

Hepatitis B



Public Health Branch

1. Case Definition

1.1 Confirmed Case of Acute Infection:

Laboratory confirmation of infection as demonstrated by:

- Hepatitis B surface antigen (HBsAg) positive PLUS immunoglobulin M antibody to hepatitis B core antigen (anti-HBc IgM) positive in the context of a compatible clinical history or probable exposure.
OR
- Loss of HBsAg within a six month period after testing HBsAg positive in the context of a compatible clinical history or probable exposure AND in the absence of recent history of Hepatitis B virus (HBV) vaccination.
OR
- Positive HBV DNA by polymerase chain reaction (PCR) followed by HBsAg and HBV core IgM antibody sero-conversion in the context of a compatible clinical history or probable exposure.

1.2 Confirmed Case of Chronic Infection:

Laboratory confirmation of infection as demonstrated by:

- HBsAg positive for longer than six months, anti-HBc IgM negative and anti-HBc positive
OR
- Detection of HBV DNA over a period greater than six months by a validated nucleic acid amplification test, anti-HBc IgM negative and anti-HBc positive (1).

1.3 Confirmed Unspecified Case:

- HBsAg positive
OR
- Detection of HBV DNA by a validated nucleic acid amplification test
AND

- Does not fit the criteria for either acute or chronic case definitions above (1).

2. Reporting Requirements

2.1 Reporting to Manitoba Health and Other Requirements

Laboratory:

- All positive laboratory results noted in the case definition are reportable to the Manitoba Health, Seniors and Active Living (MHSAL) Public Health Surveillance Unit (204-948-3044 secure fax).

Health Professional:

- Adverse events following immunization should be reported by health professional by completing and returning the form available at:
http://www.gov.mb.ca/health/publichealth/cdc/docs/mhsu_2334_20161115_aefi.pdf .
- Physicians are reminded that they must be in compliance with the CPSM By Law 11, Schedule J (5)
<http://cpsm.mb.ca/cjj39alckF30a/wp-content/uploads/ByLaws/By-Law-11.pdf> to report to the CPSM if they become aware of another physician with a bloodborne pathogen.

Regional Public Health or First Nations Inuit Health Branch (FNIHB):

- Cases are referred to regional Public Health/FNIHB for follow-up. *The Investigation Form for Hepatitis B and C Positive Cases*
http://www.gov.mb.ca/health/publichealth/surveillance/docs/mhsu_6780.pdf should be completed for all clients testing positive (this applies to all cases new to Manitoba) with assistance from the

ordering practitioner, and forwarded to the MHSAL Public Health Surveillance Unit (204-948-3044 secure fax).

2.2 Reporting to Canadian Blood Services:

- If the case has a history of blood transfusion, the MHSAL Public Health Surveillance Unit is required to notify Canadian Blood Services.

3. Clinical Presentation/Natural History

3.1 Acute Infection:

Initial infection with hepatitis B virus (HBV) may be asymptomatic in up to 50 per cent of adults and 90 per cent of children (2). When symptoms occur, they may include anorexia, abdominal pain, nausea, vomiting and jaundice (2). Fever may be absent or mild (3). Extrahepatic manifestations such as arthralgias, arthritis, macular rashes, thrombocytopenia or papular acrodermatitis (Gianotti-Crosti syndrome) can occur early in the course of illness and may precede jaundice (4). Acute illness may last up to three months and has a case fatality rate of one to two per cent, which increases with age (2). Acute HBV infection cannot be distinguished from other forms of acute viral hepatitis on the basis of clinical signs and symptoms or nonspecific laboratory findings (4).

3.2 Chronic Infection:

While the majority of individuals infected with HBV are able to clear the infection after four to eight weeks (2), some individuals fail to mount an adequate immune response, leading to chronic infection (5). Hepatitis B virus infection becomes chronic in 90% to 95% of infants, 25% to 50% of children from one to five years of age, and in 3% to 10% of adolescents and adults (2). The natural history and progression of chronic HBV is complex and non-linear, and varies from person to person (6, 7). Terms have been used to describe

different recognizable phases which are of variable duration and not necessarily sequential (7). If chronic infection is established, the spectrum of illness ranges from the healthy carrier state to all of the sequelae of chronic hepatitis, including mild to moderate fibrosis, compensated cirrhosis, hepatic decompensation and hepatocellular carcinoma (HCC) (8). Factors that may influence the natural history of chronic infection include gender, race, alcohol use, and coinfection with hepatitis A, hepatitis C or hepatitis D viruses (HDV) or human immunodeficiency virus (HIV) (4). Reactivation of resolved chronic infection is possible with immunosuppression (4). Although HCC is more common in the fifth decade of life, HCC occasionally occurs in children who become infected perinatally or in early childhood (4). It is estimated that 15% to 25% of individuals with chronic HBV infection will die prematurely of either cirrhosis or HCC (3, 4). The single most important risk factor for HCC is cirrhosis (8). Antiviral therapy can modify the natural history of chronic HBV infection (9). Acute hepatitis delta virus (HDV) is acquired as a coinfection simultaneously with HBV or as a superinfection in a patient who is already a carrier of HBV (10). Infection with HDV in HBV infected individuals is associated with more severe and/or progressive liver disease than is HBV mono-infection (10).

The natural course of acute hepatitis C virus (HCV) superinfection has not been well studied. The long-term prognosis following acute HCV superinfection is worse than that following HDV superinfection (11).

HIV coinfection increases the risk of liver decompensation, cirrhosis and HCC (10). Individuals coinfecting with the parasite *Schistosoma* (Schistosomiasis, Bilharzia) are more likely to have more severe hepatitis B manifestations and become chronic carriers of HBV (12).

