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
- Aspects
  - 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
  - Piecemeal necrosis
  - Bridging necrosis
  - Cirrhosis

Acute Viral Hepatitis

Chronic or Persistent Hepatitis

- '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 A

- Incubation period: 2-6 weeks
- Acute disease:
  - Jaundice
  - Symptoms
- Convalescence and recovery:
  - 6-12 weeks
  - IgM and IgG
  - No carrier state
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

Chronic Hepatitis B
- Infrequently a person develops chronic infection with B.
- Leads to cirrhosis

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

Alcoholic and Non-Alcoholic Fatty Liver Disease

Non Alcoholic
- DM
- Obesity
- Metabolic syndrome
- Even kids

Other Types of Cirrhosis

- 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
Gallstones

- Chronic irritation of gallstone
- Chronic cholecystitis
- Presumed oxidative damage
- Cancer

Cancer of Gallbladder

Pancreas

- Autodigestion
- Acute inflammation
- Enzyme activation
- Fat necrosis with soaponification
- Hemorrhage

Causes

- Obstruction
- Stone
- Tumor
- Alcohol

Complications

- Pseudocyst
- Shock
Acute Pancreatitis

Pancreatic Pseudocyst

Cystic Fibrosis

Pancreatic Cancer

Soaponification

Chronic Pancreatitis

- Extensive fibrosis
- Calcifications
- Cystic fibrosis

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

- 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 I Diabetes

- Trigger leads to autoimmune destruction of islets

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

- Microangiopathy
- Carotid occlusive disease
- Retinopathy
- Nephropathy
- Gangrene
- Peripheral vascular atherosclerosis
- Polyneuropathy
- Autonomic neuropathy

Diabetic vascular changes can lead to complications such as retinopathy, nephropathy, and peripheral vascular disease.