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PREVENTING, IDENTIFYING, AND MANAGING HEPATITIS B VIRUS INFECTION

- Hepatitis B is a vaccine-preventable viral infection transmitted through blood and sex, and from mother to child during childbirth.
- Chronic hepatitis B virus infection can lead to liver disease, cirrhosis, liver cancer, and premature death.
- Screen all people at risk for hepatitis B virus infection and vaccinate patients who are not immune (see page 29).
- For patients with chronic hepatitis B virus infection, provide counseling, evaluation for liver cancer, and treatment or referral for treatment if indicated.
- Refer to a specialist if you are unfamiliar with the most recent hepatitis B management guidelines.

epatitis B virus (HBV) is a bloodborne and sexually transmitted infection of the liver that can become chronic and lead to permanent liver damage, cirrhosis, liver failure, liver cancer, and

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premature death.¹ An estimated 20% to 30% of all patients with HBV infection will develop cirrhosis, and approximately 15% to 25% of those infected at birth will die from HBV-related liver disease.² HBV increases the risk of death among people coinfected with HIV.³

HBV is most commonly transmitted by perinatal exposure; percutaneous or mucosal exposure to infectious blood, semen, or vaginal fluid through sexual or close household contact (eg, sharing of razors or toothbrushes, exudates from skin lesions, and contaminated surfaces); injection drug use; or occupational exposure.^{1,4-6}



In NYC, approximately 100,000 residents have been diagnosed with chronic HBV infection.⁷ In NYC in 2016⁸:

- 8,439 people were newly reported to have chronic HBV infection.
- The highest rates of chronic HBV infection were in Sunset Park, Brooklyn, and Flushing, Queens neighborhoods with large Asian populations.
- 61 people were reported with acute HBV infection:
- \circ 38% cited heterosexual sex as a risk factor for infection.
- 18% reported being men who have sex with men (MSM) as a risk factor for infection.
- o 62% were Black or Latino.

As many as 60% of people at risk have never been tested for HBV infection.^{7,9,10} Routinely assess risk, perform testing, and take appropriate next steps based on results.

ASSESS RISK AND TEST FOR HEPATITIS B VIRUS INFECTION

Identify and test patients at risk for HBV infection (Boxes $1^{6,11}$ and $2^{6,11-13}$).

Use culturally appropriate educational materials to help patients understand the need for hepatitis B

BOX 1. INDIVIDUALS AT RISK FOR HEPATITIS B VIRUS INFECTION^{6,11}

Test people at risk for hepatitis B virus (HBV) infection

- Immigrants from areas with intermediate or high prevalence of HBV infection (**Box 2**)
- US-born people not vaccinated as infants whose mothers were born in regions of high (≥8%) HBV prevalence
- All pregnant women (hepatitis B surface antigen [HBsAg])
- Infants born to HBsAg-positive mothers (HBsAg and antibody to HBsAg)
- Men who have sex with men
- People who have ever injected drugs
- People living with HIV
- Household contacts or sexual partners of individuals with known HBV infection
- People requiring immunosuppressive therapy
- People with end-stage renal disease, including those receiving hemodialysis
- People with elevated alanine aminotransferase or aspartate aminotransferase levels
- People who have had blood or body fluid exposures (eg, needlestick) that might require postexposure prophylaxis
- Inmates in correctional facilities
- People with chronic liver disease (eg, hepatitis C infection)
- People with multiple sexual partners or a history of sexually transmitted infection

testing (**Resources for Providers** and **Patients**). Stigma or discrimination in their country of origin may deter people from testing and follow-up care, even after immigration to the US.

Routinely test for

- HBsAg, a marker of infection,
- anti-HBc (total hepatitis B core antibody), a marker of prior infection, and
- anti-HBs (antibody against hepatitis B surface antigen), a marker of immunity.

