# Gastrointestinal Physiology

# Lecture 4

## *Physiology of the Stomach and Regulation of Gastric Secretions*

**Chapter 63; pages 765-768**

**Chapter 64; pages 777-780**

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# Learning Objectives

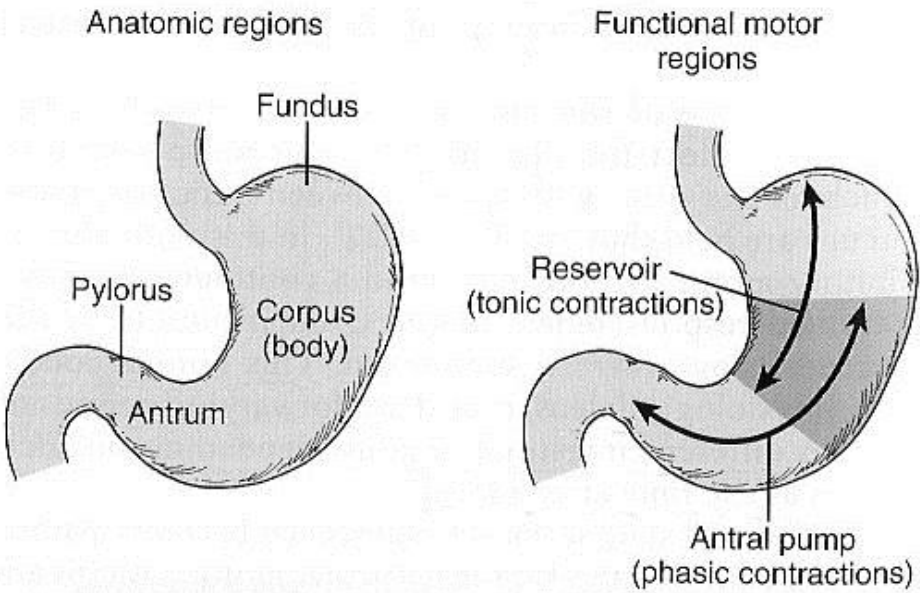
- Functions of stomach
- Gastric secretion
  - ✓ Mechanism of HCl formation
  - ✓ Gastric digestive enzymes
  - ✓ Neural & hormonal control of gastric secretion
  - ✓ Phases of gastric secretion
- Motor functions of the stomach
- Stomach Emptying
  - ✓ Gastric factors that promote stomach emptying
  - ✓ Duodenal factors that inhibit stomach emptying

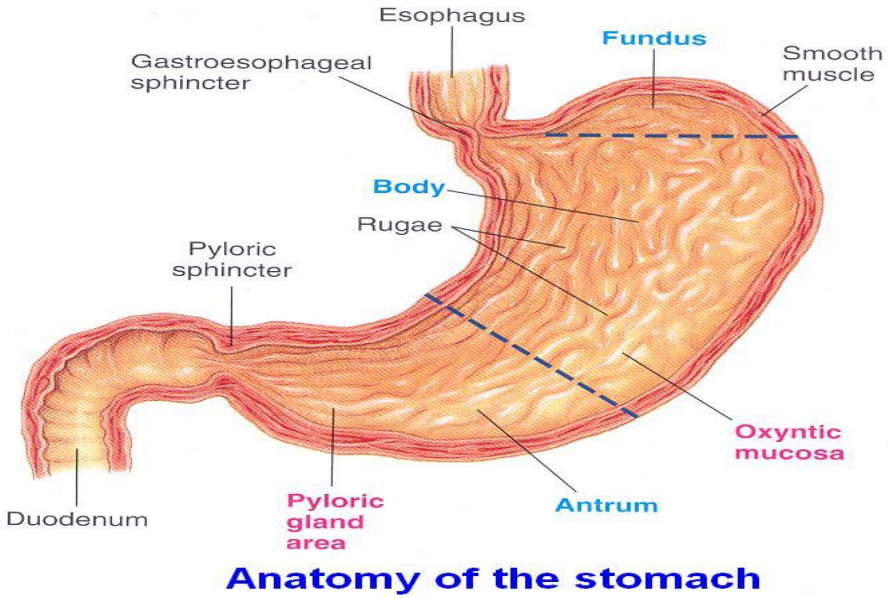
# Anatomical and Physiological Divisions of the Stomach

**Anatomically** the stomach is composed of the fundus, body and the antrum.

**Physiologically,** it is composed of :

- **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).




Anatomy of the stomach

# Functions of stomach

1- It stores food & regulates its passage to small intestine.

2- It secretes juice that liquefies & partly digests food.

3- It produces intrinsic factor necessary for vitamin $B_{12}$ absorption.

4- Gastric HCl:

- ✓Kills ingested bacteria.
- ✓Is necessary for iron & $Ca^{++}$ absorption.
- ✓Catalyzes cleavage of inactive pepsinogen into active pepsin.

7- Absorption of some water and lipid-soluble substances.

8- It has endocrine function, e.g. It produces gastrin and somatostatin.

# Gastric Secretion

**Histologically gastric mucosa is divided into 3 areas:-**

1- *The cardiac area (10 % of mucosa)*

Most of cells secrete mucus.

2- *The main gastric area (70-80 %)*

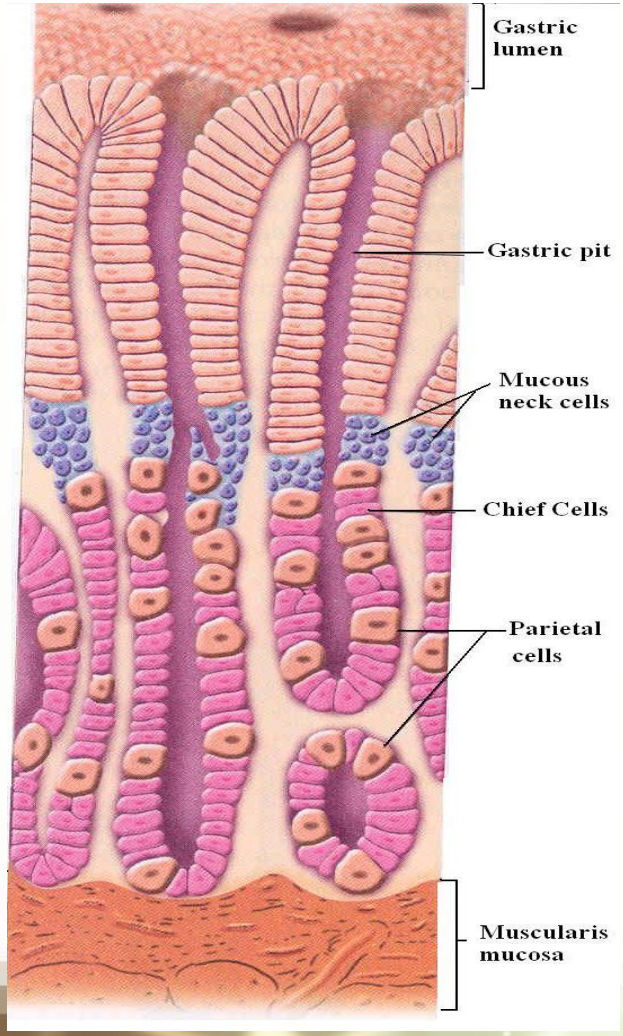
The glands in mucosa of fundus & body secrete:

- HCl & intrinsic factor from parietal (oxyntic).
- Pepsinogen from peptic (chief) cells.
- Mucus & $HCO_3^-$ from mucous neck cells.

3- *The pyloric area (15 %)*

Most of its cells are mucous cells.

Contains G- cells that secrete gastrin.



