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Hepatitis B Virus Screening and Vaccination

Uwaezu J. Umeh
University of San Francisco, joyumeh@gmail.com

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Uwaezu Joy Umeh

University of San Francisco

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Abstract

Hepatitis B is a virus that mostly affects the liver, it could be asymptomatic and if left untreated or undetected, could lead to liver cancer, cirrhosis or even death. When Hepatitis B virus enters the body, it could be detected as early as 30 days post exposure and if it persists, may develop into a chronic condition. Chronic hepatitis B is the persistence of hepatitis B surface antigen for six months or more. It is a global health problem in which an estimated 2 billion people worldwide are infected and with about 2.2 million people infected in the United States. This manuscript discusses the importance of screening for chronic hepatitis B virus in eligible individuals so as to identify infected and/or susceptible individuals. It also discusses hepatitis B vaccination as the best way to prevent the virus, the geographic distribution of chronic hepatitis B virus, and the eligibility criteria for screening following the recommendations of the Centers of Disease Control and Prevention (CDC) and United States Preventive Services Task Force USPSTF).

Keywords: *hepatitis, chronic hepatitis b, hepatitis b screening, hepatitis b vaccination,* and *hepatitis b prevention.*

Introduction

Hepatitis B virus is a life-threatening virus that affects the liver, and it is known to be the oldest virus ever found in humans [1]. Hepatitis B is a blood borne pathogen transmitted via blood contact, body fluid or sexual contact. It is spread when an uninfected person comes in contact with the body fluids (such as blood, saliva, vaginal and seminal fluids) of someone who is infected. This could happen through sharing of needles, sexual contact, or from mother to baby at birth [2]. Hepatitis B is found worldwide but regions differ in endemicity, it is worthwhile to note that most of the world's population lives in areas with high hepatitis B endemicity [3]. Hepatitis B virus can exist in both acute and chronic phases and chronic hepatitis B can lead to cirrhosis or liver cancer, hence the Centers for Disease Control and Prevention (CDC) has set forth recommendations to screen eligible patients [4, 2].

The CDC reports that about 2.2 million people in the United States are infected with chronic hepatitis B and in 2016, hepatitis B was listed in 1715 death certificates as a cause of death [5, 6]. Chronic hepatitis B is often asymptomatic and when symptoms eventually present, they could signal a late stage of liver cirrhosis, liver cancer or even death [5]. Hence, the World Health Organization (WHO) and the CDC have set forth recommendations to screen for chronic hepatitis B virus [7]. Individuals with chronic hepatitis B can still transmit the virus even when they do not have symptoms themselves [7]. Oftentimes, symptoms of chronic hepatitis B present as a vague feeling of illness which can include fatigue, poor appetite, and a discomfort in the upper abdomen. The first specific symptoms of chronic liver disease can include an enlarged spleen, redness of the palm and ascites [8]. Chronic hepatitis B virus which can lead to hepatocellular carcinoma is a rising cause of mortality and significant health burden [9]. About 15% to 40% of individuals diagnosed with chronic hepatitis B virus progress to cirrhosis, liver

failure and liver cancer if untreated [30]. Early screening will identify susceptible or infected individuals, and as a result, the former can be vaccinated while the latter can be treated in order to decrease or slow down the progression of the disease [7].

Chronic hepatitis B virus infection, defined as hepatitis B surface antigen (HBsAg) positivity for at least 6 months, is a major cause of morbidity and mortality worldwide [10]. Wilkins, Sams, and Carpenter (2019) further defined chronic hepatitis B as the persistence of hepatitis B surface antigen for more than six months. They state that although individuals who have chronic hepatitis B are at risk of hepatocellular carcinoma and cirrhosis, morbidity and mortality are reduced with adequate and timely treatment [11].

Geographic Distribution of Chronic Hepatitis B Virus

Hepatitis B virus is found worldwide but differs in endemicity (See appendix A and B). According to the World Health Organization, most of the world's population lives in countries where the prevalence of hepatitis B surface antigen (HBsAg) in the general population is high (≥8%) or intermediate (2–7%). The prevalence of hepatitis B virus remains low in certain areas of North America, Northern and Western Europe, the southern Cone of South America, Australia and New Zealand [12]. The CDC also supports the WHO's data, which found that about 45% of the world's population lives in areas of high hepatitis B endemicity where the prevalence is ≥8 and a lifetime risk of acquiring it is >60%. Another 43% live in areas of intermediate endemicity with a prevalence of 2-7% where the lifetime risk of acquiring it is 20-60%, and only about 12% of the world's population lives in areas of low endemicity where the prevalence is <2% with a lifetime risk of <20% [10].

