Mucormycosis

Mucormycosis (formerly zygomycosis) is the third most frequent cause of invasive fungal infections in immunocompromised persons. Patients with diabetes mellitus, neutropenia, and iron overload states (including deferoxamine administration) are particularly at risk. The most common mucormycetes are *Rhizopus arrhizus* and *Mucor* species. These fungi are commonly found in the environment on decaying organic debris and soil.

Infection is acute and rapidly fatal, even with early diagnosis and treatment. Major blood vessels are invaded, with ensuing ischemia, necrosis, and infarction of adjacent tissues. Mucormycosis has five major clinical forms: (1) rhinocerebral (**Figure 20**); (2) pulmonary; (3) abdominal, pelvic, gastric, gastrointestinal; (4) primary cutaneous; and (5) disseminated.

Because laboratory studies are nonspecific, diagnosis relies on a high index of suspicion in a host with appropriate risk factors and evidence of tissue invasion. Serologic tests and blood cultures offer no diagnostic benefit.

Treatment requires reversal of any predisposing conditions, extensive surgical removal of affected tissue, and early antifungal therapy. Initial treatment is high-dose liposomal amphotericin B, with de-escalation to posaconazole or isavuconazole. If amphotericin B is not tolerated, initial therapy with one of the azoles is warranted. Mortality rates remain as high as 60% to 80%, even with therapy.

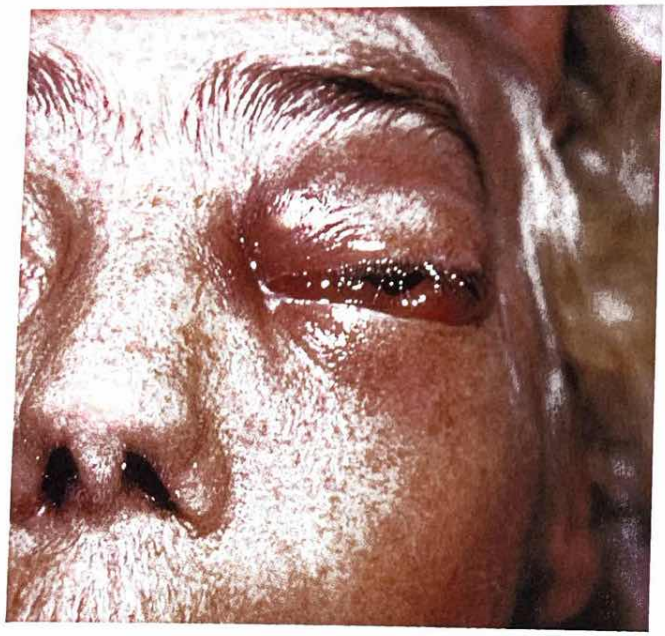

FIGURE 20. This patient presented with a case of a periorbital fungal infection known as mucormycosis, a dangerous invasive fungal infection frequently occurring in patients with uncontrolled diabetes in ketoacidosis or severely immunocompromised patients such as solid organ or hematopoietic stem cell transplantation recipients. The most common form of infection tends to affect the regions of the eye and nose, with penetration into the central nervous system (rhinocerebral form).

KEY POINTS

- Because laboratory studies are nonspecific, diagnosing mucormycosis relies on a high index of suspicion in a host with appropriate risk factors and evidence of tissue invasion.
- Treatment of mucormycosis requires reversing any predisposing condition, extensive surgical removal of affected tissue, and initial antifungal therapy with high-dose liposomal amphotericin B.

Sexually Transmitted Infections

Introduction

Sexually transmitted infections (STIs) occur most commonly in adolescents, young adults, and men who have sex with men (MSM). Most infections are asymptomatic, so a detailed sexual history, including sexual practices, is imperative to understanding individual risk. STI risk factors include a new partner, more than one current partner, a partner with an STI, or a partner who has concurrent partners. Particularly high-risk populations include persons attending STI clinics and MSM. The U.S. Preventive Services Task Force (USPSTF) recommends behavioral counseling to reduce the likelihood of acquiring STIs in sexually active adolescents and in adults at increased risk.

Unrecognized or inadequately treated STIs are a preventable cause of infertility in women. The World Health Organization and the CDC provide evidence-based guidelines for the evaluation and management of STIs; the CDC guidelines are recommended for use in the United States. Any patient diagnosed with an STI should be evaluated for other STIs, including HIV, and receive risk reduction counseling.

Chlamydia trachomatis Infection

Chlamydia trachomatis is the most commonly reported bacterial STI in the United States. Screening of all sexually active women younger than 25 years is recommended. Women aged 25 years and older should be screened if they have STI risk factors. The USPSTF concluded that evidence is insufficient to support routine screening in men; the CDC recommends screening men in settings or populations with high prevalence or burden of disease (MSM, STI clinics).

