GASTROINTESTINAL PHYSIOLOGY

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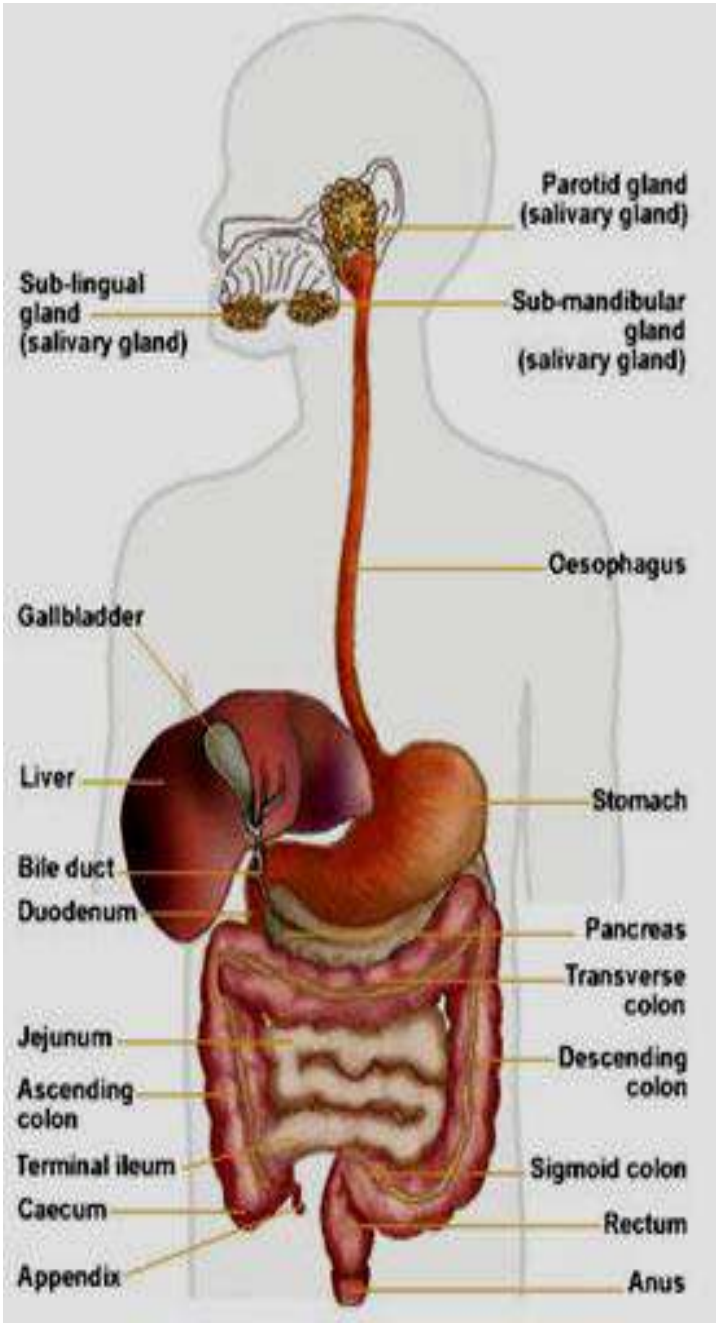
General Principles of Gastrointestinal Function-
Motility, Nervous Control, and Blood Circulation

- **The alimentary tract provides the body with a continual supply of water, electrolytes, vitamins, and nutrients.**
- ***To achieve this requires***
  - ***Movement*** **of food through the alimentary tract.**
  - ***Secretion*** **of digestive juices and digestion of the food.**
  - ***Absorption*** **of water, various electrolytes, vitamins, and digestive products.**
  - ***Circulation*** **of blood through the gastrointestinal organs to carry away the absorbed substances.**
  - ***Control*** **of all these functions by local, nervous, and hormonal systems.**

Digestive System

- It is ***5 meters*** in living persons and ***8 meters*** outside the body.
- It is a muscular tube and its lumen is continuous with the mouth and the anus.
- The digestive tract is continuous with the external environment.



Components of digestive system

It consists of :

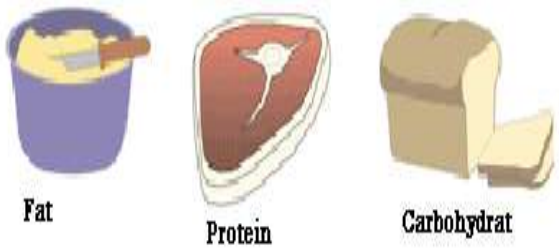
1 ***Alimentary canal*** **(starts at the mouth and ends at the anus, consists of:**

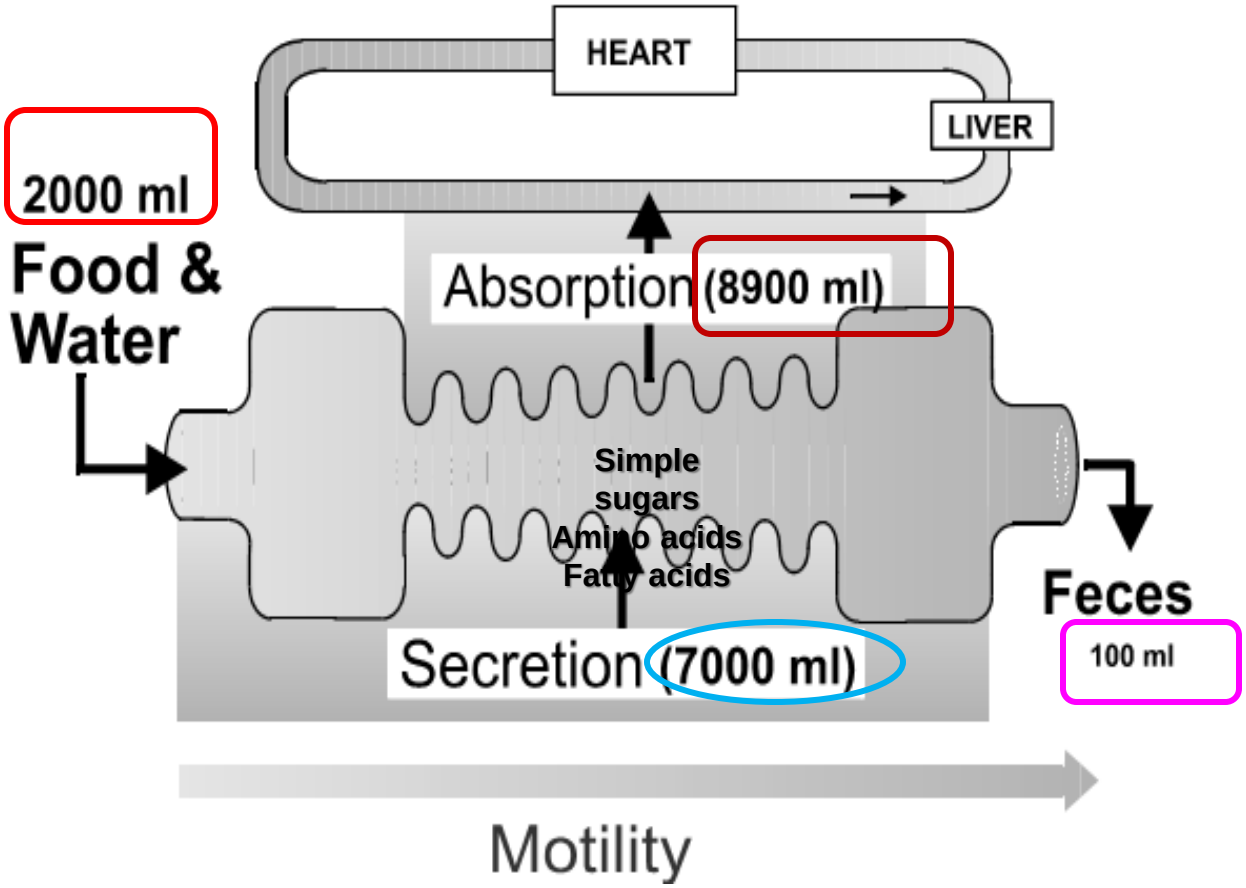
- ***Mouth , pharynx & esophagus.***
- ***Stomach.***
- ***Small intestine (duodenum, jejunum. Ileum).***
- ***Large intestine (cecum, appendix, colon & rectum).***

2 ***Digestive glands*** **(Salivary glands, Liver, Gall Bladder, Exocrine Pancreas).**

General functions of the Gut

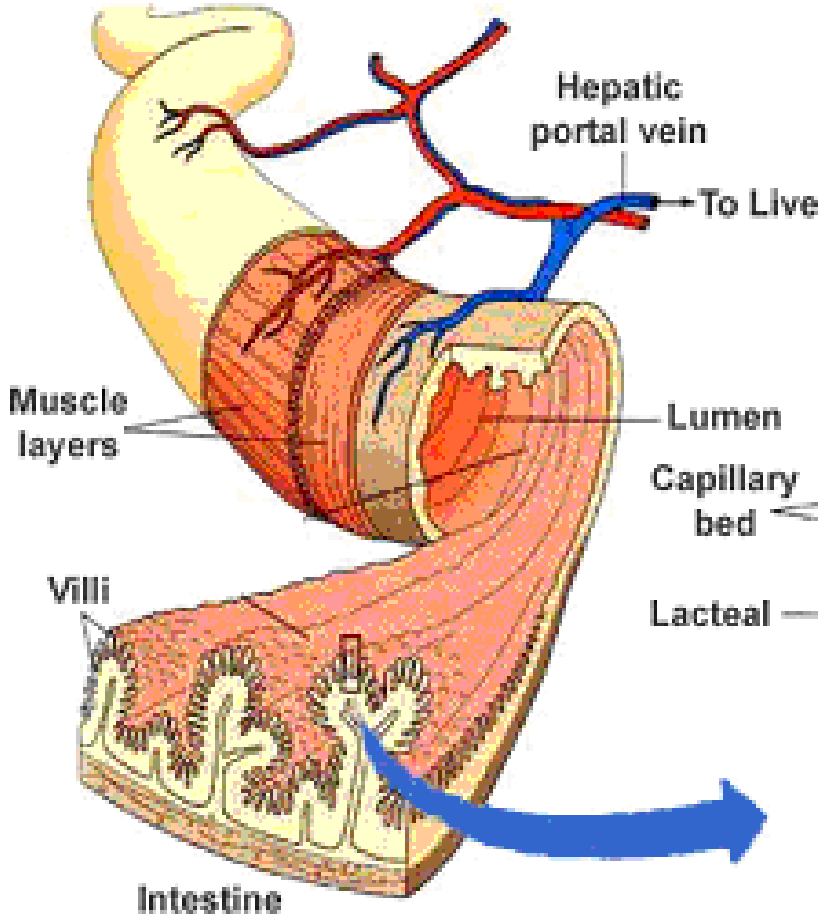
- ***Food digestion.*** **What is the definition of digestion?**
  (Digestion is the breakdown of complex molecules into simple ones to facilitate their absorption).
- **i.e. CHO⇨ Monosaccharide's, Proteins Amino Acids, Fat ⇨ Fatty Acids). The process of digestion needs:-**
  - **Secretion of digestive juices.**
  - **Wall motility**
- **Food absorption**
- **Excretion of waste products**

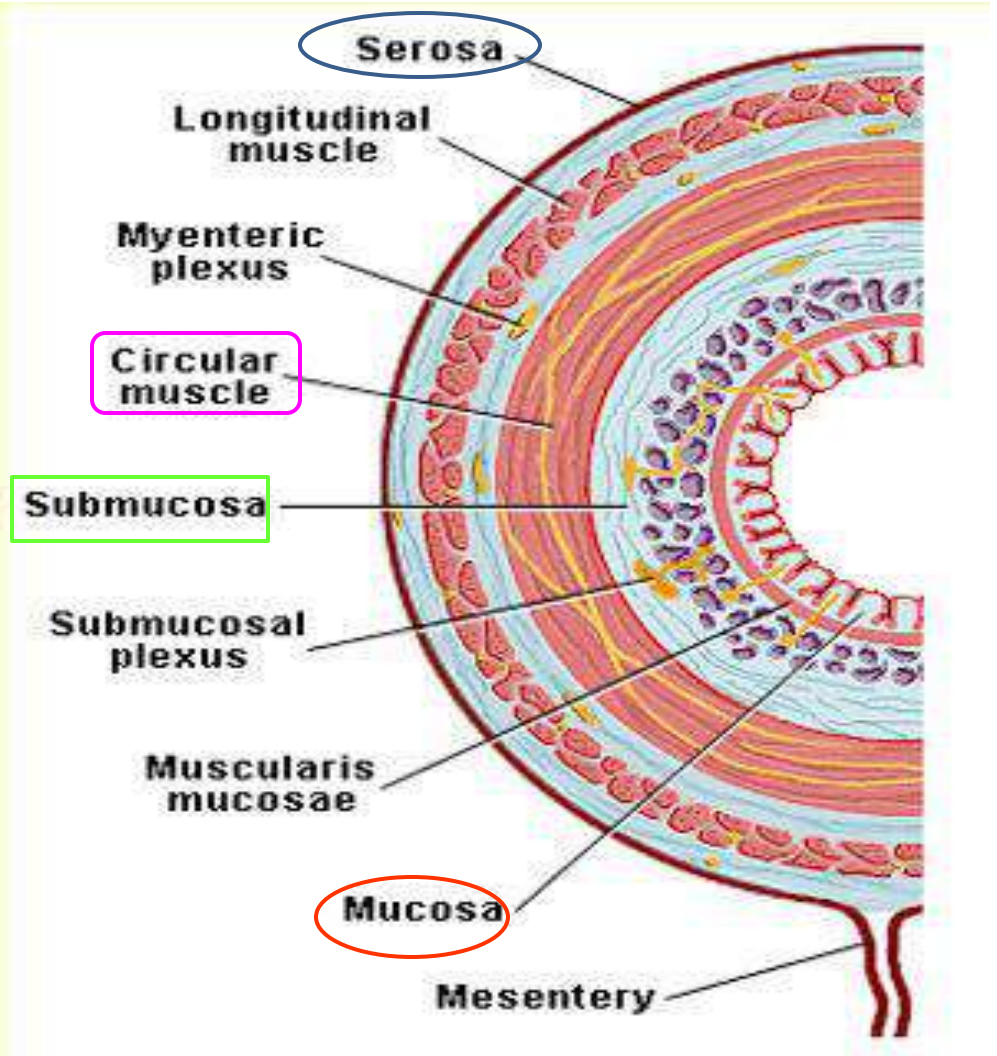


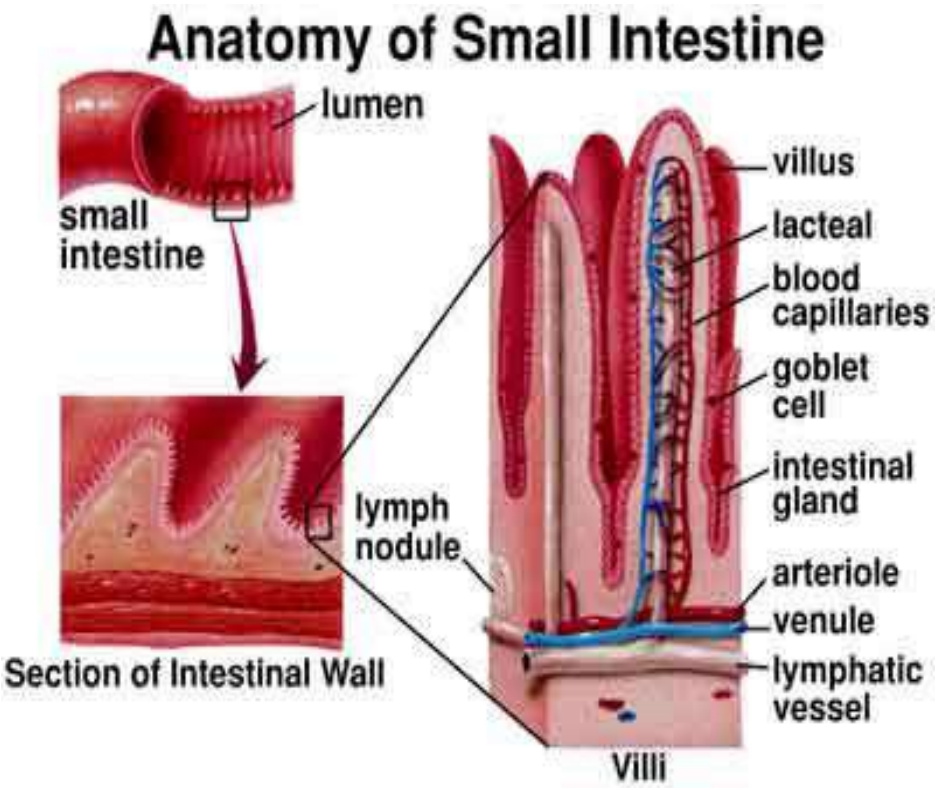


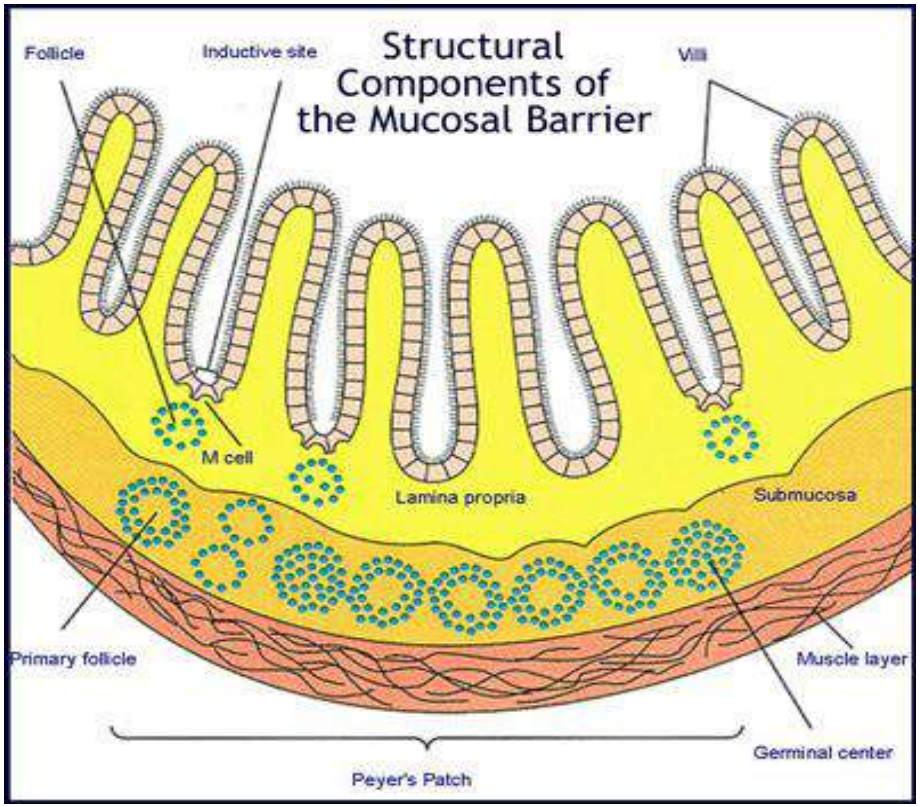
Overview of gut functions

Structure of the Gut wall







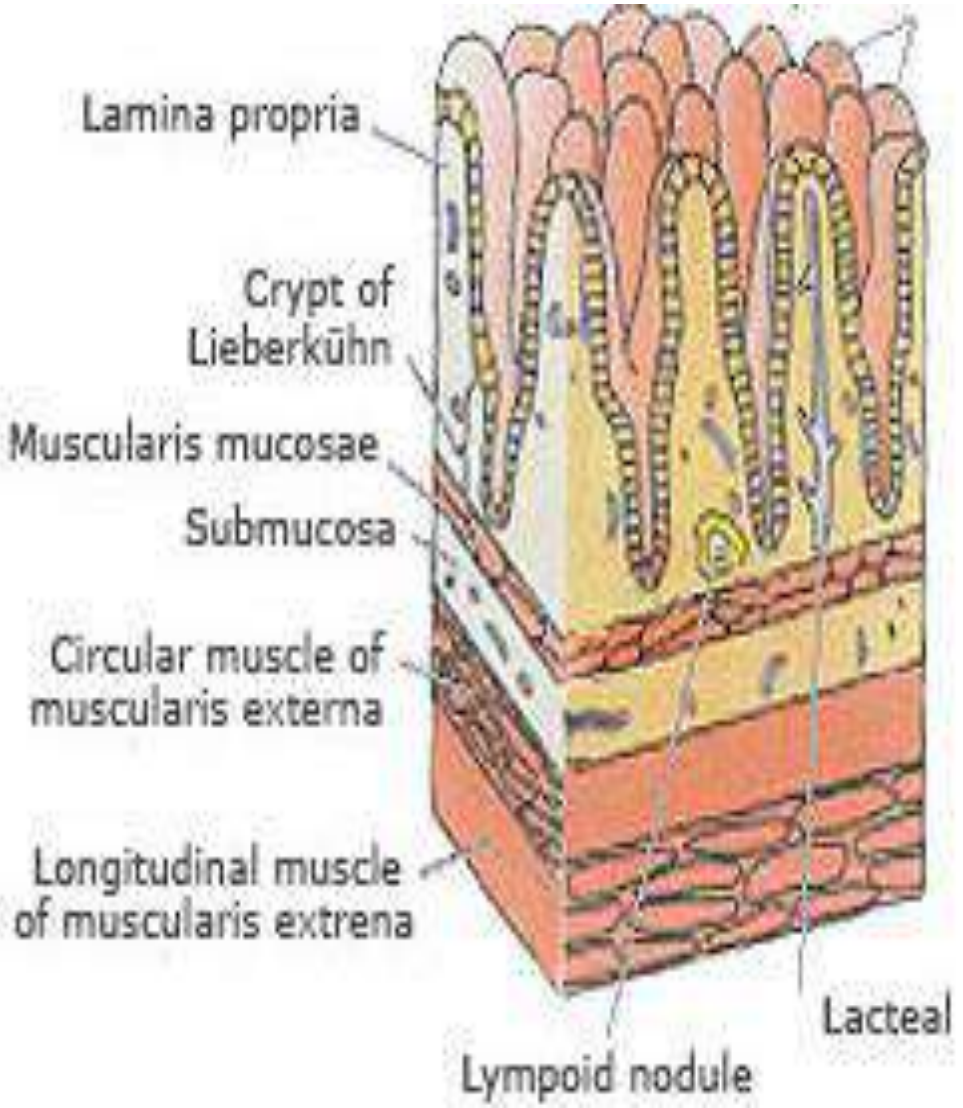


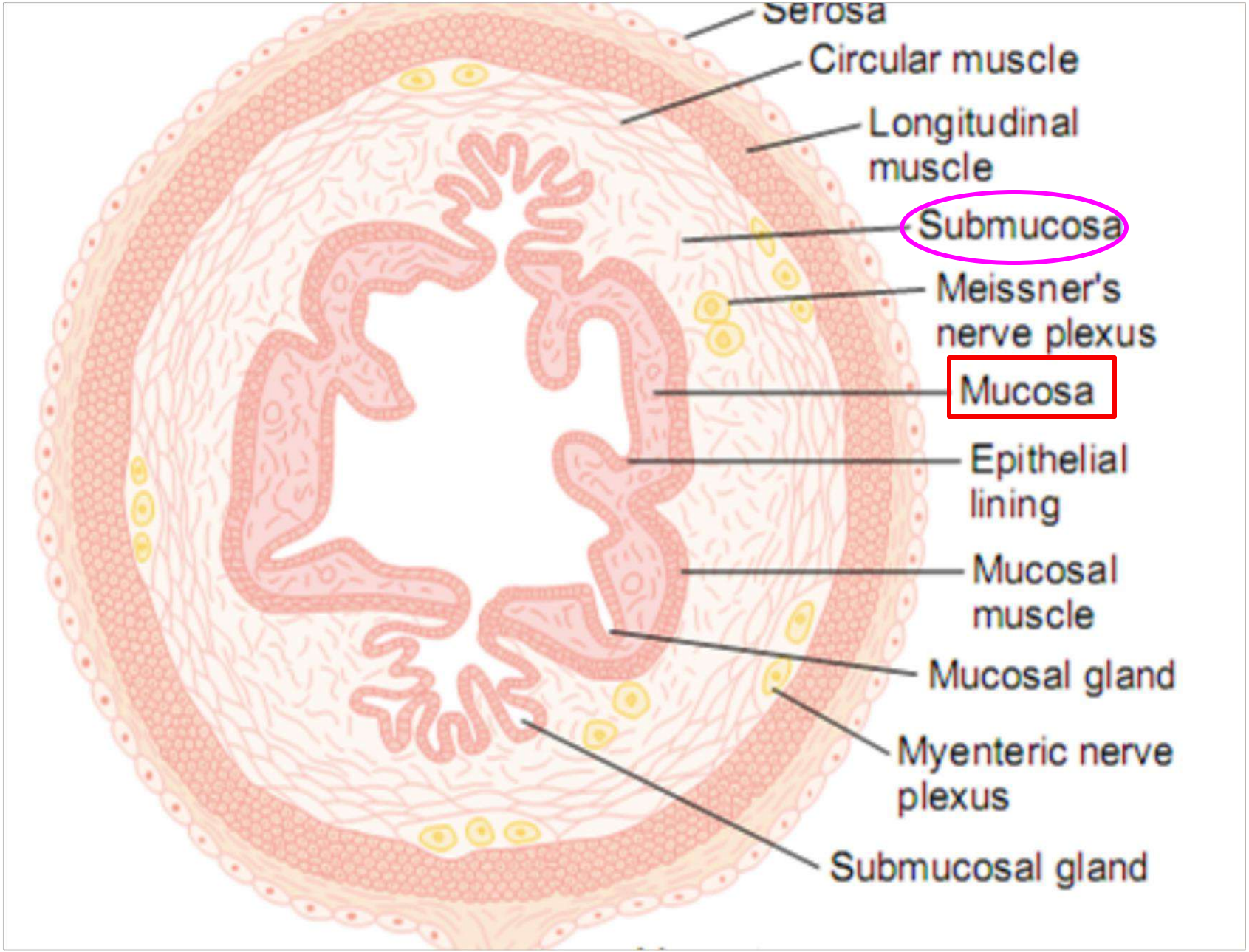
1. ***The mucosa of the gut is highly folded. Why?***

- **It is divided into:-**
  - **Mucous membrane.**
  - **Lamina propria (BV, nerves, lymphatic's & lymphoid tissue).**
  - **Muscularis mucosa (modify the pattern of folding).**

- ***The submucosa consists of:-***
  - **Blood vessels**
  - ***Meissner's plexus***
  - **Lymphatic's**
  - **Lymphoid tissue**
- ***Muscularis externa consists of :-***
  - **Outer longitudinal layer**
  - **Inner circular layer**
  - ***Nerve plexus in between (Auerbach's' s plexus)***
- ***Serosa***

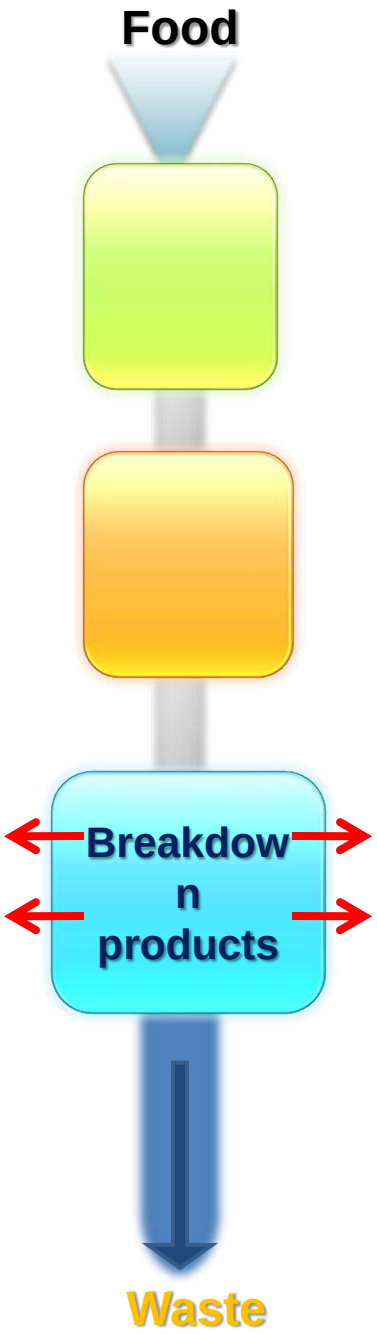
  It is the outer covering layer.




Serosa
Circular muscle
Longitudinal muscle
Submucosa
Meissner's nerve plexus
Mucosa
Epithelial lining
Mucosal muscle
Mucosal gland
Myenteric nerve plexus
Submucosal gland

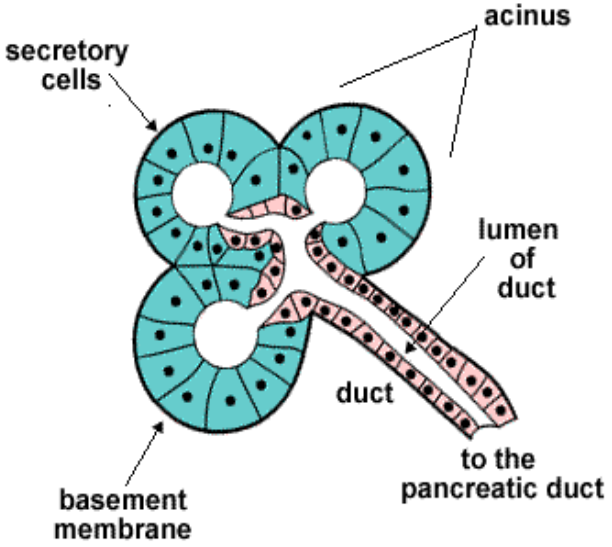
Gut layer	Function	Structure
Mucosa	1. Secretion of digestive juices and hormones. 2. Absorption of various nutrients. 3. Protection against infection.	1. Epithelial cells 2. Exocrine cells 3. Endocrine cells. 4. Muscle layer (muscularis mucosa) 5. Blood vessels , Lymph vessels & nerves
Sub mucosa	Contain the submucosal (Meissner's) nerve plexus which control GIT secretions.	1. Dense connective tissue. 2. Blood vessels, lymph vessels, and lymph nodes. 3. Submucosal (Meissner's) nerve plexus.
Musculosa	Gut motility	1. Outer longitudinal layer. 2. Inner circular layer 3. Nerve plexus in between (Auerbach's' s plexus)
Serosa	Secrete watery serous fluid. Lubricates and prevent friction	It continues with the mesentery. It contains nerves & blood vessels

Movement of materials from one container to another and mixing
Measure the concentration of hydrogen ion, the concentrations of protein, fat, and carbohydrate, and the tonicity of the digest
Addition of enzymes and fluid
Extraction of breakdown products



Gut Secretion

- There are Exocrine glands located along the wall of the gut.
- Each digestive juice consists of :-
  - Water & Electrolytes
  - Organic constituent .e.g. Enzymes & Mucus.
- The gland extract water & raw material from the plasma.
- The digestive secretion is then reabsorbed back to the blood after participation in the digestive process.
- Failure of reabsorption of digestive juices may lead to *Circulatory Shock.*



Digestion & Absorption

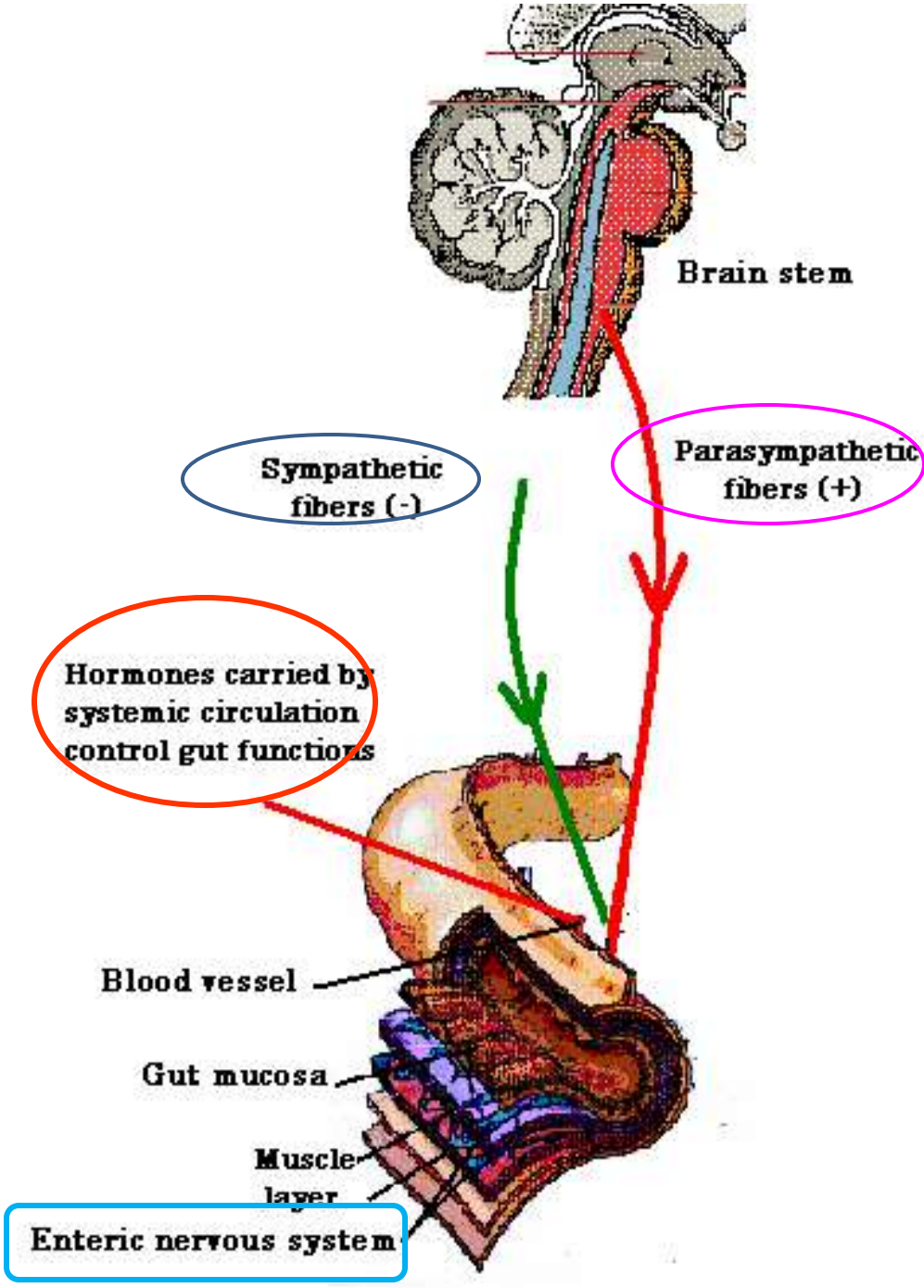
- ***Digestion*** **is the breakdown of complex molecules into simple absorbable unites.**

It is accomplished by enzymes that hydrolyze certain bonds in the food molecule.

- ***Absorption*** **occurs in the small intestine.**

Undigested & unabsorbed materials are excreted to the outside by the process of defecation .

Regulation of gut functions



Control Of gut functions

Gut functions are controlled by :-

- Autonomous Smooth Muscle Activity.
- Nervous Regulation.
- Hormonal Regulation.

Nerve supply of the gut

1-Enteric nervous system

(local nerve plexuses)

a- Meissner's plexus.

b- Auerbach's plexus.

2-Autonomic nerves:

a-Sympathetic.

