(Adapted with permission from BCCDC Communicable Disease Control Hepatitis B Guideline December 2017)

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1.0 AUTHORITY

Yukon Public Health and Safety Act (2009). Available at www.gov.yk.ca/legislation/legislation/page_p.html

2.0 GOAL

To provide prevention and control measures of hepatitis B virus (HBV) infection reported in Yukon by offering a universal infant hepatitis B immunization program for all children less than and equal to 19 years of age, and targeted immunization of all:

- individuals who are at high risk of becoming infected with HBV
- close, non-immune contacts of persons infected with HBV and,

To eliminate perinatal infection through:

- universal screening of all pregnant women for HBsAg prior to delivery
- screening for HBV DNA for pregnant women who are HBsAg and/or HBeAg positive
- consideration of antiviral prophylaxis if mother has a viral load > 200,000 IU/ml
- follow-up of infants born to mothers who are HBsAg positive, to ensure immunized infants are protected, and infants infected with HBV have been identified and engaged into care and followed-up and,
- provide post-exposure immunoprophylaxis as indicated for persons at risk of infection, and education and counselling for infected persons and their contacts.

3.0 DEFINITIONS

Alanine aminotransferase (ALT)/Aspartate Aminotransferase (AST) - Enzymes produced by the liver. Increased levels indicate inflammation of the liver, but do not always correlate with the severity of the disease process.

Anamnestic response – In response to being exposed to an antigen, the rapid reappearance of antibody in the blood an individual who had previously developed a primary immune response. This reflects one's immune memory, which is able to provide long-term protection.

Anti-viral therapy –

- Interferon (IFN) – a type of cytokine with antiviral and immunomodulatory properties
- Nucleos(t)ide Analogue (NA) – oral antiviral treatment

Attribution - Refers to the geographic area for surveillance reporting purposes.

Case Definitions - Defined here for the purpose of surveillance reporting of acute, chronic and unspecified HBV infections

Case Definitions

Acute Case

Case Definition[1]		Reportable to YCDC
Confirmed Case[3]	Hepatitis B surface antigen (HBsAg) and immunoglobulin M antibody to hepatitis B core antigen (anti-HBc IgM) 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 past 6 months in the context of a compatible clinical history or probable exposure.	**Yes**
Probable case	Acute clinical illness[2] in a person who is epidemiologically linked to a confirmed case	**Yes**

Chronic Carrier

Case Definition[1]		Reportable to YCDC
Confirmed Case[3]	HBsAg positive for more than six months **OR** Detection of HBsAg in the documented absence of anti-HBc IgM **OR** Detection of HBV DNA for more than 6 months	**Yes**

Unspecified

Case Definition[1]		Reportable to YCDC
Confirmed Case	Does not fit the definition for either acute or chronic HBV infection AND HbsAg positive OR detection of HBV DNA	**Yes**

[1] Public Health Association of Canada. Hepatitis B. Retrieved from Public Health Association of Canada website: www.phac-aspc.gc.ca/publicat/ccdr-rmtc/09vol35/35s2/Hep_B-eng.php (85)

[2] Acute clinical illness is characterized by a discrete onset of symptoms and jaundice or elevated serum aminotransferase levels (AST). Chronic infections may present with disease flares with similar symptoms and signs.

[3] Even with positive HBsAg and anti-HBc IgM results, a compatible clinical history or probable exposure is necessary. Clients with chronic HBV infection can experience a rise in anti-HBc IgM related to reactivation, or a flare.

Contact - A susceptible individual who has had exposure to potentially infectious blood or body fluids of an HBV infected person. The incubation period for HBV is 45 to 160 days, with an average of 90 days.

Exposure -

- **Percutaneous Exposure -** Contact through the skin with blood of an HBV infected person, for example, through needlestick or other sharp injury, tattooing, body piercing, electrolysis or acupuncture.

- **Perinatal Exposure -** Contact through vertical transmission from mother to infant during the perinatal period. The likelihood of transmission significantly increases when the hepatitis B surface antigen (HBsAg) positive mother is HBV DNA > 200 000 IU/mL.
- **Permucosal Exposure -** Contact through the mucous membrane lining body cavities of an HBV infected person. For example, through a lesion of the eyes, nose, mouth, vagina, rectum or urethra with blood or body fluid.

Flare or acute exacerbation of hepatitis B - Individuals with chronic HBV infection can present with intermittent elevations of aminotransferase activity to more than 10 times the upper limit of normal and more than twice the baseline value. This clinical presentation can mimic that of acute HBV infection (1).

Hepatitis B Immune Globulin (HBIg) - Passive immunoprophylaxis used in combination with hepatitis B vaccine to prevent mother-to-infant transmission and in certain other post-exposure scenarios. Prepared as a solution of hepatitis B Ig for intra-muscular administration. Waning anti-HBs levels can be detected up to 6 months later (2).

Horizontal transmission - Transmission via close person-to-person contact (e.g., household contacts). HBV somehow enters the bloodstream via extended, frequent contact with small cuts or skin rashes (3).

Iatrogenic - Unintentional and unfavourable response to a medical treatment or procedure caused by a healthcare provider.

Immunocompromised - Where the immune response is attenuated and functions at less than normal capacity due to the administration of immunosuppressive therapy, malnutrition or disease processes. Those who have HIV infection and CD4+ cell count ≤ 200 cells/mm ^{3}, chronic kidney disease, or who have been on long-term immune suppressants may not be able to mount a normal antibody response to HBV and should be vaccinated. Immunocompromised individuals with chronic HBV infection can experience reactivation and/or flares. Those with agammaglobulinemia are unable to make their own antibodies.

Liver fibrosis - An accumulation of extracellular matrix proteins that are produced in excess, inefficiently broken down, or both. Normal liver cells are replaced with fibrous tissue and this leads to disruption of the normal liver function. Main causes include chronic HBV or HCV infection, excessive alcohol intake (> 2-3 drinks/day) and non-alcoholic steatohepatitis (NASH), which is associated with obesity, diabetes or metabolic syndrome. Autoimmune hepatitis can also lead to chronic liver inflammation. Symptoms may not be present unless there is severe damage to liver function (4).

May be classified according to a histologic scoring system, such as METAVIR (5):

- F0 = no fibrosis
- F1 = portal fibrosis without septa
- F2 = portal fibrosis with few septa
- F3 = numerous septa without cirrhosis
- F4 = cirrhosis

- **Cirrhosis -** Progression of fibrosis to scarring and disruption of normally functioning structures in the liver. The presence of extensive 'bridging fibrosis' (fibrosis forming bridges between portalvascular structures) on liver histology can confirm this diagnosis. It can be predicted by noninvasive investigations, such as by Fibroscan®. Advanced cirrhosis is supported by marked coagulopathy, portal hypertension, ascites and liver failure (5).

The gold standard for determining the severity of liver damage is liver biopsy.

Non-invasive alternative tools to measure liver fibrosis:

- **Fibroscan® (Transient Elastography) -** Ultrasound method used to detect advanced fibrosis and cirrhosis. A transducer probe mounted on a vibrator transmits vibrations toward the liver. The velocities of the pulse echos that follow the vibrations directly correlate with liver stiffness. These results can be correlated with the METAVIR scoring system. Results can be influenced by hepatic inflammation, obesity (less reliable results in BMI ≥ 25-28 kg/m2), ascites, narrow intercostal spaces, and increased central venous pressure (4, 5).

- **Aspartate Aminotransferase-to-Platelet ratio index (APRI) -** An indirect method used to predict significant and severe fibrosis or cirrhosis. For the upper limit of a normal AST level, most labs use 40 IU/L. APRI score > 1.5 indicates significant fibrosis or cirrhosis, and APRI < 0.7 indicates no significant fibrosis (5)

  For an online calculator, see www.hepatitisc.uw.edu/page/clinical-calculators/apri

- **FIB-4 -** An indirect method used to help with liver fibrosis staging. FIB-4 < 1.45 indicates no significant fibrosis, and FIB-4 > 3.25 is predictive of advanced fibrosis or cirrhosis (5).

  For an online calculator, see www.hepatitisc.uw.edu/page/clinical-calculators/fib-4

Non-responder - After one complete primary hepatitis B series, when someone has anti-HBs < 10 IU/L measured at 1 to 6 months post-vaccination

- 2-series non-responder - After 2 complete hepatitis B series, when someone has anti-HBs < 10 IU/L measured at 1 to 6 months post-vaccination. Individual is considered susceptible to HBV and will require prophylaxis in post-exposure scenarios.

Number needed to treat (NNT) - in the context of post-exposure prophylaxis, the number of people needed to treat with hepatitis B vaccine and HBIg after exposure, in order to prevent one case of HBV infection over a certain time period. This estimate can help provide an indication as to the clinical effectiveness of a particular intervention or treatment.

Occult Blood infection (OBI) - Characterized by a positive HBV DNA (low viral replication) and presence of anti-HBc Total alone, or anti-HBc Total and anti-HBs, in the absence of HBsAg (6).

Post-exposure prophylaxis (PEP) - Hepatitis B vaccine and HBIg can provide susceptible individuals with protection from HBV infection after exposure to HBV in certain scenarios, when given within a certain timeframe. An assessment of the type of transmission event, and if available, the immunization histories and post-vaccination serologic testing of the source and exposed persons, will help guide the decision as to whether or not PEP is indicated.

Reactivation - Increase in HBV replication in an individual with HBsAg-positive chronic HBV infection or resolved HBV infection. HBeAg-negative chronic hepatitis can reactivate following HBeAg seroconversion. Can occur spontaneously or after initiation of immune suppressing therapy (e.g., rituximab, HIV-related immunosuppression), corticosteroid therapy, immune modulation therapy, solid organ transplant or organ transplant recipients (7).

