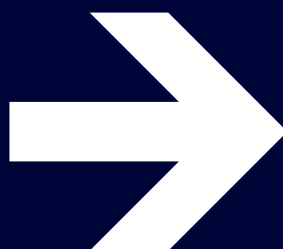
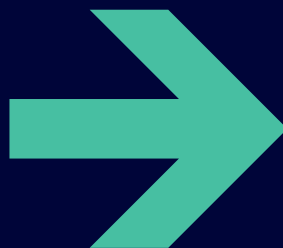


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Chronic HCV Infection:

HBV Reactivation Guide



What Is HBV Reactivation and Why Does It Occur?



Due to shared modes of transmission and known overlapping risk factors for HCV and HBV, such as injection drug use, coinfections can occur.^{1,2}



Patients with chronic or resolved HBV are at risk of HBV reactivation when undergoing immunosuppression, or when receiving DAA therapy for HCV infection.^{1,3,4}



Coinfection with HBV/HCV may lead to viral interference, when one virus (ie, HCV) may interfere or suppress replication of the other (ie, HBV).^{1,2} Therefore, treatment and clearance of HCV infection may result in HBV reactivation.^{2,5}



Though rare, cases of HBV reactivation during or after DAA therapy have been reported in patients with HCV/HBV coinfection who were not receiving HBV suppressive therapy.^{2,3,5,6}



In 2016, the FDA issued a boxed warning on the risk of HBV reactivation in patients receiving DAA therapy for HCV infection; this warning applies to all available DAA regimens as it relates to HCV clearance rather than specific DAA mechanisms of action.⁵



It is therefore important that individuals with HCV infection are also screened for HBV.¹

Potential complications of HBV reactivation

Although HBV reactivation is rare, it may be associated with significant morbidity and mortality.⁵ Coinfection with HBV/HCV is associated with an increased risk for liver disease progression and decompensated liver disease.¹

Reactivation is characterized by an increase in HBV DNA above baseline levels in chronic HBV and the appearance of HBV DNA or seroconversion to hepatitis B surface antigen (HBsAg)-positive in resolved HBV.⁴



How is HBV Reactivation Assessed?

All patients initiating HCV DAA therapy should be tested for HBV with HBsAg, hepatitis B surface antibody (anti-HBs), and hepatitis B core antibody (anti-HBc).^{1,6} Testing can be done individually, or as part of the Hepatitis B Panel, which consists of all three tests (**see table opposite**). **All three results are needed to fully understand and interpret whether a patient is infected.**⁷

HBsAg

The test detects the presence of the virus in the blood, a positive result indicates current HBV infection. In positive patients more testing is needed to determine if it is an acute or chronic infection.^{7,8}

Anti-HBs

A positive result indicates immunity against HBV either through vaccination or past infection.^{7,8}

Anti-HBc

A positive result indicates past or current HBV infection but does not provide immunity. Results can only be interpreted in combination with HBsAg and anti-HBs results.^{7,8}

How Are the Results Interpreted?

Screening Test Results, Interpretation, and Next Steps

HBsAg	Anti-HBc	Anti-HBs	Interpretation	Recommended Next Steps
			Susceptible to HBV Infection Patient has not been infected and is at risk for possible HBV infection	➔ Vaccinate for HBV No additional monitoring for HBV is required ¹⁰
			Immune due to HBV immunization Patient has immunity due to vaccine and has not been infected with HBV	➔ No vaccine is needed Continue with pre-treatment assessments No additional monitoring for HBV is required ¹⁰
			Immune due to natural infection Patient has recovered from prior HBV infection (resolved infection)	➔ No vaccine is needed Check HBV DNA*, anti-HBc Immunoglobulin M ¹ , and HBV e-antigen Regularly check liver enzymes ¹ with hepatic liver panel ^{10,11}
			Infected with HBV Indicates a current infection and presence of the HBV virus that can spread to others	➔ Consider referring to a specialist for care Patients who are HBsAg positive should be assessed for whether their HBV DNA* level meets AASLD criteria for HBV treatment ^{1,11}
			Interpretation unclear, four possibilities 1. Resolved infection (most common); 2. False-positive anti-HBc, susceptible; 3. "Low level" chronic infection; 4. Resolving acute infection	➔ More testing is needed HBV reactivation should be considered a possibility if patients experience unexplained increases in liver enzymes during and/or after completion of DAA therapy

