
VAGINITIS/CERVICITIS/ TRICHOMONIASIS



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Vaginitis

Case A:

- “Alyssa”: a 17 yo female runaway, on the streets for 6 mos living with her new boyfriend
- 10 days of “funny vaginal discharge” and mild abdominal pain
- Has never had an STD, has sex only with her boyfriend, she doesn’t think he has any symptoms or STDs.
- Engages in oral, vaginal and anal sex
- Not using birth control, LMP 6-8 weeks ago
- Only engaged in injection drug use once, shared boyfriend’s needle.

Even before you examine her, what is on your differential diagnosis list?

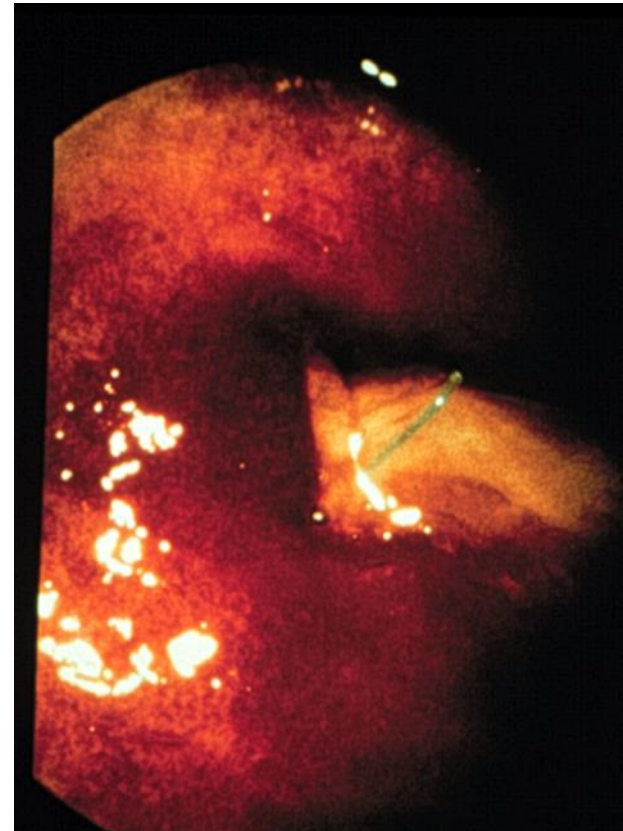
Funny Vaginal Discharge

- Cervicitis/Urethritis:
 - Chlamydia
 - Gonorrhea
 - (*Mycoplasma genitalium*)
- Vaginitis:
 - Bacterial Vaginosis
 - Trichomonas
 - Candidiasis
- PID

Other things to consider

- Sites of infection
- HIV
- HCV
- Pregnancy
- Co-morbidities
 - Drug use
 - Abuse
 - Psychiatric issues

Examination reveals



Vaginitis/Vaginal Infection

- Most women will have one during lifetime
- Symptoms: discharge, itching/irritation or odor
- Etiology:
 - Bacterial Vaginosis (40-45%)
 - Trichomonas (15-20%)
 - Vulvovaginal candidiasis (20-25%)

Clinical, economic issues

- Over six million health care visits each year are attributed to vaginitis
- Over one billion dollars are spent annually for the care and treatment of vaginitis

Back to Alyssa...

- On exam she has a vaginal discharge.
- Pregnancy test is POSITIVE.
- Wet prep of vaginal secretions shows...
 - pH of 6.0
 - Clue cells
 - +Whiff test
 - Motile trichomonads
 - No yeast

What can you diagnose her with based on the wet prep?

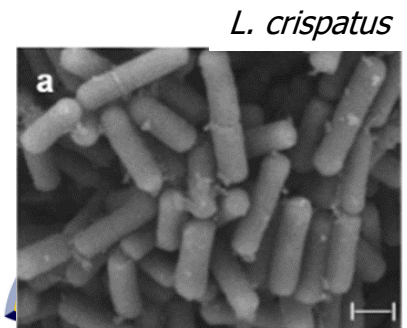
Diagnostic Criteria	Syndrome			
	Normal	Bacterial vaginosis	Candida vulvovaginitis	Trichomonas vaginitis
Vaginal pH	3.8-4.2	>4.5	≥ 4.5 (usually)	>4.5
Discharge	White, clear, flocculent	Thin, homogeneous, white, gray, adherent, often increased	White, curdy, "cottage Cheese" like, sometimes increased	Yellow, green, frothy adherent, increased
Amine odor (KOH "whiff test")	Absent	Present (fishy)	Absent	Present (fishy but not always)
Microscopic exam	Lactobacilli	Clue cells, coccoid bacteria, no WBCs	Mycelia, budding yeast, pseudohyphae with KOH	Trichomonads, WBCs >10/hpf
Main patient complaints	None	Discharge, bad odor, itching	Itching/burning, discharge	Frothy discharge, bad odor, vulvar pruritus, dysuria

Normal Vaginal Discharge

- Normal vaginal discharge is clear to white, odorless, and of high viscosity.
- Lactic acid helps to maintain a normal vaginal pH of 3.0 to 4.5.
- Acidic environment and other host immune factors inhibit the overgrowth of bacteria.
- Stratified squamous epithelial cells produce glycogen, due to estrogen stimulation → nourish lactobacilli.