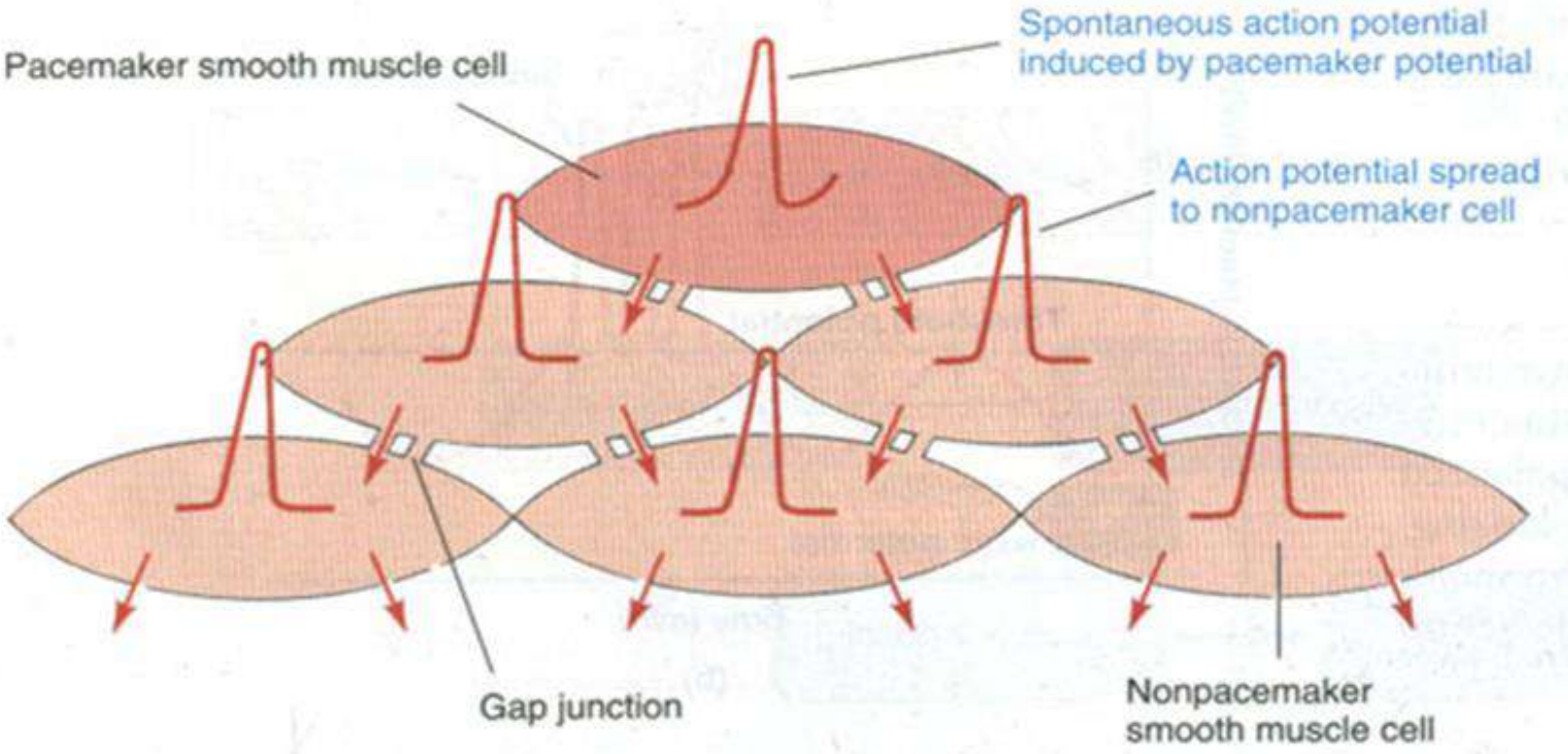
b-Parasympathetic *(vagal, sacral).*

Electrophysiology of GIT smooth muscles:

- **Gastrointestinal smooth muscle cells exhibit the following electric changes:-**
  - ***Changes in the level of smooth muscle resting potential (it is changed by sympathetic & parasympathetic stimulation as well as hormones).***
  - ***Slow wave potential (BER).***
  - ***Spike potentials***

Functional syncytium of the GIT smooth muscles:-

- **Sheets of smooth muscles cells are connected by *Gap Junctions* which are points of low electric resistance.**
- **If AP was triggered in pace maker cells, it rapidly spreads to all smooth muscles.**

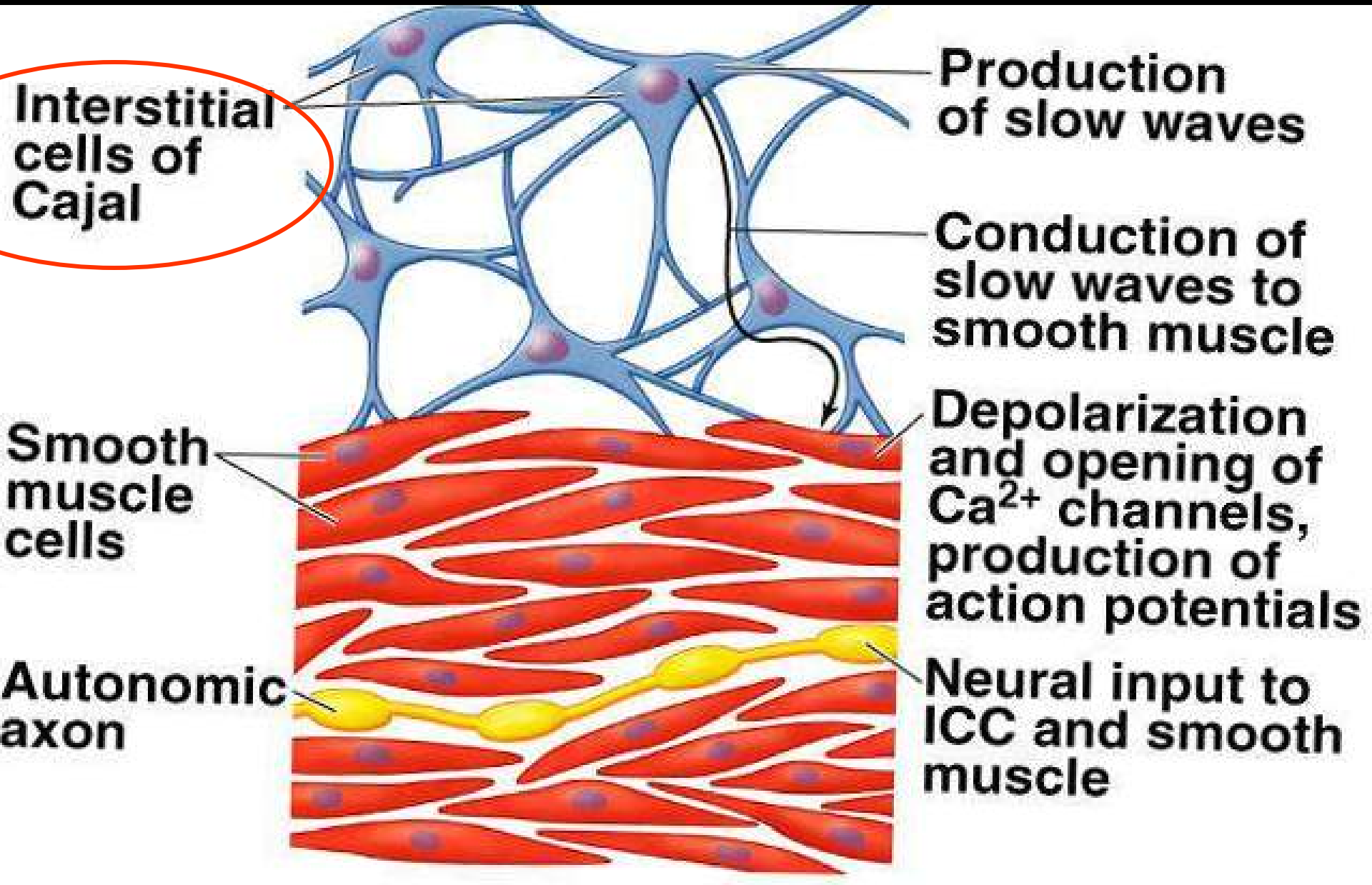


Functional syncytium of gut smooth muscles

Electrophysiology of GIT smooth muscles:

- There are ***pace maker cells*** in the GIT smooth muscles (between the longitudinal & circular smooth muscle layers) called ***(INTERSTITIAL CELLS OF CAJAL).***
- These cells are non contractile and have unstable RMP.
- They produce spontaneous depolarization and repolarization in the form of ***SLOW WAVES WHICH ARE CALLED BASIC ELECTRIC RHYTHM (BER).***

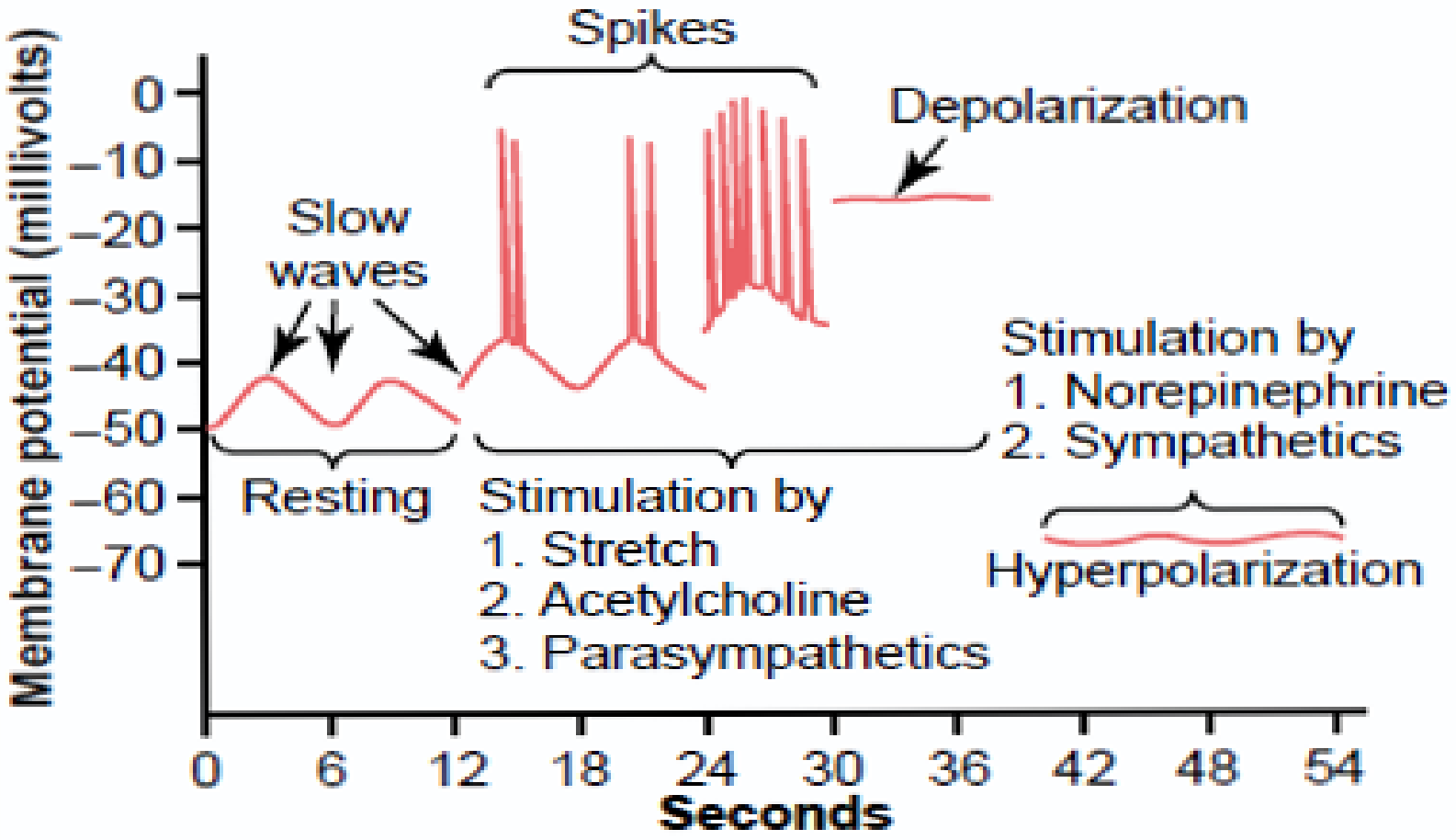
PACEMAKER OF THE GUT



- ***The frequency of slow waves depends on the section of the digestive tube***
  - **In the body of the stomach *3 / min***
  - **In the duodenum *12 /min***
  - **In the terminal ileum *8 or 9 /min.***
  - **In colon *3 /min***
- **Slow wave activity appears to be a property intrinsic to smooth muscle and not dependent on nervous stimuli or hormones.**
- **It is *Not an action potential & doesn't induce muscle contraction.* (stomach).**

Changes in Voltage of the Resting Membrane Potential.

- **The resting membrane potential averages about *-56 mill volts*, but multiple factors can change this level.**
- **When the potential becomes *less negative*, which is called *Depolarization* of the membrane, the muscle fibers become *More Excitable.***
- **When the potential becomes More negative, which is called *Hyperpolarization,* the fibers become *Less Excitable.***


Spikes
Depolarization
Slow waves
Stimulation by
1. Norepinephrine
2. Sympathetics
Resting
Stimulation by
1. Stretch
2. Acetylcholine
3. Parasympathetics
Hyperpolarization
Membrane potential (millivolts)
0
−10
−20
−30
−40
−50
−60
−70
0
6
12
18
24
30
36
42
48
54
Seconds

Factors that depolarize the membrane — that is, make it more excitable— are :

- ***Stretching*** **of the muscle.**
- **Stimulation by *Acetylcholine*.**
- **Stimulation by *parasympathetic nerves* that secrete acetylcholine at their endings,**
- **Stimulation by several *specific gastrointestinal hormones*.**

- **Important factors that make the membrane potential more negative—that is, *Hyperpolarize the membrane* and make the muscle fibers less excitable—are:**
- **The effect of *norepinephrine* or *epinephrine* on the fiber membrane .**
- **Stimulation of the sympathetic nerves that secrete mainly norepinephrine at their endings.**

Slow wave & spike potentials

	Slow wave potential	Spike potentials
Definition	Oscillatory changes in membrane potential.	Train of action potentials that occur on top of slow waves when membrane potential reaches threshold.
Nature	Muscle property	The muscle must be primed by neurotransmitters released in the vicinity due to stimulation.
Frequency	Inherent to each region.	Depend on mechanical, nervous & hormonal factors
Mechanism	Not well understood	Opening of ion channels
Significance	Determines the rate of muscle contraction	Induce muscle contraction. Number of spike potentils determines the intensity of muscle contraction

Functional Types of Movements in the Gastrointestinal Tract

- **All GIT muscle is Smooth Muscle except:**
  - **Upper 1/3 of esophagus (skeletal muscle).**
  - **Middle 1/3 of esophagus (skeletal and smooth).**
  - **External anal sphincter (skeletal muscle).**
  - **Movement of materials through the digestive tract is accomplished by smooth muscle contraction (Involuntary Control), except at the Oral & the Anal ends of the tract which contain skeletal muscles.**

TYPES OF BOWEL MOVEMENTS

(1) *Propulsive movements:*, which cause food to move forward along the tract at an appropriate rate to accommodate digestion and absorption.

(2) *Mixing movements* :which keep the intestinal contents thoroughly mixed at all times.

Propulsive Movements—Peristalsis

- **A contractile ring appears around the gut and then moves forward.**
- **Peristalsis is an inherent property of many syncytial smooth muscle tubes, stimulation at any point in the gut can cause a contractile ring to appear in the circular muscle, and this ring then spreads along the gut tube.**
- **(Bile ducts, Glandular ducts, Ureters).**

- **The usual stimulus for intestinal peristalsis is *Distention of the gut*.**

That is, if a large amount of food collects at any point in the gut, the stretching of the gut wall stimulates the enteric nervous system to contract the gut wall 2 to 3 centimeters behind this point, and a contractile ring appears that initiates a peristaltic movement.

- **Chemical or physical irritation of the epithelial lining in the gut.**
- **Parasympathetic nervous signals.**

Function of the Myenteric Plexus in Peristalsis

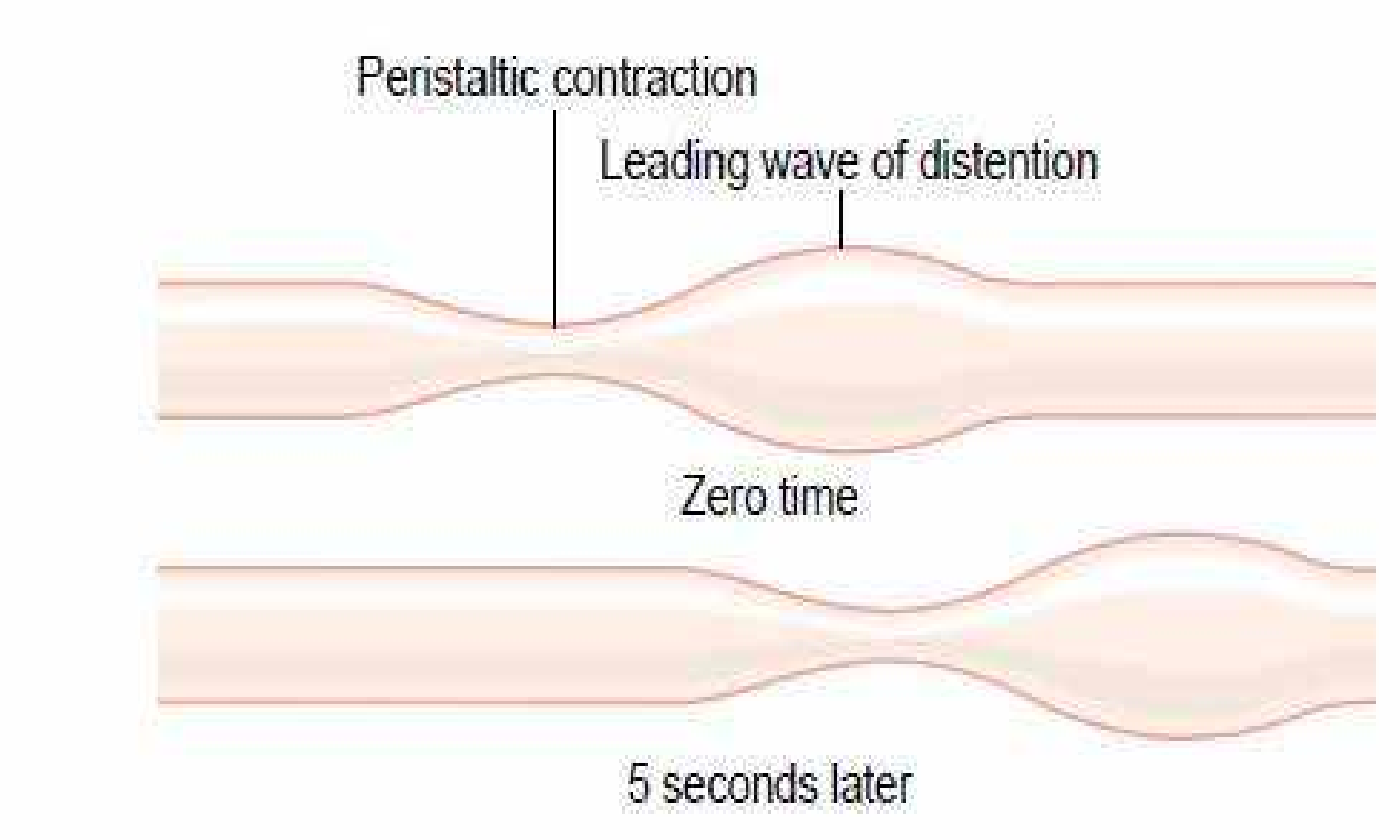
- **Peristalsis occurs only weakly or not at all in any portion of the GIT that has congenital *Absence of the Myenteric plexus*.**
- **Also, it is greatly depressed or completely blocked in the entire gut when a person is treated with Atropine to paralyze the cholinergic nerve endings of the Myenteric plexus.**
- **Therefore, *effective* peristalsis requires an active *Myenteric Plexus*.**

Directional Movement of Peristaltic Waves Toward the Anus.

- **The exact cause of this directional transmission of peristalsis has never been ascertained, although it probably results mainly from the fact that the myenteric plexus itself is *"Polarized"* in the anal direction.**

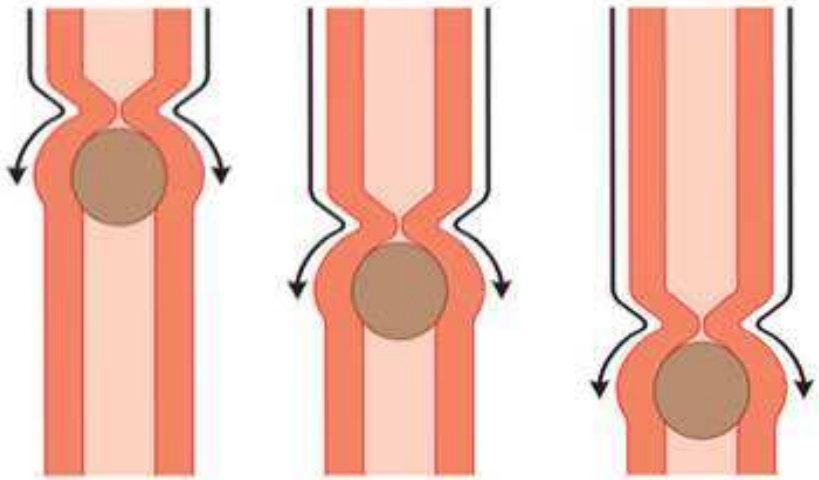
Peristaltic Reflex and the "Law of the Gut"

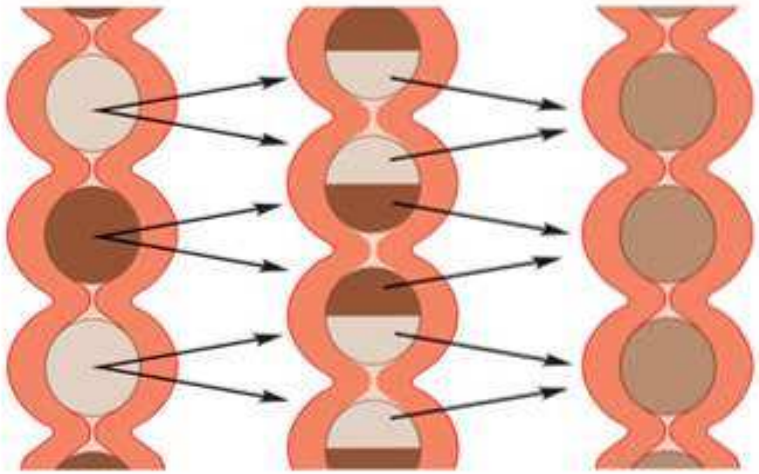
- When a segment of the GIT is excited by distention and initiates peristalsis, the contractile ring causing the peristalsis normally begins on the *oral side of the distended segment* and moves toward the distended segment, pushing the intestinal contents in the anal direction for *5 to 10 cm* before dying out.
- At the same time, the gut relaxes several centimeters downstream toward the anus, which is called *"receptive relaxation,"* thus allowing the food to be propelled more easily toward the anus than toward the mouth.
- Therefore, this complex is called the *Myenteric reflex* or the *peristaltic reflex.*
- The peristaltic reflex plus the anal direction of movement of the peristalsis is called the *"law of the Gut"*


Peristaltic contraction
Leading wave of distention
Zero time
5 seconds later

Mixing Movements

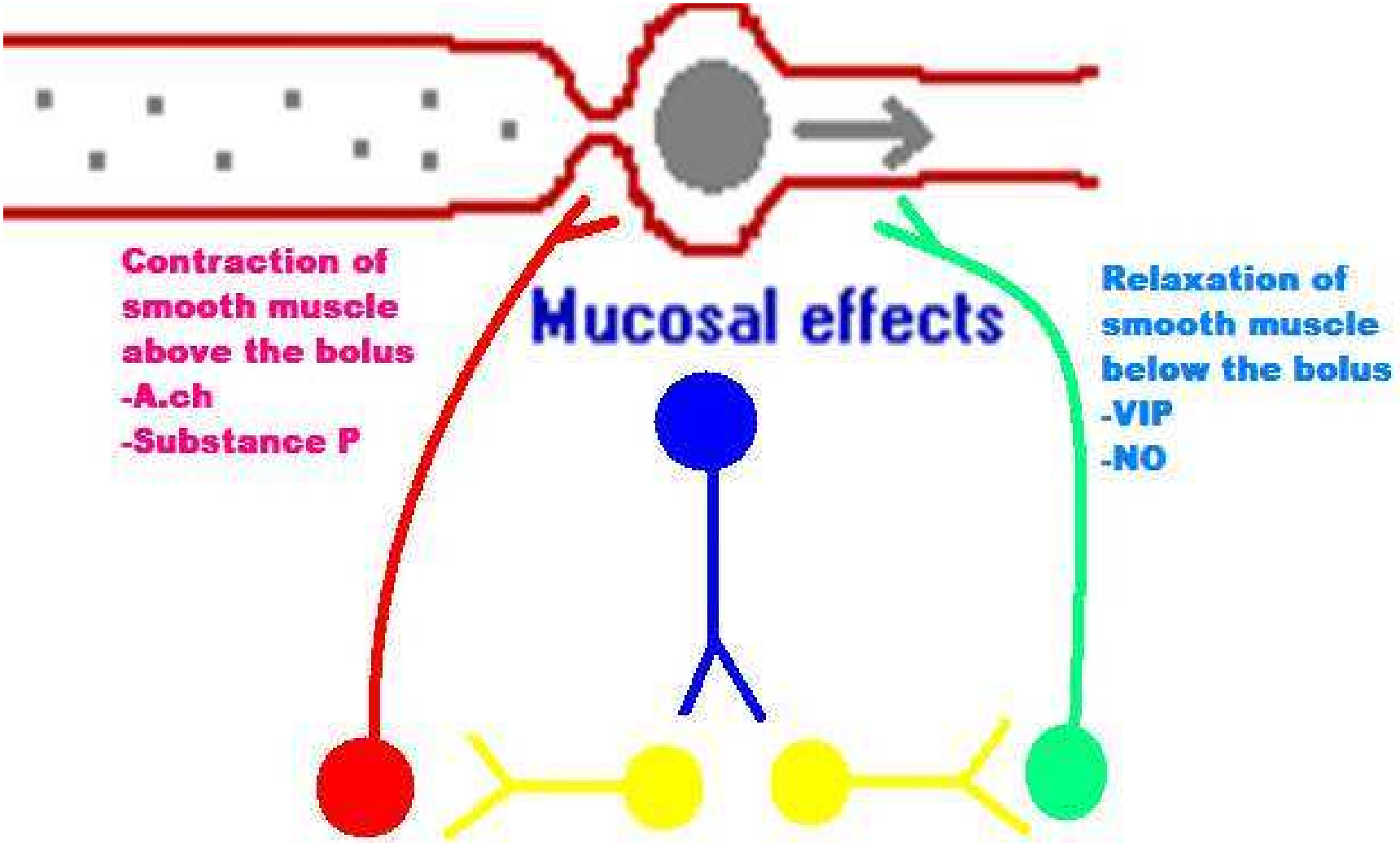
- In some areas, the peristaltic contractions themselves cause most of the mixing.
- This is especially true when *Forward Progression* of the intestinal contents is *Blocked by a sphincter*, so that a peristaltic wave can then only churn the intestinal contents, rather than propelling them forward.
- At other times, *local intermittent constrictive contractions* occur every few centimeters in the gut wall.
- These constrictions usually last only 5 to 30 seconds, then new constrictions occur at other points in the gut, thus *"Chopping" and "Shearing"* the contents first here and then there.





Peristalsis: Adjacent segments of alimentary tract organs alternately contract and relax, which moves food along the tract distally.

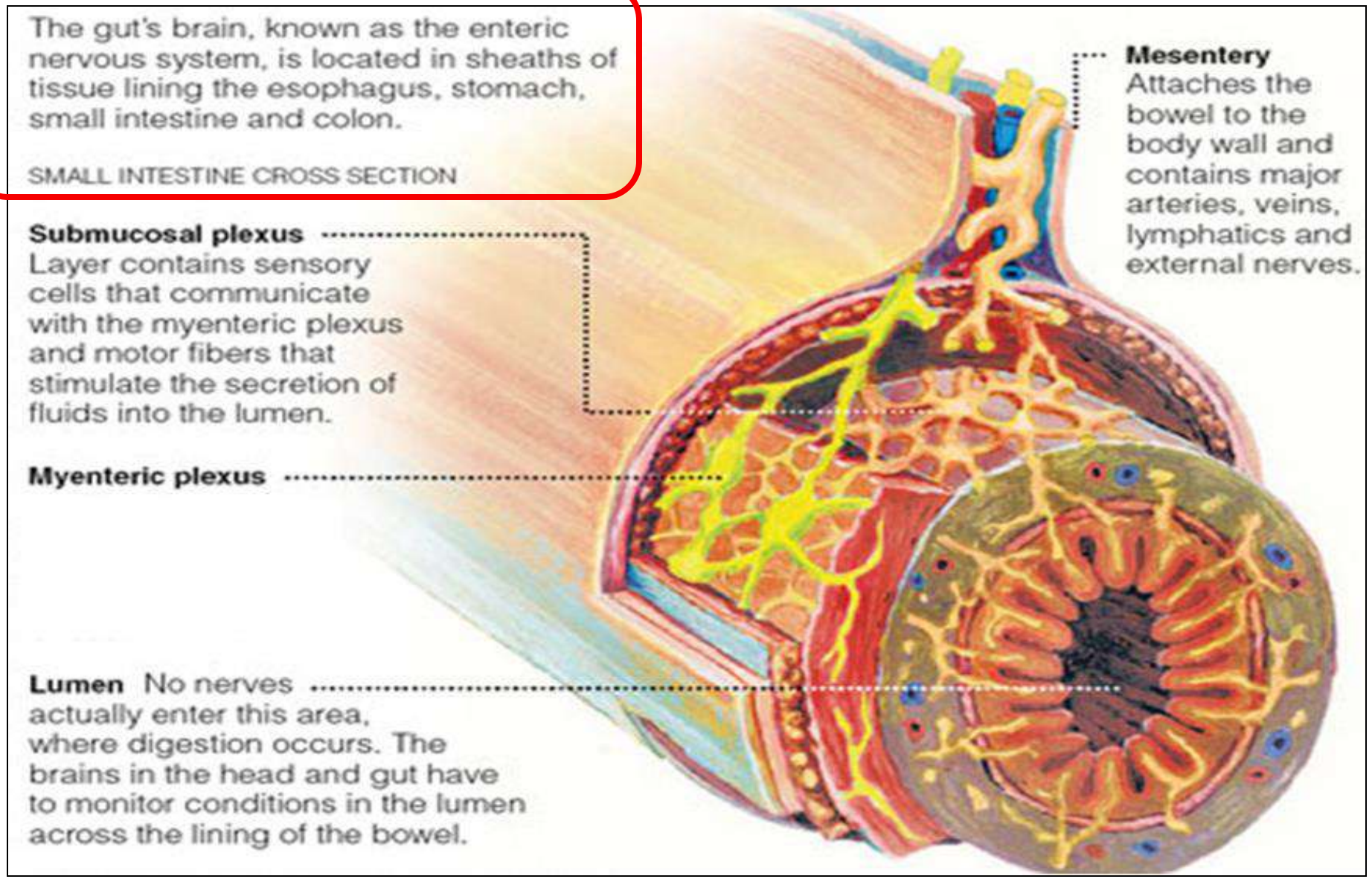
Segmentation: Nonadjacent segments of alimentary tract organs alternately contract and relax, moving the food forward then backward. Food mixing and slow food propulsion occurs


Contraction of
smooth muscle
above the bolus
-A.ch
-Substance P
Mucosal effects
Relaxation of
smooth muscle
below the bolus
-VIP
-NO

Minibrain of the gut

The gut's brain, known as the enteric nervous system, is located in sheaths of tissue lining the esophagus, stomach, small intestine and colon.

SMALL INTESTINE CROSS SECTION



Neural Control of GIT Function
Enteric Nervous System

- **GIT has a nervous system of its own called the Enteric Nervous System.**
- **It lies entirely in the wall of the gut, beginning in the esophagus and extending all the way to the anus.**
- **The number of neurons in this ENS is about 100 Million.**
- **This highly developed ENS is especially important in controlling *Gastrointestinal movements and secretion.***

Enteric nervous system

- **It is a displaced part of the CNS that is concerned with the regulation of the gastrointestinal functions.**
- ***It doesn't depend on CNS in its function.***

It consists of two plexuses;

- ***Meissner's plexus (submucosa):.***

  It controls exocrine and endocrine secretions.

- **Control local *intestinal secretion*, local *absorption*, and local *contraction of the submucosal muscle* that causes various degrees of infolding of the gastrointestinal mucosa.**

- ***Myenteric plexus*** **(Auerbach's plexus)between the 2 muscle layer).**
  - ***It Controls the GIT motility.***

- **Output neurons are either excitatory or inhibitory. What are their neurotransmitters?**
- **The neurons of the ENS secrete Ach, GABA, seretonin, and nitrous oxide (which is the major mediator for smooth muscle relaxation in GIT).**
- **Autonomic nerves terminate on it but it can functions independent of them.**
- **The parasympathetic nerve supply is generally *Stimulatory* to ENS while the sympathetic is generally *Inhibitory*.**

Types of Neurotransmitters Secreted by Enteric Neurons

1) ***acetylcholine*** **and**
2) ***norepinephrine.***
3) ***adenosine triphosphate,***
4) ***serotonin,***
5) ***dopamine,***
6) ***cholecystokinin,***
7) ***substance P,***
8) ***vasoactive intestinal polypeptide,***
9) ***somatostatin,***
10) ***leu-enkephalin,***
11) ***met-enkephalin,*** **and**
12) ***bombesin*****.**

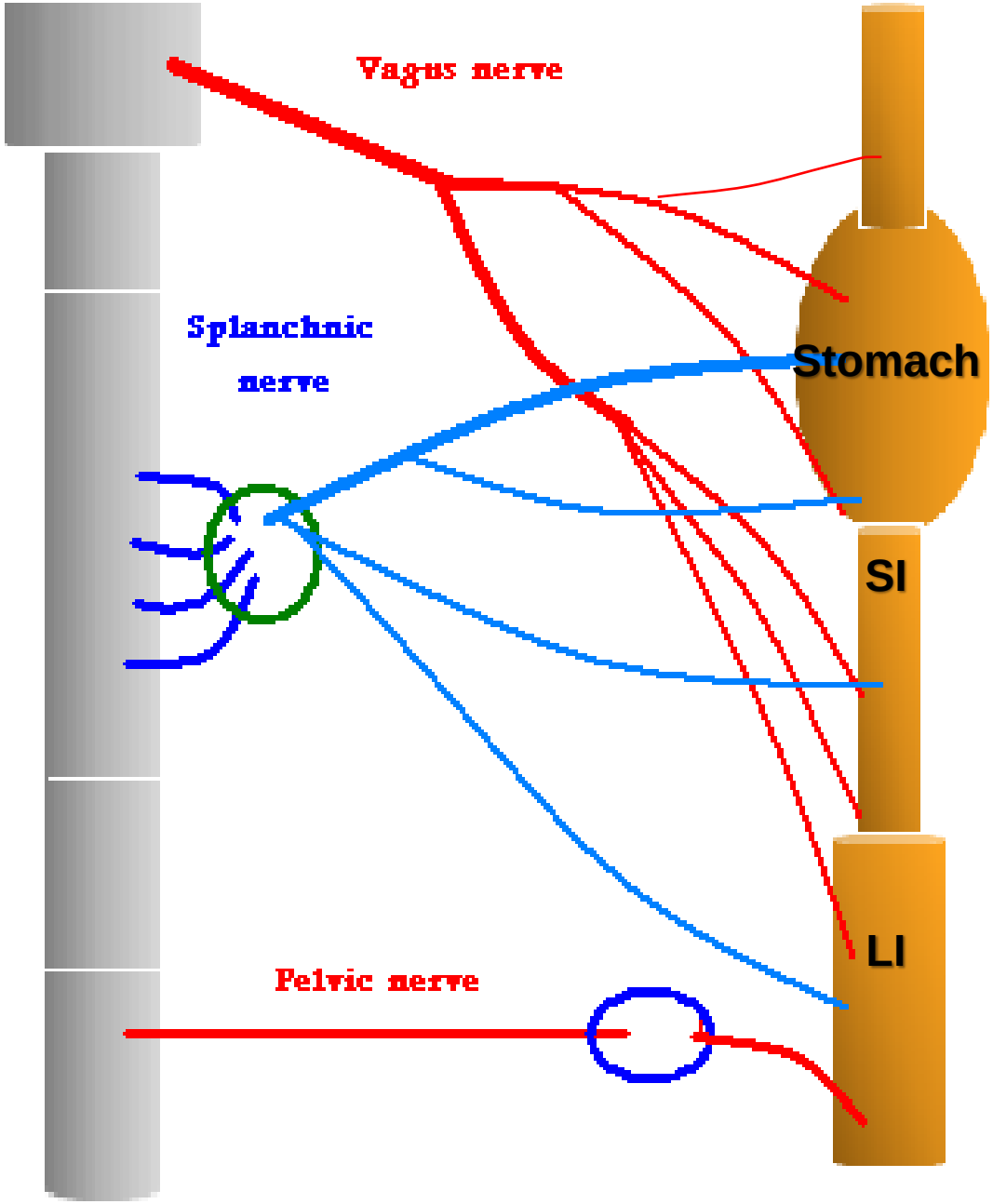
- **The *Myenteric plexus* is mainly *Excitatory* but some of its neurons are *Inhibitory, that secrete* an inhibitory transmitter, possibly *VIP .***

- **The resulting inhibitory signals are useful for inhibiting some of the intestinal sphincter muscles that impede movement of food along successive segments of the gastrointestinal tract, such as the *pyloric sphincter* and the *sphincter of the ileocecal valve.***

Autonomic Innervation

	Sympathetic	Parasympathetic
1-Origin	Thoracolumbar (T5-L2).	Cranial (mainly vagus) to esophagus till upper LI. Sacral (S2-4) pelvic nerve to lower LI, rectum, anal canal.
2-Fiber	Postganglionic	Preganglionic
3-Chemical transmitter	Norepinephrine	Acetylcholine
4-Effect	a-Relaxation of wall b-contraction of sphincters c-mainly :↓ secretions	a-Contraction of wall b-Relaxation of sphincters c-mainly :↑ secretions
5-Termination	Myenteric and Meissner's plexus others bypass:- to Blood vessels. And smooth muscles.	Myenteric and Meissner's plexus.

Nerve Supply Of The Gut



Importance of the autonomic innervation to the gut

- **Coordinate the activity between different regions of the gut.**

e.g. Chewing ⇨ Salivation , ⇨↑ Gastric secretion , ⇨ ↑ Bile , ⇨ ↑ Pancreatic secretion.

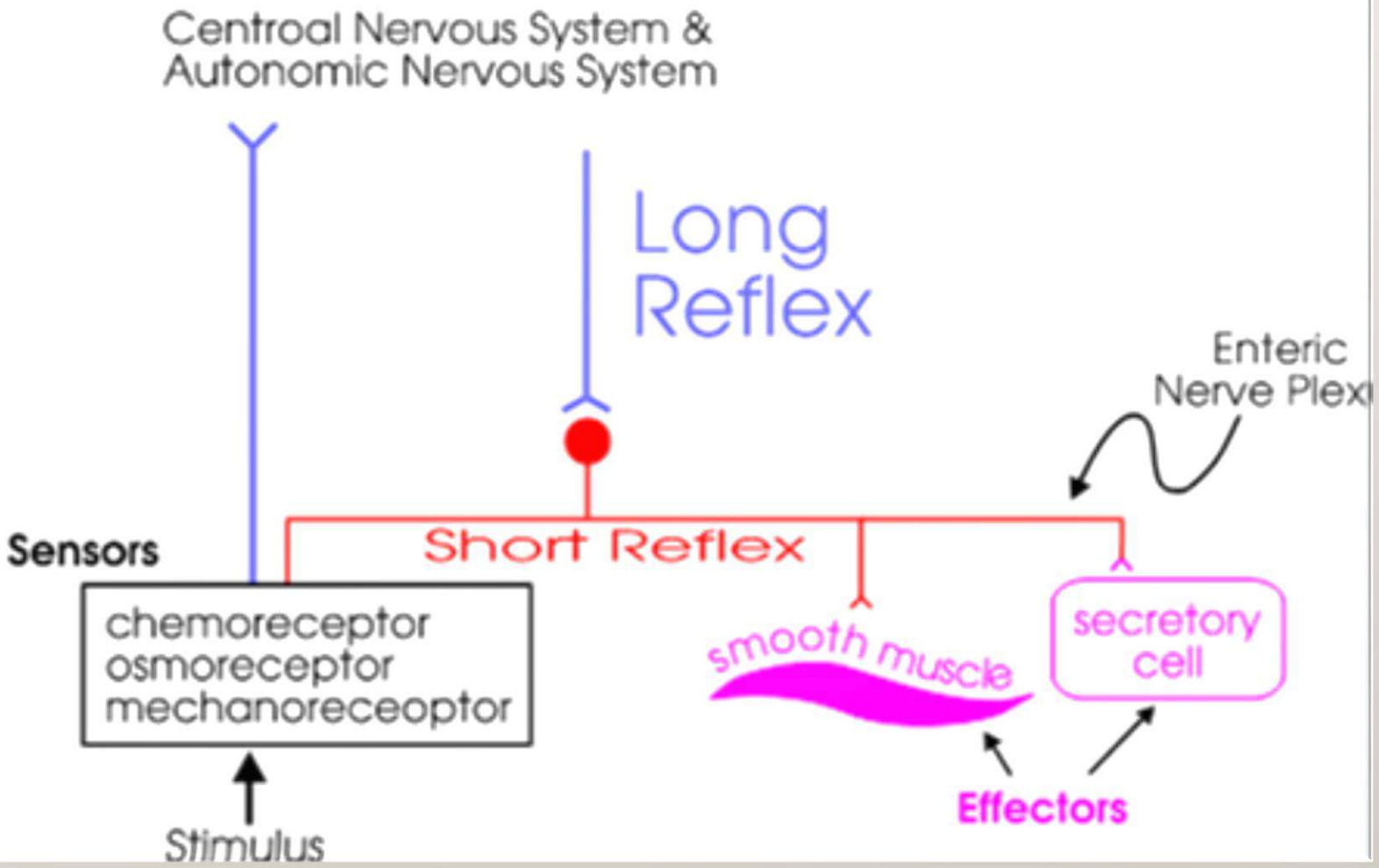
- **Make digestive system respond to the external stimuli.**

e.g. Smell or sight of food ⇨ stimulation of salivary, gastric, pancreatic & liver secretion

Gastrointestinal Reflexes

- ***Reflexes that are Integrated Entirely within the gut wall ENS*** **These include reflexes that control much gastrointestinal *Secretion, Peristalsis, Mixing contractions, Local inhibitory effects.***
- ***Reflexes from the gut to the prevertebral sympathetic ganglia and then back to the GIT.*** **Signals from the stomach to cause evacuation of the colon *(Gastrocolic reflex).***
- **Signals from the colon and small intestine to *Inhibit stomach motility and secretion (Enterogastric reflexes).***
- **Reflexes from the colon to inhibit *emptying of ileal contents into the colon* (colonoileal reflex).**

Reflexes


Centroal Nervous System &
Autonomic Nervous System
Long
Reflex
Enteric
Nerve Plex
Sensors
Short Reflex
chemoreceptor
osmoreceptor
mechanoreceptor
smooth muscle
secretory
cell
Effectors
Stimulus

Continue

- ***Reflexes from the gut to the spinal cord or brain stem and then back to the gastrointestinal tract.*** **These include *especially***
- ***Reflexes from the stomach and duodenum*** **to the brain stem and back to the stomach-by way of the vagus nerves- to control gastric motor and secretory activity.**
- ***Pain reflexes*** **that cause general inhibition of the entire GIT**
- ***Defecation reflexes*** **that travel from the colon and rectum to the spinal cord and back again to produce the powerful colonic, rectal, and abdominal contractions required for defecation (the defecation reflexes).**

Hormonal Control of Gastrointestinal Motility

- ***Polypeptide hormones*** **secreted from** ***Entero-Endocrine*** **cells in the mucosa called** ***APUD*** **cells ⇨ portal vein ⇨ liver ⇨ Systemic circulation ⇨GIT tract ⇨ gut motility &secretion.**
- **They are secreted in response to stimulation by:**
  - ***a- External autonomic nerves.***
  - ***b- Enteric nervous system.***
  - ***c- Changes in luminal contents of GIT.***
- **They are secreted in blood and circulate in it, and reach GIT to produce their effects on GIT motility and secretion (↑ or ↓).**
- **They all have** ***Trophic*** **effects:**
  - **Gastrin H. → growth of gastric mucosa.**
  - **CCK H. → growth of pancreas.**

Classification of Gut Hormones

Gastrin Family	Secretin Family	Other GIT Peptides
Gastrin Cholecystokinin (CCK)	Secretin Glucagon GIP VIP Glicentin	Motilin Somatostatin Substance P Serotonin ,guanilin, substance-P, neurotensin, GRP

- ***Gastrin*** **is secreted by the *"G"* cells of the *antrum of the stomach* in response to stimuli associated with ingestion of a meal .**

- ***Distention of the stomach .***
- ***Products of protein digestion.***
- ***Gastrin releasing peptide,*** **which is released by the nerves of the gastric mucosa during *vagal stimulation*. The primary actions of gastrin are**

(1) ***Stimulation of gastric acid secretion*** **.**

(2) ***Stimulation of growth of the gastric mucosa.***

Gastrin

- A polypeptide hormone, secreted from ***G cells*** in Antral glands of the stomach.
- It is present in different forms, the commonest of which are G_{14}, G_{17} ***(principal form for gastric secretion)***& G_{34}.

