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# *Factors Predicting the Acceptance of Herpes Simplex Virus Type 2 Antibody Testing Among Adolescents and Young Adults*

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***Background:*** **The rates and determinants of acceptance of herpes simplex virus type 2 (HSV-2) testing have not been adequately studied.**

***Objectives:*** **The objective of this study was to identify factors associated with acceptance of HSV-2 antibody testing in individuals with no history of genital herpes.**

***Study:*** **We conducted a cross-sectional survey study followed by the offer of free HSV-2 serologic testing at an urban sexually transmitted disease (STD) clinic, 2 general adult medical clinics, an urban university campus, and an urban adolescent medicine clinic. A total of 1199 individuals aged 14 to 30 years completed the survey and were offered testing.**

***Results:*** **A total of 68.4% accepted HSV-2 testing. Factors independently associated with acceptance were female sex, older age, having an STD history, having 1 or more sexual partners in the last 6 months, perceived vulnerability to HSV-2 infection, and perceived benefits of HSV-2 testing. Fear of needles predicted rejection of testing, as did attending a general medical clinic versus an STD clinic and nonwhite race.**

***Conclusion:*** **There is a substantial interest in HSV-2 antibody testing across a variety of settings. Those at greatest behavioral and historic risk for HSV-2 infection, women, and persons whose health beliefs are consistent with testing are more likely to accept serologic testing when it is offered.**

IN THE UNITED STATES, HERPES simplex virus type 2 (HSV-2) is the virus most often associated with the diagnosis of genital herpes.[1] However, the majority of persons who are HSV-2-seropositive report no history of symptoms of genital herpes,[2] although many of these individuals can be educated to recognize mild or atypical symptoms or subtle genital lesions.[3] A recent study indicates that individuals with unrecognized HSV-2 infections have rates of asymptomatic viral shedding from genital sites similar to those of HSV-2-seropositive persons known to have genital herpes.[4] These data help explain the observation that genital herpes is often spread by individuals who are unaware they are infected. Identification of undiagnosed, asymptomatic infections could facilitate public health interventions to control genital herpes.

Relatively new type-specific antibody tests that can distinguish prior HSV-2 infection from HSV-1 infection are available and have good sensitivity and specificity,[5,6] but are not yet widely used as clinical tools. Some authorities recommend HSV-2 screening as a genital herpes prevention strategy. It has been suggested that screening should be offered to all sexually experienced people or could target specific groups such as sexually transmitted disease (STD) clinic patients or pregnant women and their sexual partners.[7–10] However, others disagree, noting several problems, including the lack of cure for latent HSV-2 infection, the uncertainty that the testing would be cost-effective, concerns that the psychosocial burden of diagnosis among asymptomatic individuals may be greater than the benefit afforded by the test, some issues with test performance, and questions regarding the acceptability of HSV-2 screening.[11–14] An earlier criticism that screening should not be offered in the absence of a proven effective intervention to prevent HSV-2 transmission is less cogent in view of recent evidence that suppressive antiviral therapy can reduce the transmission of HSV-2 from symptomatic persons to susceptible partners[15] and the observation that condoms reduce transmissibility.[16]

One study found that genitourinary clinic patients were favorably disposed to the idea of serotesting for HSV-2.[17] However, because HSV-2 serologic testing was not offered in this study (it was carried out before the general availability of accurate HSV-2 serologic tests), it necessarily focused on acceptability rather than

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All subjects provided written informed consent for this study (parental permission also was obtained for subjects <18 years old) using documents approved by local institutional review boards and by the Institutional Review Board for the Centers for Disease Control and Prevention. The protocol was conducted according to federal and local guidelines for the conduct of human research.

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acceptance of testing. In a later study, STD clinic patients were offered type-specific HSV-2 serologic testing.[18] Predictors of test acceptance included free testing (as opposed to a cost of $15) and increasing age. Patients belonging to racial/ethnic minority groups were less likely to accept testing. In this study, however, predictors of test acceptance were restricted to cost and demographic factors. Attitudinal and behavioral factors were not assessed. Other recent studies have similar limitations.[19,20]

To provide more comprehensive information regarding acceptance of HSV-2 serologic testing, we recruited subjects from a variety of settings and offered them free HSV-2 antibody testing. In addition, we examined relevant demographic, attitudinal, and behavioral factors as potential predictors of HSV-2 test acceptance.