Susceptibility - A person is considered susceptible to HBV if they have no history of a protective antibody level following administration of a complete hepatitis B vaccine series (i.e., anti-HBs level less than 10 IU/L upon completion of vaccine series) OR no history of a test result indicating immunity from prior natural HBV infection

Window period - duration of time between infection and laboratory detection of infection

4.0 HBV CLINICAL DESCRIPTION

Hepatitis B is a small double stranded DNA virus from the Hepadnaviridae family that can cause chronic liver disease (8). HBV is a blood-borne virus that is highly transmissible via perinatal, percutaneous or sexual exposure to a HBV infected person's blood and/or body fluids. Household contacts are also at risk of infection.

HBV infection is most commonly acquired through sexual contact, injection drug use (IDU), and perinatal exposure from mother to infant. The likelihood of progression to chronic HBV infection is inversely related to the age at the time of infection (9). Around 95% of acute HBV infections acquired by immune competent adults will resolve within 6 months and provide lasting immunity, while 10-90% of infants born to mothers testing HBsAg reactive will acquire HBV infection, depending upon the mother's HBV DNA viral load (10-14). The incubation period for HBV is 45 to 160 days, with an average of 90 days.

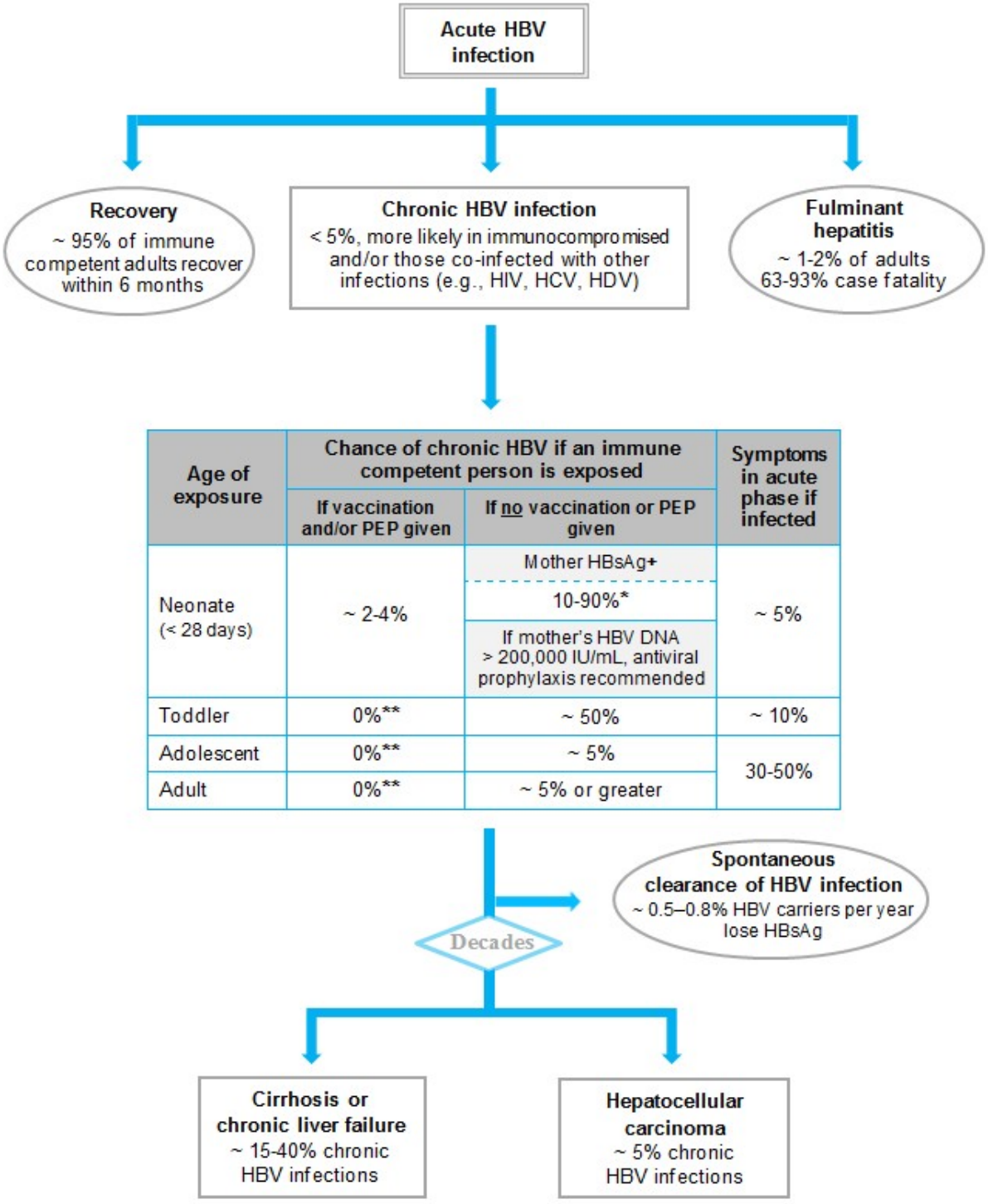
Less than 10% of children and 30–50% of adults with acute HBV infection have symptoms (refer to Figure 1.0) (10, 15). Severity ranges from asymptomatic cases detectable only by serology and liver function tests, to fatal cases of acute hepatic necrosis that have an insidious onset of clinical illness. More likely to occur in older adults and those with prior liver damage, around 1-2% of adults with acute HBV infection will progress to fulminant hepatitis, of which there is a 63-93% case fatality rate (10). Fulminant hepatitis may present as fatigue, jaundice, encephalopathy, ascites and worsening lab results. Individuals with chronic HBV infection who are withdrawing from immunosuppressive therapy, can also experience flares that could lead to fulminant hepatitis.

Chronic HBV infection is a leading cause of liver cancer and liver transplantation in Canada (16). Chronic HBV infection is most often asymptomatic, and this can lead to low rates of testing, diagnosis and reporting (17).

Table 1.0 Symptoms of acute HBV infection (2, 7, 10, 15, 18)

Acute Phase	Symptoms
Viral Replication Phase	• Asymptomatic • Abnormal liver chemistry • Serological HBV markers present
Prodromal Phase (3-10 days)	• Anorexia • Vague right upper quadrant abdominal discomfort • Nausea and vomiting • Fatigue • Malaise • Arthralgia and arthritis • Myalgia • Rash and pruritus • Fever • Headache
Icteric Phase (1-3 weeks)	• Dark urine • Light or gray stools • Jaundice • Hepatomegaly • Splenomegaly (less common)
Convalescent Phase	• Symptoms and jaundice resolve, although malaise and fatigue may persist for months • Liver enzymes return to normal

Figure 1.0: Pathogeneis of hepatitis B infection



Age of exposure	Chance of chronic HBV if an immune competent person is exposed		Symptoms in acute phase if infected
	If vaccination and/or PEP given	If no vaccination or PEP given	
Neonate (< 28 days)	~ 2-4%	Mother HBsAg+ 10-90%* If mother's HBV DNA > 200,000 IU/mL, antiviral prophylaxis recommended	~ 5%
Toddler	0%**	~ 50%	~ 10%
Adolescent	0%**	~ 5%	30-50%
Adult	0%**	~ 5% or greater	

4.1 Chronic Hepatitis B Infection

Differentiating between acute HBV infection and an acute exacerbation of a chronic HBV infection can be difficult, given the similarity in clinical presentation and serological markers. Individuals with acute HBV infection are likely to have had more recent exposures (e.g., sexual exposure), and to be symptomatic. Individuals with chronic HBV infection tend to have histories such as prior blood transfusions and/or family history in HBV endemic areas (i.e., perinatal infection or acquisition in childhood through horizontal transmission). While anti-HBc IgM is used to differentiate between acute and chronic HBV case definitions, it can be present in both acute and chronic HBV clinical scenarios (8, 19).

The phases of chronic HBV infection (refer to Figure 2.0) can vary widely from inactive, with very low levels of HBV DNA virus, to active, with very high or fluctuating levels of HBV DNA virus and liver enzyme levels. Progression through the different phases is not static and can be unpredictable. An individual's chronic hepatitis B status depends on evaluation of serial serology results and histological activity of the liver, in the context of the presenting clinical scenario.

Practitioner Alert

All individuals with chronic HBV infection are potentially infectious, regardless of clinical phase

The concepts of occult blood infection, reactivation and flares are important in understanding the nature of chronic HBV infection, testing, and ongoing transmission concerns. Risk for hepatocellular carcinoma (HCC) and cirrhosis increase during phases of active hepatitis, reactivation and hepatic flares (15).

4.1.1 HBV Occult Blood Infection

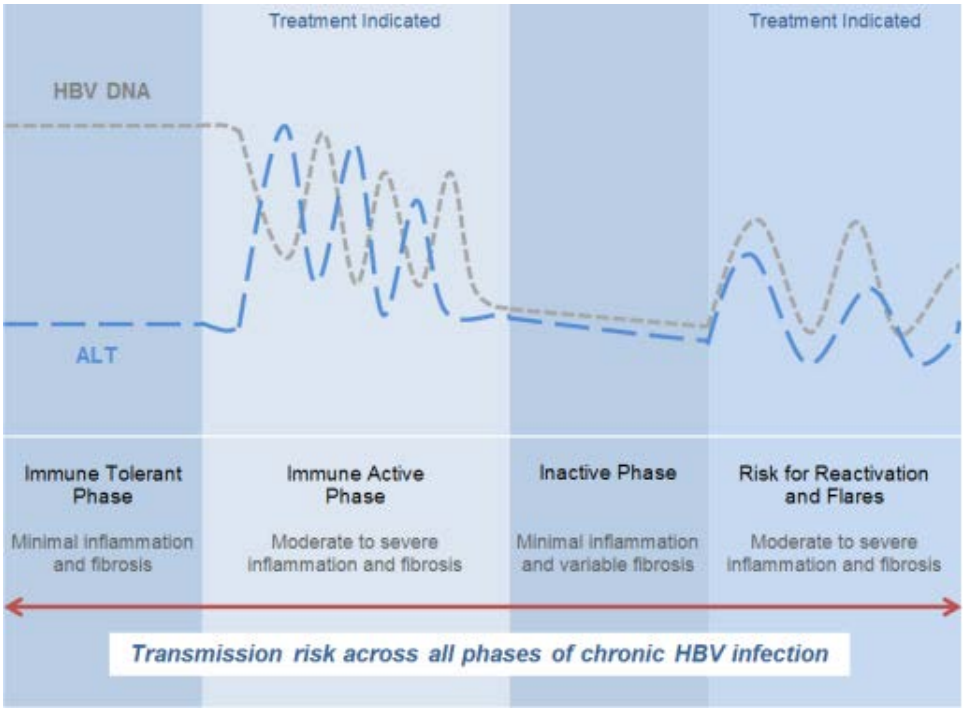
Occult Blood Infection (OBI) is characterized by a positive HBV DNA (low viral replication) and presence of anti-HBc Total alone, or anti-HBc Total and anti-HBs, in the absence of HBsAg (6). This can be seen in around 10% of HBsAg-negative/anti-HBc Total-positive individuals, where low levels of HBV DNA can be transiently detected even after successful HBsAg seroclearance. Infectivity is unclear, however liver disease can still progress in the absence of HBsAg (20-22).

4.1.2 HBV Reactivation

HBV reactivation is the reappearance of active necroinflammatory liver disease after being in an inactive chronic HBV phase or having had a resolved HBV infection (HBsAg loss), and is usually reflected by fluctuating ALT and HBV DNA levels (refer to Figure 2.0) (1). Rates have been reported as high as 50% for HBsAg-positive individuals on chemotherapy for lymphoma, and 25% for anti-HBc Total positive individuals on rituximab, compared to an overall spontaneous reactivation rate of 10-20% in inactive carriers (23, 24).

Reactivation can be prevented in the context of immunosuppressive therapy by screening for all three HBV screening markers (HBsAg, Anti-HBs and Anti-HBc Total) in all individuals, and HBV DNA levels in those with a prior history of HBV infection, before starting immunosuppressive therapy. Prophylactic antiviral treatment can help to decrease HBV reactivation and related hepatitis by 79-100% in certain cases of immunosuppressive therapy (25). Early monitoring of HBV DNA in those with a prior history of HBV infection may also help to detect reactivation in the context of OBI (26).

Figure 2.0: Natural history of chronic HBV infection (15, 24, 27, 28)



4.1.3 HBV Flares

HBV flares describe intermittent elevation of aminotransferase activity to greater than 10 times the upper limit of normal and more than 2 times the baseline value in an individual with chronic HBV infection (1). They can occur spontaneously, but are more often seen in the context of immunosuppression, chemotherapy, immune restoration (e.g., HBV/HIV coinfection) and during or upon completion of antiviral therapy. Symptoms can be absent or can vary from acute hepatitis to hepatic failure. Urgent antiviral therapy is required when HBV flares present in the context of cirrhosis (29).

Practitioner Alert

HBV reactivation or flares can occur in individuals with inactive chronic HBV infection or with HBsAg loss (OBI), if they become immune suppressed, during or upon completion of immunosuppressive therapy, or experience immune restoration.

4.2 Hepatitis B and Coinfections

Coinfection with HIV, hepatitis A (HAV), hepatitis C (HCV) or hepatitis D (HDV) can result in more severe and progressive liver disease. This can include higher rates of cirrhosis, hepatocellular carcinoma (HCC) and mortality. Coinfection is important to consider when evaluating an individual for HBV, as there are similar transmission pathways and clinical features (7, 8).

4.2.1 Coinfection with Hepatitis C Virus (HCV)

Individuals with HCV infection should be tested for HBV disease and immunity at baseline. HCV appears to play a role in interfering with HBV replication, as HBsAg clearance is 2.5 times higher, compared with HBV monoinfection, and HBV DNA levels are often low or undetectable (6, 30). While 25% of individuals with HCV infection will clear the HCV virus, 42% of those with HBV/HCV coinfection at baseline will clear the HCV infection (31, 32). Moderate to severe reactivation of HBV infection has been reported when direct-acting antivirals are used for HCV treatment (1, 7, 30, 33)

4.2.2 Coinfection with HIV

Around 9.8% of individuals with HIV infection in Canada are also coinfected with HBV (35). Compared with HBV monoinfection, coinfection with HIV increases progression of cirrhosis, HCC and liver-related mortality, and can increase HBV DNA levels (36, 37). Initiation of antiretroviral therapy (ART) in the context of advanced HIV disease and HBV coinfection could lead to flares and immune reconstitution syndrome. If ART is stopped and the agents used had anti-HBV activity, HBV reactivation and flares could occur (7, 38).

Individuals with HIV infection should be offered HBV screening at baseline, and those with isolated anti-HBc Total results should have HBV DNA testing to rule out OBI (39).

Refer to Yukon Immunization Program at www.hss.gov.yk.ca/yipm.php for further information on immunization in the immunocompromised. Refer to the Infectious Disease (ID) specialist for further information on screening for HBV infection in individuals with HIV who are non-responders to HBV vaccine.

4.3 Epidemiology

The regions of the world with the highest prevalence of infection are South-East Asia and Africa. Fortunately, twenty years of use of Hepatitis B vaccine in some of these countries has drastically reduced the incidence of Hepatitis B (87).

In Canada, the epidemiology of HBV disease has been considerably modified since the mid-1990's when the infant HBV program was implemented. In Yukon, HBV vaccine is a part of the routine immunization schedule for children. It is provided free to high risk individuals as well as everyone less than and equal to 19 years of age (90). Some provinces and territories provide HBV vaccine coverage for high risk individuals although eligibility varies across the jurisdictions (87). Despite the success of these programs, many may remain at risk of acquiring HBV.

Canada is considered an area of low endemicity. It is estimated that fewer than five per cent of residents have markers of past infection, and less than one per cent are HBsAg carriers. As a result of routine immunization programs in Canada, and increased use of vaccine in all age groups, the incidence of acute HBV has decreased dramatically. Nationally, acute HBV rates have steadily declined from 1.0 to 0.5 per 100,000 between 2005 and 2013. Caution should be used in the interpretation of national rates of chronic infection as multiple jurisdictions do not report or have inconsistent reporting practices

Acute HBV infection is limited in Yukon with only one case of acute HBV infection reported in the past nine years. Yukon began reporting chronic HBV in 2010. The average incidence of chronic hepatitis B per 100,000 population between 2013 and 2017 is 16.06 per 100,000 (91).

4.4 Transmission

HBV is thought to be 50-100 times more infectious than HIV, and more infectious than HCV (15, 46, 47). Blood contains the highest HBV titre of all bodily fluids and is the most important vehicle for transmission, whereas lower levels are found in other body fluids (refer to Table 2.0). In unvaccinated individuals, the risk of sexual or needle stick transmission may be increased if HBV DNA > 1000-2000 IU/mL (7, 48).

HBV can most efficiently be transmitted through perinatal, percutaneous and sexual contact, less so by permucosal contact. All individuals with acute and chronic HBV infection, regardless of which phase, should be considered potentially infectious.

In areas of high HBV endemicity, transmission occurs mainly through perinatal and horizontal transmission. In more industrialized areas, where the occurrence of new HBV infection is low, IDU and high-risk sexual activities are the most common means of transmission. Areas of low HBV prevalence are seeing more individuals with chronic HBV infection via immigration, who require monitoring and treatment, and identification of contacts who are in need of screening for past infection or immunization (49).

Table 2.0 Relative risk of transmission (3, 44-46)

Higher Risk	Lower Risk	Extremely low risk unless blood is present
• Blood • Serous fluid (e.g., pleural, cerebrospinal, synovial, peritoneal, pericardial, amniotic, inflammatory exudates)	• Semen and vaginal fluids (sexual transmission)	• Saliva* • Tears • Feces • Urine • Nasal secretions • Vomitus • Sputum • Sweat

* HBV transmission via casual mucosal contact to saliva that is not visibly contaminated with blood is uncommon. Although HBV has been detected in saliva, reports involving HBV transmission when a HBV-infected person bites (i.e., percutaneous) another person have involved bloody saliva. Blood was more likely the means of transmission, not the saliva (3, 50-52).

Breastfeeding is considered to be safe. If nipples are cracked or bleeding, transmission is plausible; however, given that neonates born to HBsAg positive mothers should be receiving prophylaxis immediately after birth (HBIg, a complete hepatitis B vaccine series, and follow-up post-vaccination serology), this is unlikely (3, 51).

HBV is **not** spread by casual contact such as kissing, hugging, sneezing or coughing, or via sharing food, water, eating utensils or drinking glasses. (3, 51).

Chronic HBV infection is highly stigmatized in some communities. Clear education around risk of transmission, and providing opportunities to address any concerns or fears about HBV transmission, can be crucial to help ensure successful future follow-up and outcomes for some clients.

4.5 Risk Factors and HBV Infection Testing Indications

Effective testing of HBV infection allows for the identification and timely follow-up of those requiring treatment and ongoing care to prevent cirrhosis and HCC, as well as susceptible contacts requiring vaccination. **Given the success of YT's universal vaccination programs and low incidence and prevalence rates of HBV, screening of asymptomatic, non-pregnant adolescents and adults at low risk for HBV infection is not considered beneficial. This approach is consistent with national and international findings (40, 41)**. The decision to screen for chronic infection or immunity should consider risk factors, risk for future exposure, prior testing and vaccination history.

