▶ Primary Sclerosing Cholangitis [Young ♂ with UC]

- Cholestatic disease ⇒ ↑ALP + GGT
- Frequently associated with IBD, mostly UC
- Inflammation & fibrosis of biliary tree, leads to biliary cirrhosis & PHTN

• Etiology ≫ T-cell abnormal function / Infection / Portal bacteremia

• Clinical picture ≫ ↑ALP, in setting of colitis, May be Asymptomatic.

[confirm diagnosis] → ERCP or MRCP = Abnormal cholangiogram

• Clinical presentation ≫

Asymptomatic	15 - 44%
Symptomatic	
Fatigue	75
Pruritus	70
Jaundice	30-69
Hepatomegaly	34-62
Abdominal pain	16-37
Weight loss	10-34
Splenomegaly	30
Ascending cholangitis	5-28
Hyperpigmentation	25
Variceal bleeding	2-14
Ascites	2-10

(Fatigue, Pruritus → Most common)

Fever, jaundice, RUQ pain → Charcot Triad ← Multiple (Ascending cholangitis)

\# IBD 60-80% of PSC (UC 2 : 1 crohn)

\# 4-5% of UC have PSC.

• Diagnostic criteria ≫ History of IBD + cholestatic symptoms + ↑ALP (2-3 folds) > 6 months

- MRCP (mostly used) < Non-invasive, radiation, cost-effective ; ERCP (invasive, risk of pancrititis) ← stent, ballon, biopsy

- liver tests : Always elevated : ALP / AST & ALT ↑ (شوي ومرات normal) / Bilirubin, albumin, PTT (normal) ↓ when liver cirrhosis ⇒ imparment

- Auto Ab : ↑p-ANCA (80%) Note [UC = ANCA +ve, crohns = ASKA +ve]

  ↑ANA (not specific)

- Histology : onion skin like apperance [periductal fibrosis]

∴ Small duct PSC:
- 5% of PSC, can progress to PSC
- Normal cholangiogram, Biopsy +ve
- may or not with UC

• Therapy : Dilation of stricture , IV antibiotics , manage vit. Def. (imp. ↓ AKED)

manage metabolic bone disease [osteoporosis] by → ♀ hormon replacmt
→ vit D + Ca^{2+}
→ Bisphosphonates
✗ Calcitonin
✗ steriod

manage steatorrhea that caused from
- Diminished bile salts in gut
- Chronic pancritits
- co-exist celiac disease

≠ liver Transplant
- rejection
- infection
- recurrance
- colon CA.

• Cancer risk : CholangioCA / Hepatocellular CA / Colorectal CA / pancreatic CA.

must be screened yearly to rule out colon CA.

▶ Primary Biliary Cirrhosis [AMA↑, IgM↑, Middle age ♀]

- Cholestatic liver disease (confirm diagnosis) → Biopsy by ERCP ⇒ Florid duct sign.

Biochemical: ↑ALP 3x4 folds / ↑↑ AST. ALT / Bilirubin rise late / ↑cholestrol / ↑IgM

- Associated with autoimmune thyriod disease / Sicca syndrome / smoking

• Presentation:

Symptomatic	Asymptomatic	40-60%
	Fatigue (most common)	+++
use Cholestyramine to treat	Pruritus	++
	Sicca symptoms (Dry mouth, Dry eyes, mucus membranes dryness including vagina)	+++
Portal HTN	Hepatomegaly	+
	Splenomegaly	+
	Jaundice	uncommon
Due to high cholesterol levels	Xanthelasma	uncommon

Extrahepatic Autoimmune Diseases

		(%)
1	Sicca syndrome	70
2	Thyroid disease (Patient with history of thyroid disease found to have Cholestatic disease >>> think of PBC)	40
3	Arthritis	20
4	Scleroderma	15
5	Raynaud's phenomenon	10
6	CREST syndrome	5

Sicca syndrom [Keratoconjunctivitis + Xerostomia] needs
- ↑ fluid intake
- oral sialogogues
- artificial tears
- vaginal lubricants

Metabolic bone disease [osteopenia, osteoporosis . osteomalacia] → treat same as PSC

Portal HTN, most common in cirrhotic.

⇒ UDCA : decrease liver damage (The only useful drug)

▶ Autoimmune hepatitis

- Progressive inflammatory disease, ↑IgG ↑ALT-AST, (+ve) ANA-SMA
- peri-portal hepatitis ✓Respond to corticosteroids
- Middle age, ♀, non drinker, no viral hepatitis

• Clinical feature ⇒ fatigue / arthralgias / oligomenorrhea / jaundice

• Histo ⇒ Interface hepatitis with lymphoplasmacytic infiltrate

#Autoimmune hepatitis
- Type 1 ⇒ ⊕ ANA, ASMA
- Type 2 ⇒ ⊕ LKM-1, SLA/LP

More common (80%)	Type 1	Type 2
Age at Presentation	Any age (more with adults)	Predominantly children
Female:Male (both are female-predominant)	4:1	8:1 (more associated with females)
Ig G Levels	Elevated IgG	Variable Ig G
Ig A Levels	Normal	+/- Low IgA
Auto-antibodies	ANA, SMA	LKM-1
Cirrhosis at 3 yrs	~ 40%	~ 80% (worse prognosis)

• Indications for treatment
- AST ≥ 10X normal
- AST ≥ 5X & γ globulin ≥ 2X
- Bridging necrosis

• Therapy
- Monotherapy : prednisone
  - Indications: ① sever cytopenia ② TPMT def. ③ Aza intolerance ④ Pregnancy / Malignancy
- Combination : prednisone + Azathioprine
  - Indications: ① postmenopause ② osteoporosis ③ Brittle DM ④ Obesity . HTN ⑤ Acne ⑥ Emotional lability

#liver Transplant (recurrance 30-40%)

Summary :-

	Primary sclerosing cholangitis	Primary biliary cholangitis
Epidemiology	• More common among middle-aged **men**	• More common among middle-aged **women**
Pathophysiology	• Progressive chronic inflammation of both **intrahepatic and extrahepatic** bile ducts	• Progressive destruction of **only intrahepatic** small and medium-sized bile ducts
Clinical presentation	• Pruritus • Fatigue • Jaundice • Hepatomegaly	• Similar to PSC • Potentially xanthomas and xanthelasma
Laboratory tests	• **pANCA** • ↑ ALP, GGT, and conjugated bilirubin	• Anti-mitochondrial antibodies (**AMA**) • ↑ ALP, GGT, and conjugated bilirubin
Associated conditions	• Ulcerative colitis and cholangiocarcinoma	• Autoimmune conditions

Differentiating PSC from PBC

	PSC	PBC
Cholestasis	+	+
History of colitis	+	-
AMA	-	+
Liver biopsy	onion skin fibrosis	florid duct lesion
Cholangiogram	abnormal	normal

↓

IgM

Autoimmune hepatitis » IgG

↓

Respond to corticosteriods.