Nucleic acid amplification testing (NAAT) is preferred for screening and diagnosis. First-catch urine (for men and women) and endocervical (for women) or urethral (for men) swabs can be used. NAAT of urine samples for *C. trachomatis* and *Neisseria gonorrhoeae* has been shown to have a sensitivity and specificity nearly identical to tests obtained from urethral and endocervical samples. Chlamydia may cause oropharyngeal and rectal infection, and these sites should be

evaluated using NAAT; MSM should be screened yearly for urethral and rectal infection.

Treatment of clinical syndromes caused by *C. trachomatis* is outlined in **Table 30**. Test of cure is not recommended, except in pregnancy. Because of the high risk of repeat infection, men and women should be retested after 3 months or the next time they are seen for medical care.

KEY POINTS

- Nucleic acid amplification testing is the preferred screening and diagnostic method for *Chlamydia trachomatis* infection.
- HVC Test of cure is not recommended in patients with *Chlamydia trachomatis* infection except in pregnancy; however, patients should be retested for possible repeat infection after 3 months or at their next medical visit.

Neisseria gonorrhoeae Infection

Persons aged 20 to 24 years are at highest risk for *N. gonorrhoeae* infection. In addition to cervicitis, urethritis, pharyngitis, and rectal infection, disseminated gonococcal infection (presenting as arthritis-dermatitis syndrome) can occur (see MKSAP 19 Rheumatology). Infection can be asymptomatic, especially in women, so screening is recommended for women younger than 25 years and those 25 years and older with STI risk factors. The USPSTF does not recommend screening for men; the CDC recommends screening men at high risk, as for *C. trachomatis*.

For screening and diagnosis, NAAT is preferred. Men and women can be screened using a first-catch urine sample; endocervical, urethral, rectal, and pharyngeal swabs may also be used. Pharyngeal, urethral and rectal sites should be tested at least yearly in MSM. In patients with disseminated gonococcal infection, all *N. gonorrhoeae* isolates should be tested for antimicrobial susceptibility. Patients with suspected disseminated gonococcal infection should have cultures performed on blood, joint fluid (if arthritis is present), purulent skin lesions (if present), and cerebrospinal fluid (if meningitis is suspected); however, culture yield is not high, so NAAT from all potential sites of exposure (genital, pharyngeal, rectal) should be obtained.

Treatment is outlined in Table 30. For uncomplicated gonococcal infections of the cervix, urethra, or rectum, ceftriaxone monotherapy is recommended because *N. gonorrhoeae* remains susceptible to ceftriaxone, and azithromycin resistance is increasing; the recommended ceftriaxone dose has increased. In patients with an allergy precluding use of cephalosporins, oral gemifloxacin or parenteral gentamicin plus oral azithromycin is an option.

Patients with infections caused by *N. gonorrhoeae* who do not respond to treatment should have repeat testing with NAAT and culture so that susceptibility data can be obtained; consultation with an expert in nonresponsive infections is advised.

KEY POINTS

- Screening for *Neisseria gonorrhoeae* infection is recommended for women younger than 25 years and those 25 years and older with risk factors (new partner, more than one partner, a partner with an STI, or a partner who has concurrent partners).
- Nucleic acid amplification testing is the preferred screening and diagnostic method for *Neisseria gonorrhoeae* infection.
- Parenteral ceftriaxone is the preferred regimen for the treatment of uncomplicated *Neisseria gonorrhoeae* infection.
- Test of cure in patients with *Neisseria gonorrhoeae* infection is recommended 2 weeks after therapy only when pharyngeal gonorrhea is treated with an alternate antibiotic regimen.

Mycoplasma genitalium Infection

M. genitalium is an emerging STI that is a cause of urethritis in men. It has been reported to cause up to 20% of nongonococcal urethritis and 46% of nongonococcal/nonchlamydial urethritis in men. As an STI pathogen in women, it is implicated in cervicitis and pelvic inflammatory disease (PID). The optimal role for testing with NAAT in clinical practice has yet to be defined, and no recommendations have been published for routine screening. Recommended treatment for nongonococcal urethritis is azithromycin (1-g single dose); however, azithromycin resistance is increasingly reported, and a longer course or alternate therapy may be required.

Clinical Syndromes

Cervicitis

Women with cervicitis may have vaginal discharge and intermenstrual bleeding, but many are asymptomatic. The major diagnostic criteria are visualization of mucopurulent discharge from the cervical os or on a swab obtained from the endocervical canal and eliciting bleeding by passing a swab into the cervical os. *N. gonorrhoeae* and *C. trachomatis* are the most commonly isolated pathogens; however, many cases are enigmatic. The role of *M. genitalium* is still unclear; herpes simplex virus is occasionally implicated. Noninfectious causes (for example, chemical irritation from douching) should be sought. Patients should be tested for *N. gonorrhoeae* and *C. trachomatis* with NAAT, as well as being evaluated for bacterial vaginosis and trichomoniasis (see MKSAP 19 General Internal Medicine 2).

