

What's Going On Down There?

Prevalent Sexually Transmitted Infections in
Adolescents & Young Adults with HIV



Carla London, DNP, CFNP

St Jude Children's Research Hospital

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Conflicts and Disclosures

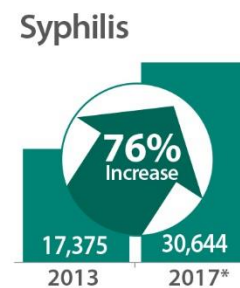
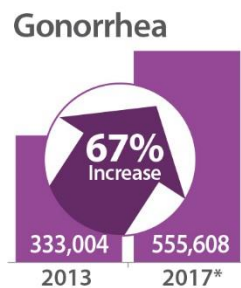
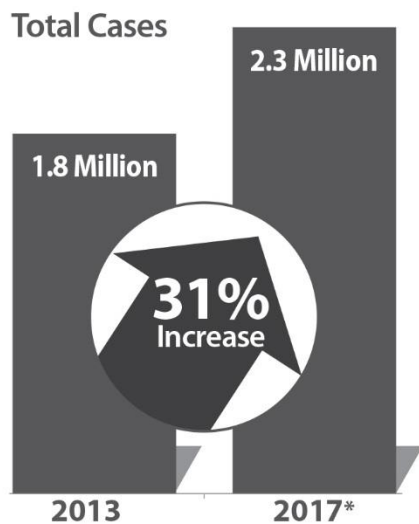
I have no conflicts of Interest to disclose.

Objectives

- Review common sexually transmitted infections (STIs) seen in adolescents and young adults
- Discuss common symptomatology for STIs
- Review recommended screening and treatment guidelines for common STIs

THE U.S. IS EXPERIENCING STEEP, SUSTAINED INCREASES IN SEXUALLY TRANSMITTED DISEASES

Combined diagnoses of chlamydia, gonorrhea, and syphilis **increased sharply over the past five years**



Chlamydia

1.7 MILLION

In 2017* chlamydia was the **most common condition** reported to CDC

*Preliminary data

For more information, visit
cdc.gov/nchhstp/newsroom



U.S. Department of
Health and Human Services
Centers for Disease
Control and Prevention

LEFT UNTREATED, STDS CAN CAUSE:



INCREASED RISK OF GIVING
OR GETTING HIV



LONG-TERM
PELVIC/ABDOMINAL PAIN



INABILITY TO GET PREGNANT OR
PREGNANCY COMPLICATIONS

HELP INTERRUPT THE STEADY CLIMB IN STDS WITH THESE THREE STEPS:

TALK

Talk openly about STDs with
your partners & healthcare
providers.

TEST

Get tested. It's the only way
to know if you have an STD.

TREAT

If you have an STD, work with
your provider to get the right
medicine.



TOUGH FACTS

- CDC estimates economic burden to be ~ \$16 billion (total medical costs)
- Youth 15-24 years of age
 - quarter of sexually active population
 - half of STIs annually
- Extragenital site testing is imperative
- Emerging pathogens and antibiotic resistance pose huge threat

Case Study # 1

John, a 19 year old AA bisexual HIV + male presents to clinic for an acute office visit after having a 2 day history of dysuria and urethral discharge. He reports having an episode of protected intercourse 1 week ago; however, “the condom broke” , with a male partner that he met on a social media app.

Case Study # 1

Pertinent History

- Practices include + anal receptive and insertive intercourse, oral sex
- Multiple history of STIs in the past
- Excellent adherence to Genvoya
- CD4-800 (32%), VL-Undetectable
- NKDA

Physical exam

- Purulent penile discharge
- Negative rash
- Remainder of exam unremarkable

Case Study #1

What Screening Test would you obtain?

