

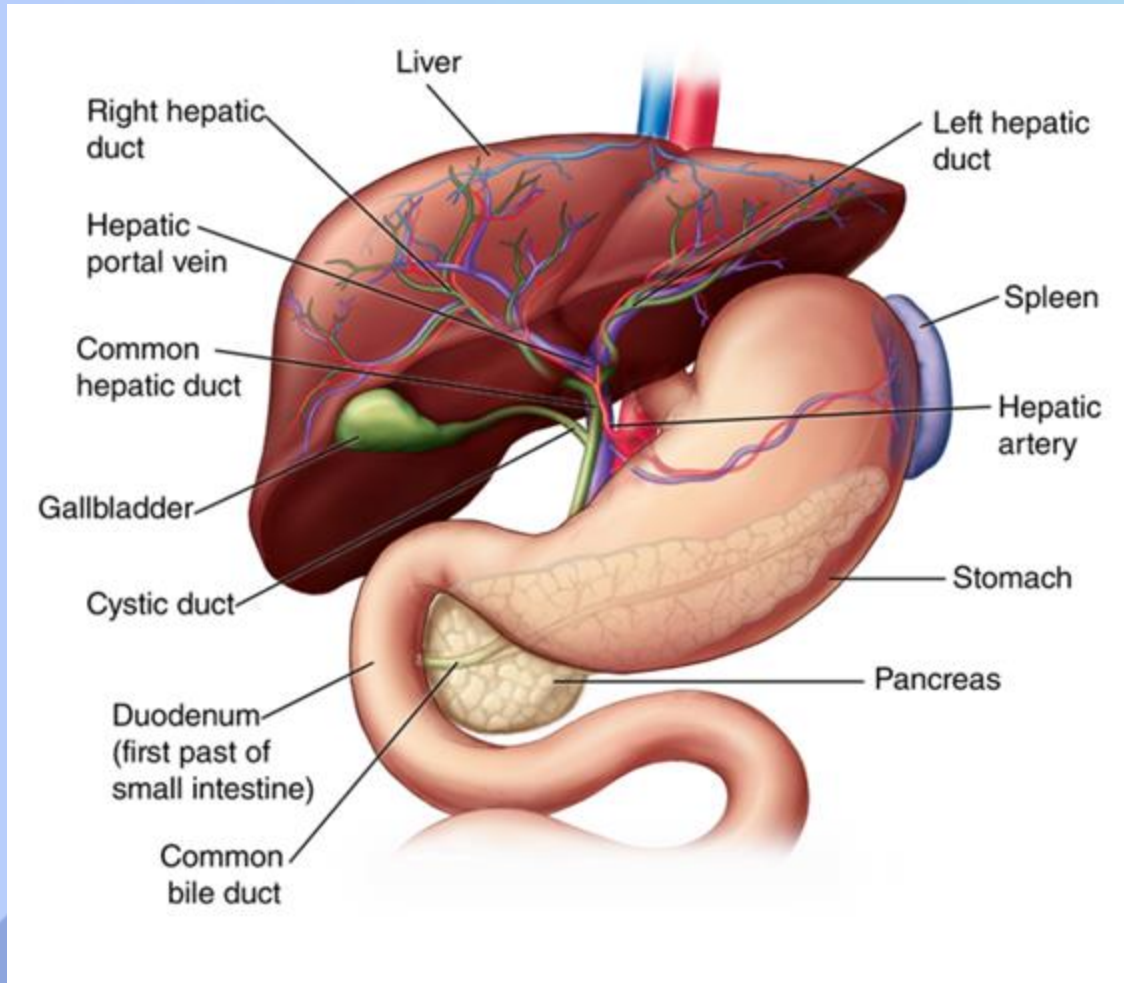
Liver and gallbladder pathology

By Josefine Holum

Overview

- Anatomy and basic function of liver and gallbladder
- Basic liver function tests
- Hyperbilirubinemia
- Gallbladder disorders
- Alcoholic and non-alcoholic liver disease

