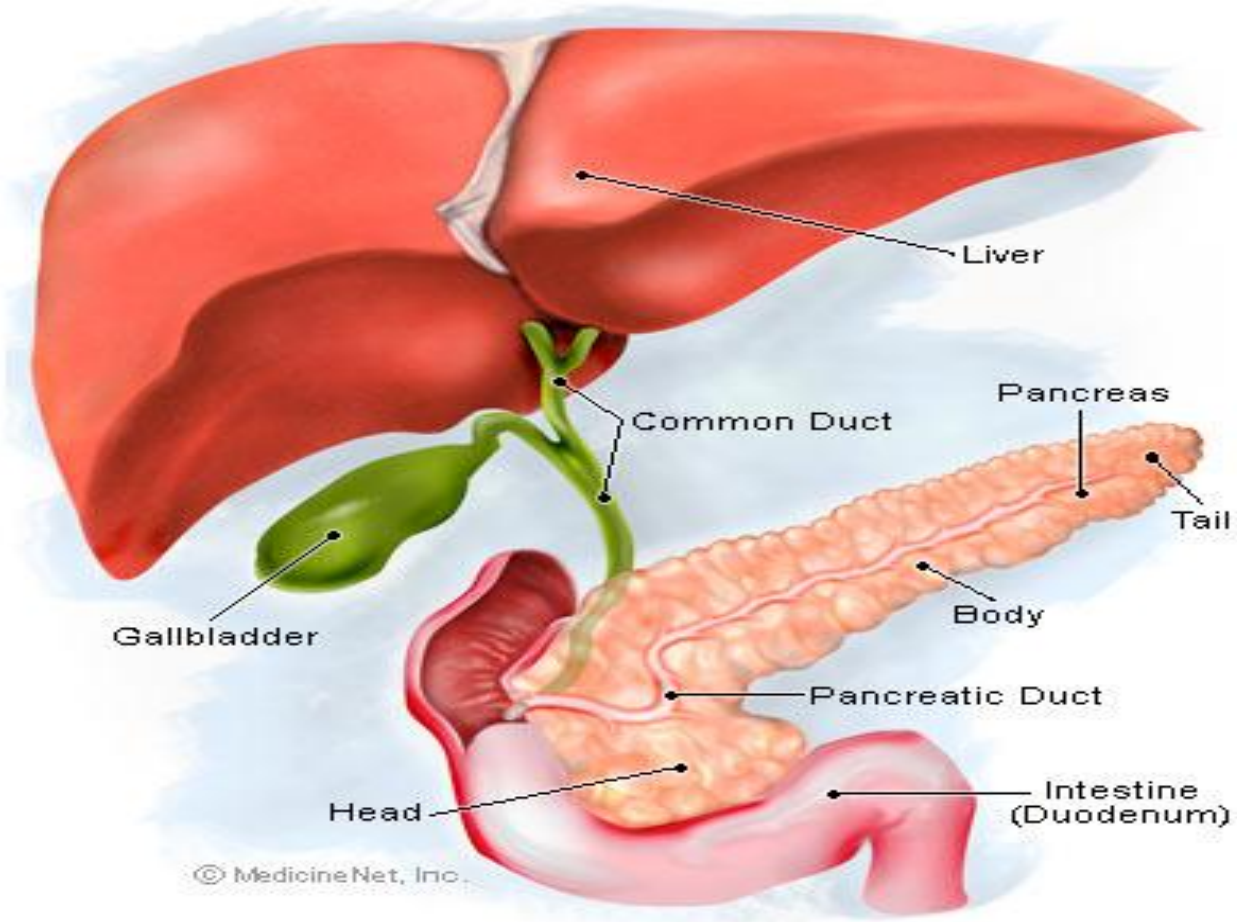
GIT Block

4th Lecture

Gastric motility and secretion



PHYSIOLOGY TEAM – 430

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Organized by: Akeel AL-Mahdaly

- ***Motor Functions of the Stomach***

The main motor functions of the stomach are:

