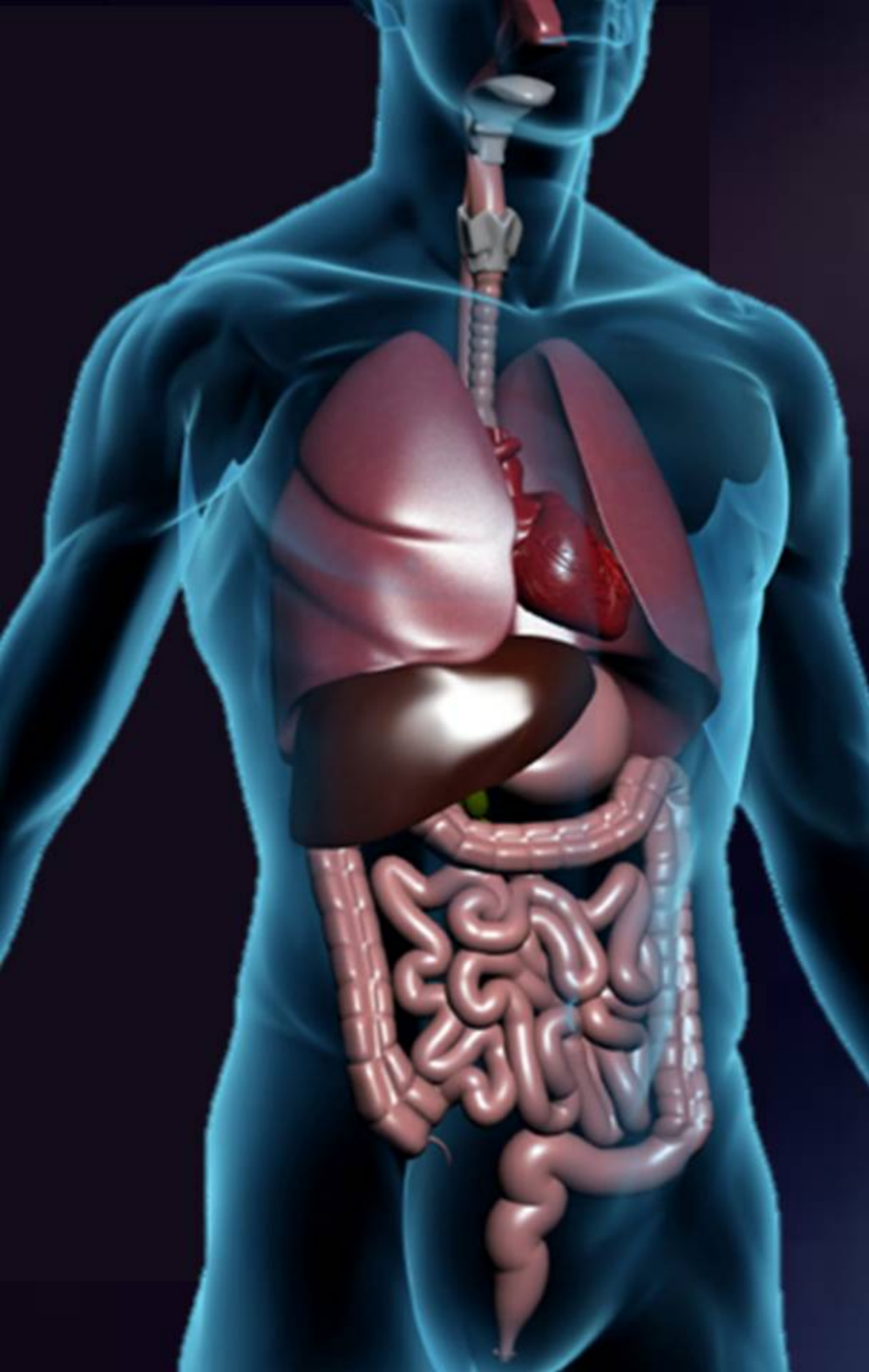


4 PHYSIOLOGY OF STOMACH & GASTRIC SECRETION

MED 433 Teams

GIT

Motor Functions of the Stomach:-

Main functions of the stomach

Storage of large quantities of food

The stomach can store 0.8-1.5 L of food. Gastric contents may remain unmixed for 1hour in the corpus.

Preparing the chyme* for digestion in the small intestine

*Is a murky semi-fluid or paste composed of food that is mixed with gastric secretions

Slow emptying of the chyme from the stomach into the small intestine

Mixing and Propulsion*الدفع* of Food in the Stomach

Major mixing activities take place in the antrum (antral pump region, phasic contraction).

Absorption of water and lipid-soluble substances (alcohol and drugs)

Anatomically and Physiologically Divisions of the Stomach:-

#Anatomically the stomach is composed of the

1-fundus

2-body

3-the antrum

#Physiologically it is composed of the stomach

1-orad portion **(fundus and upper two thirds of the body)**

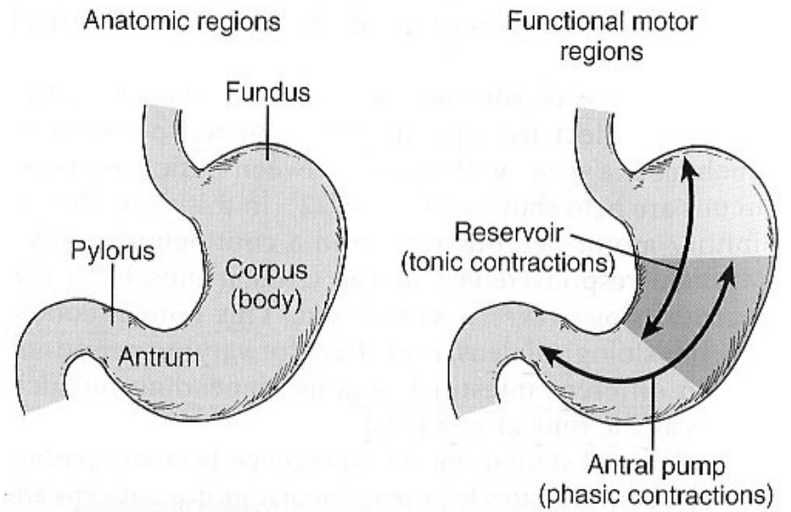
((Reservoir part **(tonic contraction)**))

2-the caudad **(lower third of the body plus antrum)**

((Antral pump **(phasic contraction)**)).

The main functions of (Reservoir part):

- To maintain a **continuous compression**
- To accommodate the received food with out significant gastric wall distention or pressure **(Storage of food)**



Relaxation Reflexes in Gastric Reservoir Part

Three Kinds of Relaxation Occur in the Gastric Reservoir:

Type of relaxation	Receptive Relaxation (vagovagal) Reflex	Adaptive relaxation (vagovagal) reflex *feel fullness or pain*	Feedback Relaxation *sends message back to tell that you are full*
the concept	When the esophageal peristaltic waves reach the stomach, the stomach relaxes through inhibition of myenteric neurons which prepares the stomach to receive the food. *Focusing on relaxation the stomach and the lowering esophageal getting the food*	when food stretches the stomach, a "vagovagal reflex" from the stomach to the brain stem and then back to the stomach reduces the tone in the muscular wall of the body of the stomach so that the wall bulges progressively outward, accommodating greater and greater quantities of food up to a limit (0.8 to 1.5 L) *Adaptive is more than receptive*	It can involve both 1- local reflex connections between stomach and small intestine (ENS). 2- hormones that are released from endocrine cells in the small intestine and transported by the blood to the gastric ENS and stimulate firing in vagal afferent terminals in the stomach then the relaxation will happen
Trigger	Triggered by swallowing reflex	Triggered by stretch receptors	Triggered by nutrients in the small intestine

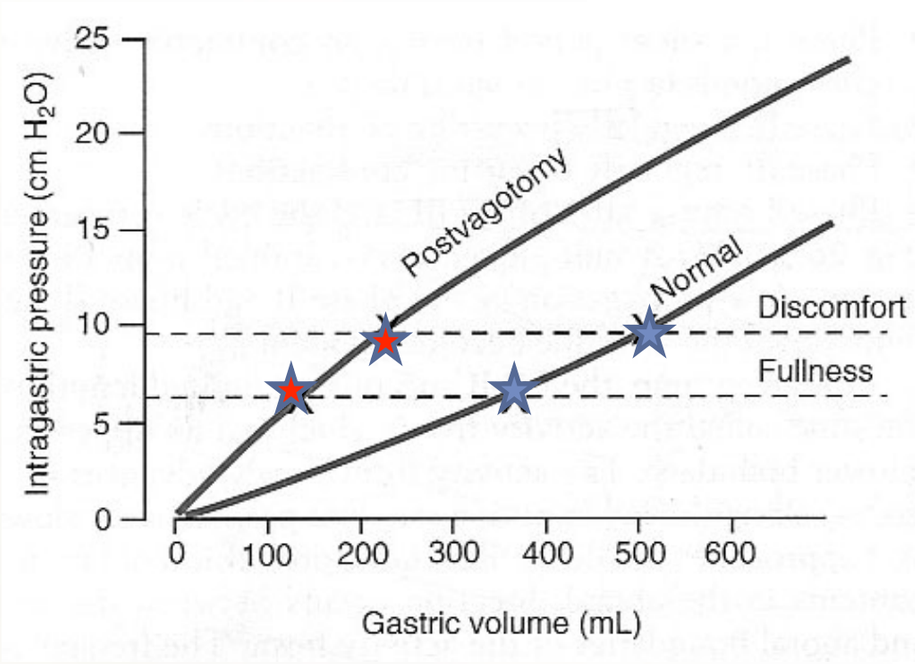
Relaxation Reflexes in Gastric Reservoir Part (continued)

Adaptive relaxation is lost in patients who have undergone a vagotomy. Following a vagotomy, increased the reservoir-muscle tone > 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.

بمعنى الي يحصل له قطع بالفيقس نيرف راح يفقد الادابتيف ريلاكسيشن بمعنى راح تزيد المصل التون لعضلات المعده ولابيحصل ريلاكسيشن استجابه للاكل ف بالتالي المريض راح يحس بالشبع والالم عند ليفل اقل من الانسان الطبيعي

★postvagotomy= the patient will feel fullness at 100 mL and pain at 200 mL

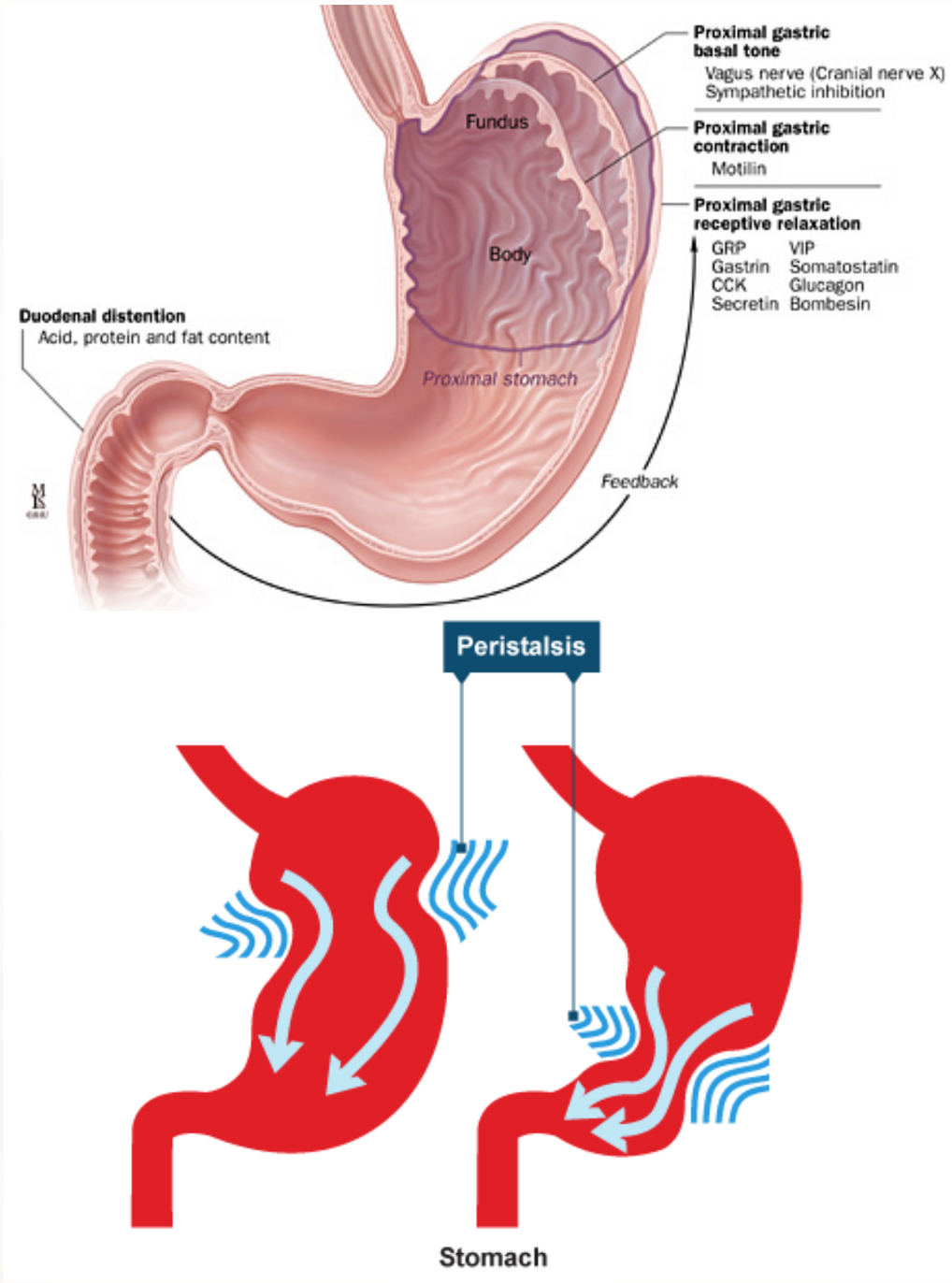
★Normal= the person will feel fullness at 350 mL and pain at 500 mL of gastric food



