Primary Sclerosing Cholangitis and Cholestatic liver diseases

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I have nothing to disclose

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Educational Objectives

- What is PSC?
- Understand the cholestatic liver diseases
  - Signs, symptoms, blood work, imaging and diagnosis
- Management plan and long term follow up.
- Appreciate conditions associated with PSC.
- Difference in PSC and PBC

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Case Introduction

- 35 year old male referred for jaundice, itching, fatigue and weakness.
- Patient has h/o diarrhea and rectal bleeding off and on for a year. Recent diagnosis of Ulcerative colitis.
- F/H of Ulcerative colitis.
- H/O Iron deficiency anemia
- On mesalamine and MVI. H/O iron supplement.

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Hepatocellular vs cholestatic liver Disease

- Hepatocellular liver disease is due to damage to hepatocytes.
    - Increase in ALT and AST.
- Cholestatic liver disease due to disease of Bile ducts and process where Bile acid flow is restricted.
    - Increase in ALP and GGT.

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PSC

- PSC is an idiopathic condition defined as the presence of beading and stricture formation of the intra and/or extrahepatic bile ducts that cannot be ascribed to another cause.
- PSC is characterized by inflammation, fibrosis, and stricturing of medium and large ducts in the intrahepatic and/or extrahepatic biliary tree
- Many, if not most, cases of PSC are associated with inflammatory bowel disease (IBD) up to 75%
- 12-15% will develop cholangiocarcinoma over life time.
- Male to female ratio is 2:1

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PSC

- Primary sclerosing cholangitis (PSC) is a chronic cholestatic liver and biliary tract disease that has a highly variable natural history.
- Pathogenesis is not understood. Disease symptoms and complications are due to fibrosis and strictures of CBD.
- PSC may be asymptomatic for long periods but may also have an aggressive course, leading to recurrent biliary tract obstruction, recurrent episodes of cholangitis, and may progress to end-stage liver disease.
- The typical cholangiography findings include focal stricturing and saccular dilatation of the bile ducts, which may lead to a “beaded” appearance

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Signs and Symptoms

- A large number (>50%) of patients present without symptoms
- Fatigue
- Pruritis
- Jaundice
- Rectal bleeding, diarrhea.
- RUQ pain

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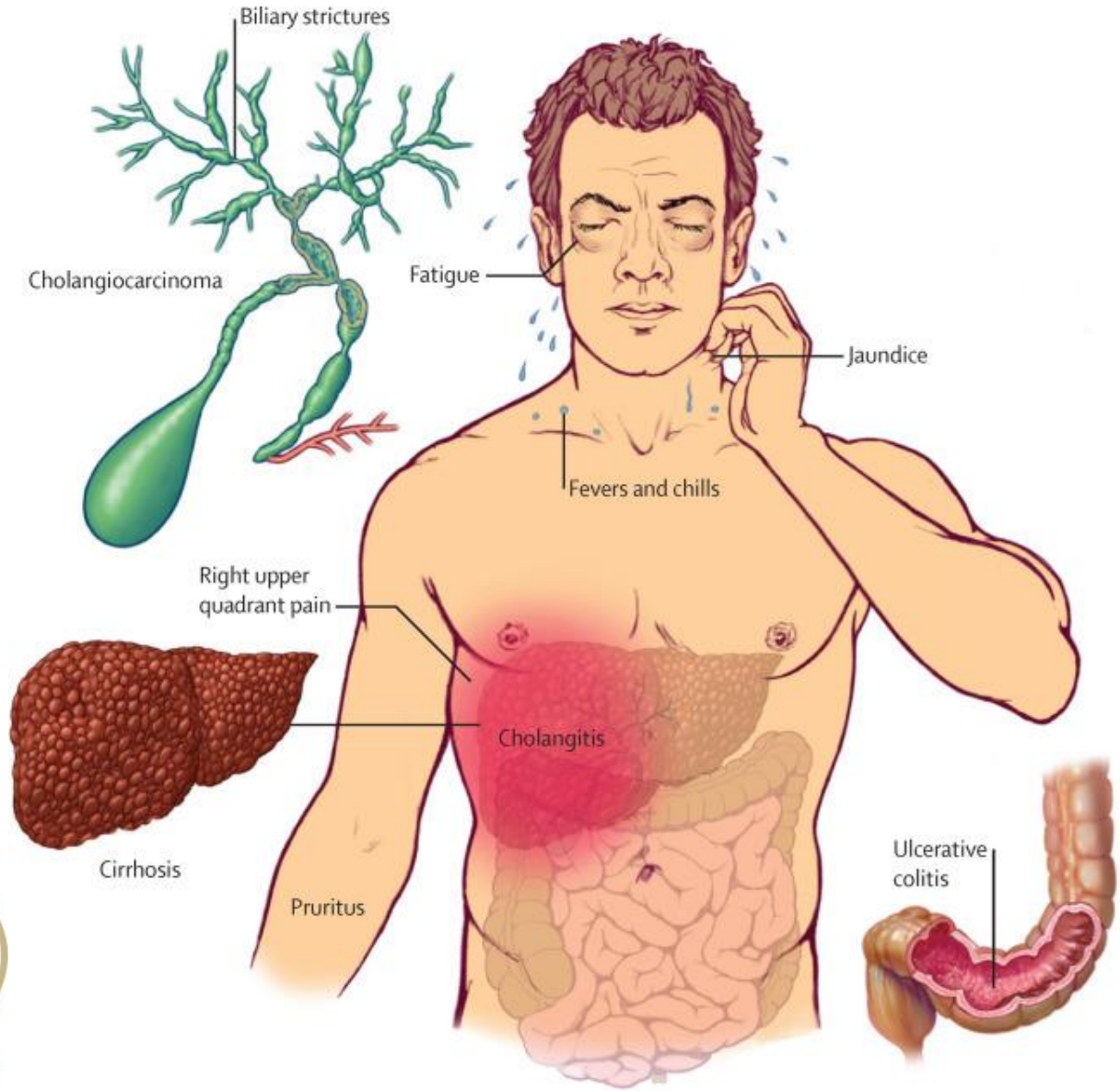

