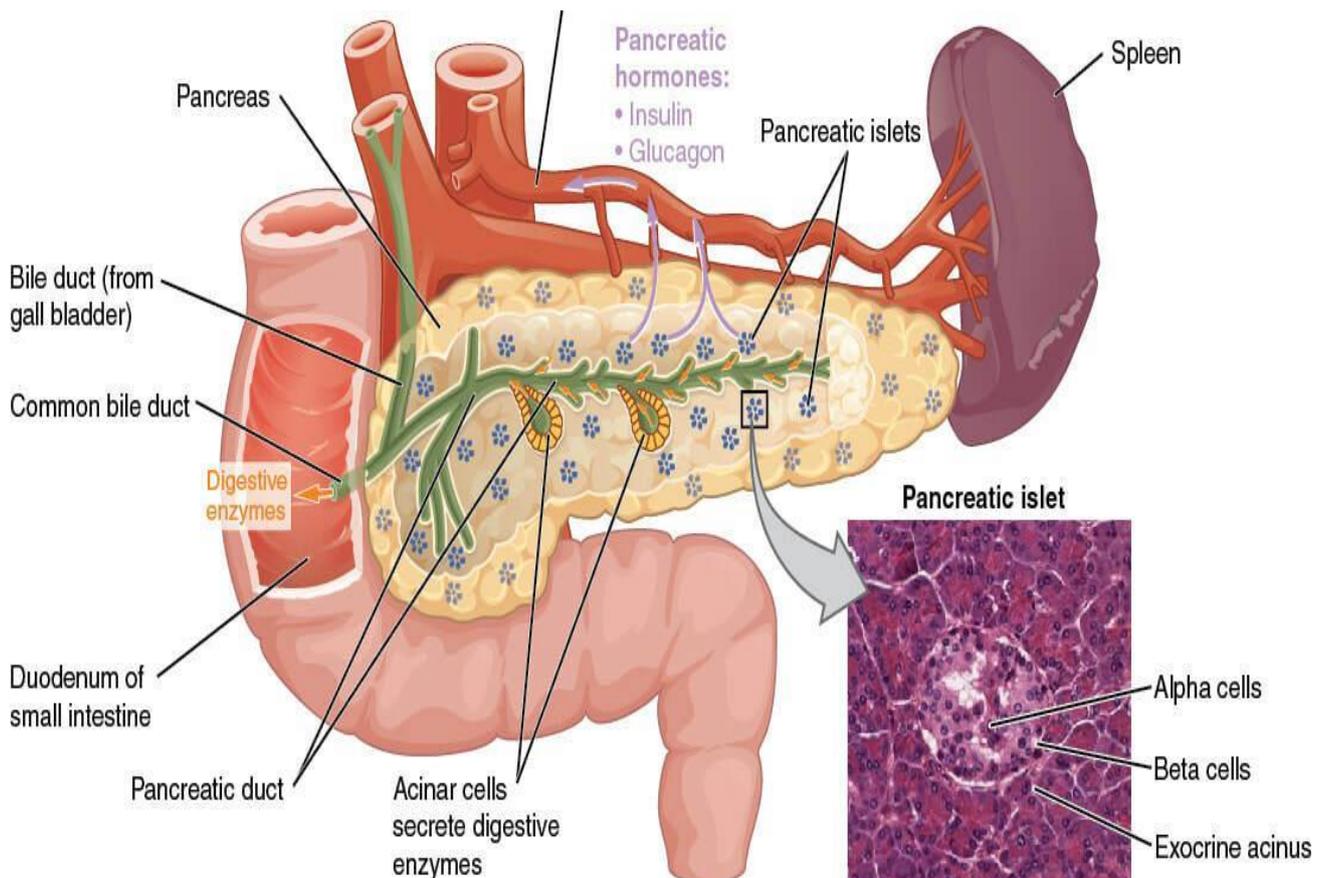


# Pancreas

## Introduction:

➤ Pancreas is **both** an endocrine and exocrine gland.

Endocrine part	Exocrine part
<ul style="list-style-type: none"> <li>• <b>Islets of Langerhans</b> which secrete hormones e.g., <i>Insulin</i></li> </ul>	<ul style="list-style-type: none"> <li>• It secretes the <b>pancreatic juice</b>.</li> <li>• It is formed of <b>acini and system of ducts</b>.</li> <li>• Ducts drain into a <b>main pancreatic duct</b> which unites with the <b>common bile duct</b> and opens in the duodenum at the <b>ampulla of Vater</b> which is guarded by <b>sphincter of Oddi</b></li> </ul>



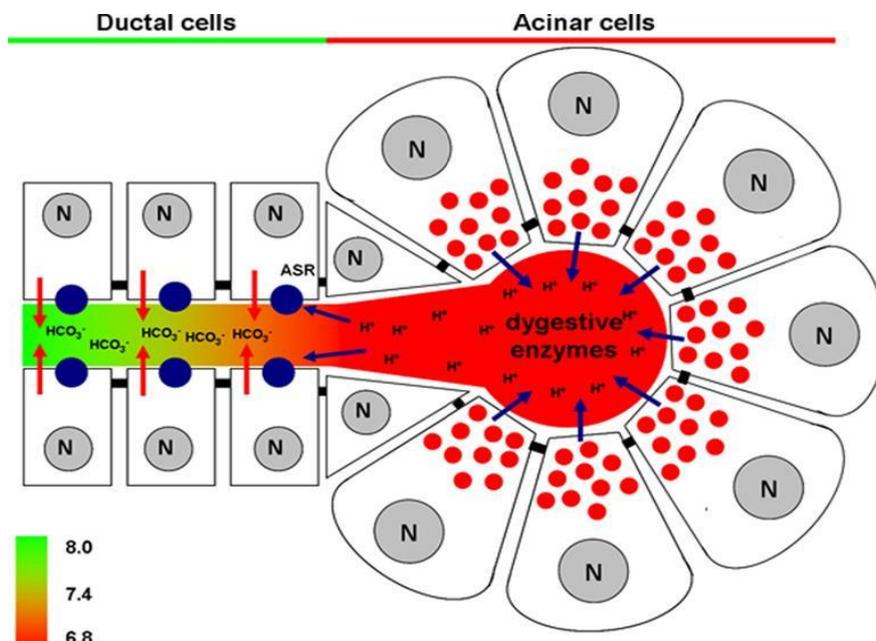
# Pancreatic juice

## Composition of pancreatic secretion:

<b>Volume</b>	• 1.5L/day	
<b>pH</b>	• It is an alkaline secretion (pH about 8).	
<b>Components:</b>	<ul style="list-style-type: none"> <li>• Water (98.5%).</li> <li>• Solids (1.5%).</li> </ul>	
	<b>Organic components</b>	<b>Inorganic components</b>
	<ul style="list-style-type: none"> <li>• Secreted by the acini, include: <ul style="list-style-type: none"> <li>➢ Pancreatic enzyme.</li> <li>➢ Trypsin inhibitor</li> <li>➢ Colipase</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• NaHCO<sub>3</sub> (mainly).</li> <li>• K<sup>+</sup>, Ca<sup>++</sup>, Mg<sup>++</sup>, Zn<sup>++</sup>, Cl<sup>-</sup>, SO<sub>4</sub><sup>-</sup>, HPO<sub>4</sub>.</li> </ul>

## Types of Pancreatic Secretion:

	<b>Aqueous part</b>	<b>Enzymatic part</b>
<b>Rich in:</b>	• Bicarbonates	• Enzymes
<b>Secreted by:</b>	• Duct cells	• Acinar cells

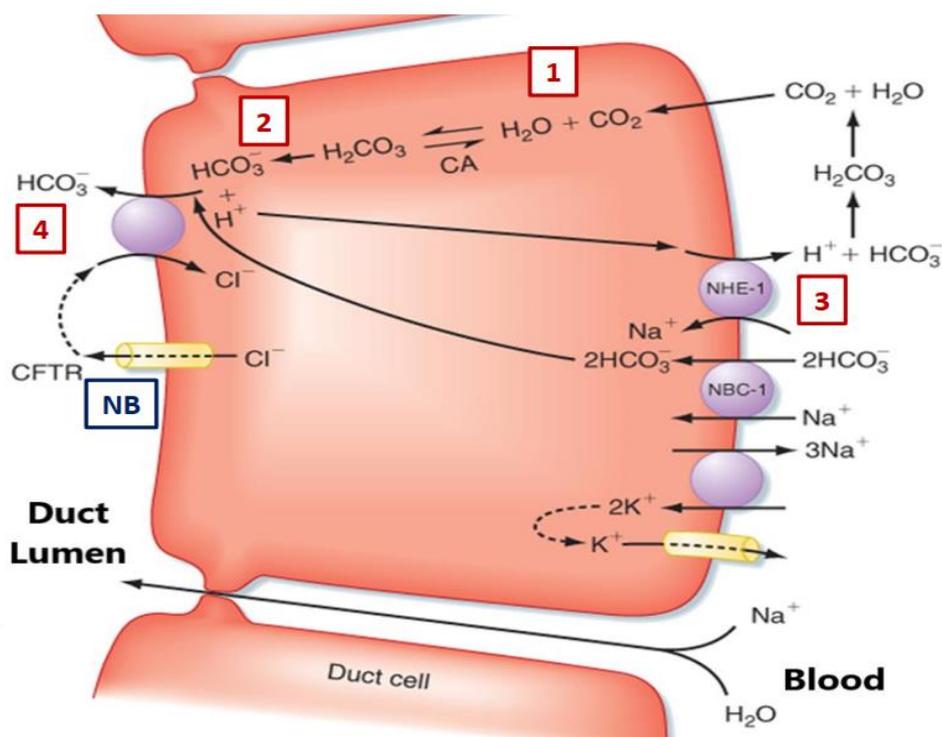


▪ **Functions of pancreatic juice:**

<p>a) <b>Secretion of sodium bicarbonate:</b></p>	<p><b>Sodium bicarbonate neutralizes the acidic chyme, thus:</b></p> <ul style="list-style-type: none"> <li>➤ Prevents development of <b>duodenal ulcer</b>.</li> <li>➤ Adjusts pH for action of <b>pancreatic enzymes</b>.</li> <li>➤ Depresses further release of <b>secretin</b>.</li> </ul>
<p>b) <b>Enzymes</b></p>	<p>See later</p>

▪ **Mechanism of NaHCO<sub>3</sub> secretion:**

<p><b>Site:</b></p>	<ul style="list-style-type: none"> <li>• In the <b>ductal cells</b> of pancreatic glands</li> </ul>
<p><b>Steps:</b></p>	<ol style="list-style-type: none"> <li>1) CO<sub>2</sub> and H<sub>2</sub>O combine in ductal cells to form <b>H<sub>2</sub>CO<sub>3</sub></b>.</li> <li>2) H<sub>2</sub>CO<sub>3</sub> dissociates into <b>H<sup>+</sup> and HCO<sub>3</sub><sup>-</sup></b>:             <ul style="list-style-type: none"> <li>➤ H<sup>+</sup> is transported into blood by <b>Na<sup>+</sup>-H<sup>+</sup> exchanger</b> at basolateral membrane of ductal cells.</li> <li>➤ HCO<sub>3</sub><sup>-</sup> is secreted into pancreatic juice by <b>Cl<sup>-</sup>-HCO<sub>3</sub><sup>-</sup> exchanger</b> at apical membrane of ductal cells, followed by osmotic flow of water.</li> </ul> </li> </ol>



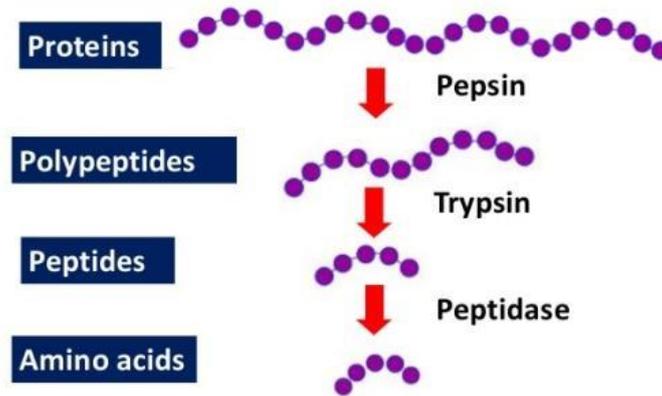
**NB:**

- The First 2 steps need **Carbonic anhydrase enzyme**.
- Cl<sup>-</sup> diffuses into the lumen by the help of **cystic fibrosis transmembrane conductance regulator**.
- Absorption of H<sup>+</sup> causes acidification of pancreatic venous blood → **Acidic Tide**.

## Pancreatic Enzymes

### 1) Digestion of proteins

Enzyme	Secreted in inactive form	Activated by	Action
<b>Trypsin</b>	Trypsinogen	<b>Enterokinase</b> (secreted from intestine) Or & <b>trypsin</b>	<ul style="list-style-type: none"><li>• It acts on proteins, proteoses and peptones to form <b>polypeptides and dipeptides</b></li><li>• Its premature activation in pancreas is <b>prevented by</b> trypsin inhibitor, a protein secreted by pancreatic acini.</li></ul>
<b>Chymotrypsin</b>	Chymo- trypsinogen	<b>Trypsin</b>	<ul style="list-style-type: none"><li>• Acts on proteins, proteoses and peptones to form <b>polypeptides and dipeptides</b>.</li></ul>
<b>Carboxy-peptidase</b>	Procarboxy-peptidases	<b>Trypsin</b>	<ul style="list-style-type: none"><li>• Acts on polypeptides to form <b>amino acids &amp; lower peptides</b>.</li></ul>
<b>Ribo and deoxy-ribonucleases:</b>			<ul style="list-style-type: none"><li>• They act on nucleic acids to form <b>nucleotides</b>.</li></ul>
<b>Elastase</b>			<ul style="list-style-type: none"><li>• Acts on elastin &amp; some other proteins</li></ul>



