

II. VIRAL HEPATITIS

A. Hepatitis A Virus (HAV)

RECOMMENDATIONS:

Clinicians should administer the HAV vaccine to HIV-infected patients who are negative for HAV IgG. The full series, consisting of an initial dose and a second dose 6 to 12 months later, should be given to ensure maximal antibody response.

Clinicians should administer HAV vaccination early in the course of HIV infection. If a patient's CD4 count is <200 cells/mm³ or the patient has symptomatic HIV disease, deferral of HAV vaccination for several months may maximize a patient's response to the vaccine. However, vaccination should not be deferred in pregnant patients or patients who are unlikely to achieve an increased CD4 count.

Clinicians should obtain a post-vaccination antibody measurement in patients who are at increased risk for hepatitis A infection (see Table 1).

Clinicians should administer HAV post-exposure prophylaxis to HAV susceptible patients (i.e., non-immune or non-vaccinated) with immune globulin (0.02 mL/kg IM) within 2 weeks of exposure. HAV vaccine is not currently indicated for post-exposure prophylaxis in patients with HIV, although it is prudent to administer it concurrently with serum immune globulin for the long-term prophylaxis of an at-risk individual.

Infection with HAV can be prevented by active immunization prior to exposure with either of the two currently licensed vaccines, which are considered equivalent in efficacy. A combined hepatitis A and B vaccine is also available and can be used in persons susceptible to both hepatitis A and B. It is given in three total doses at 0, 1, and 6 months.

HAV vaccination is effective in most HIV-infected patients, and there is no evidence of harm for patients with unsuppressed HIV infection. However, administration of HAV vaccine when CD4 counts are ≥ 200 cells/mm³, or deferring vaccination for several months in patients with symptomatic HIV disease, may maximize a patient's response to the vaccine. Vaccination should not be deferred in pregnant patients or patients who are unlikely to achieve an increased CD4 count. Follow-up HAV antibody testing should be obtained in patients who are at increased risk for HAV infection (see Table 1) to verify vaccine efficacy and to identify patients who may benefit from vaccine boosting.

| TABLE 1 |
|---|
| PERSONS WHO ARE AT INCREASED RISK FOR HEPATITIS A INFECTION |
| <ul style="list-style-type: none"> • Men who have sex with men (MSM) • Travelers to countries with high endemicity of infection • Persons who live in a community experiencing an outbreak of HAV infection • Illicit drug users, particularly injection drug users • Persons who have clotting-factor disorders • Persons at occupational risk for infection • Persons with chronic liver disease (e.g., hepatitis B or C)* |

* Persons with chronic liver disease are at increased risk for severe infection if they become coinfecting with hepatitis A.

HAV vaccines are highly immunogenic in immunocompetent adults (>95% seroconversion). However, the seroconversion rates and the geometric mean serum antibodies in HIV-infected hemophiliacs and homosexual men seem to be somewhat lower than in non-HIV-infected populations. Pre-screening for immunity to hepatitis A is optional, and its cost-effectiveness increases in populations in which the seroprevalence rates are high.

Serum immune globulin can be given to individuals who are not immune to HAV within 2 weeks after an exposure to an HAV household contact, sexual partner, or common source exposure. A single intramuscular dose of 0.02 mL/kg is effective in preventing infection or attenuating HAV infection that might result from such an exposure. HAV vaccine is not currently indicated for post-exposure prophylaxis in patients with HIV, although it is prudent to administer it concurrently with serum immune globulin for the long-term prophylaxis of an at-risk individual. The Advisory Committee on Immunization Practices recommends a single dose of single-antigen hepatitis A vaccine for healthy persons aged 12 months to 40 years for post-exposure prophylaxis to HAV.¹

B. Hepatitis B Virus (HBV)

RECOMMENDATIONS:

Clinicians should counsel patients about behavior modifications that decrease their risk of acquiring HBV infection through unprotected sexual activity and injection drug use.

