Cirrhosis

- Characterized by **diffuse hepatic fibrosis and nodule formation**

Pathological features

Fibrosis → Architectural distortion → ↓ hepatocellular mass

Regenerative nodules → ↓ hepatocellular mass

↓ hepatocellular mass → Altered blood flow → Hepatic stellate cell activation → ↑ collagen and other compounds

Causes:
- Alcohol
- Hep B, C
- Autoimmune hepatitis
- Biliary cirrhosis
- Cardiac cirrhosis
- Wilson's disease
- α_1 anti trypsin deficiency
- Cystic fibrosis

Types:
- Alcohol associated
- Due to chronic viral hepatitis
- Chronic biliary cirrhosis
- Non alcoholic fatty liver

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Alcohol associated cirrhosis

- Excess chronic alc use
- Causes fibrosis ± inflammation and necrosis
- Fibrosis is centrilobular, pericellular or periportal
- Nodules <3mm (micronodular)
- Cessation of alc use causes formation of larger nodules giving mixed appearence

Pathogenesis

Ethanol → (Alc dehydrogenase) → Acetaldehyde → (Aldehyde dehydrogenase) → Acetate

Ethanol intake → ↑ liver triglyceride → ↑ fatty acid uptak, ↓ FA oxidation

↓ FA oxidation → Reactive oxygen species

Reactive oxygen species → Acetaldehyde adducts (Proteins, Nucleic acids) → Hepatocyte damage + Kupfer cell activation

Kupfer cell activation → Profibrogenic cytokines → Stellate cell activation → Connective tissue formation → Central vein and portal triad regenerative nodules

Clinical features

- Vague upper right quadrant pain
- Fever, nausea, vomiting, diarrhea, anorexia, malaise
- Ascites
- Edema, GI hemorrhage
- Encephalopathy
- Hepatosplenomegaly
- Scleral icterus
- Palmar erythema
- Spider angioma: On release of central compression, arteriole fills from centre and spreads out peripherally
- Clubbing
- Muscle wasting
- Men: Muscle wasting
  Testicular atrophy
  ↓ body hair
  Gynaecomastia
- Women: Amenorrhea
  Menstrual irregularity
- Zieve's syndrome: Hemolytic anemia + spur cells + acanthocytes
- Enlarged parotids
- Total Bb ↑/Ⓝ
- ↑ prothrombin time
- Serum Na^+ normal but if ↓, ascites +ve
- AST > ALT 2:1 ratio

Complications: Ascites
Oedema
Upper GI hemorrhage
Jaundice
Encephalopathy

Diagnosis

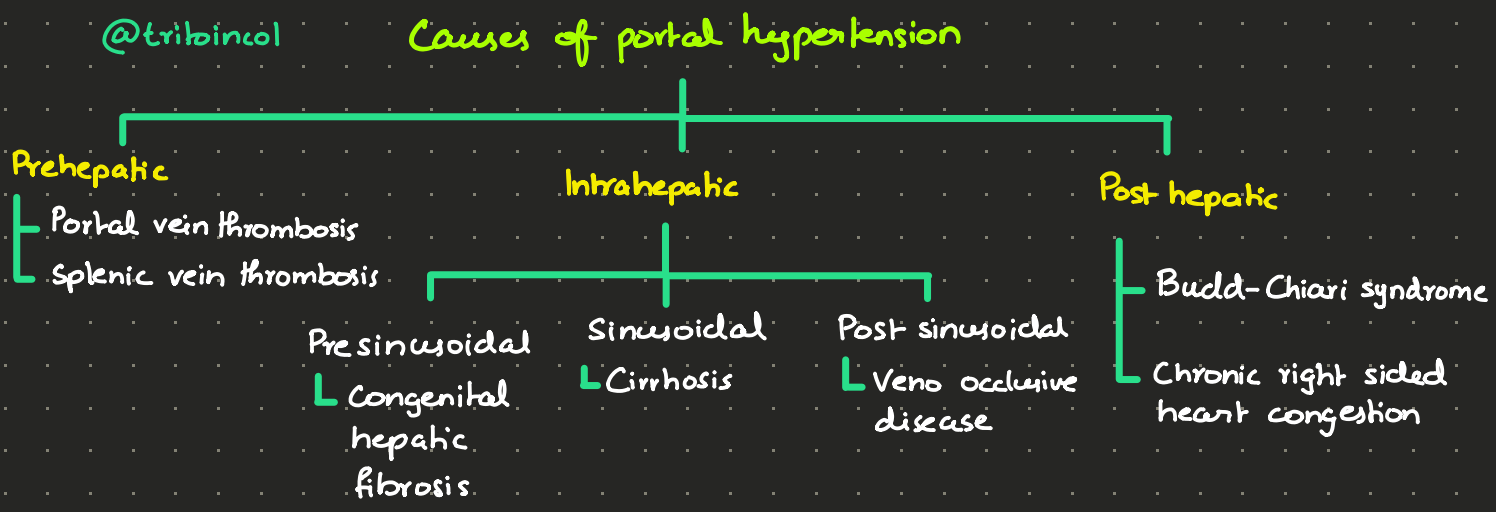
- By clinical examination
- Liver biopsy if necessary