If indicated, test for

- Immunoglobulin (Ig)M-anti-HBc (IgM antibody against HBc antigen), which can identify infections acquired within the previous 6 months. *Because false-positive IgM-anti-HBc results are often seen in those with chronic HBV infection, the test is generally useful only when acute infection is suspected.*
- HBV DNA, which can clarify infection status in cases where results are inconclusive (**Table 1**^{11,12,14}). Note that a negative HBV DNA test result should not be interpreted to mean a patient does not have current infection in the context of a positive HBsAg test.

BOX 2. REGIONS AND COUNTRIES WITH HEPATITIS B VIRUS PREVALENCE OF 2% OR HIGHER^{6,11-13}

Africa	All countries			
Asia	All countries			
Caribbean	Antigua and Barbuda, Dominica, Dominican Republic, Grenada, Haiti, Jamaica, St. Kitts, St. Lucia, and Turks and Caicos Islands			
Central America	Guatemala and Honduras			
Eastern Europe	All countries except Hungary			
Middle East	All countries except Cyprus and Israel			
North America	Indigenous populations in northern Canada			
South America	Bolivia, Brazil, Colombia, Ecuador, Guyana, Suriname, and Venezuela			
South Pacific	All countries except nonindigenous populations of Australia and New Zealand			
Western Europe	Malta and indigenous populations of Greenland			

Countries with high (≥8%) hepatitis B virus prevalence

Angola, Benin, Burkina Faso, Burundi, Cameroon, Central African Republic, Congo, Côte d'Ivoire, Djibouti, Equatorial Guinea, Gabon, Gambia, Ghana, Guinea, Haiti, Kiribati, Kyrgyzstan, Laos, Liberia, Malawi, Mali, Mauritania, Mongolia, Mozambique, Namibia, Nauru, Niger, Nigeria, Niue, Papua New Guinea, Senegal, Sierra Leone, Solomon Islands, Somalia, South Sudan, Sudan, Swaziland, Togo, Tonga, Uganda, Vanuatu, Vietnam, Yemen, and Zimbabwe

COUNSEL PEOPLE DIAGNOSED WITH HEPATITIS B VIRUS INFECTION

Counsel all HBsAg-positive patients on preventing progression of disease and transmission of HBV to others (**Box 3**). Refer people who use drugs to harm reduction services such as syringe access services and drug-use cessation programs (**Resources for Patients**). For patients without health insurance, refer to a federally qualified health center, public hospital, or other clinical care site that offers insurance enrollment and a sliding-fee scale for the uninsured. Encourage patients to inform their close contacts of their risk of exposure so they can receive prophylaxis and/or testing and vaccination if appropriate.⁴

MONITOR PATIENTS WITH ACUTE HEPATITIS B VIRUS INFECTION

Acute HBV infection is frequently asymptomatic, but patients may experience flu-like symptoms, including the following:

- loss of appetite, abdominal pain, jaundice, and dark urine;¹⁵
- extrahepatic symptoms, including skin rashes, arthralgia, and arthritis;^{1,4} and
- in rare cases, severe, life-threatening inflammation of the liver, known as fulminant hepatitis.⁴

Most immunocompetent adults recover spontaneously.⁶ Monitor patients with acute HBV infection for clearance of the virus.⁴ Evidence of ongoing infection with a positive HBsAg for more than 6 months indicates chronic HBV infection.^{4,6}

BOX 3. WHAT TO TELL HBsAg-POSITIVE PATIENTS

To prevent progression of liver disease

- See your doctor regularly to monitor your liver health, even if you feel well
- Avoid alcohol
- Maintain a healthy weight
- Consult a provider before taking any medications, including over-the-counter (eg, acetaminophen, ibuprofen, and naproxen) and herbal medicines, herbal teas, supplements, and home remedies

To prevent transmission of hepatitis B virus to other people

- Encourage all household members, sexual partners, or drug-using partners to get tested and vaccinated if not immune
- Use a condom during sex if your partner is not fully vaccinated and does not have documented immunity
- Do not share toothbrushes, razors, glucometers, nail clippers, nail files, nail scissors, washcloths, syringes, sex toys, or anything that may have come in contact with infected blood or body fluids
- Cover open cuts and scratches
- Wash hands well after touching infected blood or body fluids
- Clean blood spills with detergent or bleach
- Do not donate blood, organs, tissue, or sperm
- Never share drug-use equipment, always use new sterile equipment, wash your hands and the injection site before and after each injection, and plan ahead to avoid withdrawal

