Implementation of Routine Access to Herpes Simplex Virus Type 2 Antibody Testing in a Public Health Sexually Transmitted Disease Clinic

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Background: Testing for herpes simplex virus type 2 (HSV-2) antibody is not common in clinical practice. Client characteristics associated with HSV-2 rapid antibody test uptake and test positivity were analyzed in clients attending an urban sexually transmitted disease clinic.

Methods: This optional test was available for $30. The HerpeSelect Express assay was performed on serum. Demographic and behavioral characteristics were compared between clients who requested testing and those who did not and between those who were HSV-2 antibody positive and negative.

Results: In 4 months, 3498 individuals attended the clinic and 443 (12.7%) opted for HSV-2 testing. Clients who were black, younger, or female were less likely to request testing. Recent sexual behavior and self-reported sexual orientation were not associated with uptake of testing. Of the 442 clients with results available, 109 were positive for HSV-2 antibody (24.7%). Women were significantly ($P < 0.001$) more likely to test positive; 42 of 111 (38.4%) versus only 67 of 331 (20.2%) men. A positive HSV-2 antibody test was also associated with increasing age and black race. There was an association with the number of partners in the last 30 days, but no association with the number of partners in the last year. Of the 109 clients who had a positive HSV-2 antibody test, 71 (64.5%) accepted a prescription for suppressive acyclovir therapy.

Conclusions: Uptake of testing was modest in this population, especially among the highest risk individuals, possibly due to the cost of the test. Improved education regarding HSV-2 and subsidized testing may be needed in the populations that have the highest prevalence in order to encourage testing.

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Genital herpes remains a highly prevalent sexually transmitted infection. Nearly 22% of the US population over the age of 12 had serologic evidence of herpes simplex virus type 2 (HSV-2) infection,[1] according to the National Health and Nutrition Examination Survey III conducted between 1988 and 1994. A more recent version of the same survey conducted between 1999 and 2004 suggests that the prevalence has declined somewhat to about 17%.[2]

Because testing for HSV-2 antibody is not done commonly in clinical practice or in most municipal sexually transmitted disease (STD) clinics, most people do not know their HSV-2 serostatus. In the National Health and Nutrition Examination Survey III study, only about 10% of persons who were HSV-2 antibody positive gave a history of having been diagnosed with genital herpes.[1] In the 1999–2004 survey, 14.3% of the HSV-2 seropositive persons had an earlier diagnosis of genital herpes.[2] Although this was a statistically significant increase in the proportion that was aware of their status, the majority of HSV-2 seropositive persons remain unaware of their diagnosis. Most individuals who are HSV-2 antibody positive shed virus from the genital tract even in the absence of recognized symptoms.[3,4] These individuals are probably responsible for a large fraction of new HSV-2 infections because they are not aware that they are contagious.[5]

Assuming that a reduction in HSV-2 incidence and prevalence would be desirable, a necessary component of any program to reduce these infections is a strategy for serologic screening for HSV-2 to identify individuals who are HSV-2 positive, but are unaware of their infection as well as those who are at risk for becoming infected. Our studies have shown that there is interest among persons with no history of genital herpes in being tested for HSV-2 antibody, but the interest varies in different populations.[6] Furthermore, among persons willing to be tested for HSV-2 antibody, many failed to return to obtain their test results, including individuals who were at increased risk of having a positive test.[7] This suggests that a point-of-care test that can be done rapidly might be more successful in a control program than a test for which the patient must return for their results.

We report here our experience in implementing a program for access to HSV-2 antibody testing in an urban public health STD clinic. We report on staff training aspects of the implementation, laboratory logistic aspects, and the characteristics of the clinic clients utilizing the service.

