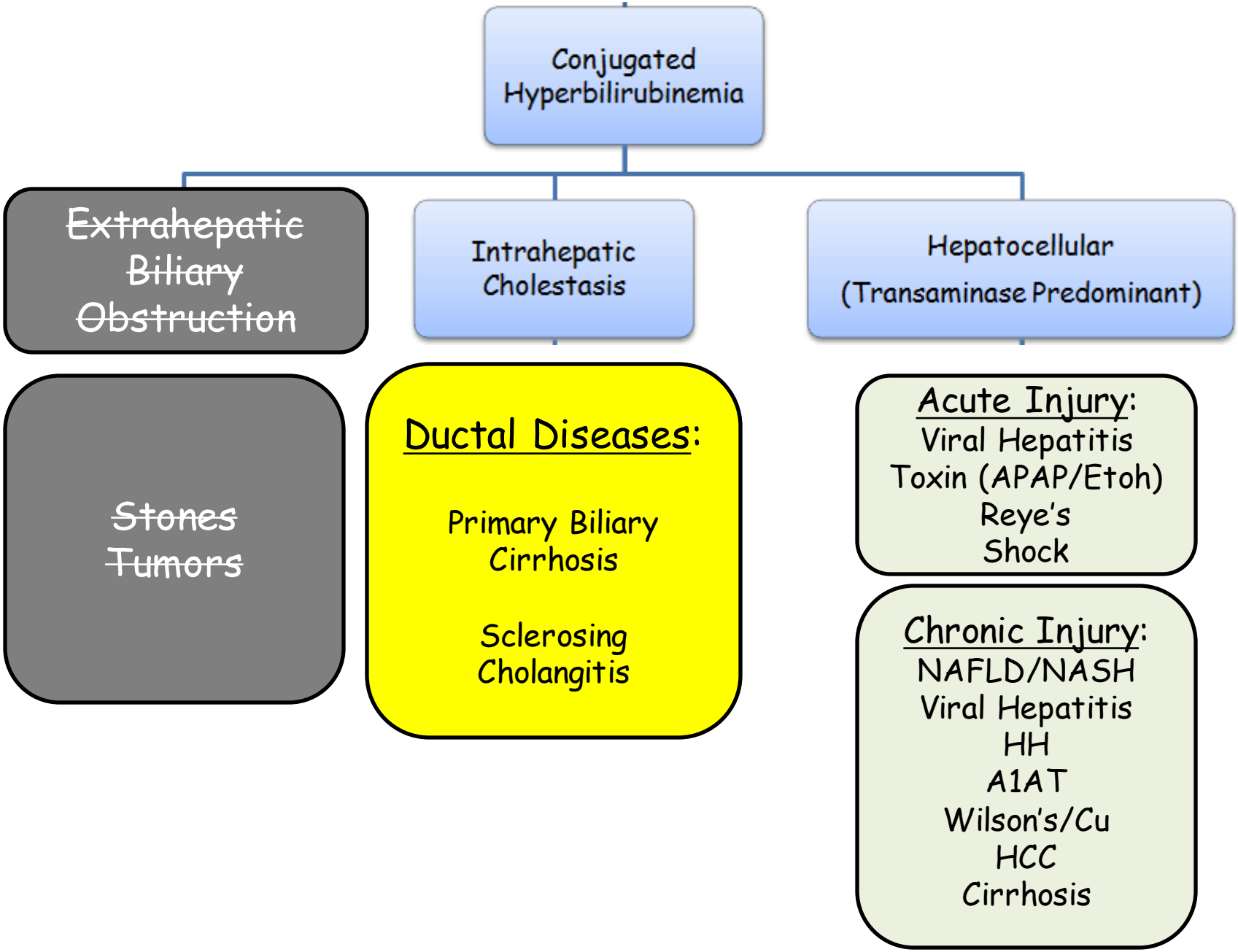
Conjugated Hyperbilirubinemia
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Sclerosing Cholangitis
Acute Injury:
Viral Hepatitis
Toxin (APAP/Etoh)
Reye's
Shock
Chronic Injury:
NAFLD/NASH
Viral Hepatitis
HH
A1AT
Wilson's/Cu
HCC
Cirrhosis

Primary Biliary Cirrhosis

That's a lousy name for this condition.
Primary = Excess Verbeage
They Don't Present With 'Biliary' (rises late in disease).
And for crying out loud, USMLE won't give you one with cirrhosis.

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Tired, Itchy, Woman, Syndrome

↓

Tired, Itchy, Woman with Elevated AlkΦ.

↓

Tired, Itchy, Woman with Elevated AlkΦ and + AMA
(and probably with xanthelasma).

