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AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

Practical Application of HBV Guidelines

To develop these guidelines, the guideline panel…

FORMULATED CLINICAL QUESTIONS

- Developed structured questions following the Population, Intervention, Comparison, and Outcome (PICO) framework
- Addressed six PICO questions covering prevention, surveillance for liver cancer, and treatment to provide evidence-based recommendations on these topics

REVIEWED EVIDENCE

- Conducted four systematic reviews of the literature and utilized two existing systematic reviews to support the recommendations

DEVELOPED RECOMMENDATIONS

- Used the Grading of Recommendation Assessment, Development, and Evaluation (GRADE) approach by first determining certainty in the evidence (from high to very low)
- Utilized the GRADE approach to determine the strength of recommendations in the evidence to decision framework considering patient values, resource use, feasibility, acceptability, equity

Objectives

By the end of this session, you should be able to:

1) Correctly identify phases of chronic hepatitis B (CHB)
2) Describe recommendations for prevention of maternal to infant transmission and horizontal transmission
3) Determine appropriate liver cancer surveillance for those who are HBsAg positive with HCV, HDV, and/or HIV co-infection as well as after HBsAg loss
4) Describe treatment indications for HBsAg positive persons in immune-tolerant or indeterminate phases
5) Describe relevant considerations regarding withdrawal of antiviral therapy

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Chronic Hepatitis B Core Concepts

Phases of CHB	
Immune-tolerant CHB	HBeAg-positive, HBV DNA > 10,000,000 IU/mL and normal ALT (< 25 U/L in women, < 35 U/L in men)
Immune active CHB	HBeAg-positive and ALT ≥ 2xULN and HBV DNA ≥ 20,000 IU/mL HBeAg-negative and ALT ≥ 2xULN and HBV DNA ≥ 2,000 IU/mL
Inactive CHB	HBeAg-negative, HBV DNA < 2000 IU/mL and normal ALT
Indeterminate CHB ("Grey zone")	HBeAg-positive or negative with HBV DNA level and/or ALT level outside those with immune-tolerant, immune active or inactive CHB
HBsAg loss	Loss of HBsAg occurring on antiviral therapy or spontaneously in a person who was previously HBsAg-positive

ALT - alanine aminotransferase, CHB - chronic hepatitis B, HBeAg - hepatitis B e antigen, HBsAg - hepatitis B surface antigen, HBV DNA - hepatitis B DNA viral load, ULN - upper limit of normal

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Ghany M., et al. AASLD Practice Guideline on Treatment of Chronic Hepatitis B. *Hepatology* 2025

Chronic HBV: Available Treatment Options

Drug with dosing regimen	Potential Long-term Side Effects	Monitoring on Treatment
Peg-IFN-α-2a (adults)/ IFN-α-2b (children) *Children ≥ age 3: 180 mcg/1.73m^2 x BSA subcutaneously once weekly *Adults: 180mcg subcutaneously weekly	• Thyroid dysfunction • Neuropsychiatric effects • Cytopenias (neutropenia, thrombocytopenia) • Autoimmune disorders and growth inhibition in children	• Hematologic testing every 2 weeks for first month then every 4-6 weeks • Biochemical tests with liver panel and uric acid monthly • TSH every 3 months • Clinical monitoring for autoimmune, neuropsychiatric and infectious complications
Entecavir (ETV) *Children ≥ age 2: weight-based to 10-30 kg, 0.5 mg orally daily for weight above 30 kg *Adults, Adolescents ≥ age 16: 0.5 mg orally daily **Must be taken 2 hours before a meal	• HIV-1 resistance in coinfected patients with untreated HIV • Lactic acidosis	• Test for HIV before treatment initiation • Lactic acid levels if there is clinical concern

Peg-IFN-α-2a – Peginterferon alfa-2a, IFN-α-2b – Peginterferon alfa-2b, BSA - body surface area, HIV-1-human immunodeficiency virus-1, TSH – thyroid stimulating hormone

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Adapted from Table 1 in Terrault N, et al. Update on Prevention, Diagnosis, and Treatment and of Chronic Hepatitis B: AASLD 2018 Hepatitis B Guidance. *Hepatology* 2018

