
السلام عليكم ورحمة الله وبركاته

Gastrointestinal Physiology

Lecture 3

Physiology of the Stomach and Regulation of Gastric Secretions

Chapter 64; pages 807-816

Chapter 65; pages 817-832

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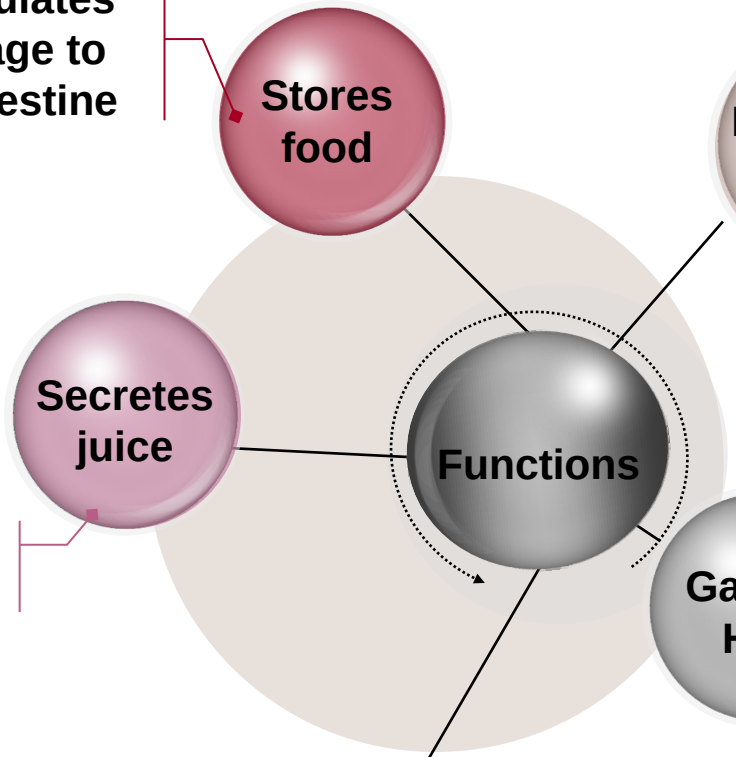
Learning Objectives

- 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

Functions of Stomach



1. And regulates its passage to small intestine

5. It produces gastrin and somatostatin.

2. Liquefies & partly digests food

4. Kills ingested bacteria.
Is necessary for iron & Ca++ absorption.
Catalyzes cleavage of inactive pepsinogen into active pepsin

3. Necessary for vitamin B_{12} absorption

In addition to, absorption of some water and lipid-soluble substances.

Gastric Secretion

Histologically gastric mucosa is divided into 3 areas:-

Cardiac area

10%

- **Cardiac glands**:- Most of cells secrete mucus

Pyloric area

15%

- **Pyloric glands**:- Secrete mucus, pepsinogen + G- cells secrete gastrin + D Cells secrete somatostatin

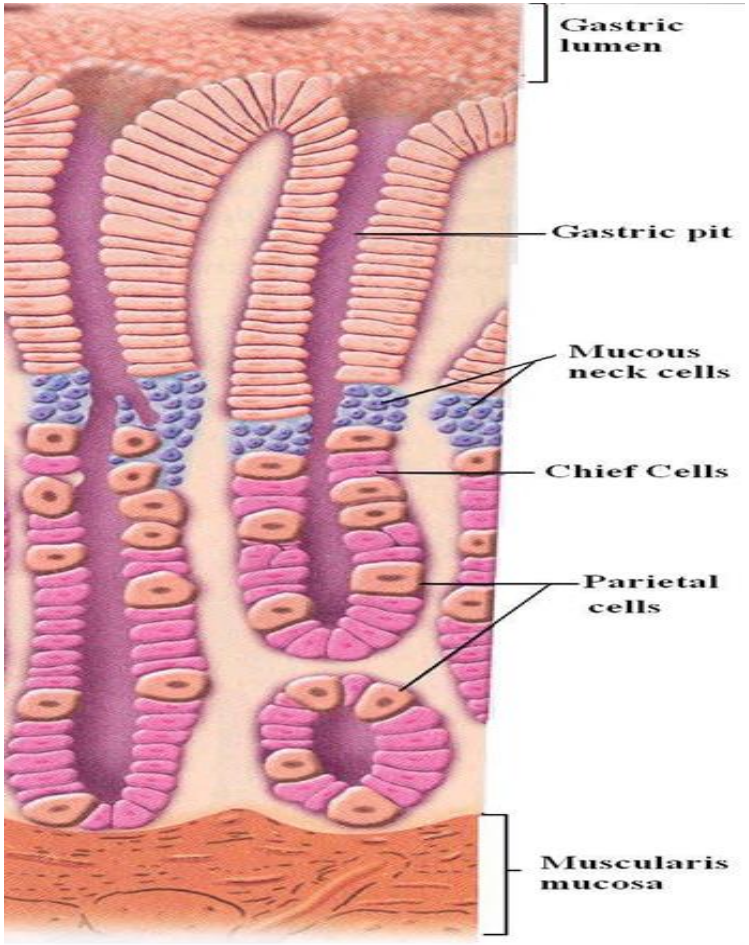
Main gastric area

70-80%

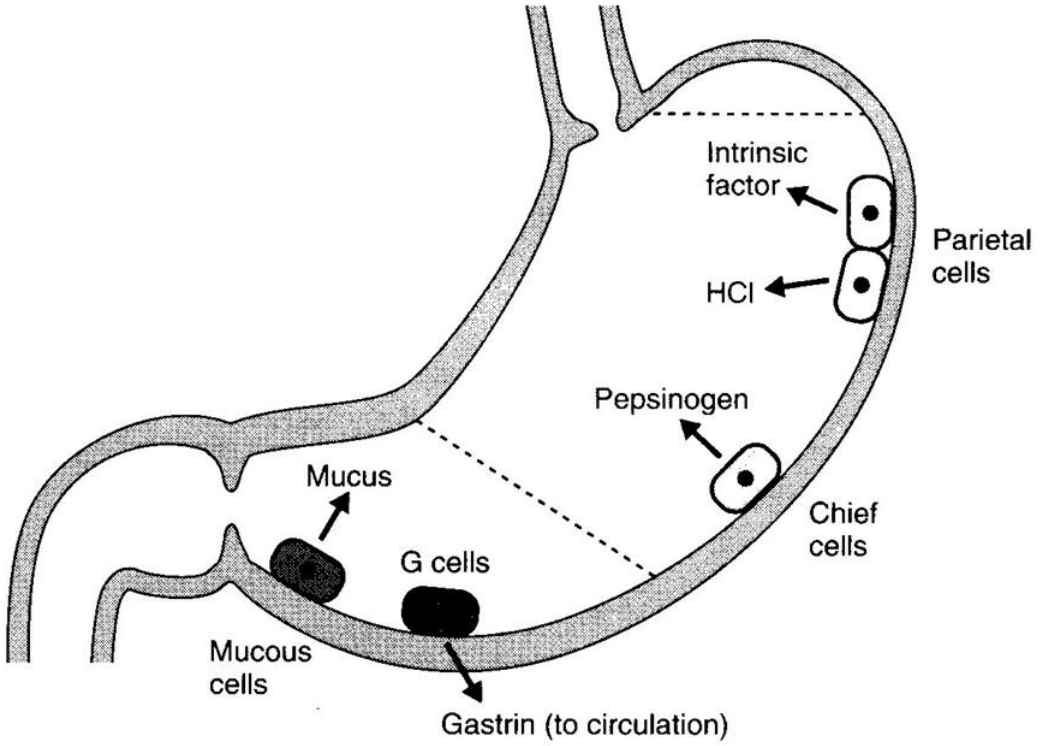
- **Oxyntic glands**:- HCl & intrinsic factor from parietal (oxyntic) cells
  Pepsinogen from peptic (chief) cells
  Mucus & HCO_3^- from mucous neck cells