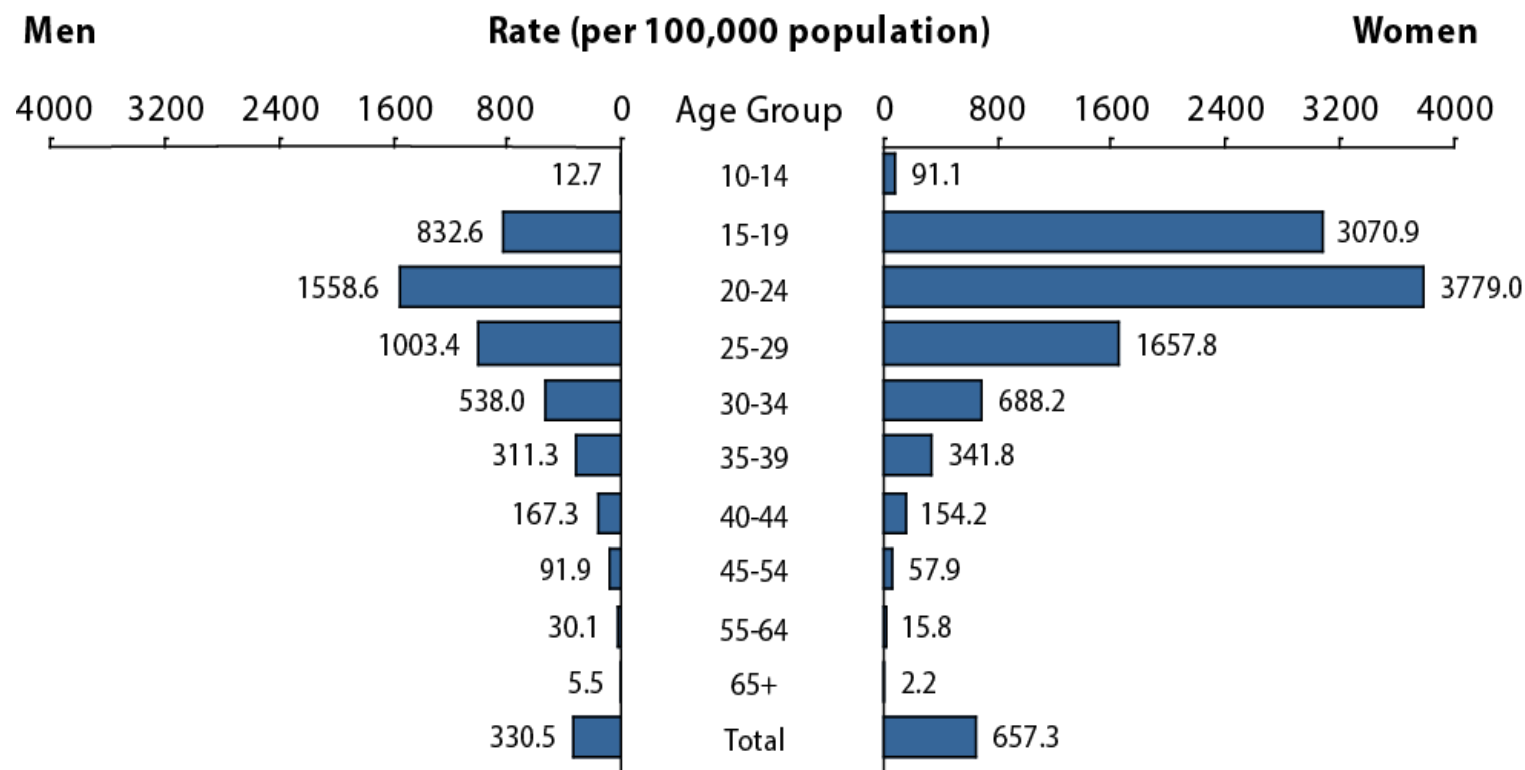
- A. Urine GC/Chlamydia testing only
- B. Urethral swab for GC/Chlamydia only
- C. 3 site testing for GC/Chlamydia
- D. Do nothing, watch and wait

Chlamydia

Chlamydia trachomatis

- Obligate intracellular bacterium
- Not identified on Gram stain and beta-lactam antibiotics not effective
- Highly-transmissible
- Incubation 7-21 days
- Most frequently *reported* STI in the US (reportable in all 50 states)
- Actual incidence higher (many asymptomatic)

Chlamydia — Rates of Reported Cases by Age Group and Sex, United States, 2016



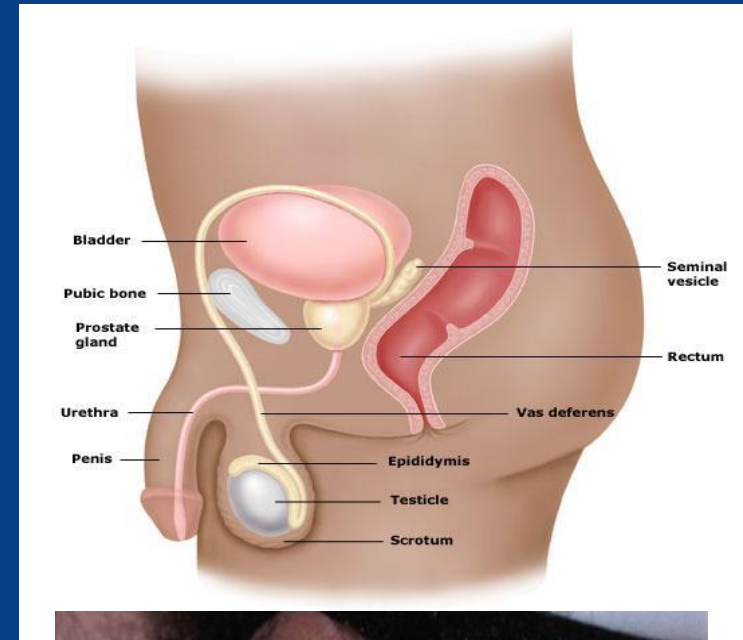
Chlamydia in Males

- Most are asymptomatic
- Urethritis
 - Mucoïd or clear penile discharge
 - Dysuria
 - Urethral pruritus
- Complications uncommon – typically epididymitis



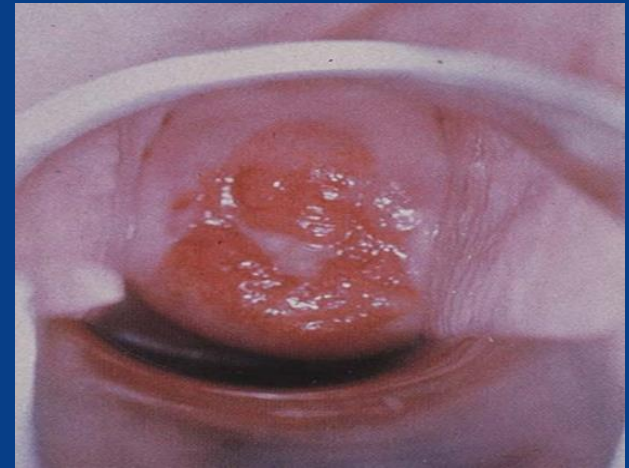
Acute Epididymitis

- Unilateral scrotal pain, epididymal swelling and tenderness
- Usually due to STI in adolescents
 - Chlamydia 70%
 - May be due to enteric gram-negative bacteria with insertive anal intercourse



