



Genital Herpes in Adolescents

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Herpes simplex virus (HSV) infections occur commonly among adolescents. Most HSV-2 infections are genital, but genital herpes can be caused by either HSV-1 or HSV-2. Weighted means were calculated based on published seroprevalence data on adolescents from the United States and found HSV-1 rates of 53.1 percent for adolescent males and 49.4 percent for adolescent females. The weighted means for HSV-2 was 15 percent for adolescent females and 12 percent for adolescent males. Most individuals who are infected with HSV-2 are unaware of their infection. Healthcare providers of adolescents should consider genital herpes even when an adolescent presents with nonspecific genital symptoms. In this article, we review current recommendations for diagnosis and management and review the psychological sequelae that can be associated with having genital herpes. Finally, we discuss biomedical interventions that are being developed to help reduce the epidemic of HSV and the challenges that these interventions face with regard to implementation.

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Genital herpes may present many clinical challenges for healthcare providers. During the period of adolescence, many individuals begin to engage in sexual behaviors. In fact, 61 percent of twelfth graders have had sexual intercourse at least once,¹ thus possibly placing them at risk for sexual transmission of herpes simplex virus (HSV) type 1 or 2, the viruses associated with genital herpes. Seroprevalence studies demonstrate that adolescents can become infected with HSV-2 early in adolescence, before reaching 13 years of age.² The potential consequences of genital herpes go beyond the immediate physical and psychological impact and the possibility of transmission to a sexual partner. Those adolescents who are infected with HSV type 2 (HSV-2) infection may be at greater risk for transmission and acquisition of human immunodeficiency virus (HIV).³ Furthermore, pregnant adolescents infected with genital HSV (particularly those with a primary infection) can transmit infection to the neonate, which can lead to serious complications for the neonate, such as neurologic problems and even death.⁴⁻⁶ Hence, healthcare providers need to be able to make an accurate diagnosis and provide appropriate treatment and counseling so that further morbidity and mortality can be avoided.

In this article, we review the literature on the seroprevalence, incidence rates, and risk factors of HSV-1 and HSV-2 among adolescents and on the physical presentation and psychological sequelae of genital herpes. We then suggest developmental-specific strategies for assessment and treatment of genital HSV infection in adolescents and provide information regarding biomedical interventions for the prevention of HSV.

Prevalence of HSV-1 and HSV-2 Infections among Adolescents

The seroprevalence of HSV-1 and HSV-2 among adolescents has been estimated both from samples of adolescents and from samples with wider age ranges (eg, 15 to 40+). Fortunately, several of these latter studies provide the HSV-1 and HSV-2 seroprevalence rates within specified adolescent age ranges. Both types of studies are reviewed for the purpose of this article.

Seroprevalence of HSV-1

Table 1 presents the data on adolescents from HSV-1 seroprevalence studies conducted within the United States. Weighted means from these data suggest that 53.1 percent of adolescent females and 49.4 percent of adolescent males are seropositive for HSV-1. Rates of HSV-1 seroprevalence outside the United States vary depending on the country. The lowest reported rates are from Spain (39.8% among urban

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Table 1 HSV-1 Adolescent Seroprevalence Data in the United States

Author	Sample/Setting	Age Range (yrs)	Seroprevalence (by Gender)	
			Females	Males
Xu, 2002 ²²	NHANES III	12-19	753/1325	609/1071
Rosenthal, 1997 ²	Teen clinics (positive STD tests) and job corps site (Ohio)	12-22	164/265	74/134
Stanberry, 2004 ¹³	Teen clinics (Ohio)	12-16	77/174	
Sucato, 2001 ¹²	Urban STD and community clinics (Washington)	14-19	112/243	73/138
Breinig, 1990 ²⁸	Family planning clinics (Pennsylvania)	17-20	747/1435	
Gibson, 1990 ¹¹	University (Southeast US)	18-23	251/517	174/540

Weighted average for HSV-1 seroprevalence is 2104/3959, or 53.1% for adolescent females.

