26. Screening for Syphilis

RECOMMENDATION

Routine serologic screening for syphilis is recommended for all pregnant women and for persons at increased risk of infection (see *Clinical Intervention*). See Chapter 62 for recommendations on counseling to prevent sexually transmitted diseases.

Burden of Suffering

Syphilis is caused by infection with the bacterium *Treponema pallidum* which can be transmitted congenitally or by sexual contact. In 1994, 20,627 cases of primary and secondary syphilis were reported in the United States.[1] Primary syphilis produces ulcers of the genitalia, pharynx, or rectum, and secondary syphilis is characterized by contagious skin lesions, lymphadenopathy, and condylomata lata.[2] Systemic spread, including invasion of the central nervous system, can occur early in infection and may be symptomatic during early or late stages of syphilis. The disease then evolves into a latent phase in which syphilis is clinically inapparent. If left untreated, as many as one third of patients progress to have potentially severe late gummatous, cardiovascular, and neurologic complications.[3] Cardiovascular syphilis produces aortic disease (insufficiency, aneurysms, aortitis), and neurosyphilis can result in meningitis, peripheral neuropathy (e.g., tabes dorsalis), meningovascular brain lesions, and psychiatric illness. Persons with tertiary syphilis may have decreased life expectancy, and they often experience significant disability and diminished productivity as a result of their symptoms. Long-term hospitalization is often necessary for patients with severe neurologic deficits or psychiatric illness. Syphilis has been associated epidemiologically with acquisition and transmission of infection with human immunodeficiency virus (HIV).[4,5]

The incidence of syphilis has decreased by 50% since 1990, but it is still high and now approximates 1970 rates.[1] A growing proportion of cases is being reported among commercial sex workers and persons who use illicit drugs, especially those using crack cocaine and those who exchange sex for drugs.[6,7] There are pronounced geographic differences in the incidence of syphilis in different communities. In recent data, nearly all counties with a high incidence of reported syphilis cases (more than 10/100,000 persons) were in large metropolitan areas or in southern states; nearly two thirds of all counties in the U.S. reported no cases of pri-

mary or secondary syphilis in the most recent year.[1] The incidence of reported infections among Hispanics and blacks is 5–60 times higher than that in non-Hispanic whites.[1] Individual communities may experience substantial fluctuations in incidence rates independent of national trends.

The incidence of congenital syphilis had increased sharply in the last 15 years, but it has fallen since 1991.[1] Congenital syphilis results in fetal or perinatal death in 40% of affected pregnancies, as well as in an increased risk of medical complications in surviving newborns.[8] The incidence of congenital syphilis increased steadily in the United States from 1978 to 1991,[9] reaching 108 cases per 100,000 live births in 1991.[1] (The reporting definition changed in 1989 to reflect both confirmed cases and infants at high risk of infection.) The rate dropped from 1991 to 1994, to 56 cases per 100,000 live births.[1]

Accuracy of Screening Tests

Serologic tests are currently the mainstay for syphilis diagnosis and management. Nontreponemal tests are used to screen patients for the presence of nonspecific reagin antibodies that appear and rise in titer following infection. Although VDRL (Venereal Disease Research Laboratory) and RPR (rapid plasma reagin) are the most commonly used nontreponemal tests, others are available. The sensitivity of nontreponemal tests varies with the levels of antibodies present during the stages of disease. In early primary syphilis, when antibody levels may be too low to detect, results may be nonreactive, and the sensitivity of nontreponemal tests is 62–76%.[10] Antibody levels rise as disease progresses; titers usually peak during secondary syphilis, when the sensitivity of nontreponemal tests approaches 100%. In late syphilis, titers decline, and previously reactive results revert to nonreactive in 25% of patients; in untreated late syphilis, test sensitivity averages only 70%.[10] Nontreponemal test titers decline or revert to normal after successful treatment.

Nontreponemal tests can produce sustained or transient false-positive reactions due to preexisting conditions (e.g., collagen vascular diseases, injection drug use, advanced malignancy, pregnancy) or infections (e.g., malaria, tuberculosis, viral and rickettsial diseases), or due to laboratory-associated errors.[10–12] The specificity of nontreponemal tests is 75–85% in persons with preexisting diseases or conditions, and it approaches 100% in persons without them.[10,13] Because nontreponemal serodiagnostic tests may be falsely positive, all reactive results in asymptomatic patients should be confirmed with a more specific treponemal test such as fluorescent treponemal antibody absorption (FTA-ABS), which has a sensitivity of 84% in primary syphilis and almost 100% for other stages, and a specificity of 96%.[14] Two less expensive and easier to perform confirmatory tests are the

MHA-TP (microhemagglutination assay for antibodies to *Treponema pallidum*) and HATTS (hemagglutination treponemal test for syphilis).[13]

Treponemal tests should not be used as initial screening tests in asymptomatic patients, as they are considerably more expensive and remain reactive in patients with previous, treated infection. Used in concert with nontreponemal tests, however, the positive predictive value of treponemal tests is high, and reactive results are likely to represent true infection with syphilis. Treponemal tests may also be useful in patients with suspected late syphilis and nonreactive nontreponemal tests, since declining antibody titers may produce false-negative nontreponemal tests. All test results should be evaluated in concert with a clinical diagnosis and history.

