CALIFORNIA
STD/HIV PREVENTION
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Guidelines for the Use of Herpes Simplex Virus (HSV) Type 2 Serologies:

Recommendations from the California Sexually Transmitted Diseases (STD) Controllers Association and the California Department of Health Services (CA DHS)

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Guideline Scope and Development

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. Prior to the development of type-specific serology tests, serological testing to diagnose genital herpes had little clinical utility. A positive HSV test could not distinguish between antibodies to HSV-1, highly prevalent in the general population from childhood orolabial disease, and antibodies to HSV-2, the virus responsible for most sexually transmitted genital herpes infections. As HSV type-specific serology tests are now becoming widely available, indications for their use have not 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 make guidelines for the use of HSV-2 type-specific serologies.

Due to the high seroprevalence of HSV-1 in the general population that represents childhood-acquired orolabial disease, the California HSV Committee limited the review and recommendations to HSV-2 serologies. This document provides guidelines for the use of HSV-2 serology for the diagnosis of symptomatic genital herpes, recommendations for screening for HSV-2 infections, and a background review of genital herpes. The strength of each screening recommendation is based on the quality of supporting evidence (Appendix A).

Executive Summary

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.

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 Appendix B for 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 section entitled *Screening for HSV-2: Discussion of the Evidence* includes a more thorough elaboration on the evidence.

SCREENING IN PATIENTS AT RISK FOR STD/HIV (CURRENT STD, RECENT STD, HIGH-RISK BEHAVIORS):

SHOULD BE OFFERED TO SELECT PATIENTS.

► **Summary:** General HSV-2 screening is not recommended 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. 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 Appendix C: Guide for genital herpes counseling). 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).[1-3]

"C" RECOMMENDATION:

Should be offered to select patients.
Evidence for efficacy is insufficient to support a general recommendation for use.

Recommendations by other groups:
No recommendations from any groups on this specific 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.

"B" RECOMMENDATION:

Should generally be offered.
Moderate evidence for efficacy, or limited evidence with expert consensus, supports a general recommendation for use.

Recommendations by other groups:

- Centers for Disease Control and Prevention (CDC); Health Resources and Services Administration (HRSA); National Institutes of Health(NIH); Infectious Disease Society of America (IDSA). Incorporating HIV prevention into the medical care of persons living with HIV: *"Some HIV experts recommend"* HSV screening for HIV-infected persons.[4]
- CA STD Controllers Association and California Coalition of Local AIDS Directors: Guidelines recommend either inquiring regarding herpes history, or HSV-2 serology testing.[5]

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).[6] 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 Appendix C: Guide for genital herpes counseling).

"B" RECOMMENDATION:

Should generally be offered.
Moderate evidence for efficacy, or limited evidence with expert consensus, supports a general recommendation for use.

Recommendations by other groups:

- CDC 2002 Treatment Guidelines: *"Asymptomatic partners of patients with genital herpes should be questioned concerning histories of genital lesions, educated to recognize symptoms of herpes, and offered type-specific serologic testing for HSV infection."*[7]

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' histories 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 cesearean 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.

"D" RECOMMENDATION:

Should generally not be offered.
Moderate evidence for lack of efficacy or for adverse outcome supports a recommendation against use.

Recommendations by other groups:

- CDC 2002 Treatment Guidelines: *"Some experts believe type-specific serologic tests are useful to identify pregnant women at-risk for HSV infection and to guide counseling with regard to the risk of acquiring genital herpes during pregnancy. Such testing may be especially important when a woman's sex partner has HSV infection".*[7]

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.

"D" RECOMMENDATION:

Should generally not be offered.
Moderate evidence for lack of efficacy or for adverse outcome supports a recommendation against use.

Recommendations by other groups:

- CDC 2002 Treatment Guidelines: *"Screening for HSV-1 or HSV-2 infection in the general population is not indicated."*[7]
- United States Preventive Services Task Force (USPSTF): *"Routine screening for genital herpes simplex in asymptomatic persons, using culture, serology, or other tests, is not recommended (D recommendation)".*[8]

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.

Recommendations by other groups:

- CDC 2002 Treatment Guidelines: *"Counseling of infected persons and their sex partners is critical to management of genital herpes. Counseling has two main goals: to help patients cope with the infection and to prevent sexual and perinatal transmission."* [7]

Genital Herpes Background

EPIDEMIOLOGY

HSV-2 is the virus most often responsible for genital herpes, a recurrent, painful, vesicular and ulcerative disease of the genitals in some adults, a cause of severe systemic disease in some neonates, as well as a known risk factor for the acquisition of HIV.[9] HSV-1, the virus primarily responsible for orolabial disease, accounts for approximately 20% of genital herpes cases.[10] The advent of type-specific serologies that distinguish between HSV-1 and 2 has enabled the study of HSV-2 prevalence in different populations.[11] A nationwide seroprevalence study, the National Health and Nutrition Examination Survey, shows that 22% of American adults are infected with HSV-2, though only 9% of these were aware of infection.[12] Prevalence ranges from as few as 4% in selected university students to 80% to 90% in HIV-infected men who have sex with men (MSM).[13, 14] With intensive education, approximately 75% of those asymptomatically infected with HSV-2 can be taught to recognize future symptoms; 20% of all HSV-2 infections are completely asymptomatic.[15, 16]

