Vaginitis and Abnormal Vaginal Bleeding

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• There are no relevant financial relationships with any commercial interests to disclose
## Vulvovaginal Symptoms: Differential Diagnosis

<table>
<thead>
<tr>
<th>Category</th>
<th>Condition</th>
<th>(VT)</th>
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<tbody>
<tr>
<td>Infections</td>
<td>Vaginal trichomoniasis</td>
<td>VT</td>
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<tr>
<td></td>
<td>Bacterial vaginosis</td>
<td>BV</td>
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<tr>
<td></td>
<td>Vulvovaginal candidiasis</td>
<td>VVC</td>
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<tr>
<td></td>
<td>Fungal vulvitis (candida, tinea)</td>
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<tr>
<td>Skin Conditions</td>
<td>Contact dermatitis (irritant, allergic)</td>
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<td></td>
<td>Vulvar dermatoses (LS, LP, LSC)</td>
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<td></td>
<td>Vulvar intraepithelial neoplasia (VIN)</td>
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<tr>
<td>Psychogenic</td>
<td>Physiologic, psychogenic</td>
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CDC 2015: Trichomoniasis Screening and Testing

• Screening indications
  – HIV positive women: annually
  – Consider if “at risk”: new/multiple sex partners, history of STI, inconsistent condom use, sex work, IDU

• Newer assays
  – Rapid antigen test: ↑ sensitivity, specificity vs. wet mount
  – Aptima TMA T. vaginalis Analyte Specific Reagent (ASR)

• Other testing situations
  – Suspect trich but NaCl slide neg → newer assays or culture
  – Pap with trich → confirm if low risk

• Consider retesting 3 months after treatment
Trichomoniasis Treatment

• Recommended regimen
  – Metronidazole 2 g PO x 1 dose
  – Tinidazole 2 g PO x 1 dose

• Alternative regimen
• Women with HIV infection
  – Metronidazole 500 mg PO BID x 7d

• Recommended regimen in pregnancy
  – Metronidazole 2 g PO x 1 dose (all trimesters)
  – Tinidazole is a Category C drug in pregnancy

• Treat sex partner(s)
• Targeted screening for other STIs: GC, Ct, syphilis, HIV
Trichomoniasis: Treatment Failure

First treatment failure, re-treat with

- Metronidazole 500 mg PO BID x 7 days

If repeat failure, treat with

- Metronidazole 2 g PO x 5 days
- Tinidazole 2 g PO x 5 days

Susceptibility testing: send isolate to CDC: 404-718-4141
BV: Pathophysiology

- Non-inflammatory bacterial overgrowth
  - 100 x increase *Gardnerella vaginalis*
  - 1000 x increase in anaerobes
  - More pathogen types (*Mobiluncus*, *Mycoplasmas*)
- Suppression of H$_2$O$_2$-producing *Lactobacillus crispatus* and *L. jensenii* (*L. acidophilus* is not present)
- >50% carry *G. vaginalis* in vaginal flora in absence of BV
  - Bacterial “C/S” of vaginal fluid doesn’t help in the diagnosis of BV….or of any other vaginal infection
BV: Sexually Associated or Transmitted?

• “Sexually associated” in heterosexuals
  – Rare in virginal women
  – Greater risk of BV with multiple male partners
  – Condom use decreases risk

  **But**
  – No BV carrier state identified in men
  – Treatment of partner does not affect recurrences

• Women having sex with women (WSW)
  – Infected vaginal fluid between women causes BV
  – Studies of concurrence in lesbian couples suggest horizontal transmission
BV: Clinical Diagnosis

- **Amsel Criteria**: 3 or more of
  - Homogenous white discharge
  - Amine odor ("whiff" test)
  - pH $\geq 4.5$ (most sensitive)
  - Clue cells $\geq 20\%$ (most specific)

- **Spiegel criteria, Nugent score**: Gram stain with
  - Few or no gram positive *Lactobacillus spp.*
  - Excess of other gram negative morphotypes
Who Should Be Tested for BV?

- **Routine screening** (asymptomatic): not indicated
- **Standard diagnostic testing**
  - Check discharge, amines, vaginal pH, clue cells
- **Microscopy not available or inconclusive**
  - Affirm VP III
  - OSOM BV Blue
  - *G vaginalis* PIP, pH + amine test cards
- “Shift in vaginal flora” on cervical cytology
  - No consensus, but poor correlation with BV...most experts recommend no further follow up
**Recommended regimens**

- Metronidazole 500 mg PO BID x 7 days
- Metronidazole gel 0.75% 5g per vagina QD x 5 days
- Clindamycin 2% cream 5g per vagina QHS x 7 days

**Alternative regimens**

- Tinidazole 2 g PO QD for 3 days
- Tinidazole 1 g PO QD for 5 days
- Clindamycin 300 mg PO BID x 7 days
- Clindamycin ovules 100 mg per vagina QHS x 3 days
CDC 2015: Recurrent BV

- Consider suppression with metronidazole vaginal gel twice weekly for 4-6 months (after full initial treatment)
- No evidence yet to support use of probiotics
- Don’t douche...with anything!
- Use of condoms by male partners may reduce recurrences
- Clean sex toys (or use condoms) between uses
- Avoid vaginal insertion after anal insertion of a finger or penis
CDC 2015: VVC Classification

- **Uncomplicated VVC (80-90%)**
  - Sporadic or infrequent VVC, and
  - Mild-to-moderate VVC, and
  - Likely to be *Candida albicans*, and
  - Immunocompetent

