# The Challenges of Vaginitis

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- No disclosures

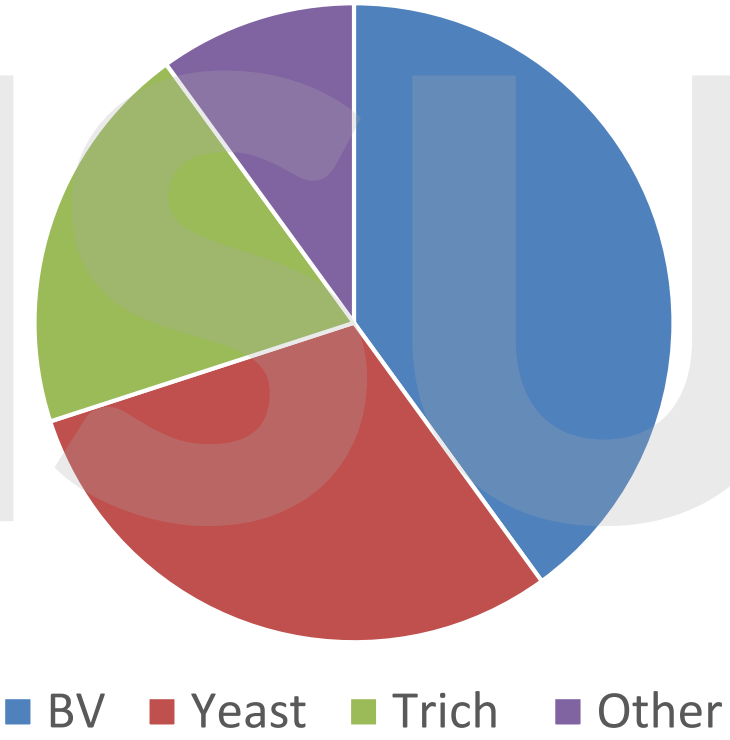
# Objectives

- Review common vaginitis
  - Pathogenesis
  - Diagnosis
  - Treatment
- Discuss difficult/unusual cases
  - Recurrent Yeast and BV
  - Resistant Trichomonaisis
  - Non-infectious vaginitis
- Understand when to refer to gyn/vulvar

# Vaginitis Basics

- Caused by infection, inflammation or changes in the normal vaginal flora

- Most common causes
  - Yeast (17-39%)
  - BV (22-50%)
  - Trich (4-35%)
  - Other (7-10%)




- Symptoms include: vaginal discharge, odor, pruritus, irritation or discomfort

# Vaginal Health and the Microbiome

- Estrogen promotes mature epithelial cell
- Glycogen in epithelial cells supports lactobacilli
- Lactobacilli produce lactic acid and lower pH
  - Normal vaginal pH is <4.5
- Acidic environment is protective
- Normal flora is heterogeneous, but in balance
  - Commonly includes *Gardrenella, E. Coli, GBS, Mycoplasma, Candida, but dominated by lactobacilli*

# Prepuberty and Menopausal Women

- lack of estrogen inhibits normal growth of the vaginal bacterial ecosystem;
- microscopy typically shows a paucity of epithelial cells and background bacteria
- Rare to see BV or yeast in these patients, so consider alternate diagnosis

# Case 1

- 36yo G0 single woman with Mirena IUD who presents with concerns of vulvovaginal itch and burn

# Office Evaluation: History

**Quality:** onset, frequency, duration, location, severity, consistency, color, & odor

**Exposure to contact irritants:** soaps, spermicide, bathing products or intra-vaginal products

**Vulvar Hair Hygiene:** shave, laser, wax

**Hormonal status** : Relation to Menstrual cycle? Estrogen depleted? (postpartum, menopausal, birth control)

**Sexuality:** partners, barrier BCMs, lubes, toys, other

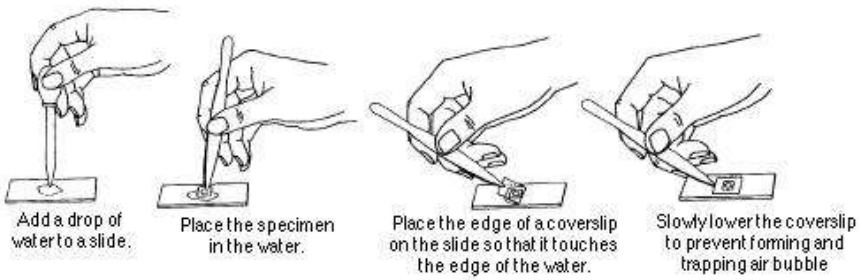
**Treatments:** OTC, CAM or prescribed medications

# Tools for Evaluation

- **Physical Exam**
  - Visual inspection of vulva , perineum, anus & vagina (speculum)
- **Microscopy**
  - pH immediately
  - Saline/KOH prep
  - Whiff test: amine odor with application of KOH
- **Vaginal Culture**: vaginal side walls or fornix, not cervix
  - Fungal culture helpful
  - General bacterial culture generally not helpful
- **Rapid tests:** when indicated or unable to do microscopy
  - BV, GC/CT,
- **Vulvar Biopsy**
  - Only when notable skin changes
  - Random biopsy not helpful and can be traumatic for the patient

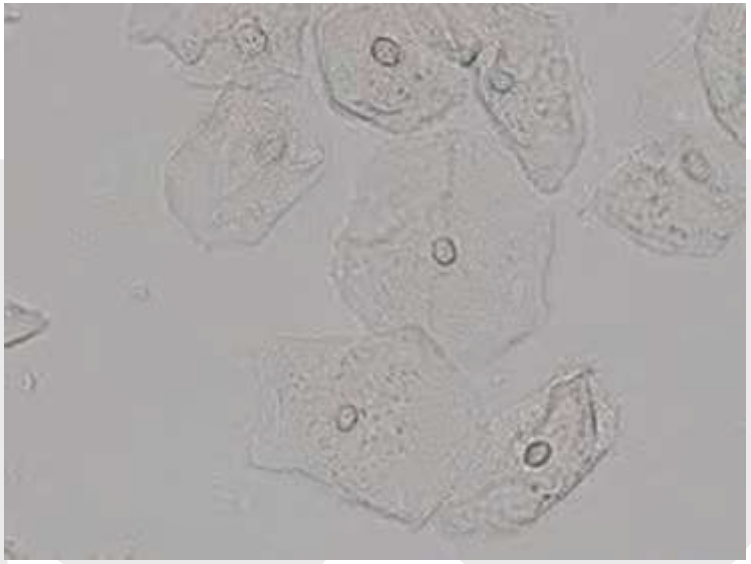
# Wet Prep


1. Check Vaginal pH
   - prior to using lidocaine, gel etc ideally
   - Using pH paper graded from 3-5.5
   - Ask about bleeding, sex and intravaginal products (affect pH)
2. Collect specimen
   - From vaginal side walls
   - Consider recollecting, I usually collect twice
3. Place specimen in saline on 2 slides (or in carrier container)
   - Check to ensure that it appears cellular, if not recollect and add more cells
4. On second slide add KOH
5. Place cover slips