Anatomy



Liver

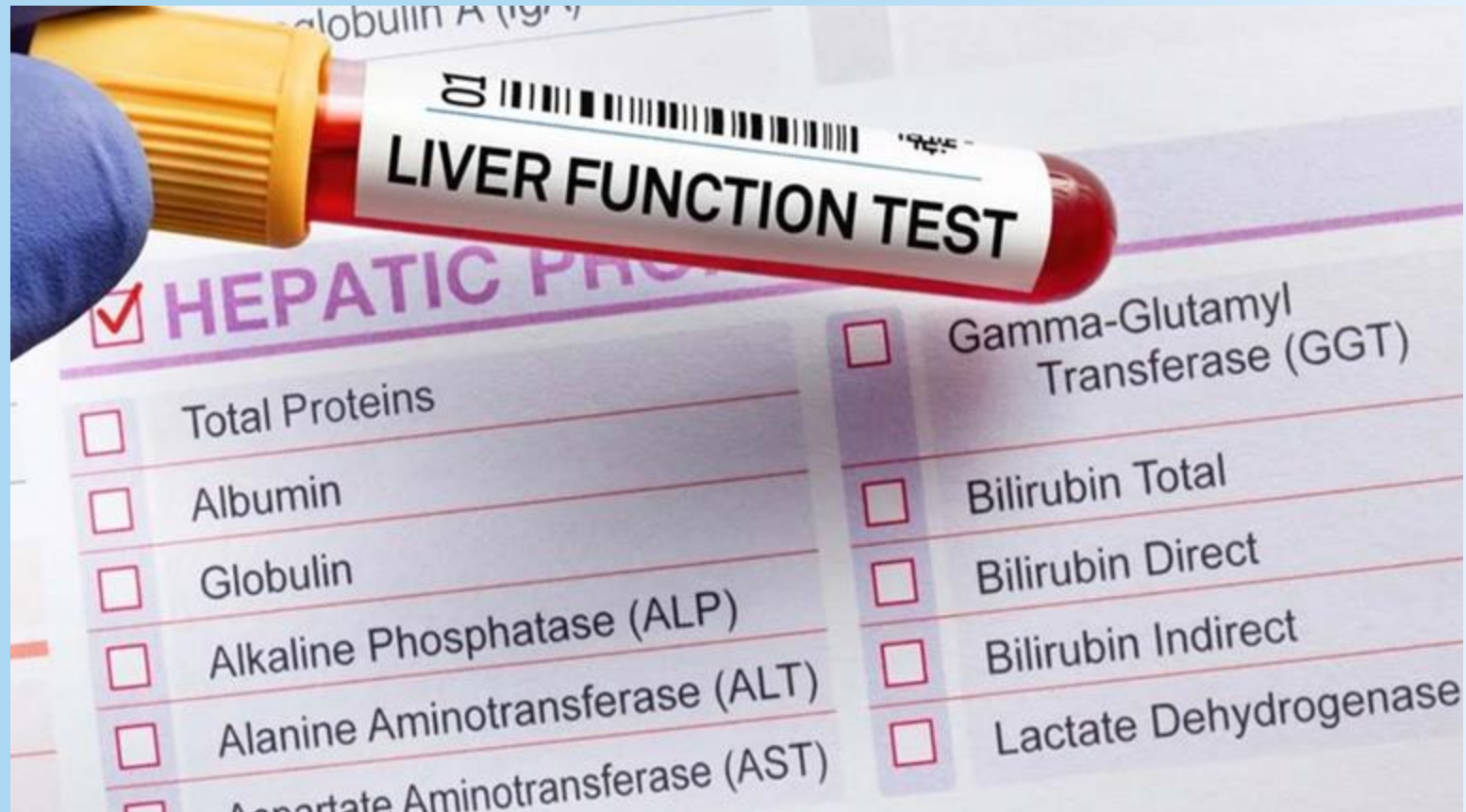
- Right upper quadrant
- Dual blood supply
 - Hepatic artery
 - Portal vein

Gallbladder

- Stores and concentrates bile
- Releases bile in response to meals

Basic liver function tests

- AST
- ALT
- ALP
- GGT
- Bilirubin
- Albumin



AST

- Aspartate aminotransferase
- Found in liver, muscle, heart and kidney
- NOT specific to the liver
- Elevated in hepatocellular injury

