LIVER MICROANATOMY GENERAL FEATURES OF LIVER INJURY

- Weight – 1.4 to 1.6 kg
- Dual blood supply – Portal vein: 60 to 70 % blood flow
- Hepatic artery: 30-40 % blood flow
- Hepatic micro-architecture based on lobular model.
- Liver is divided into 1-2 mm diameter lobules around terminal tributaries of the hepatic vein (terminal hepatic vein), with portal tracts at the lobule's periphery .

- Roughly hexagonal.
- Hepatocytes in the vicinity of central vein are centrilobular.
- Hepatocytes near portal tracts are periportal.
- Division of parenchyma into zones 1 to 3.
- It is useful because certain types of hepatic injury preferentially affect particular zones –zonal gradient of oxygenation and metabolic activities.
- Within the lobule, hepatocytes are organised into anastomosing sheets extending from portal tracts to central veins (terminal hepatic veins).

- Between the trabecular plates of hepatocytes are vascular sinusoids, are lined by fenestrated endothelial cells.
- beneath the endothelial cells ,there is a **space of Disse.**
- Scattered Kupffer cells (MPS) are attached to endothelial cells.
- Fat containing hepatic stellate cells **(Ito cells**) are found in the space of Disse.
- Between hepatocytes are 1 to 2 mm **BILE CANALICULI**.
- These channels drain into the **canals of Hering** that in turn connect to bile ductules in periportal regions.
- The ductules empty into the terminal bile ducts within portal tracts.

Liver diseases
General features

- Major primary liver diseases are ,
- Viral hepatitis
- Nonalcoholic fatty liver diseases (NAFLD)
- Alcoholic liver disease
- Hepatocellular carcinoma (HCC)
- Secondary liver diseases occurs in ,

  heart failure, Disseminated cancer and extrahepatic infections.

Mechanism of hepatic injury & repair :

- Hepatocytes can undergo number of degenerative but reversible changes.
- Accumulation of fat (steatosis)
- Accumulation of bilirubin (cholestasis)
- Hepatocytes die by 2 mechanisms

  1.necrosis

  2. apoptosis (councilman body or acidophil body)
- Widespread parenchymal loss (confluent necrosis) starts from zone 3.
- The resulting space is filled by cellular debris, macrophages and remnants of reticulin meshwork.

- Bridging necrosis : central to portal tract or bridge adjacent portal tract.
- Extensive hepatocyte loss and collapse of the supporting framework along with vascular insults via inflammation and thrombosis result into CIRRHOSIS.
- In some cases there is scar regression.
- Regeneration of hepatocytes occurs by mitotic replication.
- Hepatocytes are stem cell like, so continue to replicate even in the setting of years of chronic injury.

Scar formation & regression :

- Principle cell involved in scar formation is stellate cell in non-activated state. They are vitamin-A (lipid) storing cell, when activated are converted into highly fibrogenic myofibroblast.
- Activation of stellate cells occurs due to

  1.chronic inflammation & inflammatory cytokines

  2.cytokine & chemokine production by Kupffer cell

  endothelial cells hepatocytes & bile duct epithelial cells.

  3. In response to disruption of the extracellular matrix.

  4. Direct stimulation of the stellate cells by toxins.

- Scar formation starts from the space of Disse.
- Zones of parenchymal loss transform into dense fibrous septa.
- Other cells contribute to scar formation are portal fibroblast & epithelial mesenchymal transition.
- If injurious agent is removed or chronic injury is interrupted, then stellate cell stimulation ceases & scar becomes thin & starts to break by metalloproteinase. so scar formation can be reversed.

ACUTE LIVER FAILURE(FULMINANT LIVER FAILURE)

- It is defined as an acute liver illness associated with encephalopathy & coagulopathy that occurs within 26 weeks of initial liver injury in absence of pre-existing liver disease.
- Caused by **massive hepatic necrosis** by drugs or toxins.
- Acetaminophen, Autoimmune hepatitis, Acute hepatitis - A,B,& E.
- Liver failure within a week in acetaminophen by direct toxic damage.
- Hepatic failure due to viruses takes long time & occurs due to direct toxic damage & immune response

