

ischemic liver injury (prolonged hypotension or acute heart failure), or (3) toxin- or drug-induced liver injury.

The pattern of the aminotransferase elevation can be helpful diagnostically. In most acute hepatocellular disorders, the ALT is higher than or equal to the AST. Whereas the AST:ALT ratio is typically <1 in patients with chronic viral hepatitis and nonalcoholic fatty liver disease, a number of groups have noted that as cirrhosis develops, this ratio rises to >1 . An AST:ALT ratio $>2:1$ is suggestive, whereas a ratio $>3:1$ is highly suggestive, of alcoholic liver disease. The AST in alcoholic liver disease is rarely >300 IU/L, and the ALT is often normal. A low level of ALT in the serum is due to an alcohol-induced deficiency of pyridoxal phosphate.

The aminotransferases are usually not greatly elevated in obstructive jaundice. One notable exception occurs during the acute phase of biliary obstruction caused by the passage of a gallstone into the common bile duct. In this setting, the aminotransferases can briefly be in the 1000–2000 IU/L range. However, aminotransferase levels decrease quickly, and the biochemical tests rapidly evolve into those typical of cholestasis.

ENZYMES THAT REFLECT CHOLESTASIS The activities of three enzymes—alkaline phosphatase, 5'-nucleotidase, and γ -glutamyl transpeptidase (GGT)—are usually elevated in cholestasis. Alkaline phosphatase and 5'-nucleotidase are found in or near the bile canalicular membrane of hepatocytes, whereas GGT is located in the endoplasmic reticulum and in bile duct epithelial cells. Reflecting its more diffuse localization in the liver, GGT elevation in serum is less specific for cholestasis than are elevations of alkaline phosphatase or 5'-nucleotidase. Some have advocated the use of GGT to identify patients with occult alcohol use. Its lack of specificity makes its use in this setting questionable.

The normal serum alkaline phosphatase consists of many distinct isoenzymes found in the liver, bone, placenta, and, less commonly, the small intestine. Patients over age 60 can have a mildly elevated alkaline phosphatase (1–1.5 times normal), whereas individuals with blood types O and B can have an elevation of the serum alkaline phosphatase after eating a fatty meal due to the influx of intestinal