Hepatitis B Virus Infections

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HEPATITIS B VIRUS INFECTIONS

Etiology

- Hepatitis B is a viral disease characterized by infection of the liver by the hepatitis B virus (HBV), a small DNA virus of the family Hepadnaviridae. The virus occurs worldwide, with greatest prevalence in the developing world.

Epidemiology

- Most common cause of sexually transmitted hepatitis.
- Incubation period ranges from days after percutaneous exposure to 4–8 weeks after mucous membrane exposure.
- Incidence of acute hepatitis B in Canada is estimated to be 2.3 per 100,000.[1]
  - Incidence of acute hepatitis B in men is twice as high as in women (3.0/100,000 vs. 1.5/100,000, respectively).
  - Peak incidence rates are found in those aged 30–39 (6.1/100,000).
- Prevalence of hepatitis B in Canada is estimated to be 0.5–1.0%.[2]
- Prevalence of chronic hepatitis B varies in different populations:
  - Immigrants: 7.4%[3]
  - Inuit: 6.9%[4]
  - First Nations: 0.3%[5]
  - Sexually transmitted infection (STI) clinic patients: 0.3%[6]
- Routes of transmission:
  - Percutaneous, principally injection drug users.
  - Sexual: anal > vaginal > oral.
  - Horizontal: household contacts.
  - Vertical: mother to neonate.
- Risk factors for acquisition:[7]
  - Injection drug use (IDU): 34%
  - Multiple heterosexual sex partners: 24%
  - Men who have sex with men (MSM): 7.3%
  - Sex with HBV-infected individuals: 12%
  - Hepatitis B carrier in family: 2.4%
- Prior to donor screening, blood and blood products were important sources of infection in Canada and may still be in countries where the quality of the blood supply is questionable.
- Populations at the highest risk include the following:
  - Infants born to hepatitis B surface antigen (HBsAg)-positive mothers.
  - Injection drug users who share drug injection/preparation equipment.
  - Those with multiple sex partners.
  - Those born in or having sexual contact in areas of high endemicity.
  - Sexual and household contacts of an acute case or chronic carrier.
  - Health care workers and others with occupational blood exposure.
  - Those who are incarcerated or institutionalized.
  - Those infected with HIV or hepatitis C virus (HCV).
  - Those with a previous STI.

Prevention

Primary prevention

- Counselling/education regarding risk behaviours.
- Harm-reduction strategies (needle exchanges, etc.).
- **Hepatitis B vaccination (pre-exposure prophylaxis).**
  - A school-based universal hepatitis B immunization program aimed at children aged 9–13 was implemented in all provinces and territories in the early 1990s.
  - An infant universal hepatitis B vaccination program is run in some provinces and territories, in addition to the school-based preadolescent immunization program.

  - **Hepatitis B immunization should be routinely offered to the following risk groups (if not previously immunized)**:[8]
    - Children from HBV-endemic areas who may be exposed to HBV via extended family or the community.
    - Populations or communities in which HBV is highly endemic.
    - Residents and staff of institutions for the mentally or developmentally challenged.
    - Sex workers.
    - Hemodialysis patients.
    - People with hemophilia and others receiving repeated infusions of blood or blood products.
    - Household and sexual contacts of acute HBV cases and HBV carriers.
    - Pregnant women.
    - Injection drug users.
    - Staff and inmates of correctional facilities.
    - Travellers to HBV-endemic areas.
    - Those who have recently acquired an STI.
    - Those whose regular sex partner is HBsAg-positive.
    - Those with multiple sex partners.
    - MSM.
    - Those with occupational risk (e.g., health care workers and emergency service workers who may be exposed to blood, blood products or body fluids that may contain the virus).
    - Children in childcare settings in which there is an HBV-infected child.
    - People who are HIV-positive.
    - Sexual partners of any of those listed above.

