

2020

PHYSICIAN'S GUIDE TO

**HEPATITIS B** a silent killer

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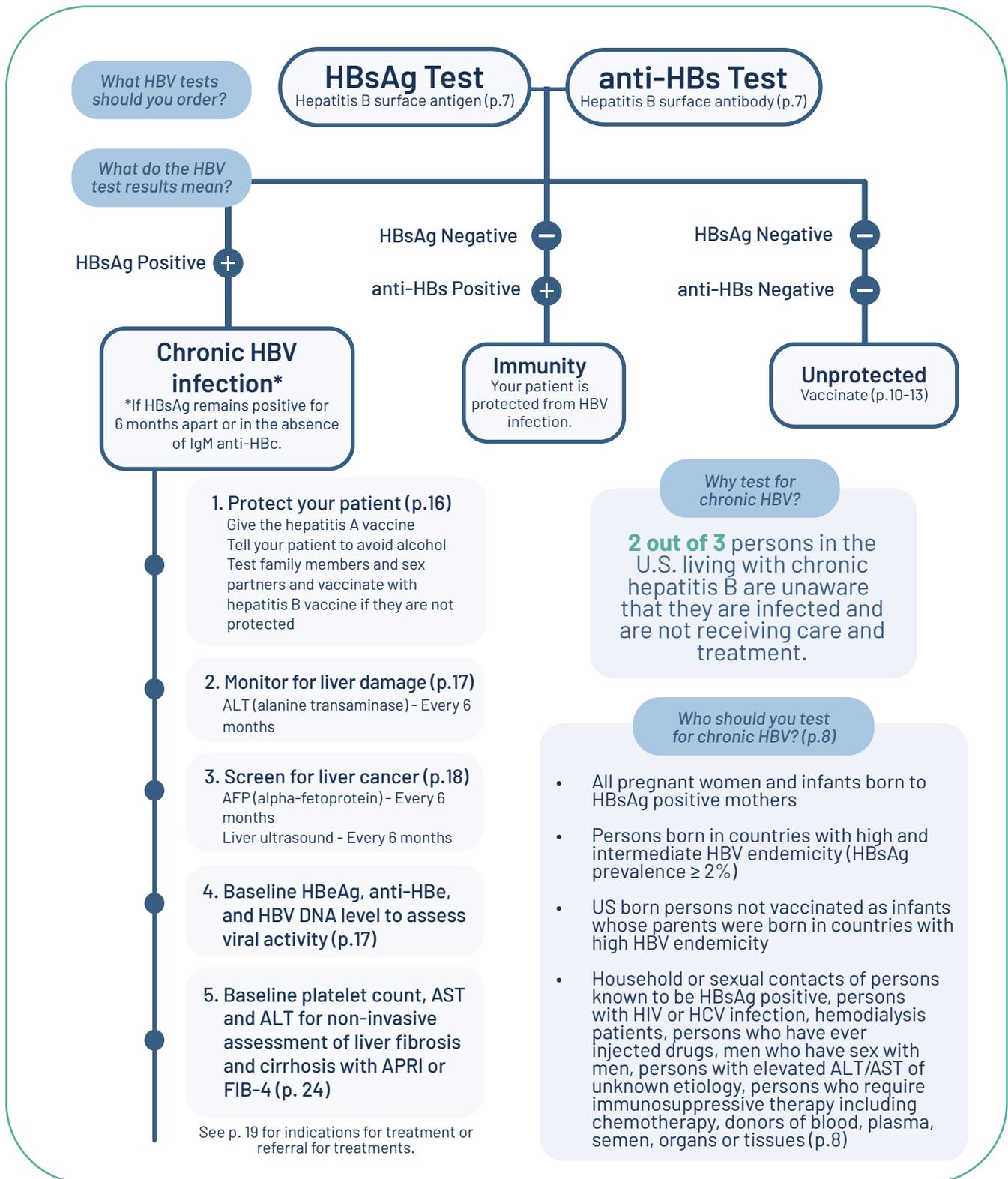
*Providers should build screening, testing, and vaccination strategies into their routine practices. Without concerted action, thousands more Americans will die each year from liver cancer or liver failure related to [hepatitis B and C].*



- Hepatitis and Liver Cancer: A National Strategy for Prevention and Control of Hepatitis B and C  
2010 Institute of Medicine Report



# Recommended Tests to Screen for Chronic Hepatitis B



Recommendations are abridged from Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices 2018,<sup>1</sup> and the 2018 practice guidelines released by the American Association for the Study of Liver Diseases.<sup>2</sup>

# HBV and Liver Cancer Facts

**Hepatitis B** is a potentially serious infection of the liver caused by the hepatitis B virus (HBV) and can lead to premature death from cirrhosis (scarring of the liver), liver failure, or liver cancer.

Worldwide, there are **7 times** more people living with chronic HBV infection than with HIV/AIDS.<sup>4</sup>

Without appropriate medical management, **15-25%** are at risk of premature death from liver cirrhosis, liver failure and liver cancer.<sup>4</sup>

In the U.S., there are as many people living with chronic HBV infection as **HIV/AIDS**.<sup>10</sup>

But **two-thirds** are not aware they are infected because they have not been tested.<sup>11</sup>

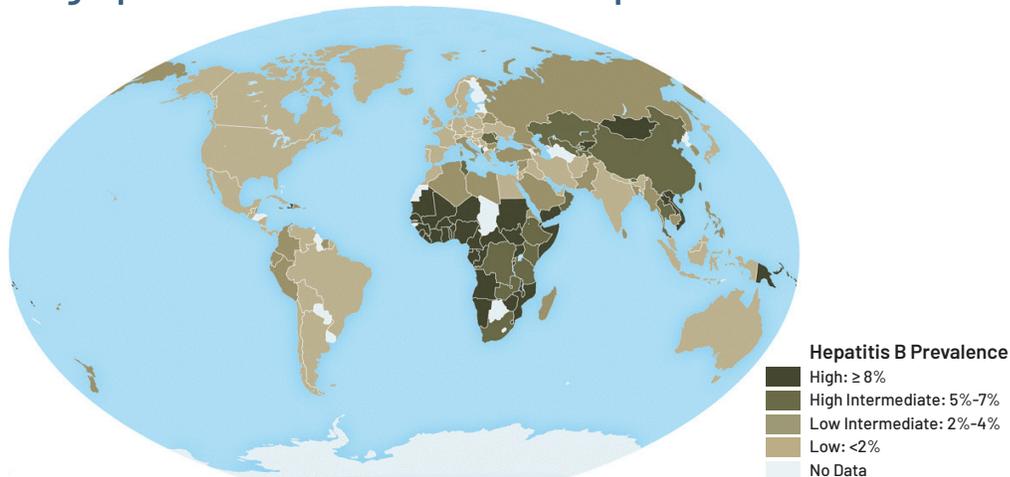
**1 in 12** Asian American adults are chronically infected with HBV.<sup>10</sup>

HBV and liver cancer are the greatest health disparities between Asian and white Americans.<sup>10</sup>

## HBV is a global epidemic

- Although a safe and effective recombinant hepatitis B vaccine has been available since 1982 and there are effective antiviral treatments, HBV still took the lives of almost a million (979,000) people worldwide in 2016.<sup>3</sup>
- About 1 in 30 people in the world (257 million in 2015) is living with chronic HBV infection.<sup>4</sup>
- The burden of disease is greatest in Asia. China alone has an estimated 93 million people chronically infected.<sup>5,6</sup>
- Every 32 seconds, one person dies from the complications of this vaccine-preventable and treatable disease.<sup>3</sup>

## Geographic Distribution of Chronic Hepatitis B Virus Infection



U.S. Centers for Disease Control and Prevention. <https://www.cdc.gov/hepatitis/global/index.htm> (accessed 9/30/2020)

