Liver disease is the most important cause of increased aminotransaminase activity in serum.The demonstration of macro–AST in serum is obtained by differential precipitation with polyethylene glycol (PEG) 6000 (see "Amylase" section later in this chapter)In viral hepatitis and other forms of liver disease associated with acute hepatic necrosis, serum AST and ALT activities are elevated even before the clinical signs and symptoms of disease (such as jaundice) appear. Activities for both enzymes may reach values as high as 100 times the URL, although 10–fold to 40–fold elevations are most frequently encountered. The most efficient aminotransferase threshold for diagnosing acute liver injury lies at seven times the URL (clinical sensitivity and specificity >95%).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 (see Chapter 37).Peak values of aminotransaminase activity occur between the 7th and 12th days; activities then gradually decrease, reaching physiological concentrations by the 3rd to 5th week if recovery is uneventful.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 acetaminopheninduced 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.Persistence of increased ALT activity for longer than 6 months after an episode of acute hepatitis is used to diagnose chronic hepatitis.Exceptions may be seen, however, in (1) alcoholic hepatitis, (2) hepatic cirrhosis, and (3) liver neoplasia.Most patients with chronic hepatitis have maximum ALT activities less than seven times theURL.In patients with acute hepatitis C, the activity of ALT should be measured periodically over the next 1 to 2 years to determine if it becomes and stays normal.The activities of aminotransferases are also elevated in nonalcoholic fatty liver disease (NAFLD).Peak activities bear no relationship to prognosis and may fall with worsening of the patient's condition.The clinical situation in toxic hepatitis is different from that in infectious hepatitis.In most types of liver disease, ALT activity is higher than that of AST.

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