Association between Acquisition of Herpes Simplex Virus Type 2 in Women and Bacterial Vaginosis

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A longitudinal cohort study of sexually active women 18–30 years of age was conducted to identify variables associated with the acquisition of herpes simplex virus type 2 (HSV-2) infections. Six hundred seventy HSV-2–seronegative women were followed up at 4-month intervals for 1 year; acquisition of HSV-2 antibodies was detected in 32 of these women. Black race, ≤12 years of education, having a new sex partner, and bacterial vaginosis (BV) were associated with HSV-2 seroconversion on univariate analysis. Antecedent HSV-1 infection was not protective against HSV-2 acquisition. After controlling for other identified risk factors in multivariable models, the diagnosis of BV remained associated with an increased risk of acquiring HSV-2 infection (hazard ratio, 2.1; 95% confidence interval, 1.0–4.5; P = .05). In this study, the population attributable risk of BV for HSV-2 seroconversion was 21%. Additional studies are needed to determine whether screening and treatment of BV could reduce susceptibility to the acquisition of HSV-2 in women.

Worldwide, herpes simplex virus type 2 (HSV-2), the primary cause of genital herpes, is one of the most prevalent sexually transmitted diseases. In the United States alone, it is estimated that 45 million individuals are seropositive for HSV-2 [1]. Moreover, the National Health and Nutrition Examination Survey (NHANES), an ongoing population-based study, showed an increase of ~30% in the seroprevalence of HSV-2 among adults between 1978 and 1990 [2]. Genital herpes is considered by many clinicians to be a relatively benign infection, but the chronic, recurrent nature of this infection can cause considerable physical discomfort and psychosexual distress [3]. HSV-2 infection also has been shown to be a significant cofactor in the transmission of HIV [4]. Because genital herpes is typically a non-reportable infection, and because HSV-2 acquisition may be asymptomatic, it has been difficult to accurately measure incidence rates. Mathematical models that incorporated the NHANES seroprevalence data estimated that >1 million new cases occur annually in the United States and that the annual incidence of HSV-2 infection increased ~82% between 1970 and 1985 [5].

Bacterial vaginosis (BV) is the most common cause of vaginal symptoms in reproductive-age women. It is characterized by an increased vaginal pH and the replacement of vaginal lactobacilli (particularly those that produce hydrogen peroxide) with Gardnerella vaginalis and anaerobic gram-negative rods. Longitudinal studies have shown that women with BV were more likely than women with normal vaginal flora to acquire Neisseria gonorrhoeae or HIV [6, 7]. Therefore, the lactobacilli-dominated vaginal ecology may be an important defense against pathogen acquisition. Possible mecha-
nisms of this protection include inactivation of organisms by the acidic environment created by lactobacilli or the ability of these hydrogen peroxide–producing organisms to act as an endogenous microbicide [8].

We have previously demonstrated an association between HSV-2 prevalence and BV [9]. However, the cross-sectional design of that study could not establish the presence of a causal relationship. The purpose of this investigation was to determine whether the presence of BV is among the risk factors associated with increased rates of HSV-2 acquisition among sexually active women.

METHODS

Study population. Women were recruited from 3 Pittsburgh-area health care clinics (the University of Pittsburgh Student Health Clinic, the Allegheny County Health Department Sexually Transmitted Diseases Clinic, and the Family Health Council of Aliquippa) for a longitudinal cohort investigation of the risk factors associated with the vaginal acquisition of group B Streptococcus. Appropriate informed consent was obtained, and the guidelines for human experimentation of the University of Pittsburgh were followed in conducting the clinical research. The use of this cohort to investigate risk factors associated with the acquisition of HSV-2 was approved by the institutional review board of the Magee-Womens Hospital in Pittsburgh. Women 18–30 years of age who were willing to return for 3 follow-up visits at 4-month intervals were eligible. Exclusion criteria included known pregnancy, vaginal bleeding, current use of systemic antimicrobials, or the use of douches, antifungals, or antifungal vaginal products in the 24 h before enrollment.

