STD Overview: Epidemiology, Clinical Presentation, Diagnosis, and Treatment of Common STDs

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Outline

Epidemiology, Clinical Presentation, Diagnosis, and Treatment of:
- Syphilis
- Gonorrhea
- Chlamydia

HIV Prevention in the Context of STDs
Syphilis
Epidemiology: Disease in Michigan
Primary & Secondary Syphilis Trends
percent of MI cases that are Male, MSM*, or HIV+
2015 P&S Syphilis by Sex and Race
Rates per 100,000 population 2015

- African American
- Caucasian
- Native American
- Asian & PI
- Hispanic

Female  Male
Clinical Presentation
Primary Syphilis

Primary lesion or "**chancre**" develops at the site of inoculation

Median incubation period before chancre appears is 21 days (range 3-90)

**Chancre**
- Progresses from macule to papule to ulcer
- Typically **painless, indurated**, and has a **clean base**
- Highly **infectious**
- Heals spontaneously within 3 to 6 weeks
- Multiple lesions can occur

**Regional lymphadenopathy:** classically rubbery, painless, bilateral

**Serologic tests** for syphilis **may not be positive** during early primary syphilis.
- Nontreponemal tests negative 20-30% of the time, treponemal test more likely to be positive
Primary Syphilis—Penile Chancre
Primary Syphilis—Labial Chancre
Primary Syphilis—Perianal Chancre
Primary Syphilis—Tongue Chancre
Secondary syphilis

Secondary lesions occur several weeks after the primary chancre appears and may persist for weeks to months.

Primary and secondary stages may overlap.

Clinical Manifestations:
- **Rash (75%–100%)**
- **Lymphadenopathy (50%–86%)**
- Malaise
- Mucous patches (6%–30%)
- Condylomata lata (10%–20%)
- Alopecia (5%)
- Liver and kidney involvement can occur
- Splenomegaly is occasionally present

**Serologic tests are usually highest** in titer during this stage.

Workowski et al. *CDC Sexually Transmitted Diseases Guidelines* 2015
Secondary Syphilis— Generalized Body Rash

Cincinnati STD/HIV Prevention Training Center

CDC/NCHSTP/Division of STD Prevention, STD Clinical Slides
Secondary Syphilis— Palmar/Plantar Rash

Seattle STD/HIV Prevention Training Center at the University of Washington, UW HSCER Slide Bank

CDC/NCHSTP/Division of STD Prevention, STD Clinical Slides
Secondary Syphilis—Condylomata lata
Latent Syphilis

- Host suppresses infection, no lesions are clinically apparent

- Only evidence is a positive serologic test

- Categories:
  - Early latent: <1 year duration
  - Late latent: ≥1 year duration

Workowski et al. CDC Sexually Transmitted Diseases Guidelines. 2015
Neurosyphilis

Occurs when *T. pallidum* invades the central nervous system (CNS)

May occur at any stage of syphilis

Can be asymptomatic

**Early neurosyphilis** occurs a few months to a few years after infection
- Clinical manifestations can include acute syphilitic meningitis, meningovascular syphilis, and ocular involvement

**Late neurosyphilis** occurs decades after infection and is rarely seen
- Clinical manifestations can include general paresis, tabes dorsalis, and ocular involvement

Ocular involvement can occur in early or late neurosyphilis

Holmes et al. Sexually Transmitted Diseases, 4th edition 2008
CDC Clinical Advisory: Ocular Syphilis in the United States 2016
Approximately 30% of untreated patients progress to the tertiary stage within 1 to 20 years.

Rare because of the widespread availability and use of antibiotics.

Manifestations:
- Gummatous lesions
- Cardiovascular syphilis
Late Syphilis—Serpiginous Gummata of Forearm
Late Syphilis - Ulcerating Gumma
Late Syphilis— Syphilis aortitis
Diagnosis
Laboratory Diagnosis

Identification of *Treponema pallidum* in lesion exudate or tissue

- Darkfield microscopy
- Tests to detect *T. pallidum* (DFA)
T. Pallidum on Darkfield Microscopy
Serologic Tests for Syphilis

Two types

- **Nontreponemal** (qualitative and quantitative)
- **Treponemal** (qualitative)

The use of only one type of serologic test is insufficient for diagnosis
Nontreponemal Serologic Tests

Nontreponemal tests include **VDRL, RPR, TRUST, USR**

Principles:

- Measure antibody directed against a **cardiolipin-lecithin-cholesterol antigen**
- Not specific for *T. pallidum*
- Titers usually **correlate with disease activity** (4-fold changes, e.g. from 1:32 to 1:8) and results are **reported quantitatively** (should only compare like tests)
- May be reactive for life, referred to as “serofast”
Treponemal Serologic Tests

Treponemal tests include TP-PA, FTA-ABS, EIA, CIA, MIA

Principles:
- Measure antibody directed against *T. pallidum* antigens
- Qualitative
- Usually reactive for life
- Titers should not be used to assess treatment response
CDC Recommended Screening

[Diagram showing a flowchart for CDC Recommended Screening with steps for RPR, TP-PA, and confirming syphilis presence or absence.]

