

#### STIs and HIV

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#### Objectives

 Discuss the importance of the role of primary care providers in the treatment and prevention of sexually transmitted infections (STIs)

• Understand the relationship between STIs and HIV

 Review CDC treatment guidelines for common STI infections, including considerations for people living with HIV



### Background

- Approximately 20 million new STI cases annually in USA
- Over half in persons aged 15-24 years
- Recent increase in rates
- STIs account for 16.9 billion in health care costs annually
- Can lead to severe reproductive health complications
- Increased risk for acquiring or transmitting human immunodeficiency virus (HIV)

https://www.cdc.gov/mmwr/volumes/68/rr/rr6805a1.htm



#### **Sexual History**

#### The Five P's

- Partners
  - Men, women, both
  - Number of partners, last 2, 12 months
  - Partner's sexual history during relationship
- Practices
  - Types of sex vaginal, anal, oral
  - Condom usage never, sometimes, always

https://www.cdc.gov/std/treatment/sexualhistory.pdf



#### **Sexual History**

The Five P's

- Prevention of Pregnancy
  - What are you doing to prevent pregnancy?
- Protection from STIs
  - What are you doing to protect yourself?
- Past History of STIs
  - Have you or your partner ever had an STI?
- \*Injection drug use, money/drugs for sex

https://www.cdc.gov/std/treatment/sexualhistory.pdf



## **Guidelines for STI Screening**

- Risk Assessment for STIs
  - Detailed sexually history at each visit
  - Annual screening for STIs in HIV-infected persons (gonorrhea(GC), chlamydia(CT), syphilis)
  - Risk reduction discussion
- Testing for hepatitis A, B, and C



## **Guidelines for STI Screening**

Men who have sex with men (MSM) should have annual 3 site testing

Women should be tested for trichomoniasis and have PAP annually

• More frequent STI screening may be indicated



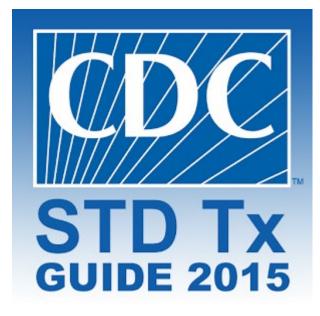
## STIs and HIV

- STIs may lead to increased risk for HIV
  - Behavioral component
  - STIs and HIV linked
  - Sore or inflammation from STI provides mode of entry
- STIs may increase risk of spreading HIV
  - Increased shedding of the HIV virus in the presence of urethritis or genital ulcer
- Syphilis coinfection in MSM

https://www.cdc.gov/std/hiv/stdfact-std-hiv-detailed.htm



#### 2015 STD Treatment Guidelines



# Diseases characterized by Ulcerative Lesions

Chancroid

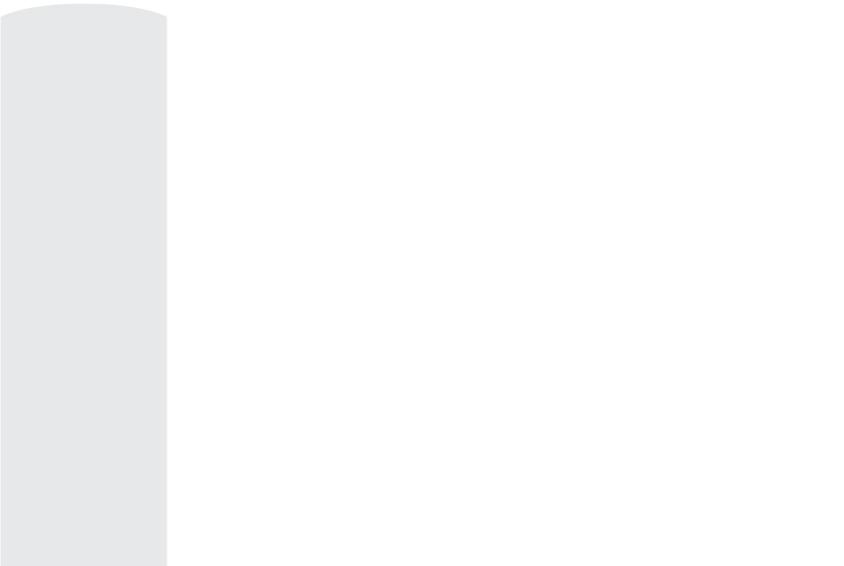
Genital HSV infections

Lymphogranuloma Venereum (LGV)

