Gynecology for the Internist...

Vaginitis again?
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No conflicts of interest
“The vaginal environment has been described as both a dynamic and a delicate ecosystem.”

Droegemueller, 3rd edition
- Recurrent yeast  
  - (1.17 million Google sites)
- Recurrent bacterial vaginosis (BV)  
  - (1.68 million)
- Recurrent trichomoniasis  
  - (111,000 sites)
Vaginitis

• The spectrum of conditions that cause vulvovaginal symptoms such as itching, burning, irritation and abnormal discharge

• Etiology:
  • 22-50% bacterial vaginosis
  • 17-39% vulvovaginal candidiasis
  • 4-35% trichomoniasis
  • 7-72% remains undiagnosed

• ACOG Practice Bulletin, #72, Reaffirmed 2015
Vaginal flora...

- Influenced by estrogen
- Very heterogeneous!
  - Lactobacilli
  - Gardnerella vaginalis
  - E. coli
  - Group B strep
  - Mycoplasmatales
  - Candida albicans

Resulting vaginal pH < 4.5
Warm....
Moist....
Lose your defensive barrier....
A. Tell her to self treat with an OTC regimen
B. Have her come to the office for evaluation that day
C. Call her in a script for an antifungal
D. Instruct her to start probiotics until your next available appointment slot
2 weeks later, she calls back with the same symptoms...

A. Retreat the same way you did the first episode
B. Retreat an alternative way from the first episode
C. Have the patient return to the office for a repeat exam
D. Hope that whatever home remedy she Googled online provides her an option for distraction
One month later...her symptoms are back. She calls back wanting to know what **YOU** are going to do about this?

A. Explain to her about the vaginal microbiome (to include diagrams)
B. Blame her husband for her symptoms
C. Assume she is crazy
D. Remember what you learned here!
Yeast (vulvovaginal candidiasis)
Vulvovaginal candidiasis (VVC)

• **Uncomplicated VVC**
  - Sporadic or infrequent
  - Mild to moderate symptoms
  - Likely *candida albicans*

• **Complicated VVC (10-20% of women)**
  - Recurrent (≥4 per year)
  - Severe symptoms
  - Nonalbicans
  - Comorbidities of diabetes, immunocompromise, immunosuppressive therapy
Uncomplicated diagnosis

- **Clinical Symptoms:**
  - External dysuria
  - Vulvar pruritus
  - Pain/swelling/redness
  - Fissures & excoriations
  - Thick curdy vaginal discharge
  - pH is typically normal (<4.5)

- **Wet prep**
  - (saline, 10% KOH) or Gram stain shows budding yeast, hyphae or pseudohyphae

- + Candida Culture
Treatment for Uncomplicated VVC:

- **OTC agents:**
  - Clotrimazole
  - Miconazole
  - Tioconazole

- **Prescription agents:**
  - Butoconazole
  - Terconazole
  - Fluconazole

Treatment days is **not = to** relief days...
“monitor if symptoms do not get better in 3 days or if they last >7 days”

No superiority of any formulation, agent or route of administration

www.cdc.gov/std/tg2015/candidiasis.htm
What year did the FDA approve over-the-counter vaginal antifungal products?

A. 1950  
B. 1970  
C. 1990  
D. 2000
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If OTC* medicines did not exist...

• **56,000** medical practitioners needed to accommodate the increase in office visits

• **$4 billion** in ED visits added to the health care system

• **$23 billion** in lost productivity due to physician visits

*Includes all OTC treatments
CHPA, Consumer Healthcare Products Association January 2012
• Estimated $275 million is spent annually on nonprescription antifungals
• Antifungals are in the top 10 of all nonprescription medications sold in the US
Office visit?

• Persistent symptoms after using an OTC preparation

• Recurrent symptoms within 2 months after treatment
Complicated Vulvovaginal candidiasis

- Recurrent.... Defined at 4 or more episodes of VVC within 1 year (~5% of women)
- Severe symptoms
- Nonalbicans on culture (10-20% of women with recurrent VVC)
- Comorbidities of diabetes, immunocompromise, immunosuppressive therapy

Obtain vaginal cultures to confirm and ID unusual species
Treatment: conventional treatment is not as effective

Goal: regain mycologic control

• Longer duration
  • Topical treatment 7-14 days
  • Oral treatment ~7 days

• Maintenance regimen
  • **Weekly** oral fluconazole (100mg, 150mg, or 200mg dose) x 6 months
    • Will successfully control > 90% of symptomatic episodes
    • Will cause a protective effect in ~50% of women

ACOG Practice Bulletin #72, 2015
Nonalbican VVC treatment?

