Chronic Hepatitis B (CHB)

KNOW IT BY THE NUMBERS

Start comprehensive biomarker testing, including quantitative and qualitative HBsAg, for more informed clinical decisions[1-4]

- Comprehensive biomarker testing may offer more clinical insights[5,6]
- HBV DNA and HBeAg are complementary biomarkers that guide CHB management—HBV DNA is a measure of viral replication that requires serial monitoring, while HBeAg helps define disease phase and differentiates between active and inactive CHB[3,7,8]
- HBsAg is an important marker of active chronic HBV infection[2]
  - **Qualitative HBsAg**[9,10]**:** Detects presence or absence of HBsAg to assist with diagnosis
  - **Quantitative HBsAg**[10]**:** Informs prognosis and clinical decisions, and tracks therapeutic progress

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Comprehensive biomarker testing may offer more clinical insights[5,6]

Real-world monitoring practices may diverge from the guideline recommendations for chronic hepatitis B (CHB)

MONITORING OF PATIENTS NOT ON TREATMENT

~50%

did not receive ALT and either HBV DNA or HBeAg testing within 12 months of CHB diagnosis[11]

MONITORING OF PATIENTS ON TREATMENT

>60%

did not receive ALT + HBV DNA testing after antiviral treatment initiation[12]

Only 40%-53%

of Asian American patients with CHB adhered to monitoring and follow-up care, which is notable because despite only making up 6% of the US population, Asian Americans account for 58% of Americans living with CHB[13]

Insufficient biomarker testing and delayed treatment initiation can increase the risk of disease progression and serious liver-related outcomes.[7,8,14-16]

CHB leads to cirrhosis, liver failure, or HCC in **15%–40%** of patients.[14,17]

Persistent viremia due to inadequate monitoring and lack of treatment adjustment contributes to **ongoing liver injury and fibrosis progression.**[7,15,16]

In 2022, HBV-related cirrhosis or HCC caused an estimated **1.1 million deaths globally.**[8]

ALT=alanine aminotransferase; DNA=deoxyribonucleic acid; HBeAg=hepatitis B e-antigen; HBV=hepatitis B virus; HCC=hepatocellular carcinoma.

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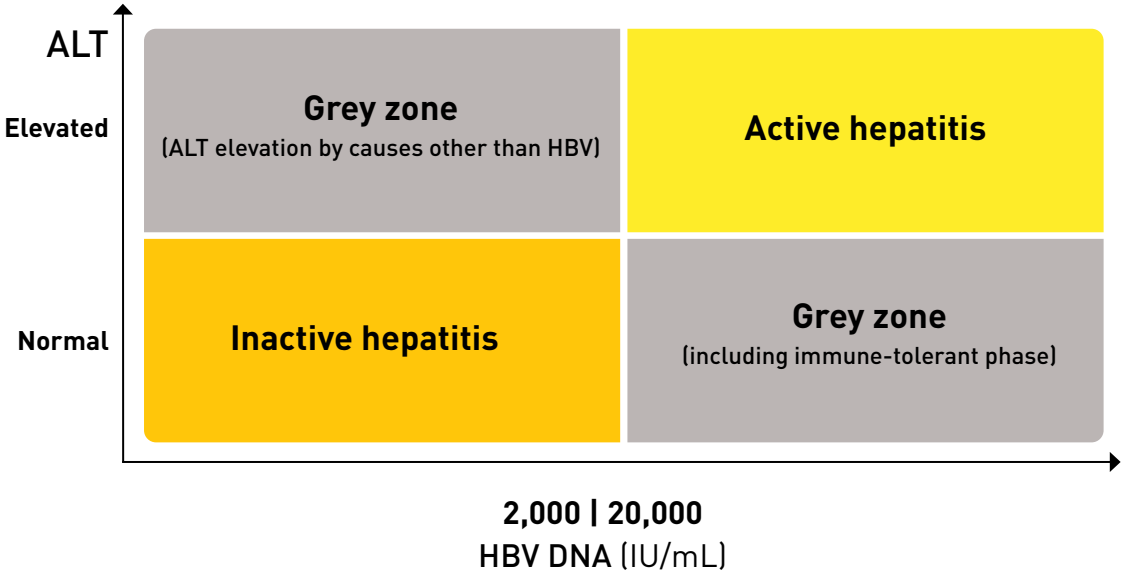
Emerging biomarkers may reveal clinical insights that complement AASLD guidelines[7]