In Canada, the most commonly identified risk factors associated with acute HBV infection are riskier sexual activities and IDU, while 70% of chronic cases are seen in individuals immigrating from high HBV prevalence areas (15). For around 30% of HBV infections, no risk factors can be identified (15).

There are many reasons to screen and/or test for HBV infection, however the decision to do so should be based on a complete history which includes:

- Report of past immunization including documentation in Panorama
- Results of previous testing (including protective antibodies)
- Risk factors for HBV infection
- Last date of testing
- Clinical presentation

Routine screening for HBV infection is not indicated in low-risk populations. Determining immune status should be done only among those individuals where a protective antibody is of great value for potential ongoing and high risk exposures. For further information, refer to Section 5.3, Post Vaccination Serology.

If previous immunity to HBV has been documented, future testing for HBV infection is not routinely recommended. Persons who are non-immune should be tested for HBV infection when ongoing risk factors exist or have occurred since last test. Focus should continue to be immunizing those who are non-immune to prevent future infection while serial testing may be indicated for non-responders or persons with contraindication to HBV immunization who are at ongoing risk.

Testing for HBV infection can be broken into 4 distinct groupings:

1. Testing due to higher exposure risk
2. Testing due to higher susceptibility or significance of infection
3. Testing due to clinical presentation
4. Contact tracing (see Section 9.2.1 Contact Tracing and Disclosure for further discussion)

Table 3.0 Risk factors for HBV infection

Risk factors for HBV infection where testing is recommended (88, 97, 98)	Population
Higher Exposure Risk	• Emigration from or a resident of a country where HBV is endemic defined as high(≥8%) and high moderate (5%-7%) prevalence – see *Map 4-04 Prevalence of Hepatitis B infection* at wwwnc.cdc.gov/travel/yellowbook/2010/chapter-2/hepatitis-b.aspx • High risk sexual behavior (i.e., sex trade work, anal sex, rough sex causing mucosal tearing) • Substance use with sharing of equipment (inhalation or injection), intravenous drug use or past or current inhalation / injection drug use • Sexual partner who is a PWID • Exposure to blood or blood products in endemic regions • Multiple transfusions of blood or blood products prior to January 1972 OR a history of receipt of blood derived coagulation products before January 1972 in Canada • Acupuncture, piercing, tattoos, scarification/body modifications, or any alternative health care that has the potential to break skin, where basic infection control practices have not been used (including while incarcerated) • Use of shared/contaminated medical devices (i.e., glucometers)
Higher Susceptibility or Significance of Infection	• All pregnant women should be routinely tested for HBsAg at the first prenatal visit. If testing has not been done during pregnancy, it should be done at the time of delivery. Repeat testing prior to delivery may be considered for women with ongoing high-risk behaviour. See Section 5.2.1 Perinatal Sera. • HIV infection • HCV, HAV infection • Hepatocellular carcinoma • Known liver disease of other etiology • Chronic renal disease and chronic hemodialysis patients • Solid organ transplant candidate/recipient • Significantly Immunocompromised persons or persons soon to be significantly immunocompromised due to medication (e.g. rituximab,)
Investigation of HBV infection due to clinical presentation	• Abnormal liver biochemistry • Hepatomegaly, splenomegaly, jaundice • Thrombocytopenia • Acute hepatitis (RUQ pain, fatigue, fever, nausea, vomiting, abnormal liver biochemistry, jaundice)

5.0 LABORATORY TESTING

In Yukon, samples for HBV serology are submitted to WGH Laboratory for shipping to BCCDC Laboratory for processing. Ensure all information required on the PHSA Laboratories Serology Screening Requisition form or direct ordering in meditech, is complete including the pertinent history and specific serological panel.

If screening for acute hepatitis infection (A, B & C) *should be used for cases that include* clinical illness and/or recent exposure. The acute panel includes *HBsAg, Anti-HBc Total, Anti-HBs, Anti-HCV, Anti-HAV IgM*. The vast majority of testing should be for chronic infection. The chronic panel includes

HBsAg, *Anti-HBc Total*, *Anti-HBs*, *Anti-HCV*. It is very important to ensure appropriate serological markers are ordered.

When testing for either acute or chronic infection, consider offering an HIV test, as there can be similar risk factors and means of transmission (53).

5.1 Significance of Hepatitis B Serological Markers

There are several HBV markers to consider when testing for HBV infection that vary according to the natural progression of the disease and immunization status. The decision as to which HBV markers to order for initial screening depends upon the indication for screening.

Table 4.0 HBV Serological Marker Interpretation

HBV serological marker	Term	Clinical Correlation
HBsAg	Hepatitis B surface antigen	Detection of acute or chronic HBV infection
Anti-HBs	Antibody to HBsAg	Immunity due to vaccination (may decline to undetectable levels over time) or past infection
Anti-HBc Total (IgM + IgG)	Total antibody to core antigen	• Identifies prior infection with HBV • Not present after immunization • May be falsely positive in areas of low HBV prevalence
Anti-HBc IgM	IgM class antibody to hepatitis B core antigen	Appears early in acute infection, lasting > 6 months • Often present during chronic HBV infection (flares, reactivation) • Requires clinical correlation for interpretation
HBeAg	Hepatitis B e antigen	Indicates viral replication and correlates with higher HBV DNA • Identifies infected individuals at higher risk for transmitting HBV • Not required for routine diagnosis
Anti-HBe	Antibody to HBeAg	• Indicates recovery from acute infection • Identifies infected individuals at lower risk for transmitting HBV • Not required for routine diagnosis
HBV DNA	Hepatitis B DNA viral load	Indicates the magnitude of HBV replication and risk of disease progression • Useful for therapeutic monitoring of chronic HBV infection • Predictor of cirrhosis and HCC development

Figure 3.0 Acute HBV infection with recovery (15, 28, 55-57)

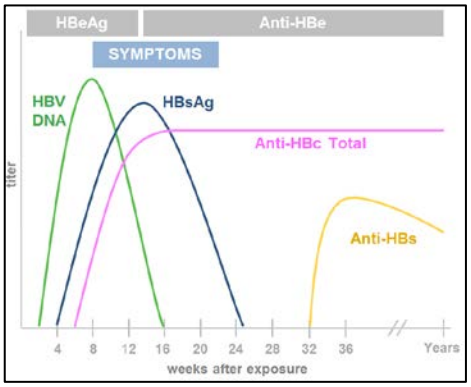
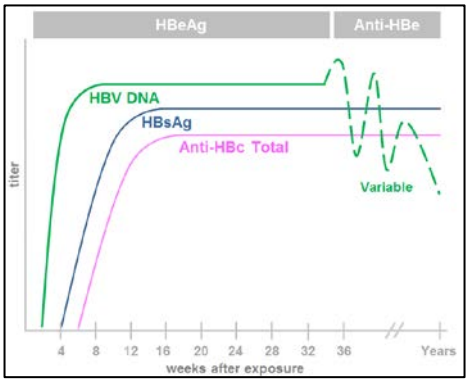


Figure 3.1 Chronic HBV infection (15, 28, 55-57)



5.2 Serologic Testing for HBV in Specific Groups

See Table 3.0 for Risk factors for complete list of groups at risk for HBV infection.

5.2.1 Prenatal Sera

All pregnant women should be screened in the first trimester for the presence of HBsAg during every pregnancy regardless of prior immunization or testing results. It is not necessary to routinely include the other screening tests to detect HBV infection, as anti-HBc Total will be positive in all HBsAg positive individuals (unless in window period) and anti-HBs is rarely positive when HBsAg positive. If testing has not been done during pregnancy, it must be done at the time of delivery.

In the absence of a documented hepatitis B vaccine series, if there are ongoing high-risk behaviors throughout pregnancy (e.g., multiple sex partners, PWID, recent history of STI), anti-HBs, HBsAg and anti-HBc Total is recommended. If susceptible, recommend a complete hepatitis B vaccine series and follow-up post vaccine serology (1 month after the last dose of vaccine) as soon as possible. If the mother refuses vaccination, consider repeating HBsAg later in pregnancy.

5.2.2 Persons from HBV Endemic Countries

Many immigrants and refugees from regions of high HBV endemicity are likely to have been previously exposed through household contact or other travels, as such testing for HBV infection is recommended. While Immigration, Refugees and Citizenship Canada (IRCC) recommends screening adults and children from countries where chronic HBV prevalence rates are greater than 2%, this is **not** a part of the routine immigration medical (1, 42). When a client who is a new immigrant from an high or high moderate HBV endemic country presents with a positive HBsAg and has no recent history of acute symptoms, the likelihood that this individual is a chronic carrier is high.

Persons from high (≥8%) and high moderate (5%-7%) endemic countries to recommend to be

tested for hepatitis B. Refer to Centers for Disease Control and Prevention, Yellow Book, 2014, Chapter 3 Hepatitis B, Map 4-04, (wwwnc.cdc.gov/travel/yellowbook/2010/chapter-2/hepatitis-b.aspx) for identification of specific countries.

Many internationally adopted children come from high Hepatitis B endemic countries. Offer hepatitis B vaccine to adoptive family members prior to the arrival of the adopted child. Screen the child for HBsAg, Anti-HBs, and Anti-HBc; consider repeating these tests six months later (since the virus can have a long incubation period).

Special efforts should be made to test those whose' exposure occurred prior to 7 years of age due to correlation between age of exposure and chronic carrier status.

