Interpreting Your Tests

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Outline

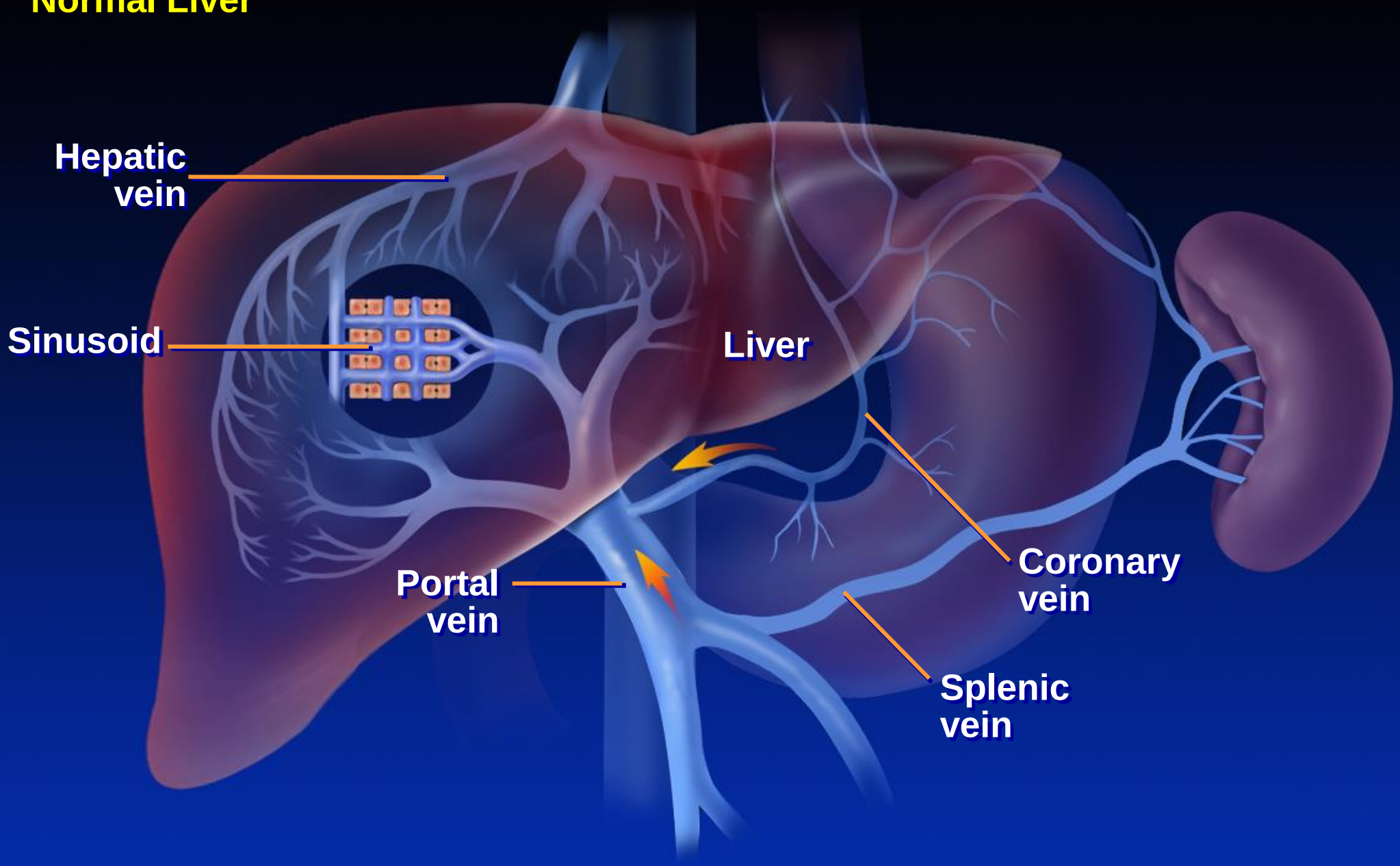
- Bile Duct Anatomy
- Lab Tests
  - LFTs
  - Tumor markers
  - MELD score
- Histologic Tests
- Radiologic Tests
- Endoscopic Tests
  - ERCP
  - EGD

The Liver has Many Functions

- Makes sugar
- Detoxifies
- Makes clotting factors
- Makes bilirubin
- Makes protein

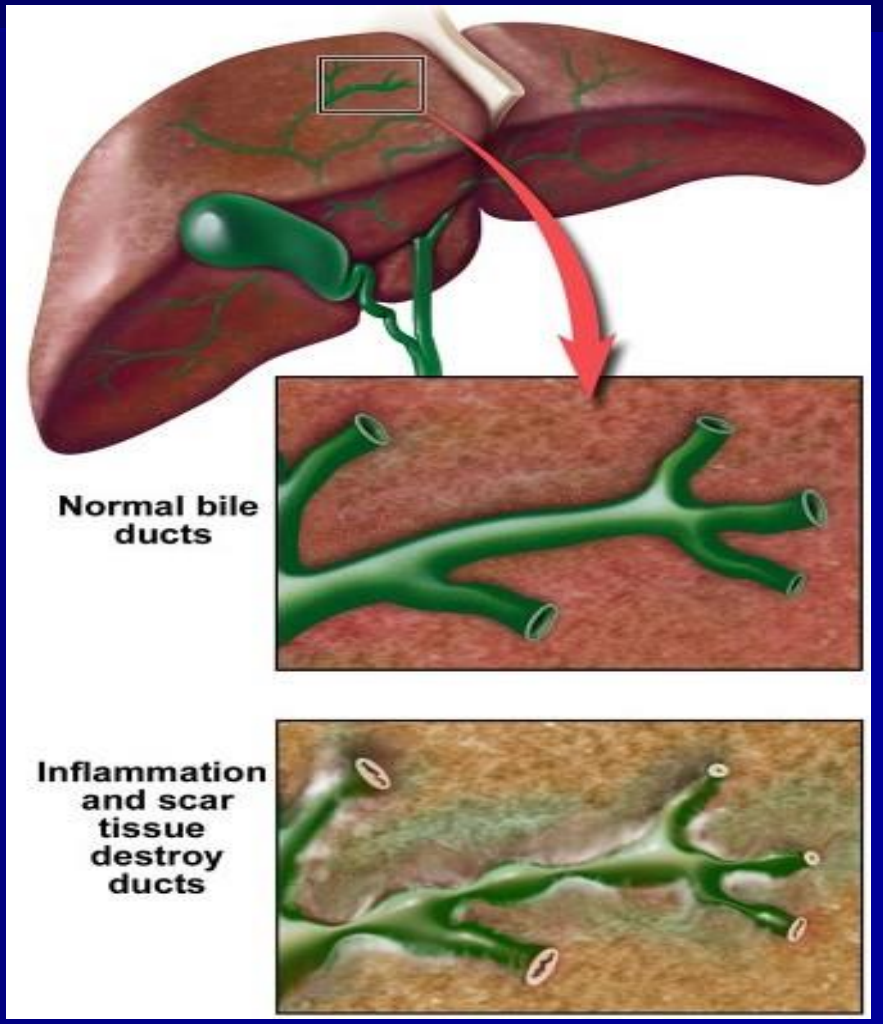
THE NORMAL LIVER OFFERS ALMOST NO RESISTANCE TO FLOW

Normal Liver



Primary Sclerosing Cholangitis

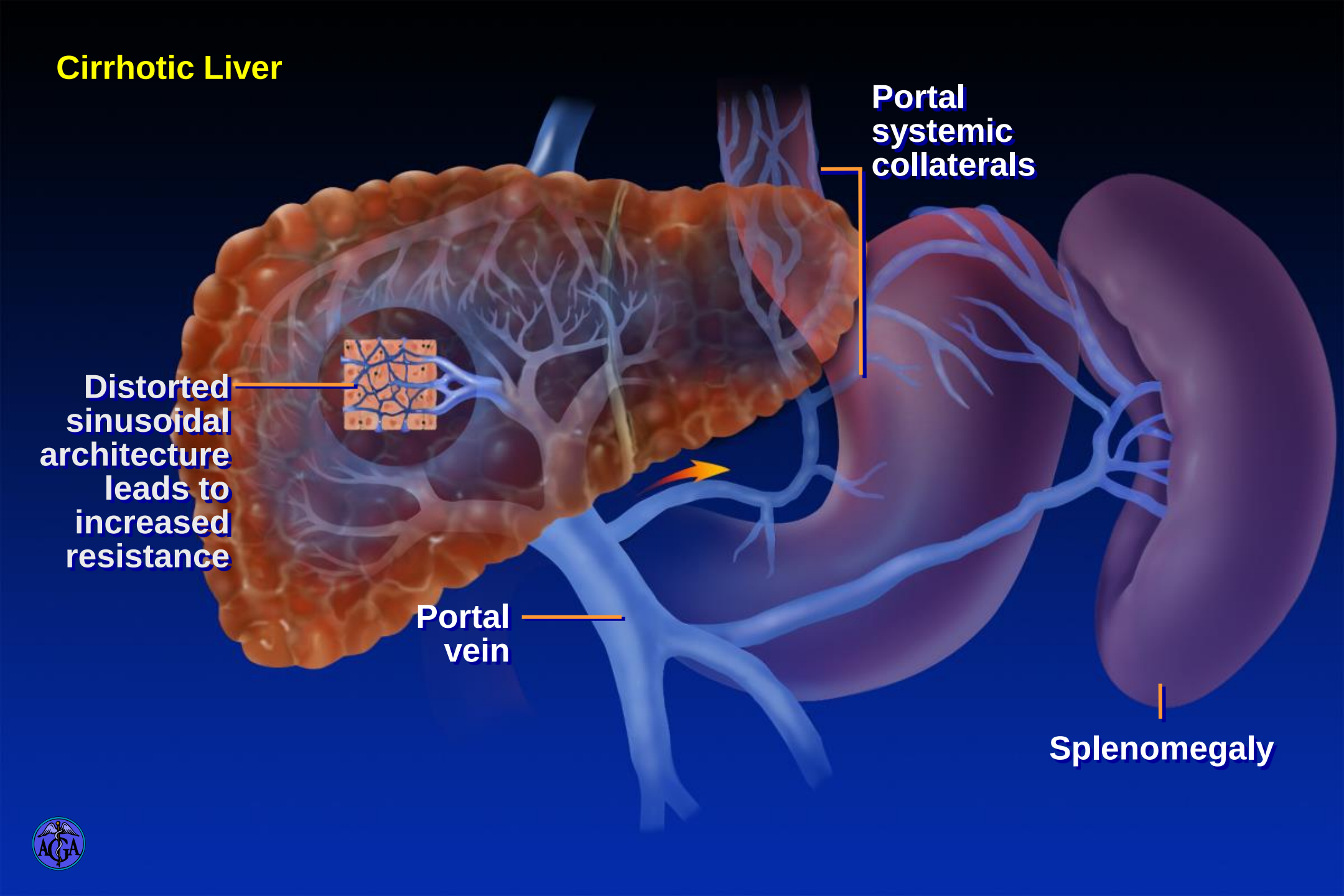
- Inflammation and destruction of intrahepatc and extrahepatc bile ducts (cholangitis). This leads to segmental scarring and stricture (sclerosing)

