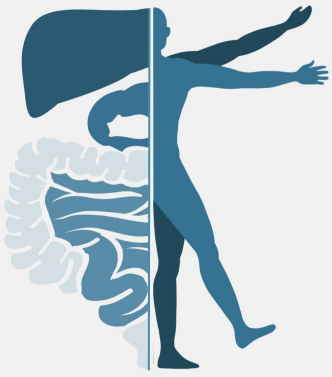
Physiology Team 439

MED439
KING SAUD UNIVERSITY

Revised & Approved
Bassam Alasmari
Rania Almutiri



Physiology of Bile Salts and Enterohepatic Circulation

Objectives:

- Liver Digestive Functions.
- Physiologic Anatomy of Biliary Secretion
- The Components of Bile
- What is the bile acid ? What are the types of the bile acid?
- Storing and Concentrating Bile in the Gallbladder
- Function of Bile Salts in Fat Digestion and Absorption
- Enterohepatic Circulation of Bile Salts
- The mechanisms of bile reabsorption back into hepatocytes
- Functions of the bile and stages of its secretion
- Characteristics & main constituents of bile.
- Functions of gall bladder.
- Control of biliary system.
- Enterohepatic circulation of bile salts.
- Absorption, uptake & functions of bile acids.

Color index:

- Important.
- Girls slide only.
- Boys slide only.
- Dr's note.
- Extra information.

Editing File

The Liver

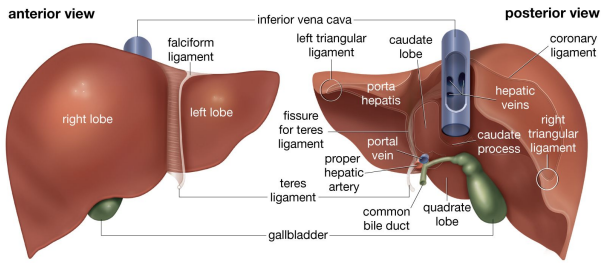
Introduction:

Facts:

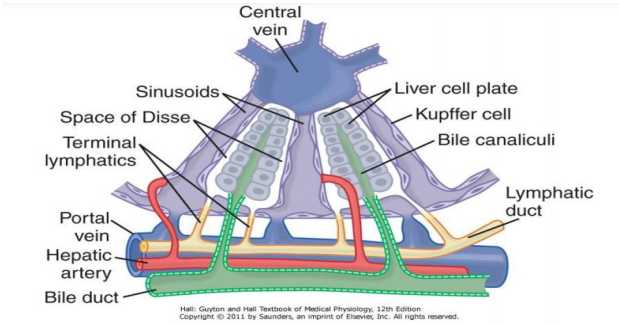
- The liver is the largest internal organ in the body, constituting about 2.5% of an adult's body weight.
- Receives 25% of the cardiac output via the hepatic portal vein and hepatic artery (dual /double blood supply). From the 5L (cardiac output) more than 1L.
- Sinusoids in the liver are unique because they contain both oxygenated (hepatic artery) and deoxygenated (portal vein which is full of nutrients from the intestines) blood.

Functions:

- Takes up, stores, and distributes nutrients and vitamins.
- Plays an important role in maintaining blood glucose levels. By synthesis of glycogen in case of hyperglycemia, and release of glucose in case of hypoglycemia.
- Regulates the circulating blood lipids by the amount of very low–density lipoproteins (LDL) it secretes.
- Synthesizes many of the circulating plasma proteins (albumin) and clotting factors (fibrinogen and prothrombin).
- Takes up numerous toxic compounds and drugs from the portal circulation.
- Performs important endocrine functions (as IGF-1, Angiotensinogen, Thrombopoietin).
- Serves as an excretory organ for bile pigments, cholesterol, and drugs.
- Continuously secretes bile, which after storage in gall bladder is discharged into duodenum.

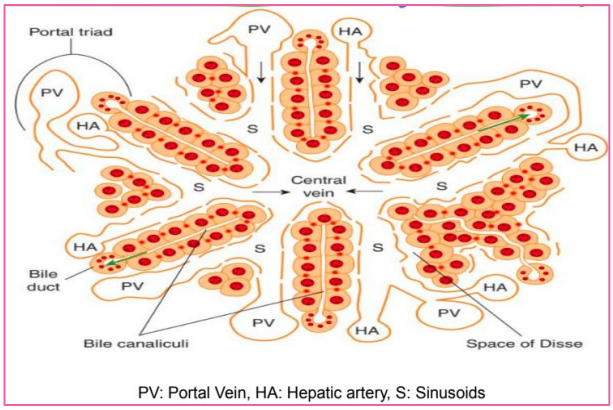


The Anatomy Of The Liver



Bile Canaliculi & Ducts

- **The diagram is important and kupffer cells are very important.**
- **Kupffer cells:** a part of the macrophage monocyte system which deals with toxins and pathogens in the liver
- Space of disse is also called perisinusoidal space
- In liver cirrhosis, We see compression of space of disse preventing lymphatic drainage. this occlusion leads to portal hypertension and the high pressure leaks fluids from the portal vein to the abdomen. This is called ascites



PV: Portal Vein, HA: Hepatic artery, S: Sinusoids

The main digestive function of the liver

The main digestive function of the liver is the secretion of bile (normally 600-1000 ml/day).

Bile serves two important functions:

It plays an important role in fat digestion and absorption by its content of bile or by the following:;

They aid in absorption of the digested fat end products through the intestinal mucosal membrane, via micelles formation.**

Emulsifying the large fat particles of the food into minute particles.**

bile serves as a means for excretion of waste products from the blood. These include especially bilirubin, an end product of hemoglobin destruction + cholesterol.

Bile is considered secretion and excretion:
1/ secretion : secret variable substance which have important physiological function. Bile acid and bile salt are important for fat digestion and absorption.
2/ excretion.

Gallbladder Bile Differs From Hepatic Bile

Bile is secreted in two stages:

1

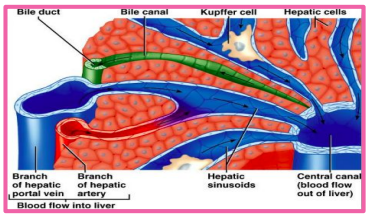
The initial portion is secreted by the hepatocytes. It is secreted into bile canaliculi that originate between the hepatic cells**.**

2

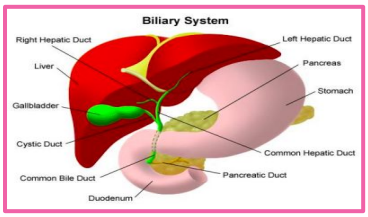
The bile flows in the canaliculi toward the hepatic duct and common bile duct. From these the bile either empties directly into the duodenum **or is diverted for** minutes up to several hours **through the cystic duct into the gallbladder (this** (gallbladder bile) **is the second portion of liver secretion which is added to the initial bile).**
In between meal, when there is no need for bile, bile is diverted and stored in the gallbladder.

