Digestive System

University of Jordan

Faculty of Medicine

Batch of 2013-2019

Medical Committee
The University of Jordan

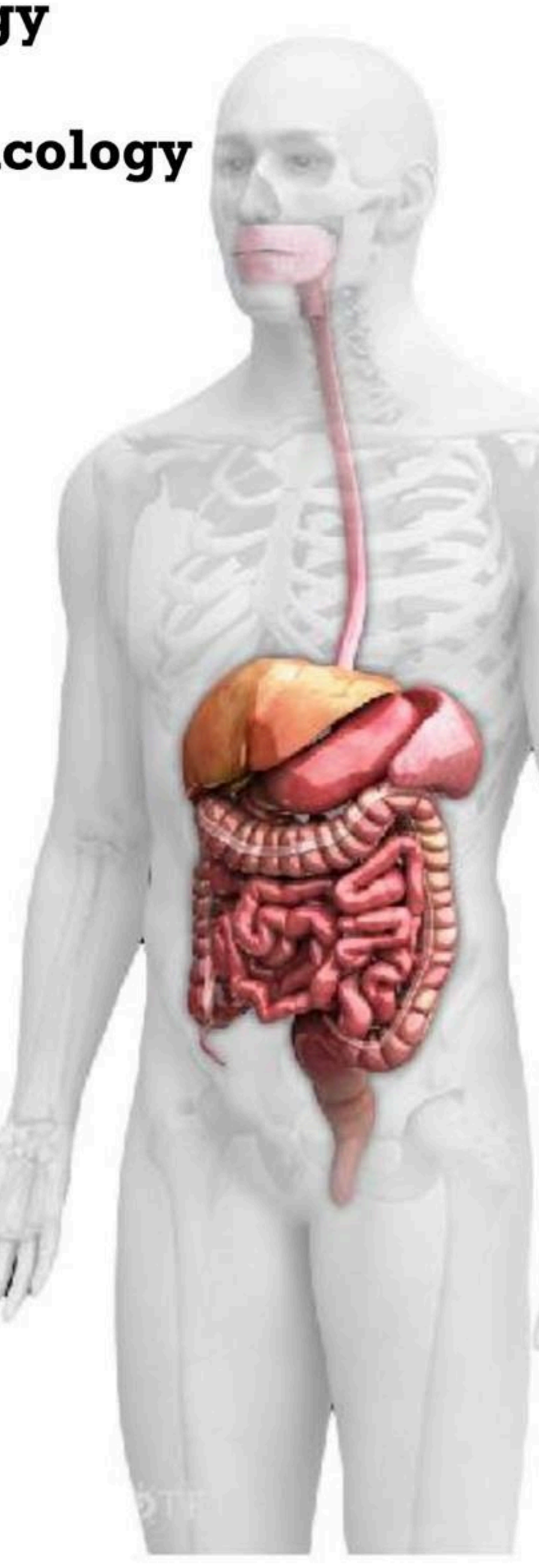
○ Slide ● Sheet ○ Handout ○ Other

☐ Anatomy ☐ Embryology

☐ Physiology ☐ Histology

☐ Pathology ☐ Pharmacology

☐ Microbiology ☐ PBL



Sheet #: 6

Done by: Hiba M Al-Atrash

Date: 6-4-2015

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DESIGNED BY: TAMER ALTAMIMI "SMILE"

بسم الله نبدأ ♥

(و أن ليس للإنسان الا ما سعى * وأن سعيه سوف يُرى) سورة النجم

About the previous lecture:

We have talked about gastric secretions, the types of the secretory cells, and the mechanism of secretion. Regarding the ionic composition, we said that there's an active transport of Cl- ions reaching the canaliculi. Once those chloride ions which are negatively charged reach the canaliculi, trans-cellular potential will be faced. "Trans-cellular: means across the whole cell". Now let's consider one layer of cell at one membrane. In this case, this will attract sodium ions from interstitial fluid toward the canaliculi. But once you've stimulated the formation & secretion of hydrogen protons, the potential becomes less negative; at the luminal membrane we only have proton pumps and potassium-hydrogen pumps thus pumping protons from inside the cells toward the canaliculi. Once you've pumped these protons, the potential will become around -30 (while before pumping it's around -70). Which of these potentials is giving more force for sodium? -70. So once you have stimulation of these cells you're releasing more sodium, but once you have stimulated the cell to release protons, you're releasing less sodium.

That's the change of the ionic composition.

At low rate, more sodium-chloride.

At high rate, more hydrochloric acid release.

This is regarding gastric secretions (the subject of the last lecture)

Now let's start with the pancreatic secretions.

Pancreatic Secretions

—

—Pancreas has many types of cells :

- **Endocrine portion**, which is forming islet. "we will take about it in the endocrine system"
- **Exocrine portion.** "we will talk about it today because it has relation with our digestive processes"