4. Etiology

Hepatitis B virus, belonging to the Hepadnaviridae family, is a small enveloped DNA virus whose partially double-stranded DNA genome is maintained in a circular conformation (2, 3, 4, 13). The nucleocapsid core antigen (HBcAg) is surrounded by an outer lipoprotein coat containing the surface antigen (HBsAg) (4). On the basis of the antibody response to HBsAg, four major subtypes of HBsAg have been recognized and designated adw, ayw, adr and ayr (3). The distribution of the four subtypes varies geographically; however, because of the common “a” antigen, protection against one subtype appears to confer protection against the other subtypes (3). No differences in clinical features have been related to subtype (3).

Worldwide, at least nine genotypes of HBV (A through I) have been identified on the basis of more than 8% difference in their genome sequences (7). Genotypes A and G are common in North America (10). Data suggests that HBV genotype may play a role in the progression from acute to chronic HBV infection (5, 14-16), and treatment outcome of HBV infection (17).

Hepatitis B primarily infects hepatocytes (13). The existence of asymptomatic hepatitis B carriers with normal liver histology and function suggests that the virus is not directly cytopathic (13).

5. Epidemiology

5.1 Reservoir and Source

Humans are the only known reservoir, although chimpanzees are susceptible to human strains (3). Individuals with chronic HBV infection are the main reservoir for infection (4). Other primates such as gibbons, orangutans, African green monkeys and squirrel monkeys have been found positive for HBsAg (13).

5.2 Transmission

The virus is transmitted by parenteral or mucosal exposure to HBsAg-positive body fluids from persons who have acute or chronic HBV infection (18). The highest concentrations of virus are found in blood and serous fluids (18). Transmission of HBV via tears, sweat, urine, stool, or droplet nuclei has not been clearly documented (18). Fecal-oral or vectorborne transmission has not been demonstrated (3, 4). HBV is not transmitted by air, food or water (7).

The highest risk of transmission and of subsequent chronic HBV carriage is in infants exposed during child birth to their mothers who are carriers of HBV (2). Perinatal transmission of HBV is highly efficient, with up to a 90% transmission risk, and usually occurs from blood exposures during labour and delivery (4). Perinatal transmission is the major mode of transmission in high prevalence areas (where the HBV carrier rate > 8 %) (13). The risk of perinatal infection is also increased if the mother has acute HBV in the second or third trimester of pregnancy or within two months of delivery (7). Although HBV can infect the fetus in utero, this appears to be uncommon, and is generally associated with antepartum haemorrhage and placental tears (7).

HBV is efficiently transmitted during heterosexual and male-to-male sex contact (17). Unprotected sex contact and injection drug use are major routes of spread in developed countries such as Canada (13, 19). Percutaneous exposures that could result in HBV transmission include: transfusion of blood or blood products, human bites, sharing needles during injection drug use, hemodialysis, acupuncture, tattooing, body piercing and needlestick or other injuries from sharp instruments sustained by health care personnel (2, 3, 18). The risk of transfusion-related HBV infection is extremely low in Canada and the USA because all blood and blood products are tested (2). Saliva is considered infectious in bite wounds

with broken skin involving the inoculation of saliva, or when it is visibly tainted with blood (2). Other types of exposure to saliva such as kissing are unlikely modes of transmission (18).

Household and community transmission may occur through sharing inanimate objects such as washcloths, towels, razors or toothbrushes (3, 4). Hepatitis B virus can survive for long periods on environmental surfaces (at least 7 days) (4, 13, 18). As such, exposure to even minute amounts of blood or contaminated secretions may transmit the virus (13). Infection can occur in settings of prolonged personal contact, such as that which occurs between children or among residents of institutions for the developmentally disabled (13). Almost one-third of people with HBV infection have no identified risk factors (2).

5.3 Occurrence

5.3.1 General:

Worldwide, an estimated 257 million people are living with hepatitis B virus infection (defined as HBsAg positive) (20). HBV prevalence is highest in the World Health Organization (WHO) Western Pacific Region and the WHO African Region, where 6.2% and 6.1% respectively of the adult population is infected (20). In the WHO Eastern Mediterranean Region, the WHO South-East Asia Region and the WHO European Region, an estimated 3.3%, 2.0% and 1.6% of the general population is infected, respectively (20). In the WHO Region of the Americas, 0.7% of the population is infected (20).

5.3.2 Canada:

Canada is a region of low endemicity; however, certain vulnerable populations are disproportionately affected including Aboriginal peoples, men who have sex with men (MSM), street-involved youth, and people who are or have been incarcerated (6). The majority of new chronic HBV cases are new immigrants from

countries where HBV is endemic. Analysis of acute HBV data reported through the Canadian Notifiable Disease Surveillance System (CNDSS) demonstrates that acute HBV rates decreased from 1.0 to 0.5 per 100,000 between 2005 and 2014 (19). Although there has been an overall increasing pattern in the rate of reported chronic HBV over the years, since 2012, it has declined slightly from 13.6 per 100,000 to 12.0 in 2014 (19). Between 2005 and 2014, chronic HBV rates were consistently higher among males than among females, with the exception of 2007 (19). The rates presented in this report likely underestimate the true burden of infection in Canada as HBV infection is asymptomatic in most individuals, who may not have been tested (19). Furthermore, provinces and territories differ in their capacity to distinguish HBV cases by their infection status (acute vs chronic); as a result, HBV reporting is not uniform across the country and many hepatitis B cases are reported as unspecified i.e. unknown infection status (19).

