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Evaluation of Abnormal Uterine Bleeding...The New Name of the Game

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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 (hypermenorrhea)
    - Prolonged duration of menses
    - Increased amount of bleeding per day
  - Hypomenorrhea
    - Shorter menses
    - Less flow per day

Abnormal Vaginal Bleeding Symptom Definitions
- Abnormal timing of bleeding: REGULAR Cycles
  - Polymenorrhea: cycle length < 24 days
  - Intermenstrual bleeding (IMB)
    - 7 days
  - Post-coital bleeding (PCB)
    - 7 days
Abnormal Vaginal Bleeding
Symptom Definitions

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

- 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 (AVB)

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

**Ovulatory = Regular**
- Menorrhagia
- Hypomenorrhoea
- Polymenorrhagia
- IMB
- PCB

**Anovulatory = Irregular or no bleeding**
- Metrorrhagia/ MMR
- Oligomenorrhea
- Amenorrhea
- Post-menopausal

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, clear cell (DES)
  - 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

Non-uterine bleeding: AUB, FIGO System 2011

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

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

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

Abnormal Ovarian Hormone Cycles

- 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

  \[
  \text{Low } T_4 \rightarrow \text{high TRH} \rightarrow \text{high TSH} \rightarrow \text{normal } T_4
  \]

  \[
  \text{high PRL} \rightarrow \text{amenorrhea + galactorrhea}
  \]

- Luteal Phase Defect (LPD)
  - Luteal phase lasts 7-10 days (vs. 14 days) or inadequate peak luteal phase progesterone (P)

  \[
  \text{Diagnosis}
  \]

  - Polymenorrhea (“periods every 2 weeks”)
  - Mid-luteal phase P level between 4-8 ng/ml
  - Endometrial biopsy >2 days out of phase

  \[
  \text{Management}
  \]

  - 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
  - Molimenal 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
- Disorders of hemostasis, as indicated
  - PT, PTT, aPTT, fibrinogen; Von Willebrand w/u

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
- 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

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Tips for Internal Os Stenosis

- Pain relief
  - Use para-cervical or intra-cervical block
  - Intrauterine 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
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, submucous myomata
  - 80% sensitivity, 69% specificity compared to hysteroscopy

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) x 10d
  - 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)

Oral MPA and COCs for Acute Uterine Bleeding

Munro MG, et al Obstet Gynecol 2006;108:924-9

- 40 women with non-anatomic AUB randomized to
  - MPA 20 mg TID x 1 week, then QD for 3 weeks vs.
  - COC (1 mg nor + 35 mcg EE) TID x 1 week, QD x 3 weeks
- Results
  - Median time to bleeding cessation was 3 days
  - Cessation in 88% OC group, 76% in MPA group
  - Surgery avoided in 100% MPA, 95% COC subjects
  - Compliance similar in both groups
  - “Would use again”...81% MPA, 69% COC

Management of Recurrent DUB

- Pregnancy: cycle with clomiphene or metformin
- Contraception: cycle with OC
- Not interested in pregnancy or contraception
  - MPA or microP first 10-14 days each month or every other month if pt prefers fewer menses
  - Place LNG-IUS (Mirena)
  - Consider endometrial ablation if childbearing completed
- Perimenopausal bleeding
  - Once hyperplasia excluded, the goal is cycle control
    - Low estrogen dose OC
    - Cyclic sequential EPT
**Post-coital Bleeding (PCB) Differential Diagnosis**

- **Anatomic**
  - Fragile (friable) ectropion
  - Urethral lesion
- **Infections**
  - Endocervix: GC, Ct, Ureaplasma, M genitalium
  - Cervical or vaginal warts
  - Endometritis (acute or chronic)
- **Neoplastic**
  - Endocervical or endometrial polyp
  - Vaginal, cervical, endocervical, or endometrial invasive cancer (not VaIN, CIN)

**Post-coital Bleeding: Evaluation**

- **Vaginal Exam**
  - Epithelial lesions; foreign body; urethral lesion
- **Cervical Exam**
  - Ectropion, cervical leukoplakia or warts, cervical mucopus, endocervical polyp
- **Cervical tests**
  - GC/Ct test, Pap (if not performed recently)
  - Endocervical curettage (ECC), as Pap is often falsely negative in women with endocervical adenocarcinoma
- **If all negative, SIS to evaluate endometrial polyp**

**Post-coital Bleeding: Treatment**

- **Endocervicitis**
  - GC, Ct: treat with cefixime, azithromycin
  - If Ureaplasma or Mycoplasma suspected, treat with doxycycline for 7 days or azithromycin 1 gm
- **Cervical or vaginal warts**
  - After biopsy, cryotherapy or 5-FU cream
- **Fragile ectropion**
  - After infection and CIN excluded, cryotherapy
- **Endometritis**
  - Doxycycline 100 mg PO BID x 14 days

**Recurrent Menorrhagia**

- **Differential diagnosis**
  - Endometrial polyp
  - Submucous myoma
  - Coagulopathy: vWD, ITP, liver disease
  - Idiopathic
- **Diagnostic**
  - Coag panel: consult with hematologist
  - Saline Infusion Sonography (SIS)
  - Hysteroscopy
  - NOT endometrial biopsy or pelvic US alone

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