The Basic Electrical Rhythm of the Stomach Wall

* The presence of food causes weak peristaltic constrictor waves called **mixing waves** once every 15-20 sec.
* **These waves are initiated by slow spontaneous electrical waves (the gut wall basic electrical rhythm). These waves progress from the body to the antrum and become intense forcing the chyme tomove under high pressure toward the pylorus. Each time a peristaltic wave passes toward the pylorus, few millimeters of antral content move into the duodenum through the pyloric sphincter.**

* **Gastric action potentials determine the duration and strength of the phasic contractions**
* **They are initiated by a pacemaker called ICC** (interstitial cell of Cajal).
* **The action potentials propagate (spread) and cause a ring-like contraction. The action potentials and associated ring-like contraction then travel more slowly toward the gastroduodenal junction.**
* **The pacemaker region in humans generates action potentials and associated antral contractions at a frequency of three slow waves per minute. *each single slow wave can give 1-10 action potential*The gastric action potential lasts about 5 seconds and has a rising phase (depolarization), a plateau phase, and a falling phase (repolarization)**



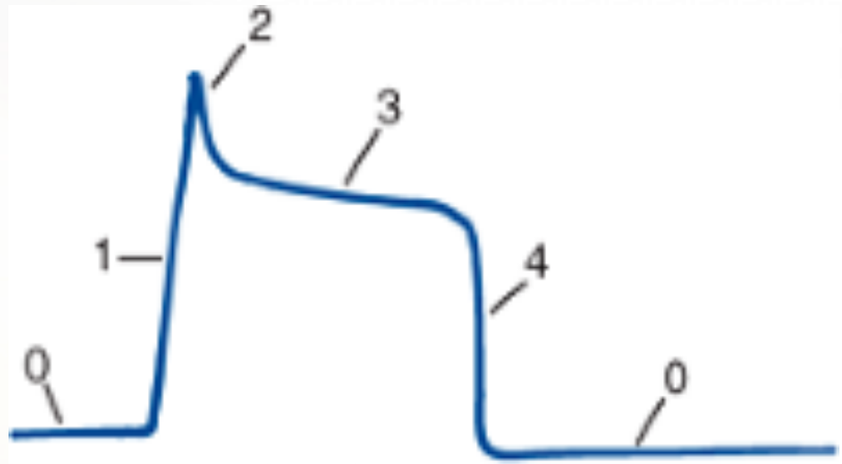
Electrical action potentials in gastrointestinal muscles occur in four phases,

Phase 0: Resting membrane potential

- **outward potassium current**

Phase 1: Rising phase (upstroke depolarization

- **activation of voltage-gated calcium channels <u>and</u> voltage-gated potassium channels**



Phase 3: Plateau phase

- **balance of inward calcium current and outward potassium current***this phase it might last 15 minutes and the calcium influx increase and the duration of contraction also increase**

Phase 4: Falling phase (repolarizatio n);

- **inactivation of <u>voltage-gated calcium channels</u> and activation of <u>calcium-gated potassium channels</u>.**

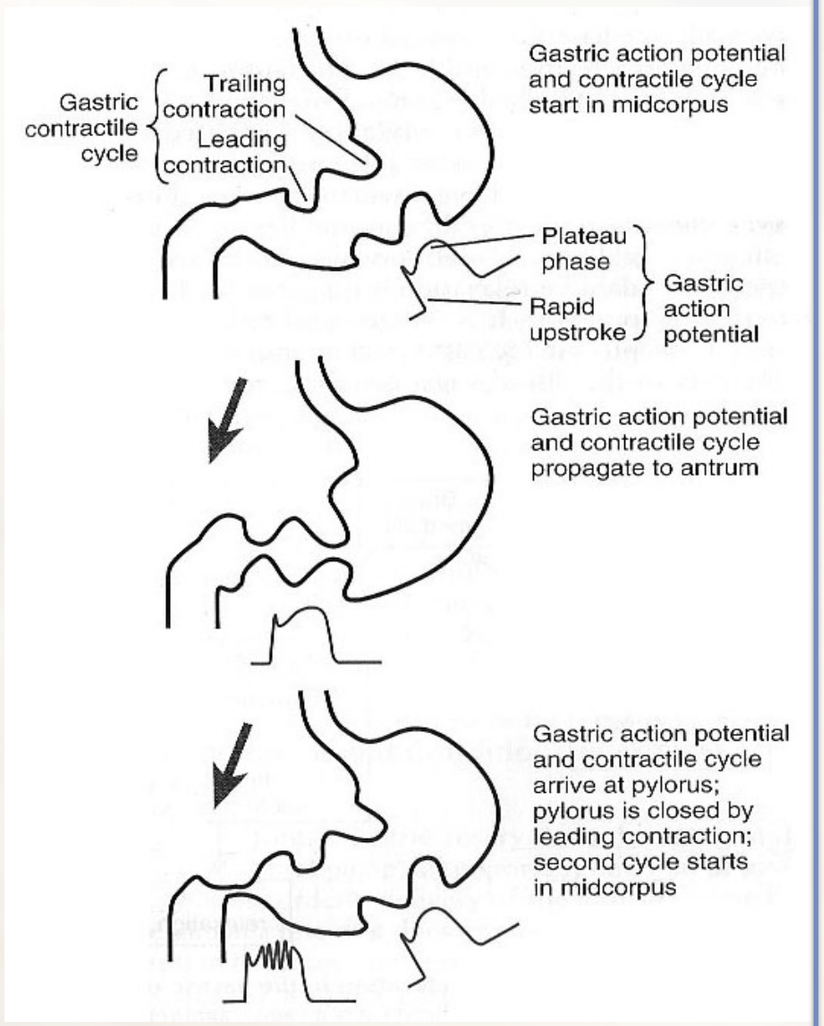
The Gastric Action Potential Triggers Two Kinds of Contractions (in the antral pump)