CDC's Recommendations for Screening

The CDC has the following recommendations of persons or groups eligible for screening for chronic hepatitis B virus (see appendix c). This includes persons born in geographic regions with HBsAg prevalence of ≥2%, US born persons not vaccinated as infants whose parents were born in geographic regions with HBsAg prevalence of ≥8%, injection-drug users, men who have sex with men, persons with elevated ALT/AST of unknown etiology, persons with selected medical conditions who require immunosuppressive therapy, pregnant women, infants born to HBsAg-positive mothers, household contacts and sex partners of HBV-infected persons, persons who are the source of blood or body fluids resulting in exposures that might warrant post exposure prophylaxis (e.g., needle stick injury to a health care worker) and persons infected with HIV [13]. The United States Preventive Services and Task Force (USPSTF) also recommends chronic hepatitis B screening in high risk individuals. They defined high risk as those from countries with a high prevalence of HBV infection, HIV-positive persons, intravenous drug users, men who have sex with men, and household contacts of persons with HBV infection [14]. The recommendation, according to USPSTF, is to screen for chronic hepatitis B using the HBsAg [15].

Prevention and Vaccination

The CDC recommends screening for chronic hepatitis B and the best way to prevent it is by getting vaccinated [16]. The American Association for the Study of Liver Diseases were of the view that Hepatitis B screening should be done using both the HBsAg and Anti-Hbs, individuals who are Anti-Hbs negative should be vaccinated [17]. The American College of Physicians and CDC recommends hepatitis B screening for adults at high risk, they also

recommend HBV vaccination for people who request it and for unvaccinated adults including pregnant women [18].

A study published in the New England Journal of Medicine noted that chronic hepatitis has become a global public health challenge and they recommend that testing and treatment of chronic HBV remains the primary means of reducing HBV related death by 65% [19]. The CDC reported that hepatitis B kills about 2,000 people in the U.S. yearly, and the hepatitis B vaccine can prevent hepatitis B and its related complications such as liver cancer and cirrhosis [20]. Hepatitis B could be preventable with the administration of the hepatitis B vaccination. The WHO has identified hepatitis as a global problem and has called for its elimination by 2030, they defined elimination as a 90% reduction in incidence rate and a 65% reduction in number of deaths [19]. Hepatitis B vaccine is made from parts of the virus and it is important to note that it cannot cause hepatitis B infection. It is usually given as 2, 3, or 4 series over one to six months period [20]. Hence, the vaccine is recommended for unvaccinated adults at risk for hepatitis B virus, this includes but is not limited to people whose sex partners have hepatitis B, men who have sex with men, healthcare and public safety workers at risk for exposure to body fluids, and people with chronic liver disease, HIV, kidney disease and diabetes [20].

Pre-exposure and post-exposure prophylaxis

Preventing hepatitis B virus prior to exposure by immunization remains the best way to prevent HBV infection, hence vaccination of newborns is recommended in most countries [21]. Pre-exposure vaccination should be offered to individuals who are not immune, healthcare workers, men who have sex with men, HIV positive patients and hepatitis C infected individuals [21]. Although prevention is more effective than therapy, post-exposure prophylaxis with hepatitis B vaccine and/or hepatitis B immune globulin (HBIG) can reduce transmission of HBV

by 70-90% after an exposure when administered within 12-24 hours of an exposure [22,23]. Post-exposure prophylaxis is indicated for individuals without previously documented HBV immunity who are exposed to blood/body fluids from a HBsAg positive or unknown HBV status source and should not be given to individuals with a known history of recovery from HBV infection [23].

Vaccine Formulations

Hepatitis B immunization can either be passive or active [22], passive immunization provides temporary immunity using HBIG while active immunization provides long-term immunity [22]. Passive immunization is not routinely recommended for healthy adults because it is typically used for immunocompromised patients [24]. There are different classes of hepatitis B vaccines: single antigen vaccines (yeast derived, mammalian cell derived, and plasma derived), and combination vaccines [25]. Plasma derived vaccines were the first vaccines but have been replaced over the years by yeast and mammalian cells using recombinant DNA technology [26]. Recombinant hepatitis B vaccines-conventional (Recombivax HB and Engerix B) are typically given in three doses over a six-month period [25,26]; and the recombinant hepatitis B vaccine (CpG-adjuvanted sold under the name Heplisav-B) is used in adults ≥18 years [27]. Hepatitis B vaccine can also be combined with another vaccine such as hepatitis A vaccine, (Twinrix-combined HepB-HepA vaccine), this is ideal and beneficial because it increases compliance and reduces the number of injections [25]. Hepatitis B vaccine is generally safe and effective in protecting against HBV, protective antibody levels achieved in ~95% of those vaccinated [26]. A booster dose is recommended if antibody levels falls <10 milli international units/mL for individuals who are immunocompromised or on dialysis [25].