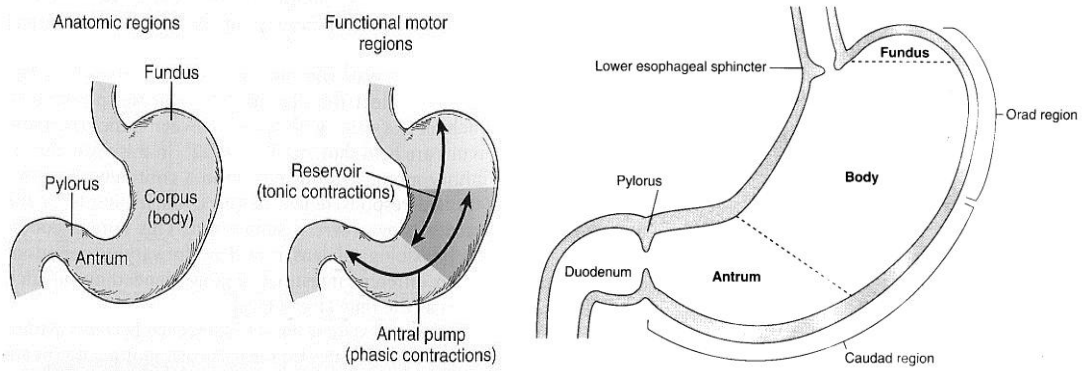
1. Storage of large quantities of food
2. Preparing the Chyme for digestion in the small intestine.
3. Absorption of water and lipid-soluble substances (alcohol and drugs)
4. Slow emptying of the Chyme from the stomach into the small intestine.

Anatomically and Physiologically Divisions of the Stomach:-

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

Physiologically, it is composed of:

1- The 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).



- ***Gastric reservoir:***

The main functions of the upper part of the stomach (Reservoir part):

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

Note: the type of contraction here is Tonic Contraction; which means a continuous contraction unlike Phasic Contraction. That is a problem because we can't accommodate that much food until we make relaxation of that Contraction, and that is mediated through 3 reflexes which will be discussed.

- ***Motor Functions Of the Stomach: -***

It's the storage and mixing function of the stomach.

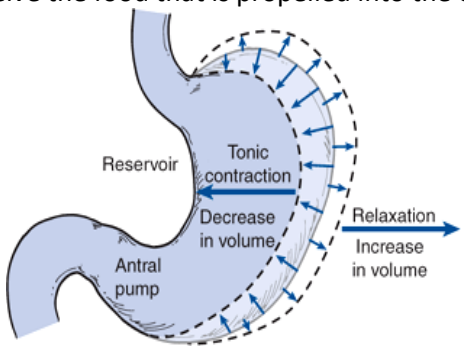
1. **Storage of food:** The stomach can store 0.8-1.5 L of food. Gastric contents may remain unmixed for 1hour in the corpus.
   - When the stomach is stretched by food, a vagovagal reflex is initiated from the stomach to the brain stem and back to the muscular wall of the stomach resulting in reduction in muscular wall tone which allows storage.
2. **Chyme:** Is a murky semi-fluid or paste composed of food that is thoroughly mixed with gastric secretions.
3. **Mixing and Propulsion of Food in the Stomach:** Major mixing activities take place in the antrum (antral pump region, phasic contraction).

Note: the type of contraction here is Phasic contraction (contraction followed by relaxation …)

Relaxation Reflexes in Gastric Reservoir Part:-

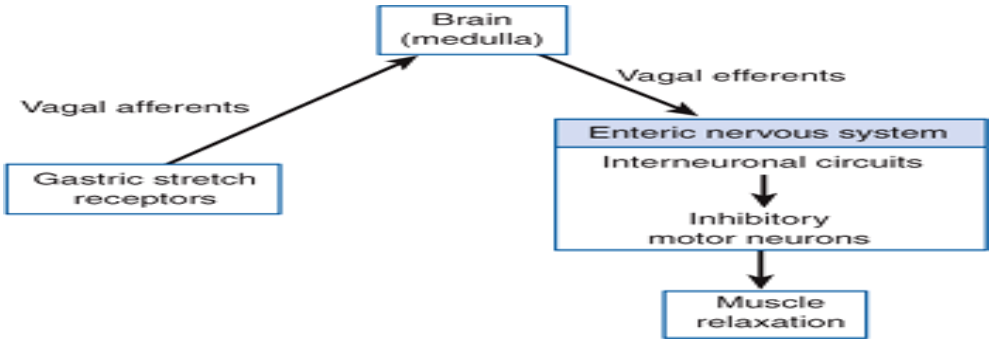
Three Kinds of Relaxation Occur in the Gastric Reservoir:

