

The Insidious Killer: Chronic Hepatitis B Virus

Disease Management and Cultural Considerations for the Asian American and Pacific Islander

Population in Primary Care

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Abstract: Chronic hepatitis B (CHB) is a significant health concern in the Asian American and Pacific Islander (AAPI) community. The lack of initial symptoms underscores the importance of early detection because it may impact the individual's quality of life and poses a risk for transmission impact in public health. The challenges in management in primary care setting for the AAPI community are multifaceted. The challenges include stigma related to cultural beliefs, lack of knowledge, and language barriers. Understanding stigma while incorporating universal screening protocols is crucial for primary care providers to utilize for early detection, reducing transmission, and lowering the risk of hepatocellular cancer (HCC).

Objective: Understanding the approach and clinician review of CHB. Discuss the challenges of treating CHB in the AAPI community. Describe universal screening protocol per CDC, identify destigmatizing approaches, and use cultural considerations to expand screening and treatment within the AAPI community. Identify evidence-based approaches from guidelines from AASLD.

Keywords: hepatitis b virus, chronic hepatitis b, asianamerican and pacific islander, cultural considerations, stigma, primary care provider, nurse practitioner

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Introduction

For every three individuals of Asian American and Pacific Islander (AAPI) descent, two are unaware of having hepatitis B virus (HBV) infection.² A study emphasized that 67% of participants that were tested positive for HBV virus did not even know that they were infected due to their attribution to a lack of presentation of symptoms.⁸ Those infected with HBV typically do not exhibit any symptoms at the onset of the infection; instead, symptoms manifest with the onset of serious disease complications like acute liver failure or chronic hepatitis B (CHB).¹¹ CHB is a known risk factor for hepatocellular carcinoma (HCC), a type of cancer, and is the leading cause of liver cancer in the AAPI community.⁹

Although vaccines offers almost a 100% protection rate against HBV and treatments are readily available, the rate of HBV worldwide is approximately 300 million and is geographically influenced in Asian and Africa.^{2, 20} Although CHB impacts about 2 million people in the United States, the AAPI population disproportionately makes up about more than 60% of HBV cases.² In the United States, 76% of CHB positive cases were immigrants and 40% of those cases were immigrants born in the Philippines, China, and Vietnam.¹⁴ The CDC reported 2,157 cases of acute hepatitis B in 2020, but estimates that the actual cases of acute hepatitis B at about 14,000

with approximately 880,000 living with CHB.² These figures may indicate a challenge in diagnosis due to lack of symptom presentation, gap in education of providers and staff due to lack of familiarity with screening methods, limited usage of evidence-based practice strategies, and need for increased prevention efforts.⁴ Furthermore, disproportionate impact emphasizes the necessity of delving deeper into tailoring treatment plans to the AAPI community.

The various complexities to be considered include cultural considerations specific to the AAPI population, language barriers, and the emotional impact of stigma.¹² Lack of education and myths associated with HBV also need to be addressed.⁵ Despite readily availability of treatment, disproportionate rates of HBV infection among the AAPI population, coupled with the absence of initial symptoms, increases the risk of the insidious progression of liver failure and cancer. The overarching goal is to provide primary care providers, like nurse practitioners, a comprehensive resource on management and general practice guidance of CHB, with culturally sensitive considerations and destigmatizing approaches tailored to the AAPI community.

