Test Definition: HBCRQ

Hepatitis B Virus Core-Related Antigen, Quantitative, Serum

Overview

Useful For

Monitoring of response to antiviral therapy in individuals with chronic hepatitis B who are negative for hepatitis B e antigen (HBeAg), positive for hepatitis B e antibody, and undetectable or low hepatitis B virus DNA levels (eg, <500 IU/mL) in serum

Testing Algorithm

For more information see Hepatitis B: Testing Algorithm for Screening, Diagnosis, and Management

Special Instructions

- Viral Hepatitis Serologic Profiles
- HBV Infection-Monitoring Before and After Liver Transplantation
- Hepatitis B: Testing Algorithm for Screening, Diagnosis, and Management

Highlights

This test measures the level of hepatitis B (HB) core-related antigen in the serum of patients with chronic hepatitis B (CHB) being monitored for response to antiviral therapy. Such measurement is especially useful in those individuals who are receiving immunotherapy or new antiviral agents to cure CHB with negative HBe antigen, positive HBe antibody, positive HB surface antigen, but undetectable or low hepatitis B virus DNA levels (eg, <500 IU/mL) in serum.

Method Name

Chemiluminescent Enzyme Immunoassay

NY State Available

Yes

Specimen

Specimen Type

Serum

Ordering Guidance

This test should be requested only in individuals with all the following:

-Chronic hepatitis B

-Confirmed positive hepatitis B surface (HBs) antigen

-Negative hepatitis B e antigen (HBeAg)

-Positive hepatitis B e antibody (anti-HBe)

-Undetectable or low hepatitis B viral DNA levels (eg, <500 IU/mL) in serum

Additional Testing Requirements

Testing for hepatitis B virus (HBV) DNA (HBVQN / Hepatitis B Virus [HBV] DNA Detection and Quantification by Real-Time PCR, Serum) and surface antigen (HBAGQ / Hepatitis B Virus Surface Antigen, Quantitative, Serum) levels in serum will be helpful in monitoring response to curative antiviral therapy for chronic hepatitis B.

Shipping Instructions

Ship specimen frozen on dry ice only. If shipment will be delayed for more than 24 hours, freeze serum at -20 degrees to -80 degrees C (up to 60 days) until shipment, and transport on dry ice.

Necessary Information

Collection date is required.

Specimen Required

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube: Serum gel
Submission Container/Tube: Plastic vial
Specimen Volume: 2 mL
Collection Instructions: Centrifuge and aliquot serum into a plastic vial

Forms

f not ordering electronically, complete, print, and send 1 of the following:
-Gastroenterology and Hepatology Test Request (T728)
-Infectious Disease Serology Test Request (T916)

Specimen Minimum Volume

0.5 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Frozen (preferred)	28 days	
	Ambient	7 days	
	Refrigerated	14 days	

Clinical & Interpretive

Clinical Information

During antiviral treatment of chronic hepatitis B (CHB), measurement of hepatitis B virus (HBV) DNA in serum or plasma is used as a marker of treatment efficacy, providing an estimate of the viral replicative activity in the treated individual. However, with nucleoside/nucleotide analogues (NA) acting on limited steps of the viral replication cycle, the production of HBV intermediate proteins (such as hepatitis B core antigen [HBcAg], hepatitis B surface antigen [HBsAg], and hepatitis B e antigen [HBeAg]) may not be affected significantly during such treatment. Therefore, measurement of such HBV proteins in serum or plasma can be useful in monitoring treatment efficacy, especially in patients receiving NA therapy when serum or plasma HBV DNA levels are undetectable. Another recently discovered group of HBV intermediate proteins, hepatitis B core-related antigens (HBcrAgs), comprises 3 related proteins sharing an identical 149 amino acid sequence: HBcAg, HBeAg, and a truncated 22-kDa precore protein.

HBcrAg levels in serum or plasma of individuals with CHB showed good correlation with intrahepatic covalently closed circular DNA (cccDNA) and total HBV DNA, serum HBV DNA, and HBsAg to a lesser extent. In situations where serum HBV DNA levels become undetectable or HBsAg loss is achieved, HBcrAg can still be detectable. Serum HBcrAg concentration correlates strongly with the serum HBV DNA concentration in a positive and linear manner, regardless of the HBeAg status. Intrahepatic total HBV DNA also correlates well with serum HBcrAg in treatment-naive or -experienced individuals. For these reasons, HBcrAg levels in serum or plasma can estimate the intrahepatic cccDNA quantity and serve as a useful marker for disease monitoring, predicting treatment response and disease outcome of CHB.