One action potential can give two contraction

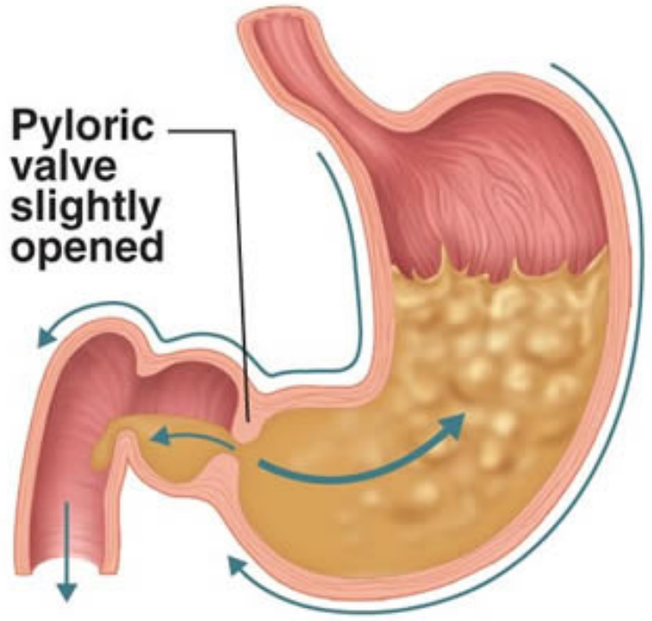
1 **A leading contraction:** **is a constant amplitude, is associated with the rising phase of the action potential**

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.

2 **a trailing contraction:** **is a variable amplitude. And it is associated with the plateau phase.**



Note\The trailing contraction follows the leading contraction by a few seconds



③ Retropulsion: The pyloric end of the stomach acts as a pump that delivers small amounts of chyme into the duodenum, simultaneously forcing most of its contained material backward into the stomach.

***)) Retropulsion (اندفاع خلفي*

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. This contraction causes increasing in gastric pressure.

Hunger contractions

1-occur when the stomach has been empty for several hours.

2-These are peristaltic contractions that can become very strong and fuse to form a continuing tetanic contraction lasting sometimes 2-3 minutes.

3-Hunger contractions are intense in young healthy people and increase by low blood glucose levels.

4-Hunger pain can begin after 12-24 hr of last food ingestion

Stomach emptying

Is the result of intense peristaltic antral contractions against resistance to passage of chyme at the pylorus.

Role of the pylorus in controling stomach emptying: The pyloric sphincter is characterized by strong circular muscle and remains tonically contracted most of the time. However, during pyloric constriction, watery chyme can still pass through the pylorus into the duodenum, but not food particles. Pyloric constriction is determined by nervous and humoral reflex signals from the stomach and the duodenum.

Regulation of Stomach Emptying

The rate of stomach emptying is controlled by signals from the duodenum and stomach. The signals from the duodenum are far stronger.

Gastric Factors that Promote Stomach Emptying	Powerful Duodenal Factors That Inhibit Stomach Emptying
1-Effect of Gastric Food Volume on Rate of Stomach Emptying ↑ **Gastric Food Volume = ↑ stomach emptying** (An increase in gastric food volume results in increased stretch in the stomach wall which elicits local myenteric reflexes that increase the activity of the pyloric pump and inhibit the tonic contraction of the pyloric sphincter)	**1-Inhibitory Effect of Enterogastric Nervous Reflexes from the Duodenum** When food enters the duodenum, multiple nervous reflexes are initiated from the duodenal wall to the stomach to regulate stomach emptying depending on the volume of chyme in the duodenum. These duodenal reflexes are mediated by three Routes **1- ENS:** hdirectly from the duodenum to stomach **2-prevertebral sympathetic ganglia:** through extrinsic nerves that go to the prevertebral sympathetic ganglia and then back through inhibitory sympathetic nerve fibers to the stomach **3-vagus:** extent through the vagus nerves reflex to the brain stem to inhibit the normal excitatory signals that are transmitted to the stomach through the vagus nerves (vagus itself is excitatory but here it get inhibited)
2-Effect of the Hormone Gastrin on Stomach Emptying **Gastrin is released from the antral mucosa in response to the presence of digestive products of meat. In turn, gastrin promotes the secretion of acidic gastric juices (ex. HCl) by the stomach gastric glands (or oxyntic glands)** **Gastrin also ↑ the activity of the pyloric pump and motor stomach function (moderate effect)**	**2-Hormonal Feedback from the Duodenum Inhibits Gastric Emptying** Releasing of CCK, secretin, gastric inhibitory peptide& GIP as a response to fat or acidity or large quantities of chyme. **1+2 inhibit the pyloric pump and increase the tone of the pyloric sphincter thus decreasing stomach emptying**

The types of factors that can initiate enterogastric inhibitory reflexes include

1) duodenal distention
2) duodenal irritation,
3) duodenal acidity,* activates S cells to release Secretin which constricts the antrum*
4) osmolality of the chyme in the duodenum,*Hyperosmotic or hyposmotic solutions delay gastric emptying *
5) protein content of the chyme in the duodenum.* Amino acids elicit inhibitory enterogastric reflexes; by slowing the rate of stomach emptying*
6) Fat (monoglycerides) in the duodenum *activates different cells to produce CCK and GIP that delay gastric emptying*

These six factors are inhibite the three reflexes that are related to Enterogastric Nervous Reflexes from the Duodenum in the previous slide

Gastric secretion :

The gastric mucosa in the stomach contains several cell types that secrete the various components of gastric juice . The cell types and their secretary products are :

1. Cardiac glands (10% of mucus) → secret mucus
2. Oxyntic glands (70 – 80) → in the fundus & the body of the stomach

	Mucus neck cells	Piptic (chief) cells	Parietal (oxyntic) cells
Location	fundus , body and antrum of the stomach	In oxyntic glands and few in pyloric glands	Oxyntic glands
Secretion	HCO_3^- Mucus	pepsinogen	HCL Intrinsic factor

