VAGINITIS!

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* No commercial disclosures or conflicts of interest

Objectives

• Review normal vaginal ecosystem
• Review three main causes of vaginitis, including current diagnostics, treatment, and management of recurrences
  – Bacterial vaginosis
  – Yeast vaginitis
  – Trichomoniasis

Today’s Questions

• What questions on …
  – History (symptoms)
  – Exam (signs)
  – Labs (office point of care tests)

… can we ask to rule in or rule out specific causes of vaginitis?
Background

- 3 out of 4 women have some type of vaginitis in their lifetime
- 1 of the top 7 reasons women seek health care
  - 10 million office visits annually
  - Procedures are billable!
- Diagnosis limited by:
  - Poor patient recognition
  - Poor provider-patient telephone triage
  - Poor provider office based prediction
    - Under-utilization of pH and microscopy

Normal Vaginal Ecosystem

= Mature vaginal squamous epithelium
  + Mucus
  + Normal vaginal flora

(-10⁶ bacterial colony forming units per gram of fluid)

= Clear to white, odorless, high viscosity discharge

(1-6 mL vaginal fluid per 24 hours, possibly increased at mid-cycle)

Mature Vaginal Squamous Epithelium

The epithelium is composed of:
- multiple layers of superficial cells (S)
- multiple layers of intermediate cells (I)
- several layers of parabasal cells (PB)
- a basal layer (B)
... that accumulate glycogen under the influence of estrogen stimulation

Source: Sharon Hillier, PhD
Protective Role of Mucus

- Provides lubrication
- Traps pathogens
- Delivers anti-microbial agents
- Constantly shed

What Is Normal Vaginal Flora?

Predominantly *Lactobacillus* (95%)

The other 5% …

- Streptococi sp.
- *Staphylococcus epidermidis*
- Diphtheroid sp.
- *Gardnerella vaginalis*
- *Peptostreptococci* sp.
- *Bacteroides* sp.
- *Anaerobic Lactobacillus*
- *Ureaplasma urealyticum*
- *Mycoplasma hominis*

Adapted from D. Eschenbach, MD, “Overview and Epidemiology of Vaginal Infections”, Dallas 12/06/98

Functions of Lactobacilli

- Produce hydrogen peroxide
  - viricidal, inhibits growth of many other bacteria such as *G. vaginalis*, anaerobes, *N. gonorrhoea*
- Produce lactic acid
- Resultant vaginal pH <4.5
- Produce bacteriocidin
- Interfere with bacterial adhesion to epithelial cells

Adapted from D. Eschenbach, MD, “Overview and Epidemiology of Vaginal Infections”, Dallas 12/06/98
“Normal” is not universal

- 96% of women without BV had communities dominated by L. crispatus or L. iners

220 women from the King County STD clinic: 44% white, 34% black

<table>
<thead>
<tr>
<th>A</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>L. crispatus</td>
<td>L. iners</td>
</tr>
<tr>
<td>L. jensenii</td>
<td></td>
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</tbody>
</table>


Ethnic variation

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>N</th>
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</thead>
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<tr>
<td>African American</td>
<td>960</td>
</tr>
<tr>
<td>Caucasian</td>
<td>330</td>
</tr>
</tbody>
</table>

Dairy Food Strains DON’T Colonize and Persist in the Vagina

- Three studies from US, Japan and Italy using DNA homology for identification of lactobacilli show that the most common vaginal species are L. crispatus and L. jensenii (not L. acidophilus)
- When women are followed over several months, H₂O₂-producing strains of L. crispatus and L. jensenii are the most likely to persist

Vallor et al., JID 2001

Source: Sharon Hillier, PhD
Etiologies of Vaginal Discharge

- Infectious 90%
  - Bacterial vaginosis
  - Candida species
  - *T. vaginalis*
  - Cervicitis
    - *N. gonorrhoeae*
    - *C. trachomatis*
  - HSV
  - Staph/Strep (TSS)
  - Group B streptococci

- Non-Infectious 10%
  - Cervical caps
  - Detergent spermicides
  - Retained foreign bodies
  - “Drying” agents
  - Allergies (latex, etc.)
  - Chemical (douching)
  - Fragranced
  - Liners/tampons
  - Cytolytic vaginitis
Less Common Causes of Vaginal Complaints

- GC and chlamydia
  - Association with vaginal discharge is UNCONFIRMED!
  - BUT age group <25 years has the peak incidence
- HSV
- Mycoplasma and ureaplasma?
- Chemical irritation
  - Latex
  - Semen
  - Douching
- Mechanical irritation

