HBV Is Primary!

Your Role in the "Call to Action" to Eliminate Viral Hepatitis By 2030

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PeerView
Live

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The Importance of Prevention and Early Detection of HBV

Current Guidelines and Standards of Care

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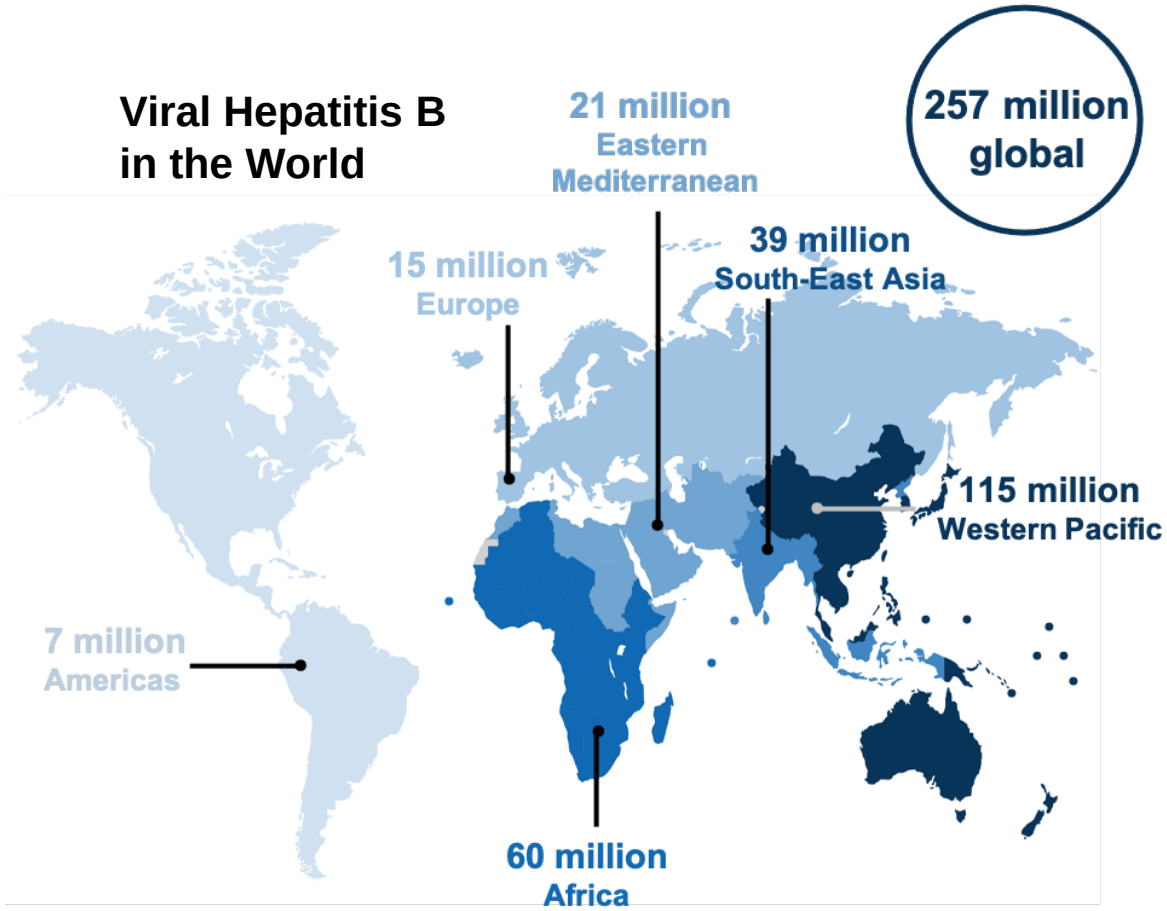
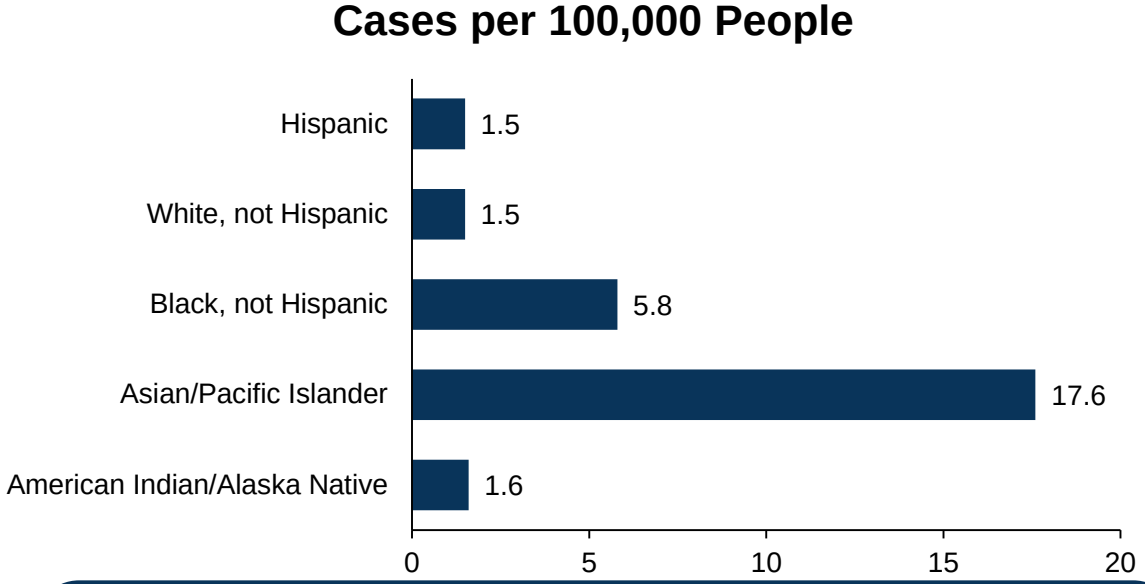
Epidemiology of HBV Infection[1-5]

>250 million people are infected with HBV, globally



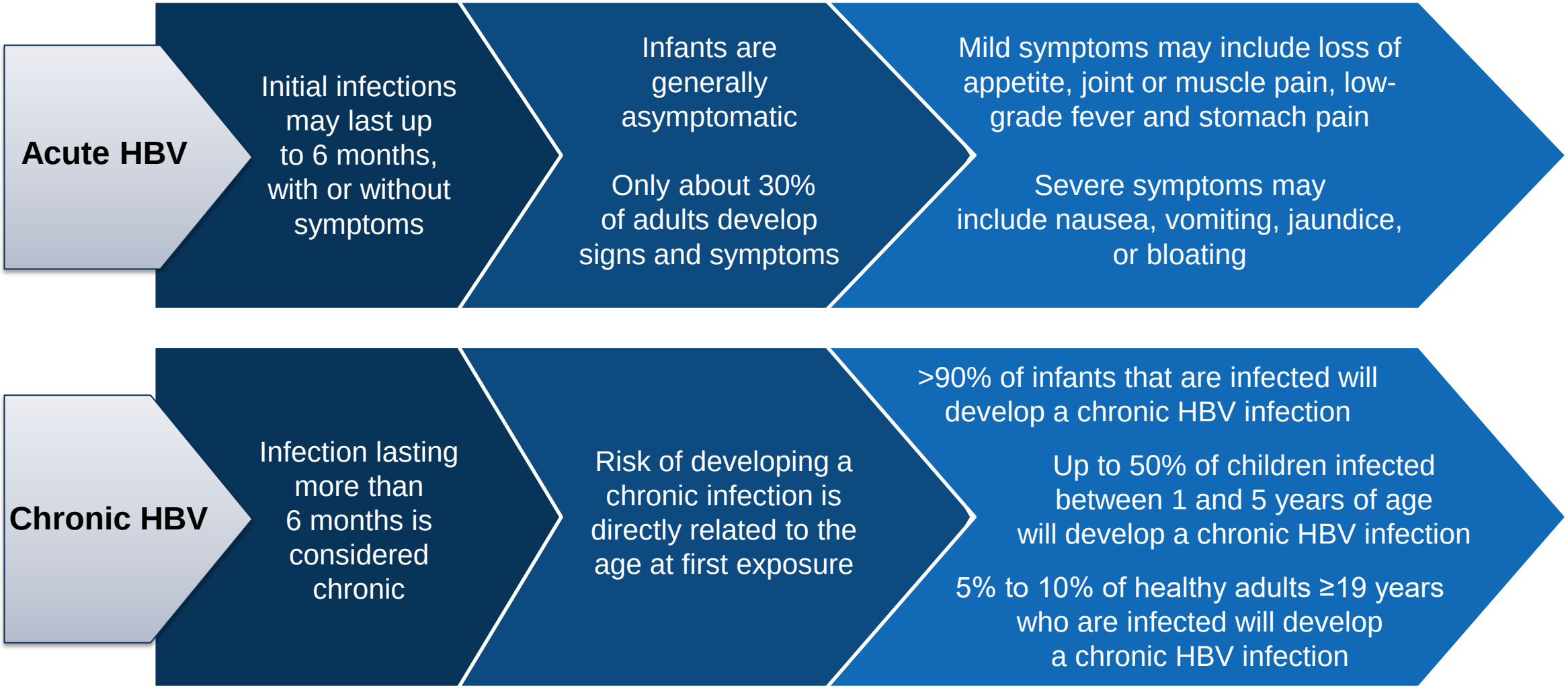


In the United States, between 880,000 and 1.89 million people are living with chronic HBV

- People not born in the United States account for 69% of the US population living with chronic HBV infection
- There are considerable racial/ethnic disparities in the incidence of reported chronic HBV infections

1. Nguyen MH et al. *Clin Microbiol Rev*. 2020;33:e00046-19. 2. https://www.who.int/news-room/fact-sheets/detail/hepatitis-b.
3. https://www.cdc.gov/hepatitis/hbv/hbvfaq.htm. 4. https://www.who.int/multi-media/details/viral-hepatitis-in-the-world-map.
5. https://www.cdc.gov/hepatitis/statistics/2020surveillance/hepatitis-b.htm.

Acute vs Chronic HBV Infection[1]



1. https://www.hepb.org/what-is-hepatitis-b/what-is-hepb/acute-vs-chronic.

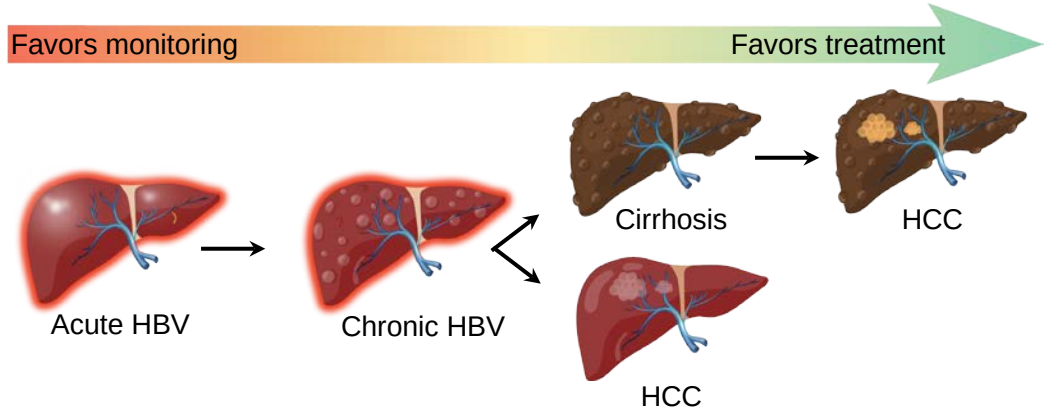
Chronic HBV Infection Is Associated With Significant Morbidity and Mortality[1-5]

HBV contributes to ~820,000 annual deaths worldwide and more than 1,600 annual deaths in the United States

15% to 40% of HBV-infected patients develop complications, such as liver cirrhosis, liver failure, or HCC

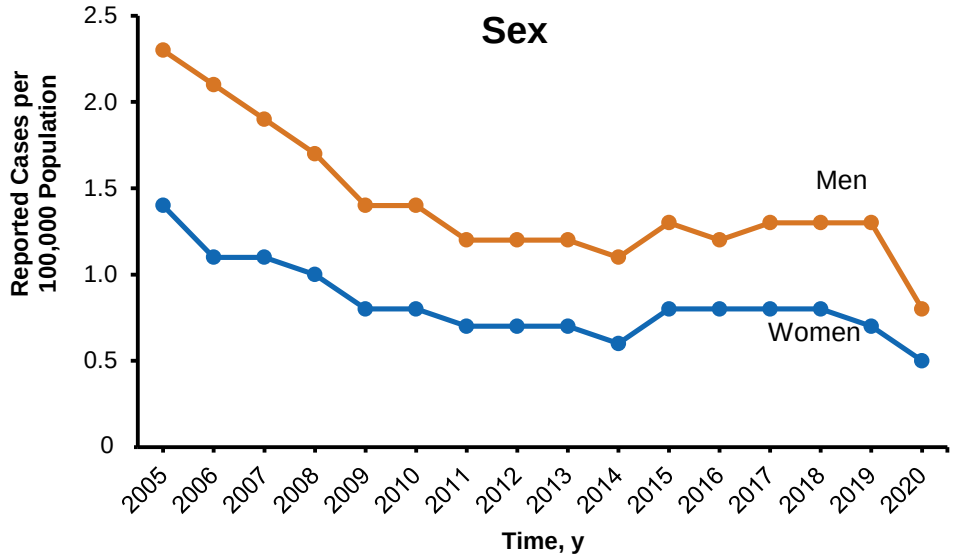
Without treatment and monitoring, 25% of persons with chronic HBV infection will die prematurely from these complications; 70% of HBV-related deaths are because of HCC

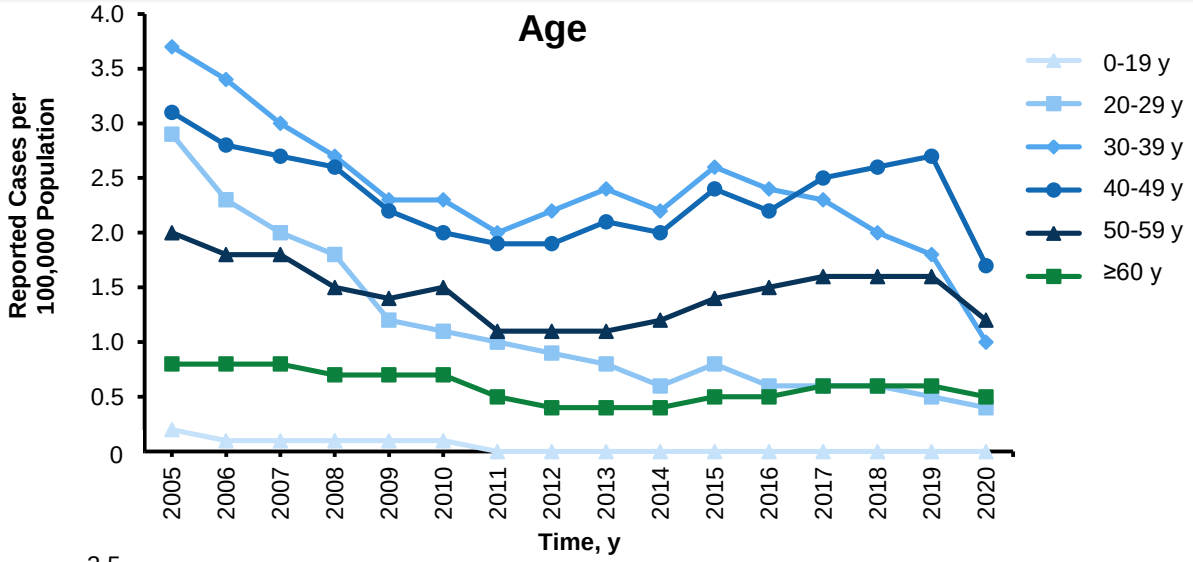
Current HBV treatment can mitigate risk, but only 10% to 15% of eligible patients receive treatment

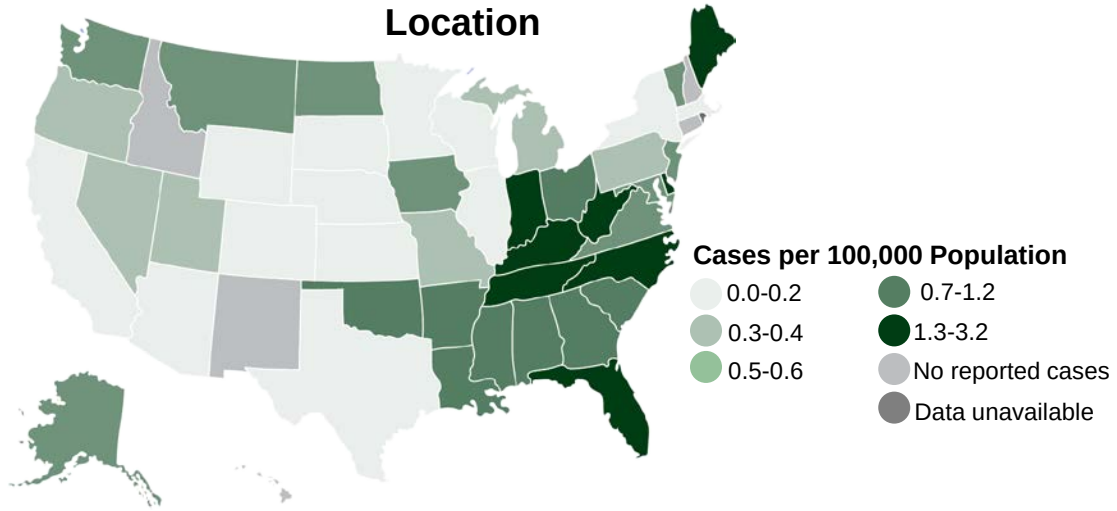


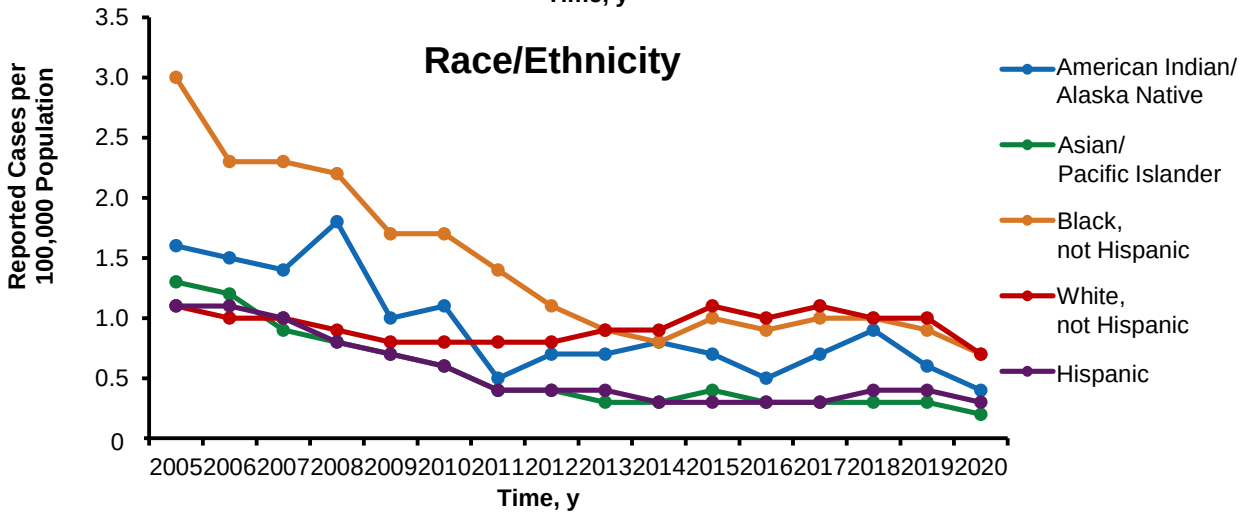
1. https://www.who.int/news-room/fact-sheets/detail/hepatitis-b. 2. https://www.cdc.gov/globalhealth/immunization/diseases/hepatitis-b/data/fast-facts.html. 3. https://www.cdc.gov/hepatitis/hbv/hbvfaq.htm. 4. Lim JK et al. *Am J Gastroenterol*. 2020;115:1429-1438. 5. Fricker ZP, Reddy KR. *Clin Gastroenterol Hepatol*. 2019;17:2644-2647.

Disparities in Acute HBV Infection[1,a]





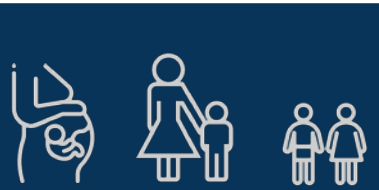




[a] The number of viral hepatitis cases reported to CDC in 2020 may be lower than in years before the COVID-19 pandemic began. This decrease may be related to fewer people seeking healthcare and being tested for viral hepatitis during the COVID-19 pandemic.

1. https://www.cdc.gov/hepatitis/statistics/2020surveillance/hepatitis-b.htm.

Transmission of HBV Infection[1,2]



- Most common route of transmission is from mother to neonate (vertical transmission) or from mother to child or child to child (horizontal)

- HBV is transmitted through percutaneous or mucosal contact with blood or body fluids

Others routes include

- Sex with a partner who has HBV infection
- Injection drug use that involves sharing needles, syringes, or drug preparation equipment
- Accidental exposures to needle sticks or sharp instruments
- Contact with blood from, or open sores on, a person who has HBV infection
- Administration of contaminated blood products, especially in resource-restricted countries

1. https://www.who.int/news-room/fact-sheets/detail/hepatitis-b. 2. https://www.cdc.gov/hepatitis/hbv/hbvfaq.htm.

ACIP Vaccination Recommendations[1,2]

Should receive HBV vaccine

- All infants
- Persons **<19 years** of age
- Adults **19 to 59 years** of age
- Adults **≥60 years** of age **with risk factors** for HBV infection

May receive HBV vaccine

- Adults ≥60 years of age **without** risk factors for HBV infection

All patients with chronic liver disease should be vaccinated for hepatitis A and B

1. Schillie S et al. *MMWR Recomm Rep*. 2018;67:1-31 2. Weng MK et al. *MMWR Morb Mortal Wkly Rep*. 2022;71:477-483.

World Health Organization Has Set a Goal to Eliminate Viral Hepatitis as a Public Health Threat by 2030[1,2]

- Chronic HBV places a huge burden on patients, their family, and the healthcare system
- Proposed as a 90% reduction in new chronic infections and a 65% reduction in mortality, compared with the 2015 baseline
- Initial roadmap focused on strategies targeted at prevention, diagnosis, treatment, and community interventions

Goals for the WHO's plan to be realized

1. Prevent new viral hepatitis infections

2. Improve viral hepatitis–related health outcomes of people with viral hepatitis

3. Reduce viral hepatitis–related disparities and health inequities

4. Improve viral hepatitis surveillance and data usage

5. Achieve integrated, coordinated efforts that address the viral hepatitis epidemics among all partners and stakeholders

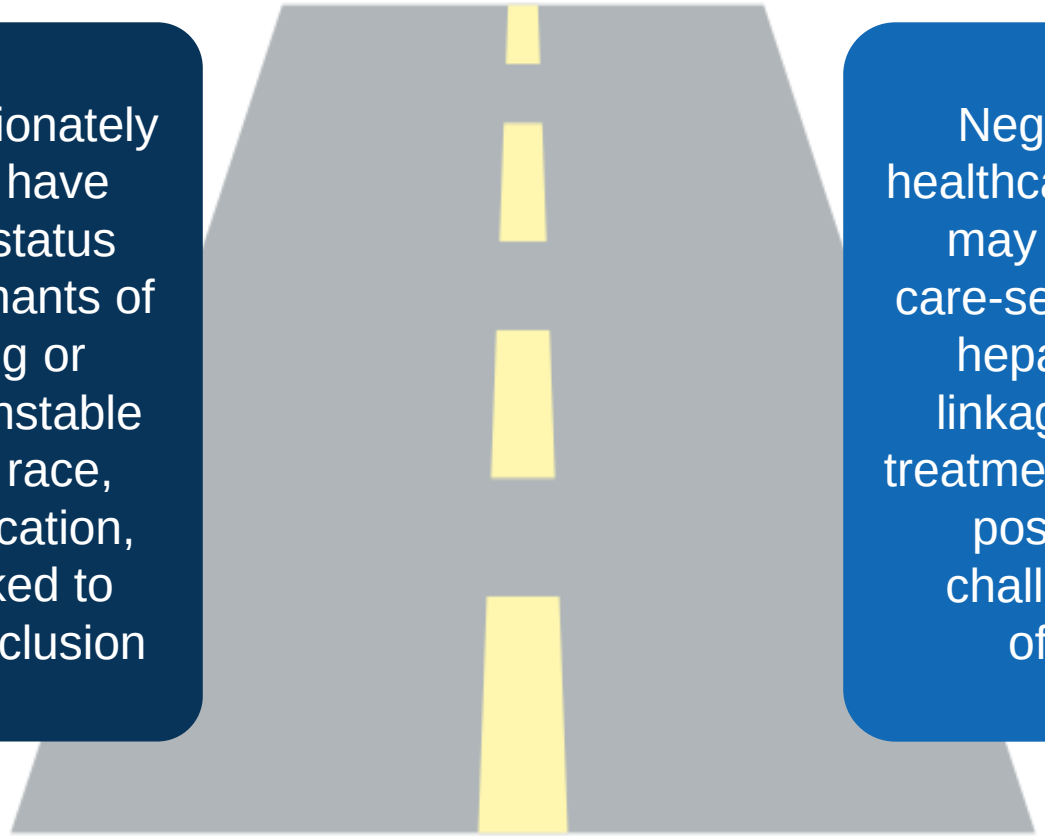
1. https://www.hhs.gov/sites/default/files/Viral-Hepatitis-National-Strategic-Plan-2021-2025.pdf. 2. https://www.who.int/news-room/fact-sheets/detail/hepatitis-b.

Viral Hepatitis: National Strategic Plan[1]

A Roadmap to Elimination for the United States, 2021-2025

The Need to Address Social Determinants of Health and Priority Populations

Many populations disproportionately impacted by viral hepatitis have faced disparities in health status related to the social determinants of health, such as low-paying or inconsistent employment, unstable housing or homelessness, race, ethnicity, and geographic location, or other characteristics linked to discrimination, stigma, or exclusion



Negative interactions with the healthcare or social services system may decrease the likelihood of care-seeking behavior, making viral hepatitis risk assessment and linkage to care, prevention, and treatment more difficult; this difficulty poses additional and unique challenges to the development of broad-based solutions

1. https://www.hhs.gov/sites/default/files/Viral-Hepatitis-National-Strategic-Plan-2021-2025.pdf.

Large Gaps in HBV Screening and Care Exist in the United States[1,2]

There are up to 2.4 million chronic HBV infections in the United States

600,000 (25%) would be eligible for treatment under guidelines

Only 33% of those with chronic HBV are aware of their infections

Only 40% of those who are aware of their infection are referred to appropriate care

Rates of acute HBV infection have risen 50% to 450% in states impacted by the opioid crisis!

1. Gish R. ECHO 2021 Session 7: Hepatitis B Treatment. Oral presentation. 2. www.hepb.org/what-is-hepatitis-b/what-is-hepb/facts-and-figures.

USPSTF HBV Screening Recommendations Were Recently Updated (in 2020)[1,a]

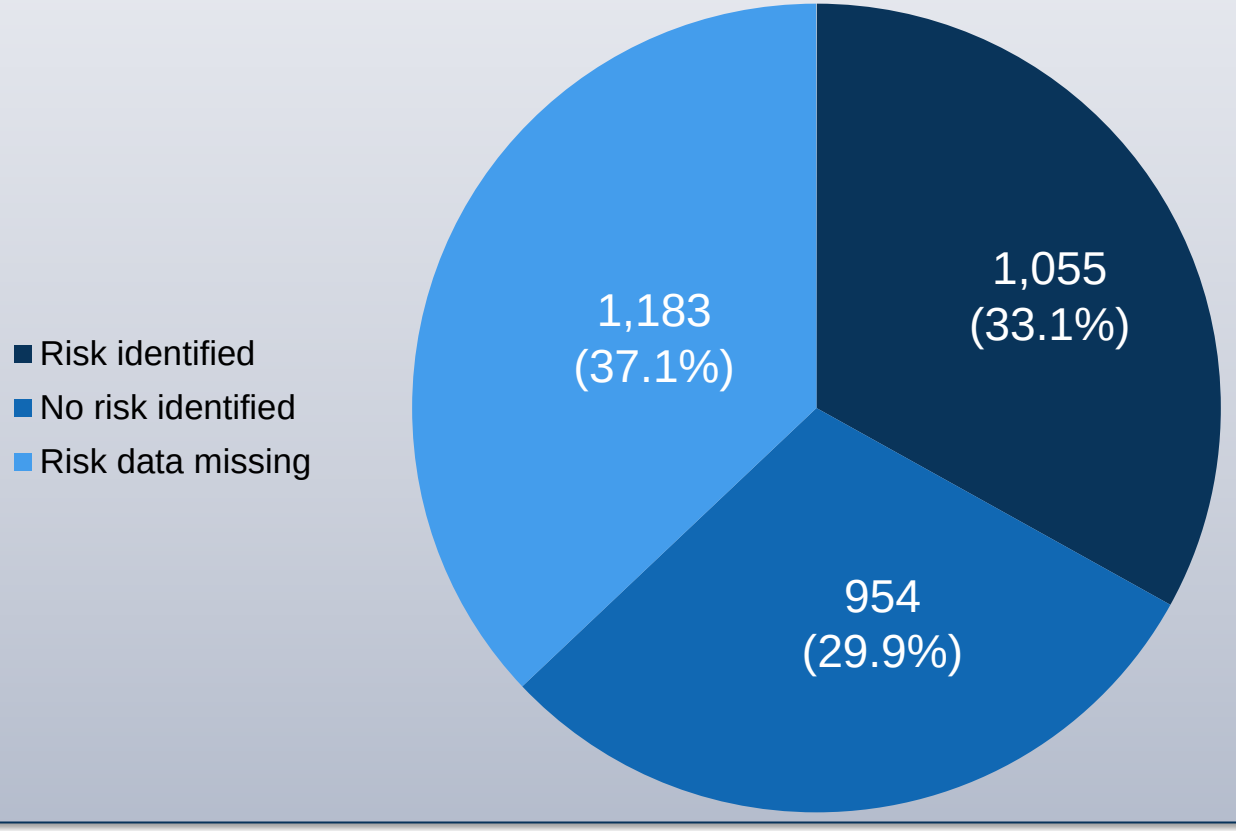
What does the USPSTF recommend?	For adolescents and adults: Screen adolescents and adults at increased risk for HBV infection
To whom does this recommendation apply?	All asymptomatic, nonpregnant adolescents and adults at increased risk for HBV infection, including those who were vaccinated before being screened for HBV infection
How should this recommendation be implemented?	Screen adolescents and adults at increased risk using HBsAg tests followed by a confirmatory test for initially reactive results; important risk groups for HBV infection with a prevalence of ≥2% that should be screened include • Persons born in countries and regions with a high prevalence of HBV infection (≥2%), such as Asia, Africa, the Pacific Islands, and parts of South America • US-born persons not vaccinated as infants whose parents were born in regions with a very high prevalence of HBV infection (≥8%) • People who are HIV positive • Persons with injection drug use • Men who have sex with men • Household contacts or sexual partners of persons with HBV infection
How often?	Periodically screen people with continued risk for HBV infection (eg, people with current injection drug use, men who have sex with men)

[a] Guidelines are risk based.

1. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/hepatitis-b-virus-infection-screening.

Limitations of a Risk-Based Approach[1]

Availability of information regarding risk behaviors or exposures[a,b] associated with reported cases of acute hepatitis B virus infection—United States, 2019



[a] Case reports with at least one of the following risk behaviors/exposures reported 6 wk to 6 mo prior to symptom onset or documented seroconversion if asymptomatic: (1) injection drug use; (2) multiple sexual partners; (3) underwent surgery; (4) men who have sex with men; (5) sexual contact with suspected/confirmed hepatitis B case; (6) sustained a percutaneous injury; (7) household contact with suspected/confirmed hepatitis B case; (8) occupational exposure to blood; (9) dialysis; and (10) transfusion. Reported cases may include more than one risk behavior/exposure. [b] Risk behaviors/exposures data from one state was classified as "missing" because of errors in reporting.

1. https://www.cdc.gov/hepatitis/statistics/2019surveillance/Figure2.7.htm.

CDC HBV Screening Recommendations: Recent Updates[1,a]

Universal hepatitis B virus (HBV) screening

- HBV screening at least once during a lifetime for adults aged ≥18 years (new recommendation)
- During screening, test for hepatitis B surface antigen (HBsAg), antibody to HBsAg, and total antibody to HBcAg (total anti-HBc; new recommendation)

Screening pregnant persons

- HBV screening for all pregnant persons during each pregnancy, preferably in the first trimester, regardless of vaccination status or history of testing
- Pregnant persons with a history of appropriately timed triple panel screening and without subsequent risk for exposure to HBV (ie, no new HBV exposures since triple panel screening) only need HBsAg screening

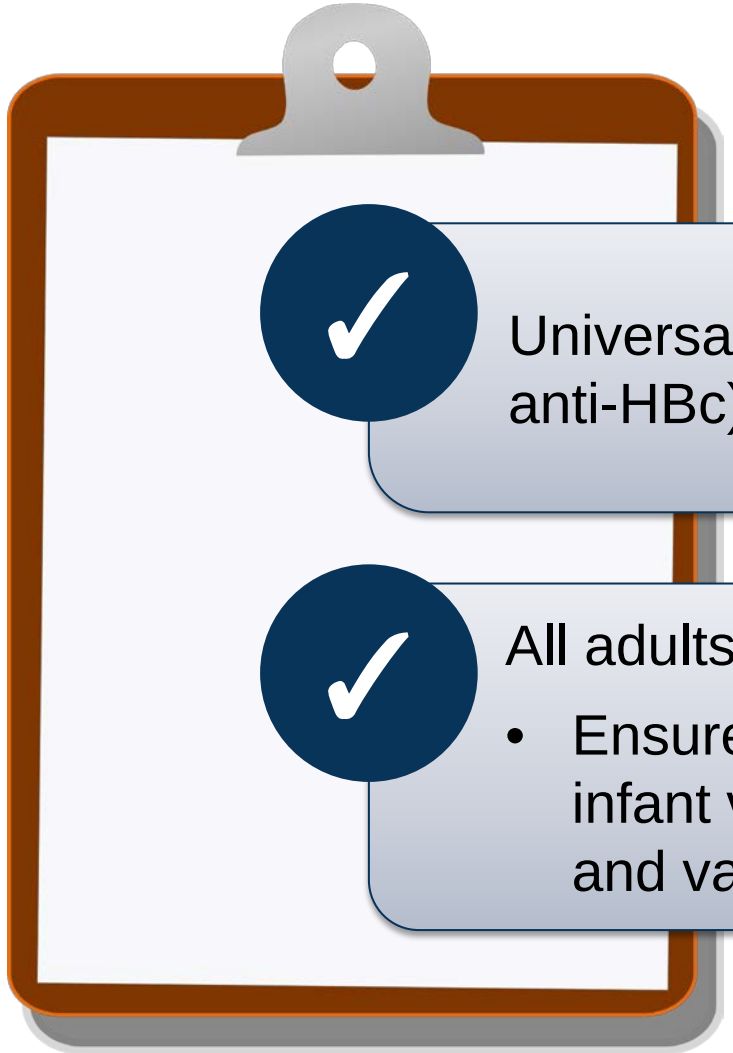
Risk-based testing

- Testing for all persons with a history of increased risk for HBV infection, regardless of age, if they might have been susceptible during the period of increased risk[b]
- Periodic testing for susceptible persons, regardless of age, with ongoing risk for exposures, while risk for exposures persists[b]

[a] Updated March 2023. [b] Susceptible persons include those who have never been infected with HBV (ie, total anti-HBc negative) and either did not complete a hepatitis B vaccine series per Advisory Committee on Immunization Practices recommendations or who are known to be vaccine nonresponders.

1. Conners EE et al. *MMWR Recomm Rep.* 2023;72:1-25.

Simplified Screening Guidance[1]



- Universal, one-time HBV screening (HBsAg, anti-HBs, and total anti-HBc) in all adults and with each pregnancy recommended
- All adults over age 18 should be screened at least once in their lifetime
  - Ensures that those who did not mount an antibody response with infant vaccination or who were never vaccinated are identified and vaccinated

1. Dieterich D et al. *Gastro Hep Advances*. 2023;2:209-218.

Serological Markers of HBV Infection: Viral Antigens[1]

HBsAg (hepatitis B surface antigen)

- Protein on the surface of HBV
- Detected in high levels in serum during acute or chronic HBV infection, and it indicates that the person is infectious

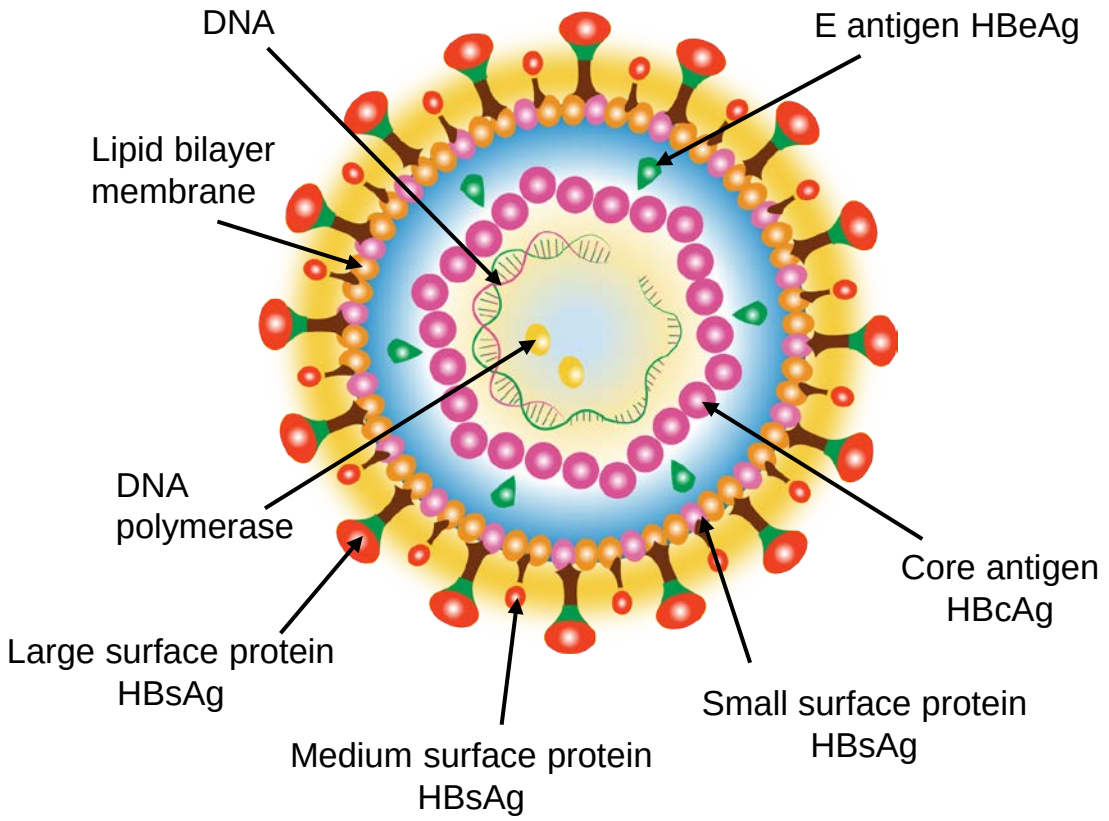
HBeAg (hepatitis B e antigen)

- Protein contained in the nucleocapsid core
- Detected in the serum of persons with high virus titers, indicating high infectivity

HBcAg (hepatitis B core antigen)

- Protein on the surface of the nucleocapsid core that is not secreted and, as a result, cannot be detected in the serum of infected individuals
- Presence indicates ongoing HBV replication during active infection

Hepatitis B Virus
Baltimore Group VII (dsDNA-RT)



1. Bousali M et al. *Microorganisms*. 2021;9:1787.

Serological Markers of HBV Infection: Antibodies[1]

anti-HBs (hepatitis B surface antibody)

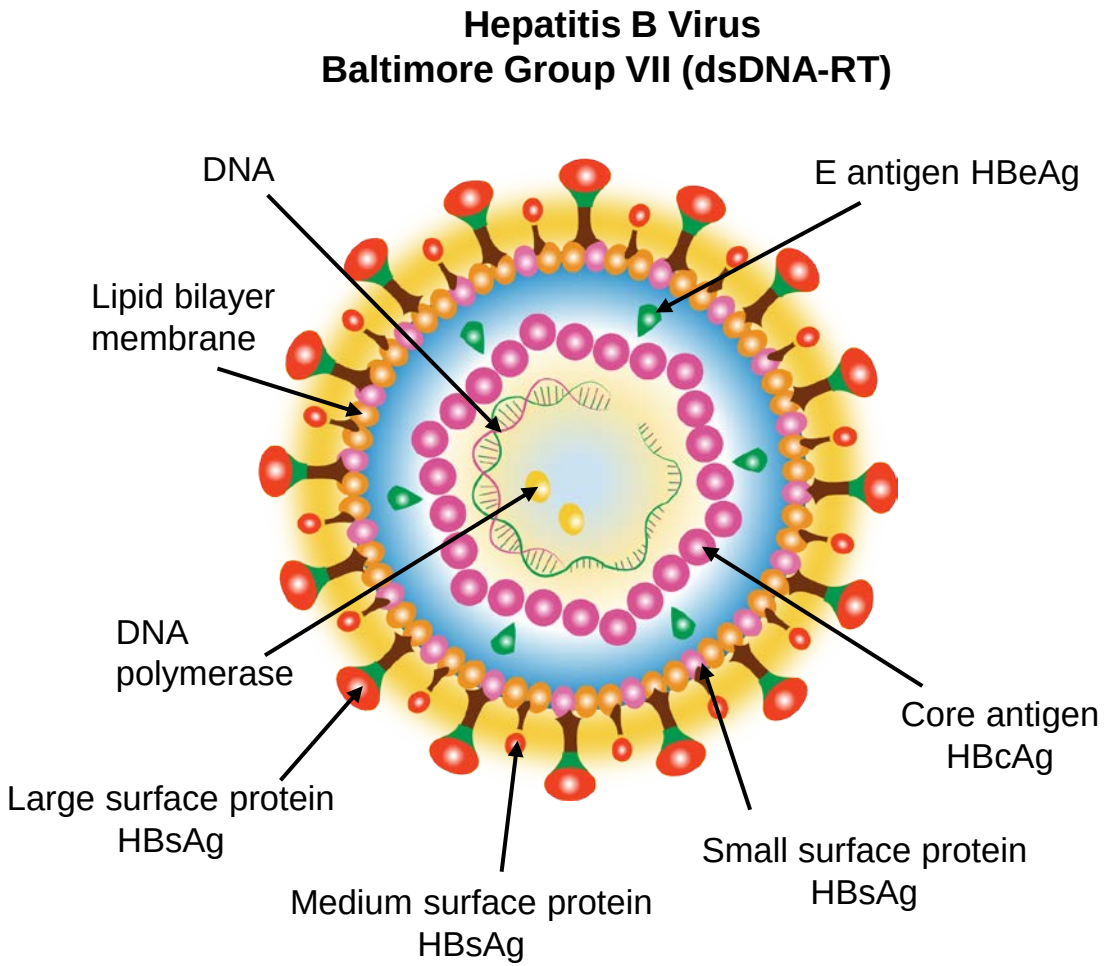
- Presence indicates recovery and immunity from HBV infection or, if also anti-HBc negative, successful vaccination against HBV

anti-HBc (total hepatitis B core antibody)