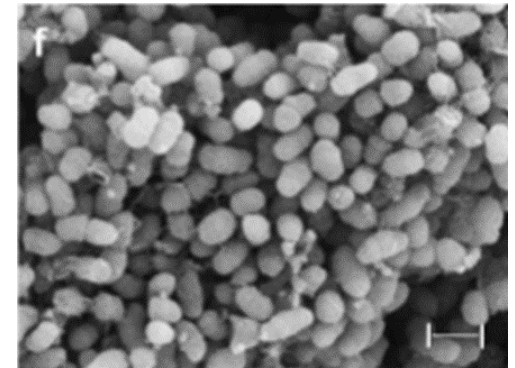
The Vaginal Microbiota (VMB)

- Communities of bacteria inhabiting the vagina
- Healthy VMB
 - *Lactobacillus* species → lactic acid → acidify the vagina
 - *L. crispatus*, *L. jensenii*, *L. gasseri*, *L. iners*
 - Protect against pathogens (STIs, *E. coli*)
 - pH, Bacteriocins, competitive binding
 - Immunomodulatory effects?



Bacterial Vaginosis

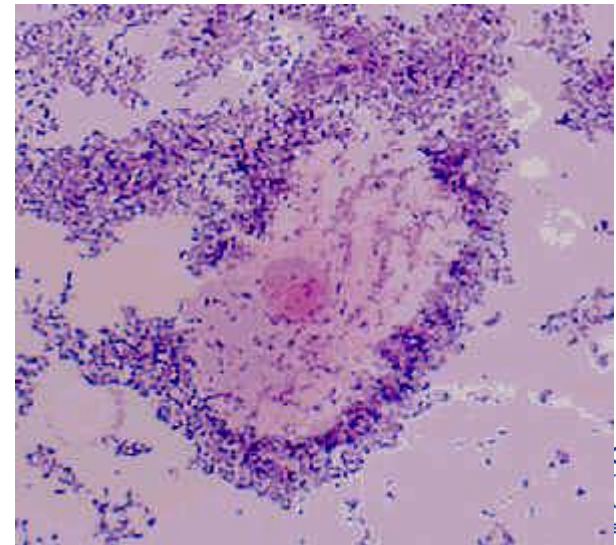
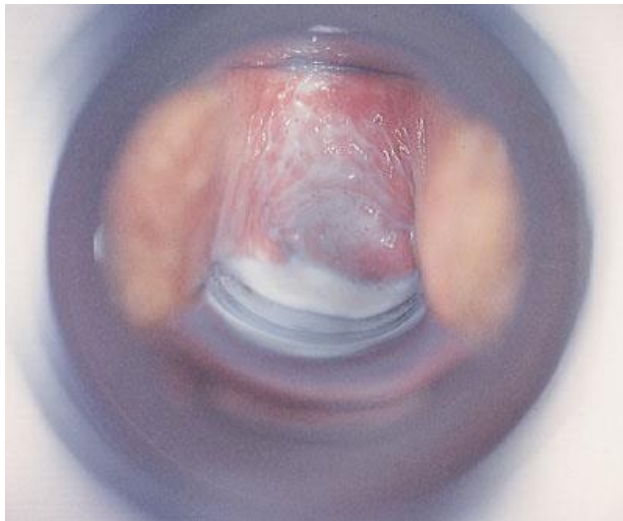
- In some women, lactobacilli replaced by an overgrowth of a variety of gram negatives/anaerobes
 - *Gardnerella vaginalis*,
Prevotella, *Mobiluncus* etc
- BV associated with
 - Inc risk acquisition TV, HSV, GC, CT
 - Inc risk acquisition & transmission of **HIV**
 - Inc risk preterm birth, chorioamnionitis.



