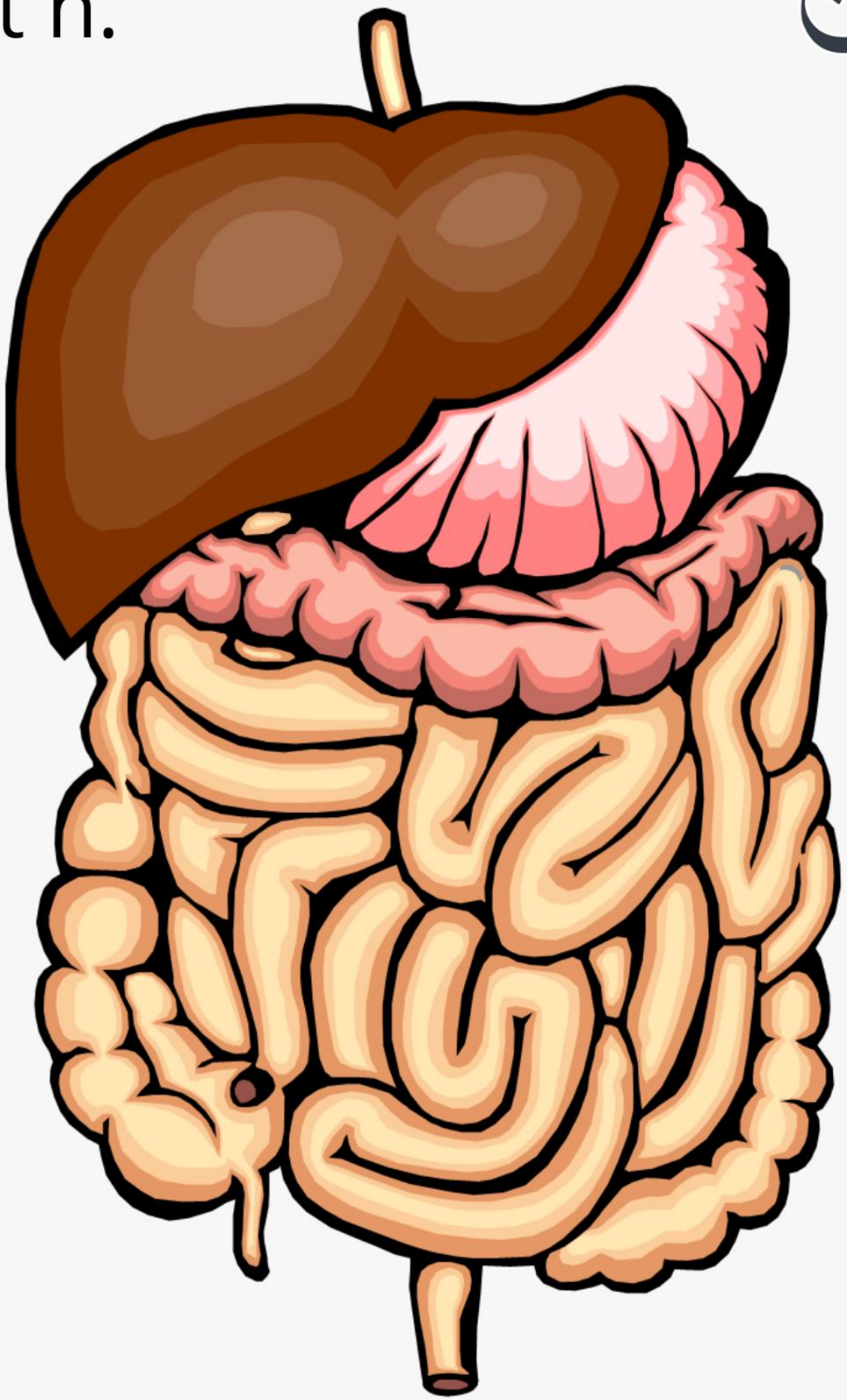
Physiology

Sheet n.



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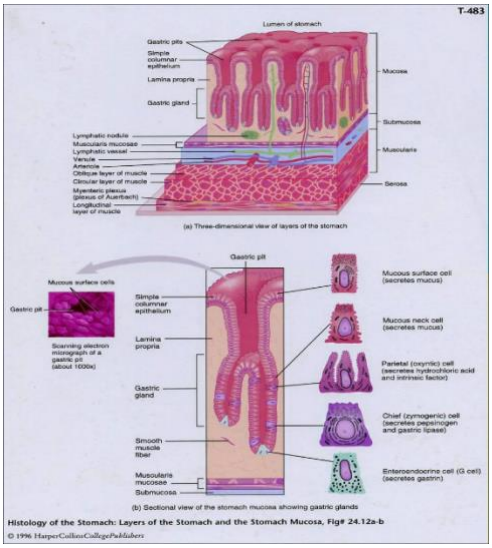
■ Doctor ■ Slides + handout ■ additional info

GASTROINTESTINAL SECRETION:

1. SALIVARY GLANDS SECRETION

2. GASTRIC SECRETION:



1. **Mucus secreting cells**:

line all the stomach surface. These cells secret **viscid mucus** which may have the following **functions**:

- **Lubricating** functions that protect against mechanical injury.