ALT

- Alanine aminotransferase
- Found in liver
- Specific to liver injury

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ALT

- Alanine aminotransferase
- Found in liver
- Specific to liver injury

ALT/AST ratio

ALT > AST - Typical for most liver diseases

ALT < AST - Indicates alcoholic liver disease

ALP



- Alkaline phosphatase
- Found in primarily gallbladder epithelium and bone

GGT

ALP ↑ GGT ↑ Gallbladder

ALP ↑ GGT ↓ Bone

- Gamma-glutamyl transferase
- Sensitive to gallbladder

Bilirubin

Unconjugated

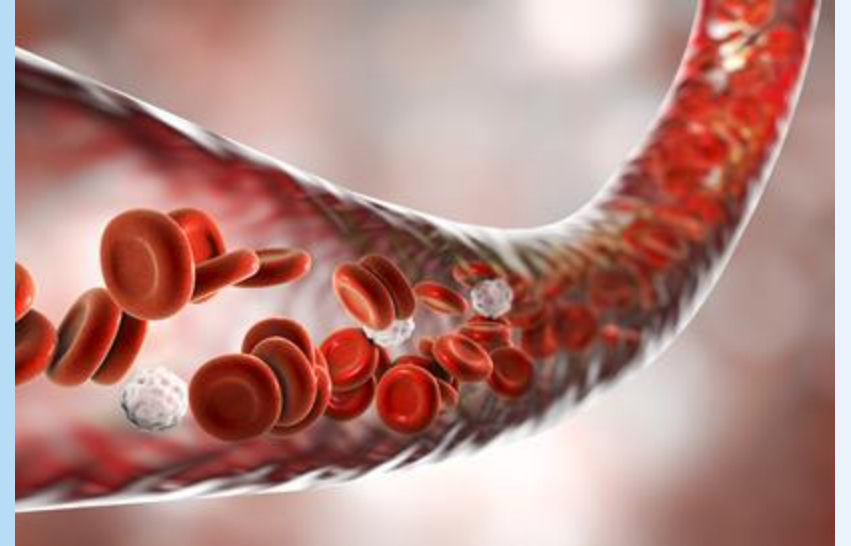
- Breakdown of hemoglobin
- Suggests hemolysis
- Prehepatic liver injury

Conjugated

- Hepatobiliary disease
- Intrahepatic / posthepatic liver injury

Albumin

- Most abundant plasma protein
- ONLY produced in the liver
- Maintains oncotic pressure in our vessels



1. Chronic liver disease
2. Malabsorption
3. Nephrotic syndrome

Overview



Anatomy and basic function of liver and gallbladder



Basic liver function tests



Hyperbilirubinemia



Gallbladder disorders



Alcoholic and non-alcoholic liver disease

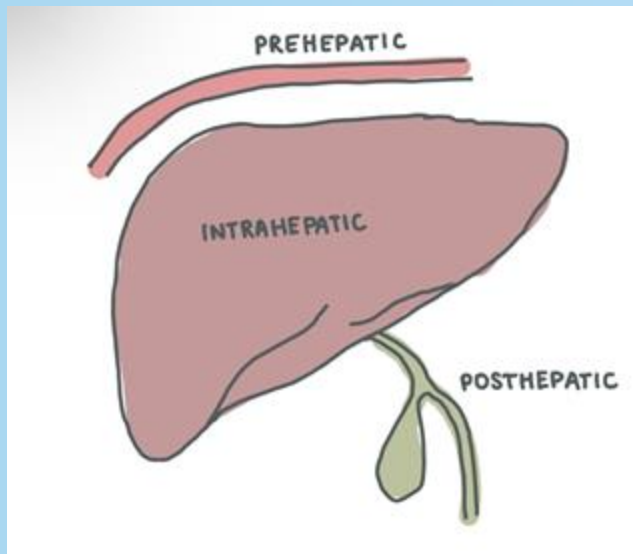
Hyperbilirubinemia

- Yellow discoloration of skin, sclera and mucous membranes due to deposition of bile pigment
- Bilirubin > 1.8 mg/dl



Hyperbilirubinemia

- Yellow discoloration of skin, sclera and mucous membranes due to deposition of bile pigment
- Bilirubin > 1.8 mg/dl
 1. Prehepatic injury
 2. Intrahepatic injury
 3. Posthepatic injury



Prehepatic injury

Total bilirubin
Unconjugated bilirubin
Conjugated bilirubin

- Problem occurs before the liver

1. Hemolysis

2. Transport problem

- Rifampin
- Probenecid

3. Conjugation problem

- Gilbert syndrome
- Crigler Najar syndrome

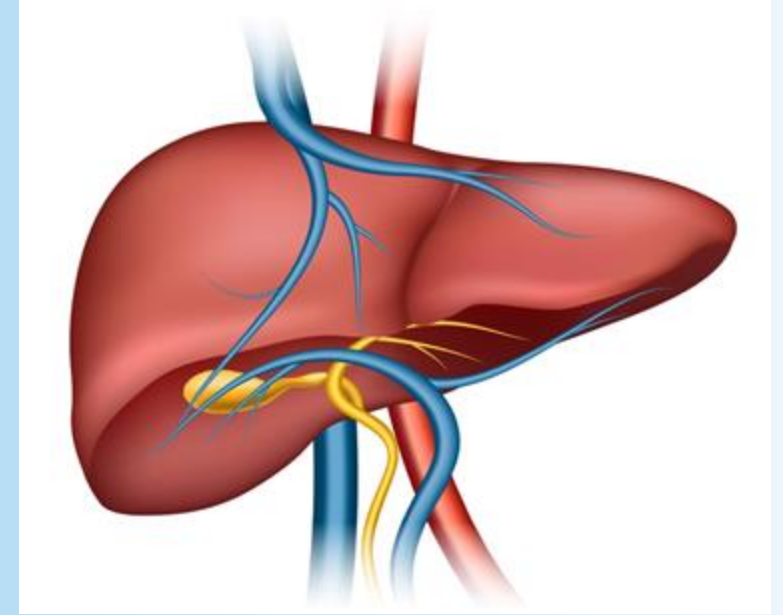


↑ Total bilirubin ↑ Unconjugated bilirubin — Conjugated bilirubin

NORMAL LFTs

Intrahepatic injury

- Problem within the liver
- Impaired uptake, impaired conjugation or impaired excretion
- Caused by hepatocellular disease, drug induced liver injury, genetic disorders

