Initial Evaluation of Persons with Chronic Hepatitis B

Key Aspects of Medical History

In addition to the standard medical history, the initial history of patients with chronic hepatitis B should focus on risk factors for HBV, including family history of HBV or liver disease, history of alcohol use, any prior evaluation for cirrhosis or hepatocellular carcinoma (HCC), prior treatment of HBV, presence of advanced liver disease, history of extrahepatic manifestations of HBV, co-occurring viral infections, and other key noninfectious comorbidities.

Identifying Risk Factors for HBV

A key aspect of the initial evaluation of persons with chronic HBV is to identify risk factors for HBV acquisition. This information helps the clinician to better assess the duration of infection, determine the risk of advanced liver disease, and provide counseling regarding prevention of HBV transmission to others. Globally, the majority of chronic HBV infections are acquired before the age of 5 years, with perinatal transmission the most common mode of infection, especially in countries with high HBV endemicity (Table 1).[6,7] For persons from these endemic regions, it is important to ask about family history of chronic HBV, particularly in mother or siblings, as that may provide a clue to perinatal transmission. In the United States, injection drug use and sex with multiple partners are the most important risk factors for acquiring HBV.[8] Important elements of the initial history include prior or current injection drug use, history of multiple sex partners, prior exposure to blood or bodily fluids (including occupational exposure), and family history of HBV or liver disease.[5] At the initial intake, some individuals may be reluctant to disclose a history of remote injection drug use or multiple sex partners. Care should be taken to establish rapport and a safe environment for ongoing discussion of these activities, whether past or current.

History of Alcohol Use

Due to its deleterious effects on the liver, it is important to inquire about alcohol use among persons with chronic HBV. Less is known about the synergistic effects of alcohol use and chronic HBV when compared to the effects of alcohol use and chronic hepatitis C virus (HCV). Although there is no clear guidance on what quantity of alcohol may be safe in persons with chronic HBV infection, studies suggest heavy alcohol use in persons with HBV can increase the risk of HCC 1.3- to 8.4-fold, in comparison to individuals with chronic HBV who are not heavy drinkers.[9,10,11,12] Accordingly, persons with chronic HBV should be counseled to avoid alcohol and be directed to educational resources, such as those provided by the National Institute on Alcohol Abuse and Alcoholism (NIAAA).[13,14] In clinical practice, it can often be challenging to obtain an accurate history of alcohol consumption. A general approach would be to assess quantity of use over a specified period of time without using qualifiers such as “heavy” or “excessive” in the inquiry. Several well-validated screening tools, as outlined below, are available to help assess for alcohol use disorder.
Prior Evaluation for Cirrhosis

Cirrhosis is a key predictor of liver-related complications such as HCC and is an indication for HCC screening. In addition, treatment of chronic HBV is indicated for all persons with cirrhosis. As such, among persons who have previously been engaged in HBV care, it is important to understand if they have undergone a prior evaluation for cirrhosis and what that evaluation revealed. Although guidelines do not specify the best method to diagnose cirrhosis in persons with chronic HBV, a variety of modalities are currently used, including liver biopsy, hepatic ultrasound, transient elastography, laboratory markers, and clinical examination. Understanding the results and timing of prior fibrosis assessments can inform the need for antiviral therapy and help triage the need for additional fibrosis assessment. A more detailed discussion on evaluating for cirrhosis in persons with chronic HBV can be found in the module When to Initiate HBV Treatment.

Prior Screening for Hepatocellular Carcinoma (HCC)

Given the oncogenic properties of HBV and the elevated risk for developing HCC among people with chronic HBV, it is also important to obtain information on prior screening for hepatocellular carcinoma, typically in the form of an abdominal ultrasound. Multiphase imaging studies, such as computed tomography (CT) and magnetic resonance imaging (MRI), are also used in some circumstances.

