Hepatitis B

Manitoba Health
Public Health
Communicable Disease Control Unit

Case Definition

Confirmed Case: Positive for one or more of following lab markers:

- Hepatitis B surface antigen (HBsAg)*
- Hepatitis B e antigen (HBeAg)
- Hepatitis B DNA
- anti-HBc (antibody to core antigen) in the absence of HBsAg and antibody† to surface antigen (anti-HBs)

* does not include positive results due to recent immunization

† presently and previously if tested

Acute case: HBsAg and anti-HBc IgM of any duration less than six months.

Chronic Case (sometimes referred to as a Carrier): Samples taken six or more months apart are HbsAg positive or a single specimen is HbsAg positive and anti-HBc IgM negative.

Clinical Case: Cases of hepatitis B cannot be diagnosed on clinical grounds alone.

Reporting Requirements

- All positive laboratory results noted above are reportable by laboratories.
- All acute cases and newly identified chronic cases are reportable by the attending health care professional.

Clinical Presentation/Natural History

Only a small proportion of acute hepatitis B cases may be clinically recognized; less than 10% of children and 30-50% of adult acute (HBV) cases will have icteric disease. In persons with clinical illness, the onset is usually insidious with anorexia, vague abdominal discomfort, nausea and vomiting, sometimes arthralgias and rash, often progressing to jaundice. Fever may be absent or mild. Severity ranges from inapparent cases detectable only by liver function tests, to fulminating, fatal cases of acute hepatic necrosis. The case-fatality rate in hospitalized patients is about 1% and is higher in those over 40 years of age.

Chronic HBV infection is found in 0.5% of North American adults and in 0.1-20% of people from other parts of the world. Persons with chronic infection may or may not have a history of clinical hepatitis. About one third have an elevated aminotransferase; biopsy findings range from normal to chronic active hepatitis, with or without cirrhosis. The prognosis of the liver disease in such persons is variable.

Following acute HBV infection, the risk of developing chronic infection varies inversely with age; chronic HBV infection occurs among about 90% of infants infected at birth, 25-50% of children infected at one to five years of age and about 1-10% of persons infected as older children and adults. Chronic HBV infection is also common in persons with immunodeficiency. An estimated 15-25% of persons with chronic HBV infection will die prematurely of either cirrhosis or hepatocellular carcinoma. HBV may be the cause of up to 80% of all cases of hepatocellular carcinoma worldwide, second only to tobacco among known human carcinogens.

Etiology

The hepatitis B virus (HBV), a hepadnavirus, is a 42-nm partially double-stranded DNA virus, composed of a 27-nm nucleocapsid core (HBcAg), surrounded by an outer lipoprotein coat containing the surface antigen (HBsAg). HBsAg is antigenically heterogeneous, with a common antigen designated “a”, and two pairs of mutually exclusive antigens, “d” and “y”, and “w” (including several subdeterminants) and “r”, resulting in four major subtypes: adw, ayw, adr and ayr. The distribution of subtypes varies geographically; because of the common “a” determinant, protection against one subtype appears to confer protection against the other subtypes, and no differences in clinical features have been related to subtype.

The third hepatitis B antigen, the "e" antigen (HBeAg), has been identified as a soluble antigen, whose sequences are a subset of those in the core antigen, but without cross-reactivity. HBV also contains DNA-dependent DNA polymerase and reverse transcriptase activities.

Epidemiology

Reservoir and Source: Humans. Chimpanzees are susceptible, but an animal reservoir in nature has not been recognized. Infected pet monkeys have been documented. Closely related hepadnaviruses have been found in woodchucks, ducks and other animals; none are thought to cause disease in humans.

Transmission: HBsAg or HBV-DNA has been found in virtually all body secretions and excretions, however, only blood (and serum-derived fluids), saliva, semen and vaginal fluids have been shown to be infectious. Blood and serum are the most infectious while saliva is the least infectious.