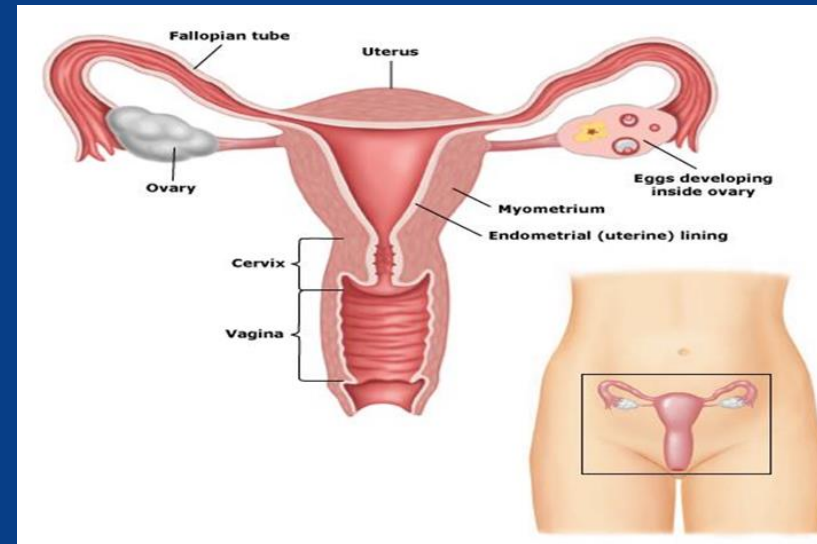
Chlamydia in Females

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



Pelvic Inflammatory Disease

- Ascending spread of micro-organisms from cervix
- Manifestations
 - Endometritis
 - Salpingitis (Fallopian tubes)
 - Tubo-ovarian abscess
 - Pelvic peritonitis



Pelvic Inflammatory Disease

- 10-15% with untreated Chlamydia
 - Subclinical in most
 - Acute presentation with lower abdominal pain
 - Pelvic examination (≥ 1 finding: cervical motion, uterine, and/or adnexal tenderness)
- PID \rightarrow scarring of Fallopian tubes
 - Infertility (20%)
 - Chronic pain (30%)
 - Ectopic pregnancy (1% of conceptions)

Other Manifestations of Chlamydia Infection

- Conjunctivitis (auto-inoculation)
- Oropharyngeal infection (asymptomatic → exudative tonsillitis)
- Proctitis/proctocolitis
 - Receptive anal intercourse (males & females)
 - Females with spread from cervical secretions
- Lymphogranuloma venereum (LGV)
- Reactive arthritis

Lymphogranuloma Venereum

- Textbook presentation: tender unilateral inguinal or femoral lymphadenopathy; ulcer or papule at site of inoculation usually resolved by time of presentation



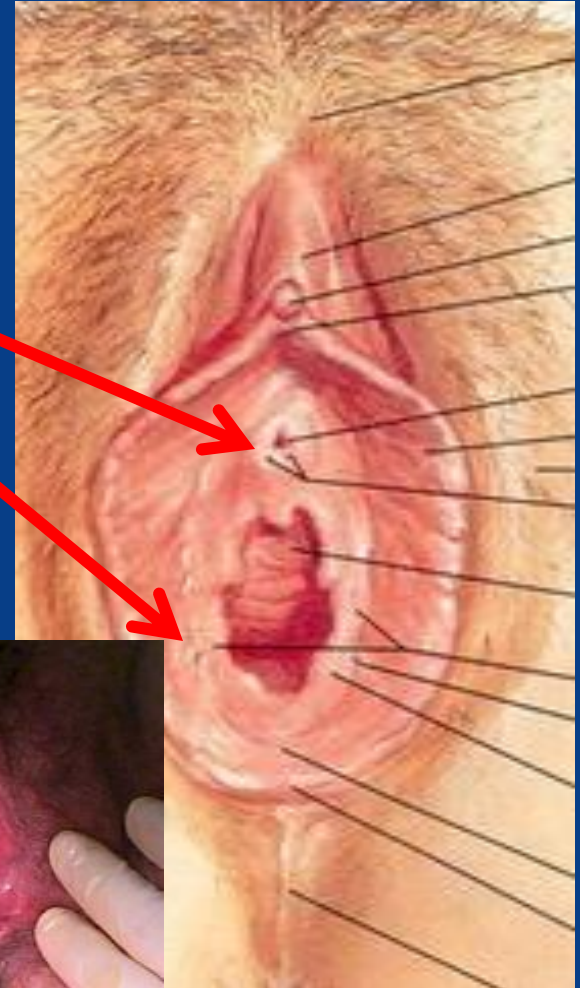
- However, most cases in the United States are rectal infection

LGV Diagnosis

- *Chlamydia trachomatis* serovars (L1-L3) that are rare in the US
- Emerging infection – outbreaks among MSM with HIV
- Diagnosis based on clinical suspicion, epidemiology, exclusion of other etiologies
- PCR not widely available
- Implications for treatment

