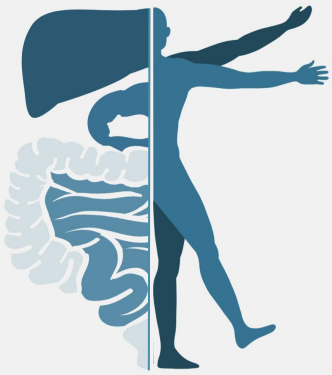
Physiology Team 439

MED439
KING SAUD UNIVERSITY

Revised & Approved
Bassam Alasmari
Rania Almutiri



Stomach and regulation of gastric secretions

Objectives:

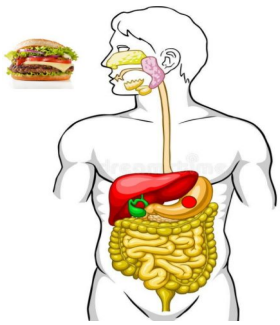
- Discuss the role of the stomach in digestion..
- Enumerate the functions of the stomach
- Discuss the secretory functions of the stomach:
  - What are the glands lining the stomach wall.
  - Discuss the cells lining the different glands and their specific secretions.
  - Discuss the mechanism of HCl 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.

Color index:

- Important.
- Girls slide only.
- Boys slide only.
- Dr's note.
- Extra information.

Editing File

Introduction*



- 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"**

General motor Functions of the Stomach*

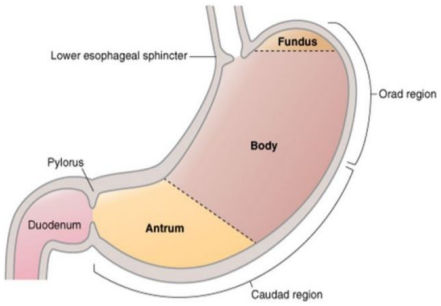
Motility functions of the stomach

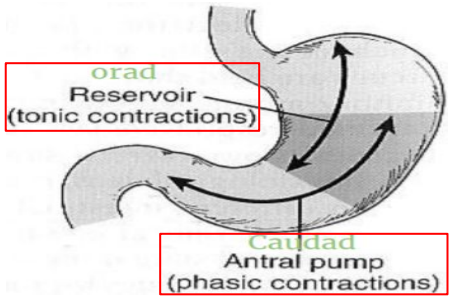
1. Storage of large quantities of food
2. Preparing the chyme for digestion in the small intestine
   It's not called bolus anymore since its mixed with digestive juices.
3. Absorption of water and lipid-soluble substances (alcohol and drugs)
4. Regulate emptying of the chyme from the stomach into the small intestine. Gradual emptying of the stomach

What are the major functions of the stomach?* Answers mentioned by doctors are mentioned above.

Functional Anatomy of the Stomach

- Stomach
  - Anatomically
    - antrum
    - Body
    - fundus
  - Physiologically
    - **Caudad (Antral Pump)** lower third of the body plus antrum **Caudad :** near legs → Phasic contraction
    - **Orad (Reservoir)** fundus and upper two thirds of the body **Orad:** near head → Tonic contraction



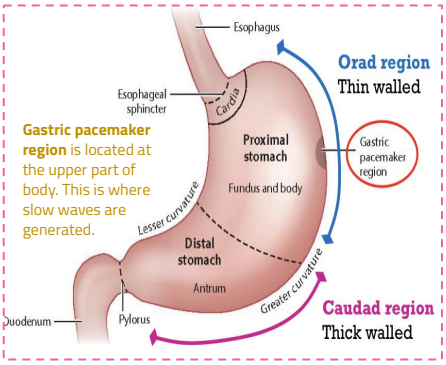


The reason behind this division is because there is a difference in motility at the two regions.

Functional Anatomy of the Stomach

Gastric Muscle Wall**

- 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.** Thickness is more in antrum than fundus -> Contraction is strongest at antrum

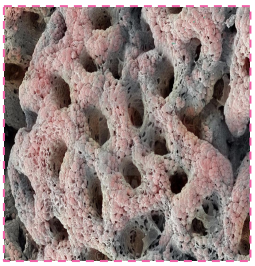


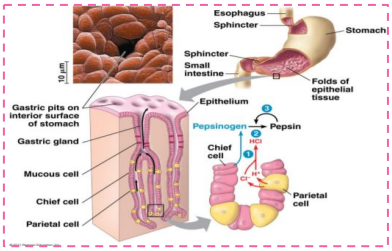
Role of pylorus:**

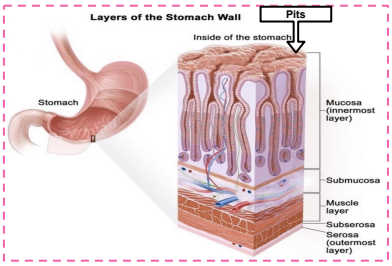
- it is slightly tonically contracted almost all the time (pyloric sphincter)
- it is usually open enough to allow water & fluids to pass.
- it is controlled by nervous and hormonal reflexes from the stomach and duodenum

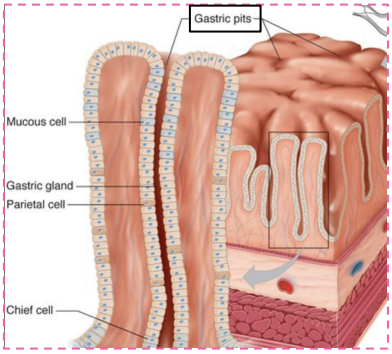
Gastric mucosa*

- Gastric mucosa is formed of columnar epithelium that is folded into "pits".
- The pits are the opening of gastric glands.
- There are Two main types of tubular (gastric) glands in the stomach and are distributed differentially in the stomach.
- Stomach lining with gastric pits, SEM BStomach lining^b. Coloured scanning electron micrograph (SEM) of the inner lining of the stomach (gastric mucosa). The indents are gastric pits. These contain cells that secrete enzymes, mucous and hydrochloric acid into the stomach. Magnification: x40 when printed 10 centimetres wide. Was skipped by girls Dr.









