Sexually Transmitted Infections in Men Who Have Sex with Men

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Introduction

The term "men who have sex with men" (MSM) describes a heterogeneous group of men with diverse sexual behaviors, identities, and healthcare needs, but who are at risk for specific STI because of specific practices [1]. MSM is a behavioral term, and as such may include men who are married to women, who do not identify as male, as well as men who identify as "gay." Hence, it is incumbent for clinicians to ask about sexual behaviors in a nonjudgmental way, since a patient's appearance or marital status may not be informative regarding specific STI risks. MSM often have higher rates of STI and HIV than demographically matched heterosexual men [2]. The reasons for these higher STI and HIV rates involve multiple intersecting variables (Fig. 11.1). This chapter will focus on (1) the biological and behavioral factors relevant to STI in MSM, (2) the STI epidemiology in MSM, (3) pertinent clinical issues unique to MSM, including the extragenital manifestations of STI, (4) current screening and diagnostic recommendations, and (5) treatment considerations.

Case 1

A 32-year-old male presents with an ulcer on the roof of his mouth. He first noticed it one day prior to presentation. He denies trauma to the area. The lesion is not painful. He has no history of such lesions in the past and denies a history of cold sores. He has no other physical complaints. He has sex with men, identifies as gay, and has had receptive oral sex with four casual partners in the last 3 months. He does not use condoms for oral sex. He was screened for STI 6 months ago at which time a serologic rapid plasma reagin (RPR) test was nonreactive. His urethral and rectal screening tests were negative for gonorrhea and chlamydia but oropharyngeal screening was positive for gonorrhea. He was appropriately treated with eradication of oropharyngeal gonorrhea noted at retesting 3 months later. Today, on examination, there is a clean-based ulcer with erythematous heaped borders on the hard palate (Fig. 11.2). Palpation of the lesion produces no pain or bleeding. The rest of the physical examination, including the skin and anogenital examinations, are normal. Based on these findings, the healthcare provider makes a clinical diagnosis of primary syphilis with an oral chancre and treats the patient with Benzathine penicillin G 2.4 million units intramuscularly in a single dose. An RPR is performed in the clinic's

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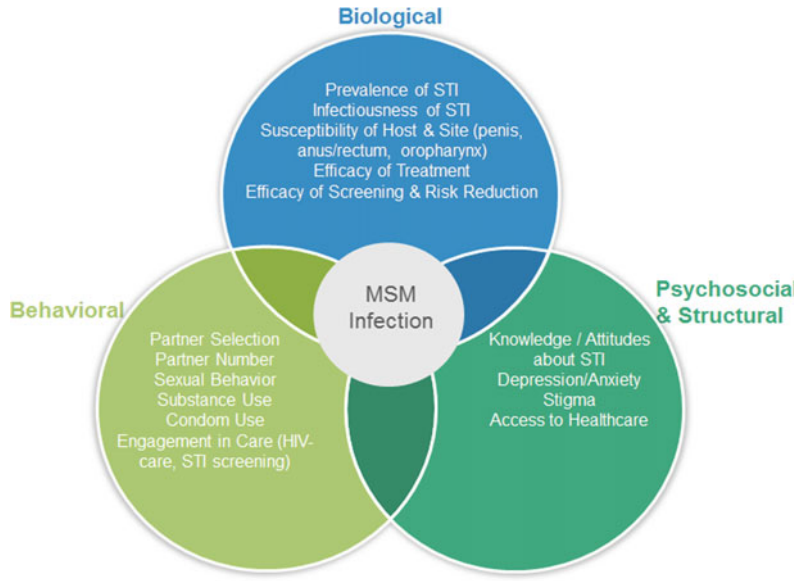

Fig. 11.1 Factors influencing STI transmission and acquisition among MSM

lab and is reactive (1:16). The *Treponema pallidum* passive particle agglutination (TP-PA) assay is sent for confirmation and is positive.

- The chancre of Primary Syphilis is seen at the site of inoculation and is often extragenital.
- When primary syphilis is suspected, providers should empirically treat at the time of presentation and prior to serologic confirmation.

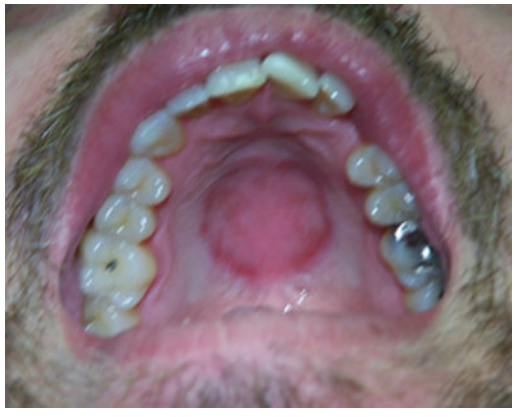

Fig. 11.2 Oral chancre of primary syphilis. Courtesy of Jeffery D. Hill, DMD

Case 2

A 23-year-old male presents for evaluation of left lower quadrant abdominal pain and rectal bleeding for the past 3 weeks. At symptom onset, he reported watery diarrhea and headache. These symptoms were followed by constant left lower quadrant pain, bloating, and intermittent cramping as well as mucoid discharge, tenesmus, and rectal bleeding that occurred with and in between bowel movements. The patient is HIV-infected on antiretroviral therapy (ART) with an undetectable HIV viral load and a CD4+ T cell count of 751 cells/μl. He has no other medical problems and specifically denies previous episodes of similar symptoms. He reports sex with men and identifies as gay. He engages in oral sex and receptive and insertive anal sex. He reports six partners in the 4 weeks preceding the start of symptoms. He has not had sex since symptoms developed. On examination, no hemorrhoids, fissures, or other perianal lesions are seen. Digital rectal examination is painful but the anal canal is smooth and the prostate is normal size and nontender. Anoscopy reveals a pink, mucoid discharge. The mucosa is friable and bleeds easily when collecting swab specimens. Polymorphonuclear leukocytes are seen on the

gram-stained smear of the exudate but no intracellular diplococci are observed. The patient is diagnosed with proctocolitis with high suspicion for Lymphogranuloma Venereum (LGV). He is prescribed doxycycline 100 mg twice a day for 21 days. Molecular testing is positive for *Chlamydia trachomatis* and negative for *Neisseria gonorrhoeae*, herpes simplex virus type 1 (HSV-1) and herpes simplex virus type 2 (HSV-2). In follow up at the end of therapy, the patient reports resolution of symptoms. The patient was rescreened for STI 3 months later, per CDC guidelines, and was negative.

- Sexually transmitted proctitis should be considered in MSM with anorectal symptoms.
- Empiric treatment for sexually transmitted causes of proctitis and/or proctocolitis should be considered while awaiting confirmation.
- Proctitis suspected or confirmed to be secondary to LGV requires longer duration (3 weeks) of therapy compared to other chlamydia infections.

