بسم الله الرحمن الرحيم

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السلام عليكم ورحمة الله وبركاته

Gastrointestinal Physiology (Lecture 10)

Bile Formation & Enterohepatic Circulation

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Learning Objectives

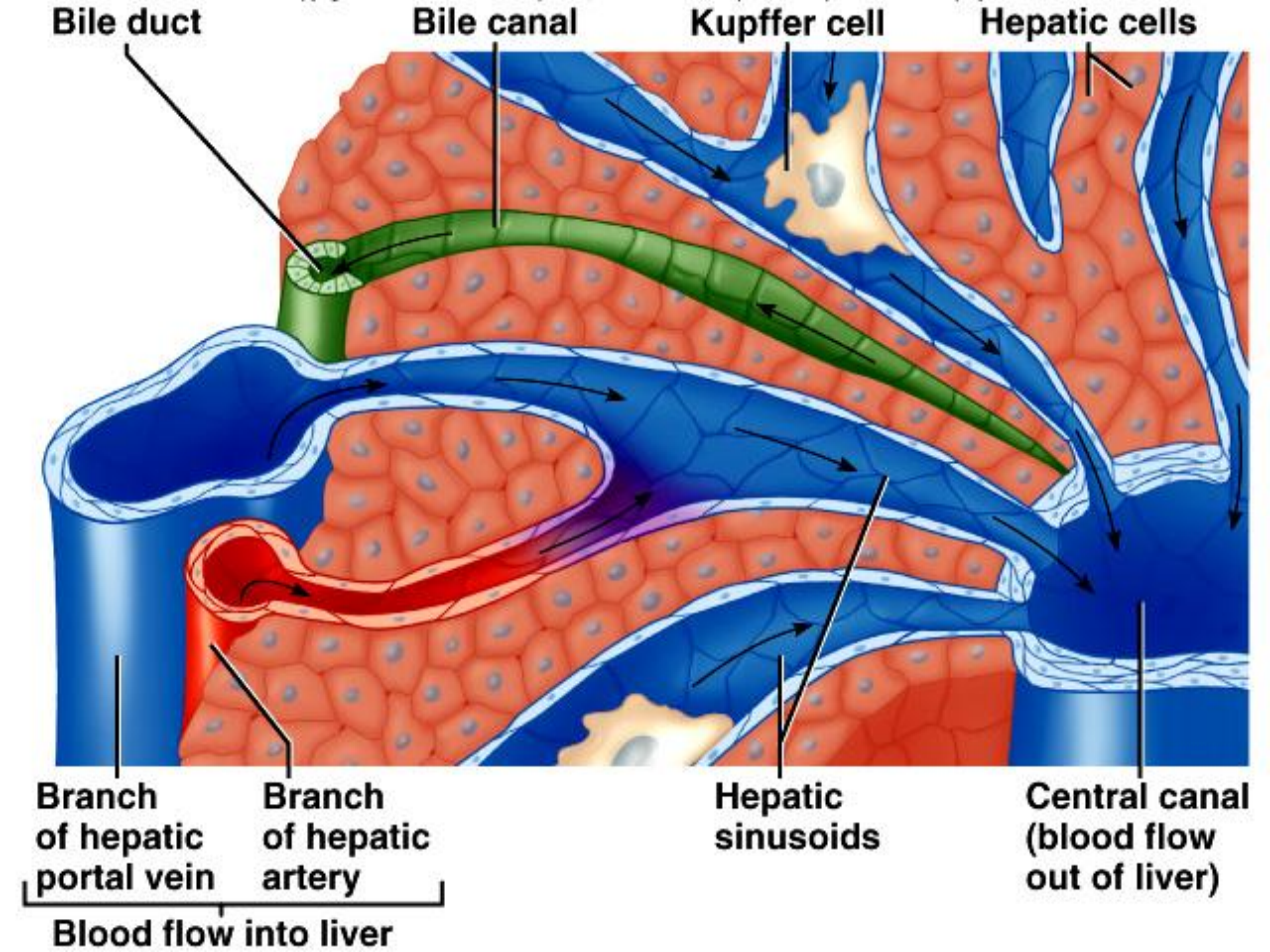
- Functions of the bile
- Stages of bile secretion
- Characteristics of bile
- The main constituents of bile
- Functions of gall bladder
- Differences between hepatic bile and gall bladder bile.
- Control of biliary system
  - Control of choleresis
    - Bile acid dependent component
    - Bile acid independent component
  - Control of the discharge of bile into the. intestine