AASLD recommendations are based on HBeAg, HBV DNA, and ALT levels[7]

Quantitative HBsAg testing can help guide management of "grey zone" patients.[7]

Conceptual definition of grey zone of chronic hepatitis B[18]



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28%–55% of patients with CHB are viremic, but fall into a grey zone without clear guidance on optimal management and treatment. HBeAg-negative patients are in the "grey zone," in which HBV DNA or ALT levels are borderline between inactive CHB and immune-active, HBeAg-negative CHB.[7,19]

- Quantitative HBsAg testing is an emerging biomarker gaining traction in international guidelines (EASL, CASL) due to its predictive and prognostic value, but it remains underutilized in US practice[20-22]

AASLD=American Association for the Study of Liver Diseases; CASL=Canadian Association for the Study of the Liver; EASL=European Association for the Study of the Liver; HBsAg=hepatitis B surface antigen.

In chronic hepatitis B (CHB):

Comprehensive testing of key biomarkers allows for more clarity when characterizing disease phase and severity, assessing patient prognosis,and evaluating treatment response[7,20,21]

Biomarkers of interest

HBV DNA | Quantitative HBsAg | Qualitative HBsAg | HBeAg | Anti-HBe antibodies

Full hepatic function panel:

ALT, AST, total bilirubin +/– direct bilirubin, alkaline phosphatase, and albumin[1]

Noninvasive tests of fibrosis:

Serum APRI or FIB-4, and elastography, FibroScan, ultrasound, or MRI[1]

For both cirrhotic and noncirrhotic patients, include HCC surveillance with ultrasound and alpha-fetoprotein.[7,20]

Anti-HBe=anti–hepatitis B e-antigen; APRI=aspartate aminotransferase to platelet ratio index; AST=aspartate aminotransferase; FIB-4=fibrosis-4; MRI=magnetic resonance imaging.

KEY BIOMARKER: Quantitative and qualitative HBsAg testing

HBsAg testing in CHB management

- HBsAg is a viral surface protein and an important marker of active chronic HBV infection[2]
- It is a measure of the total transcriptional activity of both covalently closed circular DNA (cccDNA) and integrated HBV DNA in liver cells[9]
- HBsAg is believed to promote immune evasion and disease chronicity[9]

HBsAg tests for CHB:

Qualitative HBsAg	Quantitative HBsAg
Detects only presence or absence of HBsAg in serum via standard immunoassays (eg, ELISA, CLIA)[9,10]	Measures serum concentration of HBsAg in IU/mL via automated immunoassay[3,20]
Clinical utility[1,7,10]: • Initial diagnosis of HBV and screening for at-risk individuals • Cannot inform disease activity, treatment response, or prognosis, except in rare cases of HBsAg loss	Clinical utility[10]: • Quantitative HBsAg testing may help deliver more comprehensive evaluation—informing prognosis, treatment decisions, and tracking progress toward functional cure*

*"Functional" but not sterilizing cure is achievable and should be defined as sustained HBsAg loss in addition to undetectable HBV DNA 6 months post-treatment.[23]

CLIA=chemiluminescence immunoassay; ELISA=enzyme-linked immunosorbent assay.

Quantitative HBsAg and its interpretation

qHBsAg	Below reference (<100 IU/mL)	Low (100–<1,000 IU/mL)	Elevated (≥1,000 IU/mL)
Interpretation	**Suggests inactive CHB**[7,24] • Risk of viral relapse reduced, varying by ethnicity • Increases the specificity of identifying patients with inactive CHB, but reduces sensitivity to 35%	**Suggests inactive CHB**[7] • May predict spontaneous HBsAg clearance in HBeAg-negative patients with a lower viral load • May require less frequent monitoring	**Elevated risk of cirrhosis and HCC**[10]
Cirrhosis risk[10]	HR 1 (reference)	HR 1.96	HR 3.5
HCC risk[10]	HR 1 (reference)	HR 3.2	HR 5.4

