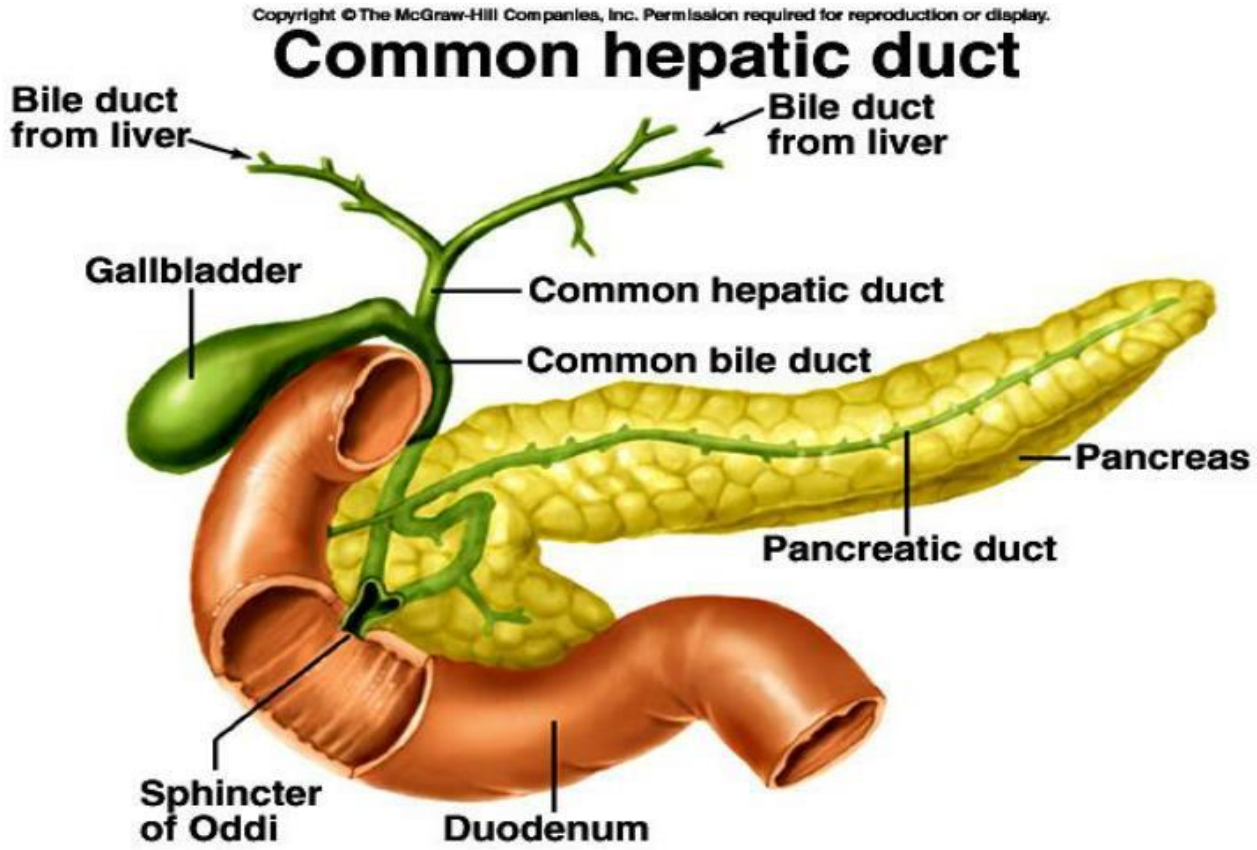
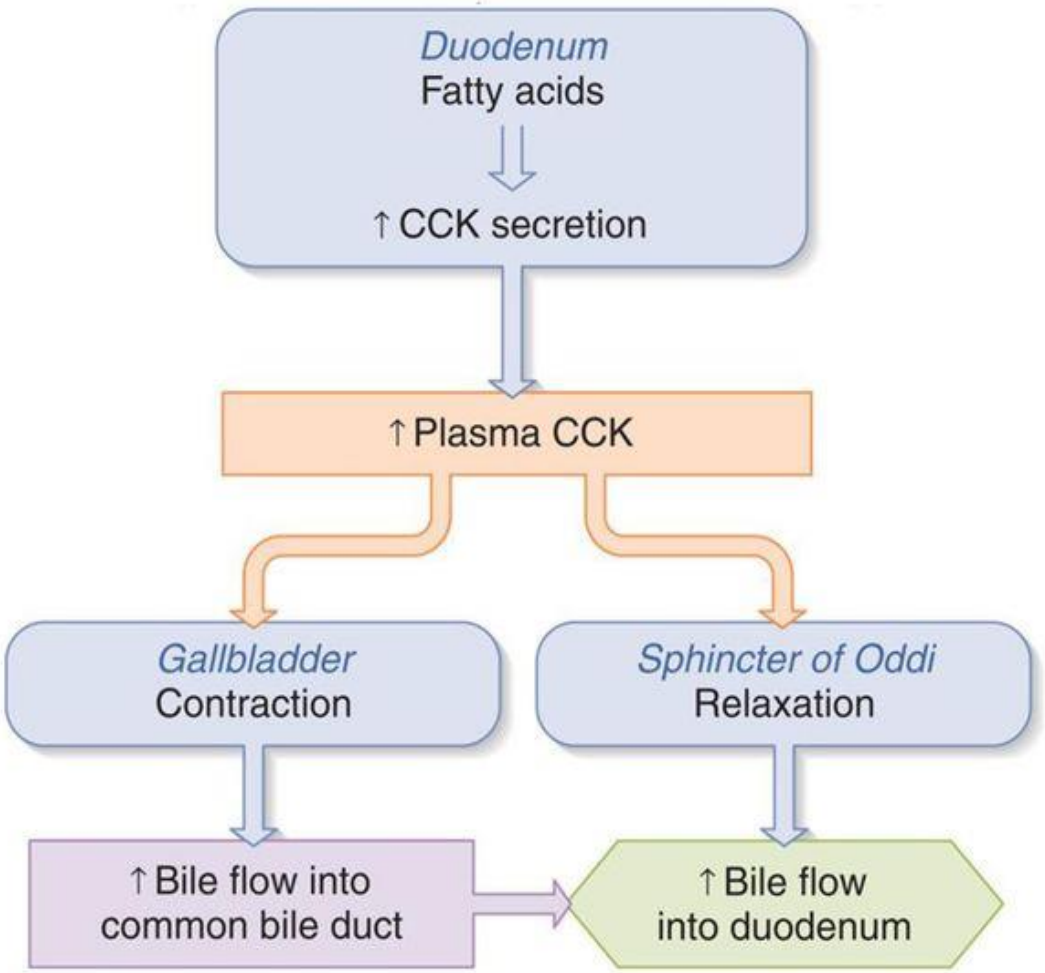
