrial Ablation System)
Electrosurgical Endometrial Resection

Slide courtesy of Raymond W. Ke, MD.
Nonhysteroscopic Endometrial Ablation

- Balloon ablation (ThermaChoice® Uterine Balloon Therapy System)
- Cryoablation (Her Option™ Uterine Cryoablation Therapy™ System)
- Radiofrequency probe
- Unipolar electrodes (Vesta system)
- Bipolar electrodes (NovaSure™ System)
HTA Treatment

- Dilate to 8 mm / 24 Fr.
- Insert Sheath under direct visualization
- Perform diagnostic hysteroscopy
- Position Sheath inside the internal cervical os
- Treatment at 90°C for 10 minutes
- One minute cool flush
### TABLE 4: ENDOMETRIAL ABLATIVE TECHNIQUES—REPORTED DATA ON EFFECTIVENESS

<table>
<thead>
<tr>
<th></th>
<th>ThermaChoice® Uterine Balloon Therapy System&lt;sup&gt;113&lt;/sup&gt;</th>
<th>Hydro ThermAblator® Endometrial Ablation System&lt;sup&gt;114&lt;/sup&gt;</th>
<th>Her Option™ Uterine Cryoablation Therapy™ System&lt;sup&gt;115&lt;/sup&gt;</th>
<th>NovaSure™ System&lt;sup&gt;116&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rate of Success</td>
<td>80%</td>
<td>68%</td>
<td>67%</td>
<td>78%*</td>
</tr>
<tr>
<td>Rate of Amenorrhea</td>
<td>15%</td>
<td>35%</td>
<td>22%</td>
<td>36%*</td>
</tr>
<tr>
<td>Treatment Time</td>
<td>8 min</td>
<td>10 min</td>
<td>10-12 min</td>
<td>4.2 min</td>
</tr>
<tr>
<td>Local+IV anesthesia</td>
<td>39%</td>
<td>45%</td>
<td>39%</td>
<td>73%</td>
</tr>
<tr>
<td>Patient-Satisfaction</td>
<td>96%</td>
<td>N/A</td>
<td>86%</td>
<td>92%</td>
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</table>

* Note that patients with a uterine cavity length greater than 6 cm had observed-success rates that were lower than the overall rates of success in the study.
AUB is a significant gynecologic health problem
Anovulatory uterine bleeding is a diagnosis of exclusion
Uterine pathology can be evaluated by: biopsy, TVS, hysteroscopy, SIS, and MRI
Medical therapy is generally preferred
Surgical treatments for AUB include removal of the anatomic lesion, hysterectomy, hysteroscopic endometrial ablation/resection, free fluid ablation, and nonhysteroscopic endometrial ablation
Sexual Assault & Domestic Violence
Sexual assault

- 1 in 4 American women/children
- 1 in 10 victims seek help
- “loss of control”
Rape Trauma Syndrome

- Acute phase: begins during assault – emotionally volatile (calm, tearful, confused)
- Gain control (shopping, cleaning)
- Readjustment: deals with reality of the victimization (counseling)
 History, assure safety
 Labs (Gonorrhea, chlamydia, HIV, syphilis, UA, preg test, hepatitis ag)
 Antibiotic prophylaxis (Doxy, amox + probenecid, erythromycin)
 Emergency contraception
 Counseling
Domestic Violence

- Physical abuse
- Sexual abuse
- Emotional or psychological abuse

SAFE (feel Safe? been Abused? Family who can help? Escape plan?)