-The secreted mucus **lines the mucosa** prevents proteolytic enzymes to act on the mucosa (protective).

-The secreted mucus has an **alkaline pH** which neutralize HCl and protect the mucosa from the chemical injury caused by HCl

2. **Tubular glands:** check the additional figure on the side.

- Could be called Oxyntic (gastric glands/gastric pits) if they are HCl forming glands or have oxyntic cells.

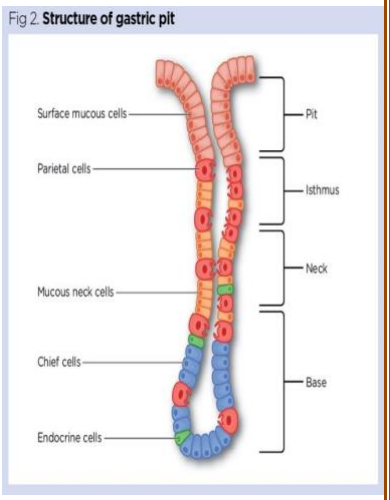
- Secrete HCl, Intrinsic factor and Mucus.

These glands are composed **of 3 types of cells**:

- ***Mucus neck cells***: secrete mucus and some pepsinogen.

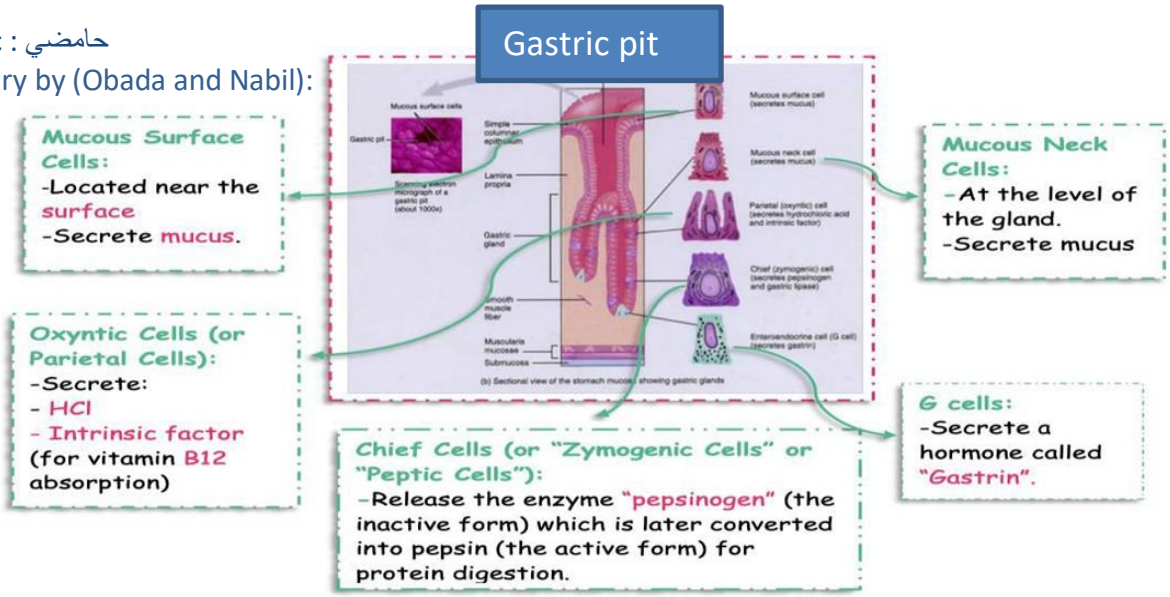
- ***Peptic or chief cells***: secrete large amount of pepsinogen.

- ***Parietal or oxyntic*** cells secrete HCl and intrinsic factor.



Oxyntic : حامضي

Summary by (Obada and Nabil):

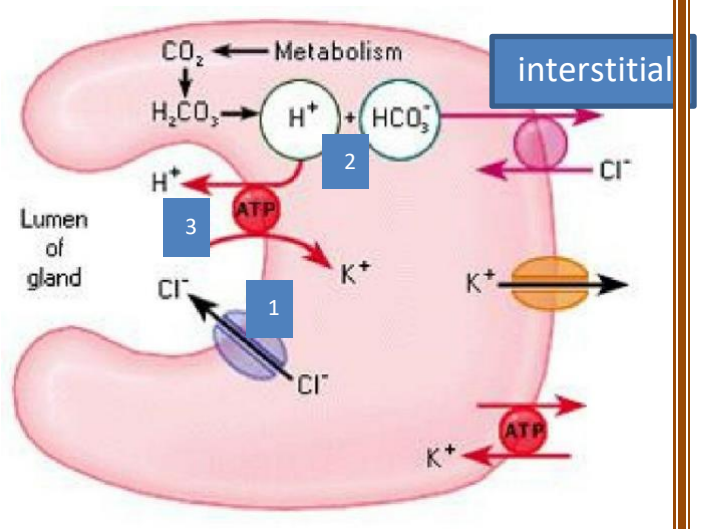


✓ The professor also mentioned another type of cells: D cells, which secrete somatostatin.

