QUICK REFERENCE FOR HEALTHCARE PROVIDERS

MANAGEMENT OF CHRONIC HEPATITIS B IN ADULTS

Ministry of Health Malaysia

Academy of Medicine Malaysia

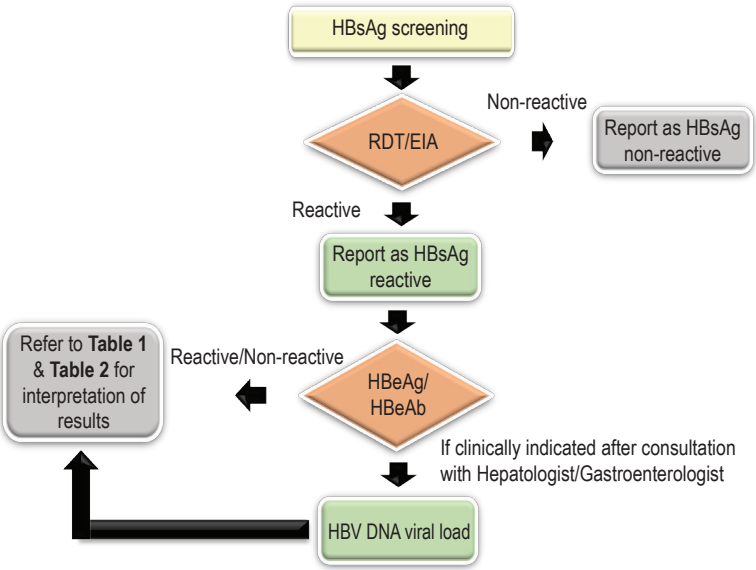
KEY MESSAGES

1. Targeted screening for hepatitis B virus (HBV) infection should be done in the following groups of people:
   - family members of hepatitis B surface antigen (HBsAg) positive persons
   - household contacts of HBsAg positive persons
   - blood donors
   - healthcare workers
   - people who inject drugs participating in harm reduction programmes
   - foreign workers
   - pregnant women
2. Screening of HBV infection should be done using either a rapid diagnostic test (RDT) or laboratory-based immunoassay. HBV deoxyribonucleic acid (DNA) should be ideally done before initiation of treatment & for assessment of its response.
3. Initial assessment of patients with chronic hepatitis B (CHB) should include:
   - phase of infection
   - degree of liver fibrosis or cirrhosis
   - presence of co-infection
4. Treatment should be initiated in CHB patients with:
   - non-cirrhotic liver
     - hepatitis B e antigen (HBeAg) positive with HBV DNA >20,000 IU/ml & alanine transaminase (ALT) twice the upper limit of normal (ULN)
     - HBeAg negative with HBV DNA >2,000 IU/ml & ALT twice ULN
   - cirrhotic liver
     - any detectable level of HBV DNA regardless of ALT & HBeAg status
5. Nucleos(t)ide analogues with high genetic barrier resistance should be used as first-line therapy in CHB i.e.
   - entecavir (ETV)*
   - tenofovir disoproxil fumarate (TDF)*
   - tenofovir alafenamide (TAF)

   *renal adjusted dose
6. ETV or TAF is preferred in CHB patients with age >60 years, bone disease or impaired renal function.
7. Human Immunodeficiency virus (HIV)/HBV co-infected patients should be treated simultaneously with dual active HBV treatment (tenofovir in combination with lamivudine or emtricitabine) plus another third agent of antiretroviral therapy.
8. Antiviral agents should be initiated in HBeAg-positive pregnant CHB women with high viral load (>200,000 IU/ml) at 28 - 32 weeks of gestation & hepatitis B immunoglobulin (HBIG) should be given to all newborns of CHB mothers within 12 hours of life.
9. All candidates for chemotherapy & immunosuppressive treatment should be tested for HBV markers prior to immunosuppression e.g. HBsAg. If HBsAg is negative, antibody to hepatitis B core antigen (anti-HBc) should be tested.
10. CHB patients who are not on treatment should be monitored for:
    - ALT
    - HBV DNA
    - liver fibrosis or cirrhosis

LABORATORY DIAGNOSIS

Laboratory Workflow for Diagnosis of Chronic Hepatitis B Infection



EIA: enzyme immunoassays; HBeAb: hepatitis B e antibody

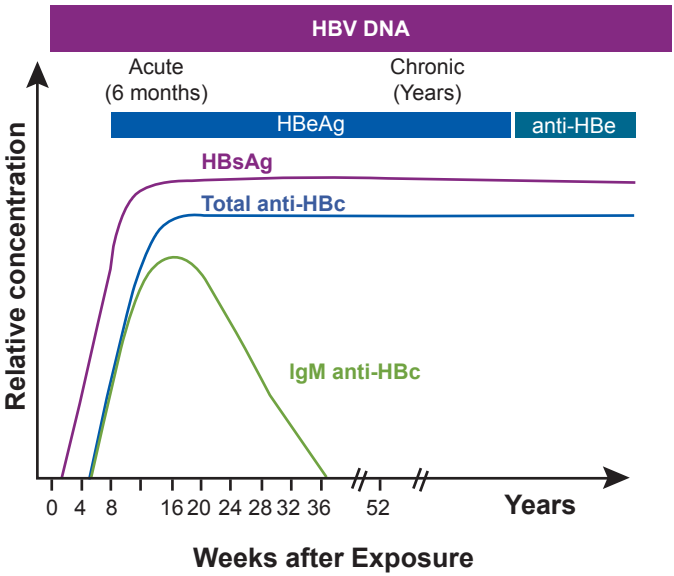
Tests to Diagnose & Monitor Hepatitis B Virus Infection

