L2

Stomach & Regulation of Gastric Secretion

GNT Physiology

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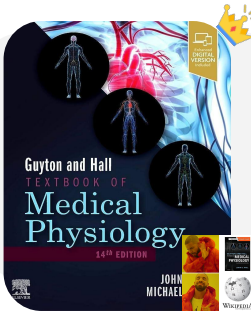
Editing File

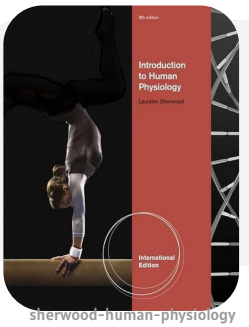
Objectives

- Discuss the role of the stomach in digestion.
- Enumerate the functions of the stomach
- Discuss the secretory functions of the stomach:
  - What are the glands lining the stomach wall.
  - Discuss the cells lining the different glands and their specific secretions.
  - Discuss the mechanism of HCl secretion by parietal cells.
  - Discuss control mechanisms of gastric secretions.
  - Enumerate and discuss the phases of gastric secretion.
- Describe the different motility patterns in the stomach and their role in digestion.
- Describe the mechanism of stomach emptying and discuss the factors controlling it.
- Discuss the role of the stomach in digesting the main food constituents.
- Discuss the pathophysiologic basis of peptic ulcer and gastritis.

Resources

Only GI chapters included





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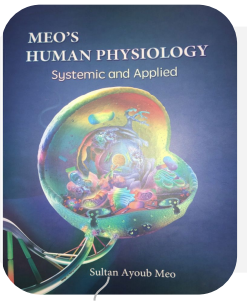


This is prof sultan meo!

Click here for a helpful channel by the team!

Summary of this Lecture will be in the channel soon..

وَاذْكُر رَّبَّكَ فِي نَفْسِكَ تَضَرُّعًا وَخِيفَةً وَدُونَ الْجَهْرِ مِنَ الْقَوْلِ بِالْغُدُوِّ وَالْآصَالِ وَلَا تَكُن مِّنَ الْغَافِلِينَ (٢٠٥)

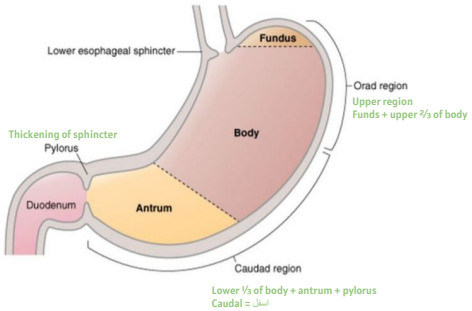
الذكر لله تعالى يكون بالقلب، ويكون باللسان، ويكون بهما، وهو أكمل أنواع الذكر وأحواله، فأمر الله عبده ورسوله محمدا أصلا وغيره تبعا، بذكر ربه في نفسه، أي: مخلصا خاليا. تَضَرُّعًا أي: متضرعا بلسانك، مكررا لأنواع الذكر، وَخِيفَةً في قلبك بأن تكون خائفا من الله، وَجِلَ القلب منه، خوفا أن يكون عملك غير مقبول، وعلامة الخوف أن يسعى ويجتهد في تكميل العمل وإصلاحه، والنصح به. وَدُونَ الجَهْرِ مِنَ القَوْلِ أي: كن متوسطا، لا تجهر بصلاتك، ولا تخافت بها، وابتغ بين ذلك سبيلا. بالْغُدُوِّ أول النهار وَالآصال آخره، وهذان الوقتان لذكر الله فيهما مزية وفضيلة على غيرهما. وَلا تَكُنْ مِنَ الْغَافِلِينَ الذين نسوا الله فأنساهم أنفسهم، فإنهم حرموا خير الدنيا والآخرة، وأعرضوا عمن كل السعادة والفوز في ذكره وعبوديته، فإن الله لا يستجيب دعاء من قلب غافل لاه.

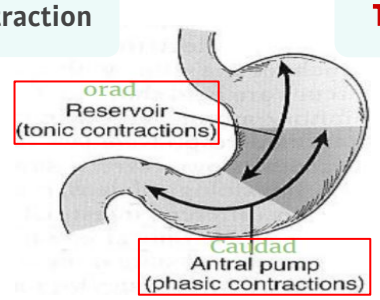
-تفسير السعدي

Introduction & Anatomy of stomach

Stomach

- **Anatomically**
  - [1] Fundus
  - Body
  - Antrum
- **Physiologically** [2]
  2 functional parts
  - **Caudad (Antral Pump)** antrum plus lower third of the body. **Caudad** :near legs
    - **Phasic** contraction
  - **Orad (Reservoir)** fundus and upper two thirds of the body. **Orad**:near head
    - **Tonic** contraction

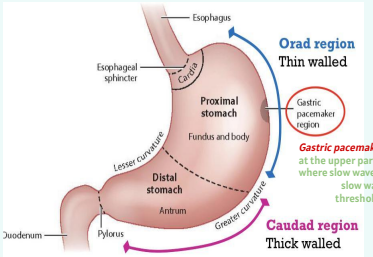




Gastric Muscle Wall

Female slides

- Gastric muscle wall is made of 3 layers:
  1. **Outer** longitudinal
  2. **Middle** circular
  3. **Inner** oblique
- **Thickness of muscle layer increases as we move from proximal to distal regions.**

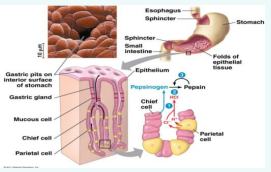


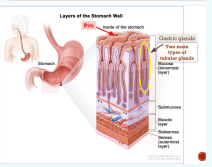
Gastric pacemaker region is located at the upper part of body. This is where slow waves are generated. slow wave more toward تطلع threshold cause contraction

Gastric mucosa

Female slides

- Gastric mucosa is formed of **columnar epithelium** that is folded into "pits".
- **The pits are the opening** of gastric glands.
- There are several types of gastric glands in the stomach and are distributed differentially in the stomach.





Role of pylorus

Female slides

- It is **slightly tonically contracted** almost all the time **"pyloric sphincter".**
- It is usually open enough to **allow water & fluids to pass.**
- It is controlled by nervous and hormonal reflexes from the stomach and duodenum.

General motor Functions of the Stomach

Important

1. Storage of large quantities of food
2. Preparing the chyme for digestion in the small intestine
3. Absorption of water and lipid-soluble substances (alcohol and drugs)
4. Regulate emptying of the chyme from the stomach into the small intestine.

Our second stop in our journey with the burger is the **stomach**
The burger that reached the stomach is no longer a burger It is called **"food bolus"** [5]

I: Upper part elevated after the junction of esophagus.
2: Cause of this division ? The function different in the 2 parts
3: Thickness is more in antrum than fundus -> Contraction is strongest at antrum
4: Mucous layer extremely thick because the wall of stomach is folded —>it form gastric gland and there is a pit in the surface of stomach مثل الحفر this pit hide in the depth of gastric gland, this gland lined by all epithelial cell that will secrete secretion done by stomach
5: How stomach deal with this food bolus? Transform it into something that intestine can handle with it

Gastric Glands

	Cell lining	Secretions	Location
Cardiac glands	-	Mucus,HCO3	Cardia
Oxyntic (gastric or parietal) glands "upper ¾of stomach, constituted 80% of gland in the stomach"	-Mucus (neck) cells -Peptic (Chief) cells **-Parietal cells** (Oxyntic cells)	HCl ,Pepsinogen, IF, Mucus	Body & fundus (above the notch)
Pyloric glands Lower part Antrum + Pylorus constituted 20% of stomach gland Minly 2 type of cell but there is other cells	Many G cells	Gastrin ,Mucus	Antrum (below the notch)

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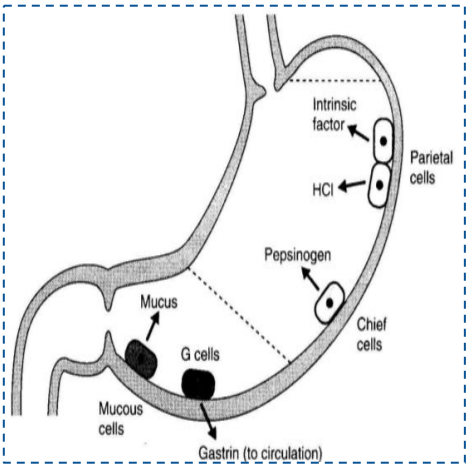
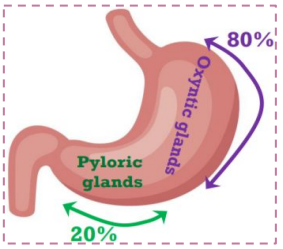
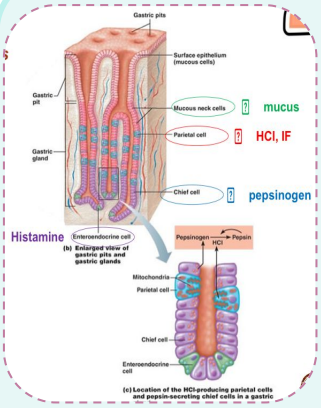




-From previous table, we can conclude that **Chief cells (peptic cells)**, they are available in oxyntic glands and <u>few in pyloric glands.</u> as well as , parietal cells.
-Oxyntic glands are <u>the most abundant gastric glands</u> found in fundus and corpus (body).