## 2) Digestion of Lipids

<p><b>a) Pancreatic lipase:</b></p>	<ul style="list-style-type: none"> <li>• It is activated by <b>bile salts and colipase</b></li> <li>• <b>Colipase</b> is protein secreted by pancreatic acini in inactive form <b>pro-colipase</b> which is activated by <b>trypsin</b>.</li> <li>• It acts on triglycerides to form <b>fatty acids, glycerol and monoglycerides</b>.</li> </ul>
<p><b>b) Cholesterol esterase:</b></p>	<ul style="list-style-type: none"> <li>• It hydrolyzes cholesterol esters to form <b>cholesterol and fatty acids</b>.</li> </ul>
<p><b>c) Phospholipase A:</b></p>	<ul style="list-style-type: none"> <li>• Its inactive form <b>pro-phospholipase A</b> is activated by <b>trypsin</b>.</li> <li>• It splits phospholipids into <b>lyso-phospholipids and fatty acids</b>.</li> </ul>

## 3) Digestion of carbohydrates

<p><b>Pancreatic amylase:</b></p>	<ul style="list-style-type: none"> <li>• It is <b>several times</b> as powerful as salivary amylase.</li> <li>• It is activated by <b>Cl<sup>-</sup></b>.</li> <li>• It digests starch, glycogen and most other carbohydrates.</li> </ul>
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# Control of Pancreatic Secretion

## 1) Nervous Control:

Sympathetic Stimulation	Vagal Stimulation	
<ul style="list-style-type: none"> <li>Causes vasoconstriction and inhibition of <b>bicarbonate</b> secretion</li> </ul>	<ul style="list-style-type: none"> <li>Causes vasodilatation and stimulation of pancreatic secretion which is small in volume, rich in <b>enzymes</b> and poor in bicarbonate.</li> </ul>	
	Conditioned Reflexes	Unconditioned Reflexes
	<ul style="list-style-type: none"> <li>Initiated by sight, smell, or thinking of food</li> </ul>	<ul style="list-style-type: none"> <li>Initiated by presence of food in mouth, stomach and small intestine.</li> </ul>

## 2) Hormonal control:

Hormones inhibit pancreatic secretion	Hormones Stimulate pancreatic secretion		
<ul style="list-style-type: none"> <li>Somatostatin.</li> <li>Glucagon</li> <li>Enkephalin</li> </ul>	Gastrin and CCK	Secretin	Other
	<ul style="list-style-type: none"> <li>Stimulate pancreatic secretion which is small in volume, rich in <b>enzymes</b> and poor in bicarbonate.</li> </ul>	<ul style="list-style-type: none"> <li>Stimulates pancreatic secretion which is large in volume, poor in enzymes and rich in <b>bicarbonate</b>.</li> </ul>	<ul style="list-style-type: none"> <li>VIP</li> <li>insulin</li> </ul>

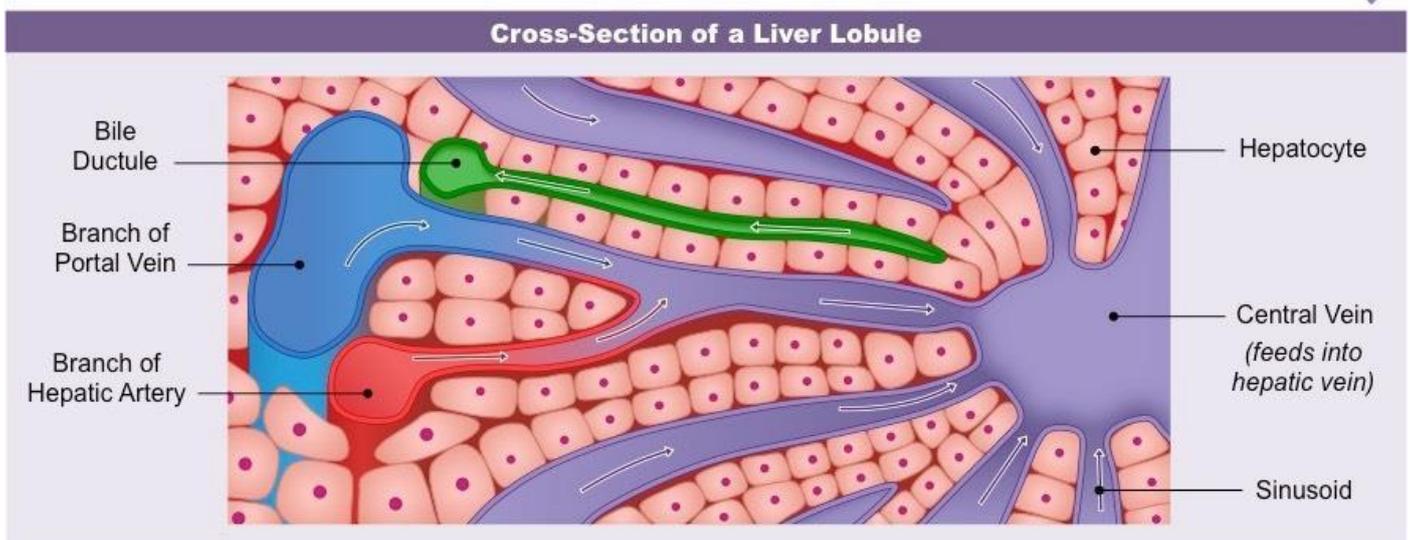
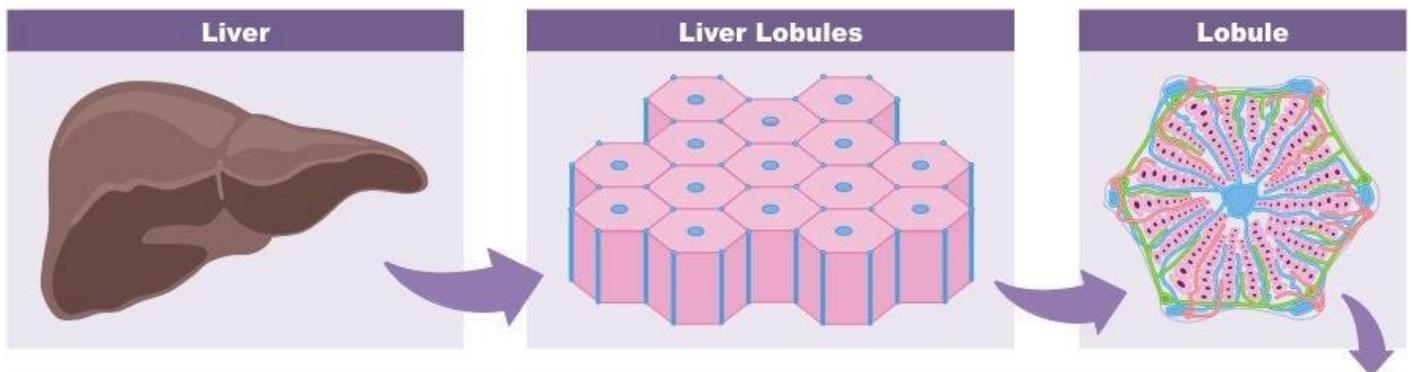
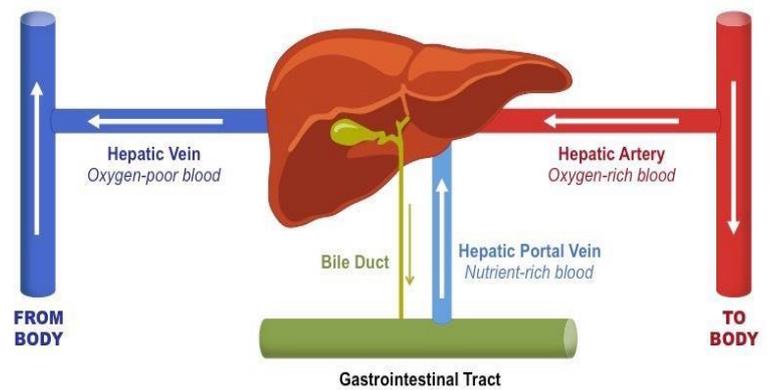
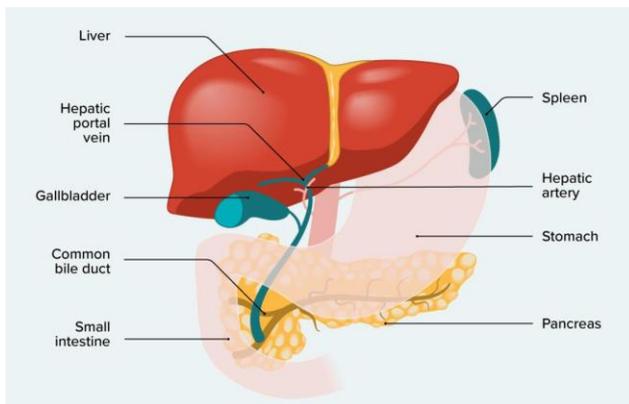
## Phases of Pancreatic Secretion

	Cephalic phase	Gastric phase	Intestinal phase
<b>Time:</b>	<ul style="list-style-type: none"> <li>• Before food reaches stomach</li> </ul>	<ul style="list-style-type: none"> <li>• When food reaches stomach</li> </ul>	<ul style="list-style-type: none"> <li>• When food reaches intestine</li> </ul>
<b>Accounts for:</b>	<ul style="list-style-type: none"> <li>• 20%</li> </ul>	<ul style="list-style-type: none"> <li>• 5-10%</li> </ul>	<ul style="list-style-type: none"> <li>• 60-70%</li> </ul>
<b>Induced by nervous:</b>	<b>Vagal stimulation</b>		
	<ul style="list-style-type: none"> <li>• Conditioned reflexes</li> <li>• Unconditioned reflexes</li> </ul>	<ul style="list-style-type: none"> <li>• Gastro-pancreatic reflex</li> </ul>	<ul style="list-style-type: none"> <li>• Entero-pancreatic reflex</li> </ul>
<b>Induced by hormonal:</b>	Gastrin		<ul style="list-style-type: none"> <li>• Secretin</li> <li>• CCK</li> </ul>
<b>Characters of the secretion:</b>	Rich in enzymes		<ul style="list-style-type: none"> <li>• Rich in <b>HCO<sub>3</sub></b> &amp; <b>enzymes</b> and large in volume</li> </ul>

# The liver

## ▪ **Def:**

- The liver is the **largest organ in the body**, contributing **about 2%** of the total body weight, or about **1.5 kilograms**.
- The human liver contains **50,000 to 100,00 lobules** which are the structural and functional units of the liver.



## Bile Secretion

▪ **Bile is:**

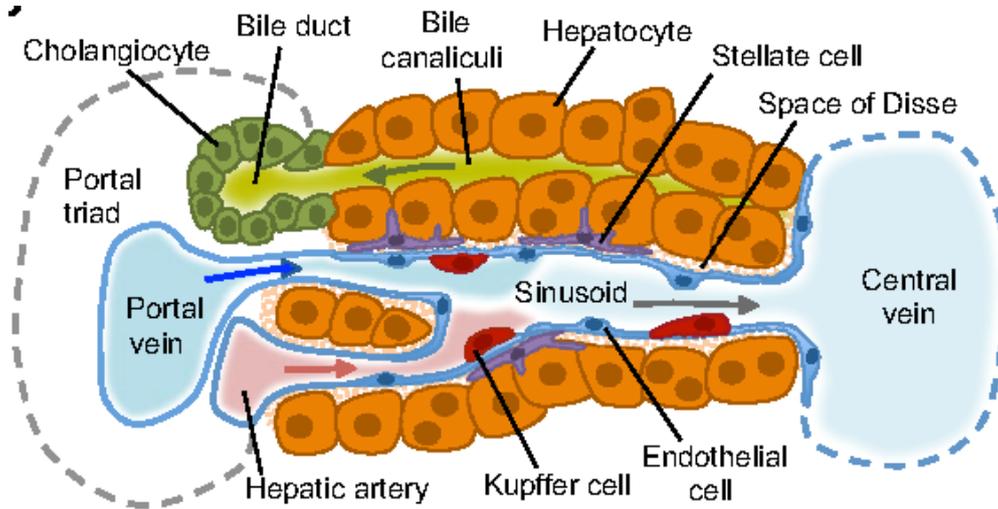
- Continuously formed and secreted by **liver**.
- It is stored, concentrated and acidified in **gallbladder** which evacuates its content into the **duodenum** mainly during the intestinal phase of digestion.

▪ **It is either:**

Ductular secretion	Canalicular secretion
<b>25%</b>	<b>75%</b>
the <b>cholangiocytes</b> are responsible for	The <b>hepatocytes</b> are responsible for.

▪ **Types of bile :**

	Hepatic Bile	Gallbladder Bile
<b>مهم جدا</b>		
<b>Volume</b>	0.6-1.2 L/day	
<b>pH</b>	Alkaline secretion (pH 7.8-8.6)	Relatively acidic (pH 6.5-7.5)
<b>Colour</b>	Golden yellow	Darker in colour
<b>Specific gravity</b>	1010	1050
<b>Composition</b>	<ul style="list-style-type: none"> <li>• 97% water</li> <li>• 3% solids :                             <ul style="list-style-type: none"> <li>a. <b>Organic:</b> include mainly bile salts and bile pigments..</li> <li>b. <b>Inorganic:</b> Na, K, Cl, HCO<sub>3</sub>, Ca and Mg</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• 92% water</li> <li>• 8% solids :                             <ul style="list-style-type: none"> <li>➤ <b>More</b> organic constituents.</li> <li>➤ <b>Less</b> inorganic constituents.</li> </ul> </li> </ul>



▪ **Control of bile secretion:**

1) **Bile salts in the enterohepatic circulation:**

- The most powerful stimulants of bile secretion (**major cholagogues**) as 50 % of canalicular bile flow is **dependent on** their active secretion by hepatocyte.