Accessory Gland Infections

- Female accessory glands – secrete lubricating mucus
 - Skene’s (paraurethral) glands
 - Bartholin’s (greater vestibular) glands
- Occlusion of ducts (may be due to STI) → abscess, usually unilateral



Bartholin's duct cyst

Chlamydia Diagnosis

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

Chlamydia Treatment – Uncomplicated Infection

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

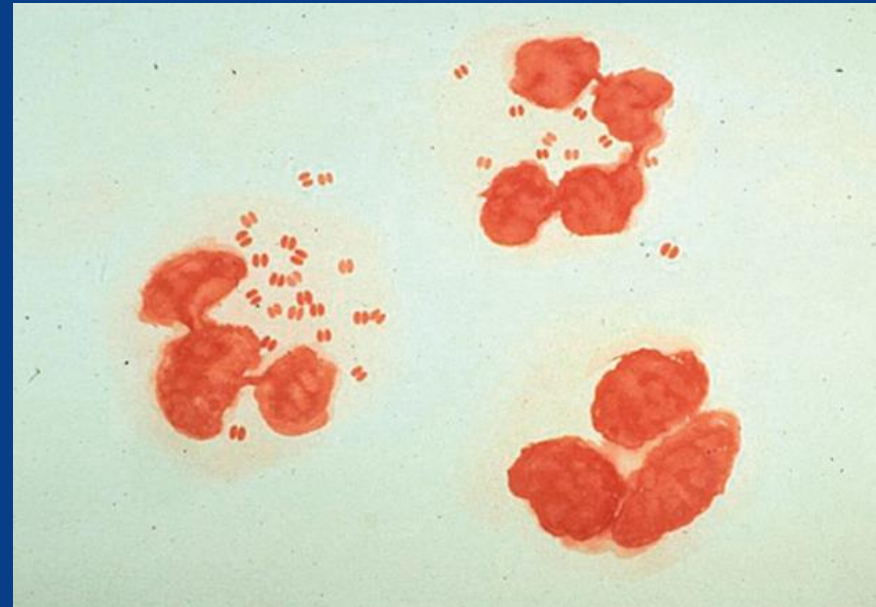
Chlamydia Treatment

- Some concern that azithromycin may be less effective for rectal infection
- Recommended treatment for LGV:
doxycycline 100 mg BID x 21 days
 - Data lacking, but azithromycin 1 g weekly x 3 probably effective