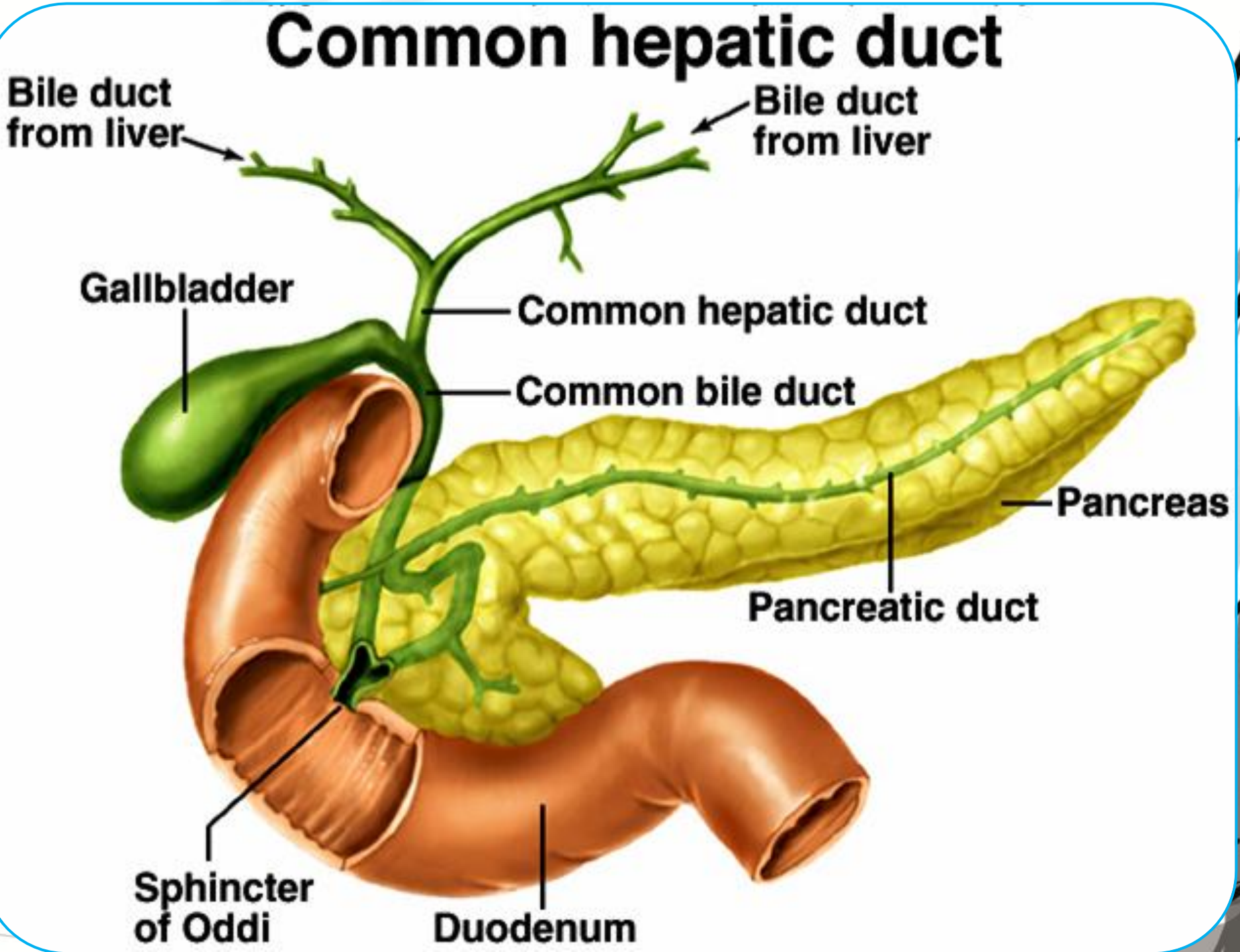
- The main digestive function of the liver is the secretion of bile.
- Bile serves two important functions:

