Light Microscopy, Culture, Molecular, and Serologic Methods for Detection of Herpes Simplex Virus

Neil W. Anderson, Blake W. Buchan, Nathan A. Ledeboer

Department of Pathology, Medical College of Wisconsin, and Dynacare Laboratories, Milwaukee, Wisconsin, USA

Herpes simplex virus 1 (HSV-1) and 2 (HSV-2) are members of the Herpesviridae family responsible for a variety of human diseases, ranging from mucocutaneous oral and genital lesions to fulminate encephalitis (1–3). The types of disease seen in patients depend on route of infection and individual host factors. Infection is relatively common, with seroprevalence approaching 80% for HSV-1 and 20% for HSV-2 in adult populations in the United States; however, prevalence can be much higher in certain demographics or in undeveloped countries (1, 4, 5). An important property of both viruses is the ability to establish latency following initial infection, leading to lifelong carriage (1–3). While there is currently no cure for latent infection, effective therapy exists for alleviating symptoms, shortening the duration of severe outbreaks, and treating some of the more life-threatening manifestations. Effective therapy for severe acute HSV infections hinges on rapid administration of appropriate antivirals. This creates the need to establish a prompt diagnosis and necessitates HSV diagnostic testing that is both rapid and sensitive (6–9). Testing must also be highly specific, since clinical manifestations of HSV are relatively nonspecific and overlap other potentially severe infections. Finally, while many tests are designed for use on mucocutaneous or skin lesions, there often is a need to test patients with rare or the patient is in pain. Sensitivity is also affected by the stage of the lesion, with the highest positivity rate being observed in early vesicular lesions (10). Even given proper sampling of vesicular lesions, a study by Durdu et al. reported a sensitivity of 84.7% in a comparison with serology and clinical findings (14). Another drawback of light microscopy is a lack of specificity. Indistinguishable CPE can be seen as a result of HSV-1, HSV-2, and varicella-zoster virus. Since the lesions caused by these organisms look similar, an effective test should be able to distinguish them from one another.

(ii) Cell culture. (a) Methods for cell culture-based detection of HSV. Prior to development of molecular methods, viral culture was the mainstay for diagnosis of acute HSV infection. Culture is dependent on the collection of a high-quality specimen, such as a swab or needle aspiration, as well as on proper transport and handling to maintain infectivity. Since the virus is enveloped and extremely labile, specimens collected using a swab must be transferred to suitable viral transport media (VTM), such as M4 (Thermo Fisher, Lenexa, KS), M6 (Thermo Fisher), or universal transport medium (UTM) (Copan, Brescia, Italy, or BD, Franklin Lakes, NJ). These media are buffered saline solutions containing albumin to aid in the stabilization of virions and are supplemented with antimicrobials, including amphotericin B, vancomycin, and colistin to reduce over-

Published ahead of print 16 October 2013

Editor: G.V. Doern

Address correspondence to Nathan A. Ledeboer, nledeboe@mcw.edu.

N.W.A. and B.W.B. contributed equally to this work.

Copyright © 2014, American Society for Microbiology. All Rights Reserved.

doi:10.1128/JCM.01966-13
growth of bacterial and fungal organisms that may be present in the specimen. Preservation of virus infectivity and reduction of overgrowth of other microbes is important when specimens will be used for cell culture. These issues are of less concern when a molecular method of detection is employed.

Following transport to the laboratory, an aliquot of specimen eluted in VTM is used to inoculate a susceptible cell line. Commonly used cell lines include Hep-2, A549, MRC-5, WI38, Vero, mink lung, rabbit kidney, and rhabdomyosarcoma cells and human diploid fibroblasts (12). Cultures of these cell lines vary in sensitivity for HSV isolation. A comparative study by Zhao et al. (11) showed that the sensitivities with both the rabbit kidney and mink lung cell lines (100% and 95%, respectively) at a low viral inoculum were higher than those with the MRC-5 and Vero cell lines (77% and 64%, respectively). Cultures are observed microscopically for CPE, including cell rounding, cytoplasmic granulation, syncytium formation, and eventually lysis (12). Virus typing is subsequently conducted using HSV-1 and -2 monoclonal antibodies (15, 16). Recovery of HSV from a lesion is evidence of acute infection. Virus-induced CPE using standard culture are typically detectable within 5 days, although they may require up to 14 days to become apparent (12). For cases that take longer to produce cytopathic effect, the use of an antigen detection system such as Herpchek (DuPont, Wilmington, DE) can decrease turnaround time (17). Shell vial culture also has a decreased average turnaround time, with high sensitivity achieved within 24 h (18).