## Materials and Methods

### *Study Population and Procedure*

The sample for this study was recruited from the following sites: an urban public health STD clinic, 2 general adult medical clinics (1 suburban, 1 urban), an urban adolescent health clinic, and an urban university campus. Inclusion criteria included ability to read English, age 14 to 30 years (14–18 in the adolescent clinic and 18–30 in the adult sites), and no known history of genital herpes. This analysis excluded persons who had reported no previous vaginal, oral, or anal sex to avoid the potential bias caused by the inclusion of people that were not at risk for genital HSV-2 infections.

The Bell Flower Clinic, located in Indianapolis, provides medical services for sexually transmitted diseases with approximately 10,000 annual patient visits. Approximately 60% of clients are African American. Subjects were recruited from the waiting room.

The Indiana University Medical Group (IUMG) is a health maintenance organization operated by the faculty of the School of Medicine. The suburban IUMG clinic used in this study serves a population that is 2% African American, whereas the population served by the urban clinic is 11% African American. Subjects were recruited from the waiting rooms of these clinics.

The Cincinnati Children's Hospital Medical Center (CCHMC) adolescent clinic handles over 5000 patient encounters yearly for residents from Ohio, Kentucky, and Indiana. The patients are 52% African American and 46% white. Healthcare providers in the adolescent clinic recruited adolescents through patient records and through the use of "snowball" recruitment techniques. To ensure recruitment of adequate numbers of adolescent males, adolescents who participated in this research study were asked to provide the names, addresses, and telephone numbers of any adolescent male friends who might be interested in participating in the study. Inclusion and exclusion criteria and study procedures, including parental permission, for these male participants were identical to those procedures used to recruit from the CCHMC clinic. Adolescents came to the clinic specifically for participation in the research (questionnaire completion). For those adolescents who elected to undergo HSV-2 screening, telephone consent from a parent was obtained before venipuncture was performed.

The University of Cincinnati (UC) had a total enrollment in 1998–1999 of 33,747 students, including 3837 African Americans, 1000 Asians, and 353 Hispanics. University students were recruited for participation in the questionnaire study through the use of e-mail and print advertisements, which were placed on bulletin boards and in the student newspaper.

This study was approved by Institutional Review Boards at Indiana University, CCHMC, and the Centers for Disease Control and Prevention. The subjects included in this study were recruited through a 2-step consent process. During step 1, participants were recruited to complete a self-report written questionnaire on attitudes about sexually transmitted diseases. Each Indianapolis participant received $15 reimbursement for the time and effort involved in completing the questionnaire. Given that Cincinnati participants were not recruited from clinic waiting rooms and therefore required additional time and effort to participate, each Cincinnati participant received $20 reimbursement. On completion of the questionnaire, participants were offered a free blood test for detection of HSV-2 antibody. No compensation was provided for agreeing to the HSV-2 antibody test.

### *Measures*

Potential predictors of acceptance of HSV-2 testing were measured by a written self-administered questionnaire. Scales and items were developed based on health belief theories and prior empiric research on HIV testing acceptance[21] and STD vaccine acceptability.[22]

*Knowledge and Beliefs.* Knowledge about genital herpes was measured with 13 true–false items that addressed a broad range of issues, including modes of transmission, symptoms, treatment, and life course. A knowledge scale was constructed by summing across the 13 items. Health belief items all were presented with a 5-point response format ranging from "strongly disagree" to "strongly agree." Constructs measured included perceived severity of genital herpes (7 items, $\alpha = 0.80$), perceived vulnerability to infection (4 items, $\alpha = 0.86$), perceived benefit of getting a test for genital herpes (2 items, $\alpha = 0.61$), fear of needles/injections (3 items, $\alpha = 0.85$), perceived stigma associated with getting an STD (11 items, $\alpha = 0.78$), and the perception that genital herpes would interfere with the establishment or maintenance of an intimate relationship (5 items, $\alpha = 0.84$).

*Sex Behavior, Sexually Transmitted Disease History, and Genital Symptomatology.* Participants were asked their number of sex partners in the last 6 months, the number of times they had sexual intercourse in the last 3 months, and the number of times a condom was used during those incidents of sexual intercourse. Potential exposure to an STD (ie, number of noncondom protected events) was measured by subtracting frequency of condom use from frequency of sexual intercourse.

To assess STD history, participants were asked to indicate if they had ever had any of 9 STDs or STD-related conditions, including chlamydia, gonorrhea, syphilis, trichomoniasis, cervical dysplasia, venereal warts, HIV/AIDS, pelvic inflammatory disease, and pubic lice or "crabs." For the purposes of data analysis, a response of "yes" to 1 or more items was considered indicative of a history of STD.

