Vaginal Discharge Syndromes

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Cervical Anatomy and Terminology

- Ectocervix
- Endocervix
- Ectopy (“Ectropion”, “Erosion”)
  - Physiologic ectopy: Migration of endocervical mucosa onto the ectocervix
    - Onset ~menarche
    - Usually regresses age 17-20
    - Can recur during pregnancy or hormonal contraception
    - Partly explains strong association of chlamydia with youth
    - Regression can generate nabothian cysts
  - Pathologic ectopy: Inflammatory edema causes eversion (“edematous ectopy”)
- Vagina has no mucus-secreting glands; presence of mucus in vaginal secretions denotes cervical origin

Courtesy: Dr. Hunter Handsfield
The normal vagina

- Lined by a mucous membrane
- Stratified, squamous, cornified epithelium
- Several layers thick
- Superficial cells are sloughed off and Lactobacillus converts glycogen into lactic acid
- Estrogen maintains vaginal wall thickness
Normal vaginal flora

• ~95% of bacteria are Lactobacillus
• Other 5% include (with approximate incidence)
  – Streptococci spp. (50-70%)
  – Staphylococcus epidermidis (40-90%)
  – Diphtheroid spp. (40-70%)
  – Gardnerella vaginalis (40-50%)
  – Peptostreptococci spp. (45-90%)
  – Bacteroides spp. (40-60%)
  – Anaerobic Lactobacillus (15-45%)
  – Ureaplasma urealyticum (50-80%)
  – Mycoplasma hominis (20-50%)
Role of Lactobacillus

- Predominant bacteria in normal flora
- Produces lactic acid and hydrogen peroxide
  - Maintains pH of 3.8-4.4, which is hostile to other bacteria
- Produces bacteriocidin which interferes with bacterial adherence to epithelial cells
- As a result, anaerobes are kept at low levels
Normal vaginal flora, cont.

- Fluctuations in vaginal microbial ecosystem likely occur day-to-day in response to:
  - Menses: more alkaline pH; lower Lactobacilli levels
  - Hormonal changes
  - Exogenous materials (douches, spermicides, diaphragm)
  - Sexual behaviors: frequency of intercourse; number of partners
    - Semen, GBS, Enterococci, E. coli (perineal residents)
  - Antibiotic use: polyamines produced by some vaginal bacteria may help to inhibit Candida
Case 1 - history

- Patient is a 23 yo heterosexual woman with 1 partner, but she thinks he may have another partner
- Vaginal discharge x 2 months, worse in last week; also noticing vague pain with intercourse during the last week
- Using oral contraceptive for birth control
Case 1 - exam

- Speculum exam reveals normal vaginal discharge
- Cervix has yellow endocervical discharge
- Gram stain of the cervical discharge shows >30 WBC/ oil immersion field
- Wet prep is normal except for increased WBC
- Urine HCG is negative
The Swab Test to Detect Mucopurulent Endocervical Discharge

Courtesy: Dr. Hunter Handsfield
Case 1 - assessment

What is the likely diagnosis for this patient?
Symptoms of Cervicitis

- Most cases are subclinical
  - Truly asymptomatic
  - Minor symptoms, e.g. small variations in quantity or quality of vaginal secretions
- Increased vaginal discharge
  - Variable color and staining
  - Little or no odor
- Dysuria (actually represents concomitant urethritis)
- Abnormal bleeding
  - Usually scant
  - Often postcoital
  - Occasionally overt menorrhagia, metrorrhagia
Diagnosis of Cervicitis

- Signs: specific, but insensitive:
  - Easily induced bleeding ("friability")
  - Mucopurulent discharge: swab test
  - Edematous ectopy
  - Discrete lesions (ulcers): can occur anywhere

- Increased PMNs ("polys;" >10-30/HPF) on Gram stain of endocervical secretions: may be sensitive for endocervicitis, but not specific; variable in ectocervicitis

Courtesy: Dr. Hunter Handsfield
STD as a Cause of Cervicitis

- Endocervicitis (mucopurulent cervicitis, MPC)
  - Gonorrhea
  - Chlamydia
  - ? *Mycoplasma genitalium* 10-15%?
  - Other/unknown 40-60%

- Ectocervicitis: often associated with vaginal infection
  - Trichomoniasis
  - *Candida albicans* (probable but infrequent)
  - Bacterial vaginosis (?)

- Discrete lesions
  - Herpes simplex virus
  - Syphilis
  - Human papillomavirus
  - Cervical cancer

Courtesy: Dr. Hunter Handsfield
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Workup of Cervicitis

• Bimanual pelvic examination to rule out PID
• Test for chlamydia and gonorrhea using most sensitive test available
• Careful examination of vaginal fluid, pH
  – Look for BV, trichomomiasis, *Candida*
• Additional diagnostic tests based on clinical judgment (HSV culture, syphilis serology)
• Consideration of STD risk (partner history etc.)

