



Hepatitis B and Primary Care Providers



The role of primary care providers in hepatitis B diagnosis and management

It is essential for primary care providers to play an active role in the testing, diagnosis and management of people with chronic hepatitis B (CHB).

Why?

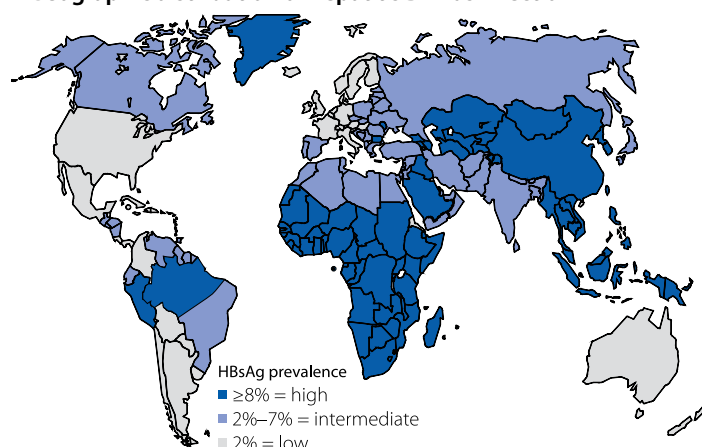
- **1 in 3** people living with CHB in Australia remain **undiagnosed**¹
- Without appropriate monitoring or treatment, up to **1 in 4** people with CHB **will die from** liver cancer or liver failure²
- Recent international evidence suggests **appropriate treatment** for CHB can reduce the risk of liver cancer by over 50%³
- Hepatitis B is a **vaccine-preventable** disease

How can primary care providers make a difference?

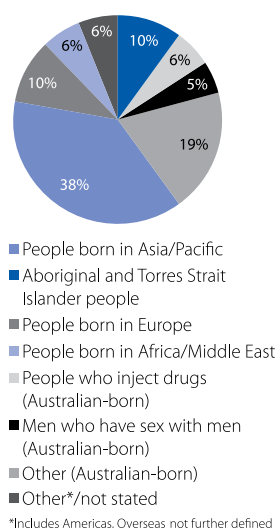
- **Opportunistically test** people from priority populations for hepatitis B
- Correctly **monitor** people with CHB to assess for phase of disease and **manage** or **refer** accordingly
- Identify when a patient should be referred for **consideration of treatment**
- **Test and vaccinate people susceptible to infection**, especially family members (parents, siblings, children), household contacts and sexual contacts of people with hepatitis B

Who has chronic hepatitis B?

Geographic distribution of hepatitis B virus infection²



Estimates of CHB distribution in Australia⁷



Globally?

Hepatitis B virus (HBV) is one of the world's most common infectious diseases. In 2008, the World Health Organization published figures estimating 2 billion people had been infected with HBV and 350–400 million were living with CHB. Worldwide, over 600,000 people die each year due to CHB complications.⁵

The world has been categorised into three areas according to the prevalence of CHB infection: high (>8%), intermediate (2–7%) and low (<2%).⁵ Many Australian migrant populations come from high and intermediate countries, including Asia, the Pacific and Sub-Saharan Africa.

In Australia?

It is estimated that approximately 200,000 people in Australia have CHB.⁶ Most newly reported infections are CHB in people who were infected at birth or in childhood.

70% of people living with CHB come from two priority populations:

1. People born overseas in countries with intermediate or high HBV prevalence

Estimates of the prevalence of chronic hepatitis B in people from overseas living in Australia are generally consistent with their country of origin.⁷ In high prevalence countries, this can be between 8–20%.^{5,8} The number of people in Australia living with CHB will continue to increase, despite universal infant vaccination being in place nationally since 2000, predominantly through migration from high prevalence areas, particularly the Asia-Pacific region.

2. Aboriginal and Torres Strait Islander people

17,000–22,000 Aboriginal and Torres Strait Islander people are estimated to be living with hepatitis B in Australia, representing 3–4% of all Indigenous Australians, compared with a prevalence of <0.5% of non-Indigenous Australians born in Australia. Aboriginal and Torres Strait Islander people make up 2.6% of the Australian population, yet account for 10% of Australians living with CHB.

Who do I test for hepatitis B?

Opportunistic testing of people at risk, particularly

- people born in intermediate and high prevalence countries and
- Aboriginal and Torres Strait Islander people.

will reduce the number of people with CHB who are undiagnosed and subsequently reduce the mortality and morbidity caused by hepatitis B.

Other patients whose HBV status should be determined include:

- pregnant women, due to the need to intervene to prevent vertical transmission;
- adults at increased risk of transmission including sexual and household contacts and family members of people with hepatitis B, men who have sex with men, people who inject drugs, people with multiple sexual partners (including sex workers) and haemodialysis patients;
- people living with hepatitis C or HIV infection, due to both increased risk factors and the presence of co-infection altering prognosis and treatment;
- patients about to commence chemotherapy or immunosuppressive therapy as patients with past or present hepatitis B infection may develop a life-threatening flare of HBV on reconstitution of the immune system;
- people with clinical presentation of liver disease and/or elevated alanine transaminase (ALT) / alpha fetoprotein (AFP) of unknown aetiology;
- health professionals who may be involved with exposure prone procedures; and
- members of the armed forces.