Pelvic Inflammatory Disease

Unrecognized PID may result in long-term sequelae, including infertility, chronic pelvic pain, and ectopic pregnancy. Symptoms include lower abdominal pain, vaginal discharge,

TABLE 30. Treatment of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* Infections and Their Complications

Clinical Syndrome	Preferred Regimen	Alternate Regimen
Cervicitis and urethritis (empiric therapy)[a]	Ceftriaxone, 250 mg IM single dose, plus azithromycin, 1 g PO single dose (preferred), *or* doxycycline[b], 100 mg PO twice daily for 7 d (only if azithromycin cannot be used)	Cefixime, 400 mg PO single dose, plus azithromycin, 1 g PO single dose (preferred), or doxycycline, 100 mg PO twice daily for 7 d
Chlamydia cervicitis, urethritis, or proctitis[a]	Azithromycin, 1 g PO single dose, *or* doxycycline, 100 mg PO twice daily for 7 d (21 d if *C. trachomatis* LGV serovars suspected or confirmed)	Erythromycin base, 500 mg PO four times daily, or erythromycin ethylsuccinate, 800 mg PO four times daily, *or* levofloxacin, 500 mg PO daily, or ofloxacin, 300 mg PO twice daily for 7 d
Gonococcal cervicitis, urethritis, or proctitis and pharyngeal infection[c,d]	Ceftriaxone, 500 mg IM single dose (1 g IM single dose for persons ≥150 kg [300 lbs]), *plus* doxycycline, 100 mg PO twice daily for 7 d; or, if pregnant, azithromycin, 1 g PO single dose (if concomitant chlamydial infection is not ruled out)	In patients allergic to cephalosporins, gentamicin, 240 mg IM single dose, plus azithromycin, 2 g PO single dose Cefixime[e], 800 mg PO single dose, *plus* doxycycline, 100 mg PO twice daily for 7 d, or, if pregnant, azithromycin 1 g PO single dose (if concomitant chlamydial infection is not ruled out) Test of cure 2 weeks after treatment for pharyngeal gonorrhea treated with an alternate regimen
Disseminated gonococcal infection[a,f]	Ceftriaxone, 1 g IM or IV every 24 h, plus azithromycin, 1 g PO single dose	Cefotaxime[g], 1 g IV every 8 h, *or* ceftizoxime[g], 1 g IV every 8 h, plus azithromycin, 1 g PO single dose
Pelvic inflammatory disease		
Parenteral therapy[h]	Cefotetan, 2 g IV every 12 h, or cefoxitin, 2 g IV every 6 h, plus doxycycline, 100 mg IV or PO every 12 h OR Clindamycin, 900 mg IV every 8 h, plus gentamicin, 2 mg/kg IV loading dose followed by 1.5 mg/kg IV every 8 hours or a single daily dose of 3-5 mg/kg/d	Ampicillin-sulbactam, 3 g IV every 6 h, plus doxycycline, 100 mg IV or PO every 12 h
Oral/IM therapy	Ceftriaxone, 250 mg IM single dose, plus doxycycline, 100 mg PO twice daily for 14 d, with or without metronidazole, 500 mg PO twice daily for 14 d, *or* cefoxitin, 2 g IM single dose, with probenecid, 1 g PO, plus doxycycline, 100 mg PO every 12 h for 14 d, with or without metronidazole, 500 mg PO twice daily for 14 d	
Epididymitis	Ceftriaxone, 250 mg IM single dose, plus doxycycline, 100 mg PO twice daily for 10 d if infection most likely due to chlamydia/gonorrhea Ceftriaxone, 250 mg IM single dose, plus levofloxacin, 500 mg PO once daily, or ofloxacin, 300 mg PO twice daily for 10 d if infection might be caused by chlamydia/gonorrhea and enteric organisms (insertive anal intercourse) Levofloxacin, 500 mg PO once daily, or ofloxacin, 300 mg PO twice daily, for 10 d if infection most likely caused by enteric organisms	

IM = intramuscularly; IV = intravenously; LGV = lymphogranuloma venereum; PO = orally.

[a]Updated CDC treatment regimens are pending.

[b]Doxycyline should be avoided or used with caution in pregnant patients.

[c]Treatment for possible chlamydial infection is recommended for all patients diagnosed with gonorrhea. Currently recommended treatment regimens for gonorrhea provide this coverage.

[d]No reliable alternative treatments are available for pharyngeal gonorrhea. For persons with a history of a β-lactam allergy, a thorough assessment of the reaction is recommended.

[e]Cefixime should be used only if ceftriaxone is unavailable because oral cephalosporin resistance to *N. gonorrhoeae* has been increasingly reported.