MORPHOLOGY

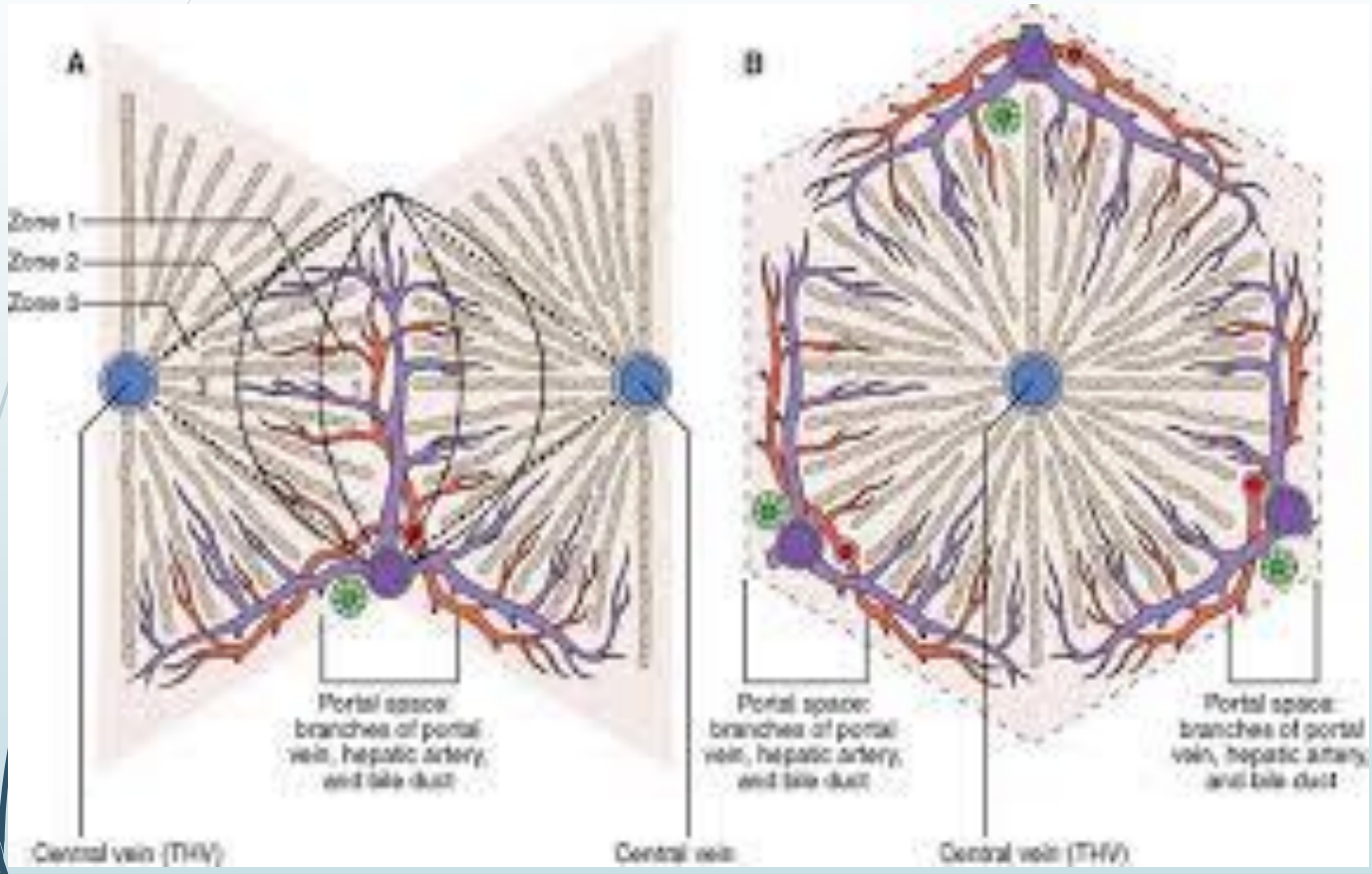
- **Massive hepatic necrosis** with broad regions of parenchymal loss surrounding islands of regenerating hepatocytes.
- Liver is initially enlarged due hepatocyte swelling inflammatory infiltrates and edema; as parenchyma is destroyed, the liver becomes small & shrunken.
- Scar & ductular reaction.
- Rarely, diffuse poisoning of liver cells without obvious cell death & parenchymal collapse .i.e. diffuse microvesicular steatosis.(fatty liver of pregnancy)
- In untreated HIV infection or post transplant immunosuppression, non hepatotropic viruses can cause fulminant liver failure.

CLINICAL COURSE

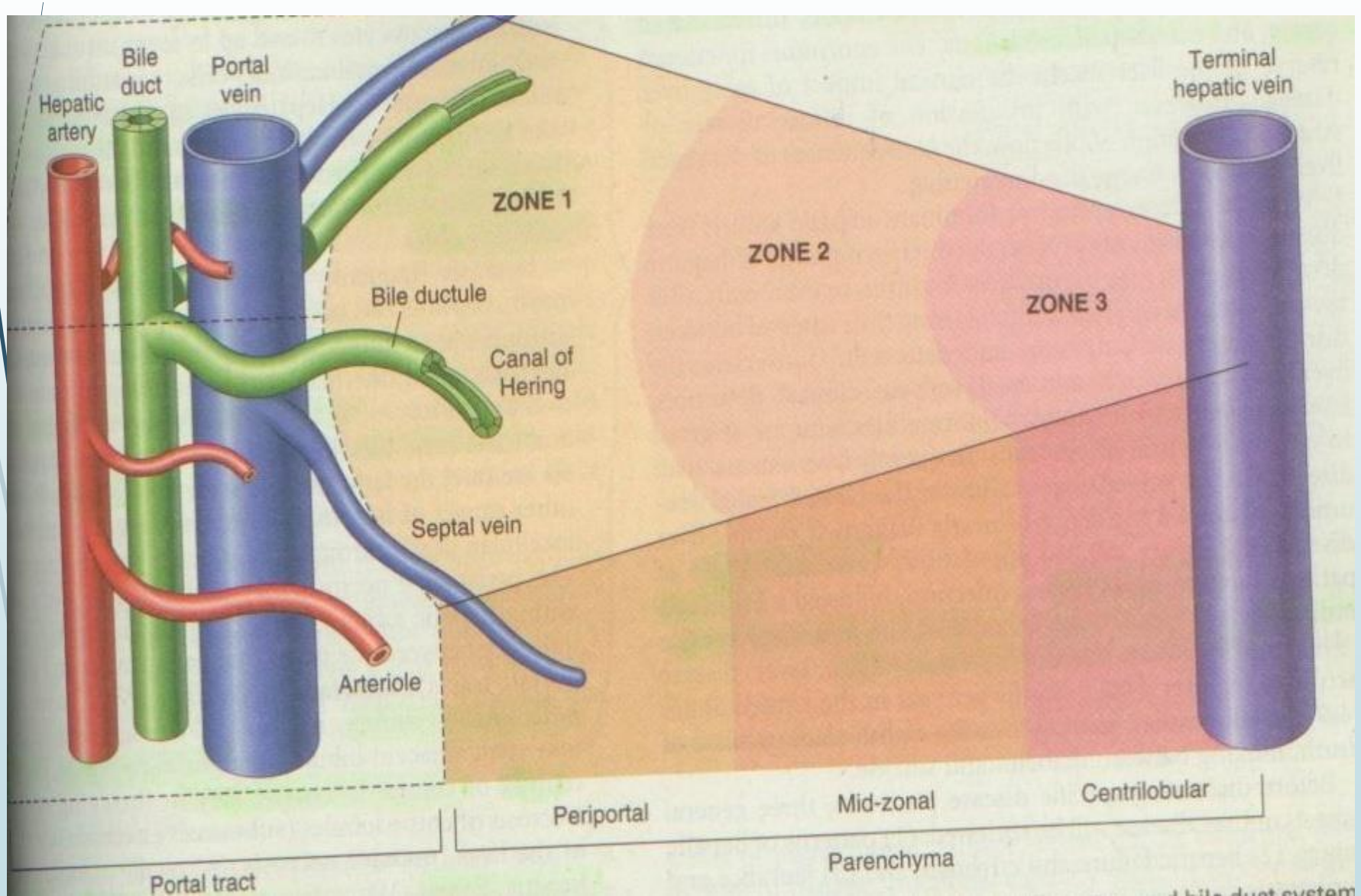
- Acute liver failure manifests first with nausea, vomiting & jaundice followed by encephalopathy & coagulopathy.
- Increased liver serum transaminases
- SGOT :(Serum Glutamic Oxaloacetic transaminase or AST ; Aspartate Amino transferase)
- SGPT : (serum glutamic pyruvic transaminase or ALT : alanine amino transferase)
- Alteration of bile formation & flow leads to jaundice & icterus.
- Cholestasis due to systemic retention of bile.

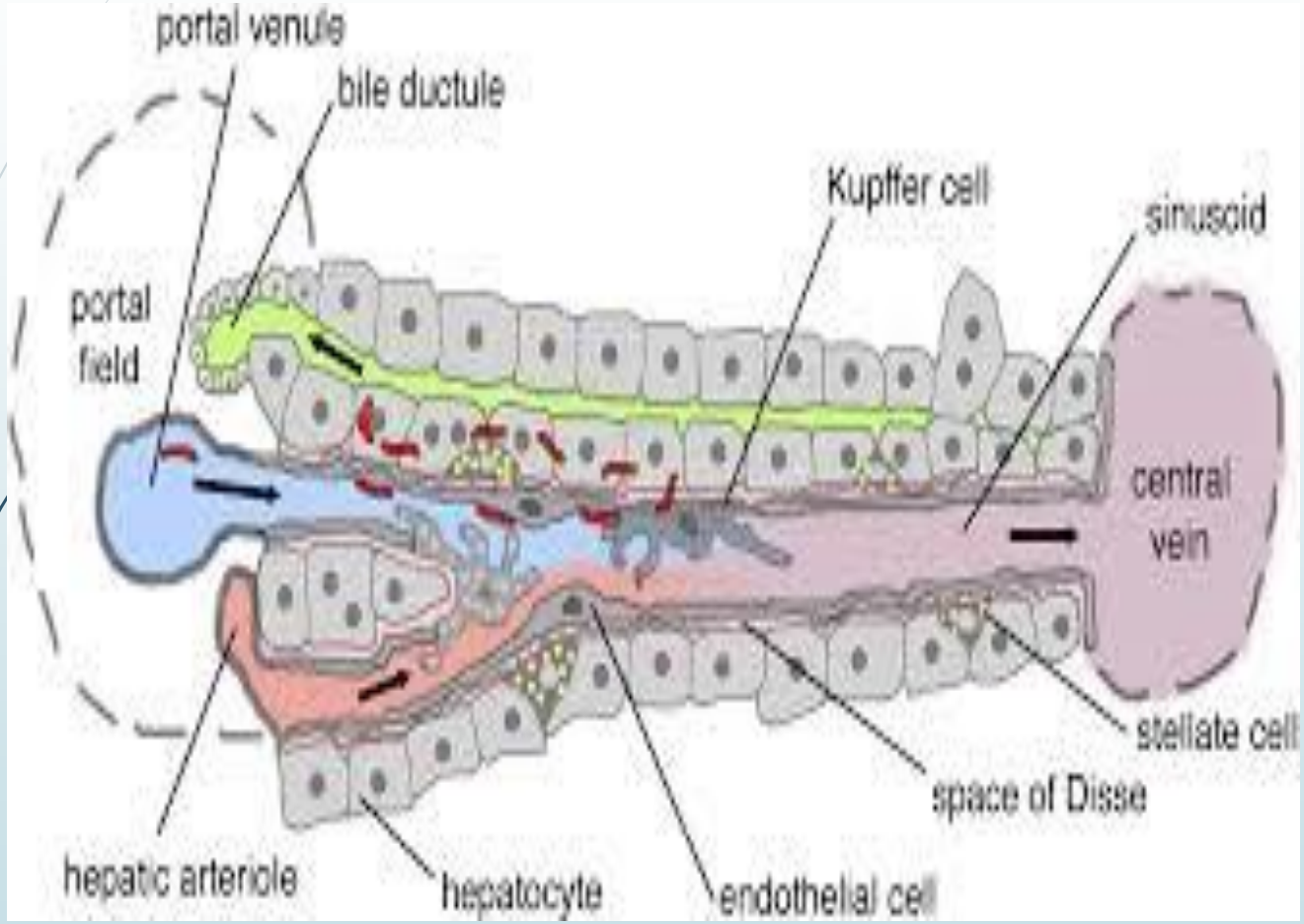
- **Hepatic encephalopathy** :disturbance in consciousness ranging from behavioural abnormalities ,to marked confusion & stupor, to deep coma & death.
- It is a disorder of neurotransmission in the CNS & neuromuscular system.
- Elevated ammonia liver in blood& CNS corelate with the impaired neuronal function & cerebral edema.
- Liver produces **vitamin-K dependent** & independent clotting factors, so with hepatic failure, coagulopathy develops easy bruising & fatal intra-cranial hemorrhage & DIC (impaired removal of activated coagulation factors by liver)

- **HEPATO-RENAL SYNDROME** : renal failure occurs in persons having liver failure.
- Sodium retention , impaired free-water excretion, decreased renal perfusion and GFR(Activation of renin-angiotensin axis)are the main renal functional abnormalities.
- Decreased urine output.
- Increased BUN & Creatinine levels.


A
Zone 1
Zone 2
Zone 3
Portal space:
branches of portal
vein, hepatic artery,
and bile duct
Central vein (THV)
Central vein
B
Portal space:
branches of portal
vein, hepatic artery,
and bile duct
Portal space:
branches of portal
vein, hepatic artery,
and bile duct
Central vein (THV)

MICROARCHITECTURE




portal venule
bile ductule
Kupffer cell
sinusoid
portal field
central vein
stellate cell
space of Disse
hepatic arteriole
hepatocyte
endothelial cell