PARTICIPANTS AND METHODS

Participants

Persons presenting to the Bell Flower Clinic, a dedicated STD clinic operated by the Marion County (Indiana) Health

Department were offered testing for HSV-2 antibody during their clinic visit for a fee (in addition to the basic service fee paid by all clinic attendees). The data reported here were collected between June 2, 2008 and September 30, 2008, the 4 months after implementation of the HSV-2 testing program. For those clients requesting HSV-2 antibody testing, the test was performed on blood drawn for syphilis antibody testing and the HSV-2 result was provided to the client before they left the clinic. For this analysis, information and test results collected routinely from all clinic attendees during the study period on a standardized computer-based encounter form were extracted from the clinic database. If a client visited the clinic more than once during the reporting period, he/she was included only on their first visit. The medical record review that was conducted was approved by the local Institutional Review Board.

HSV-2 Antibody Testing

The testing was performed on serum using the HerpeSelect Express assay (Focus Diagnostics, Cypress, CA) according to the manufacturer's instructions. This is a rapid, type-specific, point-of-care test that reportedly has sensitivity and specificity comparable to the HerpeSelect 2 enzyme-linked immunosorbent assay (ELISA).[8] The test was performed in the diagnostic laboratory in the clinic on residual serum. All positive tests were confirmed by sending serum to another laboratory where testing was performed using the HerpeSelect 2 ELISA (Focus Diagnostics, Cypress, CA) using standard cutoff values.

Data Analysis

Statistical analysis was performed using SAS version 9 (SAS Institute, Cary, NC). All tests were performed as 2-sided at the 5% α level. Patient characteristics were analyzed for differences in testing uptake and test results. Gender was analyzed using a chi square test, age was analyzed using Student *t* test, and race/ethnicity was analyzed using logistic regression. Analysis of male sexual orientation was performed using Fisher exact test. Due to skewed data distributions, analyses of number of partners during the last 30 days and the last year were performed using the nonparametric Mann-Whitney *U* test.

RESULTS

Preparation to Implement HSV-2 Antibody Testing

The decision to offer HSV-2 antibody testing was made by the clinic leadership because of a combination of (1) requests by clients of the clinic for access to this test; (2) a desire to provide more comprehensive STD services; and (3) recognition of HSV-2 as an important cofactor for HIV transmission and the impact on the minority populations served by the clinic. The process described below took nearly a year, from first concept by a few individuals to initiation of testing in the clinic. A proposal to begin this testing was presented to the governing board of the clinic for approval once the basic outline of the procedure and realistic cost estimates were established. A series of training sessions was organized for the clinic staff to provide background information that would allow them to answer questions from clinic attendees. Part of these meetings were reserved for feedback sessions so that the staff could relate questions about herpes infections that they had heard in the past and so they could express any concerns they might have regarding the test and testing process. Staff at all levels were involved in the training sessions including intake and clerical staff; nurses, nurse practitioners, and other clinicians; disease intervention specialists and other outreach workers; other administrative staff; and laboratory personnel for a total of approximately 50 individuals. Each group had somewhat different needs and concerns that were addressed in these training sessions. Brief (less than 1 page) written materials were developed to be given to clients that explained in simple terms (in English or Spanish) the circumstances under which HSV-2 antibody testing might be appropriate. These materials also explained the additional charges for this test and the amount of time required. These materials were distributed to all clinic staff for comment on content and language before finalizing. Shortly before testing was to begin, another training session was held to review a variety of clinical scenarios to allow the clinicians to reinforce their knowledge base and increase their comfort level with providing counseling messages to different kinds of clients.

