STI Update

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Learning Objectives

• Review screening recommendations for STI in different patient populations
• Describe the current epidemiology of syphilis, testing algorithm and management considerations.
• Discuss the current recommendations regarding gonorrhea treatment

Case 1

32 year old bisexual asymptomatic male presents for routine physical exam. He is usually the insertive partner and also engages in oral sex. STI screening should include

a) RPR, urine GC NAAT, rectal GC NAAT, pharyngeal Gonorrhea NAAT, HIV antigen-antibody testing
b) RPR, urine/urethral GC NAAT, HIV antigen-antibody testing
c) Syphilis EIA, urine GC NAAT, throat culture, HIV antibody
d) RPR or Syphilis EIA, urine GC NAAT, Pharyngeal Gonorrhea NAAT, HIV antigen-antibody testing
Screening for STI

- All adults and adolescents from ages 13 to 64 should be tested at least once for HIV.
- Annual chlamydia screening of all sexually active women younger than 25 years, as well as older women with risk factors such as new or multiple sex partners, or a sex partner who has a sexually transmitted infection.
- Annual gonorrhea screening for all sexually active women younger than 25 years, as well as older women with risk factors such as new or multiple sex partners, or a sex partner who has a sexually transmitted infection.
- Syphilis, HIV, chlamydia, and hepatitis B screening for all pregnant women, and gonorrhea screening for at-risk pregnant women starting early in pregnancy, with repeat testing as needed.
- Screening at least once a year for syphilis, chlamydia, and gonorrhea for all sexually active MSM or bisexual. MSM with multiple or anonymous partners should be screened more frequently (i.e., at 3-to-6 month intervals).
- Anyone who has unsafe sex or shares injection drug equipment should get tested for HIV at least once a year. Sexually active gay and bisexual men may benefit from more frequent testing (e.g., every 3 to 6 months).

Screening for Chlamydia

Screening for Gonorrhea

Screening for Trichomonas
Screening for Syphilis

Pregnant Women: All pregnant women at the first prenatal visit. Retest early in the third trimester and at delivery if at high risk.

Men Who have Sex With Men (MSM): At least annually for sexually active MSM. Every 3 to 6 months if at increased risk.

Persons with HIV:
For sexually active individuals, screen at first HIV evaluation, and at least annually thereafter
More frequent screening might be appropriate depending on individual risk behaviors and the local epidemiology.

Screening for Herpes

<table>
<thead>
<tr>
<th>Type-specific HSV</th>
<th>Population</th>
<th>Note</th>
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</table>
| gag and env       | Women      | Type-specific HSV testing should be considered for women presenting for an STD evaluation (personally or with multiple sex partners).
|                   | Men        | Evidence does not support routine HSV 2 serology screening among asymptomatic pregnant women. However, type-specific HSV testing might be considered if the patient desires testing or is at increased risk for acquiring genital herpes during pregnancy.
|                   | MSM        | Type-specific HSV testing should be considered for men presenting for an STD evaluation (personally or with multiple sex partners). Type-specific HSV testing has been associated with improved outcomes for HSV infection, and treatment of both HSV-1 and HSV-2.
|                   | Persons with HIV | Type-specific HSV serology testing should be considered for persons presenting for an STD evaluation (personally or with multiple sex partners). Persons with HIV infection, and MSM at increased risk for HSV acquisition.

Screening for Hepatitis B and C

<table>
<thead>
<tr>
<th>Type of Screening</th>
<th>Population</th>
<th>Note</th>
</tr>
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</table>
| Women             | Test for HCV at the first prenatal visit. Test for HCV and HIV at the time of the first prenatal visit (all women should be tested for HCV and HIV concurrently). Test for HCV and HIV at the time of the first prenatal visit (all women should be tested for HCV and HIV concurrently).
| Pregnant Women    | Test for HCV at the first prenatal visit. Test for HCV and HIV at the time of the first prenatal visit (all women should be tested for HCV and HIV concurrently).
| Men               | All men should be tested for HCV and HIV. Test for HCV and HIV at the time of the first prenatal visit (all women should be tested for HCV and HIV concurrently).
| MSM               | Test for HCV and HIV at the time of the first prenatal visit (all women should be tested for HCV and HIV concurrently).
| Persons with HIV  | Test for HCV and HIV at the time of the first prenatal visit (all women should be tested for HCV and HIV concurrently).

