



PSC: Recent Advances in PSC

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Disclosures



- Research – Mirum, Cymabay, BMS, Intercept, Hanmi, Target, Pliant, Ipsen, Novartis, Callidtas, and Gilead
- Advisor – Cymabay and Ipsen

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PRACTICE GUIDANCE

AASLD practice guidance on primary sclerosing cholangitis and cholangiocarcinoma

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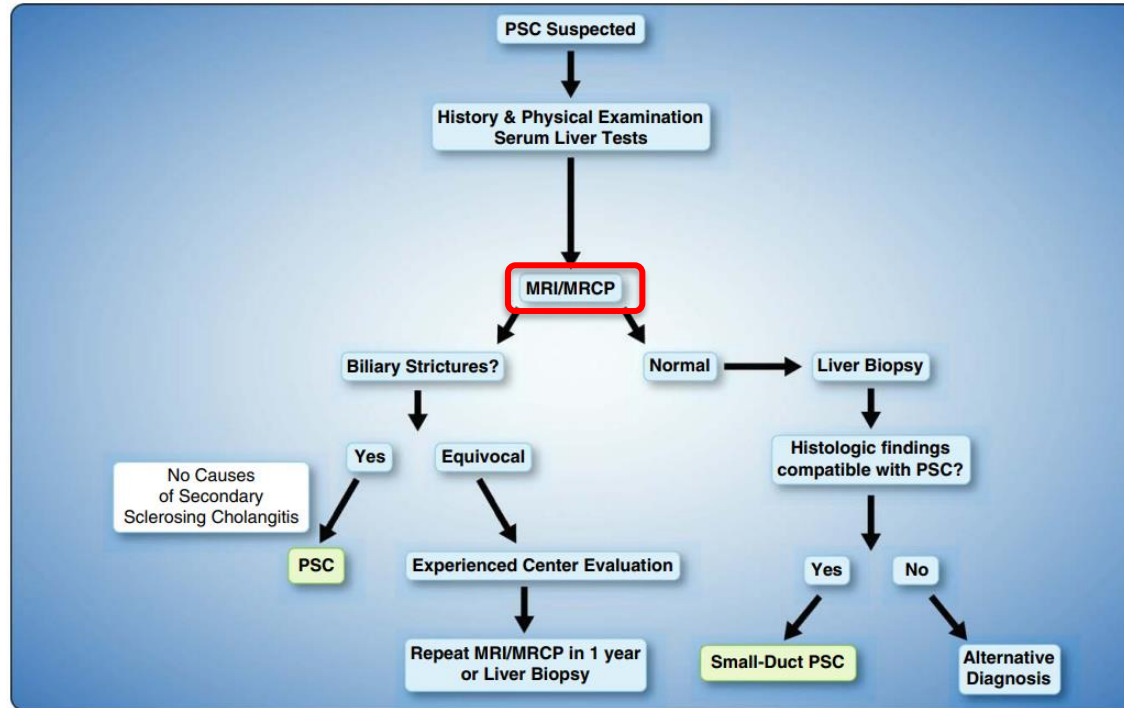
Definitions (1)

- Primary Sclerosing Cholangitis
 - Large duct PSC
 - Also known as PSC
 - Small duct PSC
 - Less common variant
 - Characterized by typical cholestatic and histological features of PSC
 - Normal bile ducts on cholangiography
 - In absence of IBD, consider other rare causes such as *ABCB4* (PFIC) mutations
 - PSC/AIH Overlap
 - Features of PSC
 - Clinical, biochemical, and histological features of AIH

Definitions (2)

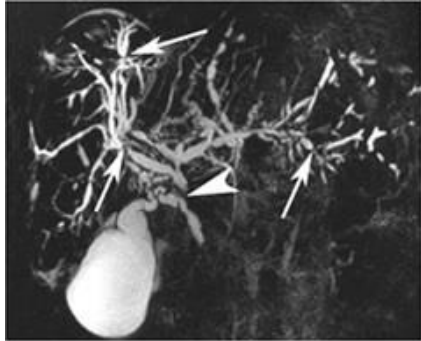
- **Strictures**
 - **Dominant (*Structural*)**
 - Stricture on ERCP with a diameter of ≤ 1.5 mm in the common bile duct or of ≤ 1 mm in the hepatic duct
 - **High-grade (*Structural*)**
 - Stricture on MRI with cholangiopancreatography with $>75\%$ reduction in the common bile duct or hepatic ducts
 - **Relevant (*Functional*)**
 - Any biliary stricture of the common bile duct or hepatic ducts associated with signs or symptoms of obstructive cholestasis and/or bacterial cholangitis
 - EASL requires it also to be of "high-grade"