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 bilirubin, an end product of hemoglobin destruction.

Bile is secreted in two stages:

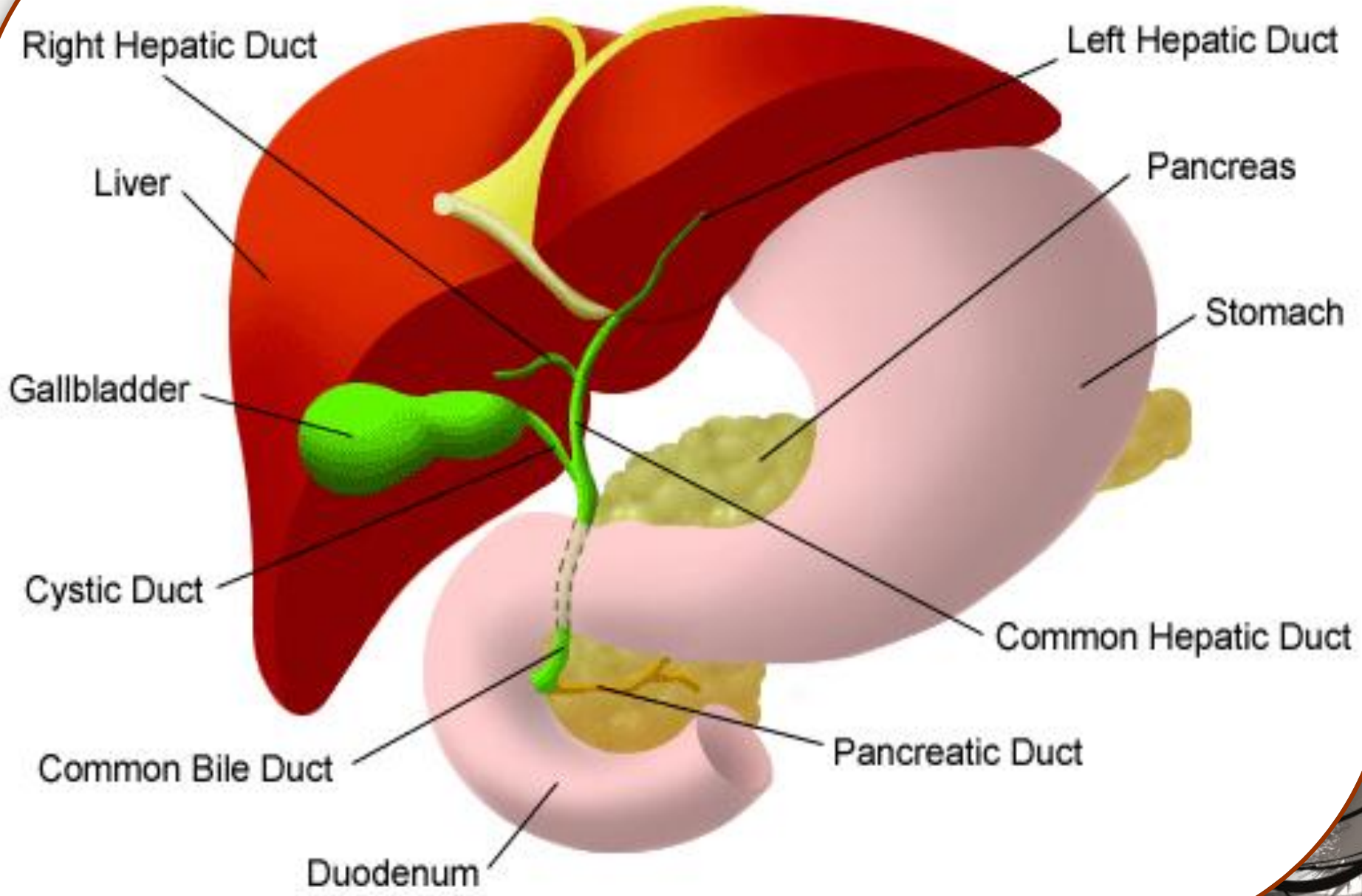
1) The initial portion is continually secreted by the hepatocytes. It is secreted into bile canaliculi that originate between the hepatic cells.
2) The bile flows in the canaliculi toward the hepatic duct and common bile duct. From these, bile either empties directly into the duodenum or is diverted 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).


Bile duct
Bile canal
Kupffer cell
Hepatic cells
Branch of hepatic portal vein
Branch of hepatic artery
Hepatic sinusoids
Central canal (blood flow out of liver)
Blood flow into liver


Common hepatic duct
Bile duct from liver
Bile duct from liver
Gallbladder
Common hepatic duct
Common bile duct
Pancreas
Pancreatic duct
Sphincter of Oddi
Duodenum

- 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).

Biliary System



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 liver produces about 5 L /day, but only 700-1200 ml/day are poured into the duodenum.

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 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.
- HCO_3^- participates with pancreatic and duodenal secretion in neutralization of acid chyme delivered from stomach.

Composition of bile

From hepatocytes

From ducts

Organic constituents

Bile salts
Cholesterol
Lecithin
bilirubin

Aqueous alkaline Solution ($NaHCO_3$)

Functions of gall bladder

I. Gall bladder not only stores bile but it 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 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 out of the lumen.

This result in drop of pH of gall bladder bile due to decreased $NaHCO_3$ concentration.

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

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 can not secret against high pressure.

	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

Control of biliary system

There are 2 aspects for control

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

2) Control of the discharge of bile into intestine.

- 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 peroids.
- Pressure in the lumen of the gall bladder varies between 0-16 cm H_2O.

