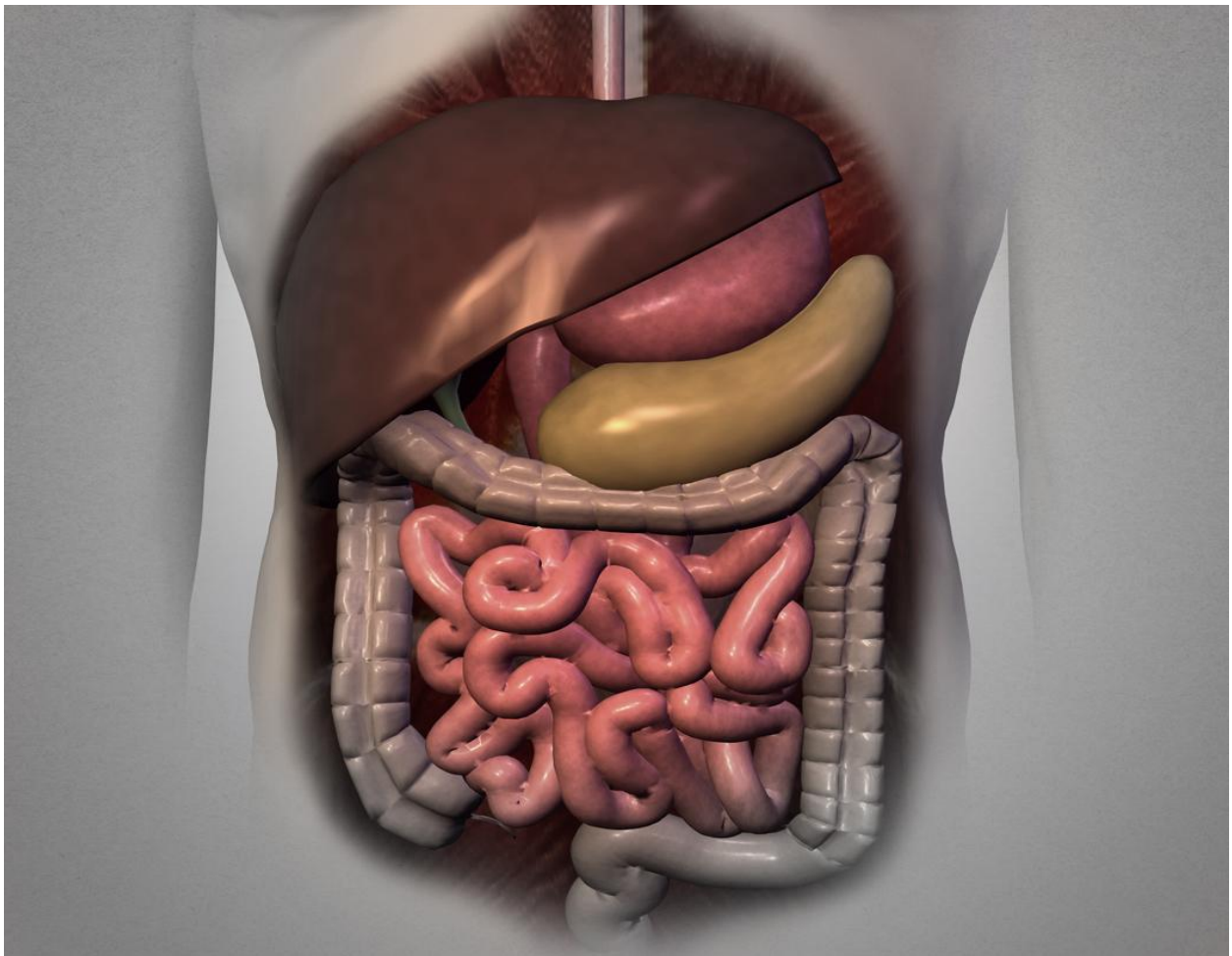


GIT Block

Physiology Team 431

Done by : Rand AL-haweal

Revised by : Nour Al-Khawajah & Mohammed Asiri

- Important
- Female's notes
- Males notes
- Extra

Gastrointestinal Physiology

(Lecture 10)

Bile Formation & Enterohepatic Circulation

Learning Objectives:

- 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
  a. Control of choleresis
  b. Bile acid dependent component
  c. Bile acid independent component
  d. Control of the discharge of bile into the. intestine

Functions of the liver: (extra info)

The liver regulates most chemical levels in the blood and excretes a product called bile, which helps carry away waste products from the liver. All the blood leaving the stomach and intestines passes through the liver. The liver processes this blood and breaks down the nutrients and drugs into forms that are easier to use for the rest of the body. More than 500 vital functions have been identified with the liver. Some of the more well-known functions include the following: (you could say secretion and excretion)

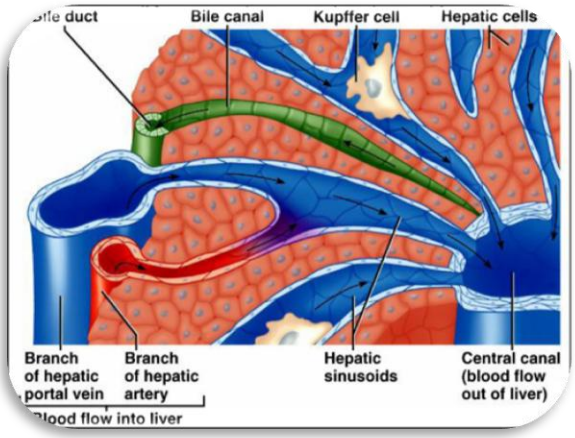
- **Production of bile, which helps carry away waste and break down fats in the small intestine during digestion**
- **Production of certain proteins for blood plasma** secretion
- **Production of cholesterol and special proteins to help carry fats through the body** secretion
- **Conversion of excess glucose into glycogen for storage**
- **Regulation of blood levels of amino acids, which form the building blocks of proteins**
- **Processing of hemoglobin for use of its iron content (the liver stores iron)**
- **Conversion of poisonous ammonia to urea (urea is an end product of protein metabolism and is excreted in the urine)**
- **Clearing the blood of drugs and other poisonous substances** excretion
- **Regulating blood clotting**
- **Resisting infections by producing immune factors and removing bacteria from the bloodstream**
- **From: http://medicalcenter.osu.edu/patientcare/healthcare_services/liver_biliary_pancreatic_disease/liver_anatomy_function/Pages/index.aspx**

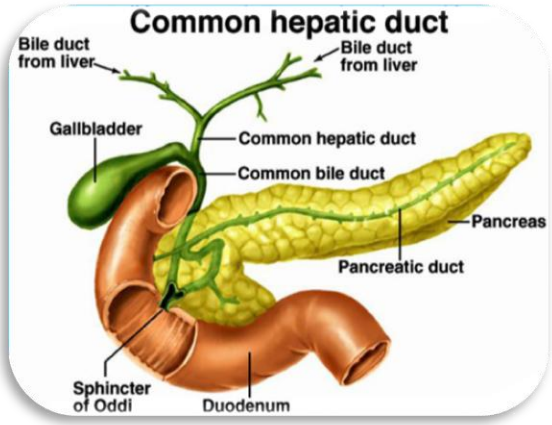
- The main digestive function of the liver is the secretion of bile.
- Bile serves two important functions:
  - It plays an important role in fat digestion and absorption by its contents of bile salts. Bile serves as a means for excretion of waste products from the blood. These include especially bilirubin (an end product of hemoglobin destruction).

