Learning Objectives

• Describe a differential diagnosis of the patient presenting with a vaginal discharge.
• Analyze the role of the office laboratory in diagnosing vaginitis.
• Identify the three most common causes of vaginitis and discuss the effective management of each.
Vaginitis

- one of the most common gynecologic disorders
- 10 million office visits/year and 7% visits to gynecologists
- 1% antibiotics prescribed in ambulatory setting
A vexing case of vaginitis

Sometimes, it is very difficult to be specific when a patient presents with vaginitis...

Therefore, you and I must act as detectives -- determining suspects, looking for clues, making decisions based upon deduction...

by Inspector Cluecell
Vaginitis: Differential Diagnosis

- **Infectious vaginitis - 60%**
  - Bacterial vaginosis
  - Candida vaginitis
  - Trichomonas vaginitis
- **Cervicitis - 20%**
- **Normal discharge - 10%**
- **Atrophic vaginitis**
Differential Diagnosis (con’t)

• Psychosomatic vaginitis
• Iatrogenic vaginitis
  Foreign body vaginitis
  Allergic / irritant vaginitis
• Miscellaneous
  Cervical polyps/ neoplasms
  Vulvar and vaginal neoplasms
  Macerated condylomata
“Finding the cause of back pain is often difficult, but let's give it a stab."
Useful historical items

- age
- menstrual status
- characteristics:
  - onset
  - color
  - consistency
  - viscosity
Associated symptoms

- pruritis
- burning
- malodor
- dysuria
- dyspareunia
Historical items

- Past medical history
  - diabetes
  - recent infection
  - medications
  - method of contraception
- Sexual history
- Hygienic practices
Physical examination

- careful gynecologic exam
- inspection of discharge
- close examination of vulvovaginal area
- careful inspection of cervix
"When did you first notice the symptoms?"
Office Laboratory Methods

- vaginal pool wet mount
  - saline prep (0.9 % saline)
  - KOH prep (10% )
- “whiff” test: (+) in BV
- vaginal pH: normal 3.5 to 4.5
- “Q-tip” test: (+) in cervicitis
“Q-tip” test:
Mucopurulent cervicitis
Office Laboratory (con’t)

- vaginal cultures- used on selective basis
  - Trichomonas:
    - modified Diamond’s, Trichosel, InPouchTV
  - Candida:
    - Sabouraud’s, Nickerson’s media
Case # 1:

A 17 y/o female HS student presents with a one day history of an increase in vaginal discharge--slightly sticky & cloudy--associated with mild soreness. Denies itching, burning, or malodor. Microscopic examination of the saline slide prep shows:
Wet mount:
Vaginal epithelial cells
Vaginal pool wet mount
Case # 1

A 17 y/o female HS student presents with a 1 day history of a vaginal discharge—slightly sticky & cloudy—associated with mild soreness. Denies itching, burning, or malodor. Microscopic exam ........

“Whiff test”- neg. Vaginal pH- 6.0
Question # 1:

What is your diagnosis?

a. Bacterial vaginosis
b. Candida vaginitis
c. Trichomonas vaginitis
d. Abnormal discharge - other
e. Normal discharge
Physiologic discharge

- responsible for 10 percent of cases of vaginal discharge
- composed of vaginal squamous cells suspended in fluid medium
- clinical characteristics:
  - clear to slightly cloudy
  - non-homogeneous
  - highly viscous
Normal vaginal discharge

- not associated with:
  - itching
  - burning
  - malodor

- normal increase in volume
  - ovulation
  - following coitus
  - after menses
  - during pregnancy
Wet mount:
Normal vaginal epithelial cell
Wet mount:
Clue cells
Wet mount:
Normal epithelial cells
Vaginal pool wet mount:
Sperm
Vaginal pool wet mount: sperm
Wet mount:
Trichomonads
**Vaginal pH**

- **normal:** pH of 3.5 to 4.5
- **pH over 4.5 is abnormal:**
  - 81 to 97% of bacterial vaginosis
  - 60% of Trichomonas vaginitis
- invalid if specimen contaminated with semen, blood, douche preps, cervical secretions
- obtain from lateral fornix
Case # 2:

28 y/o female grad student is seen for a 5-day history of a thin greyish-white discharge associated with vaginal burning and a fishy odor.....
Case # 2:

28 y/o female grad student is seen for a 5-day history of a thin greyish-white discharge associated with vaginal burning and a fishy odor. A scan of the saline prep under low power shows:
Wet mount (low power):
Wet mount (high power):
Wet mount:

Vaginal epithelial cells
Case # 2:

28 y/o female grad student is seen for a 5-day history of a thin, greyish-white vaginal discharge associated with vaginal burning and a fishy odor. Microscopic exam ..... 