Weighted average for HSV-1 seroprevalence is 930/1883, or 49.4% for adolescent males.
STD, sexually transmitted diseases.

and 52.5% among rural adolescents)⁷ and Sweden (34% among adolescent patients from an allergy clinic and 41% among upper secondary school students),^{8,9} and the highest rate (94.9%) is from rural Uganda.¹⁰

HSV-1 rates appear to differ in relation to demographic characteristics and sexual history. Research indicates that adolescents from blue-collar families tend to have higher HSV-1 seroprevalence rates than those of adolescents from families with higher level occupations.¹¹ In some studies, being of black race^{11,12} was predictive of HSV-1 seropositive status, whereas in other studies it was not.^{2,13} An effect of gender (ie, females had higher rates of HSV-1 compared with males)¹¹ also was found in one study but not others.^{2,12} The conflicting results could be attributed to a number of factors, such as differences in the type of sample (eg, university students versus patients at a clinic for sexually transmitted diseases [STDs]) and geographical location of the sample (eg, Southeast versus Midwest). In addition to demographic factors, early age of first sexual intercourse, length of time sexually active, and a previous STD history have been associated with increased rates of HSV-1 in adolescents.^{8,11}

Seroprevalence of HSV-2

The seroprevalence of HSV-2 may be rising. Within the United States between the late 1970s and early 1990s, a 30 percent increase was documented among individuals age 12 years and older. Among 12- to 19-year-old teens, the increase was much more noticeable in white teens than in black teens, increasing from 0.96 to 4.5 percent. According to the National Health and Nutrition Examination Survey III (NHANES III) data, 5.6 percent of individuals who were 12 to 19 years of age tested positive for HSV-2.¹⁴

Table 2 depicts adolescent data from other HSV-2 seroprevalence studies conducted in the United States, many of which collected their samples from selected clinic and older adolescent populations. We chose to include only those studies that provided seroprevalence data broken down by gender because of the differences in HSV-2 seroprevalence across genders.^{2,12,15-17} When we calculated weighted means from these data, we found the overall HSV-2 seroprevalence to be 15 percent for adolescent females and 12 percent for adolescent males.

HSV-2 seroprevalence studies have been conducted in

Table 2 HSV-2 Adolescent Seroprevalence Data in the United States

Author	Sample/Setting	Mean Age/Age Range (yrs)	Seroprevalence (by Gender)	
			Females	Males
Rosenthal, 1997 ²	Teen clinics (positive STD tests) and Job corps site (Ohio)	12-22	36/237	10/129
Stanberry, 2004 ¹³	Teen clinics (Ohio)	12-16	24/127	
Sucato, 2001 ¹²	Urban STD and community clinics (Washington)	14-19	41/243	6/138
Breinig, 1990 ²⁸	Family planning clinics (Pennsylvania)	17-20	143/1435	
Crosby, 2003 ²⁰	Pregnant teens (Southeast US)	17.8 (SD = 1.6)	27/127	
Cook, 2002 ¹⁶	Teen alcohol project (Pennsylvania)	14-21	18/120	0/120
Huerta, 1996 ⁶²	Juvenile detention health clinic (California)	13-18	8/41	14/94
Noell et al. ¹⁷	Homeless adolescents (Northwest US)	Females = 13-20 Males = 14-20	25/217	17/319
Gibson, 1990 ¹¹	University (Southeast US)	18-19	94/306	84/318
Lewis, 1999 ²¹	College (Ohio)	18-25	29/96	

Seroprevalence is 445/2949, or 15% overall, for HSV-2 in adolescent females.

Seroprevalence is 131/1118, or 12% overall for HSV-2 in adolescent males.

STDs, sexually transmitted diseases.