Pathophysiology

Hepatitis is inflammation in the liver that can be caused by different pathologies.¹⁰ When suspicious of viral hepatitis, consider the five different types of virus that could lead to the infection of viral hepatitis, and they are inclusive of hepatitis viruses A, B, C, D, and E.²

Hepatitis B is a type of liver infection that is caused by a virus called hepatitis B.¹³

Risk factors are attributed to contact with infectious body fluids like blood, serum, semen, and open sores or cuts of a person with HBV, shared intravenous drug use, or needlesticks.¹ HBV positive mothers giving birth and passing the infection to their baby, being infected from a family member as a child, having sex with a partner who has hepatitis B, sharing

contaminated items like toothbrushes, razors, or medical equipment are also risk factors for HBV infection.¹³ Sharing food, utensils, and kissing is not a mode of transmission.⁴

The virus is transmitted through contact with infected body fluids like blood or semen.¹³ Once the virus enters the hepatocyte, the virus is then transported to the nucleus.¹⁹ In the nucleus, the viral deoxyribonucleic acid (DNA) transforms into a molecule called a covalently closed circular DNA (cccDNA) and serves as a template for replication of HBV.¹⁹ Newly formed viruses are released from the hepatocyte.¹⁹ While cccDNA remains inside the nucleus and integrates into the DNA of the host's hepatocyte, the cccDNA continuously produces new HBV.¹⁹ The virus may also remain latent within the host's hepatocyte and may reappear years later, which then indicates that the HBV infection is chronic in nature.¹⁹

CHB infection is majorly due to acquiring the viral infection during infancy.¹³ This is believed to be due to the immaturity of the immune response against the virus at such a young age.⁷ If an individual is infected with HBV later in life, the chances of acute HBV converting to chronic is much lower and comprises 5% of cases in infected adults.⁴ When compared to the rates of hepatitis B that were infected during birth leading to CHB, it occurred in 90% of cases.⁴ This translates to the need to understand patient presentation and highlight differences of acute and CHB.

Presentation

The course of HBV can differ among each individual. In general, an individual with an HBV infection may present with fever, fatigue, loss of appetite, nausea, vomiting, diarrhea, right upper quadrant or generalized abdominal pain, dark colored urine, jaundice, and signs and symptoms of cirrhosis.⁴ Manifestations of cirrhosis include jaundice, peripheral edema, firm

liver, splenomegaly, ascites, encephalopathy, gynecomastia, and white-silver discoloration of proximal nail beds.⁴

History and Screening

Drawing from patient presentation and history can guide the primary care provider in assessing and developing strategies for the workup of HBV infection. When distinguishing between acute and CHB infection, the initial approach involves implementing universal screening. The recommended universal screening method is to screen adults who are 18 and above once in their lifetime.² All pregnant individuals be screened irrespective of vaccination status, testing history, or previous screenings, with preferences for conducting screening in the first trimester of each pregnancy.²

Recommendation for implementing universal screening method rather than the previous risk factor based screening recommendations is used because it decreases feelings of stigma associated with risk factors.² This would mean that universal screening could lead to an increased coverage and reach more individuals for screening and treatment in individuals who may have otherwise avoided treatment based on stigma due to risk factors or cultural beliefs especially in the AAPI community.

Universal screening guidelines are not listed for the pediatrics population of age 18 and under because this group has high rates of vaccinations at birth and low prevalence rates of HBV infection in the United States.² However, it may still be worthwhile to screen children and adolescents under the age of 18 if they were born or migrated from outside of the United States. The low vaccination rates among the adult population compared to the prevalent rates HBV infections of the adult population translates to the need to increase vaccination.²

Risk factors to screen for include country of origin, if they have had vaccines before and whether the patient presents with symptoms or manifestations of jaundice or cirrhosis.⁴

Medication reconciliation and polypharmacy reconciliation should be performed to ensure that medications are not inducing liver disease.⁴ Lifestyle screenings like diet, substance abuse, alcohol, and high risk sexual behavior screenings should be conducted to determine risk and causes of liver diseases.² Other risk factors to evaluate for would be inclusive of the history of household or familial HBV infection or immunity; history of familial liver cancer like HCC; sexual contacts; the risk for coinfection of hepatitis C, hepatitis D, or human immunodeficiency virus (HIV); history of being in prison or jail; and a history of receiving blood transfusions.² Healthcare workers are at risk for nosocomial HBV infections due to their direct contact with bodily fluids, whereas dialysis patients are at risk when dialysis machines and tools are not sanitized correctly.²

