Abnormal Uterine Bleeding - Cases

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Disclosure

- I have nothing to disclose
ACOG Objectives

- Describe the principle causes of AUB and the FIGO classifications
- Obtain a pertinent history and perform a physical exam to evaluate AUB
- Perform and interpret the results of diagnostic tests to determine the cause of AUB
  - Endometrial Biopsy, US/Saline Infusion US, hysteroscopy, laparoscopy
- Interpret results of other diagnostic tests
  - Serum/urine hCG, endocrinology assays, cultures of the genital tract, CBC, coagulation profile
- Treat AUB (both nonsurgically and surgically)
- Recommend appropriate follow-up that is necessary for the patient with AUB
1 of 3 outpatient gynecologic visits are for AUB

#1 indication for adolescent female urgent hospital admissions

Indication of 50% of all hysterectomies

80% of women with AUB do not have an anatomic pathologic condition
Case 1

蹋 21 yo G0 presents for a routine gynecologic exam. She is concerned about her unpredictable periods. She describes her cycles as coming the 9th of one month and the 7th of the next.

่ How would you counsel this patient? 😊
What is “Normal?”

- Duration: 2-7 days (Average 4 days)
- Cycle Length: 21-35 days (Average 29 days)
- Volume: 10-80 cc, really patient’s perception
The Menstrual Cycle

Phases of the Cycle

- Follicular – menses to LH surge
- Ovulation (30-36 hours) – LH surge to ovulation
- Luteal (14 days constant) – End of LH surge to menses

Phases of the Endometrium

- Menstrual
- Proliferative – menses to ovulation
- Secretory – ovulation to menses
Regulation – HP Axis

- Hypothalamus – pulsatile GnRH
- Anterior Pituitary – LH and FSH (gonadotropins)
- LH acts on the theca cells and FSH on the granulosa cells to produce estrogen.
- E2, P and inhibin provide negative feedback
Old Terms

- Menorrhagia – heavy flow &/or >7 days
- Metrorrhagia – intermenstrual bleeding
- Menometrorrhagia
- Polymenorrhea - <21 day cycles
- Dysmenorrhea – painful menses
- Amenorrhea – >3 months (previously regular); >6 months if irregular
- Oligomenorrhea - >35 days between menses
- Hypomenorrhea - <2 days, light menses
New Terms

- Heavy menstrual bleeding
  - Acute or chronic
- Intermenstrual bleeding
Case #2

14 year old presents with her mother through the emergency room with heavy menstrual bleeding. She reports saturating a pad every hour for 24 hours.

What is your differential diagnosis? 😊
Differential Diagnosis - AUB

- FIGO PALM-COEIN (Non Gravid Female)
- Life Cycles
  - Pre-Menarche
  - Reproductive
  - Post-Menopause
- Anatomic
- GESTATIONAL EVENT!
FIGO Classification

Differential Diagnosis

Abnormal Uterine Bleeding (AUB)
- Heavy menstrual bleeding (AUB/HMB)
- Intermenstrual bleeding (AUB/IMB)

**PALM: Structural Causes**
- Polyp (AUB-P)
- Adenomyosis (AUB-A)
- Leiomyoma (AUB-L)
  - Submucosal myoma (AUB-L_{SM})
  - Other myoma (AUB-L_{O})
- Malignancy & hyperplasia (AUB-M)

**COEIN: Nonstructural Causes**
- Coagulopathy (AUB-C)
- Ovulatory dysfunction (AUB-O)
- Endometrial (AUB-E)
- Iatrogenic (AUB-I)
- Not yet classified (AUB-N)

ACOG Practice Bulletin #128
AUB - C

- Von Willibrands
- ITP, Leukemia
- Drug induced
- Liver disease 😊
AUB-O

Causes

- Physiologic
  - Adolescence
  - Menopause Transition
  - Lactation
  - Pregnancy

- Pathologic
  - Hyperandrogenic anovulation (PCOS, CAH-NC, tumors)
  - Hypothalamic dysfunction
  - Hyperprolactinemia
  - Thyroid disease
  - Pituitary disease
  - POF
  - Iatrogenic (chemo, other meds)
AUB - I

- IUD
- Post-instrumentation
- Post-medical abortion
- Infection
Consulted by NICU for 1 week old infant with vaginal bleeding
- Estrogen withdrawal bleed
- Sarcoma botryoides (rare)

5 year old with vaginal bleeding
- Foreign body
- Infection
- Sarcoma botryoides
- Trauma
- Urethral Prolapse
- Precocious Puberty
- Ovarian Tumor
Differential Diagnosis By Age