Courtesy: Dr. Hunter Handsfield
Treatment of Cervicitis

• Treat for gonorrhea and chlamydia, unless either or both has been excluded by specific testing or prior adequate treatment

• Persistent or recurrent cervicitis
  – Azithromycin (*M. genitalium*)
  – Metronidazole (trichomoniasis)

Courtesy: Dr. Hunter Handsfield
Chronic or Persistent Non-GC, non-CT Mucupurulent Cervicitis

- A very common clinical problem, but no useful data exist on prevalence, incidence, or natural history
- Clinical significance unknown
  - One study suggests adverse pregnancy outcomes (Nugent)
- Re-evaluate at least once for gonorrhea and chlamydia
- Treat with azithromycin at least once to cover *C. trachomatis* and *M. genitalium*
- Be sure partner treated (azithromycin or doxycycline)
- Ablative therapy (laser or cryotherapy) is often used and is anecdotally successful; no data

Courtesy: Dr. Hunter Handsfield
Cervicitis: Summary

- **Established criteria**
  - Yellow pus on an endocervical swab
  - Easily induced bleeding has equal predictive value

- **WBC assessment**
  - Endocervical gram stain
    - Less useful test outside research settings
    - But maybe an occasional tie-breaker in difficult cases
  - However, *vaginal* WBC assessment is easy to perform and increases predictive value of the clinical diagnosis of cervicitis but there are many unanswered questions

- **Principal utility of diagnosis is empiric GC/CT treatment**
  - Positive predictive value (PPV) is dependent on prior probability of infection with these STDs

Courtesy: Dr. Hunter Handsfield
Case 2 - history

- An 18 year old female presents to the clinic c/o discharge with odor for two months.
- **Sexual History:** 1 new partner in the past month, 3 partners in the past 4 months. Pt states she only had vaginal sex in the past 4 months and only has sex with men. Pt reports 75% condom use in past 4 months. Pt started having sex at age 14.
Case 2 – history cont. & exam

• **STD History:** GC twice in lifetime, both over 1 year ago. Pt also tested positive for CT and Trich within the last year. Last HIV test was negative one year ago.

• **Physical Exam:** Moderate milky off-white vaginal discharge that is coating the cervix and pooling beneath the cervix. Negative CMT/adnexal tenderness.
Case 2 – laboratory

- What laboratory tests should be ordered?
Case 2 – laboratory, cont.

- What laboratory tests should be ordered?

- Tests to diagnose vaginitis:
  - Wet prep
  - KOH
  - Whiff
  - pH
  - Trichomonas?

- Additional STD testing:
  - GC/CT NAAT, HIV, RPR
Case 2 - lab results

- HIV nonreactive
- GC/CT SDA pending
- KOH negative
- NS positive clues, negative trichomonads
- Whiff positive
- pH > 5.5
Case 2 - assessment

- Based on the lab findings what is the diagnosis for this patient?
Case 2 – assessment, cont.

Based on the lab findings what is the diagnosis for this patient?

Meets Amsel criteria:

- Thin watery discharge
- Positive whiff test
- Ph >4.5
- Clue cells present

Need 3 of 4

Dx: bacterial vaginosis
The Vaginal Milieu in Bacterial Vaginosis

- Profound loss of H₂O₂ - producing *Lactobacilli*
- Overgrowth of “commensal” anaerobes
- Production of sialidase (IgA destruction), glycosidase, volatile amines
- ↑ IL-1B, IL-10; ↓ IL-8, SLPI (secretory leukocyte protease inhibitor)

Nugent = 0

Nugent = 10

Courtesy: Dr. Hunter Handsfield
Case 2- treatment

What is your treatment plan for this patient?
Nonpregnant Women

- **Recommended**
  - Metronidazole 500 mg PO bid x 7 d
  - Metronidazole gel 0.75% intravag qHS x 5 d
  - Clindamycin cream 2% intravag qHS x 7 d (*< efficacy*)

- **Alternatives**
  - Tinidazole 2 gm daily for 5 d or 1 gm daily for 7 d
  - Clindamycin 300 mg PO bid x 7 d
  - Clindamycin ovules 100 g intravag qHS x 3 d
Other Treatment Considerations in Nonpregnant Women