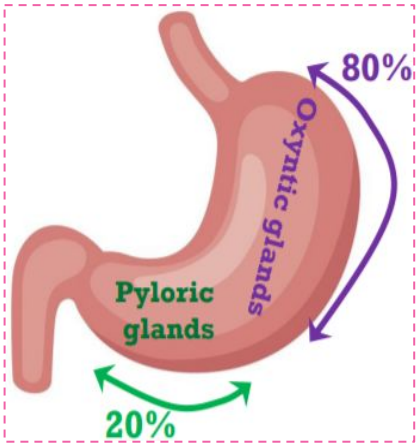
Pits= كأنها قنوات

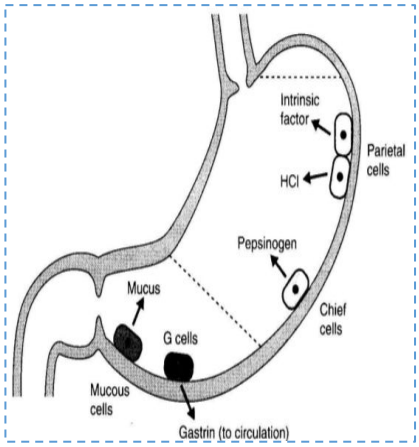
لما نشوف الميكوزا من برا\فوق راح نشوف حفر أو فتحات. كل وحده من الحفر او الفتحات عبارة عن غدة.

Each gland is lined by many type of cells.

Gastric glands

	Cell lining	Secretions	Location
Cardiac glands	-	Mucus,HCO_3	Cardia
Oxyntic (gastric or parietal) glands "most abundant glands"	-Mucus (neck) cells -Peptic (Chief) cells **-Parietal cells** (Oxyntic cells)	HCl ,Pepsinogen, IF, Mucus	Body & fundus (above the notch) Proximal 80% of stomach
Pyloric glands	Many G cells	Gastrin ,Mucus	Antrum (below the notch) Distal 20% of stomach

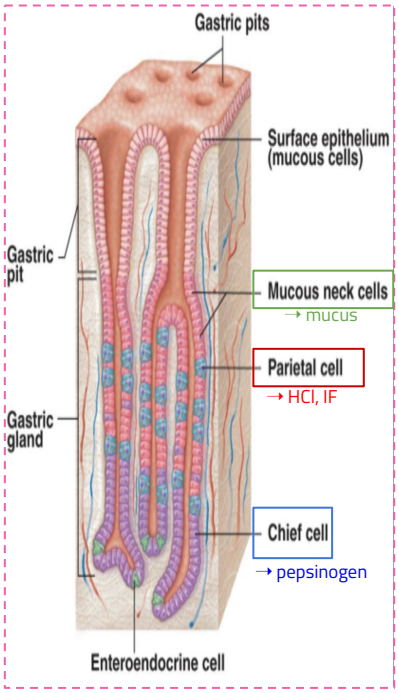




Every gland has a neck and a base.
Mucus cells are found in the neck region of glands. They neutralize acidity and **protect** the wall of stomach.
Mucus is secreted throughout the whole stomach.

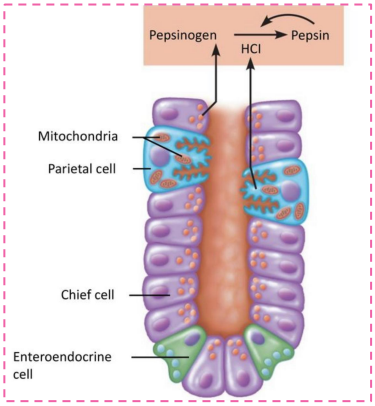
Types of Cells Present in Gastric Glands

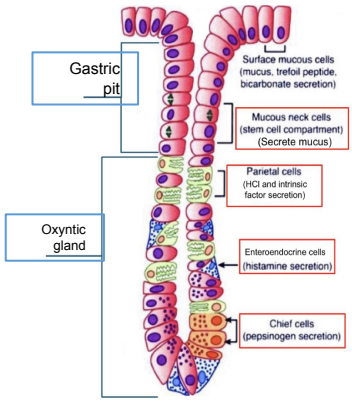
Cell	Secretions	Location
Oxyntic (parietal) cell	HCl & IF (intrinsic factor) The only cell that releases HCL in the body is the oxyntic cell.	Body (most distinctive cells in stomach)
Peptic (chief)cell	Pepsinogen inactive form	Body
Mucus (neck) cells	Mucus, HCO_3-	antrum
Enterochromaffin -like cells	Histamine	-
G cells	Gastrin (increases HCl secretion from Parietal cells) should be released in circulation to be activated	antrum
D Cells (decreases HCl secretion)	Somatostatin	antrum



Structure of Oxyntic gland

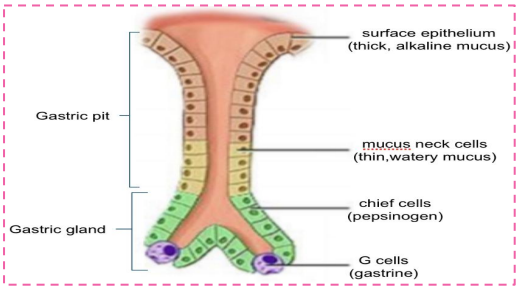
- HCl is secreted across the parietal cell microvillar membrane and flows out of the intracellular canaliculi into the oxyntic gland lumen.
- The surface **mucous cells** line the entire surface of the gastric mucosa and the openings of the cardiac, pyloric, and oxyntic glands.
- These **cells** secrete 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.





