PRIMARY CARE MANAGEMENT OF HEPATITIS B—QUICK REFERENCE

PROTECTING CANADIANS FROM ILLNESS

Public Health Agency of Canada
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LIST OF ABBREVIATIONS

AFP	alpha-fetoprotein
ALP	alkaline phosphatase
ALT	alanine aminotransferase
AST	aspartate aminotransferase
CBC	complete blood count
CMV	cytomegalovirus
CT	computerized tomography
EBV	Epstein-Barr virus
HAV	hepatitis A virus
anti-HBc	hepatitis B core antibody
anti-HBe	hepatitis B e-antibody
anti-HBs	hepatitis B surface antibody
HBeAg	hepatitis B e-antigen
HBIg	hepatitis B immune globulin
HBV	hepatitis B virus
HBsAg	hepatitis B surface antigen
HCC	hepatocellular carcinoma
HCP	healthcare provider
HCV	hepatitis C virus
HEV	hepatitis E virus
HIV	human immunodeficiency virus
HSV	herpes simplex virus
IgG	immunoglobulin G
IgM	immunoglobulin M
INR	international normalized ratio
MSM	men who have sex with men
PCR	polymerase chain reaction
PEP	post-exposure prophylaxis
PT	prothrombin time
RUQ	right upper quadrant
STI	sexually transmitted infection
ULN	upper limit of normal

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INTRODUCTION*

KEY FACTS AND FIGURES

- HBV is a vaccine-preventable disease that is highly infectious—far more so than either HIV or HCV. It is transmitted through perinatal, percutaneous, or sexual exposure to an infected person's blood/body fluids; household contacts exposed to an infected person are also at risk of infection.
- Acute and chronic HBV infections are frequently asymptomatic or present with nonspecific symptoms; about two-thirds of chronically infected people are unaware of their status, and most will only be detected through proactive screening.
- Of those infected as adults, 5% will become chronically infected; in contrast, about 90% of infants infected at birth will develop chronic infection.[1]
- Without intervention, 15%–40% of chronically infected people will go on to develop cirrhosis, end-stage liver disease, and/or HCC.

HBV is a notifiable disease in all provinces and territories in Canada. As such, it must be reported to the regional/local Medical Officer of Health.

EPIDEMIOLOGY OF ACUTE AND CHRONIC HBV IN CANADA

Acute HBV: Canada is a region of low endemicity; however, certain vulnerable populations are disproportionately affected. These include Aboriginal peoples, MSM, street-involved youth, and people who are or have been incarcerated.[2] Peak incidence is among those aged 30–39 years. The most commonly identified risk factors are high-risk sexual activities and injection drug use.

Canada has had universal HBV immunization programs in place since the mid-1990s. All provinces and territories have programs that target children aged 9–13 years, and some have also implemented a neonatal immunization program.[3] In addition, some provinces/territories provide coverage for high-risk individuals, but eligibility varies across jurisdictions (see Module 10). Despite the success of these programs, there may be many who remain at risk of acquiring HBV.

Immunization contributes to disease control by interrupting disease transmission and decreasing the pool of susceptible people. It is essential to identify those at risk who would benefit from receiving the HBV vaccine.

Chronic HBV: It is estimated that less than 1% of Canadians are chronically infected with HBV; in northern regions, serosurveys have documented the prevalence of chronic HBV at 3%–4%.[4, 5] Although the number of studies is limited, data suggest that up to 70% of chronically infected Canadians are immigrants from regions of high endemicity.

Screening immigrants from these regions will identify chronically infected individuals who can benefit from monitoring and medical management (secondary prevention); doing so will also permit vaccination of susceptible contacts, particularly infants and young children who are at risk of developing chronic infection (primary prevention).

There is an urgent need to screen, diagnose, and treat (where appropriate) chronic HBV infection so as to reduce associated morbidity and mortality and to prevent further transmission.

* This *Quick Reference* does not supersede any provincial/territorial legislative, regulatory, policy and practice requirements or professional guidelines that govern and inform the practice of care providers in their respective jurisdictions.

MODULE 1: WHO SHOULD BE TESTED FOR HBV?

In low-risk populations, routine screening for chronic infection or immunity is not recommended. Testing to determine immune status and/or to detect chronic infection is indicated for those at risk of exposure; susceptible people should be immunized.

Clinicians should maintain a high index of suspicion for HBV as infection is frequently asymptomatic; 30% of infections have no identified risk factors.[6]

The decision to screen and the selection of tests should be based on a thorough review of the following:

- ❑ Self-reported HBV immunization history and/or documentation
- ❑ Results of previous testing
- ❑ Presence of risk factors for HBV infection

WHO TO SCREEN

Risk factors for HBV infection (current or past)—screen routinely at first visit:[3,6,7]

- ❑ Birth in a region with intermediate or high endemicity†
- ❑ Infant of HBsAg-positive mother†
- ❑ Exposure before 7 years of age (e.g., child's immediate and/or extended family immigrated from a region of intermediate/high endemicity and/or child visited such a region)†
- ❑ Family history of hepatitis B or hepatoma†
- ❑ Exposure to HBsAg-positive person (e.g., percutaneous, sexual/household contact)‡
- ❑ High-risk sexual activities (e.g., unprotected sex, multiple sexual partners)‡
- ❑ Substance use with sharing of equipment (e.g., injection/inhalation drug use)‡
- ❑ Exposure to blood/blood products in endemic regions without routine precautions/screening†
- ❑ Transfusion recipient/medical procedure in Canada before 1970†
- ❑ Use of shared/contaminated materials or equipment (e.g., instruments/tools used for personal services procedures such as tattooing/piercing/body modifications, or any alternative health care that has the potential to break the skin)‡
- ❑ Use of shared/contaminated medical devices (e.g., glucometers)‡
- ❑ Occupational exposure to blood/body fluids‡
- ❑ Travel to/residence in a region of intermediate/high endemicity‡
- ❑ Incarceration‡
- ❑ Institutionalization (particularly in institutions for the developmentally challenged)‡

