

Hepatitis B, Acute

PROTOCOL CHECKLIST

- Enter available information into Merlin upon receipt of initial report
- Review background on disease, case definition, and laboratory testing
- Contact provider
- Interview patient
 - Review disease facts
 - Modes of transmission (see page 3)
 - Incubation period
 - Symptoms
 - Risk of co-infection with hepatitis A and C
 - Provide information on obtaining hepatitis A vaccine
 - Ask about exposure to relevant risk factors
 - Blood to blood contact with someone with hepatitis B
 - Occupational exposure
 - Drug use
 - Tattoos/body piercings
 - Sexual contact
 - Identify contacts
 - Refer symptomatic contacts to a health care provider
 - Refer close contacts for testing and vaccination
 - Determine if patient can be epi-linked to an existing case and if patient is part of an outbreak
 - Provide information on how to prevent further transmission (see page 3)
 - Address patient's questions or concerns
- Follow-up on special situations, including outbreaks or cases in sensitive situations
- Investigate perinatal hepatitis B or a positive hepatitis B surface antigen (HBsAg) in a pregnant woman according to corresponding guidelines
- Enter additional data obtained from interview into Merlin

Hepatitis B, Acute

1. DISEASE REPORTING

A. Purpose of reporting and surveillance

1. To identify those persons who are carriers and may still be infectious to educate and prevent further transmission
2. To identify carriers so they may seek treatment to prevent long-term complications due to hepatitis B infection
3. To identify outbreaks and other undiagnosed cases
4. To determine if there is a source of infection of public health concern and to stop transmission from such a source

B. Legal reporting requirements

Laboratories and physicians are required to report hepatitis B, acute to the county health department (CHD) within one working day of identification/diagnosis.

C. County health department investigation responsibilities

1. Begin investigation within one business day of receiving report from a provider or laboratory.
2. Contact patient and/or provider to complete case interview.
3. Report all confirmed and probable cases in Merlin.
4. Report liver enzyme results for all patients where these are available.

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic agent

The Hepatitis B virus (HBV) is a partially double-stranded DNA virus of family Hepadnaviridae. There are four subtypes and eight genotypes of HBV that vary geographically. Immunity to one subtype may confer immunity to others. There is growing evidence of differences in severity between subtypes.

B. Description of illness

People acutely infected with HBV may be asymptomatic or symptomatic. The likelihood of developing symptoms is age dependent: less than 1% of infected infants younger than one year of age, 5% to 15% of infected children one to five years of age, and 30% to 50% of infected people older than five years of age are symptomatic. Acute HBV infection cannot be

distinguished from other forms of acute viral hepatitis on the basis of clinical signs or symptoms. When present, signs and symptoms can include:

- Fever
- Fatigue
- Loss of appetite
- Nausea
- Vomiting
- Abdominal pain
- Dark urine
- Clay-colored bowel movements
- Joint pain
- Jaundice
- Cirrhosis
- Liver failure
- Hepatocellular cancer

Persistent infection with HBV (hepatitis B, chronic) depends on age at the time of acute infection. More than 90% of infants infected perinatally or in the first year of life will develop chronic hepatitis B. Between 25% and 50% of children infected between one and five years of age become chronically infected, whereas 5% to 10% of acutely infected children (over five years-old) and adults develop chronic HBV infection. Patients who become infected with HBV while immunosuppressed or with an underlying chronic illness have an increased risk of developing chronic infection.

People with chronic hepatitis B remain infectious throughout their lifetime, unless successfully treated. Infected people should be counseled to avoid hepatotoxic agents, and should be informed of the risks of excessive alcohol ingestion, which will exacerbate liver disease. All persons infected with the hepatitis C virus (HCV) should be vaccinated against hepatitis A and hepatitis B.

C. Reservoirs

Hepatitis B does not have any other known reservoirs besides humans. Although the virus has been transmitted to chimpanzees experimentally, an animal reservoir in nature has not been identified.

D. Modes of transmission

The hepatitis B virus is found in blood, seminal fluid, vaginal secretions, and other body fluids. The virus can be spread by:

- Unprotected sexual contact with an infected person, especially among persons with multiple sex partners or men who have sex with men (MSM),
- Contact with contaminated needles, especially injection drug equipment, and other items such as tattoo and body piercing instruments,
- An infected mother to her infant during delivery,
- Household contact with the body fluids from an infected person such as from razors and toothbrushes contaminated with infected blood; indirect transmission from dried blood is also possible,
- Occupational exposure through accidental needle stick,

- Lack of infection control in the health care setting (transmission used to be common in places like dialysis centers, mental hospitals and facilities for the developmentally disabled, but has been almost eliminated by better infection control and vaccination of patients and staff).

