Physiology of *Gastrointestinal System* (L7)

Physiology of Bile Salts & Enterohepatic Circulation

Chapter : 64; pages: 783-786

Dr. Hayam Gad
Associate Professor of Physiology
College of medicine, KSU

Learning Objectives

Functions of the bile and stages of its secretion.

Characteristics and main constituents of bile.

Functions of gall bladder.

Absorption, uptake and functions of bile acids.

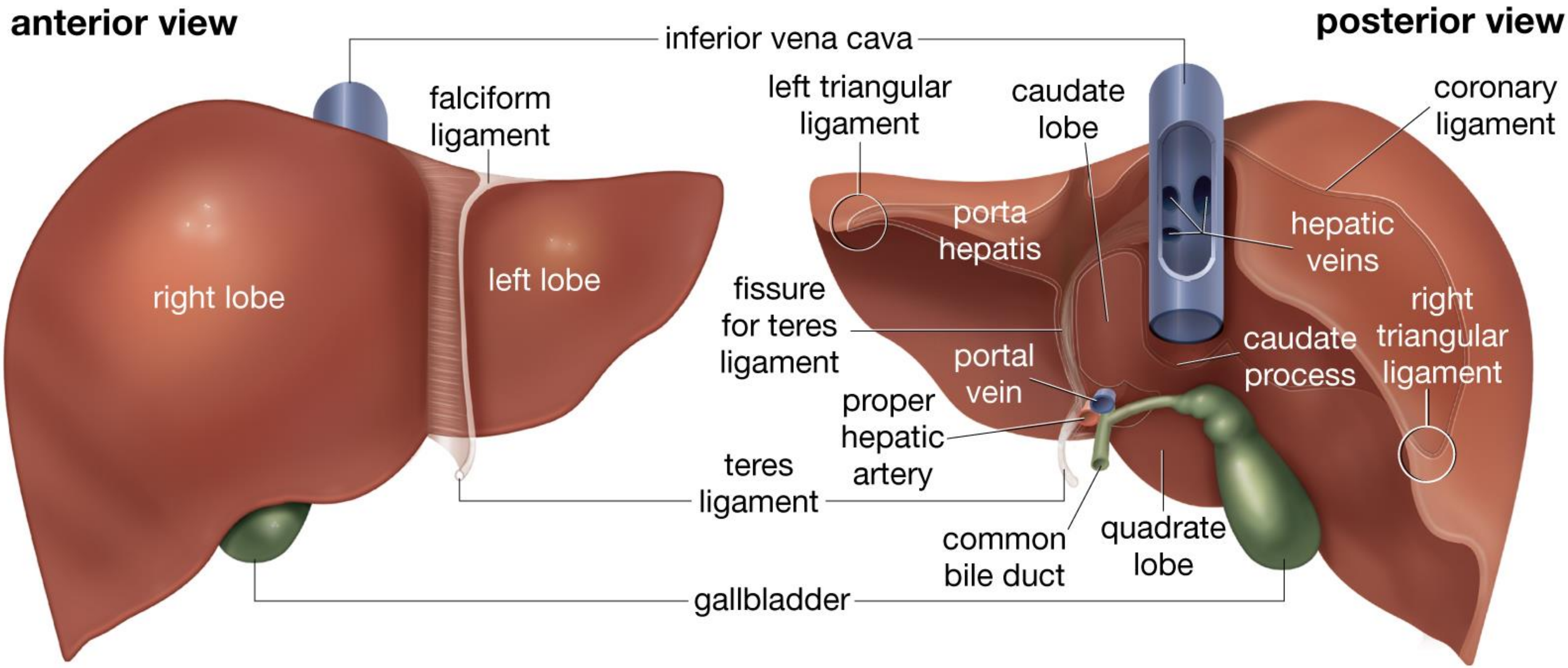
Enterohepatic circulation of bile salts.

Control of biliary system.

The Liver

- The liver is the largest internal organ in the body, constituting about 2.5% of an adult's body weight.
- Receives 25% of the cardiac output via the portal vein and hepatic artery.
- Takes up, stores, and distributes nutrients and vitamins.
- Plays an important role in maintaining blood glucose levels.
- Regulates the circulating blood lipids by the amount of very low–density lipoproteins (LDL) it secretes.
- Synthesizes many of the circulating plasma proteins.
- Takes up numerous toxic compounds and drugs from the portal circulation.
- Performs important endocrine functions.
- Serves as an excretory organ for bile pigments, cholesterol, and drugs.

The Liver


anterior view
posterior view
inferior vena cava
falciform ligament
left triangular ligament
caudate lobe
coronary ligament
porta hepatis
hepatic veins
right lobe
left lobe
fissure for teres ligament
right triangular ligament
caudate process
portal vein
proper hepatic artery
teres ligament
common bile duct
quadrate lobe
gallbladder

The Main Digestive Function Of The Liver

- The main digestive function of the liver is the secretion of bile.
- Bile serves two important functions:

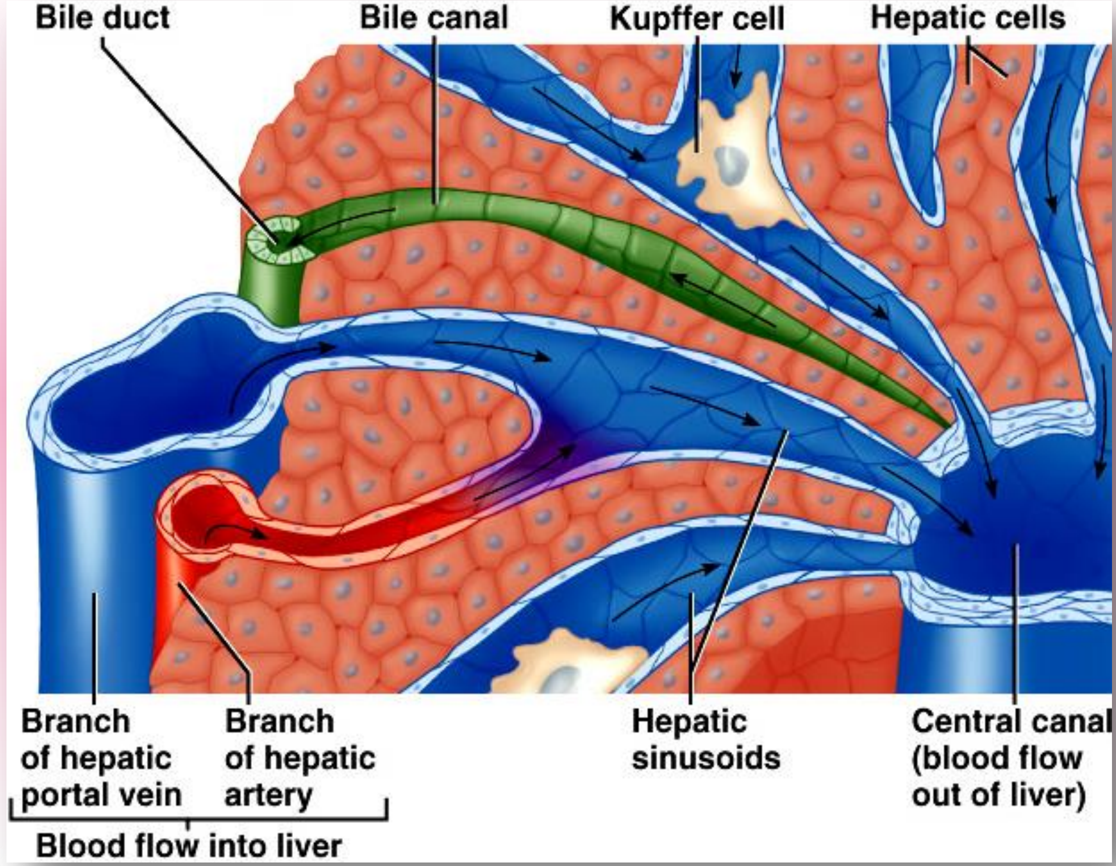
  1- It plays an important role in fat digestion and absorption by its contents of bile salts.

  2- Bile serves as a means for excretion of waste products from the blood. These include especially bilirubinan, end product of hemoglobin destruction.

