

Liver disease is the most important cause of increased aminotransaminase activity in serum. In most types of liver disease, ALT activity is higher than that of AST. Exceptions may be seen, however, in (1) alcoholic hepatitis, (2) hepatic cirrhosis, and (3) liver neoplasia. The activity of ALT may be persistently normal in 15% to 50% of patients with chronic hepatitis C, but the likelihood of continuously normal ALT activity decreases with an increasing number of measurements. In acetaminophen-induced hepatic injury, the peak of aminotransaminase activity is more than 85 times the URL in 90% of cases—a value rarely seen with acute viral hepatitis. The activities of aminotransferases are also elevated in nonalcoholic fatty liver disease (NAFLD). This disease includes a spectrum of liver pathology, from simple steatosis to nonalcoholic steatohepatitis (NASH), in which inflammatory changes and focal necrosis may progress to (1) liver fibrosis, (2) cirrhosis, and (3) hepatic failure. Twofold to fivefold elevations of the activities of both enzymes occur in patients with primary or metastatic carcinoma of the liver, with the activity of AST usually higher than ALT activity, but their values are often within the reference interval in the early stages of malignant infiltration of the liver. Slight or moderate elevations in AST and ALT activities have been observed after administration of various medications, such as (1) nonsteroidal antiinflammatory drugs, (2) antibiotics, (3) antiepileptic drugs, and (4) statins. Over-the-counter medications and herbal preparations are also implicated. In patients with (1) increased aminotransaminase activities, (2) negative viral markers, and (3) a negative history for drugs or alcohol ingestion. The diagnostic evaluation should include investigation of less common causes of chronic hepatic injury such as (1) hemochromatosis, (2) Wilson disease, (3) autoimmune hepatitis, (4) primary biliary cirrhosis, (5) .sclerosing cholangitis, (6) celiac disease, and (7)  $\alpha$ 1-antitrypsin deficiency.