STD Testing and Treatment Update

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Disclosures

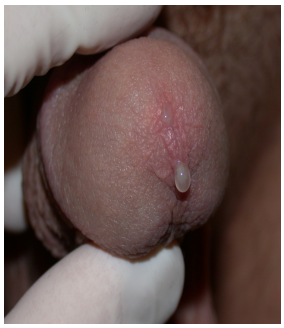
- Faculty: William M. Geisler, M.D., M.P.H.
- Has the following relevant financial relationships with ACCME-defined commercial interest: *Hologic, Inc*. The nature of that relationship is *current research and previous consulting*.
- Has the following relevant financial relationships with ACCME-defined commercial interest: *Sanofi*. The nature of that relationship is *previous consulting*.
- I will not discuss off label use and/or investigational use in my presentation

Urethritis Case

History: 26yo male presents with urethral irritation, dysuria, and intermittent urethral discharge for 7 days. He is having unprotected sexual intercourse with one female partner

Examination: cloudy urethral discharge

Diagnosis: urethritis



Urethritis Etiologies

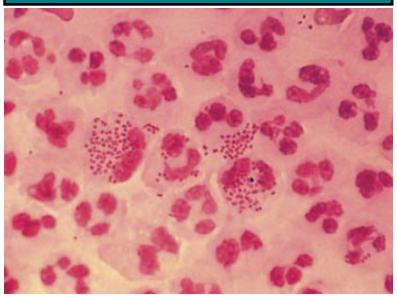
- Bacterial etiology established firmly for *Neisseria gonorrhoeae, Chlamydia trachomatis, and Mycoplasma genitalium*
  - *Neisseria meningitidis* is a rare cause
- *Trichomonas vaginalis* is an established parasitic etiology of urethritis
- Coinfection common, especially with gonorrhea and chlamydia
- Herpes simplex virus (HSV) is a viral cause of urethritis

Urethritis Testing

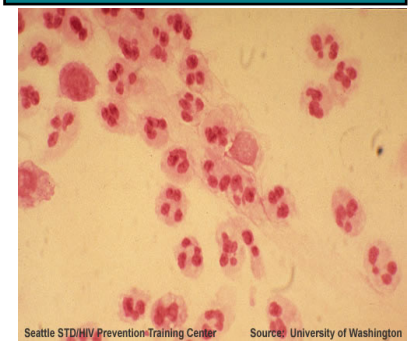
- Urethral swab Gram stain or methylene blue (MB) / gentian violet (GV) stain if urethral symptoms or exam findings
  - ≥2 WBCs (PMNs) per oil field usually present
  - Gram-negative or MB/GV purple diplococci c/w gonorrhea
- Urine leukocyte esterase if Gram stain N/A and no discharge
- Nucleic acid amplification test (NAAT) for chlamydia and gonorrhea on urethral swab or first-catch urine
- *Trichomonas* NAAT (in heterosexual men) if available

2015 CDC STD Treatment Guidelines

Presumed Gonorrhea



Nongonococcal Urethritis



Urethritis Initial Treatment

- Urethritis without Gram stain to guide treatment→ treat for gonorrhea and chlamydia
- Nongonococcal urethritis (NGU) findings on Gram stain→ treat for chlamydia
- Presumed gonorrhea findings on Gram stain→ treat for gonorrhea and chlamydia

Chlamydia Treatment

2015 CDC STD Treatment Guidelines

Recommended:

- Azithromycin 1 g PO single dose **OR**
- Doxycycline 100 mg PO twice daily for 7 days

Alternative:

- Erythromycin base 500 mg PO four times a day for 7 days **OR**
- Ofloxacin 300 mg PO twice daily for 7 days **OR**
- Levofloxacin 500 mg PO daily for 7 days

(Quinolones approved for adolescents)

ChlamydiaTreatment

Draft 2021 CDC STI Treatment Guidelines

Recommended:

- Doxycycline 100 mg PO twice daily for 7 days

Alternative:

- Azithromycin 1 g PO single dose **OR**
- Levofloxacin 500 mg PO daily for 7 days

(Quinolones approved for adolescents)

