



INDIAN HEALTH SERVICE
National Pharmacy and Therapeutics Committee
Formulary Brief: 2021 Guidelines: Sexually
Transmitted Infections



-Oct 2021-

Background:

The National Pharmacy and Therapeutics Committee (NPTC) reviewed treatment guidelines from the Centers for Disease Control and Prevention (CDC) for Sexually Transmitted Infections (STI) at the Fall 2021 meeting. The CDC guidelines were released in July 2021. A review of targeted STIs (chlamydia, gonorrhea, syphilis) at the Spring 2021 NPTC meeting led to the addition of ceftriaxone and doxycycline to the National Core Formulary (NCF) at that time. Actions taken as a result of this review included the **ADDITION of metronidazole, tinidazole, and valacyclovir to the NCF.**

Discussion:^{1,2,3}

The following list of topics was included in the meeting and are summarized below. Full details can be found in the CDC document included in the references. In addition, a web link to the CDC Web Page can be found at [here](#). Finally, a phone application that incorporates the guideline updates is expected shortly (an interim mobile friendly app is now available for [providers](#)). Detailed clinical STI training can be found in the [National STD Curriculum](#).

The issues driving development of the new guideline recommendations are (1) increasing antibiotic resistance across a large range of human pathogens, (2) rising importance of antibiotic stewardship, (3) new information on effectiveness of current therapies, and (4) continued highlighting of unique infectious risks around receptive anal and oral sex.

Topics covered during the guidelines review included the following:

Sexual History taking includes review of the six “Ps”, namely Practices, Partners, Protection, Prior STI, Pregnancy intention, and Pleasure. Sexual history is critical to assess which clinical testing or screening measures are appropriate, and guidance for prevention education.

Screening recommendations include a continued recommendation to screen for gonorrhea and chlamydia (GC/CT) in all females age 13-25 years. Local epidemiology frequently necessitates extending the female screening age to 35 years of age. Men who have sex with men (MSM) should undergo 3 anatomical site (urethral/urine, anal, oropharyngeal) screening for GC/CT at least annually due to a high incidence of unapparent, asymptomatic infection, particularly in the oropharynx and the anus. HIV and syphilis screening are also recommended at least annually and more frequently based on sexual risk for this group. A screening frequency of up to every 3 months is recommended based on risk. Finally, MSM should be offered Pre-Exposure Prophylaxis for HIV (PrEP). PrEP should also be offered to partners of people living with HIV especially when viral load is detectable or unknown, any person with gonorrhea or syphilis in the last 6 months, or people who use and share injection equipment to take drugs.

Gonorrhea and chlamydia were only briefly reviewed, due to a focused review of these infections at the Spring 2021 meeting. The treatment recommendations for GC are ceftriaxone 500 mg IM once, if under 150 kg. Ceftriaxone 1000 mg IM once is recommended for those 150 kg and over. Dual therapy utilizing ceftriaxone plus azithromycin is no longer recommended. Because oropharyngeal GC is more likely to develop antibiotic resistance than infection at other anatomic sites, GC test-of-cure is recommended 7 to 14 days after treatment for all oropharyngeal infections. Increased risk of drug resistance with oropharyngeal infection is due to difficulty achieving adequate antibiotic levels in the tissues of the oropharynx. Rescreening for reinfection within 3 months is recommended for all other anatomic sites infected with GC. Recognition of antibiotic-resistant GC is especially important and should be suspected in cases of apparent treatment failure. Drug-resistant GC can occur at any anatomical site. Reinfection is still more likely to be the cause of treatment failure. All cases of suspected treatment failure should have a GC culture collected on selective media and immediate retreatment with the recommended regimen and special attention paid to partner treatment, as well, to prevent reinfection. If continued treatment failure is apparent, then expert consultation is recommended for subsequent treatment and antimicrobial resistance testing of culture isolates in order to identify alternative treatment options promptly. Azithromycin is no longer recommended as first line for any STI due to increasing levels of azithromycin resistance in a number of different pathogens. Azithromycin has also been shown to be inferior to doxycycline for treatment of chlamydia.

The recommended *treatment for chlamydia* (CT) is now doxycycline for all infections except in pregnancy (where azithromycin is still recommended). This is based on new data which show doxycycline to be superior to azithromycin, especially in the anus. Anal CT, especially in women, even when sexual practice does not include receptive anal intercourse, is common and self-inoculation of the anus with CT is implicated.

Trichomonas vaginalis (TV) treatment is recognized as an increasingly common STI in both men and women. The recommended treatment for TV in women was changed from a one-time dose of metronidazole to metronidazole 500 mg BID for 7 days. Tinidazole 2000 mg PO once was shown to be similarly effective as the 7-day course of metronidazole.

Expedited partner therapy for male partners of women who have recurrent TV is also a new addition to the recommendations. Treatment of TV in male partners remains metronidazole 2000 mg PO once. Lifting of the concern over disulfiram reaction, the interaction of alcohol with metronidazole, is also mentioned in the guidelines.

Expedited partner therapy (EPT) is the practice of prescribing or providing medication to a person with an STI so they can also provide the medication to a partner or partners who is/are unlikely or unwilling to seek treatment in an effort to reduce re-infection. EPT is recommended as an alternate to direct patient care for GC/CT and now for TV and is discussed in detail in the guidelines. The recommended EPT for GC is cefixime 800 mg PO once, while the EPT for CT is doxycycline 100 mg PO BID for 7 days.