Chronic HBV: Available Treatment Options

Drug with dosing regimen	Potential Long-term Side Effects	Monitoring on Treatment
Tenofovir disoproxil fumarate (TDF) *Children ≥ age 2 weighing 17 to <22kg – 150mg orally daily 22 to <28kg – 200mg orally daily 28 to <35kg – 250mg orally daily ≥ 35kg – 300mg orally daily *Adults: 300 mg orally daily	• Renal biomarker changes (proteinuria, increased creatinine) • Bone mineral density decrease • Proximal tubular dysfunction, Fanconi syndrome, Hypophosphatemia • Osteoporosis • Lactic acidosis	• Baseline and (at least) annual: serum creatinine, creatinine clearance, urine glucose, urine protein; and serum phosphorus • Test for HIV before treatment initiation • Weight in children for dose adjustment • Consider bone density study at baseline and during treatment in patients with history of fracture or risks for osteopenia • Lactic acid levels if there is clinical concern
Tenofovir alafenamide (TAF) *Children ≥ age 6 weighing ≥ 25 kg: 25 mg orally daily *Adults: 25mg orally daily	• Renal biomarker changes (increased creatinine; less than TDF) • Hypophosphatemia • Bone mineral density decrease (less than TDF) • Hypercholesterolemia • Lactic acidosis	• Baseline: serum creatinine, creatinine clearance, urine glucose, urine protein; and (at least) in chronic kidney disease (include serum phosphorus) • Test serum lipids before, 4-12 weeks after initiating therapy and annually thereafter • Test for HIV before treatment initiation • Lactic acid levels if there is clinical concern

Note: TDF and TAF can be taken without food but pairing with food is preferred to aid absorption

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Adapted from Table 1 in Terrault N, et al. Update on Prevention, Diagnosis, and Treatment and of Chronic Hepatitis B: AASLD 2018 Hepatitis B Guidance. *Hepatology* 2018

Chronic Hepatitis B Core Concepts

Goals of antiviral treatment:

1) Prevention of progression to cirrhosis, decompensated liver disease, development of hepatocellular carcinoma (HCC), and liver-related death
2) Reduction in onward transmission – vertical and horizontal
3) Improvement in patient reported outcomes and quality of life

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Case 1: CHB in Pregnancy

33-year-old pregnant individual at gestational week 25 with CHB, not currently on antiviral treatment, presents to your office for follow up. Serologic testing shows continued HBsAg and HBeAg positivity along with ALT 17 U/L and HBV DNA level of 1,200,152 IU/mL.

What do you recommend for management?

A. Start peginterferon now
B. Start tenofovir disoproxil fumarate at gestational week 28
C. Continue to monitor monthly serologies with HBV DNA and ALT
D. Start entecavir at gestational week 28

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D. Start entecavir at gestational week 28

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Recommendation 1

For **pregnant persons** with **HBV DNA levels greater than 200,000 IU/mL** at any time point during pregnancy regardless of HBeAg status, AASLD recommends **initiating tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide (TAF) at gestational week 28** to prevent mother-to-child transmission. TDF has a more extensive safety record in pregnancy than TAF. Both entecavir and peginterferon use are contraindicated during pregnancy.

(Strong recommendation, moderate certainty)

***IMPLEMENTATION TIP*:**

For mothers with HBV DNA >200,000 IU/mL, if hepatitis B immunoglobulin (HBIG) use in infant is unavailable, initiate TDF/TAF prophylaxis at gestational week 16 in combination with subsequent infant vaccination

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Case 1, continued

You start tenofovir disoproxil fumarate at gestational week 28.

The patient tolerates treatment and ultimately gives birth to a healthy baby boy without any complications.

As treatment was initiated for prevention of perinatal transmission, which of the following actions can occur?

A. TDF discontinuation at delivery
B. Monitoring with HBV DNA and ALT every 1 to 3 months for up to six months if TDF discontinued
C. Continuation of TDF while breastfeeding
D. All the above

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Case 1, continued

You start tenofovir disoproxil fumarate at gestational week 28.

The patient tolerates treatment and ultimately gives birth to a healthy baby boy without any complications.

As treatment was initiated for prevention of perinatal transmission, which of the following actions can occur?

A. TDF discontinuation at delivery
B. Monitoring with HBV DNA and ALT every 1 to 3 months for up to six months if TDF discontinued
C. Continuation of TDF while breastfeeding
D. All the above

