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Summary Guidelines for the Use of Herpes Simplex Virus (HSV) Type 2 Serologies

Genital herpes is one of the most prevalent sexually transmitted diseases, affecting more than one in five sexually active adults. The advent of type-specific serology tests that distinguish between herpes simplex virus type 1 and type 2 (HSV-1 and HSV-2) has provided a tool to aid in the diagnosis of genital ulcer disease and has also made screening for asymptomatic herpes infections possible. By 2003, indications for their use have not yet been well defined. Due to this lack of formal guidelines, the California (CA) Sexually Transmitted Diseases (STD) Controllers Association* and the California Department of Health Services (CA DHS)** convened a committee to review all relevant literature and to formulate guidelines for the use of HSV-2 type-specific serologies.

This document presents an abridged version of the Guidelines for the Use of HSV 2 Serologies: Recommendations from the California Sexually Transmitted Diseases Controllers Association and the California Department of Health Services. The full text document is available on line at www.stdhivtraining.org.

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Recommended Use of HSV-2 Serologies For Diagnosis and Screening

- Diagnosis of genital lesions/symptoms: type-specific serology tests **should be available** for diagnostic purposes in conjunction with virologic tests at any clinical setting where patients are evaluated for STDs.
- Screening in patients at-risk for STD/HIV (current STD, recent STD, high-risk behaviors): **should be offered to select patients.**
- Screening in HIV-positive patients: **should generally be offered.**
- Screening in patients in partnerships or considering partnerships with HSV-2-infected people: **should generally be offered.**
- Universal screening in pregnancy: **should generally not be offered.**
- Screening in general population: **should generally not be offered.**
- Herpes education and prevention/transmission counseling is necessary for all people being tested or screened for HSV-2.

Genital Herpes Background

The natural history of HSV-2 infections in adults varies among individuals. After primary infection, often a debilitating systemic disease, the virus establishes latency in spinal cord ganglia. Infected persons experience recurrent viral reactivations that can be symptomatic, marked by recurrences less severe than primary genital herpes, or can be entirely asymptomatic. All people infected with HSV-2 shed the virus asymptotically, regardless of a history of symptomatic recurrences, thus the sexual contacts of individuals with symptomatic or asymptomatic HSV-2 are at risk of becoming infected.

At present, there is no cure for HSV-2 infections, and results of vaccine trials have been disappointing. Antivirals have been shown to decrease symptomatic recurrences of genital herpes and to decrease the frequency of viral shedding, but there is no current evidence that they prevent transmission of HSV to newborns. There are preliminary data showing that antiviral suppressive therapy of HSV-2-infected partners in discordant heterosexual relationships decreases the rate of HSV-2 acquisition in the seronegative partners. Condoms have been shown to decrease the transmission of HSV-2 to uninfected partners; however, to be effective they must be used correctly and consistently, even in the absence of lesions or prodrome.

Summary of Recommendations

DIAGNOSIS

Diagnosis of genital lesions/symptoms: type-specific serology tests SHOULD BE AVAILABLE for diagnostic purposes in conjunction with virologic tests at any clinical setting where patients are evaluated for STDs.

► **Summary:** Serology tests may be helpful in the following settings:

1. Culture-negative recurrent lesion.
2. History suggestive of herpes/atypical herpes without lesions to culture.
3. Suspected primary herpes or first presentation of genital symptoms, if culture or antigen detection testing is negative or not available and acquisition likely more than six weeks prior.

See flow sheets outlining suggested timing and interpretation of HSV-2 results by clinical presentation.

SCREENING

The purpose of screening for HSV-2 is not only to identify seropositivity, but to help seropositive people identify symptoms and protect themselves from acquiring HIV and to protect their partners and seronegative people from acquiring HSV-2 and/or HIV. The following recommendations assume that client-centered risk-reduction counseling is offered in conjunction with any HSV serologic screening. The following screening recommendation summaries are based on all available evidence. The full text document includes a more thorough discussion of the evidence.