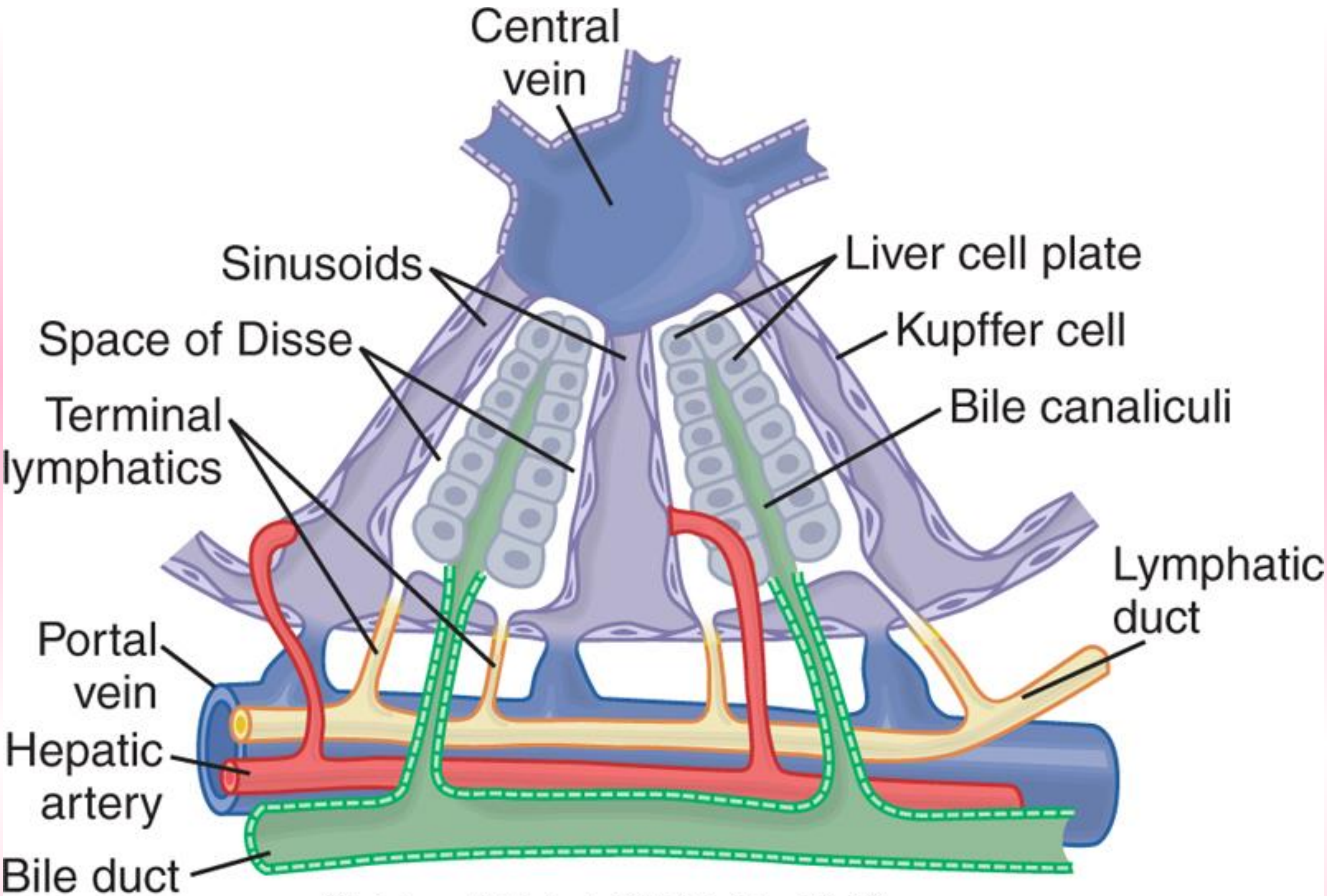
.

Bile is secreted in two stages:

- The initial portion is continually secreted by the hepatocytes.
- It is secreted into bile canaliculi that originate between the hepatic cells.
- Hepatic Bile: Isotonic secretion, with high Na^+, Cl^- and HCO_3^- and low K^+ and Ca^{2+}.
- The bile flows in the canaliculi toward the hepatic duct and common bile duct.



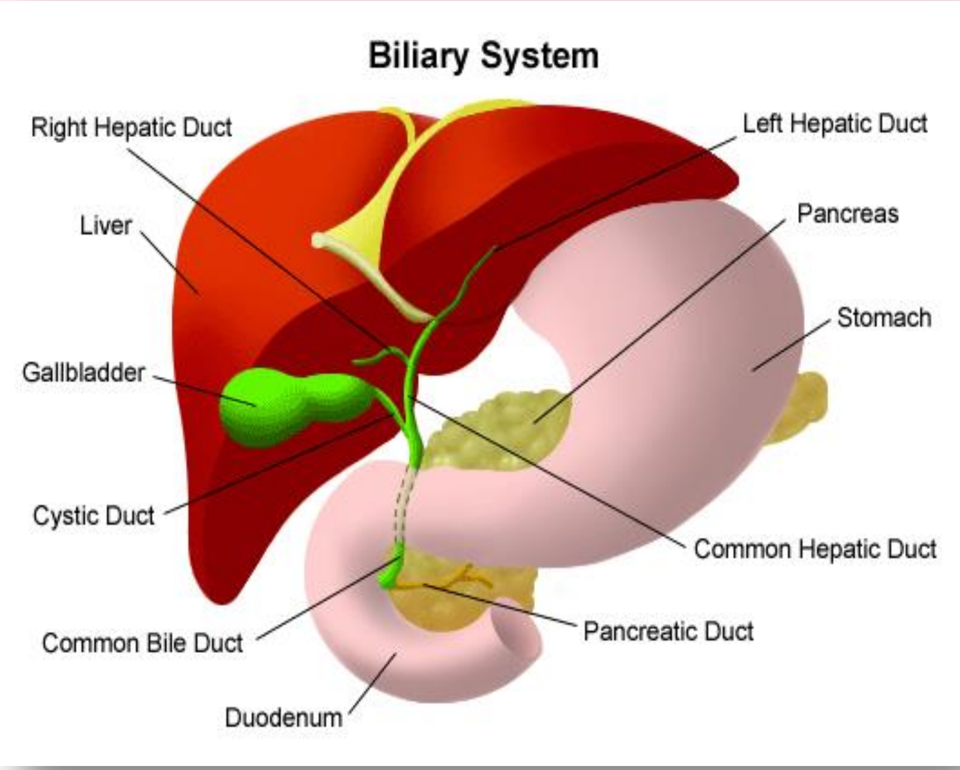
Bile Canaliculi & Ducts



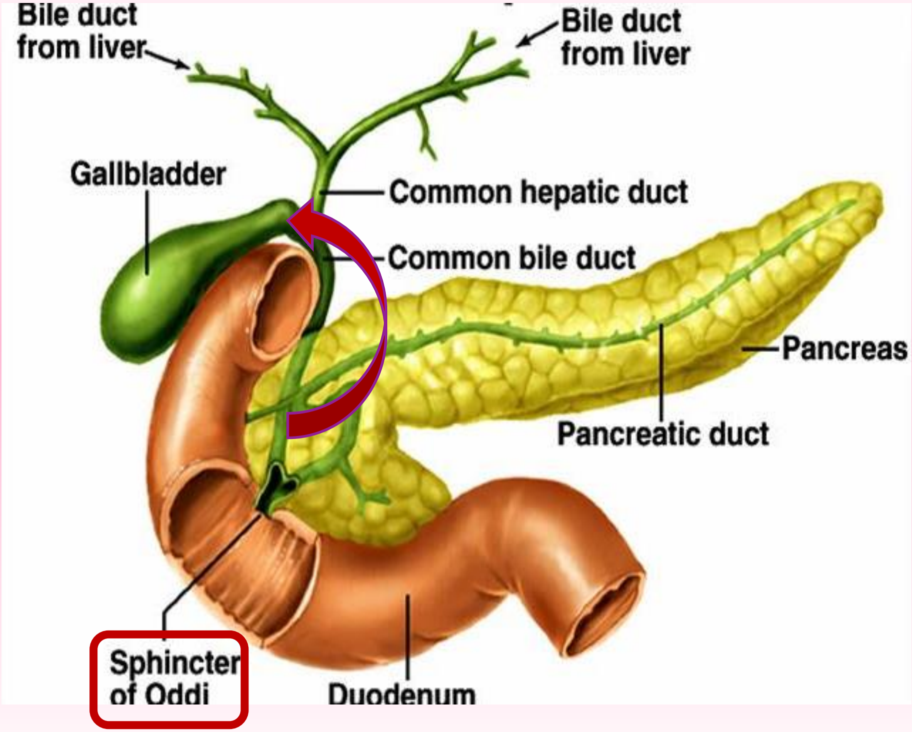
Hall: Guyton and Hall Textbook of Medical Physiology, 12th Edition

Bile is secreted in two stages: (Cont.)

- From the common bile duct, bile either empties directly into the duodenum or is diverted through the cystic duct into the gallbladder
- Gallbladder bile is the second portion which is added to the initial bile secretion.
- Gallbladder bile: high Bile acid anion and Ca^{2+} ; but low Na^{+} , Cl^{-} , HCO_3^{-} and H_2O.