Types of cells present in the Gastric Glands

Cell	Secretions	Location
Oxyntic (parietal) cell	**HCl & IF (intrinsic factor)**	Body (most distinctive cells in stomach)
Peptic (chief) cell	**Pepsinogen**	Body
Mucus (neck) cells top part of the surface	**Mucus, HCO3-** Function:protection	antrum
Enteroendocrine Or Enterochromaffin -like cells	**Histamine**	-
G cells	**Gastrin (increases HCl secretion from Parietal cells)**	antrum
D Cells (decreases HCl secretion)	**Somatostatin**	



There is a deep pit lining with epithelial cells but each epithelial cell specific and have certain function

I: Med442: Every gland has a neck and a base.
Mucus cells are found in the neck region of glands. They neutralize acidity and **protect** the wall of stomach.
Mucus is secreted throughout the whole stomach.
2: protect BI2 by bind to it to go to terminal ileum where it go to be absorbed
3:Med442:The only cell that releases HCL in the body is the oxyntic cell.
4: play important role in regulate HCL secretion
5: should be released in circulation to be activated

Gastric Glands

1 Structure of Oxyntic gland

- **HCl is secreted across the parietal cell microvillar membrane and flows out of the intracellular canaliculi into the oxyntic gland lumen.**
- **The surface mucous cells line the entire surface of the gastric mucosa and the openings of the cardiac, pyloric, and oxyntic glands.**
- **These cells secrete mucus and HCO – to protect the gastric surface from the acidic environment of the stomach.**
- **The distinguishing characteristic of a surface mucous cell is the presence of numerous mucus granules at its apex.**

Figure 1 Figure 2

2 Structure of Pyloric gland

- Med442: There are no chief cells or parietal cells in the pyloric region.
- Med442: Mucus secreting cells are near the neck region.
- Med442: Deeper within the gland, there are G cells which secrete gastrin.

Figure 3

3 Structure of parietal cells

- Med442 :HCL is secreted by parietal cells into canaliculus, then it flows into the lumen of the stomach through the opening. Canaliculus=(قناة)
- Female doctor : inactive cell the canaliculi system اخف hidden , when it got activated يزيد
- Active parietal cell have : - Apical side: side that face lumen of stomach arrange into canaliculi Basolateral side: side that face blood

Figure 4

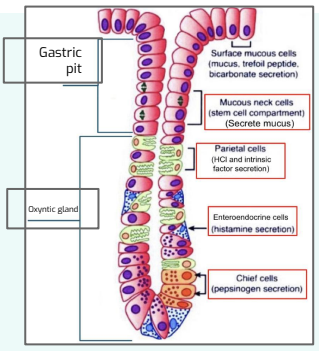


Figure 1

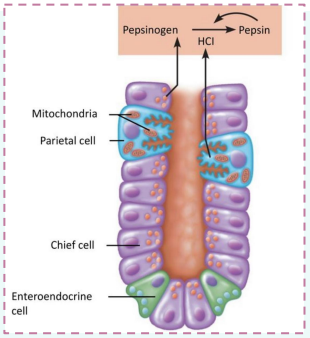


Figure 2

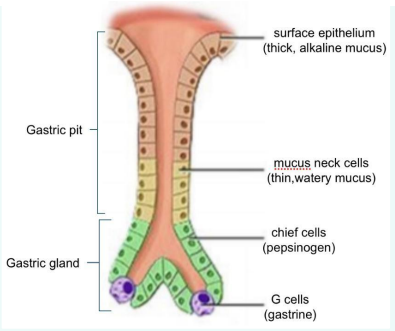


Figure 3

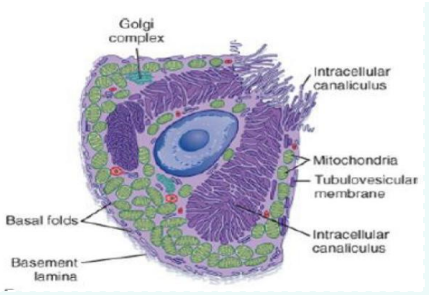


Figure 4

Gastric juice is composed of:

Male slides

- **HCL**
- **Electrolytes**
- **Mucus** (mucus gel layer)
- **Pepsinogen**
- **Intrinsic**

Mechanism of HCl Secretion by Parietal Cells

most important secretion in stomach

Important

Male slides

- **Chloride** ion is actively transported **from the cytoplasm of the parietal cell into the lumen of the canaliculus,** and **sodium ions** are actively transported **out of the canaliculus into the cytoplasm** of the parietal cell.
- **Water becomes dissociated into hydrogen ions and hydroxyl ions** in the cell cytoplasm. The hydrogen ions are then actively secreted into the canaliculus in exchange for potassium ions.
- **Carbon dioxide, either formed during metabolism in the cell or entering the cell from the blood,** combines under the influence of **carbonic anhydrase** with the hydroxyl ions to form bicarbonate ions. These then diffuse out of the cell cytoplasm into the extracellular fluid in exchange for chloride ions that enter the cell.

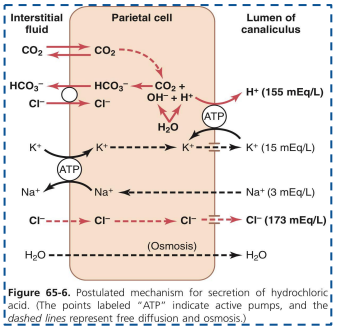
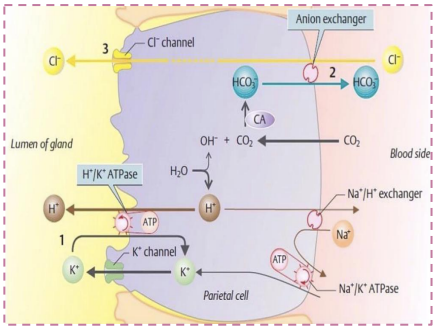
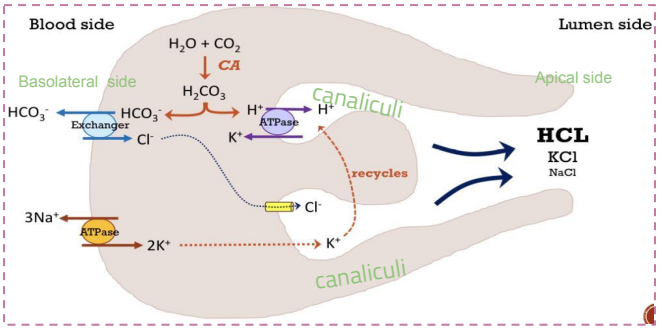


Figure 65-6. Postulated mechanism for secretion of hydrochloric acid. (The points labeled "ATP" indicate active pumps, and the *dashed lines* represent free diffusion and osmosis.)





Explanation by female doctor :

How does parietal cell secrete HCL ??

- Parietal cell on the apical side of membrane have a " H/K ATPase pump" it pump H out into lumen of stomach with exchange for K into the cell.

Note : in physiology when ever I pump an ion

1- pump in opposite direction an ion in the same charge

2- or pimp in same direction an ion with negative charge

From where come H:

- Blood
- Dissociation of HCO3

CO2+H2O $\xrightarrow{\text{Carbonic anhydrase}}$ H2CO3 $\longrightarrow$ HCO3+H

From where come K :

- Because down concentration gradient by Na/K ATPase in because basolateral membrane with pump 3 Na out and 2 K in.

