Chapter 6
Sexually Transmitted Infections

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Contents

Introduction

Sexually transmitted infections (STIs) are common infections, especially in adolescents and young adults. Primary care clinicians play an important role in the diagnosis and treatment of STIs, with approximately 22–33% of these infections diagnosed in primary care settings [1]. Depending upon proposed cuts to federally funded family planning clinics, [2] the role of the primary care clinicians could become even more important in the coming years. Thus, having a basic understanding of prevention, screening, diagnoses, and treatment of STIs is important for all primary care clinicians to have.

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This chapter will review the prevention, diagnosis, and treatment of STIs in non-pregnant, immunocompetent adults. An approach to the prevention, diagnosis, and treatment of STIs in adolescent patients can be found in Chap. 2. The prevention and diagnosis of HIV will be discussed, including the role or pre-exposure prophylaxis for HIV; however, the treatment of HIV and prevention of vertical transmission will not. The chapter is divided into three main sections: common STIs in the United States; uncommon STIs in the United States; and an emerging STI—*Mycoplasma genitalium*.

Prevention

Effective counseling on prevention of STIs is dependent on obtaining an accurate sexual history with particular attention to sexual practices. Inclusive approaches to sexual history are presented in Part 1 of this book.

Condoms offer effective prevention from STIs, especially infections transmitted by genital secretions such as gonorrhea, chlamydia, trichomonas, and HIV. The true efficacy of condoms is not known due to the reliance on observational studies with self-reported condom use. Condoms are less effective for the prevention of infections such as herpes simplex virus (HSV) and the human papillomavirus (HPV) due to the transmission being largely through skin-to-skin contact for these infections [3].

Other forms of barrier protection are often overlooked, especially when discussing sexual practices with women who have sex with women (WSW). Female condoms [4], dental dams [5], gloves during digital genital stimulation, and covers/condoms with sex toys [6] can all help prevent STI transmission.

The use of medications for prevention, where appropriate, is discussed under each disease heading.

Common Sexually Transmitted Infections in the United States

Chlamydia and Gonorrhea

Epidemiology Chlamydia is the most common reportable infection in the United States, and rates of new chlamydia infections have been increasing since at least 2000 with young women being the most commonly affected population. Although increased testing is likely part of the explanation, most experts also feel there has been an increase in actual infections. The case rate in 2016 in the United States among females was 657.3 per 100,000, and among men, it was 330.5 per 100,000 [1].

Rates of gonorrhea have also been increasing since 2009, with the greatest increases being seen in men. Similar to chlamydia, the increased rates of gonorrhea

may in part be explained by increased testing, but most experts feel there has been an increase in the actual number of infections. The case rate in 2016 in the United States among men was 170.7 per 100,000 and 121.0 per 100,000 among women [1].

Clinical Presentation Chlamydia infection is most often asymptomatic with between 84.8% and 92.9% of women reporting no symptoms and between 94.1% and 98.2% of men reporting no symptoms in one large study. For gonorrhea between 84.2% and 88.5% of women and between 86.4% and 92.6% of men reported no symptoms in the same study [7]. Cervical and urethral discharge is the most common symptom in women and men, respectively. Discharge and pain can be present rectally and orally when infections are present at these sites. Systemic manifestations including disseminated infection, septic arthritis (gonorrhea), perihepatitis, and conjunctivitis (chlamydia) are also seen but are beyond the scope of this chapter.

Screening and Testing The United States Preventive Services Task Force (USPSTF), the Centers for Disease Control (CDC), the American Academy of Family Physicians (AAFP), and the Canadian Health Agency all recommend screening sexually active women under the age of 25 and women over the age of 25 with any risk factors [8]. Neither the USPSTF nor the AAFP recommend screening in men; however, the CDC recommends screening men who are at risk, and the Canadian Health Agency recommend screening men under the age of 25 [8, 9]. Questions about sexual activity should be included as part of routine care, and men with any concerns or at high risk should be offered routine screening.

Testing is done using nucleic acid amplification tests (NAATs). In women a vaginal swab is preferred, and first catch urine is considered an acceptable alternative. In men a first catch urine is the preferred test [10].

Extragenital testing should also be offered to any persons reporting receptive oral or anal intercourse. In one study of men who have sex with men (MSM) and women who reported a history of receptive anal intercourse (RAI), over 75% of infections were found only extragenitally in men, and over 15% were found only extragenitally in women [11]. A study of self-identified gay and bisexual men looking urinary samples and anal swabs found gonorrhea and chlamydia threefold more often rectally than in urine samples [12]. Extragenital testing is done using the same NAAT swabs but is not validated in all labs and thus may not yet be available in some labs.

Treatment Treatment of chlamydia and gonorrhea in adults with genitourinary, oral, or rectal infections has recently been updated [13] and is shown in Tables 6.1 and 6.2.

Follow-Up Test-of-cure follow-up testing is not recommended for either gonorrhea or chlamydia that is treated with recommended regimens. Most follow-up testing that is positive is felt to be new infections. Additionally tests done within the first few weeks after treatment may be false positives due to the extreme sensitivity of NAAT testing.

