Managing Abnormal Vaginal Bleeding (AVB)

Vaginal Bleeding...What’s Normal?

- Onset of menses
  - By 16 years old with 2° sex characteristics
  - Start evaluation at 14 years of age if no sexual development
- Cycle length: 24-35 days
- Menstrual days: 2-7 days
- Menstrual flow: 20-80 cc. per menses
  - Average flow: 35 cc. per menses

Abnormal Vaginal Bleeding (AVB) Symptom Definitions

- Abnormal amount of bleeding
  - Menorrhagia (hypermennorrhea)
    - Prolonged duration of menses
    - Increased amount of bleeding per day
  - Hypomenorrhoea
    - Shorter menses
    - Less flow per day

Abnormal Vaginal Bleeding Symptom Definitions

- Abnormal timing of bleeding: REGULAR Cycles
  - Polymenorrhoea: cycle length < 24 days
  - Intermenstrual bleeding: (IMB)
  - Post-coital bleeding (PCB)

- Abnormal timing of bleeding: IRREGULAR Cycles
  - Metrorrhagia
    - Light “irregularly irregular” bleeding
  - Menometrorrhagia
    - Heavy “irregularly irregular” bleeding
  - Post-menopausal: bleeding >1 year after menopause

There are no relevant financial relationships with any commercial interests to disclose.
### Abnormal Vaginal Bleeding Symptom Definitions

- **Decreased frequency** of bleeding
  - Oligomenorrhea
    - No bleeding 36 days - 3 months
  - Amenorrhea
    - No bleeding for...
      - 3 cycle intervals or
      - 6 months (in oligomenorrheic women)

### Abnormal Vaginal Bleeding

- Is the patient pregnant?
- Is it uterine?
- Is the bleeding pattern ovulatory or anovulatory?

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<th>Ovulatory = Regular</th>
<th>Anovulatory = Irregular or no bleeding</th>
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### Non-Uterine Conditions: Cervix

- **Cervix Neoplasms**: IMB, PCB, PMB
  - Squamous cell carcinoma
  - Adenocarcinoma
- **Infections**: IMB, PCB, menorrhagia
  - Mucopurulent cervicitis (chlamydia, gonorrhea, mycoplasma hominis)
- **Benign cervical ectropion**: PCB
  - Exposed columnar epithelial cells on ectocervix
  - Red appearance; bleeds to touch

### Non-Uterine Conditions: Vagina

- **Vaginal inflammation** (IMB, PCB, PMB)
  - Atrophic vaginitis
  - Severe vaginal trichomoniasis
- **Trauma/ foreign body**
  - Vaginal wall laceration (PCB)
  - Hymeneal ring tear/laceration (PCB)
  - Vaginal foreign body (esp. pre-menarchal bleeding)
- **Vaginal neoplasms**
  - Squamous cell cancer
  - Childhood tumors

### Non-Uterine Conditions: Other

- **Urethra (post-void bleeding)**
  - Urethral caruncle
  - Squamous or transitional cell cancer
- **Anus (bleeding after wiping)**
  - External or internal hemorrhoid
  - Anal fissure
  - Genital warts
  - Squamous cell cancer
Hx, PE, Pregnancy test

Preg test POS

Preg test NEG

Pelvic Exam

Abnormal uterine bleeding

Non-uterine bleeding

Cervix

Vagina

Urethra

Anus

Structural (PALM)

Non-structural (COEIN)

Abnormal Vaginal Bleeding: Standard Definitions

FIGO System for AUB, 2011

Structural

Non-Structural

Polyp

Adenomyosis

Leiomyoma

Malignancy & hyperplasia

Submucosal

Endometrial

Endometrial

Not yet classified

Munro MG, et al, FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age, Int J Gynecol Obstet (2011)

AUB: Structural Conditions

• P: Endometrial polyp
  – IMB or PCB in 30-50 year old woman

• A: Adenomyosis
  – Dysmenorrhea, dyspareunia, chronic pelvic pain, sometimes menorrhagia

• L: Leiomyoma
  – Submucous myoma
  – Menorrhagia; rarely IMB; never metrorrhagia

