Screening for Genital Herpes: Recommendation Statement: United States Preventive Services Task Force

United States Preventive Services Task Force

Citation

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Abstract

This statement summarizes the U.S. Preventive Services Task Force (USPSTF) recommendations on screening for genital herpes and the supporting scientific evidence, and updates the 1996 recommendations contained in the Guide to Clinical Preventive Services, second edition.[1] Explanations of the 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 included in the brief update[2] on this topic, available through the USPSTF Web site (http://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™ (http://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. [AHRQ Pub No. 05-0573-A]

Figure 3

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Figure 2

US Department of Health and Human Services

SUMMARY OF RECOMMENDATIONS

The U.S. Preventive Services Task Force (USPSTF) recommends against routine serological screening for herpes simplex virus (HSV) in asymptomatic pregnant women at any time during pregnancy to prevent neonatal HSV infection. D recommendation.

The USPSTF found fair evidence that screening asymptomatic pregnant women using serological screening tests for HSV antibody does not reduce transmission of HSV to newborn infants. Women who develop primary HSV infection during pregnancy have the highest risk for transmitting HSV infection to their infants. Because these women are initially seronegative, serological screening tests for HSV (enzyme-linked immunosorbent assay [ELISA],

immunoblot, and western blot assay [WBA]) do not accurately detect those at highest risk. There is no evidence that treating seronegative women decreases risk for neonatal infection. There is limited evidence that the use of antiviral therapy in women with a history of recurrent HSV, or performance of cesarean section in women with active HSV lesions at the time of delivery, decreases neonatal herpes infection. There also is limited evidence of the safety of antiviral therapy in pregnant women and neonates.

The potential harms of screening include false-positive test results, labeling, and anxiety, as well as false negative tests and false reassurance, although these potential harms are not well studied. The USPSTF determined there are no benefits associated with screening, and therefore the potential harms outweigh the benefits.

The USPSTF recommends against routine serological screening for HSV in asymptomatic adolescents and adults. D recommendation.

The USPSTF found no evidence that screening asymptomatic adolescents and adults with serological tests for HSV antibody improves health outcomes or symptoms or reduces transmission of disease. There is good evidence that serological screening tests can accurately identify those persons who have been exposed to HSV. There is good evidence that antiviral therapy improves health outcomes in symptomatic persons (eg, those with multiple recurrences); however, there is no evidence that the use of antiviral therapy improves health outcomes in those with asymptomatic infection. The potential harms of screening include false-positive test results, labeling, and anxiety, although there is limited evidence of any potential harms of either screening or treatment. The USPSTF determined the benefits of screening are minimal, at best, and the potential harms outweigh the potential benefits.

CLINICAL CONSIDERATIONS

- Serological screening tests for genital herpes can detect prior infection with HSV in asymptomatic persons, and new type-specific serological tests can differentiate between HSV-1 and HSV-2 exposure (these tests cannot differentiate between oral vs genital herpes exposure); however, given the natural history of genital herpes, there is limited evidence to guide clinical intervention in those asymptomatic persons who have positive serological test results. False-positive test results may lead to labeling and psychological stress without any potential benefit to patients. Negative test results (both false-negative and true-negative results) may provide false reassurance to continue high-risk sexual behaviors.
- There is new, good-quality evidence demonstrating that systemic antiviral therapy effectively reduces viral shedding and recurrences of genital herpes in adolescents and adults with a history of recurrent genital herpes. There are multiple efficacious regimens that may be used to prevent the recurrence of clinical genital herpes.
- The USPSTF did not examine the evidence for the effectiveness of counseling to avoid high-risk sexual behavior in persons with a history of genital herpes to prevent transmission to discordant partners, or for the primary prevention of genital herpes in persons not infected with HSV. There are known health benefits of avoiding high-risk sexual behavior, including prevention of sexually transmitted infections (STIs) and HIV infection.
- Primary HSV infection during pregnancy presents the greatest risk for transmitting infection to the newborn. The fact that women with primary HSV infection are initially seronegative limits the usefulness of screening with antibody tests. The USPSTF did not find any studies testing the use of antibody screening to find and treat seronegative pregnant women (ie, those at risk for primary HSV infection) prophylactically. However, the number of seronegative pregnant women one would need to treat to theoretically avoid one primary infection would be very high, making the potential benefit small. At the same time, the potential harm to many low-risk women and fetuses from the side effects of antiviral therapy may be great.
- There is fair evidence that antiviral therapy in late pregnancy can reduce HSV recurrence and viral shedding at delivery in women with recurrent HSV infection; however, there is currently no evidence that antiviral use in women with a history of HSV leads to reduced neonatal infection. Likewise, there is limited information on the benefits of screening women in labor for signs of active genital HSV lesions, and for the performance of cesarean delivery on those with lesions.