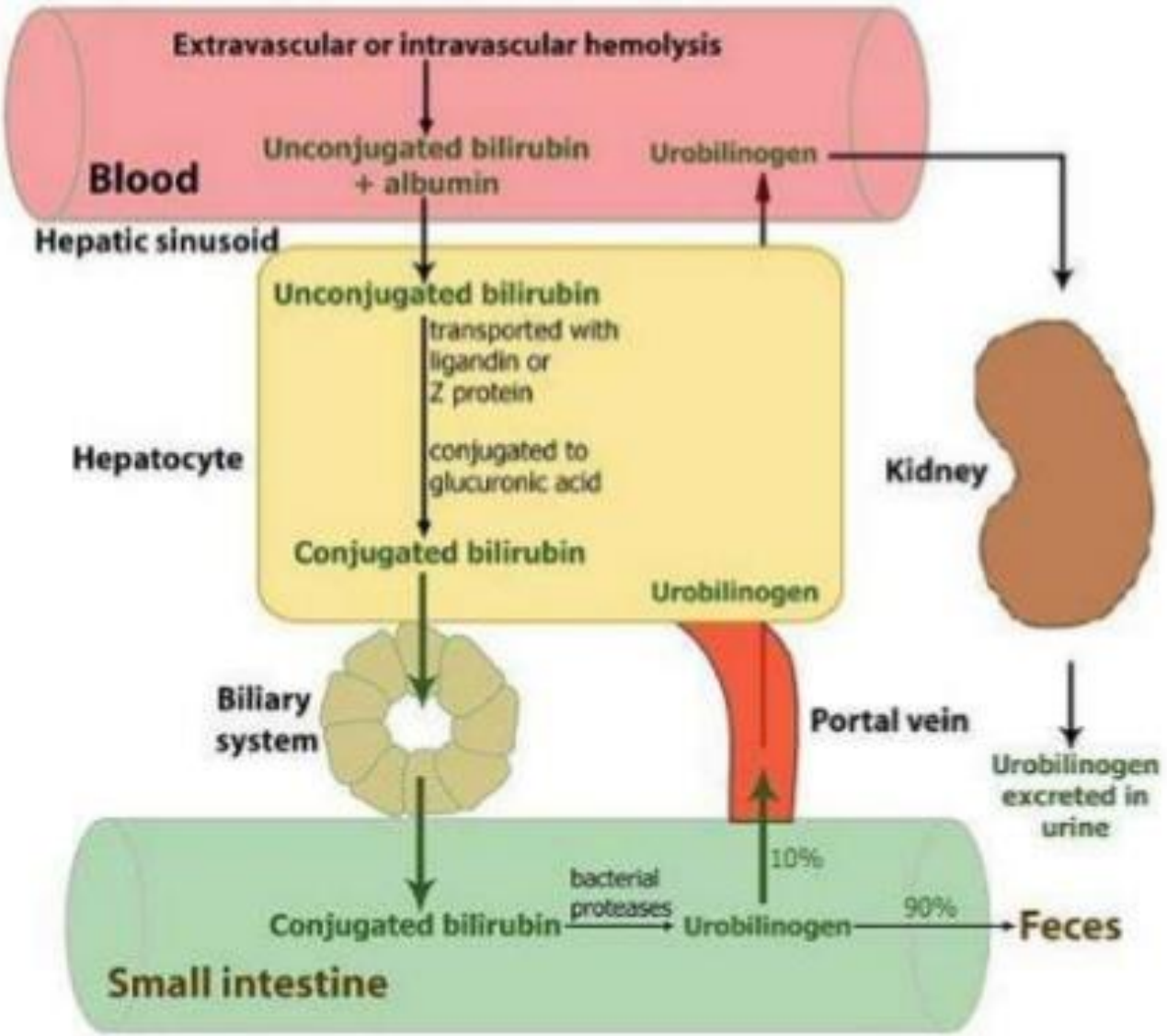
Biliary secretion lecture for second year students by Dr Riffat Sultana



