# physiology

faculty of medicine - JU2017

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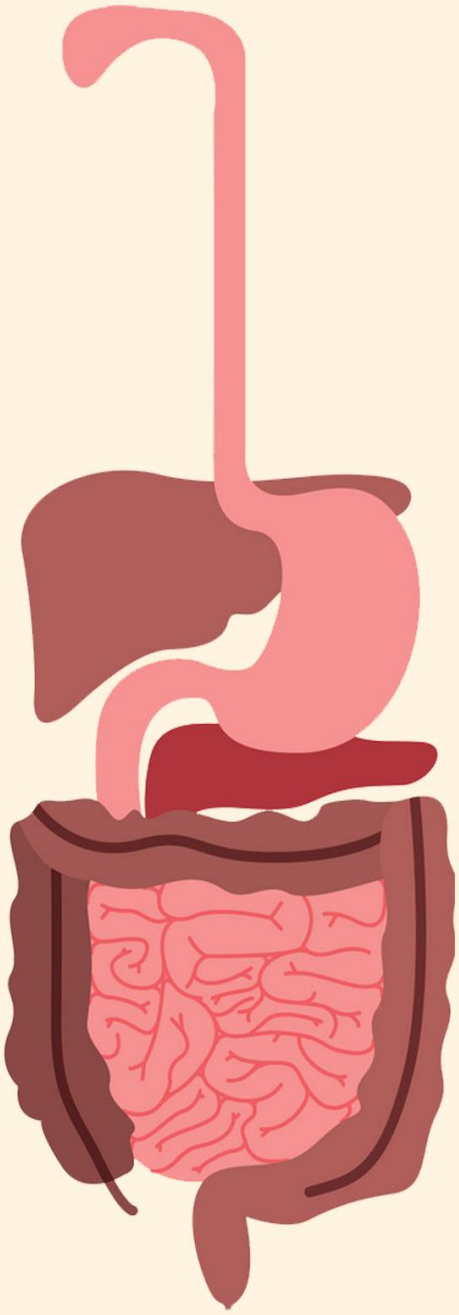


# 2nd system - GI

# pancreatic secretions (1-2L/day)

The pancreas has :

1- **Endocrine portion**(secretions are released into the blood)
   - It takes the form of many small clusters of cells called **islets of Langerhans** .
   - These cells synthesize and secrete hormones (insulin , glucagon ,somatostain and pancreatic polypeptide ).
2- **exocrine portion** (secretions are released through the canalicular system to the interstitial fluid) .
   - the exocrine portion consists of **Acinar cells** (secrete enzymes) and **duct cells** (secrete water and bicarbonate).
   - The exocrine secretions (enzymes+bicarbonate) are secreted through the **pancreatic duct** which then unites with the **common bile duct** to become the **hepatopancreatic duct** (also known as **ampulla of vater**) which empties in the duodenum through Oddi sphincter.

**Anatomical view to the Oddi sphincter :**

we have a sphincter which is guarding this opening which is important to prevent the reflux of the **pancreatic enzymes** to the pancreas again.

**Histological view:** the cells that secrete enzymes have vesicles, but duct cells don't have vesicles.

**Pancreatic enzymes(proteolytic enzymes):**

1- Trypsinogen : activated by enterokinase in the duodenum to become trypsin.
   -in the pancreas trypsinogen remains inactive by trypsin inhibitor.
2- Chemotrepsinogen : activated by trypsin.
3- ProCarboxypeptidase : activated by trypsin>

**Note**: All of these are **endopeptidases** (cut from the middle) except carboxypeptidase which is an **exopeptidase** (cuts from c end).

**Note**: All these enzymes are released as proenzymes (inactive), and the activation occurs in the duodenum.

At the duodenum, we have the enzyme enterokinase which is responsible for converting **trypsinogen** into **trypsin** (activating it by phosphorylation),and the Trypsin activates others by cutting them(**endopeptidase**).

**Note:** Pancreatic enzymes aren't released as active enzymes to protect the pancreas from eating it self

Note: (oddi sphincter) prevents the reflux of pancreatic secretions and protects the pancreas. Therefore, alcoholics suffer from acute pancreatitis because of the relaxation of the sphincter and the reflux.

**pancreatic amylase**: secreted as active enzyme to convert Starch (polysaccharide) into

disaccharides.

**Lipolytic enzymes:**

1- Lipase :
   - Is an esterase that splits triglycerides into monoglycerides and free fatty acids.
   - Their activity requires : an oil/water interface , bile salts(secreted by liver) and other co-lipase (secreted by pancreas).
2- Phospholipase.
3- cholesterol ester hydroxylase

**Note:** secreted as active and inactive enzymes.

***** pancreatic insufficiency** characterized by decreased enzyme secretion , is manifested as steatorrhea (yellowish stool due to the presence of undigested Fat).