SCREENING IN PATIENTS AT RISK FOR STD/HIV (CURRENT STD, RECENT STD, HIGH-RISK BEHAVIORS): SHOULD BE OFFERED TO SELECT PATIENTS.

- **Summary:** Because there is no recommended treatment for asymptomatic HSV-2 infections, only limited evidence at this time that risk-reduction counseling or antiviral herpes suppression significantly decreases transmission of HSV or acquisition of HIV, and limited evidence that condoms will be used consistently to prevent transmission of HSV-2 in this population, general HSV-2 screening is not recommended. Screening may be considered by the provider on an individual patient basis. If a patient is identified as at risk for STD and is motivated to reduce his/her sexual risk behavior, then HSV-2 serology could be used as an adjunct to counseling and risk reduction. HSV education and risk-reduction counseling should be available (see Herpes fact sheet and counseling points). Frequency of screening for HSV-2 negatives is unclear (annual incidence of HSV-2 ranges from roughly 3% per year in repeat HIV testers, to 4% per year in urban female adolescents, to 11% per year in a public STD clinic population).

**SCREENING IN HIV-POSITIVE PATIENTS:
SHOULD GENERALLY BE OFFERED.**

- ▶ **Summary:** Because asymptomatic HSV-2 infections in HIV-positive persons may be associated with increased transmission of HIV and may accelerate the course of HIV disease, screening should generally be offered to patients with documented HIV and without a history of genital herpes. Although there is little evidence that additional risk-reduction counseling directed at asymptomatic HSV-2-infected, HIV-positive individuals will decrease HIV transmission, and no evidence that HSV antiviral suppression will decrease HIV transmission, the theoretical risk of transmitting HIV is high enough to offer screening and patient education. If previously unidentified symptoms are uncovered with screening, HSV suppressive therapy may be offered for symptom management. In addition to the risk-reduction counseling that should be offered to all HIV-positive patients not in mutually monogamous relationships, HSV-specific education and counseling should be provided for individuals with either HSV-2-negative or HSV-2-positive results, because HSV-2-negative, HIV-infected patients have a significantly increased risk of HSV-2 acquisition. Frequency of testing for HSV-2 seronegative patients is unclear, but should be considered with acquisition of STDs or high-risk behaviors.

**SCREENING IN PATIENTS IN PARTNERSHIPS OR
CONSIDERING PARTNERSHIPS WITH HSV-2-INFECTED PEOPLE:
SHOULD GENERALLY BE OFFERED.**

- ▶ **Summary:** Screening should generally be offered to asymptomatic patients interested in reducing their risk of herpes, whose partners or potential partners have a history of genital herpes or who have known HSV-2 infections, in order to identify discordance and, therefore, to discuss strategies to prevent future acquisition. Serologic testing would be useful if results that indicate discordance motivate couples to change their behavior. Serology could then be used as an adjunct to counseling and risk reduction. Frequency of testing for those who are negative is uncertain, but should be considered prior to entry into a new partnership and for seronegative women when pregnant (likelihood of asymptomatic seroconversion is approximately 18% annually for women, and 5% annually for men, in discordant partnerships). HSV education and risk-reduction counseling should be offered at the time of screening and when the results are given. HSV-2-positive patients should be educated regarding risk of transmission in future partnerships, pregnancy risks, and risk of HIV acquisition; HSV-2-negative women and their partners should be educated about the risk of herpes acquisition during pregnancy (see Herpes fact sheet and counseling points).