Further details of people who are recommended for opportunistic testing for HBV infection can be obtained at: www.hepbhelp.org.au

How is hepatitis B transmitted?

HBV is transmitted through infected blood or bodily fluids (semen, vaginal fluids). The virus enters the bloodstream either through a break in the skin or through mucous membranes (eyes, nose, mouth).

HBV **can survive** outside the body for up to 7 days.

HBV is 50–100 times **more infectious** than HIV.

HBV may be transmitted:⁹

Vertically: from mother to child during childbirth	Common mode of transmission in high prevalence countries (in the absence of infant vaccination). Breastfeeding does not appear to increase the risk of HBV transmission to the infant and should not be discouraged if vaccination and hepatitis B immune globulin (HBIG) are administered at birth. Most guidelines do not recommend caesarean section as an intervention to reduce vertical transmission. ¹⁰
Horizontally	From an individual with hepatitis B to unvaccinated household contacts e.g. sharing toothbrushes, razors, nail-files or other personal items that may lead to exchange of body fluids. Infection acquired in early childhood after delivery is well recognised and has been attributed to parent-to-child contact ^{11,12,13} sibling contact ^{13,14} and medical procedures such as intramuscular injections.
Sexually	Through unprotected vaginal, anal or oral sex with a person who has hepatitis B
Percutaneously	Through the sharing or re-use of injecting equipment; via tattooing or body piercing including acupuncture, cupping and some other cultural practices involving blood or bodily fluids.
Medically acquired	There are still countries where blood transfusions, organ transplants and other medical interventions pose an extreme risk as they are not screened for HBV. In most countries where screening is in place, there is a very small risk of infection. Medical procedures including dentistry, surgery, dialysis and alternative health care procedures pose a risk if appropriate infection control procedures are not adhered to. Needlestick injury or splashing of infected blood or body fluids are a particular concern for health care workers and emergency services providers.

Hepatitis B is NOT transmitted by:

It is just as important to tell your patients how hepatitis B is not transmitted. HBV is NOT spread by:

- Water
- Sharing food and drink
- Coughing
- Sneezing
- Hugging
- Kissing
- Other casual contact, such as in the workplace

Negligible risk is associated with exposure to urine, faeces, sweat, tears and breast milk.

Salivary transmission is very rare and is thought to occur through human bite exposures only where blood is present.

Dispel discrimination against people with HBV

There are many myths about how HBV is transmitted. Misconceptions and fears about transmission fuel discrimination against people with hepatitis B¹⁵.

People living with hepatitis B should not experience discrimination either in health care settings or their home life.

Explain to your patients with hepatitis B that there is no reason to distance themselves from their family or other people, and they should not be excluded from work, school, or other daily activities.

How to test for hepatitis B

Serologic testing for HBV infection relies on immunoassay techniques for the detection of antigens and antibodies in patient serum. Modern hepatitis B serology techniques are highly sensitive and specific.

When testing for hepatitis B, order:

- hepatitis B surface antigen – HbsAg
- hepatitis B core antibody – anti-HBc
- hepatitis B surface antibody – anti-HBs

Ordering all three tests allows determination of **susceptibility; immunity** through vaccination or past infection; or **active infection (acute or chronic)**.

Hepatitis serology tests are Medicare rebatable.

However, **to be able to order all three diagnostic tests** (HBsAg, anti-HBc, and anti-HBs) **simultaneously and retain Medicare eligibility**, the requesting doctor should **write 'chronic hepatitis B'** or similar clinical justification for testing **on the request slip**.

If acute hepatitis B is suspected (through recent risk, presentation, or both), IgM antibody to the hepatitis B core antigen (IgM anti-HBc) can also be ordered to support clinical suspicion. IgM anti-HBc is typically elevated to a high titre in acute hepatitis B. It can however also be elevated (though usually not high titre) in a flare of chronic hepatitis B infection.

How to interpret hepatitis B diagnostic test results

The reason for requesting all three serological tests – HBsAg, anti-HBc and anti-HBs – in a patient at risk of hepatitis B infection is that systematic interpretation of these results allows categorisation of most patients by their hepatitis B status, either as susceptible (to infection); immune through vaccination or resolved infection; or chronically infected with hepatitis B. This avoids missed diagnoses, unnecessary vaccination and recalling patients or adding tests.

Test results and their interpretation ¹⁶			What if the results are inconclusive?	
Tests	Results	Interpretation	Tests	Results
HBsAg anti-HBc anti-HBs	negative negative negative	Susceptible to infection (if at risk, vaccination should be recommended)	HBsAg anti-HBc anti-HBs	negative positive negative
HBsAg anti-HBc anti-HBs	negative positive positive	Immune due to resolved infection	<p>Interpretation possibilities include:</p> <ul style="list-style-type: none"> distant resolved HBV infection – the most common interpretation, particularly in people born in HBV endemic areas; false positive result – more common in people with a low risk of past HBV infection; resolving acute HBV infection – in the period between HBsAg loss and detectable anti-HBs development; passive transfer of maternal anti-HBc – in children up to 3 years of age; and occult HBV infection – a situation when HBV DNA is detectable in the absence of positive HBsAg. This can be determined by detecting HBV DNA in serum. (Note: this test is not Medicare rebatable in the absence of HBsAg). <p>• Confirmation via repeat serology should be considered.</p>	
HBsAg anti-HBc anti-HBs	negative negative positive	Immune due to hepatitis B vaccination		
HBsAg anti-HB IgM anti-HBc * anti-HBs	positive positive positive negative	Acute HBV infection *(high titre)		
HBsAg anti-HBc anti-HBs	positive positive negative	Chronic HBV infection		

Testing for at risk individuals is covered by Medicare

Ordering HBV serology (HBsAg, anti-HBs and anti-HBc) in a patient from a hepatitis B priority population is in line with the Medicare Benefits Schedule screening provisions.¹⁷ Not testing people from priority populations is a missed opportunity to **diagnose, intervene, prevent illness and death** and to test and vaccinate contacts if required.

For more information on testing for hepatitis B see testingportal.ashm.org.au/hbv

Gaining informed consent for testing

Gaining informed consent can be a challenging process and may take more than one visit to achieve. This may be particularly relevant when dealing with patients from culturally and linguistically diverse (CALD) backgrounds with low English proficiency or Aboriginal and Torres Strait Islander people. The Good Medical Practice code of conduct recommends using whenever necessary, **qualified language interpreters or cultural interpreters to help you meet patients' communication needs**¹⁸ and information packs in the patients' first language (see the resources section for further information).



The Translating and Interpreting Service (TIS) is available, 24 hours/ 7 days per week: Contact the Doctors' Priority Line 1300 131 450

Informed consent for testing means:

that the person being tested agrees to be tested on the basis of understanding the testing procedures, the reasons for testing and is able to assess the personal implications of a positive test result, including the need for more tests.

Conveying a test result

Conveying a test result also needs to be conducted in a **culturally appropriate** and safe manner with a gender and dialect-appropriate interpreter for patients with low English proficiency. Results need to be given promptly and in person where privacy is assured. It is important to avoid information overload and it is often useful to provide **culturally and language-appropriate** written material (taking literacy levels into account) and details of support services.

Test Results	Points to discuss when conveying the test result:
Susceptible HBsAg negative anti-HBc negative anti-HBs negative	<ul style="list-style-type: none"> ■ Emphasise positive education and messages about safe behaviours. ■ Examine any difficulties or issues that the patient may have in practising safe behaviours. ■ Discuss vaccination to protect against hepatitis B.
Immune HBsAg negative anti-HBc pos/neg anti-HBs positive	<ul style="list-style-type: none"> ■ For patients immune either through natural infection or vaccination, this result should be conveyed to the patient and clearly entered in their record to avoid unnecessary repeat serologic testing or vaccination in the future. ■ Patients immune through natural infection should be advised that they may be at risk in settings of immunosuppression.

Points to discuss when conveying a hepatitis B test result: confirmed infection

- Focus on immediate needs and support.
- Modes of transmission and risk reduction.
- Who to tell and how.
- Testing of sexual partners, family members and household contacts.
- Health maintenance strategies – alcohol minimisation, weight loss, smoking cessation, IDU harm reduction as appropriate.
- Strategies for managing HBV which are flexible and appropriate to the person's needs.
- Adequate time to answer questions.
- Appropriate use of interpreters and translated resources.
- Expect to have to go through it all again.

Acute

HBsAg positive
 anti-HBc positive
 anti-HBs negative

Discuss:

- the likelihood of clearing the infection or going on to chronicity.
- medical management, referrals.

Chronic

HBsAg positive
 anti-HBc positive
 anti-HBs negative

Discuss:

- need for ongoing, potentially lifelong monitoring.
- treatment options (including no treatment) and medical management, referrals.

For more information on testing for hepatitis B see testingportal.ashm.org.au/hbv

Who should be vaccinated for hepatitis B?

The hepatitis B vaccine is effective at preventing HBV infection and subsequently liver cancer, and is often referred to as the world's first 'anti-cancer vaccine'. The universal infant program, with the first dose of hepatitis B vaccine given at birth, began nationally in 2000 and there has also been an adolescent catch-up program. There is some evidence of early vaccination program failure in some priority groups, including Aboriginal and Torres Strait Islander people.¹⁹ If in doubt, test as per page 4 to establish their hepatitis B status.