Structure of Pyloric gland *

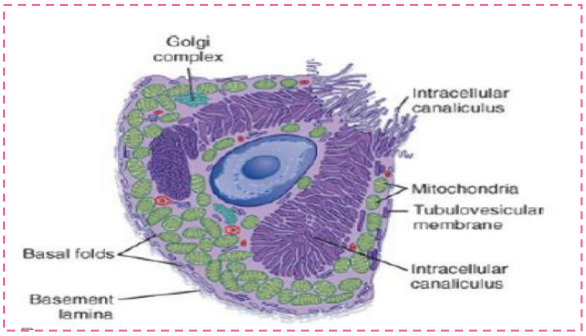
- There are no chief cells or parietal cells in the pyloric region.
- Mucus secreting cells are near the neck region.
- Deeper within the gland, there are G cells which secrete gastrin.



Structure of parietal cells *

HCL is secreted by parietal cells into canaliculus, then it flows into the lumen of the stomach through the opening.

Canaliculus(قناة)



Gastric juice is composed of:**

01 **HCL**

02 **Pepsinogen**

03 **Electrolytes**

04 **Intrinsic factor**

05 **Mucus** (mucus gel layer)

Mechanism of HCl Secretion by Parietal Cells

- 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.

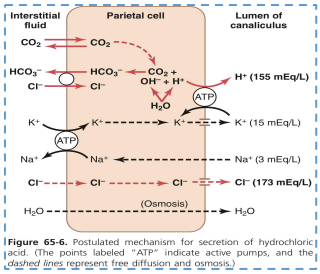
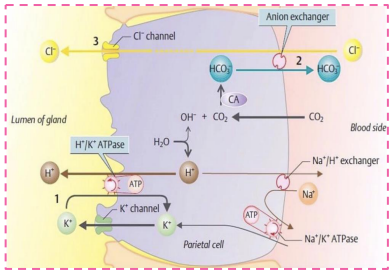
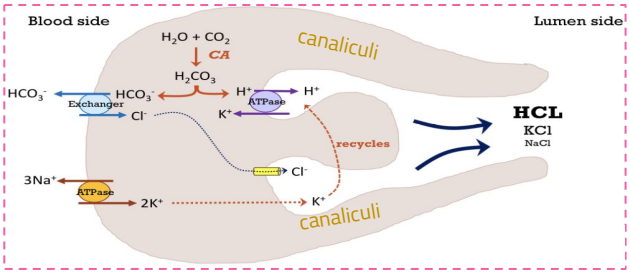


Figure 65-6. Postulated mechanism for secretion of hydrochloric acid. (The points labeled "ATP" indicate active pumps, and the *dashed lines* represent free diffusion and osmosis.)





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 celll. 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 HCO_3- in blood = amount of HCl being secreted

Control of HCL secretion(M)

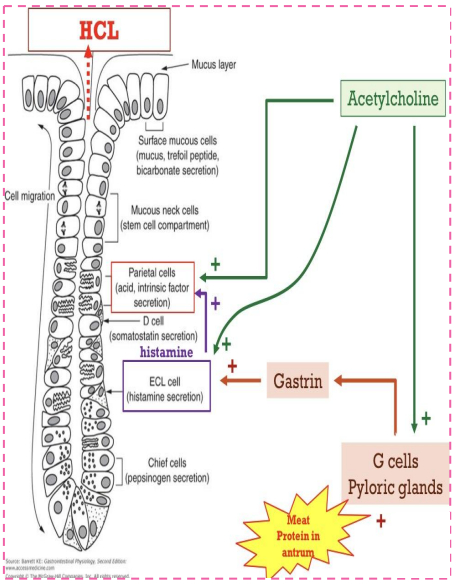
- Gastric acid secretion is mediated through **neural** (via **Vagus nerve**) and hormonal pathways (via histamine and gastrin).
- Parietal cells possess special histamine receptors, H2 receptors, whose stimulation results in increased acid secretion. they also get activated by distension
- Special neuroendocrine 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)**

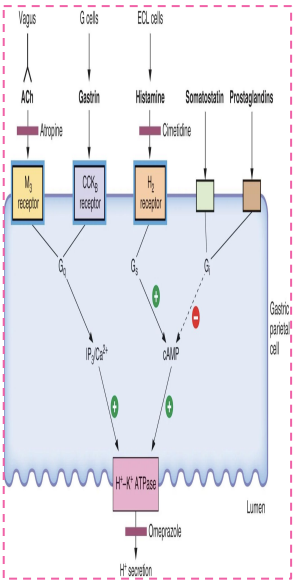
Neural via Vagus nerve	**Direct**	Ach act on parietal cells → increases HCL secretion
	Indirect	Act on G cells by releasing **Gastrin releasing peptide(GRP)** → secrete gastrin which act on CCKB receptor 4 of parietal cells → increases HCL secretion
		Act on **enterochromaffin like cells (ECL)** which 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)

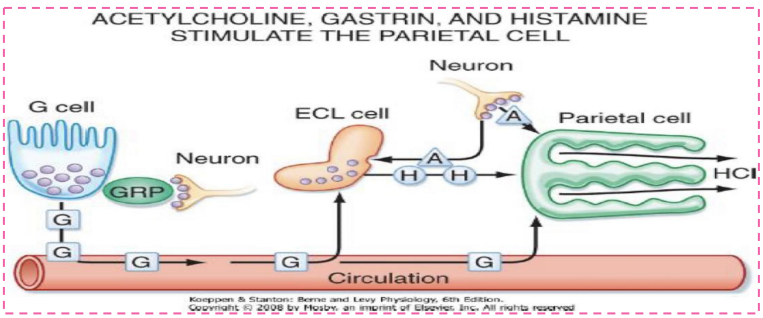
1- ECL cell is located next to parietal cell (they are neighbors). It has a paracrine effect on the the parietal cell (when a cell effects a nearby cell by a hormone or a cytokine). Histamin will got to parietal cell and stimulate it to release HCL.

