Seroprevalence of Herpes Simplex Virus Type 1 and 2 Among Pregnant Women, 1989-2010

Genital herpes during pregnancy frequently complicates management, although neonatal herpes, a potentially catastrophic complication, is rare. Maternal acquisition of genital herpes simplex virus (HSV) type 1 or 2 near the time of delivery accounts for most cases of neonatal herpes. Concurrently, a decline in HSV-1 seroprevalence, but not HSV-2, has been noted among reproductive-aged women in nationwide surveys. We determined trends in the seroprevalence of HSV-1 and HSV-2 among pregnant women who delivered newborns at a single urban academic center during 2 decades.

Methods | We reviewed the charts of women who delivered at the University of Washington Medical Center between January 1989 and May 2010. Status of HSV infection was determined with the Western blot as part of routine prenatal tests. Women transferred for management of high-risk pregnancies but who did not have their prenatal tests repeated at our institution were excluded. Selection criteria were consistent over time. The proportion of patients with prenatal HSV serological results as part of prenatal care among all those delivering at the medical center declined slightly over the study period from 54.7% during 1989-1997 to 44.8% during 1998-2010. The University of Washington human subjects review committee provided approval with a waiver of consent.

Results | We identified 15,738 women with 18,993 pregnancies who had prenatal HSV serological results. The median age was 28 years (interquartile range, 23-33 years). Forty-three percent of women were white; 12%, black; 11%, Asian; 7%, Hispanic; and 27%, other or unreported; and 26% had private insurance. Forty-one percent of women were primigravid.

Overall, 9% of pregnancies involved women who were seropositive for HSV-2 only, 15% seropositive for both HSV-1 and HSV-2, 53% seropositive for HSV-1 only, and 24% seronegative for HSV. Comparing the 2 decades, HSV-1 seroprevalence decreased from 69.1% during the first decade (1989-1999) to 65.5% during 2000-2010, whereas HSV-2 seroprevalence decreased from 30.1% to 16.3%, respectively, which is a 46% relative decline.

After adjustment, we found no significant annual trend in HSV-1 seroprevalence (0.1%/year [95% CI, 0%-0.3%/year]; P = .13); however, rates of HSV-2 seroprevalence decreased significantly by 4.8%/year (95% CI, 4.3%-5.2%/year; P < .001) (Figure and Table). Seroprevalence of HSV-1 increased slightly among black women only (0.9%/year [95% CI, 0.4%-1.3%/year]; P < .001). Seroprevalence of HSV-2 decreased significantly over time among women of all races (P < .001); however, rates per year decreased substantially less for black
women relative to white women (2.6%/year vs 5.5%/year, respectively; \( P < .001 \) for interaction of HSV-2 reduction by race).

**Discussion** | Seroprevalence of HSV-2 among pregnant women at a single urban academic center who underwent HIV-1 and HSV-2 antibody testing substantially decreased between 1989 and 2010, and this decrease was especially pronounced among white women. As a result, racial disparities between white and black women widened, as has been noted in a population-based serological survey of persons aged 14 to 49 years. In contrast to that serosurvey, HSV-1 did not decrease overall in our study and increased slightly among black women. Temporal trends in neonatal HHV-8 do not suggest a decline, although a shift toward neonatal HHV-8 has also been noted.  

Study limitations include participation at a single urban academic center, potentially limiting generalizability. Representativeness could be affected by the low proportion of women with HHV serological results. However, we compared women with prenatal serological results with all other women who had serological results at delivery during the first decade. No differences in HSV results, insurance payment, or race were noted (results available from the authors). Our findings provide new information on HSV seroprevalence specifically in the pregnant population.

