NORTHWEST AIDS EDUCATION AND TRAINING CENTER

Diagnosis and Management of Vaginitis

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Acknowledgment

- Jeanne M. Marrazzo, MD, MPH

Patient History

28 y.o. African American woman with HIV (on HAART) calls you on the phone because she has noted increased vaginal discharge for about a week.

No history of known STD.

She has a new male sex partner.

She smokes one pack of cigarettes/day.

More history

- She says that she sometimes has a lot of genital itching
- She has noted some whitish discharge at times
- Unsure about foul odor
- She says “this feels JUST like a yeast infection. I know because I have had a few before.”

What are your thoughts?

1. She probably has a reliable sense of her symptoms and you ought to call in a prescription for fluconazole
2. She probably has bacterial vaginosis and so, you will call in a prescription for metronidazole
3. Both she and her partner need testing
4. All of the above
5. None of the above

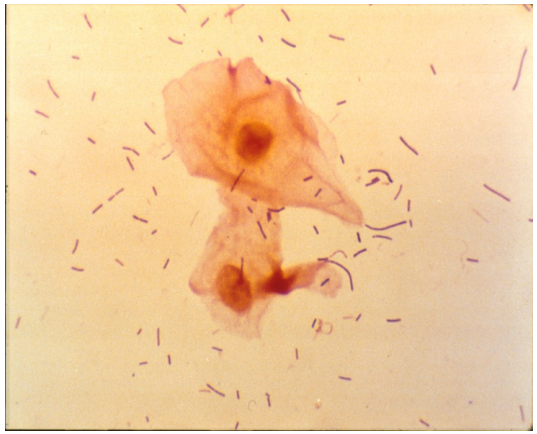
Bacterial Vaginosis: Clinical & Epidemiologic Features

- The most common cause of vulvovaginal complaints
  - 29% in population based survey in the U.S.
  - Exceedingly prevalent in areas of the world with highest HIV incidence (sub-Saharan Africa)
    - >50% in rural Ugandan villages
- Generally responds to anti-anaerobic treatment, but
  - 15% to 20% of women fail initial treatment
  - Even with initial treatment response, subsequent recurrence rates are very high (75% over one year)

Brotman 2007, Allsworth 2009, Johnson 2011, Bradshaw 2008; Sobel 2008, Marrazzo 2010

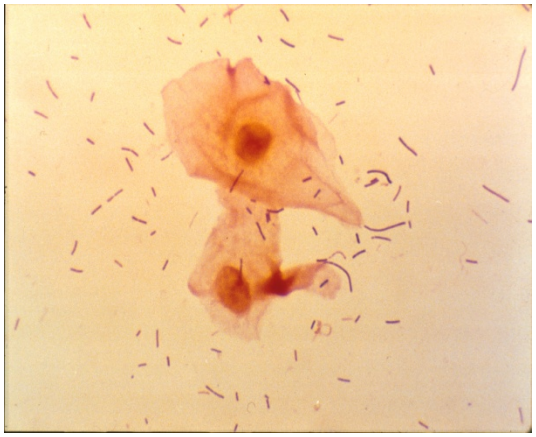
Key Features of Normal Vaginal Environment

- Normal pH <4.7:
  - Maintained by dominant vaginal bacteria, Lactobacillus, that produce lactic acid
  - Favors growth of lactobacilli and inhibits growth of other organisms (residents and invaders)

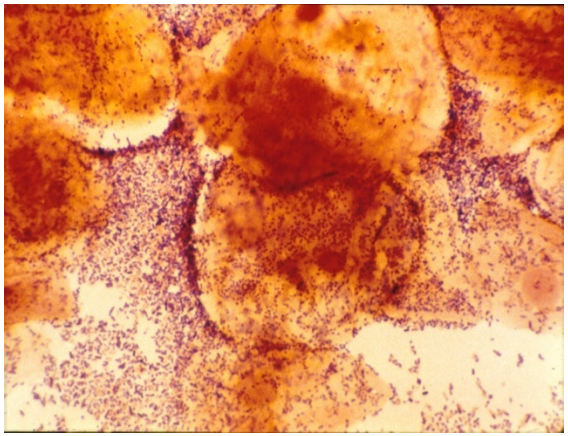


- Human lactobacilli
  - Major species: L. crispatus and L. jensenii
  - Need to produce hydrogen peroxide (H2O2) for maximal benefit