Screening in correctional facilities

Chlamydia and Gonorrhea Screening
Women ≤35 and men <30 years in correctional facilities should be screened for chlamydia and gonorrhea. Chlamydia and gonorrhea screening should be conducted at intake.

Syphilis Screening
Universal screening should be conducted on the basis of the local area and institutional prevalence of early (primary, secondary, and early latent) infectious syphilis. Correctional facilities should stay apprised of syphilis prevalence as it changes over time.
Screening for STI in HIV infected

- All women should be screened for trichomoniasis, and all women aged <25 years should be screened for Chlamydia trachomatis infection
- Men and women should be screened for gonorrhea and chlamydia infection at initial presentation and then annually thereafter if at risk for infection
- Retesting in 3 months is indicated in men and women found to be positive for gonorrhea and chlamydial infections and women found to be positive for trichomoniasis on initial screening, because of high reinfection rates

Extra-genital testing

Obtaining an accurate sexual history can be challenging in any population, and provider comfort is essential to ensure an accurate assessment. It is possible that patients may not be completely forthcoming about exposure at some of these sites, and that infections may be missed if the patient is screened based on their history (versus screened at all sites regardless of history). However, at this time it is recommended that clinicians use the patient history to guide site-specific screening.

STI presenting as genital, anal or perianal ulcer

- Specific evaluation includes 1) syphilis serology, darkfield examination, or PCR testing if available; 2) culture or PCR testing for genital herpes; and 3) serologic testing for type-specific HSV antibody
- In settings where chancroid is prevalent, a test for Haemophilus ducreyi also should be performed
- Two FDA-cleared PCR tests are available for the diagnosis of HSV-1 and HSV-2 in genital specimens. Type-specific serology for HSV-2 might be helpful in identifying persons with genital herpes. In addition, biopsy of ulcers can help identify the cause of ulcers that are unusual or that do not respond to initial therapy.

FDA approved HSV PCR

<table>
<thead>
<tr>
<th>Age</th>
<th>M/F</th>
<th>ORAL/GENITAL</th>
<th>TYPE 1 &amp; 2 DIFFERENTIATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>BD Probe Tec™</td>
<td>≥17yrs</td>
<td>M&amp;F External Anogenital</td>
<td>Yes</td>
</tr>
<tr>
<td>MultiCode-RTx</td>
<td>&gt;18yrs</td>
<td>F Vaginal</td>
<td>Yes</td>
</tr>
<tr>
<td>IsoAmp HSV Assay</td>
<td>All</td>
<td>M&amp;F Genital &amp; Oral</td>
<td>No</td>
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Treatment of Ulcerative STI

- Because early treatment decreases the possibility of transmission, public health standards require health-care providers to presumptively treat any patient with a suspected case of infectious syphilis at the initial visit, even before test results are available.
- Presumptive treatment of a patient with a suspected first episode of genital herpes also is recommended, because successful treatment depends on prompt initiation of therapy.
- 25% with genital ulcer have no diagnosis after complete laboratory evaluation.

HSV serology

- Type specific Glycoprotein G based assays
- Might be useful in the following scenarios:
  1) Recurrent genital symptoms or atypical symptoms with negative HSV PCR or culture
  2) Clinical diagnosis of genital herpes without laboratory confirmation
  3) Partner has genital herpes

Chancroid

- Incidence of chancroid has declined steadily from 1987, when over 5000 cases were reported to the CDC.
- In 2010, 24 cases were reported from 9 different states. 5 were from Texas.