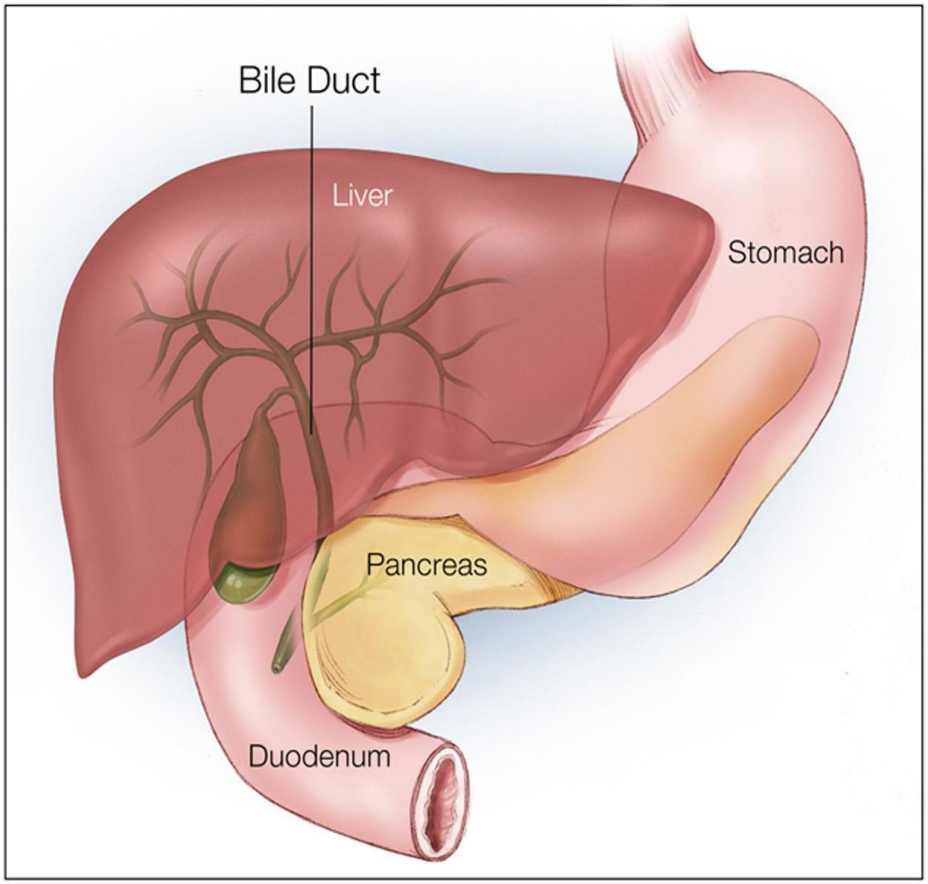


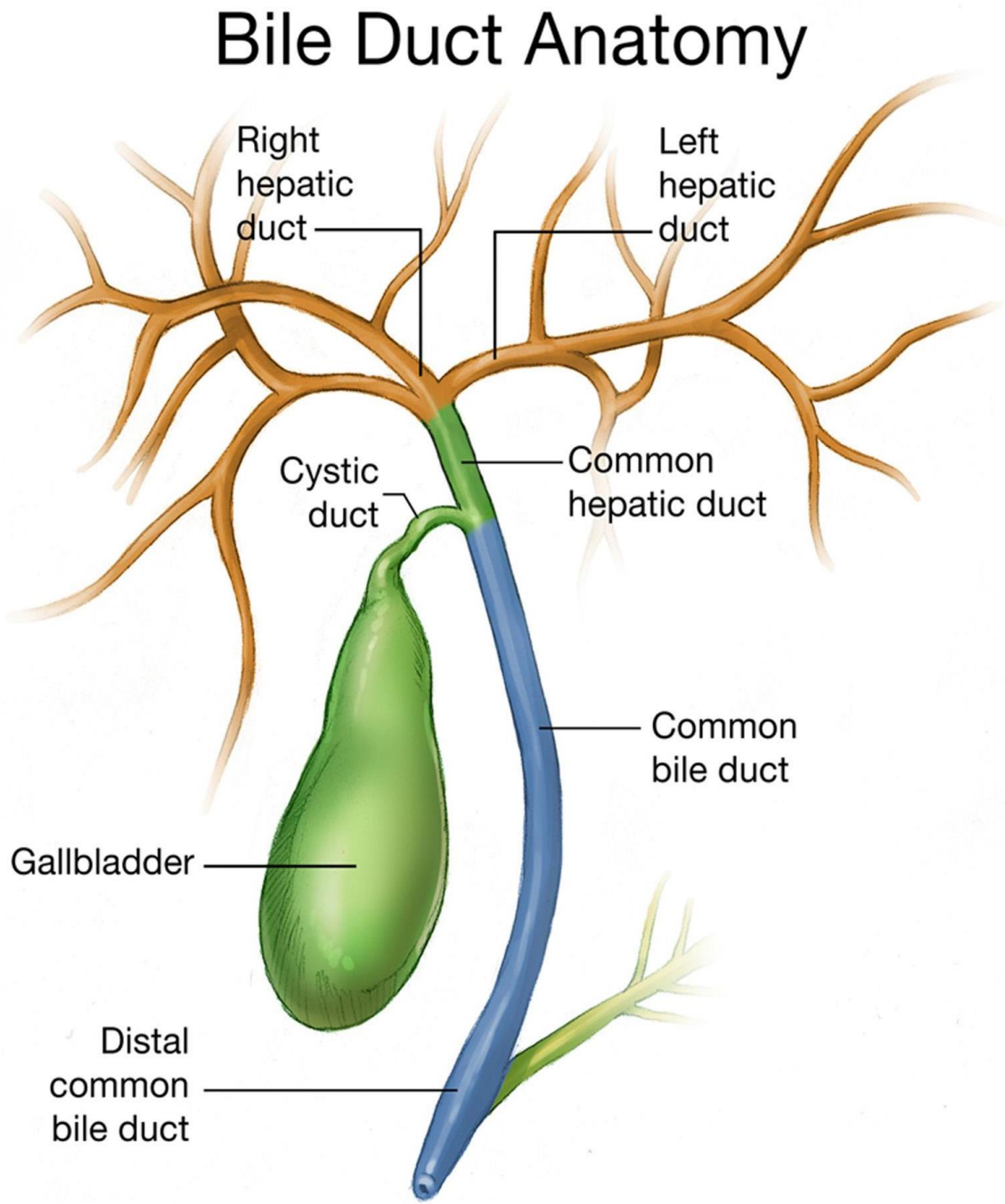
Cirrhosis

- Late stage of progressive hepatic fibrosis
- Characterized histologically by regenerative nodules surrounded by fibrous tissue
- Not all pts with PSC will develop
- Clinically there are 2 types of cirrhosis
  - Compensated (no complications)
  - Decompensated (complications)

Cirrhotic Liver




Bile Duct
Liver
Stomach
Pancreas
Duodenum


Bile Duct Anatomy
Right hepatic duct
Left hepatic duct
Cystic duct
Common hepatic duct
Common bile duct
Gallbladder
Distal common bile duct

Liver "Function" (Injury) Tests

Hepatocytes

- Aspartate aminotransferase (<35 U/L)
  - AST
  - (SGOT)
- Alanine aminotransferase (<35 U/L)
  - ALT
  - (SGPT)

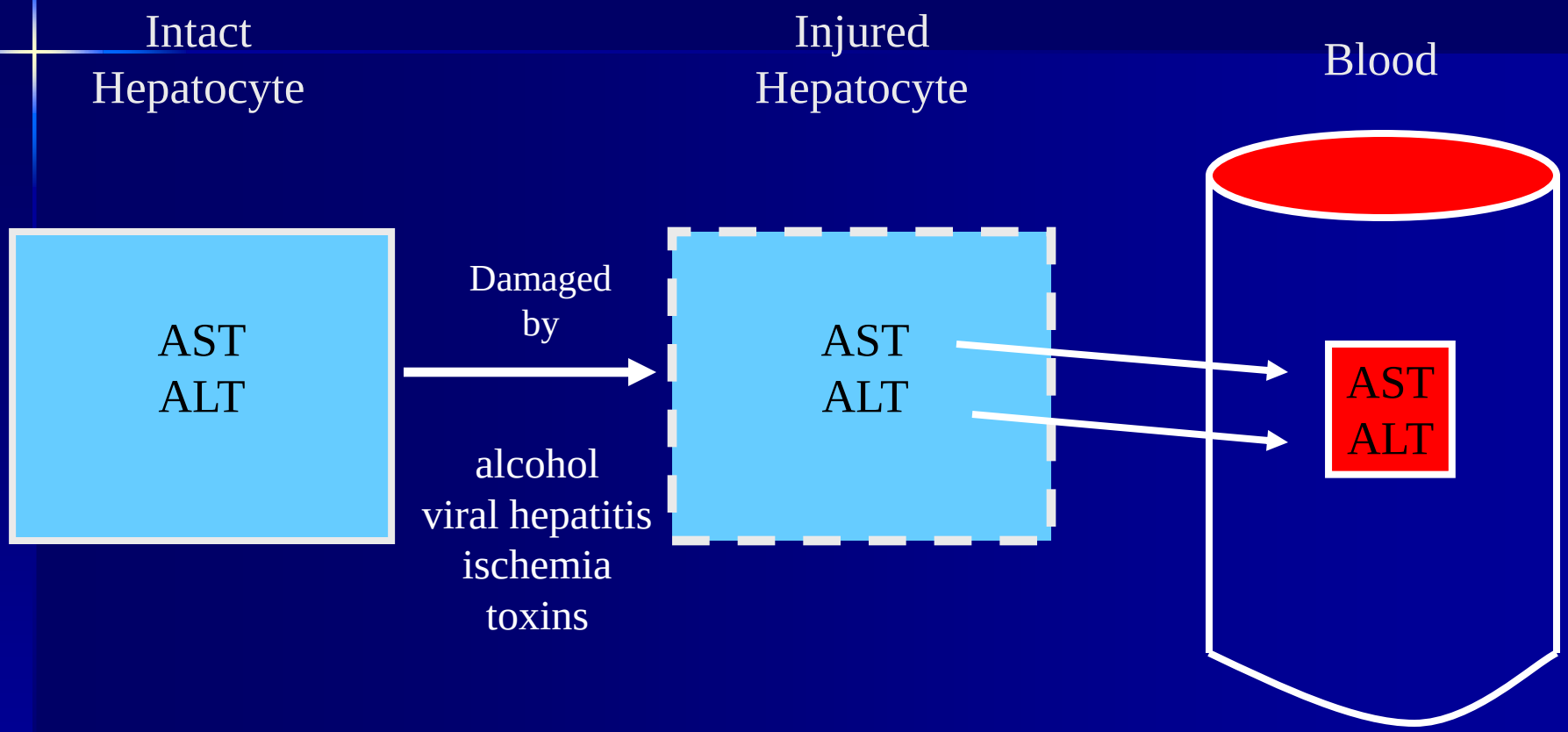
Biliary Epithelium

- Alkaline phosphatase (<130 U/L)
  - AP
- Gamma glutamyltransferase (<55 U/L)
  - GGT

Aminotransferases- ALT and AST

- increased serum aminotransferase levels caused by injury to enzyme-rich tissue
- Can be elevated 2-3x in PSC
- not specific for liver injury
- enzyme-rich tissue
  - liver
  - heart
  - muscle

Aminotransferases



Alkaline phosphatase

- enzyme that cleaves phosphate from phosphate esters at alkaline pH
- exact function is unknown
- clinical value: detection of cholestatic disease
- Marker of biliary injury
- Often elevated in pts with PSC

Alkaline phosphatase

- found in osteoblasts, canalicular membrane of hepatocytes, small intestine and placenta
- major source in serum is liver and bone
- different forms can be distinguished
  - Fractionation – separates liver and bone ALP
  - Heat labile (liver, bone), Heat stable (placenta, cancer)

Gamma glutamyl-transpeptidase

- elevated in diseases of the liver/biliary tract
- utility is determining source of elevated alk phos (bone/liver)
- often elevated in patients consuming alcohol
- highly inducible – elevated by drugs or medications without any evidence of hepatocellular damage

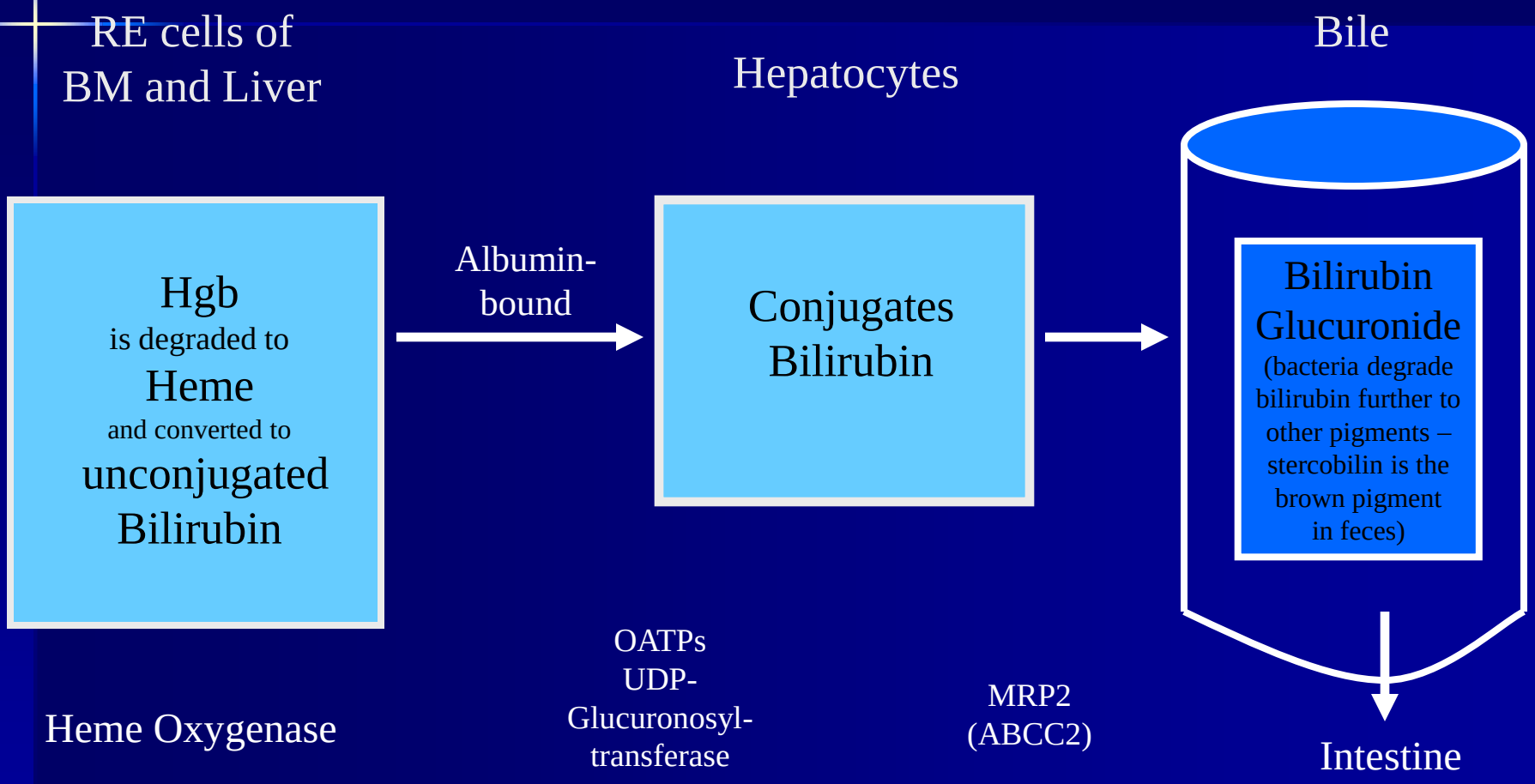
Tests of Liver Synthetic Function

- Bilirubin (<1.2 mg/dL)
- Albumin (3.5-5)
- Prothrombin Time
  - International Normalized Ratio (INR) (<=1)

Bilirubin

- is a metabolic product of heme (RBC's)
- produced in the reticuloendothelial cells (macrophages in the liver and spleen)
- insoluble, transported to hepatocyte bound to albumin

Bilirubin Metabolism



Bilirubin – causes of elevation

- hyperbilirubinemia occurs due to one or more of the following:
  1) overproduction (hemolysis)
  2) impaired metabolism (chronic liver disease)
  3) impaired excretion (biliary obstruction)

Bilirubin

- Normal <=1
- With cirrhosis or bile duct injury, >1.2
  - Yellow eyes
  - Yellow skin
  - Dark colored urine
  - Itching

Protein- Albumin

- Normal 3.5-5
- With cirrhosis, <3.5
  - Ascites
  - Edema
  - Cramping
- Can also be low with
  - Malnutrition
  - Kidney problems

Clotting Factors: INR

- Dependent on Vitamin K intake, absorption and production
- With cirrhosis, >1.2
  - Easy bruisability
  - Nose/gum bleeds
- Can also be elevated
  - Malnutrition
  - Dietary changes
  - Cholangitis

Autoantibodies

- >95% will have at least one positive
- Clinical significance unclear
- May be an indicator of overlap syndrome in proper scenario
  - Anti-nuclear antibody (ANA)
  - Anti-smooth muscle antibody (ASMA)
  - Perinuclear Anti-Neutrophil Cytoplasmic Antibodies (pANCA)
  - IgG4

IgG4

- Subclass of immunoglobulins/antibodies
- Has been linked to a variety of conditions
- Elevated in ~10% pts with PSC
- Associated with more severe disease
- May respond to steroids

Fat Soluble Vitamins

- A, D, E, K
- Should be monitored one jaundiced
  - A: night blindness
  - D: bone deficiencies, osteoporosis
  - E: neurologic symptoms
  - K: bleeding symptoms
    - INR may be elevated

Other

CBC

- WBC 4-10
  - Infection
  - Portal Hypertension
- Hgb 12-16; HCT 35-35
  - Anemia
  - Bleeding
- PLT 150-400
  - Portal Hypertension

Metabolic Panel

- Sodium, Na (133-145 mmol/L)
  - Measure of volume status
  - May be low b/c diuretics
  - Can cause confusion if abnormal
- Potassium, K (3.3-5 mmol/L)
  - Can be low b/c diuretics
  - Can cause irreg rhythms if abnl
- Creatinine, Cr (0.4-1.20 n/mL)
  - Measure of kidney function

Tumor Markers

- CA 19-9 (<35 U/mL)
- CEA (<3 ng/mL)
- AFP (<9 ng/mL)

Carbohydrate antigen 19-9

- Not sensitive to bile duct cancer
- 62% sensitivity, 63% specificity
  - May be elevated with infection and stones
- Be suspicious if rising
- >100 ng/mL
  - Used as part of CCA upgrade
- ?guidelines on monitoring

Carcinoembryonic antigen

- Elevated in many conditions
  - Colon cancer
- May be more sensitive for CCA if both CEA and CA 19-9 abnormal

Alpha-fetoprotein

- HCC risk in PSC if PSC has progressed to cirrhosis
- 20% of pts with HCC have normal AFP
- AASLD does not recommend it as a screening test

Childs Classification

Clinical or Biochemical Measurement	Points 1	2	3
Hepatic Encephalopathy	None	I-II	III-IV
Ascites	Absent	Mild	Moderate
Total bilirubin (mg/dL)	<2.0	2.0-3.0	>3.0
Serum albumin (g/dL)	>3.5	2.8-3.5	<2.8
INR	<1.7	1.7-2.3	>2.3

Class A = 5-6 **Class B = 7-9** **Class C = 10-15**

Model for End-Stage Liver Disease (MELD) Score

- Mathematical survival model created from data on patients undergoing TIPSS
- MELD score estimates risk of 3-month mortality
- Uses 3 laboratory values
  - -Serum total bilirubin
  - - Serum creatinine
  - - INR
- 6-40

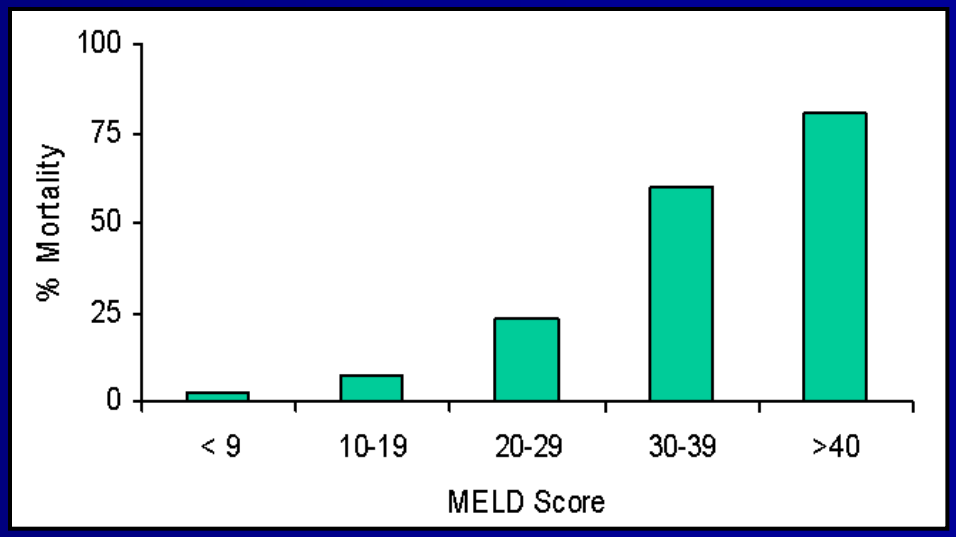
Model End Stage Liver Disease

MELD Score =

$0.378*\log_e(\text{bilirubin[mg/dL]}) +$

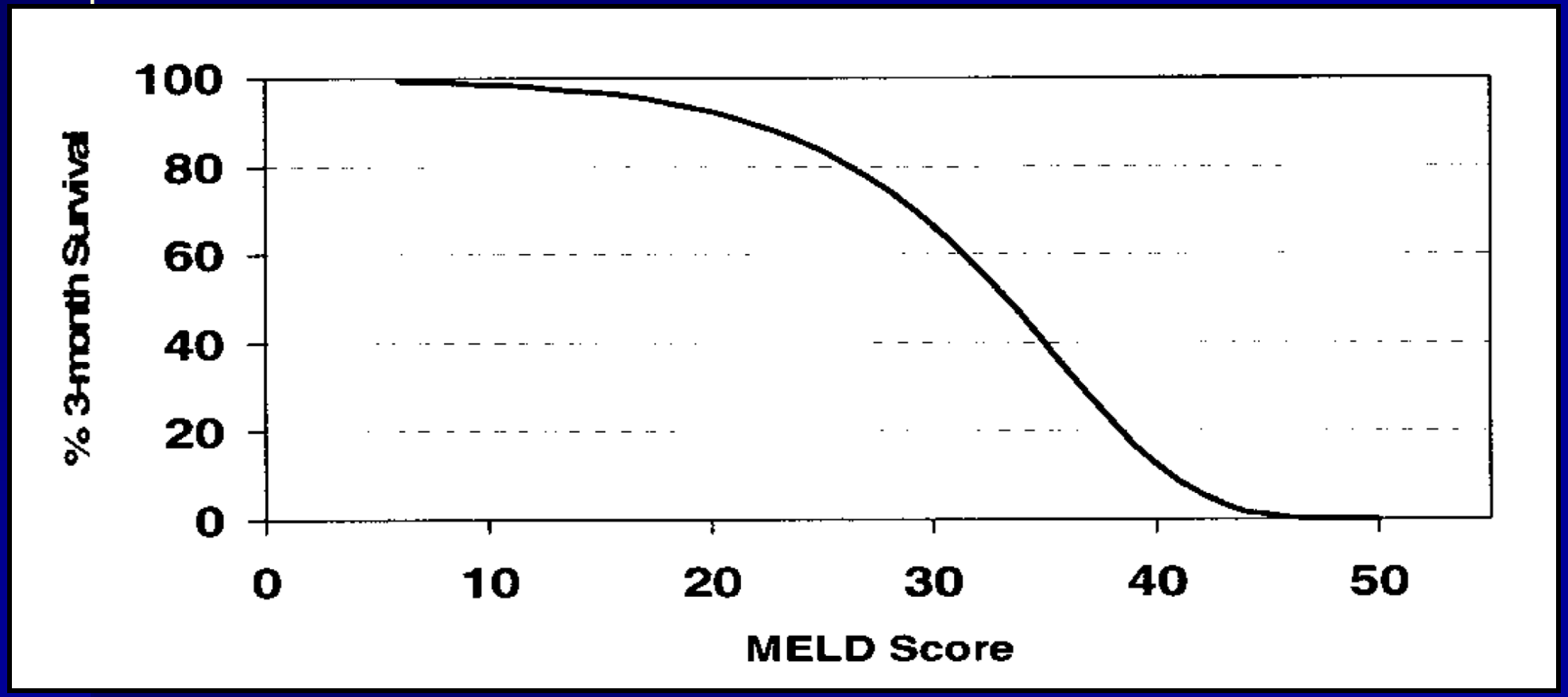
$1.120*\log_e(\text{INR}) +$

$0.957*\log_e(\text{creatinine [mg/dL]}) + 0.643$



Wiesner et al. *Gastroenterology* 2003;124:91-6

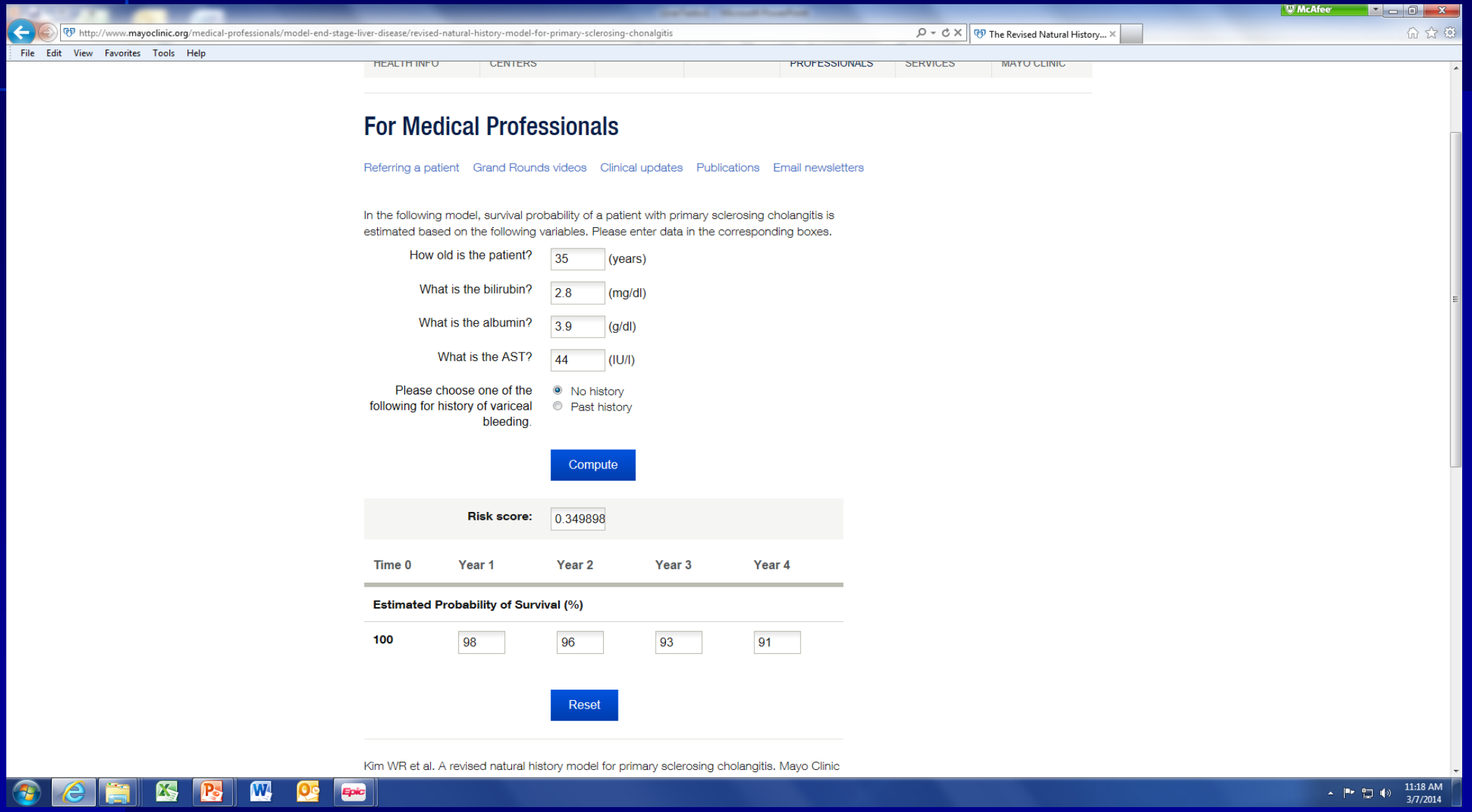
Estimated 3-Month Survival Based on Listing MELD in Patients on the Waiting List



