Complications of Cirrhosis

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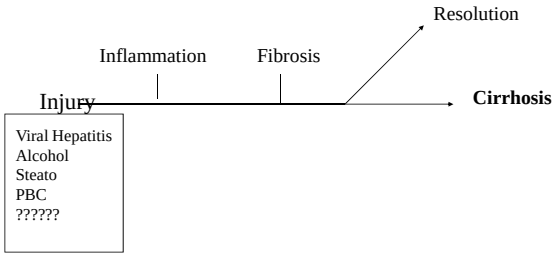
Pathway to Cirrhosis



Outline/Objectives

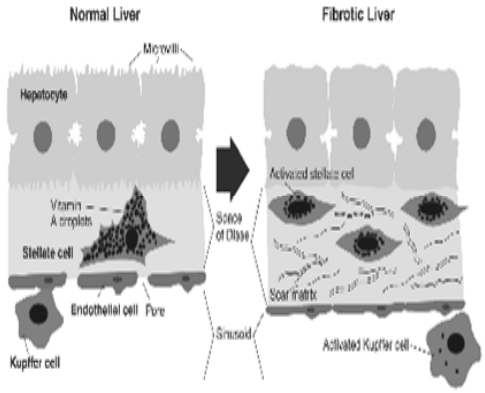
- **Cirrhosis**
  - **Etiology**
  - **Progression**
- **Complications of Cirrhosis**
  - **Portal Hypertension**
    - » **Varices**
    - » **Ascites**
    - » **Hepatohydrothorax**
    - » **Spontaneous Bacterial Peritonitis**
    - » **Hepatorenal Syndrome**
  - **Hepatic Encephalopathy**
- **Therapeutic Options**
  - **Endoscopic Therapy**
  - **Surgical Shunts**
  - **Liver Transplantation**

Cirrhosis-pathogenesis

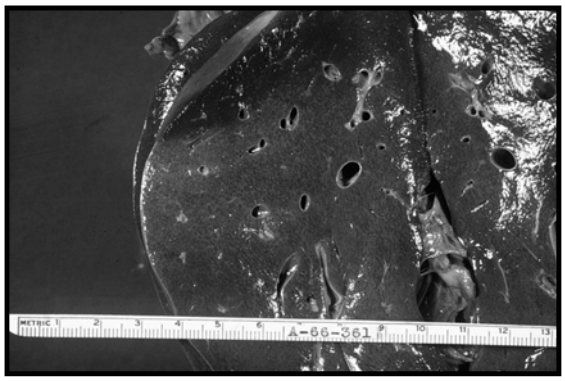
- Stellate cell or Ito cell: normally, sit in Space of Disse and store Vit. A; during cirrhosis, transform into myofibroblasts that make and deposit collagen
- Probably stimulated by inflammation, cytokines, and toxins
- Collagen types I and III are deposited in all portions of lobule
- Ultimately, architecture and vasculature are disrupted and diffusion of solutes is impaired

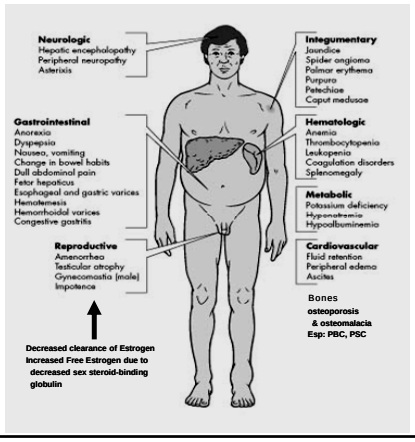
What is Cirrhosis?

- **End stage of chronic liver disease**
- **Regenerative Nodules surrounded by fibrous septa**
- **Disruption of the architecture**
- **Common Etiologies**
  - **Alcohol**
  - **Viral hepatitis**
  - **Non-alcoholic Fatty Liver Disease**
  - **Genetic/Metabolic**