[f]For arthritis-dermatitis syndrome, parenteral therapy should be used until 24 to 48 hours after substantial clinical improvement and then switched to an oral therapy based on susceptibility results for a total of 7 to 10 days of treatment. Parenteral therapy is required for the entire course of treatment for meningitis (10 to 14 days) and endocarditis (at least 28 days).

[g]Not available in the United States.

[h]Patients can be switched to oral therapy within 24 to 48 hours of clinical improvement using doxycycline, 100 mg PO twice daily, with or without metronidazole, 500 mg PO twice daily, to complete a total of 14 days of therapy.

intermenstrual bleeding or bleeding after intercourse, and dyspareunia. Some women have fever and other signs of systemic toxicity, but this is uncommon.

The presence of uterine tenderness, adnexal tenderness, or cervical motion tenderness is sufficient to make a clinical diagnosis of PID, especially if accompanied by mucopurulent cervical discharge.

PID is believed to be polymicrobial; however, testing is only indicated for *N. gonorrhoeae* and *C. trachomatis*. Most infections can be managed in the ambulatory setting with oral antibiotics (see Table 30). Indications for hospitalization include inability to exclude a surgical emergency such as appendicitis, pregnancy, severe systemic toxicity, tubo-ovarian abscess, inability to tolerate oral antibiotics, and failure of initial outpatient management.

Urethritis

Men with urethritis present with dysuria, urethral pruritus, and clinically diagnostic mucopurulent discharge. *N. gonorrhoeae*, *C. trachomatis*, and *M. genitalium* are common causes; *Trichomonas* may also be causative. A first-catch urine sample should be tested for *N. gonorrhoeae* and *C. trachomatis* by NAAT; an FDA-approved NAAT for *M. genitalium* is available. Microscopic examination of a urethral sample that reveals more than 2 leukocytes per high-powered field has a high positive predictive value for infectious urethritis, but the negative predictive value is poor. A positive leukocyte esterase test result or a microscopic examination with 10 or more leukocytes on a first-void urine specimen is also diagnostic for infectious urethritis. This testing is not required if mucoid, mucopurulent, or purulent urethral discharge is demonstrated on examination.

Epididymitis

Men with epididymitis present with unilateral pain and swelling in the epididymis; the testes may also be inflamed (epididymo-orchitis). *N. gonorrhoeae* and *C. trachomatis* are likely causes in younger, sexually active men. Older men and men who practice insertive anal intercourse may be infected with enteric gram-negative organisms such as *Escherichia coli*. NAAT for STI pathogens should be performed on first-catch urine, and a urine culture should be obtained. See MKSAP 19 General Internal Medicine 2 for further information.

Anorectal Infections

Patients who present with anorectal pain, rectal discharge, or tenesmus should be questioned regarding sexual practices. In addition to receptive anal intercourse, infection may occur in women because of autoinoculation from vaginal discharge. Causes include *C. trachomatis*, *N. gonorrhoeae*, syphilis, and herpes simplex virus (HSV). Infections caused by lymphogranuloma venereum (LGV) serovars (L1, L2, or L3) of *C. trachomatis* are an increasing cause of proctitis and proctocolitis.

Diagnostic evaluation should include NAAT for *C. trachomatis*, *N. gonorrhoeae*, and HSV as well as serologic testing for syphilis. Additional molecular testing is required to identify LGV serovars of *C. trachomatis*, but it is not widely available commercially; LGV serovars of *C. trachomatis* will be detected by currently available NAATs.

KEY POINTS

- *Chlamydia trachomatis* and *Neisseria gonorrhoeae* are the primary causative organisms in cervicitis, pelvic inflammatory disease, urethritis, epididymitis, and anorectal infections, although other organisms may also be implicated.
- The two major diagnostic criteria of cervicitis are visualization of mucopurulent discharge from the cervical os or on a swab obtained from the endocervical canal or eliciting bleeding by passing a swab into the cervical os.
- The presence of uterine tenderness, adnexal tenderness, or cervical motion tenderness is sufficient to make a clinical diagnosis of pelvic inflammatory disease, especially if accompanied by mucopurulent cervical discharge.
- *Neisseria gonorrhoeae* and *Chlamydia trachomatis* are likely causes of epididymitis in younger, sexually active men; older men and men who practice insertive anal intercourse may be infected with enteric gram-negative organisms such as *Escherichia coli*.

Treatment

Treatment of the clinical syndromes discussed previously is outlined in Table 30. Symptomatic patients evaluated in urgent care centers or emergency departments and others who may not be able to return for follow up should be treated empirically based on clinical syndrome. Diagnostic testing should still be obtained because STIs are reportable, and test results will be informative if the infection fails to respond to empiric therapy.

