Genital Herpes: A Closer Look

LEARNING OBJECTIVES
At the conclusion of this activity, participants should be able to:

- Discuss current approaches to screening/testing for HSV in order to improve diagnosis
- Encourage the counseling of infected patients and their partners to reduce the risk of transmission of HSV

Genital herpes (GH) is a common problem in primary care and women’s health practices, yet can pose difficulties in diagnosis and treatment for the clinician. The following questions and answers highlight some of these areas and will assist the provider in offering responses to patient queries.

WHAT IS GENITAL HERPES?
Genital herpes is a common viral infection affecting the genital area and adjacent keratinized skin including the buttocks, inner thighs and lower back. Two of the eight members of the herpes virus family cause genital herpes— herpes simplex virus 1 and 2. Approximately 50 million Americans are infected with HSV-2 and an estimated 10–15 million with genital HSV-1. Following initial infection, these viruses become nerve-based in the trigeminal ganglion in the face (HSV-1) and sacral ganglia in the lower back (HSV-2 and HSV-1). In these locations, the viruses are protected from clearance by the immune system; hence their designation as life-long infections. Clinical characteristics of GH include erythema, itching, burning and pain accompanied by classical inflammatory vesicular lesions that progress to ulcers and crusting, finally healing to normal appearing skin.

WHAT IS THE DIFFERENCE BETWEEN GENITAL HERPES CAUSED BY HSV-2 AND HSV-1?
GH due to HSV-2 is usually much less inflammatory in its clinical presentation than HSV-1. It is commonly caused by transmission of HSV-1 from the mouth to the genitals during oral sex. Initial HSV-1 GH outbreaks are usually shorter than those due to HSV-2 (one to three days vs. one to two weeks), less recurrent in the first few years (annual outbreaks vs. every three to four months), and less likely to be associated with asymptomatic viral shedding (AVS). Many clinical cases go undiagnosed due to a short first outbreak and infrequent clinical recurrences. Acquisition of HSV-1 GH through penile-vaginal or penile-anal intercourse is less likely than through oral sex due to infrequent genital outbreaks and limited viral shedding. It is difficult to estimate the number of individuals with sexually acquired HSV-1 GH since about two-thirds of Americans out of concern they will “open a can of worms.”

Many clinicians are hesitant to offer HSV antibody testing

intercourse. Of the 50 million infected individuals, 15–20 percent (8–10 million Americans) have the classical and easily recognized clinical presentations described previously. The remaining 40 million of those with HSV-2 were formerly thought to be asymptomatically infected. On closer examination, however, it appears that the majority of these individuals have mild to moderate recurrent lower genital tract inflammation that is rarely associated with GH by either the patient or clinician. This intermittent irritation presents as itching, redness, rashes and dysuria without the classical vesiculocerative lesions of GH. Patients often use a variety of “over-the-counter” non-prescription remedies including topical corticosteroids, antihemorrhoidal, antibacterial and antifungal creams, ointments and sprays purchased at supermarkets and pharmacies.

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are infected with orolabial HSV-1 during early childhood. Approximately half of those infected with HSV-1 will go on to develop cold sores, usually beginning in the peripubertal period. This extensive level of pre-sexually acquired HSV-1 infection may help explain the milder clinical course and less frequent rate of viral reactivation of HSV-1 GH compared to HSV-2 GH.

**WHY IS SYNDROMIC DIAGNOSIS OF GH INADEQUATE?** For decades, many - if not most - clinicians have used the appearance of vesiculoulcerative lesions and associated symptoms to make a GH diagnosis. This approach is problematic for a number of reasons. Patients with a history of genital irritation may not have lesions or symptoms at the time of their office visit. They may also not have classical stigmata, instead presenting with recurrent non-specific symptoms such as genital itching or burning, and atypical lesions such as rashes or fissures. In some cases, patients may not have any signs or symptoms of GH and yet still be infected. A syndromic diagnosis of GH also does not specify whether the cause is HSV-1 or HSV-2, conditions with different prognoses and risks of transmission to sex partners and newborns. In addition, the absence of a laboratory diagnosis for some patients may suggest uncertainty as to whether they actually have GH.⁸

**WHICH SWAB TEST FOR GENITAL HERPES IS OPTIMAL?** If the patient has a suspected GH lesion – vesiculoulcerative or atypical – a swab test should be performed. Cell cultures are inexpensive but the yield can be low, often less than 50 percent, especially if the specimen is not obtained during the first few days after the outbreak begins. Clinicians should insist that their laboratory report positive culture results by type, as either HSV-1 or HSV-2. Amplified DNA swab tests, often referred to as PCR (polymerase chain reaction), are able to identify smaller amounts of viruses later in the course of the outbreak. Although clearly superior to culture in diagnosing GH, PCRs are usually far more expensive and also may not be routinely available for use in outpatient care.⁸