Transmission occurs by percutaneous (IV, IM, SC or intradermal) and permucosal exposure to infective body fluids. 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 needlesticks or other injuries from sharp instruments sustained by hospital personnel. Blood products, including immune globulins (IG), heat-treated plasma protein fraction, albumin and fibrinolysin are considered safe. Sexual and perinatal HBV transmission usually result from mucous membrane exposures to infectious blood and body fluids. Because HBV is stable on environmental surfaces for seven days, indirect inoculation of HBV can also occur via inanimate objects.

Perinatal transmission is common in hyperendemic areas of Southeast Asia and the Far East, especially when HBsAg carrier mothers are also HBeAg positive. Infection may also be transmitted between household contacts and between sexual partners, either homosexual or heterosexual, and in toddler-aged children in groups with high HBsAg carrier rates. Communally used razors and toothbrushes have been implicated as occasional vehicles of HBV transmission causing percutaneous and mucosal inoculation. Fecal-oral or vectorborne transmission has not been demonstrated. In about 35% of cases, no transmission source can be identified.

Occurrence:

General: Worldwide; endemic with little seasonal variation. In areas of Africa and Asia, widespread infection may occur in infancy and childhood. In North America, infection is most common in young adults. In the United States and Canada, serologic evidence of previous infection varies depending on age and socioeconomic class. Overall, 5% of the adult population in the United States has anti-HBc, and 0.5% are HBsAg positive. Among those from some areas of Asia, 10-15% may be HBsAg positive. In developed countries, exposure to HBV may be common in certain high-risk groups. These include injecting drug users, heterosexuals with multiple partners, homosexual men, clients and staff in institutions for the developmentally disabled, employees in hemodialysis centers and persons in certain healthcare and public safety occupations. Percutaneous and permucosal exposure to blood or serous fluids are associated with occupationally acquired HBV infections; surgeons, dentists, oral surgeons, pathologists, operating room and emergency room staff, and clinical laboratory workers who handle blood are at highest risk.

Until 1975, recipients of blood products were at high risk. In the many countries in which pre-transfusion screening of blood donors for HBsAg is required, and where pooled blood-clotting factors (especially antihemophilic factor) are processed to destroy the virus, this risk has been virtually eliminated. However, this risk is still present in many developing countries. Contaminated and inadequately sterilized syringes and needles have resulted in outbreaks of hepatitis B among patients in clinics and physicians' offices; this has been a major mode of transmission worldwide. Occasionally, outbreaks have been traced to tattoo parlors and acupuncturists. Rarely, transmission to patients from HBsAg-positive health care workers has been documented.

Manitoba: The incidence rate of hepatitis B has been estimated to be around 19/100,000 (includes inflation for asymptomatic cases). In 1999, 17 cases were reported; in 1998, 26; 1997, 35; 1996, 66; and in 1995, 53 cases.

Incubation Period: Usually 45 to 180 days, average 60 to 90 days. As short as two weeks to the appearance of HBsAg, and rarely as long as six to nine months. The variation is related in part to the amount of virus in the inoculum, the mode of transmission and host factors.

Susceptibility and Resistance: Susceptibility is general. Usually, the disease is milder and often anicteric in children; in infants it is usually asymptomatic. Protective immunity follows infection if antibody to HBsAg (anti-HBs) develops and HBsAg becomes negative. Persons with Down's syndrome, lymphoproliferative disease, HIV infection and those on hemodialysis appear to be more likely to develop chronic infection.

Period of Communicability: The presence of one or more of HBsAg, HBeAg and hepatitis B DNA indicates that the person is potentially infectious. Communicability is highest in the acute stage of illness. Persons in the "core window period" (see **Diagnosis**), and those rare persons who are concurrently HBsAg and anti-HBs positive, should be considered infectious. In the latter case, if HBsAg disappears and anti-HBs remains, persons can be considered non-infectious. The presence of "e" antigen or high levels of viral DNA indicate high virus titres and higher infectivity, while the presence of "e" antibody and low levels of viral DNA indicate reduced infectivity. Blood from experimentally inoculated volunteers has been shown to be infective many weeks before the onset of first symptoms and to remain infective through the acute clinical course of the disease.

