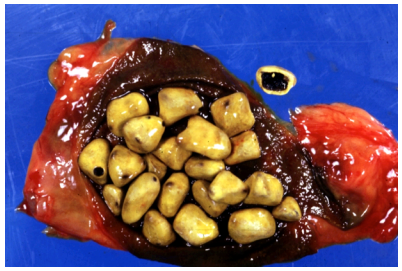
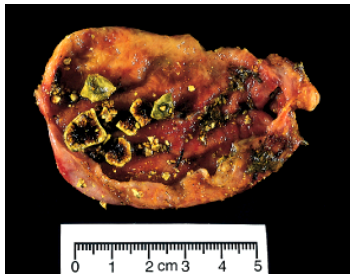
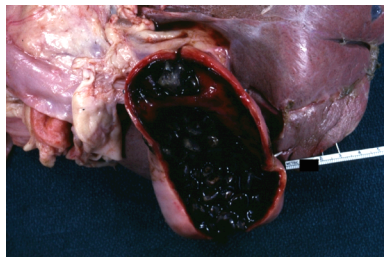
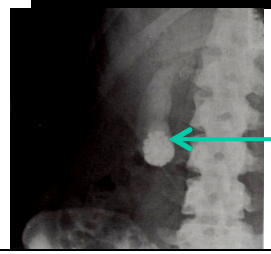
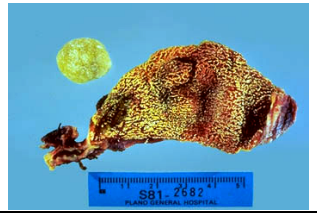
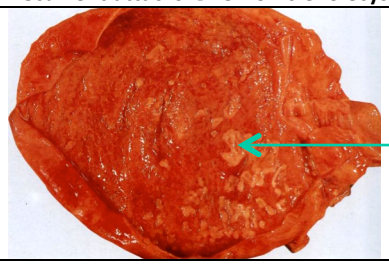
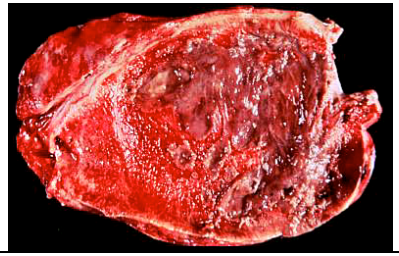
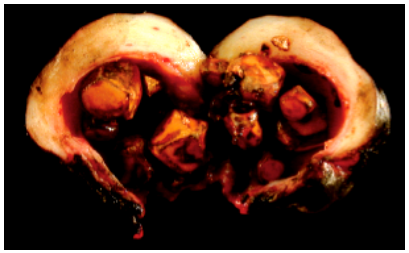
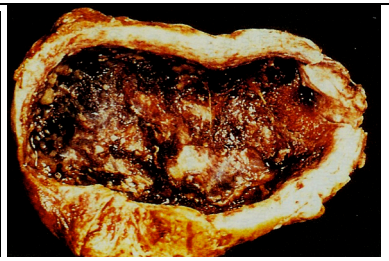
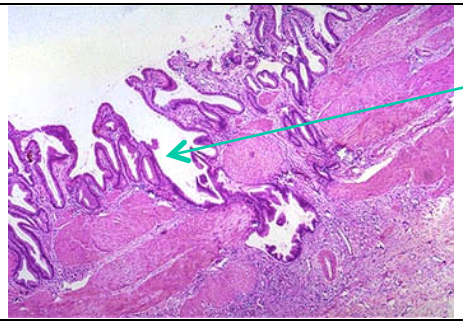
GALLBLADDER PATH

- **BILE DUCT CELL DAMAGE → ALKALINE PHOSPHATASE ELEVATED.**
- **HEPATOCELLULAR DAMAGE → TRANSAMINASES ELEVATED** – *it has to be 2-3x the amount of normal (i.e. 200, 250) to say there is damage to tissue*

	CHOLELITHIASIS (Gallstones)	
TYPES	**1. CHOLESTEROL GALLSTONES (80%)** **4 F's: Female, Forty, Fertile, Fat**	**2. PIGMENT GALLSTONES**
RISK FACTORS	Age + Gender (>40 + Female) **Native Americans** **ORAL CONTRACEPTIVES, PREGNANCY, OBESITY, ↑CHOLESTEROL** Acquired disorders (bile stasis – ***sepsis, burns***)	**Chronic Hemolytic Syndromes** – ***Hemolytic Anemia → pigment gallstones*** Bacterial infections (*E. coli*) Parasitic infections (***Ascaris lumbricoids*** **or liver fluke** ***C. sinensis***)
PATHOGENESIS	**3 Requires for Cholesterol Stone Formation:** 1. **Supersaturation** of bile with cholesterol 2. Kinetically favorable **nucleation** 3. Cholesterol **crystals** in gallbladder long enough for stone aggregation ****Gallbladder stasis plays key role***	
GROSS	50-100% cholesterol Pure cholesterol stones: **pale yellow** *May be single, but mot* **MULTIPLE + MULTIFACETED** ***RADIOLUCENT ON XRAY: ↓Ca^{2+} levels**  	**CALCIUM SALTS + UNCONJUGATED BILIRUBIN** **SMALL** & present in **GREAT NUMBER** ****50-75% of BLACK STONES – RADIOPAQUE ON XRAY** Brown stones – Radiolucent    Dilated large gallbladder w/ pigment stones – *stones same density as bone* ***BLACK STONES bc RADIOPAQUE**
COMPLICATIONS OF GALLSTONES	**Biliary Pain** – biliary tract is **contracting** & gallbladder trying to get movement past the obstruction ***Cholang*****itis** – obstruction of duct can lead to inflammation **CHOLECYSTITIS** – typically obstructs the net of the gallbladder -- **Classic presentation* **Obstructive Jaundice** – ***classically in Common Bile Duct;*** **↑CONJUGATED BILIRUBIN** *(tea-colored urine)* & **↑ALKALINE PHOSPHATASE** **Pancreatitis** – this is because the stone goes down CBD to Ampulla of Vater; if a pt gets pancreatitis secondary to obstruction, pt will have **JAUNDICE** **Gallstone Ileus** – gallbladder becomes inflamed allowing stone to pass	

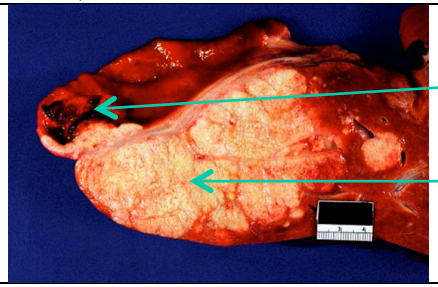
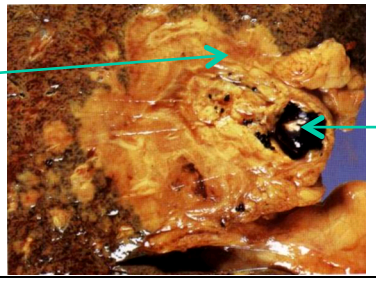
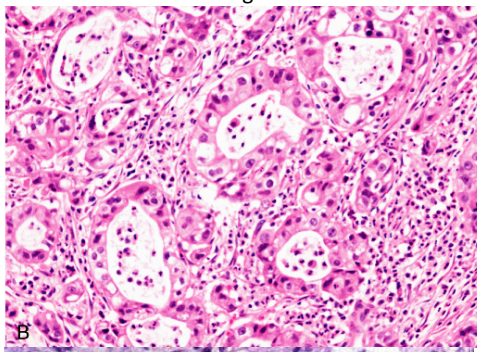
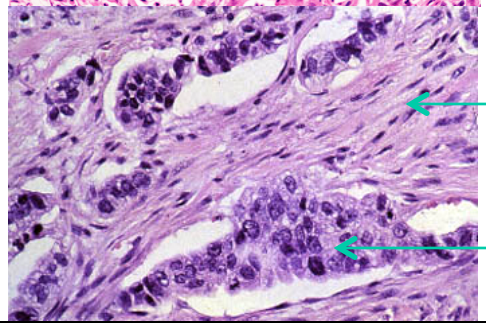
3. CHOLESTEROLOSIS	
DEFINITION	Excessive accumulation of **cholesterol esters** in the **lamina propria** of the gallbladder
CLINICAL	Incidental finding: patients are **ASYMPTOMATIC**
GROSS	Mucosal surface with minute **YELLOW FLECKS** coming out from the mucosa = **"STRAWBERRY GALLBLADDER"** 
MORPHOLOGY	**FOAMY MACROPHAGES FILLED W/ CHOLESTEROL**

4. ACUTE CHOLECYSTITIS		
DEFINITION	**Inflammation of the gallbladder wall –** *there may or may not be bacterial growth. This is different than appendicitis where you get obstruction allowing bacteria to become increased & get neutrophils, etc. Here the problem is more with the obstruction leading to inflammation.* Enlarged gallbladder with **discolored serosa; STONES** present in 90% of cases, *often* ***obstructing neck or cystic duct***	
TYPES	**GANGRENOUS CHOLECYSTITIS**: – **SEVERE COAGULATIVE NECROSIS** – Look for wall of the gallbladder to have a **BLACK color** – *Wall is weak & prone to rupture*	**ACALCULUS CHOLECYSTITIS:** – Caused by **ISCHEMIA**, not by a stone! – INSIDIOUS ONSET – Look for patient with serious illness: ***sepsis or burns*** *(will mask cholecystitis)*
CLINICAL	Presents with ***steady*** *or* ***COLICKY upper abdominal pain****, often* ***radiating to TIP OF RIGHT SCAPULA/SHOULDER*** **FATTY FOOD INTOLERANCE** since gallbladder won't be able to emulsify fatty foods **MURPHY'S SIGN – Pain on inspiration** Cardinal Signs of Inflammation: **fever, nausea, leukocytosis (LEFT SHIFT)** **Recurrent attacks → Chronic Cholecystitis**	
GROSS	 Exudate on mucosal surface 	
MORPHOLOGY	**Acute Inflammation = NEUTROPHILS = Lumen with CLOUDY or TURBID BILE**	
COMPLICATIONS	**EMPYEMA**: pus in gallbladder; ***rebound tenderness*** – Wall rupture or perforation → **PERITONITIS** *(free air under diaphragm)* **CHOLECYSTECTOMY** required for 25% of symptomatic patients	

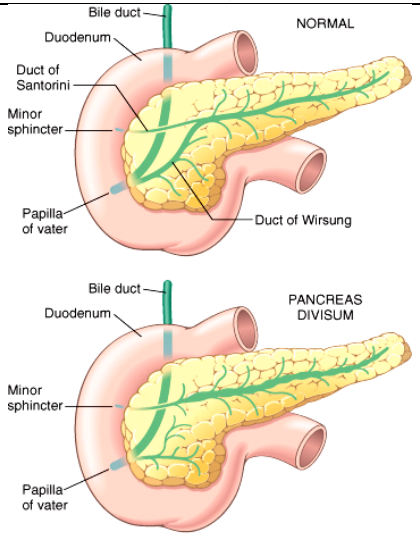
5. CHRONIC CHOLECYSTITIS	
CLINICAL	Cardinal Signs of Inflammation: fever, nausea, leukocytosis – *but usually milder than in acute cholecystitis*
PATHOGENESIS	May result from repeated bouts of acute cholecystitis or with no history of acute attacks
GROSS	 **VERY THICK WALL by Fibrosis**  Sludge in lumen – *gallbladder stasis*
MORPHOLOGY	 **ROKITANSKY-ASCHOFF SINUSES** – *mucosa invaginates down into muscular layer making a sinus*** This will eventually **calcify (DYSTROPHIC CALCIFICATION)** ***You'll see gallbladder on XR – PORCELAIN GALLBLADDER**
COURSE	Patients with **PORCELAIN GALLBLADDER** have increased incidence of **carcinoma of gallbladder**

6. CARCINOMA OF THE GALLBLADDER

FEMALE > Male; 7th Decade

DEFINITION	***Usually, adenocarcinoma which has directly invaded the LIVER at diagnosis***
CLINICAL	*Abdominal pain, jaundice, anorexia, nausea & vomiting* **HARD TO PALPATION (desmoplasia), but NO DISTENTION** ****NON-DISTENDED, PALPABLE GALLBLADDER IN ELDERLY PATIENT → THINK CARCINOMA!!**
PATHOGENESIS	Gallstones present in 95% of cases Overexpression of **ONCOPROTEIN ERBB2 (Her-2/neu)** in many cases
GROSS	 Carcinoma of the Gallbladder Liver cancer  **PIGMENTED STONES**
MORPHOLOGY	**1. EXOPHYTIC:** lesion arising form mucosa & going into the lumen **2. INFILTRATING**: lesion goes into the wall **& LIVER – *worse prognosis***  B GLANDS + HYPERCHROMATIC, PLEOMORPHIC NUCLEI *Look for desmoplasia*  Fibroblasts: *spindle-shaped cells laying down collagen* – **DESMOPLASIA** Poor differentiation
COURSE/ TREATMENT	**SILENT KILLER** – ***poor prognosis*** *(pre-op diagnosis made in less than 20% of patients)* Mean 5-year survival <10%

EXOCRINE PANCREAS PATH

	CONGENITAL ANOMALIES	
	1. PANCREAS DIVISUM	**2. ANNULAR PANCREAS**
DEFINITION	**Failure of FUSION** of the dorsal & ventral pancreatic primordial fetal duct systems ***Predisposition to CHRONIC PANCREATITIS* (& other conditions)**	**BAND-LIKE RING** of pancreatic tissue around the 2nd portion of the duodenum *May present with **duodenal obstruction***
		

3. ACUTE PANCREATITIS

FEMALE: GALLSTONES (Cholelithiasis) causing obstruction + Jaundice + Conjugated Bilirubin

MALE: ALCOHOLISM

CLINICAL

Acute onset of mild-severe **EPIGASTRIC** abdominal pain radiating to the BACK **– *pain results from NECROSIS + INFLAMMATION***

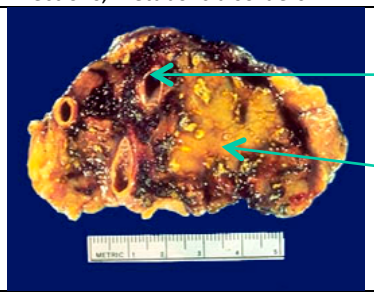
↑Pancreatic AMYLASE (1st 24 hours) **& ↑LIPASE** (72-96 hours; ***more specific***) **– 3-FOLD INCREASED!!!**

HYPOCALCEMIA, HYPERGLYCEMIA *(destruction of β cells = no insulin production)*, **jaundice** (*obstruction, probably stone from CBD*)

PATHOGENESIS

- Inappropriate intrapancreatic **ACTIVATION of TRYPSIN** → activation of other enzymes
- **ACINAR CELL INJURY** – defective intracellular transport of proenzymes within these cells; ***Kinin (vasodilation), clotting (DIC), & complement (shock – C5a, C3a) systems activated by trypsin***
- **Influx of CALCIUM** – causes **saponification** (Ca^{2+} combines w/ FAs in areas of fat necrosis) + parenchymal damage to cells
- Trauma, medications, infections, metabolic disorders

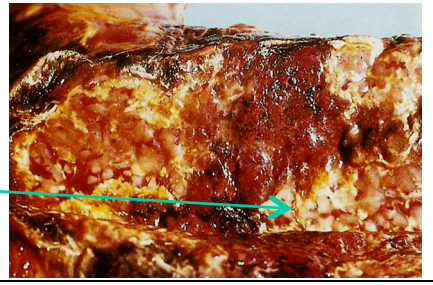
GROSS



Dark areas = hemorrhage

Light areas = fat necrosis

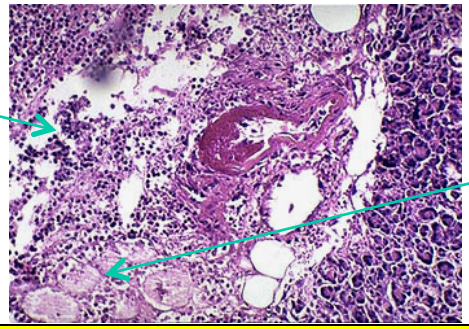
***Saponification**



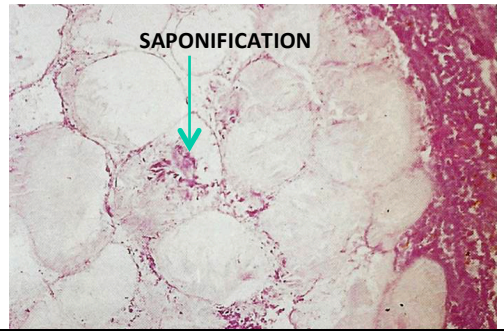
MORPHOLOGY

1. **Proteolytic destruction** of pancreatic substance
2. **Necrosis of blood vessels** with **INTERSTITIAL HEMORRHAGE:** areas of **BLUE-BLACK HEMORRHAGE**; *can lead to **hemorrhagic shock** if bleeds into abdomen*
3. **ENZYMATIC STROMAL & PERIPANCREATIC FAT NECROSIS** with **NEUTROPHILS & Ca^{2+} infiltrating pancreas**
4. Associated **acute inflammatory** reaction

Destruction of ACINAR PARENCHYMA



Fat Necrosis – *fat cells will have granular appearance; you know these are dead fat cells bc cytoplasm is seen*



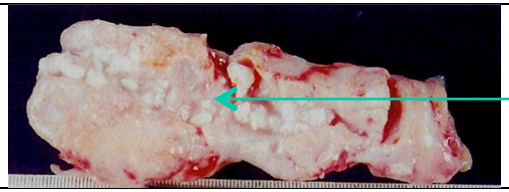
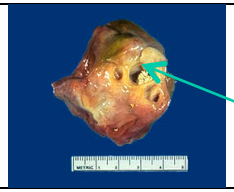
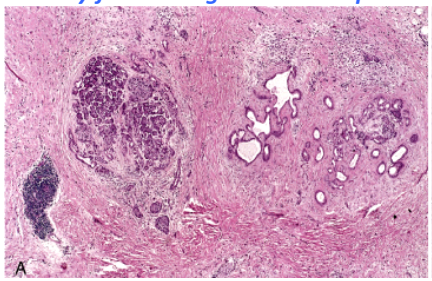
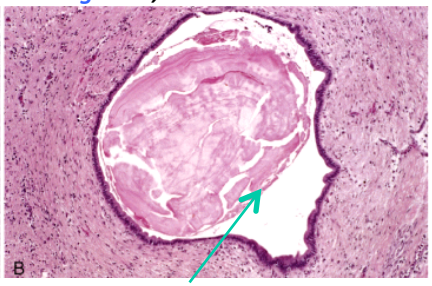
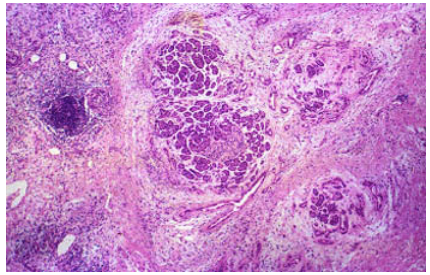
COMPLICATIONS

3 MAJOR COMPLICATIONS DUE TO TRYPSIN: DIC, SHOCK, ARDS

***Causes of Pancreatitis:** BAD HITS (Biliary, Alcohol, Drugs, Hypertriglyceridemia/Hypercalcemia, Idiopathic, Trauma, Scorpion Sting*

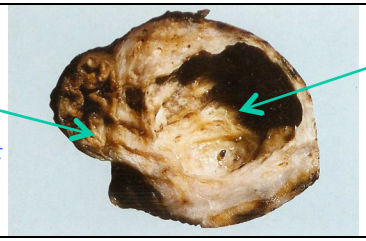
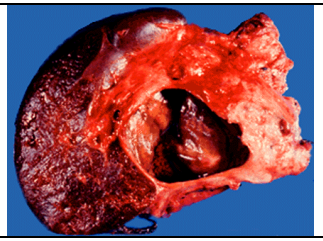
4. CHRONIC PANCREATITIS

Middle-Aged ALCOHOLIC Males

DEFINITION	Characterized by repeated bouts of mild to moderate pancreatic inflammation
CLINICAL	**Repeated attacks** of mild or severe pain, or persistent **abdominal pain** & BACK PAIN **Loss of exocrine & endocrine functions → MALABSORPTION/Pancreatic Insufficiency (diarrhea + loss of fat soluble vitamins – *Steatorrhea*) + DIABETES** **MILD ↑SERUM AMYLASE during attacks** ***Classic for Chronic Pancreatitis:** Pancreatic calcifications, Steatorrhea, Diabetes Mellitus*
PATHOGENESIS	Repeated bouts of acute pancreatitis, **LONG-STANDING OBSTRUCTION** of pancreatic duct by gallstones, pancreas divisum, autoimmune injury, hereditary pancreatitis
GROSS	 **CALCIFICATIONS** running down the middle  **Calcium stone**
MORPHOLOGY	***Densely fibrotic organ with atrophic exocrine glands*, Chronic inflammation around lobules, Ducts with PROTEIN PLUGS**    **Acinar Lobules with surrounding fibrosis** ***To ensure it is scar tissue, do Trichrome stain.*** **Acinar Parenchyma** **Dilated duct filled w/ inspissated material**
COURSE	May also lead to **PANCREATIC PSEUDOCYST** (next)

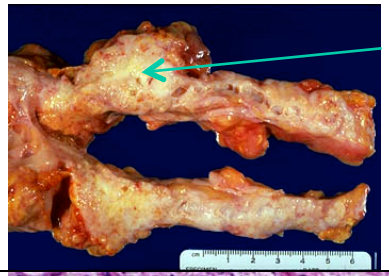
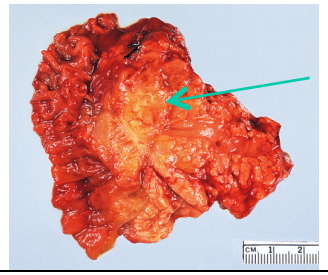
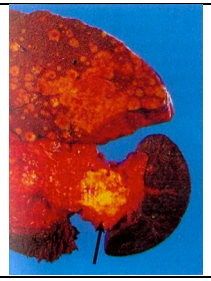
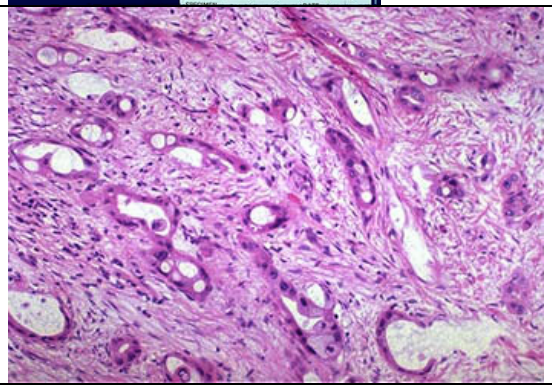
5. PANCREATIC PSEUDOCYSTS

75% of pancreatic cysts

DEFINITION	**Cystic space formed by WALL OF FIBROSIS & filled with BLOOD + NECROTIC TISSUE; not lined by epithelial tissue****
CLINICAL	*If the cyst is on the surface of the pancreas**, it may present as an abdominal mass** because of the fluid*
PATHOGENESIS	Caused by **acute or chronic pancreatitis** and **TRAUMA**
GROSS	**DUODENUM** **If you see a picture of bowel (i.e. duodenum), you know the cyst is at the HEAD of the pancreas*  **PSEUDOCYST**  **This pseudocyst is at the tail of pancreas**
MORPHOLOGY	**NO EPITHELIAL LINING**

6. SEROUS CYSTIC NEOPLASMS Women, 6th-7th Decade	7. MUCINOUS CYSTIC NEOPLASMS Women
BENIGN, multicystic neoplasms that usually occur in the **TAIL of the pancreas**	**BENIGN**, cystic neoplasm that can be **PRECURSORS TO INVASIVE CARCINOMAS** Associated with **KRAS, TP53, & RNF43** Usually in the **TAIL of the pancreas** & presents as a ***painless, slow growing mass;***

