Herpes simplex virus

Genital HSV-1 infections

A Wald

Importantly, individuals with genital HSV-1 are still at risk of HSV-2 acquisition

In the past decade, investigations have amply documented the increase in the frequency of genital herpes simplex virus type 1 (HSV-1) compared with genital HSV-2 infection. This trend has been seen both in Europe and in the United States, and it is comprehensively documented in New South Wales, Australia, on p 255 of this issue of *STI*.[1] The issues raised by this observation have implications for understanding changes in HSV seroprevalence and sexual behaviour over time, and for patient management and counselling.

What accounts for the rise in the frequency of genital HSV-1? First of all, it needs to be acknowledged that genital HSV-1 infection has been common for a long time. For example, a Japanese study of women, published in 1976, documented 43% of genital herpes as caused by HSV-1.[2] In 1977, a university health clinic study showed that 37% of women with clinical diagnosis of genital herpes had HSV-1 isolated.[3] Among people with newly acquired genital herpes in Seattle in the mid to late 1980s, 32% had genital HSV-1 infection.[4] Still, several well done studies have shown that the relative proportion of genital HSV-1 isolates has increased even more strikingly in the past two decades.[5–7] Two potential explanations that have been put forth include a decrease in HSV-1 acquisition among children, leaving them susceptible to HSV-1 in adolescence, and increase in oral-genital contact, or initiation of oral sex instead of genital-genital sex, among adolescents. Population based studies, although few have looked at secular trends in HSV-1 infection, do not suggest a prominent decrease in HSV-1 seroprevalence.[8]

Is oral sex more prevalent now than it was about 30 years ago? It seems unlikely that this practice has been invented by current youth, as occasionally portrayed by the news media, since ancient texts, including the *Kama Sutra* written between the 1st and 6th century AD, describe it. However, the concern about pregnancy among adolescents and about HIV among men who have sex with men may have tipped the balance in favour of this behaviour. In a peculiar way, abstinence proponents may have helped, as adolescents often does not regard oral sex as sex.[9] The delay in vaginal intercourse among teenagers observed in the recent surveys suggests that oral sex has replaced vaginal intercourse among the younger teens. Finally, data from several centres have shown that women, rather than heterosexual men, are at high risk for genital HSV-1.[10–12] A small proportion of these women may have sex with women, a potential risk factor for genital HSV-1, presumably because of the frequent practice of oral sex.[13] Among heterosexual women, the increase is more difficult to explain as sexual behaviour surveys suggest that fellatio rather than cunnilingus is more likely to be practised.[14 15] Most likely, these observations confirm women's inherent susceptibility to HSV infections compared with men, as the mucosal lining of the female external genitalia is likely to be more vulnerable than the thin but keratinised skin of male genitalia.

> For appropriate clinical management and complete patient counselling, the type of virus needs to be identified

What do these changes imply for clinicians? In my view, the increase in genital HSV-1 as a cause of genital herpes clearly shows the need for laboratory confirmation of the clinical diagnosis of genital herpes, and the need to identify the type of the virus. The signs and symptoms of the first episode or a recurrence are identical for both viral types. Genital HSV-1, which almost always causes a true primary infection, is likely to be more severe during the initial episode. However, genital HSV-1 causes fewer recurrences (few or none after the first year of infection) and is shed asymptomatically infrequently.[16 17] These are critical counselling points to provide to affected patients. Importantly, individuals with genital HSV-1 are still at risk of HSV-2 acquisition, and it is not known whether previous genital HSV-1 infection modifies the risk of HSV-2 acquisition more substantially than previous oral HSV-1 infection.[18] Thus for appropriate clinical management and complete patient counselling, the type of virus needs to be identified. In a patient with a first episode of lesions, this is best done using viral culture or type specific polymerase chain reaction.

The risk of genital HSV-1 infection has further muddled the issue of HSV serological testing that has been long in coming to assist in genital herpes diagnosis. For those who doubt the clinical utility of these assays, it is useful to remember that the clinical diagnosis of genital HSV-2 infection is, at best, 39% sensitive and has a 20% false positive rate.[19] Thus instead of comparing the "almost perfect" record of HIV antibody tests with HSV antibody tests, the added value of serological testing is clear when one recalls the limited accuracy of clinical diagnosis. The development of accurate serological assays has been hindered by extensive cross reactivity between antibodies to HSV-1 and HSV-2, and concerns remain about specificity and sensitivity of commercial serological tests that use only one or two antigens. However, aside from technical issues that may limit test performance, clinicians may struggle with the interpretation of the test.[20–22] The message to the patient is clear when he or she presents with recurrent genital lesions and the test indicates presence of HSV-2 antibody. But what do we tell a patient who tests positive for HSV-1 only and has no history of oral and genital lesions? In my clinic, such patients are informed that we cannot tell where they have the infection. Among those with prevalent HSV-1, most are likely to have acquired the infection in childhood. However, adults with incident HSV-1 are equally likely to be infected in the mouth or the genital area, or perhaps, both. Since these people are asymptomatic, disease management is not of concern. However, susceptibility to HSV-2, but probably not HSV-1, still remains and potential risk of transmission provides information to patients.

Counselling a person with genital HSV-1 about the risk of transmission presents an interesting predicament. While the propensity for both clinical and subclinical reactivation is dramatically lower for genital HSV-1 than for genital HSV-2, the neonatal data suggest that when reactivation recurs among HSV-1 infected women during delivery, the virus is more likely to be transmitted with an estimated relative risk of ~60.[23] Thus the infectivity, once present, appears greater for HSV-1 than for HSV-2. We do not know whether the increased risk of transmission also applies to sexual transmission. However, among 48 source partners of people with documented newly acquired genital HSV-1, HSV-1 was isolated from the genital area in seven and from the oral area in three (unpublished data). This suggests that genital to genital HSV-1 transmission is potentially not uncommon. Many people do not think that current or potential partners need to be told about oral HSV-1 infection, although this may change as

more people are aware of their status. Avoiding mucosal contact with a clinically apparent cold sore, as well as protecting newborns from such contact, seems prudent, and patients should receive such education. Condom use is unlikely to have an impact on genital HSV-1 acquired from oral sex, since most people do not use a barrier for such contact, and there is a paucity of studies of antiviral therapy for oral HSV-1 infection. We can hope that the increase in genital HSV-1 will spur research for an HSV vaccine that protects against acquisition of HSV-1 and HSV-2.

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Correspondence to: Anna Wald, MD, MPH, University of Washington Virology Research Clinic, 600 Broadway, Suite 400, Seattle, WA 98122, USA;
annawald@u.washington.edu

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Authors' affiliations
R F Miller, H Ward, Sexually Transmitted Infections Editorial Office, BMA House, London, UK

Correspondence to: Professor R F Miller, Sexually Transmitted Infections Editorial Office, BMJ Journals, BMA House, Tavistock Square, London WC1H 9HR, UK;
rmiller@gum.ucl.ac.uk

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