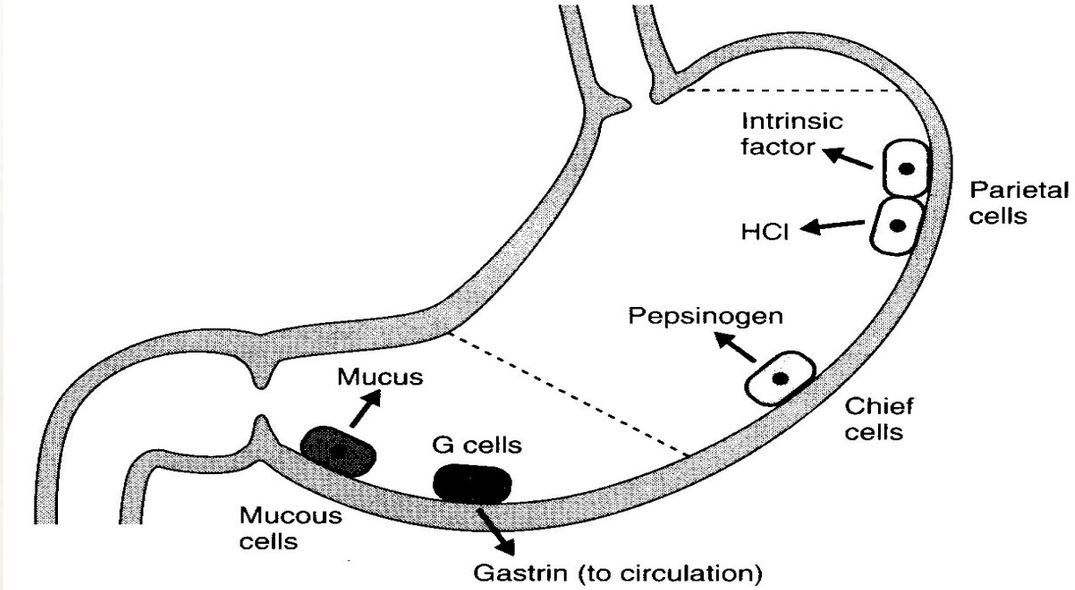
3. Pyloric glands (G cells)

secretion	Gastrin (hormon)
effect	Increase HCL secretion

4. D cells

secretion	Somatostatin (in the antrum)
effect	Decrease HCL secretion

5. Enterochromaffin-like cell → secret histamine



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

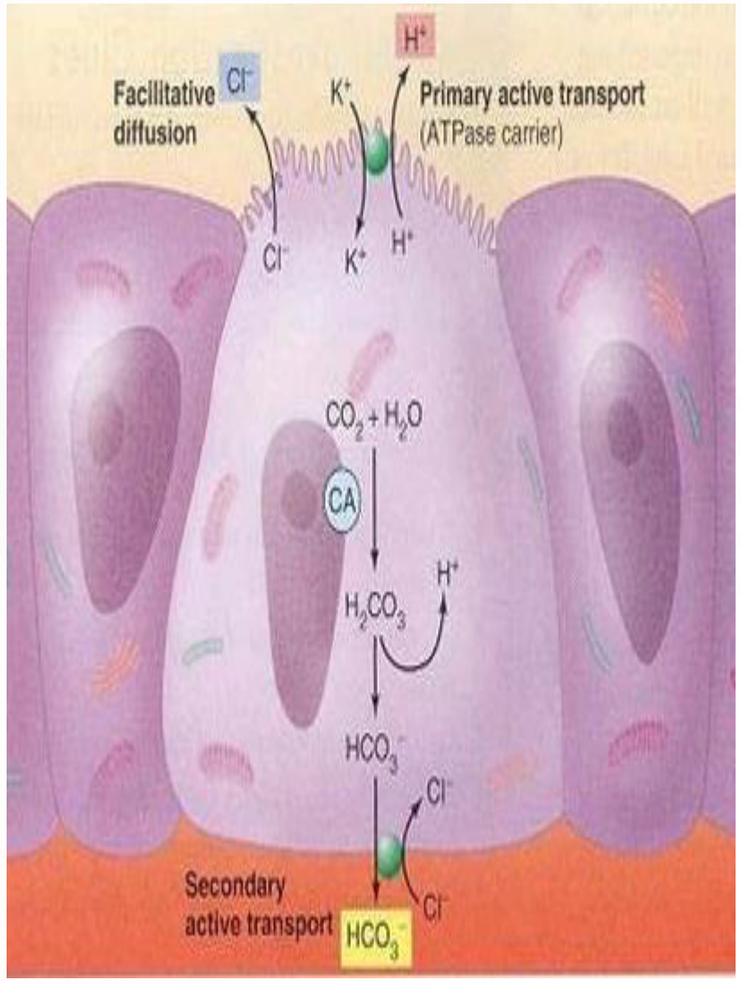
GASTRIC JUICE

- HCL
- Digestive enzymes (pepsinogen)
- eLectrolytes
- Intrinsic factors

Volume about 2-3 L/ day and it is highly acidic PH (0.8)

Gastric HCL :

❖Secreted by parietal cells.
❖They are pyramidal in shape.
❖ Their structure is unique in that they have an abundance of mitochondria* and intracellular canaliculi **"spaces between microvilli"** that are continuous with the lumen of the oxyntic gland.
❖**HCl is secreted across the parietal cell microvillar membrane and flows out of the intracellular canaliculi into the oxyntic gland lumen.**



*so they are very active cells as they have important role to concentrate H+ thousands times in order to form HCL .

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_3^- 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**.