Biological and Behavioral Factors Relevant to STI Infection in MSM

There is wide variation in sexual behaviors among MSM, and not all MSM are equally at risk for acquiring STI. However, in general, population-based surveys suggest that MSM have more sexual partners and higher rates of partner concurrency than demographically matched peers, placing them at greater risk for acquiring and transmitting STI [3]. The specific sexual practices reported by MSM are diverse, with oral sex and digital-manual stimulation of the partner's penis and anus being most common [4]. Most MSM also report experience with anal intercourse at some point during their lives [5]. Because the oropharynx and rectum are both susceptible to STI, extragenital infection is common [6, 7]. Further, STI transmission from the oropharynx and rectum to the urethra of the sex partner is well documented and confirmed by the high rates of genital infection among MSM who report only engaging in oral and/or anal insertive sex [7–10]. Oral stimulation of the anus with the tongue (i.e., rimming) is also frequently reported by MSM and has been implicated in the transmission of bacterial STI as well as enteric pathogens, including intestinal parasites, to the partner who provides the oral stimulation [10, 11]. Cytomegalovirus, Hepatitis B, and Human Herpes Virus 8 are found in saliva. Because some MSM use saliva for lubrication during digital stimulation of the anus and anal sex, these viral pathogens can be transmitted to the receptive partner, irrespective of condom use [12]. Use of saliva as a lubricant has also been suggested as an important risk factor for the transmission of gonorrhoeae [13]. Insertion of the hand into the rectum (fisting) has been reported by some MSM. Fisting carries a risk for traumatic bowel injury and has been associated with acute hepatitis C infection [14, 15]. Sex toy use (i.e., dildo, butt plug, fleshlights) can also cause mucosal trauma and act as fomites when sex toys are shared by sex partners [16]. Other sexual practices can place some MSM at risk for STI or trauma that can result in symptoms commonly associated with STI and easily confused with STI syndromes. As examples, urethral sounding is the practice of inserting an object or liquid into the urethra and is associated with urethral irritation, bleeding, and dysuria [17, 18]. Sex play (wax play, cock and ball torture, erotic electrostimulation, etc.) may lead to skin injury and ulceration with lesions mimicking those observed in genital herpes and primary/secondary syphilis.

Behaviors affecting STI risk extend beyond specific sexual practices and partner number. Rectal product use before, during or after anal sex may make the rectal mucosa more susceptible to STI and HIV. Precoital rectal douching, a popular practice among MSM, is linked to greater rates of STI and HIV [19–23]. Hyperosmolar lubricants used during anal sex may cause short term denudation of the rectal mucosa increasing susceptibility to STI and HIV [24, 25]. Postcoital douching is also commonly performed by some MSM [19]. Its relationship to STI is less well understood. Overall, condom use among MSM is declining [26]. Serosorting, the practice

of engaging in condomless sex with only men with the same HIV status, in order to decrease HIV transmission, is well documented among MSM, but has been associated with increased STI transmission [27]. As discussed below, pharmacologic advancements preventing HIV transmission also contribute to the rise in condomless sex among HIV-infected and HIV-uninfected MSM, but these factors do not fully explain recent changes in sexual behaviors among MSM [26].

Because MSM behaviors have been stigmatized by many societies, MSM may internalize societal rejection, and become depressed or anxious [28, 29]. Studies have linked high rates of depression and other behavioral health concerns with condomless sex and other adverse health outcomes, including substance use, as well as avoidance of medical care in anticipation of receiving culturally insensitive care, and/or disclosure of their homosexual behaviors to peers and/or family members [1, 30, 31]. For these reasons, knowledge of a patient's sexual behavior and substance use with focused interventions in these areas may have limited efficacy without understanding and addressing the root cause(s).

The use of recreational drugs and alcohol is common among some MSM and clearly linked to behavioral disinhibition, condomless sex, and higher STI risk [1, 32, 33]. Chemsex, is a specific term for recreational drug use that usually involves drugs that have euphoric or relaxing effects (e.g., gamma-hydroxybutyrate, methamphetamine, and mephedrone) and that alone or in combination prolong sexual sessions [34]. Dangerous in their own right, their use has been linked to STI in MSM [35]. FDA approved drugs for the treatment of erectile dysfunction are also used recreationally alone or in combination with other drugs by some MSM and are also linked to condomless sex and risk for STI and HIV [36]. Although not linked to STI, substance use among MSM extends to tobacco products with adolescent as well adults more likely to smoke tobacco than their heterosexual peers [37, 38].

Technological advancements including internet-based and geospatial sexual partner identification applications are commonly used by some MSM to identify potential sexual partners. Studies suggest that use of these platforms is linked to reporting a greater numbers of casual or unknown sex partners, condomless sex and higher rates of STI [39–41]. Further, the development of highly effective pharmacologic strategies that reduce HIV transmission and acquisition including HIV treatment as prevention and pre-exposure prophylaxis (PrEP) have been associated with higher rates of bacterial STIs and may increase STI through risk compensation (i.e., MSM feeling less concerned about HIV transmission or acquisition) [42–49].

As outlined above, sexual practices are diverse among MSM and may vary over time. Thus, the sexual history should frequently be revisited for screening purposes and discussed with MSM who present with genitourinary, gastrointestinal, or oropharyngeal symptoms. Some MSM may feel uncomfortable discussing their sexual behavior and/or recreational drug use with healthcare providers [50, 51]. Effective sexual history taking requires not only knowledge of sexual practices common to MSM but also the ability to discuss these sexual practices in a respectful way that engenders trust and ensures confidentiality.

Clinical STI Manifestations in MSM

For MSM, the primary sites of sexual exposure include the oropharynx, genitalia, anus, and rectum. When symptoms develop from infection, these are the sites usually involved, with some notable exceptions. Clinical manifestations of STI can vary depending upon HIV status and level of immune compromise.

Urogenital

Genital symptoms are not typically different in MSM and MSW and can be categorized broadly as urethral, ulcerative, and papular. As covered in greater detail elsewhere, symptoms of urethritis include dysuria, urethral itching, and urethral discharge and, in MSM, are most commonly

caused by *N. gonorrhoeae*, *C. trachomatis*, *Mycoplasma genitalium*, and other agents, which have not been fully characterized. Although there is substantial overlap, some studies suggest that the spectrum of organisms responsible for urethritis in MSM may differ from those causing urethritis in men who have sex with women (MSW) and, in MSM, may be transmitted through relatively low risk sexual practices including oral-genital sex although the specific pathogens are poorly understood [52, 53]. Enteric pathogens have also been implicated as a rare cause of urethritis in men who practice insertive anal sex. Less common causes of urethritis include HSV-1, HSV-2, and adenovirus [54, 55]. *Neisseria meningitidis* can also cause urethritis (and rarely proctitis) [56, 57]. *N. meningitidis* colonizes the nasopharynx and urethral transmission can occur through oral sex. Although reports to date do not place MSM at higher risk of *N. meningitidis* urethritis than MSW, colonization rates in oropharynx of MSM are reportedly higher than in other groups and healthcare providers should consider it a potential sexually transmitted pathogen in MSM [58]. In addition, MSM have a substantially higher risk for invasive and often life-threatening disease caused by *N. meningitidis* [59]. Vaccination against the serogroups A, C, W, Y (MenACWY or MPSV4) is currently recommended for HIV-infected MSM (Table 11.1) [60].

Genital ulcer disease is most commonly associated with *T. pallidum* and HSV-2. HSV-1 is also a frequent cause of genital ulcers in MSM [61]. Papular disease is most often caused by human papilloma virus (HPV) but can also be seen with Molluscum contagiosum, a pox virus [62, 63].

Gastrointestinal

Sexually transmitted pathogens can cause disease of both the upper and lower GI tract in MSM. In upper GI tract disease, oropharyngeal manifestations can be broadly categorized as pharyngitis, oropharyngeal ulcers, and oropharyngeal papules/patches. *N. gonorrhoeae* can cause pharyngitis, although typically infection is asymptomatic [64, 65]. *C. trachomatis* can be detected in the oropharynx and transmitted from the oropharynx, but its role in pharyngitis is unclear [66]. Whether transmitted sexually or nonsexually, HSV-1 is also a well-characterized cause of pharyngitis in adolescents and young adults and often occurs concurrently with gingivostomatitis or labial ulcers [64]. Much less commonly, HSV-2 causes an ulcerative pharyngitis [67, 68].