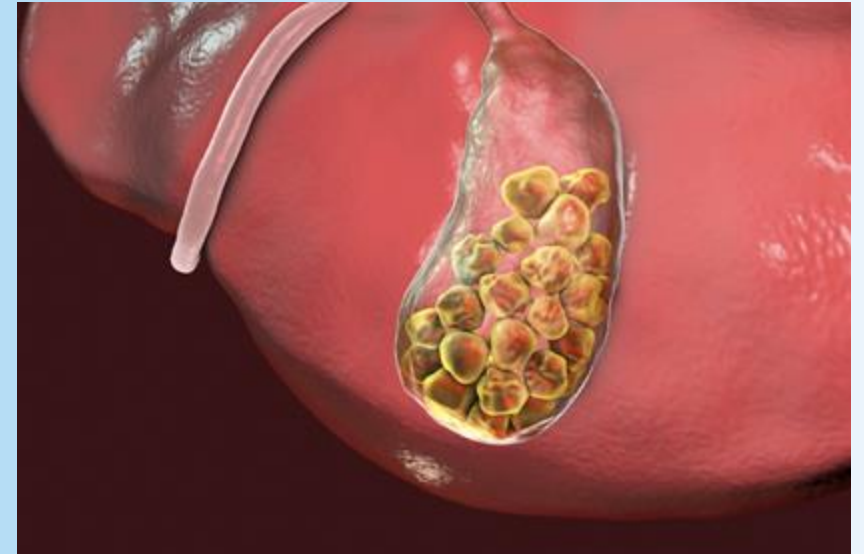


↑ Total bilirubin ↑ Conjugated ↑ Unconjugated

LFTs usually elevated

Posthepatic injury

- Problem occurs after the liver
- Typically indicating impaired bile flow
- Most common cause is gallstones



↑ Total bilirubin ↑ Conjugated — Unconjugated

Normal LFTs, elevated ALP and GGT

Overview



Anatomy and basic function of liver and gallbladder



Basic liver function tests



Hyperbilirubinemia



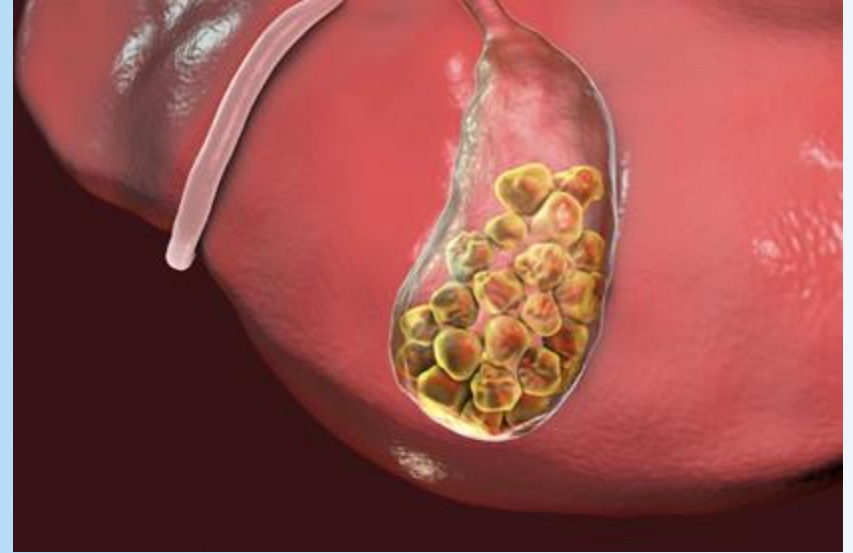
Gallbladder disorders



Alcoholic and non-alcoholic liver disease

Cholelithiasis

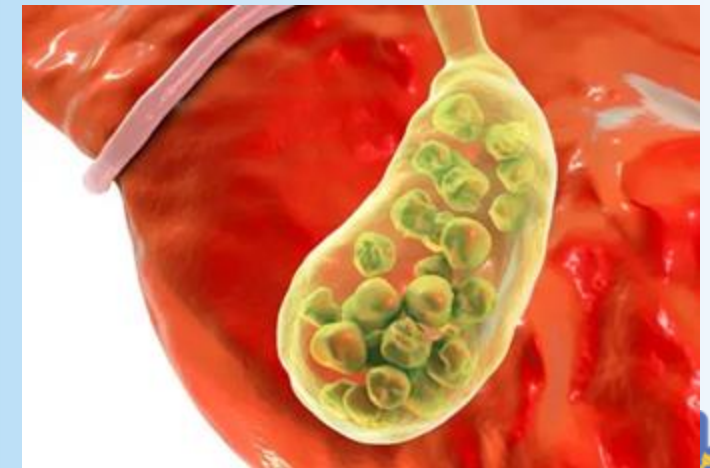
- Formation of stones in the gallbladder
- Mostly asymptomatic
- Most common type: Cholesterol