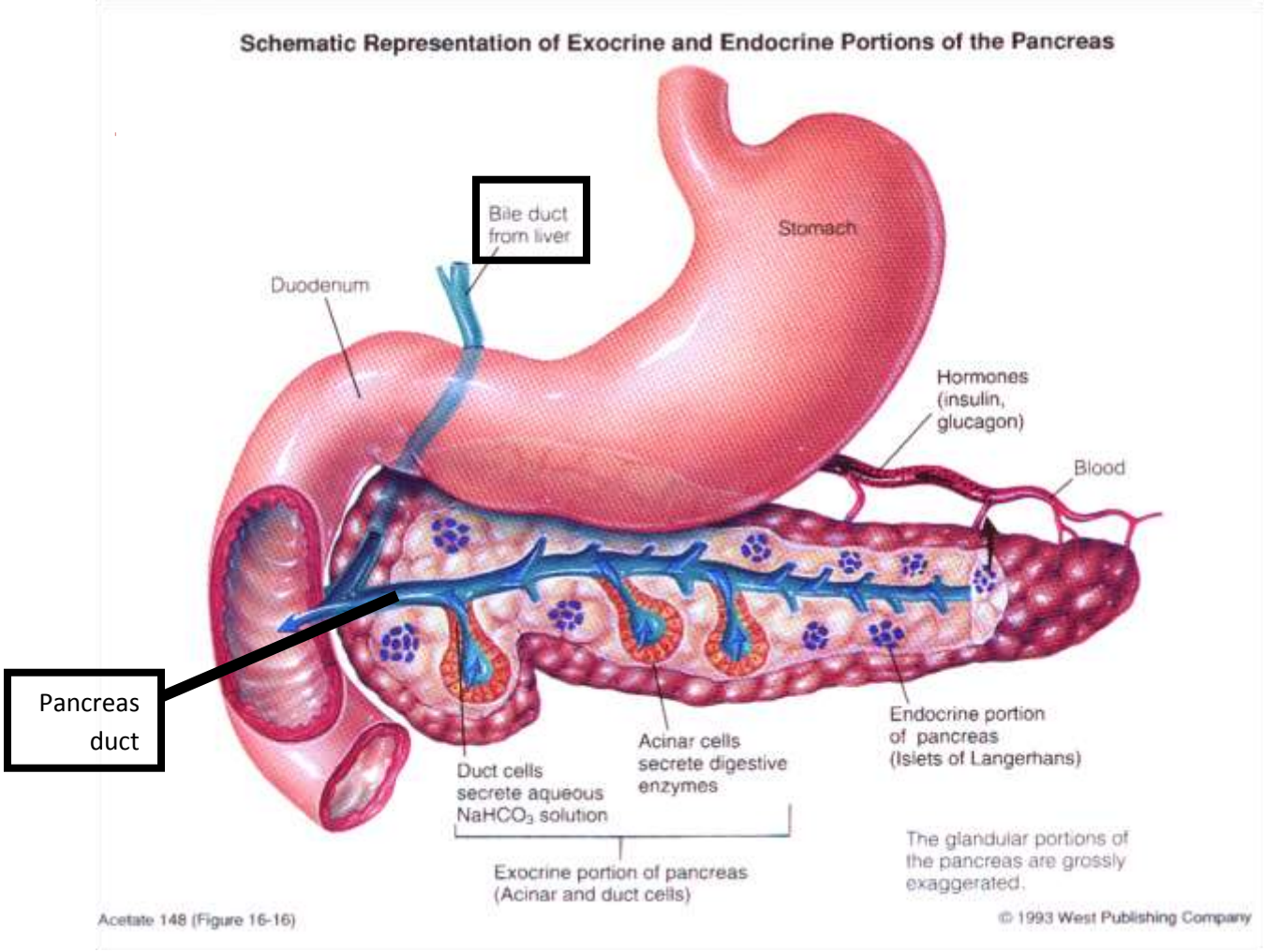
* From *functional view* pancreas is similar to *salivary gland* so we have:

1) **Acinar cells** which are involved in release of **Enzymes**
2) **Duct cells** which are involved in secretion of Water and electrolytes such as bicarbonate.

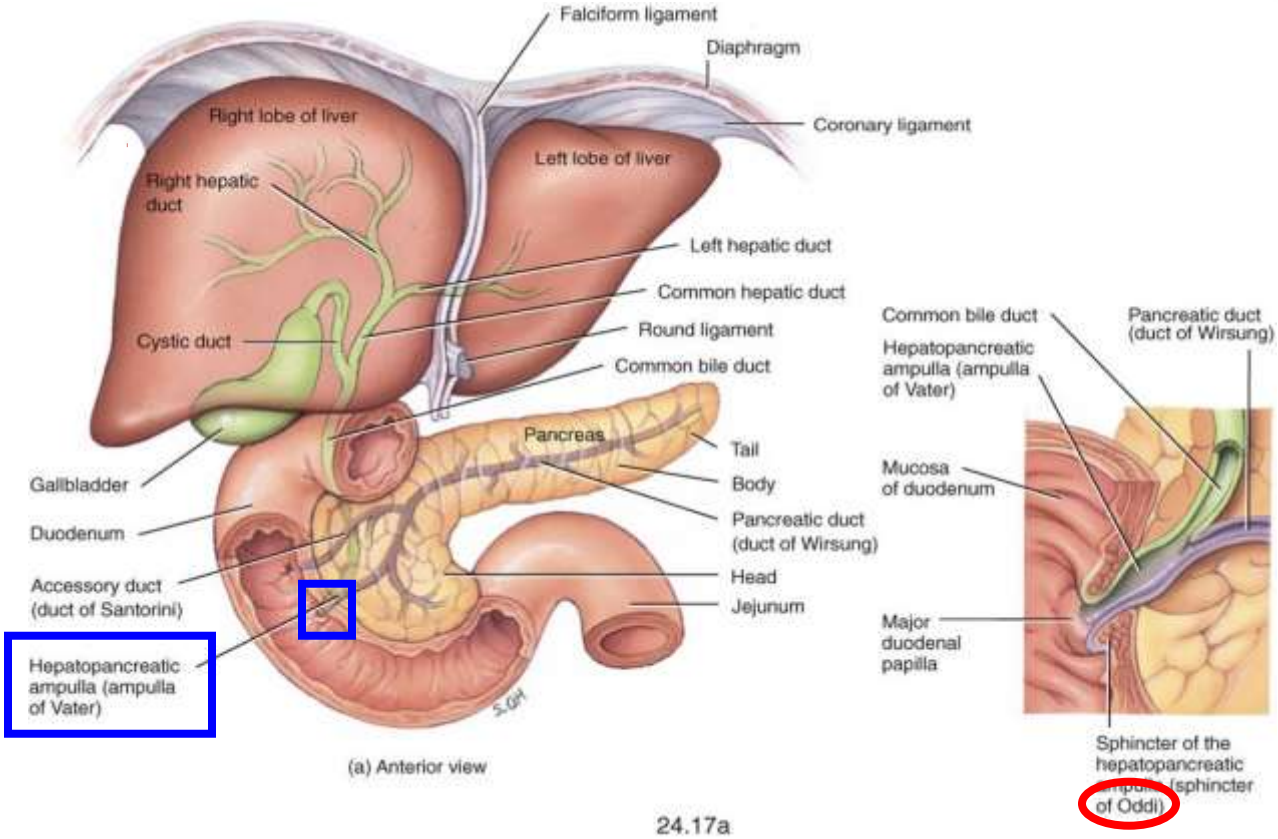
The difference between duct cell in salivary gland and pancreas:

