Herpes Viral Shedding Goes Beyond 10 Years

BY MIRIAM E. TUCKER
Senior Writer

WASHINGTON — High rates of both overall and subclinical viral shedding continue even beyond 10 years among people with genital herpes simplex virus type 2 infection, suggesting that there is a continued risk of transmission to sexual partners long after initial infection.

The findings, from a study of 377 healthy adults with a history of symptomatic herpes simplex virus type 2 (HSV-2) infection, have implications for long-term management of transmission and treatment of clinical recurrences, including long-term use of antiviral medications for clinical suppression and condom use to reduce transmission to partners,” Dr. Warren Phipps said at the jointly held annual Interscience Conference on Antimicrobial Agents and Chemotherapy and the annual meeting of the Infectious Diseases Society of America.

Previous studies suggest that rates of HSV-2 shedding during the first year of infection range from 9% to 40% of days sampled using polymerase chain reaction (PCR), and that clinical recurrences are common, with a median of about four outbreaks per year. Subclinical shedding during the first year is estimated to represent about 50% of days of recurrence. Much less is known about the natural history of genital herpes beyond the first year, and the available data conflict as to whether viral shedding decreases with time, noted Dr. Phipps of the University of Washington and the Fred Hutchinson Cancer Research Center, Seattle.

The study population included participants in several prospective observational studies, some of them funded by GlaxoSmithKline, conducted at two clinics from 1992 to 2008. Subjects collected swabs on at least 30 consecu-
tive days from perianal, vulvar, cervical, penile, and/or urethral sites. They also kept symptom diaries in which they recorded the appearance of genital lesions. The swabs were tested for HSV-2 using PCR, with a positive sample defined as greater than or equal to 150 copies/mL of HSV-2 DNA from any site.

The 377 subjects had a mean age of 39 years (range 20-76 years), were 62% female, and were 89% white. The entire group collected swabs in a total of 439 sessions with a mean of 64 days per ses-
sion, for a total of 28,372 swab days. Participants were grouped as having had “less than 1 year,” “1-9 years,” and “10 or more” years” since their initial episode.

Time since initial genital herpes episode was associ-
ated with reductions in both total and subclinical HSV-2 shedding, from 26% of sampled days within 1 year, to 16% at 10 years, and beyond for total shedding, and from 19% to 8% to 4% of sampled days, respectively, for subclinical shedding. The appearance of clinical lesions dropped insignificantly with time, from 11% to 10% to 7% of sampled days for the three groups, respectively. Although shedding was reduced, it is important to note that rates still remained high even beyond 10 years or more from the initial clinical episode,” Dr. Phipps commented.

Race had a significant impact on the change in reac-
tivation rates over time, with nonwhites having much higher rates than whites within the first year (65% vs. 26%) but dropping to a much lower level at 1-9 years (7% vs. 18%) and at 10 or more years (4% vs. 16%). Rates of subclinical shedding also de-
creased to a greater degree with time in blacks vs. whites. Small but significant decreases were seen in HSV-2 DNA copy numbers over time, from 4.8 to 4.6 log10 copies/mL between the less than 1 year and 10 years or greater groups. “It is important to note that al-
though there is no known ‘infectivity threshold,’ it is generally thought that virus is infectious at greater than 3 log10 copies/mL, so these titers remain in presumed infectious range remote from initial infection,” he said.

Duration of any reactivation and subclinical reacti-
vation episodes did not change over time, but the du-
ration of clinical episodes did decrease significantly, from a median of 8.5 days within 1 year, to 5.8 days at 1-9 years, to 5.0 days at 10 years and beyond. Dr. Phipps said that he had no financial disclosures.

Single-Day Famciclovir Found To Match 3-Day Valacyclovir

BY MIRIAM E. TUCKER
Senior Writer

WASHINGTON — Single-day famci-
clovir therapy was similar in safety and efficacy to a 3-day course of valacyclovir in the first head-to-head comparison of the two oral medications for the treat-
ment of recurrent genital herpes.

Previous data showed that, when taken within 6 hours of symptom onset, single-day famciclovir (Famvir, 1,000 mg b.i.d.) increased the proportion of patients with aborted episodes from 13% to 23%, and reduced healing time and duration of symptoms by 2 days, compared with placebo (Clin Infect Dis 2006;42:8-13).

