19
Sexually Transmitted Infections

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Key Concepts

- Nucleic acid amplification tests are superior to culture to screen for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infections. The best specimens are vaginal or endocervical swabs from women and first catch urine samples from men.
- Nucleic acid amplification tests for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* can be used for rectal and oropharyngeal specimens in addition to genital sites to increase the sensitivity of testing.
- If one suspects failure of standard antibiotic treatment for gonococcal infection then a culture needs to be performed to evaluate antibiotic susceptibility.
- Male and female patients with infections causing rectal or genital ulcerations are at increased risk for HIV infection, compared to patients with non-ulcerative STIs.
- Patients diagnosed with syphilis should be tested for HIV. Patients with HIV should be regularly screened for syphilis.
- Empiric treatment for proctitis in populations at high risk for STIs should be given at the time of evaluation rather than waiting for test results, and should consist of treatment for gonorrhea, chlamydia/lymphogranuloma venereum, and genital herpes.
- Herpes simplex virus is a common cause of proctitis in men who have sex with men and often present without visible external ulcerations.

Introduction

This chapter discusses sexually transmitted infections (STIs) that are likely to be encountered by colorectal surgeons. Clinicians must maintain a high level of suspicion for STIs to avoid delays or errors in diagnosis. A frank discussion of the patient's sexual history should direct STI testing and empiric therapy.

A substantial proportion of patients with STIs are completely asymptomatic. Overall, 7 % of men who have sex with men (MSM) undergoing screening for STI test will be positive for at least one infection. Asymptomatic MSM who report an STI exposure have a 17 % chance of testing positive for at least one STI. An HIV-positive MSM with an STI is twice as likely to be asymptomatic from the STI than an HIV-negative MSM with an STI [1].

"Sexually transmitted diseases" and "sexually transmitted infections" are interchangeably used terms, but the latter has been increasingly adopted to emphasize that infections may not cause symptoms of disease, nor may they result in development of disease. For example, infection with the human papillomavirus may not develop into the diseases of cervical cancer or anal cancer. This term is also regarded as less stigmatizing and thus may result in improved testing rates.

This chapter will discuss the diagnosis and management of STIs, as well as the risk factors for infection and public health concerns related to the infections.

Screening Guidelines for Asymptomatic High-Risk Patients

The predominant risk factor for contracting STIs is high-risk sexual behavior. Other risk factors include current infection with ulcerative STIs and HIV seropositivity. MSM, especially those who engage in unprotected receptive anal intercourse, represent the demographic group at greatest risk for STIs and should undergo regular universal testing for STIs. People in high-risk sexual networks such as swingers are also at very high risk for STIs and should also undergo universal testing for STIs. A policy of universal testing can help to stop the cycle of ongoing transmission of STIs within these networks [2].

Furthermore, MSM and other high-risk populations including prostitutes and swingers should undergo testing for STIs (mainly, chlamydia and gonorrhea) at anorectal,

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TABLE 19-1. Initial sexually transmitted infections (STI) testing and empiric therapy by symptom

Symptom	Suspected etiology	Testing	Empiric therapy
Genital, anal, perianal ulcers	Herpes Syphilis Chancroid Donovanosis	Syphilis serology HSV culture or PCR HIV *H. ducreyi* testing in settings where chancroid is prevalent	Treatment for HSV or syphilis depending on clinical suspicion
Proctitis	Gonorrhea Chlamydia Syphilis Herpes	Intra-anal swabs for chlamydia and gonorrhea and HSV culture or PCR	Treatment for gonorrhea, chlamydia/LGV, and herpes depending on clinical suspicion and risk factors
Proctocolitis	*Campylobacter*, *Shigella*, and *Entamoeba histolytica* LGV	Stool studies NAAT for chlamydia	
Enteritis	*Giardia*	Stool studies	

HSV herpes simplex virus, *LGV* lymphogranuloma venereum, *PCR* polymerase chain reaction, *NAAT* nucleic acid amplification tests

oropharyngeal, and urogenital sites, as isolated non-urogenital infections represent the majority of infections in both MSM and high-risk women. With testing at multiple anatomic sites, over 10 % of MSM had chlamydia and 6 % had gonorrhea, while 7 % of female prostitutes and swingers had chlamydia and 3 % had gonorrhea. Given that most of these infections were isolated non-urogenital infections, the practice of coincidental treatment is an inadequate strategy for controlling transmission of these infections [3].

Screening Guidelines for Symptomatic Patients

Symptoms of STIs may include painful or painless perianal or genital lesions; rectal, vaginal, or urethral discharge; or proctitis. Table 19-1 details the suspected etiologies, recommended testing, and empiric therapy by symptom class.

Perianal or Genital Lesions

Lesions or other symptoms involving the anus and perianal skin may be easily mistaken for other diagnoses, such as fissure or hemorrhoid disease, delaying appropriate treatment. Lesions in the perianal skin may also be misdiagnosed as a perianal fistula or abscess, folliculitis, hidradenitis, or pruritus ani. Patients (and sometimes their physicians) are likely to assume that any discomfort in the anal region can be attributed to hemorrhoids and will start empiric treatment for hemorrhoids without confirming the diagnosis. Thus, it is imperative to perform at least a visual inspection of the perianal skin and anal canal when evaluating any anorectal complaint. Digital exam with anoscopy should also be performed if the patient can tolerate it.

Genital lesions in young sexually active patients are most likely to be genital herpes or syphilis. Less commonly, chancroid and donovanosis may also be the cause of genital ulcers.

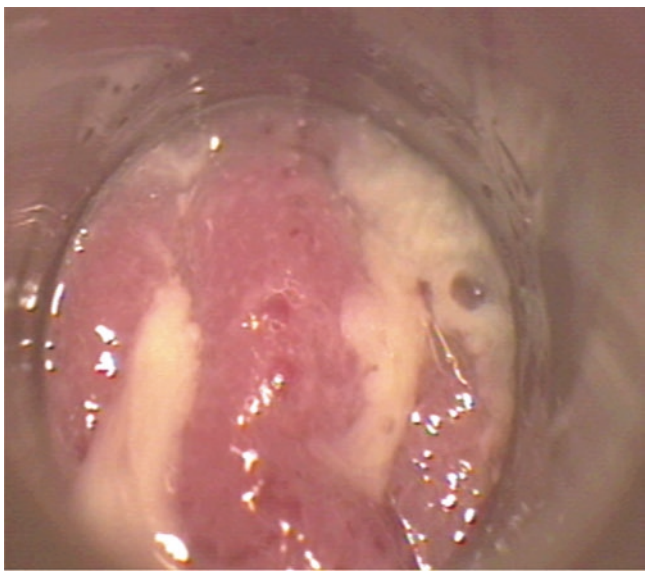

FIGURE 19-1. Patients with STIs may present with proctitis, characterized by anorectal pain, tenesmus, and mucopurulent discharge. Proctoscopy may not be possible due to pain.

Patients should undergo serologic testing for syphilis and HSV culture or PCR, as well as HIV testing. Empiric treatment of the most likely pathogen should be started. Painless lesions may be condyloma or other HPV-related dysplasia. The genital lesions of molluscum contagiosum may cause pruritus.

Proctitis

Proctitis is inflammation of the rectum, causing symptoms of anorectal pain, tenesmus, and discharge (Figure 19-1). The suspected etiologic agents are *N. gonorrhea*, *C. trachomatis*, *T. pallidum*, and HSV. Patient discomfort may preclude a proctoscopic examination, but intra-anal swabs for chlamydia and gonorrhea and HSV can and should be performed. Swabs should be taken before doing a rectal

exam with lubricant given its bacteriostatic properties. Infectious proctitis is often misdiagnosed as inflammatory bowel disease so it is important to elicit a clear sexual history to help distinguish between the two. Anorectal pain and bleeding may also signal the presence of a malignancy such as anal or rectal cancer.

Patients who present with both symptoms of proctitis as well as anal ulceration are very likely to have HSV (83 %) or gonorrhea [4]. However, as over two-thirds of MSM with HSV proctitis do not have a concomitant external ulceration, it is important to test for HSV in these patients without the classic herpetic ulcer [4].

