Centers for Disease Control and Prevention
Sexually Transmitted Disease Treatment Guidelines

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Sexually transmitted diseases (STDs) constitute an epidemic of tremendous magnitude, with an estimated 18.9 million persons acquiring a new STD each year [1]. Reported disease rates underestimate the true burden of infection because the majority of STDs are asymptomatic and therefore go undetected, and also because of underreporting. STDs have far-reaching public health consequences on the sexual and reproductive health of individuals as well as the long-term health and health care costs of the community.

The accurate identification and effective clinical management of STDs represents a critical strategy for improving reproductive and sexual health and strengthening human immunodeficiency virus (HIV) prevention efforts. This is especially relevant to women, adolescents, and infants, as untreated infections frequently result in severe, long-term complications, including tubal infertility, adverse pregnancy outcomes, cancer, and facilitation of HIV infection. For more than 20 years, the Centers for Disease Control and Prevention’s (CDC) national guidelines for managing STDs has helped clinicians deliver optimal STD care. The CDC STD treatment guidelines are the most widely referenced and authoritative source of information on STD treatment and prevention strategies for clinicians who evaluate persons with STDs or those at risk for STDs.

The 2010 Guidelines for the Treatment of Sexually Transmitted Diseases were developed in consultation with public- and private-sector professionals knowledgeable in the management of STDs [2]. Evidence-based systematic reviews were performed on peer-reviewed journal articles and abstracts that had became available since publication of the 2006 CDC STD treatment guidelines. Evidence tables developed from the systematic reviews summarized the study type, population, and setting; treatment regimens or other interventions; outcome measures; and potential limitations to the reported findings. This report contains 11 background papers that describe the available evidence in several topic areas included in the 2010 CDC STD treatment guidelines. Current advances and controversies described in this supplement include discussion regarding the prevention, evaluation, and management of various sexually transmitted infections (STIs) and syndromes that have important implications for clinical practice.

A variety of prevention interventions are available to reduce the risk of acquiring STIs. Effective prevention may involve a combination of approaches including risk reduction counseling, appropriate use of available prevention methods (male latex condoms, diaphragms, topical microbicides, male circumcision), evaluation and treatment of infected persons and their sex partners, and vaccination of persons at risk for vaccine-preventable infections. Vaccination is one of the most effective methods for preventing transmission of some STIs including human papillomavirus (HPV). Vaccination with either a quadrivalent or bivalent HPV vaccine is recommended for females aged 11–12 years to prevent cervical precancer and cancer, with catch-up vaccination for females aged 13–26 years [3, 4]. The quadrivalent vaccine is also recommended for prevention of genital warts [5] and was recently licensed for the prevention of anal cancer in males and females. In addition, HBV vaccination is
recommended for all adults being evaluated for an STD or those at risk for sexual infection [6]. While routine vaccination has been associated with declines in HBV incidence, sexual transmission still accounts for the majority of new infections, especially among men who have sex with men (MSM). Other prevention strategies discussed in the CDC STD treatment guidelines include male circumcision (shown to reduce the risk of HIV acquisition and some STIs including genital warts and genital herpes), expedited partner management, and retesting to detect repeat infection (Chlamydia trachomatis, Neisseria gonorrhoeae).

Increased rates of several STIs (early syphilis, gonorrhea, chlamydia) and greater prevalence of unsafe sexual behaviors have been reported among MSM in the United States [7]. Lymphogranuloma venereum presenting as proctocolitis after rectal exposure has also been reported in this population [8, 9]. Vaccination against hepatitis A and B is recommended for MSM if previous infection or vaccination cannot be documented. Sexual transmission of hepatitis C virus can occur, especially among HIV-infected MSM [10, 11]. Routine hepatitis C testing of HIV-infected MSM should be considered to detect acute infection in men with high-risk sexual behaviors or concomitant ulcerative STIs. Providers should assess risk factors for acquisition of STIs and should perform routine laboratory screening at least yearly for all sexually active men.

Data regarding the prevalence of STIs and the risk of infection among women who have sex with women (WSW) are limited. WSW should not be presumed to be at low risk for infection based only on sexual orientation. Screening recommendations for sexually active women (C. trachomatis and cervical cancer screening) should be followed regardless of the patient's sexual orientation [12]. Bacterial vaginosis appears to be common among WSW [13], and strain-specific genital bacteria can be shared with female partners [14]. Further research is needed to define the sexual, behavioral, and transmission risks for STIs among WSW.