A. **Receptive Relaxation Reflex:** Triggered by swallowing reflex. When the esophageal peristaltic waves reach the stomach, the stomach relaxes through inhibition of Myenteric neurons, which prepares the stomach to receive the food that is propelled into the esophagus during swallowing.



B. **Adaptive relaxation:** Triggered by stretch receptors (vago-vagal reflex). Normally, 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). This reflex is lost in vagotomy.

Note: This relaxation is more important than the receptive relaxation reflex. It regulates the feeling of fullness and feeling of discomfort; it's the reflex that tells you that you are full when you eat a lot of food.



- Adaptive relaxation is lost in patients who have 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.

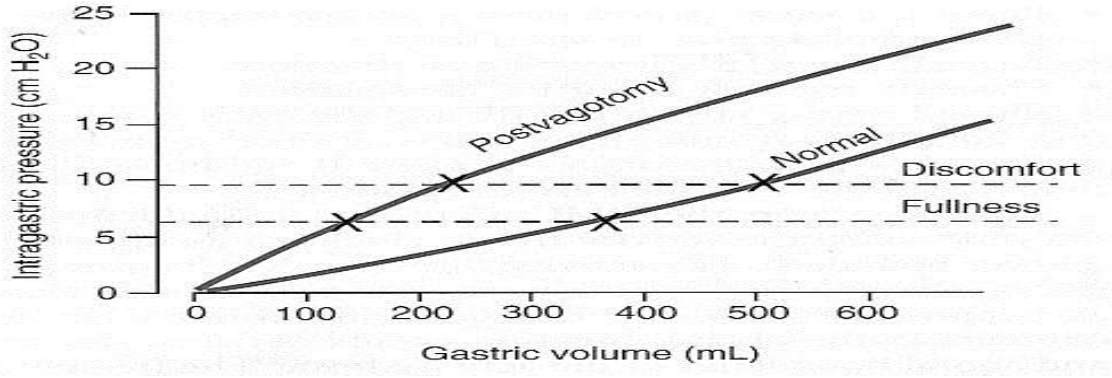


Figure 1- notice how the firing threshold is earlier in postvagotomy states.

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 transported by the blood to signal the gastric ENS and stimulate firing in vagal afferent terminals in the stomach.

Note: it's not a real Vagovagal reflex and doesn't represent much role in relaxation except when hormones are released.

- ***The Basic Electrical Rhythm of the Stomach Wall:***
  The digestive gastric juices are secreted by gastric glands and these secretions 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 waves once every 15-20 sec. These waves are initiated by the gut wall basic electrical rhythm of the slow spontaneous electrical waves. 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 to the antrum to the pylorus, few millimeters of antral content move into the duodenum through the pyloric sphincter.

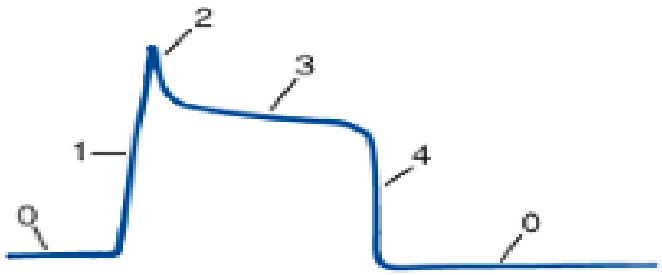
Important Note: In the gastric reservoir the type of contraction was Tonic contractions (Continuous Contraction) so slow waves are not present there. We don't need slow waves there. How come you get continuous contractions if you are building your contraction on slow waves?