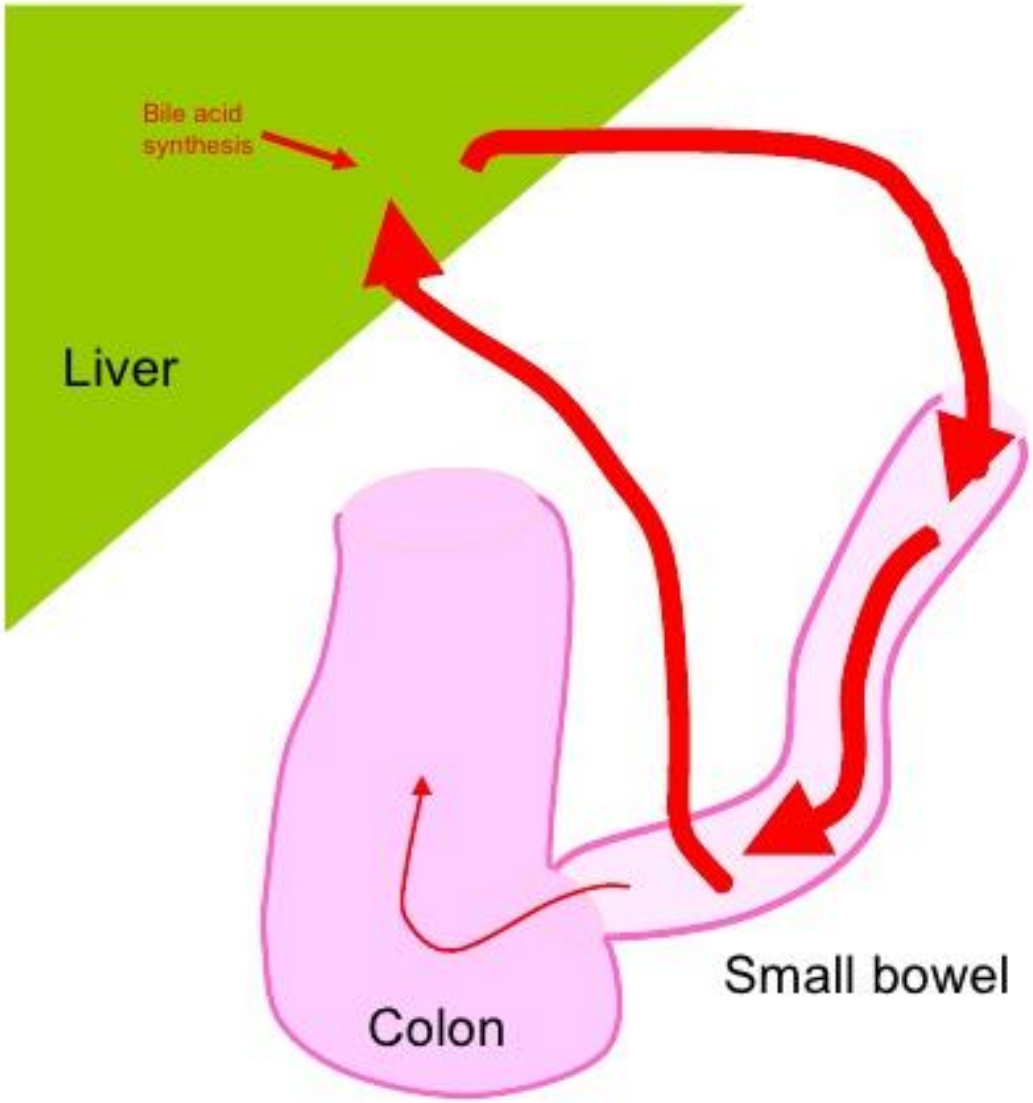
Function of CCK on biliary secretion



Bile formation



Enterohepatic Circulation of Bile Acids: recycling is efficient



Bile acids cycle between the liver and the small intestine.

