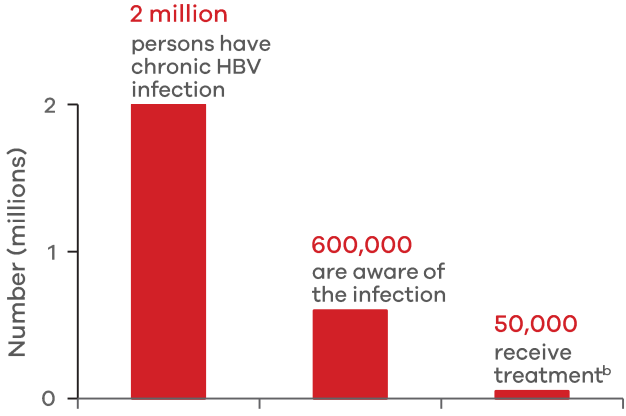
Chronic hepatitis B virus (HBV) infection

Screening & Management Guidelines

hepBMD.com®

In the U.S., chronic HBV infection is underdiagnosed and undertreated

Diagnosis and treatment of chronic HBV infection in the U.S.[1,a]



[a]2016 data.[1]
[b]Approximately 350,000-500,000 were potentially eligible for treatment.[1]

Up to **95%** of foreign-born persons with chronic HBV infection in the U.S. migrated from regions of intermediate and high endemicity[2]

About 2 out of 3 patients are unaware of their HBV infection. Those who are unaware of their infection are at risk for[1,3]:

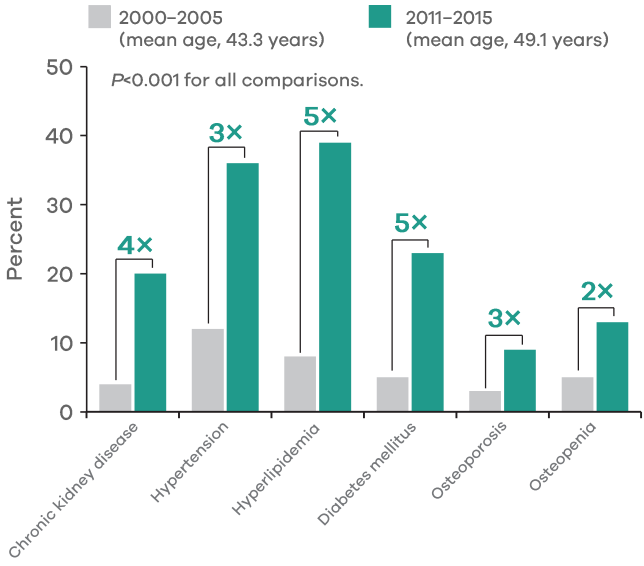
- **Transmitting the virus** to others
- Developing **serious liver disease** later in life

Vaccination without prior screening can give a dangerous perception of prevention among contagious HBV carriers.[4,5]

HBV=hepatitis B virus; U.S.=United States.

Patients with chronic HBV infection are aging and presenting with more comorbidities

Comorbidities in aging patients with chronic HBV infection (San Francisco Bay Area cohort; 15-year period)[6,a]



[a]A retrospective, observational study of 2734 patients with chronic HBV infection across 3 time periods (2000–2005, 2006–2010, 2011–2015) at a university medical center and primary care clinics in the San Francisco Bay Area.[6]

Some of these comorbidities are more prevalent in patients with chronic HBV infection vs uninfected people[7-9]

Due to the association between chronic HBV infection and comorbidities, careful evaluation and consideration are needed when managing patients with chronic HBV infection[10]

Identification of persons at risk for HBV infection

Recommendations from AASLD, ACP and CDC, and USPSTF

Patients who fall within the following risk categories may benefit from screening as early as possible[11,12]:

- Persons born in regions with prevalence of HBV infection of ≥2%[2,10,11]
- U.S.-born persons not vaccinated as infants whose parents were born in regions with prevalence of HBV infection of ≥8%[2,10]
- Household and sexual contacts of persons with HBV infection[2,10,11]
- All pregnant women[10,11,13]
- Men who have sex with men[2,10,11]
- Injection drug users[2,10,11]
- Persons with elevated liver function tests[10,11]
- Persons with certain medical conditions[10,11,14]
  - Needing immunosuppressive therapy
  - Undergoing hemodialysis
  - Infected with HCV or HIV

AASLD=American Association for the Study of Liver Diseases; ACP=American College of Physicians; CDC=Centers for Disease Control and Prevention; HCV=hepatitis C virus; HIV=human immunodeficiency virus; USPSTF=U.S. Preventive Services Task Force.