NATURAL HISTORY OF GENITAL HERPES

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. Recent evidence demonstrates that all people infected with HSV-2 shed the virus asymptomatically, regardless of a history of symptomatic recurrences.[16] The frequency of viral shedding decreases with duration of infection.[16, 17] Asymptomatic shedding of HSV-2 virus occurs from various genital sites, regardless of site of symptomatic recurrences.[16] The sexual contacts of individuals with symptomatic or asymptomatic HSV-2 are at risk of becoming infected. HSV-1 genital infections, perhaps increasing in prevalence, cause less frequent symptoms and shed virus much less frequently than do HSV-2 infections.[16, 17]

TREATMENT AND PREVENTION OF HSV-2

At present, there is no cure for HSV-2 infections, and results of vaccine trials have been disappointing. The most promising published vaccine trial showed a decrease in symptomatic herpes infections in women seronegative for both HSV-1 and HSV-2, but did not prevent HSV-2 acquisition in any groups.[18] 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.[19] 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.[20, 21]

Diagnosing Genital Herpes

LABORATORY METHODS

Laboratory confirmation of clinical genital herpes

The clinical diagnosis of genital herpes is both insensitive and non-specific.[6,22] Only approximately 20% of herpes infections have classic vesicular or ulcerative lesions. The clinical diagnosis should be confirmed by laboratory testing using virologic tests (culture or direct antigen tests) with or without type-specific serologies.[7] Distinguishing between HSV-1 and HSV-2 infections aids in patient counseling regarding the potential frequency of outbreaks, the severity of future symptoms, and the risk of transmission.

Viral Culture

Viral culture is the test of choice in patients with vesicles or moist ulcers. The sensitivity is highest with primary infection, and lower with recurrent lesions and decreases with the duration of the lesion.[23] Culture permits viral typing to distinguish between HSV-1 and HSV-2. The most important benefit of a positive culture is that it definitively identifies the etiology of an HSV-1 or HSV-2 lesion.

Direct antigen detection tests

Direct immunofluorescent antibody (DFA) or direct enzyme-linked immunosorbent assay (ELISA) methods have nearly equal sensitivity to viral culture. Only DFA can differentiate HSV type; ELISA cannot.[24]

Polymerase chain reaction (PCR)

PCR is a highly sensitive and specific test for diagnosing HSV in clinical specimens. It is not, however, Food and Drug Administration (FDA)-approved; thus not available for commercial use. It is the test of choice for detecting HSV in cerebrospinal fluid (CSF).[23]

Cytology

Cytologic detection of cellular changes of herpes virus infection is insensitive and non-specific, both in genital lesions (Tzanck preparation) and cervical Pap smears, and should not be relied on for HSV diagnosis.[23]

Non-type-specific HSV serology tests

There are serologic tests still on the market that do not distinguish between HSV types. These tests are based on crude antigen preparation and, because of cross reactivity between HSV-1 and HSV-2, cannot distinguish between antibody responses.[25] These tests should not be used; clinicians should specifically request type-specific tests based on glycoprotein G (see below).

Type-specific serology tests

Both type-specific and non-specific antibodies to HSV develop after an initial infection and persist for a person's lifetime. The type-specific tests distinguish between HSV-1 and HSV-2 by detecting antibodies to glycoprotein G, which exists in distinct variants for the different types (G1 and G2 for HSV-1 and HSV-2, respectively). Currently, there are three FDA-approved, glycoprotein G-based, type-specific assays on the market. Their performance profiles are in the following table.

Type of test	Sensitivity	Specificity
POCkit HSV-2 (Diagnology) Point-of-care test	93% -100%	94% -97%
HerpeSelect 2 ELISA IgG (Focus)	96% -100%	97% -100%
HerpeSelect 1 and 2 Immunoblot IgG (Focus)	97% -100%	98%

Adapted from Wald.[26]

Limitations to type-specific serology tests

There are limitations to using serology for the work-up of lesions. Unlike culture and antigen detection methods, type-specific serology tests cannot determine the etiology of a lesion. A positive HSV-2 test diagnoses a herpes infection but cannot specify the anatomic location of the infection. There is a risk of false negative serology results if testing is done too early, during the "window period" of seroconversion after a new herpes infection. Timing of seroconversion varies by laboratory test and among patients and has not been well documented; some experts recommend waiting at least six to twelve weeks after a suspected new herpes infection before serologic testing. It is estimated that by six weeks, more than 60% of new HSV-2 infections will have seroconverted and by twelve weeks more than 70% will have seroconverted.[27, 28] Because of the high prevalence of HSV-1, serologic testing for type 1 is less helpful in the work-up of a lesion because a positive test may result from prior orolabial disease (more than 50% of people are infected with HSV-1 during childhood).

Another limitation is the accuracy of the tests. These tests are not 100% specific; therefore, in low-prevalence populations there is an increased risk of false positive tests.[7] At present, there are no recommendations on confirmatory testing of suspected false positives.[29] See Appendix D for estimated predictive values by different population prevalences. There has been some concern regarding the subjective nature of test results and lack of concordance among test readers of the POCkit test, which may lead to more false negative or false positive results.[30]

USING TYPE-SPECIFIC SEROLOGY TESTS IN THE DIAGNOSIS OF SYMPTOMATIC PATIENTS

There are three situations in which HSV-2 serology may assist in the diagnosis of genital herpes: culture-negative recurrent lesions, history suggestive of herpes/atypical herpes without lesions, and first presentation of genital lesions when culture or antigen-detection testing is negative or unavailable. HSV-2 serology can help establish the diagnosis of a suspected but culture-negative recurrent lesion. Serology will also help confirm infection in the absence of lesions when the history is suggestive of herpes. Culture or antigen-detection tests are the tests of choice in suspected primary herpes or first presentation of herpes. If these tests are negative or not available, HSV-2 serology can assist in the diagnosis of herpes. Serology testing should be delayed for at least six to twelve weeks after suspected initial infection to avoid false negative results during the seroconversion "window period". Appendix E summarizes testing strategies and Appendix B diagrams interpretations of serology results by clinical presentation. Type-specific serology testing for HSV-1 in the work-up of genital symptoms has limited utility due to the high prevalence of HSV-1 antibodies from orolabial HSV in the adult population.