Infection with HIV may alter the clinical presentation and performance of serologic tests for syphilis. Co-infection with HIV and syphilis does not generally impair the sensitivity of syphilis testing, although there are sporadic reports of absent or delayed response to nontreponemal tests. [14,15] In contrast, HIV infection may reduce the specificity of syphilis testing; several studies have noted increased reactivity to nontreponemal tests among HIV-infected persons without syphilis. [15,16] Persistence of elevated nontreponemal titers after treatment for syphilis has also been reported in some HIV-infected persons, making it difficult to confirm the adequacy of treatment.[17,18] At the same time, treponema-specific tests may become nonreactive after treatment of syphilis in HIV-infected persons, limiting the ability to document past infection.[14,19,20]

Effectiveness of Early Detection

Early detection of syphilis in asymptomatic persons permits the initiation of antibiotic therapy to eradicate the infection, thereby preventing both clinical disease and transmission to sexual contacts. Antibiotic therapy with penicillin G benzathine (or tetracycline hydrochloride if neurosyphilis has been excluded) has been shown to be highly effective in eliminating *T. pallidum*. Early detection and penicillin treatment during pregnancy have the added benefit of reducing the risk to the fetus of acquiring congenital syphilis.[9] Prenatal antibiotic therapy is effective in preventing congenital syphilis when the mother is treated with penicillin early in pregnancy (desensitization for penicillin allergy may be required).[21] Failures can occur, however, if women are treated with erythromycin, an antibiotic with limited efficacy in preventing congenital syphilis, or if antibiotic therapy is not started until the third trimester.[21]

Recommendations of Other Groups

The American College of Obstetricians and Gynecologists and the American Academy of Pediatrics recommend routine prenatal screening for

syphilis at the first prenatal visit, after exposure to an infected partner, and in the third trimester for patients at high risk.[22,23] In the event of incomplete or equivocal data on maternal serology or treatment, neonatal testing is recommended. The American Academy of Family Physicians[24] and the American College of Physicians[25] recommend serologic screening for syphilis in high-risk adults (prostitutes, persons who engage in sex with multiple partners in areas in which syphilis is prevalent, contacts of persons with active syphilis). The American Academy of Family Physicians,[24] American Academy of Pediatrics,[22,26] American Medical Association,[27] and Bright Futures[28] all recommend routine syphilis screening for sexually active adolescents at increased risk. The Centers for Disease Control and Prevention recommends obtaining serology for syphilis from all women at the first prenatal visit.[21] In communities and populations with high syphilis prevalence or for patients at high risk, serologic testing should be repeated during the third trimester and again at delivery.[21] The Canadian Task Force on the Periodic Health Examination recommends testing for syphilis in pregnant women and sexually active persons in high-risk groups.[29]

Discussion

Since the annual incidence of syphilis is less than 10 cases per 100,000 persons,[1] routine screening of the general population is likely to have low yield. Populations at increased risk due to high-risk sexual activities include commercial sex workers, persons who exchange sex for drugs, persons with other sexually transmitted diseases (STDs) including HIV, and contacts of persons with active syphilis. The value of screening for asymptomatic infection in other persons will depend on both individual risk factors (e.g., the number and nature of sex partners) and on local epidemiology. Experience with HIV and other STDs demonstrates that sexual history is not sufficiently sensitive to identify infected persons in high-risk communities; some persons may not report risk factors, and even monogamous patients may be at risk from an infected partner. Conversely, in communities where syphilis is uncommon, screening asymptomatic persons is likely to detect few cases of syphilis, even when patients have high-risk behaviors.

Routine screening in both high- and low-risk areas is justified among pregnant women, because of the severe neonatal morbidity and mortality associated with congenital syphilis, as well as its potential preventability. Determination of sexual risk factors is often insensitive in pregnant women, who may be reluctant to admit some behaviors or unaware of risk factors in their partners.[10] Several studies have demonstrated that prenatal screening for syphilis is cost-effective, even when the prevalence of the disease among pregnant women is as low as 0.005%.[30,31] Currently, congenital syphilis occurs in 0.05% of all live births.[1]

CLINICAL INTERVENTION

Routine serologic testing for syphilis is recommended for all pregnant women and for persons at increased risk for infection, including commercial sex workers, persons who exchange sex for money or drugs, persons with other STDs (including HIV), and sexual contacts of persons with active syphilis ("A" recommendation). The local incidence of syphilis in the community and the number of sex partners reported by an individual should also be considered in identifying persons at high risk of infection. The optimal frequency for such testing has not been determined and is left to clinical discretion.

All pregnant women should be tested at their first prenatal visit. For women at high risk of acquiring syphilis during pregnancy (e.g., women in the high-risk groups listed above), repeat serologic testing is recommended in the third trimester and at delivery. Follow-up serologic tests should be obtained to document decline in titers after treatment. They should be performed using the same test initially used to document infection (e.g., VDRL or RPR) to ensure comparability.

See Chapter 62 for recommendations on counseling to prevent sexually transmitted diseases.

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