2- Presence of food (protein digestive products) stimulates the release of HCL. This is done by stimulating G cells that are found in the pyloric glands. Once G cells are stimulated they will secrete a hormone called (gastrin). Gastrin will stimulate ECL cells **indirectly .**

3- Vagus stimulation /Ach released by parasympathetic system:
a- Ach stimulates parietal cells directly to secrete HCL
b- Ach will stimulate ECL cells
c- Vagal stimulation of G cells will release GRP (not Ach) which will act on G cells -> gastrin -> stimulation of ECL cells **indirectly**

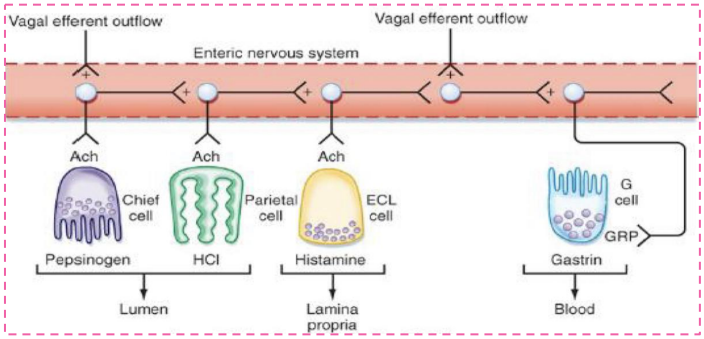






Effects of vagal activation on gastric secretion

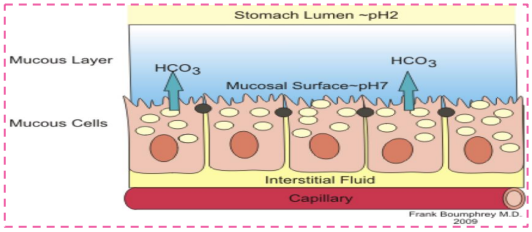
Summary
Postganglionic fibers of parasympathetic lie within ENS (found on wall of stomach). So activation of the parasympathetic system will stimulate the release of Ach -> which will act directly on chief cells, parietal cells and ECL cells. However, G cells are stimulated by GRP **not** Ach.



Other Gastric Secretions

1-Mucus:

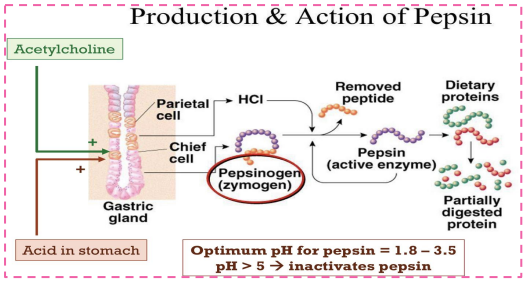
- Mucus cells secrete large quantities of viscid thick mucus that coats the muscle mucosa.
- The mucus is alkaline. **Which is rich in bicarbonate -> protects the stomach mucosa***.(Mucus is a protein and it can be degraded by digestive enzyme. So, it needs to be produced continuously because it gets degraded by pepsin)



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.



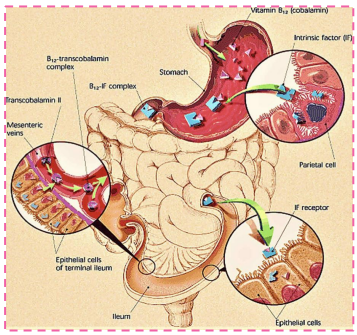
1- Chief cells in the gastric mucosa secrete pepsinogen (inactive form of pepsin)
2- Once pepsinogen reaches the lumen of the stomach, HCL will act on it.
3- HCL will activate pepsinogen -> pepsin (active enzyme)

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.

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.



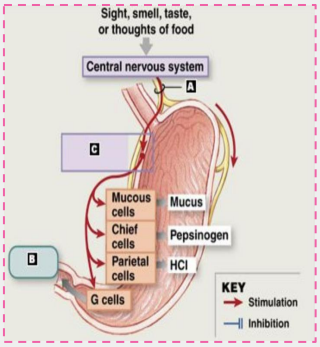
Parietal cells secrete IF along with HCL. The IF will hold onto B12 that entered the stomach with food, and protects it from being degraded by stomach acidity until they reach the terminal of the ileum "site of B12 absorption" -> IF will release vit. B12.
Any damage to parietal cells will result in anemia (no IF). -> B12 can't be absorbed -> effect on RBC synthesis and eventually will result in megaloblastic anemia (pernicious anemia)

Phases of Gastric 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:

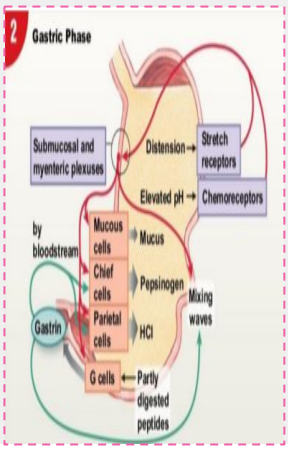
1 Cephalic phase:

- 30% of HCL is secreted in this phase.
- Before food arrives at stomach.
- Stimuli (Smelling, taste , Chewing and swallowing).
- Mechanism:
  - 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.