Total bile acid pool is about 3 grams.

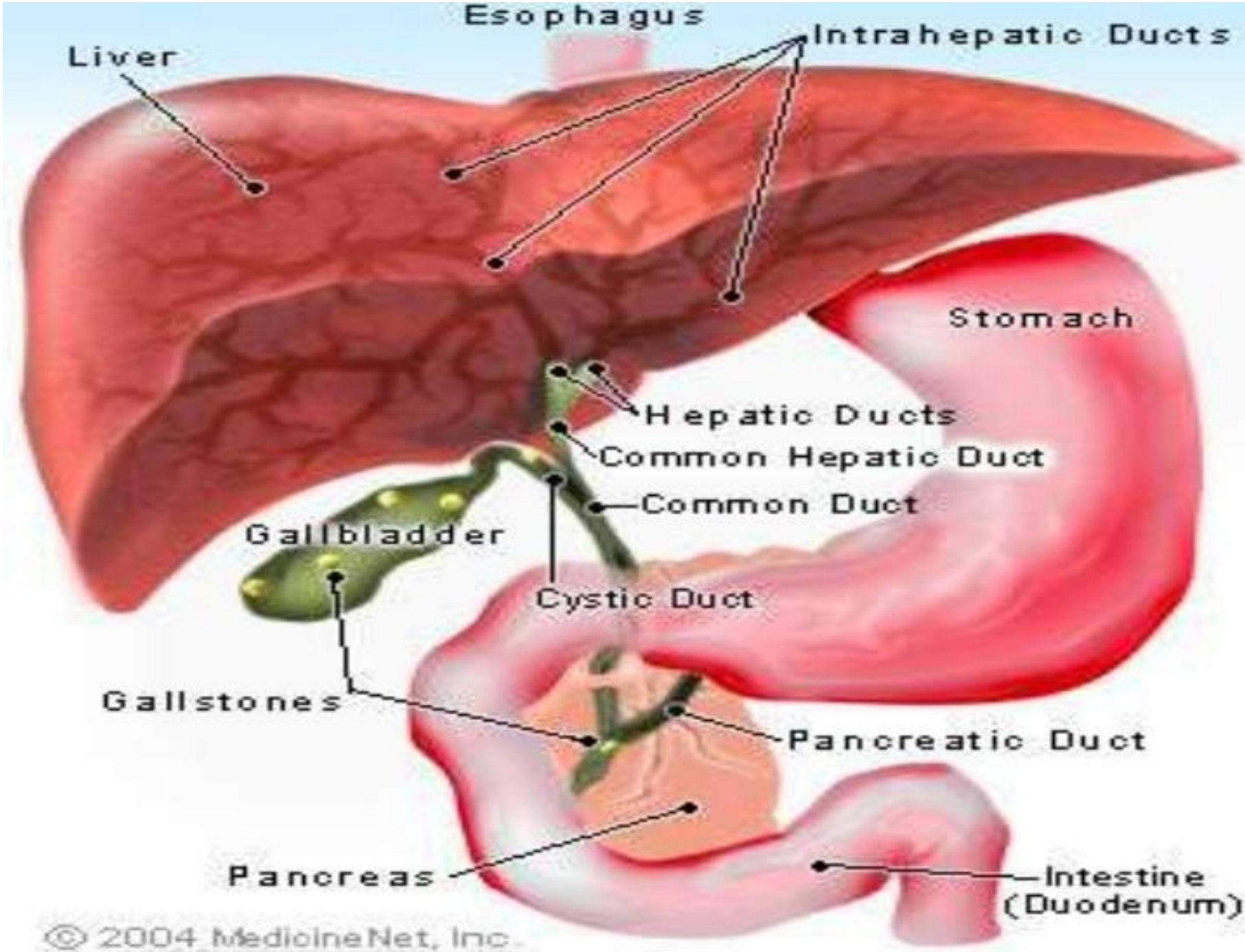
About 90% of bile acids are reabsorbed in the terminal ileum.

However about 5-10% of bile acids are lost daily into the colon. Effect?

Liver synthesizes about 5-10% of the total bile acid pool each day.

- **Bile** is a bitter-tasting, dark green to yellowish brown fluid, produced by the liver.

- **Bile** aids the process of digestion of lipids in the small intestine.
- bile is stored in the gallbladder and upon eating is discharged into the duodenum.
- Bile is a composition of the following materials: water (85%), bile salts (10%), pigments (3%),
- fats (1%), inorganic salts (0.7%) and cholesterol (0.3)


Esophagus
Intrahepatic Ducts
Liver
Stomach
Hepatic Ducts
Common Hepatic Duct
Common Duct
Gallbladder
Cystic Duct
Gallstones
Pancreatic Duct
Pancreas
Intestine
(Duodenum)
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- The secretion of bile can be considered to occur in two stages:

1. Hepatocytes secrete bile into canaliculi, from which it flows into bile ducts. This hepatic bile contains large quantities of bile acids, cholesterol and other organic molecules.
2. As bile flows through the bile ducts it is modified by addition of a watery, bicarbonate-rich secretion from ductal epithelial cells.