HBcrAg levels in serum or plasma are also helpful in differentiating HBeAg-negative CHB from HBeAg-positive CHB, predicting spontaneous or treatment-induced HBeAg seroconversion, sustained response to NA therapy, risk of HBV reactivation in occult HBV infection under immunosuppressive therapies, and risk of hepatocellular carcinoma (HCC) development as well as post-operative HCC recurrence.

Reference Values

<1,000 U/mL

Interpretation

This assay has a limit of detection of 158 U/mL and quantifies hepatitis B core-related antigen (HBcrAg) in serum within the range of 1000 to 7,500,000 U/mL (or 3.00 log to 6.88 log U/mL).

Result of <1000 U/mL indicates that the HBcrAg level present in the serum specimen tested is less than 1000 U/mL (the lower limit of quantification of this assay).

Cautions

Given the complex kinetics of hepatitis B virus (HBV) replication in chronic hepatitis B, a single undetectable result of hepatitis B core-related antigen (HBcrAg) in the serum specimen of an individual receiving antiviral therapy for chronic hepatitis B does not indicate cure or the absence of this virus in this individual. Serial measurements of HBcrAg and other tests, such as HBV DNA (HBVQN / Hepatitis B Virus DNA Detection and Quantification by Real-Time PCR, Serum) and HBsAg (HBAGQ / Hepatitis B Virus [HBV] Surface Antigen, Quantitative, Serum) levels, would be helpful or necessary to determine the definitive infection status in such individuals.

In rare cases, some individuals can develop antibodies to mouse or other animal antibodies (often referred to as human anti-mouse antibodies [HAMA] or heterophile antibodies), which may cause interference in some immunoassays. Caution should be used in interpretation of results, and the laboratory should be alerted if the result does not correlate with the clinical presentation.

Performance characteristics have not been established for the following specimen characteristics:
-Grossly icteric (total bilirubin level of >20 mg/dL)
-Grossly lipemic (triolein level of >3000 mg/dL)
-Grossly hemolyzed (hemoglobin level of >500 mg/dL)
-Containing particulate matter
-Cadaveric specimens

Clinical Reference

1.Chen EQ, Feng S, Wang ML, et al. Serum hepatitis B core-related antigen is a satisfactory surrogate marker of intrahepatic covalently closed circular DNA in chronic hepatitis B. Sci Rep. 2017;7(1):173. doi:10.1038/s41598-017-00111-0
2. Zhang ZQ, Zhang XN, Lu W, et al. Distinct patterns of serum hepatitis B core-related antigen during the natural history of chronic hepatitis B. BMC Gastroenterol. 2017;17:140. doi:10.1186/s12876-017-0703-9
3. Mak, LY,Wong DK, Cheung KS, et al. Hepatitis B core-related antigen (HbcrAg): an emerging marker for chronic hepatitis B virus infection. Aliment Pharmacol Ther. 2018;47(1):43-54. doi:10.1111/apt.14376
4. Van Halewijn GJ, Geurtsvankessel CH, Klaasse J, et al. Diagnostic and analytical performance of the hepatitis B core related antigen immunoassay in hepatitis B patients. J Clin Virol. 2019;114:1-5. doi:10.1016/j.jcv.2019.03.003

Performance

Method Description

The Lumipulse G hepatitis B core-related antigen (HBcrAg) assay includes a set of immunoassay reagents for the detection and quantification of HBcrAg in specimens based on chemiluminescent enzyme immunoassay technology with a two-step immunoassay method and the LUMIPULSE G System. Pre-treatment solution containing a detergent is added to clinical serum specimens, HBcrAg calibrator, and assay controls to the pre-treatment solution. HBcr antibodies present in clinical serum specimens are inactivated in this step. HBcr antibody-coated particles are then added to the pre-treated clinical specimens, HBcrAg calibrator, and assay controls, followed by incubation. HBcrAg present in each sample specifically bind to HBcr antibodies present on the microparticles to form antigen-antibody immunocomplexes. Excess microparticles and unbound materials are removed by washing, followed by addition and incubation with alkaline phosphatase-labeled HBcr antibodies that specifically binds to HBcrAg in the antigen-antibody immunocomplexes attached to the microparticles to form larger immunocomplexes. After additional washes to remove unbound materials, a substrate solution is added to allow an enzymatic reaction to generate luminescence that is detected by the analyzer. The resulting luminescent signal is proportionate to the amount of HBcrAg present in the sample.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Tuesday

Report Available

1 to 7 days

Specimen Retention Time

2 weeks

Performing Laboratory Location

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

82397

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
HBCRQ	HBcr Ag, Quantitative, S	97152-3

Result ID	Test Result Name	Result LOINC® Value
HBCQ2	HBcr Ag, Quantitative, S	97152-3