Motor Behavior of the Antral Pump 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). 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 three per minute. The gastric action potential lasts about 5 milliseconds and has a rising phase (depolarization), a plateau phase, and a falling phase (repolarization)

Electrical action potentials in gastrointestinal muscles:

It occurs in 4 phases:-

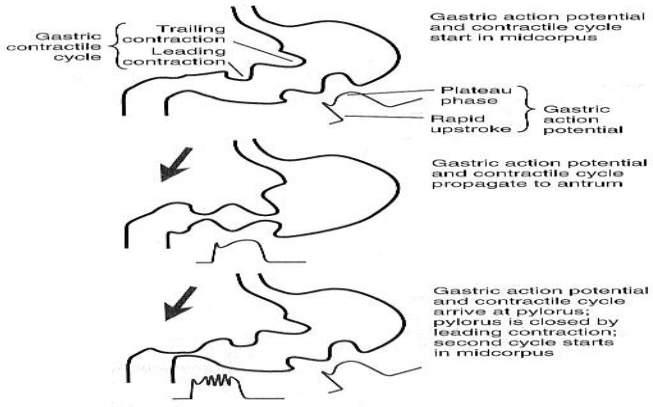


A. Phase 0: Resting membrane potential; outward potassium current.
B. Phase 1: Rising phase (upstroke depolarization); activation of voltage-gated calcium channels and voltage-gated potassium channels.
C. Phase 3: Plateau phase; balance of inward calcium current and outward potassium current.
D. **Phase 4**: Falling phase (repolarization); inactivation of voltage-gated calcium channels and activation of calcium-gated potassium channels.

Note: in this action potential we will get 2 contractions, one is during phase 1 and during the plateau phase. Between them (phase 2) it represents a fracture of milliseconds of rest between the 2 contractions. The 2 contractions are because Ca influx in both phases.

- The Gastric Action Potential Triggers Two Kinds of Contractions.
- The gastric action potential is responsible for two components of the propulsive contractile behavior in the antral pump:-

1- *leading contraction*, which has relatively constant amplitude, is associated with the rising phase of the action potential.
2- *trailing contraction*, of variable amplitude, is associated with the plateau phase.



- 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.

Note: If the food particles were big and couldn't pass the pyloric sphincter (larger than 7-mm) we will need Retropulsion Phenomena.

- ***Retropulsion phenomena:-***

as the trailing contraction approaches the closed pylorus, the gastric contents are forced into an antral compartment of ever-decreasing volume and progressively increasing pressure. This results in 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 H_2O (compared to a pressure of ~10 cm of H_2O during the mixing peristaltic contractions).

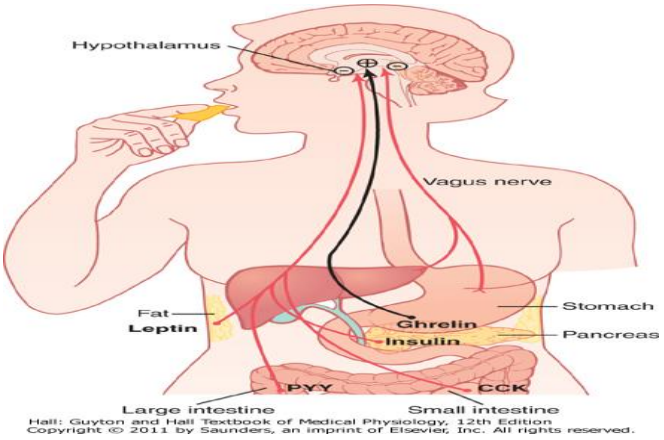
Note: Trailing Contraction is mainly responsible for Retropulsion phenomena and not leading contraction.

- ***Hunger: -***

Hunger Contractions: -

- 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.

Note: You must know that Ghrelin is responsible for regulating hunger pain to stimulate the hypothalamus so we feel hungry; on the other hand, Leptin does the opposite.



– Gastric Emptying:-

Stomach Emptying: Is the result of intense peristaltic antral contractions against resistance to passage of Chyme at the pylorus.

– Role of the Pylorus in Controlling Stomach Emptying: -

The distal opening is the pylorus. The pyloric sphincter is characterized by strong circular muscle (as compared to the antrum) 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.