AUB: Structural Conditions

• M: Malignancy and hyperplasia
  – Adenomatous hyperplasia (AH) → atypical AH → endometrial carcinoma
    – Post-menopausal bleeding
    – Recurrent perimenopausal metrorrhagia
    – Chronic anovulator (PCOS) with metrorrhagia
  – Leiomyosarcoma
  – Post-menopausal bleeding

COEIN: Coagulopathy

• Clotting factor deficiency or defect
  – Liver disease
  – Congenital (Von Willebrands Disease)

• Platelet deficiency (thrombocytopenia) with platelet count <20,000/mm³
  – Idiopathic thrombocytopenic purpura (ITP)
  – Aplastic anemia

• Platelet function defects

COEIN: Coagulopathy

Screen for underlying disorder of hemostasis if any of

• Heavy menstrual bleeding since menarche
• One of the following
  – Post-partum hemorrhage
  – Bleeding associated with surgery
  – Bleeding associated with dental work
• Two or more of the following
  – Bruising 1-2 times per month
  – Epistaxis 1-2 times per month
  – Frequent gum bleeding
  – Family history of bleeding symptoms

Munro M, Int J Gynecol Obstet (2011)
**COEIN: Ovulatory**

- Anovulation
  - Age: peri-menarche and perimenopause
  - PCOS
  - Stress
- Hypothyroidism
- Luteal phase defects

**Normal Ovarian Hormone Cycle**

- Precipitous drop of E+P
  - Synchronous
  - Universal
  - Withdrawal Bleed

**Abnormal Ovarian Hormone Cycles**

- Menometrorrhagia: heavy, irregular bleeding

**COEIN: Ovulatory**

- Mainly due to anovulatory bleeding
  - Age-related: peri-menarche, perimenopause
  - Estrogenic: unopposed exogenous or endogenous estrogen
  - Androgenic: PCOS; CAH, acute stress
  - Systemic: Renal disease, liver disease
- Diagnosis of exclusion
  - Menometrorrhagia not due to by anatomic lesion, medications, pregnancy

**COEIN: Ovulatory**

- Hyperthyroidism or hypothyroidism
  - Bleeding can be excessive, light, or irregular
  - Only severe, uncorrected thyroid disease causes abnormal bleeding patterns
  - Normal pattern when corrected to euthyroid
  - 1st hypothyroidism assoc. with 2nd amenorrhea

  | Low T4 → high TRH → high TSH → normal T4 |
  | High PRL → amenorrhea + galactorrhea |

- Luteal Phase Defect (LPD)
  - Luteal phase lasts 7-10 days (vs. 14 days) or inadequate peak luteal phase progesterone (P)
- Diagnosis
  - Poly-menorrhea (“periods every 2 weeks”)
  - Mid-luteal phase P level between 4-8 ng/ml
  - Endometrial biopsy >2 days out of phase
- Management
  - Unexplained infertility: clomiphene, P supplement
  - Pregnancy not desired: observation or OCs to cycle
**COEIN: Endometrial**
- Idiopathic
  - Unexplained menorrhagia
- Endometritis
  - Post-partum
  - Post-abortal endometritis
  - Endometritis component of PID
- In teens, PID commonly presents with abnormal bleeding (menorrhagia, IMB), not pelvic pain
  - Any teen with abnormal bleeding + pelvic pain requires bimanual exam to evaluate for PID

**COEIN: Iatrogenic Conditions**
- Anticoagulants
  - Over-anticoagulation: menorrhagia
  - Therapeutic levels will not cause bleeding problems
- Chronic steroids, opiates
- Progestin-containing contraceptives
- Intrauterine Contraception (IUC)
  - "Normal" side effect menorrhagia
  - PID, pregnancy (IUP or ectopic), perforation, expulsion

**COEIN: Not Classified**
- Chronic endometritis
- AVM
- Myometrial hypertrophy

**AVB: History**
- Is the patient pregnant?
  - Pregnancy symptoms, esp. breast tenderness
  - Intercourse pattern
  - Contraceptive use
- Is it uterine?
  - Coincidence with bowel movement and wiping, during or after urination
  - Pain or irritation of vagina, introitus, vulva, perineum, or anal skin

**AVB: History**
- Is bleeding ovulatory or anovulatory?
  - Bleeding pattern: regular, irregular, none
  - Menstrual symptoms: only in ovulatory cycles
  - Previous history of menstrual disorders
  - Recent onset weight gain or hirsutism
  - Menopausal symptoms
  - History of excess bleeding; coagulation disorders
  - Current and past medications; street drugs
  - Chronic medical illnesses or conditions
  - Nipple discharge from breasts

