Biliary and intestinal secretion

BY

Dr. Al Shaimaa Mahmoud Kotb

Assistant Professor of Medical Physiology

Faculty of Medicine- Mu'tah university

2025-2026

Biliary system

- The biliary system **refers** to the liver, gall bladder and bile ducts, and they work together to make, store and secrete bile.
- **Liver:**

 Liver is the largest gland in the body.

 It can regenerate itself. If **25%** of the healthy liver remains, it can become whole again.

FUNCTIONS OF LIVER

1. Metabolic function:

Liver is the organ where most metabolic reactions such as metabolism of carbohydrates, proteins, fats, vitamins and many hormones are carried out.

Carbohydrate metabolism:

➢ liver is essential in maintaining normal blood glucose level (glucostasis)

1- If blood glucose increases, the excess glucose is taken by liver and converts into glycogen (glycogenesis) and fat (lipogenesis).

2- If blood glucose decreases, liver adds glucose to blood by glycogenolysis and gluconeogenesis.

➢ Liver also converts galactose and fructose into glucose to be utilized by tissue.

Protein metabolism

- Synthesis plasma proteins except gamma globulin.
- Deamination of amino acids and the resulting products are either oxidized for energy or used for synthesis of carbohydrates and fat.
- Conversion of ammonia into urea (less toxic).
- Synthesis of essential amino acids and clotting factors.
- Formation of uric acids which is the end product of nucleoprotein metabolism.

Fat metabolism

- Oxidation of fatty acids for energy.
- Synthesis fat from carbohydrate (lipogenesis).
- Synthesis of lipoproteins (LDL, VLDL and HDL) which has a role in preventing precipitation of cholesterol in blood vessels and so prevent development of atherosclerosis.
- Synthesis of cholesterol from which bile salts are synthesized.
- Synthesis of phospholipids which enter in the structure of cell membrane.

2-Liver is important in erythropoiesis as

- It secretes 15% of erythropoietin.
- It stores iron in the form of ferritin.
- It stores vitamin B 12.
- It is the site of erythropoiesis in the first 7 months of fetal life.
- It forms the globin part of hemoglobin.

3- Liver participates in activation and so formation of active vitamin D through formation of 25 hdroxycholecalciferol.

4- Liver stores 200-400 ml of blood and also remove 99% of bacteria in portal blood by non specific liver macrophages (Kupffer cells).

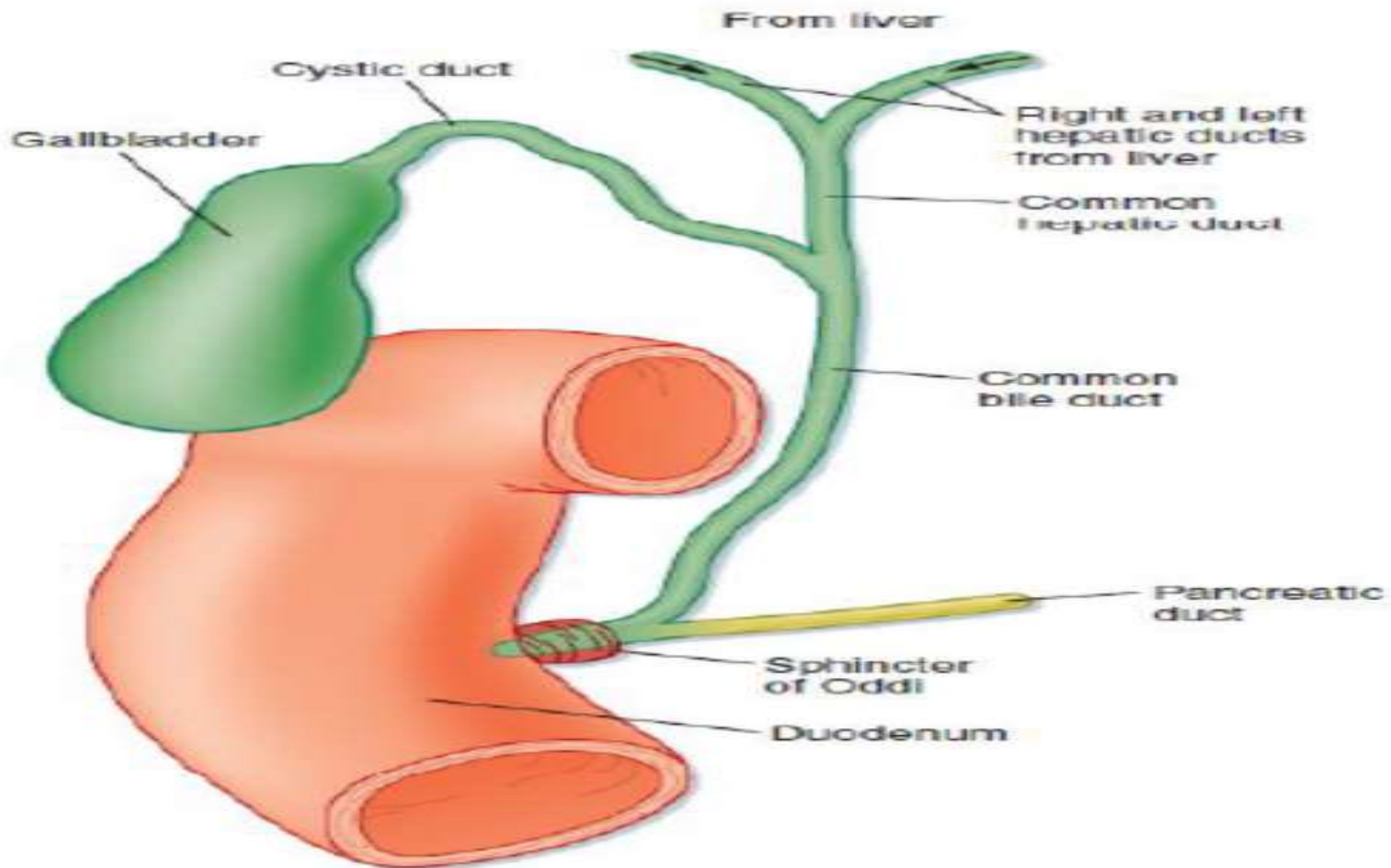
5- Liver is essential for growth as it synthesizes insulin like growth factor 1 (somatomedin).