**WHEN SHOULD TYPE-SPECIFIC ANTIBODY TESTS BE USED?** Since 2000, very accurate type-specific IgG (Immunoglobulin G) antibody (blood) tests have been available. Unlike the older non-specific GH blood tests, the new tests (e.g. HerpeSelect® 1 and 2) do not have cross reactivity problems in identifying HSV-1 and HSV-2 antibodies.⁹ The window period for the tests is three weeks for the earliest appearance of antibodies after infection and sixteen weeks for the point by which the vast majority of those infected have acquired antibodies. In fact, by twelve weeks, over 90 percent of those infected have antibodies. Although IgM (Immunoglobulin M) antibody tests are also available, they are not type-specific, are considered inaccurate, and should not be used in making a GH diagnosis.¹⁰

Point-of-care testing is also available.

The new HerpeSelect Direct kit to detect HSV-2 antibodies is more accurate and easier to use than older tests.

There are two approaches to using antibody testing to evaluate patients with suspected GH lesions. Clinicians can first perform a swab test and, if the test is negative, perform a blood test the following week. The alternative is to perform antibody testing at the same time as the swab test. Many clinicians prefer this approach since the swab test is often negative, even in the presence of herpes viruses. Also, more than half of the patients with first outbreaks due to HSV-2 already have antibodies. This is because their initial GH infection was asymptomatic, and their first outbreak does not represent true primary infection, but instead the first clinical outbreak of a previously acquired infection. In terms of whether to test for HSV-2 antibodies only or both HSV-1 and 2 antibodies, the former approach often makes more sense. A positive HSV-1 antibody test usually reflects orolabial infection acquired in early childhood rather than GH due to HSV-1. If the initial HSV-2 antibody test is negative, it should be repeated at three months. A positive HSV-2 blood test at three months reflects true primary infection. A persistently negative HSV-2 test at three months suggests that the original GH lesion was probably due to HSV-1. HSV antibody testing is also an important component of general STI evaluation and screening, and valuable in the assessment of sex partners of individuals diagnosed with GH.⁸

**WHAT SHOULD CLINICIANS TELL PATIENTS WHO HAVE HSV-2 ANTIBODIES AND NO SYMPTOMS OF GH?** Many clinicians are hesitant to offer HSV antibody testing out of concern they will “open a can of worms.” The diagnosis of GH is usually unanticipated and unsettling, especially for the asymptomatic individual or when non-specific symptoms and signs are present. Clear, concise counseling is very important and can assist patients...
in accepting and understanding their condition with less psychosocial impact.11 (Key points to emphasize are listed on the previous page.) Two or three 10-15 minute follow-up visits in the first month after diagnosis are strongly preferable to an extended first visit followed by the advice to “return if there are problems.”

**HOW COMMON IS ASYMPTOMATIC VIRAL SHEDDING?** The presence of herpes virus in the genital area when lesions are absent is a challenging concept for many patients. Our knowledge of viral shedding is the result of natural history studies and clinical trials published over the past 20 years. We now know that viral shedding not only occurs from active lesions but also from multiple locations, including the cervix, scrotum, perineum and perianal areas without any signs or symptoms of GH present. Asymptomatic viral shedding is common in HSV-2 infection, occurring about three to eight days a month; appears to be independent of whether the patient has frequent, few or no clinical outbreaks; occurs most frequently during the first year and continues at an elevated level for well over a decade; and is responsible for most new infections.6,7

**WHAT ARE THE ESSENTIALS IN TREATING PATIENTS WITH GENITAL HERPES?** The 2006 Centers for Disease Control and Prevention (CDC) Guidelines for the Treatment of STDs (CDC.org) recommends the use of guanidine nucleoside antivirals (acyclovir, valacyclovir and famciclovir) for the management of GH infection.8,14 These medications are generally safe to use and are usually well tolerated by patients.13 Patients should receive 10 days of treatment for initial outbreaks and be given medications for episodic therapy of subsequent outbreaks. Two to five day regimes appear to work equally well and reduce the outbreak duration by a day or two. Daily suppressive therapy results in 75-80 percent fewer clinical outbreaks and days of asymptomatic shedding. In the case of daily valacyclovir use, GH transmission to uninfected partners is reduced 50-75 percent.14,15 Recently, some experts have suggested that daily suppressive therapy be initiated after the first outbreak since the frequency of outbreaks and asymptomatic viral shedding are highest during the first year as are new GH infections in uninfected sex partners. For many patients, recurrent outbreaks and fear of infecting sex partners are associated with reduced self-esteem, depression, anxiety and social withdrawal.10 To the extent that daily suppressive therapy reduces the number and frequency of outbreaks and reduces the risk of transmission to others, clinical studies and anecdotal experience show that patients experience improved quality of life and fewer psychological problems.

**REFERENCES**