-Note: The signals from the duodenum are far stronger; they in reality activate certain hormones to send their message to the stomach in order to delay gastric emptying.

1- Gastric Factors That Promote Emptying:

a. ***Food Volume:*** Increased food volume in the stomach promotes emptying from the stomach (inhibits the pylorus).

b. **Gastrin hormone:** enhances the activity of the pyloric pump. Thus, it, too, probably promotes stomach emptying.

2- Powerful Duodenal Factors That Inhibit Stomach Emptying:

1. **Inhibitory Effect of Enterogastric Nervous Reflexes from the Duodenum :**
   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:-

i. **Directly through ENS**

ii. **Through extrinsic nerves that go to the prevertebral sympathetic ganglia and then back through inhibitory sympathetic nerve fibers to the stomach.**

iii. **Through the vagus nerve.**

The types of factors that can initiate Enterogastric inhibitory reflexes include the following:

1- The distention of the duodenum.
2- Acidity of the duodenum activates S cells to release Secretin which constricts the antrum.
3- Fat (monoglycerides) in the duodenum activates different cells to produce CCK and GIP that delay gastric emptying.

4- Hyperosmotic or hyposmotic solutions delay gastric emptying
5- Amino acids elicit inhibitory Enterogastric reflexes; by slowing the rate of stomach emptying.

Constriction of Pyloric Sphincter:-

- **Hormones promote constriction**

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

- **Sympathetic innervation**

Gastric Secretion: -

The stomach's mucosal lining, the glandular gastric mucosa, contains three main types of glands:

1- Cardiac Glands.
2- Oxyntic Glands, which Is composed of 3 types of cells: -
a. **Mucus neck cells**
b. **peptic (chief) cells**
c. **parietal cells (Oxyntic cells) " most important cells "**
3-Pyloric glands (many G cells)

E. The Oxyntic glands are the most abundant gastric glands, found in fundus and corpus.

- ***structure of a Gastric Oxyntic Gland: -***

- Parietal cells are the most distinctive cells in the stomach. Their structure is unique in that they have intracellular canaliculi as well as an abundance of mitochondria and ER.
- This network consists of clefts and canals 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.
- 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.

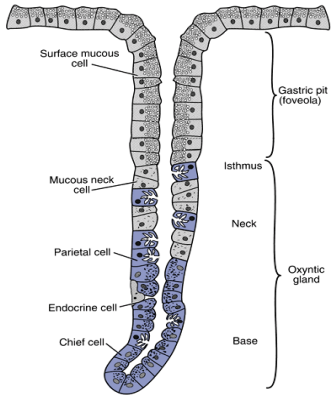
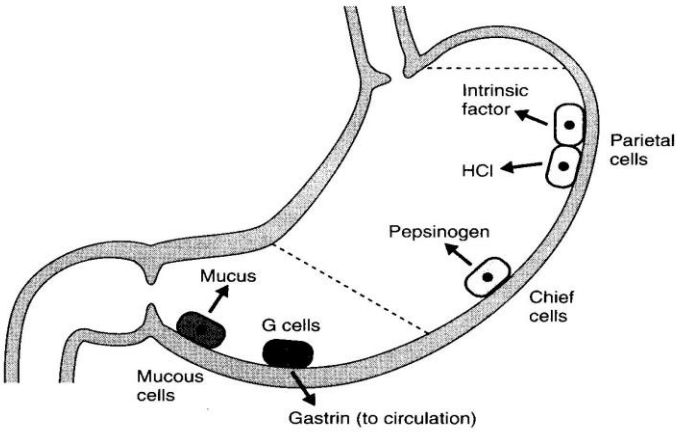


Figure 2*structure of a gastric Oxyntic gland.