• Granuloma Inguinale



#### Chancroid





## Chancroid

- Prevalence declined in United States
- Definitive diagnosis *H.ducreyi culture* 
  - *Sensitivity < 80%*
  - No FDA approved PCR test available
- Clinical diagnosis
  - One or more painful genital ulcers
  - Regional lymphadenopathy
  - No evidence of syphilis, proven by testing at least 7 days after ulcer onset
  - Negative HSV test results



#### Chancroid

**Early Stage** Photo courtesy of the CDC (1971)



Late Stage J. Pledger/CDC





#### Chancroid Genital Lesions of Chancroid

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#### Treatment

- Recommended Regimens
- Azithromycin 1 g orally in a single dose OR
- Ceftriaxone 250 mg IM in a single dose OR
- Ciprofloxacin 500 mg orally twice a day for 3 days OR
- Erythromycin base 500 mg orally three times a day for 7 days



### Follow-Up

- Uncircumcised men and persons with HIV do not respond as well to treatment
  - May require repeated or longer course of treatment
- Reexamine in 3-7 days after treatment
  - Symptoms from ulcers usually improve by 3 days
  - Resolution may be seen as early as 1 week
- Partner treatment
  - If sexual contact 10 days prior to symptoms



#### **Genital HSV Infections**





#### **Genital HSV**

- Most are asymptomatic or unrecognized
  - Shedding of the virus intermittently leads to transmission
- Chronic life-long infection
- 1 or more vesicles, leaving painful ulcers that may take 2-4 weeks to resolve
  - Absent in many
- Incubation period 2-12 days



## **Genital HSV Types**

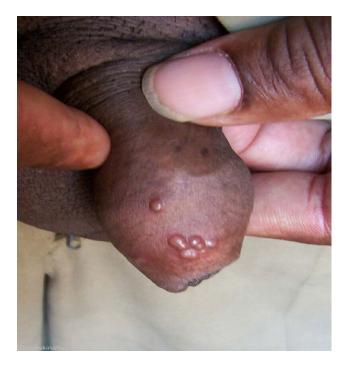
- HSV-2
  - Most cases of genital herpes
- HSV-1
  - Frequent cause of initial outbreaks in young women and MSM
    - Anogenital infection
  - Recurrences & asymptomatic shedding less common than with HSV-2



#### **Genital HSV**







# R

## **HSV** Diagnosis

- Diagnosis
  - May be difficult due to the lack of lesions present
    - Negative test does not rule out infection
  - Confirm using type-specific laboratory testing
    - Virologic and serologic testing should be available in clinic that provide treatment for STIs
- Cell Culture
  - Sensitivity low, for recurrent and healing lesion
- PCR
  - More sensitive
  - Test of choice for diagnosing CNS and systemic infections

# R

## Primary vs Recurrent

- Primary Infection
  - May be severe with painful ulcers, dysuria, fever, inguinal lymphadenopathy, and headache
  - Mild or asymptomatic
  - No difference in symptoms based on type
  - Incubation period between 2-12 days
  - Increased viremia
- Recurrent Infection
  - More common with HSV-2 than HSV-1
  - Common, but decreased severity
  - Shorter duration
  - Less viral shedding



- Antiviral chemotherapy is backbone of treatment
- Counsel on the natural course of herpes, perinatal and sexual transmission, and reduction of transmission
- Systemic antiviral medications
  - Initial episodes
  - Recurrent episodes
  - Suppressive therapy
- Topical treatment with antiviral drugs not recommended