Wiesner et al. *Gastroenterology* 2003;124;9:91-6

- MELD score does NOT take into account
  - Fatigue
  - Pruritus
  - Infection (cholangitis)

Mayo Risk Score

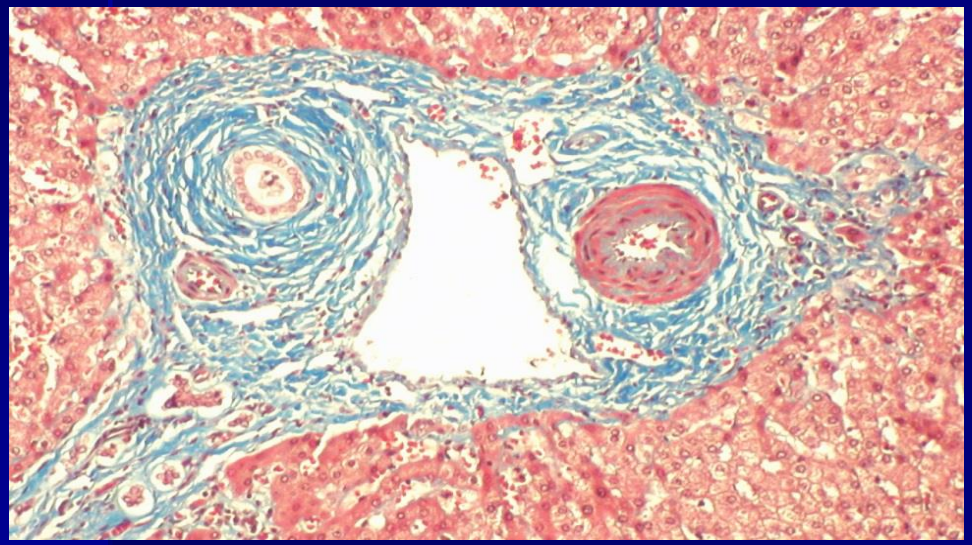


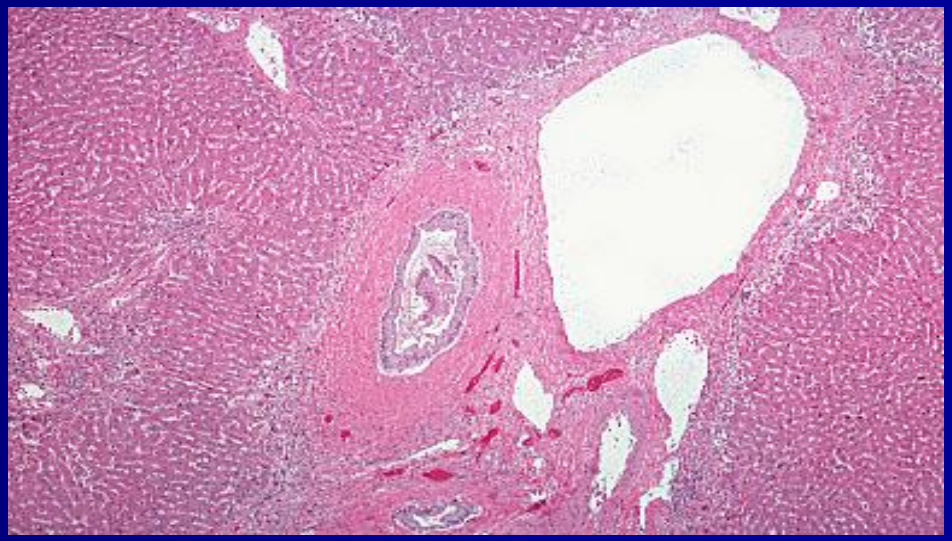
Liver Biopsy

- Exact role undefined
- Primary injury is not liver cells but medium and lg bile ducts
  - not captured in typical bx
- "onion skin" fibrosis around bile ducts

- May help exclude other diseases
  - Overlap
  - Small duct disease

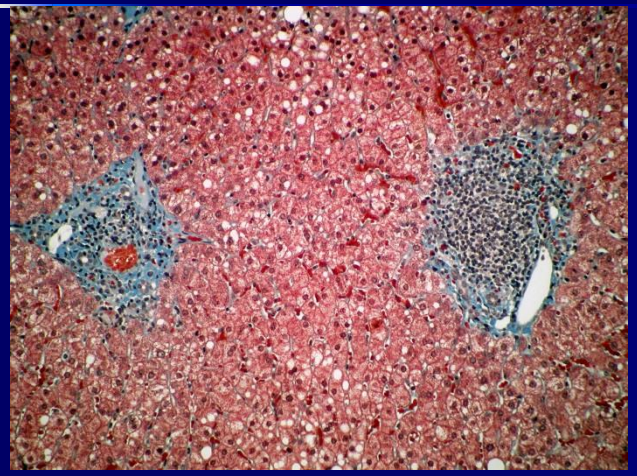
Liver Biopsy: Onion Skin





Histology Staging

1



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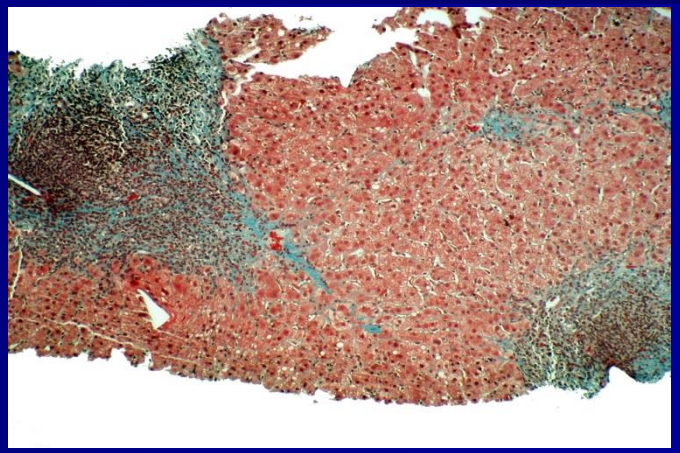
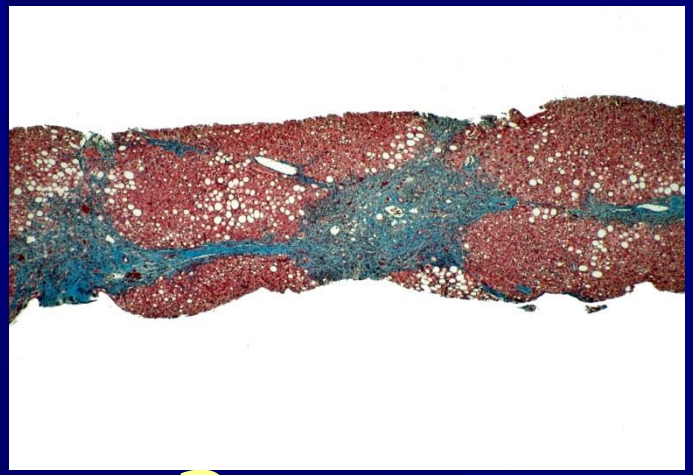




3 3

4

Radiographic Tests

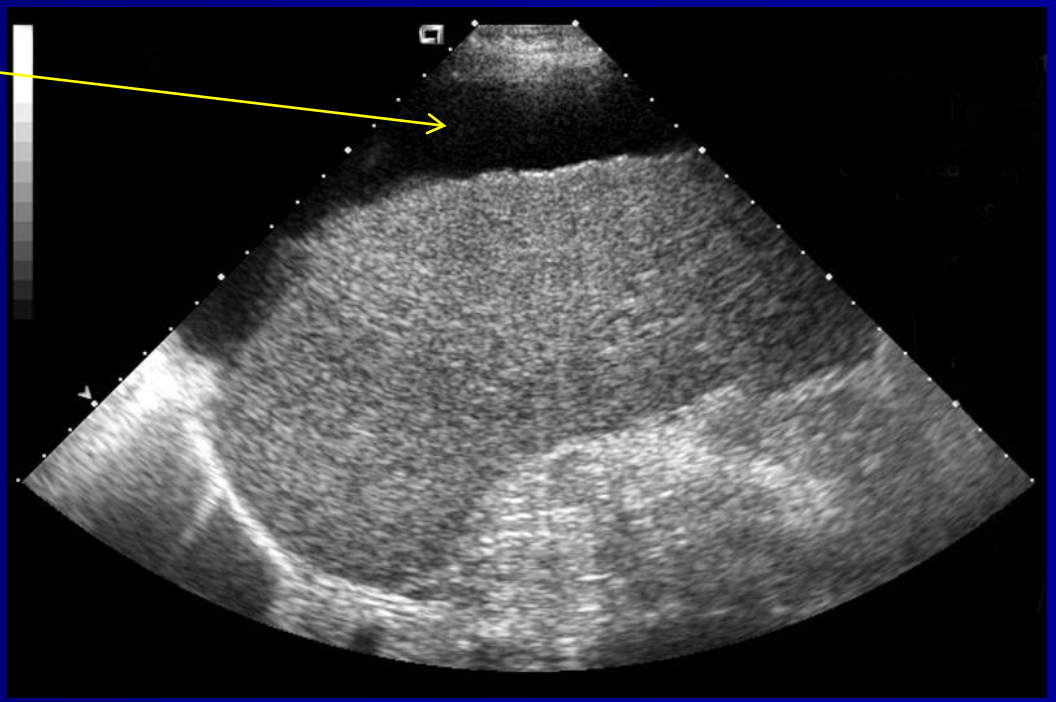
- MRI-magnetic resonance imaging
- CT-computed tomography
- Ultrasound
- Cholangiogram
  - ERCP
  - PTC

Ultrasound

- Cheap
- No radiation
- Can assess for ascites, vessel patency
- Stones, large duct dilation
- HCC screening
  - AASLD recommends
- User dependent
- Limited in obese
- Often normal

Ultrasound

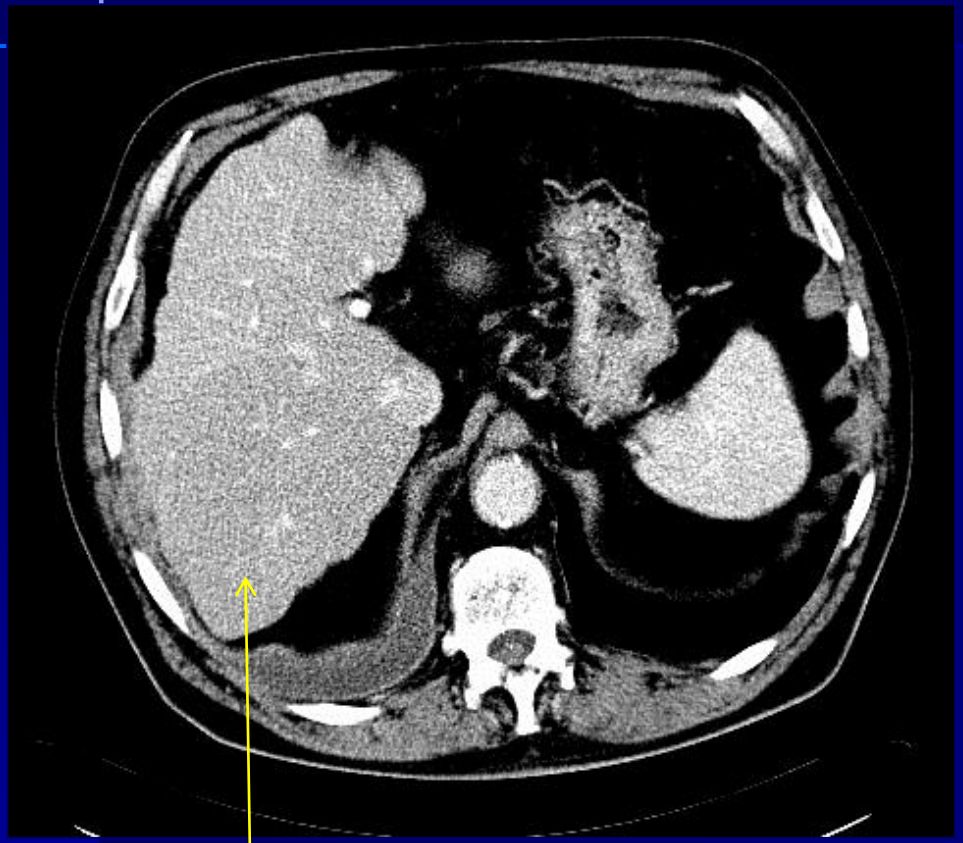
- Often normal
- Thickened bile ducts
- Can looks at size spleen
- Can detect ascites