- **The gall bladder stores and concentrates bile.**

bile is concentrated five-fold in the gall bladder by absorption of water.

COMPOSITION

- Daily secretion : 500 – 1000 ml
- Transparent alkaline fluid, light yellow in colour.
- pH : 7.8 – 8.6
- Water
- Bile Salts – These are sodium & potassium salts of bile acid.
- Bile pigments –These are biliverdin & bilirubin.
- lecithin
- Fats
- Fatty acids
- Cholesterol
- Enzyme Alkaline Phosphatase
- Electrolytes
  1. Anion – Cl- , Hco3-
  2. Cation – Na+, K+, Ca+2

Bile Salts

- These are synthesized in liver from cholesterol.
- **Primary bile acids** – Cholic acid & Chenodeoxy cholic acid.
- Conjugation – bile acids get conjugated in liver with Taurin & choline.

1. Cholic Acid + Taurine = Taurocholic Acid
2. Cholic Acid + Glycine = Glycocholic acid

- Conjugated 'Tauro' and 'Glyco' cholic acid form sodium & Potassium Salt in bile.

- Sodium tauro cholate & potassium taurocholate.
- These are K/a Bile Salts.

- Cholic acid & **Chenodeoxy cholic acid, in colon acted upon by colon Bacteria to form Deoxy cholic acid & lithocholic acid.**
- **These are k/a <u>Secondary Bile acids.</u>**

Entero Hepatic Circulation of Bile salts

- 90 – 95 % of Bile salts which enter in to duodenum are absorbed back in to Portal Vein.
- Return back to liver.
- This is k/a Entero Hepatic Circulation of Bile salts.

- Remaining 5 – 10 %, enter the colon acted upon by colon Bacteria to form Deoxy cholic acid & lithocholic acid.

- Total bile salts – 3.5 gms.
- Recycle repeatedly via Entero Hepatic Circulation.

- An ordinary meal needs 6 – 8 gm of bile salts to digest & absorb fats.
- Total bile salts circulate twice during digestion of each meal.

Bile pigment

- Bile pigments are bilirubin & biliverdin.
- These are formed from globin part of Haemoglobin (Hb) after destruction of old RBCs.
- No functional importance. Excreted in bile.
- Responsible for yellow color of bile.

- Bile acids are amphipathic,
- they contain both hydrophobic (lipid soluble) and polar (hydrophilic) faces.
- The cholesterol - derived portion of a bile acid hydrophobic ; the amino acid derived portion and hydrophilic.

- Their amphipathic nature enables bile acids to carry out two important functions:

1. Emulsification of lipid aggregates

- Bile acids have detergent action on particles of dietary fat.
- **Emulsification** causes fat globules to break down or be emulsified into minute, microscopic droplets.
- Emulsification greatly increases the surface area of fat
- make it available for digestion by lipases, which cannot access the inside of lipid

2. Solubilization and transport of lipids in an aqueous environment:

- Bile acids are lipid carriers.
- Bile acids are able to solubilize many lipids by forming **micelles.**
- **Micelles are** aggregates of lipids such as fatty acids, cholesterol and monoglycerides - that remain suspended in water.
- Bile acids are also critical for transport and absorption of the fat-soluble vitamins.

3. Role of Bile Acids in Cholesterol metabolism

- Hepatic synthesis of bile acids accounts for the majority of cholesterol breakdown in the body.
- In humans, 500 mg of cholesterol are converted to bile acids and eliminated in bile every day.
- This route for elimination of excess cholesterol is probably important in all animals, but particularly in situations of massive cholesterol ingestion