2) **Hormonal control:**

Hormone +++	Hormones ---
<ul style="list-style-type: none"> <li>• <b><u>Secretin:</u></b> <ul style="list-style-type: none"> <li>➤ Stimulates <b>bicarbonate secretion</b> by cholangiocytes (hydro-cholagogue).</li> </ul> </li> <li>• <b><u>Gastrin:</u></b> <ul style="list-style-type: none"> <li>➤ Stimulates bile secretion <b>directly and indirectly</b> through stimulation of HCl and consequently secretin release.</li> </ul> </li> <li>• <b><u>CCK:</u></b> <ul style="list-style-type: none"> <li>➤ Stimulates bile secretion from liver <b>indirectly</b> by stimulating gallbladder emptying thus <b>adding</b> more bile salts to the enterohepatic circulation.</li> </ul> </li> <li>• <b><u>Insulin.</u></b></li> <li>• <b><u>Glucagon.</u></b></li> </ul>	<ul style="list-style-type: none"> <li>• <b>Somatostatin.</b></li> <li>• <b>Estrogen.</b></li> </ul>

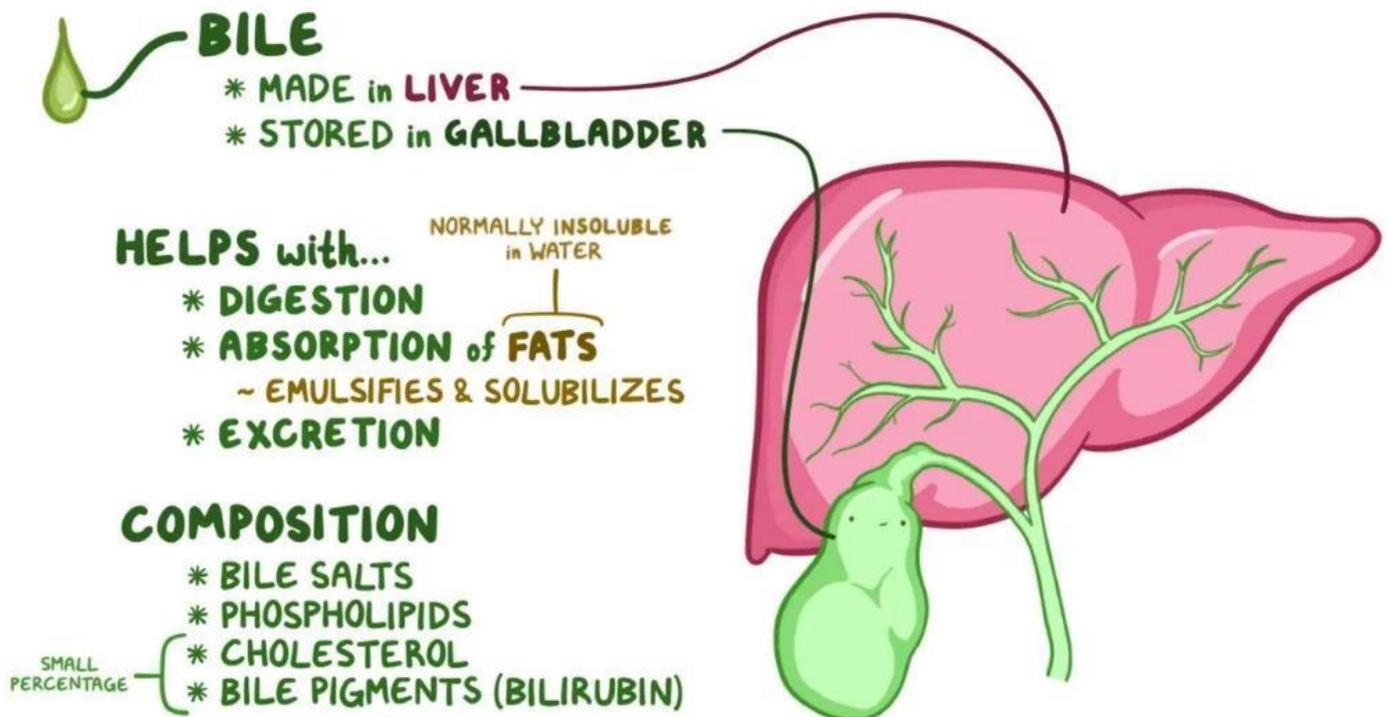
### 3) Nervous control:

Vagal stimulation:	Sympathetic stimulation:
<ul style="list-style-type: none"> <li>• <b>Stimulates bile secretion due to:</b> <ol style="list-style-type: none"> <li>a) <b>Choleretic effect of acetylcholine.</b></li> <li>b) <b>Increase hepatic blood flow by vasodilatation.</b></li> <li>c) <b>Stimulation of gastrin release.</b></li> </ol> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Decreases bile secretion secondary to decrease hepatic blood flow due to vasoconstriction of hepatic blood vessels.</b></li> </ul>

### ▪ Functions of Bile:

➤ bile as a whole functions as:

- a) **A source of alkali** to neutralize gastric HCl.
- b) **A route of excretion** of drugs and toxins.



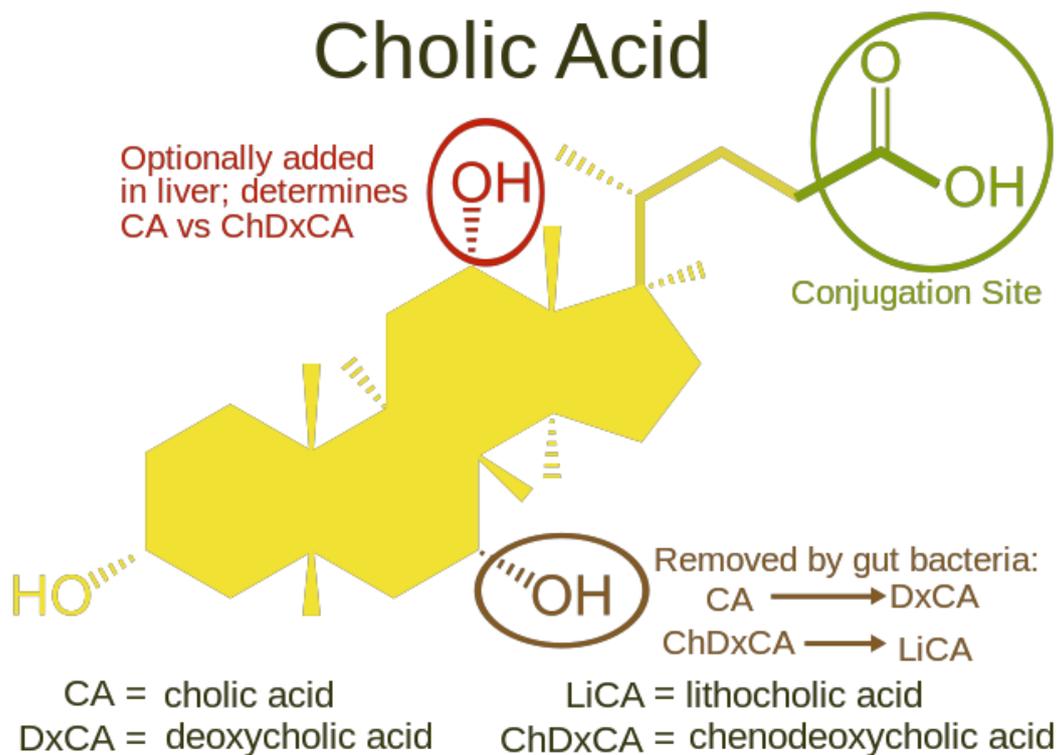
## Bile Salts

▪ **Def:**

➤ They are the sodium and potassium salts of **bile acids** conjugated with **glycine** or **taurine**.

