Hepatitis B virus (HBV) infection is a global health burden. The chronicity of this infection leads to complications such as cirrhosis and hepatocellular carcinoma, making it a leading cause of morbidity and mortality worldwide. Chronic infection commonly develops among those who acquire infection during childhood, hence the importance of effective implementation of HBV vaccination policies designed to eradicate chronic HBV. This article provides updated estimates of worldwide HBV disease prevalence and discusses how implementation of vaccination policies has affected HBV epidemiology.

Hepatitis B virus (HBV) infection is the most common chronic viral infection worldwide and remains a significant global health problem. Chronic HBV infection can progress to cirrhosis, liver failure, and hepatocellular carcinoma. Outcome of chronic HBV infections depends on the host, virus, and environmental factors. Although effective prophylactic vaccines and antiviral therapies exist, curative treatment is not yet available. Intense research into a cure for HBV is ongoing and proposed definitions of cure and endpoints for clinical trials evaluating “curative” therapy are discussed.

The prevalence of chronic hepatitis B (CHB) differs globally. CHB is responsible for 30% of all deaths from cirrhosis and 40% from hepatocellular carcinoma. The WHO developed guidelines in 2015 on prevention, care, and treatment of chronic HBV infection targeted to program managers in all health care settings, particularly in low- and middle-income countries. Several of the recommendations differ from those of the major Liver Societies, including the American Association for the Study of Liver Diseases (AASLD). This review highlights key differences between the AASLD and WHO guidelines and discusses the impact on management of CHB.
The Effects of Hepatic Steatosis on the Natural History of HBV Infection

Idrees Suliman, Noha Abdelgelil, Farah Kassamali, and Tarek I. Hassanein

Fatty liver prevalence is increasing and becoming a global health burden. Chronic hepatitis B infection (CHB) is one of the most common chronic viral infections. Steatosis in CHB patients increases risk of cirrhosis and hepatocellular carcinoma. Data from studies on the interaction between CHB and nonalcoholic fatty liver disease are not conclusive. Liver biopsy is the gold standard for diagnosis of fatty liver; however, noninvasive diagnostic tests have been developed to diagnose and predict fibrosis in CHB/NAFLD. Treatment guidelines are not clear.

Hepatitis B in Pregnant Women and their Infants

Alicia M. Cryer and Joanne C. Imperial

Chronic hepatitis B is a global health problem affecting approximately 350 million to 400 million individuals worldwide, and mother to child transmission remains the major mode of transmission. Approximately 50% of chronically infected individuals acquire infection, either perinatally or early in childhood, predominantly in areas where hepatitis B virus (HBV) is endemic. Management of HBV in pregnancy presents a unique set of challenges. All infants born of hepatitis B surface antigen–positive mothers should receive postexposure immune prophylaxis with hepatitis B immunoglobulin and HBV vaccination within 24 hours of birth and need close follow-up for the first few years of life.

HBV/HCV Coinfection in the Era of HCV-DAAs

Rashed Abdelaal, Beshoy Yanny, and Mohamed El Kabany

Epidemiologic studies suggest that 10% to 15% of patients infected with hepatitis C virus (HCV) are coinfected with hepatitis B virus (HBV) in the United States as a result of the shared modality of transmission, but the true prevalence is not known. The progression of liver disease to cirrhosis and hepatocellular carcinoma is generally faster in patients who are coinfected, and HCV is usually more predominant. Immunosuppression of the host or eradication of hepatitis C can change this paradigm, causing hepatitis B reactivation. This review describes HCV-HBV viral interactions, risks for reactivation, screening, and society guidelines for surveillance and treatment.