# What can we see in a Saline Prep?

- Epithelial Cells
  - mature squamous cells
- WBCs
- RBCs
- Parabasal Cells
  - immature squamous
- Trichomonas
- Clue Cells
- Hyphae/spores
- Debris



| | pH | WBC | Para-basals | Features | Discharge |
|---|---|---|---|---|---|
| Normal | 3.5-4.5 | Few or none | no | Mature epithelial cells<br>lactobacilli | Creamy white |

| | pH | WBC | Para-basals | Features | Discharge |
|---|---|---|---|---|---|
| Normal | 3.5-4.5 | Few or none | no | Nl lactobacilli | Creamy, mucousy, white |
| Yeast | 3.5-4.5 | no | no | Hyphae Spores (400x) | White, Curdy |
| BV | >4.5 | no | no | Clue Cell | Yellow, grey w/ odor |
| Trich | >5.0 | yes | maybe | Motile trich | Greenish yellow, frothy |
| DIV | >5.0 | yes | yes | Mixed bactertia, reduced lacto | Yellow, profuse |
| GSM | >5.0 | maybe | yes | Scant cells, few bacteria | Scant, dry |

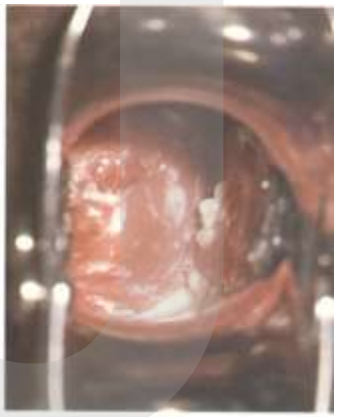
# Vaginal Culture

- Appropriate for recurrent, difficult vaginitis
- Culture for **recurrent yeast**
  - Request sensitivity and speciation
- Culture for **resistant trichomonads**
- Not helpful for recurrent or resistant BV
  - Unsure role of other coliforms, therefore not recommended to obtain bacterial culture of vagina in most cases

# Vulvovaginal candidiasis

# Vulvovaginal Candidiasis (VVC)

- 13 million cases annually in the USA
- Second most common cause of vaginitis
- Primary symptoms
  - Itching
  - Thick, curdy, white discharge

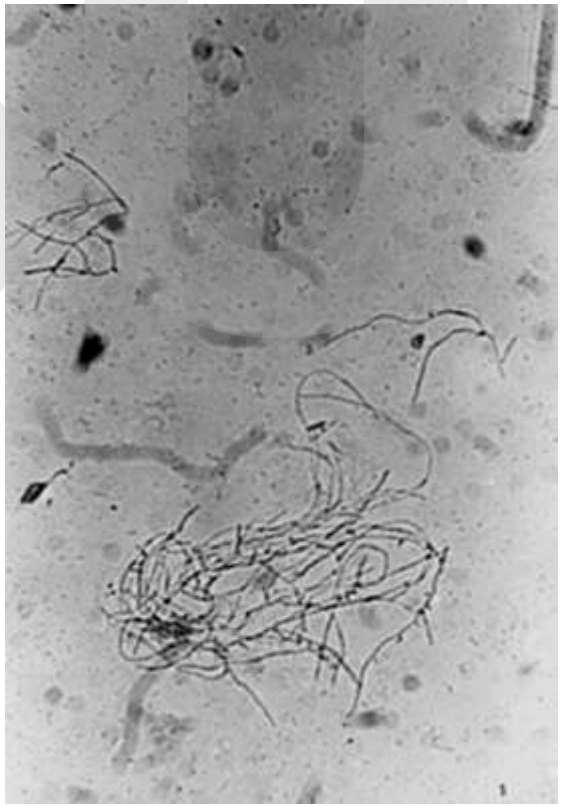


- 29-49% of women w/ at least 1 lifetime episode
- 5% of women develop recurrent infection

Foxman, 2013, CDC 2010 STD Treatment Guidelines

# Diagnosis

- Microscopy, convenient and specific
  - Only 50-70% sensitive
- Culture
  - resistant/recurrent infection
- PCR (39-99% sensitive)
  - BD AFFIRM (candida y/n)
  - BD MAX (subtype)



# Vulvovaginal Candidiasis (VVC)

- **Uncomplicated**
- Sporadic, infrequent
- Mild-moderate
- Likely *C. albicans*
- Non-immunocompromised

- **Complicated**
- Recurrent (>3/year)
- Severe (clinical exam)
- Non-albicans
- Diabetes, immunocompromise

2015 CDC STD Treatment Guideline

# Treatment of uncomplicated yeast

- Topical (vaginal) OTC azole preparation x 3-7d
- Oral fluconazole 150mg as single dose
- Very Effective >90%

- Topical tx recommended in pregnancy, as oral fluconazole was associated with increased miscarriage rate.