Patients should abstain from sexual contact until 7 days after completion of therapy and all sexual partners have been treated. Sexual partners in the previous 60 days, or the most recent partner if greater than 60 days, should be referred for evaluation and treatment. Although independent evaluation and testing of sexual partners is preferred, most states have provisions for providing empiric antibiotic therapy prescriptions to the patient for their partners (expedited partner therapy, or EPT).

KEY POINT

- Most states have provisions for providing empiric antibiotic therapy prescriptions for sexual partners (expedited partner therapy).

Genital Ulcers

Herpes Simplex Virus

In some populations, such as young heterosexual women and MSM, HSV-1 is now a more common cause of symptomatic

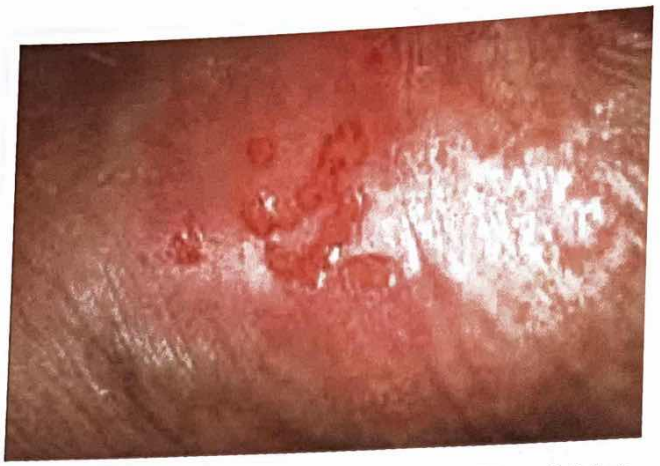

FIGURE 21. Penile lesions seen in herpes simplex virus (HSV) type 2. Patients with genital HSV infection initially have painful lesions that begin as vesicles and progress to ulcers on an erythematous base.

primary infection than HSV-2. HSV-1 is less likely than HSV-2 to cause symptomatic recurrent ulcers and subclinical shedding. Differentiation between the two viral subtypes is important in counseling patients regarding the natural history of their infection.

Primary infection presents as multiple painful lesions that begin as erythematous papules, progress to vesicles, then ulcerate, crust, and eventually heal within 2 to 3 weeks (**Figure 21**). Primary infection is often accompanied by significant systemic symptoms. Tender inguinal lymphadenopathy may be present.

NAAT for HSV-1 and HSV-2 using a swab obtained from the ulcer base is preferred to confirm the diagnosis. Type-specific serologic testing is not advised for diagnosing symptomatic ulcer disease because patients can be seropositive for HSV-1 or HSV-2 yet have genital ulcers from another cause. Serologic testing may be performed when evaluating the potential benefits of long-term suppressive therapy to decrease the transmission risk in serodiscordant couples. The CDC recommends considering HSV serologic testing in persons who present for STI evaluation, MSM, and persons with HIV infection. Serologic screening in the general population is not recommended.

Antiviral therapy for primary infection has been shown to decrease time to resolution of symptoms, lesion healing, and viral shedding (**Table 31**).

Recurrent genital HSV infections are less severe. Many patients will experience prodromal itching, burning, or tingling before ulcers appear. Atypical presentations such as fissures and excoriations may occur. Recurrent infection can be managed with either episodic self-start therapy (initiated within 24 hours of symptoms) or long-term suppressive therapy (see Table 31). Long-term suppressive therapy should be considered for persons with frequent recurrences and should be discussed with all patients because this strategy can decrease the risk of transmission to sexual partners. Laboratory monitoring is not required for patients undergoing long-term suppressive therapy; however, the continued need for therapy should be reviewed annually. Length of time since last recurrence and potential benefits of continued suppression in preventing transmission to sexual partners are factors that can inform the decision to stop suppressive therapy.

KEY POINTS

- In primary infection, the viral cause and herpes simplex virus subtype should be confirmed by nucleic acid amplification testing using a swab obtained from the ulcer base.
- Long-term suppressive therapy for recurrent herpes simplex virus infection may be preferred over self-start episodic therapy because of decreased risk of transmission to sexual partners.

Syphilis

The incidence of primary and secondary syphilis has been increasing in the United States since 2000, and an alarming increase in congenital infections has been reported. The USPSTF recommends screening all pregnant women, nonpregnant adolescents, and adults at high risk of infection. Persons at risk include MSM and commercial sex workers and those with HIV infection, multiple sexual partners, and previous syphilis.

