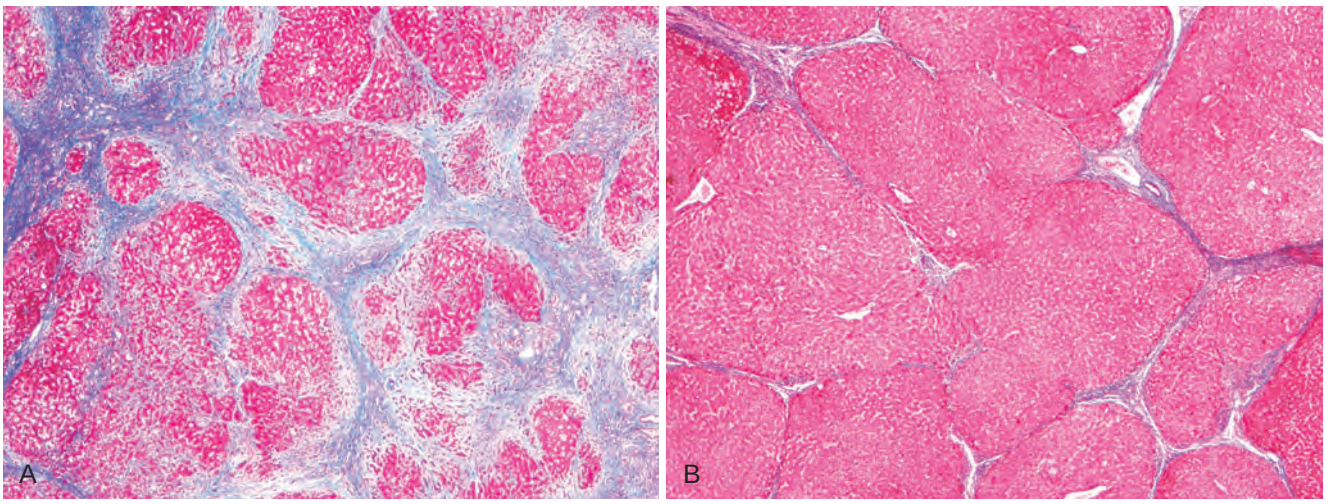

Figure 18-8 Alcoholic cirrhosis in an active drinker (A) and following long-term abstinence (B). **A,** Thick bands of collagen separate rounded cirrhotic nodules. **B,** After a year of abstinence, most scars are gone. (Masson trichrome stain) (Courtesy Drs. Hongfa Zhu and Isabel Fiel, Mount Sinai School of Medicine, New York.)

Although uncommon, regression of fibrosis, albeit rarely, in fully established cirrhosis, does occur; this is another reason why cirrhosis should not be automatically equated with end stage disease. In the past when there were no reliable ways to cure any chronic liver disease, there were no opportunities to see whether cirrhosis could regress. With increasing numbers of effective treatments for cirrhosis-causing conditions, however, we now understand that regression of scars can take place (Figs. 18-4 and 18-8). Scars can become thinner, more densely compacted, and eventually fragment. As fibrous septa break apart, adjacent nodules of regenerating parenchyma coalesce into larger islands. All cirrhotic livers show elements of both progression and regression, the balance determined by the severity and persistence of the underlying disease.

Clinical Features. **About 40% of individuals with cirrhosis are asymptomatic until the most advanced stages of the disease.** When symptomatic, they present with nonspecific manifestations: anorexia, weight loss, weakness, and, in advanced disease, symptoms and signs of liver failure discussed earlier. *The ultimate causes of death in chronic liver failure, whether cirrhotic or not, include those seen in acute liver failure, and additional grim outcomes, such as development of hepatocellular carcinoma in the context of cirrhosis.* Hepatic encephalopathy, bleeding from esophageal varices and bacterial infections (resulting from damage to mucosal barrier in the gut and Kupffer cell dysfunction) are often the the terminal events.

The course and severity of clinical manifestations of cirrhosis vary from patient to patient. In a small number of cases, as noted earlier, cessation of liver injury may give the necessary time for resorption of the fibrous tissue and "regression" of the cirrhosis. Even in such instances, the portal hypertension (from irreversible vascular shunts) and risk of hepatocellular carcinoma usually remain.

Jaundice, encephalopathy, and coagulopathy are very much the same as in acute liver failure. However, there are some significant additional features. Jaundice, when chronic, can lead to *pruritus*, that is, itching, the intensity of which can be profound. Some patients may even scratch their skin raw and risk repeated bouts of potentially life-threatening infection. Pruritus can be so severe that it can be relieved only by liver transplantation.

Impaired estrogen metabolism and consequent *hyperestrogenemia* in male patients with chronic liver failure can give rise to *palmar erythema* (a reflection of local vasodilatation) and *spider angiomas* of the skin. Each angioma is a central, pulsating, dilated arteriole from which small vessels radiate. In men, hyperestrogenemia also leads to *hypogonadism* and *gynecomastia*. Hypogonadism can also occur in women from disruption of hypothalamic-pituitary axis function, either through nutritional deficiencies associated with the chronic liver disease or primary hormonal alterations.

We next turn to a discussion of portal hypertension which as alluded to earlier can develop in acute liver failure but is much more common in chronic liver failure with cirrhosis.

Portal Hypertension

Increased resistance to portal blood flow may develop in a variety of circumstances, which can be divided into *prehepatic, intrahepatic, and posthepatic* (Table 18-2). The major *prehepatic conditions* are obstructive thrombosis, narrowing of the portal vein before it ramifies within the liver or massive splenomegaly with increased splenic vein blood flow. The main post-hepatic causes are severe right-sided heart failure, constrictive pericarditis, and hepatic vein outflow obstruction. **The dominant intrahepatic cause is cirrhosis, accounting for most cases of portal hypertension.** Far less frequent intrahepatic causes are schistosomiasis, massive fatty change, diffuse fibrosing granulomatous disease such as sarcoidosis, and diseases affecting the portal microcirculation such as nodular regenerative hyperplasia (discussed later). The pathophysiology of portal hypertension is complex and involves resistance to portal flow at the level of sinusoids and an increase in portal flow caused by hyperdynamic circulation.

The increased resistance to portal flow at the level of the sinusoids is caused by contraction of vascular smooth

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