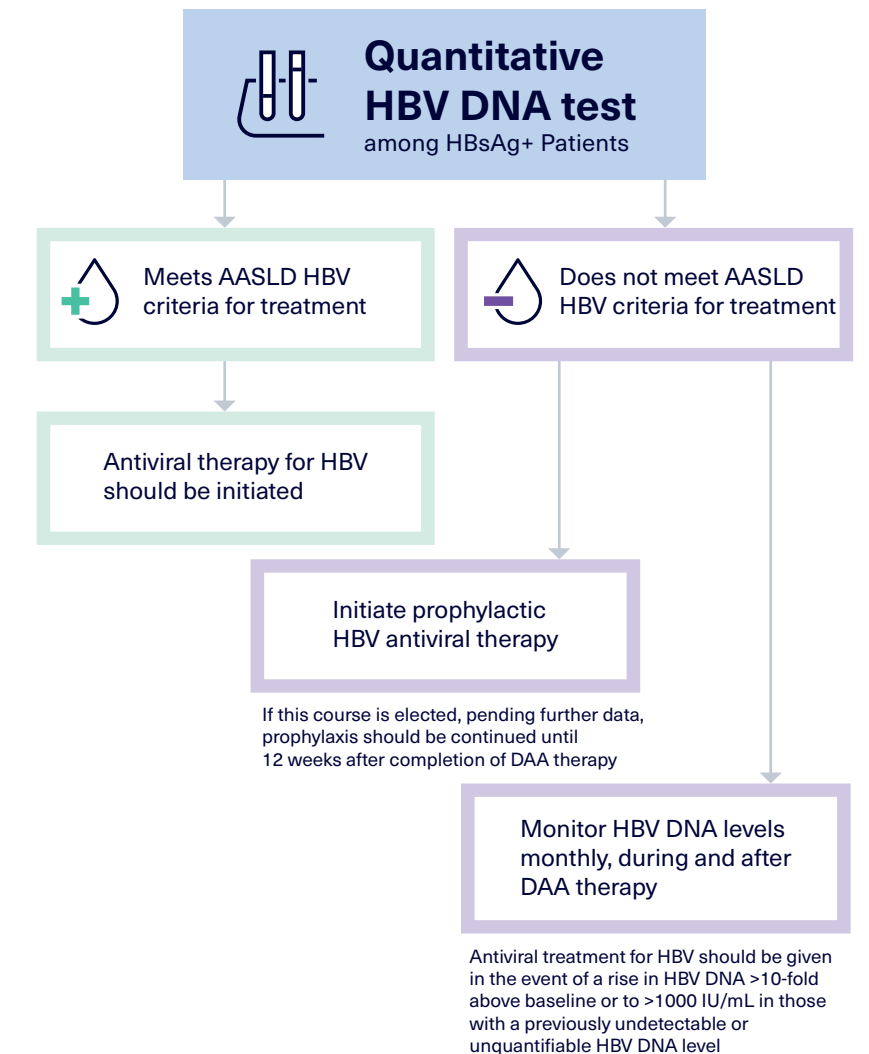
*Antiviral therapy for HBV should be initiated in patients whose HBV DNA level meets AASLD HBV guideline criteria for treatment.^{1,11}

¹Anti-HBc Immunoglobulin M positivity indicates acute infection.⁹

¹¹In patients with elevated ALT, reassess for HBsAg and HBV DNA. AASLD recommends HBV antiviral therapy for patients with elevations of ALT >2ULN plus elevated HBV DNA above the criteria for treatment.¹¹

What are the Treatment Considerations for Patients with HCV/HBV Coinfection?

Consider referring patients with HCV/HBV coinfection to a specialist.¹ The following treatment considerations are recommended for HBsAg-positive* patients who are not already on HBV suppressive therapy:¹



*There are insufficient data to provide clear recommendations for the monitoring of HBV DNA among patients testing positive either for anti-HBc alone or for anti-HBc and anti-HBs (resolved infection); however, the possibility of HBV reactivation should be considered if patients experience unexplained increases in liver enzymes during and/or after DAA therapy completion.¹

Patients who are HBsAg-positive and/or anti-HBc-positive should be monitored for reactivation while receiving HCV treatment.^{1,6,7,9,10}