**UNIVERSAL SCREENING IN PREGNANCY:
SHOULD GENERALLY NOT BE OFFERED.**

- ▶ **Summary:** Universal screening should generally not be offered to pregnant women. There has been no evidence that screening women to identify pregnancies at-risk of new infections (serologically negative pregnant women with HSV-infected partners) will effectively decrease incident infections at term. Additionally, screening to identify pregnant women with asymptomatic herpes infections has no value at present without any known safe and effective interventions to prevent an already unlikely neonatal transmission (maternal HSV antibodies are passed to the neonate and usually protect against infection). All pregnant women should be asked about their own and their partners' history of genital (and oral) herpes and examined for evidence of active herpes at delivery. Asymptomatic pregnant women whose partners have known genital HSV-2, as well as HIV-positive pregnant women, should be offered type-specific serologic testing. Serodiscordant couples (where the women are seronegative and partners are seropositive or have a history of symptomatic herpes) should be educated regarding their risk of acquiring/transmitting herpes and transmission to their newborn. Specific advice should be to avoid sex or to use condoms consistently in the third trimester. Women who are seropositive or have a history of herpes and those who seroconvert before term have a very low risk of herpes transmission to their newborn. They should be educated about their low risk of neonatal herpes and that cesarean sections are unnecessary unless they have symptoms around the time of delivery. Antiviral suppression has been shown to decrease the rate of cesarean sections for women with lesions at delivery, but not the rate of neonatal herpes.

**SCREENING IN THE GENERAL POPULATION:
SHOULD GENERALLY NOT BE OFFERED.**

- ▶ **Summary:** Because there is no current recommended treatment for asymptomatic genital herpes and no proven intervention that decreases community prevalence of HSV-2 infection, screening of the general population is not recommended.

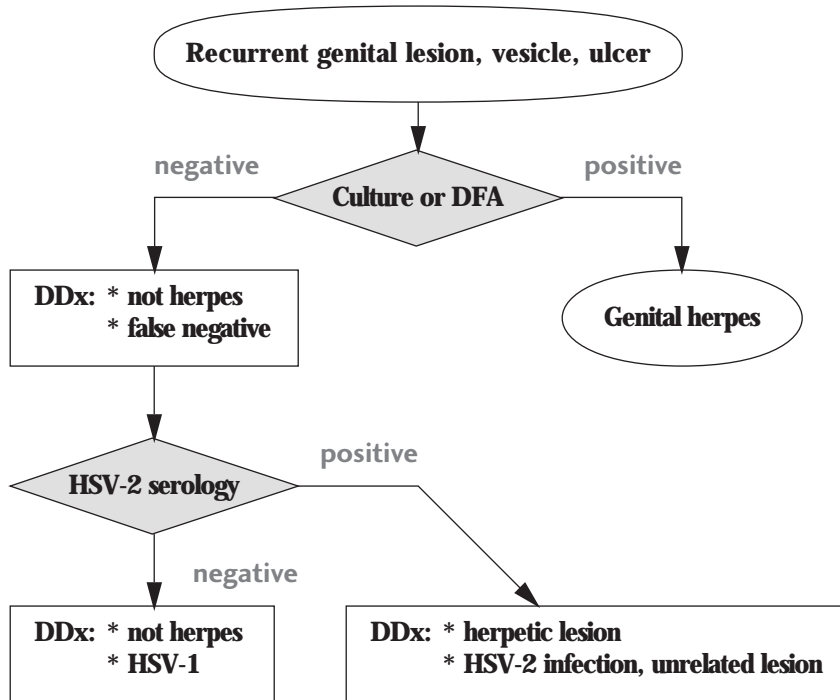
EDUCATION AND COUNSELING

HERPES EDUCATION AND PREVENTION/TRANSMISSION COUNSELING IS NECESSARY FOR ALL PATIENTS BEING TESTED OR SCREENED FOR HSV-2.

