Management of Abnormal Uterine Bleeding

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AUB

Abnormal uterine bleeding (AUB): fairly broad term referring to bleeding that occurs outside of normal cyclic menstruation

- The term “dysfunctional uterine bleeding” is no longer in favor and has been replaced by AUB
- Abnormal uterine bleeding may be ovulatory or anovulatory
AUB Affects . . .

- >10 million women in the U.S. of all ages and life stages
- 1/3 of all gynecologic visits
- 50% all hysterectomies
- Impacts daily activities and quality of life
- May cause anxiety
- May lead to iron-deficiency anemia/fatigue
- May be associated with neoplasm
## Characteristics of normal menstruation

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Abnormal</th>
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<tbody>
<tr>
<td>Duration of flow</td>
<td>4-6 days</td>
<td>&lt;2 days</td>
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<tr>
<td></td>
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<td>&gt;7 days</td>
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<tr>
<td>Volume of flow</td>
<td>30 ml</td>
<td>80 ml</td>
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<tr>
<td>Length of cycle</td>
<td>24-35 days</td>
<td>&lt;than 24 days</td>
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<td>&gt; 35 days</td>
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Normal Menstrual bleeding

- Triggered by progesterone withdrawal
- Endometrial necrosis and sloughing due to arteriolar vasoconstriction, spasm and necrosis
- PgF2 alpha mediated increase in endometrial contraction,
- Cessation of menses is a result of prolonged vasoconstriction, tissue collapse, vascular stasis and thrombin production as well as follicular recruitment and production of estradiol
(Average values. Durations and values may differ between different females or different cycles.)
Definitions of AUB

- **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
Possible 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
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
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; think pathology!
- Regular progesterone-withdrawal menses every 24-35 days—but excessive blood loss
- Loss of local endometrial hemostasis
- Alteration in PGE metabolism or fibrolytic activity
Submucosal Fibroid

Uterine myometrium

Endometrial cavity

Submucosal fibroid
Endometrial Polyps
Evaluation of Abnormal Uterine Bleeding

- **History:** frequency, duration, volume, associated symptoms, onset of bleeding, family history, general health history, medication exposure

- **Physical examination:** basic physical for signs of systemic disease, body habitus, pap smear, bimanual exam assessing uterine size, contour, tenderness
Evaluation of AUB

- Laboratory:
  - pregnancy test
  - cervical cytology
  - cultures of the cervix
  - CBC

- Evaluation of the endometrium:
  - Endometrial biopsy
  - TVUS
  - SIS
  - Hysteroscopy
Evaluation of AUB in Perimenopausal Women

Adapted from APGO Educational Series on Women’s Health Issues
Post menopausal bleeding and endometrial cancer

- Most common gyn cancer (>40,000 cases annually)
- Postmenopausal vaginal bleeding the presenting sign in >90% of cases
- Most PMB is atrophic
- 1-14% of women with PMB will have endometrial cancer
Evaluation of AUB in Postmenopausal Women

Adapted from APGO Educational Series on Women’s Health Issues
Diagnostic Techniques in AUB

ENDOMETRIAL BIOPSY
Endometrial Biopsy

- Safe, relatively simple procedure useful in perimenopausal or high risk women to exclude cancer of the uterus or precancer conditions
- Not sensitive for detecting structural abnormalities (eg, polyps or fibroids)
- Indicated for women over 35 or younger with associated risk factors
- Office-based techniques (gold standard replacing D&C)
Adequacy of EMB

Meta analysis of 39 studies, 7912 patients
Comparing endometrial sampling with definitive histopathology:

Adenocarcinoma PPV:
- 99.6% postmenopausal
- 91% premenopausal

Atypical hyperplasia PPV
- 81%

Dikhuizen et al Cancer 2000; 89:1765
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
Diagnostic Techniques in AUB

Transvaginal ultrasound
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) high NPV to exclude endometrial carcinoma in postmenopausal
- Useful with insufficient EMB or as first line evaluation with PMB
- May be used to increase index of suspicion for endometrial atrophy, hyperplasia, cancer, leiomyomas, and polyps but low specificity
Normal endometrial stripe
Diagnostic Techniques in AUB