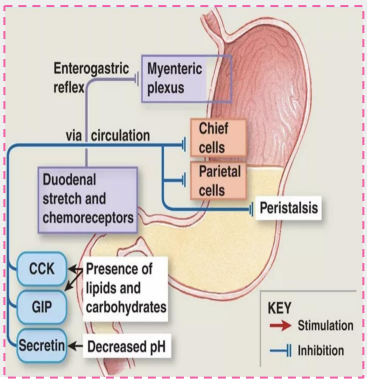
2 Gastric phase: Most important phase

- 60% of HCL is secreted in this phase.
- when food enters the stomach .
- Stimuli (distention , amino acid , small peptides).
- Mechanism :
  - 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.



3 intestinal phase: minimal effect

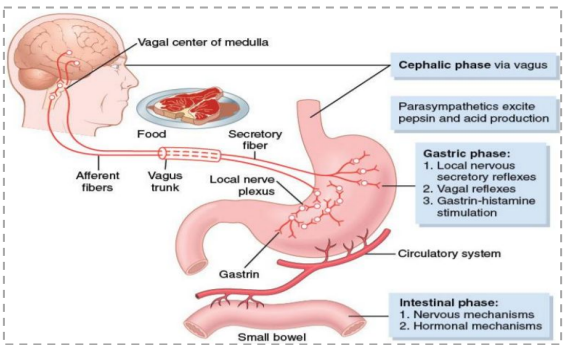
- 10% of HCL is secreted in this phase.
- when chyme enters duodenum.
- Stimuli (protein digestion products in the duodenum).
- Mechanism
  - protein digestion products in the duodenum stimulate gastric acid secretion through the action of the circulating amino acids on the parietal cells.
  - Distention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



Inhibition of Acid Secretion (Enterogastrones):*

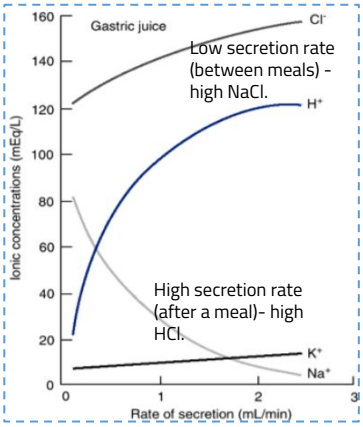
Picture in boys & girls slides

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



The Rate of Secretion **

- The Rate of Secretion Modify the Composition of Gastric Juice
- At a low secretion rate, gastric juice contains high concentrations of Na+ and Cl- and low concentrations of K+ and H+ .
- When the rate is increased:
- Na+ concentration decreases. Na+ secretion once stomach is empty is high -> makes NaCl secretion in interdigestive period (high)
- H+ concentration increases significantly.
- 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.
- Nonparietal 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

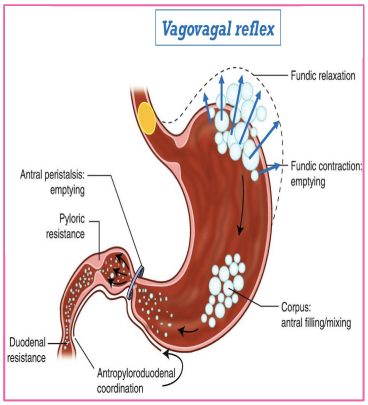
This means if we increase HCL production, that will not affect the osmolarity of secretion inside the stomach. This because having more HCL production inside the stomach after getting a meal will also increase water secretion toward the stomach (that's why we feel thirsty and we drink water after having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

Motor Function Of the Stomach

1-Storage of food:

Gastric filling

- 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.
- 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)

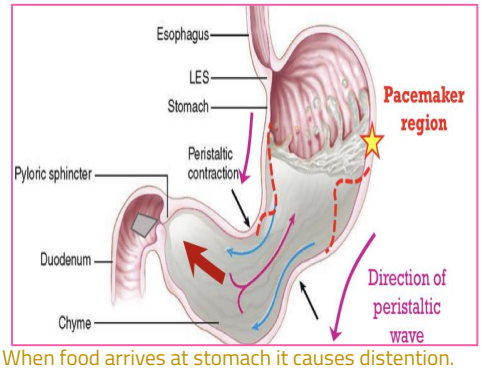


Empty stomach
50 ml

Full stomach
1000 ml

2-Mixing Propulsion of food: Gastric Mixing

- 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). ICC generates 3 slow waves per min.
- 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.

3-Regulate emptying of the chyme from the stomach into the small intestine (duodenum): Gastric Emptying

- 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**"
- **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.

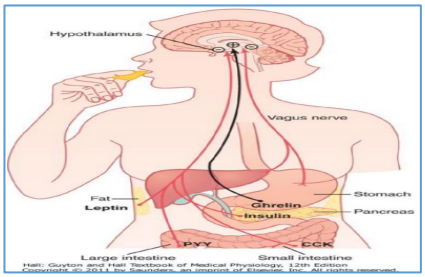
That's why once you have food between 2 contractions -> you want to mix it with digestive juices.
The leading contraction will start and squeeze food down.
If food particles are larger than 2mm, they will go back for further degradation which is done by contraction of pyloric sphincter (the leading contraction 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):

- To maintain a continuous compression.
- To accommodate the received food without significant gastric wall distention or pressure (Storage of food).

5-Hunger Contraction:

- 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.