The Vaginal Milieu in Bacterial Vaginosis



Nugent = 0



Nugent = 10

- Profound loss of H_2O_2 - producing *Lactobacilli*
- Overgrowth of "commensal" anaerobes, especially *Gardnerella vaginalis*, BVAB1, BVAB2, BVAB3, Megasphaera, Atopobium
- Production of sialidase (IgA destruction), glycosidase, volatile amines
- ↑ Il-1B, IL-10; ↓ IL-8, SLPI (secretory leukocyte protease inhibitor)

Cauci 2004; Cherpes 2008; Fredricks 2007

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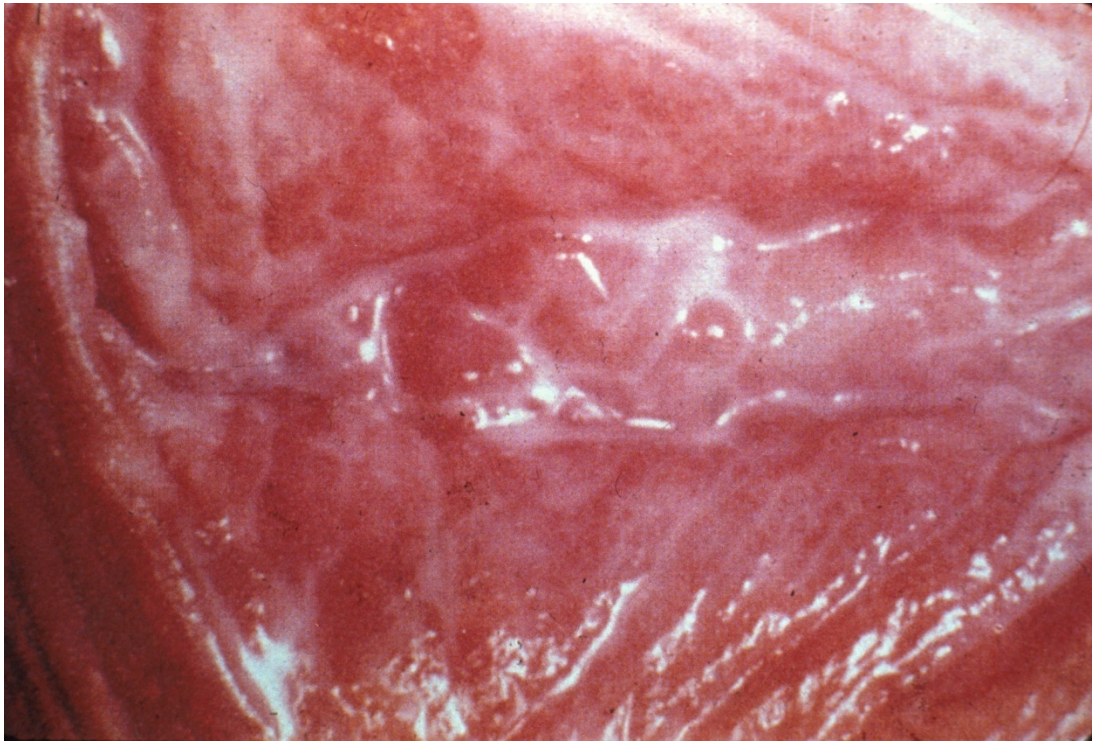
Diagnosis of Bacterial Vaginosis

- Clinical findings (Amsel criteria*): >3 of
  - homogeneous discharge
  - pH >4.5
  - clue cells (>20%)
  - amine odor on addition of KOH (+whiff test)

*No difference in performance in HIV+: Gallo *STD* 2011

Bacterial Vaginosis



Typical discharge: homogeneous, grey-white, uniformly adherent to vaginal epithelium

Bacterial vaginosis and HIV acquisition: a meta-analysis of published studies

Julius Atashili[a,b], Charles Poole[a], Peter M. Ndumbe[b], Adaora A. Adimora[a] and Jennifer S. Smith[a]

