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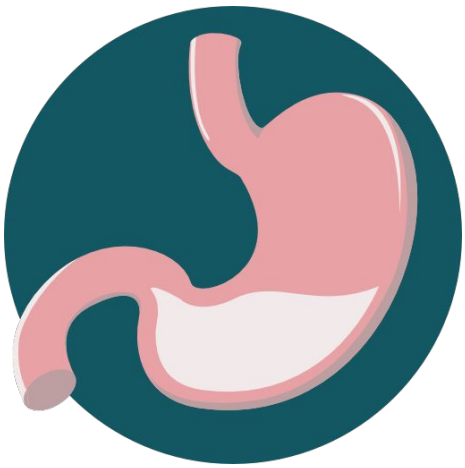

Physiology of the Stomach and Regulation of Gastric Secretions

Objectives:

- Functions of stomach
- Mechanism of gastric HCl formation
- Gastric digestive enzymes
- Control of gastric secretion
- Phases of gastric secretion
- Motor functions of the stomach
- Factors that affect gastric emptying

Done by:

- Team leader: Abdurhman Alhayssoni, Rahaf AlShammari
- Team members:
  - Reem ALQarni, Rahaf alshunaiber
  - Mohammed alhassan, Rinad alghoraiby
  - Yazeed alkhayyal, Abdullah alzaid
  - Danah alkadi, Alanoud alessa
  - Afnan almustafa, Ahad algrain

Revised By
Hadeel Awartani
Abdullah AlOmar

Colour index:
- Important
- Numbers
- Extra

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Functions of stomach

- **Stores food**
  - And regulates its passage to small intestine
  - The stomach does not through meal direct away to duodenum, the mechanism is regulated. Usually is slow emptying.
- **secrets juice**
  - Since it is partially, so we do not have a real digestion in stomach.
  - Liquefies & partly digests food
- **Endocrine function**
  - It produces gastrin and somatostatin
- **Produce intrinsic factor**
  - Necessary for vitamin B12 absorption
- **Gastric HCL**
  - 1)Kills ingested bacteria.
    2)Is necessary for iron & Ca++ absorption.
    3)Catalyzes cleavage of inactive pepsinogen into active pepsin

Divisions of the Stomach

Anatomical

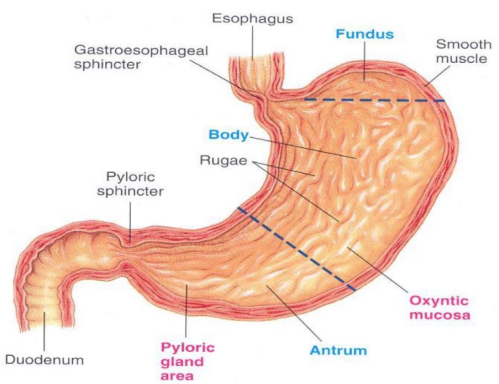
The stomach is composed of:

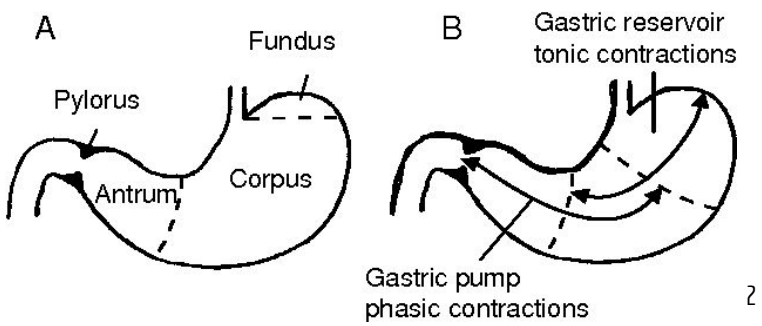
- Fundus
- Body
- Antrum

Physiological

The orad portion:
(fundus and upper two thirds of the body)
-Reservoir part (tonic contraction)

The caudal:
(lower third of the body plus antrum)
-Antral pump (phasic contraction)





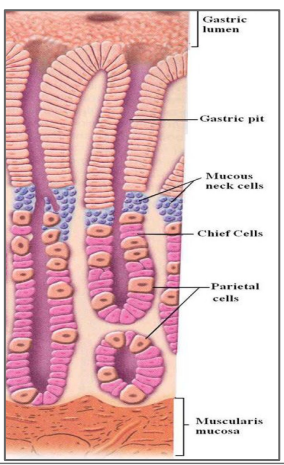
Gastric secretion

Histologically gastric mucosa is divided into 3 areas:-

1-cardiac area 10% Cardiac glands > Most of cells secrete mucus.
2-Pyloric area 15% Pyloric glands > Secrete mucus, pepsinogen + G-cells secrete gastrin + D Cells secrete somatostatin.
3-Main gastric area 70-80%: Oxyntic glands > HCl & intrinsic factor from parietal (oxyntic) cells Pepsinogen from peptic (chief) cells Mucus & HCO3- from mucous neck cells.

- Histamine is released from special neuroendocrine cells of the stomach called enterochromaffin-like (ECL) cells

Cell type	Location	secretion
Parietal cells	Body	HCL Intrinsic factor
Chief cells	Body	Pepsinogen
G cells	Antrum	Gastrin
Mucous cells	Antrum	Mucose Pepsinogen



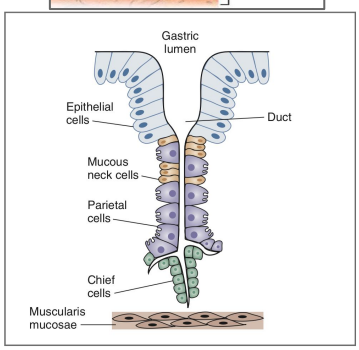
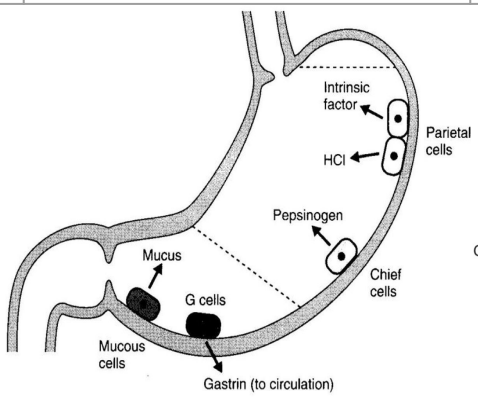


Fig. 8.16 **Structure of a gastric oxyntic gland showing the various cell types lining the gland.** The ducts open into pits on the surface of the gastric mucosa.