The most common causes of intra-oral sexually transmitted ulcers are HSV-1 and *T. pallidum*. HSV-2 is a rare cause of intra-oral ulcers. The oropharyngeal herpetic lesions of HSV-1 and HSV-2 are indistinguishable on physical examination. They are typically small but may coalesce into larger ulcers or erosions.

Table 11.1 STI vaccination recommendations for HIV-MSM[a]

Organism	Recommendation
Human papilloma virus	• Three dose series through age 26
Hepatitis A	• 2–3 dose series depending upon vaccine if not immune • Some experts recommend waiting until the CD4+ Count $\geq$ 200 cells/μl to vaccinate
Hepatitis B	• Three dose series depending upon vaccine if not immune • Some experts recommend waiting until the CD4+ Count $\geq$ 200 cells/μl to vaccinate
N. meningitidis	• If not previously vaccinated, should receive two-dose primary series of serogroups A, C, W, and Y meningococcal conjugate vaccine at least 2 months apart • Revaccinate every 5 years • Vaccination against serogroup B is not routinely recommended • Some experts recommend waiting until the CD4+ Count $\geq$ 200 cells/μl to vaccinate

[a]Created based on data from [60]

They typically have erythematous borders with a white base and are associated with mild discomfort to frank pain. In contrast, the intra-oral ulcer (chancre) of primary syphilis is typically solitary and painless (see Fig. 11.2). Secondary syphilis may also affect the oropharynx and should be considered in persons presenting with oral lesions including ulcers [69]. Sexually transmitted intra-oral papules are caused by some types of human papillomavirus [70]. Oral HPV-lesions are classically soft, pink-to-white growths most commonly observed on the buccal mucosa and soft palate but can also occur on the tongue and lips (Fig. 11.3) [70].

In STI-related lower GI tract disease, the anus, rectum, and/or colon may be involved. Clinical STI manifestations of the anus occur as ulcer disease and papules. Perianal ulcers are typically caused by HSV-2, *T. pallidum* and with increasing frequency HSV-1 in MSM. The perianal ulcers of HSV-1 and HSV-2 are indistinguishable. Perianal and anal papules are most often caused by HPV. They are typically described as pink or gray fleshy cauliflower like growths. They may extend into the anal canal and be palpated on digital rectal examination or observed by anoscopy [71]. Condyloma lata of secondary syphilis can involve the anus and perianal skin and can be confused with condyloma accuminatum. Condyloma lata typically presents with multiple moist, flat lesions whereas condyloma accuminatum are typically raised. Further, the natural history of each is different with condyloma accuminatum presenting subacutely and condyloma lata presenting more acutely. Other anal findings that may raise concern for the patient or the provider include skin tags, hemorrhoids, abrasions, and plaques associated with local trauma (including overwiping) or systemic disease. When the etiology of anal lesions is unclear, the provider should refer the patient to either a dermatologist or gastrointestinal specialist.

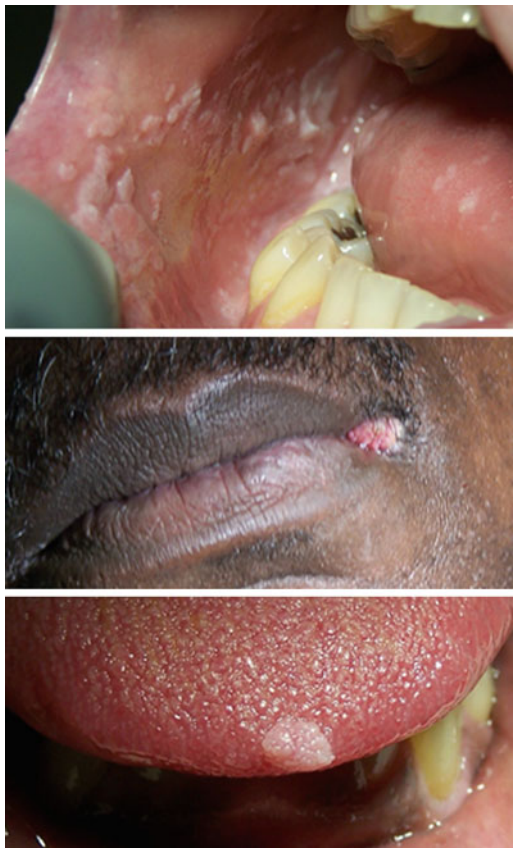

Fig. 11.3 Examples of HVP-oral lesions. Courtesy of Jeffery D. Hill, DMD

STI involving the rectum, rectum and colon, and small intestine can manifest as proctitis, proctocolitis, and enteritis, respectively. Proctitis refers to inflammation of the rectum. Symptoms and signs associated with acute proctitis include mucopurulent anal discharge, anorectal bleeding, constipation, tenesmus, and a sensation of rectal fullness or of incomplete defecation. Mucous streaking of the stool, constipation, or the sensation of incomplete defecation may indicate mild acute or chronic proctitis while anal discharge, anorectal bleeding and tenesmus indicate more severe proctitis [72, 73]. *C. trachomatis* (including LGV serovars, see below), *N. gonorrhoeae*, HSV-2, HSV-1 and *T. pallidum* are common causes of proctitis typically acquired through receptive anal sex [65, 74]. Emerging evidence suggests that *M. genitalium* may also cause proctitis [75, 76].

Proctocolitis refers to inflammation of rectum and colon. In addition to the signs and symptoms associated with proctitis, patients with proctocolitis may describe small volume diarrhea,

bloody stool, abdominal tenderness/pain and abdominal cramping [72]. Typical pathogens are acquired through receptive anal sex or through oral-anal contact. *Campylobacter* sp, *Shigella* sp, *Entamoeba histolytica*, and LGV serovars of *C. trachomatis* are causes in MSM [77–83]. Cytomegalovirus and other opportunistic pathogens (regardless of route of infection) should also be considered in persons with advanced HIV [65].

For MSM presenting with symptoms of proctitis or proctocolitis, anoscopy allows for direct visualization of the rectal mucosa. Mucous in the rectal lumen, mucosal edema, friability, easy bleeding, or ulceration may be present. Anoscopic specimen collection should include Gram stain to evaluate for Polymorphonuclear (PMN) cells and the intracellular diplococci of *N. gonorrhoeae*, a swab specimen for nucleic acid amplification tests (NAAT) for *C. trachomatis* and *N. gonorrhoeae*, and a swab specimen for HSV culture or PCR (both HSV-1 and HSV-2). Blood for syphilis serologies should also be obtained. Since diagnostic tests typically require more than 24 h to complete, empiric therapy should be given to cover the most likely pathogens [72].

Enteritis refers to inflammation of the small intestine and is characterized by symptoms that include large volume, watery diarrhea, bloody stool, abdominal cramping, and nausea with or without vomiting. STI pathogens commonly associated with enteritis in MSM include: giardia, campylobacter, and salmonella, but may include other organisms that are transmitted through oral-anal exposure. Systemic symptoms may include malaise, fever, and weight loss. With enteritis, there is typically a marked absence of proctitis or proctocolitis (unless concurrent infection with a second pathogen). Sexual history should be explored in MSM presenting with symptoms of enteritis.