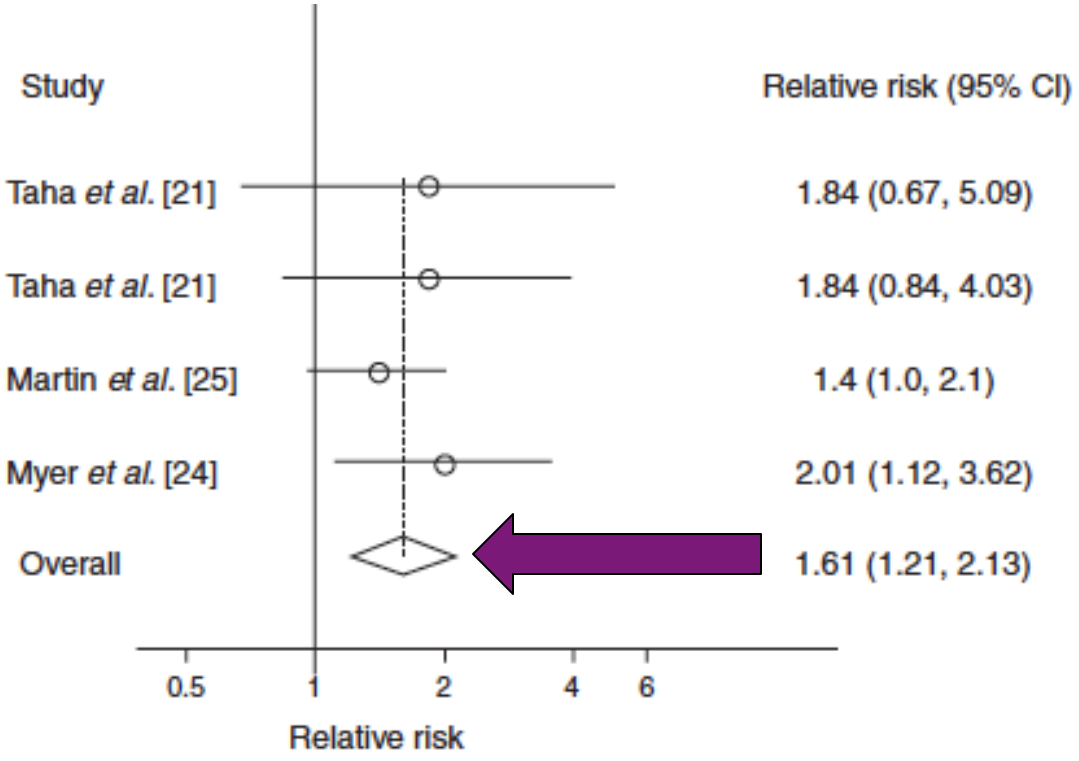


Fig. 1. Forest plot of relative risk estimates of incident HIV infection by bacterial vaginosis status, stratified by HIV-risk group. Studies are identified by the references. The horizontal lines represent the 95% confidence intervals (CI). Overall heterogeneity $P = 0.7$.

- Possible mediators
  - Loss of H2O2 (directly virucidal)
  - Activation of CD4 by alkaline pH
  - Upregulation of cytokines that promote local HIV replication (TNF-alpha, IL-1 beta)
  - Direct stimulation of HIV expression from T cells/monocytes by BV-associated bacteria

Atashili 2008

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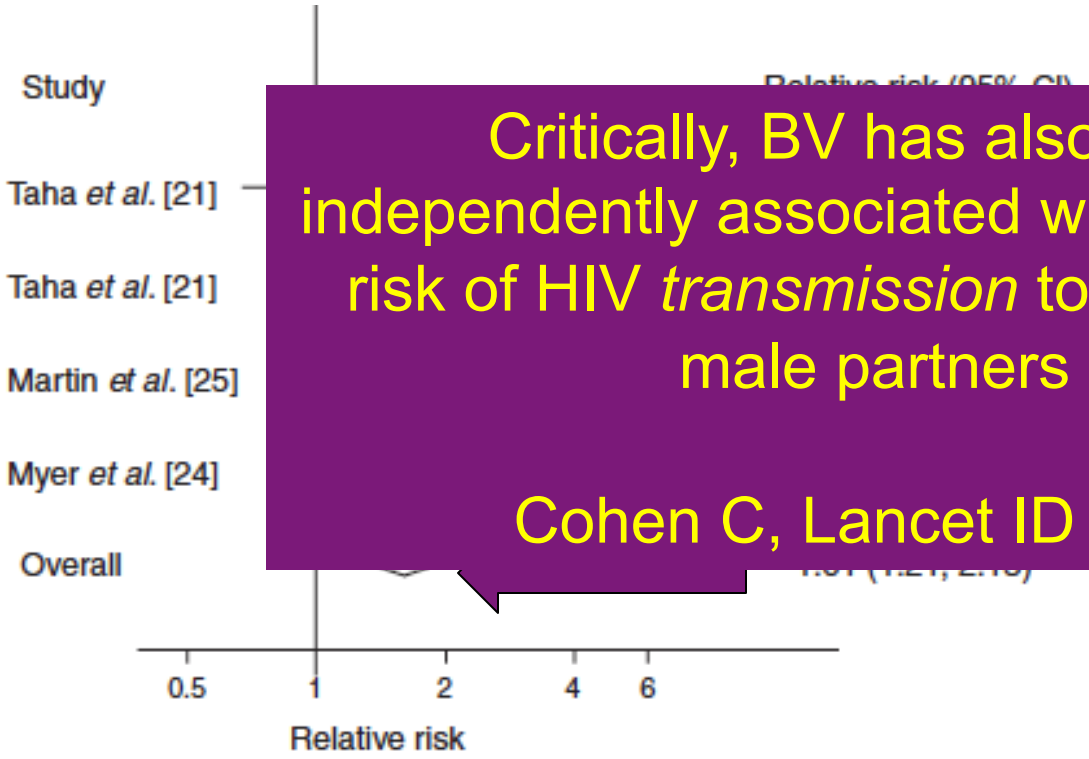

