same conditions, xanthelasma and tendon xanthomata occur as a result of retention and high serum levels of lipids and cholesterol. Slate-gray pigmentation of the skin is also seen with hemochromatosis if iron levels are high for a prolonged period. Mucocutaneous vasculitis with palpable purpura, especially on the lower extremities, is typical of cryoglobulinemia of chronic hepatitis C but can also occur in chronic hepatitis B.

Some physical signs point to specific liver diseases. Kayser-Fleischer rings occur in Wilson's disease and consist of a golden-brown copper pigment deposited in Descemet's membrane at the periphery of the cornea; they are best seen by slit-lamp examination. Dupuytren contracture and parotid enlargement are suggestive of chronic alcoholism and alcoholic liver disease. In metastatic liver disease or primary hepatocellular carcinoma, signs of cachexia and wasting as well as firm hepatomegaly and a hepatic bruit may be prominent.

DIAGNOSIS OF LIVER DISEASE

The major causes of liver disease and key diagnostic features are outlined in Table 357-3, and an algorithm for evaluation of the patient with suspected liver disease is shown in Fig. 357-1. Specifics of diagnosis are discussed in later chapters. The most common causes of acute liver disease are viral hepatitis (particularly hepatitis A, B, and C), drug-induced liver injury, cholangitis, and alcoholic liver disease. Liver biopsy usually is not needed in the diagnosis and management of acute liver disease, exceptions being situations where the diagnosis remains unclear despite thorough clinical and laboratory investigation. Liver biopsy can be helpful in diagnosing drug-induced liver disease and acute alcoholic hepatitis.

The most common causes of chronic liver disease, in general order of frequency, are chronic hepatitis C, alcoholic liver disease, nonalcoholic steatohepatitis, chronic hepatitis B, autoimmune hepatitis, sclerosing cholangitis, primary biliary cirrhosis, hemochromatosis, and Wilson's disease. Hepatitis E virus is a rare cause of chronic hepatitis, with cases occurring mostly in persons who are immunosuppressed or immunodeficient. Strict diagnostic criteria have not been developed for most liver diseases, but liver biopsy plays an important role in the diagnosis of autoimmune hepatitis, primary biliary cirrhosis, nonalcoholic and alcoholic steatohepatitis, and Wilson's disease (with a quantitative hepatic copper level in the last instance).

TABLE 357-3 IMPORTANT DIAGNOSTIC TESTS IN COMMON LIVER DISEASES

Disease	Diagnostic Test
Hepatitis A	Anti-HAV IgM
Hepatitis B	
Acute	HBsAg and anti-HBc IgM
Chronic	HBsAg and HBeAg and/or HBV DNA
Hepatitis C	Anti-HCV and HCV RNA
Hepatitis D (delta)	HBsAg and anti-HDV
Hepatitis E	Anti-HEV IgM and HEV RNA
Autoimmune hepatitis	ANA or SMA, elevated IgG levels, and compatible histology
Primary biliary cirrhosis	Mitochondrial antibody, elevated IgM levels, and compatible histology
Primary sclerosing cholangitis	P-ANCA, cholangiography
Drug-induced liver disease	History of drug ingestion
Alcoholic liver disease	History of excessive alcohol intake and compatible histology
Nonalcoholic steatohepatitis	Ultrasound or CT evidence of fatty liver and compatible histology
α_1 Antitrypsin disease	Reduced α_1 antitrypsin levels, phenotype PiZZ or PiSZ
Wilson's disease	Decreased serum ceruloplasmin and increased urinary copper; increased hepatic copper level
Hemochromatosis	Elevated iron saturation and serum ferritin; genetic testing for *HFE* gene mutations
Hepatocellular cancer	Elevated α-fetoprotein level (to >500 ng/mL); ultrasound or CT image of mass

Abbreviations: HAV, HBV, HCV, HDV, HEV: hepatitis A, B, C, D, E virus; HBsAg, hepatitis B surface antigen; anti-HBc, antibody to hepatitis B core (antigen); HBeAg, hepatitis B e antigen; ANA, antinuclear antibody; SMA, smooth-muscle antibody; P-ANCA, peripheral antineutrophil cytoplasmic antibody.