Gonorrhea Treatment

2020 Update to CDC STD Treatment Guidelines

Recommended

- Ceftriaxone 500 mg IM x 1

OR IF NOT AN AVAILABLE…

- Cefixime 800 mg PO x 1

→ **If cephalosporin allergy**: dual treatment intramuscular gentamicin 240 mg plus oral azithromycin 2 g

Gonorrhea Treatment Follow-Up

2020 Update to CDC STD Treatment Guidelines

- **If patient has pharyngeal GC: test of cure by culture or NAAT in 7-14 days**
  - Culture provides opportunity for susceptibility testing

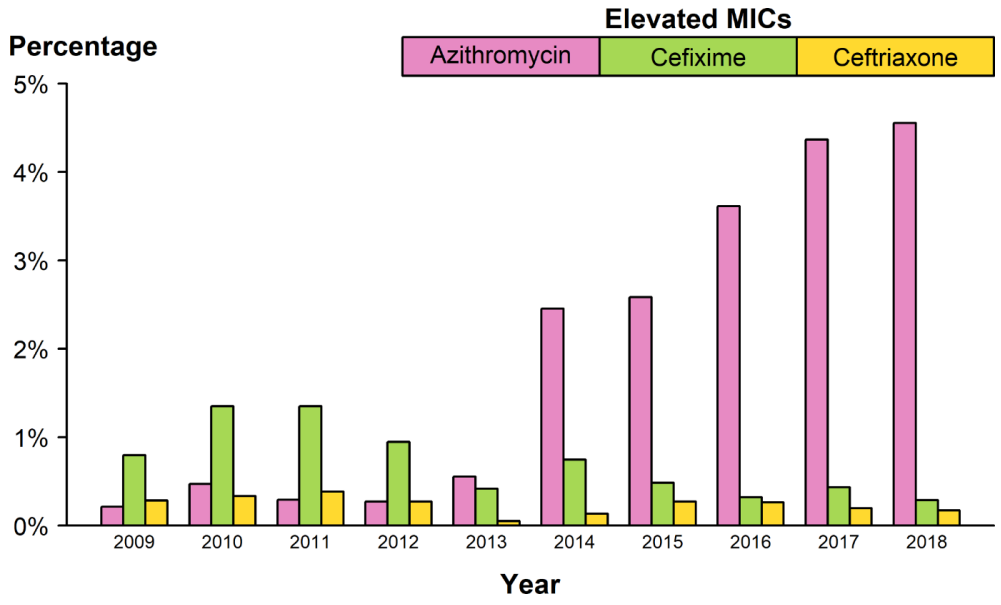
- **Recommendations for suspected GC treatment failures**
  - Gonorrhea culture and susceptibility testing
  - Consultation with ID specialist or STD clinical expert
  - Report to CDC through state and local public health authorities within 24 hours

Why is azithromycin no longer used first line in chlamydia or gonorrhea therapy?

- Doxy has higher cure rates than azithro for men with symptomatic urogenital chlamydia[1]
- Doxy has higher cure rates than azithro for rectal chlamydia[2,3]
- Rectal chlamydia detected in 33%-83% of women with urogenital chlamydia[4]
- Azithromycin resistance is increasing in gonorrhea and *M. genitalium* infections

1. Kong, et al. Clin Infect Dis. 2014 ;59:193-205.
2. Kong, et al. J Antimicrob Chemother. 2015;70:1290-7.
3. Dombrowski, et al. Clin Infect Dis. 2021 Feb 19:Epub ahead of print.
4. Dukers-Muijrers, et al.. BMC Infect Dis. 2015;15:533.

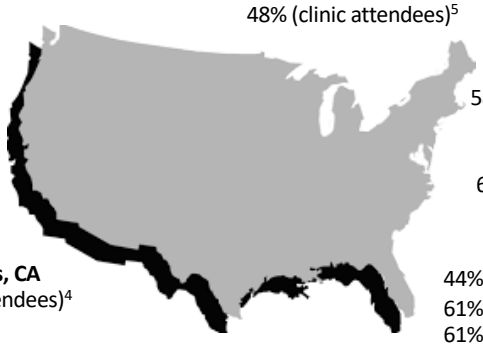
Neisseria gonorrhoeae — Percentage of Isolates with Elevated Minimum Inhibitory Concentrations (MICs) to Azithromycin, Cefixime, and Ceftriaxone, Gonococcal Isolate Surveillance Project (GISP), 2009–2018



NOTE: Elevated MIC = Azithromycin: ≥ 2.0 µg/mL; Cefixime: ≥ 0.25 µg/mL; Ceftriaxone: ≥ 0.125 µg/mL.

M. genitalium Macrolide Resistance Mutations (MRMs)* in the U.S.

MRM prevalence range from 44%-90% across U.S. sites



7 cities
48% (clinic attendees)[5]

Seattle, WA
62% (hetero men)[1]
69% (men w/urethritis)[2]
90% (MSM)[3]

Pittsburgh, PA
58% (men w/urethritis)[2]

Durham & Greensboro, NC
61% & 64% (men w/urethritis)[2]

Birmingham, AL
44% (STD Clinic)[6]
61% (hetero couples)[7]
61% (men w/urethritis)[2]
74% (HIV+ MSM)[8]

Los Angeles, CA
80% (clinic attendees)[4]

New Orleans, LA
60% (men w/urethritis)[2]

***MRMs in the 23S rRNA gene, typically A2071 and A2072 (*E.coli* numbering 2058 and 2059)**

[1]Romano 2018; [2]Bachmann 2019; [3]Chambers 2019; [4]Allan-Blitz 2018; [5]Getman 2016; [6]Xiao 2018; [7]Xiao 2019; [8]Dionne-Odom 2018

Slide Courtesy of Lisa Manhart

Other Urethritis Treatment Issues

- Rescreen men 3 months after treatment of chlamydia gonorrhea, or trichomoniasis
  - Repeat positive tests most likely due to reinfection
- Sexual partners should be evaluated and treated

2015 CDC STD Treatment Guidelines

Recurrent/Persistent NGU

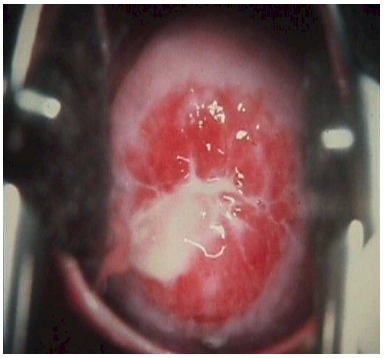
- Occurs in up to 25% of NGU cases
- If patient noncompliant with treatment or re-exposed, then treat with standard NGU regimens
- *Trichomonas vaginalis* and *Mycoplasma genitalium* are major causes
  - Test for these organisms by NAAT if not previously tested
- If patient initially compliant and exposure absent:
  - In areas of high trichomoniasis prevalence → Treat with metronidazole or tinidazole 2 g PO plus azithromycin extended dosing (assuming doxycycline used for the initial NGU episode)
  - If trichomoniasis not a concern (e.g., MSM or already tested negative)→ treat with azithromycin extended dosing (assuming doxycycline used for the initial NGU episode)
  - If fails repeat NGU treatment and remains compliant or *Mycoplasma genitalium* a concern→ treat with moxifloxacin 400mg PO daily x 7 days

Cervicitis Case

History: 16yo female presents with bleeding between menstrual periods, pain with sexual intercourse, and abnormal vaginal discharge. Having unprotected intercourse with a male partner.

Examination: Cervix shows mucopurulent exudate in the cervical os

Diagnosis: Cervicitis



Cervicitis - Etiology

- *C. trachomatis* and/or *N. gonorrhoeae* account for 40-50% of cervicitis cases

- Other etiologies (up to 50-60%)
  - Bacterial vaginosis
  - *Mycoplasma genitalium*
  - Herpes simplex viruses
  - *Trichomonas vaginalis*
  - **Idiopathic**

Cervicitis Testing

- Cervical Gram stain not recommended
- Wet mount to evaluate for bacterial vaginosis and *Trichomonas*
- NAAT for chlamydia and gonorrhea
- NAAT for *Trichomonas* (if available and wet mount w/o trichomonads)

SOUTHEAST STD/HIV PREVENTION TRAINING CENTER
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2015 CDC STD Treatment Guidelines

Cervicitis Treatment

Draft 2021 CDC STD Treatment Guidelines:

- Empirically treat for chlamydia (with doxycycline if not pregnant)
- Also empirically treat for gonorrhea (with ceftriaxone 500mg IM) if local prevalence is high
- Doxycycline and fluoroquinolones contraindicated in pregnancy
  - Use azithromycin 1g for chlamydia coverage in pregnant women

Other Cervicitis Treatment Issues

- A “test of cure” should be performed 3-4 weeks following treatment of chlamydia-infected pregnant women
- Rescreen women approximately 3 months after treatment of chlamydia, gonorrhea, or trichomoniasis
  - Repeat positive tests most likely due to reinfection
- Sexual partners should be evaluated and treated
- If cervicitis persists, get *Mycoplasma genitalium* testing

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Pelvic Inflammatory Disease (PID) Case

History: 18 yo female presents with 5 days of vaginal discharge, pelvic pain, nausea, and low grade fever. She had unprotected intercourse with a new partner 2 weeks ago

Examination: cervical motion tenderness and right adnexal pain noted

Diagnosis: pelvic inflammatory disease (PID)

PID Etiology

STI

- More common (around 40-50%)
  - *C. trachomatis*
  - *N. gonorrhoeae*
- Less common or frequency unknown (other 50-60%)
  - *Mycoplasma genitalium and M. hominis*
  - *Ureaplasma urealyticum*
  - Anaerobes: *Bacteroides fragilis*, peptostreptococci

Puerperal, Post-abortion, Post-instrumentation

Polymicrobial (*Staphylococcus*, *Streptococcus*, Coliforms, etc.)

PID Testing

- Wet mount to evaluate for bacterial vaginosis and *Trichomonas*
- NAAT for chlamydia and gonorrhea

2015 CDC STD Treatment Guidelines

Outpatient PID Treatment

2015 CDC STD Treatment Guidelines/2020 GC Treatment Update

- Ceftriaxone 500mg IM (or other parenteral 3rd generation cephalosporin) + Doxycycline 100 mg po bid to complete for 14 days w/ or w/o metronidazole 500mg PO BID for 14 days

Draft 2021 CDC STI Treatment Guidelines

- Ceftriaxone 500mg IM (or other parenteral 3rd generation cephalosporin) + Doxycycline 100 mg po bid to complete for 14 days with metronidazole 500mg PO BID for 14 days

Clinical Infectious Diseases

MAJOR ARTICLE

A Randomized Controlled Trial of Ceftriaxone and Doxycycline, With or Without Metronidazole, for the Treatment of Acute Pelvic Inflammatory Disease

Harold C. Wiesenfeld,[1,2] Leslie A. Meyn,[1,2] Toni Darville,[3] Ingrid S. Macio,[2] and Sharon L. Hillier[1,2]

[1]Department of Obstetrics, Gynecology and Reproductive Sciences, University of Pittsburgh, Pittsburgh, Pennsylvania, USA, [2]Magee-Womens Research Institute, Pittsburgh, Pennsylvania, USA, and [3]Department of Pediatrics, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA

- At 30 days following treatment:
  - Anaerobic organisms were less frequently recovered from the endometrium in women treated with metronidazole than placebo (8% vs 21%, $p<0.05$)
  - Pelvic tenderness was less common among women receiving metronidazole (9% vs 20%, $p<0.01$)

Wiesenfeld, et al. Clin Infect Dis. 2020 Feb 13:ciaa101.

Vaginitis Cases

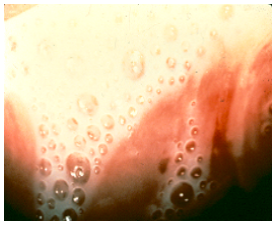
Case 1: Female with frothy vaginal discharge and vaginal itching
Diagnosis: Likely trichomoniasis (TV)

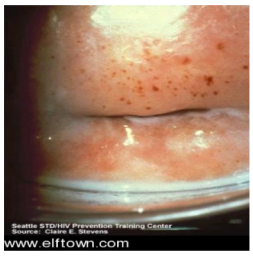
Case 2: Female with creamy vaginal discharge and odor
Diagnosis: Likely bacterial vaginosis (BV)

Case 3: Female with vaginal itching/pain and clumpy vaginal discharge
Diagnosis: Likely vaginal candidiasis (i.e. yeast infection)