- HCO3 which come from dissociation of H2CO3 will be transformers into blood by exchanger protein "HCO3/Cl exchanger" when Cl go to the cell will go again to cl channel into the lumen of stomach
- Cl will bind in lumen of stomach to H

  Finallllyyy HCL formed🤩🤩
- In addition to HCL:

  1- little KCl

  2- very little NaCl

Explanation by med442 : Our body is made of water. CO2 is released by the cell as a product of metabolism by free diffusion.

1- When CO2 and water combine together in the presence of carbonic anhydrase enzyme they will form carbonic acid. The carbonic acid will dissociate into bicarbonate and hydrogen.

2- The hydrogen will be pumped out of the cell canaliculus (luminal side) by H^+/K^+ **ATPase (primary active transport).** It will pump H+ in exchange of K+. The movement of H+ outside parietal cell depends on: H^+/K^+ **ATPase** and amount of K+ found in lumen of the stomach

Where did the K+ that will be pumped into cell come from? Inside of the cell. Na^+/K^+ **ATPase** is found on basolateral side of cell (blood side) The main function of Na^+/K^+ **ATPase** is to pump 3Na+ out and 2K+ onto the cell. This creates a high concentration of K+ inside the cell which will cause leakage of the potassium into the canaliculus side of cell through (potassium channels. In summary, the leaked potassium will be used in exchange for H+ and will enteral cell (recycled potassium).

3- The bicarbonate will be transported into blood in exchange for Cl-. When the Cl- accumulates in the cell, it will escape through the luminal side of cell via Chloride channels.

END RESULT=

The hydrogen the is pumped into the canaliculus and the Cl- that escaped the canalicular side will combine and form **HCL.** Some K+ will combine with Cl and form KCL. Na will also combine with Cl- and form NaCl (very little amount)

Summary of HCl secretion

-Depends on H/K ATPase
-Inhibited by: omeprazole
used to treat: stomach peptic ulcer and gastric reflux

-Alkaline tide
-H/K pump depends on [K]out

[HCl] drives water into gastric content to maintain osmolality

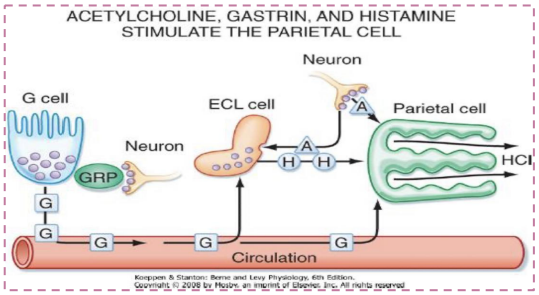
During gastric acid secretion: **amount of HCO3- in blood = amount of HCl being secreted , Alkaline tide**

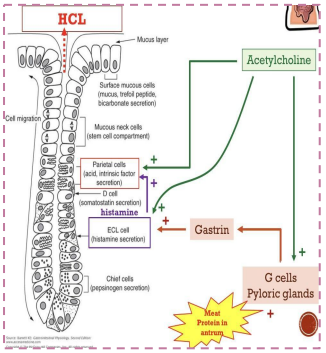
Control of HCL secretion(M)

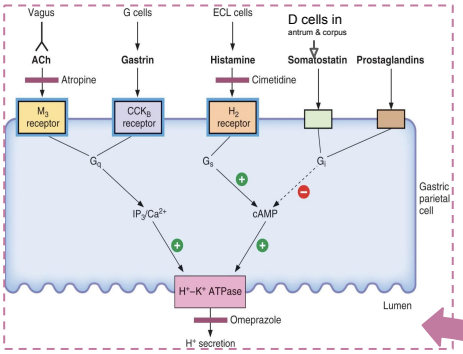
- Gastric acid secretion is mediated through **neural** (via **Vagus nerve**) and hormonal pathways (via **histamine and gastrin**).
- Parietal cells possess special histamine receptors, H2 receptors, whose stimulation results in increased acid secretion. they also get activated by distension
- Special neuroendocrine cells of the stomach, known as enterochromaffin like (ECL) cells, are believed to be the source of this histamine. They are located mostly in the acid-secreting regions of the stomach. The mechanisms that stimulate the ECL cells to release histamine are poorly understood.
- **The effectiveness of cimetidine, a H2 blocker, in reducing acid secretion has indirectly demonstrated the importance of histamine as an effector of gastric acid secretion. H2 blockers are commonly used for the treatment of peptic ulcer disease or gastroesophageal reflux disease.(M)**

Important

Neural via Vagus nerve	**Direct**	Ach act on parietal cells → increases HCL secretion
	Indirect	Act on G cells by releasing **Gastrin releasing peptide(GRP)** → secrete gastrin which act on CCKB receptor 4 of parietal cells → increases HCL secretion
		Act on **enterochromaffin like cells (ECL)** which secrete histamine → act on H2 receptor of parietal cell → increases HCL secretion.
Hormonal	**Gastrin** (Endocrine secretion)	—
Paracrine	**Histamine (M)**	Histamine activate H2 receptor on parietal cells thus increase HCL secretion. H2 blockers are used for the treatment of **peptic ulcer disease or gastroesophageal reflux disease**. (e.g, Cimetidine)





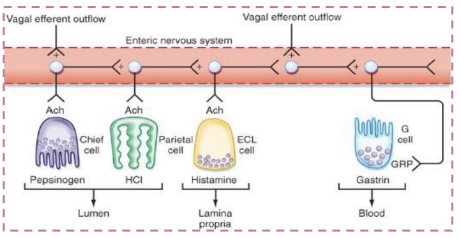


If you like to read doctor's Notes of these pictures, Your finger here please..

Agents stimulate and inhibit H+ secretion by gastric parietal cells . Mention them.

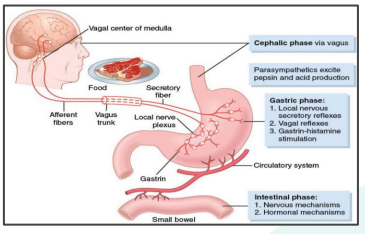
Effects of vagal activation on gastric secretion

Postganglionic fibers of parasympathetic lie within ENS (found on wall of stomach). So activation of the parasympathetic system will stimulate the release of Ach -> which will act directly on chief cells, parietal cells and ECL cells. However, G cells are stimulated by GRP **not** Ach.



Inhibition of Acid Secretion (Enterogastrones):

- **Somatostatin (D-cells)** in antrum.
- **Secretin (S-cells)** in duodenum.
- **Glucose-dependent insulinotropic peptide (GIP)** (K-cells) in duodenum.

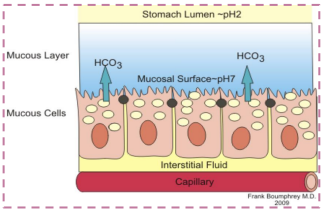


Other Gastric Secretions

1-Mucus

- Mucus cells secrete large quantities of viscid thick mucus that coats the muscle mucosa.
- The mucus is alkaline.

Which is rich in bicarbonate -> protects the stomach mucosa*.(if the surface get some erosion by gastric acid which inside lumen HCO3 can buffer acidity before it rich mucus and damage it and cause peptic ulcer)

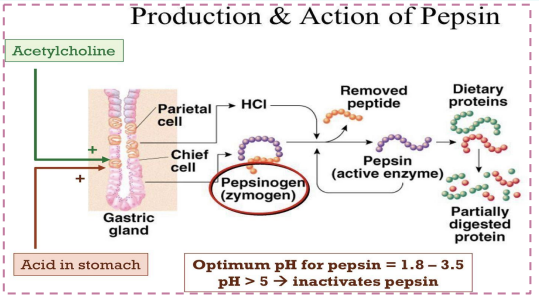


The epithelial cell layer of stomach have junction in between cell very tight to protect return anything from lumen of stomach into cell and damage it

2-Pepsin

- Peptic (chief) cells secrete pepsinogen.. What is its role in digestion?
- Several types of pepsinogen secreted from chief cells. They are activated by HCl into pepsin and once activated, they can activate more pepsinogen. These amino acids. or peptides activate G cells to secrete Gastrin thus increasing HCL secretion.
- Peptic (chief) cells secrete pepsinogen.
- **The optimum pH is (1.5-3.5) (1.8-3.5).**
- pH > 5 inactivates pepsin.
- **Pepsin breaks down proteins into peptones & polypeptides*.**
- **Pepsinogen secretion is stimulated by Ach, acid, gastrin, secretin & CCK.**

What controls the release of pepsinogen?
1- Ach secretion "direct effect on chief cells
2- Acidity in stomach. Ex: HCL in stomach can stimulate chief cells to secrete pepsinogen.