Groups at risk of exposure or significant morbidity from exposure to HBV infection should be targeted for vaccination:

The Australian National Immunisation program	People at higher risk of acquiring hepatitis B	People prone to exposure or at risk of significant morbidity from exposure	People at risk of occupational exposure
1. Infants 2. Adolescents aged 10–13 years* *These vaccines have been given as a part of a catch-up program and are now being phased out in several jurisdictions. Contact your State or Territory Health Department for details.	1. Men who have sex with men 2. People with multiple sexual partners (including sex workers) 3. Aboriginal and Torres Strait Islander people 4. People who inject drugs 5. Prison inmates and prison staff 6. Culturally and linguistically diverse communities 7. People adopting a child from a country with high prevalence rates 8. Frequent and long-term travellers to endemic areas, including those visiting families and friends in their country of origin 9. Household, family or sexual contacts of people with acute or chronic hepatitis B 10. Vulnerable populations including the homeless and people with mental health issues	1. Haemodialysis patients 2. People with clotting disorders and others who may need multiple blood or blood product transfusions, especially if they are given overseas. 3. HIV positive and other immunosuppressed people 4. Transplant recipients 5. People with chronic liver disease or hepatitis C 6. Clients and staff of facilities for the intellectually disabled	1. Health care workers 2. People who have had accidental exposure (e.g. Tattooists, body piercers, dentists) 3. People playing contact sport 4. Childcare workers 5. Embalmers 6. People working in accident and emergency services (paramedics, police, SES, volunteer first aid givers – Red Cross, St John Australia)

As there are State and Territory differences, primary care providers should check with their local Health Departments for information on which of these groups may be entitled to funded vaccine.

See *The Australian Immunisation Handbook* for further information <http://www.health.gov.au/internet/immunise/publishing.nsf/content/handbook-home>

Dosage and administration

The vaccine is administered by deep intramuscular (IM) injection in a 3-dose regimen over six months. The third dose is necessary to increase the percentage of responders and to provide long-term protection. An accelerated 2-dose regimen is available with a similar antibody response and this may be used in certain circumstances (see *The Australian Immunisation Handbook*²⁰ for more information). Hepatitis B and hepatitis A/hepatitis B combination vaccination schedules can be found in *The Australian Immunisation Handbook*.²⁰

Who should get tested before vaccination?

People from **high-risk groups should be tested** for active or resolved infection **prior to vaccination**, as vaccination is *not* beneficial for persons already exposed to HBV. Those who are chronically infected with hepatitis B instead need to be identified to receive appropriate management.

Who should get tested after vaccination?

Most people do not need to be tested for anti-HBs to confirm protection against HBV after completing the vaccination series. However, the following high-risk groups should receive post-vaccination testing:²⁰

- those at significant occupational risk (e.g. healthcare workers whose work involves frequent exposure to blood and body fluids);
- those at risk of severe or complicated disease (e.g. people with impaired immunity, and individuals with pre-existing liver disease not related to hepatitis B);
- those in whom a poor response to hepatitis B vaccination is expected (e.g. haemodialysis patients);
- sexual partners and household contacts of people diagnosed with hepatitis B.

If your patient is NOT immune after vaccination

Although uncommon, about 5% on average of those who complete the hepatitis B vaccination series may not acquire immunity. If adequate anti-HBs levels (≥ 10 mIU/mL) are not reached after the third dose:

- If unknown, test to exclude HBV infection (HBsAg and anti-HBc).
- HBsAg negative non responders should be offered further doses – given as either a fourth double dose or a further 3 doses at monthly intervals, with further testing for response at least 4 weeks after the last dose.
- Persistent non-responders should be informed that they are not protected and should minimise exposures. They should also be told about the need for Hepatitis B Immunoglobulin within 72 hours of parenteral exposure to HBV.

Natural history of ACUTE hepatitis B virus infection

In Australia, most acute hepatitis B is acquired by adults in risk groups through parenteral/percutaneous and sexual transmission. There is generally no treatment for acute hepatitis B as most will naturally clear the virus. Less than 5% will go on to have chronic hepatitis B. The progression from acute to chronic hepatitis infection is due to a failure of the immune response to remove the virus.

There are four stages of acute hepatitis B infection:²¹

Incubation phase	Can be from 4 to 12 weeks (but could be up to 6 months).
Symptomatic hepatitis	Acute hepatitis develops after the incubation period and can last from 4–12 weeks. It may be identified by elevated aminotransferase levels. Symptoms may include fever, fatigue, anorexia, nausea, dark urine, jaundice, myalgia and right upper quadrant abdominal pain. Symptoms of acute hepatitis B are common in adults but not in infants and children.
Recovery period	This results in the normalisation of alanine aminotransferase (ALT) levels.
Clearance phase	The hepatitis B surface antigen (HBsAg) clears from the serum after a few months. It coincides with the development of hepatitis B surface antibodies (anti-HBs).

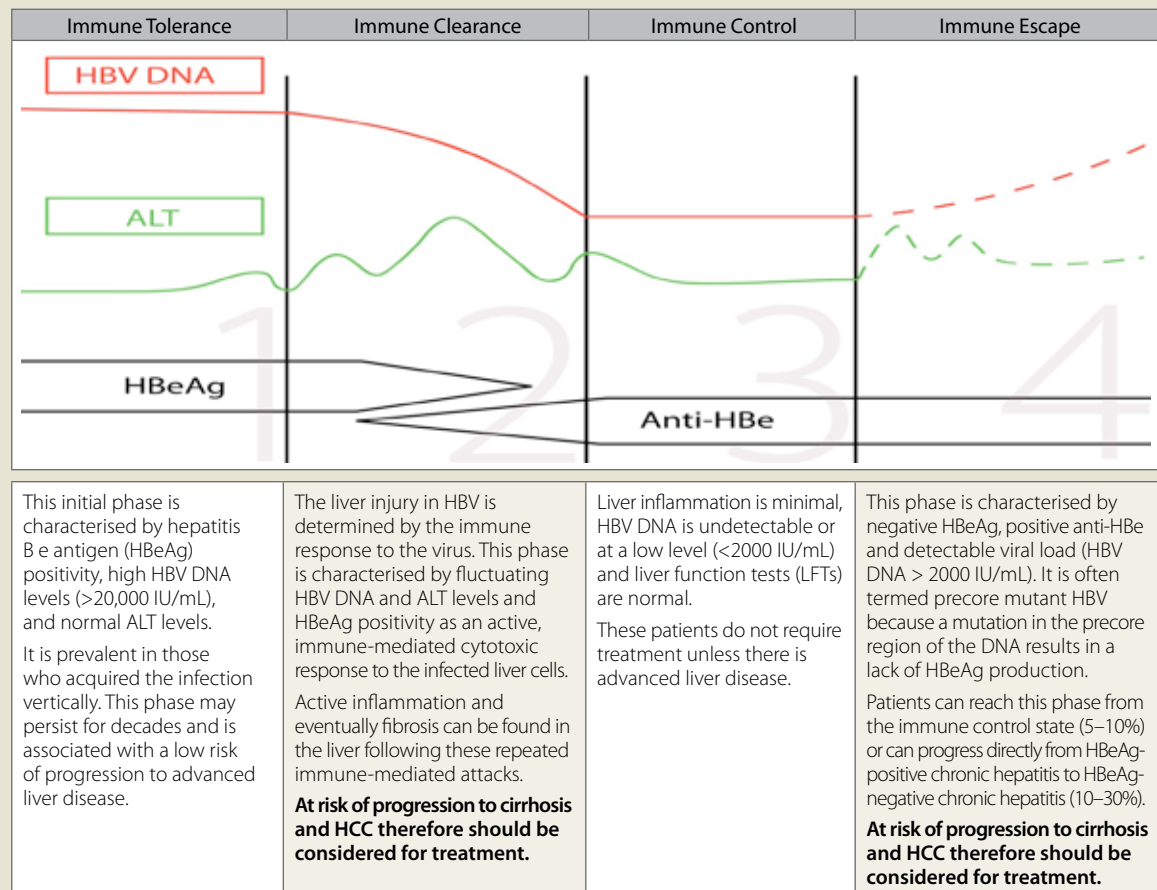
Acute hepatitis B may rarely lead to fulminant liver failure. It can be more severe with pre-existing viral hepatitis or liver disease. Fulminant disease may lead to mortality in less than 0.5% of cases.

All patients with acute hepatitis B need **follow up to document clearance.** If HBsAg persists for six months in a patient with acute hepatitis B this indicates they have progressed to CHB.

Natural history of CHRONIC hepatitis B virus infection

The four phases of chronic hepatitis B

There are 4 phases, of variable duration, that characterise chronic hepatitis B:²²



The risk of developing CHB depends on the age of the person when the virus was contracted:
>90% for infant (<5 years)
~30% during childhood
<5% of adults

People with chronic HBV infection usually exhibit **NO SYMPTOMS** until they have developed cirrhosis or liver cancer.

CHB is defined as persistent detection of **HBsAg for >6 months** after initial exposure to the virus. Positive HBsAg in most settings reflects the presence of chronic HBV.

CHB is a **dynamic disease**, patients move between phases. **Patients must be regularly re-evaluated** to determine which phase they are in.

“No Person with Chronic Hepatitis B is A Healthy Carrier!”

During the first (immune tolerance) and third phases (immune control), patients have normal liver function tests and in the past have been called ‘healthy carriers’ or ‘inactive carriers’. However, patients are always at risk of progressive liver damage and the development of cirrhosis and HCC. All patients must have regular follow-up.

Initial assessment of patients with chronic hepatitis B

All HBsAg positive patients should be assessed at baseline and at regular intervals long-term, as disease phase changes over time. The assessment of patients with CHB should commence with a thorough clinical history and physical examination. Aspects of the clinical history that deserve close attention are risk factors for acquisition of CHB, such as ethnic background, a family history of CHB, and a family history of hepatocellular carcinoma; and host or viral factors that are associated with an increased risk of cirrhosis, including older age (related to a longer duration of infection), heavy alcohol consumption, cigarette smoking and co-infection with other viruses, e.g. hepatitis C virus (HCV), hepatitis D virus (HDV), and human immunodeficiency virus (HIV). The following tests should be ordered:

Beware ‘normal’ ALT

ALT upper limits of normal have changed:

Elevated ALT levels are:

>30 U/L MEN

>19 U/L WOMEN

Test

HBsAg / Anti-HBe
HBV DNA
HAV, HCV, HDV, + HIV serology
Evaluation for co-morbidities

LFTs
FBC
Ultrasound
PT, INR
alpha fetoprotein

Why the result is important

Quantify replication, identify phase of infection, prognostication, consideration of treatment
Co-infection, vaccination
Alcohol, drug use, diabetes

Necroinflammatory activity, synthetic function
May indicate cirrhosis if thrombocytopenia is found
Assess for liver disease, portal hypertension and HCC
Synthetic function
HCC

Regular monitoring for liver damage and disease stage

Patients with CHB require regular review for change in disease activity. The frequency of monitoring is determined by age, family history, the phase of HBV infection, degree of activity and other factors such as co-morbidities. Primary care providers have a vital role in the assessment and monitoring of patients with CHB. Effective communication between GPs, specialists and referral centres is required for optimal patient management.²³ **GP Management Plans and Team Care Arrangements** are mechanisms for supporting appropriate management and are Medicare rebatable. See ASHM resources on page 12 for more information.

How to monitor and how often

Immune tolerance

Every 6–12 months
LFTs, HBV DNA*
HBsAg/anti-HBe

Immune control

Every 6–12 months
LFTs, HBV DNA*

Immune clearance or escape

Require consideration of treatment

On treatment

Regular monitoring according to treatment regimen

Monitoring CHB

Monitoring for hepatocellular carcinoma (HCC) is also necessary for certain patients.

* HBV DNA only Medicare rebatable once/year in patients not on treatment, 4 times/year on antiviral treatment

HBV prevalence and HCC incidence

Worldwide, **liver cancer** is the second most frequent cause of cancer death in males and sixth most frequent cause of death in females. **Cirrhosis** and **hepatocellular carcinoma (HCC)** are **known consequences** of **HBV infection** and are major causes of **morbidity** and **mortality**. Without intervention, 15–25% of people living with CHB will die from complications including cirrhosis and HCC.² CHB is responsible for the majority of HCC worldwide.²⁴

HBV and HCC in Australia

In Australia, liver cancer incidence has risen progressively over the last 20 years (the majority of which is attributable to chronic viral hepatitis). It now has the fastest increasing cancer incidence, and equal fastest rising cancer mortality in Australia.²⁵

Presentation with advanced HCC is associated with poor prognosis. Six monthly surveillance using ultrasound and AFP can identify small HCC lesions that may be amenable to curative treatment. Prognosis is markedly improved in patients diagnosed while undergoing regular surveillance.

Surveillance for HCC

Primary care providers can play a significant role in **surveillance for HCC**. Given that patients with early HCC may present with no symptoms, early detection is difficult. Onset of symptoms such as weight loss, lethargy, jaundice or palpable mass in the upper abdomen may indicate advanced HCC tumours.

Surveillance for HCC is recommended for patients with CHB

This includes six-monthly ultrasound (US) tests and alpha fetoprotein (AFP) level in:

- Asian males ≥ 40 years
- Asian females ≥ 50 years
- Africans ≥ 20 years
- All patients with cirrhosis
- Patients with a family history of HCC

If screening test abnormal, 4-phase CT or contrast-MRI recommended for diagnosis

Early detection is the key to improving survival

Late diagnosis of liver cancer is often the reason for very short average survival time following diagnosis.

All patients may be monitored for HCC six monthly as above if they have been viraemic for a substantial period, especially if the infection was acquired in childhood. If the screening test is abnormal, 4-phase CT or contrast-MRI is recommended for diagnosis and referral to a multidisciplinary team for management.

Other important co-factors which increase the risk of HCC in people living with HBV infection include co-infection with another hepatitis virus or the HIV virus; chronic excessive alcohol consumption (a factor of liver injury on its own and co-factor for progression of HBV-associated liver disease); age (see above); gender (liver cancer is more common in men than in women); high HBV DNA levels (see below); smoking; and family history of HCC.²⁶

The impact of HBV DNA Viral Load on liver disease

There is now substantial evidence for the link between elevated HBV DNA viral load and progressive liver disease, most notably in the REVEAL-HBV study from Taiwan.²⁷ This large cohort study has demonstrated that increasing levels of HBV DNA at baseline (especially when these persisted on follow up)²⁸ were associated with a correspondingly higher risk of developing cirrhosis and liver cancer over time.

The aims of treatment for CHB

Treatment is available for CHB based on the person's viral load. The goal of therapy is to control the viral replication. The ultimate goal of viral suppression is to limit liver damage due to immune-mediated inflammation and fibrosis; prevent the progression of liver disease to cirrhosis and reduce the risk of liver failure or the development of hepatocellular carcinoma (HCC) in patients who have established liver injury.⁹

Who and when to treat

Generally, patients in the **immune clearance** and **immune escape** phases of infection are **candidates for therapy**. Treatment is considered for patients with high HBV DNA.

Other factors important in the decision to begin antiviral therapy are:

- Phase of infection
- Patient's age
- Degree of inflammation
- Fibrosis stage
- Risk of HCC

A liver biopsy is no longer a compulsory requirement for the reimbursement of therapy for HBV.²⁹ Ultrasound elastography, known as FibroScan®, is increasingly available in some centres to provide non-invasive estimation of fibrosis and reduce the need for biopsy.

When making decisions about treatment, consideration must be given to:

- Disease severity (natural history, complications)
- The advantages and disadvantages of each therapy
- Anticipated duration of therapy
- Likelihood of response to therapy
- Likelihood of developing resistance
- Other factors (extrahepatic disease, immunosuppression, co-infection, etc)
- Likelihood of patient adherence to therapy regimens (non adherence may result in significant flares in disease activity)⁹
- Patient's life circumstance – e.g. considering starting a family.