G. vaginalis

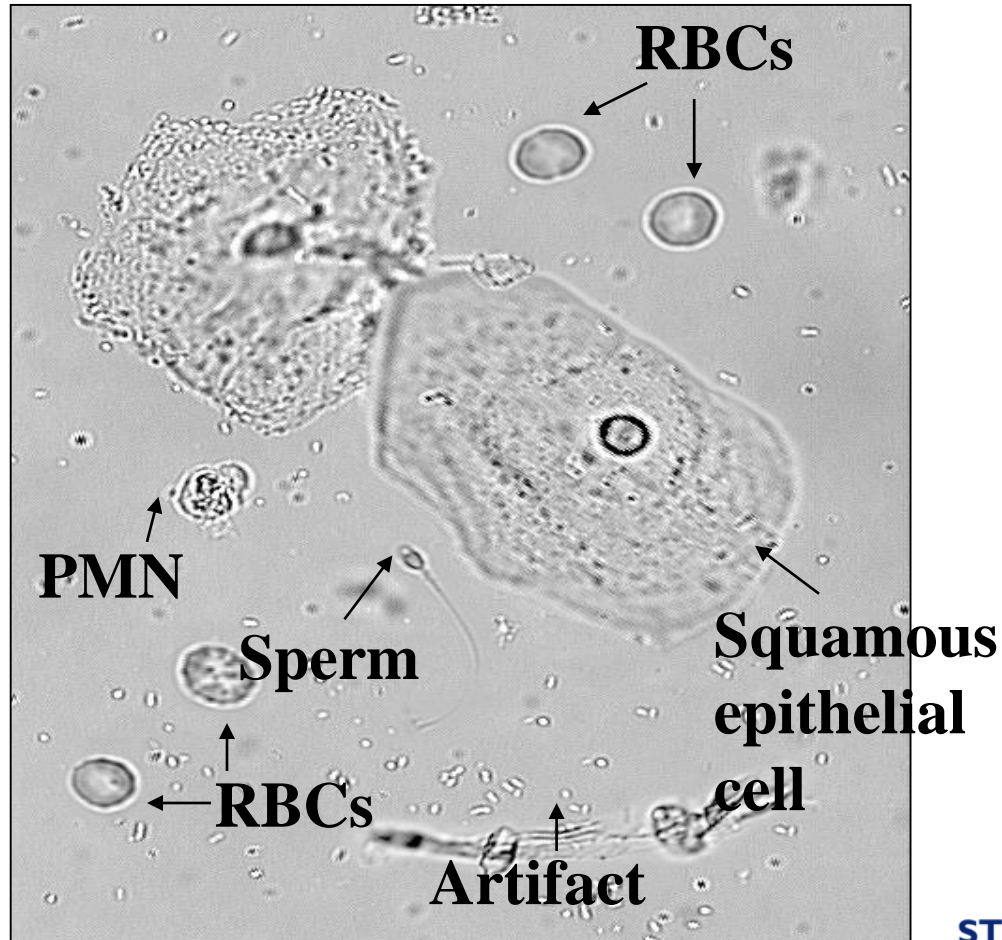
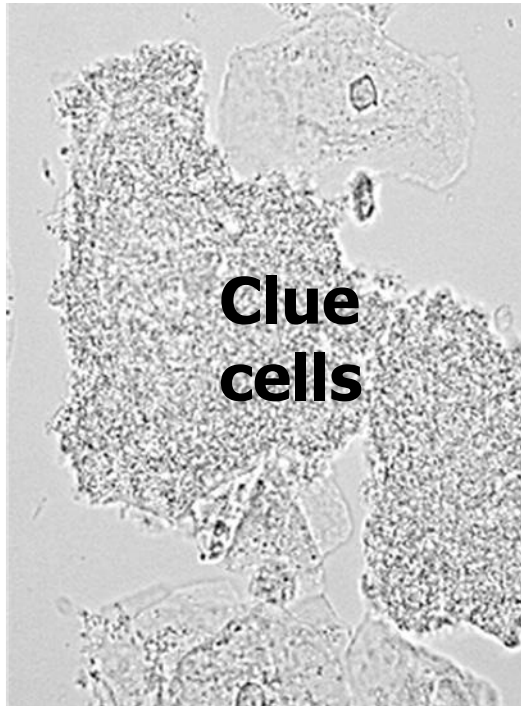
Bacterial Vaginosis

- Clinical Features- 47-50% asymptomatic
- Malodorous, thin adherent **vaginal discharge**, **pH>4.7**, **clue cells** >20% of epithelial cells, positive amine or **Whiff test**
- **Amsel's criteria**- 3 out of the above 4
- **Nugent's criteria**- quantifies the different bacteria present on gram stained vaginal fluid sample



Wet Prep: Common Characteristics

Saline: 40X objective



Source: Seattle STD/HIV Prevention Training Center at the University of Washington

Epidemiology of BV

- Most common dx for women coming in to STD clinics
- Many women asymptomatic.
- In study of 14-49yo US women:
 - BV prevalence: African-American 51%, Mexican Americans 32%, Caucasian 23%.
- Sexually associated (inc risk with inc # sexual partners and lack of barrier protection), but thus far insufficient evidence to treat partners.
- Douching? +/-

