

- Physiological functions of the liver.
- Describe the major functions of the liver with respect to metabolism, detoxification & excretion of hydrophobic substances.
- Describe the formation of bile, its constituents & its role in the excretion of cholesterol & bilirubin.
- Outline the mechanism by which the liver contributes to whole body ammonia.
- homeostasis & the consequences of the failure

of these mechanisms, particularly for brain function.

- Identify the mechanisms that permit normal functioning of the gall bladder & the basis of gallstone disease.
- Anatomy of the Liver
- Consists of 2 lobes divided by falciform ligament
- There is no known difference between the lobes
- Liver
- Basic structural unit is – lobule, made of ramifying

columns of hepatic cells. These hepatocytes are tunneled by a communicating system called – blood sinusoids which are lined by fenestrated endothelial cells. The endothelial cells contain Kupffer cells

- Portal vein and hepatic artery both empty into the sinusoids. Sinusoids open into central vein.
- Liver
- Vascular organ
 - Hepatic artery
 - Supplies O₂ rich blood from heart to liver

- Provides 20-30% of blood supply to liver
- Portal vein
 - Supplies nutrient rich blood from the digestive tract
 - Provides 70-80% of blood to liver
- Biliary system
- Bile is formed in tiny vacuoles in hepatocytes and is discharged into bile canaliculus.
- Canaliculi bile duct at portal triad (interlobular duct)
interlobar duct rt & left
hepatic duct joins cystic duct from gall bladder

joins pancreatic duct opens
at 2nd part of duodenum

- Functions of Liver
- Synthetic functions: plasma proteins, clotting factors, enzymes(SGOT,SGPT), urea
- Metabolic functions: Carbohydrates, fats, proteins, synthesis of – lipoproteins-HDL,LDL,VLDL
- Bile secretion: (bile salts&acids formation)
- Detoxification & protective
- Immunity –kupffer cells,Miscellaneous
- Synthesis

- Synthesize many biological compounds
 - **Carbohydrates**
 - Metabolism important
 - Uses glucose for its own cellular energy
 - Circulates glucose to peripheral tissue
 - Stores glucose as glycogen
 - Major player in maintaining stable glucose concentration due to glycogenesis, glycogenolysis and gluconeogenesis
 - Thus synthesis, storage and release of glucose
 - **Synthesis**
 - **Lipids**
 - Liver gathers free fatty acids from diet and breaks them down to Acetyl- CoA to form(non esterified fatty acids-to-

esterified FA-to-) triglycerides,
phospholipids or cholesterol

- Converts insoluble lipids to soluble forms
- 70% of cholesterol produced by the liver
- Thus both degradation and synthesis of fats takes place in the liver.
- Synthesis of HDL, LDL, VLDL
- **Proteins**
 - **Proteins**
 - Almost all proteins made in the liver.
 - Synthesis of enzymes and clotting factors
 - Exceptions are immunoglobulins and hgb
- **Bile secretion**

- Components of bile- bile salts and bile acids are formed by hepatocytes.
- Conjugation of bilirubin occurs in hepatocytes.
- **Detoxification**
- Liver serves as a gatekeeper between the circulation and absorbed substances-
First pass: Every substance absorbed in GI tract passes through liver
- Detoxification includes drugs and poisons, and metabolic products like ammonia, alcohol, and bilirubin
- 3 mechanisms
 - Binds material reversibly to inactivate.
 - Chemically modify compound for excretion.
 - Drug metaboliser for detoxification of drugs and poisons.

- Storage
- Glycogen
- Proteins
- Vitamins- B12 & A
- Iron
- Blood
- Others
- Hormonal inactivation:
cortisol, aldosterone, insulin,
glucagon, testosterone.
- Liver is the site for
erythropoiesis during foetal
life.

- Bile

- Is made up of bile salts, bile pigments and other substances dissolved in alkaline electrolyte solution.
- Bile salts are synthesised by hepatocytes and bile pigments are picked up from blood sinusoids.
- Daily secretion: 500 ml.
- Colour: Yellow
- Taste: Bitter
- Biliary system
- Bile is formed in tiny vacuoles in hepatocytes and is discharged into bile canaliculus.

- Canaliculi bile duct at portal triad (interlobular duct)
interlobar duct rt & left
hepatic duct joins cystic duct from gall bladder
joins pancreatic duct opens at 2nd part of duodenum
- Composition of bile
- Liver bile
- Water= 97.5gm/dl
- Bile salts= 1.1g/dl
- Bilirubin= 0.04g/dl
- Cholesterol=0.1g/dl
- Fatty acids=0.12g/dl
- Lecithin=0.04g/dl
- Na=145mEq/l
- K=5

- Ca=5 & cl= 100
- Gall bladder bile
- 92g/dl
- 6
- 0.3
- 0.3-0.9
- 0.3-1.2
- 0.3
- 130
- 23
- 23 & 25
- Bile acids
- Bile acid :Primary bile acids are produced by hepatocytes from cholesterol. They are cholic

acid & chenodeoxycholic acid.