# Quiz Question 1

Candida albicans is the most common cause of recurrent vulvovaginal yeast infections. Several **uncommon** species of yeast can also cause recurrent infection. Which species of fungus is the most common in THIS category?

a. Candida parapsilosis

b. Candida glabrata

c. Saccharomyces cerevisiae

d. Tinea

# Acute Infection: non-*albicans*?

- ~5-10% women with recurrent VVC have non-*albicans* species
  - *C. glabrata* ***
  - *C. parapsilosis*
  - *C. krusei*
  - *Saccharomyces cerevisiae*



Spinillo, A, 1995. **85**(6): p. 993-8

Sobel, Am J Obstet Gynecol, 2001

# How to treat non-*albicans*?

- Fluconazole? >50% non-response if *Candida glabrata*
- Itraconazole 200mg QD or 100mg BID x 3-7d
- Boric acid 600mg capsules intra-vaginally QHS-BID x 14ds
  - 92 women failed conventional treatment with -azoles had 98% mycologic cure with boric acid
  - Case series of resistant VVC , 81% pt responded to 600mg QDx14d boric acid compared to <50% -azole
- Flucytosine 5% cream intravaginally 5g QHS x 14d

Nyirjesy, Am J Obstet Gynecol, 1995
Guaschino, Am J Obstet Gynecol, 2001
Van Slyke, Am J Obstet Gynecol, 1981
Sobel, Am J Obstet Gynecol, 2003
Sobel JD, Clin Infect Dis 1997
Jovanovic, J Reprod Med, 1991

# Recurrent VVC Diagnosis

- Defined as 4 or more episodes/year
- Begin with office evaluation
  - Data supports women poor at self-diagnosis
- Microscopy, KOH increases sensitivity
- Consider rapid point of care test (AFFIRM®)
- Vaginal culture, most will be *C. albicans*
  - Consider ID & sensitivities for difficult case



Ferris, Obstet Gynecol 2002;99:419; Ferris, J Fam Pract. 1996;42(6):595. Sobel, AJOG 1985; 152:924
Allen-Davis, Obstet Gynecol 2002;99:18; CDC 2010 STD Treatment Guidelines

# *Can a Woman Accurately Diagnose Herself?*

Ferris, Obstet Gynecol, Vol 99 (3), 2002.

| Final Diagnosis | N | % |
|---|---|---|
| Normal | 13 | 13.7 |
| ***VVC*** | ***32*** | ***33.7*** |
| Trichomonas | 2 | 2.1 |
| BV | 18 | 18.9 |
| Other* | 10 | 10.5 |
| VVC+BV | 18 | **18.9** |
| BV+Trich | 1 | 1.1 |
| VVC+Trich | 1 | **1.1** |

# Recurrent VVC: Risk Factors

- Antibiotic use
- Estrogen excess (pregnancy, vaginal estrogen)
- Immune suppression (SLE, HIV, oral steroids)
- Vulvar dermatoses (LS, LP, psoriasis)
  - Likely due to steroid use
- Diabetes mellitus



2010 CDC STD Treatment Guideline
Sobel, JD. Candida vaginitis. Infect Dis Clin Pract 1994; 3:334.

# Complicated/Recurrent Infection

- Topical OTC azole preparation x 14days
- Oral fluconazole 150mg x 2, 3d apart
- Oral fluconazole 150mg q 3-5days x 14days
- Topical 5-Flucytosine 5g intra-vag QHSx14days



Sobel, Am J Obstet Gynecol, 2001

Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America, Clin Infect Dis. 2009 Mar 1;48(5):503-35

Rodgers, C.A. and A.J. Beardall, Int J STD AIDS, 1999.