HBsAg	Anti-HBc	IgM anti-HBc	Anti-HBs	HBeAg	HBeAb	HBV DNA	Interpretation
-	-	-	-	-	-	-	Not infected nor protected, suggest vaccination
+	-	-	-	-	-	-	Transient (up to 52 days) after vaccination
+	-	-	-	-	-	±	Early acute infection
+	+	+	-	+	-	+	Acute infection
-	+	+	±	-	±	±	Acute resolving infection
-	+	-	+	-	±	-	Recovered from past infection & immune
+	+	-	-	±	±	+	Chronic infection
-	+	-	-	-	-	±	False-positive; past infection; 'low level' chronic infection; or passive transfer of anti-HBc to an infant born to HBsAg positive mother
-	-	-	+	-	-	-	Immune if the anti-HBs concentration is ≥10 IU/ml after vaccine series completion; passive transfer after hepatitis B immune globulin administration

Anti-HBc = Antibody to hepatitis B core antigen; IgM anti-HBc = Immunoglobulin M antibody to hepatitis B core antigen; Anti-HBs = Antibody to hepatitis B surface protein
+ implies positive; - implies negative; ± may be positive or negative

PATHOPHYSIOLOGY

The figure below represents a typical serology course of hepatitis B progression from acute to chronic overtime.



The natural course of HBV infection consists of four phases as shown in the table below.

Natural History & Assessment of Patients with Chronic Hepatitis B Virus Infection

Investigation/ Terminology	HBeAg positive		HBeAg negative	
	Chronic infection	Chronic hepatitis	Chronic infection	Chronic hepatitis
HBsAg	High	High/intermediate	Low	Intermediate
HBeAg	Positive	Positive	Negative	Negative
HBV DNA	>10^7 IU/ml	10^4 - 10^7 IU/ml	<2,000 IU/ml	>2,000 IU/ml
ALT	Normal	Elevated	Normal	Elevated
Liver disease	None/minimal	Moderate/severe	None	Moderate/severe
Old terminology	Immune tolerant	Immune reactive HBeAg positive	Inactive carrier	HBeAg negative chronic hepatitis