- They reach duodenum through bile and in the small intestine and colon they are converted into secondary bile acids- deoxycholic acid and lithocholic acid by bacterial action.
- Bile salts
- Bile acids are first conjugated with taurine and glycine and then they form bile salts in combination with Na or K= Sodium taurocholate & glycocholates and

Potassium taurocholate and glycocholate.

- Functions of bile salts
- Emulsification and digestion of fats.
- Stimulate formation of bile by hepatocytes=choleretic action
- Stimulate release of bile from gall bladder=cholegauge action
- Absorption of fats
- Laxative action
- Form route for removal of cholesterol
- Bile pigments

- They are excretory products in the bile.
- Formed by breakdown of Hb in RES.
- Bilirubin is transported to liver along with plasma proteins(= unconjugated).
- Protein get separated and bilirubin gets conjugated with glucuronic acid(= conjugated).
- In intestine, bacteria act &50%of it is converted to bilinogen.
- Most of bilinogen enters liver through enterohepatic circulation and is re-

excreted through bile. About 5% of urobilinogen is excreted by kidney through urine. Some unabsorbed part is excreted through feces as stercobilinogen. This gives yellow color to urine and feces.

- **Functions of BILE**
- Required for digestion and absorption of fats :
 - A) Emulsification of fat and formation of micelle.
 - B) Active pancreatic lipase helps in digestion
- Absorption of fat soluble vitamins
- Choloretic and cholegauge action
- Endogenous synthesis of bile salts
- Bacteriostatic action

- Major route for loss of cholesterol from body
- Lubricating function due to mucus
- Alkaline helps in neutralizing acid chyme.
- Enterohepatic circulation
- About 94% of bile salts are reabsorbed into the blood from the small intestine(by diffusion in early part of intestine & by active transport from distal ileum). They then enter the portal blood and pass back to the liver. On reaching the liver, these bile salts are absorbed almost entirely

back into the hepatic cells
and are

re excreted into the bile.

In this way about 94% of all
bile salts are re circulated
into the bile, so that on the
average these salts make
the entire circuit some 17
times before being carried
out in the feces. The small
quantities of bile salts lost in
to the feces are replaced by
new amount formed
continuously by liver cells.
This recirculation of bile
salts is called enterohepatic
circulation. Necessary

because of limited pool of bile salts

- Ammonia Metabolism & Excretion.
- Ammonia must be carefully controlled because it is toxic to the CENTRAL NERVOUS SYSTEM & freely permeable across the BLOOD BRAIN BARRIER.
- The liver is the only organ in which the complete urea cycle(Kerbs) is expressed.
- Sources-Colon,Kidney,RBC lysis,Muscle metabolism.

- Hepatocytes Carbamoyl Phosphate

Ornithine-Citrulline

Arginine

/

Urea

/

Excreted
through kidney.

- Liver Failure.

Ammonia concentration increases leads to liver encephalopathy.

/

leads to Central Nervous System

impairment(Confusion,Disorientation,loss of Cognition-Memory,COMA.)

- Treatment
- Reducing load to liver by feeding non absorbable carbohydrate-lactulose it traps luminal ammonia.
- Liver transplant.

- Artificial liver assist devices that could clean the blood.
- Gall bladder
- It is sac like structure where bile is stored in between the meals. Has capacity to absorb H₂O and HCO₃
- Functions: Storage
- Concentration of bile(50times)
- Secretes mucus
- Releases bile into duodenum at a controlled rate/according to the need.
- Gallstones

- Estimated that 20 million people in USA have gallstones.
- Deposition of cholesterol or bilirubin in the gallbladder or in common biliary duct.
Cholesterol stones are the common type in Western countries.
- About 1/3 of patients will get episodes of pain in the epigastric region.
- Treatment is cholecystectomy (gall bladder removal) or sometimes endoscopic approaches to remove stones from common biliary duct or sphincter of Oddi.
- Consequence of gall bladder removal is inability to

concentrate bile, which affects fat absorption, and fatty meals may need to be avoided.

- **Summary**

- **Liver: Bile Production.**
Enterohepatic circulation – recycling

Ammonia Metabolism-Liver Encephalopathy.

- **Gallbladder: Bile Concentration and controls release**
- **CCK is a major regulator**
- **References:- Guyton & Hall, 12th edition.**

- Ganong-24th edition.
- Internet.

THANK YOU.