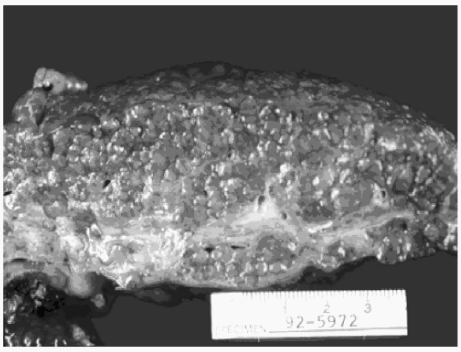


NORMAL LIVER





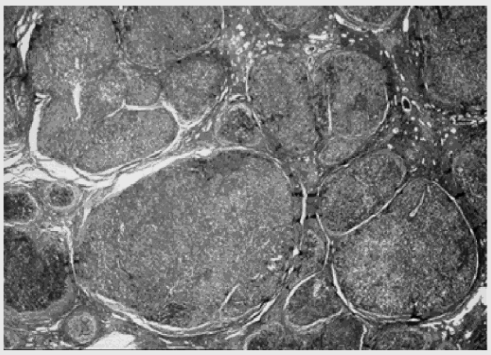
CIRRHOTIC LIVER



Complications

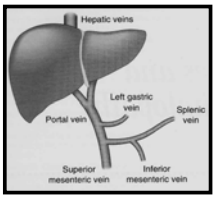
- **Portal Hypertension**
  - **Varices**
  - **Ascites**
  - **Hepato-renal Syndrome**
- **Liver Failure**
  - **Hepatic Encephalopathy**
  - **Protein Loss**
    - » **Coagulapathy**
    - » **Decrease muscle mass**
    - » **Infection**

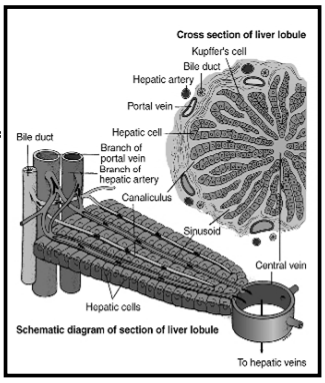
CIRRHOTIC LIVER



LIVER: Blood Flow

- **High Flow**
  - **Mesenteric vessels**
- **Low pressure**
  - **Vast network of sinusoids**





Portal Hypertension

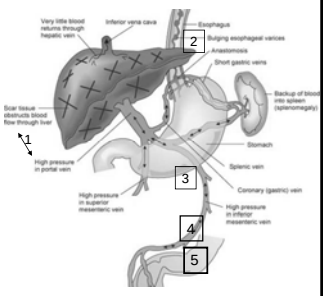
- Pre hepatic
  - Portal Vein or Splenic Vein Thrombosis
- Intra hepatic
  - Pre-sinusoidal
    - » Schistosomiasis
  - Sinusoidal
    - » Cirrhosis
  - Post Sinusoidal
    - » Veno-occlusive disease
- Post hepatic
  - Obstruction of vena cava of hepatic vein (Budd-Chiari)

Portal Hypertension
Pathophysiology

- Increased Resistance to inflow/outflow
  - Fixed scarring of the liver
  - ? reversible elements: sinusoidal blood vessels
- Increased Flow to portal system
  - Increased splanchnic flow (vasodilatation/NO)
  - Increased cardiac output
    - » Low SVR
  - Increased blood volume
- Decreased Albumin: hepatic synthetic dysfunction
  - » Decreased oncotic pressure, fluid leaks out of vascular space

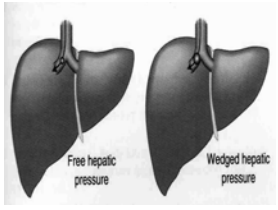
Cirrhosis: Portal Hypertension
Effects on blood flow

1. Fibrosis restricts blood flow; increased portal vein pressure
2. Collaterals acquire increased pressure, affecting spleen, esophagus, stomach (varices), gastropathy
3. Ascites due to fluid shift into peritoneum
4. Shunting of blood from liver decreases of metabolism of "toxins"
5. Portal bacteremia not cleared induces peritonitis



PHYSICAL EXAM FINDINGS

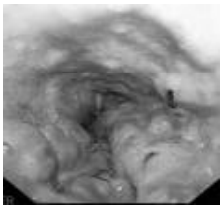
What Pressure Defines Portal HTN?
Portal Vein-Hepatic Vein Pressure Gradient



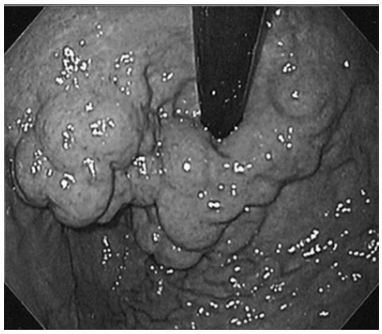
- Catheter (with deflated balloon) in Hepatic Vein measures "free HV pressure"
- Inflate Balloon in Hepatic Vein measures Portal Vein Pressure
- PV-HV pressure > 10 mmHG = "significant" portal HTN Normal gradient is less than 7

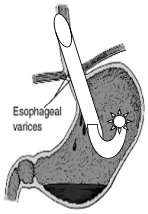
Esophageal Varices

- Risk of bleeding proportional to size and degree of portal hypertension
- Even with optimal therapy, death from initial bleed may be greater than 20%
- Non-selective Beta blockers (Propranalol, Nadolol)
- Use of Isosorbide Mononitrate controversial



