



Viral Hepatitis Testing

Effective Date: January 1, 2012

Scope

This guideline provides guidance for the use of laboratory tests to diagnose acute and chronic viral hepatitis in adults (≥ 19 years) in the primary care setting.

► General Considerations for Ordering Laboratory Tests

Prior to ordering tests for hepatitis, consider the patient's history, age, risk factors (see below), hepatitis vaccination status, and any available previous hepatitis test results.

► Risk Factors for Viral Hepatitis include:

- Substance use (includes sharing drug snorting, smoking or injection equipment)
- High-risk sexual activity or sexual partner with viral hepatitis
- Travel to or from high-risk hepatitis endemic areas or exposure during a local outbreak
- Immigration from hepatitis B and/or C endemic countries
- Household contact with an infected person especially if personal items (e.g., razors, toothbrushes, nail clippers) are shared
- Recipient of unscreened blood products*
- Needle-stick injury or other occupational exposure (e.g., healthcare workers)
- Children born to mothers with chronic hepatitis B or C infection
- Attendance at daycare
- Contaminated food or water (hepatitis A only)
- Tattoos and body piercing
- History of incarceration
- HIV or other sexually transmitted infection
- Hemodialysis

**screening of donated blood products for hepatitis C (anti-HCV) began in 1990 in Canada.¹*

► Types of Viral Hepatitis

Hepatitis A: causes acute but not chronic hepatitis

Hepatitis B: causes acute and chronic hepatitis

Hepatitis C: causes chronic hepatitis but rarely manifests as acute hepatitis

Hepatitis D: rare and only occurs in patients infected with hepatitis B

Hepatitis E: clinically similar to hepatitis A, mostly restricted to endemic areas and occasionally causes chronic infection in immunosuppressed people

Others: e.g. Epstein-Barr Virus (EBV, Mononucleosis) and Cytomegalovirus (CMV) are not addressed within this guideline

Diagnosis

► **Table 1: Diagnostic Testing²**

Clinical Indication	Lab Requisition Order	Laboratory Tests Performed	Contents
Suspect acute hepatitis: nausea, vomiting, jaundice, anorexia and elevated ALT	Acute viral hepatitis: undefined etiology	Hepatitis A: anti-HAV IgM (if reactive then anti-HAV total or IgG) Hepatitis B: HBsAg, (if reactive then anti-HBc total) Hepatitis C: anti-HCV	<ul style="list-style-type: none"> While hepatitis A infections are part of the differential for acute hepatitis, given the low prevalence of HAV infections in BC, many anti-HAV IgM positive results may reflect false positivity – clinical correlation is required. Anti-HAV IgM reactive specimens are confirmed and reported to public health. Acute HBV infections in BC are rare, most HBsAg positive results reflect chronic infection. Anti-HBc IgM testing is not included in the testing protocol because the sensitivity of current HBsAg assays is such that there usually is no window between the disappearance of HBsAg and serologic evidence of resolved infection. Most acute HCV infections will be anti-HCV reactive within 5 to 10 weeks after exposure.
Suspect chronic viral hepatitis: risk factors, persistent elevated ALT, cirrhosis or liver cancer.	Chronic viral hepatitis: undefined etiology	Hepatitis B: HBsAg, anti-HBs, anti-HBc total Hepatitis C: anti-HCV	<ul style="list-style-type: none"> Chronic hepatitis may or may not be symptomatic. Long-term complications include cirrhosis and liver cancer. ALT may or may not be elevated. If the HBsAg is positive for > 6 months, this confirms chronic hepatitis B infection. If anti-HCV is present, this indicates current or past hepatitis C infection. A HCV RNA needs to be performed to confirm current HCV infection.
Does my patient have immunity to hepatitis A?	Investigation of hepatitis immune status: hepatitis A	anti-HAV total or anti-HAV IgG	<ul style="list-style-type: none"> Testing for vaccine induced HAV immunity is not recommended as the anti-HAV total or anti-HAV IgG can be false negative even though the patient is protected.
Does my patient have immunity to hepatitis B?	Investigation of hepatitis immune status: hepatitis B	anti-HBs	<ul style="list-style-type: none"> The presence of >10 mIU/mL of anti-HBs confirms vaccine induced immunity.* Patients with a resolved HBV infection will typically be anti-HBc total and anti-HBs reactive and HBsAg non-reactive.
Exposed to blood or body fluids: needlestick, sexual assault	Hepatitis B, C and HIV serologies	Test source and exposed persons for hepatitis B and C and HIV	<ul style="list-style-type: none"> Blood should be drawn as soon as possible from both source and exposed person. When an exposure has occurred, send exposed person to the nearest emergency centre immediately. See the BCCDC Blood and Body fluid exposure management protocol. www.bccdc.ca which addresses the risk agents.