Cholelithiasis

1. Supersaturation of bile with cholesterol
 - Bile becomes too thick, affecting solubility
2. Hypomobility of the gallbladder
 - Bile sitting for too long, becoming more concentrated
3. Mucus hypersecretion
 - Mucus in gallbladder traps crystals, allowing stones to grow



Risk factors

- Fat
- Forty
- Female
- Fertile



Risk factors

- Fat
- Fertile
- Female
- Forty
- High fat diet
- Sedentary lifestyle
- Rapid weight loss over short period of time
- Periods of fasting



Cholelithiasis



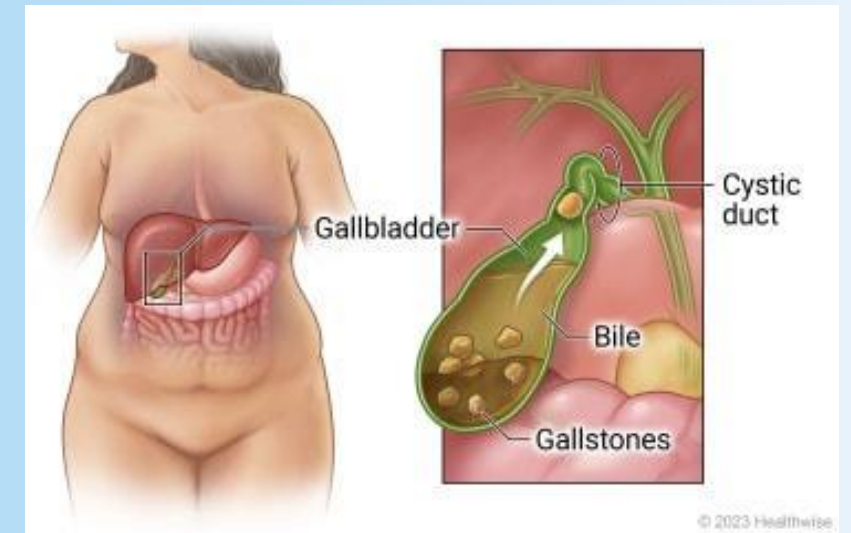
Symptoms

- Intermittent colicky pain in the RUQ
- Especially after fatty meals
- 30-60 minutes
- No systemic symptoms



Cholecystitis

- Inflammation of the gallbladder
 - Most commonly caused by a gallstone blocking the cystic duct
1. Bile stasis
 2. Gallbladder distention
 3. Inflammation
- Promote bacterial overgrowth

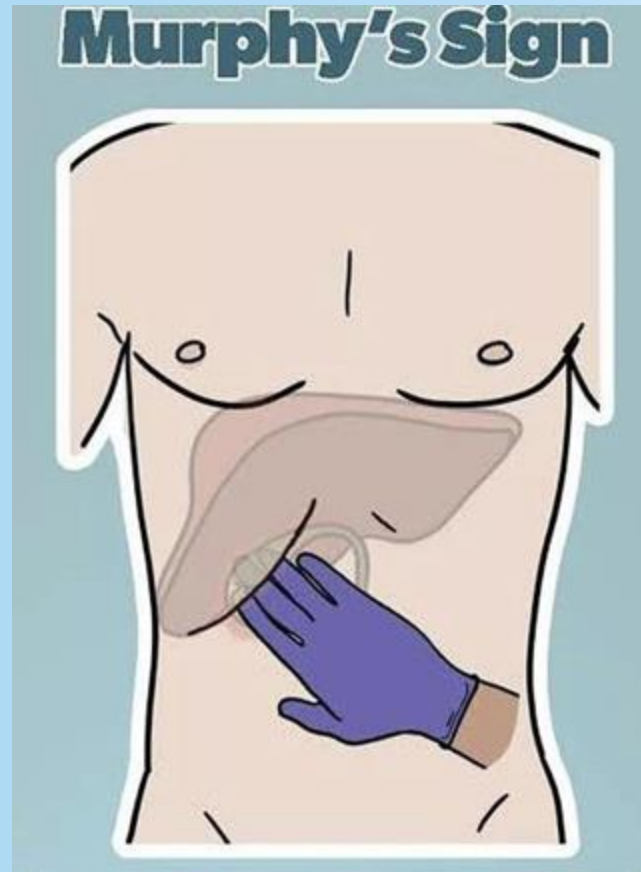


Acalculous cholecystitis

- No gallstones present
- Usually occurs in severely critically ill patients
- Sepsis, extensive trauma or burns
- Due to gallbladder ischemia and stasis

Symptoms cholecystitis

- Steady RUQ pain, often radiated to the right shoulder or back
- Systemic symptoms present
- Nausea / vomiting
- Murphys sign



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- ☐ Alcoholic and non-alcoholic liver disease

Alcoholic liver disease

Alcoholic liver disease

1. Acetaldehyde

- Ethanol is broken down to acetaldehyde in the liver

2. Reactive oxygen species

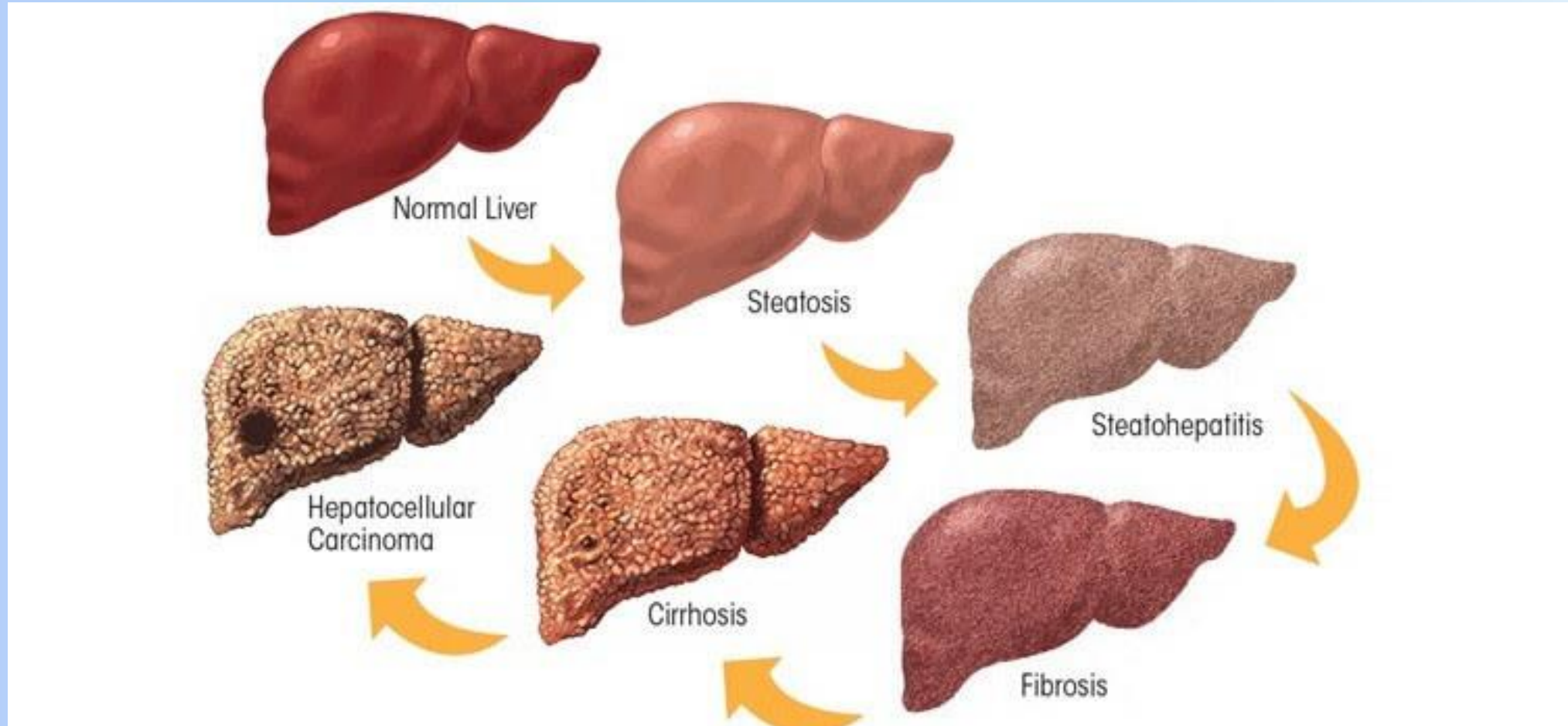
- Leads to lipidoxidation and cell injury