SD, standard deviation.

other North American countries and European countries. Among a randomized selection of students from Mexico, the HSV-2 seroprevalence was 5.7 percent.¹⁵ In Sweden, only 1 percent of female health care students from an upper secondary school tested positive for HSV-2⁸ and in Spain, 5 percent of students, ages 14 to 17 years, were seropositive for HSV-2.⁷ Among blood samples from persons in England and Wales, age 16 to 19, 2 percent of males and 3 percent of females were HSV-2 seropositive.¹⁸ In contrast, rates in Africa are quite high. For example, the seroprevalence of HSV-2 in Uganda was 34 percent among 15- to 19-year-olds.¹⁰

Many studies have found variables of both demographic and sexual history related to the presence of infection with HSV-2. As mentioned above, female adolescents are more likely than are male adolescents to be infected with HSV-2.^{2,12,15-17} HSV-2 seroprevalence rates are higher among black than white adolescents.^{2,11,12,19} The overall seroprevalence in a population obviously increases with age, but very young adolescents can be infected.² In fact, in one study, younger age was associated with an increased likelihood of acquiring HSV-2 infection.¹⁵ Sexual history variables which have been associated with HSV-2 infection include an early age of first intercourse, higher number of lifetime partners, infrequent use of condoms, history of a sexually transmitted disease, homosexual intercourse, and commercial sex work.^{2,11,15,19-21} In some populations, however, having even one lifetime partner could place a person at high risk for acquiring HSV-2 infection. In populations in which the prevalence of HSV-2 in the partner pool is high, sexual behaviors may be less relevant.^{15,21}

Adolescents/young adults with a history of alcohol¹⁶ or cocaine use¹⁹ have higher rates of HSV-2 infection, perhaps because adolescents who engage in substance use also engage in other risk behaviors (problem behavior syndrome) or because substance use diminishes judgment, leading to the engagement of high-risk sexual behaviors. Most of the research studies in this area are designed only to establish correlation between substance abuse and sexual behaviors, not causality. Regardless of whether the relationship is causal or correlational, adolescents engaging in any high-risk behaviors should be considered at risk for herpes infections and counseled accordingly.

Incidence of HSV-1 and HSV-2 among Adolescents

The incidence of HSV infections in adolescents is somewhat difficult to determine given that many infections are asymptomatic or go unrecognized.^{12,22-24} Data on attack rates or incidence of HSV-1 in adolescents are limited. A recent study examining an urban adolescent female population followed over the course of 3 years found an HSV-1 attack rate of 3.2 per 100 person-years.¹³ In another study conducted in Sweden over the course of a 2-year period, 5 percent of the girls (age range 15 to 17 years at the start of the study), regardless of sexual experience, seroconverted to HSV-1.⁸ These new infections could be either genital or oral HSV-1.

With regard to HSV-2, researchers have established attack

rates and incidence in different populations studied over the course of different lengths of time. In the same cohort of urban adolescent girls mentioned above, the attack rate of HSV-2 infection among the sexually experienced girls was 4.4 per 100 person-years.¹³ In Sweden, the yearly incidence rate of HSV-2 in a prospective evaluation was 5 per 1000 in females aged 13 to 18 years and 24 per 1000 in females aged 17 to 22 years.²⁵ In a second study conducted in Sweden over the course of a 2-year period, 1 percent of sexually experienced female adolescents (age range 15 to 17 years at start of study) seroconverted to HSV-2.⁸ Using mathematical modeling, the incidence rate of HSV-2 infection in the United States, based on the Second National Health and Nutrition Examination Survey (NHANES II) and the Third National Health and Nutrition Examination Survey (NHANES III), was calculated to be increasing between 1970 to 1985.²⁶ For example, the estimates for males (aged 12 to 19 years) increased from 4.2 per 1000 before 1970 to 7.7 per 1000 in 1985 and for females (aged 12 to 19 years) 7.9 per 1000 in 1970 to 13.8 per 1000 in 1985.²⁶ Two studies estimated the incidence for individuals from other countries. The first, from Uganda, found an incident rate of 16.7 per 1000, based on a combined adolescent and adult sample.¹⁰ The second study, which included pregnant adolescents and adults, found an incidence rate of 2.4 per 1000 Asian women from an Indian subcontinent and from Africa, 5 per 1000 white women from the British Isles, and 20 per 1000 black women from Africa, the British Isles, and the Caribbean.²⁷

