VAGINITIS
What Makes a Good Vagina Go Bad?

The 23rd Annual Charleston Advanced Practice Registered Nurses Conference

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Judith T. Burgis, MD has no disclosures related to this topic.

Learning Objectives

Review vaginal ecosystem
Update common vaginal conditions and treatments
Case studies to illustrate

Have fun
**Vaginal Ecosystem**

*Balance - normal bacteria - hormonal changes*

Epithelium – transudate  
Cervical mucous  
Uterine and fallopian tube secretions

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**Vaginal Ecosystem**

*Mucin gel layer*

Coats the vaginal epithelium  
1st line defense  
Contains antimicrobial peptides  
Protects against pathogens

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**Vaginal Ecosystem**

*Mucin gel layer*

Carries *broad antimicrobial* properties  
Innate defense mechanism  
*Changes* can alter protective properties
Vaginal Ecosystem

Antimicrobial peptides

Lysozyme
Lactoferrin
Secretory leukocyte protease inhibitor
Human beta defensins

Vaginal Ecosystem

Decreased viscosity of mucin

More permissive to penetration
Increased acquisition infections

Vaginal pH Over the Lifespan

<table>
<thead>
<tr>
<th></th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premenarchal</td>
<td>pH 7</td>
</tr>
<tr>
<td>Reproductive age w/ estrogen</td>
<td></td>
</tr>
<tr>
<td>Lactobacillus predominate</td>
<td>pH 4.0-4.5</td>
</tr>
<tr>
<td>Lactobacillus reduced or had intercourse last 24 hours</td>
<td>pH 5-4.7</td>
</tr>
<tr>
<td>BV</td>
<td>pH 4.7-5.5</td>
</tr>
<tr>
<td>Menses</td>
<td>pH 6.0</td>
</tr>
<tr>
<td>Breastfeeding</td>
<td>pH 6.5-7.0</td>
</tr>
</tbody>
</table>
Vaginal pH Over the Lifespan

Postmenopausal, no HRT  pH 6.5-7

Innate antiviral activity decreased
Increased susceptibility to HIV, HSV

Vaginal Ecosystem

Effect of pH and HIV movement

pH 4  slower
pH 6  rapid

Vaginal Epithelium

Basal
Parabasal (several layers)
Intermediate (multiple layers)
Superficial layers that progressively accumulate glycogen
Healthy Vagina

Natural protective factors
Glycogen increases at puberty
Lactobacillus begin to thrive
Lactobacilli breakdown glucose to lactic acid
pH 4.0 (lower than 4.5)

Other protective factors
- Antimicrobials
- Lysozyme, lactoferrin
- Protease inhibitors
- Beta defensins

Normal vaginal secretions
- Floccular in consistency
- White in color
- Located in the posterior fornix
Vaginal Secretions

When analyzed by wet-mount
- Superficial cells
- WBCs (less than 1/epithelial)
- Few clue cells
  
  Add KOH for fungal elements

Vaginal Ecosystem

Impact of menstruation
- pH increases to 6.0 or higher
- Lactobacilli decrease in numbers temporarily

In a study of 74 women
- lactobacillus increased over the cycle
- Non-lactobacillus highest at menses

Menses, Tampons, and Contraceptives

RBCs can decrease the numbers of lactobacilli binding to vaginal epithelial cells

Epidemiologic data support
Tampon users are more likely to have H₂O₂ producing lactobacilli
Non deodorant tampon users were 30% more likely to be colonized by H₂O₂ producing lactobacilli
Depo users less likely to have H₂O₂ LB, OCP and ring users are more likely
Healthy Vagina

A beautiful ecosystem
Cleaner than your mouth

What Makes a Good Vagina Go Bad?

- DMPA (↓ lactobacilli)
- Smoking
- Unprotected sex with a man
- Stress hormones (Cortisol)
- Sex with an infected female partner
- Failure to clean sex toys

What Makes a Good Vagina Stay Good?

- Oral contraceptives or vaginal ring
- Tampon usage (non-deodorant)
- Lack of frequent exposure to sperm cells
- Having $H_2O_2$–producing lactobacilli in the gut
- Adequate estrogen levels
What Makes a Good Vagina Stay Good?

Patient wants to douche?

