Update on Sexually Transmitted Diseases: Herpes Simplex Virus Type 2 Infections

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Most cases of HSV-2 infection are spread through sexual transmission. An infected person can have virus in his or her saliva, semen, or vaginal secretions. When a seronegative partner comes in sexual contact with these secretions, the virus can enter the body through mucosal surfaces (such as the vagina, anus, or mouth) or micro-abrasions on the skin (eg, the penile shaft, scrotum, thighs, or perineum).

Last month, I began a series of clinical updates on sexually transmitted infections that you may encounter when caring for adolescents. The first update covered the various presentations of gonorrhea and chlamydial infections. This month, the focus is on herpes simplex virus (HSV) infection. Two types of HSV exist:

• HSV-1, which causes oral childhood herpetic stomatitis infections.
• HSV-2, which causes genital herpes infections transmitted through sexual contact.

Most of this discussion is about HSV-2. However, I occasionally discuss HSV-1 because of its similarities to HSV-2—and because it, too, may be sexually transmitted. Teenagers with newly diagnosed infection have many questions for their physician and they expect to receive accurate, timely information—regardless of the clinician's level of expertise in this area. I have therefore structured most of this review around the questions that my patients have asked me when I told them about their herpes diagnosis. This list of questions is not exhaustive, but it does cover most topics that adolescents will ask you to address. A patient education guide follows (page 244).

Q: How did I get this infection?
A: Most cases of HSV-2 infection are spread through sexual transmission. An infected person can have virus in his or her saliva, semen, or vaginal secretions. When a seronegative partner comes in sexual contact with these secretions, the virus can enter the body through mucosal surfaces (such as the vagina, anus, or mouth) or micro-abrasions on the skin (eg, the penile shaft, scrotum, thighs, or perineum).

Once the virus enters the new host, it replicates and often produces the primary outbreak. Following resolution of the initial outbreak of genital HSV-2 infection, the virus enters a latent stage in which it lies dormant in the dorsal (sensory) sacral nerve routes. In oral HSV-2 (or HSV-1) infection, the trigeminal ganglion serves as the reservoir for the latent virus.

Q: My boyfriend told me that he's clean and never had genital herpes. How do you know that I don't have herpes type 1 infection?
A: Adolescents learn about HSV-1 and HSV-2 infections in their middle-school health classes. They often label HSV-2 as “the bad kind” of herpes--even though both types can lead to sores on the mouth or genitalia.

HSV-1 infections are often asymptomatic and usually occur in infancy or childhood. A person with a history of oral HSV-1 can shed the virus asymptotically and spread the infection to a partner through kissing or oral sex. However, HSV-1 is not responsible for the great majority of cases of genital herpes. (Details about confirmatory diagnostic testing follow.)

Q: What makes you sure it's herpes? Is there anything else it could be?
A: As with most sexually transmitted diseases (STDs), the history and clinical examination results provide the bulk of diagnostic clues. Primary infection with HSV-2 occurs about a week after sexual exposure, although the incubation period can be as long as 7 weeks. The patient will often describe a 1- to 2-day prodromal phase characterized by flu-like symptoms (headache, fever, and malaise) and mild genital sensations of tingling, burning, or pruritus.

An outbreak of painful vesicles in the exposed area follows this phase. In girls, vesicles may develop...
on the thighs, vaginal opening, vaginal canal, and cervix. Boys usually find the vesicles on the penile shaft or glans. If the vesicular inflammation involves the urethra, the patient may present with dysuria. Both males and females can have vesicles and inflammation in the perineum, mouth, and anus—depending on the types of sexual activity in which they have engaged.

Carefully consider other diagnoses in the differential before you give an adolescent a diagnosis with a lifelong tenure. Most of the other possible entities can be effectively ruled out with a careful physical examination.

- The chancre seen in primary syphilis is often solitary and painless.
- In chancroid, the ulcers tend to be larger, irregularly shaped, and deeper than herpetic vesicles.
- Genital warts are generally painless, raised, and fleshy.
- The lesions in molluscum contagiosum are typically firm, dome-shaped, smooth, and umbilicated in the center.
- Behet syndrome can manifest with genital lesions similar to the ones seen in HSV infection, but these are classically accompanied by oral ulcerations and uveitis.

The diagnosis needs to be confirmed once a presumptive clinical diagnosis has been made. The 3 principle diagnostic tools are HSV culture, HSV polymerase chain reaction (PCR) assay, and assays of HSV antibodies.

Culture sensitivity varies, depending on the age and stage of the HSV lesion tested. This method is not as sensitive as the PCR technique--the most sensitive means of isolating the virus. Unlike the PCR, however, cultures can distinguish between HSV type 1 and type 2 infections.

If your patient wants or needs to know which virus infection he has contracted (type 1 or 2), you can order serologic tests to determine the presence of HSV type-specific antibodies several weeks after a primary infection occurs.