## Burden of chronic HBV infection in the U.S.

- An estimated 900,000 - 2 million people in the U.S. are chronically infected with HBV compared to about 1.2 million infected with HIV.<sup>1,7,8</sup>
- A major risk factor in the U.S. for chronic HBV infection is having been born in an endemic country where many became infected at birth or during early childhood because they were not vaccinated.<sup>1</sup>
- Although Asian Americans make up only 5.9% of the U.S. population, they account for more than half of the burden of chronic HBV infection.<sup>9</sup>
- An estimated 1 in 12 Asian American adults is living with chronic HBV infection, compared to 1 in 1,000 in non-Hispanic white adults.<sup>10</sup>
- Liver cancer frequently caused by chronic HBV infection is the second leading cause of cancer death for Asian men living in the U.S.<sup>10,11</sup>
- Each year about 550 liver transplants are performed for HBV-related liver disease or liver cancer.<sup>12</sup>

# HBV and Liver Cancer Facts

## HBV is a silent killer

- Chronic HBV infection is dangerous because there are often no symptoms (even blood tests for liver enzymes may be normal).<sup>1,2</sup>
- As many as 2 out of 3 chronically infected persons are not aware that they are infected.<sup>9,10</sup>
- By the time symptoms such as abdominal pain and/or abdominal distension appear, it is often too late for treatment to be effective.
- The World Health Organization (WHO) estimated that in 2016 about 90% of HBV-related deaths were associated with chronic HBV infection (40% from hepatocellular carcinoma with or without cirrhosis and 50% from cirrhosis) while 10% were the result of acute infection.<sup>3</sup>

Asians who became chronically infected with HBV at birth or early childhood can develop liver cancer as early as when they become adolescents or young adults.

## HBV is the leading cause of primary liver cancer death worldwide<sup>3</sup>

- HBV is a carcinogen that is third only to smoking tobacco and Helicobacter pylori infection in causing the most cancer deaths worldwide.<sup>3</sup>
- 46% of hepatocellular carcinoma (HCC), the most common type of primary liver cancer, is caused by HBV.<sup>3</sup>
- People chronically infected with HBV are 100 times more likely to develop liver cancer than those who are not infected.<sup>13</sup>

Liver cancer can develop even in the absence of cirrhosis in persons with chronic HBV infection.

## Liver cancer is among the deadliest cancers

- In 2018, liver cancer was the sixth most common cancer and tied stomach cancer as the second deadliest cancer type in the world.<sup>14</sup>
- Liver cancer is a silent killer because patients typically show no symptoms until the end stages of disease.<sup>15</sup>
- If diagnosed late, liver cancer is one of the most difficult cancers to treat. Even today in the U.S., the 5-year survival rate is only 18% for all liver cancers.<sup>16</sup>
- Most of the deaths caused by cirrhosis and liver cancer associated with chronic hepatitis B can be averted by early diagnosis, long-term monitoring and antiviral therapy.<sup>15</sup>

Regular screening for liver cancer in persons with chronic HBV infection can save lives.

# How HBV is Transmitted



HBV is transmitted by infected blood and body fluids including semen or vaginal fluid.<sup>1</sup> The modes of transmission are similar to HIV and can be easily remembered using the mnemonic “BBS”: Birth, Blood, Sex.

## Birth: Mother-to-child infection

HBV can be transmitted from a chronically infected mother to her child during the birthing process. This is one of the most common modes of transmission for Asians.<sup>18</sup> Many pregnant mothers with chronic hepatitis B are unaware of their infection and end up silently passing the virus to the next generation.



## Bloodborne infection

HBV can be transmitted through percutaneous, mucosal and nonintact skin exposure with infected blood. This includes:

- Wound-to-wound contact
- Reusing or sharing needles for tattoos, piercings, acupuncture, or injection drugs
- Sharing razors or toothbrushes contaminated by blood
- Reusing syringes or medical devices including lapses in infection control practices related to blood glucose monitoring in diabetes care
- Unsafe blood transfusion



## Sexually transmitted infection

HBV can be transmitted through unprotected sex with a person infected with HBV. The use of condoms can reduce, but not eliminate, the risk of infection. Vaccination remains the most effective way to protect against HBV (p. 10-12).

## HBV is NOT transmitted through food or water

There are many myths about how HBV is transmitted. A common misconception is that HBV can be spread through contaminated food or water, like the hepatitis A virus. This is not true.

HBV is NOT spread through:

- Sharing food or water
- Sharing eating utensils or drinking glasses
- Tears, sweat, urine, or stool
- Coughing or sneezing
- Hugging or kissing
- Breastfeeding
- Mosquitoes
- Shaking hands

## Dispelling discrimination against people with HBV

Misconceptions and fears about transmission fuel discrimination against people with HBV infection.<sup>17</sup> Explain to your patients that there is no reason to distance themselves from people with chronic HBV infection. Persons with chronic HBV infection should not be excluded from work, school, or other daily activities. In the U.S., several state laws, as well as the Americans with Disabilities Act (1991), protect against discrimination related to chronic hepatitis B infection.

HBV can survive outside the body for 7 days, whereas HIV can survive for only a few hours outside the body.<sup>1</sup>

HBV is 50–100 times more infectious than HIV.<sup>12</sup>

# Acute vs. Chronic Infection

## 3 possible outcomes after initial HBV infection

### 1. Acute hepatitis B resulting in fulminant liver failure

Infection with HBV causes extensive liver cell death resulting in liver failure and sometimes death. Fortunately, this most severe form of acute hepatitis is uncommon, occurring in 0.5-1% of hepatitis B cases, with the highest risk in adults  $\geq 55$  years.<sup>1</sup>

### 2. Acute hepatitis B with full recovery and development of immunity

HBV is spontaneously cleared from the body within a few months, and immunity against future infection develops. There is currently no FDA-approved drug treatment for acute infection, and the main form of therapy is supportive care.

### 3. Chronic hepatitis B

Failure to clear the initial HBV infection will result in a chronic (lifelong) infection. Regular screening for liver damage and liver cancer is needed to determine if antiviral therapy is necessary. Without appropriate medical management, approximately 25% of persons who became chronically infected during infancy or early childhood and 15% who became infected after childhood will die prematurely from cirrhosis, liver failure or liver cancer.<sup>1</sup>

Symptoms of **acute** HBV infection include:

- Jaundice
- Fatigue
- Nausea
- Abdominal pain
- Loss of appetite

People with **chronic** HBV infection usually exhibit **NO SYMPTOMS** until they have developed cirrhosis or advanced liver cancer.

Hepatitis B vaccination at birth protects the infant from HBV infection.

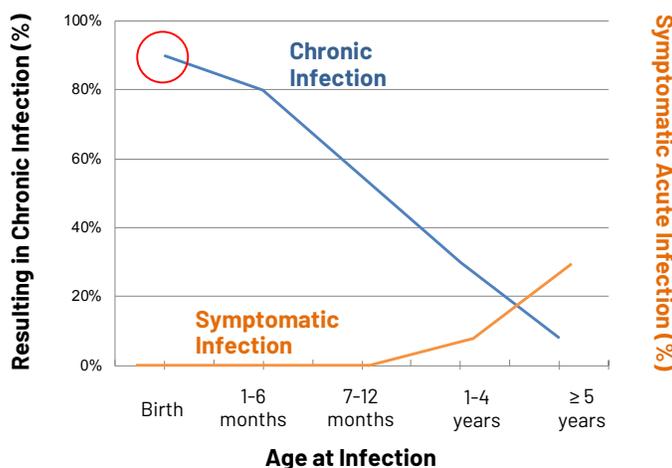
Infants born to HBV infected mothers who did not receive hepatitis B vaccination at birth have an 80-90% chance of developing chronic HBV infection.

Unvaccinated young children who became infected through unsafe injections in the healthcare setting or wound-to-wound contact also have high risk of developing chronic infection.

## Newborns are most vulnerable to chronic infection

Anyone who is not protected against HBV can become infected. However, newborns and young children who become infected with HBV have the greatest risk of developing a lifelong infection. Without appropriate immunoprophylaxis, as many as 90% of infected newborns develop chronic hepatitis B infection. This is why it is important for all newborns to be vaccinated against HBV at birth (p. 13). **When infants and children are infected, they usually exhibit few or no symptoms.** When adults are infected, 30-50% are likely to become ill with symptoms of acute infection (e.g., fatigue, loss of appetite, or jaundice), and 2-6% of infected adults will develop chronic hepatitis B infection.<sup>1</sup>

Outcome of hepatitis B virus infection by age at infection



World Health Organization. Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection. 2015.