6- Liver is essential for clotting as it synthetizes clotting factor and heparin.

7- Liver causes detoxification of drugs and alcohols and inactivation of many hormones like steroid hormone, thyroxin.

Functional anatomy of the biliary system:

- Bile is an important digestive liquid (juice) that is secreted by the liver & stored in the gall bladder.
- The liver cells secrete bile into fine biliary canaliculi which coalesce together forming the right & left hepatic ducts (one from each lobe of the liver).
- These join outside the liver forming the *common hepatic duct*, which unites with the *cystic duct* of the gall bladder forming the *common bile duct*.
- This joins the main pancreatic duct forming the ampulla of vater which opens at the duodenal papilla, & its opening is controlled by the sphincter of Oddi.


From liver
Cystic duct
Gallbladder
Right and left
hepatic ducts
from liver
Common
hepatic duct
Common
bile duct
Pancreatic
duct
Sphincter
of Oddi
Duodenum

Composition of bile:

1) ***Volume:*** ***25***0 – 1000 ml/day.

2) Color: golden yellow.

3) pH:

- Liver bile □ alkaline (pH 7.8 – 8.6).
- Gall bladder bile □ acidic (pH 6.5 –7.5).

4) Constituents:

- Water 97% (liver bile), bile salts, bile pigments, small amounts of cholesterol, lecithin, fatty acids) and electrolytes (Na^+, K^+, Ca^{++}, Cl^- and HCO_3).

- HCO_3 is secreted by biliary duct cells. High HCO_3 content is to share in neutralization of gastric HCL. The main stimulus for biliary HCO_3 secretion is secretin hormone.

Function of gall bladder

Bile continuously produced, but we **ONLY** need it during and after meals. Therefore, the gallbladder concentrates and stores bile, by removing the water and ions.

1- **Storage of bile:** in between meals and so decreases pressure in the bile ducts as high biliary pressure stops bile secretion and causes impairment of liver.

2- **Concentration of bile:**

To accommodate the large volume of bile flow from liver due to the capacity of gall bladder is 20-60 ml.

This occurs through active absorption of Na^+ followed by passive absorption of both water and HCO_3.

This results in

1. Increase concentration of bile salts in the bile of gall bladder 5-10 times than liver bile.

2- Water content in liver bile is 97%, while, water content in gall bladder is 89%.

3- As a result of HCO3 absorption, bile in gall bladder becomes acidified (pH 7-7.4), while, liver bile is alkaline (pH 7.8-8.6) the acidic bile in gall bladder prevents Ca precipitation and formation of gallstones.

3- Secretion of mucous from mucosa of gall bladder and this protects the gall bladder mucosa from highly concentrated bile salts.

4- Evacuation of bile by contraction of wall of gall bladder and relaxation of sphincter of oddi. This occurs after eating under effect of

a. CCK hormone (hormonal mechanism) is the major stimulus contraction of wall of gall bladder and relaxation of sphincter of oddi.

b. Vagal stimulation (nervous mechanism) is the less strong stimulus contraction of wall of gall bladder and relaxation of sphincter of oddi..

Bile salts

 Chemical nature & formation:

- They are formed from cholesterol mainly cholic acid and chenodeoxycholic acids forming primary bile acids. These primary bile acids are conjugated to glycin and taurine and then to the sodium & potassium forming bile salts.