Logistics of HSV-2 Antibody Testing

Clients presenting to the clinic for STD care were given a brief written handout describing the availability of HSV-2 antibody testing and the circumstances under which testing may be desirable. They were also informed that there would be an additional charge of $30 (paid in cash) above the usual clinic administrative fee of $10 for the HSV-2 antibody test. Clients who desired HSV-2 antibody testing had both fees collected at the time of registration. Their charts were flagged so that the clinician who saw the client would request the HSV-2 test from the laboratory and the clients were instructed to wait for the result (as well as the results of any other rapid tests obtained as a part of their visit). Clients who decided to undergo HSV-2 antibody testing after meeting with the clinician could return to the registration desk and pay the fee to have the test performed during that visit. The HSV-2 test was conducted in the clinic laboratory and the result was reported to the clinician. For all positive tests, an aliquot of serum was saved for later confirmation by ELISA. All positive results were provided to the clients by a clinician; clients with positive HSV-2 antibody tests were told that the result was preliminary and they were instructed to call the clinic in 1 week for the results of the confirmatory test. Clients who had a positive rapid test and negative ELISA were instructed to have repeat testing (at no additional charge) in 2 to 3 months to determine if 1 test was falsely positive or negative. All clients were offered written material that contained information about transmission, condom use, treatment, and contact information for a local support group. They also had the opportunity to ask questions or receive additional counseling to help them understand the result of the test. Clients who tested positive for HSV-2 antibody were offered a prescription for acyclovir suppressive therapy, if they wished to use it. Prescriptions were written for generic acyclovir in doses and quantities such that the clients could have them filled at local pharmacy chains that provide low cost (typically, $4–$10) filling of prescriptions for certain common drugs. Clients were given a prescription for a 3-month supply of suppressive acyclovir and they were told that they would need to see a private health care provider if they wished to continue suppressive therapy beyond 3 months.

Characteristics of the Clients Who Chose to be Tested

During the first 4 months of testing, demand for HSV-2 antibody testing was stable at a median of 112 tests per month (range, 94–125). A total of 443 of 3498 (12.7%) clinic attend-

TABLE 1. Characteristics of Clients Requesting Testing for HSV 2 Antibody

Parameter	Tested for HSV 2 Antibody n (%)	Not Tested for HSV 2 Antibody n (%)	RR: Reference OR: Scale	RR/OR (95% CI)	*P*
Gender					
Male	332 (14.3)	1998 (87.7)			
Female	111 (9.5)	1057 (90.5)	Male	0.7 (0.5, 0.8)	<0.0001
Race/ethnicity*					
Black	129 (6.5)	1865 (93.5)	Reference	NA	
White	227 (19.9)	913 (80.1)	Black	3.1 (2.5, 3.8)	<0.0001
Hispanic†	74 (23.6)	240 (76.4)	Black	3.6 (2.8, 4.7)	<0.0001
MSM‡	23 (13.1)	152 (86.9)	No	0.9 (0.6, 1.4)	0.66
Age	33.2 (32.1, 34.2)§	29.8 (29.5, 30.2)§	Each 10 yr	1.3 (1.2, 1.4)	<0.0001
Partners in last 30 days	1.25 (1.14, 1.37)§	1.30 (1.26, 1.34)§	Every partner	1.0 (0.8, 1.1)	0.31
Partners in last year	3.99 (2.88, 5.10)§	3.29 (3.06, 3.52)§	Every 10 partners	1.1 (1.0, 1.3)	0.99

*Fifty-two clients were from other racial/ethnic groups, 13 (25%) were tested for HSV 2 antibody.
†Exclusive category, not included with white or black group.
‡Men who have sex with men.
§Mean value (95% confidence interval).
RR indicates relative risk; OR, odds ratio; CI, confidence interval.

ees during that time requested HSV-2 antibody testing. The demographic and behavioral characteristics of clients requesting HSV-2 antibody testing are shown in Table 1 and are compared with the demographics of clinic attendees who were not tested during the same time period. Clients who were older, male, and white, or Hispanic were more likely to request HSV-2 antibody testing. Pairwise comparisons by race showed that black clients were significantly less likely than either white or Hispanic clients to request testing. There was no association with the number of recent sexual partners and men who have sex with men were no more likely to request testing than were other men. There was also no association with a history of a new sex partner in the last 30 days (data not shown). A total of 452 clients were tested for HSV-2 in this time period, but 9 clients were tested on visits other than their first.

