Hepatitis B in British Columbia, Update August 1st, 2008

There have been a number of changes in the reporting, laboratory processes and epidemiology of hepatitis B virus (HBV) recently in BC. This report includes:

1. New HBV surveillance case definitions and implementation issues
2. New HBV epidemiological data from BC integrated Public Health Information System (iPHIS) and the Enhanced Hepatitis Strain and Surveillance System (EHSSS)
3. Updated information developments in the laboratory system
4. HBV vaccine: long-term immunity, and vaccine effectiveness in persons with HCV
5. Changes to BCCDC Guidelines: New Core Only Guidelines and high risk infant post-immunization serology no longer includes anti-hepatitis B core testing
6. Hepatitis testing for insurance medicals

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1. Case Definitions

The Public Health Agency of Canada has developed new case definitions for HBV to improve the quality of HBV surveillance data. The following are those adapted for BC purposes.

Acute case	**Confirmed case**: Hepatitis B surface antigen (HBsAg) and immuoglobulin M antibody to hepatitis B core antigen (anti-HBcIgM) positive in the context of a compatible clinical history or probable exposure **OR** Clearance of HBsAg in a person who was documented to be HBsAg positive within the last six months in the context of a compatible clinical history or probable exposure **Probable case**: Acute clinical illness in a person who is epidemiologically linked to a confirmed case
Chronic carrier	**Confirmed case**: HBsAg positive for more than 6 months **OR** Detection of HBsAg and anti-HBcIgG in the documented absence of anti-HBcIgM
Undetermined	**Confirmed case**: HBsAg positive **AND** does not fit the criteria for either acute case or chronic carrier above.

As these new case definitions are implemented, clinical judgment will be invaluable in their application. Some potential challenges:

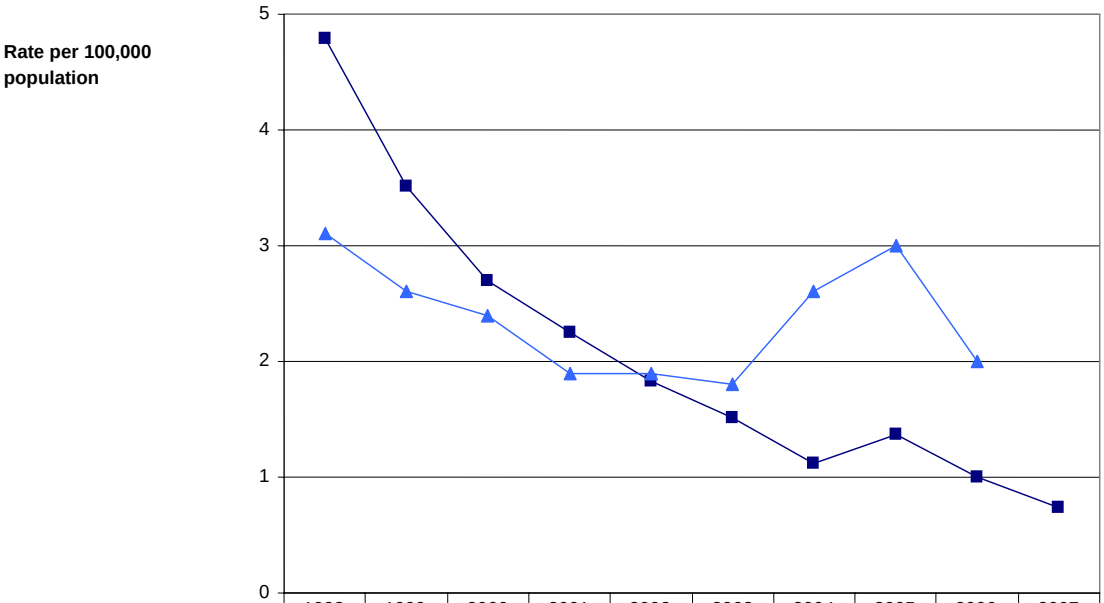
- Even with positive HBsAg and anti-HBcIgM results, the acute case definition requires a compatible clinical history or probable exposure because patients with chronic HBV infection may have a reactivation of disease activity and a corresponding rise in anti-HBcIgM. A recent review of a sample of anti-HBcIgM results found >20% of positive results were likely related to reactivation of chronic infection.[1]

- When a patient who is a new immigrant from an endemic country presents with a positive HBsAg and has no recent history of acute symptoms, the likelihood that they are a chronic carrier is high. Entering them as such in iPHIS will help improve data quality. Completing the country of origin and date of immigration fields in iPHIS will be particularly useful for helping to assess vaccine efficacy on a population level.