#### First Episode

- Acyclovir 400 mg orally three times a day for 7–10 days OR
- Acyclovir 200 mg orally five times a day for 7–10 days OR
- Valacyclovir 1 g orally twice a day for 7–10 days OR
- Famciclovir 250 mg orally three times a day for 7–10 days



#### **Suppressive Therapy**

- Acyclovir 400 mg orally twice a day OR
- Valacyclovir 500 mg orally once a day\* OR
- Valacyclovir 1 g orally once a day OR
- Famiciclovir 250 mg orally twice a day



#### **Episodic Therapy**

- Acyclovir 400 mg orally three times a day for 5 days OR
- Acyclovir 800 mg orally twice a day for 5 days OR
- Acyclovir 800 mg orally three times a day for 2 days



#### **Episodic Therapy**

- Valacyclovir 500 mg orally twice a day for 3 days OR
- Valacyclovir 1 g orally once a day for 5 days OR
- Famciclovir 125 mg orally twice daily for 5 days OR
- Famciclovir 1 gram orally twice daily for 1 day OR
- Famciclovir 500 mg once, followed by 250 mg twice daily for 2 days

# R

#### **HSV** Treatment

#### **Treatment for patients infected with HIV**

#### Recommended Regimens for Daily Suppressive Therapy

- Acyclovir 400–800 mg orally twice to three times a day OR
- Valacyclovir 500 mg orally twice a day OR
- Famciclovir 500 mg orally twice a day

#### Recommended Regimens for Episodic Infection

- Acyclovir 400 mg orally three times a day for 5–10 days OR
- Valacyclovir 1 g orally twice a day for 5–10 days OR
- Famciclovir 500 mg orally twice a day for 5–10 days

# Lymphogranuloma Venereum (LGV)



- Causative agent *C. trachomatis* serovars L1, L2, or L3
- Unilateral, tender inguinal/femoral lymphadenopathy
- Self-limited ulcer or papule at site of inoculation
- MSM or women may develop proctocolitis
  - Rectal exposure
    - Mucoid or bloody discharge, pain, constipation, or fever



#### LGV

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## LGV Diagnosis

- Diagnosis based on clinical suspicion, epidemiology, exclusion of other etiologies
- PCR not widely available
- Nucleic acid amplification tests (NAATs) for confirmation
- Specimens can be tested for *C. trachomatis* by culture, direct immunofluorescence, or nucleic acid detection
- NAATs for *C. trachomatis* rectal specimens are reliable, however not FDA approved



#### LGV Treatment

- Doxycycline 100 mg orally twice a day for 21 days
- Alternative Regimen
- Erythromycin base 500 mg orally four times a day for 21 days
- Azithromycin 1 gram orally once weekly for 3 weeks
  - Probably as effective however, clinical data insufficient



### Follow-up

- Follow until signs and symptoms resolve
- Persons with HIV infection should receive the same treatment as persons without HIV infection
  - Extended treatment might be required, and delay in symptom resolution might occur

# Granuloma Inguinale (Donovanosis)



## Granuloma Inguinale Diagnosis

- *Klebsiella* (formerly *Calymmatobacterium*) granulomatis
  - Gram-negative bacteria

• Endemic in tropics, rare in the US

- Difficult to culture
  - Requires presence of Donovan bodies on tissue or biopsy
  - No FDA-cleared molecular DNA test



#### Granuloma Inguinale

- Painless, slowly progressive ulcerative lesions
  - Genital region or perineum
- No regional lymphadenopathy
- May have subcutaneous granulomas (pseudobuboes)
   Very vascular and easy to bleed
- Extragenital infection
  - Pelvis, abdominal organs, bones, or mouth