Diagnosis

Two serologic tests are commonly used to determine if a person is a chronic or acute case of hepatitis B. They are:

- hepatitis B surface antigen (HBsAg);
- antibody to HBcAg (anti-HBc).

HBsAg can be detected in the serum from several weeks before onset of symptoms to days, weeks or months after onset in acute cases; it persists in chronic cases. HBsAg declines, disappears and is followed by the appearance of anti-HBs in acute and chronic cases which resolve.

Anti-HBc appears at the onset of illness and persists indefinitely. Demonstration of anti-HBc in serum indicates either current or past HBV infection. IgM anti-HBc is present in high titre in acute cases and usually disappears within six months, although rarely it can persist in chronic cases; thus, a positive result may reliably diagnose an acute case. In resolving cases, anti-HBc (IgM anti-HBc in acute cases) may be present while HBsAg and anti-HBs are both absent — the "core window" period.

Testing for hepatitis B DNA is a not routinely performed except by reference labs. It is used primarily to monitor the effectiveness of therapy.

Key Investigations

- Determination of risk factors for acquisition of hepatitis B.
- Contact identification and follow-up.
- Immunization history.

Control

Management of Cases:

Treatment:

- Alpha interferon is the only drug licensed for treatment of chronic hepatitis B in Canada.
- Treatment is most worthwhile during the high-replicative phase (HBeAg-positive) of infection because the patient is most likely to be symptomatic, infectious and at greatest risk of long-term sequelae.
- Studies have shown that the drug is successful in arresting viral replication in about 30-40% of patients treated.
- Approximately 10% of patients who respond lose HBsAg six months after therapy.

- Further details concerning treatment can be found in the Canadian Liver Foundation pamphlet "*Hepatitis B: Information for the Medical Profession*."

Public Health Measures:

Prevention of Transmission of Hepatitis B to Newborns:

- ***Screen prenatal women:***
  - All prenatal women should be screened for hepatitis B surface antigen (HbsAg), even if they have tested positive for HbsAg in the past.
  - Physicians are requested to tick off the "prenatal" box on the Cadham Provincial Laboratory (CPL) requisitions.

- ***Prophylactic measures for newborns:***
  - If the mother is HbsAg positive or the father or other household member is HbsAg positive and will be the primary caregiver, or there is an acute case in the household, both HBIG 0.5 ml and hepatitis B vaccine should be administered.
  - If there is a carrier in the household (other than the mother), only vaccine is required.

- ***Unscreened mother about to deliver:***
  - Screening is recommended to occur as soon as possible, even if delivery has occurred.
  - If results can be obtained from CPL within 12 hours (call (204) 945-7582), the first dose of hepatitis B vaccine should be given, with a decision to give HBIG awaiting results.
  - If results are positive for HbsAg, then HBIG should be given; if negative, HBIG is not required, but the two remaining doses of hepatitis B vaccine can be given to complete the series (see below).
  - If results will not be available within 12 hours, the first dose of vaccine should be given and administration of HBIG should be considered — taking into account the presence or absence of maternal risk factors for infection (e.g., no prenatal care, intravenous drug use, multiple sexual partners, immigration from endemic area of world* or Canadian First Nations person).
    * China, Southeast Asia, eastern Europe, the Central Asian republics, most of the Middle East, Africa, the Amazon Basin, some Caribbean islands, the Pacific Islands.

- ***Hepatitis B Immune Globulin (HBIG):***
  - The dose for newborns is 0.5 ml intramuscular. Ideally, it should be given within 12 hours of birth, with efficacy decreasing significantly after 48 hours.
  - Pediatric HBIG is available from hospital pharmacies who order it from the Biologics Order Desk at the provincial vaccine warehouse, Livingston Health Care Services Inc. ph: 633-2621.

