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TABLE 347-6 Child-Pugh Classification of Cirrhosis POINTS TOWARD TOTAL SCORE FACTOR UNITS

Serum bilirubin $\mu\text{mol/L}$ <34 34-51

“ 51 mg/dL <2.0 2.0-3.0 3.0 Serum albumin g/L 35 30-35 <30 g/dL 3.5 3.0-3.5 <3.0 Prothrombin time Seconds prolonged <4 4-6 6 INRa <1.7 1.7-2.3 2.3 Ascites None Easily controlled Poorly controlled Hepatic encephalopathy None Minimal Advanced aInternational normalized ratio. Note: The Child-Pugh score is calculated by adding the scores for the five factors and can range from 5 to 15. The resulting Child-Pugh class can be A (a score of 5-6), B (7-9), or C (≥ 10). Decompensation indicates cirrhosis, with a Child-Pugh score of ≥ 7 (class B). This level has been the accepted criterion for listing a patient for liver transplantation. classification, with a scoring system of 5-15: scores of 5 and 6 represent Child-Pugh class A (consistent with “compensated cirrhosis”), scores of 7-9 represent class B, and scores of 10-15 represent class C (Table 347-6). This scoring system was initially devised to stratify patients with cirrhosis into risk groups before portal decompressive surgery. The Child-Pugh score is a reasonably reliable predictor of survival in many liver diseases and predicts the likelihood of major complications of cirrhosis, such as bleeding from varices and spontaneous bacterial peritonitis. This classification scheme was used to assess prognosis in cirrhosis and to provide standard criteria for listing a patient as a candidate for liver transplantation (Child-Pugh class B). The Child-Pugh system has been replaced by the Model for End-Stage Liver Disease (MELD) system for the latter purpose. The MELD score is a prospectively derived system designed to predict the short-term mortality of patients awaiting orthotopic liver transplant and following a transjugular intrahepatic portosystemic shunt (TIPS). This score is calculated using three readily available objective variables: the prothrombin time expressed as the international normalized ratio (INR), the serum bilirubin level, and the serum creatinine concentration. The ability of the MELD score to predict outcome after liver transplantation is regularly monitored

and was modified to increase its accuracy and improve allocation of donated livers. These modifications include serum sodium concentration as a factor in the model and a reweighting of the MELD components. A separate scoring system, the Pediatric End-Stage Liver Disease (PELD) score, is used for children (<12 years old). Transient elastography has also been used to stage cirrhosis and has been shown to be useful in predicting complications such as variceal hemorrhage, ascites development, and liver-related death. The MELD system provides a more objective means of assessing disease severity and has less center-to-center variation than the Child-Pugh score as well as a wider range of values. The MELD and PELD systems are currently used to establish priority listing for liver transplantation in the United States. Convenient MELD and PELD calculators are available via the Internet (<https://optn.transplant.hrsa.gov>). ■

■ **NONSPECIFIC ISSUES IN THE MANAGEMENT OF PATIENTS WITH LIVER DISEASE**
Specifics on the management of different forms of acute or chronic liver disease are supplied in subsequent chapters, but certain issues are applicable to any patient with liver disease. These issues include advice regarding alcohol use, medication use, vaccination, and surveillance for certain liver diseases and complications of liver disease. Alcohol should be used sparingly, if at all, by patients with liver disease. Abstinence from alcohol should be encouraged for all patients with alcohol-related liver disease, patients with cirrhosis, and patients receiving interferon-based therapy for hepatitis B or D and during

antiviral therapy of hepatitis C. With regard to vaccinations, all patients with liver disease should receive hepatitis A and hepatitis B vaccine, if not previously vaccinated, and screened for hepatitis C if not already done. Adherence to the recommendations of the Centers for Disease Control and Prevention (CDC) on other adult vaccinations should also be encouraged. Patients with liver disease should exercise caution in using any medications other than those that are most necessary. Drug-induced hepatotoxicity can mimic many forms of liver disease and can cause exacerbations of chronic hepatitis and cirrhosis; drugs should be suspected in any situation in which the cause of exacerbation is unknown. Finally, consideration should be given to surveillance for complications of chronic liver disease such as variceal hemorrhage and HCC. Cirrhosis warrants upper endoscopy to assess the presence of varices, and the patient should receive chronic therapy with beta blockers or should be offered endoscopic obliteration if large varices are found. Moreover, cirrhosis warrants screening and long-term surveillance for development of HCC. While the optimal regimen for such surveillance has not been established, an appropriate approach is US of the liver at 6- to 12-month intervals.