Gonorrhoea

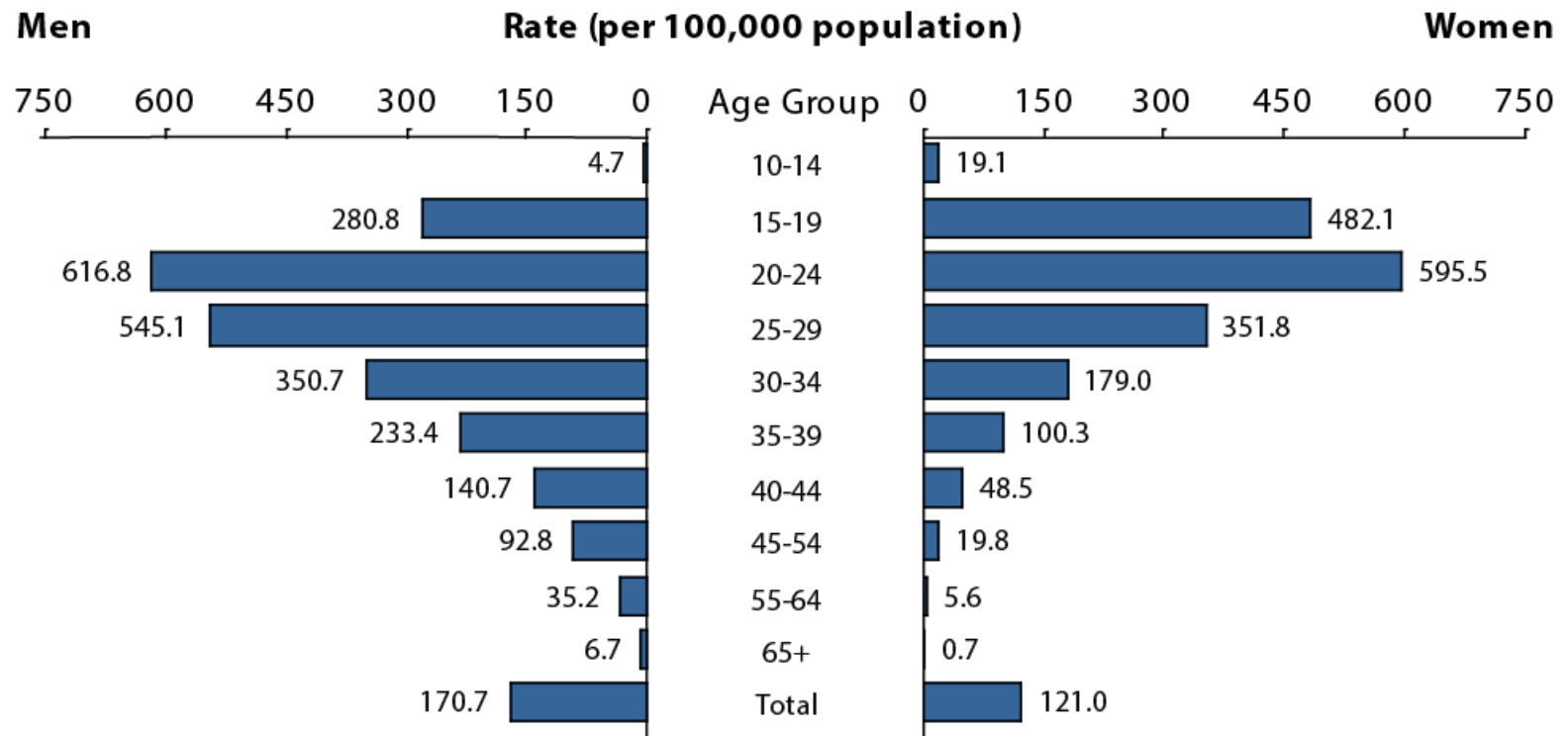
Neisseria gonorrhoeae

- Gram-negative diplococcus
- Transmission risk per intercourse:
 - Male-to-female: 50-70%
 - Female-to-male: 20%
- Often co-infection with Chlamydia



PMNs with intracellular
Gram-negative diplococci

Gonorrhea — Rates of Reported Cases by Age Group and Sex, United States, 2016



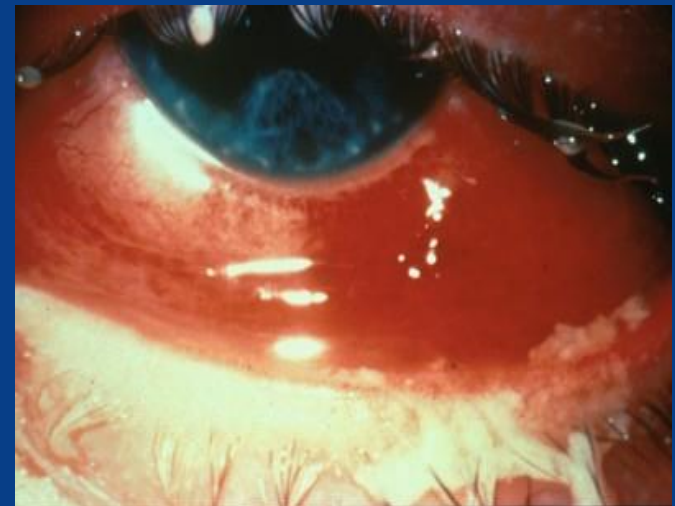
Gonorrhea Manifestations

- Males
 - Most (~90%) are symptomatic
 - Incubation period 2-5 days
 - Purulent or mucopurulent penile discharge
- Females
 - ~50% are symptomatic
 - Symptoms within 10 days of exposure
 - Cervicitis or urethritis



Other Manifestations

- Anorectal infection – may be seen in women without a history of anal intercourse
- Pharyngitis – often asymptomatic (screen in high-risk patients), may be only site of infection in oral-genital transmission
- Conjunctivitis – due to autoinoculation



Gonorrhea Diagnosis

- 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

Gonorrhoea Treatment

- Antibiotic resistance
- Quinolones no longer recommended
- Must treat with two drugs
 - To help avoid development of further resistance
 - May enhance treatment efficacy for pharyngeal infections (often unrecognized)

Gonorrhea Treatment - Uncomplicated

Recommended Regimen

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

Alternative Regimens

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

Alternative regimens are NOT
RECOMMENDED in oropharyngeal
infection (difficult to eradicate)

Applicable to both Chlamydia and
Gonorrhea

Epididymitis Treatment

- If likely caused by Chlamydia or gonorrhea:
 - Ceftriaxone 250 mg IM x 1
 - PLUS
 - Doxycycline 100 mg BID x 10 days
- In men who practice insertive anal sex, infection due to enteric organisms should be considered:
 - Use a fluoroquinolone instead of doxycycline (to cover both Chlamydia and enteric organisms): levofloxacin 500 mg daily (or ofloxacin 300 mg BID) x 10 days

PID Treatment

- Outpatient therapy:
 - Ceftriaxone 250 mg IM x 1
 - PLUS
 - Doxycycline 100 mg BID x 14 days
with or without
 - Metronidazole 500 mg BID x 14 days

Other Management Considerations

- Patient should abstain from sex
 - For 7 days after single-dose therapy
 - Until completion of 7-day regimen and resolution of symptoms
 - Until partners have been treated

Additional Testing

- Follow-up testing
 - No test of cure*, but risk of reinfection
 - Repeat test in 3 months
 - May have false positive NAAT within 3 weeks after treatment
- Additional testing
 - *Everyone diagnosed with one STI should be tested for the others (HIV, Chlamydia, gonorrhea, and syphilis)*

* Exception for oropharyngeal GC infection should have TOC in 14 days

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

Case Study # 2

Terri, a 15 year old Transgender female, reports to clinic for her Initial ID visit w/ labs after testing positive for HIV during a well child exam by her local PCP.

Pertinent history

- Diarrhea, night sweats, fatigue, cough, recurrent bronchitis, LAD; denies rashes or significant weight loss
- Anal receptive and oral sex
- History of treated GC
- Multiple partners with inconsistent condom usage (all males)
- No delay in linkage or entry into care

Case Study #2

Physical Exam

- Thin appearing w/ generalized LAD
- Bilateral tonsillar hypertrophy
- HR-RRR w/o murmur, lungs- CTA
- Abdomen-WNL
- VS WNL
- Negative for rash or skin lesions

Case Study # 2

Initial Labs

- CD4, viral load, genotype, hepatitis panel, CBC, CMP, RPR, 3 site testing, IGRA, CMV IgG/IgM, Toxo-IgG ab

RESULTS

- CD4-10 (1%), VL-36,800 copies/ml
- CMV IgG/IgM-positive, genotype-pending, CBC-mild anemia, CMP-WNL
- RPR-Non-reactive, 3 site testing-negative
- All other serology negative

Case Study #2 cont.

- Initiated Dolutegravir & Descovy and OI prophylaxis (Septra, Azithromycin)
- 1 week return- generalized pruritic body rash w/ burning and peeling of skin
- Septra discontinued and Atovaquone started w/ complete resolution of symptoms
- Toxicity labs WNL

Case Study # 2 cont.

2 week f/u visit

- Excellent adherence to HAART and OI prophylaxis w/o side effects
- Generalized maculopapular rash noted all over body w/o itching

Case study # 2 cont.

What would be your next step?

- A. Prescribe antihistamine and topical steroid cream for contact dermatitis
- B. Do nothing since the rash is not really bothering the patient
- C. Repeat RPR
- D. Refer the patient to Dermatology

Syphilis

PROZONE PHENOMENON

What is it?

A false negative response resulting from high antibody titer which interferes with formation of antigen-antibody lattice necessary to visualize a clumping (flocculation) within the serum

Prozone Phenomenon

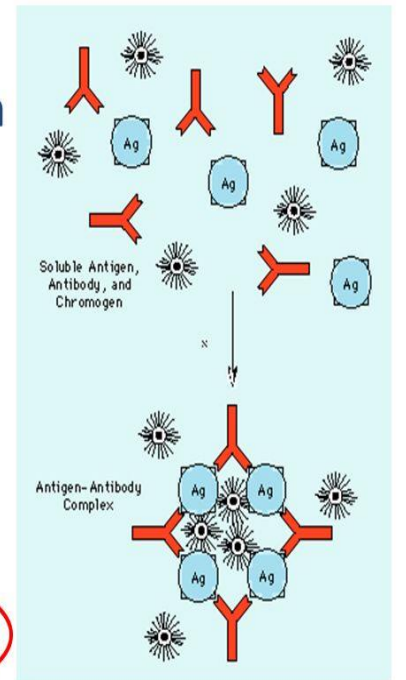
False Negative RPR

High Ab titers prevent antibody/antigen lattice formation

Rare

Occurs ~0.3-2% (early syphilis/ secondary)

May be more common in HIV+ and neurosyphilis



Jurado RL et al. Arch Intern Med 1993, 153:2496-2498.

Geisler MG. South Med Jour 2004, 97: 327-328.

Liu LL et al. Clin Infect Dis 2014, 59:384-9.



Causative Organism

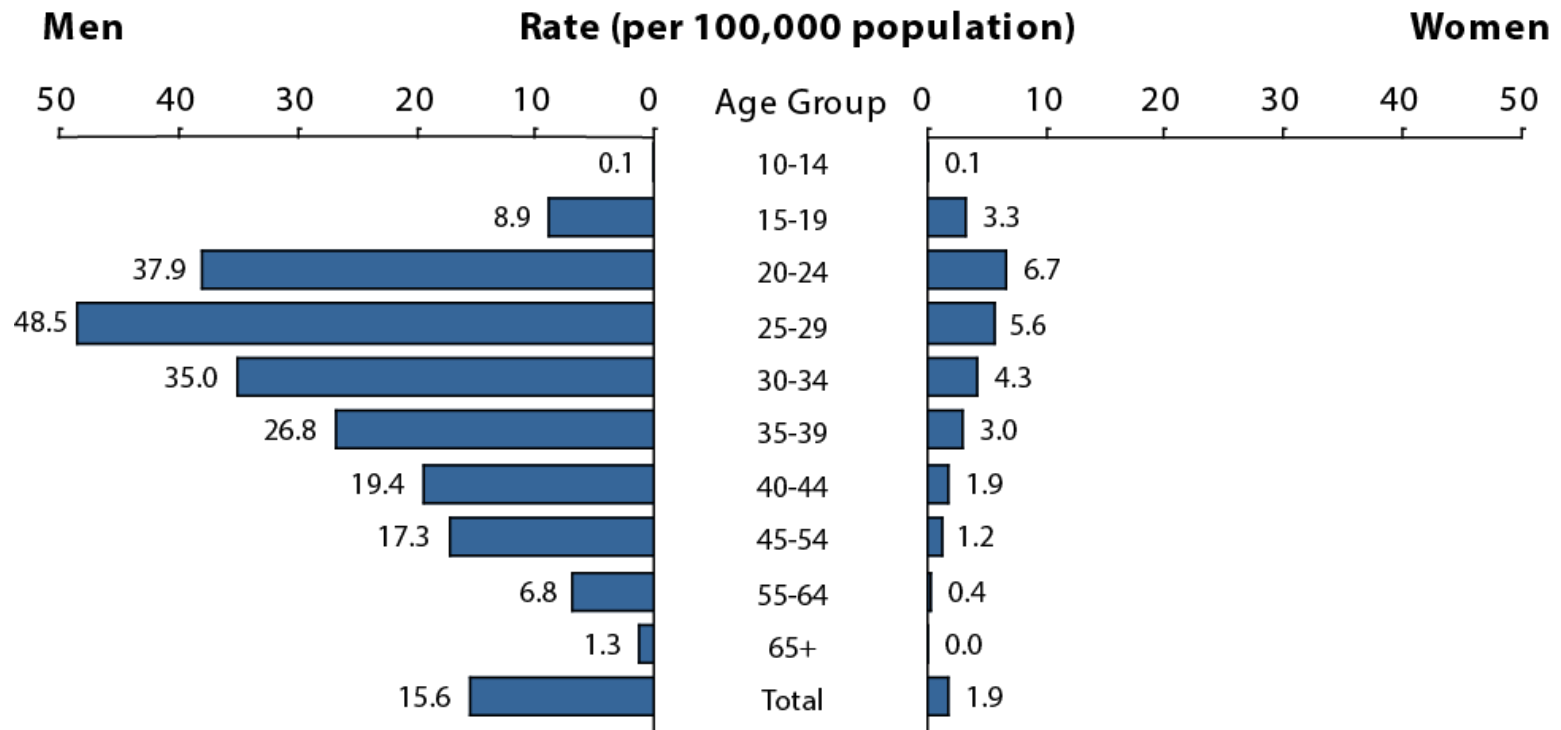
- *Treponema pallidum*
- Corkscrew-shaped, motile bacterium
- Cannot be cultured
- Cannot be viewed by normal microscopy