- Optimal regimen is unknown

- If recurrent, 600mg boric acid vaginally x 2 weeks

- No data to support the treatment of sexual partners therefore...no recommendation
Field trip....
Boric acid powder

Fatty acid base (solid, then melted)

Silica Gel

• Silica gel...a suspending agent added to the base
• Keeps the boric acid suspended
• Prevents caking at the bottom of container
• Ensures the same amount of the active ingredient in each suppository
Melted base added to silica & boric acid

Electronic Pestle and Mortar mixing

Hot plate maintains temperature
• Each suppository mold is filled by a syringe
• Molds are then left to cool and harden (couple of hours)
• Suppositories are then ready to be dispensed
Boric Acid Vaginal Suppository

Compounding pharmacies

https://members.pccarx.com/Resources/FindACompounder.aspx
ICD 10

• Uncomplicated vaginitis

• Complicated vaginitis

• B37.3 Candidiasis of vulva and vagina

• V97.33XD Sucked into jet engine, subsequent encounter
Bacterial Vaginosis

• Polymicrobial
  • Replace normal hydrogen peroxide producing Lactobacillus with...
    • Anaerobic bacteria (Prevotella and Mobiluncus)
    • G. vaginalis
    • Ureaplasma
    • Mycoplasma
    • Others
Vaginosis

A shift in the vaginal flora
Diagnosis?

- Clinically 3 of the following (Amsel’s Criteria):
  - Homogeneous, thin white discharge that smoothly coats the vaginal walls
  - Clue cells (epithelia cells studded with adherent coccobacilli on microscopic exam)
  - pH of vaginal fluid > 4.5
  - Fishy odor before or after addition of 10% KOH (“whiff test”)

- Gram Stain (“gold standard”)
  - determines the relative concentration of lactobacilli, etc.

- Other lab testing...
  - DNA hybridization probes
  - Sialidase activity levels
  - PCR testing

- NOT pap testing

www.cdc.gov/std/tg2015/bv.htm
Treatment...

Recommended Regimens:

• Metronidazole 500 mg orally twice a day for 7 days

OR

• Metronidazole gel 0.75%, one full applicator (5 g) intravaginally, once a day for 5 days

OR

• Clindamycin cream 2%, one full applicator (5 g) intravaginally at bedtime for 7 days

www.cdc.gov/std/tg2015/bv.htm
Alternative regimens...

Tinidazole 2 g po daily x 2 days
Tinidazole 1 g po daily x 5 days
Clindamycin 300mg BID x 7 days
Clindamycin ovules 100mg vaginally x 3 days
Symptoms recur....???

• Persistence? Recurrence? Resistance?
• Return of symptoms is noted up to 30% within 3 months
• Limited data on management strategies

• 2\textsuperscript{nd} case...
  • Retreatment with same regimen acceptable
  • OR...use a different recommended treatment
Multiple recurrences....

Treat longer, stronger
Options include...

1. 0.75% metronidazole gel twice weekly x 4-6 months
2. Initial oral 7 day treatment....followed by....
   boric acid 600mg intravaginally x 3 weeks....followed by...
   0.75% metronidazole twice weekly x 4-6 months
3. Monthly metronidazole 2g + 150mg fluconazole

Goal...suppressive treatment to promote colonization with normal vaginal flora
Treat sex partners?

- **Not** recommended
- Relapse or recurrence is not affected by treatment of partners
Bacterial Vaginosis

• Polymicrobial
  • Replace normal hydrogen peroxide producing Lactobacillus with...
    • Anaerobic bacteria (Prevotella and Mobiluncus)
    • G. vaginalis
    • Ureplasm
    • Mycoplasm
    • Others

• Can you put the lactobacillus back in???
• Probiotics?
No studies support this

- Not as an adjunctive treatment
- Not as a replacement therapy
- Further research is ongoing
- Quality of products vary worldwide
ICD 10

- N76.0  Bacterial vaginosis
- Recurrent bacterial vaginosis

- W61.62XZ  Struck by duck, subsequent encounter
- Z63.1  Problems with in-laws
Recurrent trich?

• Most likely represents reexposure or treatment nonadherence

• Less common: antimicrobial resistance
  • Metronidazole resistance 4-10%
  • Tinidazole resistance 1%

• Prolonged treatment is necessary

• In rare cases, susceptibility testing via CDC
  www.cdc.gov/std
  Phone: 404-718-4141
EPT

Expedited Partner Therapy

The future?

Extra credit....

What is this?
Spherical objects are various organisms enrobed in a biofilm.

Stringy sheets ("biofilm") are an extra cellular material elaborated by the microbes.

The biofilm serves as a matrix/glue that binds the organisms and forms a "protective blanket" or shield from harm.
What might the future hold?

• **Biofilm** formation helps microbes (both yeast and bacteria) to survive.

• **Biofilms** confer:
  • Greater resistance to peroxides and low pH* (natural defense of lactobacillus against other organisms).

• Work being done on disrupting the biofilms may lead to advances in treatment

• More likely that a combination of Antimicrobials, biofilm meditation and improved probiotic therapy may hold the key.

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VCU ....a leader in vaginal microbiology!

- **VaMP (Vaginal Microbiome project)** – Completed $7 million NIH grant to study the microbiome of the vagina involving 4,000 plus participants.

- **MOMS-PI** – Ongoing $11 million NIH Grant to VCU to study the microbiome of pregnancy and neonates involving 2,000 participants.
Recurrent vaginitis...