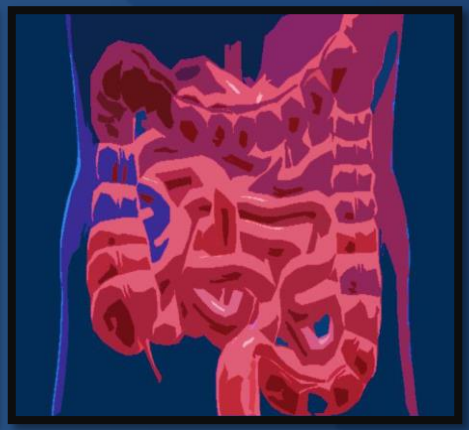
Physiology Team

GASTOINTISTINAL TRACT

LECTURE 10

Bile formation & enterohepatic circulation

Thanks for cooperation:
Mohammed AlGhammass

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OBJECTIVES

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At the end of this lecture, student should be able to describe:

- ❖Functions of the bile
- ❖Stages of bile secretion
- ❖Characteristics of bile
- ❖The main constituents of bile
- ❖Functions of gall bladder
- ❖Differences between hepatic bile and gall bladder bile.

- ❖Control of biliary system
  - ▪Control of choleresis
    - Bile acid dependent component
    - Bile acid independent component
  - ▪Control of the discharge of bile into the intestine

MIND MAP

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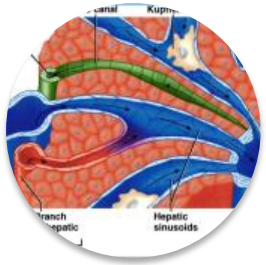
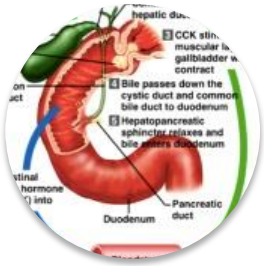


Bile

- components
- Secretion
- Characteristics
- Important functions

Gall Bladder

- Functions



Control of Biliary System

- Secretion of bile by liver cells (choleresis).
- Control of the discharge of bile into intestine.

Function of bile

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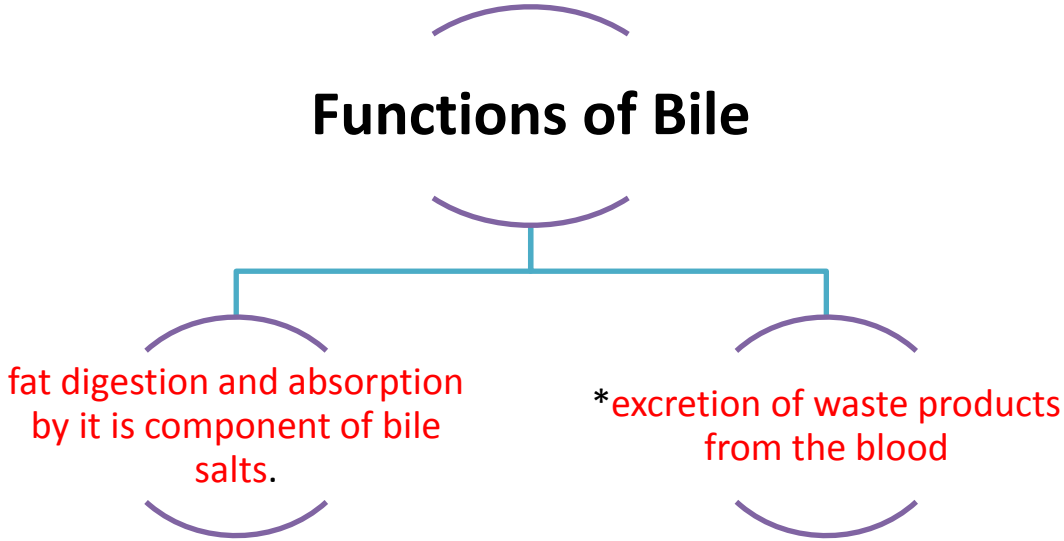
The main digestive function of the liver is the secretion of bile.