**water and bicarbonate secretion**

*Duct cells secrete water and bicarbonate ( the mechanism same as in stomach) .

-The enzyme Carbonic anhydrase catalyzes the following reaction :

$$H_2O + CO_2 \xrightarrow{CA} H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

- $HCO_3^-$ is transported at the luminal border by secondary active transport , in exchange with $Cl^-$ .($Cl^-$ moves along its chemical gradient)

-$H^+$ is transported by secondary active transport in exchange with $Na^+$ at blood border.

- $Na^+$ is transported from the cell by active transport followed by water osmosis.

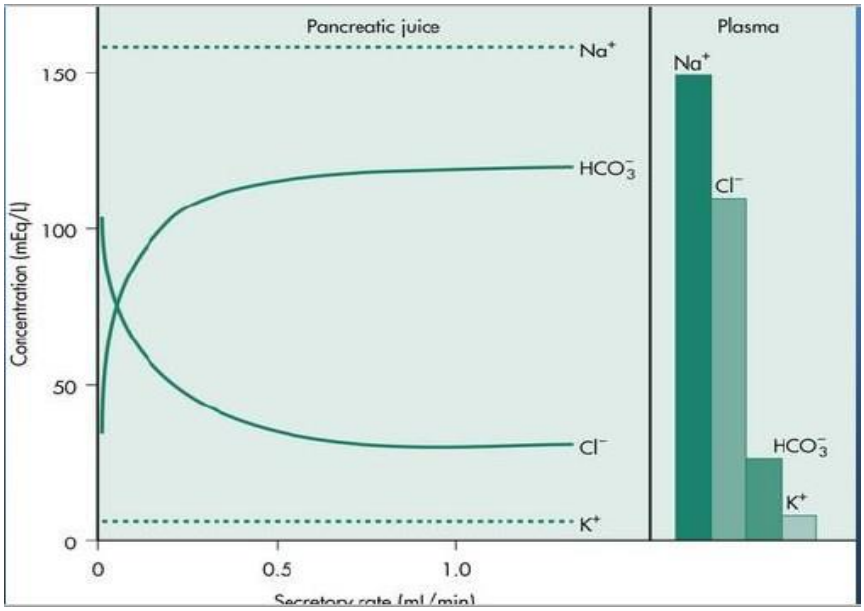
*We are forming the bicarbonate in duct cells and secreting it toward the lumen and absorbing H+ ions.

The final composition varies with the rate of secretion :

***At low secretion level**: low bicarbonate content and high Cl- .

***At higher levels** we have higher bicarbonate content (that means you formed more bicarbonate upon stimulating ) and Cl- is low.

*The absorption of Cl- is according to the potentials , once you have more releasing of bicarbonate, you are reducing the release of the other ions.




*the pancreatic secretion has an alkaline pH to neutralize the acids when emptied into the duodenum from the stomach, providing an optimal pH for enzymes function.

**Controlling of pancreatic secretions:**

1- Neural control.
2- Hormonal control.

**** Neural control (autonomic nervous system, and some enteric fibers)**

**Parasympathetic**: activation by vagal stimulation ⟹ enteric nervous system ⟹ release of Ach, VIP, and GRP (Gastrin releasing protein).

**Sympathetic**: indirect inhibition via vasoconstriction , reducing blood supply to the pancreas.

**Hormonal control:**

**1-Secretin**: it is secreted from the duodenal mucosa, and it affects duct cells (increase water and HCO3- secretion in response to the presence of of acid in the duodenum)******it's the major stimulant of water and bicarbonate secretion.

**2-Cholecystokinin(CKK**) : it is the major stimulant of enzyme secretion .

-CKK is released by duodenal mucosal cells into the blood in response to fat products and proteins in chyme.

- acts directly through CKK-A receptors on acinar cells to increase enzymatic secretion.

- it also acts indirectly through vagovagal reflex to stimulate enzyme secretions.

- Other effects of CKK include contraction of the gallbladder and relaxation of Oddi sphincter by both ways directly and indirectly.

vagovagal: vagal nerve has sensory fibers and efferent fibers (increases parasympathetic and stimulates enzyme secretion)

**Note:** this is an example proves that endocrine cells can act on the neurons and change its activity.

**3-Pancreatic polypeptide**: it inhibits the pancreatic enzyme secretion by:

*Inhibiting Ach release from enteric nervous system.