Demographic and Behavioral Features Associated With a Positive Test

Of the 443 clients tested for HSV-2 antibody, results were available for 442; 109 were positive (24.7%). There were 3 positive rapid tests (2.7%) that failed to confirm as positive by ELISA. For the analysis presented here, the 3 that failed to confirm are considered HSV-2 antibody negative. There was a considerable gender difference with 42 of 112 (37.8%) women positive for HSV-2 antibody but only 67 of 331 (20.2%) men HSV-2 antibody positive ($P < 0.001$). Several demographic and behavioral features of the clients who chose to be tested were examined to identify factors associated with a positive HSV-2 antibody test. These results are shown in Table 2. A positive HSV-2 antibody test was associated with increasing age and black race. Pairwise comparisons by race showed that black clients were significantly more likely than either white or Hispanic clients to have a positive HSV-2 antibody test while there was no difference between whites and Hispanics. There was a borderline association with the number of partners in the last 30 days, but no association with the number of partners in the last year. Men who have sex with men had a lower prevalence of HSV-2 antibody than other men, but the difference was not significant. Only 6 clients (1.4%) reported a history of genital herpes before HSV-2 antibody testing, so very few

TABLE 2. Characteristics Associated With a Positive HSV 2 Antibody Test

Parameter	HSV 2 Antibody Positive n (%)	HSV 2 Antibody Negative n (%)	RR: Reference OR: Scale	RR/OR (95% CI)	*P*
Gender					
Male	67 (20.2)	264 (79.8)			
Female	42 (37.8)	69 (62.2)	Male	1.9 (1.4, 2.6)	0.0002
Race/ethnicity*					
Black	51 (39.5)	78 (60.5)	Reference	NA	NA
White	46 (20.4)	180 (79.7)	Black	0.5 (0.4, 0.7)	0.0001
Hispanic†	12 (16.2)	62 (83.8)	Black	0.4 (0.2, 0.7)	0.001
MSM‡	3 (13.0)	20 (87.0)	No	0.6 (0.2, 1.8)	0.59
Age	38.6 (36.5, 40.8)§	31.3 (30.2, 32.4)§	Each 10 yr	1.8 (1.5, 2.2)	<0.0001
Partners in last 30 days	1.44 (1.20, 1.68)§	1.19 (1.06, 1.32)§	Every partner	1.3 (1.0, 1.7)	0.04
Partners in last year	4.90 (1.93, 7.88)§	3.67 (2.58, 4.75)§	Every 10 partners	1.1 (0.9, 1.5)	0.14

*Thirteen clients from other racial/ethnic groups were all negative for HSV 2 antibody.
†Exclusive category, not included with white or black group.
‡Men who have sex with men.
§Mean value (95% confidence interval).
RR indicates relative risk; OR, odds ratio; CI, confidence interval.

clients were attempting to confirm a previously made diagnosis. Of those who reported a history of genital herpes, all were positive for HSV-2 antibody.

Uptake of Antiviral Therapy

Clients who were found to be positive for HSV-2 antibody were informed of the availability of suppressive antiviral therapy to prevent or control symptoms and to reduce the risk of transmission of HSV-2 to a sexual partner. Of the 109 clients who had a positive HSV-2 antibody test, 71 (65.1%) were given a prescription for suppressive acyclovir therapy. There is only limited anecdotal information about why the remaining clients did not receive a prescription for acyclovir. Some specifically declined treatment, but others may have not been offered the prescription for various reasons. A few were reportedly already receiving therapy. There is no information available on how many clients had these prescriptions filled or took the medication.

DISCUSSION

Most dedicated STD clinics in the United States are operated by local public health agencies that typically have very limited budgets for providing free or low cost diagnostic and treatment services. Although the mandate of most such clinics is the treatment and control of traditional STD pathogens, such as syphilis, gonorrhea, and Chlamydia (and, more recently, HIV) that are considered to be of major public health importance, most clinics also offer some diagnostic and treatment services for conditions of lower public health priority such as trichomoniasis, vaginal candidiasis, bacterial vaginosis, external genital warts, and exoparasites. Services for genital herpes may include clinical diagnosis of lesions and, in some cases, viral culture. Few clinics offer serologic testing for HSV antibodies. Type-specific antibody testing for HSV 1 and HSV-2 has been widely available for only a few years, and rapid, point-of-care testing has been even less available until very recently.