8. CARCINOMA OF THE PANCREAS
OLDER PATIENTS**

DEFINITION	Arises from **well-defined non-invasive precursor lesions (PANCREATIC INTRAEPITHELIAL NEOPLASIA) in small ducts of the pancreas (=ADENOCARCINOMA)**
RISK FACTORS	**CIGARETTE SMOKING, HIGH FAT DIETS, chronic pancreatitis, diabetes mellitus**
CLINICAL	*Usually remain silent until there is impingement on adjacent structures* **60-70% arise in HEAD OF PANCREAS – *obstructing bile flow at the Ampullary Region* → *OBSRUCTIVE JAUNDICE* (dark urine, light stool)** BODY & TAIL lesions remain silent & invade adjacent structures (spleen, adrenals, transverse colon, stomach) – **VERY BAD PROGNOSIS** ****DISTENDED, NON-PALPABLE GALL BLADDER** ****TROUSSEAU SIGN (Migratory Thrombophlebitis – *inflammation of vein due to blood clot*)** seen in 10% of patients
PATHOGENESIS	Associated with **KRAS, TP53, & CDKN2A**
GROSS	 **Carcinomas have desmoplasia – SOLID LESIONS**  **HEAD of the PANCREAS** *(you see duodenum on L)*  **TAIL of PANCREAS** Liver shows cancer – *this is BAD! Pancreatic CA has metastasized!*
MORPHOLOGY	 **ADENOCARCINOMA** ***SPINDLE SHAPED CELLS laying down FIBROUS TISSUE leading to DESMOPLASIA** **Tumor markers:** **CA19-9** **CEA**
COURSE/ TREATMENT	**POOR PROGNOSIS *(but better if in the HEAD of the pancreas)*; 5-year survival rate <5%** ****PERINEURAL INVASION MAY BE SEEN – *This is a classic tumor that invades nerves!***** *(Prostate, Pancreas, & Adenoid Cystic Carcinoma all invade nerves)*

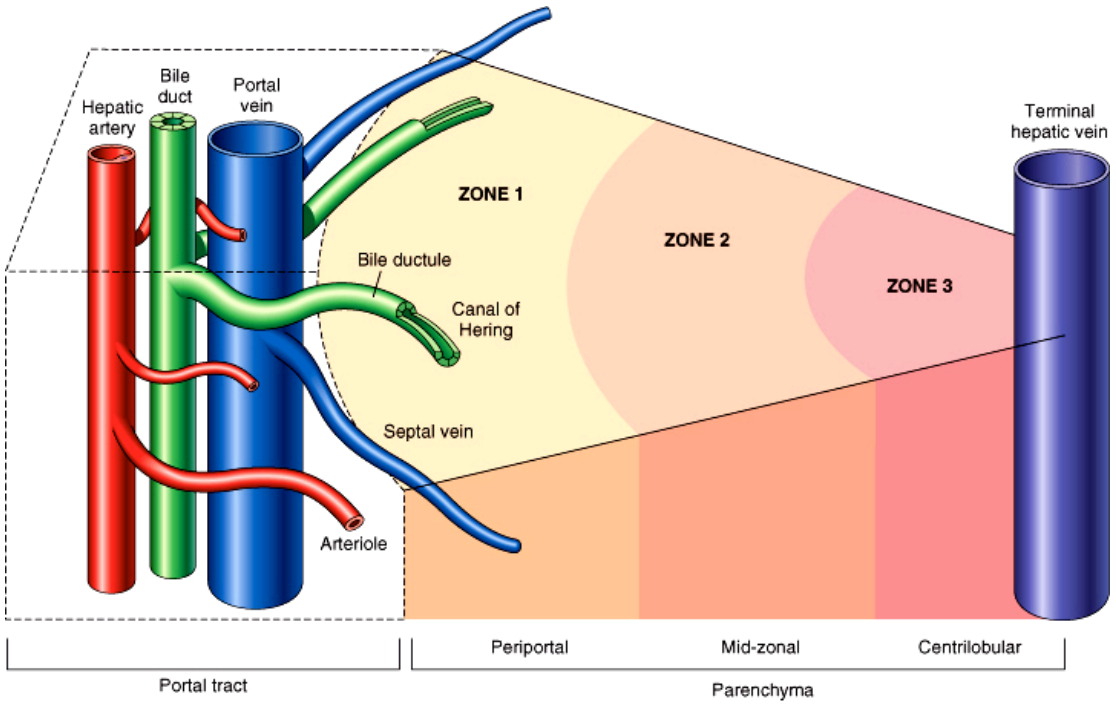
http://www.cheatography.com/ksellybelly/cheat-sheets/gi-v-pancreas-and-biliary-tract/

	ACUTE PANCREATITIS	CHRONIC PANCREATITIS	PANCREATIC NEOPLASM
ETIOLOGY	Cholelithiasis (female) ETOH (males)	ETOH	Risk Factors: elderly, obesity, tobacco, chronic pancreatitis, previous abdominal radiation, family history
CLINICAL FEATURES	***Epigastric pain radiating to the back***, improves with leaning forward or lying in fetal position, nausea/vomiting, fever, leukocytosis, sterile peritonitis	Epigastric pain radiating to the back, improves with leaning forward or lying in fetal position, nausea/vomiting, **+ fat malabsorption**, *Steatorrhea later in disease*	Abdominal pain +/- radiating pain, jaundice, palpable gallbladder (Courvoisier's sign) if cancer of pancreatic head
LAB STUDIES	↑Serum Amylase, Lipase, WBC, LFTs if biliary obstruction, Ranson's criteria = poor prognosis	↑Amylase early in disease Abdominal plain film (x-ray) shows calcifications	
TREATMENT	NPO to prevent secretion of pancreatic juices Restore + maintain fluid volume Parenteral hyperalimentation	Address underlying cause (ETOH) NPO to prevent secretion of pancreatic juices Fluid volume restoration Parenteral hyperalimentation Low-fat diet upon discharge Surgical removal for pain control	Surgery (Modified Whipple's)

LIVER PATH

SIGNS OF HEPATIC INJURY

- INFLAMMATION: **Hepatitis**
  - *Can be autoimmune or drug-induced or caused by organisms (viruses and others)*
- DEGENERATION
  - **Ballooning**: enlarged "swollen" cell with watery cytoplasm & variable nuclear damage
  - **Foamy** ("feathery"): due to **cholestasis** – *bile is inside the cell*
  - **Steatosis**: ***fatty change***
    - **MICROvesicular** – Reye Syndrome
    - **MACROvesicular** – Alcoholic & Non-Alcoholic Fatty Liver Disease
- CELL DEATH: **Necrosis, Apoptosis**
- FIBROSIS:
  - **Bridging**: bridging of portal tracts or bridging of portal tracts to the portal vein → *cirrhotic appearance*
- CIRRHOSIS = **Diffuse Fibrous Tissue + Regenerative Nodules of Hepatocytes**
- ↑ALT & ↑AST due to HEPATOCELLULAR DAMAGE

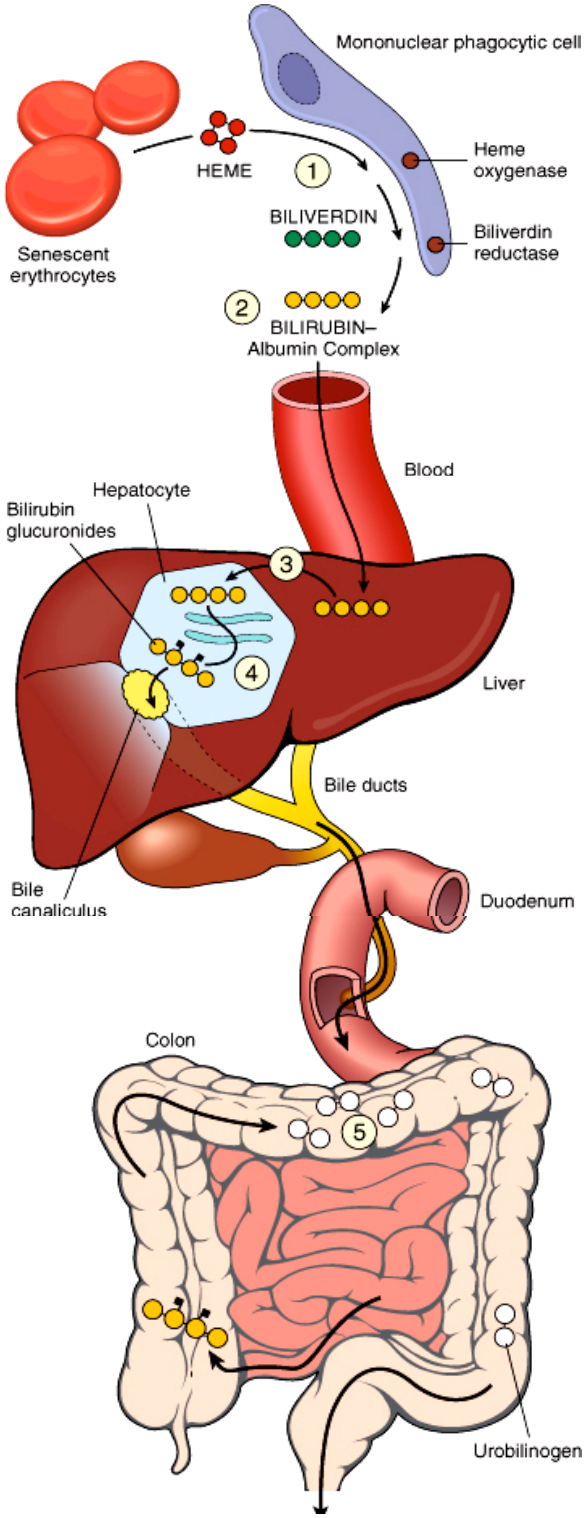


EACH ZONE IS SPECIFIC FOR A SPECIFIC TYPE OF NECROSIS

ZONE 1: PERIPORTAL (Peripheral) NECROSIS
- *Phosphorous poisoning*
- *Pregnancy*
- *Chronic viral hepatitis*

ZONE 2: MID-ZONAL NECROSIS
- ***YELLOW FEVER***

ZONE 3: CENTRAL ZONE NECROSIS
- ***Affected first by ischemia***
- *Acetaminophen poisoning (coagulative necrosis)*
- *Congestion → dilated sinuses + central necrosis =* ***nutmeg liver***



BILIRUBIN METABOLISM

1. Heme oxygenase converts *heme* to *biliverdin*
2. Biliverdin reductase converts biliverdin to ***UNconjugated*** *bilirubin*
3. Unconjugated bilirubin binds to albumin & travels in the blood to the liver
4. In the liver, unconjugated bilirubin enters the hepatocyte, where it becomes ***conjugated*** *bilirubin*
5. Conjugated bilirubin is transported into the bile canaliculi & then into the bile ducts
6. Conjugated bilirubin is acted upon in the **colon** by bacteria, which will metabolize the conjugated bilirubin into *urobilinogen* – ***this is what givens stool its brown color****; if you cannot get conjugated bilirubin to the colon, stool will be pale*

UNCONJUGATED BILIRUBIN

- Tightly complexes to serum albumin
- *Unconjugated (indirect) bilirubin is* ***not water-soluble*** *at physiologic pH, so it's NOT found in urine.*
- Increased with severe **HEMOLYTIC disease**: destruction of RBCs causes the release of unconjugated bilirubin into the blood
- Increased with displacement of bilirubin from albumin

