disrupt tumor suppressor genes and activate oncogenes. In areas of high prevalence, vaccination to prevent infection with hepatitis B virus has reduced the incidence of HCC. The exact pathophysiologic mechanisms leading to tumorogenesis in patients with other causes of cirrhosis (e.g., hemochromatosis, alcohol, hepatitis C viral infection) remain poorly understood. Risk factors for the development of HCC and its clinical manifestations are listed in (Table 43-7).

Diagnosis

Table 43-8 lists currently used imaging techniques for detection of HCC and the most common findings. A tissue specimen may be necessary to confirm the diagnosis in some cases, but it is not needed if characteristic clinical and radiologic features are present, especially if they are accompanied by a rise in serum α-fetoprotein levels. Diagnosis of small, treatable tumors is possible with intensive screening programs that employ imaging studies, although the long-term outcomes and cost-effectiveness of these strategies remain unclear.

Staging

Although many staging systems for HCC are in use, the Barcelona Clinic Liver Cancer (BCLC) system is most commonly used.

TABLE 43-7 HEPATOCELLULAR CARCINOMA

ASSOCIATIONS	
Chronic hepatitis B infection Chronic hepatitis C infection Hemochromatosis (with cirrhosis) Cirrhosis (alcoholic, cryptogenic) Aflatoxin ingestion, Thorotrast exposure α_1-Antitrypsin deficiency Androgen administration	Jaundice Hepatic or portal vein obstruction Metabolic effects Erythrocytosis Hypercalcemia Hypercholesterolemia Hypoglycemia Gynecomastia Feminization Acquired porphyria
COMMON CLINICAL PRESENTATIONS	**CLINICAL AND LABORATORY FINDINGS**
Abdominal pain Abdominal mass Weight loss Deterioration of liver function	Hepatic bruit or friction rub Serum α-fetoprotein >400 ng/mL
UNUSUAL MANIFESTATIONS	
Bloody ascites Tumor emboli (lung)	

TABLE 43-8 IMAGING CHARACTERISTICS OF HEPATOCELLULAR CARCINOMA

ULTRASONOGRAPHY
Mass lesion with varying echogenicity but usually hypoechoic
DYNAMIC COMPUTED TOMOGRAPHY
Arterial phase: tumor enhances quickly Venous phase: quick de-enhancement of tumor relative to parenchyma
MAGNETIC RESONANCE IMAGING
T1-weighted images: hypointense T2-weighted images: hyperintense After gadolinium administration, tumor increases in intensity

Treatment

Patients with well-compensated cirrhosis may undergo surgical resection or liver transplantation, with a 5-year survival rate of up to 70%. Nonsurgical options include percutaneous ethanol injection, transarterial chemoembolization (TACE), and radiofrequency ablation. Sorafenib (a receptor tyrosine kinase angiogenesis inhibitor) has been approved for use in patients with unresectable HCC and has been shown to prolong survival in such patients.

Prognosis

In patients with widespread, multifocal disease and in those with vascular invasion, the prognosis is poor, with a 5-year survival rate of 5% to 6%. Accordingly, emphasis is placed on prevention of viral hepatitis and other causes of liver disease and on screening by ultrasound of those who are at higher risk, including patients with known cirrhosis.

VASCULAR DISEASE OF THE LIVER

Disorders of the hepatic vasculature are uncommon and include portal vein thrombosis (PVT), hepatic vein thrombosis (Budd-Chiari syndrome), and veno-occlusive disease. Affected patients usually have portal hypertension with or without associated liver dysfunction, which may mimic the presentation of cirrhosis.

Portal Vein Thrombosis

Definition and Etiology

Thrombosis of the portal vein may develop after blunt abdominal trauma, umbilical vein infection, neonatal sepsis, intra-abdominal inflammatory diseases (e.g., pancreatitis), or hypercoagulable states, and in association with cirrhosis. Myeloproliferative diseases (including polycythemia vera, essential thrombocytosis, and myelofibrosis) are now being recognized as possible causes of PVT. One study observed that as many as 25% to 65% of patients with splanchnic vein thrombosis in the absence of cirrhosis had a myeloproliferative disease. The Janus kinase 2 (JAK2) mutation is a marker for myeloproliferative disease and is often checked in patients with PVT. The disease produces the manifestations of portal hypertension, but the liver histology is usually normal.

Diagnosis

The diagnosis is established by angiography, but noninvasive imaging modalities such as Doppler ultrasonography, computed tomography, and magnetic resonance imaging may reveal thrombus, collateral circulation near the porta hepatis, and splenomegaly. In long-standing PVT, tortuous venous channels develop within the organized clot, leading to cavernous transformation.

Treatment

In acute PVT, thrombolysis may be attempted, but anticoagulation with warfarin remains the mainstay of therapy. In most patients, recanalization of the thrombus occurs within 6 months after initiation of anticoagulation. Recommendations for duration of anticoagulation after an acute event vary and are usually