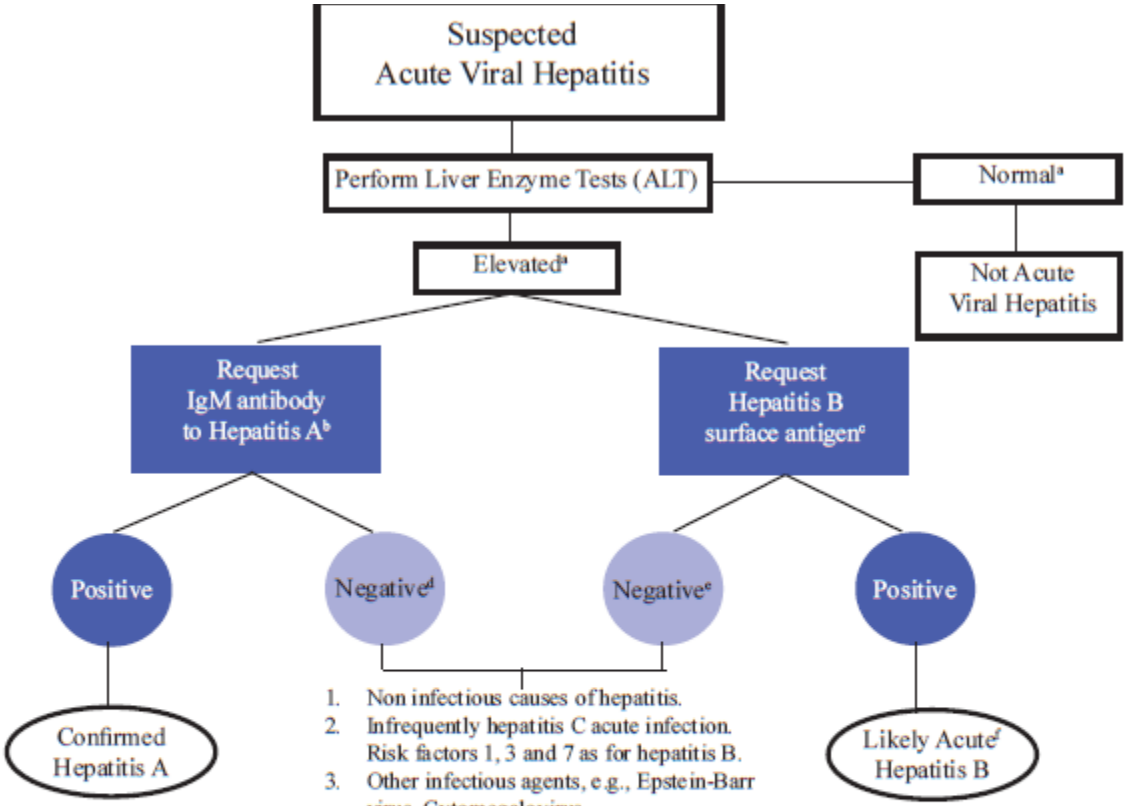
SEROLOGICAL TESTING FOR SUSPECTED VIRAL HEPATITIS

Summary of the Clinical Practice Guideline | January 2006

ALGORITHM FOR SUSPECTED ACUTE VIRAL HEPATITIS



a. • Usually ≥ X5 upper limit of normal in acute viral hepatitis.
   • At the upper limit or mildly elevated.
   - Consider common non-viral causes, e.g., medication, alcohol; **OR**
   - Patient may be in the acute prodromol phase of viral hepatitis

   Consider retesting ALT 2 to 3 days later when values will be significantly higher in acute viral hepatitis. Also consider requesting hepatitis serology at this point if indicated by the clinical history.

b. If hepatitis A alone is being considered, request only anti-HAV IgM.

c. If hepatitis B alone is being considered, request only HBsAg.

d. May be negative in early infection. Repeat test if sample collected within 5 to 7 days of onset of symptoms.

e. Consider requesting IgM antibody to hepatitis B core antigen ONLY if early "window period" is strongly suspected.

f. Retest at 6 months to exclude chronic hepatitis B infection.