The hepatitis B virus is never transmitted through casual contact such as coughing, sneezing, being in the same area as an infected person, or by consuming contaminated food or water. Transmission due to blood and blood products used in medical practice, including those used to treat hemophilia, was common but has been essentially eradicated by testing of products for hepatitis B.

E. Incubation period

The incubation period for acute hepatitis B is 60 to 150 days, with an average of 90 days.

F. Period of communicability

All persons with detectable HBV DNA in their blood are potentially infectious to others.

G. Treatment

Guidance on treatment can be found at the following site:

<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5708a1.htm>

Therapy for hepatitis B is a rapidly changing area of clinical practice. No specific therapy for acute HBV infection is available, and acute HBV infection does not usually warrant referral to a hepatitis specialist. For those that develop chronic hepatitis B, the Food and Drug Administration (FDA) has approved seven therapies for the treatment of chronic HBV infection: interferon alfa-2b, peginterferon alfa-2a, lamivudine, adefovir dipivoxil, entecavir, telbivudine, and tenofovir disoproxil fumarate (13, 106, 132, 133). In addition, at least two other FDA-approved oral antiviral medications for HIV (clevudine and emtricitabine) are undergoing phase-three trials for HBV treatment and might be approved soon for chronic hepatitis B. Treatment decisions are made on the basis of HBeAg status, HBV DNA viral load, aminotransferase (ALT), stage of liver disease, age of patient, and other factors (13, 32, 134).

H. Prophylaxis

There are two types of products available for prophylaxis and the prevention of hepatitis B infection:

- 1) **Hepatitis B vaccine** provides long-term protection against HBV infection, and is used for both pre-exposure and post-exposure prophylaxis. There are three doses of the vaccine; the second dose is given one month after the first, and the third dose is given six months after the first.
- 2) **Hepatitis B Immune Globulin (HBIG)** provides temporary protection against the hepatitis B virus for three to six months, and is used only in certain post-exposure settings.

I. Vaccination

Hepatitis B vaccination is recommended for:

- Children zero to 18 years of age
- Persons with compromised immune systems (e.g., HIV/AIDS)
- Persons with chronic liver disease or chronic hepatitis C
- Inmates of long-term correctional facilities
- Adults in one or more of the following high-risk groups:
 - i. drug users who share needles
 - ii. health care workers who have contact with infected blood
 - iii. MSM (men who have sex with men)
 - iv. people who have multiple sexual partners
 - v. household contacts of infected persons

Hepatitis B vaccination has been successfully integrated into the childhood vaccination schedule. The Advisory Committee on Immunization Practice (ACIP) recommends that children get their first dose of hepatitis B vaccine at birth and complete the series by six to 18 months-old. It is recommended that older children and adolescents that have not received the vaccine also be vaccinated. Adults who have not been vaccinated and are at high-risk for infection based on high-risk behavior or occupational risk should discuss vaccination with their physician.

J. Hepatitis B, Acute in Florida

The incidence rate for acute hepatitis B infection has declined gradually over the last ten years. In 2011, 234 cases of acute hepatitis B were reported, which is 36% lower than the five-year average from 2006 to 2010. There is no seasonal trend for acute hepatitis B infection and 93% of the infections were classified as sporadic. In 2011, the highest incidence was among those aged 35 to 44 years. During the same year, the incidence rates were equal to or lower than the previous five-year average in all age groups except those aged 1-4 and 15-19 years. Rates have always been low in children, and are even lower now with widespread hepatitis B vaccination. The most common risk factors reported in 2011 were non-injection drug use (18.1%), followed by contact with someone confirmed or suspected of having an HBV infection (11.1%), injection drug use (10.7%), and a recent tattoo (7.7%).

See *Florida Annual Morbidity and Statistics Report*: <http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/data-and-publications/fl-amr1.html>.

3. CASE DEFINITION

A. Clinical case definition

An acute illness with discrete onset of symptoms* consistent with acute viral hepatitis **and** either jaundice **or** elevated ALT levels over 100 IU/L.

*Symptoms most commonly include fever, headache, malaise, anorexia, diarrhea, vague abdominal discomfort, nausea and vomiting. Only a small proportion of acute hepatitis B infections will be clinically recognized.

A documented negative HBV antigen (HBsAg) laboratory test result followed within six months by a positive test result (either HBsAg, HBeAg, or HBV NAT including genotype) does not require an acute presentation to meet the surveillance case definition.