The enzyme-linked virus-inducible system (ELVIS; Diagnostic Hybrids, Inc., USA) enables significantly faster turnaround than standard culture or shell vial methods, with similar performance characteristics (18). ELVIS relies on a genetically engineered host cell line carrying a lacZ (β-galactosidase) reporter gene whose expression is governed by the HSV UL39 promoter (18, 19). HSV infection induces expression of lacZ within the host cell, causing increased production of β-galactosidase. This enzyme then cleaves a colorimetric substrate, resulting in the development of a blue color in infected cells. Positive ELVIS cultures can be detected within 24 h of inoculation, and the method has been reported to be 88 to 100% sensitive and 98 to 100% specific in a comparison with standard viral culture (Table 1) (18, 20–22).

Direct immunofluorescence assays (DFA) can be performed directly on patient specimens, providing a method for same-day results. DFA specificity approaches 100%, while sensitivity ranged from 50 to 100% in a comparison with viral culture (Table 1) (23–27). The best use of DFA is in combination with culture, which can increase the overall sensitivity for HSV detection from about 50% when DFA is used alone to 80% when it is used in combination with cell culture (26).

Because of well-developed culture protocols and a lack of FDA-cleared PCR tests, viral culture remains an important method of diagnosis for many laboratories, and maintenance of viral culture capabilities by clinical laboratories is still recommended by some groups (28, 29). Additionally, the emergence of resistance to first-line antivirals, such as acyclovir, underscores the necessity to maintain viral culture capabilities.

(b) Factors affecting sensitivity and specificity of cell culture methods. The primary obstacle hindering high sensitivity in all culture-based and DFA tests is virus recovery. Recovery of virus from lesions can be highly variable and is dependent on the stage of the lesion as well as primary versus recurrent infection (3). The highest culture sensitivity can be achieved using specimens obtained from vesicular-stage lesions, when virus can be recovered in up to 95% of cases (26). Test sensitivity rapidly decreases when specimens are obtained from ulcerative (32 to 72%) and crusted (17 to 30%) lesions (3, 25–27). Additionally, lesions following primary infection can harbor a viral load 3 to 4 orders of magnitude higher than recurrent lesions (3). Thus, virus recovery and subsequent culture sensitivity can be significantly lower from recurrent than from primary HSV lesions (26).

(iii) Molecular methods. (a) Targets. Molecular diagnosis of acute HSV can be accomplished via amplification and detection of specific viral genome targets. Early real-time PCR assays targeted highly conserved regions of the herpesvirus DNA polymerase in order to amplify both HSV-1 and HSV-2 (30, 31). While sensitive and specific, this method was unable to differentiate HSV-1 from HSV-2 (30, 32). An early assay capable of molecular typing of HSV utilized a LightCycler (Roche, Indianapolis, IN) for PCR combined with melting point analysis and fluorescence resonance energy transfer (FRET) probes (33). These methods have proven to be more sensitive than viral culture and also effectively differentiate HSV-1 and HSV-2 without additional steps. An alternate approach described by Whiley et al. (34) used PCR followed by melt analysis of the gene encoding glycoprotein D (gD) for accurate typing. In a comparison study with DNA polymerase-based typing, this method allowed for 100% typing accuracy (96.8% accuracy for DNA polymerase typing). Another method for typing involves amplification of a highly conserved gene encoding a viral envelope protein required for virion fusion with a host cell, glycoprotein B (gB). As with the DNA polymerase typing and gD targeti
g, amplification of gB can be used to detect both HSV-1 and -2. Polymorphisms in this target allow for type-specific probes which can be used for subtyping. Namvar et al. describe a real-time PCR assay utilizing two different TaqMan probes, specific for HSV-1 or -2 (35). Compared to culture, this method demonstrated 99.5% sensitivity, with correct typing in all but one case (n = 217).