As part of the baseline assessment, clinicians should ask patients about their HBV vaccination history and should obtain the following:

- **HBV serologies: HBsAg, HBsAb, and HBcAb (IgG or total)**
- **Hepatitis A IgG and hepatitis C IgG**

The serologic and virologic responses to hepatitis B are shown in Table 2. Active immunization and passive immunization are two types of prophylaxis for hepatitis B. Active immunization involves the administration of the hepatitis B vaccine series prior to exposure to HBV (pre-exposure prophylaxis) or after exposure (post-exposure prophylaxis) over a 6-month period.

After exposure to a known chronic HBV carrier, the hepatitis B vaccine is usually given along with passive immunization using hepatitis B immunoglobulin (HBIG).

| Stage of Infection | HBsAg | HBsAb | HBcAb IgG | HBcAb IgM | HBeAg | HBeAb | HBV Viral Load |
|----------------------------------|--------------|--------------|----------------------|----------------------|--------------|--------------|---------------------------|
| Incubation | + | – | – | – | + or – | – | Low |
| Acute hepatitis B | + | – | + | + | + | – | High |
| HBsAg-negative acute hepatitis B | – | – | + | + | +/- | – | High |
| Inactive HBsAg carrier | + | – | +++ | + or – | – | + | Low |
| Precore mutant | + | – | + or – | + or – | – | + | High |
| Occult infection* | – | – | + | + or – | – | – | High or low |
| Chronic hepatitis B | + | – | +++ | + or – | + or – | – | High or low |
| Resolved HBV infection† | – | ++ | ++ | + or – | – | + | Undetectable |
| HBV vaccination | – | ++ | – | – | – | – | Undetectable |

* Studies have found occult HBV infection in approximately 10% of HBcAb-positive and HBsAg- and HBsAb-negative HIV-infected patients.^{2,3} Occult infection may be associated with greater immunosuppression (<200 cells/mm³) and higher HIV DNA levels.⁴

† Formerly known as convalescent HBV infection.

1. Pre-Exposure HBV Prophylaxis

RECOMMENDATIONS:

Clinicians should administer the HBV vaccination series to HIV-infected patients who are negative for HBsAb, unless they are chronically infected (see [Adults Guidelines Hepatitis B Virus: Figure 3](#)).

Clinicians should test for HBsAb between 4 and 12 weeks after vaccination. Nonresponders (HBsAb <10 IU/L) should be revaccinated with another three-dose hepatitis B vaccine series (see [Adults Guidelines Hepatitis B Virus: Figure 3](#)). If a patient's CD4 count is <200 cells/mm³ or the patient has symptomatic HIV disease, revaccination may be deferred until several months after initiation of ARV therapy in an attempt to maximize the antibody response to the vaccine. However, revaccination should not be deferred in pregnant patients or patients who are unlikely to achieve an increased CD4 count.

HBsAg, HBsAb, and HbcAb IgG should be included in prevaccination screening for HIV-infected persons. This panel identifies patients with prior HBV infection as well as responders to prior hepatitis B vaccination. People who are negative for all three tests are eligible to receive the hepatitis B vaccine.

In >90% of adult immunocompetent patients, three doses of the hepatitis B vaccine are efficacious and induce protective antibody. The two commercially available vaccines are equally immunogenic. Three vaccine doses are given at 0, 1 to 2 months, and 6 months. The doses of vaccine vary by the patient's age.

Several factors reduce the vaccine's immunogenicity. These include age >40 years, tobacco use, and HIV infection, especially when CD4 counts are low. Ideally, the HBV vaccine series should be administered early in the course of HIV disease, before severe immune suppression has occurred. However, advanced immune suppression is not a contraindication to vaccination, and vaccination should not be deferred or delayed because of advanced immune suppression or in anticipation of expected immune recovery due to the effect of HAART.