In an effort to expand available clinical services in a way that would be largely revenue neutral, we initiated a program to offer HSV-2 antibody testing at a cost that would be affordable to many of our clients. We felt that it was important to monitor the characteristics of clients requesting HSV-2 antibody testing to determine whether we were reaching the most appropriate populations.

The consistent demand for HSV-2 antibody testing by about 13% of our clients despite the additional $30 cost of the testing suggests that we are offering a desired service. Nearly all of the clients requesting testing did not have a history of genital herpes, suggesting that we were reaching individuals who were unsure of their serostatus and probably asymptomatically infected, an important group to identify in any control effort. The demographic group with the highest prevalence of HSV-2 antibody in our population as well as in other prevalence surveys,[2] black women, was the group that was least likely to request testing. Although we have no information about why this group was less likely to request testing, it is probable that cost played a significant role. In an earlier study conducted in this clinic, over 90% of clients accepted HSV-2 antibody testing when it was offered at no cost.[6] In the same study (that included other clinical sites in addition to this clinic), being older and female were associated with accepting HSV-2 antibody testing while being nonwhite was associated with decreased test acceptance.[6] A survey of acceptability of HSV-2 antibody testing suggested that cost was an important factor influencing acceptability.[9] These observations should be useful in constructing approaches to promoting appropriate HSV-2 antibody testing. However, it is likely that some type of subsidy to permit free or at least lower cost HSV-2 antibody testing to be performed will be a necessary component of a more comprehensive testing program. It is also possible that allowing other forms of payment such as credit or debit cards would improve uptake of testing. Anecdotal reports by the clinic staff suggested that some clients were interested in HSV-2 antibody testing, but did not have $30 in cash at the time of their visit.

On the basis of our previous experience with testing in this setting,[7] we used point-of-care testing as the most effective way to assure that our clients would get useful information. However, our previous experience was in the context of free HSV-2 antibody testing. It is possible that clients who paid for testing would be more motivated to access their results later by telephone if, for example, a lab-based test like the HSV-2 ELISA were used. This could be a topic for future study.

While planning this testing project, we felt obligated to provide clients who were newly found to be HSV-2 antibody positive with something in addition to counseling and education about genital herpes and referral to local support groups. On the basis of the data demonstrating that persons who are HSV-2 antibody positive but have no symptoms still shed HSV-2 from the genital tract almost as often as symptomatic persons[3,4] and that antiviral therapy reduces HSV-2 shedding in this population,[10,11] we felt that antiviral treatment was justified. We also thought that it was appropriate to suggest to clients that suppressive antiviral therapy used in conjunction with condoms might reduce the risk of transmitting HSV-2 to a susceptible partner, even though the study that demonstrated this reduction was conducted under somewhat different circumstances.[12] We found it interesting that nearly two-thirds of the HSV-2 antibody positive persons identified in our clinic accepted a prescription for suppressive acyclovir treatment. However, obtaining a prescription is only 1 step in initiating suppressive acyclovir therapy and we have no information about the proportion that actually started suppressive therapy. The only information we have is the anecdotal reports by our clinic staff of clients who have returned to clinic requesting refills of their acyclovir prescriptions, suggesting that at least some clients initiated suppressive therapy. However, because clients were told they would have to go elsewhere to get suppressive acyclovir after 3 months, we would not expect most to return to our clinic with such a request.

There are several limitations that should be noted. Because this analysis was conducted without outside funding, we were limited to information contained in the clinic database. We have no information on motivation for HSV-2 antibody testing or, perhaps more importantly, reasons clients chose not to be tested. Similarly, we have very limited information about why some clients accepted prescriptions for acyclovir treatment and some did not and no information about whether clients receiving acyclovir prescriptions ever took any of the medication. We do not know whether individuals found to be HSV-2 antibody positive modified their behavior or if they felt that the information about their HSV-2 antibody status was useful to them. These are all important questions that should be addressed in the future.

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