What is the best test to detect herpes in skin lesions?

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EVIDENCE-BASED ANSWER

Polymerase chain reaction (PCR) techniques appear to be more sensitive and specific in detecting herpes simplex virus (HSV) in genital lesions (strength of recommendation [SOR]: **A**, based on 2 diagnostic cohort studies); however, viral culture remains the gold standard (SOR: **C**, based on expert opinion). Studies of serologic and antibody detection tests report higher sensitivities than viral culture (SOR: **C**, based on consensus guidelines). Cytologic tests such as the Tzanck smear and Papanicolaou (Pap) smear have poor sensitivities and specificities and should not be relied upon for a diagnosis of genital herpes (SOR: **C**, based on expert opinion).

CLINICAL COMMENTARY

Test ulcers with culture or PCR

Genital and oral lesions consistent with herpes simplex lesions are relatively common in my practice. Before PCR testing was available, ulcers could be tested via culture—which took too long to be immediately useful—or via Tzanck smear, which helped greatly if multinucleated giant cells were seen. However, both tests were relatively insensitive. As this Clinical Inquiry demonstrates, ulcers currently should be tested either with culture or with PCR. Herpes culture is most sensitive if vesicles are still intact for unroofing.

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Evidence summary

More than 50 million individuals in the United States have genital herpes. The diagnosis of genital herpes based on clinical history and physical examination is often inaccurate.[1] Clinical suspicion needs to be confirmed by laboratory testing because it has a direct impact on counseling and prognosis.[2]

Viral culture is still the gold standard test for the detection of HSV; however, the rate of positive cultures depends on the stage of the lesion, the quality of the specimen, and the transport conditions. A British study[3] found the rate of virus recovery for early vesicles to be 52% to 93%. This dropped to 41% to 72% if midstage ulcers were present. Finally, the detection for late-stage crusted lesions was only 19% to 27%. Another disadvantage is that culture is labor-intensive. A positive culture takes an average of 3 days to grow, whereas a negative culture must incubate for 10 days.[3]

PCR techniques are more sensitive and results can be available in less than 4 hours.[3] In 110 clinical samples from dermal or genital lesions of patients with suspected HSV infection, the sensitivity of PCR was 98% (positive likelihood ratio [LR+] = ∞; negative likelihood ratio [LR–] = 0.02) compared with 73% (LR+ = ∞; LR– = 0.27) for culture. The specificities of both were 100%.[4] In London, 233 samples from patients at a genitourinary medicine clinic were tested with both viral culture

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FAST TRACK

Viral culture is still the gold standard, but PCR is more sensitive and faster (and may be less expensive due to decreased labor costs)

and PCR. HSV was detected in 79 samples by culture and 132 samples by PCR. The detection by PCR was higher in early as well as late stages of infection and in both first and recurrent episodes.[3] The reference standard for these studies was not an independent standard, but a positive result on both tests or modified versions of the PCR test. The use of a version of the test of interest (PCR) as part of the reference standard, while probably unavoidable in this situation, will tend inflate the sensitivity and specificity.

In another study, daily sampling of lesions in patients with known HSV infections detected HSV DNA on 15 of 17 days with PCR and only 3 of 17 days with culture.[1] This suggests that PCR is more effective in detecting early, as well as late, stages of infection. Currently PCR is more expensive, but it may become cheaper because of decreased labor expense when compared with culture.

Genital herpes may also be detected with enzyme immunoassay testing in as little as 5 hours. In a study[5] using 275 samples from genital lesions, HSV was detected in 65% of the antigen tests and 53% of the viral cultures. The sensitivity of this method is equal to culture for early lesions, but much higher in late-stage lesions (58% vs 26%).[5]

Serologic tests are often used to detect HSV because they can differentiate between HSV-1 and HSV-2. There is an FDA-approved point-of-care test called POCkit that gives results from capillary blood or serum during an office visit. These tests are 80% to 98% sensitive and more than 96% specific. Unfortunately, they are not readily available in all countries.[2]

Other detection methods include the Tzanck smear, which is only 40% to 50% sensitive compared with culture, and the Pap smear, which is 60% to 70% sensitive.[6] These tests should not be the sole method for the diagnosis of HSV. They cannot differentiate between HSV 1 and HSV 2; furthermore, the Tzanck prep will give a positive result if varicella zoster virus is present.[6] If these tests are positive, confirmatory testing specific for HSV should be performed.

Recommendations from Others

The Centers for Disease Control and Prevention[7] recommends screening with a viral culture when a genital lesion is present, however, the sensitivity declines rapidly within a few days as the lesion begins to heal. To collect a sample the lesion must be unroofed using a Dacron swab, which is then placed in a viral transport medium and processed within 24 hours. Swabs containing calcium agglutinate are toxic to HSV.[6] Type-specific antibodies develop during the first several weeks and can be detected with serologic tests; however, these may be falsely negative in the early stages of a primary infection.[7]

The US Preventative Services Task Force[8] recommends against routine serologic screening for HSV in asymptomatic adolescents and adults. They also recommend against routine screening of asymptomatic pregnant women at any time during pregnancy as a way to decrease neonatal transmission.[8]

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