Cirrhosis & Portal Hypertension
CIRRHOSIS

- Term was 1st coined by Laennec in 1826
- Many definitions but common theme is injury, repair, regeneration and scarring
- NOT a localized process; involves entire liver
- Primary histologic features:
  1. Marked fibrosis
  2. Destruction of vascular & biliary elements
  3. Regeneration
  4. Nodule formation
Cirrhosis: Pathophysiology

• Primary event is injury to hepatocellular elements
• Initiates inflammatory response with cytokine release->toxic substances
• Destruction of hepatocytes, bile duct cells, vascular endothelial cells
• Repair thru cellular proliferation and regeneration
• Formation of fibrous scar
Cirrhosis: Pathophysiology

- Primary cell responsible for fibrosis is stellate cell
- Become activated in response to injury and lead to ↑ed expression of fibril-forming collagen
- Above process is influenced by Kupffer cells which activate stellate cells by eliciting production of cytokines
- Sinusoidal fenestrations are obliterated because of ↑ed collagen and EC matrix synthesis
Cirrhosis: Pathophysiology

- Prevents normal flow of nutrients to hepatocytes and increases vascular resistance
- Initially, fibrosis may be reversible if inciting events are removed
- With sustained injury, process of fibrosis becomes irreversible and leads to cirrhosis
Causes of Cirrhosis

- Alcohol
- Viral hepatitis
- Biliary obstruction
- Veno-occlusive disease
- Hemochromatosis
- Wilson’s disease
- Autoimmune
- Drugs and toxins
- Metabolic diseases
- Idiopathic
Classification of Cirrhosis

• WHO divided cirrhosis into 3 categories based on morphological characteristics of the hepatic nodules
  1. Micronodular
  2. Macronodular
  3. Mixed
Micronodular Cirrhosis

- Nodules are <3 mm in diameter
- Relatively uniform in size
- Distributed throughout the liver
- Rarely contain portal tracts or efferent veins
- Liver is of uniform size or mildly enlarged
- Reflect relatively early disease
Macronodular & Mixed Cirrhosis

- Nodules are >3 mm in diameter and vary considerably in size
- Usually contain portal tracts and efferent veins
- Liver is usually normal or reduced in size
- Mixed pattern if both type of nodules are present in equal proportions
Cirrhosis - Alcohol

• Also known as Laennec’s cirrhosis
• >50% of pts. with alcoholic cirrhosis die within 4 yrs of diagnosis
• Develops in only 10% to 30% of heavy drinkers
• Morphologically, micronodular pattern
• Multifactorial - genetic, nutritional, drug use and viral
Cirrhosis - Alcohol

- Fatty liver, alcoholic hepatitis
- Histology - megamitochondria, Mallory bodies, inflammation, necrosis, fibrosis
- Key mediator is acetaldehyde (ADH), the product of alcohol metabolism by alcohol dehydrogenase
- ADH directly activates stellate cells, inhibits DNA repair and damage microtubules
NAFLD/NASH

- Nonalcoholic Fatty Liver Disease and Steatohepatitis
- Becoming more common
- Infiltration of the liver with fat ± inflammation
- Pathologically similar to alcoholic liver but in absence of alcohol
- Associated with obesity, hyperlipidemia, NIDDM,
Viral Hepatitis

- Most common cause of cirrhosis worldwide (>50% of cases)
- Incidence of cirrhosis in Hepatitis B pts. is 1% and 10% in Hepatitis C pts.
- Incidence increases to 70-80% in HBV +ve pts. who are superinfected with HDV
DIAGNOSIS

• Can be asymptomatic for decades
• History
• Physical findings: Hepatomegaly, jaundice, ascites, spider angioma, splenomegaly, palmar erythema, fetor hepaticus, purpura etc.
• Elevated LFTs, thrombocytopenia,
DIAGNOSIS

• Definitive diagnosis is by biopsy or gross inspection of liver
• Noninvasive methods include US, CT scan, MRI
• Indirect evidence - esophageal varices seen during endoscop}


Manifestations of Cirrhosis

- Hepatorenal syndrome
- Hepatic encephalopathy
- Portal hypertension
- Water retention
- Hematologic
- Hepatocellular carcinoma
Portal Hypertension (PH)

- Portal vein pressure above the normal range of 5 to 8 mm Hg
- Portal vein - Hepatic vein pressure gradient greater than 5 mm Hg (>12 clinically significant)
- Represents an increase of the hydrostatic pressure within the portal vein or its tributaries
Pathophysiology of PH

- Cirrhosis results in scarring (perisinusoidal deposition of collagen)
- Scarring narrows and compresses hepatic sinusoids (fibrosis)
- Progressive increase in resistance to portal venous blood flow results in PH
- Portal vein thrombosis, or hepatic venous obstruction also cause PH by increasing the resistance to portal blood flow
Pathophysiology of PH

• As pressure increases, blood flow decreases and the pressure in the portal system is transmitted to its branches
• Results in dilation of venous tributaries
• Increased blood flow through collaterals and subsequently increased venous return cause an increase in cardiac output and total blood volume and a decrease in systemic vascular resistance
• With progression of disease, blood pressure usually falls
Portal Vein Collaterals

• Coronary vein and short gastric veins -> veins of the lesser curve of the stomach and the esophagus, leading to the formation of varices
• Inferior mesenteric vein -> rectal branches which, when distended, form hemorrhoids
• Umbilical vein -> epigastric venous system around the umbilicus (caput medusae)
• Retroperitoneal collaterals -> gastrointestinal veins through the bare areas of the liver
Etiology of PH