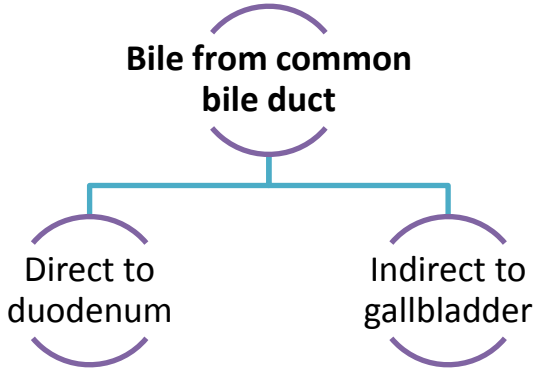


*Bile Excretes especially bilirubin and it is the main route of cholesterol excretion.

Bile is secreted in two stages

•(1) The initial portion is continually secreted by the hepatocytes into bile canaliculi that originate between the hepatic cells.

•(2) The bile flows in the canaliculi toward the common bile duct.
Then, bile either empties directly into the duodenum or indirectly diverted for minutes up to several hours through the cystic duct into the *gallbladder to be stored.
* (this is the second portion which is added to the initial bile)



Bile secretion

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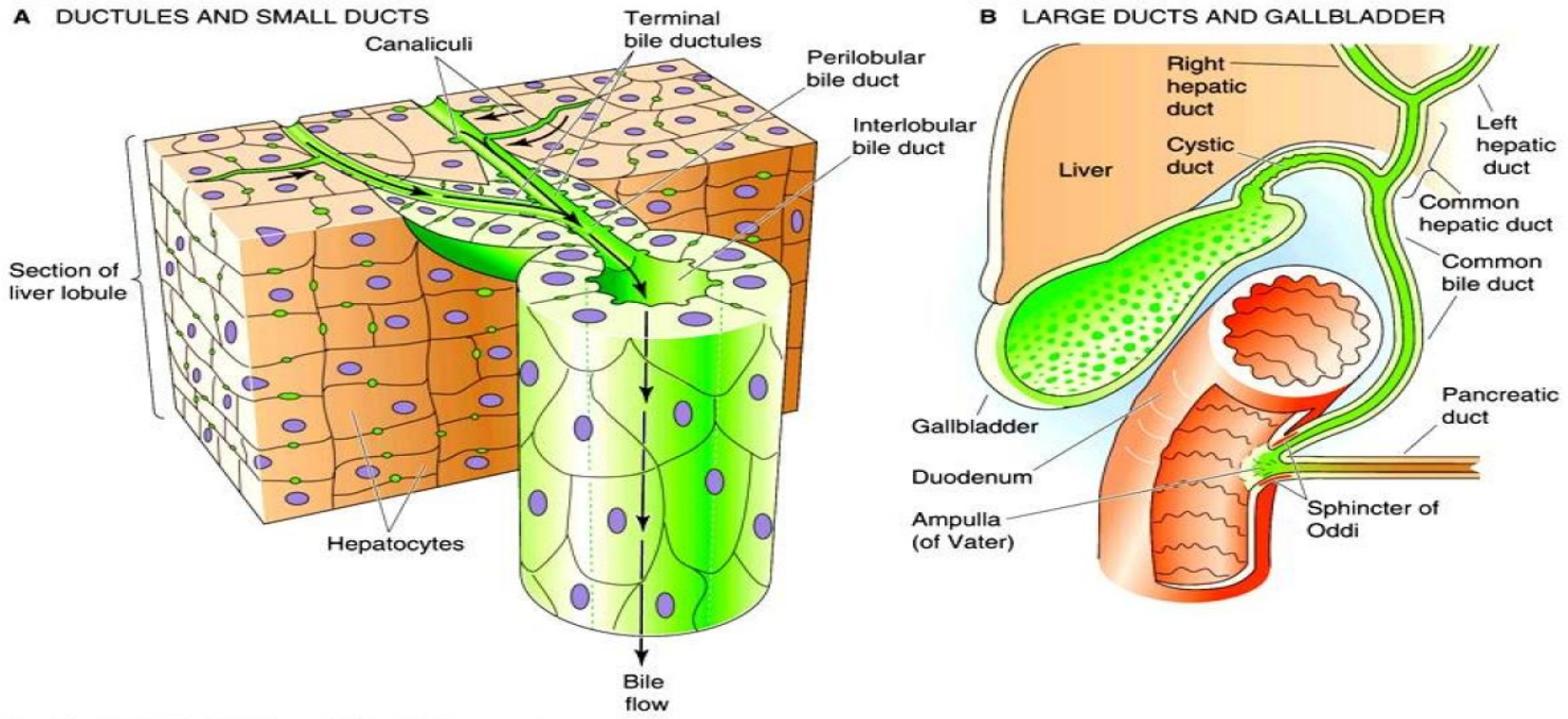
Bile is secreted by the liver, stored in the gall bladder and ejected into the small intestine



