

**TABLE 100-1** DIFFERENTIAL DIAGNOSIS OF GENITAL ULCER DISEASE

DISEASE	PRIMARY LESION	ADENOPATHY	SYSTEMIC FEATURES	DIAGNOSIS AND TREATMENT
Genital herpes (HSV-1/2)				
Primary	Incubation 2-7 days; multiple, painful vesicles on erythematous base; lasts 7-14 days	Tender, soft, and usually bilateral	Fever, malaise	Viral cultures, DFA, antibody testing, Tzanck smear Tx: acyclovir, famciclovir, or valacyclovir for 7-10 days (shorter for recurrent cases)
Recurrent	Grouped, painful vesicles on erythematous base; lasts 3-10 days	None	None	Nontreponemal tests (RPR, VDRL), treponemal tests (FTA-ABS), darkfield microscopy; cannot be cultured Tx: see Table 100-3
Primary syphilis (<i>Treponema pallidum</i>)	Incubation 10-90 days (average, 21) Chancre: painless papule that ulcerates with firm, raised border and smooth base; usually single; may be genital or almost anywhere; heals in 3-6 wk without treatment	1 wk after chancre appears; bilateral or unilateral; firm, discrete, no overlying skin changes, painless, nonsuppurative	During later stages	Nontreponemal tests (RPR, VDRL), treponemal tests (FTA-ABS), darkfield microscopy; cannot be cultured Tx: see Table 100-3
Chancroid (<i>Haemophilus ducreyi</i>)	Incubation 3-5 days; vesicle or papule to pustule to ulcer; soft, not indurated; very painful	1 wk after primary in 50%; painful, unilateral in two thirds; suppurative	None	Gram stain and culture. Tx: azithromycin, ceftriaxone, ciprofloxacin
Lymphogranuloma venereum (<i>Chlamydia trachomatis</i> serovars L1, L2, L3)	Incubation 5-21 days; self-limited, painless papule, vesicle, or ulcer; lasts 2-3 days; found in only 10-40%	5-21 days after primary; one third bilateral, tender, matted iliac or femoral groove sign; multiple abscesses; coalescent, caseating, suppurative; thick yellow pus; sinus tracts; fistulas; strictures; genital ulcerations	Fever, arthritis, pericarditis, proctitis, meningoencephalitis, keratoconjunctivitis, preauricular adenopathy, erythema nodosum	NAAT for <i>Chlamydia</i> Tx: incision and drainage, doxycycline
Granuloma inguinale (donovanosis)	Incubation 9-50 days; at least one painless papule that gradually ulcerates; ulcers are large (1-4 cm), irregular, nontender, with thickened; rolled margins and beefy red tissue at base; older portions of ulcer show depigmented scarring, white areas; advancing edge contains new papules	No true adenopathy; in one fifth of patients, subcutaneous spread through lymphatics leads to indurated swelling or abscesses of groin (pseudobuboes)	Metastatic infection of bones, joints, liver	Wright or Giemsa staining with short, plump, bipolar staining pattern, Donovan bodies in macrophage vacuoles Tx: doxycycline
Condyloma acuminatum (genital warts)	Characteristic large, soft, fleshy, cauliflower-like excrescences around vulva, glans, urethral orifice, anus, perineum	None	None	Clinical diagnosis, biopsy if necessary Tx: topical podophyllin, surgery, others

DFA, Direct fluorescent antibody test; FTA-ABS, fluorescent treponemal antibody absorption test; HSV, herpes simplex virus; NAAT, nucleic acid amplification test; RPR, rapid plasma reagin; Tx, treatment; VDRL, venereal disease research laboratory.

nadir in 2000 with a rate of 2.1 cases per 100,000 people in the general population. However, since that time, the number of reported syphilis cases has been increasing. The major at-risk group is MSM, but the disease is observed in people across all ages, genders, sexual orientations, socioeconomic status, and racial and ethnic classes.

The resurgence of a generalized syphilis epidemic among MSM with HIV infection or acquired immunodeficiency syndrome (HIV/AIDS) has had important consequences. Clinicians at STI clinics and those treating individuals with HIV/AIDS need to be aware of guidelines for the diagnosis and treatment of syphilis in this population. Given the increasing number of MSM living with HIV/AIDS, it is not uncommon to see co-infection in this population. All MSM, regardless of HIV status, should be considered for syphilis screening on an annual basis and more frequently if they have other risk factors.

Pathology

T. pallidum organisms are thinly coiled bacteria that move in a corkscrew motion. *T. pallidum* cannot be cultured, hindering diagnosis and study of the organism. *T. pallidum* infects and penetrates mucosal membranes, resulting in the classic chancre lesion. The organism then infects local lymph nodes and disseminates systemically. The median incubation period is

approximately 3 weeks. In more than 60% of infected individuals, syphilis does not progress to tertiary stages. Immune host factors are thought to contribute to the development of tertiary syphilis.

Clinical Presentation

Ninety-five percent of primary syphilis cases involve the genitals. The estimated risk of transmission from an individual with primary syphilis to an uninfected individual is 30% per sexual act. Syphilis may also be transmitted through oral-genital exposure and with any contact of a primary lesion. Inoculation of the organism by surgeons through needlesticks has been well documented and typically does not result in a chancre at the site of infection (i.e., syphilis d'emblee).

The four classic stages of syphilis are primary, secondary, latent, and tertiary. Staging is best thought of as a continuum rather than discrete stages of infection. The states can manifest individually, but individuals often have symptoms consistent with primary and secondary symptoms. The primary and secondary stages of syphilis are extremely infectious, and cases of transmission during the tertiary stage have been reported.

It can be very difficult to diagnose primary syphilis based solely on the physical examination. The primary chancre is a painless, clean-based, indurated ulcer. The borders are firm and raised.