Financial Disclosures

• None
Case

• 32 y/o African American female calls your office complaining of malodorous vaginal discharge and is concerned she has another bacterial vaginosis infection. This will be her 6th infection this year. She admits that she has been using intravaginal petroleum jelly in hopes that it would prevent infections. She is sexually active with a male partner and inconsistently uses condoms for birth control. She is frustrated that this keeps happening to her. She is asking you to call in an antibiotic. She also has several questions for you.

• 1) Why does she keep getting these infections?
• 2) Should her partner be treated as well?
Outline

• Prevalence
• Risk Factors and Associations
• Is BV an STI?
• Psychosocial Impact
• Home Remedies
• Protective Measures
• Presentation, Diagnosis, Treatment and Pathophysiology of BV
• Definition of Recurrent BV and suppressive therapy
• Theories Recurrences
• Partner treatment
• Challenges in research
• Emerging Therapies
Objectives

• Identify risk factors and home regimens
• Review appropriate diagnosis and management
• Discuss pathophysiology, theories of recurrence and challenges in research
Why Should We Care?

10-30% of the female population

1/3 of the female population

21 million women

Worldwide prevalence between 10-50%

Most common cause of vaginal discharge in the United States

5-10 million clinic visits annually in USA

Cost of over $1 billion each year in USA
Psychosocial distress, decreased quality of life and financial burden for patients.

Numerous health risk factors associated with bacterial vaginosis.
Risk Factors and Associations

- Demographics
- Lifestyle
- Sexual Practices
- Hygiene Practices
- Menstrual
- Other
Risk Factors and Associations

Demographics
- Reproductive Age
- African-American, Hispanic, Native America
- Sex workers, HIV-positive populations, women who have sex with women
- Higher BMI, prior pregnancy,
- Low social economic status
- Low education level

Sexual Practices
- Young age of first intercourse
- New sexual partner
- Multiple sex partners
- Unprotected intercourse
- Uncircumcised male
- Sharing sex toys
- Presence of other STIs
- Exposure to same pre/post treatment regular sex partner

Lifestyle
- Smoking
- Alcohol
- Drug Use
- Stress

Hygiene Practices
- Douching
- Tub baths
- Improper hygiene
- Intravaginal cleansing

Other
- IUD
- Previous BV infection
- Recent antibiotic use

Menstrual
- <3 or >35 days
- Dysmenorrhea
Is Bacterial Vaginosis an STI?

• **NO**
  - No causative/transmissible agent has been identified
  - Absence of disease counterpart in males

• “sexually associated” and “sexually facilitated”
  - BV associated bacteria can be found in male genitalia
  - Strongly associated with penile-vaginal sex
  - Rare in women only engaging in noncoital practices
  - Absent in women reporting no sexual contact
Psychosocial Impact

- confused
- self blame
- helplessness
- dirty
- ashamed
- estimated
- immoral
- frustrated
- lack of control
- isolated
- disappointed
- fearful
- deviant
- self-concious
- annoyed
- Worry
Home Management and Regimens

• Douching
• Intravaginal insertion of petroleum jelly, yogurt, or garlic
• Insertion of tampons soaked with various products
• OTC yeast infection treatments or antiseptic cream
• Manual vaginal washing

• Salt or vinegar bathes
• Avoiding hot baths, perfumed soaps or soaps in general
• Avoiding tight clothing
• Reduced alcohol intake
• Increase exercise
• Sanitary products, perfumes or deodorants
• Cotton underwear
• Oral yogurt or probiotics
70% sexual lubricants

81% of women reported either washing the inside of their vagina or inserting an over-the-counter product (other than a tampon) into their vagina over the past year

49% of women reported inserting an OTC product (other than tampons) inside the vagina over the past month

17% petroleum jelly

13% oils

20% antifungals
What Factors Are Protective?

• Higher level of education and knowledge of STIs
• Consistent condom use
• Estrogen–containing OCPs
• Male circumcision
Presentation

- Mild-to-moderate discharge
- Fishy odor
  - worse after intercourse and menses
- Little to no vulvovaginal irritation
- Occasional mild abdominal discomfort

- Discharge caused by BV is mildly adherent to the vaginal walls
- Vaginal walls do not appear inflamed
- Endocervix is unaffected
# Diagnostic Tools

<table>
<thead>
<tr>
<th>Nugent criteria</th>
<th>Amsel Criteria</th>
<th>Vaginal Fluid sialidase activity (OSOM BVBLUE Test)</th>
<th>DNA hybridization probe analysis (Affirm VP III)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Gold Standard</td>
<td>• Clinically used</td>
<td>• Chromogenic test based on sialidase produced by</td>
<td>• DNA probe testing specifically identifies</td>
</tr>
<tr>
<td>• Research</td>
<td>• Sensitivity 90-92%</td>
<td>anaerobic bacteria</td>
<td>Gardnerella vaginalis vs. Trichomonas vaginalis</td>
</tr>
<tr>
<td>• Sensitivity 83%</td>
<td>• Specificity 77%</td>
<td>• Sensitivity 88%</td>
<td>and Candida albicans based on DNA</td>
</tr>
<tr>
<td>• Specificity 92</td>
<td></td>
<td>• Specificity 95-97%</td>
<td>• Sensitivity 90%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Specificity 68%</td>
</tr>
</tbody>
</table>
**Nugent Criteria - Gold standard/Research**

**TABLE 2**

<table>
<thead>
<tr>
<th>Lactobacillus morphophytes</th>
<th>Gardnerella and Bacteroides spp. morphophytes</th>
<th>Curved gram-variable rods</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>4+</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3+</td>
<td>1+</td>
<td>1+ or 2+</td>
<td>1</td>
</tr>
<tr>
<td>2+</td>
<td>2+</td>
<td>3+ or 4+</td>
<td>2</td>
</tr>
<tr>
<td>1+</td>
<td>3+</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>0</td>
<td>4+</td>
<td></td>
<td>4</td>
</tr>
</tbody>
</table>

Review each of the first 3 columns in turn, assigning points at far right according to your exam findings. Add the points for all 3 columns for a final sum. A score of 7 or higher indicates bacterial vaginosis. Source: Nugent et al 1991.
Amsel Criteria- Clinically Used

Table 3. Amsel Criteria for Diagnosis of BV: Three of the following four criteria must be met. Establishes accurate diagnosis of bacterial vaginosis in 90% of affected women.

1) Homogeneous, non-clumping vaginal discharge (color and amount may vary)

2) Amine (fishy) odor when potassium hydroxide solution is added to vaginal secretions (commonly called the "whiff test")

3) Presence of clue cells (greater than 20%) on microscopy

4) Vaginal pH greater than 4.5
A) Normal vaginal epithelial cells

B) Clue cells with coccobaccilli
Diagnosis via Telephone?

- **3.2%** of patients with *no prior history* of bacterial vaginosis accurately diagnosed themselves.

- **4.4%** of patients *with prior history* of bacterial vaginosis accurately diagnosed themselves.
Bacterial Vaginosis on PAP Smear

- Per ACOG PAP test is an unreliable tool for diagnosing bacterial vaginosis
Treatment

- Metronidazole 500mg PO BID for 7 days
- Clindamycin 300mg PO BID for 7 days
- 0.75% metronidazole gel once daily for 5 days
- 2% clindamycin cream once daily for 7 days
- Clindamycin ovules 100mg intravaginally once at bedtime for 3 consecutive nights
- Tinidazole 2g PO for 3 days of 1g PO for 5 days
- **70-80% cure rate at 1 month follow-up**
Recurrent Bacterial Vaginosis

