TABLE 206-2 RECOMMENDATIONS FOR THE TREATMENT OF SYPHILIS[a]

Stage of Syphilis	Patients without Penicillin Allergy	Patients with Confirmed Penicillin Allergy[b]
Primary, secondary, or early latent	*CSF normal or not examined:* Penicillin G benzathine (single dose of 2.4 mU IM)	*CSF normal or not examined:* Tetracycline HCl (500 mg PO qid) or doxycycline (100 mg PO bid) for 2 weeks
	CSF abnormal: Treat as neurosyphilis	*CSF abnormal:* Treat as neurosyphilis
Late latent (or latent of uncertain duration), cardiovascular, or benign tertiary	*CSF normal or not examined:* Penicillin G benzathine (2.4 mU IM weekly for 3 weeks)	*CSF normal and patient not infected with HIV:* Tetracycline HCl (500 mg PO qid) or doxycycline (100 mg PO bid) for 4 weeks
	CSF abnormal: Treat as neurosyphilis	*CSF normal and patient infected with HIV:* Desensitization and treatment with penicillin if compliance cannot be ensured
		CSF abnormal: Treat as neurosyphilis
Neurosyphilis (asymptomatic or symptomatic)	Aqueous crystalline penicillin G (18–24 mU/d IV, given as 3–4 mU q4h or continuous infusion) for 10–14 days	Desensitization and treatment with penicillin[c]
	or	
	Aqueous procaine penicillin G (2.4 mU/d IM) plus oral probenecid (500 mg qid), both for 10–14 days	
Syphilis in pregnancy	According to stage	Desensitization and treatment with penicillin

[a]See Table 206-1 and text for indications for CSF examination. [b]Because of the documented presence of macrolide resistance in many *T. pallidum* strains in North America, Europe, and China, azithromycin or other macrolides should be used with caution only when treatment with penicillin or doxycycline is not feasible. Azithromycin should not be used for men who have sex with men or for pregnant women. [c]Limited data suggest that ceftriaxone (2 g/d either IM or IV for 10–14 days) can be used; however, cross-reactivity between penicillin and ceftriaxone is possible.

Abbreviations: CSF, cerebrospinal fluid; mU, million units.

Source: Adapted from the 2010 Sexually Transmitted Diseases Treatment Guidelines from the Centers for Disease Control and Prevention.

CD4+ T cell count of ≤350/μL. Therapy appropriate for neurosyphilis should be given if there is any evidence of CNS infection.

Late Latent Syphilis or Syphilis of Unknown Duration If the CSF is normal or is not examined, the recommended treatment is penicillin G benzathine (7.2 million units total; Table 206-2). If CSF abnormalities are found, the patient should be treated for neurosyphilis.

Tertiary Syphilis CSF examination should be performed. If the CSF is normal, the recommended treatment is penicillin G benzathine (7.2 million units total; Table 206-2). If CSF abnormalities are found, the patient should be treated for neurosyphilis. The clinical response to treatment for benign tertiary syphilis is usually impressive. However, responses to therapy for cardiovascular syphilis are not dramatic because aortic aneurysm and aortic regurgitation cannot be reversed by antibiotics.

Syphilis in Penicillin-Allergic Patients For penicillin-allergic patients with syphilis, a 2-week (early syphilis) or 4-week (late or late latent syphilis) course of therapy with doxycycline or tetracycline is recommended (Table 206-2). These regimens appear to be effective in early syphilis but have not been tested for late or late latent syphilis, and compliance may be problematic. Limited studies suggest that ceftriaxone (1 g/d, given IM or IV for 8–10 days) is effective for early syphilis. These nonpenicillin regimens have not been carefully evaluated in HIV-infected individuals and should be used with caution. If compliance and follow-up cannot be ensured, penicillin-allergic HIV-infected persons with late latent or late syphilis should be desensitized and treated with penicillin.

Neurosyphilis Penicillin G benzathine, given in total doses of up to 7.2 million units, does not produce detectable concentrations of penicillin G in CSF and should not be used for treatment of neurosyphilis. Asymptomatic neurosyphilis may relapse as symptomatic disease after treatment with benzathine penicillin, and the risk of relapse may be higher in HIV-infected patients. Both symptomatic and asymptomatic neurosyphilis should be treated with aqueous penicillin (Table 206-2). Administration either of IV aqueous crystalline penicillin G or of IM aqueous procaine penicillin G plus oral probenecid in recommended doses is thought to ensure treponemicidal concentrations of penicillin G in CSF. The clinical response to penicillin therapy for meningeal syphilis is dramatic, but treatment of neurosyphilis with existing parenchymal damage may only arrest disease progression. No data suggest that additional therapy (e.g., penicillin G benzathine for 3 weeks) is beneficial after treatment for neurosyphilis.

The use of antibiotics other than penicillin G for the treatment of neurosyphilis has not been studied, although very limited data suggest that ceftriaxone may be used. In patients with penicillin allergy demonstrated by skin testing, desensitization and treatment with penicillin are recommended.

Management of Syphilis in Pregnancy Every pregnant woman should undergo a nontreponemal test at her first prenatal visit and, if at high risk of exposure, again in the third trimester and at delivery. In the untreated pregnant patient with presumed syphilis, expeditious treatment appropriate to the stage of the disease is essential. Patients should be warned of the risk of a Jarisch-Herxheimer reaction, which may be associated with mild premature contractions but rarely results in premature delivery.

Penicillin is the only recommended agent for the treatment of syphilis in pregnancy. If the patient has a documented penicillin allergy, desensitization and penicillin therapy should be undertaken according to the CDC's 2010 guidelines. After treatment, a quantitative nontreponemal test should be repeated monthly throughout pregnancy to assess therapeutic efficacy. Treated women whose antibody titers rise by fourfold or whose titers do not decrease by fourfold over a 3-month period should be re-treated.

EVALUATION AND MANAGEMENT OF CONGENITAL SYPHILIS

Whether or not they are infected, newborn infants of mothers with reactive serologic tests may themselves have reactive tests because of transplacental transfer of maternal IgG antibody. For asymptomatic infants born to women treated adequately with penicillin during the first or second trimester of pregnancy, monthly quantitative nontreponemal tests may be performed to monitor for appropriate reduction in antibody titers. Rising or persistent titers indicate infection, and the infant should be treated. Detection of neonatal IgM antibody may be useful, but no commercially available test is currently recommended.

An infant should be treated at birth if the treatment status of the seropositive mother is unknown; if the mother has received inadequate or nonpenicillin therapy; if the mother received penicillin therapy in the third trimester; or if the infant may be difficult to follow. The CSF should be examined to obtain baseline values before treatment. Penicillin is the only recommended drug for the treatment of syphilis in infants. Specific recommendations for the treatment of infants and older children are included in the CDC's 2010 treatment guidelines.