- Appears at the onset of symptoms in acute HBV infection and persists for life
- Indicates previous or ongoing HBV infection in an undefined time frame (exposure)

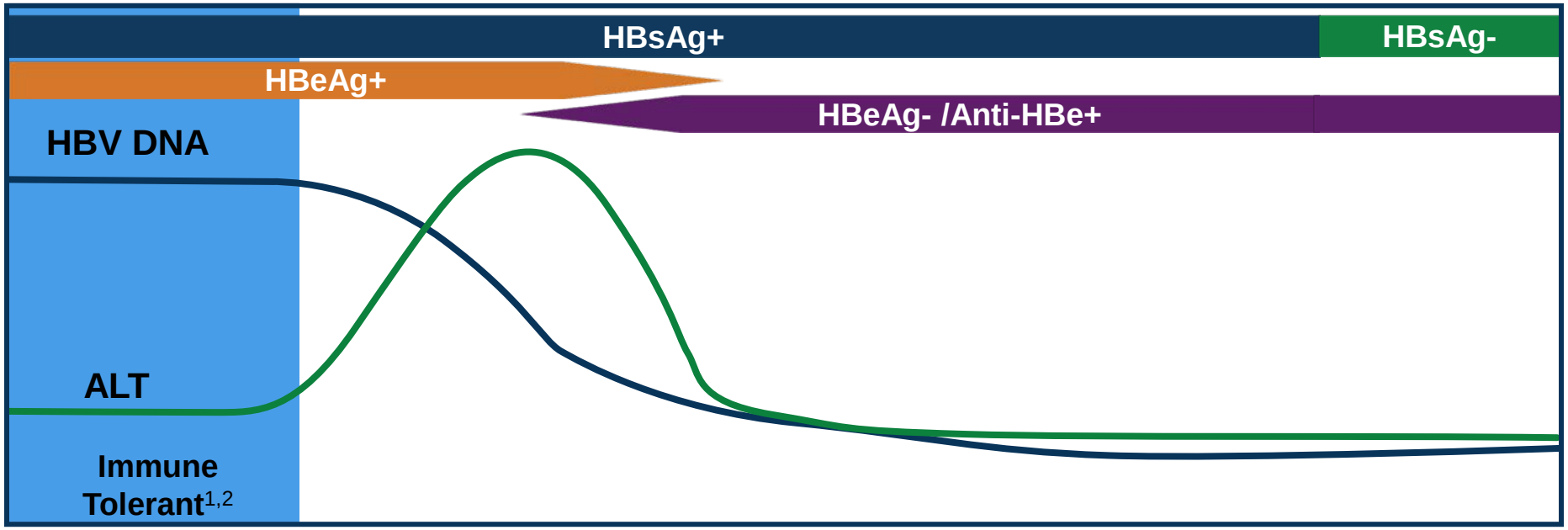
IgM anti-HBc (IgM antibody to core antigen)

- Presence indicates recent (6 months) acute HBV infection



1. Bousali M et al. *Microorganisms*. 2021;9:1787.

The Natural Course of Chronic HBV Infection: Five Phases



- This phase occurs in patients with perinatally acquired infection
- Minimal or no inflammation
- May last 1 to 4 decades
- **Chronic infection[3]**

CHB follows a nonlinear clinical course; not all patients will go through each phase

1. Tong MJ et al. *Dig Dis Sci*. 2011;56:3143-3162. 2. Yim HJ et al. *Hepatology*. 2006;43:S173-S181.
3. European Association for the Study of the Liver. *J Hepatol*. 2017;67:370-398.

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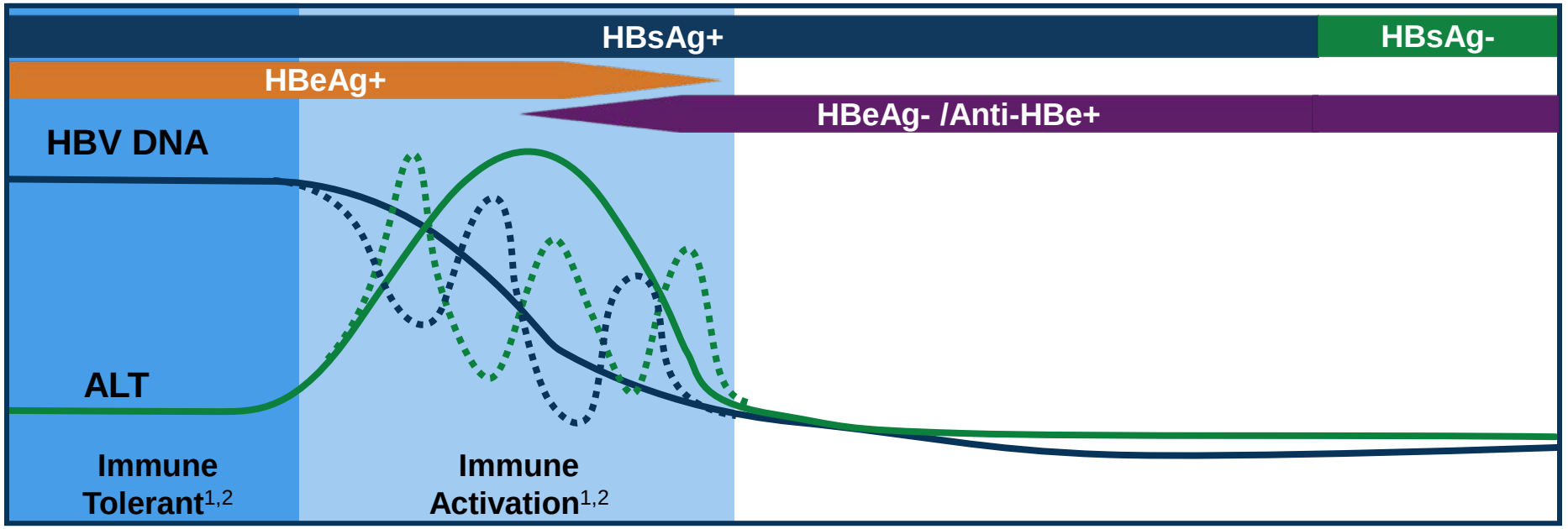

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- High or fluctuating HBV DNA levels
- Persistent or intermittent fluctuation in ALT levels
- Active inflammation and liver damage
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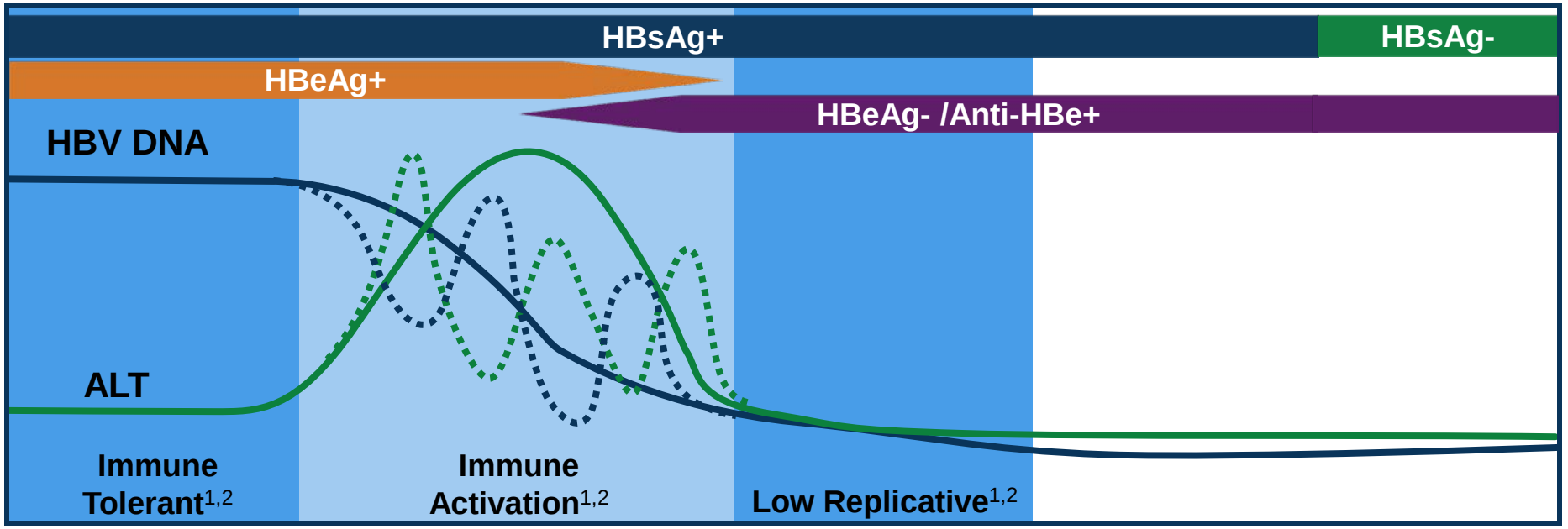

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- Low or undetectable HBV DNA levels
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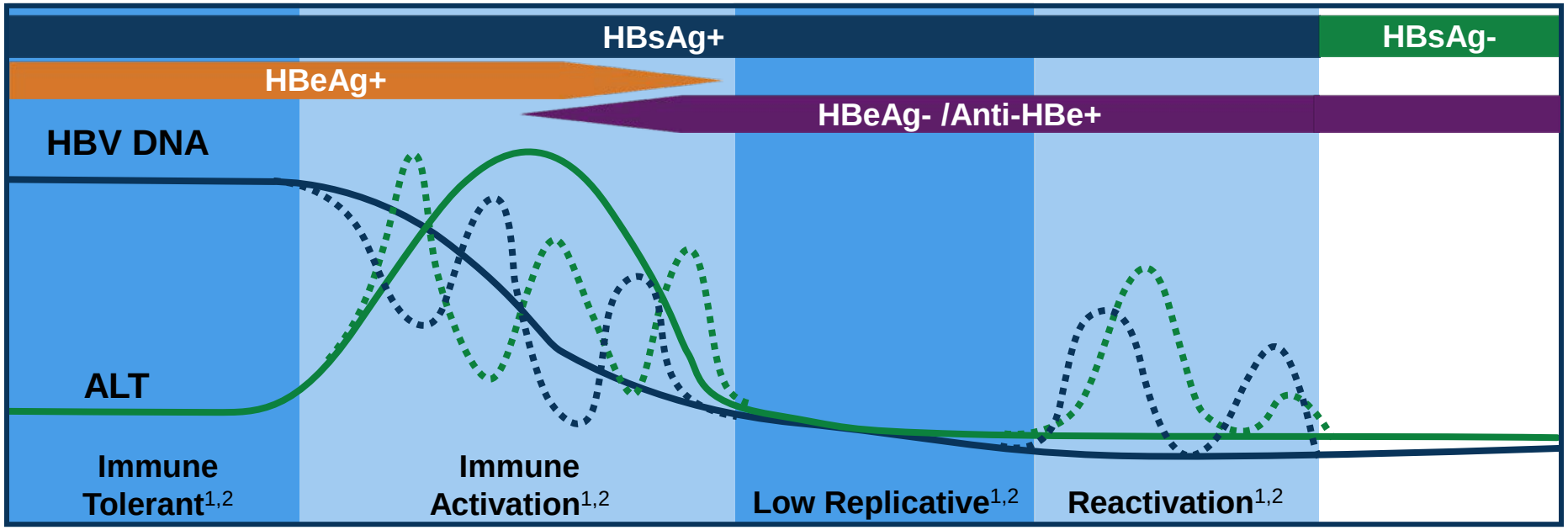

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- Some patients may have reactivation of HBV replication
- Usually older patients with more advanced liver disease
- Fluctuating levels of ALT and HBV DNA
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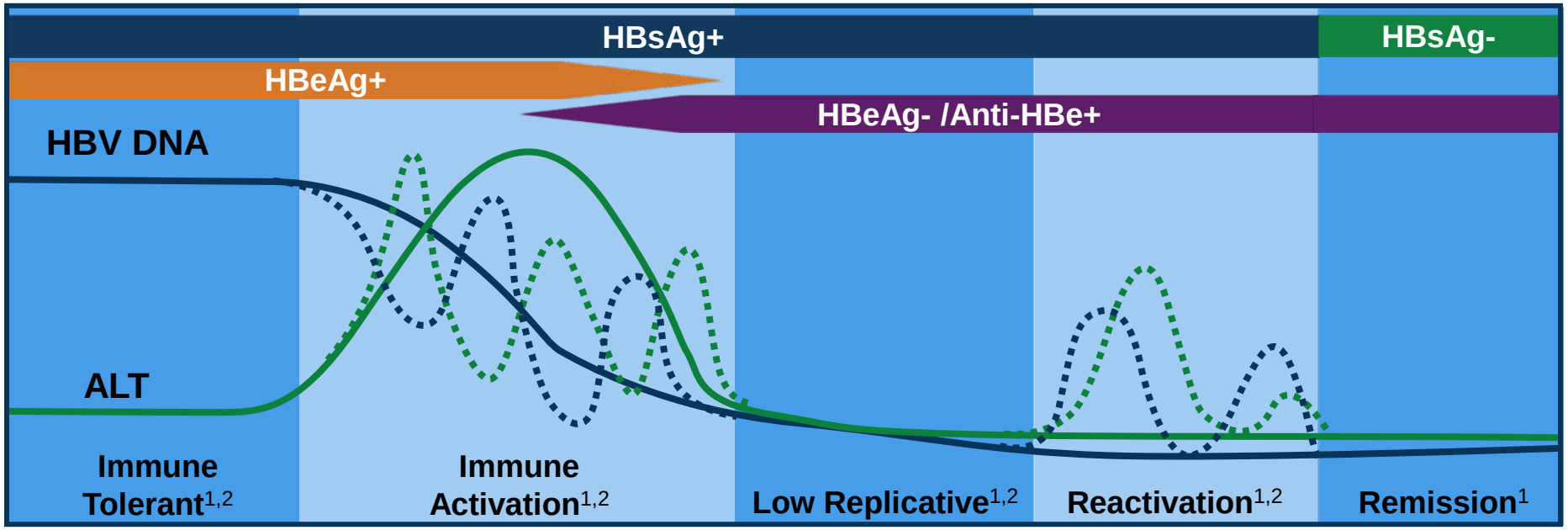

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- Usually older patients with more advanced liver disease
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- After many years, some patients may enter a remission phase
- Not considered a "cure" because intracellular HBV DNA is still present

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1. Tong MJ et al. *Dig Dis Sci*. 2011;56:3143-3162. 2. Yim HJ et al. *Hepatology*. 2006;43:S173-S181.
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Interpretation of Serological Testing Results and Recommended Actions[1]

Test Results			Action Items	Patient Education and Counseling
+ HBsAg			• Proceed to further workup	• Inform patient they have HBV infection and further evaluation is necessary to determine next steps • Counsel regarding risk of HBV transmission • Household and sexual contacts should be evaluated for HBV and vaccination
- HBsAg	+ Anti-HBs	+ Total anti-HBc	• No further action required[a]	• Inform patient they had previous HBV infection that has resolved • Counsel regarding risk of HBV reactivation
		- Total anti-HBc	• No further action required	• Inform patient they have HBV immunity due to vaccination and no further follow-up is necessary
	- Anti-HBs	+ Total anti-HBc	• No further action required[a]	• Counsel on risk of reactivation
		- Total anti-HBc	• Vaccinate at-risk patients[b]	• Inform patient they are susceptible to HBV infection; initiate HBV vaccination

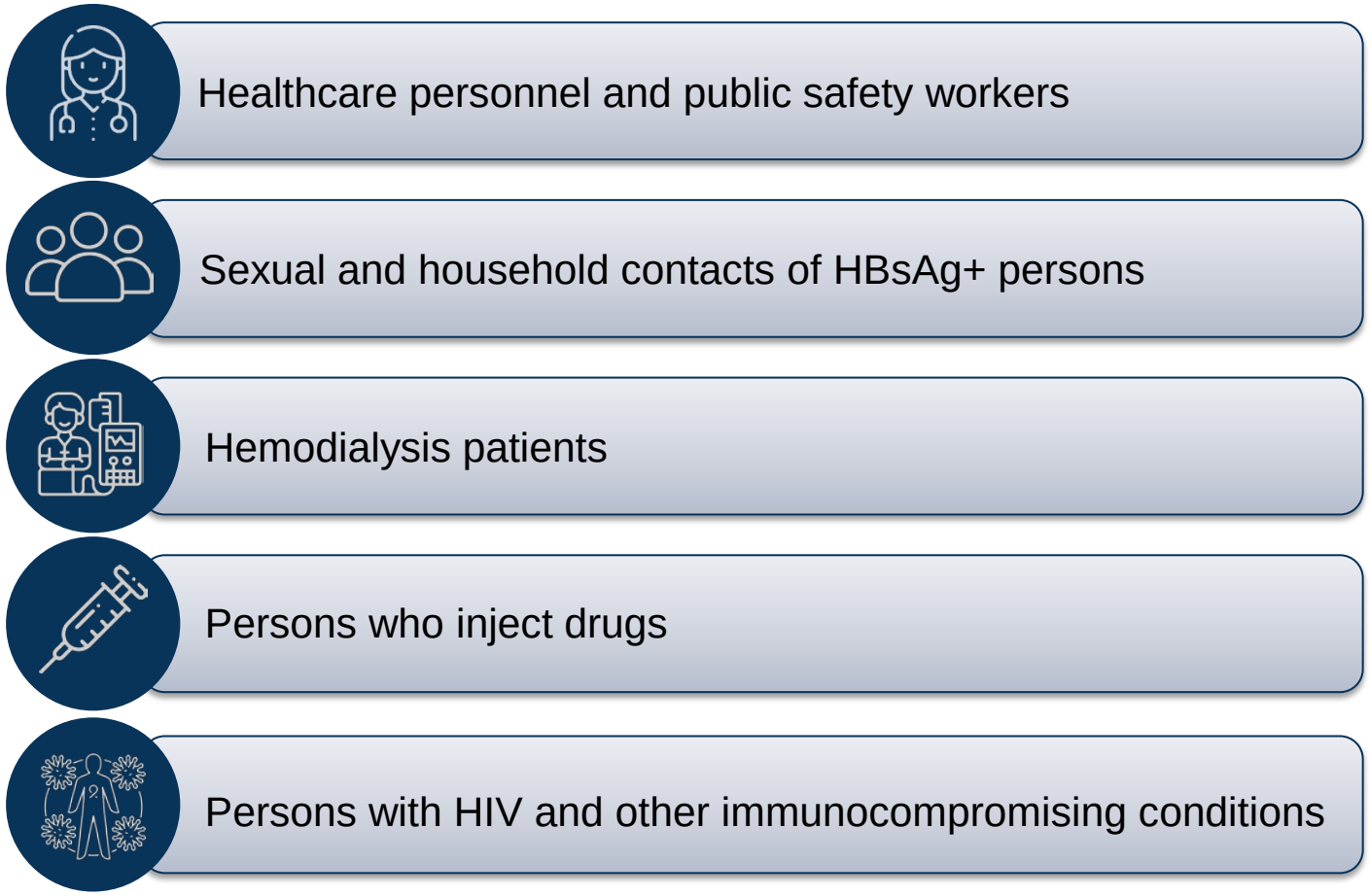
[a] Consult with a specialist if patient is on any immunosuppressive therapy. [b] Booster vaccine followed by serologic testing 1-2 mo later is only recommended for healthcare workers, sexual partners or household contacts of persons with HBV, persons who use injection drugs, persons with a history of incarceration, chronic hemodialysis patients, and immunocompromised persons (eg, those with HIV). If negative anti-HBs test, repeat the full vaccination series and retest 1-2 mo after the last vaccine dose.

1. Dieterich D et al. *Gastro Hep Advances*. 2023;2:209-218.

Post-Vaccination Serologic Testing

HBV Primary Care Workgroup Recommendations (2020)[1]

Post-vaccination serologic test of anti-HBs between 1 and 2 months
after the final dose of vaccine in all of the following adult groups at high risk for HBV



1. https://www.hepatitisB.uw.edu/hbv-pcw/guidance.

Applying Evidence in the Primary-Care Setting

Strategies for Optimizing Outcomes in Patients With HBV Infection

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Simplified Approach for HBsAg+ Patient Evaluation[1]

Severity of Liver Disease	Level of Viral Replication	Presence and Prevention of Comorbidities
• Stigmata of cirrhosis[a] • Extrahepatic manifestations[b] • CBC with platelets, INR • Liver biochemistries ALT, AST, ALP, total bilirubin, albumin, and creatinine • Calculate APRI and/or FIB-4 • Ultrasound of the liver with AFP • Other noninvasive methods such as elastography, if available	• HBV DNA quantitative	• Diabetes, metabolic syndrome, renal disease, and other liver diseases • Renal function creatinine and eGFR • Identify coinfections anti-HCV, anti-HIV, and anti-HDV • Pregnancy test for all women of childbearing age • Current medications (including as needed drugs, over-the-counter drugs, vitamins, herbals, and supplements) • Screen for STDs • Risk factors for progressive liver disease (ie, alcohol consumption, obesity)

[a] Stigmata of cirrhosis include jaundice, hepatomegaly, splenomegaly, palmar erythema, ascites, edema, spider hemangiomas, gynecomastia, asterixis, and encephalopathy. [b] Extrahepatic manifestations include vasculitis, erythematous skin rash, fever, glomerulonephritis, polyarthritis, and cryoglobulinemia.

1. Dieterich D et al. *Gastro Hep Advances*. 2023;2:209-218.

Counseling of the HBsAg+ Patient

HBV Primary Care Workgroup Recommendations (2020)[1]

Give a plan for follow-up care

- Regular (minimum every 6 months) follow-up and monitoring for disease progression

Educate and counsel on the long-term implications of chronic HBV infection

- Cirrhosis and hepatocellular carcinoma

Advise to inform all current and future medical providers of their HBsAg+ status

- Especially important if they ever need treatment for cancer or immunosuppression

Counsel to avoid or limit alcohol use

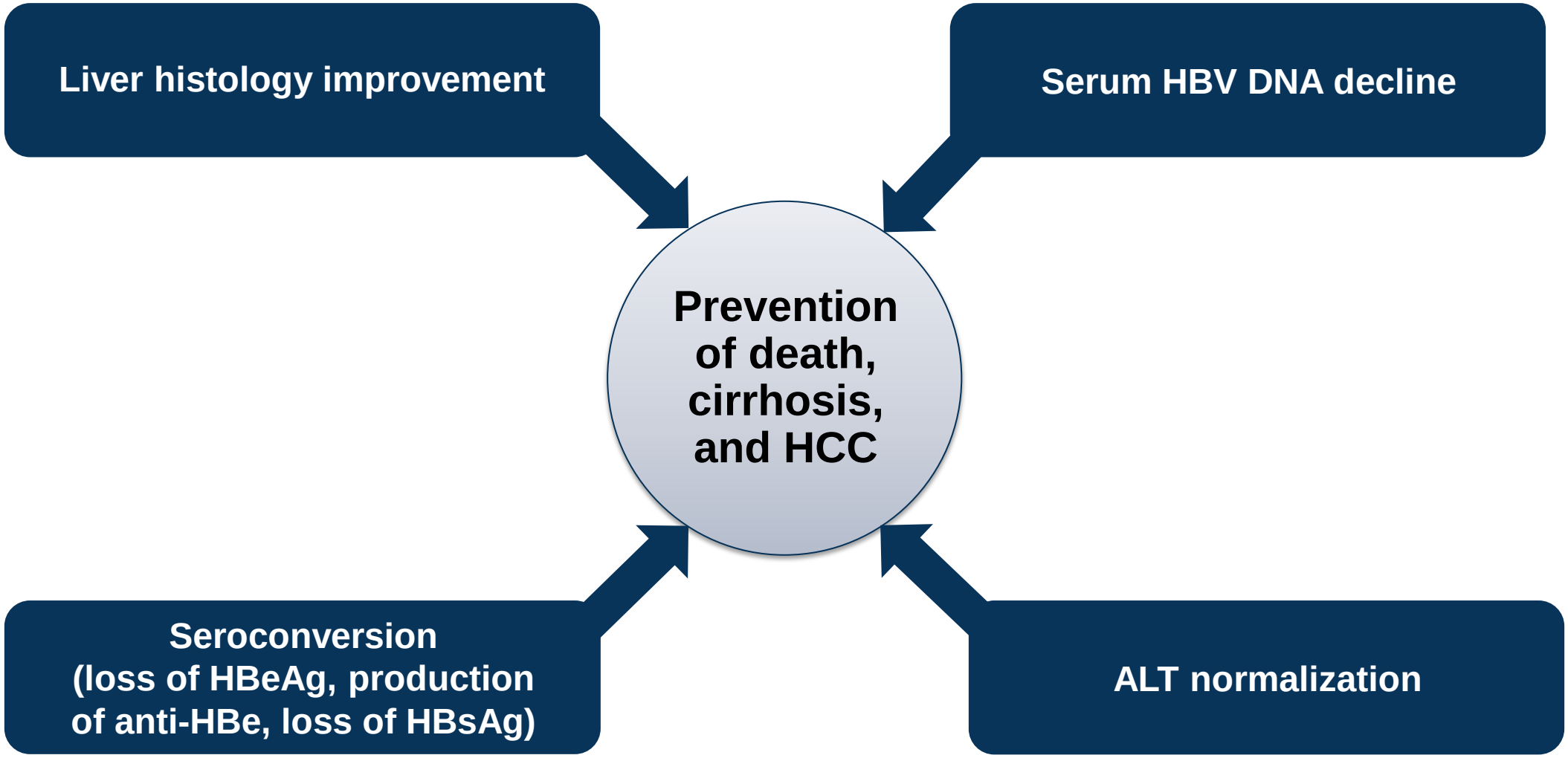
Advise to optimize body weight and address metabolic complications

- Control of diabetes and dyslipidemia

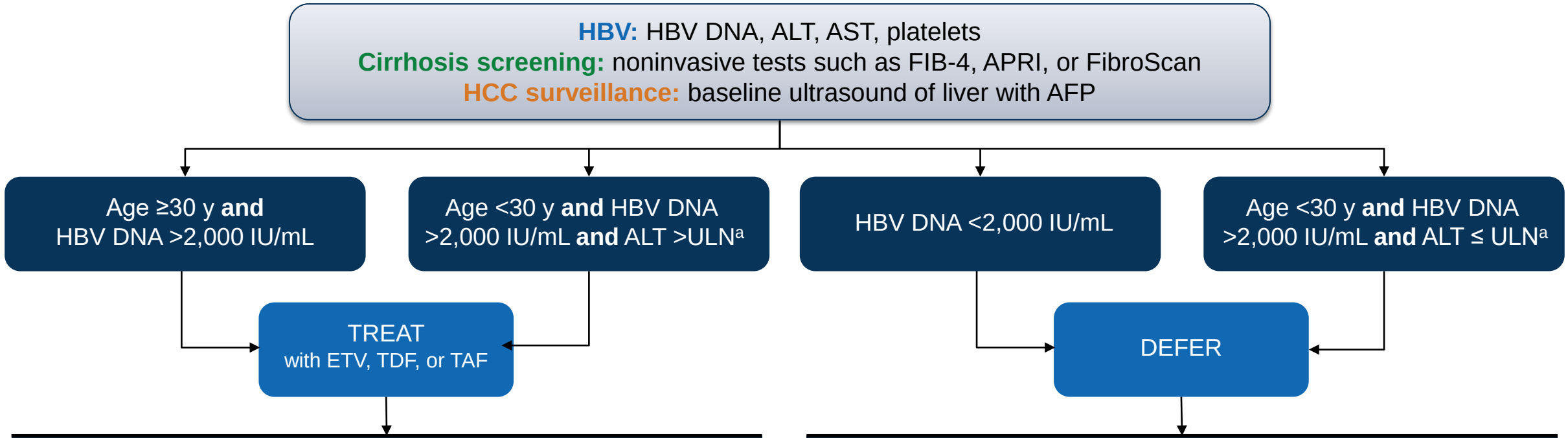
Provide education on how to prevent transmission of HBV to others

1. https://www.hepatitisB.uw.edu/hbv-pcw/guidance.