From 1998 through 2000, a total of 1248 women were enrolled. Of the 1089 women who returned for at least 1 follow-up visit, 739 had negative results of testing for HSV-2 antibodies at enrollment. Only 670 of these HSV-2–seronegative women indicated that they were sexually active on self-report; this subset of women made up the study population. At each visit, demographic and behavioral interview data were collected and a vaginal swab, a vaginal smear, and a serum sample were obtained. Serum samples were frozen and stored at −70°C until testing for HSV-1 and HSV-2 antibodies was performed.

Laboratory methods. Vaginal smears were Gram-stained and evaluated for BV according to a standardized 0–10-point scoring system [10]. Normal vaginal flora received a score of 0–3; intermediate flora, 4–6; and BV, 7–10. Serum samples were tested for type-specific antibodies to HSV-1 and HSV-2 using 2 commercially available ELISAs from Focus Technologies. Both assays use baculovirus recombinant gpG constructs, are approved by the US Food and Drug Administration for testing among sexually active adults, and were used according to the manufacturer’s instructions. As recommended in the package insert [11], index values >1.10 were considered to be positive, and values <0.90 were considered to be negative. Serum samples for which the results were equivocal (an index value of 0.90–1.10) were retested. The final result for a particular specimen was considered to be equivocal if the second index value also was between the inclusive values of 0.90 and 1.10. For samples in which antibodies to HSV-2 were found by ELISA (and on serum samples from the visits that immediately preceded and followed ELISA seroconversion), Western blot (WB) analysis was performed by the University of Washington Virology Laboratory (Seattle), using methods described elsewhere [12].

When the results of ELISA and WB were discrepant, HSV-2 PCR was performed by the University of Pittsburgh’s Clinical Molecular Diagnostics Laboratory, using the vaginal swab obtained from the visit in which seroconversion was detected by ELISA. Two microliters of extracted DNA was amplified by real-time PCR with the LightCycler instrument (Roche Diagnostics). The DNA was added to 18 μL of a master mix consisting of 0.5 μmol/L each of primers specific to the HSV-2 DNA polymerase gene, 5% dimethyl sulfoxide, and FastStart DNA Master Sybr Green I mix (Roche Diagnostics). After a 10-min incubation at 95°C, samples were amplified for 40 cycles under the following conditions: 95°C for 0 s, 60°C for 5 s, and 72°C for 10 s. Fluorescence was read after the 72°C extension step of each cycle to confirm amplification. Melting-curve analysis was then performed to detect the presence of HSV-2–specific product. The HSV-2–specific product formed has a length of 350 bp and a melting temperature of 89°C. Confirmation of HSV-2–specific product was made by comparison of the melting peak of a particular patient sample with the peaks obtained from amplification of HSV-2 genomic DNA (1000-, 100-, and 10-copy control samples). Patient samples displaying a melting peak that matched the control peaks when superimposed were considered to be positive.

Statistical analysis. Acquisition of HSV-2 was defined as a change in the ELISA index value from <0.9 (negative) at enrollment to ≥1.1 (positive) at the 4-, 8-, or 12-month follow-up visit. Cox proportional hazards models with interval-censored, time-dependent covariates were used to evaluate the risk factors associated with acquisition of HSV-2 antibody. The vaginal Gram stain score from the visit before seroconversion was used in the models. Variables were considered for inclusion in the models if the P value from the log-rank test for equality of survivor functions was <.1. Forward stepwise regression was used, and variables were retained in the model if the P value from the Wald χ² test statistic was ≤.05. The mean of the positive index values was calculated for each woman who acquired HSV-2 antibodies, and the medians of these values were compared, using the Mann-Whitney U test, between women who had positive results of both ELISA and WB and those with...
discordant results. An estimate of the proportion of HSV-2 acquisition attributable to BV was made using the incidence rates of HSV-2 acquisition in the full cohort and among women without BV. \( P < .05 \) was considered to be statistically significant.

**RESULTS**

**Characteristics of the study population.** Of the 670 women who were HSV-2 seronegative at enrollment, 488 (73%) described themselves as white, 154 (23%) as black, and 28 (4.0%) as Hispanic, Asian, Native American, or multiethnic. Those 28 women were combined in a single racial category, referred to as “other” for purposes of analysis. The number of women enrolled from each site was similar: 255 (38%) from the Student Health Clinic, 216 (32%) from the Family Health Council of Aliquippa, and 199 (30%) from the Allegheny County Health Department. The majority of the women in this investigation were <26 years of age (88%), had never been pregnant (70%), and had >12 years of education (76%). Three hundred five (46%) of the women had antibodies to HSV-1, and the remaining 365 women (54%) were seronegative for both HSV-1 and HSV-2.