Assessment

There is no specific physical exam assessment that completely confirms the diagnosis of the infection of CHB because there are various liver disease processes that present with similar presentations and requires further diagnostic workup to confirm.⁴ The physical examination of the abdomen should be performed by palpation for liver size and consistency, and ascites.¹

Palpation of four to eight centimeters away from midsternal line and percussion along right midclavicular line (MCL) from six to twelve centimeters both assess for normal liver span and estimation of size.¹ Increased dullness along the MCL may indicate hepatomegaly from acute hepatitis.¹ Palpation of the liver below the costal margin in the MCL while the patient inhales determines liver consistency, in which a firm liver edge would indicate cirrhosis.¹ Palpation above the costal margin of the MCL would assess for tenderness or masses, and may

indicate hepatitis or tumor respectively.¹ Ascites is assessed by palpation and percussion of the ascitic fluid shifting dependently to the same side the individual turned to.¹ Percussion of ascitic fluid is dull and changes in dullness is dependent shifting from side to side, also known as shifting dullness.¹

Differentials and Diagnostic Workups

HBV is only one of the many differentials that could lead to liver disease with presentations of cirrhosis and jaundice. Differentials include drug or medication induced liver failure; non-alcoholic and alcoholic fatty liver disease; primary biliary cholangitis; autoimmune hepatitis; sepsis; muscle disorders like seizures or heavy exercise that may lead to rhabdomyolysis; genetic diseases like Wilson's disease; Budd-Chiari syndrome; hemochromatosis; and in pregnant patients suspicious of HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome.^{4,10} It should be noted that this list of differentials and workups is not completely exhaustive.

Laboratory tests include complete blood count (CBC); complete metabolic panel (CMP); liver function tests that include aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, alkaline phosphatase, and albumin; international normalized ratio (INR), and prothrombin time (PT).⁴ For CHB, there is a markedly elevated serum ALT and AST, and bilirubin and alkaline phosphatase may be elevated.⁴ Hepatitis panel is ordered to determine which type of hepatitis the individual may have and determine whether infection status is current or past based on antigen and antibodies, and immunity response to vaccines.² Triple panel includes hepatitis B surface antigen (HBsAg), the antibody to the hepatitis surface antigen (anti-HBs), and antibody to hepatitis B core (anti-HBc) and is recommended as initial screening.² Any

subsequent periodic testing of both HBsAg and anti-HBc could be then used for cases in screening for pre-vaccination to determine whether there was previous exposure to infection.²

Depending on care setting, acetaminophen levels and toxicology levels should be drawn.⁴ Serum ammonia levels should be assessed in acute settings where individuals present with altered mental status or comatose state and have liver disease manifestations because severe liver damage could impair the processing of ammonia and ammonia build leads to hepatic encephalopathy which manifests as the altered mental status or coma.¹⁸ Ordering iron, total iron binding capacity (TIBC), and ferritin blood work may assist the primary care provider in determining whether a patient has hemochromatosis, hepatitis C, and hepatitis D.¹⁸ Hemochromatosis is due to an increased iron absorption or storage in the liver and may lead to liver cirrhosis.¹⁸ Increased iron absorption or storage is also seen in hepatitis B, C, and D.¹⁸ High levels of urine copper levels may indicate Wilson's disease.¹⁸ Wilson's disease is a genetic disease where the body has a build up of copper, is unable to remove extra copper from the body, and leads to liver disease.¹⁸ Screening for HIV is also recommended due to injection drug use leading to hepatitis and individuals may be coinfecting with hepatitis B, hepatitis C, and HIV.¹⁰ If there is persistent and unexplained levels of ALT and AST that is two times the upper limit or alkaline phosphatase is 1.5 times the upper limit; not responding to antiviral therapy; coinfection of hepatitis B, hepatitis C, hepatitis D, or HIV; or advanced stages of cirrhosis then the patient should be referred to consultations of gastroenterologist, hepatologist, and infectious disease specialist.¹⁸