Whiff test: (+) . Vaginal pH: 5.5
Question # 2:

What is the diagnosis?

a. Bacterial vaginosis
b. Candida vaginitis
c. Trichomonas vaginitis
d. Mixed infection
e. Normal discharge
Bacterial vaginosis

Diagnostic criteria (requires 3 of the 4):

1. thin, homogeneous discharge
2. vaginal pH over 4.5
3. positive “whiff” test
4. clue cells on wet mount
Wet mount:
Clue cells
Vaginal pool wet mount

Increased number of white cells:

- > 10 wbc/hpf
- > 1 wbc per epithelial cell
- Increase in cervicitis, trichomonas
- Variable in candida
- Reduced number in B. vaginosis
Wet mount:
Increased number of white cells
Wet mount:
Increased number of white cells
Vaginal pool wet mount

Increased number of white cells:

- > 10 wbc/hpf
- > 1 wbc per epithelial cell
- Increase in cervicitis, trichomonas
- Variable in candida
- Reduced number in B. vaginosis
Mgmt of Bacterial vaginosis

- Metronidazole- 1\textsuperscript{st} generation nitroimidazole regarded by many as “drug of choice”
- 500 mg BID x 7 days still “gold standard” (Phieffer, NEJM 1978)
Mgmt of Bacterial vaginosis

**ORAL:**
- clindamycin 300 mg BID x 7 days

**TOPICAL:**
- vaginal metronidazole gel 0.75%: 1 applicatorful qd or bid x 5 d
- vaginal clindamycin cream 2%: 5 g qd x 7 d
- vaginal clindamycin ovules: 100 mg qhs x 3 days
# Mgmt of Bacterial vaginosis

## Worst-case efficacy

<table>
<thead>
<tr>
<th>DOSE</th>
<th>relapse after 4 wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metronidazole 500 mg BID x 7 d</td>
<td>20 %</td>
</tr>
<tr>
<td>Metronidazole 2 g x 1 dose</td>
<td>50 %</td>
</tr>
<tr>
<td>Metronidazole vaginal gel</td>
<td>34 %</td>
</tr>
<tr>
<td>Clindamycin vaginal cream</td>
<td>42 %</td>
</tr>
<tr>
<td>Clindamycin vaginal ovules</td>
<td>49 %</td>
</tr>
</tbody>
</table>

Mgmt of Bacterial vaginosis

Tinidazole (2^{nd} generation)

- FDA approval in 2007 for treatment of BV
- 2 grams (4 tabs) once daily x 2 d or 1 gram (2 tabs) once daily x 5 d

* 2015 STD Guidelines rec. 2 days
Mgmt of male in B. vaginosisis

- **No benefit:**
  - Eschenbach, Scand J Inf Dis 1983
  - Swedberg, JAMA 1985
  - Vejtorp, Brit J Ob Gyn 1988
  - Moi, Genitourin Med 1989
  - Vutyavanich, Ob Gyn 1993
  - Colli, Genitourin Med 1997

- **Benefit:**
  - Mengel, J Fam Pract 1989
Mgmt of Recurrent B.V.
(Sobel et al, Am J Ob Gyn 2006;194:1283)

Prospective RCT of 112 women with recurrent BV following 10-day course of metronidazole gel

- 0.75% metronidazole gel BIW vs placebo x 16 weeks with 12-week post-Rx F/U
- RR = 0.43 (CI = 0.25-0.73) during Rx
- RR = 0.70 at end of 28 wk study period
- Adverse side effect: Candida vaginitis
Case # 3

A 34 years old female is seen for a one week history of a itchy, white, curd-like discharge. She notes that one week prior she was treated for a UTI with ciprofloxacin.
KOH prep:
Pseudohyphae
Mgmt: Topical imidazole agents

• single-day regimens:
  • clotrimazole 500 mg vaginal tab
  • tioconazole 3% - 300 mg/d x 1 d

• 3-day regimens:
  • butoconazole 2%: 120 mg/d x 3 d
  • clotrimazole 1%: 200 mg/d x 3 d

• 7-day regimens:
  • miconazole 2% - 100 mg/d x 7 d
  • clotrimazole 1% - 100 mg/d x 7 d
Mgmt of Candida vaginitis

- **Polyene antifungal agent:**
  - nystatin 100,000 units/d x 7 to 14 d

- **Triazole antifungal agents**
  - vaginal terconazole (Terazol®)
    - cream 0.4% - 20 mg/d x 7 d
    - cream 0.8% - 40 mg/d x 3 d
    - suppository - 80 mg/d x 3 d
  - oral fluconazole (Diflucan®)
    - single dose 150 mg. MR in 72 hrs
Mgmt of Recurrent Candida

- identify predisposing factors
  - diabetes, antibiotics, medications, candida in partner, HIV infection
- yeast cultures
Mgmt of Recurrent C. albicans
Options from 2015 CDC Guidelines

Extended course of therapy

- Topical therapy for 7 to 14 days
- Fluconazole 100-200 mg PO on days 1, 4, and 7

Maintenance 6 mo regimens:

- Fluconazole 100-200 mg PO q week*
- Clotrimazole 500 mg vaginal suppository q week
- Topical clotrimazole 200 mg BIW

* preferred
Case #4

A 44 years old nurse is seen for a 2 mo hx of recurrent “yeast” infections. She reports that despite treatment with several OTC as well as prescription yeast meds, her infection continues to recur. Her 10% KOH prep shows only:
KOH prep:
Question # 3

What is the cause of her discharge?