**Acquisition of HSV-2 antibodies, as demonstrated by ELISA.** During the investigation, 32 women were found by ELISA to have acquired antibodies to HSV-2. Seventeen of these women were from the Allegheny County Health Department; 11 were from the Family Health Council of Aliquippa; and 4 were among those enrolled from the University of Pittsburgh’s Student Health Clinic. The 670 women attended a total of 1833 follow-up visits (637 visits at 4 months after enrollment, 612 at 8 months, and 584 at 12 months). During these follow-up visits, 628 woman-years of follow-up were accumulated, yielding an HSV-2 acquisition incidence rate of 5.1 cases/100 woman-years. Selected characteristics of the women who were found by ELISA to have acquired antibodies to HSV-2 are shown in table 1. HSV-2 acquisition was found to be associated with enrollment from either the Family Health Council of Aliquippa or the Allegheny County Health Department on univariate analysis. Other demographic characteristics associated with HSV-2 seroconversion included black race and ≤12 years of education. There were no statistically significant differences in the acquisition of HSV-2 among women who admitted use of alcohol, tobacco, marijuana, or vaginal douche products in the 4 months before seroconversion (data not shown).

Univariate analysis of sexual behavior characteristics demonstrated that the rate of acquisition of HSV-2 infection was significantly higher among women who had had a new sex partner in the 4 months before HSV-2 seroconversion than among women who were sexually active but denied having new sexual contacts (9.3 vs. 4.0 cases/100 woman-years, respectively; hazard ratio [HR], 2.3; 95% CI, 1.1−4.6; \( P = .02 \) (table 1).

However, more frequent intercourse did not appear to significantly increase the risk of HSV-2 acquisition (5.4 cases/100 woman-years among women who reported having sexual intercourse ≤3 times/week vs. 6.6 cases/100 woman-years among those who reported having intercourse more frequently; HR, 1.4; 95% CI, 0.7−3.0; \( P = .4 \)). The rate of HSV-2 acquisition was considerably higher among women in whom BV was diagnosed at the visit before HSV-2 seroconversion than among women who had a normal vaginal morphology score (8.9 vs. 4.0 cases/100 woman-years, respectively; HR, 2.3; 95% CI, 1.1−4.8; \( P = .03 \)). Women who had antecedent HSV-1 infection were as likely to acquire HSV-2 as those who were seronegative for HSV-1 (4.7 vs. 5.4 cases/100 woman-years; HR, 0.9; 95% CI, 0.4–1.8).

Cox proportional hazards analysis demonstrated that the association between acquisition of HSV-2 and the presence of BV at the visit before HSV-2 seroconversion persisted after adjusting for potential confounders (HR, 2.1; 95% CI, 1.0–4.5; \( P = .05 \)) (table 2). The estimated population attributable risk of HSV-2 seroconversion for BV was 21.4%. In our final multivariable proportional hazards model, the other characteristics found to be independently associated with HSV-2 seroconversion were ≤12 years of education and having had a new sex partner in the 4 months before HSV-2 seroconversion.

**Comparison of ELISA and WB for detection of HSV-2 seroconversion.** WB analysis did not detect seroconversion in 8 of the 32 women who were found by ELISA to have acquired antibodies to HSV-2. The median of the mean positive index value for women with concordant ELISA and WB results was significantly greater than the median of the mean positive index value for women whose seroconversion was not confirmed by WB (5.45 vs. 1.63, respectively; \( P = .001 \)). Five of the 8 HSV-2 acquisitions that were not detected by WB occurred on the last scheduled follow-up visit of the investigation. In 3 of the 24 women who were found by both methods to have acquired HSV-2 antibodies, seroconversion was detected 4 months earlier by ELISA than it was by WB.