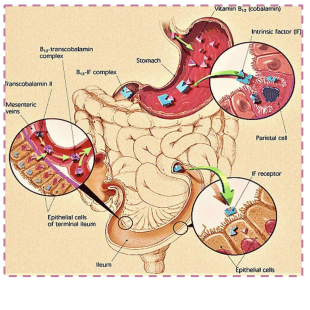


1- Chief cells in the gastric mucosa secrete pepsinogen (inactive form of pepsin) protective mechanism because will digest the cell if it activated in it
2- Once pepsinogen reaches the lumen of the stomach, HCL will act on it.
3- HCL will activate pepsinogen -> pepsin (active enzyme)
What's the role of pepsin in digestion? It plays a role in protein digestion (breaks down proteins into smaller polypeptides" dietary proteins -> parietal digested protein. 15% of ingested protein is digested in stomach by pepsin.
2 stimulator for pepsin : 1-acidity of cell 2- parasympathetic ACh by vagus nerve
A feature of active enzymes: once the active form is formed, it promotes conversion of inactive form to active يحفز نفسه

3-Intrinsic Factor:

- In addition to HCl, parietal cells secrete IF. **What is its importance?**
- It is a glycoprotein secreted by **parietal cells.**
- **It is the only essential function of stomach as it is essential for vitamin B_{12} absorption*.**
- **Atrophy of gastric mucosa leads to pernicious anemia.**

Parietal cells secrete IF along with HCL The IF will hold onto BI2 that entered the stomach with food, and protects it from being degraded by stomach acidity until they reach the terminal of the ileum "site of BI2 absorption" -> IF will release vit. BI2.
Any damage to parietal cells will result in anemia (no IF). -> BI2 can't be absorbed -> effect on RBC synthesis and eventually will result in megaloblastic anemia (pernicious anemia)



The Rate of Secretion

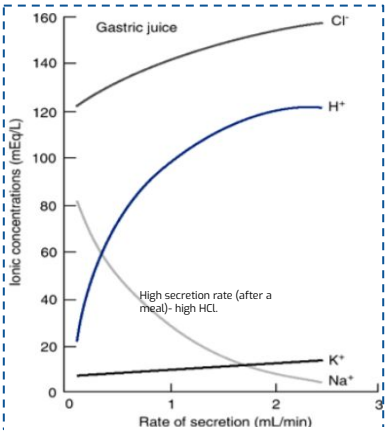
Male slides

- The Rate of Secretion Modify the Composition of Gastric Juice

- **At a low secretion rate**, gastric juice contains :
  1-high concentrations of **Na+ and Cl-** and
  2-low concentrations of **K+ and H+.**

- When the rate is **increased:**
  1-Na+ concentration **decreases**. Na+ secretion once stomach is empty is high -> makes NaCl secretion in interdigestive period (high)
  2-H+concentration **increases significantly.**
  3-Cl-concentration **increases**.

- Gastric juice is derived from the secretions of two major sources:
  -Parietal cells: its secretion (HCl secretion) **contributes mainly to the changes in electrolyte composition** with higher secretion rates.
  -Non parietal cells: constant secretion, thus **having little contribution to the electrolyte changes.**
- Interdigestive period (i.e., between meals) : production of H+out of parietal cells is very low and Cl- is high, By eating -> H+ will increase and so as Cl-



Always isotonic
This means if we increase HCL production, that will not affect the osmolarity of secretion inside the stomach. This because having more HCL production inside the stomach after getting a meal will also increase water secretion toward the stomach (that's why we feel thirsty and we drink water after having a meal, in order to regulate osmolarity

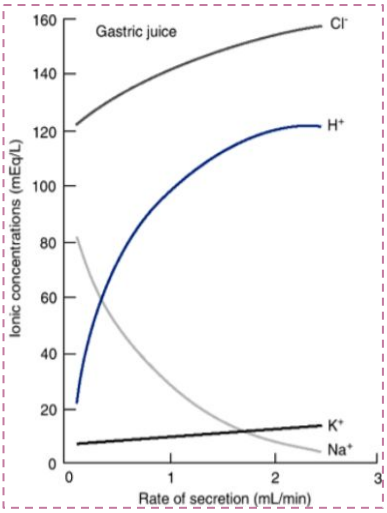
The Rate of Secretion (in summary)

female slides

-Low secretion rate —-------->high **NaCl.**
(Between meals)

-High secretion rate —-------> high **HCl.**
(After meal)

-Always isotonic.



Peptic ulcer disease

female slides

- **What causes peptic ulcer disease ?**

-is the imbalance between damaging factors and protective factors.

- **What are they ?**

Damaging factors	Protective factors
HCL	Alkaline mucus
NSAIDS	Somatostatin
H.Pylori	Prostaglandins

- **What is Zollinger—Ellison syndrome ?**

-It's a tumor that produce more gastrin hormone —-> ++ acidity secretions.

don't worry , the whole paragraph has been explained in pathology

Phases of Gastric Secretion

When does the stomach start secret this secretion

-Gastric secretion starts even before food reaches the stomach and when food is in the stomach and continues even after food leaves stomach into duodenum. Sight/smell/.. will activate cerebral cortex -> parasympathetic system will fire. Vagal stimulation through neuronal connections will stimulate stomach to start secreting its juices.

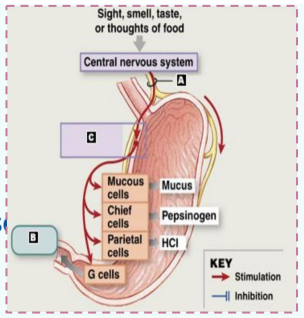
-The stimulation of acid secretion resulting from the ingestion of food can be divided into 3 phases:

Cephalic phase:

Looking , smell food

1

- 30% of HCL is secreted in this phase.
- Before food arrives at stomach.
- **Stimuli (Smelling, taste , Chewing and swallowing).**
- Mechanism: ?(long reflex) vagus
  - CNS send impulses via the vagus nerves,The nerve endings release **ACh,** which directly stimulates acid secretion from parietal cells.
  - CNS send impulses via the vagus nerves ,nerves also release gastrin-releasing peptide **(GRP),** which stimulates G cells to release gastrin, indirectly stimulating parietal cell acid secretion.

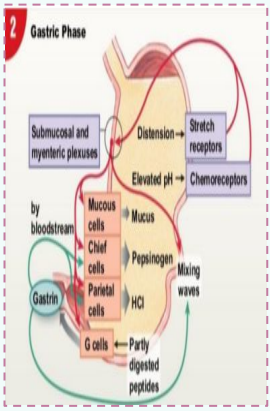


Gastric phase: Most important phase

Stimulate by destination of stomach , chemical in food

2

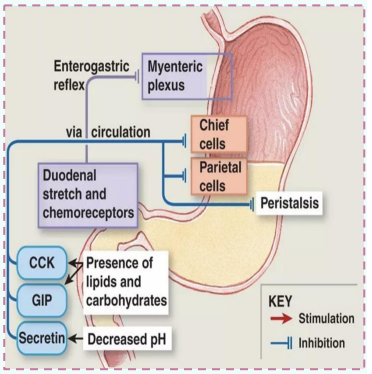
- 60% of HCL is secreted in this phase.
- when food enters the stomach .
- **Stimuli (distention , amino acid , small peptides).**
- Mechanism : (long reflex vagus) (short reflex ENS) (hormonal)
  - Distention of the stomach stimulates mechanoreceptors, which stimulate the parietal cells directly through short local (enteric) reflexes and by long vago-vagal reflexes.
  - Digested proteins in the stomach are also potent stimulators of gastric acid secretion, an effect mediated through gastrin release. Several other chemicals, such as **alcohol and caffeine, stimulate gastric acid secretion through mechanisms that are not well understood.**

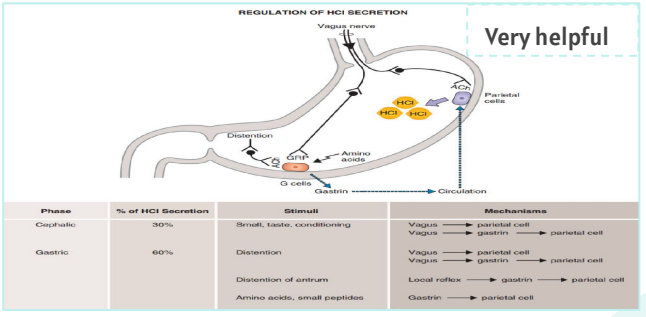


intestinal phase: minimal effect (mainly inhibit HCL more than stimulate it)

3

- 10% of HCL is secreted in this phase.
- when chyme enters duodenum.
- **Stimuli (protein digestion products in the duodenum).**
- Mechanism
  - protein digestion products in the duodenum stimulate gastric acid secretion through the action of the circulating amino acids on the parietal cells.
  - Distention of the small intestine, probably via the **release of the hormone entero-oxyntin from intestinal endocrine cells,** stimulates acid secretion.

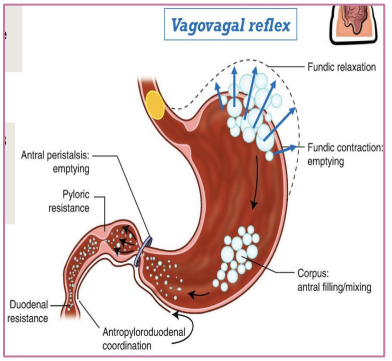




Motor Function Of the Stomach

1-Storage of food:

- Mainly in the proximal portion Involves muscle relaxation
- When bolus of food in the esophagus approaches the stomach
- A wave of relaxation recedes it that relaxes the LES & the orad region of the stomach **"Receptive relaxation"**Peristaltic wave of esophagus is preceded by a relaxation wave -> which relaxes LES as well as the upper part of stomach wall. Distend upper part of stomach to allow accommodation
- Allow food to enter and the volume of stomach increases **without an increase in intragastric pressure** this is because the stomach is relaxing as food comes in -> accommodates food without significance increase in pressure
- When the stomach is stretched by food, a **vagovagal** reflex is initiated from the stomach to the brain stem and back to the muscular wall of the stomach resulting in reduction in muscular wall tone which allows storage. Stomach can store 0.8-1.5 L of food.
- Gastric contents may remain unmixed for 1 hour in the corpus (body of stomach).
- The pressure in the stomach remains low until the volume reaches ~1.5 L of food. This function is regulated by **Receptive Relaxation Reflex (vagovagal): Triggered by swallowing reflex.**(will be discussed in the next slides)



Empty stomach 50 ml

⇩

Full stomach 1000 ml

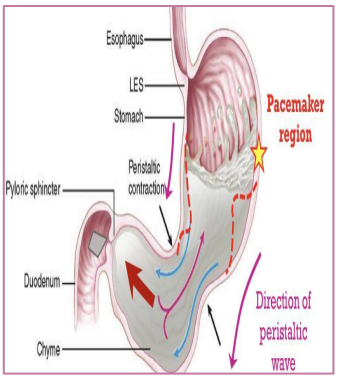
2-Mixing Propulsion of food:

- Churns food to transform it into a form that can pass through the pylorus and easy for intestine to deal with.
- Mixing of food in the stomach transforms it into a semifluid mix called "chyme".

- Major mixing activities take place in the antrum (antral pump region, **phasic contraction**).
- The **Basic Electrical Rhythm of the Stomach Wall.** The digestive gastric juices come in contact with the food lying against the mucosal surface of the stomach.
- The presence of food causes weak peristaltic constrictor waves called mixing/constrictor waves once every 15-20 seconds. **These waves are initiated by the gut wall basic electrical rhythm of the slow spontaneous electrical waves.** **Note:** If you remember, we said that slow waves can't produce contractions, except in the stomach (mixing waves). If slow waves produce a contraction, It's weak (like this one)

- These waves progress from the body to the antrum and become intense, forcing the chyme to mix and move under high pressure from the antrum toward the pylorus.
- Each time a peristaltic wave passes from the antrum to the pylorus, few millimeters of antral content move into the duodenum through the pyloric sphincter We can not depend on weak peristaltic constrictor waves in mixing/digesting/pushing

- food to duodenum. Once slow waves reach threshold, they will generate enough AP. Every single AP in this area can last 5 sec "Very long" (normal 10-20 msec).



When food arrives at stomach it causes distention.

Distention of the stomach causes the slow wave potential to reach the threshold -> generation of AP -> contraction of stomach wall (contraction stats at mid. region of body).

A peristaltic wave will cause another constrictor wave. When this wave reaches the pyloric sphincter it will be tonically contracted.
In order for food to leave the stomach via the pyloric sphincter, it's size should be less than 2mm. Whatever is bigger than 2mm will tumbled back in to antrum and goes through the same process until it's small enough to pass through pyloric sphincter.

Motor Function Of the Stomach (cont-)

3-Regulate emptying of the chyme from the stomach into the small Intestine (duodenum):

- Emptying of modified gastric contents "chyme" into duodenum
- If particles are **< 2mm they will squeezed through the tight pyloric sphincter** and get emptied into duodenum **"Pyloric pump"**
- If particles are **> 2mm they will pump into the tight pyloric sphincter and tumble back into antrum "retropulsion"** مثل هرس الطعام
- اذا فضت المعده تبدأ ال **wave** تكون اعلى **To binch more food**
- **Chyme:** Is a murky semi-fluid or paste composed of food that is thoroughly mixed with gastric secretions.
- Movement of chyme into duodenum is achieved by "Pyloric pump"
- Each time a peristaltic wave passes from the antrum to the pylorus, few millimeters of antral content move into the duodenum through the pyloric sphincter.

That's why once you have food between 2 contractions -> you want to mix it with digestive juices. The leading contraction will start and squeeze food down. If food particles are larger than 2mm, they will go back for further degradation which is done by contraction of pyloric sphincter (the leading contraction will squeeze sphincter and the trailing contraction will push food back and expose food to HCL to mix and digest "retropulsion"). Another AP will be generated to push the food down. Size of food is determined by stretch receptors that are located on pyloric sphincters. It will determine whether food will pass through sphincter or will go back.

4-The main functions of the upper part of the Stomach (Reservoir part):

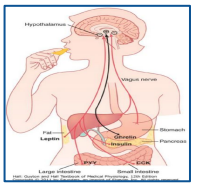
Male slides

- To maintain a continuous compression.
- To accommodate the received food without significant gastric wall distention or pressure (Storage of food).
- Upper part of stomach: storage+relaxes
- Lowe part : mixing + grinding

5-Hunger Contraction:

Male slides

- **Hunger contractions** occur when the stomach has been empty for several hours
- These are rhythmical peristaltic contractions that can become very strong and fuse to form a continuing tetanic contraction lasting sometimes 2-3 minutes.
- Hunger contractions are intense in young healthy people and increase by low blood glucose levels.
- **Hunger pain can begin after 12-24 hr of last food ingestion.**



6-Absorption of water and a few highly-lipid soluble substances (alcohol and Aspirin):

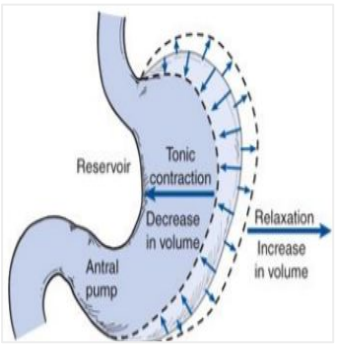
Female slides

- Stomach is a poor absorptive area of GIT:
  - ➢ It lacks the villous type of absorptive membrane.
  - ➢ It has tight junctions between epithelial cells.

Three Kinds of Relaxation Occur in the Gastric Reservoir (orad):

1-Receptive Relaxation Reflex:

- **Triggered by: swallowing reflex.**
- When the esophageal peristaltic waves reach the stomach, the stomach relaxes through inhibition of myenteric neurons which prepares the stomach to receive the food that is propelled into the esophagus during swallowing.
- Gastric fundus dilates when food passes down the pharynx and esophagus



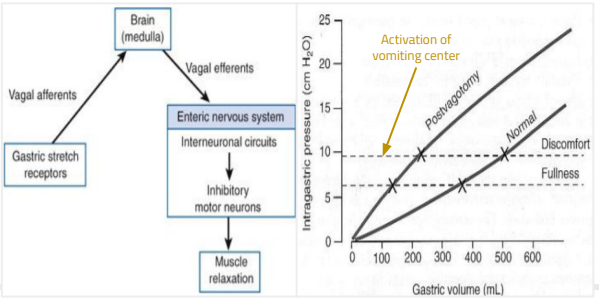
2-Feedback Relaxation:

- **Triggered by: presence of nutrients in the small intestine.**
- It can involve both local reflex connections between receptors in the small intestine and the gastric ENS (Enteric nervous system).
- or hormones that are released from endocrine cells in the small intestinal mucosa and transported by the blood to signal the gastric ENS and stimulate firing in vagal afferent terminals in the stomach
- Feedback relaxation significance is delaying gastric emptying

3-Adaptive relaxation:

Most important

- **Triggered by: stretch receptors (vago-vagal reflex).**
- Stomach dilates when filled, accommodating greater and greater quantities of food up to a limit (0.8 to 1.5 L).
- Gastric stretch receptors → Vagal afferents → brain stem (medulla oblongata) → Vagal efferents → enteric nervous system → inhibitory motor neurons → Muscle Relaxation
- **Adaptive relaxation is lost in patients undergone a vagotomy.**
- Following a vagotomy, increased tone in the musculature of the reservoir decreases the wall compliance, which in turn affects the responses of gastric stretch receptors to distention of the reservoir.
- Pressure–volume curves obtained before and after vagotomy reflect the decrease in compliance of the gastric wall. The loss of adaptive relaxation after a vagotomy is associated with a lowered threshold for sensations of fullness and pain.