3. Mitochondrial damage

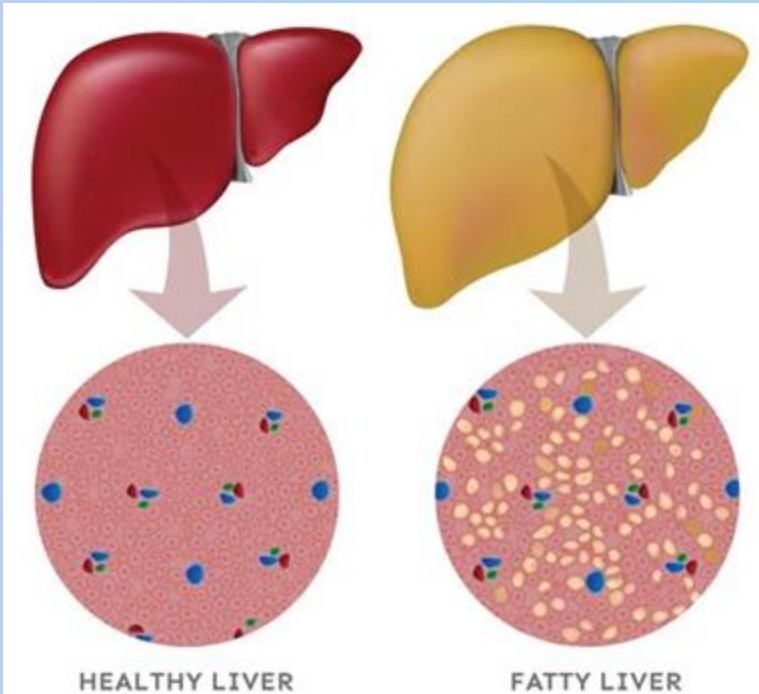
- Promotes triglyceride accumulation in liver



Alcoholic liver disease



Steatosis (fatty liver)



- Mostly asymptomatic
- Reversible with abstinence

Mitochondrial damage



Inhibition of β -oxidation of fatty acids and triglyceride accumulation in hepatocytes

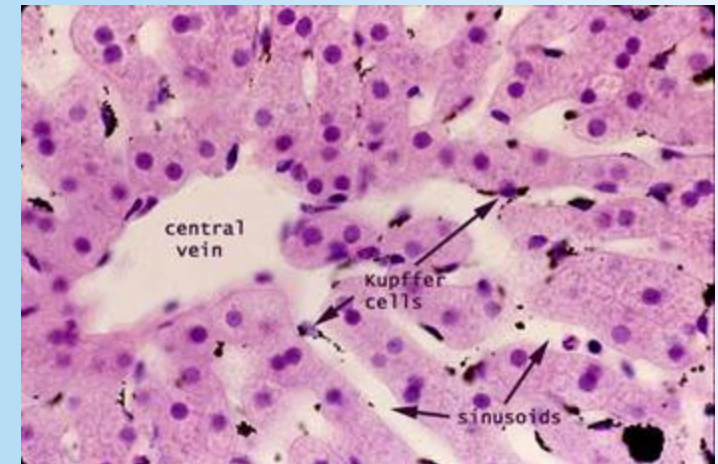


Fatty liver

Alcoholic steatohepatitis

- Continued exposure to alcohol and acetaldehyde disrupts liver function
- Continuous oxidative stress leads to inflammation
- Kupffer cells release proinflammatory cytokines which further inflammation