BV treatment

- Recommended for women with **symptoms**

BV	RECOMMENDED REGIMENS DOSE/ROUTE	ALTERNATIVE REGIMENS: To be used if medical contraindication to recommended regimen
Adults/ adolescents	Metronidazole 500 mg orally twice a day for 7 days or Metronidazole gel 0.75%, one full applicator (5g) intravaginally qd x 5 d or Clindamycin cream one full applicator (5g) intravaginally qhs x 7 d	Tinidazole 2 g po qd x 2 d or Tinidazole 1 g po qd x 5 d or Clindamycin 300 mg po bid x 7 d or Clindamycin ovules 100 mg intravaginally qhs x 3 d

(Note: no studies support the addition of any available lactobacillus formulations or probiotic as an adjunctive or replacement therapy in women with BV.)

Refrain from sex or use condoms during treatment; douching may increase relapse

A phase-3, double-blind, placebo-controlled study of the effectiveness and safety of single oral doses of secnidazole 2 g for the treatment of women with bacterial vaginosis

Jane R. Schwebke, MD; Franklin G. Morgan Jr, MD, FACOG; William Koltun, MD; Paul Nyirjesy, MD

- Secnidazole-2g po X1
- Modified intent-to-treat population, with clinical outcome responder rates of 53.3% (57/107) vs 19.3% (11/57; $P < .001$) vs. placebo
- Previous European data suggested not inferior to flagyl.
- Not better than placebo for women with ≥ 4 recurrences per year.
- Mix with pudding/applesauce

BV and Pregnancy

- Screening: Not recommended to screen in pregnancy
- Treatment of pregnant women: same as non-pregnant
 - NO association between metronidazole during pregnancy and teratogenic or mutagenic effects in newborns
 - Vaginal clindamycin also safe

Evidence is insufficient to recommend routine screening for BV in asymptomatic pregnant women at high or low risk for preterm delivery to prevent preterm birth.
(Ann Intern Med 208;148:214-219)

High Rates of BV Recurrence

- BV frequently persists/recurs after antibiotic treatment
 - 30% of women have symptomatic recurrence within 30-90 days, and 70% within 9 months
- Why? Suspected causative factors include:
 - failure to eliminate BV-associated organisms
 - re-inoculation with organisms from an outside source
 - i.e. sex partner or fomite (but thusfar efforts to treat partner have not been shown to improve response to therapy, relapse or recurrence.)
 - persistence of risk factors
 - i.e. intrauterine device, *douching*, lubricants
 - failure to re-colonize lactobacilli or bacteria which sufficiently produce lactic acid, ? microbial community important?
 - failure of lactobacilli to fully acidify the vagina
 - presence of bacteriophages that destroy lactobacilli

Fredricks, *Curr Infect Dis Rep*, 2005;

Marrazzo, *J Infect Dis*, 2002 and *J Infect Dis*, 2006;

Bradshaw, *J Infect Dis*, 2006

Persistent or recurrent BV

- Limited data regarding management
- Try different recommended treatment regimen
- If this fails:
 - Metronidazole gel twice weekly for 4-6 months reduced recurrences, but BV may recur when suppressive therapy is stopped (Sobel JD. Am J OB Gyn 2006;194:1283-89)
 - an oral nitroimidazole followed by intravaginal boric acid and suppressive metronidazole gel twice weekly for 4-6 months for those women in remission (Reichman O. Sex Transm Dis 2009;36:732-34)
 - Monthly oral metronidazole administered with fluconazole has also been evaluated as suppressive therapy which reduced the incidence of BV and promoted colonization with normal vaginal flora (McClelland RS J Infect Dis 2008;197:1361-68)
- Awaiting more data
 - Vitamin D deficiencies; contraceptives and BV risk
 - *L. crispatus* vaginal capsule (LACTIN-V) for BV prevention

Can BV affect the efficacy of PrEP in women?

- Klatt et al. Science 2017.
 - Vaginal tenofovir gel decreased HIV incidence by 61% ($p=0.013$) in Lactobacillus dominated women but only 18% ($p=0.644$) in non-Lactobacillus women
 - Detectable mucosal tenofovir was lower in non-Lactobacillus women
 - In vitro, *G. vaginalis* and other BV associated bacteria appeared to metabolize tenofovir.

Vaginal bacteria modify HIV tenofovir microbicide efficacy in African women

Nichole R. Klatt,^{1*†} Ryan Cheu,^{1‡} Kenzie Birse,^{2,3‡} Alexander S. Zevin,^{1‡} Michelle Perner,^{2,3‡} Laura Noël-Romas,^{2,3‡} Anneke Grobler,⁴ Garrett Westmacott,⁵ Irene Y. Xie,^{2,3} Jennifer Butler,^{2,3} Leila Mansoor,⁴ Lyle R. McKinnon,^{3,4} Jo-Ann S. Passmore,^{6,4} Quarraisha Abdool Karim,^{4,7} Salim S. Abdool Karim,^{4,7} Adam D. Burgener^{2,3,8*†}

But...

