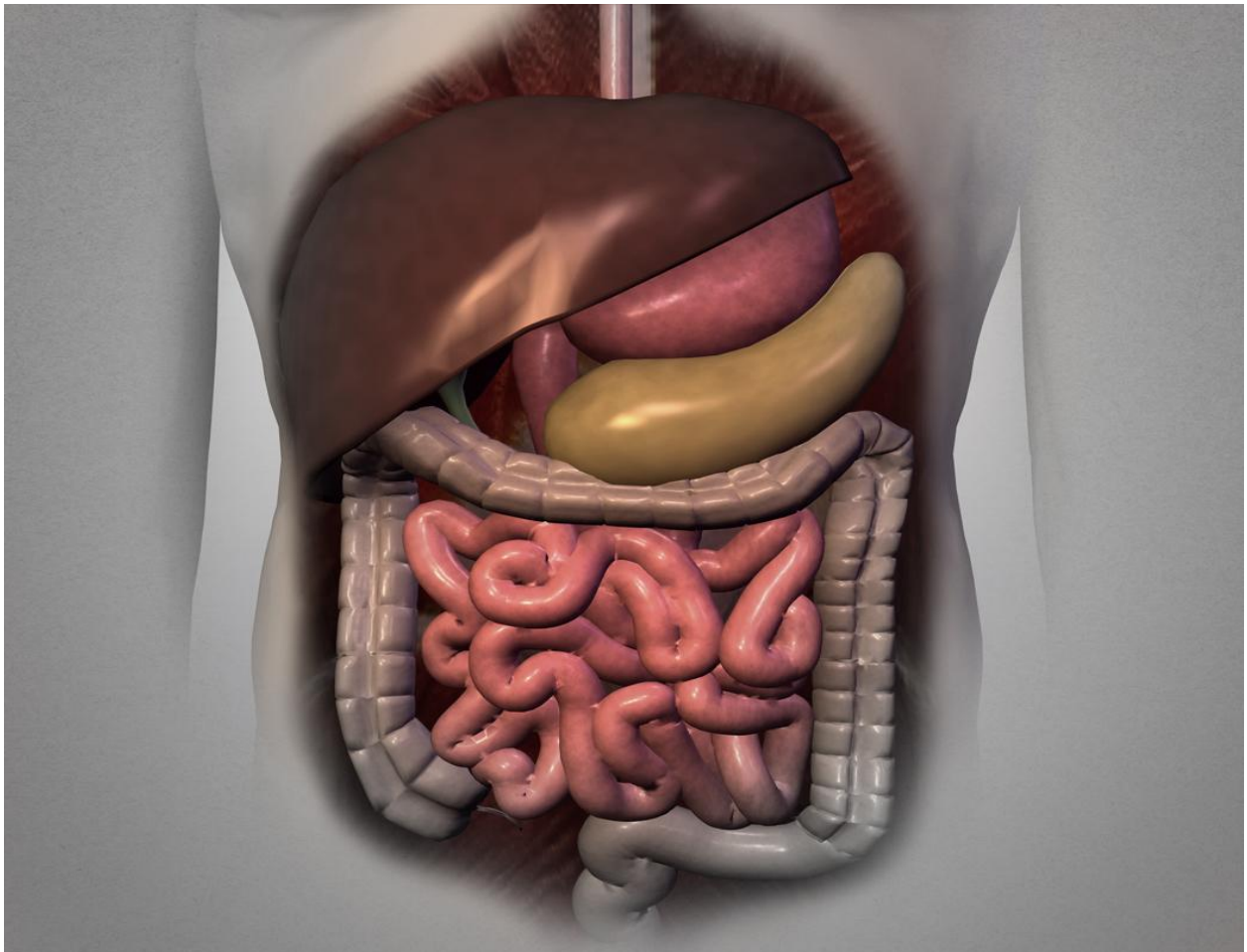

GIT Block

Physiology Team 431

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Physiology of the Stomach & Regulation of Gastric Secretion