Treatment

- Stop alcohol
- Good nutrition
- Treat complication
- Liver transplant
- Glucocorticoid if hepatitis without infection
- N-acetyl cysteine + glucocorticoid
- Consume > 21.5 KCal/Kg/day
- Max acetaminophen = 2g/day

Portal hypertension

- ↑ hepatic venous pressure gradient (HVPG) to >5mmHg
- Caused by: ↑ intrahepatic resistance (Cirrhosis, regenrative nodules)
  ↑ Splanchnic blood flow
- Initial compensated cirrhosis where HVPG b/w 5-10mmHg.
  Asymptomatic lasting ≥10 yrs
- When HVPG ≥10mmHg, variceal bleeding, ascites, encephalopathy may occur. Mortality <2 yrs



C/F

- 3 primary complications: GI varices with hemorrhage
  Ascites
  Hyperplenism
- Upper GI bleed on endoscopy
- Peripheral edema
- Splenomegaly
- Thrombocytopenia
- Leukocytopenia

Oesophageal varices

- Screen known cirrhotics, 1/3 will have varices

Diagnosis

- Portal htn usually revealed by thrombocytopenia, splenomegaly or complications
- Varies identified by endoscopy
- CT, MRI

Treatment

i) Primary prophylaxis

- Routine endoscopic surveillance every 2 yrs if liver disease active, 3 yrs if liver disease inactive
- Non selective β blockers. Goal of HR = 50-60 beats/min, systolic BP >90 mmHg
- Variceal band ligation

ii) Treat acute bleed

- Fluid and RBC replacement
- Vasoconstrictors (somatostatin, octreotide)
- Prophylactic antibiotics
- Balloon tamponade