* Patients with a history of prior vaccine induced immunity (anti-HBs >10mIU/mL) will be protected from infection when exposed to HBV or display a booster (anamnestic) antibody response when revaccinated. If a resolved HBV infection is a consideration, order an anti-HBc total in addition to an anti-HBs. Occasionally some HBV carriers may be both HBsAg and anti-HBs reactive. These persons should be considered infectious.

► **Table 2: Interpretation of Results**

Test	Positive Result Indicates
<ul style="list-style-type: none"> • ALT elevation 	<ul style="list-style-type: none"> • Hepatocyte injury and can occur in acute or chronic hepatitis and other types of liver disease. Patients with severe cirrhosis may have ALT levels within the normal range.
<ul style="list-style-type: none"> • anti-HAV IgM • anti-HAV total or anti-HAV IgG 	<ul style="list-style-type: none"> • Acute hepatitis A infection. N.B. given the low prevalence of HAV infections in BC, many anti-HAV IgM positive results may reflect false positivity – clinical correlation is required. • If the anti-HAV IgM is non-reactive, a positive result indicates immunity to hepatitis A from natural infection or vaccination.
<ul style="list-style-type: none"> • HBsAg • anti-HBc IgM • anti-HBc total • anti-HBs • HBeAg, anti-HBe, HBV DNA 	<ul style="list-style-type: none"> • Hepatitis B virus infection and infectiousness. • Acute or chronic hepatitis B infection. Rarely required for clinical management. About 20% of chronic HBV infected people display anti-HBc IgM • Antibody to this marker does not imply immunity. • Immunity to hepatitis B, due to vaccination or natural infection. If both anti-HBc total and anti-HBs reactive (and HBsAg is non-reactive) this indicates a resolved hepatitis B infection. • These tests are used to assess disease severity or for treatment eligibility/monitoring and should not be ordered for routine diagnosis
<ul style="list-style-type: none"> • anti-HCV • HCV RNA 	<ul style="list-style-type: none"> • Indicates exposure to hepatitis C. Does not imply immunity, usually represents active infection, confirm status by testing for HCV RNA. • Presence of hepatitis C virus infection.

Diagnosis of HBV infection is usually through serological and virological markers. The incubation period of HBV infection ranges from 1 to 4 months, and has a wide spectrum of clinical manifestations.³

The results of hepatitis B serologic testing and their corresponding interpretation are shown in Table 3.

► **Table 3: Hepatitis B Virology Results**

HBsAg	anti-HBc-total	anti-HBc IgM	anti-HBs	HBeAg	anti-HBe	Interpretation
+	+	+	-			Acute or chronic hepatitis B infection
+	+	-	-	+	-	Likely chronic carrier state; highly infectious
+	+	-	-	-	+	Likely chronic carrier state; infectivity lower
-	+		+			Past hepatitis B infection = immune unless immunosuppressed which can result in reactivation
-	+	-	-			Remote or past hepatitis B or false positive: Resolved infection, probably immune* See the BCCDC Communicable infectious disease manual
-	-	-	+			HBV vaccine induced immunity
-	-	-	-			No evidence of HBV infection*
+	+		+	+/-	+/-	Very rarely patients will display HBsAg, anti-HBc-total & anti-HBs. Such patients are typically chronically infected or may be resolving their infection. They are considered infectious

+ = reactive; - = non-reactive

* patients with these test profiles can be vaccinated for hepatitis B.

Rationale

There were 31 reported cases of hepatitis A in British Columbia in 2009 for an incidence of 0.7 per 100,000. A large proportion of hepatitis A cases continue to be identified in persons who have travelled to countries where hepatitis A is common, but were not immunized prior to travel.⁵ Hepatitis A is usually self-limited, but may be fatal. It does not lead to chronic disease.