TABLE 1. INTERPRETING HEPATITIS B SEROLOGIC TEST RESULTS^{11,12,14}

	Serologic Marker					
	HBsAg	anti-HBc	lgM anti-HBcª	anti-HBs	Interpretation	Next steps
	-	—		—	Susceptible	Vaccination
	-	+		+	Resolved infection	Counseling, reassurance
	-	_		+	Immune due to hepatitis B vaccination	Reassurance
	+	+	+	—	Acute infection	Link to HBV care
	+	+	_	—	Chronic infection	Link to HBV care
Result -	-	+		_	 Unclear; possibilities are: 1. Resolved infection (most common) 2. Low-level chronic infection 3. Resolving acute infection 4. Occult HBV infection (presence of HBV DNA in the absence of detectable HBsAg) 	Inform patient and general practitioner about the potential risk of HBV reactivation. HBsAg-negative patients with positive anti-HBc should be tested for HBV DNA prior to immunosuppressive therapy, chemotherapy, or receipt of direct-acting anti-viral agents such as in the treatment of HCV; if HBV DNA is detectable, patients should be treated similarly to HBsAg-positive patients.

anti-HBs, antibody to HBsAg; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; IgM-anti-HBc, immunoglobulin antibody against HBc antigen; total anti-HBc, total anti-HBc, immunoglobulin antibody to hepatitis B core antigen

^a IgM tests are most useful when there is a clinical suspicion of acute HBV infection; they can give false-positive results in people with established diagnoses of chronic HBV infection.

Refer all patients with chronic HBV infection to a specialist or primary care provider who is familiar with HBV guidelines and treatment.



MANAGE CHRONIC HEPATITIS B VIRUS INFECTION

Refer all patients with chronic HBV infection to a specialist or primary care provider who is familiar with HBV guidelines and treatment for further evaluation.

Initial evaluation

Thoroughly evaluate patients with chronic HBV infection (Box 4).

Depending on patients' risk factors, they may also require hepatitis C, hepatitis D (if from regions where infection is common, including the Mediterranean Basin, the Middle East, Pakistan, Central and Northern Asia, Japan, Taiwan, Greenland, the horn of Africa, West Africa, and the Amazon Basin),¹⁶ and HIV testing; HBV genotype testing; tests to rule out other sources of liver disease if α -fetoprotein (AFP) or γ -glutamyl transpeptidase (GGT) are elevated; or liver biopsy.⁶

Linkage to care

Antiviral therapy may help patients with active chronic HBV infection prevent or delay the progression to cirrhosis, end-stage liver disease, and hepatocellular carcinoma.¹⁷

BOX 4. INITIAL EVALUATION OF PATIENTS WITH CHRONIC HEPATITIS B VIRUS INFECTION

History and physical examination

- Signs and symptoms of cirrhosis
- Alcohol and metabolic risk factors (eg, metabolic syndrome)
- Family history of primary liver cancer
- Vaccination status

Laboratory tests

- Complete blood count, including platelets
- Liver enzyme and function tests, including ALT, AST, total bilirubin, alkaline phosphatase, albumin, and INR
- Virology: HBeAg/anti-HBe, HBV DNA (viral) quantitation, anti-HAV to determine need for vaccination

Imaging/staging studies, including

- Abdominal ultrasound
- Vibration-controlled transient elastography or serum fibrosis panel (AST to platelet ratio, FIB-4, or FibroTest, also marketed as FibroSure[®])

ALT, alanine aminotransferase; anti-HAV, antibody to hepatitis A virus; anti-HBe, antibody to hepatitis B e-antigen; AST, aspartate aminotransferase; HBeAg, hepatitis B e-antigen; HBV, hepatitis B virus; INR, international normalized ratio/standardized prothrombin time Preferred antiviral agents are pegylated interferon (Peg-IFN)- α -2a (not approved for children), IFN- α -2b, entecavir, tenofovir dipovoxil fumarate, and tenofovir alafenamide (not studied in children).⁶ Initiation of treatment depends on viral activity (as measured by hepatitis B e-antigen [HBeAg] and viral load), degree of liver injury (as measured by alanine aminotransferase [ALT] and liver pathology), age, and length of infection.

