Adolescent Sexuality

Updates to the Sexually Transmitted Infection Guidelines

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KEYWORDS

• Adolescents • Sexual health • Sexually transmitted infections
• Sexually transmitted diseases • Risk behaviors • Screening • Prevention

KEY POINTS

- Adolescents constitute one of the groups at highest risk for the acquisition and transmission of sexually transmitted infections (STI).
- Adolescents are both biologically and cognitively susceptible to acquisition of STIs.
- New guidelines are available regarding updates to the prevention, screening, diagnosis, and management of STIs in this age group.

INTRODUCTION

The Centers for Disease Control and Prevention (CDC) estimates that among the 20 million new sexually transmitted infections (STIs) diagnosed every year in the United States, one-half of these occur in young people aged 15 to 24 years.[1] Adolescents and young adults account for 53% of US reported gonorrhea cases and 65% of reported chlamydia cases.[1] Of concern, there has been an alarming increase in syphilis rates (15.1% from 2013 to 2014) among men who have sex with men (MSM), particularly those who are young and of color.

Adolescents are in a unique period of development; their psychosocial developmental stage is associated with increased risk-taking behaviors and desire for autonomy.[2] Their STI risk is multifactorial, including increased likelihood of multiple sex partners, lower levels of condom use, unprotected sex, complex structure of sexual

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networks, adolescent female susceptibility to infection owing to cervical ectopy, older sexual partners, mental health issues and substance abuse, and less access to confidential STI prevention and clinical services.[1,3–6]

This article discusses the most common STIs encountered in adolescents, with an emphasis on new guidelines for diagnosis, treatment, and prevention.

CHLAMYDIA TRACHOMATIS INFECTIONS

Clinical Manifestations

Chlamydia is the most frequently reported infectious disease in the United States and is the second most common STI in US adolescents after human papillomavirus (HPV).[1] Although most infections are asymptomatic, clinical manifestations include urethritis, epididymitis, cervicitis, proctitis, pelvic inflammatory disease (PID), and conjunctivitis and pneumonia among infants. Chlamydia is one of the leading causes of tubal factor infertility in females, which is preventable with early detection and treatment. Although the clinical significance of oropharyngeal infection is unclear, available evidence suggests that *C trachomatis* can be sexually transmitted from oral to genital sites.[7]

Diagnosis and Screening

Nucleic acid amplification tests (NAATs) have superior sensitivity and adequate specificity compared with older nonculture and non-NAAT methods for the diagnosis of *C trachomatis* genital tract infections in males and females. These US Food and Drug Administration (FDA)-cleared and recommended tests can be collected via vaginal or cervical swabs from females and first-catch urine from females or males.[8] Compared with vaginal and cervical specimens, first-catch urine may detect up to 10% fewer infections among females.[9–11] Vaginal swabs are preferred for female screening, although urine is still recommended.[9,10,12–15] Urine is preferred for male urethral screening.[8] Rectal and oropharyngeal NAATs are not FDA cleared, but are recommended by the CDC based on increased sensitivity and ease of specimen transport and processing. This testing is available commercially and most reference laboratories have already performed internal validation for Clinical Laboratory Improvement Amendments (CLIA) approval; clinicians should discuss testing availability with their local laboratories.[8]

The use and acceptability for self-collected swab testing has been described in females as young as 12 years of age and is potentially cost saving in this group.[16–21] In a recent study of STI testing using clinic-based, self-collected vaginal swabs among 310 first-year female college students, 98% of students found it easy or very easy to understand collection instructions and 93% found it easy or very easy to collect the specimen. Among all females, self-collected specimens were preferred over clinician-collected specimens, and the majority of females noted that self-collection made them feel comfortable and in control and that they were taking care of their health.[22] Currently, multiple FDA-cleared NAAT platforms can be used for patient-collected vaginal swabs in a clinical setting.[8]

The CDC, the US Preventive Services Task Force (USPSTF), and the American Academy of Pediatrics (AAP) recommend routine annual chlamydia screening for sexually active females less than 25 years of age.[7,23,24] The CDC and AAP also recommend that clinicians should consider chlamydia screening in sexually active, heterosexual young males in clinical settings with higher chlamydia prevalence (including adolescent primary care clinics, correctional facilities, and STI clinics).

The recommendation for routine chlamydia screening remains unchanged for MSM based on most current guidelines, but more frequent screening at 3- to 6-month intervals is indicated for MSM, including those with human immunodeficiency virus (HIV)

infection, based on risk factors in patients or their partners (see Special Populations: Men Who Have Sex With Men).

Treatment and Management

Recommended and alternative chlamydia treatments are outlined in **Table 1**. Recent studies suggest that doxycycline is marginally superior to azithromycin in treating genital chlamydia. Data from several studies and a metaanalysis show pooled cure rates of 97.5% for doxycycline versus 94.4% for azithromycin.[25–27] A recent randomized, controlled trial of males and females 12 to 21 years of age in a youth detention setting evaluated chlamydia directly observed therapy with doxycycline versus azithromycin. Treatment failure occurred in 5 of 155 individuals treated with azithromycin and none of the 155 individuals treated with doxycycline (cure rates of 97% and 100%, respectively.)[28] However, in settings in which directly observed therapy would not be feasible, that is, an office setting, single-dose azithromycin is still a highly effective and appropriate treatment option with a high cure rate.[29]