- No ETOH during, 24 h after MTZ; routine TX of partners not indicated; mineral oil in clindamycin preparations may weaken latex
- Metronidazole 750 mg extended-release tablets approved as a once daily dose for 7 days; however, no comparative data available
- No role for douching or for treatment with oral (OTC) lactobacilli, intravaginal yogurt
- Studies of intravaginal lactobacillus capsules not encouraging
Case 3 - history

• This patient took all her metronidazole and her symptoms resolved. Over the next 6 months she returns and is diagnosed with bacterial vaginosis each time
• She is frustrated and wants to know why she keeps getting this and how she can get over it
• What do you tell her?
BV recurrence

- Recurrence is common: up to 80% within 9 months
- Why?
  - Failure of lactobacilli to recolonize
  - Persistence of untreated ‘pathogens’
  - Re-exposure to some inciting factor (sexual)
  - Persistence of unidentified host factor
Risk factors for development of BV

- Recent douching ↑
- New sexual partner male or female
- IUD
- Condom use -- trend towards ↓, but no consistent definitive protective effect (Evans 95; Hawes 96); among women initiating sex for first time, no condom use ↑ risk 8-fold, more recent intercourse 6-fold (Hillier, PC)
- Oral contraceptives: no clear association
BV recurrence

- Suppressive MTZ regimens:
  - 14 days intravaginal metronidazole, then biweekly (q Mon and Thurs) maintenance therapy with same for 6 months


  - Condom use probably helpful, and avoid douching
21 yr old female presents for a check up and you discover she is 8 weeks pregnant

She has no history of STD’s and only has one partner. She never uses condoms

She has a slight, white homogenous vaginal discharge on exam which she has not noticed and she denies itchiness or discomfort
You decide to do a wet prep which has a positive whiff test, a pH of 5.0, and has clue cells.

You diagnose BV on the basis of meeting 3 of 4 Amsel criteria.
Case 4 - treatment

- Should you now treat this pregnant patient?
Bacterial vaginosis in pregnancy

• *Should you now treat this pregnant patient?*

• Per STD 2006 treatment guidelines BV should be treated in pregnancy if the patient is symptomatic

• Treat if the patient has a history of pre term birth whether she is symptomatic or not

• Studies that look at screening asymptomatic low risk women for BV to prevent preterm birth have conflicting results so at this time it is not recommended
If you decide to treat her, what should you treat her with?
If you decide to treat her, what should you treat her with?

Metronidazole 500 mg bid po x 7 days

No evidence of teratogenicity, even in first trimester

Alternative regimens:

- Metronidazole 250 mg po tid for 7 days
- Clindamycin 300 mg bid po x 7d
BV treatment in pregnancy

- Systemic therapy is important
- Metronidazole 500 mg bid po x 7d
- No evidence of teratogenicity, even in first trimester
- Alternative regimens:
  - Metronidazole 250 mg po tid for 7 days
  - Clindamycin 300 mg bid po x 7d
Case 5 - history

- 24 year old F presents with persistent vaginal discharge
- She is symptomatic with vulvar/vaginal irritation and itching
- Seen at the STD clinic 2 weeks ago and treated for TV with metronidazole 2 g X1
- Discharge cleared in 2 days, but then reoccurred
- Partner was treated
- No sex for the past 2 weeks
Case 5 - exam

- On examination: frothy yellow-green vaginal discharge with odor
Case 5 - laboratory

- Wet prep: numerous WBCs with trichomonas identified
Trichomoniasis: The Basics

- Etiology: *Trichomonas vaginalis*
- Sexually transmitted
  ? colonic reservoir
- Mostly asymptomatic
- Male partners generally asymptomatic; sometimes NGU
- Saline mount insensitive (~50-60%)
  - Culture ~70%;
  - PCR required to detect >90% of cases
Case 5 - discussion

• What do you want to do?
Trichomoniasis Treatment

Recommended regimen
  – Metronidazole 2 g PO x 1
  – Tinidazole 2 g po x 1

Alternative regimen
  – Metronidazole 500 mg PO BID x 7d
  – Routine use for recurrent/persistent cases

• Metronidazole is safe at all stages of pregnancy
• Vaginal therapy is ineffective
• Treat sex partner(s)
Trichomoniasis – treatment failure

- Why has this infection not cleared?

- Low level metronidazole resistance identified in 2%-5% of cases of TV
- High level resistance is rare
- Tinidazole has a longer half-life and reaches higher levels in genitourinary tissues than metronidazole
Trichomoniasis – treatment failure, cont.