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

Structure of the Gastric Oxyntic Gland



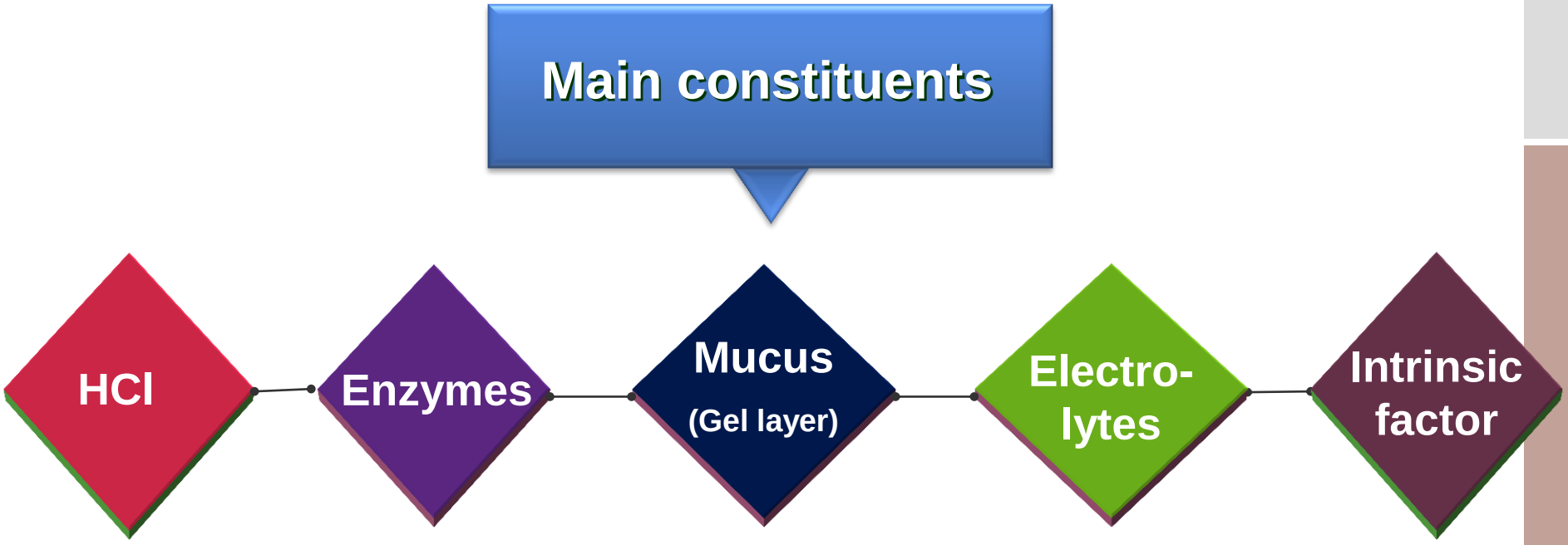
The Normal Locations of Gastric Cells



Cell Type	Location	Secretion
Parietal cells	Body	HCL Intrinsic factor
Chief cells	Body	Pepsinogen
G cells	Antrum	Gastrin
Mucous cells	Antrum	Mucus Pepsinogen

Gastric Juice

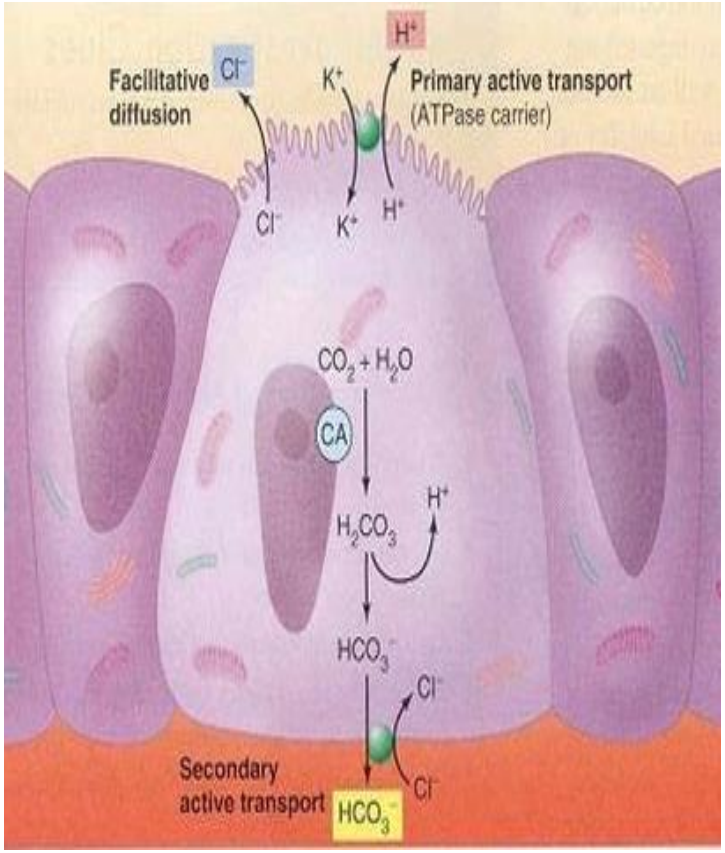
- **Volume about 2-3 L/day**



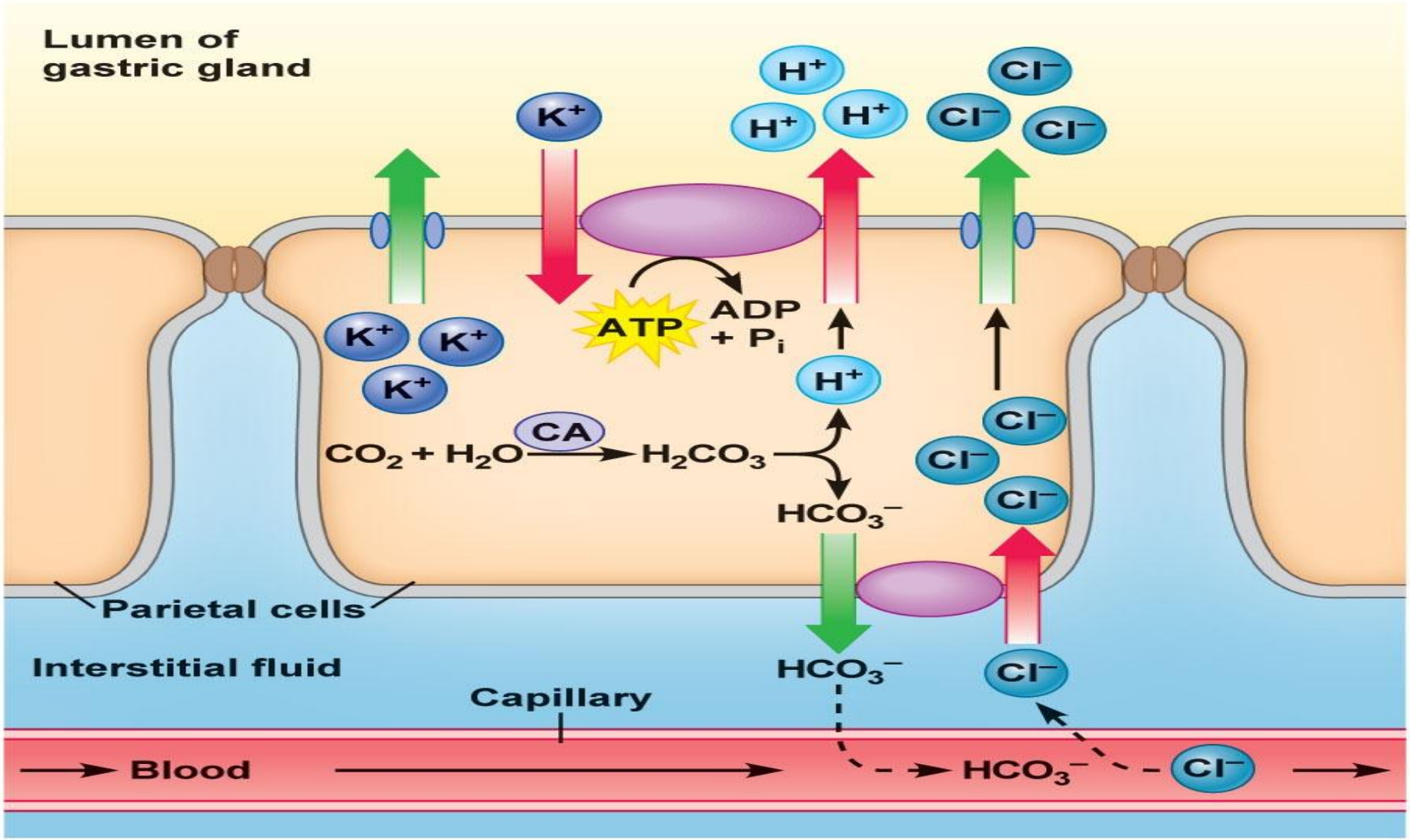
Gastric HCL

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



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 H_2O dissociate into $H^+ + OH^-$

H^+ is actively transported by H^+-K^+ ATPase which exchange H^+ with K^+

CO_2 combines under the influence of carbonic anhydrase with the OH^- to form HCO_3^-

HCO_3^- 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)

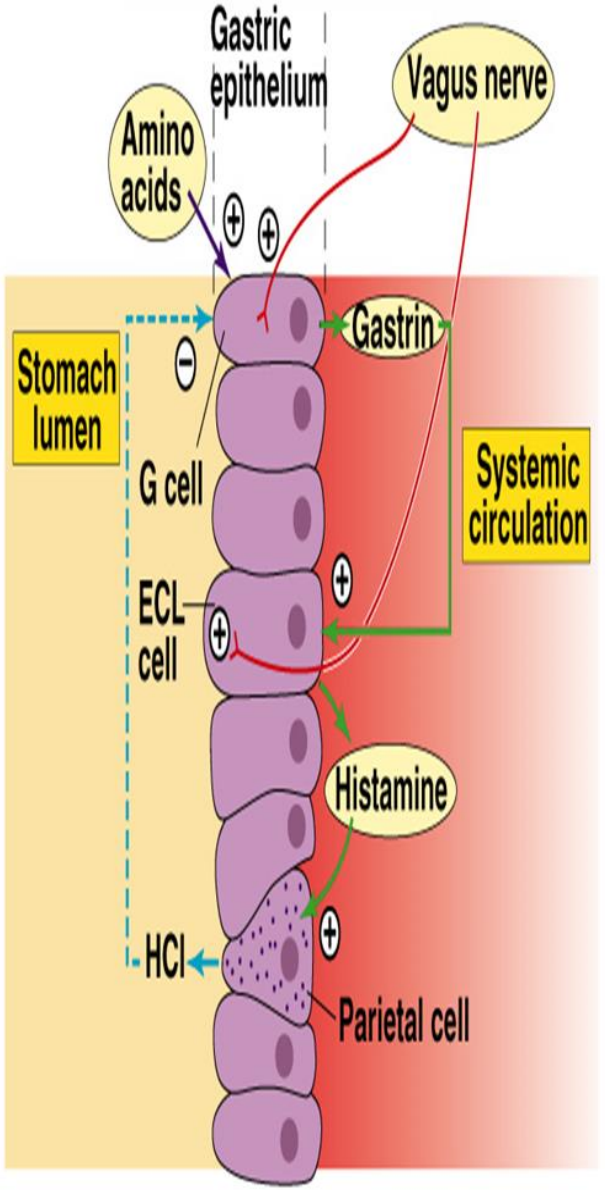
Control of HCl secretion at the level of parietal cells