Vaginitis

- Bacterial vaginosis
- Yeast
- Trichomoniasis
- Menopause

- Cervicitis
- DIV
- Physiologic leukorrhea
- Vulvodynia
- Cervical cancer
- Vulvar dermatosis
- Herpes

Etiologies of Vaginitis

<table>
<thead>
<tr>
<th></th>
<th>National</th>
<th>Anderson et al.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yeast</td>
<td>20-25%</td>
<td>17-39%</td>
</tr>
<tr>
<td>BV</td>
<td>40-50%</td>
<td>22-50%</td>
</tr>
<tr>
<td>Trich</td>
<td>15-20%</td>
<td>4-35%</td>
</tr>
<tr>
<td>Undiagnosed</td>
<td>30%</td>
<td>7-72%</td>
</tr>
</tbody>
</table>

Bacterial Vaginosis

Homogeneous, white discharge

Bacterial Vaginosis

• Most frequent cause of abnormal vaginal discharge

• Prevalence estimates from 2-30% general population; 40-50% women in STD clinics
Risk Factors for BV

- More common among African American and older women
- Douching
  - Recent douching (OR=2.1), frequent douching, douching for hygiene or symptoms
- IUD: 2-fold more likely to have BV
- Two or more sex partners in previous six months
- New sex partner
- Female sex partners*
- Past history of BV*
- Others??

Sobel JD et al. Obstet Gynecol 2006; 194;1283-9
Bradshaw CS et al. JID 2006;193:1478-86

Pathogenesis

- Lack/paucity of lactobacilli (<5%)
- Ratio of anaerobes: aerobes greatly increases
  - Overgrowth of Gardnerella vaginalis, genital mycoplasmas, anaerobic GNRs, and Mobiluncus species
- Gardnerella probably necessary but not sufficient (experimental data)
  - Synergistic process with anaerobes probably responsible
- BV pts have a higher number of sialidase-producing bacteria
  - 84% of women with BV have elevated levels of sialidase activity in their vaginal fluid (Briselden et al 1992)
  - Mainly produced by Prevotella and Bacteroides spp.

BV Pathogenesis

- Flora in healthy vaginas
  - Lactobacilli (95%)
  - Other (5%)
    - Strepococci sp.
    - Staphylococcus epidermidis
    - Diphtheroid sp.
    - Gardnerella vaginalis
    - Peptostreptococci sp.
    - Bacteroides sp.
    - Anaerobic Lactobacillus
    - Ureaplasma urealyticum
    - Mycoplasma hominis

- Flora in BV
  - Gardnerella- up 17x
  - Bacteroides- up 15x
  - Peptostreptococci- up 10x
  - Mycoplasma/Ureaplasma- up 15x
  - Lactobacilli- < 5%
Bacterial vaginosis is complex

- 386 asymptomatic women
- Deep sequencing 16S rRNA gene from vaginal swab samples

Between 70-90% of women without BV have *G. vaginalis* detected in vaginal samples

Clinical Manifestations

- 50% report malodorous vaginal discharge
  - more common after unprotected vaginal intercourse and after menses
- 50% are asymptomatic:
  - may have increased discharge
  - pruritus may or may not be present

Clinical Signs

- Elevated pH >4.7
  - surrogate for reduced numbers of lactobacilli
- Clue cells
  - an indication of increased numbers of bacteria and binding of the bacteria to the epithelial cells
- Amine odor
  - an indication that high levels of anaerobic gram negative rods are present
- Homogenous discharge
  - caused by degradation of mucins by anaerobic gram negative rods
<table>
<thead>
<tr>
<th>Sensitivity &amp; Specificity of Clinical Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sensitivity</strong></td>
</tr>
<tr>
<td>Thin homogenous discharge</td>
</tr>
<tr>
<td>pH &gt; 4.5</td>
</tr>
<tr>
<td>Positive amine test</td>
</tr>
<tr>
<td>Clue cells (&gt;20%)</td>
</tr>
<tr>
<td>pH &gt; 4.5 and discharge</td>
</tr>
<tr>
<td>pH &gt; 4.5 and amine odor</td>
</tr>
<tr>
<td>pH &gt; 4.5 and clue cells</td>
</tr>
<tr>
<td>Clue cells and amine odor</td>
</tr>
<tr>
<td>Clue cells and discharge</td>
</tr>
<tr>
<td>Amine odor and discharge</td>
</tr>
<tr>
<td>Amsel criteria (&gt;3 of 4)</td>
</tr>
</tbody>
</table>