Preexisting HSV-1 results in a decreased likelihood of being symptomatic with HSV-2 infection^{18,22,28,29} and may well provide a protective effect against incident HSV-2 infection. Several studies have found that individuals, especially females, infected with HSV-1 are less likely to get infected with HSV-2.^{13,24,28,30} However, some studies have found no reduced rate of infection of HSV-2 in persons infected with HSV-1.^{22,29,31} The studies that have found a protective effect of HSV-1 on HSV-2 infection have either conducted the analyses with female-only populations or controlled for gender in the analyses. In two of the studies that did not find a relationship,^{22,29} gender-specific effects of HSV-1 on HSV-2 were not evaluated. Therefore, HSV-1 possibly provides a protective effect for HSV-2 in females but not males. Brown and co-workers³¹ may not have found a protective effect of HSV-1 on HSV-2 in their sample of pregnant women because of possible immune factors that come into play during pregnancy. In summary, future studies will need to take into account some of these potential mediating factors (eg, gender, pregnancy, location of HSV-1 infection) when designing studies so that the relationship between HSV-1 and HSV-2 can be clarified.

Clinical Presentation of Genital Herpes

Most individuals with antibodies to HSV are not aware of their status.^{12,20,22} Some of these individuals have had symptoms that they have not recognized as being those of genital herpes (ie, nonspecific genitourinary tract symptoms, such as

itching), and other individuals are truly asymptomatic. In an adult study, asymptomatic female patients were counseled to recognize symptoms. The results indicated that subsequent to the intervention, 50 percent of the women reported symptoms of genital herpes, suggesting that they could be taught to recognize symptoms.²⁹ Whether adolescents can be taught to recognize symptoms is unclear. Adolescents possibly have more difficulty recognizing genital symptoms, because they may be less experienced and less comfortable with their developing bodies, specifically their genital areas.

Among individuals with genital herpes symptoms, no evidence has shown that the symptoms present differently in adolescents than in adults. Individuals experiencing their first episode of genital herpes may have systemic symptoms, such as fever and headache, as well as genitourinary symptoms, such as painful ulcerations or blisters, itching, and dysuria. Systemic symptoms present early, followed by lesions, which form over the course of the first week of illness and typically resolve in the next week or two.³²

Many, but not all, patients with genital herpes experience recurrences,³³ but fortunately recurrences tend to decrease in frequency over time.³⁴ Genital lesions may vary in number (ie, 1 to 20) and may last an average of 6 to 10 days. Symptoms tend to be milder, with fewer lesions, than at the first episode.³² Why some patients have recurrences but others do not is not known, but research has identified some potential contributing factors. For instance, individuals infected with genital HSV-2 appear to be more likely than individuals with genital HSV-1 to experience recurrences.^{32,33} Men tend to experience more recurrences than do women (ie, median of 5 versus 4),³³ but women tend to have more painful recurrences than those of men.³² Recurrences tend to occur more frequently when acquisition of genital herpes occurs at a younger age.³⁴ Finally, recurrences may occur more frequently in patients who experienced prolonged primary infections.³² Hypothesized triggers of recurrences may include radiation or exposure to sun, skin irritation, surgical trauma, and psychological stress.³⁵

Studies on HSV transmission/viral shedding have been conducted with adult populations but, to our knowledge, have not been performed with adolescent populations. According to the adult literature, viral shedding takes place over the course of approximately 12 days during first episodes and approximately 4 days during untreated recurrences. Viral shedding can occur in the absence of symptoms, and thus, transmission of HSV also can occur in the absence of symptoms.³²

Psychological Impact of Genital Herpes

The potential psychological impact of receiving a diagnosis of genital herpes frequently is discussed; however, little is known about how adolescents will respond over the course of time and which adolescents will adjust well and which will do poorly. Studies with adults have shown that some experience anxiety, depression, anger, and lowered self-es-

teem,^{36,37} but certainly many individuals adjust after accepting the initial diagnosis. The adolescent's previous level of psychosexual or psychological functioning may be critical,³⁸ as may the strategies he or she uses to cope with the diagnosis. One strategy used commonly by adolescents to cope with acquisition of an STD is wishful thinking.³⁹ Within the adult literature, this method of coping and self-blame in response to receiving a diagnosis of genital herpes is associated with psychological maladjustment.⁴⁰

