

Screening for Syphilis Infection: Recommendation Statement

U.S. Preventive Services Task Force

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This statement summarizes the U.S. Preventive Services Task Force (USPSTF) recommendations on screening for syphilis and the supporting scientific evidence, and updates the 1996 recommendations contained in the *Guide to Clinical Preventive Services*, second edition.¹ In 1996, the USPSTF recommended routine screening for syphilis infection for all pregnant women and for persons at increased risk for infection (A recommendation). Since then, the USPSTF criteria to rate the strength of the evidence have changed.² Therefore, this recommendation statement has been updated and revised based on the current USPSTF methodology and rating of the strength of the evidence.

Explanations of the current Task Force ratings and of the strength of overall evidence are given in Appendix A and Appendix B, respectively.

The complete information on which this statement is based, including evidence tables and references, is available in the brief update³ on this topic on the USPSTF Web site (www.preventiveservices.ahrq.gov). The recommendation statement and brief update are also available in print from the Agency for Healthcare Research and Quality (AHRQ) Publications Clearinghouse (call 1-800-358-9295, or e-mail ahrqpubs@ahrq.gov). The recommendation is also posted on the Web site of the National Guideline Clearinghouse™ (www.guideline.gov).

Recommendations made by the USPSTF are independent of the U.S. Government. They should not be construed as an official position of AHRQ or the U.S. Department of Health and Human Services.

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SUMMARY OF RECOMMENDATIONS

- The U.S. Preventive Services Task Force (USPSTF) strongly recommends that clinicians screen persons at increased risk for syphilis infection. **A recommendation.**

Although the USPSTF found no new direct evidence that screening for syphilis infection leads to improved health outcomes in persons at increased risk (see Clinical Considerations), there is adequate evidence that screening tests can accurately detect syphilis infection and that antibiotics can cure syphilis. Screening may result in potential harms (such as clinical evaluation of false-positive results, unnecessary anxiety to the patient, and harms of antibiotic use). The USPSTF concludes that the benefits of screening persons at increased risk for syphilis infection substantially outweigh the potential harms.

- The USPSTF strongly recommends that clinicians screen all pregnant women for syphilis infection. **A recommendation.**

The USPSTF found observational evidence that the universal screening of pregnant women decreases the proportion of infants with clinical manifestations of syphilis infection and those with positive serologies. The USPSTF concludes that the benefits of screening all pregnant women for syphilis infection substantially outweigh potential harms.

- The USPSTF recommends against routine screening of asymptomatic persons who are not at increased risk for syphilis infection. **D recommendation.**

Given the low incidence of syphilis infection in the general population and the consequent low yield of such screening, the USPSTF concludes that potential harms of

screening (ie, opportunity cost, false-positive tests, and labeling) in a low-incident population outweigh the benefits.

CLINICAL CONSIDERATIONS

- Populations at increased risk for syphilis infection (as determined by incident rates) include men who have sex with men and engage in high-risk sexual behavior, commercial sex workers, persons who exchange sex for drugs, and those in adult correctional facilities. There is no evidence to support an optimal screening frequency in this population. Clinicians should consider the characteristics of the communities they serve in determining appropriate screening strategies. Prevalence of syphilis infection varies widely among communities and patient populations. For example, the prevalence of syphilis infection differs by region (the prevalence of infection is higher in the southern U.S. and in some metropolitan areas than it is in the U.S. as a whole) and by ethnicity (the prevalence of syphilis infection is higher in Hispanic and African American populations than it is in the white population).
- Persons diagnosed with other sexually transmitted diseases (STDs) (ie, chlamydia, gonorrhea, genital herpes simplex, human papilloma virus, and HIV) may be more likely than others to engage in high-risk behavior, placing them at increased risk for syphilis; however, there is no evidence that supports the routine screening of individuals diagnosed with other STDs for syphilis infection. Clinicians should use clinical judgment to individualize screening for syphilis infection based on local prevalence and other risk factors (see above).
- Nontreponemal tests commonly used for initial screening are the Venereal Disease Research Laboratory (VDRL) or Rapid Plasma Reagin (RPR), followed by a confirmatory fluorescent treponemal antibody absorbed (FTA-ABS) or *T. pallidum* particle agglutination (TP-PA). The optimal screening interval in average- and high-risk persons has not been determined.
- All pregnant women should be tested at their first prenatal visit. For women in high-risk groups, repeat serologic testing may be necessary in the third trimester and at delivery. Follow-up serologic tests should be obtained to document decline initially after treatment. These follow-up tests should be performed using the same nontreponemal test initially used to document infections (eg, VDRL or RPR) to ensure comparability.