• Definition
  • 3 or more episode of bacterial vaginosis per year

• Prevalence
  • 30-50% recurrence rate after 2-3 months
Disruption of normal vaginal flora

Pathogenic shift and polymicrobial overgrowth of anaerobic bacterial flora:
- Gardnerella vaginalis
- Prevotella species
- Mobiluncus
- Atroplubium vaginae
- Mycoplasma

Formation of biofilms
Theories for Recurrence

- **Persistence** of pathogenic bacteria
- **Reinfection** from exogenous sources including sexual partner
- **Lack of recolonization** of lactobacillus flora
- **Lack of adherence** to therapeutic course secondary to side effects or cost
“Should my partner be treated?”

- CDC says NO

- Treatment **DOES NOT** prevent BV recurrence

- Female partner **should be evaluated** and treated appropriately
Suppression Therapy

- Nocturnal application of topical metronidazole 2 nights a week for 6 months
  - prevent significant regrowth of anaerobic bacteria but does not help create therapeutic lactobillus-dominant environment
- BV treatment followed by boric acid 600mg daily for 21 days and suppressive 0.75% metronidazole gel twice weekly for 4-6 months
- Monthly oral metronidazole 2g with fluconazole 150mg
Health Risk Associated with Bacterial Vaginosis

Pelvic Inflammatory disease
- Infertility
- Ectopic pregnancy
- Chronic pelvic pain

HIV Transmission

STI
- 2 fold increase risk of STI
- HIV, HPV, chlamydia, gonorrhea, syphilis

Surgical Complications
- Post hysterectomy cuff cellulitis
- Postabortal infection

OB complications
- Pregnancy loss
- Preterm birth
- PROM
- Chorioamnionitis
- Endometritis
- Low birthweight
Research Challenges

• Lacking and lagging
• Limited research--recurrent BV
• International studies
• Different diagnostic criteria
• Different treatment dosing
• Global studies--conflicting risk factors
• In vitro cultures for G vaginalis
  • limited utility
  • cultures in almost all women with symptomatic infection are positive, 50% of the cultures from healthy asymptomatic women are also positive
• Lack of a suitable animal model
Emerging Therapies

• Adjuvants of antibiotic therapy
• Plants and Plant Extracts
• Probiotics
• Antimicrobial peptides
Case

44 year old Hispanic female presents with malodorous vaginal discharge. After proper office evaluation, you diagnose her with BV. Several new therapies are available which would you recommend?

a) EcoVag with metronidazole
b) Vitamin C with metronidazole
c) L. acidophilus and rhamnosus with tinidazole and metronidazole
d) Vitamin D with metronidazole
e) Subtilosin with metronidazole

In vivo

Long term cure against BV

Reduced BV recurrence from 32.4% to 16.2%

Side effects: burning, itching, skin irritation, candidiasis and bronchitis

In vitro

Synergized with metronidazole against biofilms of G. vaginalis but no biofilms-associated vaginal lactobacilli
### Areas of Research and Emerging Therapies

<table>
<thead>
<tr>
<th>Adjuvants of Antibiotic Therapy</th>
<th>In vivo</th>
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<tbody>
<tr>
<td>EcoVag with clindamycin or metronidazole</td>
<td>Long term cure against BV</td>
</tr>
<tr>
<td>L. Acidophilus &amp; L bifidus with metronidazole</td>
<td>Low recurrence rate after 3 month-BV treatment</td>
</tr>
<tr>
<td>L. Acidophilus &amp; rhamnosus with tinidazole and metronidazole</td>
<td>Reduction of BV recurrence; recolonization of vagina with lactobacilli</td>
</tr>
<tr>
<td>L casei var rhamnosus with metronidazole</td>
<td>Increase in clinical and microbiological efficacy of antibiotic therapy and restore microbial balance in vaginal ecosystem</td>
</tr>
<tr>
<td>L rhamnosus BMX54 with metronidazole</td>
<td>Significantly replace of BV associated flora</td>
</tr>
<tr>
<td>L. rhamnosus, L acidophilus, S. thermophiles &amp; L. bularicus with metronidazole</td>
<td>Recurrence rate of 30%</td>
</tr>
<tr>
<td>Miconazole with metronidazole</td>
<td>Reduced BV during 12 month follow-up</td>
</tr>
<tr>
<td>Vitamin C with metronidazole or clindamycin</td>
<td>Reduction of BV recurrence (32.4% to 16.2%) side effects include burning, itching, skin irritation, candidiasis and bronchitis</td>
</tr>
<tr>
<td>Vitamin D with metronidazole</td>
<td>BV recurrence not reduced</td>
</tr>
</tbody>
</table>
Areas of Research and Emerging Therapies