Control of gastrin secretion:

	Stimulators	Inhibitors
Luminal factors •Mechanical •Chemical	Gastric distention Amino acids, peptides , low Hcl	Excess H^+, somatostatin
Nervous factors	Vagal stimulation (the neurotransmitter is GRP)	Sympathetic stimulation
Blood –borne	Calcium, epinephrine	Secretin, GIP, VIP , glucagon & calcitonin

Functions of Gastrin:-

- Increase gastric Hcl & pepsinogen secretion.
- Increase gastric motility.
- Increase motility of the ileum (gastroileal reflex).
- Relaxes ileocecal sphincter.
- Cause mass contractions of the colon which move feces to anus & initiate defecation.
- Trophic to the stomach & intestine.

Cholecystokinin (CCK) **is secreted by *"I"* cells in the *mucosa of the* Duodenum and Jejunum mainly in response to digestive products of *fat, fatty acids, and monoglycerides* in the intestinal contents.**
This hormone strongly contracts the gallbladder, expelling bile into the small intestine.
CCK *Inhibits stomach contraction* moderately.
CCK *Inhibits appetite* to prevent overeating during meals by stimulating sensory afferent nerve fibers in the duodenum, these fibers, in turn, send signals by way of the vagus nerve to inhibit feeding centers in the brain .

Cholecystokinin

It is secreted from:-

- ***I*** **cells in the upper small intestine.**
- **Nerves in the distal ileum.**

It is secreted in response to products of fat & protein digestion.

Function:-

- **Inhibit gastric motility, emptying & secretion.**
- **Stimulate pancreatic *Acinar cell* to secrete juice *Rich in enzymes.***
- **Trophic to exocrine pancreas**
- **Augment action of secretin.**
- **Stimulate GB contraction act as (*Cholagoque*).**
- **Involved in regulation of food intake.**

Secretin **was the first GIT hormone discovered and is secreted by the *"S"* cells in the *Mucosa of the Duodenum* in response to acidic gastric juice emptying into the duodenum from the pylorus of the stomach.**

- **Secretin has a mild effect on motility of the GIT**
- **Promote pancreatic secretion of bicarbonate, which in turn helps to neutralize the acid in the small intestine.**

Secretin

It is a polypeptide hormone secreted from specialized cells called *S cells* in the glands of the duodenum& jejunum.

It is secreted in response to:-

- **Acidic chyme in the duodenum.**
- **Products of protein digestion.**

- **Function:-**
  - **Stimulate secretion of pancreatic juice rich in *Hco_3* from pancreatic *Duct cells.***
  - **Stimulate secretion of Hco_3 from duct cells of the biliary tract which increase bile flow.**
  - **Augment the action of CCK on pancreatic cells.**
  - **Inhibit gastric acid secretion & emptying.**
  - **Has trophic effect on exocrine pancreas.**

Gastric inhibitory peptide (GIP) is secreted by the *mucosa of the upper small intestine(K cells),* is the only GI hormone that is released in response to fat, protein, and carbohydrate.

- **Inhibit gastric motility & secretion.**
- **Stimulation of insulin release: GIP, at blood levels even lower than those needed to inhibit gastric motility, also stimulates insulin secretion and for this reason is also known as *glucose-dependent insulinotropic peptide.***

Thus, oral glucose is more effective than intravenous glucose in causing insulin release and, therefore, glucose utilization.

Motilin **is secreted by the stomach and *upper duodenum* during fasting, and the only known function of this hormone is to *increase gastrointestinal motility*. Motilin is released cyclically and stimulates waves of gastrointestinal motility called *interdigestive myoelectric complexes* that move through the stomach and small intestine every 90 minutes in a fasted person. Motilin secretion is inhibited after ingestion by mechanisms that are not fully understood.**

Paracrines

- Are released from endocrine cells in the GI mucosa.
- Diffuse over short distances to act on target cells located in the GI tract.
- The GI paracrines are *Somatostatin and Histamine*

1. Somatostatin

- **Is secreted by cells throughout the GI tract in response to H+ in the lumen. Its secretion is inhibited by vagal stimulation.**
- **Inhibits the release of all GI hormones.**
- **Inhibits gastric H+ secretion.**

2. Histamine

- **is secreted by *mast cells* of the gastric mucosa.**
- **increases gastric H+ secretion directly and by potentiating the effects of gastrin and vagal stimulation.**

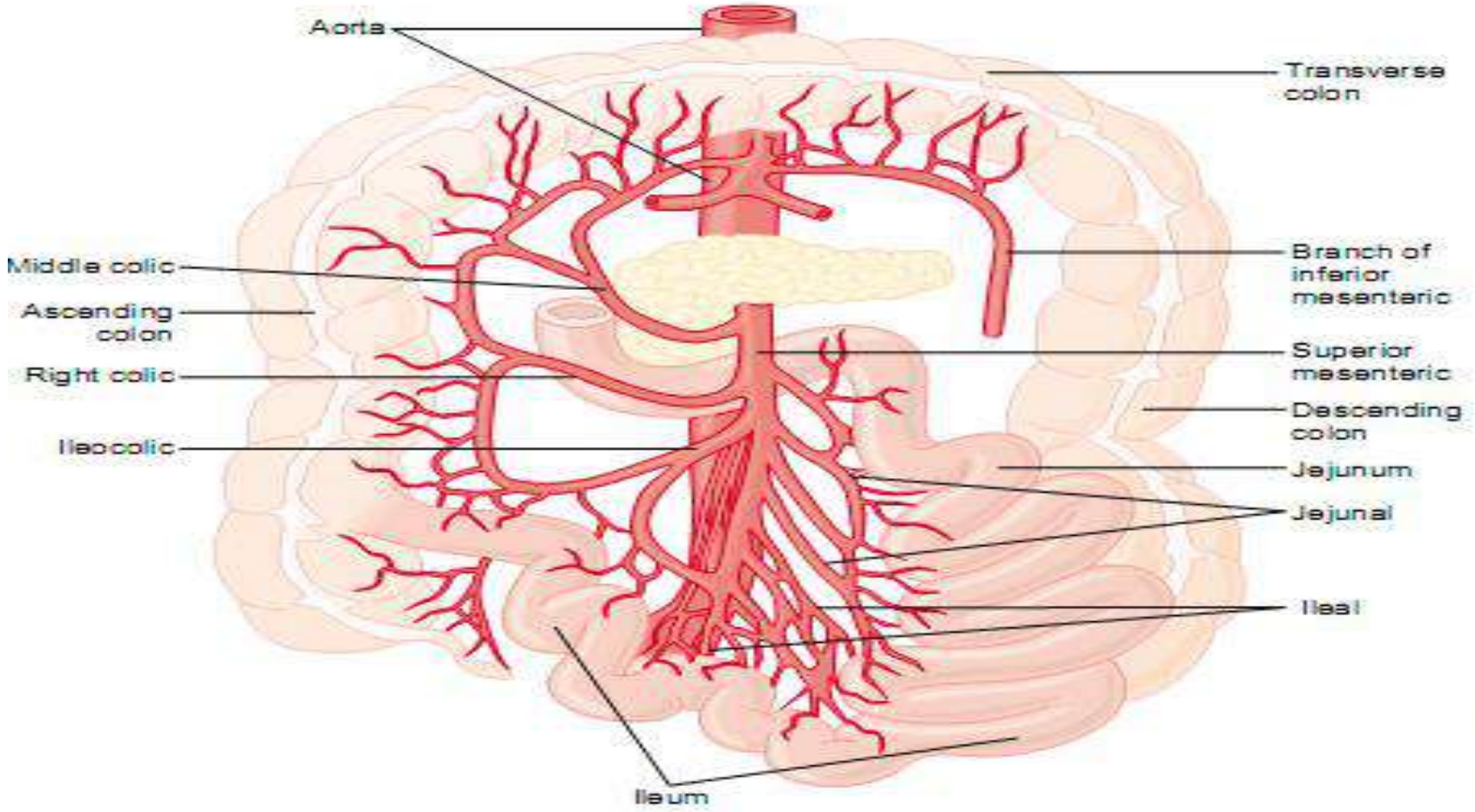
1. VIP

- Contains 28 amino acids.
- Is released from neurons in the mucosa and smooth muscle of the GI tract.
- Produces relaxation of GI smooth muscle, including the lower esophageal sphincter.
- Stimulates pancreatic HCO3 secretion and inhibits gastric H+ secretion. In these actions, it resembles secretin.
- Is secreted by pancreatic islet cell tumors and is presumed to mediate pancreatic cholera.

2. Gastrin-releasing peptide GRP (bombesin)

Is released from vagus nerves that innervate the G cells. Stimulates gastrin release from G cells.

Gastrointestinal Blood Flow "Splanchnic Circulation"



- **On entering the wall of the gut, the arteries branch and send smaller arteries *circling* in both directions around the gut, with the tips of these arteries meeting on the side of the gut wall opposite the mesenteric attachment.**
- **From the circling arteries, still much smaller arteries *penetrate* into the intestinal wall and spread**
- **Along the muscle bundles.**
- **Into the intestinal villi.**
- **Into submucosal vessels beneath the epithelium to serve the secretory and absorptive functions of the gut.**

The Non-fat, Water-soluble nutrients **absorbed from the gut (such as carbohydrates and proteins)**

- **Here, both the reticuloendothelial cells and the principal parenchymal cells of the liver, the *hepatic cells*, absorb and store temporarily from one half to three quarters of the nutrients.**
- ***Almost all of the Fats*** **(except small quantities of short- and medium-chain fatty acids) absorbed from the intestinal tract *are not carried in the portal blood* but instead are absorbed into the intestinal lymphatic's and then conducted to the systemic circulating blood by way of the Thoracic Duct, by passing the liver.**

Effect of Gut Activity and Metabolic Factors on Gastro-intestinal Blood Flow

- **Under normal conditions, the blood flow in each area of the GIT, is directly related to the *level of local activity.***
- **During active absorption of nutrients, blood flow in the *Villi and adjacent regions of the submucosa* is increased as much as Eight Fold.**
- **Blood flow in the *Muscle layers* of the intestinal wall increases with increased motor activity in the gut.**
- **After a meal, the motor activity, secretory activity, and absorptive activity all increase; likewise, the blood flow increases greatly but then decreases back to the resting level over another *2 to 4 hours*.**

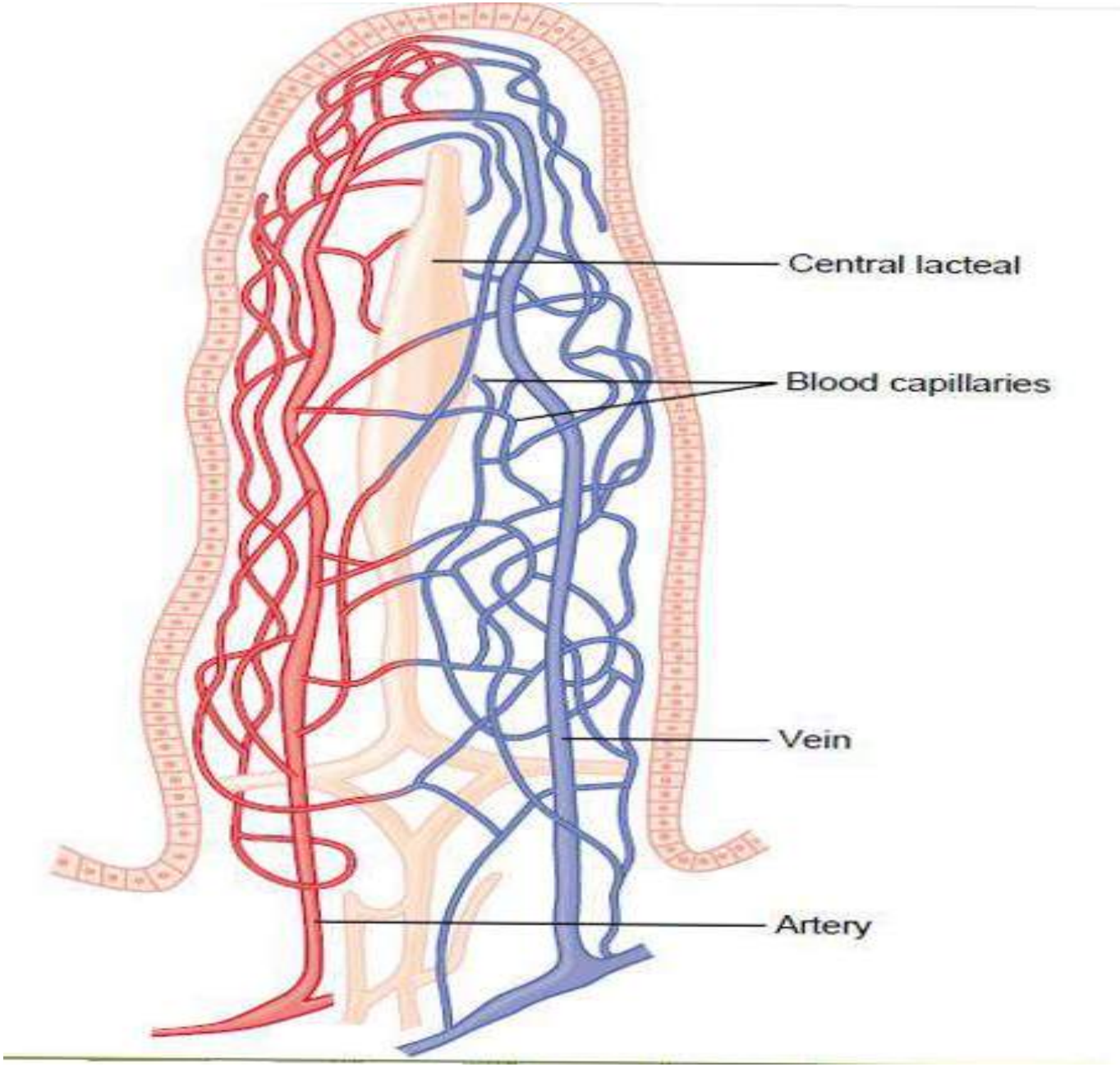
Possible Causes of the Increased Blood Flow During Gastrointestinal Activity.

- ***Several hormones*** **are released from the mucosa of the intestinal tract during the digestive process. including *cholecystokinin, vasoactive intestinal peptide, gastrin, and secretin*.**
- **Some of the gastrointestinal glands also release into the gut wall two *kinins, kallidin and bradykinin*, at the same time that they secrete their secretions into the lumen. These kinins are *Powerful Vasodilators* that are believed to cause much of the increased mucosal vasodilation that occurs along with secretion.**

- **Decreased Oxygen Concentration in the gut wall can increase intestinal blood flow at least 50 to 100 per cent; The decrease in oxygen can also lead to as much as a fourfold increase of *adenosine*, a well known vasodilator that could be responsible for much of the increased flow.**

"Countercurrent" Blood Flow in the Villi.

- **The arterial flow into the villus and the venous flow out of the villus are in directions opposite to each other, and that the vessels lie in close apposition to each other.**
- **Because of this vascular arrangement, much of the blood oxygen diffuses out of the arterioles directly into the adjacent venules without ever being carried in the blood to the tips of the villi.**
- **As much as *80 %* of the oxygen may take this short-circuit route and therefore not be available for local metabolic functions of the villi.**


Central lacteal
Blood capillaries
Vein
Artery

- **In *Circulatory Shock*, the oxygen deficit in the tips of the villi can become so bad that the villus tip or even the whole villus suffers *Ischemic Death* and can disintegrate.**

- **Therefore, for this reason and others, in many gastrointestinal diseases the villi become seriously *Blunted,* leading to greatly diminished intestinal absorptive capacity.**

Nervous Control of Gastrointestinal Blood Flow

- ***Parasympathetic Stimulation*** **of the nerves going to the *stomach* and *lower colon* increases local blood flow at the same time that it increases glandular secretion.**
- **This increased flow probably results *secondary from the increased glandular activity and not as a direct effect of the nervous stimulation.***
- **Sympathetic stimulation, by contrast, has a *Direct effect* on essentially all the GIT to cause intense vasoconstriction of the arterioles with greatly decreased blood flow.**

Autoregulatory escape

- **After a few minutes of vasoconstriction, the flow often returns almost to normal.**

- **That is, the local metabolic vasodilator mechanisms that are elicited by ischemia become prepotent over the sympathetic vasoconstriction and, therefore, redilate the arterioles, thus causing return of necessary nutrient blood flow to the GI glands and muscle.**

Importance of Nervous Depression of GIT Blood Flow When Other Parts of the Body Need Extra Blood Flow.

A major value of Sympathetic Vasoconstriction in the gut is that:

- **1-It allows shut-off of GIT and other splanchnic blood flow for short periods of time *During Heavy Exercise*, when increased flow is needed by the skeletal muscle and heart.**
- **2-Also, in *Circulatory Shock*, when all the body's vital tissues are in danger of cellular death for lack of blood flow—especially the *Brain and the Heart*—sympathetic stimulation can decrease splanchnic blood flow to very little for many hours.**

- **Sympathetic stimulation also causes *Strong vasoconstriction of the large-volume intestinal and mesenteric veins.* This decreases the volume of these veins, thereby displacing large amounts of blood into other parts of the circulation.**

- **In hemorrhagic shock or other states of low blood volume, this mechanism can provide as much as 200 to 400 milliliters of extra blood to sustain the general circulation.**

PROPULSION AND MIXING MOVEMENT OF GIT

1-Ingestion of Food

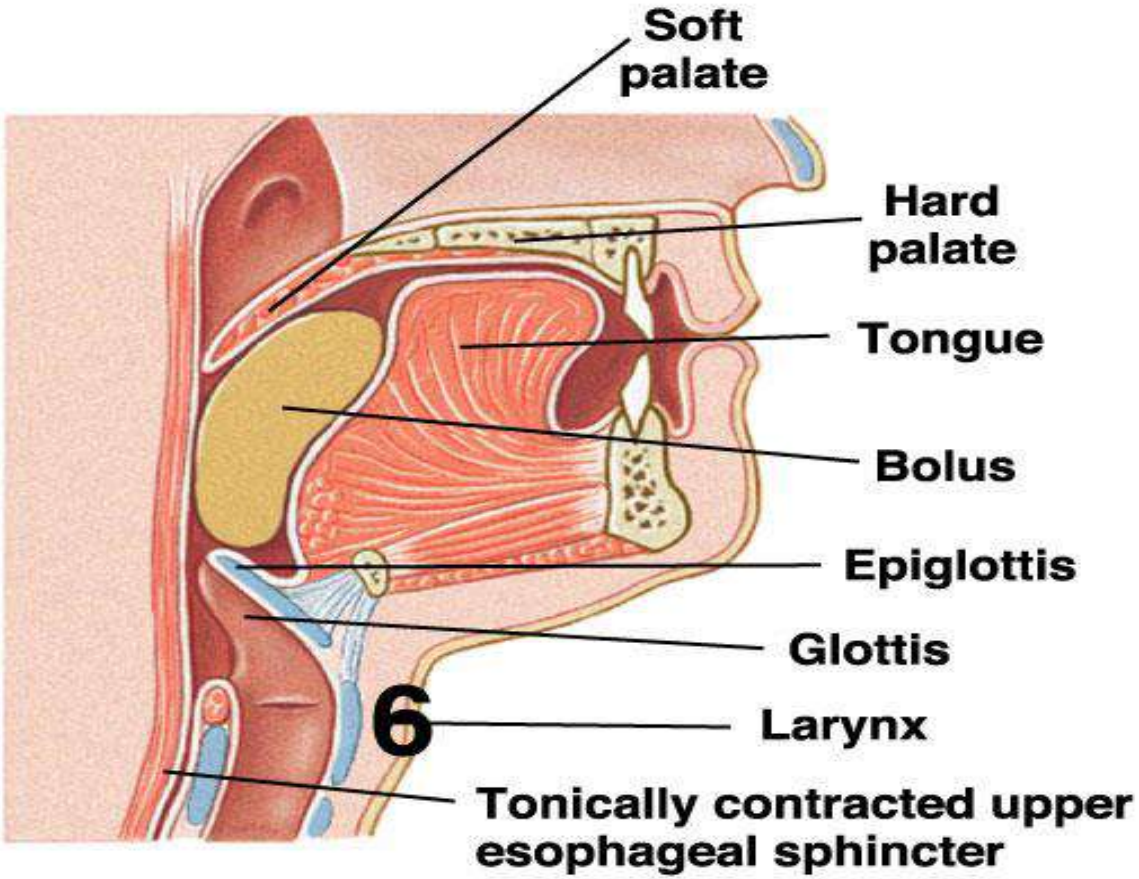
- **Mastication (Chewing) :*chewing reflex***
- ***Swallowing (Deglutition) :***
- ***Buccal Stage (Voluntary Stage)*****which initiates the swallowing process , as tongue pushes the bolus of food to pharynx.**
- ***Pharyngeal Stage*** **which is *Involuntary* and constitutes passage of food through the pharynx into the esophagus.**
- ***Esophageal Stage*** **another *Involuntary* phase that transports food from the pharynx to the stomach.**

Pharyngeal Stage of Swallowing

- **The trachea is closed, the esophagus is opened, and a fast peristaltic wave initiated by the nervous system of the pharynx forces the bolus of food into the upper esophagus, the entire process occurring in less than 2 Seconds.**
- ***Afferent nerves*: the sensory portions of the *Trigeminal and Glossopharyngeal* nerves.**
- ***Reflex centre :* The *deglutition* or *swallowing center* in the medulla and lower pons.**
- ***Efferent nerves :* To pharynx and upper esophagus by the *5th, 9th, 10th, and 12th* cranial nerves and even a few of the superior cervical nerves.**

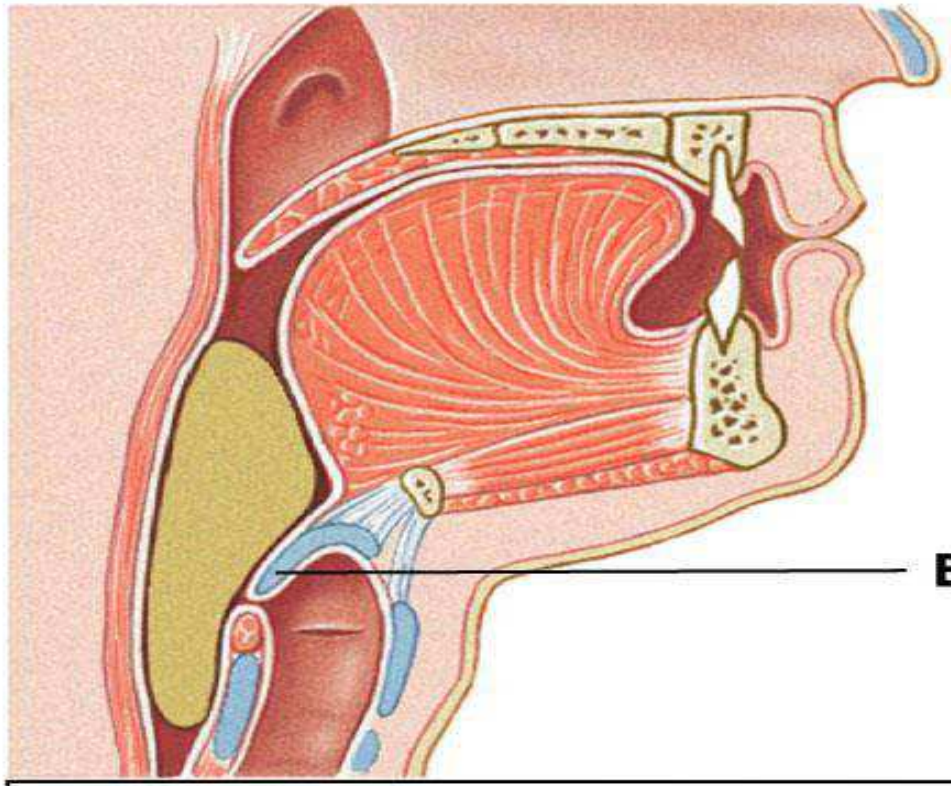
Steps of swallowing

Step 1



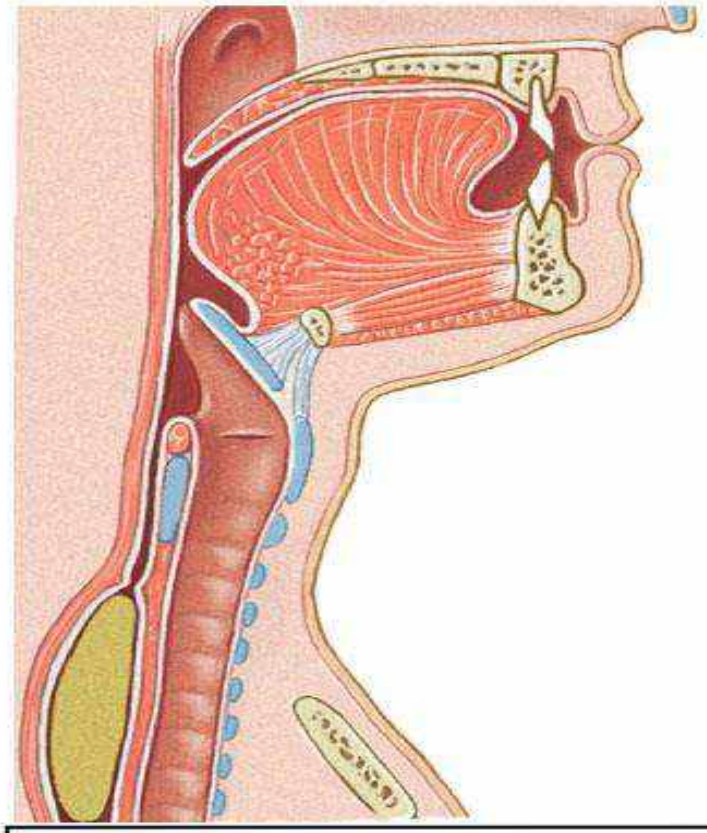
1. Tongue pushes bolus against soft palate and back of mouth, triggering swallowing reflex.

Step 2



2. Upper esophageal sphincter relaxes while epiglottis closes to keep swallowed material out of the airways.

Step 3



3. Food moves downward into the esophagus, propelled by peristaltic waves and aided by gravity.

- **Effect of the Pharyngeal Stage of Swallowing on Respiration.**

- **The entire pharyngeal stage of swallowing usually occurs in *less than 6 seconds,* thereby interrupting respiration for only a fraction of a usual respiratory cycle.**

- **The Swallowing Center specifically inhibits the Respiratory Center of the medulla during this time.**

- ***Esophageal Stage of Swallowing***
- ***Primary peristalsis :*** **is simply continuation of the peristaltic wave that begins in the pharynx and spreads into the esophagus during the pharyngeal stage of swallowing.**
- **This wave passes all the way from the pharynx to the stomach in about 8 to 10 seconds(upright position 5 to 8 seconds).**
- ***Secondary peristaltic waves*** **result from *Distention of the esophagus*** **itself by the retained food , causing stimulation of local axon reflexes**

(Myenteric plexsus) **these waves continue until all the food has emptied into the stomach.**

Receptive Relaxation of the Stomach

- **A wave of relaxation, transmitted through Myenteric inhibitory neurons, precedes the peristalsis.**
- **The entire stomach and, to a lesser extent, even the duodenum become relaxed as this wave reaches the lower end of the esophagus .**
- **Function of the Lower Esophageal Sphincter (Gastro esophageal Sphincter)**
- **This sphincter normally remains tonically constricted with an intraluminal pressure at this point in the esophagus of about 20-*30 mm Hg*, in contrast to the mid portion of the esophagus, which normally remains relaxed.**
- **When a peristaltic swallowing wave passes down the esophagus, there is *"receptive relaxation"* of the LES ahead of the peristaltic wave, which allows easy propulsion of the swallowed food into the stomach. Rarely, the sphincter does not relax satisfactorily, resulting in a condition called *Achalasia.***

stages of swallowing

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2-Motor Functions of the Stomach

Motor functions of the stomach are :

- ***Storage of large quantities*** **of food until the food can be processed in the stomach, duodenum, and lower intestinal tract .**
- ***Mixing of this food with gastric secretions*** **until it forms a semi fluid mixture called *Chyme.***
- ***Slow emptying of the chyme*** **from the stomach into the small intestine at a rate suitable for proper digestion and absorption by the small intestine.**

- ***Secretory Glands :*** **produce digestive enzymes present from Mouth to Terminal ileum.**

- ***Mucus Glands:*** **lubricants from mouth to anus.**

- *Reservoir part*

Fundus + 1/3 corpus

(tonic contraction)

- *Antral pump*

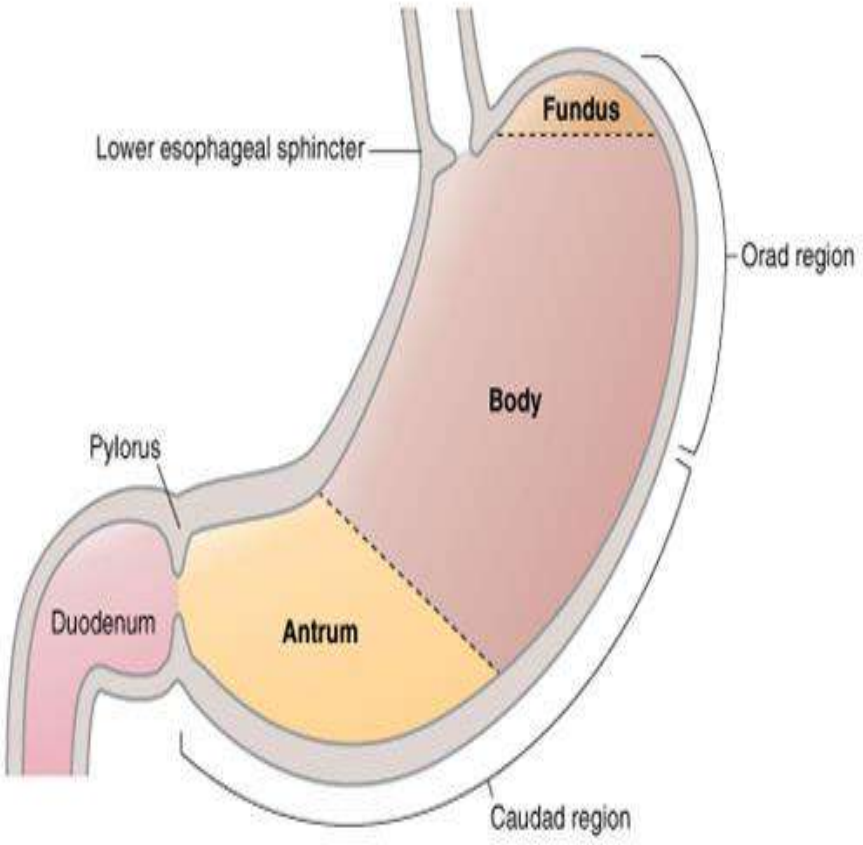
2/3 corpus + antrum & pylorus
(contraction)

- **Physiologically, it is more appropriately divided into**
- *The "Orad" Portion*:

comprising about the first *Two thirds of the body*, **and is thin wall .**

- **The "***Caudad" Portion:* **comprising the remainder**

of the *Body plus the Antrum* **, and is thick wall.**



Relaxation in gastric reservoir

- ***Receptive Relaxation***

  - Triggered by swallowing reflex.

- ***Adaptive Relaxation***

  - Triggered by stretch receptors (vago-vagal reflex) 0.8 to 1.5 liters.

  - lost in vagotomy .

  ⇒ threshold of fullness and pain.

- ***Feedback Relaxation***

  - Triggered by chyme in small intestine.