Bile secretion

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•**Between meals, bile is diverted into gall bladder.**

•The gall bladder epithelium (we will talk about it later on) extracts (absorb) salts and H2O from the stored bile, concentrating bile five fold up to twenty fold (5 to 20 times).

•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).

Characteristics of bile

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Characteristics of bile
viscous golden yellow or greenish fluid with bitter taste
Isotonic with plasma and slightly alkaline **NaHCO3 in the bile for its alkaline reaction
Daily production from liver= 5 L /day only 700-1200 ml/day are released into duodenum (with meals).

Components of bile in hepatocytes

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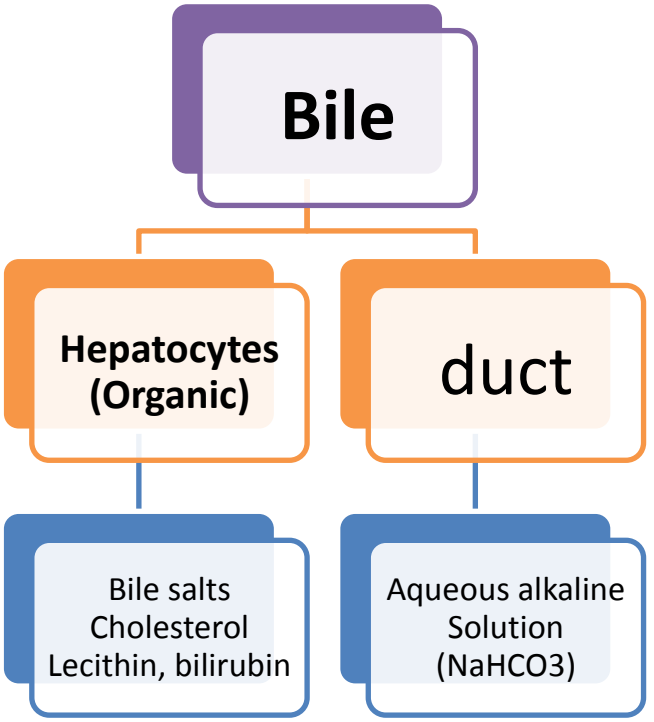
- Bile acids (**bile salts**) (65% of dry weight of bile)
- Bilirubin and bile pigments (0.3%).
- Phospholipids (20%) (90% of phospholipids are lecithin).
- Proteins (5%).
- Cholesterol (4%), the major route for cholesterol excretion is bile.

**Cholesterol solubility depends on the relative concentration of cholesterol, bile salts, and phospholipids.



Components of bile in bile ducts

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All organic constituents (in the previous slide) are secreted by hepatocytes into bile canaliculi, along with an isotonic fluid that resembles plasma in its electrolyte conc.

•Electrolytes mainly HCO3- (bicarbonate), these in addition to H2O are secreted by epithelial cells that line bile ducts, and contribute to the volume of bile leaving the liver.

•HCO3- participates with pancreatic and duodenal secretion in neutralization of acid chyme delivered from stomach

Functions of gall bladder

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**Gall bladder not only stores bile but concentrates it.

- The total secretion of bile (into duodenum) each day is about 700-1200 ml per day.
- The maximum volume of the gall bladder is only 30-60 ml as much as 12 hours bile secretion can be stored & concentrated in the gall bladder.
- Bile is normally conc. about 5 folds (5 to 20 folds).

**Gall bladder epithelium secretes mucus which has protective function.

**Buffer of biliary pressure by storing of bile, so it prevents increase in biliary pressure & enables the liver to secret bile(liver continuously secrete bile), because hepatic cells can not secret against high pressure.

Concentration of bile in the gall bladder occur by:

- Active absorption of Na+, Cl-, and HCO3- by the lining epithelium.
- Associated passive water movement out of the lumen (water follow Na).