1. Control of choleresis

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

- The deriving 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*

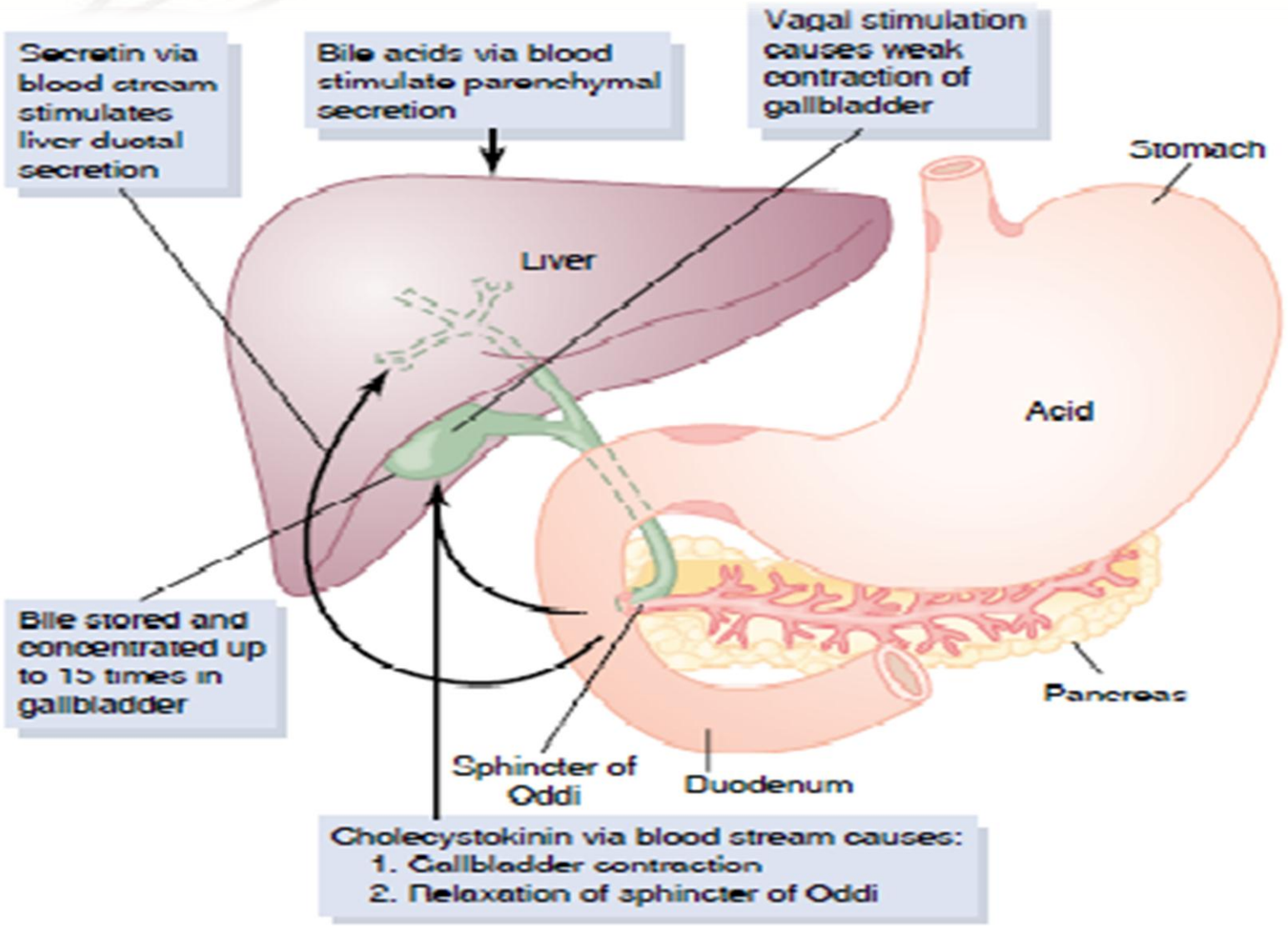
Bile acid dependent component

- 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.