CT scan

- Fast
- Can assess other abdominal organs
- Better look at liver parenchyma/masses
  - Especially if overweight
- Radiation exposure
- Contrast
  - Kidney problems

CAT Scan



Liver with irregular surface

collateral vessels

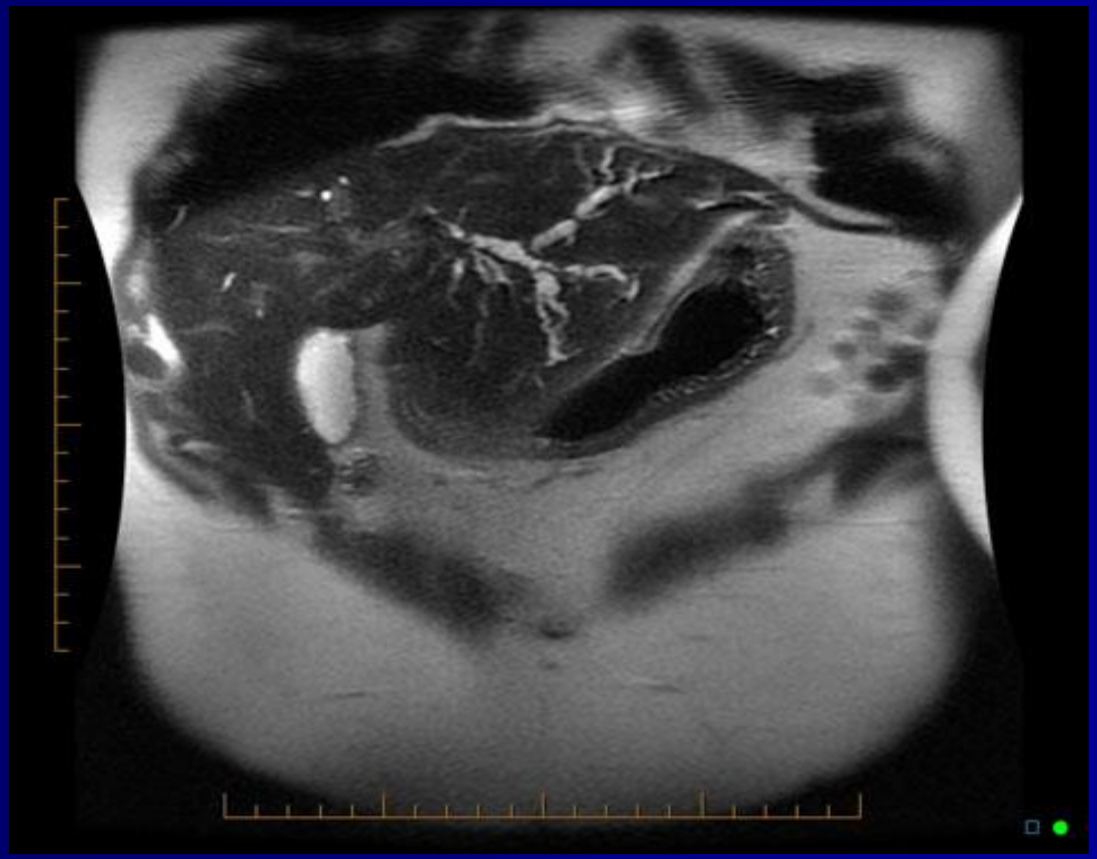
splenomegaly

Magnetic Resonace Cholangiopancreatography

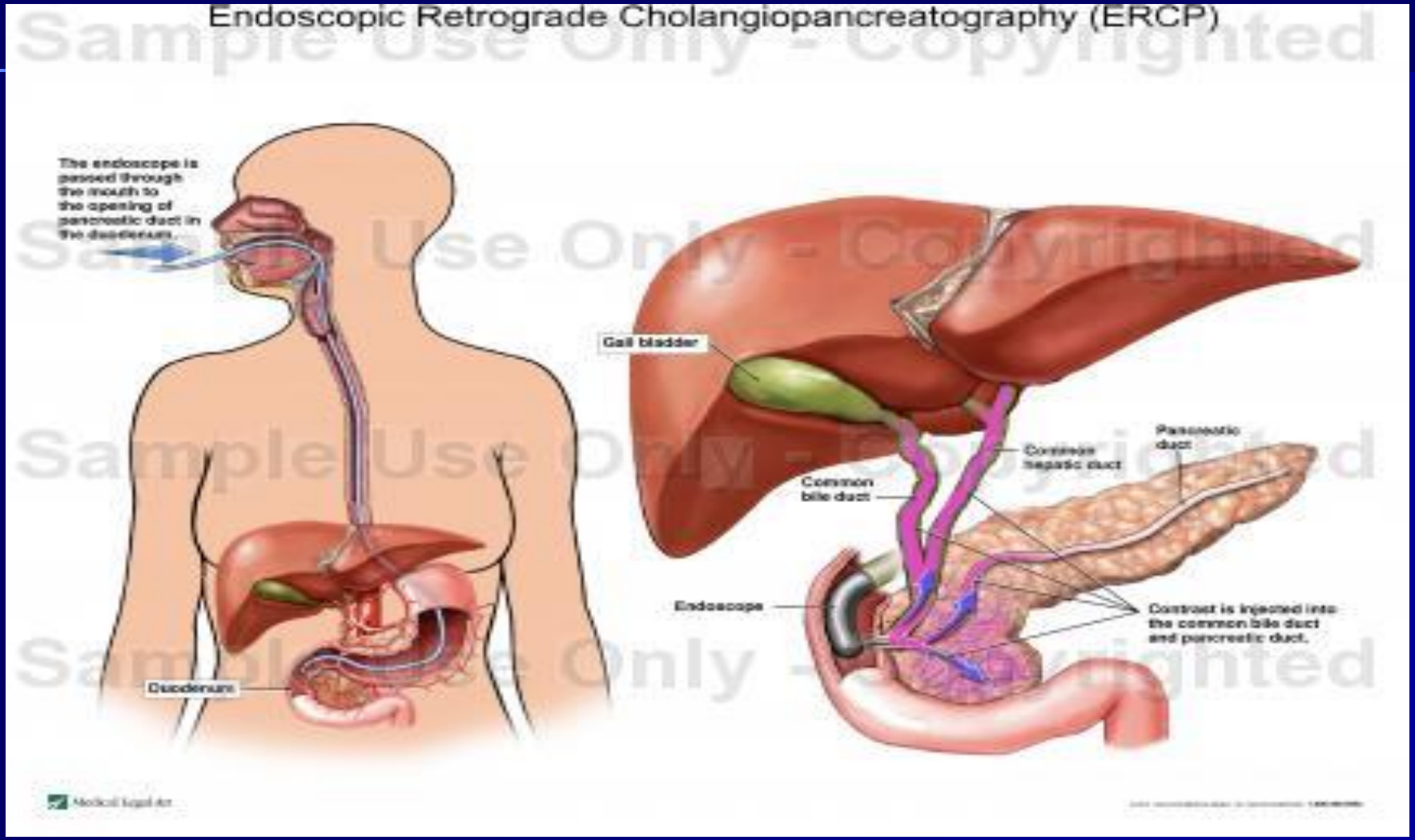
- No radiation
- Sensitive
- Can provide a roadmap
- Claustrophobia
- Gadolinium
  - Kidney problems
- Cannot intervene

MRCP

- Focal thickening and dilation of bile ducts

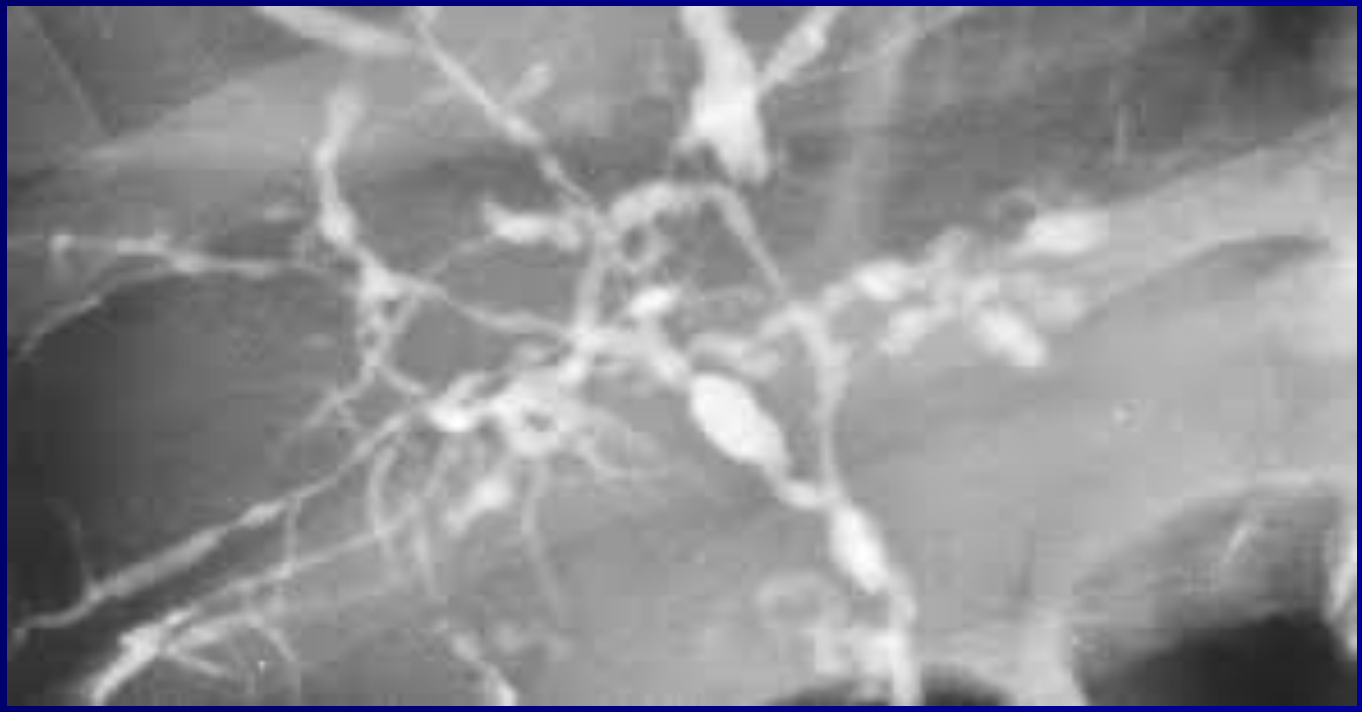


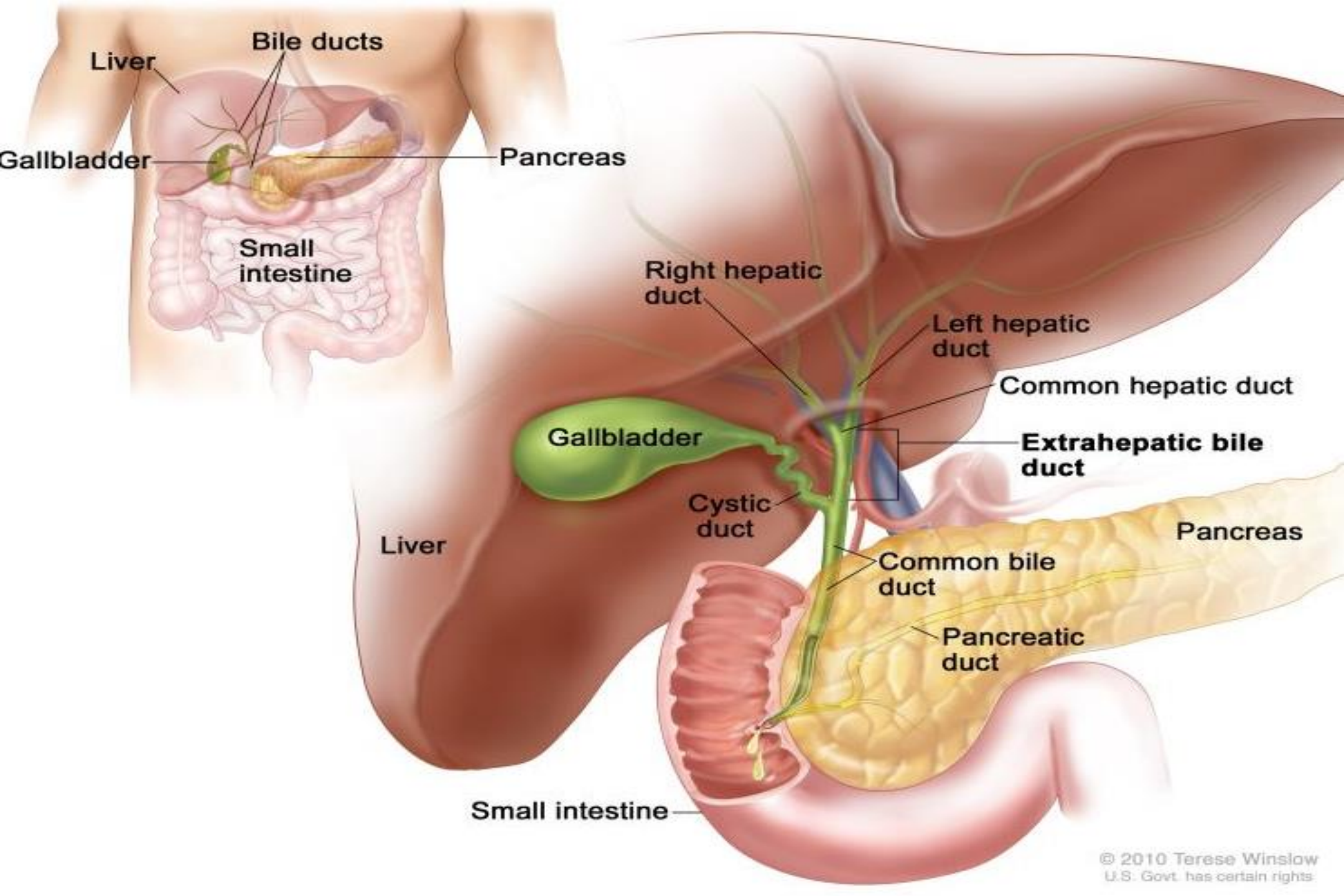
Endoscopic Retrograde Cholangiopancreatography