HCL SECRETION:

- **What is the mechanism of HCl secretion/ how oxyntic cell is functioning?**

Theory that suggests mechanism of acid secretion by oxyntic (parietal) cells is:



1. **Active secretion of Cl^-** into the canaliculus

- **What results from the continuous active secretion of Cl^-?**
  Developing a potential across the whole cell, which is called transcellular potential, it is more negative towards canaliculi, attracting positive charges from the interstitial fluid, usually attracting *Na^+ that has higher concentrations extracellularly causes negative potential which induces passive diffusion of K^+ and Na^+ (*mainly K^+).

Canaliculus: lumen of the gland

- **what is the source of (H+) protons?**

2. The H^+ is taken from dissociated water during the reaction **catalyzed by carbonic anhydrase**. In the presence of CO_2 and the activity of carbonic anhydrase, HCO_3^- and H^+ are formed.

   The reaction is:

   $H_2O + CO_2 \rightarrow H_2CO_3 \leftrightarrow HCO_3^- + H^+$

- **What is the fate of bicarbonate and protons?**
  HCO_3^- (bicarbonate) is transported toward interstitial fluid in exchange for Cl^-.

3. **Active secretion of H^+ by H^+/K^+ pump into the canaliculus.**

-Active process of Na^+ absorption at this level by Na^+ pump.

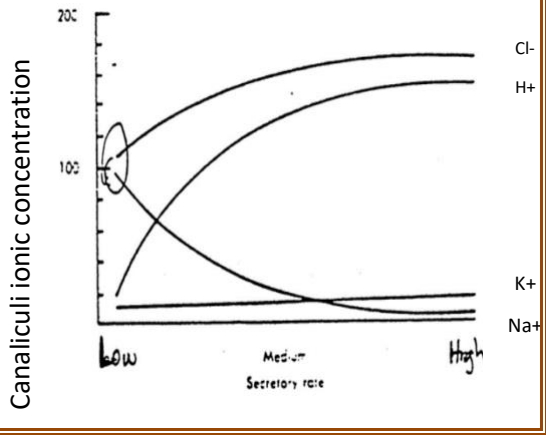
The net reactions that result in HCl secretion is: H2O + CO2 + NaCl → NaHCO3 (blood) and HCl (lumen)

- **What happens when proton pump inhibitors PPI are used?**
  The secretion of HCL is inhibited.

4. **Water is transported into the canaliculus by osmosis.**

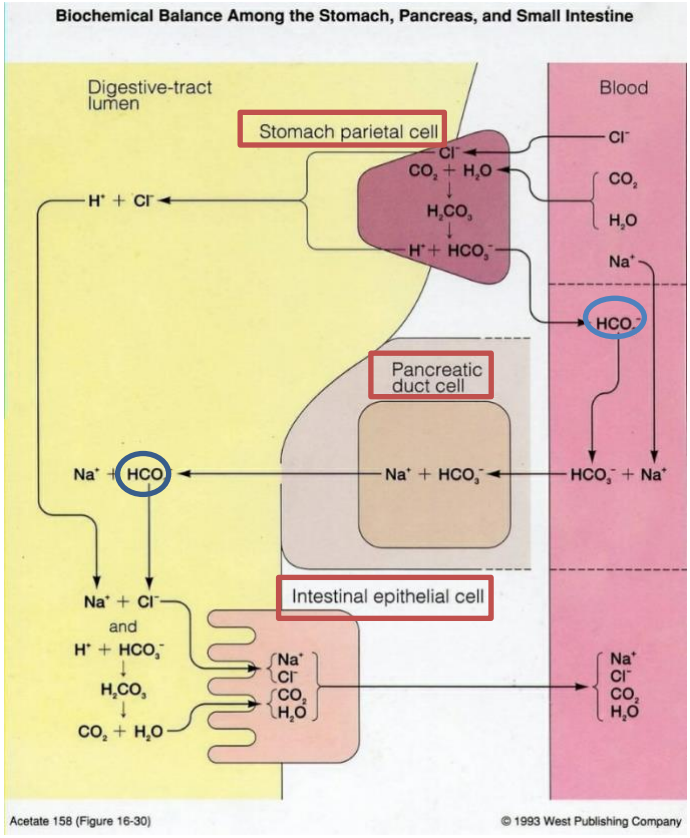
- The whole secretion process is a stimulated process, **what do you expect to have as secretion when there is no stimulation?**

  <u>At rest and at low levels of stimulation usually NaCl is secreted</u> <u>and during high rates of stimulation there is HCl secretion.</u>



Check the difference between the oxyntic cells and other types of cells which secrete bicarbonate HCO3 (like pancreatic duct cells)–:

Pancreatic cells secrete HCO_3^- towards lumen while the oxyntic cell secretes HCO_3^- towards interstitial.



