Overview

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

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

NY State Available
Yes

Specimen

Specimen Type
CSF

Specimen Required

Supplies: Aliquot Tube, 5 mL (T465)

Container/Tube:

Preferred: Aliquot Tube, 5 mL (T465)

Acceptable: Sterile vial

Specimen Volume: 0.5 mL

Collection Instructions: 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

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
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</thead>
<tbody>
<tr>
<td>CSF</td>
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Clinical and 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 immunocompromised patients.(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 (HH6-B) depending on restriction enzyme digestion patterns and on 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

Cautions

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

A negative test does not exclude infection with human herpesvirus-6 virus. 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/mcL). The 62 spiked specimens were run in a blinded manner along with 28 negative (nonspiked) plasma and 30 negative (nonspiked) CSF specimens. Of the spiked specimens, 100% were positive; of the nonspaced specimens, 100% were negative.

Analytical Sensitivity/LoD:

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

Analytical Specificity:

No PCR 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


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 bp amplicon. The LightCycler instrument (Roche Applied Science) amplifies and monitors the development of target nucleic acid sequences after the annealing step during 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 Rapid Cycle Real-Time PCR Methods and Applications. Edited by U Reischel, C Wittwer, F Cockerill. Berlin, Germany, Springer-Verlag, 2002 pp 3-30)

PDF Report

No

Day(s) and Time(s) Test Performed

Monday, Wednesday, Friday; 6 a.m.

Analytic Time

Monday through Thursday: 2 days Friday, Saturday: 3 days

Maximum Laboratory Time

5 days
Specimen Retention Time
1 week

Performing Laboratory Location
Rochester

Fees and 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 Regional Manager. 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. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information
87532

LOINC® Information

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