Hepatitis B

CASE DEFINITION

Hepatitis B is an infectious disease of the liver caused by HBV.

Estimated prevalence of HBsAg in rural Indigenous Australians is 8%, making up 16% of chronic hepatitis B in Australia[1].

HBV spread through:

- Any blood contact, including sharing injecting needles and personal items such as razors/toothbrushes
- Mother to baby at or around birth
- Unprotected sexual intercourse
- Biohazard/needlestick injury
- Household transmission in childhood (eg. open skin sores)

Case definitions:

TEST	ROLE
HBsAG	Defines current infection; if persists >6 months defines chronic infection
Anti-HBs	Defines immunity from either past infection or vaccination
Anti-HBc	Defines acute (IgM) or past/current (IgG or total) infection
HBeAg	Defines viral replication and high infectivity (can be falsely negative in immune escape phase)
Anti-HBe	Defines the immune control or immune escape phase in chronic hepatitis B
HBV DNA	Detects the state of viral replication

THE 4 PHASES OF CHRONIC HEPATITIS B	
Immune tolerance	Viral replication, minimal liver damage: high HBV DNA, normal LFTs, HBeAg positive, Anti-HBe negative
Immune clearance	Immune response, inflammation and liver injury: high HBV DNA, fluctuating LFTs, HBeAg positive → negative, Anti-HBe negative → positive
Immune control	Suppression of viral replication, minimal liver damage: low HBV DNA, normal LFTs, HBeAg negative, Anti-HBe positive
Immune escape	Viral replication, high risk cirrhosis: high HBV DNA, fluctuating LFTs, HBeAg negative, Anti-HBe positive

Hepatitis B can be divided into acute and chronic infection:

1. Acute hepatitis B

- Only 30 - 50% of adults and <10% of children will have symptoms and signs - may include tiredness, anorexia, abdominal pain, nausea, muscle and joint pain, rash, jaundice, hepatomegaly, splenomegaly, dark urine and pale faeces
- HBsAg positive, Anti-HBc IgM positive, HBV DNA high, ALT high (usually 10-100 x normal)
- 10% infants, 95% adults will have appropriate immune response with viral clearance and recovery
- 90% infants, 30% children <5 years, 5% adults will have inappropriate immune response and develop chronic hepatitis B infection
- <1% progress to fulminant hepatitis and death

2. Chronic hepatitis B

- Detection of HBsAg on two occasions 6 months apart with no evidence of acute infection (clinically or on blood tests)
- Usually asymptomatic BUT 20-30% risk of progression to advanced liver disease and hepatocellular carcinoma (HCC)
- Divided into 4 phases (see Case definitions table - don't always occur in order)

SCREENING

In Kimberley region, the routine vaccination schedule has excellent coverage – with the majority of people born on or after 01/01/1989 thought to be fully vaccinated.

Screening is NOT needed for those who have documented complete vaccination or have been shown to be immune (Anti-HBs >10IU/ml) in previous blood test.

Screening involves testing for HBsAg, Anti-HBs and Anti-HBc. Pre-test counselling should be undertaken.

Screening IS recommended in the following circumstances:

1. A single screening blood test is recommended for those with no documentation of completed Hep B vaccination schedule

   AND

   No previous blood test to determine immunity

2. High risk individuals who are not known to be immune should be screened every 2 years with adult health checks (unless high risk behaviours, positive for other STIs or named as a contact, which requires immediate testing), – These individuals need to be vaccinated (if not previously immunized) if found to be non-immune post screening. Once immunized and proven immune, they no longer need screening.

ie:

- Indigenous people born before 1989 who have not been immunised
- Sexual/household contacts for those with hepatitis B infection
- Patients born overseas in endemic areas
- Patients who are immunosuppressed or about to start immunosuppressant therapy ie including those with asthma about to start short course high dose steroids or methotrexate for RA.. If surface antigen positive – THINK TWICE
- Those infected with HIV or hepatitis C
- Men who have sex with men
- Inmates of correctional facilities
- Injecting drug users

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- People who are at occupational risk (eg. healthcare workers)
- Patients on haemodialysis
- People travelling to endemic regions

3. ALL pregnant women should be tested for hepatitis B at the first antenatal visit of each pregnancy regardless of previous vaccination or testing