  - Offer hepatitis B vaccine to all those in the above categories who do not show evidence of immunity *[A-I]* or do not have proof of immunization, and refer those showing evidence of chronic hepatitis B carriage for consideration for treatment with available agents *[A-I]*.[9,10] Some authorities suggest that preimmunization screening is not cost-effective in low-risk populations, particularly adolescents, and recommend immunization without screening tests;[11] with each passing year after the initiation of universal school-based immunization, screening will become increasingly cost-effective as the proportion of those not immunized diminishes.

Secondary prevention (post-exposure prophylaxis)

- Hepatitis B immune globulin (HBIG) can be given to recipients of percutaneous (needlestick) or mucosal exposure up to 7 days after exposure and to sexual contacts within 14 days of exposure (ideally within 48 hours), followed by hepatitis B vaccine.[8]
- **For infants born to HBV-infected mothers, the first dose of hepatitis B vaccine should be administered within 12 hours of birth and HBIG immediately after birth (efficacy decreases sharply after 48 hours).**[8]
- See Figure 1 for an algorithm on the approach to a sexual (penile-anal, penile-vaginal or oral-genital) or percutaneous/mucosal exposure to a known hepatitis B carrier or a high-risk source.
- **Postimmunization screening for the antibody to hepatitis B surface antigen (anti-HBs) is generally not recommended, except for the following**[8]:
  - Infants born to infected mothers.
  - Sexual partners and household contacts of chronic carriers.
  - Those immunized for occupational exposure.
  - Those who are immunocompromised (i.e., lose their response).
  - Hemodialysis patients.
  - Pregnant women.

Manifestations and Diagnosis

- Although HBV is hepatotropic and the liver is the sole site of infection, viremia may lead to clinical manifestations related to immune complex formation.
- All patients being assessed for STIs should be asked about their vaccination history, risk history, previous icteric illness and previous hepatitis testing.
- Acute hepatitis B infection is often not clinically apparent, with 50–70% of adult cases being asymptomatic. Symptomatic cases may be non-specific (fatigue, nausea, vomiting, anorexia, rash, arthralgia). A smaller proportion of cases are icteric; these can be clinically indistinguishable from other viral or toxic causes of hepatitis.
- Chronic hepatitis B can be detected by persistence of HBsAg, may or may not be associated with elevations in hepatic transaminases and is generally asymptomatic until clinical signs of cirrhosis, portal hypertension or hepatocellular carcinoma supervene.
- Hepatitis serologic testing can be done for a number of potential indications:
  - To diagnose acute infection in symptomatic persons.
  - To detect chronic infection in asymptomatic persons.
  - As a preimmunization screen to identify non-immune persons who may benefit from hepatitis B vaccination.
- See Table 1 for serologic markers for hepatitis B.

Table 1. Serologic markers for hepatitis B

Stage	HBsAg	HBeAg	Anti-HBc IgM	Anti-HBc IgG/total	Hepatitis B viral DNA	Anti HBs
Acute (early)	+	+	+	+	+	–
Acute (resolving)	+	–	+	+	–	–
Chronic	+	+/–	–	+	+/–	–
Resolved	–	–	–	+	–	+/–*
Vaccinated	–	–	–	–	–	+*