**Results of HSV-2 PCR using genital swab samples.** DNA was extracted from genital swabs from the 8 women with discordant results of ELISA and WB. The genital swab from the visit at which seroconversion was detected by ELISA was chosen for analysis because recent acquisition of HSV-2 has been associated with higher rates of vaginal shedding of virus [13]. Although women who acquire genital herpes do not shed detectable virus daily, HSV-2 DNA was present in the vaginal swab from 1 of these 8 women. This woman was found by ELISA to have acquired antibodies to HSV-2 on her second follow-up visit (the visit at which the sample used for PCR was obtained), and she retained a positive ELISA index value at her third and fourth follow-up visits. WB analysis of swabs from...
her second and third follow-up visits, however, demonstrated no change from the profile seen at the time of enrollment.

**DISCUSSION**

Our study detected increased acquisition of HSV-2 among women with BV, compared with those with normal vaginal flora. Cox proportional hazards analysis demonstrated that the presence of BV 4 months before the acquisition of antibodies to HSV-2 was an independent predictor of HSV-2 infection. The population attributable risk of BV for HSV-2 seroconversion was ~21%. Because the prevalence of BV among women in some communities can be as high as 50% [14], it seems likely that more-comprehensive screening and appropriate treatment of BV would reduce susceptibility to the acquisition of HSV-2 among women. Additional studies are needed to evaluate this possibility.

The capacity of the normal vaginal environment to act as an effective barrier to acquisition of infection makes teleologic sense. Like the oral cavity and the upper respiratory tract, which

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**Table 1.** Characteristics of women who were found to have acquired herpes simplex virus type 2 (HSV-2) antibodies by ELISA during follow-up investigation.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of HSV-2 acquisitions/woman-years</th>
<th>Acquisition rate, %a</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recruitment site</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>University of Pittsburgh Student Health Clinic</td>
<td>4/245.7</td>
<td>1.6</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Family Health Council of Aliquippa</td>
<td>11/199.9</td>
<td>5.5</td>
<td>3.4 (1.1–10.6)</td>
<td>.02</td>
</tr>
<tr>
<td>Allegheny County Health Department Sexually Transmitted Diseases Clinic</td>
<td>17/182.4</td>
<td>4.3</td>
<td>5.7 (1.9–16.9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>17/459.7</td>
<td>3.7</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>14/142.5</td>
<td>9.8</td>
<td>2.7 (1.4–5.7)</td>
<td>.004</td>
</tr>
<tr>
<td>Other</td>
<td>1/25.8</td>
<td>3.9</td>
<td>1.1 (0.1–8.1)</td>
<td>1.0</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;12 years</td>
<td>17/480.4</td>
<td>3.5</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>≤12 years</td>
<td>15/147.6</td>
<td>10.2</td>
<td>3.2 (1.6–6.3)</td>
<td>.003</td>
</tr>
<tr>
<td>No. of sex partners in past 4 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0/69.7</td>
<td>0</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>24/473.0</td>
<td>5.1</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>&gt;2</td>
<td>8/84.7</td>
<td>9.4</td>
<td>2.0 (0.9–4.5)</td>
<td>.07</td>
</tr>
<tr>
<td>Frequency of intercourse in past 4 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0/67.9</td>
<td>0</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>&lt;3 times/week</td>
<td>23/423.2</td>
<td>5.4</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>≥3 times/week</td>
<td>9/136.6</td>
<td>6.6</td>
<td>1.4 (0.7–3.0)</td>
<td>.4</td>
</tr>
<tr>
<td>New sex partner in the 4 months before HSV-2 seroconversion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>20/499.5</td>
<td>4.0</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>12/128.4</td>
<td>9.3</td>
<td>2.3 (1.1–4.6)</td>
<td>.02</td>
</tr>
<tr>
<td>HSV-1 seropositive at visit before HSV-2 seroconversion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>18/334.6</td>
<td>5.4</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>14/293.3</td>
<td>4.8</td>
<td>0.9 (0.4–1.8)</td>
<td>.7</td>
</tr>
<tr>
<td>Vaginal Gram stain score at visit before HSV-2 seroconversion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–3</td>
<td>15/375.7</td>
<td>4.0</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>4–6</td>
<td>5/112.4</td>
<td>4.4</td>
<td>1.1 (0.4–3.2)</td>
<td>.8</td>
</tr>
<tr>
<td>7–10</td>
<td>12/134.4</td>
<td>8.9</td>
<td>2.3 (1.1–4.8)</td>
<td>.03</td>
</tr>
</tbody>
</table>

**NOTE.** HR, hazard ratio.

*a* Calculated by dividing the no. of events by the no. of woman-years.