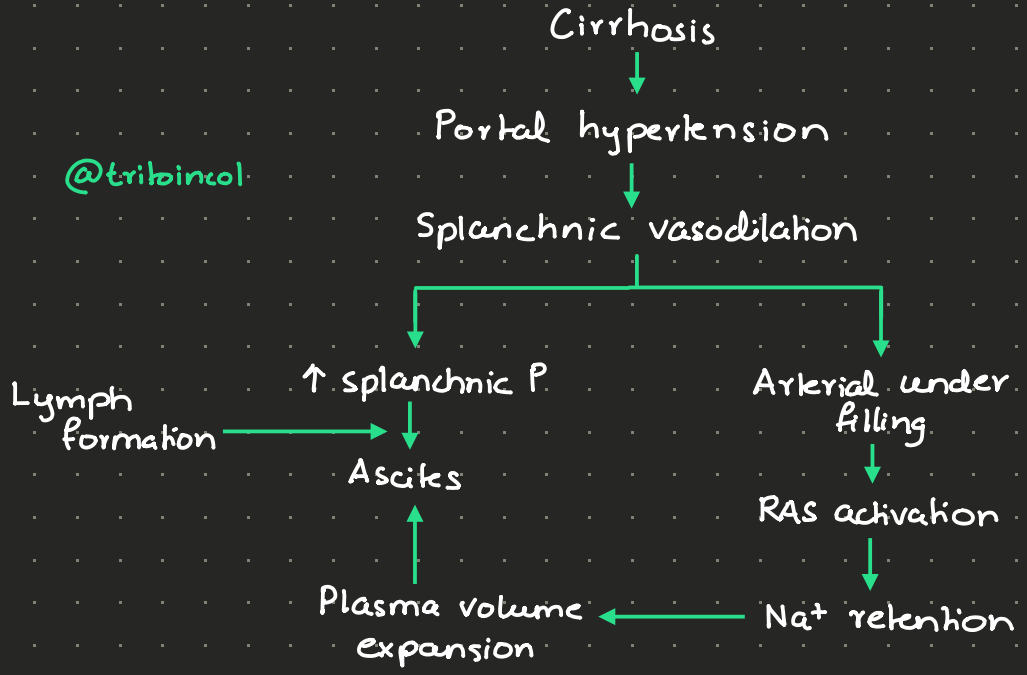
iii) Prevent rebleeding

- Endoscopy to check extent of varices
- Consider TIPS if varices extend to proximal stomach
- Balloon occluded retrograde transvenous obliteration (BRTO)
- Repeated band ligation till varices obliterated
- TIPS for long term prevention

Ascites

- Fluid accumulation in peritoneal cavity
- Most commonly due to portal htn due to cirrhosis
- Other causes: Malignant
  Infectious
  Cardiac

Pathogenesis



C/F

- ↑ abdominal girth
- Peripheral edema
- Insidious onset
- If massive, respiration compromised causing dyspnea
- Patient malnourished, muscles wasted, fatigued, weak

Diagnosis

- By physical exam, imaging
- Patients with bulging flanks have fluid wave or shifting dullness
- Small ascites detected by US/CT
- When presenting for first time, check protein and albumin content, red cell count with differential and cultures of the fluid

Treatment

- Small amount? → Dietary Na^+ restriction
- Moderate amount → Dietary Na^+ restriction
  + Spironolactone 100mg/day
  + Frusemide 40mg/day if peripheral edema +ve
- Still no recovery? Doubt compliance to Na^+ restricted diet
  If diet correct, ↑ spironolactone to max 400mg/day, frusemide to 160mg/day
- Ascites ↑ still / large ascites → Large volume paracentesis OR TIPS procedure
  (Refractory ascites)

Spontaneous bacterial peritonitis

- Ascitic fluid infection without intraabdominal source
- Gut flora transversing intestine to mysenteric lymph node is cause
- Organisms: E.Coli
  Streptococcus viridans
  Staph aureus
  Enterococcus

Diagnosis: Fluid sample with neutrophil count >250/μL
Bedside culture

C/F: Fever
Altered mental status
↑ WBC
Abdominal pain
AKI

Treatment : IV 3rd gen cephalosporin for 5 days
IV albumin
If multiple episodes → Quinolone prophylaxis

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Hepatic encephalopathy

- Altered mental status, cognitive failure in presence of liver failure
- In severe acute liver failure, encephalopathy is a criteria for diagnosis
- Usually in chronic liver disease
- Gut derived neurotoxins not removed by liver, reach brain
- ↑ ammonia level

CIF

- Brain edema → Cerebral herniation
- Usually precipitated by hypokalemia, infection, ↑ dietary protein load, volume depletion
- Patient confused, changed personality
- Violent, difficult to manage or sleepy, difficult to rouse
- If ascites +ve, rule out infection
- Asterixis : Extend arms, bend wrists back · Sudden forward movement of wrists seen (liver flap)

Treatment

- Managing precipitating factors
- Lactulose induced catharsis helps remove neurotoxins from gut
- Alternating administration of neomycin and metronidazole for peripheral neuropathy
- Rifamixin 550mg BD to prevent recurrence
- Zn supplementation