# *Gastric Juice*

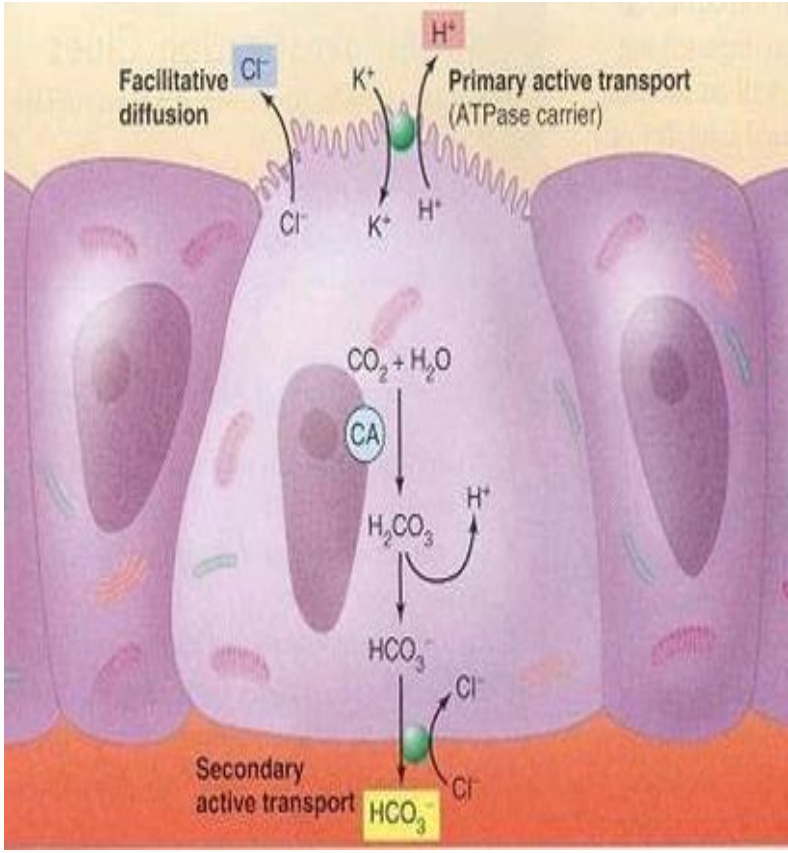
Volume about 2-3 L/day

Main constituents are:

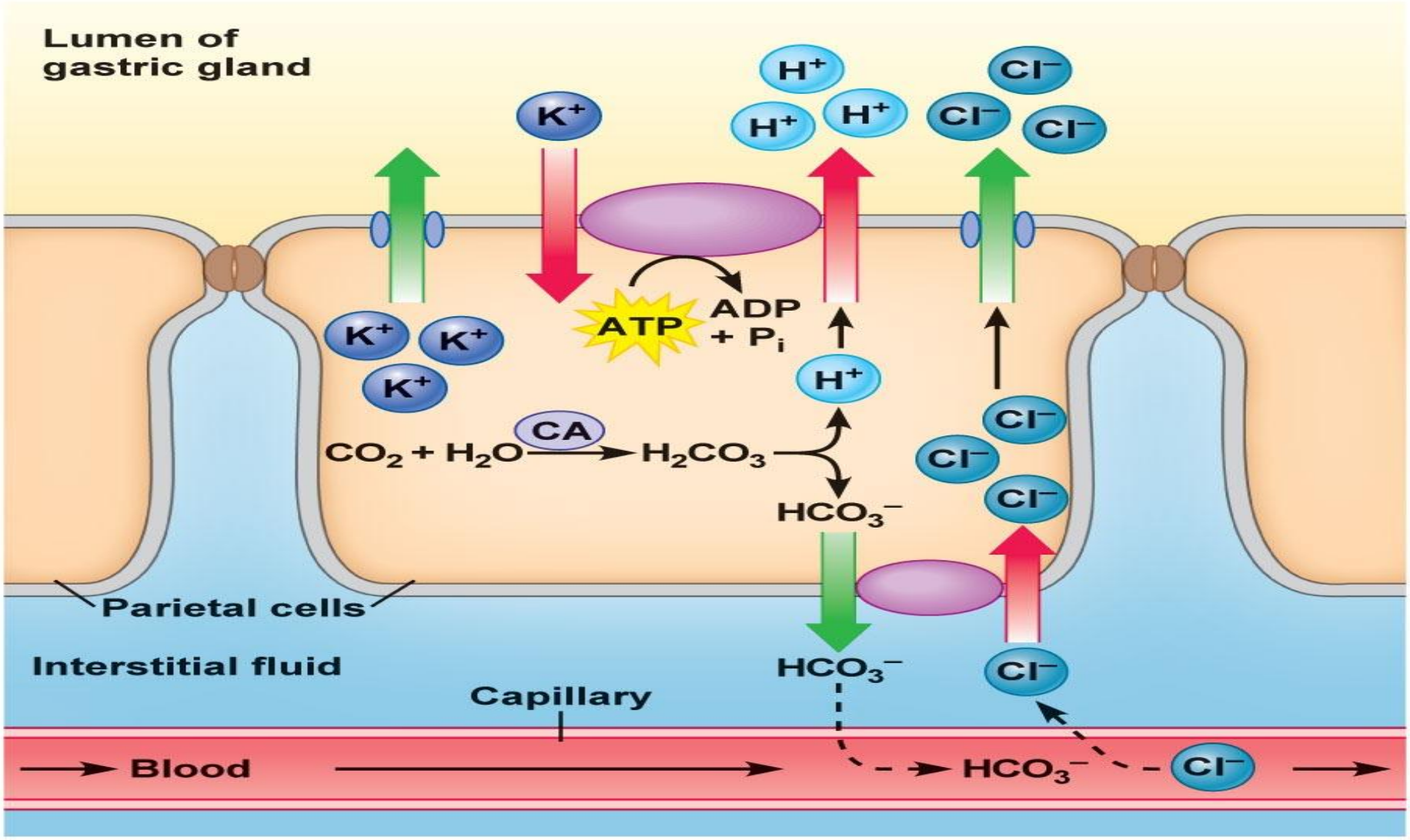
- HCl
- Digestive enzymes (Pepsinogen)
- Mucus (mucus gel layer)
- Electrolytes
- Intrinsic factor.

# Gastric HCL

- Secreted by **parietal cells**.
- They are pyramidal in shape.
- They have an abundance of mitochondria and intracellular canaliculi that are continuous with the lumen of the oxyntic gland.
- HCl is secreted and flows out of the intracellular canaliculi into the oxyntic gland lumen.



# Mechanism of HCl formation



## Mechanism of 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 $H_2O$ dissociates into $H^+$ & $OH^-$.
- $H^+$ is actively transported across canalicular membrane against concentration gradient by $H^+$-$K^+$ ATPase which exchange $H^+$ with $K^+$. It can be inhibited by omeprazole (proton pump inhibitors).
- $CO_2$, either formed during metabolism in the cell or entering the cell from the blood, combines under the influence of carbonic anhydrase with the $OH^-$ to form $HCO3^-$.
- $HCO_3^-$ diffuses from the cell to plasma (Alkaline tide) and $CL^-$ enters via a carrier mechanism that facilitates exchange between the 2 ions.

# Gastric digestive enzymes

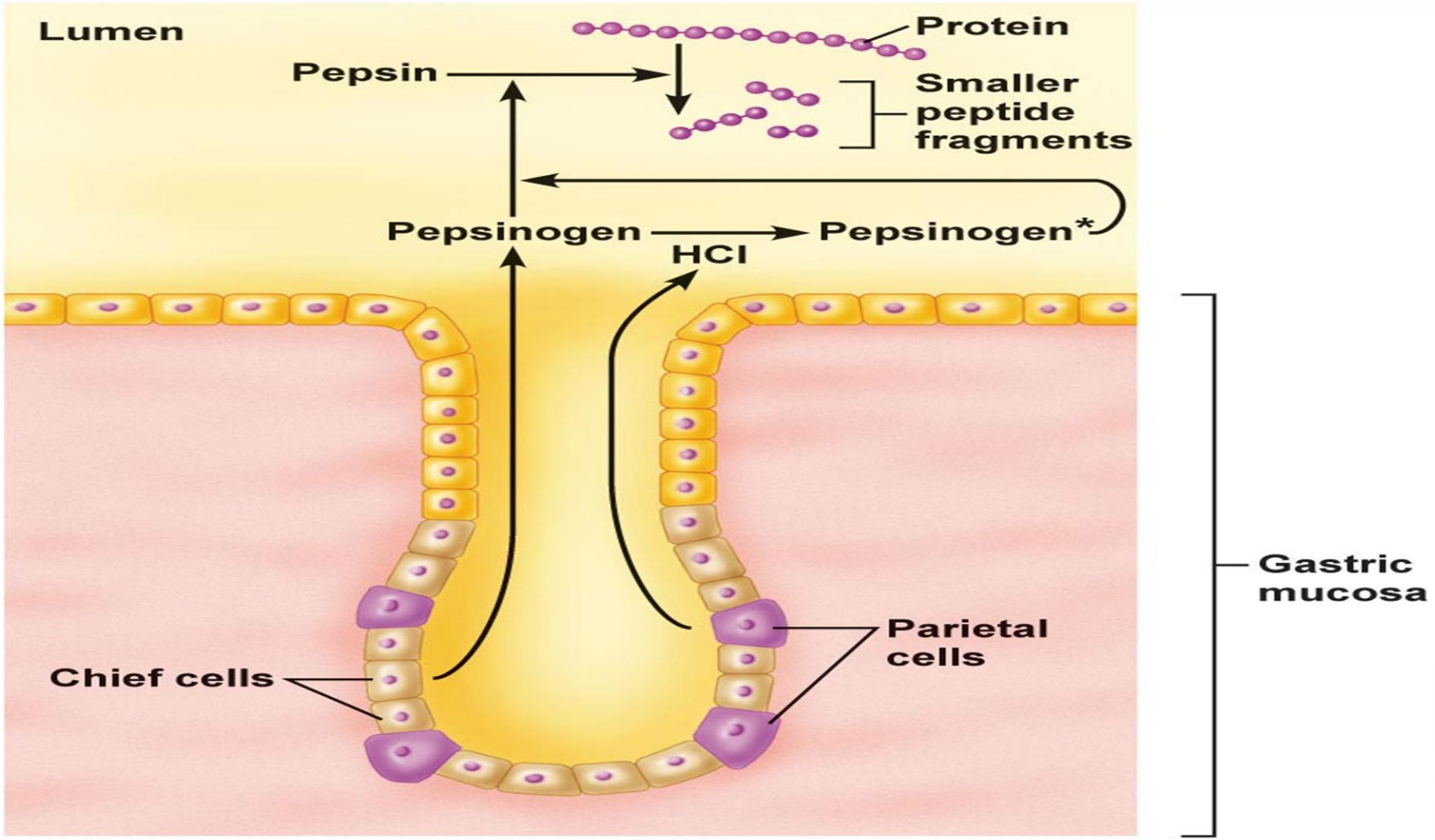
## Pepsin enzyme

Several types of pepsinogen secreted from chief cells. They are activated by HCl into pepsin and once activated, they can activate more pepsinogen. The optimum pH is 1.5-3.5. Pepsin breaks down proteins into peptones & polypeptides. Pepsinogen secretion is stimulated by Ach, acid, gastrin, secretin & CCK.

## Lipase enzyme

Secreted from fundic mucosa. It hydrolyses TG into MG & FA. Its activity is less than pancreatic lipase.

# Pepsinogen activation in the stomach lumen

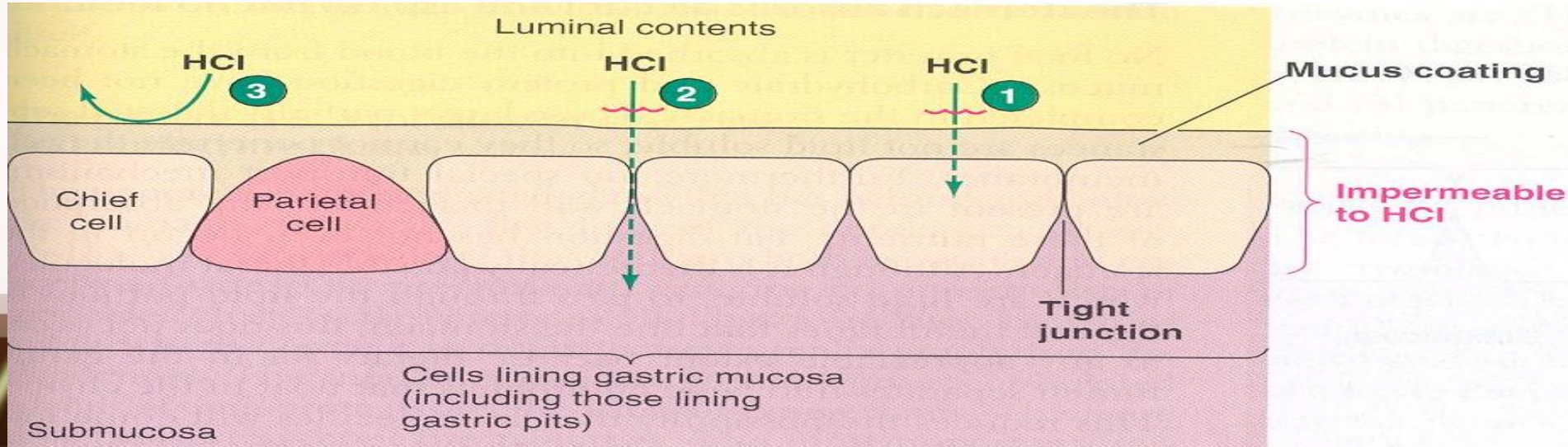


# Gastric mucus

- It is glycoprotein, about 0.2 mm thick and separate surface epithelial cells from acidic contents.

1. It protects the mucosa against mechanical injury by lubricating the chyme.
2. It protects the mucosa against chemical injury by acting together with $HCO_3^-$ as a barrier to HCl & pepsin. It also neutralize HCl and arrest action of pepsin.

Aspirin & nonsteroidal anti-inflammatory agents inhibit secretion of mucus & $HCO_3^-$. Prolonged use of these drugs may produce gastritis or ulcer.