Prior or Current Antiviral Therapy for HBV

When evaluating persons with chronic HBV, clinicians should inquire about prior or current antiviral therapy for HBV, including the type of treatment, duration of therapy, response to therapy, level of adherence, treatment-related adverse effects, and reasons for stopping therapy (if discontinued). For persons with HIV and chronic HBV coinfection, this would entail a detailed overview of past antiretroviral therapy because the nucleos(t)ide analogues emtricitabine, lamivudine, tenofovir alafenamide, or tenofovir DF are also active against HBV. This information can help guide recommendations for future treatment and predict the presence of resistance, particularly for lamivudine and adefovir—two drugs that are no longer recommended as first-line therapy due to their low barrier to resistance.

Presence of Advanced Liver Disease

The management of persons with advanced liver disease can be complex. As discussed above, it is important to understand what, if any, prior testing the patient has undergone for cirrhosis, and it is similarly important to assess for signs and symptoms of decompensated cirrhosis including current or past ascites, hepatic encephalopathy, jaundice, scleral icterus, and gastrointestinal bleeding. If advanced liver disease is suspected, the clinician can calculate the Child-Turcotte-Pugh (CTP) stage to help estimate the severity of cirrhosis (see CTP Calculator). Persons with chronic HBV who are classified as CTP stage B or C have decompensated cirrhosis and should be urgently referred to a liver specialist.

Presence of Extrahepatic Manifestations

Hepatitis B can be associated with a variety of extrahepatic manifestations, most of which are immune mediated. The most clinically significant extrahepatic manifestations include polyarteritis nodosa, glomerular disease (commonly membranous nephropathy or membranoproliferative glomerulonephritis), and...
a serum sickness-like reaction that can occur during acute HBV infection.[23,24,25]

**Key Viral Comorbidities**

During the initial evaluation of persons with chronic hepatitis B, it is important to evaluate for other viral infections, such as human immunodeficiency virus (HIV), HCV, hepatitis A virus (HAV), and possibly hepatitis D virus (HDV).

- **HIV**: Identifying persons with HIV and HBV coinfection is of particular importance, as coinfection has been shown to accelerate progressions of liver disease and increase liver associated mortality.[26] In addition, there is considerable overlap in the oral antivirals used to treat HBV and HIV, and therefore understanding the individual’s HIV status is critical to selecting an appropriate antiviral regimen for HBV (Table 2).[20,27]

- **HCV**: Coinfection with HCV can accelerate progression of liver disease in persons with chronic HBV.[28] Evaluation for HCV and HAV is especially important since there is highly effective and well tolerated treatment for HCV and persons undergoing treatment for HCV have risk of HBV reactivation.[29] Screening for HAV is important since there is a highly effective vaccine to prevent HAV infection.

- **Hepatitis D Virus (HDV)**: HDV is a unique satellite virus that requires HBsAg to replicate and can therefore only occur in the presence of chronic HBV infection.[30] Coinfection with HDV can accelerate the progression of liver disease and increase the risk of developing HCC.[13] The American Association for the Study of the Liver (AASLD) guidelines recommend screening for HDV in key populations at highest risk, including those from regions of high HDV endemcity (Figure 3), persons with a history of injection drug use, men who have sex with men (MSM), individuals coinfected with HCV or HIV, persons with multiple sex partners or any history of sexually transmitted diseases, and those with persistently elevated liver enzymes despite low or undetectable HBV DNA levels.[13,31]

**Noninfectious Comorbidities**

When evaluating persons with chronic HBV infection, the clinician should inquire about any secondary causes of liver disease, such as nonalcoholic fatty liver disease (NAFLD), alcoholic hepatitis, alpha-1 antitrypsin deficiency, hemochromatosis, or autoimmune hepatitis.[32,33,34,35,36,37,38] A past or current history of obesity is important to obtain since obesity is strongly associated with the development of NAFLD.[39]
Initial Laboratory Evaluation

The initial laboratory evaluation for patients with HBV aims to assess the stage of HBV, screen for common medical comorbidities, including renal disease, assess for abnormalities attributable to liver injury and fibrosis, and to screen for other co-occurring viral infections. Because chronic infection with HBV cannot be accurately assessed based on a single laboratory assessment, it is also advisable to repeat HBV serologies and obtain an HBV DNA level. Doing so will not only allow the provider to confirm the diagnosis of HBV, but it will also help facilitate and assessment of the immune phase of chronic HBV infection, as discussed in further detail in the module on *When to Initiate HBV Treatment*.