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<tr>
<th>Adjuvants of Antibiotic Therapy</th>
<th>In vitro</th>
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<tr>
<td>Lauramide arginine ethyl ester (LAE) with clindamycin</td>
<td>Synergized with clindamycin against biofilms of <em>G. vaginalis</em> but not biofilm-associated vaginal lactobacilli</td>
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<td>Subtilosin with clindamycin</td>
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<td>Synergized with metronidazole against biofilms of <em>G. vaginalis</em> but not biofilm-associated vaginal lactobacilli</td>
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</table>
Case

- 23 year old female who is allergic to metronidazole and cannot tolerate clindamycin presents with vaginal discharge consistent with BV. She is interested in natural plant-based BV treatments. Which one would you recommend?

a) Extracts of Brazilian pepper tree
b) Garlic tablet
c) Zataria multiflora

C) Zataria multiflora

In Vivo
High Cure rate
## Areas of Research and Emerging Therapies

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<tr>
<th>Plants and Plant Extracts</th>
<th>In Vivo</th>
<th></th>
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<tr>
<td>Extracts of Brazilian pepper tree</td>
<td>Low cure rate</td>
<td></td>
</tr>
<tr>
<td>Garlic tablet</td>
<td>Moderate cure rate</td>
<td></td>
</tr>
<tr>
<td>Zataria multiflora</td>
<td>High cure rate</td>
<td></td>
</tr>
<tr>
<td>In Vitro</td>
<td></td>
<td></td>
</tr>
<tr>
<td>19 plant extracts tested</td>
<td>7 plant extracts showed antimicrobial activity</td>
<td></td>
</tr>
<tr>
<td>Seaweed extract</td>
<td>Extracts of seaweed Ulva pertusa displayed strongest activities against G vaginalis</td>
<td></td>
</tr>
</tbody>
</table>
### Areas of Research and Emerging Therapies

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<th>Probiotics</th>
<th>In vivo</th>
</tr>
</thead>
<tbody>
<tr>
<td>L crispatus DM8909</td>
<td>High cure rate 30D after beginning BV treatment</td>
</tr>
<tr>
<td>L fermentum LF15 and L plantarum LP01</td>
<td>Lactobacilli significantly reduced the nugent score</td>
</tr>
<tr>
<td>L rhamnosus GR-1 and L reuteri RC 14</td>
<td>Normal vaginal microbiota were present in more than half of patients</td>
</tr>
<tr>
<td>VSL3</td>
<td>Absent of vaginal discharge; reduction of itching and leukorrhea</td>
</tr>
<tr>
<td><strong>In Vitro</strong></td>
<td></td>
</tr>
<tr>
<td>L fermentum LF15</td>
<td>Reduced nugent score below threshold of 7</td>
</tr>
<tr>
<td>L fermentum LF23</td>
<td>Inhibited growth of G. vaginalis</td>
</tr>
<tr>
<td>L fermentum SK5</td>
<td>Inhibit pathogenic microorganisms</td>
</tr>
</tbody>
</table>
# Areas of Research and Emerging Therapies