Chronic HBV infection is a dynamic disease with a variable course.⁶ If you do not regularly care for patients with chronic HBV infection and are not familiar with the most current guidelines (Resources for Providers), refer patients to a provider experienced with HBV infection for ongoing monitoring and evaluation for treatment.⁶

Liver cancer surveillance

People living with chronic HBV infection may develop primary liver cancer at any stage of disease, even in the absence of advanced fibrosis or cirrhosis.¹⁸ For all patients diagnosed with chronic HBV infection, evaluate liver fibrosis upon diagnosis. Initial and ongoing liver cancer surveillance with ultrasound is recommended for some patient subgroups (**Box 5**^{6,19}).

VACCINATE AGAINST HEPATITIS B VIRUS INFECTION

Vaccinate people at risk for HBV infection (**Box** 6^{12}). There are 4 licensed hepatitis B vaccines (**Table** 2^{12}).

Hepatitis B vaccine is contraindicated if the patient has had a severe allergic reaction (eg, anaphylaxis) after a previous dose or an allergy to any vaccine component. The vaccine can safely be given during pregnancy and to those who are immunocompromised¹ (**Resources**—**CDC Recommended Adult Immunization**).

BOX 5. HEPATOCELLULAR CARCINOMA SURVEILLANCE^{6,19}

Hepatocellular carcinoma (HCC) is closely associated with hepatitis B virus (HBV) infection. Perform ultrasound screening every 6 months, with or without α -fetoprotein (AFP),^{α} for patients at high risk for HCC, including

- Patients with cirrhosis
- Asian or Black men aged >40 years
- Asian women aged >50 years
- People with a first-degree family member with a history of HCC
- People with hepatitis C, hepatitis D, or HIV coinfection
- ° For individuals positive for hepatitis B surface antigen at high risk for HCC who are living in areas where ultrasound is not readily available, screening with AFP every 6 months should be performed.

PREVENT AND MANAGE PERINATAL HEPATITIS B VIRUS INFECTION

Infants born to mothers with HBV infection are at high risk for developing chronic infection themselves. Take routine measures to prevent perinatal HBV infection (**Box** 7^{6,12,20-23}).

SUMMARY

Identify patients at risk for HBV infection and provide appropriate testing and vaccination. Counsel patients with HBV infection on measures to prevent progression of liver damage and transmission to others. Monitor patients

TABLE 2. HEPATITIS B VACCINES¹²

Vaccine	Scheduleª	Notes
Recombivax HB® (Merck) ^ь	3-dose series at 0, 1-2, and 6 months	
Engerix-B (GSK)°		
Twinrix (GSK, combination hepatitis A and B vaccine) (for patients aged ≥18 years only)		
HEPLISAV-B™ (Dynavax Technologies Corp) ^d	2-dose series, 1 month apart	For patients aged ≥18 years

 $^{\circ}$ There is no need to restart the series for any of the medications listed below if the schedule is interrupted.

- ^b Three formulations are available: pediatric (5 mcg/0.5 mL) for ages <20 years, adult (10 mcg/ 1 mL) for ages >20 years, and for dialysis patients (40 mcg/1 mL)
- $^{\rm c}$ Two formulations are available: pediatric (10 mcg/0.5 ml) for ages <20 years and adult (20 mcg/1 mL) for ages >20 years

^d Licensed in 2017; recommended by the Advisory Committee on Immunization Practices on February 21, 2018.

