TABLE 43-2 CLINICAL FEATURES AND PATHOGENESIS OF CIRRHOSIS

SIGNS AND SYMPTOMS	PATHOGENESIS
CONSTITUTIONAL	
Fatigue, anorexia, malaise, weakness, weight loss	Liver synthetic or metabolic dysfunction
CUTANEOUS	
Spider angiomas, palmar erythema	Altered estrogen and androgen metabolism
Jaundice	Decreased bilirubin excretion
Caput medusae	Porto systemic shunting due to portal hypertension
ENDOCRINE	
Gynecomastia, testicular atrophy, decreased body hair in men	Altered estrogen and androgen metabolism
Decreased libido, virilization, and menstrual irregularities in women	
GASTROINTESTINAL	
Abdominal pain	Hepatomegaly, hepatocellular carcinoma
Abdominal swelling	Ascites due to portal hypertension
Gastrointestinal bleeding	Variceal hemorrhage due to portal hypertension
HEMATOLOGIC	
Anemia, leukopenia, thrombocytopenia	Hypersplenism secondary to portal hypertension
Ecchymosis	Decreased synthesis of coagulation factors
NEUROLOGIC	
Altered sleep pattern, somnolence, confusion, asterixis	Hepatocellular dysfunction: inability to metabolize ammonia to urea

ALT and AST suggest intrahepatic or extrahepatic biliary obstruction.

Radiology

Various radiologic modalities including ultrasound (with and without Doppler imaging of the portal and hepatic venous vasculature), computed tomography, and magnetic resonance imaging have complementary profiles in the evaluation of suspected cirrhosis. Findings supportive of the diagnosis of cirrhosis include relative enlargement of the left hepatic and caudate lobes as a result of right lobe atrophy, surface nodularity, and features of portal hypertension such as ascites, intra-abdominal varices, and splenomegaly.

Transient elastography (Fibroscan) is a newer noninvasive modality that provides an indirect measure of liver fibrosis and cirrhosis by calculating liver stiffness. Abnormal liver stiffness suggests underlying fibrosis; in the presence of clinical and laboratory features of cirrhosis, this finding may obviate the need for diagnostic liver biopsy in some patients. Biopsy is more invasive and is usually reserved for situations in which the results of noninvasive studies are indeterminate or the cause of the liver disease is in doubt.

COMPLICATION OF CIRRHOSIS

The major sequelae of cirrhosis are illustrated diagrammatically in Figure 43-1 and can be categorized broadly into features of hepatocellular dysfunction and portal hypertension. The pathophysiologic interrelationships among these complications are described in the following sections.

Hepatocellular Dysfunction

The loss of hepatocyte mass that occurs in cirrhosis results in impaired synthesis of many important proteins, which in turn leads to hypoalbuminemia, deficient production of vitamin K–dependent coagulation factors, and diminished capacity for hepatic detoxification (see Chapters 39 and 42 for details). In addition, there is a decline in the capacity for conjugation and excretion of bilirubin.

Portal Hypertension

Under normal circumstances, the portal circulation is a low-pressure system with only small changes in pressure as blood flows from the portal vein, through the liver, and into the inferior vena cava. The hepatic venous pressure gradient (HVPG), which reflects sinusoidal pressure, is the gradient between the wedged hepatic venous pressure and the free hepatic venous pressure measured by direct catheterization. Normal HVPG values range between 3 and 5 mm Hg. In cirrhosis, the distortion of hepatic architecture by fibrous tissue and regenerative nodules, along with an increased intrahepatic vascular tone, leads to increased resistance to portal venous flow and resultant portal hypertension. Portal hypertension is defined as an HPVG greater than 5 mm Hg, and clinically significant complications typically develop at values greater than 10 mm Hg.

Although cirrhosis is the most important cause of portal hypertension, any process that increases resistance to portal blood flow through the presinusoidal, sinusoidal, or hepatic venous outflow tracts may result in portal hypertension (Table 43-3). In addition, cirrhosis is associated with increased cardiac output, which leads to greater splanchnic blood flow, further aggravating portal hypertension. It is important to recognize that the HVPG is reliably increased only in sinusoidal portal hypertension.

With sustained portal hypertension, portosystemic collaterals are formed which have the benefit of decreasing portal pressures at the expense of bypassing the liver. Major sites of collateral formation includes the gastroesophageal junction, retroperitoneum, rectum, and falciform ligament of liver (abdominal and periumbilical collaterals). Clinically, the most important collaterals are those connecting the portal to the azygos vein through the dilated and tortuous vessels (varices) in the submucosa of the gastric fundus and esophagus.

VARICEAL HEMORRHAGE

Definition and Pathology

Varices are abnormally large veins that are most commonly recognized near the gastroesophageal junction or the stomach wall. Gastroesophageal varices usually develop when the portal pressure gradient (HVPG) exceeds 10 mm Hg, and the risk for variceal rupture increases when the gradient is higher than 12 mm Hg. Bleeding occurs most commonly from large varices in the esophagus when high tension in the walls of these vessels leads to rupture. Among gastric varices, fundal varices have the highest