



Hepatitis B Science Backgrounder

Epidemiology

Worldwide, more than two billion people (1 out of 3 people) have been infected with hepatitis B and approximately 350 to 400 million people have developed chronic infection.¹ These chronically infected persons are at high risk of death from cirrhosis of the liver and liver cancer. About one million people die each year from hepatitis B and its complications.²

In the United States, more than 12 million people (1 out of 20 people) have been infected with hepatitis B, and approximately 1.25 million people have developed chronic infection. Each year approximately 100,000 new people become infected with the disease and more than 5,000 Americans die from hepatitis B-related liver complications, including cirrhosis and hepatocellular carcinoma (HCC). It is estimated that one U.S. health care worker dies each day from hepatitis B.¹

Pathogenesis

The hepatitis B virus (HBV) is a double-stranded DNA virus that belongs to the Hepadnaviridae family of viruses. The family name refers to “*hepato*,” meaning liver, and *viral DNA*. As the only member of this family of viruses affecting humans, the hepatitis B virus has the smallest known genome of any replication-competent human virus. Related viruses cause hepatitis in ducks, ground squirrels and woodchucks.³

The hepatitis B virus primarily interferes with the functions of the liver while replicating in liver cells, also known as hepatocytes. The virus replicative intermediates and/or viral transcripts also have been found in bile duct epithelial and endothelial cells, smooth muscle tissue, adrenal glands, gonads, kidneys, lymph nodes, and thyroid glands of acute hepatitis B-infected patients.⁴

The hepatitis B virus consists of three main components.¹ These are:

1. Surface antigen (HBsAg) – This is a complex antigen found on the surface of the complete virus particle that exists outside of a host cell, also known as the virion. HBsAg also can be found circulating in the serum of patients during the early phase of the disease.
2. Core antigen (HBcAg) – This antigen is found in the core of the virion and in infected cell nuclei.
3. e antigen (HBeAg) – In contrast to the surface antigen (HBsAg) and core antigen (HBcAg), this antigen is associated with the viral nucleocapsid, which consists of the protein coat of the virus and its enclosed nucleic acid. Its presence is a marker that the virus is replicating actively, and the individual is potentially infectious.

The hepatitis B virus is roughly spherical in shape, and is commonly referred to as double-shelled. It has an outer envelope with HBsAg and an inner core, which consists of HBcAg, HBeAg and the genetic material.

The unique mode of hepatitis B virus replication takes place in the nucleus of the infected host cell. Viral entrance into the cell takes place by binding to a receptor as the envelope is shed and the viral core particle with the DNA viral genome is delivered into the nucleus of the host cell. The viral DNA is then repaired and transformed into closed circular supercoiled DNA (cccDNA) that serves as a template for transcription of four viral RNAs. These four viral transcripts undergo additional processes and travel different cellular pathways to either form and secrete new virions or amplify the viral genome inside the cell nucleus. HBeAg is secreted and the virus further replicates, with the capability to produce both cell proliferation and cell death.

Diagnosis

Most people with hepatitis B infection have no symptoms and feel healthy. If the proper tests are not administered, people infected with the virus may even appear to exhibit normal blood tests for liver function, granting them a deceptively clean bill of health.

The time between exposure to the hepatitis B virus and onset of clinical symptoms is between 45 and 180 days, with an average range of 60-90 days.³ When a person is first infected with the hepatitis B virus, this is called an “acute infection.” If the virus remains in the blood for more than six months, then a person is diagnosed as having a “chronic infection.” People with chronic hepatitis B infection are at increased risk of developing liver complications, such as the replacement of liver cells with scar tissue (the end result of extensive scarring can be liver cirrhosis), liver cancer (hepatocellular carcinoma), liver failure, and, in some cases, death. In addition, chronic hepatitis B-infected individuals can transmit the disease for many years.

The cardinal feature of chronic hepatitis B infection is the long-term presence of HBsAg in the blood and the failure to develop hepatitis B surface antibodies that provide protective immunity. All people who are HBsAg-positive are potentially infectious, and most patients receive the diagnosis of chronic hepatitis B infection long after chronicity is established. An estimated 40 percent of people who have been infected with the hepatitis B virus do not know how or when they became infected.⁵

A patient with an acute hepatitis B infection will test positive for the hepatitis B virus (HBsAg), HBeAg, and possibly the HBe-antigen (HBeAg). An acute hepatitis B infection follows a relatively long incubation period, ranging from one to six months (with or without symptoms) and infected persons are able to pass the virus to others at this stage; therefore, safe sex practices should be recommended and vaccination of close family/household members and sexual partners is advised. Repeat blood tests over a six-month period are needed to diagnose recovery or chronic infection.¹ Patients who clear acute infection by six months will be core HBeAg negative and core HBeAg positive and HBsAb positive. Patients who do not clear the infection will have evidence of HBsAg and HBeAg depending on the virus strain of infection (core or pre-core mutants).

Blood is infective many weeks before the onset of the first symptoms and throughout the acute phase of the hepatitis B infection. The infectivity of chronically infected individuals varies from highly-infectious (HBeAg-positive) to often sparingly-infectious (possessing hepatitis B surface and core antibodies).¹

Additional signs of chronic hepatitis B infection are histological evidence of chronic necroinflammatory disease on liver biopsy or persistently elevated serum alanine aminotransferase (ALT) activities.⁶ Assays exist to assess the replicative state of chronic hepatitis B and its pathogenicity, and to measure levels of HBeAg and anti-HBe antibody, HBV DNA, and liver enzymes (particularly ALT).

Treatment

The primary goal of antiviral therapy for chronic hepatitis B infection is to eliminate or significantly suppress viral replication, as measured in the reduction of HBV DNA levels, and to prevent disease progression to liver cancer.⁷ Reducing viral load and enhancing the body’s natural immune response can lower the risk of liver damage. Elevations in ALT levels make patients candidates for antiviral therapy.⁷ Antivirals and immunomodulators have been approved by the U.S. Food and Drug Administration for the treatment of chronic hepatitis B, and several additional antivirals are currently in development.⁸

Treatment responses are generally evaluated on the basis of normalization of ALT levels, clearance of HBe-Ag, and decreased or undetectable HBV DNA. If a liver biopsy is performed, histologic findings should show a decrease in liver inflammation, possibly, even reversal of damage if compared to pre-treatment biopsy results.¹

Acute hepatitis B

There is no specific treatment for individuals with acute viral hepatitis B. Hepatitis B is a viral disease, and as such, antibiotics are of no value in treatment of the infection. Further, antivirals have not been shown to alter the course or affect the risk of chronicity in patients with clinically recognized acute hepatitis B infection.⁸

Chronic hepatitis B

The ability of antiviral therapy to suppress viral replication and halt the progression of chronic liver disease have been the focus of intense interest for more than two decades.⁸ Antivirals aim to suppress or destroy HBV DNA by interfering with viral replication, and immune modulators seek to help the human immune system mount a defense against the virus.

References

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