Hepatic Bile: Isotonic secretion (similar to that of plasma), with **high Na+, Cl- and HCO3 and low K+ and Ca2+** > gallbladder bile مقارنة ب

Gallbladder bile: high Bile acid anion and Ca2+ ; but low Na+ , Cl- , HCO3 and H2O.



This show cross in liver lobule, there are 2 plates of hepatocytes radiating form the central canal. In between this 2 plates there are bile canaliculi. So, bile is secreted from hepatocytes and then bile flow through bile canaliculi.

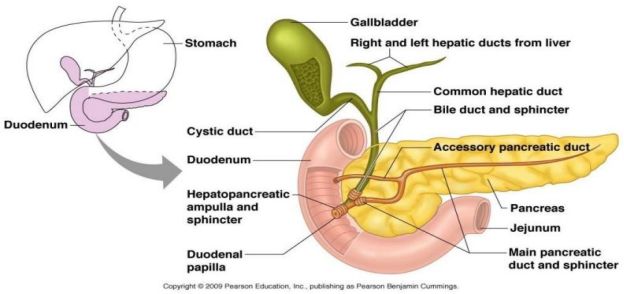


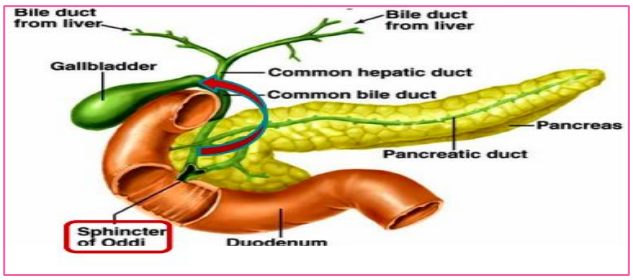
Where The Common Bile Duct Opens*

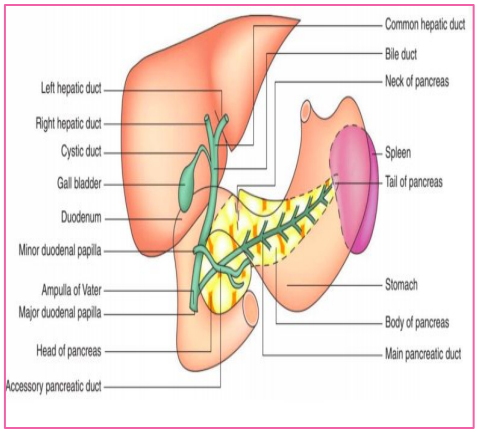
The common bile duct open into the duodenum in company with the pancreatic duct at the ampulla of vater. This opening is guarded by the sphincter of Oddi (choledochoduodenal sphincter).

The common bile duct ends below by piercing the medial wall of the second part of the duodenum, and is usually joined by the main pancreatic duct. Together they open into the hepatopancreatic ampulla (ampulla of Vater).

Gallbladder Recap:
The gallbladder is completely covered by peritoneum, composed of the fundus, body, and neck. the narrow area between the neck and the body is called the infundibulum. the fundus lies at the level of the tip of the 9th intercostal space, it is supplied by the cystic artery, which is a branch of the hepatic, and drained by the cystic vein directly to the portal vein

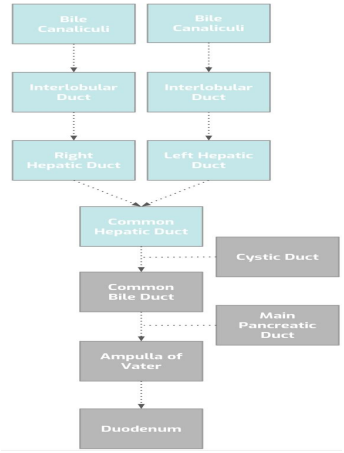






From the liver, there are 2 hepatic ducts (left and right). Join to form common hepatic duct. Common hepatic duct join the duct from the gallbladder called cystic duct and form the common bile duct. The common bile duct joining the pancreatic duct, and open by a single orifice through the second portion of the duodenum in area called ampulla of vater. This ampulla of vater is guarded by sphincter called duodenal sphincter / sphincter of oddi.

Bile Ducts,
Anatomy Team 439:



Characteristics of Bile*

Bile is	A viscous golden yellow or greenish fluid
PH	Isotonic with plasma and slightly alkaline (due to NaHCO3). It participates in neutralization of acid chyme delivered from stomach.3 alkaline GI secretions ? Intestinal, pancreatic and bile. All these secretion participate in neutralization of the acid chyme from stomach.
Volume	The liver produces about 5 L /day, but only 600-1000 ml/day are poured into the duodenum. why? Stored and concentrated on the gallbladder.

What Are The Components of Bile?

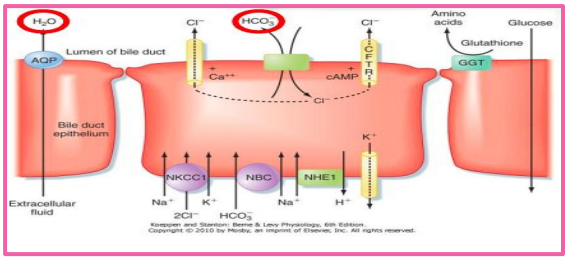
Classification is based on girls slides

From hepatocytes:

- Bile acids (bile salts) (65% of dry weight of bile)
- Phospholipids (Lecithin, 20%), phosphatidylcholine
- Proteins (5%)
- Cholesterol (4%) bile is the major route for cholesterol excretion
- Bile pigments (as bilirubin, 0.3%)
- Ions and water

From bile ducts epithelial cells*:

- Electrolytes mainly $HCO3^-$, in addition to H2O
- These contribute to the volume of hepatic bile.
- $HCO3^-$ aids in neutralization of acid chyme.



While passing through the duct, electrolytes and water will be added. So increase the volume.

Composition of Bile*

From hepatocytes (organic constituents)

- Bile salts(65%)
- Lecithin (20%)
- Proteins (5%)
- Cholesterol (4%)
- Bilirubin (0.3%) mostly excreted out to prevent jaundice

From ducts

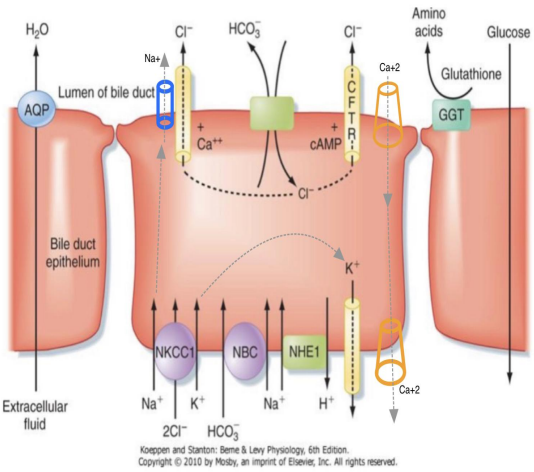
- Aqueous alkaline Solution (NaHCO3)

The major transport processes of cholangiocytes that secrete an alkaline-rich fluid*

Cholangiocytes: Epithelium lining the bile ducts

DR's explanation:

The cholangiocytes maintains Isotonic secretion, with **high** Na+, Cl- and HCO3 and **low** K+ and Ca2+ by the following:
There are three ion channels in the direction of blood:
1- Sodium-Hydrogen exchanger (NHE1)
2- Sodium-Bicarbonate cotransporter (NBC)
3-Sodium-potassium-two chloride (NKCCl):
After these ions enter, potassium immediately leaves by potassium channels.Chloride is secreted to the luminal border by the famous CFTR channels, and sodium follows chloride through sodium channels, then water follows NaCl.
on the luminal border, HCO3-Cl counter transport occurs, so HCO3 is secreted to the lumen, and Chloride enters the cell. But chloride goes again to the lumin by CFTR.
Another important protein on the luminal border Is GGT, which converts Glutathione into amino acids. There is Active reabsorption of Glucose and A.A. to prevent bacterial growth.
Hepatic Bile: Isotonic secretion, with high Na+, Cl- and HCO3 and low K+ and Ca2+.