In most cases, the clinical manifestations of STI in HIV-infected and HIV-uninfected MSM are similar. This is particularly true for HIV-infected MSM who are virologically suppressed on ART. However, a subset of MSM with HIV and low CD4+ T cell counts may present with more severe and/or atypical clinical manifestations of STI. As examples, HSV-2 in persons with advanced HIV may present as chronic mucocutaneous ulcers that last weeks to months. These ulcers may be extensive and difficult to treat [84, 85]. Other rare atypical manifestations of HSV-2 reported in persons with advanced HIV include slow growing nodular, tumoral or verrucoid masses that mimic penile or anal neoplasms [86]. Primary syphilis more frequently presents with multiple ulcers in patients coinfected with HIV than those with primary syphilis alone [87]. Immunosuppressed HIV-infected MSM may also be at increased risk for neurosyphilis. Genital ulcers are also more likely to be present during secondary syphilis in HIV-coinfected patients [88]. The influence of HIV on clinical manifestations is discussed in the context of the specific pathogen in the following sections.

Epidemiology, Diagnostics, and Treatment of STI in Msm

STI are common and on the rise in some subpopulations of MSM [89, 90]. In the following sections, the prevalence of specific pathogens including genital and extragenital infections is presented. This is followed by a discussion of clinical manifestations, diagnosis, and treatment of each STI. Special considerations related to the pathogen, its diagnosis, and/or treatment in MSM are presented.

Bacterial Pathogens Causing Oropharyngeal, Urethral, and Rectal Infection

Neisseria Gonorrhoeae

N. gonorrhoeae is common and increasing in MSM [6, 91–96]. Although the absolute number of infections is higher among MSW and women who have sex with men, the proportion *of N. gonorrhoeae* cases in MSM compared to these other groups is higher and demonstrates a substantial and growing inequality in the burden of STI in MSM [97]. A recent surveillance study of

MSM presenting to STI clinics in the U.S. reported a median site-specific *N. gonorrhoeae* prevalence of 19.0% and the burden of *N. gonorrhoeae* was greater among HIV-infected than HIV-uninfected MSM (Urethral gonorrhea: HIV-infected = 11.3%, HIV-uninfected = 6.8%; pharyngeal gonorrhea: HIV-infected = 9.2%, HIV-uninfected = 7.7%; rectal gonorrhea: HIV-infected = 17.1%, HIV-infected = 7.3%) [98]. The majority of MSM with oropharyngeal or rectal *N. gonorrhoeae* do not have concurrent urethral *N. gonorrhoeae* infection. Thus most cases of *N. gonorrhoeae* in MSM will be missed with urethral screening alone [6]. This highlights the importance of routine extragenital screening in MSM.

When symptomatic, symptoms caused by *N. gonorrhoeae* typically appear 72 h to 2 weeks after exposure [99]. The presentation of gonococcal urethritis in MSM is similar to that occurring in MSW and is described elsewhere in this book. Pharyngitis caused by *N. gonorrhoeae* is characterized by sore throat and in some cases with tonsillar involvement [64, 65]. A whitish-yellow exudate has been reported in a minority of patients with tonsillar involvement [100]. Fever and cervical lymphadenopathy are uncommon [64]. The typical mode of acquisition is receptive oral sex. Because the symptoms of gonococcal pharyngitis are nondescript and difficult to distinguish from other causes of pharyngitis, a thorough history that includes sexual exposures should be obtained from MSM presenting with symptoms of pharyngitis. Pharyngitis caused by *N. gonorrhoeae* is the exception with most infections of the pharynx being asymptomatic [6, 94, 101]. NAAT are the preferred diagnostic assays [65].

Proctitis and proctocolitis caused by *N. gonorrhoeae* are difficult to distinguish from other causes based upon symptoms and direct visualization of the rectal mucosa by anoscopy. However, a clue for proctitis caused by *N. gonorrhoeae* is the presence of a thick purulent discharge expressed from the anal crypts [99]. Gram stain may reveal intracellular diplococci but their absence does not exclude *N. gonorrhoeae* as the cause. Like pharyngeal infections, rectal infections with *N. gonorrhoeae* are often asymptomatic and screening in asymptomatic men is required to find infection [94, 102, 103].

Because of their high sensitivity and specificity, NAAT are the preferred diagnostics for *N. gonorrhoeae* [104]. NAAT for *N. gonnorrhoeae* is often performed concurrently with NAAT for *C. trachomatis* [65]. Urethral infection can be diagnosed from a provider-collected urethral specimens or from first void urine. Although not FDA approved for rectal or oropharyngeal specimens, NAAT is highly effective and can be used for diagnosis of extragenital *N. gonorrhoeae* infection in laboratories with Clinical Laboratory Improvement Amendment (CLIA)-defined performance specifications [104–106]. Self-collected rectal specimens are comparable to provider-collected specimens and may be more acceptable to patients [107, 108]. Extragenital screening is critical to finding the majority of infections in MSM.

N. gonorrhoeae has developed resistance over time to all antimicrobial regimens recommended for its treatment, though multidrug resistant gonorrheae is uncommon at present [109–120]. MSM are particularly vulnerable to infection with resistant gonorrhoeae [114, 121–125]. Several factors may contribute to the higher rates of infection with resistant strains among MSM. The oropharynx, a common site of infection in MSM, is potentially an important site for the development of resistance, sometimes through plasmid exchange with commensal *neisseriae* [126]. Studies also suggest that mechanisms that provide antimicrobial resistance may also allow for improved survival of *N. gonorrhoeae* in the rectum [127–129]. Higher rates of antimicrobial use among MSM when compared to MSW may also contribute to the selection and persistence of resistant *N. gonorrhoeae* [124]. New patterns of *N. gonorrhoeae* antimicrobial resistance have often been reported internationally prior to their presentation in the U.S [130, 131]. Some MSM may be more likely to travel internationally and report foreign-borne sex partners which may facilitate entry of resistant *N. gonorrhoeae* into the U.S. [132]. Sexual behaviors of some MSM include group sex and circuit parties that may

allow for contact between MSM from various geographic regions and facilitate spread of resistant *N. gonorrhoeae* [133–135].

Due to *N. gonorrhoeae's* propensity for rapid development of antimicrobial resistance local resistance patterns in MSM (when available) should be considered when selecting therapy [136]. Most guidelines recommend dual therapy with ceftriaxone 250 mg IM as a single dose plus azithromycin 1 g orally for uncomplicated infections of the urethra and rectum [65, 137]. The recommended alternative regimen is cefixime 400 mg orally as a single dose plus azithromycin 1 g as a single dose and should only be used if ceftriaxone is unavailable, because of emerging resistance to cefixime and its proven lower efficacy [65, 138]. The underlying philosophy for dual therapy is that use of two antibiotics with different mechanisms of action may improve treatment efficacy and slow development of further resistance [65]. Azithromycin is preferred over doxycycline because of *N. gonorrhoeae's* higher resistance to doxycycline and because of the ease of dosing of azithromycin [65, 114]. Alternative regimens are available and may be used for rectal infections in MSM who cannot tolerate first line agents. Recommended treatment regimens are the same regardless of HIV status. Test of cure for urethral or rectal *N. gonorrhoeae* infection in MSM is not currently recommended [65]. However, surveillance for *N. gonorrhoeae* antimicrobial resistance is ongoing and recommendations are updated according to new trends in its resistance [139]. Retesting of persons with uncomplicated urethral or rectal gonorrheae, is recommended 3 months after treatment whenever possible in sexually active MSM [65].

