Chapter 47: Sexually Transmitted Diseases

INTRODUCTION

- The spectrum of sexually transmitted infections (STIs) includes the classic venereal diseases—gonorrhea, syphilis, chancroid, lymphogranuloma venereum, and granuloma inguinale—as well as a variety of other pathogens known to be spread by sexual contact (**Table 47-1**). Selected clinical syndromes associated with STIs are listed in **Table 47-2**. The most current information on epidemiology, diagnosis, and treatment of STIs provided by the Centers for Disease Control and Prevention (CDC) can be found at www.cdc.gov.

TABLE 47-1

Sexually Transmitted Infections

Disease	Associated Pathogens
Bacterial	
Gonorrhea	*Neisseria gonorrhoeae*
Syphilis	*Treponema pallidum*
Chancroid	*Haemophilus ducreyi*
Granuloma inguinale	*Calymmatobacterium granulomatis*
Enteric disease	*Salmonella* spp., *Shigella* spp., *Campylobacter* fetus
Campylobacter infection	*Campylobacter jejuni*
Bacterial vaginosis	*Gardnerella vaginalis, Mycoplasma hominis, Bacteroides* spp., *Mobiluncus* spp.
Group B streptococcal infections	Group B *Streptococcus*
Chlamydial	
Nongonococcal urethritis	*Chlamydia trachomatis*
Lymphogranuloma venereum	*C. trachomatis*, type L
Viral	
Acquired immunodeficiency syndrome	Human immunodeficiency virus
Herpes genitalis	Herpes simplex virus, types I and II
Viral hepatitis	Hepatitis A, B, C, and D viruses

Condylomata acuminata	Human papillomavirus
Molluscum contagiosum	Poxvirus
Cytomegalovirus infection	Cytomegalovirus
Mycoplasmal	
Nongonococcal urethritis	*Mycoplasma genitalium*
Protozoal	
Trichomoniasis	*Trichomonas vaginalis*
Amebiasis	*Entamoeba histolytica*
Giardiasis	*Giardia lamblia*
Fungal	
Vaginal candidiasis	*Candida albicans*
Parasitic	
Scabies	*Sarcoptes scabiei*
Pediculosis pubis	*Phthirus pubis*
Enterobiasis	*Enterobius vermicularis*

TABLE 47-2

Selected Syndromes Associated with Common Sexually Transmitted Pathogens

Syndrome	Commonly Implicated Pathogens	Common Clinical Manifestations[a]
Urethritis	*C. trachomatis*, herpes simplex virus, *N. gonorrhoeae*, *Trichomonas vaginalis*, *Ureaplasma urealyticum*, *Mycoplasma genitalium*	Urethral discharge, dysuria
Epididymitis	*C. trachomatis*, *N. gonorrhoeae*	Scrotal pain, inguinal pain, flank pain, urethral discharge
Cervicitis/Vulvovaginitis	*C. trachomatis, Gardnerella vaginalis*, herpes simplex virus, human papillomavirus, *N. gonorrhoeae, T. vaginalis*	Abnormal vaginal discharge, vulvar itching/irritation, dysuria, dyspareunia
Genital ulcers (painful)	*Haemophilus ducreyi*, herpes simplex virus	Usually multiple vesicular/pustular (herpes) or papular/pustular (*H. ducreyi*) lesions that can coalesce; painful, tender lymphadenopathy[b]
Genital ulcers (painless)	*Treponema pallidum*	Usually single papular lesion
Genital/Anal warts	Human papillomavirus	Multiple lesions ranging in size from small papular warts to large exophytic condylomas
Pharyngitis	*C. trachomatis*, herpes simplex virus, *N. gonorrhoeae*	Symptoms of acute pharyngitis, cervical lymphadenopathy, fever[c]
Proctitis	*C. trachomatis*, herpes simplex virus, *N. gonorrhoeae, T. pallidum*	Constipation, anorectal discomfort, tenesmus, mucopurulent rectal discharge
Salpingitis	*C. trachomatis, N. gonorrhoeae*	Lower abdominal pain, purulent cervical or vaginal discharge, adnexal swelling, fever[d]

[a]For some syndromes, clinical manifestations can be minimal or absent.

[b]Recurrent herpes infection can manifest as a single lesion.

[c]Most cases of pharyngeal gonococcal infection are asymptomatic.

[d]Salpingitis increases the risk of subsequent ectopic pregnancy and infertility.

GONORRHEA

- *Neisseria gonorrhoeae* is a gram-negative diplococcus estimated to cause almost 500,000 new infections per year in the United States. Humans are the only known host of this intracellular parasite.

Clinical Presentation

- Infected individuals may be symptomatic or asymptomatic, have complicated or uncomplicated infections, and have infections involving several

anatomical sites. The majority of women diagnosed with gonorrhea are asymptomatic.

- The most common clinical features of gonococcal infections are presented in **Table 47-3**. Ninety percent of males experience symptoms within 2–6 days following exposure, most commonly mucopurulent penile discharge and dysuria. Approximately 10%–20% of women with gonorrhea develop pelvic inflammatory disease. Left untreated, pelvic inflammatory disease can be an indirect cause of infertility and ectopic pregnancies.
- In 0.5%–3% of patients with gonorrhea, the gonococci invade the bloodstream and produce disseminated disease. The usual clinical manifestations of disseminated gonococcal infection are tender necrotic skin lesions, tenosynovitis, and monoarticular arthritis.
- Diagnosis of gonococcal infections can be made by gram-stained smears, culture (the most reliable method), or newer methods based on the detection of cellular components of the gonococcus (eg, enzymes, antigens, or DNA) in clinical specimens.
- Nucleic acid amplification techniques (NAATs) have replaced culture in most settings as the primary diagnostic test for gonorrhea infections and when screening for asymptomatic infections.

