Management Guidelines

Chronic Hepatitis B

Hepatitis B

Pakistan Society of Hepatology

Rawalians' Research Forum

Adapted from

A Treatment Algorithm for the Management of Chronic Hepatitis B Virus Infection in the United States.

Keeffe EB, Et al. Clinical Gastroenterology and Hepatology. 2004; 2:87-106

Collaboration: Hepatitis B Consultation Forum Pakistan

Introduction

This guide is designed to assist healthcare professionals in the evaluation, diagnosis, treatment, and monitoring of patients with chronic hepatitis B infection (HBV). Here you will find evidence-based, practical approaches to the following clinical situations:

- ☐ What tests to order and how to interpret the results
- ☐ Which patients should be treated
- ☐ When patients should be treated and for how long
- ☐ What treatments are available
- ☐ How patients should be monitored

The HBV burden

- ☐ An estimated 1.25 million people in the U.S. are chronically infected with HBV
- ☐ Approximately 100,000 people in the U.S. become acutely infected each year
- ☐ HBV patients are at increased risk for developing cirrhosis, hepatic decompensation, and hepatocellular carcinoma (HCC)

Treatment goals

- ☐ Eliminate or significantly suppress HBV replication
- ☐ Prevent the progression of liver disease to cirrhosis which could lead to liver failure or HCC
- ☐ Reduce the HBV DNA level and maintain it at the lowest possible level
- ☐ Loss of HBeAg with seroconversion to anti-HBe positively for HBeAg-positive patients

Risk factors for hepatitis B virus infection

- ☐ Family history of HBV and liver cancer[3]
- ☐ Sexually active with multiple partners[4]
- ☐ Exposure to human blood or blood-contaminated body fluids[4]
- ☐ Intravenous drug use[5]
- ☐ International travel to endemic areas[5]
- ☐ Born in endemic area with high prevalence of chronic HBV[4]
- ☐ Incarceration in long-term correctional facilities[5]

Diagnosis

Serum HBsAg + for > 6 months

Initial patient evaluation

Checklist for initial patient evaluation

- ☐ History and physical examination
  - Laboratory tests to assess liver disease
  - AST
  - ALT
  - CBC
  - Prothrombin time
- ☐ Tests for HBV replication and serology
  - HBV DNA
  - HBsAg
  - HBeAg
  - Anti-HBe
- ☐ Test to rule out other causes of liver disease
  - Anti-HCV
  - Anti-HDV
- ☐ Tests to screen for hepatocellular carcinoma (HCC)
  - Alpha-fetoprotein (AFP)
  - Ultrasound (US)
- ☐ Liver biopsy to grade and stage liver disease for patients meeting the criteria for chronic hepatitis

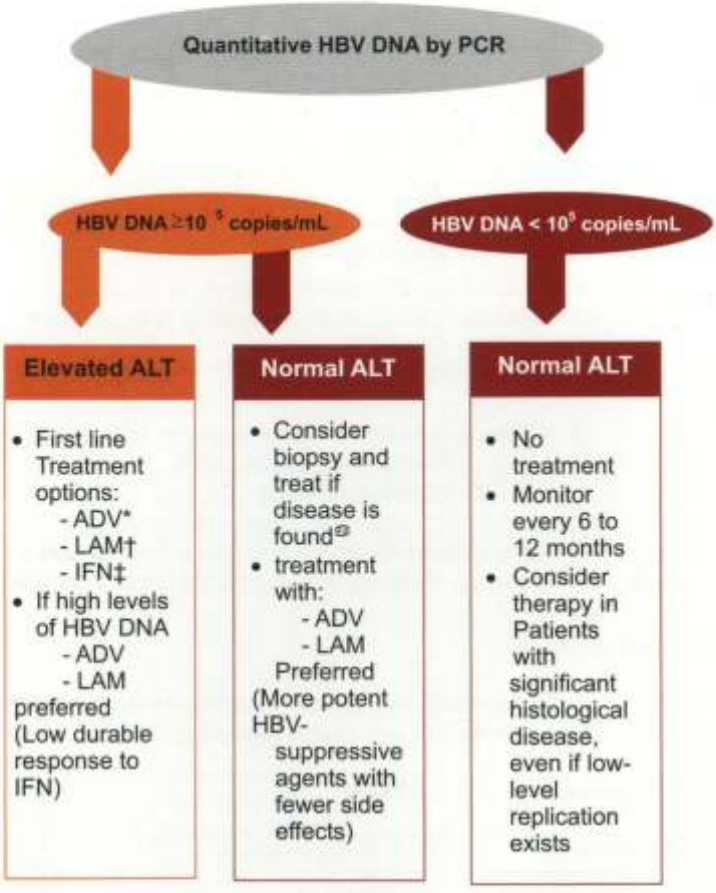
Disease status

Following the initial patients evaluation, treatment recommendations are based upon the patient's disease status described below:

Disease Status	Criteria
HBeAg+ Compensated liver disease	No cirrhosis on biopsy HBeAg + Anti-HBe- HBV DNA + by PCR
HBeAg- Compensated liver disease	No cirrhosis on biopsy HBeAg - Anti-HBe+ HBV DNA + by PCR
Compensated cirrhosis	Cirrhosis on biopsy Either HBeAg + or HBeAg- Compensated liver function
Decompensated cirrhosis	Clinical signs of decompensation or cirrhosis on biopsy Either HBeAg+ or HBeAg- Decompensated liver function ○ End-stage liver disease ○ Liver transplantation

Treatment recommendations

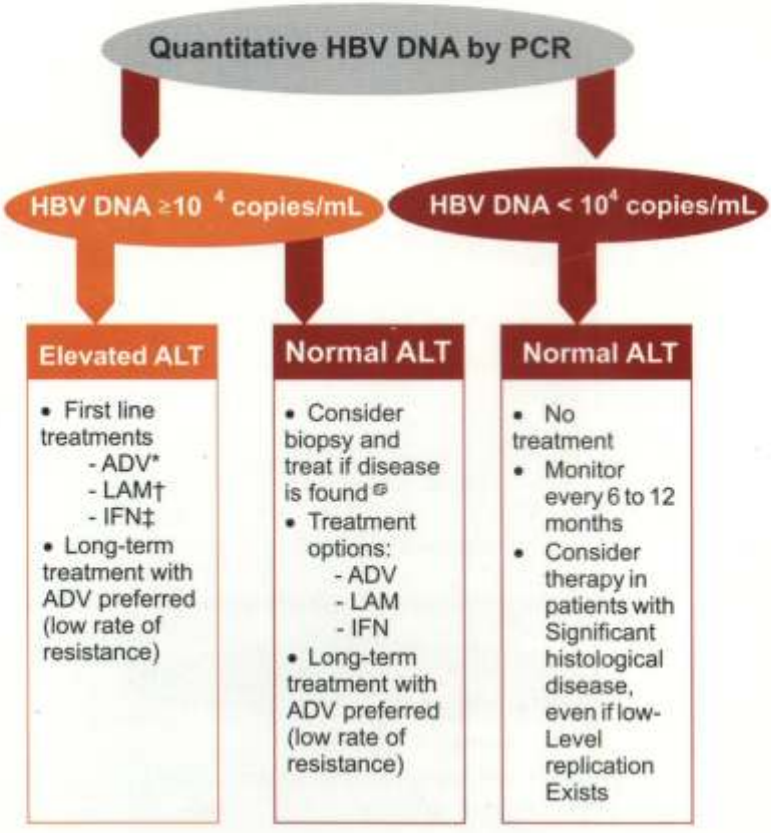
HBeAg positive patients[3]



*Adefovir dipivoxil.
† Lamivudine.
‡ Interferon alfa-2b.
If disease not found, monitor every 6 months.

HBeAg-negative patients[3]

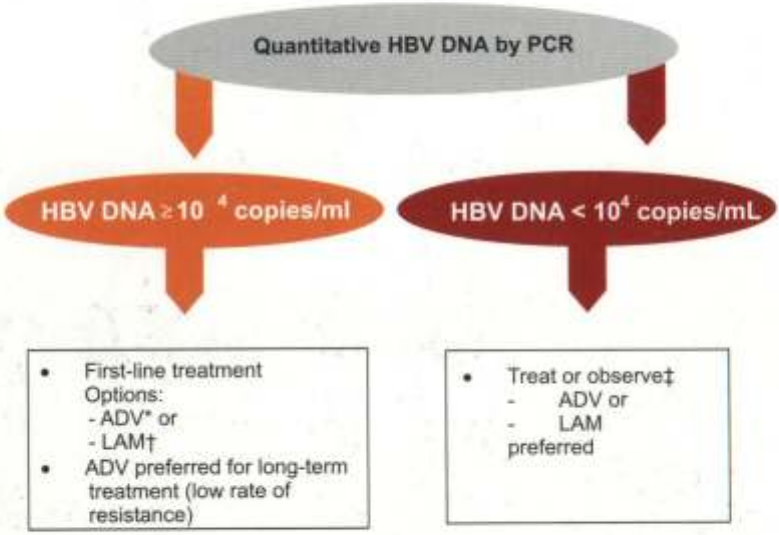
(Precore and core promoter mutations)



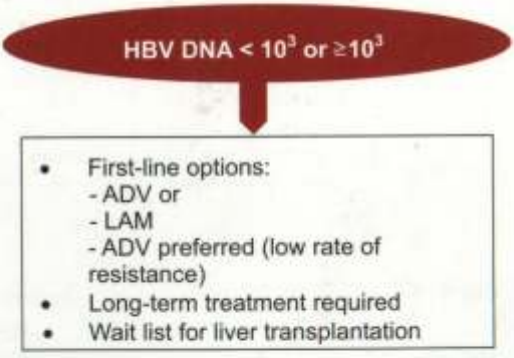
*Adefovir dipivoxil.
† Lamivudine.
‡ Interferon alfa-2b.
◎ If disease not found, monitor every 6 months.