Screening For HSV-2: Discussion Of The Evidence

PATIENTS AT RISK FOR STD/HIV

Introduction

Epidemiologic studies have shown that STD clinic populations have a high prevalence of HSV-2 infections (14% to 69%).[11] Of particular concern in this population is the increased risk of acquisition of HIV. HSV-2 infections are associated with at least a twofold increased risk of acquisition of HIV.[9] HSV-2 may be a co-factor in acquisition of HIV or may be a marker of sexual risk. Preliminary data from discordant HIV-infected couples in Rakai, Uganda showed that HSV-2-infected, HIV-negative partners had a fivefold increased risk of acquiring HIV per sexual contact, compared with the risk for HSV-2-negative partners.[31]

Examining the rationale for screening

The rationale for an HSV-2 screening program in an STD at-risk population would be to identify:

- HSV-2-positive patients to decrease their risk of HIV acquisition and to decrease their transmission of HSV-2;
- HSV-2-positive patients with unrecognized symptoms, to educate them to recognize symptoms in order to both improve their health and decrease transmission of HSV-2.

HIV acquisition and HSV-2 transmission reduction

The proposed interventions to decrease both the risk of acquiring HIV and the transmission of HSV-2 include risk-reduction counseling, condoms, and antiviral suppressive therapy.

Risk reduction

There have been no studies to investigate whether knowledge of herpes infection decreases individual risk behavior or acquisition of HIV. There have been two studies of client-centered behavioral risk-reduction interventions that were effective in decreasing incident bacterial infections in populations that were at high risk for STDs.[32, 33] Although not statistically significant, possibly due to small numbers, client-centered risk-reduction counseling appeared to decrease HSV-2 incidence in STD clients studied by the Project Respect Group.[34] Behavioral interventions targeting MSM and using STDs as an outcome measure have been limited. The only study of behavior interventions in MSM that used new STDs as endpoints showed that intensive risk-reduction counseling in group settings did not decrease STD incidence.[35] More recently, however, Dilley et al. showed that intensive one-on-one behavioral therapy did decrease self-reported risk behavior in MSM.[36]

Condom efficacy

Male condoms are protective against HIV when used consistently and correctly. There have been no studies that specifically evaluate condom efficacy in protecting HSV-2-infected people from acquiring HIV; however, there is biologic plausability that condoms, used consistently and correctly, should protect an asymptomatic HSV-infected person against HIV

acquisition. There is evidence that condoms are effective in reducing, but not eliminating, the risk of transmission of HSV-2 in heterosexuals. A recent prospective study of discordant couples showed that if condoms were used for more than 25% of sex acts, they offered protection to women.[20] An unpublished study of adults with more than four partners or an STD showed that condoms were protective against HSV-2 for men as well, if used for more than 65% of sex acts.[21] Condoms appear to be effective if used, but they need to be used regularly. In two studies of heterosexual couples, fewer than 25% of couples aware of their risk of transmission/acquisition used condoms consistently.[20, 37] There have not been, however, any specific evaluations of risk-reduction counseling interventions to determine if condom use can be increased in HSV discordant couples.

Antiviral suppression
There have been no studies to date that demonstrate that antiviral suppressive therapy for persons infected with HSV-2 reduces the acquisition rates of HIV. Theoretically, suppressive therapy should decrease the incidence of ulceration or skin breakdown, thus limiting portals of HIV entry; the role in asymptomatic HSV infections is less clear.

There is early evidence indicating that suppressive therapy does decrease transmission of HSV-2. Corey et al. reported preliminary data from a randomized controlled trial of a suppressive dose of valacyclovir compared with placebo in symptomatic HSV-2 discordant couples. Transmission to the seronegative partner was halved in the valacyclovir group, though genital herpes acquisition rates were very low in both groups (1.9% versus 3.8%).[19] This is supported by evidence that suppressive doses of acyclovir significantly decrease subclinical shedding (95% by viral culture and 80% by PCR) of HSV-2 in patients with symptomatic infections.[38] Further study of antiviral suppressive therapy and its influence on herpes transmission in different populations is needed, especially in asymptomatic HSV populations.

Identification of unrecognized symptomatic herpes

It has been established that many asymptomatic HSV-2-infected patients can be educated to recognize symptomatic disease.[15, 16] Previously unrecognized symptoms of recurrent herpes may be identified after diagnosis of infection and with education regarding symptoms of herpes. Patients may then be offered either episodic or suppressive therapy to treat recurrent outbreaks. Risk-reduction counseling that includes education to abstain from sex with recurrent lesions may decrease HSV transmission.

SCREENING IN HIV-INFECTED PATIENTS

Introduction

HSV-2 infections are highly prevalent in HIV-positive populations. More than 80% of HIV-positive MSM and more than 60% of HIV-positive heterosexuals have been shown to be co-infected with HSV-2.[14] HSV infection is a significant cause of morbidity and mortality in individuals with HIV infections. Common clinical manifestations are recurrent anogenital

or orolabial ulceration, proctitis, and significant persistent mucocutaneous herpes in AIDS patients. HIV-infected MSM have more frequent symptomatic herpes recurrences than do HIV-negative MSM.[39] There is also concern that HSV infections may accelerate the course of HIV disease progression. It has been shown that primary and recurrent HSV infections increase HIV replication in vivo.[39, 40]

Genital HSV is a potential co-factor for HIV transmission. Several studies have suggested increased HIV infectiousness in those co-infected with HSV-2. There are higher HIV virus levels in HSV genital lesions than in plasma.[41] Persons with concomitant HIV and HSV-2 infections have a threefold higher rate of symptomatic herpes recurrences and therefore increased frequency of potential HIV shedding.[39] HSV-2 viral shedding also increases with decreasing immunity.[39] Additionally, HIV transcription rate and plasma viral load increases in individuals with acute HSV, even post-outbreak.[42] There have been no prospective studies, however, to show that HSV-2 co-infections cause increased HIV transmission. Preliminary results from Gray and colleagues studying the probability of HIV transmission in discordant couples showed that HSV-2 was not associated with increased HIV transmission by HSV-2/HIV co-infected partners, although symptomatic genital ulcer disease did increase the risk of HIV transmission.[43]

Examining the rationale for screening

The rationale for an HSV-2 screening program in HIV-infected individuals has three goals. These are to identify:

- HSV-2-positive patients, in order to intervene to potentially reduce HIV and HSV transmission to others;
- HSV-2-positive patients, in order to educate them to recognize unidentified symptoms of herpes amenable to suppressive therapy, thus improving the health of the HIV/HSV-2 co-infected patient and potentially decreasing HIV transmission, as well as HSV transmission to others;
- To identify HSV-2-negative patients in order to provide counseling to reduce their risk of acquisition of HSV-2.

HIV and HSV-2 transmission reduction

The primary goal of screening in this population is to identify those at potentially higher risk for transmitting HIV due to their HSV-2 co-infection. Possible interventions to prevent both HIV and HSV-2 transmission include client-centered risk-reduction counseling and/or antiviral suppression of herpes, which, in decreasing HSV recurrences, may theoretically decrease HIV shedding.

Risk-reduction

There have been no studies to specifically evaluate the effectiveness of client-centered risk-reduction counseling in HSV-2/HIV co-infected individuals to decrease individual risk behavior or transmission of HIV. Risk-reduction counseling in other high-risk STD populations, however, has been shown to be effective. Counseling significantly decreased incident bacterial STDs in two high-risk heterosexual populations and reduced HSV-2 incidence in STD clinic populations, though the reduction was not statistically significant.[32, 34]

Condom effectiveness
Condoms are protective against HIV when used consistently and correctly. However, because condoms do not cover all exposed areas, they are likely to be less effective in preventing STDs transmitted by skin-to-skin contact, such as herpes.[7] No studies have evaluated whether HIV can be transmitted by herpetic lesions not covered by condoms.

Antiviral suppressive therapy
There have been no studies demonstrating that suppressive therapy for herpes in HSV-2/HIV co-infected patients decreases transmission of HIV. There is evidence that suppressive therapy for HSV decreases herpes viral shedding in HIV-infected patients. A randomized controlled trial of famciclovir in HSV/HIV co-infected people showed that HSV shedding detected by viral culture was decreased to 1% of days with famciclovir, compared with 11% of days with placebo.[44] However, if preliminary data from Gray et al., showing that asymptomatic HSV-2 infections are not associated with increased transmission of HIV in discordant couples bears out, then suppressive therapy may have a role only in HSV/HIV co-infections in which herpes is symptomatic.[43]

Identification and treatment of unrecognized symptomatic herpes

The second goal of screening HIV-infected persons for HSV-2 would be to improve the health of HSV-2/HIV co-infected patients. Previously unrecognized symptoms of recurrent herpes may be identified after screening, thus making the patient a candidate for herpes suppressive therapy. Suppressive therapy does significantly decrease the frequency of sympto-matic outbreaks and of subclinical viral shedding of HSV-2.[44] Additionally, the patient could be educated regarding his/her increased risk of transmission of HIV and HSV and could potentially decrease transmission with risk-reduction counseling and other behavioral interventions.

At present, there is no clear indication for treatment of asymptomatic herpes infections in patients with HIV. Acyclovir has been shown to decrease plasma HIV-1 RNA, and high doses of acyclovir have shown a survival benefit for HIV positives.[40, 45] However, further prospective, controlled studies demonstrating a benefit from HSV suppression on HIV progression are needed prior to recommending herpes suppressive therapy for asymptomatic HSV/HIV co-infected populations. The contribution of this approach to increasing levels of acyclovir-resistant HSV is unclear and would need further investigation as well.

HSV-2 acquisition reduction

The third goal of screening for HSV-2 infections in HIV-positive persons would be to identify those at-risk of acquiring HSV-2. HIV-infected persons have a fourfold increased risk of becoming infected with HSV-2.[9, 46, 47] General STD risk-reduction counseling may reduce risk of incident herpes infection in these individuals.[34]

SCREENING IN PATIENTS WITH PARTNERSHIPS OR CONSIDERING PARTNERSHIPS WITH HSV-2-INFECTED PEOPLE

Introduction

With the availability of type-specific serology tests, more people are being identified as infected with HSV-2, thus likely increasing the known number of partners with possible discordance. Screening patients whose partners or potential partners are known to have HSV-2 may assist patients in sexual health decisions. The yearly risk of acquisition in discordant symptomatic heterosexual couples aware of their serodiscordance ranges from approximately 4% to 10% per year.[19, 37]

Examining the rationale for screening

The goals of screening asymptomatic patients who report a sexual partner with a history of genital herpes or HSV-2 infection are to identify:

- HSV-2-negative patients to decrease their risk of HSV-2 infection;
- HSV-2-positive patients to recognize unidentified symptoms of HSV and to educate them about risk of transmission to other/future partners and about their risk for other STDs and HIV.