- **General Laboratory Evaluation**: Complete blood count (CBC), including platelets; chemistry panel, including serum creatinine and blood urea nitrogen. The presence of renal impairment may influence the selection or dose of antiviral therapy, as different agents are approved for use in varying stages of chronic kidney disease or may require dose adjustment.
- **Hepatic Function Testing**: Alanine aminotransferase (ALT), aspartate aminotransferase (AST), total and direct bilirubin, alkaline phosphatase, serum albumin, and international normalized ratio (INR).
- **Hepatitis B Serologic and DNA Testing**: HBV surface antibody (anti-HBs), HBV surface antigen (HBsAg), HBV core antibody (anti-HBc), HBV E antigen (HBeAg), HBV E antibody (anti-HBe), and HBV DNA.
- **HBV Genotyping and Viral Resistance Testing**: These tests are not routinely recommended for individuals with chronic HBV, particularly those who are treatment-naïve or not on antiviral therapy.
- **Laboratory Testing to Assess for Co-occurring Infections**: Hepatitis A virus (HAV) IgG antibody, hepatitis C virus (HCV) antibody (ideally with reflexive PCR), and HIV-1/2 antigen-antibody immunoassay. In select cases, as described above, testing for antibodies to the hepatitis D virus may be indicated.
- **Laboratory Screening for HCC**: For individuals with chronic HBV who meet criteria for HCC screening, the AASLD guidelines recommend abdominal ultrasound with or without alpha-fetoprotein every six months.
Evaluation of Fibrosis Stage

For persons previously engaged in clinical care for HBV, it is important to determine whether they have had prior evaluation and staging of liver fibrosis. Methods to assess liver fibrosis include serum-based aspartate aminotransferase-to-platelet ratio index (APRI), FibroTest, liver transient elastography, hepatic ultrasound, and liver biopsy [57, 58]. If a liver biopsy has previously been performed, it is important to document the sample size, fibrosis score, and fibrosis scoring system used in the report. For a detailed discussion on this topic, see the Evaluation and Staging of Liver Fibrosis on the Hepatitis C Online web site.
Immunizations for Persons with Chronic HBV and Cirrhosis

The following summarizes key vaccine recommendations for persons with chronic HBV.

- **Hepatitis A Vaccination**: Individuals with chronic hepatitis B are at increased risk for severe clinical manifestations of acute HAV infection, including fulminant liver failure.[29] As such, all persons with HBV should receive the two-dose hepatitis A vaccine series, which is administered at 0 and 6 months ([Figure 12]).[13, 59, 60] This vaccine has been shown to be highly immunogenic in adults, with an estimated 94 to 100% of adults 18 years of age or older achieving protective antibody levels 1 month after the first dose of vaccine, and all persons achieving protective antibody levels after the second dose.[61] Given the efficacy of HAV vaccine, post-vaccination serologic testing is not routinely recommended for persons with chronic HBV, even for individuals with chronic liver disease.[61]
- **Pneumococcal Vaccination**: A one-time dose of the 23-valent pneumococcal polysaccharide vaccine (PPSV23) is recommended for all persons ages 19 to 64 years who have chronic liver disease and cirrhosis.[59, 62] The PPSV23 is also recommended for all adults 65 years of age or older regardless of underlying medical conditions.[63, 64] Individuals with chronic HBV, who received the PPSV23 between the ages of 19 and 64 should receive a second dose of PPSV23 once they reach 65 years of age, ensuring there is a minimum of 5 years between the first and second dose of PPSV23.[59, 63] For persons 65 years of age or older, including individuals with liver, the Advisory Committee on Immunization Practices (ACIP) recommends offering the 13-valent pneumococcal conjugate vaccine (PCV13) using a shared decision process.[64] If the PCV13 vaccine is administered, one dose of the PPSV23 should be given at least one year following administration of PCV13, and at least 5 years after any prior dose of PPSV23.[63, 64]
- **Other Routine Vaccinations**: Entry into care for the management of chronic HBV, also presents an opportunity to ensure that the patient is up to date on other routine adult vaccinations, including yearly influenza vaccination and a one-time tetanus diphtheria acellular pertussis (Tdap) vaccine, followed by a tetanus diphtheria (Td) or Tdap booster every 10 years.[59, 64]
Summary Points