ERCP

- Diagnostic and therapeutic
- Multiple strictures and dilations of bile ducts

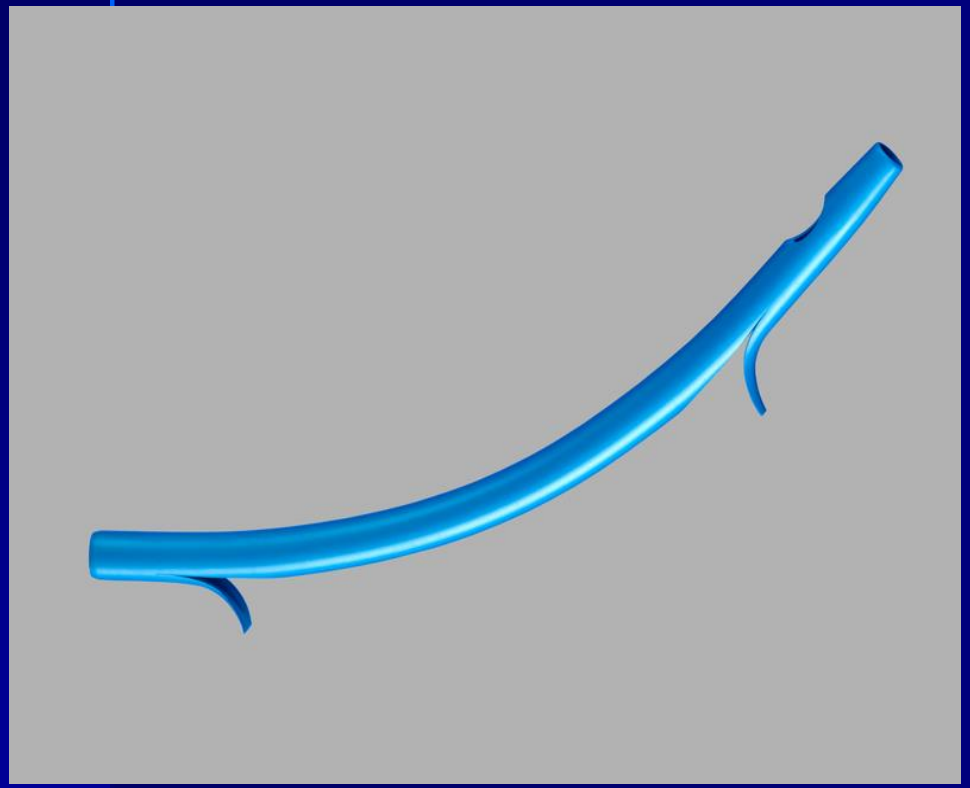


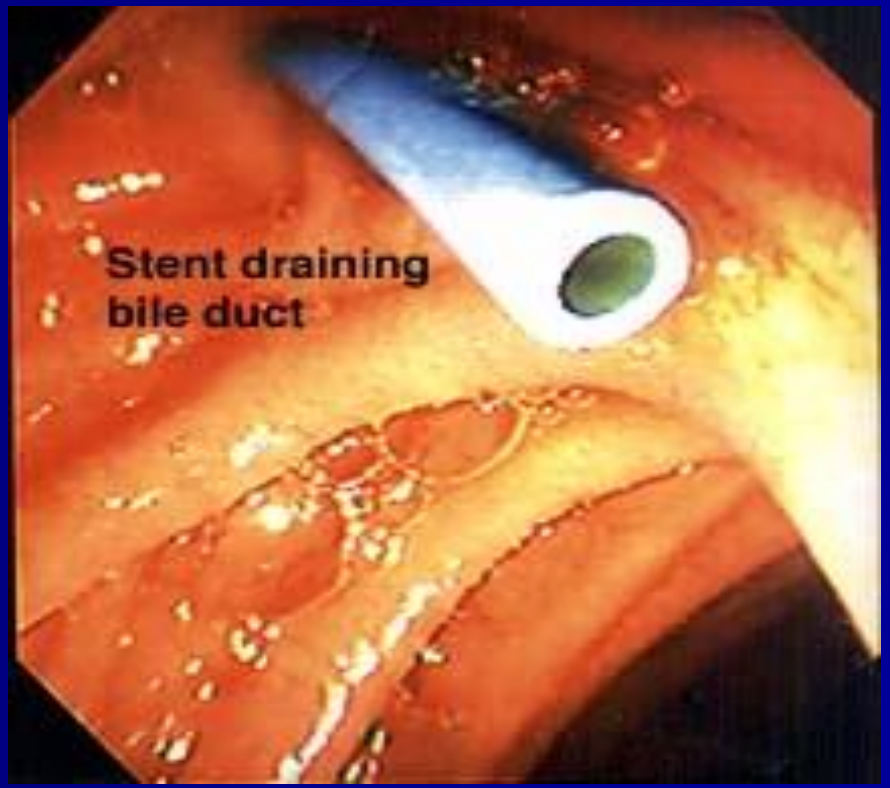


Dilation

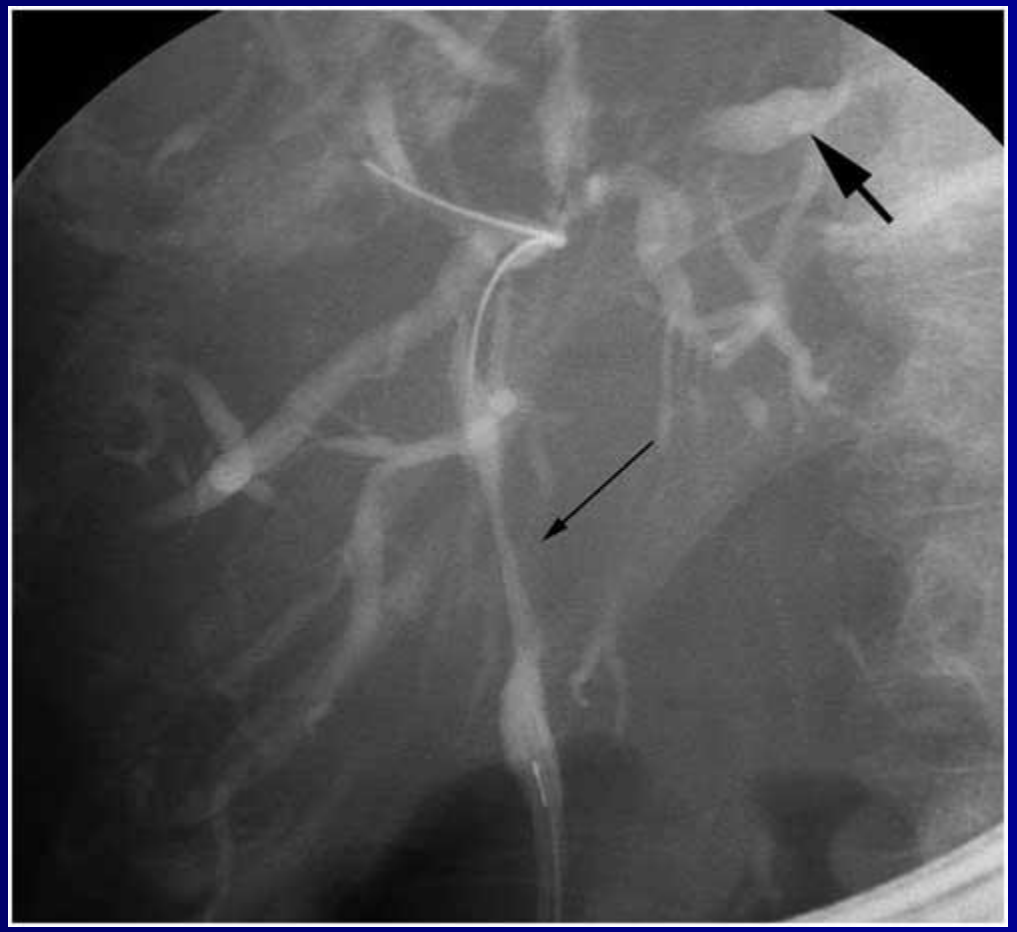
- Stretching narrowed bile duct

Stenting

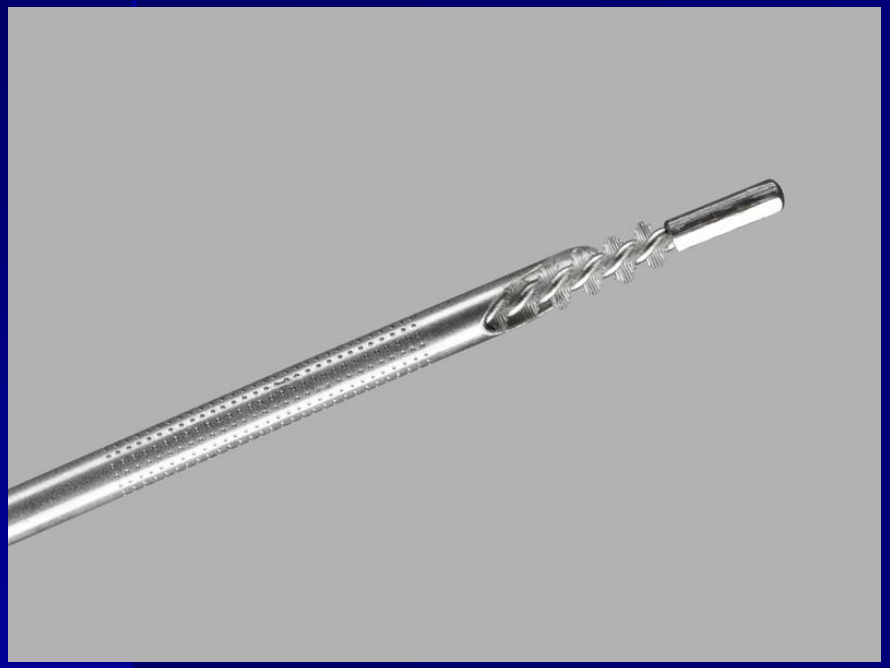




Dominant Stricture

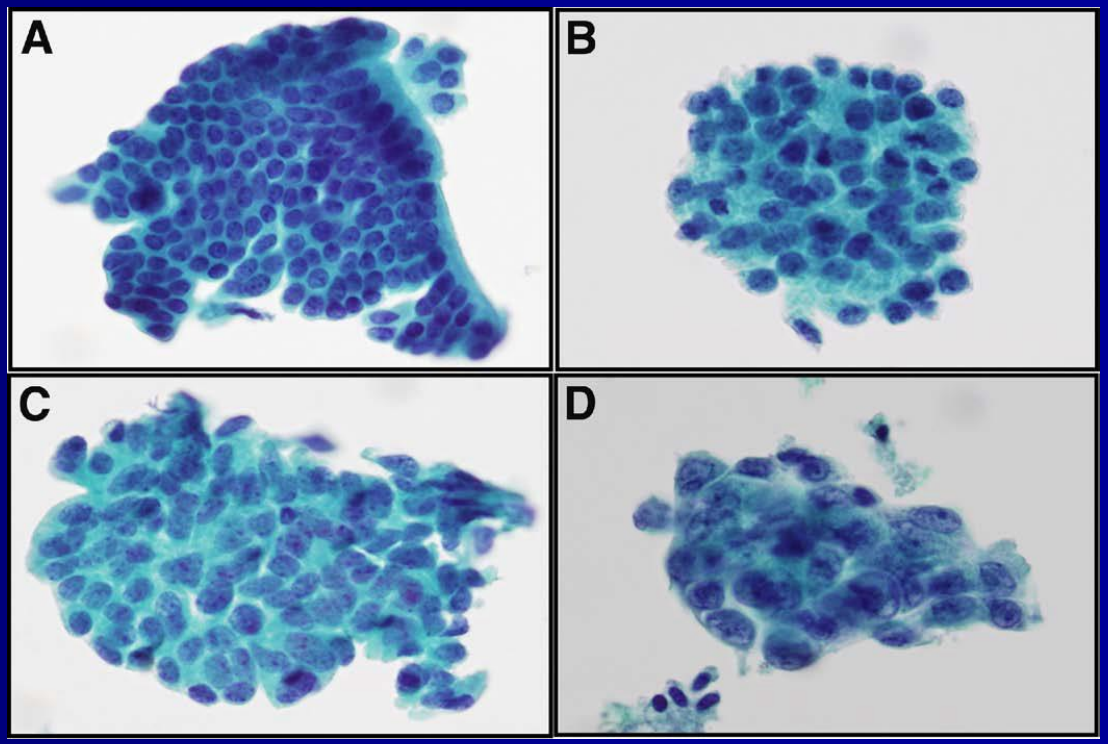


Brushing



Negative

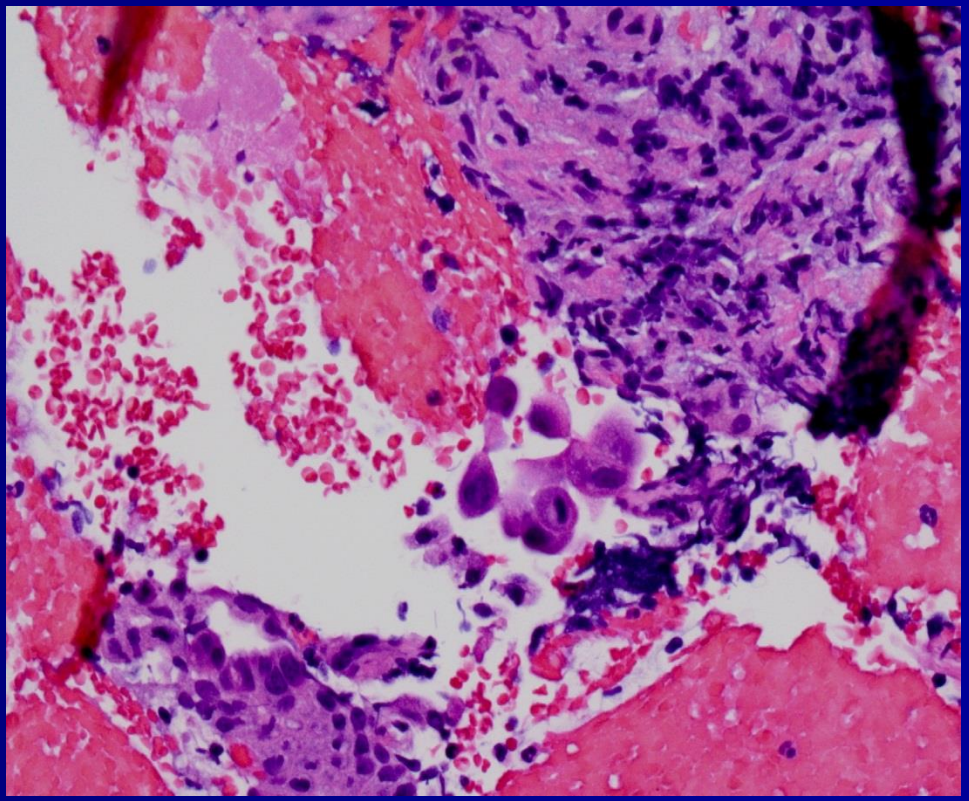
Atypical



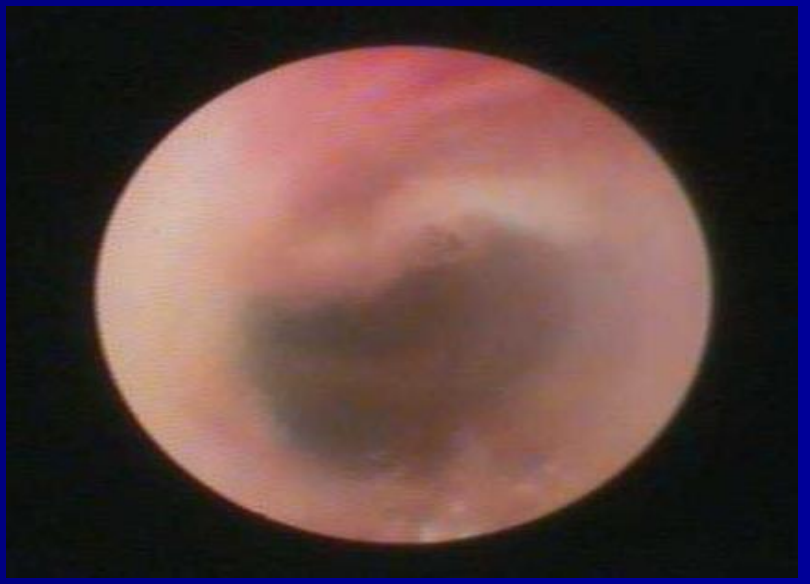
Suspicious

Positive

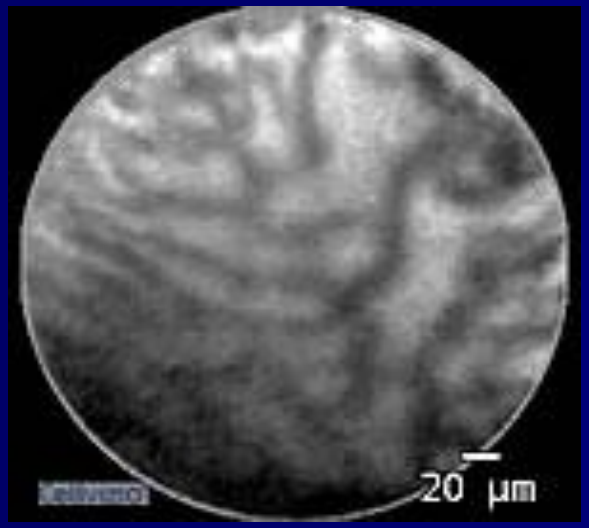
Biopsy



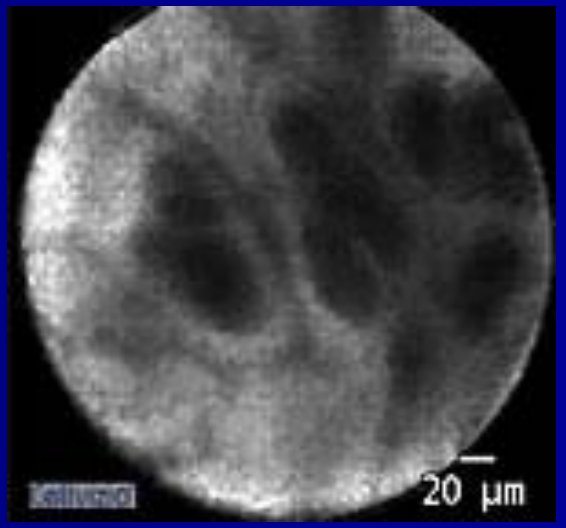