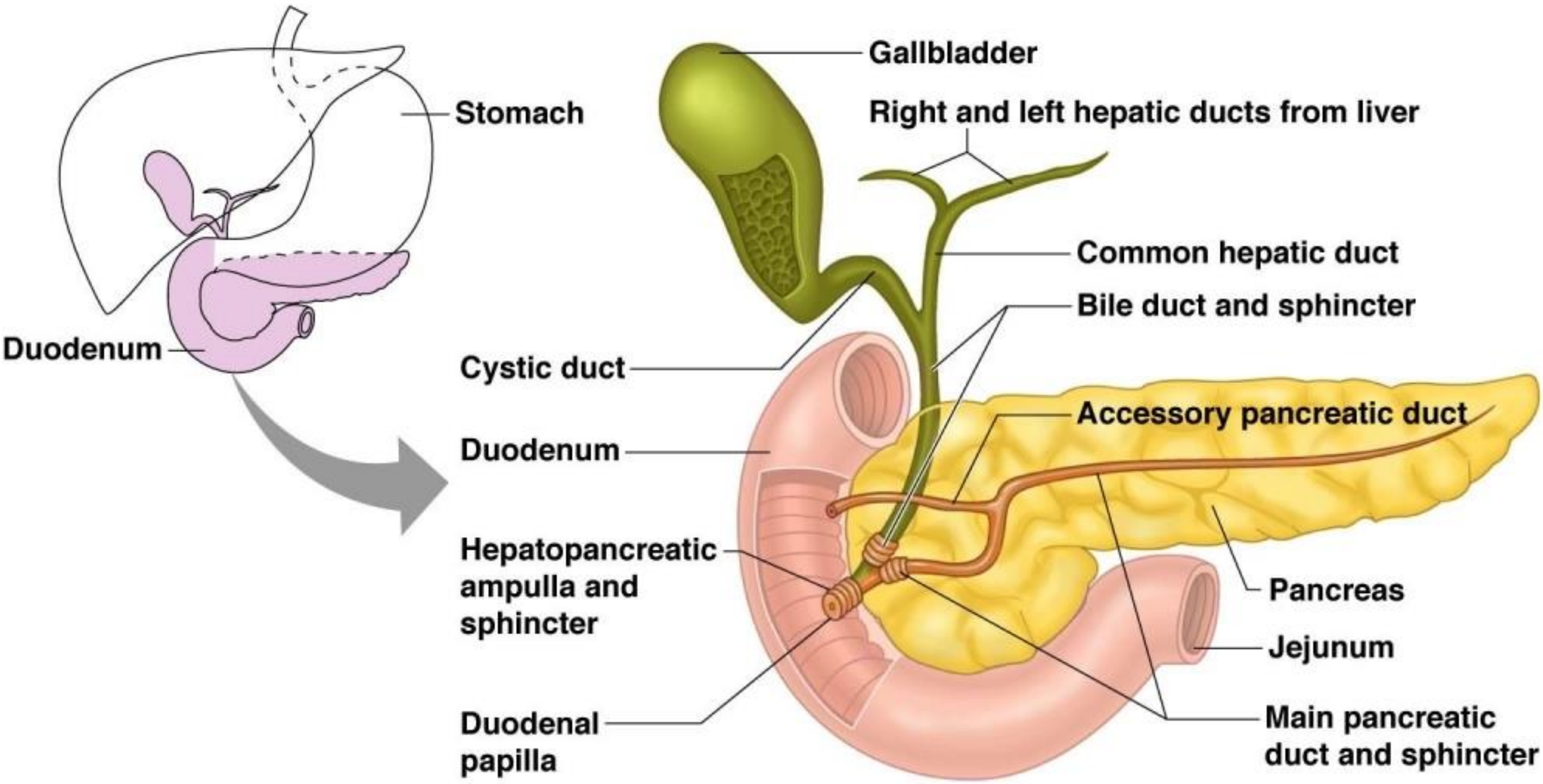
- The common bile duct open into the duodenum in company with the pancreatic duct at the ampulla of vater.
- This opening is guarded by the sphincter of Oddi (choledochoduodenal sphincter).



Differences between hepatic and gallbladder bile

	Hepatic bile	Gall bladder bile
Water	% 98	% 89
Total solids	2-4 %	11 %
Bile salts	26	145
Bilirubin	0.7	5
Cholesterol	2.6	16
Phospholipids	0.5	4
Na^+	145	130
HCO_3^-	28	10
Ca^{++}	5	23
Cl^-	100	25
K^+	5	12
pH	8.3	7.5

The Gallbladder



Characteristics of bile

- Bile is a viscous golden yellow or greenish fluid.
- It is isotonic with plasma and slightly alkaline.
- $NaHCO_3$ in bile is responsible for its alkaline reaction and participates with pancreatic and duodenal secretion in neutralization of acid chyme delivered from stomach.
- The liver produces about 5 L /day, but only 600-1000 ml/day are poured into the duodenum.

What are the components of bile?

From hepatocytes

01 Bile acids (bile salts)
(65% of dry weight of bile)

02 Phospholipids
(As lecithin, 20%)

03 Proteins (5%)

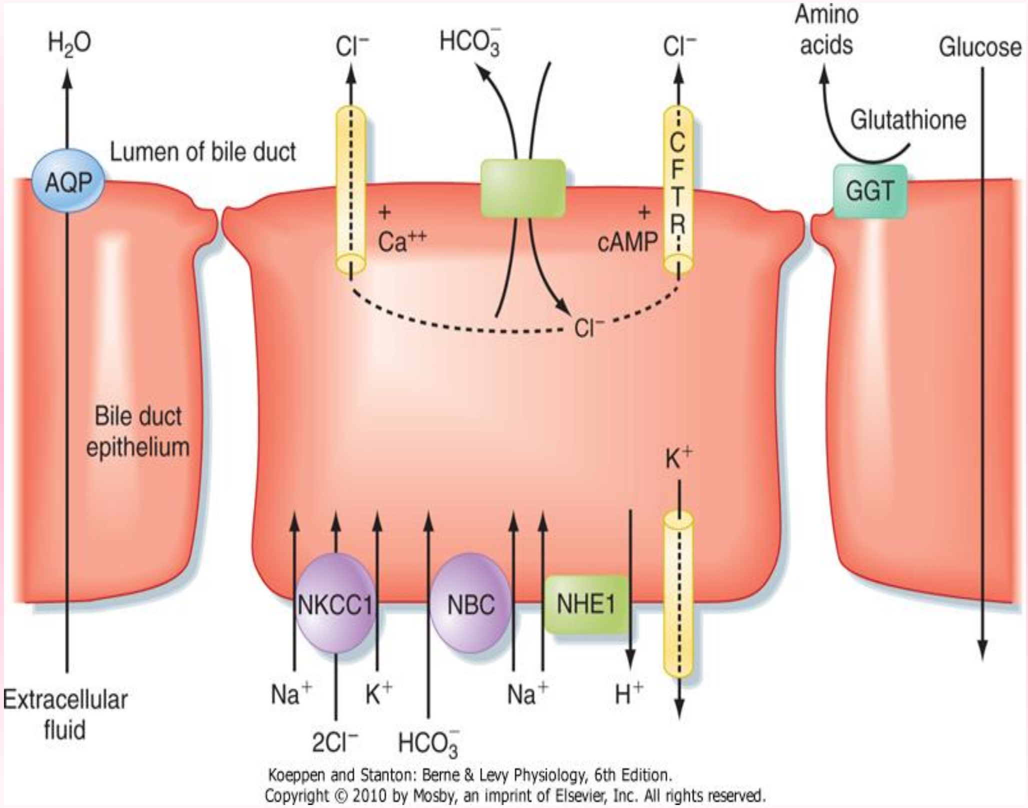
04 Cholesterol
(4%), bile is the major route for cholesterol excretion

05 Bile pigments
(as bilirubin, 0.3%)

What are the components of bile? Cont.

From bile ducts epithelial cells:

- Electrolytes mainly HCO_3^- , in addition to H_2O
- These contribute to the volume of hepatic bile.
- HCO_3^- aids in neutralization of acid chyme.



Composition of bile

From ducts

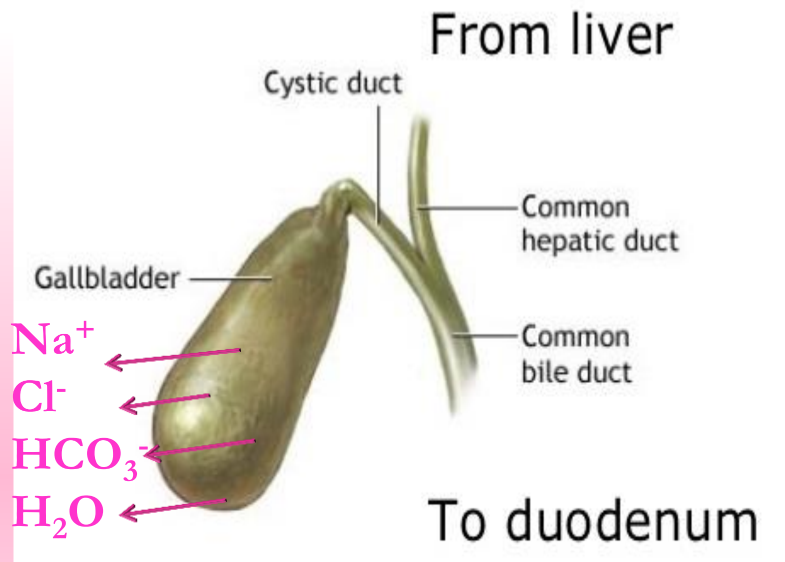
Aqueous alkaline Solution ($NaHCO_3$)

From hepatocytes

Organic constituents

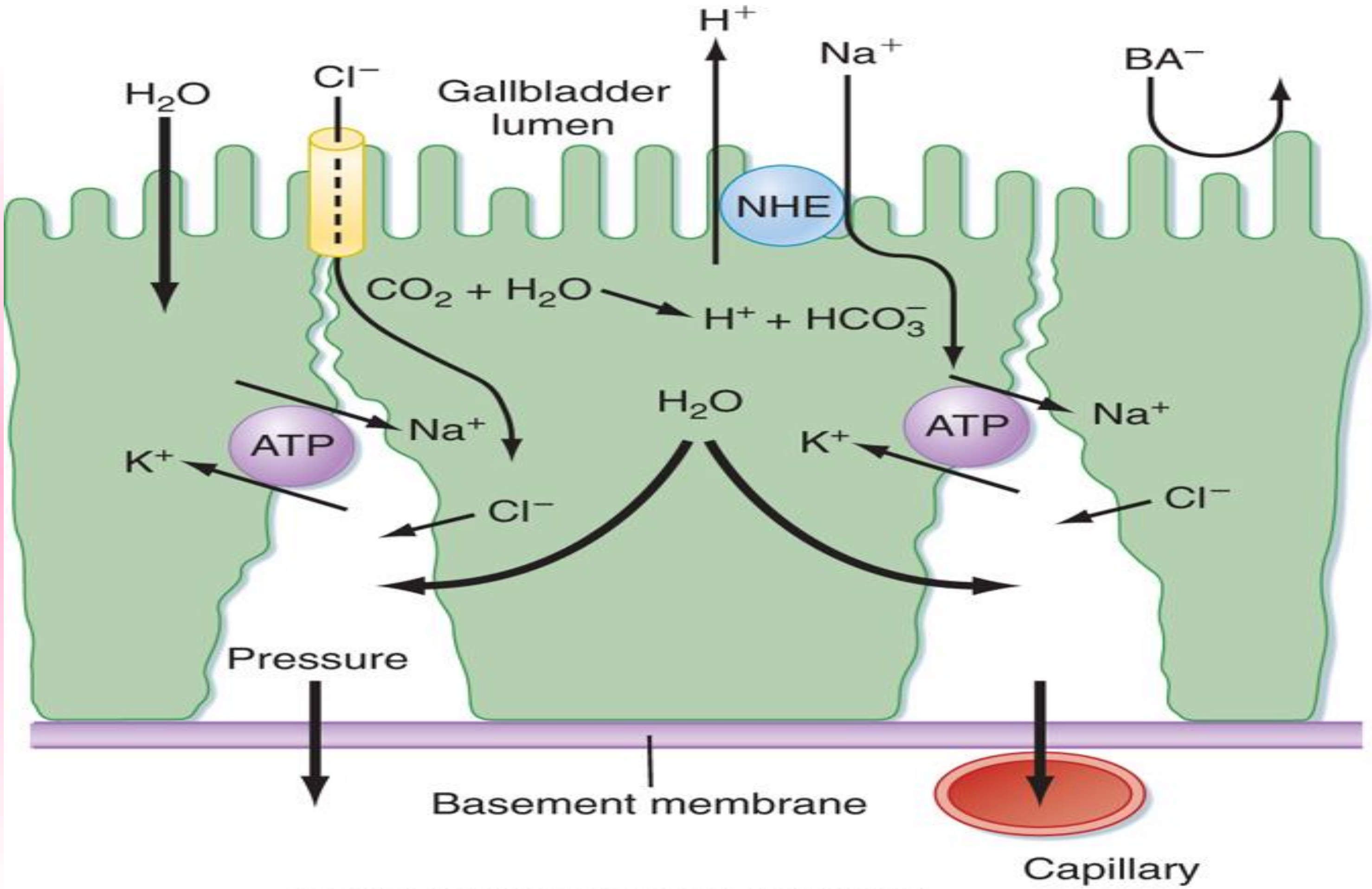
- Bile salts(65%)
- Lecithin (20%).
- Proteins (5%)
- Cholesterol (4%)
- Bilirubin (0.3%)

Storing and Concentrating Bile in the Gallbladder



- Bile is secreted continually by the liver cells and then normally stored in the gallbladder until needed (gallbladder can hold 30 to 60 mL).
- Gallbladder concentrates the bile, during every 12 hours of bile secretion (usually about 450 mL) because Na^+ is actively transport through the gallbladder mucosa.
- Then, followed by secondary absorption of Cl^-, water, and most other diffusible constituents.
- Bile is normally concentrated in this way about 5-fold, but it can be concentrated up to a maximum of 20-fold.

Concentration of Bile During Storage in The Gallbladder



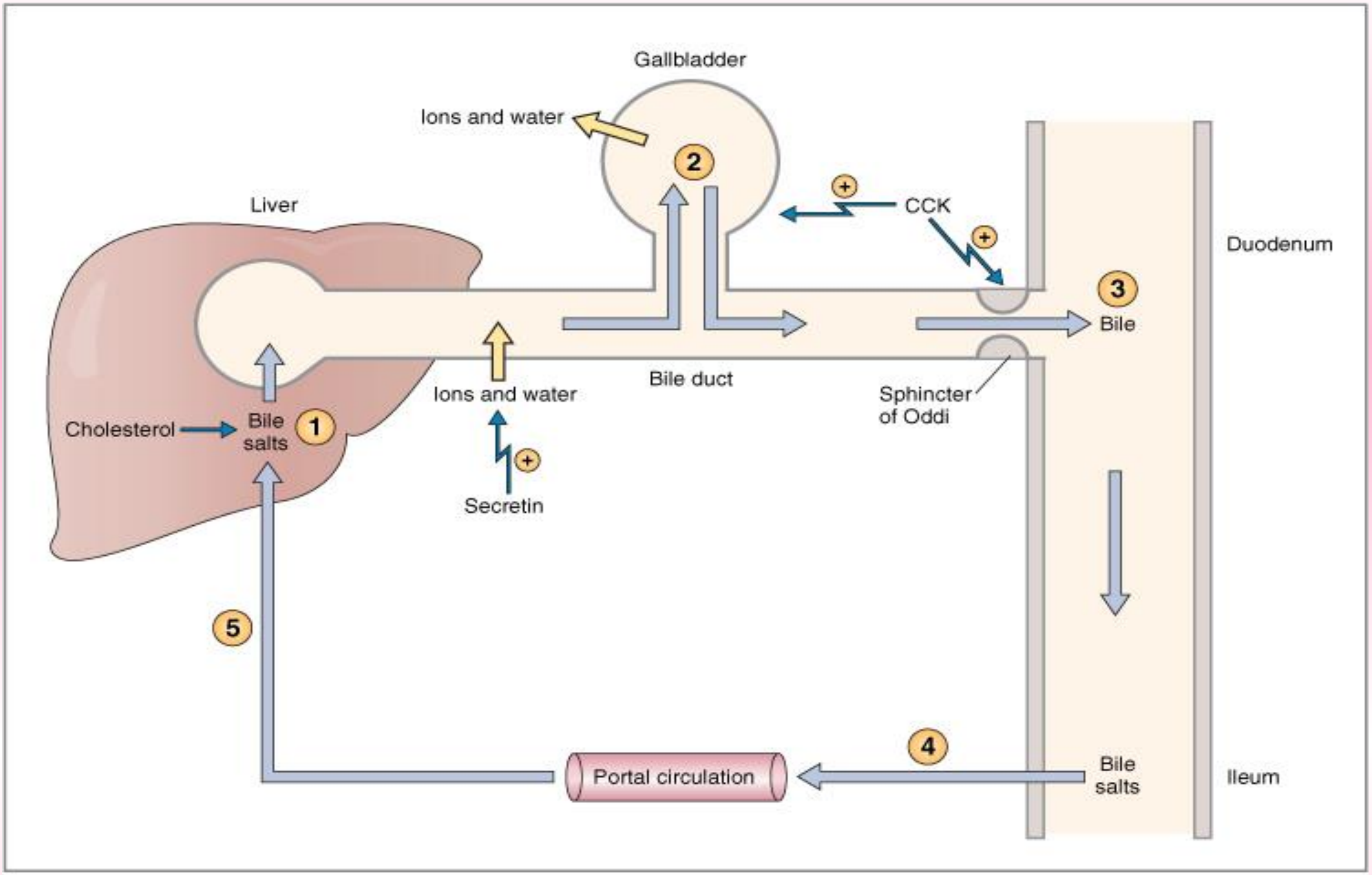
Koeppen and Stanton: Berne & Levy Physiology, 6th Edition.

CFTR: Cystic fibrosis transmembrane conductance regulator, chloride channel. The tight junctions have low permeability, they resist the passage of Bile Acid anions (BA) out of the lumen.