2. Epidemiology

Prior to the implementation of HBV vaccination, BC routinely reported acute hepatitis B rates of >5 per 100,000 population, well above the Canadian average. This is related to the relatively high prevalence of chronic HBV in BC, which is in part due to significant importation from endemic countries. Since the introduction of immunization for grade 6 students in 1992 and the addition of universal immunization of all infants in 2001, the incidence of acute HBV has plummeted in BC to <1 per 100,000, and has been consistently below the national average since 2002. In 2007 only 2 cases of acute HBV occurred in BC in persons under 25 years.

Acute Hepatitis B - Reported Cases 1998-2007



	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
BC Hepatitis B: Acute Reports	191	141	109	92	76	63	47	58	42	35
BC Hepatitis B: Acute Rate	4.8	3.5	2.7	2.3	1.9	1.5	1.1	1.4	1.0	0.8
CAN. Hepatitis B: Acute Rate	3.1	2.6	2.4	1.9	1.9	1.8	2.6	3	2	

Data Extracted March 2008

The BC Enhanced Hepatitis Strain Surveillance System, (EHSSS) collects demographic and risk factor data from all acute HBV cases reported in BC outside of the City of Vancouver. Recent analysis showed that from 2000-2007, 74% of reported HBV infections were distributed across the 20-50 age groups and men accounted for 71% of reported infections. The most commonly reported risk factor was sex with a person of the opposite sex (48%), followed by non-injection drug use (22%), injection drug use (16%), and incarceration (14%).[1]

Using iPHIS data, we identified 1,815 cases of reported chronic HBV and hepatitis C (HCV) co-infection in BC between 1991 and October 2007. Analysis showed that 3.1% of (58,361) persons with HCV also tested positive for HBV; and 5.2% of (33,261) persons reported with HBV were also reported to have HCV. The infections were identified concurrently (within 2 weeks of each other) in 905 cases; HBV was reported before HCV in 478 cases; and HCV first in 432 cases.

Given the current NACI and BCCDC recommendations to vaccinate all individuals with HCV against HBV, cases of co-infection where HCV is reported before HBV may represent missed opportunities for prevention of HBV infection. Most (95%) of anti-HCV testing occurs at BCCDC. Since 1998, all HCV reactive sera are reflex tested for anti-HBs (and hepatitis A antibodies) to determine the need for immunization. For those who tested positive for HBV first, one must ask how many HCV infections could have been prevented with a broader application of evidence-based harm reduction programs.

3. Laboratory Update

HBV serology occurs in private, hospital as well at BCCDC laboratories. There have been developments in the handling of HBV samples and testing practices in some settings that may present challenges to public health practitioners in the field.

- ***False positive HBsAg results***: Some private and hospital labs perform HBsAg testing and do not neutralize, nor repeat using a second method. Serum is generally sent to BCCDC for confirmatory testing and to identify false positives. However, if this confirmation process is delayed or disrupted, inaccurate results and counselling may be given to patients. BCCDC has requested that these labs state "provisional reactive" on any results that are sent to physicians and health authorities prior to confirmatory testing.

- ***Prenatal testing***: One of the large private laboratory corporations has decided to test prenatal sera for HBsAg despite consolidation of all other prenatal virology at BCCDC. These laboratories may not report results to the hospital of delivery or inform public health that they are prenatal tests. A process is being negotiated so these labs will send results to BCCDC after their initial testing for appropriate follow-up testing (e.g. confirmation and HBeAg to inform risk counseling) and communication of results.

BCCDC is working with labs across the province to improve collaboration so that the most reliable and safest testing and reporting practices are followed.

4. Vaccine Update

Hepatitis B vaccine is recommended for universal immunization of infants, pre-exposure immunization of high-risk groups and post-exposure intervention for those exposed to HBV, particularly infants born to HBV-infected mothers.[2]

Long-term immunity following HBV immunization: Recent studies have improved our knowledge of how vaccine-induced HBV immunity changes over time. While 95% of children <2 years of age develop protective immunity, defined as anti-HBs >10 IU/L, anti-HBs titers decline over time. However, there is mounting evidence that immunity or protection from chronic HBV infection is maintained through an anamnestic response in spite of low or absent anti-HBs levels:

- McMahon *et al* followed a group of vaccinees over 15 years in a US community where incidence rates of 50 per 1000 person-years had been the norm. They found that their incidence dropped to approximately 1 infection per 1000 person-years, despite only 66% of participants showing protective levels of anti-HBs at 15 years.[3]

- Van der Sande *et al* followed a group of vaccinees in Gambia for 15 years post-vaccination, and found that a full primary series (3 or 4 doses) protected against 67.0% of infections, and 96.6% of chronic infections. This was in spite of only a third of participants showing protective levels of antibodies at 15 years.[4]

Although studies continue to show that serological markers of immunity decline over time,[5, 6] there is no convincing evidence that there is a significant burden of illness in any cohort that has received universal vaccination as infants.[7] The current BC recommendations are that certain high-risk groups receive anti-HBs testing post-immunization, and further immunization is administered if antibodies are not protective. While there is growing evidence that low-risk, immune-competent vaccine recipients should not require a booster dose for at least 10-15 years, there remains controversy about the utility of a universal booster program at some point in adolescence. We will continue to monitor the evidence as it emerges.