Note: The same would apply for tenofovir alafenamide use in this setting

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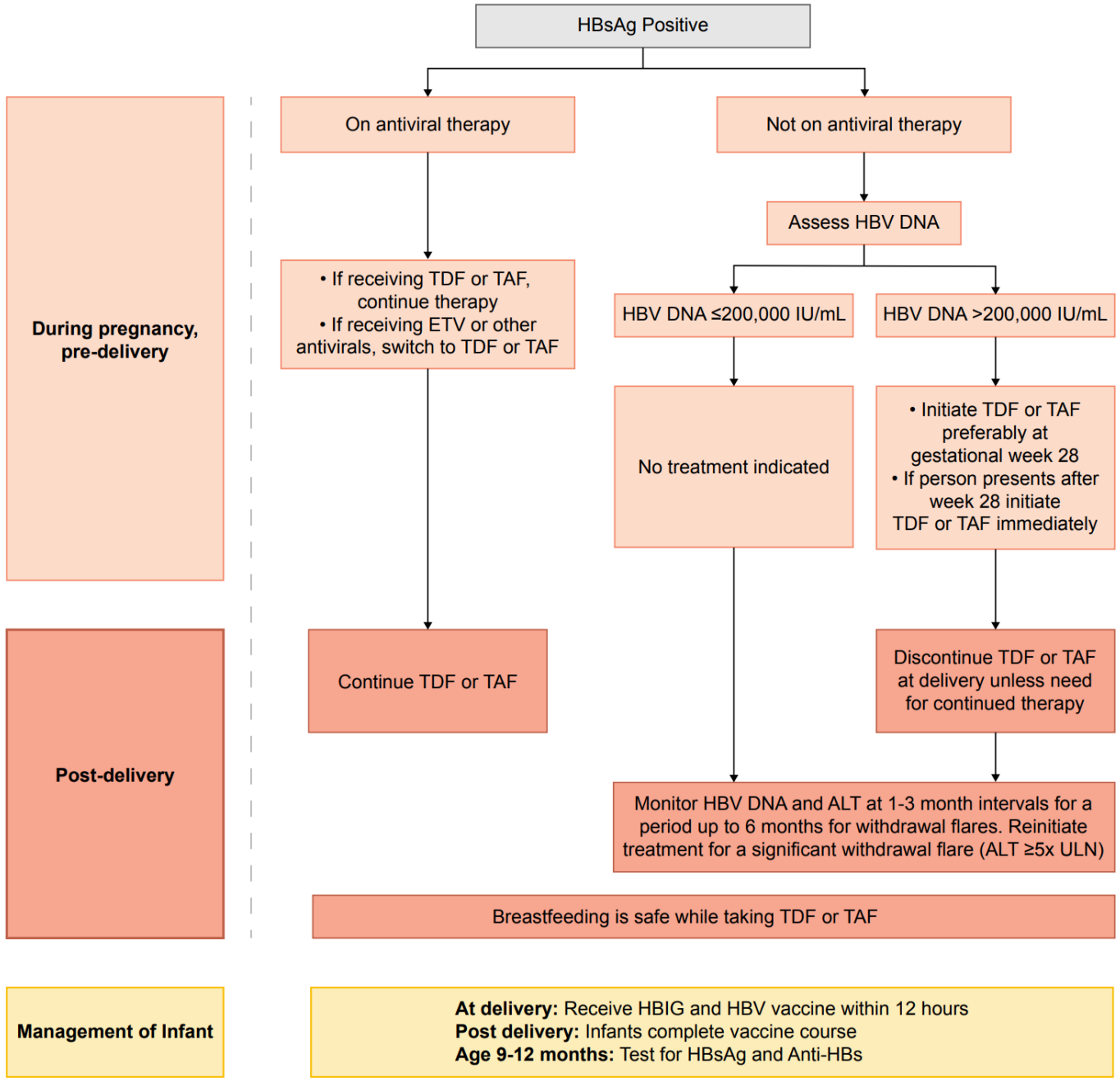
Figure 1: CHB Pregnancy Algorithm



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ALT - alanine aminotransferase, Anti-HBs - hepatitis B surface antibody, ETV - entecavir, HBIG - hepatitis B immunoglobulin, HBsAg - hepatitis B surface antigen, HBV DNA - hepatitis B DNA viral load, TAF - tenofovir alafenamide, TDF - tenofovir disoproxil fumarate, ULN - upper limit of normal

Case 2: High transmission risk

21-year-old college student presents to your office for recent diagnosis of CHB. He occasionally engages in unprotected sexual activity and does not intend to utilize barrier protection in the near-future. Serologic testing shows positive HBeAg, ALT 32 U/L, and HBV DNA 10,650,000 IU/mL.

What is the recommended advice?

