MAYO CLINIC LABORATORIES

Test Definition: HEVQU

Hepatitis E Virus RNA Detection and Quantification, Real-Time RT-PCR, Serum

Overview

Useful For

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

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

Testing Algorithm

For more information see the following algorithms:
-Hepatitis E: Diagnostic Testing Algorithm
-Hepatitis D: Diagnostic Testing Algorithm

Special Instructions

- Hepatitis E: Diagnostic Testing Algorithm

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 24 hours, freeze serum at -20 to -80 degrees C (up to 35 days) until shipment on dry ice.

Specimen Required

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube: Serum gel
Submission Container/Tube: Plastic vial
Specimen Volume: 1.8 mL
Collection Instructions:
1. Centrifuge blood collection tube per collection tube manufacturer's instructions (eg, centrifuge within 2 hours of

collection for BD Vacutainer tubes).
2. Aliquot serum into plastic vial.

Forms
If not ordering electronically, complete, print, and send 1 of the following with the specimen:
-Gastroenterology and Hepatology Test Request (T728)
-Microbiology Test Request (T244)

Specimen Minimum Volume
0.8 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum SST	Frozen (preferred)	35 days	ALIQUOT TUBE
	Refrigerated	5 days	ALIQUOT TUBE

Clinical & 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 nonsymptomatic, 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 individuals who are immunocompromised, 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 patients who are immunosuppressed.

Hepatitis E virus 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 patients who are immunosuppressed, molecular testing (eg, real-time reverse-transcriptase polymerase chain reaction 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 50 to 5,000,000 IU/mL (1.70 log to 6.70 log IU/mL), with a limit of detection (based on a 95% detection rate) of 20 IU/mL (1.40 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 20 IU/mL.

A result of "<50 IU/mL" indicates that the HEV RNA level present in the serum specimen is below 50 IU/mL (1.70 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 real-time reverse transcriptase-polymerase chain reaction (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 real-time, reverse-transcription polymerase chain reaction 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

1. Aggarwal R. Diagnosis of hepatitis E. Nat Rev Gastroenterol Hepatol. 2013;10(1):24-33. doi:10.1038/nrgastro.2012.187
2. Kamar N, Rostaing L, Izopet J. Hepatitis E virus infection in immunosuppressed patients: natural history and therapy. Semin Liver Dis. 2013;33(1):62-70. doi:10.1055/s-0033-1338115
3. Kamar N, Lhome S, Abravanel F, et al. An early viral response predicts the virological response to ribavirin in hepatitis E virus organ transplant patients. Transplantation. 2015;99(10):2124-2131. doi:10.1097/TP.0000000000000850

Performance

Method Description

This assay utilizes real-time polymerase chain reaction (PCR) technology for the qualitative and quantitative detection of hepatitis E virus (HEV) RNA in human serum. Testing involves 3 major processes with the ELITe InGenius integrated system: automated extraction and purification of viral RNA; reverse transcription of viral target RNA sequence to generate complementary DNA (cDNA); and PCR amplification of a 69-base pair sequence in the 5' end of the HEV open reading frame (ORF) 2 that encodes the viral capsid protein, followed by real-time detection of fluorescent dye-labeled oligonucleotide probes that allow the specific and simultaneous detection and quantification of the target sequence as well as an MS2 internal control. The assay is calibrated to the First World Health Organization 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[5]:1478-1487. doi:10.1128/JCM.02334-16)

PDF Report

No

Day(s) Performed

Varies

Report Available

1 to 14 days

Specimen Retention Time

2 months

Performing Laboratory Location

Test Definition: HEVQU

Hepatitis E Virus RNA Detection and Quantification, Real-Time RT-PCR, Serum

Mayo Clinic Laboratories - Rochester Superior Drive

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

87799

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
HEVQU	HEV RNA Detect / Quant, S	69961-1

Result ID	Test Result Name	Result LOINC® Value
62929	HEV RNA Detect / Quant, S	69961-1