Structure of the Gastric Oxyntic Gland

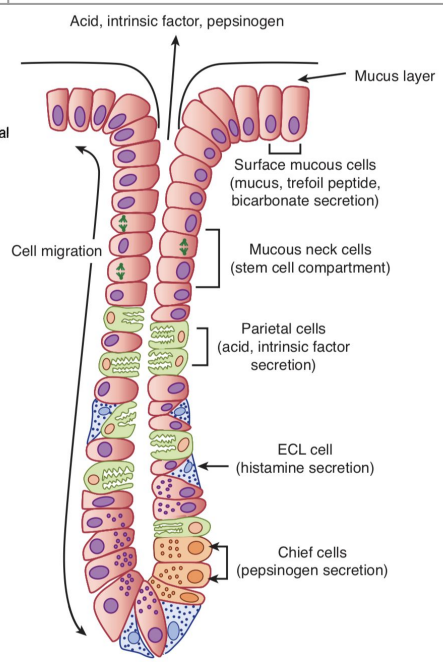


FIGURE 26–5 **Structure of a gastric gland from the fundus and body of the stomach.** These acid- and pepsinogen-producing glands are referred to as "oxyntic" glands in some sources. (Adapted from Barrett KE: *Gastrointestinal Physiology*. McGraw-Hill, 2006.)

Gastric juice

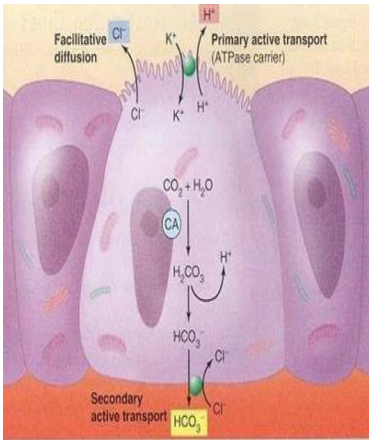
- volume 2-3L\day

Main Constituents

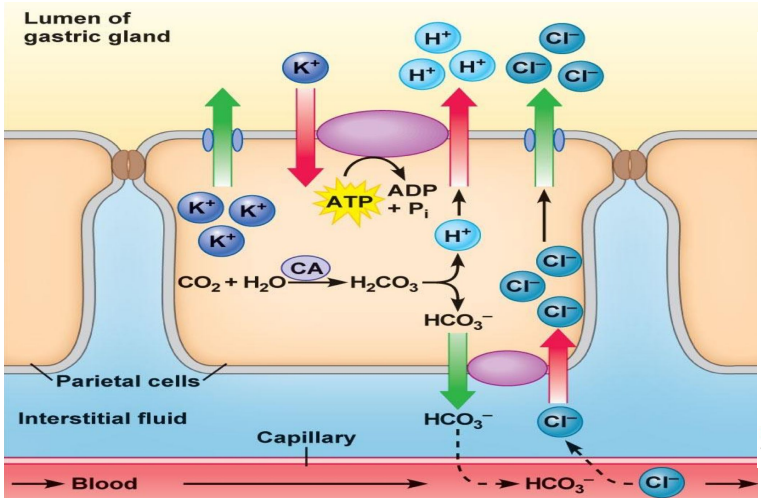
HCL | Enzyme | Mucus (gel layer) | Electrolytes | Intrinsic factor

Gastric HCL

- Parietal cells:
  - Are pyramidal in shape.
  - Have an abundance of mitochondria and intracellular canaliculi continuous with the lumen of the oxyntic gland.
  - Secrete HCl which flows out of the intracellular canaliculi into the oxyntic gland lumen.



Mechanism of gastric HCL formation



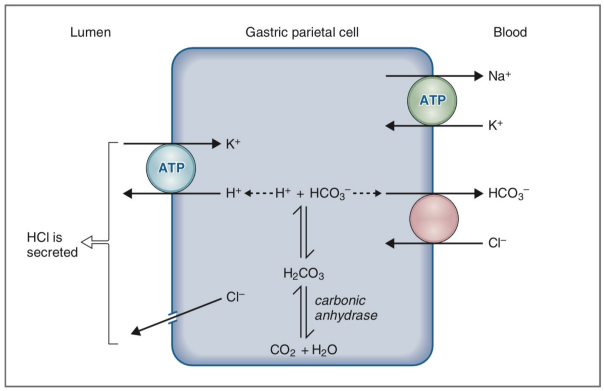


Fig. 8.17 Mechanism of HCl secretion by gastric parietal cells. *ATP,* Adenosine triphosphate.

Mechanism of gastric HCL formation

Cl- is actively transported from cytoplasm into luminal canaliculi

This create –ve potential which causes passive diffusion of K+from cytoplasm into canaliculi

Intracellular H2O dissociate into H++OH-

H+ is actively transported by H+-K+ ATPase which exchange H+ with K+. H/K pump depends on [K]out.

CO2 combines under the influence of carbonic anhydrase with the OH- to form HCO3-

HCO3- diffuses to plasma (Alkaline tide)and CL- enters via a carrier that facilitates exchange between the 2 ions.

This step can be Inhibited by proton pump inhibitors as omeprazole)

Control of HCl secretion at the level of parietal cells

Stimulation of parietal cells

- **Vagus nerve** (neural effector) (directly by Ach or indirectly by releasing gastrin releasing peptide, GRP).
- **Gastrin** (hormonal effector)
- **Histamine** (ECL cells) activates H2 receptor on parietal cells

H2 blockers (as cimetidine) are commonly used for the treatment of peptic ulcer disease or gastroesophageal reflux disease.