5.3 Post-vaccination serology

Serology to determine protective status is NOT routinely recommended, however post vaccination serology to determine protective status is recommended in the following situations:

Table 5.0 Indications for post-vaccination testing

Scenario	HBsAg	Anti-HBs	Anti-HBc Total	Notes
Infants (less than 12 months): • Born to known HBsAg positive mother • With a mother who is at high risk for HBV infection (e.g., IDU, STW), but status is unknown at time of delivery • With a father, primary caregiver or household contact who has chronic HBV infection • With a father or primary caregiver who is at high risk for HBV infection	√	√		• Anti-HBc Total testing post-vaccination is not indicated, as high levels of false positives can occur for up to 12 months due to circulating maternal antibody • Accountability mechanisms should be in place to ensure that every infant born to a HBV infected mother receive HBIg, a full course of hepatitis B vaccine, and testing for serologic response to vaccine • Infants who receive hepatitis B vaccine at birth should also be tested 1 month after the last dose of vaccine • Refer to Section 9.3
All pregnant mothers at high risk for HBV infection	√	√	√	• Multiple sex partners, PWID, recent history of STI
Immunocompromised individuals who may be expected to have a lower seroconversion rate	√	√	√	• HIV, hematopoietic stem cell transplant recipients (HSCT), solid organ transplant candidates and recipients • For complete list of immunocompromised individuals eligible for Hepatitis B vaccine, refer to Yukon Immunization Program, Section 5 Immunization of Special Populations www.hss.gov.yk.ca/yipm.php
Chronic liver disease	√	√	√	• Includes anti-HCV positive individuals • While hepatitis B vaccine is as effective in chronic HCV populations as in controls, the response is generally reduced in those clients with cirrhosis (58)
Post-exposure management: • Steady sexual partners and household contacts of persons with acute or chronic hepatitis B infection • Individuals who have had a percutaneous or permucosal exposure to hepatitis B	√	√	√	• Refer to Section 7.0, Yukon Blood and Body Fluid Exposure management for full list and indications.
Health care workers at high risk for continued percutaneous or mucosal exposure to blood or body fluids	√	√	√	• Employees and Employers are responsible for confirming vaccination is complete and documented titres are entered into the Yukon's immunization repository (Panorama).

For more information, see Yukon Immunization Program Section 5- Immunization of Special Populations at www.hss.gov.yk.ca/yipm.php

6.0 INTERPRETATION OF LAB RESULTS AND RECOMMENDED FOLLOW-UP

Testing for hepatitis B is complex and can be confusing. Ensure the correct interpretation is being applied and check for client understanding when reviewing results and follow-up care plans.

The following sections outline specific follow-up recommendations for post-vaccination serology, isolated anti-HBc total results and prenatal HBsAg testing. Various combinations of equivocal/indeterminate HBV lab results can occur. Recommended follow-up will depend on the individual's clinical scenario. Consultation with a health care provider experienced with hepatitis B is recommended.

Table 6.0 Interpretation of HBV screening results

Interpretation	Results						
	Screening Tests			other serological markers			
+ Reactive (positive) - Non-reactive (negative)	HbsAg*	Anti-HBs**	Anti-HBc (total)	Anti-HBc IgM	Anti-HBe ▲	Anti-HBe ▲	HBV DNA
Susceptible, vaccinate	–	–	–	–			
Immune due to vaccination	–	+	–	–			
Immune due to past infection Ω	–	+	+	–			
"Isolated anti-core positive" four interpretations (refer to Section 6.4): 1. False positive anti-HBc Total 2. Resolved past infection 3. Resolving acute HBV infection 4. Occult blood infection	–	–	+	–			
Recent acute infection ("convalescent window" phase)	–	–	+	+			
Acute or chronic infection ϕ	+	–	+	+			variable
Chronic infection, highly infectious	+	–	+	+/–	+/–	+/–	variable
Chronic infection, lower infectivity	+	–	+	+/–	+/–	+/–	variable
Chronic infection, lower infectivity with possible resolution	+	–	+	–	–	–	variable

* HBsAg levels may be falsely elevated for 3-4 weeks after vaccine administration

** Anti-HBs may be reported as IU/L or mIU/mL. These are equivalent units. The international threshold for vaccine-induced immunity is 10IU/L. Anti-HBs may also be passively elevated for 6 months following receipt of HBIg (2, 55).

▲ Not required for routine diagnosis. HBeAg is associated with higher HBV DNA and infectivity.

Ω Potential for reactivation in immune compromised individuals who have previously lost HBsAg

ϕ Clinical correlation required to differentiate between acute and chronic infection

6.1 Reactive HBsAg result follow-up

Individuals testing HBsAg reactive should undergo further evaluation and liver fibrosis assessment (e.g., HBV DNA, ALT and ultrasound). HBsAg levels may be falsely elevated for 3-4 weeks following hepatitis B vaccine administration.

In clinical practice anti-HBc IgM is not routinely recommended to test for when evaluating an acute HBV infection, but is used in current Public Health case definitions. While an anti-HBc IgM non-reactive result is consistent with chronic HBV infection, an anti-HBc IgM reactive (positive) result could indicate either an acute or chronic HBV infection. Clinical correlation is required to differentiate between acute and chronic HBV infection. Some individuals with chronic HBV infection can remain anti-HBc IgM reactive for many years, while others can become anti-HBc IgM reactive during exacerbations of chronic HBV infection (i.e., reactivation).

Refer to Section 8.0 and 9.0 for further follow-up information. If pregnant, refer to Section 6.3.

6.2 Post-vaccination serology follow-up: boosters and re-immunization recommendations

Immune memory persists even when anti-HBs levels decline (< 10 IU/L) over time and become undetectable. Anti-HBs ≥ 10 IU/L is the established international threshold that is correlated with vaccine induced immune protection (when HBsAg and anti-HBc Total negative). If immune competent, the individual is considered to have protection against HBV and will be able to mount an anamnestic response in the development of anti-HBs if challenged with HBV. Routine boosters of hepatitis B vaccine are not required for immune competent individuals (2).

Approximately 5-10% of immune competent individuals are non-responders to a first series of hepatitis B vaccine. Of these, 50-70% will respond to a second series of hepatitis B vaccine. Less than 5% of individuals will not respond after receiving six doses of hepatitis B vaccine. There is no benefit to further vaccinating individuals who have not responded to 2 complete series of hepatitis B vaccine. A non-responder to 2 series of hepatitis B vaccine (whether 2 or 3-dose complete series) will require HBIg post-exposure prophylaxis if exposed to HBV (2, 10).

Timing of post-vaccination serology

Recommendations for anti-HBs post-vaccination serology follow-up, in the context of anti-HBc Total and HBsAg negative results, depends on the length of time between the last dose of hepatitis B vaccine and when post-vaccination serology was done. The timing of post-vaccination serology is important in avoiding unnecessary vaccination and case management follow-up (59).

For further information on Hepatitis B vaccination including the timing of post-vaccination serology, refer to the Yukon Immunization Program Manual at www.hss.gov.yk.ca/yipm.php.

For post-exposure recommendations see Yukon Blood and Body Fluid Exposure Management:

http://www.hss.gov.yk.ca/exposure_management.php.

Practitioner Alert

A documented anti-HBs level ≥ 10 IU/L done 1 to 6 months after the last dose of a complete vaccine series is considered to be protective for life. While anti-HBs levels wane over time, immune memory persists. The absence of detectable anti-HBs in a person who previously demonstrated an adequate level of anti-HBs does not mean lack of protection.

Post-vaccination serology done more than 6 months following the last dose of vaccine requires a different approach to follow-up, as it is difficult to distinguish between those who will be able to mount an anamnestic response, and those who have inadequate immunity.

6.3 Prenatal HBsAg result follow-up recommendations

In Yukon, individuals with a positive HBsAg during pregnancy require referral to the infectious disease specialist who will then determine the appropriateness for antiviral therapy on a case-by-case basis.

The strongest predictor of HBV vertical transmission is maternal serum HBV DNA (60). If HBV DNA > 200,000 IU/mL, antiviral therapy taken during third trimester can improve HBV suppression and decrease the risk of vertical transmission from mother to neonate, compared with HBIg and hepatitis B vaccine alone. The use of telbivudine, lamivudine, and tenofovir antivirals appears to be safe in pregnancy with no increased adverse maternal or fetal outcomes (7, 30, 45, 61, 62).

Refer to Section 9.3 for recommended follow-up care along the prenatal to postnatal continuum

6.4 Reactive anti-HBc Total results (Isolated Hepatitis B Core Antibody)

Based upon the clinical situation and estimated likelihood of infection, there are four possible scenarios to consider when reviewing anti-HBc Total reactive, HBsAg nonreactive results, with anti-HBs undetectable or < 10 IU/L results (refer to Table 7.0). Although Yukon is considered to be a region of low HBV prevalence, there is a high level of immigration from HBV endemic countries. For Yukon residents born in Canada, the most probable reason for this result is a false positive. Among immigrants from endemic countries, the most likely scenario is that of a remotely resolved infection. Most chronic HBV infection cases in Yukon are seen in individuals who have immigrated from HBV endemic countries and in individuals with HIV and HCV infection.

After an acute HBV infection, there may be a gap of several weeks to months, where anti-HBc Total is the only detectable marker of HBV infection, in the absence of detectable HBsAg. This is not likely in a low HBV prevalence area, where the vast majority of HBV cases reflect chronic infections acquired in their endemic country of origin.