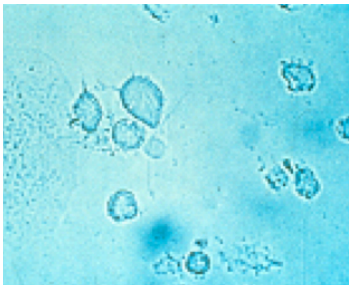
Trichomoniasis – Clinical Findings and Testing

- Clinical Findings
  - Abnormal vaginal discharge, may be frothy
  - ”Strawberry cervix” uncommon





- Testing
  - Wet mount
  - TV NAAT
  - TV Culture



Trichomoniasis Treatment

2015 CDC STD Treatment Guidelines

- Recommended Regimens:
  - Metronidazole (MTZ) 2 grams po X 1 dose
  - Tinidazole 2 grams po X 1 dose

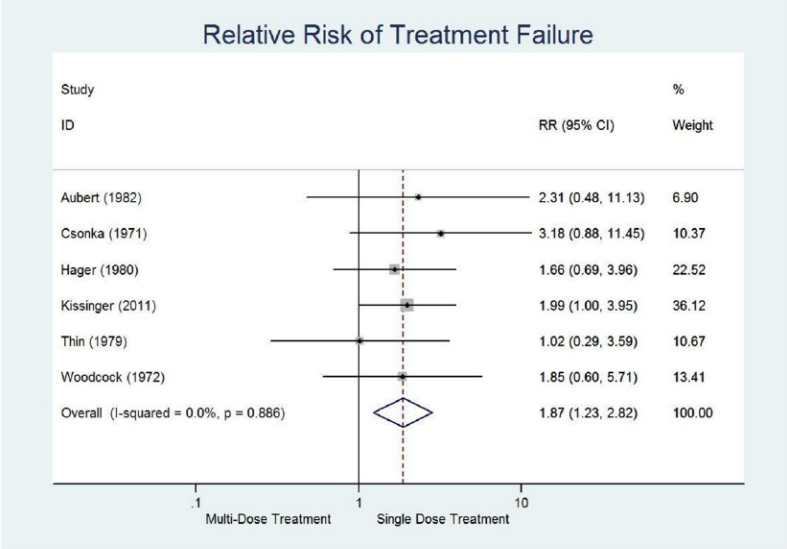
- Alternative Regimen:
  - MTZ 500 mg po bid X 7 days (recommended regimen for HIV + women)

Trichomoniasis Treatment

Draft 2021 CDC STI Treatment Guidelines

- Recommended Regimens:
  - Women - MTZ 500 mg po bid X 7 days
  - Men - MTZ 2 grams po X 1 dose
- Alternative Regimen:
  - Tinidazole 2 grams po X 1 dose

Single-dose compared to multi-dose metronidazole for the treatment of trichomoniasis in women: A meta-analysis



The pooled risk ratio indicated higher treatment failure for single dose MTZ compared to multi-dose MTZ: 1.87 (95% confidence interval, 1.23-2.82; p<0.01)

Sex Transm Dis 2017;44(1):29-34

Slide Courtesy of Christina Muzny

Single-dose versus 7-day-dose metronidazole for the treatment of trichomoniasis in women: an open-label, randomised controlled trial

Patricia Kissinger, Christina A Muzny, Leandro A Mena, Rebecca A Lillis, Jane R Schwebke, Laura Beauchamps, Stephanie N Taylor, Norine Schmidt, Leann Myers, Peter Augostini, William E Secor, Martina Bradic, Jane M Carlton, David H Martin

- Women in the 7-day-dose group were less likely to be *Trichomonas vaginalis* positive at test-of-cure than those in the single-dose group (34 [11%] of 312 vs 58 [19%] of 311, relative risk 0·55, 95% CI 0·34-0·70; p<0·0001).