INTERPRETATION OF RESULTS

Results	Interpretation	Action required
HBsAg negative Anti-HBs negative	Not immune	Consider vaccination - see prevention section
HBsAg negative Anti-HBs positive	Immune	No further testing needed Document 'the patient is immune, no further screening needed' clearly in patients file (consider alert)
HBsAg negative Anti-HBs negative Anti-HBc positive	Multiple interpretations (recovering from acute infection, false positive, low level chronic infection, low level immunity)	Seek medical and public health advice
HBsAg positive	Acute (if IgM Anti-HBc positive) or chronic infection (HBsAg positive on two occasions 6 months apart, no evidence acute infection)	Manage as per this protocol. Consider alert for infection control precautions, follow up and testing as below)

Full clinical and public health follow up is required for all patients diagnosed with acute or chronic hepatitis B and their contacts.

VACCINATION

Free vaccination program for all infants at birth, 2, 4, 6 (or 12) months; catch-up program in Yr 7 at school if needed .

In the Kimberley, free vaccination for adults ONLY if they meet the following criteria :

1. Not immune on lab testing (Anti-HBs negative, Anti-HBc negative) or no history of complete vaccination

AND

2. Are in at least one of the following categories:

- household/sexual contacts of hepatitis B carriers
- people with multiple sex partners (eg. sex workers)
- men who have sex with men
- people with chronic liver disease and/or hepatitis C
- people with HIV infection
- people who inject drugs

EXCLUDING

3. Inmates of prisons/correctional centres (have separate program) AND persons eligible for vaccines via workplace or other scheme

Adult vaccination also recommended for those in other high-risk groups (May not be free; examples include occupational exposure, travel – see The Australian Immunisation handbook)

POST VACCINATION TESTING

Testing for immunity (Anti-HBs) is only recommended post-vaccination for very high risk patients[10], such as:

1. Infants of HBsAg positive mothers (see pregnancy section)
2. Sexual partners and household contacts of recently diagnosed HBsAg positive people
3. Occupational risk (eg. healthcare workers)
4. Patients on haemodialysis
5. Those at risk of severe/complicated disease (eg. impaired immunity or with pre-existing liver disease)

Post vaccination testing should be undertaken at least 4 weeks post completion of vaccination course.

Non immune patients post vaccination[19]:

If adequate anti-HBs levels (>10mlIU/ml) are not reached after the third dose of vaccination, investigate for carriage of HBsAg.Those who are HBsAg negative should be offered further doses, either as a fourth double dose or a further 3 doses at monthly intervals with serological confirmation at least 4 weeks after the last dose.

Persistent non responders should be informed that they are not protected and should minimise exposures, and that they will need HBIG within 72 hours of parenteral exposure to HBV.

Booster doses are not recommended in immunocompetent individuals who have either completed a primary course as infants or adults who have shown previous antibody response. Booster doses ARE recommended for those with impaired immunity, especially HIV and patients with renal failure, these patients should have boosters following regular monitoring of anti-HB levels at 6 to 12 monthly intervals (discuss with physician).

Hepatitis B

PRINCIPLES OF MANAGEMENT

A thorough clinical history and examination needs to be undertaken, including:

- Risk factors for HBV infection: country of origin, family history
- Symptoms of liver disease
- Alcohol, drug and smoking use
- Abdominal examination, looking for signs of liver failure
- Examine for extrahepatic manifestations (eg. urinalysis, arthritis, skin rashes, peripheral neuropathy)

Initial tests:

- HBsAg, HBeAg, Anti-HBe, HBV DNA
- LFTs, FBC, UEC, HIV, coagulation studies, alpha-fetoprotein (αFP)
- Hepatitis A, C and D serology
- Abdominal ultrasound

Acute hepatitis B

- All suspected cases should be discussed with the regional physician and specific treatment plan made
- Consider all causes of hepatitis (eg. drugs, alcohol, non-alcoholic steatohepatitis - NASH)
- Follow up is crucial – repeat HBsAg in 6 months to see if infection resolved or progressed to chronic infection (consider repeat full STI screen)

Chronic hepatitis B

Ensure education, counselling and support provided – can be a life-long disease. Must include:

- Identification of household/sexual contacts who should be screened and potentially vaccinated
- Discussion about prevention of HBV spread and co-infection with HIV/HCV - all HBsAg-positive patients should be considered infectious

See HEALTHY LIVING protocol - encourage cessation of alcohol, drugs and smoking; BMI in normal range; diabetes control

If hepatitis A serology negative – provide free hepatitis A vaccine

Ensure influenza and pneumococcal vaccines are up to date (see HEALTHY LIVING protocol).