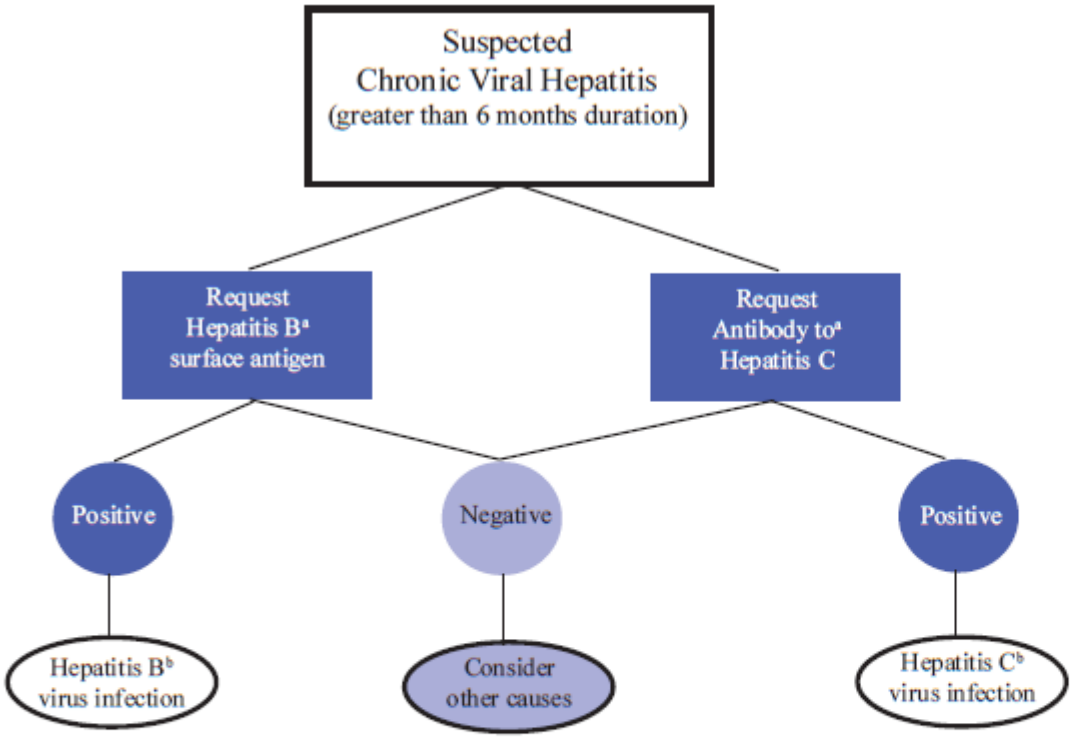
Risk Factors for Hepatitis A

1. Travel
2. Family & daycare contact
3. Poor hygienic circumstances

Risk Factors for Hepatitis B

1. Injection drug use
2. Sexual transmission
3. Percutaneous/permucosal exposure, e.g., Health Care Providers
4. Perinatal transmission
5. Renal dialysis
6. Immigration from endemic region
7. Blood transfusions & blood products
8. Close family contact

ALGORITHM FOR SUSPECTED CHRONIC VIRAL HEPATITIS



a. If hepatitis B or C is suspected, such as after receipt of a letter of notification by the Red Cross, then request HBsAg or anti-HCV as indicated.

b. Further tests may be required to determine extent of liver inflammation and cirrhosis.

Risk Factors for Hepatitis B

1. Injection drug use
2. Sexual transmission
3. Percutaneous/permucosal exposure, e.g., Health Care Providers
4. Perinatal transmission
5. Renal dialysis
6. Immigration from endemic region
7. Blood transfusions & blood products
8. Close family contact

Risk Factors for Hepatitis C

1. Injection drug use
2. Percutaneous exposure, e.g., tattooing and needle stick exposure
3. Blood transfusions & blood products

EXPLANATION OF VIRAL HEPATITIS TESTS

Test Abbreviation	Interpretation of Results and Comments
IgM Antibody to hepatitis A (Anti-HAV IgM or HAV IgM Ab)	• Positive result defines a recent HAV infection • May be negative in early infection (if collected within five to seven days after onset of symptoms) • Present for three to six months after onset of acute infection
Total Antibody to hepatitis A (Anti-HAV or HAV Ab)	• Of extremely limited value in the diagnosis of acute infection • Positive result indicates past infection and immunity to HAV • Individuals given serum immune globulin for HAV prophylaxis may test as positive for at least six months
Hepatitis B surface antigen (HBsAg)	• Used to diagnose an acute or chronic infection • First marker to appear in an acute infection • Disappearance indicates recovery from infection • Persistence for > 6 months indicates chronic infection (carrier) • Individuals tested within 72 hours after administration of the vaccine may test as positive (see anti-HBs, anti-HBc IgM and HBeAg.)
Antibody to hepatitis B surface antigen (Anti-HBs or HBs Ab)	• Only test which can be used to assess presence of protective immunity after immunization with hepatitis B vaccine • Levels of 10MIU/mL (10IU/L) are usually considered protective • Routine monitoring of levels in individuals who have received the complete course of vaccine is not considered necessary[1] • Some individuals, e.g., healthcare workers, who are believed to have been exposed to the virus by a needle injury, should have their anti-HBs levels tested to determine whether they require administration of hepatitis B immune globulin (HBIG) and hepatitis B vaccine booster[1] • Positive result in individuals with recent acute HBV infection • Indicates convalescence • Usually NOT detected when HBsAg is also present • In some cases of chronic hepatitis B infection, both HBsAg and anti-HBs can be detected. These antibodies are heterotypic and likely not protective[2] • Antibody levels may decline with time
IgM antibody to hepatitis B core antigen (Anti-HBc IgM or HBc IgM Ab)	• This test is expensive and should primarily be used if there is a high index of suspicion to indicate that the patient is in the early convalescence “window period” (two to 16 weeks post infection) when HBsAg has disappeared and anti-HBs levels are not yet detectable • Positive result in patients who are also HBsAg positive