# Screening At-Risk Populations for Chronic HBV Infection

## HBV screening is important!

Many chronically infected persons show no outward signs of HBV infection; therefore, screening for hepatitis B is necessary to:

- Identify individuals who have chronic HBV infection so they can receive appropriate medical management.
- Identify those who are unprotected so they can be vaccinated.
- Avoid unnecessary vaccination. Hepatitis B vaccination is not beneficial for persons already chronically infected with HBV and may give them a false assurance that they received protection from infection. Hepatitis B vaccination is also unnecessary for persons already immune (either through prior vaccination or a previous resolved acute infection).

Since up to 1 in 12 foreign-born Asian Americans have chronic HBV infection acquired in early childhood, it is important to test for HBsAg and anti-HBs before vaccination.



HBV screening is a simple blood test for the following hepatitis B serologic markers<sup>2</sup>

### 1. Hepatitis B surface antigen (HBsAg)

The HBsAg test is the ONLY way to definitively diagnose chronic HBV infection. By definition, if a patient remains HBsAg-positive for more than 6 months, then he/she has developed chronic (lifelong) infection. Since most Asians become infected at birth or during early childhood, most Asian patients who test positive for HBsAg will have chronic HBV infection. HBsAg-positive patients require counseling and medical management for chronic HBV infection to reduce their risk for chronic liver disease (p. 16-20).

### 2. Hepatitis B surface antibody (anti-HBs)

The anti-HBs test will tell if your patient who is HBsAg negative is protected against HBV. Anti-HBs can be produced in response to vaccination or recovery from an acute hepatitis B infection.

**HBsAg+**  
Chronic HBV Infection

**HBsAg- / anti-HBs-**  
Needs vaccination

**HBsAg- / anti-HBs+**  
Immune to HBV

Refer to p. 10 to learn about other hepatitis B serologic tests.

# Screening At-Risk Populations for Chronic HBV Infection

Quick Test Results	
Result	Interpretation
HBsAg (+) anti-HBs (-)	Chronic HBV infection*
HBsAg (-) anti-HBs (+)	Immune to HBV
HBsAg (-) anti-HBs (-)	Unprotected; needs vaccination
HBsAg (+) anti-HBs (+) (rare)	Chronic HBV infection*

\*If HBsAg remains positive for 6 months or in the absence of IgM anti-HBc

**ALL PREGNANT WOMEN** should be screened to prevent perinatal transmission.

CDC recommends routine screening of **FOREIGN-BORN PERSONS** from endemic countries regardless of vaccination history.

## Who should get screened for HBV?

Foreign-born persons from endemic countries account for over 70% of persons living with chronic HBV in the U.S.<sup>8</sup> The U.S. Centers for Disease Control and Prevention (CDC), the U.S. Preventive Services Task Force (USPSTF) and the American Association for the Study of Liver Diseases (AASLD) recommend routine HBV screening of all foreign-born persons from both high and intermediate endemic areas (HBsAg prevalence  $\geq 2\%$ ).<sup>1,2,18</sup>

All pregnant women should be screened for hepatitis B infection.<sup>1,2,19</sup> Refer to p.13 for guidelines for screening expectant mothers. Other groups recommended for HBV screening include:<sup>1,2,18</sup>

- U.S. born persons not vaccinated as infants whose parents were born in countries with high ( $\geq 8\%$ ) prevalence (including East Asia and Africa)
- Household, needle-sharing, or sexual contacts of persons known to be HBsAg-positive
- Infants born to HBsAg-positive mothers
- Persons who have ever injected drugs
- Men who have sex with men
- Persons with multiple sex partners or history of sexually transmitted infections
- Persons with elevated ALT/AST of unknown etiology
- Persons with HIV or HCV infection
- Persons who require immunosuppressive or cancer chemotherapy
- Donors of blood, plasma, semen, or tissues
- Inmates of correctional facilities

Regions of high and intermediate HBsAg endemicity include:

**Adults born in countries/regions with HBsAg prevalence of  $\geq 2\%$  (essentially all regions except Australia, New Zealand, Western Europe, North America, Argentina, Chile, Paraguay and Uruguay)**

# Screening At-Risk Populations for Chronic HBV Infection

## What can physicians do to increase screening?

If you are seeing the patient for the first time, ask whether they are foreign-born or have a foreign-born parent from an endemic country. If so, screen for HBsAg and anti-HBs. If they are not infected and not protected, recommend they receive the hepatitis B vaccine (p. 11). In addition, you can help raise awareness about hepatitis B by having educational brochures in the waiting area and at your clinic (p. 24).



*If your patient answers **yes** to either question, he/she should be screened for hepatitis B.*

## What about other hepatitis B blood tests?

- Total hepatitis B core antibody (total anti-HBc) test:**  
 Tells if your patient has been previously infected with HBV, which is useful for screening potential blood donors (the U.S. does not allow people with past HBV infections to donate blood – even if they have recovered). The test by itself does not indicate whether your patient is chronically infected with or protected against HBV infection.
- Hepatitis B core IgM antibody (IgM anti-HBc) test:**  
 Tells if your patient has recently become infected (< 6 months) with HBV.

Blood Test	Result	Interpretation
Total anti-HBc	Positive (+)	Was infected with HBV (the test alone does not tell if immunity or chronic infection has developed)
	Negative (-)	Never been infected with HBV; candidate for donating blood
IgM anti-HBc	Positive (+)	Recently acquired acute HBV infection
HBeAg	Positive (+)	Indicates high viral replication and infectivity
Anti-HBe	Positive (+)	Indicates low viral replication and infectivity (not a protective antibody)

# Vaccinating Against Hepatitis B

## 3-for-Life

Hepatitis B vaccine is safe and >95% effective at preventing HBV infection.<sup>1,8</sup> Vaccination involves a series of 3 shots given over 6 months, and can provide lifelong immunity against HBV. The hepatitis B vaccine is also known as the world's first "anti-cancer vaccine" since it prevents liver cancer caused by HBV infection. It will also protect against hepatitis D, another hepatitis virus that can only occur in persons infected with HBV. The vaccination series can be started at any age. The usual schedule is:



For adults, there is an alternate 2 dose hepatitis B vaccine (Heplisav-B®) given over 1 month. (p. 11-12)

## Who should get vaccinated against HBV?

The CDC recommends universal vaccination of all newborns and previously unvaccinated children and adolescents. Adult immunization is recommended for:<sup>1</sup>

- Anyone seeking protection from HBV infection
- Household, sex, and needle-sharing contacts of HBsAg-positive persons
- Healthcare and public safety workers
- Current and recent injection drug users
- Sexually active persons with more than one sex partner, men who have sex with men, and persons seeking evaluation and treatment of sexually transmitted infection
- Persons with HIV or HCV or other chronic liver disease or predialysis and dialysis patients
- Persons incarcerated, and residents and staff of facilities for developmentally disabled persons
- Unvaccinated adults with diabetes mellitus
- Travelers to regions with high or intermediate HBsAg prevalence

## Who should get tested after vaccination?

Routine anti-HBs testing after hepatitis B vaccination is not recommended except for the following high risk groups:

- **Infants born to HBsAg-positive or HBsAg unknown mothers:** Test for both HBsAg and anti-HBs at 9-12 months of age.<sup>1</sup>(p.14)
- **Healthcare/public safety workers, hemodialysis patients, immunocompromised persons (e.g. HIV-infected persons), sex partners of HBsAg positive persons:** Test for anti-HBs 1-2 months after completing the vaccination series.<sup>1</sup>

## If your patient is NOT immune after vaccination

Although uncommon, about 5% of those who complete the hepatitis B vaccination series may not acquire immunity (anti-HBs levels <10 mIU/mL). In these cases:

1. Administer 1 additional dose of hepatitis B vaccine and test 1-2 months later for immunity (anti-HBs > 10 mIU/mL).
2. If anti-HBs remains < 10 mIU/mL, give 2 additional doses to complete the 3 shot series and retest for anti-HBs. 44 – 100% of these patients will successfully develop immunity.