Keeping in mind that study entry criteria excluded all individuals with a known history of genital herpes, experiences of genital symptoms suggestive of genital herpes were measured with 4 items relevant to both male and female participants ($\alpha = 0.69$). Symptoms assessed were pain, itching, burning, and rashes in the genital region, buttocks, or upper thighs. A 6-point frequency-based response format was used, which ranged from "almost never (less than yearly)" to "very often (monthly or more)."

*Outcome.* The outcome was acceptance or rejection of venipuncture for the purpose of HSV-2 antibody testing. The test used was HerpeSelect enzyme-linked immunoassay for HSV-2 (Focus Technologies, Cypress, CA). Assays were interpreted according to the manufacturer's instructions. It is important to note that this particular test does not detect HSV-1 antibody. Genital herpes

infections resulting from HSV-1, therefore, were not identified in this study. Although HSV-1 is associated with an increasing number of genital herpes infections,[23] the course of disease is typically much less severe than disease caused by HSV-2.[24] Positive tests were confirmed by Western blot.[25]

*Statistical Methods*

Each of the 4 recruitment sites was selected to represent a unique target population. To adequately depict the differential demographic composition of the study sample at each recruitment site, we report the age, sex, and race distribution by site, along with site-specific HSV-2 test acceptance rates in Table 1.

Initial univariate analyses were carried out to examine the association of each predictor with acceptance of HSV-2 testing. Continuous predictors (eg, age and attitudinal scales) were evaluated by *t* tests, whereas categorical variables (eg, sex, race, STD history, data collection site, and number of sex partners) were evaluated with chi-squared tests. Multivariable logistic regression models were used to identify independent predictors of acceptance of the HSV-2 antibody testing in the study population. The logistic regression models used acceptance as the response variable. Demographic, attitudinal, and behavioral factors entered the model as covariates. Forward, backward, and stepwise model selection procedures were then performed to determine the effects of inclusion or elimination of a variable in the final model. A significance level of 0.05 was used as the criterion for variables to enter the regression model (for forward and stepwise procedures) and for variables to remain in the regression model (for backward and stepwise procedures). The 3 model-selection procedures produced the same final model. The implementation of model fitting and selections were all carried out by PROC LOGISTIC in SAS.[26]

Two of the covariates were considered categorical variables with multiple levels. Clinical site was a nominal variable that contained 4 levels (each of which represented an individual recruiting site). Number of sex partners in the past 6 months was categorized into 3 levels: no sex partner, 1 partner, and more than 1 partner. In the logistic regression analysis, a reference level was designated for each of these multilevel categorical variables; other levels of the variable were then compared with the reference level.

## Results

Sample demographics by data collection site are presented in Table 1. Overall, the 1199 participants were 59% female, 61% non-Hispanic white, and 36% African American. Participants were 14 to 30 years of age (mean, 21.8; standard deviation, 3.8). HSV-2 screening acceptance rates ranged from 47.7% at the adult general medical clinics to 91.7% at the STD clinic, with an overall rate of acceptance of 68.4%. Of those screened for HSV-2, 12.9% tested positive. Issues related to testing positive for HSV-2 are reported elsewhere.[27]

Results of the univariate analyses indicated that compared with those who refused testing, individuals who agreed to HSV-2 testing were older, had less fear of needles, greater perceived vulnerability to HSV infection, and were more likely to see testing as beneficial. In addition, acceptors reported more genital symptoms, more sexual partners over the previous 6 months, were more likely to report a history of STD, and were more likely to be recruited from the STD clinic. The complete results from the univariate analyses are reported in Table 2.

Table 3 lists all of the covariates that the logistic regression model selection process identified as significant independent predictors of HSV-2 test acceptance, along with their odds ratios and 95% confidence intervals. The adequacy of model fit was assessed with the Hosmer and Lemeshow goodness-of-fit test. The test resulted in a chi-square of 10.50 with a *P* value of 0.23, indicating an adequate fit of the model to the data (ie, the model does not deviate significantly from the data).[28]

Among the demographic predictors, female sex, white race, and older age were associated with higher rates of acceptance. Although sex and race were not significant at the univariate level, they emerged as significant predictors in the multivariable analysis as a result of their associations with other predictors such as clinic and STD history. Female participants were 1.71 times more likely than males to accept the testing. Non-Hispanic whites were 1.47 times more likely to accept the testing than others. Each 1-year increase in age was associated with a 1.07 increase in the probability of test acceptance. Among the sexual history and behavior measures, more sexual partners was independently predictive of test acceptance, whereas attending the general medical clinic was associated with refusal of testing. Participants with 1 partner in the last 6 months were 2.65 times more likely to accept testing than were those with no partners. Individuals with more than 1 partner were 3.13 times more likely to accept than those with no partners over the previous 6 months. Moreover, those who had STD histories were 1.44 times more likely to accept the testing. Compared with participants recruited from the STD clinic, those recruited from the general medical clinics were nearly 10 times less likely to accept serologic testing.