Antiretroviral Effects on HBV/HIV Co-infection and the Natural History of Liver Disease

David L. Wyles

Hepatitis B virus (HBV) coinfection is common in persons with human immunodeficiency virus (HIV) infection, contributing significantly to morbidity and mortality. Many currently used HIV antiretroviral therapy (ART) regimens provide potent anti-HBV activity and it is recommended that HBV-HIV coinfected persons be treated with ART regimens containing tenofovir. ART has multiple benefits, including increasing rates of HBV clearance after initial infection and potent suppression of HBV DNA in chronic infection. Nevertheless, long-term studies have yet to demonstrate a profound positive impact of ART on HBV-related fibrosis progression and development of endstage liver disease.
Current recommendations concerning hepatitis C virus (HBV) reactivation are limited, with nearly all guidelines focused on its occurrence in patients with hematological malignancies or some solid tumors, who are treated with immunosuppressive therapies. Few of the guidelines address reactivation in patients receiving immunosuppression with organ transplants or treatment with any of the many immunosuppressive agents in use today for the treatment of multiple different diseases, or in patients receiving the direct-acting antivirals used in the treatment of hepatitis C virus (HCV). This article covers the immunology of HBV reactivation, mechanisms of viral clearance, and recommendations for screening and prophylaxis.

Organ transplantation is a lifesaving procedure for many patients. To prevent rejection or graft-versus-host disease, recipients require long-term immunosuppression. In patients who have ever been exposed to hepatitis B, it is possible for reactivation to occur; this includes patients who are anti–hepatitis B core antibody-positive only or both anti–hepatitis B core antibody-positive and hepatitis B surface antibody-positive. The susceptibility to this varies with the nature of the transplant. Hepatitis B can be transmitted from donor to recipient. It is important to assess the hepatitis B status and formulate a strategy to prevent transmission and prevent reactivation.

Patients with malignancies require chemotherapy and other immunosuppressive therapies for treatment. Because of this immunosuppression, in patients who have ever been exposed to hepatitis B it is possible for reactivation to occur. This reactivation can be fatal. Reactivation is particularly likely in patients who receive B cell–active agents such as rituximab. The occurrence of reactivation flares may also delay further chemotherapy, which can negatively affect the outcome of the underlying malignancy. Accordingly, it is important to screen patients for markers of hepatitis B and institute antiviral prophylaxis to prevent reactivation.
Screening and Prophylaxis to Prevent Hepatitis B Reactivation: Other Populations and Newer Agents

Joe Sasadeusz, Andrew Grigg, Peter D. Hughes, Seng Lee Lim, Michaela Lucas, Geoff McColl, Sue Anne McLachlan, Marion G. Peters, Nicholas Shackel, Monica Slavin, Vijaya Sundararajan, Alexander Thompson, Joseph Doyle, James Rickard, Peter De Cruz, Robert G. Gish, and Kumar Visvanathan

Because of the relatively high prevalence of both hepatitis B infection and various forms of autoimmune inflammatory diseases treated with aggressive immunotherapy, reactivation of hepatitis B occurs in a substantial number of patients. The risk of reactivation depends on the degree and duration of immunosuppression. A large number of drug treatments have resulted in reactivation of hepatitis B virus infection and, based on the mechanisms and extent of immunosuppression, recommendations for some of the newer classes of immunosuppressive drugs are provided.

Drugs in the Pipeline for HBV

Uri Lopatin

Chronic hepatitis B remains a significant cause of morbidity and mortality worldwide. Most hepatitis B virus (HBV)-infected individuals are neither diagnosed nor treated. In those treated, nucleos(t)ide polymerase inhibitors persistently suppress viremia to the limits of quantitation; however, few achieve a “functional cure,” defined as sustained off-treatment loss of detectable serum HBV DNA with or without loss of hepatitis B surface antigen. The low cure rate has been attributed to an inability to eliminate the viral reservoir of covalently closed circular DNA from hepatocytes. This review focuses on the diverse therapeutic approaches currently under development that may contribute to the goal of HBV cure.

HBV/HDV Coinfection: A Challenge for Therapeutics

Christopher Koh, Ben L. Da, and Jeffrey S. Glenn

Chronic hepatitis D (CHD) results from an infection with the hepatitis B virus and hepatitis D virus (HDV). CHD is the most severe form of human viral hepatitis. Current treatment options consist of interferon alfa, which is effective only in a minority of patients. Study of HDV molecular virology has resulted in new approaches entering clinical trials, with phase-3 studies the most advanced. These include the entry inhibitor bulevirtide, the nucleic acid polymer REP 2139-Ca, the farnesyltransferase inhibitor lonafarnib, and pegylated interferon lambda. This article summarizes the available data on these emerging therapeutics.