A. Remind him of transmission risk related to casual and sexual contact, contact sports, and sharing meals but advise against therapy as ALT level is normal
B. Reassure him that there is no risk of HBV transmission via sexual contact, but advise that he should use barrier protection to prevent HIV
C. Review pros and cons of initiating antiviral therapy for prevention of HBV transmission to sexual partners
D. None of the above

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A. Remind him of transmission risk related to casual and sexual contact, contact sports, and sharing meals but advise against therapy as ALT level is normal
B. Reassure him that there is no risk of HBV transmission via sexual contact, but advise that he should use barrier protection to prevent HIV
C. Review pros and cons of initiating antiviral therapy for prevention of HBV transmission to sexual partners
D. None of the above

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Recommendation 2

For persons who are **HBsAg-positive with viremia not meeting disease-specific treatment indications** and who are in **high-risk** scenarios **for transmission** to others, AASLD suggests a **shared decision-making approach** regarding antiviral treatment.

(Conditional recommendation, very low certainty)

***IMPLEMENTATION TIP*:**
If the primary indication for initiating antiviral therapy is for prevention of horizontal HBV transmission, the continuation of antiviral therapy may be revisited when transmission risks are no longer high

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Positive HBsAg with viremia- transmission prevention in high-risk settings

Considerations for antiviral treatment for the main purpose to prevent onward transmission

- HBV treatment to prevent onward transmission is not necessary for average risk scenarios for transmission*
- Possible high-risk scenarios for horizontal transmission of HBV include persons who are engaging in unprotected sex or with multiple partners, persons who are injecting drugs with inconsistent harm reduction practices, persons living with susceptible household members and healthcare workers performing SHEA level III exposure-prone procedures
- Utilize a shared decision-making approach to assess overall horizontal transmission risk and the individual‘s values and preference regarding this risk and that of taking antivirals with the primary goal of preventing transmission to others
- Decisions are influenced by the individual’s hepatitis B viremia, the exposure scenario and the vaccine and immunity status of those who are potentially exposed: Situations favoring antiviral treatment of the viremic person include those where the person at risk for acquiring HBV is unvaccinated, has inadequate response to vaccine and/or has compromised immune systems,** or has unknown vaccine status
- Providers should avoid stigmatizing practices and messages
- Once initiated for the prevention of HBV transmission, antiviral therapy should be continued until the high risk of transmission is no longer present
- People starting antiviral therapy should be counselled regarding the risks of treatment cession, which may include severe liver flares
- Though there are no definitive studies on the lowest level of viral load transmissibility, *** the goal of HBV treatment is HBV DNA suppression to less than the lower limit of quantification

*HBV is not transmitted from casual contact. People with hepatitis B should not be restricted in their daily activities, contact sports, school activities or professional training, and should not be required to be treated in those settings. Within households, worksites, and other settings, it is important to emphasize that routine contact, sharing meals, and hugging are not considered routes of transmission, though sharing of personal hygiene items (eg, toothbrush, razors) should be avoided

**Groups known to have inadequate response to vaccine include those who have immunocompromising conditions, have diabetes, have advanced liver disease, have advanced kidney disease, smoke, and are obese

***For healthcare providers performing Category III procedures, SHEA guidelines suggest maintaining HBV DNA < 1000 IU/mL

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Adapted from Table 2 in Ghany M., et al. AASLD Practice Guideline on Treatment of Chronic Hepatitis B. *Hepatology* 2025

Case 3: Management of Persons in the Immune-tolerant Phase

42-year-old male is referred by his PCP for management of newly diagnosed chronic hepatitis B. Serologies reveal positive HBeAg, HBV DNA 10,880,000 IU/mL and ALT 32 U/L. FIB-4 noted to be 0.75.

Vibration-controlled transient elastography (VCTE) with LSM of 5.6 kPa.

As his ALT was 33 U/L 8 months ago, you determine that he is in the immune-tolerant phase.

Which of the following factors in this patient would lead you to recommend antiviral therapy?

A. Age > 40 years old
B. FIB-4 score
C. VCTE results
D. HBV DNA >10 million IU/mL

*LSM - liver stiffness measurement

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Which of the following factors in this patient would lead you to recommend antiviral therapy?

A. **Age > 40 years old**
B. FIB-4 score
C. VCTE results
D. HBV DNA >10 million IU/mL

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Recommendation 3

For persons in the **immune-tolerant phase**, the AASLD suggests **antiviral therapy** for those **> 40 years** or with **significant liver inflammation (≥ grade 2) or fibrosis (≥ F2)** on liver biopsy or noninvasive tests. For persons **< 40 years old** who are interested in starting treatment earlier, the AASLD suggests **shared decision-making** with consideration of risk factors as well as the benefits and risks of treatment.

(Conditional recommendation, very low certainty)

***IMPLEMENTATION TIP*:**
Accurate identification of immune-tolerant phase requires persistently normal ALT levels (≥2 measurements at ≥ 6 months apart) with HBV DNA >10^7 IU/mL in HBeAg-positive persons

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Figure 2: Algorithm for no cirrhosis, +HBsAg, +HBeAg

HBV DNA >10,000,000 IU/mL ALT ≤ ULN	HBV DNA >10,000,000 IU/mL ALT 1-<2x ULN	HBV DNA ≥20,000 to ≤10,000,000 IU/mL ALT 1-<2x ULN	HBV DNA ≥20,000 IU/mL ALT ≥2x ULN
Immune tolerant	**Indeterminate**	**Indeterminate**	**Immune active**

• Monitor ALT and HBV DNA every 6 months
  • Assess for signs of fibrosis
  • Reassess need for treatment at each visit
• If age ≥40 years or ≥F2 fibrosis by biopsy or imaged-based NITs (e.g., elastography), suggest consideration of treatment
• If age <40 years, use a shared decision-making approach to discuss the risks and benefits if treatment considered
	• Monitor ALT and HBV DNA every 6 months
	  • Assess for signs of fibrosis
	  • Reassess need for treatment at each visit
	• If age ≥40 years or ≥F2 fibrosis by biopsy or imaged-based NITs (e.g., elastography), suggest consideration of treatment
		• Monitor ALT and HBV DNA every 3-6 months (as likely to transition to immune active)
		  • Assess for signs of fibrosis
		  • Reassess need for treatment at each visit
		• If age ≥40 years or ≥F2 fibrosis by biopsy or imaged-based NITs (e.g., elastography), suggest consideration of treatment
			• Treat

*ULN for ALT: 25 U/L in women, 35 U/L in men

*NITs - non-invasive fibrosis tests

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Case 4: Management of Persons in the Indeterminate Phase

41-year-old male with history of type 2 diabetes mellitus on two oral anti-hyperglycemic medications, grade 1 obesity, and stage 2 chronic kidney disease presents for follow up of CHB.

Serologic testing shows positive HBsAg, HBeAg negative, ALT 62 U/L, and HBV DNA 562 IU/mL. VCTE demonstrates CAP 320 dB/m and LSM 4.5 kPa.

What is the recommended management?

A. Start entecavir
B. Start tenofovir disoproxil fumarate
C. Start pegylated interferon
D. Shared decision-making with patient regarding treatment initiation

*CAP - controlled attenuation parameter

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Case 4: Management of Persons in the Indeterminate Phase

41-year-old male with history of type 2 diabetes mellitus on two oral anti-hyperglycemic medications, grade 1 obesity, and stage 2 chronic kidney disease presents for follow up of CHB.

Serologic testing shows positive HBsAg, HBeAg negative, ALT 62 U/L, and HBV DNA 562 IU/mL. VCTE demonstrates CAP 320 dB/m and LSM 4.5 kPa.

What is the recommended management?

A. Start entecavir
B. Start tenofovir disoproxil fumarate
C. Start pegylated interferon
D. Shared decision-making with patient regarding treatment initiation

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Recommendation 4

In adults with **HBsAg-positive, HBeAg-negative chronic HBV infection without cirrhosis** and in the **indeterminate phase**, AASLD suggests antiviral therapy using a **shared decision-making** approach by assessing risks and benefits and to **reevaluate that decision at each follow-up** visit if treatment has not been initiated.

(Conditional recommendation, very low certainty)

***IMPLEMENTATION TIP*:**
Individuals with persistently elevated ALT but HBV DNA < 2000 IU/mL should be evaluated for other etiologies of liver injury and managed for those etiologies if found

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Figure 3: Algorithm for no cirrhosis, +HBsAg, -HBeAg

HBV DNA <2,000 IU/mL ALT ≤ ULN	HBV DNA <2,000 IU/mL ALT > ULN	HBV DNA ≥2,000 IU/mL ALT <2x ULN	HBV DNA ≥2,000 IU/mL ALT ≥2x ULN
Inactive Phase	**Indeterminate**	**Indeterminate**	**Immune active**

• Monitor HBV DNA and ALT q 3-6 months for first year then q 6-12 months
• Assess for signs of cirrhosis
• Reassess need for treatment at each visit
	• Evaluate for other etiologies of liver disease and treat accordingly
	• Monitor HBV DNA and ALT q 3-6 months for first year then q 6 months
	• Assess for signs of cirrhosis
	• Reassess need for treatment at each visit
		• Consider treatment based on shared decision-making after discussion of risks and benefits, and factors associated with increased risk for HCC including male sex, age >40 years, platelet count <180k
		• If treatment is not initiated
		  • Monitor ALT and HBV DNA q 3 months for first year then q 6 months
		  • Assess for signs of cirrhosis
		  • Reassess need for treatment at each visit
			• Treat

***ULN for ALT: 25 U/L in women, 35 U/L in men**

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Case 4, continued

The patient elects to not pursue treatment at this time given his current pill burden and desire to focus on managing his other medical conditions.