Diagnosis and interpretation of results

With 1 blood draw, you can measure 3 potential infection markers[15]

1

HBsAg

Hepatitis B surface antigen

- Hallmark of infection

2

Anti-HBs

Hepatitis B surface antibody

- Marker of immunity[a]

3

Anti-HBc

Hepatitis B core antibody

- Marker of prior exposure

Possible test results[3,11,15,16]				
HBsAg	+	–	–	–
Anti-HBs	–	+/–	+	–
Anti-HBc[b]	+	+	–	–
Interpretation	Acute or chronic infection[c]	Exposure to HBV At risk for reactivation[d]	Immunity from vaccination	At risk for HBV infection
Action	Evaluation and further testing	Follow up as appropriate[e]	No further action required	Vaccinate

> "Tests for HBV infection are **widely available, cheap,** and **accurate**"
>
> R. Rajbhandari and R.T. Chung, *Annals of Internal Medicine*[12]

[a]Through vaccination or recovery from previous HBV infection.

[b]Anti-HBc refers to total anti-HBc.[3]

[c]Patient is chronically infected if HBsAg+ for ≥6 months; patients with acute infection will be positive for anti-HBc IgM.[3]

[d]Patients undergoing immunosuppressive therapy or treatment with direct-acting antivirals for HCV coinfection should be monitored for HBV reactivation.[17]

[e]Patients with cirrhosis may need to be monitored for HCC per AASLD/ European Association for the Study of the Liver (EASL) guidelines.[10,17]

Evaluation of patients with chronic HBV infection after diagnosis

Tests that guide the management of chronic HBV infection[3,10]

Markers of HBV replication

- Hepatitis B DNA
- Hepatitis B e antigen and antibody (HBeAg, anti-HBe)

Degree of liver injury

- Alanine aminotransferase (ALT)
- Noninvasive techniques (eg, FibroScan®)
- Liver biopsy

Patient history and physical examination

- Risk factors for coinfection
- Alcohol use
- Family history of HBV infection and liver cancer
- Comorbidities

Liver cancer

- Ultrasound
- Alpha-fetoprotein (AFP)

Following an initial evaluation, all patients with chronic HBV infection should receive lifelong monitoring to assess[3]:

1 Liver disease progression, including HCC

2 Need for treatment

3 Response to treatment

HCC=hepatocellular carcinoma.

Criteria for treatment from selected treatment guidelines and algorithms

	HBeAg+	
	HBV DNA (IU/mL)	ALT (U/L)
AASLD 2018[10]	>20,000	>2×ULN[a] or significant liver disease[b]
AATA 2018[18]	>2000	>ULN[a] or significant liver disease[b]/ other risk factors[c]

	HBeAg–	
	HBV DNA (IU/mL)	ALT (U/L)
AASLD 2018[10]	>2000	>2×ULN[a] or significant liver disease[b]
AATA 2018[18]	>2000	>ULN[a] or significant liver disease[b]/ other risk factors[c]

According to the AASLD and AATA recommendations, all cirrhotic patients with detectable HBV DNA should be treated regardless of ALT[10,18]

[a]ULN criteria for men and women, respectively: AASLD 2018: 35 U/L and 25 U/L; AATA 2018: local laboratory range.

[b]Noninvasive testing showing significant fibrosis (≥F2) or liver biopsy showing moderate/severe inflammation (A2 or A3) and/or significant fibrosis (≥F2).

[c]Albumin <3.5 g/dL, platelet count <130,000/mm^3, presence of basal core promoter mutation, HCC in first-degree relative, or elevated AFP in the absence of HCC.

Chronic HBV infection is dynamic; patients who do not require treatment now may require treatment later in life[19]

Lifelong monitoring is recommended for all patients with chronic HBV infection[3]

Antiviral agents active against HBV are available and have been shown to[20]:

- **Suppress HBV replication**
- **Prevent progression to cirrhosis**
- **Reduce the risk of HCC and liver-related deaths**

AATA=Asian American Treatment Algorithm (also referred to as An Expert Consensus for the Management of Chronic Hepatitis B in Asian Americans); ULN=upper limit of normal.