Special clinical considerations—screen routinely:

- ❑ Pregnancy
- ❑ HIV or HCV infection
- ❑ Immunocompromised
- ❑ Planned therapy with immunosuppressive/immunoregulatory agents (e.g., rituximab—increased risk of hepatic flares or reactivation of hepatitis B)

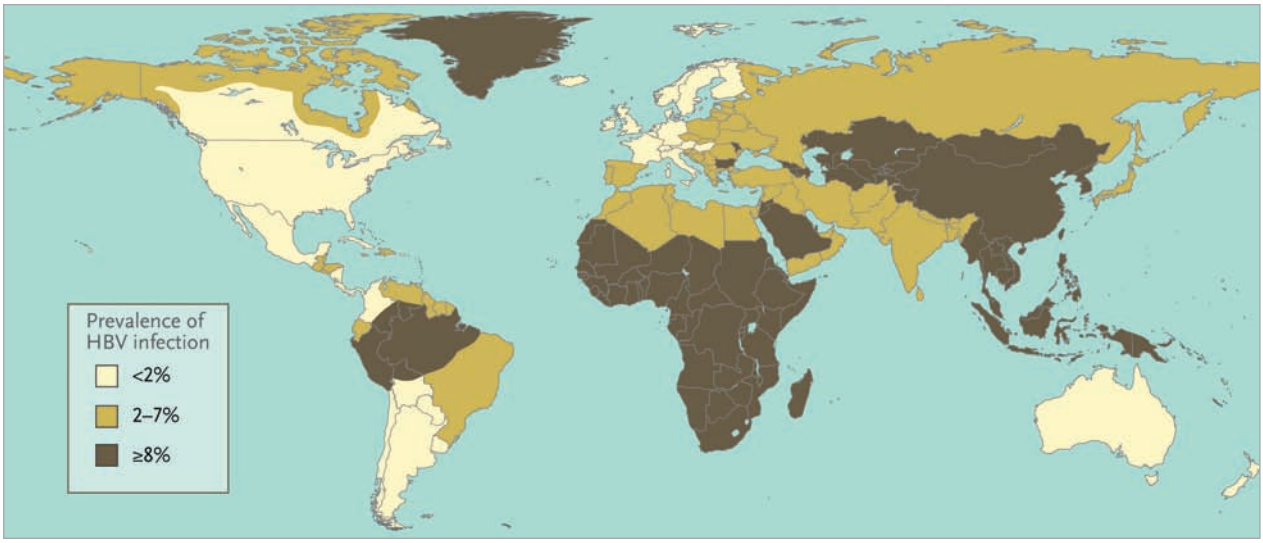
Identification of any risk factor is an indication for screening.

† Most commonly identified risk factors for chronic HBV infection.

‡ Most commonly identified risk factors for acute HBV infection in susceptible individuals; indications for vaccination; consider screening for HIV/STI in select cases.

Individuals born in regions with intermediate or high endemicity are at particular risk of having chronic HBV infection.

WHERE IS YOUR PATIENT FROM?



Reproduced with permission from NEJM 359:14 October 2008[8]

Screening populations at high risk of chronic HBV infection is essential to identify anyone who can benefit from monitoring and treatment.

WHO TO TEST

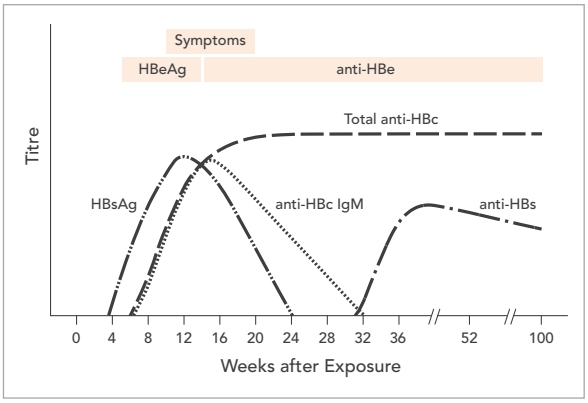
In the absence of any identified risk factors, clinicians should test anyone who presents with any of the following:

- Clinical and laboratory findings suggestive of chronic liver disease:
  - » Abnormal liver biochemistry is usually the only finding
  - » Hepatomegaly, splenomegaly, and jaundice are **late** findings
  - » Thrombocytopenia
- Signs and symptoms of acute hepatitis:
  - » RUQ abdominal discomfort, fatigue, fever, nausea, vomiting, malaise, abnormal liver biochemistry, jaundice, dark urine, rash, arthralgia
- Diagnosis of HCC
- Previous diagnosis of other liver disease

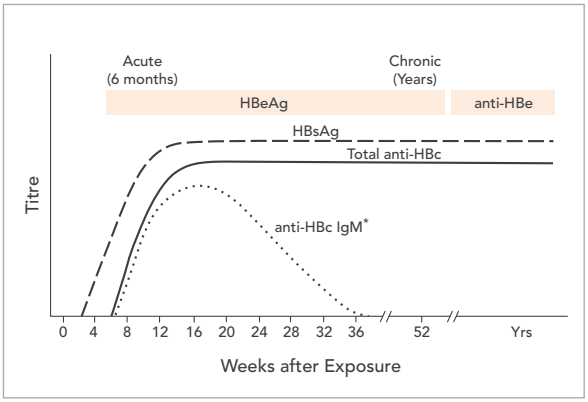
MODULE 2: APPROACH TO HBV SCREENING AND TESTING

OVERVIEW OF HBV SEROLOGICAL MARKERS

Acute HBV with recovery[9]