HIV-positive MSM presenting with proctitis are more likely than their HIV-negative counterparts with proctitis to be infected with HSV-1 (14 % vs. 7 %) or HSV-2 (22 % vs. 12 %), lymphogranuloma venereum (8 % vs. 0.7 %), or multiple STIs (18 % vs. 9 %). They are equally likely to have chlamydia or gonorrhea [4]. Empiric treatment for proctitis should be given at the time of evaluation rather than waiting for test results and should consist of treatment for gonorrhea (ceftriaxone 250 mg intramuscular × 1 day), chlamydia/LGV (doxycycline 100 mg bid × 21 days), and HSV (valacyclovir 1 g bid × 10 days). Symptom management with topical anesthetics and stool softeners will also be helpful. When test results come back, the medication regimen can be adjusted.

Proctocolitis

Proctocolitis causes symptoms of proctitis (anorectal pain, tenesmus, and discharge) along with diarrhea and abdominal cramps. Lower endoscopy reveals inflammation of the rectal and distal colonic mucosa. Stool studies may reveal fecal leukocytes. The suspected etiologic agents include *Campylobacter*, *Shigella*, and *Entamoeba histolytica*. LGV serovars of *C. trachomatis* may also cause proctocolitis. The route of transmission may be oral or oral-anal.

Enteritis

Symptoms of enteritis include diarrhea and abdominal cramping; since the rectum is not involved, patients will not present with proctitis symptoms. Enteritis acquired as an STI can be attributed to oral-anal contact. The most common etiologic agent is *Giardia lamblia*.

Diagnosis and Management of Sexually Transmitted Bacterial Infections

Testing for Chlamydia and Gonorrhea

Nucleic acid amplification tests (NAATs) are 86 % sensitive and 97 % specific for detecting gonorrhea and chlamydia, regardless of the specimen type used [5]. NAATs are also superior to other forms of testing due to the increased ease of specimen transport. The Centers for Disease Control (CDC) recommends that NAATs be used in all circumstances to detect chlamydia and gonorrhea, except for special circumstances involving prepubescent patients, and potential treatment failures in which cultures are indicated [6].

Gonorrhea

Epidemiology

Neisseria gonorrhoeae is the causative agent in gonococcal infections and represent the second most common notifiable communicable disease in the US with over 300,000 cases reported to the CDC in 2011. This is likely a gross underestimation of the actual disease burden due to underdiagnosis and underreporting. While US public health efforts have made great strides in controlling gonococcal infection, there are still groups within the population suffering from particularly high rates of gonorrhea, including MSM, HIV-positive patients, African Americans, adolescents, and young adults [7].

Clinical Presentation

Most men infected with gonorrhea experience urethritis manifesting as painful urination. They may also experience epididymitis or disseminated infection. Proctitis can also occur in those who engage in anal receptive intercourse. Gonococcal infections in women tend to be asymptomatic although they can cause cervicitis, urethritis, proctitis, and, later, pelvic inflammatory disease.

*Screening and Testing for **N. gonorrhoeae***

MSM with high-risk sexual practices such as multiple anonymous partners and unprotected oral and anal intercourse are at higher risk for gonococcal infections affecting the oropharynx and rectum. For this reason, the CDC recommends routine screening of oropharyngeal, anorectal, and urogenital sites for all MSM who are sexually active and at risk for STI.

NAATs are the recommended testing method given their high sensitivity and specificity [5]. First catch urine or urethral swab is the recommended sample type for men. In women, the recommended sample types are vaginal swabs that can be either self- or clinician-collected or endocervical swab if a pelvic examination is also indicated. First catch urine in women may miss 10 % of infections compared to the other sample types [6]. Rectal and oropharyngeal specimens can also be tested with NAATs. The CDC recommends testing extragenital sites to increase the sensitivity of screening. Patients who test positive by NAAT do not need to undergo routine repeat testing as this does not improve the positive predictive value of the test [6].

Treatment and Management of Gonorrhea

For uncomplicated gonococcal infections, the CDC recommends combination therapy with ceftriaxone 250 mg intramuscular injection plus a single dose of oral azithromycin 1 g, or a 7-day course of oral doxycycline 100 mg twice daily [8]. Azithromycin is preferred due to the high prevalence of tetracycline resistance. Patients with allergies to cephalosporins can be treated with a single oral dose of azithromycin 2 g, but *N. gonorrhoeae* isolates have demonstrated resistance to azithromycin (Figure 19-2).

N. gonorrhoeae culture testing to evaluate for antibiotic susceptibility with rectal or oropharyngeal swab, endocervical swab for women, or urethral swab for men should be performed if treatment failure is clinically suspected, or NAAT positivity persists [6].

Patients who have undergone treatment for gonorrhea should be referred to programs to reduce STI risk and also undergo retesting for gonorrhea at 3 months. Sexual partners of infected patients in the preceding 2 months should also undergo treatment with ceftriaxone and azithromycin [9].

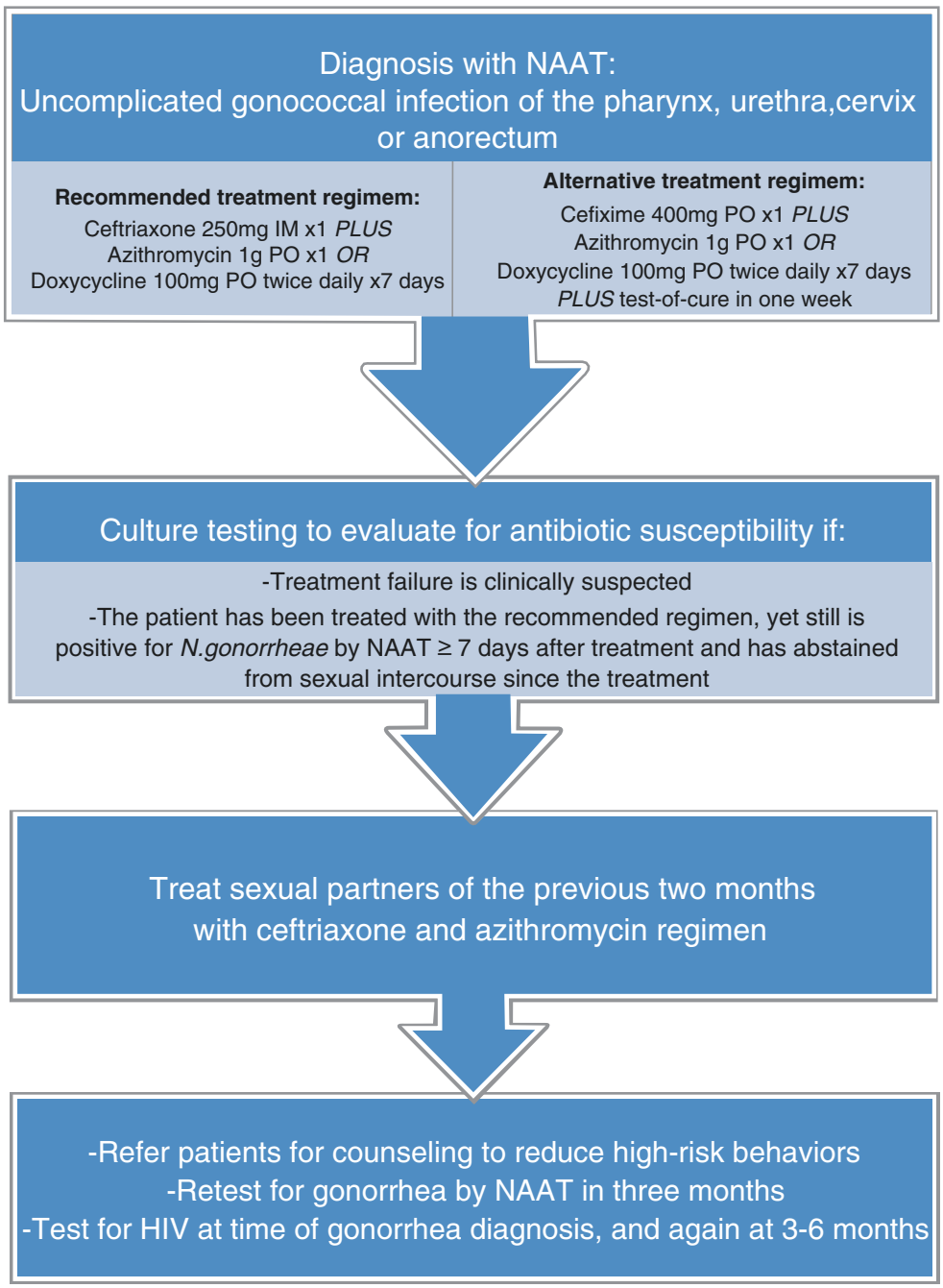

FIGURE 19-2. Treatment algorithm for patients with *N. gonorrhoeae* infection.