- duct cells in **salivary** gland ➔ Modification of primary saliva
- duct cells in **pancreas** ➔ Secretion of water and electrolytes

- Once we are getting secretions, we are having pancreatic juice flowing toward duodenum.



- But before reaching duodenum, the duct from the pancreas will unify with the duct from the liver to from **hepatopancreatic duct**.
  "We will take it in anatomy in more details."



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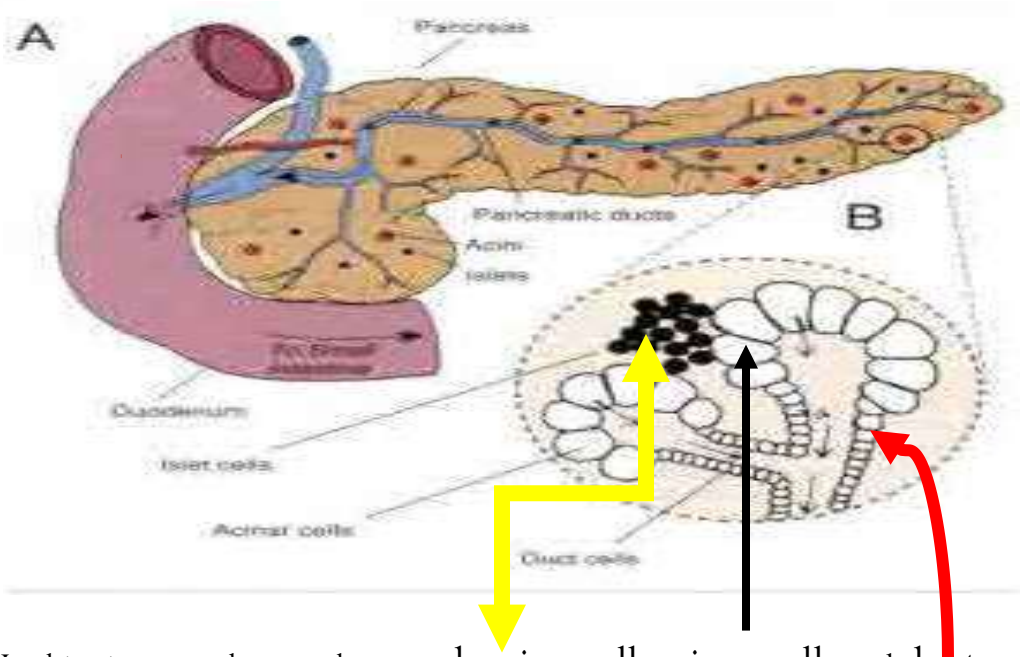
- The opening where we are getting flow of bile and pancreatic juice into duodenum, we have anatomical structure that is called ***Ampulla of Vater.***

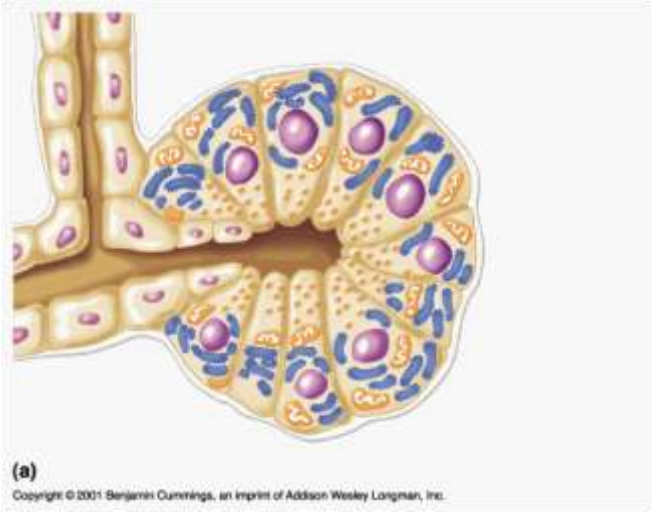
- Sphincter guarding this opening is called **ODDI sphincter**.

What's the importance of oddi sphincter?

Prevent **reflux** of duodenal content toward the biliary



In this picture we have we have endocrine cell, acinar cells and duct cells



Look here to **acinar cell**

What you have seen? High contents of ER and vesicles.

- Typically they are SECRETORY cells forming and releasing proteins (enzymes).

- No vesicles in duct cells.
- Duct cell are mainly involved in release water and electrolytes.
- You may find some secretory cells but we have much higher representation for cells that are releasing enzymes in acinar cells.

☒ Enzymes secreted by acinar cells:

- protelytic
- lipolytic
- enzyme for digestion of carbohydrate

1) PROTEOLYTIC ENZYMES: Enzymes Secreted by acinar cells

1. **Trypsin (-ogen):** activated by **enterokinase** from the duodenum acts as (endopeptidase. As long as this enzyme is in pancreas remains inactive by trypsin inhibitor.

2. **Chymotrypsin(-ogen)**: activated by trypsin and acts as endopeptidase.

3. **(Pro-) carboxypeptidase**: activated by trypsin and acts as exopeptidase.

★ From their name they are NOT active enzymes.

★ How we activate them?
Once they reach the duodenum they become active, in duodenum we have an enzyme called **enterokinase** that activate trypsinogen to become trypsin.

(Entero**kinase** phosphorylates trypsinogen once we have that trypsinogen phosphorylated; trypsinogen become trypsin (active), **then trypsin can activate** other enzymes)

★ How can trypsin activate other enzyme? By cutting amino acids.

★ Chymotrypsinogen has longer chain of amino acid after cutting it; chymotrypsinogen becomes chymotrypsin (active).

★ Process of activation takes place **inside** duodenum.

✓ **The importance of oddi sphincter :**

Imagine that these enzymes are released as active enzyme; they will destroy the pancreas (they'll digest the pancreas), so the presence of oddi sphincter prevents these active enzymes -once they're activated in duodenum- from going back toward pancreatic duct and start activation of other enzymes.

✓ **Medical condition : Acute pancreatitis**

- May happen by weakness of odd sphincter
- Result in ***reflux*** from duodenum back toward the duct thus activation of all enzymes within pancreas and destroying it.
- High complication (Patient may die after 6 hours if there is no intervention).
- People who have taken huge amount of alcohol may have weakness of the sphincter.

⇨ So this is the importance of oodi sphincter and the importance of having these enzymes released as inactive enzymes from the pancreas and undergo activation at the level of duodenum.

What is the difference between **endopeptidase** and **exopeptidase**

— we know that protein is a long chain of amino acid

Pepsin is an endopeptidase

☒ **Endopeptidase** can cut somewhere in the middle → trypsin and chymotrypsin (the active form)
☒ **Exopeptidase** removing only one amino acid from the end → carboxypeptidase

—→From the name "carboxypeptidase" → it is removing one amino acid at carboxyl end.
—

—2) Enzyme for digestion of carbohydrates

- We have some cells producing *alpha amylase*.
- Important in digestion of starch.

—3) lipolytic enzyme "Important in digestion of lipid :P "

A. Lipases.
B. Phospholipases.
C. Cholesterol ester hydroxylases.

—In addition, we can have some *co-lipase* which are helping lipase in there activity.

Note from the slide

Lipase that split
- Triglycerides → monglyceride + free fatty acids.
- Their activity requires an oil/water interface, bile salts (secreted by liver) and other co-lipase secreted by the pancreas.

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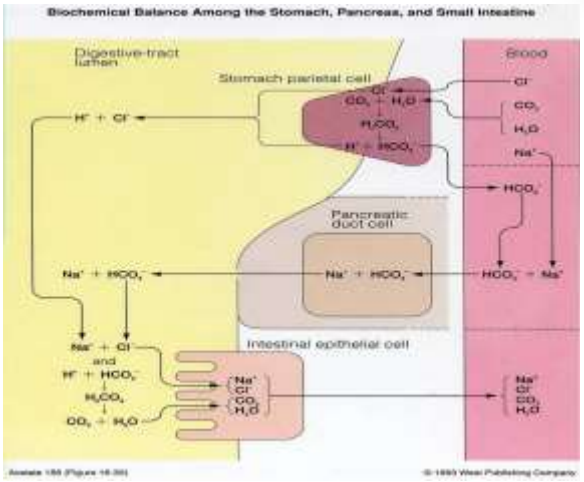
- **Duct cells :**

—Release water and electrolytes (mainly bicarbonate).



—➔ SO, what type of secretion do we have in pancreatic juice?
—Alkaline secretion.

—➔Actually , we need these alkaline secretions because:

i. We need to <u>neutralize</u> the acidic contents of the stomach.
ii. The optimal activity of all these proteolytic enzyme lipases and amylase is at alkaline pH, not acidic.

—➔ We have huge amount of bicarbonate secretion in the duodenum.