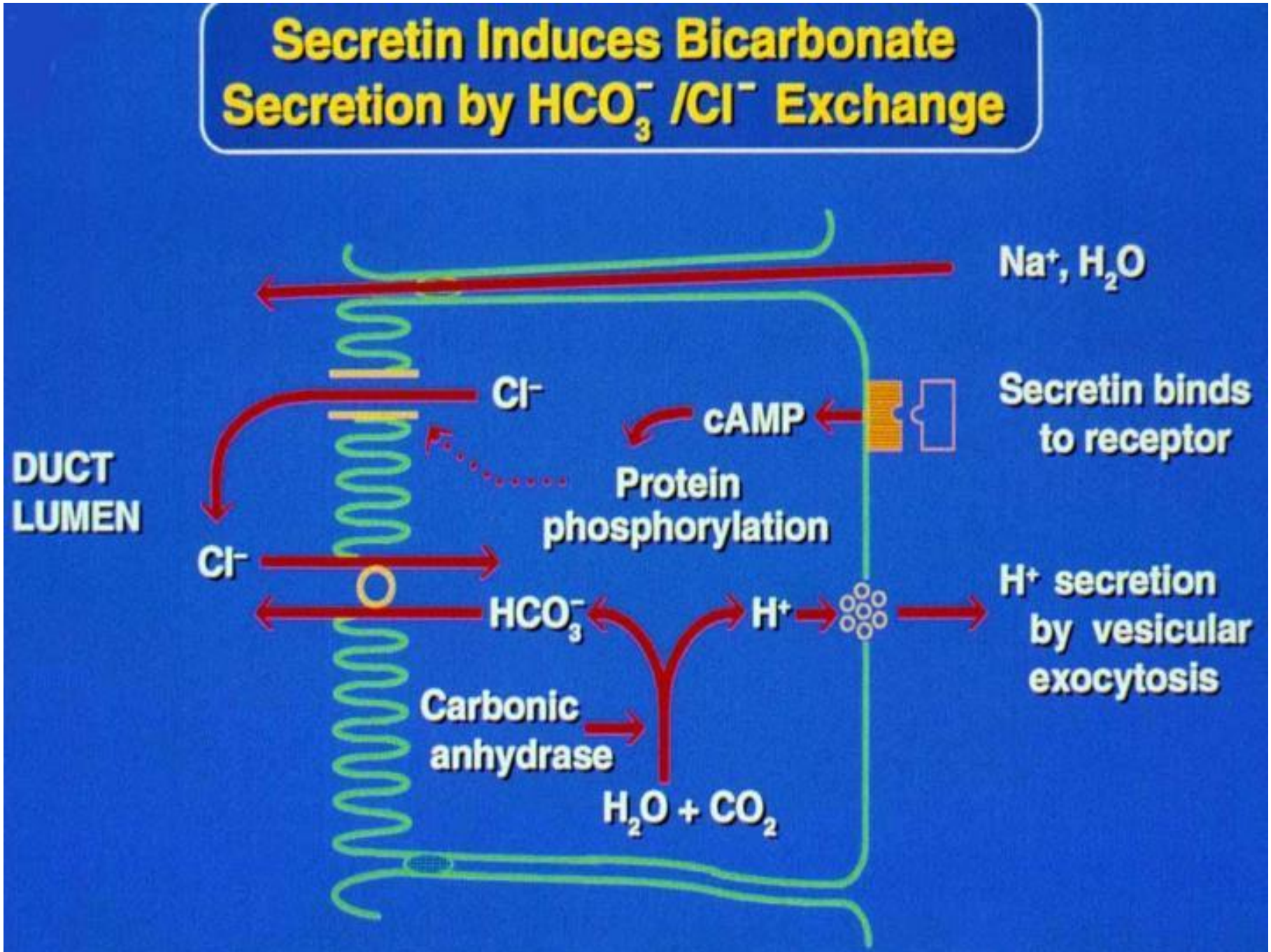
- The flow of bile is lowest during fasting, and is diverted into the gallbladder for concentration.
- When chyme enters the small intestine, acid and partially digested fats and proteins stimulate secretion of cholecystokinin and secretin.
- these enteric hormones are important for secretion and flow of bile:

Cholecystokinin

- The name of this hormone describes its effect on the biliary system –
- cholecysto = gallbladder and kinin = movement.
- The stimulus for release of cholecystokinin is the presence of fat in the duodenum.
- It stimulates contractions of the gallbladder and common bile duct, resulting in delivery of bile into the gut.

Secretin

- This hormone is secreted in response to acid in the duodenum.
- Its effect on the biliary system is very similar to what was seen in the pancreas –
- it stimulates biliary duct cells to secrete bicarbonate and water,
- which expands the volume of bile and increases its flow out into the intestine.


Secretin Induces Bicarbonate Secretion by HCO_3^- /Cl^- Exchange
Na^+, H_2O
Cl^-
cAMP
Secretin binds to receptor
DUCT LUMEN
Protein phosphorylation
Cl^-
HCO_3^-
H^+
H^+ secretion by vesicular exocytosis
Carbonic anhydrase
$H_2O + CO_2$

Gall stones

- An imbalance between these components of bile -- cholesterol, bile salts, and bilirubin -- leads to the formation of gallstones.

- Two types:
1. Cholesterol stones
2. Pigment stones

- Cholesterol is normally kept in liquid form by the dissolving action of the bile salts.

- increased amount of cholesterol in the bile overwhelms the dissolving capacity of the bile salts and leads to the formation of cholesterol gallstones.

- Similarly, a deficiency of bile salts promotes cholesterol gallstone.