5.3.3 Manitoba:

In 2016, 276 cases were reported as new to the Public Health Surveillance System at MHSAL. The cases reported included acute, chronic and unspecified cases. The surveillance system captures cases with a positive test result for the hepatitis B surface antigen (HBsAg), and in the majority of cases is unable to distinguish chronic and unspecified cases. In 2016, as in previous years, the majority (82%) of hepatitis B cases reported residence in the Winnipeg Health Region. The highest percentage (29%) of newly reported cases were in the 30-39 year age group, followed by the 40-49 year age group who had 25% of cases reported. The overall rate in Manitoba in 2016 was 20.9 cases per 100,000 population, compared with 15.2 per 100,000 for 2015.

5.4 Incubation:

The incubation period for HBV ranges from 45 to 180 days with an average of 60 to 90 days (3). Hepatitis B surface antigen (HBsAg) may be detected as early as two weeks post-infection. Incubation is dependent upon inoculum size, mode of transmission and host factors (3).

5.5 Risk Factors for Infection:

The most commonly identified risk factors for acute HBV infection in Canada are high-risk sex activities and injection drug use (6). Immunocompromised adults are at particular risk of developing chronic infection (6).

5.6 Period of Communicability:

All persons who are HBsAg positive are potentially infectious (3). When symptoms are present in individuals with acute HBV infection, HBsAg can be found in blood and body fluids for one to two months before and after the onset of symptoms (18). The presence of HBV early antigen (HBeAg) and/or high levels of HBV DNA are also indicators of communicability (3).

6. Diagnosis

NOTE: Where the testing for HBV is being done pursuant to an order issued under the *Testing of Bodily Fluids and Disclosure Act*, refer to the *Integrated Post-Exposure Protocol for HIV, HBV and HCV: Guidelines for Managing Exposures to Blood and Body Fluids* available at: http://www.gov.mb.ca/health/publichealth/cdc/protocol/hiv_postexp.pdf for testing procedure.

Diagnosis of acute or chronic hepatitis B virus infection may sometimes be very difficult. Often one needs a clear history, physical and sequential serological and/or nucleic acid tests to determine this. See “Case Definition” section. Patient history is also important to assist the laboratory in determining testing needs.

6.1 Acute Cases: Diagnosis of acute HBV infection is typically based upon the detection of both HBsAg and anti-HBc IgM. When symptoms are present in individuals with acute HBV infection, HBsAg can be found in blood and body fluids for one to two months before and after the onset of symptoms (18). HBsAg declines, disappears and is followed by the appearance of anti-HBs in acute cases which resolve. Anti-HBc IgM is present in high titer in acute cases and usually disappears within six months. See Table 1 for abbreviations and interpretation of serologic test results.

6.2 Chronic Cases: The diagnosis of chronic HBV infection is based upon the persistence of HBsAg for more than six months. The presence of HBsAg and anti-HBc, in the absence of anti-HBc IgM is also diagnostic of chronic infection. Other markers that may be tested for include HBeAg, anti-HBe and HBV DNA. See Table 1 for abbreviations and interpretation of serologic test results.

6.3 Unspecified Cases: Cases that are HBsAg positive or in which HBV DNA has been detected by a validated nucleic acid amplification test, but which do not fit the acute or chronic case definition, are termed “unspecified”. It is recommended that repeat testing for HBsAg be performed six months after initial testing to determine if chronicity can be documented.

Testing for hepatitis B DNA is not routinely performed except in uncommon circumstances by reference laboratories. Testing for HBV DNA may be used to improve the clarity of diagnosis, to determine candidacy for treatment or to monitor the effectiveness of therapy.

Hepatitis B



Public Health Branch

Table 1: Interpretation of Hepatitis B Virus Test Results

Test	Acute Hepatitis B	Immunity Through Infection	Immunity Through Vaccination	Chronic Hepatitis B
HBsAg*	+	-	-	+
Anti-HBs	-	+	+	-
HBeAg*	+/-	-	-	+/-
Anti-HBe	+/-	+/-	-	+/-
Anti-HBc	+/-	+	-	+
Anti-HBc IgM	+/-	-	-	-
HBV DNA*	+/-	-	-	+

NOTE: While occult HBV infections are believed to occur, the frequency and significance of this finding remains under investigation.

*Patients positive for one or more of HBsAg, HBeAg, and HBV DNA are considered to be infectious (2, 4).

Abbreviation

HBsAg
Anti-HBs
HBeAg
Anti-HBe
Anti-HBc
Anti-HBc IgM
HBV DNA

Marker

hepatitis B surface antigen
antibody to hepatitis B surface antigen
hepatitis B early antigen
antibody to hepatitis B early antigen
antibody to hepatitis B core antigen (total antibody)
IgM antibody to hepatitis B core antigen
hepatitis B virus nucleic acid

7. Key Investigations for Public Health Response

- Immunization history
- Determination of risk factors for acquisition of hepatitis B (e.g., exposure to blood, unprotected sex, injection drug use, recent body tattoos/piercings)
- Residence in endemic geographic region or family history of HBV infection
- Recent blood, semen or tissue donations
- Contact identification to determine source and extent of transmission of infection and to prevent further spread by immunization.

8. Control

For the purposes of this protocol, “Public Health” refers to provincial regional public health authorities as well as First Nations Inuit Health Branch.

8.1 Management of Cases

For the purposes of case and contact management, unspecified cases should be managed as acute cases unless and until further testing indicates that they fit the case definition for chronic infection.

- Any patient with hepatitis B infection believed to have been acquired through sexual transmission should be considered at high risk for other sexually transmitted infections (STIs),

including HIV, and should be offered testing. Human papillomavirus (HPV) vaccine should be discussed as per recommendations in the most current National Advisory Committee on Immunization (NACI) Statement on HPV <http://www.phac-aspc.gc.ca/naci-ccni/>.