B. Laboratory criteria for diagnosis

One or more of the following three criteria:

- Hepatitis B surface antigen (HBsAg) positive,
AND
- (if done) IgM antibody to hepatitis B core antigen (IgM anti-HBc) positive,
OR
- Negative HBsAg within six months prior to a positive test result (either HBsAg, HBeAg, or HBV DNA NAT including genotype).

C. Case classification

Confirmed:

- A case that meets the clinical case definition and is laboratory confirmed, and is not known to have chronic hepatitis B.
OR
- A case that does not have acute clinical illness but has a documented negative HBV antigen laboratory test result followed **within six months** by a positive test result **AND** no previous diagnosis of chronic hepatitis B.

Probable: A case that is IgM anti-HBc positive, lacks jaundice or elevated liver enzymes, but has discrete onset and other appropriate symptoms. Probable cases also include patients who have a discrete onset of symptoms, have a positive HBsAg and are epidemiologically linked to a confirmed acute hepatitis B case.

Comment

Report liver enzyme results for all cases in Merlin.

A chart for assisting in interpreting hepatitis B serology can be found on the CDC site below: <http://www.cdc.gov/hepatitis/HBV/HBVfaq.htm#C1>.

Note: transient hepatitis B surface antigen positivity after vaccination has been reported in the literature. A positive HBsAg result within two weeks of administration of vaccine should be interpreted with caution. It is recommended that testing be repeated two weeks after the completion of the vaccine series. Ideally, health practitioners will obtain hepatitis B serologies before vaccination, reducing the risk of false positive test results.

4. LABORATORY TESTING

A. Criteria for diagnosis

Hepatitis B serology is the only way to determine the state of infection. Hepatitis B, acute is classified by the presence of IgM antibody to the hepatitis B core antigen (IgM anti-HBc).

However, IgM anti-HBc is usually not present in infants infected perinatally. See Section D below for interpretation of laboratory results.

B. Services available at the BPHL

The Bureau of Public Health Laboratories (BPHL) runs a hepatitis screen when testing patients for hepatitis. The hepatitis screen includes hepatitis B surface antigen, hepatitis B surface antibody, hepatitis B core total antibody, and hepatitis A total antibody and hepatitis C antibody.

C. Testing requests

1. Submitting specimens/isolates to BPHL
 - a. All submissions should be accompanied by Clinical Lab Submission Form 1847: http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/surveillance-and-investigation-guidance/_documents/dh1847clinicalsubmissionform.pdf
 - b. Electronic Laboratory Ordering (ELO) is also available by entering a request into the HMS State Laboratory System, placing a bar-coded label on the O&P vial, and writing the date collected on the vial.
2. Specimen collection:

Three ml of serum or 6 to 8 ml of whole blood properly labeled (name, date of birth, and date collected) should be submitted for testing.
3. Packaging and shipping
 - a. Testing for hepatitis B is done at all BPHL facilities.
 - b. Place labeled specimen in the proper biohazard transport bag with the Clinical Lab Submission Form 1847. Pack according to International Air Transport Association (IATA) regulations, labeling the outer shipping container: *UN3373, Biological Substance Category B*.
 - c. Specimens and isolates should be sent at ambient temperature or cooler, but cool packs should not be in direct contact with vials.

Packaging and Shipping of Diagnostic Specimens Flowchart:

http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/surveillance-and-investigation-guidance/_documents/packagingflowchar0422051.pdf

Packaging and Shipping of Diagnostic Specimens Notes:

http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/surveillance-and-investigation-guidance/_documents/packagingflowchartnotes0422051.pdf

4. Contact the regional laboratory with questions: http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/_documents/investigationunitmap_11-22-13color.pdf.

D. Interpretation of results:

The fact that some people with acute HBV infection are asymptomatic and have no evidence of liver disease makes interpretation of laboratory results difficult. Below is a chart used to help determine the status of the patient based on serological testing. Other testing and liver biopsy may be necessary to determine the progression of disease. The following information is available on the CDC website:

<http://www.cdc.gov/hepatitis/HBV/HBVfaq.htm#C2>.

Hepatitis B surface antigen (HBsAg): A protein on the surface of HBV; it can be detected in high levels in serum during acute or chronic HBV infection. The presence of HBsAg indicates that the person is infectious. The body normally produces antibodies to HBsAg as part of the normal immune response to infection. HBsAg is the antigen used to make the hepatitis B vaccine. False positive HBsAg results can occur in the two weeks following receipt of the hepatitis B vaccine.

Hepatitis B surface antibody (anti-HBs): The presence of anti-HBs is generally interpreted as indicating recovery and immunity from HBV infection. Anti-HBs also develops in a person who has been successfully vaccinated against hepatitis B.