*Inhibiting vagal output of the CNS.

**Control of pancreatic secretion (summary):**

- **Cephalic phase** (activation): sight , smell ,taste or hearing . **Reflex is mediated by vagus.**

- **Gastric phase** (activation) :Distension . **Effect is mediated by vagus.**

- **Intestinal phase** (activation) : local changes are caused by : Aminoacids , Fatty acids , Distension. **Effect is mediated by CKK , secretin , enteropancreatic reflexes and other hormones.**

- **No phase** ( inhibition) : more pancreatic polypeptide in no phase.

# Liver secretions

*The liver is the largest and most important metabolic organ.

*it plays an important role in digestive mechanisms by the formation and secretion of **bile salts.**

**The liver also preforms the following functions :**

1. metabolic processes: Process all nutrients after their absorption.
2. Detoxification of body wastes, hormones, drugs, and other foreign bodies.
3. Synthesis of plasma proteins, including clotting factors (their synthesis requires vit. K), hormone transporters.
4. Storage organ of glycogen, iron (ferritin), copper, and vitamins.
5. Removal of bacteria and foreign materials by reticuloendothelial cells (Kupffer cells).
6. Excretion of cholesterol and bilirubin

*we will concentrate on Excretion of cholesterol and bilirubin.

*Bilirubin is waste material from hemoglobin, low excretion =high bilirubin= jaundice.

**Note**: In order to excrete bilirubin, it must be conjugated with (glucuronide, sulfate, other substances) to make it more soluble and hydrophilic.

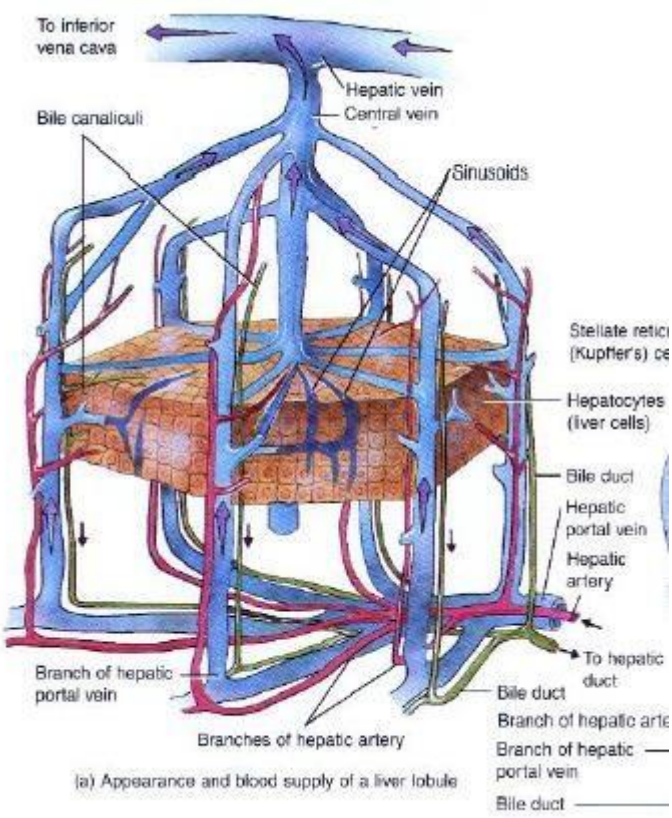
**Hepatic lobule- blood and bile paths**

The functional unit is called **hepatic lobule**. Hepatic cells in this unit have hexagonal arrangement that surround the central vein. At the outer edges of the hexagonal structure of the lobule there are three vessels:

*A branch of the hepatic artery *A branch of the portal vein. *A bile duct.

-At the center of the hepatic lobule, there is a vein called central vein.

- Blood runs from **the branch of the hepatic artery** and the **portal vein** (from periphery) into **sinusoid***, which runs between rows of hepatocytes to the **central vein.** The hepatocytes are arranged in two cell layers , so that each hepatocyte has one side faces sinusoidal blood. The other side of hepatocyte faces bile carrying channel called (**bile canaliculus**), which carries bile to a bile duct at the periphery of the lobule , bile flows into the **common bile duct**, then in duodenum. The space between sinusoid and hepatocytes (space of Disse). In this space lymphatic circulation takes place.




**Excretion of bilirubin with bile:**

-Bilirubin results from the catabolism of hemoglobin = Heme + Globin

-Heme ring is decomposed into iron + biliverdin

-**Biliverdin** is transformed into bilirubin and secreted in bile as conjugated with (glucoronide, sulfate, other substances).