A. Candida albicans
B. Candida tropicalis
C. Candida glabrata
D. Blastomyces dermatitidis
E. Torulopsis sporium
Vaginal pool wet mount

KOH prep: “budding spores and the absence of pseudohyphae”

- Candida glabrata
- Saccharomyces cerevisiae
Mgmt of Candida glabrata

- Topical imidazole agent x 7-14 days
- Topical nystatin vaginal suppository (100,000 units) q d x 14 days
- Boric acid vaginal capsules 600 mg vaginal q d x 14 d
- Topical 17% flucytosine vaginal cream q d x 14 days

28 year old housewife is seen by you for a one week history of a frothy, greenish, malodorous vaginal discharge. She also complains of dyspareunia and vaginal irritation. Vaginal pH is 6.5 and the “whiff” test is positive. Examination of cervix:
Question # 4

What is the diagnosis?

a. Herpes genitalis
b. Trichomonas vaginalis
c. Mycoplasma genitalium
d. Bacterial vaginosis
e. Chlamydia trachomatis
Vaginal pool wet mount

Trichomonas vaginalis:
- motile trichomonads
- pear-shaped, larger than WBC
- examine immediately, use fresh saline
- round up when inactive or die
Wet mount:
Trichomonads
Trichomonas vaginalis

- common non-viral STI
- 3% prevalence in the U.S.
- 3.7 million people with TV
- 1.1 million new cases per year
Trichomonas vaginalis
Prevalence

- 60% more common in women, 11% in symptomatic women over 40 yrs
- Health care disparities: 13.3% African American, 1.8% Hispanic, 1.3% white (NHES survey)
- Settings: 32% incarcerated subjects, 17% in STD clinic
Trichomonas vaginalis
Adverse outcomes and sequelae

- 2-3 X risk of acquiring HIV and 2X risk of transmission to infant
- higher risk of having CT, GC, HSV, and syphilis
- adverse pregnancy outcomes
- higher risk of PID - CDC favors TV screening in HIV-infected women
Trichomonas vaginalis
Neglected and underdetected

• “more than a nuisance” and remains a neglected often undetected STI
• asymptomatic: 70-85% with no or minimal symptoms
• lack of an available, sufficiently sensitive diagnostic test

CDC: 2015 STD Guidelines
Trichomonas vaginalis
Diagnostic Tests

Vaginal cultures- “gold standard”
• cultures: Diamond’s®, InPouch TV®, Trichosel®
• Sensitivity: 75-96 %
• expense, 2-7 day incubation period required
Trichomonas vaginalis
Diagnostic Tests

NAAT- e.g. APTIMA®, BD Probe Tech TV Q®, Xpert TV test®
- more sensitive than culture: 95.3- 100%
- new “gold standard”
- expense, need for specimen transport, hours to days for results
Trichomonas vaginalis
POC Diagnostic Tests

Vaginal pool wet mount:
• sensitivity: 44-68 % \(^1\)
• detection level: >10^4 cells/ml \(^2\)
• delay 10 min ➔ 20 % ↓ sensitivity \(^3\)

Alternative POC tests:
• Nuclear acid probe test
• Rapid antigen test

1. STI 2013;89:434
### Diagnostic tests for Trichomonas

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wet mount</td>
<td>51-65 %</td>
<td></td>
</tr>
<tr>
<td>NAPT</td>
<td>63 %</td>
<td>99.9 %</td>
</tr>
<tr>
<td>RAT</td>
<td>82-95 %</td>
<td>97-100 %</td>
</tr>
<tr>
<td>Culture</td>
<td>75-96 %</td>
<td>100 %</td>
</tr>
<tr>
<td>NAAT</td>
<td>95.3-100 %</td>
<td>95.2-100 %</td>
</tr>
</tbody>
</table>

NAPT: Nucleic acid probe test  
RAT: Rapid antigen test  

[CDC: 2015 STD Guidelines]
# NAPT versus RAT

<table>
<thead>
<tr>
<th>TEST</th>
<th>SENSITIVITY</th>
<th>TIME TO RESULT</th>
<th>EQUIPMENT</th>
<th>CLIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAPT</td>
<td>63 %</td>
<td>45 min</td>
<td>Analyzer Instrument</td>
<td>CLIA moderate complexity</td>
</tr>
<tr>
<td>RAT</td>
<td>82-95 %</td>
<td>10 min</td>
<td>None</td>
<td>CLIA-waived</td>
</tr>
</tbody>
</table>
## Diagnostic tests for Trichomonas: Sensitivity