#### Granuloma Inguinale

#### emedicine.medscape.com



### Granuloma Inguinale Treatment

Recommended Regimen

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- Azithromycin 1 g orally once per week or 500 mg daily for at least 3 weeks and until all lesions have completely healed
- Alternative Regimens
- Doxycycline 100 mg orally twice a day for at least 3 weeks and until all lesions have completely healed OR
- Ciprofloxacin 750 mg orally twice a day for at least 3 weeks and until all lesions have completely healed OR
- Erythromycin base 500 mg orally four times a day for at least 3 weeks and until all lesions have completely healed OR
- Trimethoprim-sulfamethoxazole one double-strength (160 mg/800 mg) tablet orally twice a day for at least 3 weeks and until all lesions have completely healed



#### Follow-Up

- Follow until signs and symptoms resolve
- Persons with HIV infection should receive the same treatment as persons without HIV infection
  - Consider adding an aminoglycoside (gentamicin 1 mg/kg IV every 8 hours) if no improvement within the first few days of treatment



### Syphilis



#### **Tuskegee Experiment**

- Clinical study between 1932 1972
- U. S. Public Health Service/Tuskegee University
- Purpose: To understand the natural progression in untreated syphilis
- Participants: 622 AA men from Macon County, Alabama
- Incentives: Free medical care, meals, and free burial insurance



# Syphilis

- Systemic disease caused by Treponema pallidum
- Different stages based on clinical findings
  - Primary syphilis ulcer or chancre
  - Secondary syphilis rash, mucocutaneous lesions, lymphadenopathy
  - Tertiary syphilis cardiac, gummatous lesions, tabes dorsalis, general paresis
  - Latent infections no clinical symptoms
    - Early latent
    - Late latent
    - Syphilis of unknown duration
- Neurosyphilis can occur at any stage



#### **Primary Syphilis**

#### Chancre



#### Chancre





#### Secondary Syphilis





#### Secondary Syphilis

Condyloma Lata

- Seen in 10-20%
- "teeming with spirochetes"





#### Syphilis Diagnosis

- Darkfield examination of lesions
- PCR not commercially available
- Usually diagnosed by combination of 2 types of serologic tests:
  - Nontreponemal (screening) VDRL or RPR
  - Treponemal (confirmatory) FTA-ABS, TP-PA, EIAs, chemiluminescence immunoassays, immunoblots, or rapid treponemal assays
- NOTE: some labs doing reverse sequence syphilis screening algorithm



#### Syphilis Diagnosis

Nontreponemal

- May have false positives
- Use same type of test for follow-up
- Quantitative fourfold change in titer to demonstrate clinical significance
- Declines with treatment and often become nonreactive over time
- "Serofast reaction" antibodies may linger in some patients



#### Syphilis Diagnosis

- Treponemal
- Several available tests, but only a few approved in US

 Most patients will have reactive test for life, 15% - 25% revert to nonreactive after 2-3 years

- Should not be used to determine treatment response
  - Don't distinguish between active and past infection



#### Neurosyphilis Diagnosis

- CSF studies commonly abnormal
  - If so, repeat every 6 months up to 2 years
- VDRL in CSF
  - Highly specific diagnostic in absence of substantial blood contamination
  - Not sensitive
- FTA-ABS in CSF
  - Very sensitive
  - Consider if highly suspicious but CSF VDRL nonreactive



### Syphilis Diagnosis and HIV

- Treponemal and nontreponemal tests interpretation same for persons with HIV infection
  - Unusual serologic responses may be seen in persons with HIV infection
    - Post-treatment titers that were higher than expected (high serofast) or fluctuated
    - False-negative test results and delayed appearance of seroreactivity
- Clinical picture suggestive of syphilis with nonreactive serologic tests, consider alternative tests such as, biopsy of a lesion, darkfield examination, and PCR of lesion material
- In persons with HIV and neurological symptoms, neurosyphilis should be ruled out

