HIV Module: STI Screening and HIV infection

Perry Tiberio, MD, PhD
Dana Dunne, MD

Module adapted from IAS-USA. Sexually Transmitted Infections in the HIV-infected patient.

Objectives:

- Define the incidence and prevalence of symptomatic and asymptomatic gonococcal and chlamydial infections by site of infection, with an emphasis on MSM HIV-infected patients
- Describe the approach to routine screening for STIs in HIV-infected patients including how often to screen and which tests are optimal for detection of STIs
- Determine management of STI infections in terms of treatment and treatment of sexual partners
- Understand that HIV-infected MSM are at risk for acquiring HCV through sexual exposure

Relevance:

- STIs are common among people infected with HIV.
- For individuals who are HIV negative, infection with an STI increases the risk of acquiring HIV infection.
- Early detection and treatment of STIs can prevent spread of infection and reduce the incidence of new HIV infections.
- Routine screening for STIs in the primary care setting remains low despite high prevalence of disease.
- Certain subpopulations of HIV infected individuals including MSM have demonstrated an increased incidence in STIs including syphilis, gonorrhea and chlamydia.
- Antibiotic resistance among gonococcal strains has made treatment challenging.

Although there is a high prevalence of STI coinfection among HIV-infected patients (described below) the routine screening for such infections in the outpatient setting remains low. Among HIV-infected MSM who visited 8 large STI clinics in 6 cities in the US between 2004 and 2006, annual screening for rectal chlamydia and gonorrhea infection was performed in only 2-9% and annual screening for urethral chlamydia and gonorrhea infections were 14-18%. This was compared with annual screening for syphilis at a rate of 66-76% of visits.

Case:
A 32-year-old man recently tested positive for HIV infection and he is visiting the clinic today. Laboratory tests show his CD4+ count is 390/μL and his HIV VL is 78,000 copies/mL. He discloses to you that he has hooked up with men who he met on Grindr, an online hookup app. In these hookups he was both the receptive and insertive oral and anal (versatile) sexual partner. He reports using condoms ”most of the time” for anal sex, but rarely for oral sex. His rapid plasma reagin (RPR) test is nonreactive. Serologies for hepatitis A virus (HAV), HBV, HCV and Toxoplasma gondii are pending. His medical history includes recurrent outbreaks of genital herpes, which he treats with episodic valacyclovir. He has had some fatigue recently but otherwise feels well. The physical exam today was unremarkable.

Question 1. How often should this patient receive STI screening? What is the prevalence of asymptomatic gonococcal and chlamydial infections in the MSM community? Among HIV-infected persons?

In this particular patient he reports having multiple male sex partners including high-risk contacts with anonymous partners who he met through Grindr, a phone hookup app. These all increase his risk of acquiring STIs including chlamydia and gonorrhea. Oral and anal intercourse pose a risk of acquiring both pharyngeal and rectal infections particularly but not exclusively in the MSM population. Among the MSM community STIs are more frequently detected at extragenital sites other than the urethra.

All patients who are sexually active should be screened for STIs regardless of the presence of symptoms. The anatomic locations (cervical, rectal, pharyngeal, urethral) tested should include all those which were exposed during recent sexual encounters.

The CDC recently released the 2015 Sexually Transmitted Diseases Guidelines (http://www.cdc.gov/std/tg2015/ for full the full list of recommendations). In these guidelines they generally recommend that STI screening should be considered in HIV care settings:

- at every visit if possible for risky sexual and substance-use behaviors
- annual screening of all patients for common STIs.

A systematic review by Kalichman et al reported the prevalence of STIs among persons with HIV showed a mean point prevalence of STI coinfection of 16.3%. The prevalence of STI among HIV-infected people was similar for men (mean, 13.6%) and women (mean, 15.8%). Median prevalence of common STIs included 9.5% syphilis, 9.5% gonorrhea, 5% chlamydia and 18.8% trichomoniasis.

With respect to site-specific positivity, Kent et al. defined the prevalence of chlamydial and gonococcal infections among MSM (both HIV-uninfected and HIV-infected) in San Francisco in 2003. The results from this study are summarized in the table below.

	Rectum	Urethra	Pharynx
Chlamydia	5.7-8.8%	3.3-5.5%	1.3-1.7%
Gonorrhea	3.2-7.5%	1.9-6.6%	7.8-9.4%

They found that men screened at all 3 anatomic sites had an overall prevalence of 13.3% for chlamydia and 16.7% for gonococcal infections.It is important to note that the vast majority of these extragenital infections were asymptomatic and would be missed if only urethral samples were screened for infection.