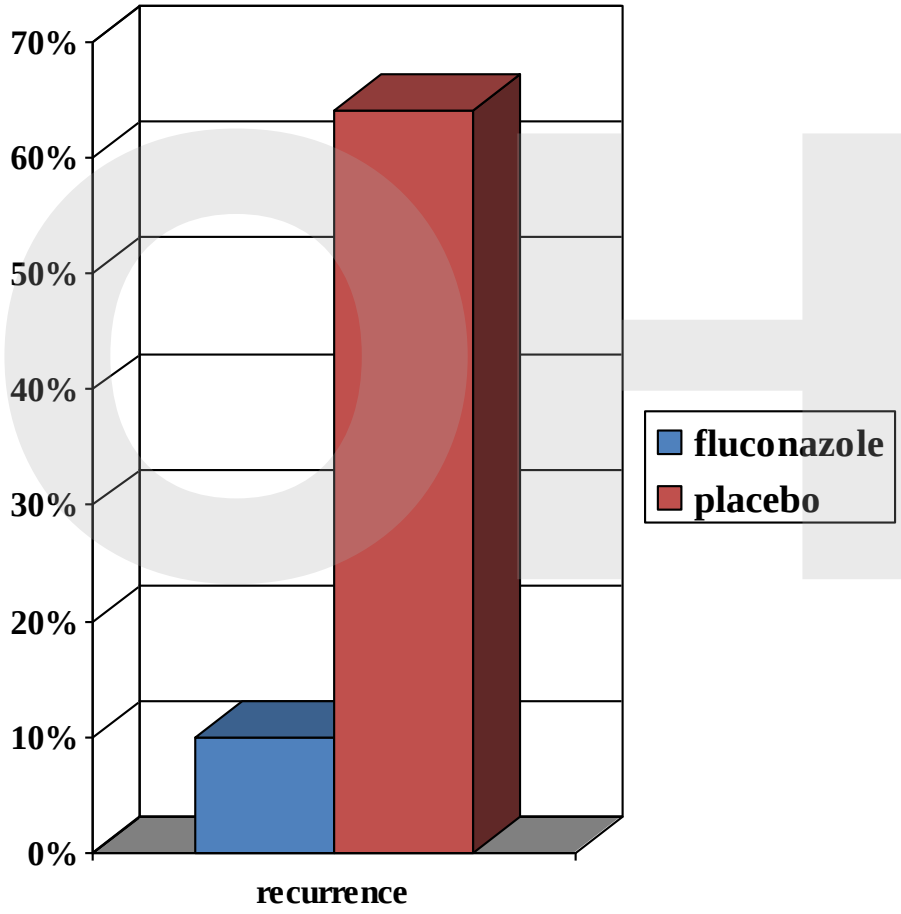
# Preventing Recurrence: Suppression

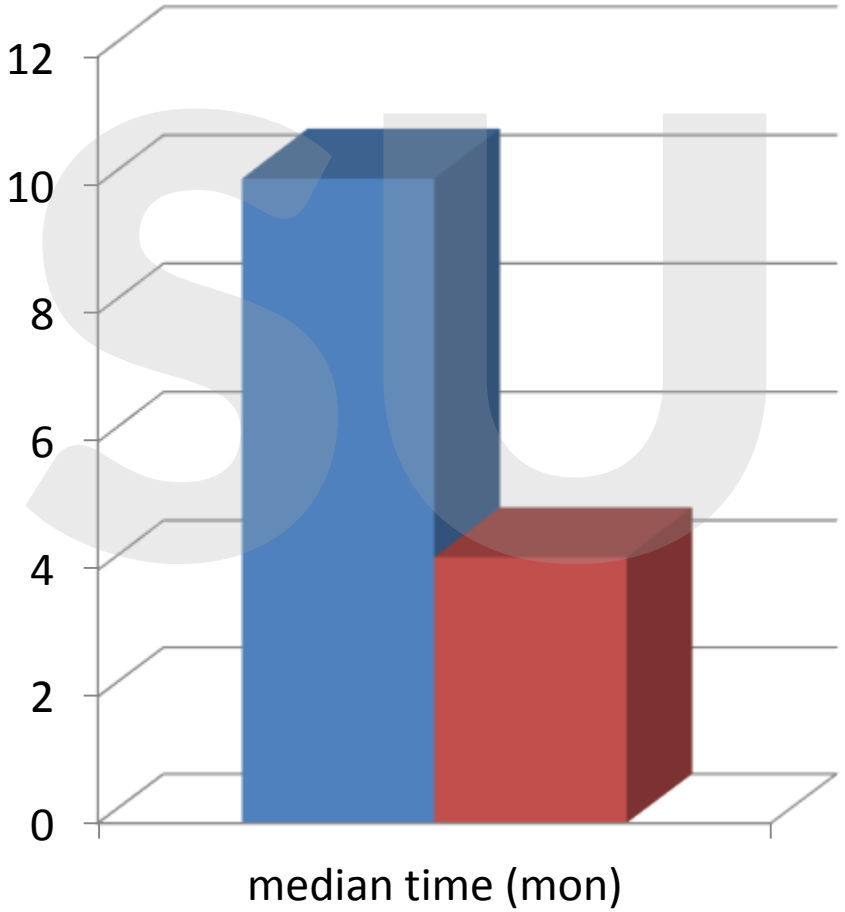
- Begin prophylaxis:
  - **Fluconazole 150mg Q week x 6 mon
  - Clotrimazole 500mg vag supp weekly x 6 mon
  - Boric acid 600mg intravag 2x/week x 6 mon

- Weekly oral fluconazole is very effective and safe
- Recurrence after suppression up to 30%
- Safety profile of long term use of boric acid not proven

Sobel, 1992  2015 CDC STD Treatment Guideline

# VVC: Why Suppression?




Sobel, NEJM 2004; 351:876

# What Predicts Recurrence?

Patel et al, AJOG 2004; 190:644

- Prospective cohort: 65 with RVVC despite maintenance, classic risks controlled, logistic regression for behaviors associated with recurrence
- **RISK:** panty-liners, pantyhose, cranberry juice, consumption of acidophilus products (oral & vaginal), hx of BV, <40yo
- **NO RISK:** OCPs, oral sex, vaginal sex

# Preventing Recurrence?

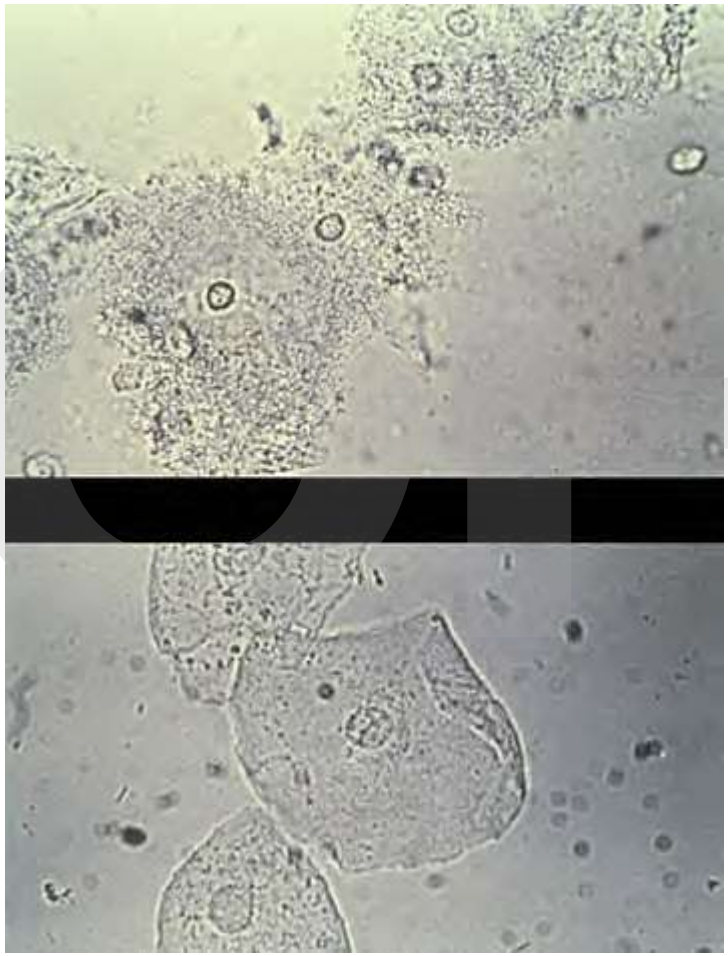
- Control Classic risk factors:
  - uncontrolled DM
  - Immuno-suppression
  - HIV+
  - antibiotic use
- Data does not support
  - use of probiotics
  - treatment of male partner

Fong 1992, William 2001, Priotta 2004, Witt, 2009

# Summary: Recurrent VVC

- Defined as 4 infections/year
- Office evaluation/culture to confirm dx & species
- Treat acute infection aggressively (*Candida albicans)*
  - Fluconazole 150mg x 3 doses, Days 1, 4 and 7
  - Intra-vaginal –azole QHS x 14d
- Suppression x 6 months
  - Fluconazole 150mg weekly
  - Intra-vaginal –azole weekly
- 30% will recur after 6 months suppression
- Long term safety established with oral Fluconazole
- Look at behaviors for risk factors