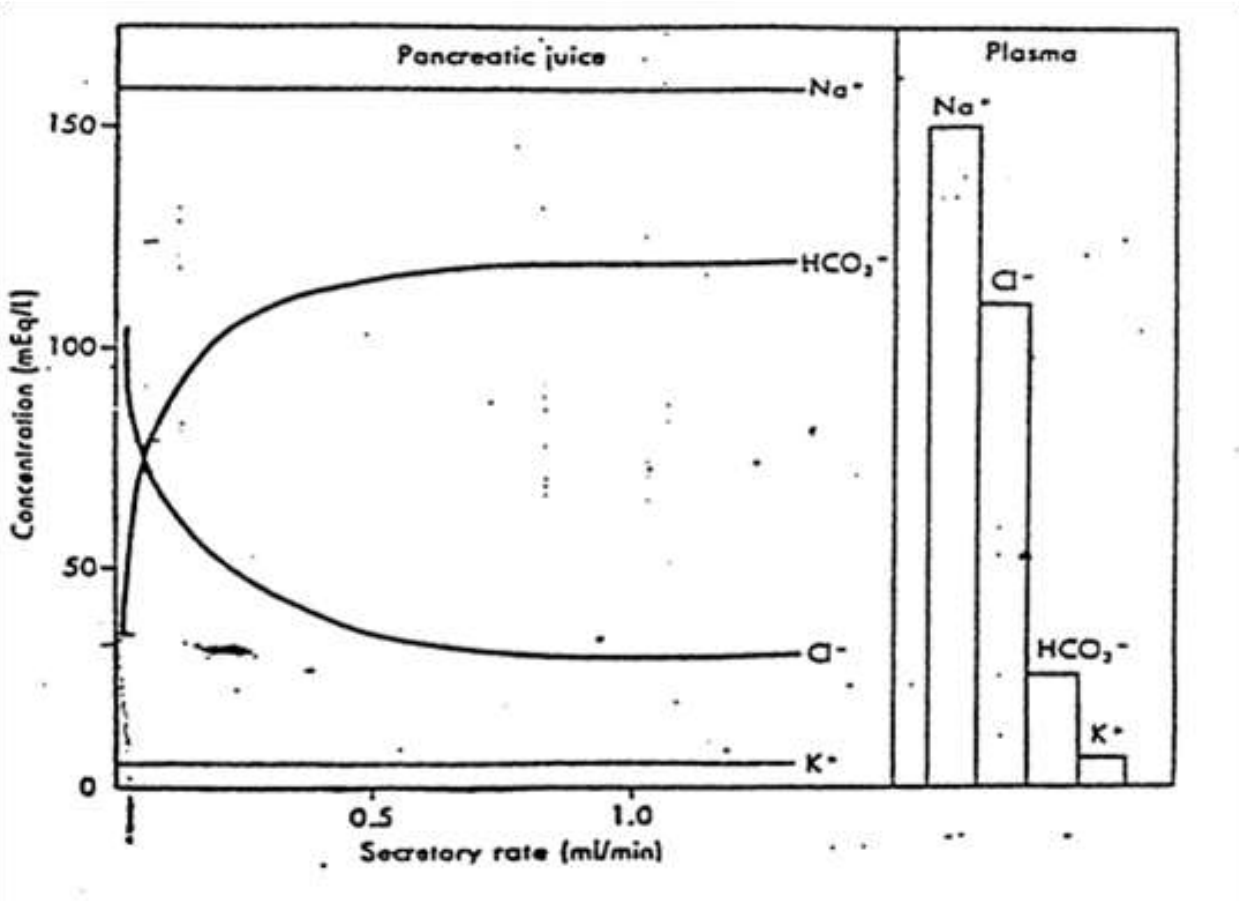
—➔ What the mechanism by which we are getting secretion and formation of bicarbonate?

—We have some complex regarding this point but you will see that the composition of pancreatic juice can change according to the stimulation process. If these cells are stimulated, they will form and secrete more bicarbonate.

- Releasing bicarbonate toward lumen and reabsorbing back hydrogen toward interstitial fluid

- Don't pay much attention to the mechanism by which we are getting bicarbonate release.

— *** composition of pancreatic juice is <u>changed</u> according to <u>stimulation</u>:**



At **low** rate of stimulation

↑ conc. of Cl^-

↓ conc. of HCO_3

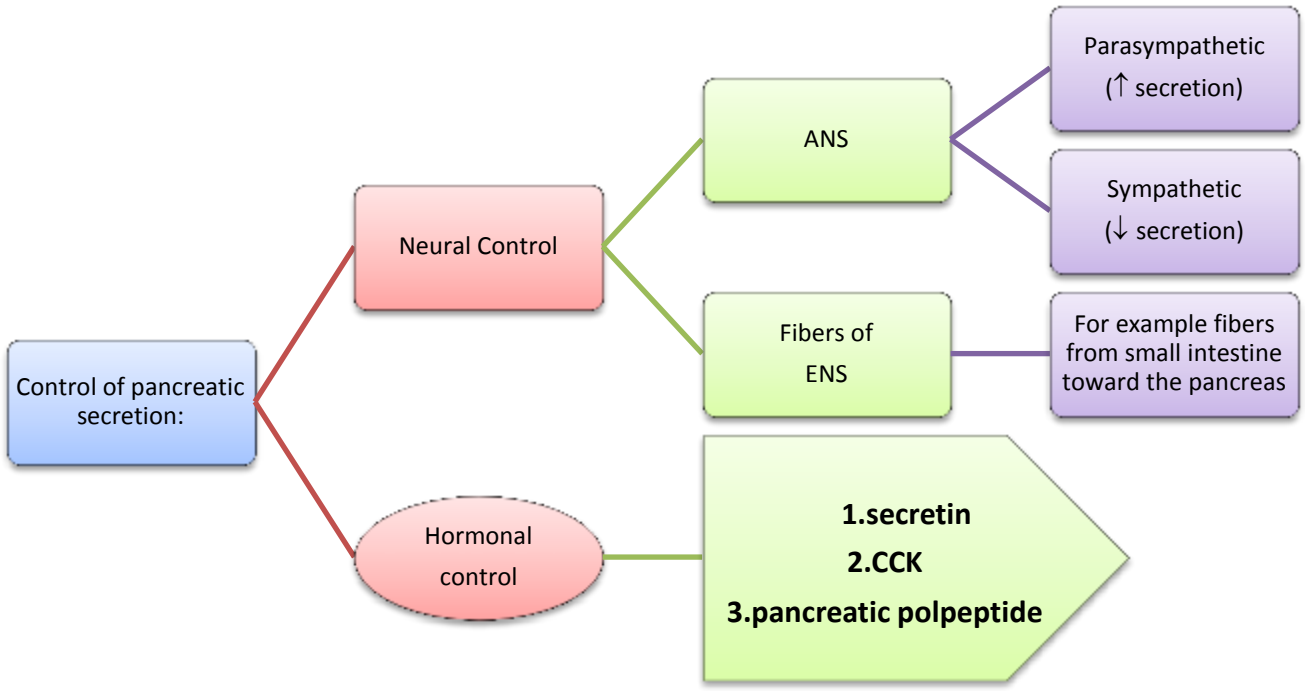
At **high** rate of stimulation

↓ conc. of Cl^-

↑ conc. of HCO_3

- ✓ Chloride is moving according to electrochemical gradient.
- ✓ At any time, the movement of chloride by secretion is favoring reabsorption toward interstitial fluid.