Mycoplasma genitalium (M gen) is recognized as an increasingly common cause of cervicitis and male urethritis. It is a relatively antibiotic-resistant organism. Treatment for M gen is a two-step process and involves a 7-day course of doxycycline 100 mg PO BID followed by 7 days of moxifloxacin 400 mg PO BID. Nucleic acid amplification testing (NAAT) for M gen is now available. Resistance testing, also through NAAT, is expected to become available for M gen in the near future. Current data suggest 40-90% of M gen is macrolide-resistant. Prior recommendations for M gen treatment utilized azithromycin as the second step in the two-step process. Suspicion for M gen infection should be raised and evaluation recommended in cases of urethritis or cervicitis where a patient has recurrent symptoms with negative GC/CT and TV testing. While M gen was previously identified in STI literature as an etiology for recurrent symptomatology, detection with commercial assays is new. Treatment for M gen is recommended only when detected in the case of unresolved or recurrent symptoms. The role of M gen in STI diagnosis and treatment is evolving as are the diagnostic capabilities around M gen in the clinical laboratory.

Herpes simplex (HSV) was addressed in the 2021 guidelines and changes were made to the use of serologic diagnosis. Direct sampling of freshly unroofed vesicles utilizing a NAAT test is still the preferred diagnostic test for herpes. However, a newly developed serologic testing sequence, employing a Western Blot test to confirm a positive IgG test for herpes simplex and differentiate between HSV1 and HSV2, is now available. This testing sequence can be utilized in cases of recurrent genital ulcers or other atypical presentations of HSV. Routine serologic HSV screening is NOT recommended. As a reminder, screening for syphilis is always recommended when an ulcerating genital infection is evaluated.

Syphilis was addressed previously which resulted in penicillin G benzathine being added to the NCF. Staging was also reviewed previously. The importance of syphilis screening in pregnancy was stressed. Congenital syphilis, a common etiology of still birth, can be prevented when syphilis is identified and treated in pregnancy. Management of penicillin allergy was detailed to provide clinical guidance to providers and reduce the use of inferior alternatives to penicillin G benzathine. There is no effective alternative to penicillin G benzathine to treat syphilis during pregnancy.

Pelvic inflammatory disease (PID) therapy was revised in the new guidelines. A one-time dose of ceftriaxone 500mg IM once PLUS doxycycline 100 mg PO BID for 14 days WITH metronidazole 500 mg BID for 14 days is the current recommendation for outpatient management of PID. Outpatient management is appropriate when clinically mild disease is present. Inpatient management of PID also was revised in the CDC guidelines to include metronidazole. See the complete guidelines for a detailed discussion of [inpatient management of PID](#).

Proctocolitis was identified as a clinical entity caused by STIs in the previous guidelines from 2015, with GC/CT identified as the most common pathogens. Outbreaks attributable to Shigella and Campylobacter as well as other enteric pathogens have been identified particularly in MSM. M gen is also identified as a potential etiology. Initial treatment aimed at GC/CT is recommended in cases where bloody anal discharge is present or tenesmus or mucosal ulceration is noted when evaluating proctocolitis. A positive CT test in this context of proctocolitis suggests serovariants of CT responsible for lymphogranuloma venereum are present and a three week course of doxycycline is recommended. Any time mucosal ulcers are noted, syphilis testing is indicated.

Vaccine preventable STI's were also addressed in the new CDC guidelines. The HPV vaccine should be offered to all people under 26 years of age, and shared decision making is recommended to offer HPV vaccine for all people under age 46. [HPV screening](#) was addressed, see the complete guidelines for details. No changes were suggested to condyloma treatment guidelines. Consideration of Hepatitis A and Hepatitis B as STIs in MSM was discussed in the guidelines. Shared decision making in this situation is encouraged and immunization is recommended when appropriate.

Sexual assault treatment guidelines were included. Coverage for TV in addition to GC/CT are recommended. Post exposure HIV prophylaxis recommendations are also included. Instructions to consider Hepatitis A, Hepatitis B exposure, and post-coital contraception are noted.

Findings:

Medications added to the NCF at the Fall 2021 NPTC meeting following review of the 2021 CDC treatment guidelines for STIs included (1) metronidazole, for treatment of PID and TV, (2) tinidazole, for treatment of TV in women, and (3)

valacyclovir, for HSV treatment and suppression. A focused review of 3 STIs, namely chlamydia, gonorrhea, and syphilis, at the Spring NPTC meeting in April 2021 resulted in the addition of ceftriaxone, penicillin G benzathine, and doxycycline. A test-of-cure for oropharyngeal gonorrhea between 7 and 14 days after completion of treatment was reiterated. Evolving laboratory methods for diagnosis of M gen, its recognition as an etiology for recurrent urethritis/cervicitis, and its difficulty to eradicate were noted.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov . For more information about the NPTC, please visit the [NPTC website](#).

References:

1. Workowski KA, Bachmann LH, Chan PA, et al. [Sexually Transmitted Infections Treatment Guidelines, 2021](#). MMWR 2021; (70):4. Published July 23, 2021.
2. Centers for Disease Control and Prevention. [STI Tx Quick Guide. Conditions](#). For directions to download mobile app, scroll to bottom of page.
3. University of Washington STD Prevention Training Center. [National STD Curriculum, Second Edition](#). Funded by the Centers for Disease Control and Prevention. Accessed Nov 14, 2021.