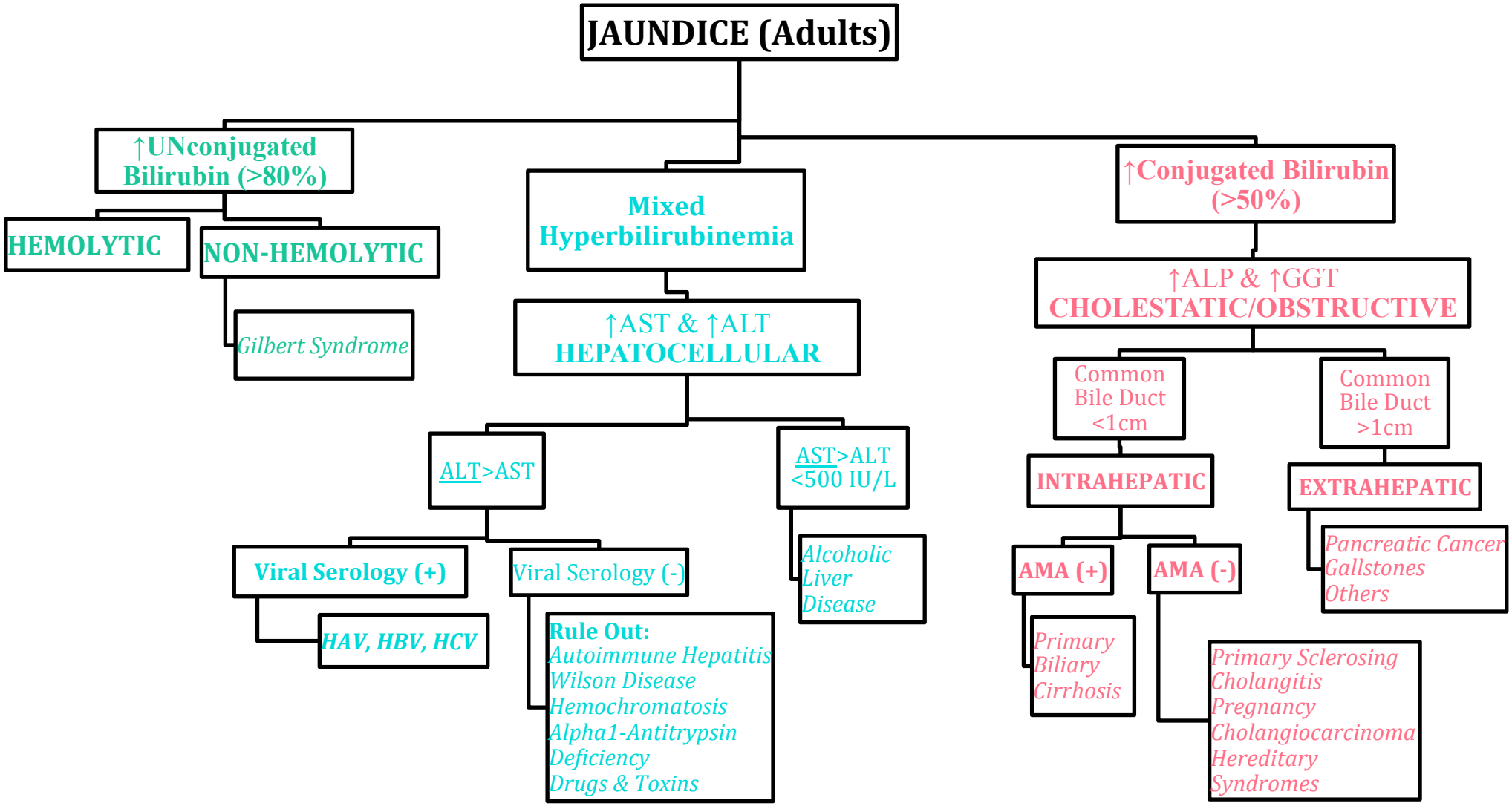
CONJUGATED BILIRUBIN

- Loosely bound to albumin
- *Conjugated (direct) bilirubin is* ***water-soluble****, so excess in plasma can be excrete in urine*
- Increased with **OBSTRUCTION of bile flow**

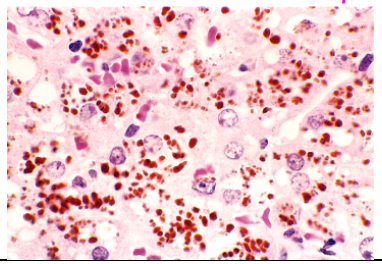
Normal Bilirubin Levels: 0.3-1.2 mg/dl

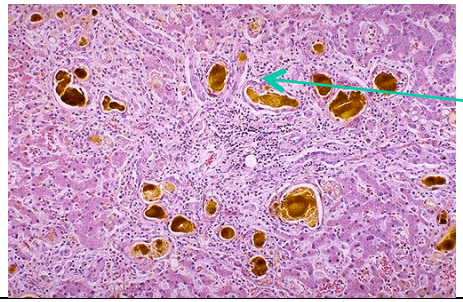
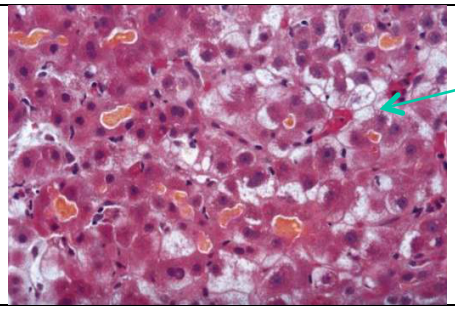
JAUNDICE: yellow discoloration of the skin & sclera that occurs when **bilirubin levels rise >2.0-2.5 mg/dl**

- Excessive production of bilirubin: *hemolytic anemias, ineffective erythropoiesis*
- Reduced hepatic uptake: *drug interference with membrane carrier systems*
- Impaired conjugation: ***neonatal jaundice***
- Decreased hepatocellular excretion: ***Dublin-Johnson*** (deficiency of canalicular membrane transporters)
- Impaired bile flow: *Intrahepatic (within the liver) vs. Extrahepatic (outside the liver)*


JAUNDICE (Adults)
↑UNconjugated Bilirubin (>80%)
HEMOLYTIC
NON-HEMOLYTIC
Gilbert Syndrome
Mixed Hyperbilirubinemia
↑AST & ↑ALT
HEPATOCELLULAR
ALT>AST
AST>ALT
<500 IU/L
Viral Serology (+)
HAV, HBV, HCV
Viral Serology (-)
Rule Out:
Autoimmune Hepatitis
Wilson Disease
Hemochromatosis
Alpha1-Antitrypsin Deficiency
Drugs & Toxins
Alcoholic Liver Disease
↑Conjugated Bilirubin (>50%)
↑ALP & ↑GGT
CHOLESTATIC/OBSTRUCTIVE
Common Bile Duct <1cm
Common Bile Duct >1cm
INTRAHEPATIC
EXTRAHEPATIC
AMA (+)
AMA (-)
Primary Biliary Cirrhosis
Primary Sclerosing Cholangitis
Pregnancy
Cholangiocarcinoma
Hereditary Syndromes
Pancreatic Cancer
Gallstones
Others

CONGENITAL UNCONJUGATED HYPERBILIRUBINEMIAS = Deficiency in UGT1A1				
	1. NEONATAL JAUNDICE	**2. CRIGLER NAJJAR I**	**3. CRIGLER NAJJAR II**	**4. GILBERT SYNDROME**
DEFINITION	**↓UDP-glucuronyltransferase (UGT1A1)**	**AUTOSOMAL RECESSIVE** *Complete lack of UGT1A1*	**AUTOSOMAL DOMINANT** ★ *Decreased UGT1A1 activity*	Relatively uncommon *Decreased levels of UGT1A1*
COURSE/ TREATMENT	Tx with **phototherapy** to degrade small amounts of bilirubin	**FATAL**, secondary to irreversible brain damage (*kernicterus*)	Less severe, **NON-FATAL**	Mild jaundice or *asymptomatic* ****ADULTS WITH LONG HISTORY OF MILD JAUNDICE****

CONGENITAL CONJUGATED HYPERBILIRUBINEMIAS		
	5. DUBLIN-JOHNSON SYNDROME	**6. ROTOR SYNDROME**
DEFINITION	**AUTOSOMAL RECESSIVE defect in TRANSPORT PROTEIN** *CAN conjugate bilirubin, but can't get it out of hepatocyte*	Variant of Dublin-Johnson Syndrome
MORPHOLOGY	**DARKLY PIGMENTED CYTOPLASMIC GLOBULES – *black hepatic tissue in a child*** 	NO dark liver pigment

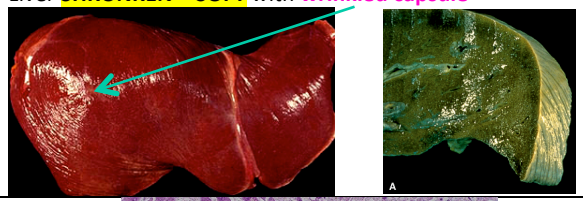
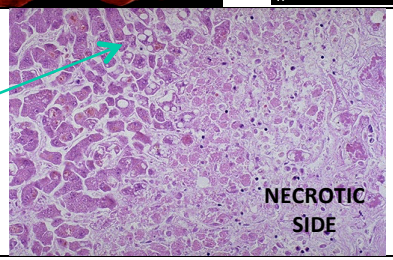
7. CHOLESTASIS: ↑ALP ↑GGT	
DEFINITION	Systemic retention of **conjugated** bilirubin & other solute eliminated in bile (*bile salts, cholesterol, etc.*)
CLINICAL	Jaundice, pruritus (*accumulation of bile salts*), skin xanthomas (*build up of cholesterol*) **↑ALP ↑GGT**
PATHOGENESIS	Caused by **HEPATOCELLULAR DYSFUNCTION;** intrahepatic or extrahepatic **biliary obstruction**
MORPHOLOGY	 Accumulation of bile pigment in hepatic parenchyma  **Foamy/feathery degeneration** *Cells are becoming vacuolated*
COURSE	*Prolonged obstruction, typically from a stone* → Portal tract fibrosis → **Secondary Biliary Cirrhosis** Ascending cholangitis secondary to obstruction

8. BILIARY ATRESIA (Fetal & Perinatal) **Within the first 3 months of life**	
DEFINITION	Complete or partial obstruction of the lumen of the **extrahepatic biliary tree**
CLINICAL	Presents with serum **bilirubin of 6-12 mg/dl** + only ***moderately*** ↑aminotransferase & ALP
GROSS	Scarring of hepatic & common bile ducts
MORPHOLOGY	Inflammation & **fibrosing stricture** of the hepatic & common bile ducts
TREATMENT	Treatment: liver transplant

HEPATIC FAILURE: Most severe clinical consequence of liver disease

>80-90% of hepatic functional capacity eroded; *usually the end point of progressive liver damage;* 80% mortality rate in patients not treated with a liver transplant

CLINICAL FEATURES: Jaundice, hypoalbuminemia, hyperammonemia, spider angiomas, testicular atrophy/gynecomastia, coagulopathy, death within weeks to months

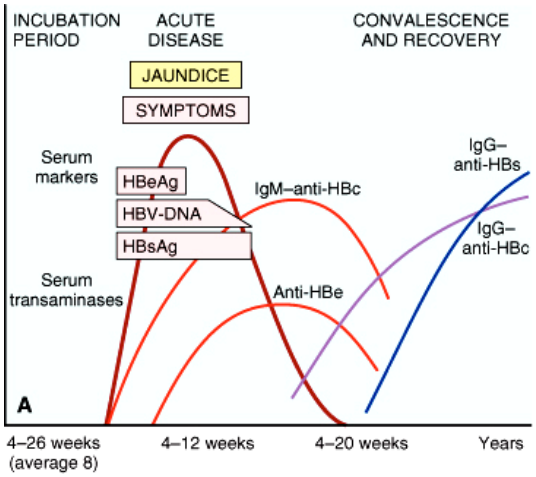
	9. MASSIVE HEPATIC NECROSIS ↑↑ALT & AST	10. CIRRHOSIS	11. REYE SYNDROME Children < age 4
DEFINITION	Acute massive liver destruction – *fulminant hepatitis*	**Most common cause of Chronic Liver Disease** *Chronic liver damage from a variety of causes leading to scarring and liver failure*	Hepatic dysfunction without overt necrosis DIFFUSE & MASSIVE FATTY CHANGE of the liver + *encephalopathy* → hepatocellular dysfunction
CLINICAL	*Jaundice, **hepatic encephalopathy, portal HTN, & heptorenal syndrome*** **(described on next page)**	**Asymptomatic (40%)** Or anorexia, weight loss, weakness, frank debilitation	Initially presents as sleeping & with vomiting episodes that can eventually progresses to come & death
CAUSES	**Fulminant Viral Hepatitis**: Acute A & B **Drugs & Chemicals:** Acetaminophen	**60-70% ALCOHOL ABUSE** *Many different causes of cirrhosis that will be discussed*	**Associated with giving child ASA during viral illness**
GROSS	Liver **SHRUNKEN + SOFT** with **wrinkled capsule** 		
MORPHOLOGY	Just fatty change over here 	**3 CHARACTERISTICS:** 1. **Narrow to broad dense bands of fibrosis** 2. **Regenerative parenchymal nodules** 3. **Entire liver architecture disruption**	**MICROVESICULAR STEATOSIS** – *diffuse & massive fatty change of the liver*
COURSE/ TX	Mortality ranges from 25-90%	**Of the top 10 causes of death in Western world** **PROGRESSIVE LIVER FAILURE. PORTAL HTN, HEPATOCELULAR CARCINOMA**	Look for a **child** presenting with signs of liver failure – *elevated transaminases, bleeding, etc.* – who just recovered from a **viral illness**