- ***Hepatitis B vaccine:***
  - The dose is 0.5 ml intramuscular (10 µg if ENGERIX™; 5 µg if RECOMBIVAX™). It should be given at the same time as the HBIG, but at a different site.
  - If immunization is delayed, attempts should be made to ensure that the vaccine is given before seven days of age.
  - Second and third doses of vaccine are required one and six months after the first dose to complete the immunization series.
  - Vaccine is available from hospital pharmacies who order from the Biologics Order Desk (see HBIG above).

- *Premature infants:*
  - Newborns weighing less than 2,000 g should receive prophylaxis in the same way as other newborns, except that an additional dose of vaccine should be given two months after the third dose.
- *Follow-up:*
  - Health care providers are asked to complete the "Hepatitis B-Prophylaxis- Record Sheet for Infants" at the time of prophylaxis. This sheet is provided with each vial of HBIG and should be returned to the CDC Unit at the address listed. The CDC Unit or Winnipeg Regional Health Authority (if in Winnipeg) will write to the infant's pediatrician or family physician, as well as to the mother, alerting them that two additional doses of hepatitis B vaccine are required at one and six months following the first dose.
  - Infants should be screened for antibody to hepatitis B surface antigen (anti-HBs) as well as hepatitis B surface antigen one to two months after receipt of the third dose of vaccine (fourth in the case of premature infants born less than 2 kg). If the anti-HBs result is less than 10 I.U./L and HbsAg is negative, an additional three doses of vaccine at zero, one and six months should be given, followed by anti-HBs and HbsAg testing as above.

Education of Acute and Chronic Cases:

- Acute and chronic cases should be educated:
  - not to share toothbrushes, razors or intravenous drug needles, or donate blood or organs;
  - how to minimize sexual transmission;
  - how to properly clean-up blood spills;
  - to inform persons providing health care services to them that they have been infected with HBV;
  - chronic cases should be advised to be immunized with hepatitis A vaccine.

Contact Identification:

- A list of sexual, needle/razor/toothbrush sharing and/or household contacts should be obtained to determine source of infection and to prevent further spread by immunization.
- For acute cases, this should include all current contacts as well as those in the previous six months.
- For chronic cases, include current contacts as well as those within the last six months; this cut-off should be extended further back if contact was frequent and after infection developed (when this can be estimated).

Follow-up Testing

- Acute cases should be tested for both HBsAg and anti-HBs six months after detection to assess whether chronicity has developed and to determine the need for ongoing precautions described above.
- If the person is in the core window at six months, re-test at six month intervals to determine if the person develops anti-HBs while remaining HBsAg negative.
- Pregnant women should be tested earlier than six months if they will deliver before that time, to establish whether or not prophylaxis of the newborn will be required. One or more tests between three months following detection and one month prior to delivery (whichever comes first), is a suggested time frame.

Management of Contacts:

- Public health nurse will contact all new chronic and acute reported cases to advise acute cases of the need for follow-up testing and identify and arrange for follow-up of contacts.