In 2009, there were 27 laboratory confirmed cases of acute hepatitis B in British Columbia (0.6 per 100,000).⁵ In contrast, there were 1311 reported cases of chronic or undetermined hepatitis B cases (29.5 per 100,000).⁴ The majority of infections are in persons who have emigrated from a country where hepatitis B is endemic.⁴ Universal hepatitis B vaccine became available in BC for grade 6 students in 1992, and the infant program was introduced province-wide in 2001.⁴

Long-term efficacy and booster policy for hepatitis B vaccines have often been a topic of discussion. Studies of long-term protective efficacy have yet to determine whether booster doses of vaccine are ever needed. However, routine boosters in immunocompetent persons are generally not necessary. Persons who have had a previously demonstrated protective antibody level will not contract the disease when exposed to HBV, whether or not the antibody is still detectable, because immune memory persists. Please see the Public Health Agency of Canada (PHAC), BC Centre for Disease Control (BCCDC) and World Health Organization (WHO) for further information. For current vaccination guidelines please refer to the BCCDC, www.bccdc.ca.

In 2009, a total of 2,444 cases of hepatitis C were reported for a rate of 54.9 per 100,000.⁵ Hepatitis C is usually a chronic slowly progressive disease which may progress to cirrhosis and liver cancer after a few decades. Hepatitis C antibodies are not protective and usually indicate active infection. There is no hepatitis C vaccine.

With the increasing curability of hepatitis C with antiviral therapy and effective hepatitis B antiviral treatments chronically infected hepatitis B or C patients should be considered for referral and treatment. Specific treatments and monitoring are beyond the scope of this guideline.

Hepatitis D and E infections are uncommon in Canada and often in the realm of specialty care.

Resources

► References

- 1 Canadian Blood Services. www.bloodservices.ca c1998-2011 cited 2011 May 30. Available from http://www.bloodservices.ca/CentreApps/Internet/UW_V502_MainEngine.nsf/page/E_Hepatitis?OpenDocument
- 2 Hamilton Regional Microbiology Laboratory Protocol for Viral Hepatitis Testing. September 20, 2010.
- 3 Kao, JH. Diagnosis of hepatitis B virus infection through serological and virological markers. *Expert Rev. Gastroenterol. Hepatol.* 2(4), 553-562 (2008).
- 4 BCCDC Public Health Microbiology & Reference Laboratory, PHSA Laboratories Guide to Programs and Services. September 2010. Available from: <http://www.phsa.ca/AgenciesAndServices/Services/PHSA-Labs/About-PHSA-Labs/BCCDC-Public-Health-Microbiology-Lab.htm>
- 5 British Columbia Centre for Disease Control. BC 2009 Annual Summary of Reportable Diseases. [Annual Report] 2010; Aug 18 Available from: http://www.bccdc.ca/NR/rdonlyres/13B44CDB-740F-4417-90C2-495F6B2424C8/0/2009_CD_Annual_Report_r1.pdf
- 6 Van Damme P, Van herck K. A review of the long-term protection after hepatitis A and B vaccination. *Travel Medicine and Infectious Disease.* 2007. 5, 79-84.
- 7 Public Health Agency of Canada. Canadian Immunization Guide 2006. Available from: www.phac-aspc.gc.ca/publicat/cig-gci/p04-hepb-eng.php#boost

► Resources

- British Columbia Centre of Disease Control www.bccdc.ca
- BC Centre for Excellence in HIV/AIDS www.cfenet.ubc.ca
- Centers for Disease Control www.cdc.gov
- HealthLinkBC www.healthlinkbc.ca
- Public Health Agency of Canada www.phac-aspc.gc.ca

► List of Abbreviations

ALT	Alanine transaminase
CDC	Centre for Disease Control
CMV	Cytomegalovirus
EBV	Epstein-Barr Virus
PHAC	Public Health Agency of Canada
WHO	World Health Organization
HAV	Hepatitis A virus
HBV	Hepatitis B virus
HCV	Hepatitis C virus

This guideline is based on scientific evidence current as of the Effective Date.

This guideline was developed by the Guidelines and Protocols Advisory Committee, approved by the British Columbia Medical Association, and adopted by the Medical Services Commission.

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- encourage appropriate responses to common medical situations
- recommend actions that are sufficient and efficient, neither excessive nor deficient
- permit exceptions when justified by clinical circumstances

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