- Heffron et al. Lancet 2017
 - No difference in women on oral PrEP in PrEP efficacy based on vaginal microbiota.

Efficacy of oral pre-exposure prophylaxis (PrEP) for HIV among women with abnormal vaginal microbiota: a post-hoc analysis of the randomised, placebo-controlled Partners PrEP Study

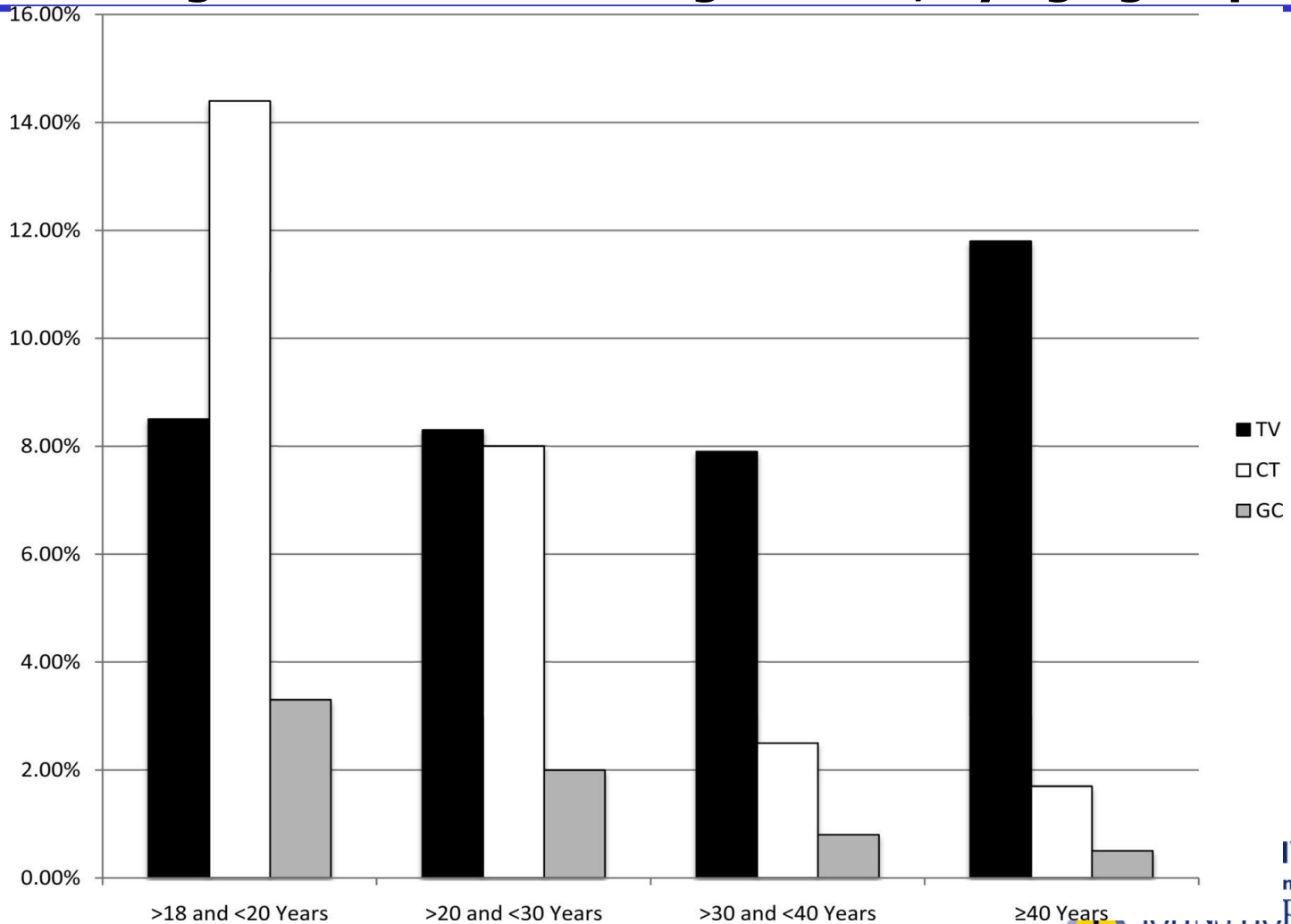
Trichomoniasis

- Most common non-viral STI.
- Transmission is almost exclusively sexual
- Up to 85% asymptomatic



Trichomonas Epidemiology

NAAT prevalence of TV, CT, and GC infections among 7593 U.S. women age 18–89, by age group