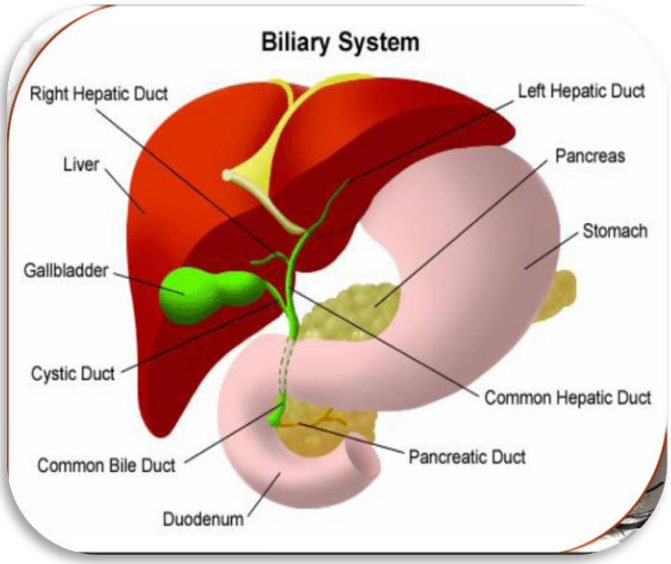
Bile is secreted in two stages:

1. The initial portion is continually 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, bile either empties directly into the duodenum or is diverted for minutes up to several hours through the cystic duct into the gallbladder (this is the second portion of liver secretion, which is added to the initial bile).

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

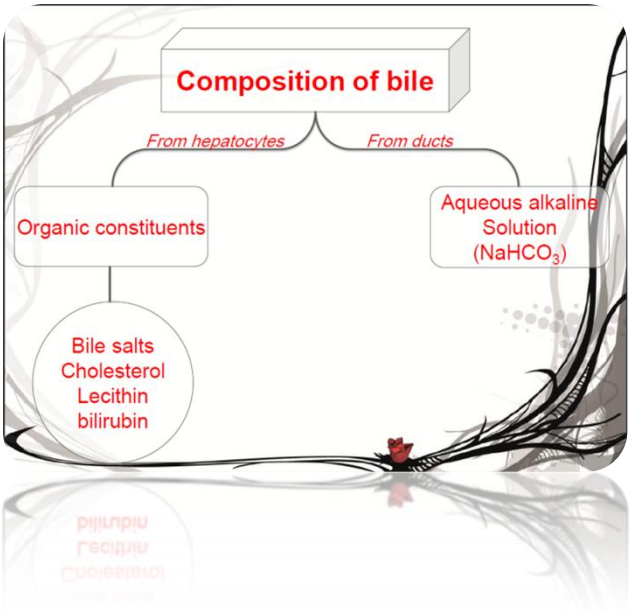
- Bile is a viscous golden yellow or greenish fluid with bitter taste.
- It is isotonic with plasma and slightly alkaline. $NaHCO_3$ in bile is responsible for its alkaline reaction.

The only non-isotonic secretion is saliva (hypo tonic).

- The liver produces about 5 L /day, but only 700-1200 ml/day are poured into the duodenum. (The rest is stored in gall bladder)

The main constituents of bile are:

- Bile acids (bile salts) (65% of dry weight of bile).
- Bilirubin and related bile pigments (0.3%).
- Phospholipids (90% lecithin) (20%).
- Proteins (5%).
- Cholesterol (4%), the major route for cholesterol excretion. (Cholesterol must be exerted or it will form gall stones). Cholesterol solubility depends on the relative concentration of cholesterol, bile salts, and phospholipids.



- All of these constituents are secreted by hepatocytes into bile canaliculi, along with an isotonic fluid that resembles plasma in its electrolyte conc.
- Electrolytes mainly HCO_3^-, these in addition to H_2O are secreted by epithelial cells that line bile ducts, and contribute to the volume of bile leaving the liver. ← they cause osmosis of water (water is added to the bile)
- HCO_3^- participates with pancreatic and duodenal secretion in neutralization of acid chyme delivered from stomach. → With the secretions from pancreas and intestine

---

Function of gall bladder:

I. Gall bladder not only stores bile but it also concentrates and lowers the pH of the bile.

The total secretion of bile 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 (up to 20 folds).

Concentration of the bile in the gall bladder occur by:

a. Active absorption of Na^+, Cl^-, and HCO_3^- by the lining epithelium.
b. Associated passive water movement = osmosis of water with the solutes(Na^+, Cl^-, and HCO_3^+ out of the lumen.

