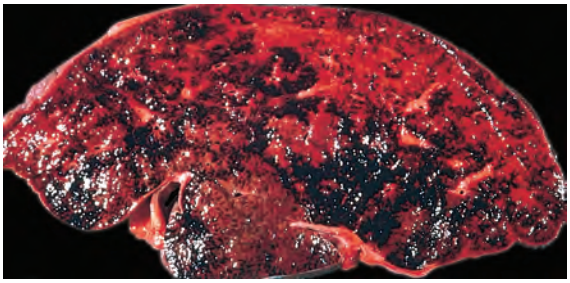

Figure 18-46 Budd-Chiari syndrome. Thrombosis of the major hepatic veins has caused hemorrhagic liver necrosis.

The mortality of untreated acute hepatic vein thrombosis is high. Prompt surgical creation of a portosystemic venous shunt permits reverse flow through the portal vein and improves the prognosis. The chronic form is far less lethal, and more than two thirds of patients are alive after 5 years.

Sinusoidal Obstruction Syndrome

Originally described in Jamaican drinkers of pyrrolizidine alkaloid–containing bush tea and named *veno-occlusive disease*, the disease is now called *sinusoidal obstruction syndrome*. It now occurs primarily in two settings: (1) following allogeneic hematopoietic stem cell transplantation, usually within the first 3 weeks; (2) in cancer patients receiving chemotherapy. The mortality rates can be higher than 30%.

Pathogenesis. **Sinusoidal obstruction syndrome arises from toxic injury to the sinusoidal endothelium.** Injured, sloughed endothelium obstructs sinusoidal blood flow. Erythrocytes enter into the space of Disse followed by necrosis of perivenular hepatocytes and downstream accumulation of cellular debris in the terminal hepatic vein.

MORPHOLOGY

Sinusoidal obstruction syndrome is characterized by obliteration of the terminal hepatic venules by subendothelial swelling and collagen deposition. In acute disease, there is centrilobular congestion, hepatocellular necrosis, and accumulation of hemosiderin-laden macrophages. As the disease progresses, obliteration of the lumen of the venule is easily identified with special stains for connective tissue (Fig. 18-47). In chronic or healed sinusoidal obstruction syndrome, fibrous obliteration of the venule may follow.

Although histology is the gold standard for diagnosis, in typical settings, diagnosis is frequently made on clinical grounds (tender hepatomegaly, ascites, weight gain, and jaundice), because of the high risk associated with liver biopsy. Early results suggest that treatment with anticoagulants and ursodeoxycholate may lower the incidence and severity of sinusoidal obstruction syndrome in patients undergoing hematopoieitic stem cell transplantation.

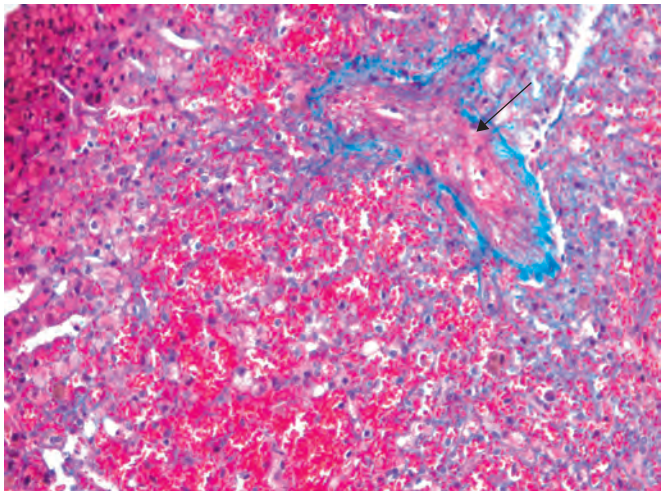

Figure 18-47 Sinusoidal obstruction syndrome. Collagen stain reveals marked sinusoidal congestion, hepatocyte atrophy and loss, and organizing thrombus within the vein lumen (arrow). (Masson trichrome stain.)

Passive Congestion and Centrilobular Necrosis

These hepatic manifestations of systemic circulatory compromise—passive congestion and centrilobular necrosis—are considered together because they represent a morphologic continuum. Both changes are commonly seen at autopsy because there is an element of preterminal circulatory failure with virtually every nontraumatic death. Components of both left and right sided heart failure can contribute to the injury variably in different clinical settings and with different forms of possibly underlying cardiac disease.

MORPHOLOGY

Right-sided cardiac decompensation leads to passive congestion of the liver. The liver is slightly enlarged, tense, and cyanotic, with rounded edges. Microscopically there is **congestion of centrilobular sinusoids.** With time, centrilobular hepatocytes become atrophic, resulting in markedly attenuated liver cell plates. Left-sided cardiac failure or shock may lead to hepatic hypoperfusion and hypoxia, causing ischemic coagulative necrosis of hepatocytes in the central region of the lobule (centrilobular necrosis). In most instances the only clinical evidence of centrilobular necrosis or its variants is transient elevation of serum aminotransferases, but the parenchymal damage may be sufficient to induce mild to moderate jaundice.

The combination of hypoperfusion and retrograde congestion acts synergistically to cause centrilobular hemorrhagic necrosis. The liver takes on a variegated mottled appearance, reflecting hemorrhage and necrosis in the centrilobular regions (Fig. 18-48*A*). This finding is known as **nutmeg liver** due to its resemblance to the cut surface of a nutmeg.

By microscopy there is a sharp demarcation of viable periportal and necrotic or atrophic pericentral hepatocytes, with suffusion of blood through the centrilobular region (Fig. 18-48*B*). Uncommonly, with sustained chronic severe congestive heart failure, **cardiac sclerosis** develops with centrilobular fibrosis, sometimes with central-central linking fibrous septa.