The rare group of people not protected after six hepatitis B vaccine doses should take care to avoid HBV transmission (e.g., cover wounds, use condoms). Nonresponders exposed to HBV-infected body fluids should get the HBIG shot to prevent chronic infection (p. 15).<sup>1</sup>



**ALL newborns** should be vaccinated.

Anyone who has not already been vaccinated or infected should be offered hepatitis B vaccination.

Revaccination or Booster dose is not generally recommended unless anti-HBs is <10 mIU/mL in:

- Infants born to HBsAg positive mothers
- Sex partners of HBsAg positive persons
- Healthcare personnel
- Hemodialysis patients

Getting the hepatitis B vaccine also protects against hepatitis D.

# Vaccinating Against Hepatitis B

## Free vaccines for children

Hepatitis B vaccine is free for children 0–18 years of age who are on Medicaid or whose vaccinations are not covered by insurance. These vaccines can be obtained through the federal Vaccines for Children program. For more information, visit <https://www.cdc.gov/vaccines/programs/vfc/about/index.html>

Anyone who has not already been vaccinated or infected should be offered hepatitis B vaccination.



## FDA-Approved hepatitis B vaccines

### Monovalent vaccines:

#### Engerix-B® and Recombivax HB®

**For any age:** These single-antigen hepatitis B vaccines are typically given as a 3-shot series at 0, 1, and 6 months. For adolescents 11–15 years old, an alternative 2-dose 10mcg Recombivax HB® regimen given at 0 and 4–6 months may be used. Engerix-B® and Recombivax HB® can be used interchangeably and administered concurrently with hepatitis B immune globulin (HBIG) or other vaccines.<sup>23</sup>

#### Heplisav-B®

**For adults only (18 years of age or older):** Suitable for any adult seeking protection from hepatitis B. This is a two-shot hepatitis B vaccine given at 0 and 1 month.

### Combination vaccines:

#### Pediarix®: hepatitis B+diphtheria+tetanus+pertussis+polio

**For children (6 weeks–7 years of age):** All newborns, regardless of their mother's HBsAg status, should receive a birth dose of the hepatitis B vaccine with either Engerix-B® and Recombivax HB®. After the initial birth dose, a 3-dose Pediarix® regimen given at age 2, 4 and 6 months can be used to complete the hepatitis B vaccine series.<sup>1</sup>

#### Twinrix®: combination hepatitis B and hepatitis A vaccine

**For adults only (18 years of age and older):** Suitable for anyone seeking protection from both the hepatitis B and hepatitis A (HAV) virus. Twinrix® is given as a 3-shot series at 0, 1 and 6 months or an accelerated schedule with 4 doses given at 0, 7, 21–30 days, and 12 months.<sup>23</sup>

## Vaccine administration and storage

Follow these simple precautions to protect your patients:

- **Shake the vaccine before use.** Hepatitis B vaccine normally looks cloudy, but if the vaccine stands for a long time, it may separate from the liquid and look like fine sand at the bottom of the vial. Shake until mixed.
- **Do NOT freeze or expose to freezing temperatures.** Store hepatitis B vaccine at 2–8°C (36–46°F). The “shake test” will determine if the vaccine has been damaged by freezing. If the vaccine fails the shake test (the vaccine and liquid do not mix) you must discard it since it may no longer be effective.
- **Administer the hepatitis B vaccine intramuscularly** (i.e., in the arm for children and adults, and in the thigh for infants). It is ineffective if given subcutaneously in fatty tissue (i.e., in the buttocks). Use a longer 1.5 inch instead of a 1 inch needle for obese adolescents or adults.

Adult Hepatitis B Vaccine Schedules <sup>1</sup>				
Age Group	Single Antigen Hepatitis B Vaccines			Combined Hep A + B Vaccine
	<i>Recombivax HB</i> <sup>®</sup>	<i>Engerix-B</i> <sup>®</sup>	<i>Heplisav-B</i> <sup>®</sup>	<i>Twinrix</i> <sup>®</sup>
<b>Adults (≥18 yrs)</b>			2 doses (0 and 1 month)  20 mcg in 0.5 mL	3 doses (0,1,6 months) or alternate accelerated 4 dose schedule (0,7,21-30days, 12 months) 20 mcg in 1 mL
<b>Adults (≥20 yrs) *</b>	3 doses (0,1,6 months) 10 mcg in 1 mL	3 doses (0,1,6 months) 20 mcg in 1 mL		
<b>Hemodialysis patients and immunocompromised adults (e.g. HIV or persons receiving chemotherapy)</b>	3 doses (0,1,6 months) 40mcg in 1 mL	4 doses (0,1,2,6 months) 40 mcg in 2 mL	2 doses (0 and 1 month) 20 mcg in 0.5 mL	

Pediatric Hepatitis B Vaccine Schedules <sup>1</sup>			
Age Group	Single Antigen Hepatitis B Vaccines		Combination hepatitis B, diphtheria, tetanus, polio and pertussis vaccine
	<i>Recombivax HB</i> <sup>®</sup>	<i>Engerix-B</i> <sup>®</sup>	<i>Pediarix</i> <sup>®</sup>
<b>Infants &gt;2,000 grams born to HBsAg-negative mothers*</b>	3 doses. (Birth dose within 24 hr after birth,1,6 months) 5 mcg in 0.5 mL	3 doses (Birth dose within 24 hr after birth,1,6 months) 10 mcg in 0.5 mL	
<b>Infants and children (6 weeks to &lt; 7 yrs old)</b>			3 doses (2,4,6 months of age) (0.5 mL each). Can be used to complete hepatitis B vaccine series in infants who have received the birth dose
<b>Children and adolescents (1-19 yrs old)*</b>	3 doses (0,1,6 months) 5 mcg in 0.5 mL	3 doses (0,1,6 months) 10 mcg in 0.5 mL	
<b>Adolescents (11-15 yrs old)</b>	2 doses (0,4-6 months) 10 mcg in 1 mL		

\*There are also alternate single antigen hepatitis B vaccine administration schedules that are appropriate for children and adults.<sup>1</sup> \*\*For infants weighing < 2000 grams born to HBsAg-negative mothers: Delay administration of the 3-dose vaccine series until age 1 month or hospital discharge (whichever comes first and even if still <2,000 grams), and then resume the 3-dose series according to the schedule (Final dose of the vaccine series should not be administered before age 6 months).

Adapted from Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. 2018.<sup>1</sup>

# Screening Pregnant Women for Chronic Hepatitis B Infection



## All pregnant women should be screened

Federal guidelines recommend that all pregnant women have a prenatal HBsAg test in the first trimester of each pregnancy, even if they have been previously tested or vaccinated.<sup>17,19</sup> The CDC Advisory Committee on Immunization Practices also recommends the following measures:<sup>19</sup>

### If your pregnant patient is HBsAg-negative:

Inform her that Federal guidelines recommend all newborns receive the hepatitis B vaccine within 24 hours after birth to protect them from hepatitis B infection which is a major cause of liver cancer and liver cirrhosis.

### If your pregnant patient is HBsAg-positive:

Send copies of the lab report:

**1. To the birth hospital** to document the woman's positive HBsAg status. A hospital notice or alert should also be included in the woman's medical record to remind the delivery hospital/nursery that the infant needs to receive HBIG in addition to hepatitis B vaccine birth dose.

**2. To the local health department** for case management by Perinatal Hepatitis B Prevention Program\* and indicate the positive test result is from a pregnant woman if not stated on the lab report (Reporting all HBsAg-positive cases is required by law in most states).

**Inform her about her HBsAg status and provide her with linguistically and culturally appropriate education pamphlet and resources** about chronic hepatitis B and prevention of mother-to-child prevention. (p. 24)

Emphasize to the expecting mother the importance of having her newborn receive HBIG and the birth dose of hepatitis B vaccine as soon as possible after birth, and the need for postvaccination testing at 9-12 months to assess whether the newborn has developed immunity or requires additional vaccine doses.

