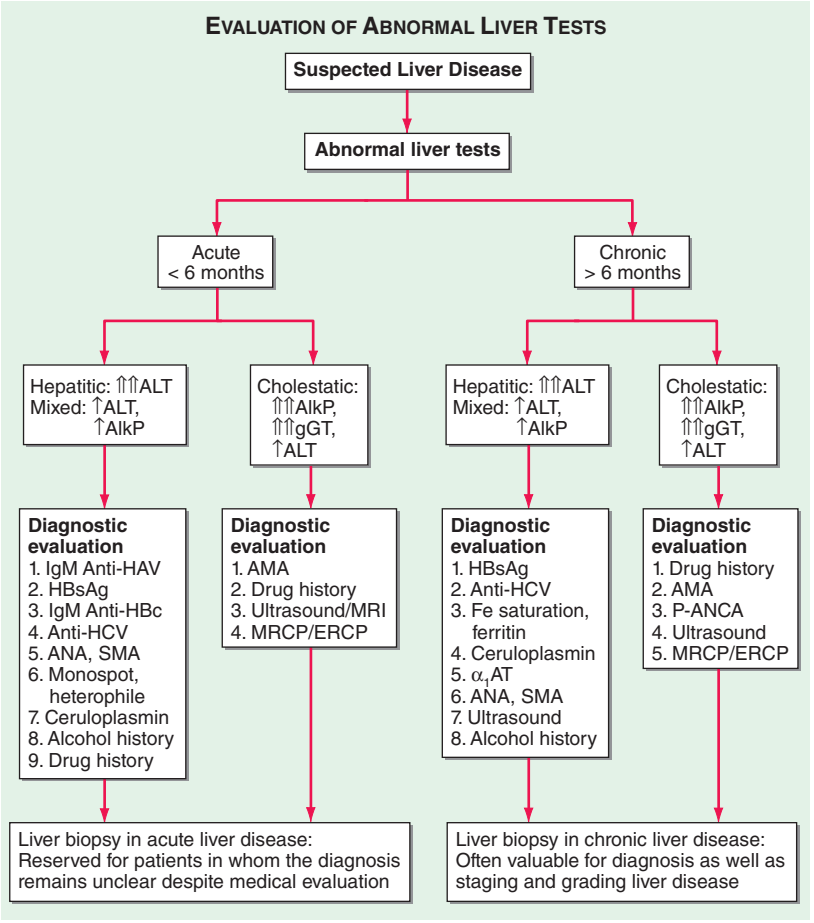

FIGURE 357-1 Algorithm for evaluation of abnormal liver tests. For patients with suspected liver disease, an appropriate approach to evaluation is initial routine liver testing—e.g., measurement of serum bilirubin, albumin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (AlkP). These results (sometimes complemented by testing of γ-glutamyl transpeptidase; gGT) will establish whether the pattern of abnormalities is hepatic, cholestatic, or mixed. In addition, the duration of symptoms or abnormalities will indicate whether the disease is acute or chronic. If the disease is acute and if history, laboratory tests, and imaging studies do not reveal a diagnosis, liver biopsy is appropriate to help establish the diagnosis. If the disease is chronic, liver biopsy can be helpful not only for diagnosis but also for grading of the activity and staging the progression of disease. This approach is generally applicable to patients without immune deficiency. In patients with HIV infection or recipients of bone marrow or solid organ transplants, the diagnostic evaluation should also include evaluation for opportunistic infections (e.g., with adenovirus, cytomegalovirus, *Coccidioides*, hepatitis E virus) as well as for vascular and immunologic conditions (veno-occlusive disease, graft-versus-host disease). HAV, hepatitis A virus; HCV, hepatitis C virus; HBsAg, hepatitis B surface antigen; anti-HBc, antibody to hepatitis B core (antigen); ANA, antinuclear antibody; SMA, smooth-muscle antibody; MRCP, magnetic resonance cholangiopancreatography; ERCP, endoscopic retrograde cholangiopancreatography; α_1 AT, α_1 antitrypsin; AMA; antimitochondrial antibody; P-ANCA, peripheral antineutrophil cytoplasmic antibody.

ablation and chemoembolization of cancerous lesions, the insertion of drains into hepatic abscesses, the measurement of portal pressure, and the creation of vascular shunts in patients with portal hypertension. Which modality to use depends on factors such as availability, cost, and experience of the radiologist with each technique.