- After confirming chronic infection with hepatitis B, the medical provider should perform a detailed history, aimed at identifying risk factors for acquiring HBV, evaluating for significant medical comorbidities, and understanding any prior evaluation and treatment for HBV.
- A complete physical examination should be performed, focusing on stigmata of chronic liver disease, including ascites, caput medusae, gynecomastia, jaundice, palmar erythema, spider angioma, and Terry's nails.
- The initial laboratory evaluation should include a complete blood count, chemistry panel, creatinine, hepatic function testing, hepatitis B serologic and DNA testing, and testing for HIV and HCV.
- Persons with chronic HBV should receive routinely recommended adult immunizations, as well as HAV and pneumococcal vaccines.
- Clinicians should be familiar with the most important nonviral causes of hepatic inflammation, but an exhaustive screening laboratory work-up for other causes of liver disease is usually not required because of the high cost and low yield.
Screening for Other Causes of Liver Disease

Overview of Screening for Other Causes of Liver Disease

In the course of a complete workup of an individual diagnosed with chronic HBV, the clinician should make an effort to determine whether additional causes of liver disease are present, especially in cases with significant abnormalities on liver function testing. Other causes of liver disease may coexist with HBV infection, including both hereditary and acquired conditions. Identifying additional causes of liver disease in persons with chronic HBV is important since the combination of diseases may result in accelerated fibrosis progression or ongoing fibrosis progression even after treatment of HBV. An exhaustive screening laboratory work-up for all these conditions would be expensive and low-yield for most patients; however, they may be relevant in special situations, such as may occur if ALT and AST do not fully normalize with antiviral therapy. Therefore, the clinician should be familiar with some of the more important nonviral causes of hepatic inflammation.

Alcoholic Liver Disease

Chronic excessive alcohol consumption is the most common cause of liver disease in the Western world and determining alcohol intake is important in persons with chronic HBV. On a practical basis, differentiating liver injury caused by alcohol use from that due to chronic HBV infection can be difficult, but the finding of an AST/ALT ratio of greater than 2.0 suggests alcohol-related injury, although this pattern may also be seen in advanced cirrhosis of any cause. In addition, screening for alcohol intake as part of the medical history, as outlined above, may provide useful information on whether alcohol is a likely contributor to liver disease. Excessive alcohol use can cause acute alcoholic hepatitis, fatty liver (steatosis), and eventually cirrhosis. In addition, alcohol use can accelerate HBV-associated fibrosis and increase the risk of developing hepatocellular carcinoma. Given that no consensus exists regarding a safe level of alcohol consumption for persons with chronic HBV, most experts recommend complete abstinence from alcohol.

Nonalcoholic Fatty Liver Disease (NAFLD)