- Any patient with hepatitis B virus infection should be considered at risk for other bloodborne pathogens (i.e., HIV and HCV) and should always be offered testing for them.

8.1.1 Management of Acute Cases

- Acute HBV does not require antiviral treatment (6). Management should focus on relief of symptoms, monitoring and prevention of hepatic complications, as well as counselling aimed at preventing transmission (6).
- Routine Practices in health care as per Manitoba Health, Seniors and Active Living's *Routine Practices and Additional Precautions: Preventing the Transmission of Infection in Health Care* available at: <http://www.gov.mb.ca/health/publichealth/cdc/docs/ipc/rpap.pdf>.
- Public Health will contact cases to advise on follow-up testing and for contact identification and follow-up. Contacts include all sex, household as well as needle, razor or toothbrush-sharing contacts within the six months prior to the symptom onset date of the cases (2, 4, 6). See "Management of Contacts" below.
- Acute cases should be tested for both HBsAg and anti-HBsAg six months after initial detection of HBsAg, to assess whether chronicity has developed and to determine the need

for ongoing precautions. See "Education of Acute and Chronic Cases to Prevent Transmission" below.

8.1.2 Management of Chronic Cases

- All patients diagnosed with chronic hepatitis B should be referred to a clinician with expertise in viral hepatitis or to the Viral Hepatitis Investigative Unit (fax: 204-789-3987) for evaluation, treatment if indicated, and other advice relevant to their care.
- The goal of monitoring chronic HBV is to prevent progression to cirrhosis, HCC, and liver decompensation (6).
- Treatment may be indicated for individuals presenting with chronic hepatitis B whether HBeAg positive or HBeAg negative.
- Routine Practices in health care as per Manitoba Health, Seniors and Active Living's *Routine Practices and Additional Precautions: Preventing the Transmission of Infection in Health Care* available at: <http://www.gov.mb.ca/health/publichealth/cdc/docs/ipc/rpap.pdf>.
- Public Health will contact cases to identify and arrange for follow-up of contacts. Contacts include all sex, household as well as needle, razor or toothbrush-sharing contacts within the six months prior to the symptom onset date of the cases (2, 4, 6). This timeframe should be extended further back if contact was frequent and after infection developed (when this can be estimated). See "Management of Contacts" below.
- Immunization against hepatitis A should be offered if the patient is not already immune (6).

- See “Education of Acute and Chronic Cases to Prevent Transmission” below.

8.1.3 Special Considerations for Management of Pregnant Women

- Some women will first receive the diagnosis of HBV as part of routine prenatal screening.
- Newly diagnosed pregnant women should be counselled on risk and prevention of transmission to household and sexual contacts.
- Consultation with a clinician with expertise in viral hepatitis or the Viral Hepatitis Investigative Unit (204-787-3630) and/or the Reproductive Infectious Diseases Clinic (204-787-1961) is recommended. Referral should be expedited if there is clinical evidence of chronic liver disease, abnormal ALT, detectable HBV DNA or evidence of cirrhosis and/or portal hypertension on ultrasound.
- Pregnant women or women who wish to become pregnant and who have hepatitis B infection should be counselled on the risk of transmission to the newborn. Methods to prevent vertical transmission (i.e. hepatitis B immune globulin and HBV vaccine for the infant) should be discussed with pregnant women as well as the expected failure rates of these prophylactic measures (up to 2% risk). Both risk of transmission and expected failure of prophylaxis are correlated to characteristics of maternal disease with high HBV DNA viral loads and maternal HBeAg being important clinical risk factors for perinatal transmission.
- Quantitative measurement of HBV DNA viral load is appropriate in the third trimester of pregnancy (around 28 weeks gestational age). Treatment for viral suppression is considered in women during the third trimester if their HBV viral loads are higher than 200,000 IU/mL or $>10^6$ copies, especially if previous children were born with HBV.
- Pregnant women with acute HBV infection should be retested one month prior to expected date of delivery to determine HBV status. If the pregnant woman is still positive, follow immunization procedures detailed under “Neonatal Contacts” below at the time of delivery.
- There is no evidence that caesarean section prevents maternal-infant transmission, and thus routine caesarean section is not recommended for this indication (13).
- All neonates born to women who are HBsAg-positive should be vaccinated against hepatitis B and receive hepatitis B immune globulin during the first 12h of life. Completion of the HBV vaccine series should be encouraged.
- Breastfeeding of the infant by an HBsAg-positive mother poses no additional risk of acquisition of HBV infection when the infant has received appropriate administration of hepatitis B vaccine and HBIG (4).
- The post-partum period is a high-risk time for hepatitis flares, especially if a patient has discontinued treatment during pregnancy or post-partum. These flares are more common in women who are HBeAg-positive. Given that some flares are only mildly

symptomatic, clinicians should have a low threshold to order liver enzymes in the post-partum period.

- Pregnancy and post-partum is a time in which women access the healthcare system more frequently. It is an ideal opportunity for health care providers to ensure that women infected with HBV have adequate follow-up for viral hepatitis prior to discharge from obstetrical care.

8.1.4 Education of Acute and Chronic Cases to Prevent Transmission

Cases should be educated about how hepatitis B virus is spread and how to limit/prevent transmission to others through the following actions.