Chronic HBV[10]



* May reappear during flares of activity

SIGNIFICANCE OF HBV SEROLOGICAL MARKERS

HBsAg (surface antigen) indicates infection. Persistence of HBsAg for 6 months or more indicates chronic infection. However, up to 50% of people with extended chronic infection will eventually clear HBsAg. By contrast, those with resolving acute HBV will clear HBsAg several months after initial infection.

Anti-HBs (surface antibody) is a protective antibody produced with recovery from infection or in response to immunization. Over time, titre may decline to undetectable levels. **NOTE:** There is a gap of several weeks to months between the disappearance of HBsAg and the appearance of anti-HBs; during this period, anti-HBc total is detectable as a marker of HBV infection.

Anti-HBc IgM (core antibody—IgM) appears early in acute HBV infection and persists for about 6 months. It may also be seen in chronic infection during flares of activity, so clinical/epidemiological correlation is required for interpretation.

Anti-HBc total (total core antibody—IgM and IgG) is a marker of past exposure or current infection. IgG usually persists for life. In low prevalence populations, a finding of isolated anti-HBc may signify a false positive result.

HBeAg (e-antigen) is a marker of viral replication; its presence indicates high infectivity. Implications for liver injury vary with stage of infection (see Module 7 for significance).

Anti-HBe (e-antibody) appears with recovery from acute infection. In chronic infection, the presence of anti-HBe is generally a marker of reduced viral replication, indicating a less infectious state. The implications for liver injury vary with stage of infection (see Module 7 for significance).

APPROACH TO TEST SELECTION

The choice of tests should be based on patient history and clinical presentation.

Screening to detect infection or determine immune status[§] in asymptomatic patients at risk of acute or chronic infection:

- HBsAg, anti-HBs
- anti-HBc IgM—in case of recent known or suspected exposure

Baseline screening to assess need for PEP (i.e., immune status unknown and recent high-risk exposure):[**]

- HBsAg, anti-HBs

Screening in patients with defined clinical conditions:

- Pregnancy (in the absence of identified risk factors)
  - » HBsAg at first prenatal visit or at delivery if there is no documented result on file
- Before starting immunosuppressive therapy (e.g., prednisone, azathioprine, chemotherapy, infliximab, rituximab)
  - » HBsAg (plus anti-HBc if to receive rituximab)
- Known HIV or HCV infection[3,11]
  - » HBsAg, anti-HBs, anti-HBc (total)
- Immunocompromised
  - » HBsAg, anti-HBc (total)

Pre-immunization screening of high-risk population:[§]

- HBsAg, anti-HBs

Post-immunization screening[§] for those with ongoing exposure or risk of exposure (e.g., HBV-positive sexual partner, injection drug use):

- anti-HBs

Testing to confirm diagnosis in patients with clinical or laboratory findings consistent with acute hepatitis:

- HBsAg, anti-HCV, anti-HAV IgM

  If these are negative, test for:
  - » HEV, HCV-RNA
  - » Consider other infectious causes (e.g., CMV, EBV, HSV) or non-infectious causes (e.g., hepatotoxic drugs, autoimmune hepatitis, Wilson's disease, vascular causes, or other pre-existing chronic liver diseases)

§ Refer to the *Canadian Immunization Guide (CIG)* or to your provincial/territorial guidelines for a discussion of pre- and post-immunization testing for HBV serologic markers.

** Refer to the *Canadian Immunization Guide (CIG)* or to your provincial/territorial guidelines for recommendations for management and follow-up including PEP.

MODULE 3: INTERPRETATION OF HBV DIAGNOSTIC TEST RESULTS

HBV SEROLOGICAL MARKERS				Interpretation and recommended action
HBsAg	anti-HBs	anti-HBc (total)	anti-HBc IgM	
Negative	Negative*	Negative	N/A	Susceptible Vaccinate
Negative	Positive*,†	Negative	N/A	Immune due to vaccination Counsel as outlined in Module 11
Negative	Positive‡	Positive	N/A	Immune due to previous infection Counsel as outlined in Module 11
Positive	Negative	Positive	Positive§	Infected—acute infection Refer to Module 4 and counsel as outlined in Module 11
Positive	Negative‡	Positive	Negative§	Infected—chronic infection Refer to Module 4 and counsel as outlined in Module 11
Negative	Negative	Positive‖	Negative	Four possible interpretations[12] See below and counsel as outlined in Module 11

* About 5%–10% of people will not respond to the vaccine or else do not produce protective levels of antibody post-vaccination (i.e., ≥ 10 IU/ml).

† Levels of anti-HBs may decline over time and become undetectable.

