Treatment

Despite the classic staging of syphilis as primary, secondary, latent, or tertiary, the disease is best thought of in terms of early infection (<1 year) or late infection (≥1 year) when considering treatment. *T. pallidum* remains sensitive to penicillin. Individuals with early syphilis can be treated with a single intramuscular injection of benzathine penicillin G (Bicillin), which achieves high and prolonged serum concentrations. Individuals with late syphilis or disease of unknown duration should be treated with three weekly injections of intramuscular benzathine penicillin G (Table 100-3). This cures most patients.

Although penicillin remains the drug of choice, doxycycline may also be used in individuals who have severe allergies to penicillin. However, every effort should be made to use penicillin because of the sensitivity of the organism. For pregnant women who are allergic to penicillin, penicillin desensitization should occur in collaboration with a pharmacist and an allergist specialist. As a result of treatment, individuals may experience a febrile reaction (i.e., Jarisch-Herxheimer reaction). Symptoms are caused by killing of the spirochetes and should not be confused with an allergic reaction.

The co-epidemic of syphilis and HIV has led to an increase in individuals with manifestations of neurosyphilis. In cases of syphilis with neurologic symptoms, a lumbar puncture is warranted to rule out neurologic involvement. Any pleocytosis or increase in protein concentration warrants treatment for neurosyphilis. A cerebrospinal fluid (CSF) sample should be sent for VDRL testing, but the test lacks sensitivity (50%), and a negative test result does not rule out neurosyphilis. Usually, HIV-negative individuals with syphilis without neurologic symptoms should not undergo a lumbar puncture. Many HIV-infected individuals with syphilis, however, have asymptomatic neurosyphilis. The clinical implications of this are unclear, but these individuals may fail intramuscular therapy at a high rate. Some experts recommend CSF examination in all HIV-infected individuals with a $CD4^+$ count lower than 350 cells/μL or a nontreponemal titer greater than 1 : 32. These criteria capture almost everyone with asymptomatic neurosyphilis.

TABLE 100-3 SYPHILIS TREATMENT

CLINICAL CATEGORY	REGIMEN OF CHOICE	ALTERNATIVE*
Early syphilis (<1 year)	Benzathine penicillin, 2.4 million units IM, given once	Penicillin desensitization Doxycycline, 100 mg PO bid for 14 days Tetracycline, 500 mg PO qid for 14 days Azithromycin 2 g PO qd
Late syphilis (≥1 year) or unknown duration	Benzathine penicillin, 2.4 million units IM, given once each week for 3 wk	Penicillin desensitization Doxycycline, 100 mg PO bid for 28 days Tetracycline, 500 mg PO qid for 28 days
Neurosyphilis	Penicillin G, 4 million units IV q4h or 24 million units by continuous infusion qd for 10-14 days	Penicillin desensitization Ceftriaxone 2 g qd IM or IV for 10-14 days

*If patient has a penicillin allergy.

Individuals with neurosyphilis should be treated with intravenous penicillin G for 10 to 14 days. In tertiary disease with manifestations of neurologic disease, treatment with intravenous penicillin halts disease progression but does not reverse existing structural damage. Ocular disease or other similar neurologic manifestations should be treated as neurosyphilis. Nontreponemal titers should be followed to ensure an appropriate response. Repeat treatment may be necessary in a small number of cases.

Prognosis

Although penicillin is the treatment of choice for syphilis, it has not been validated in clinical trials but is based on a long history of clinical use. However, a significant number of individuals with syphilis do not respond with the recommended decline in nontreponemal titer. Individuals who do not respond should be retreated.

For a deeper discussion of these topics, please see Chapter 319, "Syphilis," in Goldman-Cecil Medicine, *25th Edition.*

Herpes Simplex Virus

Definition and Epidemiology

Herpes simplex virus types 1 and 2 (HSV-1/2) cause a wide variety of clinical disease. HSV-1 is usually the cause of herpes labialis (i.e., cold sores), and HSV-2 is the cause of genital herpes, although there may be overlap. After infection occurs, HSV-1/2 enters a latent state and may later reactivate to cause disease in a subset of individuals.

The overall prevalence of HSV-1 and HSV-2 in the population is approximately 60% and 20%, respectively. However, the incidence of HSV-1 infection approaches 90% to 100% among middle-aged adults. Seroprevalence of HSV-2 is associated with a patient's sexual activity, including number of partners and history of other STIs, and with age, gender (women ae at higher risk than men), and race or ethnicity. More than 50 million people in the United States are infected with genital HSV-1/2, and most are asymptomatic. CDC guidelines do not recommend routine screening for HSV-1/2 in people without symptoms. There is no evidence that screening for HSV-1/2 reduces its spread or has an impact on the disease. HSV-1/2 is not a reportable disease in the United States.

Pathology

HSV-1 and HSV-2 are two of eight double-stranded DNA human herpesviruses. Others are varicella-zoster virus (VZV), cytomegalovirus (CMV), Epstein-Barr virus (EBV), and human herpesviruses 6, 7, and 8. Infection with one type of HSV does not prevent or increase the chances of infection with other types. After initial infection, HSV-1/2 enters a latent state within neuronal cells of sensory or autonomic peripheral ganglia. Reactivation can occur at any time and is mediated in part by immune factors. HSV-1 most commonly infects the trigeminal ganglia and HSV-2 the sacral nerve root ganglia (S2-S5).

Clinical Presentation

Transmission of HSV-1/2 is through skin-to-skin contact, including sexual contact at mucosal surfaces, including the oropharynx,