Disorders of the Liver and Pancreas

Liver Lobule
- Hexagonal plates
- Sinusoids
- Triads
- Bile duct branch
- Arteriole
- Venuole
- Blood flows from periphery to Central vein
- Space of Dissé

Lobular Microanatomy
- Hepatocytes
- Canaliculi
- Triad
- Arteriole
- Venuole
- Bile Duct Branch

Bile Formation
- Hemoglobin breakdown
- Conversion in liver to water soluble form
  - Bilirubin
  - Serum levels help diagnose liver disease
- Excretion in bile
- Some is reabsorbed
Zonal Pattern of Injury
- Peripheral
- Middle
- Central
- Triadal
  - Limiting plate
  - Piecemeal necrosis

Liver Injury, The Basics
- Lots of stuff injures the liver.
- It's the great detoxifier
- Chronic injury
  - Fibrosis
  - Regeneration
    - Providing the underlying framework remains

Cholestasis
- Slowed bile excretion
- Intracellular
  - Drugs
  - Viral infection
- By means of ducts
  - Drugs
  - Obstruction

Cirrhosis
- Many things may lead to cirrhosis
- Common features
  - Irreversible
  - Chronic inflammation
  - Scarring (fibrosis)
  - Parenchymal loss
  - Regenerative nodules
  - Altered vascularity
- Symptoms
  - Ascites
  - Gynecomastia
  - Esophageal varices
  - Splenomegaly
  - Caput medusae

Cirrhosis
- Irreversible
- Scarring
- Botched regeneration
- Vascular rearrangements
  - Caput medusae ➔ Ascites ➔ Low albumin ➔ Venous portal hypertension
**Common Etiologies**
- Inherited
- Pigmentary
- Post-necrotic
- Chronic viral
- Nutritional

**Cirrhosis**
- Stellate cell becomes real important
- Normally stores vitamin A
- Lymphocytes turn him into a collagen making machine

**Sequence of Events**
- Liver cell injury
- Cycle of chronic inflammation
  - Destruction of underlying architecture
  - Fibrosis
  - Attempts to regenerate
  - Vascular reorganization leading to shunting
  - Repeat cycle
- Progressive
- Irreversible

**Parasitic**
- There are several
- Schistosomiasis
- Clonorchis sinensis
Inflammation of Liver
- Very common, lots of things do it.
- Toxins and drugs
- Bacteria
- Cholangitis
- Abscesses
- Viruses
  - EBV
  - CMV
  - Hepatic specific
- Parasites
- Autoimmune

Viral Hepatitis
- Generally taken to mean hepatic specific viruses.
- Histologic features common to most.
- Acute
  - Necrosis of random liver cells
  - Councilman bodies = bright pink dead cells
  - Diffuse liver cell swelling
  - Bile-stasis
  - Portal (triadal) inflammation
- Chronic pattern = persistence or relapse for 6 months
  - Chronic and acute inflammation
  - Premembranous necrosis
  - Bridging necrosis
  - Cirrhosis

Acute Viral Hepatitis

Chronic or Persistent Hepatitis

Hepatitis A
- "Infectious hepatitis"
- Food handlers
- Virus in stool
- Seafood
- Self limiting
- No chronic state
- No cirrhosis
- No carrier state
- History and serology
  - IgM
  - IgG
  - Maybe virus
**Hepatitis B**
- "Serum hepatitis"
- Sexually transmitted
- Blood borne
- Longer incubation
- Common in Asia
- Most get over it fine
- Immunologic damage
- Less common
  - Chronic progressive
  - Fulminant failure and death
  - Cirrhosis
  - Chronic carrier state

**Hepatitis B Outcomes**

**Hepatitis C**
- Very high rate of persistence
- Long incubation period
- Cirrhosis

**Delta Agent**
- Incomplete virus
- Needs hepatitis B to replicate
- The two together cause terrible disease
- Fulminant loss of liver
- Can become infected later if you are a carrier of hepatitis B
Hepatitis Outcomes

- Asymptomatic infection
- Acute hepatitis like a bad case of the flu
- Overt Jaundice
- Carrier state
- Fulminant liver death
- Chronicity, +/- cirrhosis

Autoimmune Hepatitis

- Women
- Chronic hepatitis
- No viral markers
- May lead to cirrhosis

Abscesses

- Bacterial
- Parasitic
- Blood borne
- Ascends ducts

Drug and Toxin

- Too many to list
- Direct hepatocyte toxicity
- Biliary paralysis
- Conversion to a truly toxic agent