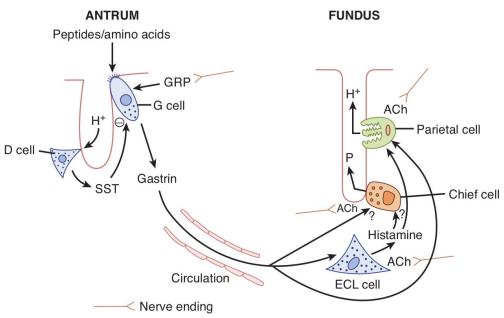
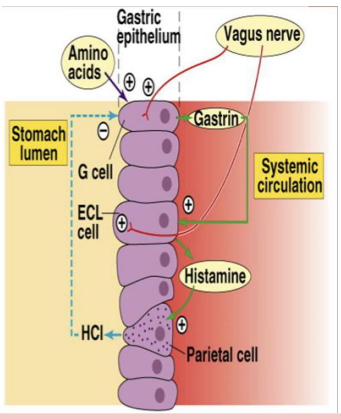


FIGURE 26–7 **Regulation of gastric acid and pepsin secretion by soluble mediators and neural input.** Gastrin is released from G cells in the antrum and travels through the circulation to influence the activity of ECL cells and parietal cells. The specific agonists of the chief cell are not well understood. Gastrin release is negatively regulated by luminal acidity via the release of somatostatin from antral D cells. (Adapted from Barrett KE: *Gastrointestinal Physiology*. McGraw-Hill, 2006.)



Agents that stimulate and inhibit H+ secretion by gastric parietal cells

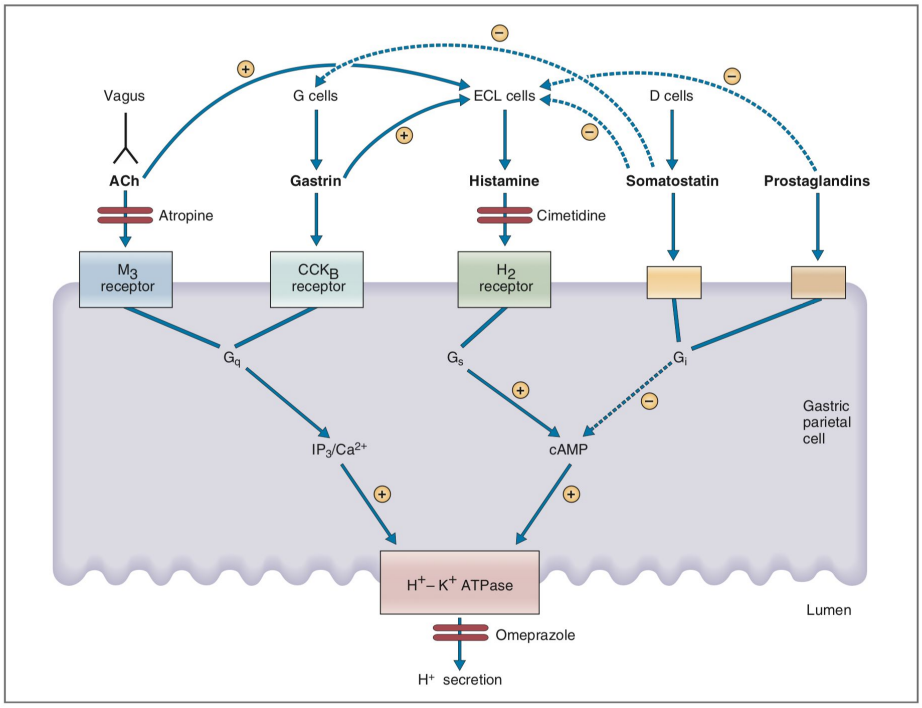


Fig. 8.18 **Agents that stimulate and inhibit H^+ secretion by gastric parietal cells.** *ACh*, Acetylcholine; *cAMP*, cyclic adenosine monophosphate; *CCK*, cholecystokinin; *ECL*, enterochromaffin-like; *IP_3*, inositol 1,4,5-triphosphate; *M*, muscarinic.

Watch from 5:21-7:21

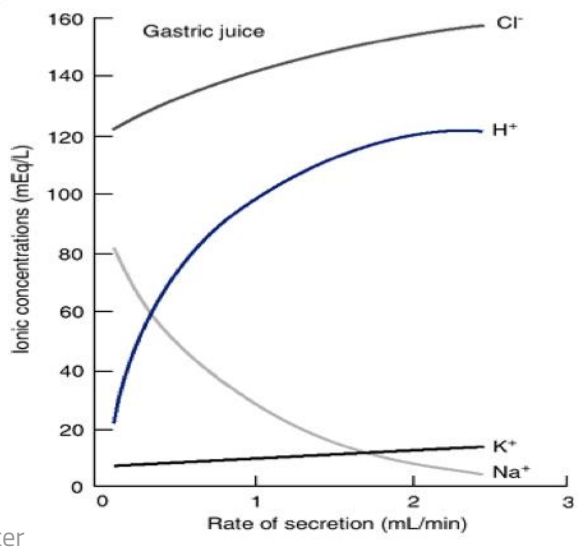
The Rate of Secretion Modifies the Composition of Gastric Juice

- The isotonic gastric juice is derived from the secretions of two major sources: parietal cells and non parietal cells.

-Secretion from non parietal cells is probably constant. Parietal HCl secretion contributes to the changes in electrolyte composition with changes of secretion rates.

-At a low secretion rate, gastric juice contains high concentrations of Na+ & Cl- and low concentrations of K+ & H+

-When the rate of secretion increases, the concentration of Na+ decreases whereas that of H+ & Cl- increases significantly.



- Low secretion rate (between meals) -high NaCl.
- High secretion rate (after a meal)- high HCl.
- Always isotonic. Because membranes are permeable for water which maintains osmolarity.