**AVB: Physical Exam**
- General: BMI ≥ 30
- Skin: acne, hirsutism, acanthosis nigricans; bruising
- Breasts: galactorrhea
- Abdomen: uterine enlargement, abdominal pain
- Pelvic exam
  - Vulva and perineum
  - Anal and peri-anal skin
  - Speculum: vaginal walls and cervix
  - Bimanual: uterine enlargement, softness, masses
**AVB: Laboratory**

- Urine highly sensitive pregnancy test
  - *Quantitative B-hCG is unnecessary*
- CBC
  - Find severe anemia; baseline value for observation
  - Platelet estimation (detect thrombocytopenia)
- TSH, Prolactin
  - Amenorrhea or recurrent anovulatory bleeds only
- FSH, LH levels are unnecessary

**AVB: Imaging Studies**

- Mainly for evaluation of ovulatory AUB if no response to treatment or suspect anatomic defect
- Not useful for demonstrating or excluding hyperplasia in premenopausal women
- Saline infusion sonogram (SIS) helpful for polyps, sub-mucus myomata
  - 80% sensitivity, 69% specificity compared to hysteroscopy

**Who Needs an EMB?**

- Purpose: detect endometrial hyperplasia or cancer
- Premenopausal women
  - Prolonged metrorrhagia
  - Unexplained post-coital or intermenstrual bleeding
  - Endometrial cells on Pap smear in anovulatory premenopausal woman
  - Abnormal glandular cells (AGC) Pap
    - Abnormal endometrial cells
    - Older than 35 years old
    - < 35 years old with abnormal bleeding
- Older than 35 years old with abnormal bleeding

**Who Needs an EMB?**

- Menopausal woman
  - Any postmenopausal bleeding, if not using HT
  - Unscheduled bleeding on continuous-sequential hormone therapy
  - Bleeding > 3 mo after start of continuous-combined hormone therapy
  - Endometrial stripe ≥ 5 mm (applies to postmenopausal woman only)
  - Pap smear: any endometrial cells or AGC Pap

**Tips for Internal Os Stenosis**

- Pain relief
  - Use para-cervical or intra-cervical block
  - Intruterine instillation of lidocaine
- Cervical dilation
  - Grasp sampler with sponge forceps 3-4 cm from tip
  - Freeze endometrial sampler to increase rigidity
  - Use cervical “os finder” device
  - Use small size Pratt or Hegar dilators
  - No studies to support misoprostol; not helpful for IUCs
**EMB Result: Non-Neoplastic**
- Proliferative: E-induced growth, but no ovulation
- Secretory: ovulatory or recent progestin exposure
- Menstrual: glandular breakdown, non-neoplastic
- Disordered: out-of-phase glands (often anovulation)
- Chronic endometritis/inflammation: plasma cells + wbc
- Atrophic: hypoplastic glands and stroma
- Cystic hyperplasia: hypoplastic glands and stroma
- Insufficient: not enough tissue for interpretation
  - If adequate sampling, atrophic endometrium likely
  - If sounding <5 cm, may not have entered cavity

**EMB Result: Neoplasms**
- Endometrial polyp
- Simple endometrial hyperplasia
  - Gland proliferation and crowding, but no atypia
  - Reversible with continuous progestin exposure
- Atypical endometrial hyperplasia
  - Hyperplasia with nuclear atypia of gland cells
  - Premalignant; often not reversible with progestin
- Endometrial carcinoma
  - Stromal invasion of malignant glands

**Management Based on EMB Results**
- Atrophic vaginitis: topical estrogen
- Chronic endometritis: + antibiotics
- Polyp: observe or hysteroscopic excision
  - Depends upon size, persistent bleeding symptoms
- Cystic hyperplasia or endometrial atrophy
  - Observe or very low estrogen dose CC-EPT
- Simple endometrial hyperplasia
  - Continuous high dose progestin; re-biopsy in 4 mos
- Atypical endometrial hyperplasia
  - Endometrial cancer: hysterectomy + XRT