Gonococcal infections of the pharynx are more difficult to eradicate than urethral or rectal infections [140]. When treated with the preferred regimen of Ceftiaxone plus azithromcyin, no test of cure is required. However, if treated with an alternative regimen, test of cure for pharyngeal infection by NAAT or culture is recommended 14 days after treatment to ensure eradication of infection [141]. If a NAAT alone is used for test of cure and is positive, confirmatory culture should be performed prior to retreatment. Positive cultures should undergo antimicrobial susceptibility testing [65]. Gonococcal culture and susceptibility testing should be performed on any patient with persistent symptoms after treatment. Further treatment decisions should be made by an infectious diseases expert and the public health system notified. Recommended treatment regimens and follow up are the same regardless of HIV status. Because *N. gonorrhoeae* infection is often asymptomatic at both genital and extragenital sites, routine screening is recommended in MSM (Table 11.2).

Chlamydia Trachomatis

Like *N. gonorrhoeae*, *C. trachomatis* is highly transmissible and common in MSM [6, 102, 142]. The U.S. STD Surveillance for 2015 showed similar rates of urethral chlamydia in MSM regardless of HIV status but much higher rates of rectal chlamydia among HIV-infected MSM presenting to STD clinics for care (urethral chlamydia: HIV-infected: 5.6%, HIV-uninfected: 6.4%; rectal chlamydia: HIV-infected: 18.6%, HIV: uninfected 8.1%) [98]. Although pharyngeal infection does occur, its clinical significance is not known and routine screening is not recommended [65]. In prevalence studies of MSM, anorectal chlamydia is more commonly observed than urethral or pharyngeal chlamydia [6, 93, 143, 144]. However, evidence suggests that *C. trachomatis* is transmissible from the oropharynx and may serve as reservoir for the organism; and some experts support pharyngeal screening in MSM [145, 146].

Genital and extragenital *C. trachomatis* infection is most often asymptomatic and may be present for extended periods of time [91, 94, 145, 147, 148]. Only about 10% of infected men are thought to develop symptoms and routine screening is recommended in MSM (see Table 11.2) [149]. When symptoms occur, their timing is not well defined but may be delayed until weeks after infection given the slow replication cycle of *C. trachomatis*. Symptomatic urethritis caused by *C. trachomatis* typically presents with a mucoid or watery urethral discharge and dysuria. Symptomatic rectal infection

Table 11.2 STI screening recommendations for HIV-Infected MSM[a]

Organism	Screening recommendation
C. trachomatis	• For sexually active MSM, screen at the first HIV evaluation at sites of exposure (urethra and/or rectum) regardless of condom use • Screen at least annually at sites of contact regardless of condom use • Screen more frequently (every 3–6 months) at sites of contact if at increased risk
N. gonorrhoeae	• For sexually active MSM, screen at the first HIV evaluation at sites of exposure (pharynx, urethra, and/or rectum) regardless of condom use • Screen at least annually at sites of contact regardless of condom use • Screen more frequently (every 3–6 months) at sites of contact if at increased risk
T. pallidum	• For sexually active MSM, screen at first HIV evaluation • Screen at least annually • Every 3–6 months if at increased risk
Herpes simplex viruses	• HSV-1 and HSV-2 type-specific testing should be considered for persons presenting for STI evaluation
Hepatitis B virus	• Screen for HBsAg and anti-HBc and/or anti-HBs
Hepatitis C virus	• Screen at the initial HIV evaluation • Screen annually

[a]https://www.cdc.gov/std/tg2015/screening-recommendations.htm 2015 STD treatment guidelines

with non-Lymphogranuloma Venereum strains of *C. trachomatis* typically presents as a mild proctitis [150].

As for *N. gonorrhoeae*, NAAT are the preferred diagnostics for chlamydia and are often combined with NAAT for other STI [65, 104]. Specimen collection is similar for *C. trachomatis* as described for *N. gonorrhoeae* including rectal specimens.

Azithromycin 1 g orally as a single dose and doxycycline 100 mg orally twice a day for 7 days are highly effective for the treatment of urogenital *C. trachomatis* infection [151]. Head-to-head comparisons of azithromycin and doxycycline in the treatment of rectal chlamydia are lacking. However, retrospective studies suggest high rates of treatment failure with azithromycin when compared to doxycycline [152, 153]. For MSM presenting with acute proctitis (and without concern for LGV, see below), doxycycline 100 mg twice daily for 7 days is preferred over azithromcyin for empiric treatment of *C. trachomatis*. As stated previously, the clinical relevance of oropharyngeal chlamydia is poorly understood and routine screening for oropharyngeal chlamydia is not recommended. However, because *N. gonorrhoeae* and *C. trachomatis* assays are often linked, asymptomatic oropharyngeal *C. trachomatis* infection is not infrequently identified in MSM. When identified, it should be treated with either azithromycin or doxycycline as outlined for urogenital infection [65]. Treatment of *C. trachomatis* infection in MSM is the same regardless of HIV status [151].

Lymphgranuloma Venereum

LGV has increased at a concerning rate among MSM and in particular among HIV-infected MSM [154, 155]. LGV is caused by *C. trachomatis* invasive serovars L1, L2, and L3 [83]. In male genital infection, LGV presents as a transient genital ulcer disease associated with inguinal/femoral lymphadenopathy [156]. Underscoring its invasive nature, if left untreated, LGV may lead to chronic complications including deep tissue abscess, strictures, fissures, and chronic pain [83]. More recently, LGV has become a leading cause of proctitis and proctocolitis in MSM in developed countries [83]. The range of prevalence of LGV in persons with proctitis and proven rectal chlamydia is 7–23% [83, 157]. Proctitis and proctocolitis caused by LGV associated serovars can be severe, mimicking inflammatory bowel disease, with symptoms that include mucoid and/or hemorrhagic rectal discharge, anal pain, constipation,

and tenesmus, or hematochezia [158–160]. Prolonged infection can result in systemic symptoms including fever, malaise, and weight loss as well as serious complications including perirectal abscesses, fissures, and fistula formation [83]. When gram-stained, anal discharge in persons with LGV proctitis is likely to show white blood cells but no organisms [157]. Erythematous, friable ulcers are frequently observed on colonoscopy [83]. Although LGV rectal infection causes a more severe proctitis and proctocolitis than other *C. trachomatis* serovars, LGV can be asymptomatic [161].

Definitive laboratory diagnosis depends on detecting *C. trachomatis* DNA followed by genotyping to specifically detect LGV-specific serovars. However, assays to detect LGV-specific serovars are currently only found in research labs and are not commercially available. In the clinical setting, the diagnosis is typically based on the epidemiological and clinical findings consistent with LGV, confirmation of *C. trachomatis* by NAAT, and exclusion of other causes of symptoms [83].

Doxycycline 100 mg twice daily for 21 days is the treatment of choice for LGV proctitis [65, 83]. The prolonged length of therapy is required because of the invasiveness of LGV and the difficulty with its eradication. HIV-infected persons with LGV proctitis or proctocolitis respond well to doxycycline. However, some may have delayed resolution of symptoms. In these cases, patients may benefit from an extended course of doxycline [83]. Erythromycin, azithromycin, and moxifloxacin have activity against LGV but efficacy data are limited and side effect profiles may compromise their use [162–164].

Syphilis

Rates of syphilis are high and have been consistently increasing in MSM [98]. Of all cases of Primary and Secondary Syphilis reported in men in the U.S. in 2015, MSM accounted for 82% [98]. Similarly, high trends of Primary and Secondary Syphilis in MSM are reported in both developed and developing countries with HIV-infected MSM more often affected [165–167]. Reinfection is common in HIV-infected MSM [168, 169]. Not only is syphilis common in HIV-infected men, it is also an important predictor for new acquisition of HIV [170, 171].