As patients with gonococcal infection have a higher risk of HIV infection, they should also undergo testing for HIV at the time of gonorrhea detection and 3–6 months later.

Emerging Antibiotic Resistance

N. gonorrhoeae has a record of developing antibiotic resistance—to penicillins and tetracyclines in the 1980s and then to fluoroquinolones in the 2000s [7]. Resistance to cephalosporins is developing as well, limiting treatment options to third-generation cephalosporins [9, 10]. MSM are more likely than heterosexual men to be infected with resistant strains of *N. gonorrhoeae* [11]. As antimicrobial susceptibility testing is not routinely performed, clinicians need to maintain a high suspicion for treatment failure and must report treatment failures [12].

Chlamydia

Epidemiology

Infection with *Chlamydia trachomatis* is the most common notifiable disease in the USA with over 1.3 million cases reported to the CDC in 2010. The prevalence of urogenital chlamydia is over 11 % and anorectal chlamydia is over 8 % among women undergoing STI evaluation [13].

Clinical Presentation

Most patients with chlamydia are asymptomatic or have such mild nonspecific symptoms that a visit to a physician never occurs, and they never become aware that they are infected. Therefore, screening is crucial to controlling this disease and preventing the severe potential sequelae of pelvic inflammatory disease that increases the risk of infertility (20 %), chronic pelvic pain (18 %), and ectopic pregnancy (9 %). Men with chlamydia infection most commonly have symptoms of urethritis; a smaller proportion has epididymitis and an even smaller proportion experiences infertility as a result of the infection. Infections affecting the rectum are usually asymptomatic and can be attributed to unprotected anal receptive intercourse (Figure 19-3). However, some patients may develop proctocolitis. Ocular infection and reactive arthritis can also occur.

*Screening and Testing for **C. trachomatis***

As for gonorrhea, the recommended testing method for *C. trachomatis* is the NAAT. The recommended sample type for men is a first catch urine or urethral swab. For women, vaginal swab is recommended and if a pelvic examination is indicated then endocervical swab is also an acceptable sample type. Urine samples from women are less sensitive. Rectal and oropharyngeal specimens should also be used for screening

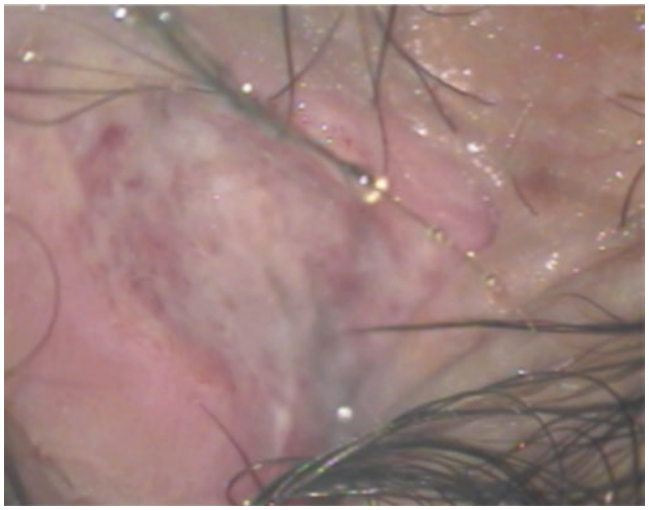

FIGURE 19-3. Chlamydia infection may present with no symptoms, mild symptoms, urethritis, ulcerations, or proctitis. Pictured is an ulcer due to chlamydia infection. Photograph courtesy of Stephen Goldstone, MD.

to increase the sensitivity of the test. Positive NAATs do not need to be routinely repeated [5, 6].

There is a high incidence of co-occurrence of anorectal and urogenital chlamydia in women—over 94 % of women with anorectal infection also have urogenital chlamydia, and over 71 % of women with urogenital infection also have anorectal infection [13].

Due to its high prevalence and serious sequelae and the potential to reduce the incidence of pelvic inflammatory disease, the CDC and the US Preventive Services Task Force recommend screening sexually active women aged 24 and younger for chlamydia, as well as older women at increased risk for infection [5, 14]. Selective testing based on symptoms and sexual history is an inadequate strategy for identifying most cases of chlamydia infection [13].

Routine universal screening for men is not recommended, as complications from chlamydia infection in men is rare. Chlamydia screening is recommended for certain high-risk male populations based on prevalence data. These populations include men in STI clinics, National Job Training Programs, and juvenile detention facilities, as well as men under 30 years old who are in the military or in jail, and men whose partners have been diagnosed with chlamydia [15]. For all MSM reporting receptive anorectal intercourse, rectal chlamydia screening is recommended [16].

Treatment and Repeat Testing

A single oral dose of 1 g of azithromycin is the recommended treatment for *C. trachomatis* infection and should be given empirically for acute nongonococcal urethritis or for suspected or proven infection in women. A 7-day course of twice daily doxycycline 100 mg is equally effective [17].

TABLE 19-2. Centers for Disease Control recommended antibiotic regimens for bacterial sexually transmitted infections (STIs) [18]

Infection	Recommended regimens	Alternative regimens
Chlamydia trachomatis	Azithromycin 1 g PO × 1 dose or doxycycline 100 mg PO twice daily × 7 days	Erythromycin base 500 mg PO four times daily × 7 days or erythromycin ethylsuccinate 800 mg PO four times daily × 7 days or levofloxacin 500 mg PO once daily × 7 days or ofloxacin 300 mg PO twice daily × 7 days
Neisseria gonorrhoeae	Ceftriaxone 250 mg IM injection × 1 dose *plus* azithromycin 1 g PO × 1 dose *or* doxycycline 100 mg PO twice daily × 7 days	Cefixime 400 mg PO × 1 *plus* azithromycin 1 g PO × 1 *or* doxycycline 100 mg PO twice daily × 7 days plus test-of-cure in 1 week
Acute proctitis in patient with recent receptive anal intercourse, with anorectal exudate or WBCs on gram-stained smear	Treat empirically with: ceftriaxone 250 mg IM × 1 dose plus doxycycline 100 mg PO twice daily × 7 days	
LGV proctitis/proctocolitis (MSM with anorectal chlamydia and proctitis or HIV)	Doxycycline 100 mg PO twice daily × 3 weeks	Erythromycin base 500 mg orally four times daily for 3 weeks
Primary, secondary, or early latent syphilis	Penicillin G benzathine 2.4 million units IM × 1 dose	Doxycycline 100 mg orally twice daily for 2 weeks or tetracycline 500 mg four times daily for 2 weeks (Penicillin-allergic pregnant women with syphilis should undergo desensitization and be treated with penicillin regimen)
Tertiary or late latent syphilis or syphilis of unknown duration	Penicillin G benzathine 2.4 million units IM once per week × 3 weeks	
Neurosyphilis	Aqueous crystalline penicillin G 18–24 million units per day, administered as 3–4 million units IV every 4 h or as a continuous infusion, × 10–14 days	
Chancroid	Ceftriaxone 250 mg IM × 1 dose or azithromycin 1 g PO × 1 dose or ciprofloxacin 500 mg PO twice daily × 3 days or erythromycin base 500 mg PO three times daily × 7 days	
Granuloma inguinale (Donovanosis)	Doxycycline 100 mg PO twice daily[a]	Azithromycin 1 g PO once per week[a] or ciprofloxacin 750 mg PO twice daily[a] or erythromycin base 500 mg PO four times daily[a] or trimethoprim/sulfamethoxazole 800 mg/160 mg PO twice daily[a]

WBC white blood count, *HIV* human immunodeficiency virus, *MSM* men who have sex with men, *LGV* lymphogranuloma venereum

[a]All regimens are for at least 3 weeks duration and should be continued until all lesions have healed

Alternative regimens include 7-day courses of erythromycin, levofloxacin, or ofloxacin (Table 19-2) [18]. Azithromycin is also effective treatment for the other infectious causes of nongonococcal urethritis aside from *C. trachomatis*, including *Mycoplasma genitalium* and *Ureaplasma urealyticum* [19]. The single dose of azithromycin is preferred as it can be given directly to the patient at the time of testing to maximize compliance. Patients should be instructed not to engage in sexual intercourse for 7 days after the single dose of azithromycin (or until they complete the full 7-day course of the other antibiotic regimens), and they should also avoid having sexual intercourse until their partners are treated as well to avoid reinfection [18]. Patients should be counseled to refer anyone with whom they have had sexual contact in the 60 days prior to chlamydia diagnosis or symptom onset for testing and treatment.