#### Syphilis Treatment

- Parenteral penicillin G
  - Benzathine PCN G 2.4 million units IM
    - Single dose: primary, secondary, early latent
    - Weekly doses x 3: late latent, latent of unknown duration, tertiary, retreatment
  - Aqueous crystalline penicillin G 3-4 million units IV every 4 hours for 10-14 days: neurosyphilis
    - Persons with HIV infection should be managed the same as HIV-negative persons with neurosyphilis
- PCN allergy
  - Regimens of doxycycline 100 mg orally BID for 14 days and tetracycline 500 mg QID daily for 14 days
  - No alternatives for pregnant women, should be desensitized and treated with PCN G
- Persons with HIV infection and primary or secondary syphilis should be treated same as HIV negative persons



#### Treatment of sex partners

- Treat all persons having sexual contact within 90 days with a person diagnosed with primary, secondary, or early latent syphilis regardless of test results
- Treat all persons having sexual contact more than 90 days prior with a person diagnosed with primary, secondary, or early latent syphilis if test results not available and follow up unlikely. If tests results negative, do not treat. If test results positive treat according to clinical and serological assessment.

### **Other Management Considerations**

- All patients with syphilis should be tested for HIV
  - If test negative, retest in 3 months
- In patients with symptoms of neurologic or ophthalmic disease
  - CSF analysis
  - Ocular slit-lamp ophthalmologic examination
  - Audiology



#### Follow-Up

- Repeat RPR at 6 & 12 months
  - Expect 4-fold decrease in titer (15% will not)
  - If not, re-test for HIV
- Treatment failure vs. Reinfection
  - Signs or symptoms that persist or recur
  - Sustained 4-fold increase in titer
  - Re-test for HIV
  - CSF analysis
  - Retreatment: benzathine penicillin G 2.4 million units IM weekly times 3



#### Follow-up

- Persons with HIV infection
  - Primary or Secondary syphilis
    - Repeat titers at 3, 6, 9, 12, and 24 months
  - Latent syphilis
    - Repeat titers at 6, 12, 18, and 24 months after therapy



#### Follow-up

- Persons with HIV infection
- Treatment failure
  - Signs or symptoms that persist or recur or fourfold increase or more in titer, manage same as HIV-negative persons
  - CSF examination and retreatment can be considered for persons whose RPR titers do not decrease fourfold within 12–24 months
    - If CSF normal, treat with benzathine penicillin G 2.4 million units IM weekly times 3
    - If titers do not decline despite a negative CSF examination and a repeated course of therapy, the need for additional therapy or repeat CSF examinations is not generally recommended

## Diseases Characterized by Urethritis and Cervicitis

• Chlamydia

Gonorrhea

Mycoplasma Genitalium



#### Urethritis

- Urethral inflammation can result from infectious and noninfectious causes
- Symptoms include dysuria, urethral pruritis, mucoid, mucopurulent, or purulent discharge



### Chlamydia

- Most frequently reported disease in US
- Highest incidence in persons ≤ 24 years of age
- Sequelae in women
  - PID
  - Infertility
  - Ectopic pregnancy
- Common for both men and women to be asymptomatic
- Yearly screening
  - Women < 25 years</p>
  - Some older women



#### Chlamydia

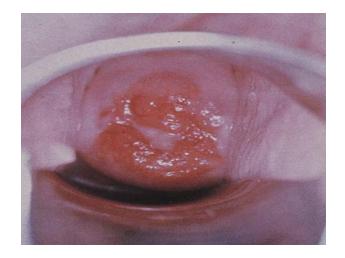
- Males
  - Most are asymptomatic
- Incubation period 7-10 days
- Urethritis
  - Mucoid or clear penile discharge
  - Dysuria
  - Urethral pruritis





### Chlamydia

- Women
  - Most are asymptomatic
- Urethritis
  - Dysuria
  - Urinary frequency
- Cervicitis (more common manifestation)
  - Mucopurulent discharge
  - Spontaneous or easy bleeding







#### Chlamydia Diagnosis

- Nucleic acid amplification testing (NAAT): most sensitive method
  - FDA-cleared for <u>cervical</u>, <u>urethral</u>, and <u>urine</u> specimens
  - Some labs have validated for use on <u>rectal</u> specimens
  - <u>Oropharyngeal</u> testing not recommended (clinical significance & transmissibility of Chlamydia isolated from oropharynx unclear)



