

# What's the best test for HSV-2 after exposure?

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## Evidence-based answer

Enzyme-linked immunosorbent assay (ELISA) tests based on herpes simplex virus 2's (HSV-2) glycoprotein G have demonstrated high sensitivity and specificity in determining seropositivity for HSV-2 antibodies (strength of recommendation [SOR]: **C**, based on cross-sectional studies).

ELISA tests not based on glycoprotein G are also highly sensitive, but they are less specific for HSV-2 and are prone to false-

positive results because of cross-reactivity with HSV-1 antibodies (SOR: **C**, based on cross-sectional studies).

Random anogenital cultures are not sensitive for diagnosing HSV-2 infection (**TABLE**) (SOR: **B**, based on extrapolation from a well-designed prospective cohort study). No studies have found patient-oriented benefits to testing asymptomatic patients for HSV-2 infection.

## Clinical commentary

### Consider offering these tests to patients at high risk of coinfection with HSV

An estimated 1.6 million new cases of genital herpes are diagnosed annually. The viral shedding among asymptomatic patients poses a great challenge in controlling its transmission. Older methods of detecting HSV infection by non-glycoprotein G-based ELISA tests are nonspecific and do not differentiate between HSV-1 and HSV-2. The newer serologic tests that detect antibodies to HSV glycoproteins G1 and G2 are available for rapid detection and typing of genital herpes. Sensitivity and specificity of

these tests are also higher than older tests.

Although US Preventive Services Task Force (USPSTF) guidelines do not recommend routine screening of all patients for HSV, it's important that you consider offering these tests to patients at high risk of coinfection with HSV, such as those who are HIV-positive. Good-quality evidence demonstrates that systemic antiviral therapy along with condom use effectively reduces the viral shedding and therefore reduces the risk of genital HSV transmission.

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## FAST TRACK

**No studies found patient-oriented benefits to testing asymptomatic patients for HSV-2**

## Evidence summary

Our literature search failed to find any randomized controlled trials comparing diagnostic tests for HSV-2 infection among asymptomatic populations. Data from cross-sectional studies, however, are available.

### Glycoprotein G ELISA has better specificity

Using the Western blot technique as the gold standard, a total of 158 serum samples from patients with either HSV-1 or HSV-2 infection—without mention of symptomatology—were used to compare

TABLE

Summary of HSV test characteristics

TEST	SN (%)	SP (%)	LR+	COST (EST.)	TIME TO RESULT
Genital culture <sup>3</sup>	5*	100	NA <sup>†</sup>	\$90	24 hours
Western blot <sup>1,6</sup>	100	100	>99 <sup>‡</sup>	\$104	2 weeks
Glycoprotein G ELISA <sup>1,6</sup>	90–100	90–100	19 <sup>‡</sup>	\$4–\$20	1–2 weeks
Non-glycoprotein G ELISA <sup>1,6</sup>	95–100	60–85	3.5 <sup>‡</sup>	Not available	Not available

\* Calculation using development of symptoms as gold standard.

† Specificity=100%, so likelihood ratio = infinity and positive predictive value = 1.

‡ LR calculated based on median sensitivity and specificity from sources cited in table.

SN, sensitivity; SP, specificity; LR+, positive likelihood ratio; ELISA, enzyme-linked immunosorbent assay.

the performance of several commercially available ELISA assays.<sup>1</sup> The glycoprotein G and non-glycoprotein G ELISA tests were both found to have sensitivities >90%, but the non-glycoprotein G ELISA tests had specificities under 90%.

In 47% to 82% of the samples tested with non-glycoprotein G ELISA, there was cross-reactivity between HSV-1 and HSV-2 antibodies.<sup>1</sup> The College of American Pathologists found that 46% to 84% of laboratories using non-glycoprotein G ELISA tests incorrectly identified an HSV-1 sample as being HSV-2. All laboratories reporting use of glycoprotein G ELISA tests correctly identified the sample as containing only HSV-1 antibodies.<sup>2</sup> Neither study included controls, delineated symptom status, or measured patient-oriented outcomes.

#### Genital culture has poor sensitivity

A prospective cohort study compared the viral shedding by Western blot among 52 asymptomatic seropositive patients with 90 seropositive and symptomatic patients.<sup>3</sup> Daily genital swabs were done for 3 months for each patient. The asymptomatic individuals had HSV-2 positive cultures on 3% of culture days.<sup>3</sup> Genital culture appears to have a very poor sensitivity (5%) for diagnosis of HSV-2 infection among asymptomatic individuals.

We found no studies that measured patient-oriented harms or benefits arising from testing asymptomatic individuals for HSV-2 infection.

#### Recommendations from others

The USPSTF recommends against routine serological screening for HSV in asymptomatic adolescents and adults (D recommendation, fair or good evidence that the service is ineffective or that the harms outweigh the benefits).<sup>4</sup> The California Sexually Transmitted Diseases Controllers Association recommends that serologic testing is likely to benefit HIV-infected patients, those whose sexual partners have genital herpes, and those at high risk of STDs motivated to reduce their sexual risk behavior.<sup>5</sup> ■

#### References

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#### FAST TRACK

**46% to 84% of labs using non-glycoprotein G ELISA tests incorrectly identified HSV-1 as HSV-2**