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Types of PSC

- Classic PSC
- Small duct PSC

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Diagnosis

1 . MRCP is preferred over endoscopic retrograde cholangiopancreatography (ERCP) to establish a diagnosis of PSC.

2 . Liver biopsy is not necessary to make a diagnosis in patients with suspected PSC based on diagnostic cholangiographic findings.

3 . Liver biopsy is recommended to make a diagnosis in patients with suspected small duct PSC or to exclude other conditions such as suspected overlap syndrome with autoimmune hepatitis, PBC

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Serologic findings in patients with PSC

- Hypergammaglobulinemia – 30 percent
- Increased serum immunoglobulin M (IgM) levels – 40 to 50 percent
- Atypical perinuclear antineutrophil cytoplasmic antibodies (P-ANCA) – 30 to 80 percent
- Human leukocyte antigen DRw52a – 0 to 100 percent in various reports

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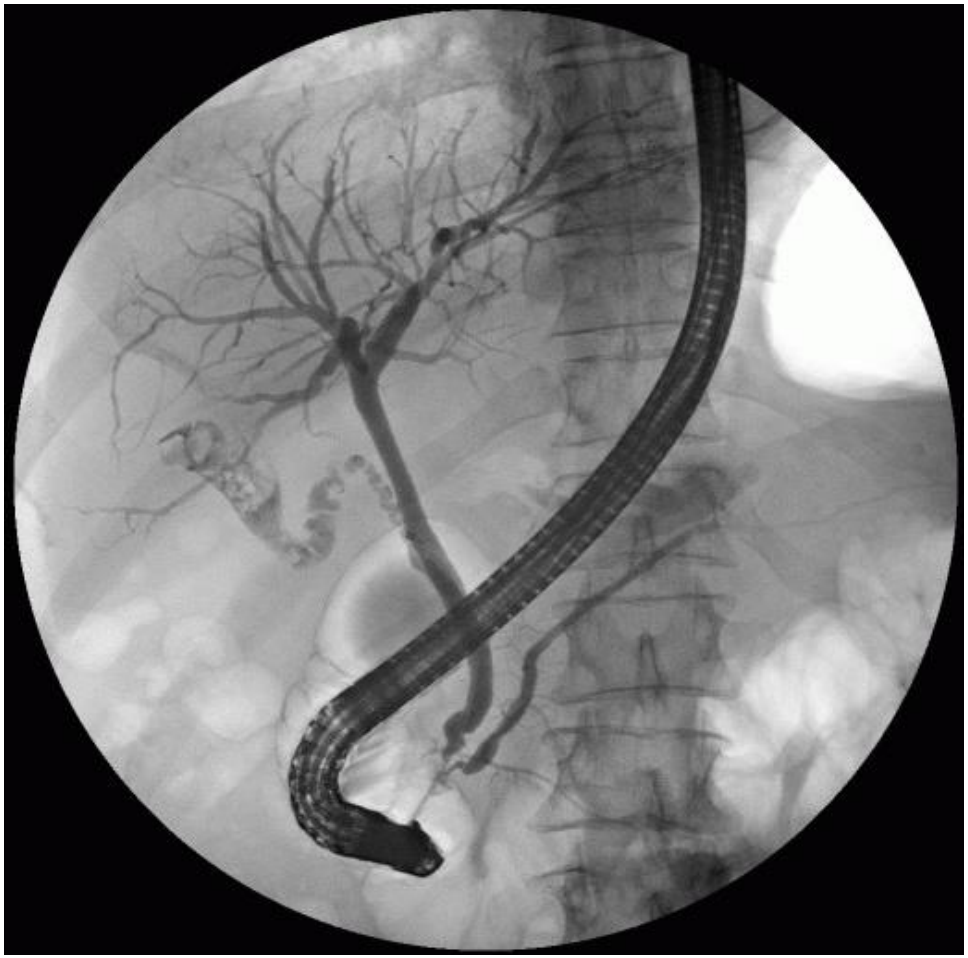
Normal ERCP and CBD



