Lecture 4

PHYSIOLOGY TEAM

PHYSIOLOGY OF STOMACH AND REGULATION OF GASTRIC SECRETION

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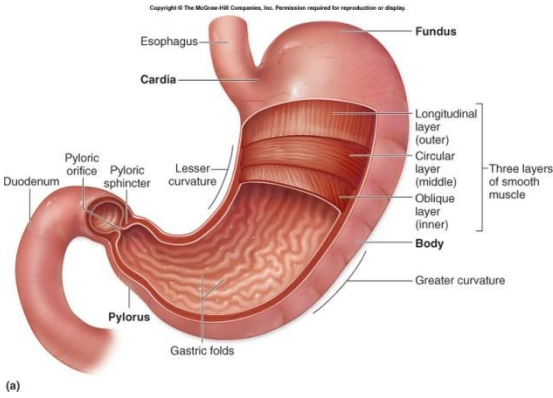
Physiology of the stomach and regulation of gastric secretions

Stomach and control of gastric secretions



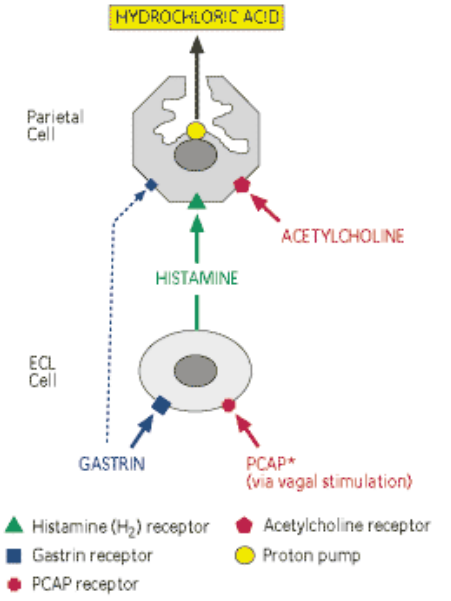
Gastric mucosa divided *into 3 areas:*

1-* cardiac area *:" at cardiac orific "

present 10% of it and secrete mucus (mucine)

***2-* main gastric area *:* present 70-80% and it contains the gastric glands and all cells which involved in secreting gastric juice:**

- **Parietal call : HCl + intrinsic factor**
- **Endocrine : histamine**
- **Peptic chief cell : pepsin**
- **Mucus neck cell : mucus + small amount of pepsin**



***3-* pyloric area : present 15% and contain the G cell that secrets gastrine hormone**

Function of the stomach :

1-food storage and regulates its passage to the small intestine by pyloric sphincter " it is open when the food is fully digested!!"

2- digestion and secretion →liquefies +partially digest the food

3-protective function by :

-HCL " hyperacidity" →to kill the ingested bacteria

-mucus +bicarbonate→provide protection for stomach cell against HCL

-vomiting → it`s a protective reflex against poisoning

4-produce intrinsic factor (IF) that helps in vitamin B12 absorption

" the only essential function of the stomach \ because other function are compensated"!!

5- gastric HCL is important in:

- absorptionof iron and Ca++

- also convert the inactive pepsinogen into active pepsin .

" 1- reduce ferric → ferrus \ 2- ca will be more soluble in acidic nature \ 3- pepsinogen → pepsin"

6- has endocrine function because it produces gastrine , somatostatine and VIP

the gastric juice : it`s highly acidic and isotonic (the na and ca concentration is same as plasma)

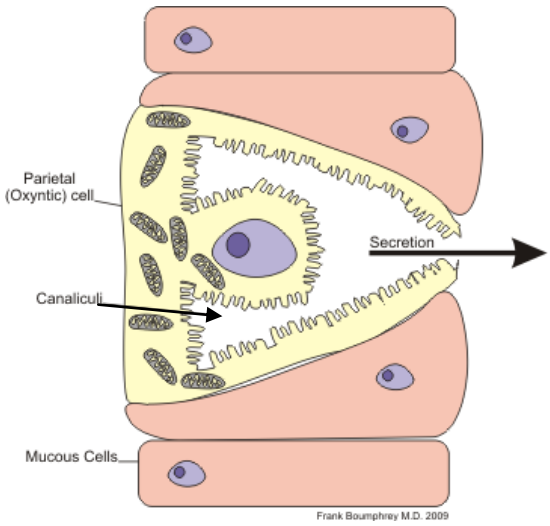
" all GIT are isotonic .. except salivary is hypotonic 'Na and Ca is less than plasma'

Gastric juice:

Volume about 2-3 L/day

PH = 2 – 3 “ Acidic”

Main constituents are HCl, digestive enzymes, mucus, intrinsic factor.



HCL formation :

-HCL is formed at canaliculi of parietal cells “not inside the cell it self”

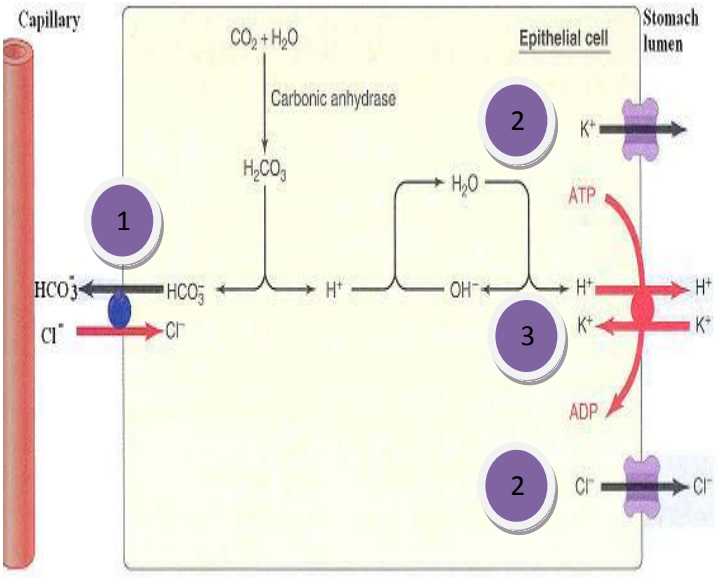
to form the HCL we need H and CL

parietal cel الفكره ببساطه رح تكون كالتالي : + كل الخطوات التاليه رح تحصل في قناة ال

1- **Cl^-\HCO_3^+** الكلورايد رح يدخل .. والبايكاربونيت رح يطلع
2- **Cl^- \ K^+** .. ويجر معاه البوتاسيوم الكلورايد يطلع → **why K will go out ? because of electrical gradient** “سالبية الكلورايد سحبت معاه موجب اللي هو البوتاسيوم"**”**
3- **H^+\K^+** والبوتاسيوم رح يدخل الهيدروجين رح يطلع .. → **why K will go in again ? because K concentration gradient “** البوتاسيوم قل داخل الخليه فرح يرجع مره ثانيه**“**

So,

HCL فالكلورايد والهيدروجين اللي طلعوا رح يكونوا



Also There is a cycle happen inside the cell :

“ the source of H^+ and HCO_3^+ “

CO_2 + H_2O → H_2CO_3 carbonic acid → H^+ + HCO_3^+

باقي نعرف كل ايون كيف نسمي دخلته :

1- **Cl^- by carrier OR active transport**
2- **K^+ by electrical gradient with Cl^-**
3- **H^+ active transport “ by H\K ATPase”**
4- **K exchange with H “ by H\K ATPase”**

Finally, after both H, CL ions are transported to the gastric lumen the HCL is formed.

Proton pump inhibitor “ omeprazole” → inhibit H^+-K^+ ATPase
So intrupt HCl formation → so, decrease acidity for peptic ulcer patient !!

Gastric digestive enzymes :

The enzyme	Secreted from	Stimulated /activated by	Function
pepsine	Chief cells(peptic cells)	- Pepsinogen secretion is stimulated by Ach, acid, gastrin, secretin & CCK. -HCL convert pepsinogen (inactive)→pepsin(active -autocatalysis →activate pepsinogen by the activated pepsine	Proteilytic(protein breakdown into polypeptides+peptones)
Gastric mucus(mucine)	Mucus cells	- mechanical & chemical irritation of mucosa. "mechnical → stretch stomach by food" "chemical→ substances of food"	-Separate gastric epithelial cells from gastric enzymes -protect the mucosa against mechanical injury by lubrication of chyme -mucus contain "HCO3 bicarbonate" alkaline → so, it neutralize acid and protect mucosa from "HCl and pepsin"
Intrinsic factor (IF)	Parietal cell		The only essential function of stomach* It is important for vitamin B12 absorption
Lipase enzyme	Fundic mucosa		hydrolyses TriGlyceride into MonoGlyceride & Fatty Acid -it`s less important than the pancreatic lipase in adult !!.

- Chyme → food after partially digested ..
- It is essential because all the fuction of stomach can be done by the intestine except the vitamin b12 absorption , and if parietal cells destroyed ex.gastritis , the person will develop pernicious anemia
- Gastric mucus : **allows neutral pH at epithelial cells** despite luminal pH about 2.
- **Lipase enzyme : Its activity is less than pancreatic lipase.**

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

Salivary secretion

1. is the only one regulated by ONLY neural mechanism

2.the only hypotonic !!

Control of gastric seretions regulated by :

1-hormonal

2-neuronal

Control of gastric secretion :

ماذا سيؤثر في افرازات المعدة ؟؟؟؟ عندما يكون الطعام في

1-cephalic phase. عندما يكون في الفم أو عند شم رائحته

2-gastric phase. عندما يكون في المعدة

3-intistinal phase. عندما يكون في الامعاء

في كل من هذه الثلاث اوضاع .. سوف تؤثر قطعة الطعام إما في /

1- **Mechanoreceptor → vagovagal reflex !! →** **neural control** ما يسمى بـ
2- **Chemically → production of hormone !! →** **Hormonal control** ما يسمى بـ

سوف اشرح كل من هاتين النقطتين .. لكي يسهل قراءة ما يليه ..

1- **Mechanoreceptor → vagovagal reflex !!**

Food it self → sensed by machanoreceptor any where "mouth,wtomach,intestine" → send signals by vagus → to medulla oblongata "vagual nucleus" → efferent by vagus again → to stomach !!

In stomach , there is paraietal cell that responsible for secreting HCl "the main component"!!

This parietal cell has 3 main receptors >> when you stimulate them → they stimulate parietal cell to activate the proton pump "as we talk about above in HCl formation" → then increase HCl secretion !!

These 3 receptors are :

1- **Histamine**
2- **Gastrin**
3- **Acetyl choline**

So, the vagus nerve stimulate secretion of ach → stimulating parietal cell → secretion of HCl !! لكل اعادة إفادة☺

2-Chemically → production of hormone !!

Components of food "aminoacid , fatty acid..." → stimulate G-cell to secrete its hormone

gastrine والهرمون الوحيد اللي في المعدة رح يطلع هو

وزي ما قلنا قبل شوي ..

Gastrin will act on its receptor on parietal cell → secretion of HCl !!!

نقطه اخيره

G-cell in pyloric antrum → has muscarinic receptor for ach !!

So, ach when act on G-cell receptor → G-cell secrete gastrin → gastrin act on parietal cell → secreting HCL

So, this condition is called " indirectly acting on parietal cell"

1-cephalic phase elicited by 2 reflexes (mainly neuronal control "vagus" + some hormonal control) :

-non-condetioned reflex

(just present of food in mouth)

-conditioned reflex:

follows psychotic stimulation by seeing, smelling, hearing or thinking of appetizing food

- **both will : stimulate receptors →afferent to vagal nucleus in medulla→efferent impulses→by vagus →to stomach →stimulate stomach secretion.**
- **Vagus has 2 actions ;**

1-direct : stimulate parietal cells -→ release HCl

2-indirect : stimulate G cell → release of gastrine → stimulate paraietal cell → release HCl

II- The gastric phase

- **It is mediated by nervous & hormonal mechanisms.**
- **It is elicited by presence of food in stomach.**
- **The stimuli are distension of stomach → stimulate mechoreceptor , presence of amino acids & peptides → stimulate hormone production**

A- Nervous mechanism

*** Distension of either body or antrum of stomach stimulates mechanoreceptors in gastric wall. Gastric secretion occurs by:**

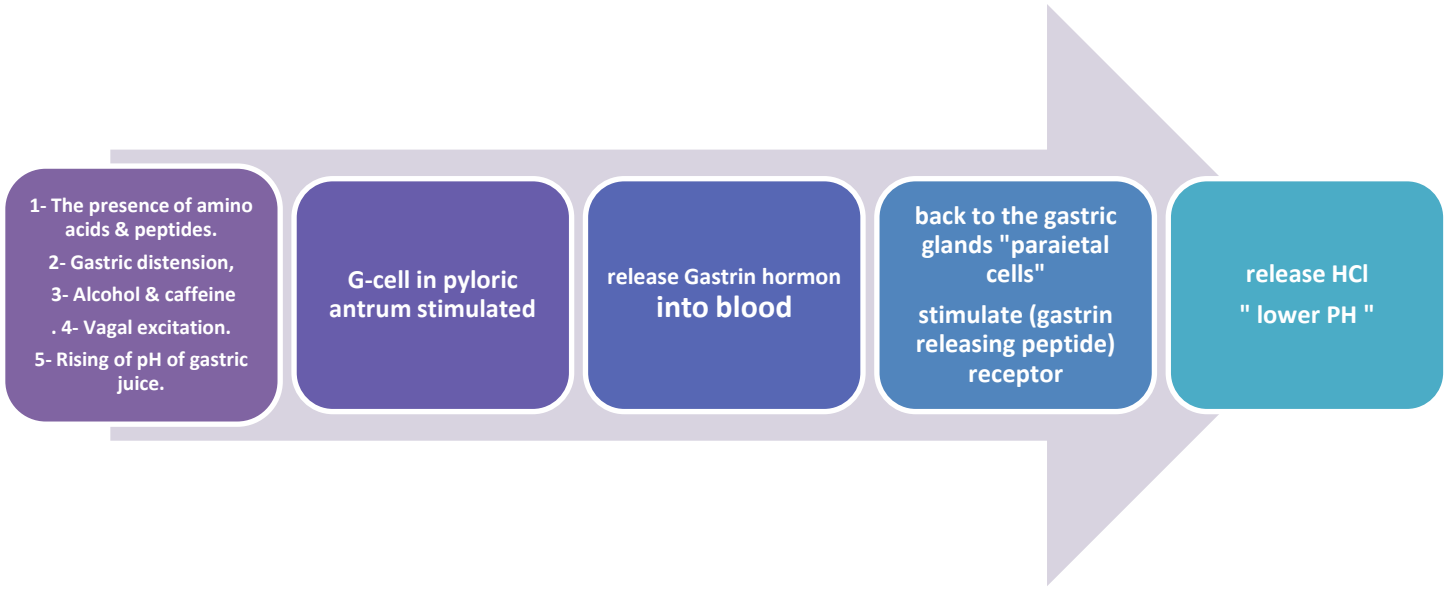
long vagovagal reflex.-

Receptors→afferent→center "medulla oblongata" →efferent→glands and smooth muscles

short intramural cholinergic reflexes.-

Receptors→intermural plexuses→glands and smooth muscles

B- Hormal mechanism (Gastrin hormone)



Other Actions of gastrin after released into blood :

A) Effect on secretion :

1 - Stimulation of gastric acid secretion " HCl " , secretion of pepsin and (intrinsic factor).
2- Stimulation of intestinal secretion.
3- Stimulation of pancreatic secretion of enzyme & HCO3-.
4- Stimulation of biliary secretion of HCO3- & H2O.

B) Effect on motility and muscles

5- Stimulation of gastric motility.

6- Stimulation of intestinal motility & relaxes ileocaecal sphincter.--> to pass the food outside the body

7- It contract LES.(lower esophageal sphincter) → due to increase stomach motility .. so, no reflux occure

8- It has trophic effect on gastric mucosa.

(stimulate the growth, development and metabolism of cells of gastric mucosa)

Control of HCl secretion at the level of parietal cells

By 3 mechanisms:

1. **Endocrine action**
2. **Neurocrine action**
3. **Paracrine action**

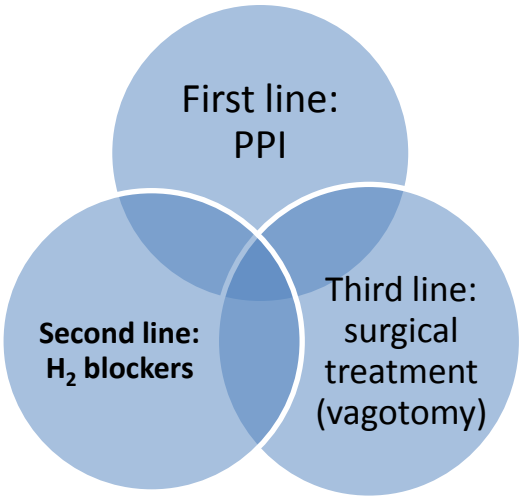
* **Gastrin** reaches parietal cells via blood stream to stimulate HCl secretion (endocrine action).

* **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(not to blood stream) to act on H2 receptors to stimulate HCl secretion (paracrine action).

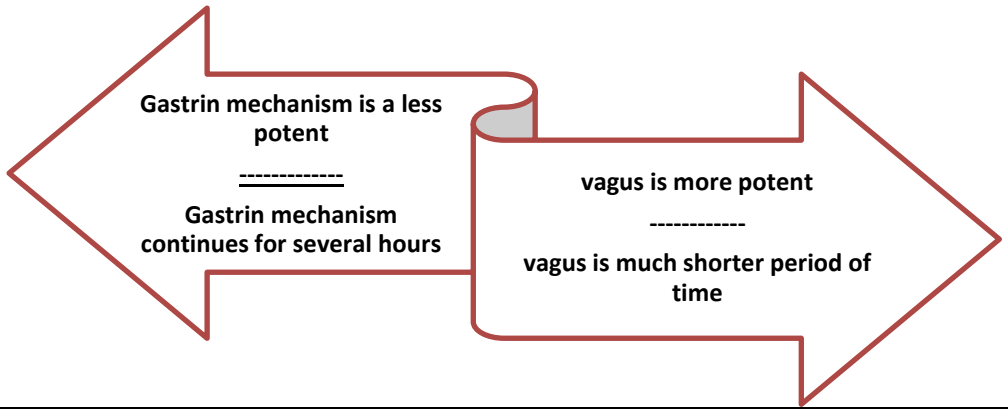
* Cimetidine & ranitidine are H2 receptor blockers and potent inhibitor of G.A secretion and both are used for treatment of peptic ulcers.

➔ **So,Treatment of peptic ulcer:**



- **vagotomy→ cutting the branch of vagus nerve that supplying gastric glands → so, no ach acting on parietal cell !!**

Differences between gastrin & vagal



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

III- The intestinal phase

رح يكون غير عن المرحلتين اللي فاتوا

1- اول ما يبدأ دخول الطعام الى الامعاء .. سوف تقول الامعاء : ادخلي المزيد من فضلك : وسوف تزيد افرازات المعدة طبقا لاوامرها
2- عندما تبدأ الامعاء بالامتلاء : سوف تقول للمعدة : توقفي من فضلك لقد امتلأت !! سوف تقف افرازات المعدة طبقا لاوامرها وهذه الاوامر سوف تكون من الامعاء الى المعدة .. اذا سوف تسمى بـ

Enterogastric reflex → neural control

Enterogastron → hormonal control

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

There is still food in the stomach , so it stimulates the stomach for further degradation of food , but later when the intestine is filled with food it will inhibit the stomach.

First : Gastric secretion is enhanced by:-

1- **Distension of duodenum, it stimulates G.A. (gastric acid) secretion by means of vagovagal reflex that stimulates parietal & G- cells (neural control)**

2- **Presence of protein digestive products as peptides & A.A. in duodenum. This stimulates G-cells in duodenum & proximal jejunum to release gastrin. (hormonal control)**

Second : The inhibitory mechanisms that limit G.A secretion

1- **The presence of food in small intestine initiates enterogastric reflex (inhibitory reflex) due to over distension of duodenum, transmitted through ENS & autonomic NS that inhibits 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 mechanisns.**

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.

Electrical activity of gastric smooth muscle

2 types of potentials can be recorded:-

1- Basal electrical rhythm **(slow wave)**

2- Action potential spikes

3- The migrating motor complex

It is bursts (occurs suddenly and powerful) 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.

After that a new wave of MMC starts.. until you eat another food !! then its activity will stop..!!

The function of MMC is to sweep remnants in stomach & small intestine into colon.

The motility function of stomach

Functionally stomach is divided into :

1- **proximal reservoir :** ***(fundus and upper 1/3 of body)***
رح تستقبل الطعام وتكون مرخيه ،، بعد ذلك سوف تدفع الطعام للاسفل

2- **distal antral pump :** ***lower 2/3 of body ,antrum & pylorus)***

The proximal stomach **As food enters stomach:**

A- **it relaxes to accommodate food (receptive relaxation).**

B- **Slow sustained tonic contraction in proximal stomach provides pressure gradient for pushing & emptying of chyme.**

The distal stomach

(The main activity in distal stomach is peristaltic contractions).

Its function is grinding of solids, liquefaction of chyme, so chyme is propelled to duodenum.

Gastric emptying (gradual)

It occurs through coordinate contraction of antrum, pylorus & duodenal bulb(first part of the duodenum) (gastroduodenal pump).

As gastric contents are propelled into distal stomach, the antrum, pylorus & proximal duodenum are relaxed.

Liquified 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

1- 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.**

Graete volume→ Distension of stomach

But over distension of stomach will delay stomach emtying

B- Effect of gastrin ***on gastric emptying***

2- 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. (chime which contains more concentration of electrolyte)**
2. **The drop of pH of chyme in duodenum to < 3.5 – 4 PH → because the intestine is alkaline.**
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 → (gastric inhibitory peptide).**
- **Gastrin slows gastric emptying due to:- 1- It stimulates duodenal motility & ↑ its resistance → (increase pressure in the duodenum)**

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