*b* A score of 0–3 was considered to be normal; of 4–6, intermediate; and of 7–10, indicative of bacterial vaginosis.
may contribute to the increased but variable susceptibility of
in a large but variable proportion of reproductive-age women
partners, and it is possible that the intermittent presence of BV
predictably transmitted from male sources to susceptible female
than female-to-male transmission [20]. HSV-2 is not, however,
that male-to-female transmission of the virus is more efficient
with men, and studies of discordant couples have demonstrated
women are at an increased risk for HSV-2 infection, compared
the genital herpes epidemic. First, serosurveys have shown that
of HSV-2 in women is consistent with observations from the
metabolize glucose to produce lactic acid [8], and the acidic
environment produced by normal vaginal flora may create an
environment that is less hospitable for invading pathogens.

The cervical mucus that coats the vaginal and cervical epithe-
also is likely to protect women from the acquisition of
genital herpes. In vitro, cervical mucus has demonstrated the
ability to trap HSV in its viscous gel [17]. However, many of
the microorganisms associated with BV are known to pro-
duce higher levels of mucinase, sialidase, and other mucin-
degrading enzymes, compared with the lactobacilli-dominated
normal vagina flora [18, 19]. Therefore, it is possible that in-
crease degradation of components of the protective mucus
layer in women with BV may facilitate attachment of HSV-2
to the underlying epithelial cells.

Evidence that BV increases the susceptibility to acquisition
of HSV-2 in women is consistent with observations from the
mgital herpes epidemic. First, serosurveys have shown that
women are at an increased risk for HSV-2 infection, compared
with men, and studies of discordant couples have demonstrated
that male-to-female transmission of the virus is more efficient
than female-to-male transmission [20]. HSV-2 is not, however,
predictably transmitted from male sources to susceptible female
partners, and it is possible that the intermittent presence of BV
in a large but variable proportion of reproductive-age women
may contribute to the increased but variable susceptibility of
women to HSV-2 infection. In our study, the frequency of BV
was 45% (9 of 20 women) among women who acquired HSV-
2 but denied having a new sex partner, compared with the 25%
prevalence (3 of 12 women) of BV among women whose se-
roconversion occurred within 4 months after the introduction
of a new sex partner (P = .5).

Behavioral variables, rather than biological susceptibility,
may explain why the seroprevalence of HSV-2 is higher among
women. For instance, older age is associated with increased
prevalence of HSV-2 [8, 21], and women are more likely than
men to choose sex partners who are older than themselves [22].
Therefore, women would be at an increased risk for HSV-2
infection. Similarly, black women are more likely to have sex
with black men than with white men [22]. Because black men
have a higher seroprevalence of HSV-2 than do white men [2],
the higher prevalence of HSV-2 seen among black women may
simply be a consequence of cumulative high-risk activity. In
our investigation, after controlling for age, BV, but not race,
remained an independent predictor of HSV-2 acquisition.
However, it is possible that behavioral factors other than those
assessed in this study may account for the association between
BV and HSV-2 acquisition.

Antecedent HSV-1 infection did not provide significant pro-
tection against the acquisition of HSV-2 in our investigation.
We found the HSV-2 incidence rate among women who were
seropositive for HSV-1 to be approximately the same as that
among women who were seronegative for HSV-1 (table 1).
Findings from our cross-sectional investigation also implied
that HSV-1 infection does not provide protective immunity;
women with antibody to HSV-1 had a higher HSV-2 sero-
prevalence at enrollment than did those who did not have HSV-
1 antibodies [9]. Likewise, the Chiron HSV Vaccine Study
Group found that previous HSV-1 infection increased the like-
lihood of asymptomatic HSV-2 seroconversion but did not
reduce the rate of HSV-2 acquisition [23]. This is in contrast
to earlier published studies that reported a partially protective
role for antecedent HSV-1 infection [19, 24].