Globally, an epidemic in chronic liver disease caused by nonalcoholic fatty liver disease (NAFLD) has emerged due to changes in lifestyle and increasing prevalence of obesity. The prevalence of obesity is high and the NAFLD prevalence in adults is estimated at approximately 24%. The AASLD defines NAFLD as (1) evidence of hepatic steatosis documented either by imaging or histologic findings on liver biopsy, and (2) lack of any secondary cause of hepatic fat accumulation, such as significant alcohol consumption, long-term use of a steatogenic medication, or monogenic hereditary disorders. Common conditions that have an established association with NAFLD include obesity, dyslipidemia, type 2 diabetes mellitus, metabolic syndrome, and polycystic ovary syndrome. The AASLD classifies NAFLD into two subcategories—nonalcoholic fatty liver (NAFL) and nonalcoholic steatohepatitis (NASH) based on histologic findings: (1) NAFL is defined as 5% or more hepatic steatosis without evidence of hepatocellular injury, and (2) NASH is defined as 5% or more hepatic steatosis with evidence of hepatocellular inflammation and injury. The development of NASH can result in progression to cirrhosis, liver failure, and hepatocellular cancer. The diagnosis of NAFLD requires documented absence of ongoing or recent substantial alcohol ingestion. Two radiographic tests—magnetic resonance imaging by spectroscopy or magnetic resonance imaging with proton hepatic assessments—appear promising as noninvasive methods to estimate the degree of hepatic steatosis, but is not routinely available in clinical settings. In addition, transient elastography controlled attenuation parameter (CAP) is a recently developed noninvasive technique for assessing steatosis and fibrosis. Liver biopsy remains the gold standard for determining the presence and severity of NAFLD.

Alpha-1 Antitrypsin Deficiency

This rare condition is characterized by deficiency of the alpha-1 antitrypsin enzyme, resulting in overly active
proteases in the body and concomitant lung and liver destruction (emphysema and cirrhosis).\[75,76\] It has a genetic basis with complex inheritance and variable penetrance, but is most prevalent in Caucasians of Scandinavian descent. In the United States and Western Europe, the prevalence of alpha-1 antitrypsin deficiency is estimated between 1 in 2,000 and 1 in 5,000 population.\[76\] A serum alpha-1 antitrypsin level below 11 μmol/L (80 mg/dL) should prompt specific genetic testing for the most common alpha-1 antitrypsin deficiency alleles.\[38\]

**Hemochromatosis**

Hemochromatosis is defined as an excessive accumulation of iron in the liver; hemochromatosis may result from excessive blood transfusions, erythrocyte disorders, or as a hereditary condition that involves a defect in iron metabolism.\[65\] With hereditary hemochromatosis, the total amount of body iron accumulates over time, which is associated with increased hepatic iron that can eventually cause tissue injury and complications that can include cirrhosis, arthropathy, or diabetes (and other endocrinologic disorders).\[77\] Type 1 hereditary hemochromatosis is the most common and best-studied hereditary hemochromatosis variant and is caused by mutations in the human factors engineering (HFE) gene.\[78\] Initial diagnostic laboratory studies that can suggest but not necessarily confirm a diagnosis of hemochromatosis include elevated serum iron, elevated serum ferritin concentration, and elevated transferrin saturation.\[77,78\] Use of these markers can be challenging since they often are elevated in patients with chronic liver disease or hepatic injury.\[79\] A definitive diagnosis of hemochromatosis requires either liver biopsy with determination of iron index, or a specific battery of genetic testing. For screening purposes, most expert guidelines, including those from the American Association for the Study of Liver Diseases (AASLD), recommend using the following cutoffs when screening for iron overload: transferrin saturation greater than 45% and a serum ferritin greater than 200 ng/mL (for men) and greater than 150 ng/mL (for women).\[32,80,81\]

**Autoimmune Hepatitis**

This relatively rare condition results from both genetic and host factors. The disorder is believed to result from the host losing tolerance to its own liver antigens, which leads to an immune response that includes activated immune cells, autoantibodies, interferons, and proinflammatory cytokines, which together cause hepatic inflammation.\[82,83\] Most experts classify autoimmune hepatitis as type 1 or type 2.\[35,83\] Autoimmune hepatitis-1 is more common than autoimmune hepatitis-2 and can affect children or adults, although it predominantly occurs in adults. Approximately 20% of persons with autoimmune hepatitis-1 will have an extrahepatic autoimmune disorder, such as autoimmune thyroid disease, arthritis, or inflammatory bowel disease.\[83\] Autoimmune hepatitis-2 most often affects children and extrahepatic autoimmune complications are common, including autoimmune thyroid disease, insulin-dependent diabetes mellitus, Addison's disease, and arthritis.\[83\] Clinical and laboratory characteristics with autoimmune hepatitis include itching, joint pain, hypergammaglobulinemia, and chronic elevations in aminotransferase levels. The diagnosis typically depends on positive autoantibody studies combined with compatible clinical and histologic features.\[84,85\] Autoantibodies commonly found in persons with autoimmune hepatitis include smooth muscle antibodies (SMA), antinuclear antibodies (ANA), antimitochondrial antibodies (AMA), liver-kidney microsomal antibodies (LKM), and soluble liver/liver-pancreas antibodies (SLA/LP).\[86\] In 2008, the International Autoimmune Hepatitis Group published revised simplified criteria for the diagnosis of autoimmune hepatitis.\[86\]
Counseling HBsAg-Positive Persons Following Diagnosis