■ **FURTHER READING** Jeng W-J et al: Hepatitis B. *Lancet* 401:1039, 2023. Manns MP et al: Breakthroughs in hepatitis C research: From discovery to cure. *Gastroenterol Hepatol* 19:533, 2022. Powell EE et al: Non-alcoholic fatty liver disease. *Lancet* 397:2212, 2021. Tapper EB, Lok AS: Use of liver imaging and biopsy in clinical practice. *N Engl J Med* 377:756, 2017. **CHAPTER 348**
Evaluation of Liver Function Emily D. Bethea, Daniel S. Pratt

Evaluation of Liver

Function There are a number of tests that can be used to evaluate liver function. These tests include biochemical tests, radiologic tests, and pathologic tests. Serum biochemical tests, also commonly referred to as “liver function tests,” can be used to (1) detect the presence of liver disease, (2) distinguish among different types of liver disorders, (3) gauge the extent of liver damage, and (4) follow the response to treatment. However, serum biochemical tests have shortcomings. They lack sensitivity and specificity; they can be normal in patients with serious liver disease and abnormal in patients with diseases that do not affect the liver. Liver tests rarely suggest a specific diagnosis; rather, they suggest a general category of liver disease, such as hepatocellular or cholestatic, which then further directs the evaluation. The liver carries out thousands of biochemical functions, most of which cannot be easily measured by blood tests. Laboratory tests measure only a limited number of these functions. In fact, many tests, such as the aminotransferases and alkaline phosphatase, do not measure liver function at all. Rather, they detect liver cell damage or interference with bile flow. Thus, no one biochemical test enables the clinician to accurately assess the liver’s total functional capacity. To increase the sensitivity and the specificity of biochemical tests in the detection of liver disease, it is best to use them as a battery. Tests usually employed in clinical practice include the bilirubin, aminotransferases, alkaline phosphatase, albumin, and prothrombin time tests. When more than one of these tests provide abnormal findings or the findings are persistently abnormal on serial determinations, the probability of liver disease is high. When all test results are normal, the probability of missing occult liver disease is low.

Serum Bilirubin (See also Chap. 52) Bilirubin, a breakdown product of the porphyrin ring of heme-containing proteins, is found in the blood in two fractions—conjugated and unconjugated. The unconjugated fraction, also termed the indirect fraction, is insoluble in water and is bound to albumin in the blood. The conjugated (direct) bilirubin fraction is water-soluble and can therefore be excreted by the kidney. Normal values of total serum bilirubin are reported between 1 and 1.5 mg/dL with 95% of a normal population falling between 0.2 and 0.9 mg/dL. If the direct-acting fraction is <15% of the total, the bilirubin can be considered to all be indirect. The most frequently reported upper limit of normal for conjugated bilirubin is 0.3 mg/dL.

Elevation of the unconjugated fraction of bilirubin is rarely due to liver disease. An isolated elevation of unconjugated bilirubin is seen primarily in hemolytic disorders and in a number of genetic conditions such as Crigler-Najjar and Gilbert’s syndromes (Chap. 52). Isolated unconjugated hyperbilirubinemia (bilirubin elevated but <15% direct) should prompt a workup for hemolysis (Fig. 348-1). In the absence of hemolysis, an isolated, unconjugated hyperbilirubinemia in an otherwise healthy patient can be attributed to Gilbert’s syndrome, and no further evaluation is required. In contrast, conjugated hyperbilirubinemia almost always implies liver or biliary tract disease. The rate-limiting step in bilirubin metabolism is not conjugation of bilirubin, but rather the transport of conjugated bilirubin into the bile canaliculi. Thus, elevation of the conjugated fraction may be seen in any type of liver disease including fulminant liver failure. In most liver diseases, both conjugated and unconjugated fractions of the bilirubin tend to be elevated. Except in PART 10 Disorders of the Gastrointestinal System Liver Tests Isolated elevation of the bilirubin Fractionate bilirubin Ducts not dilated Dilated ducts