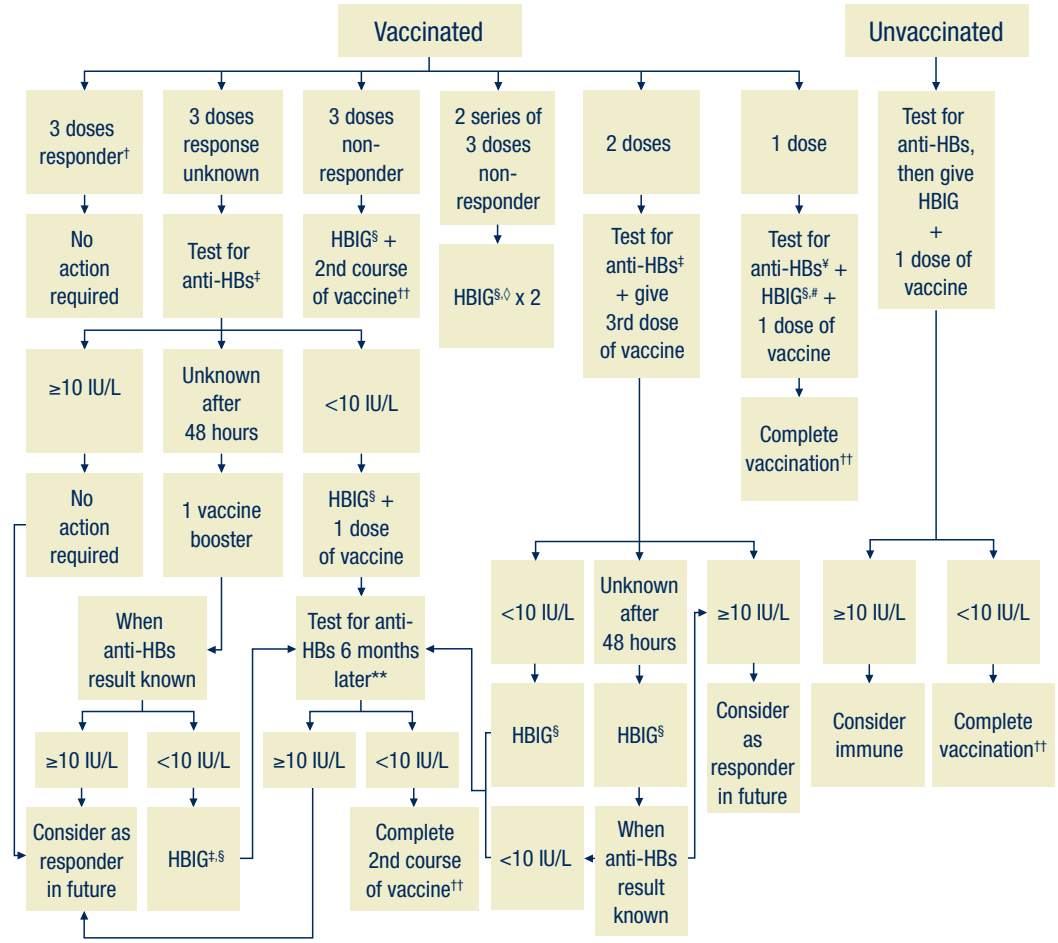
anti-HBc= antibody to hepatitis B core antigen
anti-HBs=antibody to hepatitis B surface antigen
HBeAg=hepatitis B early antigen
HBsAg=hepatitis B surface antigen
*In some patients, anti-HBs may decline over time and become undetectable.

- The choice of serologic testing for suspected acute or chronic cases is determined by the clinical situation and should be supplemented by the addition of liver function testing and hepatic transaminases. For those who are HBsAg-positive, who may be in the window period before development of anti-HBs and anti-HBc antibodies, a positive anti-HBc IgM confirms that this is due to early infection.
- There is controversy surrounding the need to prescreen high-risk individuals before vaccination, as well as the optimal choice of serologic tests for screening. For those at high risk and for whom follow-up cannot be ensured, it is prudent to give the first dose of vaccine on the initial visit after drawing blood for screening serology.
- Evaluating the status of a high-risk person should not delay immunization.

Management

Figure 1. Management of sexual/percutaneous/mucosal exposure to infected (HBsAg-positive) or high-risk source*

(adapted from the *Canadian Immunization Guide*)[8]



anti-HBs = antibody to hepatitis B surface antigen

HBIG = hepatitis B immune globulin

* A known source is high-risk if the person comes from a highly endemic region for HBV, has sexual relations with multiple partners, has a partner who is infected with HBV or is at high risk of being so, is in close family contact with an infected person, uses injection drugs or received blood or blood products prior to 1970. Wherever possible, the source should be tested. In the case of an unknown source, background circumstances may provide some indication of the degree of risk (e.g., syringe found in the street, attendance at an STI, detoxification or well-baby clinic).

