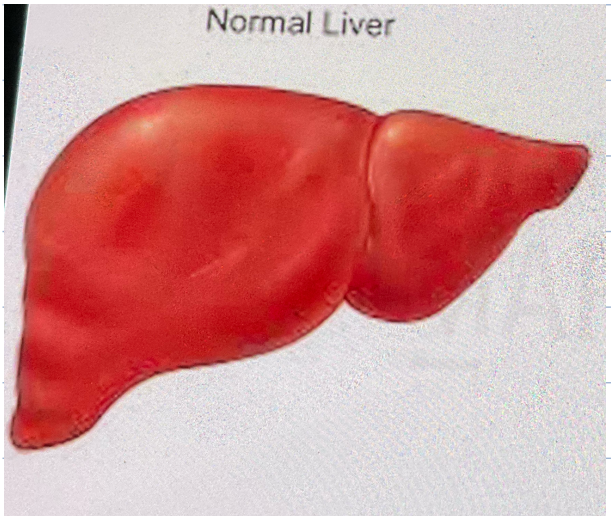
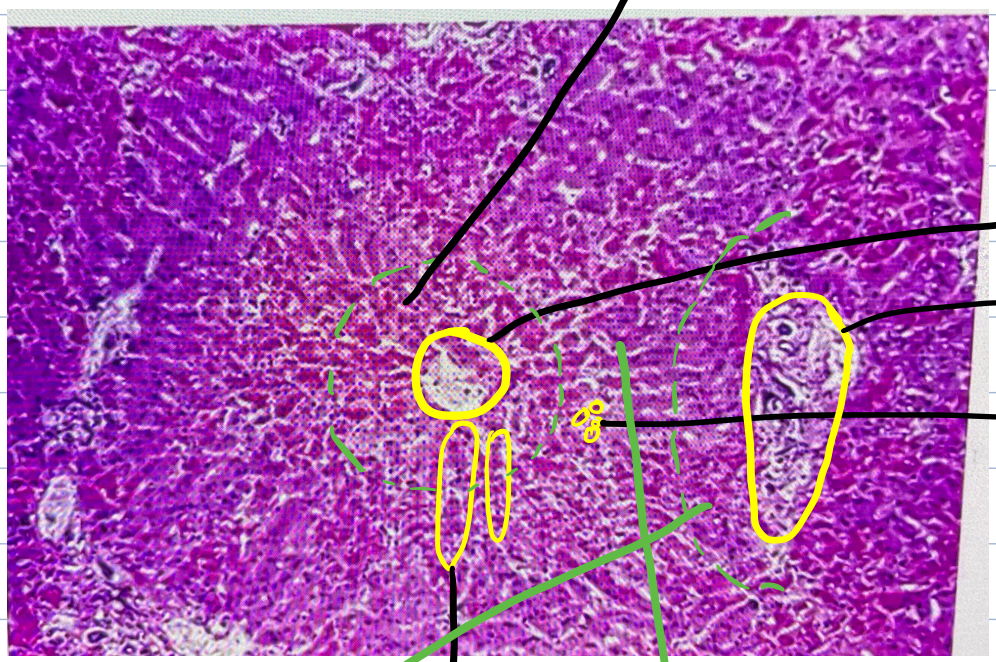
Liver:



Normal weight: 1400 - 1600 g

Portal triad = Bile duct + Portal vein + Hepatic artery



zone 3 (centrilobular)