HEPATITIS B QUIZ

1. Which of the following are at risk for HBV infection?

- A. Men who have sex with men
- B. People who have received blood transfusions
- C. People who inject drugs
- D. A and C
- E. All of the above
- 2. What is the next step for a patient whose test results are HBsAg (-), anti-HBc (+), and anti-HBs (+)?
 - A. Vaccination
 - B. Linkage to care
 - C. Counseling and reassurance
 - D. A and B

Answers: 1-D; 2-C

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with acute or chronic HBV infection for possible disease progression and/or complications. Refer patients with chronic HBV infection to a provider with experience in managing this infection if you do not routinely manage chronic HBV infection.

BOX 6. HEPATITIS B VACCINATION RECOMMENDATIONS¹²

Vaccination against hepatitis B virus (HBV) is recommended for

- All infants, beginning at birth
- Unvaccinated children aged <19 years
- People at risk for infection by sexual exposure
- sex partners of hepatitis B surface antigen (HBsAg)positive people
- sexually active people who are not in a long-term, mutually monogamous relationship (eg, individuals with more than one sex partner during the previous 6 months)
- people seeking evaluation or treatment for a sexually transmitted infection
- \circ men who have sex with men
- People at risk for infection by percutaneous or mucosal exposure to blood
 - current or recent injection drug users
 - household contacts of HBsAg-positive people
 - residents and staff of facilities for developmentally disabled individuals
 - health care and public safety personnel with reasonably anticipated risk for exposure to blood or blood-contaminated body fluids
 - hemodialysis patients and predialysis, peritoneal dialysis, and home dialysis patients
 - people with diabetes aged 19-59 years; people with diabetes aged ≥60 years at the discretion of the treating clinician
- International travelers to countries with high or intermediate levels of endemic HBV infection (HBsAg prevalence of ≥2%)
- Individuals with hepatitis C virus infection
- People with chronic liver disease (including, but not limited to, people with cirrhosis, fatty liver disease, alcoholic liver disease, autoimmune hepatitis, and an alanine aminotransferase or aspartate aminotransferase level greater than twice the upper limit of normal)
- Individuals with HIV infection
- Incarcerated people
- All other people seeking protection from HBV infection, even without a disclosed risk for infection

See Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices for full guidance.

BOX 7. PREVENTING PERINATAL HEPATITIS B VIRUS INFECTION^{6,12,20-23}

Maternal care

- In accordance with New York State (NYS) law, all pregnant women must be tested for hepatitis B surface antigen (HBsAg) and women who are HBsAg-positive must be reported to the NYS Health Department during the prenatal period and at the time of delivery.
- Screen all pregnant women for HBsAg in the first trimester or as soon as possible thereafter.
- For HBsAg-positive women, test for hepatitis B virus (HBV) DNA, alanine aminotransferase (ALT), and hepatitis B e-antigen (HBeAg).
- Refer to a liver specialist if the patient is HBeAg-positive or has ALT ≥19 or HBV DNA >20,000.
- For all pregnant women with HBV DNA >200,000, begin antiviral prophylaxis with tenofovir disoproxil fumarate at 24 to 28 weeks gestation and discontinue at delivery. Monitor mother for ALT flares every 3 months for 6 months after discontinuation.^{a,b}
- Women who are HBsAg negative but at high risk for infection should be retested at the time of delivery.

Newborn care

- Infants of HBsAg-negative mothers: vaccinate within 24 hours of birth.
- Infants of HBsAg-positive mothers: vaccinate and provide hepatitis B immune globulin (HBIG) within 12 hours of birth.

- Infants of HBsAg-unknown mothers:
 - birthweight ≥2000 g: vaccinate within 12 hours of birth and test mother for HBsAg immediately. If mother is HBsAg-positive, administer HBIG as soon as possible, no later than 7 days of life.
 - birthweight <2000 g: vaccinate and test mother immediately for HBsAg. If test results cannot be obtained quickly, administer HBIG within 12 hours of birth.
- Infants born to women for whom HBsAg testing results during pregnancy are not available but other evidence suggestive of maternal HBV infection exists^c: manage as if born to an HBsAg-positive mother.