Diagnosis



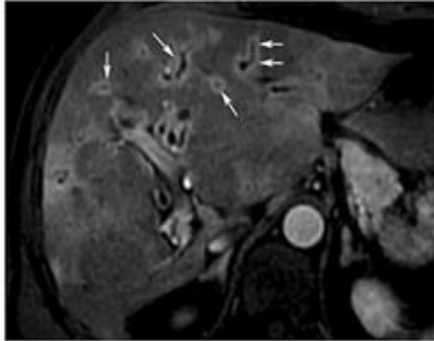
MRI Features of PSC

Strictures of intrahepatic biliary ducts

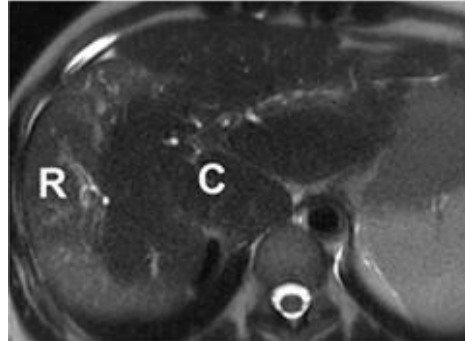


“High grade” stricture of common hepatic duct

Biliary wall thickening
Mural contrast enhancement

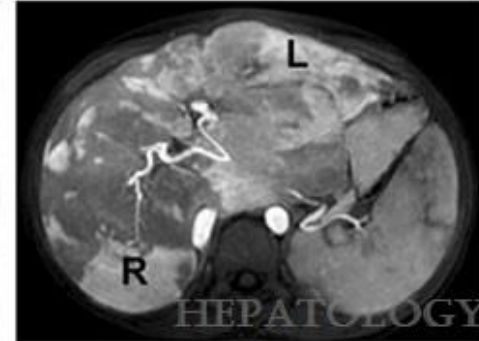


Dysmorphism

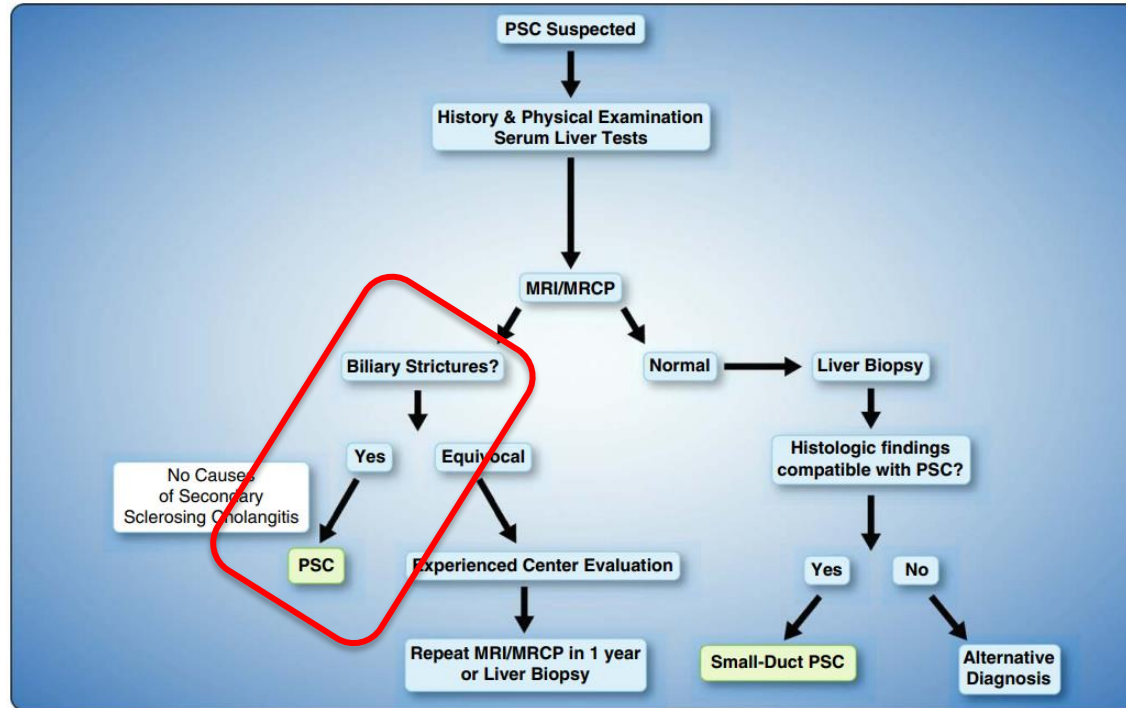


- Enlargement of the caudate lobe
- Atrophy with high signal intensity of the right liver lobe

Contrast enhancement heterogeneity



Diagnosis

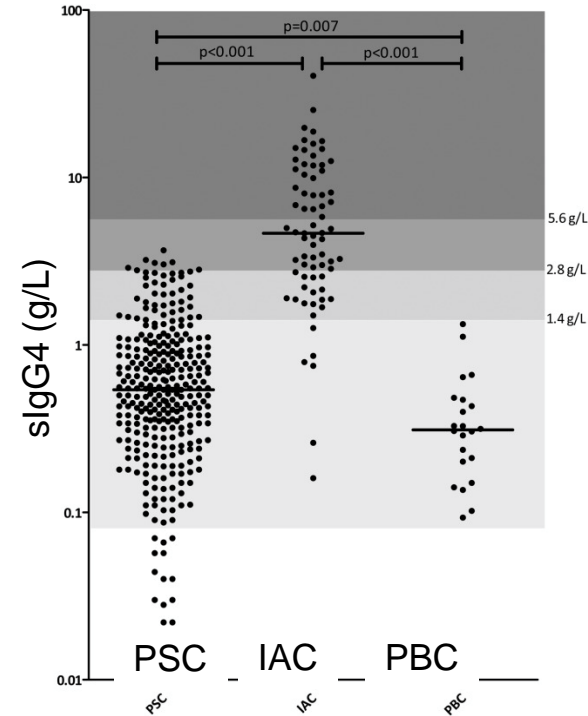


Secondary Sclerosing Cholangitis

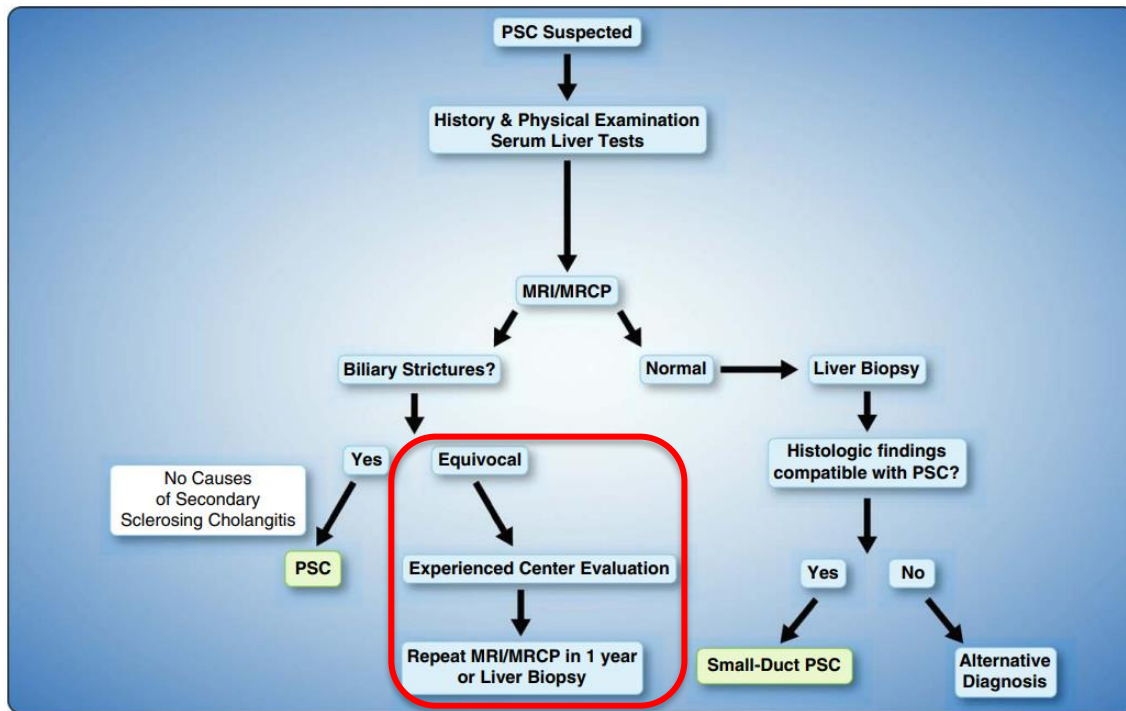
- Infectious
 - HIV-related cholangiopathy
 - Recurrent pyogenic cholangitis
 - Parasitic cholangiopathy
 - **COVID-19***
- Ischemic
 - **Critically ill patients**
 - Hereditary hemorrhagic telangiectasis
 - Intra-arterial chemotherapy
 - Hepatic artery thrombosis
- Malignant
 - **Cholangiocarcinoma**
 - **Diffuse intrahepatic metastasis**
 - Langerhans cell histiocytosis
 - Lymphoma
- Autoimmune
 - Eosinophilic cholangitis
 - Hepatic inflammatory pseudotumor
 - **IgG4-associated cholangitis**
 - Mast cell cholangiopathy
 - Sarcoidosis
- Anatomic
 - Choledocholithiasis
 - Intrahepatic lithiasis
 - Cystic fibrosis liver disease
 - **Surgical biliary trauma**
 - Anastomotic stricture
 - Portal hypertensive biliopathy
 - Recurrent pancreatitis
 - Sickle cell cholangiopathy
 - Choledochal cyst
- Drug-induced
 - **Immunotherapy with checkpoint inhibitors***