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**Wet Prep: Bacterial Vaginosis**

Saline: 40X objective

![Wet Prep Image](https://example.com/wet_prep_image.png)

Source: Seattle STD/HIV Prevention Training Center at the University of Washington

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**Bacterial Vaginosis Diagnosis: Amsel Criteria**

Amsel Criteria: Must have at least three of the following findings:

- Vaginal pH > 4.5
- Presence of >20% per HPF of "clue cells" on wet mount examination
- Positive amine or "whiff" test
- Homogeneous, non-viscous, milky-white discharge adherent to the vaginal walls
Lab Tests for Diagnosis of Bacterial Vaginosis

• Affirm VP III system (Becton-Dickinson)
  Non-amplified nucleic acid for detection of $>$10^7 CFU/g of *G. vaginalis* (*T. vaginalis* and *Candida* species).

<table>
<thead>
<tr>
<th>Clinical Criteria</th>
<th>Clue Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>97% sensitive</td>
<td>90% sensitive</td>
</tr>
<tr>
<td>71% specific</td>
<td>97% specific</td>
</tr>
</tbody>
</table>

Could be surrogate for wet mount examination of clue cells
Use in conjunction with vaginal pH and presence of amine odor (Briselden et al 1994. JCM;2:148-52)

Lab Tests for Diagnosis of Bacterial Vaginosis

• FemExam pH/amine test card (Quidel)
  – Colorimetric pH and amine test on a card

• BVBlue Test (OSOM – Genzyme – CLIA Moderate)
  – 10 minute colorimetric test requiring incubation based on detection of sialidase activity

  **Gram Stain Score:**
  91.7% sensitive
  97.8% specific

Treatment Benefits: Non-Pregnant Patients

- Relieve symptoms
- Reduce post-infection rates following hysterectomy and abortion
- May reduce STD/HIV acquisition

**THEREFORE:**
- Treat all non-pregnant women with symptoms
- Consider screening and treatment of asymptomatic women
  - prior to abortion, hysterectomy, or other invasive upper genital tract procedure

Treatment Benefits: Pregnant Patients

- Relieve symptoms
- Reduce postpartum endometritis, post C-section wound infection
- Reduce preterm labor in high-risk women?
  - 7 studies done as of 1/2012
    - 4 showed benefit, 2 no change, 1 harm- conflicting results

**THEREFORE:**
- Treat all women with symptoms

**To screen or not to screen?**

- CDC- not enough evidence
- USPSTF- not enough evidence
- Cochrane Review- evidence to support screening high risk women, then treating them with systemic therapy only

Recurrence BV

- Recurrent disease remains common
  - Rates up to 70% within 3 months
- Reasons for recurrence unclear
  - Re-infection
  - Failure of lactobacilli to re-colonize
  - Inadequate length of therapy
  - Persistence of unidentified host factor
- Despite comparable early cure rates, higher recurrence rates associated with shorter treatment
  - Single-dose 2 g metronidazole
  - 3-day clindamycin course
### Bacterial vaginosis - recurrent

**It's (probably) all about sex**

<table>
<thead>
<tr>
<th>Risk</th>
<th>Risk Factor</th>
<th># studies</th>
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<tbody>
<tr>
<td>Condom use</td>
<td>0.8*</td>
<td>43</td>
</tr>
<tr>
<td>New/multiple male partner(s)</td>
<td>1.6*</td>
<td>43</td>
</tr>
<tr>
<td>Consistent partner</td>
<td>1.91</td>
<td>2</td>
</tr>
<tr>
<td>Douching</td>
<td>1.17-1.21</td>
<td>2 (2 no)</td>
</tr>
<tr>
<td>Hormonal contraceptive use</td>
<td>0.78**</td>
<td>55</td>
</tr>
<tr>
<td>Female partner w/sx</td>
<td>HR 7.92</td>
<td>1</td>
</tr>
</tbody>
</table>

*From meta-analysis, Fethers CID 2008
**from meta-analysis, Vodstrcil PLoS One 2013

### Recurrent BV: Management

- More antibiotic is better: higher cumulative doses (longer therapy, 10-14 days) with subsequent suppression is most effective
  - Metronidazole gel, twice weekly (Sobel 2006)
  - Emerging data support the response of initial BV with higher vaginal doses of MTZ (Sanchez 2004)
- Prevent sexual transmission (condoms, no shared toys):
  - Alkaline pH of sperm (7.5) vs. reinfection? (Trabert 2007; Sanchez 2004)
- Boric acid: 7 d MTZ PO, 21 d vaginal BA (600 mg qHS) followed by MTZ vaginal gel biweekly for 16 weeks was encouraging: cure post-BA 88%-92% (Reichman 2009)