This result in drop of pH of gall bladder bile due to decreased $NaHCO_3$ concentration. By decreasing the pH so it prevent precipitation of Ca and gard against gall stones

Explanation: How does the gall bladder store secretions that exceed its capacity?

By increasing the concentration of the secretion up to 20 folds which will defiantly decrease its volume so it can be stored in gall bladder.

II. Gall bladder epithelium secretes mucus which has protective function. From the high concentration of solutes that may damage the lining epithelium.

III. Buffer of biliary pressure by storing of bile, so it prevents increase in biliary pressure & enables the liver to secret bile, because hepatic cells cannot secret against high pressure.

The hepatocytes are constantly secreting bile. So, if the bile don't get stored in gall bladder, it will increase biliary pressure (the pressure caused by accumulation of bile in the canaliculi) and then the hepatic cell will malfunction because it can't secret against high pressure.

So, buffer here means decrease constantly

	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

NUMBERS ARE FOR YOUR KNOWLEDG (NOT INCLUDED IN EXAM)

You need to know what substances are more concentrated in gall bladder more than hepatic like the ones in red

Control of biliary system:

There are 2 aspects for control

1) Secretion of bile by liver cells (choleresis). (initial portion)
2) Control of the discharge of bile into intestine. (second portion)

* The human liver secretes bile at a pressure of about 25 cm H_2O. Between the meals, the choledochoduodenal sphincter is normally closed offering a resistance of about 30 cm H_2O.
* Bile secreted by liver is thus diverted to the gall bladder during the interdigestive periods.
* Pressure in the lumen of the gall bladder varies between 0-16 cm H2O.

Cause of the difference in bile secretion into duodenum:

Between meals: the choledochoduodenal sphincter is normally closed and the gall bladder relaxed → low secretion.

While digestion: it is open and the gall bladder contract → more secretion.

1. Control of choleresis

Choleresis: stimulation of hepatic secretion of bile.

Choleretics: Substances that stimulate choleresis.

- Substances that stimulate hepatic secretion of bile (choleresis) are **choleretics.**
- The driving force for bile secretion is active transport of **bile acids** into canaliculi with passive H_2O flow along osmotic gradient.
- In the biliary ducts, **HCO_3^-** is secreted independently of bile acid secretion & is followed passively by water.
- Total bile flow is thus due to 2 components:
  - *Bile acid dependent component*
  - *Bile acid independent component*

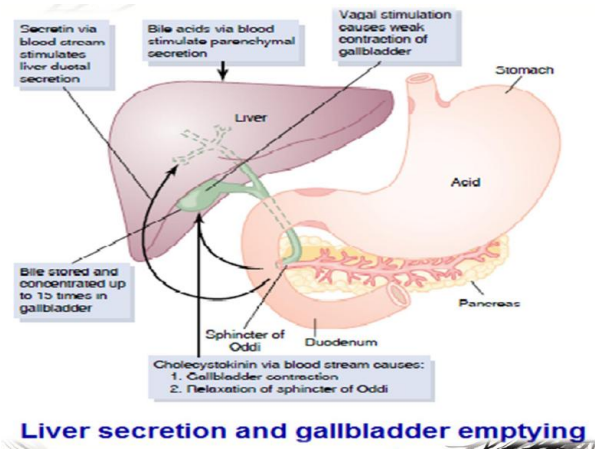
Hepatic secretion are stimulated by the presence of bile acids.

Bile acid dependent component :

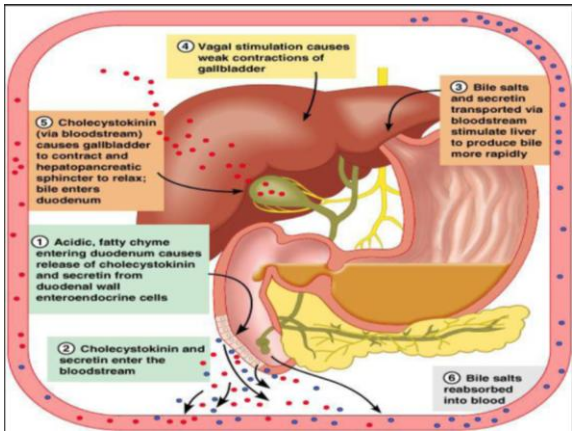
- The bile acid dependent component depends mainly on the integrity of the enterohepatic circulation.
- At least 90% of the rate of secretion of bile acids is determined by the rate of clearance of reabsorbed bile acids from the portal vein.
- The remaining 10% is due to synthesis of new bile acids by hepatocytes.
- Interruption of the enterohepatic circulation results in markedly reduced choleresis. Like thrombosis