HBsAg loss (below detection threshold of <0.05 IU/mL) serves as a reliable indicator of reduced viral DNA expression, which is associated with improved clinical outcomes.[20]

Quantitative HBsAg is an important biomarker in assessing clinical response and functional cure.[7,20]

Clinical utility of quantitative HBsAg

Prognostic Value
- Predicts risk of liver fibrosis and development of HCC[7]

Identify True Inactive HBV Carriers
- Helps guide treatment approach for patients in an indeterminate stage or "grey zone" (HBeAg-negative with borderline levels of HBV or ALT)[7]

Monitor Response
- Predictor of on-treatment virologic control—helps identify potential candidates to withdraw from therapy (in combination with HBV DNA)[25]

Determine Probability of HBsAg Loss
- Higher probability of spontaneous HBsAg clearance if <100 IU/mL[7,26]

HR=hazard ratio.

KEY BIOMARKERS: HBV DNA and HBeAg

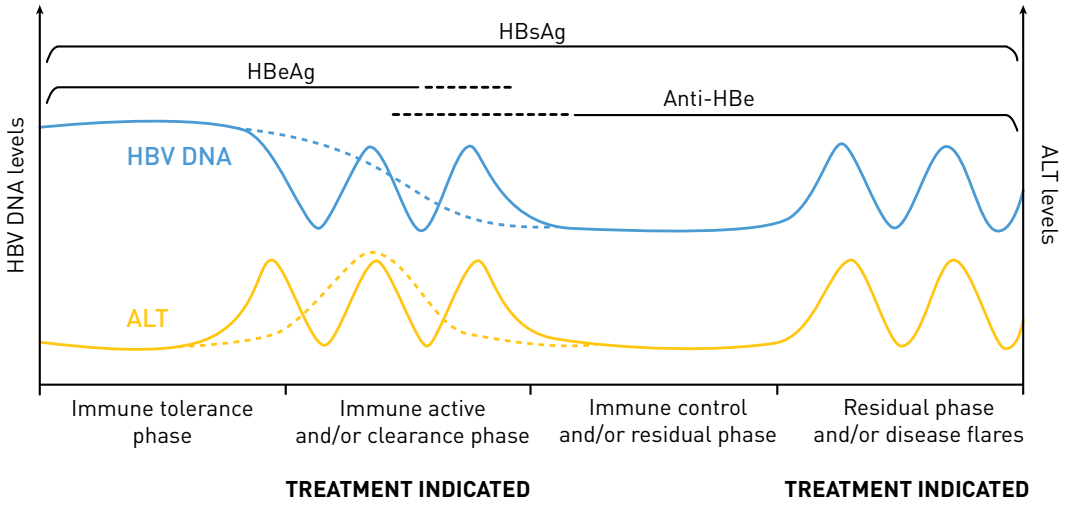
Real-world monitoring practices may diverge from the guideline recommendations for chronic hepatitis B [CHB].[7]

HBV DNA is a measure of viral replication and guides treatment decisions, but levels can fluctuate[7]

- Serial monitoring is more reliable than cutoff values
- Levels should be interpreted alongside other clinical variables

HBeAg indicates immune activity, helps define disease phase, and differentiates between active* and inactive CHB[3,7,8]

Chronic hepatitis B phases[27]



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*Per AASLD guidelines, immune-active chronic hepatitis B is defined by ALT ≥2X ULN or significant histologic disease with HBV DNA >2,000 IU/mL (HBeAg-negative) or >20,000 IU/mL (HBeAg-positive).[7]

ULN=upper limit of normal.

KNOW THE NUMBERS.
Know the complete picture.

Routine testing of all chronic hepatitis B biomarkers, including quantitative and qualitative HBsAg, may provide a fuller picture of patients' disease and better inform treatment decisions.[3,10,28]

- Quantitative and qualitative HBsAg, HBeAg, and HBV DNA tests are commercially available[10]

Scan to explore comprehensive testing on our website

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