

The Editor's Workshop

Genital Herpes and the Teen Female

Karin Batalden, MD¹, Corinne Bria, MD¹, and Frank M. Biro, MD^{1,2}

¹Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati Children's Hospital Medical Center; and

²Division of Adolescent Medicine, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA

Introduction

Herpes simplex virus is a common sexually transmitted infection of a chronic nature, with important medical and psychological consequences in the adolescent and adult populations. Recent National Health and Nutrition Examination Survey (NHANES) data estimate overall US population seroprevalence at 17.0%, with rapid increase in prevalence from 1.6% in persons aged 14 to 19 years to 10.6% of persons aged 20 to 29.¹ The attack rate for adolescent females is 4.4 cases per 100 person years among those who are sexually active.² Of note, attack rates are higher among adolescent females who did not have pre-existing antibodies to HSV1 than in those who did have HSV1 antibodies (6.6 v 2.3 cases per 100 person years, $p = 0.0002$).²

Initial infection can be extensive, lasting two to six weeks, and the median number of recurrences after initial infection is four per year, with wide interpatient variability.³ Most patients will tend to have fewer clinical recurrences the longer the time elapsed since diagnosis, but will continue to shed virus indefinitely. Of interest, 16.2% of people with HSV2 antibody, but lacking HSV1 antibody, had a history of genital herpes, as contrasted to 5.9% of those who had both HSV1 and HSV2 antibody, suggesting those without HSV1 antibody were more likely to have experienced symptoms of genital herpes.⁴ Although the 2006 Treatment Guidelines suggest evaluating type-specific serology for those who request serologic testing,⁵ the lower prevalence of HSV-2 in adolescents 19 or younger would lead to a suboptimal positive predictive value in those without symptoms. This is because of the lower prevalence of HSV-2 among adolescents (0.9–5.0%, depending on gender, race, and ethnicity),¹ and the specificity of currently available type-

specific serology is 96–97%. If one assumes prevalence of 1.6% (the seroprevalence noted in adolescents 14–19 year of age in the NHANES data generated 1999–2004), and specificity of 97%, the positive predictive value as a screening test is only 35% ($1.6 / (1.6 + 3)$). However, if the adolescent patient has a previous history of genital ulcers, the pre-test probability is much greater than 1.6%, and type-specific serology may be useful as a confirmatory test.

Pregnant women with genital herpes pose an additional clinical problem, that of vertical transmission to their infant. Of note, the vast majority of infants who develop neonatal HSV will acquire the transmitted virus near delivery, and the majority of transmission occurs in mothers who are asymptomatic.⁶

In newly diagnosed patients, a diagnosis of HSV is associated with psychological distress,⁷ and in patients who continue to have symptomatic recurrences, anxiety remains elevated.⁷ A French study noted that those with genital herpes reported that herpes interfered with sexual relationships, and when compared to controls, they had a lower health quality of life and utilized significantly more health care resources.⁸

Treatment

Since the advent of acyclovir treatment of HSV infection, there have been many advances in treatment strategies. Current opinions exist as to whom to treat, when to treat, how long to treat, and how to treat. There is fairly uniform consensus that the first episode of genital herpes warrants treatment (see Table 1).

Controversy arises over further HSV treatment. Because most patients will experience a recurrence, and because most patients are responsive to antiviral therapy, a major decision is whether to treat symptomatically at the onset of recurrence or whether to offer suppressive therapy to prevent recurrence. The 2006 Centers for Disease Control and Prevention STD Treatment Guidelines highlight the need to discuss

Address correspondence to: Frank M. Biro, MD, Division of Adolescent Medicine, Cincinnati Children's Hospital Medical Center, 3333 Burnet Avenue (ML-4000), Cincinnati, OH 45229-3039; E-mail: frank.biro@cchmc.org

Table 1. Recommended Treatment Regimens for Initial Episode of Genital Herpes⁵

Acyclovir	400 mg PO TID	7–10 days*
Acyclovir	200 mg PO five times daily	7–10 days*
Famciclovir	250 mg PO TID	7–10 days*
Valacyclovir	1 gm PO BID	7–10 days*

*Treatment can be extended if lesions are not healed

treatment options individually with each patient and offer suggested regimens for either suppressive or episodic treatment.⁵

We recommend the consideration of suppressive therapy from the time of initial diagnosis, based on data that most individuals will experience multiple recurrences. Suppressive therapy has psychological benefits particularly valuable among adolescents, such as decreasing recurrences, decreasing risk of transmission, and allowing individuals time to adjust to the diagnosis.^{9,10} Use of suppressive antiviral medication can reduce overall outbreaks by 70–80%,^{11,12} and once-daily acyclovir has been shown to decrease transmission to seronegative partners, as well as decrease HSV detected in secretions.⁹ In a double-blind, placebo-controlled study, suppressive therapy was demonstrated to be an effective approach to improve quality of life, which was sustained for the length of the study (12 months).¹³ A recent article, utilizing mathematical models to examine the impact of suppression, noted suppression reduces population incidence of HSV-2; further reduction of new cases through suppressive therapy for a greater proportion of those infected, initiating suppression closer to time of initial infection, and total years of suppression.¹⁴ Studies have shown long-term safety in the use of acyclovir for 10 years in patients for HSV suppression.¹⁵ Valacyclovir and famciclovir have been evaluated in one-year continuous suppressive therapy with excellent safety profiles.^{11,15} These studies have also shown low rates of resistant viral strains in immunocompetent patients taking continuous acyclovir, rates similar to resistance in acyclovir-naïve patients.^{15,16} There are recommended regimes for continuous suppressive therapy (see Table 2).

Episodic therapy, either patient- or provider-initiated, has been shown to decrease intensity and duration of outbreaks when started within one day of lesion onset or during prodrome.^{17–21} Benefits of

Table 2. Recommended Regimens for Continuous Suppressive Therapy⁵

Valacyclovir	500 mg PO daily
Acyclovir	400 mg PO BID
Famciclovir	250 mg PO BID
Valacyclovir	1 gm PO daily

Table 3. Recommended Episodic Therapy Regimens⁵

Acyclovir	400 mg PO TID	5 days
Acyclovir	800 mg PO BID	5 days
Acyclovir	800 mg PO TID	2 days
Famciclovir	125 mg PO BID	5 days
Famciclovir	1 gm PO BID	1 day

episodic therapy include shortened duration of lesions (3 to 5 days), reduced exposure to antiviral medication, and avoiding the need to take daily medication. However, it does not reduce overall number of outbreaks, and requires patients to be both self-aware of symptoms and promptly responsive to prodromal symptoms or outbreaks. Newer studies have established shorter duration of treatment, which may increase patient compliance and satisfaction. See Table 3 for recommended regimes.⁵

There have been several studies as well as a systematic review on antiviral prophylaxis to prevent HSV disease at delivery. A systematic review of studies published between 1966 and 2003 noted that acyclovir prophylaxis, begun at 36 weeks gestation, reduced clinical HSV recurrences at delivery, cesarean deliveries for clinical recurrences of genital herpes, HSV detected at delivery, and asymptomatic HSV shedding at delivery.²² In a randomized clinical trial, women receiving valacyclovir 500 mg bid were less likely to require cesarean delivery because of recurrent genital herpes, and less likely to have HSV detected by culture.²³

Conclusions

Adolescent genital HSV is an important clinical issue. Although older groups have higher prevalence rates, the attack rate is highest in adolescents. Review of published studies support that the clinician discusses suppressive therapy at time of initial diagnosis, in order to reduce recurrences, minimize psychological sequelae, and minimize transmission to subsequent partners. Unless the adolescent patient has a history of genital ulcers, use of type-specific serologic tests have lower clinical utility because the prevalence is lower than the specificity of the approved type-specific tests. Data also support the initiation of suppressive therapy at 36 weeks gestation for women with history of genital herpes.

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