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Critically, BV has also been independently associated with increased risk of HIV *transmission* to uninfected male partners

Cohen C, Lancet ID 2012

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Atashili 2008

Your patient, 28 yo and with a single male sex partner, comes in with her third episode of symptomatic BV in six months. She is desperate. Which recommendation is supported by published evidence?

1. Suppressive metronidazole gel biweekly for 6 months
2. Nightly boric acid for 6 months
3. Intravaginal yogurt to replenish vaginal lactobacilli
4. Treat her boyfriend with a week of oral metronidazole
5. Find a new health care provider

Randomized, Placebo-controlled Trial of Metronidazole Gel for Recurrent BV Suppression

	Recurrence		
	Metro	Placebo	P
Prophylactic Phase (4 mo): twice weekly gel			
Clinical	13/51 (26%)	26/44 (59%)	<.001
Observation Phase (3 mo): off therapy			
Clinical	26/51 (51%)	33/44 (75%)	.02

Sobel AJOG 2006

Recurrent BV

- Randomized controlled trial with 450 women with BV. All were treated with standard week-long twice daily oral metronidazole with the addition of either:

  - Vaginal clindamycin 2% cream
  - Lactobacillus vaginal probiotic
  - Placebo cream

  RESULTS: cumulative 6-month BV recurrence was 28.2%; (95%CI 24.0-32.7%) with no difference between groups, p= 0.82.

Bradshaw CS et al. PLoS One 2012

After stratifying for treatment and adjusting for age and sex frequency

- Recurrence was associated with having the same pre-/posttreatment sexual partner (adjusted HR [AHR] = 1.9; 95% CI, 1.2-3.0) and inconsistent condom use (AHR = 1.9; 95% CI, 1.0-3.3)

- And **halved** with use of an estrogen-containing contraceptive (AHR = 0.5; 95% CI, .3-.8)

Bradshaw CS et al. CID 2013

2010 CDC STD Treatment Recommendations Bacterial Vaginosis

- Recommended
  - Metronidazole 500 mg PO bid x 7

  OR

  - Metronidazole gel 0.75% intravag qHS x 5 d

  OR

  - Clindamycin cream 2% intravag qHS x 7 d

2010 CDC STD Treatment Recommendations
Bacterial Vaginosis

Alternatives

- Tinidazole 2 g orally once daily for 2 days

OR

- Tinidazole 1 g orally once daily for 5 days

OR

- Clindamycin 300 mg orally twice daily for 7 days

OR

- Clindamycin ovules 100 mg intravaginally once at bedtime for 3 days

Tinidazole

- Second-generation nitroimidazole
- Elimination ½ life twice that of MTZ (12-14 h vs. 6-7 h)
- No alcohol during and 3 days after treatment
- Category C in pregnancy, don't use
- Efficacy in BV:
  - 1 gram daily x 5 days: 64%
  - 2 grams daily for 2 days: 46%
- Report of highly recalcitrant BV treated successfully with single course 500 mg bid x 14 days (Baylson 2004)

Conclusions

- Vaginitis is common and diagnosis warrants a clinical examination
- BV is associated with risk of HIV acquisition and transmission to uninfected male partners
- BV is often recurrent
- Some research showing strong association with sex partners and inconsistent condom use
- Interesting findings to suggest a protective role for estrogen based contraception