Overview

Useful For
Virologic detection and confirmation of hepatitis E virus (HEV) infection in immunocompromised individuals at risk for or suspected to have acute or chronic hepatitis E

Monitoring HEV RNA levels and determining eradication of chronic HEV infection in immunocompromised individuals

Testing Algorithm
See Hepatitis E: Testing Algorithm for Diagnosis and Management in Special Instructions.

Special Instructions
- Hepatitis E: Testing Algorithm for Diagnosis and Management

Method Name
Real-Time Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR)

NY State Available
Yes

Specimen

Specimen Type
Serum SST

Shipping Instructions
1. Freeze serum immediately, and ship specimen frozen on dry ice.

2. If shipment will be delayed for more than 24 hours, freeze serum at -20 to -80 degrees C (up to 35 days) until shipment on dry ice.

Specimen Required

Supplies: Aliquot Tube, 5 mL (T465)

Collection Container/Tube: Serum gel

Submission Container/Tube: Plastic vial

Specimen Volume: 1.2 mL

Collection Instructions:
1. Centrifuge blood collection tube per collection tube manufacturer's instructions (e.g., centrifuge within 2 hours of collection for BD Vacutainer tubes).

2. Aliquot plasma into plastic vial.

Forms
If not ordering electronically, complete, print, and send a Gastroenterology and Hepatology Client Test Request
Test Definition: HEVQU
HEV RNA Detect / Quant, S

(T728) with the specimen.

Specimen Minimum Volume
0.6 mL

Reject Due To

<table>
<thead>
<tr>
<th>Gross hemolysis</th>
<th>OK</th>
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<tbody>
<tr>
<td>Gross lipemia</td>
<td>OK</td>
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Specimen Stability Information

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<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
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<tbody>
<tr>
<td>Serum SST</td>
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<td></td>
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<tr>
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<td>Refrigerated</td>
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Clinical and Interpretive

Clinical Information

Hepatitis E virus (HEV) is a causative agent of acute self-limited or fulminant hepatitis. HEV has been responsible for large outbreaks of disease in developing countries, primarily through waterborne transmission. Hepatitis E also can occur in industrialized countries, usually as sporadic cases due to zoonotic infection transmitted by the fecal-oral route. A major natural reservoir of HEV is pigs.

In immunocompetent individuals, hepatitis E is mainly a self-limited infection, frequently non-symptomatic and does not result in chronic infection. However, in otherwise healthy pregnant patients, hepatitis E can be severe resulting in significant morbidity and mortality. In immunocompromised individuals, such as organ transplant recipients, hepatitis E can be chronic with detectable HEV RNA levels in serum and plasma beyond 3 months after infection. HEV-specific IgM antibody is detectable by serologic testing by 4 weeks after infection in immunocompetent individuals, but it may not be detectable until 6 months after infection in immunosuppressed patients.

HEV RNA levels in serum or plasma are usually detectable in all infected individuals by 3 weeks after infection and become undetectable by 7 weeks in immunocompetent individuals. Due to the limitations of HEV serologic testing in immunosuppressed patients, molecular testing (eg, RT-PCR assay) for HEV RNA in serum or plasma is an increasingly important tool in the diagnosis of acute or chronic HEV infection in these patients.

Currently, ribavirin is used as the antiviral agent of choice for organ transplant recipients with chronic HEV, and monitoring of HEV RNA levels in serum or plasma is used to assess response to such antiviral therapy. Significant decreases in HEV viral load or clearance of HEV RNA may be important predictors of virologic response during antiviral therapy.

Reference Values
Undetected

Interpretation
The quantification range of this assay is 100 to 5,000,000 IU/mL (2.00 log to 6.70 log IU/mL), with a limit of detection (based on a 95% detection rate) of 11 IU/mL (1.04 log IU/mL).
An "Undetected" result indicates that hepatitis E virus (HEV) RNA is not detected in the serum specimen (see Cautions). Repeat testing in 1 to 2 months is recommended for those at risk of HEV infection. The limit of detection (based on a 95% detection rate) for this assay is 11 IU/mL.

A result of "<100 IU/mL" indicates that the HEV RNA level present in the serum specimen is below 100 IU/mL (2.00 log IU/mL), and the assay cannot accurately quantify the HEV RNA present below this level.

A quantitative value (reported in IU/mL and log IU/mL) indicates the HEV RNA level (ie, viral load) present in the serum specimen.

A result of ">5,000,000 IU/mL" indicates that the HEV RNA level present in the serum specimen is above 5,000,000 IU/mL (6.70 log IU/mL), and this assay cannot accurately quantify the HEV RNA present above this level.

An "Indeterminate" result suggests the presence of an atypical HEV target sequence. Since the HEV RNA sequence is atypical, repeat testing is unlikely to change this result and therefore is not recommended.

An "Equivocal" result indicates that the presence or absence of HEV RNA in the serum specimen could not be determined with certainty due to atypical RT-PCR probe reactivity. Submission of a new specimen for testing is recommended.

An "Inconclusive" result indicates that the presence or absence of HEV RNA in the serum specimen could not be determined with certainty after repeat testing in the laboratory, possibly due to RT-PCR inhibition. Submission of a new specimen for testing is recommended.

Cautions
This assay is optimized for the detection and quantification of Hepatitis E virus (HEV) genotypes 1 to 4, but due to unexpected mismatches between the RT-PCR primers and unusual or rare HEV target sequences, some serum specimens may yield "Undetected" results despite the presence of HEV RNA. Therefore, results should be interpreted with caution, considering the patient's risk factors for HEV infection, the analytical sensitivity of the assay, and possible source of the infecting HEV strain. Follow-up HEV RNA testing is recommended for patients with initially "Undetected" HEV RNA test results but at high risk for or suspected to have chronic hepatitis E.

In immunocompetent individuals, undetectable HEV RNA results indicate only the absence of HEV RNA in the specimen tested and do not exclude the diagnosis of HEV infection, given the relatively short duration of viremia (3 to 7 weeks after infection) in these individuals. Immunocompetent individuals with HEV infection would be expected to have repeatedly positive HEV-specific antibody test results (anti-HEV IgM and/or anti-HEV IgG).

Due to potential differences in assay performance, serial monitoring of HEV viral load in a given patient should be performed with the same molecular assay.

Clinical Reference
Performance

Method Description
This assay utilizes real-time PCR technology for qualitative and quantitative detection of hepatitis E virus (HEV) RNA in human serum. It involves 3 major processes: 1) automated specimen preparation by the MagNA Pure LC instrument, 2) reverse transcription of the target RNA to generate complementary DNA (cDNA), 3) PCR amplification and real-time detection of fluorescent dye-labeled oligonucleotide probes that allow the specific and simultaneous detection and quantitation of the target sequence as well as an MS2 internal control (IC) using the QuantStudio Dx Fast Real-Time PCR System. The HEV primer and probe sequences are designed to amplify a 69-bp segment of the 5’-end of HEV ORF-2 sequence. The assay is calibrated to the First World Health Organization (WHO) International Standard for HEV RNA, PEI code 6329/10. (Germer JJ, Ankoudinova I, Belousov YS, et al: Hepatitis E virus detection and quantification by an RT-PCR assay calibrated to the World Health Organization Standard for HEV RNA. J Clin Microbiol 2017; 55:1478-1487)

PDF Report
No

Day(s) and Time(s) Test Performed
Thursday

Analytic Time
1 day

Maximum Laboratory Time
10 days

Specimen Retention Time
2 months

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
87798

LOINC® Information
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