-In intestines, bilirubin is transformed (by bacterial action) into **urobilinogen**. This will be reabsorbed and secreted in urine as (urobilin) **or** secreted with feces as stercobilin.

**Note:** Jaundice (yellow discoloration of the skin) is caused by the presence of high concentration of bilirubin in the extracellular space.

**Bile synthesis and secretion:**

The digestion and absorption of lipids involve a special problem: The environment in the lumen of intestine is an aqueous environment **in which lipids are not soluble.** To make lipids soluble, bile is added to the small intestine at the level of duodenum. Bile acts as detergent to emulsify lipids and make them soluble.

-Bile is composed of bile salts, water & electrolytes, cholesterol, phospholipids and wastes intended for excretion, (bilirubin).

-Bile salts are synthesized by the liver, concentrated in the gallbladder and modified in the lumen.

**Synthesis by the Liver :**

-Liver synthesizes two bile acids from cholesterol : ***cholic acid*** and ***chenodeoxycholic acid*** (these are primary bile acids).

-Bile acids are usually secreted as bile salts rather than as bile acids.

-Transformation appears by conjugation of bile acids with either ***taurine*** or ***glycine***. Thus, bile contains 4 bile acids conjugated to one of these amino acids.

-The primary bile secretion is isotonic and contains also Na+, K+, and Cl-.

-The secretion enters the duct system where the cells lining the duct modify it by exchanging HCO3- for Cl-.

-The secretion of HCO3- is increased by the activity of the hormone secretin.

-Between meals bile is derived into Gallbladder where it is stored.

**How do the bile salts go to gall bladder?**

By the relaxation of the gall bladder, the pressure inside it is lower than in the duct, so the bile moves from the bile duct to the gall bladder and get stored in it (some absorption of water and electrolytes takes place ).

Once a meal is ingested, the bile salts are secreted from the gall bladder to the duodenum by the contraction of the bladder, and the Oddi sphincter is relaxed.

**Note**: By comparing of bile from the liver directly, and the one from the gall bladder, we find that bile salts are more concentrated in the gall bladder bile. (this is done by the epithelium of gallbladder ; which removes water and electrolytes resulting in 5-20 folds concentration of bile.

**Note:** if someone has done gall bladderectomy, this person must reduce his fat intake (must not eat fat rich meals because its bile is less efficient than in normal people).

-gallbladder contraction is mediated by neural (local and vagal) reflexes, as well as hormonal by the activity of CKK which is released by the presence of lipid and protein digestion products in the duodenum.

**Gall bladder stones**: hypomotility of gall bladder leads to more reabsorbtion of water and electrolytes from the bile, so it is less soluble, and that what makes the gall bladder stones.

**Notes:**

1- Hypomotility of gall bladder is caused by deformity or inflammation.
2- stones might cause inflammation.

**Bile salts reabsorption:**

*80 percent of bile salts are reabsorbed actively in the terminal ileum. They are then removed from the blood by the liver and resecreted into the bile.

- During a normal meal, the entire bile salt pool is recirculated twice. This is known as the **enterohepatic circulation**.

*The 20 percent lost can be compensated by de novo synthesis from cholesterol.

**Modification of bile salts in the intestine to secondary bile acid:**

-Once they are in the intestine these bile acids are modified to **secondary bile acid** by the activity of bacteria that dehydroxylate them which result in the conversion of :

-Cholic acid $\Longrightarrow$ deoxycholic acid.

Chenodeoxycholic acid $\Longrightarrow$ lithocholic acid

**Note:** the non modified bile salts can be reabsorbed unlike the modified (secondary bile acids)

**Control of hepatic secretions:**

In addition to the autonomic nervous system (contraction of the gall bladder and the release of the bile salts)

1- CCK: Its main activity is to stimulate contraction of the gall bladder, which is stimulated by the eating of fat content chyme.
2- Secretin: works over duct cells to increase water and electrolytes
3- Somatostatin: inhibitory for duct cells.

## digestion and absorption:

esophagus: no absorption small intestine: specialized organ

for absorption and digestion  colon: highly reabsorption of

fluids from the feces.

small intestine: the mucosa is folded which increases the surface area 3 times. over these folds we have villi (papillary like structure, highly capillariesed, also there is lymphatic vessels which are called central lacteals_ which has importance for absorbing some materials) with these villi, we increase the surface area 10 times, (3 times is from the folds)

we have cells which are lining the villi, the luminal membrane of these cells is also folded, forming microvilli (brush border), over the brush boarder we have some enzymes, like enterokinase.

The overall increase of the surface area of the small intestine is 600 times.

1cm of the intestine  is equal to 600cm  (functionally)