Storing and Concentrating Bile in the Gallbladder

Ion Conc. in the gallbladder is almost opposite to to that of the hepatic ducts

Bile is secreted continually by the liver cells and then normally stored in the gallbladder until needed in the duodenum (gallbladder can hold 30 to 60 mL).

Gallbladder concentrates the bile, which has the bile salts, cholesterol, lecithin, and bilirubin during every 12 hours of bile secretion (usually about 450 mL) because water, Na, Cl, and most other small electrolytes are continually absorbed through the gallbladder mucosa by active transport of sodium, and this is followed by secondary absorption of chloride ions, water, and most other diffusible constituents.
Na+ is actively transport through the gallbladder mucosa. Then, followed by secondary absorption of Cl-, water, and most other diffusible constituents.

The tight junctions have low permeability, they resist the passage of Bile Acid anions (BA) out of the lumen.

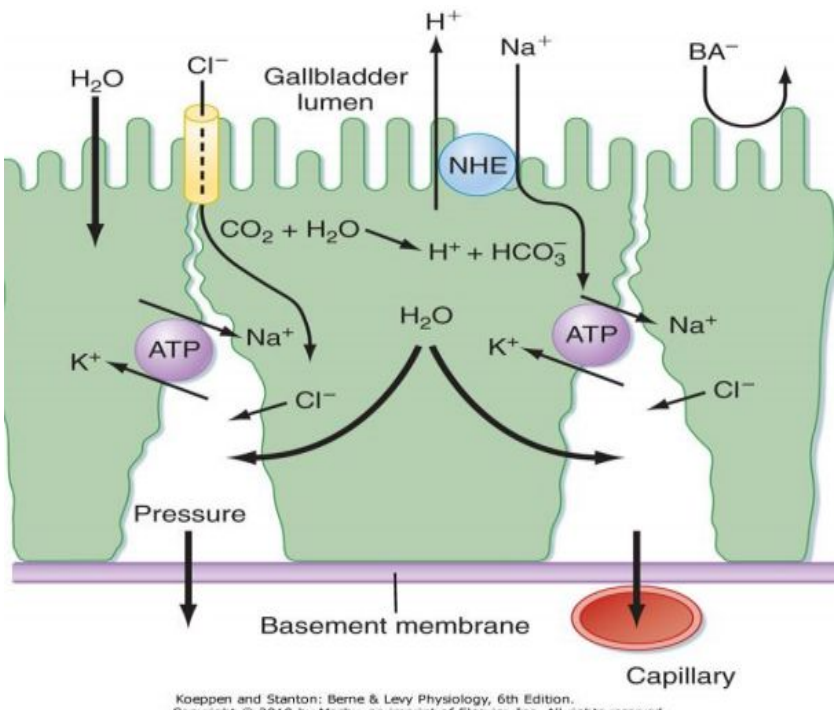
Their conc. is high in the bile of Gallbladder, but (Na^+ , HCO_3^- , H_2O, Cl^-) conc. is low in compare to hepatic bile.

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

DR's explanation:

Gallbladder bile has **high** Bile acid anion and Ca2+ ; but **low** Na+ , Cl- , HCO3 and H2O, this is done by the following:
1-Sodium-Hydrogen exchanger is present on the luminal border, which gets sodium in and hydrogen out Actively. The source of hydrogen is the Carbonic Anhydrase reaction
Sodium then is pumped to the blood in exchange for potassium by sodium-potassium ATPase. Sodium left, chloride left, water should leave to maintain the osmolarity. The tight junctions have low permeability, they **resist** the passage of Bile Acid anions (BA) out of the lumen.
CFTR: Cystic fibrosis transmembrane conductance regulator (chloride channel).Doctor: just know that it is a chloride channel
Gallbladder bile: high Bile acid anion and Ca2+; but low Na+, Cl-,HCO3 and H2O.



Koeppen and Stanton: Berne & Levy Physiology, 6th Edition.
Copyright © 2010 by Mosby, an imprint of Elsevier, Inc. All rights reserved.

The function of gallbladder is to store and concentrate bile. To store the amount that is continuously secreted by the liver, it must be concentrated, why? Gallbladder capacity is only 30-60 ml, and can store about half liter or 450ml by concentrate the bile, how? By removing water, and to remove water, Na^+ must be transported from the lumen into the gallbladder epithelial cells by active transport, then to capillary circulation. This is followed by Cl^- and HCO_3^- absorption. So, due to increase osmolarity (osmotic pressure) water will move from low to high osmotic gradient.
This cause absorption of Na^+, Cl^-, HCO_3^- and water.

Differences Between Hepatic and Gallbladder Bile*

		Hepatic Bile	Gallbladder Bile
Organic	Water (g/dl)	97.5	**92**
	Total solids	2-4 %	11 %
	Bile salts (g/dl) most important	**1.1**	**6**
	Bilirubin (g/dl)	0.04	0.3
	Cholesterol (g/dl)	0.1	0.3-0.9
	Fatty acids (g/dl)	0.12	0.3-1.2
	Phospholipids	0.5	4
Inorganic (electrolytes)	Na+(mEq/L)	145	**130**
	Cl-(mEq/L)	100	**25**
	HCO3- (mEq/L)	28	**10**
	Ca++(mEq/L)	5	23
	K+(mEq/L)	5	12
	pH	8.3 bcs of HCO3	**7.5**

مش مطلوب حفظ التركيز لكل المكونات. لكن مهم تعرفون هذه النقاط:

1/ all the constituents are concentrated in gallbladder bile in compare to hepatic bile **except** (Na^+, Cl^-, HCO_3^- and water).

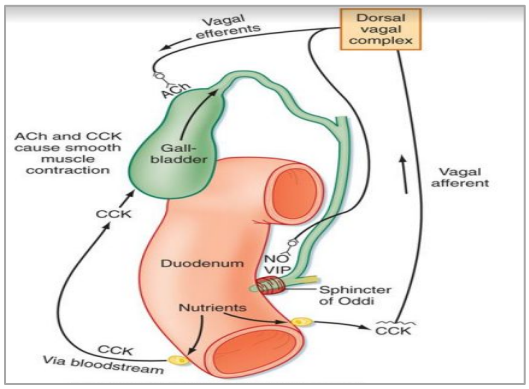
2/ (Na^+, Cl^-, HCO_3^- and water) are low conc. in compare to hepatic bile? Due to absorption.

3/ pH of gallbladder is lower than pH of hepatic, but both are alkaline, which is important physiologically, because all the constituents are concentrated, it may cause Ca^{++} stones. But since the pH is lower, Ca^{++} solubility is more in acidic medium. So, lower pH "as compared to that of hepatic bile" prevent precipitation of Ca^{++} , and guard against Ca^{++} stones.

Regulation of Bile Secretion

Bile secretion is **primarily** regulated by a feedback mechanism, with **secondary** hormonal and neural controls.

Feedback Control **Most important**	Concentration of bile acid in hepatic portal blood is the major determinant of its synthesis Bile acids after secretion, when they reach the duodenum and terminal ileum they are reabsorbed again into the liver through the portal circulation, which is essential to stimulate bile secretion more and more. كأنها تعمل تحفيز ذاتي لنفسها
Hormonal Control	Secretin, CCK, and estrogen stimulate bile secretion
Neural Control	Parasympathetic and sympathetic nerves supply the biliary system. ❖ Parasympathetic (vagal) stimulation results in contraction of the gallbladder and relaxation of the sphincter of Oddi, as well as increased bile formation. ❖ {Bilateral vagotomy (cutting of vagus nerve in left and right side) results in reduced bile secretion after a meal, suggesting that the parasympathetic nervous system plays a role in mediating bile secretion}. ❖ By contrast, sympathetic stimulation results in reduced bile secretion and relaxation of the gallbladder. + contract the sphincter.



Neurohumoral control of gallbladder contraction and biliary secretion

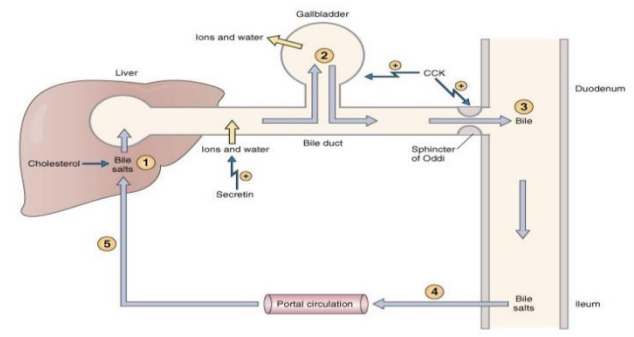
Summary: Regulators:
1- Feedback
2- Nutrients stimulate **I cells** to secrete CCK, which contracts the bladder and relaxes the sphincter of Oddi. CCK also stimulates dorsal vagal complex in the brainstem via the vagal afferents, which gives commands to the vagal efferents to stimulate the gallbladder by ACh, and also it relaxes the sphincter of Oddi by NO and VIP

CCK and vagal stimulation have the same effect

Feedback Control of Bile Secretion through Enterohepatic Circulation of Bile Salts

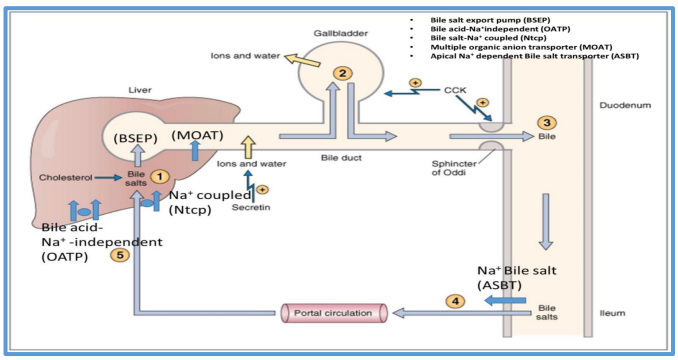
The topic was found in boys and girls slides but the text was found in boys slides only. Pictures were in both.

1	The hepatocytes of the liver continuously synthesize and secrete the constituents of bile actively by BSEP and also by MOAT (Step 1)
2	The components of bile are the bile salts, cholesterol, phospholipids, bile pigments, ions, and water. secretion of these ions by cholangiocytes is stimulated by secretin, because you know that secretin hates acidity, and these secretions contains bicarbonate. Bile flows out of the liver through the bile ducts and fills the gallbladder, where it is stored (Step 2) (Some bile goes directly to the intestine without entering the gallbladder) The gallbladder then concentrates the bile salts by absorption of water and ions.
3	When chyme reaches the small intestine, CCK is secreted. CCK has two separate but coordinated actions on the biliary system: It stimulates contraction of the gallbladder and relaxation of the sphincter of Oddi, causing stored bile to flow from the gallbladder into the lumen of the duodenum (Step 3). In the small intestine, the bile salts emulsify and solubilize dietary lipids.
4	When lipid absorption is complete, the bile salts are recirculated to the liver via the enterohepatic circulation, mediated by the active transporter ASBT (Step 4)
5	The steps involved in the enterohepatic circulation include absorption of bile salts from the **ileum** into the portal circulation, delivery back to the liver mediated by two active transporters; OATP and Ntcp, and extraction of bile salts from the portal blood by the hepatocytes. (Step 5)

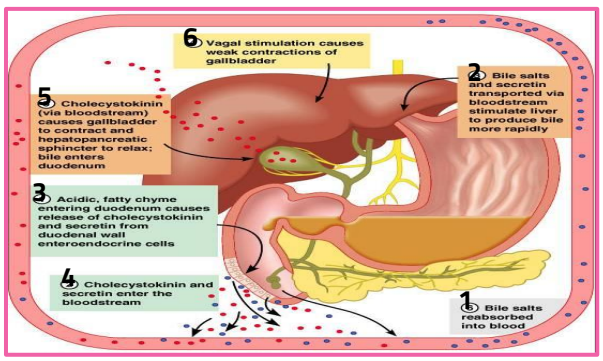


5% normally move towards the colon

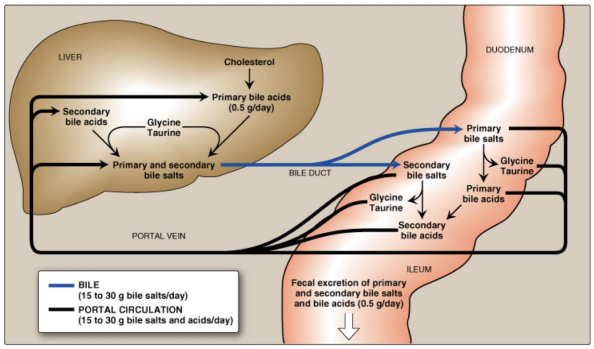
The picture is important



2+1. Bile secreted "including bile salt" from liver and Gallbladder.
4. when bile reach terminal ileum, most of Bile reabsorbed again.
5. When Bile reach the to the liver, it stimulate the liver for synthesis of more Bile and bile salts



Regulation of Bile secretion



Extra

Secretin directly stimulate hepatocytes to increase HCO_3^- in the bile (as in pancreatic secretion)

Bile acids & salts

What are bile acids ?

