Table 18-2 Location and Causes of Portal Hypertension

Prehepatic causes
Obstructive thrombosis of portal vein
Structural abnormalities such as narrowing of the portal vein before it ramifies in the liver
Intrahepatic causes
Cirrhosis from any cause
Nodular regenerative hyperplasia
Primary biliary cirrhosis (even in the absence of cirrhosis)
Schistosomiasis
Massive fatty change
Diffuse, fibrosing granulomatous disease (e.g., sarcoid)
Infiltrative malignancy, primary or metastatic
Focal malignancy with invasion into portal vein (particularly hepatocellular carcinoma)
Amyloidosis
Posthepatic causes
Severe right-sided heart failure
Constrictive pericarditis
Hepatic vein outflow obstruction

muscle cells and myofibroblasts, and disruption of blood flow by scarring and the formation of parenchymal nodules. Alterations in sinusoidal endothelial cells that contribute to the intrahepatic vasoconstriction associated with portal hypertension include a decrease in nitric oxide production, and increased release of endothelin-1 (ET-1), angiotensinogen, and eicosanoids. Sinusoidal remodeling and anastomosis between the arterial and portal system in the fibrous septa contribute to portal hypertension by imposing arterial pressures on the low pressure portal venous system. Sinusoidal remodeling and intrahepatic shunts also interfere with the metabolic exchange between sinusoidal blood and hepatocytes.

Another major factor in the development of portal hypertension is an *increase in portal venous blood flow resulting from a hyperdynamic circulation*. This is caused by arterial vasodilation, primarily in the splanchnic circulation. The increased splanchnic arterial blood flow in turn leads to increased venous efflux into the portal venous system. While various mediators such as prostacyclin and TNF have been implicated in the causation of the splanchnic arterial vasodilation, NO has emerged as the most significant one.

The four major clinical consequences of portal hypertension are (1) ascites, (2) the formation of portosystemic venous shunts, (3) congestive splenomegaly, and (4) hepatic encephalopathy (discussed earlier). These are illustrated in Figure 18-9.

Ascites. The accumulation of excess *fluid in the peritoneal cavity is called ascites*. In 85% of cases, ascites is caused by cirrhosis. Ascites usually becomes clinically detectable when at least 500 mL have accumulated. The fluid is generally serous, having less than 3 gm/dL of protein (largely albumin), and a serum to ascites albumin gradient of ≥1.1 gm/dL. The fluid may contain a scant number of mesothelial cells and mononuclear leukocytes. Influx of neutrophils suggests infection, whereas the presence of blood cells points to possible disseminated intra-abdominal cancer. With long-standing ascites, seepage of peritoneal fluid through trans-diaphragmatic lymphatics may produce hydro-thorax, more often on the right side. The pathogenesis of ascites is complex, involving the following mechanisms:

Sinusoidal hypertension, altering Starling's forces and driving fluid into the space of Disse, from where it is removed by hepatic lymphatics; this movement of fluid is also promoted by *hypoalbuminemia*.

Percolation of hepatic lymph into the peritoneal cavity: Normal thoracic duct lymph flow approximates 800 to 1000 mL/day. With cirrhosis, hepatic lymphatic flow may approach 20 L/day, exceeding thoracic duct capacity. Hepatic lymph is rich in proteins and low in triglycerides, which explains the presence of protein in the ascitic fluid.

Splanchnic vasodilation and hyperdynamic circulation. These conditions were described earlier, in relationship to the pathogenesis of portal hypertension. Arterial vasodilation in the splanchnic circulation tends to reduce arterial blood pressure. With worsening of the vasodilation, the heart rate and cardiac output are unable to maintain the blood pressure. This triggers the activation of

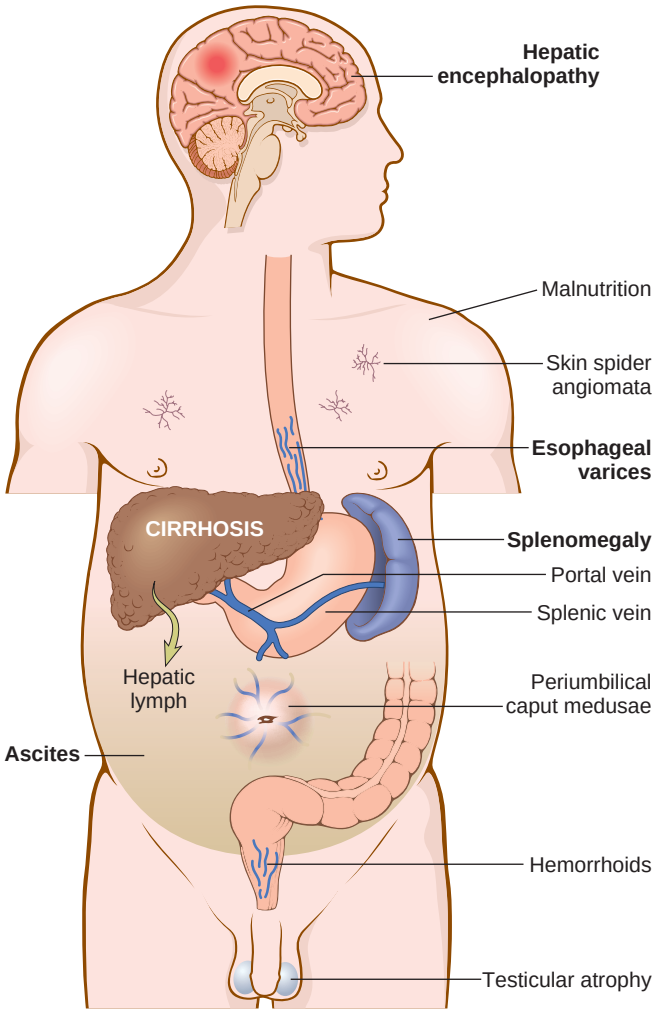

Figure 18-9 Major clinical consequences of portal hypertension in the setting of cirrhosis, shown for the male. In women, oligomenorrhea, amenorrhea, and sterility as a result of hypogonadism are frequent. Clinically significant findings are bold faced.