The Vagina is like a Self-cleaning Oven

Vaginal Infections
- *Trichomonas vaginalis*
- Vulvovaginal candidiasis
- Bacterial vaginosis
Evaluation for Vaginal Infection

Objective vulvar inflammation

Absence of vaginal pathogen
Mineral discharge

Mechanical, chemical, allergic, or other noninfectious etiology

Evaluation for Vaginal Infection

Microscopy not available

Point of care testing
Trichomonas Vaginitis

Caused by *Trichomonas vaginalis*

High transmission rate
70% of men contract after a single exposure with an infected female

Creates an anaerobic environment
*diagnosed with BV in 60% of patients*

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Trichomonas Vaginitis

*Increased risk for HIV*

*In HIV positive women*

Increased risk for PID

Routine screening in + HIV women

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“You’ve got it. Don’t flaunt it. You’ll spread it.”
Trichomonas Vaginitis

Can be transmitted through sexual abuse
Little scientific evidence for fomites
Can be carried asymptotically for years
Can emerge as a new infection following antibiotics
Careful diagnosis (NOT PAP TEST) and partner treatment are essential

Trich and the PAP Test

Detected poorly

Sensitivity on PAP is 50%

Do not treat based on PAP test

Diagnosis

Profuse purulent malodorous discharge

Vaginal secretions may exude from vagina

Vaginal erythema and strawberry cervix
  pH >5.0

Microscopy reveals motile trichomonads
Wet Mount

![Wet Mount](image)

Decreasing Shelf Life of Trichomonas Vaginalis on Wet-Mount

![Graph showing decreasing shelf life](image)

20% of initial positives become negative in 10 minutes

Ref: Kingston MA, Bansal D. Int J STD & AIDS 2003;14:28-29

Diagnosis

OSOM Trichomonas Rapid test
- Immunochromatographic capillary flow dipstick
- 10 minutes

Affirm TM VP III (BD)
- Nucleic acid probe (T vaginalis, G vaginalis, C albicans)
- 45 minutes

Sensitivity >83%, specificity >97%

Culture

![Logo: Palmetto Health USC Medical Group](image)
Treatment (CDC 2016)

Metronidazole 2g orally single dose or Tinidazole 2g orally single dose

*alternative regimen*

Metronidazole 500mg orally BID for 7 days

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Treatment (CDC 2016)

**Recommended for HIV +**

Metronidazole 500mg PO BID X 7 days

Retest in 3 months

NAAT recommended

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Treatment

Sex partners should be treated

Avoid alcohol

24 hours after completion of Metronidazole

72 hours after completion of Tindazole

**Test for other STIs**
Treatment Failure

Single dose

- **Exclude reinfection**
  - Use Metronidazole 500 BID x 7 days or Tindazole 2g single dose

Fails this, then Metronidazole or Tindazole 2g po x 5 days

Fails this, then susceptibility test CDC (404.718.4141) www.cdc.gov/std

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Treatment Failure

- Metronidazole resistance 4-10%
- Tindazole resistance 1%

Avoid single dose therapy for treatment failures

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Treatment **Pregnancy**

Metronidazole – Pregnancy B
Tindazole – Pregnancy C

Breastfeeding

- Metronidazole withhold feeding 12-24 hours after the last dose
- Tindazole withhold feeding for 72 hours after last dose
**Yeast Vaginitis**

Usually caused by *Candida albicans*

~ 75% of women have 1 episode

External dysuria, vulvar pruritus, pain, swelling, and redness

*Signs include* vulvar edema, fissures, excoriations, thick curdy discharge

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**Yeast Vaginitis**

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**Yeast Vaginitis  *Diagnosis***

- Wet prep (saline, 10%KOH)
- Gram stain
- Vaginal pH (<4.5)
- Yeast culture

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Yeast Vaginitis

Uncomplicated

Complicated
10-20% requires special diagnostic and therapeutic considerations

Yeast Colonization

Common as many as 70% will have vaginal yeast
Colonization is more frequent in women with vaginal lactobacilli, GBS, Depo users, and the sexually active
15-25% asymptomatic vaginal colonization in healthy adolescents and adults
Why do some "GET" Yeast Vaginitis?

Candida specific - Cell Mediated Immunity acquired by exposure early in life

**predominant** host defense mechanism

Why do some "GET" Yeast Vaginitis?

**Predisposing factors**

hormonal fluctuations, luteal phase, high dose estrogen OCs, HRT, antibiotic usage, uncontrolled diabetes

Why do some "GET" Yeast Vaginitis?