Mechanism of HCL formation

* Water in the inside the parietal cell becomes dissociated in to H+ and OH- , then this H+ is actively secreted to the lumen in exchange with K+ , this active exchange is catalyzed by H+_K+ ATPase

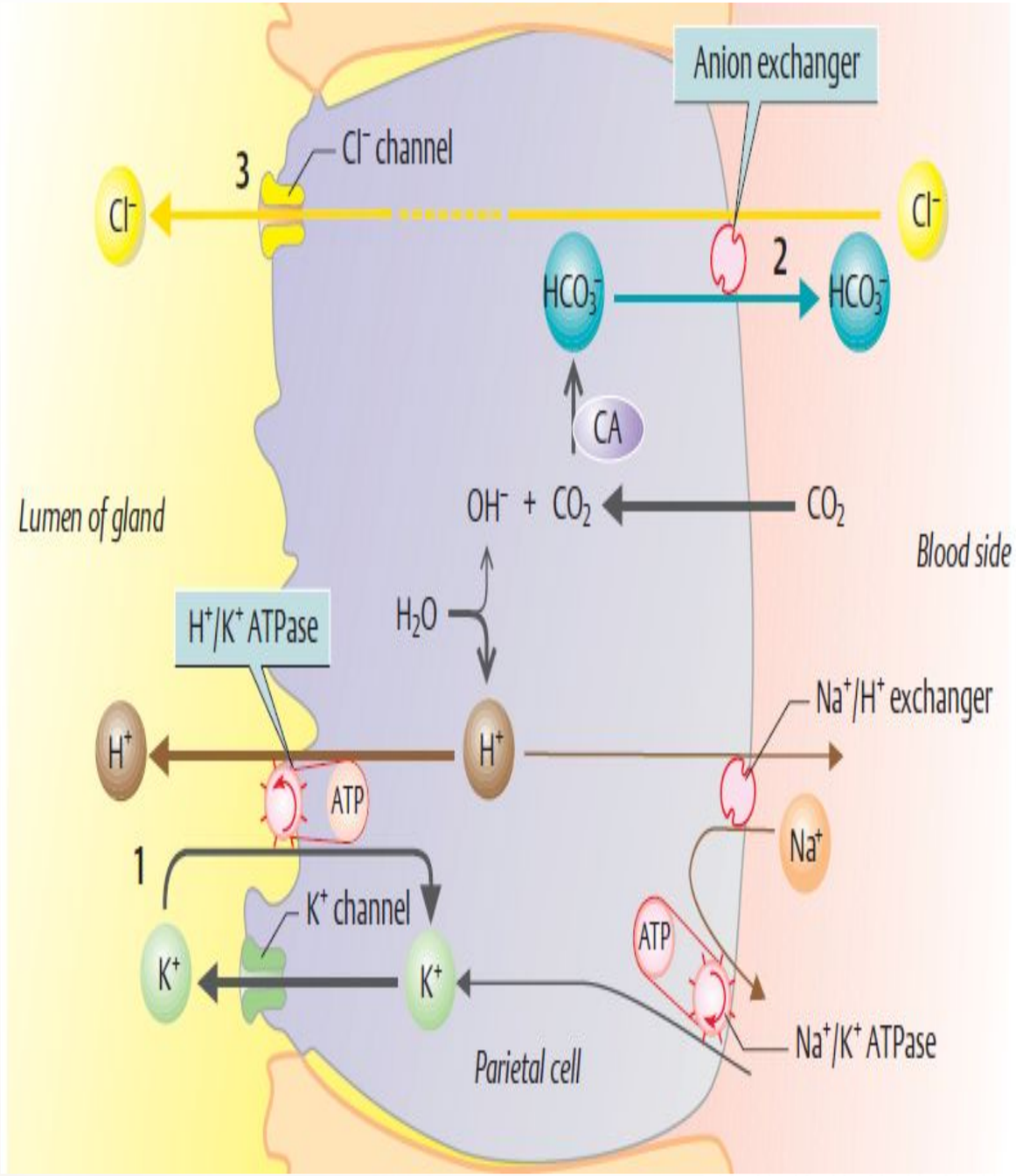
This active secretion of H+ will lead to accumulation of OH- which will be form HCO_3- from CO_2 , either formed during metabolism in the cell or entering the cell from the blood , this reaction is catalyzed by carbonic anhyd

HCO_3- is then transported into the extracellular fluid (alkaline tide) in exchange for Cl- by anion exchanger , Cl- will enter the cell and secreted through CL- channels in to the lumen

This will create –ve potential which causes passive diffusion of K+ from cytoplasm into . So the lumen will have K+ and CL- .
-K+ for exchange with H+
- Cl- for HCL formation

NOT IMPORTANT

* H+_K- ATPase can be inhibited by omeprazole (proton pump inhibitors)
-H+ is transported against its concentration gradiant



Secretion of H+ (HCL) = secretion of HCO_3-

HCL secretion :

- ✓Depends on H/K ATPase
- ✓Inhibited by: omeprazole
- ✓H/K pump depends on $[K]_{out}$ (K+ count)
- ✓[HCl] drives water into gastric content to maintain osmolality
- ✓Alkaline tide

Neural control

Vagus nerve

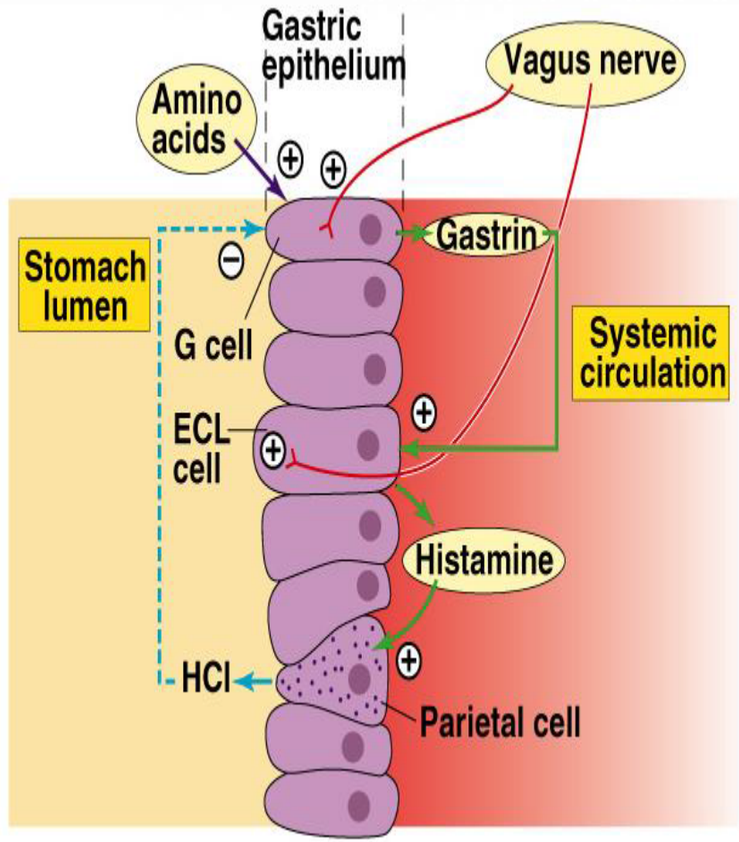
- Direct activation of the parietal cells by releasing of Ach
- Indirect activation of the parietal cells by releasing of gastrin releasing peptides (GRP)

Hormonal control

Gastrin

Histamine

Histamine is released from Enterochromaffin-like cells , which will activates activates H_2 receptor (parietal cells) → increase HCL secterion



Phases of gastric secretion :

1.CEPHALIC PHASE 30% OF HCL SECRETION

Stimuli	Mechanism of action
Smelling Chewing Swallowing of food	The impulses will be sent via vagus nerve to vagal necleus which wil send impulses to the parietal cells and G cells this will stimulate secretion of HCL by two ways : 1. Direct way : by releasing of Ach from the nerve endings → increase HCL secretion 2. Indirect way : releasing of GRP from the nerve endings this will stimulates G cells to secret gastrin → increase HCl secretion .