### Adherent Biofilms in Bacterial Vaginosis

*Fig. 4 in common bile duct vs. bacterial biofilm on the vaginal epithelial surface in women with recurrent bacterial vaginosis.*

*Fig. 4 in common bile duct vs. bacterial biofilm on the vaginal epithelial surface in women with recurrent bacterial vaginosis.*

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*Slide courtesy of Marrazzo, IDSA 2011*
Treatment

- **Recommended**
  - Metronidazole 500 mg PO bid x 7 days OR
  - Metrogel 0.75% 5 g intravaginally qhs x 5 days OR
  - Clindamycin cream 2% 5 g intravaginally qhs x 7 days
  - Oil-based, might weaken latex condoms and diaphragms for 5 days after use
- **Alternative**
  - Tinidazole 2 g PO qd x 2 days
  - Tinidazole 1 g PO qd x 5 days
  - Clindamycin 300 mg PO bid x 7 days OR
  - Clindamycin ovules 100 mg intravaginally qhs x 3 days
  - Oil-based, might weaken latex condoms and diaphragms for 5 days after use
- **Pregnant**
  - Same as recommended regimens for non-pregnant women
  - **Suppressive treatment:**
    - Metrogel 0.75% twice weekly for 4-6 months
    - Oral nitroimidazole course, followed by boric acid 600 mg intravaginally for 21 days and suppressive metronidazole gel for 4-6 months (limited data)

2015 CDC STD Treatment Guidelines

Treatment efficacy for BV

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Cure rate at 1 month FDA (Amsels)</th>
<th>Cure rate at 3-6 months FDA (Amsels)</th>
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</thead>
<tbody>
<tr>
<td>Metronidazole</td>
<td>500 mg po bid x 7d</td>
<td>77% (71%)</td>
<td>48-57%</td>
</tr>
<tr>
<td></td>
<td>0.75% gel qhs x 5d</td>
<td>74% (71%)</td>
<td>~50%</td>
</tr>
<tr>
<td></td>
<td>1.3% gel x 1</td>
<td>16.8% (37.2%)</td>
<td></td>
</tr>
<tr>
<td>Clindamycin</td>
<td>2% cream qhs x 7d</td>
<td>(54-77%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>300mg po bid x 7d</td>
<td>85%*</td>
<td>83%*</td>
</tr>
<tr>
<td>Tinidazole</td>
<td>1g po daily x 5d</td>
<td>36% (52%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2g po daily x3d</td>
<td>27% (35%)</td>
<td></td>
</tr>
<tr>
<td>Secnidazole</td>
<td>2g PO x 1</td>
<td>(53%)</td>
<td></td>
</tr>
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</table>

Should we treat male partners?

- Yes Treatment
- No Treatment

Purell treatment of penis also ineffective

Mehta STD 2012
**Partner Management**

- Routine treatment of male sexual partners of women with BV is not recommended
- Data from clinical trials indicate that a woman’s response to therapy and the likelihood of relapse or recurrence are not affected by treatment of her sex partner(s)

- Female partners of women with BV could be examined and treated if BV is present, but this approach has not been validated
  - Increase awareness of signs & symptoms of BV in women
  - Encourage healthy sex practices: avoid shared sex toys, clean sex toys, use barriers

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**Probiotics - Prevention**

![Graph showing L. Rhamnosus GR effectiveness]

<table>
<thead>
<tr>
<th>N</th>
<th>125</th>
<th>450</th>
<th>95</th>
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<td>Tx</td>
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<td>6d</td>
<td>6m</td>
<td>28d</td>
<td>7d</td>
<td>7m</td>
</tr>
<tr>
<td>Fu</td>
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<td>30d</td>
<td>60d</td>
<td>14d</td>
<td>30d</td>
<td>28d</td>
<td>28d</td>
<td>60d</td>
<td>66d</td>
<td></td>
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</tr>
<tr>
<td>Route</td>
<td>PO</td>
<td>V</td>
<td>V</td>
<td>V</td>
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<td>P</td>
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**Vulvovaginal Candidiasis**
Epidemiology and Causes