This result in drop of pH (but still slightly alkaline 7.5) of gall bladder bile due to decreased NaHCO3 concentration (that is important to prevent some substance like Ca from precipitating in more alkaline media) .

This explanation is from male slides

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.

Functions of gall bladder

Not to remember

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This is just for comparison and to show that all components get concentrated except Na, Cl- , HCO3- & water which get absorbed by the epithelium of gall bladder.

Water	Hepatic bile (98%)	Gall bladder (89%)
Total solids	2-4	11
Bile salts	26	145
Bilirubin	0.7	5
Cholesterol	2.6	16
Phospholipids	0.5	4
Ca++	5	23
K+	5	12
pH	8.3	7.5
Na+	145	130
Cl-	100	25
HCO3-	28	10

Control of biliary system

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There are 2 aspects for control

1. Secretion of bile by liver cells (choleresis) (in the next slide).
2. Control of the discharge of bile into intestine (in bile duct).

•The human liver secretes bile at a pressure of about 25 cm H2O. Between the meals, the cholechoduodenal sphincter is normally closed offering a resistance of about 30 cm H2O (the pressure in the sphincter higher than that in bile duct so no bile will be secreted to dudenum).

•Bile secreted by liver is thus diverted to the gall bladder during the interdigestive peroids.

•Pressure in the lumen of the gall bladder varies between 0-16 cm H2O

Control of choleresis

Substances that stimulate hepatic secretion of bile (choleresis) are choleretics.

•Bile secretion from hepatocytes is active transport of bile acids into canaliculi with passive H2O flow along osmotic gradient.

•In the biliary ducts HCO3- is secreted independently of bile acid secretion & is followed passively by water.

Total bile flow is due to 2 components:

•Bile acid dependent component
•Bile acid independent component

Bile acid dependent component

•The bile acid dependent component depends mainly on the integrity of the enterohepatic circulation.

•At least 90% of the rate of secretion of bile acids is determined by the rate of clearance of reabsorbed bile acids from the portal vein (90% reabsorbed & 10% excreted in stool).

•The remaining 10% is due to synthesis of new bile acids by hepatocytes (to compensate the amount that lost in stool) .

•Interruption of the enterohepatic circulation results in markedly reduced choleresis (low rate of bile secretion).

Bile acid independent component

•This fraction of bile secretion is due to secretion of HCO3- followed by water by the biliary duct cells. It depends on active sodium transport.

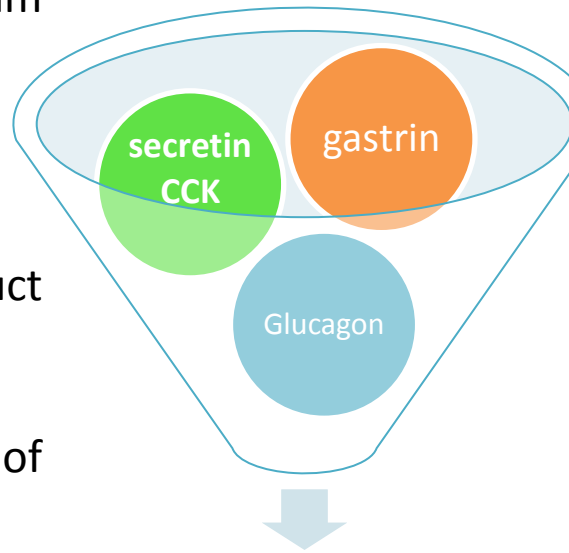
•Bile acid independent fraction of bile secretion is stimulated by:

1. Hormones as secretin, glucagon, CCK and gastrin.

They all stimulate HCO3- & passive water transfer by the biliary duct cells.

1. Vagal stimulation also stimulates bile flow.

The effect is mediated mainly indirectly, through stimulation of gastric acid secretion, which leads to release of secretin & CCK.



