There is considerable variability in the anatomy of biliary atresia. When the disease is limited to the common duct (type I) or right and/or left hepatic bile ducts (type II), the disease is surgically correctable (Kasai procedure). Unfortunately, 90% of patients have type III biliary atresia, in which there is also obstruction of bile ducts at or above the porta hepatis. These cases are not correctable, since there are no patent bile ducts amenable to surgical anastomosis. Moreover, in most patients, bile ducts within the liver are initially patent, but then are progressively destroyed.

Clinical Features. Infants with biliary atresia present with neonatal cholestasis, but exhibit normal birth weight and postnatal weight gain. There is a slight female preponderance. Initially normal stools change to acholic stools as the disease evolves. At the time of presentation, serum bilirubin values are usually in the range of 6 to 12 mg/dL, with only moderately elevated aminotransferase and alkaline phosphatase levels. The success of surgical resection and bypass of the biliary tree is limited by ascending cholangitis and/or intrahepatic progression of the disease. Liver transplantation remains the primary hope for salvage of these young patients. Without surgical intervention, death usually occurs within 2 years of birth.

Autoimmune Cholangiopathies

This section discusses the two main autoimmune disorders of intrahepatic bile ducts: primary biliary cirrhosis (PBC) and primary sclerosing cholangitis (PSC). The features of these two conditions are contrasted in Table 18-11. It should be noted that intrahepatic bile ducts are frequently damaged as part of other liver diseases, including viral hepatitis, drug- or toxin-induced liver injury, liver transplantation, and graft-versus-host disease that follows hematopoietic stem cell transplantation.

Table 18-11 Main Features of Primary Biliary Cirrhosis and Primary Sclerosing Cholangitis

Parameter	Primary Biliary Cirrhosis	Primary Sclerosing Cholangitis
Age	Median age 50 years (30 to 70)	Median age 30 years
Gender	90% female	70% male
Clinical course	Progressive	Unpredictable but progressive
Associated conditions	Sjögren syndrome (70%) Scleroderma (5%) Thyroid disease (20%)	Inflammatory bowel disease (70%) Pancreatitis (≤25%) Idiopathic fibrosing diseases (retroperitoneal fibrosis)
Serology	95% AMA-positive 50% ANA-positive 40% ANCA-positive	0-5% AMA-positive (low titer) 6% ANA-positive 65% ANCA-positive
Radiology	Normal	Strictures and beading of large bile ducts; pruning of smaller ducts
Duct lesion	Florid duct lesions and loss of small ducts only	Inflammatory destruction of extrahepatic and large intrahepatic ducts; fibrotic obliteration of medium and small intrahepatic ducts

AMA, Antimitochondrial antibody; ANA, antinuclear antibody; ANCA, antineutrophil cytoplasmic antibody.

Primary Biliary Cirrhosis (PBC)

PBC is an autoimmune disease characterized by nonsuppurative, inflammatory destruction of small and medium-sized intrahepatic bile ducts. Large intrahepatic ducts and the extrahepatic biliary tree are not involved. Most patients are diagnosed in the early stages of disease when cirrhosis is a distant possibility. Moreover, not all end-stage PBC is fully cirrhotic. Thus, the name is a misnomer for many patients. At best this name leads to confusion, at worst patients think they have an imminently fatal disease requiring transplantation, a fate that is not, in fact, the norm.

PBC is primarily a disease of middle-aged women, with a female predominance of 9:1. Occurring between the ages of 30 and 70 years, its peak incidence is between 40 and 50 years of age. The disease is most prevalent in Northern European countries (England and Scotland) and the Northern United States (Minnesota) where the prevalence is as high as 400 cases per million. Recent increases in incidence and prevalence along with geographic clustering suggest that genetic and environmental factors are important in its pathogenesis. Family members of PBC patients have an increased risk for development of the disease.

Pathogenesis. PBC is thought to be an autoimmune disorder, but as with other autoimmune diseases, the triggers that initiate PBC are unknown. *Antimitochondrial antibodies are the most characteristic laboratory finding in PBC.* They recognize the E2 component of the pyruvate dehydrogenase complex (PDC-E2). PDC-E2–specific T cells are also present in these patients, further supporting the notion of an immune-mediated process. Other findings suggestive of altered immunity include aberrant expression of MHC class II molecules on bile duct epithelial cells, accumulation of autoreactive T cells around bile ducts, and antibodies against other cellular components (nuclear pore proteins, and centromeric proteins, among others).

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Interlobular bile ducts are actively destroyed by lymphoplasmacytic inflammation with or without granulomas (the *florid duct lesion*) (Fig. 18-35). Some biopsy specimens, however, show only absence of bile ducts in portal tracts. The disease is quite patchy in distribution; it is common to see a single bile duct under immune attack in one level of a biopsy specimen, while deeper levels, less than a millimeter away, remain unaffected. Ductular reactions follow duct injury, and these in turn participate in the development of portal-portal septal fibrosis (Fig. 18-36).

In patients who follow a classic path to end stage, there is increasingly widespread duct loss, slowly leading to cirrhosis and, in the end stages, to profound cholestasis (Fig. 18-37). The bile accumulation in such cholestasis is not centrilobular, unlike in drug-induced or sepsis-associated cholestatsis, but is periportal/periseptal. It is associated with feathery degeneration and ballooned, bile-stained hepatocytes, often with prominent