Trichomonas

- Prevalence:
 - 50%-60% in female prison inmates & commercial sex workers
 - Approx 20% of females at STD clinics
 - 18-50% of women with vaginal complaints
 - **10-43% in HIV+ women, recent study at HIV clinic: 17.4% of women tested were positive via NAAT. (Muzny et al. STD 2016)**
- Increases risk for HIV acquisition.
- Screening recommended for HIV+ women (proposed interval: at least annually)
 - Associated with inc risk of preterm birth and other adverse pregnancy outcomes and PID in HIV infected women
- Consider screening in those at high risk for infection or negative sequelae
 - new or multiple partners, history of STDs
 - exchange sex for payment, use injection drugs
 - pregnant

Trichomonas

- Maximum growth at pH 4.9-7.5
- Motile at high pH
- Less prominent signs & symptoms at low pH
- Kills and ingests lactobacilli
- Clinical Features
 - In men, urethritis, epididymitis, or prostatic OR asymptomatic
 - In women, ranges from asymptomatic to severe vaginitis
 - Purulent vaginal discharge
 - Abnormal vaginal bleeding/post coital bleeding
 - Vulvar edema, erythema
 - Dyspareunia, pruritis



Diagnosis

- pH is usually >5
- Examine saline wet prep of fresh vaginal fluid for motile trich - sensitivity is about 51-65%
- Culture on Diamond medium was gold standard: sensitivity 75-96%
- NAATs is $>95\%$ sensitive and $> 95\%$ specific
 - Several assays are FDA-cleared for vaginal, endocervical or urine specimens from women with or without symptoms and for urine or urethral swabs (preferred) from men if lab is CLIA certified to run the test
- CLIA waved Point of care tests for women:
 - OSOM Trich Rapid test (10 minutes with 82-95% sensitivity and $>97\%$ specificity and self-testing is option)
 - Affirm VP III (45 minutes, with sensitivity 63% and specificity 99%)
- No for Pap tests: too many false negatives and false positives

Treatment

- Metronidazole 2 g PO in a single dose OR
- Tinidazole 2 g PO in a single dose

Alternate regimens

- Metronidazole 500 mg PO BID for 7 days

No alcohol (24 hours MTZ; 72 hours TNZ);
Metronidazole gel is not recommended (less efficacious);
Tinidazole is not recommended in pregnancy (animal studies)

Retest 3 mo after treatment (for HIV pos and neg women)

T vaginalis and HIV infection

- Women with HIV infection should receive screening at entry to care and annually if sexually active
 - associated with PID (Moodley 2002)
 - Treatment reduces genital HIV shedding (Kissinger 2009, Anderson 2012)
- Longer treatment course better in women
 - metronidazole 500mg BID x7d (vs. 2g)-less TV at TOC/3 mo RR 0.46, CI:0.21–0.98 (*Kissinger, 2010*)
 - Potential factors- BV infection, arv, changes in vaginal ecology
- No data to recommend extended treatment in men

HIV + women should get Flagyl 500mg po BID X 7d

Treatment for Persistent or Recurrent Trichomoniasis

- Metronidazole 500 mg PO BID for 7 days

If this regimen fails:

- Metronidazole 2 g PO for 7 days OR
- Tinidazole 2 g PO for 7 days

If this regimen fails, do susceptibility tests

May need to consider 2-3g po tinidazole X14 days plus intravaginal tinidazole, ?intravaginal boric acid?

Management

- Sex partner management- all contacts should be treated
- Note: Patients should be counseled to refrain from sexual intercourse until all partners have been treated and symptoms have subsided.

Epidemiology- VVC

- Affects most females during lifetime
- Most cases caused by *C. albicans* (85%-90%)
- Second most common cause of vaginitis
- Estimated cost: \$1 billion annually in the U.S.

Vulvovaginal Candidiasis (VVC)

- Inflammatory vaginitis and, if vulvar area is involved, vulvitis
- Etiology: *C. albicans* 80-92%, *C. glabrata*
- Candida is normal flora of the vagina
- 20% women are colonized with Candida

Classification of VVC

- Uncomplicated- sporadic or infrequent, mild to moderate, likely to be *C. albicans*, non-immunocompromised host
- Complicated- recurrent, severe, non-*albicans* species, uncontrolled diabetes, debilitation, pregnancy, other immune suppression

Risk Factors

- oral contraceptive users
- pregnancy
- antibiotic use
- steroid use
- uncontrolled diabetes
- prior history of candida infections

Clinical Manifestations

- Pruritis
- vaginal irritation, vaginal discharge
- vulvar edema/excoriation
- dysuria, dysparenuia
- fissures

