Sexually Transmitted Infections in LGBT Populations

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Learning Objectives

- Describe the epidemiology of STIs in the LGBT community *(PC5)*
- Discuss how risk for different STIs varies by sexual behavior *(KP4, PC5)*
- List the different treatment and management strategies for various STIs *(PC5, PC6)*

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Introduction

LGBT Populations and Sexually Transmitted Infections

As mentioned elsewhere in this text, LGBT persons are estimated to make up some 5–10 % of the US population, yet are at disproportionately increased risk of many health conditions. One of the areas in which this was initially appreciated was with sexually transmitted infections (STI), particularly in men who have sex with men (MSM). For example, MSM accounted for about 50 % of all new HIV infections in 2011 [1]. In the same year at CDC STD Surveillance Network sites, 72 % of newly diagnosed primary and secondary syphilis was in MSM [2]. We begin this chapter with a discussion of sexual behavior and how to elicit appropriate information in a sexual history. We then discuss, briefly, the limitations presented by the literature that focuses more on behavior than on identity, and how identity plays a role in STI transmission via networks. The next major section of this chapter is a discussion of the epidemiology, clinical presentation, treatment, and prevention of the key STI pathogens. The final section deals with the common clinical syndromes encountered in STI, including the diagnostic approach to each.

One other caveat: as is evident by the references and discussion that follow, the literature has

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been dominated by STI in MSM, to the relative exclusion of any other LBT populations. Where possible, we have included discussion of the extant literature on women who have sex with women (WSW), lesbian, bisexual, and trans populations.

Sexual Behavior and STI Risk

The distinctions amongst sex, gender, and sexuality are particularly important in the discussion about STI and STI risk. It is imperative to note that an individual's sexual behavior—not identity—is the primary determinant of his or her risk of STI exposure and acquisition. Some providers will make decisions about screening based either on how a patient identifies (e.g., "Only gay patients need to be screened for HIV"), or worse, based on how the provider *perceives* their identification/sexual orientation (e.g., "Well, I wouldn't screen him for HIV because he doesn't seem gay"). Whether a man identifies as "gay" or "straight", it is clear that if that man participates in unprotected receptive anal intercourse with another man (amongst other behaviors), there is a higher risk of acquisition of HIV, and that man should be screened for HIV. The sexual history, then, should focus on behavior first. If a clinician can clarify patients' specific sexual acts, he/she can appropriately assess their potential sites of infection and pathogen exposures.

Consider a self-identified straight male who regularly has insertive oral and anal sex with other men. These *behaviors* put him at risk for urogenital STI acquisition from his male sexual partner(s) regardless of his discordant sexual identity. A different self-identified straight male may have insertive *and* receptive oral and anal sex with other men. This man is thus at risk for STI exposure at his pharynx and anorectum in addition to his urogenital tract. Even though both of these men identify as straight and have sex with other men, their individual STI risks are different. Now consider a self-identified straight male who only participates in receptive oral and anal sex with other men but also has penetrative oral and vaginal sex with women. This man is at risk for urogenital, pharyngeal, and anorectal STI acquisition. However, he is likely exposed to different types of pathogens at his urogenital tract in comparison to his pharynx and anorectum based on the variability of pathogens that affect WSM versus MSM. It may seem challenging and cumbersome to delve into the details of patients' sexual activities but these specific behaviors differentiate patients' risks on an individual basis and permit appropriate risk reduction counseling and screening. It is thus important that culturally competent providers become comfortable with discussing sex and sexual behaviors with *all* of their patients.

Behavior Versus Sexual Orientation

The terms "MSM" and "WSW" have been widely incorporated into sexual health literature because of their inherent objectivity in differentiating populations of sexual minorities from their heterosexual counterparts. This methodology was intended to give researchers the advantage of generalizing a non-heterosexual population based solely on its members' sexual behaviors without implicating their social variability. As stated previously, sexual behavior is what primarily determines STI risk. However, opponents of this research model argue that this cultural stripping inhibits effective interpretation of data associated with specific sexual behaviors as an individual's sexual identity and behavior are intrinsically interconnected [3, 4]. From a health care provider's perspective, it is important to note that subpopulations of MSM (e.g. openly gay men versus men "on the DL") may have different social networks, may engage in different specific sexual behaviors, and, thus, may have different STI risks. This point highlights the need for clinicians to assess patients' sexual identities *and* behaviors when taking sexual histories. Further, research strategies that assess the variance within "MSM" and "WSW" from population perspective are needed so health care providers can recognize the risks associated with specific sexual identities within the generalized MSM and WSW groups.

A Discussion of Key Pathogens

Human Immunodeficiency Virus

Epidemiology

Human immunodeficiency virus (HIV), the etiologic agent of the Acquired Immunodeficiency Syndrome (AIDS), infects approximately 2.3 million people globally and 50,000 people in the United States annually [5, 6]. While treatment standards and implementation differ markedly for developed versus developing nations, overall our ability to treat HIV (with highly active antiretroviral therapy, or HAART) has improved the overall survival of those infected with HIV. With mortality rates lower than incidence rates, the prevalence of HIV has increased overall, and there are an estimated 35.3 million people globally, and 1.1 million people in the US, living with HIV [5, 6].

HIV is an infection that is disproportionately represented in those with barriers to access of health care. The largest proportion of those newly diagnosed with HIV and living with HIV overall are MSM. In addition, racial/ethnic minority populations are overrepresented in HIV infections. According to Centers for Disease Control and Prevention (CDC) data, MSM, while only 2–5 % of the US population, accounted for 63 % of all new HIV infections in 2010 [7]. Likewise, African-American males are infected with HIV at an eightfold higher rate than white males [8]. The highest rate of HIV infection is currently in young (ages 13–24) MSM of color [8].

It is also important to note that accurate statistics for HIV infection are somewhat compromised by barriers to testing (see Clinical Presentation and Diagnosis, below). The CDC estimates that 16 % of those currently living with HIV in the US are unaware of their diagnosis [6]. There are also data to show that this fact has implications for the propagation of HIV in communities (see Prevention, below).

Clinical Presentation

HIV is a retrovirus that replicates in host immune cells (primarily CD4+ T cells) and, as a part of viral replication, causes destruction of many of those cells. HIV infection and the host response are dynamic, with most infected individuals mounting a robust, but ultimately ineffective immune response. After infection, an initial high viral load is usually brought under some level of control, while destruction and regeneration of immune cells reaches a steady state. When this process shifts in favor of viral replication, the immune system deteriorates and opportunistic infections (OIs) may ensue. In the absence of effective immune reconstitution, infections may progress unchecked, leading to morbidity and, ultimately, mortality. This process is summarized graphically in Fig. 14.1.

Clinical manifestations depend primarily on when in the course of infection a patient is encountered. In the initial viremic phase (acute HIV), symptomatic patients often present with a mononucleosis-like syndrome (fevers, generalized lymphadenopathy, occasionally with sore throat). However, approximately half of all individuals infected with HIV may be asymptomatic, even in the acute phase of the illness [9]. In advanced HIV disease (AIDS), symptoms such as fever, night sweats, weight loss, and inappetance are common. Likewise, as patients with advanced HIV disease are at risk for opportunistic infections, symptoms of OI may predominate, based on pathogen and/or site of infection. Common clinical syndromes encountered with OI in AIDS include meningitis/encephalitis, pneumonia, gastroenteritis/colitis, and undifferentiated fever.

Diagnosis

The United States Preventive Services Task Force (USPSTF) has issued recommendations for screening patients for HIV (see Table 14.1) [10]. The standard testing protocol includes use of an HIV enzyme-linked immunosorbent assay (ELISA) for initial screening, and then Western blot for confirmatory testing. As both of these rely on an immune response (antibody formation), neither is sensitive for screening for acute HIV. For acute HIV, nucleic acid testing or antigen testing would be more appropriate. Screening may sometimes lead to an "indeterminate" result. In such cases, though there are many causes of a false positive ELISA (and occasionally even a

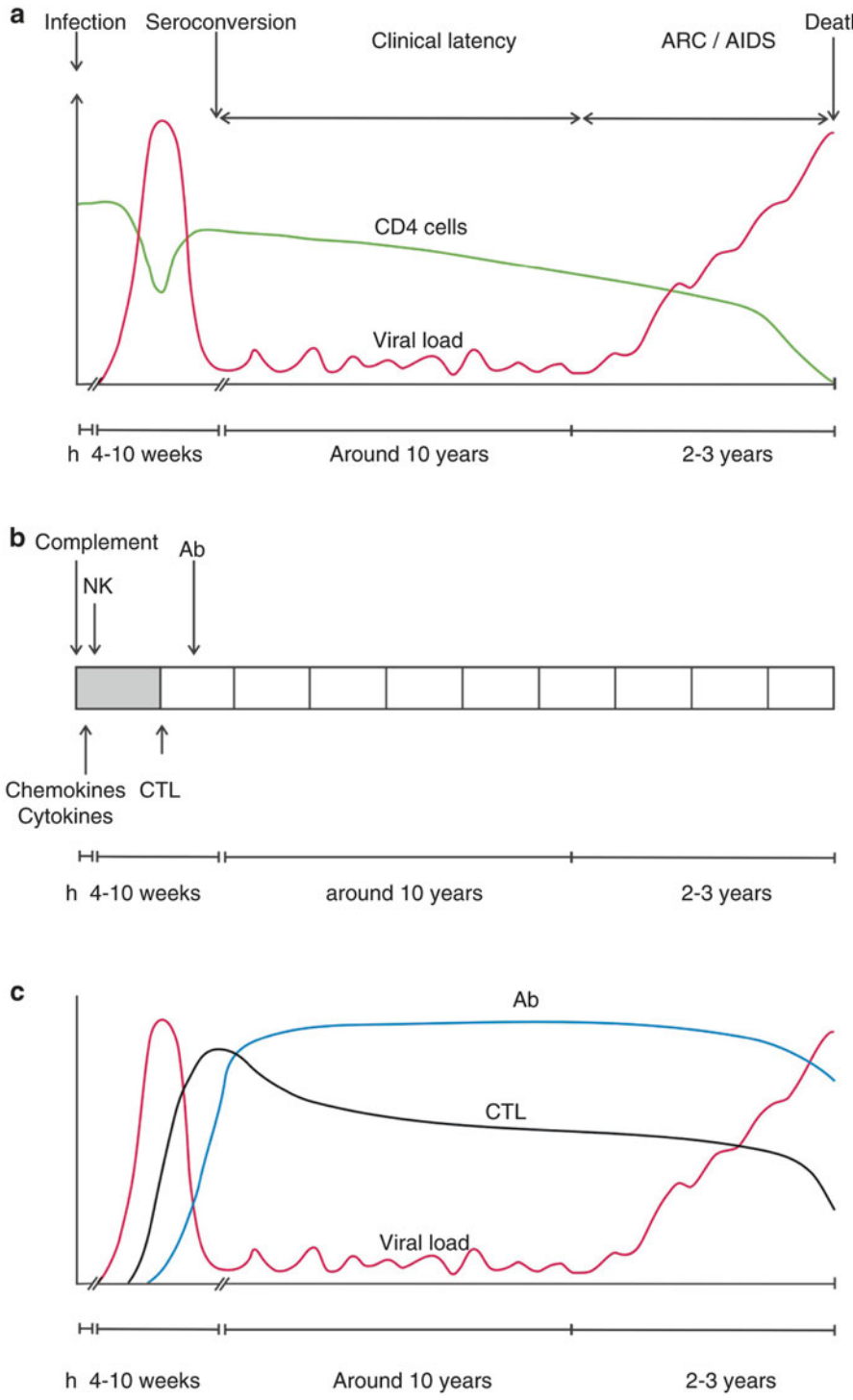

Fig. 14.1 This graph depicts the natural history of HIV infection without antiretroviral therapy. Note initial surge in viral load at disease onset. Over time, the CD count declines and there is an associated, steep rise in the viral load when CD4 numbers are depleted. As the CD4 count is depleted, patients are at increased risk for opportunistic infections and certain malignancies

Table 14.1 United States Preventive Services Task Force (USPSTF) Guidelines for screening patients for HIV

Recommended Populations for Screening
Adolescents and adults aged 15–65
Younger adolescents and older adults at increased risk for infection
Pregnant women
Populations at Higher Risk
Men who have sex with men (MSM)
Active injection drug users
Those who are being tested for other sexually transmitted infections (STI)

false positive Western blot), it is usually best to repeat the testing process in a few weeks to see if there has been evolution of an immune response.