Non-immune household and sexual contacts should be offered:

- Immunoglobulin (ideally within 48 hours of acute infection)
- Hepatitis B vaccination (free vaccines available)
- Advice on how to prevent HBV spread (protected sexual intercourse, avoid sharing toothbrushes/razors)

Avoid medications, including over-the-counter preparations, which may worsen liver function. If medication required, monitoring of liver function should occur in consultation with GP.

THERAPEUTIC PROTOCOLS

The primary health care provider is responsible for assessing suitability for and patient's desire for treatment of hepatitis B. The aim of treatment is to prevent progression of liver disease, not to cure infection. To do this:

- Undertake a shared care meeting early – should include patient, medical officer, clinic staff and community members/family if requested by patient.
- Significant patient education needs to occurs to allow the individual and their family to consider future treatment options and lifestyle choices
- Determine suitability for treatment. This requires an assessment by the primary health care provider of the following:

  Ability of the patient to comply with daily medications (which may be life-long), regular investigations and review by physician

  Willingness of the patient to abstain from alcohol during treatment
- The patient suitability/willingness to accept treatment should be reviewed regularly

If deemed **suitable** for treatment:

1. Decision when/if to treat is guided by HBV DNA viral load, degree of liver damage, patient's other co-morbidities and lifestyle factors. Please note, not all patients deemed suitable actually need treatment but all need monitoring. Whether treatment is actually required will be determined by the Regional Physician.
2. If no record of these tests having been done in last 12 months order:
   - FBP, UEC, TFTs, uric acid, coagulation studies, Alpha-fetoprotein (αFP) and abdominal ultrasound, (hepatocellular carcinoma screening), HCV Ab, HIV, HAV total Ab
3. If LFTs abnormal (i.e ALT > 30 in males and >19 in females) and no record of the following test results in patient file (as once off screening) order a parenchymal liver disease screen, which is.:
   - ferritin, iron studies, antinuclear antibody, smooth muscle antibody, anti-mitochondrial antibodies, copper, alpha-1 antitrypsin level, caeruloplasmin
4. Discuss all results with local regional physician (by MMEx message or telephone)
5. To appreciate, participate in and help educate patient on the physician's monitoring/treatment advice – please see appendix 1 in reference manual.

If patient deemed **not suitable** or declines treatment:

Monitoring and referral to regional physician as per table 1

CHRONIC HEPATITIS B

HBSAG POSITIVE MOTHERS: antenatal care and follow up for child

All pregnant women should be screened for hepatitis B at the first antenatal visit of each pregnancy, request HBsAg[11].

Women who are found to be HBsAg positive:

- Order HBeAg, Anti-HBe, HBV DNA level, LFT, FBP, INR

- A shared care meeting to occur with local midwife and obstetrics DMO by 20 weeks gestation, in which blood results will be available; with discussion to include 1) counselling and education re HBV, 2) consideration of specialist input and anti-viral therapy, 3) planning of follow up for child

- Counselling needs to occur with family due to a risk of up to 10% for transmission from mothers with high HBV DNA viral load to babies despite immuno-prophylaxis (vaccine + immunoglobulin at birth)[12].

For infants born to mothers who are HBsAg positive:

- Give hepatitis B (HBV) vaccine AND hepatitis B immunoglobulin (HBIG) at the same time within 12 hours of birth at different body sites (eg. one each thigh)

- Midwife to refer infant prior to hospital discharge to:

1. Paediatrician – for bloods and follow up as needed
2. Local child health nurse, GP, local AMS/clinic as appropriate to ensure follow up, education and support

- Subsequent vaccination as per normal schedule

- Hepatitis serology (HBsAg + Anti-HBs) needed at 9-15 months of age (at least 3 months after the full hepatitis B vaccination schedule). Local services to coordinate with paediatric team to ensure completion. If HBsAg positive OR Anti-HBs negative will need further specialist follow up.

The mother can safely breastfeed her child provided the HBV vaccine and HBIG were given at birth[13]. Educate mothers to take good care of her nipples and avoid cracking or bleeding.

FOLLOW UP

Chronic hepatitis B can be a life-long disease, appropriate education, counselling and support needs to be provided.

If deemed **suitable** for treatment: follow up and monitoring as per physician recommendations

If patient deemed **not suitable** or **declines** treatment: follow and monitoring up as per table 1

Ensure all household contacts have been vaccinated

WHEN TO REFER

If **deemed suitable** for treatment – refer as per discussion with local regional physicians (see therapeutic protocols)

If patient **deemed not suitable** or **declines** treatment: referral to regional physician as per table 1

For further information in regards to chronic hepatitis B management in **suitable for treatment** patients – see appendix 1 in reference manual.

REFER/DISCUSS

Position	Role	Contact details
Blood borne virus public health nurse	To provide information, education and support to staff and patients in relation to hepatitis treatment and prevention	9194 1644
Kimberley Physician	Provide follow up and treatment access	91941657 0417 911 595
Regional pharmacist	To advise on treatment and side effects	91942822
Broome hospital hepatitis nurse	To provide support to patients undergoing treatment	91942274
Royal Perth Hospital Hepatitis CNC	To provide support and information to patients undergoing treatment	92242244 Page 3186
Hepatitis council WA	Counselling and support for patients with hepatitis	93288538 1800 800 070
WASUA (WA Substance Users Assocation)	Support to injecting drug users	92277866
Kinway Broome	Counselling support	91942499
Kinway Kununurra	Counselling support	91665000
Kimberley Mental Health and Drug Service	Counselling support	91923322

Hepatitis B Table 1 and Appendix 1

Table 1: Primary care monitoring of patients not suitable for or declining treatment [3]

Patient is HBeAG positive	
Monitoring	If ALT levels <2 x ULN (upper limit normal)
	HBsAg, Anti-HBs, HBeAg, Anti-HBe and LFTs every 12 months If ALT levels >2 x ULN HBsAg, Anti-HBs, HBeAg, Anti-HBe and LFTs every 6 months
Refer#	If ALT levels are persistently >2 x ULN (or 1-2 xULN if aged >40 years) or if HBeAg remains positive for over 6 months
Patient is HBeAg negative	
Monitoring	HBV DNA and LFTs every 12 months. If ALT high: exclude other possible causes of ALT elevation
Refer#	If HBV DNA >2,000 IU/mL AND ALT remains elevated with no other cause found
HCC screening in high risk patients*: LFTs + αFP 6 monthly, ultrasound yearly (discuss with regional physician)	

*High risk groups: 1) Indigenous patients aged 40+ 2) Asian males aged 40+ 3) Asian females aged 50+ 4) All cirrhotic patients 5) Family history of HCC 6) Africans aged 20+

Consider physician referral for consideration of treatment if above referral parameters fulfilled and patient is now willing to accept treatment.

APPENDIX 1: Primary care management and referral advice for patients suitable for treatment[15 16 17 18]

Task	1. Immune tolerance	2. Immune clearance	3. Immune control	4. Immune escape
Description	Viral replication, minimal liver damage	Immune response, inflammation and liver injury	Supression of viral replication, minimal liver damage	Viral replication, high risk cirrhosis
HBsAG	>6 months positive	>6 months positive	>6 months positive	>6 months positive
HBeAG	Positive	Positive	Negative	Negative
Anti-HBe	Negative	Negative → positive	Positive	Positive
ALT	Normal	Fluctuating, raised	Normal	Fluctuating, raised
HBV DNA	>20,000 IU/ml	>20,000 IU/ml, fluctuating	<2000 IU/ml	>2000 IU/ml
Physician referral	No	If high ALT persists >3 months AND/ OR HBeAg remains positive >6 months - Yes	No	Yes
Follow up	Order LFT, HBsAG, HBeAg, Anti-HBe, HBV DNA in 12 months	Order LFT in 3 months; if LFT normal – HbsAg, HBeAg, anti-HBe in 6 months and HBV DNA in 12 months; if refer – as per physician recommendations	Order LFT, HBsAg, HBeAg, HBV DNA in 12 months	As per physician recommendations
HCC screening in high risk patients: LFTs + αFP 6 monthly, ultrasound yearly (discuss with regional physician)*				

*High risk groups: 1) Indigenous patients aged 40+ 2) Asian males aged 40+ 3) Asian females aged 50+ 4) All cirrhotic patients 5) Family history of HCC 6) Africans aged 20+

Acronyms

HBV, hepatitis B virus; HBsAg, hepatitis B surface antigen; Anti-HBs, hepatitis B surface antibody; Anti-HBc, hepatitis B core antibody; HBeAg, hepatitis B e antigen; Anti-HBe, hepatitis B e antibody; HCC, hepatocellular carcinoma

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