Complications of Hepatic Failure

	12. HEPATIC ENCEPHALOPATHY	13. HEPTORENAL SYNDROME	14. PORTAL HYPERTENSION
DEFINITION	Metabolic disorder of the CNS & neuromuscular system Feared complication of **acute & chronic hepatic failure**	Appearance of **renal failure** in patients with liver failure *LIVER DYSFUNCTION 1ST, then KIDNEY FAILURE	Increased resistance to portal flow
CLINICAL	**Marked stupor & confusion**, deep coma, & death **NEUROLOGIC SIGNS:** rigidity, hyperreflexia, seizures, or **ASTERIXIS (flapping tremor)**	Associated with sodium retention, impaired free-water excretion, & decreased renal perfusion & GFR	Ascites, congestive splenomegaly, portosystemic venous shunts leading to varices, caput medusa, hepatic encephalopathy
PATHOGENESIS	Important physiologic factors: 1. Severe loss of hepatocellular function 2. Shunting of blood around chronically diseased liver 3. Deranged neurotransmission	No intrinsic morphologic or functional causes for renal failure – *Renal function promptly improves if hepatic failure is reversed*	**PRE-HEPATIC:** obstructive thrombosis **HEPATIC:** cirrhosis, shistosomiasis, massive fatty change **POST-HEPATIC:** severe R heart failure, constrictive pericarditis, hepatic vein obstruction **(BUDD CHIARI)**
MORPHOLOGY			**NUTMEG LIVER** – *usually due to R heat failure*

Viral Hepatitis – *Do not progress to chronic disease*		
	15. HAV (Picornaviridae): ssRNA **Schools, Daycare Centers, UNDERDEVELOPED COUNTRIES**	**16. HEV (Calciviridae): ssRNA** ****High mortality rate amount PREGNANT FEMALES****
DEFINITION	***Benign*, self-limited** disease	Self-limited disease in most cases
CLINICAL	Incubation period of 2-6 weeks; *patients presents with acute hepatitis symptoms – flu-like symptoms, pale stools, brown urine, icterus, etc.*	Incubation period of 2-8 weeks
PATHOGENESIS	Spread by ingestion of contaminated water & foods (Raw or steamed **SHELLFISH**) Shed in the stool (fecal-oral)	Fecal-oral transmission
MORPHOLOGY	*Massive hepatic necrosis possible*	
COURSE/TX	**NO CHRONIC HEPATITIS OR CARRIER STATE**	**NO CHRONIC HEPATITIS**
DIAGNOSIS	**IgM-anti-HAV**	HEV RNA or IgM/IgG

Viral Hepatitis – *Can progress to chronic disease*			
	17. HBV (Hepdnaviridae): partially dsDNA	**18. HCV (Flaviviridae): ssRNA**	**19. HDV (Deltaviridae): defective ssRNA**
CLINICAL	Prolonged incubation period 4-26 weeks	Prolonged incubation period 2-26 weeks Symptoms are milder than HBV **PERSISTENT ↑ AST/ALT**	Seen in 2 settings: 1. Acute coinfection from serum with both viruses 2. Superinfection of HBV in Chronic HBV patient
PATHOGENESIS	Present in all physiologic & pathologic body fluids Transmitted via **IV drug use, sex, birth**, **TRANSFUSIONS**	Major route of transmission: **IV drug use, sex** ****HCV via blood transfusions is basically NONE in US****	**Dependent on HBV coinfection for replication**
COURSE/ TX	Can produce: *acute hepatitis, **chronic hepatitis, cirrhosis, fulminant hepatitis, & asymptomatic carrier state*** ***Hepatocellular carcinoma (ONCOGENIC)**	**90% PROGRESS TO CHRONIC HEPATITIS** *Cirrhosis occurs in ~20% of patients with Chronic HCV*	**Superinfected** patients more often progress to **SEVERE CHRONIC HEPATITIS (Fulminant)**
DIAGNOSIS	***Serum Markers ***	**HCV RNA** + ↑transaminases	**IgM-anti-HDV**



*****HBV Serum Markers*****

HBsAg (surface) peaks during **ACTIVE** infection; *patient is **symptomatic***

HBeAg (envelope) signifies infectivity/viral replication

IgM-anti-HBc (core) & anti-HBe seen during WINDOW PERIOD, but aren't specific for hepatitis!

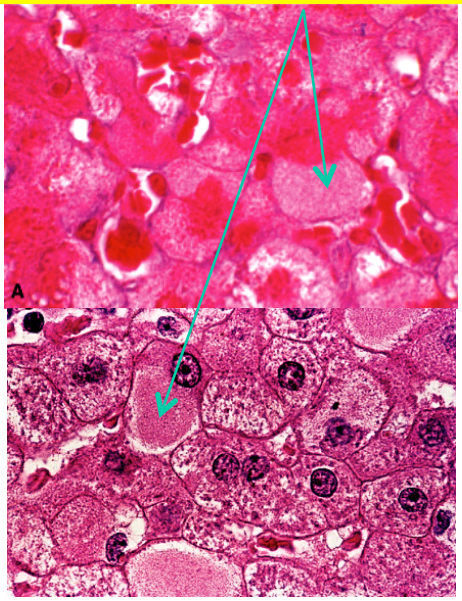
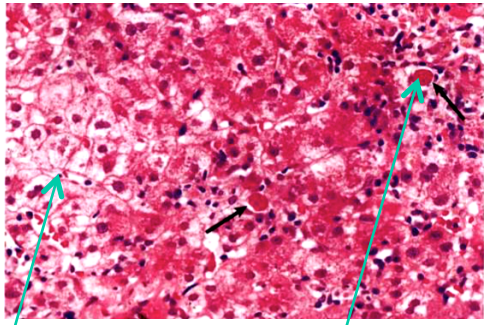
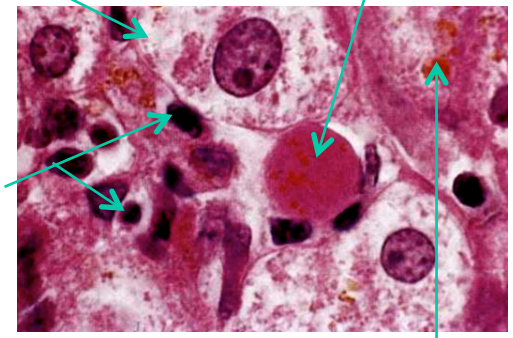
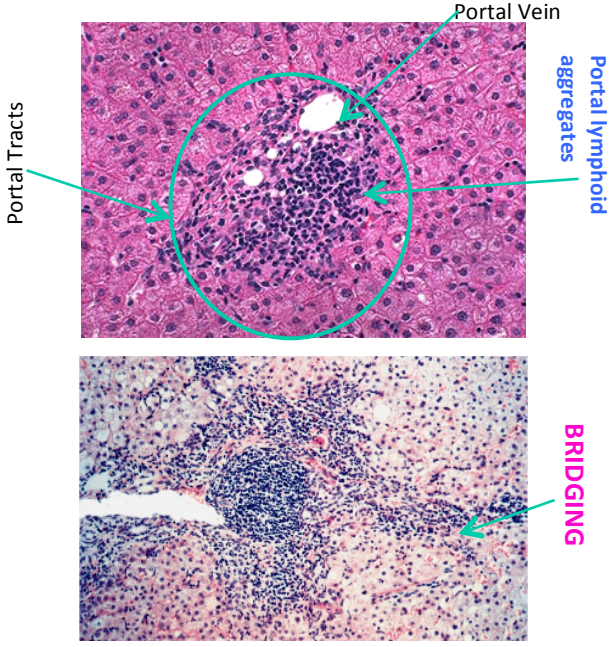
***Check for anti-HB**c** & anti-HBe – After the initial acute/symptomatic phase, HBsAg can go really low when the patient is asymptomatic, but the patient can still transmit the infection!*

IgG-anti-HBs denotes PREVIOUS EXPOSURE after acute phase

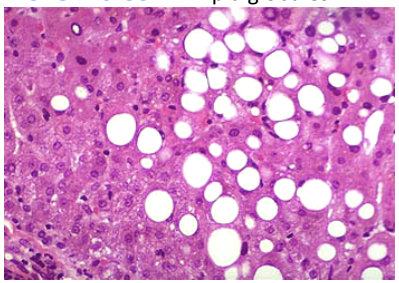
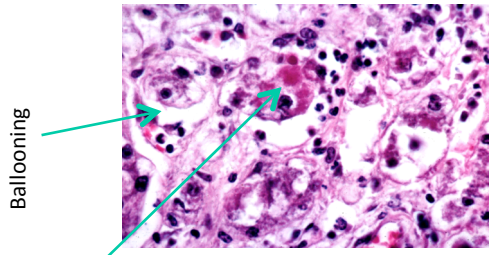
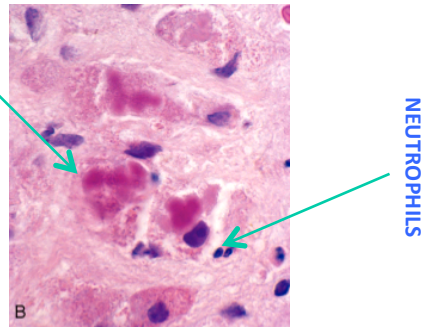
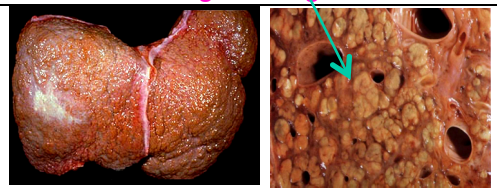
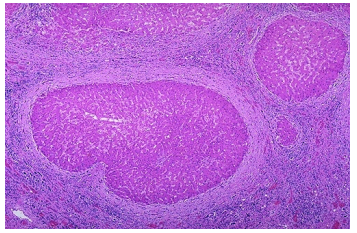
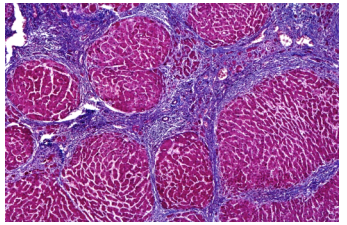
*Patient has a blood transfusion & gets HBV. After about 8 weeks, HBsAg + HBeAg increase. Antibody against core antigen (IgM-anti-HBc) will rise. **WINDOW PERIOD:** HBsAg + HBeAg disappear. **IgM-anti-HBc PEAKS & it's ALL you see.** No detection of Ig-anti-HBs because they are bound to HBsAg. Eventually, your IgM antibodies will drop & IgG antibodies will increase, indicating **recovery phase**.*

Window Period is the time between the disappearance of HBsAg & the appearance of Anti-HBs antibodies.

