

Jugular venous distention, a sign of right-sided heart failure, suggests hepatic congestion. Right pleural effusion in the absence of clinically apparent ascites may be seen in advanced cirrhosis.

The abdominal examination should focus on the size and consistency of the liver, on whether the spleen is palpable and hence enlarged, and on whether ascites is present. Patients with cirrhosis may have an enlarged left lobe of the liver, which is felt below the xiphoid, and an enlarged spleen. A grossly enlarged nodular liver or an obvious abdominal mass suggests malignancy. An enlarged tender liver could signify viral or alcoholic hepatitis; an infiltrative process such as amyloidosis; or, less often, an acutely congested liver secondary to right-sided heart failure. Severe right-upper-quadrant tenderness with respiratory arrest on inspiration (Murphy's sign) suggests cholecystitis. Ascites in the presence of jaundice suggests either cirrhosis or malignancy with peritoneal spread.

Laboratory Tests A battery of tests are helpful in the initial evaluation of a patient with unexplained jaundice. These include total and direct serum bilirubin measurement with fractionation; determination of serum aminotransferase, alkaline phosphatase, and albumin concentrations; and prothrombin time tests. Enzyme tests (alanine aminotransferase [ALT], aspartate aminotransferase [AST], and alkaline phosphatase [ALP]) are helpful in differentiating between a hepatocellular process and a cholestatic process (Table 358-1; Fig. 58-1)—a critical step in determining what additional workup is indicated. Patients with a hepatocellular process generally have a rise in the aminotransferases that is disproportionate to that in ALP, whereas patients with a cholestatic process have a rise in ALP that is disproportionate to that of the aminotransferases. The serum bilirubin can be prominently elevated in both hepatocellular and cholestatic conditions and therefore is not necessarily helpful in differentiating between the two.

In addition to enzyme tests, all jaundiced patients should have additional blood tests—specifically, an albumin level and a prothrombin time—to assess liver function. A low albumin level suggests a chronic process such as cirrhosis or cancer. A normal albumin level is suggestive of a more acute process such as viral hepatitis or choledocholithiasis. An elevated prothrombin time indicates either vitamin K deficiency due to prolonged jaundice and malabsorption of vitamin K or significant hepatocellular dysfunction. The failure of the prothrombin time to correct with parenteral administration of vitamin K indicates severe hepatocellular injury.

The results of the bilirubin, enzyme, albumin, and prothrombin time tests will usually indicate whether a jaundiced patient has a hepatocellular or a cholestatic disease and offer some indication of the duration and severity of the disease. The causes and evaluations of hepatocellular and cholestatic diseases are quite different.

Hepatocellular Conditions Hepatocellular diseases that can cause jaundice include viral hepatitis, drug or environmental toxicity, alcohol, and end-stage cirrhosis from any cause (Table 58-2). Wilson's disease occurs primarily in young adults. Autoimmune hepatitis is typically seen in young to middle-aged women but may affect men and women of any age. Alcoholic hepatitis can be differentiated from viral and toxin-related hepatitis by the pattern of the aminotransferases: patients with alcoholic hepatitis typically have an AST-to-ALT ratio of at least 2:1, and the AST level rarely exceeds 300 U/L. Patients with acute viral hepatitis and toxin-related injury severe enough to produce jaundice typically have aminotransferase levels >500 U/L, with the ALT greater than or equal to the AST. While ALT and AST values <8 times normal may be seen in either hepatocellular or cholestatic liver disease, values 25 times normal or higher are seen primarily in acute hepatocellular diseases. Patients with jaundice from cirrhosis can have normal or only slightly elevated aminotransferase levels.

When the clinician determines that a patient has a hepatocellular disease, appropriate testing for acute viral hepatitis includes

TABLE 58-2 HEPATOCELLULAR CONDITIONS THAT MAY PRODUCE JAUNDICE

Viral hepatitis
Hepatitis A, B, C, D, and E
Epstein-Barr virus
Cytomegalovirus
Herpes simplex virus
Alcoholic hepatitis
Drug toxicity
Predictable, dose-dependent (e.g., acetaminophen)
Unpredictable, idiosyncratic (e.g., isoniazid)
Environmental toxins
Vinyl chloride
Jamaica bush tea—pyrrolizidine alkaloids
Kava Kava
Wild mushrooms— <i>Amanita phalloides</i> , <i>A. verna</i>
Wilson's disease
Autoimmune hepatitis

a hepatitis A IgM antibody assay, a hepatitis B surface antigen and core IgM antibody assay, a hepatitis C viral RNA test, and, depending on the circumstances, a hepatitis E IgM antibody assay. Because it can take many weeks for hepatitis C antibody to become detectable, its assay is an unreliable test if acute hepatitis C is suspected. Studies for hepatitis D and E viruses, Epstein-Barr virus (EBV), and cytomegalovirus (CMV) may also be indicated. Ceruloplasmin is the initial screening test for Wilson's disease. Testing for autoimmune hepatitis usually includes an antinuclear antibody assay and measurement of specific immunoglobulins.

Drug-induced hepatocellular injury can be classified as either predictable or unpredictable. Predictable drug reactions are dose-dependent and affect all patients who ingest a toxic dose of the drug in question. The classic example is acetaminophen hepatotoxicity. Unpredictable or idiosyncratic drug reactions are not dose-dependent and occur in a minority of patients. A great number of drugs can cause idiosyncratic hepatic injury. Environmental toxins are also an important cause of hepatocellular injury. Examples include industrial chemicals such as vinyl chloride, herbal preparations containing pyrrolizidine alkaloids (Jamaica bush tea) or Kava Kava, and the mushrooms *Amanita phalloides* and *A. verna*, which contain highly hepatotoxic amatoxins.

Cholestatic Conditions When the pattern of the liver tests suggests a cholestatic disorder, the next step is to determine whether it is intra- or extrahepatic cholestasis (Fig. 58-1). Distinguishing intrahepatic from extrahepatic cholestasis may be difficult. History, physical examination, and laboratory tests often are not helpful. The next appropriate test is an ultrasound. The ultrasound is inexpensive, does not expose the patient to ionizing radiation, and can detect dilation of the intra- and extrahepatic biliary tree with a high degree of sensitivity and specificity. The absence of biliary dilation suggests intrahepatic cholestasis, while its presence indicates extrahepatic cholestasis. False-negative results occur in patients with partial obstruction of the common bile duct or in patients with cirrhosis or primary sclerosing cholangitis (PSC), in which scarring prevents the intrahepatic ducts from dilating.

Although ultrasonography may indicate extrahepatic cholestasis, it rarely identifies the site or cause of obstruction. The distal common bile duct is a particularly difficult area to visualize by ultrasound because of overlying bowel gas. Appropriate next tests include CT, magnetic resonance cholangiopancreatography (MRCP), endoscopic retrograde cholangiopancreatography (ERCP), and endoscopic ultrasound (EUS). CT scanning and MRCP are better than ultrasonography for assessing the head of the pancreas and for identifying choledocholithiasis in the distal