Integrated Hepatitis B Prevention, Screening, and Testing Consideration Among Adults: Frequently Asked Questions

Hepatitis B Triple Panel Screening: Indications

Why should I do hepatitis B triple panel screening for an adult patient who has written documentation of previous completion of a hepatitis B (HepB) vaccine series?
Hepatitis B triple panel screening[1] is important for vaccinated adults to determine if they have evidence of current or past hepatitis B virus (HBV) infection, which might have occurred before vaccination. Antiviral treatment may be needed in certain situations (1).

Hepatitis B Triple Panel Screening: Hepatitis B Surface Antigen (HBsAg)

What does it mean for a reactive HBsAg to be confirmed? Why is confirmation of reactive HBsAg test results important?
Initially reactive HBsAg test results may require confirmation with a licensed neutralizing confirmatory test according to the manufacturer's labeling. Confirmatory testing involves adding a reagent containing antibodies to HBsAg to the specimen. If HBsAg is present, the antibodies will bind to the antigen, neutralizing it and reducing test signal. A reactive HBsAg specimen that can be neutralized is considered positive for HBsAg. A reactive HBsAg specimen that cannot be neutralized is considered a false-positive result. For some HBsAg test assays, it is recommended that a reactive HBsAg assay be reflexed to a confirmation test in cases when the HBsAg assay is used as a standalone test for HBV infection, such as in pregnancy. The HBsAg test package insert provides information on when HBsAg confirmatory testing is indicated. When indicated, confirmation of reactive HBsAg test results is important for accurate identification and management of HBV-infected persons. A confirmed reactive HBsAg test signifies current HBV infection, either acute or chronic (2).

All HBV-infected pregnant women should be tested for HBV DNA to guide the use of maternal antiviral therapy during pregnancy for prevention of perinatal HBV transmission. For additional details, please refer to the 2018 Advisory Committee on Immunization Practices (ACIP) recommendations for hepatitis B prevention (2).

[1] Hepatitis B triple panel screening includes hepatitis B surface antigen (HBsAg), antibody to hepatitis B surface antigen (anti-HBs), and total antibody to hepatitis B core antigen (total anti-HBc).

What are some common reasons for false positive HBsAg test results?

In general, HBsAg false positives can occur for several reasons, including recent hepatitis B vaccination, presence of heterophile antibodies, and ingestion of high levels of biotin (3, 4, 5). Heterophile antibodies are naturally-occurring human antibodies that bind and react to antigens and antibodies used in chemical immunoassays that can lead to false positivity of HBsAg (3). Transient HBsAg positivity can occur up to 18 days following vaccination and is clinically insignificant (2). Biotin is a water-soluble vitamin B and can be found in dietary sources such as egg yolk, liver, cereals, vegetables (spinach, mushrooms), rice, and vitamin supplements (5, 6). In addition, high-dose biotin may be used for certain medical conditions such as multiple sclerosis (7). Ingestion of high levels of biotin can significantly interfere with certain commonly used biotinylated immunoassays and cause false-positive or false-negative laboratory test results (4, 5).

Hepatitis B Triple Panel Screening: Antibody to Hepatitis B Surface Antigen (anti-HBs)

If an adult patient has written documentation of previous completion of a hepatitis B vaccine series and the hepatitis B triple panel screening showed non-reactive HBsAg and anti-HBs ≥10 IU/mL, can I assure the patient that they are protected from hepatitis B virus infection and require no further testing?

Yes, the presence of anti-HBs is generally interpreted as evidence of immunity. Immunocompetent children and adults with vaccine-induced anti-HBs levels of ≥10 mIU/mL measured 1-2 months after completion of a documented hepatitis B vaccine series are considered seroprotected. An anti-HBs level ≥10 mIU/mL is a known correlate of protection only when testing follows a documented complete HepB vaccine series. Different assays have different cutoff values and reported levels of anti-HBs might vary depending on the assay used. Refer to the package insert of the test for the determination of appropriate level of anti-HBs (2).

If an adult patient has written documentation of previous completion of a hepatitis B vaccine series and the hepatitis B triple panel screening showed non-reactive HBsAg, and anti-HBs <10 mIU/mL, can I assure the patient that they are protected from hepatitis B virus infection and require no further testing?

Yes, for patients with normal immune status who are not healthcare personnel. However, when anti-HBs is tested years after vaccination (rather than 1-2 months after completion of the vaccine series as part of post vaccination serologic testing), a result <10 mIU/mL may reflect one of two scenarios: 1) the patient initially responded to the vaccine , but antibody levels waned over time; protection likely persists because immune memory remains intact, or 2) the patient did not respond to hepatitis B vaccine and is not protected (2).

Revaccination is not generally recommended for persons with a normal immune status who were vaccinated as infants, children, adolescents, or adults. Revaccination when anti-HBs is <10 mIU/mL is recommended for the following persons: infants born to HBsAg-positive mothers, health care personnel, hemodialysis patients, and other immunocompromised persons (2).

A study by Middleman et al. on adolescents who received infant hepatitis B vaccination published in 2014 showed that 92% of adolescents in the study who received hepatitis B vaccination as infants demonstrated a seroprotective response after a challenge dose, suggesting immune memory (8). A challenge dose of hepatitis B vaccine may be used to determine the presence of vaccine-induced immunologic memory through generation of an anamnestic response (2). For individuals with increased risk behaviors for hepatitis B such as injection drug use and condomless sex with multiple partners you can consider a challenge dose of hepatitis B vaccine followed by repeat anti-HBs testing 1-2 months post challenge dose to determine immunity (2).

If initiating HIV preexposure prophylaxis (PrEP) that does not treat hepatitis B (e.g., lenacapavir, LEN; cabotegravir, CAB) or switching from tenofovir-based PrEP to non-tenofovir-based PrEP (LEN, CAB), clinicians should determine if the patient has HBV infection or is immune to HBV.

For more information, please see:

1. Clinical Recommendation for the Use of Injectable Lenacapavir as HIV Preexposure Prophylaxis — United States, 2025 | MMWR
2. Preexposure prophylaxis for the prevention of HIV infection in the United States -- 2021 update: a clinical practice guideline

Hepatitis B Triple Panel Screening: Antibody to Hepatitis B Core Antigen (anti-HBc)

If an adult patient has an isolated positive total anti-HBc result, how do I interpret it?
There are several potential interpretations of an isolated positive total anti-HBc result (i.e., a positive total anti-HBc with a negative HBsAg and anti-HBs <10 mIU/mL). Additional evaluation of the patient's immune status and risk history is needed. A 2011-2018 national survey found that the prevalence of isolated positive total anti-HBc is about 0.8%. However, the prevalence of occult HBV infection[2] is likely higher among populations with risk factors (e.g., HIV, HCV, hemodialysis, injection drug use) or advanced chronic liver disease (1, 10). An occult HBV infection is defined as the presence of HBV covalently closed circular DNA in the

[2] Defined as the presence of HBV covalently closed circular DNA in the liver or HBV DNA in the blood of persons who test negative for HBsAg (10).

liver of HBV DNA in the blood of persons who test negative for HBsAg (10). The total anti-HBc tests are very accurate, with upwards of 99% specificity reported. If a person has no risk factors for hepatitis B, the result may be a false positive, but this is much less common with currently available total anti-HBc test assays compared to earlier assays (1, 9). Other possibilities include a previous infection with waning or loss of anti-HBs over time; an occult infection; a resolving HBV infection where testing occurred during the brief period before anti-HBs is detectable and after HBsAg has already disappeared; or a chronic HBV infection with a mutant HBsAg not detectable by available assays but would be identified by detectable HBV DNA (1). A consultation with a specialist may be helpful.

For additional resources, please see: https://www.cdc.gov/hepatitis-b/media/pdfs/2025/08/FINAL-7.25.25-interpretation-differentiation-isolated-positive-hepatitis-b-core-antibody.pdf

Hepatitis B Triple Panel Screening, Special Populations: Pregnant Women

I have an adult pregnant woman with chronic HBV infection. Should this patient receive triple panel screening with each pregnancy?

