



GP Companion Resource to the "12 questions to ask your doctor if you have been diagnosed with hepatitis B"

This resource provides General Practitioners with suggested answers to the consumer flyer "12 questions to ask your doctor if you have been diagnosed with hepatitis B". It has been developed for National Hepatitis Awareness Week, 18 May - 24 May 2009.

The GP Companion Resource is available for download from www.ashm.org.au/publications. The consumer flyer can be downloaded from www.hepatitisaustralia.com.

In Australia, up to 160,000 people have chronic hepatitis B, the majority of whom were born overseas. Hepatitis B is the leading cause of liver cancer in Australia.

1 What are the symptoms of hepatitis B and how will it affect my liver?

Symptoms

Acute hepatitis B virus (HBV) infection

The outcome and symptoms of acute infection vary depending on the age that the infection is acquired:

Acute HBV in infancy and childhood

- 90% of infants acquiring the infection at birth will develop chronic hepatitis B
- Mostly asymptomatic
- Mostly vertical and horizontal (skin, mucosal cuts) transmission

Acute HBV in late teens and adulthood

- 95% will clear the virus and not develop chronic hepatitis B
- Around half of newly acquired HBV cases in Australia are associated with injecting drug use and about 16% are associated with heterosexual contact
- Higher risk of severe acute hepatitis
- Many are asymptomatic but if there are symptoms, these can include fever, fatigue, anorexia, nausea, vomiting, jaundice, dark urine, pale stools, pain in right upper quadrant, myalgia, arthralgia.

Those who clear the infection have life-long immunity, maintain anti-HBc (core), and may or may not preserve anti-HBs (surface) which can reactivate during transplantation, chemotherapy or HIV co-infection.

Chronic HBV infection

- Mostly asymptomatic
- If symptoms, mostly mild and non specific, e.g. fatigue, lethargy or nausea, pruritis, abdominal discomfort, intolerance to alcohol, fatty foods, jaundice
- 20% will develop some extrahepatic manifestation e.g. polyarteritis nodosa or glomerulonephritis
- Exacerbations may be symptomatic and mimic acute infection
- Symptoms often increased in advanced liver disease: lethargy, ankle swelling, abdominal swelling, easy bruising, prolonged bleeding, haematemesis, melaena, encephalopathy (reversal sleep pattern, forgetfulness, inappropriate behaviour, drowsiness)

Outcome of chronic HBV

30% of individuals with chronic HBV will develop cirrhosis. Overall individuals with chronic HBV, have a 15-25% premature mortality from cirrhosis and hepatocellular carcinoma. Hepatocellular carcinoma can even occur before developing cirrhosis, especially in males.

5-year rates of progression

- Chronic hepatitis B to cirrhosis: 12-20%
- Compensated to decompensated cirrhosis: 20%
- Cirrhosis to hepatocellular carcinoma: 5-15%

Those with chronic HBV and a positive HBsAg are infectious to others.

How will hepatitis B affect the liver?

There are 4 main phases of chronic HBV and the host immune response in each phase determines the outcome of infection and the severity of liver injury.

The 4 phases are:

- Immune tolerance. No immune response to the virus (decades in infants but mostly brief or absent in adults). Normal ALT, HBeAg positive, high viral load (HBV DNA)
- Immune clearance: fluctuating ALT and HBV DNA levels; HBeAg seroconversion to anti-HBe associated with HBV DNA declines
- Immune control: Non-replicative (latent) infection. HBeAg negative, low or undetectable HBV DNA, normal ALT levels (but continue surveillance as about 20% may have reactivation of HBV with immune escape)
- Immune escape: Reactivation - spontaneous reactivation occurs in 20% of those in immune control phase; negative HBeAg, positive anti-HBe, detectable viral load

Chronic hepatitis B cases can be divided into those who are HBeAg positive (indication of hepatitis B viral replication and high infectivity) and those who are HBeAg negative (less viral replication and less infective).

Predictors of progression to cirrhosis include:

- High HBV viral load
- Recurrent exacerbations (LFT flares)
- Longer duration of infection
- HBeAg positive and high viral load: increase risk hepatocellular carcinoma
- Family history of hepatocellular carcinoma
- Severe liver fibrosis and inflammation
- Older age > 45 years
- Immunosuppression
- Male
- Co-infection with hepatitis C, hepatitis D virus, and/or HIV
- Heavy alcohol intake > 40-50 gm/day

2 How is hepatitis B transmitted?

Transmission

HBV infection is transmitted by blood or bodily fluids (saliva, semen and vaginal secretions) containing hepatitis B virus entering another person's body.

Most cases of hepatitis B result from perinatal and vertical transmission. Higher risk groups in Australia are injecting drug users, Indigenous Australians, men who have sex with men and immigrants from highly endemic countries such as China, South East Asia and Pacific Island nations.

In adults, HBV transmission is mainly via sexual contact and injecting drug use. Other potential modes of transmission include:

- Unsterile tattooing or body piercing
- Blood-to-blood contact through open wounds
- Sharing household items such as toothbrushes, razors and tweezers
- Occupational – the risk of transmission by percutaneous exposure such as a needle-stick injury is about 30% if the person with HBV infection has replicative disease or 3% for those with HBV infection with non-replicative disease

Prevention

- Newborn babies of mothers with HBV infection should receive HBIG and be started on an HBV vaccination course at birth
- Immunisation with hepatitis B vaccine is recommended for people at risk of household, blood-to-blood or sexual contact and all infants at birth, and 12-year-old children who were not vaccinated at birth. See ASHM. *HIV, viral hepatitis and STIs: a guide for primary care*. 2008. Table 5.6 Available at: www.ashm.org.au/publications
- Using safe injecting practices
- Avoiding sharing and re-using contaminated objects that pierce the skin
- Using standard infection control procedures in a medical setting
- Practising safe sex

Post exposure prophylaxis

- Should be offered for all contacts.

3 Do I have to tell anyone I have hepatitis B?

Hepatitis B is a notifiable disease

Practitioners who are uncertain about their statutory or common law obligations to patients or to the local Health Department, including privacy and reporting obligations, are strongly advised to contact their local health department, applicable privacy office or seek independent legal advice.

Discrimination

Australian Commonwealth law prohibits discrimination against someone with an infectious disease, unless the discrimination is necessary to protect public health. Most states and territories have corresponding laws.

Confidentiality

Health practitioners have a duty of care to maintain the confidentiality of their patients. There are health specific laws requiring that medical practitioners not disclose any information regarding a person who has tested positive to an infectious disease.

Disclosure

In almost all cases, it is up to the individual whether or not to disclose their HCV infection. Generally speaking, infected individuals do not have to tell anyone they have hepatitis C except:

- if they are donating blood, blood products, ova or semen (they will not be accepted as a donor)
- if they are a health care or dental worker involved in exposure-prone procedures
- if they are in or want to join the Australian Defence Force
- if they are applying for insurance and superannuation, especially life insurance

Further information for patients and practitioners:

Contact Hepatitis Australia, website: www.hepatitisaustralia.com or call the helpline: 1300 437 222 (1300 HEP ABC).

Contact ASHM, website: www.ashm.org.au or call 02 8204 0700.

4 What tests will I need in order to know how hepatitis B is affecting me?

Tests

Hepatitis B testing is quite complicated, and can be difficult to interpret. The introduction of the HBV DNA test on Medicare has made testing for active disease simpler.

Tests to complete before referral to a specialist include:

- Viral load (HBV DNA) – a marker of active replication and strongest predictor of future cirrhosis risk
- HBsAg – a marker of ongoing infection
- Anti-HBs – an indication of immunity to hepatitis B (from natural infection or vaccination)
- Anti-HBc – antibody to hepatitis B core antigen and a marker of prior infection
- HBeAg – indication of hepatitis B viral replication and high infectivity
- Anti-HBe – indication of hepatitis B viral clearance and occurs following loss of HBeAg. May also occur in the presence of pre-core mutant disease in association with abnormal ALT and elevated HBV DNA
- Liver function tests (particularly serum ALT). If there is damage to liver may be raised but LFTs are often a poor indicator of illness outcome and severity
- Albumin and prothrombin time give an indication of the synthetic function of the liver
- Full blood count (FBC): decreased platelet count may indicate the development of portal hypertension and hypersplenism
- Bilirubin to assess hepatic secretory function
- HCV or HIV testing in patients at risk as co-infection may alter prognosis and treatment options
- HAV – if not immune, then vaccinate
- Thyroid function tests are useful to exclude associated thyroid disorders
- Transferrin saturation, ferritin levels, alpha-1-antitrypsin, caeruloplasmin and copper levels to exclude other hepatic pathologies (haemochromatosis, alpha-1-antitrypsin deficiency and Wilson's disease)
- ANA (antinuclear antibody), SMA (smooth muscle antibody) and LKMA (liver kidney microsomal antibody) – to exclude auto-immune liver disease
- Abdominal ultrasound and portal venous Doppler if available to screen for hepatoma and evidence of cirrhosis or portal hypertension

The specialist will determine if a liver biopsy should be undertaken. It is required before commencing government-subsidised treatment for hepatitis B and can provide a more detailed and reliable indication of liver damage.