Stimulation of parietal cells

Vagus nerve
(neural effector) (directly by Ach or indirectly by releasing gastrin releasing peptide, GRP)

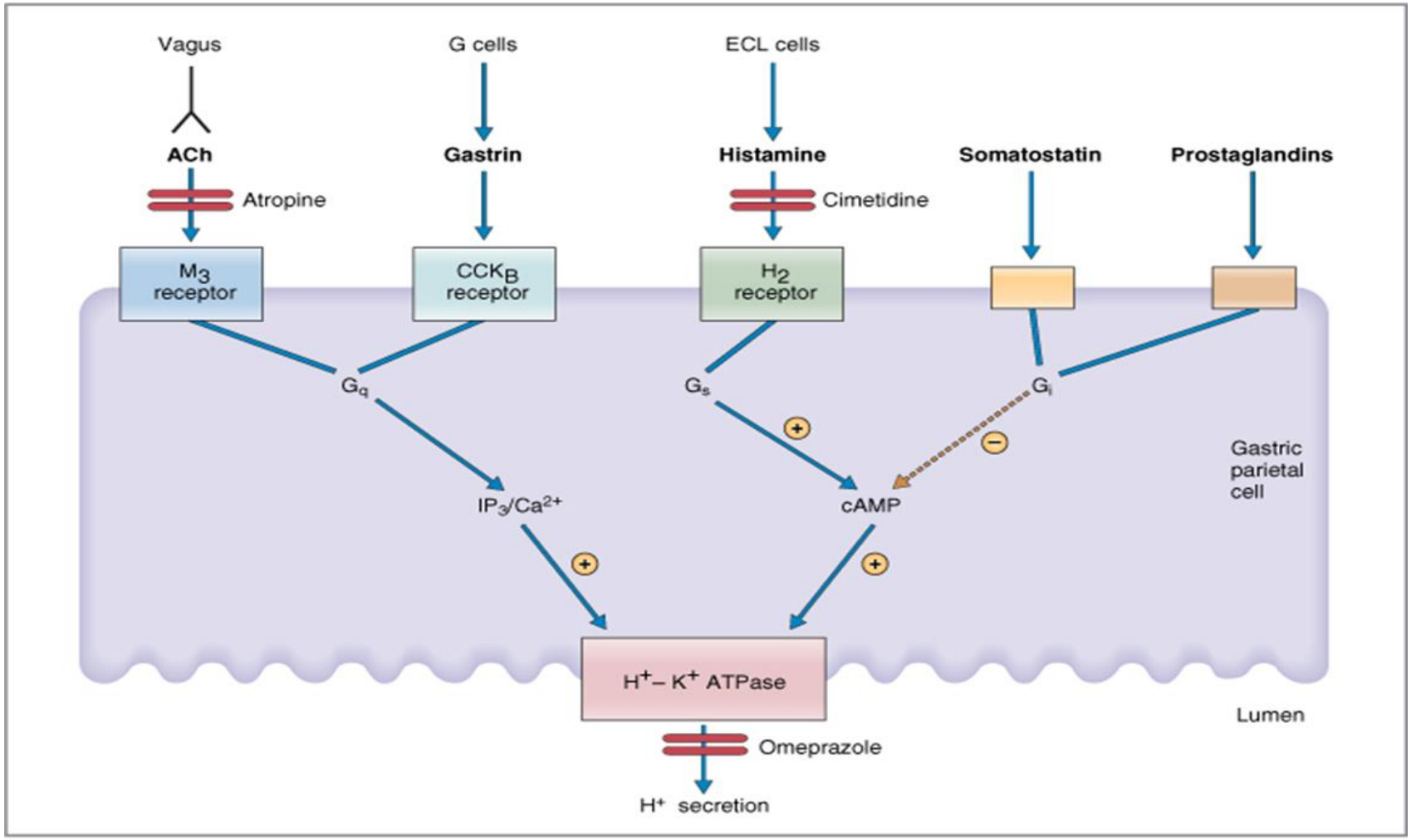
Gastrin
(hormonal effector)

Histamine
(ECL cells) activates H_2 receptor on parietal cells



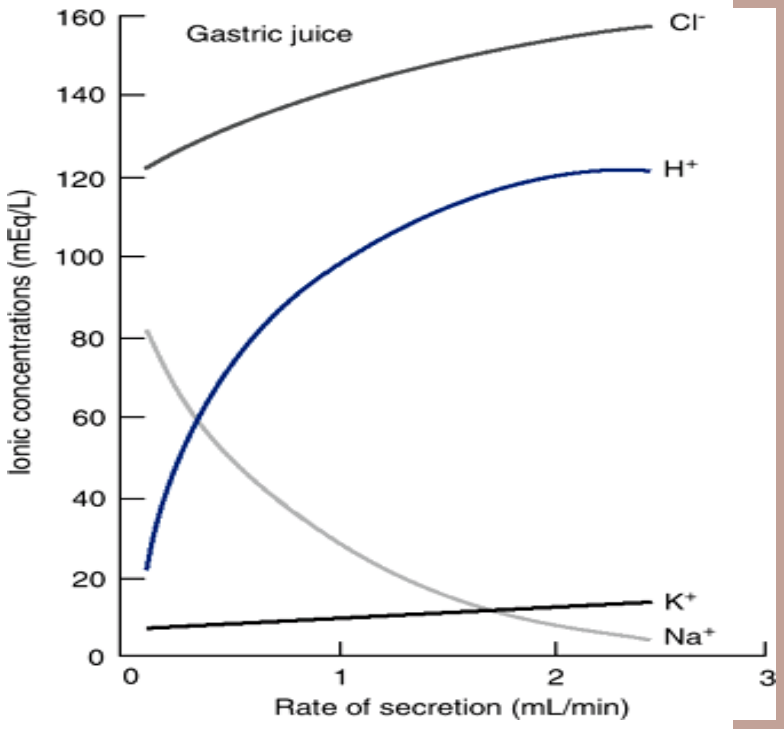
H_2 blockers (as cimetidine) are commonly used for the treatment of peptic ulcer disease or gastroesophageal reflux disease.

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

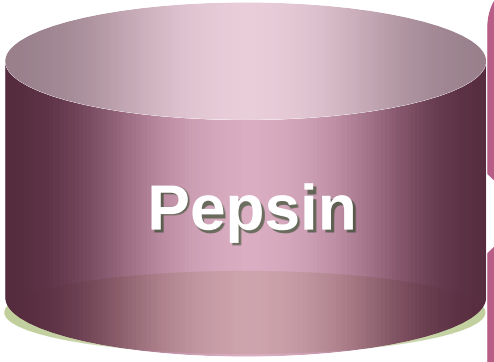


The Rate of Secretion Modifies the Composition of Gastric Juice

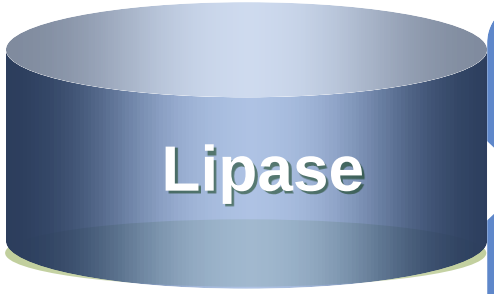
- The isotonic gastric juice is derived from the secretions of two major sources: parietal cells and nonparietal cells.
- Secretion from nonparietal cells is probably constant.
- Parietal HCl secretion contributes to the changes in electrolyte composition with changes of secretion rates.
- At a low secretion 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.