Cirrhosis/End-stage liver disease

Compensated cirrhosis patients[3]



Decompensated cirrhosis patients



* Adefovir dipivoxil
† Lamivudine
‡ Observe 6 months.

Duration of therapy and monitoring

Disease Status	Duration and monitoring
HBeAg+ Compensated liver disease	**Monitoring:** every 6 months@ - HBV DNA (PCR) - ALT **Duration of treatment#:** Discontinue treatment when - HBeAg- -Anti-HBe+ - HBV DNA (PCR)- } On two observations 6 months apart
HBeAg- Compensated liver disease	**Monitoring:** every 6 months@ - HBV DNA (PCR) - ALT **Duration of treatment:** - Long-term/indefinite treatment required**
Compensated cirrhosis and Decompensated cirrhosis	**Monitoring:** every 3 months†† - HBV DNA (PCR) - ALT - Renal function: Serum creatinine **Duration of treatment:** - Long-term / indefinite treatment requirEd**

@Possibly more frequently with lamivudine to facilitate early detection of resistance.

Monitoring patients closely following treatment discontinuation. Hepatic flares are observed in up to 25% of patients following discontinuation of nucleoside/nucleotide analogs.

** Continue treatment until:

- HBV DNA (PCR)-
- HBsAg-

††Close monitoring is required because drug resistance can result in liver decompensation.

Serum HBV DNA assays[3]

Optimal management of chronic hepatitis B patients requires the use of HBV DNA testing. HBV DNA assays can help determine whether the hepatitis B virus is actively replicating, stable, or reduced to an undetectable level. There are two categories of HBV DNA assays:

PCR assays[3]

- Preferred in the initial evaluation and monitoring of both treated and untreated patients
- Detect HBV DNA to lower levels of qualification (e.g., 10^2 copies/ml)
  - More rapid detection of viral rebound due to drug resistance
  - More accurate identification of active disease

Nonamplified hybridization assays[3]

- Unable to detect HBV DNA below 10^5 to 10^6 copies/ml
  - Lacks sensitivity to detect HBV DNA rebound due to drug resistance
  - May not identify active disease in HBeAg-negative (precore mutant) patients due to lower DNA levels

- The threshold of HBV DNA levels associated with disease in unknown
  - There is some evidence that patients can have advanced disease even if their serum HBV DNA levels are persistently < 10^5 copies/mL[3]
  - Patients who are HBeAg+ have an increased risk of HCC[6]
  - Likelihood of HCC in individuals with detectable HBV DNA is four times more than in those with undetectable HBV DNA[6]

Recommendation / References

AASLD recommendations for treatment: Summary

HBeAg-positive disease, ALT > 2 x ULN, HBV-DNA>10^5 copies/ml

- IFN-á* for 16 weeks, or LAM or ADV for minimum 1 year
- Endpoint: Seroconversion to anti-HBe

HBeAg-positive disease, ALT > 2 x ULN, HBV-DNA>10^5 copies/ml

- IFN-á* for 1 year, or LAM or ADV for minimum 1 year
- IFN- á or ADV preferred for long-term treatment, due to possibility of resistance with LAM
- Endpoint: Sustained normalization of ALT; undetectable HBV-DNA by PCR assay

Cirrhosis, HBV-DNA>10^5 copies/ml, HBeAg-positive or HBeAg-negative disease

- Compensated: LAM or ADV
- Decompensated: LAM (or ADV), refer for liver transplant
- IFN- á contraindicated

Cirrhosis, HBV-DNA>10^5 copies/ml, HBeAg-positive or HBeAg-negative disease

- Compensated: Observe
- Decompensated: Refer for liver transplant

- Use LAM or ADV if IFN- á contraindicated or no response

Lok ASF, McMahon BJ. Chronic hepatitis b: Update of recommendations. Hepatology 2004; 39: 857-861.

References

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3. Keeffe EB, Dieterich DT, Han SHB, et al. A treatment algorithm for the management of chronic hepatitis B virus infection in the United States. Clin Gastroenterol Hepatol. 2004; 2: 87-106.
4. Centers For Disease Control and Prevention. Public health service inter-agency guidelines for screening donors of blood, plasma, organs, tissues, and semen for evidence of hepatitis B and hepatitis C. MMWR, 1991; 40: 1-17.
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6. Yang HI, Lu SN, Liaw YF, et al, for the Taiwan Community-Based Cancer Screening Project Group. Hepatitis B e antigen and the risk of hepatocellular carcinoma. N Engl J Med. 2002; 347: 168-174.

Please contact to inquire further

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