CHRONIC HEPATITIS B (CHB)
Screening and management
CHB is a major global health problem\textsuperscript{1}

**CHB has far-reaching consequences\textsuperscript{1}**

- An estimated 240 million people worldwide are living with CHB\textsuperscript{2}
- If left untreated, up to 1 in 4 people with CHB develop liver problems, such as cirrhosis and hepatocellular carcinoma (HCC)\textsuperscript{3}
- Approximately 15\%-25\% of persons with CHB die of cirrhosis or HCC\textsuperscript{4}

The highest prevalence of hepatitis B is in sub-Saharan Africa and East Asia.\textsuperscript{2}

Map adapted from CDC\textsuperscript{5} and Vijayadeva V, et al.\textsuperscript{6}
In the US, CHB is underdiagnosed and undertreated⁷

About 2 out of 3 persons with CHB in the United States are unaware of their infection.³

- Persons with CHB can be without symptoms for many years⁵
- Unaware of their infection, CHB patients are at risk for transmitting the virus to others, and for developing serious liver disease later in life⁵
- Identification and management of CHB-infected individuals may help prevent serious sequelae of chronic liver disease⁵

Persons with CHB die an average of 22 years earlier than uninfected persons.⁸
Screening at-risk patients

- Screening for HBV identifies people with CHB who may benefit from treatment or surveillance for disease progression\(^4\)
- Analysis of a model that simulates disease progression found that screening and early treatment of CHB may reduce the incidence of HCC and cumulative mortality, compared to late treatment\(^9\)

Alignment of screening recommendations from the USPSTF, CDC, and AASLD\(^{4,10,11}\)

<table>
<thead>
<tr>
<th>USPSTF</th>
<th>CDC</th>
<th>AASLD</th>
</tr>
</thead>
<tbody>
<tr>
<td>People born in regions where the prevalence of HBV infection is &gt;2%</td>
<td>US-born people not vaccinated as infants and whose parents were born in regions having an HBV prevalence of &gt;8%</td>
<td></td>
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<tr>
<td>Household and sexual contacts of persons with HBV infection</td>
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<tr>
<td>All pregnant women</td>
<td></td>
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<tr>
<td>Men who have sex with men</td>
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<tr>
<td>Injection drug users</td>
<td></td>
<td></td>
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<tr>
<td>Individuals infected with HIV</td>
<td></td>
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<tr>
<td>People with certain medical conditions</td>
<td></td>
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<tr>
<td>— Needing immunosuppressive therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>— Undergoing hemodialysis</td>
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<td></td>
</tr>
</tbody>
</table>

USPSTF = United States Preventive Services Task Force; CDC = Centers for Disease Control; AASLD = American Association for the Study of Liver Disease.

Patients who fall within these risk factors may benefit from screening as early as possible.\(^{12}\)
## Diagnosis and interpretation of results

**CHB can be diagnosed with these simple blood tests.**

<table>
<thead>
<tr>
<th>Hepatitis B surface antigen (HBsAg)</th>
<th>Hepatitis B surface antibody (anti-HBs)</th>
<th>Total hepatitis B core antibody (anti-HBc)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg</td>
<td>Anti-HBs</td>
<td>Anti-HBc</td>
</tr>
<tr>
<td>+</td>
<td>-</td>
<td>+</td>
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<td>-</td>
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</tbody>
</table>

### Interpreting HBV serology markers

#### Test results and recommended follow-up

<table>
<thead>
<tr>
<th>Possible test results</th>
<th>Interpretation</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg</td>
<td>Acute or chronic infection(^a)</td>
<td>Contact patient for evaluation and further testing</td>
</tr>
<tr>
<td>Anti-HBs</td>
<td>Immune resolved infection</td>
<td>Follow up as appropriate(^b,d)</td>
</tr>
<tr>
<td>Anti-HBc(^a)</td>
<td>Immune: by vaccination</td>
<td>None required</td>
</tr>
<tr>
<td></td>
<td>Susceptible to HBV infection</td>
<td>Vaccinate</td>
</tr>
</tbody>
</table>

\(^a\) Anti-HBc refers to Total Anti-HBc.\(^5\)
\(^b\) Patient is chronically infected if HBsAg+ for ≥6 months.\(^5\)
\(^c\) Patients who are anti-HBc–positive should be monitored closely during and after the administration of cytotoxic chemotherapy for signs of HBV reactivation.\(^5\)
\(^d\) Patients with cirrhosis may need to be monitored for hepatocellular carcinoma per the AASLD guidelines.\(^15\)

#### HBV vaccination is effective in preventing infection

- **First dose (0 month):**
  - 1 month
  - ~30%-55% with protective immunity\(^*\)

- **Second dose (1 month):**
  - 5 months
  - ~75% with protective immunity\(^*\)

- **Third dose (6 months):**
  - >90% with protective immunity\(^*\)

\(^*\)Percentage varies with age.

