

---

## Overview

### Useful For

An aid in the diagnosis of congenital herpes simplex virus (HSV) infection in patients younger than 35 days old through the recovery of HSV using viral culture (shell-vial)

### Method Name

Virus Culture by Shell-Vial

### NY State Available

Yes

## Specimen

### Specimen Type

Varies

### Ordering Guidance

**This test should only be performed on patients younger than 35 days old. It is intended for the recovery of herpes simplex virus in suspected cases of congenital herpes.**

If enterovirus or hand, foot, and mouth disease is suspected order test VIRNR / Viral Culture, Non-Respiratory. Indicate "Looking for Enterovirus" in order comments.

Spinal fluid (CSF) specimens: order HSVC / Herpes Simplex Virus (HSV), Molecular Detection, PCR, Spinal Fluid.

### Shipping Instructions

**Specimen must be transported at refrigerate temperature.**

### Necessary Information

**Specimen source is required.**

### Specimen Required

**Submit only 1 of the following specimens:**

**Specimen Type:** Swab

**Supplies:**

-M4-RT (T605)

-Bartels FlexTrans VTM-3 mL (T892)

-Jiangsu VTM-3 mL (T891)

**Sources:** Ocular, Rectal, Skin, Dermal, Mouth, Nasopharynx, Conjunctiva, Eye, Anus

**Container/Tube:** Multimicrobe media (M4-RT) (T605) or other viral transport media (M4 or M5)

**Specimen Volume:** Swab

**Collection Instructions:** Place swab back into multimicrobe media (M4-RT, M4, or M5)

**Additional Information:** Swab with a wood handle has been shown to be toxic to some viruses and is not acceptable for culture.

**Specimen Type:** Urine

**Container/Tube:** Sterile container

**Specimen Volume:** 1 mL

**Specimen Type:** Stool

**Container/Tube:** Sterile container

**Specimen Volume:** 5 to10 g

**Reject Due To**

Other   Frozen Swab with wood handle   Gel swabs   Blood   Bone marrow/bone Tissue   Lymph node

**Specimen Minimum Volume**

Stool: 5 g

Urine: 0.5 mL

**Specimen Stability Information**

Specimen Type	Temperature	Time	Special Container
Varies	Refrigerated (preferred)	7 days	

**Clinical & Interpretive****Clinical Information**

Herpes simplex virus (HSV) types 1 (HSV-1) and 2 (HSV-2) are DNA viruses that cause localized infections of the skin, oral mucosa, oral cavity, eyes, genital tract, and central nervous system (CNS).(1,2) Systemic disease may occur. Primary infection typically results in no symptoms or localized pain and lesions at the site of infection (usually the oral or genital areas). After a primary infection, the virus enters a latent state. Latent virus may or may not reactivate in the future. Typically, the primary infection is more severe than subsequent reactivations. However, not all individuals have symptoms during the primary infection and the first recognized symptoms may be in the setting of a reactivation.

HSV infections are common. Seroprevalence of HSV-1 and HSV-2 in the United States (2005-2010) is 53.9% and 15.7%, respectively.(3) HSV-1 has historically been associated with oral lesions, but increasingly it is also a cause of genital herpes. Both HSV-1 and HSV-2 can cause severe CNS disease. In particular, HSV encephalitis in neonates is considered a medical emergency. Even with antiviral medication, there is significant morbidity and mortality associated with HSV encephalitis, especially in neonates.

Fetal and neonatal HSV infections can be acquired in utero or at the time of delivery. The greatest risk for transmitting HSV is when the mother experiences a primary HSV infection, but there is also increased risk of transmission during periods of reactivation. Primary infection and reactivation may not be symptomatic, but nevertheless result in viral transmission to the fetus or newborn.

Diagnostic methods for HSV include routine viral culture, molecular testing by PCR, and serology. It is difficult to recover HSV from spinal fluid (CSF) specimens using viral culture, and a serologic response to HSV is not detectable immediately after infection.