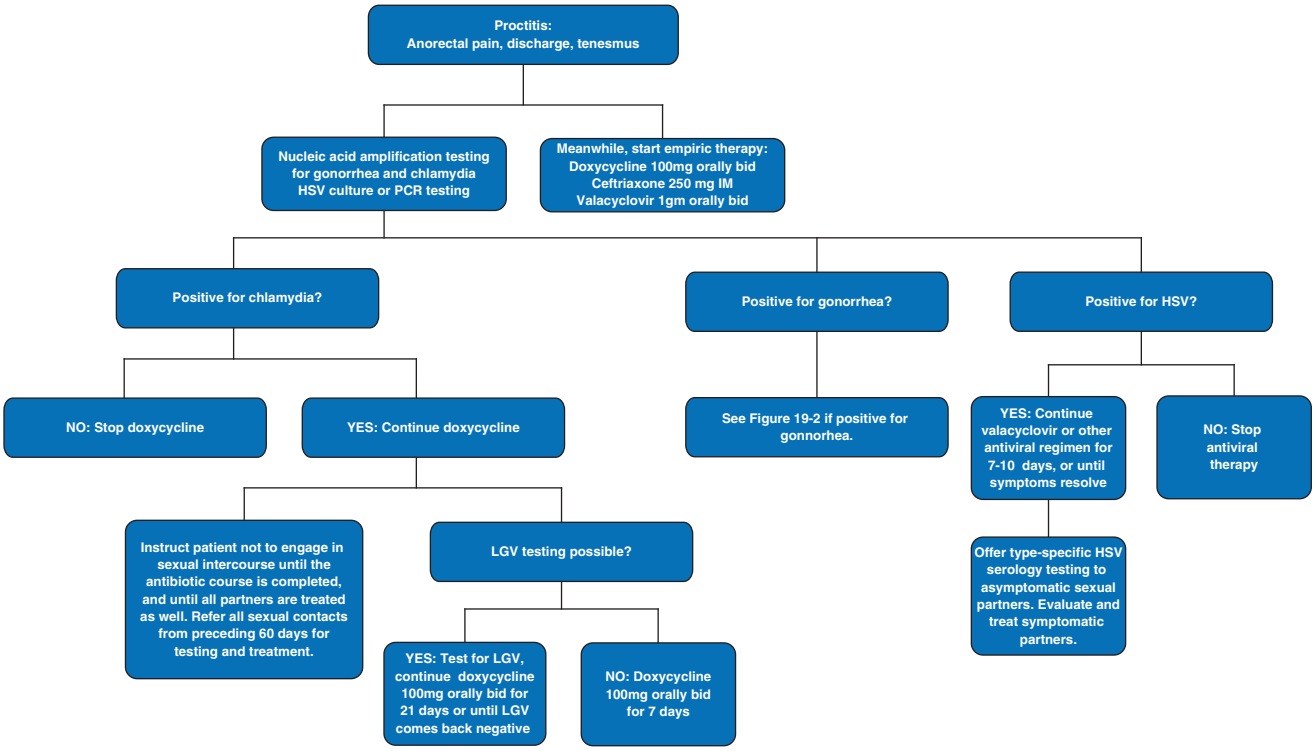

FIGURE 19-4. Management algorithm for MSM with proctitis reporting receptive anal intercourse.

Routine test-of-cure several weeks after treatment for chlamydia is not recommended by the CDC if the patient has undergone appropriate treatment and is asymptomatic with no suspicion of reinfection. However, as recurrent chlamydial infections are common in both men and women after treatment due to reinfection, repeat testing should be performed three months after treatment [15, 18].

Lymphogranuloma Venereum

Epidemiology

C. trachomatis serovars L1, L2, and L3 cause lymphogranuloma venereum. L2b has been identified as the main causative agent of the recent epidemic [20]. While anorectal infection with non-LGV *C. trachomatis* serovars A-K is mild and often asymptomatic, the LGV serovars cause severe inflammation and invasive infection. LGV has reemerged recently in its anorectal form due to outbreaks within MSM sexual networks. Infection has been associated with attendance at sex parties as well as HIV seropositivity. Hemorrhagic proctitis due to LGV has only been reported in MSM [21–24]. Risk factors for LGV proctitis include HIV seropositivity and chlamydia with concurrent ulcerative disease, previously diagnosed STI, unprotected receptive anal intercourse with casual partners, MSM, having sex at sex parties, and having sex with HIV-positive partners [16, 25]. MSM with anorectal chlamydia should undergo LGV testing; if it is not available, then MSM with anorectal chlamydia and either proctitis, >10 white blood cells per high-power field on anorectal smear, or HIV seropositivity should be treated empirically for LGV [16]. A recommended algorithm for testing and treatment of chlamydia and LGV for MSM reporting anal intercourse is detailed in Figure 19-4.

Clinical Presentation

Depending on the site of primary inoculation (genital vs. anorectal), patients will manifest different syndromes. Patients with the inguinal syndrome (genital inoculation) experience unilateral painful inguinal or femoral lymphadenopathy (buboes), possibly with a genital ulcer. Patients with the anorectal syndrome experience ulcerative proctocolitis or proctitis characterized by mucopurulent discharge and tenesmus, along with systemic constitutional symptoms (Figures 19-5 and 19-6) [20]. Untreated LGV infection can result in severe complications including colorectal fistulas and strictures, elephantiasis, infertility, and pelvic fibrosis [21].

The proper diagnosis of LGV is frequently delayed because symptoms can be misleading, physicians may be unfamiliar with the disease, and there is no routine diagnostic

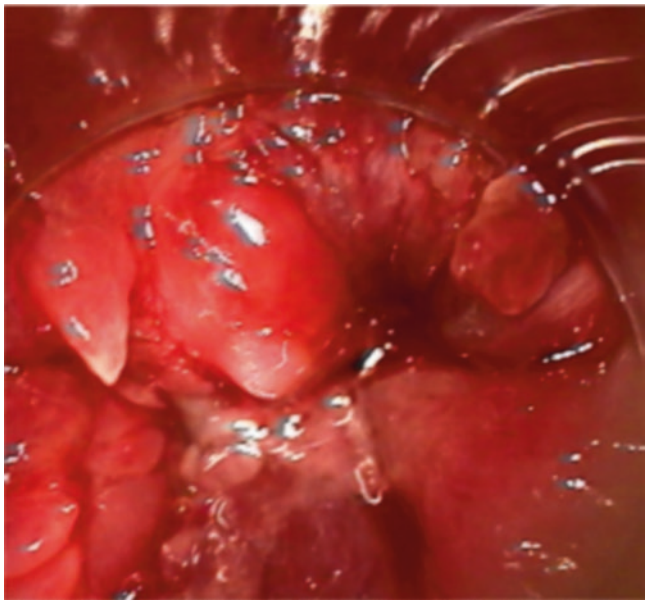

FIGURE 19-5. Proctitis due to lymphogranuloma venereum, demonstrating marked inflammation one week after treatment started. Photograph courtesy of Stephen Goldstone, MD.

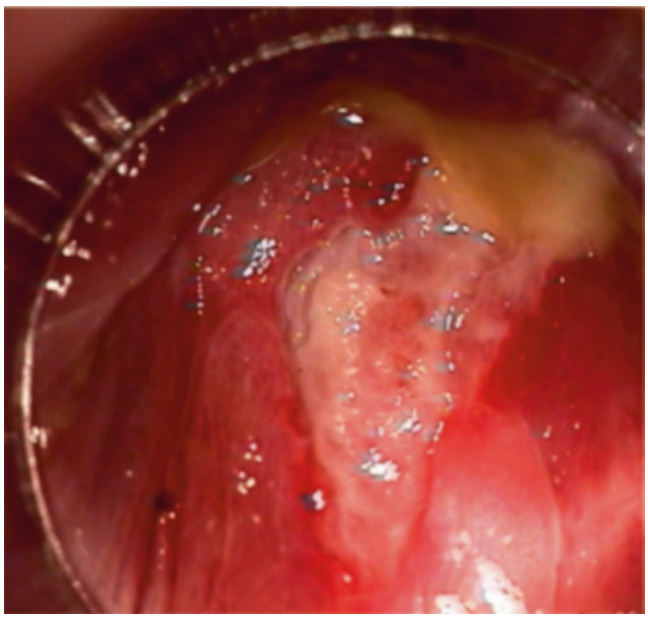

FIGURE 19-6. After two months of treatment for lymphogranuloma venereum, proctitis has resolved and ulcerations are healing. Photograph courtesy of Stephen Goldstone, MD.

test for LGV serovars [20]. Since LGV proctocolitis presents with bleeding, pain, and tenesmus, it can be mistaken as inflammatory bowel disease [21, 22]. Even pathologic specimens from endoscopic examination can be confusing, as mucosal ulcers, cryptitis, crypt abscesses, and granulomas are common histological findings that can also be attributed to inflammatory bowel disease [22, 23].