central vein

portal triad

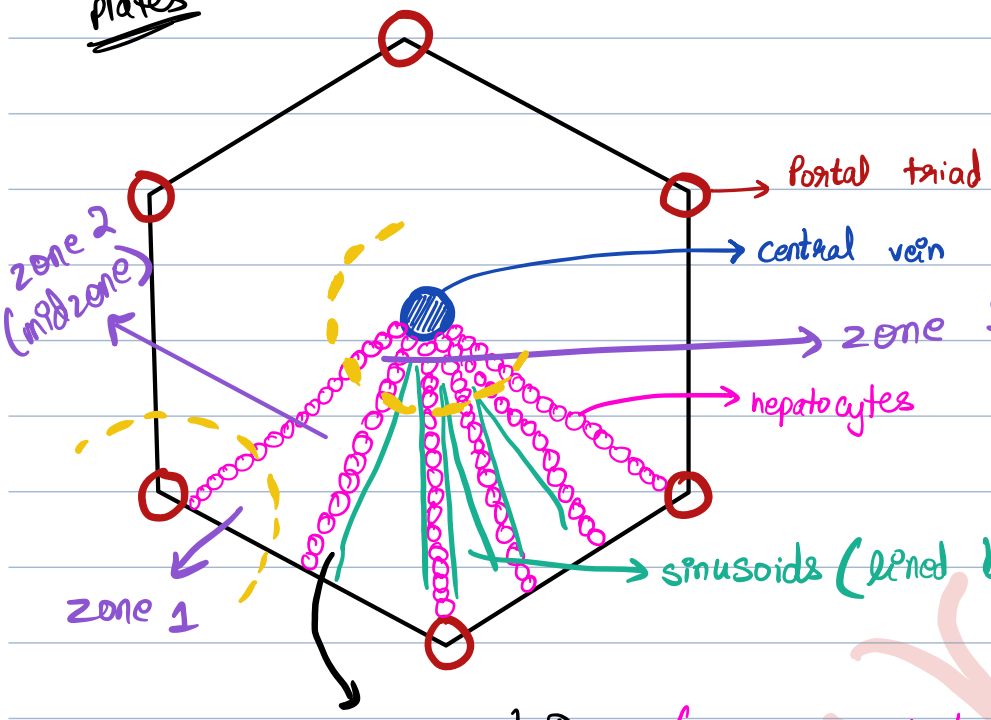
hepatocytes (abundant pink, eosinophilic cytoplasm due to excess mitochondria)

cords of hepatocytes

Zone 1 (periportal zone) [zone of cells near the portal triad]

mid zone

Hexagonal plates



→ zone which is most susceptible to hypoxia / ischaemia : **zone 3**

→ zone which is most susceptible to toxin-induced damage : **zone 1**

→ **midzone** : yellow fever affects it

Space of Disse:

→ Amyloid first affects this area

→ it contains the **Ito cells** (for storage of vit. A)

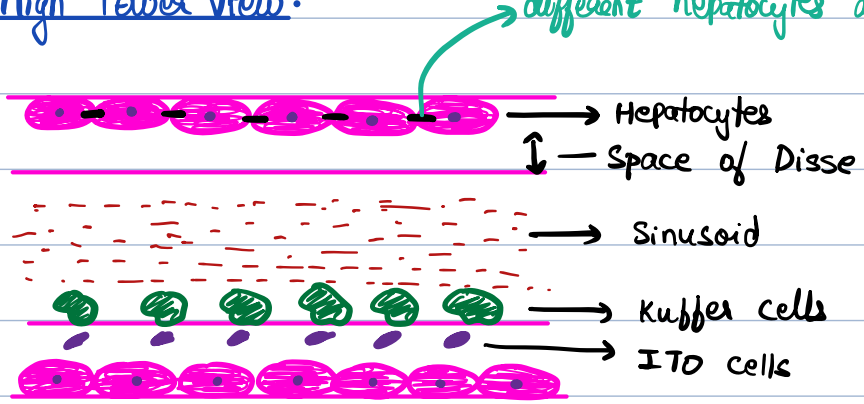
↓ if stimulated

stellate cells

↓

fibrosis → • Type I & Type III collagen
• myofibroblasts.

High Power View:



↓

Contain oval cells (stem cells of liver)

Jaundice : hyperbilirubinemia

Unconjugated Hyperbilirubinemia

- Hemolytic Anemia
- Crigler - Najjar Syndrome
  - Type I
  - Type II
- Gilbert Syndrome