#### **Recommended Regimens**

- Azithromycin 1 g orally in a single dose OR
- **Doxycycline** 100 mg orally twice a day for 7 days
- Alternative Regimens
- Erythromycin base 500 mg orally four times a day for 7 days OR
- Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days OR
- Levofloxacin 500 mg orally once daily for 7 days OR
- **Ofloxacin** 300 mg orally twice a day for 7 days

\*Persons with HIV infection and Chlamydia should be treated same as HIV negative persons



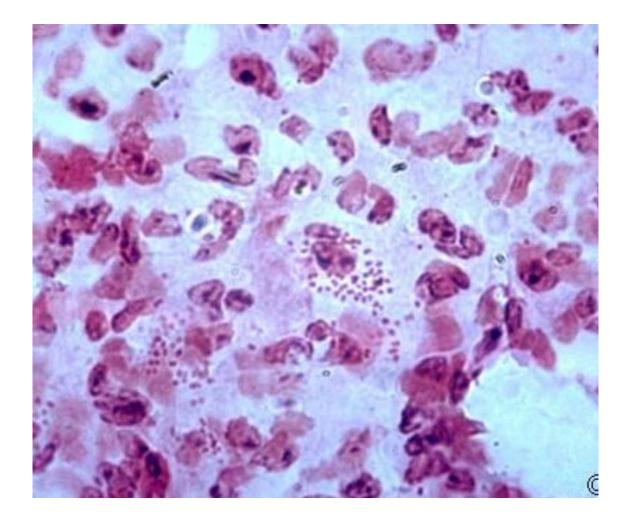
#### Follow-up

- Test-of-cure to detect treatment failure (i.e., repeat testing 3–4 weeks after treatment) is not advised if recommended or alterative regimens used
- Retest approximately 3 months after treatment, regardless if sex partners were treated to rule out reinfection



#### Gonorrhea

- Second most commonly reported STI in the United States
  - 820,000 cases yearly
  - 53% of cases diagnosed in 15
    24 years old
- Neisseria gonorrhoeae
  - Gram-negative, oxidasepositive diplococcus
- Incubation period 2-7 days





#### Gonorrhea

Males

Most are symptomatic Incubation period 2-5 days Purulent or mucopurulent penile discharge

Females

Most are asymptomatic

Symptoms within 10 days of exposure

Late onset of symptoms until complications







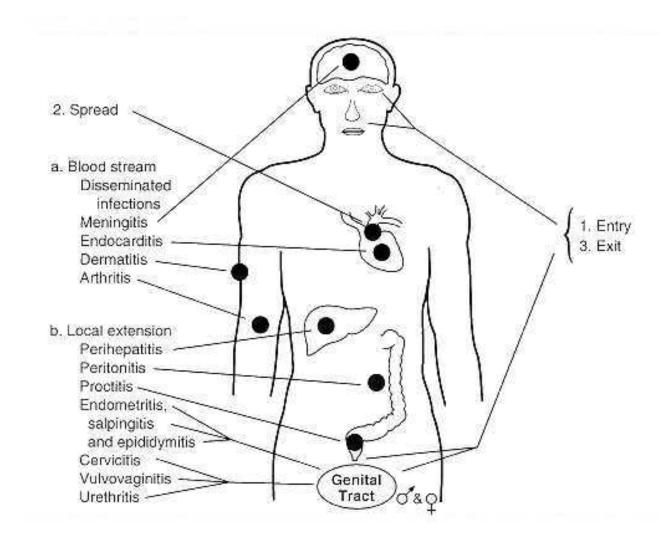
#### Gonorrhea

- Anorectal infection
  - MSM
  - May also be seen in women with/without history of anal intercourse

- Pharyngitis
  - Asymptomatic
  - Screen in high-risk patients
- Conjunctivitis
  - Autoinoculation