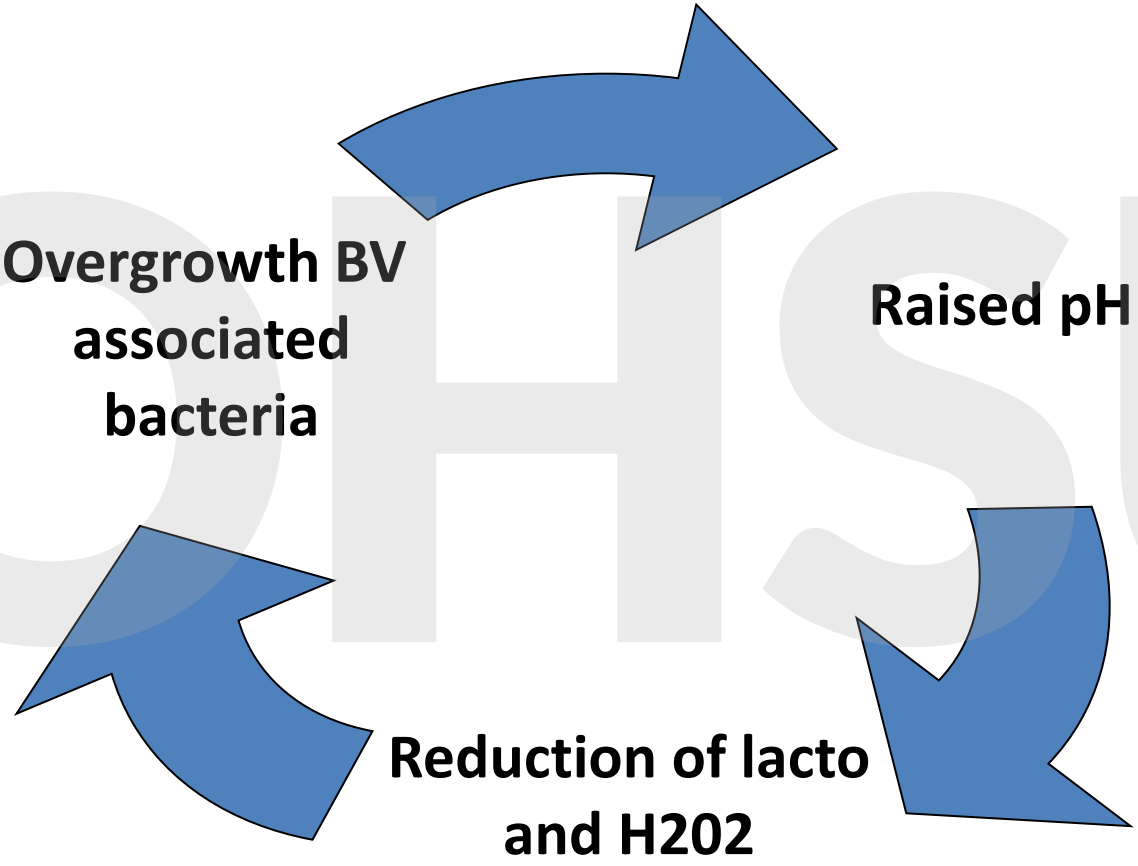
# Bacterial Vaginosis



# Quiz Question 2

True or False:  Most bacterial vaginosis is asymptomatic.

# BV: Etiology




Wilson, STI 2004;80: 8-11;  Ling BMC Genomics 2010; 11: 488.

# BV: Risk Factors & Associations

- Sexual activity (hetero and lesbian)
- AA ethnicity
- Multiple sex partners
- Douching
- Smoking
- STIs (CDC recommends STI testing)

2015 CDC STD Treatment Guidelines

# BV: Diagnosis

## Amsel criteria: 3 of 4 findings

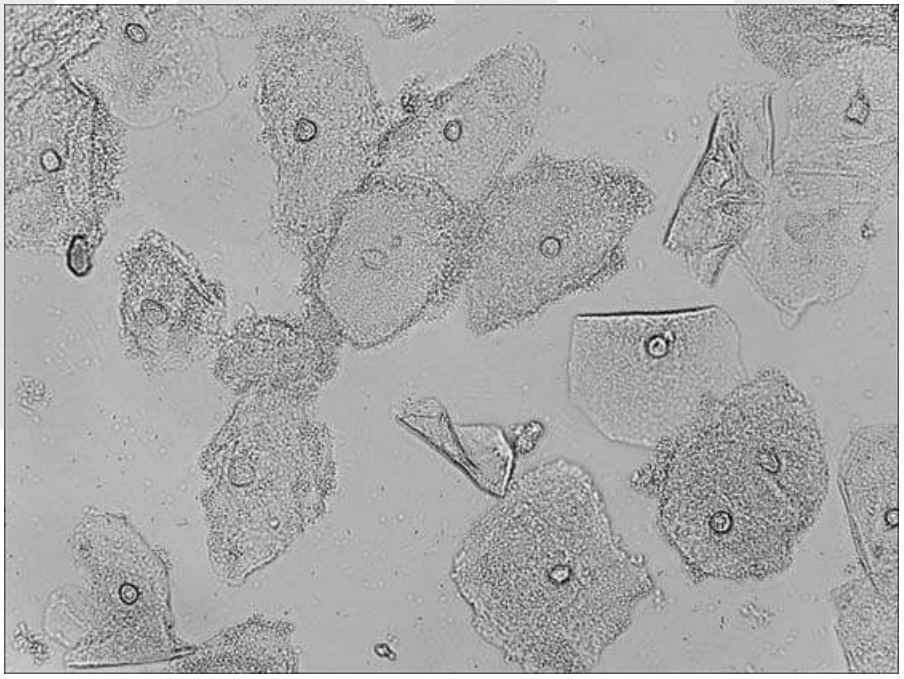
(1) Homogeneous, thin grayish-white vaginal discharge

(2) clue cells > 20%

(3) positive whiff test

(4) vaginal pH >4.5

A positive test for gardrenella on BD affirm, is not diagnostic for BV.



*Gardnerella vaginalis*, *Prevotella* species, *Porphyromonas* species, *Bacteroides* species, *Peptostreptococcus* species, *Mycoplasma hominis*, and *Ureaplasma urealyticum*, as well as *Mobiluncus*, *Megasphaera*, *Sneathia*, and *Clostridiales* species *Fusobacterium* species and *Atopobium vaginae* are also common

# Other Tests

- Gram Stain with Nugent scoring
- Non-amplified nucleic-acid test for *Gardnerella*
  - BD affirm
- Chromogenic test of sialidase enzyme activity
  - OSOM BV Blue
- PCR testing
  - Evaluates presence of lactobacilli and BV assoc bacteria
  - self or clinician collected
- Over diagnosis of BV is common!