C. trachomatis infection is the most common bacterial STD in the United States with an estimated 3 million cases occurring annually [15]. Reported rates of chlamydial infections have increased over the past decade, reflecting expansion of chlamydial screening with highly sensitive nucleic acid amplification tests (NAATs) as well as improvements in information systems used for reporting. However, many women who are at risk for this infection are still not being screened appropriately, reflecting in part lack of awareness among some providers and limited resources. Diagnosis is typically associated with screening, as symptomatic infection is relatively uncommon. Annual screening of all sexually active women aged ≥25 years is recommended [4], as is screening of older women with risk factors (eg, those who have a new sex partner or multiple sex partners). There is insufficient evidence to recommend routine screening for C. trachomatis in sexually active young men, based on feasibility, efficacy, and cost-effectiveness; however, screening should be considered in high-prevalence areas, such as adolescent clinics, correctional facilities, and STD clinics. NAATs are the most sensitive method for diagnosis especially at extragenital sites of exposure [16]. Efficacious therapeutic regimens for chlamydia include azithromycin or doxycycline. Treatment should be provided promptly as delay in chlamydial treatment has been associated with complications in some persons [17]. Due to the high prevalence of repeat infection, women and men should be retested for chlamydial infection 3 months after treatment [18, 19].

The diagnosis and treatment of gonococcal and chlamydial infections in pregnant women is the best method for preventing neonatal gonococcal and chlamydial disease. However, all infants should receive ocular prophylaxis to prevent possible gonococcal ophthalmia neonatorum because not all women receive prenatal care and some may have untreated infection. The efficacy of ophthalmic prophylaxis in prevention of chlamydial ophthalmia is less certain. Erythromycin ophthalmic ointment 0.5% is the only recommended antibiotic treatment for neonates. However, if erythromycin ointment is not available, infants at risk for exposure to N. gonorrhoeae (ie, mother with untreated gonococcal infection or without prenatal care) should be presumptively treated as recommended in the CDC treatment guidelines [2].

The identification of a sexually transmissible pathogen in a child beyond the neonatal period suggests sexual abuse; however, the significance varies by pathogen. STI screening in this setting should be independent of symptoms [20]. Data on the use of NAATs for N. gonorrhoeae in children are limited, and performance is test dependent [21, 22]. When using NAATs in this context, expert consultation is recommended to minimize the possibility of cross-reaction with nongonococcal Neisseria species and commensals (eg, Neisseria meningitidis, Neisseria sicca, Neisseria lactamica, Neisseria cinerea, and Moraxella catarrhalis). NAATs can be used as an alternative to culture with vaginal specimens or urine from girls. However, culture remains the preferred method for urethral specimens or urine from boys and for extragenital specimens (pharynx and rectum) from all children. NAATs can be used for detection of C. trachomatis in vaginal specimens or urine from girls. No data are available regarding the use of NAATs in boys or for extragenital testing in boys and girls. Chlamydial culture remains the preferred method for extragenital sites.

Syphilis remains an important problem given the recent increases in primary and secondary syphilis [15], especially in MSM and because of biological interactions that facilitate HIV acquisition and transmission [23]. Long-acting preparations of penicillin remain the treatment of choice for all stages of syphilis. Enhanced antibiotic therapy has not been shown to improve treatment outcomes, regardless of HIV status [24]. The use of alternative therapeutic regimens (eg, ceftriaxone, doxycycline) for syphilis has been limited by the lack of data on the management of syphilis in pregnancy.
of early syphilis in those with penicillin allergy. Azithromycin has been a suggested alternative regimen due to its oral dose administration and demonstrated efficacy [25–27]. However, Treponema pallidum chromosomal mutations associated with azithromycin resistance and treatment failure have been documented [28]. Thus, azithromycin should always be used with caution and only when penicillin or doxycycline treatment is not feasible. Most HIV-infected persons respond appropriately to benzathine penicillin for primary and secondary syphilis. Cerebrospinal fluid (CSF) examination should be performed in all persons with serologic evidence of syphilis who have neurologic symptoms. However, CSF examination is not recommended for HIV-infected persons who have asymptomatic late latent syphilis; evidence of clinical benefit of this procedure is lacking. HIV-infected persons with syphilis of any stage whose rapid plasma reagin titers are $\geq 1:32$ and/or whose CD4 cell counts are $<350$ cells/mm$^3$ may be at increased risk for asymptomatic neurosyphilis [29]. However, unless neurologic symptoms are present, CSF examination in this situation has not been associated with improved clinical outcomes. The use of antiretroviral therapy in individuals with HIV infection and syphilis may decrease the risk of neurologic complications, decrease the risk of serologic failure following syphilis therapy, and enhance clinical responses in HIV-infected persons with neurosyphilis [30–32].