The broad range of clinical manifestations associated with primary, secondary, and tertiary syphilis are covered in detail elsewhere in this book. Most HIV-infected patients with *T. pallidum* present with the typical dermatologic manifestations of primary and secondary syphilis. However, notable differences have been observed. As mentioned, in HIV-infected individuals, primary syphilis more frequently presents with multiple ulcers and genital ulcers are more likely to be present during secondary syphilis [87, 88]. Atypical chancres have been reported but are uncommon [172–174]. Unusual rashes in secondary syphilis have also been reported in patients with HIV but also in patients who are HIV-negative [175–179]. It remains unclear whether the presence of HIV influences the rash of secondary syphilis. Neurosyphilis can occur at any stage of infection. HIV-infected persons with early syphilis appear to possibly have an increased risk for developing neurological involvement [180]. Ocular syphilis, a type of neurosyphilis, may also occur with greater frequency in HIV-infected patients. Ocular syphilis can involve any part of the eye but panuveitis and posterior uveitis are the most common types of ocular inflammation documented [181]. Common signs and symptoms include eye redness, blurred vision, and vision loss. Other possible symptoms include eye pain, floaters, flashing lights, eye pressure, and photophobia [182]. Ocular syphilis may not be accompanied by manifestations of neurosyphilis or positive cerebrospinal fluid findings [183, 184]. Thus, ocular syphilis should be considered in MSM at risk for syphilis and presenting with eye complaints with or without other findings consistent with neurosyphilis. Although the skin, mucous membranes, and CNS are most frequently involved, syphilis is a systemic disease and can affect any organ system. A high index of suspicion should be maintained when assessing MSM at risk for syphilis who present with symptoms involving other organs systems.

As with all STI, a careful history and physical examination are central to interpreting risk and identifying clinical manifestations of syphilis. In MSM, the painless primary lesion may involve the mouth or rectum and go unnoticed by the patient and the provider. The cutaneous rash and mucous patches may be subtle and resolve without treatment. Because syphilis is characterized by periods of latency, many infected persons will have no evidence of infection at the time of their healthcare visits supporting the need for routine screening (see Table 11.2).

Laboratory diagnosis of syphilis requires two steps, a nontreponemal and a treponemal test. Nontreponemal tests include the Venereal Disease Research Laboratory (VDRL) and the RPR assays. Both are equally valid but not directly comparable because RPR titers are often slightly higher than VDRL titers. Nontreponemal antibody titers correlate with disease activity in most cases and are used to both diagnose and follow treatment response. A fourfold change in titer in the 6 months posttreatment is considered initial evidence of a successful response to therapy. However, lack of a fourfold change does not necessarily indicate treatment failure. With treatment, nontreponemal tests usually decline and may become nonreactive. False positives are possible with nontreponemal tests and thus require confirmation with Treponemal tests. False positive nontreponemal tests may be more common in people with autoimmune diseases, and multiparous women. In some parts of the world, infection with non-syphilitic treponemes (e.g., Pinta, Bejel) may result in biological false positive tests. The treponemal tests most often used are the fluorescent treponemal antibody absorbed (FTA-ABS) and the *T. pallidum* passive particle agglutination (TP-PA) assays. These tests are qualitative and typically remain positive throughout life. The sensitivity of treponemal and nontreponemal tests increases with duration of infection ranging from 75% in primary syphilis to virtually 100% in secondary syphilis. The clinician should take this into account when evaluating patients with findings concerning for syphilis. In late syphilis the treponemal test almost always remains positive while nontreponemal tests may decline with time. With the development of automation, some laboratories invert the classic algorithm and first test with a treponeme-specific test and confirm with a non-treponemal test.

The diagnostics used for syphilis are the same regardless of sex, sexual behavior, or HIV status. For most patients with HIV, these assays are accurate for diagnosing and monitoring treatment of syphilis. However, interpretation of these tests in the diagnosis and when following treatment can be more complicated in HIV-infected persons.

Genital Herpes

Genital herpes is the major cause of genital ulcer disease world worldwide [185]. It's primary cause is HSV-2 and is most often transmitted through anogenital-anogenital contact. HSV-2 is common in several studies of MSM and observed with high frequency among HIV-infected MSM [186–188]. In addition, HSV-1 is increasingly observed among young MSM as the cause of genital herpes, often reflecting oral-genital contact [189]. Genital HSV-1 infection is believed to recur at lower frequency than HSV-2 [190, 191]. However, the anogenital clinical manifestations of HSV-1 and HSV-2 are indistinguishable and require laboratory tests to identify the responsible virus. The major mode of transmission of HSV-1 is thought to be oral-anogenital contact but penile-anogenital transmission is also thought to be possible. Active genital herpes is an important risk factor for acquisition of HIV [192, 193]. Furthermore, HIV transmission to others is believed to be increased by HSV-2 coinfection [185].

Genital herpes is characterized by life-long infection and recurrent episodes. Classic and atypical manifestations of first-episode and recurrent genital herpes are covered elsewhere in detail and do not differ between MSM and MSW. However, MSM are more likely to have anorectal exposure and herpes simplex infection should be considered in MSM presenting with anal pain, perianal lesions, and proctitis [72, 74]. Reactivation of genital herpes in persons with HIV and who are immunosuppressed can be more severe,

of longer duration and occur more frequently than in the immunocompetent host [185]. Persons with HIV–HSV-2 coinfection not receiving ART also have higher rates of subclinical reactivation and asymptomatic viral shedding. CD4+ T cell count inversely correlates with rates of shedding [194]. High rates of HSV-2 shedding and clinical disease are seen in coinfected persons during the first 3–6 months after initiating ART and may represent an immune reconstitution syndrome [195]. Limited studies suggest that ART, in persons with well-controlled HIV, reduces the frequency of genital herpes recurrence. However, ART appears to have less effect on asymptomatic shedding of HSV-2 [196].

The diagnostic approach to genital herpes depends on the presence and stage of clinical manifestations at the time of presentation for care. Cell culture and NAAT are preferred when genital ulcers or other mucocutaneous lesions are present [65]. NAAT are more sensitive than culture. However, the use of cell culture or nucleic acid amplification is often determined by availability within the healthcare system. When cell culture is used, the practitioner should maintain a high level of suspicion even when cultures are negative especially when assays for other causes of genital ulcers are nonrevealing [197]. Type-specific serologic tests can be used alone or in combination with viral tests (when lesions are present) to interpret cause and proximity of infection. Because several weeks is required for antibodies to develop, persons presenting with genital lesions and a positive cell culture or nucleic acid amplification test but negative type-specific serologic tests have early infection. The presence of type-specific positive cell culture or nucleic acid amplification plus a positive serologic test suggest long standing infection with recurrence [197]. Serologic tests alone may be useful in persons with recurrent anogenital symptoms in whom HSV PCR or culture are negative, in persons who carry a clinical but unconfirmed diagnosis of genital herpes, or in persons who have a partner with genital herpes. In these cases, if serologic tests are positive for HSV-2, the provider can be relatively assured that the patient has genital infection. For HSV-1, seropositivity alone does not distinguish orolabial from anogenital infection [65].

Serologic test performance overall is good but reduced sensitivity and/or specificity is reported in some populations including persons with HIV [198, 199]. To optimize sensitivity and specificity of HSV-2 serologic assays, experts recommend using a higher than-standard-index cutoff [200].