Diagnosis and Treatment of Genital Herpes

When an adolescent presents with genital symptoms, a complete sexual history should be obtained and appropriate laboratory tests should be performed. Healthcare providers should ask the adolescent direct questions about his/her specific sexual behaviors (eg, kissing, masturbation with partners, oral sex, vaginal intercourse, anal sex, sexual behaviors with the same sex) in a nonjudgmental, accepting manner. Regardless of whether the symptoms are typical or atypical for genital herpes, the current recommendation is that laboratory evaluation, such as culture or polymerase chain reaction, be performed, rather than relying on clinical impression alone.⁴¹

Type-specific serological testing may help distinguish whether the symptoms result from HSV-2 or HSV-1. Transmission occurs through either genital-genital or oral-genital contact. In the United States, the more common cause of first-episode genital herpes is HSV-2, whereas in some European countries, the more common cause is HSV-1.⁴² For instance, in two studies of patients with STDs in Seattle, approximately 20 percent of first-episode genital herpes cases were caused by HSV-1,^{34,43} whereas in Sweden, almost half of first-episode genital herpes cases resulted from HSV-1.⁴⁴ However, because recurrences are more common with HSV-2 than HSV-1,^{34,43} most genital herpes cases are caused by HSV-2. Why differences exist across countries with regard to first-episode disease is unclear, but some researchers have suggested that the difference can be attributed to the varying sexual practices or differing rates of childhood-acquired HSV-1.^{42,45}

Before testing an adolescent for HSV, the healthcare provider should ask the adolescent what he/she might think and feel about having a positive diagnosis for genital herpes. This feedback provides the healthcare provider information about how prepared the adolescent is to hear that he/she has genital herpes. If the HSV test is negative, counseling about safe-sex behaviors still should be discussed.⁴⁶ If a genital herpes diagnosis is confirmed, the provider will need to provide further education and counseling as well as treatment. Because information given at the first visit will be forgotten as the adolescent absorbs the initial diagnosis, additional counseling should be provided during subsequent multiple visits.

When addressing the adolescent's needs, one should remember that not all adolescents have the ability to think abstractly and that they vary considerably in their sexual

experience. Therefore, healthcare providers may find that providing information in a very basic, concrete manner is helpful. Referrals to adolescent-specific materials, brochures, and web pages also may be useful.⁴⁷

With regard to the content of the education/counseling given after the diagnosis has been established, healthcare providers should educate the adolescent about the course of the disease (eg, recurrent episodes) and the risk of transmission. Decisions about when to use antiviral medications for suppression should be discussed in the context of the adolescent's life. Although the concept of asymptomatic shedding and contagion may be particularly difficult for the adolescent to understand, he or she should be advised of it. As with adults, adolescents may benefit from being given help in deciding how and when to tell partners. They should be encouraged to avoid engaging in sexual activity when lesions and other symptoms are present. Adolescents should be informed that latex condoms, if used consistently and correctly, have been shown to prevent transmission of HSV-2 infection at least in females.^{48,49} Whether to tell parents and friends will be another important discussion. Adolescents have the right to confidential care for STDs in the United States,⁵⁰ but many of them choose to tell their parents and find that their parents are supportive. The healthcare provider can help the adolescent make a decision about what is right for him or her. For those adolescents who choose not to tell their parents, the provider can help make sure that confidentiality is protected throughout the treatment process (eg, where to keep medication so that parents do not find it). Screening for other STD infections should be offered. At a later visit, the provider should discuss with the adolescent the link between HIV and HSV.^{47,49}