No, testing pregnant women known to be chronically infected with HBV using triple panel screening during each pregnancy is not needed. However, pregnant women should be tested for HBsAg during each pregnancy as it provides documentation of the positive HBsAg test result obtained during pregnancy and helps to ensure that their infant(s) will be identified for timely prophylaxis. In addition, all HBsAg-positive pregnant women should be tested for HBV DNA to guide the use of maternal antiviral therapy during pregnancy for the prevention of perinatal HBV transmission (2).

Hepatitis B Triple Panel Screening, Special Populations: Healthcare Personnel

Should an adult healthcare personnel who needs to be tested for anti-HBs to confirm immunity after hepatitis B vaccination have the hepatitis B triple panel screening instead of only an anti-HBs test?

The CDC recommends that all adults aged ≥18 years receive hepatitis B triple panel screening at least once in a lifetime (1). If the healthcare personnel has never received hepatitis B triple panel screening, it is indicated.

Should HBV DNA be included as a fourth hepatitis B triple panel screening test for adult patients, alongside HBsAg, anti-HBs, and anti-HBc?

No, the 2023 CDC hepatitis B triple panel screening recommendation includes hepatitis B screening for three laboratory tests (i.e., HBsAg, anti-HBs, and anti-HBc) at least once during a lifetime for adults aged ≥18 years and expands risk-based testing recommendations. The updated screening recommendations were based on a guideline development process that

incorporated systematic reviews, meta-analyses, and cost-effectiveness analyses when available (1). An HBV DNA test should be performed in HBsAg positive pregnant women to guide maternal antiviral therapy during pregnancy to prevent perinatal HBV transmission (2). HBV DNA testing is also helpful in determining next steps for anyone whose triple panel results show an isolated positive total anti-HBc. HBV DNA is not an FDA-approved diagnostic test; however, HBV DNA testing, either quantitative or qualitative, is used to detect hepatitis B virus in a person with known or suspected HBV infection and to guide antiviral treatment (11).

Timing of Hepatitis B Triple Panel Screening and Hepatitis B Vaccination

What is the reason behind the CDC's recommendation (1) for hepatitis B vaccination for adults in locations, like many pharmacies, where hepatitis B triple panel screening is not available?

Expanded access to vaccination may be available in the community, including at pharmacies. While the hepatitis B triple panel screening can identify people who are not vaccinated against hepatitis B, or have current infection or resolved infection, it should not be a barrier to vaccination, especially in populations that have decreased engagement with or access to care (1). Vaccination of persons immune to HBV because of current or resolved infection or previous HepB vaccination does not increase the risk for adverse events (12).

If an adult patient has not been screened using the hepatitis B triple panel, should I screen them before I vaccinate?

No, adult patients without written documentation of a completed hepatitis B vaccine series should be offered vaccination at the same visit or associated provider visit. However, blood should be collected for hepatitis B triple panel screening before administering the first dose. Results of the hepatitis B triple panel should be used to determine whether to continue the vaccine series (1).

What should I do if I have an adult patient who needs hepatitis B triple panel screening but recently received the first dose of hepatitis B vaccine elsewhere?

Hepatitis B vaccination may cause a false positive HBsAg screen up to 18 days after vaccination (1). Wait at least one month after receipt of the hepatitis B vaccine dose before drawing blood for hepatitis B triple panel screening.

Hepatitis B Vaccination: Hepatitis B Vaccine Type

What hepatitis B vaccines are available and how are they different?

There are three different single-antigen hepatitis B vaccines (Engerix-B, Heplisav-B, and Recombivax HB) approved and available for adults, in addition to the Twinrix combination hepatitis A-hepatitis B vaccine (13). Each vaccine is FDA-licensed and approved for use in the United States. Engerix-B and Recombivax HB can be administered to individuals from birth

through adulthood, while Heplisav-B and Twinrix are approved for adults 18 years and older. Heplisav-B is administered as a two-dose series given one month apart, whereas the other vaccines require a three-dose series given over a period of six months. All four vaccines (Engerix-B, Heplisav-B, Recombivax HB, and Twinrix) are safe for use during pregnancy (15). Two vaccines (Engerix-B, Recombivax HB) are approved for use in hemodialysis patients. For more information, please refer to Hepatitis B Vaccine Administration | Hepatitis B | CDC (13).

Are the available hepatitis B vaccines inter-changeable?
Ideally, the same vaccine product given as the initial dose should be used for subsequent doses to complete the series (2). However, if a different brand is administered, the dose should be considered valid and does not need to be repeated. The exception is Heplisav-B, as the two-dose vaccine series only applies when both doses in the series are Heplisav-B (2, 14). A two-dose series of Heplisav-B administered at least four weeks apart is valid, irrespective of the interval from doses received using vaccines by other manufacturers (14). A vaccine series consisting of a combination of one dose of Heplisav-B and a vaccine from a different manufacturer should consist of three total vaccine doses. The series should adhere to the three-dose schedule minimum intervals of four weeks between dose one and dose two, eight weeks between dose two and dose three, and 16 weeks between dose one and dose three (14, 16). Doses administered at less than the minimum intervals are not valid and should be repeated (14, 16, 17).

Hepatitis B Vaccination: Incomplete Hepatitis B Vaccination Series

What do I do if my patient has written documentation of one dose of hepatitis B vaccine a few years ago, but never finished the complete hepatitis B vaccine series?
If the dates of hepatitis B vaccine administration are documented but vaccine type is not available, the vaccine series does not need to be restarted (2). Continue the vaccine series from the last dose that the patient received and ensure minimal intervals between vaccine doses are followed (2).

Hepatitis B Vaccination: Documentation

What do I do for my patients who don't have records of hepatitis B vaccination, but are sure they were immunized?
According to the CDC's General Best Practice Guidelines for Immunization, providers should only accept written, dated records as evidence of vaccinations (16). If records are unavailable, persons without evidence of vaccination should be considered susceptible and should initiate the hepatitis B vaccine series (16).

Hepatitis B Vaccination: Breakthrough Infections

Can my patient still get hepatitis B if they received the complete hepatitis B vaccine series?
While breakthrough infections can occur, they are very uncommon in an otherwise healthy adults who have completed the hepatitis B vaccine series. The hepatitis B vaccine series produces immunity to hepatitis B in approximately 95% of healthy infants and >90% of healthy adults aged <40 years (18, 19, 20). A small subset of the population who may not respond adequately to the hepatitis B vaccine series; these people are known as vaccine non-responders. Vaccine non-responders are defined as persons who have an anti-HBs level l<10 mIU/mL after completing two full hepatitis B vaccine series. In certain settings, post-vaccination serologic testing is recommended to determine if an individual has developed protective immunity from the hepatitis B vaccine, or if they remain susceptible to HBV infection. Different assays have different cutoff values and reported levels of anti-HBs might vary depending on the assay used (2). Refer to the package insert of the test for the determination of appropriate level of anti-HBs (2).

Hepatitis B Vaccination: Birth Dose Vaccine and Hepatitis B Immune Globulin (HBIG)

What do I do if I give hepatitis B birth dose vaccine and HBIG in the same limb?
The 2018 ACIP hepatitis B recommendations state that all infants born to HBsAg-positive women should receive both hepatitis B birth dose vaccine and hepatitis B immune globulin (HBIG) within 12 hours of birth, administered at different injection sites (i.e., separate limbs) (2). Although there are no data on the effectiveness of hepatitis B vaccine and HBIG when both are administered in the same limb, there is a theoretical risk of HBIG neutralizing the antigen in hepatitis B vaccine in this situation. Some experts suggest that even if binding of hepatitis B vaccine and HBIG does occur, the dose of HBIG would not need to be repeated as they considered the amount of antibody from the dose of HBIG to still be protective. Given the favorable safety profile of the hepatitis B vaccine and the poor outcomes associated with HBV transmission to newborns, it is reasonable to repeat the hepatitis B vaccine in the opposite limb as soon as the error is recognized. However, this approach requires an individualized conversation with the parent or caregiver to discuss the potential risks and benefits for the infant.

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Footnote

*Immunization Schedules | Vaccines & Immunizations | CDC