Lancet Infect Dis 2018; e-published online 10/5/18

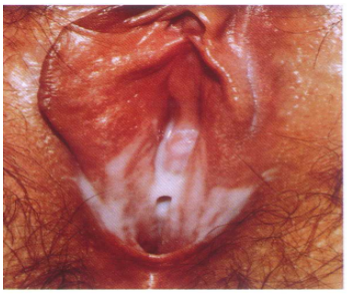
Persisting Trichomoniasis Treatment

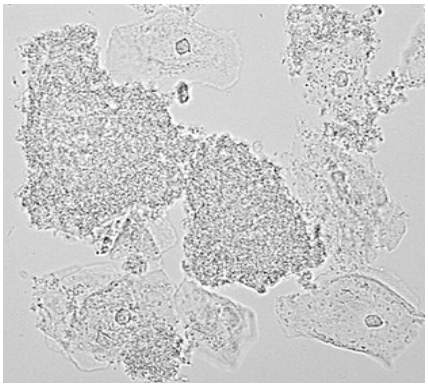
2015 CDC STD Treatment Guidelines

- Recommended Regimens:
  - MTZ 500 mg po bid X 7 days (if initially took single dose regimen)
  - MTZ or tinidazole (TIN) 2 grams po daily for 5-7 days
  - High dose TIN at 2–3g po daily in combination with intravaginal TIN 500 mg twice daily for 14 days
  - High-dose oral TIN (1 gram three times daily) plus intravaginal paromomycin (4 g of 6.25% intravaginal paromomycin cream nightly) for 14 days

Bacterial Vaginosis – Clinical Findings and Testing

- Clinical Findings
  - Homogenous, thin, gray/white discharge smoothly coating the vaginal walls
  - Vaginal odor
- Diagnosis
  - Amsel Critieria (3 of 4)
    - Homogenous vaginal discharge smoothly, vaginal pH >4.5, + whiff test, and clue cells on a vaginal wet mount
  - NAAT (for BV-associated bacteria)
  - DNA Probe





Bacterial Vaginosis Treatment

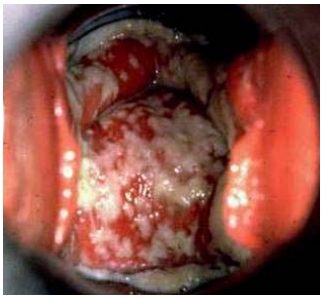
2015 CDC STD Treatment Guidelines

- Recommended Regimens:
  - Metronidazole 500 mg orally BID X 7 days
  - Metronidazole gel 0.75%, one full applicator (5g) intravaginally, daily X 5 days
  - Clindamycin cream 2%, one full applicator (5 g) intravaginally qhs X 7 days

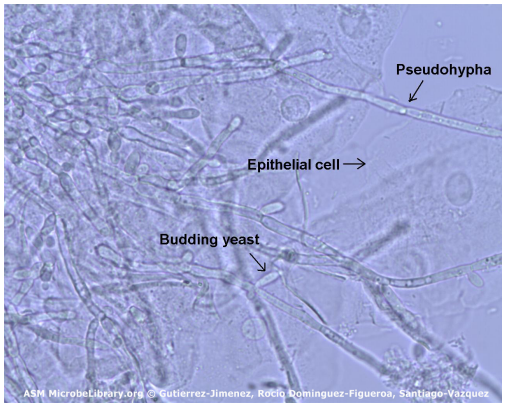
- Alternative Regimens:
  - Tinidazole 2 g orally once daily X 2 days
  - Tinidazole 1 g orally once daily X 5 days
  - Clindamycin 300 mg orally BID X 7 days
  - Clindamycin ovules 100 mg intravaginally qhs X 3 days

Candidiasis – Clinical Findings, Testing, Treatment

- Clinical Findings
  - vulvar/vaginal erythema, fissures, excoriation,
  - thick curdy vaginal discharge



- Testing
  - Wet Prep with or without 10% KOH



- Treatment
  - Fluconazole 150mg PO x 1
  - OTC azole cream

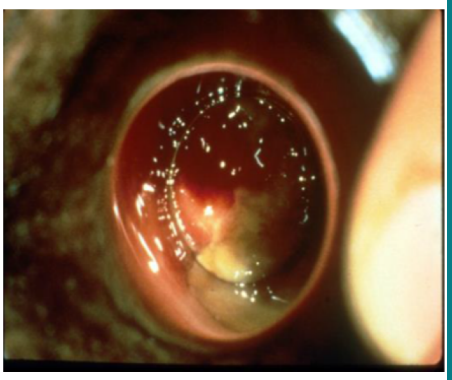
2015 CDC STD Treatment Guidelines

Proctitis Case

History: 24yo MSM presents with rectal pain and discharge and a sense of urgency to defecate for 2 days . Having unprotected receptive anal intercourse