15% Direct Check AMA <15% Direct AMA positive AMA negative Evaluation for hemolysis Dubin-Johnson or Rotor syndrome W/U positive W/U negative Hepatocellular pattern (see Table 348-1) Hemolysis Gilbert's syndrome Review drug list Hepatitis C antibody Hepatitis B surface Ag Iron, TIBC, ferritin ANA, SPEP Ceruloplasmin (if patient <40) Ultrasound to look for fatty liver W/U negative R/O Celiac disease Consider other nonhepatic cause W/U negative Consider liver biopsy FIGURE 348-1 Algorithm for the evaluation of chronically abnormal liver tests. Ag, antigen; AMA, antimitochondrial antibody; ANA, antinuclear antibody; Bx, biopsy; CT, computed tomography; ERCP, endoscopic retrograde cholangiopancreatography; GGT, γ -glutamyl transpeptidase; MRCP, magnetic resonance cholangiopancreatography; R/O, rule out; SPEP, serum protein electrophoresis; TIBC, total iron-binding capacity; W/U, workup.

the presence of an isolated hyperbilirubinemia, fractionation of the bilirubin is rarely helpful in determining the cause of jaundice. Although the degree of elevation of the serum bilirubin has not been critically assessed as a prognostic marker, it is important in a number of conditions. In viral hepatitis, the higher the serum bilirubin, the greater is the hepatocellular damage. Total serum bilirubin correlates with poor outcomes in alcoholic hepatitis. It is also a critical component of the Model for End-Stage Liver Disease (MELD) score, a tool used to estimate survival of patients with end-stage liver disease, prioritize patients awaiting liver transplantation, and assess operative risk of patients with cirrhosis. An elevated total serum bilirubin in patients with drug-induced liver disease indicates more severe injury. Total bilirubin has also been shown to be of prognostic value in primary biliary cholangitis. Unconjugated bilirubin always binds to albumin in the serum and is not filtered by the kidney. Therefore, any bilirubin found in the urine is conjugated bilirubin; the presence of bilirubinuria implies the presence of liver disease or obstructive jaundice. A urine dipstick test can theoretically give the same information as fractionation of the serum bilirubin. This test is almost 100% accurate. Phenothiazines may give a false-positive reading with the Ictotest tablet. In patients recovering from jaundice, the urine bilirubin clears prior to the serum bilirubin. Serum Enzymes The liver contains thousands of enzymes, some of which are also present in the serum in very low concentrations. These enzymes have no known function in the serum and behave like other Cholestatic pattern (see Table 348-1) Isolated elevation of the alkaline phosphatase Review drugs Ultrasound CT/MRCP/ERCP ERCP/Liver Bx Liver Bx Fractionate the alkaline phosphatase or check GGT or 5' nucleotidase to assess origin of alkaline phosphatase Alkaline phos. of liver origin Alkaline phos. of bone origin Bone Eval Ultrasound Review drug list Check AMA Dilated ducts Ducts not dilated and/or AMA positive MRCP Liver biopsy

serum proteins. They are distributed in the plasma and in interstitial fluid and have characteristic half-lives, which are usually measured in days. Very little is known about the catabolism of serum enzymes, although they are probably cleared by cells in the reticuloendothelial system. The elevation of a given enzyme activity in the serum is thought to primarily reflect its increased rate of entrance into serum from damaged liver cells. Serum enzyme tests can be grouped into two categories: (1) enzymes whose elevation in serum reflects damage to hepatocytes and (2) enzymes whose elevation in serum reflects cholestasis. ENZYMES THAT REFLECT DAMAGE TO HEPATOCYTES The amino transferases (transaminases) are sensitive indicators of liver cell injury