Following the diagnosis of HBV, medical providers should counsel HBsAg-positive individuals on the natural history and key clinical aspects of HBV, expectations for follow-up care, the risk of HBV transmission to others, and ways to promote liver health, as outlined below.\[13,87\]

- Natural history and key clinical aspects of HBV Infection
  - Educate and counsel individuals on the long-term implications of chronic HBV infection, including the potential for development of cirrhosis and HCC.
  - Advise persons with HBV to inform all medical providers of their HBsAg-positive status. This is of particular importance if the person will require chemotherapy or other immunosuppressive therapies for autoimmune or other immunologic diseases.
  - Advise pregnant women and women of childbearing age that their newborns should receive both the hepatitis B vaccine and hepatitis B immune globulin (HBIG) at the time of birth.

- Expectations for follow-up care
  - Counsel that HBV is a chronic illness that requires regular follow-up and monitoring, at least every 6 months.

- Risk of HBV transmission to others
  - Persons with HBV should verify that their household, sex, and needle-sharing partners have been screened and vaccinated for HBV.
  - Advise persons with HBV to use barrier protection (e.g. condoms) during sexual intercourse to prevent transmission to susceptible partners.
  - Advise persons with HBV to cover their cuts and clean up blood and bodily fluid spills with diluted bleach (1:10).
  - Individuals with HBV should refrain from sharing items such as toothbrushes, razors, nail clippers, earrings, personal injection equipment, or other articles that may be contaminated with blood and pose a transmission risk to susceptible individuals.
  - Advise persons with HBV to not donate blood, plasma, tissue or semen.
  - Counsel that HBV is not spread through kissing, hugging, coughing, sharing food or water, breastfeeding, or casual contact.

- General recommendations to promote liver health
  - Counsel individuals with HBV to avoid alcohol.
  - Advise persons with HBV to maintain a healthy body weight and control their blood sugars and cholesterol to prevent the development of nonalcoholic steatohepatitis.
  - Recommend persons with HBV receive hepatitis A vaccine if they are not immune to HAV.
Citations


27. Panel on Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the prevention
and treatment of opportunistic infections in adults and adolescents with HIV: recommendations from
the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine
Association of the Infectious Diseases Society of America. Hepatitis B virus infection. Last Updated:
November 13, 2018.
[HIV.gov] -

[PubMed Abstract] -

29. Win NN, Kanda T, Ogawa M, et al. Superinfection of hepatitis A virus in hepatocytes infected with
[PubMed Abstract] -

30. Shah PA, Choudhry S, Reyes KJC, Lau DTY. An update on the management of chronic hepatitis D.
[PubMed Abstract] -

[PubMed Abstract] -

32. Bacon BR, Adams PC, Kowdley KV, Powell LW, Tavill AS. Diagnosis and management of
hemochromatosis: 2011 practice guideline by the American Association for the Study of Liver
[PubMed Abstract] -

33. Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of non-alcoholic fatty liver
disease: practice guideline by the American Gastroenterological Association, American Association for
[PubMed Abstract] -

34. Czaia AJ. Review article: next-generation transformative advances in the pathogenesis and
[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

38. Nelson DR, Teckman J, Di Bisceglie AM, Brenner DA. Diagnosis and management of patients with
[PubMed Abstract] -

2017;377:2063-72.