TABLE 31. Treatment of Herpes Simplex Virus Genital Infections

Clinical Syndrome	Recommended Regimen[a]
Primary infection[b]	Acyclovir, 400 mg three times daily, *or* acyclovir, 200 mg five times daily, *or* famciclovir, 250 mg three times daily, *or* valacyclovir, 1 g twice daily; all regimens for 7-10 days
Recurrent infection	Acyclovir, 400 mg three times daily for 5 days, *or* acyclovir, 800 mg twice daily for 5 days, *or* acyclovir, 800 mg three times daily for 2 days, *or* famciclovir, 125 mg twice daily for 5 days, *or* famciclovir, 1 g twice daily for 1 day, *or* famciclovir, 500 mg once followed by 250 mg twice daily for 2 days, *or* valacyclovir, 500 mg twice daily for 3 days, *or* valacyclovir, 1 g once daily for 5 days
Suppressive therapy	Acyclovir, 400 mg twice daily, *or* famciclovir, 250 mg twice daily, *or* valacyclovir, 500 mg daily[c], *or* valacyclovir, 1 g daily

[a]All regimens are given orally; topical preparations are not recommended for treatment of genital herpes simplex virus.

[b]Therapy can be extended if healing is incomplete after 10 days of treatment.

[c]The 500-mg dose of valacyclovir may be less effective than the 1-g dose in patients who have very frequent recurrences (≥10 episodes per year).

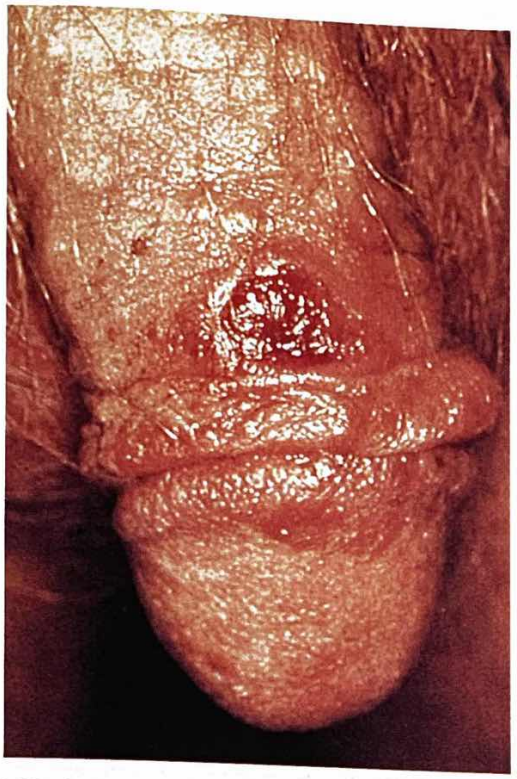

FIGURE 22. The primary ulcerative lesion (chancre) in patients with syphilis develops approximately 3 weeks after infection occurs, has a clean appearance with heaped-up borders, and is indurated and usually painless. It is often unrecognized.

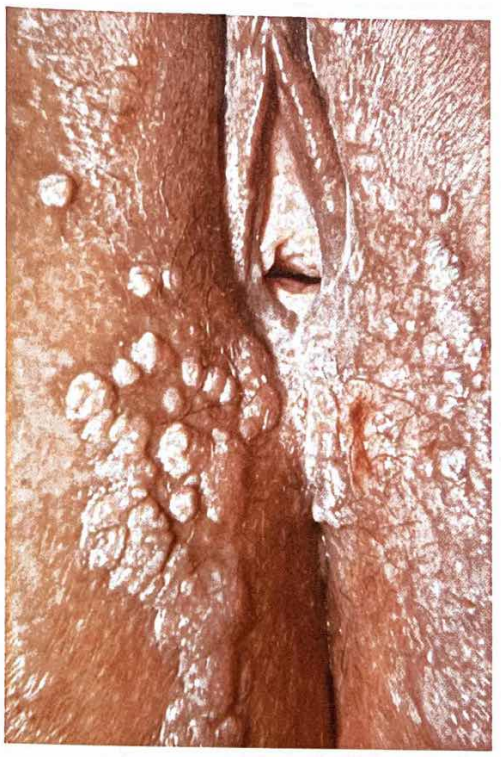

FIGURE 23. In patients with rash caused by secondary syphilis, papules may coalesce in intertriginous areas to form plaque-like lesions called condyloma lata.

Primary syphilis presents as a painless genital ulcer (chancre) with a raised regular border that demonstrates firm induration on palpation (**Figure 22**). Several chancres may be present and may occur in the oral cavity. Regional lymphadenopathy may be present. Serologic test results may be negative in early primary infection. Even without treatment, lesions heal spontaneously in 3 to 6 weeks.

The most common manifestation of secondary syphilis is rash. Various forms are described; involvement of the palms and soles is characteristic. In intertriginous areas, papules may coalesce to form condyloma lata (**Figure 23**). Mucous patches (superficial erosions on mucosal surfaces) may occur in the oral cavity and moist genital regions and are highly infectious (**Figure 24**). Prominent systemic symptoms and generalized lymphadenopathy are common. Uveitis and neurosyphilis (meningitis) can occur. Secondary syphilis manifestations can also resolve without treatment, followed by latent infection (a positive serologic test result without clinical manifestations). If latent infection is of less than 12 months' duration, it is termed early latent; if greater than 12 months' duration, it is late latent. Practically, these determinations can be made only if past serology results are available. Otherwise, patients are considered to have syphilis of unknown duration.