As mentioned, although routine oropharyngeal screening is not recommended, chlamydia can be transmitted sexually from oral to genital sites and should be treated if detected.[30,31] The efficacy of any of the alternative regimens is unknown for this indication.[7] Last, more recent retrospective studies including a systematic review and metaanalysis have raised some concern about the efficacy of single-dose azithromycin compared with doxycycline for rectal chlamydia infections.[32–34] More studies are needed comparing the 2 regimens before definitive recommendations can be made.[7]

Secondary to high reinfection rates, retesting in 3 months after chlamydia treatment is indicated in males and females.[35–37] NAAT testing should not be performed any sooner than approximately 1 month postinfection secondary to residual chlamydial DNA or RNA despite appropriate therapy.[7] Sexual partners in the past 60 days before diagnosis should be evaluated and treated. Or, if the last sexual exposure was more than 60 days before the onset of symptoms or diagnosis, the most recent sex partner should be treated. Partners should avoid sexual intercourse for at least 7 days after treatment to avoid reinfection.[7]

NEISSERIA GONORRHOEAE INFECTIONS

In the United States, gonorrhea is the second most frequently reported communicable disease after chlamydia.[1] *N gonorrhoeae* has evolved to resist each single antimicrobial agent used formerly as first-line therapy and cephalosporin resistance with accompanying treatment failures have been described worldwide (although not yet in the United States).[38–40] In a 2013 report, CDC designated *N gonorrhoeae* as antibiotic resistance threat level "urgent."[41]

Clinical Manifestations

N gonorrhoeae typically infects mucous membranes and may remain localized but can disseminate. Manifestations include urethritis, epididymitis, proctitis, conjunctivitis, cervicitis, PID, pharyngitis, and disseminated infection. Vertical transmission from infected mothers to their infants occurs. Gonorrhea can also increase rates of HIV sexual transmission up to 5-fold.[42]

Oral sex is highly prevalent among youth and prevalence of pharyngeal gonorrhea has increased in parallel. In 2 Los Angeles STI clinics, 65% of patients 15 to 24 years of age reported having oral sex and prevalence of pharyngeal gonorrhea in this group was 6%, compared with 7% for urogenital gonorrhea.[43]

Table 1
Recommended and alternative treatments for the major STDs in adolescents greater than 45 kg

Infection	Recommended Treatments	Alternative Treatments
Syphilis		
Primary, secondary or early latent (<1 y)	Benzathine penicillin G 50,000 units/kg IM once, up to adult dose of 2.4 million units	No specific alternative regimens exist.
Late latent (>1 y) or latent of unknown duration	Benzathine penicillin G 50,000 units/kg IM (up to adult dose of 2.4 million units) for 3 doses at 1 wk intervals (up to total adult dose of 7.2 million units)	No specific alternative regimens exist.
Gonorrhea		
Urogenital, pharyngeal and rectal	Ceftriaxone 250 mg IM once *plus* Azithromycin 1 g orally once	**Note: Use of an alternative regimen for pharyngeal gonorrhea should be followed by a test-of-cure 14 d after treatment.**[a] If ceftriaxone is *not* available: Cefixime 400 mg orally once[b] *plus* Azithromycin 1 g orally once *or* in case of azithromycin allergy Doxycycline[c] 100 mg orally 2 times a day for 7 d **For azithromycin allergy:** **Ceftriaxone 250 mg IM once *plus*** **Doxycycline[c] 100 mg orally 2 times a day for 7 d** **For cephalosporin allergy or IgE-mediated penicillin allergy:** **Gemifloxacin 320 mg orally once *or*** **Gentamicin 240 mg IM once** ***plus*** **Azithromycin 2 g orally once**
Conjunctival	Ceftriaxone 1 g IM once ***plus*** **Azithromycin 1 g orally once**, *plus* consider lavage of infected eye with saline solution once	No specific alternative regimens exist.
Chlamydia		
Urogenital, pharyngeal[d] and rectal[e]	Azithromycin 1 g orally once *or* Doxycycline[c] 100 mg orally 2 times a day for 7 d *or* Doxycycline hyclate[c] delayed-release tabs, 200 mg orally once daily for 7 d[f,g]	Erythromycin base 500 mg orally 4 times a day for 7 d[h] *or* Erythromycin ethylsuccinate 800 mg orally 4 times a day for 7 d[h] *or* Levofloxacin[i] 500 mg orally once a day for 7 d *or* Ofloxacin[i] 300 mg orally 2 times a day for 7 d

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Table 1
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Infection	Recommended Treatments	Alternative Treatments	
Trichomoniasis	Metronidazole 2 g orally once *or* Tinidazole 2 g orally once	Metronidazole[j] 500 mg orally 2 times a day for 7 d	
Genital herpes simplex virus			
First clinical episode[k]	Acyclovir 400 mg orally 3 times a day for 7–10 d *or* Acyclovir 200 mg orally 5 times a day for 7–10 d *or* Valacyclovir 1 g orally 2 times a day for 7–10 d *or* Famciclovir[l] 250 mg orally 3 times a day for 7–10 d		
Recurrent disease (episodic therapy)	Acyclovir 400 mg orally 3 times a day for 5 d *or* Acyclovir 800 mg orally 2 times a day for 5 d *or* Acyclovir 800 mg orally 3 times a day for 2 d *or* Valacyclovir 500 mg orally 2 times a day for 3 d *or* Valacyclovir 1 g orally once a day for 5 d *or* Famciclovir[l] 125 mg orally 2 times a day for 5 d *or* Famciclovir[l] 1 g orally 2 times a day for 1 d *or* Famciclovir[l] 500 mg orally once, followed by 250 mg orally 2 times a day for 2 d		
Recurrent disease (suppressive therapy)	Acyclovir 400 mg orally 2 times a day *or* Valacyclovir 500 mg orally once a day *or* Valacyclovir 1 g orally once a day *or* Famciclovir[l] 250 mg orally 2 times a day		
Anogenital human papillomavirus			
External or perianal		Urethral meatus	Vaginal[p], cervical[q] or intraanal[r]

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Table 1
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Infection	Recommended Treatments	Alternative Treatments	
Provider administered • Cryotherapy with liquid nitrogen or cryoprobe. Repeat applications every 1–2 wk if necessary *or* • Surgical removal *or* • TCA or BCA 80% −90%. Apply small amount only to warts. Allow to dry. If excess amount applied, powder with talc, baking soda or liquid soap. Repeat weekly if necessary. Patient Applied • Imiquimod 5% cream[m]—apply once daily at bedtime 3 times a week for up to 16 wk; wash treatment area with soap and water 6–10 h after application *or* • **Imiquimod 3.75% cream[m]—apply once daily at bedtime every day for up to 16 wk; wash treatment area with soap and water 6–10 h after application** *or* • Podofilox 0.5% solution or gel[n]—apply 2 times a day for 3 d, followed by 4 d of no therapy, 4 cycles maximum; total wart area should not exceed 10 cm^2 and total volume applied daily not to exceed 0.5 mL *or* • Sinecatechins 15% ointment[o]—applied 3 times a day for up to 16 wk; do not wash off	• Cryotherapy with liquid nitrogen *or* • Surgical removal	• Cryotherapy with liquid nitrogen *or* • Surgical removal *or* • TCA or BCA 80%-90%: apply small amount only to warts; allow to dry; if excess amount applied, powder with talc, baking soda or liquid soap; repeat weekly if necessary	

Revisions from the prior 2010 Centers for Disease Control and Prevention (CDC) STD Treatment Guidelines are emphasized in bold. See complete CDC Guidelines for management in pregnancy and in HIV infection.

Abbreviations: BCA, bichloroacetic acid; IgE, immunoglobulin E; IM, intramuscular; STD, sexually transmitted disease; TCA, trichloroacetic acid.

[a] Test of cure is no longer necessary in cases of uncomplicated urogenital or rectal gonorrhea treated with recommended or alternative regimens.

[b] Cefixime is not appropriate for pharyngeal gonococcal infections. See text.

[c] Doxycycline is not recommended during pregnancy or lactation.

[d] The efficacy of any of the *alternative* regimens is unknown for pharyngeal chlamydia; only recommended regimens should be used. See text.

[e] The efficacy of single-dose azithromycin compared with doxycycline for rectal chlamydia infections has yet to be studied in large trials. See text.

[f] This newer formulation comes in delayed-release 50 and 200 mg tabs and seems to be as effective as generic doxycycline with lower frequency of gastrointestinal side effects. Cost may be prohibitive for patients (approximately $340 for a 7-day course; in comparison, 7-day course of generic doxycycline ranges from $33–70).

[g] Thomson Reuters Micromedex Clinical Evidence Solutions [Internet]. Thomson Reuters; c2016. RED BOOK drug references; c2016 [cited 2016 Feb 11]. Available from: http://thomsonreuters.com/products_services/healthcare/healthcare_products/clinical_deci_support/micromedex_clinical_evidence_sols/med_safety_solutions/red_book/.

[h] If patient cannot tolerate high-dose erythromycin, change to lower dose for longer (refer to CDC Guidelines for details).

[i] Quinolones are not recommended for use in patients less than 18 years of age and are contraindicated in pregnancy.

[j] Regimen of 7 days of metronidazole may be more effective than single dose metronidazole in females coinfected with trichomoniasis and human immunodeficiency virus (HIV).

[k] Treatment can be extended if healing is incomplete after 10 days of therapy.
[l] Famciclovir efficacy and safety has not established in patients less than 18 years of age.
[m] May weaken condoms and vaginal diaphragms. Data from studies of humans are limited regarding use of imiquimod in pregnancy, but animal data suggest imiquimod poses low risk.
[n] Podofilox is contraindicated in pregnancy.
[o] Sinecatechins are not recommended for HIV-infected persons, immunocompromised persons, or persons with clinical genital herpes. Safety of sinecatechins in pregnancy is unknown.
[p] Cryoprobe is not recommended secondary to risk for vaginal perforation and fistula formation.
[q] Exophytic cervical warts warrant biopsy to exclude high-grade squamous intraepithelial lesions before treatment is initiated. Management should include consultation with a specialist.
[r] Many persons with anal warts may also have them in the rectal mucosa. Inspect rectal mucosa by digital examination or anoscopy. Management should include consultation with a specialist.
Adapted from Massachusetts Department of Public Health, Summary of the 2015 CDC STD Treatment Guidelines. Available at: http://www.mass.gov/eohhs/docs/dph/cdc/std/ma-std-tx-guidelines-2016.pdf. Accessed September 14, 2016.

Diagnosis and Screening

Similar to that for *C trachomatis* (see *Chlamydia trachomatis* infections), optimal detection of genital tract infections caused by *N gonorrhoeae* in males and females is achieved with NAATs collected via cervical or vaginal swabs (either clinician or patient collected in a clinical setting) from females and first-catch urine from females or males.[8] Clinicians should discuss testing availability with their local laboratories. Similar to chlamydia, the CDC, AAP, and USPSTF recommend routine gonorrhea screening for sexually active females less than 25 years of age.