Saline infusion sonography (SIS)
Saline Infusion Sonography (SIS)

- 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
- Able to determine penetration depth of uterine fibroids
- Disadvantage: small irregularities may be misinterpreted as polyps
Transvaginal sonography
Saline infusion sonography
Posterior Class 3 Fibroid
Diagnostic Techniques in AUB

Hysteroscopy

Telescope angled 30°

Inflow port

Outflow port

Light post is always opposite of the scope angle.
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
Normal Endometrium
Endometrial Polyps
Endometrial Hyperplasia

Slide courtesy of Linda Darlene Bradley, MD.
Vascular Polyp
Medical Treatment of AUB in the Reproductive years

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

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

- Local (IUD) progestin: reductions in bleeding volume of 79% to 94%;

- 82% of women elected to cancel hysterectomies

Barrington et al BJOG 1997;90:257
Lahteenmaki P et al. BMH 1998;316:1122
Estrogens + Progestins (OCs)

- Most commonly prescribed treatment in the U.S.
- Effective for ovulatory AUB and anovulatory uterine bleeding.
- Choose an OC containing 30-35 μg of ethinyl estradiol.
- May have a role as add-back therapy for women taking GnRH agonists.
Parenteral Estrogens (CEE(s))

- IV or IM conjugated equine estrogens (CEE(s)): most widely prescribed emergent treatment for acute, rapid, and excessive uterine bleeding
- Acts to elevate thrombin and stabilize endometrial shedding
- May be effective for both ovulatory AUB and anovulatory uterine bleeding: 71% bleeding cessation vs. 38% for placebo
GnRH Agonists/Antagonists

- May be effective for the treatment of both ovulatory AUB and anovulatory uterine bleeding
- Best role in patients with anticipated coagulation defects (i.e. Chemotherapy)
- Agonists induce amenorrhea by shrinking total uterine volume by 40% to 60%
- Gonadotropin “flare” associated with agonists may induce bleeding in 2nd week of treatment
- Cost and adverse effects (eg, osteopenia) may limit utility in women with AUB,
- Often regarded as a treatment of last resort
Anti-progestational 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

Murno J Am Assoc Gynecol Laprosc 1999:393
Medical Therapy: Ovulatory AUB

- If contraception desired: combination OCs or progestin IUDs are good initial treatment
- If fertility desired: NSAIDs 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—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
Hysteroscopic Endometrial Ablation

- Electrosurgical techniques (e.g., rollerball, loop electrode, vaporization)

- Hydrothemoablation: heated free fluid (HydroThermoAblator® Endometrial Ablation System)
Electrosurgical Endometrial Resection

Slide courtesy of Raymond W. Ke, MD.
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
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)
## Endometrial Ablation

### Reported Effectiveness

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<tr>
<th></th>
<th>Thermachoice Balloon system</th>
<th>Hydro-ThermAblator</th>
<th>Cryo-ablation</th>
<th>Novasure</th>
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<tbody>
<tr>
<td><strong>Success</strong></td>
<td>80%</td>
<td>68%</td>
<td>67%</td>
<td>78%</td>
</tr>
<tr>
<td><strong>Amenorrhea</strong></td>
<td>15%</td>
<td>35%</td>
<td>22%</td>
<td>36%</td>
</tr>
<tr>
<td><strong>Treatment time</strong></td>
<td>8 min</td>
<td>10 min</td>
<td>10-12 min</td>
<td>4 min</td>
</tr>
<tr>
<td><strong>Patient satisfaction</strong></td>
<td>96%</td>
<td>95%</td>
<td>86%</td>
<td>92%</td>
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Medical vs Surgical therapy

- Cochrane Database review: ablation vs hysterectomy vs medical therapy
- 8 studies 821 women
- 58% randomized to medical Rx had surgery within 2 years
- Endometrial ablation more effective than oral medicine; less side effects
- QOL no different between ablation, hysterectomy and IUS
Summary

- 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