**Q:** Is there any way for me to know if this outbreak was caused by my current partner or by my ex?

**A:** There is no test that can accurately "tell" which partner gave the patient HSV infection. That said, however, results of serologic tests for HSV do at least suggest whether the patient has a primary infection or a secondary outbreak. HSV antibodies are not detectable early in a primary infection. But they can be detected several weeks after a primary infection and remain present indefinitely. Therefore, if you test a patient who has had lesions for only a few days and his HSV serology demonstrates anti-HSV antibodies, then he probably had an initial infection at some point in the past. (Thus, the current outbreak indicates a recurrence). Conversely, the absence of these antibodies (with a positive type-specific culture) suggests that the patient has a primary HSV infection.

**Q:** My friend got herpes and had to stay in the hospital. Will that happen to me?

**A:** HSV-2 infection can vary in severity. While most cases present with self-resolving ulcers, the breakdown in the mucosal and skin surfaces can lead to complications. Secondary bacterial infections can lead to localized cellulitis of the anogenital region. Uncircumcised males with lesions over the urethral area can present with urinary retention or phimosis. Vaginal outbreaks can result in labial adhesions and urinary retention. Anorectal HSV infection outbreaks often present with pain, bleeding, discharge, tenesmus, and inability to defecate.

Serious secondary complications involve herpetic involvement of the brain and meninges. Most cases of herpes encephalitis are caused by HSV-1 infection. A significant minority of cases of HSV meningitis and transverse myelitis result from primary infection with HSV-2. Unlike HSV-1 encephalitis, however, complications of HSV-2 infection tend to be nonfatal and infrequently require hospitalization.

**Q:** What's the chance that I will have another outbreak?

**A:** As mentioned, the latent virus that resides in the sensory nerve roots reactivates intermittently. Because patients often do not recognize specific "triggers" for reactivation, advise them to be aware of potential contributing factors. Trauma (eg, from sexual intercourse), stress, or fatigue can lead to an outbreak. Physiologic stresses, such as fever and infection, occasionally reactivate the latent virus.

A prospective study revealed that almost 90% of patients have at least one recurrence during the first year following the primary infection--and that 38% of these patients have 6 or more recurrences during that year. That same study also demonstrated that while males tend to have higher recurrence rates than do females, the outbreak severity in females tends to be worse. Genital infections with HSV-2 have more reactivations than do HSV-1 genital infections. Primary outbreak
severity (defined as an outbreak that lasts longer than 35 days) correlated with an increased frequency of recurrences. These statistics may be disheartening to an adolescent with newly diagnosed disease. The "good" news is that the number of outbreaks decreases over time. Patients with recurrences often benefit from antiviral medications. Bear in mind, however, that taking antiviral medications during the initial infection or an outbreak does not modulate the recurrence risk.

Q: My first outbreak was miserable. If I get a recurrence, do you think it will be as bad?
A: Recurrent episodes are usually less severe than the primary outbreak (ie, the duration is shorter and the number and size of lesions are smaller). The lesions are often unilateral—similar to what one might expect in shingles. In recurrent outbreaks, lower amounts of virus are shed and the patient is contagious for about 3 days. Patients tend to have minimal systemic symptoms and can usually recognize the prodromal signs and symptoms before lesion eruption. This is often an important cue to initiate antiviral treatment (described later), which will further minimize the intensity of the outbreak.

Q: What is the chance that the herpes can spread from my penis/vagina to other parts of my body?
A: In an otherwise immunocompetent person, disseminated outbreaks are very rare. Theoretically, if a person touches an active herpetic lesion with a finger and then places that finger on another vulnerable body part (eg, mouth, eyes, etc), the infection could be spread. Fortunately, the body's anti-HSV antibodies minimize the possibility of such an occurrence. If the self-inoculation occurs before the body mounts an antibody response, however, transmission could still occur. This holds true for both HSV-1 and HSV-2 infections.

Q: Can I give my partner herpes if we don't have intercourse?
A: A person with genital herpes (both HSV types 1 and 2) can transmit the infection through oral or anal sexual contact. For example, a person with active HSV-1 mouth lesions who performs fellatio on another person can readily spread the virus to their partner's genitalia (and vice versa). Conversely, a partner with HSV-2 lesions on his penis could give his oral sex partner an infection on the lips or oropharynx.

Many teenagers mistakenly believe that avoiding sexual intercourse is equivalent to "safe sex." This gravity of this misperception cannot be overemphasized. While it may minimize the risk of pregnancy, it can readily lead to the spread of herpes (as well as many other STDs). When counseling your adolescent patient about sexual risk reduction (regardless of whether the patient has a known diagnosis of HSV), be sure to inquire about sexual practices other than intercourse and address that patient's specific sexual behaviors.

Q: I heard that condoms don't protect you against herpes. Is that true?
A: Aside from total sexual abstinence, correct use of a condom is the most effective way to prevent the spread of STDs. Unfortunately, this statement needs to be somewhat qualified when it comes to HSV infections and genital wart infections. In these infections, the condom only effectively protects the areas that it covers. For example, if herpes lesions are present along the penile shaft, then a condom will reduce the likelihood of spreading the infection to a partner. However, condoms do not cover the scrotum, thighs, or perineal area. Thus, if the male partner has a herpetic outbreak on the scrotum (or at the base of the penile shaft not covered by the condom) and the area comes into contact with a female's labia majora or thighs, the virus will be transmitted to those areas.