Examination: Anoscopy shows purulent exudate, erythema, and bleeding in the anorectal area

Diagnosis: Proctitis



Proctitis - Etiology

- *C. trachomatis* (including LGV serovars)
- *N. gonorrhoeae*
- Syphilis
- HSV
- *M. genitalium* has been detected in proctitis
- If concomitant colitis (i.e., proctocolitis), then pathogens also include *Campylobacter, Shigella,* and *Entamoeba histolytica*

Proctitis Testing

- Gram stain of anorectal specimen
- NAAT for chlamydia
  - If positive, send for LGV typing if available
- NAAT or culture for gonorrhea
- HSV PCR or culture
- Syphilis serologic testing (and darkfield microscopy if available)

2015 CDC STD Treatment Guidelines

Proctitis Treatment

2015 CDC STD Treatment Guidelines:

- Ceftriaxone 500 mg IM x 1 and doxycycline 100mg PO twice daily for 7 days
  - If anorectal ulcers visualized and either anorectal CT NAAT is positive patient or patient is HIV-positive, then extend the doxy for 3 weeks total to cover LGV
- If painful ulcers are noted, then provide presumptive herpes treatment

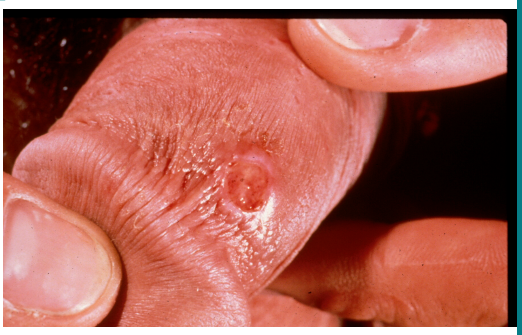
2015 CDC STD Treatment Guidelines

Genital Ulcer Disease Cases

Case 1: A sexually active male presents with a single genital ulcer that is painless.

Diagnosis: genital ulcer disease

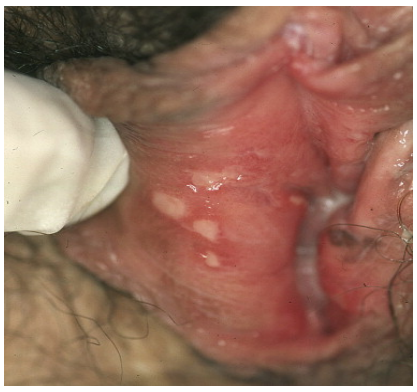
(mostly likely syphilis, but could be HSV or LGV)



Case 2: A sexually active female presents with several genital ulcers that are painful.

Diagnosis: genital ulcer disease

(mostly likely HSV, but could be syphilis)

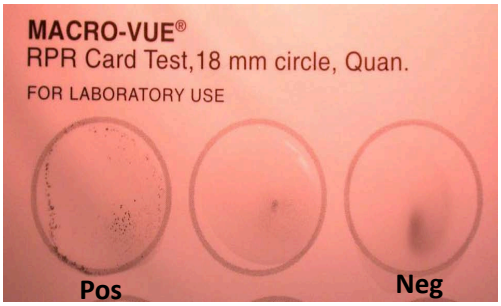


GUD Etiologies (in the U.S.)

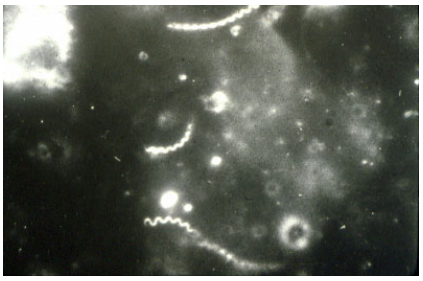
- Primary Syphilis
- Herpes simplex virus (HSV) Types 1 and 2
- Lymphogranuloma venereum is a rare cause of genital ulcers in the U.S.