Ongoing management and routine monitoring

Patients should be informed that adherence and regular follow-up visits are essential[18]

Appropriate patient support and care will improve patient adherence and treatment outcomes[18]

Laboratory monitoring after initiating treatment[18]

ALT	HBV DNA	HBeAg	HBsAg
• Every 3 months • 3–6 months if ALT is within normal limits	• Every 3 months • 3–6 months if HBV DNA is undetectable	• Every 6 months until seronegative • Then initiate anti-HBe testing	• Every 12 months after HBeAg sero-conversion • Every 12 months after sustained suppression of HBV DNA in HBeAg– patients

HCC surveillance for those with risk factors is an important component of monitoring and should be done routinely in patients with chronic HBV infection[18]

Recommendations for HCC surveillance

AASLD 2018[10]

Tests

- Ultrasound ± AFP
- Every 6 months

At-risk populations

- HBsAg+ Asian or African American men >40 years of age
- HBsAg+ Asian women >50 years of age
- Patients with cirrhosis
- People with a family history of HCC
- Patients with fatty liver
- People coinfected with HCV, HDV, or HIV

Routine surveillance for HCC has demonstrated significant benefits for patients with chronic HBV infection[21]

2×
Improvement in early tumor detection

2×
Improvement in 3-year survival

HDV=hepatitis D virus.

Call to action
Linking your patients to care

AASLD Recommendations[22]

To reduce the morbidity and mortality of chronic HBV infection in the United States and worldwide...

1. **Identify infected individuals** through targeted screening
2. **Prevent new infections** through vaccination
3. **Monitor and treat those at risk** for complications of their chronic HBV infection, including surveillance for HCC

> "Reducing the burden of chronic HBV infection by increasing vaccination, screening at-risk adults, and providing linkage to care is a **public health priority**"
>
> – ACP and CDC Best Practice Advice[11]

References

1. Cohen C, et al. *J Viral Hepat*. 2011;18:377-383; **2.** LeFevre ML; USPSTF. *Ann Intern Med*. 2014;161:58-66; **3.** CDC. *MMWR Recomm Rep*. 2008;57:1-20; **4.** Asian Liver Center. Physician's Guide to Hepatitis B 2013. http://med.stanford.edu/content/dam/sm/liver/documents/resources/guides/2013Handbook.pdf. Accessed August 8, 2018; **5.** Navarro N, et al. *BMC Infect Dis*. 2014;14:269; **6.** Liu A, et al. *Clin Transl Gastroenterol*. 2018;9:141; **7.** Nguyen MH, et al. *Hepatology*. 2018 Sep 2. [Epub ahead of print]; **8.** Chen CH, et al. *Medicine (Baltimore)*. 2015;94:e2276; **9.** Chen YC, et al. *Kidney Int*. 2015;87:1030-1038; **10.** Terrault NA, et al. *Hepatology*. 2018;67:1560-1599; **11.** Abara WE, et al. *Ann Intern Med*. 2017;167:794-804; **12.** Rajbhandari R, Chung RT. *Ann Intern Med*. 2014;161:76-77; **13.** USPSTF. *Ann Intern Med*. 2009;150:869-873; **14.** USPSTF. Hepatitis B virus infection: Screening, 2014. May 2014. www.uspreventiveservicestaskforce.org/uspstf/uspshepb.htm. Accessed August 8, 2018; **15.** CDC. Epidemiology and Prevention of Vaccine-Preventable Diseases. 13th ed; 2015. https://www.cdc.gov/vaccines/pubs/pinkbook/index.html. Accessed August 8, 2018; **16.** CDC. Interpretation of Hepatitis B Serologic Test Results. www.cdc.gov/hepatitis/HBV/testingchronic.htm. Updated November 21, 2017. Accessed August 8, 2018; **17.** EASL. *J Hepatol*. 2017;67:370-398; **18.** Tong MJ, et al. *Aliment Pharmacol Ther*. 2018;47:1181-1200; **19.** Martin P, et al. *Clin Gastroenterol Hepatol*. 2015;13:2071-2087.e16; **20.** WHO. Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection. Geneva, Switzerland: WHO Press; 2015; **21.** Singal AG, et al. *PLoS Med*. 2014;11:e1001624; **22.** Terrault NA, et al. *Hepatology*. 2016;63:261-283.

GILEAD

GILEAD, the GILEAD Logo, HEPBMD, the HEPBMD Logo and the Liver Icon are trademarks of Gilead Sciences, Inc. All other marks referenced herein are the property of their respective owners.

©2018 Gilead Sciences, Inc. All rights reserved. UNBP4333 11/18