- Pigment gallstones
- excessive breakdown of red blood cells
- increased amounts of bilirubin (breakdown product of red cells) in the bile,
- thus causing bilirubin gallstone formation

steatorrhea

- In the absence of bile, fats become indigestible and are instead excreted in feces, a condition called steatorrhea.
- Feces are white or gray, and greasy.
- Steatorrhea can lead to deficiencies in essential fatty acids and fat-soluble vitamins.

Review:
Components of Pancreatic Secretion

1. Exocrine
   i. Digestive enzymes
      - Secreted by acinar cells
   i. HCO_3- -
      - Secreted by duct cells
1. Endocrine
   i. Insulin
   ii. Glucagon

Contd.....

Pancreatic Digestive Enzymes

- For digestion of Proteins
  - Trypsin
  - Chymotrypsin
  - Carboxypeptidase
  - Elastase
- For digestion of Carbohydrates
  - Pancreatic Amylase
- For digestion of Fats
  - Lipase
  - Cholesterol Esterase
  - Phospholipase
  - Colipase (Activated by Trypsin)
  - Bile salt activated Lipase

About 1 liter per day

HCO_3^- Secretion by Pancreas

- Functions of HCO_3^- in duodenum

1. To neutralize acidic pH of Stomach as the duodenum cannot resist acidic pH
2. To block the peptic digestive activity of the gastric juices
3. To provide a appropriate pH for pancreatic digestive enzymes

Phases of Pancreatic Secretion

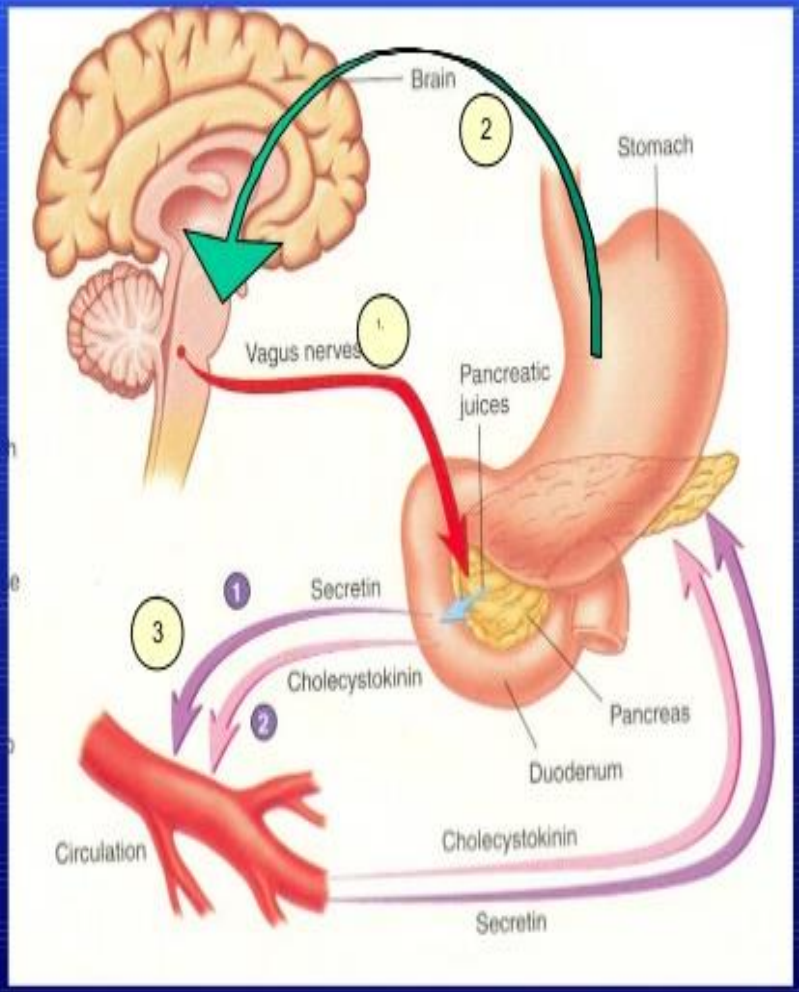
- Three phases:
  - Cephalic phase
  - Gastric phase
  - Intestinal phase.

Phases of Pancreatic juice (Enzymes) secretion

1. **Cephalic** Phase (20%)

2. Gastric Phase (10%)

3. Intestinal Phase (70%)



Prof .Dr. Rashid Mahmood

Cephalic Phase of Pancreatic Secretion

- The same nervous signals from the brain that cause secretion in the stomach also cause acetylcholine release by the vagal nerve endings in the pancreas.
- 20 per cent of the total secretion of pancreatic enzymes
- But little of the secretion flows immediately through the pancreatic ducts into the intestine because only small amounts of water and electrolytes are secreted along with the enzymes.

Gastric Phase of Pancreatic Secretion

- Nervous stimulation of enzyme secretion continues
- Another 5 to 10 per cent of pancreatic enzymes
- But, again, only small amounts reach the duodenum because of continued lack of significant fluid secretion.