TABLE 47-3

Presentation of Gonorrhea Infections

	Males	Females
General	Incubation period: 1–14 days	Incubation period: 1–14 days
	Symptom onset in 2–8 days	Symptom onset in 10 days
Site of infection	Most common: urethra Others: rectum (usually caused by rectal intercourse in MSM), oropharynx, eye	Most common: endocervical canal Others: urethra, rectum (usually caused by perineal contamination), oropharynx, eye
Symptoms	Commonly symptomatic, may be asymptomatic Urethral infection: dysuria and urinary frequency Anorectal infection: asymptomatic to severe rectal pain Pharyngeal infection: asymptomatic to mild pharyngitis	Can be asymptomatic or minimally symptomatic Endocervical infection: usually asymptomatic or mildly symptomatic Urethral infection: dysuria, urinary frequency Anorectal and pharyngeal infection; symptoms same as for men
Signs	Purulent urethral or rectal discharge can be scant to profuse Anorectal: pruritus, mucopurulent discharge, bleeding	Abnormal vaginal discharge or uterine bleeding; purulent urethral or rectal discharge can be scant to profuse
Complications	Rare (epididymitis, prostatitis, inguinal lymphadenopathy, urethral stricture) Disseminated gonorrhea	Pelvic inflammatory disease and associated complications (ie, ectopic pregnancy, infertility) Disseminated gonorrhea (three times more common than in men)

MSM, men who have sex with men.

Treatment

- Single-dose intramuscular (IM) **ceftriaxone** remains the only recommended agent for treating gonorrhea as ceftriaxone-based regimens are the only regimens with well-documented efficacy in the treatment of urethral, cervical, rectal, and pharyngeal infections (**Table 47-4**). Ceftriaxone 250 mg should be administered IM in combination with a 1000-mg single dose of oral **azithromycin**. Dual antibiotic therapy with different mechanisms of action is recommended in an effort to delay further development of antimicrobial resistance and increase treatment efficacy. A

400 mg oral dose of **cefixime** may be substituted if ceftriaxone is unavailable.

- Ceftriaxone is the recommended therapy for disseminated gonococcal infection (DGI) including meningitis and endocarditis, and any type of gonococcal infection in children.
- Pregnant women infected with *N. gonorrhoeae* should be treated with ceftriaxone.
- Treatment of gonorrhea during pregnancy is essential to prevent ophthalmia neonatorum. The CDC recommends that **erythromycin (0.5%) ophthalmic ointment** be instilled in each conjunctival sac immediately postpartum to prevent ophthalmia neonatorum.

TABLE 47-4

Treatment of Gonorrhea

Type of Infection	Recommended Regimens[a]	Alternative Regimens[a]
Uncomplicated infections of the cervix, urethra, and rectum in adults	Ceftriaxone 250 mg IM once *plus* Azithromycin 1 g orally once	Cefixime 400 mg orally once *plus* Azithromycin 1 g orally once, or doxycycline 100 mg PO twice daily for 7 days[b] *or* Gemifloxacin 320 mg orally once or gentamicin 240 mg IM *plus* Azithromycin 2 g orally once
Uncomplicated infections of the pharynx	Ceftriaxone 250 mg IM once *plus*	Consult with infectious disease expert
Disseminated gonococcal infection in adults (>45 kg)	Ceftriaxone 1–2 g IM or IV every 12–24 hours[c] *plus* Azithromycin 1 g orally once	Cefotaxime 1 g IV every 8 hours[c] or ceftizoxime 1 g IV every 8 hours[c] *plus* Azithromycin 1 g orally once
Uncomplicated infections of the cervix, urethra, pharynx, and rectum in children (<45 kg)	Ceftriaxone 25–50 mg/kg IV or IM once (not to exceed 125 mg)	
Disseminated gonococcal infection in children (<45 kg)	Ceftriaxone 50 mg/kg IV or IM once daily × 7 days (not to exceed 1 g)	
Gonococcal conjunctivitis in adults	Ceftriaxone 1 g IM once[d] *plus* Azithromycin 1 g orally once	
Ophthalmia neonatorum	Ceftriaxone 25–50 mg/kg IV or IMf once (not to exceed 125 mg)	

Disseminated gonococcal infection in neonates	Ceftriaxone 25–50 mg/kg/day IV or IM once daily or cefotaxime 25 mg/kg IV or IM twice daily for 7 days, or 10–14 days if meningitis is suspected[f]	
Infants born to mothers with gonococcal infection	Prophylaxis: Erythromycin (0.5%) ophthalmic ointment in a single application[e] Treatment: Ceftriaxone 25–50 mg/kg IM or IV once (not to exceed 125 mg)	

[a]Recommendations are those of the CDC.

[b]Tetracyclines are contraindicated during pregnancy. Pregnant women should be treated with recommended cephalosporin-based combination therapy. In severe cephalosporin allergy, consultation with an infectious diseases expert is recommended.