#### Disseminated Gonococcal Infection

- Infrequent
- More common in women
- High index of suspicion: sexually active adolescent with septic arthritis





#### **Disseminated Gonococcal Infection**

#### Wikipedia



#### Grepmed.com





#### Gonorrhea Diagnosis

- Culture and NAAT
- Culture
  - Available for rectal, oropharyngeal, and conjunctival specimens
  - Requires endocervical or urethral swab specimens
- Nucleic acid amplification testing (NAAT)
  - Most sensitive method
  - FDA-cleared for cervical, urethral, and urine specimens
  - Some labs have validated for use on rectal, oropharyngeal, and conjunctival specimens



#### Gonorrhea Treatment

Infections of the Cervix, Urethra, and Rectum

**Recommended Regimen** 

- Ceftriaxone 250 mg IM in a single dose PLUS
- Azithromycin 1g orally in a single dose

\*Persons with HIV infection and Gonorrhea should receive same treatment as HIV negative persons



#### Gonorrhea Treatment

#### Alternative Regimens

- If ceftriaxone is not available:
- Cefixime 400 mg orally in a single dose PLUS
- Azithromycin 1 g orally in a single dose



## Follow-up

- Persons with pharyngeal gonorrhea treated with an alternative regimen should return 14 days after treatment for a test-of cure
- Test-of-cure to detect treatment failure for urogenital or rectal gonorrhea is not advised if recommended or alternative regimen used
- Retest approximately 3 months after treatment, regardless if sex partners were treated to rule out reinfection



# Expedited Partner Therapy (EPT)

 Treating sex partners of patients diagnosed with Chlamydia or gonorrhea by providing prescriptions of medications for the patient to take to the partner without the health care provider first examining the partner

Not permissible in all states

Permissible in Tennessee for Chlamydia only



#### Mycoplasma genitalium



### Mycoplasma genitalium

- Cause of 15-25% non-GC/non-CT male urethritis
- Often more common than gonorrhea
- Organism grows slowly
  - Culture may take as long as 6 months
- NAAT preferred method of diagnosis (not FDA-approved in United States)
   Available in some large medical centers and commercial laboratories
- Consider with persistent or recurrent urethritis, cervicitis, PID



# Mycoplasma genitalium Treatment

- No cell wall antibiotics such as PCN and cephalosporins ineffective
- Only 31% cure rate with 7-day doxycycline course
- Single-dose azithromycin, 1 gram, preferred regimen
  - Concern for developing resistance
- Consider moxifloxacin (400 mg daily for 7, 10, 14 days) for treatment failures

\*Persons with HIV infection and M. genitalium should be treated same as HIV negative persons



#### Follow-up

 If validated *M. genitalium* testing is available, persons with persistent urethritis, cervicitis, or PID and persistent detection of *M. genitalium* may be treated with moxifloxacin

Routine tests-of-cure in asymptomatic persons are not recommended

# Diseases Characterized by Vaginal Discharge

• Bacterial Vaginosis (BV)

• Trichomoniasis







• Most common cause of vaginal discharge or odor

• Most women with BV were asymptomatic

• Results from alteration in normal bacterial flora

 Risk factors include multiple partners, new sex partner, douching, lack of condom use, and lack of vaginal lactobacilli



Women who have never been sexually active are infrequently affected

Increases risk for other STIs

• Increases the risk for HIV transmission to male sex partners

• Treatment of male sex partners not recommended



#### **Clinical Criteria for Diagnosis**

- 3 of the following:
  - Homogenous, thin, white discharge that smoothly coats vaginal walls
  - Clue cells on wet prep
  - Vaginal pH >4.5
  - Positive "whiff test" fishy odor (before or after addition of 10% KOH)





#### **Bacterial Vaginosis Treatment**

Recommended Regimens

- Metronidazole 500 mg orally twice a day for 7 days
   OR
- Metronidazole gel 0.75%, one full applicator (5 g) intravaginally, once a day for 5 days
   OR
- **Clindamycin** cream 2%, one full applicator (5 g) intravaginally at bedtime for 7 days