Non-invasive diagnostics like an abdominal ultrasound may be useful in viewing whether the liver had developed any scar tissue like in various stages of fibrosis, cirrhosis, nodules, and fatty liver diseases.⁴ However, abdominal ultrasound may not always pick up lesions due to body

composition, and cross sectional imaging with contrast computed tomography (CT) or magnetic resonance imaging (MRI) is considered when monitoring HCC risk.¹⁷ Vibration-controlled transient elastography (VCTE) is another non-invasive method to assess for fibrosis.¹⁶ Liver biopsy would be most useful in situations where an individual has persistently elevated ALT and low HBV DNA; when the individual does not meet criteria for treatment and is at risk for advanced liver disease; or elevated HBV viral load for more than six months with an ALT that is either normal or two times the upper limit with the risk factor of being older than 40 years old and family history of HCC.¹⁰ Liver biopsy is recommended when there is a lack of an identifiable cause of the manifestations of liver disease.¹⁶

Diagnosis

The triple panel is the primary serological markers used to determine status of HBV infection, but these values may change during the resolution of an acute infection or development of a chronic infection.² HBsAg presence indicates that there is an HBV infection, which could be either acute or chronic, but is transiently positive shortly after a dose of the HepB vaccine.¹⁰ Recovery from the HBV infection occurs when Anti-HBs appear after there is a decline of the HBsAg.¹⁰ Acute hepatitis B is defined as the detection of the HBsAg and the immunoglobulin M (IgM) to anti-HBc, in which infection lasts less than six months.¹⁰ CHB is defined as the detection of HBsAg that is present for longer than six months and negative IgM anti-HBc.^{4,10} ALT or AST levels can either be normal or elevated, while a liver biopsy would show chronic hepatitis with necroinflammation or fibrosis.¹⁶

Other types of markers for hepatitis B also include HBV DNA, hepatitis B e antigen (HBeAg), and antibodies to hepatitis B e antigen (anti-HBes).² The HBV DNA is a blood test that confirms infection, but a negative result does not completely rule out

disease.¹⁶ HBeAg presence is for viral replication and high infectivity, whereas anti-HBe is used to monitor whether there is response to treatment and the progression of CHB infection.¹⁰ Once the individual is diagnosed with HBV infection, ordering tests for HBeAg, anti-HBe, and HBV DNA can offer insights into the extent of the viral replication and infectivity, in which it can provide insight on the guide to clinical management of the individual.¹⁰

Education, Prevention, and Treatment

For prevention, it is important to educate individuals to practice safe sex, proper sanitation and hygiene, avoidance of exposure to blood and blood products, avoid intravenous drug use, and proper sanitation and hygiene techniques.² For vaccinations, recommendations are to vaccinate all adults aged 19 to 59, but each HBV vaccine dose and schedule varies by brand, age, risk factors, and conditions.² Pregnant persons are vaccinated each pregnancy, and antiviral therapy is recommended in the third semester for every pregnant person that has an HBV DNA of above 200,000 IU/mL.⁴ Vaccination is recommended at birth for newborns within the first 24 hours of life and at scheduled intervals when following up with primary care during developmental milestone physical exams.² The second recommended dose is between one to two months of life, whereas the third dose is recommended anywhere from six to 18 months.²

For immunocompromised individuals, have never been infected with HBV, and have completed specifically the HepB vaccine series 1-2 months afterwards, the levels of anti-HBs above or equal to 10 mIU/mL means there is immunity.¹⁰ Hepatitis B immunoglobulin (HBIG) is typically given post-exposure, and can provide anti-HBs for about four to six months.¹⁰ Testing for anti-HBs before six months is not accurate when attempting to determine the immunity status of an individual that received HBIG.¹⁰

For CHB infected individuals with cirrhosis, antiviral therapy is still continued despite clinical response or even if HBV DNA levels are low at less than 2,000 IU/mL.⁴ However, antiviral therapy could be discontinued if there is no presentation of cirrhosis and the anti-HBe is negative.⁴ For all cases of CHB who have not been started on antiretroviral therapy, ALT should be monitored at least every three to six months.⁴

Antivirals are recommended on the general guidelines provided and updated in 2018 by the American Association for the Study of Liver Disease (AASLD).¹⁶ Antiviral treatment is only utilized to decrease morbidity and mortality through suppressing the virus from replicating and preventing HBV from developing into worsening liver diseases like chronic hepatitis or cirrhosis, end-stage liver disease, and HCC.¹⁶ This means that currently there is no treatment to cure HBV. Measurable outcomes of suppression of the replication process of HBV are achieved when ALT is normal, no detection of anti-HBe and HBeAg, and liver tissue improvement.¹⁶

There are various antivirals that could be used to treat CHB, but precautions and individualized treatment should be tailored specifically to each patient. Furthermore, the list of approved antiviral therapy's adult and pediatric dosage, frequency of intake, recommendations of follow up laboratory monitoring frequency, pregnancy category risk factors, and potential side effects vary between each medication.¹⁶ The list of approved antiviral therapy according to the AASLD is inclusive of Peg-IFN- α 2a for adults, IFN- α 2b for children, Lamivudine, Telbivudine, Entecavir, Adefovir, Tenofovir dipovoxil fumarate, and Tenofovir alafenamide.¹⁶ Depending on which medication is selected for therapy based on individual case, additional labs may be required like lactic acid due to risk for lactic acidosis; HIV testing; thyroid stimulating hormone (TSH) levels every three months; CBC every one to three months; serum creatinine and serum phosphorus; creatinine clearance, urine glucose, and urine protein as baseline and during

antiviral therapy.¹⁶ Medication reference guides and the AASLD guideline should be utilized to accurately order indicated labs prior, during, and after treatment to evaluate effectiveness and toxicities.

Non-pharmacological interventions include abstaining from alcohol, avoiding large doses of liver metabolizing drugs like acetaminophen and iron, and vaccinating against other viral hepatitis.⁴ Some AAPI cultures use herbal remedies and traditional eastern medicine.¹⁷ Providers should emphasize with individuals to refrain from starting new medications, over the counter medications, and herbal medications without first consulting with a provider to prevent further harm to the liver.

Liver transplant is required if there are extensive complications like sudden or severe onset of liver failure due to HBV infection, severe cases of exacerbation of CHB, decompensated cirrhosis and detectable HBV DNA.^{10,18} Pre and post liver transplant requires antiviral therapy to prevent HBV from replicating.³ Although there are various treatments, HBV still poses some challenges for initiating treatment due to challenges of stigma and cultural beliefs.

Cultural Considerations

Cultural considerations must be taken into account as cultural beliefs and practices can significantly influence a patient's non-compliance or refusal of treatment. Although patients have the right to make decisions about their healthcare, primary care providers should prioritize having meaningful interactions with their patient by exploring the specific reasons influencing the patient's decision. Practicing culturally competent care is a key strategy in addressing these challenges, as it involves recognizing and respecting the patient's beliefs, values, and practices. This approach not only provides insight into the reasons behind the patient's decisions, but also strengthens the patient-provider relationship.

In addition to cultural practices, lack of awareness or knowledge, myths, cultural beliefs, and language barriers also influence the stigma associated with CHB.^{15,21} In a study that provided HBV education workshops that were culturally tailored, it was found that some individuals of the AAPI community have expressed that there is stigma and discrimination against individuals with hepatitis B.²¹ Participants of the study stated that they would try to isolate and use different utensils while eating with a family member that was a carrier of HBV.²¹ Stigma related to HBV also varied based on social, structural or institutional, and workplace stigma.¹⁵ Some participants expressed concern with bringing shame and challenges for their family and did not want to appear “dirty” if positive for HBV.¹⁵ Other findings included fear of not being able to either find or losing a job, being isolated from social gatherings, fear of putting others at risk, and feel that they are not a desirable partner or spouse.¹⁵ Some participants expressed fear disclosing HBV status due to fear of being treated like an HIV patient.¹⁵ HBV infected mothers expressed fear of their child being ostracized in school and throughout life.¹⁵ Other participants expressed unwillingness to accept any gifts, let their children play, have dinner, hug or shake hands from those with HBV.¹⁵