Table 6.1 Treatment of genitourinary, oral, and rectal chlamydia infections (Ref. [10])

Recommended regimens
Non-Pregnant Adults: Doxycycline 100 mg orally twice a day for 7 days Pregnant Adults: Azithromycin 1 gram orally as a single dose
Alternative regimens
Erythromycin base 500 mg orally four times a day for 7 days OR Erythromycin succinate 800 mg orally four times a day for 7 days OR Levofloxacin 500 mg orally once daily for 7 days OR Ofloxacin 300 mg twice a day for 7 days

Table 6.2 Treatment for genitourinary, oral, and rectal gonorrhea infections (Ref. [10])

Recommended regimen
Ceftriaxone 500 mg IM in a single dose
Alternative regimen
Cefixime 800 mg orally as a single dose PLUS Azithromycin 1 gram orally as a single dose

Treatment of Sex Partners Both chlamydia and gonorrhea are reportable conditions, and the laboratories that do the testing should notify their respective State Health Departments. Sexual partners in the last 60 days and the last potential exposure if the last sexual encounter was more than 60 days ago should be referred for counseling, testing, and treatment. Persons should abstain from sex for at least 7 days after receiving treatment. If there are concerns about sexual partners getting in for testing and treatment, expedited partner therapy (EPT) can be given in most states (for a list of states where EPT is legal, go to https://www.cdc.gov/STI/ept/legal/default.htm). EPT involves either prescribing for the partner or providing the patient with a prescription for the partner (doxycycline 100 mg orally twice daily for 7 days for chlamydia and cefixime 800 mg as a single dose for gonorrhea) [13]. The CDC does not recommend the routine use of EPT for MSM due to a higher risk of other STIs such as HIV that may be missed with EPT [14]. However, each patient should be assessed individually, and there are situations where EPT can be appropriate for MSM.

Trichomonas

Epidemiology It is estimated that there are over a one million new infections caused by *Trichomonas vaginalis* in the United States annually [15] with self-identified heterosexual Black women being the most heavily affected population. Of note, any such observations regarding racial inequities should be interpreted as a manifestation of social and structural forces, not biological differences between races, and the application of these data individualized to each patient or community.

Clinical Presentation Seventy to eighty-five percent of persons may be asymptomatic. Women may present with vaginal discharge that may be malodorous and have associated vulvar irritation. Men may present with urethritis, epididymitis, or prostatitis [14]. Infection may last for years, and it is estimated that prevalence may be 3 – 4fold greater than the incidence of disease [14, 15].

Screening and Testing NAAT is considered is the preferred method of detecting trichomonas. In women vaginal swabs and urine testing are considered equally sensitive (95.3–100%) and specific (95.2–100%, Ref. 14). Recently NAAT has also been found to have a sensitivity 97.2% and a specificity of 99.9% in male urine samples [16]. Wet mount microscopy can be a rapid way to diagnose trichomonas and is available in many clinics but suffers from poor sensitivity (51–65%) compared to NAAT [14].

Treatment Treatment is with metronidazole or tinidazole, both 2 grams orally as a single dose. Metronidazole 500 mg orally twice daily for 7 days is an alternative.

Follow-Up Follow-up test of cure is recommended by the CDC due to high rates of reinfections and emerging resistance to metronidazole (4–10%). Retesting with NAAT can be done within 2 weeks of completing therapy [14].

Treatment of Sex Partners All sex partners should be treated as well with the same regimens used for patients. Patients and their partners should abstain from sex until both have been treated and symptoms have resolved [14].

Syphilis

Epidemiology The rates of primary and secondary (P & S) syphilis (i.e., new infections) have been increasing every year since about 2000 when they were at an all-time low. In 2016 the rate among men was 15.6 per 100,000 and 1.9 per 100,000 among women. During most of this time, the increase has largely been in MSM; however, starting in 2013 rates in women also started to increase. Congenital syphilis cases tend to rise when rates in women increase, and indeed rates of congenital syphilis have increased from 8.4 per 100,000 in 2012 to 15.7 per 100,000 in 2016 [1].

Clinical Presentation Syphilis is often called the great masquerader and can present with protean manifestations. The most common presentation of primary syphilis is a clean based, painless ulcer at the infection site. For secondary syphilis a rash, often involving the palms and soles of the feet is the most common symptom. A discussion of all the manifestations of secondary and tertiary syphilis is beyond the scope of this chapter. However, anyone with unexplained symptoms and risk factors for syphilis should be tested [14]. The CDC website offers a concise discussion of the presentation of syphilis in its various stages (https://www.cdc.gov/STI/syphilis/

STIfact-syphilis-detailed.htm) along with images of its various manifestations (https://phil.cdc.gov/QuickSearch.aspx).

Screening and Testing Screening is recommended in HIV positive men and MSM with intervals as often as every 3 months for persons with multiple sexual partners [17]. It is also the opinion of the author that any person requesting STI testing should be offered syphilis screening.

In the primary care setting, testing for syphilis is generally done using serologic testing. Two sets of serologic tests are available, treponemal (TPPA, FTA-ABS) and non-treponemal tests (RPR, VRDL). Neither test alone is sufficient to diagnosis syphilis [14]. Characteristics of the tests are shown in Table 6.3. Although the reported specificity of both tests is high [17, 18], there is no gold standard to truly base this on, and false positives are more commonly reported with non-treponemal tests. Most centers today first perform a treponemal test (i.e., TPPA) and if this is positive will reflex to a non-treponemal test (i.e., RPR). Interpretation of testing is often confusing for providers without a lot of experience, and Table 6.4 offers interpretations of the most common scenarios seen in primary care.