The detection of discordant results by ELISA and WB in our
investigation is perplexing. Two recent studies concluded that
HSV-2 type-specific ELISAs are sufficiently accurate to warrant
their use without confirmatory testing [25, 26]. In an analysis
adjunctive to the present study, we found the Focus HSV-2
ELISA to have excellent longitudinal reliability; <1% of HSV-
2 antibody–positive women had a subsequent negative result
[27]. Recent evidence suggests that seroconversion is typically
detected 3 weeks sooner by the Focus HSV-2 ELISA than by
WB [28]. Therefore, it is possible that some or all of the WB-
negative women who were found by ELISA to have acquired
antibodies to HSV-2 on their last follow-up visit would also
have been found to have seroconverted by WB if they had been
retested at a later date. We would have required access to ad-

Table 2. Results of adjusted analysis of the association
between risk factors and acquisition of herpes simplex virus
type 2 (HSV-2), as demonstrated by ELISA.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Education &lt;12 years</td>
<td>2.8 (1.4–5.9)</td>
<td>.005</td>
</tr>
<tr>
<td>New sex partner in past 4 months</td>
<td>2.6 (1.2–5.4)</td>
<td>.02</td>
</tr>
<tr>
<td>Vaginal Gram stain score at visit before HSV-2 seroconversion a</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–3</td>
<td>1.0</td>
<td>—</td>
</tr>
<tr>
<td>4–6</td>
<td>1.2 (0.4–3.4)</td>
<td>.7</td>
</tr>
<tr>
<td>7–10</td>
<td>2.1 (1.0–4.5)</td>
<td>.05</td>
</tr>
</tbody>
</table>

NOTE. Variables shown here are those included in the final multi-
variable proportional hazards regression model. HR, hazard ratio.

a A score of 0–3 was considered to be normal; of 4–6, intermediate;
and of 7–10, indicative of bacterial vaginosis.
ditional follow-up serum samples from the women who had discordant results to test this hypothesis.

Our investigation underscores the fact that neither WB nor ELISA represents a reference standard for the detection of HSV-2 infection. Because the women with discordant results of ELISA and WB were more likely to have lower positive index values, it is possible that nonspecific IgG binding may have produced false-positive ELISA values. However, a recent investigation of discordant HSV-2 ELISA (positive) and WB (negative) results, which used an HSV–2–inhibition assay to further analyze these inconsistencies, found that WB yielded false-negative results for 67% of the discrepant samples [29]. Furthermore, our detection of HSV-2 DNA in a specimen from the vaginal swab of a woman who was found to have antibodies by ELISA, but not by WB, suggests that evidence of viral infection and antibody response to HSV-2 will occur in some women without a discernable change in the HSV-2 WB result. HSV-2 PCR or antigen testing of genital lesions would be more accurate, but, because these lesions are inconsistently present, use of these tests is clinically impractical. Widespread future use of the HSV-2 ELISAs is likely, and further work to clarify the discrepancies between ELISA and WB is needed.

There are limitations to the present study. Foremost among them is the lack of testing for possible coinfections with other sexually transmitted diseases. Therefore, it is possible that the association between BV and the acquisition of HSV-2 infection was confounded by the acquisition of other infections. However, in our analysis of the cross-sectional enrollment data from this investigation, Chlamydia trachomatis and N. gonorrhoeae test results were available. After we accounted for these cervical pathogens, BV remained independently associated with HSV-2 infection [9]. In addition, a recent study from the United Kingdom reported that a history of BV was significantly associated with HSV-2 seropositivity [30]. Another limitation of the present study is intrinsic to its design. Although the diagnosis of BV preceded acquisition of HSV-2 antibodies, it is impossible to know whether BV was actually present when infection occurred.

Our investigation appears to be the first to recognize an increased risk of HSV-2 acquisition among women with BV, an association consistent with that seen previously between BV and HIV. Because of the high prevalence of BV and the incurable nature of HSV-2 infection, widespread screening and treatment of BV may represent an opportunity to reduce the incidence of HSV-2 infection in women.

Acknowledgments

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References

22. Laumann E, Gagnon J, Michael R, Michaels S. Sexual networks. The

Reference Image