Syphilis Evaluation

- Serologic test
  - Nontreponemal (RPR, VDRL)
  - Treponemal (EIA, FTA-ABS, MHA-TP, TPPA)



- Darkfield microscopy if available



2015 CDC STD Treatment Guidelines

Early Syphilis Treatment (primary, secondary, early latent)

2015 CDC STD Treatment Guidelines

- Recommended
- Benazthine Penicillin G, 2.4 Mu IM

- Penicillin Allergy
- Doxycyline 100 mg PO, BID x 14d

- Limited Data
- Ceftriaxone 1.0 g IM or IV x 8-10d
- Azithromycin 2.0g PO

Genital Herpes Evaluation

- PCR on an ulcer specimen (preferred due to higher sensitivity)
- Culture of an ulcer specimen
- HSV Type specific IgG test on a blood specimen
  - can be negative in primary HSV infection
  - helpful when a lesion cannot be swabbed for PCR or culture

2015 CDC STD Treatment Guidelines

Genital Herpes Treatment

2015 CDC STD Treatment Guidelines

Initial

- Acyclovir: 400 mg 3 times a day for 7-10 days or 200 mg 5 times a day for 7-10 days
- Valacyclovir: 1 g twice a day for 7-10 days
- Famciclovir: 250 mg 3 times a day for 7-10 days

Recurrence

- Acyclovir: 400 mg 3 times a day for 5 days or 800 mg twice a day for 5 days or 800 mg 3 times a day for 2 days
- Valacyclovir: 500 mg twice a day for 3 days or 1 g once a day for 5 days
- Famciclovir: 125 mg twice a day for 5 days or 1 g every 12 hr for 2 doses or 500 mg for 1 dose followed by 250 mg twice a day for 2 days.

STI Screening Women <25yo or 25+ w/ STI risks

- NAAT for chlamydia and gonorrhea
  - genital exposure→ self- or clinician-collected vaginal swab specimen of choice, cervical swab fine
  - anorectal exposure→ consider screening by self- or clinician-collected rectal swab
  - oropharyngeal screening not recommended
- If high risk or in high STI prevalence setting--> screen for *Trichomonas* (vaginal swab wet mount +/- NAAT), syphilis, and HIV
- Screening for *M. genitalium,* bacterial vaginosis, and HSV not recommended
- Address pre-exposure vaccination (Hep A/B, HPV), PrEP/PEP, and sexual risk behaviors

2015 CDC STD Treatment Guidelines

STI Screening Heterosexual Men at Risk or in High STI Prevalence Venue

- NAAT for chlamydia and gonorrhea
  - genital exposure→ first-catch urine specimen of choice; urethral swab fine
  - oropharyngeal screening not recommended
- Screen for syphilis and HIV
- Consider screening for *Trichomonas*
- Screening for *M. genitalium* and HSV not recommended
- Address pre-exposure vaccination (Hep A/B, HPV), PrEP/PEP, and sexual risk behaviors

2015 CDC STD Treatment Guidelines

STI Screening Men Who Have Sex With Men

- NAAT for chlamydia and gonorrhea
  - genital exposure→ first-catch urine specimen of choice; urethral swab fine
  - anorectal exposure→ self- or clinician-collected rectal swab
  - oropharyngeal exposure → screen only for gonorrhea by oropharyngeal swab
- Screen for syphilis, HIV, and Hepatitis B (HBsAg), and also Hepatitis C if not screened before, if at risk, or if HIV positive
- Consider HSV screening if at increased risk for HIV
- Screening for *M. genitalium* and *Trichomonas* not recommended
- Address pre-exposure vaccination (Hep A/B, HPV), PrEP/PEP, sexual risk behaviors

2015 CDC STD Treatment Guidelines and the 2020 CDC Hepatitis C Screening Recommendations

STI Screening Pregnant Women

- NAAT for chlamydia and gonorrhea at first prenatal visit if <25yo or 25+yo and at risk
  - repeat screening third trimester if at risk
- Screen for syphilis, HIV, and Hepatitis B (HBsAg) at first prenatal visit
  - rescreen for syphilis early third trimester if at risk or in high prevalence setting
- Screening for *M. genitalium, Trichomonas,* BV, and HSV not recommended
- Address Hepatitis B vaccination if indicated and sexual risk behaviors

2015 CDC STD Treatment Guidelines

Thank You!

Contact me with questions:

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