Part 1

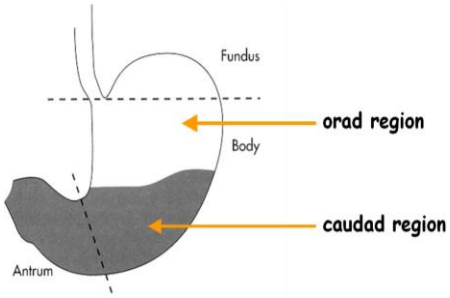
GREEN: mentioned by doctor
BLUE: team's notes
RED: very important
GREY: not important
Other than that is just a format

➢ Anatomical and Physiological 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) (Not mediated by Slow waves)

  2- The caudal (lower third of the body plus antrum)- Antral pump (phasic contraction).



➢ Functions of the stomach:

1- Stores food & regulates its passage to small intestine.
2- Secretes juice that liquefies & partly digests food.
3- Produces intrinsic factor necessary for vitamin B12 absorption.
4- Gastric HCl:
- Kills ingested bacteria. ●Is necessary for iron & Ca++ absorption.
- Catalyzes cleavage of inactive pepsinogen into active pepsin.

5- Absorption of water and lipid-soluble substances (alcohol and drugs).
6- It has endocrine function, e.g. It produces gastrin and somatostatin.(means that those hormones are secreted into blood then into the target tissue)

➢ Gastric secretion:

Histologically gastric mucosa is divided into 3 areas:-

1. The cardiac area (10 % of mucosa) "near the gastro-esophageal junction"
   Most of cells secrete mucus.
2. The main gastric area (70-80 %)
   Includes mucosa of fundus & body.
   It contains the oxyntic glands which secrete all of gastric juice constituents:
   - Parietal (oxyntic) cells secrete HCl & intrinsic factor.
   - Peptic (chief) cells secrete pepsinogen.
   - Mucous neck cells secrete mucus & HCO3-.
3. The pyloric area (15 %)

4. Most of its cells are mucous secreting cells. Contains G- cells that secrete gastrin hormone.

➢ Gastric Juice

Volume about 2-3 L/day

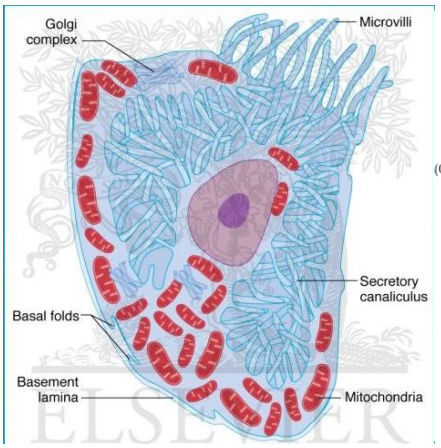
Main constituents are:

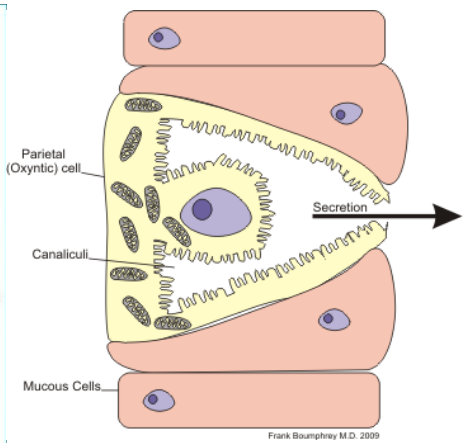
- HCl
- Mucus (mucus gel layer)
- Digestive enzymes (Pepsinogen)
- Electrolytes
- Intrinsic factor.

➢ Gastric HCL:

- Secreted by parietal cells, the most distinctive cells in the stomach.
- They are pyramidal in shape.
- Their structure is unique in that they have an abundance of mitochondria and intracellular canaliculi 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.