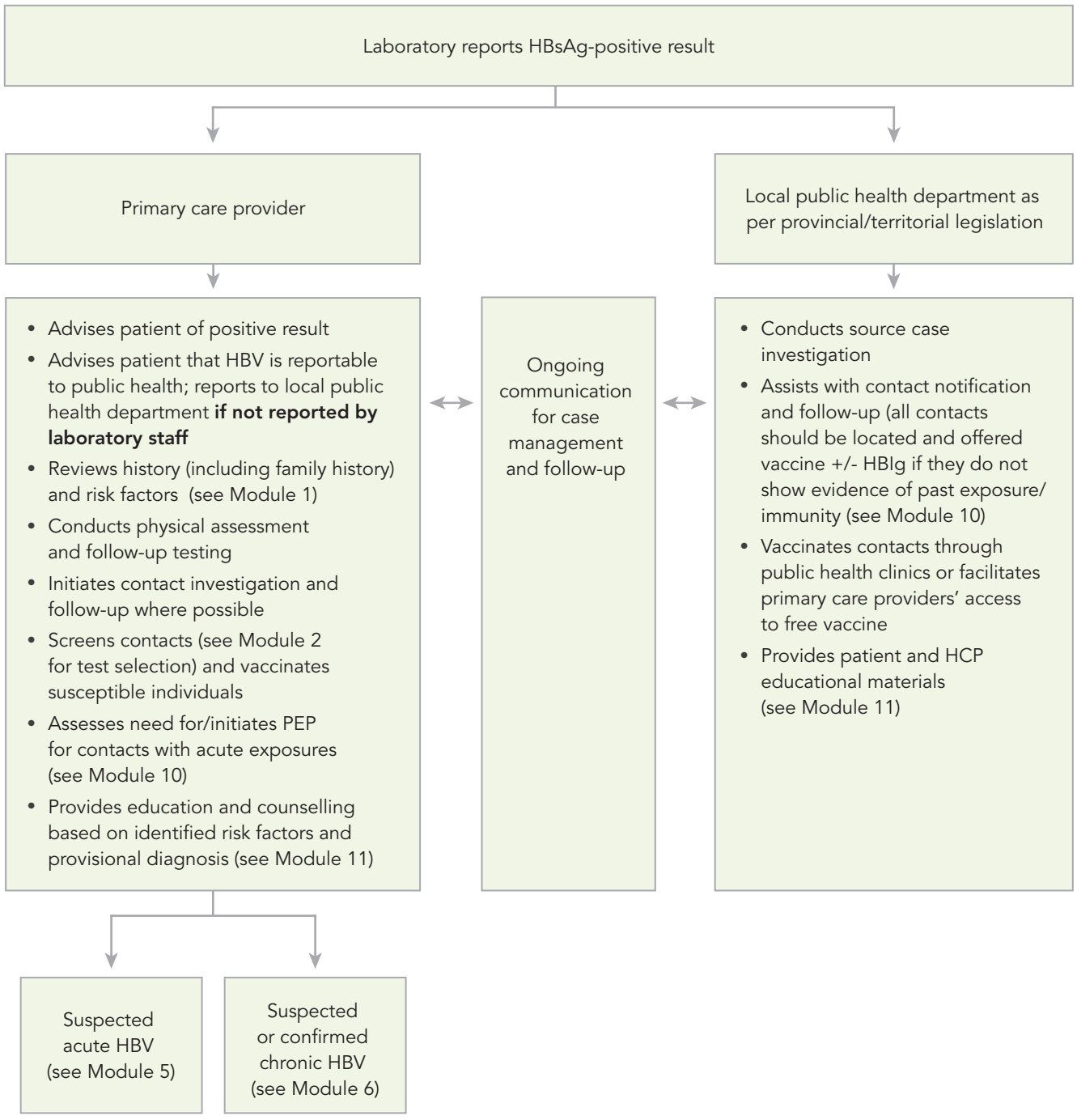
‡ A small percentage of people with chronic infection will have both HBsAg and anti-HBs markers present.

§ Since anti-HBc IgM can be detected in acute HBV, this test may be helpful when acute infection is suspected. It may also reappear in a flare of chronic infection.

‖ On rare occasions, an isolated anti-HBc total will be the only detectable marker. Although there are four possible interpretations for this finding, it is more common in immunocompromised people and in those who are co-infected with HIV or HCV.

- In low prevalence populations this finding is **most often** a false positive result or due to lab error. Repeat test if lab error is suspected.
- Less frequently this finding may reflect
  - » resolving acute infection before the appearance of anti-HBs
  - » natural immunity with undetectable anti-HBs due to a decline in antibody titre over time
- Rarely, this finding may represent a chronic infection with undetectable HBsAg.
  - » Consult a specialist for guidance.

MODULE 4: INITIAL MANAGEMENT OF PATIENTS WITH HBsAg-POSITIVE RESULTS



MODULE 5: NATURAL HISTORY AND MANAGEMENT OF ACUTE HBV

INCUBATION

The incubation period ranges from 45–180 days (average is 60–90 days).[1]

SIGNS AND SYMPTOMS

Whereas infants and children rarely have symptoms, 30%–50% of adults are symptomatic.[1] Symptoms tend to be insidious and can include fatigue, malaise, fever, nausea, vomiting, anorexia, rash, arthralgia, dark urine, and abdominal discomfort. Most will have elevated ALT/AST; a small proportion will develop acute icteric viral hepatitis.

A flare of chronic HBV may present like acute HBV, and should be included in the differential diagnosis.

RESOLUTION TIME AND CLINICAL COURSE OF INFECTION

The majority (95%) of immunocompetent adults will recover within 6 months and develop lifelong immunity; the remainder will be chronically infected. Immunocompromised adults are at particular risk of developing chronic infection. The risk of developing chronic infection is also much higher for those who acquired the infection in infancy (70%–90%) or before 7 years of age (10%–30%).[3,13,14]

Acute HBV does not require antiviral treatment. Management should focus on relief of symptoms, monitoring and prevention of hepatic complications, as well as counselling aimed at preventing transmission. Persistence of HBsAg for 6 months indicates chronic infection.