And that is the correct name:

Tired, Itchy, Woman with Elevated AlkΦ and + AMA.

Tired, Itchy, Woman with Elevated AlkΦ and + AMA

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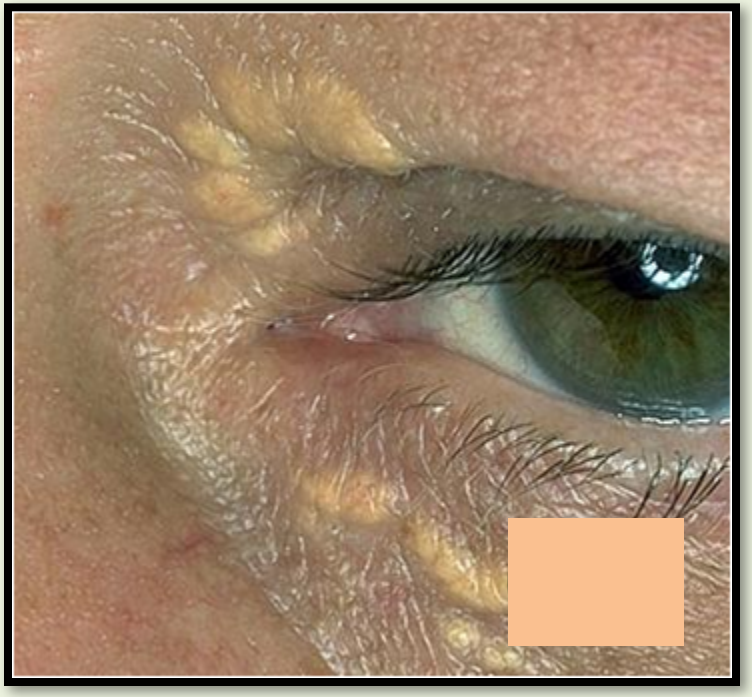


Let's get familiar with disease associations and pathology and we're done.

Primary Biliary Cirrhosis

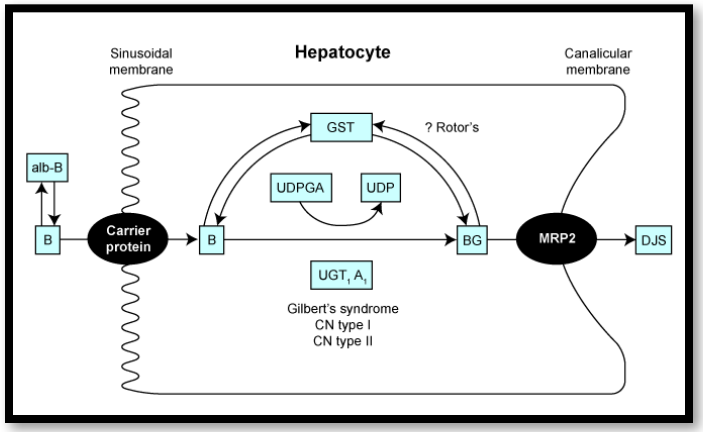
-
-

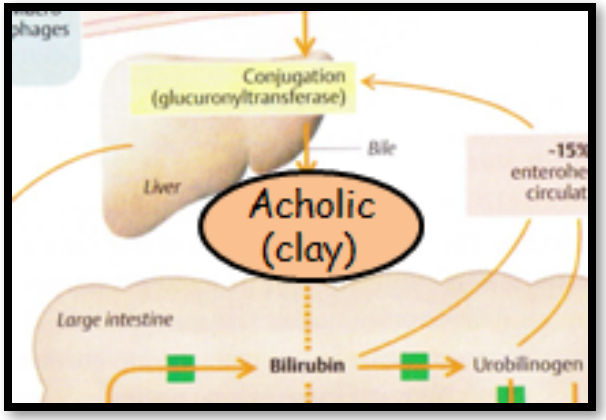
Primary Biliary Cholangitis

Primary Biliary Cirrhosis
(Female, Fatigue, Itch plus Alk Phos and AMA)

- Background
  - Results from autoimmune destruction of intrahepatic bile ducts
  - Effects middle aged women
  - Concommitant autoimmune dz (Sjogren's, etc).