(b) Available tests. Currently only three FDA-cleared molecular tests for HSV-1 and -2 detection are available. The PCR-based MultiCode-RTx kit (Luminex, Austin, TX) for the detection of HSV-1 and -2 in vaginal swabs has a reported sensitivity of 92.4% and a specificity of 98.3% for the detection of HSV-1, as well as a sensitivity of 95.2% and specificity of 93.6% for the detection of HSV-2 (Table 2) (36). This test is cleared for vaginal swab samples of symptomatic females greater than 10 years of age. The ProbeTec HSV Q assay (BD) detects both HSV-1 and HSV-2 from anogenital lesions in both men and women. In a comparison with viral culture, the reported sensitivity and specificity for HSV-1 detection are 96.8% and 97.6%, respectively, while the reported sensitivity and specificity for HSV-2 detection are 98.4% and 83.7%, respectively (37). A study by Van Der Pol et al. (38) demonstrated that the BD ProbeTec HSV Q assay had a specificity of 97% for HSV-2 detection compared to that of another molecular method (38). A third test, the IsoAmp HSV assay (Biohelix, Beverly, MA), is FDA cleared for testing on both male and female genital or oral lesions. It uses isothermal helicase-dependent amplification of the HSV gB gene and detection with a target-specific colorimetric probe. Compared to ELVIS, this assay had 97.1% sensitivity and 93.4% specificity for detecting HSV-1 or HSV-2 from genital lesions (39). An advantage of this assay is that it does not require thermocycling, allowing it to be performed using only a heat block (40). A potential drawback to this assay is its inability to distinguish between HSV-1 and HSV-2, which can have implications for patient management, given the higher rate of recurrence of HSV-2 than of HSV-1 in genital ulcers. Tong et al. (41) describe a modified version of this assay, known as the IsoClow HSV

---

**TABLE 1 Comparison of culture-based and direct fluorescence-based HSV detection assays**

<table>
<thead>
<tr>
<th>Detection assay (vs standard or shell vial culture) and type status</th>
<th>Sensitivity or range (%) for:</th>
<th>Specificity or range (%) for:</th>
</tr>
</thead>
<tbody>
<tr>
<td>ELVIS</td>
<td>HSV-1</td>
<td>HSV-2</td>
</tr>
<tr>
<td>Typing</td>
<td>92.9</td>
<td>100</td>
</tr>
<tr>
<td>Not typing</td>
<td>88.0–95.0</td>
<td>98.6–100</td>
</tr>
<tr>
<td>DFA</td>
<td>Typing</td>
<td>53.9–75.8</td>
</tr>
<tr>
<td>Not typing</td>
<td>76.6–96.0</td>
<td>90.0–100</td>
</tr>
</tbody>
</table>

*ELVIS, enzyme-linked inducible virus system; DFA, direct immunofluorescence assay; NR, not reported.*
Laboratories developed an efficacious use of PCR-based HSV detection is from CSF (4). While HSV from cutaneous and mucocutaneous lesions, perhaps the most clinically significant, are the most widely used for serologic diagnosis of HSV. However, ELISAs require a spectrophotometric plate reader for interpretation and also utilize a lack of internal positive controls that prohibit point-of-care testing in clinics or undeveloped regions of the world. Additionally, false-negative HSV-2 results, although rare, can occur in individuals who are seropositive for HSV-1. This is due to a strong amnestic response to HSV-1 common antigens, resulting in obscuring antibodies on the blot (49, 50).

Early enzyme-linked immunosorbent assays (ELISAs) also utilized whole-antigen preparations from HSV-1- or HSV-2-infected cell lines. These assays are sensitive (92 to 100%) and are less expensive, are easier to perform, and provide significantly faster turnaround than WB. However, a major drawback is the lack of specificity for HSV-1 and -2, which ranges from 61 to 85% (Table 3). This is due primarily to the use of whole-antigen preparations used to construct these assays. The advent of type-specific tests based on HSV glycoprotein G has rendered crude antigen-based assays obsolete.

(b) gG-based detection methods. Newer serologic methods incorporate type-specific assays based on HSV gG. These type-specific proteins are easily differentiated based upon an additional HSV-2-specific domain that is not present in HSV-1. Commercial, type-specific ELISAs utilize purified recombinant or native gG-1 and gG-2 for increased specificity. HSV-1 and -2 testing requires separate assays, which adds to workload but also provides versatility. The sensitivity and specificity for HSV-1 (69.0 to 98.8% and 93.8 to 99%, respectively) and HSV-2 (82.6 to 100% and 93.0 to 100%, respectively) can approach 100% when convalescent-phase serum is used (Table 2) (51–56). The availability of well-validated formats that accommodate high-throughput testing, a low per-test cost, and a rapid turnaround time of approximately 2 to 3 h have allowed this type of test to be the most widely used for serologic diagnosis of HSV. However, ELISAs require a spectrophotometric reader for interpretation and also utilize a lack of internal positive controls that prohibit point-of-care testing in clinics or undeveloped regions of the world. Additionally, false-negative HSV-2 results, although rare, can occur in individuals who are seropositive for HSV-1. This is due to a strong amnestic response to HSV-1 common antigens, resulting in obscuring antibodies on the blot (49, 50).

Table 2 Molecular assays for detection of HSV

<table>
<thead>
<tr>
<th>Test name</th>
<th>FDA approved</th>
<th>Targets</th>
<th>Patient population</th>
<th>Specimen type(s)</th>
<th>Sensitivities (%)</th>
<th>Specificities (%)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>LightCycler HSV 1/2 kit</td>
<td>No</td>
<td>HSV-1 and -2</td>
<td>Symptomatic patients</td>
<td>CSF and vesicle swabs</td>
<td>ND</td>
<td>ND</td>
<td>75</td>
</tr>
<tr>
<td>Affigen HSV 1/2 kit</td>
<td>No</td>
<td>HSV-1 and -2</td>
<td>Pediatric</td>
<td>Skin, respiratory, or genital swabs</td>
<td>ND</td>
<td>ND</td>
<td>76</td>
</tr>
<tr>
<td>LDT</td>
<td>No</td>
<td>HSV-1 and -2, HIV</td>
<td>Hospitalized patients</td>
<td>CSF</td>
<td>ND</td>
<td>ND</td>
<td>30</td>
</tr>
<tr>
<td>LDT</td>
<td>No</td>
<td>HSV-1 and -2, Treponema pallidum</td>
<td>Symptomatic patients</td>
<td>Genital lesion specimens</td>
<td>ND</td>
<td>ND</td>
<td>77</td>
</tr>
<tr>
<td>LDT</td>
<td>No</td>
<td>HSV-1 and -2, VZV</td>
<td>Women with genital ulcers</td>
<td>Cervical and vaginal swabs</td>
<td>ND</td>
<td>ND</td>
<td>31</td>
</tr>
<tr>
<td>LDT</td>
<td>No</td>
<td>HSV-1, -2, VZV, EBV, CMV, HHV-6 and -7</td>
<td>Symptomatic patients</td>
<td>Blood, CSF, serum, plasma</td>
<td>ND</td>
<td>ND</td>
<td>43</td>
</tr>
</tbody>
</table>

(a) Whole-antigen-based (non-gG-specific) detection methods. Western blotting (WB) assays have been described for serologic detection and differentiation of HSV-1 and -2. Whole-antigen preparations from HSV-1 or -2-infected cell lines are separated by electrophoresis, adsorbed to a nitrocellulose gel, and exposed to patient serum. HSV status is determined by banding patterns specific to HSV-1 or -2 (49). Specifically, the presence of a 92,000-M, band corresponding to HSV-2-specific glycoprotein G (gG) is a key factor in differentiating between HSV-1 and -2 infections. A significant drawback to WB is that assays are expensive and time-consuming (32). Additionally, false-negative HSV-2 results, although rare, can occur in individuals who are seropositive for HSV-1. This is due to a strong amnestic response to HSV-1 common antigens, resulting in obscuring antibodies on the blot (49, 50).

(b) gG-based detection methods. Newer serologic methods incorporate type-specific assays based on HSV gG. These type-specific proteins are easily differentiated based upon an additional HSV-2-specific domain that is not present in HSV-1. Commercial, type-specific ELISAs utilize purified recombinant or native gG-1 and gG-2 for increased specificity. HSV-1 and -2 testing requires separate assays, which adds to workload but also provides versatility. The sensitivity and specificity for HSV-1 (69.0 to 98.8% and 93.8 to 99%, respectively) and HSV-2 (82.6 to 100% and 93.0 to 100%, respectively) can approach 100% when convalescent-phase serum is used (Table 2) (51–56). The availability of well-validated formats that accommodate high-throughput testing, a low per-test cost, and a rapid turnaround time of approximately 2 to 3 h have allowed this type of test to be the most widely used for serologic diagnosis of HSV. However, ELISAs require a spectrophotometric plate reader for interpretation and also utilize a lack of internal positive controls that prohibit point-of-care testing in clinics or undeveloped regions of the world. Additionally, false-negative HSV-2 results, although rare, can occur in individuals who are seropositive for HSV-1. This is due to a strong amnestic response to HSV-1 common antigens, resulting in obscuring antibodies on the blot (49, 50).

Downloaded from http://jcm.asm.org/ on August 30, 2017 by guest.
spheres with different physical properties, i.e., size, fluorescence, and conjugation to a unique antigen, such as gG-1, gG-2, or a nonspecific control. Serum antibody binds a specific bead-antigen conjugate, and the complex is detected using flow cytometry (58). These assays are rapid (~120 min) and demonstrate high sensitivities and specificities for HSV-1 (95.8 to 99.2%) and HSV-2 (92.6%–98.3% and 85.5%–98.7%, respectively) compared to those of ELISAs (59, 60) (Table 2). In addition to a fully automated platform, a major advantage of MFIs is the inclusion of internal controls for calibration and nonspecific binding. This removes subjectivity and intertest variability encountered with rapid and standard ELISAs and reduces equivocal results. Like ELISAs, MFIs require laboratory instrumentation, which prevents point-of-care use. Additionally, MFIs have a high per-test cost and their throughput is low compared to that of the standard 96-well ELISA.

Rapid ELISAs, which do not require additional reagents or instrumentation, are available for point-of-care use and provide the fastest turnaround time, with results in approximately 6 min. Specificities of the tests are high (98.0% to 98.4%), but sensitivities can vary (59.0 to 96.0%), owing to the subjectivity of visual interpretation of test results (51, 61–63). Performance of these tests can also be affected by population characteristics, including geographic location and concurrent infection with other sexually transmitted disease etiologies (discussed later).

(c) Factors affecting the sensitivities and specificities of serologic detection methods. Because immunoassays are dependent on the presence of HSV antibodies, the sensitivities of these tests are affected by the time elapsed since initial infection. Optimal sensitivity is achieved when the test is conducted a minimum of 21 days after initial infection and may improve if the test is run >40 days after primary infection (49, 53, 64).

The specificity of type-specific (gG-based) tests may be dependent on regional and population characteristics. Studies conducted using populations from Kenya, Uganda, and South Africa all report reduced specificities of various HSV-2 ELISAs, ranging from 44.3 to 96.2% (32, 65, 66), of note, tests demonstrating the best specificities (>90%) within these populations often suffered reduced sensitivity (32, 66). A meta-analysis conducted by Biraro et al. includes data from 10 publications and further details these findings (67).

In populations with low HSV-2 endemicity, e.g., 3.4 to 13.0%, test specificity remains high; however, rare false-positive results combined with a low number of “true” HSV-2 infections can result in low positive predictive values (PPVs): 37.5 to 84.0% (52, 57). HSV-1 seropositivity has also been reported to affect the performance of HSV-2 ELISAs (51, 57). Modifying the ELISA fluorescence index value used to define a positive result or reflex testing of positive results using rapid antigen tests can increase the overall PPV of testing with minimal added effort and cost (57, 62). In one study, an increase in PPV from 80% to 96% was achieved when a rapid antigen test was used to confirm positive ELISA results.

HIV status of an individual does not appear to affect the performance of HSV ELISAs (66). This is an important point because of the high rate of coinfection and increased risk of transmission and acquisition of HIV by HSV-positive individuals (51, 68). Among other common sexually transmitted diseases, only coinfection with Neisseria gonorrhoeae significantly reduced HSV immunoassay performance (51).

(d) Other serological detection methods. An important limitation to the utility of HSV IgG-based serology is the challenge of result interpretation. The high overall prevalence of infection, which approaches 100% for HSV-1 in some demographics, makes differentiating between chronic carriage and acute disease challenging (1). IgM-based serology assays have been evaluated as a method to detect HSV infection at an early stage as well as to differentiate between chronic and acute infection. In one report, approximately 33% of early HSV-2 infections (~7 days following the appearance of lesions) and 8% of midphase infections (7 to 30 days) were positive for anti-HSV IgM only (69). Despite the ability to detect some early infections, the sensitivity and specificity of IgM-based tests can be as low as 74% and 90%, respectively, resulting in a positive predictive value of 71% (70). Additional factors also limit the utility of such tests to discriminate between recent and chronic infection. For example, anti-HSV IgM may persist for 48 to 89 days in some instances and can reappear following subsequent HSV episodes in up to one-third of infected individuals (69, 71, 72). Therefore, recent infection should be considered only if a positive IgM result is accompanied by a negative IgG result. Further, IgM may not be detectable in 50% of culture-confirmed initial infections (71).