Goals of Therapy for HBV Infection



Simplified Treatment Algorithm for HBsAg+ Patient Care[1]



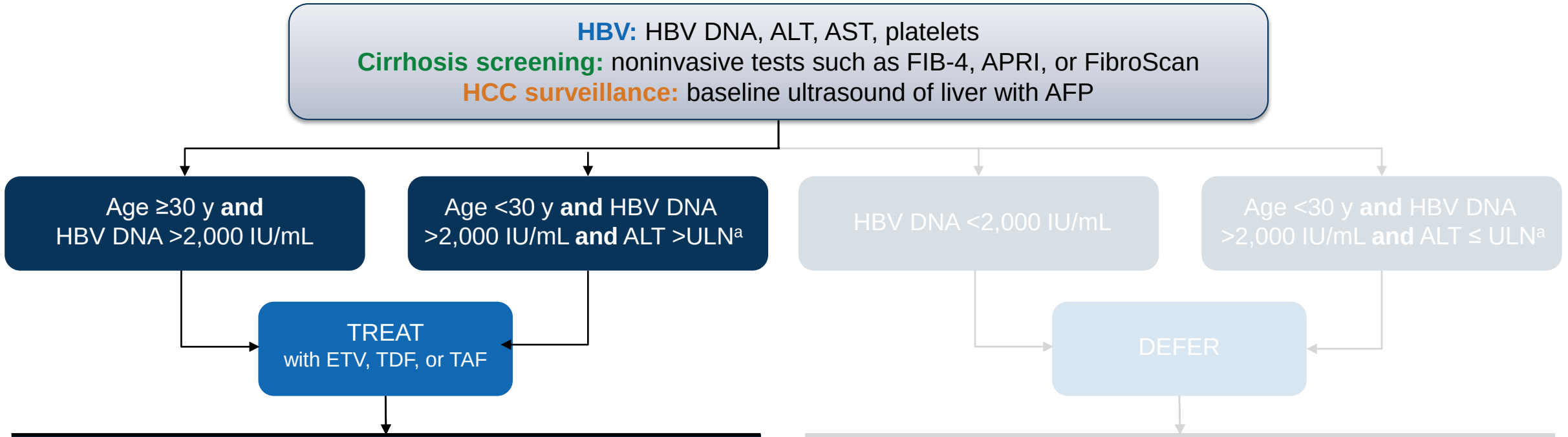
Monitor	
Antiviral therapy	• ALT + HBV DNA every 3-6 mo until viral suppression achieved then every 6 mo • HBsAg every year • Creatinine at least every year
Cirrhosis screening	• FIB-4, APRI, or FibroScan every year
HCC surveillance	• Ultrasound with AFP every 6 mo

Monitor	
HBV	• ALT + HBV DNA every 6 mo for 2 y, and then annually if no change • HBsAg every 2 y
Cirrhosis screening	• FIB-4, APRI, or FibroScan every 2 y
HCC surveillance	• Ultrasound with AFP every 6 mo for age ≥40 y

[a] The upper limit of normal for ALT in healthy adults is 30 U/L for men and 19 U/L for women.

1. Dieterich D et al. *Gastro Hep Advances*. 2023;2:209-218.

Simplified Treatment Algorithm for HBsAg+ Patient Care[1]



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1. Dieterich D et al. *Gastro Hep Advances*. 2023;2:209-218.

Simplified Treatment Algorithm for HBsAg+ Patient Care[1]

HBV: HBV DNA, ALT, AST, platelets
Cirrhosis screening: noninvasive tests such as FIB-4, APRI, or FibroScan
HCC surveillance: baseline ultrasound of liver with AFP

Age ≥30 y **and** HBV DNA >2,000 IU/mL

Age <30 y **and** HBV DNA >2,000 IU/mL **and** ALT >ULN[a]

HBV DNA <2,000 IU/mL

Age <30 y **and** HBV DNA >2,000 IU/mL **and** ALT ≤ ULN[a]

TREAT
with ETV, TDF, or TAF

DEFER

Monitor	
Antiviral therapy	• ALT + HBV DNA every 3-6 mo until viral suppression achieved then every 6 mo • HBsAg every year • Creatinine at least every year
Cirrhosis screening	• FIB-4, APRI, or FibroScan every year
HCC surveillance	• Ultrasound with AFP every 6 mo

Monitor	
HBV	• ALT + HBV DNA every 6 mo for 2 y, and then annually if no change • HBsAg every 2 y
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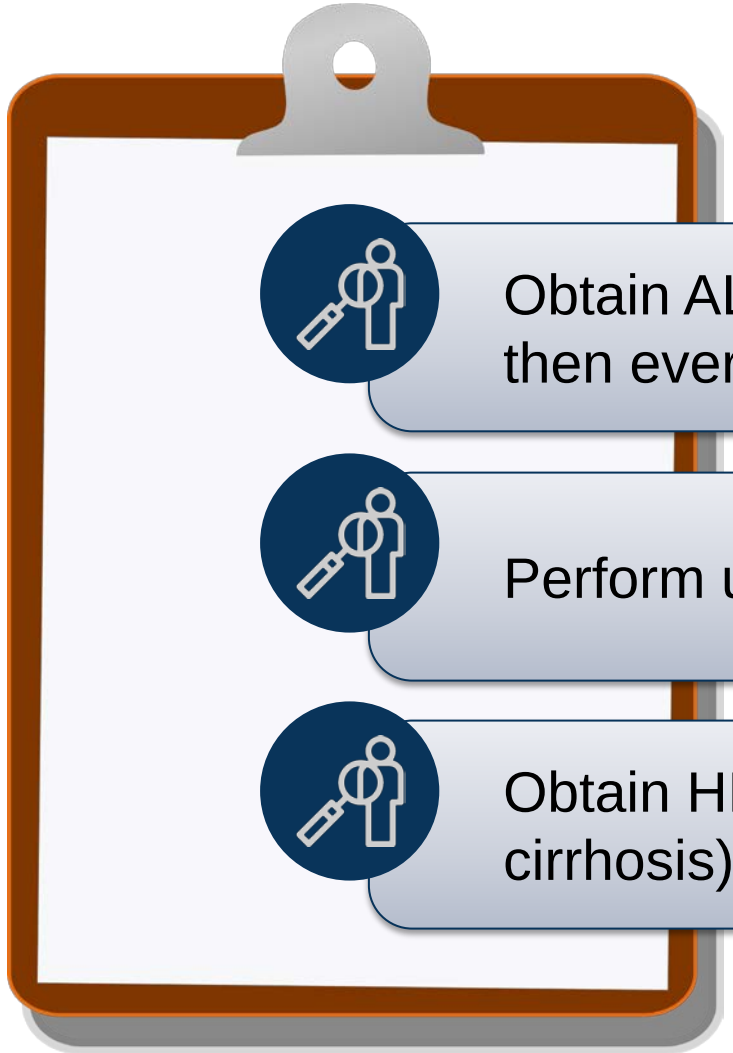
[a] The upper limit of normal for ALT in healthy adults is 30 U/L for men and 19 U/L for women.

1. Dieterich D et al. *Gastro Hep Advances*. 2023;2:209-218.

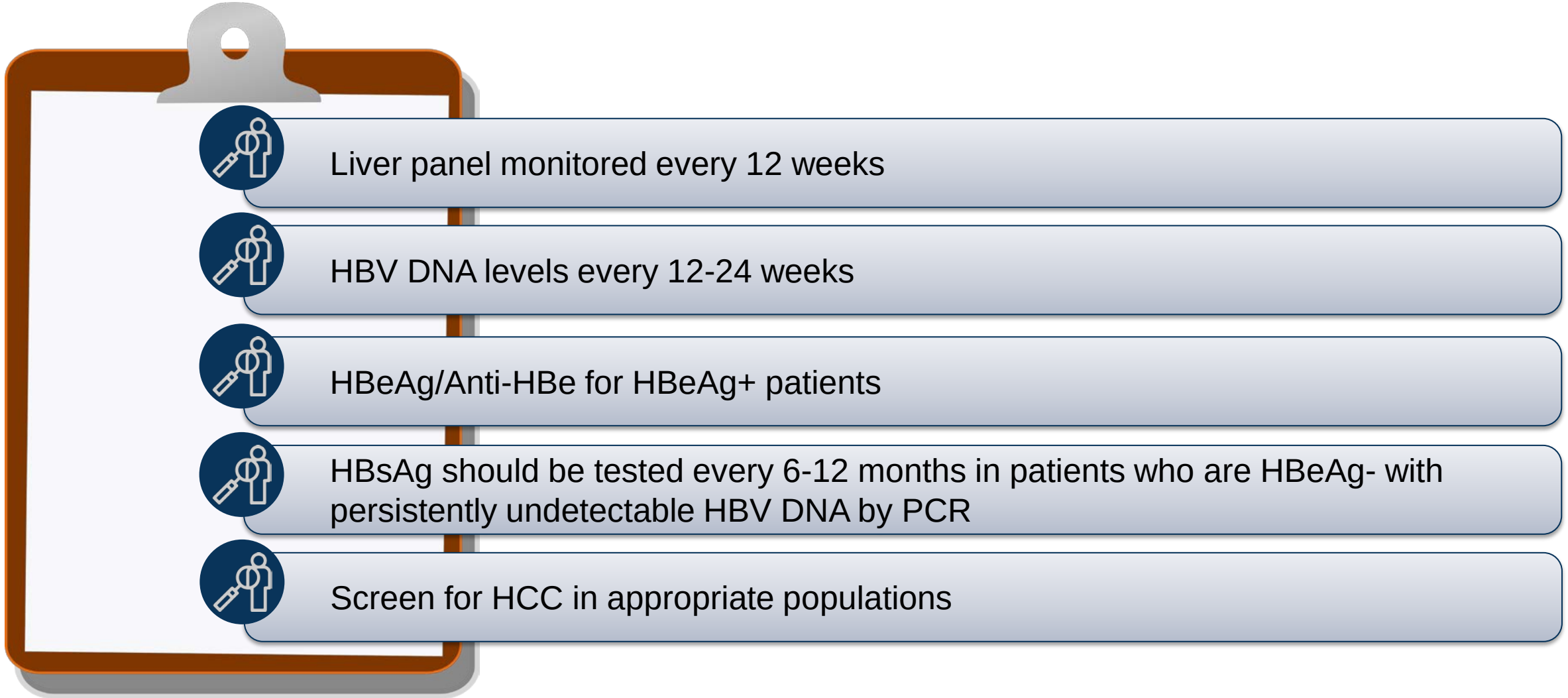
Monitoring Disease in HBsAg+ Patients[1]



- Obtain ALT and HBV DNA every 3 months for the first year and then every 6 months thereafter
- Perform ultrasound with AFP every 6 months
- Obtain HBsAg and assess fibrosis (testing consistent with cirrhosis) annually

1. Dieterich D et al. *Gastro Hep Advances*. 2023;2:209-218.

Monitoring Patients Who Are Not Treated[1,2]



1. Terrault NA et al. *Hepatology.* 2016;63:261-283. 2. Terrault NA et al. *Hepatology*. 2018;67:1560-1599.

First-Line Treatments for Hepatitis B Infection[1,2]

Key Considerations	Entecavir (ETV)	Tenofovir disoproxil fumarate (TDF)	Tenofovir alafenamide fumarate (TAF)
Dosage and administration			
No cirrhosis or compensated cirrhosis	0.5 mg tablet QD	300 mg QD	25 mg QD
Decompensated cirrhosis	1 mg QD	300 mg QD	25 mg QD
Prior treatment failure with lamivudine or telbivudine	Not recommended	300 mg QD	25 mg QD
Use in renal impairment	Dosage adjustment in eGFR <50 mL/min	Dosage adjustment in eGFR <50 mL/min	Not recommended in eGFR <15 mL/min not on HD
Use in pregnancy	Insufficient human data to assess risk; avoid in pregnant patients	Extensive data from pregnant women with HIV or HBV infections indicate no increase in pregnancy complications or major birth defects	Emerging safety database; still immature
Most common side effects	Headache, fatigue, dizziness, and nausea[a]	Nausea[b]	Headache[c]
Key drug–drug interactions[d]	Drugs that reduce renal function or compete for active tubular secretion		Drugs that strongly affect P-gp and BCRP activity, carbamazepine, phenytoin, rifampin, St. John's wort
	N/A	Adefovir, didanosine, protease inhibitors, HCV antivirals	

[a] Most common adverse reactions of any severity in ≥3% of subjects with at least a possible relation to study drug. [b] Most common adverse reactions in HBV-treated subjects with compensated liver disease. [c] Most common adverse reactions of any severity in ≥10% of subjects. [d] Healthcare providers should consult prescribing information, their local pharmacist, and/or online tools to confirm if interaction for specific drugs within a class, as exceptions may exist.

