its meaning in any situation. First, "hepatitis" is the name of each of the *hepatotropic viruses* (hepatitis A, B, C, D, and E) that have a specific affinity for the liver. Second, "hepatitis" stands for the histologic patterns of hepatitic injury, both acute and chronic (depending on the specific virus), that are seen in the livers infected by hepatotropic viruses (and in autoimmune and drug or toxin induced hepatitis, as well). Third, to a more minor degree, it is any form of hepatocellular injury due to infection by other, usually systemic viruses, such as (1) mild Epstein-Barr virus hepatitis sometimes seen in infectious mononucleosis; (2) cytomegalovirus, herpes virus, and adenovirus infections, particularly in the newborn or immunosuppressed patient; and (3) yellow fever (yellow fever virus), a major and serious cause of hepatitis in tropical countries. We first present the main features of each hepatotropic virus, followed by a discussion of the clinicopathologic characteristics of acute and chronic viral hepatitis.

Hepatitis A Virus

Hepatitis A virus (HAV) is a usually benign, self-limited disease with an incubation period of 2 to 6 weeks. HAV does not cause chronic hepatitis or a carrier state and only uncommonly causes acute hepatic failure, so the fatality rate associated with HAV is only about 0.1-0.3%. HAV occurs throughout the world and is endemic in countries with poor hygiene and sanitation. Many individuals in these countries have detectable anti-HAV antibodies by the time they are 10 years old. Clinical disease tends to be mild or asymptomatic and is rare after childhood.

In developed countries, the prevalence of seropositivity (indicative of previous exposure) increases gradually with age, reaching 50% by age 50 years in the United States. In this population, acute HAV tends to be a sporadic febrile illness. Affected individuals have nonspecific symptoms such as fatigue and loss of appetite, and often develop jaundice. Overall, HAV accounts for about 25% of clinically evident acute hepatitis worldwide and an estimated 2000 new cases per year in the United States.

Discovered in 1973, HAV is a small, nonenveloped, positive-strand RNA picornavirus that occupies its own genus, *Hepatovirus*. Ultrastructurally, HAV is an icosahedral capsid 27 nm in diameter. The receptor for HAV is HAVcr-1, a 451–amino acid class I integral-membrane mucin-like glycoprotein. HAV is spread by ingestion of contaminated water and foods and is shed in the stool for 2 to 3 weeks before and 1 week after the onset of jaundice. Thus, close personal contact with an infected individual or fecal-oral contamination during this period accounts for most cases and explains the outbreaks in institutional settings such as schools and nurseries, and the water-borne epidemics in places where people live in overcrowded, unsanitary conditions. HAV vaccine, available since 1992, is effective in preventing infection. Immunization of toddlers in Israel has eliminated outbreaks in day care centers.

HAV can also be detected in serum and saliva. *Because HAV viremia is transient, blood-borne transmission of HAV occurs only rarely; therefore, donated blood is not specifically screened for this virus.* In developed countries, sporadic infections may be contracted by the consumption of raw or steamed shellfish (oysters, mussels, clams), which concentrate the virus from seawater contaminated with human sewage. Infected workers in the food industry may also be the source of outbreaks. HAV itself does not seem to be cytopathic. Cellular immunity, particularly CD8+ T cells, plays a key role in hepatocellular injury during HAV infection.

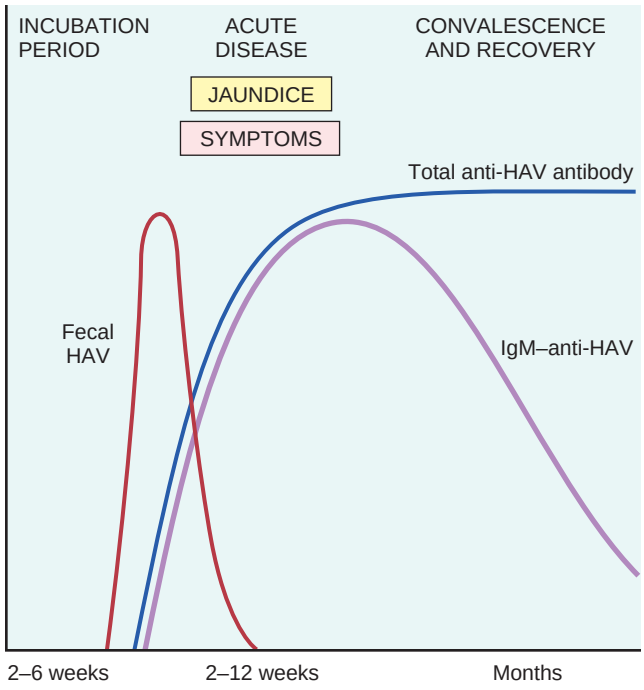

Figure 18-10 Temporal changes in serologic markers in acute hepatitis A infection. HAV, Hepatitis A virus.

Specific IgM antibody against HAV appears with the onset of symptoms, constituting a reliable marker of acute infection (Fig. 18-10). Fecal shedding of the virus ends as the IgM titer rises. The IgM response usually begins to decline in a few months and is followed by the appearance of IgG anti-HAV. The latter persists for years, perhaps conferring lifelong immunity against reinfection by all strains of HAV. Since there are no routinely available tests for IgG anti-HAV, the presence of IgG anti-HAV is inferred from the difference between total and IgM anti-HAV.

Hepatitis B Virus

Hepatitis B virus (HBV) can produce (1) acute hepatitis followed by recovery and clearance of the virus, (2) nonprogressive chronic hepatitis, (3) progressive chronic disease ending in cirrhosis, (4) acute hepatic failure with massive liver necrosis, and (5) an asymptomatic, "healthy" carrier state. HBV-induced chronic liver disease is also an important precursor for the development of hepatocellular carcinoma even in the absence of cirrhosis. The approximate frequencies of clinical outcomes of HBV infection are depicted in Figure 18-11.

Liver disease due to HBV is an enormous global health problem. One third of the world population (2 billion people) have been infected with HBV and 400 million people have chronic infection. Seventy-five percent of all chronic carriers live in Asia and the Western Pacific rim. The global prevalence of chronic hepatitis B infection varies widely, from high (>8%) in Africa, Asia, and the Western Pacific to intermediate (2% to 7%) in southern and eastern Europe, to low (<2%) in Western Europe, North America,