Approximately 18 months later, he has lost weight with diet and exercise, and his diabetes is now diet-controlled. ALT is 45 U/L. Another in-clinic discussion determines to hold off on treatment.

Two years later, his serologies show continued positive HBsAg and negative HBeAg though ALT is 125 U/L with HBV DNA 2,505 IU/mL.

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Case 4, continued

Laboratory results over this time are displayed in the table below

	Initial	+6 months	+12 months	+18 months	+36 months	+42 months
ALT (U/L)	82	78	72	75	94	125
HBV DNA (IU/mL)	562	1,767	1,715	1,802	2,011	2,505

What is the recommended management?

A. No treatment indicated. Continue to monitor ALT and HBV DNA every 6 months
B. Start peginterferon
C. Start entecavir
D. None of the above

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Case 4, continued

Laboratory results over this time are displayed in the table below

	Initial	+6 months	+12 months	+18 months	+36 months	+42 months
ALT (U/L)	82	78	72	75	94	125
HBV DNA (IU/mL)	562	1,767	1,715	1,802	2,011	2,505

What is the recommended management?

A. No treatment indicated. Continue to monitor ALT and HBV DNA every 6 months
B. Start peginterferon
C. Start entecavir
D. None of the above

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Case 4, key concepts

- Initiate treatment for progression to advanced fibrosis/ cirrhosis or transition to HBeAg-negative immune active phase
- Patient is now immune active (HBeAg negative, ALT ≥ 2x ULN, HBV DNA ≥ 2,000 IU/mL) which warrants treatment
- History of kidney disease makes tenofovir alafenamide or entecavir the preferred treatments

Phases of CHB	
Immune-tolerant CHB	HBeAg-positive, HBV DNA > 10,000,000 IU/mL and normal ALT (< 25 U/mL in women, < 35 U/mL in men)
Immune active CHB	HBeAg-positive and ALT ≥2xULN and HBV DNA ≥ 20,000 IU/mL HBeAg-negative and ALT ≥2xULN and HBV DNA ≥ 2,000 IU/mL
Inactive CHB	HBeAg-negative, HBV DNA < 2000 IU/mL and normal ALT
Indeterminate CHB ("Grey zone")	HBeAg-positive or negative with HBV DNA level and/or ALT level outside those with immune-tolerant, immune active or inactive CHB
HBsAg loss	Loss of HBsAg occurring on antiviral therapy or spontaneously in person who was previously HBsAg-positive

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Case 5: Treatment withdrawal

52-year-old individual on entecavir for four years asks to discontinue therapy. Prior to treatment initiation, labs showed positive HBsAg, negative HBeAg, and HBV DNA 1,275,608 IU/mL. Today, labs show HBsAg 1196 IU/mL and undetected HBV DNA for the past 2.5 years. There is no evidence of advanced fibrosis/cirrhosis or HCC. There is no history of hepatic decompensation or extrahepatic complications of HBV.

How should you proceed with their management?

A. Recommend withdrawing therapy with monitoring every 3 months for a year then every 6 months indefinitely
B. Counsel patient that therapy withdrawal is not advised until HBsAg loss
C. Counsel patient that therapy withdrawal is not advised until HBV DNA remains undetectable for >5 years
D. None of the above

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How should you proceed with their management?

A. Recommend withdrawing therapy with monitoring every 3 months for a year then every 6 months indefinitely

B. Counsel patient that therapy withdrawal is not advised until HBsAg loss

C. Counsel patient that therapy withdrawal is not advised until HBV DNA remains undetectable for >5 years

D. None of the above

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Recommendation 5

In adults with chronic hepatitis B, who are **HBeAg-negative without cirrhosis**, **with sustained undetectable HBV DNA on nucleos(t)ide analogue therapy**, AASLD suggests **not withdrawing nucleos(t)ide analogous therapy until HBsAg loss**.

