

# Testing Options to Support Diagnosis and Screening of Herpes Simplex Virus (HSV)

## Key highlights

- HSV-1 and HSV-2 infections can be detected using several laboratory methods
- Culture and polymerase chain reaction (PCR) tests are useful when a lesion is present, and these methods can detect and often differentiate HSV-1 and HSV-2
- Type-specific serological tests that detect IgG responses to HSV-1 and HSV-2 are available to determine if a patient has been exposed to HSV-1 and/or HSV-2 in the past

## Introduction

Herpes simplex is a viral infection caused by herpes simplex virus (HSV) and characterized by systemic and local symptoms, including the formation of vesicular lesions where the virus is found in high concentrations. After a primary infection, HSV establishes latency and exhibits a tendency for localized recurrence. HSV is differentiated into two subtypes, HSV-1 and HSV-2, which generally produce distinct clinical syndromes, depending on the portal of entry. HSV-1 and HSV-2 can infect the genital tract and oral mucosa, although HSV-2 has been historically associated with genital infection.

HSV-1 and HSV-2 infections can be detected using several laboratory methods. Culture and polymerase chain reaction (PCR) tests are useful when a lesion is present, and these methods can detect and often differentiate HSV-1 and HSV-2. Type-specific serological tests that detect IgG antibody responses to HSV-1 and HSV-2 are available to determine if a patient has been exposed to HSV-1 and/or HSV-2 in the past. Best-practice recommendations for laboratory tests to diagnose HSV in different clinical scenarios are described below.

## Genital herpes

In the United States, the majority of sexually active patients presenting with genital or perianal ulcers have genital herpes or syphilis, with genital herpes being the most prevalent.<sup>1</sup> Genital herpes is a lifelong, chronic viral infection with most cases of recurrent genital herpes caused by infection with HSV-2. However, an increasing proportion of anogenital herpetic infections are attributed to HSV-1.<sup>1</sup> Diagnosis of genital HSV infections can be challenging as lesions are often absent at the time of clinical evaluation and symptoms can be absent or mild. Intermittent viral shedding can occur in the absence of symptoms, and most infections are believed to be transmitted by individuals who are either unaware that they are infected and/or asymptomatic at the time of transmission.<sup>1</sup> It is estimated that 11.9% of 14-49-year-olds in the U.S. are infected with HSV-2.<sup>1</sup>

Current guidelines and recommendations do not recommend routine screening for HSV-1 and/or HSV-2 in asymptomatic adolescents and adults, including those that are pregnant.<sup>1-3</sup> Screening using type-specific antibody assays may be useful in patients at higher risk of infection, including those who have (or have had) a sex partner with genital herpes or those seeking testing for sexually transmitted infections.<sup>1-2,4-5</sup> Additionally, type-specific serological testing can be useful for identifying pregnant individuals at increased risk for acquiring HSV-2 during pregnancy (e.g., have a partner with a known HSV-2 infection).<sup>1,3</sup> Type-specific HSV antibodies develop during the first weeks post infection and persist indefinitely.

- In individuals with genital, anal and/or perianal lesions, nucleic acid amplification testing (NAAT) or culture of lesion exudates or swabs should be used to confirm HSV infection.<sup>1,4</sup> NAAT for HSV-1 and HSV-2 is the recommended testing method as it is highly sensitive and specific.<sup>1,4</sup>
- In individuals without visible genital lesions, random genital swabs should not be submitted for NAAT or culture due to low sensitivity in the absence of visible lesions. In the absence of visible lesions, a negative result for HSV-1 and/or HSV-2 is insufficient for ruling out HSV infection.<sup>1</sup> Serological testing can be useful for diagnosis of HSV infection in individuals presenting without visible lesions but with a known exposure to HSV or with recurrent or atypical genital symptoms that are negative for HSV by NAAT and/or culture.<sup>1-2,4</sup> The use of IgM antibody testing for HSV-1 and/or HSV-2 is not recommended per current guidelines as IgM tests are not type-specific and have a higher rate of false-positivity, and the presence of IgM cannot differentiate between primary and recurrent infection.<sup>1-2,4,5</sup>

### **Herpes simplex CNS involvement**

Central nervous system (CNS) involvement may appear in association with primary HSV infection or during viral reactivation. HSV-1 is a cause of meningoencephalitis and HSV-2 has been associated with aseptic meningitis, myelitis and radiculitis. Diagnosis of HSV CNS infection can be confirmed by HSV NAAT, which is the preferred diagnostic approach since it is highly sensitive and specific. Moreover, NAATs for HSV can be performed within hours of CSF collection compared to days for viral cultures for HSV-1/HSV-2.<sup>1-4</sup>