Current recommended first-line therapies

It is important to choose an antiviral therapy with a high likelihood of HBV DNA suppression and a low chance of resistance. Therefore the current first-line therapies for treatment-naïve patients are:

Antiviral Therapy	Comments
Entecavir (ETV)	ETV is a nucleoside analogue and has excellent tolerability, high potency and a high barrier to resistance (only 1.2% at 6 years in treatment naïve patients). A higher rate of resistance occurs if used in patients with lamivudine-resistant HBV, therefore avoid ETV in this context.
Tenofovir (TDF)	TDF is a nucleotide analogue and has high potency and a high barrier to resistance (0% at 3 yrs in treatment-naïve patients). TDF retains high activity against lamivudine-resistant HBV and is also active against HIV. It should be avoided in patients with renal disease. There is increasing safety in pregnancy data, so it is the treatment of choice in women with childbearing potential requiring prolonged antiviral therapy for treatment of CHB.
Pegylated Interferon (PEG-IFN)	PEG-IFN is less likely to be prescribed because of the side effects, but has a defined one year duration of therapy and the possibility of HBsAg clearance. PEG-IFN can be useful in selected younger patients, particularly women who are intending to get pregnant in the future. A response is more likely in HBeAg-positive patients with high ALT and low HBV DNA viral load.

Lamivudine was the first nucleoside analogue licensed for HBV (it is also active against HIV polymerase). It is well tolerated, but has a major problem with regards to resistance. Approximately 70% of patients after 5 years on lamivudine have resistant HBV (YMDD mutation). It also causes cross-resistance with entecavir and telbivudine. It is no longer first line therapy in Australia, though it is still used in special circumstances or continued in patients with sustained response over years. For lamivudine resistant patients combination therapy of tenofovir and lamivudine is used.

Definitions of a response in CHB

The ideal response to CHB therapy in all patients is HBsAg seroconversion, as this is associated with definitive remission and improved prognosis. However, this occurs in less than 10% of patients in the short to mid term. In HBeAg positive patients, durable HBeAg seroconversion represents a good response, as this is associated with sustained viral suppression in most patients, and with improved prognosis. In HBeAg negative patients (and HBeAg positive without seroconversion), **persistently undetectable HBV DNA** by sensitive assay is next best endpoint and this is **currently the aim of therapy**.

Monitoring on treatment

It is important to encourage treatment adherence to avoid antiviral resistance and risks associated with sudden cessation. **It is necessary to regularly monitor patients on therapy** to record their adherence to the treatment, response to antiviral therapy with HBV DNA levels, adverse effects and to facilitate early detection of antiviral resistance. Patients on nucleos(t)ide analogues are monitored every three to six months; patients on PegIFN alfa 2a are tested more frequently due to the risk of adverse effects.

HBV in the setting of immune suppression

People with resolved or chronic HBV infection may develop a severe flare of HBV when treated with chemotherapy or immunosuppressive medications (including Rituximab, Infliximab, Etanercept etc). The risk of a flare in a person with chronic hepatitis B undergoing chemotherapy is between 33–67%, and mortality rates, primarily related to liver failure, range from 4–60%. Reactivation is reported in up to 25% HBsAg negative/anti-HBc positive patients (resolved infection) with Rituximab-containing chemotherapy.³⁰

All patients should be screened for HBsAg and anti-HBc prior to chemotherapy or intense immunosuppression.

Patients who have CHB should be referred to a specialist and must be given prophylaxis with an oral antiviral agent from the start of treatment and for at least 12 months after the completion of treatment to prevent HBV flares. Those that are HBsAg negative/anti-HBc positive (resolved infection) should be considered for either prophylactic treatment or close monitoring.

HBV and pregnancy

All pregnant women should be offered hepatitis B screening antenatally. Those who are found to be HBsAg positive should be referred to an infectious diseases specialist or hepatologist for information, advice and follow-up. It is crucial that pregnant women receive information regarding the risk of HBV transmission to the infant, as well as possible interventions to reduce this risk. Without intervention there is a 95% chance of transmission to the baby, whereas with intervention, this can be as low as 5%.

All babies of HBsAg positive mothers should:

- Be given HBIG and first dose of HBV vaccine within 12 hours of birth
- Three subsequent doses of HBV vaccine should be given at two, four and either six or twelve months of age
- The newborn should be tested for HBsAg and anti-HBs, at least 3 months after the final dose of HBV vaccine

Other considerations:

- Mothers are at risk of flares of hepatitis during or after pregnancy;
- Women of childbearing age who are already on antiviral therapy must weigh up possible risks of the drug on foetal development vs. risk of flare in the mother (or transmission to the baby);
- Breastfeeding is NOT associated with an increased risk of transmission of HBV if vaccination and HBIG is administered at birth. Therefore breastfeeding should NOT be discouraged.
- Mothers with HBV DNA greater than 10^7 IU/mL have substantial risk of transmission and should be counselled about the potential role of antiviral therapy and the options available;
- Mode of delivery has no effect when prophylaxis given; and

Mothers SHOULD NOT be lost to follow-up after birth.