Generally, in HIV-infected patients who do not respond to the vaccine series, a rapid loss of induced antibody occurs. These patients are, therefore, at risk for HBV infection following exposure. The clinician should test for HBsAb between 4 and 12 weeks after completion of the third vaccine dose. HBV seroconversion may be enhanced by immune reconstitution (≥ 200 cells/mm³) prior to revaccination. However, revaccination should not be deferred in pregnant patients or patients who are unlikely to achieve an increased CD4 count.

A combined hepatitis A and B vaccine is available and may be used in persons susceptible to both hepatitis A and B. It is given in three total doses at 0, 1, and 6 months.

2. Post-Exposure HBV Prophylaxis

RECOMMENDATION:

The hepatitis B vaccine series should be initiated in *non-HBV-immune* patients who sustain a blood or body fluid exposure.

Administration of prophylactic hepatitis B immune globulin (HBIG) and the initiation of the hepatitis B vaccine series (at different sites) are recommended when the non-HBV-immune patient sustains a blood or body fluid exposure to a source with known acute or chronic HBV (see Table 3). Both HBIG and the hepatitis B vaccine should be ideally administered within 24 hours of exposure; prophylaxis should not be given later than 14 days post-exposure.

Needlestick injuries and wounds should be washed with soap and water and should not be squeezed. Mucous membranes should be flushed with water.

Initiation of the HBV vaccine series within 12 to 24 hours of an exposure has been demonstrated to be 70% to 90% effective in preventing HBV infection. The combination of vaccine and HBIG achieves a similar level of efficacy. Among known non-responders to vaccination, one dose of HBIG is 70% to 90% effective in preventing HBV when administered within 7 days of percutaneous HBV exposure,⁵ and multiple doses have been shown to be 75% to 95% effective.⁶ The maximum effective interval is likely within 14 days for sexual exposure.⁷⁻¹¹ Pregnant women can safely receive both the HBV vaccination and HBIG. When considering nPEP for HBV exposures, both the source HBsAg status and the exposed person's vaccination status and antibody response should be considered (see Table 3). Both HBIG and the hepatitis B vaccine should be ideally administered within 24 hours of exposure; prophylaxis should not be given later than 14 days post-exposure. Hepatitis B antibodies should be obtained 1 to 2 months after

completion of the third dose of the vaccine; however, levels may be falsely elevated if the exposed person received HBIG within the past 3 to 4 months.

| TABLE 3 RECOMMENDED POST-EXPOSURE PROPHYLAXIS FOR NON-OCCUPATIONAL EXPOSURE TO HEPATITIS B VIRUS | | | |
|---|--|-------------------------------|---|
| Vaccination and/or antibody response status of exposed patient* | Treatment when source is: | | |
| | HBsAg positive | HBsAg negative | Source unknown or not available for testing |
| Unvaccinated/ non-immune | HBIG† ×1; initiate HB vaccine series | Initiate HB vaccine series | Initiate HB vaccine series |
| Previously vaccinated, known responder‡ | No treatment | No treatment | No treatment |
| Previously vaccinated, known non-responder‡ | HBIG† ×2 or HBIG† ×1 and initiate revaccination§ | No treatment | If known high-risk source, treat as if source were HBsAg positive |
| Previously vaccinated, antibody response unknown | Test exposed person for anti-HBs: - If adequate,‡ no treatment - If inadequate,‡ HBIG ×1 and vaccine booster | No treatment | Test exposed person for anti-HBs: - If adequate,‡ no treatment - If inadequate,‡ initiate revaccination |

Reprinted from the Updated US Public Health Service Guidelines for the Management of Occupational Exposures to HBV, HCV, and HIV and Recommendations for Post-Exposure Prophylaxis. *MMWR Morb Mortal Wkly Rep* 2001;50(RR-11):1-42. Available at: www.cdc.gov/mmwr/preview/mmwrhtml/rr5011a1.htm.

HBsAg, hepatitis B surface antigen; HBIG, hepatitis B immune globulin; anti-HBs, antibody to hepatitis B surface antigen.

* Persons who have previously been infected with HBV are immune to re-infection and do not require PEP.

