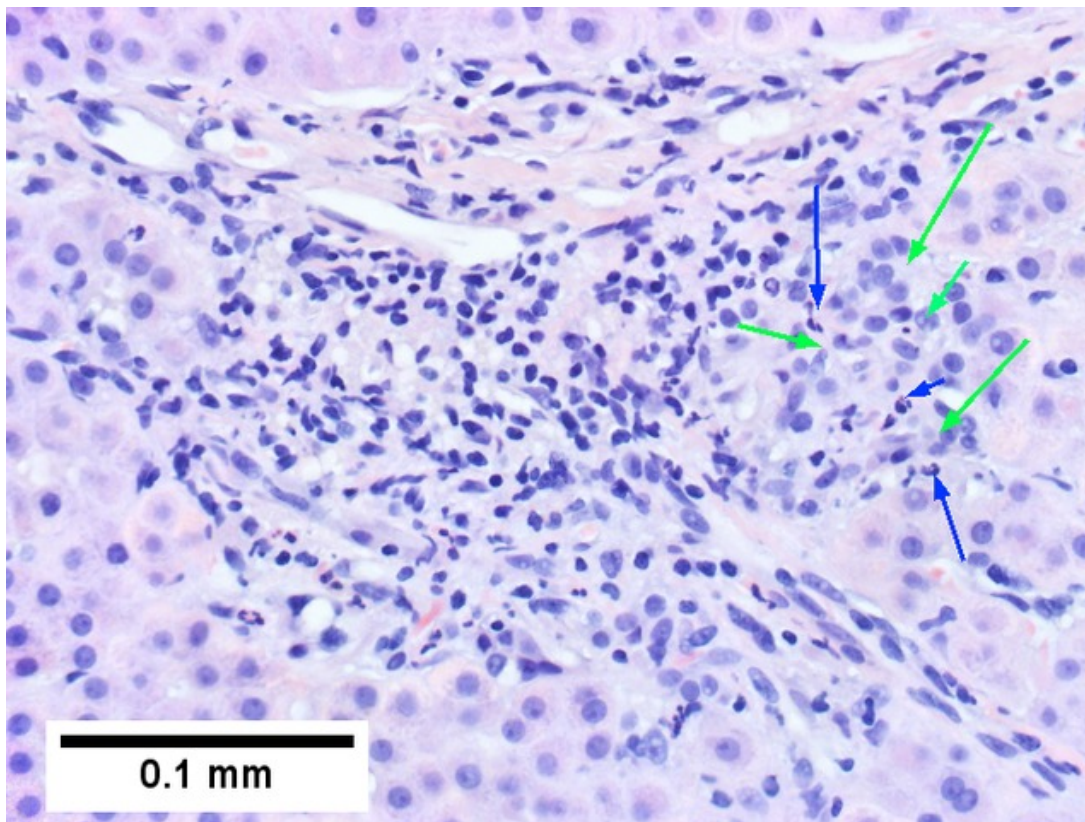


Primary Sclerosing Cholangitis (PSC) — Symptoms and Life Expectancy

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Primary sclerosing cholangitis is a common cause of chronic liver disease in patients with ulcerative colitis. It is an autoimmune disorder and patients usually present with jaundice, fever, abdominal pain, and elevated alkaline phosphatase. Endoscopic retrograde cholangiopancreatography is the best diagnostic tool to confirm the diagnosis of primary sclerosing cholangitis. Multiple strictures and dilations of the biliary system are usually observed. Symptomatic treatment, immunosuppression, and ursodeoxycholic acid are used in early stage PSC. In later stages, liver transplantation might be the only option available to alter prognosis and survival.



Definition and Epidemiology of Primary Sclerosing Cholangitis

Primary sclerosing cholangitis (PSC) is defined as a chronic process of cholestasis associated with inflammation and fibrosis of the liver and eventually leading to **chronic liver disease**. Primary sclerosing cholangitis is an [autoimmune disease](#) and is associated with other autoimmune disorders such as [ulcerative colitis](#).

The prevalence of PSC is approximately **6.3 cases per 100,000**. The diagnosis of PSC is highly dependent on **endoscopic retrograde cholangiopancreatography (ERCP)**. People of Jewish descent are more likely to develop [inflammatory bowel disease](#) and the associated complication of PSC. Additionally, patients with PSC are more likely to develop [colorectal cancer](#) and should be screened for it.

The majority of the patients are middle-aged men.

Etiology of Primary Sclerosing Cholangitis

The exact etiology of PSC is still unknown but different risk factors have been linked to the development of the condition. It is believed that the condition is autoimmune and associated with inflammatory bowel diseases especially ulcerative colitis.

Additionally, **genetic predisposition** is thought to play a role. Certain HLA alleles such as A1, B8, and DR3 have been associated with PSC and other autoimmune disorders.

Pathophysiology and Clinical Presentation of Primary Sclerosing Cholangitis



[Image](#): "Cholangiogram of primary sclerosing cholangitis." by Joy Worthington, Roger Chapman - Primary sclerosing cholangitis. Orphanet Journal of Rare Diseases 2006, 1:41doi:10.1186/1750-1172-1-41. License: [CC BY 2.0](#)

Up to 90% of the patients with PSC also have a known history of ulcerative colitis. Certain autoantibodies are known to be elevated in the serum of PSC patients such as **antineutrophil cytoplasmic antibodies (ANCA)**, **anticardiolipin (aCL)** and **antinuclear antibodies (ANA)**.

Chronic inflammation of the **intrahepatic bile ducts** ensues in PSC which predisposes to cholestasis and eventually bacterial infection of the bile ducts. The chronic infection of the intrahepatic bile ducts and exposure to toxic bile acids eventually lead to **fibrosis**. ANCA is also reported to be high in certain forms of **vasculitides** and some postulate that patients with PSC may have some form of vasculitis and ischemic injury to the bile ducts system.

To connect all of these theories, our current understanding of PSC allows us to postulate that patients at first develop autoimmune injury of the intrahepatic bile duct system. This leads to **cholestasis**, repeated injury and bacterial infection of the bile ducts. If this happens in a genetically predisposed individual, along with the **high risk of ischemic injury** due to the elevated ANCA, patients eventually develop chronic liver disease and fibrosis.

Patients present with tiredness, jaundice, pruritus, and right upper abdominal pain. Due to the high risk of intrahepatic bile duct infection, patients might present with fever.

40% of patients with PSC are **asymptomatic**. ERCP findings, when combined with an **elevated alkaline phosphatase level** in a patient with a known history of ulcerative colitis can be the presenting feature in asymptomatic PSC.

If left untreated, patients are at increased risk for developing **cholangiocarcinoma**. Physical examination reveals weight loss, hepatomegaly, and splenomegaly. Jaundice is also evident in these patients. In late-stage disease, patients might develop signs of [liver failure](#) such as ascites and spider angiomas.

Stages of Primary Sclerosing Cholangitis

PSC is a progressive disorder that has four stages. In stage 1, patients have **hepatitis** and if a biopsy is taken, the bile ducts have inflammatory cell infiltrates. Stage 2 disease presents with a **clear decrease in the number of the bile ducts**. **Septal fibrosis and necrosis** are present in stage 3. Patients with stage 4 PSC have **liver cirrhosis** and [end stage liver failure](#).

Diagnostic Work-up for Primary Sclerosing Cholangitis

Patients with PSC present with an elevated serum alkaline phosphatase, aminotransferases, and hypergammaglobulinemia.

Alkaline phosphatase is usually elevated up to 5 times the normal upper limit due to cholestasis. **Serum bilirubin levels** are usually increased in patients with PSC. **Gamma-glutamyl transpeptidase levels** are elevated in patients with PSC.

Immunoglobulin M (IgM) can be elevated in 50% of the patients. **ANCA, aCL, and ANA** are also elevated in patients with PSC.

Endoscopic retrograde cholangiopancreatography (ERCP) is the gold standard imaging modality for the diagnosis of PSC. ERCP can reveal strictures and dilations of the intrahepatic and extrahepatic biliary ducts.

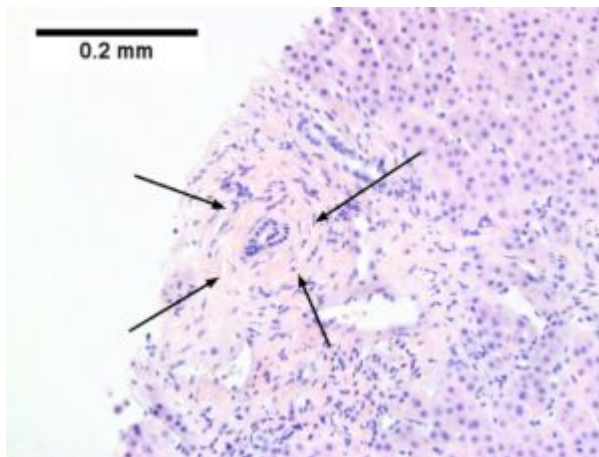


Image: "Primary sclerosing cholangitis in a patient with a history of ulcerative colitis." by TexasPathologistMSW - Own work.
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Magnetic resonance cholangiopancreatography (MRCP) is a new imaging modality that has comparable sensitivity and specificity to ERCP but is non-invasive.

Patients with PSC might benefit from a **liver biopsy study** to determine the stage of the disease for prognosis and treatment decisions. The biopsy can show **periductal concentric fibrosis** around the bile ducts also known as onion skin fibrosis. This pattern is only found in 10% of the patients but is pathognomonic of PSC. Usually, the biopsy shows **inflammatory cell infiltrates** and **necrosis**.

Treatment of Primary Sclerosing Cholangitis

Unfortunately, there is no definitive medical treatment for PSC. **Symptomatic treatment** is indicated for pain.

Patients in the early stages of the disease can be prescribed **steroids** or other **immunosuppressants** to delay disease progression but this approach has not been found to alter the overall prognosis. **Ursodeoxycholic acid supplementation** decreases cholestasis, improves the liver function profile and may improve survival in early stage PSC. Patients who are on medical treatment might also benefit from **stricture dilation by endoscopy**.

Medical treatment and endoscopic dilation can relieve symptoms in a subset of patients but are not known to lower the risk of **malignant transformation**.

Diet modifications might be necessary for patients with cholestasis. These patients are known to develop pancreatic insufficiency as well and this can lead to fat-soluble vitamins deficiency. Accordingly, **fat-soluble vitamin supplementation** is indicated in patients with associated pancreatic enzyme insufficiency.

Patients who develop **variceal bleeding** due to liver cirrhosis, intractable ascites, **hepatic encephalopathy**, and recurrent bacterial cholangitis are possible candidates for liver transplantation. **Liver transplantation** is the only known treatment for TSC to significantly alter the prognosis and survival.

Unfortunately, patients who also have ulcerative colitis are known to develop **recurrent PSC** in the transplanted liver. **Immunomodulation** for the liver transplantation can also worsen inflammatory bowel disease or even cause inflammatory bowel disease in patients who had PSC without concurrent ulcerative colitis. One possible approach to lower the risk of recurrent PSC is to provide a **proctocolectomy** in a patient with

ulcerative colitis.

References

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