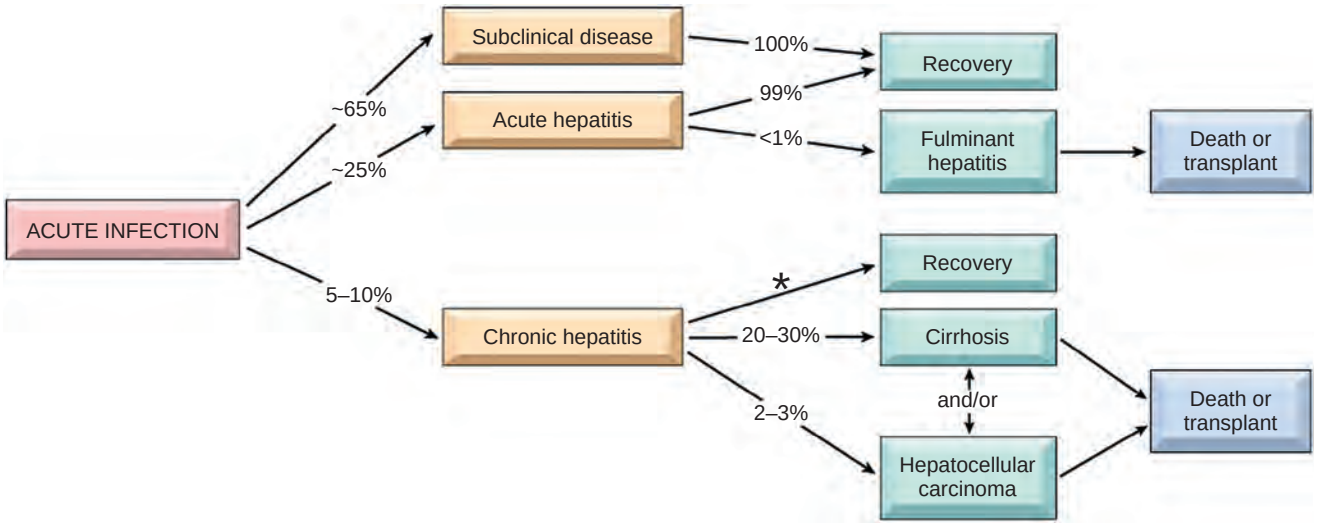

Figure 18-11 Potential outcomes of hepatitis B infection in adults, with their approximate frequencies in the United States. *Spontaneous HBsAg clearance occurs during chronic HBV infection at an estimated annual incidence of 1 to 2% in Western countries. As mentioned in the text, fulminant hepatitis and acute hepatic failure are used interchangeably

and Australia. As discussed later, the carrier rate is largely dictated by the age at infection, being the highest when infection occurs in children perinatally and the lowest when adults are infected.

The mode of transmission of HBV also varies with geographic areas. In high prevalence regions of the world, transmission during childbirth accounts for 90% of cases. In areas with intermediate prevalence, horizontal transmission, especially in early childhood, is the dominant mode of transmission. Such spread occurs through minor breaks in the skin or mucous membranes among children with close bodily contact. In low prevalence areas, unprotected sex and intravenous drug abuse (sharing of needles and syringes) are the chief modes of spread. The incidence of transfusion-related spread has dwindled greatly in recent decades due to screening of donated blood for HBsAg and exclusion of paid blood donors. Vaccination induces a protective anti-HBs antibody response in 95% of infants, children, and adolescents. Universal vaccination has had notable success in Taiwan and Gambia, but unfortunately, has not been adopted worldwide. Broad childhood population vaccination programs in endemic countries (e.g., Taiwan) are expected to curtail the disease in coming years.

HBV has a prolonged incubation period (2 to 26 weeks). Unlike HAV, HBV remains in the blood until and during active episodes of acute and chronic hepatitis. Approximately 65% of adults newly acquiring HBV have mild or no symptoms and do not develop jaundice. The remaining 25% have nonspecific constitutional symptoms such as anorexia, fever, jaundice, and upper right quadrant pain. In almost all cases the infection is self-limited and resolves without treatment. Chronic disease occurs in 5%-10% of infected individuals. Fulminant hepatitis (acute hepatic failure) is rare, occurring in approximately 0.1% to 0.5% of acutely infected individuals.

HBV was first linked to hepatitis in the 1960s when Australia antigen (later known as HBV surface antigen) was identified. The virus is a member of the *Hepadnaviridae*, a family of DNA viruses that cause hepatitis in multiple animal species. There are eight HBV genotypes that are distributed around the globe. The mature HBV virion is a 42-nm, spherical double-layered "Dane particle" that has an outer surface envelope of protein, lipid, and carbohydrate enclosing an electron-dense, 28-nm, slightly hexagonal core. The genome of HBV is a partially double-stranded circular DNA molecule having 3200 nucleotides with four open reading frames coding for:

- A nucleocapsid "core" protein (HBcAg, hepatitis B core antigen) and a longer polypeptide transcript with a precore and core region, designated HBeAg (hepatitis B e antigen). The precore region directs the secretion of the HBeAg polypeptide, whereas HBcAg remains in hepatocytes, where it participates in the assembly of complete virions.
- Envelope glycoproteins (HBsAg, hepatitis B surface antigen), which consist of three related proteins: large, middle, and small HBsAg. Infected hepatocytes are capable of synthesizing and secreting massive quantities of noninfective surface protein (mainly small HBsAg).
- A polymerase (Pol) that exhibits both DNA polymerase activity and reverse transcriptase activity. Replication of the viral genome occurs via an intermediate RNA template, through a unique replication cycle: DNA → RNA → DNA
- HBx protein, which is necessary for virus replication and may act as a transcriptional transactivator of both viral genes and a subset of host genes. It has been implicated in the pathogenesis of hepatocellular carcinoma in HBV infection.

The natural course of the disease can be followed by serum markers (Fig. 18-12)

- HBsAg appears before the onset of symptoms, peaks during overt disease, and then often declines to undetectable levels in 12 weeks, although it may persist in some individuals for as long as 24 weeks.
- Anti-HBs antibody does not rise until the acute disease is over, concomitant with the disappearance of HBsAg