DISCUSSION

Genital herpes simplex (commonly caused by HSV-2, occasionally by HSV-1) is the most prevalent STI in the United States.[3] Seroprevalence surveys show that 1 in 5 people aged 12 years and older in the United States has been infected with HSV-2, and the rate is even higher among adults and women.[3] An estimated 1.6 million new HSV-2 infections occur in the United States annually.[4] Symptoms vary based on phase of infection: primary infection manifests as tender vesicular lesions, dysuria, itching, lymphadenopathy, fever, malaise, and/or myalgia; recurrent infections manifest as localized lesions; and viral shedding is usually asymptomatic. HSV in pregnant women can be vertically transmitted to the infant, primarily at the time of delivery. Primary infection during pregnancy, although less prevalent than recurrent infection, is associated with a much higher transmission rate (33% vs 3% transmission rates in primary and recurrent infection, respectively).[5] Neonatal HSV disease is diagnosed in approximately 1 of every 3,000 deliveries in the United States, resulting in an estimated 1,500 cases annually.[6] Infants infected with HSV may be born prematurely and with low birth weight; symptoms vary from mild localized disease to severe disseminated infection. Encephalitis and disseminated disease secondary to neonatal HSV infection are associated with long-term morbidity and mortality.[7] Intrauterine infections (congenital herpes) are very rare (1/100,000) although they result in serious sequelae including hydrocephalus, microcephaly, and chorioretinitis.

The USPSTF reviewed the evidence from 1996-2002 and found no direct evidence that screening asymptomatic adolescents and adults, including pregnant women, for genital HSV reduces symptomatic recurrences or transmission of disease.

Methods for HSV detection include viral culture, polymerase chain reaction (PCR), and antibody-based tests including the WBA and type-specific glycoprotein G serological tests. Viral culture has a sensitivity of 50% and a specificity of nearly 100%. PCR has a sensitivity of 80% to 90% for specimens obtained from lesions. Serological tests are used to detect previous infection with herpes in asymptomatic patients, or to diagnose infection in a symptomatic patient when culture is not feasible or the clinical syndrome is unclear. The WBA is considered the gold standard, with a sensitivity and specificity of greater than 99%.[8,9] Currently, 2 type-specific glycoprotein G serological tests, the ELISA and immunoblot tests, are commercially available in the United States; they have a sensitivity and specificity comparable to the WBA.[10]

The USPSTF examined the evidence for the efficacy of antiviral therapy in reducing symptomatic recurrences and transmission in adolescents and adults. Three good-quality randomized controlled trials (RCTs) and one fair-quality RCT examined the effectiveness of antiviral agents in the suppression of HSV recurrences.[11,12,13,14] These studies showed that in those persons with 6 or more recurrences annually, those taking antiviral therapy had a significantly longer delay in the time to first recurrence compared with those receiving placebo. One good-quality RCT of women with a history of recurrent HSV showed that the relative risk for subclinical viral shedding was lower in women who received acyclovir compared with women who received placebo.[15]