PSC versus IgG4-associated cholangitis

- Cholangiograms can look similar
- 5-15% of PSC patients have elevated IgG4
 - Original reports of worse prognosis have not been validated
 - Unclear if they benefit from steroids
- IgG4-SC is clinically distinct
 - Older men
 - <10% have IBD
 - Steroid Responsive
 - Serum IgG4 > 2.8 g/L



Diagnosis



MRI Standards

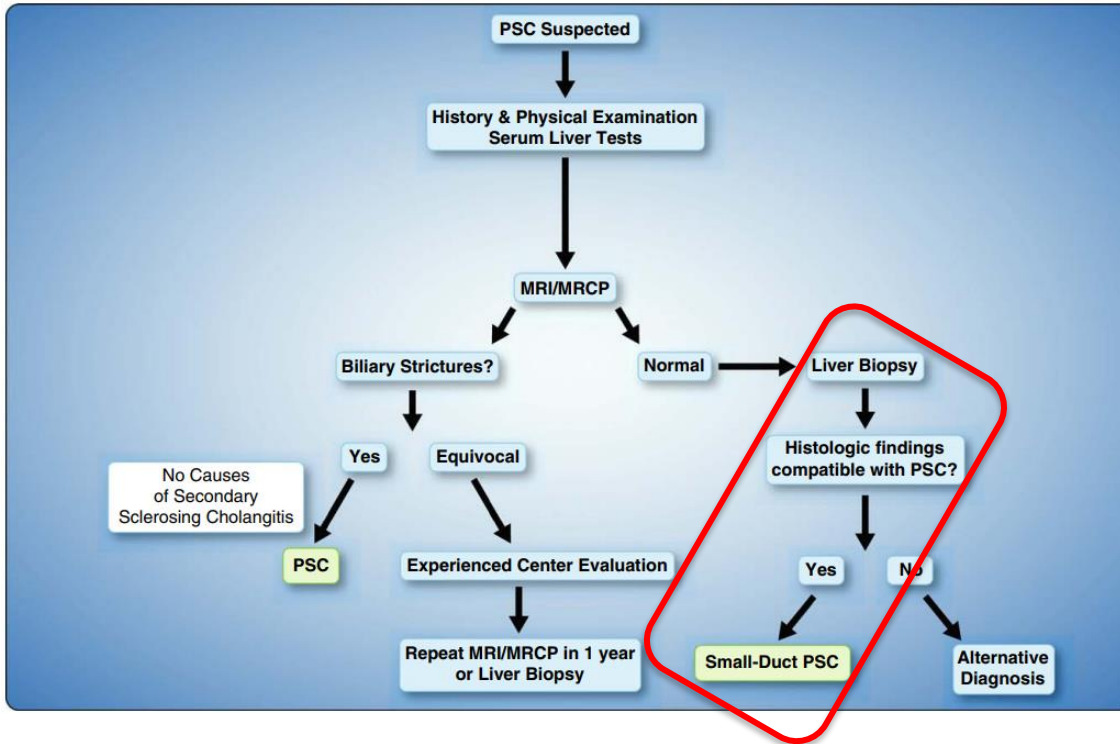
- Minimum of a 1.5-Tesla
- 3D MRCP with 1-mm slices
- Axial imaging including T1w and T2w
- Contrast enhancement