To some extent, this concept presents a dilemma for physicians who work with adolescents. Older adolescents and adults understand the fundamental limitations of a condom's effectiveness, but adolescents often think in concrete "black-and-white" terms (ie, "condoms either work or they don't . . . period"). If the labeling on the condom box implies that the product will not be effective, many younger to middle adolescents may react by not wearing the condoms at all. A few extra minutes spent with these adolescents to clarify this discrepancy can make a huge impact on managing their sexual health and safety.

Q: My friend told me that if you have herpes, you are only contagious when you see the blisters. So, if I look "clean," I shouldn't need to use protection . . . right?
A: A person is obviously contagious during a prodrome or an active outbreak. But asymptomatic shedding is one of the most difficult concepts for an adolescent to grasp. A recent study employing daily PCR analysis of skin swabs revealed that a newly infected person can shed HSV-2 virus up to 40% of the time--regardless of the presence of prodromal symptoms or active lesions. Emphasize to your adolescent patients that they can potentially infect another person--even when
no prodromal or active symptoms are present. Condoms must therefore be used consistently. Also discuss the role of antivirals (discussed later) as an effective way to decrease infectivity in a sexually active teenager.

**Q:** If my partner and I are both infected with HSV-2, does that mean we don't need to use protection?

**A:** The answer to this question presents an ethical dilemma. Ample evidence suggests that existing HSV antibodies (of both types 1 and 2) offer some protection against reinfection (or even infection with the other herpes type). That said, adolescents need to understand the importance of protecting themselves from other infections--especially hepatitis B and HIV. Even micro-ulcerations in the skin function as a breach in the body’s prime defenses against HIV. Current data suggest that a person with HSV infection is twice as likely to contract HIV infection if he or she is exposed to the virus.³

**Q:** Is herpes treatable?

**A:** Medications such as acyclovir, famciclovir and valacyclovir do not eradicate the herpes virus--but they are extremely effective in treating both primary and recurrent outbreaks (Table). In primary outbreaks, these antiviral agents decrease local pain, time to lesion crusting, viral shedding, and constitutional symptoms. These medications do not attenuate the risk of future recurrences, however.

<table>
<thead>
<tr>
<th>Table – Recommended treatment regimens for HSV type 2 genital infections</th>
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<tr>
<td><strong>First clinical episode</strong></td>
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<tr>
<td>Acyclovir (400 mg PO tid 7 - 10 days)</td>
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<tr>
<td>or Acyclovir (200 mg PO 5 times a day for 7 - 10 days)</td>
</tr>
<tr>
<td>or Famciclovir (250 mg PO tid for 7 - 10 days)</td>
</tr>
<tr>
<td>or Valacyclovir (1 g PO bid for 7 - 10 days)</td>
</tr>
<tr>
<td><strong>Episodic therapy</strong></td>
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<tr>
<td>Acyclovir (400 mg PO tid 5 days)</td>
</tr>
<tr>
<td>or Acyclovir (200 mg PO 5 times a day for 5 days)</td>
</tr>
<tr>
<td>or Acyclovir (800 mg PO bid for 5 days)</td>
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<tr>
<td>or Famciclovir (125 mg PO tid for 5 days)</td>
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<tr>
<td>or Valacyclovir (500 mg PO bid for 3 - 5 days)</td>
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<td>or Valacyclovir (1 g PO qd for 5 days)</td>
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<td><strong>Suppressive therapy for recurrent genital herpes</strong></td>
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<tr>
<td>Acyclovir (400 mg PO bid)</td>
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<td>or Famciclovir (250 mg PO bid)</td>
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<td>or Valacyclovir (500 mg PO qd)</td>
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In recurrent outbreaks, antiviral medications also reduce the symptoms and infectivity. They tend to be most effective when started during a prodromal stage or within a day of the outbreak. Patients with recurrent outbreaks need a filled prescription available at all times to ensure that treatment initiation is not delayed past the time of maximal response. In addition, sitz baths, loose-fitting clothing, and analgesia may be employed as adjunctive therapies. Local outbreaks may occasionally require hospitalization when the lesions are complicated by secondary infections, urinary retention, or dissemination. Topical treatments do not adequately treat genital herpes infections. These agents should not be employed as a treatment modality.

**Q:** Can't anything be done to prevent the outbreaks?

**A:** In patients with multiple yearly recurrences, acyclovir, famciclovir, and valacyclovir decrease the
frequency of outbreaks as well as the degree of viral shedding. Taken daily, the medications are effective and antiviral resistance patterns are rarely seen.

Remind your patient that these treatments ameliorate the disease's course, but that future outbreaks are possible even if the virus has been silent for years. Condom use is still essential to reduce the risk of disease transmission to new partners.

**PARTING COMMENTS**

As I mentioned last month, sexually transmitted infections tend to travel in groups. If my patient has newly diagnosed HSV-2 infection, I often screen for chlamydial and HIV infection, as well as for gonorrhea and syphilis. If pain or swelling precludes a pelvic examination, these screens can be performed at a follow-up visit.

**References: REFERENCES:**


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