- Inform health care providers (e.g., physicians, nurses, dentists) and other providers of personal services with piercing of the skin (e.g., acupuncturist, tattooist) of your infection (6).
- Do not donate blood, organs, semen or tissues (6).
- Do not share personal hygiene materials/sharp instruments (e.g., razors, nail clippers, toothbrushes, glucometers) (6).
- Safely dispose of articles contaminated with blood (e.g., feminine hygiene products, dental floss, bandages, needles, broken glass) (6).
- Cover all cuts and sores (6).
- Clean up blood spills with freshly made diluted household bleach (9 parts water to 1 part bleach). Leave the solution on the surface for 10 minutes before wiping it away. Persons who clean up blood spills should wear protective gloves and wash their hands thoroughly after removing them (6).
- Use condoms with all sex partners until testing shows the case is no longer infectious, or the partner is immune (6).
- Do not share any equipment used to prepare, inject, or inhale drugs (e.g., syringes/needles, spoons, drug solutions, water, wash filters, cookers, pipes, straws, devices for snorting drugs) (6).

8.2 Management of Contacts:

For management of neonatal contacts see “Neonatal Contacts” below.

A risk assessment should be done to inform the contact management plan. The regional Medical Officer of Health may be consulted for assistance.

Contacts of cases are: all sex, household as well as needle, razor or toothbrush-sharing contacts within the six months prior to the symptom onset date of the cases.

Refer to the *Integrated Post-Exposure Protocol for HIV, HBV and HCV: Guidelines for Managing Exposures to Blood and Body Fluids* available at: http://www.gov.mb.ca/health/publichealth/cdc/protocol/hiv_postexp.pdf for complicated exposure to blood and body fluids situations that are not covered in this protocol (e.g., motor vehicle accidents, occupational needlestick injuries).

Contacts who are immunocompromised or have chronic diseases may require a higher vaccine dose and/or booster doses (2). Refer to the current *Canadian Immunization Guide*. To ensure appropriate care, consult a specialist physician.

Public Health will attempt to locate contacts of cases and inform them of the potential risk of acquiring infection and the need for immunization of non-immune contacts. For sex partners, barrier methods such as condoms should be used until immunization is administered and adequate anti-HBs demonstrated (21).

- Contacts should be identified and interviewed as soon as possible to support early initiation and maximize efficacy of immunoprophylaxis. The *Notification of Sexually-Transmitted and Blood-Borne Infections* form http://www.gov.mb.ca/health/publichealth/surveillance/docs/mhsu_6782.pdf may be used to assist with contacts of hepatitis B cases.
- When the case is asymptomatic, the date of onset is the date testing was done.
- **Pre-immunization screening of all contacts:** Contacts should be tested for hepatitis B infection (HBsAg) and susceptibility or immunity (anti-HBs). The blood specimen for pre-immunization screening should be drawn before the administration of hepatitis B vaccine and hepatitis B immune globulin (HBIG) to prevent the immunization(s) from interfering with testing results. The requisition should be marked “Urgent” or “STAT” if there is immediacy attached to the test results. If after hours processing is required, consultation with the on-call CPL physician is recommended. See Table 2 below for follow-up.
- **Immunoprophylaxis:** Contacts should be offered the first dose of hepatitis B vaccine immediately after blood has been drawn for testing. See “Acquisition and Administration of HBV Vaccine and HBIG.” If indicated (i.e., HBsAg negative and anti-HBs negative), second and third doses of vaccine should be given one and six months after the first dose to complete the immunization series (2).
 - **For contacts of acute hepatitis B cases:** The following groups should be offered hepatitis B immune globulin (HBIG) in addition to hepatitis B vaccine (2, 21).
 - All sex contacts within the last 14 days
 - All needle/toothbrush/razor-sharing contacts within the last seven days
 - All sex and needle/toothbrush/razor-sharing contacts, regardless of the interval since last exposure, if there is any chance of future, similar exposures to the case.
 - With the exception of infants born to a HBV-infected mother, HBIG is not indicated for household contacts of acute or chronic HBsAg carriers not already discussed immediately above (2).
 - HBIG may be considered for children younger than 12 months of age who have close contact with a primary caregiver with acute or chronic HBV if the child has received less than two doses of HBV vaccine (4).
 - **For contacts of chronic hepatitis B cases:** HBIG (in addition to provision of vaccine) should be considered if sex or needle/razor/toothbrush sharing contact occurred for the first time in the previous 14 days. See section below “Acquisition and Administration of HBV Vaccine and HBIG” for indications and clinical use information.

NOTE: Vaccine and HBIG may be given at the same time but at different injection sites using separate needles and syringes.

- Post-immunization testing** for anti-HBs should be undertaken one to six months after completion of the vaccine series as recommended by the current *Canadian Immunization Guide*. In individuals who received HBIG in addition to the vaccine, determination of anti-HBs titre should be delayed for six months after completion of the vaccine series (2). Individuals who do not develop anti-HBs titre of at least 10 IU/L after the initial HBV vaccine series should receive a second HBV vaccine series (2). Additional vaccine doses (up to three) received in a second immunization series will produce a protective antibody response in 50% to 70% of healthy adults and children who did not respond to the initial vaccine series (2). Individuals who fail to respond to three additional doses of vaccine are unlikely to benefit from further immunization and should be counselled on alternative risk reduction measures (2).

Table 2: Recommended Follow-up of Contacts Based on Pre-immunization Serological Test Results

Antibody to HBs Antigen Result	HBs Antigen Result	
	HBsAg Positive	HBsAg Negative
Anti-HBs Positive	Rare inconsistent finding: Call CPL for clarification and possible repeat testing.	Individual is immune. No further HBV immunization is required.
Anti-HBs Negative	Individual is infected. See “Management of Cases”. Discontinue immunization if already started.	Individual is susceptible. Complete HBV immunization series. Administer HBIG in the indicated groups detailed above.