Baseline laboratory testing to assess liver function and screen for other infections:

- Bilirubin (total and direct), albumin, INR (PT), creatinine
- ALT, AST, ALP
- CBC
- anti-HBc IgM (if not already done)
- Testing for STIs, including HIV, and for HCV, where appropriate
- Repeat HBsAg at least 6 months after baseline, to confirm/rule out chronic infection. (NOTE: symptomatic patients may demonstrate seroconversion and recovery from acute infection at 3 months from baseline). See Module 6 for additional testing recommendations for those with confirmed chronic HBV.

ACUTE HBV WITH SEVERE PRESENTATION

Presentation of acute HBV as fulminant hepatitis is uncommon but can nevertheless be life threatening. Those most at risk include patients with pre-existing chronic liver disease of any etiology. Manifestations include fatigue, jaundice, altered mental status (encephalopathy), and abdominal swelling (ascites).

In patients with chronic HBV infection, spontaneous flares of disease or flares precipitated by withdrawal from immunosuppressive therapy can result in fulminant hepatitis. It is important to maintain a high index of suspicion and watch for signs of impending liver failure (see below).

Indications for urgent and immediate referral to a specialist:

- Worsening symptoms/signs of liver failure (e.g., encephalopathy)
- Laboratory tests indicating deteriorating liver function or liver failure
  - » Elevated or rising INR
  - » Elevated or rising bilirubin
  - » Low or falling platelet count

MODULE 6: INITIAL EVALUATION OF CONFIRMED CHRONIC HBV[2]

Baseline clinical evaluation includes:

- History, particularly risk factors for hepatitis acquisition, and family history of liver disease including HCC
- Physical examination to look for signs of liver failure (e.g., jaundice, ascites, encephalopathy)

Initial laboratory evaluation

- HBeAg/anti-HBe,* quantitative HBV DNA (viral load)*
- ALT,*† AST, ALP, bilirubin (total and direct)
- CBC, albumin, INR (PT)‡
- Creatinine
- anti-HAV (IgG) (vaccinate if negative)
- HIV-antibody testing, if not already done
- HCV-antibody testing, if not already done

Imaging

- Abdominal ultrasound

All patients with chronic HBV should be referred to a specialist at some point.

There are certain situations where referrals should be expedited.

Indications for urgent referral to a hepatologist:

- Signs of liver failure—acute or chronic
- Pregnant patients (HBV DNA detected during pregnancy)
- Imaging results suggestive of HCC

Indications for semi-urgent referral:

- Co-infection with HCV or HIV (refer to a hepatologist or an infectious disease specialist/primary care physician experienced in HIV and hepatitis care)
- Suspected cirrhosis‡ (provide counselling as outlined in Module 11)

* HBeAg status, ALT, and viral load will determine long-term management (i.e., monitoring/consulting versus referral to a specialist for treatment—see Module 8).

† The ULN of ALT for men is < 30 U/L; for women, < 20 U/L. **NOTE: liver injury may be present despite normal ALT**.

‡ **IMPORTANT NOTE: Decreased platelet count (< 150 x 10^9/L) is highly suspicious for cirrhosis even if liver biochemistry is normal.**

MODULE 7: NATURAL HISTORY OF CHRONIC HBV[15,16]

The natural history and progression of chronic HBV is complex and non-linear, and varies from person to person. Familiarity with the natural history can help guide decisions related to treatment and monitoring.

IMMUNE TOLERANT PHASE

The immune tolerant phase is mainly seen in people infected at birth or in early childhood. During this phase, the body does not recognize the virus as foreign. HBeAg is present; HBV DNA levels are high; ALT levels are normal; and hepatic fibrosis is minimal or non-existent. Immune tolerant individuals may stay in this phase for up to 40 years or more before eventually progressing to the immune active phase.

HBeAg-POSITIVE IMMUNE ACTIVE CHRONIC HBV PHASE

Progression to the HBeAg-positive immune active chronic HBV phase occurs when the host immune system recognizes the virus as foreign. During this phase, ALT levels are elevated (sometimes only intermittently); HBV DNA levels are also elevated but not as high as in the immune tolerant phase; and mild to severe liver inflammation with/without fibrosis is found on biopsy. **This phase can be prolonged, which may result in severe liver injury.** Over 5–25 years, 90% of cases seroconvert to e-antibody-positive, which generally represents a transition to the inactive HBsAg phase.[15] Of these, approximately 4% are at risk of seroreversion (i.e., become HBeAg-positive again) with associated flares of activity.[14]

HBeAg-NEGATIVE IMMUNE ACTIVE CHRONIC HBV PHASE (anti-HBe POSITIVE)

Even after seroconversion to anti-HBe, approximately 20% of people remain in the immune active phase due to a mutant form of the virus. Their HBV DNA levels are elevated, although these are not as high as in the HBeAg-positive immune active phase, and ALT is elevated (this may be intermittent). Depending on the host immune response during this phase, liver injury may occur, increasing the risk of progression to cirrhosis and HCC.