Treatment

Treatment of HIV is complex and rapidly evolving; thus, a thorough discussion of management of HIV is beyond the scope of this chapter, and only key points are mentioned here. The Department of Health and Human Services (DHHS) produces and maintains guidelines for the treatment of both HIV and opportunistic infections associated with HIV [11, 12]. Guidelines for treatment as of the writing of this chapter are summarized in Table 14.2. In general, treatment should consist of three antiretroviral agents, from at least two different classes of medication (Table 14.2B). Treatment should be initiated as close to the time of diagnosis as possible, with the possible exception of those who are concomitantly diagnosed with an opportunistic infection. In the case of a diagnosis in the setting of OI, data are clear about the need for early HAART in some infections (e.g., tuberculosis), but equivocal in others. It is clear, however, that early therapy confers a morbidity and mortality benefit, especially when treatment forestalls the onset of immune compromise. It is also clear that treatment, once started, should not be interrupted. Even transient interruption of therapy and other episodes of non-adherence to an established regimen increase the risk of virologic resistance, virologic failure, and immunologic failure.

Guidelines are also available for the primary care physician to help guide the care of the patient with HIV who is establishing care and who presents for maintenance of care. These are generated and reviewed regularly by the HIV Medical Association of the Infectious Diseases Society of America [13].

Prevention

HIV prevention has been studied extensively using many approaches, including many behavioral and biomedical methods. Behavioral methods (such as encouraging testing, and safer sex practices) have been part of prevention efforts from the time the HIV transmission cycle was elucidated, though results of such efforts have been disappointing overall. More recently, biomedical methods, especially pre-exposure prophylaxis (PrEP), have shown promising results in both rates of HIV prevention and rates of in-study adherence. One study in particular merits mention here. The iPrEx study looked at the effect of daily tenofovir/emtricitabine (Truvada) in the prevention of HIV acquisition in MSM and transgender women (MTF) who have sex with men. The study showed that PrEP reduced the acquisition of HIV 47 % in all those who were assigned to receive it, and was even more effective (93 %) in those who demonstrated adherence to the PrEP regimen (detectable levels of medication in the blood) [14]. Other studies of the PrEP approach have yielded similar results. Studies are currently underway to see if other dosing strategies provide equal (or better) rates of prevention.

When providing prevention counseling to an individual patient, it is helpful to target risk mitigation, leading to an open and frank conversation about what the patient feels are realistic expectations. It is important to note that patients may engage in many such behaviors to limit their risk of HIV acquisition, including serosorting, seroadaptation, and PrEP. Ultimately, the strategies that are employed are individual, and these should be discussed regularly with each sexually active patient.

Lastly, the role of prevention with the patient living with HIV should also be discussed. From data in the last decade from the CDC, it has been shown that knowing one's status can have an impact on transmission of HIV. As many states have laws pertaining to sexual acts and the need to disclose HIV status, it is also important for providers to be aware of pertinent laws/statutes and to discuss them with their patients who have

Table 14.2 Department of Health and Human Services (DHHS) guidelines for when to initiate treatment (A) and what to initiate (B) in the treatment of persons living with HIV

A. When to Treat			
Clinical condition	Recommendation	Strength of recommendation	
For patients who are HIV+, to prevent progression and complications of disease			
CD4 > 500 cells/mm^3	Treat	BIII	
CD4 350–500 cells/mm^3	Treat	AII	
CD4 < 350 cells/mm^3	Treat	AI	
For patients who are HIV+, to prevent transmission of HIV			
Risk group	Strength of recommendation		
Heterosexuals	AI		
Perinatal/Pregnancy	AI		
Other	AIII		
B. What to Start			
Recommended (AI)	Backbone	Plus other agent	
	TDF/FTC	DRV/r	PI-based regimen
	TDF/FTC	ATV/r	
	TDF/FTC	EFV	NNRTI-based regimen
	TDF/FTC	RAL	INSTI-based regimen
	TDF/FTC	EVG/COBI	
	TDF/FTC	DTG	
	ABC/3TC	DTG	
Recommended only for patients with a pre-ART plasma HIV RNA <100,000 copies/mL			
	ABC/3TC	EFV	
	TDF/FTC	RPV	
	ABC/3TC	ATV/r	
Notes			
1. ABC-containing regimens should only be used for patients who test negative for HLA-B*5701			
2. The combination TDF/FTC/RPV should only be used in patients with a pre-treatment CD4 of >200 cells/mm^3			
3. The agents FTC and 3TC may be used interchangeably			
(1) DHHS guidelines, available at http://aidsinfo.nih.gov			
Strength of recommendation	A = strong, B = moderate, C = optional		
	I = data from randomized controlled trials; II = data from well-designed, non-randomized trials or observational cohort studies with long-term follow up; III = expert opinion		

HIV. It is also important to discuss with patients with HIV that they are still at risk for other STI (as noted elsewhere in this chapter) and should thus be screened appropriately for STI.

Chlamydia trachomatis

Epidemiology

Chlamydia trachomatis (CT) is a small obligate intracellular Gram-negative bacterium that causes a wide spectrum of disease. From a sexual health perspective, the most important CT serotypes are D-K, which are known to cause the common chlamydial genitourinary syndromes. CT has been the most commonly reported STD to the US Center for Disease Control (CDC) since 1994, and more than 1.4 million cases of CT infections were reported in the US in 2012 [15]. Yearly incidence of CT infections has been increasing for the past 20 years, which may partially be due to improved population screening strategies. Within the context of the LGBT population, there is significant data available on CT infections affecting

MSM. Approximately 6–22 % (variation based on site) of MSM who received care at the CDC STD Surveillance Network clinics in 2012 were infected with CT [15]. Unfortunately, little data is available on the association between female-to-female sexual contact and CT transmission. Some self-identified lesbians and other WS(M)W also have oral, insertive vaginal, and/or insertive anal sex with men, however, and these sexual behaviors put these populations of women at risk for CT exposure and infection.

Clinical Presentation

The most common sites of CT inoculation are the cervix, urethra, anorectum, pharynx, and conjunctivae. Depending on the site and host, a majority of those infected with CT are asymptomatic. Current literature shows that CT urethritis in men can be asymptomatic in over 80 % of those infected [16, 17]. Two studies done in San Francisco, California and Columbus, Ohio independently found that 85 % of rectal CT infections in MSM were asymptomatic [18, 19]. Similarly, as much as 80 % of female urogenital CT infections are asymptomatic [20]. Asymptomatic CT infections in the female urogenital tract put patients at risk for complications as severe as infertility, pregnancy complications, and chronic pain secondary to pelvic inflammatory disease (PID) if left untreated. Further, asymptomatic carriers of CT at any anatomical site serve as an unknowing reservoir of CT transmission and spread.

Symptomatic urogenital CT infection in men most commonly manifests as urethritis (see Urethritis below). A small minority of these men develops prostatitis or epididymitis from urethral spread. MSM who participate in receptive anal intercourse can develop CT proctitis (infection of the anorectum). Symptomatic urogenital infection in women most commonly presents as cervicitis (see Cervicitis below). Some female patients with cervicitis develop a concurrent CT urethritis, while others develop urethritis without a corresponding cervicitis. CT proctitis in women can result from either direct receptive anal intercourse with an infected male or from self-inoculation by infected cervicovaginal secretions. Urogenital CT infection in women can progress to PID, a process characterized by inflammation of the uterine lining, fallopian tubes, ovaries, and/or adjacent pelvic organs, in approximately 10 % of untreated cases [20]. CT conjunctivitis can occur in men or women either by direct or indirect (via the hands) inoculation by infected urogenital secretions. Although CT can infect the pharynx, it is not known to be a major cause of symptomatic pharyngitis. A systemic autoimmune process called reactive arthritis (Reiter's syndrome) is characterized by recent urogenital CT infection, ocular inflammation (usually conjunctivitis), and a large joint polyarthritis.

Diagnosis

Nucleic acid amplification testing (NAAT) has largely replaced culture for all sites, and is the preferred diagnostic method for genitourinary CT infections in both men and women. For women, a vaginal swab for NAAT is currently the most sensitive and specific specimen collection method for CT detection, though first-catch urine, endocervical swabs, and urethral swabs are also viable specimens in women [21]. A first-catch urine sample for NAAT is the preferred collection method for urogenital CT infection in men [22]. A urethral swab is a viable alternative but is typically less comfortable for the patient. For men at risk for rectal CT, many laboratories have been approved for rectal NAAT specimens under the Clinical Laboratory Improvement Amendment (CLIA) regulations despite its lack of FDA approval. There are currently no recommendations for routine NAAT of pharyngeal specimens in men or women; although, the pharynx is likely a contributing reservoir for the spread of CT.

As mentioned above, the majority of CT cases are asymptomatic. Therefore, screening patients based on their sexual behaviors is imperative, as swabbing at one inoculable site does not indicate CT positivity or negativity at a different location. Kent et al. found that 53 % cases of rectal CT in MSM would have been missed if patients were screened only with urogenital samples [18]. This finding highlights the importance of routinely

screening patients for CT at susceptible sites based on an individual's sexual behavior.

Treatment

According to the 2010 CDC treatment guidelines, 1 g of azithromycin in one dose or 100 mg of doxycycline taken twice daily for 7 days are equally effective in treating a non-LGV chlamydial infection [22]. Other macrolides or fluoroquinolones are alternative therapies but may be less effective. The one-time-dose of azithromycin is preferable for patients in whom medication noncompliance may be an issue, but gastrointestinal distress and subsequent medication loss with emesis must be considered. If diagnosed with CT, patients are recommended to abstain from further sexual activity for 7 days and until all symptoms have diminished. When a patient is diagnosed with CT, all sexual partners of the patient within the past 60 days should be contacted and recommended for testing at susceptible sites. Infected patients should follow-up with their provider in approximately 3 months for retesting regardless of whether they believe their sexual partner(s) were screened and treated appropriately. Contrary to *Neisseria gonorrheae* (GC), little concern exists for the development of antibiotic resistance in CT.

Lymphogranuloma Venereum

Lymphogranuloma venereum (LGV) is a particular form of invasive CT disease, commonly manifest as proctitis and suppurative inguinal adenopathy, and is typically caused by L1–L3 serovars of CT. Clusters of LGV have been reported in MSM, most often in the context of a sexual network, though it should be noted that many cases can be traced back to en endemic exposure (e.g., travel to endemic tropical/subtropical area). Overall, rates of LGV are higher amongst MSM than in the general population. It is unclear whether this represents an increase in the prevalence of the LGV-causing serovars in MSM, or the increased incidence of CT in MSM, as has also been reported when compared with other populations. For LGV, the standard treatment is oral doxycycline, 100 mg, taken twice daily for 21 days.