8.2.1 Neonatal Contacts

Infants Born to HBsAg Positive Mothers:

All infants born to HBV-infected mothers should be given a dose of monovalent hepatitis B pediatric vaccine within 12 hours of birth and an intramuscular dose of HBIG as soon as possible, preferably within 12 hours after birth (2). Although the efficacy of HBIG decreases significantly after 48 hours, it may be given up to seven days after birth (2). Vaccine and HBIG may be given at the same time but at different injection sites, using separate needles and syringes (2).

- For term infants, the second and third doses of the HBV vaccine series should be given at one and six months of age. Other hepatitis B virus containing vaccines (instead of the monovalent vaccine) can be used for the sixth month vaccine dose. See section below “Acquisition and Administration of HBV Vaccine and HBIG” for indications and clinical use information.
- Health care providers should complete the *Hepatitis B-Prophylaxis Record Sheet for Infants* http://www.gov.mb.ca/health/publichealth/cdc/protocol/hepb_infantrecord.pdf at the time of prophylaxis and enter the immunization data (HBIG and HBV vaccine) directly into Panorama, the Manitoba immunization registry. Where direct data entry or submission of the tariff code(s) through claims is not possible, immunization providers are to complete the *Immunization Inputting Form for Health Care Providers* <http://www.gov.mb.ca/health/publichealth/cdc/div/docs/iifhcb.pdf>. These forms should be returned along with the infant’s post-partum referral to the regional public health office of the parent/guardian’s

region of residence for **appropriate public health follow-up including:**

- Generating follow-up form letters (to be signed by Regional Medical Officer of Health or designate or First Nations Inuit Health) to the infant's physician/practitioner and parent/guardian. The follow-up letters will advise that two additional doses of HBV vaccine should be given at one and six months following the first dose.
- Ensuring a plan is in place for completion of the HBV vaccine immunization series and post-immunization testing (i.e., notifying the patient/guardian and the infant's physician/practitioner by letter of what needs to be done). Immunizations should be entered into Panorama (by either direct entry or through submission of claims by the infant's physician/practitioner), once the infant's Personal Health Information Number (PHIN) is assigned. If a provider does not have direct access to the immunization registry or claims, complete and submit to the local public health office as soon as possible the *Immunization Inputting Form for Health Care Providers* <http://www.gov.mb.ca/health/publichealth/cdc/div/docs/iifhpc.pdf>.
- **Post-immunization Testing:** Infants born to HBV-infected mothers should not be tested for anti-HBs prior to nine months of age, to avoid detection of passive anti-HBs from HBIG administered at birth and maximize the likelihood of detecting late HBV infection (2). Testing should be

conducted at least one month and no more than four months after the last dose of vaccine is administered (2). If HBsAg is present, the child will likely become a chronic carrier (refer to "Management of Chronic Cases") (2). If the infant is a vaccine non-responder (negative for both HBsAg and anti-HBs), additional doses of vaccine should be given with repeated serologic testing for antibody response (2), after each dose. Additional vaccine doses (up to three) received in a second immunization series will produce a protective antibody response in 50% to 70% of healthy adults and children who did not initially respond to the vaccine (2). Individuals who fail to respond to three additional doses of vaccine are unlikely to benefit from further immunization (2).

Pre-term Infants Born to HBsAg-Positive Mothers:

- Pre-term infants (less than 37 weeks gestation) weighing 2,000 grams or more at birth require three doses of hepatitis B pediatric vaccine as described above under *Infants Born to HBsAg Positive Mothers*.
- The response to hepatitis B vaccine may be diminished in pre-term infants weighing less than 2,000 grams at birth (2). Therefore, these infants require four doses of hepatitis B pediatric vaccine, given at **birth**, and at **one, two** and **six** months of age (2). Monovalent hepatitis B vaccine should be given for the doses at birth and one month. Other hepatitis B virus containing vaccines (instead of the monovalent vaccine) can be used for the two month and six month vaccine doses.
- Refer to "Post-immunization Testing" above for post-immunization testing.

Unscreened Mother About to Deliver:

- Pregnant women whose hepatitis B status is unknown at time of labour/delivery should undergo blood (HBsAg) testing as soon as possible and preferably before delivery to determine their infection status (call Cadham Provincial Laboratory at 204-945-6123 to arrange).
- While awaiting test results, the infant should receive HBIG and the first dose of hepatitis B pediatric vaccine (0.5 mL) within 12 hours of birth (as described above under *Infants Born to HBsAg-Positive Mothers*).
- If the mother is found to have hepatitis B infection (i.e., HBsAg-positive), the hepatitis B pediatric vaccine series should be completed in the infant and post-immunization testing performed as described above under *Infants Born to HBsAg-Positive Mothers*. If the mother tests negative subsequent to initiation of immunoprophylaxis, completion of the hepatitis B vaccination series in the infant is still recommended; however, post-immunization testing of the infant is not necessary.

Other HBsAg-Positive Household Members:

- If a household member of the infant's family other than the mother is HBsAg-positive, hepatitis B pediatric vaccine (0.5 mL) should be administered to the infant as described above under *Infants Born to HBsAg-Positive Mothers*. HBIG is not indicated. See section below "Acquisition and Administration of HBV Vaccine and HBIG."

Mother's Infection Recognized During the First Year of the Infant's Life:

- The infant's HBV status should be assessed urgently and the infant started

immediately on the full immunoprophylaxis with hepatitis B vaccine and HBIG as described under *Infants Born to HBsAg-Positive Mothers*. Immunoprophylaxis should be completed if the infant is found not to be already infected or immune (2).

8.3 Acquisition and Administration of HBV Vaccine and HBIG

During Regular Business Hours:

Sites authorized to stock adult and pediatric formulations of HBIG and hepatitis B vaccines include hospitals and some health centres outside Winnipeg. Specific formulations may or may not be stocked at these sites. If HBIG and HBV vaccine are not available at a particular site, contact the Provincial Vaccine Warehouse at 204-948-1333 or Toll-free 1-855-683-3306. A current Biologics Vaccine Order Form is available at <http://www.gov.mb.ca/health/publichealth/cdc/protocol/vaccinebiologics.pdf>. HBIG and HBV vaccine can be released to a hospital, Public Health Unit or physician. HBIG and HBV vaccine can also be released to a health care professional who is registered or licensed to provide health care under an Act of the Legislature and who is authorized under that Act to administer vaccines. Assistance in determining the need for HBIG and HBV vaccine can be obtained from the local Medical Officer of Health (MOH). Contact information is available at: <http://www.gov.mb.ca/health/publichealth/contactlist.html>.

After Hours:

For sites providing health care after regular warehouse hours, the on-call warehouse staff may be contacted at 204-805-4096. After regular hours, the Medical Officer of Health on call (204-788-8666) or Infectious Diseases on call (204-787-2071) may order HBIG and HBV vaccine.

Immunization providers should consult the respective product monograph prior to administering HBIG and HBV vaccine for information such as storage and handling requirements, administration schedule, injection site, dose specific to age and weight (for HBIG) etc. to ensure appropriate use.

NOTE: Vaccine and HBIG may be given at the same time but at different injection sites using separate needles and syringes (2).

- **HBIG:**
 - Administration is intramuscular (anterolateral thigh muscle of infants; deltoid muscle of children and adults) (2).
 - The standard HBIG dose for newborns and children up to 8.3 kg is 0.5 mL; the dose for children over 8.3 kg and adults is 0.06 mL/kg.
- **HBV Vaccine:**
 - Administration is intramuscular (anterolateral thigh muscle of infants; deltoid muscle of children and adults) (2).
 - There are various vaccine schedules, formats, strengths.
 - Infants born to HBV-positive (or suspected to be positive) mothers should receive 0.5 mL of the pediatric formulation for each dose.
 - Preferred schedule: second and third doses of HBV vaccine should be administered one and six months after the start of the immunization series unless otherwise indicated (e.g., serologic testing demonstrates HBsAg positivity).

8.4 Management of Outbreaks:

- A thorough investigation should be undertaken to determine source and institute preventive measures if possible.
- Consider mass immunization in situations where control of transmission is likely to be difficult (e.g., correctional facilities).

8.5 Preventive Measures:

8.5.1 Screening

- Prenatal screening is strongly recommended for all women for each pregnancy, even if they were HBsAg positive in the past, so that newborns can receive prophylaxis if necessary (2). Practitioners are requested to tick-off the “prenatal” box on the Cadham Provincial Laboratory (CPL) requisition.
- Women with ongoing risk factors for HBV infection during pregnancy should be re-screened in the third trimester even if their initial prenatal screening was HBsAg-negative.
- Screening of blood donors and individuals at high risk of infection, including but not limited to: individuals entering a health care profession, persons or adopted children from countries or family situations in which there is a high prevalence of infection, persons who have been institutionalized (e.g., incarcerated), persons on dialysis, men who have sex with men, bisexual males and heterosexual males or females with multiple sex partners or with a recent history of sexually transmitted infection, injection drug users and those with a hepatitis B carrier in the household (2, 4, 6).

8.5.2 Immunization

- Universal pre-exposure immunization programs as well as ongoing immunization of populations at increased

risk. Please see eligibility criteria for provision of publicly funded vaccine on the Communicable Disease Control Branch web site at:

<http://www.gov.mb.ca/health/publichealth/cdc/vaccineeligibility.html> .

- Please refer to the most recent edition of the *Canadian Immunization Guide* for indications and clinical use information.
- Pregnant women who are unvaccinated and have ongoing risk factors for HBV infection should be offered the HBV vaccine during pregnancy as pregnancy is NOT a contraindication to HBV vaccination.

8.5.3 Contact Investigation and Follow-up

Appropriate identification and follow-up of:

- Contacts of acute and chronic cases
- Perinatal contacts
- Individuals who have sustained an exposure to blood and body fluids (e.g., needlestick injury in a health care worker) and are deemed at risk of acquiring infection. Refer to the *Integrated Post-Exposure Protocol for HIV, HBV and HCV: Guidelines for Managing Exposures to Blood and Body Fluids* available at: http://www.gov.mb.ca/health/publichealth/cdc/protocol/hiv_postexp.pdf .

8.5.4 Post-immunization Testing

- For individuals who may respond sub-optimally to hepatitis B vaccine (e.g., immunocompromised);
- For high risk pregnant women who are immunized before or during pregnancy;
- For individuals at high risk of exposure or re-exposure to HBV-infected individuals which may include the following:
 - Infants born to HBV-infected mothers after completion of the primary vaccine series;

- Sexual partners and household contacts of acute cases and chronic carriers of hepatitis;
- Patients on dialysis; and
- Those who have been immunized because of risk of occupational exposure or percutaneous or mucosal exposure to hepatitis B (2, 4).

8.5.5 Health Care Precautions

- Routine Practices including the safe disposal of sharps.
- Adequate sterilization of instruments used in invasive procedures, including personal care services (e.g., piercing, tattooing).
- Avoidance of personal services that penetrate the skin (e.g., piercing, tattooing).
- Single-use, disposable syringes and needles (including acupuncture needles), and lancets for finger puncture (3).
- Appropriate disinfection measures following body fluid spills.
- Restricting the performing of exposure-prone procedures for medical and dental personnel who are infected with HBV, unless they have sought counsel from an expert review panel and have been advised under what circumstances, if any, they may continue to perform these procedures (3, 22, 23).