ASHM resources

Other ASHM resources are available from the ASHM website: www.ashm.org.au/publications

Profession Based Booklets

- An Overview of Hepatitis C: Clinical Management in Opiate Pharmacotherapy Settings
- Correctional Officers and Hepatitis C
- Dental Health and Hepatitis C
- Dentists and HIV
- General Practitioners and Hepatitis C
- Nurses and Hepatitis C
- Police and Blood-Borne Viruses
- Emergency Service Providers and Blood-borne Viruses
- Decision Making in Hepatitis B
- Hepatitis C in Brief – A Factsheet
- Hepatitis C Management and Treatment for Clients of Pharmacotherapy Services
- HIV Patient Fact Sheet

Monographs

- ASHM Directory of HIV, Hepatitis and Related Services
- B Positive: all you wanted to know about hepatitis B – a guide for primary care
- Co-infection: HIV & Viral Hepatitis – a guide for clinical management
- Hepatitis C: clinical management in opiate pharmacotherapy settings
- HIV and viral hepatitis C: policy, discrimination, legal and ethical issue
- HIV Management in Australasia: a guide for clinical care
- HIV, Viral Hepatitis and STIs: a guide for primary care

Distance-learning Kit

- Clinical Science of HIV Medicine CD Manuals
- Australasian Contact Tracing Manual

Online resource

- Guide to Australian HIV Laws and Policies for Healthcare Professionals. Available online only at www.ashm.org.au/HIVlegal
- Hepatitis B GP Management Plan template at www.ashm.org.au/images/hbv/hbv_gpmp.rtf

DVD

- C Me, Hear Me. Hepatitis C in our own words

Hepatitis B and Primary Care – Online Learning Module

Online learning modules incorporating interactive self-assessment activities have been developed. To access these online education modules visit the ASHM website at www.ashm.org.au/e-learning

Detailed references

Detailed references are available at the ASHM website at www.ashm.org.au/publications

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Critical situations and the need for referral

The following is not an exhaustive list, but aims to highlight some examples of when to seek urgent advice and/or referral.

Severe acute exacerbation (or acute HBV)

- Potential for fulminant disease – how to recognise/react
- See page 7: Natural history of ACUTE hepatitis B virus infection

Reactivation during immunosuppression/chemotherapy

- Urgent antiviral therapy required
- See page 11: HBV in the setting of immune suppression

Cirrhosis (especially where suggestion of decompensation)

- Needs immediate discussion, triage prioritisation with specialist service

Possible HCC found on surveillance

- See page 9: Surveillance for HCC

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This booklet was sent out for focus testing and received responses from 17 health professionals.

Further information and contacts

HepBHelp is an independent website which aims to assist GPs in the further investigation and management of patients diagnosed with chronic hepatitis B virus (HBV) infection <http://www.hepbhelp.org.au>

Multilingual patient factsheets on hepatitis B are available to order for free:

Hepatitis B. It's family business http://www.multiculturalhivhepc.net.au/images/pdf/hbv_orderform.pdf
Hepatitis B factsheet for people newly diagnosed www.ashm.org.au/publications

RACGP: Using interpreters A guide for GPs, <http://www.racgp.org.au/afp/201004/201004phillips.pdf>

Translating and Interpreting Service

http://www.immi.gov.au/living-in-australia/help-with-english/help_with_translating/medical-practitioners.htm

Find the closest Aboriginal Medical Service: contact AH&MRC <http://www.ahmrc.org.au/>

Cultural Respect & Communication Guide. A resource to assist sexual health service delivery to Aboriginal communities http://www.tvgnp.org.au/Welcome_files/Programs/ATSI_Health/Sexual_Health_guide.pdf

Communicating positively: A guide to appropriate Aboriginal terminology

http://www.health.nsw.gov.au/pubs/2004/pdf/aboriginal_terms.pdf

The Australian Immunisation Handbook

<http://www.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook-hepatitisb>

Chronic Hepatitis B (CHB) Recommendations – Australia and New Zealand 2nd Ed;

Digestive Health Foundation, Gastroenterology Society of Australia 2010, available online http://www.gesa.org.au/files/editor_upload/File/Professional/CHB.pdf

Cirrhosis a management guide, Medicine Today, Gokulan Pavendranathan, Simone Strasser, September 2007, Vol 8, Number 9. <http://www.medicinetoday.com.au/home/article/view/665>

The Medicare Benefits Schedule

<http://www.health.gov.au/internet/mbsonline/publishing.nsf/Content/Medicare-Benefits-Schedule-mbs-downloads>

Policy advice on HIV, hepatitis C and hepatitis B testing, <http://testingportal.ashm.org.au/>

Hepatitis Australia website at www.hepatitisaustralia.com. National hepatitis helpline: 1300 437 222

Gastroenterological Society of Australia website at www.gesa.org.au

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Supporting the HIV, Viral Hepatitis and Sexual Health Workforce

www.ashm.org.au



Hepatitis B and Primary Care

SUPPLEMENTARY

Detailed References

Detailed references are available at the ASHM website at www.ashm.org.au/publications

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