# BV: Treatment

**Recommended Treatment Regimens**

1. Metronidazole 500mg PO BID x7d
   - most effective treatment with **90% clinical cure**
2. Metronidazole Gel 0.75% 5g vaginal once daily x 5d
   - **as effective** as oral metronidazole
3. Clindamycin 2% cream 5g intravaginally daily x 7d

**Alternatives**

- Tinidazole 2g PO daily x 2 d
- Tinidazole 1g PO daily x 5d
- Clindamycin 300mg oral bid x 7d
- Clindamycin ovules 100mg intravaginally daily x 3d

CDC 2015

# BV: Recurrence

- 30% women recur within 3 month
- 58% recur within 12 months
- Chronic defined as 3 episodes/year

Wilson, 2004 Bradshaw, 2006, Powell 2014

# Recurrent BV:

## Step 1: Treat the Acute Infection

- Treat longer, 10-14d
- Change agent

## Step 2: Consider Suppression

- Twice weekly MetroGel (or Clindamycin)

Baylson, Obstet Gynecol 2004; 104:931-2
2010 CDC STD Treatment Guidelines

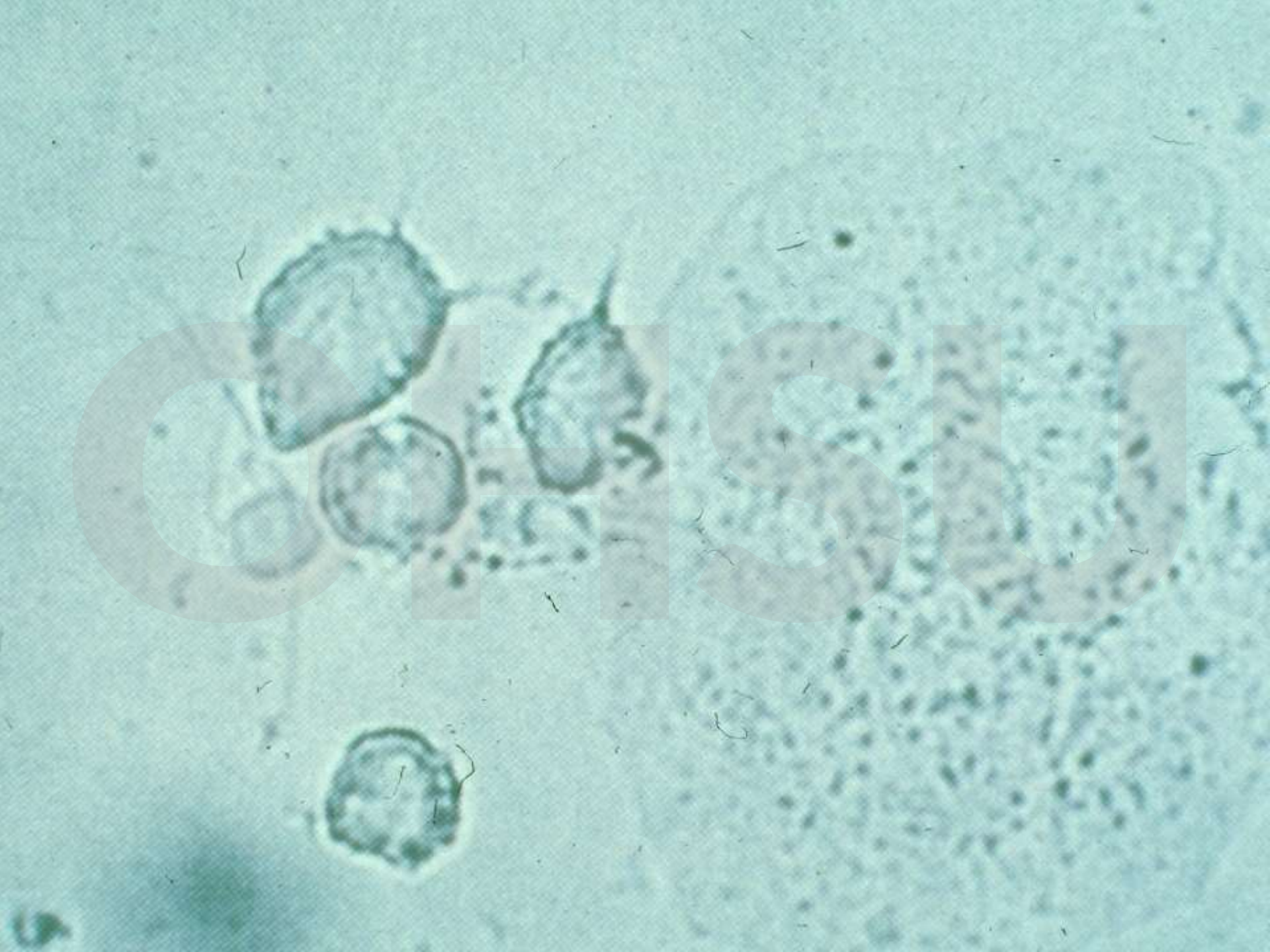
# Probiotics or Alternative Treatments?