- Recurrent yeast - 4 or more more infections per year (5-10% of women)

- Suggested that host mediated immune response plays a role (nonprotective inflammatory leukocytic response)
Diagnosis of VVC

Accurate diagnosis crucial to treatment success

- Signs and symptoms **PLUS**
- Positive saline of 10% KOH microscopy **OR**
- Positive culture

**Clinical signs are NOT specific**

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Accuracy of Self-diagnosis
(95 women)

<table>
<thead>
<tr>
<th>Actual diagnosis</th>
<th>#</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>13</td>
<td>14%</td>
</tr>
<tr>
<td>Candiasis</td>
<td>32</td>
<td>34%</td>
</tr>
<tr>
<td><em>with BV</em></td>
<td>18</td>
<td>18%</td>
</tr>
<tr>
<td>BV alone</td>
<td>18</td>
<td>19%</td>
</tr>
<tr>
<td>Trichomoniasia</td>
<td>3</td>
<td>3%</td>
</tr>
<tr>
<td>Other</td>
<td>10</td>
<td>11%</td>
</tr>
</tbody>
</table>

Ferris, Obstet Gynec 2002;99:419

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Treatment of Uncomplicated VVC

**How to Choose Therapy**

**Efficacy**
- Topical and oral azoles >80% in women who complete therapy
- Nystatin 70% to 80% effective

**Ease of administration**

**Duration of therapy**
- Little significance in uncomplicated VVC
2016 CDC Treatment Guidelines (uncomplicated)

Over the counter Intravaginal agents

- Clotrimazole
- Miconazole
- Tioconazole

Prescription Intravaginal Agents

- Butoconazole 2%
- Terconazole

Oral Agent

- Fluconazole

Complicated Vulvovaginal Candidiasis

Recurrent (RVVC) is usually defined as 4 or more symptomatic episodes per year

Small percentage (< 5%)

Pathogenesis poorly understood

*Obtain vaginal yeast cultures*
Treatment of Complicated Candidiasis

Responds well to short duration of oral or topical azoles

Longer duration of therapy
- 7 to 14 days of topical treatment
- 100mg, 150mg, or 200mg oral fluconazole every third day for 3 doses

Maintenance for RVVC

Oral fluconazole weekly for 6 months

Topical Clotrimazole 200mg twice a week

Clotrimazole 500mg vaginal suppository weekly

Severe VVC

Characterized by extensive erythema, edema, excoriation, and fissures

7-14 days of topical azole or 2 doses of 150mg fluconazole

Midpotency topical corticosteroid
Non-albicans VVC
Optimal therapy unknown (yeast culture)
Longer duration with non-fluconazole (7-14 days)
600mg boric acid in a gelatin capsule administered vaginally qd x14

Compromised Host
Debilitating medical conditions
Correct modifiable conditions
7-14 days of conventional anti-mycotic treatment

Pregnancy
Topical azole therapy for 7 days
Treat Sexual Partners?

**58 monogamous couples**

All women had RVVC
All women treated with 400mg ketoconazole for 7 days
Male partners randomized to:
  a. Ketoconazole 200mg/d x5days
  b. placebo

Fong, Genitourin Med 1992;68:174-6

<table>
<thead>
<tr>
<th>Relapse period</th>
<th>Ketoconazole</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month</td>
<td>31%</td>
<td>32%</td>
</tr>
<tr>
<td>3 months</td>
<td>65%</td>
<td>61%</td>
</tr>
<tr>
<td>6 months</td>
<td>65%</td>
<td>71%</td>
</tr>
<tr>
<td>12 months</td>
<td>85%</td>
<td>82%</td>
</tr>
</tbody>
</table>

Why Maintenance in RVVC?

Sensitive organisms but high persistence of vaginal yeast following therapy

Goal – suppress vaginal colonization because it is the primary risk for recurrent disease
Fluconazole Suppression of RVVC

494 women with RVVC

- White – 67%
- African American – 26%
- Hispanic – 6%
- Asian – 1%

Treatment

- Open label treatment 150mg fluconazole x2 doses
- Maintenance 150mg fluconazole weekly vs placebo

Fluconazole Suppression for RVVC

Cumulative Failures

<table>
<thead>
<tr>
<th>Follow-up (mos.)</th>
<th>Fluconazole</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4%</td>
<td>15%</td>
</tr>
<tr>
<td>2</td>
<td>5%</td>
<td>33%</td>
</tr>
<tr>
<td>3</td>
<td>6%</td>
<td>45%</td>
</tr>
<tr>
<td>4</td>
<td>7%</td>
<td>54%</td>
</tr>
<tr>
<td>5</td>
<td>10%</td>
<td>59%</td>
</tr>
<tr>
<td>6</td>
<td>10%</td>
<td>64%</td>
</tr>
</tbody>
</table>