Treatment Penicillin is the preferred treatment for all stages of syphilis. Treatments for syphilis are shown in Table 6.5 and are based on CDC guidelines [14]. According to the CDC, secondary syphilis can be treated the same as primary and early latent syphilis (infection of less than 1 year's duration); however, given the frequent uncertainty in the staging of syphilis, consideration should be made to treat with three injections of benzathine penicillin. Thus, the recommended treatment can be separated into three clinical scenarios. (1) Infection of less than 1 year should be treated with benzathine penicillin 2.4 million units one time. (2) Infection that is of unknown duration or more than 1 year's duration but does not involve the central nervous

Table 6.3 Characteristics of serologic tests for syphilis (Ref. [10, 14, 15])

	Treponemal	Non-treponemal
Test names	TPPA, FTA-AB	RPR, VDRL
Antigens tested	*Treponemal pallidum*	Cardiolipin, cholesterol, lecithin
Remains positive after treatment	Yes	Not usually. Should decline and hopefully become undetectable with therapy
Can be used to follow response to therapy	No	Yes, titer should drop with therapy. A fourfold or greater drop is considered an appropriate response
Sensitivity		
Primary Secondary Latent Late	84–88% 100% 97–100% 94–96%	78–86% 100% 96–98% 71–73%
Specificity	96–97%	98% False positive seen in autoimmune diseases, HIV, pregnancy, intravenous drug abuse

Table 6.4 Interpretation of syphilis tests

Clinical scenario	Treponemal test (TPPA, FTA-AB)	Non-treponemal test (RPR, VDRL)	Interpretation
Asymptomatic screening	Positive	Negative	In most cases, this represents previously treated syphilis. However, this scenario could be seen in late disease, and confirmation of prior treatment is essential
Asymptomatic screening	Positive	Positive with a titer of 1:2 or greater	In most cases this means active disease and treatment are indicated. However, this could also be seen in someone with prior disease that has been treated. If a fourfold drop in the titer is documented from pre-treatment levels, this may indicate an appropriate response to therapy and not active disease
Symptomatic testing	Positive	Positive with a titer of 1:2 or greater	This indicates active disease. Unless documentation of a fourfold drop in titer with prior treatment and a good alternative for patients symptoms is available, treatment is indicated
Symptomatic testing or asymptomatic screening	Negative	Positive with a titer or 1:2 or greater	This usually indicates a false positive non-treponemal test. This scenario is less common today due to most laboratories doing the treponemal assay first and only doing the non-treponemal test if that is positive

Table 6.5 Treatment of syphilis (Ref. [10])

Clinical scenario	Treatment
Primary syphilis or disease of less than 1 year's duration (i.e., prior screening test done less than a year ago was negative)	Benzathine penicillin G 2.4 million units IM in a single dose ALTERNATIVES Doxycycline 100 mg orally twice daily x 14 days OR Ceftriaxone 1–2 grams IM or IV for 10–14 days
Disease duration unknown or greater than 1 year, but not neurosyphilis	Benzathine penicillin G 2.4 million units IM × 3 doses, each a week apart ALTERNATIVE Doxycycline 100 mg orally twice daily × 28 days
Neurosyphilis	Aqueous crystalline penicillin 3–4 million units every 4 hours or 18–24 million units as a continuous drip for 10–14 days. ALTERNATIVES Procaine penicillin G 2.4 million units IM daily for 10–14 days PLUS Probenecid 500 mg orally four times daily for the same duration OR Ceftriaxone 2 grams IM or IV daily for 10–14 days

system (CNS) should be treated with three injections, each a week apart of benzathine penicillin 2.4 million units each. (3) Neurosyphilis should be treated with IV penicillin 3–four million units every 4 hours and usually requires hospital admission to at least begin therapy (Table 6.5).

Follow-Up All persons with syphilis require close follow-up to assess response to therapy. The non-treponemal (RPR or VDRL) titer should be followed, with a response to therapy considered a fourfold or greater drop in the titer (i.e., 1:16 drops to 1:4), although ideally these titers become undetectable. In some patients these titers will not drop, and in those cases they should be evaluated for possible undertreated syphilis, and consideration should be given to getting a lumbar puncture (LP) if not done as part of the initial work-up. However, in many cases these patients are what's known as serofast. The serofast state is when the titers do not drop despite appropriate therapy and represent the imperfection of antibody-based tests [14].

Treatment of Sex Partners Syphilis is only considered transmittable during the primary and secondary stages. Persons who have had sexual contact with the patient in the last 90 days during either of these stages should be tested and then treated presumptively for syphilis. Persons who have had a sexual exposure with the patient within the first year of infection should be tested, and consideration should be given to presumptive treatment. Long-term sexual partners should be tested and treated based on the results of testing [14].

Genital Herpes Simplex Virus (HSV)

Epidemiology Approximately 50 million Americans are infected with HSV-2, the most common cause of genital ulcers in the United States. Although HSV-1 is more commonly associated with oral mucosal ulcers, it can also cause genital ulcers [14].