- The potential difference across the cell is about –70mV at rest and drops to about (-30 mV) during stimulation Concentration of H+ [H+] in canaliculus is about 3 million times that in blood which results in a decreased pH during gastric secretions.
- This process needs ATP for H+ pump activity.
- **What is the function of hydrochloric acid (HCL)?**

  Importance of HCl:

  1. HCl does not usually digest anything, but it is important in the **conversion of the proteolytic enzyme pepsinogen into Pepsin** (active form of enzyme with proteolytic activity).
  2. Helps in **decomposition of connective tissue**.
  3. Helps in **defense** by killing most microorganisms ingested with food.

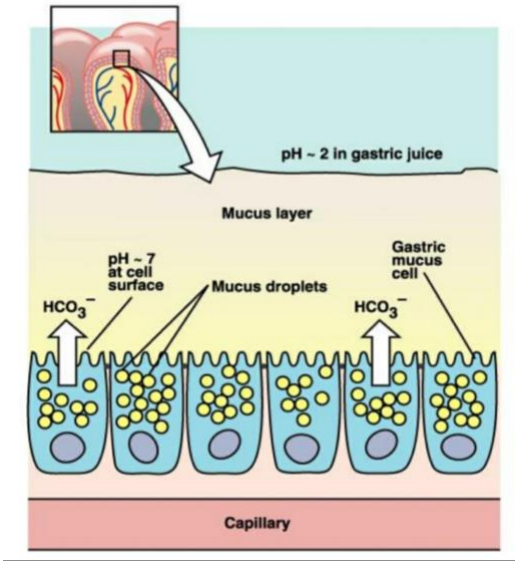
PEPSINOGEN SECRETION:

- **What is the difference between pepsin and pepsinogen?**
  Pepsinogen is secreted by peptic (chief) and *mucus cells. When secreted, it is inactive. The active form of pepsinogen is ***pepsin***: which is an active proteolytic enzyme with an **optimal activity at acidic pH (1.8-3.5).**
- ***The bulk secretion of pepsin is from?**
  Chief (peptic) cells

- **What is the function of pepsin?**
  Importance of Pepsin: - helps in cleaving longer polypeptides into smaller peptides.(incomplete digestion of proteins)
- **Recall: What is the function of stomach?**
  Storage, mixing with secretions to form chyme, grinding (mechanical digestion), note it just starts the digestion, it is not the main function, the real digestion is the chemical one in the intestine.

MUCUS SECRETING CELLS

- **what is the importance of mucus secreting cells?**
  Check the figure: secreting the mucus will create a barrier between the lumen of the stomach and the tissue Function:
  - Lubricating functions.
  - **Protect the mucosa** from the chemical **injury by:**
    - ✓ Preventing the activity of the proteolytic enzymes (pepsin) to act on the mucosa.
    - ✓ Neutralizing HCl by its alkaline character.



GASTRIN SECRETION

- **What stimulates the secretion of gastrin?**
  secreted by G cells of the pyloric glands into blood.

  stimulated by: (local changes)
  - gastric distention.
  - presence of proteins in chyme.
  - vagal stimulation. (parasympathetic, rest and digest)

  !! Functions: This hormone acts on the body of the stomach to
  - **Increase HCl and pepsinogen secretion.**
  - **trophic effect on gastric mucosa to maintain growth of mucosal cells.**

    trophic means keeping survival of mucosal cells as it exposed to highly acidic destroying environment.

Pyloric glands:

- **Contain Mucus cells and G cells that secret Gastrin.**
- **The mucus secreting cells are similar to mucus neck cells of the gastric glands.**

SECRETION OF INTRINSIC FACTOR

It is secreted by parietal cells (oxyntic cells).

This factor is essential for B12 absorption.

- **How does gastric atrophy contribute to the development of anemia?**

In the defective production of intrinsic factor such as in gastric mucosal atrophy, causes pernicious anemia with failure of RBC maturation may occur.

• REGULATION OF GASTRIC SECRETIONS:

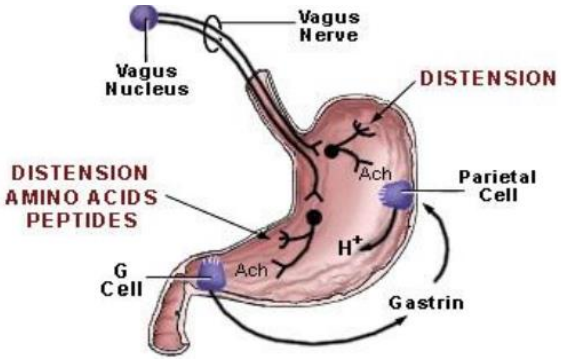
Regulation of HCl secretion: (neural, hormonal, paracrine, feedback)

1. Neural:

- **ENS**

Ach neurons → parietal and peptic cells.