Reye’s Syndrome

- Young kids
- Follows flu
- Got aspirin
- Liver and brain
- Fulminant liver failure

Alcoholic Liver Disease

- Acute and chronic
- Acute hepatitis
- Fatty liver
- Cirrhosis
Acute Alcoholic Hepatitis
- Liver cell necrosis
- Balloon degeneration
- Neutrophils
- Mallory bodies

Alcoholic Cirrhosis
- About 15-20% of alcoholics
- Micronodular pattern, so called "hobnails"
- Increased portal pressures

Other Types of Cirrhosis
- Pigmentary
  - Iron
  - Oxidative injury
  - Scarring
  - Congenital problem with excessive absorption
- Wilson’s Disease
  - Copper metabolism
  - Absence of transport protein
  - Builds up in various organs
  - Cirrhosis
  - Brain degeneration
  - Corneal ring
Alpha-1 Anti-trypsin Deficiency

- Neutralizes proteases and elastases
- Made in the liver
- Can't finish the process
- Constipated cells fill up with partially completed anti-trypsin
- Causes cell death and scarring
- Emphysema

Intrahepatic Biliary Disease

- Drug related
  - Bile stasis
  - Inflammation
  - Scarring
- Primary conditions of the biliary tree
  - Autoimmune, often leading to cirrhosis
  - Sometimes associated with other conditions

Primary Biliary Cirrhosis

- Women
- Granulomatous destruction of medium sized bile ducts
- High serum cholesterol
- Xanthomas
- Cirrhosis
- Antimitochondrial antibodies
- Sicca syndrome
  - Dry eyes & mouth
  - Scleroderma
  - Rheumatoid arthritis
  - All autoimmune in nature

Primary Sclerosing Cholangitis

- Concentric fibrosis of smaller bile ducts
- Onionskin
- Seen with ulcerative colitis
- No antibodies
- No other problems, like Sicca syndrome
Vascular Related
- Congestion
- Infarcts
- Cirrhosis altered vascularity of liver

Hepatic Infarct

Pregnancy Related
- HELLP syndrome
  - Hepatic enzymes
  - Low platelets
- Eclampsia
  - High blood pressure
  - Fatty liver
  - May be life threatening

Eclampsia
Tumors of the Liver

- Hyperplasia vs. true tumor
  - Estrogens
- Benign vs. malignant
- Primary vs. metastatic
  - Bowel
  - Lung
  - Kidney
  - Breast

Metastatic Cancer

Hepatocellular Carcinoma

- Malignant hepatocytes
- Associated with
  - Hepatitis B
  - Cirrhosis
- May be multiple foci

Cholangiocarcinoma

- Comes from bile duct epithelium
- Adenocarcinoma
- Much desmoplasia
- Not associated with the stuff seen in hepatocellular cancer

Gallstones

- Ethnicity
- Age
- Sex
- Fatty foods
- Cholesterol and mixed stones
- Pigmentary stones
- Obstruction
  - Painful
  - Infection
Cancer of the Gallbladder
- Chronic irritation of gallstone
- Chronic cholecystitis
- Presumed oxidative damage
- Cancer

Pancreas

Acute Pancreatitis
- Autodigestion
- Acute inflammation
- Enzyme activation
- Fat necrosis with soaponification
- Hemorrhage
- Causes
- Obstruction
- Stone
- Tumor
- Alcohol
- Complications
- Pseudocyst
- Shock
Soaponification

Pancreatic Pseudocyst

Chronic Panreatitis
- Extensive fibrosis
- Calcifications
- Cystic fibrosis

Cystic Fibrosis
- Inherited problem of chloride pump
- Thick mucus
- Clogs
  - Bowel
  - Pancreas
    - Fibrosis
    - Malabsorption
  - Bronchi

Pancreatic Cancer
- Often advanced at the time of discovery
- Adenocarcinoma
- From ductal epithelium
- Spreads to liver
- Not hormonally active
- Painless jaundice

Islet Cell Tumors
- Insulin secreting
  - Hypoglycemic episodes
- Gastrinoma
- Zollinger-Ellison
- Glucagonomas
- VIPomas
Insulin Secretion and Peripheral Utilization

Type I Diabetes
- Lack of insulin
- Trigger causes autoimmune destruction of beta cells.
- Ketosis prone

Type II Diabetes
- Insulin release problem
- Peripheral resistance
- Non-ketosis prone

Glycosylated Proteins
- Small vessel vascular disease
- This is what diabetes becomes
Diabetic Vascular Changes