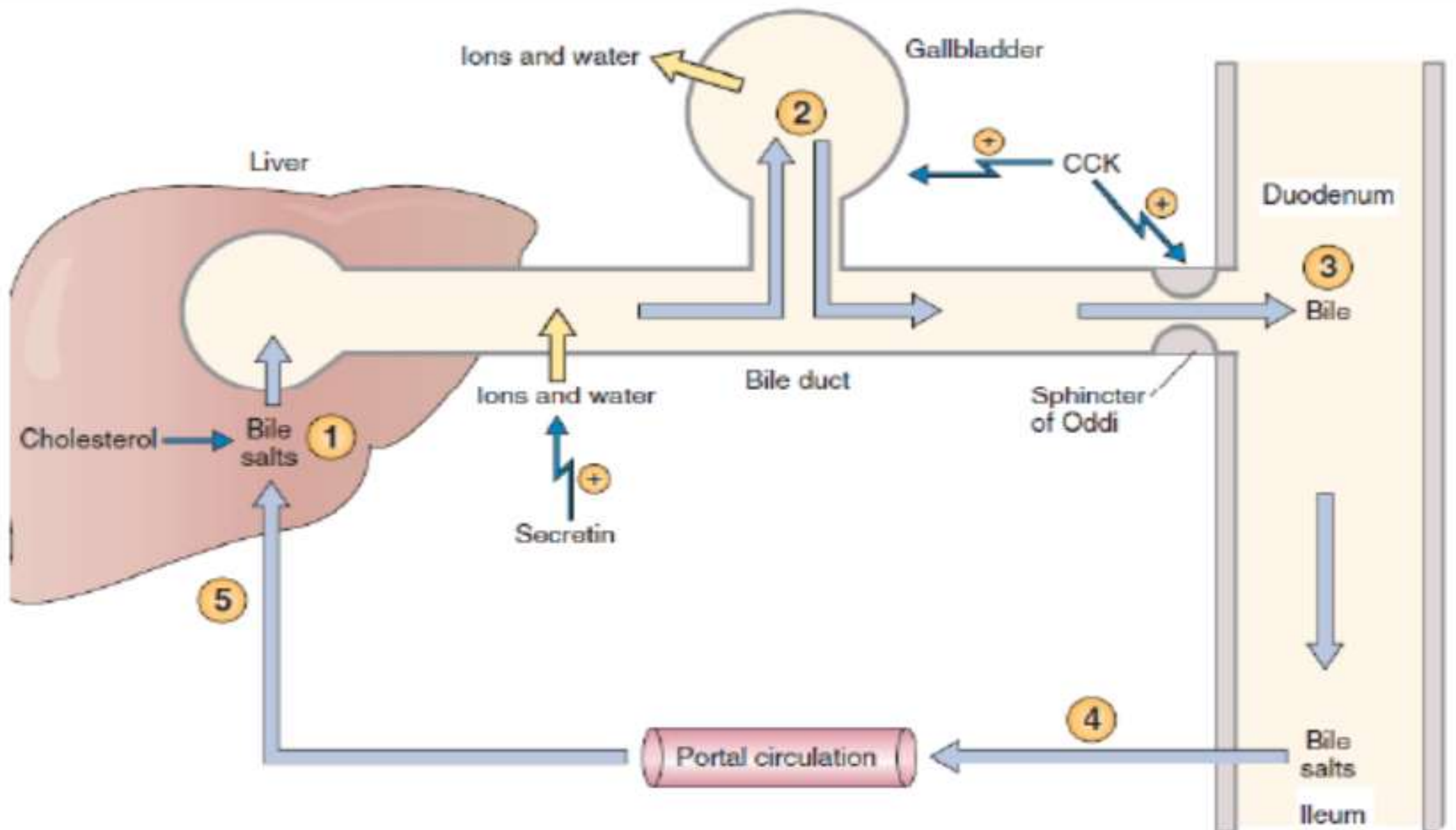
- The liver cells form about 2.5 g/day.

□ Fate of bile salts:

90-95 % of bile salts are absorbed from the terminal ileum by an active transport mechanism. The absorbed bile salts pass in portal circulation to the liver to be secreted in bile. This circulation of bile salts between liver & intestine is called *the* entero-hepatic circulation of bile salts.

5-10 % of bile salts pass to the colon to be excreted in stool.

So, the enterohepatic circulation allows the liver recycle and preserve bile acids.



Ions and water
Gallbladder
2
Liver
CCK
Duodenum
3
Bile
Bile duct
Ions and water
Sphincter of Oddi
Cholesterol
Bile salts
1
Secretin
5
4
Portal circulation
Bile salts
Ileum

Functions of bile salts:

[1] Digestion of fat:

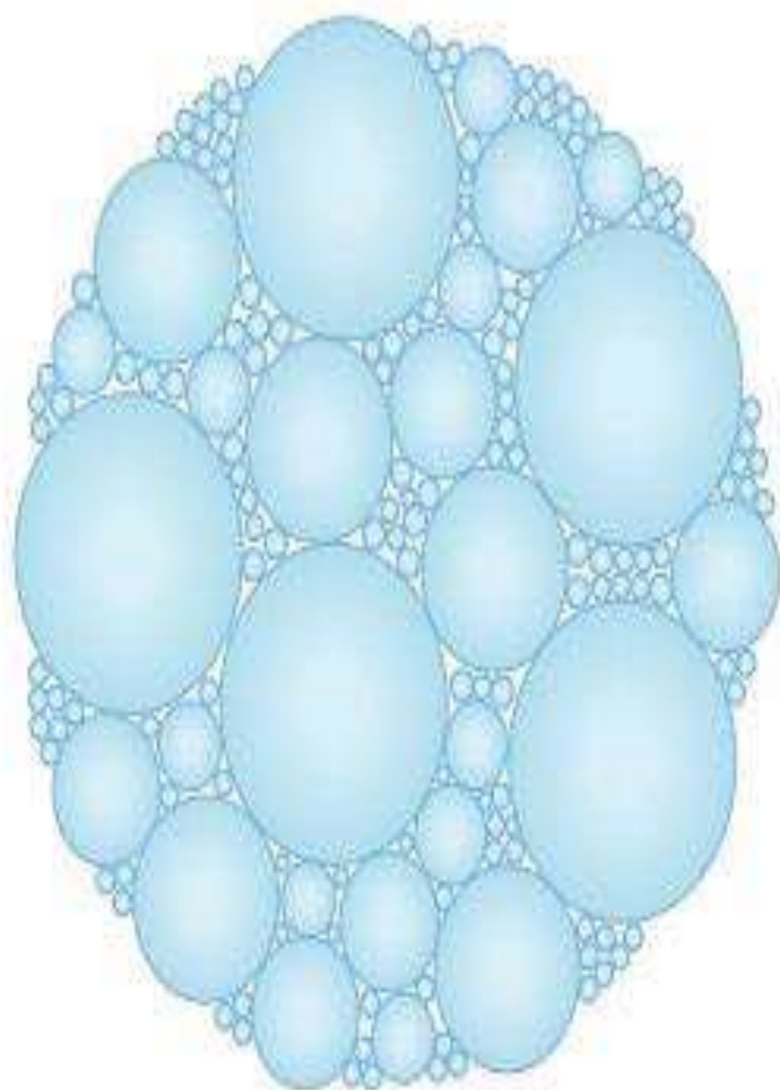
- Bile salts are **amphipathic** which means they have a hydrophobic end which is lipid-soluble and a hydrophilic end which is water-soluble. This structure allows bile salts to emulsify fats(converting it into fine globules by reducing surface tension (detergent action) and increasing surface area for action of lipase.

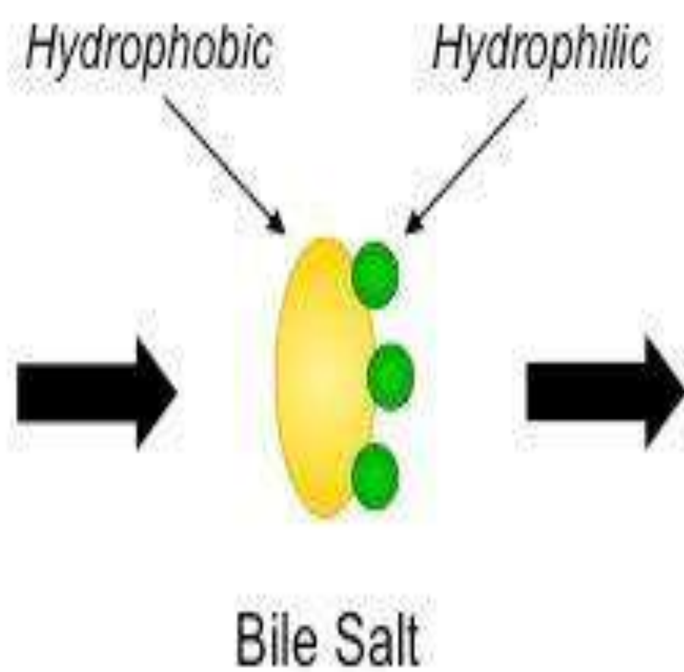
[2] Absorption:

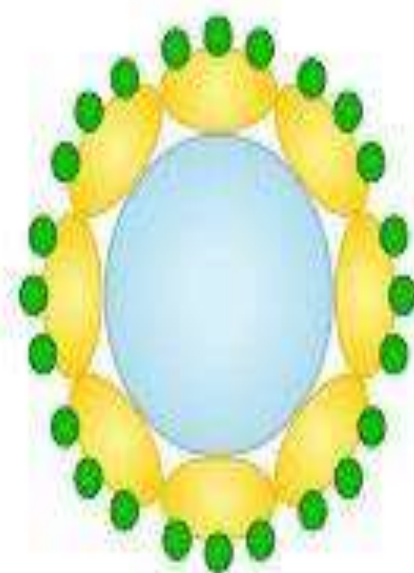
- Bile salts help absorption of fat & fat-soluble vitamins (A, D, E, K).

- Bile salts by their hydrophilic part form with fat digestive products & fat-soluble vitamins particles. These particles are soluble & easily diffusible, & are called micelles.