**Order prenatal HBV DNA and ALT blood tests.** If she is not receiving care for chronic hepatitis B, refer her to a primary care provider experienced in hepatitis B management or specialist to assess whether she requires tenofovir antiviral therapy for treatment of active hepatitis B associated with elevated ALT level or for prophylaxis to further eliminate the risk of perinatal transmission.

**Identify her household, family and sex partner for screening** and hepatitis B vaccination if they are not protected.

Link to perinatal hepatitis B prevention program: <https://www.cdc.gov/vaccines/programs/perinatal-hepb/index.html>

## FAQs for Moms-to-be

### Is breastfeeding safe?

HBV is not transmitted through breast milk. Breastfeeding is safe for all newborns, regardless of the mother's HBV infection status.<sup>1</sup>

### Can C-sections prevent HBV?

Cesarean sections cannot prevent HBV transmission from mother to child. Hepatitis B vaccination plus the HBIG shot is the best way to protect newborns against HBV.<sup>1</sup>

### Can women with chronic HBV infection be treated during pregnancy?

Antiviral treatment with tenofovir disoproxil fumarate (TDF) is indicated if the pregnant woman has active hepatitis. AASLD also recommends TDF given in the last trimester to pregnant women with high HBV DNA level (>200,000 IU/mL) to further reduce or eliminate the risk of perinatal transmission.<sup>2</sup>

# Preventing Mother-to-Child Transmission of HBV

Timely hepatitis B vaccine birth dose and hepatitis B immune globulin (given as soon as possible and within 12 hours after birth), and completion of the hepatitis B vaccine series is important to prevent perinatal transmission.

Newborns and infants infected with HBV have the highest risk of developing chronic hepatitis B infection. Without immunoprophylaxis, 80-90% of newborns to HBsAg positive women will develop chronic hepatitis B infection. Infants who developed chronic infection are also at the highest risk of death from liver cancer and liver cirrhosis later in adulthood. Therefore, the pillar of the U.S. and global HBV elimination strategy is infant immunization and the prevention of mother-to-child transmission.

Infants born to HBsAg positive mothers should be tested for anti-HBs and HBsAg after completing the vaccine series to check for immunity and infection. Pregnant women with high viral load are at increased risk for perinatal transmission. Women with HBV DNA > 200,000 IU/mL is recommended by AASLD to receive TDF antiviral therapy starting at 28-32 weeks of pregnancy until delivery.

**Prevention of Hepatitis B Mother-to-Child Transmission<sup>1,2</sup>**

HBsAg positive pregnant women	Single antigen hepatitis B vaccine		Hepatitis B Immune Globulin (HBIG)	Postvaccination serologic testing (HBsAg, anti-HBs) of infants born to HBsAg positive mothers	Antiviral therapy for infected pregnant women recommended by AASLD <sup>2</sup>
	<i>Recombivax HB</i> <sup>®</sup>	<i>Engerix-B</i> <sup>®</sup>			
Antenatal HBV DNA level < 200,000 IU/mL	3 doses (Birth dose as soon as possible and within 12 hrs after birth, 1,6 months)*  5 mcg in 0.5 mL	3 doses (Birth dose as soon as possible and within 12 hrs after birth, 1,6 months)*  10 mcg in 0.5 mL	As soon as possible and within 12 hrs after birth  0.5 mL	At 9-12 months of age or 1-2 months after completing the last vaccine dose.  If HBsAg negative and anti-HBs < 10 mIU/mL: revaccinate with 1 vaccine dose or 3 doses. Repeat PVST 1-2 months after the last dose	Not recommended
Antenatal HBV DNA level > 200,000 IU/mL	3 doses (Birth dose as soon as possible and within 12 hrs after birth, 1,6 months)*  5 mcg in 0.5 mL	3 doses (Birth dose as soon as possible and within 12 hrs after birth, 1,6 months)*  10 mcg in 0.5 mL	As soon as possible and within 12 hrs  0.5 mL	At 9-12 months of age or 1-2 months after completing the last vaccine dose.  If HBsAg negative and anti-HBs < 10 mIU/mL: revaccinate with 1 vaccine dose or 3 doses. Repeat PVST 1-2 months after the last dose.	TDF 300mg/day, starting at 28-32 wks until birth. After stopping TDF, check ALT for hepatitis flare every 3 months for 6 months

**For infants weighing less than 2000 grams who are born to HBsAg positive mothers or HBsAg status unknown mothers:** Give the HBIG shot and hepatitis B vaccine within 12 hours of birth, but do not count the initial vaccine dose as part of the 3 dose series. Start the 3-dose vaccine series beginning at chronological age 1 month or hospital discharge (Final dose of the vaccine series should not be administered before age 6 months).

\* After the hepatitis B birth dose, according to ACIP recommendations, Pediarix<sup>®</sup> can be used to complete the hepatitis B vaccine series at 2, 4, and 6 months in infants born to HBsAg positive or negative mothers.<sup>1</sup>

Adapted from Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. 2018.<sup>1</sup>

# Preventing HBV Transmission in Healthcare Settings



## Avoiding needlestick injuries

### How to protect yourself:

- Practice universal precautions to prevent transmission of HBV and other bloodborne pathogens, including safe needle handling and the use of gloves.
- Vaccinate all health care workers against HBV infection with the complete vaccine series, then test for anti-HBs 1-2 months after completion of the vaccination series to confirm protection (anti-HBs level  $\geq 10$  mIU/mL). See page 10 for healthcare workers that did not develop immunity.

## Preventing patient-to-patient transmission

- Do NOT reuse needles and syringes. Always use sterile syringes, preferably with auto-disable features to prevent reuse.<sup>20</sup>
- Immediately dispose used needles into puncture-resistant safety containers.
- Avoid use of multi-dose vials. Use of single-dose vials greatly reduces the risk of patient-to-patient transmission.
- Adhere to Standard Precaution and aseptic technique principles. Relatively safe procedures such as dialysis, glucose monitoring, and endoscopy can become sources of hepatitis B outbreak when infection control practices are not followed. Fingertick devices should never be used for more than one person.<sup>21</sup> Ensure that shared equipment is properly sterilized between patients and that disposable parts are used when available.<sup>20</sup>



## Preventing physician-to-patient transmission

The updated CDC recommendation reaffirmed that HBV-infected healthcare providers and students who conform to infection control standards do not require curtailing of their practices. HBV-infected providers can perform exposure-prone procedures if an undetectable or low ( $<1,000$  IU/mL) HBV viral load is documented every 6 months.<sup>22</sup>

## Post-exposure prophylaxis

### HBIG (Hepatitis B Immune Globulin)

#### For any age:<sup>1</sup>

HBIG should be administered to unprotected persons as soon as possible after exposure to blood or bodily fluids infected with HBV (e.g., when infants are born to HBsAg-positive women, after needlestick injuries, and after sexual contact with an infected person). Administration of HBIG more than 7 days after percutaneous or perinatal exposure and after 14 days after sexual exposure is unlikely to be effective.

#### When you are exposed to a needlestick from a HBsAg positive person:<sup>1</sup>

1. Perform baseline testing for anti-HBs, total anti-HBc, HBsAg, and ALT.
2. If you are unvaccinated, uncertain of hepatitis B vaccination history, or anti-HBs titer  $< 10$  mIU/mL, get the HBIG shot (0.06 mL/kg or 5 mL for adults) preferably within 24 hours of exposure, and initiate the 3-shot hepatitis B vaccine series.
3. If you are a known nonresponder (anti-HBs  $< 10$  mIU/mL after hepatitis B vaccination), give HBIG and repeat a second HBIG dose a month later.
4. If you are a known responder or baseline testing anti-HBs level  $\geq 10$  mIU/mL, no treatment is recommended.
5. Perform follow up testing for anti-HBs, total anti-HBc, HBsAg, and ALT after 6 months.