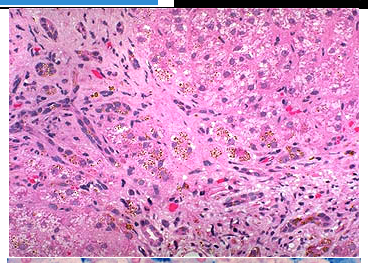
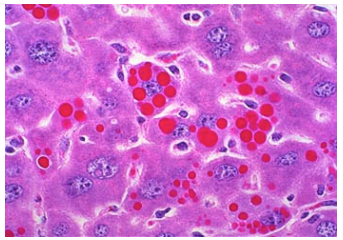
Different Presentations of Viral Hepatitis

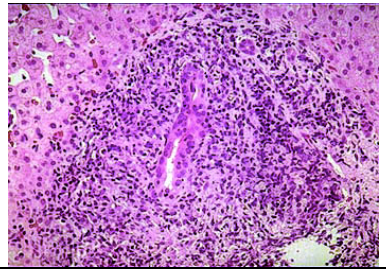
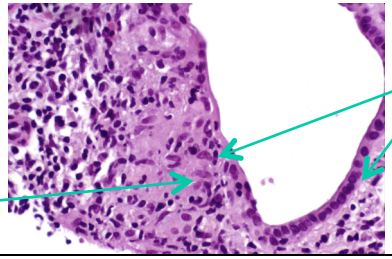
	20. CARRIER STATE	21. ACUTE HEPATITIS: ↑ ALT/AST	22. CHRONIC HEPATITIS: ↑ ALT/AST
CLINICAL	Typically seen with **HBV** **ASYMPTOMATIC**, but **can still transmit infection** **Infected early in life: 90-95% carrier state** Infected in adulthood: 1-10% carrier state	LESS THAN 6 MONTHS 4 Phases: Incubation, Pre-icteric, Icteric, Convalescence **PRE-ICTERIC:** *non-specific, constitutional symptoms; malaise followed by fatigability, nausea, loss of appetite* **ICTERIC:** *jaundice from ↑conjugated & unconjugated bilirubin,* ***dark urine, clay-colored stools, pruritus***	Continuing or relapsing hepatitis for >6 MONTHS **HBV, HCV, HDV** Variable clinical features – *fatigue most common* **↑ PROTHROMBIN TIME**, Hyperglobulinemia, Hyperbilirubinemia, **MILD ↑ ALP**
MORPHOLOGY	*Fine, granular eosinophilic cytoplasm* **GROUND GLASS CELLS + "SANDED" NUCLEI**  ***Ground glass appearance comes from the accumulation of HBsAg in the cells***	**KUPFFER CELL HYPERPLASIA** **PORTAL TRIADITIS:** inflammation around portal triad; *looking for lymphocytic infiltration in the parenchyma* **LOBULAR DISARRAY**: lose hexagon shape, no lines or divisions  Ballooning/feathery degeneration **COUNCILMAN BODIES** ★ ***Apoptosis, EXTRACELLULAR***  Lymphocytes **CHOLESTASIS** ***Brown pigment*** ****NO FATTY CHANGE****	**BRIDGING NECROSIS + FIBROSIS** **PERIPORTAL** (patchy, focal) **NECROSIS**  Portal Vein Portal Tracts Portal lymphoid aggregates **BRIDGING** **This looks like **active severe hepatitis** → **CIRRHOSIS*** Portal Tracts

ALCOHOLIC LIVER DISEASE: Leading cause of liver disease in most Western countries

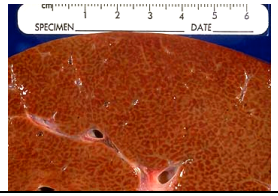
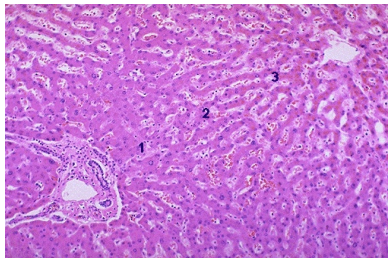
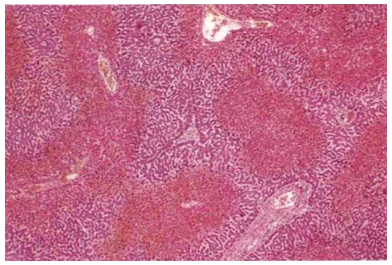
	23. HEPATIC STEATOSIS	24. ALCOHOLIC HEPATITIS: ↑AST>>ALT★	25. CIRRHOSIS: ↑AST>>ALT
DEFINITION	Fatty liver	15-20 years of ETOH abuse is necessary for disease state	
CLINICAL		Anorexia, malaise, upper abdominal discomfort, *tender hepatomegaly* **HYPERBILIRUBINEMIA, ↑ALP, NEUTROPHILIC LEUKOCYTOSIS**	1st signs relate to **portal HTN**, S/S **Hepatic Failure** **HYPERBILIRUBINEMIA, ↑ALP, HYPOPROTEINEMIA**
PATHOGENESIS	Alcohol toxicity → no apolipoproteins to transport lipids out of the hepatocytes	Alcohol toxicity to hepatocytes → accumulation of pre-keratin intermediate filaments inside the liver forming Mallory Body	
GROSS	Large, yellow, greasy liver	**MICRONODULAR CIRRHOSIS** <3mm	**SHRUNKEN + FIRM LIVER (scarring)** **MICRONODULAR regenerating nodules**
MORPHOLOGY	**MACROVESICULAR** lipid globules  *You never see a nucleus inside the vacuole	**HEPATOCYTE SWELLING + NECROSIS**: *clear vacuole, **eccentric nucleus***  **MALLORY BODIES – INTRA**cellular eosinophilic material ***INTERMEDIATE KERATIN FILAMENTS** 	  *Only hepatocytes regenerate, but not portal v, a, ducts.  **TRICHROME STAIN FOR COLLAGEN (scar tissue)**
COURSE/TX	**REVERSIBLE** with alcohol withdrawal	**Repeated bouts → Cirrhosis**	

	26. NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)	27. NON-ALCOHOLIC STEATOHEPATITIS (NASH)
DEFINITION	The presence of hepatic steatosis in individuals who do NOT consume alcohol ***Most common cause of chronic liver disease in the U.S.***	Overt clinical features of **liver injury**, such as ↑AST/ALT & **histologic features of hepatocyte injury seen in alcoholic liver disease**
PATHOGENESIS	**ASSOCIATED WITH METABOLIC SYNDROME (insulin resistance)**	
MORPHOLOGY	**FATTY CHANGE**	Signs of Hepatic Injury – ballooning, scarring, etc.
COURSE/TX	**↑ risk for Hepatocellular Carcinoma**	**↑ risk for Hepatocellular Carcinoma** – *MORE than NAFLD due to hepatic injury*

	28. HEMOCHROMATOSIS Males >40 y/o	29. WILSON DISEASE	30. α_1-ANTITRYPSIN DEFICIENCY
DEFINITION	Accumulation of iron in tissues – *can be either hereditary (mutation in **HFE** gene) or acquired*; METABOLIC liver disorder leading to CIRRHOSIS	Autosomal recessive mutation in **ATP7B** gene associated with the **accumulation of copper** METABOLIC liver disorder leading to CIRRHOSIS	Autosomal recessive disorder with abnormal gene on **Chromosome 14 (PiZZ)** associated with PANACINAR EMPHYSEMA (*early onset in a pt who never smoked)*
CLINICAL	**LIVER:** **CIRRHOSIS** (tissue DAMAGE*), hepatomegaly, abdominal pain **PANCREAS:** deposits in islets → **DIABETES** **HEART:** arrhythmias, **DILATED CARDIOMYOPATHY** **SKIN:** **BRONZE DIABETES** **(Classic Triad of cirrhosis with hepatomegaly, skin pigmentation, & diabetes mellitus)** ★	**LIVER:** Hepatitis → **CIRRHOSIS** **BRAIN:** deposits in Basal Ganglia → **extra-pyramidal symptoms (Parkinson's)** **EYE:** **KAYSER-FLEISCHER RING** ↓ **Serum CERULOPLASMIN**	***Most commonly diagnosed INHERITED HEPATIC DISORDER in Infants & Children** **CIRRHOSIS does not occur until ADULTHOOD**
PATHOGENESIS	**HEREDITARY/PRIMARY –** autosomal recessive mutation in **HFE** gene → **DEFICIENCY IN HEPCIDIN** – Hepcidin is what helps keep the iron in the liver & OUT of the blood; thus, if you have ↓levels, you will have ↑ **iron in the blood & in other tissues** **ACQUIRED/SECONDARY –** due to iron overload from acquired causes, such as **multiple transfusions** **(pt w/ hx of anemia)** or ineffective erythropoiesis		
GROSS			
MORPHOLOGY	 Brown granular pigment in liver; *Stains with **PRUSSIAN BLUE***		**AAT retained in hepatocytes as** **EOSINOPHILIC CYTOPLASMIC GLOBULES – PAS+** 
TREATMENT	Treat with phlebotomy	Chelation or Zinc-based therapy	Orthotopic liver transplant is curative

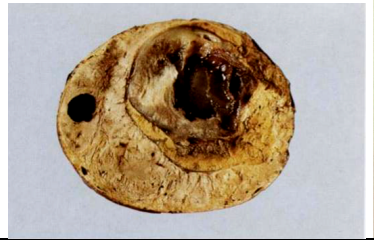
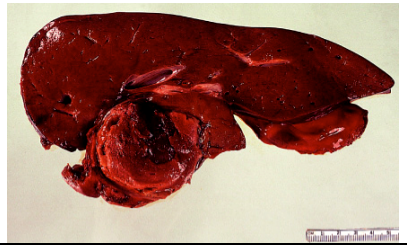
31. PRIMARY BILIARY CIRRHOSIS: ↑ALP & ↑GGT Females 40-50 y/o	
DEFINITION	An autoimmune disorder associated with Chronic Cholestatic Liver Disease & AMA+ ***AMA is against mitochondrial in the BILE DUCT CELLS, not in hepatocytes. Thus, this can present similar to Obstructive Jaundice w/ hyperbilirubinemia & ↑ALP***
CLINICAL	***Pruritus*** *(bile salt buildup)* *skin xanthomas of the eyelids; cirrhosis occurs later in the disease* ↑ALP & ↑GGT + ↑Cholesterol + ↑Conjugated bilirubin (later)
MORPHOLOGY	NON-SUPPURATIVE, GRANULOMATOUS destruction of INTRAhepatic ducts   Macrophages **Notice how you see normal BILE DUCT CELLS all along the Right side & then when you move towards the middle of the picture, there are NO BILE**

32. PRIMARY SCLEROSING CHOLANGITIS: PERSISTENT ↑ALP	
CLINICAL	Presents similarly to Primary Biliary Cirrhosis, except it also affects EXTRAhepatic ducts
PATHOGENESIS	Coexists in ~70% of individuals with ULCERATIVE COLITIS
GROSS	"BEADING" of the ducts seen on radiograph
MORPHOLOGY	**Inflammation &** OBLITERATIVE FIBROSIS **of** INTRAhepatic & EXTRAhepatic bile ducts with DILATION of preserved segments
COURSE	Progressive fatigue, pruritus, & obstructive jaundice may develop along with acute bouts of **Ascending Cholangitis**

33. PASSIVE CONGESTION RIGHT SIDED HEART FAILURE	
DEFINITION	CONGESTION of the centrilobular sinusoids from back up of blood into systemic circulation secondary to *right sided heart failure*
GROSS	**CONGESTION of the centrilobular sinusoids** (*from R CHF*) **+ ISCEHMIA** (*from L CHF*) → **CENTROLOBULAR NECROSIS = NUTMEG LIVER**  
MORPHOLOGY	 
COURSE	UNCOMMONLY, sustained chronic severe CHF → **CARDIAC SCLEROSIS** (centrilobular fibrosis only around the CENTRAL VEIN & secondary to the heart failure)

34. BUDD CHIARI SYNDROME (Hepatic Vein Thrombosis)	
DEFINITION	Obstruction of the hepatic vein via **thrombosis**
CLINICAL	**POST-HEPATIC PORTAL HTN;** *Hepatomegaly, weight gain, ascites, & abdominal pain;*
PATHOGENESIS	Associated with **POLYCYTHEMIA VERA** (& other myeloproliferative disorders), pregnancy, **ORAL CONTRACEPTIVES (**young female of reproductive age)
MORPHOLOGY	**SEVERE CENTRILOBULAR CONGESTION & NECROSIS → NUTMEG LIVER**
COURSE	High mortality of untreated

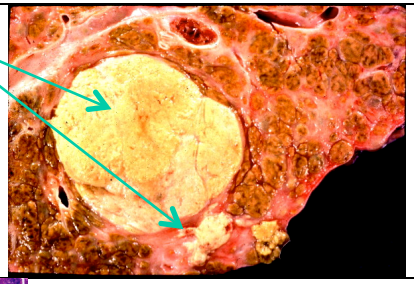
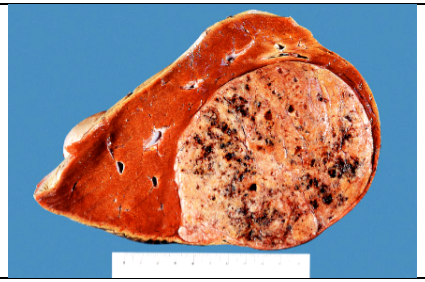
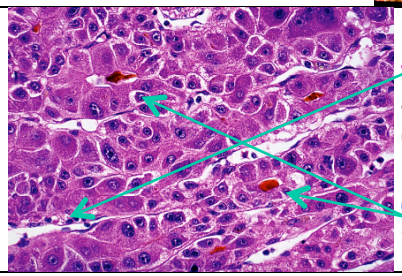
35. CAVERNOUS HEMANGIOMA Most common benign liver tumor!	
DEFINITION	**BENIGN** tumor of the blood vessels;
CLINICAL	***May be mistaken radiographically or intraoperatively for metastatic tumors*** – meaning that their can be **MULTIPLE** of them
GROSS	Discrete, red-blue, **SOFT NODULES**, <2cm in diameter
MORPHOLOGY	**DILATED VASCULAR CHANNELS IN A BED OF FIBROUS CONNECTIVE TISSUE**