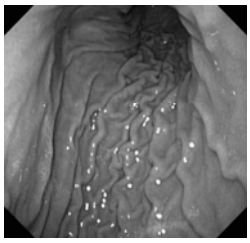
Gastric Varices



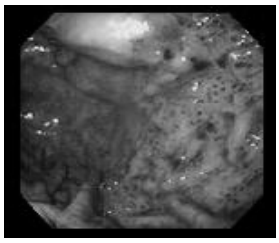


Varices/ Banding

Portal Gastropathy



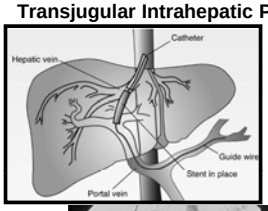
Normal

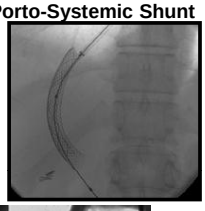


Gastropathy

TIPS

Transjugular Intrahepatic Porto-Systemic Shunt





Esophageal Varices

- **Bleeding Control: Acute**
  - **Stabilize hemodynamics**
  - **Decrease portal Pressure**
    - **» Octreotide, Somatostatin**
  - **Endoscopy**
    - **» Sclerotherapy: past**
    - **» Banding: present**
  - **TIPS**
  - **Surgical Shunt**
  - **Chronic therapy**
    - **» Beta Blockers/Nitrates**
    - **» Banding ablation**
  - **Transplantation**

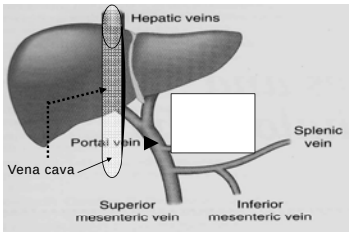
TIPS

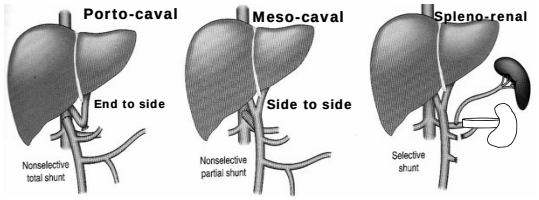
- **Functional side to side shunt**
- **Produces connection from Portal Vein to Hepatic Vein**
  - **Increase Hepatic vein pressure, RV volume**
  - **Decrease Portal pressure, hepatic perfusion**
- **TIPS improves sodium and water handling**
  - **Hepatic hydrothorax**
  - **Refractory ascites**
- **Caution:**
  - **CHF, Bili > 4, Inc Creat, PSE, Older pt**

Surgical shunts

- **Limited indications: for endoscopic, medical failure, not OLT candidates**
  - **Cirrhosis: Child's A**
  - **Budd Chiari syndrome**
  - **Non-cirrhotic portal hypertension**
- **Selective vs non-selective**
  - **Goal is to preserve portal perfusion**

Surgical Shunts





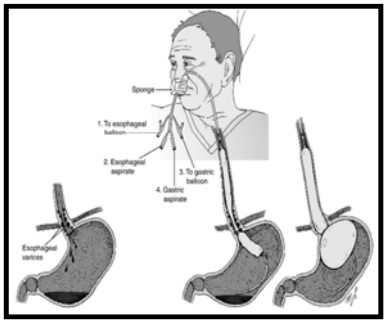
Ascites

Clinical Diagnosis

- **History: increasing abdominal girth**
- **Physical Examination:**
  - **shifting dullness, fluid wave**
  - **very poor in detecting modest amounts of ascites**
- **Radiology: ultrasound, CT scan more sensitive**

Blakemore Tube

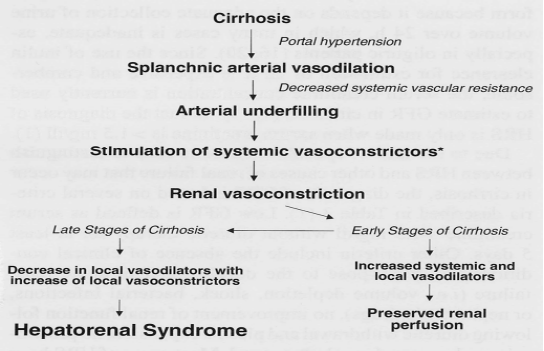
- **Historically, an important way to stabilize a patient with variceal bleeding prior to:**
  - **Surgery**
  - **Transplant**
- **Now, only used in emergencies**
  - **Prior to TIPS**
  - **To Transport a patient from hospital to hospital**



Ascites

- **Differential dx:**
  - **Portal hypertension**
  - **Hepatic (or portal vein) occlusion**
  - **Heart failure**
  - **Peritoneal inflammation**
    - **» TB peritonitis**
    - **» Carcinomatosis (sometimes chylous ascites)**
  - **Ovarian Cancer**
  - **Nephrogenic ascites (nephrotic syndrome)**
  - **Pancreatic ascites**
  - **"Other" (Schistosomiasis, non-cirrhotic portal HTN, polycystic liver disease,**

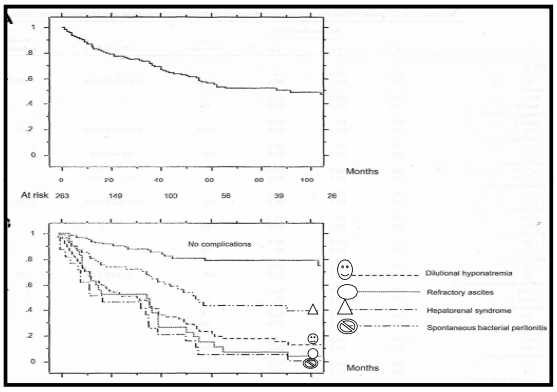
Portal HTN and Ascites



Ascites: Treatment

- Bedrest
  - Na^+ restriction; 1.5-2 gms/day
  - fluid restriction: 1.5 liters if Na+ < 120
- Diuretics (maximum doses):
  - Spironolactone 400mg , Furosemide (200 mg)
  - Amiloride, HCTZ, Metolazone, Zaroxyln
- Large-volume paracentesis
- TIPS
- Surgery: Liver transplantation
  - Leveen or Denver Shunt (historical value, ? If valuable now, radiologists now place these

Probability of Survival After Ascites Diagnosed



Large-Volume Paracentesis

- Advantages: Fast, ↓ hospital time, less expensive
  - Patients should have normal creatinine
  - Better if volume overloaded (peripheral edema)
- Disadvantages:
  - Precipitate renal insufficiency
  - Removes proteins (e.g., opsonins)
- Use of volume expansion
  - Albumin: 6 gms/liter of ascites removed
  - May not be required for < 2-3 liter paracentesis

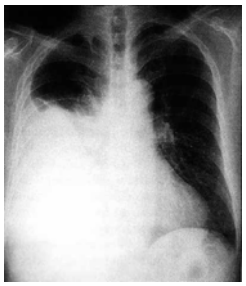
Characteristics of Ascites due to Portal Hypertension

- Transudate; i.e., ascites protein < 3 g/dl; most < 1 g/dl
- WBC < 50 cc/mm^3; mostly mononuclear
- Normal ascitic fluid amylase
- Serum - ascites Albumin gradient (SAG) > 1.1 g/dl due to portal HTN

LeVeen/Denver peritoneo-venous shunt

- Coagulopathy:
  - DIC almost universal
  - severity can be limited by replacing ascites with saline
- Infection
  - generally requires removal of shunt
- Occlusion
  - Venous side of shunt
- Heart failure
  - Volume overload

Hepatic Hydrothorax



- Ascites leaks through rents in the diaphragm
- Diagnosis: Fluid should have characteristics similar to ascites
- Treatment: AVOID CHEST TUBES. Surgical repair not usually effective
- TIPS is treatment of choice for diuretic-refractory cases
- Liver transplantation

Spontaneous Bacterial Peritonitis:Treatment

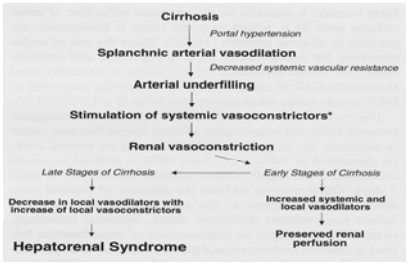
- Most common organisms are E. coli, Klebsiella, Pneumococcus, Enterococcus
- Broad Spectrum antibiotics and then narrow antibiotic spectrum if culture results are known
- ? re-tap after 48 hours to confirm response to therapy

SBP

Spontaneous Bacterial Peritonitis

- Infection independent of another intra-abdominal source
- Monomicrobial
- Enteric flora enters portal circulation, not cleared
- Ascites WBC > 500 or 250 with greater than 50% polys
- Culture negative neutrocytic ascites
- Culture positive neutrocytic ascites
- Culture positive non-neutrocytic ascites
  - If gm negative : treat
  - If gm positive: likely contaminant