Mycoplasma genitalium has been associated with acute and chronic nongonococcal urethritis in men. Limited data in women suggest that M. genitalium may be associated with urethritis, cervicitis, and pelvic inflammatory disease. However, the public health impact of M. genitalium and its influence on empiric treatment recommendations has been difficult to determine due to the lack of a commercially available diagnostic test. Infections with M. genitalium in men with urethritis appear to respond better to azithromycin than to doxycycline [33]. However, there have been reports of azithromycin treatment failure in men with persistent urethritis, in which moxifloxacin has proven effective [34, 35].

Persistent oncogenic HPV infection is the strongest risk factor for development of cervical precancer, and for cervical and other anogenital cancers [36]. Recent data have also described the association of HPV 16 with oropharyngeal cancers, including those in the tonsils, base of tongue, and oropharynx [37]. HPV diagnostic tests that detect viral nucleic acid are available for clinical use in women undergoing cervical cancer screening. These tests should not be used for women <20 years of age, for prevaccination testing, or for STI screening apart from use as indicated in cervical cancer screening. HPV tests can be misleading when used in other settings (eg, screening men, screening partners, and screening women <30 years of age). There has been limited new information from clinical trials of existing therapeutic modalities for external genital warts, although vitiligo has recently been described as a side effect of imiquimod therapy [38]. A new patient-applied therapeutic modality is available for external genital warts, Veregen 15% ointment (150 mg sinecatechins). No clinical data are available regarding the efficacy or safety of sinecatechins compared with other available anogenital wart treatment modalities.

Trichomonas vaginalis is the most prevalent curable STI in the United States [15]. Diagnostic evaluation for T. vaginalis should be performed in women seeking evaluation of vaginal discharge. Screening for this infection can be considered in individuals at high risk for infection, including women who report new or multiple partners, a history of STIs, exchange of sex for payment, or use of injection drugs, although further research is needed to address the optimal frequency and cost benefit of this intervention. NAATs can provide optimal sensitivity and acceptable specificity for T. vaginalis diagnosis in various specimens from males and females. Metronidazole or tinidazole are the recommended regimens for trichomoniasis treatment. Randomized controlled trials suggest that tinidazole is equivalent to, or superior to, metronidazole in achieving parasitologic cure and resolution of symptoms [39]. Some strains of T. vaginalis can have diminished susceptibility to nitroimidazoles; however, most infections will respond to higher doses of metronidazole or tinidazole. In vitro data and clinical investigation support the efficacy of tinidazole when treatment with metronidazole fails [40–42]. The standard treatment recommendations for trichomoniasis have been based on studies that were conducted in HIV-negative persons. However, a recent randomized clinical trial demonstrated that among HIV-infected women, metronidazole 2-gram single oral dose was not as effective as metronidazole 500 mg twice daily for 7 days for trichomoniasis [43]. Therefore, a multidose treatment regimen for T. vaginalis may be considered in HIV-infected women. In addition, due to high rates of repeat infection [44] and possible persistent infection [45], rescreening for T. vaginalis 3 months after initial infection can be considered.

Health care providers can assist in the prevention of STIs through education and counseling of persons at risk, identification of asymptomatic infection, appropriate diagnosis and treatment of infected persons and their sex partners, and pre-exposure vaccination of persons at risk for a vaccine-preventable infection. The publication of national guidelines for management of STDs provides the clinical guidance necessary to deliver optimal care in both the public and private sectors. Treatment recommendations will continue to evolve reflecting advances in basic and clinical research, emerging antimicrobial resistance, and changing sexual and health care behaviors. Utilization of new, more effective treatment regimens, more sensitive tests for screening for asymptomatic infection, improvements in counseling of patients and their sexual partners, and new vaccines for STIs are crucial to achieve the broader public health goals of improving sexual and reproductive health.
Notes

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