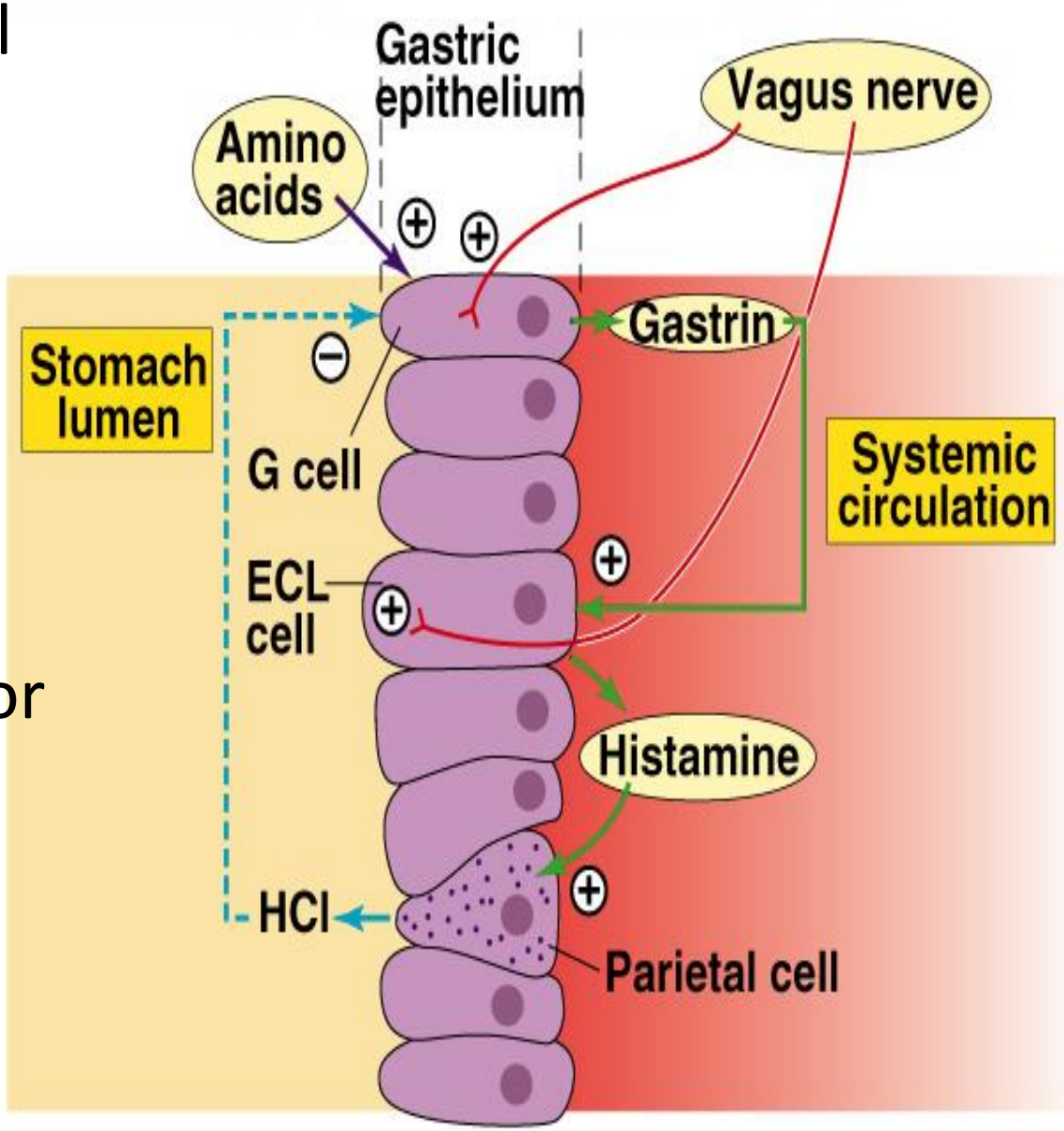


# *Intrinsic Factor*

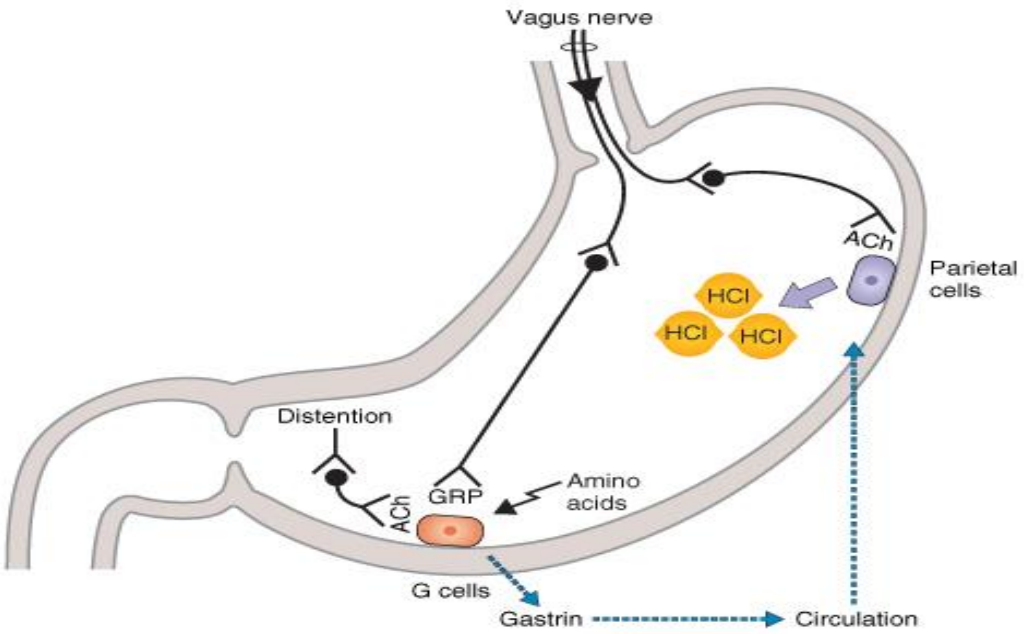
- It is glycoprotein secreted by **parietal cells**.
- It is the only essential function of stomach as it is essential for vitamin $B_{12}$ absorption.
- Atrophy of gastric mucosa leads to pernicious anemia.

# *Control of HCl secretion at the level of parietal cells*

- ☑ Vagus nerve (neural effector)
- ☑ Gastrin (hormonal effector)
- ☑ Enterochromaffin-like cells release Histamine→ activates $H_2$ receptor (parietal cells) → increases acid secretion