DISCUSSION

In 2002, the reported nationwide incidence rate of primary and secondary cases of syphilis infection was 2.4 per 100,000 persons (state incidence rates ranged from 0-5.4 per 100,000 persons), and the rate of congenital syphilis infection nationwide was 11.1 per 100,000 live births (state incident rates ranged from 0-31.1 per 100,000 live births).⁴ Rates of primary and secondary syphilis infection had been steadily decreasing during the 1990s; however, in 2001, the rate increased for the first time in a decade. This increase was evident only in men and was associated with outbreaks in several urban areas among

men who have sex with men, high reported rates of HIV co-infection, and high-risk sexual behavior. The prevalence of syphilis infection differs by region (3.1 and 1.7 per 100,000 persons for the South and Northeast U.S., respectively) and by ethnicity (9.8, 2.7, and 1.2 per 100,000 persons for African Americans, Hispanics, and whites, respectively).⁴ The median seropositivity has been reported as 2.1% to 12.2% in incarcerated women and 0.9% to 5.2% in incarcerated men.⁴ Commercial sex workers and persons who exchange sex for drugs have a higher incidence of syphilis infection.^{5,6} Late-stage syphilis includes gummatous, cardiovascular, and neurological complications that can lead to significant disability and premature death. Congenital syphilis infection results in fetal or perinatal death in 40% of affected pregnancies,¹ as well as disease complications in surviving newborns, including central nervous system abnormalities; deafness; multiple skin, bone, and joint deformities; and hematological disorders.⁷

The USPSTF examined the evidence from 1994 to 2003 to determine the efficacy of syphilis screening in decreasing syphilis-related morbidity and mortality in the general population, as well as in high-risk populations and in pregnant women.³ The USPSTF found no direct evidence that screening for syphilis infection in the general population or in high-risk populations reduces morbidity or mortality. The USPSTF did find observational evidence that screening for syphilis infection in pregnant women and/or neonates reduces the prevalence of congenital syphilis infection in neonates.^{8,9}

Traditionally, screening for syphilis infection is a 2-step process that involves an initial nontreponemal test (VDRL or RPR) followed by a confirmatory treponemal test (FTA-ABS or TP-PA). Sensitivity of the RPR and VDRL tests are estimated to be 78% to 86% for detecting primary syphilis infection, 100% for detecting secondary syphilis infection, and 95% to 98% for detecting latent syphilis infection. Specificity ranges from 85% to 99% and may be reduced in individuals who have preexisting conditions (ie, collagen vascular disease, pregnancy, intravenous drug use, advanced malignancy, tuberculosis, malaria, and viral and rickettsial diseases) that produce false-positive results. The FTA-ABS test has a sensitivity of 84% for detecting primary syphilis infection and almost 100% sensitivity for detecting syphilis infection in other stages, and a specificity of 96%.¹⁰ Several new screening tests are currently being studied, including Immunochromatographic Strip (ICS), Line Immunoassay (LIA), Enzyme-linked Immunosorbent Assay (ELISA), RPR card, and Rapid Syphilis Test (RST).³ New screening tests currently being studied for use in pregnant women and infants include: IgM immunoblotting and Polymerase Chain Reaction (PCR) assay of serum and cerebrospinal fluid for central nervous system infection in infants, placenta histopathology, and umbilical cord blood testing.³

The yield of screening using a two-step process (RPR followed by confirmatory FTA-ABS) can be estimated using test characteristics and the incidence of syphilis infection in a given population. For example, in the general population (assuming a prevalence of 5 per 100,000, an RPR sensitivity of 91% and specificity of 95%, and FTA-ABS sensitivity of 92% and specificity of 96%), one would have to screen more than 24,000 patients to detect a single case of syphilis infection (number needed to screen [NNS] = 24,000); 200 per 100,000 people screened would have false-positive test results. On the other hand, in

a high-risk population of incarcerated women (assuming a prevalence of 12%, an RPR sensitivity of 91% and specificity of 95%, and FTA-ABS sensitivity of 92% and specificity of 96%), one would have to screen 10 patients to detect 1 case of syphilis infection (NNS = 10); almost 2,000 per 100,000 people screened would have false-negative test results.

Antibiotic therapy is highly effective in eliminating *T. pallidum* and in preventing congenital infection when administered early to pregnant women.¹¹ Penicillin G has long been an effective regimen for all stages of syphilis,¹² and new trials focus on antibiotics that are easier to administer or are alternatives for penicillin allergic individuals. A number of small poor-quality cohort and RCT studies on the use of oral azithromycin have been published and report comparable outcomes to penicillin treatment.¹³⁻¹⁶ Little evidence is available to guide therapy in pregnancy.

No studies have directly looked at the harms of screening or treatment. Potential harms of screening may include opportunity costs to the clinician and patient (time, resources, etc.) and false-positive results which may lead to stress, labeling, and further work-up. Harms of treatment include adverse drug-related effects including anaphylaxis from penicillin allergy and the Jarisch-Herxheimer reaction (febrile reaction with headache, myalgia, and other symptoms) that may occur within the first 24 hours after any therapy for syphilis.

Seven cost studies done in different countries support continued universal testing during pregnancy.⁷ In a study done in the UK, universal prenatal screening of pregnant women was about as cost-effective as targeted screening programs.¹⁷

RECOMMENDATIONS OF OTHER GROUPS

Guidelines of the Centers for Disease Control and Prevention can be accessed at: www.cdc.gov/mmwr/preview/mmwrhtml/00050909.htm.

Guidelines of the American Academy of Family Physicians can be accessed at: www.aafp.org/x24973.xml.

Guidelines of the American Academy of Pediatrics and American College of Obstetricians and Gynecologists can be found in *Guidelines for Perinatal Care*.¹⁸

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APPENDIX A

U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS AND RATINGS

The Task Force grades its recommendations according to one of 5 classifications (A, B, C, D, I) reflecting the strength of evidence and magnitude of net benefit (benefits minus harms):

- A.** The USPSTF strongly recommends that clinicians provide [the service] to eligible patients. *The USPSTF found good evidence that [the service] improves important health outcomes and concludes that benefits substantially outweigh harms.*
- B.** The USPSTF recommends that clinicians provide [the service] to eligible patients. *The USPSTF found at least fair evidence that [the service] improves important health outcomes and concludes that benefits outweigh harms.*
- C.** The USPSTF makes no recommendation for or against routine provision of [the service]. *The USPSTF found at least fair evidence that [the service] can improve health outcomes but concludes that the balance of benefits and harms is too close to justify a general recommendation.*
- D.** The USPSTF recommends against routinely providing [the service] to asymptomatic patients. *The USPSTF found at least fair evidence that [the service] is ineffective or that harms outweigh benefits.*
- I.** The USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing [the service]. *Evidence that [the service] is effective is lacking, of poor quality, or conflicting and the balance of benefits and harms cannot be determined.*

APPENDIX B

U.S. PREVENTIVE SERVICES TASK FORCE STRENGTH OF OVERALL EVIDENCE

The USPSTF grades the quality of the overall evidence for a service on a 3-point scale (good, fair, poor):

Good: Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes.

Fair: Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies, generalizability to routine practice, or indirect nature of the evidence on health outcomes.

Poor: Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.