---

### TABLE 3 Serology-based HSV detection assays

<table>
<thead>
<tr>
<th>Type test (manufacturer)</th>
<th>Sensitivity or range (%)</th>
<th>Specificity or range (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ELISAs with crude antigen</td>
<td>HSV-1</td>
<td>HSV-2</td>
</tr>
<tr>
<td>Immunoprecipitation HSV (Diamedix)</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>HSV-1 or 2 IgG (Inverness)</td>
<td>98.0</td>
<td>95.0</td>
</tr>
<tr>
<td>HSV-1 or 2 IgG enzyme immunoassay (Zeus Scientific)</td>
<td>92.0</td>
<td>98.0</td>
</tr>
<tr>
<td>gG-specific ELISAs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Premier HSV-1 or -2</td>
<td>98.0–98.8</td>
<td>90.0–83.2</td>
</tr>
<tr>
<td>HerpeSelect 1 or 2 (MRL/Focus Diagnostics)</td>
<td>69.0–98.2</td>
<td>82.6–100</td>
</tr>
<tr>
<td>Kalon HSV-2 ELISA (Kalon Biological)</td>
<td>NA</td>
<td>90.8–100</td>
</tr>
<tr>
<td>Rapid gG-specific ELISA</td>
<td>Sure-Vue HSV-2 (Biokit USA)</td>
<td>NA</td>
</tr>
<tr>
<td>Multiplex flow immunoassays</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AthenA Multi-Lyte HSV (Zeus Scientific)</td>
<td>95.8–99.2</td>
<td>92.6–97.4</td>
</tr>
<tr>
<td>BioPlex 2200 (Bio-Rad)</td>
<td>99.2</td>
<td>98.3</td>
</tr>
<tr>
<td>Plexus HerpeSelect (Focus Diagnostics)</td>
<td>96.5</td>
<td>93.2</td>
</tr>
</tbody>
</table>

---

a Formerly Wampole Laboratories.
b No longer available.
c Formerly POCkit HSV-2 (Diagnology).
DISCUSSION

HSV is one of the most common sexually transmitted diseases in the United States and worldwide. Clinical diagnosis of HSV-2 infection can be as low as 50%, and 50 to 90% of seropositive individuals do not report a history of lesions (73). Therefore, sensitive and accurate methods to detect and differentiate HSV-1 and -2 infections are critical.

The choice of assay is dependent on the purpose of the test. For diagnosis of acute lesions, nucleic acid amplification assays are most appropriate because of sensitivities superior to those of culture-based techniques. The use of serologic tests to diagnose suspected HSV-2 genital lesions is inappropriate because positive results may be due to chronic infection, while negative results may overlook recent infection. Further, the prevalence of HSV-1 as the cause of genital lesions in on the rise (74). Serologic tests are of value only for determination of past exposure to HSV-1 or -2 and should not be used to diagnose acute infection. The primary value of HSV serologic tests is in prenatal screening and as part of general screening for sexually transmitted diseases (STDs) in high-risk individuals to aid in prevention of transmission of the virus. If serology indicates HSV-2 infection, suppressive therapy may reduce asymptomatic shedding and potentially reduce transmission of the virus. Currently, routine screening of patients presenting to STD clinics is not conducted. Studies have suggested a negative psychological effect on individuals presented with a positive result, and appropriate counseling of these individuals is not often available.

In conclusion, there is a wide array of tests available for the detection of HSV. The diagnostic goals, patient population, specimen type, and environment in which the test will be used must all be considered when an appropriate test is selected. Selection of a test that best fits each situation will provide reliable results that can be trusted to guide patient management and therapy.

REFERENCES


Biohelix Corp. 2012. IsoAmp HSV assay product insert. Biohelix Corp, Beverly, MA.


Nathan A. Ledebor received his B.A. degree from Dordt College in 2000 and his Ph.D. degree in microbiology from the University of Iowa in 2005. Following 2 years of fellowship training in clinical and public health microbiology at Washington University School of Medicine in Saint Louis, MO, he became an assistant professor of pathology at the Medical College of Wisconsin and medical director of clinical microbiology and molecular diagnostics at Froedtert Hospital and Dycare Laboratories in Milwaukee, WI, where he has remained for more than 5 years. In addition to serving as director of clinical microbiology and molecular diagnostics at a large academic medical center, Ledebor continues to develop his research career. His research endeavors, particularly in the area developing diagnostic tools for infectious diseases, have led to numerous publications in peer-reviewed journals. He has been chair of public and professional affairs for the South Central Association for Clinical Microbiology and served on the American Society for Microbiology’s ad hoc review for numerous other journals in infectious diseases and clinical microbiology. He has delivered nearly 100 invited lectures in various medical-science educational forums worldwide and has served as an investigator on more than 75 funded research projects. In 2011, he received the distinguished Siemens Young Investigator Award from the American Society for Microbiology.