- **Types of cells in the stomach: -**
- **Parietal cells (Oxyntic cells):**
  most distinctive cells in stomach (Releases HCl & intrinsic factor)
- **Chief cells (peptic cells);** they are available in Oxyntic glands and few in pyloric glands.
  Releases pepsinogen
- **Mucus neck cells:** Releases
  - HCO_3^-
  - Mucus
- **G Cells:** releases Gastrin (hormone), which increases HCl secretion
- **D Cells: releases:** Somatostatin (antrum) which decreases HCl secretion
- **Enterochromaffin-like cell: releases >**Histamine.
- **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: -**

The gastric juice consists of: -

- HCL
- Pepsinogen
- Electrolytes
- Intrinsic factor
- Mucus (mucus gel layer)

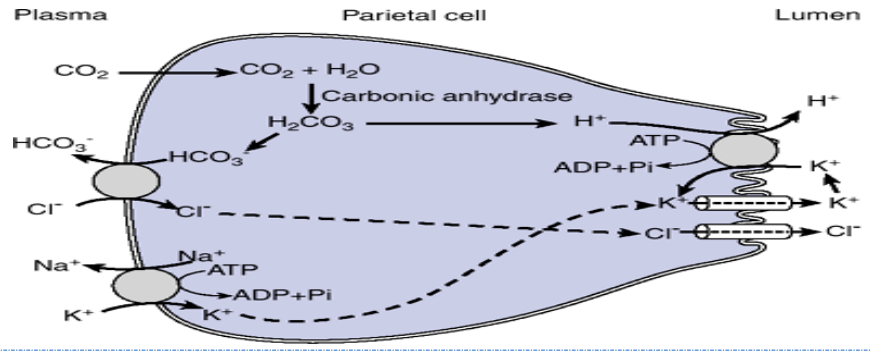
Note: the most important point here is the mechanism of production HCL.

- **Mechanism of HCL formation:-**

1. **Chloride (Cl^-) ion is actively transported from the cytoplasm of the parietal cell into the lumen of the canaliculus, and sodium (Na^+) ions are actively transported out of the canaliculus into the cytoplasm of the parietal cell.**

2. **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 through H^+-K^+ ATPase pump**; it can be inhibited by omeprazole.

3. **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.**



Mechanism of HCL production: -

-Depends on H/K ATPase.

-Inhibited by: omeprazole.

-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, this will lead to alkaline tide (in the blood).

- ***Control of Gastric Secretion: -***

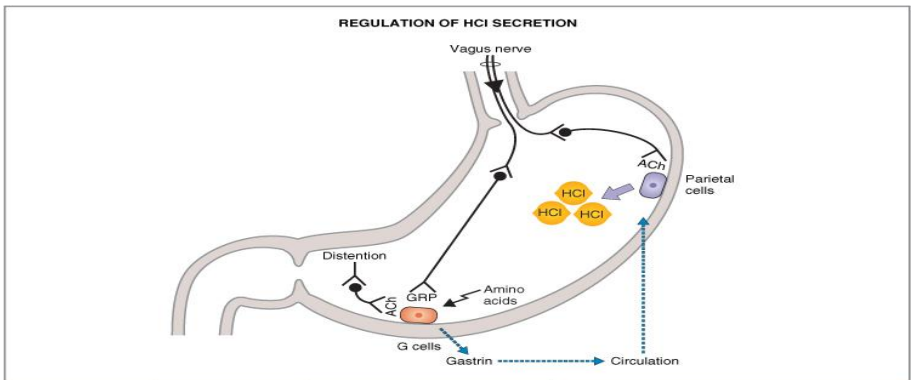
Gastric secretion is under neural & hormonal control.