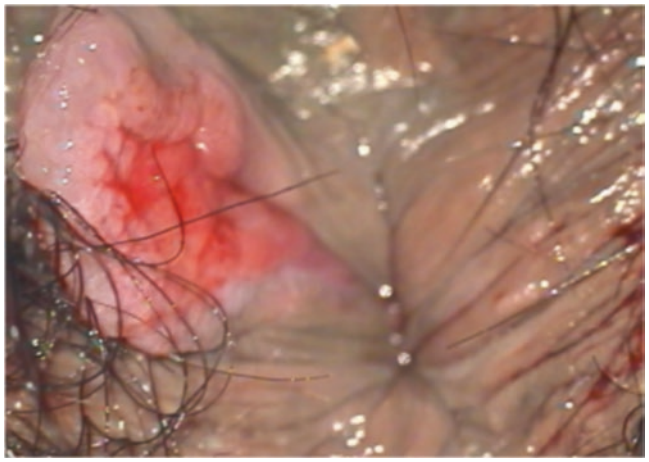

FIGURE 19-7. Chancre due to primary syphilis. Photograph courtesy of Stephen Goldstone, MD.

Treatment

The recommended treatment for LGV proctitis is twice daily doxycycline 100 mg orally for 3 weeks or for as long as anorectal symptoms persist. Buboes may require aspiration or incision and drainage to prevent ulcerations. Clinical follow-up should be continued until signs and symptoms have resolved. Sex partners from the preceding 60 days should undergo testing for chlamydia and be treated for chlamydia (one oral dose of azithromycin 1 g or one week of doxycycline) (Table 19-2) [20].

Syphilis

Epidemiology

Rates of primary and secondary syphilis, after declining for many years to a nadir of 2.1 cases per 100,000 in the year 2000, have experienced a concerning resurgence to over double that rate to 5.3 per 100,000 in 2013. Over 90 % of cases of primary and secondary syphilis occur in men, and the rise in syphilis rates is attributable to increases in men [26, 27]. Men in their 20s, MSM, black men, and Hispanic men have had the greatest increases. Rates of syphilis among women increased in the mid 2000s but have since decreased again. Similar to their male counterparts, the rate among black and Hispanic women is higher than in white women [27]. Half to a third of MSM infected with syphilis are coinfected with HIV, and the rates of HIV seroconversion following syphilis infection are high [27].

Clinical Presentation

Syphilis, caused by the spirochete *Treponema pallidum*, presents classically in its primary form as a solitary nontender genital chancre, but it can also present with multiple chancres or proctitis with bleeding, pain, and tenesmus (Figures 19-7, 19-8, and 19-9). Only a third of patients are

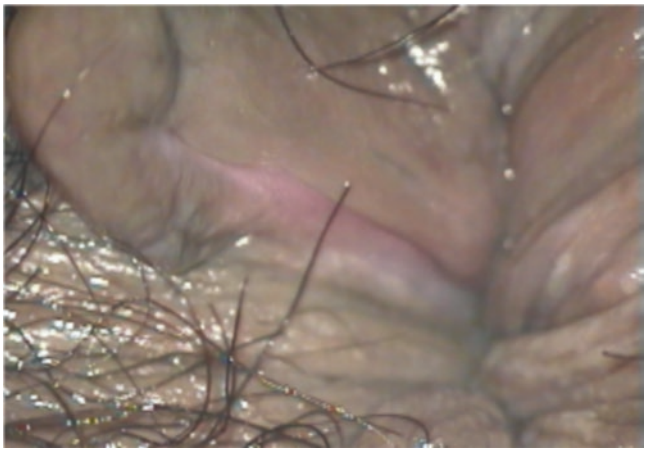

FIGURE 19-8. Healed chancre after resolution of primary syphilis. Photograph courtesy of Stephen Goldstone, MD.

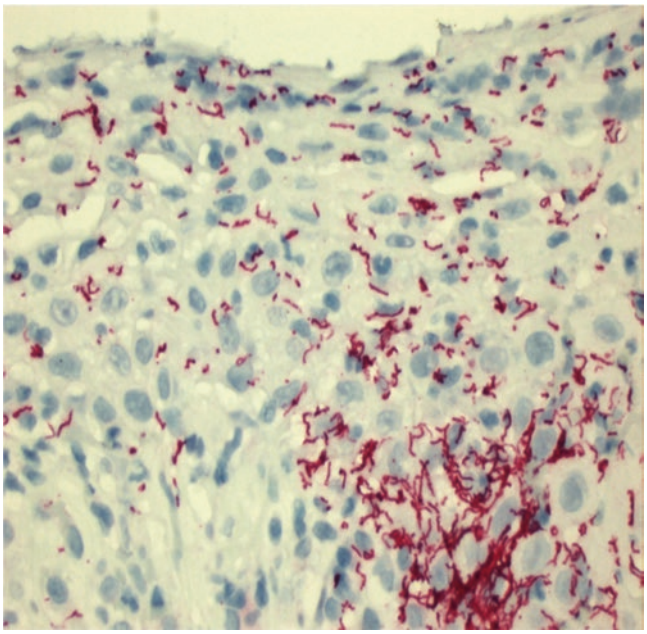

FIGURE 19-9. Immunohistochemistry staining for spirochetes, indicative of syphilis infection. Photograph courtesy of Stephen Goldstone, MD.

diagnosed during the primary infection as the primary chancre can be quite small and unnoticeable. HIV-positive patients have a higher rate of asymptomatic primary syphilis, may experience more aggressive secondary infection, and are at increased risk of developing neurosyphilis [28].

Testing Recommendations

Two types of serologic tests are used to make a presumptive diagnosis of syphilis. The nontreponemal tests include the Venereal Disease Research Laboratory (VDRL) and RPR tests and are used for screening as they become positive within 3 weeks of the primary chancre. Dark field examination to detect *T. pallidum* in lesion exudate or tissue may be successful in diagnosing early syphilis, as the nontreponemal tests may be negative in these early stages. Some patients may manifest a serofast reaction, causing the nontreponemal test to be elevated for a long period of time [26]. Treponemal tests include the fluorescent treponemal antibody absorbed tests, *T. pallidum* passive particle agglutination assay, and other immunoassays. These tests usually remain reactive for life in patients who have had a reactive test at one point. Patients with a positive nontreponemal test should undergo a confirmatory treponemal test. Patients with a negative VDRL or RPR but with strong clinical indicators of primary syphilis should undergo repeat nontreponemal testing two weeks later [18, 26]. Confirmed cases of syphilis must be reported to local and state health departments.

Due to the rebound in syphilis rates disproportionately affecting MSM, all sexually active MSM should be screened at least annually for syphilis, more frequently if they engage in high-risk sexual practices such as having multiple or anonymous sex partners [18, 27]. Due to the high rate of coinfection with HIV, patients with syphilis should undergo HIV testing, and all patients with HIV should undergo regular syphilis screening [18, 28].

Treatment

The CDC recommends a single intramuscular dose of 2.4 million units of penicillin G benzathine for primary, secondary, and early latent syphilis [18, 26]. Patients coinfected with HIV should be treated with the regimen recommended for the treatment of neurosyphilis and should be closely monitored due to increased rates of relapse [28]. The Jarisch-Herxheimer reaction, an acute febrile reaction characterized by headache, myalgia, and fever, may develop within 24 h of treatment and occurs most commonly in patients with early syphilis. Patients with penicillin allergy should be treated with doxycycline, tetracycline, ceftriaxone, or azithromycin. Pregnant women with syphilis and a penicillin allergy should undergo desensitization and treated with penicillin. Sexual contacts of patients with primary, secondary, or early latent syphilis should undergo presumptive treatment.