Total Hepatitis B core antibody (anti-HBc): Appears at the onset of symptoms in acute hepatitis B and persists for life. The presence of anti-HBc indicates previous or ongoing infection with HBV in an undefined time frame.

IgM antibody to Hepatitis B core antigen (IgM anti-HBc): Positivity indicates recent infection with HBV (six months or less). Its presence indicates acute infection.

Hepatitis B envelope antigen (HBeAg): A secreted product of the nucleocapsid gene of HBV that is found in serum during acute and chronic hepatitis B. Its presence indicates that the virus is replicating and the infected person has high levels of HBV.

Hepatitis B envelope antibody (HBeAb or anti-HBe): Produced by the immune system temporarily during acute HBV infection or consistently during or after a burst in viral replication. Spontaneous conversion from e antigen to e antibody (a change known as seroconversion) is a predictor of long-term clearance of HBV in patients undergoing antiviral therapy and indicates lower levels of HBV.

Interpretation of Hepatitis B Serologic Test Results		
Test	Result	Interpretation
HBsAg anti-HBc anti-HBs	Negative Negative Negative	Susceptible
HBsAg Anti-HBc Anti-HBs	Negative Positive Positive	Immune due to natural infection
HBsAg Anti-HBc Anti-HBs	Negative Negative Positive	Immune due to hepatitis B vaccination
HBsAg anti-HBc IgM anti-HBc anti-HBs	Positive Positive Positive Negative	Acutely infected
HBsAg anti-HBc IgM anti-HBc anti-HBs	Positive Positive Negative Negative	Chronically infected
HBsAg HBsAb HBV DNA	Positive Positive Negative	Consistent with recent immunization; retest two weeks after completion of vaccine series
HBsAg anti-HBc anti-HBs	Negative Positive Negative	Interpretation unclear; four possibilities: 1. Resolved infection (most common) 2. False-positive anti-HBc, thus susceptible 3. "Low level" chronic infection 4. Resolving acute infection

5. CASE INVESTIGATION

A. Contact the physician or hospital

1. Confirm acute hepatitis B infection has been diagnosed in the reported patient and symptoms are consistent with an acute hepatitis B infection.
2. Obtain as much information as possible about the case, such as:
 - b. Contact information
 - c. Demographic information (e.g., DOB, gender, race, ethnicity)
 - d. Date of onset
 - e. Symptoms
 - f. Laboratory tests performed

- g. Hepatitis A and B vaccine history
 - h. Underlying conditions
3. Ask what information has been given to the patient, including whether the patient knows about the diagnosis.
4. Notify the physician that you will be contacting the case as DOH follows up on all cases of hepatitis B, acute to assess risk factors, to better characterize the occurrence of hepatitis B, acute in Florida and to take necessary steps to prevent additional cases. Also, review infection control recommendations and address any concerns in regards to the CHD contacting the case.

B. Interview the case

1. Complete an interview as soon as possible after the patient is reported to optimize recall.
 - a. Make at least three phone call attempts to reach the patient; calls should be made at different times of the day with at least one call being made in the evening.
 - b. If phone calls are unsuccessful, mail a letter to the patient requesting that he/she contact the CHD and/or conduct a home visit or leave a letter for the patient.
 - c. If the patient is unable to provide information, interview a proxy (e.g., a spouse, parent) to gather further information.
2. Once contact is made, education about hepatitis B infection should be provided and an interview should be conducted to obtain any further information not already gathered from the provider or hospital. A viral hepatitis Case Report Form is available to guide the investigation and assist in follow-up:
http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/_documents/crf-hepatitis-viral.pdf.
3. Pertinent items to cover during the interview include:
 - a. Education
 - b. Demographic information
 - c. Identification of possible exposures and risks during exposure period (six weeks to six months prior to onset of symptoms)
 - i. Close contact (e.g., household member, sexual partner) with any person who had an illness compatible with hepatitis B or any person with a known acute or chronic hepatitis B infection
 - ii. Injection and non-injection drug use
 - iii. Tattoos and/or body piercings
 - iv. Surgery, dental work, other invasive procedures
 - d. Information on where to obtain the hepatitis A vaccine

C. Merlin data entry

Create a case in Merlin under disease code **HEPATITIS B, ACUTE-07030**. Enter available data, being sure to include all required fields on the Basic Data screen, complete the Case Symptoms screen and attach all relevant laboratory results. Please note that liver function test results should be entered as a laboratory result. The extended data screens (Hepatitis Common, and Hepatitis B, Acute) should also be completed in Merlin. If laboratory results and/or physician diagnosis are received that indicate perinatal hepatitis B or a positive hepatitis B surface antigen (HBsAg) in a pregnant woman, the CHD can access the case,

enter relevant results and manually change the disease code from 07030 to the corresponding disease code. If the case has already been reported, it will remain so, if not, it will move to the hepatitis B task list for further investigation and completion by the CHD.