Theme causes of stigma are due to misconceptions of how the virus is transmitted and the fear of being infected.¹⁵ Stigma could negatively influence the daily life of people due to misconceptions and lack of awareness.¹⁵ This means that stigma could lead to deterrence of treatment, feelings of shame, and unnecessary isolation based on infection status. Using universal screening, as opposed to risk factor based type of screening, allows for a destigmatizing approach. Cultural considerations and ensuring that the individual’s preferred language is utilized has positive impacts on treatment, adherence, and follow up care.¹¹ Support for culturally tailored HBV public education and outreach programs that target both the infected

HBV and general population would help further advance HBV immunization and awareness, and increase efforts to destigmatize HBV in the AAPI community.^{12,15}

Follow-up Recommendations

Continuous screening and evaluation is recommended to evaluate the progression of disease process; immunity status from vaccines and immunoglobulins; decreasing replication process of viruses through antivirals; and to measure whether treatment has been effective. The recommendations for follow up depend on each individual case. For the individual with acute hepatitis B, follow-up should be six months after acute illness and lab workup to measure HBsAg and HBeAg to determine whether chronic infection is present.¹⁰ Lifelong monitoring and management of CHB is needed to assess whether treatment is needed and during treatment to assess whether treatment needs revision.¹⁰ For HBsAg positive individuals, HCC should be screened every six months by abdominal ultrasound along with serum alpha-fetoprotein (AFP).¹⁶ Additional screening for HCC is if there is advanced fibrosis per ultrasound results, if the patient is an adult Asian or Black man over 40 years old or an Asian woman over 50 years old, if there is a history of first-degree relative with HCC, and if there is HDV coinfection.⁴ Liver function tests should be monitored every three to six months to evaluate AST and ALT trends.¹⁰ Failure to recommend follow-ups or failure of the individual to come back for follow-up may lead to negative outcomes of health.

Conclusion

The initial lack of symptoms in CHB makes early detection and initiation of treatment challenging and increases risk of complications like acute liver failure and HCC especially in the AAPI community. Understanding differential diagnoses is crucial for guiding the primary care provider in diagnostic workup to determine whether manifestations of liver disease are caused by

HBV or through other liver disease processes. The utilization of a universal screening protocol, adherence to treatment guidelines from AASLD, and recognizing that stigma is multifaceted while integrating cultural considerations would combat challenges of treatment in individuals with CHB. While evidence-based practice is considered the best course of action, a holistic approach with emphasis on combating stigma, incorporating cultural considerations, and individualization based on each patient's case should be equally regarded as important to include. This approach ensures the patient's dignity and can lead to measurable improvements in their health as a result of the comprehensive management of care by the primary care provider and healthcare team.

Table 1
Terminology

Abbreviations	Definition
HBV	Hepatitis B Virus
HBV DNA	Hepatitis B Virus DNA
HBsAg	Surface antigen: marker for current infection. Positive could be acute or chronic
Anti-HBs	Surface antibody: marker for immunity Positive is an immune response to either vaccination or infection
Anti-HBc	Antibody to core antigen Used in pre-vaccination to determine previous exposure to infection
IgM anti-HBc	Immunoglobulin M antibody to anti-HBc

	Positive means acute infection, usually within the last 6 months.
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Sources: Centers for Disease Control and Prevention. 2021; Lok. 2021; Terrault NA, Lok ASF, McMahon BJ, Chang K, Hwang JP, Jonas MM, Brown RS, Bzowej NH, Wong JB. 2018.