Treatment of primary and secondary syphilis should result in a decline of the nontreponemal test titers over the ensuing months. Repeat testing with nontreponemal tests should be performed at 6 and 12 months after treatment [18]. Retreatment for relapse should consist of 2.4 million units of intramuscular penicillin G benzathine weekly for three weeks (Table 19.2) [18].

Chancroid

Chancroid, caused by *Haemophilus ducreyi*, has declined worldwide but is a common cause of genital ulcer disease, a risk factor for HIV transmission. It usually presents with

multiple painful purulent genital ulcers that progress through pustular and ulcerative stages, as well as painful regional lymphadenopathy with bubo formation. Perianal chancroid is less common than genital chancroid but can occur in MSM. Diagnosis can be difficult due to its rarity. There are no FDA-approved tests for it in the USA. Thus, diagnosis of chancroid is made based on symptoms of painful genital ulceration and regional lymphadenopathy in the absence of syphilis and HSV [18].

First-line treatment of chancroid includes azithromycin, erythromycin, ceftriaxone, and ciprofloxacin, detailed in Table 19.2 [29]. HIV-positive patients may have a higher risk of treatment failure with single-dose regimens. Inguinal bubo formation requires at least a two-week course of antibiotic therapy and may also require aspiration or incision and drainage to prevent spontaneous rupture [30, 31].

Granuloma Inguinale (aka Donovanosis)

Granuloma inguinale is a rare tropical genitoulcerative disease caused by *Klebsiella granulomatis* (formerly *Calymmatobacterium granulomatis*), endemic in Papua New Guinea, South Africa, India, Brazil, and Australia. The mode of transmission is via sexual contact, fecal contamination, and autoinoculation [32]. Clinical presentation includes papules or nodules that progress into a painless ulcer, usually in the genital area. Disseminated disease may cause cervical ulceration, pelvic lymphadenopathy, and septic arthritis and can be mistaken for cervical and ovarian cancer [32, 33]. Coinfection with HIV may worsen the course of the disease with more ulceration and tissue damage and thus the need for prolonged antibiotic therapy. Malignant transformation can also occur in HIV-positive patients [34, 35]. Testing is performed using tissue smears from the lesions and microscopic identification of characteristic intracytoplasmic inclusion bodies (Donovan bodies). PCR has recently become available as well. Treatment regimens include three-week courses of doxycycline, ciprofloxacin, erythromycin base, or trimethoprim/sulfamethoxazole [32].

Diagnosis and Management of Sexually Transmitted Viral Infections

Herpes

Epidemiology

Herpes simplex virus types 1 and 2 (HSV-1 and HSV-2) are common in the population with a seroprevalence of 54 % and 15.7 %, respectively [36]. Both may cause anogenital herpes infection. While most cases are caused by HSV-2, HSV-1 is an increasing etiologic agent in anogenital herpes, especially among heterosexual women and young MSM [37, 38]. The overall seroprevalence of HSV-2 has decreased among the 14–49-year-old population in the USA over the last two decades—from 21.2 % in the late 1980s and early 1990s to 15.5 % in the late 2000s. However, this decrease is due mainly to decreases among whites while the rates in black men and women have not changed, thus representing increased racial disparity. Over 90 % of patients with genital herpes are unaware that they have it [39]. Primary prevention of genital herpes is difficult due to the high rates of unrecognized infection [40]. HSV has been found to be frequently reactivated for short periods of time (less than 12 h) and then rapidly cleared without causing clinical symptoms, likely by the peripheral mucosal immune system. These subclinical reactivations may also contribute to increased transmission [41, 42]. Men with HSV infection, even when asymptomatic, also have higher rates of HIV shedding which has implications for increased HIV transmission.

Clinical Presentation

HSV infections classically present with multiple painful vesicular ulcers, although not all infected patients have these symptoms (Figure 19-10). HSV is the most common cause of proctitis among HIV-positive men, occurring in more than a third of HIV-positive MSM with proctitis. HSV is the cause of proctitis in 20 % of HIV-negative men with proctitis [4]. Only a third of patients with HSV proctitis have external ulcers as well, thus underscoring the need to test and treat for herpes in MSM with proctitis, regardless of the presence of ulcers [4]. HSV-2 infection is more likely to cause recurrences than HSV-1 infection. Patients who also have HIV are more likely to have more severe and painful lesions, and increased HSV shedding, even when they are asymptomatic.

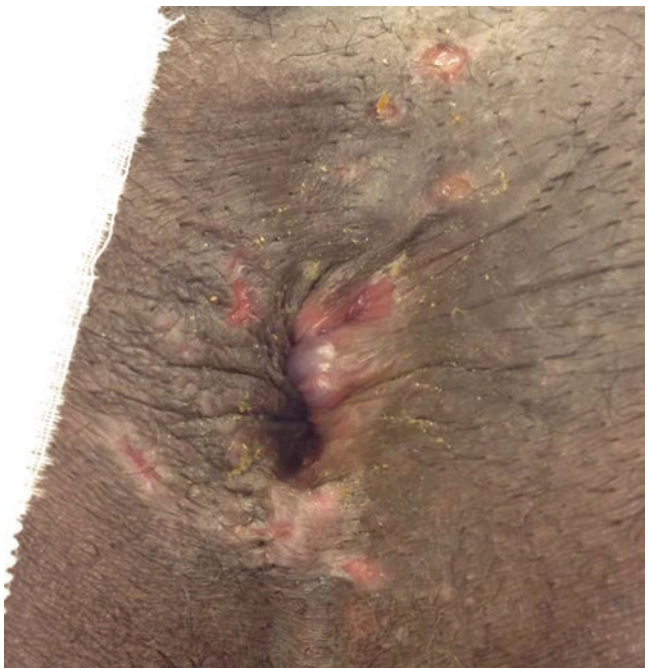

FIGURE 19-10. Perianal herpes lesions that have started to resolve.

Testing and Screening

HSV testing can be performed with cell culture or PCR, although a negative result may be attributed to intermittent viral shedding. Type-specific HSV serologic assays are also available and can be used to evaluate patients with symptoms of genital herpes but with negative HSV cultures, patients who have a partner with genital herpes, patients seeking an STI evaluation, HIV-positive patients, and MSM at high risk for being infected with HIV. Routine screening of the general population is not recommended.

Treatment

The first clinical episode of genital herpes can cause severe ulcerations as well as systemic symptoms. Therefore, treatment with antiviral therapy—acyclovir, famciclovir, or valacyclovir—is recommended to shorten the course of the episode. Suppressive antiviral therapy can decrease the number of recurrences in patients with frequent recurrences (at least four per year) [43]. Suppressive therapy may also be indicated to decrease the risk for transmission to sexual partners, especially when the patient's sexual partner is not positive for HSV, or if the patient has multiple partners [44]. Condom use and avoidance of sexual activity during recurrences offer additional protection against transmission to HSV-negative partners [45]. Another option for recurrent genital herpes is the use of episodic treatment. Recommended regimens for treatment of the first clinical episode, suppressive therapy, and episodic therapy are detailed in Table 19-3. Rarely, HSV can cause severe complicated disease requiring hospitalization and intravenous acyclovir therapy. For patients coinfected with HIV, suppressive herpes treatment with valacyclovir has also been shown to decrease rectal, seminal, and plasma HIV levels [46–51]. HSV resistance to acyclovir, valacyclovir, and famciclovir may result in persistent infections, which will need to be treated with alternative regimens such as foscarnet or cidofovir. Asymptomatic sex partners should be offered type-specific serologic testing for HSV infection, and symptomatic sex partners should be evaluated and treated accordingly.

Human Papillomavirus

Epidemiology

Over 40 different HPV types can cause genital infection, and most infections are asymptomatic and self-limited. Sexually active people have at least a 50 % risk of becoming infected at least once in their lifetime, if they are not vaccinated. Low-risk HPV types include HPV types 6 and 11, and these are the most common etiologic agents for genital warts, while the high-risk HPV types 16 and 18 are associated with cancers of the anus, cervix, penis, vulva, and vagina. Genital warts may also harbor more high-risk HPV types 16, 18, 31, 33, and 35 and may contain areas of high-grade dysplasia. These precursor lesions are common among high-risk populations such as MSM- and HIV-positive patients, occurring in over half of HIV-positive MSM and over a third of HIV-negative MSM [52].