Bile acid independent component

- This fraction of bile secretion is due to secretion of HCO_3^- 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, CCK, gastrin and glucagon. They all stimulate HCO_3^- & passive water transfer by the biliary duct cells. Like in pancreas
  2. Vagal stimulation stimulates bile flow indirectly, through stimulation of gastric acid secretion, which leads to release of secretin & CCK



Liver secretion and gallbladder emptying



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.

2. control of discharge of bile into the intestine

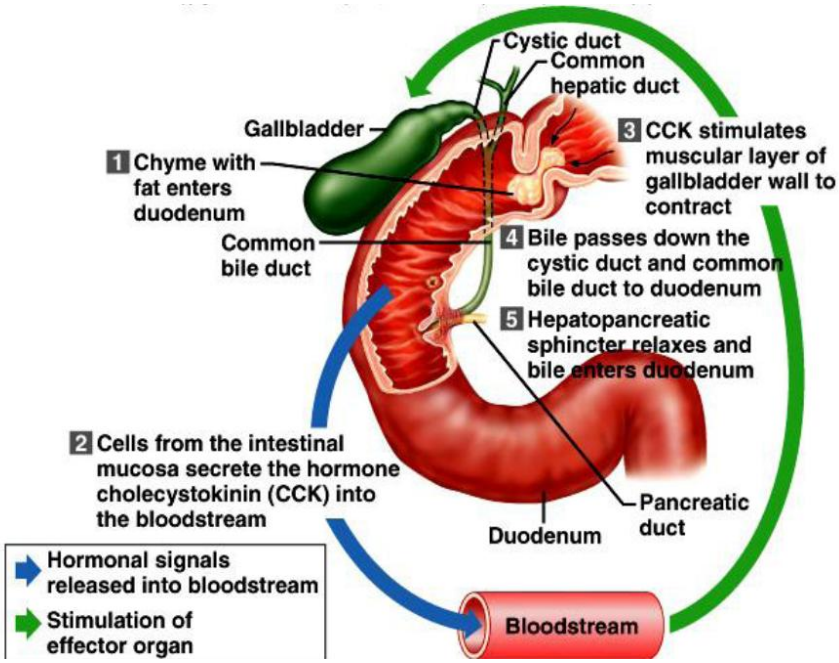
- Discharge of bile into the duodenum occurs by contraction of gall bladder wall and relaxation of Oddi sphincter. The highest rate of gall bladder emptying occurs during the intestinal phase. Gall bladder evacuants are called **cholagogues.** ← **different from choleretics**
- Discharge of bile into the duodenum is regulated by nervous & hormonal mechanisms:

a) The nervous component:

- 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 PNS plays a role in mediating bile secretion.
- Stimulation of the sympathetic nervous system results in relaxation of the gallbladder and reduced bile secretion.

b) The hormonal component

It is mediated by CCK. The presence of digestive products of fat & proteins releases CCK from the upper intestine into the blood. CCK contracts gall bladder and relaxes sphincter of Oddi, thus discharging bile into the duodenum. Both vagal excitation & secretin augment the action of CCK on the gall bladder.



Questions

1/ After secretion of bile, it is drained into:
a) Common bile duct
b) Hepatic duct
c) Portal vein
d) Bile canaliculi

2/ Upon emptying the gallbladder:
a) The walls contract and sphincter of the oddi relaxes
b) The walls relax and sphincter of the oddi contracts
c) Sympathetic stimulation increases
d) Will remain closed until it is completely filled with bile

Answers

D,A