INACTIVE HBsAg PHASE

Most people enter the inactive HBsAg phase after they undergo seroconversion to anti-HBe positive. This phase is characterized by an HBeAg-negative status, normal ALT, and low levels of HBV DNA (often undetectable by PCR). **Most individuals (70%–80%) remain in this inactive phase for life.**

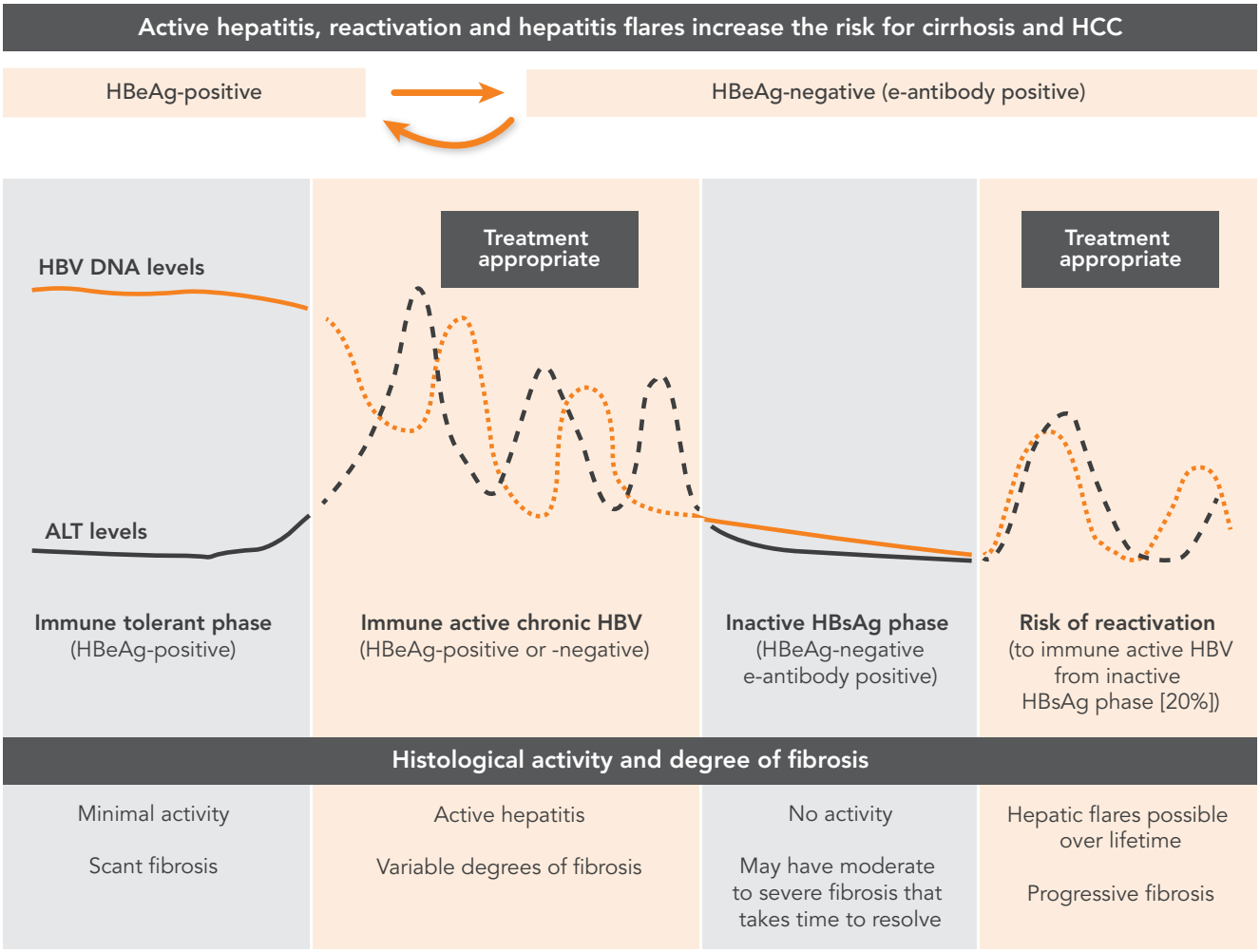
- An estimated 20% risk reactivating to the HBeAg-negative or returning to the HBeAg-positive immune active phase. They can have hepatitis flares over their lifetime, which in turn can lead to cirrhosis or HCC. Either initiation of, or withdrawal from, immunosuppressive therapy may precipitate reactivation.
- Increasing ALT and HBV DNA levels are a sign of reactivation.[17]

HBsAg CLEARANCE

Over many years, 50% of chronically infected individuals who are in the inactive phase will clear HBsAg; of those, most—but not all—will develop anti-HBs. During this phase, individuals who developed cirrhosis pre-clearance and those who do not develop anti-HBs are at increased risk of HCC.

- Reactivation (seroreversion to HBsAg-positive) is possible, although rare. Continued monitoring for reactivation is important for patients who remain anti-HBs negative and particularly for those who are receiving immunosuppressive therapy (e.g. rituximab).[2,18]

Phases of Chronic HBV



MODULE 8: LONG-TERM MANAGEMENT OF CONFIRMED CHRONIC HBV[15]

The goal of managing chronic HBV is to prevent progression to cirrhosis, HCC, and liver decompensation by:

- Monitoring blood work regularly, regardless of phase
- Determining who requires or would benefit from antiviral therapy (see table page 14)
- Monitoring for portal hypertension and evidence of progression to cirrhosis or HCC
- Determining who would benefit from a liver biopsy to assess disease severity (ultrasound will detect most—but not all—cases of cirrhosis).††

The following patients with chronic HBV should have lifelong screening for HCC at 6-month intervals using abdominal ultrasound:

- Any patient with cirrhosis
- Any patient with HIV or HCV co-infection
- People of African descent 20 years of age or older
- Men 40 years of age or older[2]
- Women 50 years of age or older[2]
- Any patient with a family history of hepatoma

Alpha-fetoprotein (AFP) is not an effective screening test for HCC and is not recommended for this purpose. It may be used, along with ultrasound with/without a CT scan, as a follow-up test to monitor patients undergoing treatment for HCC.