Chronic hepatitis cases are automatically reported in Merlin. However, Merlin does not automatically match hand-entered cases of acute hepatitis B with cases that have been automatically reported as chronic. Checking the CHD "Chronic Hepatitis B and C" list for preexisting cases before entering a new one will save time and reduce duplication of cases.

6. CONTROLLING FURTHER SPREAD

A. Patient/Household education on prevention recommendations

1. Disinfect all items that may come in contact with blood and body fluid.
2. Do not share personal items that may have blood on them: razorblades, toothbrushes.
3. Cuts and sores on the skin should be covered to prevent the spread of infected blood or body fluid.
4. Patients should be informed of the risk of sexual transmission. Hepatitis B virus-positive persons engaged in high-risk sexual activities* should be counseled to use latex barriers correctly every time they have sex.
5. Do not share needles or syringes. Disposable needles should be used only once then discarded. As a last resort, undiluted household bleach can be used to clean syringes and needles.
6. Active injection drug users should be directed to needle exchange programs and drug rehabilitation services.
7. Blood spills, including dried blood, still carry a risk of infection. All blood spills should be cleaned using 1:10 dilution of one part bleach to 10 parts water.

B. Isolation of cases

Standard precautions should be observed to prevent exposures to blood and body fluids in health care settings.

C. Management of contacts

To identify who may be a contact, see Modes of Transmission. Case contacts should be Epi-linked in Merlin.

Symptomatic contacts: If the probable case definition is met, the contact should be reported, investigated, and managed in the same manner as a confirmed case.

Asymptomatic contacts: Should be vaccinated with the three-dose series of hepatitis B vaccine. If a known exposure has occurred, the contact should receive HBIG and begin the three-dose series of hepatitis B vaccine. For previously vaccinated and exposed contacts, refer to the most updated Epidemiology and Prevention of Vaccine-Preventable Diseases: <http://www.cdc.gov/vaccines/pubs/pinkbook/hepb.html#vaccine>.

Use universal precautions for individuals in contact with body fluids in health care settings. High-risk groups for infection include:

- drug abusers who share needles

- health care workers who have contact with infected blood
- men who have sex with men
- people who have multiple sexual partners
- household contacts of infected persons
- infants born to mothers who are HBsAg carriers

* High-risk sexual activities are any type of penetrative sexual contact without using barrier protection, especially if the person has multiple sexual partners (even if one is a steady) regardless of vaccination status.

7. MANAGING SENSITIVE SITUATIONS

A. Identifying a sensitive situation

As defined by *Florida Administrative Code* 64D-3.208, a sensitive situation is a setting in which the presence of a case would increase significantly the probability of spread of the diagnosed or suspected disease or condition and would, therefore, constitute a public health hazard. Examples of such settings are schools, childcare facilities, hospitals and other patient care facilities.

B. Work or childcare restrictions

No occupational, school, or child care restrictions are necessary for hepatitis B infected individuals.

C. Needle stick and similar exposure

Accidental needle sticks carry a risk for transmission of hepatitis B depending on the status of the infected person. If the source patient is positive for both hepatitis B surface antigen (HBsAg) and hepatitis B envelope antigen (HBeAg), the risk of transmission is 22% to 31% and the risk of developing serological symptoms of an HBV infection is 37% to 62%. For those that are positive for hepatitis B surface antigen (HBsAg) and negative for hepatitis B envelope antigen (HBeAg), the risk of transmission is 1% to 6% and the risk of developing serological symptoms of a hepatitis B infection is 23% to 37%.

D. Case is a recent blood donor or recipient

Notify the blood bank immediately so that any unused product can be recalled.

8. IMPORTANT LINKS

A. Viral Hepatitis Case Report Form:

http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/_documents/crf-hepatitis-viral.pdf

B. CDC Hepatitis B Page

<http://www.cdc.gov/hepatitis/HBV/index.htm>

C. Florida Department of Health Bureau of HIV/AIDS and Hepatitis
<http://www.floridahealth.gov/diseases-and-conditions/aids/index.html>

D. Health care Investigation Guide
<http://www.cdc.gov/hepatitis/Outbreaks/PDFs/HealthcareInvestigationGuide.pdf>

9. REFERENCES

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