Stages of Syphilis

- Primary – initial infection, chancre
- Secondary – variety of manifestations
- Latent – no clinical manifestations
 - Early Latent – infection within the last year
 - Late Latent – infected more than a year before
 - Latent of Unknown Duration
- Tertiary – complications decades later

Primary and Secondary Syphilis — Rates of Reported Cases by Age Group and Sex, United States, 2016



<https://www.cdc.gov/std/stats16/>

Primary Syphilis

Chancre = painless lesion at site of inoculation



Secondary Syphilis

- Timing
 - May occur when chancre is healing or several weeks after
 - Chancre often not recognized, so timing often not known
- May have a variety of symptoms
 - Fever, lymphadenopathy, sore throat, alopecia, headache, myalgia, fatigue, weight loss
- $\geq 75\%$ have a maculopapular, nonpruritic rash, typically involving palms and soles

Rash of Secondary Syphilis



Secondary Syphilis



Secondary Syphilis – Condyloma Lata

- Seen in 10-20%
- “teeming with spirochetes”



Secondary Syphilis – Oral Lesions



Latent Syphilis

- Laboratory diagnosis – no symptoms
- Early Latent = within 1 year of infection (known prior testing results)
- Late Latent = known to be > 1 year after infection
- Latent of unknown duration (what most of them wind up being)

Tertiary Syphilis

- 10-15 years after infection:
gummas
 - Soft, gummy (rubbery)
destructive tumors that may
involve any organ system

- 20-30 years after infection:
aortic lesions



Neurosyphilis

Neurosyphilis is NOT a stage – it may occur at ANY stage of syphilis

Neurosyphilis

- Early manifestations
 - Cranial nerve dysfunction
 - Meningitis
 - Stroke
 - Acute altered mental status
 - Auditory
 - Ophthalmologic
- Late manifestations (10-30 years later)
 - Tabes dorsalis
 - General paresis

Syphilis Diagnosis

- Darkfield examination of lesions
- PCR not commercially available
- Usually diagnosed by combination of 2 types of serologic tests:
 - Nontreponemal (screening)
 - Treponemal (confirmatory)
- NOTE: some labs doing reverse sequence syphilis screening algorithm



Nontreponemal Tests

- RPR or VDRL
- May have false positives
- Use same type of test for follow-up
- Quantitative – fourfold change in titer is clinically significant
- Usually decline with treatment and often become nonreactive with time
- “Serofast reaction” – some may have positive titers for long periods of time

Treponemal Tests

- Many types
 - FTA-ABS (fluorescent treponemal antibody absorbed)
 - TP-PA (*Treponema pallidum* passive particle agglutination assay)
 - EIAs (enzyme immunoassays)
 - Chemiluminescence immunoassays
- Typically remains positive for life

Diagnosis of Neurosyphilis

- 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 Treatment

- Treat empirically pending test results if infectious syphilis suspected
- 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
- No alternatives for pregnant women – if allergic, should be desensitized and treated with PCN G
- Treat all contacts (regardless of testing) exposed within 90 days

Follow-Up After Early Syphilis

- Repeat RPR at 6 & 12 months
 - Expect 4-fold decrease in titer (15% will not)
- Treatment failure v. reinfection?
 - Signs or symptoms that persist or recur
 - Sustained 4-fold increase in titer
 - CSF analysis
 - Retreatment: benzathine penicillin G 2.4 million units IM weekly times 3

Who to Test?

- All sexually active adolescent & young adult MSM
 - At least annually
 - Every 3-6 months if high risk
- Consider for youth whose behaviors put them at higher risk