Contraindications, Precautions and Adverse Events

According to Hibberd (2019), administering a live vaccination to an individual who is immunocompromised is contraindicated. Vaccination should be avoided only if a true contraindication exists such as previous anaphylactic reaction to a specific vaccine, history of anaphylaxis to eggs and/or neomycin. In the event of an adverse reaction, it should be reported to the United States Department of Health and Human Services [24].

Summary

Chronic hepatitis B virus has become a major global threat, one that leads to liver cirrhosis and hepatocellular carcinoma and claims about 1 million lives worldwide annually [28]. It is imperative to note that the disease burden of chronic hepatitis B is high in the Asian Pacific region, hence the United Nations Sustainable Development Goals for 2030 include combating hepatitis [29]. About 15% to 40% of people with chronic hepatitis B progress to cirrhosis if not treated [30]. As part of the discussion in this manuscript, the recommendation therefore, is to screen for chronic hepatitis B virus using the HbsAg blood test, in order to identify individuals who are infected and treat them to prevent/reduce the progression of the disease. And, it is also critically important to screen using the Anti-Hbs in order to identify susceptible individuals and vaccinate them to further prevent exposure to the virus. The USPSTF has enough evidence that hepatitis B vaccination is effective in decreasing the chances of acquiring the virus [14]. Hence, the need for healthcare providers to screen eligible patients, vaccinate susceptible individuals and treat those with the virus in order to slow down the progression of the disease.

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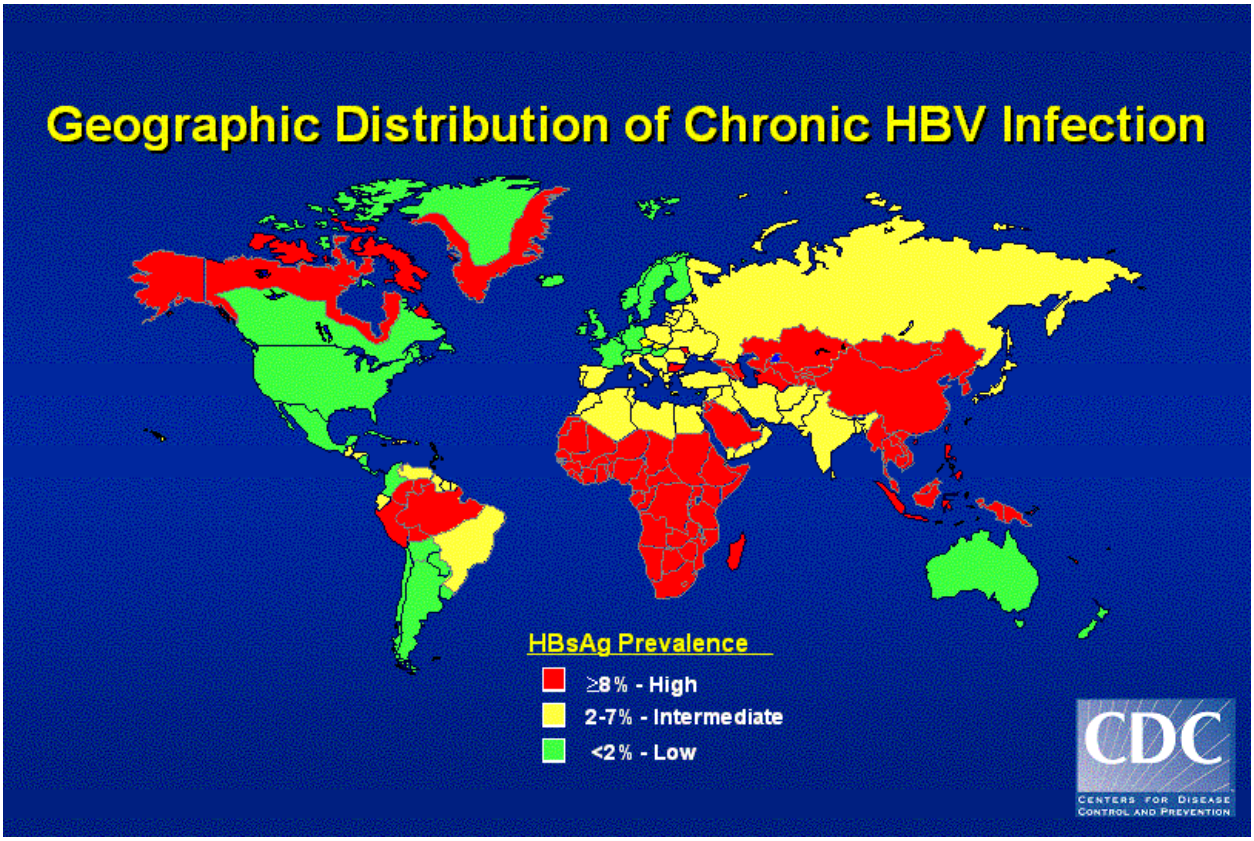
Appendix A: Geographic Distribution of Chronic HBV Infection