Storage Function of the Stomach

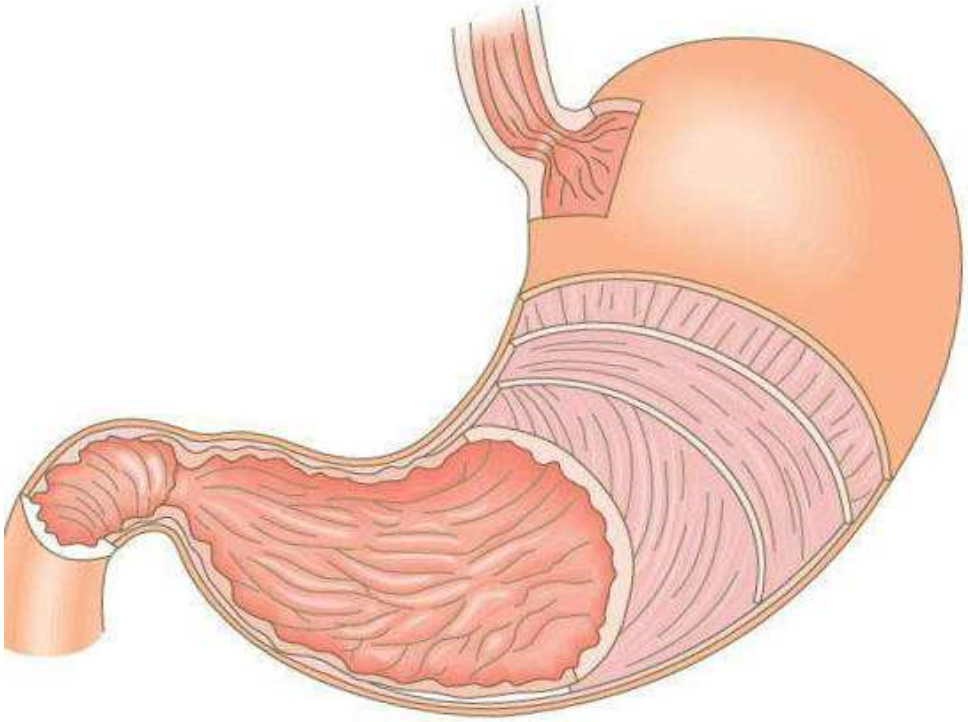
- **As food enters the stomach, it forms concentric circles in the orad portion of the stomach, the newest food lying closest to the esophageal opening and the oldest lying nearest the outer wall of the stomach.**

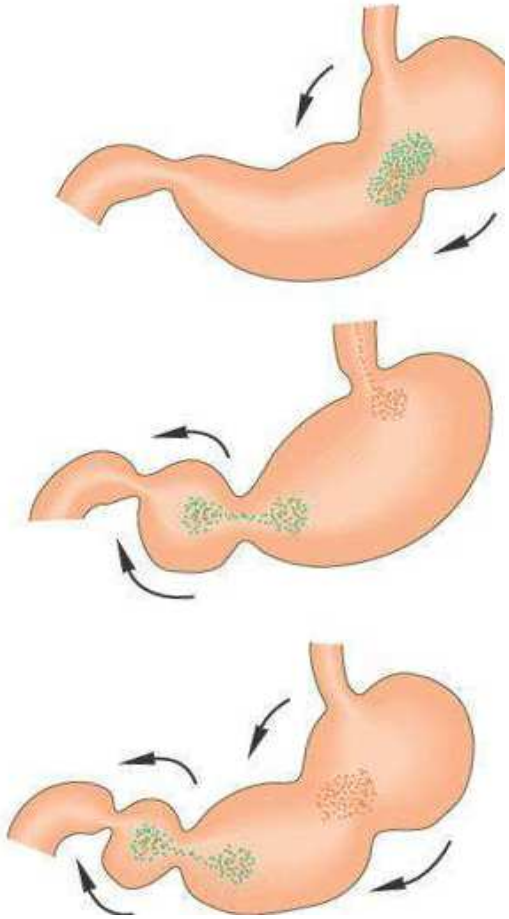
- **Normally, when food stretches the stomach, a *"VagoVagal Reflex"* reduces the tone in the muscular wall of the body of the stomach so that the wall bulges progressively outward, accommodating greater and greater quantities of food up to a limit in the completely relaxed stomach of *0.8 to 1.5 liters.***
- **The pressure in the stomach remains low until this limit is approached.**

Mixing and Propulsion of Food in the Stomach

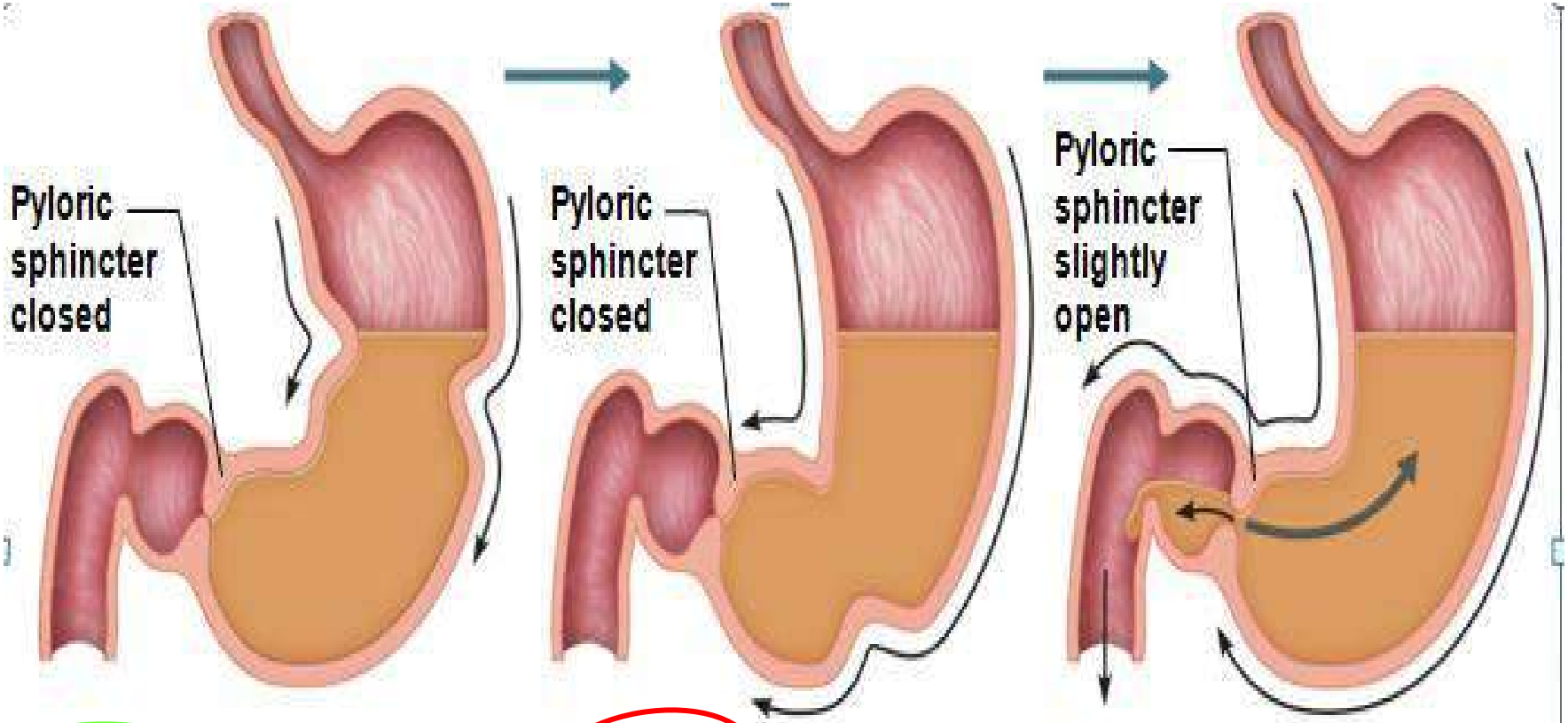
- ***The Basic Electrical Rhythm of the Stomach Wall***
- **As long as food is in the stomach, weak peristaltic *Constrictor Waves* , called *Mixing Waves,* begin in the mid- to upper portions of the stomach wall and move toward the antrum about once every 15 to 20 seconds.**
- **These waves are initiated by the gut wall *Basic electrical rhythm* consisting of electrical "slow waves" that occur spontaneously in the stomach wall.**

- **As the constrictor waves progress from the body of the stomach into the antrum, they become more intense, some becoming extremely intense and providing powerful *peristaltic action potential*–driven constrictor rings that force the antral contents under higher and higher pressure toward the pylorus.**





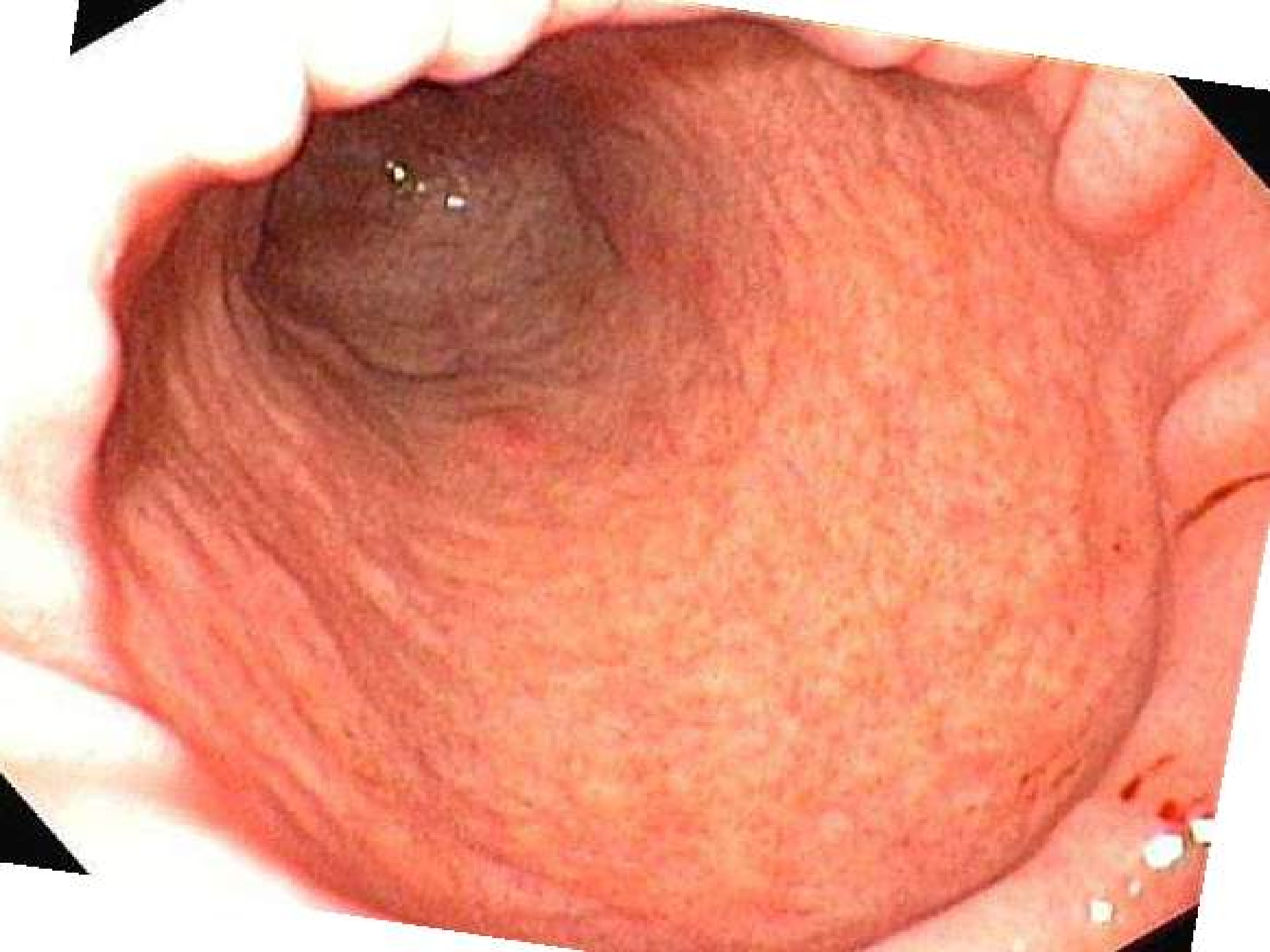
- *These constrictor rings also play an important role in mixing the stomach contents in the following way:*
- **As *peristaltic wave* passes down the Antral wall toward the pylorus, it digs deeply into the food contents in the antrum.**
- **Yet the opening of the pylorus is still small enough that only a few milliliters or less of chyme is expelled into the D1 with each peristaltic wave.**
- **As each peristaltic wave reach the pylorus, the pyloric muscle contracts, which impedes emptying through the pylorus.**
- **So, most of the Antral contents are squeezed upstream through the peristaltic ring toward the body of the stomach, not through the pylorus.**
- *The moving peristaltic constrictive ring, combined with this upstream squeezing action, called "Retropulsion,"* **is an very important *Mixing mechanism* in the stomach.**

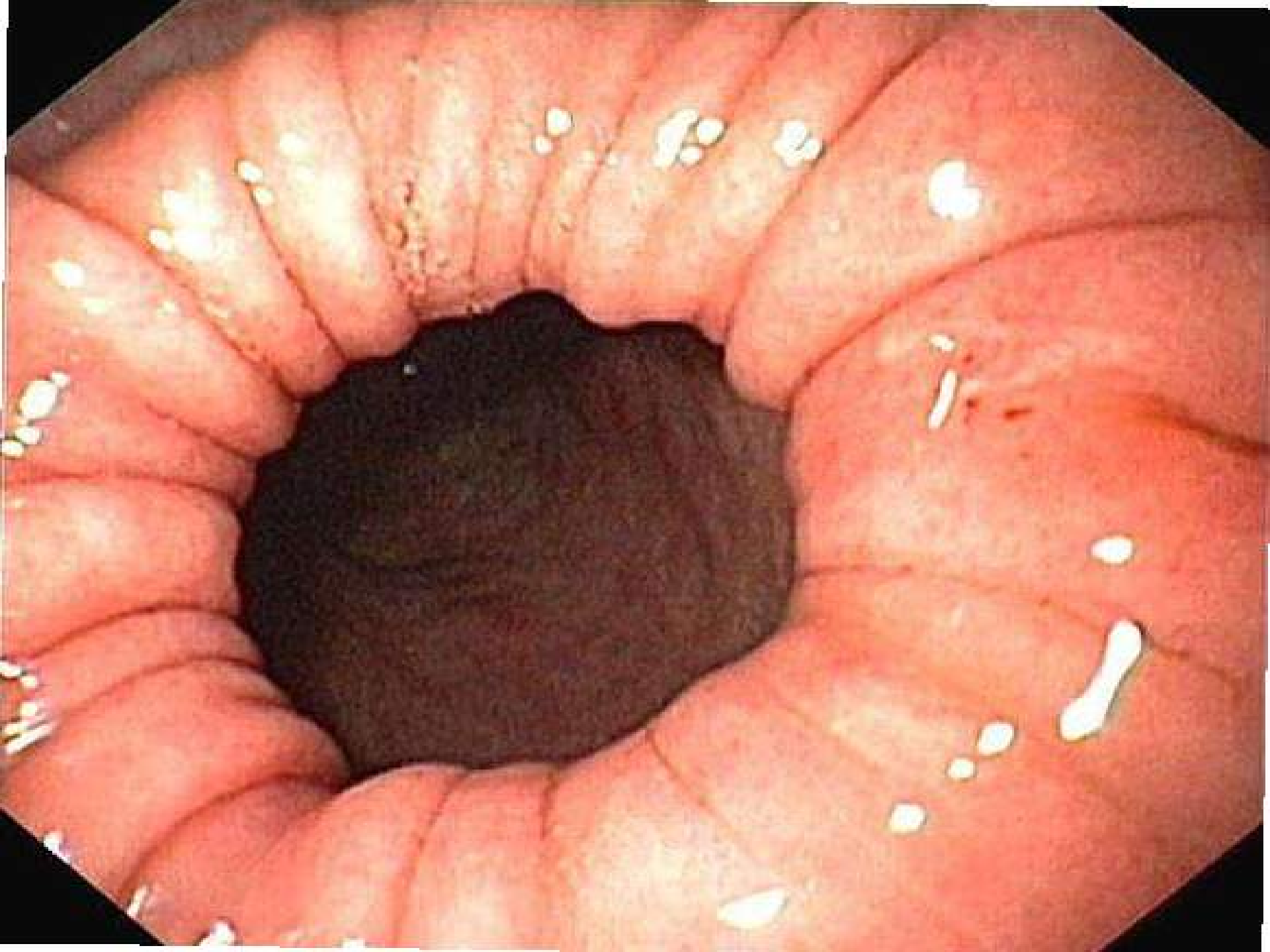


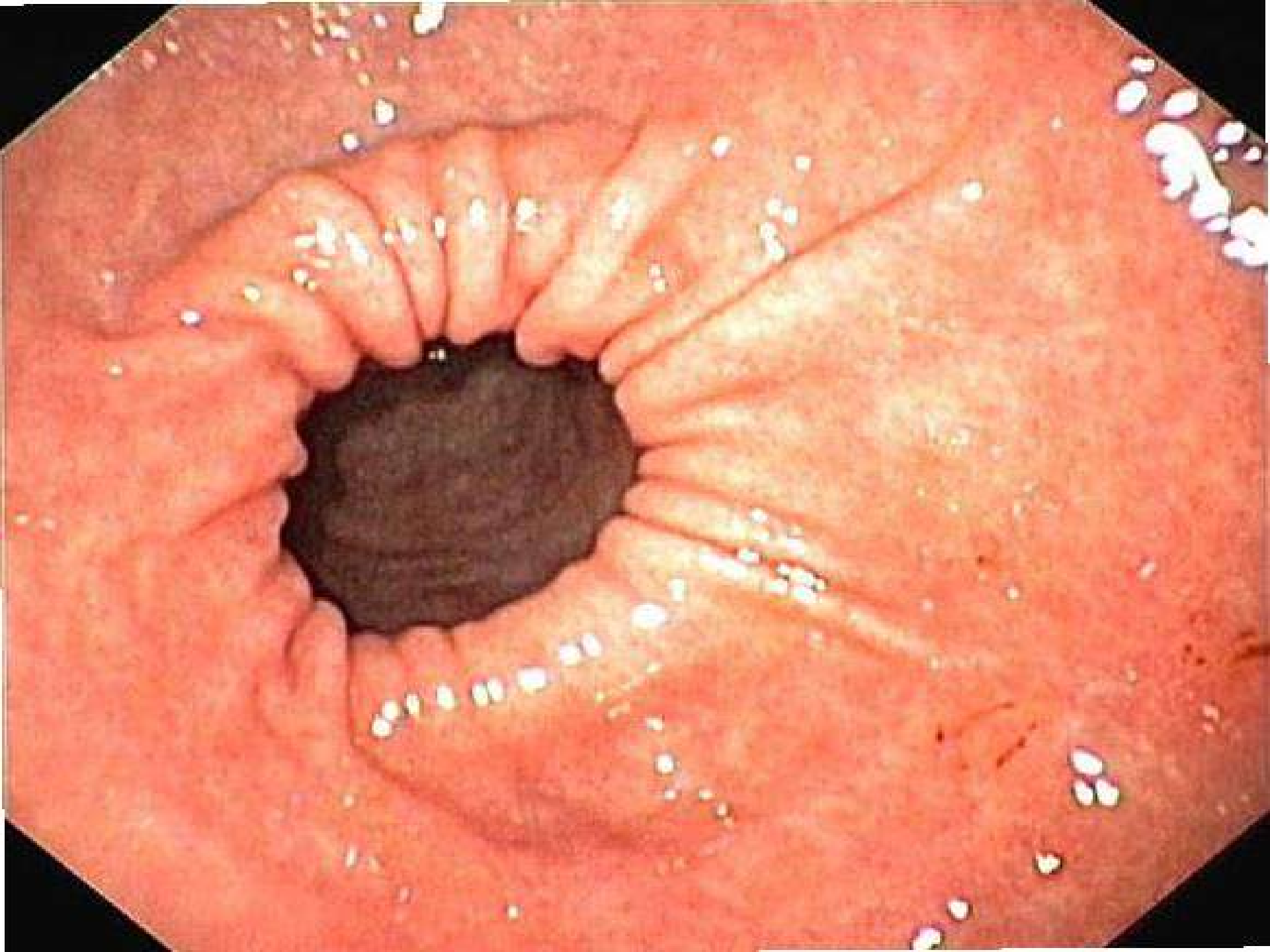
(1) Propulsion: Peristaltic waves move from the fundus to the pylorus.

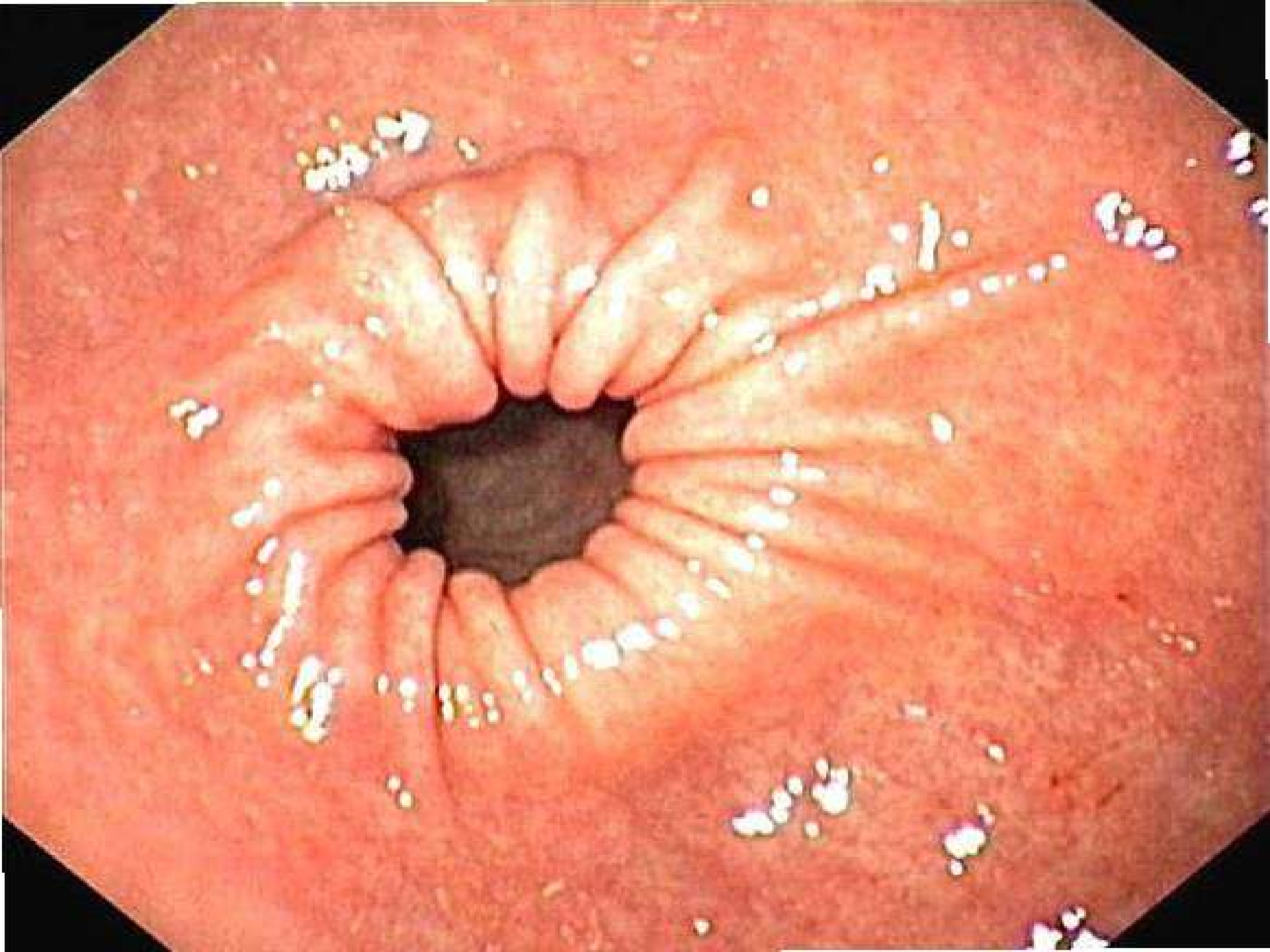
(2) Grinding: The most vigorous peristalsis and mixing action occur close to the pylorus.

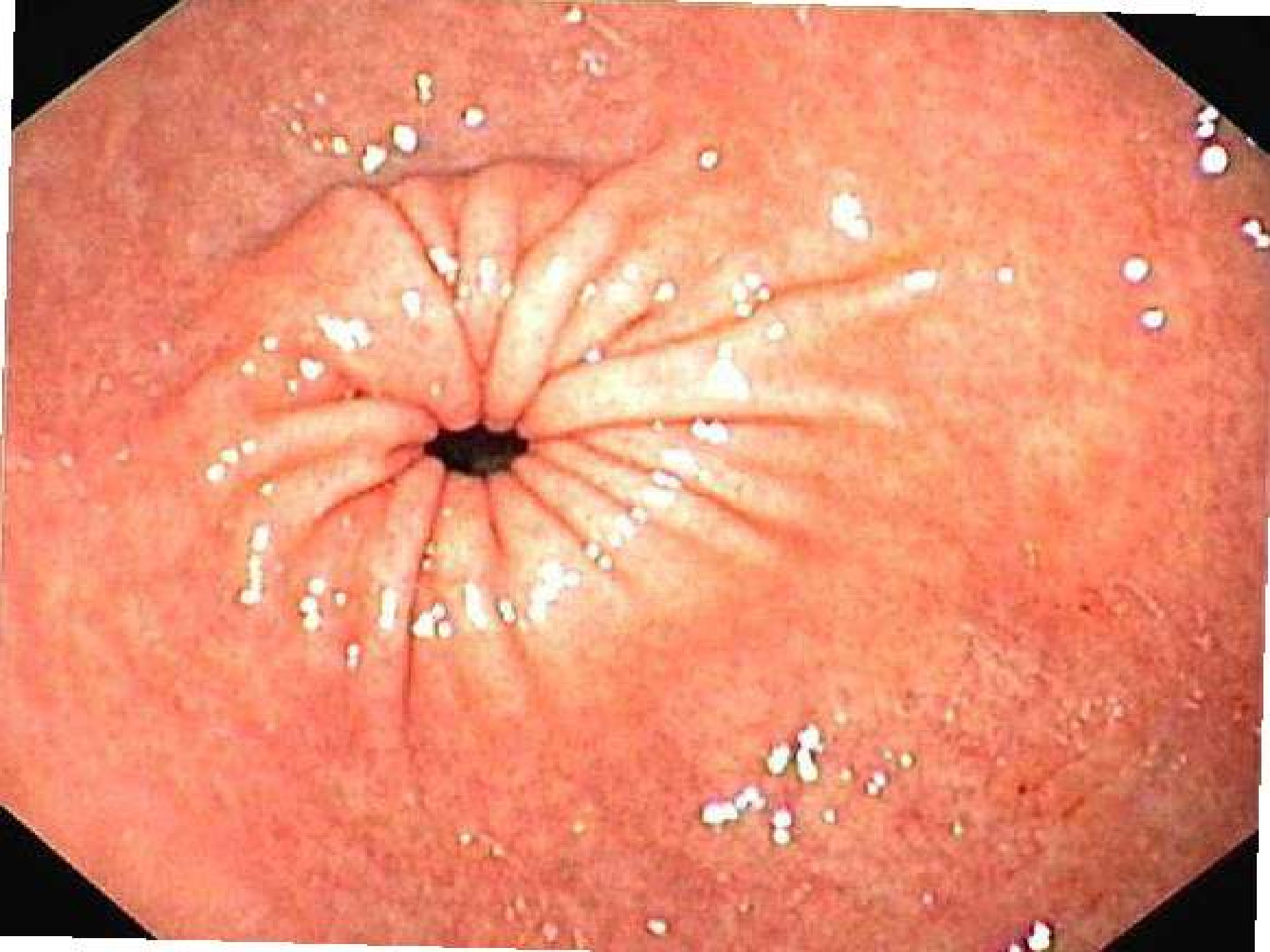
(3) Retropulsion: The pyloric end of the stomach pumps small amounts of chyme into the duodenum, while simultaneously forcing most of its contents backward











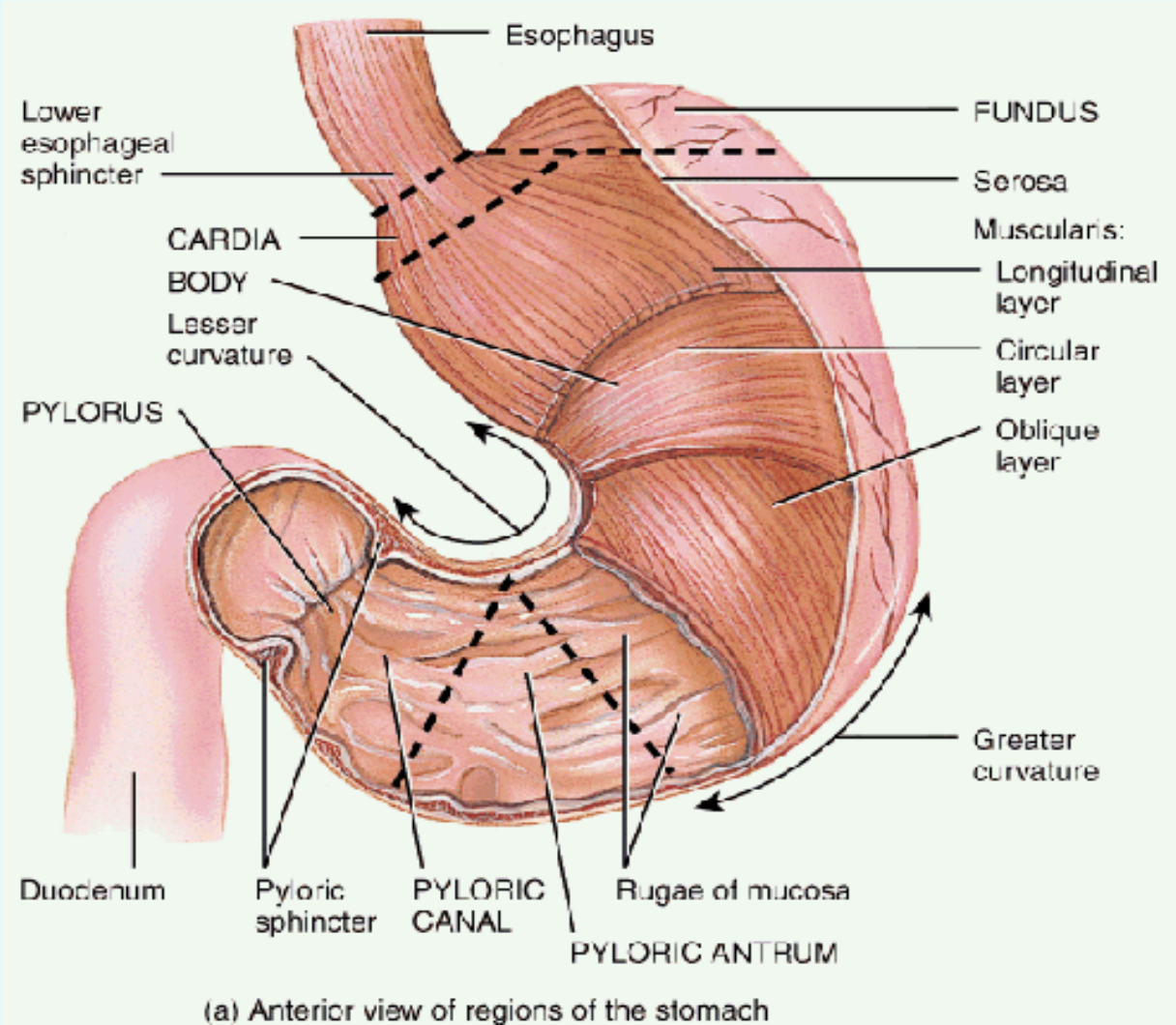
- ***Chyme:*** **After food in the stomach has become thoroughly mixed with the stomach secretions, the resulting mixture that passes down the gut is called Chyme.**
- **The degree of fluidity of the chyme depends on the relative amounts of food, water, and stomach secretions and on the degree of digestion that has occurred.**
- **The appearance of chyme is that of a *Murky Semifluid or Paste.***

Stomach Emptying is due to

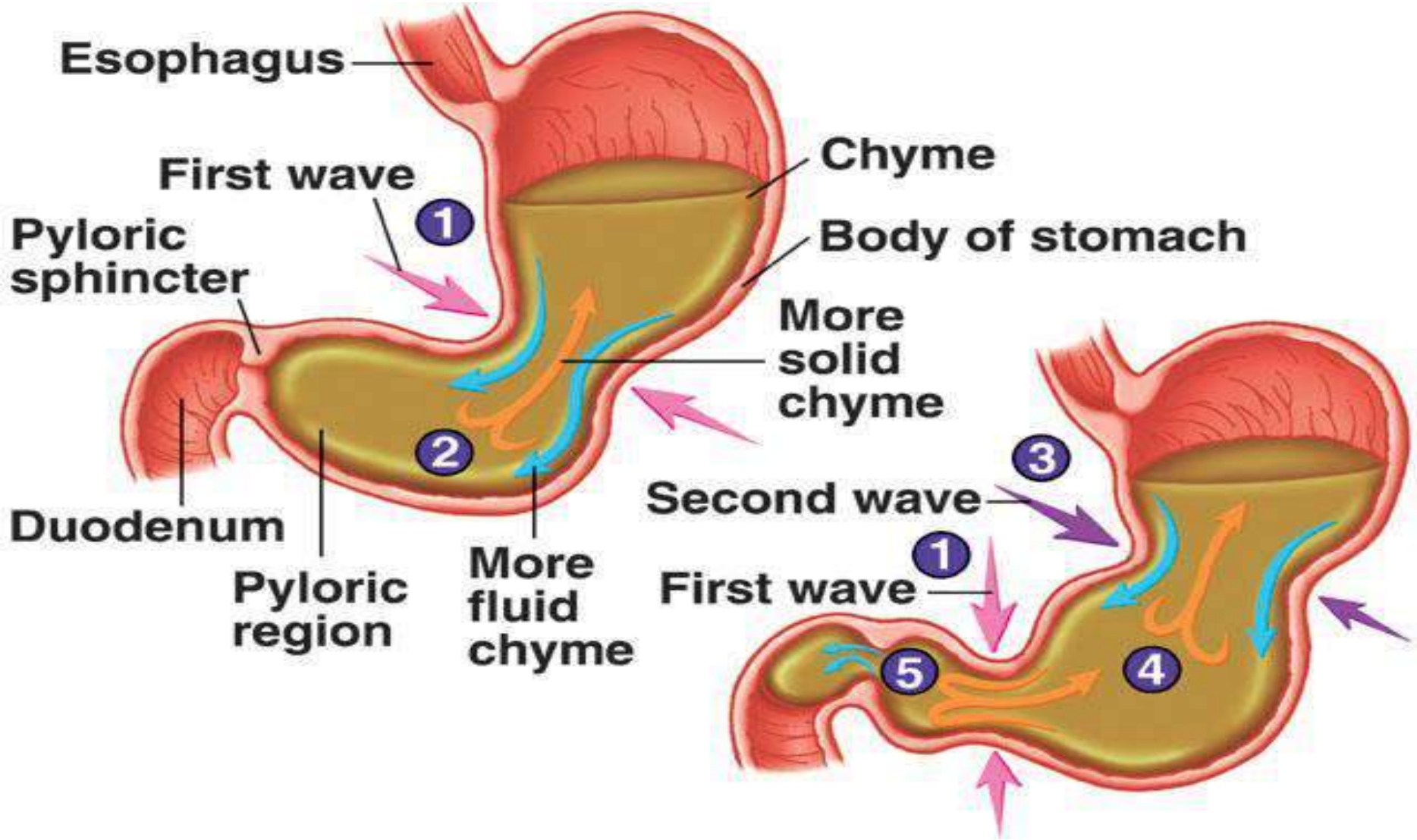
- **Intense Antral Peristaltic Contractions *"Pyloric Pump."***
- **Role of the Pylorus in Controlling Stomach Emptying**
  - **Despite normal tonic contraction of the pyloric sphincter, the pylorus usually is open enough for water and other fluids to empty from the stomach into the duodenum with ease.**
  - **Conversely, the constriction usually prevents passage of food particles until they have become mixed in the chyme to almost fluid consistency.**

EMPTYING OF THE STOMACH (PYLORIC PUMP)

Peristalsis + relaxation of pyloric sphincter



(a) Anterior view of regions of the stomach


Esophagus
First wave
1
Pyloric sphincter
Chyme
Body of stomach
More solid chyme
2
Duodenum
Pyloric region
More fluid chyme
3
Second wave
1
First wave
5
4

Regulation of Stomach Emptying

Gastric Factors That Promote ↑ Emptying:

- **Effect of *Gastric Food Volume* on Rate of Emptying.**

(Stretching of stomach produce local axon reflex which stimulate contraction of wall and inhibition of pyloric sphincter)

- **Effect of the *Hormone Gastrin* ↑ Stomach Emptying by increase contractility of antrum muscles.**

Powerful Duodenal Factors That *Inhibit* Stomach Emptying

A-*Inhibitory* Effect of *Entero Gastric Nervous Reflexes* from the Duodenum

- **Multiple nervous reflexes are initiated from the duodenal wall:**
  - **Directly from the D1 to the stomach through *ENS* in the gut wall.**
  - **Through *Extrinsic Nerves* that go to the prevertebral sympathetic ganglia and then back through *inhibitory sympathetic nerve .***

All these parallel reflexes have two effects on stomach emptying:

- **First, they strongly *Inhibit the "pyloric pump" propulsive contractions.***
- ***Second, they increase the tone of the pyloric sphincter.***

Factors that initiate Entero Gastric *Inhibitory Reflexes* include the following:

- **The degree of *Distention* of the duodenum .**
- **The presence of any degree of *Irritation* of the duodenal mucosa.**
- **The degree of *Acidity* of the duodenal chyme.**
- **The degree of *Osmolality* of the chyme.**
- **The presence of certain breakdown products in the chyme, especially breakdown products of *Proteins and, perhaps to a lesser extent, of fats.***

***These factors become strongly activated within as little as 30 seconds*.**

B-Hormonal Feedback from the Duodenum Inhibits Gastric Emptying-Role of Fats and the Hormone *Cholecystokinin.*

C-Other possible inhibitors of stomach emptying are the hormones *Secretin and Gastric inhibitory peptide (GIP).*

- **These feedback inhibitory mechanisms work together to slow the rate of emptying when**
- **(1) *Too much chyme* is already in the small intestine or**
- **(2) the chyme is *Excessively Acidic*, contains too much unprocessed protein or fat, is hypotonic or hypertonic, or is irritating.**

Stomach emptying

Gastric factors

VE + + + + +

1- volume of gastric contents

2- gastrin hormone.

Duodenal factors

Ve - - - - -

1 Entero gastric reflex

2 hormones :

CCK ,GIP, Secretin somatostatin

Others

1 chemicals

2 autonomic

Sympathetic and parasymp.

3-emotions

4-consistency

&type of food

Hunger contraction

In empty stomach

Strong peristalsis in the body
after 12-24 h of last meal
Reach its max. 3-4 days
Due to hypoglycemia

If very Strong Fuse Tetanic contraction

“Hunger pain”

3-Movements of the Small Intestine

- ***Mixing Contractions (Segmentation Contractions)***

- **It is the slow waves in the smooth muscle itself that cause the segmentation contraction, (Myogenic) these contractions are not effective without background excitation mainly from the Myenteric nerve plexus.**

- ***Propulsive (Peristalsis)Movements(progression and spread out of chyme)***

0.5 to 2.0 cm/min faster in the proximal intestine and slower in the terminal intestine. (1 cm /min).