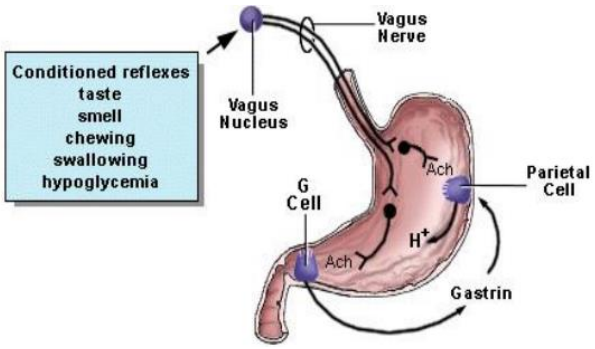
Enteric Nervous System: can control by **direct** stimulation of parietal cells and peptic cells. The effect is mediated by Ach.



- **ANS (Parasympathetic):**

By local changes or long reflexes to activate gastric secretions, it can act directly, it also Acts indirectly by activation of enteric neurons (ENS).

vagal activation during cephalic and gastric phases (via long arc reflex) **activate:**



◊ **enteric excitatory** neurons to →release **Ach.** → muscarinic receptors

◊ **enteric neurons** that innervate→ **enterochromaffin-like cells** in the stomach to →secrete **Histamine.** →*It can also activate paracrine control.

◊ **enteric neurons** that secrete **GRP**→ (gastrin releasing peptide)→ that acts on G cells →to cause secretion of **Gastrin.** → **gastric secretion**

2. Hormonal control:

- Gastrin:

secreted from G cells **into the blood** and acts on parietal cells to increase HCl secretion.

The release is stimulated by gastric distention, presence of proteins in chyme and vagal stimulation.

- **Through which receptor does gastrin affect HCl secretion?**

!! This hormone **acts on a receptor at parietal cells known as CCK-B receptor to** increase the intracellular Ca^{+2} and **activation of oxyntic cells to secrete HCl.**

A hormone called CCK is released by the intestine in the intestinal phase of digestion. **This receptor can also be activated to a lesser extent/** stimulation **by CCK (cholecystokinin).**it reduces the effects of gastrin.

Gastrin →activates CCK-B receptor → higher stimulation → induces the gastric secretion.

CCK → activates CCK-B receptor →prevents the effects of gastrin→ lesser stimulation → prevents the gastric secretion.

gastrin and cholecystokinin (CCK) can compete for the same receptor, specifically the CCK-B receptor, Gastrin primarily regulates gastric acid secretion and mucosal growth, while CCK's actions are more focused on pancreatic and biliary functions. However, they may still have overlapping effects in certain contexts, and competition for the CCK-B receptor may occur, particularly in conditions where both hormones are present in elevated concentrations.

3. Paracrine:

- **What is the meaning of paracrine?**

In paracrine signaling, the signaling molecules are released by one cell and affect neighboring cells within a short range of the secreting cell without circulating in blood.

  - Histamine: secreted by enterochromaffin-like cells in response to vagal stimulation and local inflammation.

- **Through which receptor does histamine affect HCl secretion?**

  Diffuses in the extracellular space and activates parietal **cells via H2 receptor (histamine type receptors 2)** by increasing c-AMP as a second messenger.

  Net effect = increase HCl secretion

- **What is the effect of H2 blockers, and could you mention alternative methods that produce a similar effect?**

> ***Note:*** Some antihistaminic drugs that block H2 receptors such as Cimetidine reduces acid secretions.

- or inhibition of proton pump by PPI

- Somatostatin (SS):

it is a hormone; at the level of stomach it acts through a paracrine control

released from paracrine cells in the mucosa and acts on SS receptors of parietal cells to decrease cAMP.

Net effect → decrease HCl secretion.

4.*Role of HCl in controlling secretion*

3. HCl acts indirectly by initiating **enteric reflexes** that causes an increase in pepsinogen secretion by peptic cell.

> ***Note***: Excess of acids causes feed back inhibition of gastric secretions by 2 ways:
>
> - Reduction of gastrin release
> - Initiation of inhibitory reflexes.
>
> As a result, this will maintain pH NOT to fall below 3.