Retropulsion Phenomena

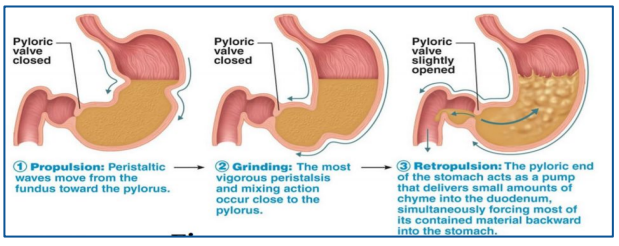
1

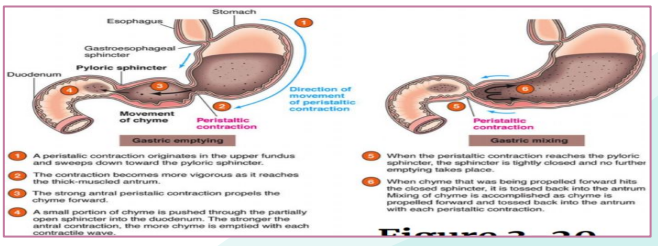
As the trailing contraction (explained later) approaches the closed pylorus, the gastric contents are forced into an antral compartment of ever-decreasing volume and progressively increasing pressure.

This will Result in

2

jet-like retropulsion through the orifice formed by the trailing contraction. Repetition **at 3 cycles/min** reduces particle size to the 1-mm to 7-mm range that is necessary before a particle can be emptied into the duodenum. **These intense peristaltic contractions that cause emptying increase the pressure in the stomach to 50–70 cm of H2O (compared to a pressure of ~10 cm of H2O during the mixing peristaltic contractions).**





Motor Behavior of the Antral Pumps Is Initiated by a Dominant Pacemaker (Motility in the Antrum):

Male slides

- Gastric action potentials determine the duration and strength of the phasic contractions of the antral pump.
- **They are initiated by a dominant pacemaker (ICC)** (interstitial cells of Cajal).

1 **The action potentials (AP) propagate rapidly around the gastric circumference and trigger a ring-like contraction**

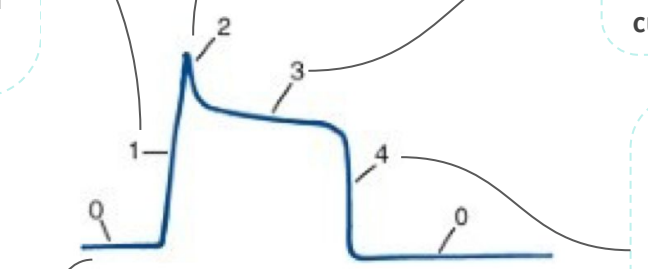
2 **The AP and associated ring-like contraction then travel more slowly toward the gastroduodenal junction.**

- **Electrical syncytial properties** of the gastric musculature account for propagation of the action potentials <u>from the pacemaker site to the gastroduodenal junction.</u>
- The pacemaker region in humans generates AP and associated antral contractions at a frequency of **three per minute.** "Slow waves"
- The gastric action potential lasts about **5 seconds**, it has:
  - **Rising phase (depolarization)**
  - **Plateau phase**
  - **Falling phase (repolarization)**
- Electrical action potentials in gastrointestinal muscles occur in four phases, determined by specific ionic mechanisms:

Phase I: Ca+2 influx Rising phase (upstroke depolarization) - Activation of voltage-gated calcium channels and voltage-gated potassium channels

Phase 2: Initial repolarization. K+ efflux

Phase 3: Balance between K+ efflux and Ca+2 influx **Plateau phase; balance of inward calcium current and outward potassium current.**



Phase 0: Resting membrane potential; **outward potassium current**

Phase 4: **Falling phase** (repolarization); **inactivation of voltage-gated calcium** channels and activation of calcium-gated potassium channels.

There are two phases of Ca+2 influx = 2 contractions
1- Leading contraction (due to depolarization)
2- Trailing contraction (due to plateau) long period of Ca+2 influx.

The Gastric Action Potential Triggers Two Kinds of Contractions

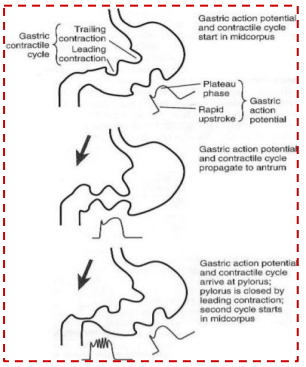
Male slides

- The gastric action potential is responsible for two components of the propulsive contractile behavior in the antral pump:

Contraction	Trailing Contraction
It has a relatively **constant** amplitude	**Variable** amplitude
Associated with the **rising phase** of the action potential.	Associated with the **plateau** phase.

The **two** contractions happen because of the extremely long duration of the Action Potential

- The leading contractions have negligible amplitude as they propagate to the pylorus. As the rising phase reaches the terminal antrum and spreads into the pylorus, contraction of the pyloric muscle closes the orifice between the stomach and duodenum.
- The trailing contraction follows the leading contraction by a few seconds.



Stomach emptying

- Stomach emptying is the result of intense peristaltic antral contractions against resistance to passage of chyme at the pylorus.

- **Role of the Pylorus in Controlling Stomach Emptying.** The distal opening is the pylorus
- The pyloric sphincter is characterized by strong circular muscle (as compared to the antrum) and remains slightly tonically contracted most of the time. However, during pyloric constriction, it is usually open enough to allow watery chyme and fluids to still pass through the pylorus into the duodenum, but not food particles.

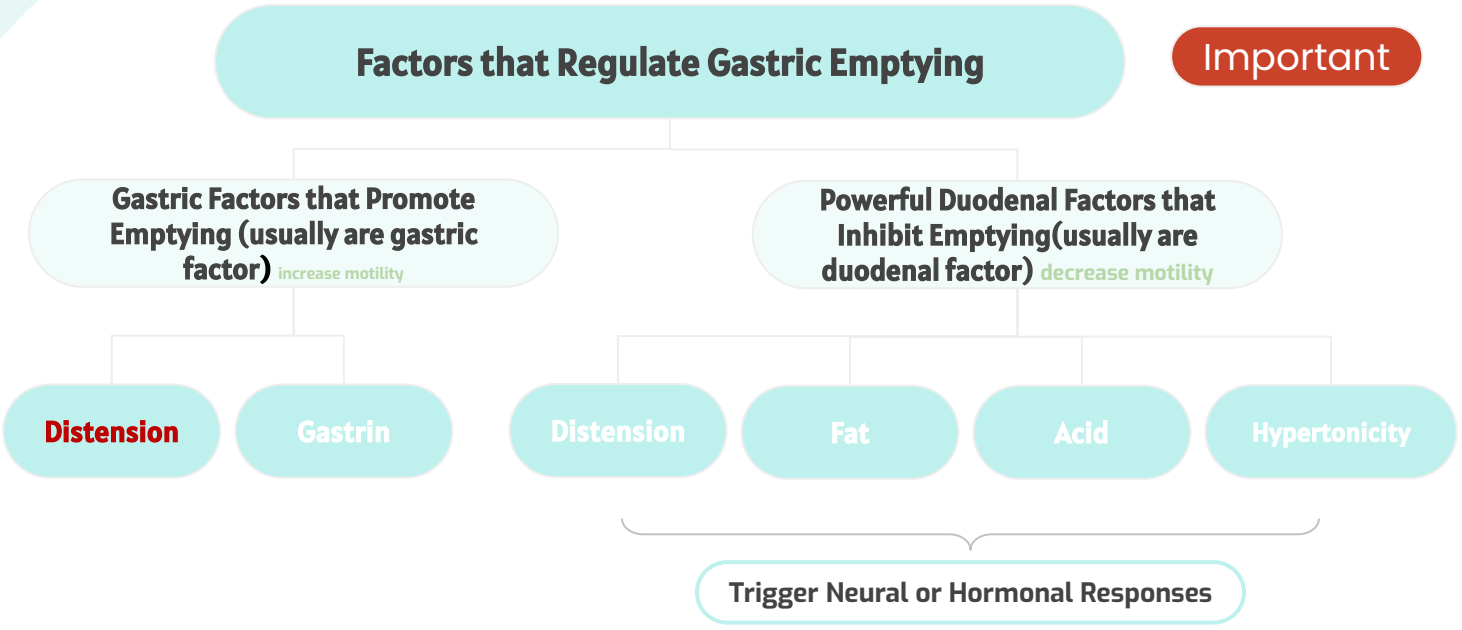
- Pyloric constriction is determined by (both are from the duodenum and stomach):
  - Nervous reflex signals
  - Humoral reflex signals