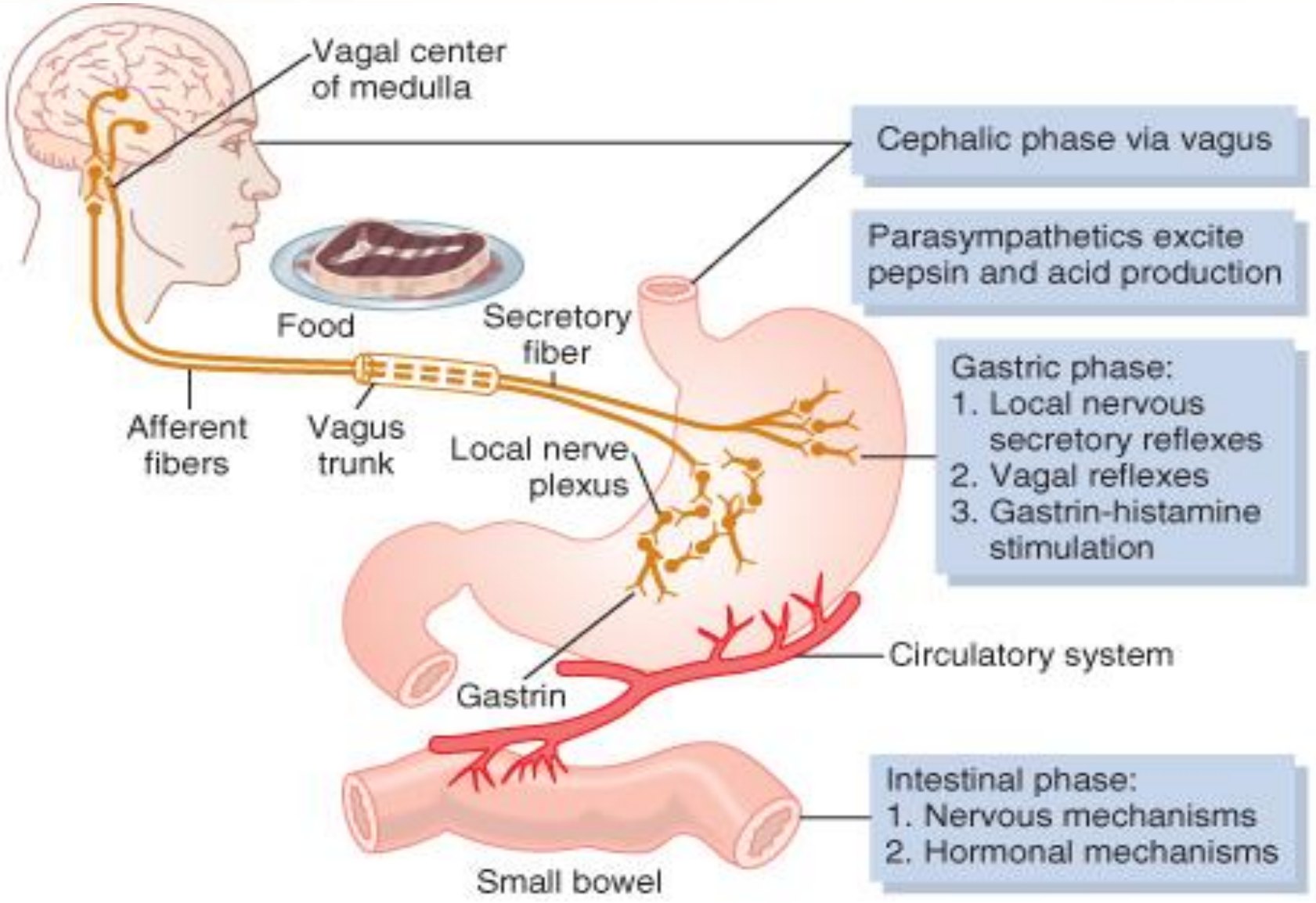


# Gastric Secretion Occurs in Three Phases



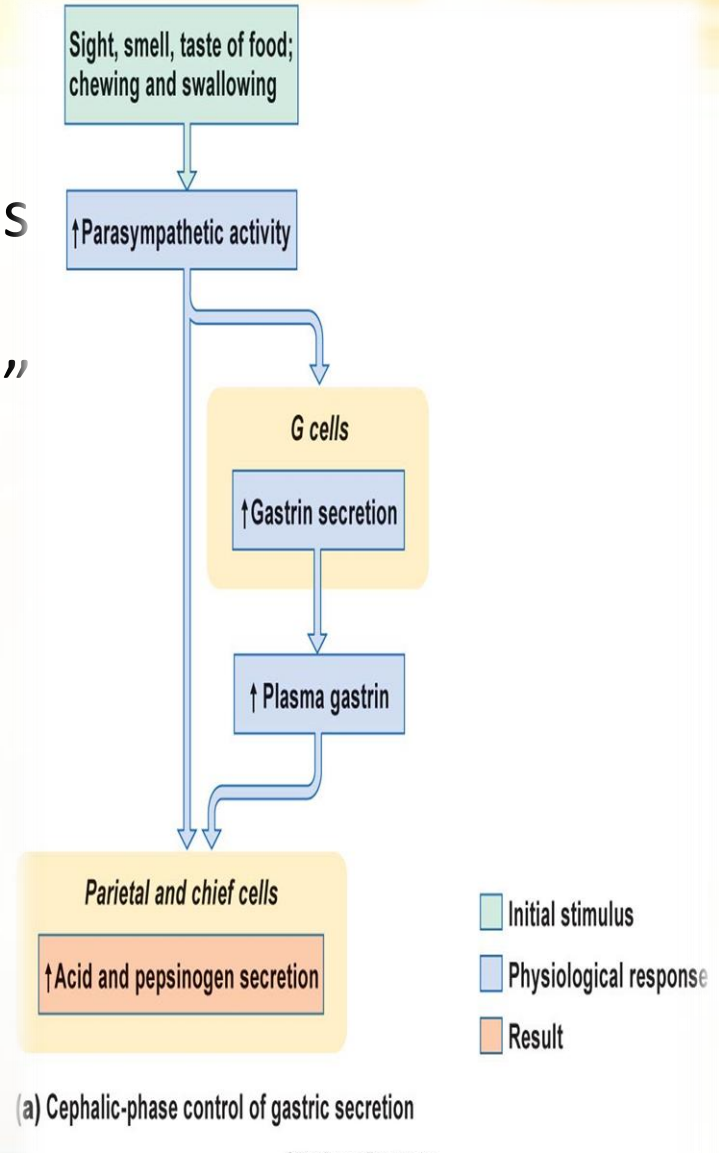

| Phase | % of HCl Secretion | Stimuli | Mechanisms |
|---|---|---|---|
| Cephalic | 30% | Smell, taste, conditioning | Vagus → parietal cell<br>Vagus → gastrin → parietal cell |
| Gastric | 60% | Distention | Vagus → parietal cell<br>Vagus → gastrin → parietal cell |
| | | Distention of antrum | Local reflex → gastrin → parietal cell |
| | | Amino acids, small peptides | Gastrin → parietal cell |
| Intestinal | 10% | Duodenal distension<br>Amono acids, small peptides | Vagus<br>Enterogastrone |

# Phases of Gastric Secretion



# 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 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, indirectly stimulating parietal cell acid secretion.




(a) Cephalic-phase control of gastric secretion

# 2. The gastric Phase

It is elicited by presence of food in stomach.

It is mediated by nervous & hormonal mechanisms.

## *a. Nervous mechanism*

Distension of either body or antrum of stomach stimulates mechanoreceptors in gastric wall.

Gastric secretion occurs by long vagovagal reflex and also by short intramural cholinergic reflexes.

## *b. Hormonal mechanism (Gastrin hormone)*

- Gastrin is secreted from "G" cells in antrum, enters the blood and then stimulates gastric glands.

- Stimuli of gastrin release:

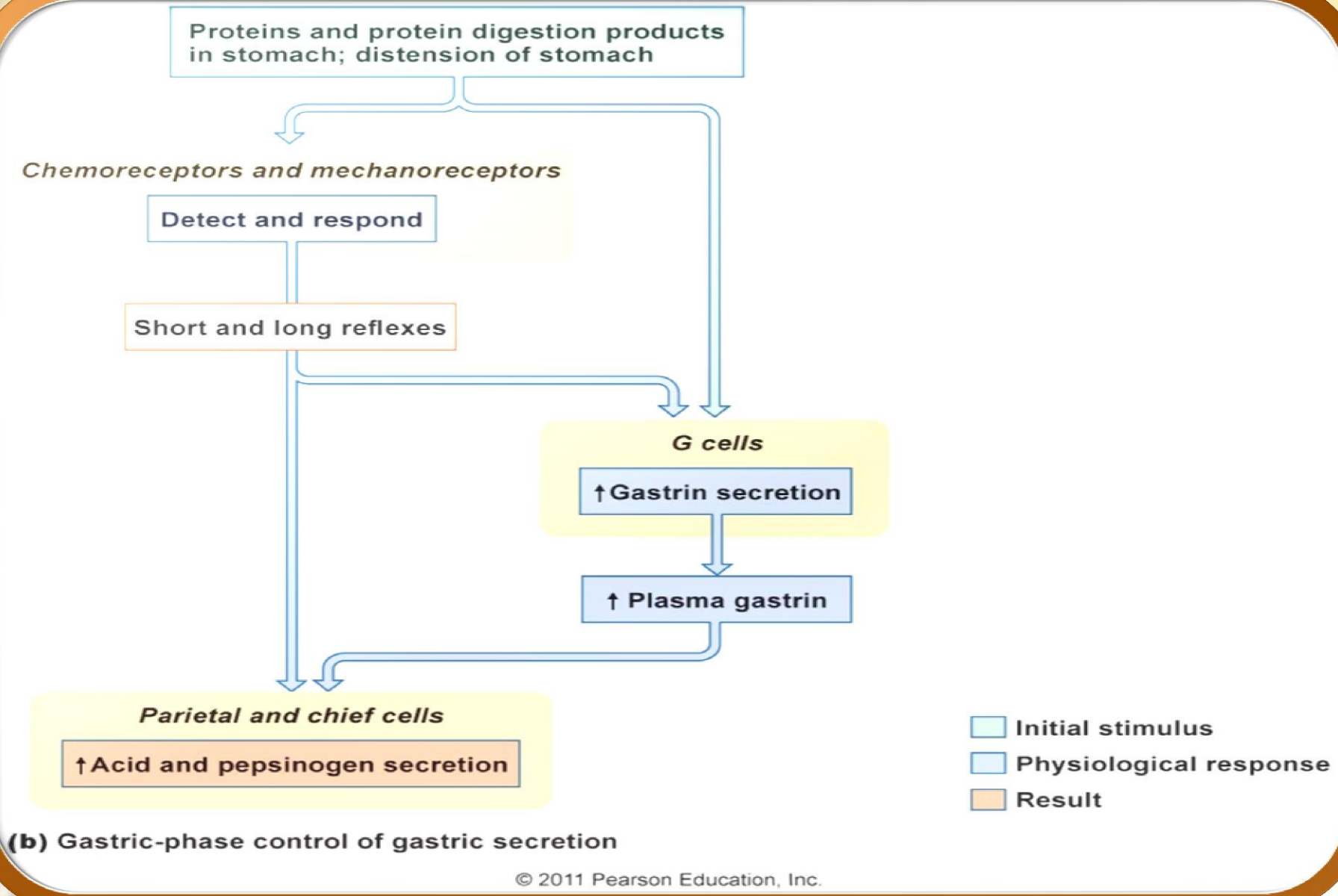
  1- The presence of amino acids & peptides.

  2- Gastric distension,

  3- Alcohol & caffeine.

  4- Vagal excitation.

  5- Rising of pH of gastric juice.




**(b)** Gastric-phase control of gastric secretion

## Actions of gastrin:

1- It stimulates gastric acid secretion, secretion of pepsin and intrinsic factor.

2- It stimulates intestinal secretion.

3- It stimulates pancreatic secretion of enzyme & $HCO_3^-$.

4- It stimulates biliary secretion of $HCO_3^-$ & $H_2O$.

5- It stimulates gastric motility.

6- It stimulates intestinal motility & relaxes ileocaecal sphincter.

7- It contract LES.

8- It has trophic effect on gastric mucosa.

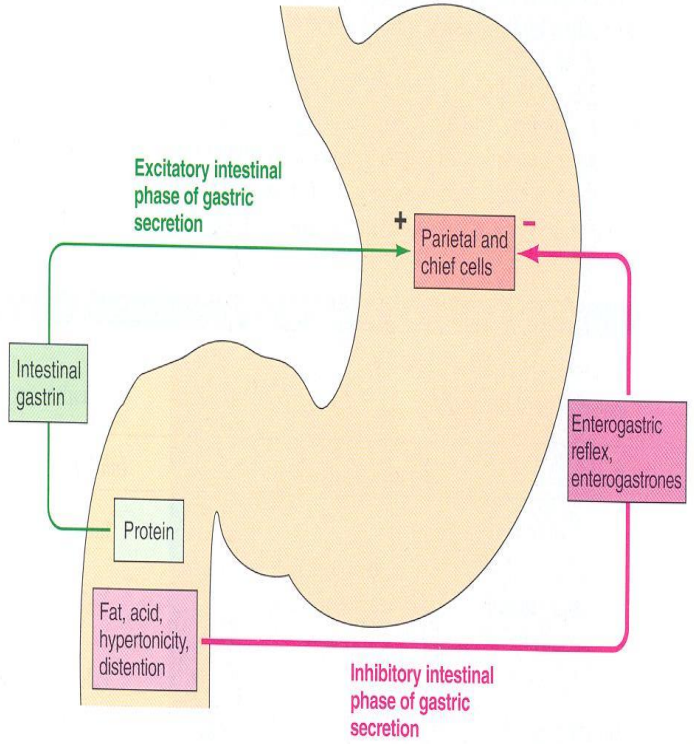
# 3. The intestinal phase

The presence of chyme in duodenum causes neural & hormonal responses that first stimulates & later inhibits gastric acid secretion.

**Gastric secretion is enhanced by:-**

i. Distension of duodenum stimulates G.A. secretion by means of vagovagal reflex and the release of the hormone entero-oxyntin from intestinal endocrine cells that stimulates parietal & G- cells.

ii. Presence of protein digestive products in duodenum stimulates G- cells in duodenum & proximal jejunum to release gastrin.