Clinical Presentation

While the majority of infections with HPV are asymptomatic and self-limited, some patients may develop genital warts, dysplastic lesions, or cancer depending on the virus type. Genital warts, or condyloma, present as growths on the genital mucosa, anal mucosa, and perianal skin (Figure 19-11). Patients with warts within the anal canal may have a history of receptive anal intercourse but not necessarily. Symptoms may include pain, pruritus, discomfort, or bleeding, depending on the location and size of the warts. Patients with HIV infection or another source of immunosuppression are more likely to develop genital warts, and these warts are less likely to respond to treatment and more likely to recur.

The high-risk HPV types can cause invasive squamous cell cancers of the anus. Squamous cell carcinoma occurs more frequently in patients who are immunosuppressed, especially in patients who are coinfected with HIV. Disturbances in the peripheral immune function in the anal mucosa may explain this increased risk to progress to invasive anal cancer [53–56].

Testing

HPV testing can be used to screen women for cervical cancer, but screening for HPV is not indicated for men, sex partners of women with known HPV, adolescent women, or for other HPV-related malignancies such as anal cancer [18].

As certain high-risk populations such as HIV-positive MSM have seen a rise in incidence of invasive anal squamous cell carcinoma, screening programs to detect precursor lesions have been developed to prevent progression to invasive cancer [52]. Liquid-based anorectal cytology specimens are the preferred specimen type to screen for high-grade anal dysplasia [57]. Self-collected samples are less sensitive than clinician-collected samples [52]. Patient with positive findings should be referred to a specialist for high-resolution anoscopy or routine anoscopy and monitoring.

Treatment

The indication to treat anogenital warts is to relieve symptoms. Untreated genital warts may self-resolve or worsen. Treatment does not affect the risk of transmission of HPV. External genital warts can be treated in a variety of ways (Table 19-3). Patients may apply their own treatment at home

TABLE 19-3. Centers for Disease Control recommended treatment regimens for viral STIs [18]

Infection	Recommended regimens
Genital herpes (HSV-1 or HSV-2): first clinical episode	Acyclovir 400 mg PO three times daily for 7–10 days or acyclovir 200 mg PO five times daily for 7–10 days or famciclovir 250 mg PO three times daily for 7–10 days or valacyclovir 1 g PO twice daily for 7–10 days
Suppressive therapy for recurrent genital herpes (frequent recurrences)	Acyclovir 400 mg PO twice daily or famciclovir 250 mg PO twice daily or valacyclovir 500 mg PO once daily[a] or valacyclovir 1 g PO once daily
Suppressive therapy for patients coinfected with HSV and HIV	Acyclovir 400–800 mg PO twice to three times per day or famciclovir 500 mg PO twice day or valacyclovir 500 mg PO twice daily
Episodic therapy for recurrent genital herpes	Acyclovir 400 mg PO three times daily for 5 days or acyclovir 800 mg PO twice daily for 5 days or acyclovir 800 mg PO three times daily for 2 days or famciclovir 125 mg PO twice daily for 5 days or famciclovir 1000 mg PO twice daily for 1 day or famciclovir 500 mg once, then 250 mg PO twice daily for 2 more days or valacyclovir 500 mg PO twice daily for 3 days or valacyclovir 1 g PO once daily for 5 days
Episodic therapy for patients coinfected with HSV and HIV	Acyclovir 400 mg PO three times daily for 5–10 days or famciclovir 500 mg PO twice daily for 5–10 days or valacyclovir 1 g PO twice daily for 5–10 days
External genital warts (HPV) Patient applied	Podofilox 0.5 % solution or gel: application with cotton swab twice daily for 3 days, then 4 days without therapy; can repeat cycle up to four times (max 0.5 mL per day) or imiquimod 5 % cream: apply three times per week up to 16 weeks, washing treated area with soap and water 6–10 h afterward or sinecatechins 15 % ointment: apply three times daily for up to 16 weeks
External genital warts (HPV) Provider administered	Cryotherapy with liquid nitrogen or cryoprobe or podophyllin resin 10–25 % in a compound tincture of benzoin or trichloroacetic acid (TCA) or Bichloroacetic acid (BCA) 80–90 % or surgical removal
Anal warts (HPV) Provider administered	Cryotherapy with liquid nitrogen or trichloroacetic acid (TCA) or bichloroacetic acid (BCA) 80–90 %: can be applied weekly as needed or surgical removal

HIV human immunodeficiency virus, *HSV* herpes simplex virus, *HPV* human papillomavirus

[a]This regimen may be less effective than the others for patients with over ten recurrences per year

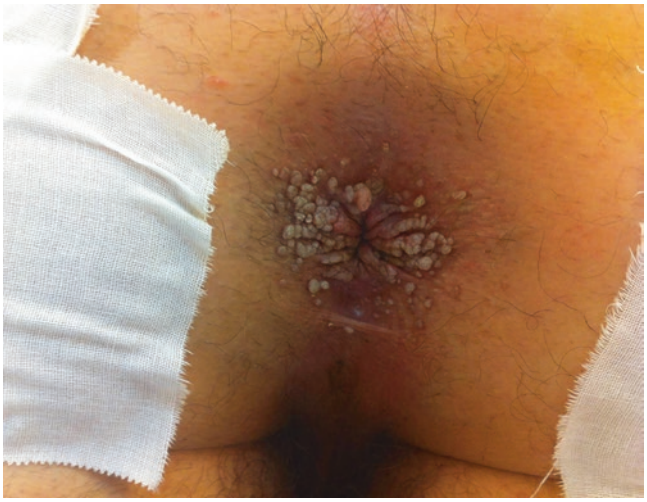

FIGURE 19-11. Perianal condyloma due to HPV infection.

using podofilox solution or gel, imiquimod cream, or sinecatechins ointment. Provider-administered options include cryotherapy, podophyllin resin, or trichloroacetic or bichloroacetic acid. The latter compounds should be applied sparingly to avoid adjacent tissue damage, and if the treatment causes pain or if too much acid is accidentally applied, soap, talc, or sodium bicarbonate (baking soda) can be used to neutralize the acid. Patients with extensive genital warts may warrant surgical management.

Anal condyloma—including warts in the anal canal and the distal rectum—can be treated with cryotherapy, TCA or BCA, or surgical therapy. High-resolution anoscopy may be indicated to inspect for high-grade dysplasia as well.

The management of high-grade anal dysplasia, the precursor to invasive squamous cell carcinoma, remains a controversial topic. While some clinicians view ablation or destruction of high-grade dysplasia as an important strategy to prevent progression to invasive cancer, others disagree with this approach. Patients with high-grade intra-anal dysplasia who undergo ablation have recurrence rates of about 50 % overall (higher in HIV-positive patients) but a low risk of developing anal cancer [58–62]. This controversy is discussed more thoroughly in the chapter on Anal Malignancies.

Vaccine

The two HPV vaccines available are the bivalent vaccine, which protects against high-risk oncogenic HPV types 16 and 18, and the quadrivalent vaccine which protects against HPV types 6, 11, 16, and 18 and should be given before one become sexually active. Both are approved for girls and boys aged 9–26 years old [18]. The quadrivalent vaccine has been shown to reduce the rates of high-grade anal dysplasia among MSM and may help to reduce the risk of anal cancer [63].

HIV and AIDS

Epidemiology

Over one million people in the USA have HIV, and over half of those infected are MSM. A quarter of those patients reported high-risk sexual practices such as unprotected sexual intercourse with a casual partner, or sex in exchange for money or drugs, and almost half of those patients reported using noninjection drugs over the past year [64].

Testing

HIV screening is recommended for all patients who present for STI testing. Positive screening tests for HIV antibody require confirmatory testing before a diagnosis can be made. If patient is suspected of having acute HIV infection, then a nucleic acid test should be performed in addition to the antibody test, and the patient should be referred immediately to an infectious disease specialist [18]. The FDA has recently approved combination tests detecting both HIV antigen and antibody, as well as tests that differentiate HIV-1 from HIV-2 [65].

Anorectal Issues

Anorectal complaints such as pain due to fissures may be the presenting symptom of patients with HIV infection. Fissures in HIV-positive patients may be a manifestation of HIV but could also represent coinfection with other STIs such as HSV or syphilis. Treatment of fissures in patients with HIV should consist of the same treatment undertaken for fissures in the general population. Special attention should be given to controlling diarrhea symptoms as well as avoidance of anal receptive intercourse.

Anal ulcers are another source of anal pain in patients with HIV and are located in a more proximal location within the anal canal—often above the dentate line—and are broader and more ulcerative than fissures. There may be evidence of destruction of the underlying sphincter muscle.