and are most helpful in recognizing acute hepatocellular diseases such as hepatitis. They include aspartate aminotransferase (AST) and alanine aminotransferase (ALT). AST is found in the liver, cardiac muscle, skeletal muscle, kidneys, brain, pancreas, lungs, leukocytes, and erythrocytes in decreasing order of concentration. ALT is found primarily in the liver and is therefore a more specific indicator of liver injury. The aminotransferases are normally present in the serum in low concentrations. These enzymes are released into the blood in greater amounts when there is damage to the liver cell membrane, resulting in increased permeability. Liver cell necrosis is not required for the release of the aminotransferases, and there is a poor correlation between the degree of liver cell damage and the level of the aminotransferases. Thus, the absolute elevation of the aminotransferases is of no prognostic significance in acute hepatocellular disorders. The normal range for aminotransferases varies widely among laboratories, but generally ranges from 10 to 40 IU/L. The interlaboratory variation in normal range is due to technical reasons; no reference standards exist to establish upper limits of normal for ALT and AST. Some have recommended revisions of normal limits of the aminotransferases to adjust for sex and body mass index, but others have noted the potential costs and unclear benefits of implementing this change. Any type of liver cell injury can cause modest elevations in the serum aminotransferases. Levels of up to 300 IU/L are nonspecific and may be found in any type of liver disorder. Minimal ALT elevations in asymptomatic blood donors rarely indicate severe liver disease; studies have shown that fatty liver disease is the most likely explanation. Striking elevations—that is, aminotransferases >1000 IU/L—occur almost exclusively in disorders associated with extensive hepatocellular injury such as (1) viral hepatitis, (2) 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 alcohol-related liver disease. The AST in alcohol-related 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 alkaline phosphatase into the blood. It is also elevated in children and adolescents undergoing rapid bone growth because of bone alkaline phosphatase and late in normal pregnancies due to the influx of placental alkaline phosphatase. Elevation of liver-derived alkaline phosphatase is not totally specific for cholestasis, and a less than threefold elevation can be seen in almost any type of liver disease. Alkaline phosphatase elevations greater than four times normal occur primarily in patients with cholestatic liver disorders, infiltrative liver diseases such as cancer and amyloidosis, and bone conditions characterized by rapid bone turnover (e.g., Paget's disease). In bone diseases, the elevation is due to increased amounts of the bone isoenzymes. In liver diseases, the elevation is almost always due to increased amounts of the liver isoenzyme. If an elevated serum alkaline phosphatase is the only abnormal finding in an apparently healthy person or if the degree of elevation is higher than expected in the clinical setting, identification of the source of elevated isoenzymes is helpful (Fig. 348-1). This problem can be approached in two ways. First, and most precise, is the fractionation of the alkaline phosphatase by electrophoresis. The second, best substantiated, and most available approach involves the measurement of serum 5'-nucleotidase or GGT.

CHAPTER 348 In the absence of jaundice or elevated aminotransferases, an elevated alkaline phosphatase of liver origin often, but not always, suggests early cholestasis and, less often, hepatic infiltration by tumor or granulomata. Other conditions that cause isolated elevations of the alkaline phosphatase include primary biliary cholangitis, primary or secondary sclerosing cholangitis, Hodgkin's disease, diabetes, hyperthyroidism, congestive heart failure, and amyloidosis.

Evaluation of Liver Function The level of serum alkaline phosphatase elevation is not helpful in distinguishing between intrahepatic and extrahepatic cholestasis. There is essentially no difference among the values found in obstructive jaundice due to cancer, common duct stone, sclerosing cholangitis, or bile duct stricture. Values are similarly increased in patients with intrahepatic cholestasis due to drug-induced hepatitis, primary biliary cholangitis, sepsis, rejection of transplanted livers, and, rarely, alcohol-induced steatohepatitis. Values are also greatly elevated in hepatobiliary disorders seen in patients with AIDS (e.g., AIDS cholangiopathy due to cytomegalovirus or cryptosporidial infection and tuberculosis with hepatic involvement).