13-18 year old
- Hypothalamic immaturity
- Coagulopathy
- Eating disorder
- Hormonal contraceptive use
- Pelvic infection
- Ovarian tumor
Differential Diagnosis By Age

19-39 year old
- Pregnancy
- Structural lesions (fibroids, polyps)
- Anovulatory cycles
- Hormonal contraception
- Endometrial hyperplasia
- Cancer

40-Menopause
- Anovulatory bleeding
- Endometrial hyperplasia or cancer
- Endometrial atrophy
- Fibroids
Differential Diagnosis By Age

- Post-Menopausal
  - Cancer
  - Vaginal atrophy
  - E2 replacement
  - Anatomic
Case #2

14 year old presents with her mother through the emergency room with heavy menstrual bleeding. She reports saturating a pad every hour for 24 hours.

- What is your differential diagnosis? 😊
- How would you evaluate this patient?
- Let’s start with history... 😊
History

- Onset, quantity, duration
- Associated Symptoms
  - Pain, dysmenorrhea
  - Infection
  - Weight changes
  - Hair distribution
  - Bruising/bleeding
  - Could it be from another source?
History

- Menstrual history
- Contraception
- Sexual history
- Genital infections
- Gynecologic history
- Obstetric history
History

- Family History
- Surgical History
- Nutrition and exercise
- Past Medical History
  - Chronic conditions
  - Anemia
  - Medications (psych, blood thinners, etc)
  - Thyroid disease
Pertinent History

- Menarche at 11
- Her cycles have always been heavy, but not this heavy. They last 7 days and are “monthly.”
- She has moderate cramping on the first 2 days
- PMH – Asthma, but otherwise healthy
- PSH – T&A (complicated by postoperative bleeding)
- FHx – Adopted
- Social Hx – sexually active, excellent grades, is active in middle school sports.
- Medications – Ventolin prn
- Pertinent ROS – (+) Fatigue, (+) bruises easily, (+) bleeding with flossing, (+) moliminal symptoms; (-) lightheadedness, (-) headache, (-) heat/cold intolerance, (-) sweating
Case #2

14 year old presents with her mother through the emergency room with heavy menstrual bleeding. She reports saturating a pad every hour for 24 hours.

- What is your differential diagnosis?
- How would you evaluate this patient?
  - Let’s start with history...
  - Physical Exam
Physical Examination

- Hemodynamically stable??
- VS: BP 110/70, P 100, AF
- Gen'l – pale, NAD, normal BMI, (-) insulin resistance signs
- Skin – (+) ecchymosis along shins
- Chest – CTAB/RRR
- Abd – S/NT/ND
- Ext – No CCE
- GU – moderate amount of menstrual blood in the vaginal vault
- Pad counts initiated
Case #2

- 14 year old presents with her mother through the emergency room with heavy menstrual bleeding. She reports saturating a pad every hour for 24 hours.

- What is your differential diagnosis? 😊
- How would you evaluate this patient?
  - Let’s start with history…😊
  - Physical Exam 😊
  - What is your next step in the evaluation? 😊
Next step in evaluation?

- Labs
  - Standard – hCG, CBC, T&C, TSH, (GC/Chl)
    - Negative hCG
    - Hemoglobin 6. platelets 160
    - TSH normal
  - Coagulopathy work-up? 😊
Von Willebrand’s

- VW Factor binds FVIII and platelets in vessels to form the platelet wall
- 3 main types
Heavy menstrual bleeding since menarche:
One of the following:
- Postpartum hemorrhage
- Surgery-related bleeding
- Bleeding associated with dental work

Two or more of the following symptoms:
- Bruising one to two times per month
- Epistaxis one to two times per month
- Frequent gum bleeding
- Family history of bleeding symptoms

ACOG PB#128
Imaging

- Based on clinical judgement
- SIS is superior to TVS alone for evaluating abnormalities of the uterine cavity
- MRI precisely localizes sub-mucosal fibroids, but is not superior to TVS and SIS in overall diagnostic potential
Case #2

14 year old presents with her mother through the emergency room with heavy menstrual bleeding. She reports saturating a pad every hour for 24 hours.

- What is your differential diagnosis? 😊
- How would you evaluate this patient?
  - Let's start with history... 😊
  - Physical Exam 😊
  - What is your next step in the evaluation? 😊
- How would manage this patient? 😊
Goals of Treatment

- Control the current episode of bleeding
- Reduce menstrual flow in subsequent cycles
- Monitor VS, O2, IVF, T&C
- Medical therapy is preferred first line
- Consider IU Foley
- Surgical management may be indicated in certain situations
### Medical Treatment

**Table 2. Medical Treatment Regimens**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Source</th>
<th>Suggested Dose</th>
<th>Dose Schedule</th>
<th>Potential Contraindications and Precautions According to FDA Labeling*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conjugated equine estrogren</td>
<td>DeVore GR, Owens O, Kase N. Use of intravenous Premarin in the treatment of dysfunctional uterine bleeding—a double-blind randomized control study. Obstet Gynecol 1982;59:285–91.</td>
<td>25 mg IV</td>
<td>Every 4–6 hours for 24 hours</td>
<td>Contraindications include, but are not limited, to breast cancer, active or past venous thrombosis or arterial thromboembolic disease, and liver dysfunction or disease. The agent should be used with caution in patients with cardiovascular or thromboembolic risk factors.</td>
</tr>
<tr>
<td>Combined oral contraceptives†</td>
<td>Munro MG, Mainor N, Basu R, Brisinger M, Barreda L. Oral medroxyprogesterone acetate and combination oral contraceptives for acute uterine bleeding: a randomized controlled trial. Obstet Gynecol 2006;108:924–9.</td>
<td>Monophasic combined oral contraceptive that contains 35 micrograms of ethinyl estradiol</td>
<td>Three times per day for 7 days</td>
<td>Contraindications include, but are not limited to, cigarette smoking (in women aged 35 years or older), hypertension, history of deep vein thrombosis or pulmonary embolism, known thromboembolic disorders, cerebrovascular disease, ischemic heart disease, migraine with aura, current or past breast cancer, severe liver disease, diabetes with vascular involvement, valvular heart disease with complications, and major surgery with prolonged immobilization.</td>
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## Medical Treatment

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<tbody>
<tr>
<td>Medroxyprogesterone acetate*</td>
<td>Munro MG, Mainor N, Basu R, Brisinger M, Barreda L. Oral medroxyprogesterone acetate and combination oral contraceptives for acute uterine bleeding: a randomized controlled trial. Obstet Gynecol 2006;108:924–9.</td>
<td>20 mg orally</td>
<td>Three times per day for 7 days</td>
<td>Contraindications include, but are not limited to, active or past deep vein thrombosis or pulmonary embolism, active or recent arterial thromboembolic disease, current or past breast cancer, and impaired liver function or liver disease.</td>
</tr>
<tr>
<td>Tranexamic acid</td>
<td>James AH, Kouides PA, Abdul-Kadir R, Dietrich JE, Edlund M, Federici AB, et al. Evaluation and management of acute menorrhagia in women with and without underlying bleeding disorders: consensus from an international expert panel. Eur J Obstet Gynecol Reprod Biol 2011;158:124–34.</td>
<td>1.3 g orally⁵ or 10 mg/kg IV (maximum 600 mg/dose)</td>
<td>Three times per day for 5 days (every 8 hours)</td>
<td>Contraindications include, but are not limited to, acquired impaired color vision and current thrombotic or thromboembolic disease. The agent should be used with caution in patients with a history of thrombosis (because of uncertain thrombotic risks), and concomitant administration of combined oral contraceptives needs to be carefully considered.</td>
</tr>
</tbody>
</table>
Continued Treatment

- Estrogen containing contraception
- Progestins (POP, cyclic, depo provera, levonorgestrel IUD, subcutaneous implant)
- TXA
- NSAIDs
- Lupron
36 yo G4P4 presents to your office for 3 years of abnormal periods. She has 2-3 periods a year and they are very heavy, lasting 12 days. She goes through 5 boxes of tampons and has to wear overnight pads, as well. She is not bleeding today. She is not on any treatment for this and has had a tubal ligation. BMI is 35.

How would you evaluate this patient?
Evaluation?

- Detailed history of physical exam
- TSH, prolactin, CBC, FSH, hCG
- +/- Androgens, AMH
- Pelvic ultrasound

What is the sensitivity of EMBx at detecting cancer? 😊

What is your criteria for an endometrial biopsy? 😊
Endometrial Biopsy

- EM Bx is 95-99% sensitive in diagnosing cancer

- However, it misses 50% of other benign diagnosis
  
  - If medical management fails with a negative EMBx further investigation for structural lesions is warranted either by Hysteroscopy or SIS.
  
  - EMBx should not be considered an end-point if the test is negative and there is persistant AUB.
Criteria for EMBx

- 45 years old or older

- If <45 and:
  - PCO/obese. Prolonged anovulation
  - Failed medical Management
  - Persistent AUB
  - History of unopposed estrogen
  - >30 BMI
  - Genetic risk factors
Case 4

38 yo G4P4 presents for chronic heavy menstrual bleeding. 6 days of flow with 2-4 day requiring 18 pads/day. She has been told in the past that she is anemic. She has tried COC for 5 months with minimal improvement. You do a complete history, physical exam and evaluation (labs, pelvic US, EMBx) and determine she is a good candidate for endometrial ablation. The patient elects for ablation.