Clinical Presentation HSV usually presents as painful blistering ulcer on an erythematous base. Infection is generally self-limited in the absence of immune compromising conditions. HSV is a lifelong infection and can recur throughout a person's life, although many patients may only have one episode in their life.

Screening and Testing Routine screening for HSV is not recommended. Testing in patients with symptoms is done with either viral culture or more commonly polymerase chain reaction (PCR) of active lesions [14].

Treatment Acyclovir, valacyclovir, and famciclovir can all be used to treat herpes infections. Various dosing regimens can be used; common ones are shown in Table 6.6. For outbreaks treatment is most likely to be beneficial if started within the first 24 hours of lesion appearance and will shorten the duration of illness by 1–2 days. For persons with HIV or who may be immunecompromised, higher dos-

Table 6.6 Treatment for genitourinary herpes simplex infections. Other dosing regimens are available (Ref. [10])

Drug (duration of therapy)	Primary infection (7–10 days)	Recurrent infection (5 days)	Chronic suppressive therapy (indefinite)
Acyclovir	400 mg thrice a day	400 mg thrice a day	400 mg twice a day
Valacyclovir	1 gram twice a day	1 gram daily	1 gram daily
Famciclovir	250 mg thrice a day	125 mg twice a day	250 mg twice a day

ages and longer treatment durations should be considered [14]. Daily suppressive therapy can be given for patients with recurrent infections. The decision of when it is appropriate to do this relies on patient preference and shared decision-making. Factors such as how bothersome they find the outbreaks, the likelihood of transmission to a partner, and their feelings about daily medication should all be considered.

Follow-Up Follow-up is not required for HSV although patients should be told to contact their provider if symptoms fail to improve.

Treatment of Sex Partners Treatment of sex partners is not required. Suppressive therapy for persons who are concerned about transmitting the virus to a partner can be given. Serologic testing of the partner to see if they have already been infected is reasonable in this setting.

Human Papillomavirus (HPV)

Epidemiology Human papillomavirus is the most common STI in the United States [15], and most sexually active persons will become infected at least once in their lifetime [14].

Clinical Presentation Most of these infections are asymptomatic and clear on their own, but persistent infection can lead to genital warts and cancer depending upon the serotype present. Most cervical, vulvar, vaginal, penile, anal and oropharyngeal cancers are caused by HPV [14]. There are more than 200 serotypes of HPV that can infect humans with 12 serotypes that are associated with human cancers (16,18,31,33,35,39,45,51,52,56,58,59) (Ref. 19).

Screening and Testing It is well agreed that screening for cervical cancer with cervical cytology decreases the incidence and mortality from cervical cancer [20]. Since the initiation of pap smear screening of women, mortality from cervical cancer has dropped almost fivefold [20]. Cervical cancer screening for average risk

patients is covered in more detail in Part 1 of this book. Screening for other forms of HPV-related cancer is more controversial. The HIV Medical Association recommends anal pap smears for HIV-positive MSM, women with a history or receptive anal intercourse or abnormal pap smears, and anyone with genital warts [21]. There are currently no guidelines that recommend anal cancer screening in HIV-negative individuals who have receptive anal intercourse. Despite this, many providers feel anal paps should be offered to any individuals at risk for HPV-related anal cancer. Anal paps can be done by inserting a moistened polyester fiber swab into the anal canal and turning several times and then sending the swab for cytology. No other extragenital screening for HPV and or its manifestations is currently recommended.

Treatment and Prevention There is no available therapy to treat the HPV. When abnormalities are noted on cervical cytology, women should generally be referred for colposcopy. Patients with abnormal cytology on anal pap smears should generally be referred for high resolution anoscopy (HRA) which is analogous to colposcopy of the rectum. HRA is not available at all centers, further complicating the question of screening for anal cancer.

There are three licensed vaccines to prevent HPV, but currently only the nine-valent vaccine is available in the United States. The vaccine appears to be greater than 96.0% effective in preventing HPV-related infection from the strains included in the vaccine. The nine valent offers protection against serotypes 16, 18 (which cause the majority of HPV-related cancers), 31, 33, 45, 52, and 58 (together these 7 strains cause 75% or more of HPV-related cancers). It also offers protection against serotypes 6 and 11 that are responsible for 90% of genital warts [22]. The vaccine can be given as a two shot series for girls and boys between the ages 9 and 14. For persons ages 15–26, it is recommended as a three-shot series [23].

Human Immunodeficiency Virus (HIV)

This section will focus on screening and testing for HIV, along with prevention through pre-exposure prophylaxis (PrEP). The treatment of HIV and the use of antiretrovirals to prevent vertical transmission of HIV are beyond the scope of this book.

Epidemiology There are approximately 1.1 million people over the age of 13 with HIV in the United States, with an estimated 37,600 new infections in 2014. The number of new infections has declined since 2008 when there were 45,700 new infections [24].

Screening and Testing HIV screening is recommended for all persons age 15–65 at least once. Persons younger and older than this should also be screened if risks for HIV are identified. Persons at high risk for HIV, such persons reporting unprotected vaginal or anal intercourse with more than one partner, persons who use

injection drugs, and persons who report sex with HIV-positive partners or exchanging sex for money or drugs, should be screened annually or more often depending upon provider judgement of risks [25]. Most laboratories now use a fourth or fifth generation assay for HIV that combines both antibody detection as well as detection of the HIV p24 antigen. Such infection can usually be detected 11–14 days after infection [26]. If there is concern that an infection may be more recent than 14 days, HIV quantitative PCR testing can be ordered. If all of this is negative and concern remains high, testing should be repeated in 4 weeks.

Pre-exposure Prophylaxis (PrEP) PrEP consists of taking one tablet of the fixed-dose formulation Truvada (tenofovir disoproxil fumarate and emtricitabine) daily to prevent HIV. Truvada has been a part of many HIV treatment regimens since its approval in 2004. Eight randomized control trials have been performed evaluating the efficacy of PrEP [27–34]. In the five trials with the highest-risk patients, the number of persons that would need to be treated for a year to prevent one case of HIV (NNT) was between 12.8 and 52.6 [27, 28, 30, 33, 34]. Most cases in which persons on PrEP have acquired HIV are thought to be due to poor adherence to the study medication. However, recently a case of transmission despite good adherence and absence of drug resistance mutations has been documented [35], highlighting the continued importance of condoms and limiting the numbers sexual partners.

In the PrEP trials, the following side effects were more common in patients given Truvada: nausea and/or vomiting [27, 29–31, 33], an elevation in creatinine [32, 33], and grade 1 or 2 ALT elevation [31]. None of these differences were noted in all studies, and discontinuation of Truvada due to toxicity was rare. Only one study assessed the effect on bone mineral density, and this study did show a greater decrease in patients on Truvada [30].

Target Population PrEP should be considered for HIV negative men and women who are sexually active and may have sex with someone who is or may be HIV-positive, as well as persons who use intravenous drugs and may share their drug paraphernalia. The epidemiology of HIV suggests MSM are at the greatest risk. However, before PrEP is prescribed, a detailed sexual history should be obtained. A man who only engages in oral sex is unlikely to benefit from PrEP, whereas a man who has receptive and/or insertive anal intercourse without condoms, with multiple different partners, clearly could. Individuals with opposite sex partners may also benefit from PrEP if they are having sex with HIV-positive persons or persons of unknown HIV status. Because many variables play into a person's risk of contracting HIV, an online risk calculator has been developed [36] that may helpful in some situations when either the patient or the provider are unsure about starting PrEP (https://prephere.org/). Further, unless contraindications exist, PrEP should generally be considered for any patient who requests it, regardless of the sexual practices that individual is comfortable sharing with the clinician. The CDC estimates the number of people in the United States who could qualify for PrEP to be about 1.2 million [37].

Monitoring Recommended laboratory testing and monitoring for PrEP is shown in Table 6.7. Hepatitis B testing should be included as part of baseline testing. The

Table 6.7 Laboratory testing for pre-exposure prophylaxis (PrEP) with Truvada

Test	Baseline	Every 3–6 months
HIV Ag/Ab	Yes	Yes
HIV pcr	If concern for acute infection within the last 14 days. See text	If concern for acute infection within the last 14 days. See text
Renal function	Yes	Yes
Hepatitis B sAg, sAb	Yes	Depends on results of baseline testing[a]
Gonorrhea and chlamydia testing[b]	Yes	Offer

[a]See text
[b]Consider extragenital testing if patient report any history of receptive anal intercourse or receptive oral sex

reason for this is that both medications in Truvada have activity against hepatitis B. If a person has active hepatitis B, the Truvada will suppress its replication but not cure the infection. If the Truvada is stopped after a prolonged period of time, there can be recurrence similar to acute hepatitis B. Any person who is not immune to hepatitis B at baseline should be vaccinated. Patients should be seen every 3–6 months, and testing for HIV and renal function should be repeated. Providers should have a very low threshold for testing for other STIs at these follow-up visits Guidelines have recently been updated to recommend HIV pcr testing along with HIV Ag/Ab testing at each visit [38].

On-demand PrEP For individuals who are sexually active on an intermittent basis and can reliably predict when they will be sexually active, on-demand PrEP may be an option. On-demand PrEP has been evaluated in a randomized control trial and was found to be efficacious, with a number need to treat (NNT) of 17.6. In this study patients took two Truvada tablets with food 2–24 hours before sex, a third tablet 24 hours after the first tablets, and a forth tablet 24 hours later [34]. On-demand PrEP has an A1a recommendation (highest recommendation) from the International Antiviral Society—USA Panel (IAS-USA) and should be considered an option for persons who are intermittently sexually active [39].

Newer Options for PrEP Descovy (Tenofovir alafenamide and emtricitabine) has recently been approved for PrEP [40]. Descovy is very similar to Truvada but has a better safety profile with regard to kidney function and bone density [41]. Descovy has not been studied for on-demand PrEP. Cabotegravir is a long-acting antiretroviral that can be injected every 2 months and was approved in December 2021. Cabotegravir has been shown to be more effective in preventing HIV among MSM, transgender women and heterosexual women than Truvada [42, 43]. Traditional PrEP with Truvada failed to show benefit in heterosexual women [29, 30], thus the dramatic benefits of Cabotegravir are very exciting [43].