Sobel. NEJM 2004;351:876

Fluconazole Suppression for RVVC

Cured at 6 months

- Fluconazole: 91%
- Placebo: 36%

Total remaining cured after:

- 3 months: Fluconazole 73%, Placebo 69%
- 6 months: Fluconazole 43%, Placebo 22%
Yeast

Effect of Lactobacillus in Preventing Post-antibiotic Yeast

235 women being treated with antibiotics

Random assignment

- Oral and vaginal Lactobacillus
- Oral Lactobacillus and vaginal placebo
- Oral placebo and vaginal Lactobacillus
- Oral and vaginal placebo

Treatment for 10 days (6 during antibiotics and 4 after)

Pirotta. BMJ 2004;329:548

<table>
<thead>
<tr>
<th>Oral:</th>
<th>Placebo</th>
<th>Lacto</th>
<th>Placebo</th>
<th>Lacto</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal:</td>
<td>Placebo</td>
<td>Placebo</td>
<td>Lacto</td>
<td>Lacto</td>
</tr>
</tbody>
</table>

Rate of yeast vaginitis after therapy:

- 17% 24% 29% 24%

Baseline swab positive for yeast:

- 13% 23% 24% 24%

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**Bacterial Vaginosis**

Polymicrobial clinical syndrome

Replacement of normal $\text{H}_2\text{O}_2$ producing *Lactobacillus* with anaerobic bacteria

Most *prevalent* cause of vaginal discharge

Most are asymptomatic

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**Bacterial Vaginosis**

Multiple partners

No condoms

No *Lactobacilli*

Sexually naïve rarely affected

Increased risk for HIV

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**Bacterial Vaginosis**

*Increase in vaginal sialidases*

Represents the virulence factor in BV

Alter the vaginal sialidase

Weaken the mucin layer

---
Bacterial Vaginosis

Infections renders

Increased HIV acquisition male to female
Increased transmission female to male

BV – Diagnosis

Clinical criteria require 3 of the following:

a. homogenous, thin, white discharge that smoothly coats the vaginal walls
b. presence of clue cells on micro exam (>20%)
c. vaginal pH >4.5
d. a fishy odor of vaginal discharge before or after adding 10% KOH

Bacterial Vaginosis
Diagnosis of BV

Using pH and amine odor *greatly increases* accuracy
G. vaginalis cultures are *not* recommended

PAP tests have **NO** clinical utility

Gram stain, Affirm VPIII, DNA probe, OSOM card

BV treatment

*In nonpregnant women*

relieve symptoms
reduce post-surgical/post procedure risk
reduce risk for other infections

2016 CDC Treatment Guidelines

Metronizadole 500mg po BID x7d

Metronizadole gel 0.75%, one applicator intravaginally qd x5d

Clindamycin cream 2%, one applicator intravaginally qd x7d
2016 CDC Treatment Guidelines

Alternative Regimens
- Tinidazole 2 g PO for 2 days
- Tinidazole 1 g PO for 5 days
- Clindamycin 300mg PO BID for 7 days
- Clindamycin ovules 100mg vaginally for 3 days

Follow-up unnecessary if symptoms resolve

Routine treatment of sex partners is not recommended

Test for HIV and other STIs

2016 CDC Regimens for Pregnant Women

- Metronizadole 500mg po BID x7d
- Metronizadole 250mg po TID x7d
- Clindamycin 300mg po BID x7d

The treatment benefit of asymptomatic pregnant women is unclear
Oral and Intravaginal Metronidazole are Equally effective for BV

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Pregnant</th>
<th>Oral</th>
<th>Intravaginal</th>
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<tbody>
<tr>
<td>Ferris</td>
<td>1995</td>
<td>No</td>
<td>16/19 (84%)</td>
<td>18/24 (75%)</td>
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<tr>
<td>Hanson</td>
<td>2000</td>
<td>No</td>
<td>32/45 (71%)</td>
<td>29/41 (71%)</td>
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<td>Yudin</td>
<td>2003</td>
<td>Yes</td>
<td>43/52 (83%)</td>
<td>42/50 (84%)</td>
</tr>
<tr>
<td>All</td>
<td></td>
<td></td>
<td>91/116 (78%)</td>
<td>89/115 (77%)</td>
</tr>
</tbody>
</table>