# Checklist for Managing Chronic HBV Infection

## 7 Steps to care for your chronic HBV patients

### 1. Help your patients understand their hepatitis B status

Make sure test results are clear, and give your patient HBV informational brochures that are culturally and linguistically appropriate.

See page 24

### 2. Monitor patients regularly for liver damage and cancer

People with chronic HBV infection can live completely normal lives as long as they are monitored regularly for liver damage and liver cancer. Early detection and treatment will increase your patient's chance of long-term survival.<sup>2,15</sup>

See pages 17-18

### 3. Give the hepatitis A vaccine

Hepatitis A is an infection of the liver caused by a different virus known as hepatitis A virus (HAV) that is transmitted by contaminated food or water. Hepatitis A vaccination is recommended for unprotected patients with chronic liver disease including chronic viral hepatitis to reduce the risk of further liver damage.<sup>2,24</sup>

### 4. Tell your patients to avoid regular alcohol consumption

Alcohol is toxic to the liver and may accelerate the progression of liver damage to cirrhosis and liver failure. Drugs, herbal supplements, and other substances with known liver toxicity should also be avoided.<sup>1</sup>

### 5. Test and vaccinate your patients' close contacts

Your patient's family members and sex partner(s) should be tested for HBsAg and anti-HBs. This will help determine if they are 1) also chronically infected with HBV and need medical management, 2) vulnerable and need vaccination, or 3) already protected.<sup>2</sup>

See page 7

### 6. Educate your patients about how to minimize the risk of infecting others

Cover wounds, use condoms, and do not share toothbrushes or razors. If diabetic, do not share blood glucose monitoring equipment that could be contaminated by blood. Advise your patients not to donate blood, organs, tissue, or semen.<sup>1</sup>

See page 5

### 7. Give antiviral treatment if indicated

Not everyone with HBV needs drug treatment, but medication may be appropriate for patients with high levels of both ALT and HBV DNA, patients with cirrhosis, or patients receiving cancer chemotherapy.<sup>2,23</sup>

See pages 19-20

# Monitoring for Liver Damage

Test	Monitors	Frequency of Test
ALT (alanine aminotransferase)	Liver damage	Every 6 months
AFP (alpha-fetoprotein)	Liver cancer	Every 6 months
HBV DNA level	Viral activity	Every year
Ultrasound	Liver cancer	Every 6 months

## Monitor for liver damage regularly

Many chronically infected persons show no symptoms and feel perfectly healthy, even though they may already have cirrhosis or be in the early stages of liver cancer. Therefore, it is important for physicians who see patients with chronic HBV infection to remain vigilant about monitoring for flare-ups of hepatitis, liver damage, or cirrhosis, and to schedule regular screenings for liver cancer (p. 18).<sup>2,23</sup>

Every 6 months, order ALT to monitor for liver damage, and AFP and liver ultrasound to monitor for liver cancer.

HBV DNA level indicates if liver damage is due to HBV, and helps evaluate treatment response.

HBeAg and anti-HBe help monitor treatment response in patients HBeAg positive pre-treatment.

Platelet count and albumin monitor for cirrhosis.

## ALT blood test – every 6 months

The ALT (alanine transaminase) test is one of the most useful and low cost tests to assess whether treatment against HBV is needed. An elevated ALT level is indicative of active liver damage. *If ALT is elevated, but HBV DNA level is undetectable or low, the patient should be evaluated for other causes of liver damage including medications, alcohol and metabolic fatty liver disease.* If ALT is persistently normal, there is no evidence to support HBV treatment (unless the patient has cirrhosis or for prophylaxis to prevent perinatal transmission or to prevent hepatitis flare in patients receiving hepatitis C or cancer chemotherapy/immunosuppressive therapies).<sup>1,2</sup>

## HBV DNA level by PCR

The HBV DNA test is a direct measure of HBV viral load. It is a recommended baseline test after initial diagnosis of chronic hepatitis B. If your patient's ALT level is elevated, the HBV DNA test will help verify whether his/her liver damage is caused by increased viral activity, and determine whether HBV treatment is appropriate. HBV DNA levels that become undetectable or decrease significantly are a good measure of treatment response.<sup>2</sup> For patients on antiviral treatment, rising HBV DNA levels may indicate patient non-compliance or the emergence of drug resistant mutant virus.

## HBeAg (hepatitis B e antigen), anti-HBe (hepatitis B e antibody)

Recommended baseline tests after initial diagnosis of chronic HBV infection. HBeAg is generally a marker of high viral replication and infectivity. If HBeAg is positive, the test should be repeated yearly. HBeAg seroconversion, which is the loss of HBeAg and development of anti-HBe, is a sign of favorable response to treatment, but can also occur spontaneously in the course of chronic HBV infection. This seroconversion can take years. The development of anti-HBe does not mean that your patient is cured and does not mean that treatment is unnecessary. Some individuals carry mutant HBV strains that do not secrete HBeAg; thus, the HBV DNA test is preferred when measuring HBV viral load.<sup>2</sup>

## Platelet count and albumin

Platelet count is a sensitive indicator of significant fibrosis and cirrhosis. A low platelet count (generally less than 150,000 platelets/mm<sup>3</sup>) combined with a low albumin level (3.5 gm/dL or lower), with or without prolonged prothrombin time, are signs suggestive of cirrhosis with impaired liver function.<sup>2</sup>

Non-invasive tests are used increasingly in place of liver biopsy to assess liver fibrosis/cirrhosis. (p.19) Liver biopsy is sometimes recommended to determine whether a person with mildly elevated ALT and DNA level is a candidate for antiviral treatment. Liver biopsy is unwarranted if there is a clear cut indication for antiviral treatment.

# Screening for Liver Cancer

## Screen for liver cancer regularly

Chronic hepatitis B infection increases the risk of developing hepatocellular carcinoma (HCC), the most common type of primary liver cancer by 50-100 times. Regular liver cancer screening with both AFP and ultrasound tests is recommended because liver cancer can occur even in patients without cirrhosis and in the presence of normal ALT levels. AFP is elevated in only 40-60% of liver cancers in patients with chronic hepatitis B. Ultrasound tests miss about 20% of liver cancers, especially in patients who are obese or have heterogeneous livers due to fatty liver or cirrhosis. Therefore, it is important for both tests to be performed regularly.<sup>2</sup>

### AFP blood test – every 6 months

The AFP (alpha-fetoprotein) test is the most widely used blood test to detect liver cancer. **A rising AFP level on serial measurements** even below 30 ng/mL or an AFP level >400 ng/mL is usually associated with liver cancer (normal range is <10 ng/mL). Since AFP levels may appear normal in 40% of liver cancers, an ultrasound is needed to help detect tumors.<sup>2,25,26</sup>

### Ultrasound – every 6 months

Ultrasound is used to screen for liver tumors. Since use of ultrasound can catch only 80% of liver cancers, it must be performed along with the AFP test. If the ultrasound result is inconclusive (common in patients with cirrhosis or fatty liver) or your patient shows rising AFP levels, you should evaluate using a triphasic spiral CT scan or MRI scan of the liver or refer him/her for further assessment. A lesion that enhances on the arterial phase and washes out to become less dense than the rest of the liver in the delayed venous phase of scanning is characteristic of HCC (see example at right). **A patient with a new lesion detected on ultrasound or CT scan and/or rising AFP levels should be referred immediately for liver cancer evaluation and treatment.**<sup>2</sup>

### Cirrhosis and family history increase the risk of liver cancer

If your patient develops cirrhosis or has a family history of liver cancer, an ultrasound of the liver should be performed every 6 months regardless of age.<sup>2</sup>

## Early Detection is Key to Improving Survival

Liver cancer caused by chronic HBV infection often develops between 30 to 65 years of age, when people are maximally productive and have family responsibilities. It is reasonable to start regular ultrasound screenings in non-cirrhotic men at the age of 30-40 years and in women at the age of 50 years and even earlier if there is a family history of liver cancer.<sup>2,25,26</sup>

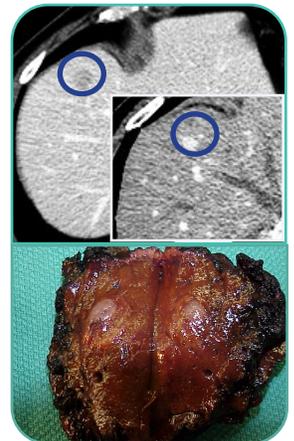
Late diagnosis of liver cancer is often the reason for the 6 to 12-month average survival time following diagnosis. It also explains the approximate 18% survival rate of liver cancer patients. However, regular screening to detect the cancer while it is small can lead to successful treatment by surgical and nonsurgical treatments, resulting in long-term survival.<sup>2,23</sup>

Liver cancer screening is important because:<sup>2,25,26</sup>

- Most patients have the appearance of perfect health without showing any symptoms until it is already too late.
- Small tumor lumps are impossible to feel because of the shielded location of the liver underneath the ribs.
- Pain is uncommon until the tumor is large; even then, some tumors do not cause pain.
- Liver cancers can grow rapidly.