Rare Sexually Transmitted Infections in the United States

Chancroid

Epidemiology Chancroid is caused by *Haemophilus ducreyi* and is rare in the United States. Prevalence has declined in both the United States and the world; however, due the difficulty in culturing this organism, it's true prevalence may be underreported [1, 14].

Clinical Presentation The presence of a painful genital ulcer and tender, suppurative inguinal lymphadenopathy should raise suspicion for Chancroid.

Diagnosis Culturing of *H. ducreyi* requires special media that may not be available in all labs. A clinical diagnosis of chancroid can be made if the above clinical scenario is met and the patient tests negative for both syphilis and HSV.

Treatment Treatment for chancroid is shown in Table 6.8. All sex partners of the patient should be examined, and anyone with symptoms OR who has had sex with the patient within 10 days of symptom onset should be treated [14].

Lymphogranuloma Venereum (LGV)

Epidemiology Lymphogranuloma venereum is caused by *Chlamydia trachomatis*, serovars L1, L2, or L3. This has previously been thought to be rare disease in developed countries, but more recent studies suggest it may be more common than previously thought, especially in persons who have receptive anal intercourse [39].

Clinical Presentation Typical presentations include tender, usually unilateral, inguinal lymphadenopathy. A self-limited genital ulcer may also be present at the site of inoculation [14]. Patients who have anal receptive sex may present with proctitis and proctocolitis that can resemble inflammatory bowel disease [14, 39].

Table 6.8 Treatment for chancroid, *Haemophilus ducreyi* (Ref. [10])

Azithromycin 500 mg orally × 1
OR
Ceftriaxone 250 mg IM × 1
OR
Ciprofloxacin 500 mg orally twice a day for 3 days
OR
Erythromycin base 500 mg orally thrice a day for 7 days

Diagnosis NAAT do not distinguish between LGV-chlamydia and non-LGV-chlamydia and will be positive in both settings. Tests to distinguish between the two types of chlamydial infections have been developed but are not commercially available outside or research settings. The diagnosis of LGV is made based on proper epidemiology and clinical findings along with a positive chlamydia NAAT and the exclusion of other possible etiologies [14, 39].

Treatment Treatment of LGV is with either doxycycline 100 mg orally twice daily or erythromycin base 500 mg orally four times daily. Both should be given for 21 days. Anyone who has had sex with the patient within 60 days of symptoms onset should be examined and tested for chlamydial infection. Presumptive therapy of a sex partner, in the absence of disease manifestations, is with antichlamydial therapy (i.e., Azithromycin 1 gram orally × 1).

Granuloma Inguinale (Donovanosis)

Epidemiology Granuloma inguinale is caused by *Klebsiella granulomatis* and is rare in the United States but is endemic in some tropical and developing areas such as India, Papua New Guinea, the Caribbean, Central Australia, and Southern Africa [14].

Clinical Presentation Granuloma inguinale is characterized by painless, slowly progressive, highly vascular ulcers on the genitals and in the perineum. Lymphadenopathy is typical absent although subcutaneous granulomas may be present. Lesions can spread to involve intra-abdominal organs, bone, and the mouth. Ulcers may become superinfected [14].

Diagnosis The diagnosis is made by visualization of "Donovan bodies" on biopsy specimens. The organism is difficult to culture, and no FDA-approved molecular tests exist [14].

Treatment Treatment for granuloma inguinale is shown in Table 6.9, but data clearly demonstrating the superiority of one regimen over another are lacking [14].

Sexually Transmitted Disease Uncertainty

Mycoplasma Genitalium

Mycoplasma genitalium may be the cause of 20–25% of cases nongonococcal/non-chlamydia urethritis and perhaps as high as 30% of persistent urethritis cases [10]. Several factors make the development of clear guidelines on the diagnosis and management of this organism difficult. First is the lack of a FDA-approved test to diagnose this infection [14, 44], although non-FDA-approved tests are available in some

Table 6.9 Treatment of granuloma inguinale (donovanosis) (Ref. [10])

Recommended regimen
Azithromycin 1 gram weekly for 3 weeks and until all lesions have resolved OR Azithromycin 500 mg daily for 3 weeks and until all lesions have resolved
Alternative regimens
Doxycycline 100 mg twice daily for 3 weeks and until all lesions have resolved OR Ciprofloxacin 750 mg twice daily for 3 weeks and until all lesions have resolved OR Erythromycin base 500 mg four times daily for 3 weeks and until all lesions have resolved OR Trimethoprim/sulfamethoxazole DS (160/800) twice daily for 3 weeks and until all lesions have resolved

centers [44]. Second is the lack of a clear correlation between this infection and adverse health outcomes—although associations exist. The difficulty of isolating this organism has made studying its epidemiology difficult. Third, there is a rising rate of antibiotic resistance among isolates, but currently there is no commercially available test for resistance [44]. Currently, the CDC recommends 1 gram azithromycin one time for nongonococcal urethritis that may be due to *Mycoplasma genitalium*. If this treatment if ineffective, then a 5-day course of azithromycin (500 mg on day 1, followed by 250 mg daily for 4 days) may be more effective. If this is ineffective, then moxifloxacin 400 mg daily for 7–14 days is recommended [14, 44]. Because resistance in this organism has arisen so quickly, some authors now recommend combination therapy, although this is not part of a guideline currently [44]. Sexual partners should be tested (if available) and treated like the source patient [14, 44].