HSV-2-negative patients

Risk reduction in discordant couples

There have been no studies directly evaluating the impact of knowledge of HSV discordance on acquisition of herpes in the at-risk partner. The effectiveness of risk-reduction counseling in serodiscordant couples has not been evaluated adequately. There have been two prospective, observational studies of non-pregnant, serodiscordant heterosexual couples. Among a series of 144 heterosexual couples in which one had recurrent genital herpes and the other was identified as HSV-2 negative, all were educated regarding the risks of skin-to-skin contact during active episodes, and regarding the risks of transmission during asymptomatic periods. Despite counseling, only 15% of couples used condoms routinely, and more than 70% of new infections occurred during asymptomatic episodes.[37] In 528 monogamous, heterosexual discordant couples prospectively studied to evaluate the efficacy of an HSV-2 vaccine, 39% never used condoms and 30% used them for fewer than 25% of sex acts, despite education at each clinic visit to use condoms for all sex acts.[20] Though neither of these studies was designed to evaluate the effectiveness of education regarding HSV discordance, they do suggest that knowledge of risk of herpes acquisition/transmission may not significantly impact discordant couples' risk-reduction behavior.

Condom efficacy

There is evidence that condoms, when used for more than 25% of sex acts, are effective in preventing the acquisition of HSV-2 in women at risk of infection from a seropositive male partner.[20] There are unpublished data that indicate that condoms are protective against HSV-2 acquisition in males as well as females, if condoms are used for more than 65% of sex acts.[21]

Antiviral suppression for the infected partner

There is preliminary evidence from Corey et al. that suppression of HSV shedding with antivirals in the infected symptomatic partner decreases transmission to the susceptible partner. Heterosexual couples randomized to valacyclovir had a 1.9% annual infection rate, compared with a 3.8% rate for those using placebo.[19] Though both groups had a low rate of acquisition of HSV-2, there was a significant benefit in the antiviral suppressive group. Acyclovir has been shown, using culture detection, to decrease HSV viral shedding by 95%, and, using more sensitive PCR techniques, by 80%.[38]

Identify HSV-2-positive patients

Concordant couples

Screening to identify concordance for individual couples has no beneficial impact on public health but does have a likely beneficial impact on the couple. A theoretical concern in identifying concordance would be decreased condom use and therefore potential risk of other STDs. There is no evidence to support this concern. General STD counseling should be conducted if concordance is identified, as well as herpes counseling regarding symptoms and risk of transmission in future or concurrent partners, pregnancy risks, and risk of HIV acquisition (see Appendix C: Guide for herpes counseling).

SCREENING IN PREGNANCY

Introduction

Newly acquired genital herpes is a major concern in pregnancy, due to the risk of neonatal herpes. The incidence of neonatal herpes is much lower than the prevalence of HSV-2 in the pregnant population.[11] Neonatal herpes affected one in 8,700 live births in California in 1995.[48] It is an often devastating disease; more than 50% of affected infants have moderate or more severe neurological impairment, with a 20% overall mortality.[49] Approximately 90% of all neonatal herpes infections are transmitted during delivery and at least 5% transmitted in utero.[50, 51] HSV-2 is implicated in more than half (55%) of neonatal herpes infections.[52] More than 80% of infants with neonatal herpes are born to women without any history of symptomatic herpes during that pregnancy or at delivery.[50] Women at highest risk (30% to 50%) of transmitting genital herpes to their infants are those with primary infections acquired during the peripartum period who deliver prior to developing protective antibodies.[53, 54] The risk of vertical herpes transmission is lowest for women with an already established genital herpes infection, i.e., seroconversion completed (<0.04%).[49, 53-55] The best evidence regarding the natural history of women at risk for neonatal herpes transmission was provided by a prospective study of 7,046 pregnant woman seronegative for either HSV-1 or HSV-2, followed for seroconversion through delivery. There were 94 (2%) seroconversions before term, and no cases of neonatal herpes. There were, however, nine infants born to women who acquired HSV infections at the time of delivery, prior to developing HSV antibodies. Four of those infants developed neonatal herpes, half of whom were HSV-1-infected.[53] This study illustrates the low risk of transmission once antibodies develop, and the high morbidity of perinatal primary HSV infections in pregnancy.

Examining the rationale for screening

The goal for serological screening for herpes in pregnant women would be to identify:

- HSV-2-negative women at-risk of acquiring herpes in late pregnancy, to reduce acquisition of herpes and therefore reduce vertical transmission;
- HSV-2-positive women at low risk of vertical transmission.

Identify at-risk population: HSV-2-negative women

There is little evidence that determining risk of primary herpes infection would decrease the incidence of neonatal herpes. Identifying women at risk for herpes would need to be the first step of a screening program. There is some evidence to suggest that the highest-risk pregnancies may be the least likely to get a prenatal HSV screen; 5 of the 9 women with primary HSV infections at delivery had either no prenatal care, or prenatal care at an outside facility.[53] Screening partners may also be difficult; more than 45% of husbands of pregnant women in a middle-upper-class obstetric community refused serologic testing.[56] Possible interventions once a pregnant patient is identified as potentially at risk for HSV are condoms, abstinence, and/or antiviral therapy for the HSV-positive sex partner.