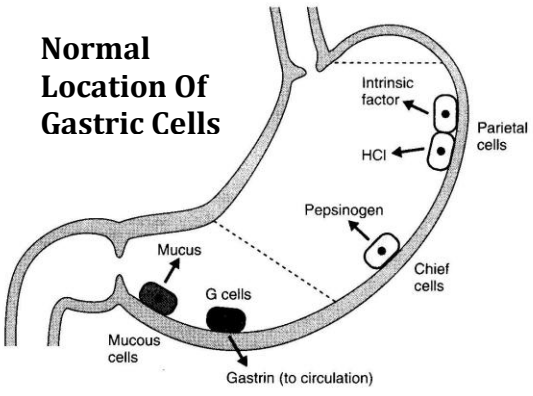
Parietal cell



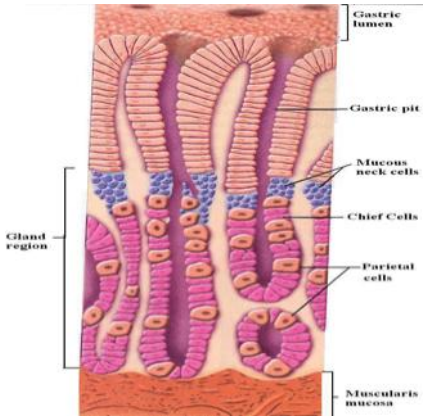


➢ Mechanism of HCL formation: (The HCl acid is secreted first toward canaliculi then into the lumen)

- Cl- is actively transported from cytoplasm into luminal canaliculi. This create –ve potential



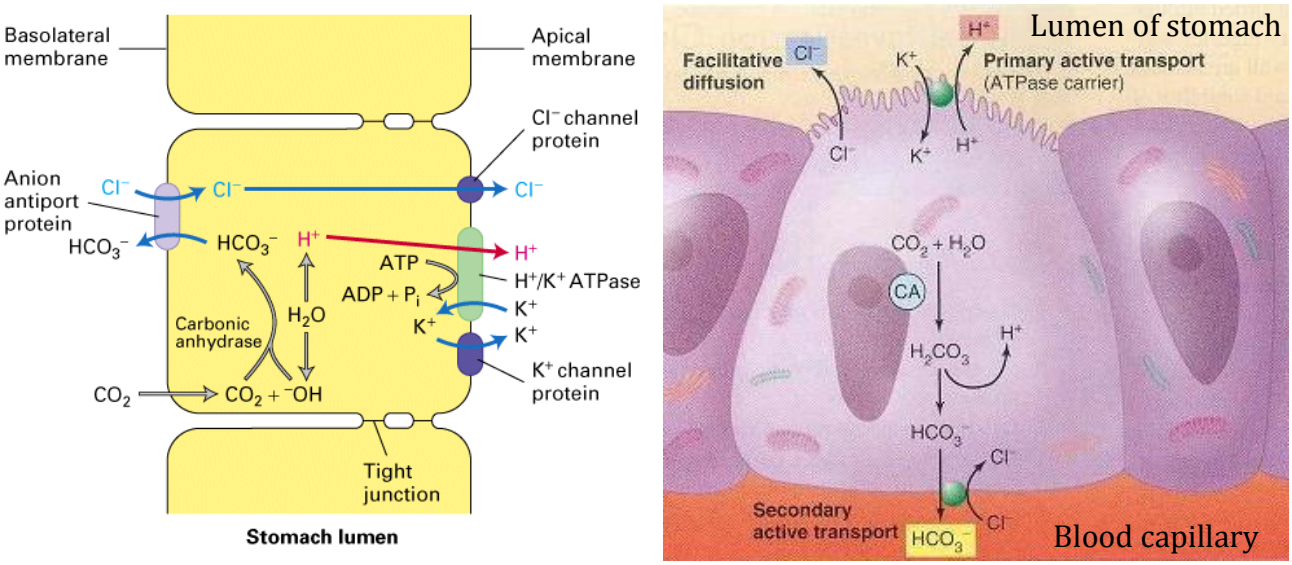
Cell Type	Location	Secretion
Parietal cells	Body	HCL Intrinsic factor
Chief cells	Body	Pepsinogen
G cells	Antrum	Gastrin
Mucous cells	Antrum	Mucus Pepsinogen



which causes passive diffusion of K+ from cytoplasm into canaliculi. Thus K+ & Cl- enters canaliculi.

- Intracellular H2O 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).**
- CO2, 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-.
- HCO3- diffuses from the cell to plasma "blood" (Alkaline tide) and CL- enters via a carrier mechanism that facilitates exchange between the 2 ions.

Alkaline tide refers to a condition, normally encountered after eating a meal, where during the production of HCl by parietal cells in the stomach leads the parietal cells also secreting bicarbonate ions across their basolateral membrane and into the interstitial fluid causing a temporary increase in pH.

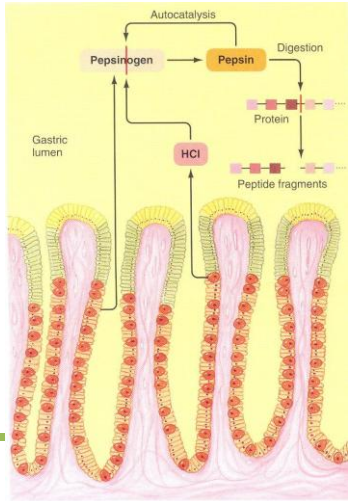


Mechanism of HCL formation

➢ Gastric digestive enzymes: "carbohydrates digested in the mouth and the small intestine"

- Lipase enzyme "for lipids":

Secreted from fundic mucosa. It hydrolyses TG "triglycerides" into MG "monoglyceride" & FA "fatty acid". Its activity is less than pancreatic lipase. "Lipase is weaker than pancreatic lipase which is the most strong lipolytic enzyme"



Pepsinogen activation in the stomach lumen

*Pepsin enzyme "for proteins":

Several types of pepsinogen secreted from chief cells. They are activated by HCl into pepsin. then the activated pepsin can activate more pepsinogen by a process called autoctalyzing. The optimum pH is 1.5-3.5 "acidic". Pepsin breaks down proteins into peptones & polypeptides. Pepsinogen secretion is stimulated by Ach, acid, gastrin, secretin & CCK.

➢ Gastric mucus:

- It is a 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.

-Mechanical irritation: Food entering the stomach.
-Chemical Irritation: Secretions.
-Chyme: The pulpy acidic fluid that passes from the stomach to the small intestine, consisting of gastric juices and partly digested food

- Function:

1. It protects the mucosa against mechanical injury by lubricating of chyme.
2. It protects the mucosa against chemical injury by acting together with HCO3- 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 & HCO3-. Prolonged use of these drugs may produce gastritis or ulcer.

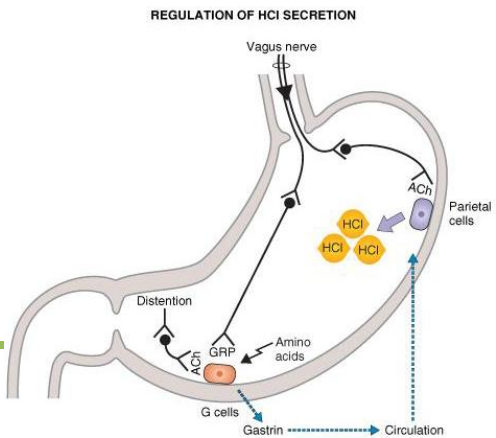
- **Also there is another factor for how the NSAID can predispose an ulceration is by inhibition of Prostaglandins that enhance blood flow in the tissue, also the prostaglandins reduce the excess amount of pepsin and acids.**

➢ Intrinsic factor:

- It is a glycoprotein secreted by **parietal cells**.
- It is the only essential function of stomach as it is essential for vitamin B12 absorption.
- Atrophy of gastric mucosa leads to pernicious anemia (Megaloblastic anaemia).

