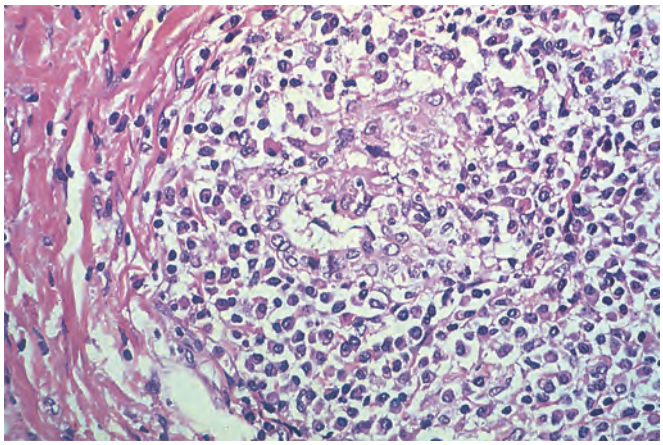

Figure 18-35 Primary biliary cirrhosis. A portal tract is markedly expanded by an infiltrate of lymphocytes and plasma cells surrounding a destructive granulomatous reaction centered on a bile duct (the "florid duct lesion").

Mallory-Denk bodies, as seen in chronic duct obstruction. Such end-stage livers show established cirrhosis and intense green pigmentation, matching the patient's icteric state.

Alternatively, some patients develop prominent portal hypertension rather than severe cholestasis. In these individuals there is widespread nodularity without the surrounding scar tissue seen in cirrhosis—a feature called nodular regenerative hyperplasia. Why this takes place in a disease that appears to be primarily biliary in nature is not understood.

In both cases, with little hepatocyte loss and often regenerative hyperplasia, there is **marked hepatomegaly**, a point of distinction from the shrunken, end-stage cirrhotic livers of chronic hepatitis, alcoholism, and non-alcoholic fatty liver disease.

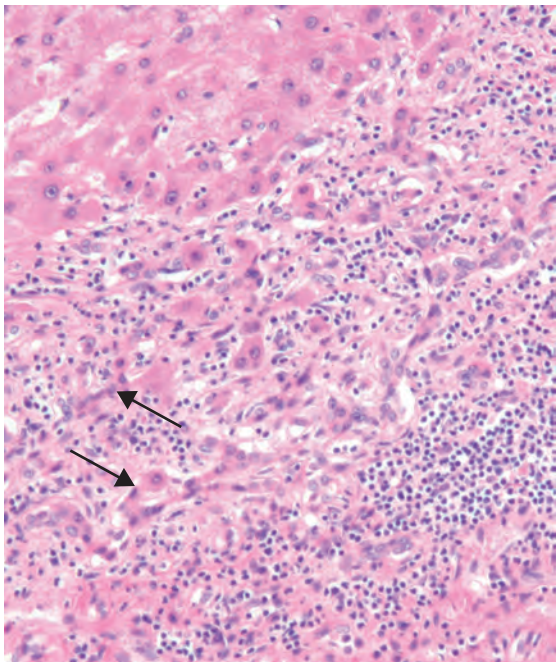

Figure 18-36 Ductular reaction (arrows) in primary biliary cirrhosis. In the earlier stages of disease, these structures may help maintain bile flow past destroyed segments of biliary tree, but later they may contribute to subsequent scarring.

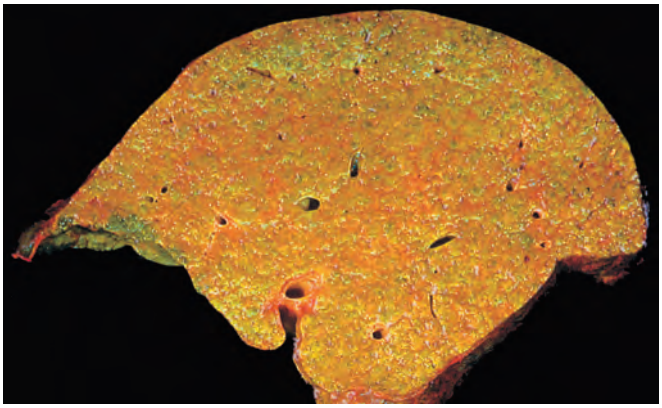

Figure 18-37 Primary biliary cirrhosis. This sagittal section demonstrates liver enlargement, nodularity indicative of cirrhosis, and green discoloration due to cholestasis.

Clinical Features. Most cases are diagnosed when asymptomatic, with elevated serum alkaline phosphatase and γ-glutamyltransferase. Both of these are markers of cholestasis and indicate the need for a liver disease work-up. Hypercholesterolemia is common. Antimitochondrial antibodies are present in 90% to 95% of patients. They are highly characteristic of PBC, although other autoantibodies may be seen in a small number of cases. *The disease is confirmed by liver biopsy, which is considered diagnostic if a florid duct lesion is present.* When symptomatic, the onset is insidious, presenting with fatigue and pruritus, which increase slowly over time.

Over a period of two or more decades, untreated patients follow one of two pathways to end-stage disease, one in which hyperbilirubinemia predominates and another with prominent portal hypertension. However, treatment of early stage disease with oral ursodeoxycholic acid greatly slows progression. Its mechanism of action is uncertain, but is presumably related to the ability of ursodeoxycholate to enter the bile acid pool and alter the biochemical composition of bile.

With progression, secondary features may emerge: skin hyperpigmentation, xanthelasmas, steatorrhea, and vitamin D malabsorption–related osteomalacia and/or osteoporosis. Individuals with PBC may also have extrahepatic manifestations of autoimmunity, including the sicca complex of dry eyes and mouth (Sjögren syndrome), systemic sclerosis, thyroiditis, rheumatoid arthritis, Raynaud phenomenon, and celiac disease. Ursodeoxycholate is not effective in advanced disease, and for these patients liver transplantation is the best form of treatment.

Primary Sclerosing Cholangitis (PSC)

PSC is characterized by inflammation and obliterative fibrosis of intrahepatic and extrahepatic bile ducts with dilation of preserved segments. Characteristic "beading" on radiographs of the intrahepatic and extrahepatic biliary tree is attributable to these irregular, biliary strictures and dilations (Fig. 18-38). *Inflammatory bowel disease* (Chapter 17), *particularly ulcerative colitis, coexists in approximately 70% of individuals with PSC.* Conversely, the prevalence of PSC in persons with ulcerative colitis is about 4%. Like inflammatory bowel disease, PSC tends to occur in the third through fifth decades of life and males predominate 2:1 (Table 18-11).

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