Gastric digestive enzymes

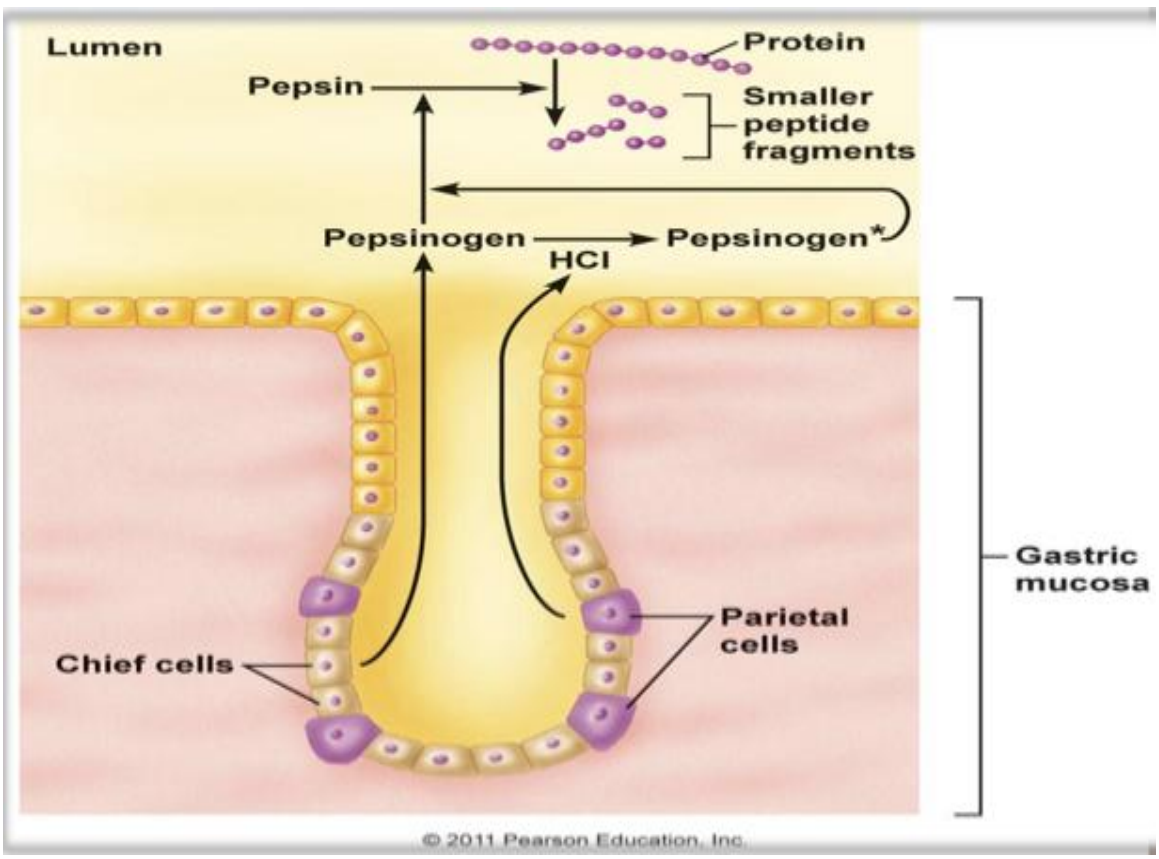
Pepsin

- Pepsinogen is activated by HCL into pepsin.
- Pepsin can activate more pepsinogen
- The optimum pH is 1.5 - 3.5
- Pepsin breaks down proteins into peptones and polypeptides
- Pepsinogen secretion is stimulated by Ach,acid,gastrin, Secretin and CCK

Lipase

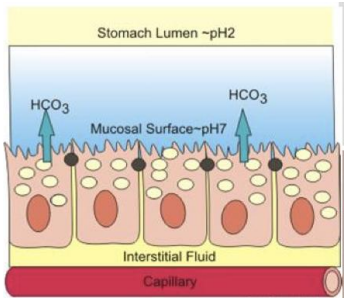
- Secreted from fundic mucosa
- It hydrolyzed TG into MG and FA
- It's activity is less than pancreatic lipase

Pepsinogen activation in the stomach lumen



Gastric Mucus

- Its glycoprotein (0.2 mm thick), separate surface epithelial cells from acidic contents .
- It protects the mucosa against :

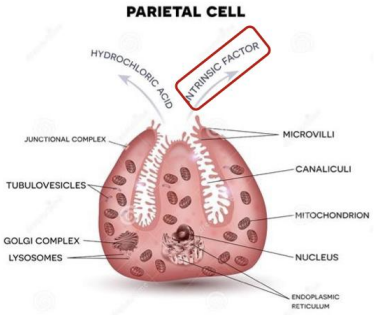


- mechanical injury by lubricating the chyme
- Chemical injury by acting together with HCO3- as a barrier to HCL and pepsin, it also neutralize HCL and arrest action of pepsin .

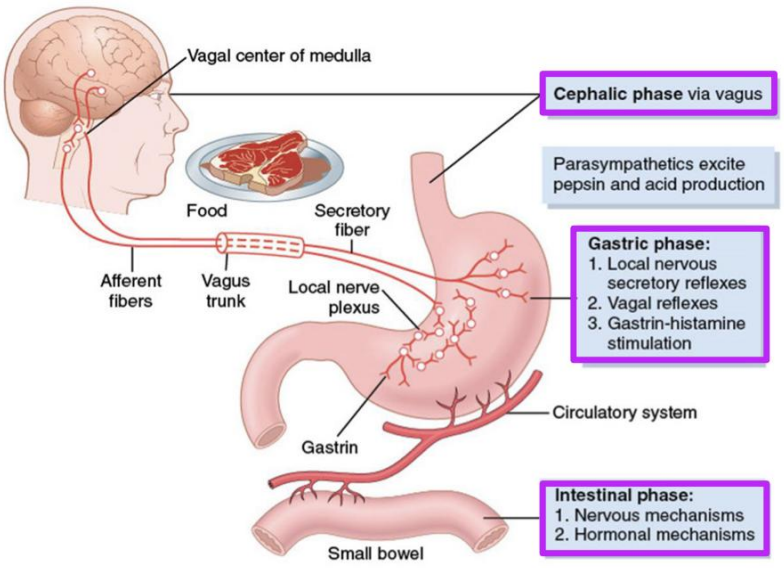
- Aspirin and nonsteroidal anti-inflammatory agents inhibit secretion of mucus and HCO3,prolonged use of these drugs may produce gastritis or ulcer .