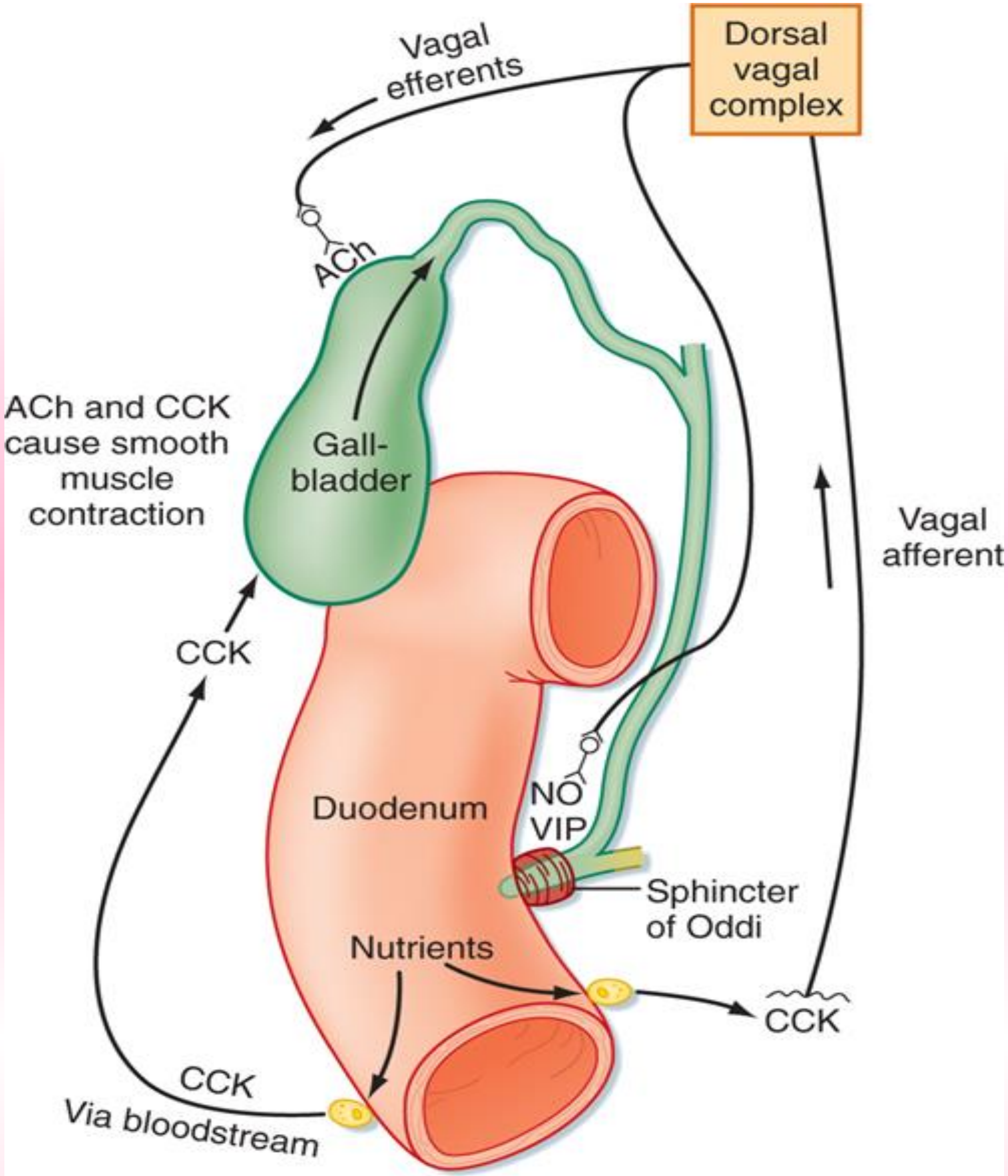
Regulation of Bile Secretion

- Bile secretion is primarily regulated by **a <u>feedback</u>** mechanism, with secondary **<u>hormonal</u>** and **<u>neural</u>** controls
- The major determinant of bile acid synthesis is its concentration in hepatic portal blood (feedback control)
- CCK, secretin and estrogen (hormonal control)
- Parasympathetic (vagal) stimulation results in contraction of the gallbladder and relaxation of the sphincter of Oddi, as well as increased bile formation.
- Bilateral vagotomy results in reduced bile secretion after a meal, suggesting that the parasympathetic nervous system plays a role in mediating bile secretion.
- By contrast, stimulation of the sympathetic nervous system results in reduced bile secretion and relaxation of the gallbladder.

Feedback Control Of Biliary Secretion (Enterohepatic Circulation Of Bile Salts)

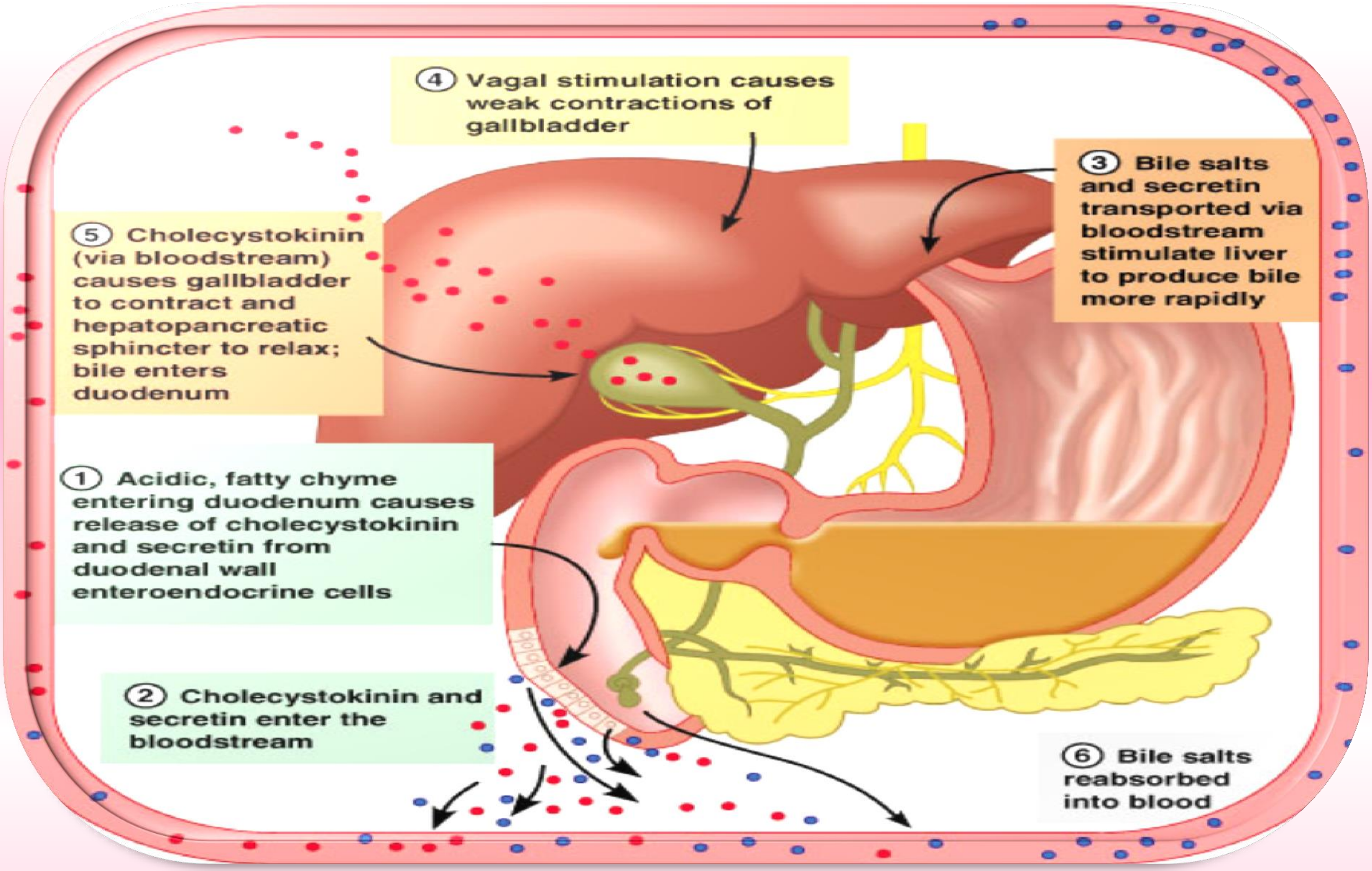


Neurohumoral control of gallbladder contraction and biliary secretion



Koeppen and Stanton: Berne & Levy Physiology, 6th Edition.

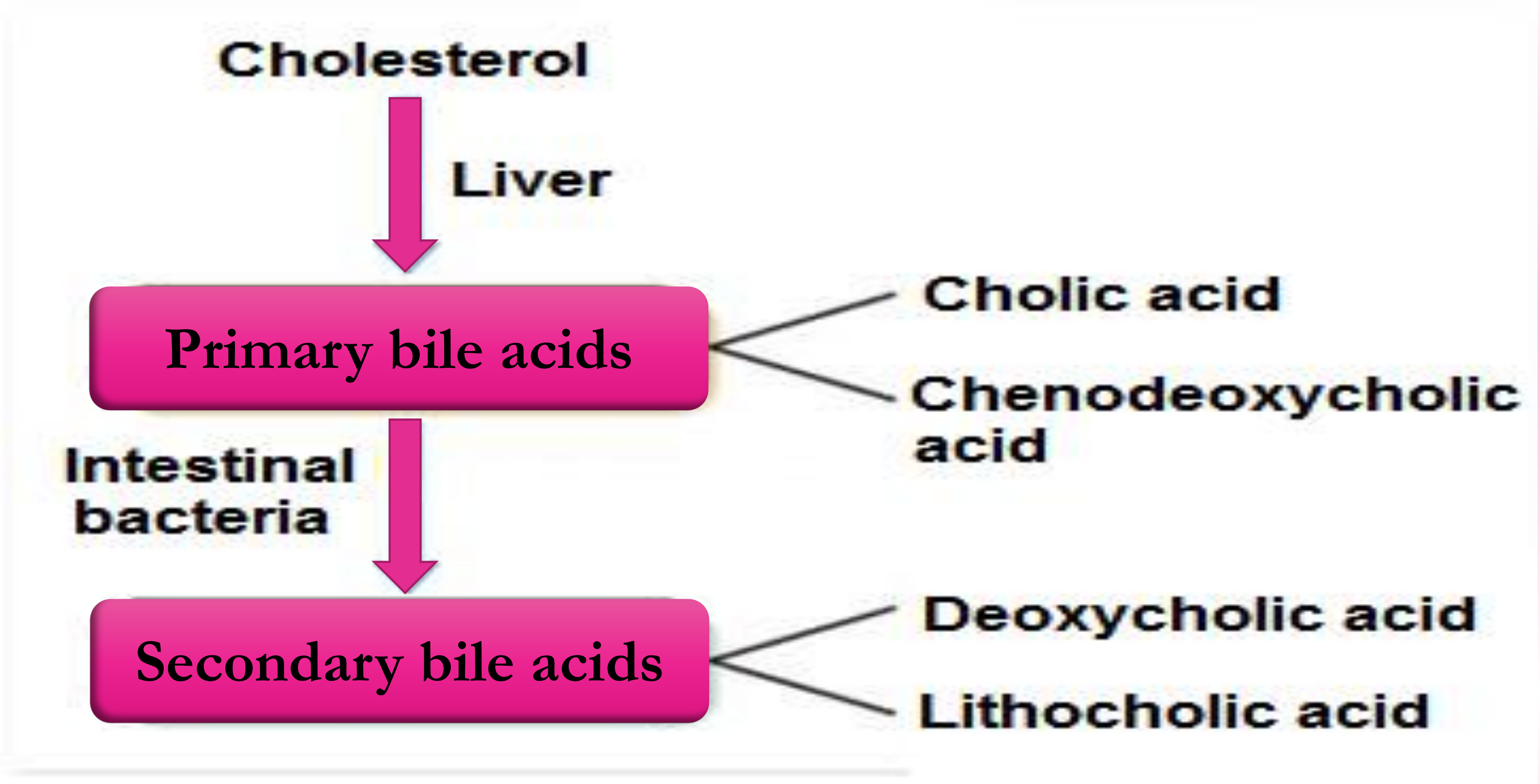
Regulation of Bile Secretion



Bile acids & salts

- Bile acids are steroid acids, synthesized in the liver from cholesterol by the enzyme ***cholesterol 7α-hydroxylase.*** Bile acids include:
  - Primary: cholic, chenodeoxycholic acids.
  - Secondary: deoxycholic, lithocholic acids.
- The principle primary bile acids conjugate with glycin or taurine to form glyco and taurocholic bile acids.

Primary and secondary bile acids

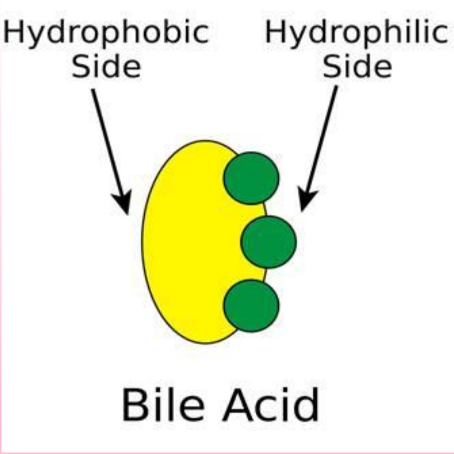


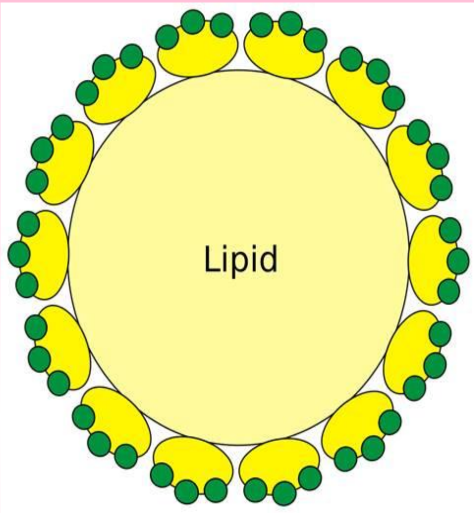
Bile acids & salts (Cont.)

- ✓ At a neutral pH, conjugated bile acids are mostly ionized, more water soluble and are present almost entirely as salts of various cations (mostly Na^+) e.g., sodium glycocholate and are called bile salts.
- ✓ Bile salts are much more polar than bile acids and have greater difficulty penetrating cell membranes. Consequently, the small intestine absorbs bile salts much more poorly than bile acids.
- ✓ This property of bile salts is important because they play an integral role in the intestinal absorption of lipid. Therefore, it is important that the small intestine absorb bile salts only after all of the lipid has been absorbed.

Bile acids & salts (Cont.)

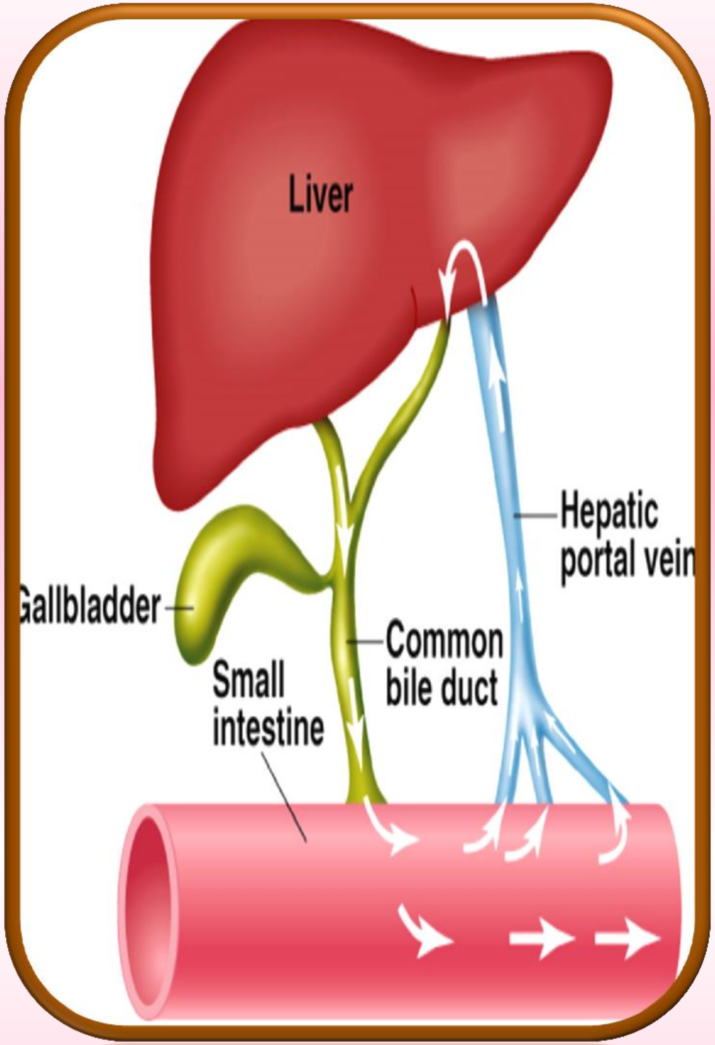
- Bile acids are amphipathic that is having both hydrophilic & hydrophobic domains and tend to form molecular arrangement called micelles.
- In bile acid micelle, the hydrophobic side of bile acid faces inside & away from water. The hydrophilic surface faces outward towards the water.
- Bile acid micelles form when the conc. of bile acids exceed a certain limit ***(critical micelle conc.).*** Above this conc., any additional bile acid will join the micelle.
- Normally bile acid conc. in bile is much greater than critical micelle conc.



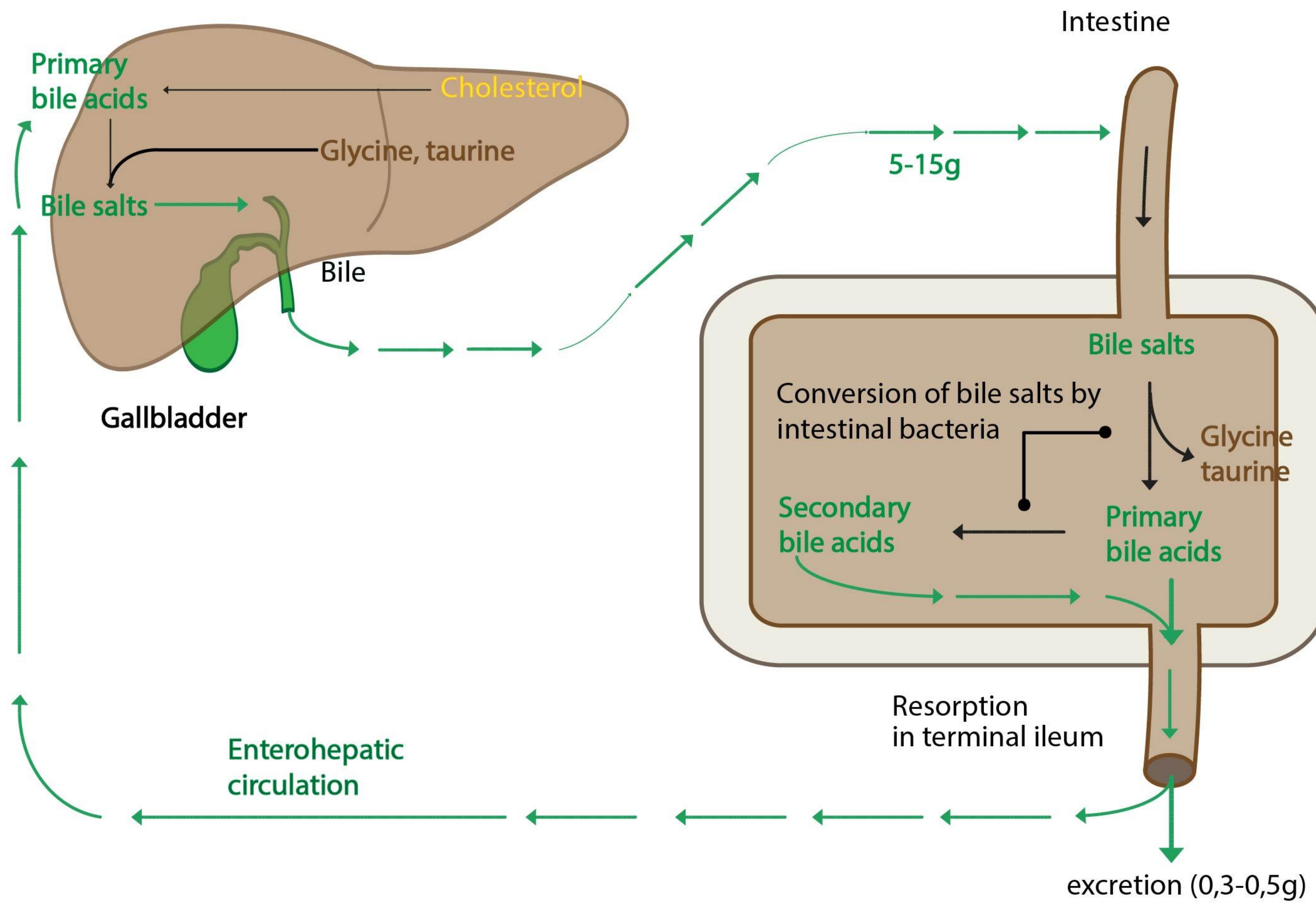


Enterohepatic Circulation of Bile Salts.

