

Hepatitis B reactivation and screening

1. Why are cancer patients screened for hepatitis B virus (HBV)?

Cancer patients with chronic or prior infection of hepatitis B virus (HBV) are at risk of reactivation following immunosuppressive therapy. The clinical presentation of HBV reactivation (also called a “flare”) can vary from asymptomatic hepatitis to potentially fatal fulminant hepatic failure.^{1,2} In general, the risk of reactivation in hepatitis B carriers undergoing chemotherapy ranges from 20% to 50%, and peaks just after chemotherapy is withdrawn. As the patient recovers from chemotherapy, the immunocompetent cells attack the hepatocytes that became infected during treatment, causing a flare of the HBV disease.² Associated mortality rates have been reported in up to 30% of patients.^{1,3} Risk factors include the type of cancer, degree and type of immunosuppression (i.e. long-term corticosteroid use), selective immunosuppressive medications such as rituximab and fludarabine, and status of the hepatitis B infection.¹ HBV serology testing is used to identify patients at risk for reactivation, and antiviral prophylaxis with lamivudine is recommended for these patients.

2. Who should be screened?

The BC Cancer Agency recommends routine HBV screening for all patients with lymphoid malignancies (including Hodgkin lymphoma, non-Hodgkin lymphoma, myeloma and lymphocytic leukemia) prior to receiving immunosuppressive therapy.⁶ This is because patients with lymphoid malignancies are at particular high risk for reactivation due to their exposure to the immunosuppressive effects of both chemotherapy treatment and their disease.⁴

HBV reactivation has also been reported in some patients undergoing chemotherapy for solid tumours such as breast, lung and gastrointestinal cancers.³ The American Society of Clinical Oncology (ASCO) does not currently recommend routine HBV screening in these patients unless they exhibit other risk factors for reactivation (i.e. born in high/intermediate

HBV endemic regions, HIV carriers, receiving highly immunosuppressive therapy such as hematopoietic cell transplantation, prior parenteral drug abuse and regimens containing rituximab).⁵

3. How do you interpret the results of the Hepatitis B screening tests?

Hepatitis B serology testing can be used to identify patients at risk for HBV reactivation by measuring serum concentrations of HBV-specific antigens and antibodies (see table 1).

HBsAg and HBcoreAb (Anti-HBc) are hepatitis B screening tests required at baseline for [Lymphoma and Myeloma](#) protocols. If either result is positive, antiviral treatment should be started as outlined in the applicable protocol summary. For example, see the **Precautions** section of the [LYCHOP](#) protocol. Different combinations of serology markers are used to determine the clinical status of the hepatitis B infection (see table 2).

Hepatitis B Screening

Table 1. Common Hepatitis B Serology Markers

Marker	Definition	Note
HBsAg	Hepatitis B surface antigen	<ul style="list-style-type: none"> § General marker of Hepatitis B infection § Usually disappears in 4 to 6 months after infection § Persistence for more than 6 months suggests chronic hepatitis B infection
Anti-HBc § IgM anti-HBc § IgG anti-HBc	Hep B core antibody	<ul style="list-style-type: none"> § Confirmed prior exposure to HBV (resolved or acute/chronic infection) § IgM anti-HBc : Acute Hepatitis B infection (usually disappear within 6 months) § IgG anti-HBc: Resolved or chronic Hepatitis B infection
Anti-HBs	Hepatitis B surface antibody	<ul style="list-style-type: none"> § Immunity to Hepatitis B from resolved infection or from vaccination

Table 2. Interpretation of Hepatitis B Serology Test Results

Tests	Results	Interpretation	At Risk For Reactivation
HBsAg	–	Susceptible to future hepatitis infection	No
Anti-HBc	–		
Anti-HBs	–		
HBsAg	–	Immune due to natural infection	Yes
Anti-HBc	+		
Anti-HBs	+		
HBsAg	–	Immune due to hepatitis B vaccination	No
Anti-HBc	–		
Anti-HBs	+		
HBsAg	+	Acutely infected	Yes
Anti-HBc	+		
IgM anti-HBc	+		
Anti-HBs	–		
HBsAg	+	Chronically infected	Yes
Anti-HBc	+		
IgM anti-HBc	–		
Anti-HBs	–		
HBsAg	–	Four Possible Interpretations: 1. Resolved infection ^a (most common) 2. False positive anti-HBc, thus susceptible 3. ‘Low level’ chronic infection ^b 4. Resolving acute infection ^c	Yes
Anti-HBc	+		
Anti-HBs	–		

a After many years of acute hepatitis B recovery, anti HBs may fall to undetectable levels

b After many years of chronic hepatitis B infection, HBsAg may fall to undetectable levels

c May occur in patients with fulminant hepatitis B where virus clearance tends to be more rapid. During this window, HBsAg may disappear while anti-HBs is still not detected. The sole marker that indicates acute hepatitis B infection is the presence of IgM-anti HBc.

4. How do you minimize the risk for Hepatitis B reactivation?

Patients who test positive for either HBsAg or Anti-HBc antibody are at risk for HBV reactivation and should receive antiviral prophylaxis. Lamivudine, a reverse transcriptase inhibitor, is recommended by BC Cancer. The recommended dose is 100 mg daily to be started the week before immunosuppressive therapy and continued for six months after immunosuppressive therapy is completed. In patients undergoing chemotherapy,

lamivudine has been shown to reduce the risk of reactivation by 79% or more when compared to placebo.³ Although resistance against lamivudine is more common than with other reverse transcriptase inhibitors (i.e. adefovir, tenofovir, entecavir), these agents are not considered the standard of care because of the lack of long-term safety data, and are not as cost effective.⁴

Viral load (HBV DNA) and liver function tests should be evaluated at baseline and monitored minimally every 2 months.⁶ Such patients should also be monitored with frequent liver function tests and hepatitis B virus DNA at least every two months. If the hepatitis B virus DNA level rises during this monitoring, management should be reviewed with an appropriate specialist with experience managing hepatitis and consideration given to halting chemotherapy. Lamivudine is a limited coverage benefit under British Columbia PharmaCare, and a Special Authority request can be used to apply for drug coverage.

References: (Oetomo E, Ferrier L. Hepatitis B Screening and Prophylaxis In Cancer Patients. Systemic Therapy Update Newsletter. [2012;15\(1\):7.](#))

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