Table 2 General guideline for diagnostics and differentials*

Diagnostic work ups	Approaches and differentials
Complete blood count (CBC) Complete metabolic panel (CMP) Liver function tests (LFTs): ALT, AST, bilirubin, alkaline phosphatase PT/PTT and INR	<ul style="list-style-type: none"> - Gather baseline lab work - Chronic hepatitis B: markedly elevated ALT and AST; may be elevated bilirubin and alkaline phosphatase - Rule out rhabdomyolysis: abnormal liver function tests - Rule out cirrhosis, HELLP,: impacting PT, PTT, INR and clotting factors - Rule out alcohol induced liver disease: AST:ALT ratio of more than 2 <ul style="list-style-type: none"> - AST is more elevated compared to ALT
Hepatitis Panel	<ul style="list-style-type: none"> - Determines which hepatitis virus type - Rules out: Coinfection of other hepatitis viruses
Hepatitis B virus serological markers	<ul style="list-style-type: none"> - Determines immunity, pre/post infection, acute/chronic HBV
HBsAg = Negative	<ul style="list-style-type: none"> - Susceptible to infection, there is no infection, but also no immunity

Anti-HBc = Negative Anti-HBs = Negative	- Vaccinate
HBsAg = Positive Anti-HBc = Negative Anti-HBs = Negative	- Either early acute infection or within 18 days of a vaccine. - Continue to monitor
HBsAg = Negative Anti-HBc = Negative Anti-HBs = Positive	- Immunity acquired due to vaccination if anti-HBs is above or equal to 10 mIU/mL after vaccine series are completed.
HBsAg = Negative Anti-HBc = Positive Anti-HBs = Positive	- Immunity acquired due to past resolved infection
HBsAg = Positive Anti-HBc = Positive IgM anti-HBc = Positive Anti-HBs = Negative	- Treat for acute hepatitis B virus infection
HBsAg = Positive Anti-HBc = Positive IgM anti-HBc = Negative Anti-HBs = Negative	Treat for chronic hepatitis B virus infection <ul style="list-style-type: none"> - Positive HBV DNA: active disease - Negative HBV DNA: no active disease - AASLD recommends: peg-IFN, entecavir, or tenofovir (TDF) as preferred initial treatment for immune-active CHB. <ul style="list-style-type: none"> - Immune-active CHB: elevation of ALT ≥ 2 the upper normal limit or evidence of significant histologic disease, and HBV DNA above 2,000 IU/mL (for HBeAg negative) or HBV DNA above 20,000 IU/mL (for HBeAg positive).
HBsAg = Negative Anti-HBc = Positive Anti-HBs = Negative	Four differentials <ol style="list-style-type: none"> 1. Patient could be recovering from acute HBV 2. Patient could be distantly immune = Testing cannot detect very low levels of the anti-HBs and may lead to a false negative 3. False positive of anti-HBc, risk for HBV infection 4. Patient could have an undetectable level of HBsAg leading to false negative, and the patient is a carrier of HBV.
HIV testing	- Rule out: Coinfection

Serum ammonia	- Rule out: Hepatic encephalopathy
Iron, total iron binding capacity (TIBC), and ferritin	- Rule out: hemochromatosis, hepatitis C, hepatitis D
Urine copper level	- Rule out: Wilson's Disease
Acetaminophen levels and toxicology levels	- Rule out: Acetaminophen or drug/medication induced liver failure
Abdominal ultrasound	- Rule out: HCC, Budd-Chiari syndrome cirrhosis, fibrosis

*Diagnostic workups, approaches, and differentials are not entirely comprehensive and exhaustive.

Sources: Centers for Disease Control and Prevention. 2021; Colombo M, Sirlin CB. 2022;

Hollier A. 2021; Lok. 2021; Terrault NA, Lok ASF, McMahon BJ, Chang K, Hwang JP, Jonas

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