High-quality study

- No artifact or blurring
- Third-order biliary branches

30% probability of PSC even if the MRCP is negative in patients with high pre-test probability

Diagnosis



Liver Histology

- Concentric “onion skin” periductal fibrosis infrequent and non-specific.
- **Typical** features
 - periductal fibrosis
 - fibro-obliterative duct lesions
- **Compatible** features
 - bile duct loss
 - ductular reaction
 - biliary pattern of interface activity
 - chronic cholestatic changes in periportal hepatocytes.

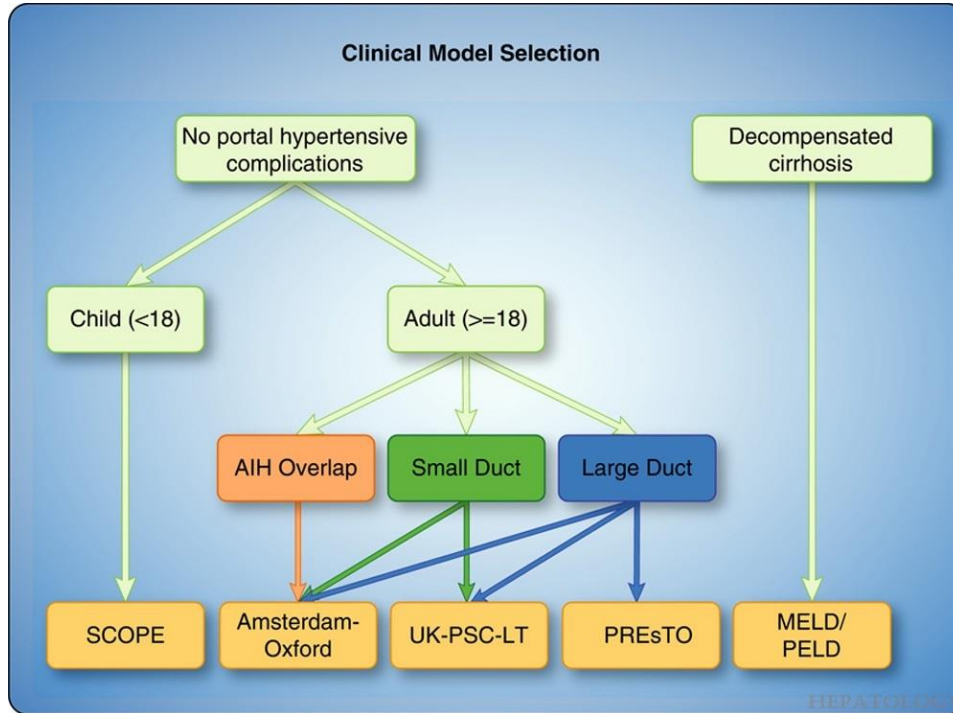
Small-Duct PSC

- Normal cholangiogram
- Typical or compatible histology
- In absence of IBD rule out *ABCB4*
- Monitor for transition to large-duct PSC

PSC-IBD

- 70% of patients with PSC have IBD
 - 2/3 ulcerative colitis
 - 1/3 Crohn's disease or indeterminate colitis.
- Frequently localized to the right colon and asymptomatic
- Histological evidence of IBD without endoscopic changes of IBD is frequent
- Increased risk of colon cancer starting at time of diagnosis
- High rate of pouchitis
- Response to anti-TNFs, vedolizumab, and JAK inhibitors appears to be similar to IBD patients without PSC
- Ileocolonoscopy with biopsies at the time of diagnosis (if no known IBD)
- Considered repeating at 5-year intervals if negative for IBD
- In patients with PSC in whom IBD is diagnosed, high-definition surveillance colonoscopy with biopsies should start at age 15 years and be repeated at 1-year to 2-year intervals to evaluate for colonic dysplasia.

