recombinant HBV vaccines. Prophylaxis with HBIG after blood or mucosal exposure should be given within 7 days along with HBV vaccine. Preventive vaccination is currently recommended for high-risk individuals—health care professionals, patients undergoing hemodialysis, patients with chronic liver disease, residents and staff of custodial care institutions, and sexually active homosexual men—and is advocated universally for children.

No accepted prevention strategies other than universal precautions are available for HCV, and serum immunoglobulin is not useful for postexposure prophylaxis. The advent of widespread blood product screening for hepatitis C has made such infection after transfusion a rarity.

## Alcoholic Liver Disease

Alcohol abuse continues to be a major cause of liver disease in the Western world. The three major pathologic findings resulting from alcohol abuse are fatty liver, alcoholic hepatitis, and cirrhosis. These findings are not mutually exclusive and may all be present in the same patient. The first two conditions are potentially reversible. Alcoholic cirrhosis is discussed in Chapter 43.

### Mechanism of Injury

The mechanisms of liver injury caused by alcohol are complex. Ethanol and its metabolites, acetaldehyde and nicotinamide adenine dinucleotide phosphate, are directly hepatotoxic and cause a large number of metabolic derangements. Induction of cytochrome P-450 (i.e., CYP2E1) and cytokine pathways, particularly tumor necrosis factor-α (TNF-α), are also critical in initiating and perpetuating hepatic injury.

Hepatotoxic effects from alcohol vary considerably among individuals. Nevertheless, consumption by men of 40 to 80 g of alcohol per day for 10 to 15 years carries a substantial risk for the development of alcoholic liver disease. Women appear to have a lower threshold of injury than men. Malnutrition and other forms of chronic liver disease may potentiate the toxic effects of alcohol on the liver. Genetic factors contribute to individual susceptibility as well.

### Clinical and Pathologic Features

Alcoholic fatty liver may manifest as incidentally discovered hepatomegaly or elevated aminotransferase levels on screening blood tests. Vague discomfort in the right upper quadrant of the abdomen may be the only symptom. Jaundice is rare, and aminotransferases are only mildly elevated (<5 times normal). Liver biopsy shows either diffuse or centrilobular fat occupying most of the hepatocytes.

Alcoholic hepatitis is much more severe and is characterized on liver biopsy by the histologic triad of Mallory bodies, infiltration by polymorphonuclear leukocytes, and a network of interlobular connective tissue surrounding hepatocytes and central veins (pericellular, perivenular, and perisinusoidal fibrosis). Patients with alcoholic hepatitis may be asymptomatic, or they may be extremely ill with hepatic failure. Other common symptoms are anorexia, nausea, vomiting, weight loss, and abdominal pain. For those with fever, infection needs to be ruled out. Jaundice is commonly present and may be pronounced, with cholestatic features that require differentiation from biliary tract disease (see Chapters 40 and 44). Physical examination may reveal cutaneous signs of chronic liver disease, including spider angiomas and palmar erythema. In addition, gynecomastia, parotid enlargement, testicular atrophy, and loss of body hair may be found. The presence of ascites and hepatic encephalopathy suggests cirrhosis. Aminotransferases are only moderately increased (200-400 U/L) in alcoholic hepatitis compared with other forms of acute hepatitis. The ratio of AST to ALT almost always exceeds 2 : 1, in contrast to viral hepatitis, in which the aminotransferases are usually increased in parallel. The white blood cell count may be strikingly increased.

### Diagnosis

A history of excessive and prolonged alcohol intake is frequently difficult to obtain from patients with alcoholic liver disease. However, historical, clinical, and biochemical features of alcoholic hepatitis are often sufficient to establish the diagnosis. Many patients suspected or found to imbibe alcohol excessively may have causes in addition to alcohol contributing to liver disease (e.g., chronic viral hepatitis). Therefore, when other causes of liver disease are suggested and alcohol intake is uncertain, appropriate serologic testing and a liver biopsy may be needed to establish a diagnosis.

### Treatment

Complete abstinence from alcohol is the most important step. Meticulous supportive care, including tube feeding for those with severe anorexia, is the cornerstone of treatment for acute alcoholic hepatitis. In the absence of contraindications (i.e., infection, gastrointestinal bleeding, or renal failure), some patients with alcoholic hepatitis may benefit from treatment with corticosteroids. A calculated discriminant function (DF) value greater than 32 (where DF = 4.6 × [prothrombin time (in seconds) − control (in seconds)] + total bilirubin [in mg/dL]) may identify a subgroup of patients who are more likely to benefit from the use of corticosteroids, but these patients have advanced liver disease and a high mortality rate. Pentoxifylline, an oral TNF-α antagonist, was shown to reduce the risk of renal failure but not mortality in a single randomized trial.

### Complication and Prognosis

Alcoholic fatty liver disease completely resolves with cessation of alcohol intake. Alcoholic hepatitis can also resolve, but it commonly progresses either to cirrhosis, which may already be present at the time of initial diagnosis, or to hepatic failure and death. The development of encephalopathy, ascites, acute kidney injury, and gastrointestinal bleeding from varices often complicates alcoholic hepatitis (see Chapter 43). Patients with a DF greater than 32 have a high risk of death. The Lille model combines six reproducible variables (age, renal insufficiency, albumin, prothrombin time, bilirubin, and evolution of bilirubin at day 7) and is highly predictive of death at 6 months. A score greater than 0.45 predicts a 6-month survival rate of 25%, compared with 85% survival when the score is less than 0.45.

## Drug-Induced Liver Injury

Drug-induced liver injury (DILI), also known as hepatotoxicity, refers to liver injury caused by drugs or other chemical agents and represents a special type of adverse drug reaction. More than