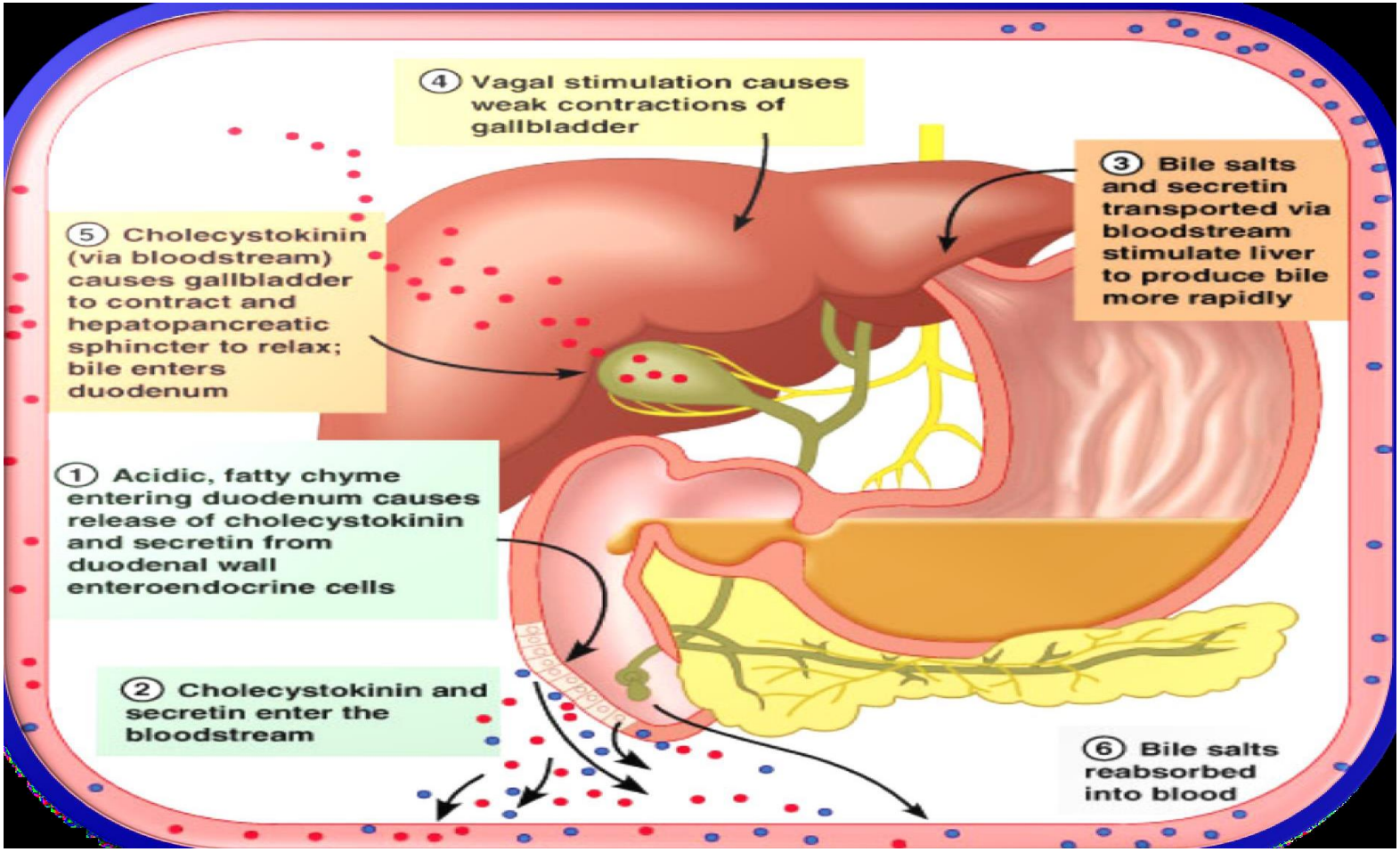
HCO3- secretion followed by water passively

N.B.

•Increase portal blood flow during digestion increases bile secretion.

•But when the liver is markedly congested bile secretion stops due to increase intrahepatic vascular pressure.

Control of biliary system



Control of the discharge of bile into the intestine

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The nervous component	The hormonal component
•**Parasympathetic (vagal)** stimulation results: 1. contraction of the gallbladder 2. relaxation of the sphincter of Oddi 3. increased bile formation. • Bilateral vagotomy results in reduced bile secretion after a meal, suggesting that the PNS plays a role in mediating bile secretion. •Stimulation of the **sympathetic** nervous system results in: 1. relaxation of the gallbladder 2. reduced bile secretion. 	• Mediated by CCK. • The presence of digestive products of fat & proteins releases CCK from the upper intestine into the blood. • CCK: 1. ontracts gall bladder 2. relaxes sphincter of Oddi, thus discharging bile into the duodenum. •Both vagal excitation & secretin augment the action of CCK on the gall bladder. •Also MgSO-4 (magnesium Sulfate) contract the gall bladder and discharge bile into the intestine as it releases.

