MAYO CLINIC LABORATORIES

Test Definition: LHSVZ

Herpes Simplex Virus (HSV) and Varicella-Zoster Virus (VZV), Molecular Detection, PCR, Varies

Overview

Useful For

Rapid diagnosis of herpes simplex virus and varicella-zoster virus infections

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
LHSV	Herpes Simplex Virus PCR	Yes	Yes
LVZV	Varicella-Zoster Virus PCR	Yes	Yes

Testing Algorithm

This test distinguishes herpes simplex virus (HSV)-1 from HSV-2 genotypes.

Method Name

LightCycler Polymerase Chain Reaction (PCR)

NY State Available

No

Specimen

Specimen Type

Varies

Necessary Information

Specimen source is required.

Specimen Required

Submit only 1 of the following specimens:

Specimen Type: Swab
Supplies:
-Culturette (BBL Culture Swab) (T092)
-M4-RT (T605)
Sources: Genital, dermal, eye, or throat
Container/Tube: Multimicrobe media (M4-RT)
Specimen Volume: Swab
Collection Instructions: Place swab back into multimicrobe media (M4-RT, M4, or M5).

Additional Information: Source information should include the main anatomical source of collection.

Supplies: Sarstedt Aliquot Tube 5 mL (T914)
Specimen Type: Fluid
Sources: Pleural, peritoneal, ascites, pericardial, amniotic, or ocular
Container/Tube: Sterile container
Specimen Volume: 0.5 mL
Collection Instructions: Do not centrifuge.

Specimen Type: Respiratory
Sources: Bronchial washing, bronchoalveolar lavage, nasopharyngeal aspirate or washing, sputum, or tracheal aspirate
Container/Tube: Sterile container
Specimen Volume: 1.5 mL

Specimen Type: Tissue
Supplies: M4-RT (T605)
Sources: Brain, colon, kidney, liver, lung, etc
Container/Tube: Sterile container containing 1 mL to 2 mL of sterile saline or multimicrobe medium (M4-RT, M4, or M5)
Specimen Volume: Entire collection
Collection Instructions: Submit only fresh tissue in multimicrobe media (M4-RT) or a sterile container with 1 to 2 mL sterile saline.

Specimen Minimum Volume

Body Fluid or Ocular Fluid: 0.3 mL; Respiratory: 1 mL

Reject Due To

Calcium alginate-tipped swab, wood swab, or transport swab containing gel	Reject

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Herpes simplex virus (HSV) types 1 and 2 are members of the *Herpesviridae* family and produce infections that may range from mild stomatitis to disseminated and fatal disease. Clinical conditions associated with HSV infection include gingivostomatitis, keratitis, encephalitis, vesicular skin eruptions, aseptic meningitis, neonatal herpes, genital tract infections, and disseminated primary infection.

Infections with HSV types 1 and 2 can differ significantly in their clinical manifestations and severity. HSV type 2 primarily causes urogenital infections and is found almost exclusively in adults. HSV type 1 is closely associated with orolabial infection, although genital infection with this virus can be common in certain populations.

The diagnosis of HSV infections is routinely made based on clinical findings and supported by laboratory testing using PCR or viral culture. HSV causes various clinical syndromes. Anatomic sites infected include skin, lips and oral cavity, eyes, genital tract, and central nervous system.(1)

Varicella-zoster virus (VZV) causes both varicella (chickenpox) and herpes zoster (shingles). VZV produces a generalized vesicular rash on the dermis (chickenpox) in normal children, usually before age 10. After primary infection with VZV, the virus persists in latent form and may emerge (usually in adults age 50 and older) clinically to cause a unilateral vesicular eruption, generally in a dermatomal distribution (shingles).

Reference Values

HERPES SIMPLEX VIRUS (HSV) PCR
Negative

VARICELLA-ZOSTER VIRUS PCR
Negative

Interpretation

Herpes Simplex Virus (HSV) PCR:
This is a qualitative assay; results are reported either as negative, positive, or indeterminate for HSV type 1 or HSV type 2.

Detection of HSV DNA in clinical specimens supports the clinical diagnosis of infection due to the virus.

Varicella-Zoster Virus (VZV) PCR:
Detection of VZV DNA in clinical specimens supports the clinical diagnosis of infection due to this virus.