Vulvovaginal Candidiasis



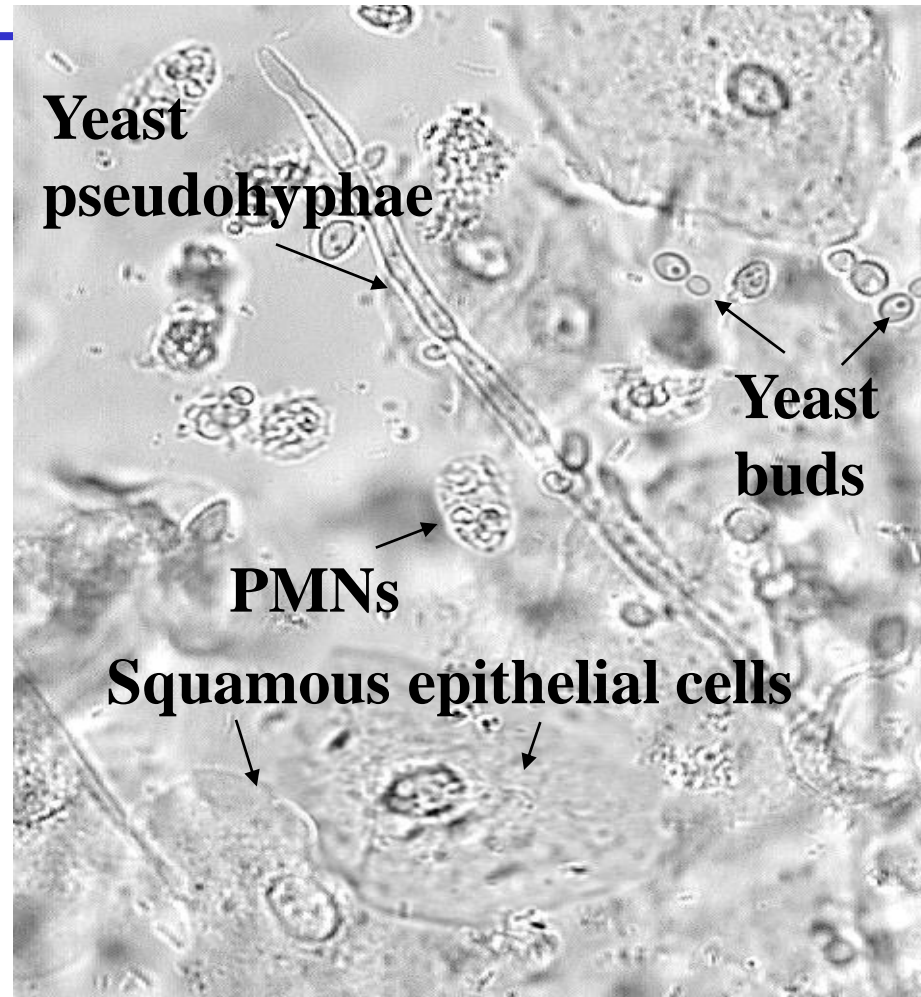
Source: Health Canada, Sexual Health and STI Section, Clinical Slide Gallery

Diagnosis

- Diagnosis: clinical exam, pH <4.5 (pH can be high with co-infections with TV or BV), KOH prep budding yeast and/or pseudo-hyphae, 50% may have negative microscopy, culture is gold standard

PMNs and Yeast Pseudohyphae

Saline: 40X objective



Source: Seattle STD/HIV Prevention Training Center at the University of Washington

Treatment

- Uncomplicated- OTC (butaconazole, clotrimazole, miconazole 3,7 day regimens)
- Single dose butaconazole available
- Other azoles- terconazole (non-OTC)
- Oral agent- fluconazole 150 mg po once

Management

- Severe: 7–14 days of topical azole or 150 mg of fluconazole in two sequential oral doses (second dose 72 hours after initial dose)
- Complicated-recurrent VVC: (4 or more episodes in a year), 7-14 days of topical azole or 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])
- Maintenance: Oral fluconazole (i.e., 100-mg, 150-mg, or 200-mg dose) weekly for 6 months is the first line maintenance regimen.
 - If this regimen is not feasible, topical treatments used intermittently can also be considered