Chancroid

- Definite — Isolation of H. ducreyi from the lesion
- Probable — Clinical findings compatible with the diagnosis plus negative darkfield microscopic examination for Treponema pallidum, negative serologic test for syphilis, and negative culture for HSV or a clinical presentation not typical for herpes

NY State H. ducreyi PCR
Chancroid Treatment

<table>
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<tr>
<th>Recommended Regimens</th>
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<tr>
<td>Azithromycin 1 g orally in a single dose</td>
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<tr>
<td>OR</td>
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<tr>
<td>Ceftriaxone 250 mg IM in a single dose</td>
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<td>OR</td>
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<tr>
<td>Ciprofloxacin 500 mg orally twice a day for 3 days</td>
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<tr>
<td>OR</td>
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<tr>
<td>Erythromycin base 500 mg orally three times a day for 7 days</td>
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</table>

Repeat HIV and Syphilis serology 3 months after treatment.

Granuloma inguinale (Donovanosis)

- *Klebsiella granulomatis (Calymmatobacterium granulomatis)*
- Rare in USA. Endemic in India, Papua, New Guinea, Caribbean, Central Australia and Southern Africa.
- Painless, slowly progressive, ulcerative, vascular, beefy without regional lymphadenopathy, subcutaneous granulomas (pseudobuboes)
- Donovan bodies on crush stain or biopsy
- Azithromycin 1 gm weekly or 500 mg daily for 3 weeks or till lesions resolved

Lymphogranuloma Venereum

- Chlamydia serovars L1, L2, L3
- Self limited genital ulcer or papule followed by unilateral tender inguinal or femoral lymphadenopathy
- Women or MSM—Proctocolitis. Untreated-colorectal fistula, reactive arthropathy.
- NAAT for CT. PCR genotyping distinguish LGV CT from non LGV CT
- Chlamydia serology might be supportive. CFT >1:64 or MIFT >1:256
- Doxycycline 100 mg twice a day x 21 days. Azithromycin 1 gm weekly x 3 weeks. Aspiration of buboes or I & D as needed.
Syphilis Treatment

Recommended Regimens for Adults*

Early Latent Syphilis
Benzathine penicillin G 2.4 million units IM in a single dose

Late Latent Syphilis or Latent Syphilis of Unknown Duration
Benzathine penicillin G 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals

Tertiary Syphilis with Normal CSF Examination
Benzathine penicillin G 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals

Neurosyphilis and Ocular Syphilis
Aqueous crystalline penicillin G 10–24 million units per day, administered as 3–4 million units IV every 4 hours or continuous infusion, for 10–14 days.

* (a, b) Marked chorioretinitis with predominance of plasma cells, mononuclear cells (c) Marked destruction of the muscle cells and fragmenation of the reticulin.
Ocular Syphilis

- Cases of ocular syphilis should be reported to your state or local health department within 24 hours of diagnosis.
- Ocular syphilis cases diagnosed since December 1, 2014, should be reported to your local or state health department. The case definition for an ocular syphilis case is as follows: a person with clinical symptoms or signs consistent with ocular disease (i.e. uveitis, panuveitis, diminished visual acuity, blindness, optic neuropathy, interstitial keratitis, anterior uveitis, and retinal vasculitis) with syphilis of any stage.
- Pre-antibiotic clinical samples (whole blood, primary lesions and moist secondary lesions, CSF or ocular fluid) should be saved and stored at -80°C immediately upon collection for molecular typing.
- If you are a healthcare provider and need advice from CDC regarding the clinical management of ocular syphilis, contact Dr. Kimberly Workowski at 404-639-1898 or kgw2@cdc.gov. If you are planning on collecting clinical specimens for molecular typing and need assistance with the collection procedure or shipment of samples, please contact Dr. Allan Pillay at 404-639-2140 or ajp7@cdc.gov.

Ocular syphilis ongoing questions

- Lack of clarity whether this represents:
  - Outbreak of a more neuro/ocular-tropic syphilis strain versus
  - Increased awareness of a known complication of syphilis in the setting of rising number of syphilis cases
- Limitations of current surveillance system to detect/record ocular syphilis cases
Syphilis follow up

- Clinical and serologic evaluation should be performed at 6 and 12 months after treatment
- Definite criteria for cure or failure have not been well established
- Decline in titer is variable
- RPR titers might decline more slowly for:
  - persons previously treated for syphilis.
  - person’s stage of syphilis (earlier stages are more likely to decline fourfold and become negative)
  - Initial nontreponemal antibody titers (lower titers are less likely to decline fourfold than higher titers)
- Optimal management of persons who have less than a fourfold decline in titers after treatment of syphilis is unclear.
- If CSF pleocytosis was present, CSF every 6 months until cell count is normal.