Control of pancreatic secretion:



- ✓ Fibers of ENS : from small intestine going back toward pancreas , could be fibers of :

  - ach
  - VIP
  - GRB (Gastrin Releasing Peptide)

• HORMONAL CONTROL :

o SECRETIN :

★ Secretin is released from some endocrine cells in duodenum.

★ How we stimulate the release of secretin?
  - Stimulation of secretion is by acidic pH.

★ Once the gastric contents enter the duodenum; these cells are activated.

★ Secretin is acting over duct cell to increase their activity, so the secretion of water and electrolyte is increased.

o CCK (CHOLECYSTOKININ)

Complex control →

- CCK-A receptors act on acinar cells (direct control)
- vago-vagal reflex to stimulate enzyme secretions (indirect control by parasympathetic fibers)

☒ another effect for CCK : "effect over oddi sphincter"

CCK causes relaxation of oddi sphincter.... and having flow of pancreatic juice into duodenum.

"CKK has more effects which we'll see when we talk about bile secretions."

o PANCREATIC POLYPEPTIDE:

Pancreatic cell:
- alpha : glucagon
- beta : insulin

→ Released from a type of pancreatic cells.
→ Have inhibitory effect over cells releasing enzymes thus →
→ inhibits the release of enzymes by its inhibitory effect that:

1) Inhibits Ach release from enteric NS. OR
2) Inhibits vagal output of the CNS.

♣ WE CAN SUMMERIZE THE CONTROL OF PANCREATIC SECRETION BY 3 PHASES :

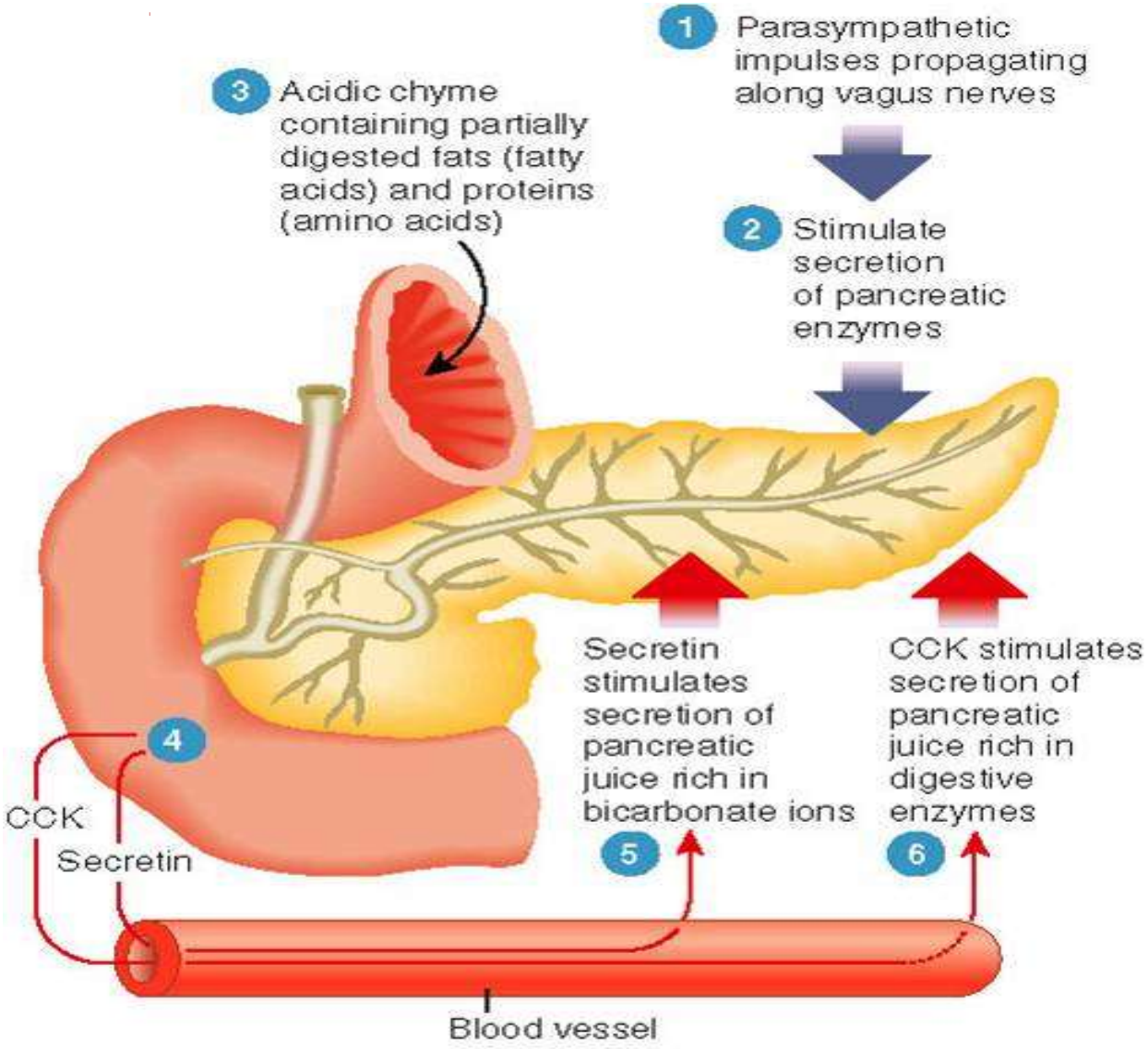
♣ (All of them increase secretions)

1. **Cephalic phase**:
   Increase parasympathetic stimulation → increase pancreatic secretions.
   Sight, smell, taste or hearing. Mediated by vagus.