Neisseria gonorrheae (Gonorrhea)

Epidemiology

Neisseria gonorrheae, or gonococcus (GC), is a diplococcal, Gram-negative bacterium that exhibits a similar spectrum of disease as *Chlamydia trachomatis* (CT). GC is the second most common bacterial sexually transmitted pathogen following CT. Over 330,000 GC infections in the US were reported to the CDC in 2012 [15]. Interestingly, the lowest recorded GC infection rate was in 2009, yet GC prevalence rates over 2010–2012 progressively increased. This trend highlights both the impact of improved screening strategies and the possibility of increasing GC burden in the US population. Similar to CT, data shows that MSM are disproportionately affected by GC. A study looking at the rates of GC in San Francisco from 1999 to 2008 showed that 72 % of GC infections were detected in MSM [23]. Approximately 10–30 % of MSM (variability based on location) screened through the CDC STD Surveillance Network tested positive for GC in 2012 [15]. Again, similar to CT, female-to-female transmission of gonococcal infections is not well documented. WS(M)W and self-identified lesbians can have sex with men, however, and put themselves at risk for pharyngeal, urogenital, and anorectal GC acquisition.

Clinical Presentation

Symptomatic GC infection exhibits considerable clinical overlap with symptomatic CT infections. Urogenital infections in men are likely to present as urethritis (see Fig. 14.2), which can spread locally to cause prostatitis or epididymitis. Contrary to CT, GC urethritis is largely symptomatic in men. In a study assessing around 1800 cases of GC urethritis, only 10.2 % were entirely asymptomatic [24]. Female urogenital infections are likely to present as cervicitis (most common), urethritis, or a combination of both. A majority of female urogenital GC infections are asymptomatic [25]. Urogenital GC in women can progress to pelvic inflammatory disease (PID), a process characterized by inflammation of the upper female genital tract (i.e. uterine lining, fallopian tubes, ovaries) and other pelvic organs [26].

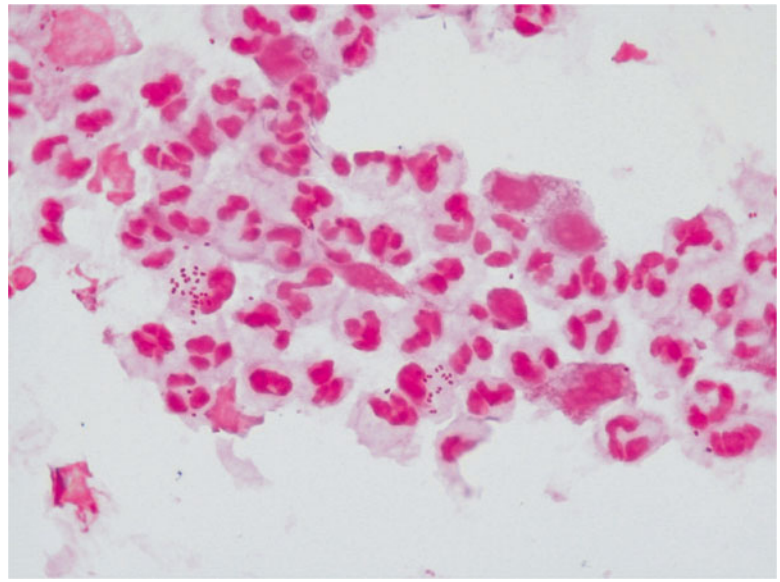

Fig. 14.2 This image shows the polymorphonuclear cells seen histologically in bacterial urethritis. Note the associated Gram-negative diplococci characteristic of an infection with *Neisseria gonorrhoeae*

The risk of progression of asymptomatic urogenital GC in women to PID and its associated morbidities is a serious concern for those infected. This highlights the need for sufficient screening and treatment of women at risk for GC acquisition.

Proctitis (infection of the anorectum) can occur in both men and women and is largely asymptomatic in both sexes. As mentioned above, Kent et al. showed that approximately 85 % of rectal gonococcal infections in their San Francisco MSM study population were asymptomatic [18]. Rectal GC in females occurs from either direct inoculation from an insertive male sexual partner or from autoinoculation by infected cervicovaginal fluids [27]. Pharyngeal gonorrhea is mostly asymptomatic and may be a concerning source of pathogen transmission and spread in the sexually active population.

Although rare, disseminated infection can present in men and women as gonococcal bacteremia with migratory polyarthritis, tenosynovitis, and/or cutaneous lesions. GC is the most common cause of polyarthritis in sexually-active, healthy young adults.

Diagnosis

The diagnostic approach to anogenital GC infections is largely comparable to CT. Nucleic acid amplification testing (NAAT) is recommended and approved by the FDA for the detection of urogenital gonococcal infections in both men and women [22]. In women, vaginal and endocervical swabs and urine can be used for NAAT. In men, viable NAAT collection methods include a urethral swab or urine. Using urine for NAAT may be easier for providers and more comfortable to patients in comparison to direct urogenital swabs. Of note, in symptomatic men, Gram stain of a urethral specimen is a specific and sensitive method of diagnosing urogenital GC; however, its sensitivity diminishes if the patient is asymptomatic [22]. Although not officially approved by the FDA, NAAT can also be used for the detection of rectal or pharyngeal gonococcal infections in men and women when laboratories receive independent authorization to perform these diagnostic tests. The specific NAAT kit used is relevant for the detection of pharyngeal and rectal specimens as commensal Neisseria flora can generate false-positive results in certain kits.

Providers should be aware of the need for antibiotic susceptibility testing when patients experience possible treatment failure (i.e. persistent symptoms after completion of prescribed antibiotic course) as these cases may represent instances of antibiotic-resistance. Antibiotic susceptibility can only be determined from cultured

Neisseria gonorrhoeae and not from routine NAAT. Treatment is discussed further in the next section.

Treatment

Since 2012, the CDC has recommended treating all GC infections with both ceftriaxone 250 mg injected intramuscularly and oral azithromycin 1 g in one dose [22]. GC treatment regimens have varied significantly in the past few decades as it has developed resistance to multiple classes of antibiotics [22]. Rates of resistance to fluoroquinolones rose to levels that led to their removal from recommendation guidelines in 2007. Interestingly, these resistant strains of GC were predominantly found in MSM in the 1990s before spreading more diffusely throughout the population. Cephalosporins (ceftriaxone, cefixime) became the standard of care for GC infection at all anatomical locations following the discontinuation of quinolone utilization. Mirroring the trend seen with fluoroquinolones a few years prior, resistance toward cefixime was seen in sporadic cases of gonococcal infections in MSM in 2011. This finding prompted a national effort by the CDC to maximally reduce the development of cephalosporin resistance. Cefixime was removed from the first-line therapy recommendations for GC. Ceftriaxone is now the only first-line cephalosporin therapy indicated for GC infections. The mandatory addition of azithromycin to ceftriaxone is intended to reduce selection for cephalosporin-resistant strains of GC due to their anti-gonococcal properties. Both of these antibiotics are also effective at eliminating CT in a patient co-infected with GC and CT.

If a patient experiences therapeutic failure with persistent symptoms of GC after antibiotic treatment, a follow-up culture with antibiotic susceptibility testing is indicated as mentioned above. Although many cases of GC infection on follow-up are due to reinfection instead of treatment failure, screening the patient for cephalosporin-resistant strains of GC is important in the context of public sexual health. This is especially important for MSM, who are reported to be at increased risk for resistant infection [29].

Herpes Simplex Virus

Epidemiology

Herpes simplex virus type 1 (HSV-1) and herpes simplex virus type 2 (HSV-2) are classically known to cause lifelong, recurrent cutaneous and mucosal ulcerative lesions of the mouth and genitalia. Despite the historical notion that HSV-1 inoculation was limited to the mouth and HSV-2 was limited to the genitals, both HSV-1 and -2 are now known to be present at both sites, and both can cause the clinical syndrome known as genital herpes.

An analysis of data collected from the National Health and Nutrition Examination Survey (NHANES) showed that HSV-1 and HSV-2 affect a significant proportion of the US population [30]. From 2005 to 2010, 53.9 % of those aged 14–49 in the US were seropositive for HSV-1. HSV-2 had a seroprevalence of 15.7 % in the same age range over the same time period. Interestingly, in comparison to data from 1999 to 2004 from the same survey, HSV-1 seroprevalence decreased dramatically in the 14–19 year old age group. This correlates with recent hypotheses that childhood, non-sexual HSV-1 transmission is declining. It is unsurprising that genital HSV-1 infections have become more common as these increasing numbers of HSV-1 seronegative teenagers and young adults practice increasing rates of oral sex [31]. HSV-2 seroprevalence did not change significantly between 1999–2004 and 2005–2010 [30]. Because HSV-1 and -2 are lifelong infections, data on HSV incidence is logistically challenging to obtain, especially in older populations, and is less available than prevalence data.

Within the context of the LGBT population, both HSV-1 and HSV-2 are relevant. A study that looked at NHANES data from 2001 to 2006 showed that 18.4 % of men who had had sex with men in their lifetime were seropositive for HSV-2 [32]. A study done in New York City showed that as many as 32.3 % of their MSM population had serological evidence of HSV-2 infection, highlighting the variability of HSV-2 seroprevalence based on study population and local sexual culture [33]. Data available on HSV-1 in MSM shows a similar trend to that of

the general population; rates of anogenital HSV-1 are on the rise [34]. A study assessing the prevalence of HSV in a study population of approximately 400 WSW showed that 46 % were seropositive for HSV-1 and 7.9 % were positive for HSV-2 [35]. The authors of this study emphasized the point that genital HSV-1 may be especially predominant in the WSW population as oral sex is a major component of female-to-female sexual contact. An interesting study assessing HSV-2 seropositivity in self-identified bisexual men showed that HSV-2 infection was significantly associated with the number of lifetime female sexual partners but not with the number of male partners [36]. Thus, heterosexual behaviors were directly implicated in HSV exposure and acquisition in the MSM population.

Transmission and Acquisition

HSV is transmitted by viral particles shed from the skin or mucosal surface of an infected individual [37]. This viral shedding can occur in the setting of an active HSV outbreak (i.e. ulcerative lesions on the skin or mucosal surface) or asymptomatically. If an individual is suceptible to the virus and is exposed at an inoculable site, he/she can experiene a local, primary "outbreak" as well as develop a latent HSV infection as the virus ascends the nerve roots present in the inoculated tissue and establishes dormancy in the nerve cell bodies. The virus then periodically reactivates, causing intermittent subclinical viral shedding and recurrent cutaneous vesicular/ulcerative lesions at the initial inoculation site.

HSV seropositive patients should be educated on their risk of transmitting HSV to their sexual partner(s). The greatest quantity of viral shedding and thus transmission risk, is associated with sexual activity when active genital (or orolabial) lesions are present [38]. Any type of sexual activity—even body contact involving the affected region—should be avoided by patients with active lesions. However, asymptomatic viral shedding occurs frequently and is likely the cause of the majority of cases of HSV transmission [39]. Data suggests that HSV-2 has a greater tropism than HSV-1 for the anogenital region; this means that it is more likely to establish recurrent HSV-2 infection in this region [40]. The same holds true for HSV-1 and the orolabial region. Yet, HSV-1 can be acquired genitally from oral secretions. Within the context of the viruses' natural histories, genital HSV-1 sheds asymptomatically less often, causes breakouts less frequently, and exhibits more dramatic decreases in yearly recurrence rates compared to HSV-2 [41].