➢ Neural & hormonal Control of Gastric Secretions:

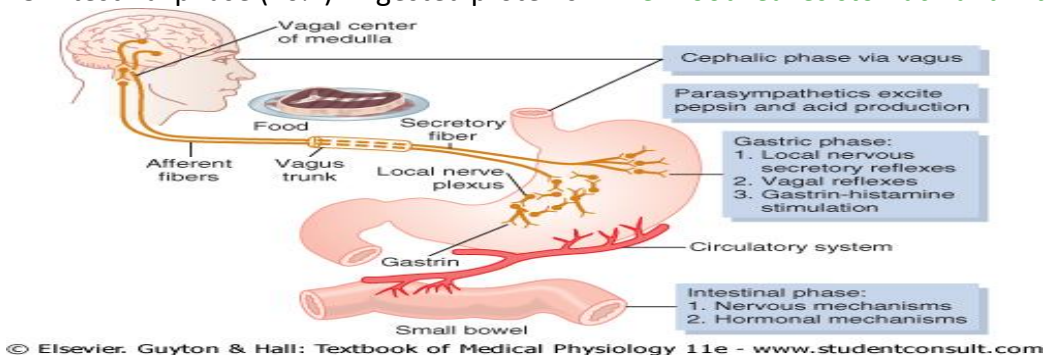
- Vagus nerve (neural effector) either by releasing Ach (direct activation of parietal cells) or by releasing, GRP "gastrin releasing peptide" (indirect activation) by secreting Gastrin which in turn will go to parietal cell and stimulate them to release HCl
- Gastrin (hormonal effector)
- Enterochromaffin-like cells release Histamine→activates H2 receptor (parietal cells) →increases acid "HCl" secretion.



➢ 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(30%): Smelling, Chewing and swallowing Stimulates parietal & G-Cells GRP
2.Gastric phase (60%): Gastric distention and presence of proteins "when food reaches stomach"
3.Intestinal phase (10%): Digested proteins "when food leaves stomach and inter duodenum



1- Cephalic phase:

- It involves the central nervous system. Seeing, smelling, thinking of appetizing food, chewing, and swallowing food send afferent impulses to vagal nucleus which sends 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. "gastrin will travel through the blood circulation to reach the parietal cells and stimulates acid secretion"

2- Gastric phase:

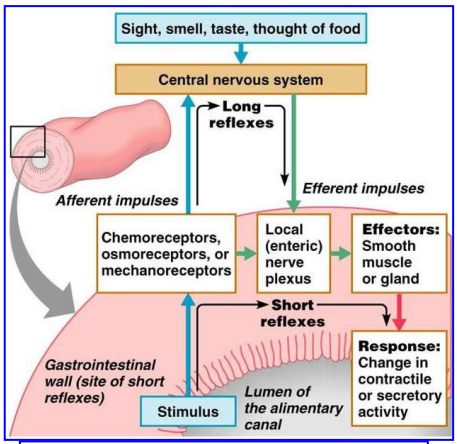
It is mediated by nervous & hormonal mechanisms. It is elicited by presence of food in stomach. The stimuli are distension of stomach and presence of amino acids & peptides.

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 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.



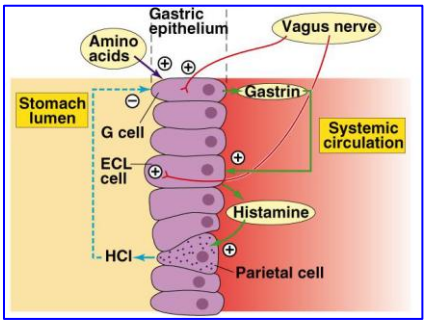
Long and short neural reflexes

▪ Actions of gastrin:

1- Stimulates gastric acid secretion, secretion of pepsin and intrinsic factor.
2- Stimulates intestinal secretion.
3- Stimulates pancreatic secretion of enzyme & HCO3-.
4- Stimulates biliary secretion of HCO3- & H2O.
5- Stimulates gastric motility.
6- Stimulates intestinal motility & relaxes ileocaecal sphincter.
7- Contract LES "lower esophageal sphincter".
8- Has trophic "increase the development and growing of the cell" effect on gastric mucosa.

▪ 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 H2 receptor blockers and potent inhibitor of gastric acid secretion and both are used for treatment of peptic ulcers and gastroesophageal reflux



▪ Inhibition of acid secretion:

Inhibitory hormones **(Enterogastrones)** **"from intestine"**:

- Somatostatin (secreted by D-cells) in antrum
- Secretin (secreted by S-cells) in duodenum
- Glucose-dependent insulinotropic peptide (GIP)"gastric inhibitory peptide" in duodenum

3.Intestinal phase:

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

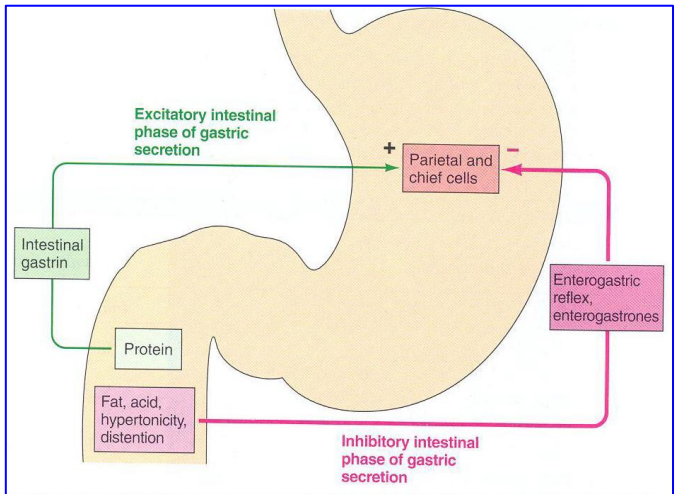
Gastric secretion in Intestinal phase is enhanced by:-

1.Distension of duodenum stimulates gastric acid secretion by means of vagovagal reflex and the release of the hormone entero-oxyntin from intestinal endocrine cells that stimulates parietal & G- cells. **It should not be mentioned because Dr-Mohammed has confirmed that this factor is wrong and confusing.**

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

The inhibitory mechanisms in Intestinal phase 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 "gastric acid" secretion.
2. Drop the pH in pyloric antrum to < 2.5 reduces gastric acid 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 gastric acid secretion. These effects are mediated mainly by hormonal mechanisms.



Excitatory and inhibitory components af intestinal phase of gastric secretion

➢ Enterogastrones :

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

1. Bulbogastrone
2. Gastric inhibitory peptide.
3. Secretin (It is the antagonist of Gastrin) & CCK "Cholecystokinin".
4. Pancreatic glucagone.
5. Other peptides as VIP "Vasoactive intestinal peptide", 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.

Recommended Video:
http://www.youtube.com/watch?v=VQnU0xL93nk&feature=related

Questions:

1-Why stomach PH is acidic despite the presence of HCO- in the stomach?

Because the HCO3- is not found in the gastric lumen as the HCl, but it is attached to the mucosa in the gastric wall so provide a strong protection to the gastric wall from acidity.

2- HCl production depends in which ion:

A- Na+
B-Cl-
C- K+
D-Ca++

3-What is the antagonist of gastrin in term of function:

A- Secretin
B- CCK
C- Motilin
D- GIP

Answers: 2-C, 3-A