- **Complicated VVC (10-20%)**
  - Recurrent VVC, or
  - Severe VVC, or
  - Non-albicans candidiasis, or
  - Uncontrolled DM, immunosuppression, pregnancy
VVC: Laboratory

- KOH suspension
  - *C. albicans*: pseudohyphae and blastospores (buds)
  - *C. glabrata*: blastospores only
- NaCl suspension: many WBC, normal lactobacillus
- pH: 4-6
- Amine test: negative
- Confirmatory tests
  - Point of care test: Affirm VP III
  - Candida culture (*not*: fungus culture)
  - Candida PCR
### Treatments for VVC

<table>
<thead>
<tr>
<th>Drug</th>
<th>OTC</th>
<th>Prescription</th>
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<tbody>
<tr>
<td><strong>Length of Treatment</strong></td>
<td><strong>7 d</strong></td>
<td><strong>3 d</strong></td>
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<tr>
<td>Butoconazole</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Clotrimazole</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Miconazole</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Terconazole</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Tioconazole</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Fluconazole (PO)</td>
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</table>
Uncomplicated VVC Treatments

- **Non-pregnant women**
  - 3 and 7 day topicals have equal efficacy and price
  - Offer *either*: 1 or 3 day topical *or* oral fluconazole
    - Topical: quickly soothing, but inconvenient
    - Oral: convenient, but effect is not immediate

- **If first treatment course fails**
  - Re-confirm diagnosis (*r/o* dual infection)
  - Treat with an alternate antifungal drug
  - Perform Candida *culture* to confirm and speciate

- **No role for nystatin, candididin**
Complicated VVC Treatment

Severe VVC
- Advanced findings: erythema, excoriation, fissures
- Topical azole therapy for 7-14 days, or

Compromised host
- Topical azole treatment for 7-14 days
- Fluconazole 150 mg PO; repeat Q3 days 1-2 times

Pregnancy
- Topical azoles for 7 days
Complicated VVC Treatment

Recurrent VVC (RVVC)

- > 4 episodes of symptomatic VVC per year
- Most women have no predisposing condition
  - Partners are rarely source of infection
- Confirm with *Candidal* culture before maintenance therapy; also checks for non-albicans species
- Early treatment regimen: self-medication 3 days with onset of symptoms
Complicated VVC Treatment

- Recurrent VVC: Treatment
  - Treat for 7-14 days of topical therapy or fluconazole 150 mg PO q 72° x3 doses, then
  - Maintenance therapy x 6 months
    - Fluconazole 100-200 mg PO 1-2 per week
    - Itraconazole 100 mg/wk or 400 mg/month
    - Clotrimazole 500 mg suppos 1 per week
    - Boric acid 600 mg suppos QD x14, then BIW
    - Gentian violet: Q week x2, Q month X 3-6 mo
Vaginal Bleeding...What’s Normal?

- **Onset of menses**
  - By 16 years old *with* $2^\circ$ 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 (hypermenorrhorea)
    - Prolonged duration of menses
    - Increased amount of bleeding per day
  - Hypomenorrhrea
    - 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)
  - Post-coital bleeding (PCB)
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
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 (AVB)

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

**Ovulatory = Regular**
- Menorrhagia
- Hypomenorrhea
- Polymenorrhea
- IMB
- PCB

**Anovulatory = Irregular or no bleeding**
- Metrorrhagia/ MMR
- Oligomenorrhea
- Amenorrhea
- Post-menopausal
Hx, PE, Preg test

Preg test POS
- Pregnant
  - Location
  - Viability
  - GA Dating

Preg test NEG
- Pelvic Exam
  - Abnl Uterine bleeding
    - Cervix
      - Cervicitis
      - Ectropion
      - Cancer
    - Vagina
      - Inflam’n
      - Trauma
      - Neoplasm
    - Urethra
      - Caruncle
      - Cancer
    - Anus
      - Hemorr’d
      - Fissure
      - Cancer
  - Non-uterine bleeding
Hx, PE, Preg test

Preg test POS
- Pregnant
  - Location
  - Viability
  - GA Dating

Preg test NEG
- Pelvic Exam
  - Abnormal Uterine Bleeding
    - Structural (PALM)
    - Non-structural (COEIN)
  - Non-uterine bleeding
    - Cervix
    - Vagina
    - Urethra
    - Anus
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
- Hypothyroidism
- Luteal phase defects
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
Normal Ovarian Hormone Cycle

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

Estrogen

Progesterone

ovulation menses
Abnormal Ovarian Hormone Cycles

- Estrogen
- Progesterone

- Amenorrhea
- E withdrawal bleed
- Menometrorrhagia: heavy, irregular bleeding
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

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

\[ \downarrow \]

\[ \text{high PRL} \rightarrow \text{amenorrhea + galactorrhea} \]
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, perinuem, 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 hirsuitism
  - 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*
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
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
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, submucus 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) 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)
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, then QD for 3 weeks vs
  - COC (1 mg nor + 35 mcg EE) TID x1 week, QD x3 wks

- 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, Liletta, etc)
  – Consider endometrial ablation if childbearing completed
• Perimenopausal bleeding
  – Once hyperplasia excluded, the goal is cycle control
    • Low estrogen dose OC
    • Cyclic sequential EPT
Recurrent Menorrhagia

• Differential diagnosis
  – Endometrial polyp
  – Submucus 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
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)
References