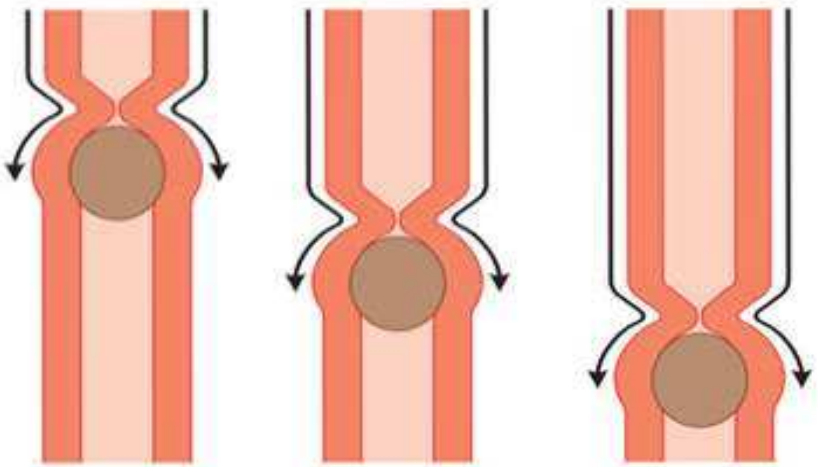
Food need 3-5 h transient time in small bowel

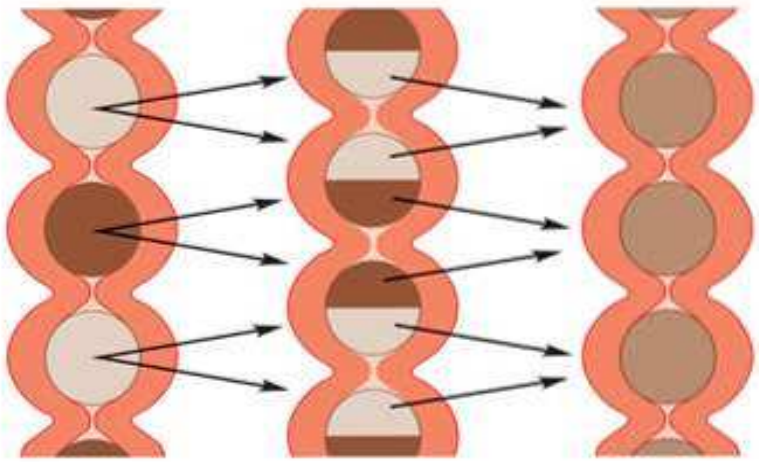
- **Control of Peristalsis by Nervous and Hormonal Signals**

Control of Peristalsis by Nervous and Hormonal Signals

- Peristaltic activity is ↑ after meal.
  Stretch of small bowel by chyme ↑ peristalsis.
- Gastro-enteric reflex ↑ Peristaltic activity in SB.
- Hormones gastrin , Motilin ,CCK ,Insulin ↑ Peristalsis
- Secretin and glucagon ↓ peristalsis.

site	Frequency of BER
Stomach	3/min
Duodenum	12/min
Distal ileum	8/min
Cecum	9/min
sigmoid	3 /min

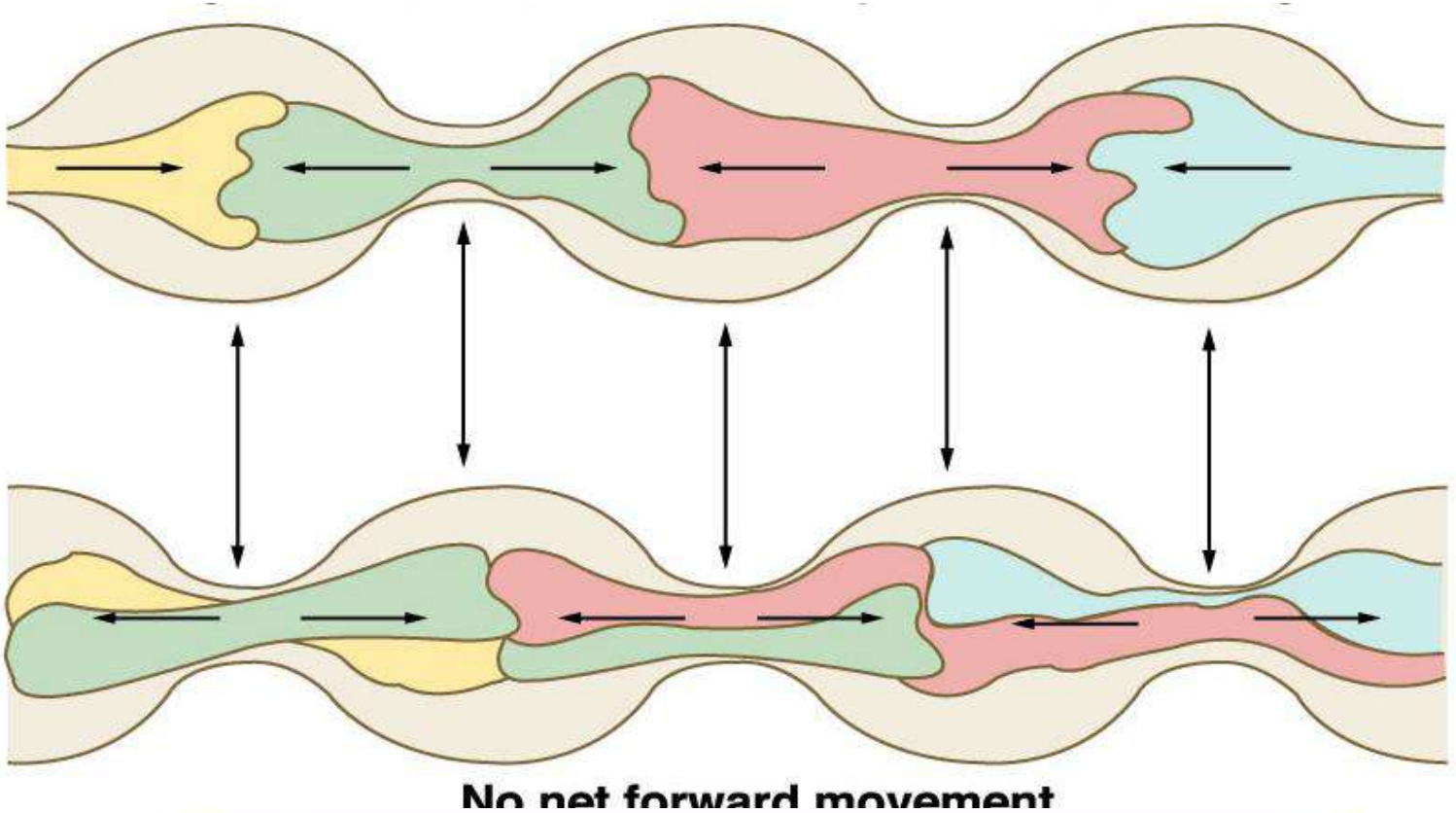


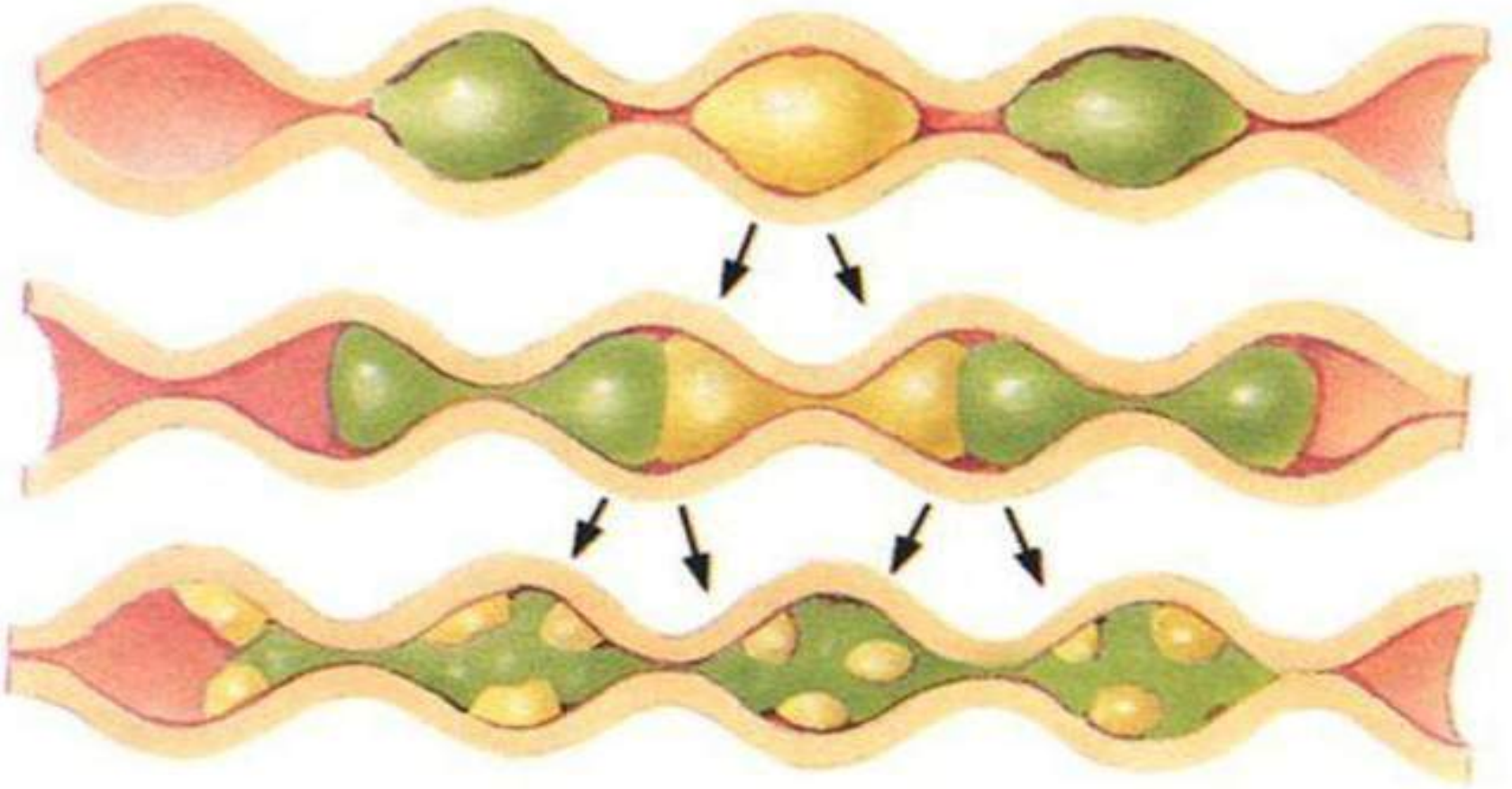


Peristalsis: Adjacent segments of alimentary tract organs alternately contract and relax, which moves food along the tract distally.

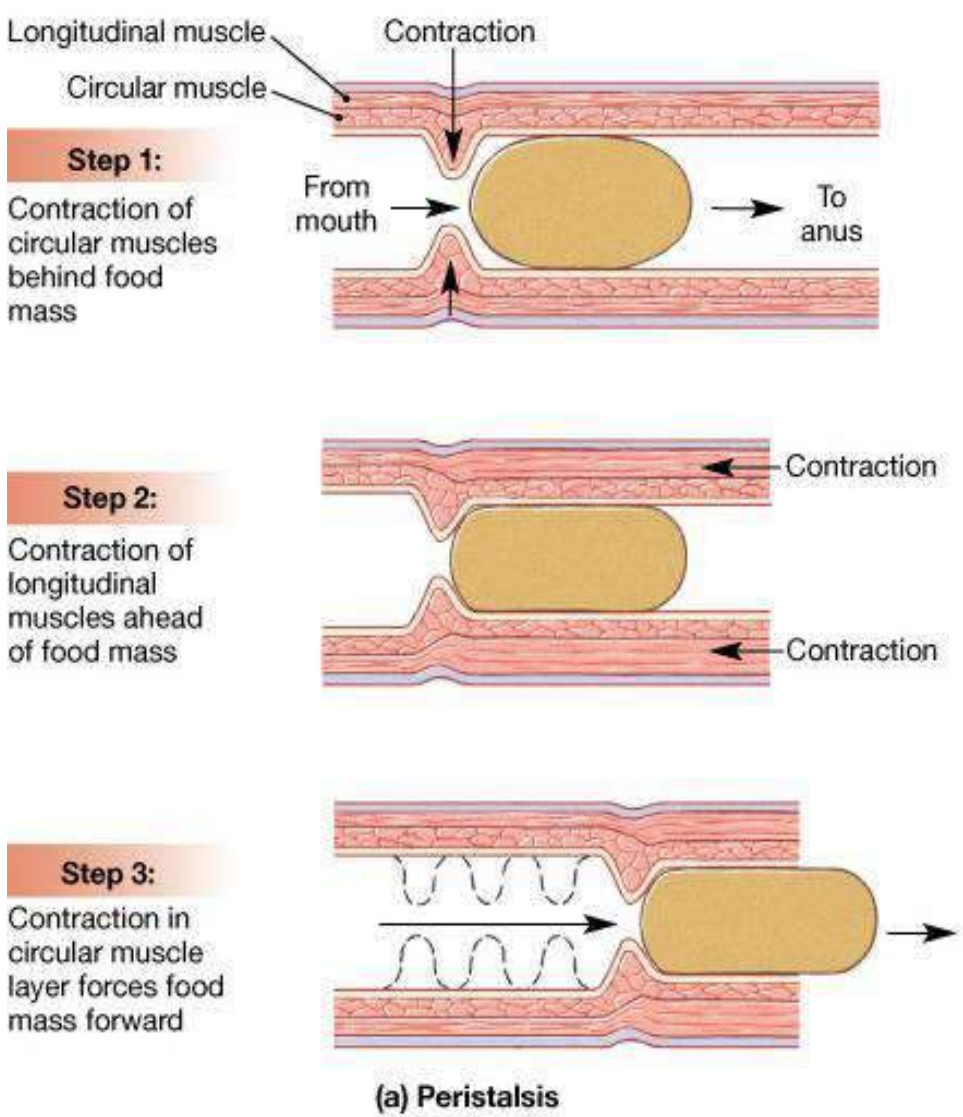
Segmentation: Nonadjacent segments of alimentary tract organs alternately contract and relax, moving the food forward then backward. Food mixing and slow food propulsion occurs

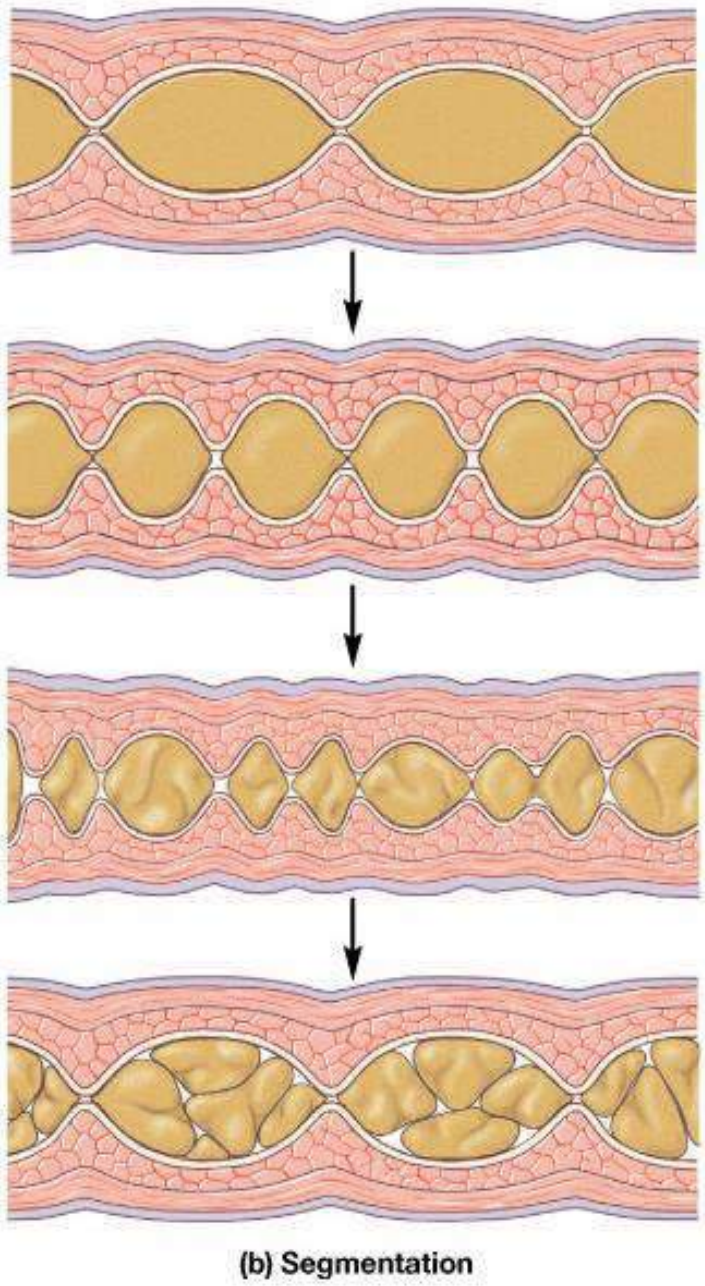
1-Segmentation: **Mix contents to promote Digestion & absorption. It is *Myogenic* i.e. controlled by the basic electric rhythm (BER).**

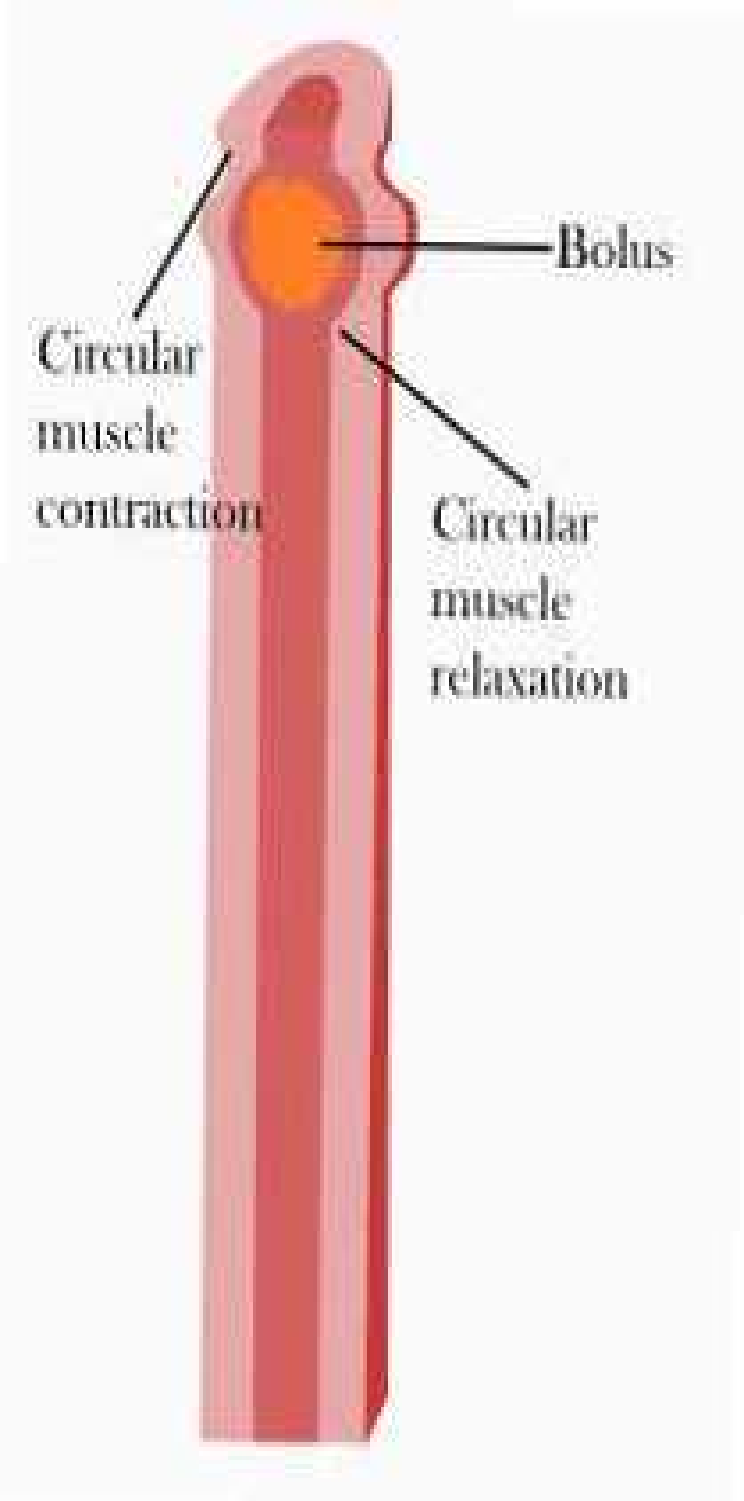


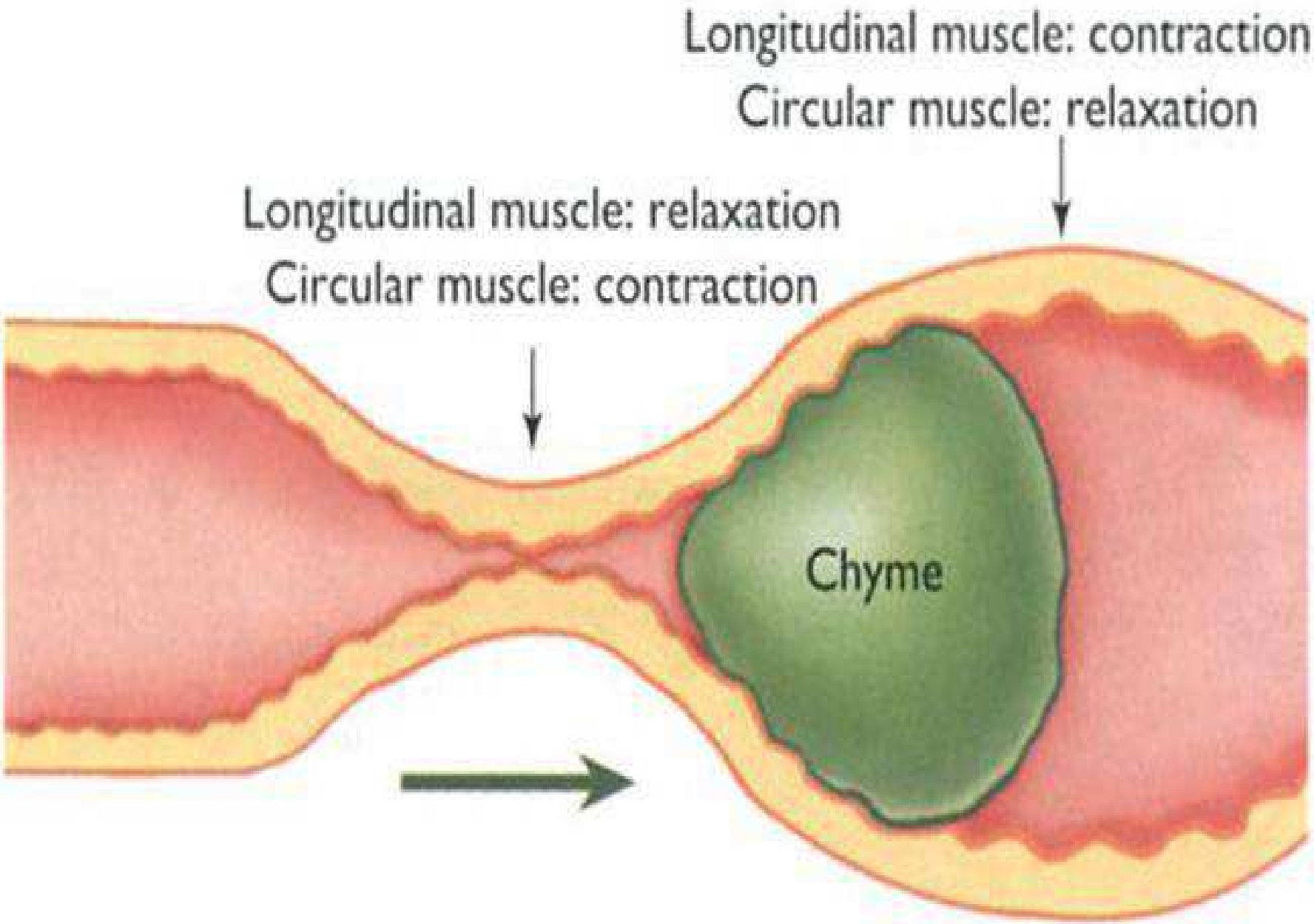


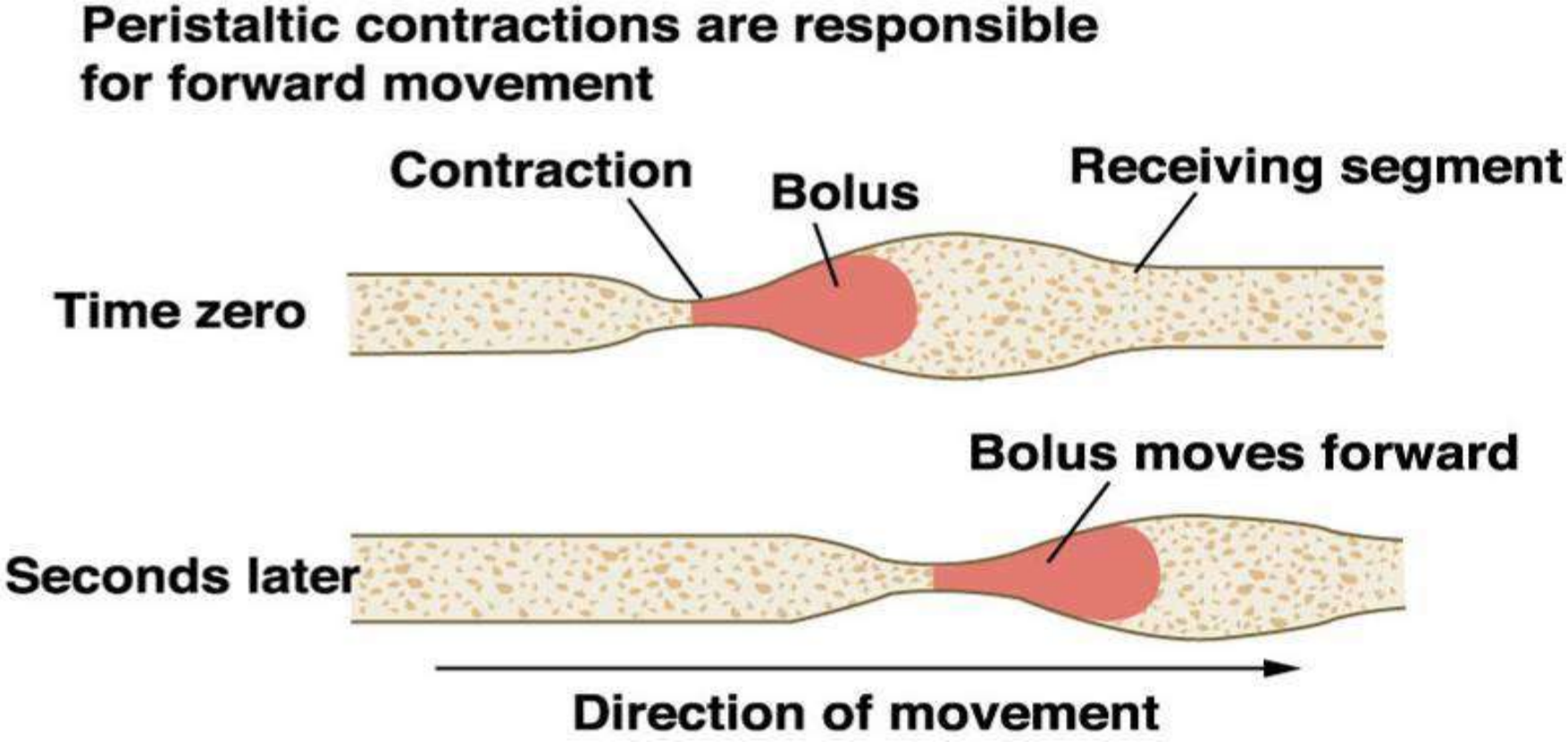
Mixing contraction of the Small Intestine. Rhythmic Segmentations Bring Through Mixing of the Intestinal Content


Longitudinal muscle
Circular muscle
Contraction
Step 1:
Contraction of circular muscles behind food mass
From mouth
To anus
Step 2:
Contraction of longitudinal muscles ahead of food mass
Contraction
Contraction
Step 3:
Contraction in circular muscle layer forces food mass forward
(a) Peristalsis


(b) Segmentation

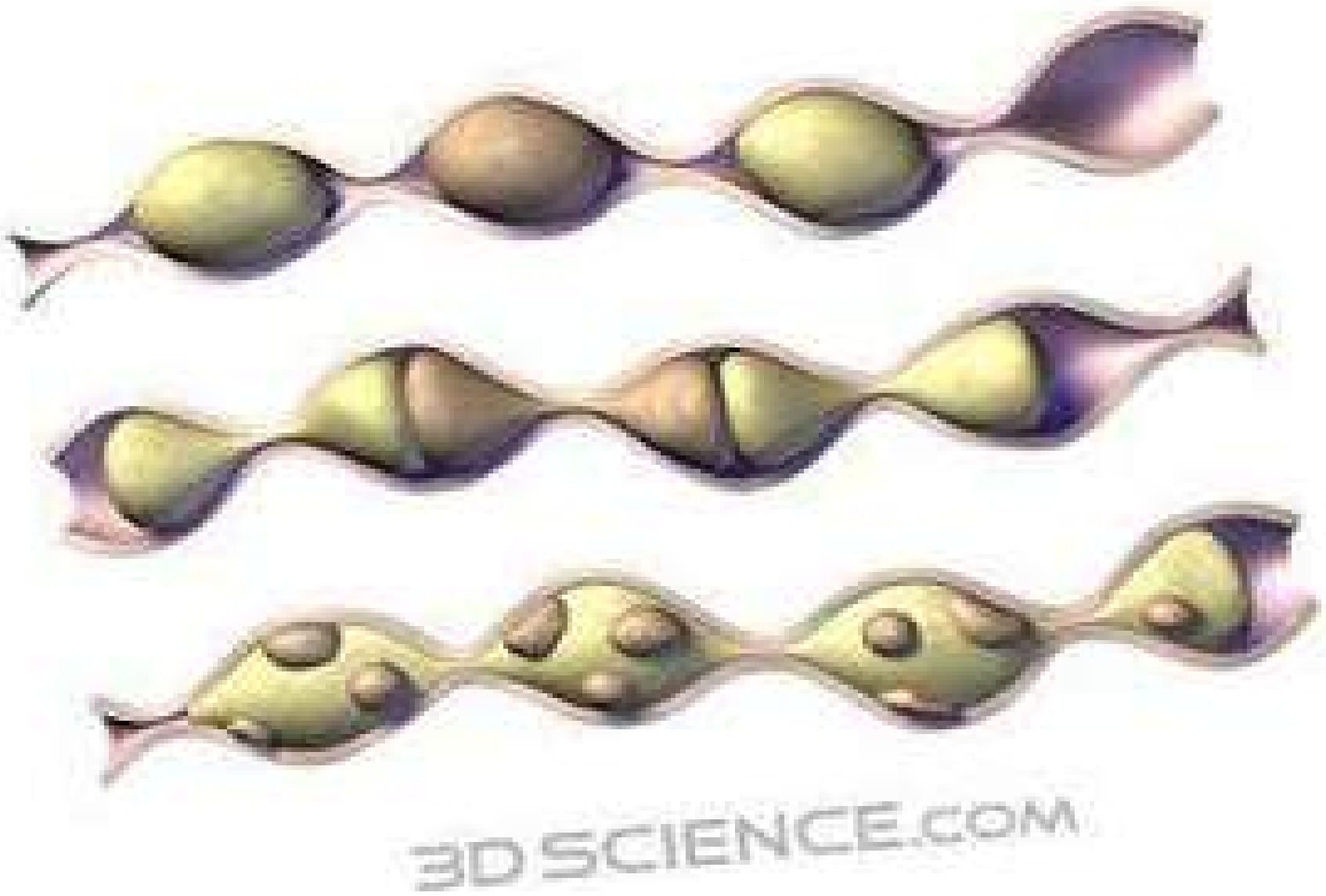

Bolus
Circular muscle contraction
Circular muscle relaxation


Longitudinal muscle: contraction
Circular muscle: relaxation
Longitudinal muscle: relaxation
Circular muscle: contraction
Chyme



"law of the Gut"

- The peristaltic reflex plus the anal direction of movement of the peristalsis is called the law of gut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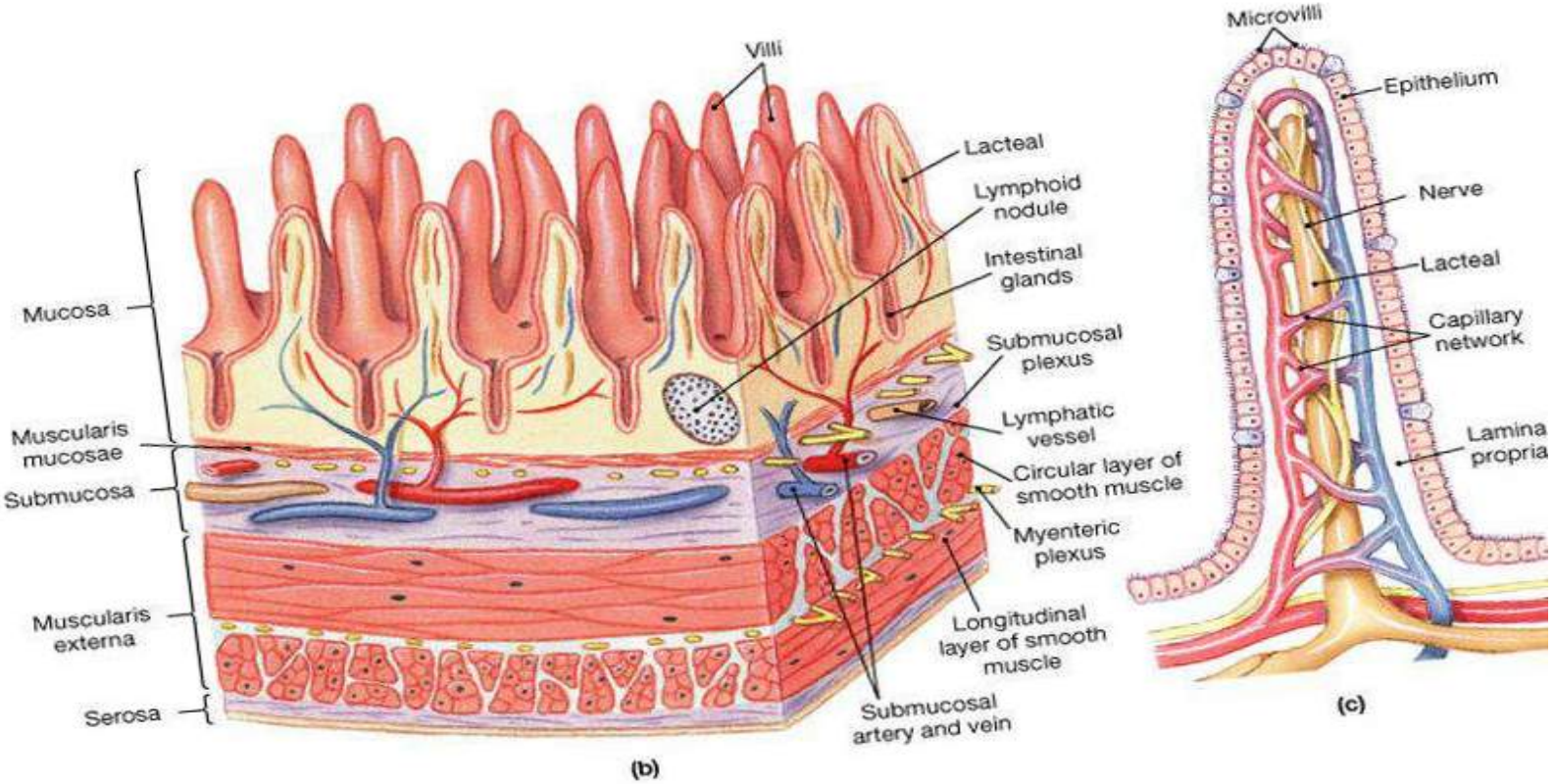
Intestinal Motility

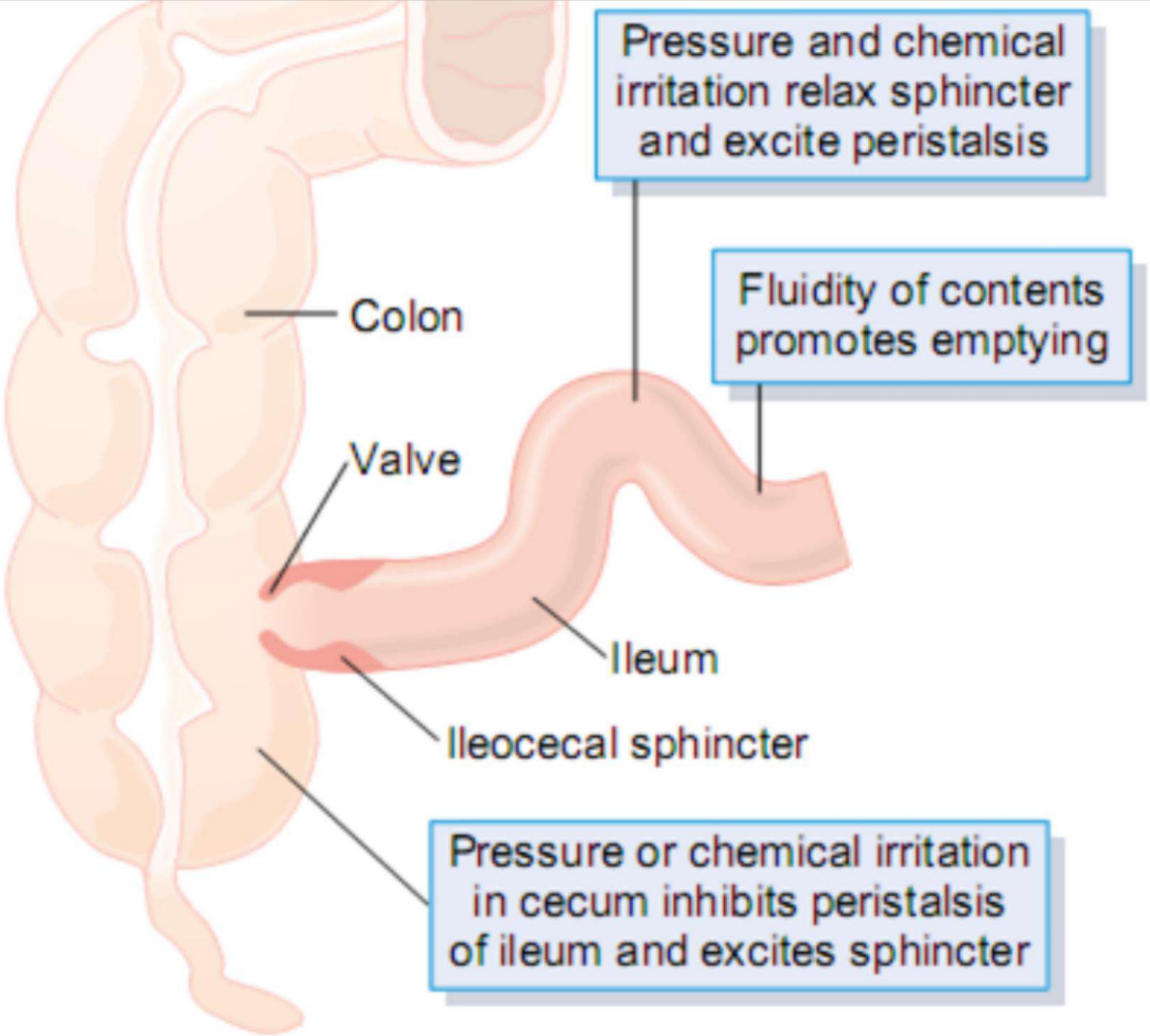
Peristaltic movement	***Segmentation movement***
Stimulus **1-Distension of the duodenum or the stomach (gastro-enteric reflex).** **2- mechanical or physical irritation.**	**Distension with chyme in the small intestine .**
Rate or velocity **Velocity=0.5-2 cm/min slower distally, then die out after few cms.**	**Rate= 11-12 in the duodenum** **8-9 in the terminal ileum**
Control *Neurogenic:* Local Myenteric reflex (law of the gut)	***Myogenic* in nature (slow wave + spike potential on top)**

Movements Caused by the Muscularis Mucosae and Muscle Fibers of the Villi

- **The *muscularis mucosae* can cause short folds to appear in the intestinal mucosa.**
- ***"Milk"* the villi, lymph flows freely from the central lacteals of the villi into the lymphatic system.**
- ***Function of the Ileocecal Valve:* to prevent backflow of fecal contents from the colon**
- **1000 milliliters of chyme empty into the cecum each day.**
- ***Feedback Control of the Ileocecal Sphincter***
- **Reflexes from the cecum(distention& irritation) cont .of sphincter, inhibit peristalsis thus delay emptying.(coloileal reflex).**

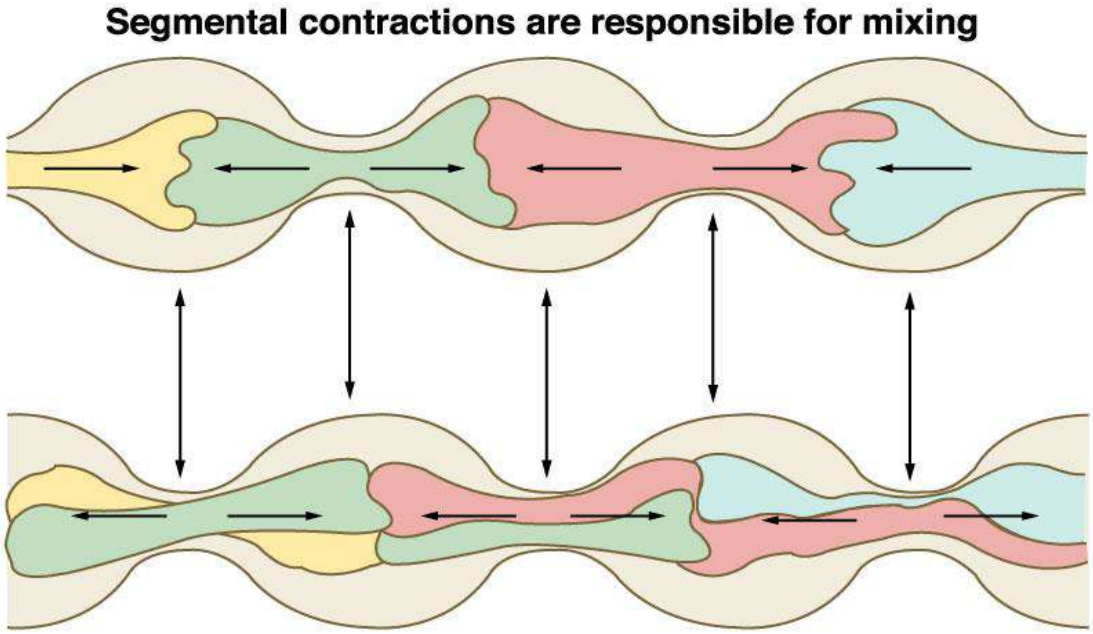
Movement of Villi by Villikinin




Pressure and chemical irritation relax sphincter and excite peristalsis
Fluidity of contents promotes emptying
Colon
Valve
Ileum
Ileocecal sphincter
Pressure or chemical irritation in cecum inhibits peristalsis of ileum and excites sphincter

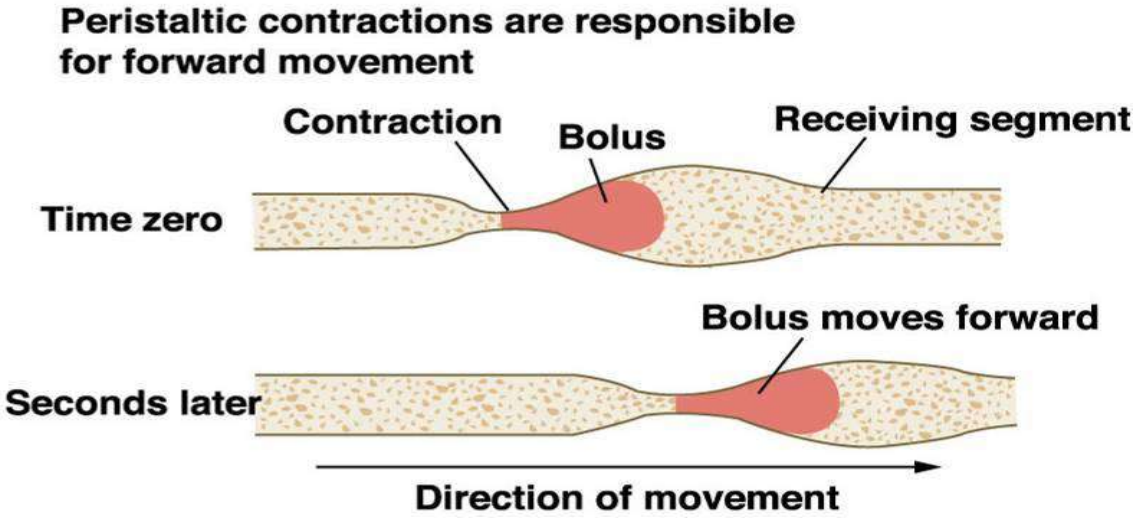
4-Movements of the Colon

- **The principal functions of the colon are :**
- **Absorption of water and electrolytes from the chyme to form solid feces *(Proximal1/2).***
- **Storage of fecal matter until it can be expelled (Distal1/2).**
- ***Mixing Movements-"Haustrations***
- **80 to 200 milliliters of feces are expelled each day.**
- ***Propulsive Movements-"Mass Movements.***
- **Persistent haustral contractions, requiring as many as *8 to 15 hours* to move the chyme from the ileocecal valve through the colon.**
- ***(1-3times daily) After breakfast by one hour.***



Large intestinal motility patterns

- **Segmental contraction *(Haustration)***



- ***Peristalsis***

A Mass Movement : is a Modified Type of Peristalsis Characterized by

- *First, A constrictive ring* **occurs in response to a distended or irritated point in the colon, usually in the Transverse colon.**
- *Then,* **Rapidly, the** *20 or more centimeters* **of colon** ***distal to the constrictive ring*** **lose their Haustrations and contract as a unit, propelling the fecal material in this** *Segment En Masse* **further down.**
- **The contraction develops progressively more force for about 30 seconds, and relaxation occurs during the next 2 to 3 minutes.**
- **A series of mass movements usually persists for** *10 to 30 minutes.* **Then they cease but return perhaps a half day later.**

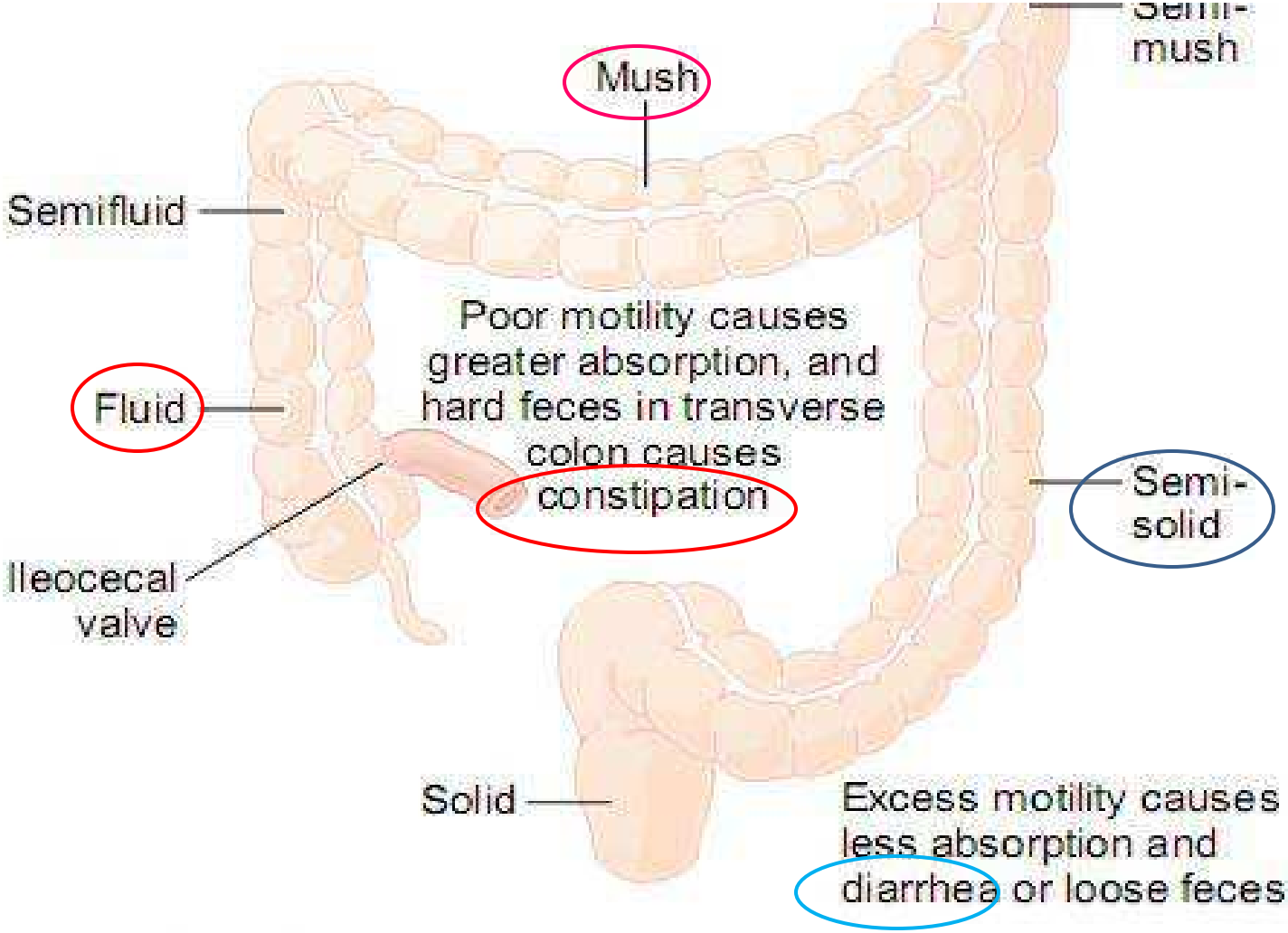

Semi-
mush
Mush
Semifluid
Poor motility causes
greater absorption, and
hard feces in transverse
colon causes
constipation
Fluid
Semi-
solid
Ileocecal
valve
Solid
Excess motility causes
less absorption and
diarrhea or loose feces

Figure 63–5

- **Initiation of Mass Movements by Gastrocolic and Duodenocolic Reflexes.**

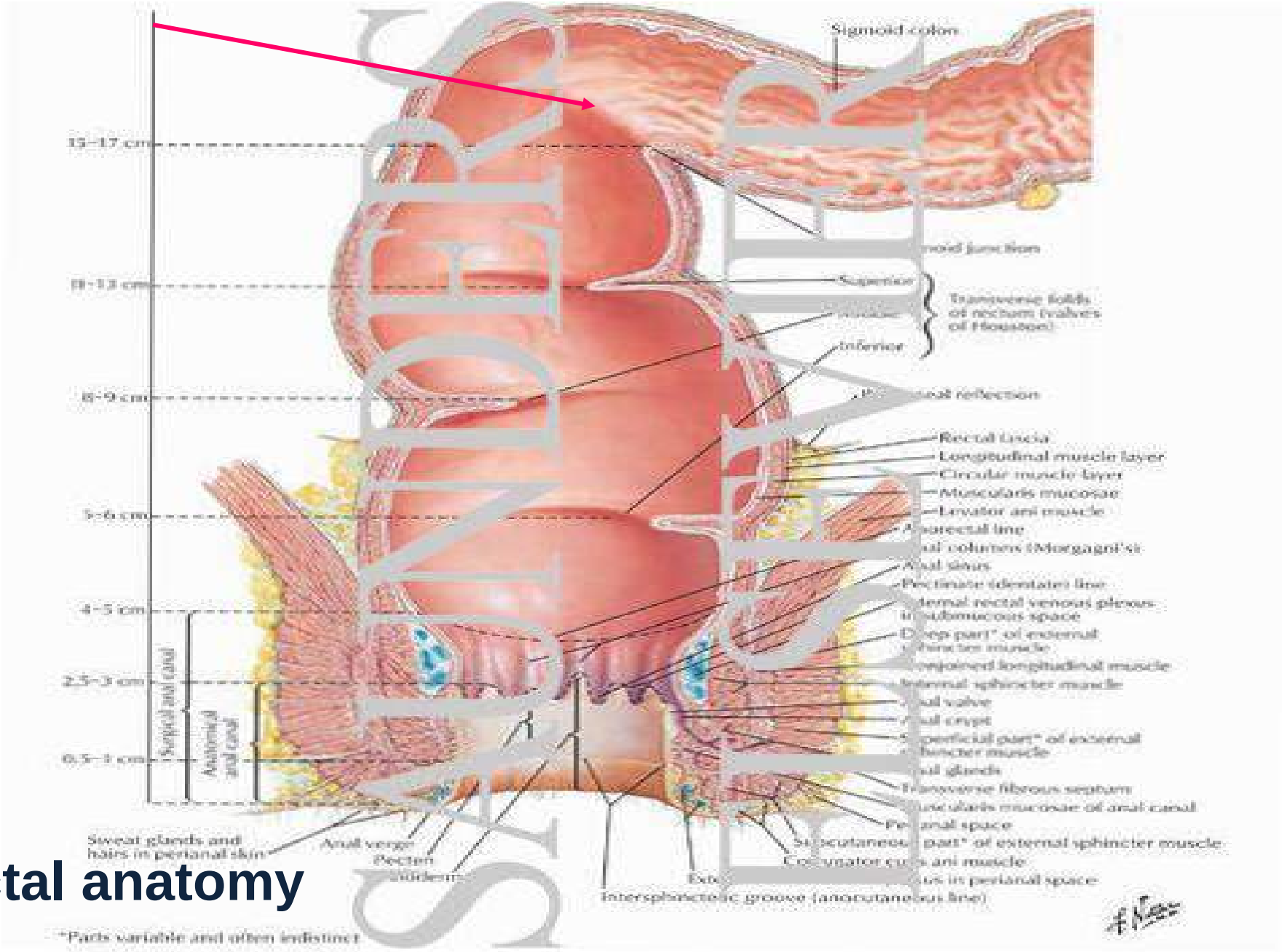
Appearance of mass movements after meals is facilitated by *Gastro Colic and Duodeno Colic reflexes.*

These reflexes result from Distention of the stomach and Duodenum.

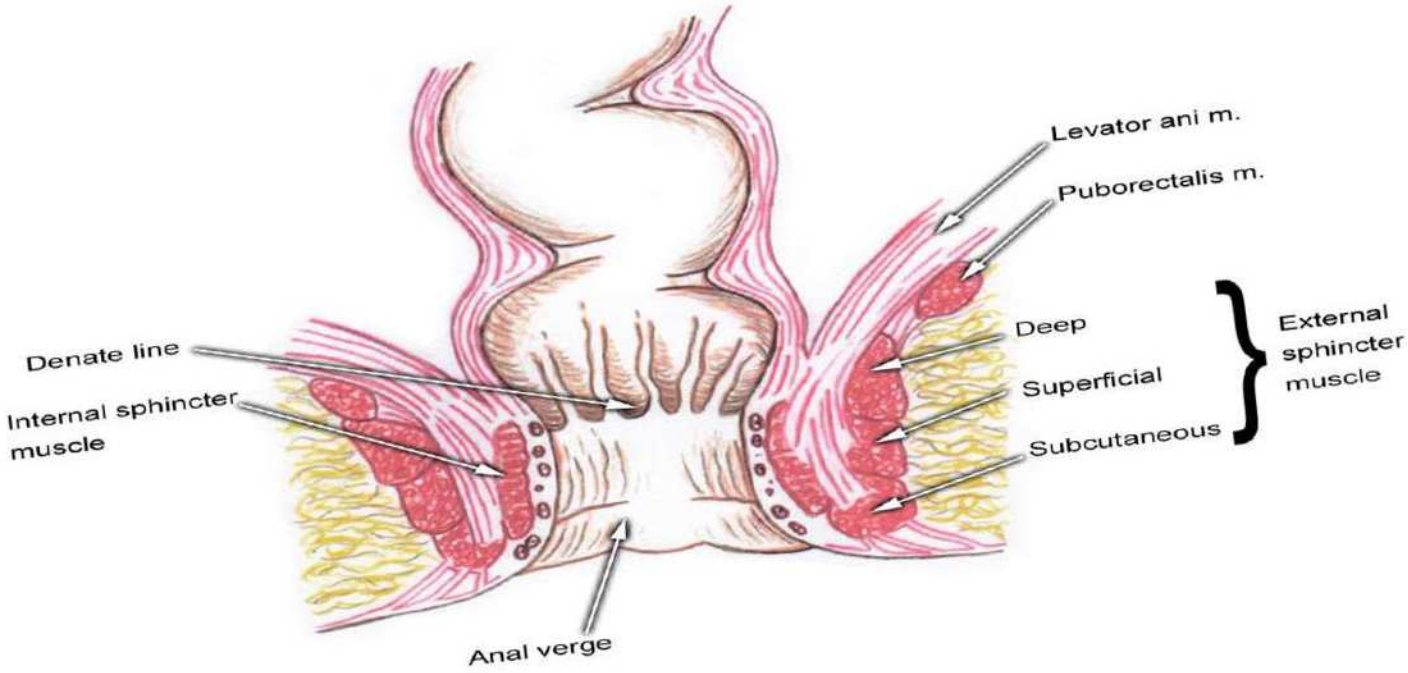
Irritation in the colon can also initiate intense mass movements.(in *ulcerative colitis* mass movements persist almost all the time).

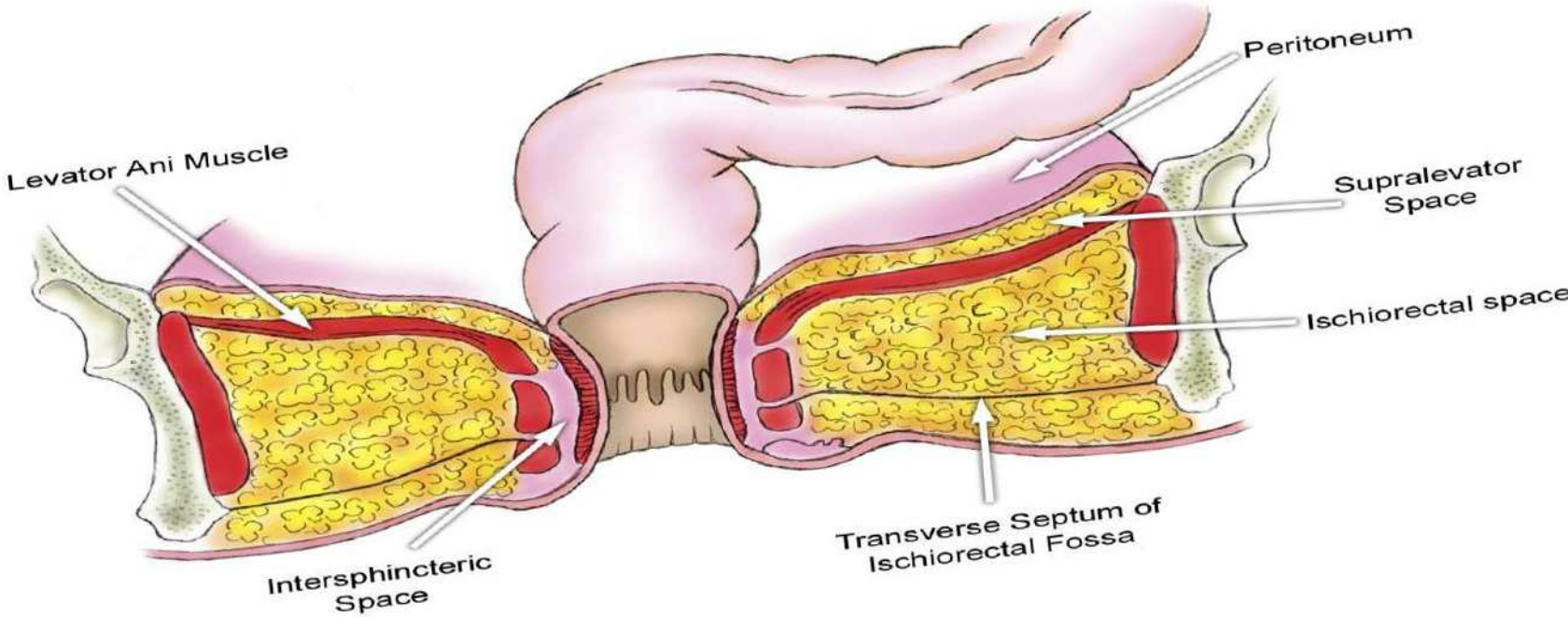
Defecation

- **Most of the time, the rectum is empty of feces as a result of:**
- ***Weak functional sphincter*** **exists about** ***20 cm*** **from the anus at the junction between the sigmoid colon and the rectum.**
- **There is also a** ***Sharp Angulation*** **here that contributes additional resistance to filling of the rectum.**
- ***Defecation Reflexes :***
- ***Intrinsic myenteric reflex:*** **is relatively weak ??.**
- ***Parasympathetic Defecation Reflex:*** **powerful process of defecation .**



ectal anatomy

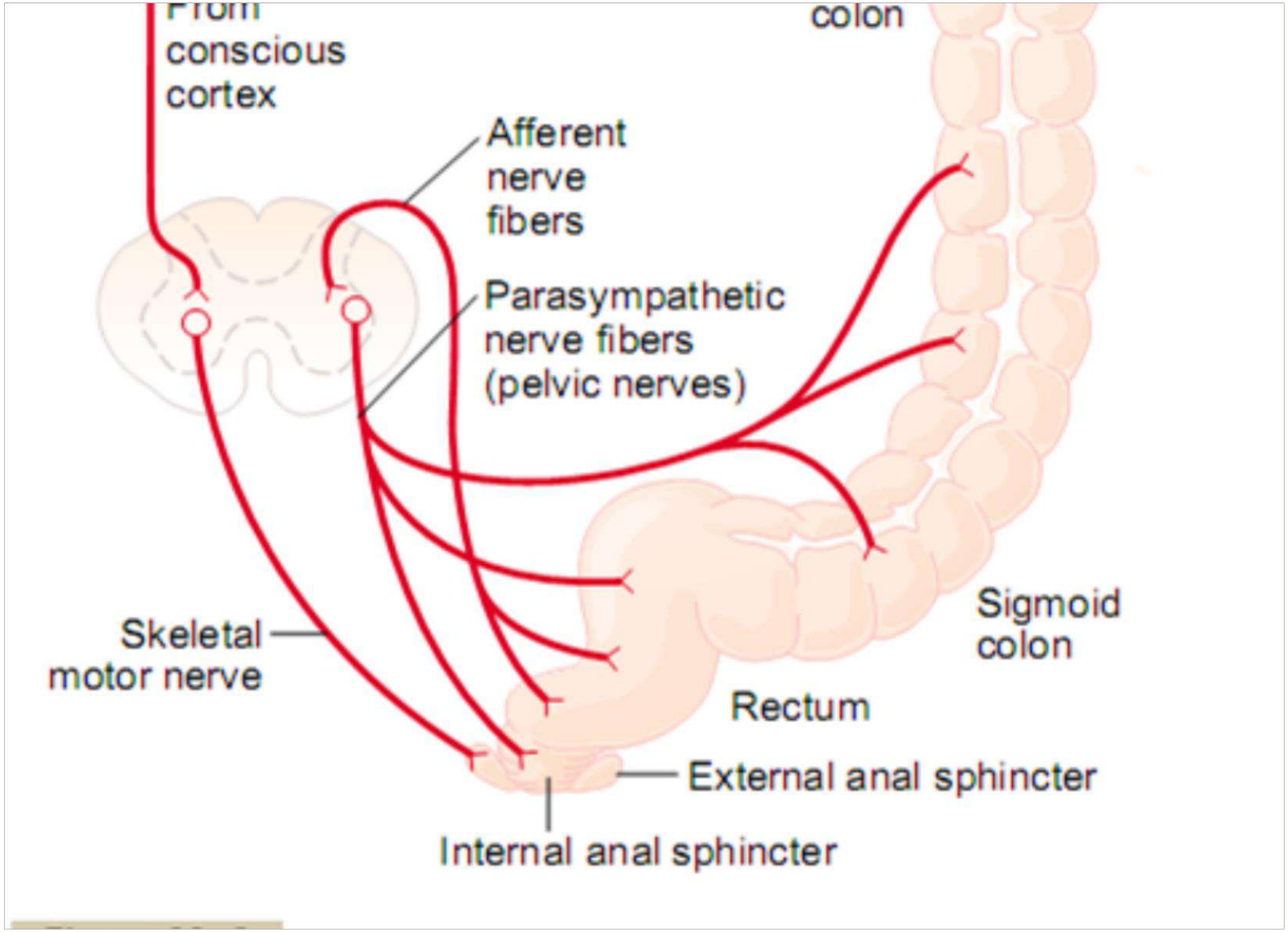

Levator ani m.
Puborectalis m.
Denate line
Internal sphincter muscle
Deep
Superficial
Subcutaneous
External sphincter muscle
Anal verge


Peritoneum
Levator Ani Muscle
Supralevator Space
Ischiorectal space
Transverse Septum of Ischiorectal Fossa
Intersphincteric Space

- ***Defecation signals :*** **entering the spinal cord initiate other effects, such as taking a Deep breath, Closure of the glottis, and Contraction of the abdominal wall muscles to force the fecal contents of the colon downward and at the same time cause the pelvic floor to relax downward and pull outward on the anal ring to evaginate the feces.**
- **People who too often inhibit their natural reflexes are likely to become severely constipated.**

5-Other Autonomic Reflexes That Affect Bowel Activity

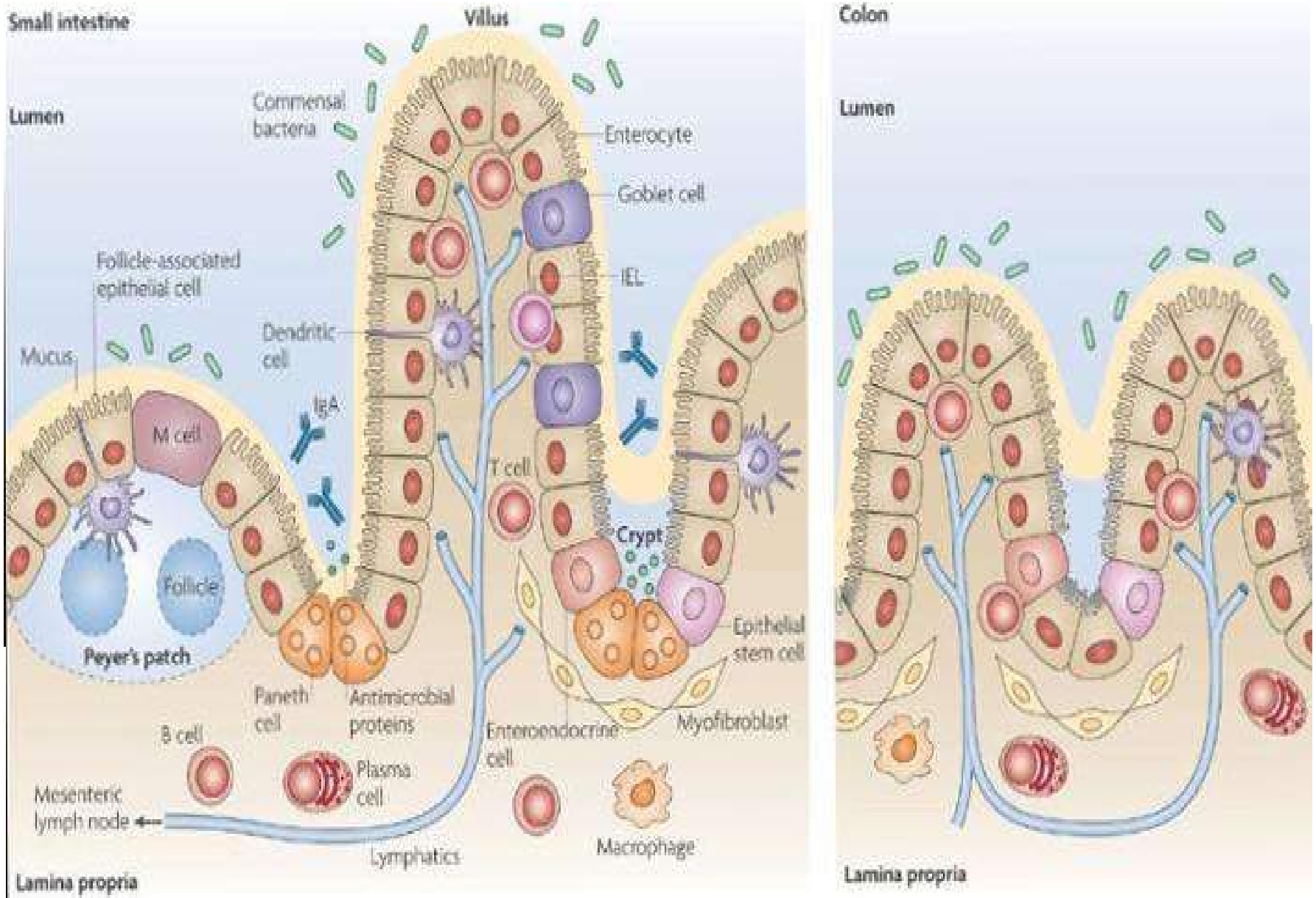
- **Peritoneo-intestinal reflex. (peritonitis)**
- **Reno-intestinal reflex.**
- **Vesicoi-ntestinal reflex.**
- **All** ***Inhibit Intestinal Activity***


From
conscious
cortex
colon
Afferent
nerve
fibers
Parasympathetic
nerve fibers
(pelvic nerves)
Skeletal
motor nerve
Sigmoid
colon
Rectum
External anal sphincter
Internal anal sphincter

SECRETORY FUNCTION OF GIT

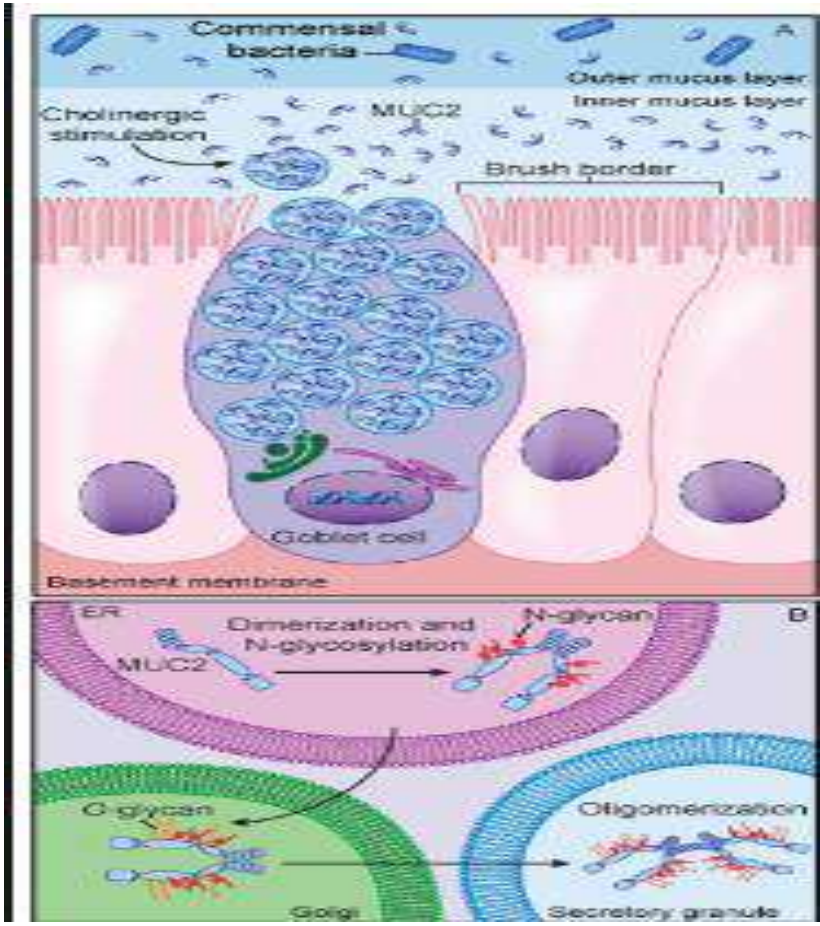
- ***Secretory glands*** **produce digestive enzymes present from mouth to terminal ileum.**

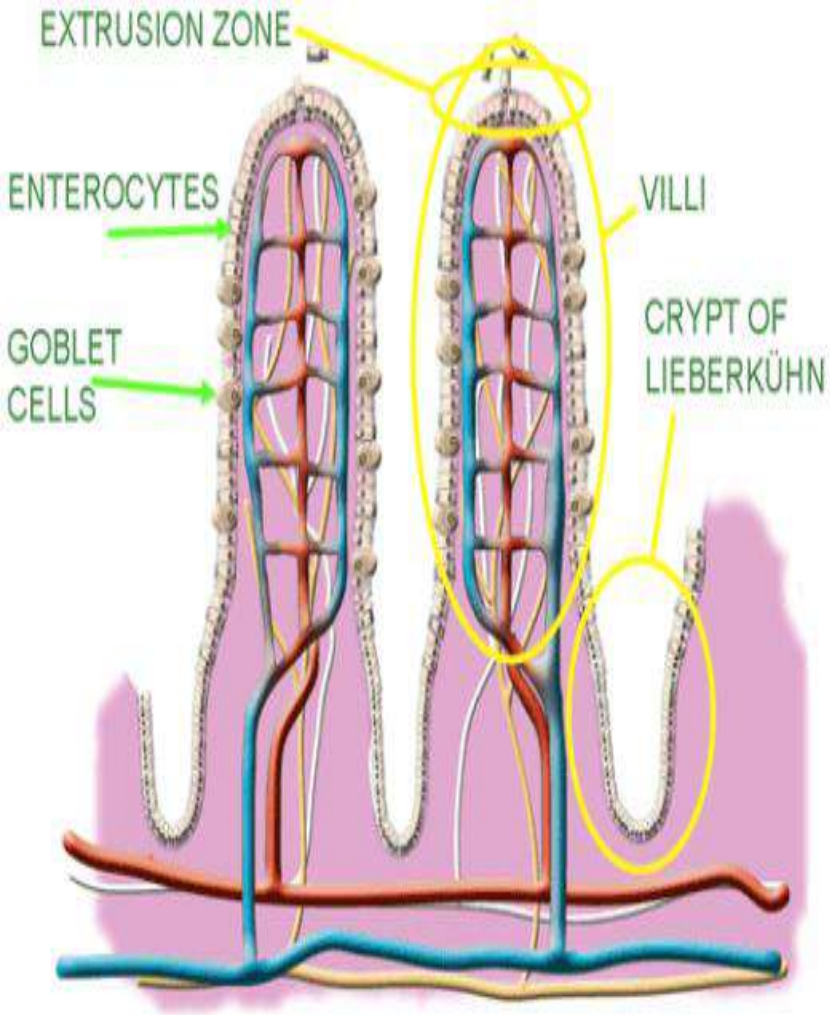
- ***Mucus glands*** **lubricants from mouth to anus.**

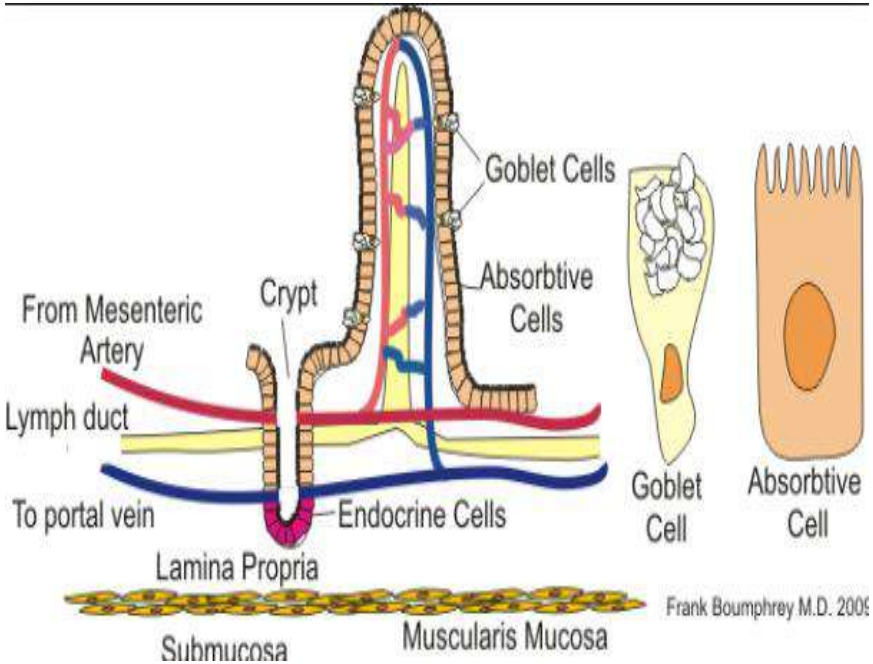

Small intestine
Villus
Lumen
Commensal bacteria
Enterocyte
Goblet cell
Follicle-associated epithelial cell
IEL
Dendritic cell
Mucus
IgA
M cell
T cell
Crypt
Follicle
Peyer's patch
Epithelial stem cell
Paneth cell
Antimicrobial proteins
Myofibroblast
B cell
Enteroendocrine cell
Plasma cell
Mesenteric lymph node
Lymphatics
Macrophage
Lamina propria
Colon
Lumen
Lamina propria

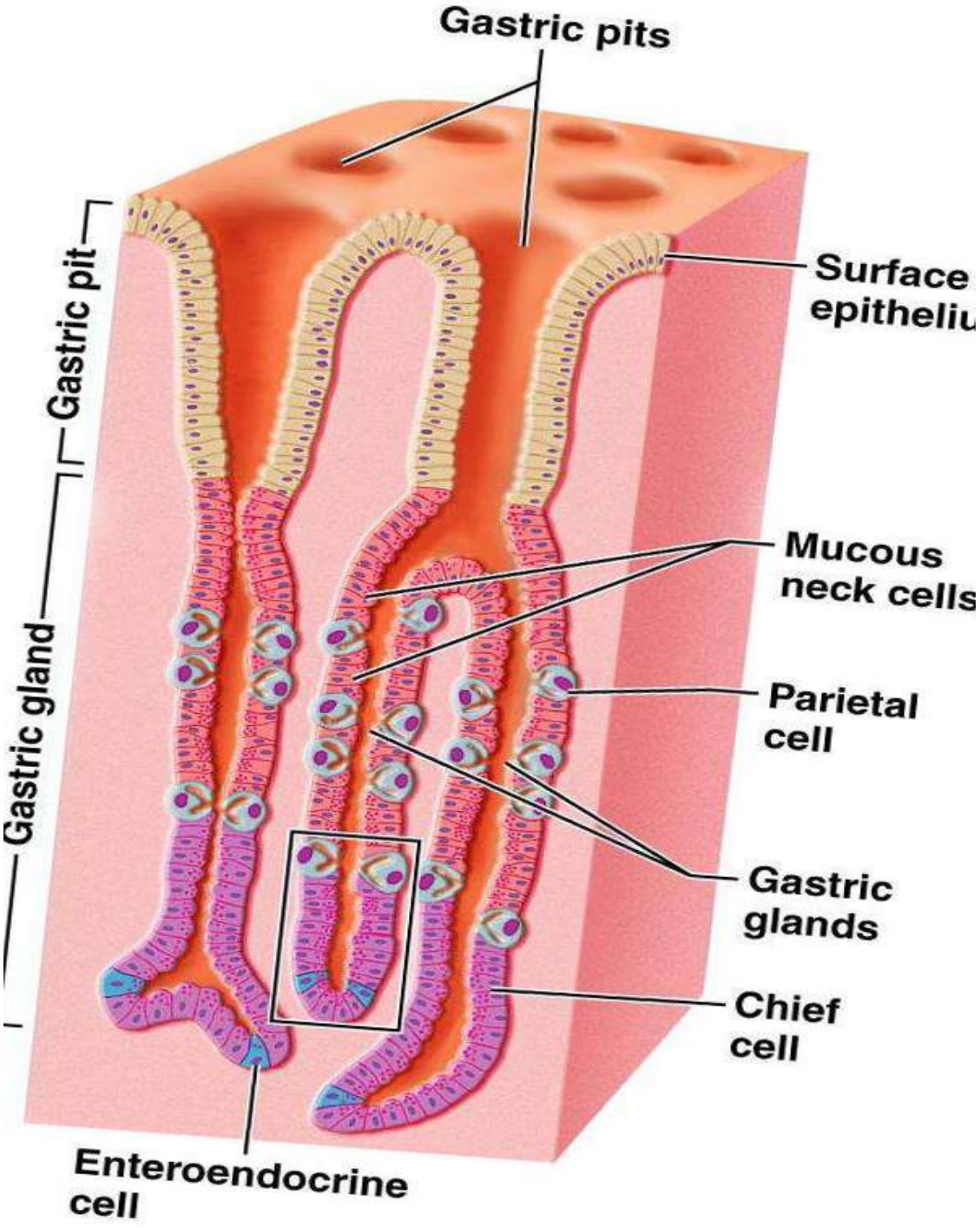
Anatomical type of glands

- *Goblet cells* **single mucus secretion gland.**
- **Specialized glands lie in pits like crypts of Lieberkühn.**
- **Deep tubular glands oxyntic cells.**
- **Several complex glands salivary ,pancreas liver.**




EXTRUSION ZONE
ENTEROCYTES
GOBLET CELLS
VILLI
CRYPT OF LIEBERKÜHN


Goblet Cells
Absorbtive Cells
Crypt
From Mesenteric Artery
Lymph duct
To portal vein
Endocrine Cells
Lamina Propria
Submucosa
Muscularis Mucosa
Goblet Cell
Absorbtive Cell
Frank Boumphrey M.D. 2009


Gastric pits
Gastric pit
Gastric gland
Surface epitheliu
Mucous neck cells
Parietal cell
Gastric glands
Chief cell
Enteroendocrine cell

Basic mechanism of stimulation of alimentary tract glands

- **Mechanical stimulation by presence of food especially mucus gland *Direct contact***
- ***Function of Enteric Nervous Stimuli.***
  - **Tactile stimulation.**
  - **Chemical irritation.**
  - **Distention of the gut wall.**
- ***Autonomic Stimulation of Secretion***
- **Parasympathetic Stimulation.**
- **sympathetic Stimulation.**
- ***Regulation of Glandular Secretion by Hormones***
- **Chemically, the gastrointestinal hormones are polypeptides or polypeptide derivatives.**

Importance of Mucus in the Gastrointestinal Tract

- **Mucus is a thick secretion composed mainly of**
- **Water Electrolytes, Mixture of several glycoproteins, (large polysaccharides bound with much smaller quantities of protein).**

- **Mucus is slightly different in different parts of the gastro-intestinal tract.**
- **But everywhere it has several important characteristics that make it both an excellent *Lubricant and a Protectant* for the wall of the gut.**

- Mucus has Adherent qualities that make it adhere tightly to the food or other particles and to spread as a thin film over the surfaces.
- It has *Sufficient body* that it coats the wall of the gut and prevents actual contact of most food particles with the mucosa.
- Mucus has a *low resistance for slippage*, so that the particles can slide along the epithelium with great ease.
- Mucus causes *fecal particles to adhere to one another* to form the feces that are expelled during a bowel movement.
- Mucus is *Strongly resistant to digestion* by the gastrointestinal enzymes.
- The glycoprotein of mucus have ***amphoteric properties***, which means that they are capable of Buffering small amounts of either acids or alkalis.
- Also, mucus often contains moderate quantities of bicarbonate ions which specifically *Neutralize acids*.

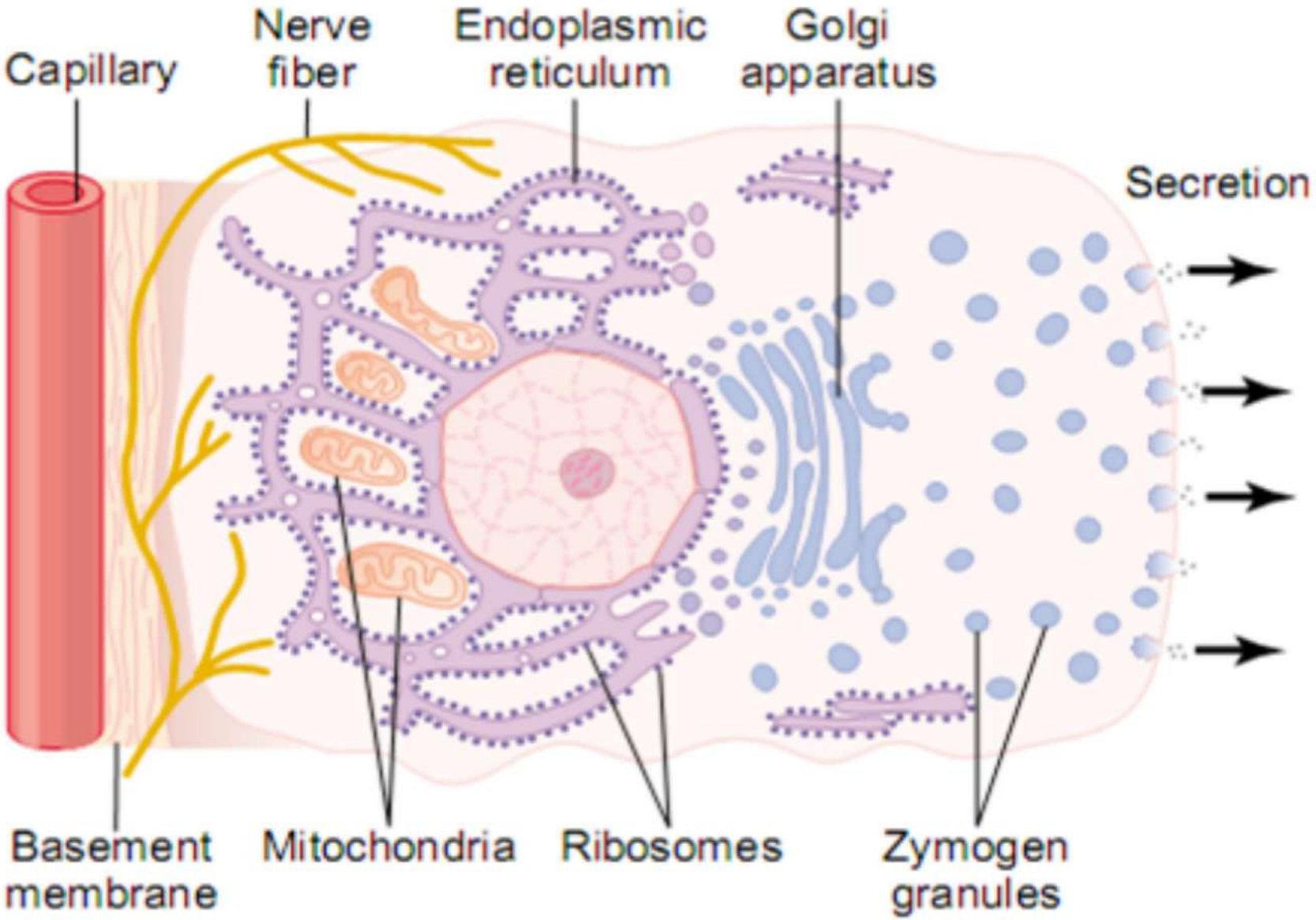

Capillary
Nerve fiber
Endoplasmic reticulum
Golgi apparatus
Secretion
Basement membrane
Mitochondria
Ribosomes
Zymogen granules

Figure 64–1

Composition of gastrointestinal secretions

Type of secretion	Volume	Na^+	K^+	Cl^-	Hco_3
Salivary	1000	20	26	50	50
Stomach	1500	70	10	100	0
Small bowel	2500	140	20	104	30
Bile	1000	140	5	100	35
Pancreas	1000	140	5	70	115

Chemical composition of body fluids

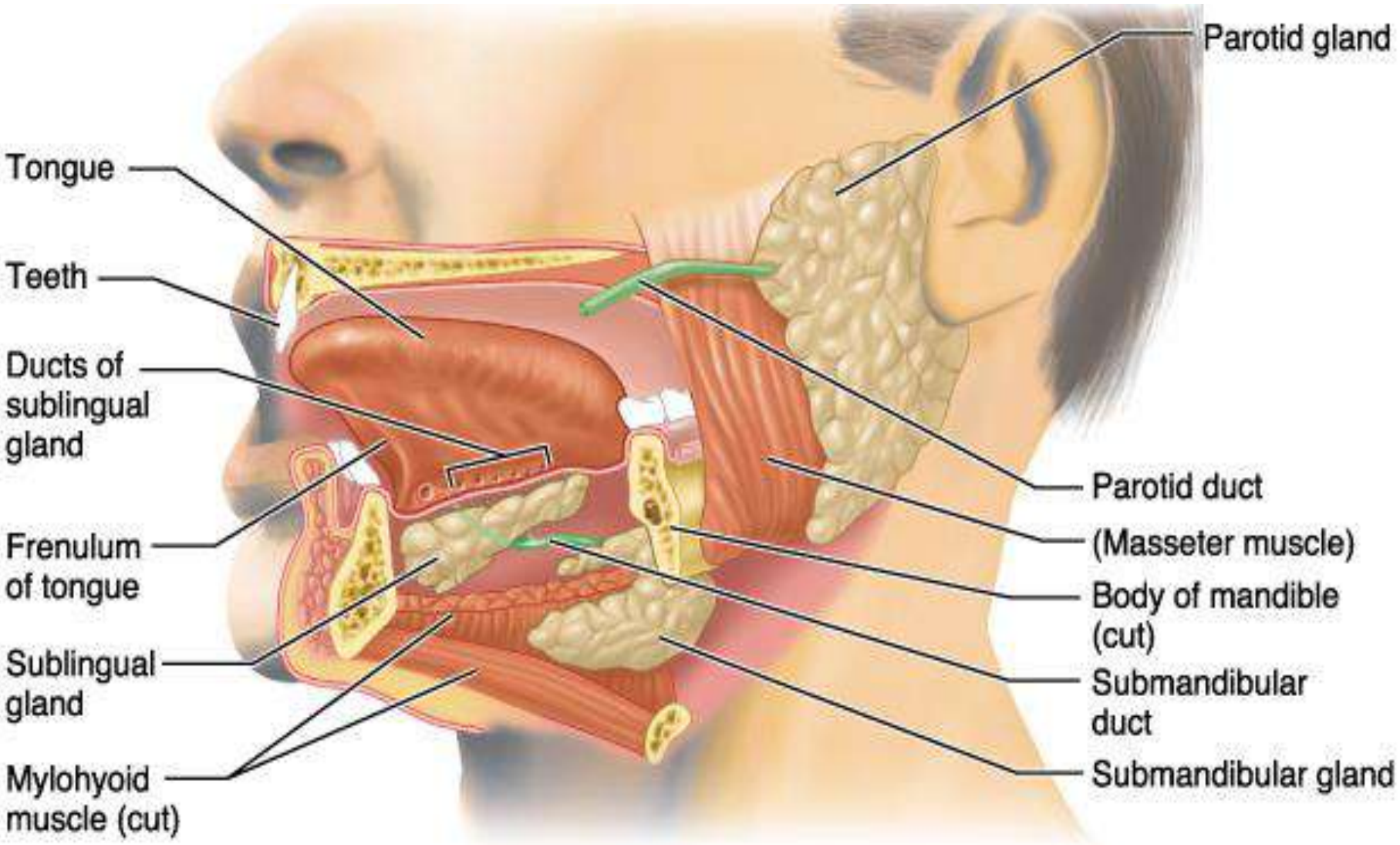
Fluid	Na	K	Mg	Hco3	Protein	PO4	CL
Intracellular	10	150	40	10	40	120	3
Interstitial	144	4	2	30	1	3	114
Plasma	142	4	3	27	16	3	103
Ringer lactate	130	4	-	28	-	-	109

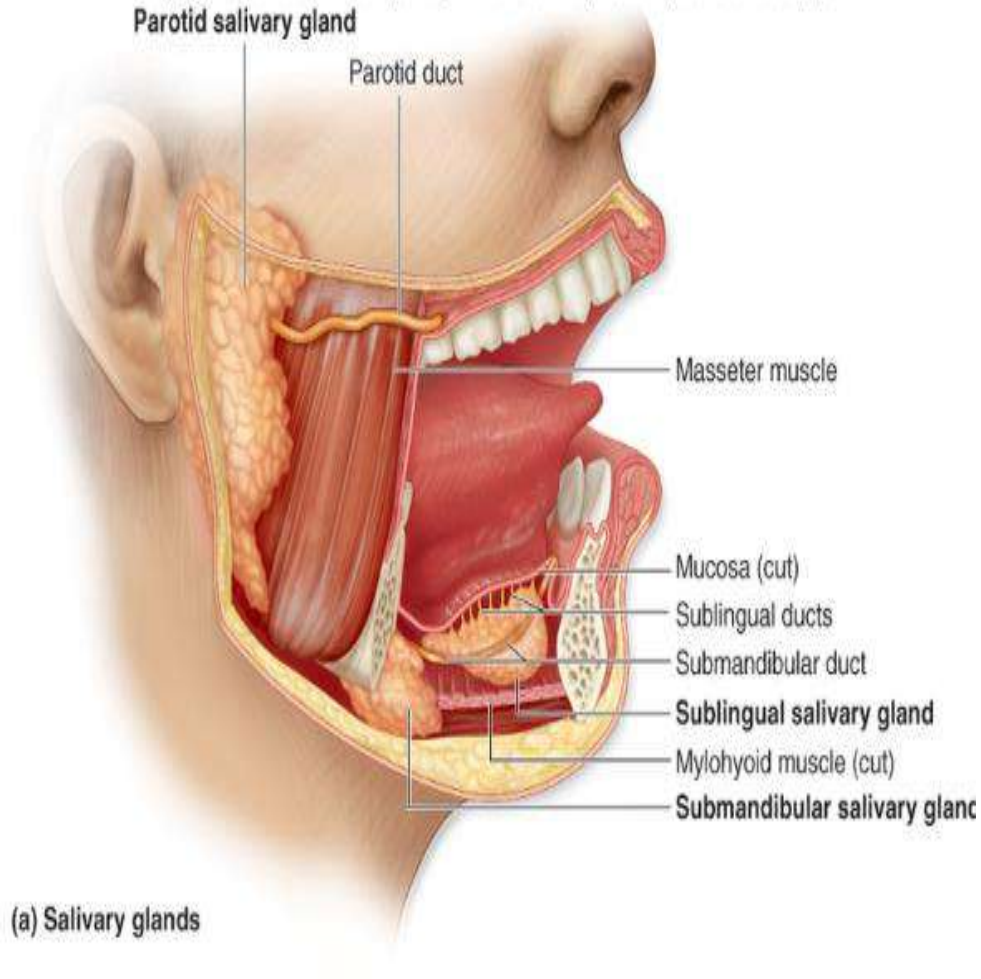
2-Secretion of Saliva

Daily Secretion of Intestinal Juices

	Daily Volume (ml)	pH
Saliva	1000	6.0–7.0
Gastric secretion	1500	1.0–3.5
Pancreatic secretion	1000	8.0–8.3
Bile	1000	7.8
Small intestine secretion	1800	7.5–8.0
Brunner's gland secretion	200	8.0–8.9
Large intestinal secretion	200	7.5–8.0
Total	6700	

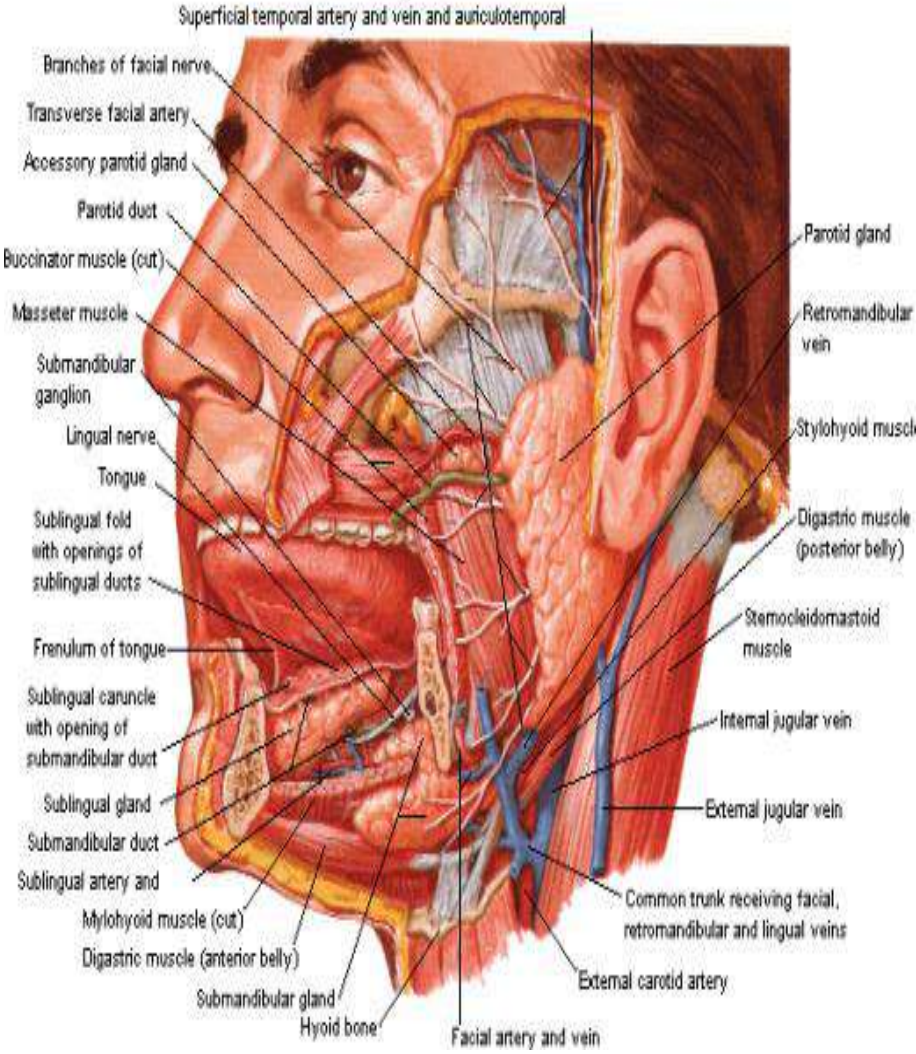
- **Saliva Contains a *Serous Secretion* and a *Mucus Secretion***
- **The principal glands of salivation are the**
- **Parotid: Serous type of secretion**
- **Submandibular: Serous secretion and Mucus(70)%**
- **Sublingual :serous secretion and mucus.**
- **Buccal glands: only mucus**
- **Daily secretion of saliva normally ranges between 800 and 1500 milliliters, as shown by the average value of 1000 milliliters**


Parotid gland
Tongue
Teeth
Ducts of sublingual gland
Frenulum of tongue
Sublingual gland
Mylohyoid muscle (cut)
Parotid duct
(Masseter muscle)
Body of mandible (cut)
Submandibular duct
Submandibular gland

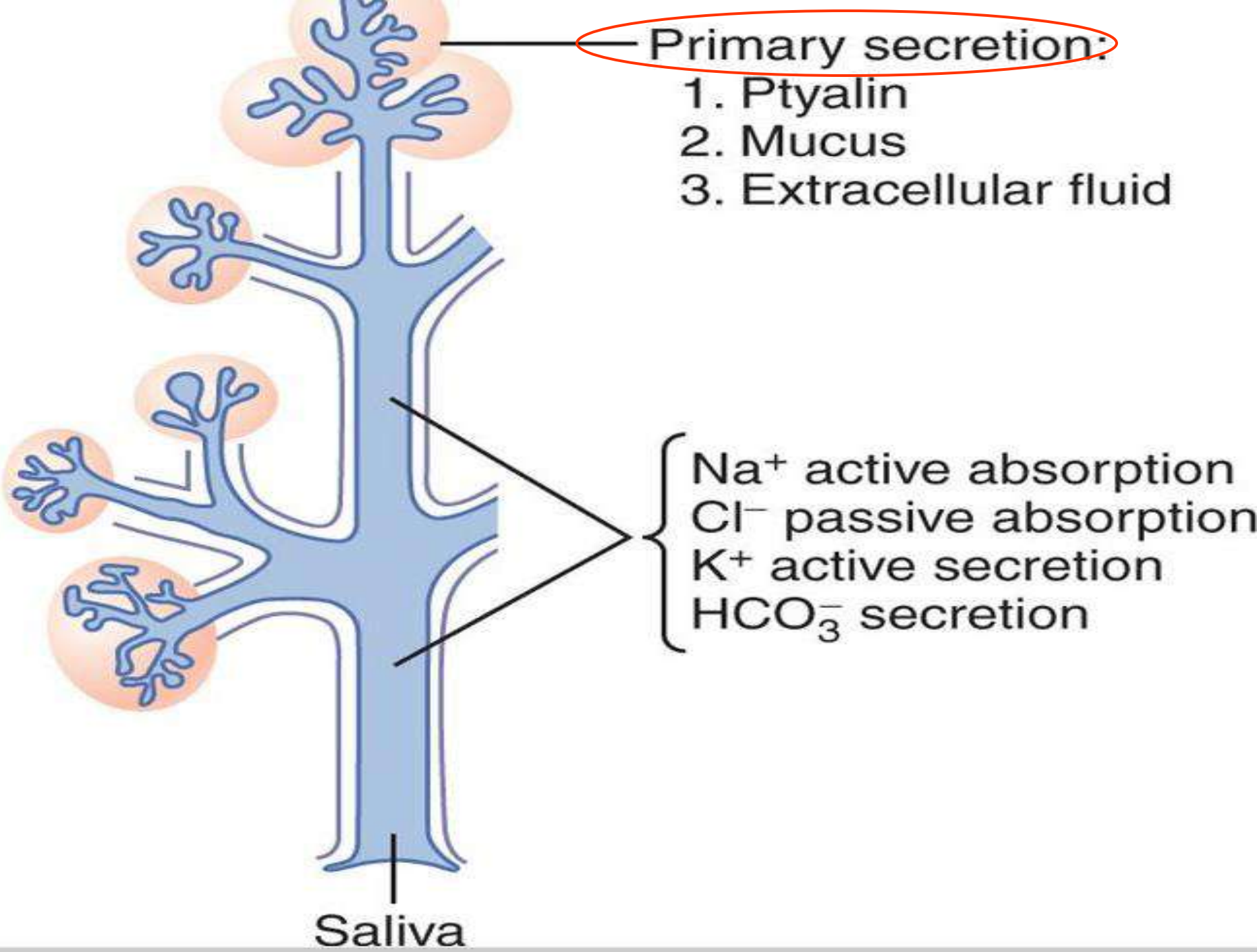


(a) Salivary glands

Salivary Glands



- **Saliva contains two major types of protein secretion:**
- **(1) *Serous secretion* that contains ***Ptyalin*** (an α-amylase), which is an enzyme for digesting starches.**
- **(2) *Mucus secretion* that contains ***Mucin*** for lubricating and for surface protective purposes.**
- **Saliva has a pH between 6.0 and 7.0, a favorable range for the digestive action of ptyalin.**


Primary secretion:
1. Ptyalin
2. Mucus
3. Extracellular fluid
Na^+ active absorption
Cl^- passive absorption
K^+ active secretion
HCO_3^- secretion
Saliva

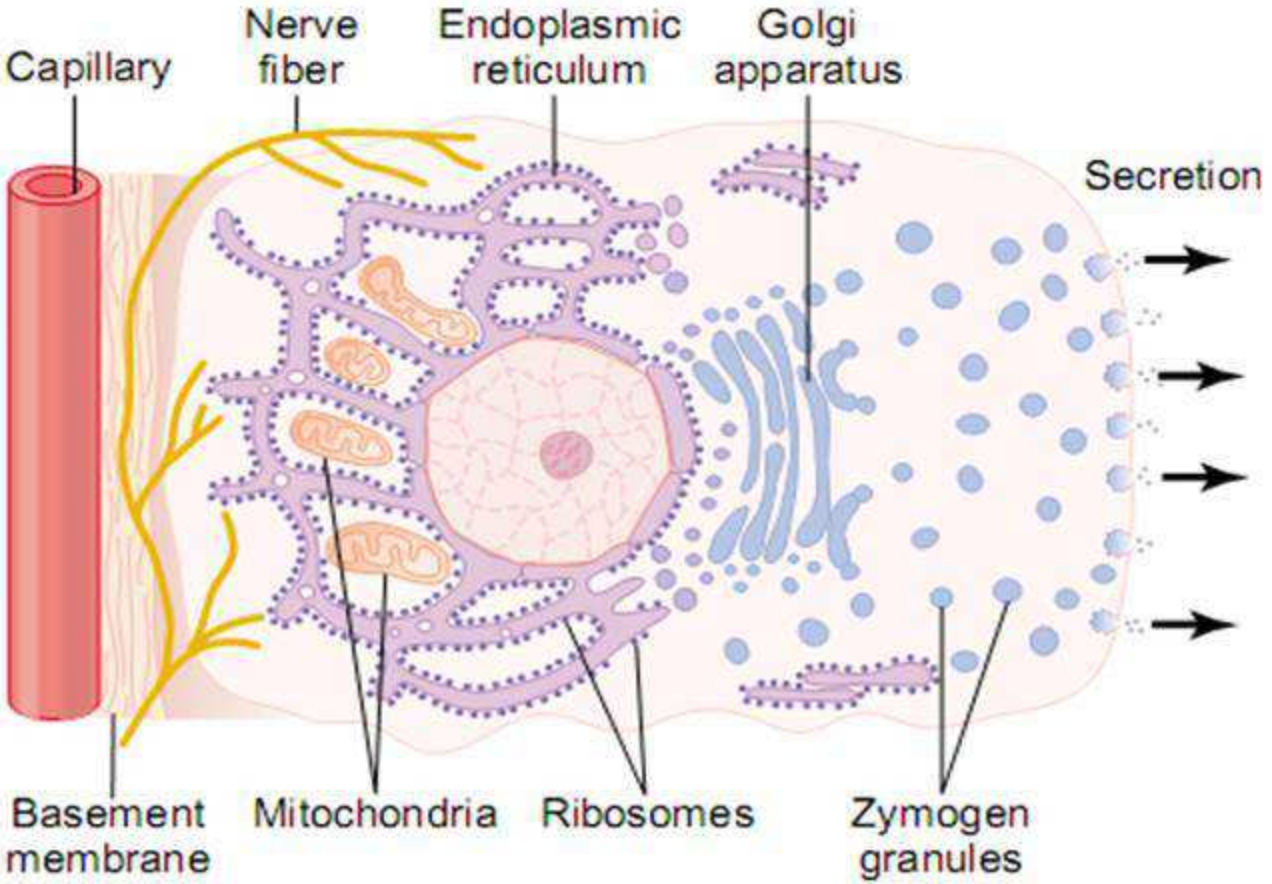
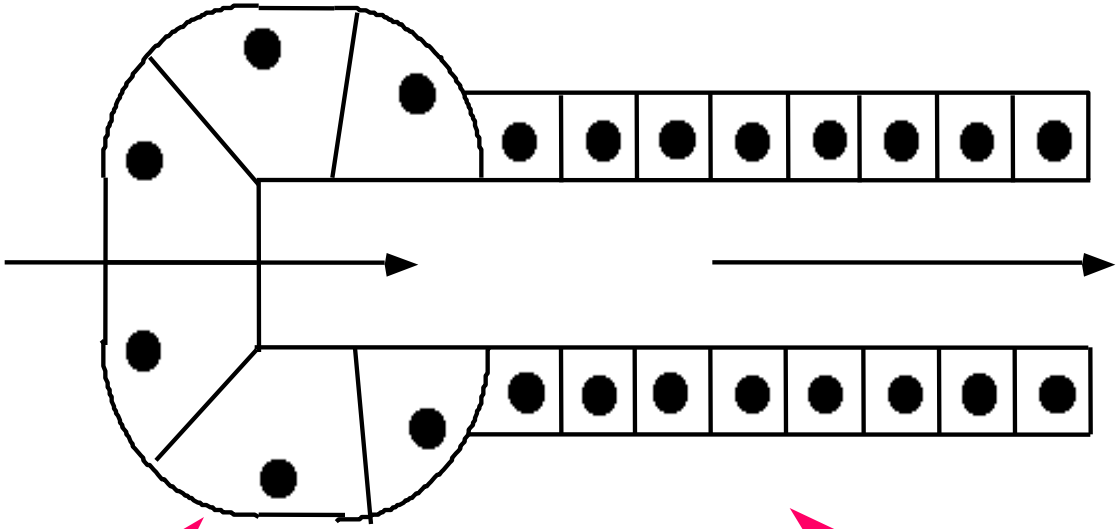

Capillary
Nerve fiber
Endoplasmic reticulum
Golgi apparatus
Secretion
Basement membrane
Mitochondria
Ribosomes
Zymogen granules

Figure 64–1

THE SECRETORY UNIT

The basic building block of all salivary glands



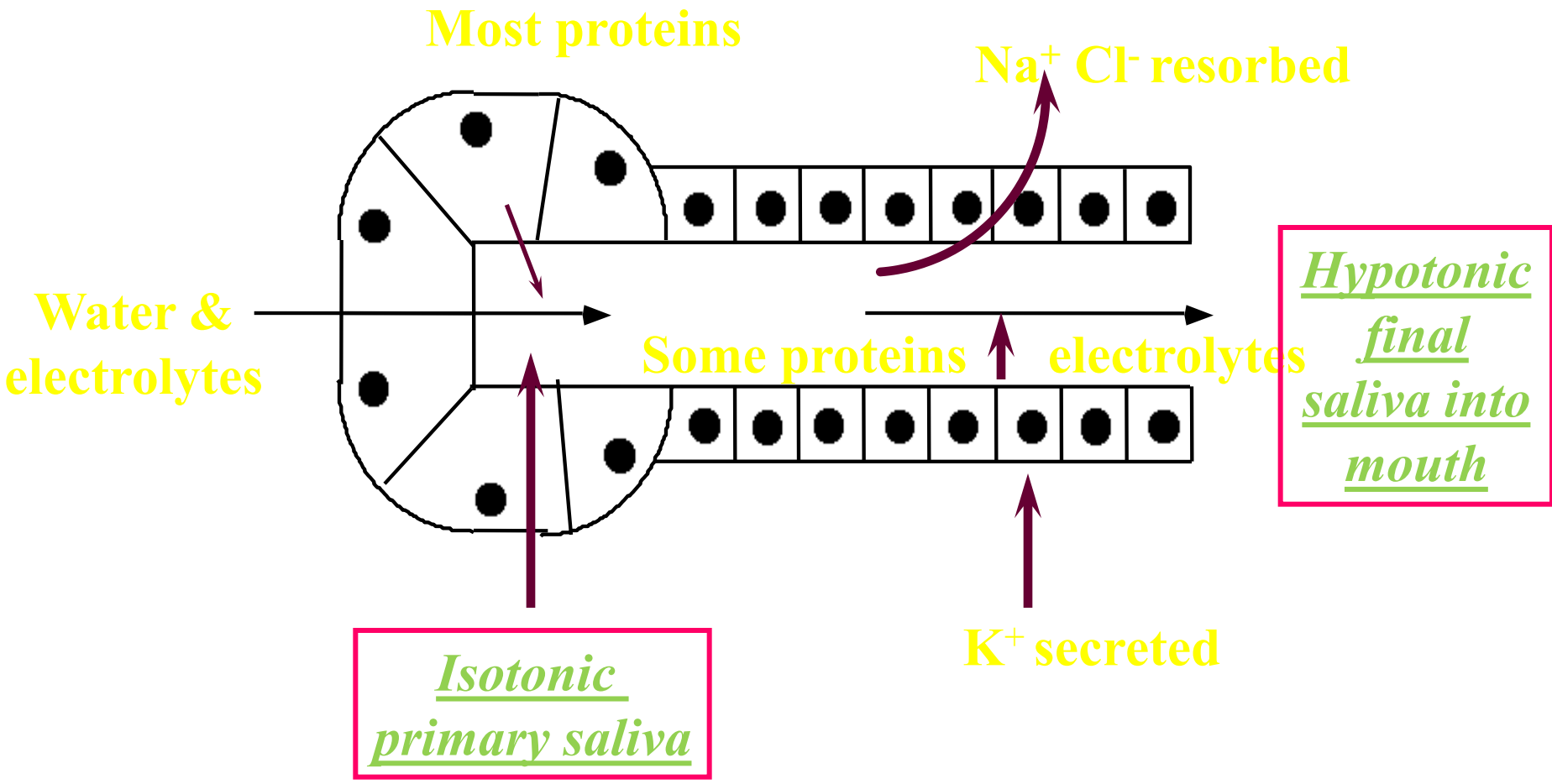
- **ACINI - water and ions derived from plasma.**
- **Saliva formed in acini flows down DUCTS to empty into the oral cavity.**

Secretion of Ions in Saliva :

- Saliva contains especially *large* quantities of Potassium and Bicarbonate ions.
- *Sodium and Chloride* ions are several times *less* in saliva than in plasma.
- Mechanism of saliva secretion:
- The *Acini* secrete a *primary secretion* that contains ptyalin and/or mucin in a solution of ions in concentrations not greatly different from those of typical extracellular fluid.
- As the primary secretion flows through the *Ducts*, *two major active transport processes take place* that markedly modify the ionic composition of the fluid in the saliva.

- First, ***sodium*** ***ions*** are ***actively reabsorbed*** from all the salivary ducts and ***potassium*** ***ions*** are ***actively secreted*** in exchange for the Na
- Second, ***bicarbonate*** ***ions*** are secreted by the ductal epithelium into the lumen of the duct
- Under resting conditions***:***
- ***Sodium and chloride:*** ions in the saliva are only about 15 mEq/L each, about one-seventh to one-tenth their concentrations in plasma.
- Conversely, the concentration of potassium ions is about 30 mEq/L, seven times as great as in plasma, and the concentration of bicarbonate ions is 50 to 70 mEq/L, about two to three times that of plasma.

SALIVA FORMATION



During maximal salivation:

- **The rate of formation of primary secretion by the acini can increase as much as *20-fold.***
- **This acinar secretion then flows through the ducts so rapidly that the ductal reconditioning of the secretion is considerably reduced. Therefore, when copious quantities of saliva are being secreted, *NaCl* concentration is about *One-half or two-thirds* that of plasma, and the *K* concentration rises to only *Four times* that of plasma.**

MAJOR FUNCTIONS OF SALIVA

- Solvent
- Buffering
- Lubrication
- Remineralization
- Digestion
- Anti-bacterial
- Anti-fungal
- Temperature regulation
- Production of growth factors and other regulatory peptides

Function of Saliva for Oral Hygiene

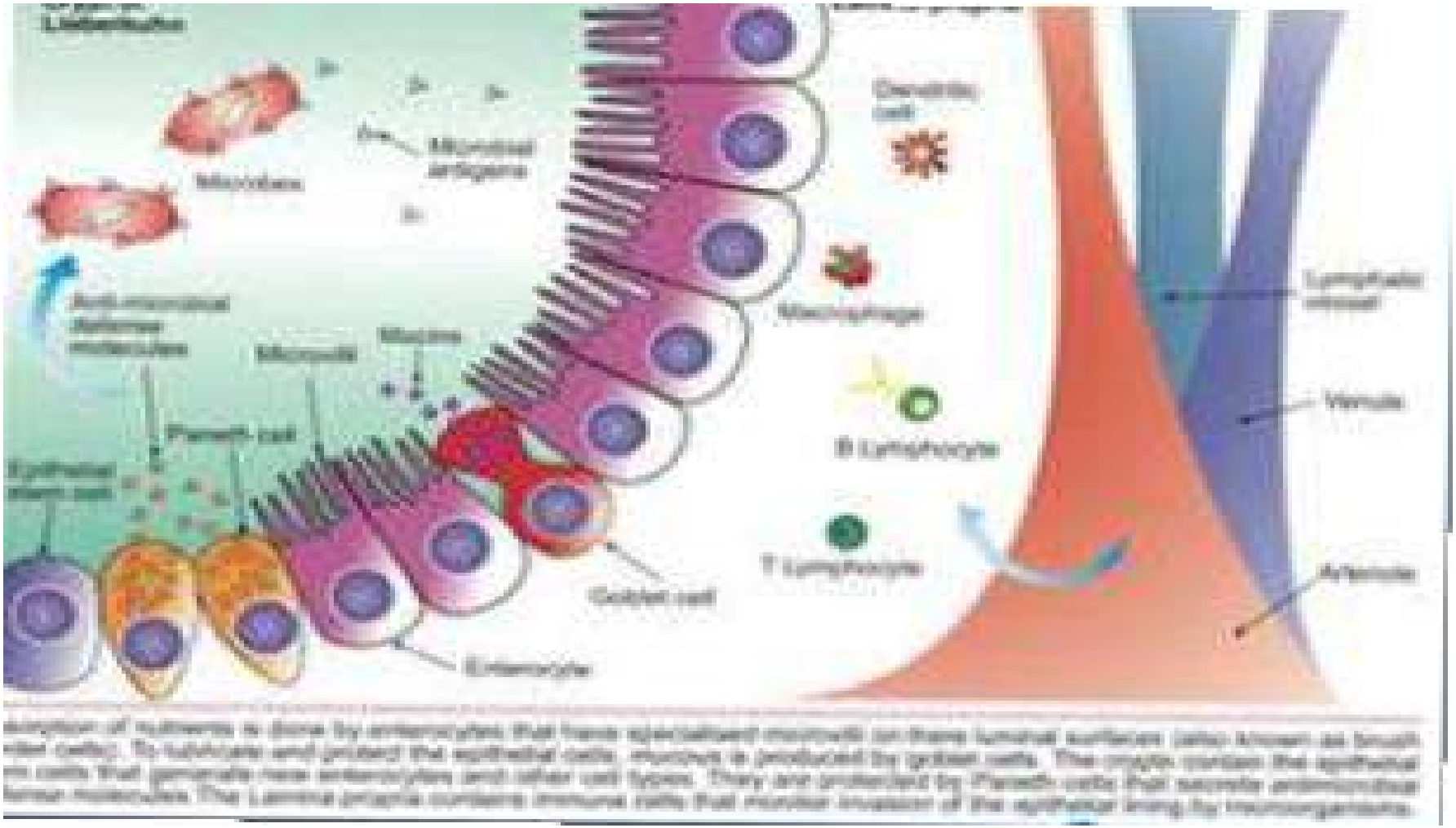
About *0.5 milliliter* of saliva, almost entirely of the mucous type, is secreted each minute.

- The flow of saliva itself helps wash away pathogenic bacteria, as well as food particles
- Saliva contains several factors that destroy bacteria. One of these is *thiocyanate ions* and another is several *proteolytic enzymes*-most important, *lysozyme.*
- Saliva often contains significant amounts of *Protein antibodies* that can destroy oral bacteria.