8.5.6 Harm Reduction Activities

- The risk of HBV transmission through injection drug use (IDU) can be significantly reduced by use of a new needle, syringe, and all other IDU equipment (e.g., filters, water, spoon) for each injection.
- Harm reduction activities such as safe injection practices may help to reduce

HBV transmission within injection drug using populations.

9. Additional Resources

9.1 Canadian Liver Foundation

<http://www.liver.ca/>

9.2 Canadian Association for the Study of the Liver

<http://www.hepatology.ca/>

9.3 *Cadham Provincial Laboratory Guide to Services*

<http://www.gov.mb.ca/health/publichealth/cpl/docs/guide.pdf>

10. References

1. Public Health Agency of Canada. Case Definitions for Communicable Diseases under National Surveillance. *Canada Communicable Disease Report CCDR* 2009; 35S2: 1-123.

2. Government of Canada. Page 7: *Canadian Immunization Guide: Part 4 – Active Vaccines – Hepatitis B Vaccine*. Updated March 2017.

Available at: <https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-7-hepatitis-b-vaccine.html>

3. Heymann David L. Hepatitis B (type B hepatitis, serum hepatitis, homologous serum jaundice, Australia antigen hepatitis, HB). In: *Control of Communicable Diseases Manual 20th ed*, American Public Health Association, Washington, 2014; 257-264.

4. American Academy of Pediatrics. Hepatitis B. In Pickering LK ed. *Redbook: 2012 Report of the Committee on Infectious Diseases 29th ed*. Elk Grove Village, IL: American Academy of Pediatrics, 2012; 369-390.

5. Conly JM and Johnston BL. Treatment options for hepatitis B. *Can J Infect Dis Med Microbiol* 2007; 18 (3): 173-176.

6. Public Health Agency of Canada. Primary Care Management of Hepatitis B – Quick Reference

(HBV – QR) 2014. Available at:

<http://www.phac-aspc.gc.ca/publicat/hep/hbv-vhb/index-eng.php>

7. World Health Organization. Guidelines for the Prevention, Care and Treatment of Persons with Chronic Hepatitis B Infection, March 2015.

http://apps.who.int/iris/bitstream/10665/154590/1/9789241549059_eng.pdf .

8. Pungapong S, Kim WR and Poterucha JJ. Natural History of Hepatitis B Virus Infection: An Update for Clinicians. *Mayo Clin Proc* 2007; 82(8): 967-975.

9. Yim HJ and Lok AS. Natural History of Chronic Hepatitis B Virus Infection: What We Knew in 1981 and What We Know in 2005. *Hepatology* 2006; 43(2) Suppl.1; S173-S181.

10. Coffin CS, Fung SK and Ma MM. Management of chronic hepatitis B: Canadian Association for the Study of the Liver consensus guidelines. *Can J Gastroenterol* 2012; 26 (12): 917-938.

11. Liaw Y, Chen Y, Sheen I et al. Impact of Acute Hepatitis C Virus Superinfection in Patients with Chronic Hepatitis B Virus Infection. *Gastroenterology* 2004; 126: 1024-1029.

12. Abruzzi A, Fried B and Alikhan SB. Chapter Three – Coinfection of *Schistosoma* Species with Hepatitis B or Hepatitis C Viruses. *Advances in Parasitology* 2016; 91: 111-231.

13. Thio CL and Hawkins C. Hepatitis B Virus and Hepatitis Delta Virus. In: Mandell, Douglas and Bennett's *Principles and Practice of Infectious Diseases 8th ed*. Elsevier, Philadelphia, 2015.

14. Lok AS and McMahon BJ. American Association for the Study of Liver Diseases Chronic Hepatitis B Practice Guidelines. *Hepatology* 2007; 45(2): 507-539.

15. Fung SK and Lok AS. Hepatitis B Virus Genotypes: Do they play a role in the outcome of infection? *Hepatology* 2004; 40(4): 790-792.
16. Chen C, Lee C, Lu S et al. Clinical Significance of Hepatitis B Virus (HBV) Genotype and Precore and Core Promoter Mutations Affecting HBV e Antigen Expression in Taiwan. *Journal of Clinical Microbiology* 2005; 43 (12): 6000-6006.
17. Van Damme P, Ward J, Shouval D et al. Hepatitis B vaccines In: Plotkin SA, Orenstein WA, Offit PA, eds. *Vaccines Sixth Edition*. China: Elsevier Saunders Inc. 2013: 205-234.
18. Centers for Disease Control and Prevention. Chapter 9 – *Hepatitis B*. *Epidemiology and Prevention of Vaccine-Preventable Diseases, The Pink Book: Updated 13th Edition* 2015: 149-174.
19. Public Health Agency of Canada. Report on Hepatitis B and C in Canada: 2014. <https://www.canada.ca/en/services/health/publications/diseases-conditions/report-hepatitis-b-c-canada-2014.html>
20. World Health Organization. Hepatitis B Fact Sheet Updated April 2017. <http://www.who.int/mediacentre/factsheets/fs204/en/>
21. Centers for Disease Control and Prevention. 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 II: Immunization of Adults. *MMWR Morb Mortal Wkly Rep* 2006; 55 (RR-16): 1-33.
22. Public Health Agency of Canada. Proceedings of the Consensus Conference on Infected Health Care Workers: Risk for Transmission of Bloodborne Pathogens. *Canada Communicable Disease Report* 1998; 24 S4: 1-32.
23. Centers for Disease Control and Prevention. Updated CDC Recommendations for the Management of Hepatitis B Virus-Infected Health-Care Providers and Students. *MMWR Morb Mortal Wkly Rep* 2012; RR-61(3): 1-12.