Among the knowledge and belief measures, increases in perceived vulnerability to HSV-2 infection and perceived benefits of HSV-2 testing predicted acceptance of the test, whereas increased fear of needles predicted nonacceptance. The odds ratio associated with a 1-point increase in the vulnerability score was 1.10 and the odds ratio associated with a 1-point increase in the benefit score was 1.29. In contrast, the odds ratio associated with a 1-point increase in the fear-of-needle score was 0.89.

## Discussion

The results of this study suggest that a substantial percentage of individuals with no history of genital herpes, across clinical settings, will agree to a free offer of HSV-2 antibody testing. Not surprisingly, interest was strongest among participants attending

TABLE 1. Sample Demographic Characteristics and Test Acceptance Rates by Data Collection Site

| Site | N | % Female | % Non-Hispanic White | % African-American | Mean Age (SD) | % HSV-2 Test Acceptance |
|---|---|---|---|---|---|---|
| STD clinic | 336 | 46.3 | 51.9 | 45.9 | 23.1 (3.6) | 91.7 |
| General medical clinics | 327 | 81.0 | 85.3 | 12.0 | 23.1 (3.6) | 47.7 |
| College campus | 315 | 57.8 | 78.2 | 18.0 | 22.2 (2.8) | 70.2 |
| Adolescent medical clinic | 221 | 49.8 | 18.9 | 80.7 | 17.5 (1.7) | 61.1 |
| Total sample | 1,199 | 59.4 | 61.4 | 36.2 | 21.8 (3.8) | 68.4 |

TABLE 2. Univariate Associations With HSV-2 Serological Test Acceptance*

| Variable | Acceptors (n = 820) | Non-Acceptors (n = 379) | *P* Value |
|---|---|---|---|
| Sex | | | NS |
| Male | 70% | 30% | |
| Female | 68% | 32% | |
| Age | 22.1 (3.7) | 21.2 (3.8) | <0.001 |
| Race | | | NS |
| Non-Hispanic white | 68% | 32% | |
| Others | 69% | 31% | |
| Site | | | <0.0001 |
| STD clinic | 92% | 8% | |
| General med clinics | 48% | 52% | |
| College campus | 70% | 30% | |
| Adolescent clinic | 61% | 39% | |
| Knowledge | 11.6 (1.5) | 11.5 (1.6) | NS |
| Severity | 19.9 (5.6) | 20.5 (5.6) | NS |
| Vulnerability | 9.4 (4.3) | 7.0 (3.1) | <0.0001 |
| Benefits | 8.3 (1.7) | 7.4 (1.9) | <0.0001 |
| Fear of needles | 7.2 (3.1) | 8.2 (3.4) | <0.0001 |
| STD stigma | 2.0 (2.2) | 2.2 (2.6) | NS |
| Relationship interference | 18.2 (4.6) | 18.2 (4.6) | NS |
| Non-condom protected sex | 18.3 (38.4) | 12.6 (23.4) | <0.01 |
| Genital symptoms | 1.9 (2.9) | 1.2 (2.4) | <0.0001 |
| STD history | | | <0.0001 |
| Yes | 80% | 20% | |
| No | 63% | 37% | |
| No. of partners in last 6 mo | | | <0.0001 |
| 0 | 44% | 56% | |
| 1 | 67% | 33% | |
| >1 | 80% | 20% | |

*Data are expressed as mean (SD) unless otherwise noted.

TABLE 3. Factors independently associated with HSV-2 serological test acceptance: Multiple variable logistic regression results

| Variable | Odds Ratio | 95% Confidence Interval | *P* Value |
|---|---|---|---|
| Sex | | | |
| Male* | 1 | | |
| Female | 1.71 | 1.23–2.38 | <0.01 |
| Age | 1.07 | 1.02–1.12 | <0.01 |
| Site | | | |
| STD clinic* | 1 | | |
| General med clinics | 0.11 | 0.06–0.18 | <0.001 |
| College campus | 0.42 | 0.25–0.72 | <0.01 |
| Adolescent clinic | 0.38 | 0.22–0.68 | <0.001 |
| Vulnerability | 1.15 | 1.05–1.15 | <0.001 |
| Benefits | 1.29 | 1.19–1.41 | <0.001 |
| Fear of Needles | 0.89 | 0.85–0.93 | <0.001 |
| Race | | | |
| Non-Hispanic white* | 1 | | |
| Others | 0.68 | 0.48–0.97 | <0.05 |
| STD history | | | |
| Yes* | 1 | | |
| No | 1.44 | 1.01–2.07 | <0.05 |
| No. of Partners in last 6 mo | | | |
| 0* | 1 | | |
| 1 | 2.65 | 1.69–4.14 | <0.001 |
| >1 | 3.13 | 1.84–5.30 | <0.001 |