(Conditional recommendation, very low certainty)

***IMPLEMENTATION TIP*:**
Shared decision-making process between patient and provider should consider the benefits (HBsAg loss) and risks (hepatitis flare, liver decompensation, and need for re-treatment) as well as need for frequent monitoring

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Criteria for discontinuing antiviral therapy

☑	No history of cirrhosis, any hepatic decompensation (variceal bleed, HE, HRS), HCC or extrahepatic complications of HBV
☑	HBeAg-negative/anti-HBe positive for a minimum of one year (if HBeAg-positive at start of treatment)
☑	HBV DNA undetectable for a minimum of 2 years
☑	HBsAg level <100 IU/mL
☑	No co-infection with HIV or HDV
☑	Agree to frequent monitoring

- Persons who have a strong desire to discontinue therapy should engage in a shared decision-making process with their provider
- All criteria must be met to proceed

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Anti-HBe - hepatitis B e antibody, HBeAg - hepatitis B e antigen, HBsAg - hepatitis B surface antigen, HBV DNA - hepatitis B DNA viral load, HCC - hepatocellular carcinoma, HDV- hepatitis Delta virus, HE - hepatic encephalopathy, HRS - hepatorenal syndrome

Case 5, continued

Two years later he expresses a preference to discontinue therapy again. Repeat HBsAg is 97 IU/mL. Repeat VCTE shows minimal fibrosis. After reviewing the pros and cons, the decision is made to stop entecavir.

What monitoring protocol should the patient adhere to following treatment withdrawal?

A. ALT and HBV DNA every 1-3 months for the first 18 months
B. ALT and HBV DNA every 6 months for 2 years
C. ALT and HBV DNA every 1-3 months for 6 months, then every 3 months for 18 months
D. ALT and HBV DNA every 1-3 months for 6 months, then every 3 months for 18 months with HBV DNA obtained only if ALT is elevated

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Case 5, continued

Two years later he expresses a preference to discontinue therapy again. Repeat HBsAg is 97 IU/mL. Repeat VCTE shows minimal fibrosis. After reviewing the pros and cons, the decision is made to stop entecavir.

What monitoring protocol should the patient adhere to following treatment withdrawal?

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B. ALT and HBV DNA every 6 months for 2 years
C. ALT and HBV DNA every 1-3 months for 6 months, then every 3 months for 18 months
D. ALT and HBV DNA every 1-3 months for 6 months, then every 3 months for 18 months with HBV DNA obtained only if ALT is elevated

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Recommended monitoring schedule after stopping treatment

HBV DNA and ALT levels every 1- 3 months for the first 6 months

HBV DNA and ALT levels every 3 months for the next 6-12 months

HBV DNA and ALT levels every 3-6 months thereafter

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Case 5, continued

He agrees to follow the monitoring schedule and expresses understanding regarding the risk for withdrawal flare.

For which of the following scenarios should treatment be restarted?

A. HBV DNA ≥ 10,000 IU/mL regardless of ALT
B. ALT ≥ 5 times ULN, regardless of HBV DNA
C. Total bilirubin > 2.5 mg/dL
D. All the above

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Case 5, continued

He agrees to follow the monitoring schedule and expresses understanding regarding the risk for withdrawal flare.

For which of the following scenarios should treatment be restarted?

A. HBV DNA ≥ 10,000 IU/mL regardless of ALT
B. ALT ≥ 5 times ULN, regardless of HBV DNA
C. Total bilirubin > 2.5 mg/dL
D. All the above

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Aside: If this individual (52-year-old man without prior evidence of cirrhosis or HCC) were to experience HBsAg loss, should he continue to undergo HCC surveillance?

Recommendation 6

In persons who achieve **HBsAg loss**, AASLD suggests **continued HCC surveillance** for those with cirrhosis, with family history of HCC, men who experienced HBsAg loss after age 40, and women who experienced HBsAg loss after age 50.

(Conditional recommendation, very low certainty)

***IMPLEMENTATION TIP*:**

For persons in whom the timing of HBsAg loss is unknown, the decision to undergo surveillance should be individualized, with consideration of cirrhosis and family history of HCC

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Case 6: Co-infection HCC surveillance

An addiction provider at a local methadone clinic asks for your recommendations regarding surveillance of persons with other viral co-infections in CHB.

Match the HCC surveillance recommendations with the correct co-infection.

HBV-HCV co-infection	adults independent of cirrhosis status
HBV-HDV co-infection	men ≥ 18 years old and women ≥ 40 years old
HBV-HIV co-infection	as per criteria for HBV mono-infection

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Case 6: Co-infection HCC surveillance

An addiction provider at a local methadone clinic asks for your recommendations regarding surveillance of persons with other viral co-infections in CHB.

Match the HCC surveillance recommendations with the correct co-infection.

