Hepatitis B virus infection remains a global public health problem with changing epidemiology due to several factors including vaccination policies and migration.

Hepatitis B was discovered by researchers who were investigating jaundice associated with blood transfusions as well as parenterally administered medications. Through trial and error, the HBV was identified. There are specific tests that detect HBV infection, whether it is a previous exposure or active infection. The various HBV serologies are reviewed in this work as well. Hepatitis B surface antigen has emerged as a tool in defining treatment endpoint and its significance is reviewed. HBV genotypes are distributed uniquely throughout the world, in particular, genotype C is associated with higher rates of hepatocellular carcinoma. Various HBV genotypes and their impact on the clinical course are discussed. The relationship of HBV serologies and HBV DNA to disease progression is outlined. There are specific recommendations on monitoring those infected with HBV and this is reviewed here. HBV mutations have an impact on the disease course and those of significance are also discussed.

This article reviews the incidence of acute hepatitis B virus (HBV) infection, its clinical course, strategies to prevent acute HBV infection in susceptible individuals, and the management of patients with acute HBV.

Nucleoside analogues are the drugs most commonly used in the treatment of chronic hepatitis B. They act by inhibiting viral replication and have minimal impact on HBsAg loss. Nucleoside analogues are indicated in patients with chronic hepatitis, cirrhosis, decompensated cirrhosis, hepatocellular carcinoma, and in those with extrahepatic manifestations. Real-world experience has been ongoing for more than 10 years, and the efficacy and safety results obtained are similar to those reported in clinical trials. Prolonged use is needed to maintain suppression of viral replication,
prevent the development of liver cirrhosis and decompensated cirrhosis, and to decrease the risk of hepatocellular carcinoma.

Controversies in Treating Chronic HBV: The Role of PEG-interferon-alfa

Phunchai Charatcharoenwitthaya, Apichat Kaewdech, and Teerha Piratvisuth

Pegylated interferon-alpha therapy is one of the first-line chronic hepatitis B treatment. Finite treatment duration, absence of drug resistance, delayed response, and higher hepatitis B surface antigen loss than nucleos(t)ides analog therapy are the advantages of pegylated interferon-alpha treatment. Common side effects and subcutaneous injections requirement limit its use. Identifying patients likely to respond to pegylated interferon-alpha and optimizing treatment is reasonable. Motivating patients to complete the 48-week treatment is necessary. Treatment is stopped or switched to other treatment strategies in patients with stopping rule criteria. Combination therapy with nucleos(t)ides analog may improve response, but remains controversial.

Controversies in Treating Chronic Hepatitis B virus: The Role of Hepatitis B Virus DNA and Surface Antigen Titer

Daniel Q. Huang, Guan Sen Kew, and Seng Gee Lim

Controversial areas in chronic hepatitis B (CHB) are those where there is uncertainty, or differences of opinion in management, or where evidence may be insufficient. Areas of controversy include whether patients with high viral load but normal liver function tests should be treated to prevent hepatocellular carcinoma (HCC) or liver disease progression to cirrhosis. Another area is whether quantitative hepatitis B surface antigen (qHBsAg) can be used to better characterize phases of CHB and prognosticate. Finally, the utility of qHBsAg in the management of patients on antiviral therapy such as interferon and nucleoside analogues could improve management practices.

Controversies in the Management of Hepatitis B: Hepatocellular Carcinoma

Stuart K. Roberts, Ammar Majeed, and William Kemp

Hepatitis B is the leading cause of hepatocellular cancer (HCC) worldwide. Untreated, annual HCC incidence rates in chronic hepatitis B subjects are 0.4% in noncirrhotics and 2% to 3% in cirrhotics. Surveillance with ultrasound with/without α-fetoprotein at 6-month intervals is recommended in at-risk persons including children. Antiviral therapy in chronic hepatitis B with entecavir or tenofovir significantly lowers the risk of HCC across all stages of liver disease, and lowers the risk of HCC recurrence following curative therapy. There are insufficient data to recommend use of tenofovir over entecavir in the prevention of de novo or recurrent HCC postcurative therapy.