1. Dieterich D et al. *Gastro Hep Advances*. 2023;2:209-218. 2. https://www.hepatitisB.uw.edu/hbv-pcw/guidance.

Assessing Treatment Response[1]

After initiation of HBV antiviral, recheck HBV DNA every 3 months until undetectable and then every 6 months

If HBV DNA is not undetectable after 1 year of antiviral therapy and the HBV DNA levels are not downtrending, obtain expert consultation or refer to a specialist

Persons with cirrhosis: Do not stop antiviral treatment, unless guided by expert consultation

In patients without cirrhosis, treatment should continue until therapeutic response has been achieved, defined as meeting all the following criteria

- Loss of HBsAg plus completing at least 1 additional year of treatment
- Maintaining persistently normal ALTs and undetectable HBV DNA
- Willingness to undergo monitoring for HBsAg seroreversion for at least 2 additional years

1. Dieterich D et al. *Gastro Hep Advances*. 2023;2:209-218.

Hepatocellular Carcinoma Surveillance: HBV Primary Care Workgroup Recommendations (2020)[1]

Indications for HCC Surveillance

Chronic HBV at increased risk for HCC, including

- All people with cirrhosis, including people who become HBsAg-
- The following populations, even in the absence of cirrhosis
  - Asian or Black men >40 years of age
  - Asian women >50 years of age
  - People with a family history of HCC
  - People with HDV coinfection

Recommended HCC Surveillance Methods

- HCC surveillance should be performed in the primary care setting with liver ultrasound with or without AFP every 6 months
- More frequent monitoring or other imaging modalities such as CT or MRI, with and without contrast, may be indicated to further evaluate new liver lesions

1. https://www.hepatitisB.uw.edu/hbv-pcw/guidance.

Patients Undergoing Immunosuppressive and Cytotoxic Therapy: AASLD Recommendations[1]

There is a proliferation of immunosuppressive and cytotoxic therapies for oncologic and immune-mediated diseases that may lead to hepatitis B reactivation

HBsAg[a] and anti-HBc (total or IgG) testing should be done before initiation of immunosuppressive, cytotoxic, or immunomodulatory therapy

HBsAg+, anti-HBc+ → Initiate anti-HBV prophylaxis before immunosuppressive or cytotoxic therapy

HBsAg-, anti-HBc+ → Carefully monitor with ALT, HBV DNA, and HBsAg testing with the intent for on-demand therapy, except for patients receiving anti-CD20 antibody therapy or undergoing stem cell transplantation, for whom anti-HBV prophylaxis is recommended[b]

- Tenofovir disoproxil, tenofovir alafenamide, and entecavir are all appropriate choices when therapy is required (prophylaxis or on demand); continue until 6-12 months after completion of immunosuppressive or cytotoxic therapy

[a] Risk of HBV reactivation in HBsAg- patients receiving immunosuppressive or cytotoxic therapy is lower than HBsAg+ patients. [b] If you choose not to use prophylaxis, you do have to monitor ALT, HBV DNA, and HBsAg.

1. Terrault NA et al. *Hepatology*. 2018;67:1560-1599.

An Emerging Approach to HBV Management: 5 x 5 x 5[1]

5 Reasons to Treat ✖ **5 Guidelines for Management** ✖ **5 Key Messages About HBV**

1. Stigma/discrimination
2. QOL/extrahepatic diseases
3. Infectivity
4. CLD cirrhosis prevention
5. HCC prevention

1. Wong RJ et al. *Clin Infect Dis*. 2023;76:e791-e800.

An Emerging Approach to HBV Management: 5 x 5 x 5[1]

5 Reasons to Treat ✖ **5 Guidelines for Management** ✖ **5 Key Messages About HBV**

1. Test all for HBV with the HBV triple panel
2. Vaccinate all for HBV who are triple panel negative
3. Link all HBsAg+ patient to HBV DNA NAT testing and delta antibody screening
4. All HBV DNA + patients are stated on Nuc therapy
5. Stage all patients, and decide on HBV surveillance

1. Wong RJ et al. *Clin Infect Dis*. 2023;76:e791-e800.

An Emerging Approach to HBV Management: 5 x 5 x 5[1]

5 Reasons to Treat ✖ **5 Guidelines for Management** ✖ **5 Key Messages About HBV**

1. HBV therapy is not lifelong; there are many new therapies in the pipeline that can lead to functional cure, HBsAg loss, and HBV DNA-
2. There are no “healthy” carriers; treatment results in improvement in the components of the five pillars
3. We always need more “research,” but we have the research data now to take action to implement the five-line guideline
4. Delta testing should be provided to all HBV+ patients; “D” is for “deadly”
5. The only way forward to HBV elimination is to follow the five-line guidelines; the current guidelines are too complex and lead to nontesting, nontreatment, and nonvaccinations

1. Wong RJ et al. *Clin Infect Dis*. 2023;76:e791-e800.

Case 1: Marcus

28-year-old man

Presenting as a new patient → Laboratory testing → Next steps

Medical History

- Born in Samoa, and emigrated to the United States at age 5 y
- Stomach pain for several months
- History of IV drug use
- Unknown HBV vaccination status

Test Results

HBsAg	Negative
Anti-HBc	Positive
Anti-HBs	Positive

Next Steps in HBV Screening and Management

- What is this patient's HBV risk?
- What is this patient's HBV infection status?
- Does this patient require vaccination?
- Should this patient be treated with antivirals or referred for additional testing?
- How should you counsel his family?

Case 1: Marcus

28-year-old man

Presenting as a new patient → Laboratory testing → Next steps

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- Stomach pain for several months
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Test Results

HBsAg	Negative
Anti-HBc	Positive
Anti-HBs	Positive

Next Steps in HBV Screening and Management

- Patient is at risk of HBV infection due to history of IV drug use and being a native Pacific Islander
- He has resolved hepatitis B
- There is no transmission risk but there is a risk of reactivation
- No need to vaccinate

Case 2: Amma

42-year-old woman

Existing patient → Laboratory testing → Next steps

Medical History

- Born in Nigeria, and emigrated to the United States in her late 30s
- No history of IV drug use
- Positive home pregnancy test
- Male partner recently received positive HBV results
- Unknown vaccination status

Test Results

HBsAg	Negative
Anti-HBc	Negative
Anti-HBs	Negative
Pregnancy test	Positive

Next Steps in HBV Screening and Management

- What is this patient's HBV risk?
- What is this patient's HBV infection status?
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- Male partner recently received positive HBV results
- Unknown vaccination status

Test Results

HBsAg	Negative
Anti-HBc	Negative
Anti-HBs	Negative
Pregnancy test	Positive

Next Steps in HBV Screening and Management

- Elevated HBV risk due to partner with positive HBV testing and birth in Africa
- Patient had not been previously exposed or vaccinated, so she should be vaccinated[a] and counseled about risk reduction

[a] Advisory Committee on Immunization Practices recommendations indicate: Data on Heplisav-B and PreHevbrio are currently insufficient to inform vaccine-associated risks in pregnancy. Thus, providers should vaccinate pregnant women needing hepatitis B vaccination with Engerix-B, Recombivax HB, or Twinrix.[1]

1. Weng MK et al. *MMWR Morb Mortal Wkly Rep.* 2022;71:477-483.

Case 3: Ahn

32-year-old woman

Existing patient → Laboratory testing → Next steps

Medical History

- Born in Vietnam, and emigrated to the United States as a child
- Mother has hepatitis B
- Father died of liver cancer
- Recently engaged
- Unknown vaccination status

Test Results

HBsAg	Positive
Anti-HBc	Positive
FIB-4	1.2
Pregnancy test	Negative

Next Steps in HBV Screening and Management

- Order HBV DNA
- CMP, CBC/Plts
- Screen for HCV, HDV, and HIV
- Ultrasound
- Ensure fiancé is vaccinated against HBV

Case 3: Ahn

32-year-old woman

Existing patient → Laboratory testing → Next steps

Medical History

- Born in Vietnam, and emigrated to the United States as a child
- Mother has hepatitis B
- Father died of liver cancer
- Recently engaged
- Unknown vaccination status

Test Results

HBsAg	Positive
HBV DNA	2,500,000 IU/mL
ALT	38 IU/mL
Ultrasound	normal

Next Steps in HBV Screening and Management

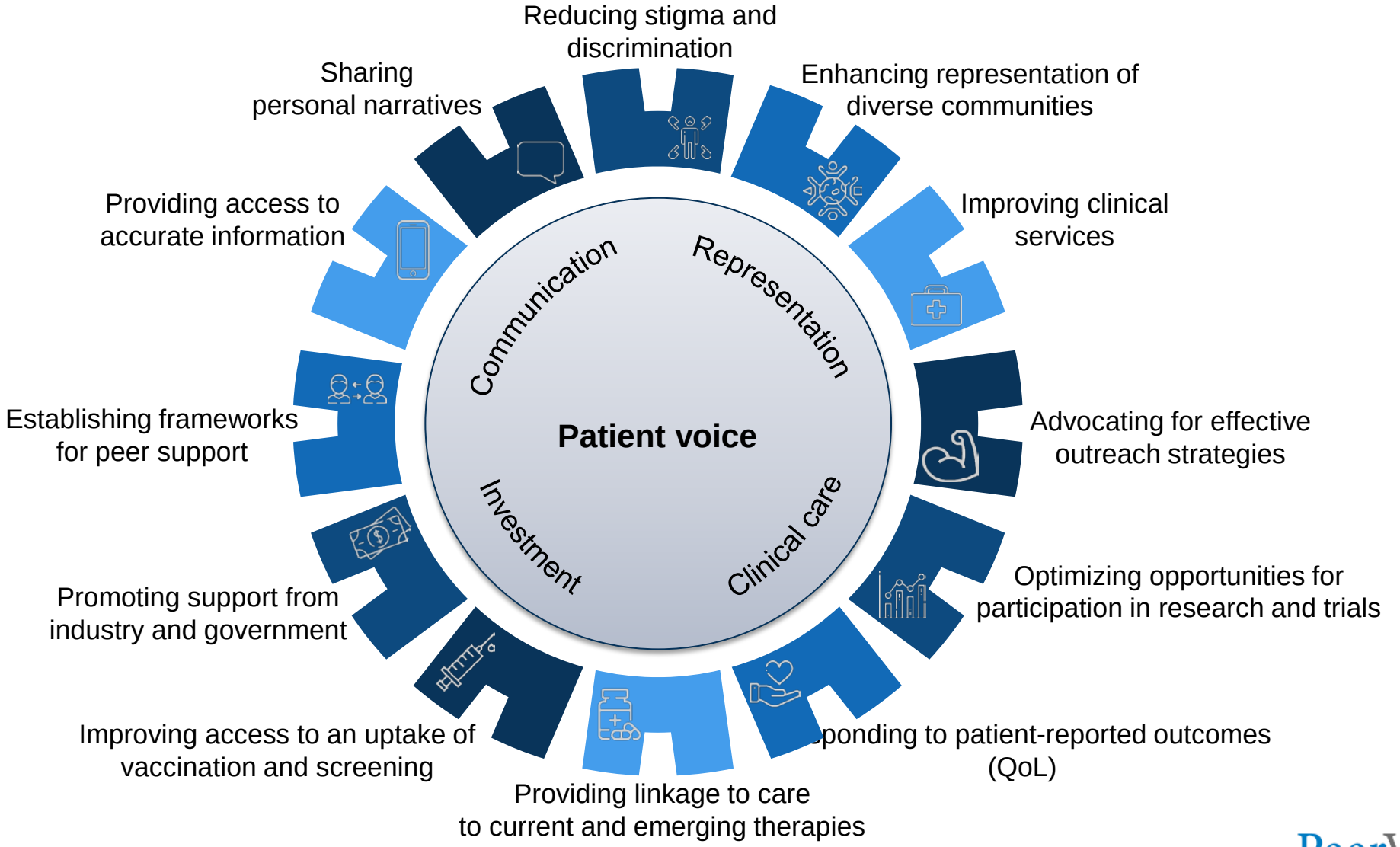
- Treat hepatitis B
- Monitor HBV DNA and CMP every 3 months until HBV DNA not detected
- Screen for HCC with ultrasound and AFP every 6 months

Referring Patients to Specialty Care

Approaches for Multidisciplinary Care

PeerView Live

Developing Strategies To Better Address Gaps in Eradicating HBV[1]



1. Matthews P at al. *Lancet Gastroenterol Hepatol*. 2022;7:282-285.

Defining the Roles and Responsibilities of Primary Care Providers and Specialists in Eradicating HBV[1,2]

What can be managed in primary care?

- HBV screening and interpretation
- HBV and HAV vaccination
- Initial evaluation and counseling of HBsAg+ patients
- HBV lab monitoring every 6 mo for both patients on and not on treatment
- Liver cancer surveillance ultrasound every 6 mo for men >40 y, women >50 y, people with cirrhosis or family history of liver cancer
- Substance use screening/harm reduction counseling
- Management of metabolic syndrome risk factors such as obesity, diabetes, hyperlipidemia, and hypertension

Dependent on comfort level of the PCP, may be managed in **primary care** or **in consultation with a specialist**

- Initiation of and monitoring on HBV antiviral treatment
- Perinatal HBV management

Refer

When should patients be referred to a liver specialist?

- Cirrhosis and/or liver mass
- Platelets <100 x 10^9/L
- HDV, HCV, and/or HIV coinfection
- Lack of response to treatment or rebound of HBV DNA levels[a]

[a] Failure of drug to reduce HBV DNA levels by ≥1 x $\log_{10}$ IU/mL within 3 mo of initiating treatment or rebound of ≥1 x $\log_{10}$ IU/mL in patients with initial response.

1. Wang S et al. *Curr Hepatol Rep*. 2021;20:34-42. 2. Dieterich D et al. *Gastro Hep Advances*. 2023;2:209-218.

Case 4: James

19-year-old man

Presenting as a new patient → Laboratory testing → Next steps

Medical History

- Born on US military base in England
- Experiences periodic homelessness
- No history of IV drug use
- Is unsure of vaccination status
- Father died of HCC

Test Results

HBsAg	Positive
Anti-HBc	Positive
Anti-HBs	Negative

Next Steps in HBV Screening and Management

- What is this patient's HBV infection status?
- Does this patient require vaccination?
- Should this patient receive additional testing?
- Should this patient be referred to a liver specialist?