59. Advisory Committee on Immunization Practices (ACIP). Recommended Adult Immunization Schedule by Medical Condition and Other Indications, United States, 2020. [ACIP] -


64. Advisory Committee on Immunization Practices (ACIP). Recommended Immunization Schedule for Ages 19 Years or Older, United States, 2020. [ACIP] -


References

Figures

Figure 1 CAGE Questionnaire for Detecting Alcoholism

The CAGE Questionnaire is a simple 4-question screening tool. The acronym CAGE is derived from the question evaluation of Cutting down, Annoyance by criticism, Guilty feeling, and Eye-openers.

Figure 2 AUDIT-C Questionnaire for Detecting Alcoholism

The AUDIT-C is a 3-item screening questionnaire to help identify individuals who have alcohol use disorders (alcohol abuse or dependence). The AUDIT-C is a truncated version of the 10-question AUDIT screen.

Figure 3 Global Prevalence of anti-HDV Among HBsAg-Positive People

Figure 4 Body Mass Index (BMI) Formula

Body Mass Index (BMI) represents a number calculated based on a person's weight and height and it provides a good rough estimate of a person's body fat. The BMI may overestimate body fat in athletes and underestimate body fat in older persons, or individuals who have lost significant muscle.

Source: National Heart Lung and Blood Institute
Figure 5 Ascites

The presence of bulging flanks suggests a possible diagnosis of ascites; this should be confirmed with a shifting dullness test.

Illustration by Jared Travnicek, Cognition Studio
Figure 6 Caput Medusa

Caput medusa results from portal hypertension and is manifested as distended abdominal veins radiating around the umbilicus.

Illustration by Jared Travnicek, Cognition Studio
**Figure 7 Gynecomastia**

In men with cirrhosis, benign enlargement of the breasts may occur and manifest as gynecomastia.

Illustration by Jared Travnicek, Cognition Studio
**Figure 8 Jaundice**

This illustration shows yellow discoloration of the sclera that results from excess deposition of biliary pigments.

Illustration by Jared Travnicek, Cognition Studio
Figure 9 Palmar Erythema

With palmar erythema, the redness is most prominent in the thenar and hypothenar eminence, with sparing of the central region of the palm.

Illustration by Jared Travnicek, Cognition Studio
Figure 10 Spider Angiomata

Spider angiomata are enlarged cutaneous blood vessels that resemble the appearance of spider. Compression of the central aspect of the lesions causes the entire lesion to blanch; with release of compression the blood quickly refills and the red color reappears.

Illustration by Jared Travnicek, Cognition Studio
Figure 11 Terry’s Nails

Note the white-silver discoloration of the proximal nail bed and the pink band on the distal portion of the nail bed.

Illustration by Jared Travnicek, Cognition Studio
### Recommended Hepatitis A Virus Vaccine Dosages and Schedules for Adults

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Dosage</th>
<th>Dosing and Route</th>
</tr>
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<tbody>
<tr>
<td><strong>Havrix</strong></td>
<td>1440 EL.U.</td>
<td>2-Dose Schedule: 1 mL given IM at 0 and 6-12 months</td>
</tr>
<tr>
<td><strong>Vaqta</strong></td>
<td>50 U</td>
<td>2-Dose Schedule: 1 mL given IM at 0 and 6-18 months</td>
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### Table 1.

