TABLE 39-1 LABORATORY TESTS OF HEPATIC FUNCTION

LIVER ASSAY*	LIVER FUNCTION	ABNORMALITY
Serum albumin (3.5-5.5 g/dL)	Assess the biosynthetic capacity of the liver (days to weeks)	Decreased synthetic capacity Protein malnutrition Nephrotic syndrome Protein-losing enteropathy
Prothrombin time (11-14 sec)	Assess the biosynthetic capacity of the liver (hours to days)	Decreased synthetic capacity (especially factors II and VII) Vitamin K deficiency Consumptive coagulopathy
Serum bilirubin (0.2-1.3 mg/dL) (3.4-22.2 µmol/L)	Extraction of bilirubin from blood; conjugation and excretion into bile	Hemolysis Diffuse liver disease Cholestasis Extrahepatic bile duct obstruction Congenital disorders of bilirubin metabolism
Serum alkaline phosphatase (39-136 units/L)	Present in the cells lining the biliary tree	Bile duct obstruction Cholestasis Infiltrative liver disease (neoplasms, granulomas) Bone destruction, remodeling Pregnancy
γ-glutamyl transpeptidase (7-45 units/L)	Highly sensitive to hepatocyte damage and cholestasis	
5'-nucleotidase (2-17 units/L)	More specific for the liver and for cholestasis than GGT	
Aspartate aminotransferase (AST) or SGOT (5-40 Units/L)	Represent hepatocyte inflammation and damage	Hepatocellular necrosis Cardiac or skeletal muscle necrosis
Alanine aminotransferase or SGPT (5-65 Units/L)	Represent hepatocyte inflammation and damage	Same as AST; however, more specific for liver cell damage

*The reference intervals given here in conventional metric units and in SI units are from several large medical centers. Always use the reference intervals provided by your clinical laboratory, since intervals may be method-dependent.

An isolated elevated ALP level may be the only clue to obstruction of the common bile duct or neoplastic or granulomatous hepatic disease. Elevated serum ALP levels with normal 5′-NT and GGT usually suggests a nonhepatic cause (e.g., bone disease, pregnancy, chronic renal failure, lymphoma, congestive heart failure). Electrophoretic fractionation of ALP isoenzymes may be useful to confirm alternative sources.

Elevated bilirubin levels also are characteristic of cholestasis. Bilirubin is present in the serum in two forms: unconjugated (indirect) and conjugated (direct). Under normal conditions, total serum bilirubin levels are less than 1 mg/dL, with the conjugated fraction representing up to 30% of the total. The serum bilirubin level reflects a balance between bilirubin production and its conjugation and excretion into bile by the liver.

The differential diagnosis for hyperbilirubinemia (see Chapter 42) requires consideration of an extensive list of disorders in which there are alterations of bilirubin production (hematologic disorders with predominantly unconjugated hyperbilirubinemia), hepatic metabolism (congenital abnormalities of bilirubin conjugation, liver disease), or excretion (congenital abnormalities of bilirubin excretion or biliary obstruction with predominantly conjugated hyperbilirubinemia). Hence, an elevated serum bilirubin is not specific but should initiate a more detailed evaluation for more specific causes.

Importantly, individual tests often do not indicate the nature of the underlying liver disease; hence, the common use of the LFT panel of tests. The overall pattern of liver test abnormalities and the relative magnitudes of abnormalities in individual tests often provide significant insights, including categorization as to whether the liver disease is primarily hepatocellular or cholestatic. Figure 39-1 outlines common patterns of liver test abnormalities and common accompanying diagnostic evaluation.

Hepatic Synthetic Function

The serum albumin level and the PT (expressed as the international normalized ratio [INR]) reflect the hepatic capacity for protein synthesis. The PT is dependent on coagulation factors II, V, VII, and X and responds rapidly to altered hepatic function because of the short serum half-lives of factors II and VII (about 6 hours). This makes measurement of PT a useful marker of hepatic synthetic function that can be measured as frequently as daily. However, because serum levels of factors II, VII, IX, and X are dependent on vitamin K, coexistent vitamin K deficiency must be excluded or treated before PT can be used as a measure of intrinsic hepatic function. In contrast, the serum half-life of albumin is 14 to 20 days, and serum levels fall with prolonged liver dysfunction or acute liver impairment. Malnutrition and renal or gastrointestinal losses merit consideration in the evaluation of significant hypoalbuminemia, especially if the PT is relatively well preserved.

QUANTITATIVE TESTS OF LIVER FUNCTION

Quantitative liver tests that depend on the capacity of the liver to transform or transport a test agent have been developed but have not received widespread application. These include indocyanine green clearance, galactose elimination capacity, aminopyrine breath test, antipyrine clearance, monoethylglycinexylidide, and caffeine clearance. They may be superior to conventional biochemical tests in predicting prognosis, but their clinical utility has not been established, and they are limited primarily to research centers.

Specific Disease Markers

Elevations of individual γ-globulins can be suggestive of specific diseases. For example, autoimmune hepatitis is associated with an elevated total immunoglobulin G (IgG) level and the presence of autoantibodies such as antinuclear antibody (ANA), anti–smooth muscle antibody (ASMA), and anti–liver/kidney microsomal antibody type 1 (anti-LKM1). IgG4-related disease is an autoimmune phenomenon in which increased IgG4 levels cause dysfunction in multiple organs, including autoimmune cholangitis and autoimmune pancreatitis. Alcoholic cirrhosis is associated with high IgA levels, and primary biliary cirrhosis is associated with elevated IgM levels.

Viruses are detected by polymerase chain reaction (PCR), enzyme assays, and genotyping. Screening can be performed for specific diseases such as hemochromatosis (iron panels and *HFE* gene mutation testing). Levels of α_1-antitrypsin and serum ceruloplasmin are measured to evaluate patients with liver disease