†† Non-invasive measures of hepatic fibrosis, e.g., Fibroscan, are being evaluated; they may be available in some jurisdictions.

SUGGESTED FOLLOW-UP BY PHASE OF INFECTION (AS DETERMINED BY SEROLOGICAL AND HISTOLOGICAL FINDINGS)

PHASE	HBeAg	ALT (see Module 6 for ULN)	HBV DNA LEVEL		HISTOLOGICAL ACTIVITY AND DEGREE OF FIBROSIS	SUGGESTED FOLLOW-UP
			IU/ML	$\log_{10}$ (IU/mL)		
Immune tolerant	Positive	Normal	≥ 200,000	≥ 5.3 Usually > 7	Minimal activity and scant fibrosis Close to normal	Biopsy not indicated. Monitor ALT q 6 months. If ALT is elevated for 6 months and is not associated with a drop in HBV DNA, rule out other causes of liver disease and refer to a specialist as treatment may be indicated. **See Module 6 for urgent referral recommendations.**
HBeAg-positive immune active chronic HBV	Positive	Elevated, usually persistently	≥ 20,000	≥ 4.3	Active hepatitis with variable degrees of fibrosis	Treatment may be indicated to prevent severe liver injury. Biopsy may be indicated. Monitor ALT q 6 months. If ALT remains elevated after 6 months of follow-up or if there is any evidence of liver failure, **refer to/consult a specialist for treatment and monitoring recommendations**. **See Module 6 for urgent referral recommendations.**
HBeAg-negative immune active chronic HBV (e-antibody positive)	Negative	Elevated, may fluctuate between normal and abnormal, and may flare intermittently	2000 to ≥ 20,000	Can fluctuate between 3.3 and ≥ 4.3	Active hepatitis with variable degrees of fibrosis	
Inactive HBsAg (e-antibody positive)	Negative	Normal	Often undetectable ≤ 2000	≤ 3.3	No activity, but may have moderate to severe fibrosis that may resolve over time if the disease remains inactive	Biopsy not indicated. Monitor ALT q 6 months. If ALT > 1–2 times ULN, check HBV DNA level and rule out other causes of liver disease. Check HBV DNA annually. **If elevated, refer back to the specialist.**
HBsAg clearance	Negative	Normal	Undetectable in serum; low levels may be present in the liver		No activity, but may already have fibrosis and/or cirrhosis that may slowly resolve	Biopsy not indicated. Monitor ALT q 6 months. Monitor q 6 months for development of anti-HBs; once detected, repeat × 1. HCC surveillance q 6 months is important in those who do not develop anti-HBs and in those who were cirrhotic pre-HBsAg clearance.

MODULE 9: TREATMENT OF CHRONIC HBV AND MONITORING OF PATIENTS ON TREATMENT

The goal of treating chronic HBV is to prevent disease progression and induce disease regression to minimize liver damage and its complications (i.e., cirrhosis, liver failure, and HCC).

The current approved treatments for HBV are interferon injections (standard or pegylated interferon) or oral nucleoside/nucleotide analogues (entecavir, lamivudine, tenofovir). As oral antivirals are excreted by the kidney, dose adjustments are required in renal failure.

Not all patients with chronic HBV infection need to be treated. The decision to treat depends on several factors including age, serial ALT and HBV DNA levels, and severity of liver disease. Co-infection, particularly with HIV and HCV, needs to be considered when deciding on which medications to use.

Treatment should be initiated by a hepatologist **or** other physician with experience in the management of viral hepatitis.

The duration of therapy depends on the type of treatment. Interferon is used for up to 48 weeks; oral antiviral medication is used indefinitely or until the treatment endpoint is achieved (i.e., seroconversion from e-antigen-positive to e-antibody-positive OR loss of HBsAg with seroconversion to anti-HBs). NOTE: Treatment cannot be stopped in organ transplant recipients or infected individuals who require immunosuppressive therapy for another disorder.

All patients being treated for chronic HBV require laboratory monitoring of HBV DNA levels and liver biochemistry every 3–6 months. This is necessary both to assess response to treatment and to permit early detection of resistance to antiviral therapy.

In addition to close, ongoing monitoring of patients on treatment, certain patients require follow-up with a specialist. These include patients:

- who have been treated for HBV in the past
- with cirrhosis with/without liver failure
- co-infected with HIV or HCV
- with a history of renal failure (whether induced by or unrelated to antiviral therapy)
- who are pregnant

For in-depth information on the selection of patients for treatment and treatment options/regimens, refer to the *Management of chronic hepatitis B: Canadian Association for the Study of the Liver consensus guidelines 2012.*[2] These guidelines contain helpful information on selecting treatment regimens and recommendations for on-treatment monitoring.

MODULE 10: PREVENTION AND VACCINATION CHECKLIST

The Public Health Agency of Canada website has information on risk eligibility criteria for publicly funded HBV vaccine‡‡ and routine infant and childhood vaccination programs across Canada by jurisdiction.§§

Contact your local public health department for guidance and information on obtaining publicly funded HBV vaccine.

- ❑ **Review patient records** for history of HBV immunization and adherence to vaccine schedule. See the *Canadian Immunization Guide* (*CIG*)*** or your provincial/territorial immunization guidelines for recommended dosages and schedules.

  NOTE: If a recommended HBV immunization schedule has been interrupted, it is not necessary to restart the series: the missed dose should be given at the earliest opportunity and the schedule completed as per the recommendations.(19)

- ❑ **Assess patient risk factors** for HBV infection in those with no immunization history. (See Module 1 for risk factors and, if identified, screen as per Module 2). Offer vaccine to those without serological evidence of immunity.‡‡,§§

- ❑ **Discuss immunization for infants and children under 7 years of age** who may be at high risk of exposure (e.g., frequent contact with an HBV-positive person and/or travel to an endemic country).‡‡,§§

- ❑ **Assess immune response post-immunization** in previous non-responders to the vaccine who are at risk of repeated exposure or at increased risk of adverse outcomes if they were to acquire HBV infection. Otherwise, assessment of immune response is not generally recommended. See the *CIG*** or your provincial/territorial immunization guidelines for who should be tested and the recommended follow-up for non-responders.

- ❑ **Routinely screen all pregnant women for HBsAg.**

  If negative and at risk of exposure, offer vaccine; HBV vaccine is not contraindicated in pregnancy.‡‡,§§

  ***If positive*, refer to a specialist for assessment before the third trimester of pregnancy.** HBV DNA levels $\geq 10^6$ IU/mL are an indication to initiate treatment during the last 3 months of pregnancy. Treatment can be discontinued early in the postpartum period once the child has received HBIg and the HBV vaccine series.

- ❑ **Ensure follow-up for infants exposed to HBV at birth.**

  All infants born to HBsAg-positive mothers should receive HBIg and the initial dose of HBV vaccine within 12 hours of birth, followed by a second and third dose of the vaccine at 1 and 6 months of age. Ideally, this should be discussed during prenatal visits.

  Post-vaccination serological testing should be done as early as 9 months of age, but no sooner than 1 month after the last dose of vaccine is administered. Testing should take place no more than 4 months after the final dose of vaccine is administered.(20)

‡‡ www.phac-aspc.gc.ca/im/ptimprog-progimpt/table-4-eng.php

§§ www.phac-aspc.gc.ca/im/ptimprog-progimpt/table-1-eng.php

*** www.phac-aspc.gc.ca/publicat/cig-gci/p04-hepb-eng.php

- **Testing for both HBsAg and anti-HBs** is required to assess outcomes. Post-vaccination testing will help to identify:
  - » Susceptible infants, who should be revaccinated and retested
  - » Infected infants, who should be referred to a specialist for continuing medical care.

- **Routinely screen for HBV infection and immunity (HBsAg and anti-HBs) in all individuals** who are immunocompromised/immunosuppressed, are infected with HIV or HCV, or have chronic liver or kidney disease. Also screen those who will be undergoing immunosuppressive therapy (including anti-tumour necrosis factor drugs and rituximab). (See Module 2)

IMMUNE STATUS	RECOMMENDED ACTION
Susceptible	Vaccinate
Susceptible and recently exposed	See the *CIG*[***] or your provincial or terrritorial immunization guidelines for PEP recommendations
HBsAg-positive	Refer to a specialist
Immune	No action required

*** www.phac-aspc.gc.ca/publicat/cig-gci/p04-hepb-eng.php

MODULE 11: PATIENT EDUCATION AND COUNSELLING

Specific Guidance for All Patients to Reduce the Risk of Transmission

- ❑ Inform 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.
- ❑ Do not donate blood, organs, semen, or tissues.
- ❑ Do not share personal hygiene materials/ sharp instruments (e.g., razors, nail clippers, toothbrushes, glucometers).
- ❑ Safely dispose of articles contaminated with blood (e.g., feminine hygiene products, dental floss, bandages, needles, broken glass).
- ❑ Cover all cuts and sores.
- ❑ Clean up blood spills with diluted household bleach (9 parts water to 1 part bleach). Leave the solution on the surface for 10 minutes before wiping it away. If others must clean up blood spills, they should wear protective gloves and wash their hands thoroughly after removing them.
- ❑ Ensure sexual partner(s), household members, and drug use partner(s) are tested and immunized if susceptible. **Hepatitis B vaccine is free for susceptible contacts**.†††
- ❑ Use condoms with all sexual partners until testing shows they are immune.†††
- ❑ Do not share any equipment used to prepare, inject, or inhale drugs (e.g., syringes/needles, spoons, drug solutions, water, wash filters, cookers, pipes, straws, devices for snorting drugs).†††

Pregnant Women and Infants

- ❑ If you are pregnant or considering pregnancy, consult your HCP for advice on reducing the risk of mother-to-child transmission. Pregnant women need to be assessed before their third trimester to see if treatment is indicated.
- ❑ Infants born to HBV-positive women require PEP including HBIg and HBV vaccine to reduce the risk of mother-to-child transmission. **See Module 10 for prevention, vaccination, and follow-up recommendations for infants exposed to HBV at birth**.

For Patients with Acute HBV

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

††† Contact your local public health department for information on the availability of risk reduction and immunization programs in your community.

FOR PATIENTS WITH CHRONIC HBV

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.[21]
- ❑ Maintain a healthy weight.
- ❑ Get vaccinated against hepatitis A if you are not already immune—talk to your HCP or contact your public health department.
- ❑ 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 abdominal 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. See *Canada's Food Guide*,[§§§] which is also available for First Nations/Inuit/Métis.[****] The US Department of Agriculture also has a variety of ethnic/cultural food pyramids.
- ❑ Allow children to go to school or daycare and to play with other children.
- ❑ Kissing or sharing food/utensils pose no risk for transmission.

§§§ www.hc-sc.gc.ca/fn-an/food-guide-aliment/index-eng.php

**** www.hc-sc.gc.ca/fn-an/pubs/fnim-pnim/index-eng.php

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