- Infection is common
  - 75% at least once
  - 40% to 45% two or more
  - < 5% recurrent VVC
- Not sexually transmitted
  - may be associated with frequency of intercourse, but not # of partners
- Most infections caused by
  - *Candida albicans* (85%)
  - *C. glabrata* (5% - 15%)
  - Misc. species (1% - 5%)
Candidiasis Curriculum

Pathogenesis

- Candida species are normal flora of the skin and vagina
- Symptomatic clinical infection is caused by overgrowth of *C. albicans* or other non-albicans species
- Yeast grows as oval budding yeast cells or as a chain of cells (pseudohyphae)
- Disruption of normal vaginal ecology or host immunity can predispose to vaginal yeast infections

Clinical Manifestations

- Intense itching and irritation of vulva
  - Not specific
- Thick, non-odorous discharge
  - Not sensitive
- External dysuria
- Exam
  - Thick, clumpy, adherent, white discharge
  - Erythema and edema of vulva, vagina
  - Sometimes see satellite lesions or shallow linear fissures or excoriations around posterior introitus

Diagnosis

- Based upon clinical presentation, signs, and office tests
  - pH < 4.5; negative amine test
  - Wet mount shows pseudohyphae and/or mycelial elements
    - 10% KOH prep improves visualization by disrupting cells that might be obscuring yeast
- When to use culture?
  - Symptoms present, pH normal, but yeast not seen on wet mount
  - Recurrent VVC (to confirm diagnosis)
  - To identify unusual species
    - *C. glabrata* buds, but doesn’t form pseudohyphae or hyphae, so it’s harder to see on wet mount
  - No improvement with therapy
  - Relapse within 2 months
Wet Prep: PMNs and Yeast Buds

Saline: 40X objective

Source: CDC and Seattle STD/HIV Prevention Training Center at the University of Washington

Wet Prep: PMNs and Pseudohyphae

Saline: 40X objective

Yeast pseudohyphae

PMNs

Squamous epithelial cells

Source: CDC and Seattle STD/HIV Prevention Training Center at the University of Washington

Classification

- **Uncomplicated VVC**
  - Sporadic or infrequent
  - Mild to moderate symptoms
  - Likely to be *C. albicans*
  - Normal host

- **Complicated VVC**
  - Recurrent
  - Severe symptoms
  - Non- *C. albicans*
  - Immunosuppressed host
    - Uncontrolled diabetes
    - Pregnancy
    - HIV
    - Immunosuppressive therapy
  - Not associated with
    - nylons, type of underwear
    - colored toilet paper, tampons
    - wiping back to front

2006 CDC STD Treatment Guidelines
Principles of Treatment: Uncomplicated Infections

- Treat only symptomatic women
- No need to treat sex partners unless sx
- Topical azole drugs ( clotrimazole, miconazole, butoconazole, etc.) more effective than nystatin
- Treatment with azole results in cure rates of 80-90% in women who comply with regimen

Treatment

- **Uncomplicated VVC**
  - Multiple topical azoles for 1-14 days* OR
  - Single-dose fluconazole 150 mg PO**

- **Recurrent VVC**
  - Induction:
    - Multiple topical azoles for 7-14 days* OR
    - Fluconazole 100-200 mg PO every 72 hrs x 3**
  - Maintenance to decrease recurrence
    - First-line: Fluconazole 100-200 mg orally weekly** OR
    - Other topical treatments used intermittently
    - Discontinue and re-assess after 6 months

*All oil-based and may weaken condoms
**Not to be used in pregnancy

2015 CDC STD Treatment Guidelines

Treatment: Severe and Non- *C. albicans* VVC

**Severe VVC**
- Lower response rates to shorter courses of treatment
- 7 to 14 days of non-fluconazole topical therapy, OR
- Fluconazole 150 mg x 2 doses (second dose 3 days after first dose)

**Non- *C. albicans* VVC**
- Optimal treatment unknown
- Confirm with culture
- 7 to 14 days of non-fluconazole topical therapy
- For recurrences: boric acid 600 mg intravaginally daily x 14 days (70% clinical and mycologic cure rates)