Control of the discharge of bile into the intestine

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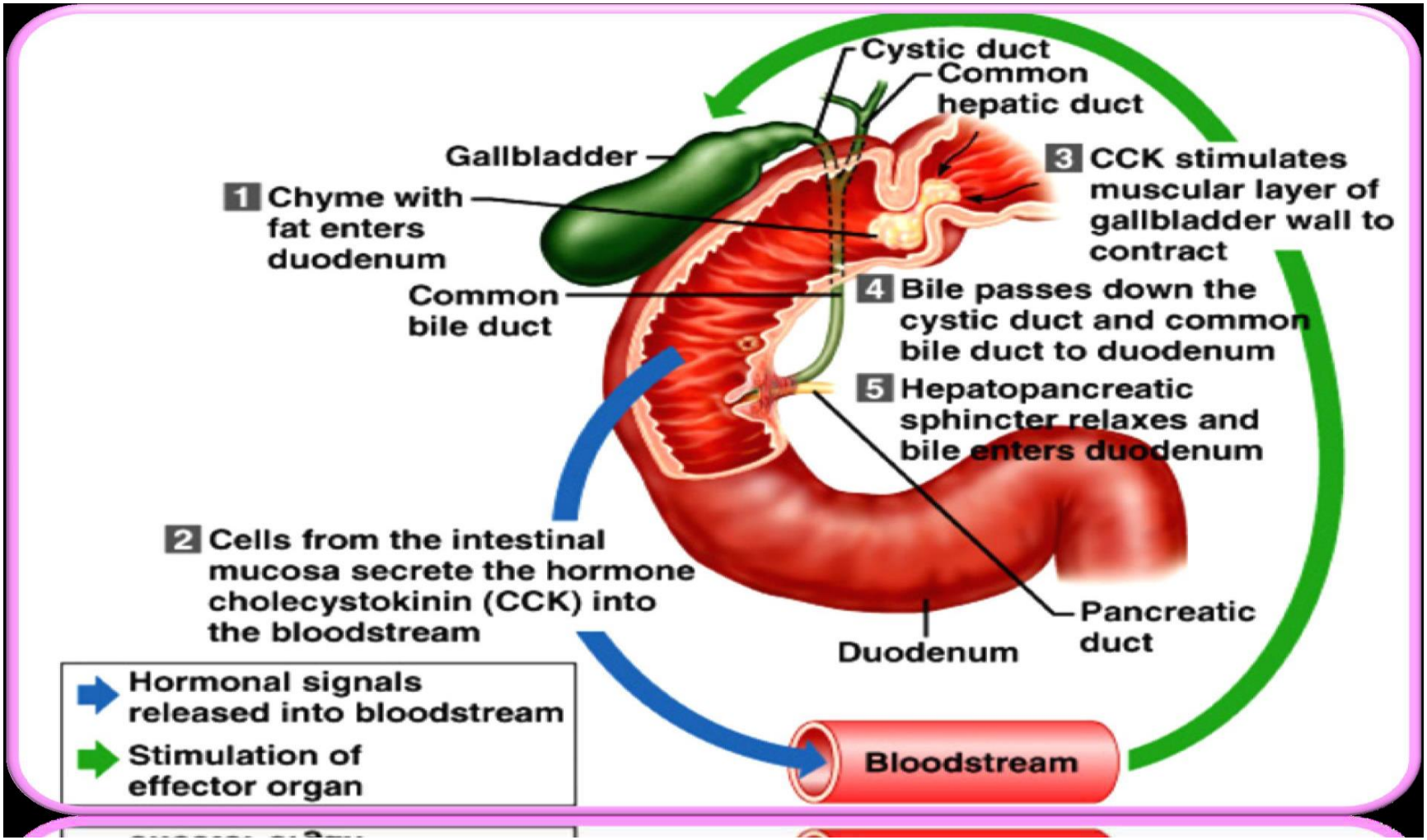

Bile secretion is primarily regulated by a feedback mechanism, with secondary hormonal and neural controls

- **The major determinant of bile acid synthesis is its concentration in hepatic portal blood (feedback control)**

- CCK, Secretin and estrogen (hormonal 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 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.