Portal HTN and HRS



- Early-Decrease in SVR is compensated by increased HR, CO Stimulation of RA and SNS, ADH
- Late-Splanchnic circulation is resistant to AngII, Vasopression,
- pressure is maintained by local vasoconstriction

Spontaneous Bacterial Peritonitis: Prevention

- Risks:
  - GI bleeding/hypotension
  - Advanced liver disease
  - Previous history !
- Early treatment of other infections
- Prophylactic antibiotics to GI bleeders
- Volume expand with Albumin
  - Effective to reduce hepato-renal syndrome
- Oral Quinolones, Bactrim can prevent recurrence when given chronically
- Liver transplantation

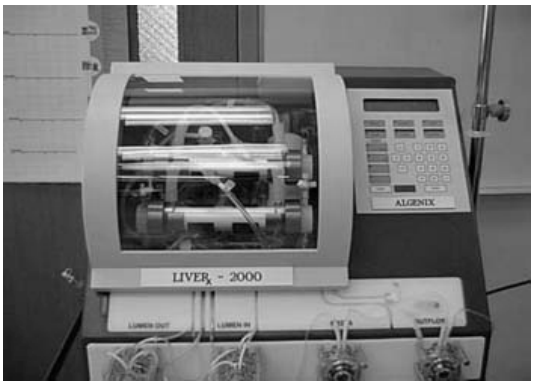
Hepato-Renal Syndrome

- Etiology: Unclear, but likely an exaggeration of mechanisms involved in ascites formation
- Precipitants:
  - Gi Bleed
  - Nephtotoxins (NSAID's, Aminoglycosides, sepsis)
  - Iatrogenic (diuresis, paracentesis)
- Diagnosis:
  - Euvolemic patient
  - Urine output < 800 cc/day, U_{Na} < 10 mEq/l,
  - "clean urine sediment"
- Treatment: TIPS, MARS, Glypressin, Terlipressin, Transplantation
  - Midodrine 5-15mg po tid
  - Octreotide sq100-200 mcg sq tid

Portal Systemic Encephalopathy: Hepatic Encephalopathy

- Inability to clear "encephalopathogenic agents" (Ammonia, Gaba, Mercaptans, endogenous Benzos)
  - Cirrhosis
  - Portal Hypertension
  - Shunting (TIPS, surgical shunt)
  - Protein load
    - » Usually GI bleed, Gastropathy, less common PO proteins
  - Acute Liver Failure:
    - PSE defines fulminant Hepatic Failure
    - Cerebral Edema (not in chronic!!)
    - Emergency Liver Transplantation is therapy

BAL



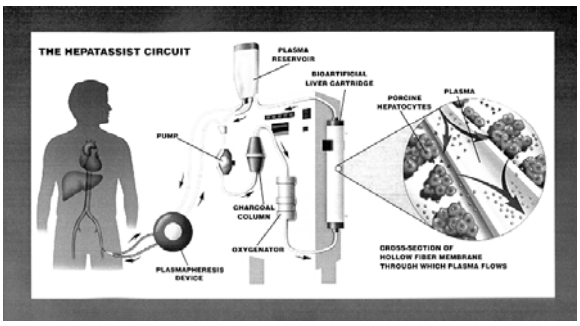
Treatment

- Decrease encephalopathic agent:
  - Lactulose 30cc po q 2 until effect (traps NH3 in colon or NH3 incorporated into bacterial proteins)
  - Rectal Tube
    - » Tap water Enema
    - » Lactulose 200 cc in 300 cc tap water
- Decrease production/block EA:
  - Rifaximin
  - Neomycin 500 mg po q 6 (watch Creatinine and hearing)
  - Flagyl 500 mg po q 8 (neuropathy, antabuse effect)
- "Brain Stabilizers"
  - Zinc and/or L-Carnitene
- Cathartic:
  - Mg Citrate, Miralax, Go-lytely

Indications for Liver Transplantation

- Manifestations of Portal HTN not controlled by alternative measures
  - » Esophageal and/or gastric variceal bleeding
  - » Bleeding from portal hypertensive gastropathy.
  - » Hepatic encephalopathy
  - » Spontaneous Bacterial Peritonitis
  - » Significant Ascites, hydrothorax
  - » Hepatocellular Carcinoma

HepatAssist® Bioartificial Liver Support System



Summary

- Cirrhosis is the end stage of many diseases that cause liver inflammation
- Complications of cirrhosis are related to loss of synthetic function and portal hypertension
- Portal Hypertension is the cause of variceal bleeding, ascites and hepatorenal syndrome in patients with liver disease
- All offered therapies other than liver transplant are supportive not curative of end-stage liver disease.