2015 CDC STD Treatment Guidelines
### List of Topical Azoles

- Butoconazole 2% cream 5g intravag x 3 days * or
- Butoconazole 2% cream 5g (sustained release), intravag once or
- Clotrimazole 1% cream 5g intravag x 7-14 days* or
- Clotrimazole 2% cream 5g intravag x 3 days* or
- Clotrimazole 100 mg vaginal tablet x 7 days
- Clotrimazole 100 mg vaginal tablet, x 3 days*
- Miconazole 2% cream 5 g intravag x 7 days* or
- Miconazole 4% cream 5 g intravag x 3 days* or
- Miconazole 100 mg vaginal suppository, one x 7 days* or
- Miconazole 200 mg vaginal suppository, one x 3 days*
- Miconazole 1,200 mg vaginal suppository x 1 dose*
- Tioconazole 6.5% ointment 5 g intravag once* or
- Terconazole 0.4% cream 5 g intravag x 7 days.
- Terconazole 0.8% cream 5 g intravag x 3 days
- Terconazole 80 mg vaginal suppository, one x 3 days

* Available Over-The-Counter

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### Persistent yeast vulvovaginitis

Consider non-*albicans* species or resistance and get a culture to evaluate this

- > 50% *C. glabrata* resistant to azoles:
  - Boric acid 600mg pv qHS x 14d
  - Flucytosine 15.5%- 5g pv qHS x 14d
  - Amphotericin B, 50mg suppository x14d

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### Treating resistant *C. albicans*

- Initial: Boric acid 600mg PV qhs
- Maintenance:
  - Low MIC (2-4 mcg/mL): Twice weekly Fluconazole
  - Higher MIC
    - Ketoconazole
    - Itraconazole
    - Boric acid 3x/week
    - Vaginal amphotericin
    - Vaginal gentian violet

*C. albicans* maintains sensitivity to medications at low pH, but not all isolates do.
Partner Management

- VVC is not usually acquired through sexual intercourse
- Treatment of sex partners is not recommended but may be considered in women who have recurrent infection
- A minority of male sex partners may have balanitis and may benefit from treatment with topical antifungal agents to relieve symptoms

Source: CDC

Yeast - Modifiable risk factors?

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Risk</th>
</tr>
</thead>
</table>
| Oral contraceptives | 4 studies no difference  
                     | 5 studies increased risk (1.4-10.15)                               |
| Diabetes          | ↑risk with poorly controlled diabetes                               |
| Diet              | Higher gtt values in women with RVVC  
                     | ↑risk with fewer servings of milk  
                     | ↑risk with more servings of dairy  
                     | ↑risk with ≥2 servings of bread |
| Sexual practices  | ↑risk with frequent oral sex  
                     | ↑risk with frequent sex                                               |
| Clothing choice   | No clear association with +culture, but worse symptoms with tight clothes |

Van de Wijgert JACO 2013; Donders AJOG 2002; Reed B Jl Womens Health Gender Based Medicine 2000; Reed BD Jl womens health 2003

Vulvar care

- Water
- Vaseline/Coconut oil/olive oil
- Cotton
- Avoid pads/pantyliners
- Benadryl at night

Less is more
Trichomoniasis

• Frothy vaginal discharge
• “Strawberry cervix” or colpitis macularis

Source: Claire E. Stevens/Seattle STD/HIV Prevention Training Center at the University of Washington

Trichomonas Vaginitis

Source: http://www.brooksdepress.org/Products/ORGYN_101

Strawberry Cervix due to Trichomoniasis

Source: PHIL, CDC
**Trichomonas vaginalis**
- Pear-shaped, flagellated, anaerobic protozoa
- Four anterior flagella
- Undulated membrane
- Posterior axostile
- Wet mount: jerky, swaying motion; increased PMNs
- Other *Trichomonas* species (body site specific):
  - *T. tenax* (oral commensal)
  - *T. hominis* (rare, GI tract)

**Epidemiology**
- Most common curable STD
- Estimated 7.4 million cases/yr ($375 million) in the U.S.
- Estimated prevalence:
  - 50%-60% in female prison inmates and commercial sex workers
  - 18%-50% in females with vaginal complaints
  - 3% in U.S. women 14–49 years of age (NHANES data)*
- Factors associated with increased likelihood of infection in multivariable analysis
  - Black, non-Hispanic race/ethnicity
  - Birth in United States
  - Greater number of lifetime sex partners
  - Increasing age
  - Lower educational level
  - Poverty
  - Douching
  - NOT symptoms

*Sutton et al. CID 2007; 45:1319-26

**Route of Infection**

**Inoculation:**
- Sexual contact
- Incubation 4-28 days
- Long duration of infection (months to years!)
  - 4 months in men
  - 5 years in women (Bowden, 2000)
- Seen in heterosexual and WSW couples

**Transmission:**
- Highly transmissible!
- Male to female: 85%
- Female to male: 20-60% (Krieger, 1995)
  - 70% (Sena, 2003)
Clinical Manifestations