- How do you counsel her regarding the procedure? (risks, benefits, failure, expectations, fertility etc)
- What are the contraindications to ablation?
- Which ablation device do you use and why?
Patients are more satisfied with resectoscope ablation vs medical mgt at 5 years (Cooper et al, 2001)

Patients were equally satisfied (QOL measures) with levonorgestrel IUD vs endometrial ablation at 1 year.

Hysterectomy rates are around 24% at 4 years after ablation

10% risk of postablation TL syndrome

Contraindications – recent pregnancy, recent infection, cancer, hyperplasia, possibly prior uterine surgery, mullerian anomalies.
<table>
<thead>
<tr>
<th>Method</th>
<th>Pretreatment</th>
<th>Outside Diameter (mm)</th>
<th>Approximate Treatment Time (min)</th>
<th>*Sounded Uterine Length (cm) Minimum</th>
<th>Maximum</th>
<th>Published Evidence</th>
<th>Type</th>
<th>Diameter (cm)</th>
<th>U.S. Food and Drug Administration Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>ThermaChoice (thermal balloon)</td>
<td>Mechanical (suction aspiration)</td>
<td>5.5</td>
<td>8</td>
<td>4</td>
<td>10</td>
<td>Yes (Level I)</td>
<td>II</td>
<td>Smaller than or equal to 3</td>
<td>No</td>
</tr>
<tr>
<td>Her Option (cryotherapy)</td>
<td>Gonadotropin-releasing hormone agonist</td>
<td>4.5</td>
<td>10–18</td>
<td>Not specified</td>
<td>10</td>
<td>None</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>No</td>
</tr>
<tr>
<td>HydroThermAblator (heated free fluid)</td>
<td>Gonadotropin-releasing hormone agonist</td>
<td>7.8</td>
<td>14</td>
<td>4</td>
<td>10.5</td>
<td>Yes (Level II-3)</td>
<td>I†, II</td>
<td>Not specified</td>
<td>No</td>
</tr>
<tr>
<td>Microwave Endometrial Ablation System (microwave energy)</td>
<td>Gonadotropin-releasing hormone agonist</td>
<td>8.5</td>
<td>2.5–4.5</td>
<td>6</td>
<td>14</td>
<td>Yes (Level I)</td>
<td>I†, II</td>
<td>Smaller than or equal to 3†</td>
<td>Yes</td>
</tr>
<tr>
<td>NovaSure (radiofrequency electricity)</td>
<td>None</td>
<td>7.2</td>
<td>1–2</td>
<td>6</td>
<td>10</td>
<td>Yes (Level II-2)</td>
<td>I, II</td>
<td>Smaller than or equal to 3</td>
<td>No</td>
</tr>
</tbody>
</table>

*Data adapted from U.S. Food and Drug Administration.
# Ablation

## Table

<table>
<thead>
<tr>
<th>Device</th>
<th>Satisfaction Rate</th>
<th>Amenorrhea Rate$^{†}$</th>
<th>Diary Success (Score: 75 or Less$^‡$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ThermaChoice (thermal balloon)</td>
<td>96/99$^{‡}$</td>
<td>13.2/27.2</td>
<td>80.2/84.3</td>
</tr>
<tr>
<td>Hydro ThermAblator (heated free fluid)</td>
<td>35.3/47.1</td>
<td>68.4/76.4</td>
<td></td>
</tr>
<tr>
<td>Her Option (cryotherapy)</td>
<td>86/88$^{¶}$</td>
<td>22.2/46.5</td>
<td>67.4/73.3</td>
</tr>
<tr>
<td>NovaSure (radiofrequency electricity)</td>
<td>92/93$^{‡}$</td>
<td>36/32.2</td>
<td>77.7/74.4</td>
</tr>
<tr>
<td>Microwave Endometrial Ablation System</td>
<td>92/93$^{‡}$</td>
<td>55.3/45.8</td>
<td>87/83.2</td>
</tr>
</tbody>
</table>

*Based on U.S. Food and Drug Administration pivotal trials.

$^{†}$Based on intent to treat.

$^{‡}$Patients reported being satisfied or very satisfied.
Overview

- Etiology varies depending on Life Cycle
- Don’t ignore coagulopathies
- Don’t forget to screen for pregnancy
- Know treatment options for acute bleed
- Know when to do an EMBx
References

- ACOG PB 136
- ACOG CO 557
- Munro, MG, et al, FIGO Classification System (PALM-COEIN) for causes of AUB in non gravid women of reproductive age. Int J Gynaecol Obstet 2011; 113:3-13