Patients should be aware that while condoms can be somewhat effective in preventing HSV transmission from asymptomatic viral shedding, any infected mucosal or skin surface can shed viral particles (as a large cutaneous surface area may be innervated by the peripheral nerves infected during the initial inoculation event) [37, 42]. For example, if a patient has a genital HSV infection, he/she may shed the virus from his/her thighs, buttocks, upper abdomen, or perineum in addition to the genitals directly.

Some data suggest that HSV-1 provides some host immunity protection against future acquisition of HSV-2 [39]. However, a patient with a genital HSV-1 infection can become infected with HSV-2 genitally as well [43]. Therefore, it is important for patients to both know their serologic status with respect to HSV-1 and -2 and continue to maintain safe sexual practices regardless of whether or not they have had a genital herpes outbreak as they may only have genital HSV-1.

Clinical Presentation

The initial, or primary, infection with HSV-1 or -2 and the associated symptoms are typically more severe than the subsequent symptomatic episodes characteristic of recurrent genital herpes [37]. Symptoms of primary infection occur a few days to a week after exposure. Primary HSV infection of the anogenitalia can manifest as local cutaneous lesions (clustered vesicles, unroofed vesicles, or crusted-over lesions), cutaneous pain, pruritus, dysuria, genital discharge, or painful inguinal lymphadenopathy (see Fig. 14.3). Systemic symptoms such as fever, malaise, headache, and muscle aches are also common in both men and women. More serious sequelae of a disseminated primary infection uncontrolled by host immune factors include encephalitis or aseptic meningitis, but these neurological conditions are rare.

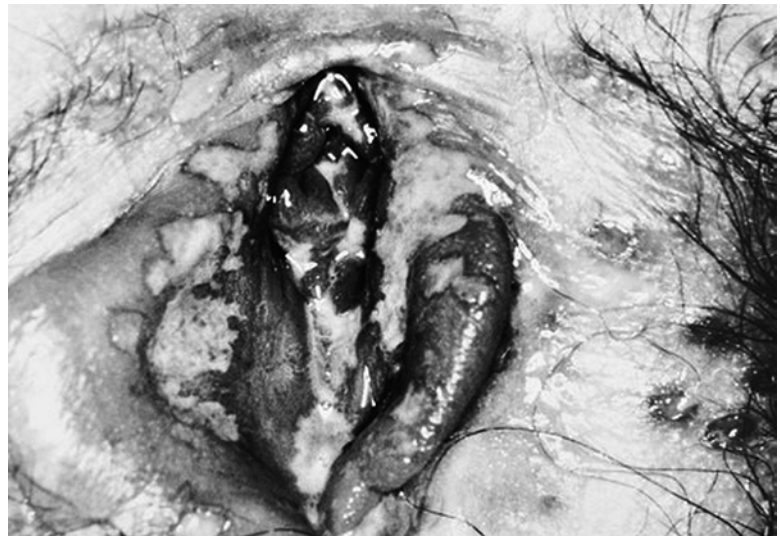

Fig. 14.3 This image depicts a very severe case of genital HSV in a female. Recurrent outbreaks of HSV are typically less extensive than the case shown here

HSV-1 and -2 outbreak recurrences typically occur at the initial site of inoculation with less severe cutaneous symptoms and few to no systemic findings [37]. Some patients may experience a prodrome characterized by tingling or pruritus in the area that later exhibits HSV vesicular lesions. As mentioned above, genital HSV-1 infections are typically milder in course compared to genital HSV-2 [41]. Individuals with HSV-1 or -2 may be entirely asymptomatic and not experience the typical symptoms of a primary infection or recurrent lesions. Others may exhibit signs and symptoms of the primary infection but never experience a recurrent outbreak and vice-versa. Atypical presentations of genital HSV are common and range from fissures to patchy erythema to excoriations. The wide variability in the appearance of genital herpes highlights the need for proper screening and diagnosis of patients with HSV from a public health perspective to decrease transmission and morbidity associated with the disease.

Diagnosis

Some cases of genital HSV may be diagnosed clinically, though laboratory confirmation is recommended [22]. Serologic testing specifically may play a role in the screening and diagnosis of HSV infection in asymptomatic individuals who may unknowingly transmit the virus to seronegative sexual partners.

The recommended confirmatory testing of an active lesion is HSV PCR performed on a swab of the base of an unroofed vesicular lesion. HSV PCR has proved superior to viral culture in terms of sensitivity, reproducibility, and time until available results [44, 45]. If HSV testing is indicated in a patient without active lesions, serological studies are available to diagnose and differentiate between HSV-1 and -2. Other indications for serologic testing include an atypical or questionable presentation of HSV infection, a negative viral culture or HSV PCR, a history of HSV lesions but no active lesions at the time of presentation, the presence of mostly healed lesions, or a person with an HSV seropositive sexual partner looking to confirm their status after exposure. Serologically differentiating between HSV-1 and -2 at the genital site has implications in quantifying a patient's risk of asymptomatic viral shedding (i.e. risk of transmission to a seronegative partner) and viral acquisition, as mentioned above, depending on the serological statuses of an individual and his/her partner(s).

Treatment

For recurrent, symptomatic genital herpes by HSV-1 or HSV-2, two treatment strategies are available: episodic and suppressive therapy. Patients with psychosocial issues related to their HSV infection, with serodiscordant sexual

partner(s) (even in the absence of outbreaks), or with frequent, painful recurrent episodes of HSV lesions, may benefit from the suppressive approach. Suppressive therapy reduces asymptomatic HSV viral shedding and symptomatic flare-ups, decreasing the risk of HSV transmission to seronegative sexual partners [46]. A typical suppressive regimen would involve acyclovir 400 mg two times per day or valacyclovir 500 mg once per day. Despite its moderately higher cost, valacyclovir may be a preferred regimen when patient noncompliance is an issue as only one dose is administered daily. Current data show that there is little risk of HSV developing antiviral resistance on long-term therapy [47]. If a patient on a suppressive regimen experiences a breakthrough recurrence, following the episodic treatment plan outlined below is appropriate. This treatment regimen conveniently uses the same dosages per pill as the suppressive regimen with a greater number of pills taken each day (see below). Of note, patient's experiencing the more severe primary outbreak may require a longer treatment course [22].

For patients who have less frequent recurrences or who are less concerned with HSV from a psychosocial or sexual transmission standpoint, episodic treatment initiated when lesions appear may be appropriate. A typical treatment regimen would involve acyclovir 500 mg three times per day for 5 days or valacyclovir 500 mg two times per day for 3 days.

As genital HSV-1 infection typically exhibits a milder course compared to genital HSV-2 [41], is serologically more common, has less frequent recurrences, and is asymptomatically shed less often at an anogenital site, suppressive therapy in patients with symptomatic genital HSV-1 may not be indicated, though patient concern may make suppression preferred.

Treponema pallidum (Syphilis)

Epidemiology

Syphilis, a disease known since antiquity, is an infection caused by the spirochete *Treponema pallidum*. Given its ability to remain asymptomatic and the concern for long-term sequelae, syphilis remains a concern to public health deserving attention. This infection is of particular interest within the LGBT community as it disproportionately affects MSM. Syphilis rates in the US declined throughout the 1990s to a nadir in 1998 of 6993 [48]. Unfortunately the 1999–2000 rates of syphilis increased, predominantly in MSM populations within large metropolitan areas such as New York City [49]. 2000–2003 saw a 19 % increase in the rate of syphilis [50]. These outbreaks often occurred among networks MSM and were aided by newer technologies such as the widespread use of the internet, as was the case with one prominent outbreak in San Francisco from a single internet chat room [51]. Even within MSM, the burden of this disease is disproportionately borne by black, Hispanic, and young MSM [52]. Multiple factors have been proposed as reasons for this increase including rising rates of HIV, less adherence to barrier methods, and lack of education about acquisition and testing for syphilis.

It is important for the provider to educate patients on the ability of syphilis to be spread in manners besides anal and vaginal penetrative sex. In one cohort, 6 % of cases of syphilis were reported in men who denied anal sex and 25 % in those who endorsed consistent condom use. Though syphilis burden is much lower in WSW populations they are also at risk for infection given the transmissibility of *Treponema pallidum* via spread of sexual secretions and cases of syphilis between female partners has been reported in the literature [53].

Clinical Presentation

Syphilis is spread via direct contact, typically during sexual intercourse. It is a fairly infectious agent with efficiency of transmission of about 30 %. It is known in medicine as "The Great Imitator" due to its myriad presentations in patients. This section by no means attempts to provide an exhaustive description of possible presentations but instead focuses on the most common presentations of the different stages of infection: primary, secondary, latent, and tertiary.

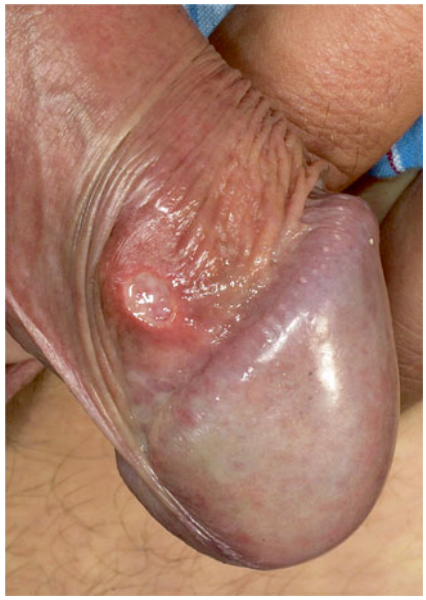

Fig. 14.4 This image depicts a penile chancre typical of a primary syphilis infection. Note the indurated, erythematous base surrounding the lesion

Primary syphilis is characterized by the classic painless ulcer, or chancre (see Fig. 14.4). The median incubation period between exposure and manifestation of chancre is 21 days. The chancre appears at the site of inoculation and is classically described as 1–2 cm, non-painful, and non-purulent. Many presentations of primary syphilis may stray from this classical presentation and thus a high level of suspicion with low threshold to test should be used with high-risk patients. The chancre may be accompanied by regional lymphadenopathy. There is usually only one chancre; however, among HIV positive patients there have been reports of multiple chancres at presentation. Due to the largely asymptomatic nature of the chancre these can go unnoticed, especially when present in the anus, oropharynx, or vaginal vault as opposed to the labia or penile shaft. The ulcer usually heals within 2–3 weeks. During this period the disease is transmissible and patients should refrain from further sexual contact until treatment is complete.

Secondary syphilis develops in about 25 % of untreated patients and usually manifests within weeks to a few months after the primary infection. Though it typically appears after resolution of the primary chancre, in immunocompromised patients secondary syphilis may appear sooner. Most patients experience rash as the predominant symptom of secondary syphilis. This rash may take many forms, excepting a vesicular rash, and is classically a maculopapular rash that does not spare the palms and soles (see Figs. 14.5 and 14.6). These are usually reddish brown 0.5–2 cm lesions that may present with or without scale. Some patients develop condyloma lata, or raised, large, white-grey lesions on mucous membranes or perineum, often adjacent to the location of the primary chancre. Condyloma lata can be mistaken for genital warts. These lesions have a very high organism burden and are highly infectious. Other systemic symptoms of secondary syphilis include fever, headache, malaise, sore throat, orogenital mucous patches, and generalized lymphadenopathy. Patients may also experience gastrointestinal symptoms, hepatitis, renal abnormalities, muscle aches, and ocular symptoms such as uveitis.