Conclusion

Sexually transmitted infections are common and contribute to significant morbidity. Up to a third of infections are diagnosed in a primary care setting [1], and primary care clinicians play a critical role in the prevention, diagnosis, and treatment. Depending upon what changes are made to healthcare coverage and funding, the role of the primary care provider is likely to only become more critical in the future.

References

1. Centers for Disease Control and Prevention. Sexually transmitted disease surveillance 2016. https://www.cdc.gov/STI/stats16/default.htm. Downloaded 3 Jan 2018.
2. Davis, JH. Trump signs law taking aim at planned parenthood funding. NY Times, April 13, 2017. https://www.nytimes.com/2017/04/13/us/politics/planned-parenthood-trump.html. Last accessed 3 Jan 2018.

3. Condoms and STIs: Fact Sheet for Public Health Personnel. https://www.cdc.gov/condomeffectiveness/docs/Condoms_and_STIS.pdf. Last accessed 8 Jan 2018.
4. Female Condom Use. https://www.cdc.gov/condomeffectiveness/Female-condom-use.html . Last accessed 5 Sept 2018.
5. Dental Dam Use. https://www.cdc.gov/condomeffectiveness/Dental-dam-use.html. Last accessed 5 Sept 2018.
6. Rowen TS, Breyer BN, Lin TC, Li CS, Robertson PA, Shindel AW. Use of barrier protection for sexual activity among women who have sex with women. Int J Gynaecol Obstet. 2013;120(1):42–5.
7. Detels R, Green AM, Klausner JD, Katzenstein D, Gaydos C, Handsfield H, et al. The incidence and correlates of symptomatic and asymptomatic chlamydia trachomatous and Neisseria gonorrhoeae infections in selected populations in five countries. Sex Transm Dis. 2011;38(6):503–9.
8. LeFevre ML, USPSTF. Screening for chlamydia and gonorrhea: U.S. preventive services task force recommendation statement. Ann Intern Med. 2014;161(12):902–10.
9. Lee KC, Ngo-Metzger Q, Wolff T, Chowdhury J, Lefevre ML, Meyers DS. Sexually transmitted infections: recommendations of the U.S. preventive services task force. Amer Fam Phy. 2016;94(11):907–15.
10. Papp JR, Schachter J, Gaydos C, Van Der Pol C. Recommendations for the laboratory-based detection of chlamydia trachomatous and Neisseria gonorrhea. MMWR. 2014;63(0):1–19.
11. Danby CS, Cosentino LA, Rabe LK, Priest CL, Damare KC, Macio IS, Meyn LA, et al. Patterns of Extragenital chlamydia and gonorrhea in women and men who have sex with men reporting a history of receptive anal intercourse. Sex Transm Dis. 2016;43(2):105–9.
12. Grov D, Cain D, Rendia J, Ventuneac A, Parsons JT. Characteristics associated with urethral and rectal gonorrhea and chlamydia diagnoses in a U.S. National Sample of gay and bisexual men: results from the one thousand strong panel. Sex Transm Dis. 2016;43(3):165–17.
13. St. Cyr S, Barbee L, Workowski KA, Bachmann LH, Pham C, Schlanger K, et al. Update to CDC's Treatment Guidelines for Gonoccoccal Infection 2020. MMWR. 2020;69(50):1911–6.
14. Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015;64(3):1–137.
15. Satterwhite CL, Torrone E, Meites E, Dunne DF, Mahajan R, Banez Ocfemia MC, et al. Sexually transmitted infections among US women and men: prevalence and incidence estimates, 2008. Sex Transm Dis. 2013;40(3):187–93.
16. Schwebke JR, Gaydos CA, Davis T, Marrazzo J, Furgerson D, Taylor SN, et al. Clinical evaluation of the Cepheid Xpert TV assay for detection of trichomonas vaginalis with prospectively collected female and male specimens. J Clin Microbiol. 2017;56(2):e01091–17.
17. Cantor AG, Pappas M, Daegas M, Nelson HD. Screening for Syphilis: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. 2016;315(21):2328–37.
18. Larsen SA, Steiner BM, Rudolph AH. Laboratory diagnosis and interpretation of tests for syphilis. Clin Microbiol Rev. 1995;8(1):1–21.
19. Araldi RP, Sant Ana TA, Modolo DG, de Melo TC, Spadacci-Morena DD, de Cassia SR, et al. The human papillomavirus related cancer biology: an overview. Biomed Pharmocother. 2018;106:1537–56.
20. Saslow D, Solomon D, Lawson HW, Killackey M, Kulasingam S, Cain J, et al. American Cancer Society, American Society of Colposcopy and Cervical Pathology screening guidelines for the prevention and early detection of cervical cancer. CA Cancer J Clin. 2012;62(3):147–72.
21. Aberg JA, Gallant JE, Ghanem KG, Emmanuel P, Zingman BS, Horberg MA. Primary care guidelines for the care of persons infected with HIV: 2013 update by the HIV Medical Association of the Infectious Diseases Society of America. Clin Infect Dis. 2014;58(1):1–10.

