58th Annual T. Hart Baker, MD
OB/GYN Symposium
Recalcitrant and Recurrent Candidiasis and Bacterial Vaginosis

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The University of Michigan
Center for Vulvar Diseases

Disclosures
Hope Haefner, MD is on an advisory board for Merck Co. Inc.
Learning Objectives

At the conclusion of the symposium the participants should be able to:

1. Identify at risk patients
2. Recognize and manage refractory and recurrent vaginitis

Vaginal discharge in lactating dairy cattle in New Zealand
CDC STD TREATMENT GUIDELINES

The 2010 Treatment Guidelines are now online

Resistant/Recurrent disease focus

Question 1

I see patients with chronic vaginitis

- Yes
- No
**Question 2**

I like to see patients with chronic vaginitis

- [ ] Yes
- [ ] No

### pH and Wet Mount

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### Classification of VVC

**Uncomplicated VVC**
- Sporadic or infrequent vulvovaginal candidiasis or
- Mild-to-moderate vulvovaginal candidiasis or
- Likely to be *C. albicans* or
- Vulvovaginal candidiasis in nonimmunocompromised women

**Complicated VVC**
- Recurrent vulvovaginal candidiasis (RVVC) or
- Severe vulvovaginal candidiasis or
- Non-albicans candidiasis or
- Vulvovaginal candidiasis in women with uncontrolled diabetes, debilitation, or immunosuppression
**Candida albicans KOH**

Torulopsis (Candida) glabrata on Cornmeal-Tween 80 agar: Small, compacted blastoconidia with no pseudohyphae formed.

10-20% of women with VVC will have complicated VVC; Estimated cost: $1 billion annually in the U.S.
Recurrent VVC
Four or more symptomatic episodes/year

Vaginal culture should be obtained to confirm diagnosis and identify species

2010 CDC STD Treatment Guidelines

Sensitivity of Microscopy vs. Culture

Yeast 22 -50%
Antifungal Susceptibilities of *Candida* Species Causing Vulvovaginitis and Epidemiology of Recurrent Cases

Sandra S. Richter, Rudolph P. Galask, Shawn A. Messer, Richard J. Hollis, Daniel J. Diekema, and Michael A. Pfaller

*Department of Pathology and Department of Obstetrics and Gynecology, University of Iowa Carver College of Medicine, Iowa City, Iowa*


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**Microbiology of Vulvovaginal Candidiasis 429 pts**

- C. albicans 70.8 %
- C. glabrata 18.9 %
- C. parapsilosis 5.0 %
- C. krusei 2.0 %
- S. cerevisiae 1.5 %
- C. tropicalis 1.4 %
- C. lusitaniae 0.2 %
- Trichosporon sp. 0.2 %

Pathogenesis

Stopping oral contraceptives not recommended

Unless additional risk factors, no need to screen:
  Diabetes mellitus in premenopausal women
  HIV

Glucose Tolerance Test

• In post-menopausal females with RVVC, a GTT should be obtained

Candida and HIV


• 88.8% of HIV-infected (HIV+) women had yeast infection, whereas 58.6% of HIV seronegative (HIV-) women had the infection. The correlation coefficient (r) for yeast and HIV infections was 0.266 (p < 0.05), and the odds ratio was 5.59 (95% Confidence Interval = 3.03 - 10.297).

Vulvovaginal Candidiasis

Management of Sex Partners

VVC is not usually acquired through sexual intercourse; no data support the treatment of sex partners. A minority of male sex partners might have balanitis, which is characterized by erythematous areas on the glans of the penis in conjunction with pruritus or irritation. These men benefit from treatment with topical antifungal agents to relieve symptoms.

2010 CDC STD Treatment Guidelines
Candidiasis

Recurrent VVC

• To maintain clinical and mycologic control, a longer duration of initial therapy (e.g., 7–14 days of topical therapy or a 100-mg, 150-mg, or 200-mg oral dose of fluconazole every third day for a total of 3 doses [day 1, 4, and 7]) then 100-mg, 150-mg, or 200-mg dose weekly for 6 months
After 6 months of fluconazole therapy, therapy is discontinued. Some patients achieve a prolonged remission, while others relapse. A short-term relapse, with culture confirmation of the diagnosis, merits reinduction therapy with three doses of fluconazole, followed by repeat weekly maintenance fluconazole therapy, this time for one year.

Fluconazole - Adverse Effects

- Nausea and vomiting in 3-4% (long term therapy)
- Liver effects
  - Chronic therapy (check LFTs if daily use of ketoconazole, itraconazole, or >6 mos fluconazole)
  - AIDS patients
- Pregnancy - More than single dose use Category D
Fluconazole Resistance

C. glabrata
C. krusei
Cases of fluconazole resistance in C. albicans increasing

Recurrent Vulvovaginal Candidiasis

If fluconazole is not feasible, some specialists recommend topical clotrimazole 200 mg twice a week, clotrimazole (500-mg dose vaginal suppositories once weekly), or other topical treatments used intermittently
Antifungals

Imidazole

- Ketoconazole
- Clotrimazole
- Miconazole

Triazoles

- Itraconazole
- Fluconazole
- Voriconazole
- Posaconazole

Recurrent yeast before treatment
Candida Glabrata

Low vaginal virulence

Rarely causes symptoms, even when identified by culture

Exclude other co-existent causes of symptoms and only then treat for C. glabrata
Candida glabrata is found on culture. What treatments have been used for C. glabrata?

- **a** Boric acid per vagina
- **b** Butoconazole nitrate per vagina
- **c** 5-flucytosine per vagina
- **d** All of the above
Other Antifungals
Boric Acid

- Puratronic, 99.99995% (metals basic)
- Formula: H₃BO₃
- Formula Weight: 61.83
- Form: Crystalline Powder
- Melting Point: 170.9°C
- Merck Number: 11,1336
Boric Acid

Fill 0-gel capsule halfway (600 mg)
   For treatment of acute infection; insert *per vagina* qhs x 14 days
   For prevention of recurrence; insert *per vagina* twice weekly

KEEP AWAY FROM CHILDREN
Nystatin

Can also be used for recurrent disease prevention
100,000 U per day per vagina for 3-6 months

Nystatin

Rachel Fuller Brown and Elizabeth Lee Hazen developed the drug in the 1950s
Gentian Violet

- 0.25 – 1% aqueous solution of aniline dye
- Paint on mucous membrane weekly
- Use 1% in office only
May cause ulceration
Safe in pregnancy

Erythematous / Irritated Vulva

Rx with combination topical antifungal and steroid
(nystatin/triamcinolone acetonide ointment)
Other Treatments

Amphotericin B vaginal suppositories

Flucytosine

Supports probiotics for preventing and treating candida infections

Probiotics for Candida

Safety generally accepted
List of patients for whom caution might be warranted:
  - immunocompromised, premature infants, short bowel syndrome, those with central venous catheters, elderly and patients with cardiac valve disease

Bacterial Vaginosis

Microbiology

- Overgrowth of bacteria species normally present in vagina with anaerobic bacteria
- BV correlates with a decrease or loss of protective lactobacilli
  - Vaginal acid pH normally maintained by lactobacilli through metabolism of glycogen
H$_2$O$_2$ -Producing Lactobacilli

- All lactobacilli produce lactic acid
- Some species also produce H$_2$O$_2$.
- Hydrogen peroxide (H$_2$O$_2$) is a potent natural microbicide
- In vitro, H$_2$O$_2$ is toxic to viruses such as HIV, as well as bacteria

New Thoughts  STD

1975 round table discussion, Dr. Josey stated “In my opinion, H.V. vaginitis is a form of venereal disease.