Screening for hepatocellular carcinoma guidelines include ultrasound and AFP (alpha-fetoprotein) levels every 6 months.

Pathology tests indicating more severe fibrosis include:

- An inverted AST/ALT ratio (where AST is higher than ALT)
- Low platelets
- Low albumin
- Raised prothrombin time
- Elevated direct bilirubin (severe liver injury indicated if ALT falls and bilirubin rises)

5 Is there a treatment for hepatitis B?

Treatment

The initial aim of treatment is to control viral replication. The ultimate aim is to prevent the progression of liver disease to cirrhosis and reduce (or eliminate) the risk of liver failure or the development of hepatocellular carcinoma in patients with established liver injury. In HBeAg-positive patients, HBe seroconversion is an endpoint of therapy. In HBeAg negative-patients, no therapeutic endpoint exists and

therapy is usually indefinite.

There are 2 main classes of therapy: direct antiviral agents which inhibit the function of the viral polymerase to prevent viral replication (lamivudine 100 mg daily and entecavir 0.5 mg daily), and the interferons, synthetic cytokines which act via multiple intracellular biological pathways to eradicate the viral infection (pegylated interferon 180 µg weekly). These treatments are subsidised through Section 100 of the PBS. Adefovir dipivoxil is also approved although only subsidised in patients with lamivudine-resistance HBV. Another nucleoside analogue, telbivudine, is also approved but not yet subsidised.

Lamivudine (100 mg daily) is well tolerated and highly effective in suppressing HBV replication and improving liver histology. Unfortunately, lamivudine therapy is associated with a high risk of emergence of resistant strains.

Optimal duration of therapy is unknown, but the current recommendation is to continue for at least 6-12 months after seroconversion. Once therapy has stopped, at least 15% of patients will undergo seroconversion.

Side effects: see Question 10

The specialist will discuss the treatment and associated side effects in more detail.

6 How do I know that I need treatment? When should I start it?

When is treatment needed?

- Before starting treatment, patients should have a liver biopsy to provide an accurate assessment of the degree of necroinflammatory activity and the extent of hepatic fibrosis. If there is no damage, treatment may not be recommended. Liver biopsy should only be performed on the recommendation of a specialist clinician
- Patients should be monitored regularly while on therapy to document their response to treatment, detect adverse side effects of treatment and to facilitate the early detection of antiviral resistance. Monitoring needs to be more frequent for those receiving pegylated interferon, as there is a risk of bone marrow suppression, neuropsychological side effects and other complications

The specialist will discuss the treatments in more detail.

7 When do I need to see a liver specialist; will I have to pay for tests and treatment?

When to refer?

Discuss with your patient the appropriate time of referral and where to go.

- Patients with acute HBV should be referred to a specialist if they have elevated prothrombin time, INR or serum bilirubin concentration, signs of decompensated liver disease such as encephalopathy or ascites or an uncharacteristically long illness
- All patients who are HBsAg-positive should be referred to a specialist, especially if they have HBV DNA > 2000 IU/mL, elevated ALT levels or features of significant liver damage
- Investigations to be performed before referral include complete HBV serology (HBsAg, anti-HBs, anti-HBc, HBeAg, anti-HBe), viral load (HBV DNA), liver function tests, full blood count, coagulation profile, hepatitis C antibody, hepatitis D antibody

Please refer to the ASHM Directory for local specialists and hepatitis treatment services at: www.ashm.org.au/directory

Costs for medications

To attend specialists and to undergo investigations will vary depending on whether the patient has a health care concession card, is a private patient or is receiving care under Medicare. For medications under the PBS, patients will be charged the normal PBS prescription amount for each item (\$5.30 for concession card holders and \$26.30 for all others). If the patient does not receive Medicare benefits, the cost for medications will exceed \$1000 per month.

8 Should I be tested for, and vaccinated against, other forms of hepatitis?

Yes definitely.

Anyone with chronic HBV should complete hepatitis A vaccination, if not immune. Anyone with HBV infection should be tested for other forms of hepatitis, in particular hepatitis C (and other tests as in Question 4)

Why?

- Co-infection with another hepatitis virus is associated with more severe liver disease
- Super infection with hepatitis A infection (HAV) in a patient with chronic hepatitis B or C can precipitate acute liver failure
- Patients with HBV and HCV co-infection are more likely to progress to cirrhosis and to develop hepatocellular carcinoma

You should ensure all household family members and sexual partners of patients with chronic HBV are fully vaccinated and immune to hepatitis B. Discuss any possible costs involved with your patient.