Table 7.0 Recommended follow-up for anti-HBc Total reactive, HBsAg nonreactive results, with anti-HBs undetectable or < 10 IU/L result (Isolated Hepatitis B Core Antibody)

Possible Scenario*	Estimated likelihood	Anti-HBs is undetectable	Anti-HBs is detectable, but <10 IU/L
False positive anti-HBc Total	**Most likely scenario in Canadian born in Yukon (YT)**	• **Offer one complete hepatitis B vaccine series** • **No routine follow-up, unless required for work/school** • **If there is ongoing risk of infection, test for anti-HBs 4 weeks after series completion**	
Remote resolved infection, with persistence of anti-HBc Total and waning anti-HBs level	Most likely scenario in YT residents **born in endemic countries.** **More likely to be a true positive if individual has HIV or chronic HCV infection**. If immunosuppressed, reactivation of latent HBV infection with detectable HBsAg can occur.	**Offer one complete hepatitis B vaccine series** • No routine follow-up, unless required for work/school, or beginning immunosuppressive medication • If ongoing risk of infection, test for anti-HBs 4 weeks after series completion	• **No follow-up required unless beginning immunosuppressive medication** • Additional doses of vaccine have not been shown to improve anti-HBs levels • Assure anti-HBc Total is likely a true positive

Resolving acute HBV infection, prior to the appearance of anti-HBs level	Rare, given the high levels of immunizations in YT.	• **If acute HBV infection is suspected**:
		  • Test for anti-HBc IgM (note: anti-HBc IgM can also be positive with chronic HBV infection)
		  • Repeat HBV screening tests (anti-HBc Total, HBsAg and anti-HBs) in 2 to 4 weeks	

Chronic infection, with undetectable HBsAg level (Occult Blood Infection)	Patient may have a low level of viremia and could be infectious.
	Although rare in the general population, this is **more likely to be a true positive if individual has HIV or chronic HCV infection, or is from an endemic HBV area.**
	If immunosuppressed, reactivation of latent HBV infection with detectable HBsAg can occur.
		• If there is evidence of HIV or HCV coinfection, immunosuppression or liver disease, **recommend HBV DNA, and ALT testing**
		• If a chronic HBV infection is present:
		  • Offer hepatitis A, pneumococcal and annual Influenza vaccines
		  • Offer susceptible household and sexual contacts HBV testing and hepatitis B vaccine	

* HIV and HCV testing is recommended in all scenarios, as these results are seen more frequently in the presence of HIV infection or HIV/HCV co-infection

7.0 POST-EXPOSURE HBV PROPHYLAXIS

For post-exposure prophylaxis management, including accidental exposure, refer to the Yukon Blood and Body Fluid Guidelines at www.hss.gov.yk.ca/exposure_management.php.

8.0 CASE IDENTIFICATION

YCDC will investigate all clinically identified and laboratory reports of Hepatitis B infection as soon as possible. For detailed case definition, refer to Section 3.0.

8.1 Case History

Hepatitis B is an infection that is not always easy to classify in terms of its stage. Hepatitis B is not a static infection. The staging of acuity or chronicity has many different patterns.

In order to properly interpret laboratory results, consideration should be given to both clinical and epidemiological information along with laboratory information. Prior immunization history, risk factors and timing of sample collection relative to disease onset are all factors that must be considered in the interpretation of lab results for the purpose of confirming a diagnosis of Hepatitis B.

A person with acute infection should be retested at six months, to determine if they have become a chronic carrier.

8.2 Incubation and Communicability

The period of incubation for Hepatitis B ranges from 45 – 180 days with an average of 90 days.

Determine the period of communicability: ***all persons with a positive HBsAg are potentially infectious***, and blood can be infectious for several weeks before the onset of clinical symptoms. The infectivity of chronically infected individuals varies from high (HBeAg positive) to modest (anti-HBe positive)

8.3 Reporting to YCDC

All cases of Hepatitis B will be reported to Yukon Communicable Disease Control by fax or electronic lab messaging via routine process as per the Yukon Reportable Diseases list, www.hss.gov.yk.ca/pdf/comm_diseases.pdf

When a new case of HBV infection is identified via lab confirmation, YCDC will provide the reporting provider the Case Report Form to be completed and returned to YCDC.

If risk factors indicate the possibility of a transfusion-transmissible infection (where client has been donor or recipient), notify YCDC, who will then provide the appropriate forms to the health care provider for reporting to Canadian Blood Services.

9.0 CASE MANAGEMENT

All persons who are HBsAg positive are potentially infectious. The level of infectivity depends on the HBV DNA levels, with greater risk when levels are above 1000-2000 IU/mL (7, 48).

In Yukon, a medical evaluation is required for referral to the infectious disease specialist who will then determine the appropriateness for antiviral therapy on a case-by-case basis.

The decision to treat a person with chronic HBV include the following criteria: age, serial ALT and HBV DNA levels, as well as severity of disease. The goal of treatment to prevent progression and induce disease regression to minimize liver damage and its complications, including cirrhosis, liver failure, and hepatocellular carcinoma (PHAC, 2013). The presence of co-infections also plays a role in terms of treatment choices.

9.1 New Case Follow-up Overview

If the initial testing provider is unable to provide ongoing care (e.g., a community health nurse or emergency physician) then the ordering provider is responsible for connecting the patient with a health care provider who can provide further clinical evaluation and ongoing care including referral to infectious specialist if chronic infection is identified. Testing should be repeated after 6 months to determine if there is chronic infection.

Comprehensive care should include the following if appropriate:

- Immunization update
- Alcohol harm reduction strategies
- Drug harm reduction strategies (e.g., opioid agonist therapy, naloxone training)
- Mental health and addictions counselling
- STI, hepatitis A and C screening
- General health and education resources (e.g., diet, housing resources)
- Community services and support groups

All new case of HBV should receive counseling from a health care provider on the following topics:

- Hepatitis B transmission and prevention of transmission
- Disclosure and potential stigma
- Contact tracing process including follow-up of household and sexual contacts, including local testing and immunization resources

Refer to Section 6.3 and Section 9.3 if the client is pregnant.

9.1.1 Contact Tracing and Disclosure

Provide newly identified cases of HBV infection with a rationale for the purpose of the interview and provide reassurance regarding privacy and confidentiality. It is recommended that the first health care professional (e.g., community health/primary care provider) who interviews the client discuss contacts, as there may not be another opportunity to do so.

Contact tracing should occur for:

- All Infants borne to HBsAg positive mothers. Refer to Yukon Immunization Program, Immunization of Special Populations, www.hss.gov.yk.ca/pdf/im_manual_section5.pdf for post-vaccination testing details
- Susceptible individuals who had exposure to potentially infectious blood or body fluids (ie, percutaneous, sexual or household contact) of a HBV infected person (HBsAg positive). The incubation period for hepatitis B is 45 to 180 days, with an average of 90 days. Identify any case contacts that fit the criteria outlined below.

For an acute HBV infection:

- Obtain a history of risk factors and potential exposure(s) for the **6 month** period preceding serological diagnosis.
- Identify case contacts in the **6 months** prior to the onset of symptoms, or if asymptomatic, 6 months prior to the date of diagnosis
- Initiate appropriate immunoprophylaxis of contacts.

If the client has a newly identified chronic HBV infection and there is no determination of when acute HBV infection occurred, it is recommended that the testing provider offer screening and vaccination to current household and sexual partners for the **6 months** prior to the chronic status being known.

Counsel susceptible contacts about minimizing further HBV transmission while waiting to determine if they have developed HBV infection. Refer to Section 9.2.2 for Health Teaching to Prevent HBV Infection.

9.1.2 Health Teaching to Prevent HBV Transmission

Counsel cases and case contacts about minimizing further transmission of hepatitis B virus. This may include:

- Informing HCPs (e.g., dentist, physician, nurse) and other providers of personal services whose care involves piercing of the skin (e.g., acupuncturist, tattoo artist) of your infection
- Informing sexual partner(s) and household members to follow-up with their health care provider for HBV testing and hepatitis B vaccine as needed. Protection from infection cannot be ensured until receipt of a complete vaccine series and/or when a protective anti-HBs level has been demonstrated through post-vaccination testing. **Hepatitis B Vaccine is publically funded for all susceptible contacts**.
- If HBsAg positive and pregnant or considering pregnancy, consultation with a specialist is advised to discuss reduction of risk for perinatal transmission. Infants born to HBV-positive women require PEP including HBIg and HBV vaccine to reduce the risk of mother-to-child transmission. See Section 9.3 for more detail.
- Harm reduction education: do not share any drug use equipment (e.g., needles, syringes, cookers, filters, straws or pipes)

- Use latex condoms to reduce the risk of HBV and other STI transmission
- Keep all open cuts and sores covered with a bandage until healed
- Put articles with blood on them (e.g., tampons, pads, Kleenex, dental floss and bandages) in a separate plastic bag before disposing into household garbage
- Disposing of bloody sharp items (e.g., razor blades, needles) into a hard container and tape shut
- Using bleach to clean up blood spills. Wet surfaces with 1-part bleach to 9-parts water and leave sitting for 10 minutes before wiping off. Anything that is "tuberculocidal" will kill HBV. Although not obligated, advise health care providers and anyone who might come into contact with their blood (e.g., during electrolysis, acupuncture, body piercing, and tattooing) of the HBV infection
- Inquire about infection control policies and procedures if engaging in any activities that involve tattooing, body piercing or other percutaneous exposures
- Do not share needles or ink used for tattooing nor needles for body piercing
- Do not donate blood, semen, breast milk, body organs or tissues
- Do not share toothbrushes, dental floss, razors, earrings, glucometers, manicure equipment or any other articles that might have traces of blood
- Do not pre-chew food for babies

Practitioner Alert

HBV infection is **NOT** transmitted by sharing eating utensils, hugging, kissing, hand holding, coughing or sneezing. HBV does not spread via water or food. Individuals who are HBsAg positive can safely:

- share meals and cutlery with others
- participate in all activities, including contact sports
- attend and interact with other children in daycare or school, because of Yukon's universal vaccination program

9.1.3 Breastfeeding

Breastfeeding is considered to be safe with proper immunization of neonates. If nipples are cracked or bleeding, transmission is plausible; however, given that neonates born to HBsAg positive mothers should be receiving HBIg, a complete hepatitis B vaccine series, and follow-up post-vaccination serology, this is unlikely (3, 51).