22. Petrosky E, Bocchini JA, Hariri S, Chesson H, Curtis R, Saraiya M. Use of the 9-valent human papillomavirus (HPV) vaccine: updated HPV vaccination recommendations of the advisory committee on immunization practices. MMWR. 2015;64(11):300–4.
23. Meites E, Kempe A, Markowitz LE. Use of a 2-dose schedule for human papillomavirus vaccination—updated recommendations of the advisory committee on immunization practices. MMWR. 2016;65(49):1405–8.
24. CDC HIV Statistics. https://www.cdc.gov/hiv/basics/statistics.html. Last accessed 01/23/18.
25. Moyer VA, USPSTF. Screening for HIV: a United States preventive services task force recommendation statement. Ann Intern Med. 2013;159:51–60.
26. Alexander TS. Human immunodeficiency virus diagnostic testing: 30 years of evolution. Clin Vaccine Immunol. 2016;23(4):249–53.
27. Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, et al. Preexposure chemophrphylaxis for HIV prevention in men who have sex with men. NEJM. 2010;363(27):2587–99.
28. Baeten JM, Donnell D, Ndase P, Mugo NR, Campbell JD, Wangisi J, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. NEJM. 2012;367(5):399–410.
29. Damme LV, Corneli A, Ahmed K, Agot K, Lombaard J, Kapiga S. Preexposure prophylaxis for HIV infection among African women. NEJM. 2012;367(5):411–22.
30. Thigpen MC, Kebaabetswe PM, Paxton LA, Smith DK, Rose CE, Segolodi TM, et al. Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana. NEJM. 2012;367(5):423–34.
31. Choopanya K, Martin M, Suntharasamai P, Sangkum U, Mock PA, Leethochawalit M, et al. Anitretroviral prophylaxis for HIV infection in injection drug users in Bangkok, Thailand (the Bangkok Tenofovir study):a randomized, double-blind, placebo-controlled phase 3 trial. Lancet. 2013;381:2083–90.
32. Marrazzo JM, Ramjee G, Richardson BA, Gomez K, Mgodi N, Nair G, et al. Tenofovir-based preexposure prophylaxis for HIV infection among African women. NEJM. 2015;372(6):509–18.
33. Molina JM, Capitant C, Spire B, Pialoux G, Cotte L, Charreau I, et al. On-demand preespsure prophylaxis in men at high risk of HIV-1 infection. NEJM. 2015;373(23):2237–46.
34. McCormack S, Dunn DT, Desai M, Dolling DI, Gafos M, Gilson R, et al. Pre-exposure prophylaxis to prevent the acquistion of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. Lancet. 2016;387:53–60.
35. Hoornenborg E, Prins M, Achterbergh RCA, Lr W, Cornelissen S, Jurriaans N, et al. Acquisition of Wild-Type HIV-1 infection in a patient on pre-exposure prophylaxis with high intracellular concentrations of Tenofovir diphosphate: a case report. Lancet HIV. 2017;4(11):e522–8.
36. Beymer MR, Weiss RE, Sugar CA, Bourque LB, Gee GC, Morisky DE, et al. Are Centers for Disease Control and Prevention Guidelines for preexposure prophylaxis specific enough? formulation of a personalized HIV Risk score for pre-exposure prophylaxis initiation. Sexually Transmitted Diseases. 2017;44(1):49–57.
37. Smith DK, Van Handel M, Wolitski RJ, Stryker JE, Hall HI, Prejean J, et al. Vital signs: estimated percentages and numbers of adults with indications for preexposure prophylaxis to prevent HIV acquisition—United States, 2015. MMWR. 2015;64(46):1291–5.
38. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf
39. Saag MS, Benson CA, Gandhi RT, Hoy JF, Landovitz RJ, Mugavero MJ, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults 2018 recommendations of the international antiviral society–USA Panel. JAMA. 2018;320(4):379–96.Stoner BP, Cohen SE. Lymphogranuloma venereum 2015: clinical presentation, diagnosis and treatment. Clin Infect Dis 2015:61(Suppl 8):S865-S873.
40. https://www.fda.gov/news-events/press-announcements/fda-approves-second-drug-prevent-hiv-infection-part-ongoing-efforts-end-hiv-epidemic.
41. Mayer KH, Molina JM, Thompson MA, Anderson PL, Mounzer KC, De WEJJ, et al. Emtricitabine and tenofovir alafenamide vs emtricitabine and tenofiovir disoproxil fumarate

for HIV pre-exposure prophylaxis (DISCOVER): primary results from a randomized, double-blind, multicenter, active-controlled, phase 3, non-inferiority trial. Lancet. 2020;396:239–54.
42. Landovitz RJ, Donnell D, Clement ME, Hanscom B, Coelho L, et al. Cabotegravir for HIV Prevention in Cisgender Men and Transgender Women. NEJM. 2021;385(7):595–608.
43. https://www.hptn.org/news-and-events/announcements/hptn-084-study-demonstrates-superiority-of-injectable-cabotegravir-to.
44. Sethi S, Zaman K, Jain N. Mycoplasma genitalium infections: current treatment options and resistance issues. Infect Drug Resist. 2017;10:283–91.