These two phases are excitatory

2.GASTRIC PHASE 60% OF HCL SECRETION

Stimuli	Mechanism of action
distention and presence of food (amino acid and small peptide = digested proteins) in stomach. *Several other chemicals, such as alcohol and caffeine, stimulate gastric acid secretion through mechanisms that are not well understood	It is under control of to mechanism : 1. nervous mechanism : Distension of either body or antrum of stomach stimulates mechanoreceptors in gastric wall . Which stimulate the parietal cells directly through: -Long vagovagal reflex -Short intramural cholinergic reflexes 2. Hormonal mechanism:** 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.

3.INTESTINAL PHASE 10% OF HCL SECRETION

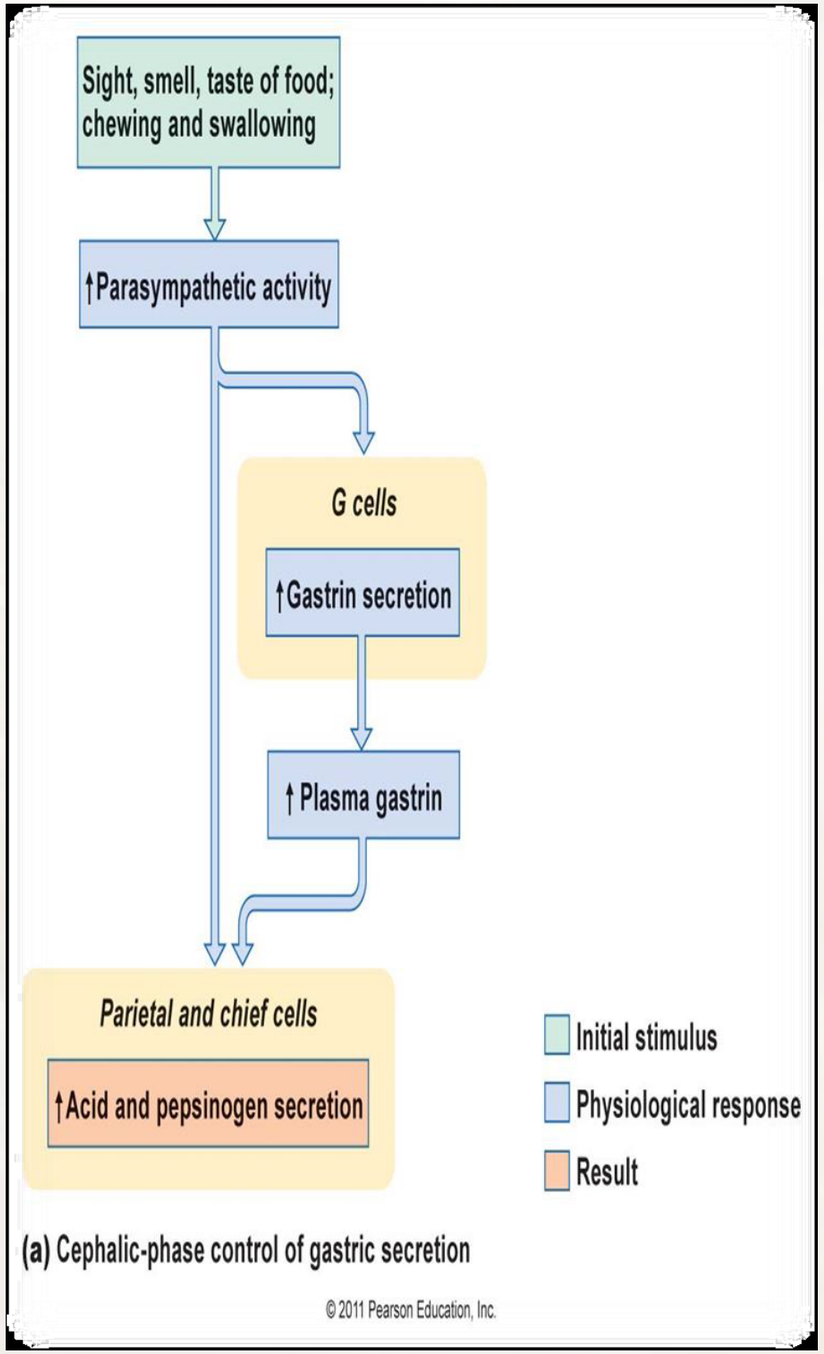
Stimuli	Mechanism of action
-Duodenal destention -presence of chyme(amino acid & peptide) in duodenum	The presence of chyme in duodenum causes neural & hormonal responses that first stimulates & later inhibits gastric acid secretion. 1- excitatory mechnism: secretion is enhanced by:- ❖ Distension of duodenum stimulates gastric acid (G.A) secretion by means of : -Neural : vagovagal reflex -Hormonal : the release of the hormone entero-oxyntin from intestinal endocrine cells that stimulates parietal & G- cells ❖Presence of protein digestive products in duodenum : this will stimulates G- cells in duodenum & proximal jejunum to release gastrin 2- inhibitory mechanism : -enterogastric reflex : the precense of food in small intestine will initiate this reflex , which will be transmitted through ENS & autonomic NS that inhibits G.A secretion. -Drop the pH in pyloric antrum to < 2.5 reduces G.A secretion via release of somatostatin from antral & duodenal “D” cells. - 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 .