- The public health nurse can also assist in identifying and following up contacts of previously identified carriers, as well as contacts in complicated "significant exposure to blood or body fluids" situations (e.g., motor vehicle accident).
- Contacts need to be informed of the potential risk of acquiring infection and the need for immunization, unless screening (see below) indicates immunity. For sexual partners, barrier methods should be used until immunizations have been completed and anti HBs demonstrated (see Contact Screening/Testing) or the case is HBsAg negative and anti-HBs positive.
- **Contacts of Acute Cases**
  - An acute case's sexual, as well as needle, razor or toothbrush sharing contacts should be offered hepatitis B vaccine to prevent against the current and possible future exposures.
  - HBIG should also be given as soon as possible, regardless of the interval since last exposure, if there is any chance of future similar exposures to the case.
  - If exposures will not occur again, then follow the guidelines in this section below regarding timing of exposure and provision of HBIG.
  - Household contacts under the age of five years should receive HBIG and hepatitis B vaccine; those five years and older should receive hepatitis B vaccine alone.
- **Contacts of Chronic Cases**
  - Chronic case household, sexual, as well as needle, razor or toothbrush sharing contacts should be given hepatitis B vaccine.
  - HBIG should be given to infants if their mother or primary care giver is a chronic case. It should also be given if sexual or needle/razor/toothbrush contact occurred for the first time in the previous two weeks (also see guidelines in this section below regarding timing of exposure and provision of HBIG).
  - **At every new contact with the health care system, all carriers should be questioned as to whether their household contacts have been immunized, since previous immunization policies were not as liberal with the provision of vaccine.**
- **Potential Case Contacts (via "Significant Exposure to Blood or Body Fluids" e.g., needlestick injury)**
  - Please consult the Manitoba Health "*Integrated Post-Exposure Protocol*" in this manual.
- **How to Obtain and Use HBIG:**
  - **HBIG, (5 ml and possibly 1 ml formats) for situations other than birth of a child to a HBsAg positive mother, is stocked only at certain locations because of expense and limited supply. These are normally:**
    - **St. Boniface General Hospital Bloodbank**
    - **Health Sciences Centre**
    - **Misericordia Health Centre**
    - **Brandon General Hospital**
    - **Flin Flon General Hospital**
    - **Thompson General Hospital**
    - **Churchill Health Centre Pharmacy**
    - **Dauphin Regional Health Centre**
  - **To obtain HBIG and hepatitis B vaccine at a site other than those listed above, contact Livingston Health Care Services Inc., (204) 633-2621 (phone) or (204) 694-2380 (fax). After 5:00 p.m. call (204) 781-5342. Assistance in determining the need for HBIG and hepatitis B vaccine can be obtained from the local Medical Officer of Health (MOH). If the MOH is unknown, call Health Links with the patient's address; (204) 788-8200 or 1-888-315-9257. During evenings, weekends and holidays, contact the MOH on-call at (204) 945-0183.**
  - **Dosage is 0.06 ml/kg IM.**

  - HBIG should be given as soon as possible since efficacy decreases with time. The maximum time after exposure during which HBIG is still effective is not known. For needlestick and mucosal exposures, benefit exists for at least seven days. For sexual contacts, it is unlikely to exceed 14 days.

- **Contact Screening/Testing:**
  - Pre-immunization screening of acute and chronic case contacts for markers of infection may be performed at the same time as the first dose of vaccine and/or HBIG is given (CPL will automatically screen for anti-HBs, HbsAg and core antibody according to a predetermined algorithm). **When requesting screening tests, please indicate "High Risk Group Pre-immunization Hep B screening."**
  - Post-immunization testing for anti-HBs should be undertaken for persons likely to have ongoing household, sexual or needle-sharing contact with an acute or chronic case. Testing should occur one to two months following the third dose of hepatitis B vaccine or four months after the receipt of HBIG, whichever is later. If negative for both markers, immunization with an additional three-dose series of hepatitis vaccine should be undertaken with anti-HBs testing as above.

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., prisons.

Preventive Measures:

- Universal immunization programs as well as ongoing immunization of high-risk groups.
- Investigation and follow-up of contacts of acute and chronic cases.
- Investigation and follow-up of persons with "significant exposures to blood or body fluids."
- Routine precautions.
- Prenatal screening for all women for each pregnancy, even if they were HBsAg positive in the past, so that newborns can be receive prophylaxis if necessary.
- Screening of blood donors, adopted children from countries or family situations in which there is a high prevalence of infection, homosexual and bisexual males, heterosexual males or females with multiple sexual partners or with a recent history of a sexually transmitted disease and injection drug users.
- Adequate sterilization of instruments used in invasive procedures, including personal care services (e.g., ear piercing, tattooing).
- Appropriate disinfection measures following body fluid spills.
- Medical and dental personnel who are infected with HBV should not perform exposure-prone procedures 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.

Additional Resources

1. *Hepatitis B: Information for the Medical Profession*. Canadian Liver Foundation.
2. *Hepatitis B: Advice for hepatitis B carriers and their families*. Canadian Liver Foundation.