Liver Functions:

o- The main digestive function of the liver is the secretion of bile (normally 600-1000 ml/day), which has **2 main functions** :

1. fat digestion and absorption
2. 2. excretion of waste products from the blood

Bile serves two important functions:

1. It plays an important role in fat digestion and absorption by the following:

- Emulsifying the large fat particles of the food into minute particles
- Help in digestion of fat through the intestinal mucosal membrane

2. Excretion of waste products (Mainly Bilirubin)

Bile secretion portions:

1) **Initial portion:**
2) Secretion of bile from the hepatocytes directly into the duodenum
3) **2) Second portion:**
4) The bile secreted from the hepatocytes get stored in the Gallbladder and secreted when needed

Storing and Concentrating Bile in the Gallbladder:

- During storage of bile, Gallbladder concentrates the bile (bile salts, cholesterol, lecithin, and bilirubin)
- The increased concentration of bile is due to absorption of water, Na, and Cl through the Gallbladder mucosa
- Absorption happens by active transport of Na, followed by secondary absorption of Cl, water, and others
- In Gallbladder, bile is concentrated about 5-fold, but it can reach up to 20-fold

Components of bile:

1- Bile acids (bile salts)
2- Cholesterol
3- Phospholipids (Lecithin)
4- Bile pigments
5- Ions and water

o**Characteristics of bile:**

1.Viscous , greenish fluid with bitter taste.
2.isotonic with plasma and slightly alkaline.
3.the liver produces about 5 L /day, but only 700-1200 ml/day are poured into the duodenum.

Composition of bile :

1- From ducts: ($NaHCO_3$)

2- **From hepatocytes:** (Bile salts,Cholesterol, Lecithin, bilirubin.)

Bile secretion:

-It is regulated by feedback mechanism, also hormonal and neural control.

Feedback control: depends on bile concentration in hepatic portal blood, if concentration is high, bile secretion will be inhibited, and vice versa

Hormonal control:

- ✓ CCK, Secretin, and Estrogen

Neural control:

- ✓ **Parasympathetic stimulation (vagus):** contraction of Gallbladder, relaxation of sphincter of Oddi, and increase bile formation
- ✓ **Sympathetic stimulation:** relaxation of Gallbladder and reduced bile secretion

Functions of of gall bladder :

1. Not only stores bile but concentrates it.(Bile is normally conc. about 5 up to 12-20 folds).
2. protective function
3.Buffer of biliary pressure

Control of biliary system :

1.Secretion of bile by liver cells (choleresis).

Substances that stimulate hepatic secretion of bile (choleresis) are choleretics.

2.Control of the discharge of bile into intestine.

Gall bladder evacuants are called cholagogues.

QUESTIONS

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1. **Concentration of bile in the gall bladder occur by :** A
   - A. Active absorption of Na+, Cl-, and HCO3 + Associated passive water movement B
   - B. Blood pressure A
   - C. Intestinal absorption
   - D. Active transport of glucose + Associated passive water movement

2. **Increase portal blood flow during digestion ……. bile secretion. But when the liver is markedly congested bile secretion……. ?**
   - A. Decreases- stops
   - B. Increases- stops
   - C. Decreases - increases
   - D. Increases- increases

3. **In the biliary ducts ……is secreted independently of bile acid secretion & is followed passively by…….. ?**
   - A. HCO3- / water
   - B. Na+ / K+
   - C. Water/ Hco3
   - D. Na+/ ca++

4. Bile Contains All Of The Following Except:

A. Fructose.
B. Phospholipids.
C. Bile Pigment.
D. Electrolytes.

A

B

A. 5. Bile Salt:

A. Are Formed From Fatty Acids.
B. Have Enterohepatic Circulation
C. Are Secreted From Stomach.
D. None Of The Above.

D

6. Which ONE of the following is a function of bile salts?

A. They are powerful cholagogues
B. They are essential for protein absorption
C. They inhibit bile secretion
D. They emulsify fat

THE END

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If there are any Problems or Suggestions,
Feel free to contact us:

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THANK YOU

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Actions Speak Louder Than Words