Reverse Sequence Screening

[Diagram showing a flowchart for Reverse Sequence Screening with steps for EIA or CIA, quantitative RPR, and confirming syphilis presence or absence.]

Screening Process:
- **Screening** (RPR or TP-PA)
  - **Confirmation** (Quantitative RPR or TP-PA)
    - **Reconfirmation** (TP-PA for presence or absence of syphilis)

Syphilis Diagnosis:
- RPR positive
- TP-PA positive
  - Syphilis present
  - Syphilis unlikely

EIA or CIA:
- EIA positive
- EIA negative
  - Confirmatory test or repeat screening
Diagnosis of Latent Syphilis: Early vs. Late Latent Syphilis

Criteria for *early latent* syphilis, if *within the year* preceding the evaluation:

- Documented *seroconversion* or *4-fold increase* in comparison with a prior serologic titer
- Unequivocal *symptoms of primary or secondary syphilis* reported by patient
- *Contact* to an infectious case of syphilis
- Only possible exposure occurred within past 12 months

Patients with latent *syphilis of unknown duration* should be managed clinically as if they have *late latent syphilis*

*Workowski et al. CDC Sexually Transmitted Diseases Guidelines 2015*
Neurosyphilis: Indications for CSF Examination

Patients with syphilis who demonstrate any of the following criteria should have a CSF evaluation:

- Neurologic or ophthalmic signs or symptoms
- Evidence of active tertiary syphilis (e.g., gummatous lesions)
- Treatment failure
- HIV infection with a CD4 count ≤350 and/or a nontreponemal serologic test titer of ≥1:32

Workowski et al. CDC Sexually Transmitted Diseases Guidelines 2015
No test can be used alone to diagnose neurosyphilis

**VDRL-CSF**: highly *specific*, but *insensitive*

Diagnosis usually depends on **the following factors**:
- Reactive serologic test results
- Abnormalities of CSF cell count or protein
- A reactive VDRL-CSF with or without clinical manifestations

CSF *leukocyte count usually is elevated* (>5 WBCs/mm³) in patients with neurosyphilis.
Patient Management
Therapy for Primary, Secondary, and Early Latent Syphilis

**Benzathine penicillin** G 2.4 million units intramuscularly in a single dose (Bicillin L-A®)

If penicillin allergic:
- Doxycycline 100 mg orally twice daily for 14 days, or
- Tetracycline 500 mg orally 4 times daily for 14 days

Treat partners within past 90 days presumptively
Therapy for Late Latent & Tertiary Syphilis

**Benzathine penicillin G** 7.2 million units total, administered as **3 doses** of 2.4 million units intramuscularly each **at 1-week intervals**

If penicillin allergic
- Doxycycline 100 mg orally twice daily for 28 days or
- Tetracycline 500 mg orally 4 times daily for 28 days

Workowski et al. *CDC Sexually Transmitted Diseases Guidelines 2015*
Treatment of Neurosyphilis

1. **Aqueous crystalline penicillin G** 18–24 million units per day, administered as 3–4 million units IV every 4 hours or continuous infusion, for 10–14 days

   OR

2. **Procaine penicillin G** 2.4 million units IM once daily PLUS **Probenecid** 500 mg orally four times a day, both for 10–14 days

If concerned for **late latent syphilis:**

**Benzathine penicillin**, 2.4 million units IM once per week for **up to 3 weeks**, can be considered **after completion a neurosyphilis treatment regimen**
Other Important Treatment Points:

**Syphilis in pregnancy:**
- Treat with penicillin according to stage of infection. **Desensitize** to penicillin if allergic.

- **Jarisch-Herxheimer reaction:**
  - Self-limited reaction to antitreponemal therapy; **Not an allergic reaction**
  - Occurs **within 24 hours** after therapy
  - More frequent after **treatment of early syphilis**
  - Fever, malaise, nausea/vomiting; may be associated with chills and exacerbation of secondary rash
Follow Up

**Primary or secondary syphilis**
- Reexamine at 6 and 12 months.
- Follow-up titers should be compared to the maximum or baseline nontreponemal titer obtained on day of treatment.