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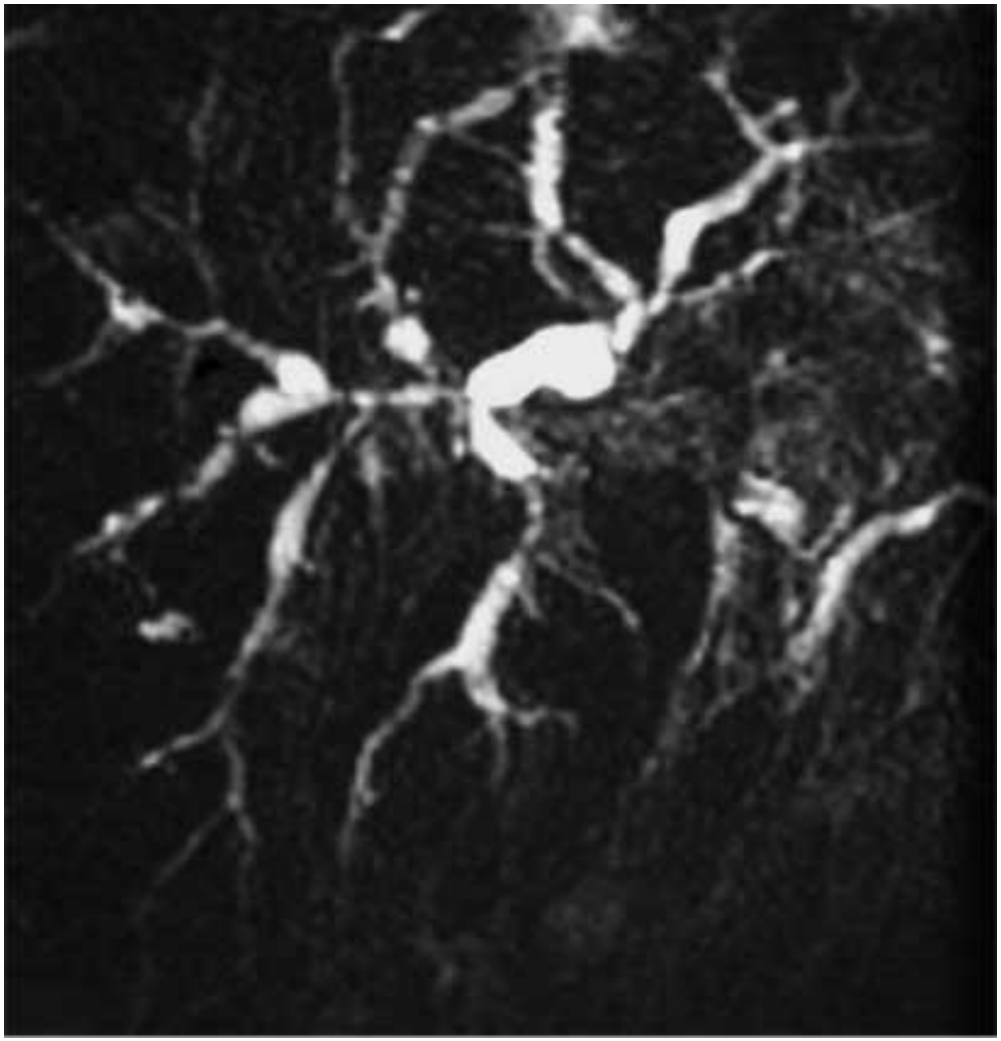

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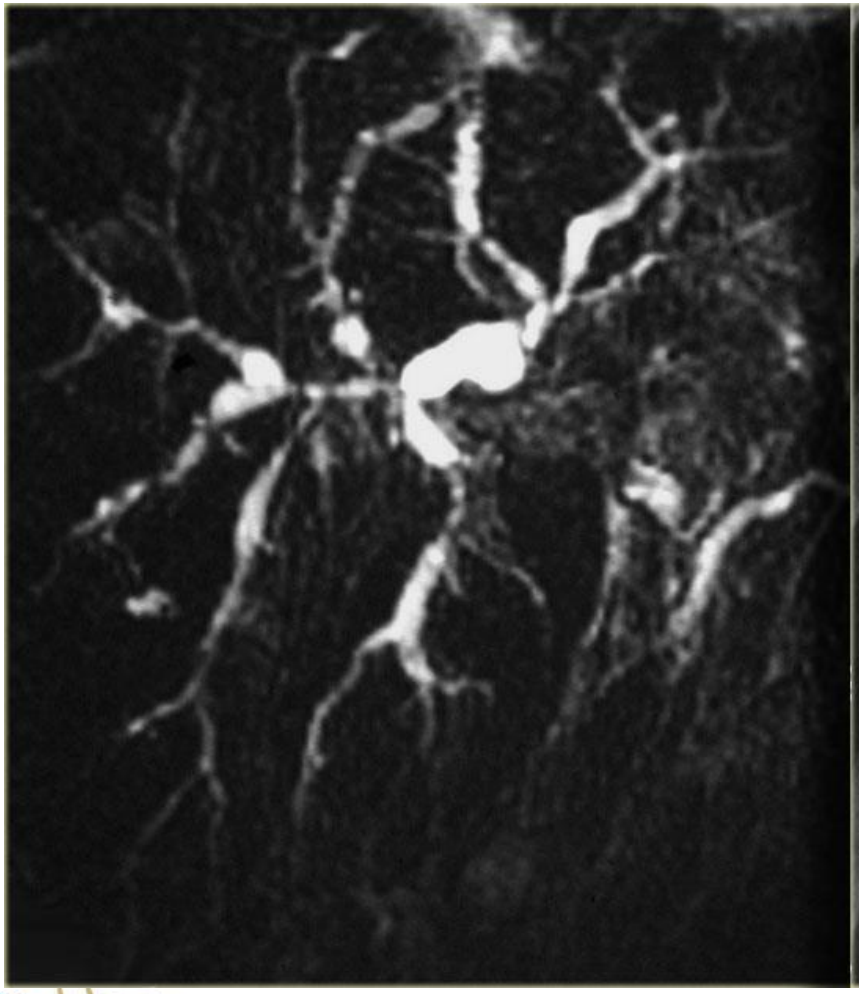