- Presentation
  - Fatigue & Pruritis w/ elevated Alk Phos (bili goes up late in disease)
    - Conjugated or unconjugated bilirubin?
  - Jaundice and progressive liver failure
  - S/s Fat-soluble vitamin deficiency due to bile salt deficiency
  - Xanthelasma: inability to secrete cholesterol
  - Pale (acholic) stool due to inability to excrete bilirubin





Primary Biliary Cirrhosis
(Female, Fatigue, Itch plus Alk Phos and AMA)

Xanthomas: yellow, plaque-like (or nodular) soft tissue masses found around the eyes or over extensor surfaces (especially the Achilles tendon)

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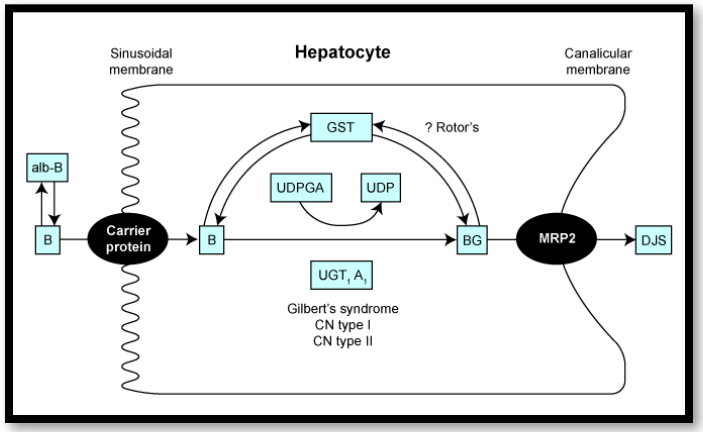