Case 4: James

19-year-old man

Presenting as a new patient → Laboratory testing → Next steps

Medical History

- Born on US military base in England
- Experiences periodic homelessness
- No history of IV drug use
- Is unsure of vaccination status
- Father died of HCC

Additional Test Results

HBV DNA	6,000,000 IU/mL
ALT	38 IU/mL
Anti-HBs repeat	Negative

Next Steps in HBV Screening and Management

- Patient has current HBV infection and meets treatment criteria
- Patient should undergo baseline abdominal ultrasound and AFP

Case 4: James

19-year-old man

Presenting as a new patient → Laboratory testing → Next steps

Medical History

- Born on US military base in England
- Experiences periodic homelessness
- No history of IV drug use
- Is unsure of vaccination status
- Father died of HCC

Additional Test Results

Abdominal ultrasound	Shows a liver mass
AFP	55 mg/mL

Next Steps in HBV Screening and Management

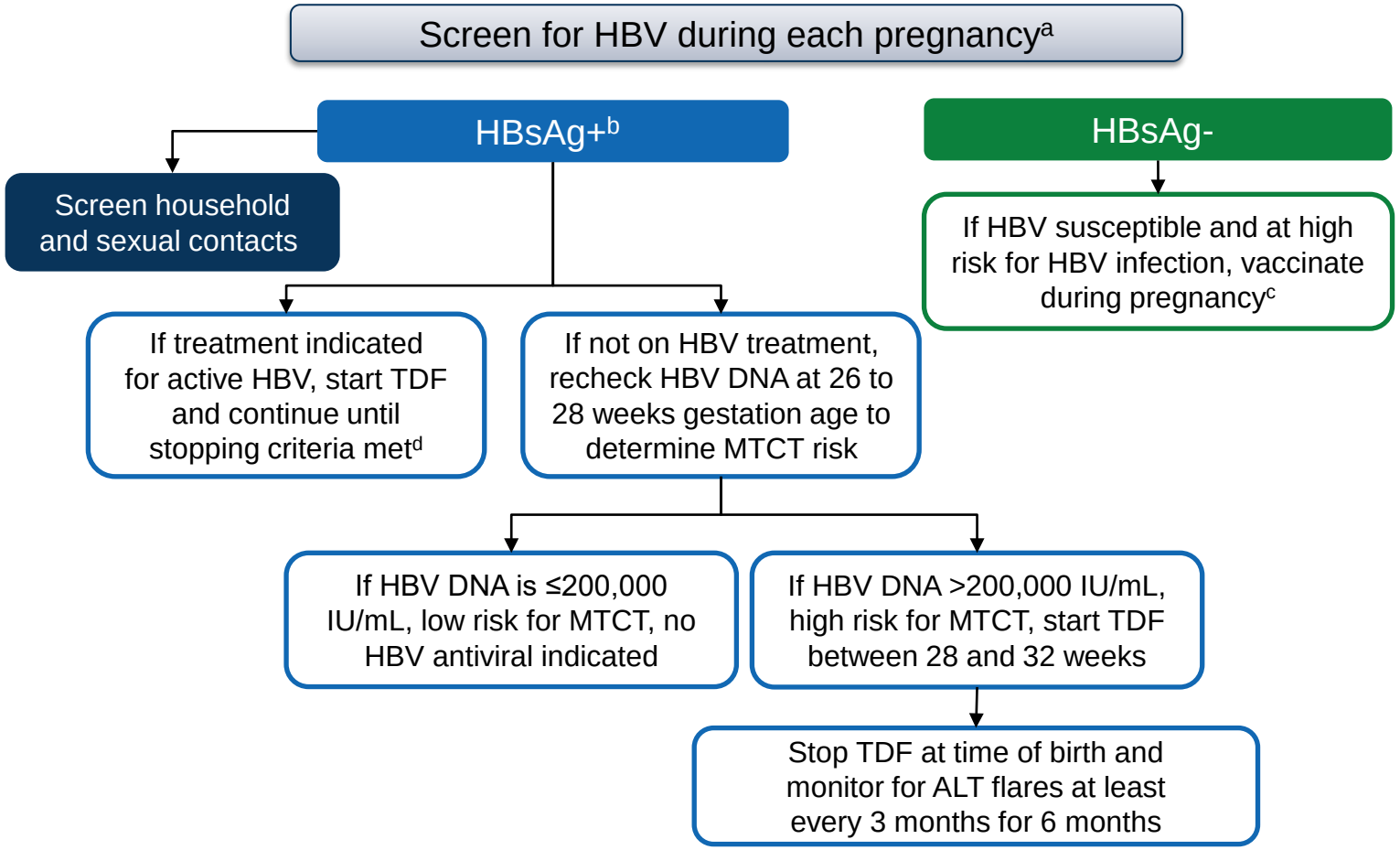
- Would you treat this person?
- Would you refer for subspecialty opinion?

Special Considerations With HBV Infection in Vulnerable Populations

PeerView
Live

Perinatal HBV Prevention and Management[1,2]

HBV Primary Care Workgroup Recommendations (2020)



Infant management

ALL infants of HBsAg- women should receive birth dose HBV vaccine within 24 hours of birth

ALL infants of HBsAg+ women should

- Receive birth dose HBV vaccine and HBIG within 12 hours of birth
- Complete HBV vaccine series on schedule[e]
- Receive a post-vaccination serology test at 9-12 months of age with HBsAg and anti-HBs to assess for mother-to-child transmission and confirm immunity

HBV and Breastfeeding

- All HBsAg+ mothers, including those on TDF, should be educated on the value and safety of breastfeeding and that HBV is not transmitted through breast milk
- Breastfeeding mothers with cracked nipples should practice proper nipple care and be informed that HBV vaccination and HBIG will protect against transmission from such blood exposures

[a] All pregnant women should be screened for HBV (with HBsAg at minimum) during each pregnancy, regardless of prior HBV screening results. For complete HBV profile, add anti-HBs to determine immunity and anti-HBc IgG or total for evidence of prior infection. [b] All HBsAg+ mothers should be educated on importance of regular follow-up during and after pregnancy, so that appropriate HBV monitoring can occur. [c] ACIP recommendations indicate: Data on Heplisav-B and PreHevbrio are currently insufficient to inform vaccine-associated risks in pregnancy. Providers should vaccinate pregnant women needing hepatitis B vaccination with Engerix-B, Recombivax HB, or Twinrix.[2] [d] If an HBsAg+ woman is already on antiviral therapy when she becomes pregnant, antiviral regimen should immediately be switched to TDF (if she is not already taking this medication). [e] For infants weighing less than 2,000 g, birth dose does not count toward vaccine series and infant should receive another HBV vaccine 1 mo after birth.

1. https://www.hepatitisB.uw.edu/hbv-pcw/guidance. 2. Weng MK et al. *MMWR Morb Mortal Wkly Rep*. 2022;71:477-483.

The Immunization Action Coalition Recommends a Universal Birth Dose of HBV Vaccine[1]

ACIP of the CDC, AAP, AAFP, and ACOG recommend

the first dose of HBV be administered prior to hospital discharge for every newborn in the United States

It prevents mother-to-infant transmission

Prevents 70% to 95% of transmission to infants born to HBsAg+ women

It prevents household transmission

Protects infants from infected family members and other caregivers

It provides protection if medical errors occur

Provides a safety net to prevent perinatal transmission when medical errors occur

1. https://www.immunize.org/protect-newborns.

Risk-Based Testing Fails to Identify Many Patients With HIV and HCV: Lessons for HBV Elimination[1]

For HIV, HBV, and, HCV

- Risk factors for infection are complicated and stigmatized
- Risk factors are inadequately assessed

Screening Solutions in HIV and HCV

- All persons ages 13-64 years are screened for HIV
- All persons ages 18-79 years are screened for HCV

Recommendations for HBV screening and prevention

- Test all adults for HBV infection
- Vaccinate all adults who lack evidence of prior HBV infection or vaccination and are susceptible to infection

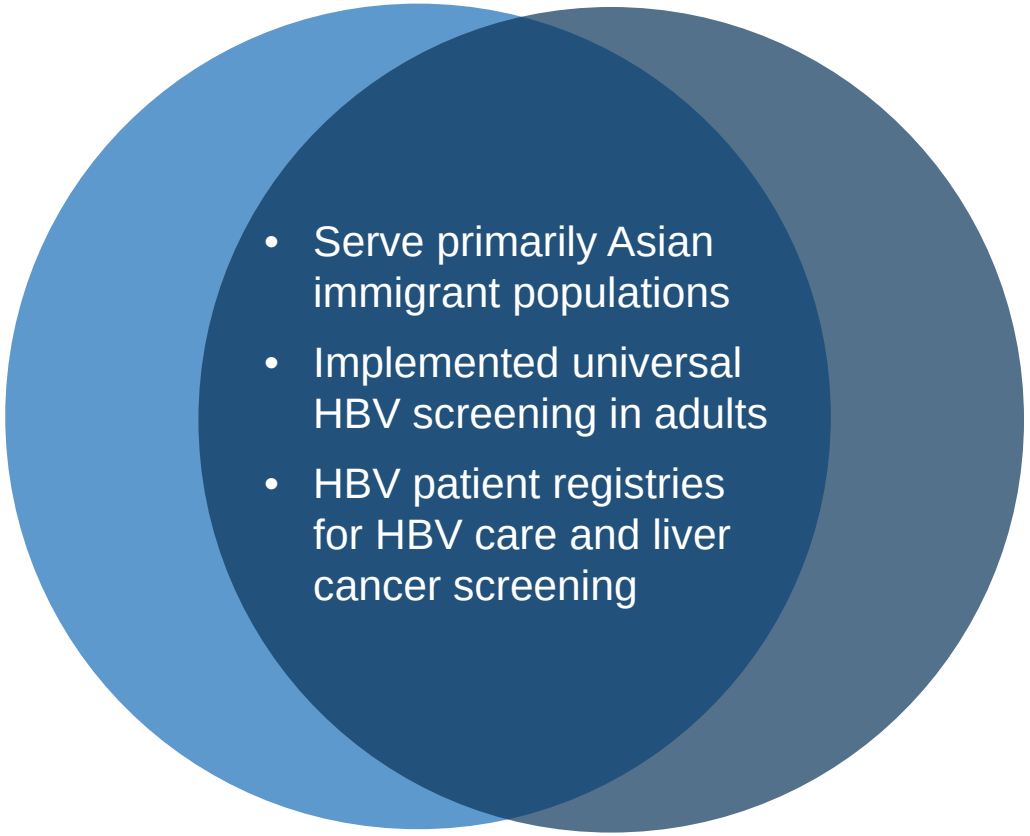
1. Wang S et al. *Curr Hepatol Rep*. 2021;20:34-42.

Effectively Delivering HBV Care to Highly Affected Populations[1]

Community groups and health centers have developed innovating strategies for delivering primary care–based HBV management to marginalized and highly affected populations

Charles B. Wang Community Health Center
New York City

Participates in NYC's Check Hep B Program to utilize patient navigators to ensure all patients with HBC are linked to care with an HBV provider and coordinate specialty care when needed



North East Medical Services
San Francisco Bay Area

In-house radiology department adopted Ultrasound Liver Imaging Reporting and Data System (US LI-RADS) for HCC surveillance of chronic HBV patients with EHR prompts for ordering US and serum AFP for men over age 40 years and women over age 50 years

1. Wang S et al. *Curr Hepatol Rep*. 2021;20:34-42.

Paraphrasing Dr. William Osler

"[Addiction] is a social disease with a medical aspect"

1. Cooper SM et al, eds. *The Quotable Osler*. Philadelphia, PA: American College of Physicians; 2003.

Harm Reduction and Hepatitis B (and C)

- Increasing evidence base for its effectiveness
- Nonjudgmental approach
- “Housing first”
- Diseases and deaths of despair
- *Undoing Drugs*, by Maia Szalavitz[1]
  - Eloquent book on the history of harm reduction

1. Maia Szalavitz. *Undoing Drugs: How Harm Reduction is Changing the Future of Drugs and Addiction.* New York, NY: Hachette Go; 2021.

Conclusions

Screen

- Consider universal screening for HBV; current standards are risk-based screening but are under revision
- Use HBsAg, anti-HBs, and total anti-HBc as serologic markers for screening

Vaccinate

- Vaccinate those who have not been exposed to hepatitis B

Treat

- Treat all patients >30 years of age and HBV DNA >2,000 IU/mL if they have no evidence of cirrhosis
- Those with cirrhosis should be treated regardless of viral level
- Use ETV, TDF, or TAF as first-line agents for treatment of HBV and monitor during therapy; ensure compliance with therapy
- Screen for HCC as appropriate

Refer

- Refer to a specialist if decompensated cirrhosis is suspected, a liver mass is suspected, HIV coinfection exists, or if a patient is not responding to treatment

It is important to identify the large undiagnosed population of individuals infected with HBV and link them to care

Audience Q&A

PeerView Live

Please remember to complete and submit Program Evaluation

PeerView.com/HBV-AYK

Thank you and have a good day.

PeerView Live

Abbreviations

AFP: alpha-fetoprotein
ALP: alkaline phosphatase
Anti-HBc: antibody to hepatitis B core antigen
Anti-HBe: antibody to hepatitis B e antigen
Anti-HBs: antibody to hepatitis B surface antigen
APRI: AST to Platelet Ratio Index
BCRP: breast cancer resistance protein
CD: cluster of differentiation
CHB: chronic hepatitis B
CMP: comprehensive metabolic panel
dsDNA-RT: double-stranded DNA reverse transcriptase
ETV: entecavir
FIB-4: Fibrosis-4 Index for Liver Fibrosis
HBeAg: hepatitis B e antigen
HBsAg: hepatitis B surface antigen
HCC: hepatocellular carcinoma
HDV: hepatitis D virus
INR: international normalized ratio
P-gp: P-glycoprotein
QD: once daily
TAF: tenofovir alafenamide
TDF: tenofovir disoproxil fumarate