Intrinsic Factor

- It's a glycoprotein secreted by parietal cells
- It's the only essential function of stomach as it's essential for vitamin B12 absorption
- Atrophy of gastric mucosa leads to pernicious anemia



Phases of Gastric Secretion



Gastric Secretion Occurs in Three Phases

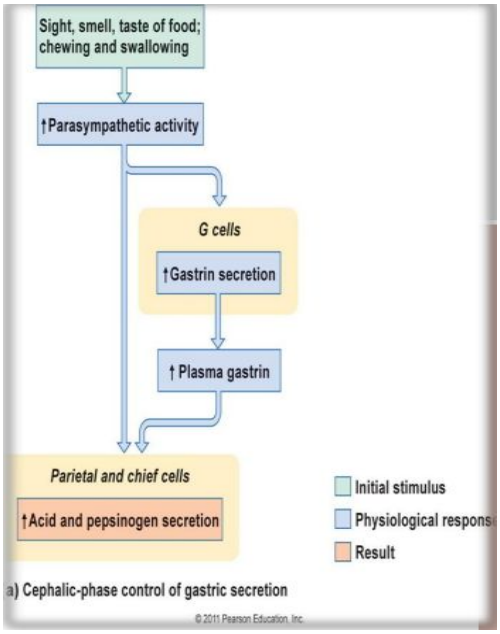
	Cephalic (30%)	Gastric (60%)	Intestinal (10%)
2 Stimuli	Smell, taste, conditioning	Distension, amino acids, small peptides	Duodenal distension AA, small peptides
3 Mechanism	• Vagus → parietal cells • Vagus → gastrin → parietal cells	• Local reflex → gastrin → parietal cells • Gastrin → parietal cells	• Vagus → parietal cells Enterogastrone

1. The Cephalic Phase

●Seeing, smelling, chewing, and swallowing food send afferent impulses to vagal nucleus which sends impulses via the vagus nerves to parietal, chief and "G" cells in the stomach.

●The nerve endings release ACh, which directly stimulates acid secretion from parietal cells.

●The nerves also release gastrin-releasing peptide (GRP), which stimulates "G" cells to release gastrin (nerves indirectly stimulate parietal cell acid secretion).



2. The Gastric Phase

Most important phase because majority of HCl secretion occurs here.

- It is mainly a result of gastric distention and chemical agents such as digested proteins. It is mediated by nervous & hormonal mechanisms

Nervous	Hormonal (Gastrin hormone)	Gastrin stimulates

- Distention of the stomach stimulates mechanoreceptors, which stimulate the parietal cells directly through short local (enteric) reflexes and by long vago-vagal reflexes.

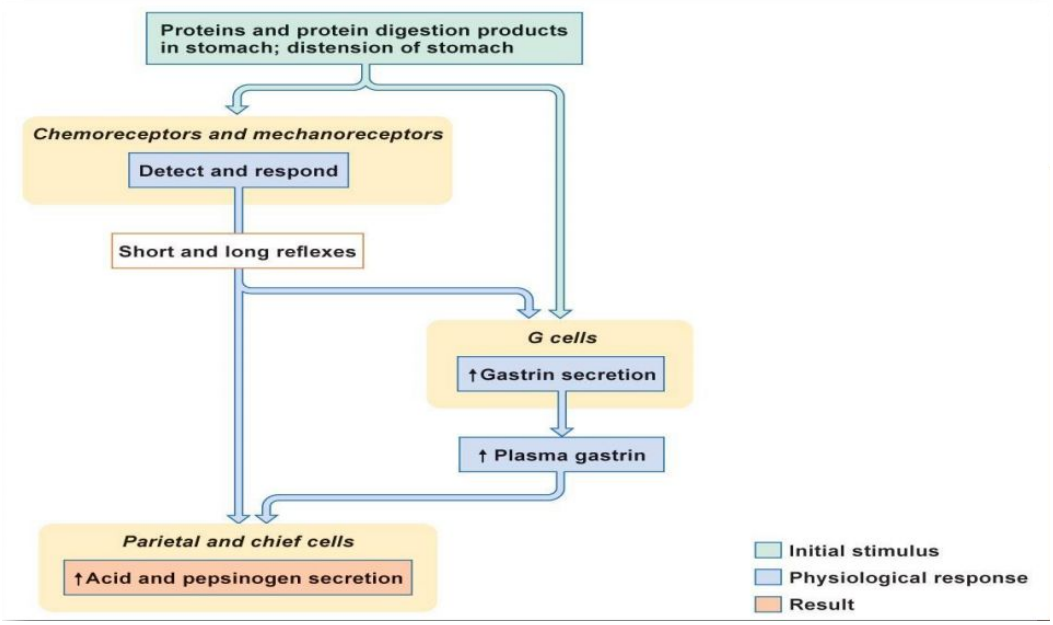
- Digested proteins in the stomach stimulates gastrin hormone release from "G" cells in antrum

Other Stimuli:

1. Gastric distension
2. Vagal excitation.
3. Rising of pH of gastric juice.

1-Gastric acid, pepsin and intrinsic factor secretion.
2-Intestinal secretion.
3-Pancreatic secretion of enzyme & HCO3 - .
4-Biliary secretion of HCO3 - & H2O.
5.Gastric motility.
6-Intestinal motility
7.Relaxation of ileocaecal sphincter.
8-Contraction of LES.
9-Trophic effect on gastric mucosa.