Data lacking therefore unclear benefit

- Evidence does not support replacing lactobacilli oral or vaginally
- Difficult to obtain specific species (*L. crispatus* and *L jensenii*) that adhere to vaginal walls and produces H202 used to maintain ecosystem
- Douching with H202 may exert a short term disinfection but does nothing to restore balance and can actually kill *Lactobacillus*
- Role of boric acid is unclear, may have some benefit in supporting vagina but not primary treatment

# Recurrent BV: Helpful Hints

- Treat longer 10-14d for acute infection
- Consider suppression with MetroGel
- Condom first 4 weeks after treatment
- Clean sex toys
- Careful hygiene, no douching
- Suppress periods

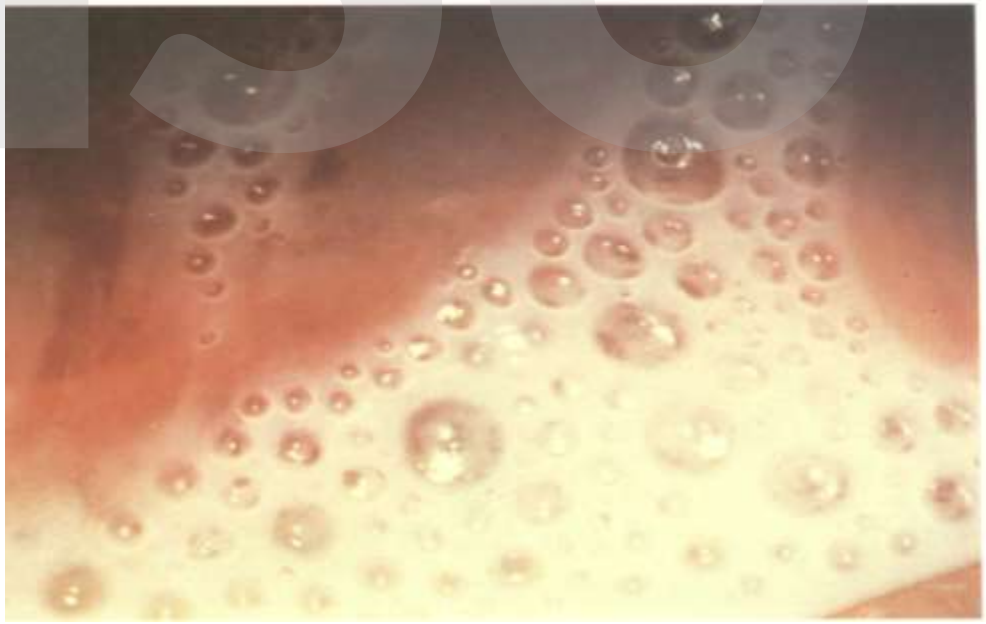


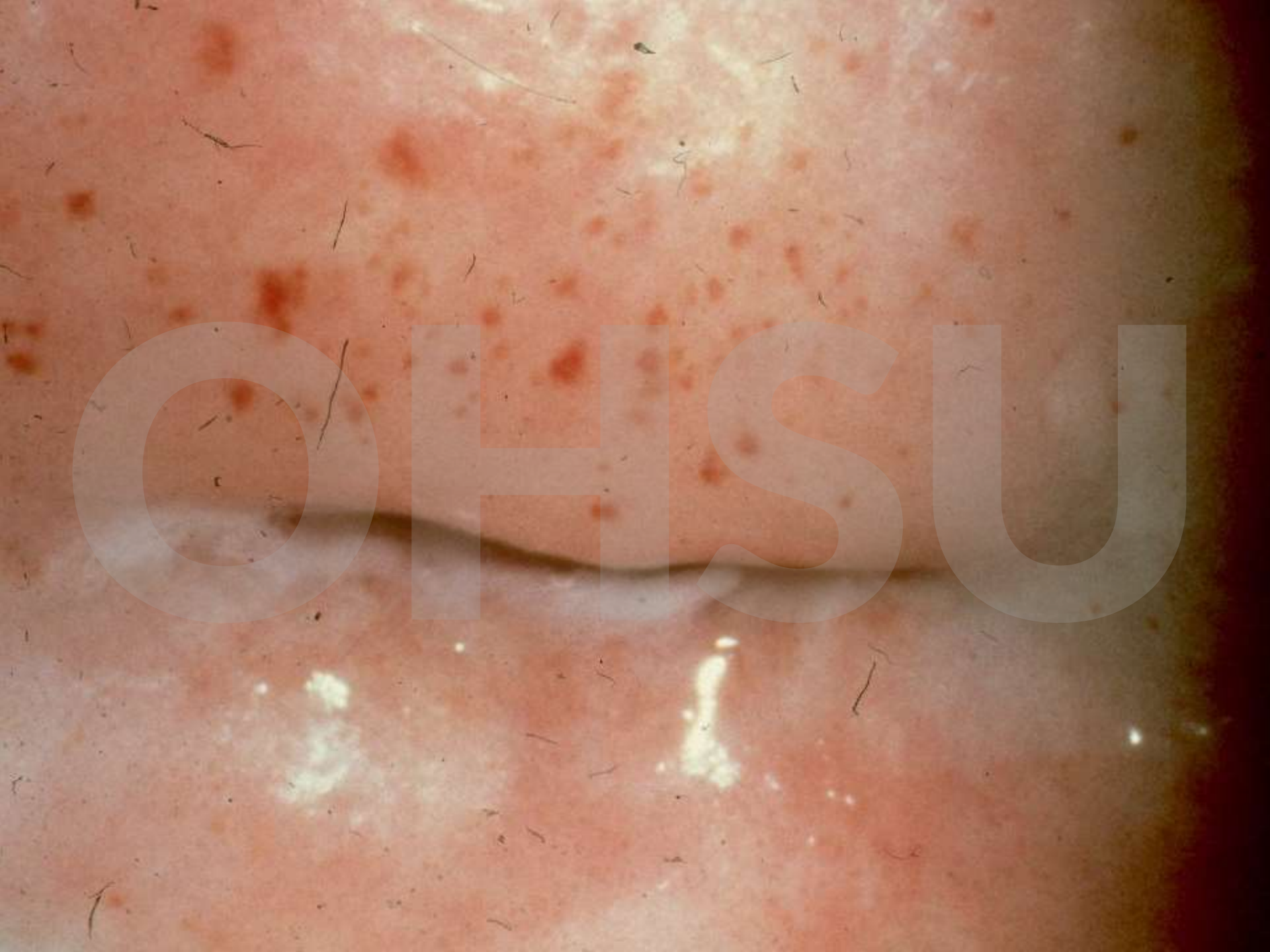
# Trichomonas vaginalis: Fast facts

- Prevalence **3.1%**
- Virtually always sexually transmitted, assoc w/ other STIs
- Asymptomatic carriage for prolonged periods of time possible. . . . ? Not always able to establish vector
- If female diagnosed, most male partners +
- Risk Factors
  - Black race
  - Number of sex partners
  - Low SE status
  - douching

# Symptoms

- Symptoms range from none to severe
- <10% have classic frothy discharge, suspect if pH>5.0 and WBC on wet mount