Infant care

- Infants must complete the 3-dose hepatitis B vaccine series with the last dose given on or after age 6 months (168 days).
- All infants should receive postvaccine serology testing (HBsAg, quantitative anti-HBs) at age 9 to 12 months or 1 to 2 months after the final dose of the vaccine series, if the series is delayed.
- Nonimmune infants who completed a 3-dose vaccine series should receive one additional dose of hepatitis B vaccine followed by repeat testing 1 to 2 months later. If testing indicates child is still not immune, give 2 more doses (at 4 weeks and 16 weeks after the additional hepatitis B dose) and repeat testing 1 to 2 months later.
- If the child is still not immune after a second 3-dose series, counsel the parent or caregiver on risk reduction strategies for nonresponders.

Report all cases of HBV infection in a pregnant or postpartum woman to the NYC Health Department using Reporting Central or the IMM-5 form. Call 347-396-2403 for more information.

- ° In most of the studies reviewed, antiviral therapy was started at 28 to 32 weeks of gestation and discontinued at birth to 3 months postpartum.6
- ^b Breastfeeding is not contraindicated. These antiviral agents are minimally excreted in breast milk and are unlikely to cause significant toxicity. The unknown risk of low-level exposure to the infant should be discussed with the mother.⁶
- ^c For example, presence of HBV DNA, an HBeAg-positive result, or a mother known to be chronically infected with HBV.

See Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices for full guidance.



RESOURCES FOR PROVIDERS

General information

- NYC Health Department. Hepatitis B and C resources: www1.nyc.gov/site/doh/providers/health-topics/hepatitis.page
- American Association for the Study of Liver Diseases. Chronic hepatitis B: www.aasld.org/publications/hepatitis-b-chronic
- Centers for Disease Control and Prevention (CDC). Viral Hepatitis: www.cdc.gov/hepatitis/hbv/index.htm
- Hepatitis B Vaccination, Screening, and Linkage to Care: Best Practice Advice from the American College of Physicians and the Centers for Disease Control and Prevention: annals.org/ aim/fullarticle/2664089/hepatitis-b-vaccination-screeninglinkage-care-best-practice-advice-from
- Hepatitis B Foundation: www.hepb.org Information about hepatitis B in 12 languages
- NYC Health Department reporting information: www1.nyc.gov/site/doh/providers/reporting-and-services/ notifiable-diseases-and-conditions-reporting-central.page

Immunization recommendations

- Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices (ACIP): www.cdc.gov/mmwr/volumes/67/rr/pdfs/ rr6701-H.PDF
- ACIP child and adolescent immunization schedule: www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html
- ACIP adult immunization schedule: www.cdc.gov/vaccines/ schedules/hcp/adult.html

Alcohol and drug use resources

 NYC Health Department Alcohol & Drug Use provider resources: www1.nyc.gov/site/doh/providers/health-topics/alcohol-anddrugs.page

RESOURCES FOR PATIENTS

General information

- NYC Health Department. Hepatitis B: www.nyc.gov/health/hepatitis Downloadable fact sheets in English, Spanish, Russian, French, Chinese, and Korean. Information about HBV infection and free/low-cost immunization clinics.
- American Liver Foundation. Hepatitis B: www.liverfoundation.org/abouttheliver/info/hepatitisb
- NYC Health Department. Hepatitis B and C resources: www1.nyc.gov/site/doh/health/health-topics/hepatitis.page
- CDC. Know Hepatitis B: www.cdc.gov/knowhepatitisb
- NYC Hep B Coalition: www.hepfree.nyc

Specialist care

 NYC Hepatitis testing and care locator: www.nyc.gov/health/sitelocator and click Hepatitis

All mental health concerns

- NYC WELL: 888-NYC-WELL/888-692-9355
 - TTY hard of hearing, call 711
 - www.nyc.gov/nycwell
 Free, confidential crisis counseling, and mental health and substance misuse support, information, and referral

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ASK CHI

Have questions or comments about Hepatitis B? **E-mail** AskCHI@health.nyc.gov

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