[c]Parenteral treatment duration should be determined in consultation with an infectious diseases expert. Parenteral therapy for meningitis should be continued for at least 10–14 days and at least 4 weeks in endocarditis.

[d]A single lavage of the infected eye with normal saline should be considered; empiric therapy for *C. trachomatis* is recommended.

[e]Efficacy in preventing chlamydial ophthalmia is unclear.

[f]Caution should be taken when administering ceftriaxone to hyperbilirubinemic neonates.

CDC, Centers for Disease Control and Prevention; *C. trachomatis, Chlamydia trachomatis*; NAAT, nucleic acid amplification test; *N. gonorrhoeae, Neisseria gonorrhoeae*.

SYPHILIS

- The causative organism of syphilis is *Treponema pallidum*, a spirochete.
- Syphilis is usually acquired by sexual contact with infected mucous membranes or cutaneous lesions, although on rare occasions it can be acquired by nonsexual personal contact, accidental inoculation, or blood transfusion.

Clinical Presentation and Diagnosis

- The clinical presentation of syphilis is varied, with progression through multiple stages possible in untreated or inadequately treated patients.

Primary Syphilis

- Primary syphilis is characterized by the appearance of a chancre on cutaneous or mucocutaneous tissue exposed to the organism and is highly infectious. Chancres heal within 4–6 weeks, although lymphadenopathy may persist longer.
- Incubation period: 10–90 days (mean, 21 days).
- Site of infection: External genitalia, perianal region, mouth, and throat.
- Signs and symptoms: Single, painless, indurated lesion (chancre) that erodes, ulcerates, and eventually heals (typical); regional lymphadenopathy is common; multiple, painful, purulent lesions possible but uncommon.

Secondary Syphilis

- The secondary stage of syphilis is characterized by a variety of mucocutaneous eruptions, resulting from widespread hematogenous and lymphatic spread of *T. pallidum.* There is multisystem involvement secondary to hematogenous and lymphatic spread.
- Develops 2–8 weeks after initial infection in untreated or inadequately treated individuals.
- Signs and symptoms of secondary syphilis disappear in 4–10 weeks; however, if untreated, secondary syphilis disappears spontaneously within 1–6 months.
- There is pruritic or nonpruritic rash, mucocutaneous lesions, flu-like symptoms, lymphadenopathy.

Latent Syphilis

- Persons with a positive serologic test for syphilis but with no other evidence of disease have latent syphilis. It develops 4–10 weeks after secondary stage in untreated or inadequately treated individuals.
- There is potentially multisystem involvement (dormant) involving the CNS, heart, eyes, bones, and joints.
- Most untreated patients with late latent syphilis are asymptomatic and have no further sequelae; however, approximately 20% of patients progress either to neurosyphilis or to late syphilis with clinical manifestations other than neurosyphilis.

Tertiary Syphilis and Neurosyphilis

- Develops in approximately 30% of untreated or inadequately treated individuals 10–30 years after initial infection.
- Tertiary syphilis may include cardiovascular syphilis (aortitis or aortic insufficiency), neurosyphilis (meningitis, general paresis, dementia, tabes dorsalis, eighth cranial nerve deafness, blindness), gummatous lesions involving any organ or tissue.
- If left untreated, syphilis can slowly produce an inflammatory reaction in virtually any organ in the body. Forty percent of patients with primary or secondary syphilis exhibit CNS infection.
- Because *T. pallidum* is difficult to culture in vitro, diagnosis is based primarily on dark-field or direct fluorescent antibody microscopic examination of serous material from a suspected syphilitic lesion or on results from serologic testing.
- Serologic tests are the mainstay in the diagnosis of syphilis and are categorized as nontreponemal or treponemal. Common nontreponemal tests include the venereal disease research laboratory (VDRL) slide test, rapid plasma reagin (RPR) card test, unheated serum reagin (USR) test, and the toluidine red unheated serum test (TRUST).
- Treponemal tests are more sensitive than nontreponemal tests and are used to confirm the diagnosis (ie, the fluorescent treponemal antibody absorption).

Treatment

- Treatment recommendations from the CDC for syphilis are presented in **Table 47-5**. Parenteral penicillin G is the treatment of choice for all stages of syphilis. **Benzathine penicillin G** is the only penicillin effective for single-dose therapy. The recommended treatment for syphilis of less than 1 year's duration is benzathine penicillin G 2.4 million units as a single IM dose.
- Alternative regimens recommended for penicillin-allergic patients are **doxycycline** 100 mg orally twice daily or **tetracycline** 500 mg orally four times daily for 2–4 weeks depending on the duration of syphilis infection.
- For pregnant patients, penicillinis the treatment of choice at the dosage recommended for that particular stage of syphilis. To ensure treatment success and prevent transmission to the fetus, some experts advocate an additional IM dose of benzathine penicillin G, 2.4 million units, 1 week after completion of the recommended regimen.