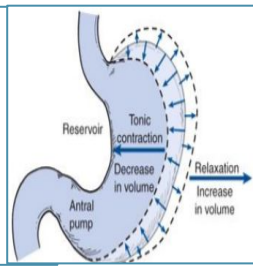
6-Absorption of water and a few highly-lipid soluble substances (alcohol and Aspirin):

- 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



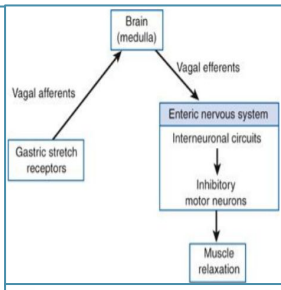
2-Feedback Relaxation:

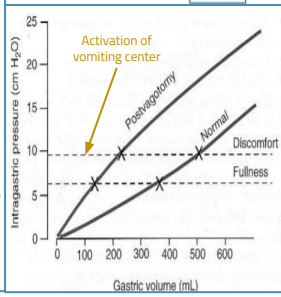
- **Triggered by:** presence of nutrients in the small intestine.
- It can involve both local reflex connections between receptors in the small intestine and the gastric ENS (Enteric nervous system).
- or hormones that are released from endocrine cells in the small intestinal mucosa and transported by 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**

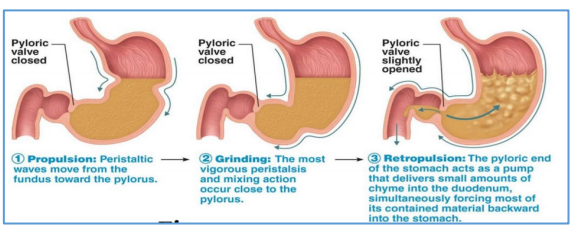
1

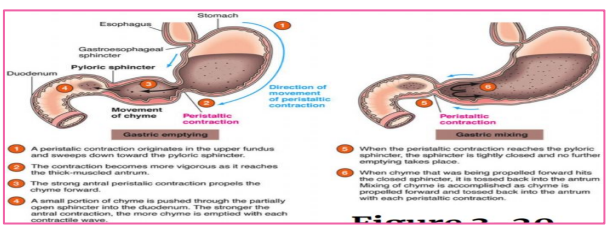
As the trailing contraction (explained later) approaches the closed pylorus, the gastric contents are forced into an antral compartment of ever-decreasing volume and progressively increasing pressure.

This will Results 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):

- 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 from the pacemaker site to the gastroduodenal junction.
- The pacemaker region in humans generates AP and associated antral contractions at a frequency of three per minute.
- 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:

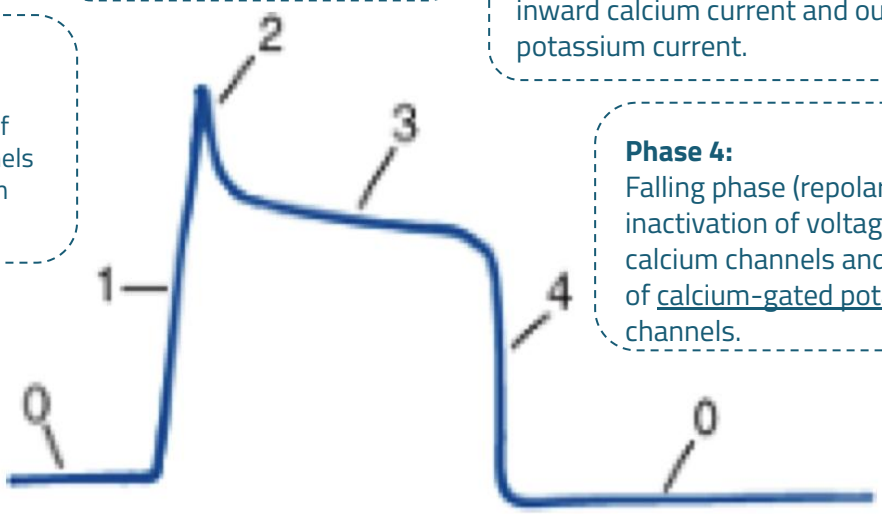
Phase 2: Initial repolarization. K+ efflux

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

Phase 1: Ca+2 influx Rising phase (upstroke depolarization) - Activation of voltage-gated calcium channels and voltage-gated potassium channels

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

Phase 0: Resting membrane potential; outward potassium current



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.

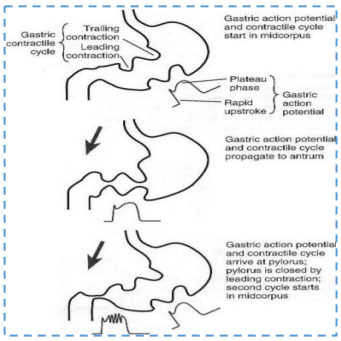
The Gastric Action Potential Triggers Two Kinds of Contractions *Males slides only*