- Bile acids are formed in the liver from cholesterol (Doctor: we asked about this in previous exams). During the conversion, hydroxyl groups (by 7 α- hydroxylase) and a carboxyl group are added to the steroid nucleus.*
- Bile acids are steroid acids, synthesized in the liver from cholesterol by the enzyme cholesterol 7 α-hydroxylase.*

Bile acids are classified as:

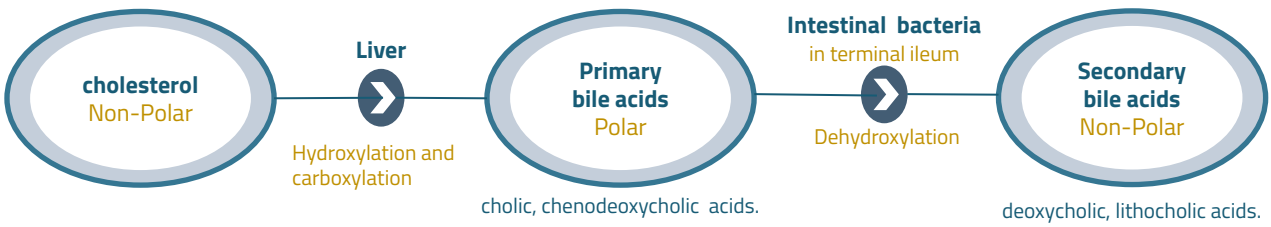
Primary
- cholic acid
- chenodeoxycholic acid

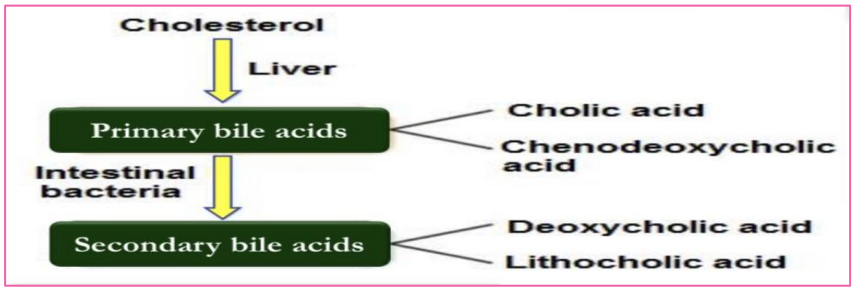
Secondary
- deoxycholic acid
- lithocholic acid

In intestine by bacterial flora, they convert primary bile acids to secondary bile acids.

Bile acids conversion

- The hepatocytes synthesize the primary bile acids (by C 27-dehydroxylase)*
- The principle primary bile acids conjugate with glycine or taurine to form glyco and taurocholic bile acids. Bile acids are secreted as conjugates of taurine or glycine.
- When bile enters the GI tract, bacteria present in the lumen act on the primary bile acids and convert them to secondary bile acids by dehydroxylation.*:
  1-Cholic acid is converted to deoxycholic acid.*
  2-Chenodeoxycholic acid to lithocholic acid.*
  Which is cytotoxic and can be sulfated by the liver if it presents in high concentration.*





Properties of Bile acids & salts

1

At a neutral pH, the bile acids are mostly ionized, more water soluble, and are referred to as bile salts. Conjugated bile acids ionize more readily than the unconjugated bile acids and, thus, usually exist as salts of various cations (mostly Na+) e.g., sodium glycocholate. Bile salt are more polar and more water soluble. So, they cross the cell membrane of intestinal epithelium poorly (cross the membrane at slower rate than Bile Acid). So, they remain for a sufficient time in the small intestine until most of the fat and fat soluble vitamin are Absorbed
(we need Bile acids to form micelles to help fat Absorption)

2

The conjugation biochemical reaction decreases the pKa of the compound and make it more ionized.*

3

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.

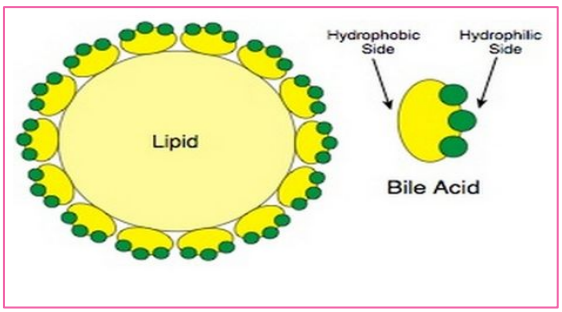
4

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.*

معناها انهم دائمًا موجودين في حالة ال micelles للمساعدة في fat absorption.

Also, make the cholesterol in the bile globule form > prevent formation of cholesterol stones.

Only in boys slides



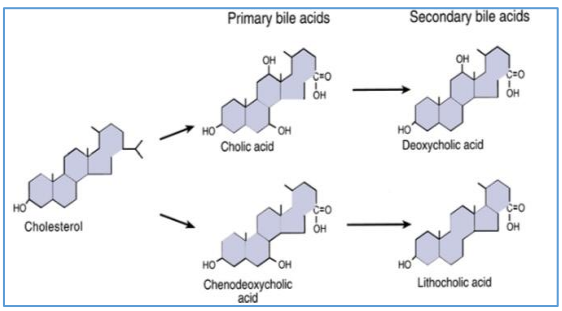
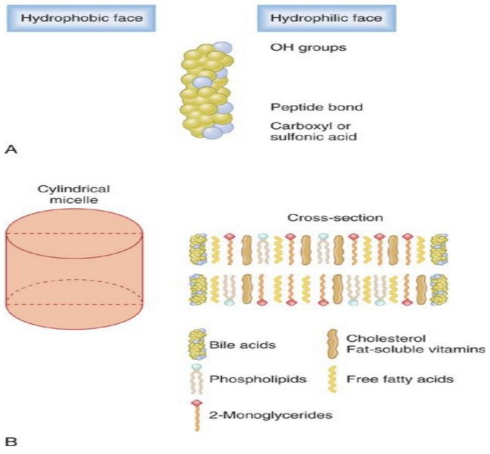


Figure 26.13

Figure 26.13: Bile acids are formed from cholesterol in the liver.
Bile acids are conjugated with the amino acid, glycine, and taurine (which is an organic compound available in animal tissue) in the liver.
At neutral pH, the bile acids are mostly ionized and referred to as bile salts.

Role of Bile Salts to Accelerate Fat Digestion Formation of Micelles*

- Bile salts have the ability to form micelles, (each bile salt molecule is composed of a sterol nucleus that is fat-soluble and a polar group that is water-soluble.
- Micelles are small spherical, cylindrical globules 3 to 6 nm in diameter composed of 20 to 40 molecules of bile salt.
- The polar groups are (-) charged, they allow the entire micelle globule to dissolve in the water of the digestive fluids and to remain in stable solution.
- The micelles act as a transport medium to carry the monoglycerides and free fatty acids to the brush borders of the intestinal epithelial cells.