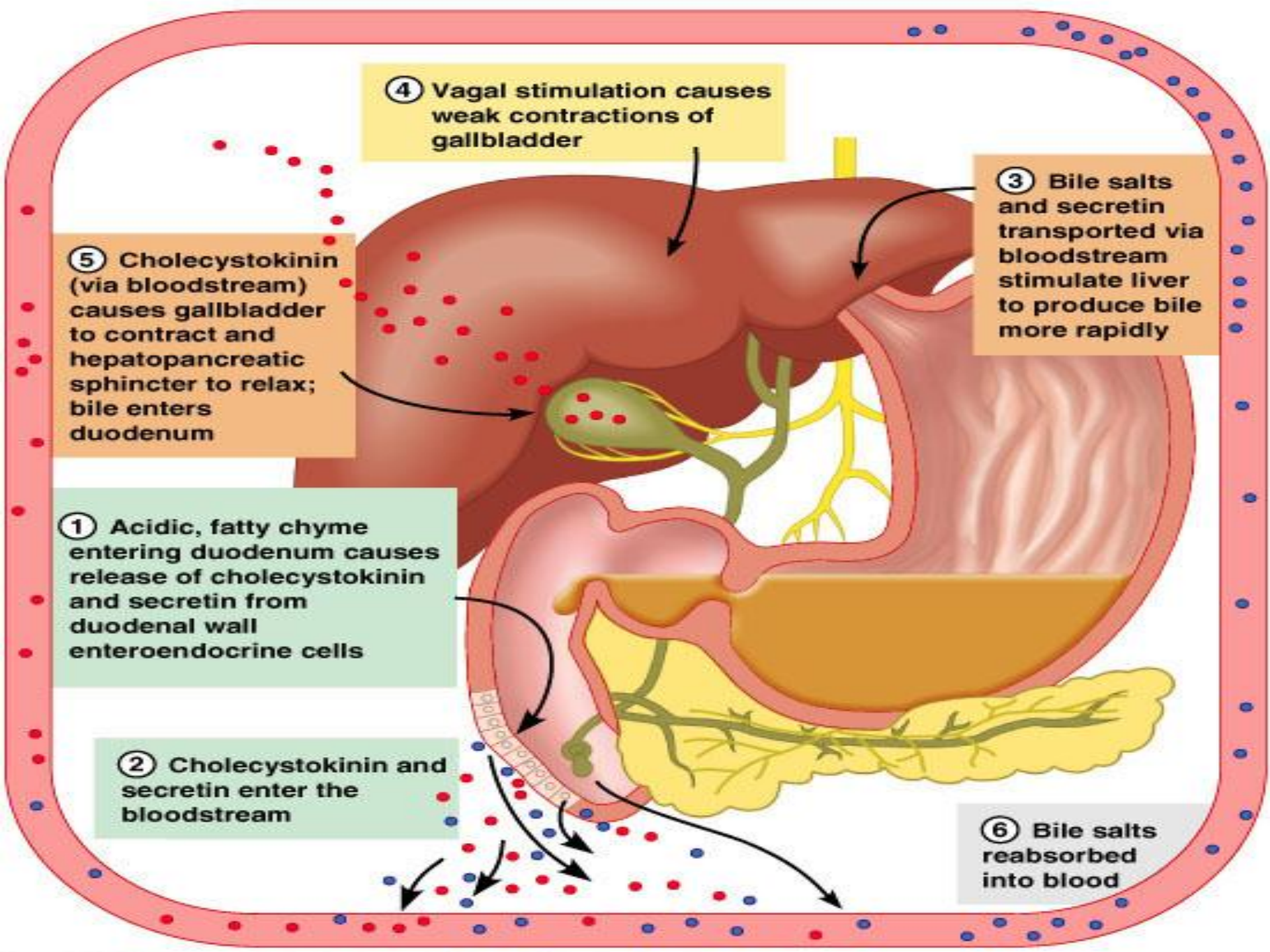
Bile acid independent component

- 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.
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


4 Vagal stimulation causes weak contractions of gallbladder
3 Bile salts and secretin transported via bloodstream stimulate liver to produce bile more rapidly
5 Cholecystokinin (via bloodstream) causes gallbladder to contract and hepatopancreatic sphincter to relax; bile enters duodenum
1 Acidic, fatty chyme entering duodenum causes release of cholecystokinin and secretin from duodenal wall enteroendocrine cells
2 Cholecystokinin and secretin enter the bloodstream
6 Bile salts reabsorbed into blood

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 the discharge of bile into the intestine