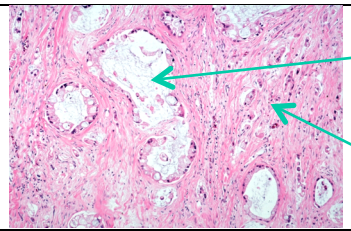
36. LIVER CELL ADENOMA	
DEFINITION	**BENIGN** tumor
CLINICAL	***May be detected incidentally with abdominal imaging*** **RUPTURE** may lead to **INTRA-ABDOMINAL BLEEDING** – *i.e. abdominal trauma from car accident*
PATHOGENESIS	**Associated with ORAL CONTRACEPTIVES* (**young female of reproductive age) **& ANABOLIC STEROIDS** *(anytime something is associated with steroid use, you have to be worried about patients who reserve steroid therapy – autoimmune, status post transplant, anti-inflammatory, RA, etc.)*
GROSS	**Well-circumscribed, BILE-STAINED**  
COURSE	*Typically they can regress, but some can go on to carcinoma*

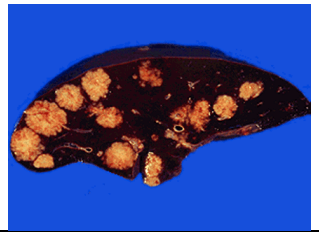
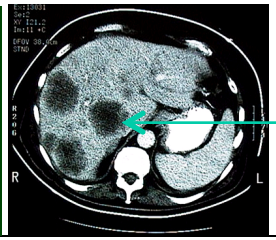
37. HEPATOCELLULAR CARCINOMA: ↑AFP >400

Most common PRIMARY cancer of the liver

Males 8:1; Blacks/Asians, 3rd to 5th Decades

CLINICAL	*May present as **SILENT HEPATOMEGALY*** Often seen in the setting of **CIRRHOSIS** with worsening symptoms
ETIOLOGY	**HBV infection seen in >85% of cases worldwide!** **Cirrhosis** (via chronic liver disease) ***AFLATOXINS** – "moldy grains" & peanuts
PATHOGENESIS	Associated with **activation of β-catenin** & **inactivation of p53**
GROSS	Large, **UNIFOCAL** lesion *With a smaller satellite lesion* *Looking at the picture, what do you think this carcinoma is caused from? It looks like cirrhotic liver (nodules, large areas of scar tissue, etc.), so maybe alcohol*  
MORPHOLOGY	 **WELL-DIFFERENTIATED** hepatocytes arranged in **CORDS or SMALL NESTS** *(lose of hexagon architecture)* **CHOLESTASIS** *because you don't' have typical portal tracts, etc.* **Tumor markers:** α-fetoprotein
COURSE	Median survival ~7 months – **BAD PROGNOSIS** Death from profound cachexia, GI or esophageal varices bleeding, or liver failure with hepatic coma

	38. ANGIOSARCOMA	39. CHOLANGIOCARCINOMA
PATHOGENESIS	**POLYVINYL CHLORIDE** ***History might be a pt who builds houses for years*** **ARSENIC** *Rat poisoning* **THOROTRAST** *Contrast dye they don't use anymore*	Incidence higher in **CHINA** & associated with ***Opisthorchis sinensis* Liver Fluke** Arises from the **BILE DUCT CELLS** – *angiocarcinoma* ***(glandular)***
MORPHOLOGY	'ANGIO-' means **VASCULAR LESION** But it is a **SARCOMA**, so looking for vascular channels lined by **spindle shaped cells** that are **pleomorphic, hyperchromatic, + mitotic figures** ***Don't confuse this with Cavernous Hemangioma – they are both vascular, but in a hemangioma, the cells are uniform!***	 **GLANDULAR** **Stromal invasion w/ DESMOPLASIA**

40. METASTATIC DISEASE **Most common malignancy in the liver**	
PATHOGENESIS	**Most common primary sources: COLON, BREAST, LUNG, & PANCREAS CARCINOMA** *If a tumor spreads hematogenously, usually sarcoma. But even though carcinomas initially spread via lymphatics, when they become very advanced, they spread hematogenously → LIVER*
GROSS	**MULTIPLE NODULAR METASTASES**    Multifocal areas of metastatic tumors
MORPHOLOGY	**SHOULD RESEMBLE PRIMARY TUMOR** (bc they cells are CLONAL)

GALLBLADDER (GB)	Cholelithiasis (Cholesterol + Pigment stones) Cholesterolosis Acute Cholecystitis Chronic Cholecystitis Carcinoma of the Gallbladder	
PANCREAS (P)	Pancreatic Divisum Annular Pancreas Acute Pancreatitis Chronic Pancreatitis Pancreatic Pseudocyst Serous & Mucinous Cystic Neoplasms Carcinoma of the Pancreas	
LIVER (L)	Jaundice – *Hemolytic, Hepatocellular, Obstructive* Hereditary Hyperbilirubinemias Congenital Unconjugated Hyperbilirubinemia Neonatal Jaundice Crigler-Najjar Syndrome Type I Crigler-Najjar Syndrome Type II Gilbert Syndrome Congenital Conjugated Hyperbilirubinemia Dubin Johnson Syndrome Rotor Syndrome Cholestasis Biliary Atresia Hepatic Failure Massive Hepatic Necrosis Chronic Liver Disease Hepatic Dysfunction Without Overt Necrosis Hepatic Encephalopathy Hepatorenal Syndrome Portal Hypertension (*Pre-hepatic, Intra-hepatic, Extra-hepatic*) Viral Hepatitis – HAV, HBV, HCV, HDV, HEV Carrier State Acute Viral Hepatitis Chronic Viral Hepatitis Fulminant Hepatitis	Alcoholic Liver Disease Fatty Liver Disease (Hepatic Steatosis) Alcoholic Hepatitis Alcoholic Cirrhosis Non-Alcoholic Fatty Liver Disease (NAFLD) Metabolic Liver Diseases Hereditary Hemochromatosis Wilson Disease α1-Antitrypsin (AAT) Deficiency Reye Syndrome Non-Alcoholic Cirrhosis Primary Biliary Cirrhosis Primary Sclerosing Cholangitis Vascular Disorders Passive Congestion Hepatic Vein Thrombosis (Budd-Chiari Syndrome) Hepatic Neoplasms (Benign) Cavernous Hemangioma Liver Cell Adenoma Primary Hepatic Neoplasms (Malignant) Hepatocellular Carcinoma (HCC) Cholangiocarcinoma Angiosarcoma Metastatic Cancer

	VIRAL HEPATITIS	**ALCOHOLIC HEPATITIS**
DIAGNOSTICS	↑AST = ↑ALT	**↑↑AST >> ↑AST**
MORPHOLOGY	Surrounded by LYMPHOCYTES COUNCILMAN BODIES: ***extra***cellular; apoptosis	Surrounded by **NEUTROPHILS** **MALLORY BODIES: *intra***cellular; hyaline inclusions

Alkaline phosphatase elevated. You think?	Bile duct damage	Histology of fat cells in fat necrosis	Granular appearance
Morphological change due to cholestasis	"Feathery" or "foamy"	Most common complication of HCV	Chronic disease
Failure of Fusion of fetal duct systems (P)	Pancreas Divisum	Examples of MID-ZONAL Necrosis	Yellow Fever
4 F's of Cholesterol Gallstones	Female, Forty, Fertile, Fat	Inflammation of GB + Coagulative necrosis	Gangrenous Cholecystitis
Hepatitis from Underdeveloped Countries	HAV	Transaminase elevated 2-3x normal. You think?	Hepatocellular damage
Examples of PERIPORTAL Necrosis	Phosphorous poisoning, pregnancy	Causes of Pancreatic Pseudocysts	Acute/**Chronic** Pancreatitis & Trauma
Oncoprotein Erbb2 (Her-2/Neu)	Carcinoma of the Gallbladder	What type of bilirubin may be found in urine?	Conjugated (water-soluble)
Decreased UDP-glucuronyltransferase (UGT1A1)	Neonatal Jaundice	Most common cause of chronic liver disease	Cirrhosis
Dark pigment cytoplasmic globules + kid	Dublin-Johnson Syndrome	HDV needs what for replication?	Coinfection with HBV
Almost all progress to chronic hepatitis	HCV	Thick fibrotic wall + "sludge" in GB lumen	Chronic Cholecystitis
Ground glass cells	Carrier state (hepatitis)	Lumen with "cloudy or turbid bile" (GB)	Acute Cholecystitis
Where is bilirubin conjugated?	Liver hepatocytes	Tumor Markers: Pancreatic Carcinoma	**CA19-9 & CEA**
Mucosal surface with "yellow flecks"	Cholesterolosis	Acute Pancreatitis classic presentation (male)	Alcoholic
Gross appearance of Cholesterol Gallstone	Pale yellow	What actually is Porcelain Gallbladder?	Dystrophic calcifications seen in X-ray
3 month old with increased AST/ALT & ALP	Biliary Atresia	Type of Fat Necrosis in Acute Pancreatitis	Enzymatic
Type of cellular injury in Acute Pancreatitis	Acinar cell injury	Common age group of Carcinoma of Gallbladder	Elderly
Liver shrunken + SOFT	Massive Hepatic Necrosis	Strawberry Gallbladder	Cholesterolosis
Non-distended, palpable GB. You think?	Carcinoma of the Gallbladder	Acetaminophen poisoning causes...	Coagulative necrosis of Central Zone
3X Increase Amylase + Increase Lipase	Acute Pancreatitis	Most common cause of Cirrhosis	Alcohol abuse (60-70%)
Clinical signs of Hepatic Failure	(8) Jaundice, hypoalbuminemia, hyperammonemia, spider angiomas, testicular atrophy, gynecomastia, coagulopathy, death within weeks to months	Consequences of Massive Hepatic Necrosis	(3) Hepatic encephalopathy, Portal HTN, Hepatorenal Syndrome
8 RFs for Cholesterol Gallstones (not F's)	4F's (F, 40, Fat, Fertile); Native American, oral contraceptives, ↑cholesterol, bile stasis (sepsis, burns)	Mucosa invaginates down into muscularis creating a sinus	Rokitansky-Aschoff Sinuses
Trousseau Sign+	Migratory Thrombophlebitis (Pancreatic CA)	Asterixis (flapping tremor)	Hepatic encephalopathy
Serum levels in Cholestasis	Increased ALP & GGT	Enlarged GB w/ discolored serosa	Acute Cholecystitis
Marked stupor & confusion	Hepatic encephalopathy	Systemic retention of conjugated bilirubin	Cholestasis
Pancreatic CA w/ worse prognosis	Body + Tail of pancreas (silent)	What causes ground glass appearance?	HBsAg accumulation in hepatocytes
What are Councilman bodies?	Extracellular; apoptotic bodies	What may Annular Pancreas present with?	Duodenal obstruction
Fatty change in acute hepatitis?	None	Most severe consequence of liver disease	Hepatic failure
Epigastric pain radiating to the back	Acute or Chronic Pancreatitis	Serum levels with Chronic Hepatitis	Increase AST/ALT & PT, mild increase ALP
Congenital Unconjugated Hyperbilirubinemia	(4) Neonatal Jaundice, Crigler Najjar I, Crigler Najjar II, Gilbert Syndrome	What radiologic finding increases incidence of Gallbladder Carcinoma?	Porcelain Gallbladder in Chronic Cholecystitis
Massive fatty change in 4 year old child	Reye Syndrome	What gives stool its brown color?	Urobilinogen (made in COLON)
Mutations in Mucinous Cystic Neoplasm (P)	KRAS, TP53, **RNF43**	Morphological features of Chronic Hepatitis	Bridging necrosis + periportal necrosis
What zone is 1st affected by ischemia?	Zone 3 – Central Zone Necrosis	Pt w/ Acalculus Cholecystitis often has...	Severe illness (sepsis or burns)
Most common symptom of Chronic Hep	Fatigue	Treat with phototherapy	Neonatal Jaundice (Decreased UGT1A1)
Acute Hep phase w/ hyperbilirubinemia	Icteric	Where do you find Kupffer hyperplasia?	Acute viral hepatitis
Clinical findings of Acute Pancreatitis	Hypocalcemia, hyperglycemia, jaundice	Multiple + Multifaceted (GB)	Cholesterol Gallstones
What causes pruritus?	Accumulation of bile salts	Leading cause of liver disease in West	Alcoholic liver disease
Complete lack of UGT1A1	Crigler Najjar I (AR)	Carcinoma of ductal cells	Adenocarcinoma
Gallstones radiopaque on X-ray	Black PIGMENT Stones	Wrinkled liver	Massive Hepatic Necrosis
Causes of Pancreatitis	BAD HITS – Biliary, Alcohol, Drugs (meds), Hypercalcemia, Idiopathic, Trauma, Scorpion	Band of ring-like tissue around 2nd portion of duodenum	Annular Pancreas
↑Unconjug. bilirubin + mild jaundice + adult	Gilbert Syndrome	Hepatitis from raw shellfish	HAV
Serum marker for Active HBV infection	HBsAg	"Classic" location for Obstructive Jaundice	Common Bile Duct