- Patients treated for primary and secondary syphilis experience the Jarisch–Herxheimer reaction after treatment, characterized by flu-like symptoms such as transient headache, fever, chills, malaise, arthralgia, myalgia, tachypnea, peripheral vasodilation, and aggravation of syphilitic lesions. The Jarisch–Herxheimer reaction should not be confused with penicillin allergy. Most reactions can be managed symptomatically with analgesics, antipyretics, and rest.
- CDC recommendations for serologic follow-up of patients treated for syphilis are given in **Table 47-5**. Quantitative nontreponemal tests should be performed at 6 and 12 months in all patients treated for primary and secondary syphilis and at 6, 12, and 24 months for early and late latent disease.
- For women treated during pregnancy, monthly, quantitative, nontreponemal tests are recommended in those at high risk of reinfection.

TABLE 47-5

Drug Therapy and Follow-up of Syphilis

Stage/Type of Syphilis	Recommended Regimens[a,b]	Follow-up Serology
Primary, secondary, or early latent syphilis (<1 year's duration)	Adults: benzathine penicillin G 2.4 million units IM in a single dose Children: Benzathine penicillin G 50,000 units/kg IM in a single dose, up to 2.4 million units	Quantitative nontreponemal tests at 6 and 12 months for primary and secondary syphilis; at 6, 12, and 24 months for early latent syphilis[c]
Late latent syphilis (>1 year's duration) or latent syphilis of unknown duration or tertiary syphilis or retreatment	Adults: benzathine penicillin G 2.4 million units IM once a week for 3 successive weeks (7.2 million units total) Children: benzathine penicillin G 50,000 units/kg IM once a week for 3 successive weeks, up to 7.2 million units total	Quantitative nontreponemal tests at 6, 12, and 24 months[d,e]
Neurosyphilis	Aqueous crystalline penicillin G 18–24 million units IV (3–4 million units every 4 hours or by continuous infusion) for 10–14 days[f] *or* Aqueous procaine penicillin G 2.4 million units IM daily plus probenecid 500 mg orally four times daily, both for 10–14 days[f]	CSF examination every 6 months until the cell count is normal; if it has not decreased at 6 months or is not normal by 2 years, retreatment should be considered
Congenital syphilis (infants with proven or highly probable disease)	Aqueous crystalline penicillin G 50,000 units/kg/dose IV every 12 hours during the first 7 days of life and every 8 hours thereafter for a total of 10 days *or* Procaine penicillin G 50,000 units/kg IM daily for 10 days	Serologic follow-up only recommended if antimicrobials other than penicillin are used
Penicillin-allergic patients[g]		
Primary, secondary, or early latent	Doxycycline 100 mg orally two times daily for 14	Same as for non–penicillin-allergic patients

syphilis	days[g,h] *or* Tetracycline 500 mg orally four times daily for 14 days[h] *or* Ceftriaxone 1–2 g IM or IV daily for 10–14 days	
Late latent syphilis (>1 year's duration) or syphilis of unknown duration	Doxycycline 100 mg orally twice a day for 28 days[h,i] *or* Tetracycline 500 mg orally four times daily for 28 days[h,i]	Same as for non–penicillin-allergic patients

[a]Recommendations are those of the CDC.

[b]The CDC recommends that all patients diagnosed with syphilis be tested for HIV infection.

[c]More frequent follow-up (ie, 3, 6, 9, 12, and 24 months) recommended for HIV-infected patients.

[d]More frequent follow-up (ie, 6, 12, 18, and 24 months) recommended for HIV-infected patients.

[e]No specific recommendations exist for tertiary syphilis because of the lack of available data.

[f]Some experts administer benzathine penicillin G 2.4 million units IM once per week for up to 3 weeks after completion of the neurosyphilis regimens to provide a total duration of therapy comparable to that used for late syphilis in the absence of neurosyphilis.

[g]For nonpregnant patients; pregnant patients should be treated with penicillin after desensitization.

[h]Pregnant patients allergic to penicillin should be desensitized and treated with penicillin.

[i]Limited data suggest that ceftriaxone may be effective, although the optimal dosage and treatment duration are unclear.

CDC, Centers for Disease Control and Prevention; CSF, cerebrospinal fluid; HIV, human immunodeficiency virus.

CHLAMYDIA

- Infections caused by *Chlamydia trachomatis* are believed to be the most common STI in the United States. *C. trachomatis* is an obligate intracellular parasite that has some similarities to viruses and bacteria.

Clinical Presentation

- In comparison with gonorrhea, chlamydial genital infections are more frequently asymptomatic, and when present, symptoms tend to be less noticeable. **Table 47-6** summarizes the usual clinical presentation of chlamydial infections.
- Similar to gonorrhea, chlamydia may be transmitted to an infant during contact with infected cervicovaginal secretions. Nearly two-thirds of infants acquire chlamydial infection after endocervical exposure, with the primary morbidity associated with seeding of the infant's eyes, nasopharynx, rectum, or vagina.
- Culture of endocervical or urethral epithelial cell scrapings is the most specific method (close to 100%) for detection of chlamydia, but sensitivity is

as low as 70%. Between 3 and 7 days are required for results.

- Tests that allow rapid identification of chlamydial antigens and nucleic acid provide more rapid results, are technically less demanding to perform, less costly, and in some situations have greater sensitivity than culture. Nucleic acid amplification tests (NAATs) are the most sensitive tests for first-catch urine, endocervix and vaginal swab specimens in women, and urethral swab specimens in men, and are therefore the recommended tests for detecting chlamydia infection.