<table>
<thead>
<tr>
<th>Test Method</th>
<th>All patients (n = 330)</th>
<th>Symptoms (n=210)</th>
<th>No symptoms (n=120)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wet mount</td>
<td>50.8 %</td>
<td>57.5 %</td>
<td>38.1 %</td>
</tr>
<tr>
<td>Culture</td>
<td>75.4 %</td>
<td>77.5 %</td>
<td>71.4 %</td>
</tr>
<tr>
<td>RAT</td>
<td>82.0 %</td>
<td>92.5 %</td>
<td>61.9 %</td>
</tr>
<tr>
<td>TMA</td>
<td>98.4 %</td>
<td>97.5 %</td>
<td>100 %</td>
</tr>
</tbody>
</table>

RAT: Rapid antigen test  
TMA: transcription-mediated amplification  
Mgmt of Trichomoniasis

- Metronidazole- 1st generation nitroimidazole long regarded as “treatment of choice”

- Two regimens prescribed:
  - 2 grams as single dose
  - 500 mg BID x 7 days

- Single dose regimen preferred
Mgmt of Trichomoniasis
Alternative to Metronidazole

- Tinidazole ("Tindamax®")
- FDA approval 5/04
- antiprotozoal agent (nitroimidazole)
- dose: 2 grams as single dose with food
- longer half-life
- less GI side effects
Mgmt of Trichomonas vaginitis

- adverse reactions: side effects including antabuse reaction (24 hr for metronidazole, 72 hr for tinidazole)
- use during pregnancy
- use in patient who is breastfeeding
- Trichomonas is a STD requiring STD measures
“I’m sure you’ll agree, we don’t want an epidemic.”
Mgmt of Trichomonas

STD measures:

- partner(s) require Rx
- evaluation for other STDs
- counseling re HIV testing and need for safer sexual practices
Case # 6

42 years old married female attorney is seen by you for her annual physical examination. Pap smear reveals evidence for trichomonas. Her husband (of 10 years) is also a patient of yours and both he and the patient adamantly deny any instance of infidelity.
Question # 5

What is the explanation?

a. False positive test
b. He cheated
c. She cheated
d. Acquisition prior to marriage
e. Use of public toilet
Trichomonas on Pap smear

- sensitivity: 60 percent
- specificity: 92 percent (standard Pap); 96 percent (liquid-based)
- Bayes theorem

**PREVALENCE**

- 20 % - 1 in 2 is false (+)
- 1 % - 19 in 20 is false (+)
  (9 in 10 if liquid-based*)
Trichomonas on Pap smear

- sexual transmission
  - recent acquisition
  - remote acquisition (dormant)
- non-venereal transmission?
  - ? rare
  - isolation from fomites (i.e. toilet seat)
Trichomonas Vaginalis (con't)


Vaginal material "teeming" with trichomonas

**Table IX**

*Time of survival (min.) of T. vaginalis on lavatory seats*

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Bakelite</th>
<th>Polished Wood</th>
<th>Absorbent Wood</th>
<th>Control</th>
<th>Room Temperature (°C.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>45</td>
<td>45</td>
<td>20</td>
<td>+</td>
<td>+15</td>
</tr>
<tr>
<td>2</td>
<td>30</td>
<td>45</td>
<td>30</td>
<td>+</td>
<td>+12.5</td>
</tr>
<tr>
<td>3</td>
<td>45</td>
<td>45</td>
<td>30</td>
<td>+</td>
<td>+11.2</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>+</td>
<td>+10.5</td>
</tr>
</tbody>
</table>
Trichomonas Vaginalis (con't)


Patients with heavy T. Vaginalis infections asked to "pass water" in water closet

Table X

Contamination by T. Vaginalis of lavatory seats

<table>
<thead>
<tr>
<th>Total No. of Patients</th>
<th>Sat on Seat</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>30</td>
<td>17</td>
</tr>
</tbody>
</table>

Seat Dry after Use

<table>
<thead>
<tr>
<th>Seat Dry after Use</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>11</td>
<td>8</td>
</tr>
</tbody>
</table>

Material left on Seat after Use

<table>
<thead>
<tr>
<th>Material left on Seat after Use</th>
<th>T. v. positive</th>
<th>T. v. negative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>3</td>
</tr>
</tbody>
</table>
Vaginitis: Meeting the Clinical Challenge

- Common gynecologic problem
- Key to management is accurate diagnosis
  - History and examination
  - Office lab: wet mount, pH, “whiff test”, Q-tip test
- Specific dx allows for effective Rx