- It is the recycling of bile salts between the small intestine and the liver.
- The total amount of bile acids in the body, primary or secondary, conjugated or free, at any time is defined as the ***total bile acid pool***.
- In healthy people, the bile acid pool ranges from 2 to 4 g.



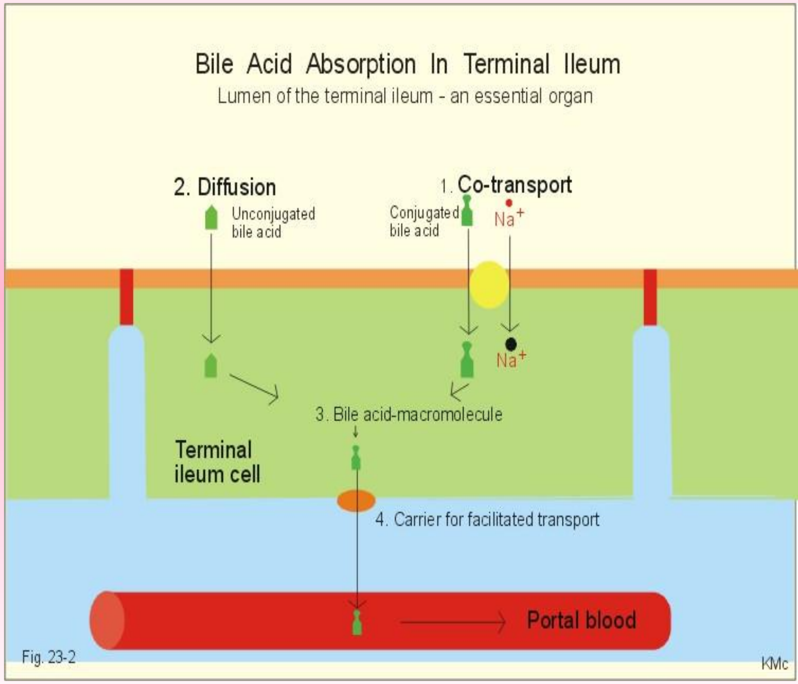
- ♠ About 5-15 g of bile acids are poured into the duodenum /day.
- ♠ In the intestine, some of bile acids are deconjugated and dehydroxylated in the 7 α position by intestinal bacteria that normally colonize in the digestive tract.
- ♠ Dehydroxylation results in the production of **secondary bile acids**. Cholic acid is converted to deoxycholic acid and chenodeoxycholic acid to lithocholic acid.
- ♠ On reaching the terminal ileum, about 95% of bile acids are absorbed and reach the liver through the portal vein.
- ♠ About 0.3-0.5 g of bile acids are lost in feces daily (15-35% of total bile acid pool). These are replaced by new synthesis in liver.



Intestine
Primary bile acids
Cholesterol
Glycine, taurine
Bile salts
Bile
Gallbladder
5-15g
Bile salts
Conversion of bile salts by intestinal bacteria
Glycine taurine
Secondary bile acids
Primary bile acids
Resorption in terminal ileum
Enterohepatic circulation
excretion (0,3-0,5g)

Absorption of bile acids in the intestinal lumen

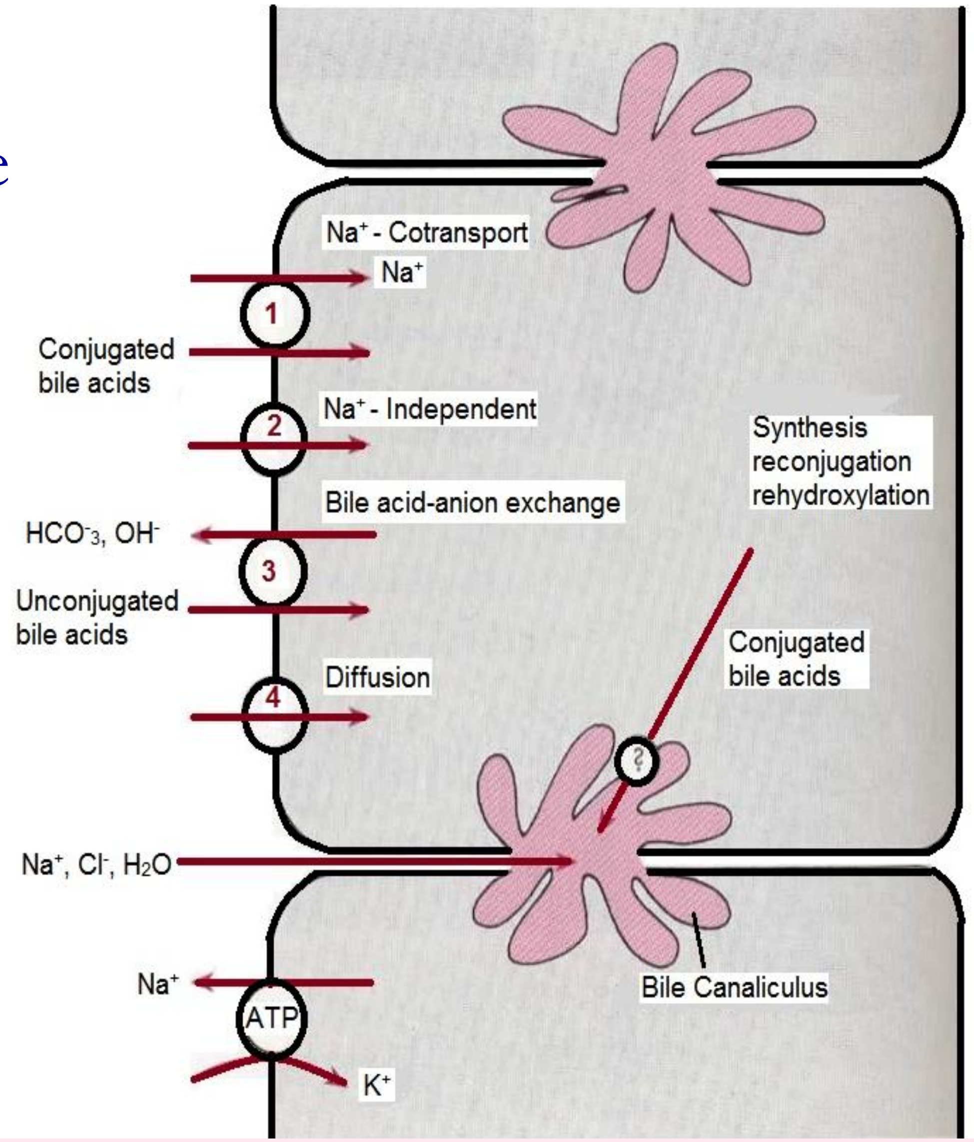
- Bile acids are absorbed largely in the terminal part of the ileum. They cross the brush border plasma membrane by two routes:
  - Conjugated bile acids are 2^{ry} active transported powered by the Na^+ gradient across the brush border membrane.
  - Unconjugated bile acids are less polar and are better absorbed by simple diffusion.



Absorption of bile acids or bile salt back into hepatocytes

Multiple transport mechanisms are located in the hepatocyte plasma membrane for uptake of bile acids from sinusoidal blood.

- ❖ An active carrier-mediated process.
- ❖ Facilitated diffusion.
- ❖ Bile acid-HCO_3^- or OH^- exchange.
- ❖ Passive diffusion (very little).



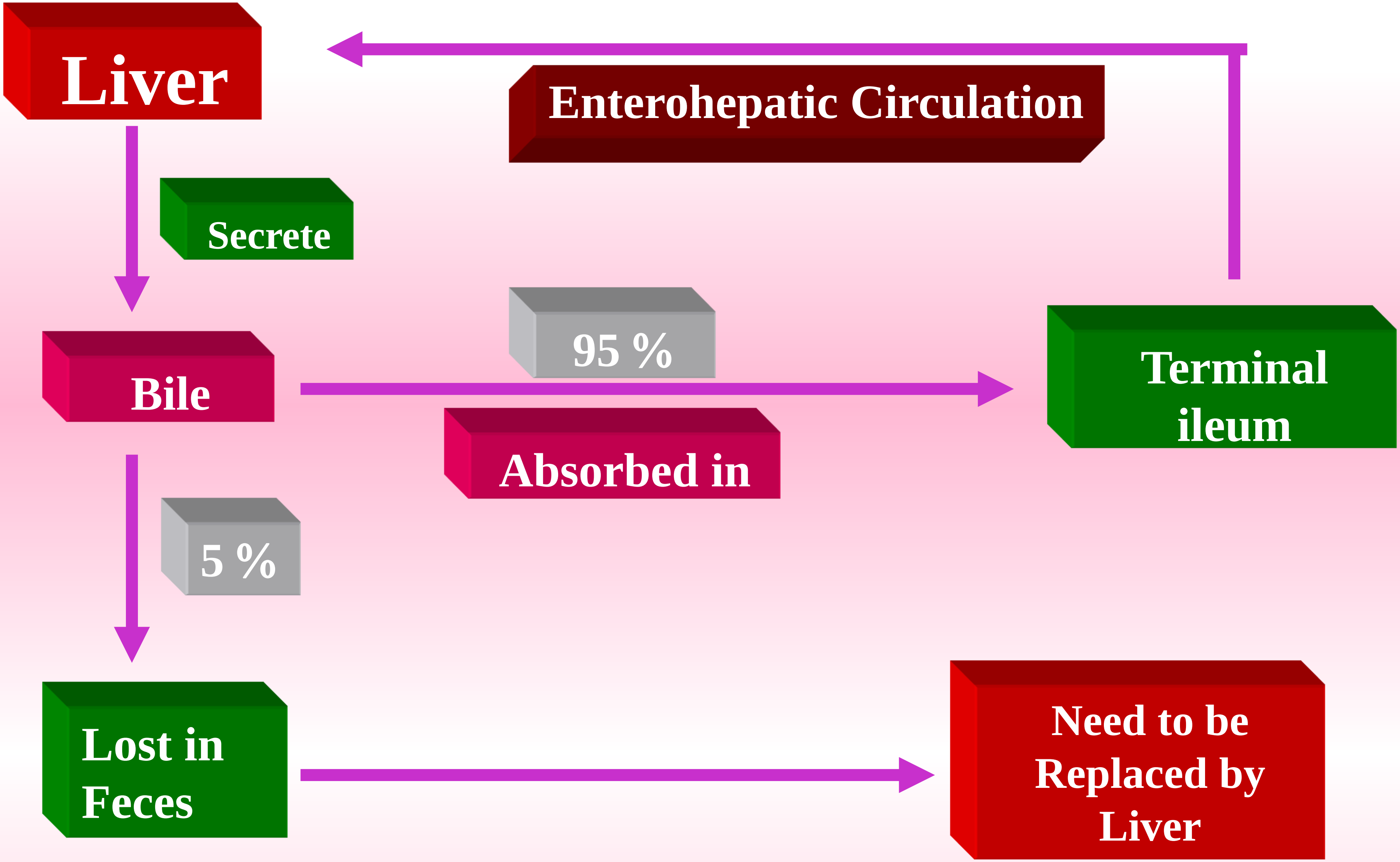
- Hepatocytes extract bile acids, essentially clearing the bile acids from the blood in a single pass through the liver.
- In the hepatocytes, most deconjugated bile acids are reconjugated & some 2^{ry} bile acids are rehydroxylated.
- The reprocessed bile acids, together with newly synthesized bile acids, are secreted into bile.