Kupffer cells



Alcoholic steatohepatitis

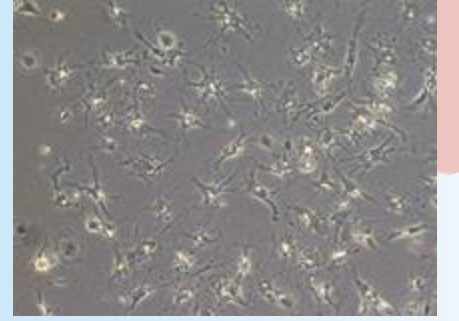
Symptoms

- RUQ pain, fever, jaundice
- Reversible with abstinence

Liver function tests

ALT < AST

Fibrosis and cirrhosis



Stellate cells become activated



Production of type 1 and type 3 collagen



Fibrous septa formation in the liver



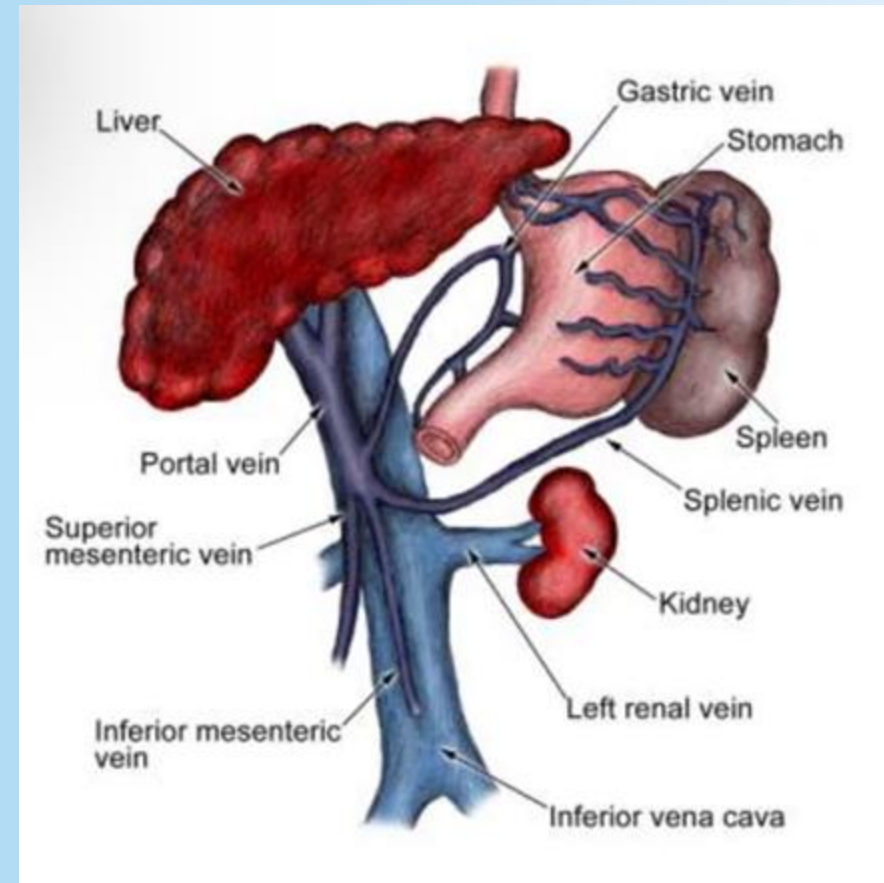
Fibrosis and cirrhosis

Fibrosis and cirrhosis

- RUQ pain
- Hepatomegaly
- Fatigue and weakness

Fibrosis and cirrhosis

- RUQ pain
- Hepatomegaly
- Fatigue and weakness
- Portal hypertension



Fibrosis and cirrhosis

- RUQ pain
- Hepatomegaly
- Fatigue and weakness
- Portal hypertension
- Esophageal varices



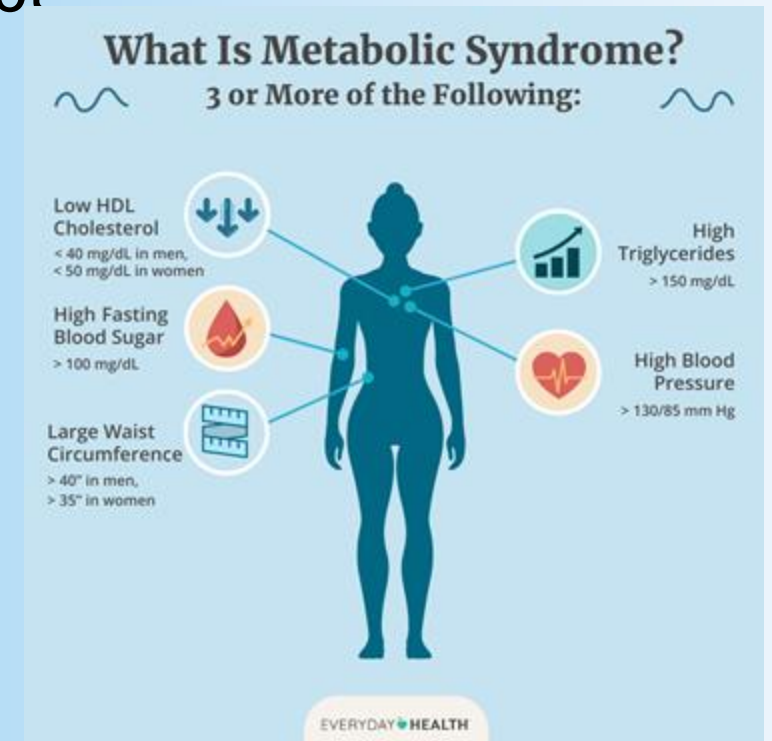
Fibrosis and cirrhosis

- RUQ pain
- Hepatomegaly
- Fatigue and weakness
- Portal hypertension
- Esophageal varices
- Ascites
- Increased risk of bleeding



Non-alcoholic fatty liver disease

- Occurs in people who consume little to no alcohol
- Strongly associated with metabolic syndrome
- Insulin resistance



Non-alcoholic fatty liver disease

Insulin resistance



Increased free fatty acids in the liver



Fat deposition in liver



Steatosis



Liver is more vulnerable to oxidative damage, mitochondrial dysfunction and inflammation

Non-alcoholic fatty liver disease

- Mostly asymptomatic
- Cirrhosis develops silently over time
- Fatigue, mild RUQ pain, elevated LFTs

ALT > AST

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QUESTIONS?