Laboratory Testing Diagnosis of liver disease is greatly aided by the availability of reliable and sensitive tests of liver injury and function. A typical battery of blood tests used for initial assessment of liver disease includes measurement of levels of serum alanine and aspartate aminotransferases, alkaline phosphatase, direct and total serum bilirubin and albumin, and prothrombin time. The pattern of abnormalities generally points to hepatocellular versus cholestatic liver disease and helps determine whether the disease is acute or chronic and whether cirrhosis and hepatic failure are present. On the basis of these results, further testing over time may be necessary. Other laboratory tests may be helpful, such as γ-glutamyl transpeptidase to define whether alkaline phosphatase elevations are due to liver disease; hepatitis serology to define the type of viral hepatitis; and autoimmune markers to diagnose primary biliary cirrhosis (antimitochondrial antibody), sclerosing cholangitis (peripheral antineutrophil cytoplasmic antibody), and autoimmune hepatitis (antinuclear, smooth-muscle, and liver-kidney microsomal antibody). A simple delineation of laboratory abnormalities and common liver diseases is given in Table 357-3.

The use and interpretation of liver function tests are summarized in Chap. 358.

Diagnostic Imaging Great advances have been made in hepatobiliary imaging, although no method is adequately accurate in demonstrating underlying cirrhosis. Of the many modalities available for imaging the liver, ultrasound, CT, and MRI are the most commonly employed and are complementary to one another. In general, ultrasound and CT are highly sensitive for detecting biliary duct dilation and are the first-line options for investigating cases of suspected obstructive jaundice. All three modalities can detect a fatty liver, which appears bright on imaging studies. Modifications of CT and MRI can be used to quantify liver fat, and this information may ultimately be valuable in monitoring therapy in patients with fatty liver disease. Magnetic resonance cholangiopancreatography (MRCP) and endoscopic retrograde cholangiopancreatography (ERCP) are the procedures of choice for visualization of the biliary tree. MRCP offers several advantages over ERCP: there is no need for contrast media or ionizing radiation, images can be acquired faster, the procedure is less operator dependent, and it carries no risk of pancreatitis. MRCP is superior to ultrasound and CT for detecting choledocholithiasis but is less specific. MRCP is useful in the diagnosis of bile duct obstruction and congenital biliary abnormalities, but ERCP is more valuable in evaluating ampullary lesions and primary sclerosing cholangitis. ERCP permits biopsy, direct visualization of the ampulla and common bile duct, and intraductal ultrasonography. It also provides several therapeutic options in patients with obstructive jaundice, such as sphincterotomy, stone extraction, and placement of nasobiliary catheters and biliary stents. Doppler ultrasound and MRI are used to assess hepatic vasculature and hemodynamics and to monitor surgically or radiologically placed vascular shunts, including transjugular intrahepatic portosystemic shunts. Multidetector or spiral CT and MRI with contrast-enhancement are the procedures of choice for the identification and evaluation of hepatic masses, the staging of liver tumors, and preoperative assessment. With regard to mass lesions, the sensitivity of hepatic imaging continues to increase; unfortunately, specificity remains a problem, and often two and sometimes three studies are needed before a diagnosis can be reached. Recently, ultrasound transient elastography has been approved for the measurement of hepatic stiffness—providing an indirect assessment of cirrhosis; this technique can eliminate the need for liver biopsy if the only indication is the assessment of disease stage. Magnetic resonance elastography is now undergoing evaluation for its ability to detect different degrees of hepatic fibrosis. Studies are ongoing to determine whether hepatic elastography is an appropriate means of monitoring fibrosis and disease progression. Finally, interventional radiologic techniques allow the biopsy of solitary lesions, the radiofrequency