Treatment Failure

- Signs or symptoms that persist or recur and those with at least a fourfold increase in nontreponemal test titer persisting for >2 weeks likely experienced treatment failure or were re-infected
- Because treatment failure usually cannot be reliably distinguished from reinfection with T. pallidum, a CSF analysis also should be performed; treatment should be guided by CSF findings
- Failure of nontreponemal test titers to decline fourfold within 6-12 months after therapy for primary or secondary syphilis. 15%-20% of persons with primary and secondary syphilis treated with the recommended therapy will not achieve the fourfold decline in nontreponemal titer used to define response at 1 year after treatment
- For retreatment, weekly injections of benzathine penicillin G 2.4 million units IM for 3 weeks is recommended, unless CSF examination indicates that neurosyphilis is present.

Case 2

Our patient’s RPR is reactive at 1:8 dilution and TP-PA confirms syphilis diagnosis. RPR was non reactive 11 months ago. Physical exam was negative for ulcer, gumma or rash. For contact tracing, testing and treatment, which of his sex partners should be notified?

a) None. He has latent syphilis
b) Partners in last 30 days
c) Partners in last 90 days
d) Partners in past year.
Management of Sex Partners

- Sexual contact with a person who receives a diagnosis of primary, secondary, or early latent syphilis within 90 days preceding the diagnosis should be treated presumptively for early syphilis, even if serologic test results are negative.
- Persons who have had sexual contact with a person who receives a diagnosis of primary, secondary, or early latent syphilis >90 days before the diagnosis should be treated presumptively for early syphilis if serologic test results are not immediately available and the opportunity for follow-up is uncertain. If serologic tests are negative, no treatment is needed. If serologic tests are positive, treatment should be based on clinical and serologic evaluation and stage of syphilis.
- Long-term sex partners of persons who have late latent syphilis should be evaluated clinically and serologically for syphilis and treated on the basis of the evaluation’s findings.
- The following sex partners of persons with syphilis are considered at risk for infection and should be confidentially notified of the exposure and need for evaluation: partners who have had sexual contact within 1) 3 months plus the duration of symptoms for persons who receive a diagnosis of primary syphilis, 2) 6 months plus duration of symptoms for those with secondary syphilis, and 3) 1 year for persons with early latent syphilis.

Gonorrhea by Age, Sex and Sexual behavior

- NAAT Recommended for genital and extra genital testing by CDC. Extra genital not FDA cleared and needs individual lab verification.
- Preferred specimens
  - Male: First catch urine
  - Female: Vaginal (equivalent to cervical, superior to urine)
- Exceptions:
  - Child sexual assault involving boys, rectal and oropharyngeal infections in prepubescent girls, Potential gonorrhea treatment failure

Chlamydia

- NAAT Recommended for genital and extra genital testing by CDC. Extra genital not FDA cleared and needs individual lab verification
- Preferred specimens
  - Male: First catch urine
  - Female: Vaginal (equivalent to cervical, superior to urine)
- Exceptions:
  - Child sexual assault involving boys, rectal and oropharyngeal infections in prepubescent girls, Potential gonorrhea treatment failure
Antimicrobials used for Gonorrhea

