Table 18-3 The Hepatitis Viruses

Virus	Hepatitis A	Hepatitis B	Hepatitis C	Hepatitis D	Hepatitis E
Type of virus	ssRNA	partially dsDNA	ssRNA	Circular defective ssRNA	ssRNA
Viral family	Hepatovirus; related to picornavirus	Hepadnavirus	Flaviviridae	Subviral particle in Deltaviridae family	Hepevirus
Route of transmission	Fecal-oral (contaminated food or water)	Parenteral, sexual contact, perinatal	Parenteral; intranasal cocaine use is a risk factor	Parenteral	Fecal-oral
Mean incubation period	2 to 6 weeks	2 to 26 weeks (mean 8 weeks)	4 to 26 weeks (mean 9 weeks)	Same as HBV	4 to 5 weeks
Frequency of chronic liver disease	Never	5%-10%	>80%	10% (co-infection); 90%-100% for superinfection	In immunocompromised hosts only
Diagnosis	Detection of serum IgM antibodies	Detection of HBsAg or antibody to HBcAg; PCR for HBV DNA	3rd-generation ELISA for antibody detection; PCR for HCV RNA	Detection of IgM and IgG antibodies; HDV RNA serum; HDAg in liver	Detection of serum IgM and IgG antibodies; PCR for HEV RNA

dsDNA, Double-stranded DNA; ELISA, enzyme-linked immunosorbent assay; HBcAg, hepatitis B core antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCV, hepatitis C virus; HDAg, hepatitis D antigen; HDV, hepatitis D virus; HEV, hepatitis E virus; IV, intravenous; PCR, polymerase chain reaction; ssRNA, single stranded RNA.
From Washington K: Inflammatory and infectious diseases of the liver. In Iacobuzio-Donahue CA, Montgomery EA (eds): Gastrointestinal and Liver Pathology. Philadelphia, Churchill Livingstone; 2005.

asymptomatic or symptomatic infection. HAV and HEV (in immunocompetent hosts) do not cause chronic hepatitis and only a small number of HBV-infected adult patients develop chronic hepatitis. In contrast, HCV is notorious for chronic infection. Fulminant hepatitis (acute liver failure) is unusual and is seen primarily with HAV, HBV, or HDV infection depending on region. HEV can cause fulminant hepatitis in pregnant women. Although HBV and HCV are responsible for most cases of chronic hepatitis, there are many other causes of similar clinicopathologic presentation, especially autoimmunity and drug/toxin-induced hepatitis, described later. Therefore, *serologic and molecular studies are essential for the diagnosis of viral hepatitis and for distinguishing between the various types.*

Acute Asymptomatic Infection with Recovery. Patients in this group are identified only incidentally on the basis of minimally elevated serum transaminases or, after the fact, by the presence of antiviral antibodies. Worldwide, HAV and HBV infection are frequently subclinical events in childhood, verified only in adulthood by the presence of anti-HAV or anti-HBV antibodies.

Acute Symptomatic Infection with Recovery. Regardless of the virus, the disease is more or less the same and can be divided into four phases: (1) an incubation period, (2) a symptomatic preicteric phase, (3) a symptomatic icteric phase, and (4) convalescence. The incubation period for the different viruses is given in Table 18-3. Peak infectivity occurs during the last asymptomatic days of the incubation period and the early days of acute symptoms.

Acute Liver Failure. Viral hepatitis is responsible for about 10% of cases of acute hepatic failure. The causative virus differs depending on the geographic location. Globally, hepatitis A and E are the most common causes; HBV is more common in Asian and Mediterranean countries. Morphologic details of massive necrosis under these circumstance were previously described in the section on Acute Liver Failure. There are no specific histologic findings which are indicative of hepatotropic virus causation.

Survival for more than a week may permit the replication of residual hepatocytes. Activation of the stem/progenitor cells in the canals of Hering gives rise to very prominent ductular reactions, although these are usually insufficient to accomplish full restitution; recovery depends on surviving hepatocytes undergoing cell division to restore missing parenchyma. The treatment for acute hepatic failure that follows acute viral hepatitis is to provide supportive care. Liver transplantation is the only option for patients whose disease does not resolve before secondary infection and other organ failure develop.

Chronic Hepatitis. **Chronic hepatitis is defined as symptomatic, biochemical, or serologic evidence of continuing or relapsing hepatic disease for more than 6 months.** Etiology rather than the histologic pattern is the most important determinant of the probability of developing progressive chronic hepatitis. The clinical features of chronic hepatitis are extremely variable and are not predictive of outcome. In some patients the only signs of chronic disease are persistent elevations of serum transaminases. Laboratory studies may also reveal prolongation of the prothrombin time and, in some instances, hyperglobulinemia, hyperbilirubinemia, and mild elevations in alkaline phosphatase levels. In symptomatic individuals, the most common finding is fatigue; less common symptoms are malaise, loss of appetite, and occasional bouts of mild jaundice. In precirrhotic chronic hepatitis, physical findings are few, the most common being mild hepatomegaly, hepatic tenderness, and mild splenomegaly. Occasionally, in cases of HBV and HCV infection, immune complex disease may develop secondary to the presence of circulating antibody-antigen complexes, in the form of vasculitis (Chapter 11) and glomerulonephritis (Chapter 20). Cryoglobulinemia is found in about 35% of individuals with chronic hepatitis C infection.

The Carrier State. A "carrier" is an individual who harbors and can transmit an organism, but has no manifest symptoms. In the case of hepatotropic virus this definition is somewhat confusing, as it can be interpreted to mean: (1) individuals who carry one of the viruses but have no liver disease; (2) those who harbor one of the viruses and have non-progressive liver damage, but are essentially free of symptoms or disability. In both cases, particularly the