Conjugated Hyperbilirubinemia

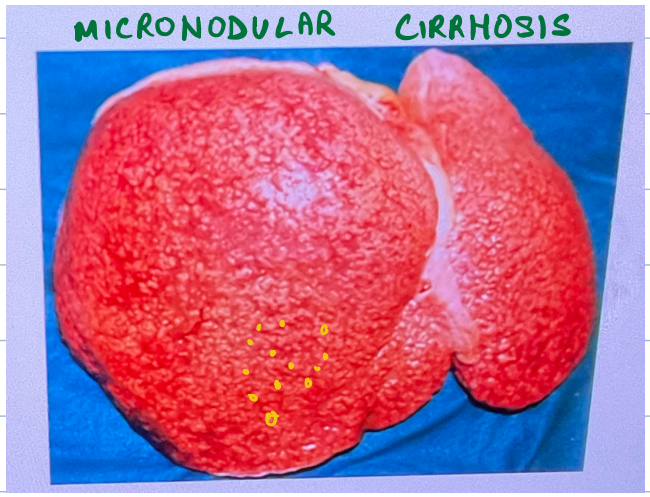
- Biliary tract disease
  - Primary Biliary Cirrhosis
  - Primary Sclerosing Colangitis
- Obstruction
  - Stone
  - Cancer
  - Stricture
- Dubin Johnson Syndrome
- Rotor Syndrome.

Hereditary Hyperbilirubinemias :

Crigler Najjar Type 1	Crigler Najar Type 2	Gilbert Syndrome
→ autosomal recessive → complete deficency of UDP-glucoronyl transferase A1 → totally fatal	→ autosomal dominant → partial deficiency of UDP glucoronyl transferase A1 (UGTA1)	→ very very mild defect in UGTA1

Dubin Johnson Syndrome	Rotor Syndrome
→ defect in canalicular MRP - 2 (multidrug resistance protein) ↓ accumulation of epinephaine ↓ pigmented liver	→ defect in ATP transport proteins → non - pigmented liver

Cirrhosis : end-stage liver disease

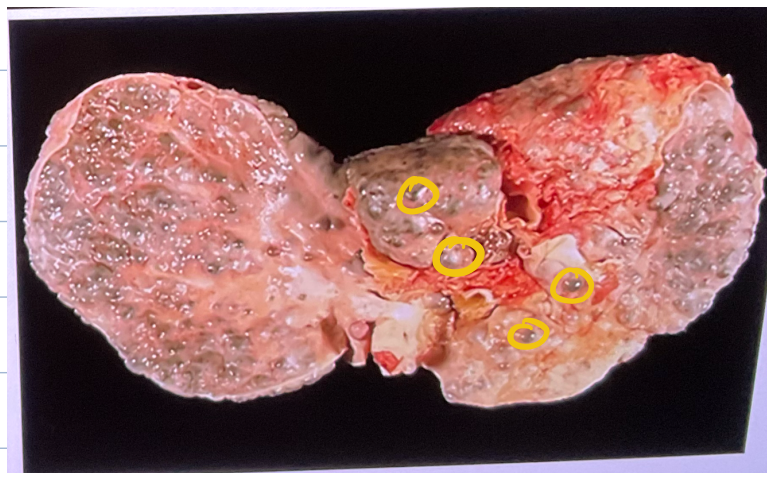


Characteristics :

- disruption of the entire lobular architecture
- regenerating parenchymal nodules
- fibrosis

Micronodular Cirrhosis: nodules < 3 mm

Macronodular Cirrhosis: nodules > 3 mm



Pathogenesis :

→ In a normal liver, type I & III collagen is present in periportal & centrilobular area;
type 4 collagen is present in space of Disse

→ in cirrhosis, type 1 & 3 collagen are present in space of Disse

↓

Loss of fenestration of sinusoids ⇒ Capillarization of sinusoids

∵ Ito cells are activated into stellate cells which produce type 1 & 3 collagen in the space of Disse.

Micronodular Cirrhosis < 3mm

- Early alcoholic liver disease
- Haemachromatosis
- Primary biliary cirrhosis
- Indian childhood cirrhosis

Macronodular Cirrhosis > 3mm

- Late stages of alcoholic liver disease
- Wilson's disease
- $\alpha 1$ antitrypsin deficiency
- Drug induced hepatitis
- Viral hepatitis

Clinical Presentation:

→ h/o jaundice
→ testicular atrophy
→ gynecomastia
→ palmar erythema
→ spider angioma
→ purpura
→ petechiae
→ caput medusae
→ amenorrhea, impotence

Haematologic abnormalities:

→ thrombocytopenia
→ anemia
→ leukopenia
→ coagulation disorders
→ splenomegaly

Metabolic Abnormalities:

→ hypokalemia
→ hyponatremia
→ hypoalbuminemia

Cardiovascular:

→ fluid retention
→ peripheral edema
→ Ascites

GI abnormalities:

- → anorexia
- → dyspepsia
- → nausea, vomiting
- → change in bowel habits
- → dull abdominal pain
- → Esophageal & gastric varices
- → Gastritis
- → Haematemesis
- → Haemorrhoidal varices
- → Fetor hepaticus

Neurological:

- → hepatic encephalopathy
- → peripheral neuropathy
- → Asterixis

Stain: Masson Trichrome

↳ collagen fibres appear blue

Alcoholic Liver Disease (ALD): (ASH)

→ only 15% of people who consume alcohol will develop ALD
→ intake of 60-80 mL / day for 10 years ⇒ ALD.
→ common cause of cirrhosis in western countries

Gross: → liver: soft, yellow, greasy (due to excess fat)

Microscopy: → Steatosis
→ Hepatitis
→ Cirrhosis

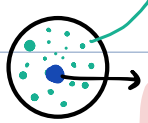
① Steatosis: fatty change

→ earliest change in ALD
→ reversible stage

Stains: - oil Red O
- Sudan Black B

Microvesicular Steatosis

→ small lipid droplets in hepatocytes



→ nucleus remains in the center

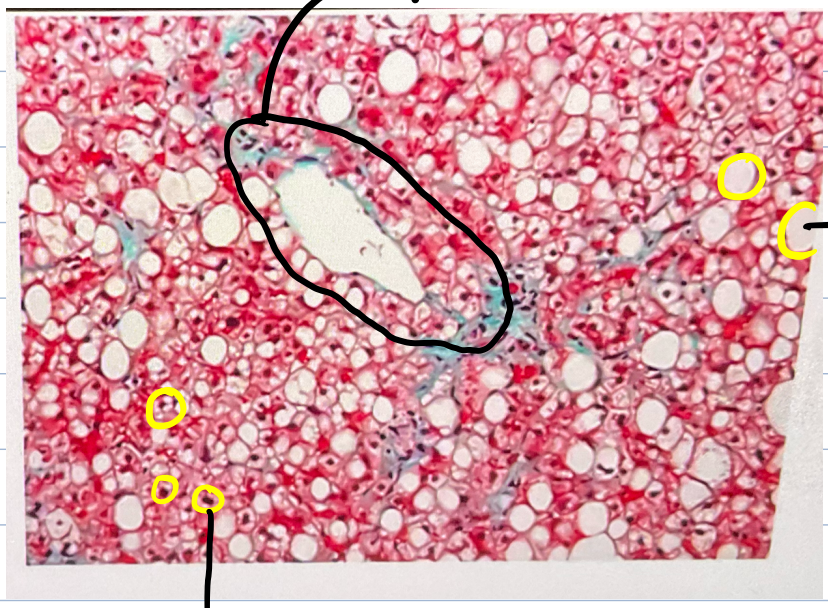
- early ALD
- Fatty liver of pregnancy
- Reye's syndrome
- Chronic viral hepatitis

Macrovesicular Steatosis

→ large lipid droplets which push the nucleus to the periphery.

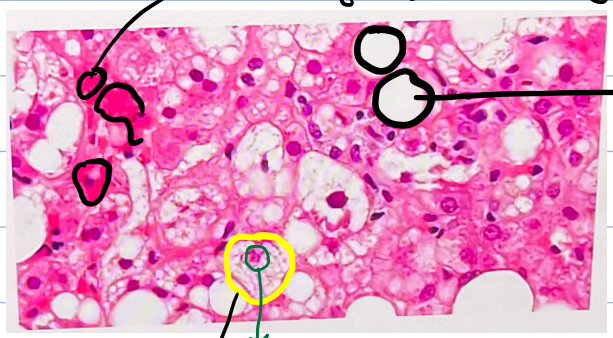
- Late ALD
- Haemachromatosis
- Obesity
- PEM
- Chronic Hepatitis B
- Non-alcoholic steato-Hepatitis