■ ■ **TESTS THAT MEASURE BIOSYNTHETIC FUNCTION OF THE LIVER**

Serum Albumin Serum albumin is synthesized exclusively by hepatocytes. Serum albumin has a long half-life: 18–20 days, with ~4% degraded per day. Because of this slow turnover, the serum albumin is not a good indicator of acute or mild hepatic dysfunction; only minimal changes in the serum albumin are seen in acute liver conditions such as viral hepatitis, drug-related hepatotoxicity, and obstructive jaundice. In hepatitis, albumin levels <3 g/dL should raise the possibility of chronic liver disease. Hypoalbuminemia is more common in chronic liver disorders such as cirrhosis and usually reflects severe liver damage and decreased albumin synthesis. However, hypoalbuminemia is not specific for liver disease and may occur in protein malnutrition of any cause, as well as protein-losing enteropathies, nephrotic syndrome, and chronic infections that are associated with prolonged increases in levels of cytokines that inhibit albumin synthesis, such as serum interleukin 1 and/or tumor necrosis factor. Serum albumin should not be measured to screen patients in whom there is no suspicion of liver disease. A general medical clinic study of consecutive patients in whom no

indications were present for albumin measurement showed that although

12% of patients had abnormal test results, the finding was of clinical importance in only 0.4%.

Serum Globulins Serum globulins are a group of proteins made up of γ globulins (immunoglobulins) produced by B lymphocytes and α and β globulins produced primarily in hepatocytes. γ Globulins are increased in chronic liver disease, such as chronic hepatitis and cirrhosis. In cirrhosis, the increased serum γ globulin concentration is due to the increased synthesis of antibodies, some of which are directed against intestinal bacteria. This occurs because the cirrhotic liver fails to clear bacterial antigens that normally reach the liver through the hepatic circulation. Increases in the concentration of specific isotypes of γ globulins are often helpful in the recognition of certain chronic liver diseases. Diffuse polyclonal increases in IgG levels are common in autoimmune hepatitis; increases $>100\%$ should alert the clinician to this possibility. Increases in the IgM levels are common in primary biliary cholangitis, whereas increases in the IgA levels occur in alcoholic liver disease. ■ ■

COAGULATION FACTORS With the exception of factor VIII, which is produced by vascular endothelial cells, the blood clotting factors are made exclusively in hepatocytes. Their serum half-lives are much shorter than albumin, ranging from 6 h for factor VII to 5 days for fibrinogen. Because of their rapid turnover, measurement of the clotting factors is the single best acute measure of hepatic synthetic function and helpful in both diagnosis and assessing the prognosis of acute parenchymal liver disease. Useful for this purpose is the serum prothrombin time, which collectively measures factors II, V, VII, and X. Biosynthesis of factors II, VII, IX, and X depends on vitamin K. The international normalized ratio (INR) is used to express the degree of anticoagulation on warfarin therapy. The INR standardizes prothrombin time measurement according to the characteristics of the thromboplastin reagent used in a particular lab, which is expressed as an International Sensitivity Index (ISI); the ISI is then used in calculating the INR.

PART 10 Disorders of the Gastrointestinal System The prothrombin time may be elevated in hepatitis and cirrhosis as well as in disorders that lead to vitamin K deficiency such as obstructive jaundice or fat malabsorption of any kind. Marked prolongation of the prothrombin time, >5 s above control and not corrected by parenteral vitamin K administration, is a poor prognostic sign in acute viral hepatitis and other acute and chronic liver diseases. The INR, along with the total serum bilirubin, creatinine, albumin, and sodium, are components of the MELD 3.0 score, which is used as a measure of hepatic decompensation and to allocate organs for liver transplantation. ■ ■

OTHER DIAGNOSTIC TESTS Although tests may direct the physician to a category of liver disease, additional biochemical testing, radiologic testing, and procedures are often necessary to make the proper diagnosis, as shown in Fig. 348-1. The most commonly used ancillary tests are reviewed here, as are the noninvasive tests available for assessing hepatic fibrosis. **Ammonia** Ammonia is produced in the body during normal protein metabolism and by intestinal bacteria, primarily those in the colon. The liver plays a role in the detoxification of ammonia by converting it to urea, which is excreted by the kidneys. Striated muscle also plays a role in detoxification of ammonia, where it is combined with glutamic acid to form glutamine. Patients with advanced liver disease typically have significant muscle wasting, which likely contributes to hyperammonemia. Some physicians use the blood ammonia for detecting encephalopathy or for monitoring hepatic synthetic function, although its use for either of these indications has problems. There is very poor correlation between either the presence or the severity of acute encephalopathy and elevation of blood ammonia; it can be occasionally useful for identifying occult liver disease in patients with mental status changes. There is also a poor correlation of the blood serum ammonia and hepatic function.