Vaccine effectiveness in persons with HCV: Buxton and Kim recently reviewed the evidence of effectiveness of HAV and HBV vaccines in persons with HCV. In some studies HBV vaccine appeared to be as effective in chronic HCV population as in controls, however response was generally reduced in patients with cirrhosis.[8] This led the authors to make two modifications to existing recommendations:

- When possible, HBV vaccine should be given early in the course of HCV disease in order to increase the likelihood of good response.

- In people with cirrhosis, post-immunization anti-HBs antibody testing should be provided, with boosters offered as indicated.

Note The current immunization policy states that individuals with chronic liver disease (including cirrhosis and liver transplant) who are eligible for HBV vaccine should receive a double dose for age.

5. Changes to BCCDC Guidelines

In addition to the new national case definitions, BCCDC is updating its guidelines to help improve management of HBV cases.

- "Core only" cases, where anti-HBc is positive, HBsAg is negative and anti-HBs is negative (<1 IU/L) or intermediate (1 to 10 IU/L), have long been difficult to interpret. This can indicate that the patient is:
    a) Recovering from acute HBV infection
    b) Immune from old infection
    c) Susceptible with a false positive anti-HBc
    d) Chronically infected, with undetectable level of HBsAg

  In these cases, further testing and/or immunization may be indicated. The revised BCCDC guidelines include a testing algorithm to help resolve these "core only" conundrums.

- Post-immunization serology recommendations for infants born to HBV positive mothers no longer includes anti-HBc. Post-immunization testing determines protective immune response to vaccine (ie. anti-HBs level >10 IU/L), or current infection (HBsAg). Anti-HBc was performed as the 3 tests are usually done together, but also to determine infants who had been infected and had cleared the virus. As anti-HBc may be due to maternal antibody, further serology was necessary at 12 months. Data collected for the BC high-risk infant study found >60% anti-HBc in infants 1-6 months post immunization were false-positives, and the true-positive rate is close to zero. Thus causing unnecessary follow-up tests, and having little benefit. This change aligns BC guidelines with those of the Canadian Immunization Guide and of the US Centre for Disease Control.

6. Hepatitis testing for insurance medicals

BCCDC is receiving an increasing number of HBV (and HCV) test results from insurance companies who use out of province physicians and/or labs to assess their clients. Most often, these are from laboratories in Ontario, and have been ordered and interpreted by physicians in that province who act on behalf of the insurance company. In most cases, the testing laboratory fulfills its duty to report positive results to the relevant health authorities, via BCCDC. However, the physicians involved often do not inform the patient of the positive results. *Health authorities should be aware that the patient's primary care provider does not usually receive the test results, and the appropriate follow-up counseling is often not performed.* In order to determine which patients have not been previously identified, BCCDC links these results to iPHIS and informs the appropriate health authorities of HBV cases, which have not previously been reported as chronic HBV and new HCV cases.

This practice may mean a gap of weeks between positive test results and appropriate counselling of the patient. These tests are not performed for clinical reasons and therefore are likely chronic HBV infections, however it is possible that contacts of the patient may be unknowingly exposed to HBV under entirely preventable circumstances. BCCDC has contacted the College of Physicians and Surgeons of Ontario (CPSO) who verified that these physicians have a duty to inform the patients of their results even when the patient is out of province. The CPSO expressed concern about this practice, but will only act if a complaint is lodged by a patient. If you have cases that you would like to elevate, please contact:

The College of Physicians and Surgeons of Ontario,
80 College Street,
Toronto, Ontario M5G 2E2
General Inquiries telephone**:** toll free: 1 (800) 268-7096 ext. 603,
E-mail Questions: feedback@cpso.on.ca

More Information

For background information on hepatitis B virus, please consult the relevant Health File, available at: http://www.bchealthguide.org/healthfiles/. For information on the management of hepatitis B cases, please see: 2007 Consensus Guidelines Hep B on BCCDC website, hepatitis Division

References

[1] BCCCDC EHSSS Site Field Report 2008 on BCCDC web site http://www.bccdc.org/downloads/EHSSS%20BCCDC%20Site%20Report%202000-07.ppt

[2] National Advisory Committee on Immunizations. *Canadian Immunization Guide, 7th ed, 2006*. Public Health Agency of Canada. 2006, Ottawa, Canada.

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[5] Whittle HC, *et al*. Long-term efficacy of continuous hepatitis B vaccination in infancy in two Gambian villages. *BMJ* 325:569-572.

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[8] Buxton JA, Kim JH. Hepatitis A and hepatitis B vaccination in persons with chronic hepatitis C infections: a review of the evidence and current recommendations. *Can J Infect Dis Med Microbiol* 2008;19(2):197-202.