SO INHIBITION OF GASTRIC ACID WILL BE BY INHIBITORY HORMONES (ENTEROGASTRONES):

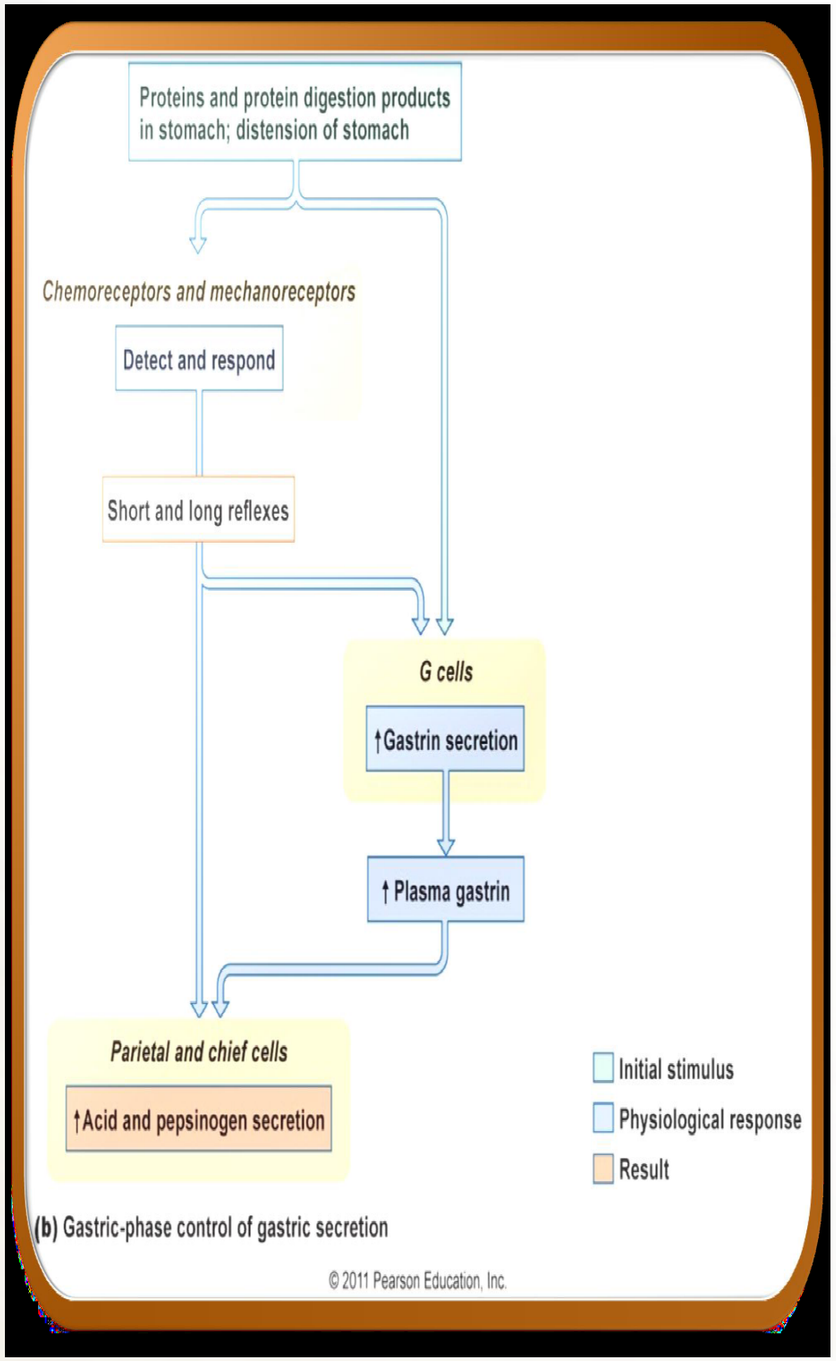
- Somatostatin (D-cells) in antrum
- Secretin (S-cells) in duodenum
- Glucose-dependent insulinotropic peptide (GIP) in duodenum

This phase is Excitatory at the beginning then inhibitory.

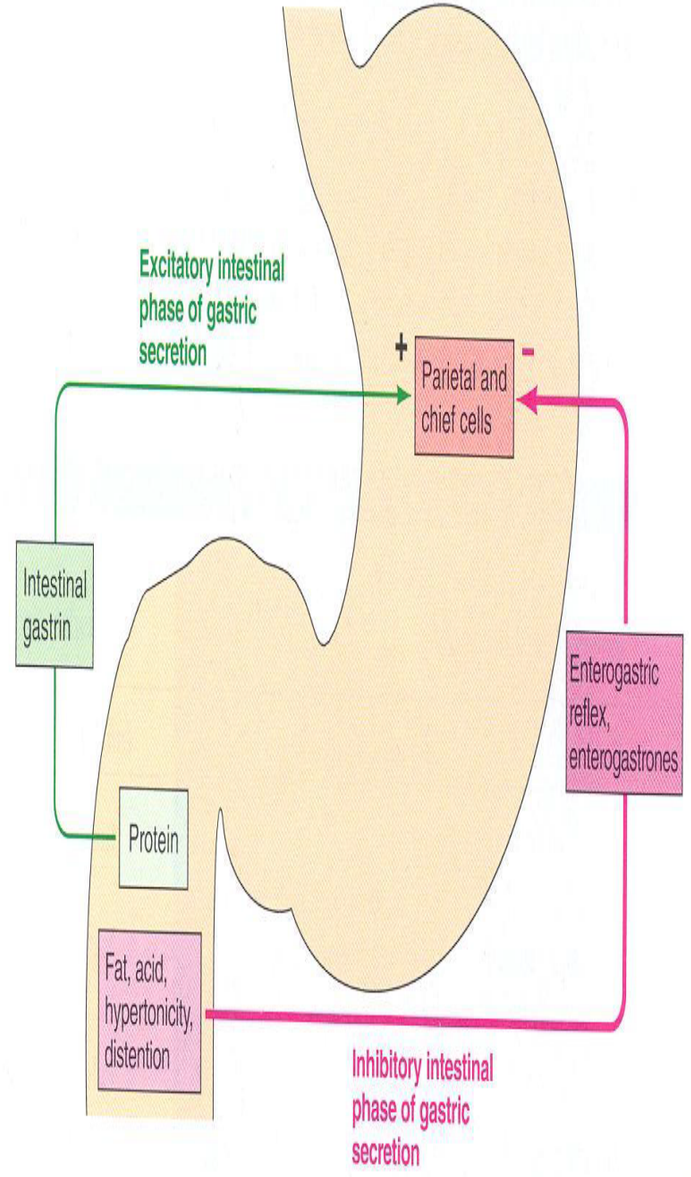
CEPHALIC PHASE



GASTRIC PHASE



INTESTINAL PHASE



Excitatory and inhibitory components af intestinal phase of gastric secretion

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GOOD LUCK