VZV DNA is not detected in cerebrospinal fluid from patients without central nervous system disease caused by this virus.

This LightCycler PCR assay does not yield positive results with other herpesvirus gene targets (cytomegalovirus, Epstein-Barr virus).

Cautions

A negative result does not eliminate the possibility of herpes simplex virus (HSV) or varicella-zoster virus (VZV) infection. Inhibitors of PCR may be present in some specimens.

The reference range is typically "negative" for this assay. This assay is only to be used for patients with a clinical history and symptoms consistent with VZV or HSV infection, and must be interpreted in the context of the clinical picture. This test is not used to screen asymptomatic patients.

Supportive Data

Herpes Simplex Virus (HSV)

Accuracy/Diagnostic Sensitivity and Specificity:
To assess the accuracy of the Roche HSV-1/2 analyte specific reagents, clinical specimens (n=50) were tested and the results compared to those of a laboratory-developed reference PCR method.

Roche HSV-1/2 ASR		**HSV-1/2 LDT**	
		Positive	Negative
	Positive	20	0
	Negative	0	30
	Total	20	30

Sensitivity (95% CI): 100% (81-100)
Specificity (95% CI): 100% (86-100)

Analytical Sensitivity/Limit of Detection (LoD):
The lower limit of detection (LoD) of the HSV assay is 10 DNA target copies per microliter. This was established in anogenital swabs and confirmed in each specimen type accepted for this assay.

Analytical Specificity:
No PCR signal was obtained from extracts of 27 bacterial, viral, and fungal isolates that could be found as normal flora in sites normally tested for this organism or that could cause similar symptoms.

Precision:
Interassay and intra-assay precision were 100% and 100%, respectively.

Varicella-Zoster Virus (VZV)

Accuracy/Diagnostic Sensitivity and Specificity:
To assess the accuracy of the VZV analyte specific reagents, clinical specimens (n=50) were tested and the results compared to those of a laboratory-developed reference PCR method.

VZV ASR		**VZV LDT**	
		Positive	Negative
	Positive	20	0
	Negative	0	30
	Total	20	30

Sensitivity (95% CI): 100% (81-100)

Specificity (95% CI): 100% (86-100)

Analytical Sensitivity/Limit of Detection (LoD):
The LoD of the VZV assay is 10 to 20 DNA target copies per microliter in specimen matrix.

Analytical Specificity:
No PCR signal was obtained from extracts of 27 bacterial, viral, and fungal isolates that could be found as normal flora in sites normally tested for this organism or that could cause similar symptoms.

Precision:
Interassay precision was 100% and intra-assay precision was 97%.

Reportable Range:
This test is a qualitative assay and results are reported as negative or positive for targeted VZV or HSV DNA.

Clinical Reference

1. Schiffer JT, Corye L. New concepts in understanding genital herpes. Curr Infect Dis Rep. 2009;11(6):457-464
2. Espy MJ, Uhl JR, Svien KA. Laboratory diagnosis of herpes simplex virus infections in the clinical laboratory by LightCycler PCR. J Clin Microbiol. 2000;38(2):795-799
3. Espy MJ, Ross TK, Teo R. Evaluation of LightCycler PCR for implementation of laboratory diagnosis of herpes simplex virus infections. J Clin Microbiol. 2000;38(8):3116-3118
4. Sauerbrei A, Eichhorn U, Hottenrott G, Wutzler P. Virological diagnosis of herpes simplex encephalitis. J Clin Virol. 2000;17(1):31-36
5. Mitchell PS, Espy MJ, Smith TF, et al. Laboratory diagnosis of central nervous system infections with herpes simplex virus by PCR performed with cerebrospinal fluid specimens. J Clin Microbiol. 1997;35(11):2873-2877
6. Yi-Wei T, Mitchell PS, Espy MJ, Smith TF, Persing DH. Molecular diagnosis of herpes simplex virus infections in the central nervous system. J Clin Microbiol. 1999;37(7):2127-2136
7. Cinque P, Bossolasco S, Vago L, et al. Varicella-zoster virus (VZV) DNA in cerebrospinal fluid of patients infected with human immunodeficiency virus: VZV disease of the central nervous system or subclinical reactivation of VZV infection? Clin Infect Dis. 1997;25(3):634-639
8. Brown M, Scarborough M, Brink N, et al: Varicella zoster virus-associated neurological disease in HIV-infected patients. Int J STD AIDS. 2001;12(2):79-83
9. Studahl M, Hagberg L, Rekabdar E, Bergstrom T. Herpesvirus DNA detection in cerebrospinal fluid: differences in clinical presentation between alpha-, beta-, and gamma-herpesviruses. Scand J Infect Dis. 2000;32(3):237-248
10. Iten A, Chatelard P, Vuadens P, et al. Impact of cerebrospinal fluid PCR on the management of HIV-infected patients with varicella-zoster virus infection of the central nervous system. J Neurovirol. 1999;5(2):172-180

Performance

Method Description

Herpes Simplex Virus (HSV):

Viral nucleic acid is extracted from genital, dermal, and ocular specimens. Primers directed to the DNA polymerase gene of HSV produce 215-base pair and 239-bp amplicons, respectively. The LightCycler instrument amplifies and monitors by fluorescence the development of target nucleic acid sequences after the annealing step during PCR cycling. This is an automated PCR system that can rapidly (30-40 minutes) detect amplicon development through stringent air-controlled temperature cycling and capillary cuvettes. The detection of amplified products is based on the fluorescence resonance energy transfer (FRET) principle. For FRET product detection, a hybridization probe with a donor fluorophore, fluorescein, on the 3' end is excited by an external light source and emits light that is absorbed by a second hybridization probe with an acceptor fluorophore, LC-Red 640, at the 5' end. The acceptor fluorophore then emits a light of a different wavelength that can be measured with a signal that is proportional to the amount of specific PCR product. LightCycler hybridization probes were designed for HSV type 2, and sequence differences between HSV type 2 and HSV type 1 are detected by melting curve analysis. Melting curve analysis is performed following PCR amplification. Starting at 40 degrees C, the temperature in the thermal chamber is slowly raised to 95 degrees C, and the fluorescence is measured at frequent intervals. Sequence differences between the PCR product and hybridization probes result in shifts in the melting temperatures (57.5 degrees C for HSV type 1 and 65.8 degrees C for HSV type 2) that are detected. Analysis of the PCR amplification and probe melting curves is accomplished through the use of LightCycler software.(Espy MJ, Uhl JR, Svien KA, et al. Laboratory diagnosis of herpes simplex virus infections in the clinical laboratory by LightCycler PCR. J Clin Microbiol 2000;38:795-799)

Varicella-Zoster Virus (VZV)
Viral nucleic acid is extracted from dermal specimens. Primers directed to gene 28 of VZV produce a 287-bp amplicon. The LightCycler instrument amplifies and monitors by fluorescence the development of target nucleic acid sequences after the annealing step during PCR cycling. This is an automated PCR system that can rapidly (30-40 minutes) detect amplicon development through stringent air-controlled temperature cycling and capillary cuvettes. The detection of amplified products is based on the fluorescence resonance energy transfer (FRET) principle. For FRET product detection, a hybridization probe with a donor fluorophore, fluorescein, on the 3' end is excited by an external light source and emits light that is absorbed by a second hybridization probe with an acceptor fluorophore, LC-Red 640, at the 5' end. The acceptor fluorophore then emits a light of a different wavelength that can be measured with a signal that is proportional to the amount of specific PCR product. Analysis of the PCR amplification is accomplished through the use of LightCycler software.(Espy MJ, Uhl JR, Svien KA, et al: Laboratory diagnosis of herpes simplex virus infections in the clinical laboratory by LightCycler PCR. J Clin Microbiol 2000;38:795-799)

PDF Report
No

Day(s) Performed
Monday through Sunday

Report Available
Same day/1 to 3 days

Specimen Retention Time
1 week

Performing Laboratory Location

Jacksonville

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

87529 x2 HSV-1 and HSV-2
87798-VZV
87999 (if appropriate for government payers)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
LHSVZ	HSV and VZV, PCR	94585-7

Result ID	Test Result Name	Result LOINC® Value
SS001	Specimen Source	39111-0
34797	HSV 1, PCR	94581-6
34798	HSV 2, PCR	94582-4
SRC70	Specimen Source	39111-0
36046	Varicella-Zoster Virus PCR	94584-0