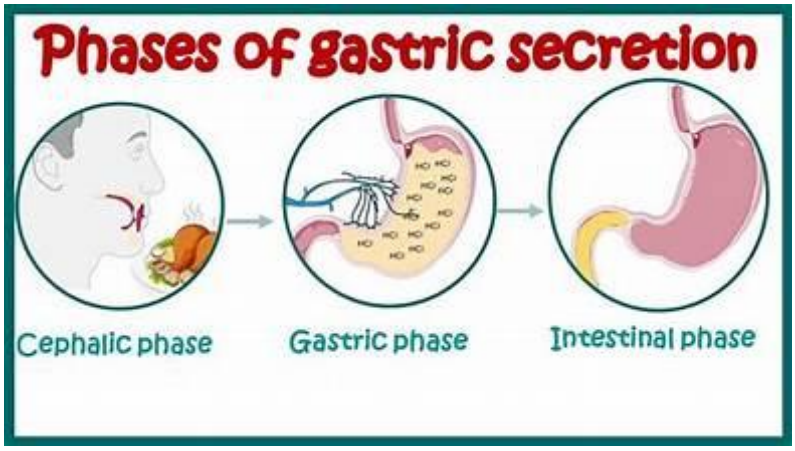
4. **Regulation of pepsinogen secretion**:

Ach, Gastrin, HCl: HCl acts indirectly by initiating enteric reflexes that causes an increase in pepsinogen secretion by peptic cell.

SUMMARY OF CONTROL

• Cephalic phase • Gastric phase • Intestinal phase

Additional figure:



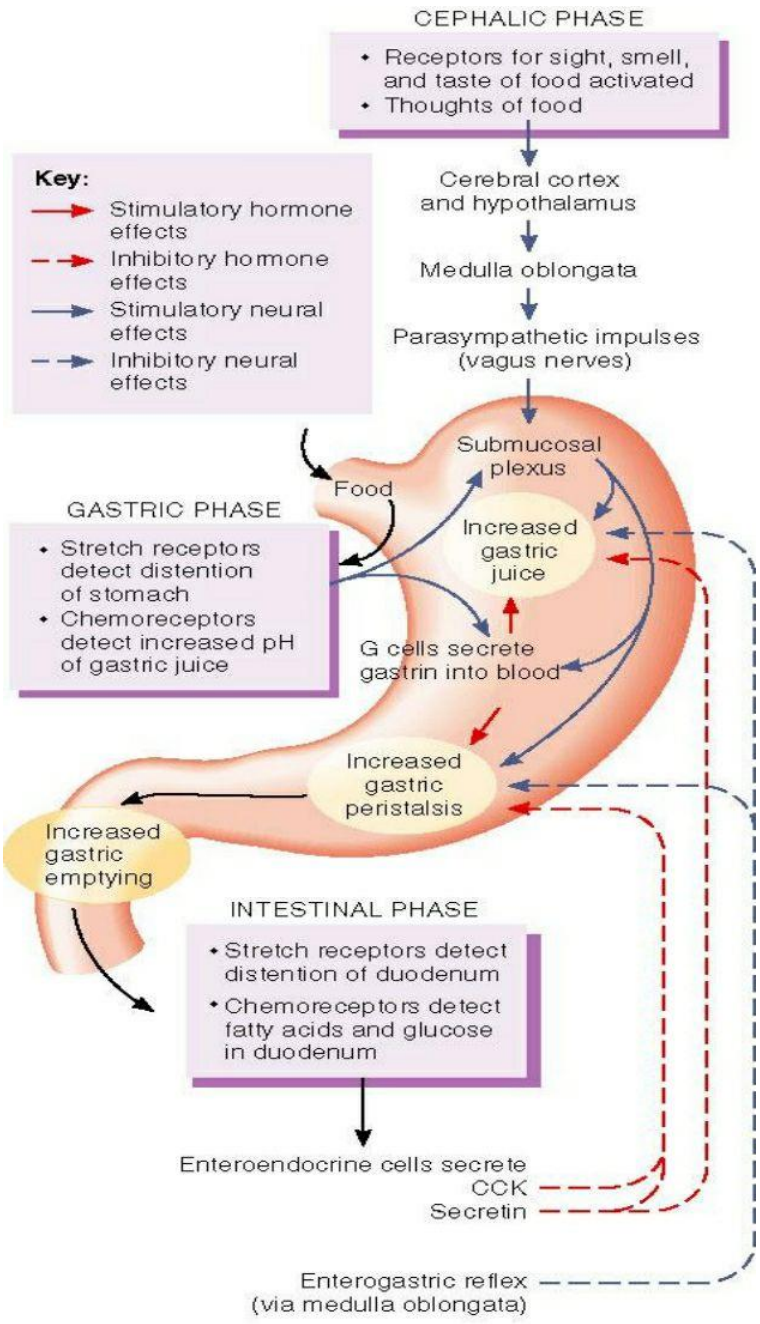
3 PHASES OF CONTROL OF GASTRIC SECRETIONS: -

1-Cephalic phase:

- by thinking about, smelling, tasting, chewing or swallowing. In this phase vagal stimulation is involved. These acting **before food the stomach reaching to stimulate parietal cells and G cells.**
- **<u>via parasympathetic ANS</u>**

2- Gastric phase:

- Acts when **food reaches the stomach to cause maximal stimulation of gastric secretions.**
- **Distension and the presence of proteins in food stimulates local reflexes and long reflexes which results in increased gastric secretion.**
- **Caffeine and alcohol also stimulate acid secretions even no food is present in the stomach.**
- **<u>via ENS, ANS and Hormones, paracrine</u>**



24.14

3- Intestinal phase:

- **why there is a slightly stimulation at the beginning of the intestinal phase?**
  - **Excitatory:** Distension of the upper portion of the duodenum can **slightly stimulate** gastric secretions. This effect is probably by the release of gastrin from the G cells in the duodenum.
- **What is the bulk effect of the intestinal phase on the gastric secretion?**
  - **<u>Inhibitory:</u>** the presence of chyme in intestine usually inhibits gastric secretions. The presence of food and acids in duodenum initiates neural reflexes (enterogastric reflex) and <u>causes the release of hormones (GIP, CCK, secretin, enterogastrone). These hormones inhibit acid secretions.</u>

YOU CAN SKIP

These 2 terms have been repeated many times, you rather know them!!

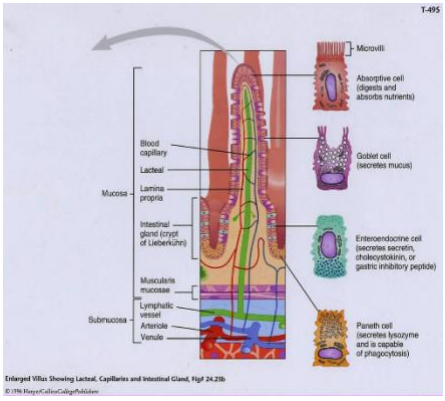
Long Reflexes/ extrinsic	Short Reflexes:/local /intrinsic
▪ Involve communication between distant parts of the nervous system. ▪ Sensory input is transmitted to the central nervous system (CNS) for processing. ▪ Responses may affect distant organs or tissues. ▪ Examples include reflexes involved in homeostatic regulation, such as heart rate or blood pressure regulation.	▪ Occur entirely within a specific organ or tissue. ▪ Sensory input is processed locally without involving the CNS. ▪ Responses are localized to the area where the sensory input was received. ▪ Examples include reflexes within the gastrointestinal tract, such as peristalsis or local secretion in response to stimuli.
▪ both short and long reflexes can interact with the Enteric Nervous System (ENS) and the Autonomic Nervous System (ANS) to regulate various physiological functions, particularly within the gastrointestinal tract and in homeostatic control systems	

3. INTESTINAL SECRETIONS

SMALL INTESTINAL SECRETION

(1500ml/day)

- **What type of secretions are produced by the small intestines?**
  - Cells of mucosal epithelium secrete mucus, water and electrolytes.
  - Tubular glands in submucosa of duodenum (duodenal glands). These invaginations of epithelium known as **crypts of Leiberkuhn** which empty into the lumen of duodenum. These glands secrete **serous secretion mainly.**



The doctor said the he wont ask about the histology of intestinal glands shown in the figure nor about amounts of secretions

REGULATION:

- **Neural**

How secretions are controlled by VIP?

- ENS: Local **neural mechanisms** that activates secretions is mediated by Ach and **VIP** (vasoactive intestinal peptide) neurons , increasing the vasodilation increases the availability of fluids for secretion.
- ANS

- **Hormonal**

What is the primary hormone responsible for regulating small intestines secretions?

- **Secretin: increases duodenal and pancreatic secretion**. This is an important factor to neutralize the acid delivered into the duodenum from the stomach, it also has inhibitory effects on the stomach.

COLONIC SECRETION:

- **What type of secretions does colon secrete compared to the small intestines?**

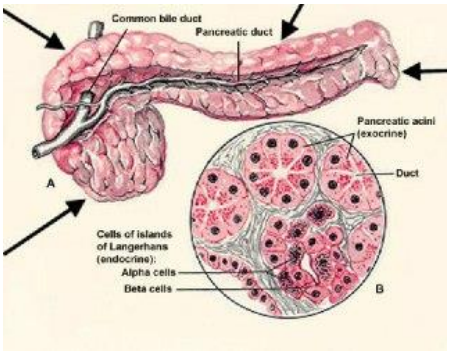
- Mostly mucus secretion.

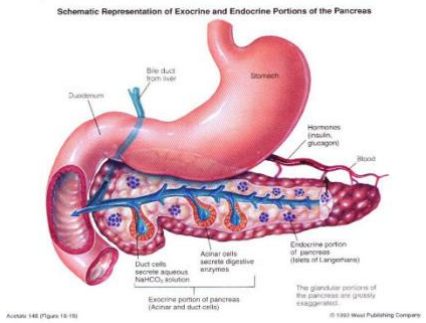
- Small amount of serous secretions which is rich in K+ and HCO3-.

PANCREATIC SECRETION:

(1-2L/day)

FUNCTIONAL ANATOMY:





What is the difference between exocrine and endocrine?