Can Antibiotic Resistance Explain the High Failure Rates seen with BV

119 women
90% previously diagnosed with BV

Randomized to Clindamycin ovules or Metronidazole
Clinical efficacy similar at 7-12d post treatment and 35-45d
Evaluated for susceptibility to Metronidazole and Clindamycin

Antibiotic Resistance After Treatment

Clindamycin resistance *is common*
53% after clindamycin therapy
Metronidazole resistance *is rare*

Antibiotic resistance did not predict clinical failure but clindamycin resistance is concerning
**BV – New Therapies**

Oral and intravaginal therapy equal
New vaginal gel (MVG 1.3%)

Phase 2 trial

1 Day 3 Day and 5 Day treatment all had higher therapeutic cure rates!

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**Recurrent BV – Peroxide Douche?**

$\text{H}_2\text{O}_2$ producing lactobacilli continually produce low levels of $\text{H}_2\text{O}_2$, reacts with myeloperoxidase and Cl- to form hypochlorous acid

Simply adding $\text{H}_2\text{O}_2$ causes short-term disinfection but **DOES NOT** restore normal balance

$\text{H}_2\text{O}_2$ LB are killed by ↑ concentration of peroxide

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**What about Probiotic Lactobacilli?**

**Women colonized by $\text{H}_2\text{O}_2$ LB are less likely to develop BV**

Following BV treatment - 50% of women are colonized with $\text{H}_2\text{O}_2$ producing LB

Application of $\text{H}_2\text{O}_2$ LB vaginally ↑ colonization and ↓ recurrent BV
LEAF Study
Randomized trial of probiotic vaginally BID x3d versus placebo
BV at enrollment and were treated with single 2g oral metronidazole

One month follow-up
Analyzed Colonization with probiotics
H₂O₂ production by endogenous lactobacillus in each group
Treatment efficacy

LEAF Study Results
If H₂O₂ lactobacilli were present - anaerobes were suppressed

Use of probiotics *suppressed endogenous recolonization by lactobacilli*

Suppressed women are **MORE LIKELY** to get recurrent BV

Lactobacillus GR-1 and RC-14 vs Metronidazole gel

Nigeria
HIV concerns

2 groups 20 in each group
Symptoms at 30 days
Lactobacillus group 12%
Metronidazole group 33%
**Metronidazole Gel for Recurrent BV**

157 women - All with recurrent BV
5g Metronidazole gel vaginally qhs x10d
Reevaluated → 88% efficacy
“Cured” subjects randomized to Metronidazole gel versus placebo applied 2 nonconsecutive nights for 16 weeks

All observed an additional 12 weeks

<table>
<thead>
<tr>
<th>Metronidazole Gel for Recurrent BV</th>
<th>Gel</th>
<th>Placebo</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prophylactic phase (16 weeks)</td>
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<tr>
<td>Clinical</td>
<td>26%</td>
<td>59%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Observation Phase (12 weeks)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical</td>
<td>51%</td>
<td>75%</td>
<td>0.02</td>
</tr>
</tbody>
</table>

**Counseling for Recurrent BV**

Abstain from vaginal sex during treatment

Do not douche

Taking a longer course of therapy (10-14) is needed

Use condoms first month following treatment
Counseling for Recurrent BV

Clean all sex toys before and after use

Avoid vaginal insertion following anal insertion of fingers or toys

Consider suppressive therapy but remember relapse rate is high

No value in treating partners
Case Studies

- 24 year old
- Complains of malodorous, yellow discharge and slight dysuria
- One week
- No STI
- except Trich one year ago
- Last exam one year ago

Physical exam

- Normal vitals
- EGBSU normal
- Vagina pink with frothy, yellow, malodorous discharge
- Normal bimanual exam
Differential diagnosis

What tests would you order?
Saline wet mount, whiff, pH, GCC

Lab Results

- pH 6.0
- Many motile trichomonads, no clue cells
- Negative KOH

What is the first line CDC treatment?

- Metronidazole 2 grams orally in a single dose
- Her partner should be treated
- Abstain from intercourse until partner is treated (7 days)
Follow up

- Patient returns 3 weeks later
- Same symptoms
- Wet mount - same
- What next?

Common reason for treatment failure is reinfection

Metronidazole 500 mg orally twice daily for 7 days or tinidazole 2 g orally single dose.

If treatment failure of either of these regimens, consider retreatment with tinidazole or metronidazole 2 g orally once a day for 5 days.
If repeated treatment failures occur, contact the Division of STD Prevention, CDC, for metronidazole-susceptibility testing.

telephone: 404-718-4141
website: www.cdc.gov/std