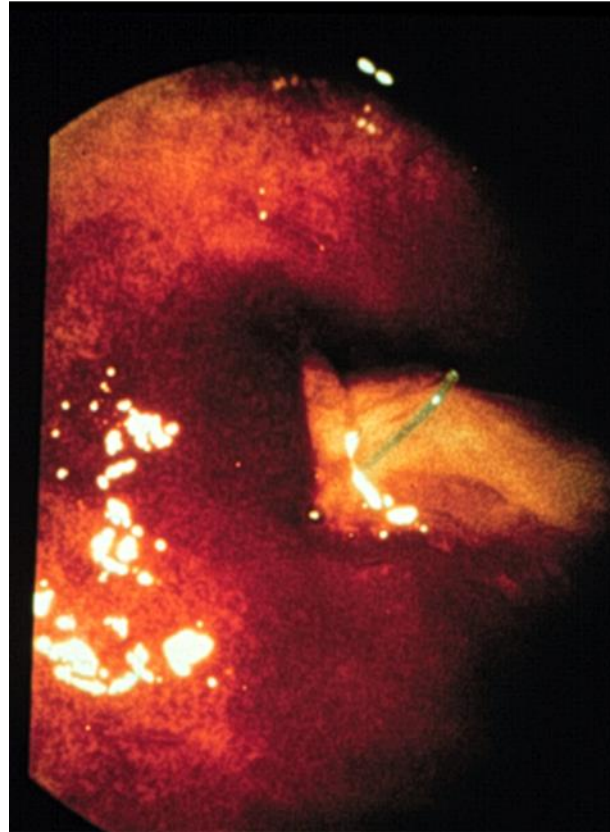
Management

- Pregnancy: only topicals recommended.
- Immunocompromised may need 7-14 day regimen.

Back to Alyssa...

- Pregnancy test +, has vaginal discharge.
- Wet prep of vaginal secretions shows...
 - pH of 6.0
 - Clue cells
 - +Whiff test
 - Motile trichomonads
 - No yeast
- She has BV and Trichomonas!

But wait...



CERVICITIS

Definitions

- Endocervicitis- also known as mucopurulent cervicitis(MPC)
- Inflammation of the cervical epithelium
- Yellow/Green exudate visible in the endocervical canal OR yellow exudate on the endocervical swab
- Other features- edema/erythema of the zone of ectopy

Mucopurulent Cervical Discharge (Positive swab test)



Source: Seattle STD/HIV Prevention Training Center at the University of Washington/
Claire E. Stevens and Ronald E. Roddy

Definitions

- Purulent discharge
- Easily induced cervical bleeding

Endocervicitis Etiology

- *C. trachomatis*, *N. gonorrhoea*, HSV
- Others: *Mycoplasma genitalium*?
- No infectious etiology is identified in a significant number of these cases.

Ectocervicitis Etiology

- Ectocervicitis- *T. vaginalis*, HSV, Candida, CMV
- Non-infectious: trauma (chemical or mechanical), neoplasia.

Epidemiology

- Percentage distribution of the causes of MPC
- No infection- 38%
- CT- 15%
- GC- 8%
- HSV- 6%
- Multiple etiologies- 1-5%

Diagnosis

- Clinical- very difficult, utilized where there are no lab facilities or if patient is high risk
- Clues for clinical diagnosis- friability of cervix, mucopus in endocervical canal, change in color of endocervical swab

Diagnosis

- Nucleic acid tests- DNA detection e.g genprobes, DNA amplification e.g PCR/LCR (NAAT) for Chlamydia, Gonorrhea
- Higher sensitivity and specificity, compared to culture
- PCR/LCR- sens/spec up to 98-99%

Treatment

- Empiric tx for women at increased risk, esp if there are concerns re: followup
 - Inc risk: aged <25 years, new sex partner, a sex partner with concurrent, partners, or a sex partner who has a sexually transmitted infection).
- All partners (last 60 days) should be evaluated and treated.

Empiric Treatment

- Treat for gonorrhea and chlamydia

Ceftriaxone 250mg IV X1 Plus

Azithromycin 1g po X1

(consider tx CT alone if community prevalence low)

- Persistent cervicitis:
 - Further testing, Treatment for Mycoplasma genitalium with Moxifloxacin? (400 mg daily x 7, 10 or 14 days)

What should Alyssa be treated with?

- Doxycycline 100mg po BID for 7 days
- Flagyl 500mg po BID for 7 days plus Ceftriaxone 250mg IM X1 plus Azithromycin 1g po X1
- Benzathine penicillin G IM X1 plus flagyl 500mg po BID for 7 days plus ceftriaxone 250mg IM X 1 plus doxycycline 100mg po BID for 7 days

The rest of Alyssa's test results

- Oral NG/CT NAT: positive for gonorrhea
- Rectal NG/CT NAT: negative
- Vaginal NG/CT NAT: positive for gonorrhea
- HCV ab: Positive
- HIV ab: Negative

Patient Counseling and Education

- Nature of the disease
 - Normal vs. abnormal vaginal discharge, signs and symptoms
- Transmission Issues- importance of partner evaluation and treatment
- Risk reduction
 - Avoid douching, avoid unnecessary antibiotic use, complete course of treatment, abstain from sex until treatment is complete

Risk Reduction

The clinician should:

- Assess patient's potential for behavior change
- Discuss individualized risk-reduction plans with the patient
- Discuss prevention strategies such as monogamy, use of condoms, and limiting the number of sex partners
- Latex condoms, when used consistently and correctly, can reduce risk

Thank You!

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