- What is the purpose of gastric emptying?
  - To deliver chyme to the intestine to continue its **digestion and absorption.**
  - **The rate at which chyme is delivered matters!**

- The rate of stomach emptying is controlled by **signals from the stomach and duodenum** (will be discussed in the next slides), with the latter being far stronger and controls emptying of the chyme at a rate that allows the proper digestion and absorption in the small intestines.

Stomach emptying

Male slides



I-Gastric Factors that Promote Stomach Emptying:

Note: The first 2 detailed boxes are in the males slides only. Alternatively, you can find the females doctors' simple explanation in the 3rd box.

A-Effect of Gastric Food Volume on Rate of Stomach Emptying:

↑ food volume -> pressure on pyloric sphincter = ↑ gastric emptying

- Increased gastric food volume → increased stretch in the stomach wall (which elicits local myenteric reflexes) →increased pyloric pump activity & the tonic contraction of the pyloric sphincter gets inhibited, leading to increased stomach emptying.

B-Effect of the Hormone Gastrin on Stomach Emptying:

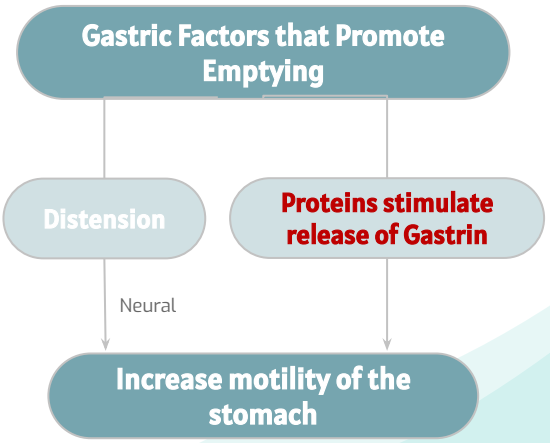
Gastric activates oxyntic cells to secrete GCl, ot also ↑ activity and motility of pyloric pump & Antrapump region = promote emptying.

- Gastrin is released **from the antral mucosa** in response to the presence of digestive products of meat.
- It promotes the secretion of acidic gastric juices (e.g. HCl) by the stomach gastric glands (or oxyntic glands) located on the inside surface of the **body and fundus of the stomach;** (i.e. proximal 80% of the stomach).
- It also enhances the activity of the pyloric pump and motor stomach function (moderate effect) and **probably promotes stomach emptying.**

Females Doctor: The presence of food in the stomach causes:

1. Distension of the stomach, which will trigger neural response by the Vagus nerve and the Enteric Nervous System.(long reflex vgus)
2. The proteins in the food stimulate G cell to release of Gastrin.

Both of these factors **increase** the motility of the stomach.



Stomach emptying

2-Powerful Duodenal Factors That Inhibit Stomach Emptying:

Note: The first 2 detailed boxes are in the males slides only. Alternatively, you can find the females doctors' simple explanation in the 3rd box in the next slide.

A-Inhibitory Effect of Enterogastric Nervous Reflexes from the Duodenum:

- When food enters the duodenum, multiple nervous reflexes are initiated from the duodenal wall and pass back to the stomach to regulate stomach emptying depending on the volume of chyme in the duodenum.
- These duodenal reflexes are mediated by three routes: goal: delay or reduce stomach emptying
  - Directly from the duodenum to stomach through the ENS (enteric nervous system) in the gut wall.
  - Through extrinsic nerves that go to the **prevertebral sympathetic** ganglia and then back through **inhibitory sympathetic nerve** fibers to the stomach.
  - Through the **vagus nerves reflex (to a slight extent)** → the brain stem → inhibit the normal excitatory signals that are transmitted to the stomach through the vagus nerves.
- These reflexes inhibit the pyloric pump and increase the tone of the pyloric sphincter thus decreasing stomach emptying.
- The duodenal factors that can initiate the enterogastric inhibitory reflexes include:
  Factors that activate 3 different routes
  - Duodenal distension.
  - Duodenal irritation.
  - Duodenal acidity.
  - Osmolality of the chyme in the duodenum.
  - Protein (and may be fat) content of the chyme in the duodenum.

Fat is mediated by CKK, which is secreted when fatty acids arrive in duodenum. CKK slows gastric emptying, ensuring that gastric contents are delivered slowly to duodenum and provide adequate time for fat to be digested and absorbed.

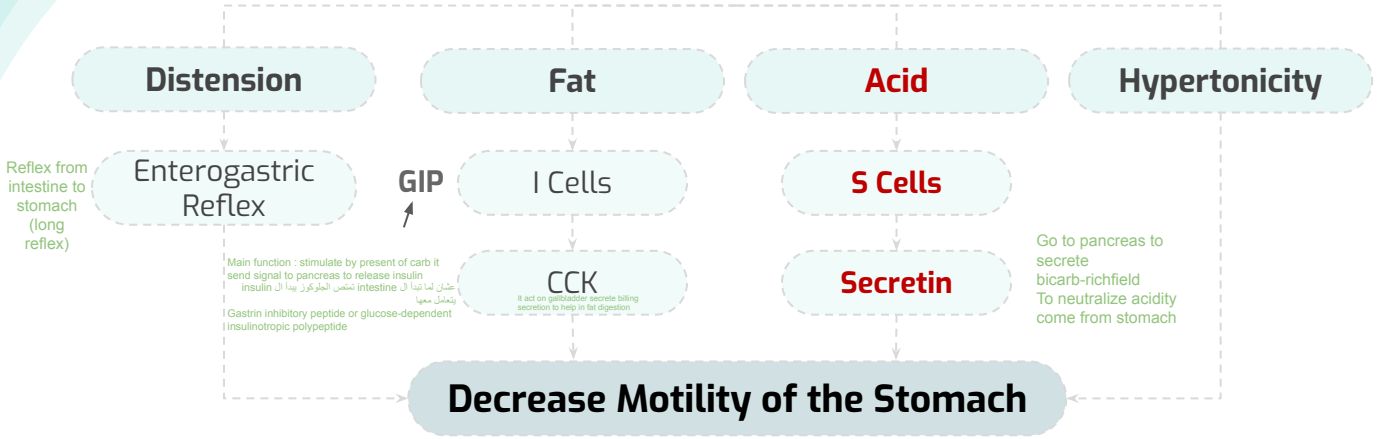
Very Important: The Inhibitory Effect of Enterogastric Nervous Reflexes from the Duodenum is what causes the Feedback Relaxation (Mentioned earlier).

B-Hormonal Feedback from the Duodenum Inhibits Gastric Emptying – Role of Fats and the Hormone Cholecystokinin:

- Fat entering the duodenum or acidity of chyme or excess quantities of chyme causes (probably a receptor mediated mechanism) the release of:
  - Cholecystokinin (CCK) , acts as an inhibitor to block increased stomach motility caused by gastrin.
  - **Other inhibitory hormones** such as secretin and gastric inhibitory peptide (GIP) from the epithelium of the duodenum and jejunum.
- Release of CCK (and probably secretin, and GIP) circulate and inhibit the pyloric pump and increase the tone of the pyloric sphincter, thus decreasing stomach emptying.