Gastric Digestive Enzymes

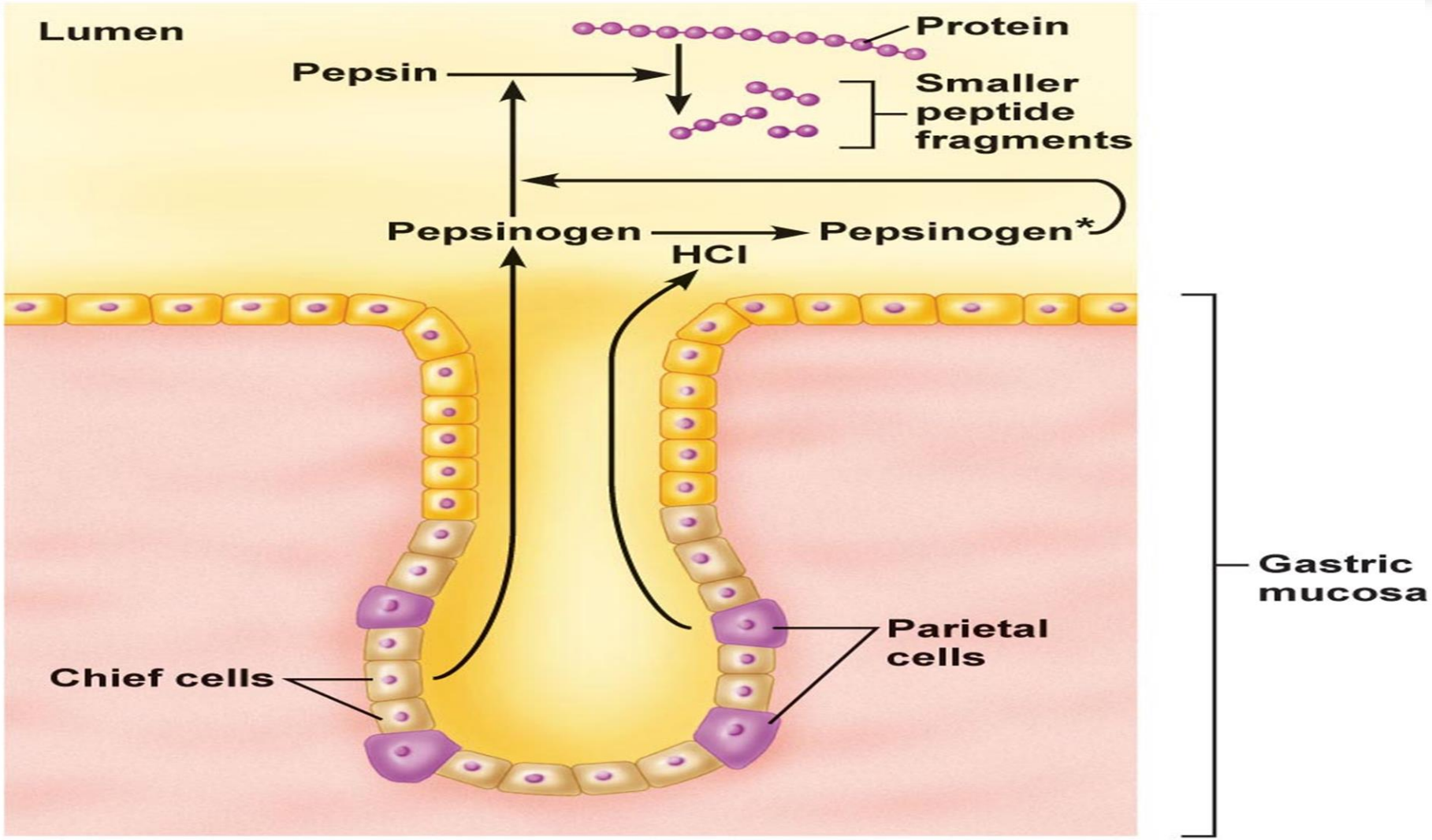


- Pepsinogen is activated by HCl into pepsin.
- Pepsin can activate more pepsinogen.
- The optimum pH is 1.5-3.5.
- Pepsin breaks down proteins into peptones & polypeptides.
- Pepsinogen secretion is stimulated by Ach, acid, gastrin, secretin & CCK.



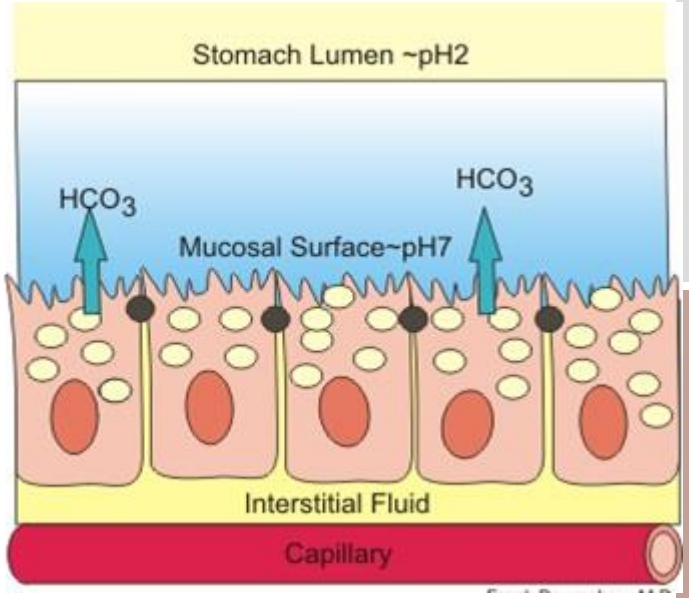
- Secreted from fundic mucosa.
- It hydrolyses TG into MG & FA.
- Its activity is less than pancreatic lipase.

Pepsinogen Activation in The Stomach Lumen



Gastric Mucus

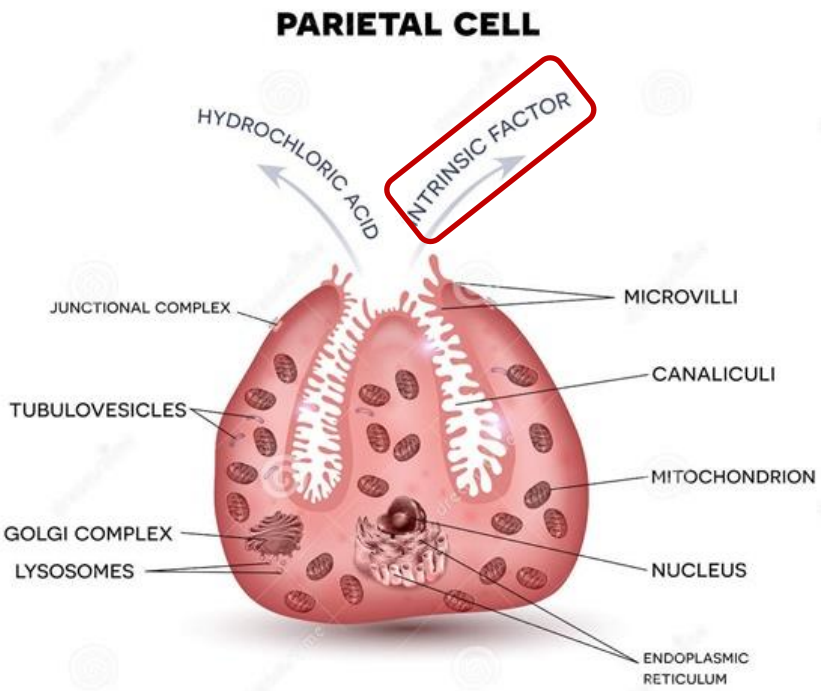
- It is glycoprotein (0.2 mm thick), separate surface epithelial cells from acidic contents.
- It protects the mucosa against:-
  - Mechanical injury by lubricating the chyme.
  - Chemical injury by acting together with HCO_3^- as a barrier to HCl & pepsin. It also neutralize HCl and arrest action of pepsin.



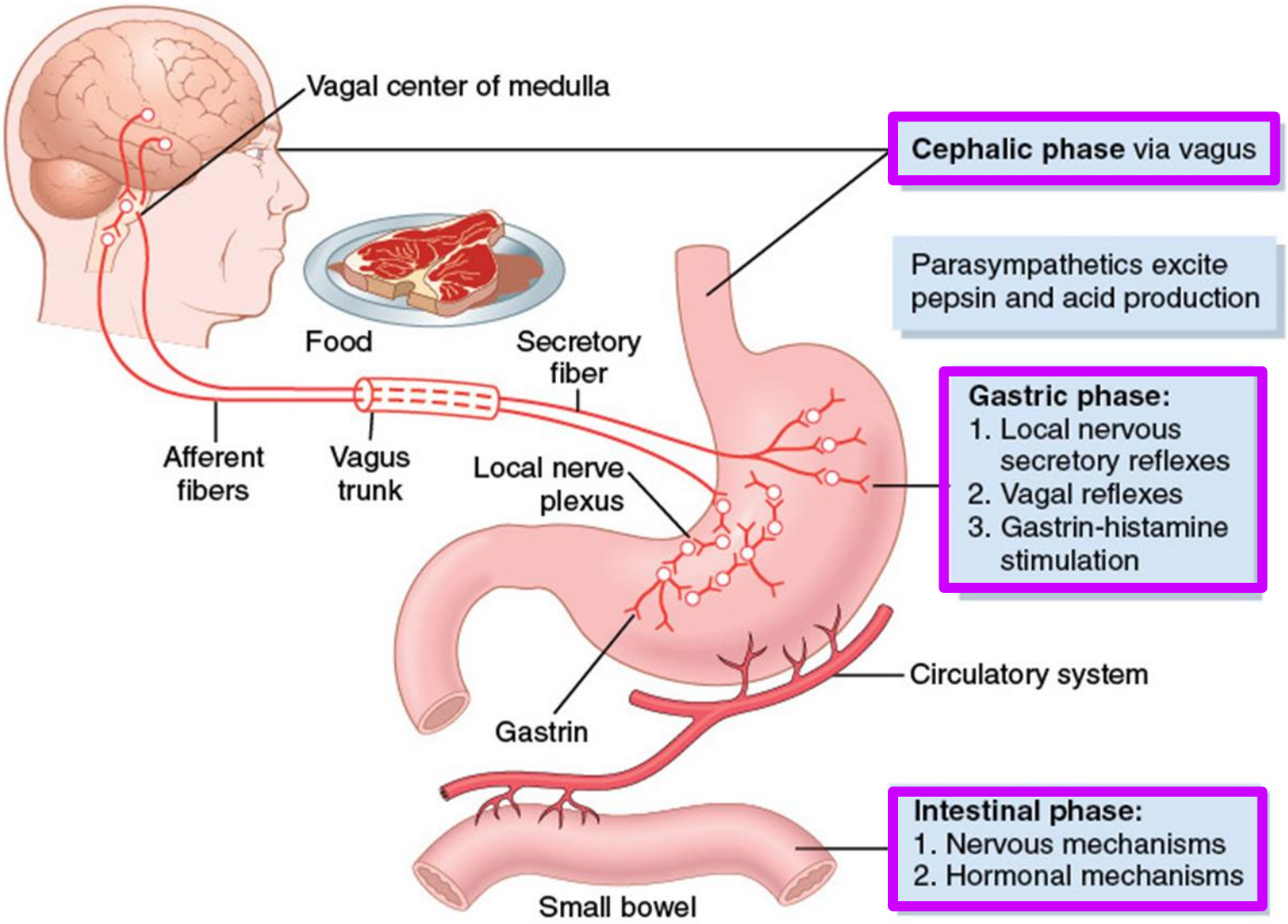
- Aspirin & nonsteroidal anti-inflammatory agents inhibit secretion of mucus & HCO_3^-. Prolonged use of these drugs may produce gastritis or ulcer.