2. **Gastric phase**:
   Activating parasympathetic fibers → increase pancreatic secretions.
   Distension. Mediated by vagus.

3. **Intestinal phase**:
   We're also increasing pancreatic secretions.
   Amino acids (aa), Fatty acids, H+, Distension.
   Mediated by CCK, secretin, enteropancreatic reflexes, other hormones

♣ When we finish intestinal phase, we are reducing pancreatic secretions and activities.



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— What is the stimulus for CCK release? Presence of fat in duodenum. I have content that stimulate the cells that release CKK thus more activation and release of enzymes. Once you have finished the intestinal phase → the content is in the lower part (ileum for eg.) → decrease pancreatic secretions.

Liver Secretions

— Liver has a lot of function functions, the dr. will focus on specific functions. (there is a lot of functions in the slide , the dr. will not ask questions about them)

—

—**Bile secretion** is important in lipid digestion and absorption.

- Bile acts as detergent to emulsify lipids and make them soluble.

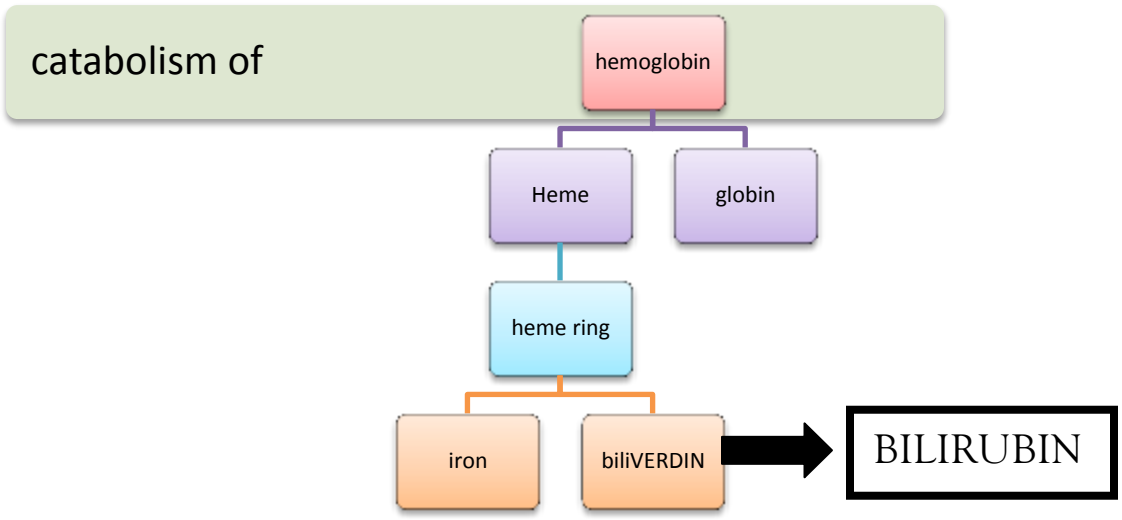
☒ **Bile is composed of:**

1. bile salts
2. water
3. electrolytes
4. cholesterol
5. phospholipids
6. Wastes intended for excretion, (bilirubin).

☒ What we have in bile which is important in the process of absorption and digestion is **bile salts**.

☒ **Bilirubin** is formed by destruction of RBC's.

Excretion of bilirubin in the bile



- The doctor will not ask about these details, but at least we should know that:

- Bilirubin secreted with bile as waste material.
- Bilirubin is taken from blood by destruction of RBC, **conjugated** with (glucoronide , sulfate , and other materials), and then released with bile.

⊙ What is the purpose of this conjugation?
To make it **more hydrosoluble.** Once it becomes more hydrosoluble, bilirubin can be dissolved with **bile** and **intestinal fluid** later on.

➔ One important thing regarding bilirubin: its concentration can be an indicator for hemolytic process in our body.

❖ What happens if we have increased conc. of bilirubin in our blood? **Jaundice** (yellow discoloration of the skin).

High conc. of bilirubin can happen because of:

❶ **Increase** of the destruction of RBC's.
OR
❷ **Decrease** conjugation, or "decrease release from the liver."

★ In labs, there are direct and indirect bilirubin, which may refer to conjugated and unconjugated bilirubin.

- If there is an increase in unconjugated bilirubin in the blood →that means the problem is **before** the liver ➔ high destruction of RBC's.

- In which conditions the conjugated bilirubin is increased? To say that we have increased conjugate bilirubin and we have **Obstruction** of the duct that is collecting the bile and taking this bile toward the duodenum .This obstruction is caused by stones or cancer of pancreatic head which presses these ducts ➔ resulting in an increase in the conjugated bilirubin in the blood.

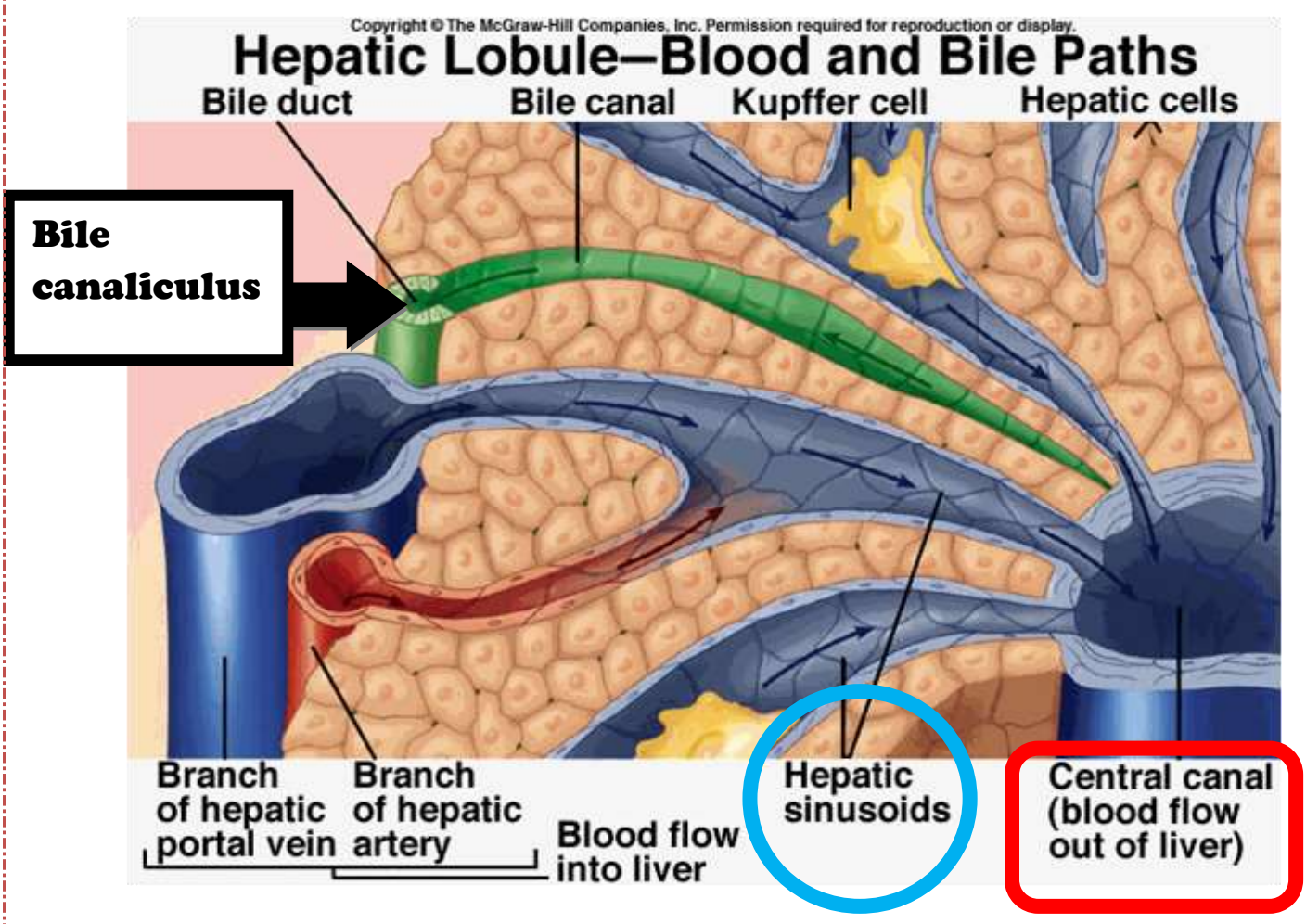
- so the bilirubin has been conjugated, but because of reflux of this bilirubin toward the blood ➔ the amount of conjugated bilirubin increase.

- *Distraction of hepatitis cell,* **hepatitis** for example, causes increase in both conjugated and unconjugated bilirubin.

SO, these are indicators for diagnosing hepatic disease and problems before and after liver.

Functional structure of the liver:

The liver is composed of **hepatic lobules**, which have hexagonal structure.

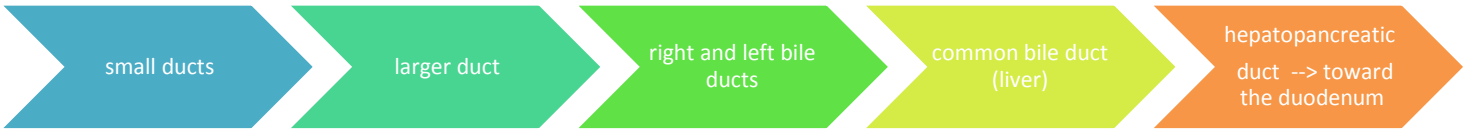


⇨ So the hepatic lobule is the functional structure of the liver with hexagonal structure. At the edges of this lobule, there's a branch of the portal vein which collects blood from small intestine toward the liver.

⇨ In the center of the lobule, there's another type of veins → the central vein.

★ So the blood is flowing from the periphery (edges) toward the center through sinusoids (capillaries).

- bile is collected in:



- From functional view , Each hepatic cell has:
  - one part of membrane facing blood vessel
  - the other part facing bile canaliculus

✓ So at any time these cells can take anything from blood and secrete it with bile.

✓ For example, bilirubin can be taken from blood and secreted into bile canaliculi.

✓ once bilirubin reaches small and large intestines , it can be:

1. Transformed (by bacterial action) into **urobilinogen** which will be reabsorbed and secreted in urine as **(urobilin)**. OR
2. Not reabsorbed back, instead released with feces as **stercobilin.**

THESE DETAILS IS NOT IMPORTANT BECAUSE IT IS BIOCHEMISTRY, BILE SALTS ARE MORE IMPORTANT "WE WILL TAKE IT NEXT LECTURE."

* DON'T mix bilirubin with bile salts.

إن الذين في قمة الجبل لم يسقطوا فجأة من السماء

THE END =)