Endocrine → release into blood. Exocrine → release through duct

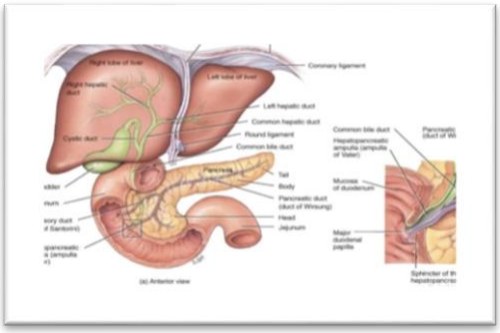
1. **Endocrine portion**:

Islets of Langherhans secrete insulin, glucagon, somatostatin, and pancreatic polypeptide **release into the blood.**

2. **Exocrine portion:**

pancreas has a similar structure of salivary glands however there are some differences, Compare the acinar and duct cells in the pancreas and salivary:

salivary glands:
acinar cells: Secretion of water and electrolytes and proteins.
duct cells: flow of saliva through the ducts + changing the ionic composition of saliva.

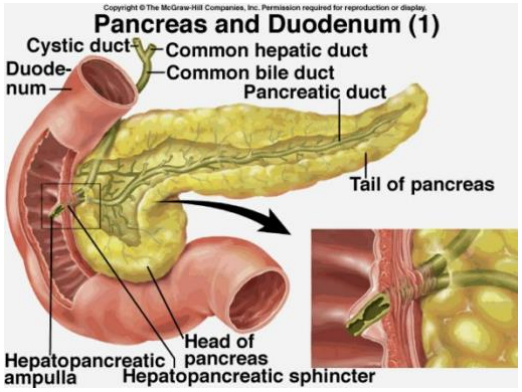


PANCREAS:

- Enzymes: secreted from **acinar cells**
- Water, electrolytes and bicarbonate are secreted by **duct cells.**

These are **secreted into the duodenum via pancreatic duct** and common bile duct. Which empty at ampulla of Vater through **sphincter of Oddi**. The net pancreatic secretion is high in enzymes and is hypotonic and alkaline.

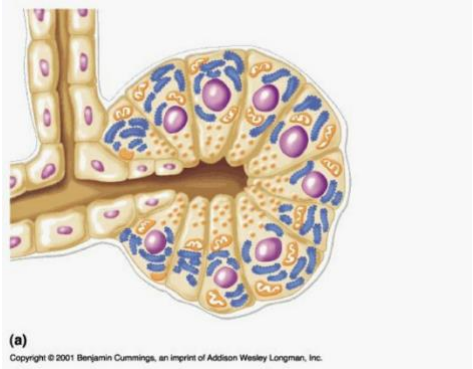
- **What is the functional importance of Oddi sphincter?**



It prevents the reflux of duodenal content back to duct system. Hint: proteolytic enzymes next page

ENZYME SECRETION BY ACINAR CELLS

Check the figure



The acinar cells are filled with vesicles which are important for the secretion of proteins (enzymes), while the duct cells don't have vesicles as they are specialized in secreting water and electrolytes.

Secretion of Pancreatic enzymes:

Pancreatic enzymes are synthesized by acinar cells and stored in **zymogen** granules. The proteolytic enzymes are **stored as inactive**

enzymes and become **activated in the duodenum**

- **Proteolytic enzymes:** all of them are released as inactive enzymes from acinar cells, **Describe the activation process for each enzyme?**
  - ✓ **Trypsinogen (unactivated trypsin): activated by enterokinase** from the duodenum (become trypsin). Trypsin acts as an **endopeptidase**. As long as it is in pancreas, Trypsinogen remains inactive by trypsin inhibitor**.**

    it activates other enzymes by cutting the peptide in a specific point.
  - ✓ **Chymotrypsin(ogen):** activated by trypsin and acts as an endopeptidase.
  - ✓ **(Pro) carboxypeptidase:** activated by trypsin and acts as exopeptidase.

- **What happens if they are released in the active form from the beginning?**
  Hint: the importance of the Oddi sphincter
  They would destroy the pancreas as the reflux of these active enzymes mainly trypsin toward the duct system activates other enzymes destroying pancreas. acute pancreatitis could happen in alcoholic persons due the relaxation / weakness of Oddi sphincter.

- **Pancreatic Amylase: Enzyme for Digestion of Carbohydrates,**

  <u>secreted in an active form</u> to convert polysaccharide into disaccharide.

- **Lipolytic enzymes:**
  - ✓ **Lipase: esterase that splits triglycerides into→ monoglyceride and free fatty acids.**

    Their activity requires an oil/water interface, bile salts (secreted by liver) and other co-lipase secreted by the pancreas.
  - ✓ **Phospholipase.**
  - ✓ **Cholesterol ester hydroxylase.**

> ***Note:*** Pancreatic insufficiency (characterized by decreased enzyme secretion) is manifested as steatorrhea (yellowish stool due to the presence of undigested fat).

V2 :figure was added to page 12