MANAGEMENT OF CHRONIC HEPATITIS B IN ADULTS

DRUG DOSAGE, ADMINISTRATION & COMMON SIDE EFFECTS OF HEPATITIS B ANTIVIRAL IN MALAYSIA

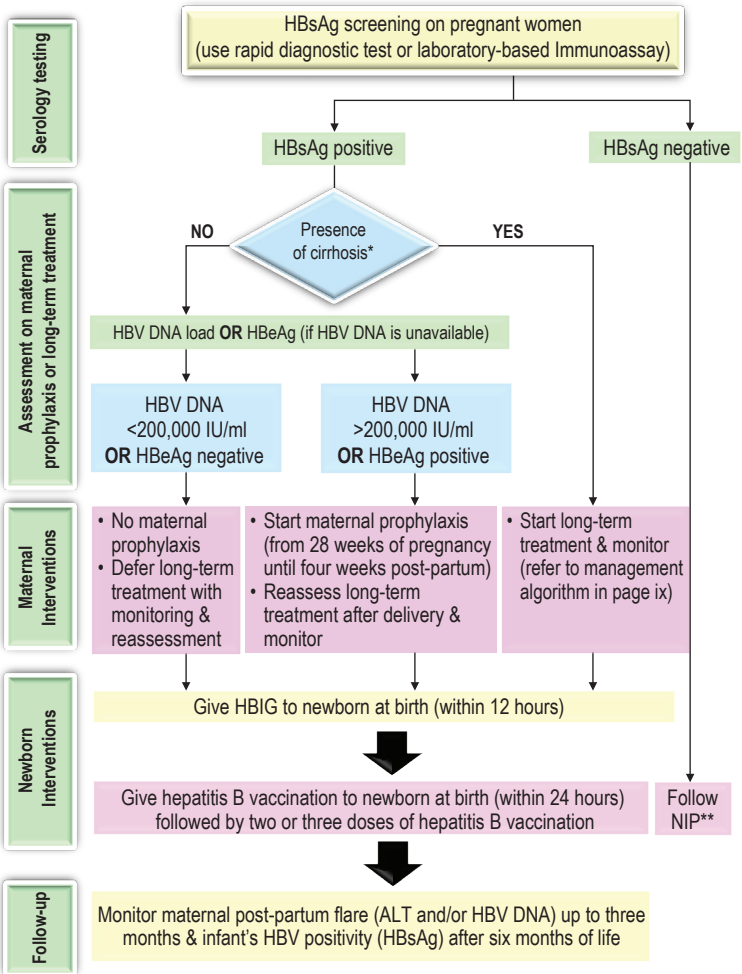
Drug	Standard dosage	Administration	Renal Adjustment (based on Creatinine Clearance, CrCl)* (ml/min)			Potential Side effects
			30 - <50	10 - <30	<10/ Hemodialysis (HD)	
Preferred (high barrier to HBV resistance)						
Pegylated Interferon-α 2a	180 mcg once weekly	Subcutaneous Injection	No dosage adjustment	135 mcg once weekly	90 - 135 mcg once weekly	Flu-like symptoms, fatigue, mood disturbances, cytopenia, autoimmune disorders
Entecavir[a]	0.5 mg once daily	Oral tablet, take on empty stomach, 2 hours apart from food	50% of usual dose **OR** 0.5 mg every 48 hours	30% of usual dose **OR** 0.5 mg every 72 hours	10% of usual dose **OR** 0.5 mg every 7 days	Lactic acidosis
Tenofovir Disoproxil Fumarate	300 mg once daily	Oral tablet, take with or without food	300 mg every 48 hours	300 mg every 72 to 96 hours	Avoid use. If no alternative, 300 mg every 7 days	Nephropathy, Fanconi syndrome osteomalacia, lactic acidosis
Tenofovir Alafenamide	25 mg once daily	Oral tablet, after food	**CrCl >15 ml/min:** No dose adjustment **CrCl <15 ml/min:** Use is not recommended			Lactic acidosis
Non-Preferred (low barrier to HBV resistance)						
Lamivudine	100 mg once daily	Oral tablet, take with or without food	**CrCl 30 - ≤50 ml/min:** 50 mg once daily **CrCl <5 - <15 ml/min:** 15 mg once daily **CrCl <5 ml/min:** 10 mg once daily			Pancreatitis, lactic acidosis
Adefovir[b] Dipivoxil	10 mg once daily	Oral tablet, take with or without food	10 mg every 48 hours	10 mg every 72 hours	Non-HD: No data HD: 10 mg every 7 days	Acute renal failure, Fanconi syndrome, lactic acidosis
Telbivudine[c]	600 mg once daily	Oral tablet, take with or without food	600 mg every 48 hours	600 mg every 72 hours	600 mg every 96 hours	Creatine kinase elevations & myopathy, peripheral neuropathy, lactic acidosis

*Creatinine clearance (CrCl) calculated by Cockcroft-Gault formula
[a]Entecavir dose is 1 mg once daily if the patient has decompensated cirrhosis
[b]Product discontinued
[c]Deregistered in Malaysia in 2022

PREGNANCY

A summary of prophylaxis & treatment in pregnant CHB patients is shown below.

Prophylaxis & Treatment of Mother-to-Child Hepatitis B Virus Transmission



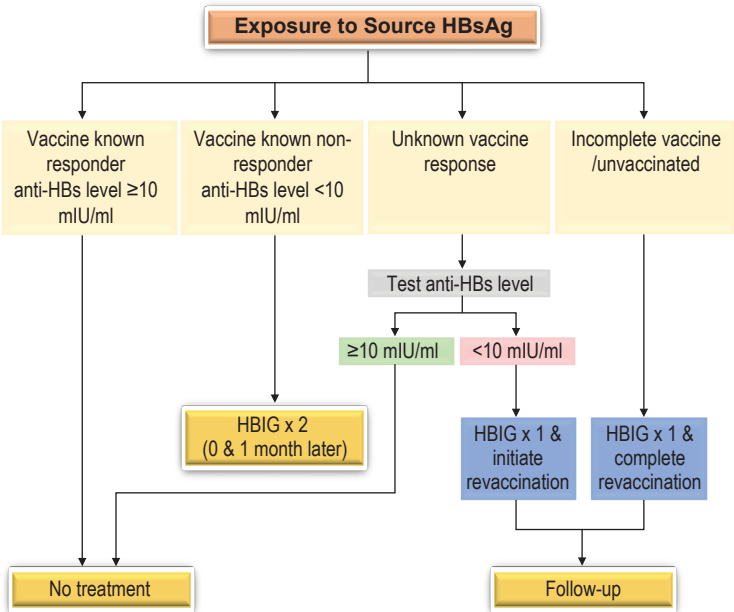
*Based on recommended methods of assessment for fibrosis in CPG

** NIP = National Immunisation Programme

EXPOSURE AT WORK PLACE

Post-exposure prophylaxis (PEP) management of healthcare provider (HCP) with possible exposure to HBV depends on the immune status of the HCP & HBsAg status of the source patient. Serological markers, i.e. baseline anti-HBs & HBsAg, are important in deciding the requirement for PEP.

POST-EXPOSURE PROPHYLAXIS WORKFLOW



This Quick Reference provides key messages & a summary of the main recommendations in the Clinical Practice Guidelines (CPG) Management of Chronic Hepatitis B in Adults.

Details of the evidence supporting these recommendations can be found in the above CPG, available on the following websites: Ministry of Health Malaysia: www.moh.gov.my
Academy of Medicine Malaysia: www.acadmed.org.my

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