Regarding need for frequent screening, Rieg et al. evaluated the prevalence of asymptomatic bacterial STIs (gonococcal, chlamydial) in 212 HIV-infected MSM over three visits during a 12 month period. At the start of the study they identified 14% prevalence of infection with gonococcal infections and gonococcal infections were identified more commonly than chlamydial infections. Importantly 68% of these identified infections were from rectal or

pharyngeal samples. Upon follow up visit at 6 months they determined that 9.4% of individuals had an incident STI, and at 12 months 12.5% of individuals had an incident STI. They determined that compared to testing every 6 months, annual screening would have delayed a diagnosis of STI in up to 46% of cases.

Case (continued):
During the interview the patient reports 8 sexual partners in the past 3 months. Most of these partners he met through Grindr or Scruff on his iPhone or he met anonymous at a local adult bookstore. He also occasionally travels to NYC and goes to a bathhouse a few months a year. He has a few "regular" hookup buddies that he reports not using condoms with and he further discloses that while he attempts to use condoms with his anonymous encounters he is not always successful. His physical exam, including genitourinary, was normal.

Question 2. What tests should be ordered for this patient?

Most commercial laboratories have a variety of highly sensitive nucleic acid amplification tests (NAATs) for gonorrhea and chlamydia that can be used at rectal and pharyngeal sites. While pharyngeal infection with C. trachomatis has been reported, the pharynx is not believed to be receptive to long-term infection with this organism. For this reason it is not recommended to routinely test for chlamydia in the pharynx.

Compared with cell culture methods for detection gonorrhea and chlamydia, NAAT-based tests have improved sensitivity and detects infections that are routinely missed through culture methodologies.

Approach to screening for STIs in HIV-infected Patients:

First Visit:
Syphilis serology: RPR/VDRL, Treponemal EIA
Gonorrhea: Urine nucleic acid amplification test (NAAT)
Chlamydia: Urine nucleic acid amplification test (NAAT)
HSV-2 serology: consideration

For women: Trichomoniasis- Vaginal swab NAAT

For patients reporting receptive anal sex: Rectal NAAT for gonorrhea and chlamydia
For patients reporting receptive oral sex: Pharyngeal NAAT for gonorrhea

Subsequent Routine Visits:
Repeat all first visit tests at least annually for all sexually active patients (and every 3-6 months for those with high risk activity as defined below).

According to the 2015 CDC STD Treatment Guidelines, screening for STIs should be performed annually at a minimum. For patients with risk factors for acquiring STIs screening for STIs such as syphilis, gonorrhea, and chlamydia should be performed as frequently as every 3-6 months.

Risk factors include multiple and anonymous sex partners, concomitant substance use (especially methamphetamine), and frequenting commercial sex venues and hookup sites and apps. Condom use should not direct whether or not to perform the screening test as self-reported condom use could be influenced by the person asking the question about condom use.

Case (continued):
You send off samples to evaluate for *C trachomatis* and *N gonorrhoeae* at the rectum and urethra and *N gonorrhoeae* at the pharynx using NAAT-based tests. Test results come back and reveal that patient has gonorrhea in his pharynx only. He has no known drug allergies and only occasionally takes Ibuprofen for headaches and a daily vitamin.

Question 3: What is the appropriate treatment regimen for his gonococcal infection?

Both nationally and globally there is growing resistance among strains of *N gonorrhoeae.* For this reason quinolones including ciprofloxacin are no longer recommended for treatment of gonococcal infections in the United States. This patient should be treated with 250mg IM Ceftriaxone and 1g PO azithromycin. All gonococcal infections should be treated with 2 agents (ceftriaxone plus either azithromycin or doxycycline) regardless of the chlamydial NAAT results. It is believed that routine dual treatment may reduce the development of antimicrobial resistance among strains of *N gonorrhoeae.*

If ceftriaxone is unavailable for treatment of urogenital or rectal gonococcal infections, cefixime 400mg PO with 1g azithromycin PO can be given or cefixime with 7 days of doxycycline 100 mg po BID (note: the rate of doxycycline resistance are high among circulating strains of *N gonorrhoeae*). Any patient who is treated with an alternative regimen who has pharyngeal gonorrhea for should return to the clinic for test of cure (TOC) using a culture sample 1 week after treatment is finished. The culture is necessary to determine active infection and to be able to test for drug susceptibility/examine for antibiotic resistance. TOC is not currently recommended if cefixime is being used for uncomplicated anogenital gonorrhea.
In the case of a severe cephalosporin allergy, 2g azithromycin, which was once recommended as alternative treatment, is no longer recommended due to concerns about rapid emergence of macrolide resistance. Two regimens have been recently studied that have high cure rates for urogenital gonorrhea: 1) gentamicin 240 mg IM x 1 plus azithromycin 2 gm po x 1 or 2) gemifloxacin 320 mg po x 1 plus azithromycin 2 gm po x 1. While cure rates of pharyngeal gonorrhea also appeared high in this study, there were inadequate numbers of patients with gonorrhea to promote this regimen definitively.