Appendix B: Geographic Regions with a Prevalence of Hepatitis B Surface Antigen ≥2% (USPSTF 2014)

Region	**Countries**
Africa	All
Asia	All
Australia and South Pacific	All except Australia and New Zealand
Middle East	All except Cyprus and Israel
Eastern Europe	Malta, Spain, and indigenous populations in Greenland
North America	Alaska natives and indigenous populations in northern Canada
Mexico and Central America	Guatemala and Honduras
South America	Ecuador, Guyana, Suriname, Venezuela, and Amazonian areas of Bolivia, Brazil, Colombia, and Peru
Caribbean	Antigua and Barbuda, Dominica, Grenada, Haiti, Jamaica, St. Kitts and Nevis, St. Lucia, and Turks and Caicos Islands

Appendix C: CDC's Recommendation for Routine Testing and Follow-up for Chronic Hepatitis B Virus Infection (CDC, 2008)

Population	**Testing**	**Vaccination/Follw-up**
Persons born in regions of high and intermediate HBV endemicity (HBsAg prevalence ≥2%)	Test for HBsAg, regardless of vaccination status in their country of origin, including immigrants, refugees, asylum seekers and internationally adopted children	If HBsAg-positive, refer for medical management. If negative, assess for on-going risk for hepatitis B and vaccinate if indicated
US born persons not vaccinated as infants whose parents were born in regions with high HBV endemicity (≥8%)	Test for HBsAg regardless of maternal HBsAg status if not vaccinated as infants in the United States	If HBsAg-positive, refer for medical management. If negative, assess for on-going risk for hepatitis B and vaccinate if indicated
Injection-drug users	Test for HBsAg, as well as anti-HBc or anti-HBs to identify susceptible persons	1st vaccine dose should be given same visit as testing. Susceptible persons should complete a 3-dose hepatitis B vaccine series
Men who have sex with men	Test for HBsAg, as well as anti-HBc or anti-HBs to identify susceptible persons	1st vaccine dose should be given same visit as testing. Susceptible persons should complete a 3-dose hepatitis B vaccine series
Persons needing immunosuppressive therapy, including chemotherapy, immunosuppression related to organ transplantation, and immunosuppression for rheumatologic or gastroenterologic disorders	Test for all markers of HBV infection (HBsAg, anti-HBc, and anti-HBs)	Treat persons who are HBsAg-positive. Monitor closely persons who are anti-HBc positive for signs of liver disease
Persons with elevated ALT/AST of unknown etiology	Test for HBsAg along with other appropriate medical evaluation	Follow up as indicated
Donors of blood, plasma, organs, tissues, or semen	Test for HBsAg, anti-HBc, and HBV-DNA as required	

Hemodialysis patients	Test for all markers of HBV infection (HBsAg, anti-HBc, and anti-HBs)	Vaccinate against hepatitis B and revaccinate when serum anti-HBs titer falls below 10mIU/m
All pregnant women	Test for HBsAg during each pregnancy, preferably in the 1st trimester. Test at the time of admission for delivery if prenatal HBsAg test result is not available of if mother was at risk for infection during pregnancy	If HBsAg positive, refer for medical management. To prevent perinatal transmission, infants of HBsAg-positive mothers and unknown HBsAg status mothers should receive vaccination and post-exposure immunoprophylaxis in accordance with recommendations and within 12 hours of delivery
Infants born to HBsAg positive mothers	Test for HBsAg and anti-HBs 1-2 months after completion of at least 3 doses of a licensed hepatitis B vaccine series (ie., at age 9-18 months, generally at the next well-child visit to assess effectiveness of post-exposure immunoprophylaxis). Testing should not be performed before age 9 months or within 1 month of the most recent vaccine dose	Vaccination in accordance with recommendations
Household, needle-sharing, or sex contacts of persons known to be HBsAg positive	Test for HBsAg, as well as anti-HBc or anti-HBs to identify susceptible persons	1st vaccine dose should be given same visit as testing. Susceptible persons should complete a 3-dose hepatitis B vaccine series
Persons who are the sources of blood or body fluids resulting in an exposure (e.g., needlestick, sexual assault) that might require post-exposure prophylaxis	Test source for HBsAg	Vaccinate healthcare and public safety workers with reasonably anticipated occupational exposures to blood or infectious body fluids. Provide post-exposure prophylaxis to exposed person if needed

HIV-positive persons	Test for HBsAg, as well as anti-HBc or anti-HBs to identify susceptible persons	Vaccinate susceptible persons against hepatitis B