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

Leading 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

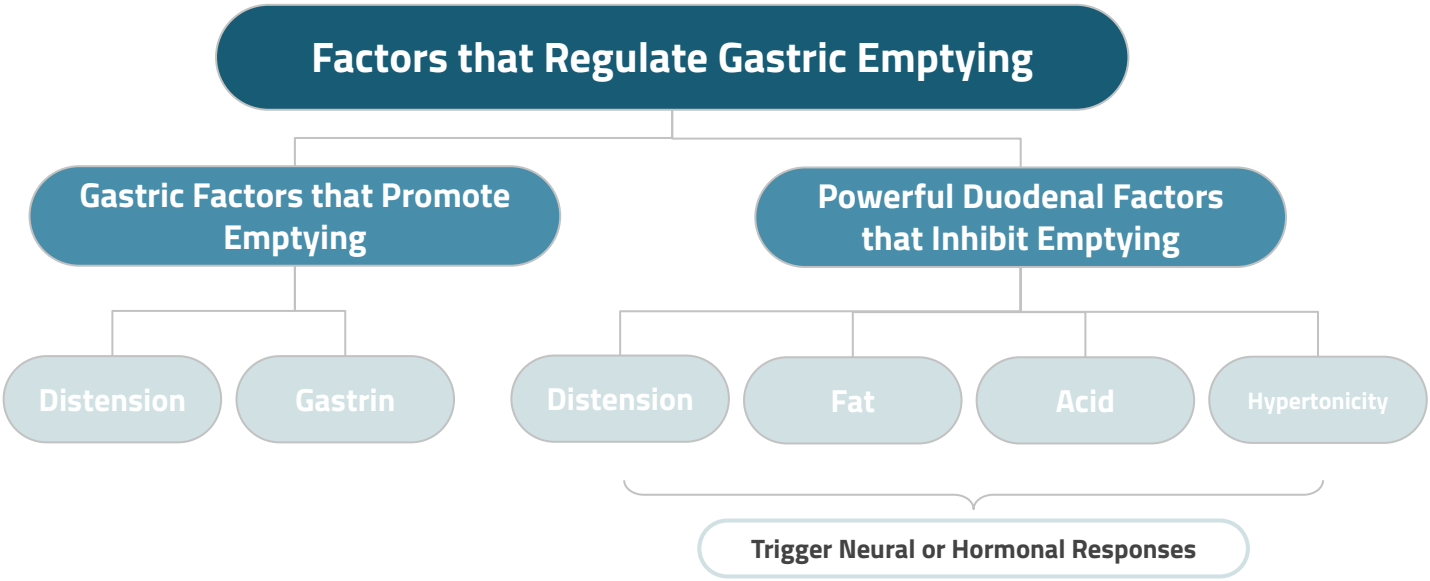
- The leading contractions have negligible amplitude as they propagate to the pylorus. As the rising phase reaches the terminal antrum and spreads into the pylorus, contraction of the pyloric muscle closes the orifice between the stomach and duodenum.
- The trailing contraction follows the leading contraction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



1-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: *Males slides only*

↑ 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: *Males slides only*

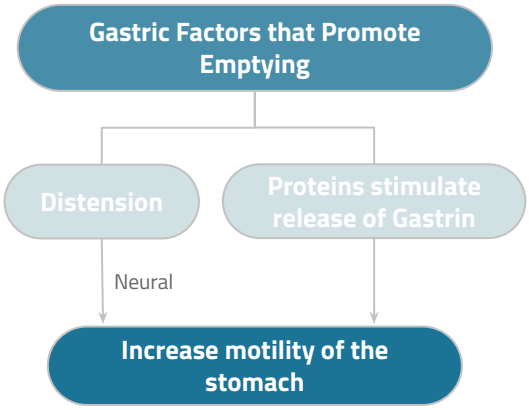
Gastric activates oxyntic cells to secrete GCL, ot also ↑ activity and motility of pyloric pump & Antrapump region = promote emptying.

- 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.
2. The proteins in the food stimulate the release of Gastrin.

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



This page is in the males slides only

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: *Males slides only*

- 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 distention.
  - 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.

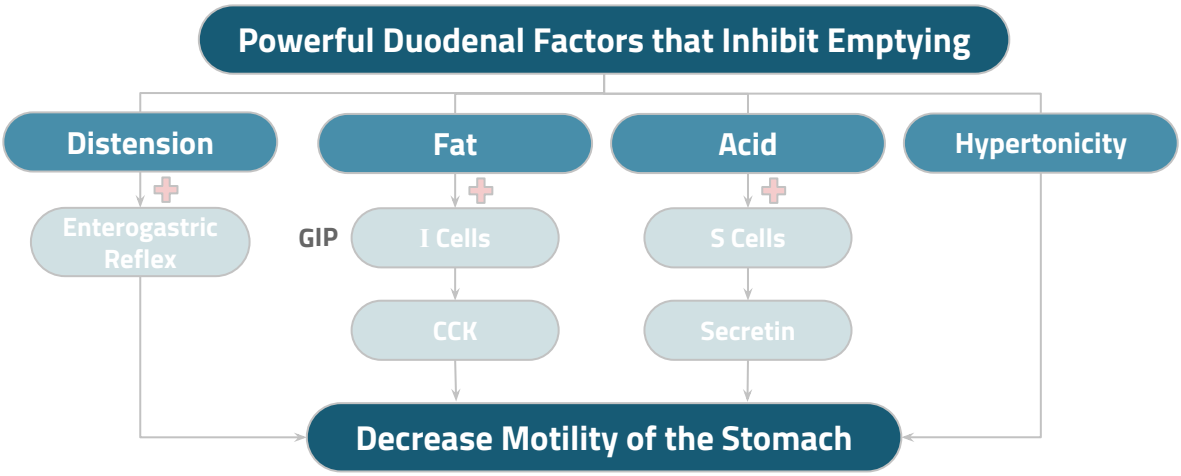
Very Important: **The Inhibitory Effect of Enterogastric Nervous Reflexes from the Duodenum is what causes the Feedback Relaxation** (Mentioned earlier).

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

- 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.

This page is in the females slides only

Stomach 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.

