EDITORIAL COMMENTARY

An Evolving Understanding of Genital Herpes Pathogenesis: Is It Time for Our Approach to Therapy to Change As Well?

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(See the article by Tata et al, on pages 499–504.)

In this issue of the Journal, Tata and co-workers present data from a small, intensively studied group of women with genital herpes due to herpes simplex virus (HSV) type 2, demonstrating that during a 30-day period these women experienced both symptomatic and asymptomatic genital viral shedding bilaterally and at areas innervated by dorsal root nerve ganglia on both sides of the midline [1]. These findings challenge widely held beliefs that genital HSV infection resides in solitary or adjacent dorsal root ganglia on just one side of the body, suggesting that the infection may occur on both sides of the midline and in more ganglia than previously thought. Although the data need to be validated by additional investigations, they encourage conceptualization of genital herpes as a chronic, nearly continuously active infection rather than an infection characterized by periodic recurrences interspersed with periods of disease inactivity. Tata et al studied a small number of patients and did not include any men; moreover, as they acknowledge, 3 of their 4 patients had become infected within the preceding year and were thus in a period of infection when both recurrences and asymptomatic viral shedding are more frequent than in persons with older infections. Nonetheless, the data are of great potential importance, because they further challenge widely held beliefs regarding genital herpes and, by extension, its management. They also suggest that it is time to use these sorts of data to guide the evolution of our approach to genital herpes management and prevention.

Thirty years ago there were no easily taken, highly effective medications for genital herpes treatment and no reliable serological tests to help diagnose infection with the virus. In 1982, herpes was characterized as “Today’s Scarlet Letter” in a cover story in Time magazine [2]. Much has changed since that time. We now know that about 1 in 5 American adults has genital herpes but that only ∼10% of them are aware of their infection [3, 4]. We know that “classic herpes” is not typical herpes and that in many persons with genital herpes the manifestations of initial and recurrent genital infections are subtle, varied, and frequently overlooked [5]. Furthermore, we have learned that the vast majority of HSV transmission occurs through contact with sexual partners who are unaware of their infections and are asymptomatic when the infection is transmitted [6, 7].

Our tools for herpes diagnosis and management have evolved as well. Type-specific serological tests can now provide reliable information about the presence or absence of infection [8, 9], and polymerase chain reaction testing has both substantially increased the sensitivity of tests for the virus and simplified specimen acquisition and transport [10]. There are also multiple highly effective antiviral therapeutic agents that not only are proved to accelerate lesion healing and reduce the discomfort associated with symptomatic recurrence of infection but that also, when taken continuously as suppressive therapy, reduce asymptomatic shedding of the virus and have been proved in a rigorously conducted clinical trial to significantly reduce transmission of infection between sexual partners [7, 11].

For most clinicians however, the approach to therapy has not kept pace with our evolving understanding of this widespread infection. All too many clinicians treat most patients with newly diagnosed
herpes with episodic therapy directed at managing the signs and symptoms of periodic symptomatic recurrences. The data presented by Tata et al [1] add to the argument, from a patient and public health perspective, that a national campaign for serological testing of those at risk would provide the foundation for more effective efforts to control HSV transmission to others, and that suppressive therapy should be the preferred approach for most sexually active persons with HSV-2 whose sex partners are not known to be infected. This would not be a simple task. Clinicians would need to reconceptualize their approach to diagnosis and management. In addition, there would be a need to portray genital herpes not as a “scarlet letter” but rather as a widespread untoward consequence of human sexuality, the impact of which on personal and public health could be reduced through broader testing and more aggressive treatment. That is where the data take us; when will we act?

References