Intrinsic Factor

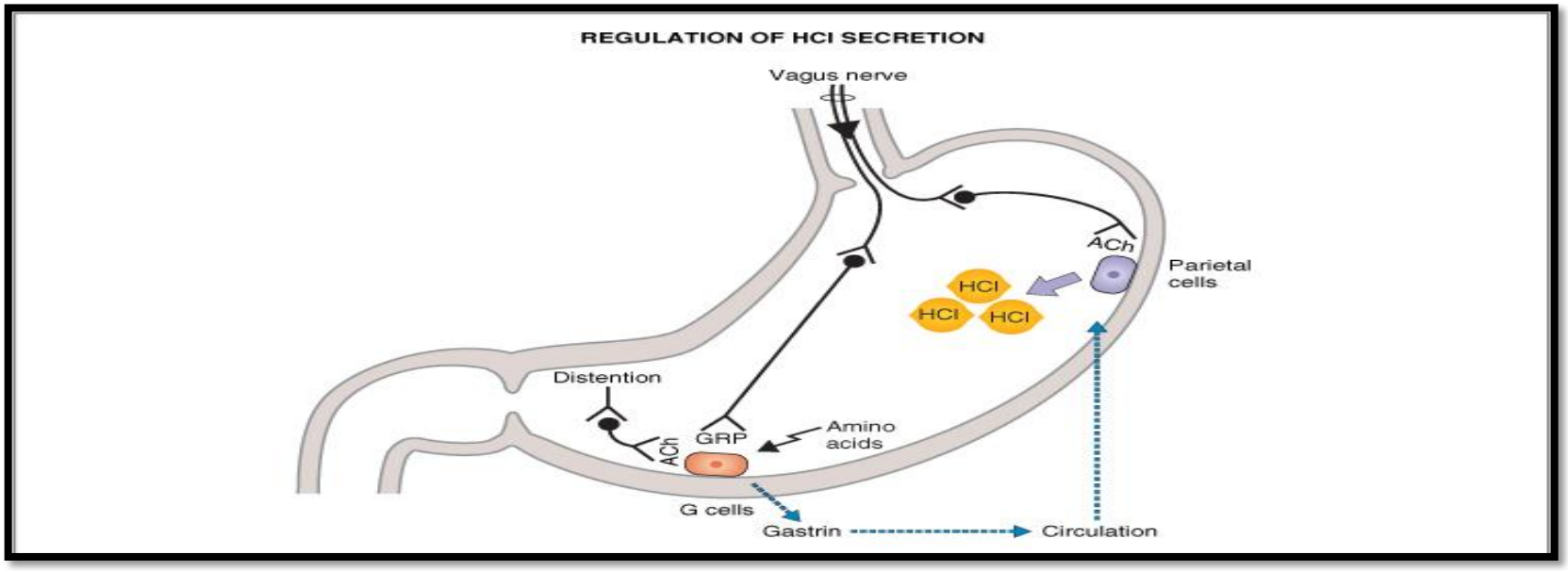
- It is glycoprotein secreted by **parietal cells**.
- It is the only essential function of stomach as it is essential for vitamin B_{12} absorption.
- Atrophy of gastric mucosa leads to pernicious anemia.



Phases of Gastric Secretion



Gastric Secretion Occurs in Three Phases



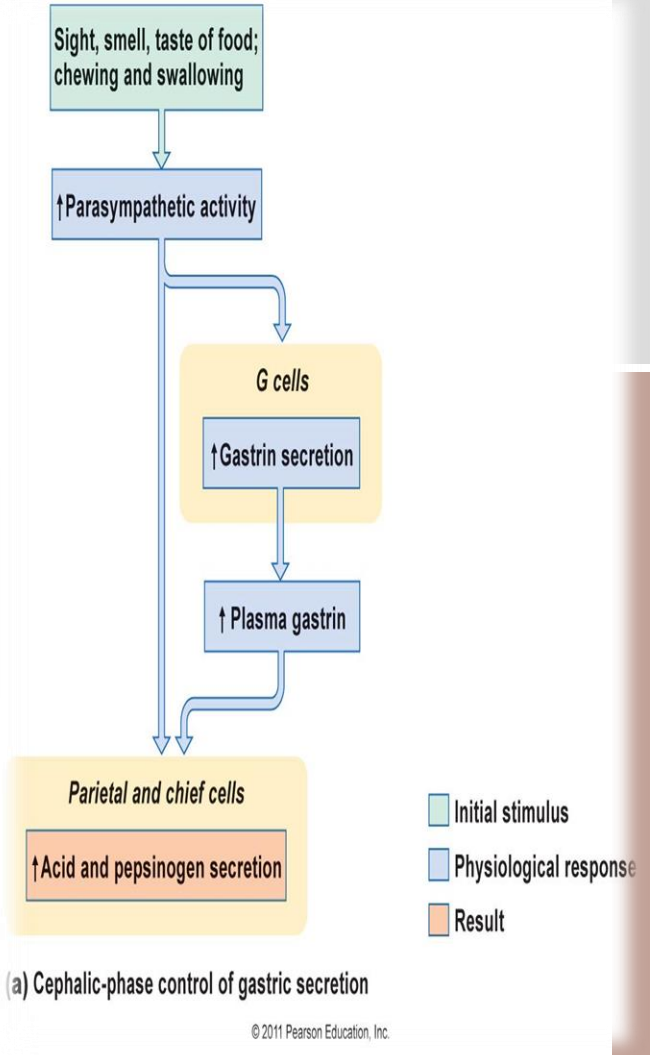
Phase	Cephalic (30%)	Gastric (60%)	Intestinal (10%)
Stimuli	Smell, taste, conditioning	Distension, amino acids, small peptides	Duodenal distension AA, small peptides
Mechanism	-Vagus → parietal cells -Vagus → gastrin → parietal cells	-Local reflex → gastrin → parietal cells -Gastrin → parietal cells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

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

Nervous

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

Hormonal (Gastrin hormone)

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

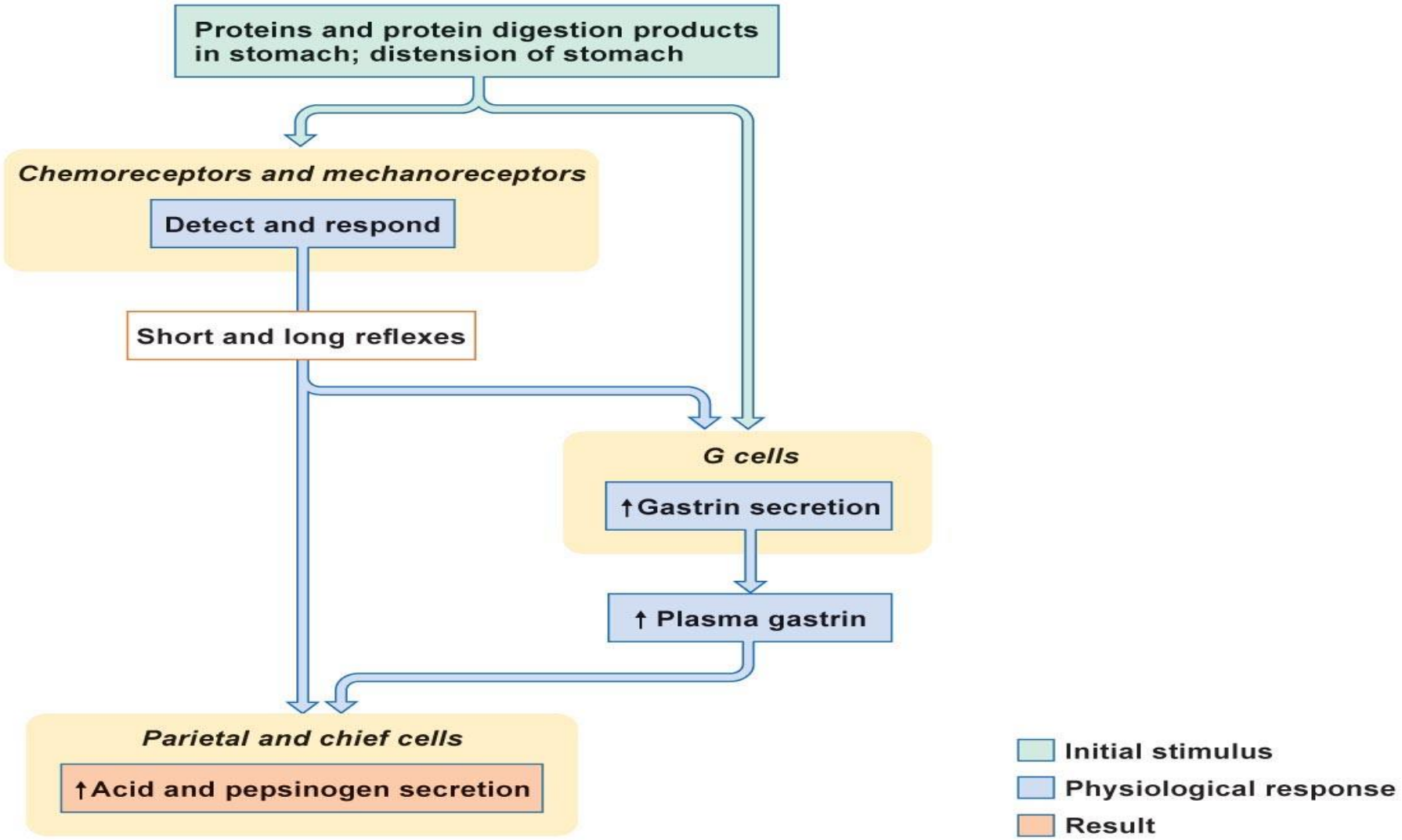
Other Stimuli:

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

Gastrin stimulates

1. **Gastric acid, pepsin and intrinsic factor secretion.**
2. **Intestinal secretion.**
3. **Pancreatic secretion of enzyme & HCO_3^-.**
4. **Biliary secretion of HCO_3^- & H_2O.**
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



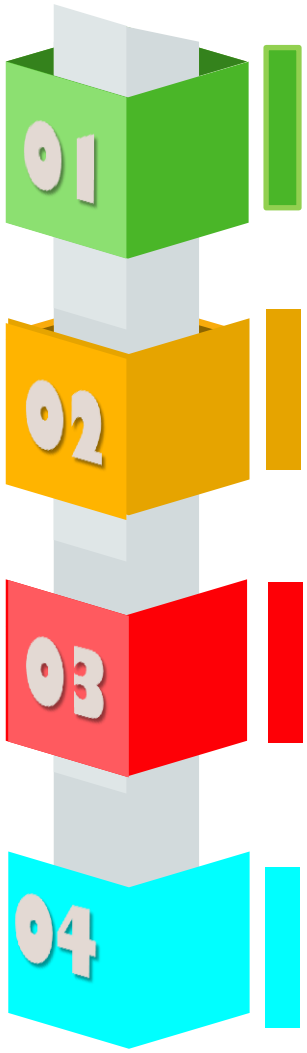
3. The intestinal Phase

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 (S-cells) 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.

Hormone	Site of Secretion	Stimuli for Secretion	Actions
Gastrin	**"G" cells** of the stomach	Small peptides and amino acids Distention of the stomach Vagal stimulation	↑ Gastric H^+ secretion Stimulates growth of gastric mucosa
Cholecystokinin (CCK)	**"I" cells** of the duodenum and jejunum	Small peptides and amino acids Fatty acids	↑ Pancreatic enzyme secretion ↑ Pancreatic HCO_3^- secretion Stimulates contraction of the gallbladder and relaxation of the sphincter of Oddi Stimulates growth of the exocrine pancreas and gallbladder Inhibits gastric emptying
Secretin	**"S" cells** of the duodenum	H^+ in the duodenum Fatty acids in the duodenum	↑ Pancreatic HCO_3^- secretion ↑ Biliary HCO_3^- secretion ↓ Gastric H^+ secretion Inhibits trophic effect of gastrin on gastric mucosa
Glucose-Dependent Insulinotropic Peptide (GIP)	**"K" cells** of the Duodenum and jejunum	Fatty acids Amino acids Oral glucose	↑ Insulin secretion from pancreatic β cells ↓ 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.

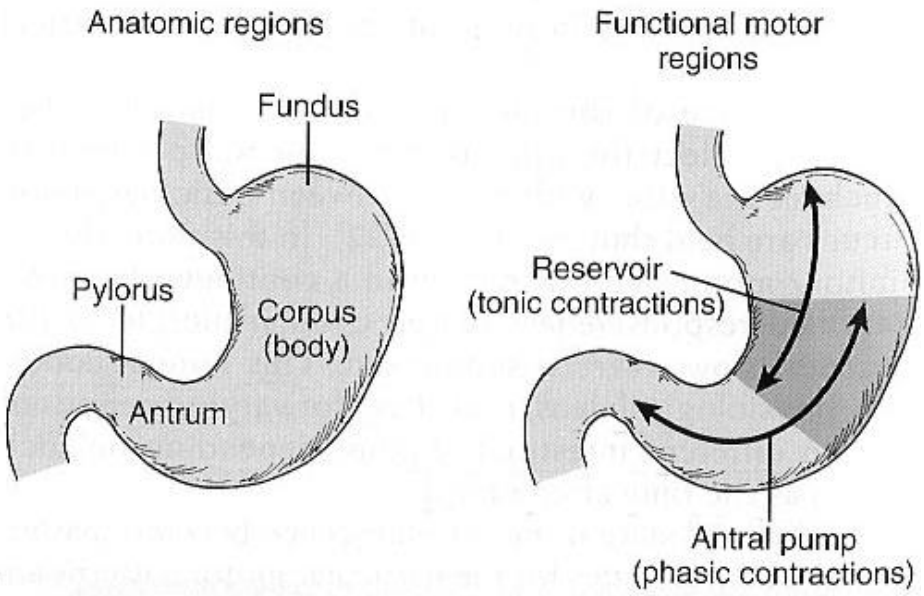
   (Chyme is a semi-fluid or paste composed of food that is thoroughly mixed with gastric secretions.
3. Absorption of some water and lipid-soluble substances (alcohol and drugs)
4. Regulate emptying of the chyme from the stomach into the small intestine

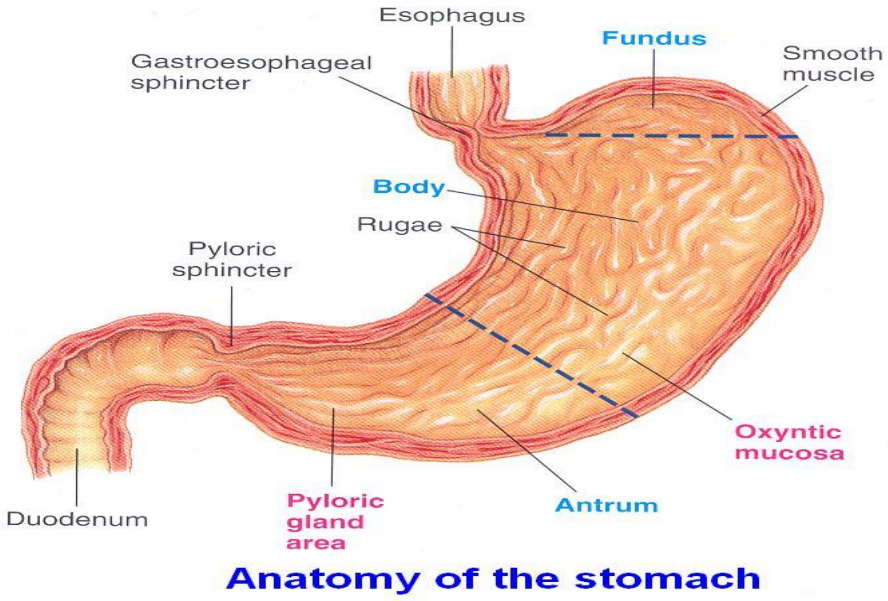
Anatomical and Physiological Divisions of the Stomach

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

Motor Functions of the Stomach (Cont.)

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.

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

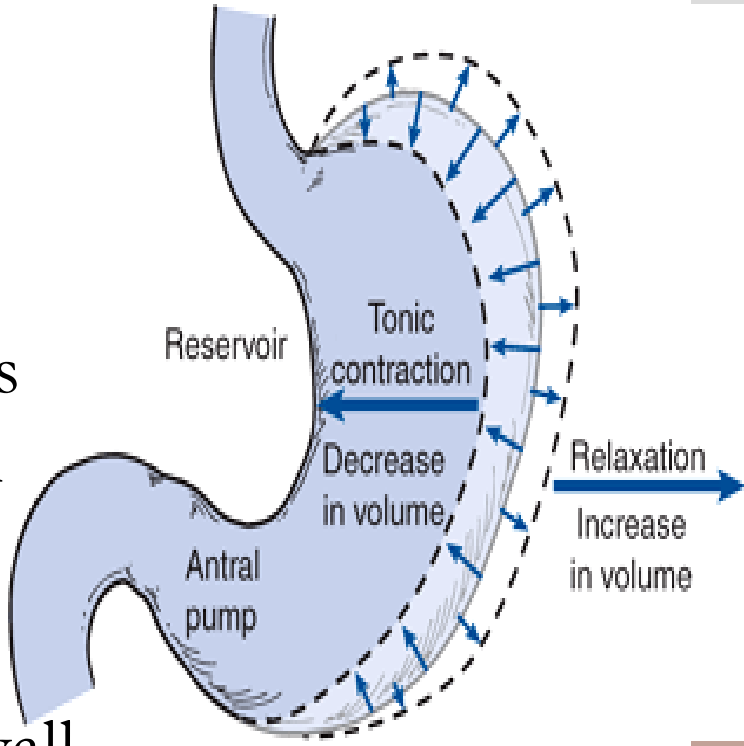
Three Kinds of Relaxation Occur in the Gastric Reservoir:

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

Types of Motor Activity of the Reservoir Part (Cont.)