- Causes of PH can be divided into
  1. Pre-hepatic
  2. Intra-hepatic
  3. Post-hepatic
Pre-hepatic PH

- Caused by obstruction to blood flow at the level of portal vein
- Examples: congenital atresia, extrinsic compression, schistosomiasis, portal, superior mesenteric, or splenic vein thrombosis
Post-hepatic

- Caused by obstruction to blood flow at the level of hepatic vein
- Examples: Budd-Chiari syndrome, chronic heart failure, constrictive pericarditis, vena cava webs
Budd-Chiari Syndrome

• Caused by hepatic venous obstruction
• At the level of the inferior vena cava, the hepatic veins, or the central veins within the liver itself
• result of congenital webs (in Africa and Asia), acute or chronic thrombosis (in the West), and malignancy
Budd-Chiari Syndrome

- Acute symptoms include hepatomegaly, RUQ abdominal pain, nausea, vomiting, ascites
- Chronic form present with the sequelae of cirrhosis and portal hypertension, including variceal bleeding, ascites, spontaneous bacterial peritonitis, fatigue, and encephalopathy
- Diagnosis is most often made by US evaluation of the liver and its vasculature
- Cross-sectional imaging using contrast-enhanced CT or MRI
Budd-Chiari Syndrome

- Gold standard for the diagnosis has been angiography
- Management has traditionally been surgical intervention (surgical decompression with a side-to-side portosystemic shunt)
- Minimally invasive treatment using TIPS may be first-line therapy now
- Response rates to medical therapy are poor
Portal Vein Thrombosis

• Most common cause in children (fewer than 10% of adult pts.)
• Normal liver function and not as susceptible to the development of complications, such as encephalopathy
• Diagnosis by sonography, CT and MRI
• Often, the initial manifestation of portal vein thrombosis is variceal bleeding in a noncirrhotic patient with normal liver function
Portal Vein Thrombosis - Causes

- Umbilical vein infection (the most common cause in children)
- Coagulopathies (protein C and antithrombin III deficiency),
- Hepatic malignancy, myeloproliferative disorders
- Inflammatory bowel disease
- Pancreatitis
- Trauma
- Most cases in adults are idiopathic
Portal Vein Thrombosis

- Therapeutic options are esophageal variceal ligation and sclerotherapy
- Distal splenorenal shunt
- Rex shunt in patients whose intrahepatic portal vein is patent (most commonly children)
Splenic Vein Thrombosis

- Most often caused by disorders of the pancreas (acute and chronic pancreatitis, trauma, pancreatic malignancy, and pseudocysts)
- Related to the location of the splenic vein
- Gastric varices are present in 80% of patients
- Occurs in the setting of normal liver function
- Readily cured with splenectomy (variceal hemorrhage), although observation for asymptomatic patients is acceptable.
Complications of PH

- GI bleeding due to gastric and esophageal varices
- Ascites
- Hepatic encephalopathy
Varices

- Most life threatening complication is bleeding from esophageal varices
- Distal 5 cm of esophagus
- Usually the portal vein-hepatic vein pressure gradient >12 mm Hg
- Bleeding occurs in 25-35% of pts. With varices and risk is highest in 1st yr.
Prevention of Varices

- Primary prophylaxis: prevent 1st episode of bleeding
- Secondary prophylaxis: prevent recurrent episodes of bleeding
- Include control of underlying cause of cirrhosis and pharmacological, surgical interventions to lower portal pressure
Prevention of Varices

- Beta blockade: Beta blockade (Nadolol, Propranolol)
- Nitrates: Organic nitrates
- Surgery: No longer performed*
- Endoscopy: Sclerotherapy (no longer used*) and variceal ligation

* Refers to primary prophylaxis
Treatment of Varices

• Initial Management:
  1. Airway control
  2. Hemodynamic monitoring
  3. Placement of large bore IV lines
  4. Full lab investigation (Hct, Coags, LFTs)
  5. Administration of blood products
  6. ICU monitoring
Pharmacologic Treatment of Varices

• Decreases the rate of bleeding
• Enhances the endoscopic ability to visualize the site of bleeding
• Vasopressin - potent splanchnic vasoconstrictor; decreases portal venous blood flow and pressure
• Somatostatin: decrease splanchnic blood flow indirectly; fewer side effects
• Octreotide: Initial drug of choice for acute variceal bleeding
Endoscopic Therapy for Varices

- **Endoscopic Sclerotherapy**: complications occur in 10-30% and include fever, retrosternal chest pain, dysphagia, perforation
- **Endoscopic variceal ligation**: becoming the initial intervention of choice; success rates range from 80-100%
Balloon Tamponade

• Sengstaken-Blakemore tube
• Minnesota tube
• Alternative therapy for pts. who fail pharmacologic or endoscopic therapy
• Complications: aspiration, perforation, necrosis
• Limited to 24 hrs; works in 70-80%
TIPS

• Transjugular inrahepatic portasystemic shunt
• 1st line treatment for bleeding esophageal varices when earlier-mentioned methods fail
• Performed in IR
• Success rates 90-100%
• Significant complication is hepatic encephalopathy
Surgical Intervention

• Liver transplantation: only definitive procedure for PH caused by cirrhosis
• Shunts
  – Totally diverting (end-side portacaval)
  – Partially diverting (side-side portacaval)
  – Selective (distal splenorenal shunt)
• Devascularization