Functions of Bile Salts/ acids

1-In Fat Digestion and Absorption

1-**Digestion:**

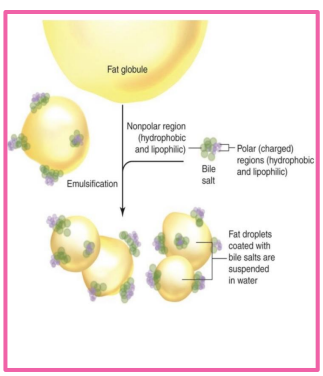
- They have a detergent action (emulsifying) on the fat particles in the food which decreases the surface tension of the particles.*
- Bile salts have a detergent action that help fat digestion by decreasing fat surface tension resulting in emulsification of fats into small particles. This increase the surface area upon which the digestive enzymes will act.*

2-**Absorption**

- They help in the absorption of fatty acids, monoglycerides, cholesterol, and other lipids from the intestinal tract.*
- 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).*

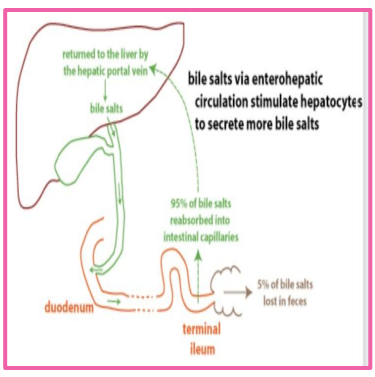
2-Other Functions of Bile Salts

- Bile salts are essential for **absorption of fat soluble vitamins** (A, D, E and K).(اكيد)
- In the liver, bile salts are important for **stimulating bile secretion and flow (choleretic action)**. They also take part in the formation of micelles which **render cholesterol soluble in bile.**



Micelles formation

Bile salts intersperse Between the fat molecules and decrease the surface tension. Decrease attraction force and divide the fat globules into smaller particles. Increase surface area for the action of pancreatic lipase enzyme, this action is called emulsification of fat.



Guard against formation of cholesterol stones (gallbladder stone)

Enterohepatic Circulation (Portal circulation) of Bile Salts*/ Enterohepatic Circulation of Bile Acids*

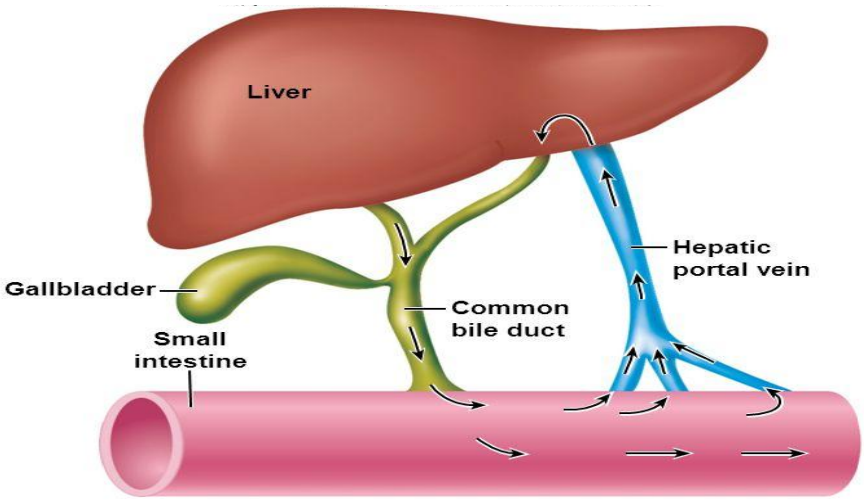
Enterohepatic Circulation of Bile Salts:

is the recycling of bile salts between the small intestine and the liver.

Total Bile Acid Pool

The total amount of bile acids in the body, primary or secondary, conjugated or free, at any time.

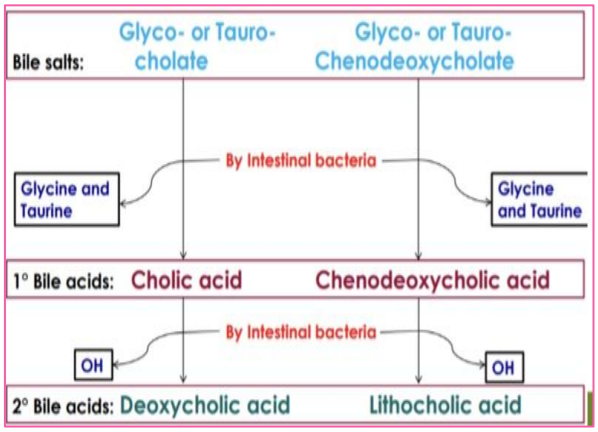
- In healthy people, the bile acid pool ranges from 2 to 4 g.
- The enterohepatic circulation of bile acids in this pool is physiologically extremely important. By cycling several times during a meal, a relatively small bile acid pool can provide the body with sufficient amounts of bile salts to promote lipid absorption. In a light eater (little fat in the diet), the bile acid pool may circulate three to five (3-5) times a day; in a heavy eater (high fat in the diet), it may circulate 14 to 16 times a day. So, enterohepatic circulation depend on the diet.
- The intestine is normally extremely efficient in absorbing the bile salts by carriers located in the distal ileum. Inflammation of the ileum can lead to their malabsorption and result in the loss of large quantities of bile salts in the feces e.g., inflammatory bowel diseases (Crohn's disease and Ulcerative Colitis).*
- If enterohepatic circulation is interrupted (e.g. due to obstruction or surgical removal or inflammation of the terminal ileum + thrombosis in portal circulation , bile flow is markedly reduced.*
- Large quantities of bile salts enter the colon (diarrhea) and lost in the feces.
  Depending on the severity of illness, malabsorption of fat may result in steatorrhea (fat in stool) because bile salt pool was depleted following the ileal inflammation or resectioning. Presence of bile salt in the colonic lumen will activate Cl secretion, Na and water will follow Cl into the intestinal lumen, producing secretory diarrhea.
- Steatorrhea is Due to :
  - deficiency of bile.
  - insufficiency of pancreatic lipase.
  -Malabsorption and maldigestion.

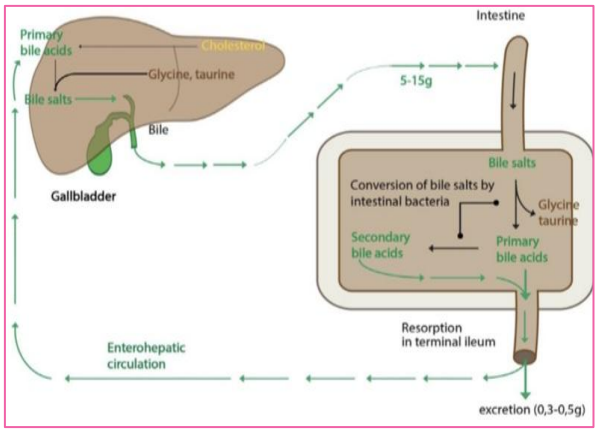


Enterohepatic Circulation (Portal circulation) of Bile Salts*/ Enterohepatic Circulation of Bile Acids* Continuation...

