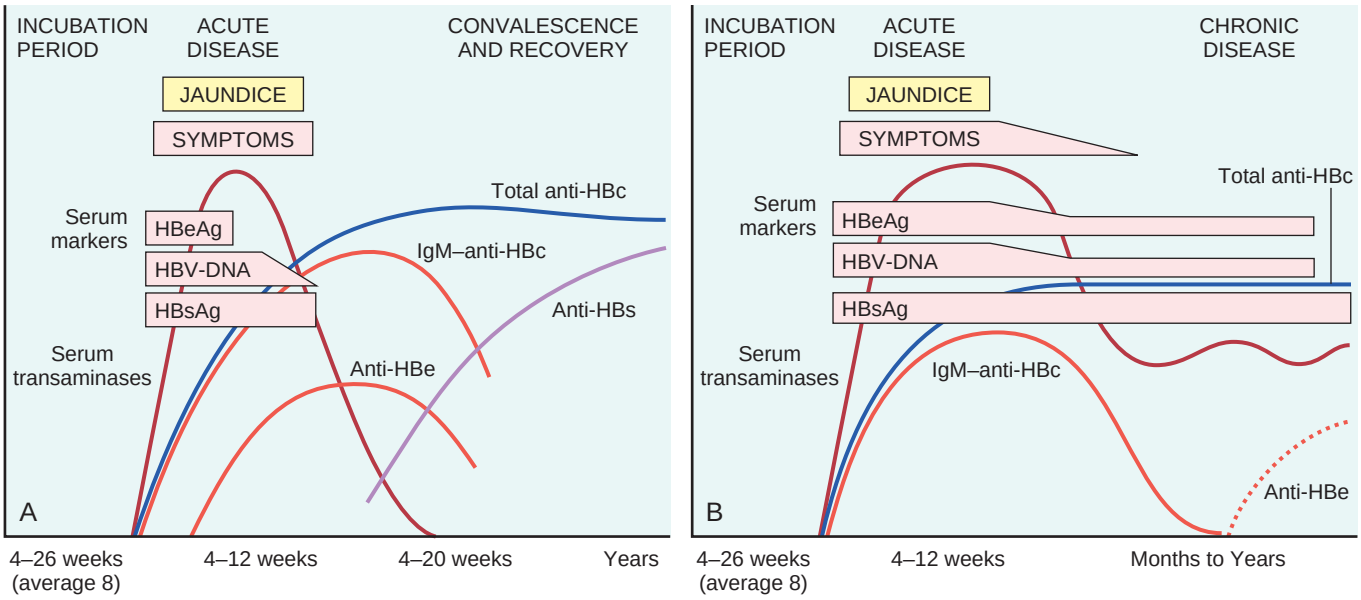

Figure 18-12 Temporal changes in serologic markers in hepatitis B viral infection. **A,** Acute infection with resolution. **B,** progression to chronic infection. Note in some cases of chronic HBV, serum transaminases may become normal.

(Fig. 18-12*A*). In some cases, however, Anti-HBs antibody is not detectable for a few weeks to several months after the disappearance of HBsAg. During this window period, serologic diagnosis can be made by detection of IgM anti-HBc antibody (see below and Fig. 18-12). Anti-HBs may persist for life, conferring protection; this is the basis for current vaccination strategies using noninfectious HBsAg.

- HBeAg, HBV-DNA, and DNA polymerase appear in serum soon after HBsAg, and all signify active viral replication. Persistence of HBeAg is an important indicator of continued viral replication, infectivity, and probable progression to chronic hepatitis. The appearance of anti-HBe antibodies implies that an acute infection has peaked and is on the wane.
- IgM anti-HBc antibody becomes detectable in serum shortly before the onset of symptoms, concurrent with the onset of elevated serum aminotransferase levels (indicative of hepatocyte destruction). Over a period of months the IgM anti-HBc antibody is replaced by IgG anti-HBc. As in the case of anti-HAV, there is no direct assay for IgG anti-HBc; its presence is inferred from decline of IgM anti-HBc in the face of rising total anti-HBc.

Occasionally, mutated strains of HBV emerge that do not produce HBeAg but are replication competent and express HBcAg. In such patients, the HBeAg may be low or undetectable despite the presence of serum HBV DNA. A second, ominous development is the appearance of vaccine-induced escape mutants, which replicate in the presence of vaccine-induced immunity.

The host immune response to the virus is the main determinant of the outcome of the infection. Innate immune mechanisms protect the host during the initial phases of the infection, and a strong response by virus-specific CD4+ and CD8+ interferon (IFN)-γ–producing cells is associated with the resolution of acute infection. HBV generally does not cause direct hepatocyte injury. Instead, injury is caused by CD8+ cytotoxic T cells attacking infected cells.

Age at the time of infection is the best predictor of chronicity. The younger the age at the time of HBV infection, the higher the probability of chronicity. Despite progress in the treatment of chronic HBV infection, complete cure is extremely difficult to achieve even when treated with highly effective antiviral agents. The difficulty in achieving cure has been attributed to the ability of the virus to insert itself in the host DNA, thus limiting the development of an effective immune response (HBsAb development). This allows the virus to persist in the face of drugs that impair its replication. Hence, the goal of the treatment of chronic hepatitis B is to slow disease progression, reduce liver damage, and prevent liver cirrhosis or liver cancer.

Hepatitis B can be prevented by vaccination and by the screening of donor blood, organs, and tissues.Vaccination induces a protective anti-HBs antibody response in 95% of infants, children, and adolescents.

Hepatitis C Virus

Hepatitis C Virus (HCV) is a major cause of liver disease worldwide, with approximately 170 million people affected. Approximately 3.6 million Americans, or 1.3% of the population, have antibodies to HCV, indicative of past or current infection. Of these, 2.7 million have chronic HCV based on presence of HCV RNA. Notably, there has been a decrease in the annual incidence of infection from its mid-1980s peak of more than 230,000 new infections per year to a current 17,000 new infections per year, due primarily to a marked reduction in transfusion-associated cases as a result of donor blood screening. Nevertheless, the number of patients with chronic infection will continue to increase, as a result of potential lifelong persistence of HCV infection.

According to data from the USA Centers for Disease Control, the most common risk factors for HCV infection are: