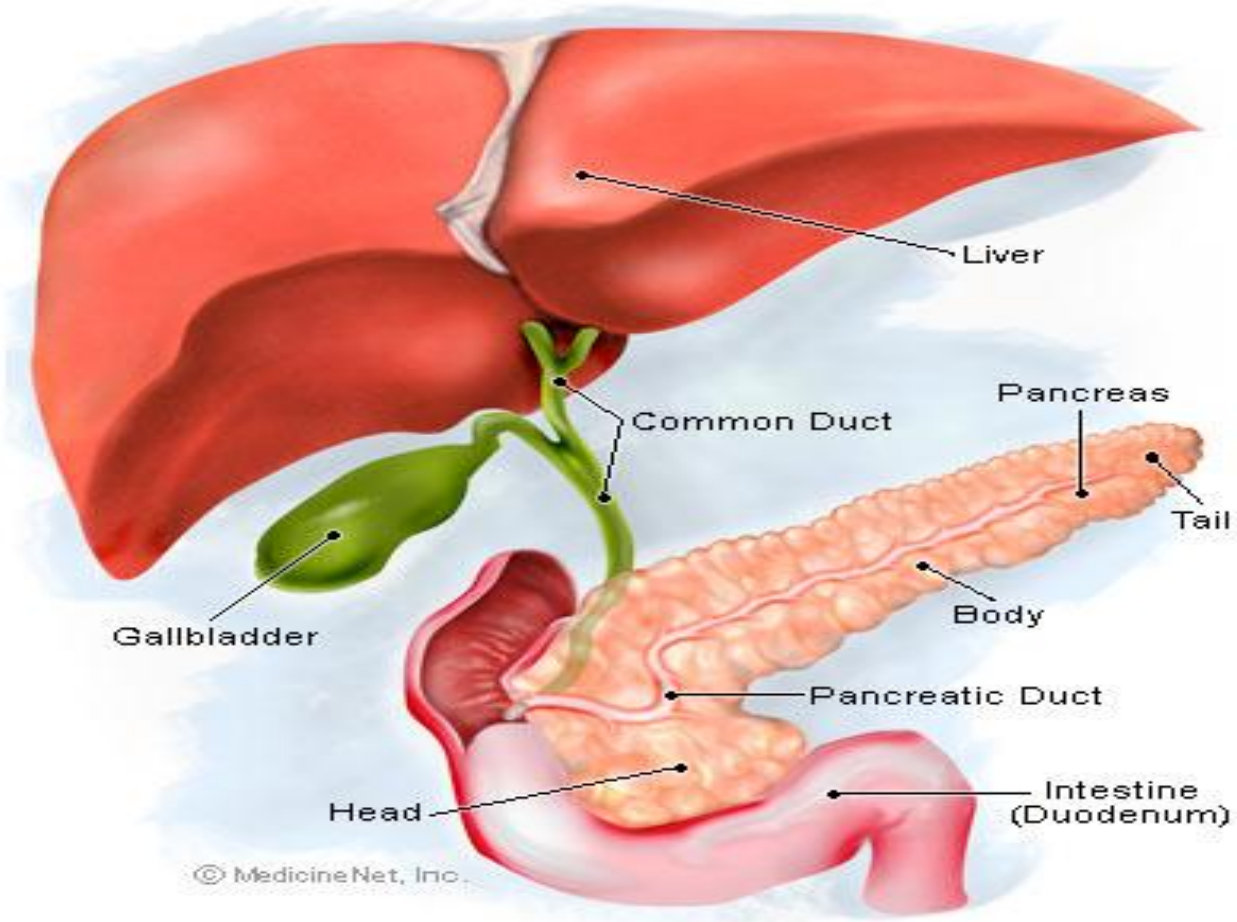
GIT Block

4th Lecture

Physiology of the Stomach and Regulation of Gastric Secretion



PHYSIOLOGY TEAM – 430

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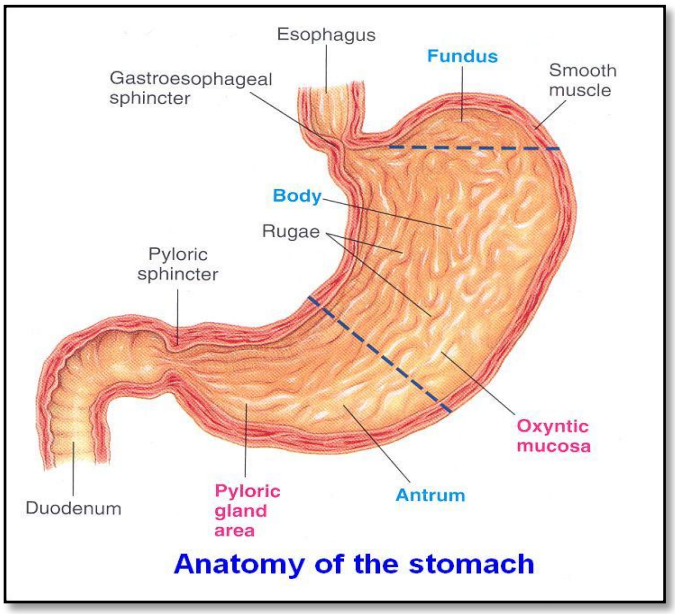
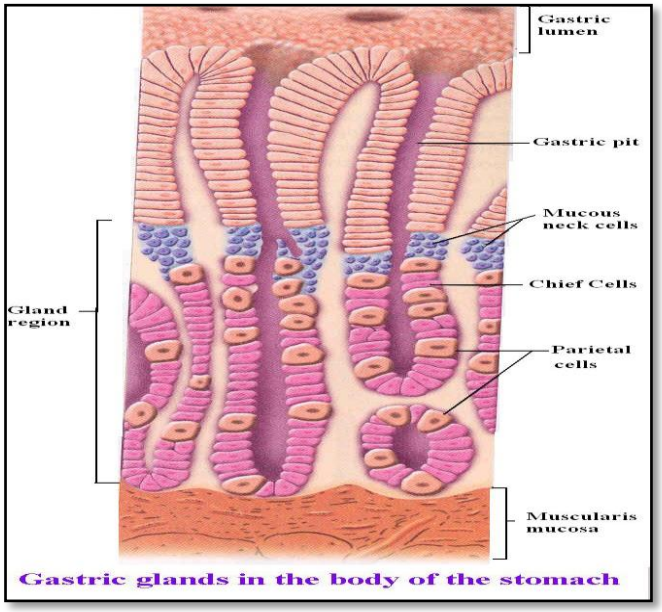
The Stomach:

Histologically the gastric mucosa is divided into 3 areas:-

The cardiac area (10 % of mucosa)	• Most of cells secrete **mucus.**
The main gastric area (70-80 %) *Includes mucosa of fundus & body. Its glands secrete all constituents of gastric juice.*	• **Parietal (oxyntic)** cells secrete **HCl & intrinsic factor.** • **Peptic (chief) cells** secrete **pepsinogen.** • **Mucous neck cells** secrete **mucus** & pepsinogen. • **Endocrine cells** secrete **peptides** & amines as histamine.
The pyloric area (15 %)	• Most of its cells are mucous cells. **Contains G- cells that secrete gastrin.**



Anatomy of the stomach



Gastric glands in the body of the stomach

Functions of the stomach:

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

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

3- Stomach has protective function:

- HCl kills ingested bacteria.
- Mucus & HCO_3^- protect stomach.
- Vomiting is a protective reflex.

4- Stomach produces intrinsic factor necessary for vitamin B_{12} absorption.

5- Gastric HCl is necessary for iron & Ca^{++} absorption.

6- Gastric HCl catalyzes cleavage of inactive pepsinogen into active pepsin.

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

8- Stomach has endocrine function. It produces gastrin, somatostatin, VIP.

Gastric Juice:

The main constituent of gastric juice is **HCL**

- Volume about 2-3 L/day.
- Main constituents is HCl, digestive enzymes, mucus, intrinsic factor.

Gastric HCl

- Secreted by parietal cells. ← These are pyramidal in shape.
- They have to concentrate H^+ more than 10^6 times to secrete it into gastric juice. This is provided by presence of numerous mitochondria & enzymes.

Mechanism of HCl formation (From lecture)

1-Cl^- is actively transported from cytoplasm into luminal canaliculi. This create –ve potential which causes passive diffusion of K^+ from cytoplasm into canaliculi. Thus K^+ & Cl^- enters canaliculi.

2- Intracellular H_2O dissociates into H^+ & OH.

3-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.

4- Water passes through the cell into caniliculi by osmosis.

5- CO^2 & H_2O form H_2CO_3 which dissociate into H^+ and HCO_3^- . H^+ combine with OH^- released in step (2) to form water.

6- HCO_3^- diffuses from the cell to plasma (Alkaline tide) and CL^- enters via a carrier mechanism that facilitates exchange between 2 ions.

Mechanism of HCl formation (Simplefied)

Cl^- inters the luminal canaliculi

- Through active transport
- Creates -ve pressure

↓

K+ Inters the luminal canaliculi

- Through Passive diffusion
- Because of -ve pressure created by Cl- intrance (In previous step)

↓

Intracellular H_2O dissociates into H & OH

- H+ is activly transported across canalicular membrane
- Transported against conentration gradient
- Transported by H^+-K^+ ATPase

↓

Water passes through the cell into caniliculi

By Osmosis

↓

CO^2 & H_2O form H_2CO_3

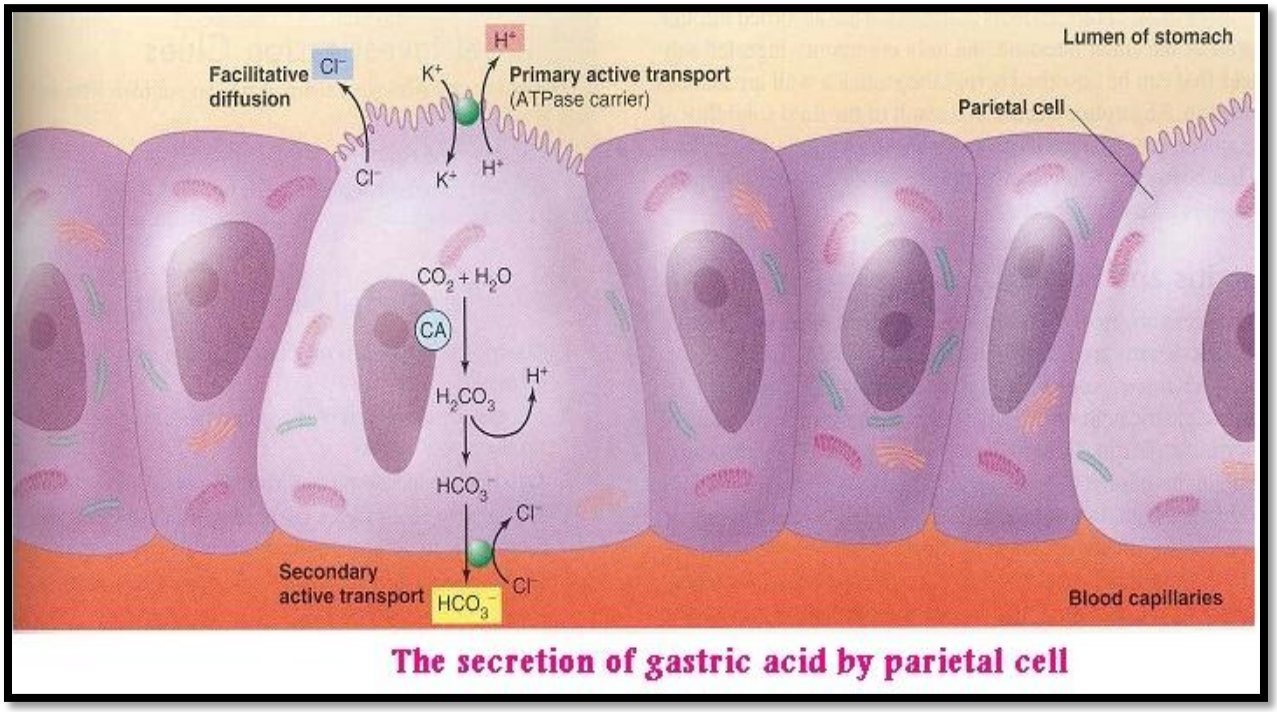
- Dissociate into H^+ and HCO_3^- .
- H^+ combine with OH^-

↓

HCO_3^- diffuses from the cell to plasma (Alkaline tide) and CL^- enters via a carrier mechanism that facilitates exchange between 2 ions.

OH from this step

H^+-K^+ ATPase is inhibited by **Omeprazole.**



The secretion of gastric acid by parietal cell

Gastric digestive enzymes:

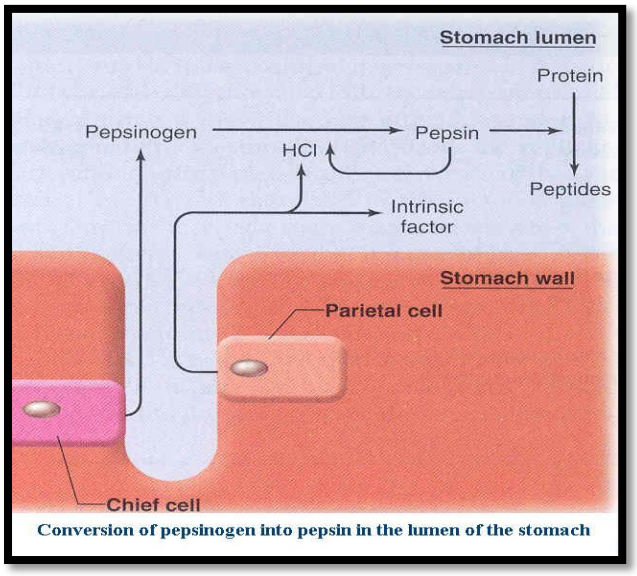
Pepsin enzyme

- Several types of pepsinogen secreted from **chief cells.**
- Pepsinogens are activated by **HCL** into **Pepsin**
- Once they're activated the activate more pepsinogen
- The optimum pH is **1.5-3.5**
- Peptsin breaks down protiens into **peptones & polypeptides**
- Pepsinogen secreation is stimulated by **Ach, Acid, Gastrin, Secretin & CCK**

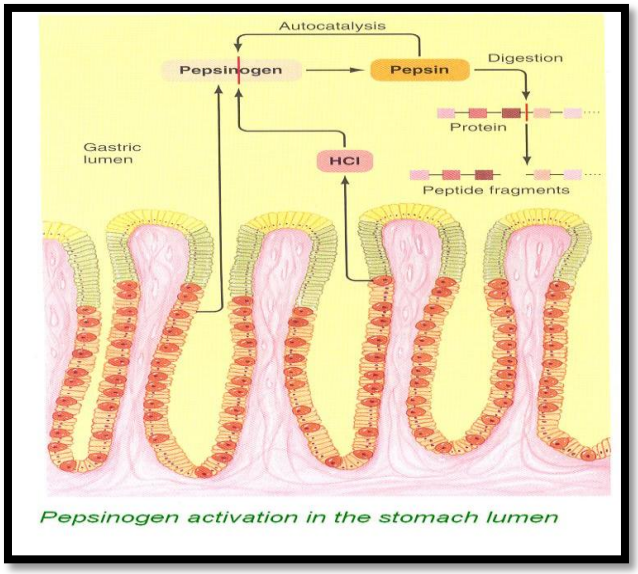
Lipase Enzyme

- Secreted from **fundic mucosa**.
- It hydrolyses TG into MG & FA. Its activity is less than pancreatic lipase.
- Additional note: It is the main enzyme that breaks down dietary fats in the human digestive system,
  converts triglyceride substrates found in ingested oils
  to monoglycerides and two fatty acids.

Pepsin enzyme



Conversion of pepsinogen into pepsin in the lumen of the stomach



Pepsinogen activation in the stomach lumen

Gastric Mucous:

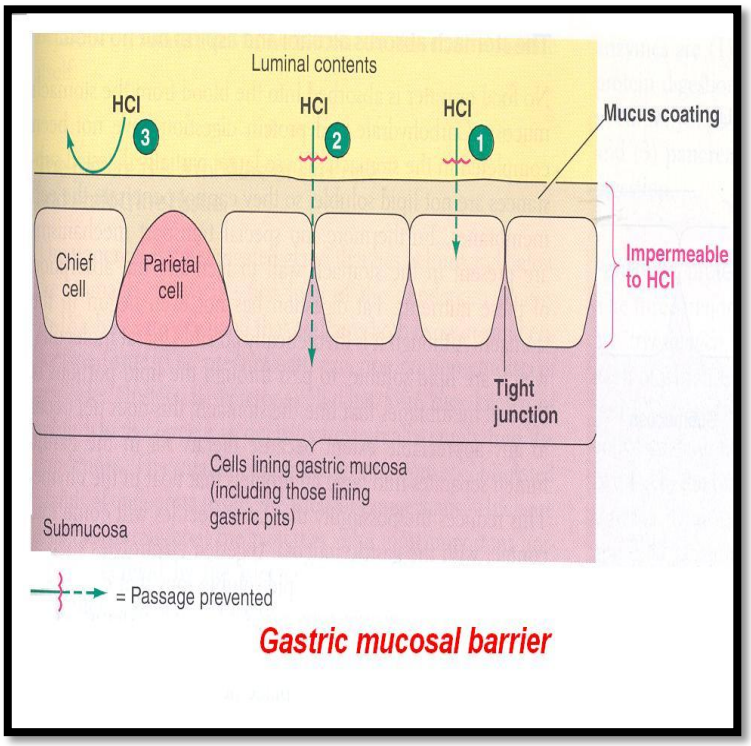
Gastric Mucous:

- It is **glycoprotein.**
- Its secretion is stimulated by **mechanical & chemical** irritation of mucosa.
- It is about 0.2 mm thick and separate surface epithelial cells from acidic contents thus **it allows neutral pH at epithelial cells despite luminal pH about 2.**

Notes:

Mechanical irritation → Food entering the stomach.

Chemical Irritation → Secretions.



Functions:-

- It protects the mucosa against mechanical injury by lubricating of chyme.
- 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 both mucus & HCO_3-. Prolonged use of these drugs may produce gastritis or ulcer.

What is "Chyme"?

The pulpy acidic fluid that passes from the stomach to the small intestine, consisting of gastric juices and partly digested food

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 Gastric Secretions:

Cephalic phase

- elicited before food reaches stomach and responsible for 1/10 of gastric secretion

Gastric phase

- elicited by presence of food in stomach, accounts for 2/3 of total gastric secretion in response to eating a meal.

Intestinal phase

- elicited by mechanisms that originate in duodenum & jejunum.

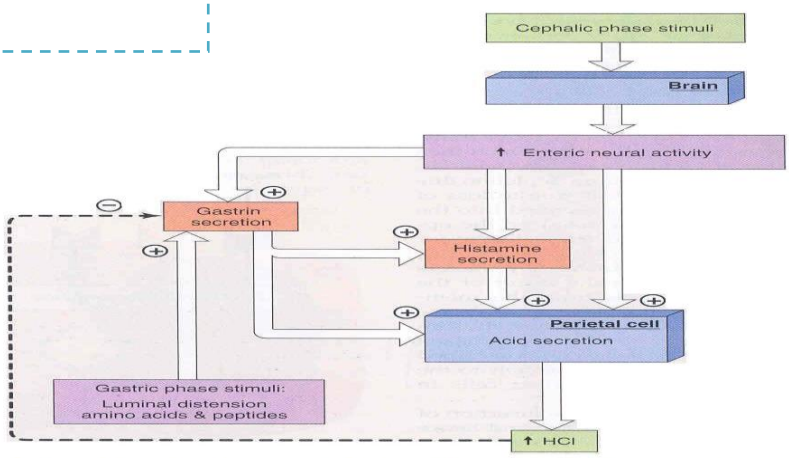
1- Cephalic Phase:

- It occurs by **conditioned** & **non conditioned reflexes**
- In non conditioned reflex, presence of food in mouth stimulates receptors
- The conditioned reflex follows psychic stimulation by seeing, smelling, hearing or thinking of appetizing food.
- Afferent impulses travel to vagal nucleus which sends impulses to gastric glands through vagi.
- Vagal impulses descending to stomach stimulates gastric glands to secrete gastric juice by 2 mechanisms:
  - **Directly** through the release of **Ach.**
  - **Indirectly** by release of **gastrin hormone.**

← To sum up:

- **Non conditional** reflex → Food enters mouth → Stimulation of receptors
- **Conditional** reflex → Seeing, smelling, hearing, thinking of appetizing food
- Afferent impulses → Vagal neuclie → Vagus nerve → Gastric glands
- Vagal impulses → Stomach → Gastric juice secretion → **Directly (release of Ach**) or **Indirectly (** release of **Gastrin Hormone)**

Cephalic and Gastric Phase of HCl Secretion



Cephalic and gastric phases controlling acid secretion by the stomach

2- Gastric Phase:

- It is mediated by **nervous** & **hormonal** mechanisms.
- It is elicited by **presence of food in stomach**.
- The stimuli are **distension of stomach** and presence of **amino acids & peptides.**

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)

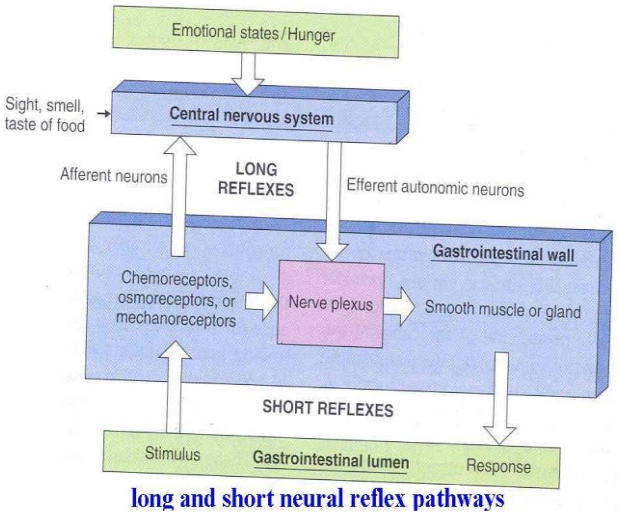
- **Gastrin** is secreted from **G cells in antrum**,
- Enters the blood and stimulates gastric glands via release of **gastrin releasing peptide.**

Actions of Gastrin:

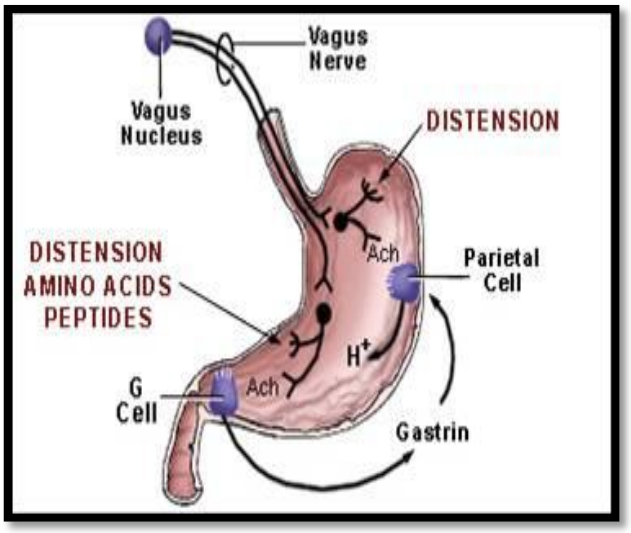
- Stimulation of **gastric acid** secretion, secretion of **pepsin and I.F**. (Intrinsic Factor)
- Stimulation of **intestinal secretion**.
- Stimulation of **pancreatic secretion** of enzyme & HCO_3^-.
- Stimulation of **biliary secretion** of HCO_3^- & H_2O.
- Stimulation of **gastric motility**.
- Stimulation of **intestinal motility & relaxes ileocaecal sphincter.**
- It **contract LES**. (lower esophageal sphincter)
- It has **trophic effect on gastric mucosa**. (Growth-promoting influence on the gastric mucosa.)

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.



long and short neural reflex pathways



Definitions:

Endocrine → Of, relating to, or denoting glands that secrete hormones or other products directly into the blood: "the endocrine system"
Neurocrine → denoting an endocrine influence on or by the nerves
Paracrine → denoting the secretion of a hormone by an organ other than an endocrine gland.

Control of HCl secretion at the level of parietal cells:

- Gastrin reaches parietal cells via blood stream to stimulate HCl secretion (endocrine action).
- Ach is released near parietal cells by cholinergic nerve endings to stimulate HCl secretion (neurocrine action).
- Histamine is released from enterochromaffin cells in gastric mucosa and diffuses to parietal cells to act on H2 receptors to stimulate HCl secretion (paracrine action).
- **Cimetidine & ranitidine** are H_2 receptor blockers and potent inhibitor of G.A secretion and both are used for **treatment of peptic ulcers.**

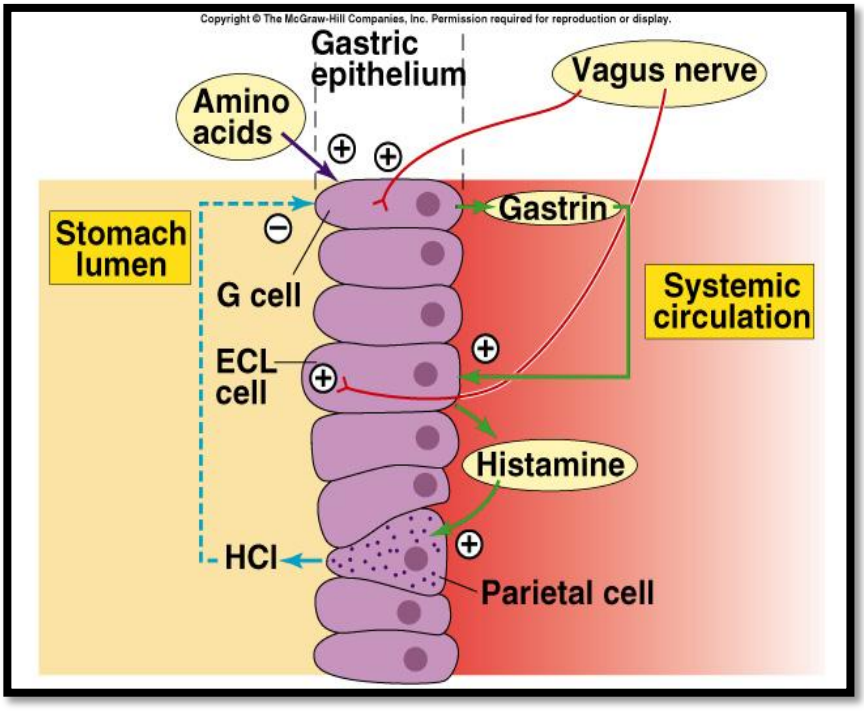
← HCL secretion stimulation:

Endocrine action → Gastrin → Parietal cells → HCL secretion

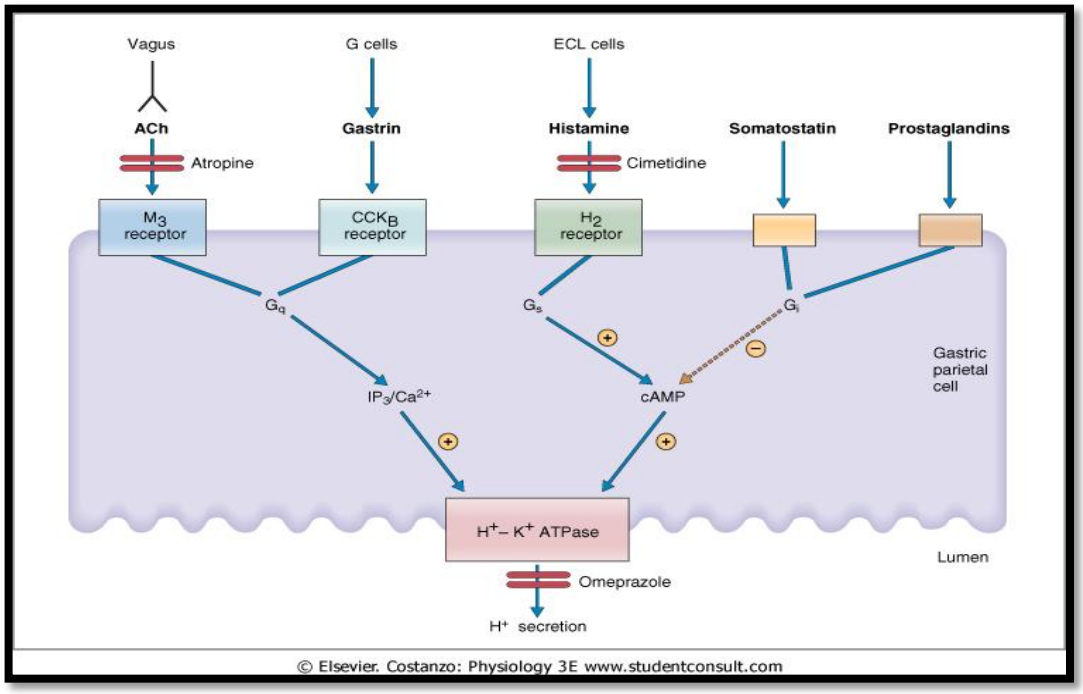
Neurocrine action → Ach released by cholinergic nerve endings→ Near Parietal cells → HCL secretion

Paracrine action → Histamine from enterochromaffin cells diffuses to parietal cells → HCL secretion

Control of HCl secretion at the level of parietal cells



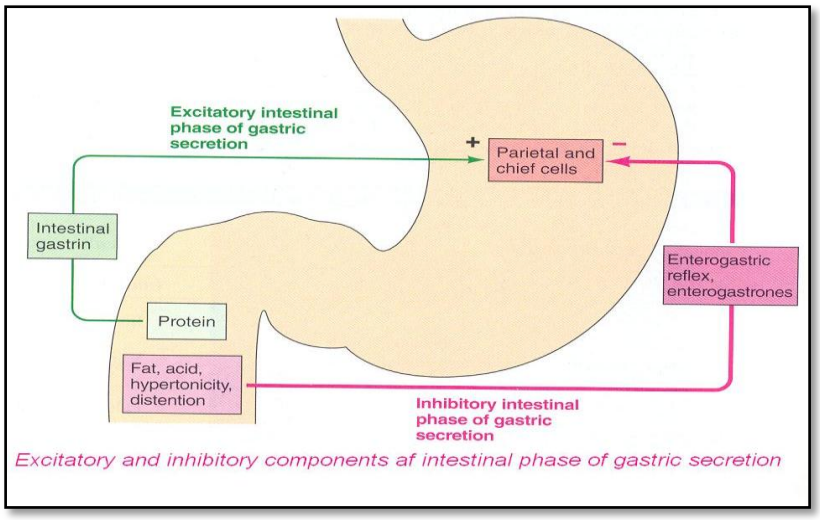
Agents that stimulate and inhibit H+ secretion by gastric parietal cells



Differences between the Gastrin Mechanism & Vagal Stimulation

Gastrin Mechanism	Vagal Stimulation.
• Less potent • Long period (Several hours)	• More potent • Shorter period then the Gastric Machanism

Gastrin mechanism is as equally important as Vagal mechanism, the 2 multiply each other.



Excitatory and inhibitory components af intestinal phase of gastric secretion

- **G.A** → Gastric Acid
- **A.A** → Amino Acid
- **CCK** → Cholecystokinin
- **VIP** → *Vasoactive intestinal peptide*

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:-

1- **Distension** of duodenum, it stimulates G.A. secretion by means of vagovagal reflex that stimulates parietal & G- cells.
2- **Presence of protein digestive products** as peptides & A.A. in duodenum. This stimulates G- cells in duodenum & proximal jejunum to release gastrin.

The inhibitory mechanisms that limit G.A secretion:

1- The presence of food in small intestine → initiates enterogastric reflex → transmitted through ENS & autonomic NS → 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.

Electrical activity of gastric smooth muscle

* 2 types of potentials can be recorded:-

1- Basal electrical rhythm
2- Action potential spikes

Enterogastrones :

* Are hormones released from intestine and affect G.A secretion as:-
1- Bulbogastrone
2- Gastric inhibitory peptide.
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.**

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.**

The Motility Function of the Stomach:

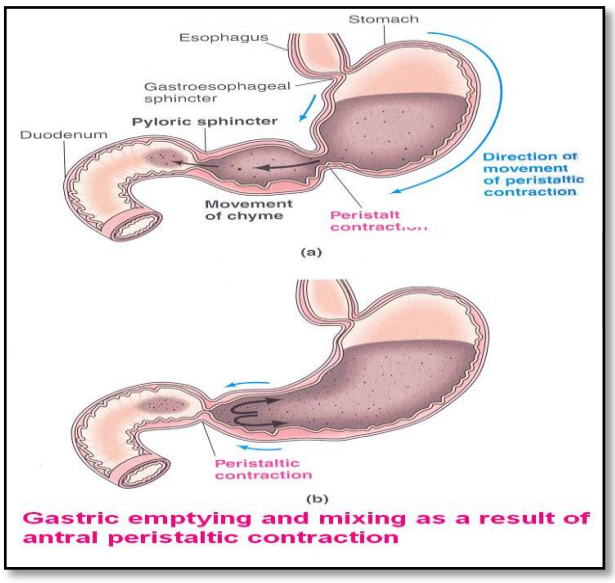
*Functionally stomach is divided into a proximal reservoir & distal antral pump.

The proximal stomach (fundus and upper 1/3 of body)

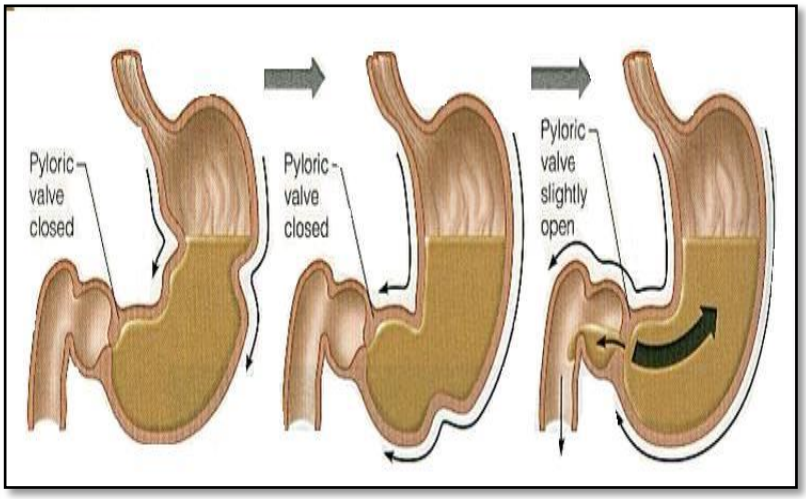
- As food enters stomach, it relaxes to accommodate food (receptive relaxation).
- **Slow sustained tonic contraction** in proximal stomach provides pressure gradient for pushing & emptying of chyme.

The distal stomach (lower 2/3 of body ,antrum & pylorus)

- The main activity in distal stomach is peristaltic contractions. Its function is grinding of solids, liquefaction of chyme to be propelled to duodenum.



Gastric emptying and mixing as a result of antral peristaltic contraction



Gastric Emptying:

Occurs through **coordinate contraction of antrum, pylorus & duodenal bulb** (gastroduodenal pump). As gastric contents are propelled into distal stomach, the antrum, pylorus & proximal duodenum are relaxed. Liquefied chyme is pushed into duodenum by tonic contraction of proximal stomach.

The terminal antrum then contracts aiding food propulsion. This is followed by contraction of pylorus which closes off stomach & arrests emptying to allow grinding of solids. The proximal stomach then contracts moving the contents into distal duodenum & jejunum. The antrum, pylorus & duodenal bulb then relax & the sequence is repeated.

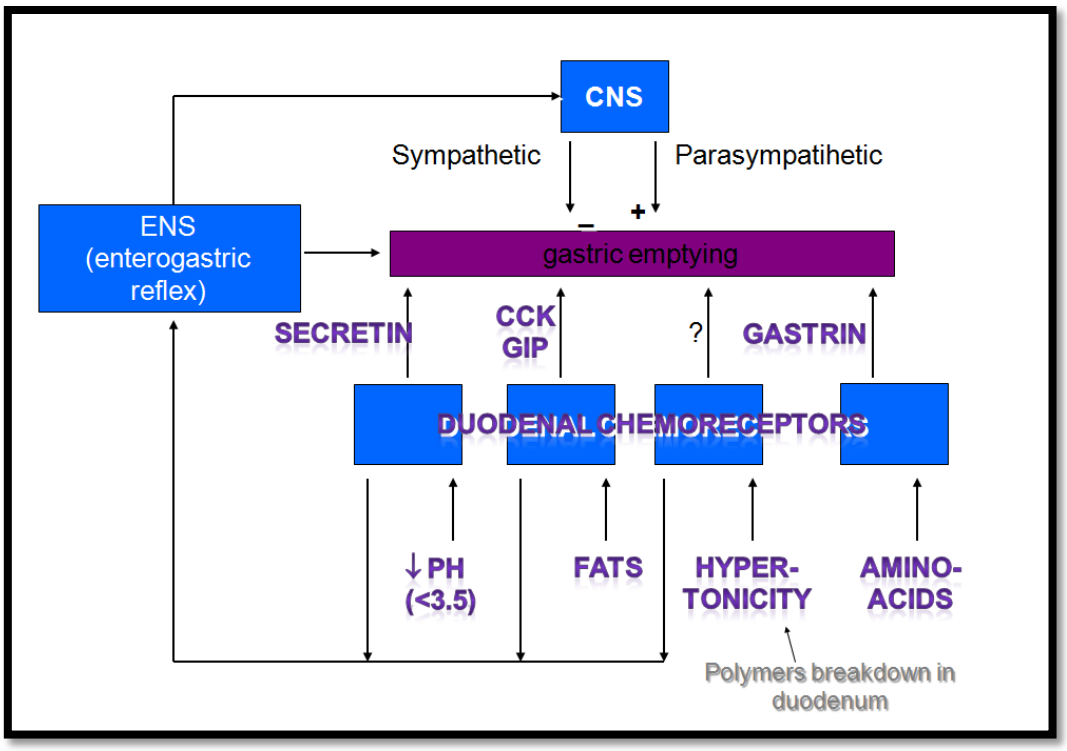
Control of gastric emptying:

* Gastric factors that promote emptying

A. Gastric food volume
   - The greater the volume of gastric contents, the faster the rate of emptying.
   - Liquids are emptied more rapidly than solids.

B. Effect of gastrin on gastric emptying

Regulation of stomach emptying



Duodenal factors that inhibit emptying

A- Enterogastric reflex

When chyme arrives in duodenum, its chemical characteristics affect various duodenal receptors. Reflex nerve signals are transmitted from duodenum to stomach to inhibit its motility, thus reducing further release of acidic contents into duodenum until chyme is neutralized.

The type of factors that can elicit enterogastric reflex include:-

1- The presence of hypertonic chyme in duodenum.

2- The drop of pH of chyme in duodenum to < 3.5-4.

3- The presence of emulsified fat, peptides & A.A in duodenum.

4- The presence of any degree of irritation of duodenal mucosa.

5- Duodenal distension.

6- Emotion as fear prolongs gastric emptying.

B- Hormonal feedback mechanisms from duodenum that inhibit emptying

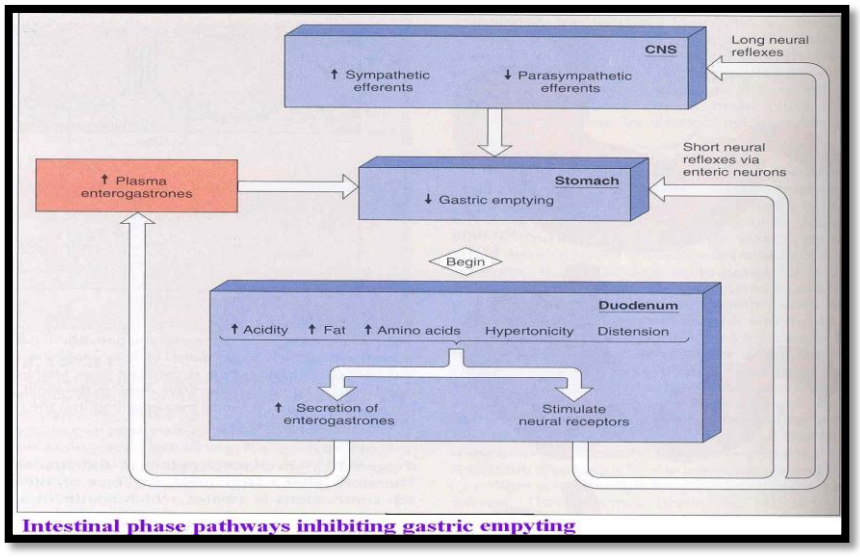
Mixture of hormones called **enterogastrone** are released from upper intestine by acids, fats & hypertonic chyme and slow gastric emptying. These hormone include:-

Secretin , CCK, GIP.

Gastrin slows gastric emptying due to:-

- 1- It stimulates duodenal motility & ↑ its resistance
- 2- It stimulates gastric acid secretion that stimulate release of secretin & CCK. Both ↓ **gastric emptying.**

Intestinal Inhibition of Gastric emptying Stomach



Intestinal phase pathways inhibiting gastric emptying

Pathophysiology

Dumping Syndrome:-	•Uncontrolled gastric emptying due to lack of •feedback inhibition by duodenum. • Post-surgical • Neurological deficit • Un-digested food makes it to the colon • Patient barely makes it to the bathroom
Pyloric Stenosis:-	•Projectile vomiting •Pediatric disease •Failure to thrive