Chronic hepatitis B increases the risk of liver cancer 100x.

Both the AFP and ultrasound tests must be done **regularly** because either test alone can miss the cancer.



Liver ultrasound every 6 months is important particularly in patients with cirrhosis or a family history of liver cancer because of their increased risk of developing liver cancer.

# Principles of Drug Treatment for Chronic HBV Infection

All HBsAg positive persons require long-term monitoring for liver damage and liver cancer, but not all of them will require antiviral drug treatment.

Initiation of HBV treatment is indicated if there is evidence of liver damage with elevated ALT and HBV DNA levels, or cirrhosis.

Prophylactic antiviral therapy is recommended to prevent viral activation while receiving HCV treatment or immunosuppressive therapy, and to eliminate perinatal transmission in HBsAg positive pregnant women with high viral load.

## Rationale for treatment

Although **there is no cure yet for chronic hepatitis B**, treatment when indicated can prevent disease progression and reduce the risk of liver cancer. Regular screening for liver damage is necessary to determine if and when initiation of HBV treatment is appropriate (p. 17-18).

**Not every patient with chronic hepatitis B needs to be on treatment.**

Patients should be informed about the treatment rationale, as well as options, side effects, and risks associated with each treatment.

### Treatment indicated

#### Patients without Cirrhosis or Significant Fibrosis

Persistently Elevated ALT level\*  
Men  $\geq 70$  U/L, Women  $\geq 50$  U/L  
**And** HBV DNA level  
HBeAg positive  $\geq 20,000$  IU/mL  
HBeAg negative  $\geq 2,000$  IU/mL

#### Patients with Significant Fibrosis (F2-F3)

Persistently Elevated ALT level\*\*  
Men  $> 35$  U/L, women  $> 25$  U/L  
**And** HBV DNA level  
HBeAg positive  $\geq 20,000$  IU/mL  
HBeAg negative  $\geq 2,000$  IU/mL

#### Patients with Cirrhosis (compensated or decompensated)

Regardless of ALT, HBV DNA levels and HBeAg status

### Prophylactic antiviral therapy is recommended

#### To reduce risk for flare up of the hepatitis B infection that can potentially lead to liver failure:

HBsAg positive patients (regardless of baseline ALT and HBV DNA levels or HBeAg status) receiving immunosuppressive/ cancer therapy or hepatitis C antiviral therapy. \*\*\*

#### To further reduce/eliminate the risk of perinatal transmission of hepatitis B in HBsAg pregnant women with very high antenatal HBV DNA level ( $>200,000$ IU/mL):

Patients are recommended to receive TNF from 28-32 weeks of pregnancy until birth. (p.14)

Adapted from Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance.<sup>2</sup> \* ALT  $\geq 2x$  upper limit of normal, \*\* ALT  $>$  upper limit of normal, but less than  $2x$ .

\*\*\*HBsAg-negative, but anti-HBc positive patients receiving immunosuppressive therapy e.g. anti-CD20 therapy would also need to be monitored for HBV reactivation.

Non-invasive tests are used increasingly in place of liver biopsy to assess liver fibrosis/cirrhosis. They include transient elastography that measures liver stiffness with ultrasound or with MRI (magnetic resonance elastography) using a low frequency pulse applied over the liver. When transient elastography is not available, assessment can be made using blood markers to generate a fibrosis score (e.g. FibroTest, APRI and FIB-4).

To access the APRI and FIB-4 calculator, visit KnowHBV.org or download the Know HBV app on chronic hepatitis B treatment decision tool for adults at the Apple app store or Google Play. (p.24)

# Medications for Chronic Hepatitis B Treatment

## Oral Antivirals

Oral antivirals are nucleoside and nucleotide analogues that inhibit replication of HBV. Patient compliance in taking the medication daily is important to minimize the development of mutant or drug-resistant viruses. Treatment with oral antivirals will likely require long-term suppressive therapy.<sup>2</sup>

### Entecavir (ETV)

Available as generic or brand drug, Baraclude<sup>®</sup>. FDA approved in 2005. Pill or oral solution (normal dose 0.5mg) taken once a day, normal dose.

### Tenofovir disoproxil fumarate (TDF)

Available as generic or brand drug, Viread<sup>®</sup>. FDA approved in 2008. Pill (300 mg) once a day. Need to monitor renal function (test for blood levels of blood urea nitrogen and creatinine).

### Tenofovir alafenamide (TAF)

Available as brand drug, Vemlidy<sup>®</sup>. FDA approved in 2016. Pill (25mg) once a day. Lower risk of reduced renal function and bone density than TDF. Need to monitor renal function (test for blood levels of blood urea nitrogen and creatinine).

## Possible side effects

For oral antivirals, side effects are uncommon and usually mild. Tenofovir can potentially increase the incidence of osteopenia and osteoporosis and has potential renal toxicity, though it is uncommon.<sup>2</sup>

For injection immunostimulators, side effects may be severe and include flu-like symptoms, hair loss, leukopenia, and psychiatric effects.<sup>2</sup>

## Injection Immunostimulators

The earliest FDA approved treatment of chronic hepatitis B is interferon alfa-2b that is administered subcutaneously 3-5 times a week for 6-12 months (Intron A<sup>®</sup>, approved in 1991). In 2005, a once a week injection, peginterferon alfa-2a (Pegasys<sup>®</sup>), was also approved by the FDA. However, treatment with these injection immunostimulators that stimulate the immune system to kill infected liver cells are now seldom prescribed for HBV treatment because of their side effects that could be severe (including flu-like symptoms, hair loss, leukopenia, psychiatric effects), and the generally low treatment response rate especially in patients with low pre-treatment ALT levels, high viral load and long duration of chronic infection. They are also not recommended for elderly patients and patients with decompensated cirrhosis.

## Favorable responses to HBV treatment

- Sustained viral suppression: loss or marked reduction of HBV DNA levels
- Normalization of serum ALT levels
- HBeAg seroconversion: loss of HBeAg, development of anti-HBe
- Loss of HBsAg
- Improvement in liver inflammation and fibrosis
- Long-term reduction in the risk of liver cancer

## What about herbal treatments?

Herbal treatments have not been proven to prevent or treat HBV infection. Some herbs can also cause liver damage.

Note: There are no large-scale clinical studies that support combining the use of oral antivirals and injection immunostimulators in chronic HBV treatment.<sup>2</sup>

# Frequently Asked Questions

**Q:** My doctor told me that I have hepatitis B, but that I have normal liver function tests and am a “healthy carrier.” What does this mean?

**A:** The term “healthy carrier” is misleading and should be discontinued. An HBV carrier is someone who has chronic HBV infection. Many chronically infected patients do not show symptoms and have normal liver function tests, but are still at increased risk for liver cancer and liver damage. Therefore, it is critical to remain vigilant about regular monitoring for liver damage (with ALT blood test every 6 months) and liver cancer (with AFP blood test and liver ultrasound every 6 months)

**Q:** Isn't hepatitis B transmitted through contaminated food and water?

**A:** No. HBV is transmitted like HIV: from an infected mother to her child at birth, through contaminated blood, or through unprotected sex. A different virus, the hepatitis A virus, is spread through food and water contaminated by human fecal waste.