OHSU

# Diagnosis

- Basic microscopy
  - Elevated pH, WBCs on wet mount, trichomonads
  - Low sensitivity (50-60%), not first line
- Gold Standard
  - NAAT
  - antigen-detection
  - PCR test
  - Culture (alternative)

# Perks & Pitfalls of Making the Diagnosis

| | Wet mount | Diamond's Medium | AFFRIM Culture Kit | OSOM Trich Rapid Test | Pap Smear |
|---|---|---|---|---|---|
| Sensitivity<br>Specificity | 60-70% | >95% | >95%<br>>95% | >88%<br>98% | 50% |
| Pitfall | High false negative<br>Dry slide | Obtain culture, Takes 7d | Not office based, sent to lab | Purchase kit | unreliable |
| What is it? | Slides + microscope | Culture medium | Swab inoculated into tube | Swab + dipstick + reagent | Slides, ? Liquid base |
| Perk | Available most offices | Accurate | <2 hrs Yeast&BV | In office kit, <10 min | Increase suspicion |
| Logistics | Office + lab | Office swab then incubate in micro lab | Becton Dickenson, San Jose, CA | GenZyme 1-800-330-3591, Office | Office + lab |

# Quiz Question 3

True or False:  Trichomoniasis can be equally and effectively treated with either oral or vaginal medicines.

# Treatment of Trichomoniasis

**Recommended Regimens:**

1. **Metronidazole 2 g** orally as single dose
2. **Tinidazole 2 g** orally as single dose

**Alternative Regimen**

Metronidazole 500 mg orally twice a day for 7 days

CDC 2015 STD Treatment Guidelines

# Treatment of Trichomoniasis

- **90-95% cured**
  - with Metronidazole or Tinidazole
- MUST treat partner
  - Concurrent partner ~75% positive trich by PCR
- NO VAGINAL preparations
- No ETOH for 1-3d after use of medication
- Refrain from sex for 7d AFTER completed

- **Re-infection & Noncompliance are COMMON**
- Compliance enhanced with single 1 DAY Tx



Sena, Clin Infect Dis. 2007 Jan 1;44(1):13-22.
CDC 2010 STD Treatment Guidelines

# Resistant Trichomoniasis

- If resistant then try. . . .
  - 1. Tinidazole 2g x 5d
    - Some Metro-resistant trich (2-5%) respond to high dose Tinidazole
  - 2. Metronidazole 500mg BID x 7d
- Most will respond to higher and longer doses
- If not, consider culture for resistant strain (1-2%)
- In patients with suspected resistance to Metronidazole, CDC recommends in vitro culture and drug susceptibility testing (CDC, # 404-718-4141)



Schwebke , Antimicrob Agents Chemother. 2006 Dec;50(12)

2015 CDC STD Treatment Guideline

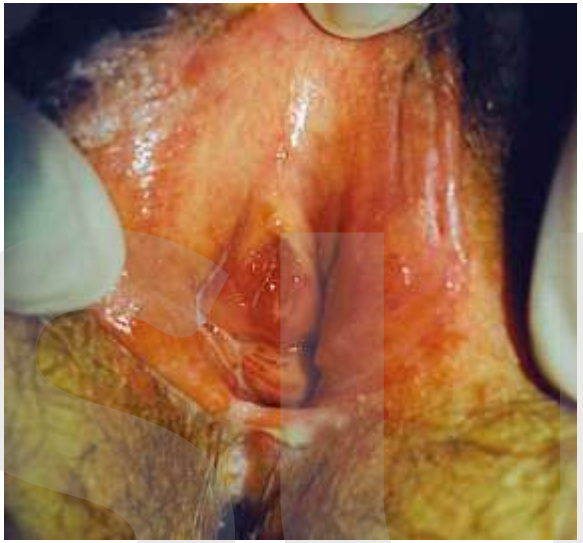
# Recurrent Vaginitis: think outside the box!

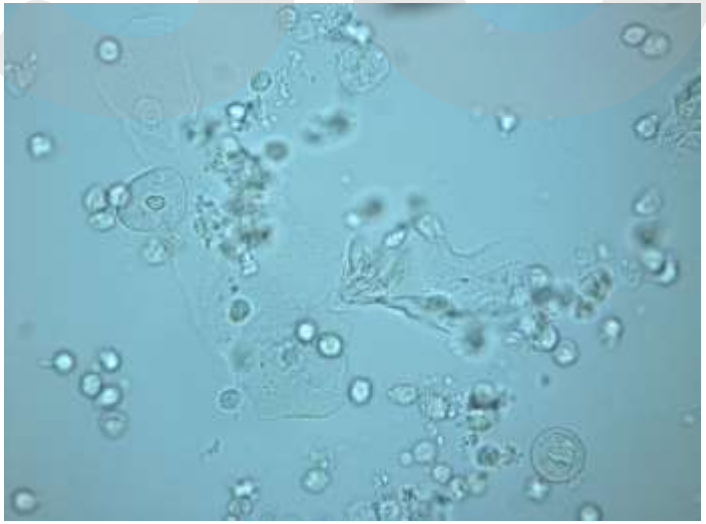
- Chemical, allergic or hypersensitivity reaction
- Foreign body, retained tampon
- Mucopurulent cervicitis (GC/CT)
- Vulvar Skin diseases
  - Erosive Lichen planus
  - Lichen sclerosus
- Vulvodynia
- Genitourinary Syndrome of Menopause (Atrophy)
- Desquamative inflammatory vaginitis (DIV)

Sobel, NEJM 1997 Vol 337

# Desquamative Inflammatory Vaginitis

- Symptoms
  - Burning
  - Pain with sex
- Exam
  - Profuse purulent discharge
  - Erythema, petichiae
  - Elevated vaginal pH >4.5
- Microscopy
  - WBCs, parabasal cells
- Treatment
  - 6 week course of intravaginal clindamycin 2% or hydrocortisone 10%





# Genitourinary Syndrome of Menopause

- Symptoms
  - Dryness, irritation, itching
  - Burning, Pain with sex
- Exam
  - Erythema, lack of rugae
  - Elevated vaginal pH >4.5
- Microscopy
  - Lack of cellularity,
  - Parabasal cells
- Treatment
  - Topical or systemic estrogen
  - Vaginal moisturizers
  - Topical Lidocaine