The recommendation for routine gonorrhea screening remains unchanged for MSM based on most current guidelines, but more frequent screening at 3- to 6-month intervals is indicated for MSM, including those with HIV infection, based on risk factors in patients or their partners (see Special Populations: Men Who Have Sex With Men).

Treatment and Management

Recommended and alternative gonorrhea treatments are outlined in **Table 1**. Dual therapy is recommended to improve treatment efficacy and potentially slow the emergence and spread of cephalosporin resistance. Importantly, doxycycline is no longer recommended as part of dual therapy based on the substantially higher prevalence of gonococcal resistance to tetracycline.[7] Ideally, patients should receive dual therapy simultaneously and under direct observation in the clinic. If a prescription is given for azithromycin, it is critical to review with the patient the importance of dual therapy and that the azithromycin prescription should be filled and taken as soon as possible. If ceftriaxone is not available, then single-dose oral cefixime can be given in addition to azithromycin; however, this regimen is not appropriate for pharyngeal infections because cefixime has limited treatment efficacy for oral infections (92.3% cure [95% confidence interval, 74.9%–99.1%] compared with 97.5% cure [95% confidence interval, 95.4%–99.8%] in anogenital infections).[44,45]

A test of cure is only needed for individuals with pharyngeal gonorrhea treated with an alternative regimen; either culture or NAAT should be performed 14 days after treatment and any positive testing should be followed by antimicrobial susceptibility testing. Secondary to high reinfection rates, retesting in 3 months after therapy is indicated.[35,36] Sexual partners in the past 60 days before diagnosis should be evaluated and treated. Or, if the last sexual exposure was more than 60 days before onset of symptoms or diagnosis, the most recent sex partner should be treated. Partners should avoid sexual intercourse for at least 7 days after treatment to avoid reinfection.[7]

For those with cephalosporin or immunoglobulin E–mediated penicillin allergy, options are limited but include intramuscular gentamicin or oral gemifloxacin plus azithromycin based on a noncomparative randomized trial and in vitro studies.[46,47] Unfortunately, there is a current shortage of gemifloxacin in the United States; although the FDA approved a generic formulation in June 2015, it is unclear when this will become more available. Clinicians can find updates on the availability of gemifloxacin online via the CDC.[48]

Treatment Failures

Treatment failure should be considered in (1) persons whose symptoms do not resolve within 3 to 5 days after appropriate treatment and report no sexual contact during the posttreatment follow-up period and (2) persons with a positive test-of-cure (ie, positive culture $\geq$72 hours or positive NAAT $\geq$7 days after receiving recommended treatment) when no sexual contact is reported during the posttreatment follow-up period. In the adolescent population, a patient who is reinfected from an untreated or partially treated partner is the most commonly encountered situation rather than a case of resistant gonorrhea. If this situation is suspected, a careful history should be obtained and the patient should be retreated with ceftriaxone and azithromycin.[7] Clinicians should ensure that the patient's sex partners from the preceding 60 days are evaluated promptly with culture and presumptively treated using the same regimen used for the patient. A test of cure with a simultaneous NAAT at relevant clinical sites should be obtained 7 to 14 days after retreatment. It should be emphasized with the patient that he or she should abstain from sex for at least 1 week after treatment to avoid reinfection or transmission to a new partner.

In contrast, if treatment failure is truly suspected, clinicians should obtain relevant clinical specimens, including both NAAT and culture, and contact the local health department for guidance before retreatment.

TREPONEMA PALLIDUM INFECTIONS

Syphilis is caused by the spirochete *T pallidum* and is divided into stages (primary, secondary, latent, and tertiary) to guide management. As mentioned, there is a current epidemic of syphilis specifically in young MSM of color. Over time, there has been a 50% increase in HIV and a 200% increase in syphilis in this group.[1] In addition, a recent CDC *Morbidity and Mortality Weekly Report* alerted clinicians to an outbreak of ocular syphilis (a manifestation of neurosyphilis) in the Western United States in late 2014/early 2015, which has been of particular concern.[49,50]

Clinical Manifestations

Symptoms of syphilis depend on the stage and duration of infection; asymptomatic patients may only be diagnosed via screening. Patients with primary syphilis may present with painless ulcers or chancres on the genitalia, extremities, or oral mucosa depending on the location of exposure. Secondary syphilis symptoms can include skin rash, mucocutaneous lesions, and lymphadenopathy; tertiary syphilis presents with cardiac, neurologic, or gummatous manifestations decades after initial infection. Neurosyphilis can occur at any stage of disease.

As mentioned, 12 cases of ocular syphilis (including uveitis associated with rapidly progressive ocular symptoms and blindness) were initially identified in Seattle, Washington, and San Francisco, California, between December 2014 and March 2015. As of the latest update in March 2016, more than 200 cases have been reported from a total of 20 states. Most cases have been among HIV-positive MSM with a few cases in

HIV-negative patients including heterosexual males and females.[51] Although this outbreak has not yet affected adolescents, considering the syphilis epidemic in young MSM of color, clinicians should remain vigilant for this manifestation.