**Table. Herpes Simplex Virus (HSV) Seroprevalence Among Pregnant Women**

<table>
<thead>
<tr>
<th>HSV type</th>
<th>1989-1999</th>
<th>2000-2010</th>
<th>Yearly % Change (95% CI)</th>
<th>P Value</th>
<th>Adjusted Yearly % Change (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSV type 1</td>
<td>Overall</td>
<td>6839/9897 (69.1)</td>
<td>5955/9096 (65.5)</td>
<td>-0.3 (-0.5 to -0.2)</td>
<td>&lt;.001</td>
<td>0.1 (0 to 0.3)</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td>White</td>
<td>2254/3989 (56.5)</td>
<td>2176/4140 (52.6)</td>
<td>-0.5 (-1.0 to -0.3)</td>
<td>&lt;.001</td>
<td>-0.1 (-0.3 to 0.2)</td>
</tr>
<tr>
<td></td>
<td>Black</td>
<td>1162/1597 (72.8)</td>
<td>751/962 (78.1)</td>
<td>0.7 (0.3 to 1.2)</td>
<td>&lt;.001</td>
<td>0.9 (0.4 to 1.3)</td>
</tr>
<tr>
<td></td>
<td>Asian</td>
<td>948/1082 (87.6)</td>
<td>883/1085 (81.4)</td>
<td>-0.7 (-1.0 to -0.3)</td>
<td>.001</td>
<td>-0.2 (-0.6 to 0.3)</td>
</tr>
<tr>
<td></td>
<td>Hispanic</td>
<td>504/595 (84.7)</td>
<td>791/891 (88.8)</td>
<td>0.3 (-0.2 to 0.9)</td>
<td>.19</td>
<td>0.3 (-0.2 to 0.8)</td>
</tr>
<tr>
<td>HSV type 2</td>
<td>Overall</td>
<td>2981/997 (31.0)</td>
<td>1480/9096 (16.3)</td>
<td>-4.9 (-5.3 to -4.5)</td>
<td>&lt;.001</td>
<td>-4.8 (-5.2 to -4.3)</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td>White</td>
<td>1217/3989 (30.5)</td>
<td>618/4140 (14.9)</td>
<td>-5.4 (-5.9 to -4.9)</td>
<td>&lt;.001</td>
<td>-5.5 (-6.0 to -4.9)</td>
</tr>
<tr>
<td></td>
<td>Black</td>
<td>775/1597 (48.5)</td>
<td>356/962 (37.0)</td>
<td>-2.1 (-3.0 to -1.3)</td>
<td>&lt;.001</td>
<td>-2.6 (-3.5 to -1.8)</td>
</tr>
<tr>
<td></td>
<td>Asian</td>
<td>168/1082 (15.5)</td>
<td>96/1085 (8.8)</td>
<td>-4.1 (-5.8 to -2.4)</td>
<td>&lt;.001</td>
<td>-3.8 (-5.5 to -2.1)</td>
</tr>
<tr>
<td></td>
<td>Hispanic</td>
<td>160/595 (26.9)</td>
<td>123/891 (13.8)</td>
<td>-5.1 (-6.7 to -3.5)</td>
<td>&lt;.001</td>
<td>-5.9 (-7.5 to -4.3)</td>
</tr>
</tbody>
</table>

* Relative risk (RR) from Poisson models using first deliveries among women of each race/ethnicity separately were used to calculate the yearly percentage changes in seroprevalence: 100 × (RR − 1).

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**Author Contributions:** Drs Magaret and Wald had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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COMMENT & RESPONSE

Tadalafil for Erectile Dysfunction Prevention After Radiotherapy for Prostate Cancer

To the Editor Dr Pisansky and colleagues1 did not find any beneficial effect of daily tadalafil administration in preventing erectile dysfunction (ED) in men treated with radiotherapy for prostate cancer. Concerns about the methodology of this study parallel those raised after previous trials testing penile rehabilitation after radical prostatectomy. These include inadequate patient selection,1 short-term follow-up,2 and possibly improper tadalafil administration.3

First, selected patients with a high probability of erectile function recovery after radiotherapy were enrolled. The majority of men were free from any significant comorbidity and had no or mild ED at treatment initiation. Such a favorable baseline profile may have diluted the effect of tadalafil on erectile function recovery, given the high probability of these patients to maintain erectile function after radiotherapy with or without any medication. Moreover, no detailed description of cardiovascular risk factors was provided by Pisansky et al.1 This is important given the effect on recovery of erectile function after radiotherapy.2 Second, longer follow-up and longer exposure to phosphodiesterase type 5 inhibitors (PDE5-I) may be needed to evaluate the efficacy of penile rehabilitation after radiotherapy. The reason for this lies in the pathophysiology of postradiotherapy ED, which includes neurovascular damage as well as induced chronic oxidative stress. The latter seems to be the primary step in a gradual fibrotic process that takes place over several years.3 Therefore, evaluating postradiotherapy erectile function at 1 year may underestimate the cavernosal damage induced by radiotherapy, as well as the potential beneficial effect of any penile rehabilitation after radiotherapy.4

Third, whether a possible beneficial effect of PDE5-I administered prior rather than after penile neurovascular damage exists needs to be tested, as shown in the setting of damage from ischemia reperfusion.5 For all these reasons, we believe that further research is needed to properly assess the effectiveness of PDE5-I use for ED after radiotherapy. Targeting the right patient and using proper administration schedules represent the main factors in the success of any penile rehabilitation protocol.

Fabio Castiglione, MD
Francesco Montorsi, MD
Alberto Briganti, MD

In Reply Although our study did not identify a role for tadalafil to prevent radiotherapy-related ED, Dr Castiglione and colleagues urge cautious interpretation of our results based on inadequate participant inclusion criteria and follow-up duration, and on possibly improper tadalafil administration. We do not agree that our participants’ favorable baseline (erectile function) profile negatively affected the trial’s outcome.

It is important to distinguish between penile rehabilitation after urological surgery (an ED preventive strategy after radiotherapy) and a therapeutic intervention for established ED. In the first, an acute vasogenic or neurogenic event (ie, radical prostatectomy) precipitates a sudden loss of function, from which recovery is sought—thus, rehabilitation. Radiotherapy-related injury to erogenous tissue accumulates slowly and as a delayed response to treatment administered over several months—thus, a strategy seeking to prevent loss of existing function. We selected trial participants without ED because we sought to preserve spontaneous off-drug erectile function. Inclusion of participants with ED or with a significant burden of conditions contributing to its occurrence6 potentially would have confounded the results.