• Women – symptomatic 20-50% of the time
  – profuse, malodorous discharge; genital irritation
  – Erythema of mucosa, profuse frothy discharge
  – Cervical petechiae (“Strawberry cervix”)
  – May also infect Skene's glands and urethra (rare), organism may not be susceptible to topical therapy

• Men – most asymptomatic
  – Non-gonococcal urethritis (etiology in up to 20% of cases)

Diagnosis

• Wet mount (saline prep)
  – Sensitivity 60-70% (highest with symptoms)
  – Motile pear-shaped trichomonad
  – Best read within 5 minutes on warm slide
  – Also see many PMNs

• pH >4.5 (90% sensitive, not specific)
• KOH may have positive whiff (50%)

Wet Prep: Trichomoniasis

Saline: 40X objective

Yeast buds
Trichomonas
PMN
Squamous epithelial cells

*Trichomonas shown for size reference only; must be motile for identification
Source: Seattle STD/HIV Prevention Training Center at the University of Washington
Newer Testing Options for Trich

- Microscopy is inferior to new options, including
  - Rapid antigen testing (OSOM)
  - Nucleic acid amplification testing
    - APTIMA TMA Trichomonas vaginalis assay
    - BD ProbeTec TV O Amplified DNA assay
    - May use same specimen types as used with gc/chl NAATs (i.e. vaginal swab, endocervical swab, urine)

<table>
<thead>
<tr>
<th>Test</th>
<th>Sens</th>
<th>Spec</th>
</tr>
</thead>
<tbody>
<tr>
<td>APTIMA TMA</td>
<td>98%</td>
<td>98%</td>
</tr>
<tr>
<td>OSOM</td>
<td>90%</td>
<td>100%</td>
</tr>
<tr>
<td>Culture</td>
<td>83%</td>
<td>100%</td>
</tr>
<tr>
<td>Wet prep</td>
<td>56%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Huppert CID 2007

Test Sens Spec
APTIMA TMA 98% 98%
OSOM 90% 100%
Culture 83% 100%
Wet prep 56% 100%

Slide courtesy of Marrazzo, IDSA 2011

Trichomoniasis: Diagnosis

Nucleic Acid Amplification Tests
- (Vaginal swab +/- other samples)
  - AmpliVue (Quidel)
  - APTIMA (Hologic)
  - MAX, ProbeTec TV (BD)
  - Solana (Quidel)
  - Xpert (Cepheid)

Sens/Spec: 88-100%, 97-99.9%

Point-of-care tests
- OSOM trichomonas rapid antigen test (Genzyme)
- Affirm VP III (BD)

OSOM Sens/Spec: 67-100%, 92-100%
Affirm VP Sens/Spec: 89-93 %, ~100%

Saline Wet Mount
- Motile trichomonads
- pH >4.5
- Whiff test may be +

Sens/Spec: 36-70%, ~100%

Culture
- Diamond’s
- InPouch TV, BioMed Diagnostics

Sens/Spec: 75-95%, 100%

Trich Testing in Men

- No approved point of care tests
  - Wet prep not sensitive
- Culture available- urethral swab, semen or urine
  - No conclusive studies on sensitivity/specificity
- Urine and urethral swab NAAT offered through certain labs using analyte-specific reagents (check before sending)

**MSM- T. vaginalis does not infect oral sites, rectal prevalence low. Do not test these sites.**
Treatment Benefits

- In women
  - Infection is associated with HIV acquisition and transmission
  - Treatment of trich reduces HIV in vaginal secretions
    - Viral RNA decreased from 4677 to 1122 (Wang, 2001)
  - Infection is predictive of *N. gonorrhoea* infection

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>% with GC TV+</th>
<th>TV-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fouts, 1980</td>
<td>400 sx women</td>
<td>37 vs 22</td>
<td></td>
</tr>
<tr>
<td>Wolner-Hanssen, 1989</td>
<td>779 women</td>
<td>31 vs 11</td>
<td></td>
</tr>
<tr>
<td>Huppert, 2004</td>
<td>92 sx teens</td>
<td>61 vs 17</td>
<td></td>
</tr>
</tbody>
</table>

Treatment

- Recommended regimens
  - Metronidazole 2 g PO x 1 dose OR
  - Tinidazole 2 g PO x 1 dose
- Alternative regimen
  - Metronidazole 500 mg PO bid x 7 days
- Pregnancy:
  - Metronidazole 2 g orally in a single dose
    - No evidence of teratogenicity (pregnancy category B)
    - Tinidazole pregnancy category C, not recommended
- HIV-infected
  - Metronidazole 500 mg PO bid x 7 days
    - More effective than single-dose therapy