Abbreviations

AASLD

American Association for the Study of Liver Diseases

ALT

Alanine aminotransferase

Anti-HBc

Antibody to hepatitis B core antigen

Anti-HBs

Antibody to hepatitis B surface antigen

CPT

Current procedural terminology

DAA

Direct-acting antiviral

DNA

Deoxy-ribonucleic acid

FDA

Food and Drug Administration

HBsAg

Hepatitis B surface antigen

HBV

Hepatitis B virus

HCV

Hepatitis C virus

IDSA

Infectious Diseases Society of America

ULN

Upper limit of normal

References

1. AASLD and IDSA. HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C. Last updated December 2019. www.hcvguidelines.org. Accessed August 2020
2. Chen G, et al. *Hepatology* 2017;66(1):13–26
3. Mucke MM, et al. *Lancet Gastroenterol Hepatol* 2018;3(3):172–80
4. Myint A, et al. *Clin Liv Dis* 2020;15(4):162–7
5. Pockros PJ. *Gastroenterol Hepatol (NY)* 2017;13:536–40
6. CDC. Hepatitis C FAQs for Health Professionals. Last reviewed January 2020. <https://www.cdc.gov/hepatitis/hcv/hcvfaq.htm>. Accessed August 2020
7. Hepatitis B Foundation. Understanding Your Test Results. <https://www.hepb.org/prevention-and-diagnosis/diagnosis/understanding-your-test-results/>. Accessed August 2020
8. Hepatitis B Foundation. Hepatitis B Blood Tests. <https://www.hepb.org/prevention-and-diagnosis/diagnosis/hbv-blood-tests/>. Accessed August 2020
9. CDC. Interpretation of Hepatitis B Serologic Test Results. <https://www.cdc.gov/hepatitis/hbv/pdfs/serologicchartv8.pdf>. Accessed August 2020
10. Terrault NA, et al. *Hepatology* 2018;67:1560–99
11. Terrault NA, et al. *Hepatology* 2015;63:261–83
12. Quest Diagnostics™. Hepatitis B Surface Antigen with Reflex Confirmation. <https://testdirectory.questdiagnostics.com/test/test-detail/498/hepatitis-b-surface-antigen-with-reflex-confirmation?cc=MASTER>. Accessed August 2020
13. LabCorp. Hepatitis B Surface Antigen (HBsAg) Screen, Qualitative. [https://www.labcorp.com/tests/006510/hepatitis-b-surface-antigen-hbsag-screenqualitative#:~:text=006510%3A%20Hepatitis%20B%20Surface%20Antigen,HBsAg\)%20Screen%2C%20Qualitative%20%7C%-20LabCorp](https://www.labcorp.com/tests/006510/hepatitis-b-surface-antigen-hbsag-screenqualitative#:~:text=006510%3A%20Hepatitis%20B%20Surface%20Antigen,HBsAg)%20Screen%2C%20Qualitative%20%7C%-20LabCorp). Accessed August 2020
14. LabCorp. Hepatitis B Core Antibody, Total. <https://www.labcorp.com/tests/006718/hepatitis-b-core-antibody-total>. Accessed August 2020
15. Quest Diagnostics™. Hepatitis B Core Antibody, Total. <https://testdirectory.questdiagnostics.com/test/test-detail/501/hepatitis-b-core-antibody-total?cc=MASTER>. Accessed August 2020
16. Quest Diagnostics™. Hepatitis B Surface Antibody Immunity, Qualitative. <https://testdirectory.questdiagnostics.com/test/test-detail/8475/hepatitis-b-surface-antibody-immunity-quantitative?cc=MASTER>. Accessed August 2020
17. LabCorp. Hepatitis B Surface Antibody, Qualitative. <https://www.labcorp.com/tests/006395/hepatitis-b-surface-antibody-qualitative>. Accessed August 2020
18. LabCorp. Hepatitis B Core Antibody, IgM. <https://www.labcorp.com/tests/016881/hepatitis-b-core-antibody-igm>. Accessed August 2020
19. Quest Diagnostics™. Hepatitis B Core Antibody (IgM). <https://testdirectory.questdiagnostics.com/test/test-detail/4848/hepatitis-b-core-antibody-igm?cc=MASTER>. Accessed August 2020
20. LabCorp. Hepatitis Be Antigen. <https://www.labcorp.com/tests/006619/hepatitis-be-antigen>. Accessed August 2020
21. Quest Diagnostics™. Hepatitis Be antigen. <https://testdirectory.questdiagnostics.com/test/test-detail/555/hepatitis-be-antigen?cc=MASTER>. Accessed August 2020
22. LabCorp. Hepatitis B Virus (HBV) Evaluation Profile. <https://www.labcorp.com/tests/037215/hepatitis-b-virus-hbv-evaluation-profile>. Accessed August 2020

HBV Testing

HBsAg with reflex confirmation:

CPT code: 87341¹² | Quest Diagnostics™ code: 498¹² | LabCorp code: 006510¹³

Anti-HBc:

CPT code: 86704¹⁴ | Quest Diagnostics™ code: 501¹⁵ | LabCorp code: 006718¹⁴

Anti-HBs:

CPT code: 86706¹⁶ | Quest Diagnostics™ code: 499¹⁶ | LabCorp code: 006395¹⁷

Anti-HBc Immunoglobulin M:

CPT code: 86705¹⁸ | Quest Diagnostics™ code: 4848¹⁹ | LabCorp code: 016881¹⁸

HBV e-antigen:

CPT code: 87350²⁰ | Quest Diagnostics™ code: 499²¹ | LabCorp code: 006619²⁰

HBV Evaluation Panel:

LabCorp code: 037215²²