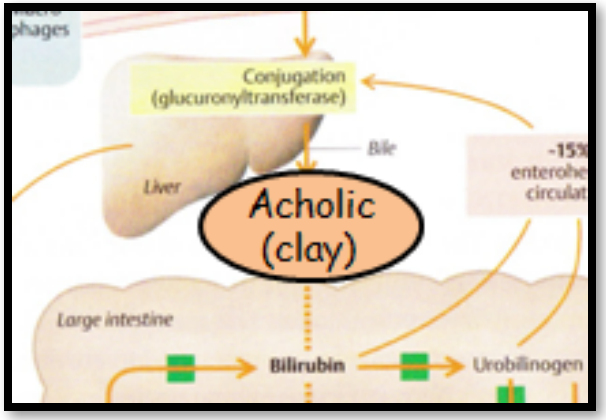

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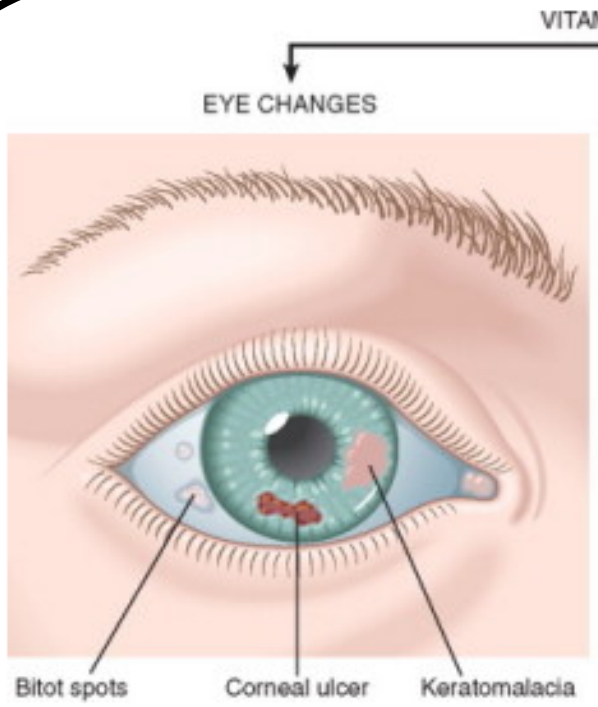
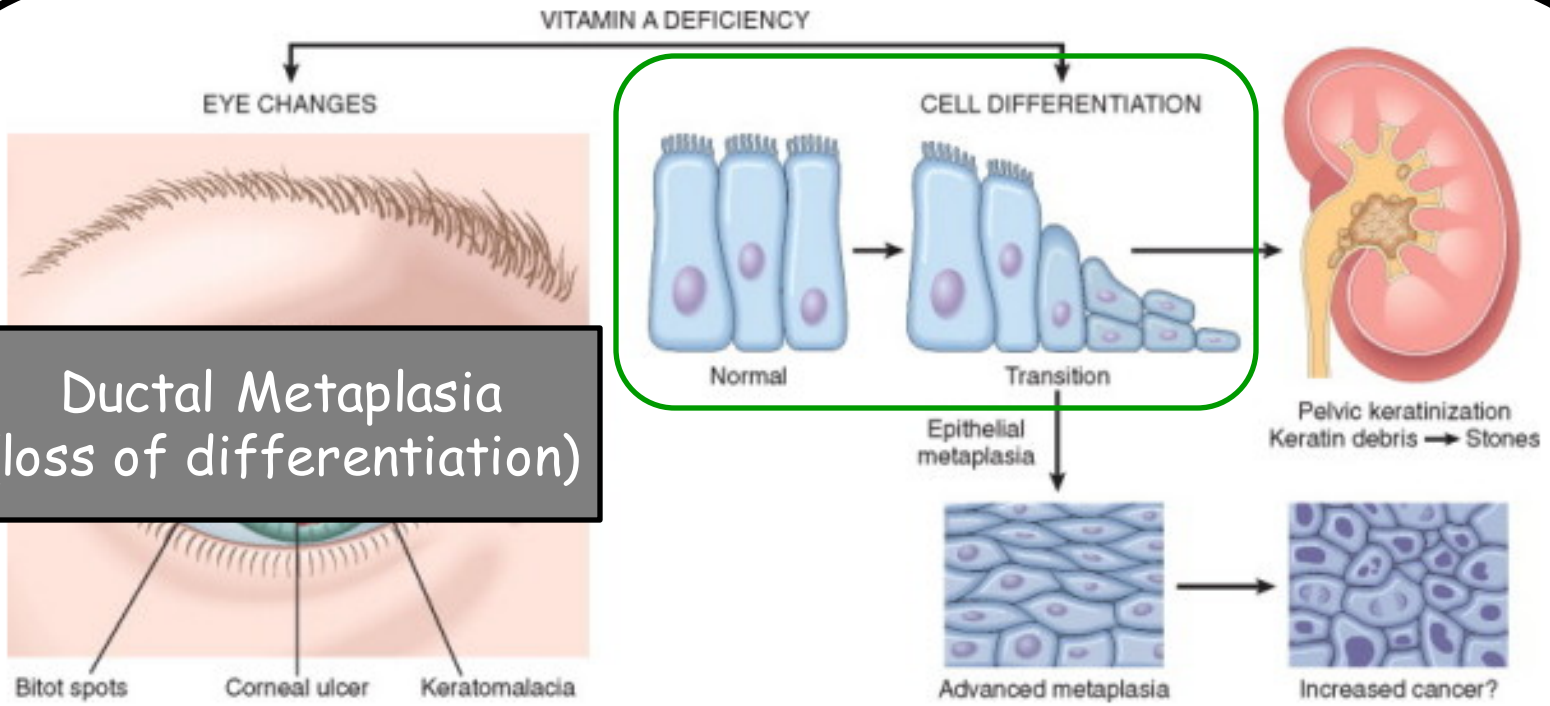
Vitamin A Deficiency

D – covered w/ bone
K – covered w/ coagulation
E – (never see – will cover in GI)



Ocular Manifestations:

- Cornea (ulcer, scar)
- Retina (loss of visual pigments)