<table>
<thead>
<tr>
<th>Antimicrobial Peptides In Vitro</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Fermenticin HV6b</td>
<td>Inhibition of G. Vaginalis; immobilization and spermicidal activity</td>
</tr>
<tr>
<td>Retrocyclin</td>
<td>Inhibited pathogenic vaginal bacteria</td>
</tr>
</tbody>
</table>
### Areas of Research and Emerging Therapies

<table>
<thead>
<tr>
<th>Other In Vivo</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin C</td>
<td>Improves abnormal vaginal pH and microflora but it is not well tolerate</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>Moderate cure rate (63.5%) effective in eliminating asymptomatic BV</td>
</tr>
<tr>
<td>Octenidine dihydrochloride spray application</td>
<td>High initial cure rate Moderate cure after 12 m post-BV treatment Complete resistance in some patients</td>
</tr>
<tr>
<td>Estriol vaginal tables and prebiotic lactoferrin</td>
<td>Recolonization of vagina with lactobacilli detected after 1m to start the treatment</td>
</tr>
<tr>
<td>In Vitro</td>
<td></td>
</tr>
<tr>
<td>DNAase</td>
<td>50% inhibition of biofilms</td>
</tr>
<tr>
<td>Subtilosin within covalently cross-linked polyethylene glycol based hydrogels</td>
<td>Inhibit growth of G vaginalis</td>
</tr>
<tr>
<td>Benzoyl peroxide formulated polycarbophil/carbopol 934P hydrogel</td>
<td>Inhibition of growth of G. vaginalis; limited effect on lactobacilli</td>
</tr>
</tbody>
</table>
Take Away Points

• Health burden (USA and Global)
• Ask about home remedies and regimens
• Patient education--risk factors
• Support the psychosocial aspects
• Bring to the office
• Male partners do NOT need to be treated
• More research is needed for emerging therapies
Resources

- Clinical Key
- ACOG Practice Bulletin
- AAFP
- CDC website
- Conn's Current Chapter on BV
- Comprehensive Gynecology Chapter on BV
- Goldman-Cecil Chapter on BV
- Roberts and Hedges’ Clinical Procedures in Emergency Medicine and Acute Care, Seventh Edition chapter on BV
- Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, Updated Edition, Eighth Edition Chapter on BV
- 2015 STD Treatment Guidelines Section on BV
Resources – PubMed Articles

Recurrent vulvovaginitis
Best Practice & Research Clinical Obstetrics and Gynecology
Anna Powell MD, Paul Nyirjesy MD

Experts explore the state of bacterial vaginosis and the unmet needs facing women and providers
Gynecology and Obstetrics
Steven Chavoustie, Scott Eder etc.

Women’s Management of Recurrent Bacterial Vaginosis and Experiences of Clinical Care: A Qualitative Study
PLOS
Jade Bilardi, Sandra Walker, etc.

Women’s Views and Experiences of the Triggers for Onset of Bacterial Vaginosis and Exacerbating Factors Associated with Recurrence
PLOS
Jade Bilardi, Sandra Walker, etc.
The Burden of Bacterial Vaginosis: Women’s Experience of the Physical, Emotional, Sexual and Social Impact of Living with Recurrent Bacterial Vaginosis
PLOS
Jade Bilardi, Sandra Walker, etc.

High Recurrence Rate of Bacterial Vaginosis over the Course of 12 months after oral metronidazole therapy and factors associated with recurrence
Journal of Infectious Diseases
Catriona Bradshaw, Anna Morton, etc.

Evidence of African-American women’s frustrations with chronic recurrent bacterial vaginosis
American Academy of Nurse Practitioners
Sandra Payne, Pamela Cromer, etc.

Recurrence of bacterial vaginosis is significantly associated with posttreatment sexual activities and hormonal contraceptive use
Catriona Bradshaw, Lenka Vodstrcil, etc.