Screening for HSV-1 and HSV-2 is not recommended in asymptomatic adolescents and adults [201]. However, some experts suggest a benefit to screening persons with HIV and MSM at increased risk for acquiring HIV (see Table 11.2). Since genital herpes is a well-characterized risk factor for HIV acquisition, knowledge of genital herpes may lead to behavioral modifications that reduce the risk of acquiring HIV and also of transmitting HSV-2 [202]. Of note, daily suppressive therapy with a thymidine kinase inhibitor (TKI) (acyclovir) in HIV–HSV-2 coinfected persons did not reduce transmission of HSV-2 to susceptible partners [203]. This is in contrast to observations in HIV-uninfected persons in which daily suppressive therapy with a TKI (valacyclovir) reduced HSV-2 transmission to sexual partners by almost 50% [204]. Studies also suggest that HSV-2 may increase infectiousness of HIV while daily suppressive TKI reduces HIV viral load and HIV infectiousness [205–207]. Despite these findings, daily suppressive therapy with TKIs does not reduce HIV transmission [208]. These studies were performed in heterosexuals but suggest that TKI would also have limited benefit in reducing transmission of either HIV or HSV-2 from coinfected MSM to their sexual partners.

Antiviral therapy is available for the treatment of clinical episodes and for suppression of recurrences in persons with frequent outbreaks. Recommended agents include the TKIs acyclovir, valacyclovir, and famciclovir. Dosing varies by indication (i.e., first clinical episode, recurrence, or suppression) and is covered elsewhere. For persons with HIV, recommended regimens for recurrent infection and suppression differ in dosage and length of therapy [65].

Thymidine kinase resistance is more commonly observed in immunocompromised persons, including those with HIV and should be considered in immune-compromised persons who do not respond to treatment [209]. When concern for resistance arises, a viral isolate should be obtained for culture and resistance testing [85]. Foscarnet is often an effective treatment in thymidine kinase resistant HSV-2 [210]. Cidofovir and imiquimod are alternative options [211].

Human Papillomavirus

Sexual transmission of human papillomaviruses is very common with approximately 40 different types of HPV that infect the anogenital and upper digestive tract [212, 213]. Low risk HPV types cause anogenital and upper digestive tract warts and mild dysplasia whereas high-risk HPV types can cause high grade dysplasia with progression to anogenital, penile, and oropharyngeal cancers [214]. Incidence of genital HPV infection is similar between MSM and MSW [215]. Genital warts also occur at similar rates in MSM and MSW [63]. In contrast, detection of anal infection is more common in MSM and reported prevalence is between 42 and 72% while oropharyngeal infection is between 3 and 11% and penile infection is between 15 and 18% [216–219]. The burden of HPV-associated manifestations at the anus, including cancer, is higher in MSM. HIV-positive MSM carry the highest burden of HPV including high-risk HPV types and suffer a higher prevalence of HPV-associated malignancies [186, 216, 220].

Many HPV infections are subclinical, and self-limited [221]. Routine screening for HPV in asymptomatic patients, including MSM, using molecular methods is not recommended. Clinical manifestations of HPV include oral and anogenital warts the majority of which are caused by the non-oncogenic HPV types 6 and 11. Oral and anogenital warts are usually asymptomatic but may cause pain and itching depending upon size and location. Intra-anal warts are seen most often in persons who have receptive anal sex and may not be visible on external inspection but palpated on digital rectal examination [65]. Anogenital warts are typically diagnosed based upon clinical appearance [221]. Molecular testing for HPV in persons with anogenital warts is not required. In support, among MSM requiring surgical removal of anogenital warts, intraepithelial neoplasia or squamous cell carcinomas were identified in the excised tissue in 26% of HIV-negative MSM and 47% of HIV-positive MSM [222]. With these high rates of intraepithelial neoplasia and squamous cell carcinomas, providers should maintain a low threshold for biopsy of anogenital warts, especially in immune-compromised persons. Any atypical lesion, characterized by pigmentation, induration, fixation to underlying tissue, bleeding or ulceration, should undergo biopsy [221]. Digital rectal examination may reveal palpable lesions. When lesions are palpated but not visualized, further evaluation is warranted, especially among HIV-infected MSM. Referral for anoscopy, with direct visualization and excision is recommended.

Several treatment options are available for treatment of anogenital warts. Choice of treatment is determined by wart characteristics (size, number, location) and patient/provider preference (cost, convenience, adverse effects) [65]. Efficacy is similar between treatments.

Despite higher prevalence of squamous cell carcinoma of the anus in MSM particularly those who are HIV-infected, data are currently insufficient to recommend routine screening. Large prospective studies are underway to better define when and how often to test for anal cytology in MSM. Although abnormal anal cytology is easily identified, its significance is not well-understood. One recent study reported abnormal anal cytology in 25% of HIV-uninfected MSM and higher prevalence among HIV-infected MSM that inversely correlated with CD4+ T cell count (47% among HIV-positive MSM with CD4 count <350 cell/mm). However, repeat screening in MSM with abnormal anal cytology, including high grade squamous intraepithelial lesions, showed regression of the abnormal anal cytology in the majority of cases [223]. Further confounding, anal intraepithelial neoplasia may occur in the absence of abnormal cytology [224].

Further studies are needed to establish if there is a benefit to anal cancer screening in MSM and which screening modality(ies) is best.

HPV vaccination is highly effective and widely available. Quadrivalent and nine-valent forms are licensed and available for use in males. These vaccines target the HPV types commonly associated with genital warts and with cancer. HPV vaccination is recommended through age 26 year for MSM (regardless of HIV status) who have not been previously vaccinated (see Table 11.1) [225]. Although the epidemiology suggests that many older MSM may be susceptible to one or more of vaccine-targeted HPV types, vaccination of MSM over the age of 26 years is not recommended at this time, but studies are underway to determine if there may be some benefit.

Hepatitis A

The Hepatitis A Virus (HAV) is a single-stranded RNA virus that is most commonly transmitted by the fecal-oral route. It infects the oral mucosa, survives in the intestine, and then infects the liver. Replication occurs in the liver and is transported by the biliary system to the intestinal tract where it is shed in the feces [226]. In most cases, HAV causes a self-limited illness most commonly characterized by fevers, malaise and jaundice [227]. Rarely, HAV causes fulminant liver failure and death. In high-income countries MSM are more likely to test positive for Hepatitis A antibodies than the general population and the likelihood of having antibodies to HAV correlates with the number of same-sex sex partners and time since same-sex sexual debut [228]. Numerous outbreaks of HAV have been reported in MSM [229–231]. In MSM with HIV, peak HAV viral loads and duration of viremia are longer [232].

The diagnosis of acute Hepatitis A requires serologic confirmation through detection of serum immunoglobulin (Ig) M anti-HAV antibodies. Anti-HAV IgM antibodies are present at the time of symptom onset and can persist for 3–6 months. Anti-HAV IgG antibodies appear in the convalescent phase, persist for decades, and are associated with life-long protective immunity. There is no treatment for hepatitis A and care is supportive [233]. Effective prophylactic vaccines are available for Hepatitis A and vaccination is recommended for MSM (see Table 11.1) [234]. Durability of the serological response to Hepatitis A vaccination is impaired in HIV-infected persons, especially persons with low CD4+ T cell counts [235]. Although not currently recommended, long-term durability of response in HIV-infected persons is better with 3 rather than 2 doses of HAV vaccine [236].