Evolution of Gonorrhea treatment

- The epidemiology of antimicrobial resistance guides decisions about gonococcal treatment recommendations.
- In 2007, emergence of fluoroquinolone-resistant N. gonorrhoeae in the United States prompted CDC to cease recommending fluoroquinolones for treatment of gonorrhea, leaving cephalosporins as the only remaining class of antimicrobials available for treatment of gonorrhea in the United States.
- Reflecting concern about emerging gonococcal resistance, CDC’s 2010 STD treatment guidelines recommended dual therapy for gonorrhea with a cephalosporin plus either azithromycin or doxycycline, even if NAAT for C. trachomatis was negative at the time of treatment.
- 2006-2011, the MIC for Cefixime in the United States and many other countries increased, suggesting that the effectiveness of cefixime might be waning. Treatment failures with cefixime or other oral cephalosporins have been reported in Asia, Europe, South Africa, and Canada.
- Ceftriaxone treatment failures for pharyngeal infections have been reported in Australia, Japan, and Europe. As a result, CDC no longer recommends the routine use of cefixime as a first-line regimen for treatment of gonorrhea in the United States.
- In addition, U.S. gonococcal strains with elevated MICs to cefixime also are likely to be resistant to tetracyclines but susceptible to azithromycin.

Recommended Rx for Uncomplicated GC infections of Cervix, urethra, rectum and Pharynx

- Cefixime 250mg IM x1 dose plus
- Azithromycin 1gm PO x1 dose
- Doxycycline 100mg PO BID X7days acceptable for azithro allergic
Cephalosporin allergy alternatives

- Gemifloxacin 320mg po plus Azithromycin 2gms
- Gentamicin IM 240mg (6ml in 2 divided doses) plus Azithromycin 2gms

Contraindicated in pregnancy
If used for pharyngeal infection, test of cure in 14days either with NAAT or culture.

Other Practical Considerations

Timing: Often in clinical practice, patients are treated with azithromycin for urethritis on one day, and screening tests return positive for gonorrhea on the next. The goal of dual therapy is to have both drugs active simultaneously.

Because azithromycin’s half-life is 68 hours, it is probably safe to administer ceftriaxone within five days of the azithromycin dose. However, the converse is not true. Ceftriaxone’s half-life is much shorter (5.8–8.7 hours), thus, if a patient is given ceftriaxone in a clinic, and fails to pick up azithromycin at the pharmacy for a couple of days, the patient should receive a second dose of ceftriaxone when they take the azithromycin.

Other practical considerations

EPT- Expedited Partner Therapy
Delivery of antibiotic therapy by index patient—either by prescription or actual medication
- Not recommended for MSM due to high risk of coinfection
- NYS EPT for CT only: 1gm Azithromycin single oral dose

GC and CT- Sex partner management

- Sex partners should be evaluated, tested and treated if they had sexual contact with the patient during the 60days preceding the onset of symptoms or diagnosis of GC or Chlamydia
- The most recent sex partner should be evaluated and treated even if the time of the last sexual contact was >60days before symptom onset or diagnosis.
Chlamydia

- Azithromycin favored over doxycycline due to adherence issue
- Concern azithromycin less effective especially for rectal Chlamydia
- Some use doxycycline preferentially for second episode/treatment failure for rectal Chlamydia

Mycoplasma genitalium

Emerging STI
Cause of male urethritis
- 15-20% of NGU
- 20-25% of non Chlamydial NGU
- 30% of persistent or recurrent urethritis
Unknown if can cause male infertility or male anogenital tract disease syndromes
Pathogenic role in women also less clear
? enhanced HIV risk

Mycoplasma genitalium

- Very slow growing organism. Difficult to recover in culture
- NAAT preferred method. Not commercially available
- 7 day doxycycline ineffective (median cure rate 31%)
- 1gm single dose azithromycin more effective
- Failure associated with macrolide resistance
- Moxifloxacin 400mg x7, 10 or 14 days for treatment failures.

Post Test Case 1

32 year old bisexual asymptomatic male presents for routine physical exam. He is usually the insertive partner and also engages in oral sex. STI screening should include

a) RPR, urine GC NAAT, rectal GC NAAT, pharyngeal Gonorrhea NAAT, HIV antigen-antibody testing
b) RPR, urine/urethral GC NAAT, HIV antigen-antibody testing
c) Syphilis EIA, urine GC NAAT, throat culture, HIV antibody
d) RPR or Syphilis EIA, urine GC NAAT, Pharyngeal Gonorrhea NAAT, HIV antigen-antibody testing
Questions?