Intestinal Phase of Pancreatic Secretion

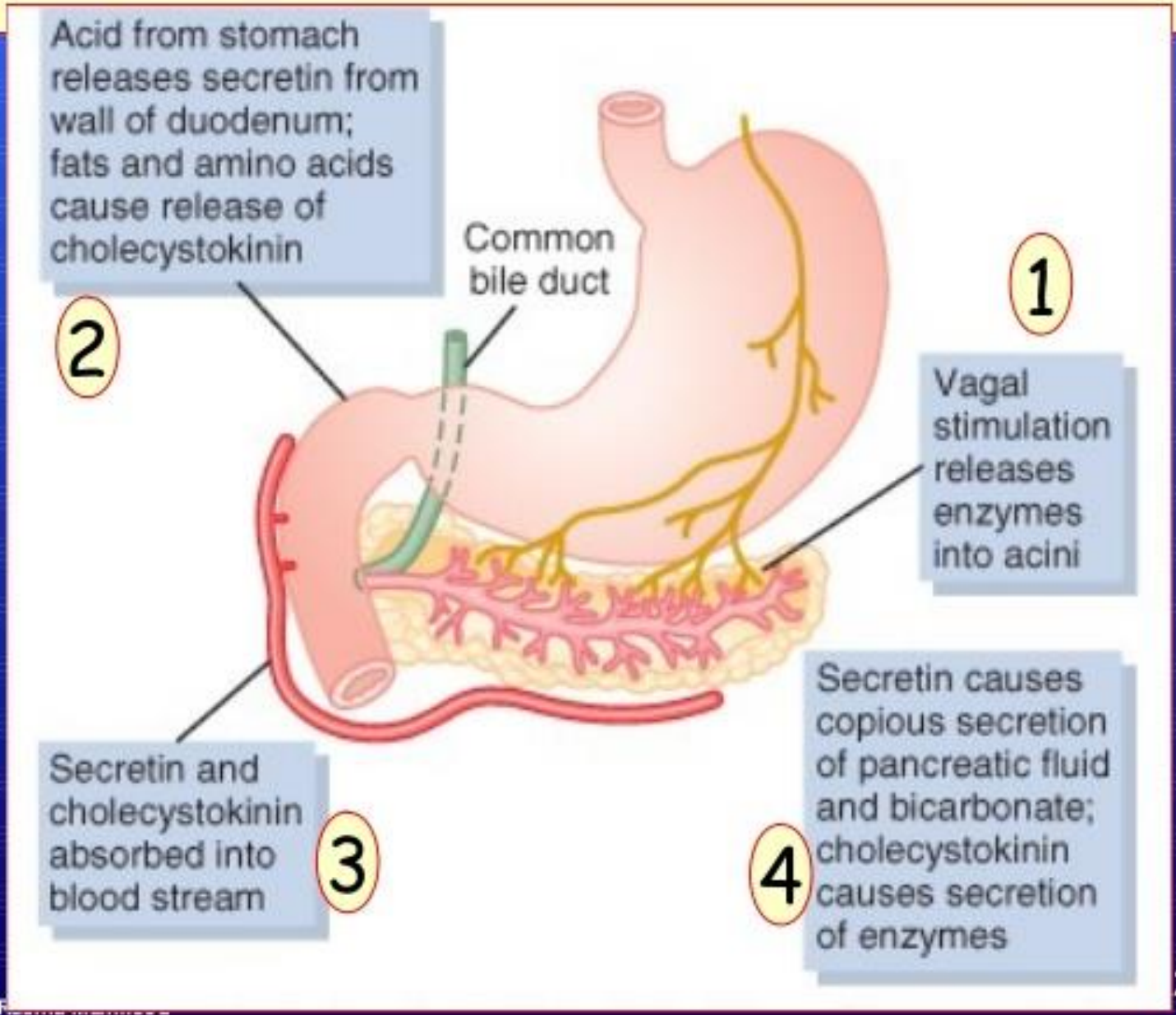
- Chyme enters the small intestine, pancreatic secretion becomes copious, mainly in response to the hormones

1. **Cholecystokinin:** Digestive Enzyme Secretion

   65 to 80 per cent

1. **Secretin:** Secretion of Copious Quantities of Bicarbonate Ions—Neutralization of Acidic Stomach

Regulation of Pancreatic Secretion



Hormonal control of pancreatic secretion

Hormone	Site of secretion	Stimulus	Function
Secretin	"S" cells of duodenum	Acidic gastric juice	1.Mild effect on GIT motility(↓) 2.Pancreatic secretion of bicarbonate 3.Bicarbonate secretion by Bile duct
Cholecys-tokinin	"I" cells of duodenum & jejunum	Digestive products of fats, fatty acids & monoglycerids	•Strong contraction of gall bladder •Inhibition of stomach contraction •Pancreatic secretion of enzymes

Contd…..

Hormonal control of pancreatic secretion