Reinfection is common among patients who have been diagnosed and treated for gonococcal infections (as discussed above in the study results by Rieg et al.). Most infections are from reinfection rather than treatment failure. If this is the case it is important to emphasize the referral and treatment of sex partners and use the opportunity to discuss preventative measures to reduce the risk of reinfection (discussed further below).

Case (continued)
You treat the patient with 250mg IM ceftriaxone and 1g PO azithromycin. You provide the patient with risk reduction counseling including condom use and his use of Grindr to meet his sexual partners. You also instruct him to abstain from all sexual conduct for the following week. He makes an appointment for 3 month follow up for STI screening. He is worried that if is his boyfriend finds out about his gonorrheal infection he we break up with him. He tells you that his boyfriend does not know about his extramarital affairs and that the couple has had serious conflict about this topic in the past.

Question 4: What do you do about partner notification?

Treatment of sexual partners is a necessary and important aspect in the management of STIs and HIV. Partner services are an integral component of treating STIs to reduce the risk of reinfection and horizontal transmission in the community. Such services include both individual and public health activities that focus on treating persons infected with STIs to reduce further transmission in the community. This is also an opportunity for linkage to medical care where prevention counseling, STI and HIV testing, hepatitis screening and vaccination should be offered.

Various strategies have been used for notifying partners that they have been exposed to HIV or another STI. The main difference among the services is who is actually delivering the information. The various methods of notifying partners include:

- Public health official trained in locating and notifying partners of their possible exposure to STI and HIV.
- The infected person
- The practitioner treating the patient with the initial infection

It is important to note that partner services are confidential and voluntary. A wide range of materials, including educational tools, patient brochures, links to STI and HIV testing sites, and information to support STI care and prevention may be found at the STD Awareness Resource Site at http://www.cdcnpin.org/stdawareness/Home.aspx.

Other options including expedited partner therapy are not covered in this module and are not available for MSM due to rates of gonococcal antibiotic resistance.

This patient has not only exposed his multiple sex partners to gonococcal infection but also to HIV and it is important to have an open dialogue with the patient about this. He should be directly referred to public-health based partner services. Specifically you can give the patient referral slips to the local public health clinic for all the partners he has had in the past 60 days so that they may be tested and treated as contacts to gonorrhea. You should also refer the case to the health department for partner services and contact tracing, if the resources are available.

In Connecticut, as in many states, there is a dual reporting system to the State Department of Public Health (DPH) for reportable diseases including the STIs chlamydia, gonorrhea, syphilis, HIV, neonatal HSV, and Chancroid. This means that state, commercial, and hospital labs will

report positive tests for these conditions to the DPH and that a designee in the clinical department will submit a report that (STD-23 form) includes more information like disease manifestation, treatment used, however. Clinicians should not rely on these reporting mechanisms to serve as partner notification, however. The time lag of up to a month before State health officials receive these reports can result in ongoing disease transmission and morbidity. Therefore, it is advised that you directly contact the State DPH at **860-509-7920** and let them know you have a patient for partner notification services.A referral form and more contact information is available http://www.ct.gov/dph/lib/dph/infectious_diseases/std/partner/Partner_services_referral_form.pdf

Required Readings:

1. Rieg, G., et al., *Asymptomatic sexually transmitted infections in HIV-infected men who have sex with men: prevalence, incidence, predictors, and screening strategies.* AIDS Patient Care STDS, 2008. **22**(12): p. 947-54.
2. JL Marcus, KT Bernstein, RP Kohn, S Liska, SS Philip *Infections missed by urethral-only screening for chlamydia or gonorrhea detection among men who have sex with men*. Sexually transmitted diseases, 2011. 38; 10:922-28.

Selected Support References:

1. Kalichman, S.C., J. Pellowski, and C. Turner, *Prevalence of sexually transmitted co-infections in people living with HIV/AIDS: systematic review with implications for using HIV treatments for prevention.* Sex Transm Infect, 2011. **87**(3): p. 183-90.
2. Centers for Disease Control and Prevention. Sexually Transmitted Diseases Treatment Guidelines, 2015.
3. van der Helm, J.J., et al., *The hepatitis C epidemic among HIV-positive MSM: incidence estimates from 1990 to 2007.* AIDS, 2011. **25**(8): p. 1083-91.
4. Rauch, A., et al., *Unsafe sex and increased incidence of hepatitis C virus infection among HIV-infected men who have sex with men: the Swiss HIV Cohort Study.* Clin Infect Dis, 2005. **41**(3): p. 395-402.
5. Wandeler, G., et al., *Hepatitis C virus infections in the Swiss HIV Cohort Study: a rapidly evolving epidemic.* Clin Infect Dis, 2012. **55**(10): p. 1408-16.

Module adapted from IAS-USA. Sexually Transmitted Infections in the HIV-infected patient.