† Responder known to have ≥10 IU/L anti-HBs. No measures are required if the person has developed an immunity following an infection.

‡ Anti-HBs titre should be determined as soon as possible to avoid needless administration of HBIG and because efficacy is unknown if given after 7 days for percutaneous/mucosal exposures and up to 14 days for sexual exposures.

§ The administration of HBIG can be omitted if the high-risk source can be tested within 48 hours and the result is negative. In that case, see Figure 2.

‖ The second dose of HBIG should be given 1 month after the first.

¶ This test does not change the continuation of vaccination, but may reassure the exposed individual about the immediate risk of becoming infected.

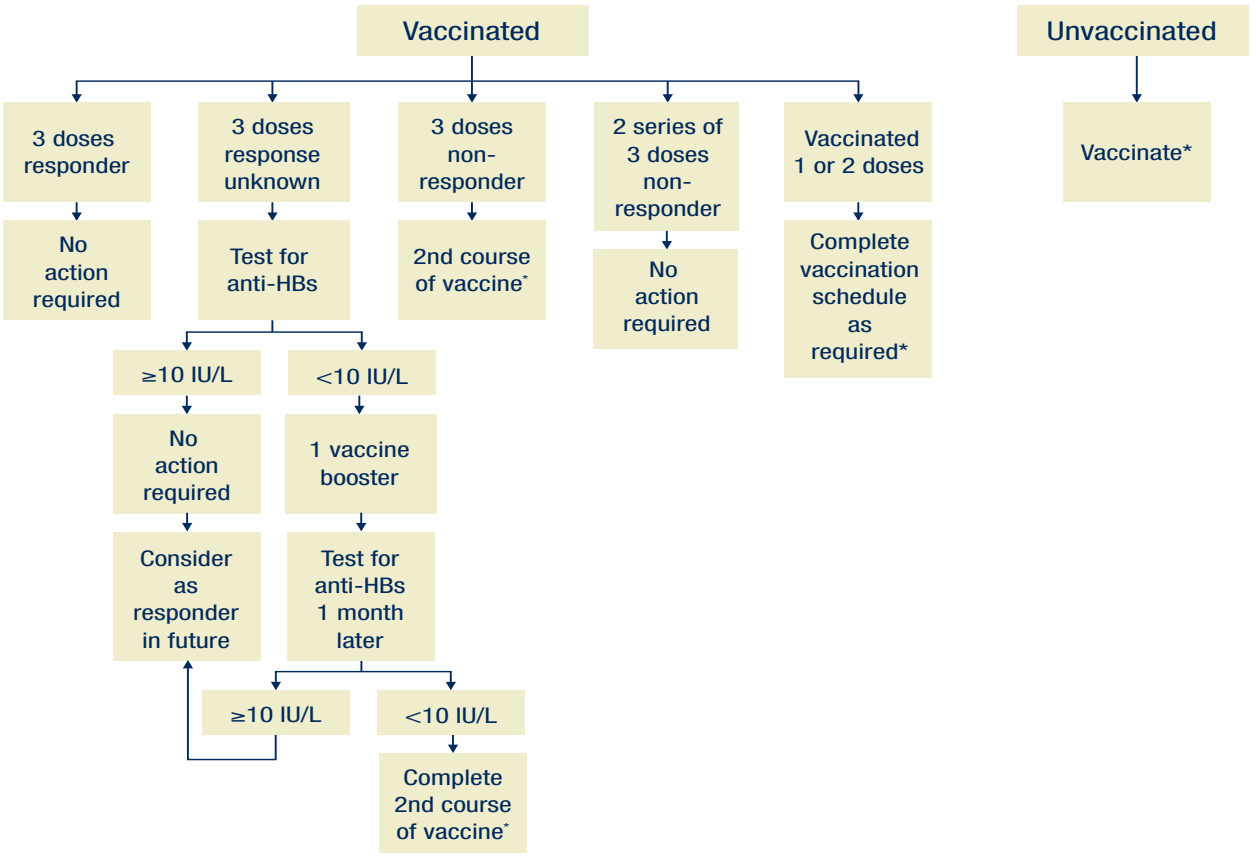
If it is possible to quickly obtain an anti-HBs titre confirming ≥10 IU/L, administration of HBIG should be omitted.

** Determination of anti-HBs titre should be delayed for 6 months to allow HBIG antibodies to wane.

†† Test for anti-HBs 1–6 months after the course of vaccine.

Figure 2. Management of sexual/percutaneous/mucosal exposure to uninfected (HBsAg-negative) or low-risk source

(adapted from the *Canadian Immunization Guide*[8])



anti-HBs = antibody to hepatitis B surface antigen

* Test for anti-HBs 1–6 months after the course of vaccine.

Treatment

- A discussion of the treatment of clinical hepatitis B is beyond the scope of these guidelines. **Any patient known to have chronic hepatitis B should be referred to an expert for further management.** Those wishing further details on initial workup of the patient with chronic hepatitis B are referred to *Management of Viral Hepatitis: A Canadian Consensus Conference 2003/2004*[12] and *The Management of Chronic Viral Hepatitis: A Canadian Consensus Conference 2004*.[13] Some brief comments can be made:
  - There is no indication for antiviral intervention in acute hepatitis B.
  - Acute cases of hepatitis B should abstain from sexual contact or practice safer-sex until partners and/or relevant contacts have been appropriately screened and/or immunized.
  - In the case of chronic active hepatitis B, there are data to support the efficacy of interferon-α,[9] lamivudine,[10] famciclovir,[14] adefovir,[15] ribavirin[16] and other agents under study. In Canada, most patients are managed with interferon-α and/or lamivudine (3TC) as primary therapeutic modalities *[A-I]*.

Consideration for Other STIs

- Any patient with hepatitis B infection believed to have been acquired sexually should be considered to be at risk for other STIs, including HIV, and should be offered testing for gonorrhea, chlamydia, syphilis and HIV.
- Discuss HPV vaccine with women as per the recommendations outlined in the Canada Communicable Disease Report, Volume 33 ACS-2, (2007) *National Advisory Committee on Immunization (NACI) statement on Human papillomavirus vaccine*.
- Any patient with hepatitis B infection believed to have been acquired parenterally should be considered to be at risk for HIV and HCV, and should be offered testing for both.
- Concurrent HIV and hepatitis B infection can lead to more rapid progression of liver damage and is more likely to lead to chronic infection and impaired hepatic function, which may limit the therapeutic options for treatment of the HIV co-infection.[17]

Reporting, Partner Notification and Follow-up

- Acute hepatitis B is a reportable infection in all Canadian jurisdictions.
- Partner notification/contact tracing is essential to identify those at risk of acquiring hepatitis B, both to clarify their immune status and to provide vaccine protection to the non-immune. Contacts include the following:
  - Sexual and percutaneous exposures during the period of infectivity.
  - Children of hepatitis B–infected mothers who did not receive HBIG and vaccine at birth.
  - Those living in the household of the index case.

Special Considerations

- **Pregnant women with no history of hepatitis B immunization should be screened at their initial prenatal visit for HBsAg**. A pregnant woman who has no markers of acute or chronic HBV infection but who is at high risk of acquiring HBV should be offered vaccine at the first opportunity and tested for antibody response.[8] Pregnancy is not a contraindication to immunization.[8] If testing has not been done during pregnancy, it should be done at the time of delivery. Repeat testing before delivery may be considered in uninfected and non-immunized women with continuing high-risk behaviour. Infants born to HBsAg-positive women should receive postexposure prophylaxis.
- **Children adopted from areas or family situations in which there is a high prevalence of HBV infection should be screened for HBsAg**, and if they are positive, household contacts should be immunized before adoption.