Stomach emptying

Powerful Duodenal Factors that Inhibit Emptying



Females Doctor: Chyme in the duodenum causes:

1. Distension of duodenum, which will trigger the Enterogastric reflex.
2. Fat stimulates I cells to secrete CCK.
3. Acid damages the duodenum, so it will:
   a. Stimulates S cells to secrete Secretin.
   b. Stimulates the pancreas to release Bicarbonate to neutralize the acidity. (Will be discussed in the next lecture)
4. Hypertonicity

All of these factors **decrease** the motility of the stomach.
#med442

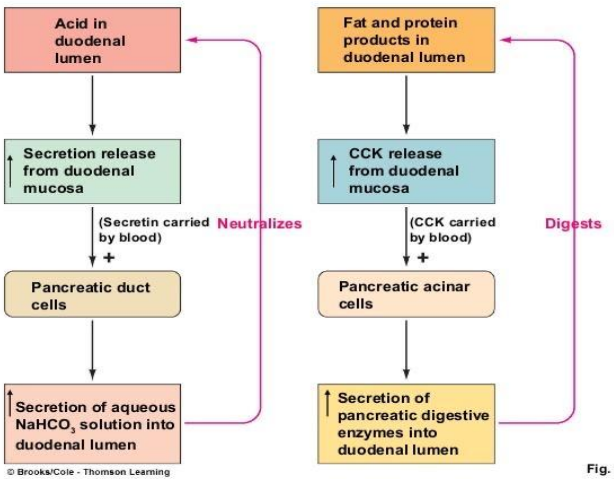


Fig.

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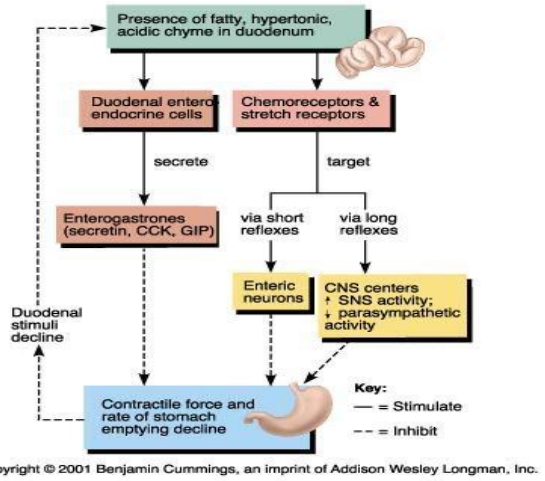

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Digestion in the Stomach

Carbohydrates	Carbs in diet include; • Cellulose. • Starch. • Disaccharides. Stomach digests 30-40% of consumed starch to maltose by action of salivary amylase.
Fat	Fat in diet include; • TGs. • Cholesterol Stomach digests <10% of consumed TGs by action of lingual lipase.
Protein	- Initiates protein digestion. - By action of pepsin. - Stomach digests 10-20% of consumed proteins transforming them into polypeptides, peptones.

Summaries

These summaries are written in the boys' slides, they are not extra effort from us

Phases of Gastric Secretion:

1. Cephalic phase(30%): Smelling, Chewing and swallowing Stimulate parietal G-Cells (via GRP).
2. Gastric phase (60%): gastric distention proteins
3. Intestinal phase (10%): digested proteins

Regulation of Stomach Emptying:

I. **Gastric Factors That Promote Emptying:**

- Food Volume: Increased food volume in the stomach promotes emptying from the stomach (inhibits the pylorus).
- Gastrin hormone: enhances the activity of the pyloric pump. Thus, it, too, probably promotes stomach emptying.

I. **Powerful Duodenal Factors That Inhibit Stomach Emptying:**

- At the presence of food in the duodenum, multiple nervous reflexes are initiated from the duodenal wall that pass back to the stomach to slow or even stop stomach emptying via one of the following routes:
- Directly through ENS
- Through extrinsic nerves that go to the prevertebral sympathetic ganglia and then back through inhibitory sympathetic nerve fibers to the stomach.
- Through the vagus nerves.

I. **The types of factors that can initiate enterogastric inhibitory reflexes include the following:**

- The distention of the duodenum.
- Acidity of the duodenum activates S cells to release Secretin which constricts the antrum.
- Fat (monoglycerides) in the duodenum activates different cells to produce CCK and GIP that delay gastric emptying.
- Hyperosmotic or hypoosmotic solutions delay gastric emptying.
- Amino acids elicit inhibitory enterogastric reflexes; by slowing the rate of stomach emptying.

Constriction of Pyloric Sphincter:

- **Hormones promote constriction of pyloric sphincter and <u>inhibit stomach emptying:</u>**

I. Cholecystokinin (CCK)
2. Secretin
3. Glucose-dependent insulinotropic peptide (GIP)

- Sympathetic innervation

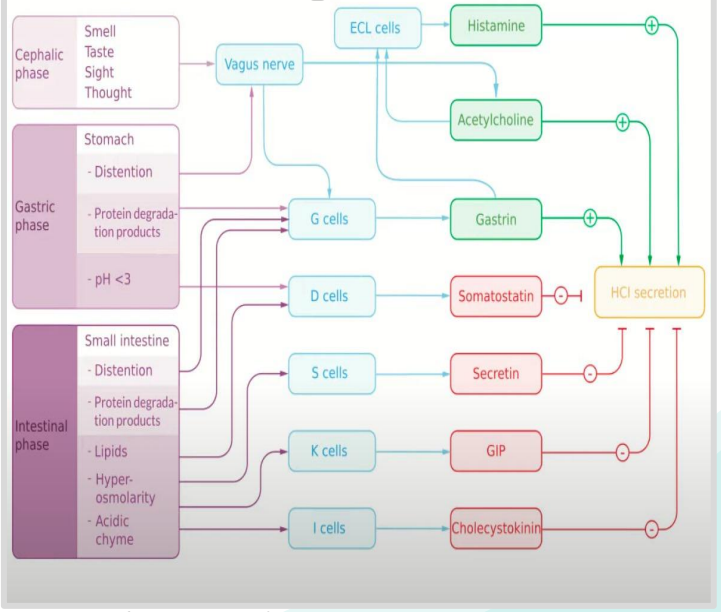
Summaries

You can fill this table Here

★الجدول مهم Hormone	Site of secretion	Stimuli for secretion	Actions	
			Stimulates:	Inhibits:
Gastrin(M)	**G** cells of the: - Antrum - Duodenum - Jejunum	(Acid inhibit its release) - Protein - Distention of the stomach - Vagal stimulation - (GRP)	- Gastric H^+ secretion - Growth of gastric mucosa	-
Cholecystokinin (CKK)	**I** cells of the: - Duodenum - Jejunum - Ileum	- Protein - Fatty acids - Acids	- Pancreatic enzyme secretion - Pancreatic HCO^-_3 secretion - Gallbladder contraction - Growth of the exocrine pancreas - Relaxation of sphincter of Oddi	Gastric emptying
Secretin	**S** cells of the: - Duodenum - Jejunum p - Ileum	- Acids & fat in the duodenum	- Pepsin secretion - Pancreatic HCO^-_3 secretion - Biliary HCO^-_3 - Growth of the exocrine pancreas	Gastric H^+ secretion
Glucose-Dependent Insulinotropic Peptide (GIP)	**K** cells of the: - Duodenum - Jejunum	- Protein - Fatty acids - Oral glucose	- Insulin secretion from pancreatic β cells	
Motilin	**M** cells of the: - Duodenum - Jejunum	- Fat - Acid - Nerve	- Gastric motility - Intestinal motility	-

هو نفسه حق المحاضرة الاولى

Phases of gastric secretion



TEST YOURSELF !

MCQ:

Q1) Receptive relaxation reflex triggers by?

A) stretch receptor

B) swallowing reflex

C)presence of nutrients in small intestine

D) all of them

Q2) Atrophy of gastric mucosa leads to?

A) protein Malabsorption

B) jaundice

C) pernicious anemia

D) diarrhea

Q3) Pepsinogen is converted to pepsin by?

A) Secretin

B) CCK

C) Somatostain

D) HCL

Q4) Which one of the following is "Hormone acts as inhibitor to block increased stomach motility caused by Gastrin" ?

A) Gastrin

B) Secretin

C) Motilin

D) CCK

Answers: Q1:B | Q2:C | Q3:D | Q4:D

SAQ:

Q1) What are the three types of relaxation occur in gastric reservoir?

1. Receptive relaxation
2. Adaptive relaxation
3. Feedback relaxation

Q2) Mention factors that promote stomach emptying?

- Increased gastric food volume
- Gastrin promotes the secretion of acidic gastric juices, and enhances the activity of the pyloric pump and motor stomach function

Here.. for you! After studying this lecture.

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