*Note: Topical vaginal therapy is ineffective*

2015 CDC STD Treatment Guidelines

Partner Management

- Sex partners should be treated
- Patients should be instructed to avoid sex until they and their sex partners are cured (when therapy has been completed and patient and partner(s) are asymptomatic)
### SUMMARY: Differential Diagnosis of Vaginitis

<table>
<thead>
<tr>
<th>Diagnostic Criteria</th>
<th>Vaginal pH</th>
<th>Discharge</th>
<th>Amine odor (KOH &quot;whiff&quot; test)</th>
<th>Microscopic</th>
<th>Common patient complaints</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>3.8 - 4.2</td>
<td>White, clear, frothy</td>
<td>Absent</td>
<td>Lactobacilli</td>
<td>None</td>
</tr>
<tr>
<td>Bacterial Vaginosis</td>
<td>&gt; 4.5</td>
<td>Thin, homogeneous, white, gray</td>
<td>Present (fishy)</td>
<td>Yeast</td>
<td>Discharge, bad odor, itching may be present</td>
</tr>
<tr>
<td>Candida Vulvovaginitis</td>
<td>&gt; 4.5 (usually)</td>
<td>White, curdy, &quot;cottage cheese&quot;</td>
<td>Present (fishy), (not always)</td>
<td>Mycelia, budding yeast, pseudohyphae with KOH prep</td>
<td>Itching/burning, discharge</td>
</tr>
<tr>
<td>Trichomonas Vaginosis</td>
<td>&gt; 4.5</td>
<td>Yellow, green, frothy, adherent</td>
<td>Present (fishy), (not always)</td>
<td>Trichomonads, WBCs &gt; 10,000</td>
<td>Frothy discharge, bad odor, vulvar pruritus, dysuria</td>
</tr>
</tbody>
</table>

### SUMMARY: Utility of Hx and Exam for Vaginitis

- No single symptom has enough predictive power to confidently diagnose any of 3 main causes of vaginitis
- Symptoms & signs can suggest a dx
  - Yeast: assoc w/ itching, cheesy d/c, redness and self-dx; watery d/c or odiferous d/c makes it less likely
  - BV: assoc w/ sensation of increased d/c and c/o of odor; absent d/c makes it less likely
  - Inflammation relatively specific for yeast, but not always there, and sometimes assoc w/ trich

### SUMMARY: Office Lab Tests for Vaginitis

- Wet mount often remains best way to make dx
  - No yeast or trich on microscopy does not mean no yeast or trich as cause
  - Presence of clue cells makes yeast unlikely
  - Lack of lactobacilli and presence of bacilli with corkscrew motility highly assoc with BV
- Use pH testing
  - Yeast: normal pH!!!

---

Obtaining Vaginal Samples

• How to obtain pH
  – Swab lateral wall of vagina 1/3-1/2 way in
  – Roll swab on narrow range pH paper (3.8-5.5)
  – Compare color to reference
  – Note - pH may be affected by cervical mucus, blood, sperm

Obtaining and Preparing Vaginal Samples (1)

• Wet mount method #1
  – Swab lateral vaginal wall and place in 0.5 cc room-temperature saline
  – Agitate swab in saline to mix; place drop on slide, add coverslip and read under microscope
• Wet mount method #2
  – Place drop of saline on slide
  – Collect sample from vagina, mix into saline
• KEY POINT: keep sample warm and wet on the way to the microscope!

Obtaining and Preparing Vaginal Samples (2)

• KOH preparations
  – swab lateral wall of vagina
  – roll swab onto slide
  – add 10% KOH and mix with swab
  – whiff immediately- fishy odor is “positive”
  – add coverslip and wait 2-5 minutes for KOH to digest cells
Unknown #1

- Why is recurrent BV so common?
  - Is it due to inappropriate treatment of the biofilm?
  - Is it recurrence or re-infection?
  - Is it due to a pathogen phenotype or a host phenotype?

Mitchell, 2017

Unknown #2

- If vaginal colonization with *Candida albicans* is present in up to 30% of women, why don’t they all have symptoms? What prompts development of the inflammatory response?
  - Is it different strains of yeast?
  - Differences in host immune response?
  - Differences in environmental triggers?

Mitchell, 2017

Unknown #3

- Is the optimal microbiota the same for everyone?
- How do we promote an optimal vaginal microbiota?