Antiviral treatment can be offered for abortive therapy (ie, providing therapy when prodromal symptoms first develop) or prophylactic therapy (ie, suppressive therapy to help reduce recurrences, viral shedding, and transmission). The recommended antiviral therapy for first-episode genital herpes is acyclovir (400 mg orally 3 times a day for 7 to 10 days or 200 mg orally 5 times a day for 7 to 10 days), famciclovir (250 mg orally 3 times a day for 7 to 10 days) or valacyclovir (1 g orally 2 times a day for 7 to 10 days). One advantage of the valacyclovir is that it needs to be taken only twice a day and, as such, the adolescent does not have to take it during school hours. Episodic therapy should be given within 24 hours of onset of symptoms (ie, lesions or prodromal symptoms). The recommended regimens for episodic therapy are acyclovir (400 mg orally 3 times a day for 5 days or 200 mg orally, 200 mg orally 5 times a day for 5 days), famciclovir (125 mg orally 2 times a day for 5 days), or valacyclovir (500 mg orally 2 times a day for 3 to 5 days or 1 g a day for 5 days). Suppressing therapy recommended regimens are acyclovir (400 mg orally twice a day), famciclovir (250 mg orally 2 times a day), or valacyclovir (500 mg orally 1 time a day or 1 g orally 1 time a day).⁴⁹ In addition to antiviral treatment, other helpful strategies to reduce pain and discomfort, such as taking analgesics, using topical anesthetics, and wearing loose clothing, should be suggested.⁴⁷

The Future: Serological Screening and Vaccines

Many individuals mistakenly believe that screening for herpes is included in their STD evaluations.⁵¹ However, only recently have routine serological screening tests become commercially available. At the present time, universal screening is not recommended. According to recent guidelines, HSV-2 screening should be offered to individuals who present with another STD or HIV or who have an HSV-2-infected partner. In those cases, no reason exists to exclude adolescents from screening.⁴⁶

The benefits of screening include the identification of individuals with asymptomatic infections who then could be treated or counseled to reduce transmission.^{52,53} The disadvantages include the costs involved in screening, the risk of false-positive results in populations with a low prevalence, and concerns that it will cause undo psychosocial distress. Although individuals who screen positive experience a variety of emotional responses, such as surprise, sadness, and relief, and may have concerns about transmission to others,⁵⁴ research has found that asymptomatic individuals with positive screening tests do not show adverse psychological effects over the course of 3- and 6-month periods.⁵⁵

Whether an adolescent can use the information from a positive serological test to reduce their risk of transmitting HSV to others or of acquiring HIV is unclear. In other words, will an asymptomatic adolescent use condoms consistently if he/she is not already doing so and/or willing to take antiviral medication for suppression?⁵⁶ Further research is needed to answer these questions.

Another prevention option, which is likely to be available in the future, is vaccines.⁵⁷ Vaccines are in phase III clinical trials, and evidence indicates that parents and adolescents/young adults will be accepting of vaccines for STDs.⁵⁸⁻⁶⁰ This topic is covered in more detail in the article in this issue by Rupp and colleagues.⁶¹

Conclusion

The diagnosis of a genital HSV infection in an adolescent can present a significant challenge for the adolescent and his/her healthcare provider. It requires sensitively managing sexuality, addressing needs for confidentiality, and providing guidance regarding symptomatic relief of what can be an extremely painful but very private disease. In addition, it requires the adolescent to consider making behavioral changes (consistent condom use) for a disease that they cannot see and would prefer to forget they have acquired. It is a lifelong infection, which may require disclosure to individuals (ie, partners) whose opinion of the adolescent may matter greatly to them. Thus, it is incumbent on the healthcare provider to be knowledgeable about the disease prevalence and current diagnostic and treatment guidelines, to be comfortable discussing sexuality with adolescents (and their parents), and to have and take the time to anticipate and address the adolescent's concerns. However, with appropriate man-

agement, genital herpes is a manageable disease, with which most individuals cope quite well. As future tools for prevention (eg, serological screening, antiviral treatment, and vaccines) become available or are better understood, it will be incumbent on professionals to evaluate their specific use in an adolescent population.

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