If electing not to breastfeed while nipples are cracked or bleeding, mothers may consider expressing and discarding breast milk until their nipples are healed to prevent cessation of milk supply. Breastfeeding is not recommended for mothers co-infected with HIV.

9.1.4 Immunizations

In addition to routine vaccinations, the following are recommended for individuals with chronic HBV infection:

- hepatitis A vaccine series, if susceptible
- pneumococcal vaccine and 5 year booster
- annual influenza vaccine

For more information, refer to Yukon Immunization Program Manual at www.hss.gov.yk.ca/yipm.php

9.2 Pregnancy - Perinatal Case Management

BCCDC Laboratory Services provide prenatal screening for Hepatitis B to Yukon. Approximately 40,000 specimens from BC and YT are submitted yearly, with <1% testing positive for HBsAg. All positive specimens are tested for HBeAg, a marker of infectivity.

Results of positive tests are forwarded to the requesting provider, the expected hospital of delivery and YCDC. Results are identified as Prenatal Assessment, and the expected date of delivery is included, if available.

Unimmunized infants born to mothers who are HBsAg positive during pregnancy, have a 10-90% risk of developing HBV infection (10, 13, 14). Around 25% of these infants will go on to develop cirrhosis and HCC (14). In Yukon, clinical practice continues to recommend HBIg and hepatitis B vaccine at birth, in addition to post-vaccination serology for all neonates born to HBsAg positive women (63).

If maternal testing has not been conducted during pregnancy:

- it should be done at the time of delivery
- if maternal HBV status is not available within 12 hours of delivery, serious consideration should be given to administering vaccine and HBIg while the results are pending, taking into account the mother's risk factors and erring on the side of providing vaccine and HBIg if there is any suspicion that the mother could be infected.

When a mother is infected with HBV, testing of the infant for HBsAg and Anti-HBs is recommended one month after completion of the vaccine series to monitor the success of immunoprophylaxis. **Testing for anti-HBc Total is not indicated as maternal core antibodies can also be detected, which is non-diagnostic in this scenario.** If HBsAg is found, the child is likely to become a chronic carrier. If an infant is negative for both HBsAg and Anti-HBs (i.e., a non-responder), additional doses up to a second full course of vaccine should be given, with repeated serologic testing for antibody response.

The benefits of prenatal screening depend on the timely administration of post-exposure prophylaxis. This is dependent upon the timely and accurate transfer of information between the healthcare provider, the delivering hospital, the post-natal care provider and community health (69).

For further information on infants at high risk for Hepatitis B, perinatal protocols for Hepatitis B and a prophylaxis record for infants at high risk of Hepatitis B, see Yukon Immunization Program manual, Section 5, Immunization of Special Populations, Infants at High Risk for Hepatitis B www.hss.gov.yk.ca/pdf/im_manual_section5.pdf

Overview of recommended perinatal HBsAg processes:

1. Prenatal Care

The following should be taken into consideration as part of routine prenatal care:

- Test for HBsAg in first trimester for each pregnancy regardless of prior immunization or testing results
- If there is risk for the acquisition of HBV infection during pregnancy, it is recommended that prenatal providers screen for hepatitis B (HBsAg, anti-HBs and anti-HBc Total) unless there is proof of immunity (i.e., natural HBV infection or immunization)
- It is recommended that prenatal providers offer at risk, susceptible pregnant women a full hepatitis B vaccine series
- Inquiry into HBV infected household or sexual contacts is recommended to determine if a birth dose of hepatitis B vaccine is indicated
- Results of prenatal testing should be routinely forwarded to attending HCP

2. Client Education

All pregnant women with HBV infection should receive counseling from a health care provider about their diagnosis, the implications for the health of their infant, and the required follow-up. Consider giving a copy of the lab result to the mother to facilitate understanding around the care needed, and to help communicate with other members of the health care team. Topics for counseling should include:

- the need for HBV DNA testing in pregnancy and possible referral to a specialist
- post-natal prophylaxis (i.e., HBIg and first dose of HBV vaccine) at birth
- immunization of all susceptible household and sexual contacts
- transmission prevention
- general prenatal and liver health education (e.g., avoid alcohol)

3. Intrapartum care

- Although hepatitis B serology results are included in the Perinatal Record, it is best practice for admitting staff to independently verify hepatitis B lab reports prior to delivery
- If no prenatal HBsAg result is available, arrange for immediate HBsAg testing
- If prenatal HBV antiviral therapy has been initiated, it may be stopped after delivery or may continue past delivery, as per the specialist's prior recommendations
- Give HBIg and hepatitis B vaccine immediately after birth (within 12 hours)
- Document the date of prophylaxis administration in Panorama. If provided in the acute care setting these doses must be communicated to YCDC, client's community health centre and the primary HCP.

4. Post-partum/post-natal care

- Post-discharge, care providers should ensure that HBIg and vaccine were given at birth and entered in Panorama.
- Post-partum, the care plan should be reviewed. This includes:
  - Routine vaccination with hepatitis B vaccine at 2, 4 and 6 months of age
  - Post-vaccination serology 1 month after the last dose of hepatitis B vaccine
- Provide mother a lab requisition for HBsAg and anti-HBs post-vaccine serology. **Anti-HBc Total is not indicated as maternal core antibodies can also be detected, which can cause confusion.**
- If the infant is HBsAg positive, refer the infant to a liver specialist. The neonate will be highly infectious. Immunize susceptible household or close contacts.
- If the infant is HBsAg negative and anti-HBs < 10 IU/L, contact YCDC for further follow-up and management.

10.0 APPENDIX A: Case Studies

YCDC has adapted this guideline from the BCCDC Communicable Disease Control Hepatitis B Guideline, including the below case studies. These case studies were put together with the goal of addressing commonly occurring scenarios and other frequently asked questions. **They are not meant to be prescriptive, as there may be other considerations and alternate recommendations applicable to individual clinical scenarios that are not addressed here.**

Note that throughout the case studies:
Non-reactive = Negative
Reactive = Positive
IU/L = mIU/mL

Case study #1
Isolated core (HBsAg nonreactive, anti-HBc Total reactive, anti-HBs undetectable)

Clinical History/Lab results

Immune competent individual with no prior documented hepatitis B vaccinations or HBV testing, born in Canada.

HBsAg	Nonreactive
Anti-HBs	Undetectable
Anti-HBc Total	Reactive

Explanation

If the individual was born in Canada, this is more likely to be a false positive. If the individual emigrated from an HBV endemic country, this is more likely to be the result of a remote resolved infection with persistence of anti-HBc Total and undetectable anti-HBs level. Such individuals may be at risk of reactivation if immunocompromised.

Recommended follow-up

- Offer one complete hepatitis B vaccine series. No routine follow-up indicated unless there is ongoing risk of infection, or documentation is required for work or school purposes.
- Testing for HIV and HCV is recommended, as isolated anti-HBc Total is more common with HIV, and potentially with HCV infection as well

For further information, refer to:

- Section 6.4 Reactive anti-HBc Total results (Isolated Hepatitis B Core Antibody)
- Section 6.2 Post-vaccination serology follow-up for immune competent individuals

Case study #2
HBsAg nonreactive, anti-HBc Total reactive, anti-HBs detectable but less than 10 IU/L

Clinical History/Lab results:
Immune competent individual with no prior documented hepatitis B vaccinations or HBV testing, born in China.

HBsAg	Nonreactive
Anti-HBs	Detectable, but less than 10 IU/L
Anti-HBc Total	Reactive

Explanation:
If the individual was born in Canada, this is more likely to be a false positive. If the individual immigrated from an HBV endemic country, this is more likely to be the result of a remote resolved infection with persistence of anti-HBc Total and a detectable, but less than 10 IU/L, anti-HBs level. Such individuals may be at risk of reactivation if immunocompromised. Consider HIV or HCV coinfection as a cause of anti-HBs loss.

Clinical history is required to rule out a recently resolved acute infection. Additional doses of vaccine have not been shown to improve anti-HBs levels

Recommended follow-up:
- If symptomatic, or an acute infection is suspected, refer as appropriate and assess for any household contacts that require HBV testing and hepatitis B vaccination
- Test for HIV and HCV
- No further follow-up required unless beginning immunosuppressive medication

For further information, refer to:
- Section 6.4 Reactive anti-HBc Total results (Isolated Hepatitis B Core Antibody)

Case study #3
Anti-HBs detectable, but less than 10 IU/L, after prior vaccination

Clinical History/Lab results
Immune competent individual presents without documentation of any prior hepatitis B vaccinations or HBV testing. Born in 1980, raised in YT, and completed elementary and high school in YT. This individual is a HCP requiring hepatitis B immunization for work purposes.

HBsAg	Nonreactive
Anti-HBs	9.2 IU/L
Anti-HBc	Nonreactive

Explanation
We know that after vaccination, anti-HBs levels will wane and people will be protected from chronic HBV, because they will develop a protective anamnestic immune response. Most people will be protected for multiple decades post-vaccination. If there are on-going risks, a booster of HBV vaccine is recommended.

This detectable, but not protective anti-HBs level is considered to be just at the immune threshold of the internationally accepted anti-HBs protective level of 10.0 IU/L.
When an individual presents without documentation of prior vaccine history, a verbal history of immunization is generally not considered proof of immunity.