Perianal abscesses and fistulas are common in patients with HIV or AIDS. Patients with well-controlled HIV and normal CD4 counts who develop abscesses and fistulas can be treated with the same surgical techniques as one would do for patients without HIV. However, abscesses in patients with AIDS should be treated with smaller incisions, favoring drain placement over larger incisions. Fistulas in patients with advanced or poorly controlled AIDS should be treated with placement of draining setons rather than fistulotomy to avoid the creation of a nonhealing wound.

External thrombosed hemorrhoids in patients with HIV or AIDS should be treated in the same manner as those occurring in patients without HIV. Symptomatic internal hemorrhoids should be treated with first-line therapy with fiber and improvement of bowel habits. A more proximal source of

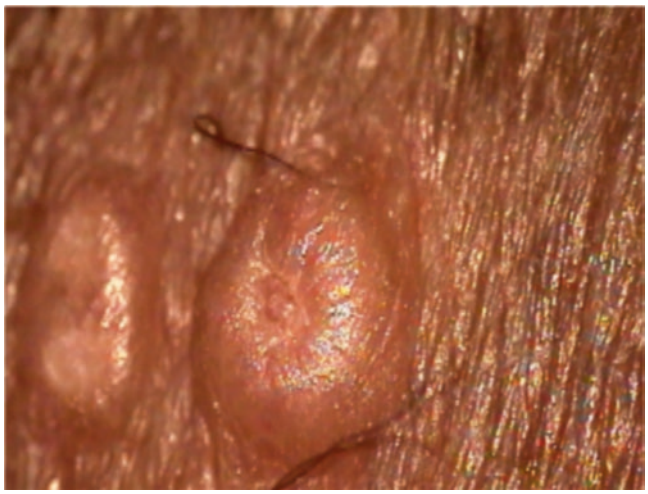

FIGURE 19-12. Molluscum contagiosum lesions present as waxy dome-shaped umbilicated papules.

bleeding should be ruled out with lower endoscopy. Patients who fail nonoperative management may safely undergo rubber band ligation of internal hemorrhoids. Hemorrhoidectomy is safe in HIV-positive patients without AIDS; patients with advanced or poorly controlled AIDS and severe hemorrhoids not amenable to banding may have wound healing problems.

Molluscum Contagiosum

Molluscum contagiosum is a common cutaneous viral infection caused by the *Molluscipoxvirus*, causing small, waxy, dome-shaped umbilicated papules (Figure 19-12). It is second only to genital warts as the most common nonulcerative STI, affecting up to 5 % of the population, 18 % of patients with immunosuppression, and 30 % of patients with advanced AIDS [66]. Secondary bacterial infection may occur especially if patients tend to scratch the lesions. Mollusca contagiosa occur frequently in young children, but their occurrence in adults is usually considered an STI and involves the pubic area. Risk factors include shaving. Transmission occurs through skin-to-skin contact, and autoinoculation can also occur to spread to other sites, especially in the 30 % of patients who develop an eczematous reaction around the lesions, which cause pruritus. Sexual contact can lead to transmission from the genitalia to the oral mucosa, conjunctiva, and cornea [67]. Diagnosis can be made by visual inspection although if there is difficulty then dermatoscopy revealing orifices, vessels, and specific vascular patterns can help confirm the diagnosis [68]. A recent PCR test has been developed as well for the molluscum contagiosum virus [69].

Immunocompetent patients will self-resolve these lesions over a period of months to years, so most patients prefer treatment. Treatment consists of removal of the lesions, similar to the treatment of genital warts. Curettage excision and cryotherapy are the most common methods of treatment [70, 71]. These treatments should not be performed in patients with immunosuppression due to the risk of nonhealing wounds and superinfection with other bacterial, viral, or fungal organisms. For these patients topical treatments such as imiquimod 5 % cream may be helpful without incurring the risk of open surgical wounds [72].

FIGURE 19-13. Pubic lice infestation causes severe pruritus and can be treated with permethrin 1 % cream. Photograph courtesy of Stephen Goldstone, MD.

Pubic Lice: *Phthirus pubis*

Pubic lice are obligate blood-sucking parasites and infestation is diagnosed by finding lice on pubic hair (Figure 19-13). As lice can neither jump nor fly, transmission is due to close contact. Therefore, the diagnosis of pubic lice should prompt testing for other STIs. Pubic lice infestation affects 2–10 % of the population worldwide [73]. The increased incidence of pubic hair removal has been associated with a lower incidence of pubic lice infections due to destruction of their natural habitat [74].

The CDC recommends permethrin 1 % cream or pyrethrins 0.3 %/piperonyl butoxide 4 % cream as the first-line therapy for pubic lice. Alternative regimens include malathion 0.5 % lotion or oral ivermectin. Permethrin should be used on the day of diagnosis and again 7–10 days later to completely

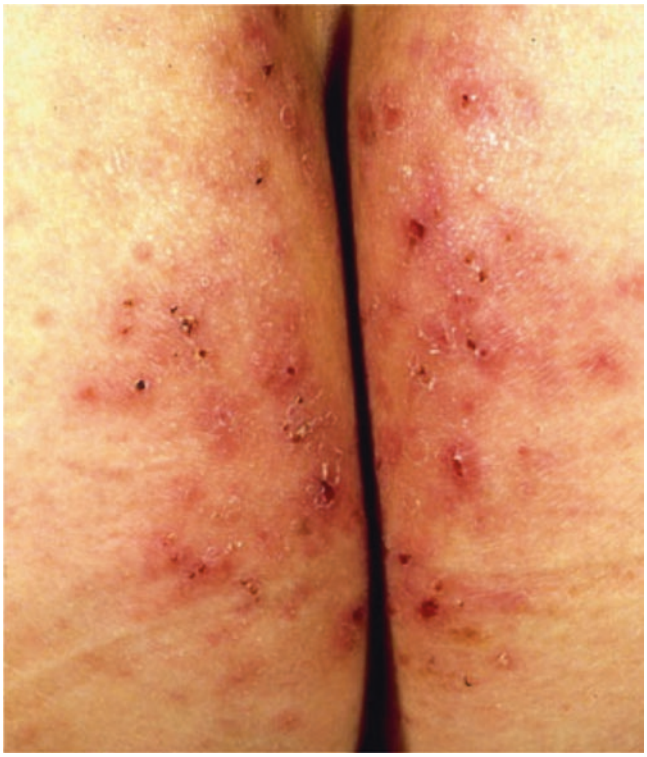

FIGURE 19-14. Scabies infestation causing an intensely pruritic rash can be treated with permethrin 5 % cream. Photograph courtesy of Stephen Goldstone, MD.

eradicate the infestation as the treatment does not kill the eggs. Laundering clothes and bedding in hot water should be done as well to prevent reinfection and transmission [18, 75].

Scabies

Scabies is caused by the mite *Sarcoptes scabiei* var. *hominis*. Scabies transmission is via skin-to-skin contact, as the mites neither jump nor fly. Scabies most commonly occurs in young children but can also occur in patients subject to overcrowded conditions, poor hygiene, homelessness, and via sexual contact. The mites burrow into the skin, creating wavy scaly lines on the skin surface, usually located on the hands and feet, typically in finger webs. The infestation causes an intense pruritic rash localized in a characteristic distribution in the armpits, elbow creases, wrists, and groin areas (Figure 19-14). Infants, children, and immunosuppressed patients may develop a more severe vesicular and pustular rash. Diagnosis can be made by visual inspection and history. Skin scrapings of the burrows, papules, and vesicles can be performed by applying mineral oil to the skin and scraping laterally across the lesion with a scalpel and examining the scraping microscopically for mites, eggs, and fecal pellets.

First-line treatment of scabies is with topical permethrin 5 % cream, which is rather effective as there is not much resistance [76]. The cream should be applied to all areas of the body from the neck down, and then washed off 8–14 h later. Reapplication of the cream should be performed 1 week later to ensure eradication. The pruritus may persist for up to 2 weeks after treatment. Oral ivermectin can also be used as first-line therapy or second-line therapy if the permethrin cream does not work [18]. Clothing and bedding should be washed in hot water and dried in a hot dryer to prevent re-infestation and transmission. Crusted scabies results when uncomplicated scabies goes untreated. Treatment involves both ivermectin orally on days 1, 2, 8, 9, and 15, as well as permethrin 5 % cream daily for 1 week, then twice a week until the disease is cured [77].

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