

Overview

Useful For

As an adjunct in the rapid diagnosis of human herpesvirus-6 infection using cerebrospinal fluid specimens

This test **should not be used** to screen asymptomatic patients.

Method Name

Real-Time Polymerase Chain Reaction (PCR)/DNA Probe Hybridization

NY State Available

Yes

Specimen

Specimen Type

CSF

Specimen Required

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)

Container/Tube:

Preferred: Aliquot tube

Acceptable: Sterile vial

Specimen Volume: 0.5 mL

Collection Instructions: Collect specimen from second collection vial. **Do not centrifuge.**

Forms

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

Specimen Minimum Volume

0.3 mL

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Human herpesvirus-6 (HHV-6) is a member of the Herpesviridae family. These viruses contain DNA surrounded by a lipid envelope. Among members of this group, this virus is most closely related to cytomegalovirus (CMV) and HHV-7. As with other members of the herpesvirus group (herpes simplex virus [HSV] 1, HSV 2, varicella-zoster virus, CMV, Epstein-Barr virus, HHV-7, HHV-8), HHV-6 may cause primary and reactivated infections subsequent to latent association with cells.(1) Infection with HHV-6 occurs early in childhood. Most adults (80%-90%) have been infected with this virus.

HHV-6 was first linked with exanthem subitum (roseola infantum) in 1998; since then, the virus has been associated with central nervous system disease almost exclusively in patients who are immunocompromised.(1) HHV-6 is commonly detected in patients posttransplantation. Clinical symptoms associated with this viral infection include febrile illness, pneumonitis, hepatitis, encephalitis, and bone marrow suppression. However, the majority of HHV-6 infections are asymptomatic.(2) The incidence of HHV-7 infection and its clinical manifestations posttransplantation are less well characterized.

HHV-6 is designated as variant A (HHV-6A) or variant B (HHV-6B) depending on restriction enzyme digestion patterns and its reaction with monoclonal antibodies. Generally, variant B has been associated with exanthem subitum, whereas variant A has been found in many immunosuppressed patients.(3)

Reference Values

Negative

Interpretation

A positive result indicates the presence of specific DNA from human herpesvirus-6 (HHV-6) and supports the diagnosis of infection with this virus.

A negative result indicates the absence of detectable DNA from HHV-6 in the specimen, but it does not negate the presence of the virus or active or recent disease.

Cautions

The sensitivity of the assay is very dependent upon the quality of the specimen submitted.

A negative test does not exclude human herpesvirus-6 virus infection. Therefore, the results obtained should be used in conjunction with clinical findings to make an accurate diagnosis.

This assay detects nucleic acid and, therefore, cannot distinguish between viable and nonviable virus. Test performance depends on viral load in the specimen and may not correlate with cell culture performed on the same specimen.

Supportive Data

A total of 32 plasma samples and 30 cerebrospinal fluid (CSF) samples were spiked with human herpesvirus-6 (HHV-6) plasmid control at the limit of detection (LOD) (25-50 copies/mL). The 62 spiked specimens were analyzed in a blinded manner along with 28 negative (non-spiked) plasma and 30 negative (non-spiked) CSF specimens. Of the spiked

specimens, 100% were positive; of the non-spiked specimens, 100% were negative.

Analytical Sensitivity/LOD:

The lower LOD of this assay is 25 to 50 DNA target copies per mL (in plasma).

Analytical Specificity:

No polymerase chain reaction signal was obtained from extracts of 25 viral, bacterial, and fungal isolates that can cause similar symptoms as HHV-6 infection.

Precision:

Interassay precision was 100% and intra-assay precision was 100%.

Reference Range:

Although the reference range is typically "negative" for this assay, this assay may detect viremia in asymptomatic individuals. However, this assay is only to be used for patients with a clinical history and symptoms consistent with HHV-6 infection and must be interpreted in the context of the clinical picture. This test should not be used to screen asymptomatic patients.

Reportable Range:

This is a qualitative assay and results are reported either as negative or positive for targeted HHV-6 DNA.

Clinical Reference

1. Agut H, Bonnafeous P, Gautheret-Dejean A: Laboratory and clinical aspects of human herpesvirus 6 infections. *Clin Microbiol Rev.* 2015 Apr;28(2):313-335
2. De Bolle L, Naesens L, De Clercq E: Update on human herpesvirus 6 biology, clinical features, and therapy. *Clin Microbiol Rev.* 2005 Jan;18(1):217-245
3. Dockrell DH, Paya CV: Human herpesvirus-6 and -7 in transplantation. *Rev Med Virol.* 2001 Jan-Feb;11(1):23-36
4. Abdel-Haq NM, Asmar BI: Human herpesvirus 6 (HHV6) infection. *Indian J Pediatr.* 2004 Jan;71(1):89-96
5. Dockrell DH, Smith TF, Paya CV: Human herpesvirus 6. *Mayo Clin Proc.* 1999 Feb;74(2):163-170

Performance**Method Description**

Viral nucleic acid is extracted by the MagNA Pure automated instrument (Roche Applied Science) from clinical specimens. Primers directed to the immediate early gene of human herpesvirus-6 (HHV-6) produce a 195 base pairs amplicon. The LightCycler instrument (Roche Applied Science) amplifies and monitors the development of target nucleic acid sequences after the annealing step during polymerase chain reaction (PCR) cycling. This automated PCR system can rapidly (1 hour) 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 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 are designed for exact homology to HHV-6.(Cockerill FR III, Uhl JR: Applications and challenges of real-time PCR for the clinical microbiology laboratory. In: Reischel U, Wittwer C, Cockerill F. Rapid Cycle Real-Time PCR - Methods and Applications. Springer-Verlag; 2002:3-30)

PDF Report

No

Day(s) Performed

Monday, Wednesday, Friday

Report Available

2 to 5 days

Specimen Retention Time

1 week

Performing Laboratory Location

Rochester

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

87532

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
HHV6V	HHV-6 PCR, Varies	33942-4

Result ID	Test Result Name	Result LOINC® Value
SS012	Specimen Source	31208-2
56092	HHV-6 PCR, Varies	33942-4