Now, the findings of a multicenter, randomized, double-blind, parallel group study of 751 adults with recurrent geni-
tal herpes suggest that single-day fam-
ciclovir is as safe and effective as 3-day valacy-
clovir (Valtrex, 500 mg b.i.d.), Dr. Stephen Tyring said at the jointly held annual Interscience Conference on Antimicrobial Agents and Chemotherapy and the annual meeting of the Infectious Diseases Society of America.

Patients were at least 18 years of age and had experienced at least 4 outbreaks of lesions on the external genitalia or anogenital area in the preceding 12 months, with positive herpes simplex virus of oral culture in 90% or more of the lesions of a female, and most had used suppressive therapy in the previous 12 months. Of the 1,179 patients who were random-
ized, 751 initiated the study medication within 6 hours of their next recurrence and were included in the analysis. The proportion of patients with abort-
ed lesions in the intent-to-treat popula-
tion was 32.7% among the 370 famci-
clovir patients and 33.6% among the 381 valacyclovir patients. Time to healing of nonaborted lesions was 2.25 days with single-day famciclovir and 4.08 days with 3-day valacyclovir, an insignificant dif-
ference. There were also no differences in time to resolution of burning, pain, tingling, itching, tenderness, or all symp-
toms together, said Dr. Tyring of the Center for Clinical Studies at Texas Med-
cal Center, Houston.

Adverse events were reported in about one-fifth of each group, with drug-relat-
ed events reported in 11% with famci-
clovir and 9% with valacyclovir. Headache was the most common adverse event, re-
sulted in 8% with famciclovir and 4% with valacyclovir. Dr. Tyring receives research funding and is on the speakers bureau for Novar-
tis, manufacturer of Famvir, and Glaxo-
SmithKline, manufacturer of Valtrex.

HSV Shedding Unaffected by Outbreak Frequency, Duration

BY HEIDI SPLETE
Senior Writer

WASHINGTON — People infected with the herpes simplex virus shed virus no matter how long they have been in-
fected or how frequently they have out-
breaks, according to data from adults aged 18 years and older with newly ac-
quired and long-term herpes infections.

Previous studies have suggested that herpes recurrences are more frequent within the first year after infection, and that viral shedding occurs on nearly 40% of days in patients with herpes simplex virus (HSV) infection for 6 months or less, said Clare A. Brennan and Cathy K. Heitman, Ph.D., of the in-
fected diseases medicine development center at GlaxoSmithKline in Research Triangle Park, N.C.

But the current study is the first to show a viral shedding rate on more than 50% of days in patients with new infections, they noted.

To study the natural history of viral shedding in patients with HSV-2, the re-
searchers conducted a post hoc analysis of a placebo group of 69 patients who were part of a larger study that com-
pared valacyclovir, acyclovir, and place-
bo. The group comprised 27 patients who had had HSV-2 for 6 months or less, and 42 patients with HSV-2 for more than 6 months and at least six re-
currences per year. The new-infection group comprised 18 men and 24 women.

The researchers presented their re-
results in a poster session at the jointly held annual Interscience Conference on Antimicrobial Agents and Chemotherapy and the annual meeting of the In-
fected Diseases Society of America.

Overall, the clinical shedding was more than twice as high in patients with newly acquired infections as it was in those with established infec-
tions (31% vs. 14%, respectively).

When the researchers examined sub-
clinical shedding as a function of HSV-
2 duration, the rate of subclinical shed-
ing was 33% in 29 patients diagnosed within a year, 14% in 17 patients in-
fected for 1-5 years, 15% in 9 patients infec-
ted for 6-10 years, and 11% in 13 patients infected for 11 years or longer. (Complete data were not available for one patient.)

Patients with the least number of outbreaks shed virus at the highest rate, the researchers noted. The per-
centage of days with subclinical shed-
ing for those who had 0-3, 4-5, and more than 5 outbreaks within the past 6 months was 24%, 17%, and 16%, re-
spectively.

The results suggest that people with few HSV outbreaks or with long-term infections are not exempt from sub-
clinical shedding and they still can transmit the virus to an uninfected partner, the researchers noted.

The study was sponsored by Glaxo-
SmithKline.