Without treatment, most cases go on to a latent, non-infectious period. During this period the disease may be spread vertically but not between sexual partners; however, about one-fourth of patients experience a recurrent secondary infection wherein they may transmit the disease. Latent syphilis can be defined as early or late latent infection, with the cutoff point between the two at 1 year. In latent syphilis, often the date of infection is not known, so the cutoff is interpreted with respect to the last known negative test. The dichotomy is important from a public health perspective given that early latent cases may identify sexual partners that should be notified from the last year, while late latent syphilis requires a longer duration of therapy than primary, secondary, and early latent infection.

About one third of untreated patients will go on to develop tertiary syphilitic symptoms. These can develop as soon as a year after infection or more indolently occur even up to 25–50 years later. These are more likely to occur more rapidly or with a more dramatic presentation in HIV-infected patients. Typically syphilis is unable to be transmitted during this stage. Classic manifes-

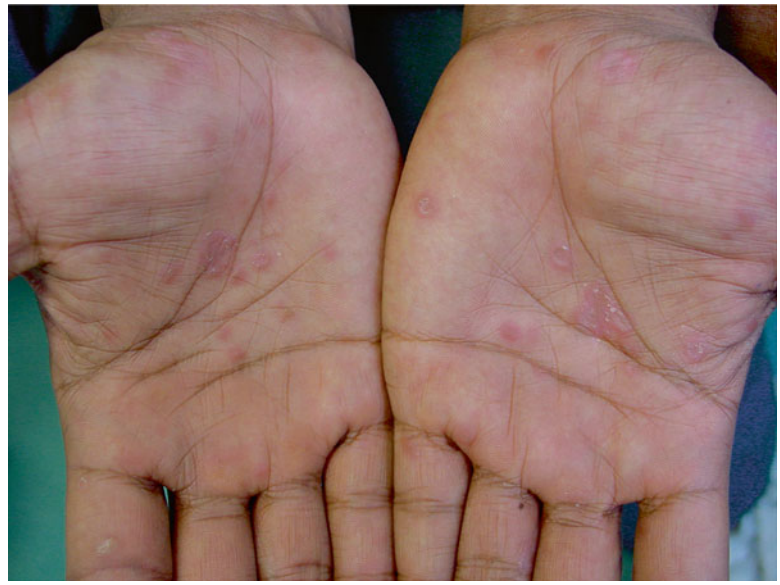

Fig. 14.5 This figure shows the palmar rash typical of secondary syphilis

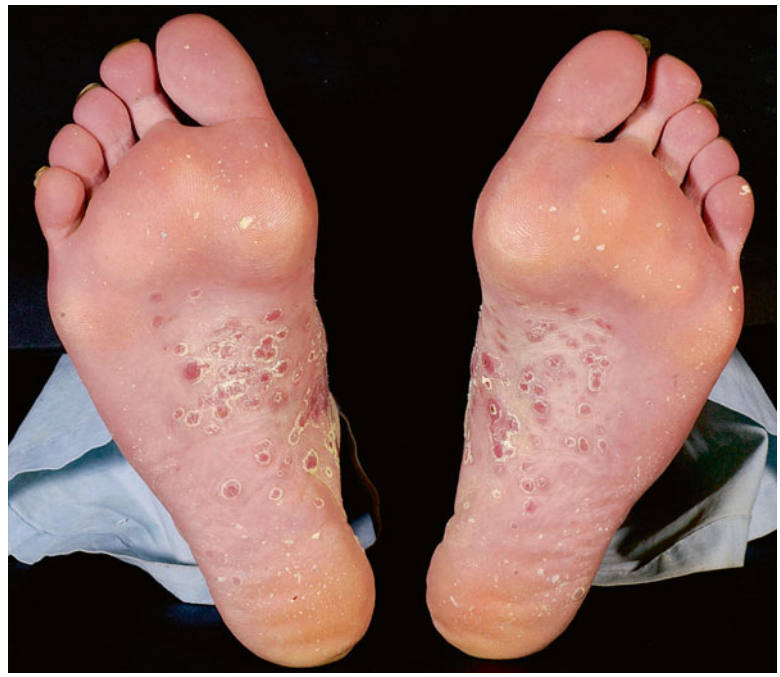

Fig. 14.6 This figure shows the rash on the soles of the feet typical of secondary syphilis

tations of this late stage of infection are gummas, cardiovascular, and neurologic findings. Gummas are the most rare manifestation and present as granulomatous lesions on the skin, bones, or internal organs (see Fig. 14.7). The classic cardiovascular symptom of tertiary syphilis is dilation of the ascending aorta. Neurosyphilis can present with symptoms ranging from meningitis to ocular symptoms (e.g., the Argyll-Robertson pupil), otologic manifestations, and tabes dorsalis. Meningitic symptoms are characteristic of early neurosyphilis and are usually seen in the first 12 months of infection, or after treatment of early syphilis in patients co-infected with HIV.

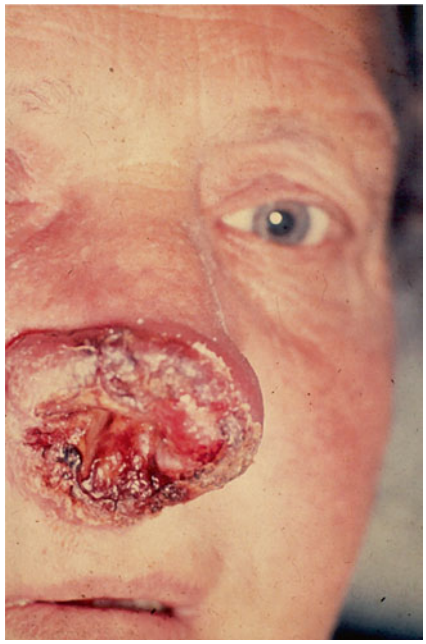

Fig. 14.7 This image shows a severe gumma on the nose of a man affected by tertiary syphilis

Late neurosyphilis occurs 10–25 years after initial infection and, while it can present with a range of neurologic symptoms, typically includes the classic tabes dorsalis and gummatous parenchymal presentations [54]. Given the varying presentations, late-stage syphilis is an important part of many differential diagnoses and the stage of this presentation has important implications for dosing and duration of treatment.

Diagnosis

Syphilis is notorious for its difficulty to culture, making live study and direct diagnosis more difficult. The classic method for diagnosis is dark-field microscopy in which the spiral treponemes light up brightly. Unfortunately this technique is not sensitive and it is rarely available in the clinical setting. Indirect serologic assays are the mainstays of syphilis testing and recommended by the CDC for diagnosis of syphilis. There are both non-treponemal and treponemal tests. Non-treponemal tests, such as the rapid plasma reagin (RPR) and the Venereal Disease Research Laboratory test (VDRL), are sensitive but not specific and are used for screening. The more specific treponemal tests, the fluorescent treponemal antibody absorption test (FTA-ABS), the *Treponema pallidum* particle agglutination test (TPPA), and the microhemagglutination-*Treponema pallidum* (MHA-TP), are used as confirmatory testing for those who test positively with screening tests. Newer PCR methods are described but not yet widely available [55]. Both screening and confirmatory tests must be positive for a diagnosis of syphilis. In the case where a patient has already been treated for syphilis, a fourfold or greater increase in non-treponemal titers represents presumptive reinfection.

Neurosyphilis can only be diagnosed via lumbar puncture and direct testing of the CSF. This should be a consideration in any patient who is displaying neurologic or ocular symptoms of syphilis infection, HIV co-infected patients with syphilitic infection of unknown duration, or patients who have failed treatment on a regimen that does not sufficiently cross the blood-brain barrier. Routine testing for neurosyphilis is not advised as early syphilis can have positive CSF findings that do not correlate with later sequelae of neurosyphilis. While CSF VRDL is very specific, its low sensitivity requires other testing including protein, cell count, and CSF-FTA. CSF-FTA is one of the most sensitive tests for neurosyphilis available and is a good test for ruling out neurosyphilis in the general population; however, as with all testing, it should be borne in mind that such a test cannot definitively rule out neurosyphilis, particularly when there is a high pre-test probability of syphilis in the patient under consideration (as may be the case, for example, with MSM populations) [56]. In otherwise healthy patients with symptoms of neurosyphilis, the CDC recommends cut-off of >5 white blood cells per mL of CSF be used to support diagnosis (a cut-off of >20 white blood cells per mL of CSF is recommended for patients with HIV). The results of these tests must be clinically correlated to patient symptoms and overall health. Patients with borderline CSF results often benefit from expert guidance in determining management with treatment versus watchful waiting with serial LPs.

Anytime there is a concern for syphilis, there should also be concern for other STI, especially HIV, and HIV testing is indicated.

Treatment

Penicillin remains the antibiotic of choice in the treatment of syphilis. There is currently no evidence of penicillin resistance in the organism. The duration and dosage of treatment depends upon the stage and symptoms of disease (see Table 14.3). Alternate regimens do exist for penicillin-allergic patients except in the cases of neurosyphilis or pregnancy, wherein desensitization therapy is the recommended treatment in these groups.

Practitioners should warn patients of the potential for the Jarisch-Herxheimer reaction upon initiation of treatment. Characterized by rash, headache, myalgias, and hypotension, this usually occurs within 1–2 h of treatment and resolves within 24–48 h. It can be managed with antipyretics and analgesics. This reaction is more common in patients who are being treated for early syphilis, those with higher RPR titers, and those who are co-infected with HIV.

Response to treatment and follow-up is somewhat specific to each stage of the disease and can be found in the CDC's Guidelines for STI Treatment [22]. In general, follow-up of non-treponemal testing is done at 6 and 12 months with a desired fourfold drop in titers at 12 months representing cure. More frequent 3-month intervals may be advisable in HIV-infected patients who are more likely to fail treatment. Finally, in patients who are not responding to treatment as expected it may be prudent to test for HIV and to consider to LP for possible CSF involvement.

Sexual partners should be offered testing. Though syphilis transmission is thought to only occur when patients have mucocutaneous lesions, sexual partners of those with latent or tertiary syphilis should still be offered testing. The guidelines for partner testing and treatment can also be found in the CDC Guidelines for STD Treatment.

Human Papillomavirus

Epidemiology

The human papillomavirus (HPV) has over 100 serotypes and 75–80 % of sexually active adults acquire some form of genital infection with HPV by age 50 [22]. Named for the visible wart lesions that it causes, it is increasingly appreciated for its role in many forms of cancer (cervical, anal, penile, vaginal, vulvar, oropharyngeal). This section focuses mainly on the manifestation of genital warts. For information on the relationship of HPV to cancer and HPV vaccination please see Chap. 17.

Within the LGBT community there are some special considerations around HPV infection. A common misconception is that WSW are at lower risk for this infection; however, HPV has been seen in WSW with no history of male partners [57]. For WSW who do have male partners, increased number of male partners represents a risk factor for HPV acquisition/infection. There is evidence that insertive toys present a potential risk for HPV transmission [58]. WSW should undergo routine Pap screening. Within the MSM population, 57 % of patients in one study were found to have anal infection with HPV with HPV 16 being the most common agent [59]. Some experts recommend that MSM who engage in receptive anal intercourse should be tested every 3–5 years with anal pap smears [60]. Again both populations may present with anogenital warts.