*Excitatory and inhibitory components af intestinal phase of gastric secretion*

# *The inhibitory mechanisms that limit G.A secretion*

1. The presence of food in small intestine initiates enterogastric reflex, transmitted through ENS & autonomic NS that inhibits G.A secretion.

2. Drop the pH in pyloric antrum to < 2.5 reduces G.A secretion via release of somatostatin from antral & duodenal "D" cells.

3. The presence of acid, fat, protein digestive products, hypertonic solution in upper intestine inhibits G.A secretion. These effects are mediated mainly by hormonal mechanisms.

# Enterogastrones

Are hormones released from intestine and decrease G.A secretion as:-

1) Bulbogastrone
2) Gastric inhibitory peptide (GIP).
3) Secretin & CCK.
4) Pancreatic glucagone.
5) Other peptides as VIP, somatostatin, and certain types of prostaglandins.

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

# Motor Functions of the Stomach

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

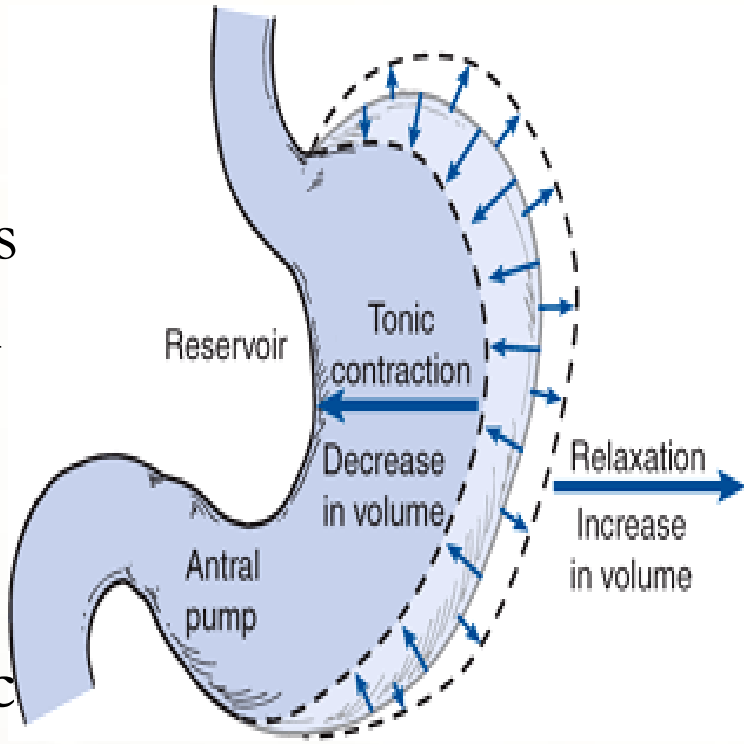
The stomach can store 0.8-1.5 L of food.

# Relaxation Reflexes in Gastric Reservoir Part

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

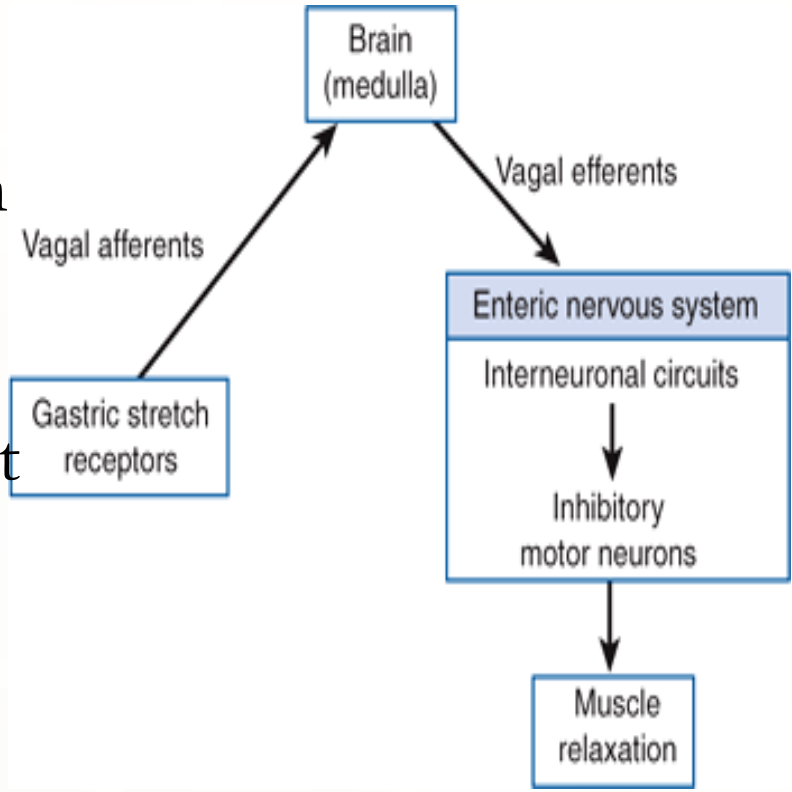
## A- Receptive Relaxation Reflex:

- 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 resulting in reduction in muscular wall tone and the stomach relaxes through inhibition of myenteric neurons.



# B- Adaptive relaxation:

- Triggered by stretch receptors (vago-vagal reflex).
- 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:

- The presence of nutrients in the small intestine triggers feedback relaxation.
- It can involve both local reflex connections between receptors in the small intestine and the gastric ENS or hormones that are released from endocrine cells in the small intestinal mucosa and signal the gastric ENS.

# II- Motor Behavior of the Antral Pump region, (phasic contraction)

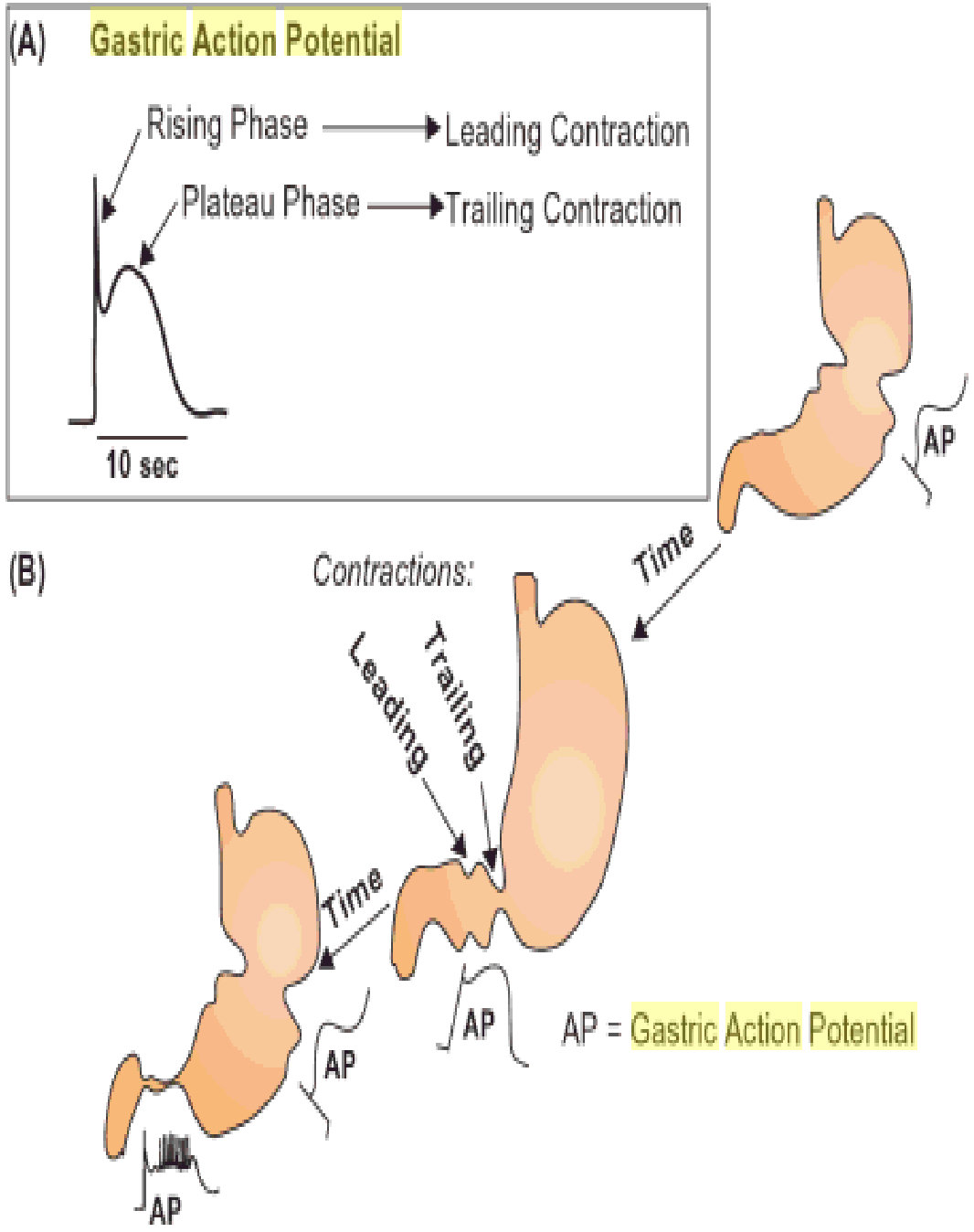
Major mixing activities take place in the antrum

- Contact of gastric chyme with the mucosal surface of the stomach, causes mixing waves, initiated by the basic electrical rhythm.
- 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 wave passes from to the antrum to the pylorus, few millimeters of antral content move into the duodenum through the pyloric sphincter.