A- Receptive Relaxation Reflex:

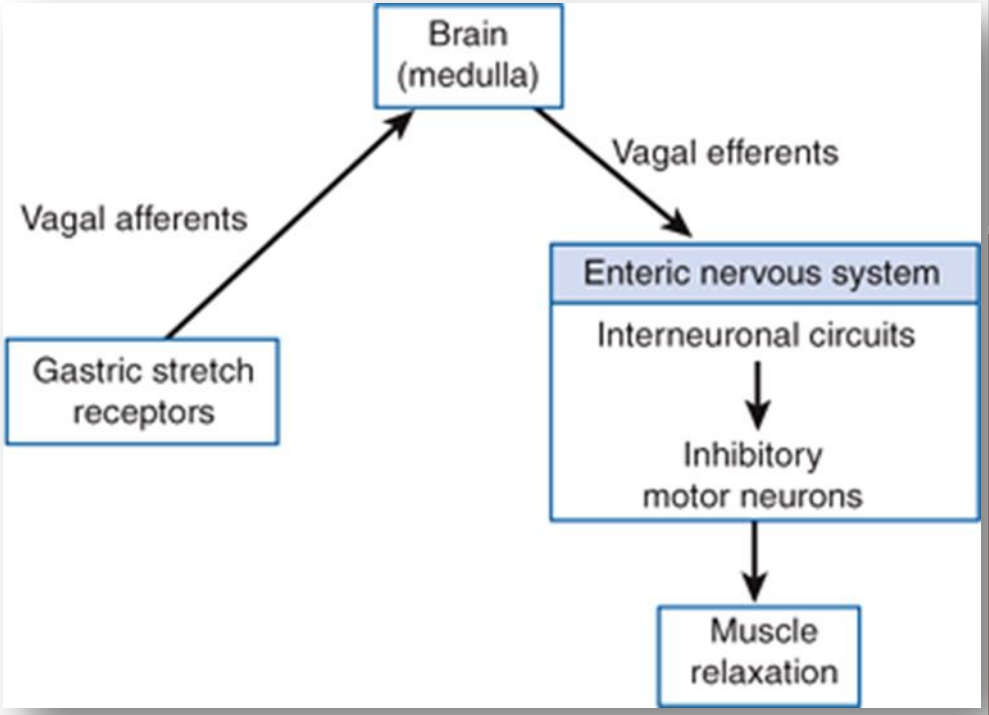
- Triggered by swallowing reflex.
- When the esophageal peristaltic waves reach the stomach, a vagovagal reflex is initiated from the stomach to the brain stem and back to the muscular wall of the stomach.
- This results in reduction in muscular wall tone and the stomach relaxes through inhibition of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



Types of Motor Activity of the Reservoir Part (Cont.)

B- Adaptive relaxation:

- 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.



Types of Motor Activity of the Reservoir Part (Cont.)

C- Feedback Relaxation:

- 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

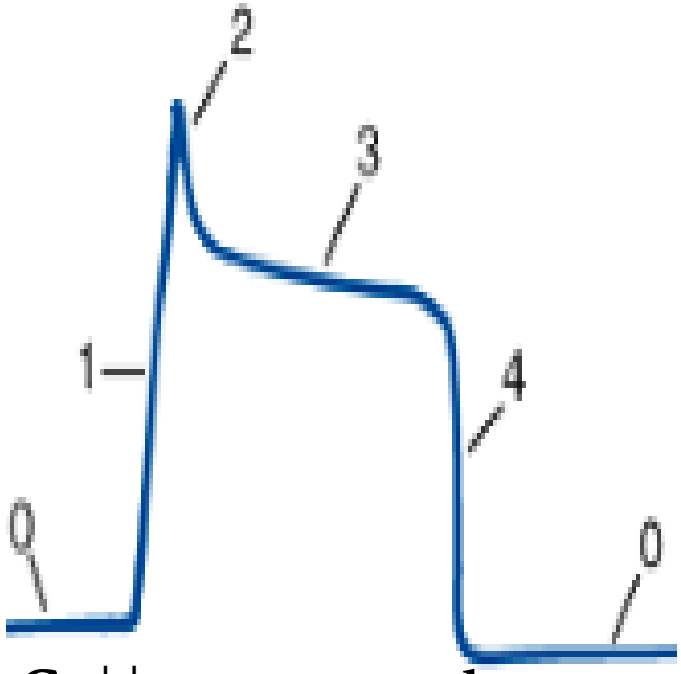
- Gastric action potentials determine the duration and strength of the phasic contractions of the antral pump.
- They are initiated by a dominant pacemaker (ICC).
- The action potentials propagate rapidly around the gastric circumference and trigger a ring-like contraction.
- The action potentials and 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 four phases:-

Phase 0: Resting membrane potential

Phase 1: Rising phase (upstroke depolarization); activation of voltage-gated Ca^{++} channels and voltage-gated K^{+} channels.



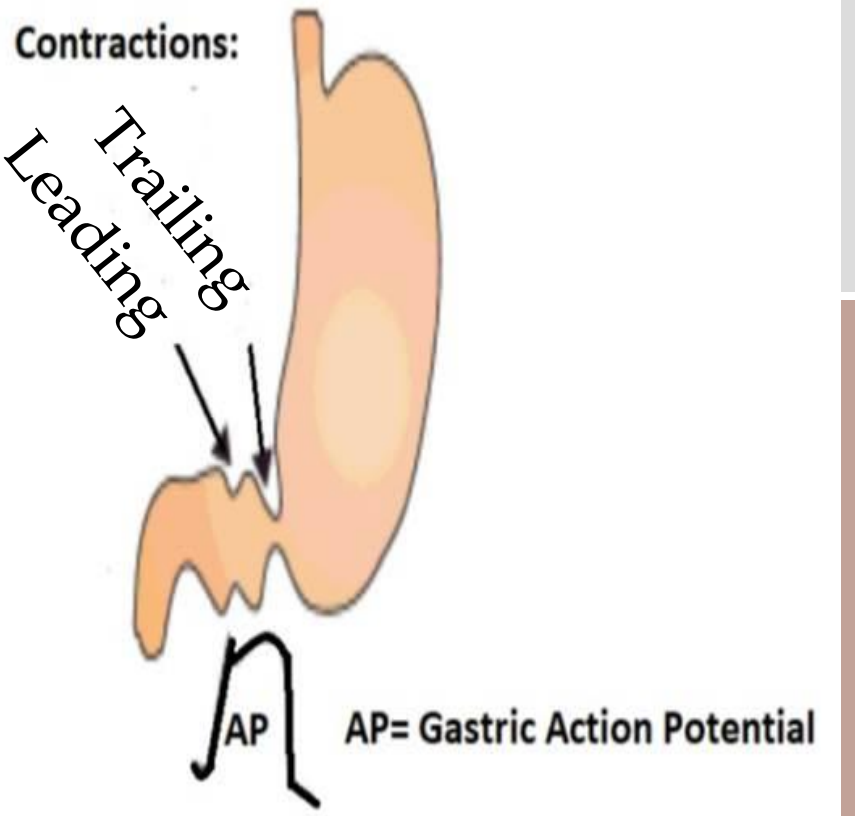
Phase 3: Plateau phase; balance of inward Ca^{++} current and outward K^{+} current.

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

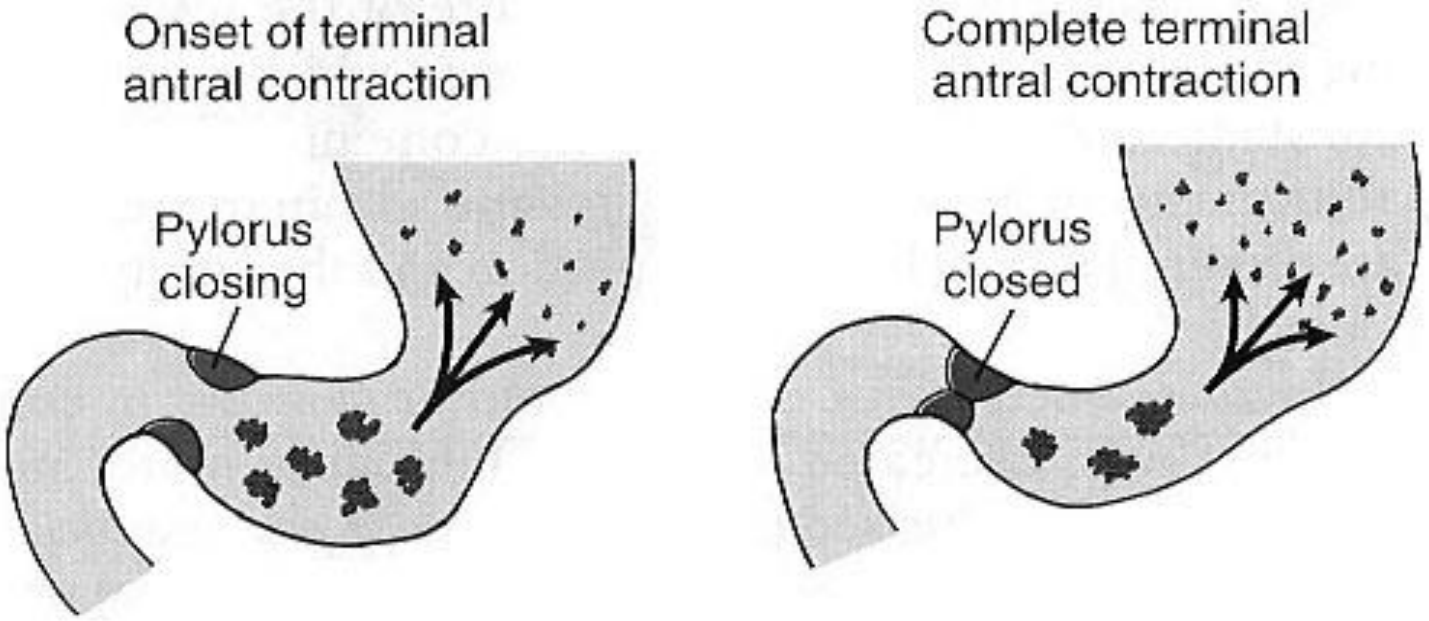
(1) **A leading contraction**, which has relatively constant (negligible amplitude), is associated with the rising phase of the action potential. As the rising phase reaches the terminal antrum and spreads into the pylorus, contraction of the pyloric muscle closes the orifice between the stomach and duodenum.

(2) **A trailing contraction**, of variable amplitude, is associated with the plateau phase. It follows the leading contraction by a few seconds.



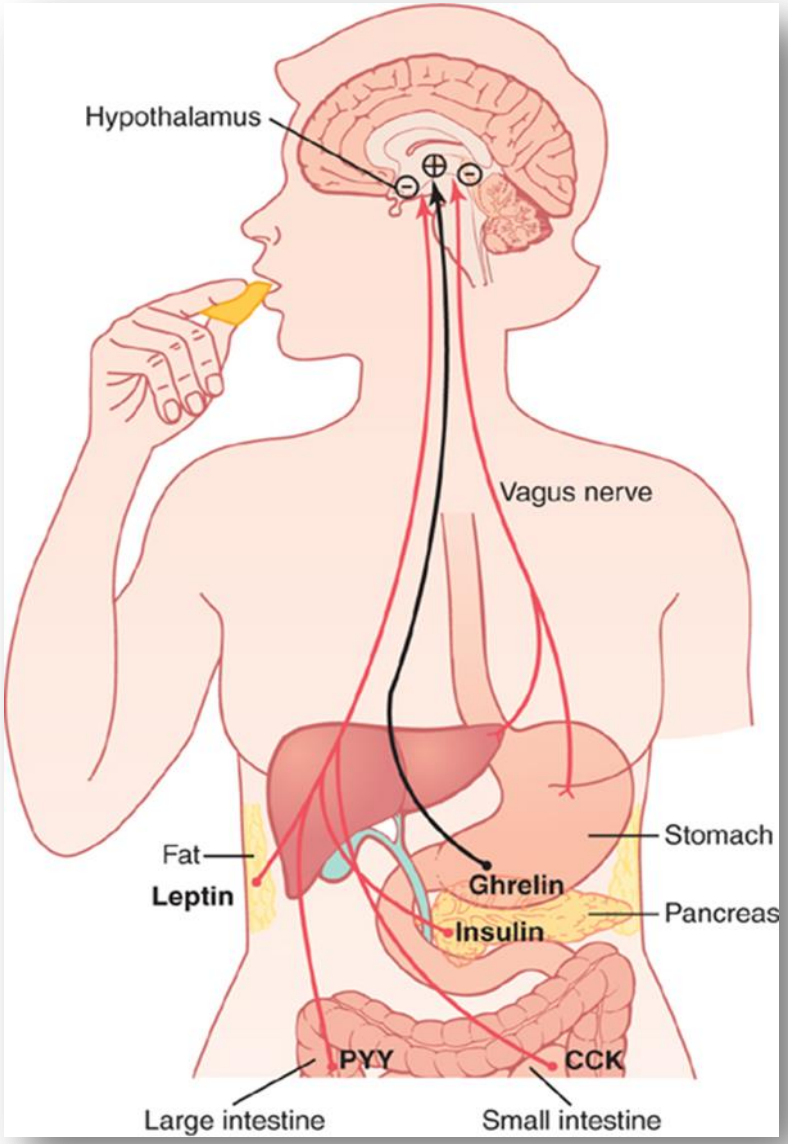
Retropulsion Phenomena

- 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.



Hunger Contractions:

- ✓ Occur when the stomach has been empty for several hours.
- ✓ Hunger pain can begin after 12-24 hr 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 and increase by low blood glucose levels.

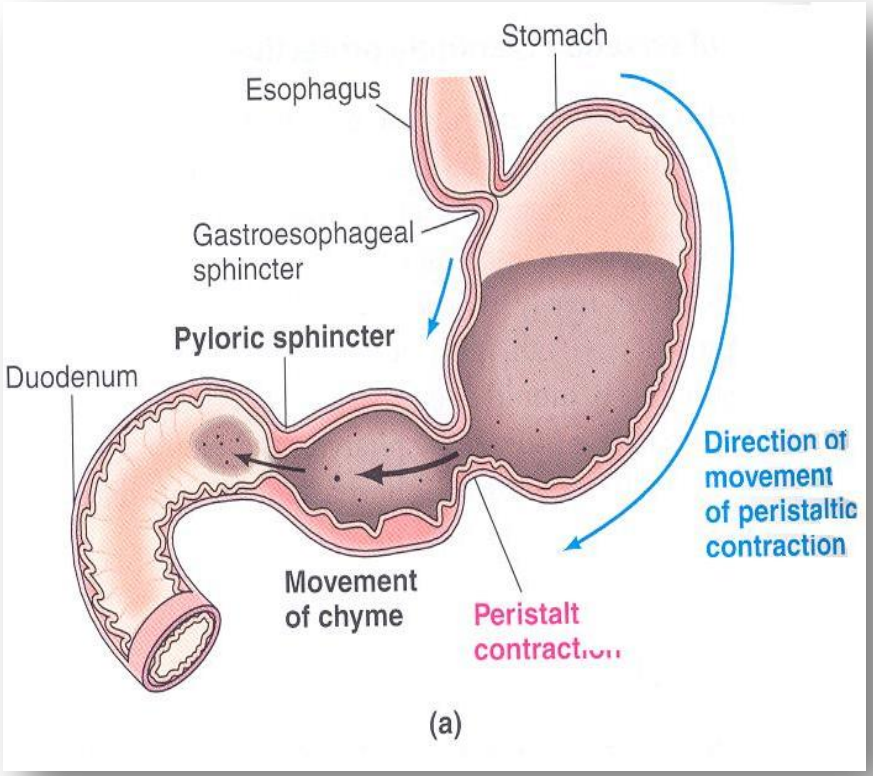


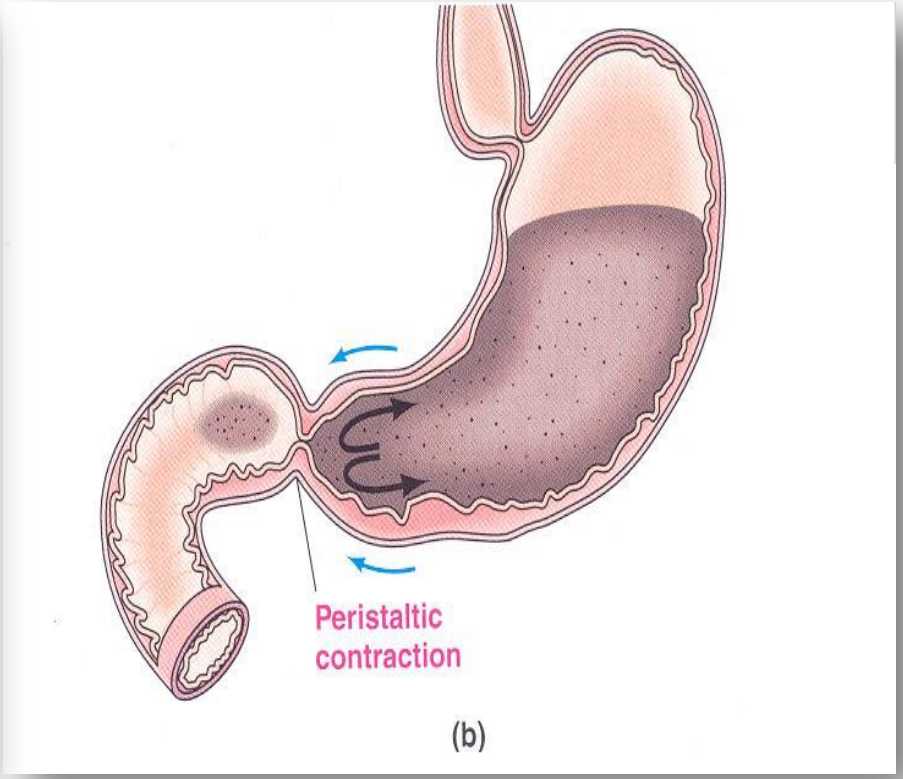
Gastric Emptying

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 Empting and Mixing as A Result of Antral Peristaltic Contraction





Factors Control Gastric Emptying

Gastric Promoting Factors

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.

Duodenal Factors that Initiate Enterogastric Inhibitory Reflexes

Distention and irritation

Acidity:- releases secretin which constricts the antrum

Hyperosmotic or hyposmotic 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 and <u>inhibit gastric emptying:</u>

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

- Sympathetic innervation

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