- The bile acids coat the products of lipid breakdown as well as cholesterol and phospholipids to form spherical structures known as **micelles**.
- Micelles play an important role in transport their contents to the intestinal epithelium where they can be absorbed.
- Bile salts by their hydrophilic part form with fat digestive products & fat-soluble vitamins particles, are soluble & easily diffusible through the water layer lining the intestinal epithelium and then by their lipophilic part, become soluble and easily diffusible through the intestinal epithelium.


Fat Globule


Hydrophobic
Hydrophilic
Bile Salt


Emulsified
Fat Droplets

[3] Choleretic action:

i.e. stimulation of bile secretion by liver.

[4] Solvent action:

- Bile salts by their solvent action keep cholesterol in solution.
- This prevents its precipitation in gallbladder & formation of gall stones.

[5] Laxative action:

- Bile salts stimulate intestinal movements □ prevention of constipation.

[6] Antiputrefactive action:

- In absence of bile salts, the undigested fat envelops protein particles preventing their digestion. So, intestinal bacteria attack the undigested protein & cause putrefaction & gases formation.

Effects of obstruction of common bile duct:

- In that condition, bile does not reach the intestine & return back to the blood leading to:

1) <u>Digestive disturbances:</u>

a) Deficient fat digestion & absorption □ steatorrhea (= fatty diarrhea).

b) Decrease absorption of fat soluble vitamins (A, D, E, K) e.g. vitamin K deficiency causes bleeding tendency.

c) Protein putrefaction in the intestine occurs.

d) Constipation (due to absence of the laxative effect of bile salts).

2) <u>Back pressure on liver cells</u> □ injury & atrophy of its cells □ impaired liver functions.

3) <u>Regurgitation of bile:</u>

a) Bilirubin (bile pigments) increase in blood □ obstructive jaundice.

b) Bile salts increase in blood □ pruritus (itching) & bradycardia (decreased heart rate) due to (+) cardio-inhibitory center [CIC] & (-) sino-atrial node [SAN].

Control of bile secretion:

Any factor which stimulate bile secretion is called "**choleretic**".

Bile secretion is controlled by:

1) <u>Bile salts in the enterohepatic circulation:</u>

- Are the most powerful stimulants of bile secretion (major choleretics).

- The more the bile salts in the enterohepatic circulation, the more the bile flow (as during meals).

NB:

- In persons who have had an **ileal resection** (removal of the ileum), the recirculation of bile salts to the liver is interrupted and large quantities of bile salts are excreted in feces decreased bile salt content of bile impaired absorption of dietary lipids and steatorrhea.

2) Secretin hormone:

- It stimulates bicarbonate secretion by the hepatocytes (hydrocholeretic).

3) Vagal stimulation: Vagal stimulation stimulates bile secretion due to:

- Choleretic effect of acetyl choline.
- Increase hepatic blood flow by vasodilatation.

Sympathetic stimulation:

Causes relaxation of gall bladder wall & contraction of the sphincter of Oddi and inhibits gall bladder emptying.

Fasting state
Bile
Liver
Gallbladder
Sphincter of Oddi
Duodenum

On eating
Bile
Liver
Gallbladder
Sphincter of Oddi
CCK
Food
Duodenum

Choleretics and Cholagogues

These are substances that increase bile flow in the duodenum

1- Choleretics

They are substances that increase bile flow through increasing its formation by liver

a. Bile salts (through enterohepatic circulation) are the most powerful.

b. Secretin (hydrocholertic) as it increases bicarbonate and water secretion

c. Acetyl choline (vagal stimulation of the liver).

2- Cholagogue Action

Cholagogue is an agent which causes contraction of gallbladder and release of bile into the intestine.

a. Cholecystokinin.
b. Acetylcholine (vagal stimulation to the gall bladder).
c. Mg^{++} & sulphate.

BILE PIGMENTS

Bile pigments are the excretory products in bile. Bile pigments are formed during the breakdown of heme present inside hemoglobin, which is released from the destroyed RBCs in the reticuloendothelial system every 120 days.

1- Bilirubin Plasma Transport:

Bilirubin bind to plasma albumin forming unconjugated bilirubin (hemobilirubin).

2- Hepatic phase of bilirubin metabolism:

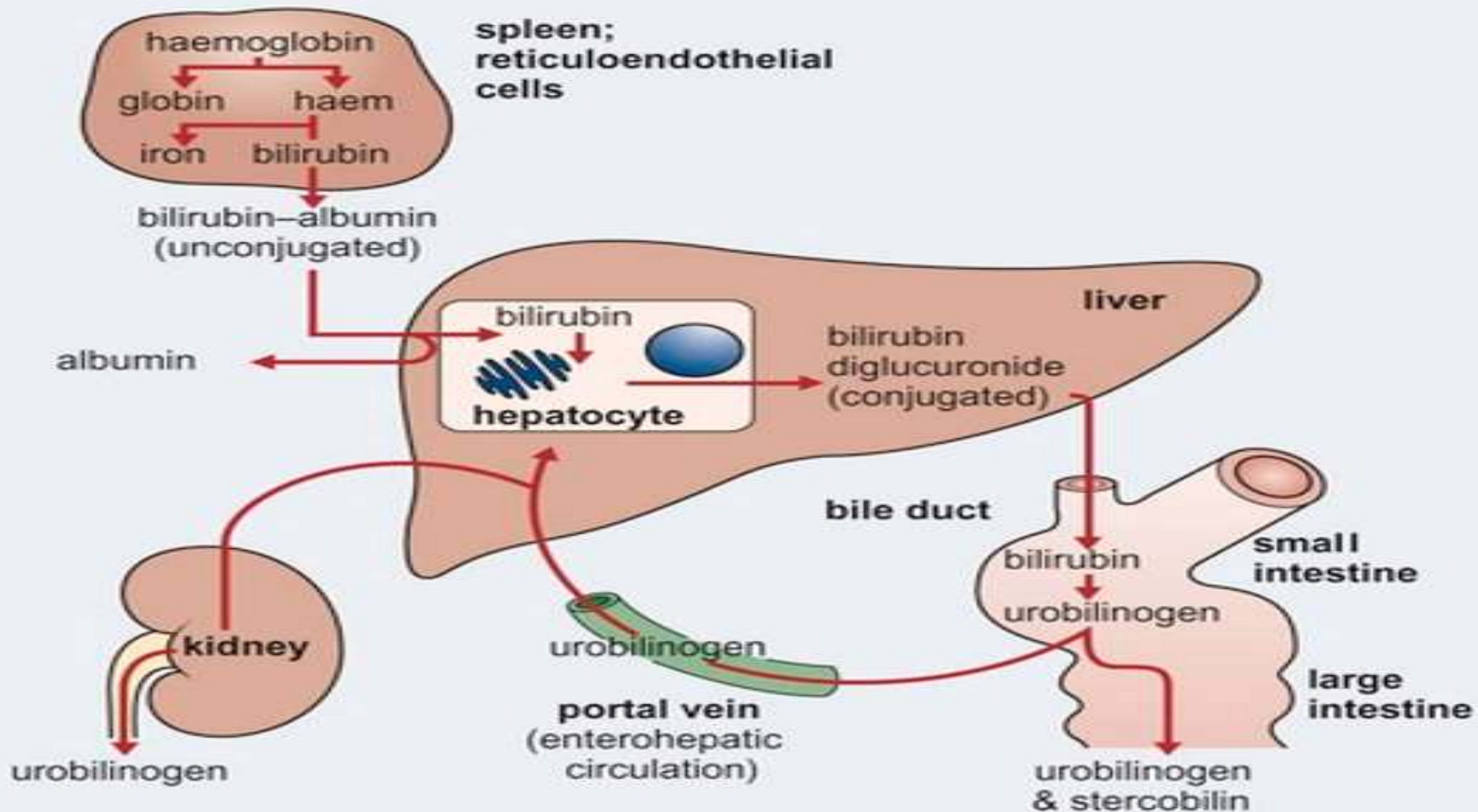
a) Hepatic Uptake: Unconjugated bilirubin is transported through blood (complex to albumin) to liver.

b) Conjugation: Bilirubin is taken into liver and conjugate with glucuronic acid.

c) Secretion in bile: Bile is secreted into intestine where glucuronic acid is removed and the resulting bilirubin is converted to urobilinogen.

3- Intestinal excretion:

- A portion of urobilinogen is reabsorbed into blood, where it is converted to yellow urobilin and excreted by kidneys.
- Urobilinogen is oxidized by intestinal bacteria to the brown stercobilin


spleen;
reticuloendothelial
cells
haemoglobin
globin
haem
iron
bilirubin
bilirubin–albumin
(unconjugated)
liver
bilirubin
albumin
hepatocyte
bilirubin
diglucuronide
(conjugated)
bile duct
small
intestine
bilirubin
urobilinogen
kidney
urobilinogen
large
intestine
portal vein
(enterohepatic
circulation)
urobilinogen
urobilinogen
& stercobilin

Jaundice

- It is a yellow pigmentation of the skin, sclera and mucous membranes occurs when serum bilirubin levels exceed **2 mg/dl.**
- **The three main types of jaundice are**

1. Haemolytic jaundice,
2. Hepatocellular jaundice, and
3. Obstructive jaundice.

Points	Haemolytic Jaundice	Obstructive Jaundice	Hepatocellular Jaundice
Cause	When red blood cell lysis exceeds liver capacity to conjugate bilirubin All causes of haemolytic anaemia (e.g. hereditary spherocytosis, sickle cell anaemia, poison). Also, it occurs physiologically in the first week in newly born infants.	• When the flow of bile out from liver is blocked so liver can conjugate bilirubin but bilirubin can not reach small intestine. And so there is stagnation in biliary passages (cholestasis) followed by regurgitation into blood stream. • Stones in the common bile duct (CBD). • Cancer head of pancreas.	• Liver dysfunction limits uptake of hemobilirubin and conjugation of bilirubin (decrease cholebilirubin formation) so decrease formation of urobilinogen in the intestine and so decrease excretion of stercobilinogen in the stool and also decrease excretion of conjugated bilirubin • as in hepatitis, cancer or certain toxic drugs