† Dose 0.06 mL/kg intramuscularly.

‡ Responder is defined as person with adequate levels of serum antibody to HBsAg (serum anti-HBs >10 mIU/mL); non-responder is a person with inadequate response to vaccination (serum anti HBs <10mIU/mL).

§ The option of giving one dose HBIG and re-initiating the vaccine series is preferred for non-responders who have not completed a second 3-dose vaccine series. For persons who previously completed a second vaccine series but failed to respond, two doses of HBIG are preferred.

For information regarding prophylaxis for perinatal HBV transmission, refer to the Women's Committee guidelines *Management of HIV-Infected Pregnant Women Including Prevention of Perinatal HIV Transmission*.

C. Hepatitis C Virus (HCV)

Coming soon!

REFERENCES

1. Advisory Committee on Immunization Practices (ACIP) Centers for Disease Control and Prevention (CDC). Update: Prevention of hepatitis A after exposure to hepatitis A virus and in international travelers. Updated recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep* 2007;56(41):1080-1084. Available at: www.cdc.gov/mmwr/preview/mmwrhtml/mm5641a3.htm
2. Shire NJ, Rouster SD, Rajicic N, et al. Occult hepatitis B in HIV-infected patients. *J Acquir Immune Defic Syndr* 2004;36:869-875. [[Abstract](#)]
3. Re VL 3rd, Frank I, Gross R, et al. Prevalence, risk factors, and outcomes for occult hepatitis B virus infection among HIV-infected patients. *J Acquir Immune Defic Syndr* 2007;44:315-320. [[Abstract](#)]
4. Tsui JI, French AL, Seaberg EC, et al. Prevalence and long-term effects of occult hepatitis B virus infection in HIV-infected women. *Clin Infect Dis* 2007;45:736-740. [[Abstract](#)]
5. Weinbaum C, Lyerla R, Margolis HS. Prevention and control of infections with hepatitis viruses in correctional settings: Centers for Disease Control and Prevention. *MMWR Recomm Rep* 2003;52(RR-1):1-36. [[Abstract](#)]
6. Centers for Disease Control and Prevention. Recommendations for prevention and control of hepatitis C virus infection and HCV-related chronic disease. *MMWR Recomm Rep* 1998;47(RR-19):1-39. [[Abstract](#)]
7. Redeker AG, Mosley JW, Gocke DJ, et al. Hepatitis B immune globulin as a prophylactic measure for spouses exposed to acute type B hepatitis. *N Engl J Med* 1975;293:1055-1059. [[Abstract](#)]
8. Szmunes W, Stevens CE, Harley EJ, et al. Hepatitis B vaccine: Demonstration of efficacy in a controlled clinical trial in a high-risk population in the United States. *N Engl J Med* 1980;303:833-841. [[Abstract](#)]
9. Papaevangelou G, Roumeliotou-Karayannis A, Richardson SC, et al. Postexposure immunoprophylaxis of spouses of patients with acute viral hepatitis B. In: Zuckerman AJ, ed. *Viral Hepatitis and Liver Disease*. New York, NY: Alan R. Liss, Inc.; 1988:992-994.
10. Roumeliotou-Karayannis A, Dandolos E, Richardson SC, et al. Immunogenicity of a reduced dose of recombinant hepatitis B vaccine. *Vaccine* 1986;4:93-94. [[Abstract](#)]
11. Perrillo RP, Campbell CR, Strang S, et al. Immune globulin and hepatitis B immune globulin. Prophylactic measures for intimate contacts exposed to acute type B hepatitis. *Arch Intern Med* 1984;144:81-85. [[Abstract](#)]

Further Reading

Mast EE, Margolis HS, Fiore AE, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: Recommendations of the Advisory Committee on Immunization Practices (ACIP) part 1: Immunization of infants, children, and adolescents. *MMWR Recomm Rep* 2005;54(RR-16):1-31. Available at: www.cdc.gov/MMWR/preview/mmwrhtml/rr5416a1.htm