**AVB: Presentation-based Management**
- Acute dysfunctional (anovulatory) bleeding
- Recurrent dysfunctional bleeding
- Post-coital bleeding
- Recurrent (ovulatory) menorrhagia
- Postmenopausal bleeding (PMB)

*Note: a menstrual calendar will help to differentiate these conditions*

**Management of Acute DUB**
- Substitute a pharmacologic luteal phase for missed physiologic luteal phase
- If minimal bleeding for a few days
  - Rx MPA 10-20 mg QD (or microP, 200 BID) x10d
  - Bleeding stops < 3 d; menses after progestin ended
- Moderate or heavy bleeding > 3 days
  - Monophasic OC taken BID-TID x 7 days, then daily OC for 3 weeks (or longer)
  - Using “OC taper” and then stopping is illogical
- Torrential bleed: surgical curettage (MUA)

**Mechanism of “Chemical Curettage”**
- High dose OCs x 7 days
  - E stabilizes EM
  - P matures EM
- Estrogen
- Progesterone
- OCs
- Anovulation
Recurrent Menorrhagia

• Submucous myoma (fibroids)
  – Medical: OCs, progestins, tranexamic acid
  – LNG-IUS (Mirena)
  – Myomectomy
    • Laparoscopy, hysteroscopy, or laparotomy
  – Uterine artery embolization (UAE)
  – GnRH-a (Lupron) is given for 1-3 months only
    • To facilitate surgery by reducing myoma volume
    • To induce amenorrhea to treat severe anemia

LNG-IUS and Fibroids

• Small studies with mixed results
  – Mercorio (2003): 75% persistent menorrhagia
  – Starczewski (2000): 92% reduced bleeding

• Recommendations
  – Off-label use; may violate precaution regarding cavity depth and distortion of uterine cavity
  – Reasonable to attempt treatment with Mirena
  – Documentation of informed consent content a must

Tips for IUC Insertion in Women with Fibroids

• Determine fibroid location by ultrasound
  – Fundal fibroids (intramural, sub-serous) that do not distort uterine cavity do not preclude IUC use
  – Large sub-mucous fibroids, especially in lower uterine segment, contraindicate IUC use
  – Evaluate for other pathology, e.g., polyp
• Ultrasound guidance may facilitate safe placement

Recurrent Menorrhagia

• Idiopathic menorrhagia
  – Oral contraceptives (extended regimen or cycle)
  – NSAIDS (before and during menses)
    • Ibuprofen (400 mg tid), naproxen Na (275 mg every 6 hours after a loading dose of 550 mg)
  – LNG intrauterine system (Mirena)
  – Tranexamic acid (Lysteda)
  – Endometrial ablation
  – Hysterectomy (VH, LAVH, LASH)

Tranexamic Acid (Lysteda) for HMB

• FDA: treatment of cyclic heavy menstrual bleeding
• Mechanism of action is antifibrinolytic
• Use: 1,300 mg (two 650 mg tablets) TID for up to 5 days
• Contraindications
  – Active thromboembolic disease
  – History or intrinsic risk of DVT
• Cautions
  – Concomitant therapy with OCs may further increase the risk of blood clots, stroke, or MI
  – Women using CHC should use only if a strong medical need and benefit outweighs risk of TE event

Global Endometrial Ablation

• Bipolar Dessication (NovaSure™)
• Cryoablation (Her Option™)
• Thermal Balloon (Thermachoice ™, Cavitur™)
• Microwave Endometrial Ablation (Microsulis)
• Hydrothermal Ablation (Hydro ThermAblator ™)
• Radiofrequency Thermal Balloon
Endometrial Ablation vs Hysterectomy

• **Advantages**
  – Office procedure or outpatient surgery
  – Very low rate of major complications
  – Rapid post operative recovery period
  – Less time consuming and costly vs hysterectomy

• **Disadvantages**
  – Amenorrhea in 50-70%, but >95% have less bleeding
  – May fail over time: 2nd ablation required in 5-10%
  – Reduces fertility, but not highly effective contraception
  – Cervical, endometrial cancer may occur

References

• Munro MG, Critchley HO, Fraser IS; FIGO Menstrual Disorders Working Group. The FIGO classification of causes of abnormal uterine bleeding in the reproductive years. Fertil Steril. 2011;95(7):2204-8

References

• Pitkin J. Dysfunctional uterine bleeding. BMJ 2007;334:1110