Gastric Phase Control of Gastric Secretion



3. The intestinal Phase

- It is mainly a result of protein digestion products in the duodenum and duodenal distension

1-Protein digestion products stimulate gastric acid secretion through the action of the circulating amino acids on the parietal cells.

2-Distention of the duodenum stimulates acid secretion by means of vagovagal reflex and via the release of the hormone entero-oxyntin from intestinal endocrine cells.

Inhibition of Gastric Acid Secretion

Enterogastrones
Are hormones released from intestine and decrease gastric acid secretion

e.g. Somatostatin (D-cells) in antrum, Secretin (Scells) in duodenum, Glucose-dependent insulinotropic peptide (GIP) in duodenum.

Stimuli for their release: drop the pH in pyloric antrum to < 2.5, the presence of acid, fat, protein digestive products, hypertonic solution in upper intestine

The functional purpose of the inhibition of gastric acid secretion by intestinal factors is to slow the release of chyme from stomach when the small intestine is already filled.

Helpful videos

- https://youtu.be/pqgcEIaXGME

Crash course

- https://youtu.be/raPhtaTmxNk

Watch from 10:47 till 21:36

- https://youtu.be/NIbclTo3duU

Ninja nerd: The cephalic & Gastric phase

- https://youtu.be/9UFiapkutFI

The intestinal phase

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 and 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, and 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, and 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

Motor Functions of the Stomach

The main motor functions of the stomach are:

1. Storage of large quantities of food
2. Preparing the chyme for digestion in the small intestine.

(Chyme is a semi-fluid or paste composed of food that is thoroughly mixed with gastric secretions)

3. Absorption of some water and lipid-soluble substances (alcohol and drugs)
4. Regulate emptying of the chyme from the stomach into the small intestine

Motor Functions of the Stomach

Upper part of the stomach (Reservoir part)

- The main functions of the upper part of the stomach:

1. To maintain a continuous compression (tonic contraction).beside to give stomach enough time to expose bolus to HCl.

2-To accommodate the received food without significant gastric wall distention or pressure (Storage of food).

- The stomach can store 0.8-1.5 L of food.

Antral pump region (Phasic contraction)

- Mixing waves, initiated by the basic electrical rhythm progress from the body to the antrum and become intense forcing the chyme toward the pylorus.
- Each time a wave passes from antrum to pylorus, few millimeters of antral content move into the duodenum through the pyloric sphincter.

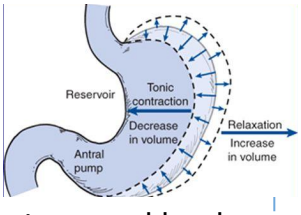
Types of Motor Activity of the Reservoir Part

Three Kinds of Relaxation Occur in the **Gastric Reservoir**:

As we have tonic contraction in reservoir part of stomach, how it can be relaxed. It is relaxed by 3 mechanism as follows. These mechanisms aim to accommodate food and keep it for long time.

A- Receptive Relaxation | B- Adaptive Relaxation | C- Feedback Relaxation

A- Receptive Relaxation

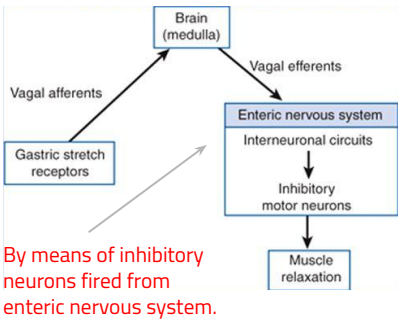


- Triggered by swallowing reflex.
- When the esophageal peristaltic waves reach the stomach, a vagovagal reflex is initiated from the stomach to the brain stem and back to the muscular wall of the stomach.
- This results in reduction in muscular wall tone and the stomach relaxes through inhibition of myenteric neurons.

B- Adaptive Relaxation

More important

- Triggered by stretch receptors when food stretches the stomach.
- A "vagovagal reflex"reduces the tone in gastric muscular wall so that the wall bulges outward, accommodating greater quantities of food up to a limit (0.8 to 1.5 L).
- This reflex is lost in vagotomy.



C- Feedback Relaxation

Isn't a vagovagal reflex

- Triggered by the presence of nutrients in the small intestine causing feedback relaxation.
- It can involve:
  - Local reflex connections between receptors in the small intestine and the gastric ENS.
  - Hormones that are released from endocrine cells in the small intestinal mucosa and signal the gastric ENS and stimulate firing in vagal afferent terminals in the stomach.

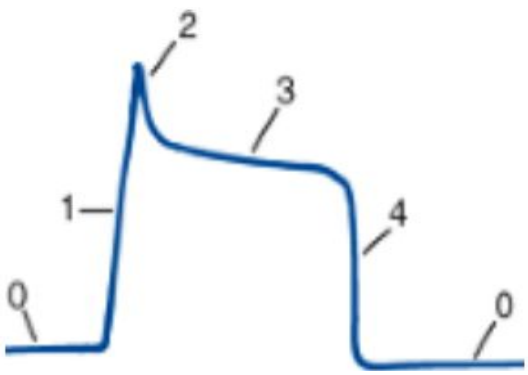
Motor Behavior of the Antral Pump

- Gastric action potentials determine the duration and strength of the phasic contractions of the antral pump.
- They are initiated by a dominant pacemaker (ICC).
- The action potentials propagate rapidly around the gastric circumference and trigger a ring-like contraction.
- The action potentials 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 action potentials and associated antral contractions at a frequency of 3/min and lasts about 5 seconds.

Gastric Action Potentials

Electrical action potentials in gastrointestinal muscles occur in 4 phases:

- **Phase 0:** Resting membrane potential.
- **Phase 1:** Rising phase (upstroke depolarization); activation of voltage-gated Ca++ channels and voltage-gated K+ channels. .
- **Phase 3:** Plateau phase; balance of inward Ca++ current and outward K+ current.
- **Phase 4:** Falling phase (repolarization); inactivation of voltage-gated Ca++ channels and activation of voltage-gated K+ channels.