# Gastric action potentials

- They are initiated at a frequency of 3/min and lasts about 5 seconds .
- They propagate rapidly around the gastric circumference and trigger a ring-like contraction.
- Electrical syncytial properties of the gastric musculature account for propagation of the action potentials to the gastroduodenal junction.

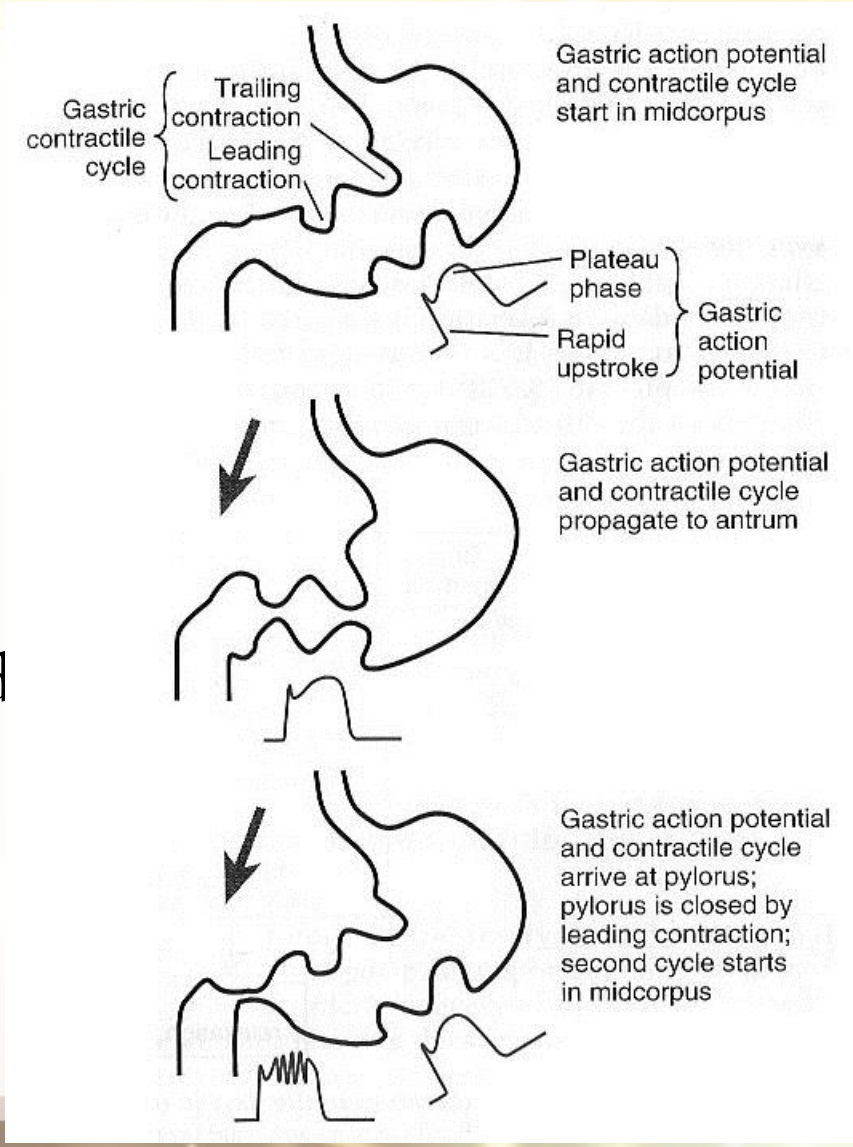
Gastric Action Potentials are characterized by an initial rapidly rising upstroke, followed by a plateau phase, and then a falling phase back to the baseline membrane potential



# The Gastric Action Potential Triggers Two Kinds of Contractions

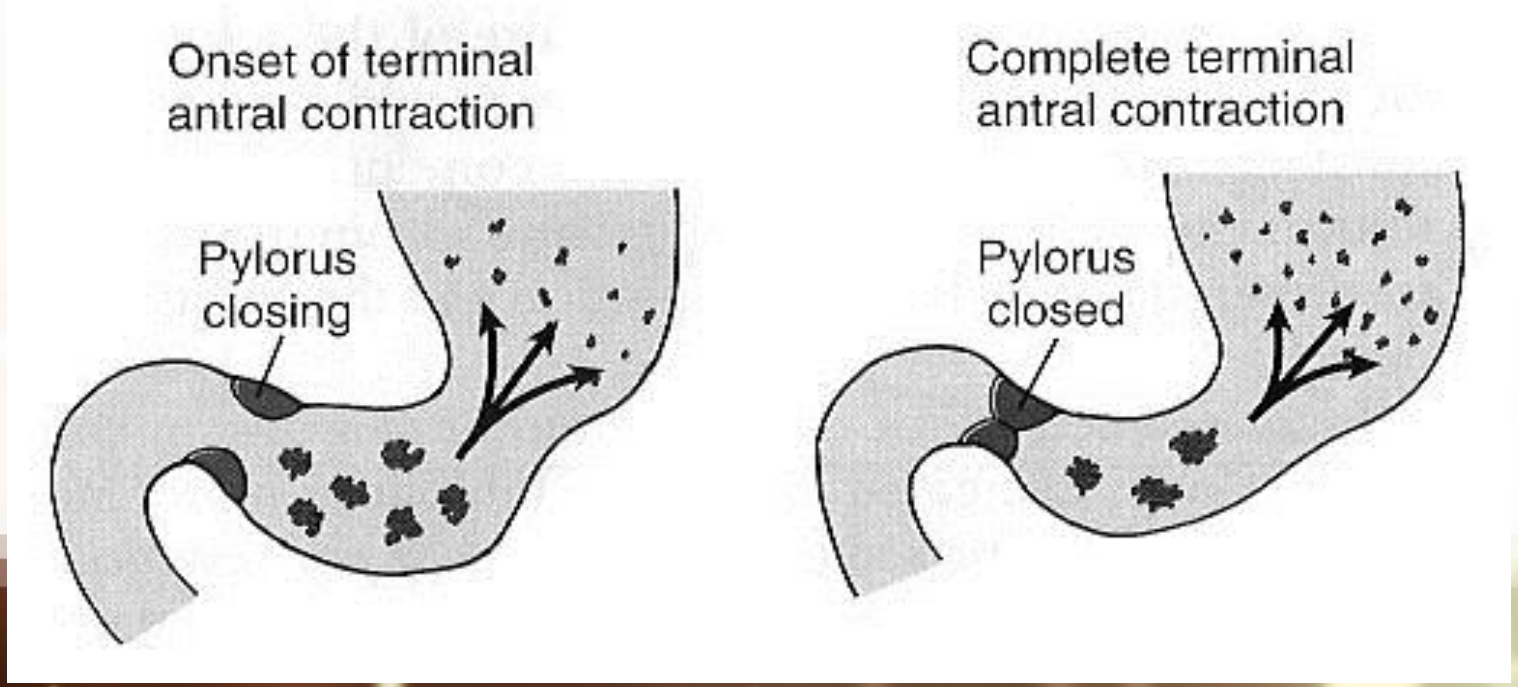
(1) A leading contraction, which has relatively constant amplitude, is associated with the rising phase of the action potential