Risk-reduction in seronegative pregnant women

There have been no studies to evaluate behavioral interventions on the acquisition of HSV during pregnancy. There has been one prospective study of 227 pregnant women and 190 partners enrolled in prenatal care who were tested for serologic discordance. The 18 couples who were identified as discordant, with the woman susceptible to HSV-2 acquisition, were educated to abstain from sex or to use condoms to prevent maternal acquisition of HSV. More than half of couples (10 couples) did not use condoms at all after diagnosis of discordance, and had sex a mean of 5.5 times per month.[56] Other prospective observational studies of non-pregnant couples with serodiscordance showed that condom use is infrequent, despite knowledge of risk of developing herpes.[20, 37]

Condom efficacy

The use of condoms by male HSV-2-infected partners appears to decrease the risk of transmission to the uninfected woman. Pregnant couples who used condoms had a lower risk for seroconversion than did those who had unprotected sex (11% versus 20% annualized incidence of seroconversion).[56] Condoms used during more than 25% of sex acts were protective for non-pregnant women.[20]

Antiviral suppressive therapy for partner of seronegative pregnant woman

Antiviral suppressive therapy for a known HSV-2-infected male partner to prevent transmission to the at-risk pregnant woman has not been evaluated. Antivirals do suppress viral shedding in those infected with herpes, and preliminary evidence from Corey et al. indicates that daily valacyclovir therapy for HSV-2-infected people significantly decreases herpes transmission to susceptible partners.[19] This is an appealing management option, in addition to abstention or condom use, to reduce the risk of maternal acquisition of herpes near term in couples, but has yet to be evaluated.

Identify HSV-2-seropositive women

The second goal of type-specific screening in pregnancy would be to identify asymptomatic HSV-2-positive women to educate them regarding their very low risk of viral transmission at delivery. Historically, this has been the group targeted by viral cultures at delivery and cesarean section with any signs or symptoms of recurrence to prevent neonatal herpes. It has been assumed that cesarean sections interrupt transmission of herpes to infants by bypassing the vaginal canal and they have been routinely performed for any positive culture or herpetic lesion at delivery. Although this surgical procedure remains the current standard of care for women with lesions at the time of delivery,[57] no firm data supports this strategy. In a recent study by Brown et al., cesarean section was shown to be protective against neonatal herpes infection, but results were no longer significant when adjusted for stage of infection.[52] Surveillance shows that 20% to 30% of infected infants are born by cesarean, including 8% of infected infants born to women with intact membranes.[50, 51] Further evidence by Prober et al. demonstrates that infants born to mothers with recurrent herpes have high protective neutralizing antibodies to HSV-2 and low risk of acquiring herpes. His group showed that none of 34 infants inadvertently exposed to vaginal HSV-2 by visible lesions or positive cultures (56% with noted genital lesions) developed herpes infections.[54] In an analysis of maternal and neonatal outcomes associated with cesarean section in women with recurrent herpes, using cesarean section effectiveness of 80%, it was determined that more than 1580 excess cesareans would be performed to prevent one severe neonatal HSV-2 infection, and cause 0.57 maternal deaths for every neonatal death prevented.[55] There is a general concern that universal serologic screening for HSV-2 in pregnant women will lead to the identification of significant numbers of asymptomatic HSV-2 infections that may result in unnecessary cesarean sections and maternal morbidity, and may not be an effective strategy to prevent neonatal HSV.

Antiviral suppressive therapy in established herpes infections

The use of antiviral suppressive therapy in women with recurrent herpes has not been shown to impact on neonatal herpes, but has been shown to decrease symptomatic recurrences. Because the incidence of neonatal herpes is so low in this population, it is difficult to adequately evaluate the effectiveness of this intervention. There have been two small randomized controlled trials that have shown a decrease in cesarean rates in women with a history of genital herpes by decreasing the frequency of herpetic recurrences at term. One trial was not statistically significant, but did show a trend towards decreased recurrences and cesarean sections.[58] The other study, a randomized controlled trial of 46 pregnant women with first-episode herpes who were randomized to acyclovir or placebo in their 36th week of pregnancy, showed no recurrences and, therefore, no cesarean sections for herpes in the 21 women treated with acyclovir, and 9 (36%) recurrences in the placebo group of 25 women treated with cesarean sections. There were no cases of neonatal herpes in either group, and none of the 46 women were found be shedding herpes virus at delivery.[59] The safety of acyclovir in pregnancy has not been well established. There have been no reported adverse fetal outcomes above the normal population reported to the acyclovir registry; however, routine use of acyclovir is not being recommended.[60]

Adverse impact of screening

A disadvantage to universal screening of asymptomatic women in pregnancy would be the increase in the number of women who would be serologically positive, and, therefore, identified by the provider and patient as at theoretical risk of neonatal transmission; this may increase the rate of prophylactic cesarean deliveries. Marrazzo et al. found that pregnant women with a known history of herpes (but without symptoms during the studied pregnancy) were 1.2 times more likely to have a cesarean section delivery, compared with pregnant women without herpes in hospitals where cesarean section rates were greater than 20%.[61] Though these results were not statistically significant (p=0.058), this is the only study investigating this potential adverse effect of screening in pregnancy. Education of obstetricians regarding the likely protective nature of HSV-2 antibodies would be critical prior to implementing large screening programs in pregnancy.

Cost effectiveness

The cost effectiveness of screening all pregnant women to prevent neonatal herpes infections is undetermined. A cost-effectiveness analysis by Rouse et al. of screening pregnant women for HSV-2 estimated that the cost to prevent one case of moderate to severe neonatal HSV ranged from $891,000 to $4,000,000, concluding that routine screening of pregnant women from a public health perspective was ill advised.[62]

SCREENING IN GENERAL POPULATION

Because there is no current treatment of asymptomatic HSV-2 infections or proven intervention that decreases community prevalence of HSV-2, universal screening of the general population is not recommended.