Test Abbreviation	Interpretation of Results and Comments
	• Usually indicates acute infection. • Usually detectable for three to 12 months. • Depending upon the threshold level of sensitivity, low levels may be detected in patients with chronic infection and reactivation.[3]
Hepatitis B e antigen (HBeAg)	• Marker of active HBV replication • Also a marker of infectivity. However, the absence of HBeAg in a person who is HBsAg-positive does not imply that the individual is NOT infectious. • Can be used to monitor therapy of patients with chronic HBV infection
Antibody to hepatitis B e antigen (Anti-HBe or HBe Ab)	• Appears as HBeAg disappears • In chronic hepatitis B infection, a positive result indicates resolving or minimal liver disease • However, individuals who are HBsAg-positive and have anti-HBe present must still be considered infectious
Total antibody to hepatitis B core antigen (Anti-HBc or HBc Ab)	• A positive result indicates past infection with hepatitis B virus • Usually persists for life • This antibody is absent in individuals who are immune solely as a result of vaccination • Up to 10% false-positive rate has been described in individuals with no documented infection to HBV. If uncertain, presence of one other marker, e.g., anti-HBs or anti-HBe would confirm previous exposure with HBV. Alternatively a negative repeat test later may indicate an earlier false-positive result.
Hepatitis B viral DNA (HBV DNA)	• Available by special request only. Of very limited value in the diagnosis of HBV infection. • Used to determine the presence of HBV DNA circulating in the blood which is a measure of virus replication in the liver. • Primary use is in monitoring treatment and clarifying some complex situations.
Antibody to hepatitis C (Anti-HCV or HCV Ab)	• Enzyme immunoassay (EIA) tests are the most common screening test used to detect antibody • With present EIA tests, a reactive result may be obtained after eight to 12 weeks to several months following infection with HCV.[4] Earlier generations of EIA tests often gave negative antibody results for up to one year. • False-positive results are found in patients with autoimmune chronic active hepatitis, alcoholic liver disease and other disorders relating to hypergammaglobulinemia • Presence of antibody can be due to acute or chronic infection. It may represent only evidence of an infection with HCV • Presence of antibody does not imply immunity to HCV • Persistently elevated ALT levels suggest chronic infection. Repeatedly normal levels do not exclude chronic infection, but suggest low grade inflammation. • ALT values in some patients with HCV infection are within normal ranges

Test Abbreviation	Interpretation of Results and Comments
Recombinant immunoblot for antibody to hepatitis C (RIBA)	• Supplementary test for the verification of EIA reactive results to HCV • Indeterminate results may be found in early seroconversion, immunosuppressed patients or those unable to mount a completer antibody response. Some of the conditions which give false-positives in the EIA may well give an indeterminate or non-specific result in the RIBA.
Polymerase chain reaction for hepatitis C (PCR for HCV)	• Available by special request only, as it is a research tool • Used to determine the presence of HCV RNA circulating in the blood which is a measure of virus replication in the liver • Can be used to assess the infectivity of the patient and monitor therapy • May be of use in early infection when antibody to the virus is undetectable, and in immunocompromised patients who may not seroconvert • Can be of use in resolving indeterminate RIBA results
Antibody to hepatitis D virus (Anti-HDV or HBV Ab)	• HDV occurs as a co-infection with HBV or super-infection of a chronic HBsAg carrier • Antibodies appear late during the course of acute infection • HDV in uncommon in Alberta
Antibody to hepatitis E virus (Anti-HEV or HEV Ab)	• Routine tests not presently available for detection of this agent • This test may be available by special request only from reference laboratories
ALT (Alanine aminotransferase)	• Liver enzyme test • Used to assess extent of liver inflammation • Can be used to monitor resolution of inflammation following acute or chronic infection

REFERENCES

1. National advisory committee on immunization. Statement on hepatitis B vaccine. CCDR 1993;19-14:104-15.
2. Shiels MT, Taswell HF, Czaja AJ, Nelson C, Swenke P. Frequency and significance of concurrent hepatitis B surface antigen and antibody in acute and chronic hepatitis B. Gastroenterology 1987;93:675-80
3. Sjogren M, Hoofnagle jH. Immunoglobulin M antibody to hepatitis B core antigen in patients with chronic type B hepatitis. Gastroenterology 1985;15:33-40.
4. deMedina M, Schiff ER. Hepatitis C: diagnostic assays. Semin Liver Dis 1995;15:33-40.