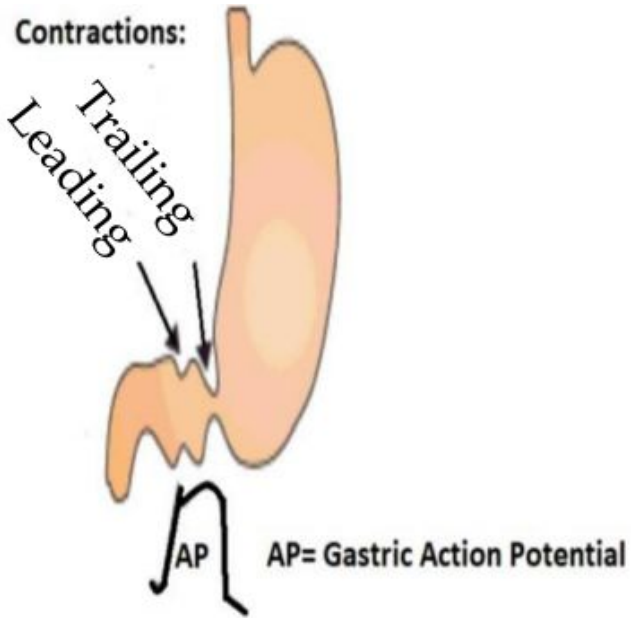
The Gastric Action Potential Triggers Two Kinds of Contractions

1) A leading contraction:

which has relatively constant (negligible amplitude), is associated with the rising phase of the action potential.
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.

2) A trailing contraction:

of variable amplitude, is associated with the plateau phase. It follows the leading contraction by a few seconds.

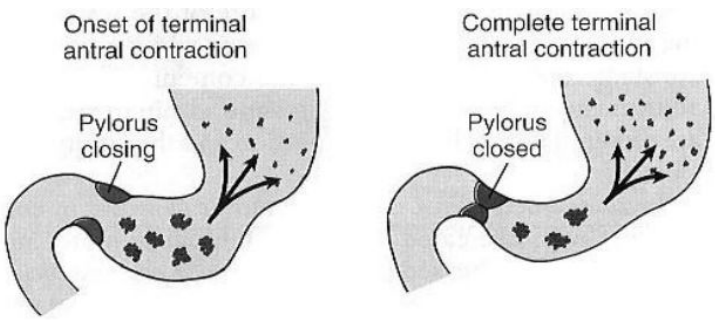


Doctor's summary: 3 slow waves are generated every minute. Each slow wave can give 1-10 spikes. Each spike represent an action potential(AP). Each AP can give two contraction (leading and trailing). Each AP lasts for 5s which is very long to guarantee enough Ca can influx. Depolarizing phase (phase 1) shows leading contraction. Plateau phase (phase 3) shows trailing contraction which is stronger than leading contraction because Ca influx more in plateau phase.

Retropulsion Phenomena:

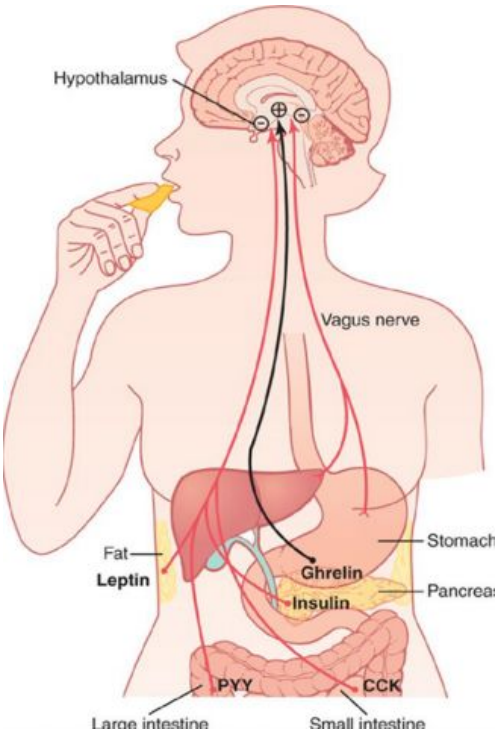
As the trailing contraction approaches the closed pylorus, the gastric contents are forced into the antrum. This results in jet-like retropulsion through the pyloric orifice at 3 cycles/min to reduce particle size before they can be emptied into the duodenum. These intense peristaltic contractions increase the pressure in the stomach.

Dr's note :When a food particle is not below 7mm , it cannot pass pyloric sphincter is closed by leading contraction. So, it has to returned to upper stomach by trailing contraction for further breaking down.(retropulsion)