Diagnosis and Screening

Syphilis diagnosis requires both nontreponemal (eg, Venereal Disease Research Laboratory or rapid plasma reagin) and treponemal (eg, fluorescent treponemal antibody absorbed tests, the *T pallidum* passive particle agglutination assay, or enzyme immunoassay) testing. Because false-positive nontreponemal testing occurs in some situations (including pregnancy, autoimmune disease, HIV, and others), patients should always receive confirmatory treponemal testing.[7]

A growing number of clinical laboratories are screening samples initially using treponemal rather than nontreponemal tests, typically by enzyme immunoassay or chemiluminescence immunoassays, called the reverse screening algorithm. Such testing can be automated (in contrast, rapid plasma reagin is a manual test), has high sensitivity, and is optimal for populations with high prevalence of disease. In contrast, reverse screening cannot distinguish previous from new disease or treated from untreated disease, and secondary treponemal confirmation is required. False-positive initial treponemal results can occur in low-prevalence populations. Clinicians should be aware of the testing options at their institutions, and if reverse algorithm screening is available, they must be able to receive all treponemal and nontreponemal testing results to interpret the test results appropriately.[52] Of note, in 2014, the FDA granted a CLIA waiver for the Syphilis Health Check, a point-of-care test allowing for rapid screening in multiple clinical settings.[53] Local health departments and infectious diseases specialists can be contacted for discussion regarding testing availability and the most appropriate testing methodologies based on local epidemiology.

Patients with ocular symptoms consistent with syphilis should have serologic testing for syphilis in addition to immediate ophthalmologic evaluation and examination of the cerebrospinal fluid. Clinicians should contact their local health departments for guidance regarding suspected ocular syphilis cases.[50]

Treatment and Management

Syphilis treatments are outlined in **Table 1**. Of note, no adolescent or young adult-specific data exist. Primary and secondary syphilis-infected patients should be evaluated clinically and serologically for treatment failure at 6 and 12 months; those with latent syphilis should be evaluated clinically and serologically for treatment failure at 6, 12, and 24 months. Those with suspected neurosyphilis should be managed in collaboration with an infectious diseases specialist. In cases of suspected ocular syphilis, clinicians should contact their local health departments for discussion and guidance within 24 hours of diagnosis.[7]

TRICHOMONAS VAGINALIS INFECTIONS

Trichomoniasis is caused by the parasite *T vaginalis* and is the most prevalent nonviral STI in the United States. Although both males and females can be infected, this organism affects black females specifically (13% compared with 1.8% of non-Hispanic white females).[7] Infection may increase HIV acquisition risk by up to 3-fold, and it is particularly important in those coinfected with HIV based on studies of females 18 to 61 years of age: treatment can reduce genital HIV-1 shedding even in those not on antiretroviral therapy.[54–57] Therefore, sexually active HIV-positive females should

be screened for trichomoniasis at care entry and then at least annually thereafter. The AAP recommends considering screening females at higher risk of infection.[58]

Clinical Manifestations

Most patients with trichomoniasis have few to no symptoms, and untreated infections can last for months or years. Symptoms in females include diffuse, malodorous or yellow-green vaginal discharge with or without vulvar irritation, and vaginitis or cervicitis on examination. Males may have urethritis, epididymitis, or prostatitis.

Diagnosis and Screening

All symptomatic individuals, particularly those with high-risk sexual behaviors, should be tested for trichomoniasis. Data are lacking on whether screening and treatment for asymptomatic trichomoniasis in high-prevalence settings or in persons at high risk can definitively reduce any adverse health events and health disparities or reduce community burden of infection.[58]

NAAT has the highest sensitivity and acceptable specificity for diagnosis of trichomoniasis and is available for females only from vaginal, endocervical, or urine specimens; however, the APTIMA assay may be used with male urine or urethral swabs if validated per CLIA regulations. The CLIA-waived point-of-care OSOM Trichomonas Rapid Test (Sekisui Diagnostics, Framingham, MA) relies on immunochromatographic antigen detection of *T vaginalis* in vaginal secretions, provides results in 10 minutes and has a sensitivity of 82% to 95% and specificity of 97% to 100%. The Affirm VP III (Becton Dickinson, Sparks, MD) is a DNA hybridization probe test that evaluates for *T vaginalis*, *Gardnerella vaginalis*, and *Candida albicans* in vaginal secretions. The trichomonas test sensitivity is 63% and specificity is 99.9%, and results are typically available in 45 minutes. The DNA hybridization probe test or culture have lower sensitivity and specificity and are not recommended as first-line screening tests if amplified molecular detection methods are available.[7] The microscopic evaluation of wet preparations (wet mount) is the most common method for *T vaginalis* diagnosis because of convenience and relatively low cost. However, it requires immediate specimen evaluation for optimal results, and has suboptimal sensitivity (51%–65% in vaginal specimens; even lower in male urethral, urine, or semen specimens).

Treatment and Management

Recommended and alternative trichomoniasis treatments are outlined in **Table 1**. Secondary to high reinfection rates, patient retesting in 3 months is indicated.[35,36]

HERPES SIMPLEX VIRUS INFECTIONS

Genital herpes is a chronic, life-long viral infection of 2 types: herpes simples virus (HSV)1 and HSV2. Most cases of recurrent genital herpes are caused by HSV2; however, HSV1 is becoming more prominent as a cause of first-episode genital herpes. Recent studies have supported the increase and/or stability in the rates of oral sex behaviors in both male and female adolescents and adults.[59–61] Over the last decade, HSV1 seroprevalence has decreased, leaving young people more susceptible to HSV disease and incident HSV1 infections at sexual debut. HSV1 now causes most first genital HSV episodes in young adults, specifically young females and MSM.[62]

Clinical Manifestations

Patients with HSV infection may have vesicular or ulcerative anogenital or oral lesions, but may also have episodes of asymptomatic viral shedding, which is much more

frequent for genital HSV2 than for HSV1. Those with newly acquired disease can also have fever, malaise, and lymphadenopathy. Neonates can acquire devastating disease from vertical transmission. HSV2 also increases the risk of HIV acquisition.