Points	Haemolytic Jaundice	Obstructive Jaundice	Hepatocellular Jaundice
Blood Anaemia Bilirubin	Present Haemobilirubin	Absent Cholebilirubin	Absent Both due to mild biliary obstruction due to swelling of liver cells that leads to regurgitation of some cholebilirubin into blood stream so both hemobilirubin and cholebilirubin are increased
Liver function	Normal	Impaired due to pressure on liver cells by the stagnant bile	impaired

points	Haemolytic Jaundice	Obstructive Jaundice	Hepatocellular Jaundice
Fat digestion and absorption Purities and bradycardia	Normal Not present	Marked disturbed due to decreased flow of bile salts present	Disturbed due to decrease formation and excretion of bile salts swelling of cells and inflammation cause intrahepatic biliary obstruction . Present (less than obstructive jaundice)
Urine Colour	Normal due to hemobilirubin cannot filtered through the renal glomeruli	Dark brown due to cholebilirubin is filtered through the renal glomeruli But its urobilinogen content is low	brown
Stool Colour	Darker than normal due to excess stercobilinogen is excreted in the stool.	Very pale due to ↓↓↓↓↓ stercobilinogen	Pale due to ↓↓↓ stercobilinogen

Small intestine

- In the small intestine , the chyme delivered by stomach is mixed with the intestinal secretion, pancreatic juice & bile (which complete food digestion).
- The products of digestion are then absorbed together with most vitamins, minerals & fluids.
- It is the digestive secretion of the small intestine: **(= Succus-Entericus)**

➢Volume/24 h. = 2 liters.

➢pH: alkaline 8.1 – 8.3 an alkaline fluid secreted by crypts of LiberKuhn that contains mainly HCO_3.

➢H_2O: 97%.

➢Solids: 3 % includes:

a) Organic: mucous & intestinal enzymes (1.5 %).

b) Inorganic: salts of Na^+, Ca^{++} & K^+, mainly. $NaHCO_3$ (1.5%).

Mucous is secreted by the surface epithelium and goblet cell, it lubricates and protects the intestinal epithelium. While, that secreted by Brunners glands plus HCO_3 secreted from pancreas protects the duodenal mucosa from gastric HCL.

- Mucosal cells: which are normally sloughed daily into intestinal lumen, and then they are replaced by new cells formed from cells located in the crypts.
- As a result of sloughing , about 30 grams of protein is secreted in the intestinal lumen.

Intestinal enzymes

- They are present in the membranes of mucosal cells mainly at the brush borders where intestinal digestion takes place

1) **Enterokinase**: it activates trypsinogen into trypsin.

2) **Exopeptidase** : it acts on small peptides and poly peptides releasing amino acids.

3) Disaccharidases: These act on disaccharides coverting them into monosaccharides.

- Maltase breaks maltose into glucose
- Lactase breaks lactose into glucose- and galactose.
- Sucrase breaks sucrose into glucose and galactose

4) intestinal lipase: It completes the action of lingual and pancreatic lipase.

5) Nucleases:

a. **Ncleotidase** which splits nucleotides into nucleosides and phosphoric acids

b. **Nucleosidase** splits nucleosides into their constituent sugars and purine and pyrimidine bases.

Regulation of intestinal secretion:

1. **Local stimuli:** like mechanical (distension) or chemical (digestive product or acid chyme) stimulates intestinal secretion directly or through local enteric reflex.
2. **Nervous:** vagus stimulates intestinal secretion especially Brunner ,s glands.
3. **Hormonal:** VIP, Secretin, CCK stimulate intestinal secretion from crypts of Liberkuhun. Secretin also stimulates secretion from Brunner ,s glands.

Intestinal movements (motility):

(1) Segmenting movements (mixing contents):

It is the most common type of movement by small intestine.

During it the circular muscle contracts at regular intervals dividing small intestine into segments. A few seconds later, new contractions occur in the middle of each segment with relaxation of the previous contraction (disappear) & so on.

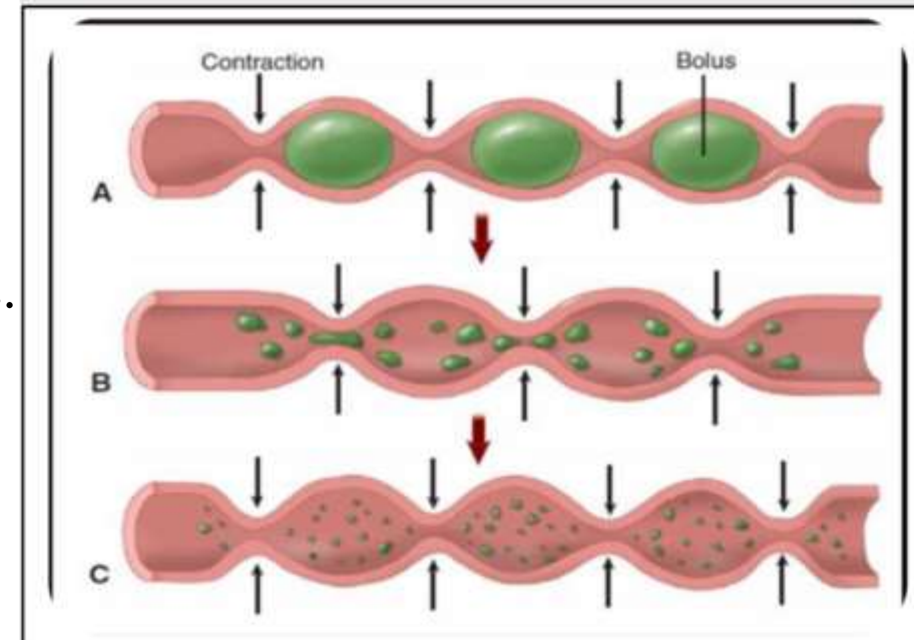
This cycle occurs at a rate of 12 /minute in the duodenum and jejunum and 8-9 /minute in the ileum.

It is myogenic not nervous, controlled by the basic electric rhythm.

 Functions*:*

1) It help digestion by mixing intestinal content with digestive enzymes.

2) It help absorption; through increase contact of the food with intestinal mucosa.



(2) Peristaltic movements: (propulsive movements)

- Peristaltic waves that propel the chyme along the intestine at a velocity of 0.5 – 2 cm/sec and dies off after few cm.

- Contraction behind the bolus and, simultaneously, relaxation in front of the bolus cause the chyme to be propelled caudally.

Control: 1- **Nervous**

a. It is a local enteric reflex evoked by distention of the intestine.

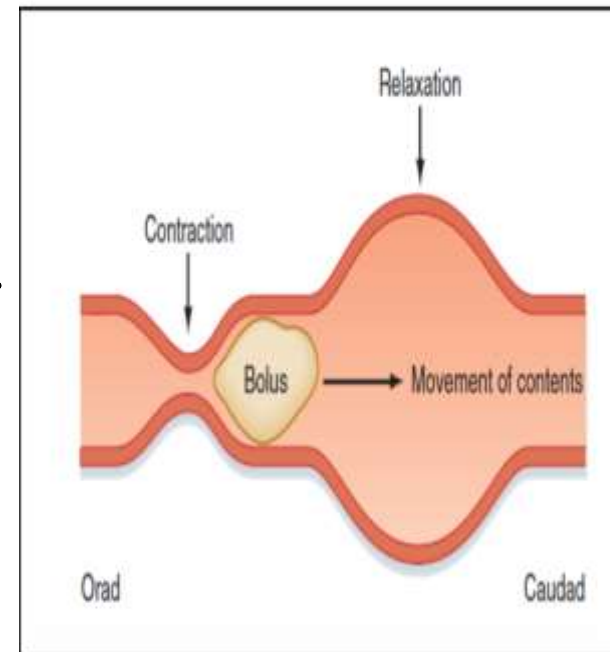
b. Gastro-enteric reflex: caused by stomach distension with reflex stimulation of intestinal peristalsis.

2- Hormonal:

a. CCK, gastrin, motilin and insulin enhance intestinal motility.

b. Glucagon and secretin inhibits intestinal motility.

Functions: Propulsion of intestinal contents towards the colon.



3) Peristaltic rush:

- Are strong peristaltic contractions that travels for along distance to evacuate the intestinal contents rapidly into the colon (leading to diarrhea).

- Do not occur normally but when there is intense irritation of mucosa or excessive distension to relieve small intestine from them.

4) **Migrating motor complex (MMC)**

- Repeated waves of peristalsis occur during the periods fasting and in-between meals and stopped by food digestion.

Control*:*

It is myogenic not nervous, controlled by the basic electrical rhythm (BER).

Function*:*

1. It moves undigested substances remaining in the small intestine to large intestine.

2. Prevents extensively growth and multiplication of bacteria from remaining in the small intestine

- **Adynamic (Paralytic) ileus:**
- Diffuse decrease in peristaltic activity, leading to inhibition or complete loss of intestinal motility that start in the ileum and spread upward.
- It occurs in response to excessive sympathetic stimulation due to trauma or excessive manipulation of the intestine and irritation of peritoneum after open abdominal operation.

Ileocecal Valve and Sphincter

Definition:

- The ileocecal valve is situated at the junction of the ileum and the colon, and its lips protruded into the colon.
- However, the ileocecal sphincter is a thickened muscle at the last few centimeters of the ileum (before the valve).

Function:

- Normally, it is kept tonically contracted to promote absorption in the ilium and prevent regurgitation of the colonic contents.
- When food enters the stomach, emptying of ileal contents into the cecum is accelerated as a result of both increased intestinal peristalsis and relaxation of ileocecal valve (gastroileal reflex)

Thank you