*Reference category.

the STD clinic, with 92% of participants agreeing to the test. However, among the participants recruited from the general medical clinics, less than 50% decided to accept testing. It is possible that the relatively higher acceptability among the STD clinic participants related to the fact that only at this site was drawing blood a routine part of the clinic procedure, so all subjects had blood drawn whether they accepted HSV-2 antibody testing or not. At all other sites, the blood draw was more likely to be an additional procedure not otherwise required.

Individuals most likely to accept HSV-2 serologic testing were characterized by a variety of demographic, behavioral, and attitudinal factors. Female participants and individuals closer to the upper age range in this study (30 years of age) were more likely to agree to be tested. It may be that women are more amenable to testing because of an awareness of greater vulnerability to many sexually transmitted infections, an orientation to reproductive health care, and/or greater concern about the risks of neonatal herpes. Older individuals may be aware of cumulative risk for HSV-2 infection over time and therefore have a greater interest in testing. African American participants were less likely to agree to serologic testing. In light of the relatively higher prevalence of HSV-2 infection among African Americans, it would appear to be important to gain a better understanding of barriers to testing among African Americans and to develop interventions to overcome these barriers.

Those who recognized their potential increased behavioral/historical risk for infection (more noncondom-protected intercourse and more sexual partners) were more accepting of serologic testing. Furthermore, those who perceived themselves to be at risk, independent of their actual behavioral/historical risk, were also more likely to accept the test, as were those who perceived testing to be beneficial to their health. Finally, participants who reported greater fear of needles were less likely to agree to serologic testing. In general, the factors identified as significant predictors of accep-

tance of HSV-2 serologic testing are similar to those identified in HIV antibody testing research.[21]

These data suggest that some aspects of HSV-2 test acceptance are amenable to public health and clinical intervention. Public health education programs could emphasize the potential benefits of testing, including diagnosis of persons with unrecognized HSV infection for whom suppressive therapy might reduce transmission to sex partners. Tailored risk appraisal and counseling, similar to successful programs for HIV risk reduction, should be designed and evaluated. Tailored risk appraisal coupled with brief office-based interventions (eg, motivational interviewing[29]) would allow accurate assessment of risk along with a personalized plan for risk management that might include HSV-2 screening. Such a program would require counselors trained to recognize and manage anxiety associated with testing. Provision of appropriate supportive services for those testing positive would also be a necessary part of any HSV-2 screening program. In addition, healthcare providers may be in a position to take advantage of coincident opportunities, which may help to overcome reluctance related to dislike of venipuncture. Given that fear of needles was identified as a significant barrier to test acceptance, the offer of HSV-2 testing when blood has to be drawn for other reasons may be 1 way to optimize acceptance.

There are a number of limitations to this study, which suggest that the results should be interpreted with some caution. First of all, although we found a relatively high rate of acceptance and identified demographic, behavioral, historical, and attitudinal characteristics associated with the decision to undergo serologic testing, this study clearly does not address the issue of when, with whom, and in what way HSV-2 serologic testing should be offered. Second, although our subjects represented a diverse group of individuals, they were not randomly selected or necessarily representative of the larger population of potential subjects. For example, we did not include pregnant women and their partners, which are important groups to consider for HSV-2 serologic testing given the problem of neonatal herpes.

Factors other than those identified in this study might be more relevant for other populations such as pregnant women. There may also be unique issues and considerations that motivate testing. Finally, it is possible that elements of the study design might have influenced acceptance of HSV-2 serologic testing. Offering the test for free might have prompted some to accept the test who would have declined it had it been associated with out-of-pocket cost. Likewise, the questionnaire itself might have sensitized the subjects in this study to issues related to herpes and other sexually transmitted infections, thereby artificially inflating HSV-2 serologic testing acceptance rates. Although this potential problem clearly is unavoidable in this type of research, the acceptance results should be considered with the sensitization issue in mind. Despite the various limitations noted here, the results of this research study provide new and important information that will help to guide the development of future HSV-2 serologic testing programs and research.

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