Clinical Presentation

Anogenital warts can range in appearance from pink to flesh colored and from flat, smooth lesions to hyperkeratotic raised lesions, to the classic condyloma acuminata (cauliflower-shaped, verrucous lesions, see Fig. 14.8). Though infection is often asymptomatic, patients can present with pruritis, bleeding, pain, or vaginal discharge (see Fig. 14.9). In certain instances, the lesions can become large and interfere with intercourse or defecation.

Diagnosis

When diagnosing the lesion, careful attention should be given to the size and extent of the lesions. Providers should use anoscopy and/or pelvic examination to search for other lesions outside of the perineal, penile, or vulvar areas. Additionally, the oral cavity should also be examined for lesions. Anogenital warts are usually diagnosed by visual inspection; however, when unclear a biopsy may be performed. Additionally, 5 % acetic acid can be applied to the area to assess for extent of disease, though this is not

Table 14.3 Pathogen, presentation, and treatment

Pathogen/Disease	Classic patient complaint(s)	Treatment recommendations
Genital herpes (HSV-1, HSV-2)	Primary infection: painful anogenital vesicular rash with associated lymphadenopathy and constitutional symptoms (e.g. fever, malaise) Recurrent outbreak: painful anogenital vesicular rash (commonly to lesser extent than primary infection) with surrounding erythema; possible prodrome	Suppressive: acyclovir 400 mg PO BID, valacyclovir 500 mg PO QD Episodic: acyclovir 400 mg PO TID ×5 d, valacyclovir 500 mg PO BID ×3 d (unless primary outbreak: acyclovir 400 mg PO TID ×7–10 d, valacyclovir 1 g PO BID ×7–10 d)
Chlamydia trachomatis serovars D-K	Urethritis: dysuria, urethral pruritis, urinary frequency, penile discharge Cervicitis: dyspareunia, postcoital bleeding, vulvovaginal irritation, cervical discharge, dysuria, urinary frequency Proctitis: bleeding (particularly with bowel movements), tenesmus, anal discharge, perianal pruritis	Azithromycin 1 g PO ×1 dose Doxycycline 100 mg PO BID ×7 d
Gonorrhea (*Nessieria gonorrhoeae*)	Similar spectrum of disease as anogenital chlamydial infections	Ceftriaxone 250 mg IM ×1 dose + azithromycin 1 g PO × 1 dose Treatment failure on follow-up: consider antibiotic resistance in addition to reinfection
Lymphogranuloma venereum (*Chlamydia trachomatis* serovars L1, L2, L2a, L3)	Painless genital ulcer that progresses to painful lymphadenopathy, late-stage disease associated with permanent lymphatic stricture	Doxycycline 100 mg PO BID × 21 d
Syphilis (*Treponema pallidum*)	Primary syphilis: painless, non-purulent genital ulcer (i.e. chancre) Secondary syphilis: maculopapular rash involving the palms/soles, condyloma lata (raised, large, white-grey lesions on mucous membranes), systemic lymphadenopathy, constitutional symptoms Latent syphilis: asymptomatic Tertiary syphilis: cutaneous gummas (granulomatous lesions with central necrosis), tabes dorsalis and other neurological manifestations, cardiovascular disease	Primary, secondary, early-latent syphilis: Benzathine penicillin G 2.4 million units IM single dose Late-latent syphilis, latent syphilis of unknown duration, non-neurological tertiary syphilis: Benzathine penicillin G 7.2 million units in 3 divided doses of 2.4 million units given a week apart Neurosyphilis: Aqueous crystalline penicillin G 18–24 million units per day, administered as 3–4 million units IV every 4 h or continuous infusion, for 10–14 days
Bacterial vaginosis	Malodorous ("fishy") clear vaginal discharge, mild vaginal pruritis	Metronidazole 500 mg PO BID × 7 d
Vulvovaginal candidiasis (Candida spp.)	Vaginal pruritus, vaginal soreness, dyspareunia, dysuria, white/curd-like ("cottage cheese") vaginal discharge	Fluconazole 150 mg PO × 1 dose Various topical azole therapies

(continued)

Table 14.3 (continued)

Pathogen/Disease	Classic patient complaint(s)	Treatment recommendations
Trichomoniasis (Trichomonas vaginalis)	Malodorous yellow-green vaginal discharge, vulvar pruritis Consider as possible etiology of urethritis (see above for symptoms) in men if refractory to empiric GC/CT therapy	Metronidazole 2 g PO × 1 dose
Pubic lice (*Pediculosis pubis*)	Anogenital pruritis, visible organisms in pubic hair	1 % Permethrin cream rinse applied and washed off after 10 min Pyrethrins + piperonyl butoxide applied and washed off after 10 min
Scabies (*Sarcoptes scabiei*)	Crusted linear/serpentine cutaneous lesions with associated pruritis	5 % Permethrin cream applied to body from neck down, washed off after 8–14 h (i.e. overnight) Ivermectin 200 μg/kg with repeated dose at 2 weeks

Note: Viable alternative therapies are available, see 2015 CDC Treatment Guidelines for more information

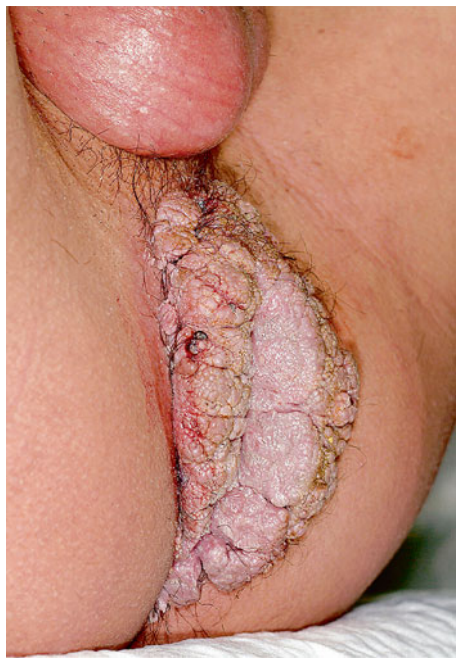

Fig. 14.8 This image shows a severe case of anorectal genital warts, also known as condylomata acuminata (singular: condyloma acuminata). These lesions are associated with an infection with human papilloma virus (HPV)

specific. In immunocompromised patients, those who lesions are growing or large in size, or with atypical features such as induration or ulceration it is prudent to biopsy for potential pre-malignant or malignant lesions.

Treatment

Treatment can generally be classified as chemical/physical ablation, immunomodulation, or surgical removal. The type of treatment initiated should be selected based on extent of the disease and patient follow-up. Podophyllin, tricholroacetic acid (TCA), and 5-fluorouracil (5-FU)/epinephrine gel have all been used as chemical agents. Imiquimod and interferon alpha are two immunomodulating agents used for treatment. Cryotherapy, laser ablation, and surgical excision are also options for removal.

Prevention

The quadrivalent HPV vaccine provides protection from the two most common HPV strains causing anogenital warts. For more information about the HPV vaccines please see Chap. 17.

Bacterial Vaginosis

Epidemiology

Bacterial vaginosis (BV) is a common infection in women caused by the loss of normal vaginal flora of lactobacilli and the overgrowth of polymicrobial facultative anaerobes. This infection is of particular importance to sexual health providers of WSW, as multiple studies have shown an association between female sexual partners and BV. During 2001–2004, the NHANES found the

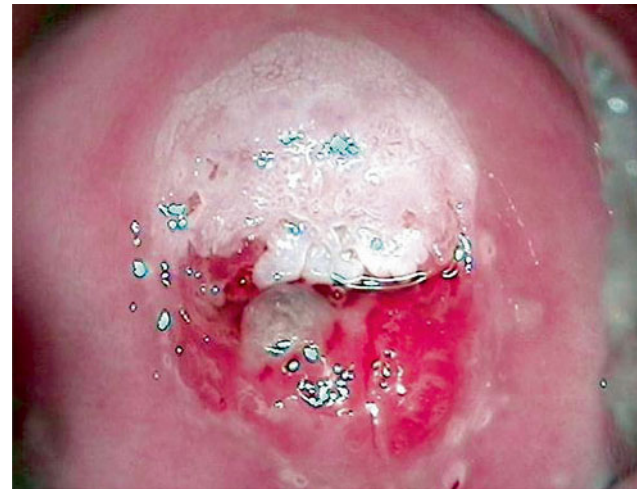

Fig. 14.9 This image shows a HPV-related genital wart on the cervix. Note the associated inflammation and bleeding

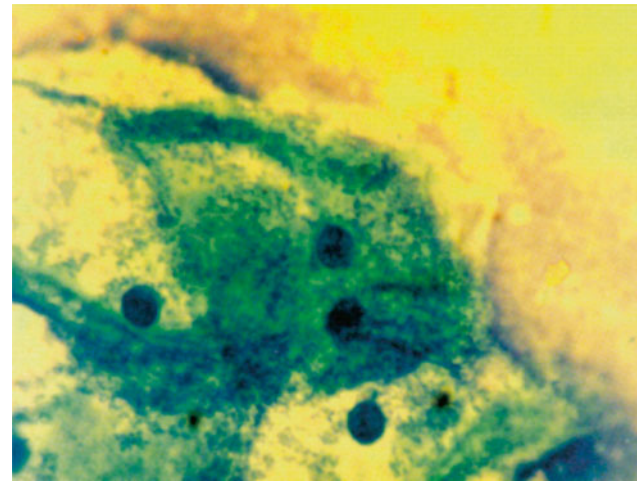

Fig. 14.10 This image shows the appearance of clue cells typical of bacterial vaginosis on light microscopy. Note the numerous bacteria coating the sloughed epithelial cells from the female genital tract

prevalence of BV in women who reported sex with a woman was significantly higher at 45.2 % than the overall prevalence of 29.2 % [61]. Additionally, self-identified lesbian women in an age-matched study in the UK showed an increased odds (of 2.5) for BV [62]. There is some evidence that a monogamous, long-term same-sex relationship is protective against BV, while more partners promote a disruption in the vaginal microbiota and increase BV rates [63]. Providers should be aware of this increased risk when treating and counseling WSW.

Clinical Presentation

BV can present with urethritis and vaginitis, though patients more often complain of increased vaginal discharge and of a "fishy" odor. This odor classically worsens with sexual intercourse and menstruation. Many patients will be asymptomatic. The diagnosis of BV is made when they meet 3 of 4 Amsel's Criteria: abnormal gray discharge, vaginal pH of greater than 4.5, a positive amine "whiff" test, and clue cells on wet prep (see Fig. 14.10).

Diagnosis

Common bacterial pathogens identified include *Gardnerella vaginalis*, *Mycoplasma hominis*, *Bacteroides* species, *Peptostreptococcus* species, *Fusobacterium* species, *Prevotella* species, and *Atopobium vaginae*. These can also be normal vaginal flora but become pathogenic when an as yet unidentified change in the vaginal microenvi-

ronment allows overgrowth of these species. The diagnosis of BV is clinical. Given the normal presence of these bacterial species in healthy vaginal flora, a positive culture for does not diagnose BV without corresponding clinical symptoms. The exception to this is in research wherein the Nugent criteria use gram stain to diagnose.

Treatment

Current treatment recommendations include metronidazole and clindamycin, with the former preferred. These come in both topical and oral administrations. Typically the oral regimens are more expensive, though many patients prefer the oral route. Often BV is recurrent and may require multiple or extended courses of antiobiotics. Additionally, patients who smoke cigarettes should be counseled on cessation as smoking has been linked to this infection [63]. BV should be treated regardless of symptoms due to increased risk for other pelvic and post-operative infections. Extra consideration of this diagnosis should be given to pregnant patients or those seeking to become pregnant as BV has been associated with low birth weight, premature rupture of membranes, and prematurity [64].