General Considerations In Screening

ADVERSE EFFECTS

When evaluating screening proposals, potential adverse consequences of screening need to be considered. The actual serology test is unlikely to have adverse consequences, as it is minimally invasive: either a simple venipuncture or finger stick. The psychosocial impact of newly diagnosed herpes infection through screening has been a concern. Symptomatic genital herpes infections can be very traumatic, often resulting in depression and on-going emotional stress.[63] Results from an American Social Health Association survey of the perceived trauma of a potential herpes infection showed that two-thirds of respondents thought the diagnosis would be "very traumatic".[64] Results from the three small randomized or prospective studies of psychological impact of HSV screening have shown no effect on mood post diagnosis.[65-67] Though all three trials were small and had a high rate of loss to follow-up, their results suggest that most non-pregnant sexually active people may have no significant psychosocial dysfunction after diagnosis of asymptomatic herpes infections.

COST-EFFECTIVENESS

An acceptable cost to prevent new HSV-2 infections has not yet been established. Additional costs that should be considered are the costs of pre- and post-test counseling and the prices of the actual screening tests (which range from $5 to $30). If used, the cost of daily suppressive therapy for identified seropositives would range from $100 to $160 per month. Whether health insurance companies would reimburse suppressive therapy for seropositive partners in order to prevent transmission to enrollees is unclear. The potential inappropriate utilization of care after diagnosis with asymptomatic genital herpes is another concern. Further research is needed to evaluate the cost-effectiveness of HSV-2 screening in high-risk populations.

Conclusion

These guidelines represent the first practical recommendations for using type-specific herpes serologies. Due to the recent accessibility of type-specific herpes technology and as-yet-unproven benefit to screening, the guidelines were limited to diagnosis of genital symptoms and screening in four specific populations. These guidelines were written from a public health perspective, applying a screening rationale to each group, using the strength of existing data and, where data were insufficient, expert opinion. By the conclusion of this literature review, there was little strong evidence to support screening recommendations. These guidelines will be revised as additional data become available.

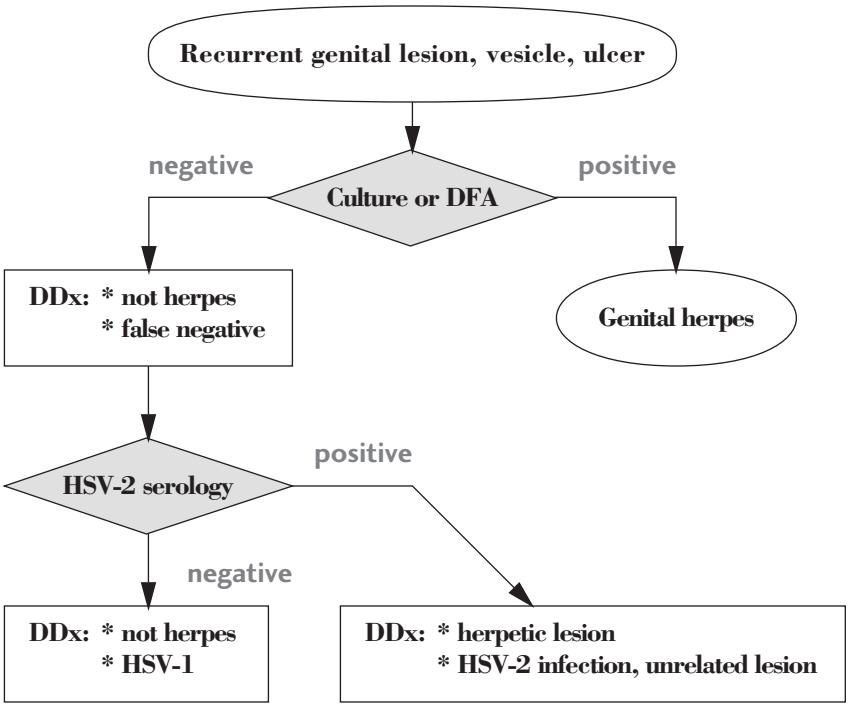
Appendices

Appendix A.
RATING SYSTEM FOR RECOMMENDATIONS

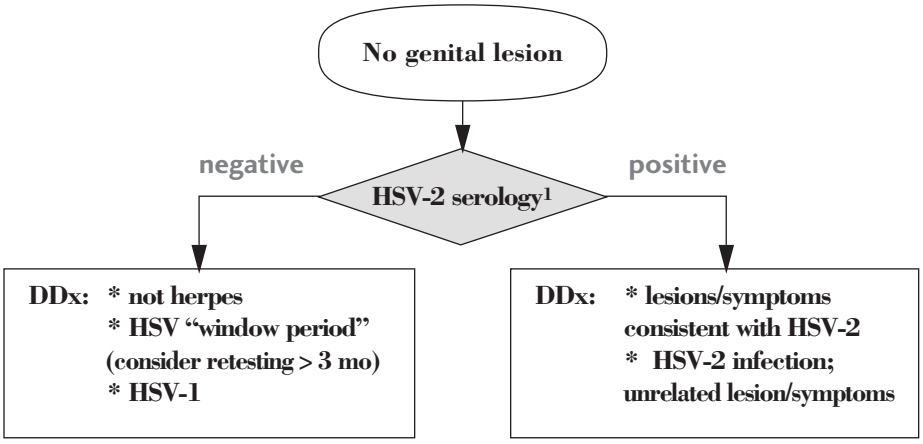
Rating	Strength of the Recommendation
A	Should always be offered. Both strong evidence for efficacy and substantial benefit support recommendation for use.
B	Should generally be offered. Moderate evidence for efficacy, or limited evidence with expert consensus, supports a general recommendation for use.
C	Should be offered to select patients. Evidence for efficacy is insufficient to support a general recommendation for use.
D	Should generally not be offered. Moderate evidence for lack of efficacy or for adverse outcome supports a recommendation against use.
E	Should never be offered. Strong evidence for lack of efficacy or for adverse outcome supports a recommendation against use.