9 What can I do to look after my health?

Ways to protect the liver and prevent disease progression include:

- Limit or cease alcohol intake: excessive alcohol consumption >50g/day and likely less, leads to disease progression and increased risk of hepatocellular carcinoma. Referral to local Drug and Alcohol Services can assist in reduction or cessation
- Limit or cease smoking and cannabis use
- Cease current medical or complementary medicines that may harm the liver
- Vaccination – make sure fully vaccinated for hepatitis A
- Healthy eating and reduction in abdominal obesity and body mass index to normal range. Overweight patients should be encouraged to reduce weight gradually, often under the guidance of their GP or dietician
- Maintain good overall health, reinforcing need for relaxation and stress reduction – if low mood is a problem, consider cognitive behaviour therapy (CBT), referral to a psychologist and antidepressant medication
- Monitor for symptoms and signs of liver progression (6– 12 monthly examination) with GP
- Nutrition. Strong recommendation against restrictive calorie diets. Instead, a well balanced diet is recommended. For most people with hepatitis, dietary recommendations are the same as for the general population (encouraging: grilled rather than fried food; lean meats and fish; reduced-fat products; wholemeal bread; vegetables and fruit; pasta; minimising fat for spreading and cooking)
- Planning rest periods and incorporating light-to-moderate exercise may reduce symptoms of fatigue, headache, aching muscles and joints
- There is little evidence that herbal medicines have an antiviral effect despite many patients reporting some symptomatic improvement, and the ability of some agents to induce a fall in ALT. Most preparations are safe, but some have reported hepatotoxicity and should be avoided (e.g. mistletoe, valerian, heliotropium, kombucha tea). Close monitoring of liver biochemistry is recommended at the commencement of any herbal medicine course
- Behaviours which increase the risk of HIV or HCV should be addressed as these can dramatically affect your patient's

health and cause further liver damage. Encourage safe sex and safe injecting drug use.

For more information, refer patients to the Hepatitis Australia website: www.hepatitisaustralia.com or call the helpline 1300 437 222.

10 Are there any side effects to treatment?

Side effects

- Pegylated interferon: flu-like symptoms, fatigue, leucopenia, irritability, sleep disturbance, mood disorders and depression
- Lamivudine is well tolerated with no significant side effects
- Entecavir is well tolerated with few side effects, the most common being headache and fatigue
- Adefovir is well tolerated

The specialist will discuss the side effects of treatment in more detail.

11 How often should I come back and see you?

Regular surveillance is very important for anyone diagnosed with chronic hepatitis B. A 6-12 monthly medical review is recommended depending on the clinical characteristics summarised below. The review includes:

- A check for signs of chronic liver disease or decompensation
- Serum liver enzymes, FBC, coagulation studies and alpha feto protein (AFP)
- Liver ultrasound (especially if a family history of hepatocellular carcinoma)

Women with HBsAg+, HBeAg-negative, no evidence of active liver disease or family history of hepatocellular carcinoma, and minimal alcohol intake, are generally at low risk of progression and require only 12-monthly check-ups.

For reasons that remain unclear, men with the same serological status, particularly those with infection since infancy, remain at risk of hepatocellular carcinoma development regardless of the presence or absence of cirrhosis. They should be seen twice a year for review.

Patients with known cirrhosis should undergo serum AFP testing and ultrasound every six months to screen for hepatocellular carcinoma. Patients with active liver disease (i.e. with abnormal liver enzymes) should be closely monitored and considered for antiviral therapy.

12 Where can I go for more information and support?

Patients should see their regular GP for more information. GPs can obtain contact details for local specialists and Hepatitis Treatment Services from the ASHM Directory at: www.ashm.org.au/directory.

GPs can also contact ASHM (on 02 8204 0700) or via email ashm@ashm.org.au for information on training and additional resources.

GPs can also refer patients for more information to the Hepatitis Australia website: www.hepatitisaustralia.com or call the helpline 1300 437 222. The helpline can direct you to multilingual resources and local multicultural hepatitis support agencies.

References

- ASHM, (2008). HIV, Viral Hepatitis and STIs. A Guide for Primary Care.
- ASHM, (2008). B positive: All You Wanted to Know About Hepatitis B.

The above resources are available to order or download from the ASHM website: www.ashm.org.au/publications

This resource is produced by the:

Australasian Society for HIV Medicine Inc
Locked Mail Bag 5057 Darlinghurst NSW 1300
Tel: 02 8204 0700
Fax: 02 9212 2671
Email: ashm@ashm.org.au

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