Detection of HSV by real-time PCR is now recognized as the most sensitive approach to diagnose HSV infection, especially CNS-associated HSV disease. However, it is still recommended to test neonates by viral culture when testing for potential congenital herpes by peripheral (eg, skin) swab, since PCR may detect low levels of HSV DNA or inactive virus in the absence of infectious viral particles. Infants younger than 4 weeks of age may have detectable HSV DNA on them that was shed by an infected mother, even in the absence of active HSV infection in the infant. On the other hand, a positive result by viral culture indicates the presence of live virus, suggesting active infection in the newborn.(4)

**Reference Values**

No virus isolated

**Interpretation**

Recovery of herpes simplex virus (HSV) from clinical specimens supports the diagnosis of congenital HSV infection. A negative result by shell vial assay should be interpreted in the context of the patient's clinical presentation and exposure history. Furthermore, testing by real-time PCR for this virus should be considered prior to ruling out HSV disease.

**Cautions**

This test should not be performed on patients older than 4 weeks of age. It is intended for the recovery of herpes simplex virus (HSV) in suspected cases of congenital herpes. For patients older than 4 weeks of age, detection of HSV by real-time PCR is recommended.

A negative result does not rule out the possibility of congenital HSV infection.

Real-time PCR for HSV is the recommended test for all cases of central nervous system disease caused by this virus. Viral culture is an insensitive approach for detection of HSV in spinal fluid.

**Supportive Data**

Herpes simplex virus (HSV) shell-vial is a standard method that has been compared to real-time PCR in several published studies. Data from these studies suggest that real-time PCR increased the detection rate for HSV-1 and HSV-2 by up to 62.5%.<sup>(5,6)</sup>

Despite the increased sensitivity of real-time PCR compared to routine viral culture, detection of live virus may be useful in cases of suspected congenital herpes infection when the ability to distinguish between the presence of active, replicating virus and inactive virus or viral nucleic acid is important.

**Clinical Reference**

1. Schiffer JT, Corye L: New concepts in understanding genital herpes. *Curr Infect Dis Rep* Nov 2009;11(6):457-464
2. Sauerbrei A, Eichhorn U, Hottenrott G, Wutzler P: Virological diagnosis of herpes simplex encephalitis. *J Clin Virol* 2000;17(1):31-36
3. American Academy of Pediatrics. *Red Book: 2012 Report of the Committee on Infectious Diseases. Herpes Simplex*. Edited by LK Pickering. 29th edition. Elk Grove Village, IL: American Academy of Pediatrics, 2012
4. Bradley H, Markowitz LE, Gibson T, McQuillan GM: Seroprevalence of Herpes Simplex Virus types 1 and 2-United

---

States, 1999-2010. J Infect Dis 2014 Feb 1;209(3):325-333

5. Stranska R, Schuurman R, de Vos M, van Loon AM: Routine use of a highly automated and internally controlled real-time PCR assay for the diagnosis of herpes simplex and varicella-zoster virus infections. J Clin Virol 2004 May;30(1):39-44

6. Espy MJ, Uhl JR, Mitchell PS, et al: Diagnosis of herpes simplex virus infections in the clinical laboratory by LightCycler PCR. J Clin Microbiol 2000;38(2):795-799

## Performance

### Method Description

This test is intended for use in the identification and typing of herpes simplex virus (HSV) in cell culture. The test can detect and distinguish between HSV-1 and HSV-2 in shell-vial cultures (MRC-5 cells) before the development of cytopathic effect (Pre-CPE). This test uses monoclonal antibodies (DHI/Quidell), labeled with fluorescein isothiocyanate, which react specifically with HSV-1 and HSV-2. The testing process involves the inoculation of shell vials containing a monolayer of cells on a 12-mm circular cover slip at the base of the vial. Specimen is inoculated into the shell vial and infection of the cells is enhanced by low-speed centrifugation, which is thought to enhance viral infection of the cell monolayer. After incubation at 35 degrees C to 37 degrees C, monoclonal antibodies directed against immediate early antigens of replicating HSV are added, and viral-specific foci visualized by fluorescence microscopy.(Paya CV, Wold AD, Smith TF: Detection of cytomegalovirus infections in specimens other than urine by the shell vial assay and conventional tube cell cultures. J Clin Microbiol 1987;25:755-757)

### PDF Report

No

### Specimen Retention Time

Until Reported

### Performing Laboratory Location

Rochester

## Fees & Codes

### Test Classification

This test has been cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

**CPT Code Information**

87254 x 2

**LOINC® Information**

Test ID	Test Order Name	Order LOINC Value
VHSV	HSV Culture from Neonates	43697-2

Result ID	Reporting Name	LOINC®
VHSV	HSV Culture from Neonates	43697-2