Recommended follow-up
Offer one dose of hepatitis B vaccine and repeat anti-HBs in 1 month
- If anti-HBs ≥ 10 IU/L, consider immune. No further hepatitis B vaccination is required.
- If anti-HBs < 10 IU/L, consider a non-responder. Complete a second hepatitis B vaccine series and repeat anti-HBs 1 month after the last dose of hepatitis B vaccine.
- If anti-HBs ≥ 10 IU/L, consider immune. No further hepatitis B vaccination is required.
- If anti-HBs < 10 IU/L, consider a 2-series non-responder and susceptible to HBV infection. If exposed,

individual will require appropriate post-exposure prophylaxis.
For further information, refer to: • Section 5.2 Post-vaccination serology • Section 6.2 for Post-vaccination serology follow-up for immune competent individuals • Yukon Immunization Program Manual, www.hss.gov.yk.ca/yipm.php

Case study #4
Undetectable surface antibody levels after prior vaccination

Clinical History/Lab results:

Immune competent individual presents without documentation of any prior hepatitis B vaccinations or HBV testing. Born in 1980, raised in YT, and completed elementary and high school. This individual is a HCP, requiring hepatitis B immunization for work purposes.

HBsAg	Nonreactive
Anti-HBs	0.9 IU/L (Undetectable)
Anti-HBc Total	Nonreactive

Explanation

If tested at BCCDC PHL, anti-HBs < 3.1 is undetectable. This is below the internationally accepted anti-HBs protective level of 10.0 mIU/mL (or 10.0 IU/L).

In this scenario, the nurse used Panorama to verify that there were no previously documented Hepatitis B immunizations. Ideally, attempts should be made to locate any documentation prior to drawing serology unless there are potential past immunizations but documentation that is not available (ie., immunized in another province or lost records). In the absence of such, the individual is considered susceptible and immunization should commence.

Recommended follow-up

- Provide a complete hepatitis B vaccine series
- If anti-HBs ≥ 10 IU/L, consider immune. No further hepatitis B vaccination is required.
- If anti-HBs < 10 IU/L, consider a 2-series non-responder and susceptible to HBV infection. If exposed, individual will require appropriate prophylaxis.
- Offer an HIV test every time you test for or diagnose hepatitis B

For further information, refer to:

• Section 5.2 Post-vaccination serology
• Section 6.2 Post-vaccination serology follow-up for immune competent individuals

Case study #5
Post-sexual assault follow-up

Clinical History/Lab results

A 24 year old female born in Canada, presented in the ER following a reported sexual assault the night prior. HBIg was not administered at the ER and the client was advised to follow-up with Public Health for hepatitis B vaccinations. The client presented at YCDC one day later. YCDC staff where unable to locate any documentation of prior hepatitis B vaccine. As far as the nurse could tell, this individual appeared to be immune competent. HBV screening tests were ordered.

HBsAg	Nonreactive
Anti-HBs	4.2 IU/L
Anti-HBc Total	Nonreactive

Explanation

Post-exposure prophylaxis is indicated in this scenario. In the case of a sexual assault, or if the source individual is known to have acute or chronic hepatitis B infection, HBIg is indicated to provide passive immunity. In addition, an assessment of the individual's capacity to mount an active immune response to a potential HBV infection is required, in ensuring anti-HBs levels are ≥ 10 IU/L.

As in case study #4, these HBV results could reflect waning immunity or failure of a first complete hepatitis B vaccine series. When an individual presents without documentation of prior vaccine history, it is best practice to consider them susceptible and to immunize as appropriate.

Recommended follow-up

- Refer to Yukon Blood and Body Fluid Exposure Management guideline at www.hss.gov.yk.ca/exposure_management.php
- HBIg should be given as soon as possible, preferably within 48 hours of exposure. Follow Yukon Blood and Body Fluid guideline for process related to release of HBIg. HBIg may be given up to 14 days after exposure.
- Complete one hepatitis B vaccine series and repeat HBV screening tests (HBsAg, anti-HBs and anti-HBc Total) 1 month after the last dose of hepatitis B vaccine, or 6 months after HBIg was given, whichever is longer.
- Assess for the need to test/treat for other sexually transmitted infections and address potential for unwanted pregnancy and forensic involvement (e.g., HIV PEP, CT/GC treatment, managing forensic samples, emergency contraception), and refer as appropriate
- Review follow-up plan with the individual:
    - Dates for remainder of hepatitis B vaccines and post-vaccination serology
    - Document the prophylaxis and immunization in Panorama
    - Provide notification to primary HCP

Connect individual with other appropriate supports (e.g., crisis counselling, advocacy and support)

For further information, refer to:

- Section 7.0 Post-exposure Prophylaxis
- Section 6.2 Post-vaccination serology follow-up for immune competent individuals

Case study #6
Reactivation

Clinical History/Lab results

82 year old male of Korean ancestry received routine HBV testing related to lymphoma in 2017. History of colon cancer and lymphoma.

2013		
HBsAg	Nonreactive	Client asymptomatic. No risk factors. Testing related to colon cancer
Anti-HBs	15 IU/L	
Anti-HBc Total	Reactive	

In 2013, the client was diagnosed and treated for colon cancer. No HBV antiviral prophylaxis was administered.

In 2017, the client was diagnosed and treated for lymphoma. No HBV anti-viral prophylaxis was administered prior to starting treatment.

2017		
HBsAg	Reactive	Client asymptomatic. No risk. No sexual partners in the past 5 years.
Anti-HBs	Undetectable	
Anti-HBc Total	Reactive	
AST	101 (normal < 36) *	
ALT	193 (normal <50) *	

* Normal ranges noted on lab can vary, depending on reporting laboratory

Explanation

In 2013, this individual had evidence of a past HBV infection which had resolved. In 2017, HBsAg converted to reactive, suggesting reactivation of HBV infection. HBV reactivation is more common in the scenario of immunosuppressive therapy (e.g., chemotherapy, biologic therapy) and has been reported when direct-acting antivirals are used for HCV treatment. Further lab testing should be done to confirm this individual's status.

2017	
Hep B DNA	DNA detected
HBsAg	Reactive
Anti-HBs	Undetectable
Anti-HBc Total	Reactive
AST	94 (normal < 36)*
ALT	199 (normal < 50)*

The detection of HBV DNA and persistently elevated liver enzymes in the context of previously cleared HBV infection (i.e., HBsAg nonreactive) is further supportive of HBV reactivation. HBV prophylaxis prior to chemotherapy would have ideally been recommended to help decrease risk for reactivation of HBV infection.

Recommended follow-up

Refer to infectious disease specialist for further follow-up care. This individual will require ongoing clinical assessments (e.g., bloodwork, ultrasounds, Fibroscan®).

Assess for any household contacts that require HBV testing and hepatitis B vaccination

For further information, refer to:

- Section 4.1.2 HBV Reactivation
- Section 4.2.1 Coinfection with Hepatitis C Virus (HCV)
- Section 6.1 Reactive HBsAg result follow-up and Section 6.4 Isolated anti-HBc Total results

Case Study #7
HBsAg reactive, anti-HBc Total reactive and anti-HBs greater than 10 IU/L

Clinical History/Lab results

A 65 year old female China had HBV testing done related to an Immigration Medical Examination (IME). This individual appears to be immune competent and does not have any other medical conditions. Prior history of hepatitis B vaccine or disease is unknown.

HBsAg	Reactive
Anti-HBs	44 IU/L
Anti-HBc Total	Reactive

Explanation

There are a few possible scenarios:

- Most common: This individual is in the process of resolving a HBV infection and mounting an immune response. This is more commonly seen in people from countries where HBV is endemic. Further clinical assessment is required to determine whether this is an acute HBV infection.
- False positive results
- Hepatitis B vaccine was given within the past 3-4 weeks and/or HBIg was given within the prior 6 months.

This individual should be considered infectious.

Recommended follow-up

- Refer to a liver specialist for further assessment. This individual will require additional clinical assessments (e.g., bloodwork, ultrasounds)
- If this individual is symptomatic and an acute infection is suspected, recommend re-testing (HBsAg, anti-HBc Total and anti-HBs) in 1 month
- Assess for any household contacts that require HBV testing and hepatitis B vaccination

For further information, refer to:

- Section 5.0 Laboratory and Testing Information
- Section 5.2 Post-vaccination serology

11.0 APPENDIX B: Patient Education and Counselling

(Adapted from Primary Care Management of Hepatitis B- Quick reference, PHAC, 2013)

For Patients with Acute HBV

- Acute HBV does not require anti-viral treatment
- A follow-up blood test is required 6 months later to determine if the infection has resolved

For Patients with Chronic HBV

Ongoing primary care provider is critical to successful management of this chronic infection.

Reducing the risk of liver damage (fibrosis progression)

- Have liver enzymes monitored every 6-12 months
- Reduce or eliminate alcohol
- Stop smoking, as it increases the risk of liver cancer
- You may drink coffee; 3 or more cups per day may reduce the risk of liver cancer
- Maintain a healthy weight
- Get vaccinated against hepatitis A if you are not already
- Stick to your medication schedule and your regular lab testing and follow-up visits.
- Tell your HCP before starting any immunosuppressive therapy

About medications for patients with cirrhosis

- Avoid aminoglycosides (a type of antibiotic), benzodiazepines and narcotics including codeine (even in cough syrup)
- Whenever possible, avoid ASA or NSAIDs. Acetaminophen, oral contraceptive pills, and statins are safe to use
- Do not drink alcohol
- Treat any infection immediately
- If you require surgery, discuss it with your specialist first
- If you have black stools, call your specialist immediately or go to the ER
- Tell your HCP(s) about any complementary/alternative therapies or over the counter supplements including herbal remedies that you are taking
- Follow your HCP's advice on how frequently you require follow-up including ultrasounds

Living well with HBV

- Stay actively involved in your care plan. It is provided by your HCP to monitor and follow-up on your infection
- Access accurate and up-to-date information on HBV; examples of credible sources include the specialist's office, your family doctor, public health departments, and the Canadian Liver Foundation
- Enjoy physical activities. There are no restrictions on working out or sports, including contact sports
- Eat a healthy diet
- Allow children to go to school or daycare and to play with other children
- Kissing or sharing food/utensils pose no risk for transmission

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