2009 Editorial commentary Dr. Schwebke...It is time to accept (again) that BV is sexually transmitted.
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## Diagnosis- pH

### Causes for Elevated Vaginal pH
- Menses
- Heavy cervical mucus
- Semen
- Ruptured membranes
- Hypoestrogenism
- Desquamative vaginitis
- Trichomoniasis
- Bacterial vaginosis
- Foreign body with infection
- Streptococcal vaginitis (group A)
Clue Cells with Coccobaccilli

Absence of lactobacilli
Loss of WBC (hence vaginosis, not vaginitis)
Bacteria between cells

BV Diagnosis Amsel Criteria

At least three criteria must be present

● Homogeneous, thin, grayish-white discharge that smoothly coats the vaginal walls
● Vaginal pH >4.5
● Positive whiff-amine test, defined as the presence of a fishy odor when a drop of 10 percent potassium hydroxide (KOH) is added to a sample of vaginal discharge
● Clue cells on saline wet mount
Question 3
The sensitivity of Amsel’s criteria for BV is

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<td></td>
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<td>b</td>
<td>62%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>c</td>
<td>22%</td>
<td></td>
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<td>d</td>
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Sensitivity of Microscopy vs. Culture

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Other Diagnostic Tools

- Cytology not reliable
- Vaginal Gram stain (Nugent or Speigel criteria - mostly for research)
- Culture - No role in diagnosis
- DNA probe
- Point of care tests for pH and amines, and proline iminopeptidase are commercially available

Complications with BV

- Preterm delivery
- Increased risk of pelvic inflammatory disease (?causal factor vs. independent risk) and infertility
  - Endometrial bacterial colonization
  - Postabortal infection
  - Postpartum fever
  - Plasma cell endometritis
- Post hysterectomy cuff cellulitis
- Acquisition of HSV and Increased susceptibility to HIV acquisition/transmission
Recurrent Bacterial Vaginosis 3 or more in 12 months

~30 percent of patients with initial responses to therapy have a recurrence of symptoms within three months

More than 50 percent experience a recurrence within 12 months

Recurrence may be a result of persistence of BV-associated organisms and a failure of lactobacillus flora to recolonize

Recurrent Bacterial Vaginosis Treatments

- Treat for longer periods (10 – 14 days) with same agent
- Switch Agent
- ? Suppression (twice weekly for 6 months)
- ? Condom use
- Acidification of vagina has not been helpful
- Emergence of clindamycin-resistant anaerobic gram-neg rods
Other Treatment Thoughts

Hormonal contraception decreases the risk of BV


Other Treatment Thoughts

Boric acid per vagina for bacterial vaginosis

Reichman, Akins and Sobel used 600 mg per vagina x 21 days for recurrent BV.

Limited data suggest that oral nitroimidazole followed by intravaginal boric acid and suppressive metronidazole gel might be a treatment option after multiple occurrences.
New Treatment Thoughts

Rifaximin vaginal tablets


Another Treatment

Hydrogen peroxide 3% vaginal irrigations

• Non-controlled study by Wincesalus SJ, Claver G. Int J STD AIDS 1996;7:284-7
• Chaithongwongwatthana et al. J Med Assoc Thai 2003;86:S379-84
  Randomized controlled study using 20 ml single dose per vagina in lithotomy for 3 mins
• Cardone A et al. Minerva Ginecol 2003;55:483-92
  Non-controlled trial using 30 ml qhs x 1 week per vagina
Tea Tree Oil

Multiple methods. One is to use a 5-day course of pessaries, each with 200mg Tea Tree oil in a vegetable Oil base.

CONCERN FOR CONTACT DERMATITIS

Other Treatment Thoughts

Decrease dietary fat intake


Hormonal contraception decreases the risk of BV

Probiotics for Bacterial Vaginosis

AKA

To lactobacilli or not lactobacilli… that is the question

Which strains or combination of strains are most effective (e.g., *Lactobacillus* rhamnosus GR-1, *Lactobacillus reuteri* RC-14, *Lactobacillus acidophilus*)

OBGYN Management
December 2010;22(12)50.

- Probiotic blend containing 8 billion colony-forming units of various lactobacilli po bid
- Dr. Firestone Aventura, Florida
Bacterial Vaginosis
Management of Sex Partners

Response to therapy and the likelihood of relapse or recurrence are not affected by treatment of her sex partner(s). Therefore, routine treatment of sex partners is not recommended

2010 CDC STD Treatment Guidelines
The phone is neither a diagnostic nor a therapeutic tool....