Shedding of HSV-2 Persists 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 longterm 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 (that is, shedding without lesions) during the first year is estimated to represent



& Gilman's The Pharmacological Basis of Therapeutics. 10th ed. New York, NY: McGraw-Hill; 2001;687-731. 3. Emmerson BT. The management of gout. In: Hochberg MC, Silman AJ, Smolen JS, Weinblatt ME, Weisman MH, eds. Rhezmatology. 3rd ed. Edinburgh: Mosby; 2003:1929-1936. ©2008Takeda Pharmaceuticals America, Inc. TXF-00012 Printed in U.S.A. 09/08

about 50% of days of reactivation. Much less is known about the natural history of genital herpes beyond the first year, noted Dr. Phipps of the University of Washington and the Fred Hutchinson Cancer Research Center, Seattle.

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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 consecutive days from perianal, vulvar, cervical, penile, and/or urethral sites. They also kept symptom diaries. The swabs were tested for HSV-2 using PCR.

The 377 subjects had a mean age of 39 years (range 20-76 years); 62% were female and 89% were white. The entire group collected swabs on a total of 28,252 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 associated with reductions in both total and subclinical HSV-2 shedding, from 26% of sampled days within 1 year, to 16% at 1-9 years, to 14% 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.

Nonwhites had much higher reactivation rates than whites within the first year (65% vs. 26%), but rates were much lower at 1-9 years (7% vs. 18%) and at 10 or more years (4% vs. 16%). Rates of subclinical shedding also decreased to a greater degree with time in blacks vs. whites. There were no associations with rates of shedding by gender, sexual orientation, HSV antibody status, age at first sexual contact, or age at first herpes lesion.

Small but significant decreases were seen in HSV-2 DNA copy numbers, from 4.8 to 4.6 log10 copies/mL between the less than 1 year and 10 years or greater groups. "Although 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," Dr. Phipps said.

Duration of any reactivation and subclinical reactivation episodes did not change over time, but the duration of clinical episodes did decrease significantly over time, 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. These data support the notion that a virologic set point may be established in genital herpes infections, with lower rates and copy numbers after the first year of infection, but with ultimately persistent reactivation, he commented.

Dr. Phipps said that he had no financial disclosures.