Diagnosis and Screening

Cell culture or DNA polymerase chain reaction (PCR) are preferred for diagnosis in those with lesions. Although culture is highly specific, it is insensitive, may have a slow turnaround time, and testing is qualitative. PCR is highly sensitive and specific, type specific, automated, has a rapid turnaround time, and can be quantitative. It is the test of choice for central nervous system or systemic infections (including neonatal disease). Resistance testing can be done on culture but not on PCR. Importantly, failure to detect HSV by culture or PCR (especially in the absence of lesions) does not rule out HSV, because viral shedding is intermittent. Other tests, including the Tzanck preparation or direct immunofluorescence, have low sensitivity and/or specificity and are not recommended.

Serology with glycoprotein immunoglobulin G testing is type specific and accurate with sensitivities (HSV2) of 80% to 98%, although false-negatives may occur in early disease. The HerpeSelect HSV1 ELISA (Focus Diagnostics, Cypress, CA) is insensitive for detection of HSV1 antibody. The HerpeSelect HSV2 Elisa may have high false positives. HSV immunoglobulin M serology is not useful because is not type specific and may be positive during recurrent oral/genital episodes.

Because nearly all HSV2 infections are acquired sexually, the presence of HSV2 antibody implies anogenital infection. In contrast, the presence of HSV1 antibody alone is difficult to interpret because many individuals with positive testing may have been exposed in childhood with no implications for future disease or transmission to sexual partners. However, acquisition of genital HSV1 is increasing and can be asymptomatic. Lack of symptoms in a person who is HSV1 seropositive does not distinguish anogenital from orolabial or cutaneous infection, and regardless of site of infection, these persons remain at risk for acquiring HSV2.

Type-specific HSV serologic assays might be useful for (1) recurrent or atypical genital symptoms with negative HSV PCR or culture, (2) clinical diagnosis of genital herpes without laboratory confirmation, and (3) a patient whose partner has genital herpes. Screening for HSV1 and HSV2 in the general population is not indicated.

Treatment and Management

Recommended treatments for genital HSV infections are outlined in **Table 1**. Systemic antiviral therapy for HSV disease can treat symptomatic disease and control shedding, although famciclovir is less effective for the latter indication. Treatment also has no effect on latent virus, and it does not decrease risk of recurrence, frequency, or severity of episodes once it is discontinued. No topical therapy has been proven effective for HSV infection. In those with HIV, treatment decreases clinical symptoms but does not reduce HSV or HIV transmission risk to the uninfected partner; antivirals do not reduce risk of HIV acquisition in those who are HSV2 seropositive.

Daily suppressive therapy may be warranted for those with frequent episodes (>6 outbreaks per year) and can reduce the frequency of outbreaks by 70% to 80%. Treatment also is effective in patients with less frequent recurrences. Safety and efficacy has been studied in acyclovir (up to 6 years of documented experience) and valacyclovir and famciclovir up to 1 year. Any suppressive treatment should be reassessed yearly for necessity, as recurrences often decrease over time.[7]

Most persons with genital HSV remain undiagnosed and have mild or unrecognized infections, shedding virus intermittently. Most HSV transmission occurs via persons

unaware of their infection. Thus, management must include counseling regarding the chronic nature of disease and the concept of asymptomatic shedding, rather than focusing solely on treating symptomatic episodes. The psychological effect of HSV infection can be substantial for patients. Strategies for HSV prevention in discordant couples include barrier methods (condoms), antivirals (for treatment and/or suppression), and avoidance of intercourse during symptomatic episodes. Disclosure can have a significant impact on disease acquisition. In a study of HSV1- and HSV2-infected patients aged 15 to 58 years (median, 26 years), those whose partners informed them that they had herpes had up to one-half of the risk of acquiring herpes compared with those with partners who did not inform them.[63]

HUMAN PAPILLOMAVIRUS INFECTIONS

Genital HPV is the most common STI in the United States and worldwide.[1,64] One-half of new infections occur in those 15 to 24 years of age, and 75% to 80% of sexually active adults will acquire genital tract HPV infection before the age of 50 years. Of note, 1 in 5 females with only 1 lifetime sexual partner has been infected with high-risk HPV.[1]

Clinical Manifestations

Although most infections are self-limited and/or asymptomatic, persistent infection can cause cervical cancer in females, as well as anogenital and oropharyngeal cancer, anogenital warts (AGW), and recurrent respiratory papillomatosis in males, females, and children. There are approximately 40 types of genital HPV, which can be categorized by their epidemiologic association with cervical cancer; the high-risk types are oncogenic while the low-risk types are primarily responsible for AGW.[65]

Diagnosis and Screening

Diagnosis of AGW is usually clinical. Acetic acid application is not a specific test for HPV infection. Therefore, the routine use of this procedure for screening to detect mucosal changes attributed to HPV infection is not recommended.[7] Routine cervical cancer screening should be performed in females 21 to 65 years and Pap testing every 3 years in those 21 to 29 years. HPV testing is never appropriate in any female younger than 21 years of age or in males, and should not be done as a screening test before vaccination, for STI screening, or for diagnosis of AGW.[66]

Treatment and Management

Recommended treatments for AGW are outlined in **Table 1**. There is no "best" or curative therapy and all have potential side effects and high recurrence rates, even with repeated therapy (20%–50% by 6 months).[7] The type of therapy is dictated by multiple factors including provider experience, patient preference and ability, size/number/location of warts, potential side effects, availability and expense. Although 10% to 30% of AGW may resolve on their own, persistent lesions can cause irritation and bleeding during intercourse, because lesions are typically friable. The removal of AGW likely reduces but is unlikely to completely eradicate infectivity.[7]

A diagnosis of AGW is not indicative of a partner's infidelity and it is unknown how long HPV remains contagious after treatment. Asymptomatic partners of patients with AGW do not need to be tested for HPV, and patients do not necessarily need to inform their future sex partners about a prior history of AGW, because this may not benefit the health of those partners.

Vaccination

The Advisory Committee on Immunization Practices now recommends immunization with HPV9. HPV9 is licensed for females 9 to 26 years of age. Although HPV9 is only licensed for males 9 to 15 years, the Advisory Committee on Immunization Practices has reviewed available bridging data and recommends HPV9 for all ages where HPV4 vaccine is recommended, including a routine vaccine for 13- to 21-year-old males and for 22- to 26-year-old MSM and HIV+ males and a permissive recommendation for other 22- to 26-year-old males. See Chapter 3 on the HPV Vaccine Update.

EMERGING ISSUES: *MYCOPLASMA GENITALIUM* INFECTIONS

Clinical Manifestations

M genitalium was first isolated in 1981 from urethral specimens of males with nongonococcal urethritis.[67] It is more common than gonorrhea but less common than chlamydia; similar to other STIs, prevalence varies based on the population studied.[7] In studies including young adults 18 to 24 years of age, *M genitalium* has been identified in approximately 15% to 20% of nongonococcal urethritis, 20% to 25% of nonchlamydial nongonococcal urethritis, and approximately 30% of persistent or recurrent urethritis cases.[68–71] It is unknown if *M genitalium* causes infertility or other anogenital tract disease besides urethritis in males; it can also be found in the rectum in asymptomatic males.

M genitalium's pathogenic role is less definitive in female reproductive tract disease because it can be found in the vagina, cervix, and endometrium of asymptomatic females. It has also been detected in 10% to 30% of clinical cervicitis cases.[72–78] Evidence suggests that *M genitalium* can cause PID, but less frequently than *C trachomatis*.[79,80]

Diagnosis and Screening

There is currently no FDA-approved diagnostic test for *M genitalium*, although many commercial laboratories have developed their own CLIA-certified PCR tests. Hologic, Inc (formerly Gen-Probe) recently launched its APTIMA *M genitalium* TMA assay and it is commercially available as an analyte-specific reagent platform.[81] Although FDA approval is pending, laboratories may obtain CLIA approval to use it as part of the APTIMA platform if they already use APTIMA NAATs (which are currently available for chlamydia, gonorrhea, and trichomoniasis testing). Clinicians are encouraged to contact their laboratories for information regarding availability of this assay.

Treatment and Management

In the absence of widely available testing, clinicians should consider treatment for *M genitalium* in cases of persistent or recurrent urethritis, cervicitis or PID unresponsive to standard empiric STI syndromic therapy. *M genitalium* lacks a cell wall; thus, antibiotics that target cell-wall biosynthesis, such as penicillins and cephalosporins, are ineffective. Cure rates with doxycycline range from 30% to 45% and for azithromycin, 40% to 87%.[25,26,82] The current recommended regimen is azithromycin 1 g orally once; however, there are emerging data regarding *M genitalium* azithromycin resistance. For suspected azithromycin treatment failures, clinicians may consider treatment with moxifloxacin 400 mg orally once daily for 7 to 14 days based on cure rates of 100% in initial reports.[83,84] Of note, data from Japan, Australia, and the United States show moxifloxacin treatment failures in some cases after the 7-day regimen.[85–88]

EMERGING ISSUES: HEPATITIS C INFECTIONS

Hepatitis C virus (HCV) is not efficiently transmitted sexually except in those with HIV. Incidence has been increasing in HIV+ MSM in the United States and Europe.[7] In the United States, a significant increase in new HCV infections, including in adolescents, has been noted concurrently with the drug use epidemic. In 2013, among all age groups, those aged 20 to 29 years had the highest rate (2.01 cases per 100,000 population) of acute disease.[1]

Clinical Manifestations

Those with acute HCV are usually asymptomatic or have mild symptoms. Chronic HCV develops in 70% to 85% of these patients and 60% to 70% of those with chronic disease develop active hepatitis. Chronic HCV may progress to cirrhosis and hepatocellular carcinoma.[7]

Diagnosis and Screening

The CDC and the USPSTF recommend HCV screening for those born between 1945 and 1965, with past or current injection or intranasal drug use, receiving a blood transfusion before 1992, on long-term hemodialysis, born to a mother with HCV infection, with an unregulated tattoo, or other related exposures. It is also now recommended to perform at least annual HCV screening for MSM because sexual transmission of HCV can occur, especially among MSM with HIV infection. An FDA-cleared HCV antibody test should be used first (ie, immunoassay, enzyme immunoassay) followed by NAAT if results are positive. Of note, antibody false negativity can occur in HIV-positive patients with a low CD4 counts and NAAT is particularly important in those cases.[7]