Prognostic Models



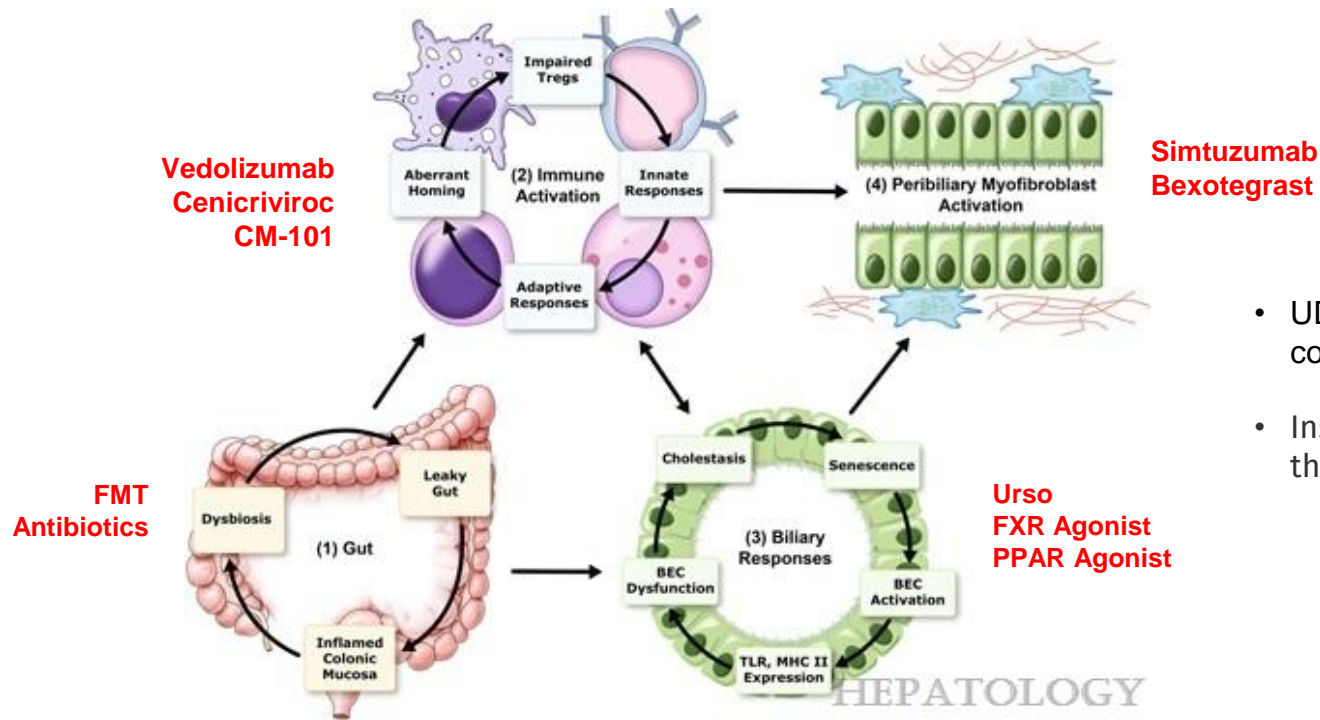
Transient elastography or MR elastography are the preferred methods for estimation of fibrosis stage.

Liver biopsy is not recommended for fibrosis staging in clinical practice.