The USPSTF examined the evidence for the efficacy of antiviral therapy and condom use in reducing HSV-2 transmission in adolescents and adults. A good-quality, randomized, multi-center, placebo-controlled trial showed that once-daily valacyclovir reduced sexual transmission of genital HSV-2 in monogamous heterosexual couples who were discordant for HSV-2 infection.[16] In this study, fewer of the susceptible partners developed clinical symptoms, and fewer of the source partners had evidence of viral shedding in the treatment group compared with the placebo group. One prospective cohort study suggested that male condom use in 25% of episodes of sexual intercourse was associated with a lower risk for HSV-2 acquisition among women but not among men; however, condom use was low throughout the study, with only 61% of couples reporting ever using condoms and only 8% reporting condom use for each sexual act, despite counseling at each clinic follow-up visit.[17] In a second prospective cohort study, use of condoms for more than 65% of episodes of sexual intercourse offered significant and comparable protection against HSV-2 acquisition for both men and women.[18]

The USPSTF examined the evidence for interventions in pregnant women to reduce HSV recurrence at the time of delivery, including antiviral use in late pregnancy and cesarean section delivery. One fair-quality RCT of women with recurrent genital HSV infection evaluated the use of suppressive acyclovir after 36 weeks' gestation and found that 6% of patients treated with acyclovir had clinical HSV at delivery compared with 14% of patients treated with placebo.[19] No patients in the acyclovir group had positive

HSV cultures, compared with 6% of placebo-treated patients. Three poor-quality studies examined reduction of neonatal infection as an outcome of antiviral therapy in pregnant women with a history of HSV.[20,21,22] One poor-quality study examined the use of cesarean section to reduce neonatal infection.[23]

Potential harms of screening for HSV-2 include labeling, anxiety, and disrupting partner relationships. A qualitative assessment of the psychosocial impact of a serological diagnosis of HSV-2 concluded that patients may experience strong psychological responses to their diagnoses.[24] False-positive test results may lead to needless work-up and anxiety. Negative test results may potentially provide false reassurance to continue high-risk sexual behavior. Potential harms of antiviral treatment may include drug hypersensitivity and renal impairment; however, antiviral treatments are generally well tolerated with mild harms.[11,12,13] There is limited evidence on the safety of antiviral treatments during pregnancy.[25,26]

A cost analysis of oral acyclovir prophylaxis in late pregnancy was compared with the current standard of cesarean delivery for genital HSV lesions. This analysis demonstrated that prophylactic acyclovir and follow-up of infants exposed to HSV during a non-cesarean delivery was least expensive ($400,000 per case of neonatal infection prevented), while the use of cesarean section alone for women with active lesions at the time of delivery was most expensive ($1.3 million per case of neonatal infection prevented).[27] Another study found that screening at-risk pregnant women and suppressive therapy in their seropositive partners were more cost-effective interventions (at a cost of $363,000 per case of neonatal infection prevented) compared with no management or cesarean section delivery for women with lesions.[28] Further research is needed to define the clinical significance and natural history of asymptomatic persons who have seropositive test results, to identify effective strategies to decrease HSV transmission, and to examine the benefits of antiviral suppression and cesarean section delivery for pregnant women in reducing neonatal infection. Previous literature examining various vaccines under study have reported poor efficacy[29,30] and vaccine research is ongoing.

RECOMMENDATIONS OF OTHER GROUPS

The American College of Obstetricians and Gynecologists (ACOG) and the American Academy of Pediatrics (AAP) guidelines are available in print form.[31] ACOG recommends that all women and their partners be asked about a history of HSV infection; women with a history of genital HSV infection should be questioned about recent symptoms and should undergo careful examination of the perineum before delivery. ACOG recommends cesarean delivery for all women with active primary and recurrent lesions at the time of delivery. ACOG does not recommend screening nonpregnant women for HSV; ACOG makes treatment recommendations, including methods to reduce the risk for transmission among discordant couples. The Centers for Disease Control and Prevention HSV treatment recommendations can be accessed at: http://www.cdc.gov/STD/treatment/2-2002TG.htm#GenitalHerpes.[32]

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*Members of the Task Force at the time this recommendation was finalized. For a list of current Task Force members, go to http://www.ahrq.gov/clinic/uspstfab.htm.

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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.

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