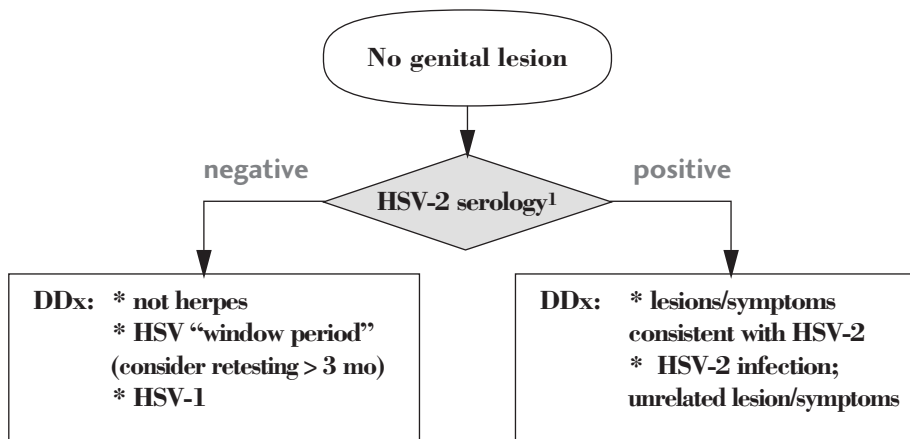
- ▶ **Summary:** Genital herpes education and prevention/transmission counseling is a critical part of any HSV-2 screening program. Ideally, both pre- and post-test counseling should be conducted. In pre-test counseling, the provider can determine patient preparedness for the diagnosis of a chronic disease, as well as motivation to reduce risk behavior if diagnosed. Post-test counseling can provide support and reassurance to patients testing positive, as well as educate them about the natural history of the disease and its transmissibility. Those identified as uninfected with HSV-2 can be informed of how to prevent future acquisition of herpes and other STDs.

**PROVIDER PULL-OUT:
 CLINICAL APPLICATIONS AND INTERPRETATIONS OF TYPE-SPECIFIC
 HSV-2 SEROLOGIES BY PRESENTATION (DDx: differential diagnosis)**

1. Presentation with recurrent genital lesion:

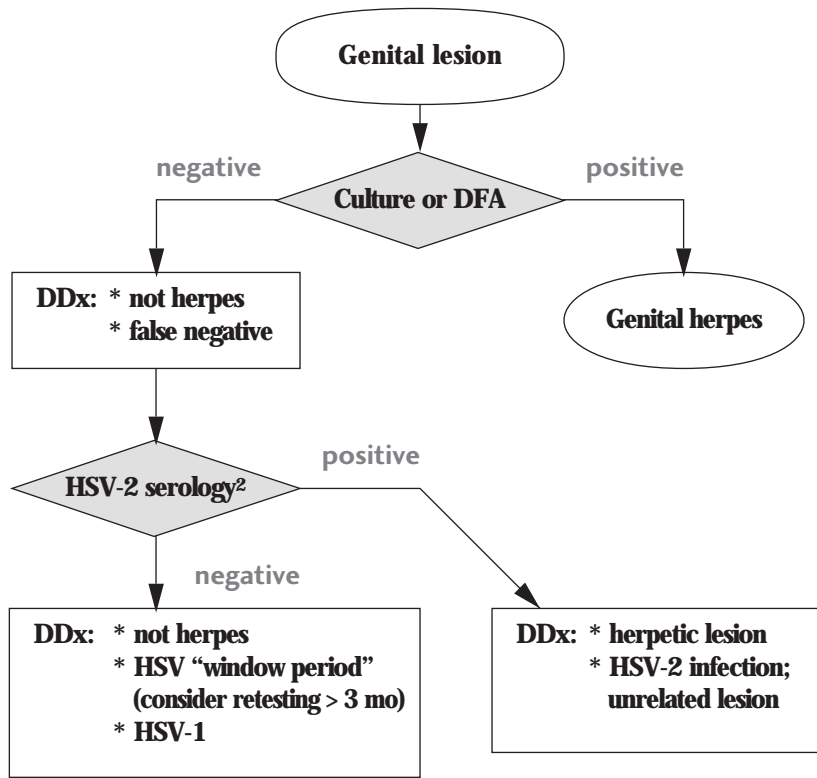


2. History suggestive of first, recurrent, or atypical herpes--no lesion to culture:



¹If suspected primary infection, wait at least 6 weeks prior to testing.

3. First presentation with genital lesions:¹



¹ Evaluation of new genital lesions should include syphilis screening with RPR or VDRL, as well as screening for other STDs or HIV, depending on risk factors.

² If suspected primary infection, wait at least 6 weeks prior to testing.

PROVIDER PULL-OUT: HERPES FACT SHEET AND COUNSELING POINTS

Epidemiology

- Twenty-two percent of adults in the United States are infected with HSV-2.
- Ninety percent of people seropositive for HSV-2 are unaware of infection.

Symptoms and Natural History

- Genital herpes causes a wide variety of signs and symptoms ranging from classically painful vesicles/ulcers to the atypical, including: urethritis, cervicitis, skin or mucosal fissures, and non-specific itching, burning, or tingling of anogenital skin.
- Probably all people infected with HSV-2, regardless of a history of symptomatic outbreaks, have episodes of asymptomatic viral shedding.
- Virtually all patients with HSV-2 have genital herpes. Oral HSV-2 is very rare. HSV-1 is responsible for approximately 20% of new genital herpes infections. These infections cause less frequent symptoms and shed virus less frequently than do HSV-2 genital infections.

Diagnosis and Treatment

- Genital lesions suspicious for herpes should have laboratory confirmation. Culture or antigen-detection tests should be performed if lesions are present. If no lesion is present, or patient has culture-negative recurrent lesions, HSV-2 serology should be offered to aid in diagnosis. A positive HSV-2 serologic test result indicates prior infection but, while supportive, cannot confirm etiology of symptoms.
- Recommended antiviral regimens using acyclovir, famcyclovir, or valacyclovir are equally effective in ameliorating symptoms and shortening duration of primary and recurrent genital herpes. Suppressive therapy decreases frequency and duration of recurrences.

Counseling Points (Adapted from CDC 2002 STD Treatment Guidelines)

Specific counseling messages for all patients with clinical or serologic diagnosis of HSV-2 infection should include the following information:

- Information about the natural history of the disease, with emphasis on the potential for recurrent episodes, asymptomatic viral shedding, and attendant risks of sexual transmission.
- Information about episodic or suppressive treatment with antiviral medication to shorten the duration of or prevent symptoms.

- All patients with genital HSV infection should be encouraged to inform their current sex partners that they have genital herpes and to inform future partners before initiating a sexual relationship.
- Persons with genital herpes should be informed that sexual transmission of HSV can occur during asymptomatic periods. Asymptomatic viral shedding is more frequent in genital HSV-2 infection than in genital HSV-1 infection and is most common in the first 12 months following acquisition of HSV-2, but may persist for years, less frequently, in some individuals.
- Patients should be advised to abstain from sexual activity when lesions or prodromal symptoms are present.
- Latex condoms, when used consistently and correctly, can reduce the risk for genital herpes when the infected areas are covered or protected by the condom. Because condoms do not cover all exposed areas, they are likely to be more effective in preventing infections transmitted by fluids from mucosal surfaces than in preventing those transmitted by skin-to-skin contact (e.g., HSV).
- Sex partners of infected persons should be advised that they may themselves be infected even if they have never experienced symptoms. Type-specific serologic testing of asymptomatic partners of persons with genital herpes can determine whether they are at risk for HSV acquisition.
- The risk of neonatal infection should be explained to all patients, including men.
- Pregnant women and women of childbearing age who have genital herpes should inform their providers who care for them during pregnancy, as well as those who will care for their newborn infants.
- Pregnant women who are not infected with HSV-2 should be advised to avoid intercourse during the third trimester with men who have genital herpes. Similarly, pregnant women who are not infected with HSV-1 should be counseled to avoid genital exposure to HSV-1 (e.g., cunnilingus with a partner with oral herpes) during the third trimester.
- Patients with a positive HSV-2 serologic test should be taught to recognize the common manifestations of genital herpes. Antiviral therapy is not recommended for patients without clinical manifestations of infection.
- HSV-2 infections are associated with a significantly increased risk of acquiring HIV. Infected people should be educated about their increased risk of HIV acquisition and should protect themselves against HIV, as well as prevent HSV transmission to partners.

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