Though not classically considered a sexually transmitted infection, there may be a case for partner testing and treatment of BV in the case of WSW. In the aforementioned UK study, a significantly higher correspondence rate of 87 % was seen in lesbian-identified couples [63]. While this was not associated with sexual practices that increase the risk of exchange of vaginal secretions (such as toys) or with receptive oral sex, this significant concordance may necessitate partner testing and treatment. This is an especially important consideration in refractory cases.

Vulvovaginal Candidiasis

Candida infections are one of the three leading causes of vaginitis. This common infection happens in up to 75 % women and up to 5 % of these patients will experience recurrent episodes [65]. This is not traditionally considered in a sexually transmitted infection but has been associated with higher numbers of female partners in WSW [66]. This is similar to heterosexual studies linking a higher number of male partners to increased risk for vulvovaginal candidiasis (VVC). There is no established link between any particular sexual practice, such as use of toys, and the development of VVC.

Symptoms of infection include a thick, white, curd-like discharge as well as accompanying pruritus, burning, dysuria, and dyspareunia. Candida spp. are considered part of the natural vaginal flora and symptomatic candidiasis is typically caused by an overgrowth of these organisms. The diagnosis requires both clinical symptoms and evidence of the yeast on either probe testing or microscopic visualization on wet prep with 10 % KOH (see Fig. 14.11).

VVC can be defined as either uncomplicated or complicated. Complicated infections are those that present with severe symptoms, infections with non-*albicans* spp., four or more recurrent infections in 1 year, or infections in high-risk patient groups such as women with diabetes, other vulvovaginal pathology, immunosuppression, or pregnancy. Patients with complicated VCC may require more extended treatment and are more likely to fail standard treatment [67]. In patients presenting with complicated VVC with otherwise normal risk factors it is prudent to test for an underlying risks such as diabetes or an immunocompromised state, such as previously unknown HIV infection.

There are many treatment regimens and antifungal agents available for VVC. Many patients prefer oral fluconazole and the standard regimen of a one-time dose of 150 mg. For recurrent infections a more intensive regimen with a second dose of 150 mg fluconazole 3 days after the first has been shown to increase cure rates. In infections that fail -azole therapy, a 2-week regimen of 600-mg capsule boric acid intravaginally daily for 2 weeks is effective.

Trichomonas vaginalis (Trichomoniasis)

Trichomonas vaginalis is a protozoan parasite that is largely sexually transmitted. Though principally transmitted through intercourse, there

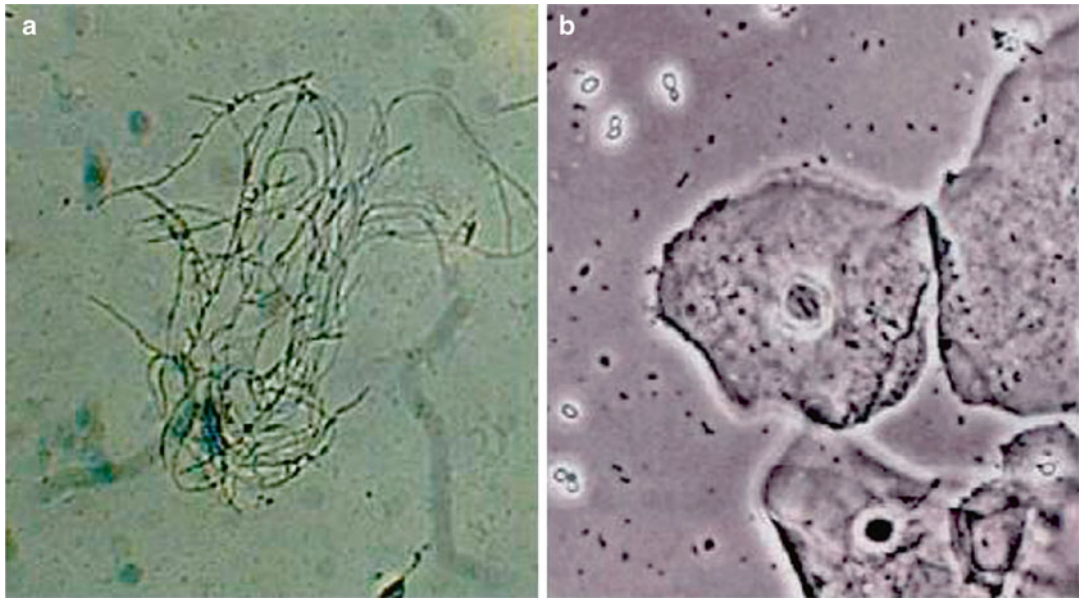

Fig. 14.11 This image shows the hyphae and associated budding typical of vaginal candidiasis seen on light microscopy

have been reports of trichomonads spread through passive transmission through vectors such as shared damp washcloths or towels. In one study of lesbian couples with trichomoniasis, this was the suggested route of transmission in one concordant couple [68]. This infection may be present along with other causes of vaginitis, especially BV. Treatment of this condition is important to reduce partner transmission as well as reduction of transmission of HIV. In a recent study of trichomoniasis in HIV positive women, trichomoniasis was associated with higher HIV-1 viral shedding [69]. In the same study, trichomoniasis synergistically increased HIV viral shedding in patients who also had BV.

Typically these infections are asymptomatic; however, it is one of the three most common causes of vaginitis in female patients. Rarely, it has been a cause of urethritis in male patients. Signs of infection with *Trichomonas* are typical vaginitis symptoms of odor, discharge, dyspareunia, and itching. The discharge of trichomoniasis tends to be copious, frothy, and often has a yellow-green tinge. Discharge of this quality should raise suspicion for this disease. Diagnosis can often be accomplished with microscopic examination of vaginal discharge (wet mount), on which trichomonads can be seen as motile flagellated organisms (see Fig. 14.12). There are also DNA probes for *T. vaginalis*, which may be of use if organisms are not found on wet mount

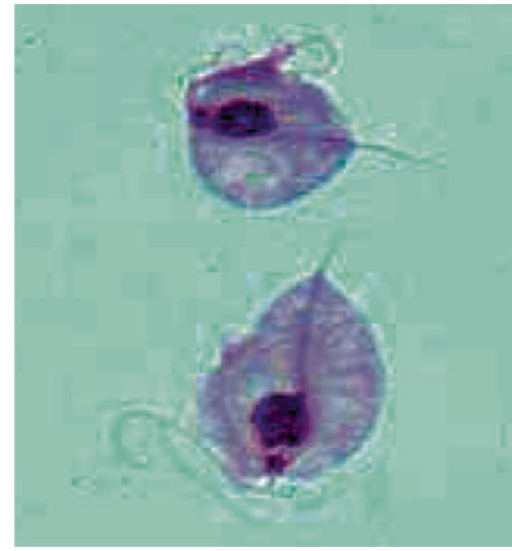

Fig. 14.12 This image shows trichomoniasis as seen on light microscopy. These organisms are often confused with cervical squamous cells on Pap smear analysis

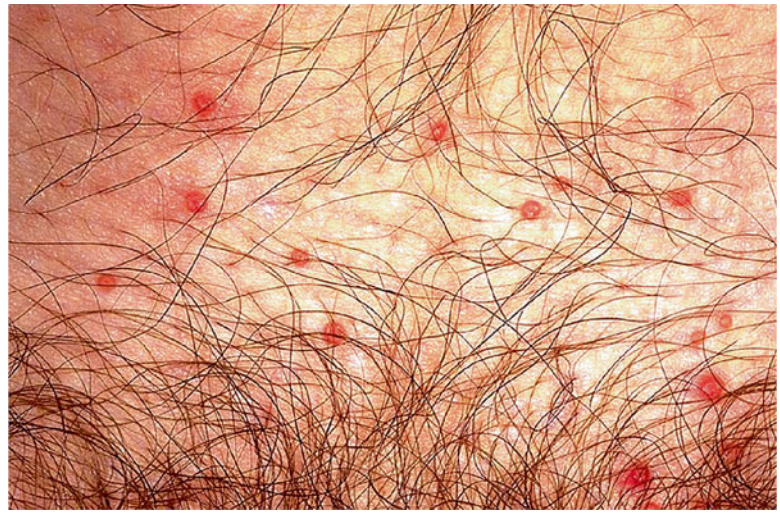

Fig. 14.13 This image depicts the dome-shaped, pearly lesions typical of an infection with molluscum contagiosum virus

but diagnosis seems probable. Treatment of trichomoniasis is usually metronidazole as a one-time 2 g oral dose, though metronidazole at 500 mg given orally three times daily for 7 days is an alternative. There is evidence of metronidazole-resistant *T. vaginalis*, including a case report in a lesbian couple [70]. Tinidazole is a reasonable first option in the case of metronidazole-resistant infections.

Pediculosis pubis: Pubic Lice

Pubic Lice (or "crabs") is an infestation with the louse *Pedculosis pubis* and characterized by pruritus in the genital and perianal region. The adult organism and nits are visible to the naked eye and are diagnostic of this infection. Spread through sexual contact, the lice are predominant in the genital area. Though rarely infesting the scalp, any region of hair is a potential site of infection, especially the axilla. Treatment is with topical drugs such as malathion 0.05 % or permethrin 5 %. Oral ivermectin 200 mcg/kg in two doses a week apart is a systemic option. Additionally, nitcombs can be used to aid in decontamination. Sexual partners should also be examined and treated. Patients should be instructed to wash all bedding and towels and dry on high heat. Anything that cannot be washed should be bagged for 72 h or longer to kill remaining lice.

Infection with *Pediculosis pubis* should prompt testing for other sexually transmitted infections, as up to 30 % of patients with pubic lice are found to have another sexually transmitted infection [71].

Molluscum Contagiosum

Molluscum contagiosum is a poxvirus spread by skin-to-skin contact. Traditionally thought of as a disease of children, these lesions are also a sexually transmitted infection and, when spread in this manner, are found in the anogenital region, inner thighs, and lower abdomen. Typically the virus manifests as 2–5 mm diameter flesh-toned, papular lesions with central umbilication (see Fig. 14.13). Most often the disease is self-limited, and lesions are cleared within a few months, though rarely they may persist for years. In the immunocompromised patient, a more severe infection can occur with confluence of multiple lesions. These can mimic other infections and biopsy may be required for diagnosis.

Diagnosis is usually made by visual inspection with the classic lesions; however, when performed, biopsy shows intracellular pox inclusion bodies. While the disease is most often self-limited, treatment may be warranted for faster clearance and to prevent further spread via autoinoculation or to others via sexual contact.

There is no standard of care for treatment of the lesions, though most first-line therapies are ablative (such as cryotherapy, curettage or electrocautery). Podophyllotoxin and, to a lesser extent, imiquimod have also been used for treatment. In immunocompromised patients with disseminated infection, trichloroacetic acid and cidofovir have been studied as possible treatment options.

Infection with molluscum contagiosum should prompt further testing for other sexually transmitted infections.

Scabies

Sarcoptes scabiei (var. *hominis*) is a human parasitic mite that burrows into the epidermis and lays eggs therein. In an immunocompetent host this typically results in a strong immunologic response characterized by intense pruritus and raised, scaled lesions that follow the burrowed path of individual mites. Transmission of mites is almost completely through skin-to-skin contact and, with a predilection for intertriginous and genital regions, often can be transmitted during sexual activity. The burden of scabies infections varies widely across the globe, being as high as 43 % of persons in some developing-world communities, though the prevalence in developed countries has been reported around 2–3 per 1000 [72].