HBV-HCV co-infection	**as per criteria for HBV mono-infection**
HBV-HDV co-infection	**adults independent of cirrhosis status**
HBV-HIV co-infection	**men ≥ 18 years old and women ≥ 40 years old**

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Recommendation 7

In persons with HBV-HDV co-infection, AASLD suggests HCC surveillance of adults independent of cirrhosis status. The decision to undertake surveillance in children should be individualized due to the risk of HCC being unknown in this population. *(Conditional recommendation, very low certainty)*

Recommendation 8

In persons with HBV-HIV co-infection, AASLD suggests HCC surveillance for men ≥ 18 years of age and women ≥ 40 years of age. *(Conditional recommendation, very low certainty)*

Recommendation 9

In persons with HBV-HCV co-infection, AASLD recommends treatment for HCV and suggests HCC surveillance as per criteria for HBV mono-infection. *(Conditional recommendation, very low certainty)*

HCC surveillance with ultrasound and serum AFP performed at semiannual (approximately every 6 months) intervals is recommended as the most cost-effective approach per the 2023 AASLD HCC guideline

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Table 4: Target Groups for HCC Surveillance

Chronic HBV infection with cirrhosis	Child Pugh A-B, and transplant eligible Child-Pugh C
Chronic HBV infection without cirrhosis with increased HCC risk	Man from endemic country age > 40-years-old
	Woman from endemic country age > 50-years-old
	Person from Africa at earlier age
	Family history of HCC
	PAGE-B score ≥ 10
Co-infection without cirrhosis	HBV/HDV coinfection: all persons
	HBV/HIV coinfection: men ≥ 18-years-old and women ≥ 40-years-old
HBsAg loss with increased risk	All persons with cirrhosis
	Man > 40-years-old at time of HBsAg loss
	Woman > 50-years-old at time of HBsAg loss
	Family history of HCC

PAGE-B score - Platelet-Age-Gender-Hepatitis B score for predicting risk of HCC in CHB

AASLD

Ghany M., et al. AASLD Practice Guideline on Treatment of Chronic Hepatitis B. *Hepatology* 2025
Singal A. G., et al. AASLD Practice Guidance on prevention, diagnosis, and treatment of hepatocellular carcinoma. *Hepatology* 2023

Summary of Recommendations

1	For pregnant persons with HBV DNA levels greater than 200,000 IU/mL at any time point during pregnancy regardless of HBeAg status, AASLD recommends initiating tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide (TAF) at gestational week 28 to prevent mother-to-child transmission (MTCT). TDF has a more extensive safety record in pregnancy than TAF. Both entecavir and peginterferon use are contraindicated during pregnancy.
2	For persons who are HBsAg-positive with viremia not meeting disease-specific treatment indications and who are in high-risk scenarios for transmission to others, AASLD suggests a shared decision-making approach regarding antiviral treatment.
3	For persons in the immune-tolerant phase, the AASLD suggests antiviral therapy for those > 40 years or with significant liver inflammation (≥ grade 2) or fibrosis (≥ F2) on liver biopsy or noninvasive tests. For persons < 40 years old who are interested in starting treatment earlier, the AASLD suggests shared decision-making with consideration of risk factors as well as the benefits and risks of treatment.
4	In adults with HBsAg-positive, HBeAg-negative chronic HBV infection without cirrhosis and in the indeterminate phase, AASLD suggests antiviral therapy using a shared decision-making approach by assessing risks and benefits and to reevaluate that decision at each follow-up visit if treatment has not been initiated.

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Summary of Recommendations

5	In adults with chronic hepatitis B, who are HBeAg-negative without cirrhosis, with sustained undetectable HBV DNA on nucleos(t)ide analogue therapy, AASLD suggests not withdrawing nucleos(t)ide analogous therapy until HBsAg loss.
6	In persons who achieve HBsAg loss, AASLD suggests continued HCC surveillance for those with cirrhosis, with family history of HCC, men who experienced HBsAg loss after age 40, and women who experienced HBsAg loss after age 50.
7	In persons with HBV-HDV co-infection, AASLD suggests HCC surveillance of adults independent of cirrhosis status. The decision to undertake surveillance in children should be individualized due to the risk of HCC being unknown in this population.
8	In persons with HBV-HIV co-infection, AASLD suggests HCC surveillance for men ≥ 18 years of age and women ≥ 40 years of age.
9	In persons with HBV-HCV co-infection, AASLD recommends treatment for HCV and suggests HCC surveillance as per criteria for HBV mono-infection.

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Acknowledgments

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See more about the AASLD CHB guidelines

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