MAYO CLINIC LABORATORIES

Test Definition: HSVC

Herpes Simplex Virus, PCR, CSF

Overview

Useful For

Aids in the rapid diagnosis of herpes simplex virus (HSV)-1 and HSV-2 infections of the central nervous system

Testing Algorithm

See Meningitis/Encephalitis Panel Algorithm in Special Instructions.

Special Instructions

- Meningitis/Encephalitis Panel Algorithm

Method Name

Real-Time Polymerase Chain Reaction (RT-PCR)

NY State Available

Yes

Specimen

Specimen Type

CSF

Specimen Required

Supplies: Aliquot Tube, 5 mL (T465)

Container/Tube: Aliquot tube (12- x 75-mm screw cap vial: T465)

Specimen Volume: 0.2 mL

Collection Instructions: Do not centrifuge or heat-inactivate.

Additional Information:

1. The high sensitivity of amplification by PCR requires the specimen to be processed in an environment in which contamination of the specimen by herpes simplex virus DNA is not likely.

2. Specimens that are received with less than the minimum volume required for all testing requested will be canceled.

Forms

If not ordering electronically, complete, print, and send a Microbiology Test Request (T244) with the specimen.

Reject Due To

Heat-treated spinal fluid	Reject

Specimen Minimum Volume

0.1 mL

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Herpes simplex virus (HSV)-1 and HSV-2 are members of the Alpha herpesviridae subfamily. HSV is an enveloped virus with a capsid containing viral DNA. Although HSV-1 and HSV-2 are closely related, the 2 viruses are serologically and genetically distinct.(1,2)

HSV-1 and -2 are common causes of dermal and genital infections; however, in some cases, infection with HSV may result in central nervous system (CNS) disease that is considered a medical emergency. HSV infection of the CNS may result in encephalitis (more commonly associated with HSV-1) or meningitis (more commonly associated with HSV-2).

Encephalitis is inflammation of the brain associated with clinical evidence of neurologic dysfunction. Of the pathogens reported to cause encephalitis, the majority are viruses.(3) In general, the most commonly identified etiologies in the United States are HSV, West Nile virus, and the enteroviruses, followed by other herpesviruses.(3)

HSV causes about 5% to 10% of all encephalitis cases, and is one of the most common causes of identified sporadic encephalitis globally.(3) HSV encephalitis occurs in all ages, and during all seasons. HSV-1 encephalitis is more common in adults, and HSV-2 encephalitis is more common in neonates.(3) One study reported a neonatal herpes rate of 1 case per 3,200 live births in the United States.(4)

Clinical features involved with HSV encephalitis include fever, hemicranial headache, language and behavioral abnormalities, memory impairment, and seizures.(3)

Reference Values

Negative

Interpretation

A positive result suggests the presence of herpes simplex virus (HSV)-1 and/or HSV-2 DNA in the cerebrospinal fluid (CSF) sample.

A negative result suggests that HSV-1 and HSV-2 DNA are not present in the CSF sample.

An invalid result points to the inability to determine presence or absence of HSV-1 or HSV-2 DNA in the CSF sample.

Cautions

This test is not validated for sample types other than cerebrospinal fluid (CSF).

Negative results do not preclude herpes simplex virus (HSV)-1 or HSV-2 infection and should not be used as the sole basis for treatment or other patient management decisions.

False-negative results may occur if the viruses are present at a level that is below the analytical sensitivity of the assay or if the virus has genomic mutations, insertions, deletions, or rearrangements, or if the assay is performed very early in the course of illness.

For encephalitis patients with a negative herpes simplex PCR result, consideration should be given to repeating the test 3 to 7 days later for patients demonstrating a compatible clinical syndrome or temporal lobe localization on neuroimaging.(3)

The performance of this test has not been established for immunocompromised individuals, nor has it been established for monitoring treatment of HSV infection of the central nervous system.

Supportive Data

Accuracy:

To assess the accuracy of the Diasorin(Focus) Simplexa (herpes simplex virus)-1 and -2 Direct assay, clinical

cerebrospinal fluid specimens (n=100) were tested and the results compared to those of the Roche HSV-1/2 analyte specific reagents.(6) Samples showing discordant results were tested by a third method (artus HSV-1/2; Qiagen). The results are summarized below in Tables 1 and 2:

Table 1. Comparison of the Simplexa HSV-1 Direct Assay to the Roche ASR using Clinical CSF Samples (n=100)(a).

