# Hepatitis B, Chronic

## PROTOCOL CHECKLIST

- ☐ Merlin automatically assigns diagnosis status and reports chronic Hepatitis B cases
  - ☐ Follow up any special situations as time allows
- ☐ Enter additional data obtained from physician/ lab into Merlin
- ☐ Manually change disease code from chronic to acute pending lab/physician diagnosis if necessary
  - ☐ Investigate acute Hepatitis B, perinatal Hepatitis B or a positive Hepatitis B surface antigen (HBsAg) in a pregnant woman according to corresponding guidelines

# Hepatitis B, Chronic

## 1. DISEASE REPORTING

### A. Purpose of reporting and surveillance

To identify those persons who are chronic carriers and may still be infectious to educate and prevent further transmission. To identify chronic carriers so that they may seek treatment to prevent long term complications due to Hepatitis B infection.

### B. Legal reporting requirements

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

### C. County health department investigation responsibilities

Chronic Hepatitis B cases are automatically reported in Merlin and may not require further investigation. Special situations, such as children and young adults, may require follow up. See section 5, **Case Investigation** for further details.

## 2. THE DISEASE AND ITS EPIDEMIOLOGY

### A. Etiologic agent

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

### B. Description of illness

Persons with chronic HBV infection might be asymptomatic, have no evidence of liver disease, or have a spectrum of disease ranging from chronic hepatitis to cirrhosis or hepatocellular carcinoma (a type of liver cancer).
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

**People with chronic Hepatitis B remain infectious throughout their lifetime, unless successfully treated.** The presence of signs and symptoms varies by age. Most children

under age 5 years and newly infected immunosuppressed adults are asymptomatic; whereas 30%–50% of persons aged ≥5 years have initial signs and symptoms.

**C. Reservoirs**

Hepatitis B does not have any other known reservoirs besides humans. Although chimpanzees are susceptible, an animal reservoir in nature has not been identified.

**D. Modes of transmission**

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. Other items such as tattoo and body piercing instruments, razors, and toothbrushes may be contaminated with infected blood
- An infected mother to her infant during delivery
- Household contact with an infected person
- Occupational exposure through accidental needle stick
- Lack of infection control in the healthcare 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 not an airborne virus, and 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, including those used to treat hemophilia, used to be common and has been essentially eradicated by testing of products for Hepatitis B.

**E. Incubation period**

Although the incubation period for chronic Hepatitis B is difficult to determine due to the absence of clinical symptoms, serologic Hepatitis B markers of infection may be present as early 6 to 24 weeks following exposure, with an average of 8 to 12 weeks. Chronic Hepatitis B may persist for up to 20 years before onset of cirrhosis or liver cancer.

**F. Period of communicability**

All persons who are Hepatitis B surface antigen positive or have detectable HbsAg or HBeAg are potentially infectious to others. Infectivity of chronically infected persons varies from high to moderate depending on the severity of disease and viremia.

**G. Treatment**

Guidance on treatment can be found at the following sites:
http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5708a1.htm
and
http://www.aasld.org/practiceguidelines/Documents/Bookmarked%20Practice%20Guidelines/Chronic_Hep_B_Update_2009%208_24_2009.pdf

Therapy for Hepatitis B is a rapidly changing area of clinical practice. Seven therapies have been approved by FDA 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-3 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, 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:

- **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 1 month after the first, and the third dose is given 6 months after the first.
- **Hepatitis B Immune Globulin (HBIG)** provides temporary protection against the Hepatitis B virus for 3 – 6 months, and is used only in certain post exposure settings.

### I. Vaccination

Hepatitis B vaccination is recommended for:

- Adults in one or more of the high risk groups
- Children 0 – 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

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 6-18 months. It is recommended that older children and adolescents that have not received the vaccine also be vaccinated. Adults who have not been vaccinated that are at high-risk for infection based on high-risk behavior or occupational risk should discuss vaccination with their physician.

### J. Chronic Hepatitis B in Florida

Chronic Hepatitis B became reportable in FL in 2001. There has been a steady increase in the number of reports received up to at least 4000 a year from 2009-2011. Florida data indicate a higher prevalence of HBV for persons 50 years old and older; male gender; white race; and non-Hispanic ethnicity

## 3. CASE DEFINITION

### A. Clinical description

Persons with chronic Hepatitis B infection may have no evidence of liver disease or may have a spectrum of disease ranging from chronic hepatitis to cirrhosis or liver cancer. Persons with chronic infection may be asymptomatic.

**B. Laboratory criteria for diagnosis**

Confirmed:

- IgM antibodies to Hepatitis B core antigen (referred to as anti-HBc or IgM HBcAg) negative AND a positive result on one of the following tests: Hepatitis B surface antigen (HBsAg), Hepatitis B e antigen (HBeAg), or nucleic acid for Hepatitis B virus (HBV) DNA (including quantitative, qualitative and genotype testing)

OR

- HBsAg positive, or nucleic acid test for HBV DNA positive (including quantitative, qualitative and genotype testing), or HBeAg positive two times at least 6 months apart (any combination of these tests performed six months apart is acceptable)

Probable:

Any single positive result: HBsAg positive, or nucleic acid test for HBV DNA positive (including quantitative, qualitative and genotype testing), or HBeAg positive

**C. Case classification**

Confirmed: A case that is laboratory confirmed.

Probable: A case with a single HBsAg positive, HBV DNA positive, or HBeAg positive lab result and does not meet the case definition for Hepatitis B, acute.

**D. Note**

Multiple laboratory tests indicative of chronic HBV infection may be performed simultaneously on the same patient specimen as part of a "hepatitis panel." Testing performed in this manner may lead to seemingly discordant results e.g., HBsAg-negative AND HBV DNA-positive. For the purposes of this case definition, any positive result among the three laboratory tests mentioned above is acceptable, regardless of other testing results. Negative HBeAg results and HBV DNA levels below positive cutoff level do not confirm the absence of HBV infection.

A table for assisting in interpreting Hepatitis B serology can be found on the CDC site below: http://www.cdc.gov/ncidod/diseases/hepatitis/b/Bserology.htm

## 4. LABORATORY TESTING

**A. Criteria for diagnosis**

Hepatitis B serology is the only way to determine the state of infection. Chronic Hepatitis B is classified as the presence of Hepatitis B surface antigen (HBsAG) in serum for at least six months or by the presence of HBsAG in a person who tests negative for IgM antibody to the Hepatitis B core antigen (IgM-anti-HBc).

**B. Services available at the BPHL**

The Bureau of Public Health Laboratories (BPHL) runs a Chronic Hepatitis Screen when testing patients for chronic hepatitis. The Chronic 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.doh.state.fl.us/lab/addpages/BOL_Forms.html).
   b. Electronic Laboratory Ordering (ELO) may also be used by entering request into the HMS State Laboratory System, placing bar coded label on the O&P vial, and writing the date collected on the vial.
2. Specimen collection
   Three ml of serum or 6-8 ml of whole blood that is properly labeled (name, date of birth, date collected) should be submitted for testing.
3. Packaging and shipping
   a. Testing for chronic 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. Package 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.
   d. http://www.doh.state.fl.us/lab/PDF_Files/Packaging_Flowchart_0422051.pdf
   e. http://www.doh.state.fl.us/lab/PDF_Files/Packaging_Flowchart_notes_0422051.pdf
4. Contact the regional laboratory with questions: http://www.doh.state.fl.us/lab/addpages/BOL_Contacts.html.

## D. Interpretation of results:

The fact that many people with chronic infection by HBV are asymptomatic and have no evidence of liver disease makes interpretation of laboratory results difficult. The following 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

**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 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 (≤6 months). Its presence indicates acute infection.

**Hepatitis B e 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 e 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**<br>**anti-HBc**<br>**anti-HBs** | Negative<br>Negative<br>Negative | Susceptible |
| **HBsAg**<br>**Anti-HBc**<br>**Anti-HBs** | negative<br>positive<br>positive | Immune due to natural infection |
| **HBsAg**<br>**Anti-HBc**<br>**Anti-HBs** | negative<br>negative<br>positive | Immune due to Hepatitis B vaccination |
| **HBsAg**<br>**anti-HBc**<br>**IgM anti-HBc**<br>**anti-HBs** | positive<br>positive<br>positive<br>negative | Acutely infected |
| **HBsAg**<br>**anti-HBc**<br>**IgM anti-HBc**<br>**anti-HBs** | positive<br>positive<br>negative<br>negative | Chronically infected |
| **HBsAg**<br>**anti-HBc**<br>**anti-HBs** | negative<br>positive<br>negative | Interpretation unclear; four possibilities (below) |

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. Chronic Hepatitis case management

In most populations, investigation of chronic cases of Hepatitis B is not required. Children and young adults with chronic Hepatitis B are unusual and should be investigated as time allows, as this could also be an indication of an acute Hepatitis B infection. A viral Hepatitis Case Report Form is available to guide the investigation and assist in follow-up: http://www.cdc.gov/hepatitis/PDFs/vhsp02.pdf. Hepatitis cases are automatically reported in Merlin. If laboratory results or physician notes indicate a diagnosis of acute Hepatitis B, perinatal Hepatitis B or a positive Hepatitis B surface antigen (HBsAg) in a pregnant woman the disease code will be manually changed and a case investigation will be conducted following the corresponding guidelines.

**B. Merlin data entry**

Create a case in Merlin under disease code **HEPATITIS B**-07032. Enter available data. The Hepatitis B disease code is automatically assigned as chronic and reported in Merlin. Based on the completeness of the laboratory results, the diagnosis status will be set as confirmed, suspect or probable. In the instance of an incomplete case status, the case will automatically be assigned a suspect category until completed information is entered. Once the completed data is entered, the case will automatically be reported. When laboratory results and/or physician diagnosis are received that specifically indicate acute Hepatitis B, 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 chronic 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. Merlin will 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. If a patient is reported with a positive IgM but the CHD believes the infection is actually chronic Hepatitis B, then the IgM positive laboratory report must be unattached from the case to save the report as a chronic case. This type of laboratory report is frequently received on immunosuppressed patients and persons who are 60 years of age and older.

## 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 and 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 healthcare settings.

**C. Management of contacts**

To identify who may be a contact, see Modes of Transmission.
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 3-dose series of Hepatitis B vaccine. If a known exposure has occurred the contact should receive HBIG and begin the 3-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

* 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. Work or childcare restrictions**
No occupational, school, or child care restrictions are necessary for Hepatitis B infected individuals.

**B. 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 between 22%-31% and the risk of developing serological symptoms of an HBV infection is between 37%-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%-6% and the risk of developing serological symptoms of a Hepatitis B infection is between 23%-37%.

**C. 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.doh.state.fl.us/disease_ctrl/epi/surv/Hepatitis_Viral_CRF.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.doh.state.fl.us/disease_ctrl/aids/index.html

**D. Healthcare Investigation Guide**
http://www.cdc.gov/hepatitis/Outbreaks/PDFs/HealthcareInvestigationGuide.pdf

## 9. REFERENCES

**A. American Academy of Pediatrics. (2012). *Red Book: 2012 Report of the Committee on Infectious Diseases* (29th ed.). Grove Village, IL: American Academy of Pediatrics.**

**B. Heymann, D.L. (2008). Control *of Communicable Disease Manual* (19th ed.). Washington DC: American Public Health Association.**

**C. CDC. (2001). MMWR: Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HBV, HCV, and HIV and Recommendations for Postexposure Prophylaxis. June 29, 2001/ 50(RR11);1-42.**