Neural Control: -

- **Vagus nerve stimulation is the neural effector.**

Hormonal Control: -

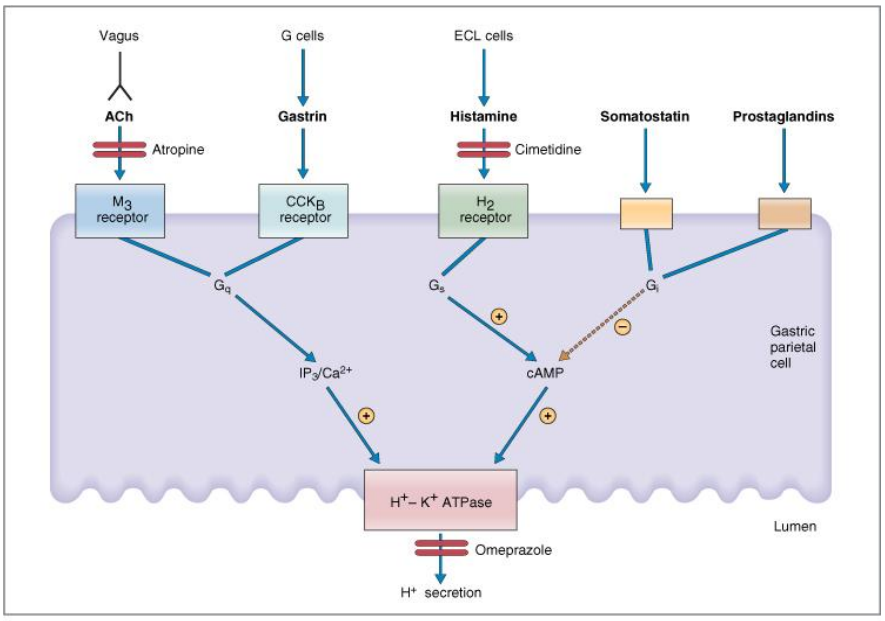
- **Histamine and gastrin are the hormonal effectors.**
- **Parietal cells possess special histamine receptors, H_2 receptors, whose stimulation results in increased acid secretion.**
- **Special neuroendocrine cells of the stomach, known as Enterochromaffin like (ECL) cells, are believed to be the source 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 H_2 blocker, in reducing acid secretion has indirectly demonstrated the importance of histamine as an effector of gastric acid secretion. H_2 blockers are commonly used for the treatment of peptic ulcer disease or gastroesophageal reflux disease.**



Phase	% of HCl Secretion	Stimuli	Mechanisms
Cephalic	30%	Smell, taste, conditioning	Vagus → parietal cell Vagus → gastrin → parietal cell
Gastric	60%	Distention	Vagus → parietal cell Vagus → gastrin → parietal cell
		Distention of antrum	Local reflex → gastrin → parietal cell
		Amino acids, small peptides	Gastrin → parietal cell

- Vagus nerve (neural effector) either by releasing Ach (direct activation of parietal cells) or by releasing Gastrin releasing peptide, GRP (indirect activation).
- Gastrin (hormonal effector)
- Enterochromaffin-like cells release Histamine→ activates H_2 receptor (parietal cells) → increases acid secretion
- Cimetidine (H_2 receptor blocker)→ peptic ulcer and gastroesophageal reflux

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



Rate of Secretion: -

- ***<u>The Rate of Secretion Modify the Composition of Gastric Juice.</u>***
- At a low secretion rate, gastric juice contains high concentrations of Na^+ and Cl^- and low concentrations of K^+ and H^+.
- When the rate of secretion increases, the concentration of Na^+ decreases whereas that of H^+ increases significantly. Also coupled with this increase in gastric secretion is an increase in Cl^- concentration.
- To understand the changes in electrolyte composition of gastric juice at different secretion rates, remember that gastric juice is derived from the secretions of two major sources: parietal cells and nonparietal cells.
- Secretion from nonparietal cells is probably constant; therefore, it is parietal secretion (HCl secretion) that contributes mainly to the changes in electrolyte composition with higher secretion rates.
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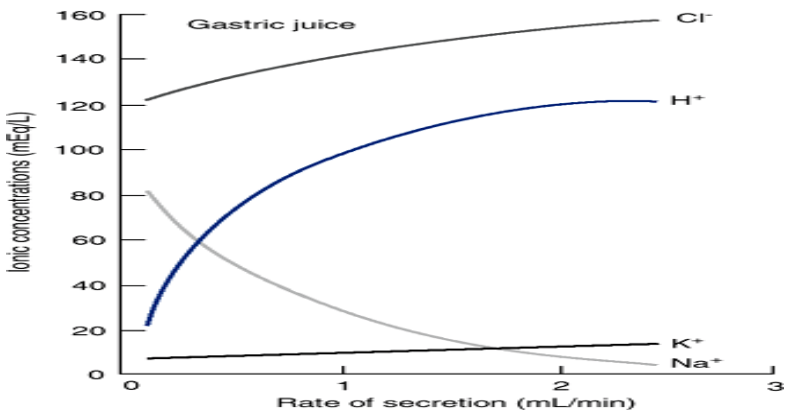


Gastric Secretion Phases: -

- Gastric secretion occurs in 3 phases.
  The stimulation of acid secretion resulting from the ingestion of food can be divided into three phases:

1) Cephalic Phase (before food reaches the stomach).
2) Gastric Phase (begins when actually food reaches the stomach).
3) Intestinal Phase.