Simplexa HSV-1		**Roche HSV-1 ASR (b)**	
		Positive	Negative
	Positive	11	0
	Negative	0	85
	Total	11	85

Sensitivity (95% CI): 100% (70-100)

Specificity (95% CI): 100% (94.8-100)

Table 2. Comparison of the Simplexa HSV-2 Direct Assay to the Roche ASR using Clinical CSF Samples (n=100)(a).

Simplexa HSV-2		**Roche HSV-2 ASR (b)**	
		Positive	Negative
	Positive	37	1
	Negative	0	58
	Total	37	59

Sensitivity (95% CI): 100% (88.8-100)

Specificity (95% CI): 98.3% (90.2-99.9)

(a) Only 96 samples are summarized. This is because 4 samples were found to be HSV detected-type indeterminate by the Roche ASR. These results are summarized in footnote b.

(b) One sample was HSV detected-type indeterminate by the Roche ASR and positive for HSV-1 by the Diasorin (Focus) Simplexa assay. In addition, 3 samples were HSV detected-type indeterminate by the Roche ASR but negative by the Simplexa HSV-1 assay. These 3 samples were tested by a third method (artus HSV-1/2; Qiagen) and were negative for HSV-1 and -2. Testing was also repeated by the Roche ASR and the results were negative upon repeat testing.

Clinical Reference

1. Lawrence C: Herpes Simplex virus. In Principles and Practice of Infectious Diseases. Sixth Edition. Edited by GL Mandell, JE Bennet, R Dolin. Philadelphia, Elsevier, Churchill and Livingstone, 2004, pp 1762-1780

2. Szpara ML, Parsons L, Enquist LW: Sequence variability in clinical and laboratory isolates of herpes simplex virus 1 reveals new mutations. J Virol 2010;84(10):5303-5313

3. Tunkel AR, Glaser CA, Bloch KC, et al: The management of encephalitis: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis 2008 Aug 1;47(3):303-327

4. Brown ZA, Wald A, Morrow RA, et al: Effect of serologic status and cesarean delivery on transmission rates of herpes simplex virus from mother to infant. JAMA 2003;289(2):203-209

5. Clinical Management Guidelines for Obstetrician-Gynecologists. ACOG Practice Bulletin No. 57, 104 (5 pt 1). 2004;1111-1118

6. Binnicker MJ, Espy MJ, Irish CL: Rapid and direct detection of herpes simplex virus in cerebrospinal fluid using a commercial real-time PCR assay. J Clin Microbiol 2014 Oct 1. PMID 25274992

Performance

Method Description

The Simplexa HSV (herpes simplex virus)-1 and -2 Direct assay system is a real-time PCR that enables the direct amplification, detection, and differentiation of HSV-1 and HSV-2 DNA from unprocessed spinal fluid specimens without nucleic acid extraction.

In this assay, bifunctional fluorescent probe primers are used together with corresponding reverse primers to amplify HSV-1, HSV-2, and internal control targets. Well-conserved regions of the HSV-1 and HSV-2 DNA polymerase genes are targeted to identify HSV-1 and HSV-2 DNA, respectively, in the specimen. An internal control is used to detect PCR failure or inhibition.(Binnicker MJ, Espy MJ, Irish CL: Rapid and direct detection of herpes simplex virus in cerebrospinal fluid using a commercial real-time PCR assay. J Clin Microbiol. Oct 1. PMID 25274992; Package insert: Simplexa HSV 1 and 2 Direct, Focus Diagnostics, Cypress, CA, 07/07/2014)

PDF Report

No

Specimen Retention Time

1 week

Performing Laboratory Location

Rochester

Fees & Codes

Test Definition: HSVC

Herpes Simplex Virus, PCR, CSF

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

87529 x 2

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
HSVC	Herpes Simplex Virus, PCR, CSF	92865-5

Result ID	Reporting Name	LOINC®
36858	HSV 1 PCR, C	16952-4
36859	HSV 2 PCR, C	16960-7