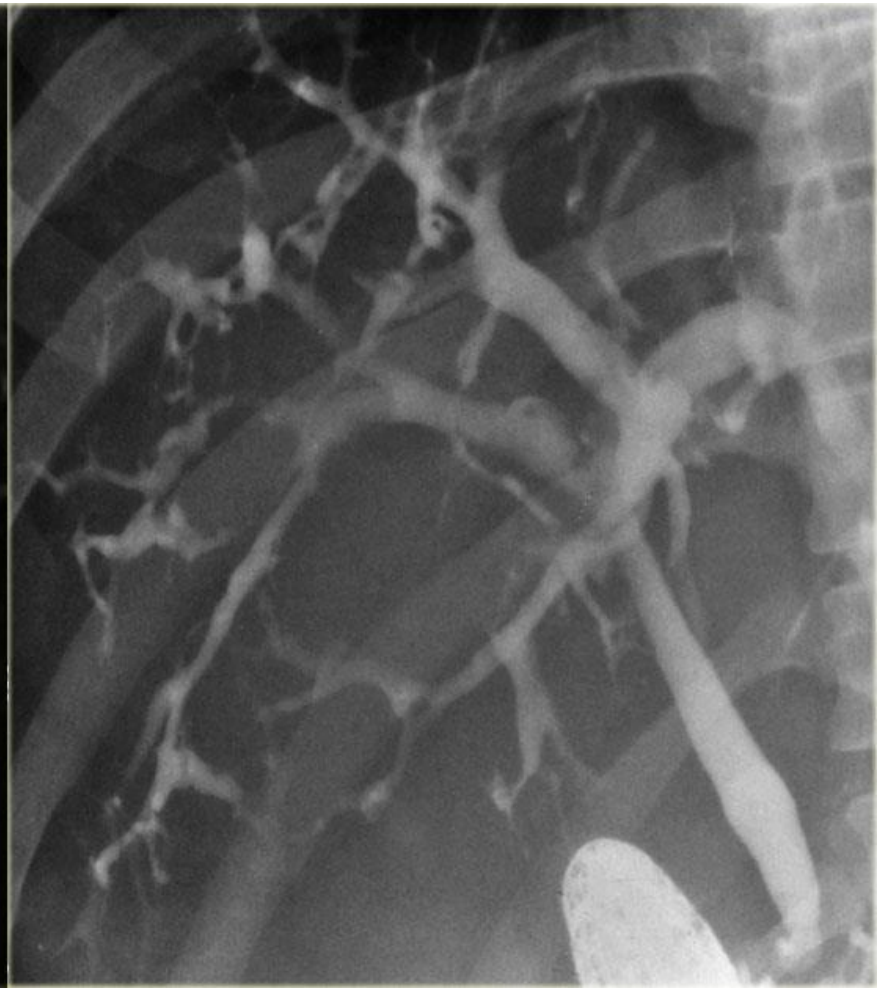

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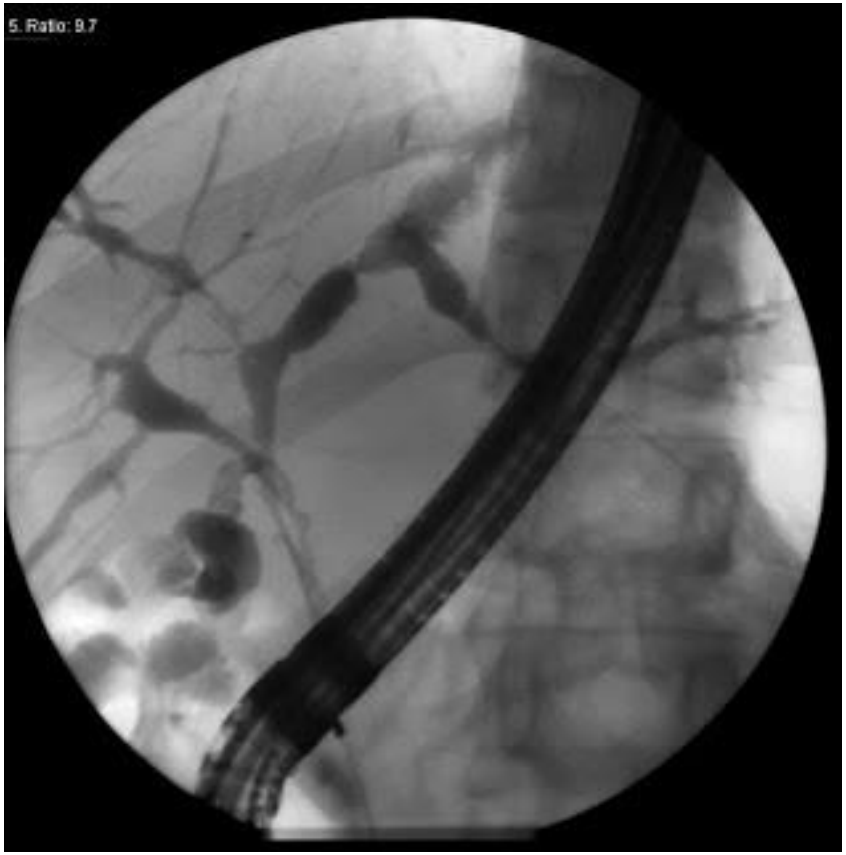

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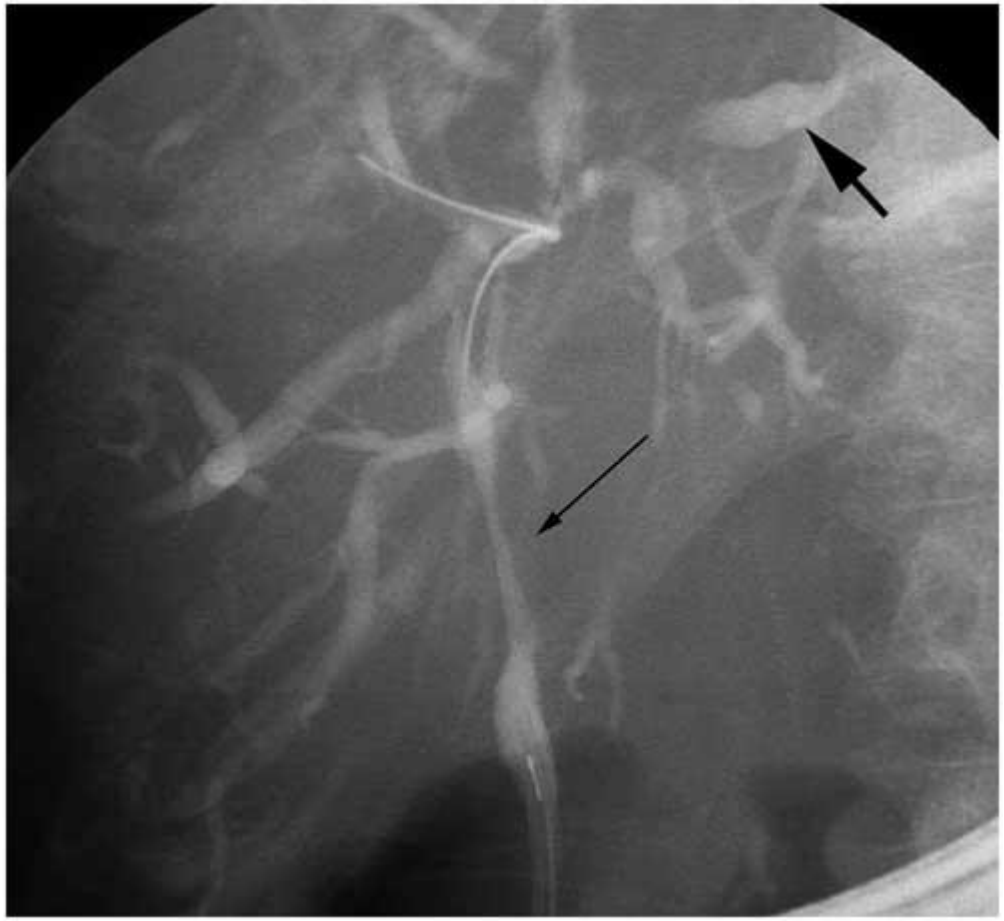
ERCP image in PSC



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Differential diagnosis of primary sclerosing cholangitis

- **Secondary sclerosing cholangitis**
- Cholangiocarcinoma
- **IgG4-associated cholangitis**
- Histiocytosis X
- Autoimmune hepatitis
- HIV syndrome
- Bile duct strictures
- Choledocholithiasis.
- **Primary biliary cirrhosis**
- Papillary tumors

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Small duct PSC Differential Diagnosis

- Liver biopsy is recommended to make a diagnosis in patients with suspected small duct PSC or to exclude other conditions such as suspected overlap with autoimmune hepatitis.

- Antimitochondrial autoantibody testing can help exclude (PBC) primary biliary cirrhosis.

- Patients with PSC should be tested at least once for elevated serum immunogloblulin G4 (IgG4) levels.

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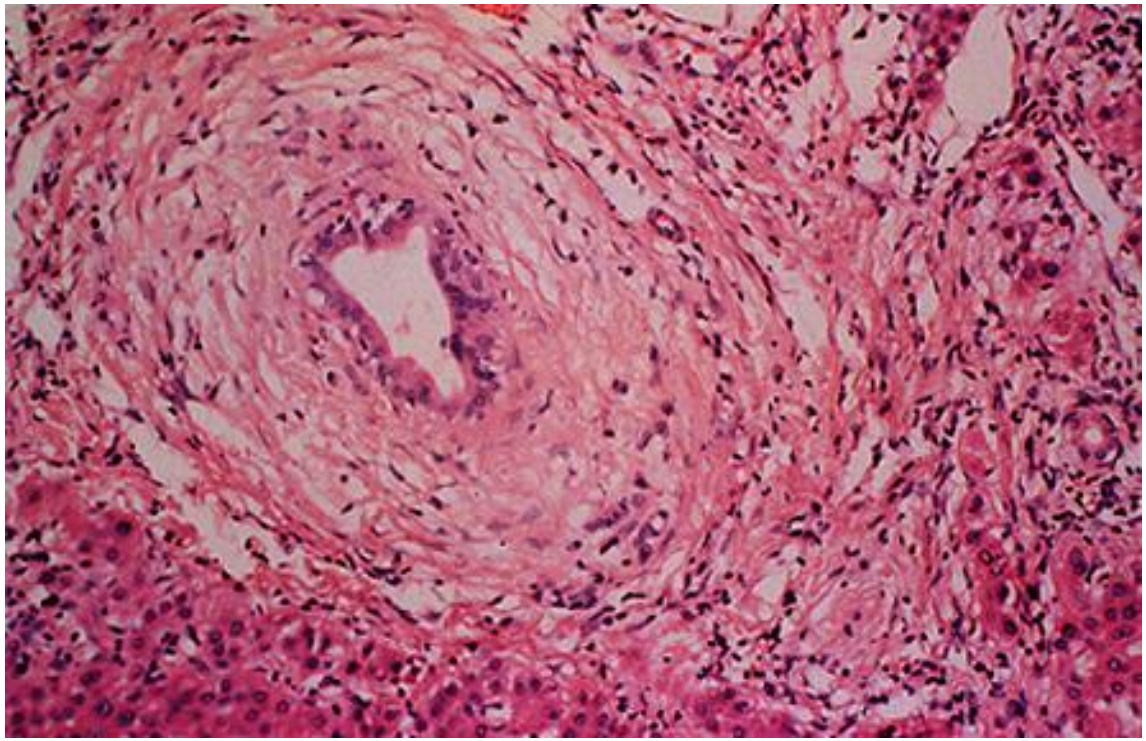

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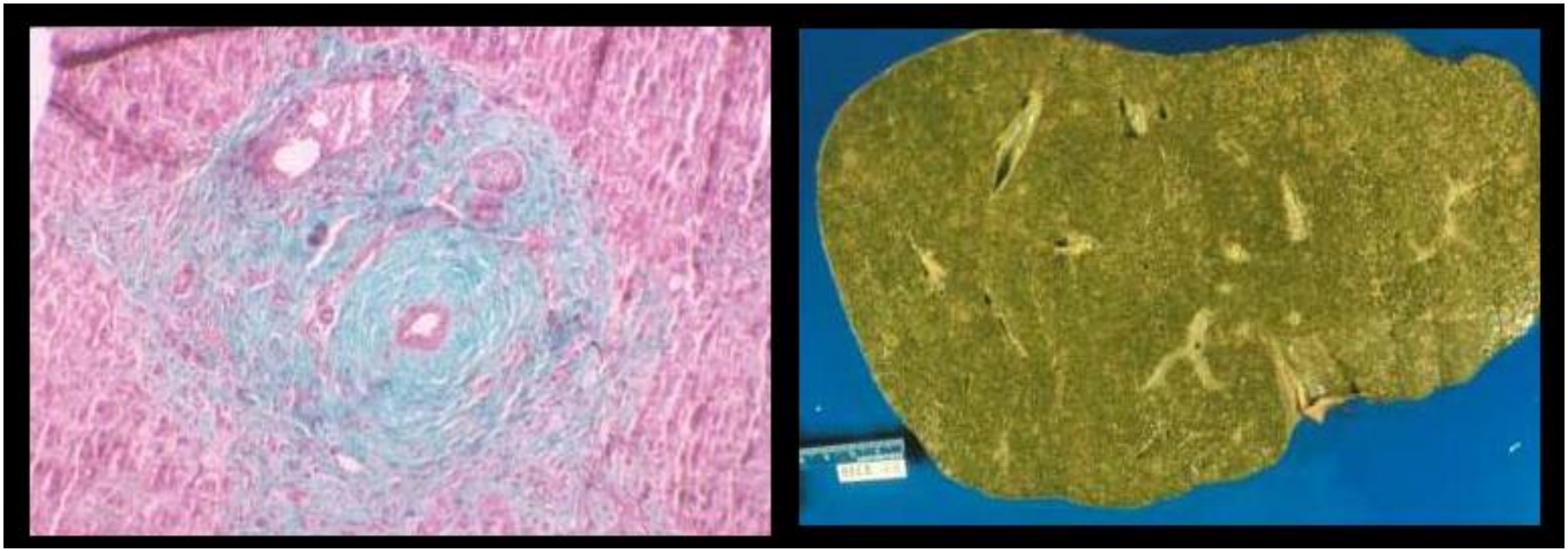
Histology



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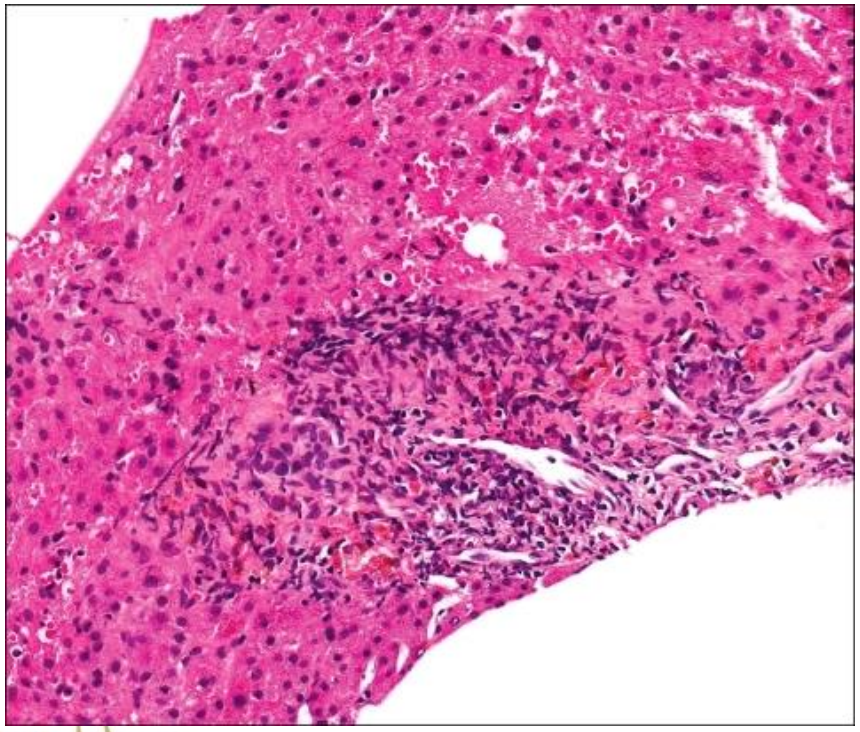
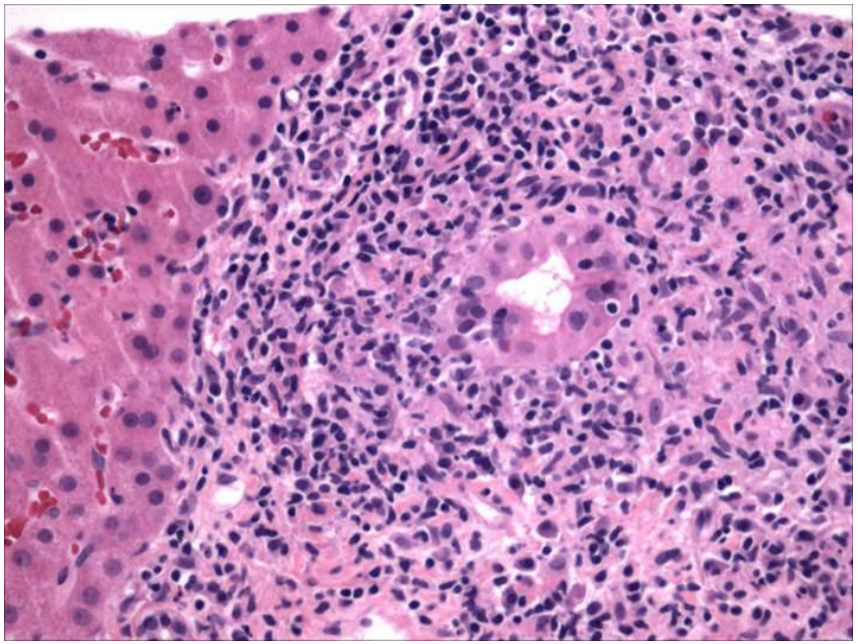
PBC





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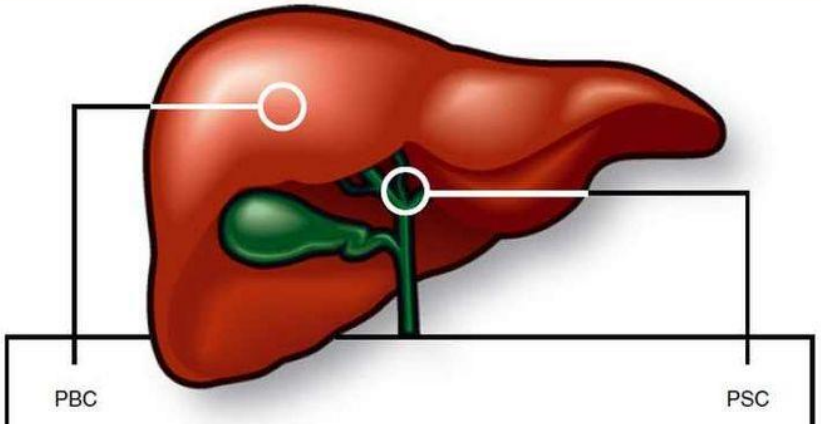
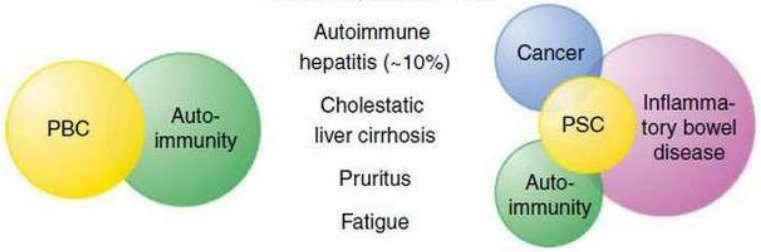


PBC PSC

Interlobular bile duct destruction	Intra-/extrahepatic bile ducts
Prevalence: 0.6–40 per 100.000	Prevalence: 0.2–14 per 100.000
Gender: F>M, 10:1	Gender F<M, 1:2
Age at onset: 50–60 years	Age at onset: 30–40 years
Smoking increases risk	Smoking decreases risk
>28 known risk genes	>16 known risk genes
Autoantibodies (AMA)	Autoantibodies (ANCA?)
Known T cell targets	Unknown T cell targets

Shared hepatic features:



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PSC and IBD

- Annual colon surveillance preferably with chromoendoscopy is recommended in PSC patients with colitis beginning at the time of PSC diagnosis.

- A full colonoscopy with biopsies is recommended in patients with PSC regardless of the presence of symptoms to assess for associated colitis at time of PSC diagnosis.

- Some advocate repeating the exam every 3–5 years in those without prior evidence of colitis.

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Medications

- Ursodeoxycholic acid

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ENDOSCOPIC MANAGEMENT

1 . ERCP with balloon dilatation is recommended for PSC patients with dominant stricture and pruritus, and/or cholangitis, to relieve symptoms.

2 . PSC with a dominant stricture seen on imaging should have an ERCP with cytology, biopsies, and fluorescence *in-situ* hybridization (FISH), to exclude diagnosis of cholangiocarcinoma.

3 . PSC patients undergoing ERCP should have antibiotic prophylaxis to prevent post-ERCP cholangitis

4 . Routine stenting after dilation of a dominant stricture is not required, whereas short-term stenting may be required in patients with severe stricture.

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Complications of PSC

- Fat-soluble vitamin deficiencies (A, D, E, and K)
- Metabolic bone disease
- Dominant biliary strictures
- Cholangitis and cholelithiasis
- Cholangiocarcinoma
- Gallbladder cancer
- Hepatocellular carcinoma (in patients with cirrhosis)
- Colon cancer (in patients with concomitant ulcerative colitis)

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Liver Transplant

- Liver transplantation, when possible, is recommended over medical therapy or surgical drainage in PSC patients with decompensated cirrhosis, to prolong survival.
- Patients should be referred for liver transplantation when their Model for End-Stage Liver Disease (MELD) score exceeds 14.
- Outcomes for liver transplantation in PSC compare favorably to transplants for other indications,

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special circumstances in which liver transplantation may be indicated despite low MELD score

- Recurrent or refractory cholangitis
- Intractable pruritus
- Peripheral or hilar cholangiocarcinoma <3 cm in diameter (in the context of a clinical trial)

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CANCER SCREENING

- Gallbladder carcinoma and cholangiocarcinoma
- An annual ultrasound examination to detect mass lesions in the gallbladder.
- Ultrasound or magnetic resonance imaging (MRI) to look for evidence of cholangiocarcinoma every 6 to 12 months.
- Serum levels of the tumor marker cancer antigen (CA) 19-9 every 6 to 12 months to detect cholangiocarcinoma.
- Cholecystectomy in patients found to have a gallbladder polyp >8 mm (of note, some guidelines recommend cholecystectomy for gallbladder masses of any size
- Evaluation for cholangiocarcinoma in patients with deterioration of constitutional performance status or liver biochemical tests.

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