APPENDIX B.
CLINICAL APPLICATIONS AND INTERPRETATIONS OF TYPE-SPECIFIC HSV-2 SEROLOGIES BY PRESENTATION (DDx: DIFFERENTIAL DIAGNOSIS)

1. Presentation with recurrent genital lesion:

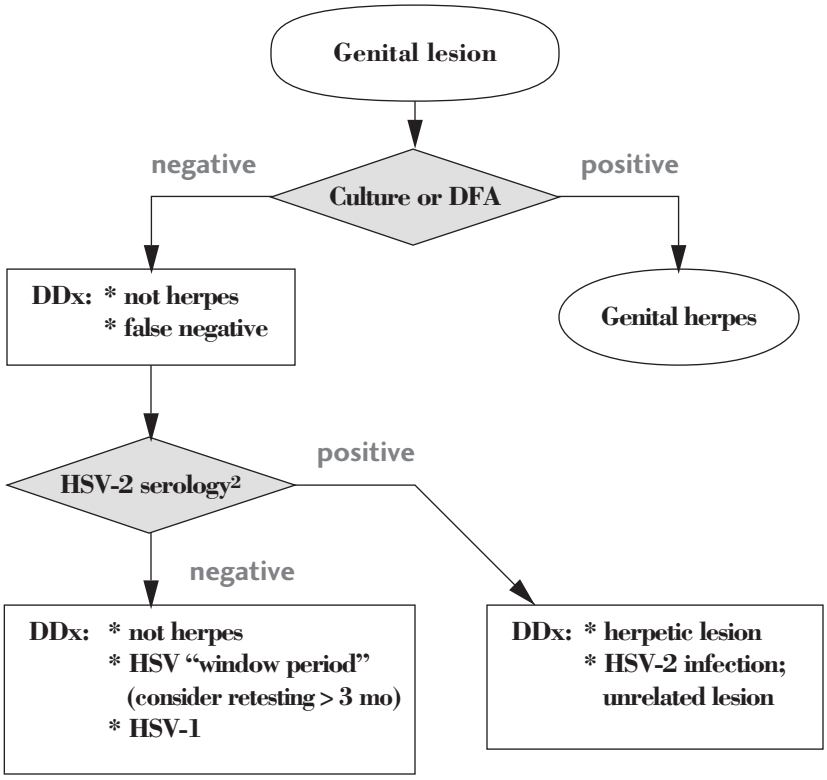


2. History suggestive of first, recurrent, or atypical herpes--no lesion to culture:



[1]*If 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.

Appendix C.
GUIDE TO GENITAL HERPES COUNSELING

(Adapted from CDC STD Treatment Guidelines.)[7]

"Counseling of infected patients and their sex partners is critical to the management of genital herpes. Counseling has two main goals: to help patients cope with the infection and to prevent sexual and perinatal transmission. Although initial counseling can be provided at the first visit, many patients benefit from learning about the chronic aspects of the disease after the acute illness subsides."

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 of acquiring HSV-2, but may persist, less frequently, for years 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.

Appendix D.
ESTIMATED POSITIVE AND NEGATIVE PREDICTIVE VALUES OF TWO HYPOTHETICAL SEROLOGY TESTS IN DIFFERENT POPULATIONS

Population	Estimated prevalence[a]	TEST 1[b]		TEST 2[c]	
		PPV[d]	NPV[e]	PPV	NPV
STD clinic: lower risk	20%	89%	99%	92.5%	99.5%
STD clinic: higher risk	50%	97%	96%	98%	98%
HIV-infected	80%	99.2%	85.8%	99.5%	92.5%
Pregnant women	30%	93.2%	98.3%	95.5%	99.1%
General population: family planning clinic	10%	78.0%	99.5%	84.5%	99.8%

a These percentages represent estimates of prevalences in each population.

b Sensitivity 96%, specificity 97%

c Sensitivity 98%, specificity 98%

d Positive predictive value: the probability that a patient with a positive serology test result actually reflects an HSV-2 infection

e Negative predictive value: the probability that a patient with a negative serology test result actually does not reflect an HSV-2 infection

Appendix E .
USES OF TYPE-SPECIFIC SEROLOGY TESTS

I. Diagnostic	
A. Culture-negative recurrent lesion **B.** History suggestive of herpes/atypical herpes without lesions to culture **C.** Suspected primary herpes or first presentation of genital symptoms, if culture or antigen detection testing is negative or unavailable and acquisition likely more than six weeks prior	
II. Screening	**Rating**
A. Patients at risk for STD/HIV	**C**
B. HIV-infected patients	**B**
C. Patients with a partner with genital herpes	**B**
D. Pregnant women	**D**
E. General population	**D**

Appendix F.
PROVIDER PULL-OUT: PROVIDER HERPES FACT SHEET AND SUMMARY OF USE OF HSV-2 SEROLOGIES

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.)[7]

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.

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.

Open-ended questions to guide counseling prior to HSV-2 serologic testing:

- How would a positive herpes diagnosis (or having genital herpes) change your sexual behavior?
- How would a negative herpes diagnosis change your sexual behavior?
- Tell me some ways you would protect yourself (if negative)/your partners (if positive).
- What changes in your relationships or sexual behaviors would having herpes mean for you?
- How would you change your behavior if you were pregnant or your partner were pregnant?

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