Only in girls slides

- 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:
  1-Cholic acid is converted to deoxycholic acid
  2-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. Stimulate more bile secretion (feedback control).
- 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. So, total bile acids remain constant. Feedback regulation will stimulate liver to synthesis the same amounts of BA that is secreted out with feces.





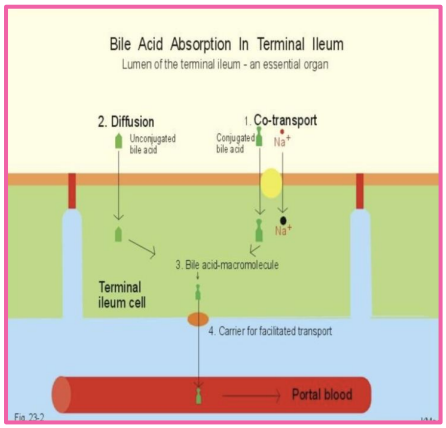
What is the difference between primary and secondary ?
Primary bile acids contain hydroxyl group and conjugate with amino acids (glycine and taurine).
So, it converts to secondary by deconjugation and dehydroxylation (in intestine by intestinal flora).

Absorption of Bile Acids in The Small intestines*

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 **2ry active transported** (Sodium dependent) powered by the Na+ gradient across the brush border membrane.The same as amino acids, glucose and galactose

Unconjugated bile acids are better absorbed by **simple diffusion**. (They are less polar).



Absorption of Bile Acids into portal circulation*

Bile salts or bile acids in the intestine lumen are absorbed via four pathways into portal circulation (enterohepatic circulation):

1. Passive diffusion
2. An active carrier-mediated process **(Apical Na+ dependent Bile salt transporter (ASBT).**
3. De-conjugation and/or transforming of bile salts to bile acids (by bacteria)
4. Transforming the primary bile acids to secondary bile acids (by bacteria)

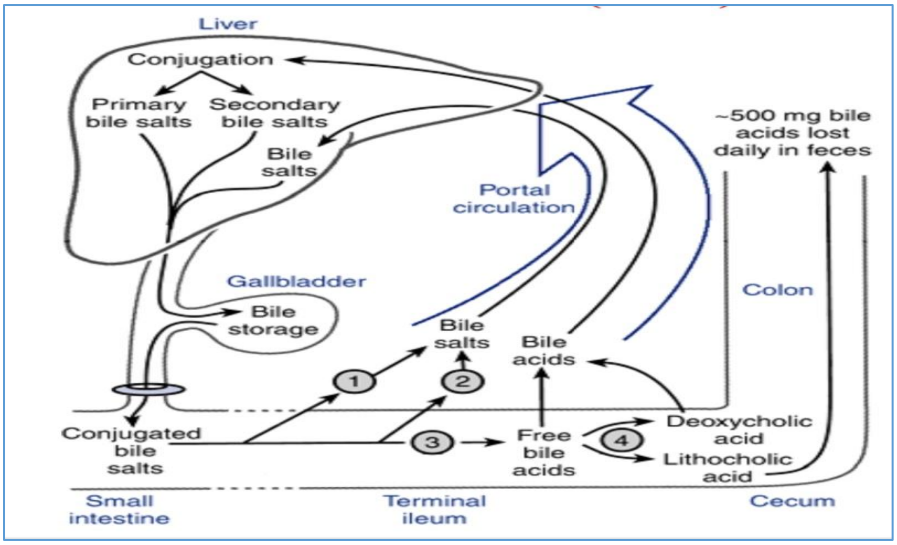
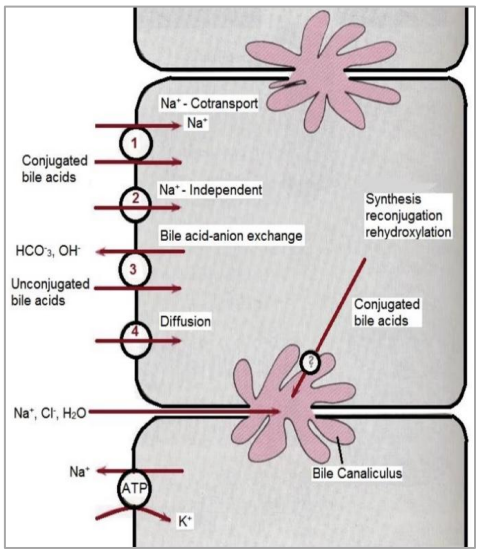


Figure 26.16 Bile salts are recycled.

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.*
Bile salts or bile acids in the portal circulation are absorbed via four pathways into hepatocytes*:

1. **An active carrier-mediated process:**
   conjugated bile acids-Na co-transport (Bile salt-Na+ coupled (Ntcp).
2. Na-independent pathway (Bile acid-Na+ independent (OATP).
   Facilitated diffusion (Sodium independent)
3. Bile acid-HCO3 or Bile acid-OH exchange.
   - OH^- and HCO_3^- = reabsorbed or leave the cell.
   - unconjugated bile acid - enter into the cell.
4. Passive diffusion (very little).



Only in girls slides

1

Hepatocytes extract bile acids, essentially clearing the bile acids from the blood in a single pass through the liver.

2

In the hepatocytes, most deconjugated bile acids are reconjugated & some 2ry bile acids are rehydroxylated.

ترجعه primary عكس اللي حصل في intestine.

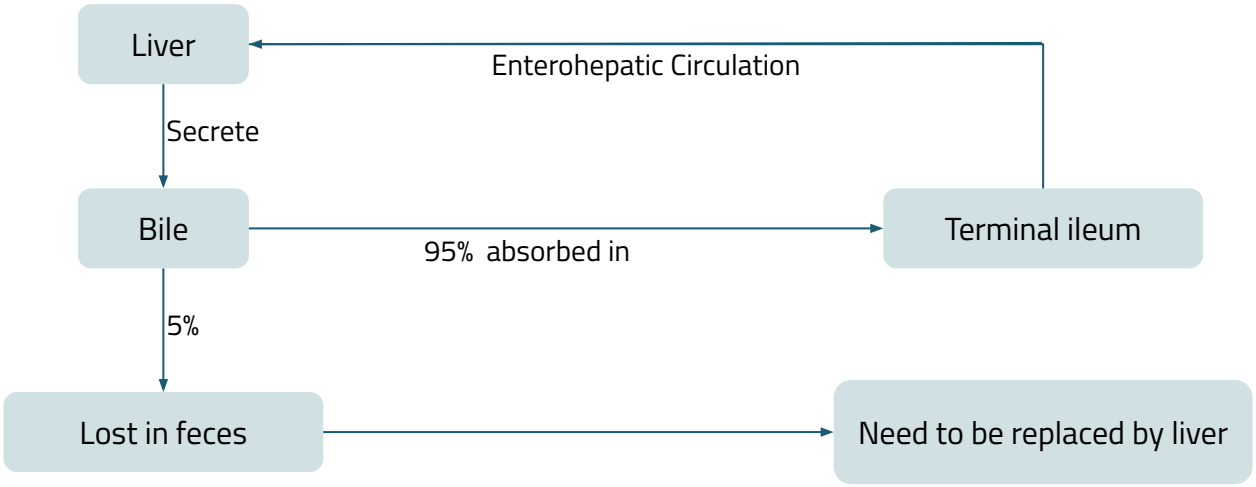
- Intestine: deconjugation and dehydroxylation.
- Liver: reconjugation and rehydroxylation