The typical presentation of scabies is crusted linear or serpentine lesions with intense itching; often these are located in the hands, wrists, ankles, elbows, and genitals and intertriginous regions. Crusted, or Norwegian, scabies is a superinfection of thousands to millions of mites and has been described in immunocompromised hosts such as patients with advanced HIV infection [73]. Unlike the typical presentation of scabies, these patients present with non-pruritic, hyperkeratotic, scaled plaques typically with an acral distribution and resembling psoriasis. Diagnosis in either case is made through skin scrapings demonstrating mites, ovum, or feces. Identification of burrows may be aided by application and subsequent removal of washable marker as a means of highlighting the lesions. If infection is suspected highly and no mites are seen, it is prudent to treat empirically as diagnostic tests for scabies are not sensitive, and mites are often difficult to isolate.

Scabies infestations require medical and environmental measures. Medical management of the infestation can be accomplished with 5 % permethrin cream overnight. This may require two treatments 1 week apart. An oral option is two doses of oral ivermectin (200 mcg/kg each, 1 week apart). Both may be required for patients with crusted scabies. Sexual partners should be examined for scabies and treated appropriately. The hypersensitivity reaction to scabies infestations can last for weeks after the mites have been killed, so continued itching does not necessarily imply treatment failure. Patients may respond to sedating antihistamines, while corticosteroids should largely be avoided to prevent missed treatment failure. In addition to medical management, patients should be advised to machine wash and dry on high heat any items with which they have come into contact. Non-washable items should be bagged and stored for 72 h to kill remaining mites.

Other Pathogens

While this chapter has discussed some of the major pathogens causing STI in the US (LGBT) population(s), there are others that are of interest, and which should be kept in mind in the appropriate clinical context.

It is important to note that human herpesviruses (HHV) can be spread through sexual contact (specifically, the exchange of body fluids). While not considered classic STI, both Epstein-Barr virus (the etiologic agent of mononucleosis) and cytomegalovirus can cause a mononucleosis-like syndrome, with fever and adenopathy (including inguinal adenopathy). There are case reports of Kaposi sarcoma (KS) in MSM who are not HIV+ [74]. Human herpesvirus-8, the etiologic agent of KS, can be spread sexually, and should be considered in immunocompromised MSM who present with the characteristic skin/mucous membrane findings of KS.

The hepatitis viruses can also be spread by sexual contact. With case reports in the late 1990s, hepatitis A was noted to be increasingly common epidemiologically in MSM, and shortly after, was added to the list of vaccines to be considered in special populations (specifically, MSM) [75]. More recently, sexual activity has been appreciated as an important mode of transmission of hepatitis C, and the cause of several clusters of cases [76]. Both hepatitis C and hepatitis B are relatively highly prevalent and incident in MSM populations, especially those who are co-infected with HIV, and this remains the case despite the universal recommendation for hepatitis B vaccination [77, 78].

In addition to these sexually transmitted pathogens, some pathogens may be spread by intimate (not necessarily sexual) contact and may travel along networks. As LGB populations are, in part, defined by their sexual activity, and sexual activity often occurs within the context of a network, some pathogens may be encountered disproportionately in LGB populations (as well as T populations) or subpopulations regardless of sexual contact.

For example, methicillin-resistant *Staphylococcus aureus* (MRSA), which can be spread by any form of intimate or close contact (amongst other modes of transmission), has been reported in clusters of MSM whose only exposure was sexual contact [79]. Not all cases of transmission of MRSA lead to identifiable disease; some lead to colonization, though the two are correlated. Some studies have not shown higher rates of carriage of MRSA in MSM when compared to the general population [80], lending support to the hypothesis that the increase in MRSA infections seen in MSM may be due to spread along (sexual) networks, or in some other more limited way, rather than by higher colonization rates of the MSM population in general.

Recently, an outbreak of invasive meningococcal disease has been reported in MSM in certain urban areas [81]. In these cases, it is unclear that sexual contact has played a role in transmission. Regardless, many have advocated immunization of MSM against meningococcus, and recently some public health departments have started immunization campaigns in select cities [82].

Thus, it is important for those who provide care for LGBT populations to be attuned to both traditional STI and non-traditional pathogens that may be transmitted along the networks of our LGBT patients.

A Brief Discussion of Clinical Syndromes

Genital Ulcerative Lesions

Patients presenting with ulcerative lesions of the genitals almost immediately raise concern for sexually transmitted infection. Though other non-infectious etiologies (Behcet's disease, Crohn's disease, drug reactions) may be the culprit, in sexually active adults a sexually transmitted infection is the most common etiology. HSV and primary/secondary syphilis, respectively, make up the vast majority of these cases. In 2012 HSV was the cause of about 240,000 office visits [15]. 15,667 cases of primary and secondary Syphilis cases were reported to the CDC in 2012 [15]. Chancroid (caused by the bacterium *Haemophilus ducreyi*) is the other most common cause, and in comparison had 15 reported cases in 2012 [15]. Other sexually transmitted infections that cause ulcerative lesions are lymphogranuloma venereum (*C. trachomatis*) and granuloma iguinale (*Klebsiella granulomatia*). Though these are both rarer, of note LGV when seen in more developed countries was associated with MSM sexual activity [83].

History and physical exam are the most useful in determining the etiologic agent of ulcerative genital disease. The typical HSV presentation is multiple, painful and burning vesicular lesions with occasional bilateral lymphadenopathy. Primary syphilitic lesions are classically painless, indurated, and with clean bases. Chancroid often presents with multiple, painful, ragged-edged ulcerations with classically unilateral, suppurative lymphadenopathy. In contrast, the ulcerative lesion of LGV is less commonly seen,

while bilateral, suppurative adenopathy raises suspicion for this etiology. Finally granuloma iguinale has a classic beefy, granular ulceration without true adenopathy.

Given the potential overlap in presentation, and the possibility of atypical presentation, diagnostic testing becomes critical. The most useful tests are HSV PCR of a swab of the lesion (though culture and/or Tzanck smear may be useful in certain circumstances), RPR (or treponemal antibody test), and Gram stain from the edge of the ulcer (if chancroid is suspected). In the MSM population, especially those with recent international travel, LGV PCR or serology may be considered. When the etiology remains unclear with the above means, biopsy is warranted. For more information on HSV, Syphilis, and LGV please see the respective pathogen sections above.

Urethritis

Symptomatic urethritis in men is classically characterized by mucopurulent or purulent urethral discharge, dysuria (pain on urination), and/or urethral pruritus. Infectious urethritis as a syndrome is classically divided by etiology into gonococcal urethritis and non-gonococcal urethritis (NGU). Gonococcal urethritis is caused by *Neisseria gonorrhoeae* as its name suggests. NGU most commonly results from infection with *Chlamydia trachomatis*, but *Mycoplasma genitalium*, *Trichomonas vaginalis*, HSV-1 and -2, and adenovirus may also be responsible [84]. Many cases of NGU may not have an identifiable etiology upon comprehensive laboratory analysis [85]. Empiric therapy is thus recommended regardless of the outcome of diagnostic studies when treating men with symptoms of urethritis.

A health care provider's first step in assessing a patient with possible urethritis should be to establish clinical evidence of disease. Providers should look for urethral discharge when examining a patient. If available, Gram stain of discharge can detect elevated white blood cell counts (≥5 WBC per oil immersion field, suggestive of urethritis) and/or Gram-negative intracellular diplococci (diagnostic for gonococcal urethritis). First-void urinalysis can be used to look for presence of leukocyte esterase (a nonspecific indicator of urogenital tract infection) or white blood cells on microscopy (≥10 WBC per high-power field). Once a diagnosis of urethritis is made (or heavily suspected), further etiological testing is indicated to ensure proper treatment. This primarily includes NAAT for GC and CT.

Treatment should be started immediately upon diagnosis. Specific therapy for GC and CT are discussed in their respective sections above. It is important to note that, although azithromycin and doxycycline are approved antibiotic regimens for the treatment of NGU, azithromycin has proved superior in the treatment of *M. genitalium* urethritis [85]. If a patient fails initial therapy and noncompliance and pathogen reexposure are ruled out, further diagnostic testing for HSV or *T. vaginalis* may be indicated. HSV diagnosis and treatment is discussed above. Of note, MSM are at low-risk for *T. vaginalis* unless they also participate in sexual intercourse with women [22].

Proctitis

Clinically, proctitis in men is characterized by inflammation of the distal 10–12 cm of the anorectum and is associated with anorectal pain, anorectal discharge, and/or tenesmus (a persistent sensation of needing to pass stool despite an empty rectal vault). This syndrome must be differentiated from proctocolitis and enteritis, which involve more proximal regions of the gastrointestinal tract and are caused by different pathogens despite possible overlapping clinical pictures. As mentioned above, the majority of cases of gonococcal and chlamydial proctitis in MSM are asymptomatic, highlighting the need for effective screening strategies. Besides CT and GC, *Treponema pallidum* (i.e. syphilis) and HSV-1 and -2 must also be considered as possible etiologies of infectious proctitis [22].

Providers should ensure they are completing effective sexual histories to screen for men who may participate in receptive anal intercourse as this is the sexual behavior that primarily puts patients at risk for infectious proctitis. Patients should be

examined for rectal discharge or any external ulcerative lesions. Anoscopy may be necessary to visualize more proximal areas of the distal rectal mucosa. Diagnostic and therapeutic information for the pathogens mentioned above (i.e. GC, CT, HSV-1 and -2, syphilis) are discussed in their respective sections.

Cervicitis

Inflammation of the uterine cervix is often an asymptomatic condition discovered on routine health maintenance. When patients present with symptoms, typical complaints include mucopurulent discharge, post-coital bleeding or intermenstrual spotting, dysuria, dyspareunia, or vulvovaginal irritation. The most common causes of this condition are gonorrhea and *chlamydia*, which are discussed in detail earlier in the chapter.

Patients with the above symptoms warrant a pelvic exam. If cervical motion or adnexal tenderness is elicited, NAAT for gonorrhea and chlamydia should be performed. There are no prominent reports of transmission of the aforementioned pathogens between female partners, though male partners of WSW should be tested and treated for these infections. Empiric treatment should cover both pathogens. Untreated cervicitis may progress to pelvic inflammatory disease, tubo-ovarian abscess, and salpingitis. It is important to test regularly for these infections in WSMW, as untreated cervicitis may progress to these more serious infectious as well as infertility.

Vaginitis

Vaginitis is a common clinical complaint of female patients characterized by vaginal burning, itching, odor, and abnormal discharge. The vast majority of these cases are caused by three etiologies: bacterial vaginosis, candidiasis, and trichomoniasis. Of note WSW patients are at equal—and in the case of BV, increased—risk for these infections. These three causes are each elaborated within the specific pathogen sections above. Though inflammatory and atrophic changes can also be to blame, these are not discussed here.

This clinical syndrome should raise concern for an infectious cause as over 90 % of cases are due to an infection or overgrowth of natural flora. When seeing a patient with these complaints a pelvic exam with careful examination of the vulvar skin for evidence of infection is warranted. Samples for wet mount, potassium hydroxide testing, the amine whiff test, and pH testing are advisable in almost all cases. These should be taken from the mid-portion of the vagina to avoid contamination with cervical mucus. Specific DNA probes for the most common causes may be warranted if the above testing and physical exam are non-diagnostic. Finally, depending upon the risk factors of the patient, remembering that identity does not determine sexual behavior, DNA amplification testing for gonorrhea and *Chlamydia* may also be a consideration.

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