#### **Bacterial Vaginosis Treatment**

Alternative Regimens

- Tinidazole 2 g orally once daily for 2 days
   OR
- Tinidazole 1 g orally once daily for 5 days
   OR
- Clindamycin 300 mg orally twice daily for 7 days OR
- Clindamycin ovules 100 mg intravaginally once at bedtime for 3 days\*



#### **Bacterial Vaginosis and HIV**

• BV may recur more often in women with HIV infection

 Women with HIV who have BV should receive the same treatment regimen as those who do not have HIV infection

No follow-up necessary for women with or without HIV if symptoms resolve



#### Trichomoniasis

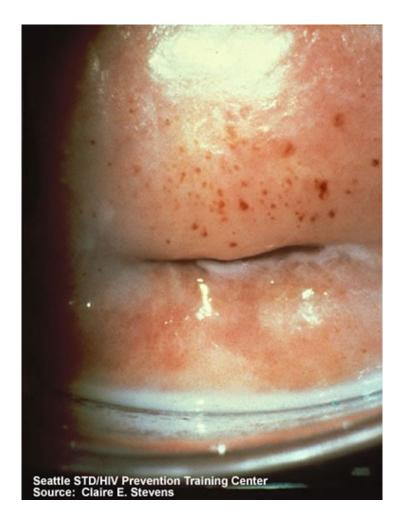


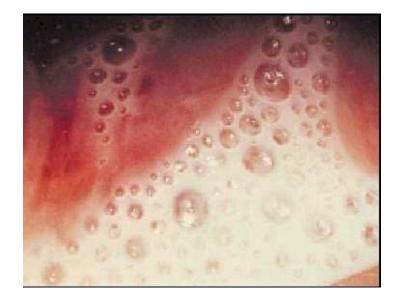
#### Trichomoniasis

- Protozoan Trichomonas vaginalis
- Minimal or no symptoms
- Women
  - Diffuse, malodorous, yellow-green vaginal discharge with vulvar irritation
- Men
  - Urethritis, epididymitis, or prostatitis
- Associated with two- to threefold increased risk for acquiring HIV



#### Trichomonasis









# **Trichomonasis Diagnosis**

- Wet prep
  - Most common
  - Only 51-65% sensitive in women
  - Even less sensitive in men
- NAAT
  - Very sensitive for women 3-5x higher yield
- APTIMA *T. vaginalis* assay
  - Vaginal, endocervical, or urine specimens in women
  - Sensitivity 95.3%–100%, specificity 95.2%–100



### **Trichomonaisis Diagnosis**

#### Culture

- Once considered gold standard
- Vaginal 75-96% sensitive, specificity up to 100%, less sensitive for urine
- Men urethral swab, urine sediment, or semen

- Cervical cytology
  - Not considered diagnostic
  - False negatives and false positives



#### **Trichomonasis Treatment**

#### Recommended Regimen

- Metronidazole 2 g orally in a single dose
   OR
- Tinidazole 2 g orally in a single dose
- Alternative Regimen
- Metronidazole 500 mg orally twice a day for 7 days
- \* Metronidazole gel not recommended



#### Follow-Up

• Retest in 3 months following initial treatment

 Testing by nucleic acid amplification can be conducted as soon as 2 weeks after treatment

• Insufficient data on retesting men



## Trichomonasis and HIV

- 53% of women with HIV infection are infected with *T. vaginalis* 
  - Associated with PID
  - Treatment decreases genital-tract HIV viral load and viral shedding
- Screening at entry to care and annually

• NAAT testing because of higher sensitivity



#### Trichomoniasis and HIV

Recommended Regimen for Women with HIV Infection

• Metronidazole 500 mg orally twice daily for 7 days

• Retest in 3 months following initial treatment

• Use NAAT testing



#### Thank you for your Attention!