- If treatment failure occurs with 2 g metronidazole, options include:
  - Metronidazole 500 mg: orally twice a day for 7 days
  - Tinidazole 2 g: orally in a single dose
- If treatment failure with either of these regimens:
  - Tinidazole or metronidazole 2 g orally for 5 days
- If these therapies are not effective:
  - Consultation and susceptibility testing through CDC
Case 6 - history

- 24 year old F presents with a 1 week history of vaginal discharge
- She is complaining of vulvar irritation and itching with dysparuenia and dysuria
- She has tried some OTC medications without help
Case 6 – exam and laboratory

- On examination:
  - Vulvar erythema
  - Vaginal discharge that is thick, curdy white which adheres to the walls of the vagina
- Wet prep: yeast and pseudohyphae identified
- PH < 4.5
- Negative whiff test
Case 6 - discussion

• *What do you want to do?*

• *How do you want to treat this patient?*
Fluconazole 150 mg PO, single dose
Any 3-7 day vaginal imidazole regimens (miconazole, clotrimazole, terconazole, butaconazole, tioconazole)
Single dose of intravaginal butoconazole sustained-release cream
Nystatin 100K unit vaginal tablet qd x 14 d
Pregnancy: 7 days of vaginal imidazoles (Avoid fluconazole; clotrimazole category B, others imidazoles category C)
VVC risk factors

- Diabetes
- Corticosteroid use
- Repeated course of antibiotics
- Pregnancy
- HIV disease
- Occlusive clothing
- Most healthy women with uncomplicated VVC have no precipitating factors
Treatment - comments

- Treatment indicated for relief of symptoms
- Oral and topical therapy achieve comparable clinical cure rates
- Since absence of superiority of any formulation, agent, and route of administration—consider cost, patient preference, and contraindications
- Fluconazole 150mg:
  - therapeutic concentration in vaginal secretions for at least 72 hours
  - Side effects: mild/infrequent; interacts with multiple medications
  - Generic, so cost less than OTC topical therapy
Treatment – comments, cont.

- Majority of infections uncomplicated (90%)
- Criteria for uncomplicated infections
  - Sporadic, infrequent episodes
  - Mild/moderate signs/symptoms
  - Probable infection with C. albicans
  - Healthy, non-pregnant woman
Treatment – comments, cont.

• Complicated infections criteria:
  – Poorly controlled diabetes, immunosuppression, debilitation
  – Severe signs/symptoms
  – Candida species other than C. albicans
  – Pregnancy
  – History of recurrent (≥4/year) infections

• Treatment: prolonged therapy
  – Topical for 7-14 days
  – Two doses of oral therapy-fluconazole 150mg 72 hours apart
Questions?
Additional comments on vaginitis
Vaginitis: etiologies

- Trichomoniasis: 40%
- Candidiasis: 20%
- Bacterial vaginosis: 20%
- Other: 20%

“Other” includes atrophic, irritant/chemical, desquamative interstitial vaginitis; erosive lichen planus
Vaginitis: common chemical irritants

- Can cause an inflammation of the vagina: reactive/chemical vaginitis
  - Perfumed or deodorant soap
  - Adhesive on minipads
  - Perfumes, hair products, powder
  - Chemically treated clothing, tap water
  - Deodorant hygiene products
  - Douches and home remedies (yogurt)
  - Laundry detergent

- Treatment: eliminate offending agent, sodium bicarb sitz baths and topical vegetable oils for local relief; avoid topical steroids
Atrophic vaginitis

- Seen in estrogen deficiency (postpartum, postmenopausal)
- Unrecognized cause in younger women with hypoestrogenic states
  - Breast feeding
  - Female athletes who are not menstruating
  - Tamoxifen in premenopausal women
  - Ovarian non-function due to chemotherapy radiation, Lupron, Danazol
  - Can be seen in some women on DMPA
- Discharge often thin, scanty, may be purulent, bloody
- Vagina appears smooth, thin, dry, pH 6-7; may appear granular, with patchy inflammation or shallow ulcerations; at risk for superinfection
- Treatment: estrogen replacement therapy
Management of atrophic vaginitis

• For women in whom systemic hormone replacement therapy is contraindicated:
  – Vaginal lubricants (without N-9, water-based)
  – Estring: estradiol vaginal ring inserted into the upper vagina, releases 7.5µg/24 hours over 90 days; replace after 3 months: little systemic absorption
  – Contraindicated: pregnancy, lactation, breast cancer
  – Newer SERMs (raloxifene) do not treat genitourinary effects of estrogen deficit
Problems in accurate diagnosis of vaginitis

- Failure to do microscopy
  - Or appropriate point-of-care test
- Poor quality microscopy
- Insensitivity of wet prep for trich, yeast
- Failure to do pH/amine test
- Inappropriate reliance on vaginal bacterial cultures
- Mixed infections present, undetected
- Use of OTC products for self-treatment can obscure diagnosis
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