Tertiary syphilis is uncommonly seen in the United States, although neurologic disease still occurs, including stroke, altered mental status, and auditory or ophthalmic abnormalities. Spinal fluid should be examined in any patient with unexplained neurologic symptoms and serologic evidence of syphilis as well as in those who do not demonstrate an appropriate serologic response to syphilis treatment.

Secondary and tertiary syphilis diagnosis relies on serologic testing. Many laboratories use the "reverse" serologic testing strategy, starting with an automated enzyme immunoassay followed by a nonspecific test (rapid plasma reagin or Venereal Disease Research Lab test). Patients with a positive enzyme immunoassay result but negative rapid plasma reagin or Venereal Disease Research Lab test result should have a second specific treponemal antibody test to confirm the result.

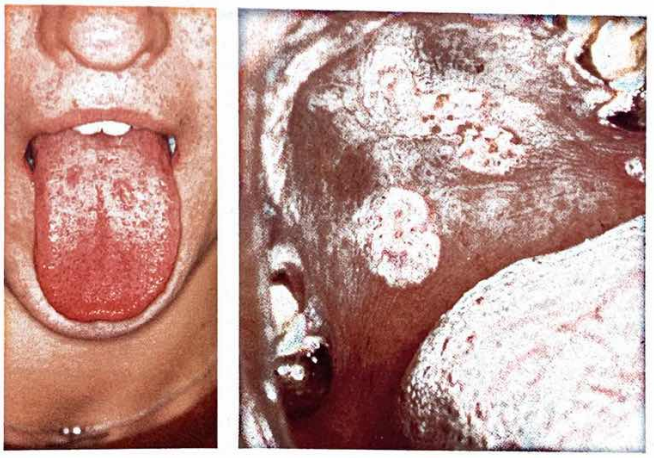

FIGURE 24. Mucous patches are often slightly raised, plaque-like lesions that can be seen in the oral or genital mucosal regions. They occasionally ulcerate and are covered by a grayish membrane.

TABLE 32. Treatment of Syphilis

Stage	Recommended Regimen[a]	Alternate Regimen for Penicillin-Allergic Patients
Primary and secondary	Benzathine penicillin G, 2.4 million units IM single dose	Doxycycline, 100 mg PO twice daily, *or* tetracycline, 500 mg PO four times daily, for 14 days
Early latent	Benzathine penicillin G, 2.4 million units IM single dose	Doxycycline, 100 mg PO twice daily, *or* tetracycline, 500 mg PO four times daily, for 14 days
Late latent or syphilis of unknown duration	Benzathine penicillin G, 2.4 million units IM at 1-week intervals for 3 doses	Doxycycline, 100 mg PO twice daily, *or* tetracycline, 500 mg PO four times daily, for 28 days
Neurosyphilis	Aqueous crystalline penicillin G, 18-24 million units daily given as 3-4 million units IV every 4 hours or by continuous infusion for 10-14 days, *or* procaine penicillin, 2.4 million units IM daily, plus probenecid, 500 mg PO four times daily, both for 10-14 days	Ceftriaxone, 2 g IM or IV daily for 10-14 days[b]

IM = intramuscularly; IV = intravenously; PO = orally.

[a]Penicillin is the only effective antimicrobial agent for treatment of syphilis at any stage in pregnancy; therefore, pregnant penicillin-allergic patients should be desensitized and treated with the appropriate penicillin regimen as outlined above.

[b]Limited data are available to support the use of this alternate regimen, and the possibility of cross-reaction in penicillin-allergic patients must be considered. In patients who cannot take ceftriaxone, penicillin desensitization is recommended.

Those with a confirmed positive result and no history of syphilis treatment should be offered treatment for syphilis of unknown duration.

Syphilis treatment is outlined in **Table 32**. Sexual partners of those with primary, secondary, or early latent syphilis exposed in the preceding 90 days should be treated regardless of serologic results.

KEY POINTS

- Primary syphilis presents as a painless genital ulcer (chancre) with a raised regular border that demonstrates firm induration on palpation; lesions heal spontaneously in 3 to 6 weeks even without treatment.
- The most common manifestation of secondary syphilis is rash, with characteristic involvement of the palms and soles; in intertriginous areas, papules may coalesce to form condyloma lata, and mucous patches may occur in the oral cavity and moist genital regions and are highly infectious.

(Continued)

KEY POINTS *(continued)*

- Secondary and tertiary syphilis diagnosis relies on serologic testing; patients with a positive enzyme immunoassay result and positive rapid plasma reagin or Venereal Disease Research Lab test result and no history of syphilis treatment should be offered treatment for syphilis of unknown duration.

Chancroid and Lymphogranuloma Venereum

Except for proctitis or proctocolitis caused by the LGV serovars of *C. trachomatis*, these two STIs are rarely seen in the United States. The clinical presentation, evaluation, and treatment are outlined in **Table 33**.

Genital Warts

Genital warts have a variety of appearances, including papular or pedunculated lesions (**Figure 25**). Larger, verrucous, exophytic lesions can occur. Most are

TABLE 33. Clinical Presentation, Diagnosis, and Treatment of Chancroid and Lymphogranuloma Venereum

Clinical Entity	Causative Agent	Presentation	Diagnosis	Recommended Regimen
Chancroid	*Haemophilus ducreyi*	Painful genital ulcer; tender inguinal lymph nodes, which often suppurate	Culture is difficult; consider diagnosis if painful ulcer with tender and suppurative regional lymphadenopathy, no evidence of syphilis by dark-field examination or serology, and negative HSV PCR or HSV culture	Azithromycin, 1 g PO single dose, *or* ceftriaxone, 250 mg IM single dose, *or* ciprofloxacin, 500 mg PO twice daily for 3 days, *or* erythromycin base, 500 mg PO three times daily for 7 days
LGV	L1, L2, and L3 serovars of *Chlamydia trachomatis*	Painless genital papule or ulcer with unilateral tender inguinal lymphadenopathy; proctitis, proctocolitis in MSM	NAAT for *C. trachomatis*; does not distinguish the serovars, so diagnosis is made based on clinical and epidemiologic findings	Doxycycline[a], 100 mg PO twice daily for 21 days (preferred), *or* erythromycin base, 500 mg PO four times daily for 21 days (alternate)

HSV = herpes simplex virus; IM = intramuscularly; LGV = lymphogranuloma venereum; MSM = men who have sex with men; NAAT = nucleic acid amplification test; PCR = polymerase chain reaction; PO = orally.

[a]*Doxycyline should be avoided or used with caution in pregnant patients.*

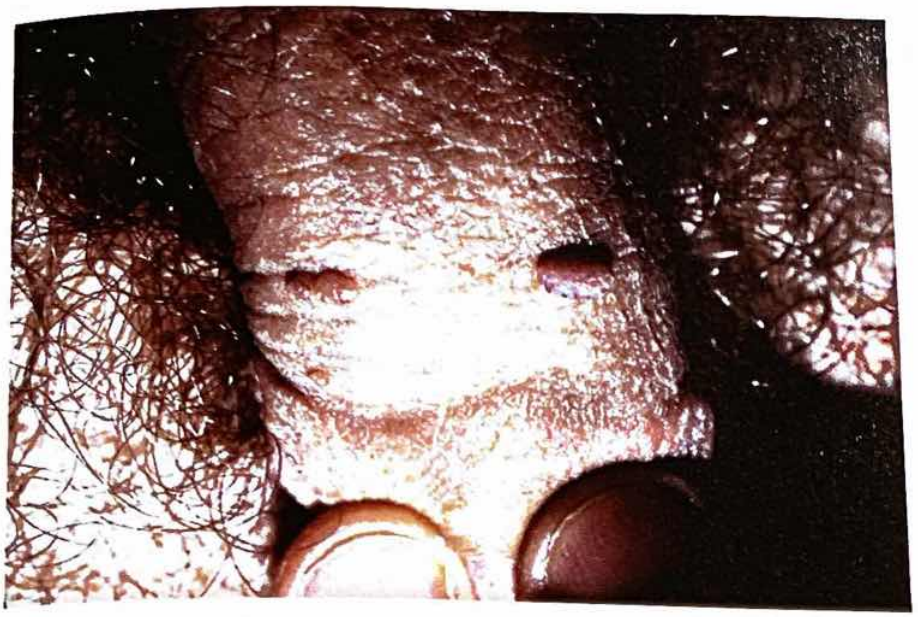

FIGURE 25. Genital warts caused by human papillomavirus infection are typically flesh colored and exophytic; pedunculated lesions often occur.

asymptomatic; however, large lesions may cause irritation or pain depending on their location. Nononcogenic types of human papillomavirus (HPV) are responsible for most lesions. Specific testing for HPV is not recommended for diagnosis.

Warts often resolve without therapy, but treatment is indicated for symptomatic warts or psychological distress. Patients should be counseled that successful treatment might not eliminate the risk of transmission. Patient-applied therapies include imiquimod, podofilox, and sinecatechins; provider-administered therapies include trichloroacetic or bichloroacetic acid, cryotherapy with liquid nitrogen or cryoprobe, or surgical removal. No evidence indicates any recommended modality is superior. Ulcerated or pigmented warts and those that fail to respond to or worsen after therapy should be biopsied to exclude a cancerous lesion.

KEY POINT

- Nononcogenic types of human papillomavirus are responsible for most genital warts, which often resolve without therapy.