Other STIs

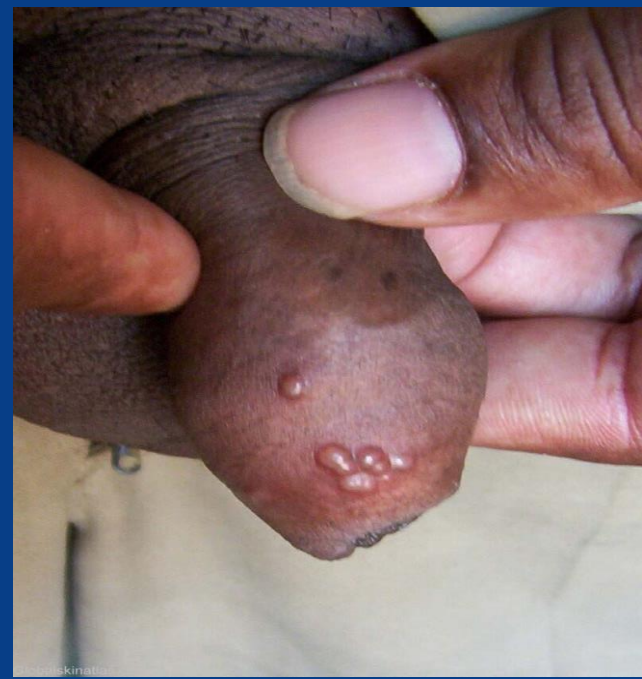
Herpes Simplex Virus

Genital HSV Infection

- HSV-1 or HSV-2
- Most transmission by undiagnosed persons, or diagnosed but asymptomatic
- HSV-2 causes most cases of recurrent genital herpes
- HSV-1 becoming more common, especially in young women and MSM

Genital HSV Infections

- If symptomatic: 1 or more vesicles, leaving painful ulcers that may take 2-4 weeks to completely heal
- Incubation period 2-12 days



Initial Episode v. Recurrences

- Initial episode:
 - Longer duration of lesions
 - Increased viral shedding
 - Systemic symptoms: fever, myalgia, lymphadenopathy, headache
- Recurrences:
 - Common, particularly in first year after initial episode
 - Shorter duration, less severe
 - About half have prodrome: pain or tingling

HSV Diagnosis

- Cell culture
 - Low sensitivity, declines with recurrences and healing lesions
- PCR
 - Negative tests do not exclude infection (intermittent shedding)

HSV Treatment

- First episode (treat empirically)
- Episodic therapy
 - Start within 1 day of lesions, or during prodrome
- Suppressive therapy for frequent recurrences
 - Decreases frequency by 70-80%
 - Decreases transmission to partners
 - Data demonstrating safety & efficacy of daily acyclovir therapy for up to 6 years, newer agents for 1 year
 - Reassess yearly need for continued treatment

HSV TREATMENT

Initial or Recurrent Genital Lesions (Duration: 5–10 Days)

- Valacyclovir 1 g PO BID (AI), or
- Famciclovir 500 mg PO BID (AI), or
- Acyclovir 400 mg PO TID (AI)

Chronic Suppressive Therapy

- Valacyclovir 500 mg PO BID (**AI**), *or*
- Famciclovir 500 mg PO BID (**AI**), *or*
- Acyclovir 400 mg PO BID (**AI**)

Evaluate ongoing need for suppressive therapy annually.

Trichomoniasis

- Protozoan *Trichomonas vaginalis*
- Most have no-few symptoms – untreated infections may last years
- Diffuse, malodorous, yellow-green vaginal discharge with vulvar irritation
- Diagnosis:
 - Microscopy of wet prep – motile protozoa
 - Nucleic acid testing of vaginal secretions (results in 10-45 minutes)
 - Culture
- Infection in men
 - Urethritis or asymptomatic
 - Diagnosis: wet prep not sensitive and no point-of-care testing options



Trichomoniasis - Diagnosis

- Wet prep (wet-mount microscopy)
 - Most common – convenient, low-cost
 - Only 51-65% sensitive in women
 - Even less sensitive in men
- NAAT
 - Very sensitive for women – 3-5x higher yield
- Culture
 - Vaginal 75-96% sensitive
 - Less sensitive for urine
- Cervical cytology
 - Not considered diagnostic – false-negatives and false-positives



Seattle STD/HIV Prevention Training Center
Source: Claire E. Stevens

Trichomoniasis Treatment

Recommended Regimen for Women with HIV Infection

Metronidazole 500 mg orally twice daily for 7 days

- Topical treatment NOT an option
- High rate of reinfection – consider re-testing women in 3 months
- Partners must be treated

Mycoplasma genitalium

- First identified in early 1980s
- 15-25% non-GC/ 20-25% non-CT urethritis
- Often more common than gonorrhea
- Diagnosis: NAAT (no FDA-approved test); culture may take 6 months & few labs can do
- Consider with persistent or recurrent urethritis, cervicitis, PID

Mycoplasma genitalium Treatment

- No cell wall – beta-lactams (PCN, cephalosporins) ineffective
- Only 31% cure rate with 7-day doxycycline course
- Single-dose azithromycin preferred, but resistance emerging concern
- Consider moxifloxacin (400 mg daily for 7, 10, 14 days) for treatment failures

Take Aways

- 3 site testing helps to avoid missed infections
- Emerging GC resistance limits treatment options (tx with ceftriazone & azithromycin)
- Repeat testing is necessary in high risk populations (3 months after treatment)
- If GC/CT (-) in symptomatic patients consider treatment for Mycoplasma Genitalium
- If patient is positive for one STI – Screen for All

Consider Holistic Approaches

- Target underlying conditions
 - Low self esteem
 - Low socioeconomic status
 - Substance abuse
- Use of Motivational Interviewing techniques
- Novel approaches to testing and education

Acknowledgments

- St. Jude Children's Research Hospital
 - HIV Clinical Staff
 - Katherine Knapp, MD
 - Patients
- AETC

National Guidelines



www.cdc.gov/std/treatment

apps available for Apple and Android devices

Thanks for Your Attentiveness!