The ammonia can be elevated in patients with severe portal hypertension and portal blood shunting

around the liver even in the presence of normal or near-normal hepatic function. Elevated arterial ammonia levels have been shown to correlate with outcome in fulminant hepatic failure. Liver Biopsy Percutaneous biopsy of the liver is a safe procedure that is easily performed with local anesthesia and ultrasound guidance. Liver biopsy is of proven value in the following situations: (1) hepatocellular disease of uncertain cause, (2) prolonged hepatitis with the possibility of autoimmune hepatitis, (3) unexplained hepatomegaly, (4) unexplained splenomegaly, (5) hepatic lesions uncharacterized by radiologic imaging, (6) fever of unknown origin, and (7) staging of malignant lymphoma. Liver biopsy is most accurate in disorders causing diffuse changes throughout the liver and is subject to sampling error in focal disorders. Liver biopsy should not be the initial procedure in the diagnosis of cholestasis. The biliary tree should first be assessed for signs of obstruction. Contraindications to performing a percutaneous liver biopsy include significant ascites and prolonged INR. Under these circumstances, the biopsy can be performed via the transjugular approach. Noninvasive Tests to Detect Hepatic Fibrosis Although liver biopsy is the standard for the assessment of hepatic fibrosis, noninvasive measures of hepatic fibrosis have gained favor. These measures include multiparameter tests aimed at detecting and staging the degree of hepatic fibrosis and imaging techniques. FibroTest (marketed as FibroSure in the United States) is the best evaluated of the multiparameter blood tests. The test incorporates haptoglobin, bilirubin, GGT, apolipoprotein A-I, and α 2-macroglobulin and has been found to have high positive and negative predictive values for diagnosing advanced fibrosis in patients with chronic hepatitis C, chronic hepatitis B, alcoholic liver disease, or metabolic dysfunction-associated steatotic liver disease (MASLD) and patients taking methotrexate for psoriasis. The Enhanced Liver Fibrosis (ELF) test is a multiparameter blood test that uses markers of fibrogenesis and cytolysis to estimate hepatic fibrosis: type III procollagen peptide, hyaluronic acid, and tissue inhibitor of metalloproteinase-1. It has been validated in patients with MASLD and is gaining favor in cholestatic liver disease. The FIB4 index is a liver fibrosis biomarker that is easily calculated using age and three routine laboratory parameters: ALT, AST, and platelet count. While originally proposed to help assess hepatic fibrosis in patients with human immunodeficiency virus and hepatitis C virus coinfection, it has been validated for hepatitis C virus, hepatitis B virus, and MASLD. Transient elastography (TE), marketed as FibroScan, and magnetic resonance elastography (MRE) both have gained U.S. Food and Drug Administration approval for use in the management of patients with liver disease. TE uses ultrasound waves to measure hepatic stiffness noninvasively. TE has been shown to be accurate for identifying advanced fibrosis in patients with chronic hepatitis C, primary biliary cholangitis, hemochromatosis, nonalcoholic fatty liver disease, and recurrent chronic hepatitis after liver transplantation. MRE has been found to be superior to TE for staging liver fibrosis in patients with a variety of chronic liver diseases but requires access to a magnetic resonance imaging scanner and is more expensive. Ultrasonography Ultrasonography is the first diagnostic test to use in patients whose liver tests suggest cholestasis, to look for the presence of a dilated intrahepatic or extrahepatic biliary tree or to identify gallstones. In addition, it shows space-occupying lesions within the liver, enables the clinician to distinguish between cystic and solid masses, and helps direct percutaneous biopsies. Ultrasound with Doppler imaging can detect the patency of the portal vein, hepatic artery, and hepatic veins and determine the direction of blood flow. This is the first test ordered in patients suspected of having Budd-Chiari syndrome. ■

■USE OF LIVER TESTS As previously noted, the best way to increase the sensitivity and specificity of laboratory tests in the detection of liver disease is to employ a battery of tests that includes the

aminotransferases, alkaline phosphatase, bilirubin, albumin, and prothrombin time along with the

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