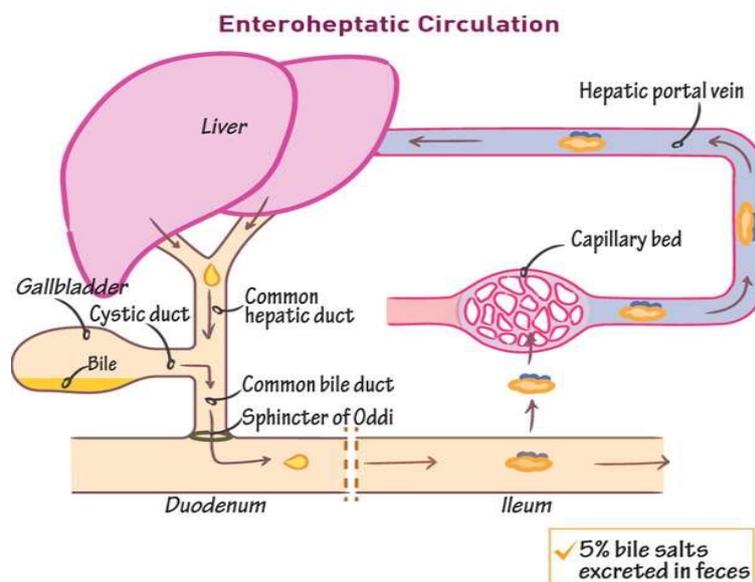
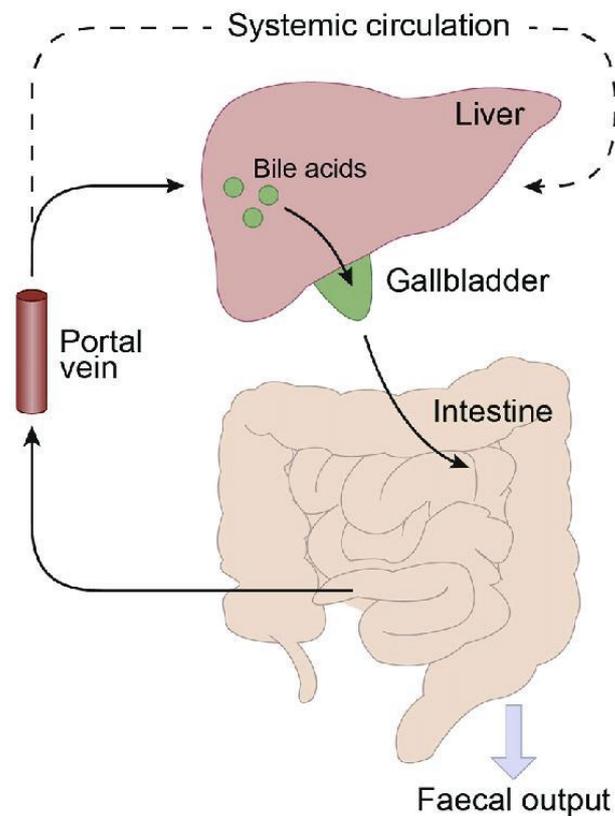
▪ **The bile acids are 2 types:**

	<i>1ry bile acids</i>	<i>2ry bile acids</i>
<b>Formation</b>	<ul style="list-style-type: none"> <li>Formed in liver from <b>cholesterol</b>.</li> </ul>	<ul style="list-style-type: none"> <li>From <b>1ry bile acids</b> by the action of colonic bacteria.</li> </ul>
<b>Example</b>	<ul style="list-style-type: none"> <li>Cholic acid.</li> <li>Chenodoxy-cholic acid.</li> </ul>	<ul style="list-style-type: none"> <li>Deoxycholic acid.</li> <li>lithocholic acid.</li> </ul>



## ■ Entero-hepatic Circulation of Bile Salts:

- The bile salts circulate twice during a meal and **6-8 times per day**.
- **90-95%** of bile salts are absorbed from GIT (**50%** by  $\text{Na}^+$  dependent 2ry active transport from the **terminal ileum**).
- Absorbed bile salts pass in portal circulation to liver to be re-secreted in bile.
- The rate of loss of bile salts in stool is **0.2- 0.4 gm/day** which are replaced by new synthesis in liver the total circulating pool of bile salts (**3.5gm**) is kept constant.



▪ **Functions of bile salts:**

<p><b>1- Help digestion of fat by:</b></p>	<ul style="list-style-type: none"> <li>• <b>Emulsification of fat</b> i.e. converting it into fine globules by <b>reducing</b> surface tension (detergent action).</li> <li>• <b>Dissolving fatty acids</b> thus exposing deeper layers of fat for action of lipase.</li> <li>• Activation of <b>lipase</b>.</li> </ul>
<p><b>2- Help absorption of fat and fat soluble vitamins:</b></p>	<ul style="list-style-type: none"> <li>• Bile salts, by <b>their hydrotropic action</b> , form with fat digestion products and fat soluble vitamins , water soluble easily diffusible particles called <b>micelles</b>.</li> </ul> <div data-bbox="572 824 1390 983" data-label="Diagram"> </div>
<p><b>3- Help absorption of Ca, Mg and iron:</b></p>	<ul style="list-style-type: none"> <li>• Indirectly through facilitating fat absorption which <b>impairs</b> their absorption</li> </ul>
<p><b>4- Solvent action:</b></p>	<ul style="list-style-type: none"> <li>• keep cholesterol dissolved.</li> <li>• This <b>prevents</b> its precipitation in gallbladder and formation of gall stones</li> </ul>
<p><b>5- Laxative action:</b></p>	<ul style="list-style-type: none"> <li>• Bile salts <b>stimulate</b> intestinal movements.</li> </ul>
<p><b>6- Choleric action:</b></p>	<ul style="list-style-type: none"> <li>• Stimulation of <b>bile secretion</b> by liver.</li> <li>• <b>About 50%</b> of canalicular bile secretion is dependent on bile salts.</li> </ul>
<p><b>7- Anti-putrifactive action:</b></p>	<ul style="list-style-type: none"> <li>• In absence of bile salts, the undigested fat <b>envelops</b> protein particles <b>preventing</b> their digestion.</li> <li>• So <b>intestinal bacteria</b> attack the undigested protein and cause <b>putrefaction</b>.</li> </ul>