**Global Prevalence of Chronic HBV Infection, by Country**

<table>
<thead>
<tr>
<th>Prevalence Category</th>
<th>Country</th>
</tr>
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<tbody>
<tr>
<td><strong>High</strong> (≥8%)</td>
<td>Angola, Benin, Burkina Faso, Burundi, Cameroon, Central African Republic, Congo, Côte d’Ivoire, Djibouti, Equatorial Guinea, Gabon, Gambia, Ghana, Guinea, Haiti, Kiribati, Kyrgyzstan, Laos, Liberia, Malawi, Mali, Mauritania, Mongolia, Mozambique, Namibia, Nauru, Niger, Nigeria, Niue, Papua New Guinea, Senegal, Sierra Leone, Solomon Islands, Somalia, South Sudan, Sudan, Swaziland, Togo, Tonga, Uganda, Vanuatu, Vietnam, Yemen, and Zimbabwe.</td>
</tr>
<tr>
<td><strong>Intermediate</strong> (5.0-7.9%)</td>
<td>Albania, Bhutan, Cape Verde, China, Democratic Republic of the Congo, Ethiopia, Kazakhstan, Kenya, Marshall Islands, Moldova, Oman, Romania, Rwanda, Samoa, South Africa, Tajikistan, Tanzania, Thailand, Tunisia, Tuvalu, Uzbekistan, and Zambia.</td>
</tr>
<tr>
<td><strong>Low Intermediate</strong> (2.0-4.9%)</td>
<td>Algeria, Azerbaijan, Bangladesh, Belarus, Belize, Brunei Darussalam, Bulgaria, Cambodia, Colombia, Cyprus, Dominican Republic, Ecuador, Eritrea, Federated States of Micronesia, Fiji, Georgia, Italy, Jamaica, Kosovo, Libya, Madagascar, Myanmar, New Zealand, Pakistan, Palau, Philippines, Peru, Russia, Saudi Arabia, Singapore, South Korea, Sri Lanka, Suriname, Syria, Tahiti, and Turkey.</td>
</tr>
<tr>
<td><strong>Low</strong> (≤1.9%)</td>
<td>Afghanistan, Argentina, Australia, Austria, Bahrain, Barbados, Belgium, Bolivia,</td>
</tr>
<tr>
<td>Prevalence Category</td>
<td>Country</td>
</tr>
<tr>
<td>--------------------</td>
<td>---------</td>
</tr>
<tr>
<td>Prevalence Category</td>
<td>Bosnia and Herzegovina, Brazil, Canada, Chile, Costa Rica, Croatia, Cuba, Czech Republic, Denmark, Egypt, France, Germany, Greece, Guatemala, Hungary, Iceland, India, Indonesia, Iran, Iraq, Ireland, Israel, Japan, Jordan, Kuwait, Lebanon, Lithuania, Malaysia, Mexico, Morocco, Nepal, Netherlands, Nicaragua, Norway, Palestine, Panama, Poland, Portugal, Qatar, Serbia, Seychelles, Slovakia, Slovenia, Spain, Sweden, Switzerland, Ukraine, United Kingdom, United Arab Emirates, United States of America, and Venezuela.</td>
</tr>
<tr>
<td>No data</td>
<td>Andorra, Antigua and Barbuda, Armenia, The Bahamas, Botswana, Chad, Comoros, Cook Islands, Dominica, El Salvador, Finland, Grenada, Guinea-Bissau, Guyana, Honduras, Latvia, Lesotho, Lithuania, Luxembourg, Macedonia, Maldives, Malta, Mauritius, Monaco, Montenegro, North Korea, Paraguay, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, San Marino, Sao Tome and Principe, Timor-Leste, Trinidad and Tobago, Turkmenistan, and Uruguay.</td>
</tr>
</tbody>
</table>

**NOTE:** This table is based on data from the Centers for Disease Control and Prevention (CDC)

Source:

Table 2.

**Key Characteristics of Oral Antiviral Agents Used to Treat HBV and/or HIV***

<table>
<thead>
<tr>
<th>Medication</th>
<th>Hepatitis B Virus</th>
<th>Potency Against HBV</th>
<th>Barrier to HBV Resistance</th>
<th>Potency Against HIV</th>
<th>Barrier to HIV Resistance</th>
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<tr>
<td>Adefovir</td>
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<td>Low</td>
<td>Moderate</td>
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<tr>
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<td>High</td>
<td>High</td>
<td>High</td>
<td>High</td>
</tr>
</tbody>
</table>

*Telbivudine is not included as it is no longer manufactured in the United States*