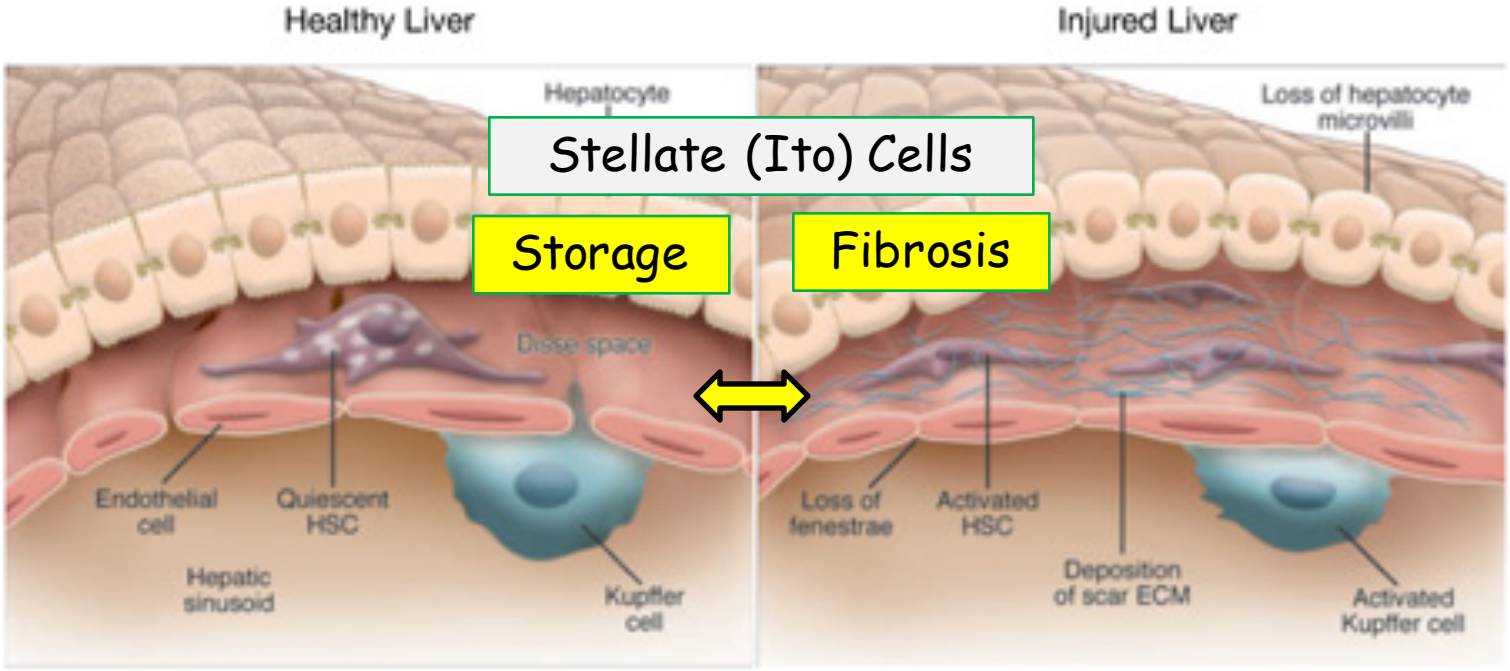


Ductal Metaplasia
(loss of differentiation)

Keratinizing, Proliferating Squamous Cells

- Cornea
- Ducts
- Skin

USMLE



In healthy liver, hepatic stellate cells are kept quiescent and their main function is to store vitamin A droplets. When the liver is injured, hepatic stellate cells transform into activated myofibroblast-like cells to generate scar tissue. (adopted from Iredale, 2007. The Journal of Clinical Investigation 117(3): 539-548).

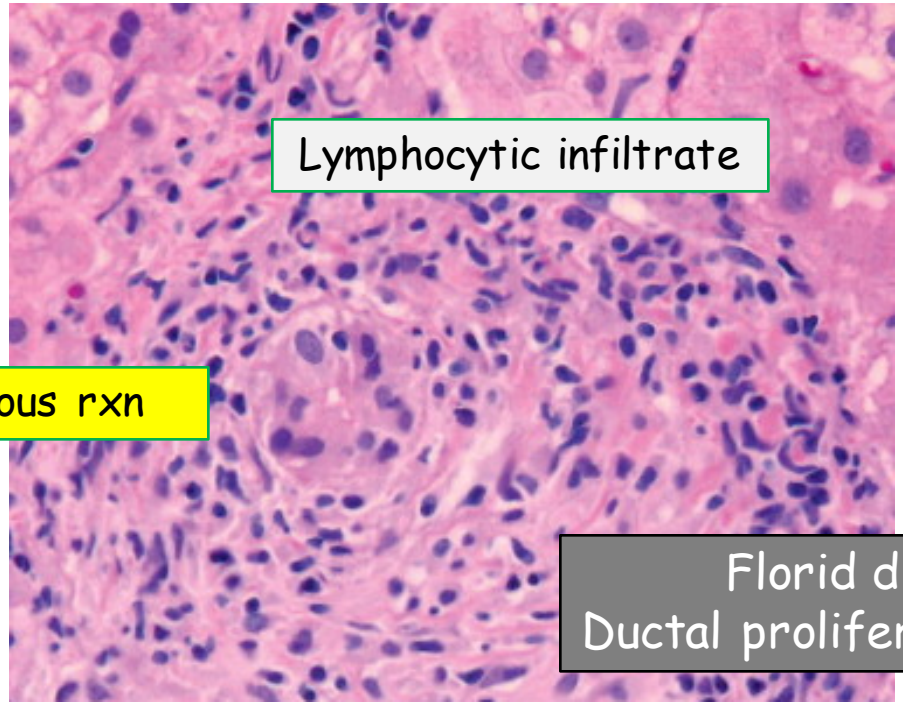
Hepatic Stellate Cells (or Ito cells) in Space of Disse

1. Store Vitamin A
2. Tranform into myofibroblasts → fibrosis

Primary Biliary Cirrhosis
(Female, Fatigue, Itch plus Alk Phos and AMA)

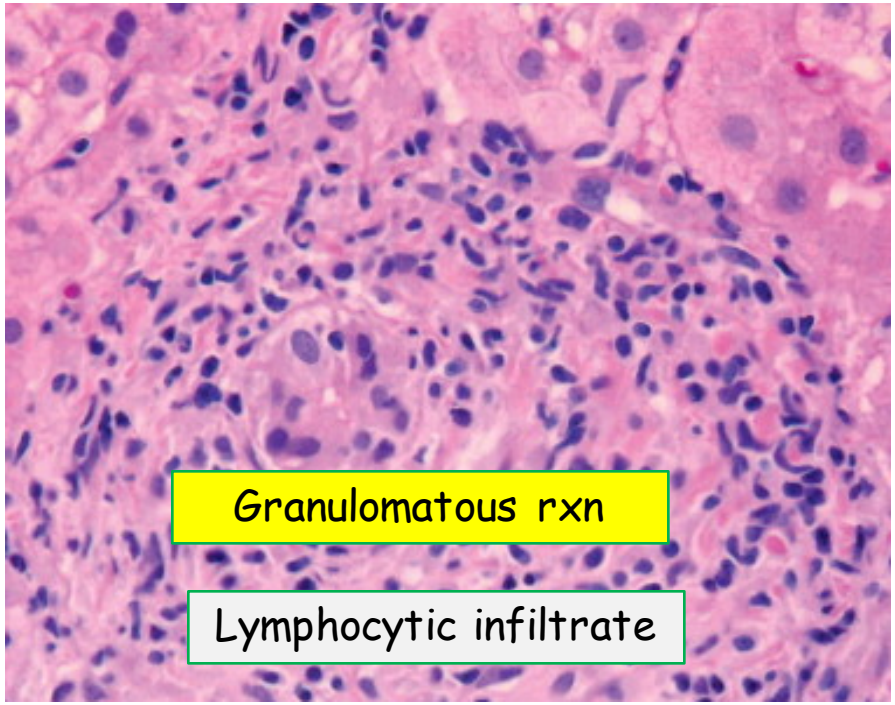
- Diagnostics
  - Elevated Alkaline Phosphatase
    - Bone v Liver??? Distinguish with γ-GT
  - Anti-Mitochondrial Antibody
    - Elevated transaminase, cholesterol
  - Liver biopsy:
    - Lymphocytic infiltrate in portal region
    - Granulomas
    - Loss of bile ductules ('florid duct' lesion)

PBC: Pathology



- A portal tract is markedly expanded by an infiltrate of lymphocytes and plasma cells.
- There is a granulomatous reaction to a bile duct undergoing destruction (florid duct lesion).
- Portal tracts upstream from damaged bile ducts show ductule proliferation, inflammation, and necrosis of the adjacent periportal hepatic parenchyma.

PBC: Pathology



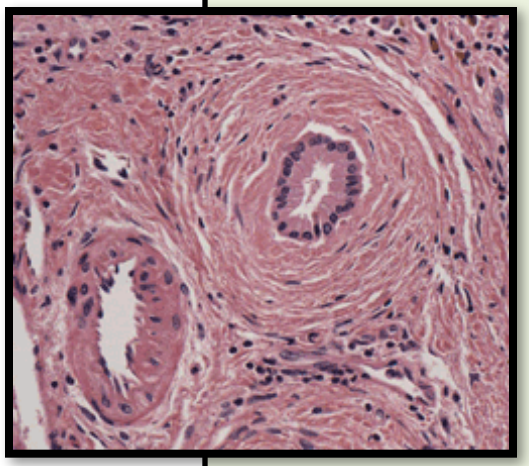
The relevance of the pathology is in distinguishing from PSC

(i.e. 'sclerosing' = fibrotic process)

Definition–PSC

Primary Sclerosing Cholangitis

= Fibrosis



…in distinction to PBC

Macro: Obliterative fibrosis of intra- AND extra-hepatic bile ducts
Micro: Not granulomatous; Onion skin fibrotic process on bx;
Dx: Cholangiogram reveals: 'Beading'

Complication of Ulcerative Colitis

ClinicalPresentation

Primary Sclerosing Cholangitis

Clinical Presentation

Asymptomatic	**15 - 44%**
Symptomatic	
Fatigue	**75**
Pruritus	**70**
Jaundice	**30-69**
Hepatomegaly	**34-62**
Abdominal pain	**16-37**
Weight loss	**10-34**

UC and elevated Alk Φ

Fatigue & Pruritis.
Sound familiar?...how will you know???

Major differences:

- Ulcerative Colitis
- Not a tired, woman (but Alk Φ is ↑)
- Fibrosis v Granuloma

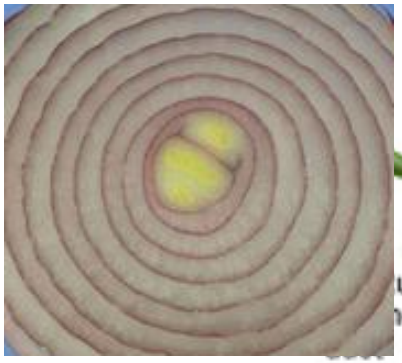
DifferentiatingPSCfromPBC

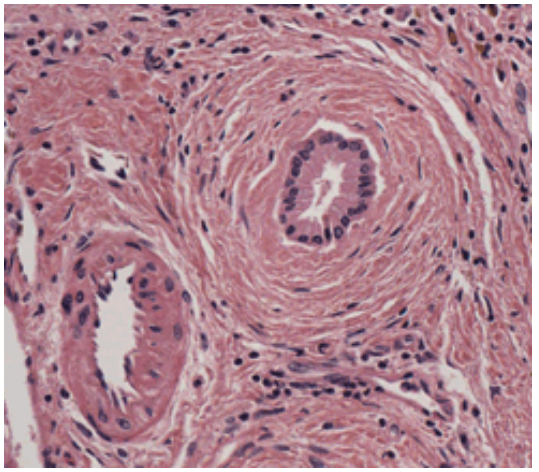
Primary Sclerosing Cholangitis

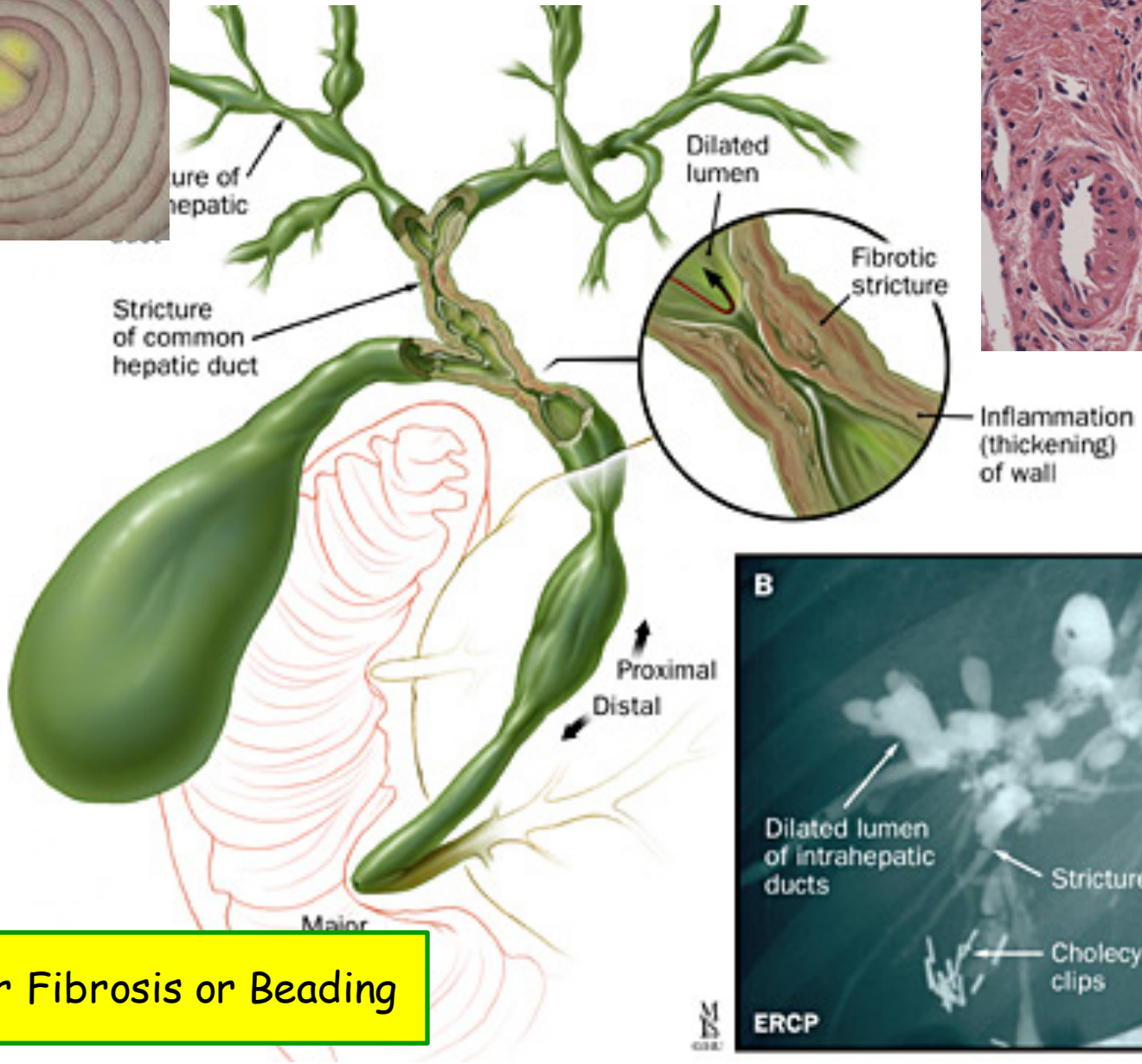
Differentiating PSC from PBC

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

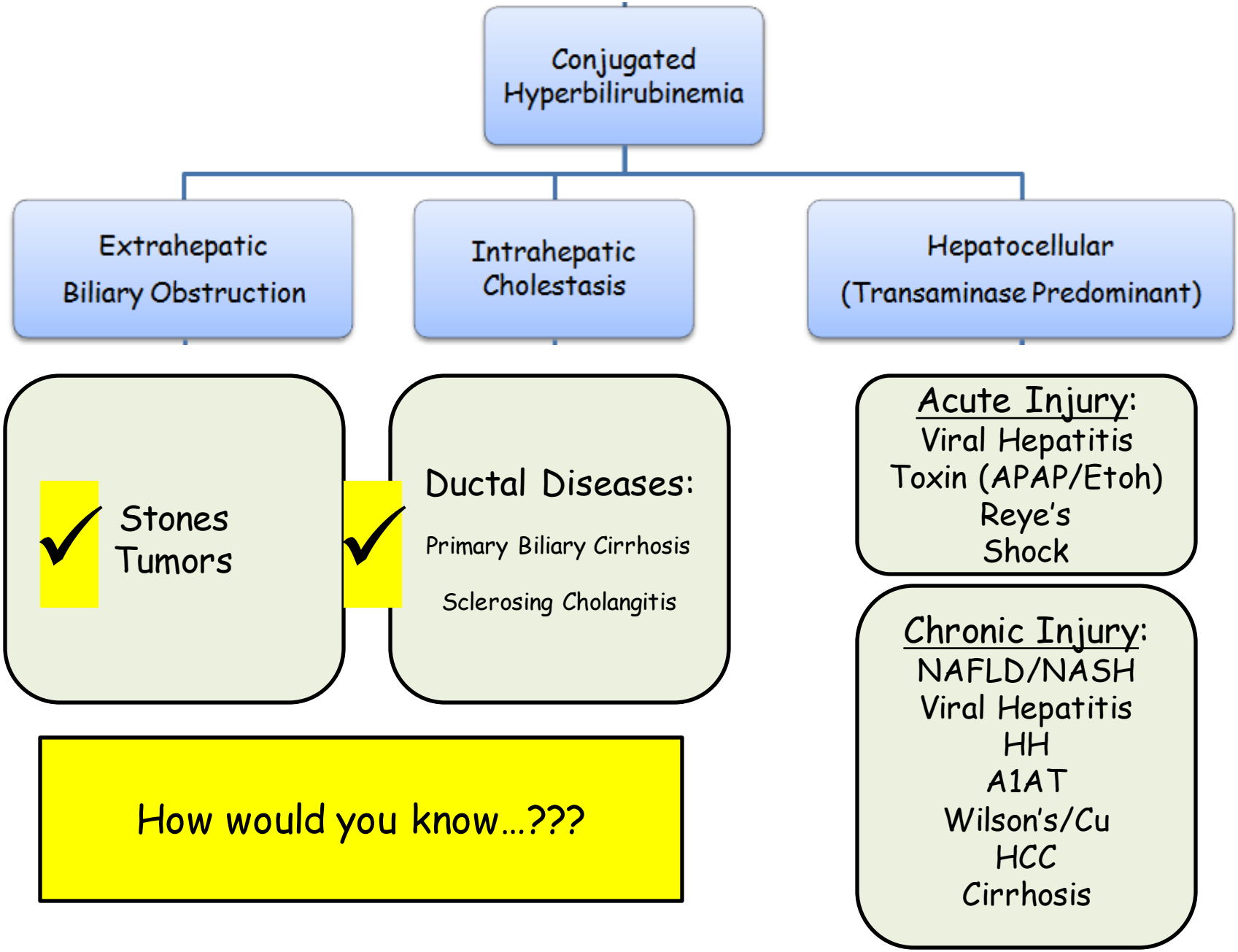
Biopsy plays little role in diagnosing PSC; used more for staging/prognosis and differentiating from other conditions BUT be familiar with the pathology for USMLE Step One.







Either Fibrosis or Beading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How would you know…???