Controversies in Treating Chronic Hepatitis B Virus Infection: Discordant Serologic Results

Arif Sarowar, Grishma Hirode, Harry L.A. Janssen, and Jordan J. Feld

Despite effective vaccines and approved therapeutic agents, hepatitis B virus (HBV) remains a prevalent global health problem. Current guidelines
rely on a combination of serologic, virological, and biochemical markers to identify the phase in the natural history of chronic HBV infection. Discordant serologic results can occur, which may lead to misclassification. Commonly encountered results that differ from the typical profiles seen in chronic HBV infection are described. For each scenario, the frequency of occurrence, possible explanations, and recommendations for clinical management are discussed. Recognition of discordant serologic findings is crucial for optimal clinical decision.

Chronic Hepatitis B Virus in Patients with Chronic Hepatitis C Virus 817
Nelson E. Airewele and Mitchell L. Shiffman

Many patients with hepatitis C virus (HCV) have also been exposed to hepatitis B virus (HBV). The 2 viruses interact and in most cases HCV suppresses HBV. When HCV is treated with direct antiviral agents, this suppressive effect is removed, HBV replication may increase, and a flare in liver enzymes with liver injury may occur. All patients with chronic HCV should therefore be checked for serologic evidence of HBV. Patients with hepatitis B surface antigen are at the highest risk for reactivation, and these patients should receive prophylactic treatment of HBV during and for 6 months after HCV treatment.

New Treatments for Chronic Hepatitis B Virus/Hepatitis D Virus Infection 831
Lisa Sandmann and Heiner Wedemeyer

Chronic hepatitis D virus (HDV) infection is the most severe form of viral hepatitis with high rates of end-stage liver disease and hepatocellular carcinoma. Therefore, effective antiviral treatment strategies are needed desperately. Until recently, antiviral treatment was limited to pegylated interferon-alpha. With the conditional approval of the entry inhibitor bulevirtide by the European Medicines Agency, new treatment options are now available. In addition, multiple other antiviral compounds are currently tested in clinical phase II and III trials and represent promising agents for the treatment of chronic HDV infection.

Use of Hepatitis B Virus–Positive Organs in Organ Transplantation 841
Saro Khemichian, Jeffrey Kahn, and Norah A. Terrault

The significant morbidity and mortality of people with end-stage renal, liver, heart, and lung diseases in need of transplantation provides rationale for use of organs from donors who are hepatitis B positive. The recipient’s hepatitis B status plays a key role in defining the prophylactic strategy. The availability of safe and effective therapies (hepatitis B antivirals and hepatitis B immune globulin) has contributed to the safety of using hepatitis B–positive donors. The outcomes in both liver and nonliver solid organ transplant recipients given hepatitis B–positive organs have been excellent if appropriate prophylactic therapies provided.
Hepatitis B and Health Care Workers

Stephen C. Pappas

Owing to standard precautions and initiatives for universal hepatitis B virus (HBV) vaccination in the general population and health care workers, risk of transmission of HBV infection from the patient to a health care worker (and vice versa) is very low. The need for mandatory HBV screening and vaccination in health care workers is less clear than in the past. Health care workers with chronic HBV infection neither require restrictions on professional practice nor disclosure of infection status to a patient. Further study is required to develop effective revaccination strategies to manage health care workers who are vaccine nonresponders.

Novel Therapies That May Cure Chronic Hepatitis B Virus

Alessandro Loglio, Mauro Viganò, and Pietro Lampertico

Despite the significant improvement of long-term outcomes in CHB patients long-term treated with NA, none of these drugs can directly target and efficiently clear the cccDNA, which persists in the nuclei of the infected hepatocytes. New anti-HBV strategies that target directly or indirectly HBsAg to achieve “functional cure”, ie. Loss of serum HBsAg coupled with serum undetectable HBV DNA, are based on the short-term administration of combination therapies with complementary and synergistics mechanisms of action, targeting in one or multiple critical steps of viral life.