TABLE 47-6

Presentation of Chlamydia Infections

	Males	Females
General	Incubation period: 35 days Symptom onset: 7–21 days	Incubation period: 7–35 days Usual symptom onset: 7–21 days
Site of infection	Most common: urethra Others: rectum (receptive anal intercourse), oropharynx, eye	Most common: endocervical canal Others: urethra, rectum (usually caused by perineal contamination), oropharynx, eye
Symptoms	More than 50% of urethral and rectal infections are asymptomatic Urethral infection: mild dysuria, discharge Pharyngeal infection: asymptomatic to mild pharyngitis	More than 66% of cervical infections are asymptomatic Urethral infection: usually subclinical; dysuria and frequency uncommon Rectal and pharyngeal infection: symptoms same as for men
Signs	Scant to profuse, mucoid to purulent urethral or rectal discharge Rectal infection: pain, discharge, bleeding	Abnormal vaginal discharge or uterine bleeding, purulent urethral or rectal discharge can be scant to profuse
Complications	Epididymitis, Reiter's syndrome (rare)	Pelvic inflammatory disease and associated complications (ie, ectopic pregnancy, infertility) Reiter's syndrome (rare)

Treatment

- **Azithromycin** 1000 mg orally as a single-dose and **doxycycline** 100 mg orally twice daily for 7 days are the regimens of choice for the treatment of uncomplicated urogenital chlamydia infections (**Table 47-7**).
- Treatment of chlamydial infections with the recommended regimens is highly effective; therefore, posttreatment cultures are not routinely recommended.
- Infants with pneumonitis should receive follow-up testing because **erythromycin** is only 80% effective.
- For infected pregnant women azithromycin is the recommended treatment.

TABLE 47-7

Treatment of Chlamydia Infections

Infection	Recommended Regimens[a]	Alternative Regimen
Uncomplicated urethral, endocervical, or rectal infection in adults	Azithromycin 1 g orally once, or doxycycline 100 mg orally twice daily for 7 days	Erythromycin base 500 mg orally four times daily for 7 days, or erythromycin ethylsuccinate 800 mg orally four times daily for 7 days, or levofloxacin 500 mg orally once daily for 7 days, or ofloxacin 300 mg orally twice daily for 7 days
Urogenital infections during pregnancy	Azithromycin 1 g orally as a single dose or amoxicillin 500 mg orally three times daily for 7 days	Amoxicillin 500 mg orally three times daily for 7 days, or erythromycin base 500 mg orally four times daily for 7 days, or erythromycin base 250 mg orally four times daily for 14 days, or erythromycin ethylsuccinate 800 mg orally four times daily for 7 days, or erythromycin ethylsuccinate 400 mg orally four times daily for 14 days
Conjunctivitis of the newborn or pneumonia in infants	Erythromycin base or ethylsuccinate 50 mg/kg/day orally in four divided doses for 14 days[b,c]	Azithromycin suspension 20 mg/kg/day orally once daily for 3 days[c]

[a]Recommendations are those of the CDC.

[b]Topical therapy alone is inadequate for ophthalmia neonatorum and is unnecessary when systemic therapy is administered. Effectiveness of erythromycin treatment is approximately 80%; therefore, a second course of therapy may be required.

[c]An association between oral erythromycin and azithromycin and IHPS has been reported in infants aged <6 weeks. Infants treated with either of these antimicrobials should be followed for signs and symptoms of IHPS.

CDC, Centers for Disease Control and Prevention; IHPS, infantile hypertrophic pyloric stenosis.

GENITAL HERPES

- The term ***herpes*** is used to describe two distinct but antigenically related serotypes of herpes simplex virus (HSV). HSV type 1 (HSV-1) is most commonly associated with oropharyngeal disease; type 2 (HSV-2) is most closely associated with genital disease.

Clinical Presentation

- A summary of the clinical presentation of genital herpes is provided in **Table 47-8**.
- Complications from genital herpes infections result from both genital spread and autoinoculation of the virus and occur most commonly with primary first episodes. Lesions at extragenital sites, such as the eye, rectum, pharynx, and fingers, are not uncommon. CNS involvement is seen occasionally and can take several forms, including encephalitis, aseptic meningitis, and transverse myelitis. A major concern is the effect of genital herpes on neonates exposed during pregnancy.
- Tissue culture is the most specific (100%) and sensitive method (80%–90%) of confirming the diagnosis of first-episode genital herpes; however, culture is relatively insensitive in detecting HSV in ulcers in the latter stages of healing and in recurrent infections.