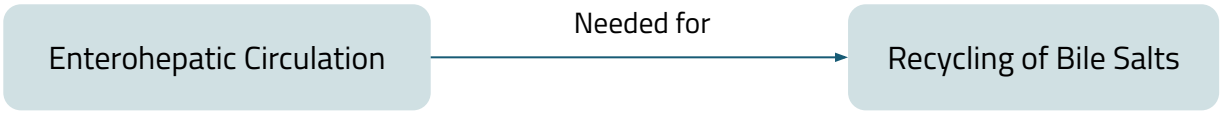
3

The reprocessed bile acids, together with newly synthesized bile acids, are secreted into bile.

Importance of Enterohepatic Circulation of Bile Acids

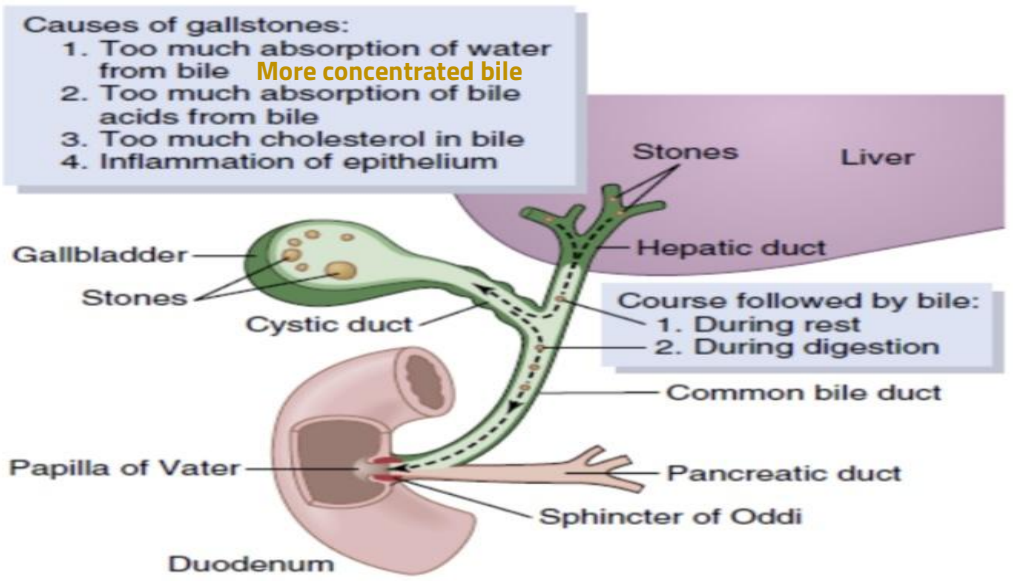
1. It is essential for stimulating & maintaining the secretion of bile by hepatocytes.*
2. The greater the quantity of bile salts in the enterohepatic circulation, the greater the rate of bile secretion.*the greater bile is absorbed the greater will be secreted when there is food and need it ,and less synthesis
3. By cycling several times, a relatively small bile acid pool can provide the body with sufficient amounts of bile salts to promote lipid absorption.





Why Recycling Bile salts is needed?

Gallstones



MCQ & SAQ:

Q1: Hepatic bile secretion is containing:
A. High Bile acid anion and Ca2+
B. Low Na+ , Cl- , HCO3 and H2O
C. Low K+ and Ca2+
D. B + C

Q2: Which of the following transporters carries the bile salts back to the liver through the portal vein?
A. BSEP
B. ASBT
C. MOTP
D. OATP

Q3: The absorption of bile salts occur in:
A. 3rd part of the duodenum
B. Jejunum
C. Ileum
D. Colon

Q4: Which of the following is the action of bile salt on the digestion of fat:
A. Break triglycerides to FFA
B. Emulsify fat to small particles
C. Increase fat surface tension
D. Reduce cholesteryl ester

Q5: Chenodeoxycholic acid is converted to lithocholic acid by:
A. Liver enzymes
B. Intestinal mucosa
C. Intestinal bacteria
D. Micelles

Q6: Which of the following is a pathway for absorption of bile acids or salts back into the hepatocytes:
A. Bile acid-H exchange
B. Apical Na+ dependent bile salt transporter
C. Na-independent pathway
D. all are true

answer key:
1: C
2: D
3: C
4: B
5: C
6: C

1- What provides hydrogen ions for the process of bile concentrations?

2- What is the main determinant of bile acid synthesis?

3-Name 2 pathways for absorption of bile acids into the portal circulation ?

4-Mention two functions of bile acids?

A1: Carbonic Anhydrase reaction

A2: Its concentration in the hepatic portal blood

A3:1-passive diffusion. 2-active carrier-mediated process. 3-Transforming bile salts to bile acids. 4-Transforming primary bile acids to secondary bile acids.

A4: 1-essential for absorption of fat soluble vitamins (A, D, E and K). 2-Emulsify fat to small particles. 3-They help in the absorption of fatty acids. 4-stimulate bile secretion and flow (choleretic action).

Leaders:

- Abdulaziz Alsuhaim.
- **Yara Alasmari.**

Co-leader:

- Mayasem Alhazmi.

Organizers:

- **Rawan baqader**
- Haya Alanazi
- Shaden Alobaid
- Mayasem Alhazmi.
- Basel Fakeeha
- Leen Almadhyani

Note takers:

- Shaden Alobaid
- **Raghad Albarrak**
- **Homoud Algadheb**.

Revisers:

- Abeer Awwad.
- **Shayma Alghanoum**

MEMBERS:

- Abdulaziz Alamri
- Basel Fakeeha
- Ahmad Alkhayatt
- Aljoud Algazlan
- Almaha Alshathri
- Abdulrahman Barashid
- Nada Bin Obeid
- Tarfa Alkaltham
- Yara alzahrani
- Sarah AlQuwayz
- Abdulrhman Alsuhaibany
- Abeer Awwad
- Mohammed alkathiri
- ziyad alhosan
- Rand Alrefaie
- **Omar Alhalabi**
- Joud Alarifi
- Ibrahim Alnamlah
- Hamad Almousa
- Abdullah Alburikan
- Leen Almadhyani
- Abdullah Alanzan
- Bader Alrayes
- Faisal jazzar
- Khalid Almutlaq
- Yara Alomar
- Reem Alqahtani
- Aljoharah Albnyan
- **Saud Alhasani**
- Muneerah Alsadhan

Physiology439@gmail.com