# Cirrhosis

- define, classify → Cirrhosis.
- pathogenesis / morphology → ALD.

→ Etiopathogenesis - cirrhosis.
→ 4 causes.

## Cirrhosis.

- Cirrhosis is a condition marked by the diffuse transformation of the entire liver into regenerative parenchymal nodules surrounded by fibrous bands and variable degree of vascular shunting.

→ Cirrhosis is the morphologic change associated with chronic liver disease.

# Pathogenesis

① Hepatocyte injury and death

- loss of liver cell architecture due to hepatocyte injury.
- mechanism of injury varies depending on etiological agent.
  eg: alcohol, viral hepatitis etc...

② Fibrosis formation.

Stellate cells.

myofibroblasts.

# Classification

## Morphologic Classification

→ micronodular
→ macronodular
→ mixed.

## Etiological Classification

- alcohol (M/C)
- chronic viral hepatitis
  HBV and HCV
- NASH
- Autoimmune hepatitis.
- biliary cirrhosis
  eg: Primary biliary cholangitis.
- Inherited metabolic disorder:
  - hemochromatosis
  - wilson disease
  - $\alpha_1$-antitrypsin deficiency.
- cystic fibrosis.
- cryptogenic/idiopathic
- Indian childhood cirrhosis
- cardiac cirrhosis

FIGURE 5.C:

liver injury occurs due to.

↓

alcohol, viral infections, toxins, metabolic diseases etc..

↓

Hepatocytes undergo stress, damage or death.

↓

damaged cells release

- Damage - Associated molecular Pattern. (DAMPs.)
- ROS.

↓

microbial toxins, DAMPs and ROS are detected by.

Kupffer cells. {first line of Immune defense in the liver}

↓

they release Inflammatory cytokines.

TNFα, IL-1 & IL-6, TGF-β.

- TNFα → amplify Inflammation
- IL-1 & IL-6 → recruit more immune cells
- TGF-β → activate stellate cells → fibrosis.

↓

Kupffer cells send cytokines & chemokines, to recruit additional immune cells.

- Monocytes & macrophages. → enter from blood & ↑ inflammation.
- lymphocytes.
- Neutrophils in active ~~inflammation~~ infection.

Activated Stellate cells.

Kupffer cells.

TGF-β, IL-17, PDGF → stimulate hepatic stellate cells.

↓

myofibroblasts.

Inflammatory cells.

↓

Inflammatory cytokines.

↓

TNF, lymphotoxin, IL-1β, IL-1, IL-6, TN-F2

cytokine & eg TGF-β. chemokine.

↓ by

Kupffer cells, endothelial cells, hepatocytes

ROS.

↓

activation of stellate cells

↓

myofibroblasts.

↓

Secrete Type I & III collagen in space of Disse.

↓

Continuous ECM deposition forms fibrous bonds (septa)

↓

blood flow is disrupted leading to PHTN.

↓

liver tries to regenerate by proliferating hepatocytes.

↓

due to fibrotic barriers, hepatocytes proliferate in an abnormal manner

↓

forming nodules.

↓

"regenerative ~~tissue~~ nodules are surrounded by fibrous tissue."

↓

Characteristic feature of Cirrhosis

# MORPHOLOGY

## GROSS features

→ Early: JH ✓
→ late:

- Nodular architecture.
  {micro | macronodules}
- Liver ~~may be~~ shrunken
- Brown, firm.

## MICROSCOPY

✓ diffuse loA in.

1. loss of architecture - entire liver.
2. regenerative nodules.
3. fibrosis
4. vascular reorganization.

### • regenerating nodules lack

the normal structure of liver lobules or acini

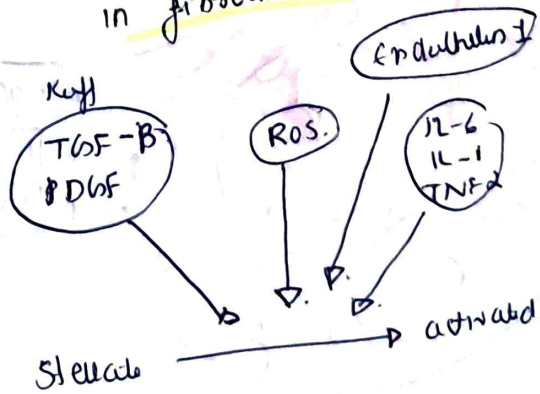
- Initially micro → macro later
  < 3mm > 3mm.
  or mixed.

### • fibrosis

- Initially delicate.
  & expands through sinusoids
- → later broad bands.

### vascular reorganization

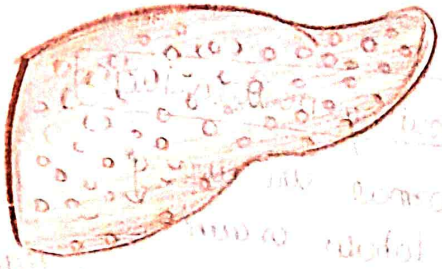
- new vessels are formed in fibrous septa



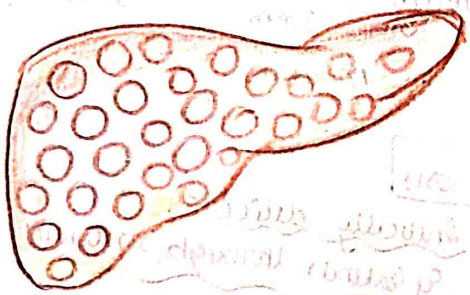
## GROSS

Early stage → enlarged, yellow, fatty.

Late stage → shrunken, brown, Non-fatty, diffuse Nodular & firm.

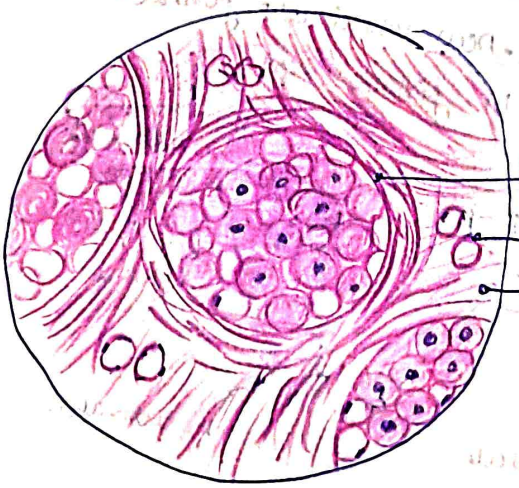


uniform. microscopic architecture. (< 3mm)



Macronodular. >3mm.

## MICROSCOPY




loss of architecture

① regenerating nodules

② FIBROUS SEPTA.