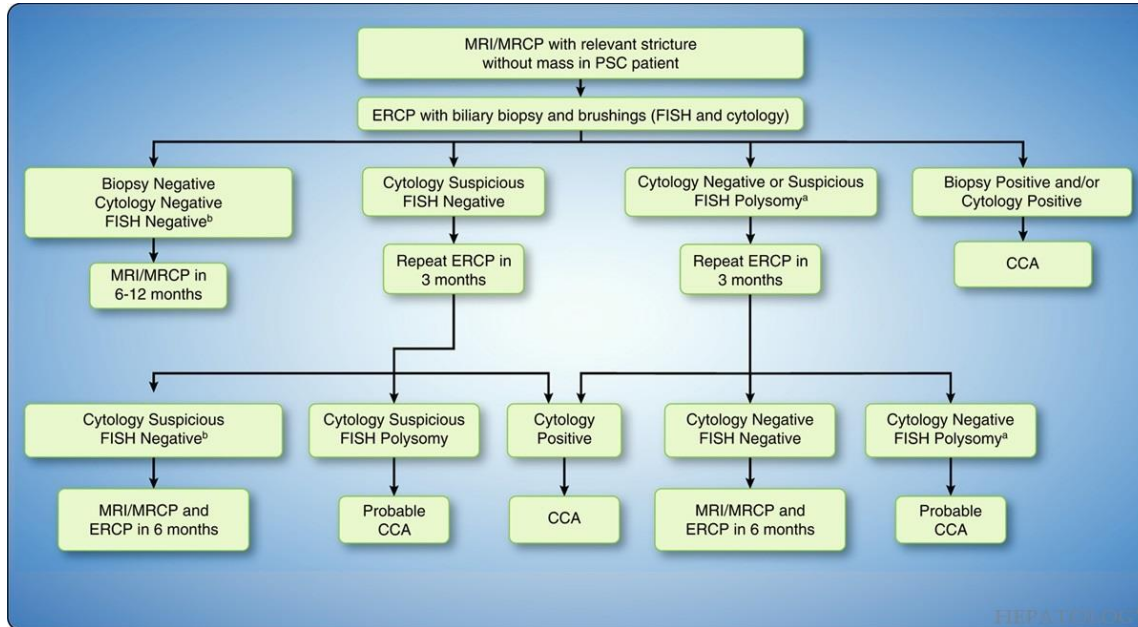
PSC Treatment

PSC Treatment



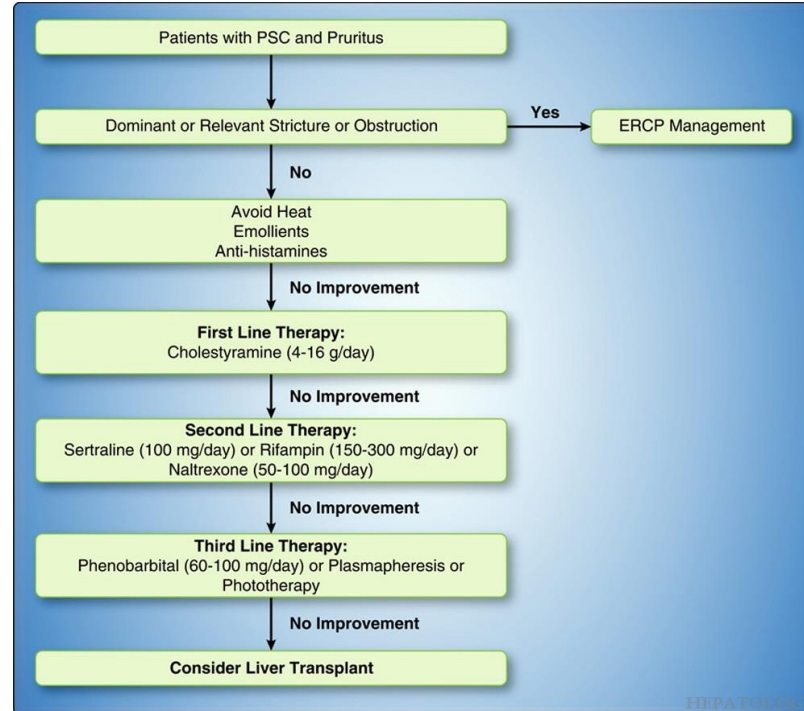
- UDCA 13–23 mg/kg/day can be considered
- Insufficient evidence to recommend the use of oral vancomycin

Cholangiocarcinoma – Surveillance/Diagnosis



- Annual surveillance
 - MRI preferred
 - +/- CA 19-9
 - Not necessary in pediatric patients or small-duct PSC
- Cytology and FISH should be performed routinely during ERCP

Pruritus



Recent Advances in PSC

- Diagnosis is based upon MRI/MRCP
 - Liver biopsy only to exclude AIH or diagnose small-Duct PSC
 - ERCP only for therapeutic intervention
- Screen all patients for IBD, even if asymptomatic
- TE and prognostic models can be helpful
- Urso (or nothing) is OK, oral vanco is not
- Cancer surveillance for CCA, colon cancer