Only the completion of the 3-dose vaccine series is associated with >90% of healthy adults developing protective immunity.\(^16\)
• Key elements in the initial evaluation of CHB infection include a thorough history and physical examination, with particular attention to family history of HBV infection and liver cancer, risk factors for coinfections, and alcohol use\textsuperscript{17}

• Pretreatment laboratory tests should include assessment of liver disease (CBC, hepatic panel, and PT), markers of HBV replication, HBV genotype in selected patients, tests for coinfection with other viruses, such as HCV, HDC or HIV, for at-risk individuals, and assessment of renal function\textsuperscript{10,17}

• Liver biopsy is the gold standard for assessing the extent of fibrosis; however, non-invasive transient elastography may also be used\textsuperscript{17}

• USTA recommends HBsAg+ persons with a family history of primary HCC should be screened twice annually for HCC, regardless of age\textsuperscript{17}

Tests that guide CHB management\textsuperscript{10,13,18}

- **Hepatitis B DNA**
- **Alanine aminotransferase (ALT)**
- **Hepatitis B e antigen (HBeAg)**
- **Hepatitis B e antibody (HBeAb or anti-HBe)**
- **Alpha-fetoprotein (AFP)/ultrasound**
Evaluate and treat as appropriate

**Goals of treatment**

The goals of treatment for patients with chronic hepatitis B are to:

- Achieve sustained suppression of HBV replication
- Reduce the risk of liver disease progression to cirrhosis, liver failure, or HCC

**Overview of selected CHB treatment guidelines and algorithms (AASLD, USTA, EASL)**

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<tr>
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<th>ALT (U/L)</th>
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<tr>
<td><strong>HBeAg+</strong></td>
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</tr>
<tr>
<td>AASLD 201519</td>
<td>&gt;20,000</td>
</tr>
<tr>
<td>USTA 201517</td>
<td>≥2000</td>
</tr>
<tr>
<td>EASL 201220</td>
<td>≥2000</td>
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<tr>
<td>AASLD 201519</td>
<td>&gt;2x ULN or noninvasive test/biopsy (+)³</td>
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*Noninvasive testing/TE or liver biopsy showing significant histological disease (defined as fibrosis ≥2/4 and necroinflammatory score ≥2/4) particularly in HBeAg+ patients aged >35-40 years.

*ULN for EASL (2012) is 40 U/L. In patients with normal ALT, treatment may be considered if HBV DNA >2000 IU/mL and there are signs of liver disease.

*Moderate to severe active necroinflammation and/or at least moderate fibrosis demonstrated with liver biopsy (or noninvasive markers once validated in HBV-infected patients).

USTA = US Treatment Algorithm; EASL = European Association for the Study of the Liver; ALT = alanine aminotransferase; ULN = upper limit of normal; TE = transient elastography.

Patients with signs and symptoms suggestive of advanced liver disease or indicative of cirrhosis should be evaluated by a specialist. These patients frequently require ongoing evaluation and management of liver-related complications.

- The USTA and AASLD recommend 19 U/L and 30 U/L as the ALT ULN for women and men, respectively.
  - Previously established ALT ULN values and those used by commercial laboratories are significantly higher.

Approximately 30% of patients with persistently normal ALT levels may have significant fibrosis or inflammation.
Recommendations for HCC surveillance

According to the USTA, all HBsAg+ persons 20 years and older, or any HBsAg+ persons with a family history of HCC, regardless of age, are advised to receive HCC screening twice annually, including a baseline ultrasound at initial presentation whether or not they are receiving treatment for CHB.17

Overview of AASLD recommendations10

Recommended HCC surveillance of HBV carriers at high risk for HCC
- Ultrasound surveillance every 6-12 months
- Periodic screening for AFP alone when ultrasound is not available or is cost-prohibitive

Populations at high risk for HCC
- Asian men >40 years of age
- Asian women >50 years of age
- Patients with cirrhosis
- Persons with a family history of HCC
- Africans >20 years of age
- Any carrier >40 years of age with persistent or intermittent ALT elevation and/or high HBV DNA level >2000 IU/mL

Overview of USTA recommendations17

Recommended tests and frequency for HCC screening and surveillance
- Ultrasound and AFP testing
- Every 6 months

Candidates for HCC screening and surveillance
- All HBsAg+ persons 20 years of age and older
- All HBsAg+ persons with a family history of primary HCC, regardless of age
Recommendations on monitoring CHB patients

Overview of USTA recommendations
By managing CHB in your patients, you may reduce the risk of liver complications such as cirrhosis, liver failure, or HCC.17

Monitoring CHB patients on treatment

Suggested follow-up for patients not receiving treatment (HBeAg+ or HBeAg- CHB with HBV DNA ≥2,000 IU/mL and normal ALT)17

- Assess ALT levels every 3 to 6 months
- Consider liver biopsy or transient elastography to assess fibrosis
- Consider initiating treatment when ALT levels increase or fibrosis is present

HBV DNA <2,000 IU/mL and normal ALT17

- Assess ALT levels every 6 to 12 months
- If ALT levels increase, check serum HBV DNA and exclude other causes of disease

Recommended on-treatment monitoring17

- Monitor serum HBV DNA levels
  - At 12 weeks to identify primary treatment failure
  - At 24 weeks to confirm continued virologic suppression
- Monitor HBV DNA every 3 to 6 months during the first year to confirm adequate viral suppression and detect viral breakthrough
- Monitor HBV DNA and ALT every 6-12 months thereafter

a HBV DNA decline of <1 log10 IU/mL.
Key steps that may help reduce the burden of disease

- **Identify at-risk patients in your practice for HBV screening, as recommended by the USPSTF, CDC, and AASLD**
  - HBV screening involves simple blood tests for HBsAg, anti-HBs, and anti-HBc
- **Screening allows interventions to be implemented, which may help reduce the risk of transmission**
- **Screening can identify CHB early, so that necessary care, including antiviral therapy if appropriate, may be considered**
  - Treatment guidelines (eg, AASLD, USTA, EASL) can help healthcare providers deliver clinically appropriate care for their patients

"Identification and appropriate management of persons with CHB can help prevent serious sequelae of chronic liver disease and complement immunization strategies to eliminate HBV transmission in the US."

— Centers for Disease Control and Prevention

The information contained in this brochure is based on published recommendations and is not a substitute for the professional judgment of the healthcare provider in diagnosing and treating patients.

References: