CDC

CENTERS FOR DISEASE CONTROL AND PREVENTION

UDC

THE UNIVERSAL DATA COLLECTION PROGRAM

For People with Bleeding Disorders

Surveillance Testing Algorithms

SAFER • HEALTHIER • PEOPLE ™

DEPARTMENT OF HEALTH & HUMAN SERVICES

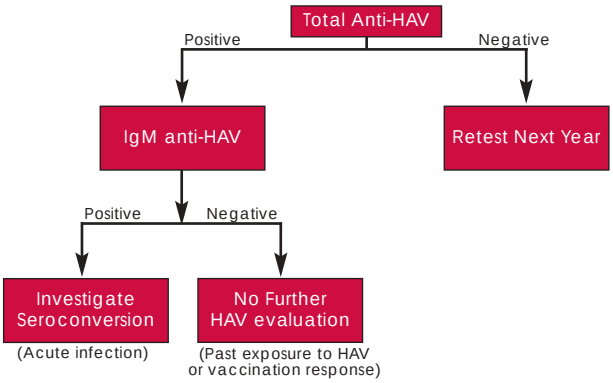
How is surveillance testing different from clinical care testing, and how do I evaluate test results?

As part of the Universal Data Collection program (UDC), CDC conducts blood product safety monitoring for persons with bleeding disorders. UDC participants are tested for past and present exposure to hepatitis A, B, and C viruses (HAV, HBV, and HCV). The algorithms for determining the sequence of tests performed on UDC blood samples are described below. As you read, you may notice that UDC testing algorithms differ from those used in routine clinical practice. In clinical care testing, if the patient tests positive, the goal is to establish the level of infection so that progression of disease can be established and monitored over time.

In contrast, the goal of surveillance testing is to determine the prevalence of infection in a population and to detect seroconversions that might indicate a breakdown in blood safety measures. Once a positive test has been established, the patient is no longer a candidate for seroconversion to that virus and will not be tested for that virus again. However, if a patient's test results are negative, the patient will be retested in subsequent years to ensure that the test remains negative and a seroconversion has not occurred.

Even if a patient has been determined to have positive results on all the tests, a plasma specimen should be submitted each year for UDC (with patient consent) in the event that testing for new agents is required.

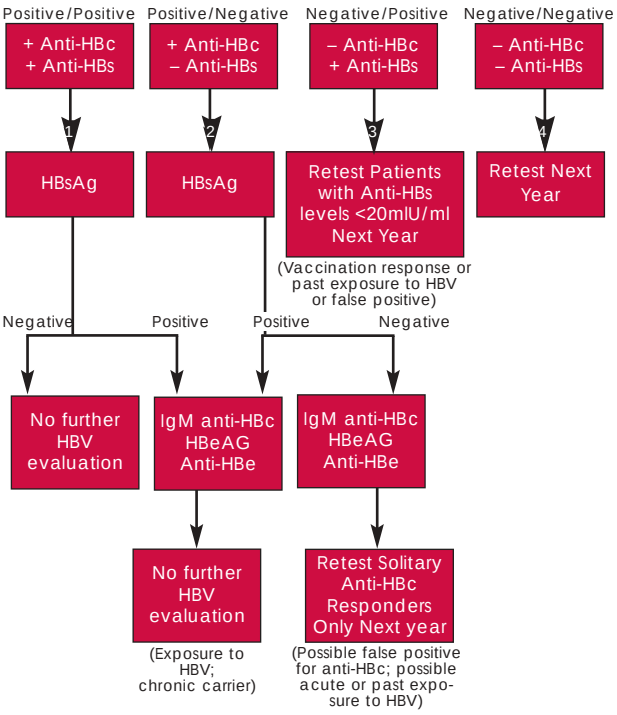
Algorithm for Hepatitis A Virus (HAV) Testing



HAV Testing

HAV testing evaluates total antibody levels to HAV (anti-HAV) among patients. If a patient tests positive for anti-HAV, a further test for anti-HAV IgM is performed to determine presence of acute infection. It is important to note that HAV vaccination may not produce detectable levels of antibody using current assays. Currently approved assays do not detect less than 100 mIU/ml of antibody, yet levels as low as 10 to 20 mIU/ml are thought to confer protection. Thus, a vaccinated individual may have a negative test result for total anti-HAV. In most cases, this person will probably be protected against serious disease. The CDC does not currently recommend revaccination of healthy individuals with undetectable antibody levels. If a patient's test results are positive or if there is evidence of vaccination response, no further testing is required. If a test result is contrary to information in the patient's medical records, the discrepancy should be reported to CDC so that the cause can be clarified.

Algorithm for Hepatitis B Virus (HBV) Testing



HBV Testing

All enrollees are tested for anti-HBs (antibody to hepatitis B surface antigen) and anti-HBc (antibody to hepatitis B core antigen). Depending on the results of these two lab tests, additional testing will be performed, as follows:

1. **POSITIVE/POSITIVE** If the patient has positive results for both tests, the HBsAg (hepatitis B surface antigen) is measured. This test is done to determine whether patients are chronic carriers of HBV infection. In cases in which the HBsAg test is negative, no further tests are performed, and the results are interpreted as indicating a patient exposed to hepatitis B virus who has cleared the virus. If the HBsAg test is positive, the person is identified as a chronic carrier of hepatitis B. Patients positive for HBsAg are further tested for the presence of antibody for hepatitis B core antigen IgM (IgM anti-HBc), hepatitis B e antigen (HBeAg), and antibody to hepatitis B e antigen (anti-HBe) to evaluate the level of viral replication.

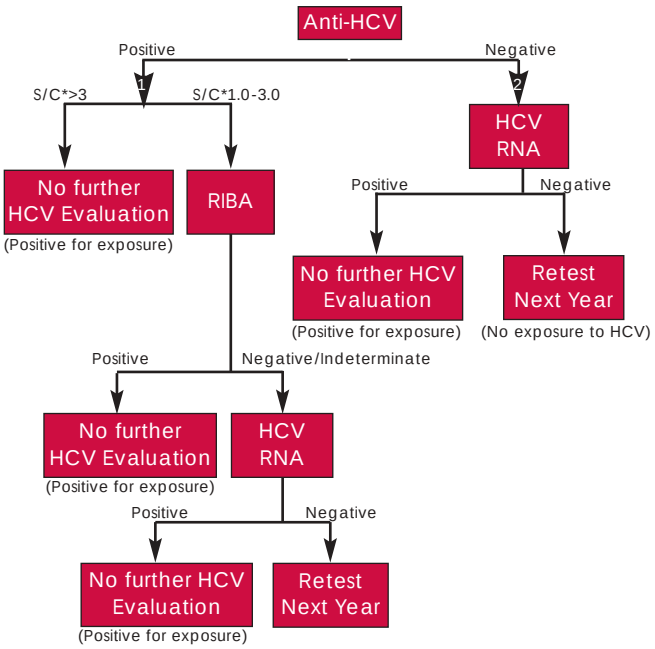
2. **POSITIVE/NEGATIVE** Patients testing positive for anti-HBc only are then tested for HBsAg. Whether the HBsAg test is positive or negative, the plasma is further tested for IgM anti-HBc, HBeAg, and anti-HBe to evaluate the level of viral replication. Any positive result in this series of tests indicates that the patient is a chronic HBV carrier.

3. **NEGATIVE/POSITIVE** Patients testing negative for anti-HBc but positive for anti-HBs may have been either vaccinated or exposed naturally to HBV, or this may represent a false-positive result (no exposure). These persons will be retested the following year.

4. **NEGATIVE/NEGATIVE** Patients testing negative for both anti-HBs and anti-HBc have not been exposed to HBV and will be retested the next year.

These results can be interpreted only in the context of the patient's clinical history. For example, persons with HIV infection are more likely to lose their antibody response to anti-HBs and anti-HBc. Persons who were infected with HBV in the remote past are likely to lose their antibody to HBs. These persons would test positive for anti-HBc only. If any of the hepatitis B results from UDC testing are inconsistent with the results at your center, please call the CDC to clarify any discrepancies.

Algorithm for Hepatitis C Virus (HCV) Testing



* ratio of optical density of sample signal to optical density of cutoff signal

HCV Testing

UDC protocol for HCV testing begins with screening patient plasma for the presence of antibody to HCV (anti-HCV).

1 **POSITIVE** If the patient tests positive for anti-HCV with an S/C* ratio between 1.0 and 3.0, a confirmatory RIBA test is done to rule out a false-positive anti-HCV result. If the RIBA is positive, the result is classified as a true positive. If the RIBA test is indeterminate or negative, patient plasma is tested for presence of HCV RNA by PCR. If the PCR result is positive, then positive anti-HCV result will be considered a true positive.

If the RIBA is negative and the plasma is negative for presence of HCV RNA, then the positive anti-HCV result is considered to be a false-positive.

If the RIBA is indeterminate and the plasma is negative for presence of HCV RNA, then the interpretation of the positive anti-HCV result is uncertain. It could be a false-positive, or the person could be chronically infected with HCV or in the process of seroconversion.

All persons who are found to have no or questionable evidence of past exposure to HCV (see the algorithm) will be retested the following year.

It is important to note that participants who test positive for anti-HCV with an S/C ratio >3.0 are considered positive for past exposure to HCV. No further testing will be done on that patient's plasma in the year of enrollment or subsequent years. If the UDC test result is inconsistent with that recorded in the patient's medical records, these differences should be reported to CDC so that discrepancies can be clarified.

2 **NEGATIVE** If the anti-HCV test is negative, PCR testing for the presence of HCV RNA is conducted to rule out a possible false-negative anti-HCV test. If the PCR result is positive, the patient is considered HCV infected and no further testing will be performed. If the PCR result is negative, the patient will be retested the next year.

TESTING

TABLE OF SEROLOGIC TESTS

INTERPRETATION

Table of Serologic Tests Provided by UDC

TEST	INTERPRETATION OF A POSITIVE RESULT
IgM Anti-HAV Hepatitis A IgM antibody	Acute infection with HAV; detectable IgM persists for 4 to 6 months after infection.
Total Anti-HAV Total hepatitis A antibody	One of the following: - Previous infection with HAV - Previous HAV vaccination
Anti-HBs Hepatitis B surface antigen antibody	One of the following: - Previous infection with HBV - Previous HBV vaccination - Recent hepatitis B immune globulin prophylaxis - Passive antibody from mother
IgM Anti-HBc Hepatitis B core IgM antibody	One of the following: - Current or recent HBV infection (past 4 months) - Chronic hepatitis B with active viral replication (rare)
Total Anti-HBc Total hepatitis B core antibody	Previous HBV infection; timing and chronicity unknown if both HBsAg and anti-HBs are not detected.
HBsAg Hepatitis B surface antigen	Acute or chronic HBV infection; patient may infect others through sexual contact and blood-to-blood contact.
HBeAg Hepatitis B e antigen	Acute or chronic HBV infection with active viral replication; patient may infect others through sexual contact and blood-to-blood contact.

Table of Serologic Tests Provided by UDC (cont.)

Anti-HBe	
Hepatitis B e antigen antibody	Suppression of HBV replication (positive individuals are considered less infectious than anti-HBe negative individuals).
HBV DNA	
Hepatitis B DNA	Acute or chronic HBV infection (test used for research purposes only); not currently utilized in the testing algorithm.
Anti-HCV	
Hepatitis C antibody	Previous or chronic infection with HCV.
RIBA	
Hepatitis C antigen by positive anti-HCV recombinant immunoblot assay	Previous infection with HCV; used to evaluate suspected false-positive results.
HCV RNA	
Hepatitis C RNA by polymerase chain reaction	Active HCV replication, either acute or chronic.

Modified after Neusschwander-Tetri. Postgrad Med 1995;98(1):55.

Printed Resources

*Epidemiology and prevention of vaccine-preventable diseases, 4th edition.
www.cdc.gov/nip/publictions/pink/e&p_vpd.html.

*The hepatitis B virus: a comprehensive strategy for eliminating transmission in the United States through universal childhood vaccination: recommendations of the Immunization Practices Advisory Committee (IPAC). MMWR 1991;40(RR-13):1-19.

*Interpretation and use of the western blot assay for serodiagnosis of human immunodeficiency virus type 1 infections. MMWR 1990;38(S-7):1-7.

Lemon SM, Thomas DL. Vaccines to prevent viral hepatitis. N Engl J Med 1997;336:196-202.

Mannucci PM, Gringeri A, Morfini M, De Biasi R, et al. Immunogenicity of a recombinant hepatitis B vaccine in hemophiliacs. Am J Hematol 1988;29:211-214.

Maris JM, Butler RB, Cohen AR. Loss of detectable antibody to hepatitis B surface antigen in immunized hemophilia but without human immunodeficiency virus infection. J Pediatr 1995;126(2):269-271.

*Prevention of hepatitis A through active or passive immunization: recommendations of the Immunization Practices Advisory Committee. MMWR 1996;45(RR-15):1-30.

Tilzey AJ, Palmer SJ, Harrington C, O'Doherty MJ. Hepatitis A vaccine in HIV-positive persons with hemophilia. Vaccine 1996; 14(11):1039-1041.

*UDC Surveillance Reports
www.cdc.gov/ncidod/dastlr/hematology.

*CDC Publications

Health Surveillance

Information for life.

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