### **Neonatal/congenital herpes simplex infections**

Neonatal herpes simplex infections can be present as disseminated infections involving multiple organs, encephalitis and/or localized infection of the skin, eyes or mouth.<sup>3</sup> Infections are most frequently due to HSV-2, but HSV-1 is also common. Typically, only HSV shedding at the time of delivery is dangerous to the newborn, although intrauterine infections can occur in rare instances. The risk of transmission is highest among individuals who acquire primary infection during the third trimester of pregnancy.<sup>1,3</sup> Congenital herpes infections can be diagnosed using NAAT performed on amniotic fluid specimens, neonatal blood specimens and swab specimens if herpetic lesions are visible at the time of delivery.<sup>1,3-4</sup>

Labcorp offers a variety of testing options to support the diagnosis of HSV-1 and HSV-2 infections. See the table on Page 3 for more details.

## Testing options for HSV-1 and HSV-2

Test No.	Test Name	Intended Use	Specimen Type(s)
<b>138651</b>	Herpes Simplex Virus (HSV) Types 1/2, DNA PCR	Aid in the diagnosis of acute HSV infection and differentiate between HSV-1 and HSV-2. PCR testing of blood, serum or plasma is clinically useful ONLY in potential cases of disseminated infection (neonates, immunosuppressed individuals) and not as an aid in the diagnosis of either mucosal or CNS disease. <sup>1,4</sup>	Swab in universal or viral transport media (UTM/VTM), whole blood, serum or plasma
<b>188056</b>	Herpes Simplex Virus (HSV) Types 1 and 2, NAA	Detection of active HSV-1 and HSV-2 shedding in genital or cervical specimens	Aptima® Swab Transport or ThinPrep® Liquid Cytology vial
<b>164099</b>	Herpes Simplex Virus (HSV) Types 1 and 2-Specific Antibodies, IgG	Detection of HSV-1 and HSV-2 type-specific IgG antibodies for determination of immunostatus and in cases of suspected exposure to HSV-1 and/or HSV-2 <sup>1-4</sup>	Serum
<b>164897</b>	Herpes Simplex Virus (HSV) Type 1-Specific Antibodies, IgG	Detection of HSV-1 type-specific IgG antibodies for determination of immunostatus and in cases of suspected exposure to HSV-1 <sup>1-4</sup>	Serum
<b>164098</b>	Herpes Simplex Virus (HSV) Type 2-Specific Antibodies, IgG	Detection of HSV-2 type-specific IgG antibodies for determination of immunostatus and in cases of suspected exposure to HSV-2 <sup>1-4</sup>	Serum
<b>138594</b>	Herpes Simplex Virus (HSV) Types 1/2, Amniotic Fluid, DNA PCR	Diagnosis of congenital HSV infection <sup>1,4</sup>	Amniotic fluid
<b>139800</b>	Herpes Simplex Virus (HSV) Types 1/2, Cerebrospinal Fluid (CSF), DNA PCR	Detection and differentiation of HSV-1 and HSV-2 DNA in cerebrospinal fluid to support diagnosis of HSV CNS disease (encephalitis and meningitis) <sup>1,4</sup>	Cerebrospinal Fluid (CSF)
<b>008250</b>	Herpes Simplex Virus (HSV) Culture and Typing	Aid in the diagnosis of acute HSV infection and differentiate between HSV-1 and HSV-2. Molecular methods (e.g., PCR, NAA) are recommended for the diagnosis of HSV-associated encephalitis, meningitis and congenital infection. <sup>1,4</sup>	Vesicular fluid, ulcerated lesions, pharyngeal and throat swabs, urine, CSF, autopsy and biopsy material, eye exudates, vaginal swabs

For additional testing options, or details about specimen requirements and CPT codes, visit our online Test Menu at [www.labcorp.com](http://www.labcorp.com).

### References

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4. Miller JM, Binnicker MJ, Campbell S, et al. A Guide to Utilization of the Microbiology Laboratory for Diagnosis of Infectious Diseases: 2018 Update by the Infectious Diseases Society of America and the American Society for Microbiology. *Clin Infect Dis*. 2018 Aug 31;67(6): e1-94.
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