Importance of enterohepatic circulation of bile salts

- It is essential for stimulating and maintaining the secretion of bile by hepatocytes.
- The greater the quantity of bile salts in the enterohepatic circulation, the greater the rate of bile secretion.
- By cycling several times during a meal, a relatively small bile acid pool can provide the body with sufficient amounts of bile salts to promote lipid absorption.

- In a light eater, the bile acid pool may circulate 3-5 times a day; in a heavy eater, it may circulate 14 to 16 times a day.
- If enterohepatic circulation is interrupted (e.g. due to obstruction by disease or surgical removal or inflammation of the terminal ileum), bile flow is markedly reduced and large quantities of bile salts are lost in the feces.
- Depending on the severity of illness, malabsorption of fat may result (steatorrhea).

N.B: Excess amount of bile acids entering the colon may result in diarrhea.


Liver
Enterohepatic Circulation
Secrete
95 %
Bile
Terminal ileum
Absorbed in
5 %
Lost in Feces
Need to be Replaced by Liver

Enterohepatic Circulation

Needed for

Recycling of Bile Salts

Why Recycling of Bile Salts is needed?

Single meal

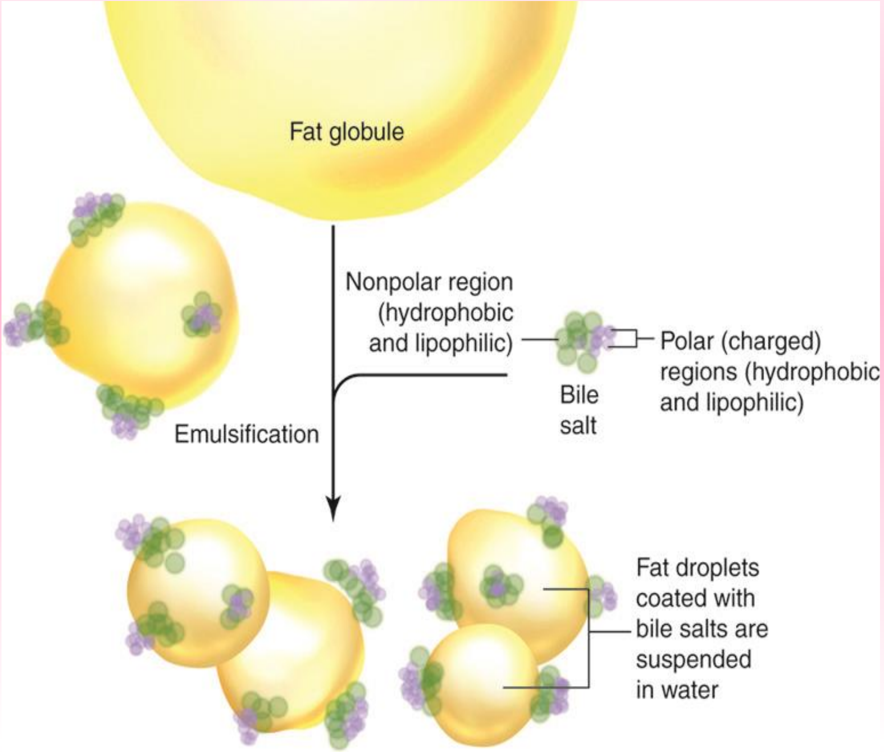
Requires

Up to 5 times the available Bile Salts

Functions of bile acids

1. Digestion of fats:-

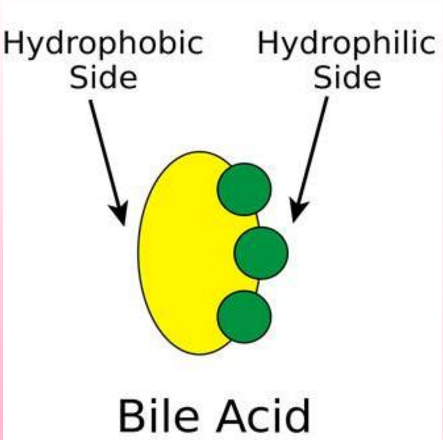
Bile salts have a detergent action that help fat digestion by decreasing fat surface tension resulting in emulsification of fats into small particles. This increase the surface area upon which the digestive enzymes will act.

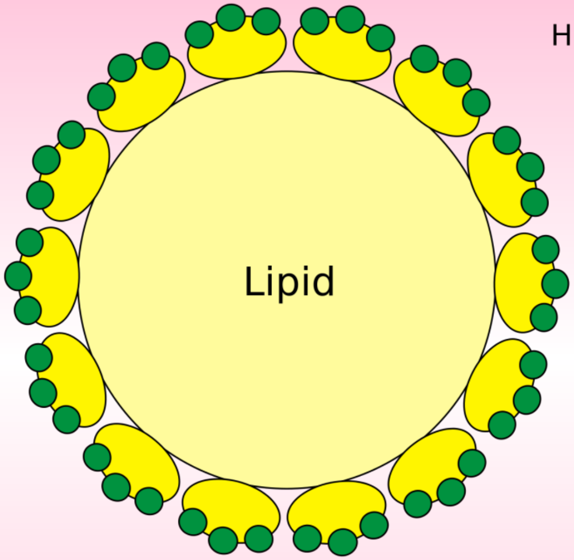


Functions of bile acids (Cont.)

2. Absorption of fats:-

- Bile salts combine with fats to form micelles (water soluble compounds) from which fatty acids, monoglycerides, cholesterol, and other lipids can be absorbed from the intestinal tract.
- Without the presence of bile salts in intestinal tract up to 40% of lipids are lost into the stools (steatorrhea).



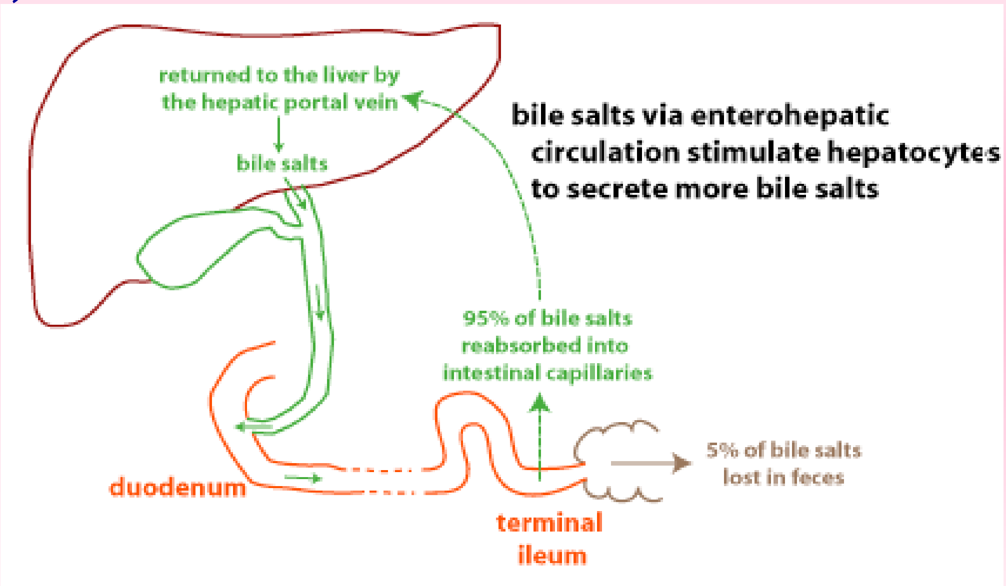


H

Functions of bile acids (Cont.)

3. **Bile salts** are essential for absorption of **fat soluble vitamins** (A, D, E and K).

4. In the liver, bile salts are important for **stimulating bile secretion and flow** (choleretic action).



5. **Bile salts** also take part in the formation of micelles which render cholesterol soluble in bile.


Thanks!
spicecomments.com