Hunger Contractions

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

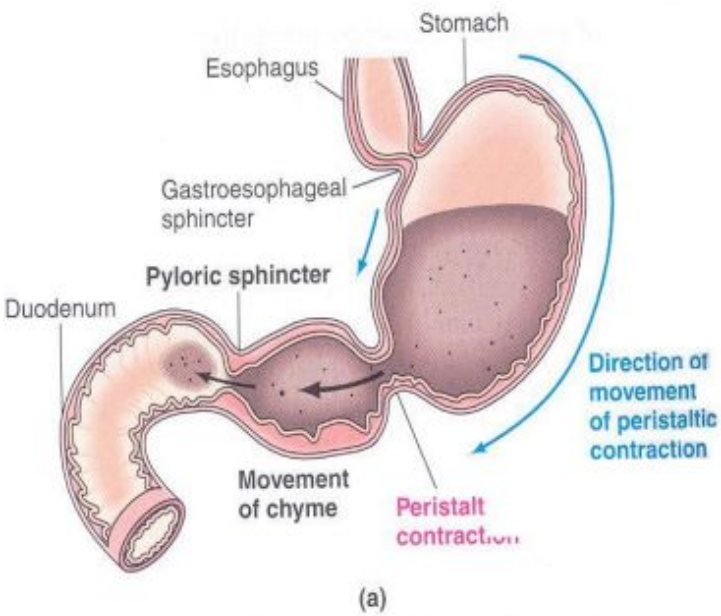


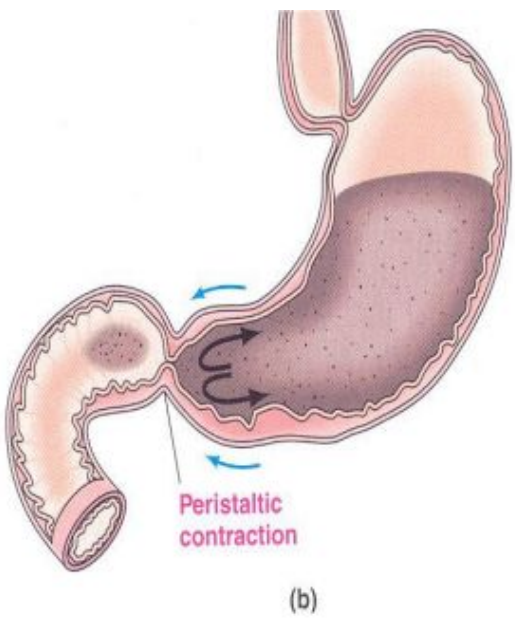
Gastric Emptying

Results from intense peristaltic antral contractions against resistance to passage of chyme at the pylorus. Gastric emptying is regulated by 2 factors (gastric and duodenal).

- The rate of stomach emptying is controlled by signals from the duodenum and stomach.
- The signals from the duodenum are far stronger and control emptying of chyme at a rate that allows the proper digestion and absorption in the small intestines.

Gastric Emptying & Mixing as a Result of Antral Peristaltic Contraction





Factors Control Gastric Emptying

Gastric Promoting Factors 2 Factors
An increase in gastric food volume results in increased stretch in the stomach wall and increased stomach emptying. Increasing of gastric volume lead to increase gastric emptying.
Gastrin hormone moderately increases the activity of the pyloric pump and motor stomach function and probably promotes stomach emptying. فيها اختلافات بعض الكتب يقولون انها تهبط السفينكتر والبعض يقول انها تحفز

Duodenal Factors that Initiate Enterogastric Inhibitory Reflexes
Distention and irritation
Acidity: releases secretin which constricts the antrum
Hyperosmotic or hypoosmotic chyme
Protein content of the chyme
Fat activates CCK & GIP release that increase pyloric sphincter tone

Summary

(Constriction of Pyloric Sphincter)

- Hormones promote constriction of pyloric sphincter & inhibit gastric emptying:
    - Cholecystokinin (**CCK**)
    - Secretin
    - Glucose-dependent Insulinotropic Peptide (**GIP**)
- Sympathetic innervation

Summary

Types of Motor Activity of the Reservoir Part			
	Receptive Relaxation	Adaptive Relaxation	Feedback Relaxation
Triggered by	swallowing reflex.	stretch receptors	the presence of nutrients in the small intestine
Notes	When the esophageal peristaltic waves reach the stomach, a **vagovagal reflex** is initiated from the stomach to the brain stem and back to the muscular wall of the stomach.	A "**vagovagal reflex**"reduces the tone in gastric muscular wall so that the wall bulges outward, accommodating greater quantities of food up to a limit (0.8 to 1.5 L).	**It can involve:** **-**Local reflex connections -Hormones that are released from endocrine cells in the small intestinal mucosa

Motor Functions of the Stomach	
Upper part of the stomach (Reservoir part)	Antral pump region (Phasic contraction)
-maintain a continuous compression -accommodate the received food without significant gastric wall distention or pressure	-Mixing waves, initiated by the basic electrical rhythm progress from the body to the antrum and become intense forcing the chyme toward the pylorus.

Factors Control Gastric Emptying	
Gastric Promoting Factors	Duodenal Factors that Initiate Enterogastric Inhibitory Reflexes
An increase in gastric food **volume** results in increased stretch in the stomach wall and increased stomach emptying. Gastrin **hormone** moderately increases the activity of the pyloric pump and motor stomach function and probably promotes stomach emptying.	-Distention and irritation -Acidity: releases secretin which constricts the antrum -Hyperosmotic or hypoosmotic chyme -Protein content of the chyme - Fat activates CCK & GIP release that increase pyloric sphincter tone

MCQs

1.Where can we find the oxytocin glands?

A. Cardiac area
B. Pyloric area
C. Main gastric area
D. B+C

2.Which one of the following is the hormonal effector that stimulates the parietal cells?

A. Histamine
B. Gastrin
C. Ach
D. Vagus nerve

3.When the rate of secretion increase the conc. of ..... increase.

A. Na
B. K
C. Cl
D. A+C

4.A patient diagnosed with gastric mucosal atrophy,he may develop:

A. Pernicious anemia
B. Megaloblastic anemia
C. PUD
D. GERD

5.Stimulation of gastric and intestinal motility occur due to stimulation of which hormone?

A. Gastrin
B. CCK
C. Motilin
D. A+C

6.Feedback relaxation trigger is

A. Swallowing reflex
B. Stretch receptors
C. Presence of nutrients in s.intestine

7.When does the hunger pain start?

A. 6H after meal
B. 10H after meal
C. 12H after meal
D. 35H after meal

8.Which one of the following best describes the function of gastric emptying:

A. Acidification of the Antrum increase gastric empyting
B. Meals containing fat empity faster than carbohydrates
C. Hyperosmolality Of deudenal initiate decrease in gastric emptying
D. Vagal stimulation decrease receptive relaxation in the upper portion of the stomach

SAQ

1.What're the kinds of relaxation occur in gastric reservoir?

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

2.Write 2 of main motor functions of stomach.

1. Storage large quantities of food.
2. Preparing the chyme for digestion.

Answers:
1. C
2. B
3. C
4. A
5. D
6. C
7. C
8. C