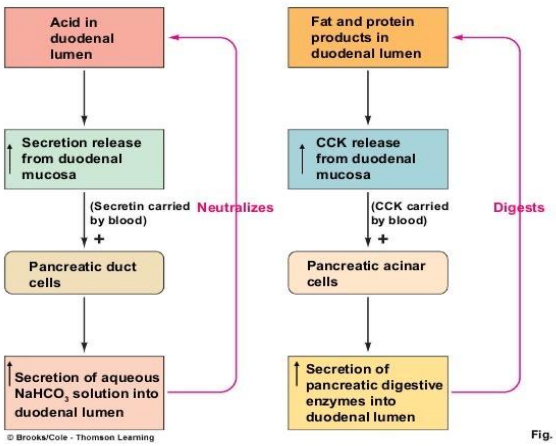
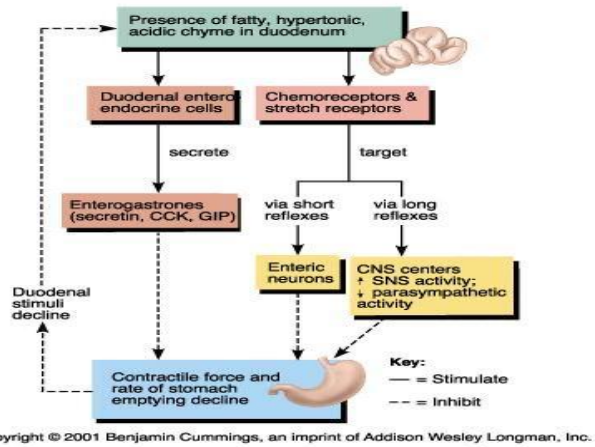


Fig.

Both images were Skipped



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.

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

Summaries

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:

- **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.

- **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.

- **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 hyposmotic 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>**
  - Cholecystokinin (CCK)
  - Secretin
  - Glucose-dependent insulinotropic peptide (GIP)
  - Sympathetic innervation

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

Summaries

Hormone	Site of Secretion	Stimuli for Secretion	Actions
Gastrin	G cells of the antrum, duodenum and jejunum	Protein Distention of the stomach Vagal stimulation (GRP) (Acid inhibits release)	**Stimulates:** -Gastric H+ secretion -Growth of gastric mucosa
Cholecystokinin (CCK)	I cells of the duodenum, jejunum, and ileum	Protein Fatty acids Acids	**Stimulates:** -Pancreatic enzyme secretion -Pancreatic HCO_3-secretion -Gallbladder contraction -growth of the exocrine pancreas -Relaxation of the sphincter of Oddi. **Inhibits:** gastric emptying
Secretin	S cells of the duodenum, jejunum, and ileum	Acids and Fat in the duodenum	**Stimulates:** -Pepsin secretion -Pancreatic HCO_3- secretion -Biliary HCO_3- secretion -Growth of the exocrine pancreas. **Inhibits:** Gastric H+ secretion
Glucose-Dependent Insulinotropic Peptide (GIP)	K cells of the Duodenum and jejunum	Protein Fatty acids Oral glucose	**Stimulates:** -Insulin secretion from pancreatic β cells **Inhibits:** Gastric H+ secretion
Motilin	M cells of the duodenum and jejunum	Fat Acid Nerve	**Stimulates:** -Gastric motility -Intestinal motility

MCQ & SAQ:

Q1: Which of the following cells secrete Pepsinogen

A. G cells
B. Peptic cells
C. Oxyntic Cells
D. Mucus cells

Q2: Which of the following is not Component of gastric Juice

A.HCL
B. Pepsinogen
C. Fatty acids
D. Intrinsic factor

Q3: When the rate of secretion increase the conc. of ..... decreases

A. Na
B. K
C. Cl
D. non of them

Q4: .Feedback relaxation trigger is

A. Swallowing reflex
B. Stretch receptors
C. Presence of nutrients in small intestine
D. non of them

Q5: Which of the following increases gastric emptying?

A.Distension of the duodenum
B.Duodenal Hypertonicity
C.Distention of the stomach
D.Decreased concentration of Gastrin

Q6: Which of the following is responsible for the Feedback relaxation?

A.Distension of the duodenum
B.Duodenal Hypertonicity
C.Distention of the stomach
D. Decreased concentration of CCK

answer key:
1: B
2: C
3: A
4: C
5: C
6: A

1- Mention the gastric glands and where are they located?

2- What are the kinds of relaxation occur in gastric reservoir?

3-Mention the duodenal factors that inhibit gastric emptying.

4- Brief description on the control of Hcl secretion .

A1: slide 5

A2: (1. Receptive relaxation 2. Adaptive relaxation 3. Feedback relaxation)

A3: Distension, presence of Acid, presence of Fat, Hypertonicity.

A4: slide 7

Leaders:

- Abdulaziz Alsuhaim.
- **Yara Alasmari.**

Co-leader:

- Mayasem Alhazmi.

Organizers:

- Rawan baqader
- Haya Alanazi
- Shaden Alobaid
- Mayasem Alhazmi.
- **Basel Fakeeha**
- Leen Almadhyani

Note takers:

- **Shaden Alobaid**
- Raghad Albarrak
- **Homoud Algadheb.**

Revisers:

- **Shayma Alghanoum**
- **Abeer Awwad.**

MEMBERS:

- Abdulaziz Alamri
- Basel Fakeeha
- Ahmad Alkhayatt
- **Aljoud Algazlan**
- Almaha Alshathri
- Abdulrahman Barashid
- Nada Bin Obeid
- Tarfa Alkaltham
- Yara alzahrani
- Sarah AlQuwayz
- **Abdulrhman Alsuhaibany**
- Abeer Awwad
- Mohammed alkathiri
- **Ziyad Alhosan**
- Rand Alrefaie
- Omar Alhalabi
- Joud Alarifi
- Ibrahim Alnamlah
- Hamad Almousa
- Abdullah Alburikan
- Leen Almadhyani
- Abdullah Alanzan
- Bader Alrayes
- Faisal jazzar
- Khalid Almutlaq
- Yara Alomar
- Reem Alqahtani
- Aljoharah Albnyan
- Saud Alhasani
- Muneerah Alsadhan

Physiology439@gmail.com