Treatment and Management

Any patient with positive HCV testing should be evaluated by specialists (typically infectious diseases physicians and/or gastroenterologists) for counseling and management. Therapy is available for HCV disease and can be curative. Vaccination against hepatitis A and B is also recommended. Specific recommendations for HCV management and treatment are available from the American Association for the Study of Liver Diseases and the Infectious Disease Society of America.[89]

SPECIAL POPULATIONS: MEN WHO HAVE SEX WITH MEN, WOMEN WHO HAVE SEX WITH WOMEN, AND TRANSGENDER INDIVIDUALS

Men Who Have Sex with Men

Recommendations for routine annual HIV screening, syphilis serologic testing, and chlamydia and gonorrhea screening remain unchanged for MSM based on most current guidelines. More frequent STI screening (ie, for syphilis, gonorrhea, and chlamydia) at 3- to 6-month intervals is indicated for MSM, including those with HIV infection, if risk behaviors persist in patients or their partners.

Studies in the 1980s and 1990s have shown increases in oral sex among heterosexual individuals, MSM, and adolescents.[90–93] In MSM, there was a decline in anal intercourse as a response to the HIV epidemic and studies show that recent sexual contacts reported by MSM are more likely to be orogenital or non–ano-penetrative.[94] Thus, it is critical to obtain a careful history about the type of sex (eg, oral, anal, or vaginal) and screen for STIs at all potentially exposed sites using NAAT testing to optimize sensitivity and specificity.

Women Who Have Sex With Women

Adolescent WSW may be at increased risk for STI and HIV acquisition based on reported risk factors.[95–99] Risk varies by the specific STI and sexual practice[100,101] and reported sexual identity does not always reflect sexual behavior. Studies show that 53% to 97% of self-identified WSW describe having male sexual contact in the past, and up to 28% have had male partners within the past year.[102–104] Thus, clinicians should ask about specific sex practices and partner types to identify the most appropriate screening types, modalities and sites for their patients.

WSW are at risk for acquiring HPV from partners of both sexes and should be offered routine cervical cancer screening and HPV vaccine as per current guidelines.[105] Transmission of HSV2 is inefficient in WSW, but they remain at risk for acquisition of both HSV2 and HSV1.[103,104] Transmission of bacterial infections between female partners, including syphilis, chlamydia, and bacterial vaginosis, is less clear. Bacterial vaginosis is generally common in women and especially in those with female partners,[106,107] but routine screening and partner therapy for such in WSW are not recommended at this time.

Transgender Individuals

Those who are transgender express a gender identity differing from the one corresponding with sex assignment at birth. In general, transgender women have a higher HIV prevalence compared with transgender men, but specific differences in other STIs have not yet been identified.[7] Clinicians should assess STI and HIV-related risks for their transgender patients based on current anatomy and specific sexual practices to determine the most appropriate screening.

SPECIAL ISSUES: EXPEDITED PARTNER THERAPY AND PREEXPOSURE PROPHYLAXIS

Expedited Partner Therapy

Expedited partner therapy (EPT) is the clinical practice of treating the sex partners of patients diagnosed with chlamydia or gonorrhea by providing prescriptions or medications to the patient to take to his/her partner without the health care provider first examining the partner. EPT is legal in most states but varies by type of STI authorized.[7] Information regarding state-specific EPT laws can be found on the CDC website (available: http://www.cdc.gov/std/ept/). The US EPT trials and a metaanalysis in females 14 years and older and males 16 years and older have shown reduced reinfection rates compared with patient referral strategies; across trials, reductions in chlamydia and gonorrhea prevalence at follow-up were 20% and 50%, respectively.[108–111] Several national organizations, including the AAP, endorse EPT use as a strategy to improve treatment and prevent reinfection in adolescents and young adults.[112–115]

Preexposure Prophylaxis for Human Immunodeficiency Virus Infection

HIV preexposure prophylaxis (PrEP) is the preventive use of daily oral antiretroviral therapy with a combination of tenofovir disoproxil fumarate and emtricitabine in HIV-negative patients at high risk for HIV acquisition. Although PrEP has been FDA approved in adults[116,117] and the CDC PrEP guidance targets this population,[118–120] the combination of tenofovir disoproxil fumarate and emtricitabine may be used off-label in those under 18 years of age. PrEP has been shown to be effective in reducing new HIV infections by 44% to 75% in adult MSM, heterosexuals, and injection drug users taking daily PrEP.[121–124] PrEP has also been found to be an acceptable and feasible intervention in young MSM.[125,126] Ongoing studies of PrEP in persons less than 18 years of age may lead to a PrEP indication in younger adolescents in the

near future.[127] Barriers may exist to PrEP access, including parental consent requirement[128] and potential cost. PrEP may be paid for via Medicaid, participation in clinical trials, or industry-sponsored patient assistance programs.

SUMMARY

Adolescents are in a unique period of psychosocial and biologic development, placing them at high risk for STI acquisition and transmission. Some STIs are more prevalent among adolescents and young adults than among older men and women. Unfortunately, many providers who care for adolescents fail to discuss sexuality, even at health maintenance visits. Primary care visits present opportunities to educate adolescents on sexual health and development, to promote healthy relationships and to discuss prevention of STIs and HIV. (See Chapter 1 on Interviewing Adolescents about Sexual Matters). A confidential sexual history and STI screening are essential components of routine care for adolescents and young adults and updated guidelines should be used to guide prevention, screening, diagnosis, and management of STIs in this age group.

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