Liver Biopsy Liver biopsy remains the criterion standard in the evaluation of patients with liver disease, particularly chronic liver disease. Liver biopsy is necessary for diagnosis in selected instances but is more often useful for assessment of the severity (grade) and stage of liver damage, prediction of prognosis, and monitoring of the response to treatment. The size of the liver biopsy sample is an important determinant of reliability; a length of 1.5–2 cm is necessary for accurate assessment of fibrosis. In the future, noninvasive means of assessing disease activity (batteries of blood tests) and fibrosis (elastography and fibrosis markers) may replace liver biopsy for the staging and grading of disease.

GRADING AND STAGING OF LIVER DISEASE

Grading refers to an assessment of the severity or activity of liver disease, whether acute or chronic; active or inactive; and mild, moderate, or severe. Liver biopsy is the most accurate means of assessing severity, particularly in chronic liver disease. Serum aminotransferase levels serve as convenient and noninvasive markers for disease activity but do not always reliably reflect disease severity. Thus, normal serum aminotransferase levels in patients with hepatitis B surface antigen in serum may indicate the inactive carrier state or may reflect mild chronic hepatitis B or hepatitis B with fluctuating disease activity. Serum testing for hepatitis B e antigen and hepatitis B virus DNA can help sort out these different patterns, but these markers can also fluctuate and change over time. Similarly, in chronic hepatitis C, serum aminotransferase levels can be normal despite moderate disease activity. Finally, in both alcoholic and nonalcoholic steatohepatitis, aminotransferase levels are quite unreliable in reflecting severity. In these conditions, liver biopsy is helpful in guiding management and identifying appropriate therapy, particularly if treatment is difficult, prolonged, and expensive, as is often the case in chronic viral hepatitis. Of the several well-verified numerical scales for grading activity in chronic liver disease, the most commonly used are the histology activity index and the Ishak histology scale.

Liver biopsy is also the most accurate means of assessing stage of disease as early or advanced, precirrhotic, and cirrhotic. Staging of disease pertains largely to chronic liver diseases in which progression to cirrhosis and end-stage disease can occur but may require years or decades. Clinical features, biochemical tests, and hepatic imaging studies are helpful in assessing stage but generally become abnormal only in the middle to late stages of cirrhosis. Noninvasive tests that suggest advanced fibrosis include mild elevations of bilirubin, prolongation of prothrombin time, slight decreases in serum albumin, and mild thrombocytopenia (which is often the first indication of worsening fibrosis). Combinations of blood test results have been used to create models for predicting advanced liver disease, but these models are not reliable enough to use on a regular basis and only separate advanced from early disease. Recently, elastography and noninvasive breath tests using ^{13}C-labeled compounds have been proposed as a means of detecting early stages of fibrosis and liver dysfunction, but their reliability and reproducibility remain to be proven. Thus, at present, mild to moderate stages of hepatic fibrosis are detectable only by liver biopsy. In the assessment of stage, the degree of fibrosis is usually used as the quantitative measure. The amount of fibrosis is generally staged on a scale of 0 to 4+ (Metavir scale) or 0 to 6+ (Ishak scale). The importance of staging relates primarily to prognosis and to optimal management of complications. Patients with cirrhosis are candidates for screening and surveillance for esophageal varices and hepatocellular carcinoma. Patients without advanced fibrosis need not undergo screening.

Cirrhosis can also be staged clinically. A reliable staging system is the modified Child-Pugh 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 357-4). This scoring system was initially devised to stratify patients into risk groups before portal