**Latent syphilis**
- Reexamine at 6, 12, and 24 months.

**HIV-infected patients**
- 3, 6, 9, 12 and 24 months for primary or secondary syphilis
- 6, 12, 18, and 24 months for latent syphilis

**Neurosyphilis**
- Serologic testing as above
- Repeat CSF examination at 6 month intervals until normal (normalization of WBCs)
Gonorrhea & Chlamydia
Epidemiology: Disease in Michigan
Chlamydia Cases in Michigan, 2015
N= 44,843

Rate per 100,000 cases
Chlamydia Cases by Sex 2015
\( n = 47,702 \)

- Female
- Male
2015 Chlamydia by Sex and Race
(Rates per 100,000 population 2015)

- **African American**
  - Female: 1400
  - Male: 800

- **Caucasian**
  - Female: 200
  - Male: 100

- **Native American**
  - Female: 400
  - Male: 200

- **Asian & PI**
  - Female: 100
  - Male: 50

- **Hispanic**
  - Female: 500
  - Male: 400
Gonorrhea Cases in Michigan, 2015
N= 10,615

Rate per 100,000 cases
Gonorrhea Cases by Sex 2015
(n= 10,615)
2015 Gonorrhea by Sex and Race Rates per 100,000 population 2015

- African American
- Caucasian
- Native American
- Asian & PI
- Hispanic

Female & Male categories are indicated by different colors.
Clinical Presentations
### Manifestations of Gonorrhea and Chlamydia

<table>
<thead>
<tr>
<th><strong>Gonorrhea and Chlamydia:</strong></th>
<th><strong>Gonorrhea:</strong></th>
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<tbody>
<tr>
<td>• Urethritis</td>
<td>• Disseminated gonococcal infection (DGI)</td>
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<tr>
<td>• Cervicitis</td>
<td>• Skin lesions, tenosynovitis, arthralgia</td>
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<tr>
<td>• Epididymitis</td>
<td>• Occasionally meningitis or endocarditis</td>
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<tr>
<td>• Prostatitis</td>
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<tr>
<td>• Pelvic Inflammatory Disease</td>
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<td>• Pharyngitis</td>
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<td>• Anorectal infections</td>
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<td>• Fitz-Hughes-Curtis Syndrome</td>
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<th><strong>Chlamydia:</strong></th>
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<tr>
<td>• Pneumonia in newborns</td>
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<tr>
<td>• Sexually-associated reactive arthritis</td>
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<tr>
<td>• Lymphogranuloma venereum (LGV)</td>
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Nongonococcal Urethritis: Mucoid Discharge
Gonococcal Urethritis: Purulent Discharge
Epididymitis
Chlamydia Cervicitis
Gonococcal Cervicitis
Pelvic Inflammatory Disease
Pelvic Inflammatory Disease
Disseminated Gonorrhea
Diagnosis
Diagnosis

Preferred testing: **Nucleic acid amplification tests (NAAT)**, typically detect both organisms in same specimen

• Can perform on:
  • Urethra swab in men
  • Cervical or vaginal swab in women
  • Urine from women and men

• Not FDA approved (but are CDC recommended, especially in MSM):
  • Rectal swab
  • Pharyngeal swab

**Culture** also available, typically only used when there is concern for **gonococcal resistance**

Workowski et al. *CDC Sexually Transmitted Diseases Guidelines 2015*
Gram Stain of Urethral Discharge
Patient Management
Treatment

Uncomplicated genital chlamydia infection:

• Azithromycin 1 g orally in a single dose, or

• Doxycycline 100 mg orally twice daily for 7 days
  • Some evidence this is better for rectal chlamydia infection

• Alternative for pregnant women: Amoxicillin 500 mg orally three times a day for 7 days

Uncomplicated genital gonorrhea infection:

• Ceftriaxone 250 mg IM in a single dose PLUS azithromycin 1 gram orally in a single dose OR doxycycline 100 mg orally twice a day for 7 days

• If ceftriaxone allergy, gentamicin 240 mg IM in a single dose (or gemifloxacin 320 mg orally in one dose) PLUS azithromycin 2 grams orally in a single dose
Treatment

**Epididymitis**
- Ceftriaxone 250 mg IM single dose **PLUS** Doxycycline 100 mg orally twice daily for 10 days

**Pelvic Inflammatory Disease**
- Lots of options
  - Common outpatient regimen: Ceftriaxone 250 mg IM single dose **PLUS** Doxycycline 100 mg orally twice daily for 14 days **WITH OR WITHOUT** metronidazole 500 mg orally twice daily for 14 days

- Treat all sexual partners with contact in past 60 days
- Counsel to avoid sexual intercourse until partners are treated and for 7 days after treatment

*Workowski et al. CDC Sexually Transmitted Diseases Guidelines 2015*
Follow Up

**Test of cure** recommended only if:
- if symptoms persist after treatment
- second line therapy used

**Test of reinfection** recommended for all at 3 months

1st trimester screening for all pregnant women, repeat in third trimester for those at continued risk
Gonorrhea Resistance
Gonorrhea isolates from 7 individuals in Honolulu April and May of 2016
  ◦ All had high resistance to azithromycin & 5 had reduced susceptibility to ceftriaxone
  ◦ All successfully treated with ceftriaxone 250mg IM and azithromycin 1g po

Gonorrhea Resistance

What we can do:

Adhere to 2015 CDC Treatment Guidelines

Recommended: ceftriaxone 250mg IM & azithromycin 1g po

If patient does not have clinical response to recommend treatment, send gonorrhea culture and susceptibility.

Future directions:

Phase II RCT of ETX 0914 (single dose oral treatment) in December 2015, 98% effective at eradicating urogenital gonorrhea infection

Two more drugs “in the pipeline” per recent CDC press release

Local Outbreak
Local Outbreak: Lymphogranuloma Venerum (LGV)

**Chlamydia trachomatis:** Serovars L1-L3

**Three stages:**
- Painless genital ulcer
- Tender inguinal lymphadenopathy, sometimes suppurative
- Genitoanorectal syndrome: proctocolitis, damage of lymphatic system with genital swelling, colorectal fistulas
Local Outbreak: Lymphogranuloma Venerum (LGV)

August 2015-April 2016

MDHHS received 38 reports of LGV in HIV-infected MSM, 21 cases confirmed by CDC

Recommendations for suspected LGV cases:
- Report to local health department and/or MDHHS
- Test anatomic sites of exposure for Chlamydia trachomatis
  - May also be advised to send specimen to CDC
- Offer presumptive treatment at initial visit
  - Doxycycline 100 mg po bid for 21 days

Asymptomatic sexual contacts:
- Test for chlamydia at exposed sites and treat presumptively
  - Doxycycline 100 mg po bid for 7 days

De Voex et al. MMWR 2016
HIV Prevention
HIV Prevention in the Context of STDs

• STDs increase the risk of HIV acquisition

• Persons with STDs should be screened for HIV, and if negative, undergo HIV prevention counseling

• In addition to traditional HIV prevention techniques, such as changes in sexual practices, condoms, lubricant, etc., we now have HIV pre-exposure prophylaxis (PrEP) as a tool
HIV incidence among men diagnosed with syphilis is high; one in 20 MSM were diagnosed with HIV within a year. Our data have implications for syphilis and HIV screening and may be useful for further targeting HIV negative populations for pre-exposure prophylaxis.
MSM were at the greatest risk for HIV diagnosis after being diagnosed as having rectal gonorrhea (HIV incidence, 4.1 per 100 person-years), followed by early syphilis (2.8), urethral gonorrhea (1.6), rectal chlamydial infection (1.6), pharyngeal gonorrhea (1.1), late syphilis (1.0), and urethral chlamydial infection (0.6; P < 0.0001 overall). These men should be prioritized for more intensive prevention interventions, including PrEP.
What is PrEP?

HIV pre-exposure prophylaxis (PrEP) is a medication taken daily to prevent HIV infection.
What is PrEP?

2012: The FDA approved Truvada® (emtricitabine 200 mg/ tenofovir 300 mg) one tablet daily for PrEP use in individuals 18 years of age and older. This is the only approved regimen for PrEP.

- When taken consistently, reduces the risk of HIV acquisition by approximately 90%

2014: CDC released PrEP clinical practice guidelines

2015-Present: Increased PrEP marketing and implementation
CDC Indications for PrEP (abbreviated)

MSM/MSMW/Transgender women
- Condomless anal sex in the past 6 months (insertive or receptive)
- Any STD in the past 6 months (early syphilis and rectal gonorrhea especially high risk for HIV acquisition)

Anyone in an ongoing sexual relationship with an HIV-positive partner
- especially if partner has detectable viral load

Commercial sex workers

Injection drug users who share needles/preparation equipment
PrEP in Clinical Practice

- Patients need to have negative HIV testing (every 3 months) and creatinine clearance >60 mL/min to be prescribed PrEP

- In addition to HIV testing every 3 months, also need STD testing every 3-6 months, and monitoring of renal function every 6 months

- Prescription coverage can be challenging, there are several assistance programs to help with this

- Recommended to use in combination with other HIV prevention strategies
Questions?