TABLE 47-8

Presentation of Genital Herpes Infections

General	Incubation period: 2–14 days (mean, 4 days) Can be caused by either HSV-1 or HSV-2
Classification of infection	
First-episode primary First-episode nonprimary Recurrent	Initial genital infection in individuals lacking antibody to either HSV-1 or HSV-2 Initial genital infection in individuals with clinical or serologic evidence of prior HSV (usually HSV-1) infection Appearance of genital lesions at some time following healing of first-episode infection
Signs and symptoms	
First-episode infections	Most primary infections are asymptomatic or minimally symptomatic Multiple painful pustular or ulcerative lesions on external genitalia developing over a period of 7–10 days; lesions heal in 2–4 weeks (mean, 21 days) Flu-like symptoms (eg, fever, headache, malaise) during first few days after appearance of lesions Others—local itching, pain, or discomfort; vaginal or urethral discharge, tender inguinal adenopathy, paresthesias, urinary retention Severity of symptoms greater in females than in males Symptoms are less severe (eg, fewer lesions, more rapid lesion healing, fewer or milder systemic symptoms) with nonprimary infections Symptoms more severe and prolonged in immunocompromised patients On average viral shedding lasts approximately 11–12 days for primary infections and 7 days for nonprimary infections
Recurrent	Prodrome seen in approximately 50% of patients prior to appearance of recurrent lesions; mild burning, itching, or tingling are typical prodromal symptoms Compared to primary infections, recurrent infections associated with (1) fewer lesions that are more localized, (2) shorter duration of active infection (lesions heal within 7 days), and (3) milder symptoms Severity of symptoms greater in females than in males Symptoms more severe and prolonged in immunocompromised patients On average viral shedding lasts approximately 4 days Asymptomatic viral shedding is more frequent during the first year after infection with HSV
Therapeutic implications of HSV-1 vs. HSV-2 genital infection	Primary infections caused by HSV-1 and HSV-2 virtually indistinguishable Recurrent infections and subclinical viral shedding are less frequent with HSV-1 Recurrent infections with HSV-2 tend to be more severe
Complications	Secondary infection of lesions; extragenital infection because of autoinoculation; disseminated infection (primarily in immunocompromised patients); meningitis or encephalitis; neonatal transmission

HSV-1, herpes simplex virus type 1; HSV-2, herpes simplex virus type 2.

Treatment

- Goals of Treatment: To relieve symptoms and to shorten the clinical course, prevent complications and recurrences, and to decrease disease

transmission.

- Specific treatment recommendations are given in **Table 47-9**.
- Oral **acyclovir, valacyclovir**, and **famciclovir** are the treatments of choice for outpatients with first-episode genital herpes.
- Suppressive with oral antiviral agents reduces the frequency and the severity of recurrences in 70%–80% of patients experiencing frequent recurrences.
- Acyclovir, valacyclovir, and famciclovir have been used to prevent reactivation of infection in patients seropositive for HSV who undergo transplantation procedures or induction chemotherapy for acute leukemia.
- The safety of acyclovir, famciclovir, and valacyclovir therapy during pregnancy is not well established, although experience with both agents in animal studies suggests a low risk of fetal harm.

TABLE 47-9

Treatment of Genital Herpes

Type of Infection	Recommended Regimens[a,b]	Alternative Regimen
First clinical episode of genital herpes[c]	Acyclovir 400 mg orally three times daily for 7–10 days[d] *or* Acyclovir 200 mg orally five times daily for 7–10 days[d] *or* Famciclovir 250 mg orally three times daily for 7–10 days[d] *or* Valacyclovir 1 g orally twice daily for 7–10 days[d]	Acyclovir 5–10 mg/kg IV every 8 hours for 2–7 days or until clinical improvement occurs, followed by oral therapy to complete at least 10 days of total therapy[e]
Recurrent infection		
Episodic therapy	Acyclovir 400 mg orally three times daily for 5 days[f] *or* Acyclovir 800 mg orally twice daily for 5 days[f] *or* Acyclovir 800 mg orally three times daily for 2 days[f] *or* Famciclovir 125 mg orally twice daily for 5 days[f] *or* Famciclovir 1 g orally twice daily for 1 day[f]	

	or Famciclovir 500 mg orally once, followed by 250 mg orally twice daily for 2 days[f] *or* Valacyclovir 500 mg orally twice daily for 3 days[f] *or* Valacyclovir 1 g orally once daily for 5 days[f]	
Suppressive therapy[g]	Acyclovir 400 mg orally twice daily *or* Famciclovir 250 mg orally twice daily[h] *or* Valacyclovir 500 mg or 1000 mg orally once daily[i]	

[a]Recommendations are those of the CDC.

[b]HIV-infected patients can require more aggressive therapy.

[c]Primary or nonprimary first episode.

[d]Treatment duration can be extended if healing is incomplete after 10 days.

[e]Only for patients with severe symptoms or complications that necessitate hospitalization. HSV encephalitis requires 21 days of IV therapy.

[f]Requires initiation of therapy within 24 hours of lesion onset or during the prodrome that precedes some outbreaks.

[g]Consider discontinuation of treatment after 1 year to assess frequency of recurrence.

[h]Famciclovir appears less effective for suppression of viral shedding.

[i]Valacyclovir 500 mg appears less effective than other valacyclovir and acyclovir regimens in patients with 10 or more recurrences per year.

CDC, Centers for Disease Control and Prevention; HIV, human immunodeficiency virus; IV, intravenous.

TRICHOMONIASIS

- Trichomoniasis is caused by *Trichomonas vaginalis,* a flagellated, motile protozoan that is responsible for 3–4 million cases per year in the United States.
- Coinfection with other STIs (eg, gonorrhea) is common in patients diagnosed with trichomoniasis.

Clinical Presentation

- The typical presentation of trichomoniasis in men and women is presented in **Table 47-10**.

- *T. vaginalis* produces nonspecific symptoms also consistent with bacterial vaginosis; thus, laboratory diagnosis is required.
- The simplest and most reliable means of diagnosis is a wet-mount examination of the vaginal discharge. Trichomoniasis is confirmed if characteristic pear-shaped, flagellating organisms are observed. Newer diagnostic tests, such as monoclonal antibody or DNA probe techniques, as well as PCR tests that can detect small amounts of trichomonal DNA and are highly sensitive and specific.