1) Cephalic Phase: -

It refers to the increased secretion of HCL and pepsinogen (HCL is the main topic) that occurs in response to stimuli acting in the head (cephalic means head).

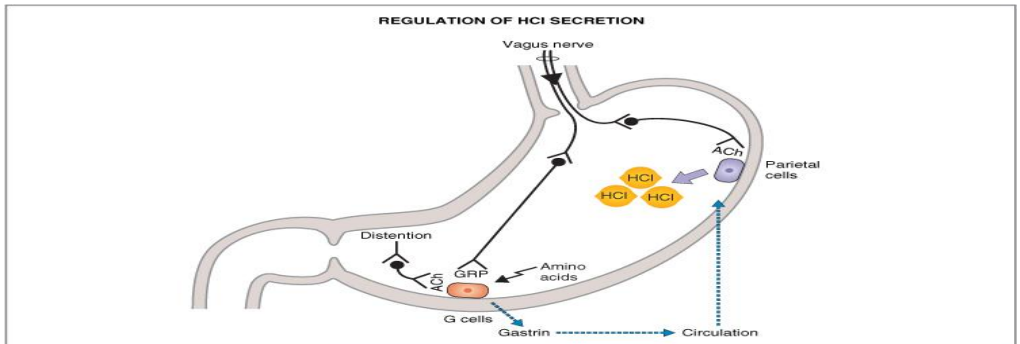
- **Thinking about, smelling, tasting, chewing, and swallowing food increase gastric secretion by vagal nerve activity in two ways.**
- **Stimuli in the head (smelling, chewing…) send impulses via the vagus nerves to the parietal and G cells in the stomach. The nerve endings release ACh, which directly 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.**

2) Gastric phase: -

- **The gastric phase is mainly a result of gastric distention and chemical agents such as digested proteins.**
- **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: -

- **During the intestinal phase, 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.**



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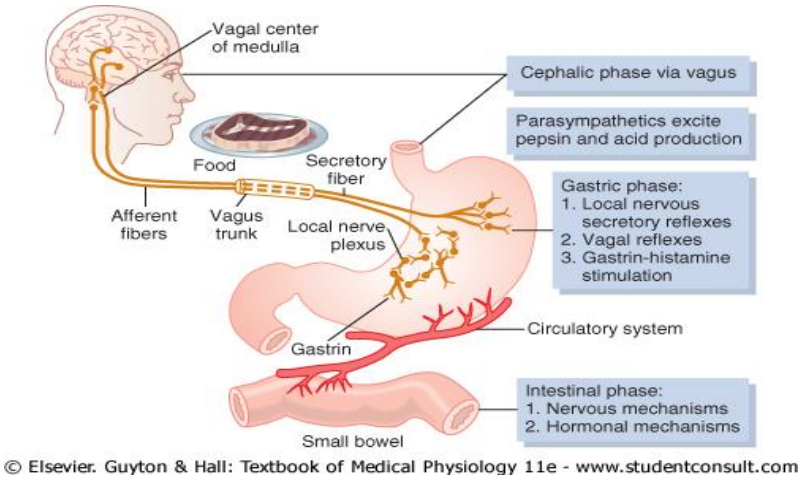
- **Cephalic phase (30%):**
  Stimuli: Smelling, Chewing and swallowing…
  it Stimulates parietal G-Cells GRP.
- **Gastric phase (60%):**
  stimuli: gastric distention - proteins.
- **Intestinal phase (10%):**
  Stimuli: digested proteins.



Inhibition of Acid Secretion: -

Inhibitory hormones (Enterogastrones) inhibit gastric acid secretion: -

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