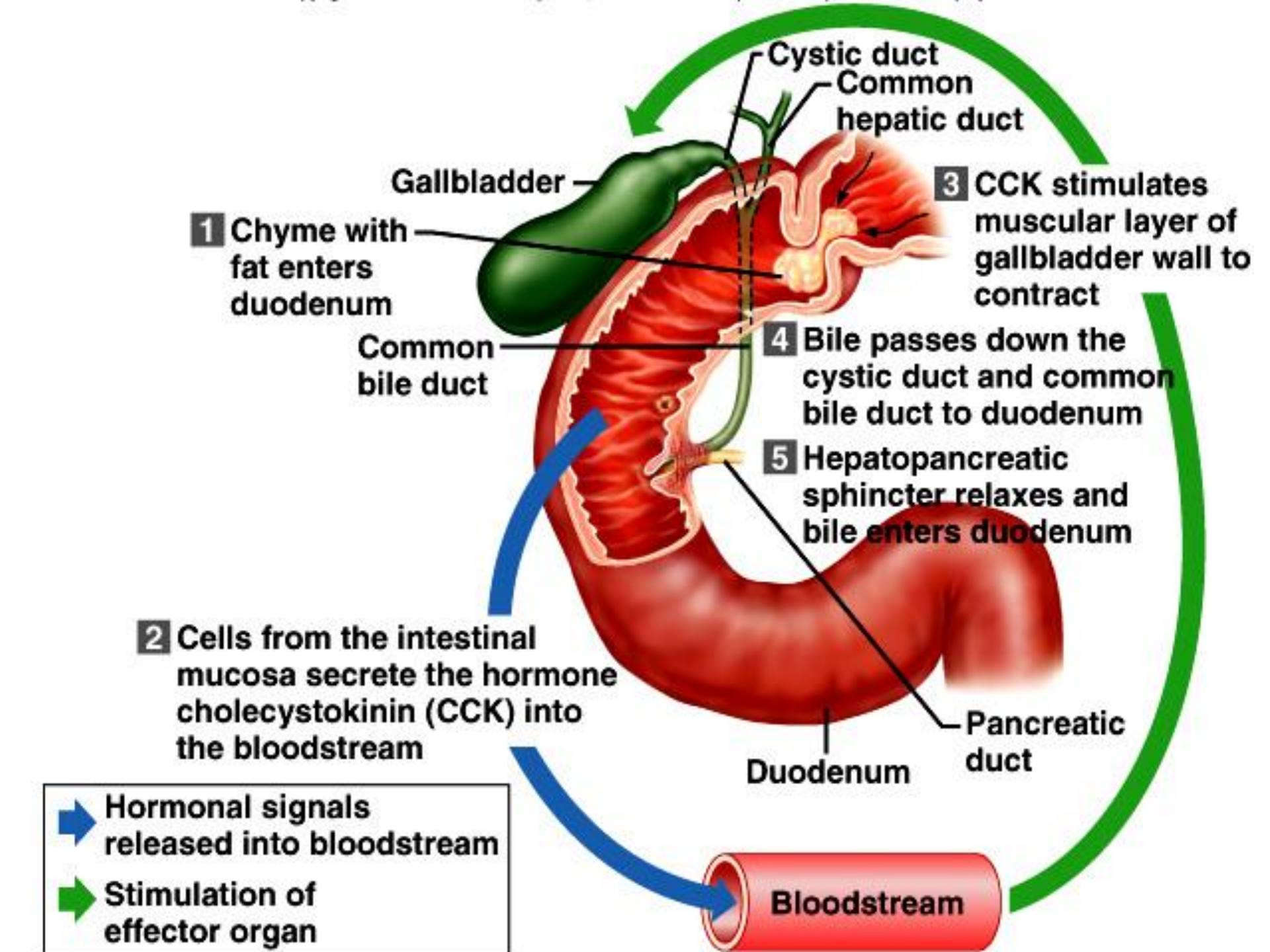
- Discharge of bile into the duodenum occurs by contraction of gall bladder wall and relaxation of Oddi sphincter. The highest rate of gall bladder emptying occurs during the intestinal phase. Gall bladder evacuants are called ***cholagogues.***
- Discharge of bile into the duodenum is regulated by nervous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


Cystic duct
Common hepatic duct
Gallbladder
1 Chyme with fat enters duodenum
3 CCK stimulates muscular layer of gallbladder wall to contract
Common bile duct
4 Bile passes down the cystic duct and common bile duct to duodenum
5 Hepatopancreatic sphincter relaxes and bile enters duodenum
2 Cells from the intestinal mucosa secrete the hormone cholecystokinin (CCK) into the bloodstream
Pancreatic duct
Duodenum
Hormonal signals released into bloodstream
Stimulation of effector organ
Bloodstream

Thank You