A blinded, randomized controlled trial of high-dose vitamin D supplementation to reduce recurrence of bacterial vaginosis
AJOG
Abigail Norris Turner, Patricia Carr Reese etc.
Intravaginal practices and risk of bacterial vaginosis and candidiasis infection among a cohort of women in the United States
Joelle M. Brown, Kristen L Hess etc.

Prevalence and Risk Factors for Bacterial Vaginosis and Other Vulvovaginitis in Population of Sexually Active Adolescents from Salvador, Bahia, Brazil
Rita Elizabeth Moreira Mascarenhas, etc.

Prevalence of and risk factors for bacterial vaginosis among women of reproductive age attending cervical in southeastern Brazil
Camila Marconi, Marli T.C. Duarte etc

Risk of associated with bacterial vaginosis in infertility patients: a systematic review and meta-analysis
Noortje van Oostrum, Petra De Sutter etc

Sexual Risk Factors and bacterial vaginosis: a systematic review and meta-analysis
Clinical Infectious Disease
Katerine A. Fethers, Christopher Fairley, etc
Resources – PubMed Articles

Finding associated with recurrence of bacterial vaginosis among adolescents attending sexually transmitted disease clinics
Journal Pediatric Adolescents Gynecology
Rebecca M. Brotman, Emily J. Erbelding etc

Risk factors for bacterial vaginosis: results from a cross-sectional study having a sample of 53,652 women
X.-D. Lim C.-C. Wang etc

Aetiology & risk factors of recurrent vaginitis & its association with various contraceptive methods
Jyoti Thulkar, Alka Kriplani etc

Behavioral and medical predictors of bacterial vaginosis recurrence among female sex workers: longitudinal analysis from a randomized controlled trial
BMC Infectious Disease
Fernand A. Guedou, Lut Van Damme etc.

Cochrane Library Antibiotic Treatment for the sexual partners of women with bacterial vaginosis (review)
Resources – PubMed Articles

Bacterial vaginosis: a synthesis of the literature on etiology, prevalence, risk factors and relationship with chlamydia and gonorrhea infections
Christian T. Bautista, Eyako Wurapa etc.

The influence of behaviors and relationships on the vaginal microbiota of women and their female partners: the WOW Health Study
Catriona Bradshaw, Sandra Walker etc.

Cochrane Library Probiotics for the treatment of bacterial vaginosis (review)

Suppressive antibacterial therapy with 0.75% metronidazole vaginal gel to prevent recurrent bacterial vaginosis
Jack Sobel, Daron Ferris etc.

Bacterial vaginosis: A practical review
Paulette Bagnail Denise Rizzolo etc.

Managing Recurrent Bacterial Vaginosis: Insights for Busy Providers
Alison Marshall
Resources – PubMed Articles

Current Treatment of Bacterial Vaginosis---Limitation and Need for Innovation
Catriona Bradshaw, Jack Sobel

The global epidemiology of bacterial vaginosis: a systemic review
AJOG
Chris Kenyon Robert Colebunders

Risk of Bacterial Vaginosis in Users of the Intrauterine Device: A longitudinal Study
Tessa Madden, Jaclyn Grentzer

Effects of Probiotics on the Recurrence of Bacterial Vaginosis: A Review
Aiz Homayouni, Parvin Bastani etc.

Differences in vaginal microbiome in African American women versus women of European ancestry
Microbiology
Jennifer Fettweis, Paul Brooks
Resources – PubMed Articles

Evaluation of Health Disparity in Bacterial Vaginosis and the Implications for HIV-1 Acquisition in African American Women
Donald J. Alcendors

Can one size fit all? Approach to bacterial vaginosis in sub-Saharan Africa
Zenda Woodman

Best Practices to Minimize Risk of Infection With Intrauterine Device Insertion
Sheila Caddy, Mark Yudin etc.


Short- and long-term influence of the levonorgestrel-releasing intrauterine system (Mirena®) on vaginal microbiota and Candida.