TABLE 47-10

Presentation of Trichomonas Infections

	Males	Females
General	Incubation period: 3–28 days Organism can be detectable within 48 hours after exposure to infected partner	Incubation period: 3–28 days
Site of infection	Most common: urethra Others: rectum (usually caused by rectal intercourse in MSM), oropharynx, eye	Most common: endocervical canal Others: urethra, rectum (usually caused by perineal contamination), oropharynx, eye
Symptoms	Can be asymptomatic (more common in males than females) or minimally symptomatic Urethral discharge (clear to mucopurulent) Dysuria, pruritus	Can be asymptomatic or minimally symptomatic Scant to copious, typically malodorous vaginal discharge (50%–75%) and pruritus (worse during menses) Dysuria, dyspareunia
Signs	Urethral discharge	Vaginal discharge Vaginal pH 4.5–6 Inflammation/erythema of vulva, vagina, and/or cervix Urethritis
Complications	Epididymitis and chronic prostatitis (uncommon) Male infertility (decreased sperm motility and viability)	Pelvic inflammatory disease and associated complications (ie, ectopic pregnancy, infertility) Premature labor, premature rupture of membranes, and low-birth-weight infants (risk of neonatal infections is low) Cervical neoplasia

MSM, men who have sex with men.

Treatment

- Recommended and alternative treatment regimens for *T. vaginalis* include either **metronidazole** or **tinidazole**, both of which produce high cure rates.
- Treatment recommendations for *Trichomonas* infections are given in **Table 47-11**.
- GI complaints are more common with the single 2 g dose of either metronidazole or tinidazole and some patients also complain of a bitter metallic taste in the mouth with metronidazole.

- Patients intolerant of the single 2 g dose because of GI adverse effects usually tolerate the alternative metronidazole multidose regimen.
- To achieve maximal cure rates and prevent relapse with the single 2 g dose of metronidazole, simultaneous treatment of infected sexual partners is necessary.
- In patients who fail to respond to an initial course of metronidazole therapy, a second course of therapy with metronidazole 500 mg twice daily for 7 days or a single 2 g dose of tinidazole is recommended.
- Patients taking metronidazole should be instructed to avoid alcohol ingestion during therapy and for 1 or 2 days after completion of therapy because of a possible disulfiram-like effect.
- Because metronidazole is secreted in breast milk, it is recommended that breast-feeding be interrupted for 12–24 hours after maternal ingestion of a single 2 g dose. Metronidazole (pregnancy category B) and tinidazole (pregnancy category C) are contraindicated during the first trimester of pregnancy based on FDA-approved labeling. However, the CDC now recommends that all symptomatic pregnant women, regardless of pregnancy stage, be tested and considered for treatment with metronidazole.
- Follow-up was previously considered unnecessary in patients who become asymptomatic after treatment with recommended therapy; however, retesting is now recommended for all sexually active women within 3 months following initial treatment due to the high rates of reinfection.
- When patients remain symptomatic, it is important to determine if reinfection has occurred. In these cases, a repeat course of therapy, as well as identification and treatment or retreatment of infected sexual partners, is recommended.

TABLE 47-11

Treatment of Trichomoniasis

Type	Recommended Regimens[a]	Alternative Regimen
Symptomatic and asymptomatic infections	Metronidazole 2 g orally in a single dose *or* Tinidazole 2 g orally in a single dose[b]	Metronidazole 500 mg orally two times daily for 7 days[c,d]
Persistent or recurrent infections	Metronidazole 500 mg orally two times daily for 7 days[c]	Metronidazole 2 g orally for 7 days[e] *or* Tinidazole 2 g orally for 7 days[e]
Treatment in pregnancy	Metronidazole 2 g orally in a single dose[e,f]	

[a]Recommendations are those of the CDC.

[b]Randomized controlled trials comparing single 2 g doses of metronidazole and tinidazole suggest that tinidazole is equivalent to, or superior to, metronidazole in achieving parasitologic cure and resolution of symptoms.

[c]Metronidazole labeling approved by the FDA does not include this regimen. Dosage regimens for treatment of trichomoniasis included in the product labeling are the single 2 g dose; 250 mg three times daily for 7 days; and 375 mg twice daily for 7 days. The 250 mg and 375 mg dosage regimens are currently not included in the CDC recommendations.

[d]Recommended treatment regimen for women with HIV coinfection.

[e]For treatment failures with metronidazole 2 g as a single dose and metronidazole 500 mg orally two times daily for 7 days.

[f]Symptomatic pregnant women can be treated with this regimen at any stage of pregnancy.

OTHER SEXUALLY TRANSMITTED INFECTIONS

- Several STIs other than those previously discussed occur with varying frequency in the United States and throughout the world. Although an in-depth discussion of these diseases is beyond the scope of this chapter, recommended treatment regimens are given in **Table 47-12**.