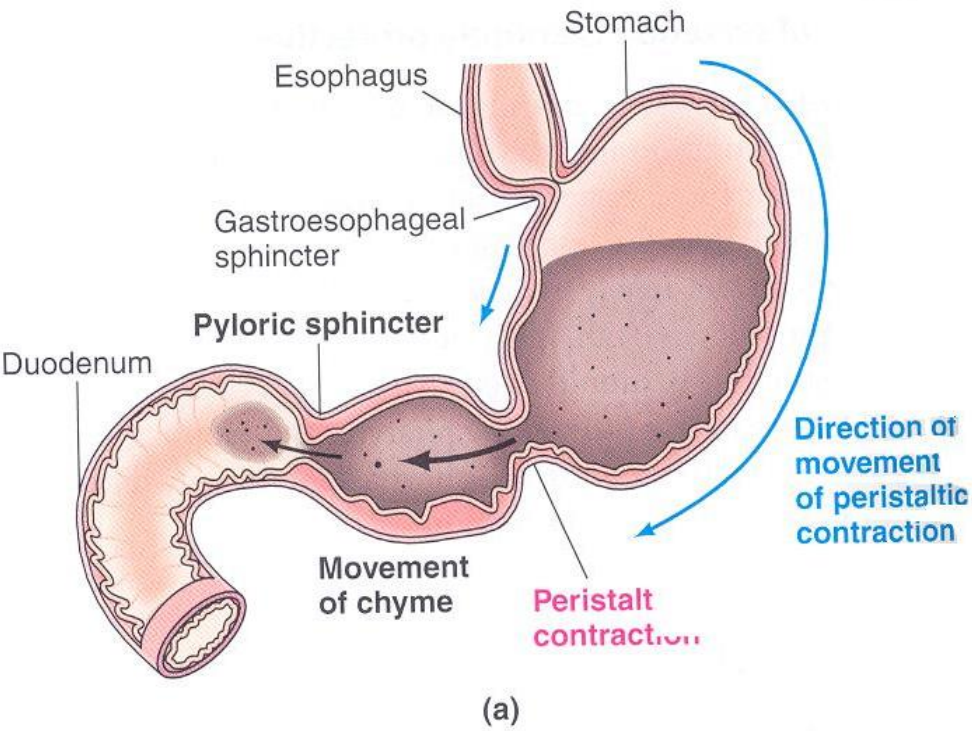
(2) A trailing contraction, of variable amplitude, is associated with the plateau phase.

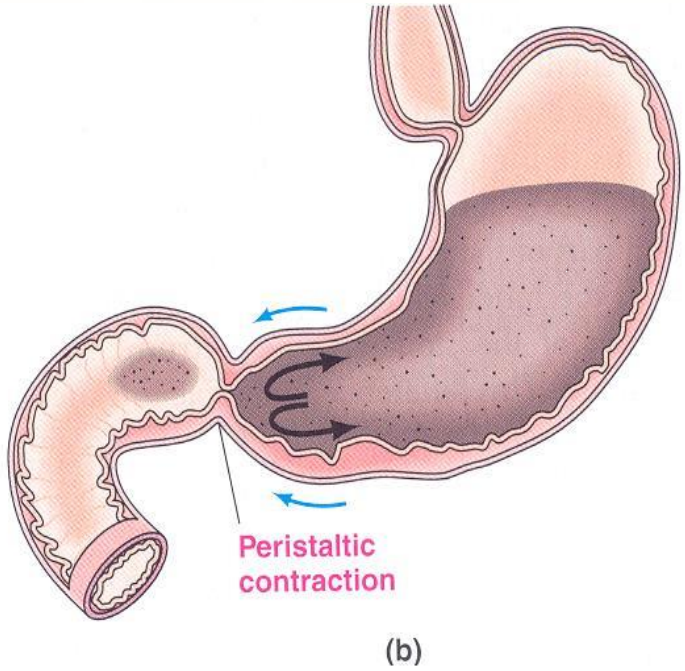


# Retropulsion Phenomena

- 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.



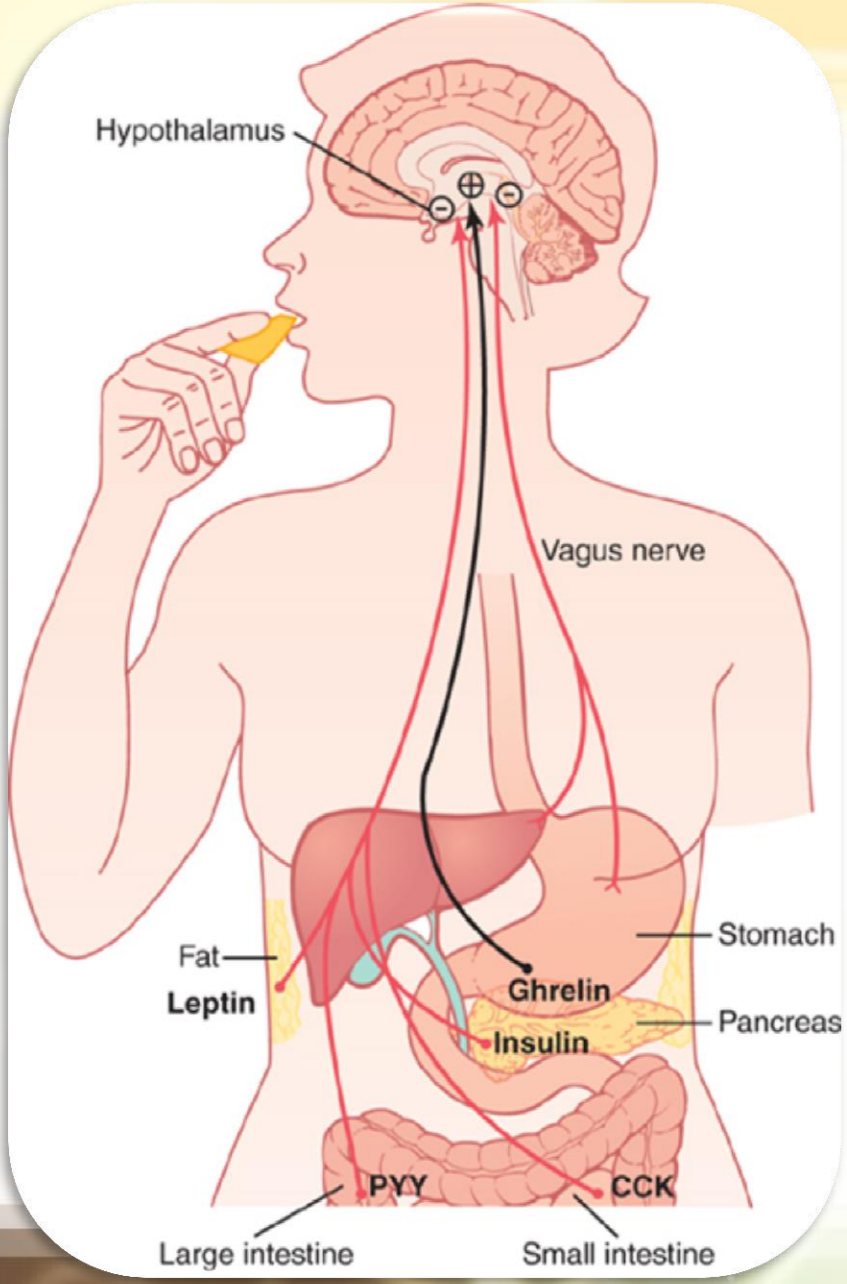



**Gastric emptying and mixing as a result of antral peristaltic contraction**

# 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 2-3 minutes.
- ✓ They 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.



# The migrating motor complex

- It is bursts of depolarization accompanied by peristaltic contraction that occur in empty stomach during interdigestive period.
- MMC moves on a long whole length of small intestine to reach ileocaecal valve after 1.5-2 h where it disappears. A new wave of MMC starts.
- The activity of MMC terminates as soon as food is ingested.
- The function of MMC is to sweep remnants in stomach & small intestine into colon.

# Stomach Emptying

Results from intense peristaltic antral contractions against resistance to passage of chyme at the pylorus.

- 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 Factors that Promote Stomach Emptying

1. **Gastric Food Volume:** An increase in gastric food volume results in increased stretch in the stomach wall and increased stomach emptying.

2. **Gastrin Hormone:** Gastrin increases the activity of the pyloric pump and motor stomach function (moderate effect) and probably promotes stomach emptying.

## The duodenal factors that can inhibit stomach emptying include:

(1) Distention and irritation.

(3) Acidity activates "S" cells to release secretin which constricts the antrum

(4) Hyperosmotic chyme in the duodenum

(5) Protein content of the chyme in the duodenum.

(6) Fat (monoglycerides) in the duodenum activates different cells to produce CCK and GIP that increase the tone of the pyloric sphincter and decrease stomach emptying.

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