Cholangioscopy: direct visualization of bile ducts



Confocal Microscopy



Normal bile duct

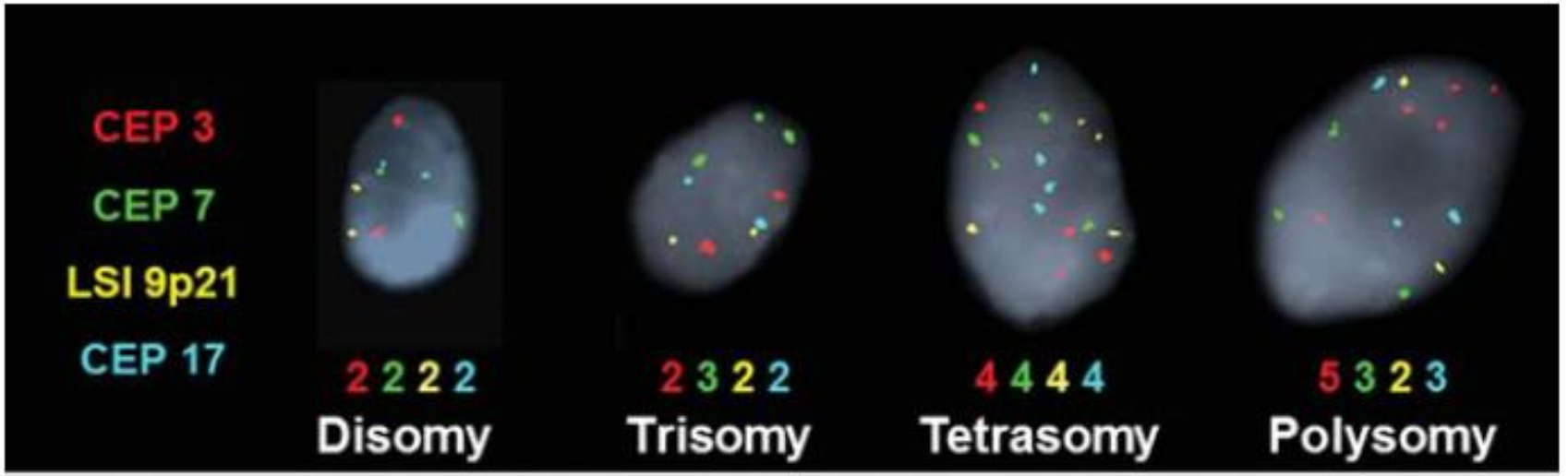


Abnormal dark glands

Fluorescence *in situ* Hybridization

- FISH
- Cytologic technique
- Increases sensitivity and accuracy of biliary tract malignancies
- Uses fluorescently labeled DNA probes to detect chromosomal abnormalities in cells
- Can be used in correct scenario

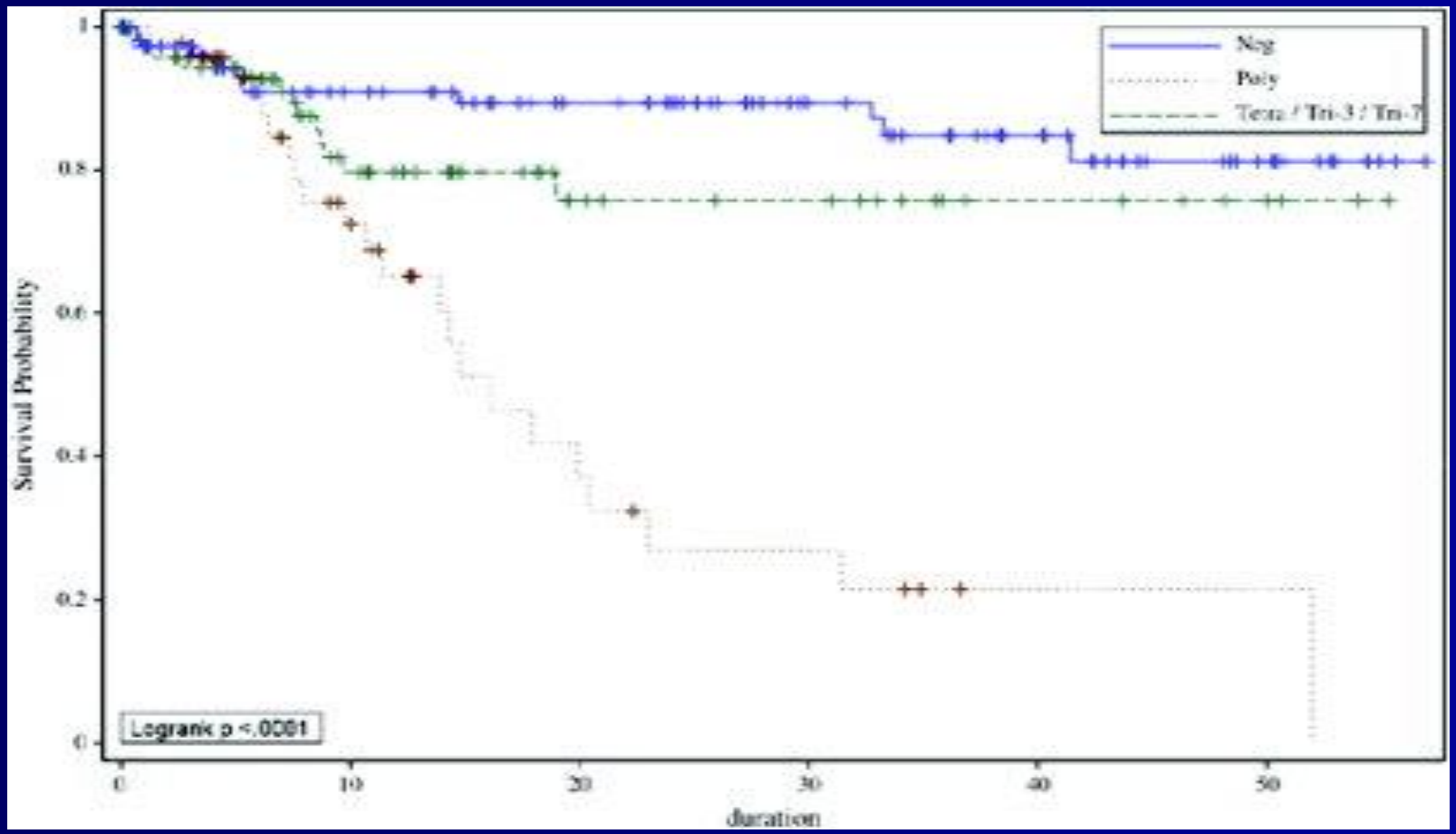
FISH



	Disomy	Trisomy	Tetrasomy	Polysomy
Definition	2 copies per locus	>2 copies of a single locus	4 copies of each locus	>2 copies of at least 2 loci*
Cut-off	N/A	≥10 cells	≥10 cells	≥5 cells