**Q:** If I have hepatitis B, am I going to die from liver cancer or liver failure?

**A:** People with chronic hepatitis B can lead completely normal and active lives. With regular monitoring for liver damage and liver cancer every 6 months, liver disease can be detected early and treated quickly to prevent further damage, which will increase the probability of long-term survival.

**Q:** If I am pregnant and have chronic hepatitis B, will my child be infected as well?

**A:** Hepatitis B is NOT a hereditary disease. Mothers with high HBV DNA levels or who test positive for HBeAg are at the greatest risk of infecting their newborns. HBsAg-positive mothers can protect their newborns from becoming chronically infected with HBV if the newborn receives the first dose of the hepatitis B vaccine and the hepatitis B immune globulin (HBIG) shot within 12 hours of birth, and completes the hepatitis B vaccination series. Even pregnant women with very high HBV DNA levels can protect their newborns from infection by taking an antiviral medicine from 28-32 weeks of pregnancy until delivery.

**Q:** I have already received my 3-shot hepatitis B vaccination. Do I need a booster shot?

**A:** The CDC does not recommend a routine booster shot of the hepatitis B vaccine for persons with a normal immune status who have previously completed the hepatitis B vaccine series. Completion of the hepatitis B vaccine series provides long-term protection against HBV in most of those vaccinated.

**Q:** Why is hepatitis B so common in Asians?

**A:** There is no clear explanation for the endemic persistence of HBV in Asia, though lack of symptoms, testing, vaccination, and awareness are all contributing factors. Because mother-to-child transmission is common in Asians, HBV infection is often passed silently from generation to generation. However, anyone (regardless of race or gender) without proper vaccination is susceptible to HBV infection.

# Glossary of Key Terms

<b>Acute HBV infection</b>	Initial infection with hepatitis B virus. May result in liver failure and sometimes death, but over 90% of adult cases will recover completely and develop immunity.
<b>AFP</b>	Alpha-fetoprotein is a biomarker for liver cancer. Elevated or rising AFP levels can indicate liver cancer.
<b>ALT</b>	Alanine transaminase (or alanine aminotransferase). Elevated ALT levels can indicate active liver damage. Also referred to as SGPT (serum glutamate pyruvate transaminase).
<b>AST</b>	Aspartate transaminase (or aspartate aminotransferase). Elevated AST levels can indicate active liver damage, but it's less specific than ALT. AST may also be elevated with heart and skeletal muscle damage. Also referred to as SGOT (serum glutamic-oxaloacetic transaminase).
<b>Anti-HBc</b>	Hepatitis B core antibody. A negative HBsAg but a positive total anti-HBc test indicates past HBV infection. A positive IgM anti-HBc test indicates the person has acute hepatitis B and has only been recently infected (< 6 months) with HBV. Not a protective antibody.
<b>Anti-HBe</b>	Hepatitis B e antibody. Generally indicates low viral replication and infectivity. Not a protective antibody.
<b>Anti-HBs or HBsAb</b>	Hepatitis B surface antibody. Levels $\geq 10$ mIU/mL indicate protection against HBV.
<b>Chronic HBV infection</b>	Clinical term used to describe lifelong HBV infection, indicated by presence of hepatitis B surface antigen (HBsAg) in the blood for more than six months.
<b>Cirrhosis</b>	Severe scarring of the liver that can lead to liver failure and death. Common causes include chronic hepatitis B or C, excessive alcohol consumption, and nonalcoholic fatty liver disease.
<b>HBeAg</b>	Recommended baseline test after initial diagnosis of chronic HBV infection. HBeAg is a marker of high viral replication and infectivity (though some mutant HBV strains have increased viral replication but negative HBeAg).
<b>HBeAg seroconversion</b>	Loss of HBeAg and development of anti-HBe, is indicative of a favorable response to HBV treatment. It can also occur spontaneously in the course of chronic HBV infection.
<b>HBIG</b>	Hepatitis B immune globulin. Provides short-term protection against HBV infection and is given in combination with the 3-dose hepatitis B vaccine, especially to unprotected individuals exposed to HBV or newborns born to chronically infected mothers.
<b>HBsAg</b>	Hepatitis B surface antigen. The gold standard test to diagnose chronic hepatitis B. Its presence for at least six months after initial infection indicates chronic HBV infection.
<b>HBV DNA</b>	Hepatitis B virus deoxyribonucleic acid. The basis of the most direct blood test used to measure the hepatitis B viral load. It is used to assess and monitor the treatment of chronic HBV patients.
<b>Hepatitis</b>	General term meaning "inflammation of the liver," which can be caused by bacterial infections, trauma, adverse drug reactions, and a range of viruses including hepatitis A, B, C, D, and E.
<b>Hepatitis A</b>	Disease of the liver caused by infection with the hepatitis A virus (HAV). HAV is transmitted through food or water contaminated by fecal matter from humans infected with HAV. It is vaccine-preventable. HAV does not cause a chronic infection or liver cancer.
<b>Hepatitis B</b>	Disease of the liver caused by infection with the hepatitis B virus (HBV). Chronic infection with HBV can lead to death caused by cirrhosis, liver failure, or liver cancer. It is vaccine-preventable.
<b>Hepatitis C</b>	Disease of the liver caused by infection with the hepatitis C virus (HCV). Largely a bloodborne infection. Chronic hepatitis C infection can also cause liver cancer and cirrhosis. Over 95% of patients with chronic hepatitis C infection are cured after a 2-3 months course of oral hepatitis C antiviral therapy. There is no vaccine to prevent HCV infection.
<b>Hepatitis D</b>	Disease of the liver caused by the Hepatitis D or delta virus. Largely a bloodborne infection that can cause chronic infection, liver cirrhosis and liver failure. Hepatitis D only infects a person who is also infected with hepatitis B, hence the hepatitis B vaccine will also protect against hepatitis D.
<b>Hepatitis E</b>	Disease of the liver caused by the hepatitis E virus. Like hepatitis A, it is transmitted by contaminated food or water in endemic regions of the world. Pregnant women who became infected can develop severe liver disease and liver failure. Chronic hepatitis E infection is rare but has occurred in immunocompromised persons and transplant recipients. There is only one hepatitis E vaccine and it is only approved in China.
<b>Hepatocellular carcinoma (HCC)</b>	Most common type of primary liver cancer. Worldwide, an estimated 80% of HCC is caused by chronic HBV or HCV infection. Other causes of HCC include alcoholic cirrhosis, non-alcoholic fatty liver disease associated with obesity, and aflatoxin, a heat resistant toxin produced by certain mold that have contaminated food crops including peanuts and cottonseed. <sup>26</sup>

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# Additional Resources



## Know HBV: A Chronic Hepatitis B Treatment Decision Tool for Adults

Free Mobile App: Apple app store/Google Play

- Also available on the web: <https://knowhbv.org>

## APRI and FIB-4 Calculator

Non-invasive tests to assess liver fibrosis and cirrhosis.

- Available on Know HBV mobile app or <https://knowhbv.org>



## Hepatitis B Calculator

Provides country-specific, cost-effectiveness analysis of chronic hepatitis B treatment.

- <https://hepbcalculator.org>



## Hepatitis B Health Risk Assessment

Online confidential self assessment for HBV risk.

- <https://med.stanford.edu/liver/education/hra.html>
- <https://hepbhra.org>

## HBV Informational Resources for Patients, Clinics, and Birth Hospitals (Multiple Languages)



For HBsAg positive pregnant women

- <https://www.cdc.gov/hepatitis/hbv/patienteduhbv.htm>
- <https://www.hepbmoms.org/brochures>

For Asian Americans, Pacific Islanders, African Americans and general population

- <https://www.cdc.gov/hepatitis/hbv/patienteduhbv.htm>
- <https://www.hepbmoms.org/brochures>

HBsAg positive pregnant women diagnosis and delivery hospital discharge packets

- <https://www.hepbmoms.org/brochures>



## Jade Ribbon and JoinJade

Global call to action to eliminate hepatitis B and liver cancer



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#JOINJADE

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