# Bile Pigments

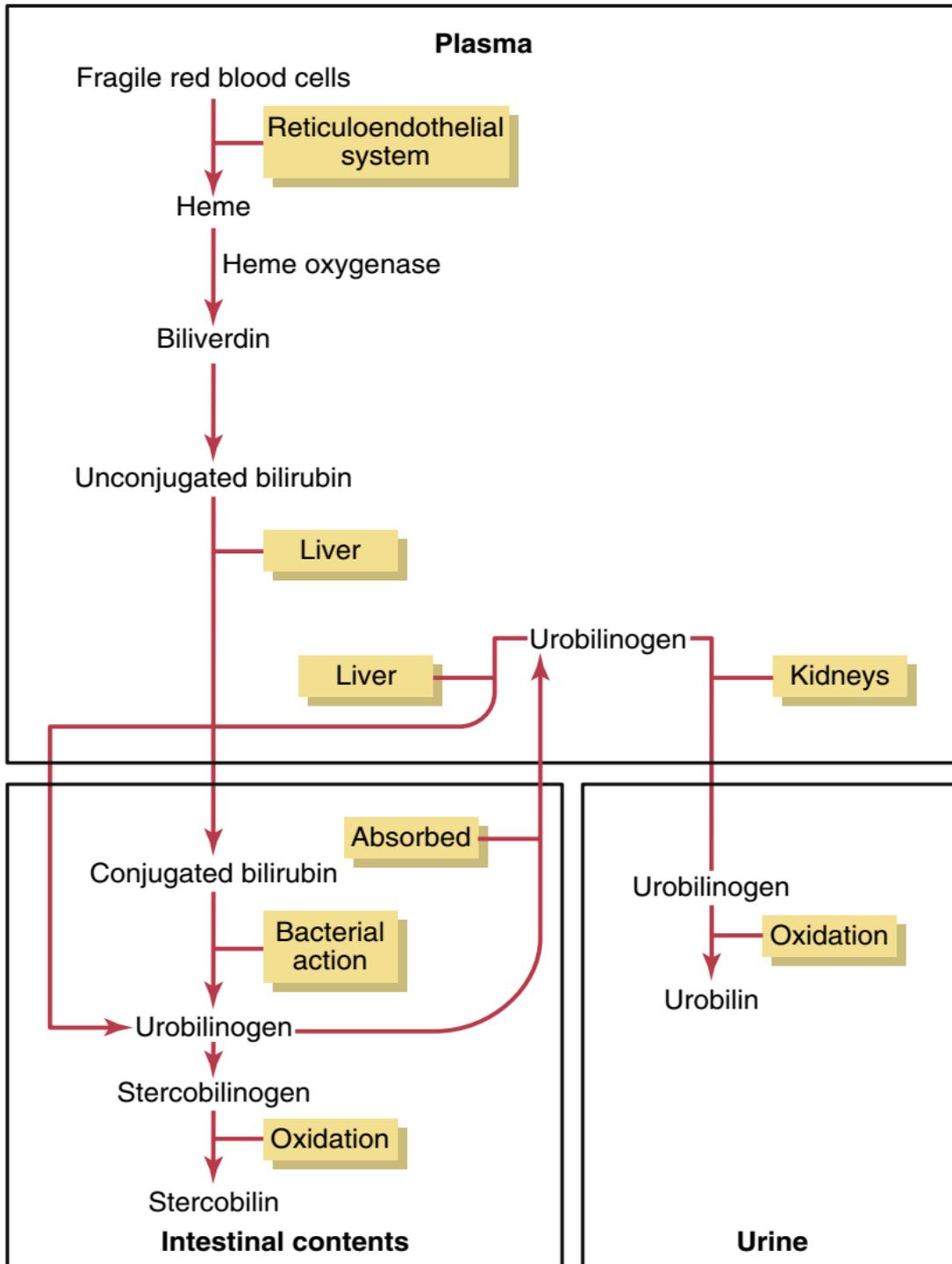
▪ **Formed from:**

➤ **old or damaged RBCs.**

▪ **Formation:**

<p><b>A) In the reticuloendothelial cells:</b></p>	<ul style="list-style-type: none"> <li>• Hb is <b>spitted</b> into globin and heme.</li> <li>• Iron in heme is released to give <b>biliverdin</b>.</li> <li>• Biliverdin is reduced to <b>bilirubin</b> which is the principal bile pigment.</li> </ul>
<p><b>B) In blood:</b></p>	<ul style="list-style-type: none"> <li>• Bilirubin is released into plasma and immediately combined with plasma albumin to form <b>free (Indirect) (Unconjugated) bilirubin</b>.</li> </ul>
<p><b>C) In the liver:</b></p>	<ul style="list-style-type: none"> <li>• Bilirubin is actively <b>up taken</b> where it is released from albumin and <b>conjugated</b> mainly with glucuronic acid (catalyzed by glucuronyl transferase enzyme) and to lesser extent with sulfate.</li> <li>• <b>The conjugated bilirubin (Direct)</b> is actively transported into bile canaliculi with small amount passes to blood.</li> </ul>
<p><b>D) In the intestine:</b></p>	<ul style="list-style-type: none"> <li>• The conjugated bilirubin is converted to <b>Urobilinogen</b> by the action of bacteria.</li> </ul>
<p><b>E) Fate of Urobilinogen:</b></p>	<ul style="list-style-type: none"> <li>• Most of it passes with feces as <b>Stercobilinogen</b> which gives feces its normal brown color.</li> <li>• Some of it is absorbed by portal circulation to the liver to be re-excreted (<b>enterohepatic circulation</b> of urobilinogen).</li> </ul>

- **Small amount** escapes from liver and enter the general circulation where it is excreted by kidneys into **urine** giving it its **normal yellow color**.



# Jaundice

## ▪ Def:

- It is the **yellow coloration** of skin, sclera and mucous membrane due to increased concentration of bilirubin in plasma **more than 2mg %**.

## ▪ Normal value of Plasma Bilirubin:

<b>Total bilirubin:</b>	<b>0.3 to 1.0 mg/dL</b>
<b>Direct (conjugated) bilirubin:</b>	<b>0.0 to 0.3 mg/dL</b>
<b>Indirect (unconjugated) bilirubin:</b>	<b>0.2 to 0.8 mg/dL</b>



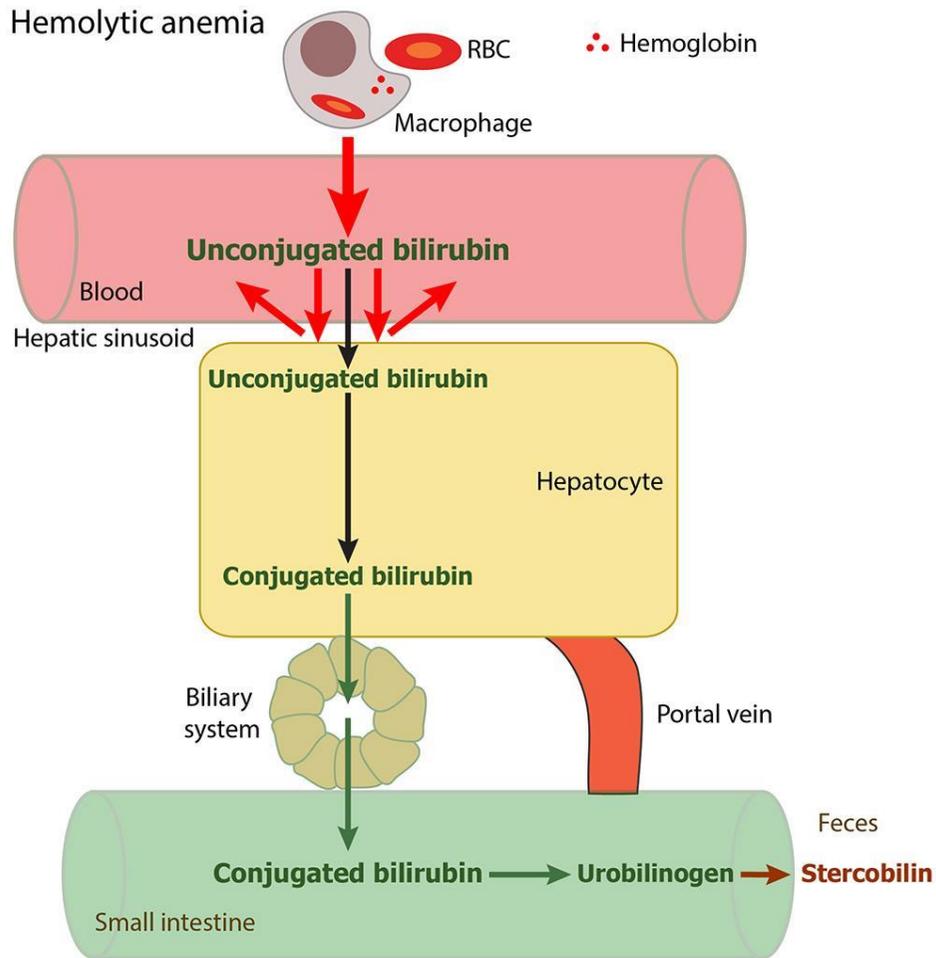
## ▪ Types of Jaundice:

- 1- Hemolytic (Prehepatic) jaundice:
- 2- Hepatocellular (Intrahepatic) Jaundice:
- 3- Obstructive (Post-hepatic) Jaundice:

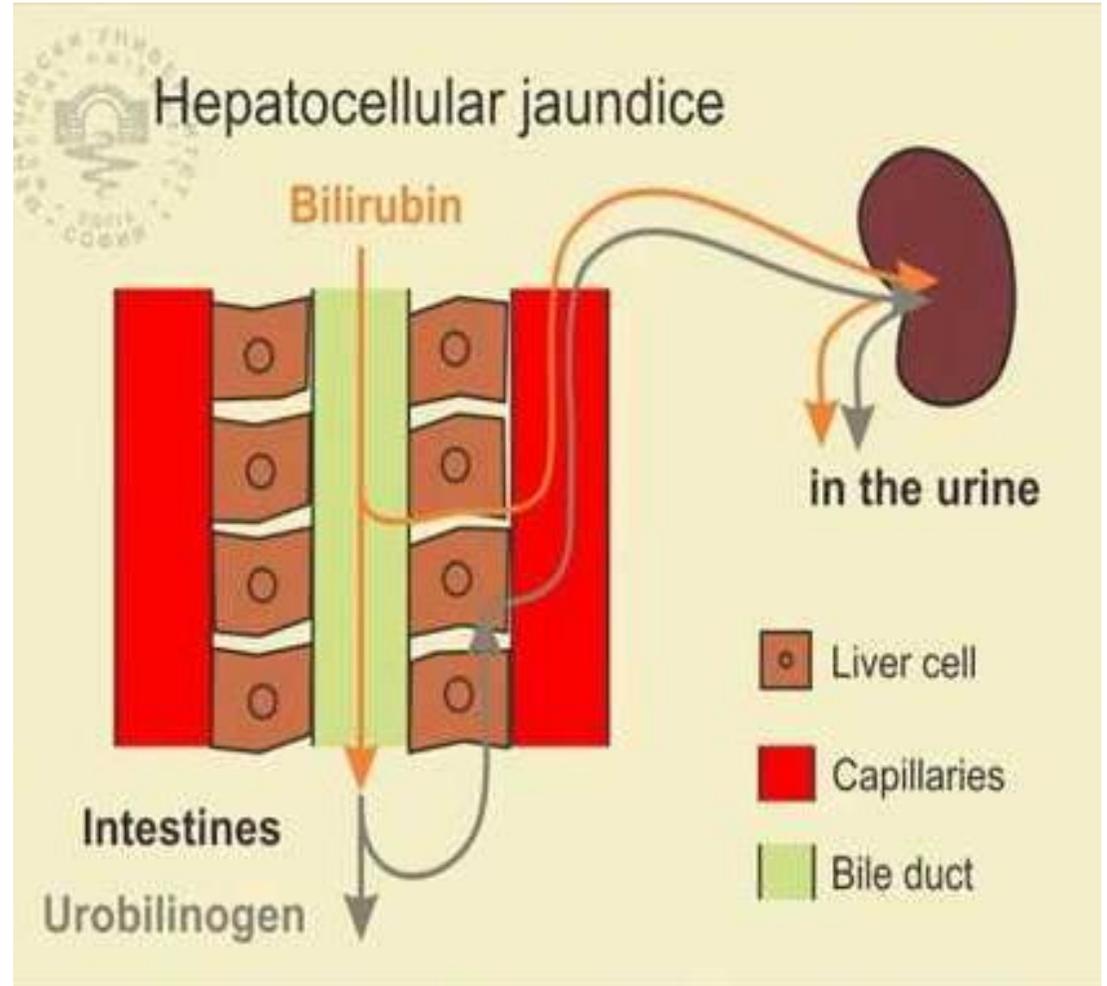
### **NB:**

- The commonest type of jaundice is **mixed** hepatocellular and obstructive jaundice in cases complicated with **cirrhosis**.
- **Fibrosis** compresses the intra-hepatic portions of the biliary tree to cause a **degree of obstruction**.

	<b>1- Hemolytic (Prehepatic) jaundice:</b>	<b>2- Hepatocellular (Intrahepatic) Jaundice:</b>	<b>3- Obstructive (Post-hepatic) Jaundice:</b>
<b>Causes:</b>	<ul style="list-style-type: none"> <li>• ↑ <b>destruction (hemolysis) of RBCs</b> → ↑ production of <b>bilirubin</b> more than its removal by liver e.g. Incompatible blood transfusion &amp; RH incompatibility.</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Damage of liver cells</b> e.g. Viral hepatitis, and liver cirrhosis.</li> <li>• <b>Immature hepatic system</b> as in physiologic jaundice of the newly born</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Obstruction of bile flow</b> in biliary passages e.g. gall stones, cancer head of pancreas.</li> </ul>
<b>Characters:</b>	<ul style="list-style-type: none"> <li>• ↑ <b>unconjugated bilirubin</b> in plasma.</li> <li>• ↑ <b>urobilinogen</b> formation in intestine.</li> <li>• ↑ excretion of <b>urobilinogen</b> in urine and feces so <b>stool and urine</b> is darker than normal.</li> </ul>	<ul style="list-style-type: none"> <li>• ↑ <b>unconjugated bilirubin</b> in plasma.</li> <li>• ↓ excretion of <b>conjugated bilirubin</b> and ↓ formation of <b>urobilinogen</b> in intestine so stool is lighter in color than normal.</li> <li>• The urine is <b>dark</b> due to ↑ <b>urobilinogen</b> (not reabsorbed in the liver) and ↑ <b>conjugated bilirubin</b> (leaked from damaged hepatocytes).</li> </ul>	<ul style="list-style-type: none"> <li>• ↓ excretion of <b>conjugated bilirubin</b> and ↓ formation of <b>urobilinogen</b> in intestine and its excretion in urine so stool becomes pale.</li> <li>• ↑ <b>conjugated bilirubin</b> in blood and urine which becomes darker than normal.</li> <li>• ↓ excretion of <b>bile salts</b> in the intestine leading to steatorrhea.</li> <li>• <b>Back flow</b> of bile salts into blood leading to itching and bradycardia.</li> </ul>



**Hemolytic (Prehepatic) jaundice**



**Hepatocellular (Intrahepatic) Jaundice**