*Unless 4 copies of each locus, then classified as tetrasomy

Survival based on FISH results



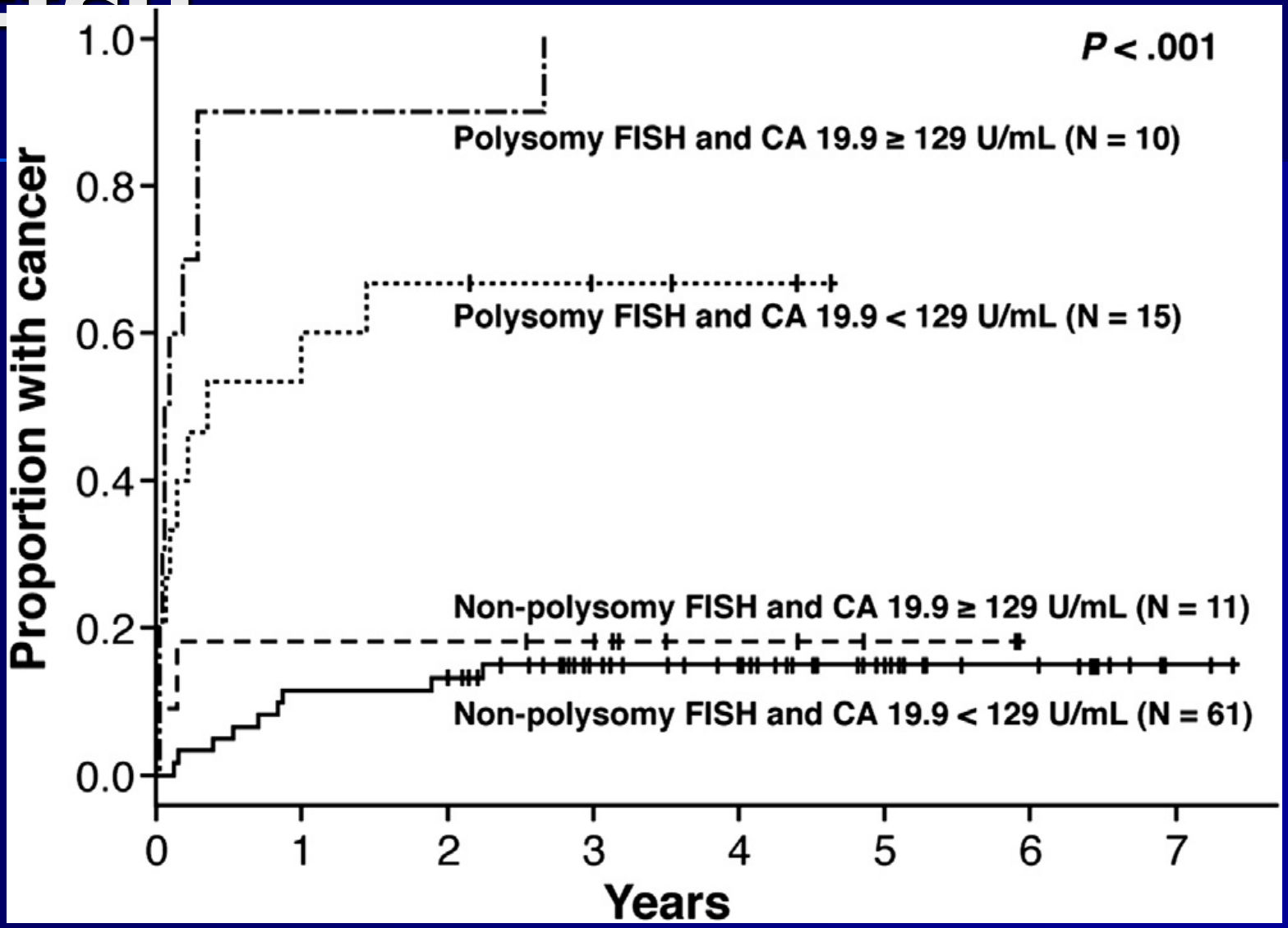
Negative

Trisomy 3/Trisomy 7/Tetrasomy

Polysomy

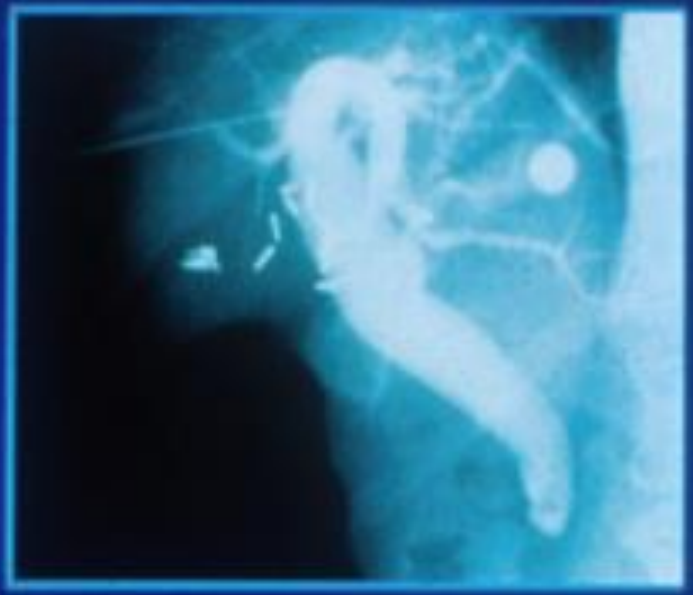
Hepatology 2010;51:174-80

FISH



Gastroenterology 2013;145:1215-1229

PERCUTANEOUS TRANSHEPATIC CHOLANGIOGRAPHY



ADVANTAGES

- Direct visualization of bile ducts
- Proximal extent of obstruction/lesion
- Therapeutic options: stenting
  stricture dilatation
- Less operator dependent than ERCP

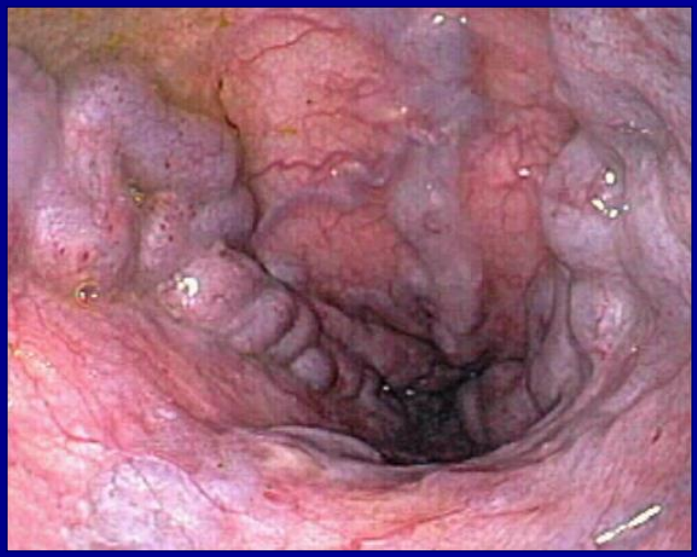
LIMITATIONS

- Pancreatic duct not seen
- Biliary-venous connection
- Complications: sepsis
  bile leak
- Success related to duct size

Esophagogastroduoedenoscopy

- Upper endoscopy
- Screen varices
- Evaluate abdominal pain

Varices

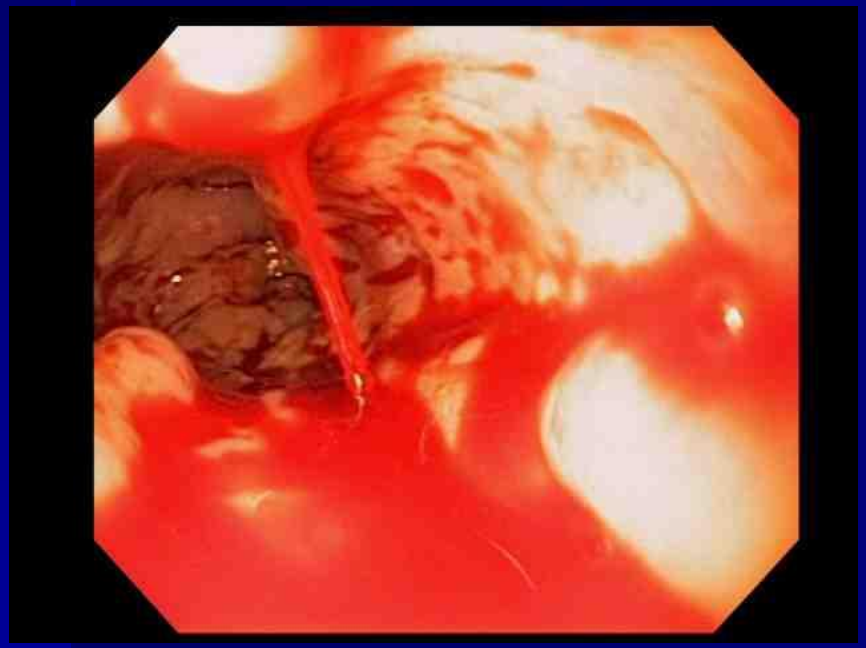


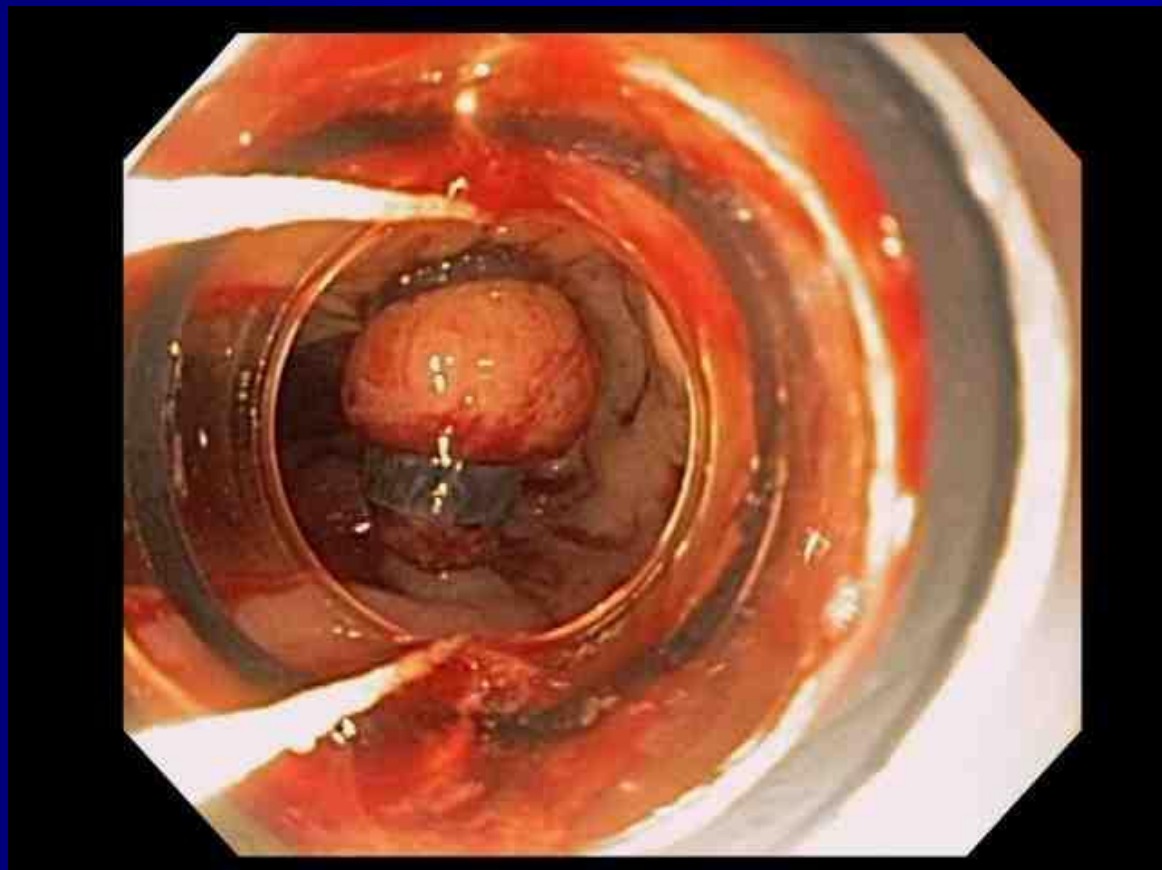
No varices **Small varices** **Large varices**

Increased risk of bleeding as varices get bigger

5-15%/year

Bleeding/Banding





Questions?