Hepatitis B

The Hepatitis B Virus (HBV) is a partially double-stranded DNA virus that is found in blood and other body fluids including semen [237]. In MSM, the rates of infection far exceed those in the general population and are mediated by unprotected anal sex [228]. The incubation period from exposure to symptoms varies from 6 weeks to 6 months [65]. HBV infection can be self-limited or chronic. The clinical presentation of HBV varies from asymptomatic to fulminant hepatitis and liver failure. About half of newly acquired HBV infections are believed to produce symptoms and in rare cases leads to acute liver failure [238]. The likelihood of developing chronic hepatitis B inversely correlates with age of infection. Chronic hepatitis B is more common in MSM, particularly HIV-infected MSM [239]. In MSM, 6–10% of HBV-infected men are coinfected with HIV [240]. In the HIV–HBV coinfected and untreated individual, HBV is more rapidly progressive. The HbsAg carrier rates and HBV viral loads are higher and episodes of HBV activation are more frequent in HIV-infected individuals than those who are HIV-uninfected. End-stage consequences of HBV infection including cirrhosis and hepatocellular carcinoma are also more frequent in HIV-infected MSM [240].

The diagnosis of both acute Hepatitis B, chronic Hepatitis B, and immunity to Hepatitis B (either through resolved infection or through

vaccination) is based on interpreting serologic markers for HBV. The presence of Hepatitis B surface antigen (HBsAg) indicates active infection. The presence of anti-Hepatitis B core IgM helps distinguish acute from chronic infection. The presence of anti-Hepatitis B surface antibodies (Anti-HBs) indicates immunity to Hepatitis B. In combination with total anti-Hepatitis B core antibody (Total anti-HBc), the presence of anti-HBs Ab mean recovery from past infection and immunity. The presence of anti-HBs Ab alone is consistent with immunity after immunization [239]. No treatment is available for acute hepatitis B. However, treatment is available for chronic hepatitis B. As a priority, adults, adolescents and children with chronic hepatitis B and clinical evidence of compensated or decompensated cirrhosis should be treated. Treatment is also recommended for adults over 30 years of age with chronic Hepatitis B without clinical evidence of cirrhosis, who have elevated alanine transferase and high level of HBV replication. For HBV monoinfected person, nucleos(t)ide analogs with a high barrier to drug resistance including tenofovir or entecavir are recommended. All HBV and HIV-coinfected individuals should be treated for both HIV and HBV [241]. Tenofovir plus emtricitabine or lamivudine as a part of the antiretroviral regimen will concurrently treat HIV and HBV, and need to be used for life to avoid HIV rebound and hepatic inflammation from HBV [241].

Universal vaccination of children and adolescents against HBV has helped reduce the burden of HBV infection. However, some groups including MSM remain at risk and, if unvaccinated, they should receive the HBV vaccine series [65, 234]. The HBV vaccine is also recommended for all persons living with HIV (see Table 11.1) [234]. Lower HBsAb seroconversion rates after vaccination are observed in persons with HIV. Further, in those who do respond to vaccination, rapid declines in antibody titers are observed more often in persons with HIV [242–244]. It is recommended that persons with HIV infection should be tested for anti-HBsAb 4–8 weeks after completing the vaccination series [65]. Although not yet included in guidelines, new studies suggest that immune responses to HBV vaccination are improved by higher concentrations and by increased number of doses in the vaccine series in persons with HIV [245]. Clinicians may want to recheck HBsAb levels periodically in HIV-infected patients who engage in condomless sex.

Hepatitis C

Hepatitis C Virus (HCV) is a single-stranded RNA virus and primarily considered to be a blood–borne pathogen transmitted through exposure to blood through needle-sharing, transfusion of contaminated blood products and unsafe medical practices [246]. Worldwide the most common mode of transmission is intravenous drug use (IDU) [247]. However, among HIV-infected MSM, increasing rates of HCV infection have been observed and are believed to represent sexual transmission [246]. Supporting sexual transmission, IDU is reportedly low in cohorts of HIV–HCV coinfected MSM and high-risk sexual behaviors (i.e., unprotected anal sex and fisting), concurrent diagnosis of chlamydia, and methamphetamine use are linked to HCV infection [248, 249]. Further supporting sexual transmission, HCV is shed in ejaculate and from the rectum (even in the absence of rectal bleeding) at sufficient levels to cause infection, though concentrations in blood are generally higher [250, 251]. Rates of reinfection are also high in HIV-infected MSM successfully treated for HCV who continue to engage in mucosally traumatic sex and methamphetamine use during sex [249]. While sexual transmission of HCV occurs among HIV-infected MSM, sexual transmission in non-IDU, HIV-uninfected MSM remains uncommon [246]. The factors that result in higher rates of HCV transmission in HIV-infected MSM are incompletely understood but thought to be related to both biological and behavioral factors. Biologically, HIV leads to chronic gastrointestinal inflammation weakening the mucosal immune system and facilitating HCV transmission [252]. Ulcerative STIs, including syphilis, LGV, and Herpes are common among HIV-infected MSM and may also

increase risk of HCV [253, 254]. Certain sexual practices may place some MSM at risk for sexual transmission of typically blood–borne pathogens. Group sex, receptive fisting, use of sex toys, and enema use before anal sex may induce mucosal trauma facilitating HCV transmission [255, 256]. Sexualized drug use is associated with HCV transmission in HIV-infected MSM and may result in higher rates of condomless sex, greater numbers of sex partners, and anal/rectal trauma resulting from longer and more intense sexual encounters while under the influence of drugs [257, 258]. Because HCV RNA is more frequently found in the semen of HCV/HIV coinfected versus HCV monoinfected persons, the practice of serosorting (HIV-infected men choosing other HIV-infected men as sex partners) may also facilitate higher rates of HCV transmission among HIV-infected MSM [259].

Most often, acute HCV infection is asymptomatic. When present, symptoms are indistinguishable from those caused by HAV and HBV. Unlike HAV and HBV acquired in adolescence and adulthood, HCV more often causes chronic infection, cirrhosis, and hepatocellular carcinoma. The natural history of HCV is influenced by coinfection with HIV, resulting in more severe clinical disease in dual-infected persons. Clinical manifestations of acute HCV may differ [260]. Further, HIV infection may accelerate liver fibrosis in chronic HCV infection [261].

HCV screening is recommended for one-time testing in MSM born between 1945 and 1965 [262]. MSM with risk factors for HCV infection including IDU should be screened periodically according to active risk [263]. HIV-infected MSM should be screened annually for HCV infection (see Table 11.2). Anti-HCV antibody tests should be used for screening. When positive, confirmatory testing by nucleic acid amplification evaluating for viremia confirms chronic infection [263]. In persons with low CD4+ T cell counts, false negative anti-HCV results may be observed. In such cases where clinical suspicion is high, nucleic acid amplification should be performed [65]. Patients with HCV should be evaluated for treatment [264]. Prophylactic vaccines are not available for the prevention of HCV. Prevention is mediated by risk reduction in vulnerable populations. Highly active treatment is available for Hepatitis C and all persons with Hepatitis C should be evaluated for treatment.

Conclusions

MSM are at high risk for STI. Healthcare providers caring for HIV-infected MSM should maintain an open dialogue with their patients regarding potential exposures to STI, vaccinate, and screen when appropriate. For MSM presenting with symptoms concerning for STI syndromes, treatment should be offered while awaiting diagnostic tests. Furthermore, when treatment is unsuccessful, the provider should explore sexual behavior to identify causes of symptoms other than STI.

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