Type of bilirubin increased in Hemolysis	Unconjugated	Murphy's sign+	(Acute) Cholecystitis
Morphologies in Acute Pancreatitis	1. Proteolytic destruction 2. Necrosis of blood vessels w/ interstitial hemorrhage 3. Peripancreatic fat necrosis 4. Acute inflammation	Morphologies in Chronic Pancreatitis	1. Densely fibrotic w/ atrophic exocrine glands 2. Chronic inflammation around lobules 3. Ducts with protein plugs 4. Dilated ducts with inspissated material
Micronodular regenerating nodules	Alcoholic Cirrhosis	AR defect in transport protein	Dublin-Johnson Syndrome
Non-suppurative granulomatous destruction; intrahepatic	Primary Biliary Cirrhosis	4 yo w/ fatigue & vomiting then encephalopathy	Reye Syndrome
Example when AST:ALT ratio 2:1?	Alcoholic Hepatitis	Increased Conjug. Bilirubin + Increased ALP. You think?	Obstructive Jaundice (of the CBD)
Morphological features of Cirrhosis	(3) dense bands of fibrosis, regenerative nodules, entire architecture disruption	Time between disappearance of HBsAg & appearance of Anti-HBs antibodies	Window Period
Opisthorchis sinensis liver fluke. You think?	Cholangiocarcinoma	What serum level is more specific for Pancreatitis?	Lipase
Tumor marker for Hepatocellular Carcinoma	AFP >400	What type of viral hepatitis is oncogenic?	HBV
Appearance of renal failure in liver patient	Hepatorenal Syndrome	Serum levels of Alcoholic Hepatitis	Increased AST 2x greater than ALT
Portal HTN from Budd Chiari	Post-hepatic	'Beading' of the ducts on radiograph	Primary Sclerosing Cholangitis
'Sanded' nuclei	Carrier state (hepatitis)	Foamy macrophages filled w/ Cholesterol (GB)	Cholesterolosis
Serum levels in Wilson Disease	Decreased ceruloplasmin	Carcinoma at head of pancreas presents how?	Obstructive Jaundice
Classic triad of Hemochromatosis	Cirrhosis w/ hepatomegaly, skin pigmentation, & diabetes mellitus	Clinical findings of Alcoholic Hepatitis	Hyperbilirubinemia, elevated ALP/AST/ALT, neutrophilic leukocytosis
Portal HTN from Obstructive thrombus	Pre-hepatic	Most common diagnosed inherited hepatic disorder in infants & children	AAT deficiency
Councilman bodies	Acute viral hepatitis	Deficiency in hepcidin	Hemochromatosis
Manifestations of Alcoholic Liver Disease	(3) Hepatic steatosis, hepatitis, cirrhosis	GB Carcinoma with worse prognosis	Infiltrating (invasion through wall to liver)
Describe Pancreatic Pseudocyst.	Cystic space formed by Wall of Fibrosis & filled with Blood + Necrotic tissue; ***not lined by epithelial tissue***	Clinical manifestations of Wilson Disease	(4) Cirrhosis, extra-pyramidal symptoms, Kayser-Fleischer right, decreased ceruloplasmin
Cholestatic liver disease that is AMA+	Primary Biliary Cirrhosis	Serum marker for infectivity of HBV	HBeAg
Macrovesicular lipid globules	Fatty Liver Disease (Alcoholic & NAFLD)	Acute Pancreatitis pain results from what?	Necrosis + Inflammation
Gallstones radiolucent on X-ray	CHOLESTEROL Gallstones	Difference between NAFLD & NASH	Hepatocyte injury in NASH
High mortality in pregnant women	HEV	Migratory Thrombophlebitis	Carcinoma (Pancreatic)
Mallory bodies	Alcoholic hepatitis	Organs affected most by Hemochromatosis	Liver, Pancreas, Heart, Skin
Mutation in hemochromatosis	HFE gene	PAS+ eosinophilic cytoplasmic globules	AAT deficiency
Tx for SYMPTOMATIC Acute Cholecystitis	Cholecystectomy (25%)	Autoimmune destruction of bile duct cells	Primary Biliary Cirrhosis
Saponification	Ca2+ combines w/ FAs in areas of fat necrosis	Acute Pancreatitis classic presentation (female)	Cholelithiasis (Gallstones)
Transmission of HBV	IVD, sex, transfusion, birth	Common age with Hemochromatosis	Middle aged male
Pancreatic Carcinoma arises from...	Well-defined, non-invasive lesions of small ducts	Increased resistance to portal flow	Portal HTN
Common, HY cause of Pigment Gallstones	Hemolytic Anemias	Shrunken + firm liver	Alcoholic Cirrhosis
Rokitansky-Aschoff Sinuses	Chronic Cholecystitis	Type of bilirubin increased in obstructive disease	Conjugated
Associated with Liver Cell Adenoma	ORAL CONTRACEPTIVES & anabolic steroids	Example of acquired Hemochromatosis	Transfusions, ineffective erythropoiesis
Asymptomatic, but can still transmit disease	Carrier state (hepatitis)	Associated with Metabolic Syndrome	NAFLD
Causes of Chronic Pancreatitis (5)	1. Repeated bouts of Acute Pancreatitis **2. Long-standing obstruction of pancreatic duct** 3. Pancreas divisum 4. Autoimmune injury 5. Hereditary pancreatitis	Requirements for Cholesterol Gallstones	1. **Supersaturation** of bile w/ cholesterol 2. Kinetically favorable **nucleation** 3. Cholesterol **crystals** in GB long enough
2 Parasites for Pigment Gallstones	*Ascaris lumbricoids* & Liver Fluke *C. sinensis*	Serum levels of Primary Sclerosis Cholangitis	Persistent elevated ALP
Serum marker seen in Window Period (HBV)	IgM-anti-HBc & anti-HBe	Infiltration of what cells in Alcoholic Hepatitis?	Neutrophils
Cardiac sclerosis associated with what?	Passive Congestion (severe CHF)	When does Cirrhosis occur in AAT deficiency?	Adulthood
Morphology of Primary Sclerosis Cholangitis	Obliterative fibrosis + dilation of preserved area	Mutations in Pancreatic Carcinoma	KRAS, TP53, **CDKN2A**
Spindle shaped cells lining vascular bed	Angiosarcoma of the liver	Can be mistaken for metastatic tumors (multiple)	Cavernous hemangiomas
Dilated Cardiomyopathy	Hemochromatosis	What ducts don't fuse in Pancreas Divisum?	Duct of Wirsung & Duct of Santorini

RFs for Pancreatic Carcinoma	Smoking, High Fat Diets, Chronic Pancreatitis, DM	Perineural invasion seen in what 3 carcinomas?	Prostate, **Pancreas**, Adenoid Cystic
Viral hepatitis from blood transfusions	HBV	Serum marker denoting previous HBV exposure	IgG-anti-HBs
Common location for Pancreatic Carcinoma	Head of the pancreas	Most common malignancy of the liver	Metastatic cancer
Aflatoxins – You think?	Hepatocellular carcinoma	Polyvinyl chloride	Angiosarcoma of liver
Stain used to confirm Alcoholic Cirrhosis	Trichrome Stain	Major complications of Acute Pancreatitis	1. DIC, 2. Shock, 3. ARDS – *all due to Trypsin*
Increased risk for Hepatocellular Carcinoma	HBV, NAFLD, NASH, Cirrhosis	Nutmeg liver is usually from what?	Right heart failure
Kayser-Fleischer Ring	Wilson Disease	What type of viral hepatitis can be fulminant?	HBV
Obstruction of hepatic v. due to thrombosis	Budd Chiari	Dilated vascular channels in fibrous CT; benign	Cavernous Hemangioma
Portal HTN from R heart failure	Post-hepatic	dsDNA hepatitis virus	HBV
What shows on X-ray w/ Peritonitis?	Free air under the diaphragm	Porcelain Gallbladder	Chronic Cholecystitis
If you see DUODENUM, where is lesion? (P)	Head of the pancreas	Extra-pyramidal symptoms	Wilson Disease
Serum levels of HCV	Persistent elevated AST/ALT	Serum Amylase levels in Chronic Pancreatitis	Mild elevation
Accumulation of copper	Wilson Disease	3 systems activated by Trypsin in Pancreatitis	Kinin (vasodilation, clotting, complement (shock)
Benign + multicystic + 70 + tail of pancreas	Serous cystic neoplasm	ATP7B mutation	Wilson Disease
Well-defined, non-invasive lesions of small ducts	Pancreatic Intraepithelial Neoplasia	Accumulation of iron	Hemochromatosis
"Silent hepatomegaly"	Hepatocellular Carcinoma	Inflammation of GB due to ischemia	Acalculus Cholecystitis
2 Main morphological features of cirrhosis	Diffuse fibrous tissue + Regenerative nodules	Precursor to invasive carcinoma + pancreas tail	Mucinous cystic neoplasm
Describe Mallory bodies.	Intracellular; intermediate filaments (keratin)	Activation of β-catenin	Hepatocellular carcinoma
Portal HTN from Cirrhosis	Hepatic	Distended, non-palpable gallbladder. You think?	Carcinoma of the pancreas
Abnormal chromosome in AAT deficiency	PiZZ (Chr14)	"Classic" presentation of gallstones	Cholecystitis
Most common benign liver tumor	Cavernous hemangioma	Decreased activity of UGT1A1	Crigler Najjar II (AD)
Incidental finding with abdominal imaging	Liver Cell Adenoma	Associated with Budd Chiari	Polycythemia vera, ORAL CONTRACEPTIVES
Serum levels in Primary Biliary Cirrhosis	Elevated ALT & GGT	Microvesicular steatosis example	Reye Syndrome
GB Carcinoma usually presents after what?	Invasion to Liver at diagnosis	Serum levels in Massive Hepatic Necrosis	Marked elevated ALT & AST
Difference between Primary Biliary Cirrhosis & Primary Sclerosing Cholangitis (histology)	PBC affects only intrahepatic ducts PSC affects intra & extrahepatic ducts	Primary Biliary Cirrhosis can present similar to what in later stages?	Obstructive jaundice
Classic Triad for Chronic Pancreatitis	Pancreatic Calcifications, Steatorrhea, DM	Infiltration of what cells in Viral Hepatitis?	Lymphocytes
'Fibrosing stricture' of hepatic ducts & CBD	Biliary atresia	Most common virus seen in HCC	HBV
Pain radiating to tip of R scapula	Acute Cholecystitis	Common cause of passive congestion	Right sided heart failure
Thorotrast	Angiosarcoma of liver	Increased incidence in CHINA	Cholangiocarcinoma of the liver
Vascular tumors we discussed	Cavernous hemangioma & angiosarcoma	Tumor that can rupture & cause massive bleed	Liver Cell Adenoma
Most hep carriers are infected with? When?	HBV early in life	Viral hepatitis that can progress to chronic	HBV, HCV, HDV
Associated with Ulcerative Colitis	Primary Sclerosing Cholangitis	Pancreas Divisum predisposes to what?	Chronic Pancreatitis
Most common primary sources of mets	Colon, breast, lung, pancreas	Centrilobular fibrosis only around central vein	Cardiac sclerosis
Constituents of Nutmeg Liver	Congestion of centrilobular sinusoids + ischemia		