TABLE 47-12

Treatment Regimens for Miscellaneous Sexually Transmitted Infections

Infection	Recommended Regimens[a]	Alternative Regimen
Chancroid (*H. ducreyi*)	Azithromycin 1 g orally in a single dose *or* Ceftriaxone 250 mg IM in a single dose *or* Ciprofloxacin 500 mg orally twice daily for 3 days[b]	

	or Erythromycin base 500 mg orally four times daily for 7 days	
Lymphogranuloma venereum	Doxycycline 100 mg orally twice daily for 21 days[c]	Erythromycin base 500 mg orally four times daily for 21 days[d]
Nongonococcal urethritis (NGU)	Azithromycin 1 g orally in a single dose *or* Doxycyline 100 mg orally twice daily for 7 days	Erythromycin base 500 mg orally four times daily for 7 days, or erythromycin ethylsuccinate 800 mg orally four times daily for 7 days, or levofloxacin 500 mg orally once daily for 7 days, or ofloxacin 300 mg orally twice daily for 7 days
NGU (persistent or recurrent or due to *Mycoplasma genitalium*)	Azithromycin 1 g orally in a single dose	Fail initial regimen of azithromycin: moxifloxacin 400 mg orally daily for 7 days
HPV infection		
External genital/Perianal warts	*Provider-administered therapies* Cryotherapy (eg, liquid nitrogen or cryoprobe); repeat weekly as necessary *or* Podophyllin resin 10%–25% in compound tincture of benzoin applied to lesions; repeat weekly as necessary[e,f] *or* TCA 80%–90% *or* BCA 80%–90% applied to warts; repeat weekly as necessary *or* Surgical removal (tangential scissor excision, tangential shave excision, curettage, or electrosurgery) *Patient-applied therapies* Podofilox 0.5% solution or gel applied twice daily for 3 days, followed by 4 days of no therapy; cycle is repeated as necessary for up to four cycles[f] *or* Imiquimod 3.75% or 5% cream applied at bedtime three times weekly for up to 16 weeks[f] *or* Sinecatechins 15% ointment applied three times daily for up to 16 weeks	Intralesional interferon *or* Photodynamic therapy *or* Topical cidofovir
Vaginal and anal warts	Cryotherapy with liquid nitrogen, or TCA or BCA 80%–90% as for external HPV warts; repeat weekly as necessary[g]	

	Surgical removal (not for vaginal or urethral meatus warts)	
Urethral meatus warts	Cryotherapy with liquid nitrogen, or podophyllin resin 10%–25% in compound tincture of benzoin applied at weekly intervals[f,h]	
Prevention (ages 9–14 years)	Gardasil (HPV quadrivalent [types 6, 11, 16, and 18]) recombinant vaccine 0.5 mL IM on day 1; a second dose administered 6–12 months following the first dose[i,j,k] Cervarix (HPV bivalent [types 16 and 18]) recombinant vaccine 0.5 mL IM on day 1; a second dose administered 6–12 months following the first dose[i,l] Gardasil9 (HPV 9-valent [types 6, 11, 16, 18, 31, 33, 45, 52, 58]) recombinant vaccine 0.5 mL IM on day 1; a second dose administered 6–12 months following the first dose[i]	
Prevention (age ≥15 years)	Gardasil (HPV quadrivalent [types 6, 11, 16, and 18]) recombinant vaccine 0.5 mL IM on day 1; a second and third dose are administered 2 and 6 months following the first dose[i,j,k] Cervarix (HPV bivalent [types 16 and 18]) recombinant vaccine 0.5 mL IM on day 1; a second and third dose are administered 1 and 6 months following the first dose[i,l] Gardasil9 (HPV 9-valent [types 6, 11, 16, 18, 31, 33, 45, 52, 58]) recombinant vaccine 0.5 mL IM on day 1; a second and third dose are administered 1 and 6 months following the first dose[i]	

[a]Recommendations are those of the Centers for Disease Control and Prevention (CDC).

[b]Ciprofloxacin is contraindicated for pregnant and lactating women and for persons aged <18 years.

[c]Azithromycin 1 g PO once weekly for 3 weeks can be effective.

[d]Pregnant patients should be treated with erythromycin.

[e]Some experts recommended washing podophyllin off after 1–4 hours to minimize local irritation.

[f]Safety during pregnancy is not established.

[g]Surgical removal of anal warts is also a recommended treatment.

[h]Some specialists recommend the use of podofilox and imiquimod for treating distal meatal warts.

[i]CDC recommendations: vaccination is recommended in girls 11–12 years of age, and in females aged 13–26 years who either were not previously vaccinated, or who did not complete the vaccination series.

[j]FDA-approved labeling for Gardasil: indicated in girls and women 9 through 26 years of age for the prevention of cervical, vulvar, vaginal, and anal cancer caused by HPV types 16 and 18, genital warts (condyloma acuminata) caused by HPV types 6 and 11, and precancerous or dysplastic lesions caused by HPV types 6, 11, 16, and 18.

[k]Vaccination is recommended in males aged 9–26 years to prevent genital warts and anal cancer.

[l]FDA-approved labeling for Cervarix: indicated in females 9 through 25 years of age for the prevention of cervical cancer, cervical intraepithelial neoplasia grade 2 or worse, adenocarcinoma in situ, and cervical intraepithelial neoplasia grade 1 caused by HPV types 16 and 18.

BCA, bichloracetic acid; HPV, human papillomavirus; NGU, nongonococcal urethritis; TCA, trichloroacetic acid.

See Chapter 135, Sexually Transmitted Infections, authored by Bryson Duhon, and Yvonne Burnett, for a more detailed discussion of this topic.