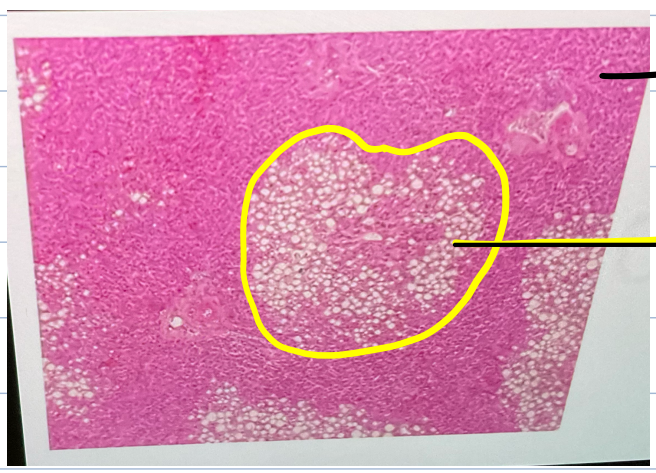
green fibrosis ⇒ chicken wire fibrosis



macrovesicular steatosis

microvesicular steatosis

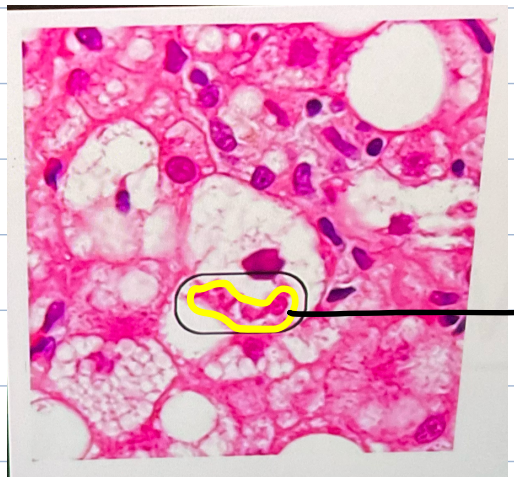




② Hepatitis : inflammation of liver parenchyma

→ neutrophilic infiltrate

→ Malory Hyaline Bodies / Malory Denk bodies → Chicken wire fibrosis



composed of intermediate filaments like CK 8 , CK 18

Mallory Hyaline Bodies (dense eosinophilic bodies inside hepatocytes)

→ also seen in: *

→ not seen in:
① haemachromatosis
② secondary biliary cirrhosis

* New ⇒ NASH
Indian ⇒ Indian childhood cirrhosis
W ⇒ Wilson's disease
A ⇒ α1 AT deficiency
T ⇒ Tumours like HCC
C ⇒ Primary biliary cirrhosis
H ⇒ Focal nodular hyperplasia.

Chicken Wire Fibrosis: perisinusoidal fibrosis

→ Stain ⇒ Masson Trichrome

③ Cirrhosis :

Lennac cirrhosis : conversion of liver into fibrous scar.

" " Fatty Liver Disease / Non-alcoholic Steato Hepatitis (NASH):

→ most common cause of cirrhosis in western countries
→ increases the risk of HCC
→ no h/o alcohol intake / very little alcohol intake
→ usually occurs in:
- obesity
- diabetes mellitus
- insulin resistance
- metabolic syndrome
- hypercholesterolemia.

ASH	NASH
① h/o alcohol intake	① No h/o of alcohol intake
② Obesity, Diabetes mellitus, Hypercholesterolemia } usually absent	② Obesity, Diabetes mellitus, Hypercholesterolemia } present
③ Mallory hyaline bodies are more prominent	③ less prominent.
④ Perisinusoidal inflammation is more	④ Periportal inflammation is more
⑤ neutrophils are more prominent	⑤ monocytes are more prominent
⑥ More increase in GGT	⑥ Less / no increase in GGT
⑦ AST : ALT > 2	⑦ AST : ALT < 1

Reye's Syndrome :

→ usually develops in children

↓

that have viral fever

↓

Tx with Aspirin

↓

child develops features of

- hepatic encephalopathy
- hypoglycemia
- vomiting.

} ⇒ child has Reye's syndrome

→ Biopsy shows extensive microvesicular steatosis.

Metabolic Liver Diseases:

- Hemachromatosis
- Wilson's disease
- α1 AT deficiency

Haemachromatosis: excessive iron deposition

→ autosomal recessive

→ most common cause of cirrhosis due to metabolic disorder.

TYPES

Hereditary / Congenital

- mutation of HFE gene on chromosome 6p
- HAMP gene mutation
- HJV gene mutation

Acquired

ISHITA
KANODIA