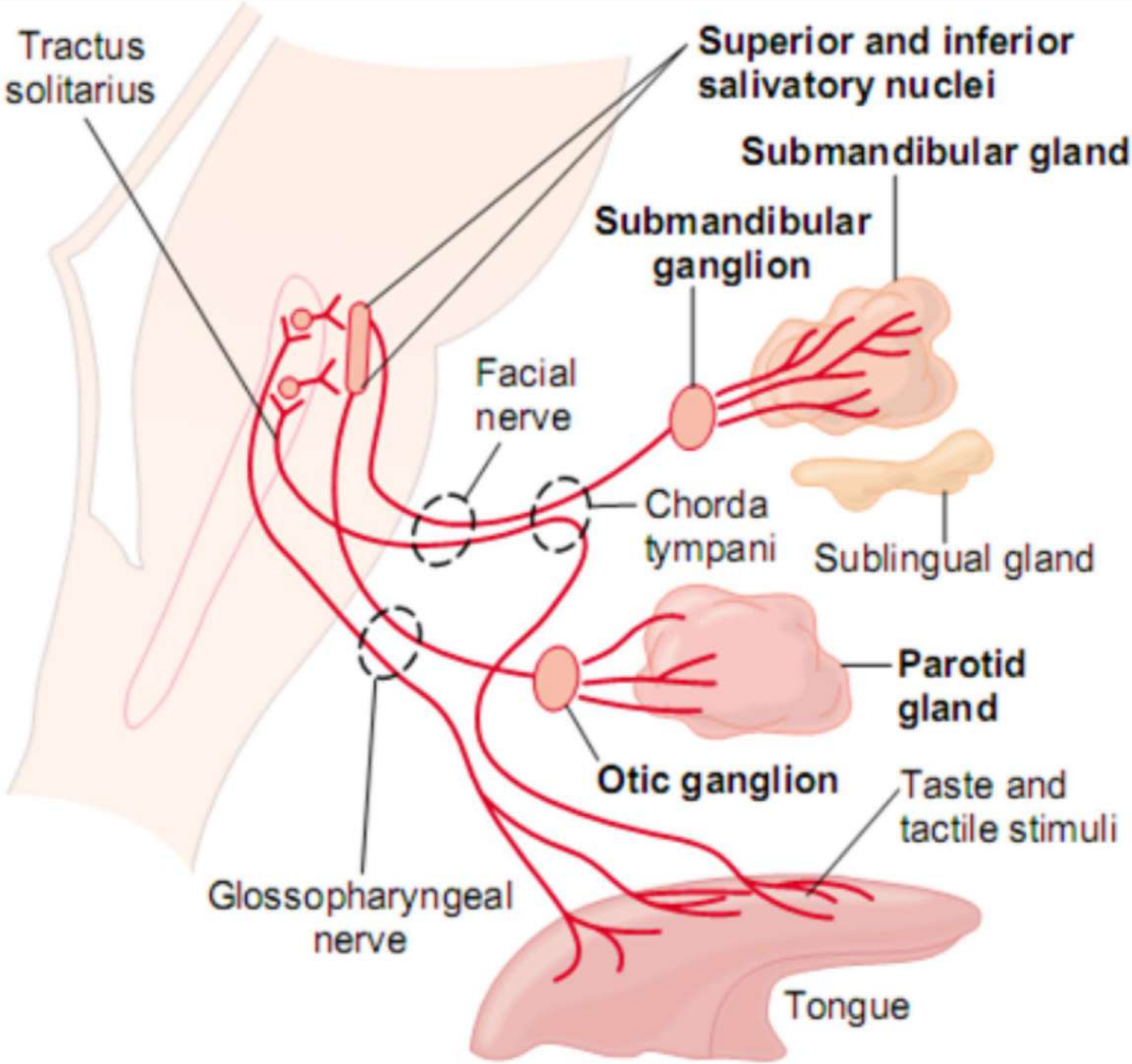
Nervous Regulation of Salivary Secretion

- The salivary glands are controlled mainly by *parasympathetic nervous signals* all the way from the *superior* and *inferior salivatory nuclei* in the brain stem.
- Taste and tactile stimuli from the tongue and other areas of the mouth and pharynx.
- Many *Taste stimuli*, especially the Sour taste (caused by acids), elicit copious secretion of saliva-often *8 to 20* times the basal rate of secretion.
- *Tactile stimuli*, such as the presence of smooth objects in mouth causes marked salivation.

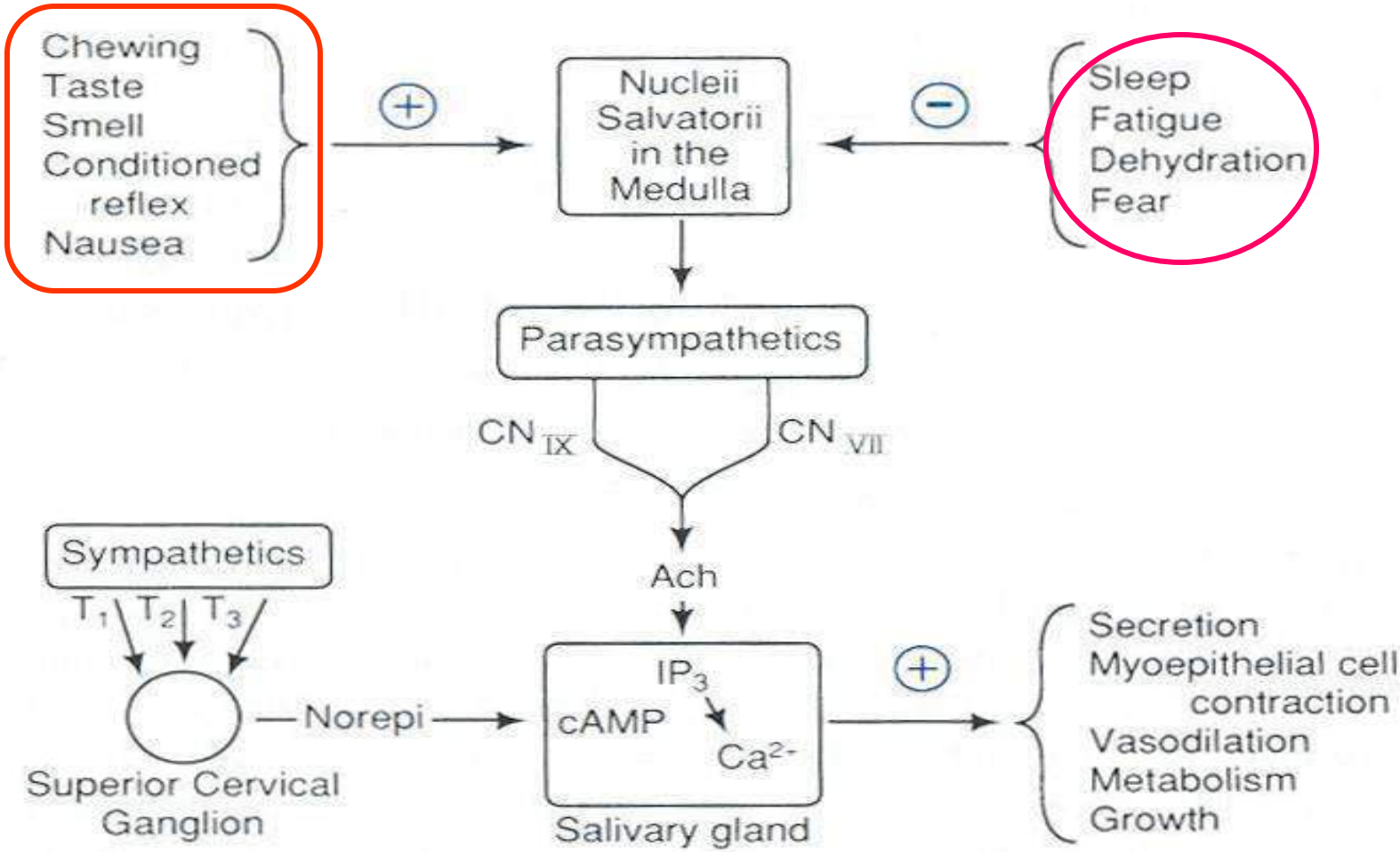
- ***Higher* centers control:** when a person smells or eats favorite foods, salivation is greater than when disliked food is smelled or eaten(*appetite area* of the brain) .
- ***Reflexes originating in the stomach and upper small intestines-*** particularly when irritating foods are swallowed or when a person is nauseated .The saliva, when swallowed, helps to remove the irritating factor in the GIT by diluting or neutralizing the irritant substances.
- ***Sympathetic stimulation*** can also increase salivation a slight amount
- ***Blood supply to the glands kallikrein, bradykinin.***



absorption of nutrients is done by enterocytes that have specialized microvilli on there luminal surfaces (villi). Known as brush border cells). To lubricate and protect the epithelial cells, mucins is produced by goblet cells. The crypts contain the epithelial stem cells that generate new enterocytes and other cell types. They are protected by Paneth cells that secrete antimicrobial tumor molecules. The Lamina propria contains immune cells that monitor invasion of the epithelial lining by microorganisms.


Tractus solitarius
Superior and inferior salivatory nuclei
Submandibular gland
Submandibular ganglion
Facial nerve
Chorda tympani
Sublingual gland
Parotid gland
Otic ganglion
Taste and tactile stimuli
Glossopharyngeal nerve
Tongue

Neural regulation of secretion



3-Esophageal Secretion

- **The esophageal secretions are *Entirely Mucous* and mainly provide lubrication for swallowing.**

- ***Simple mucous glands: main body.***

- ***Compound mucous glands :At lower end& to lesser extent the* initial portion ,which prevent peptic ulceration.**

4-Gastric Secretion

Characteristics of the Gastric Secretions

- ***Oxyntic glands*** **(also called *Gastric* glands) and *Pyloric glands.***
- ***The Oxyntic*** **(acid-forming) glands**
- **Secrete *hydrochloric acid.***
- ***Pepsinogen.***
- ***Intrinsic factor.***
- **M*ucus***
- **located at the body and fundus.**
- **Constituting the proximal 80 % of stomach.**

Pyloric glands

- Secrete mainly ***mucus*** for protection of the pyloric mucosa from the stomach acid.
- They also secrete the hormone ***Gastrin***.
- located in the Antral portion of the stomach, the distal 20 %of the stomach.

Types of Cells

- ***Parietal(oxyntic) cells***
  - **Most distinctive cells in stomach (HCl & intrinsic factor).**
- ***Chief(peptic) cells***
  - **pepsinogen**
- **Mucus neck cells:**
  - **- HCO_3^-**
  - **- Mucus**

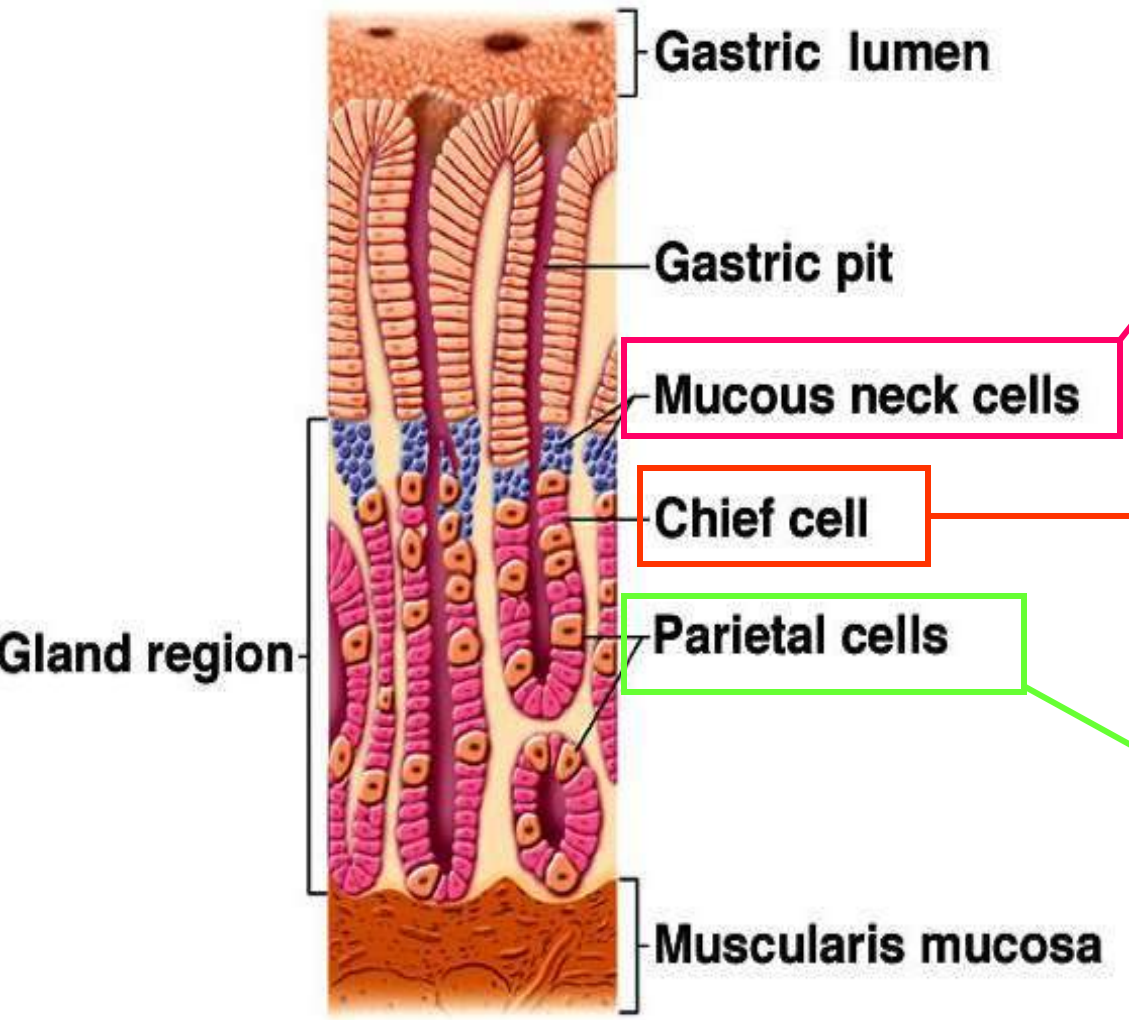
Types of Cells

- ***G Cells:*** **Gastrin (hormone) ---> ↑ HCl secretion**
- ***D Cells:*** **Somatostatin (antrum).**
- ***Enterochromaffin-like cell:*** **Histamine**
- **Present in a recess in deep part of gastric pits**

Gastric juice

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

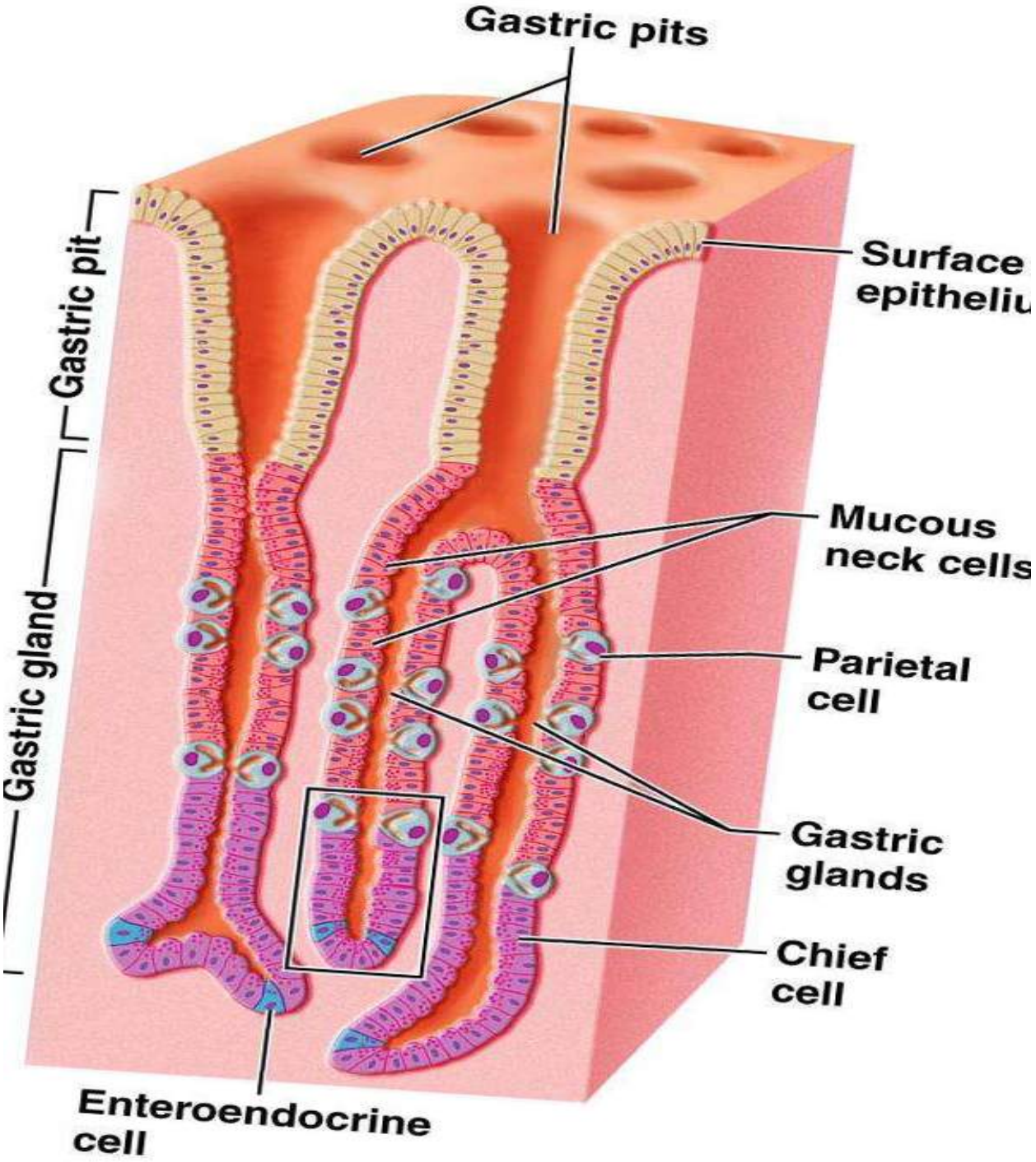
Exocrine gland cells of gastric pits

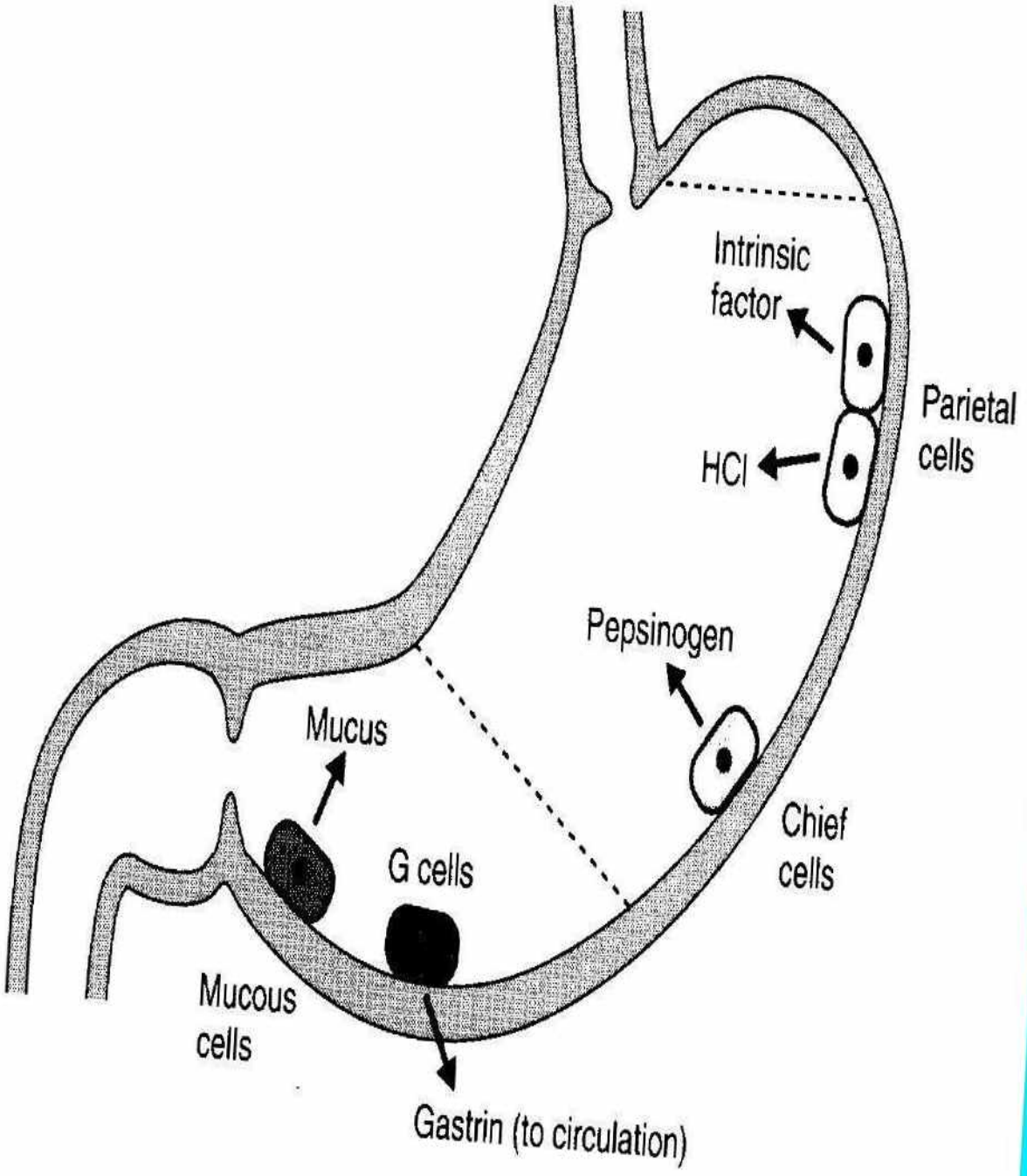


Produce alkaline mucus that covers mucosa layer

Synthesize and secrete the protease precursor known as pepsinogen.

Synthesize and secrete the HCl acid responsible for the acidic pH in the gastric lumen.


Gastric pits
Gastric pit
Gastric gland
Surface epitheliu
Mucous neck cells
Parietal cell
Gastric glands
Chief cell
Enteroendocrine cell



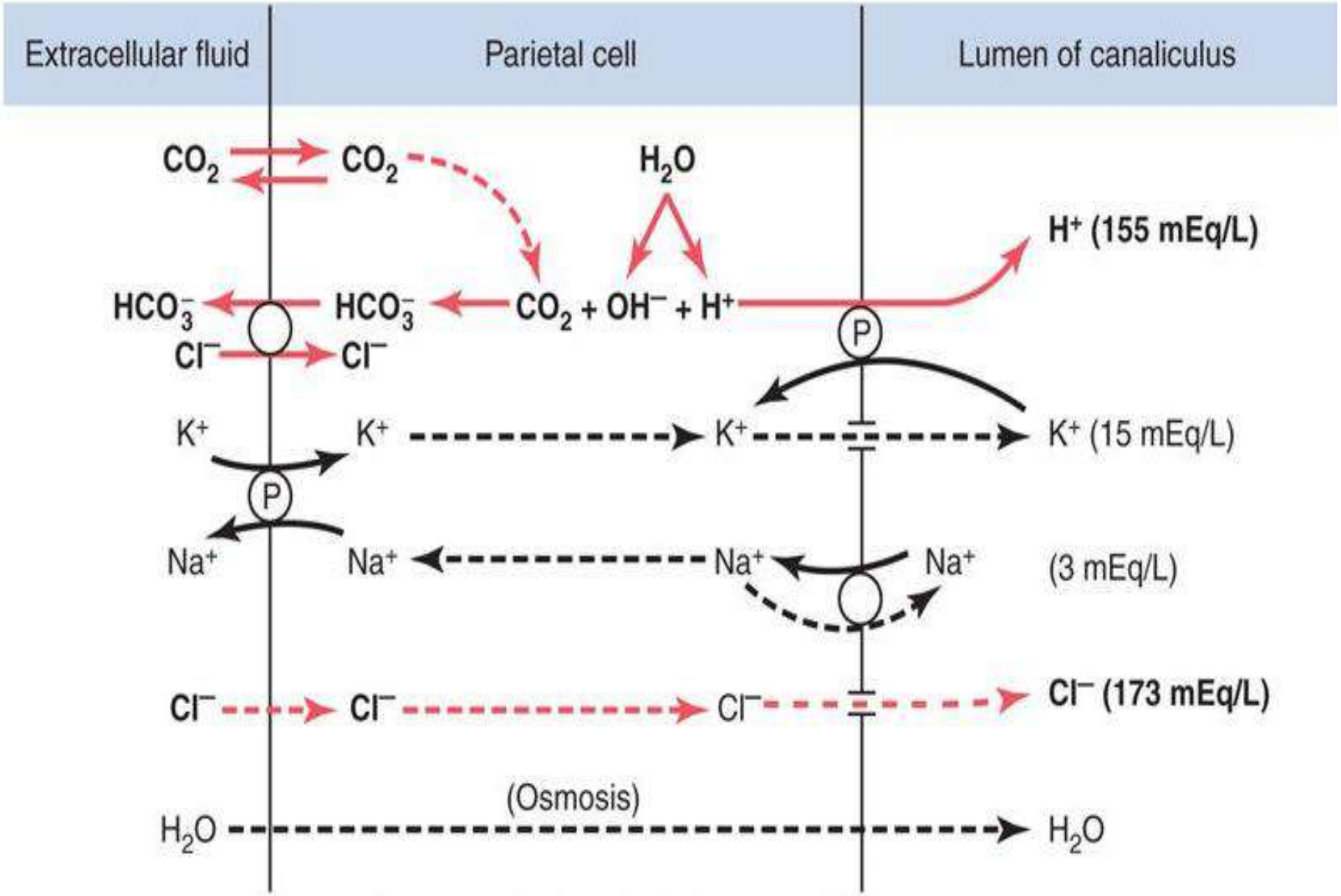
Cell Type	Location	Secretion
Parietal cells	Body	HCL Intrinsic factor
Chief cells	Body	Pepsinogen
G cells	Antrum	Gastrin
Mucous cells	Antrum	Mucus Pepsinogen

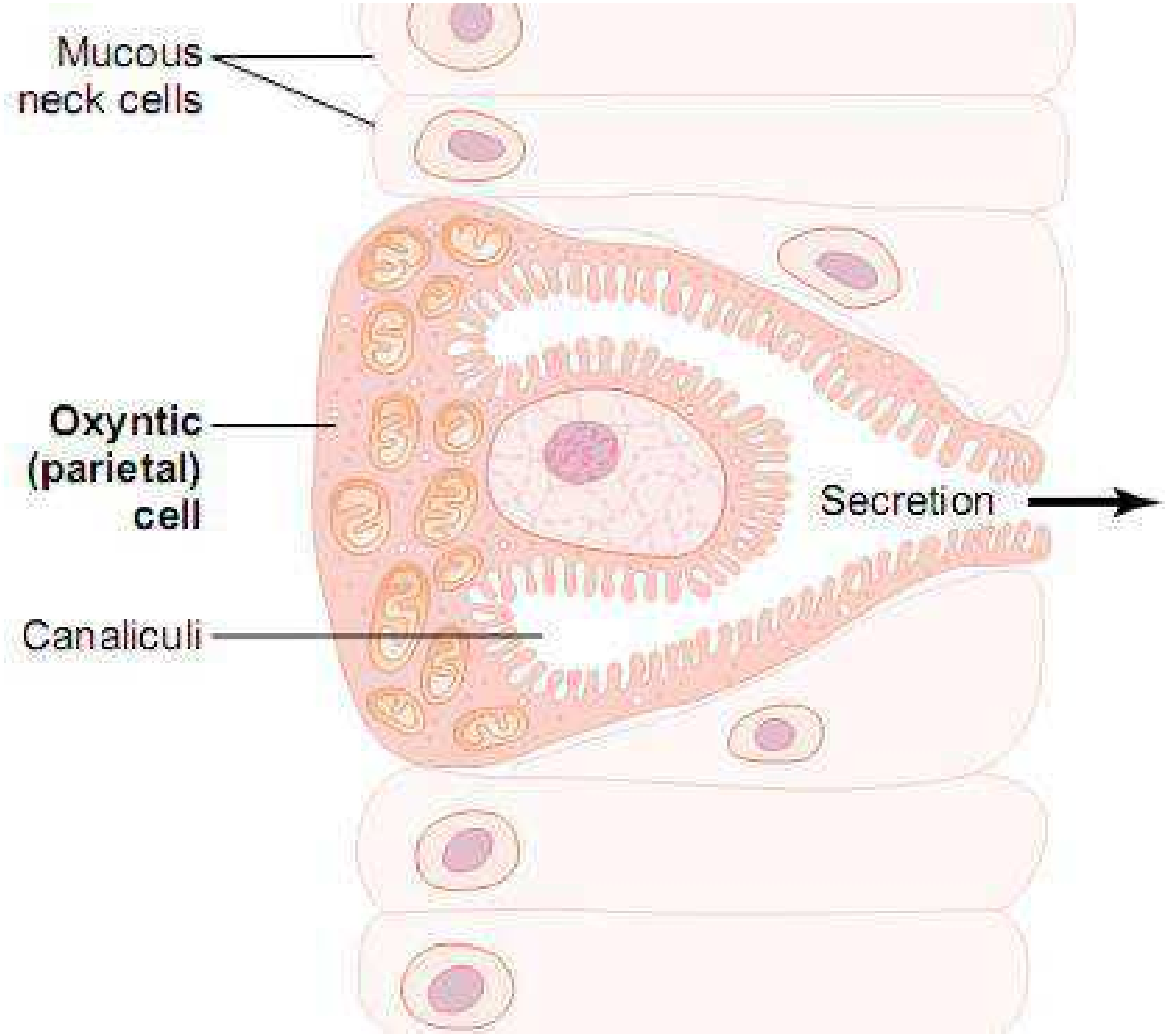
Secretion of hydrochloric acid

- Parietal cells secrete an isotonic acid solution that contains about 160 mmol/L of hydrochloric acid.
- This has pH about 0.8, which is extreme acidic. At this pH, the hydrogen ion concentration is about 3 million times that of the arterial blood. At the same time that hydrogen ions are secreted, bicarbonate ions diffuse into the blood so that gastric venous blood has a higher pH than arterial blood when the stomach is secreting acid *(alkaline tide.)*

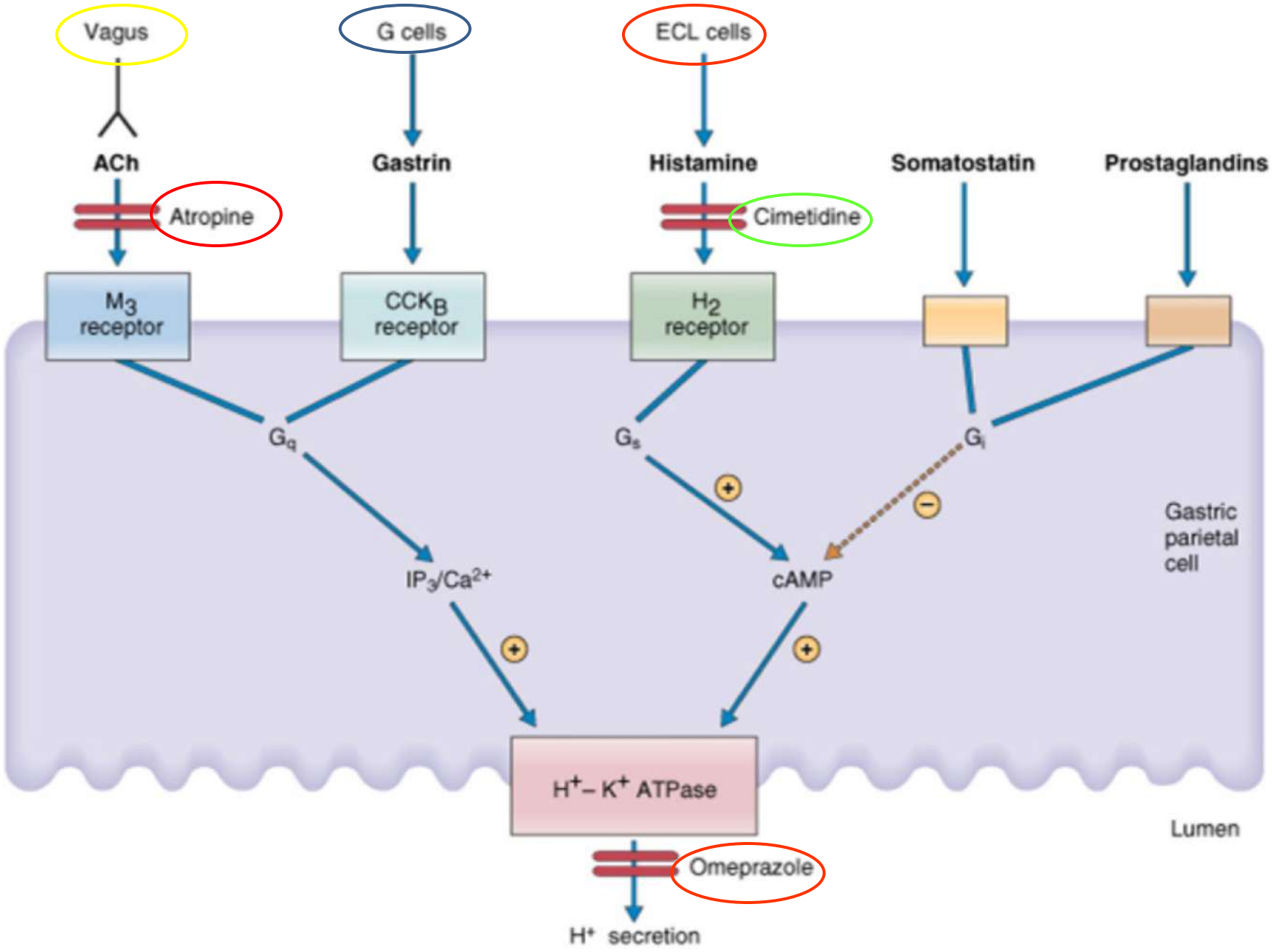
Basic mechanism of HCL secretion

- Water is dissociated in cytoplasm into H^+,OH^-,H+ is actively secreted into (Can),in exchange of K^+ by H-K ATPase shunt.
- CL^- is actively transported from cytoplasm of cell into lumen of canaliculus (Can)
- Na^+ is actively transported in other direction
- K^+, and few Na+ ions passively diffuse as a result to lumen of (Can)
- Na^+ is actively reabsorbed by separate shunt
- Water pass to (Can) by osmosis
- CO2 in cytoplasm combine with OH^- by carbonic anhydrase in to Hco_3 which diffuse to plasma in exchange of CL^-

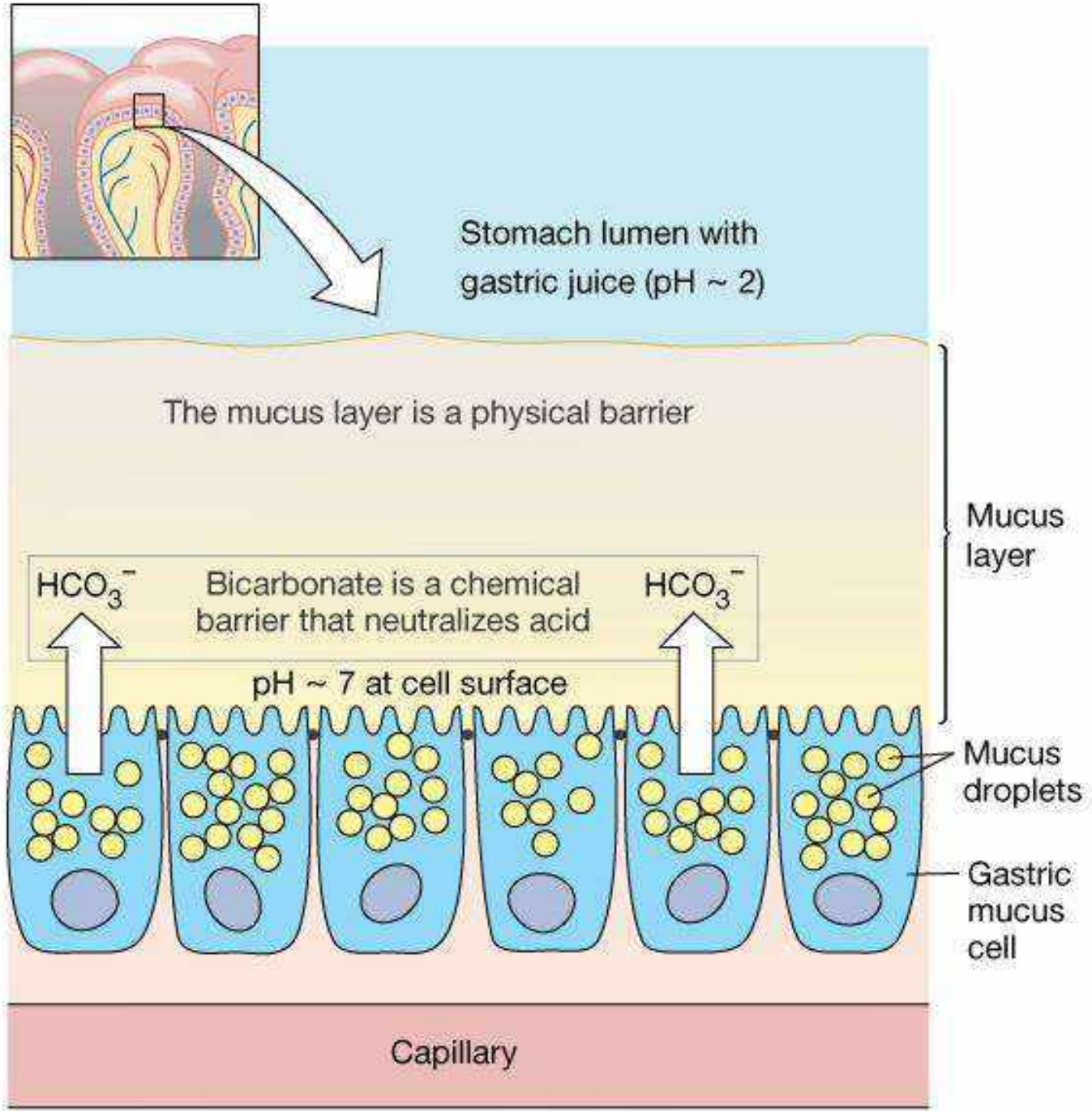

Extracellular fluid
Parietal cell
Lumen of canaliculus
CO_2
CO_2
H_2O
H^+ (155 mEq/L)
HCO_3^-
HCO_3^-
$CO_2 + OH^- + H^+$
Cl^-
Cl^-
P
K^+
K^+
K^+
K^+ (15 mEq/L)
P
Na^+
Na^+
Na^+
Na^+
(3 mEq/L)
Cl^-
Cl^-
Cl^-
Cl^- (173 mEq/L)
(Osmosis)
H_2O
H_2O


Mucous neck cells
Oxyntic (parietal) cell
Canaliculi
Secretion

- **Basic Factors That Stimulate Gastric Secretion *Are Acetylcholine, Gastrin, and Histamine***
  - **Secretion and Activation of Pepsinogen.**
  - **Secretion of Intrinsic Factor by Parietal Cells .**
  - **Pyloric Glands-Secretion of Mucus and Gastrin .**
  - **Surface Mucous Cells :They secrete large quantities of *viscid mucus(it is alkaline)* that coats the stomach mucosa with a gel layer of mucus often more than *1 millimeter thick*, thus providing a major shell of protection for the stomach wall, as well as contributing to lubrication of food transport**



- **The stomach's ability to prevent back leak of acid can be attributed to the Gastric barrier due to the formation of alkaline mucus and to tight junctions between epithelia cells .**
- **If this barrier is damaged by toxic substances, such as occurs with excessive use of *Aspirin or NSAIDS, Steroids,Alcohol*, *Vinegar, Bile salts* the secreted acid does leak down an electrochemical gradient into the mucosa, causing stomach mucosal damage.**



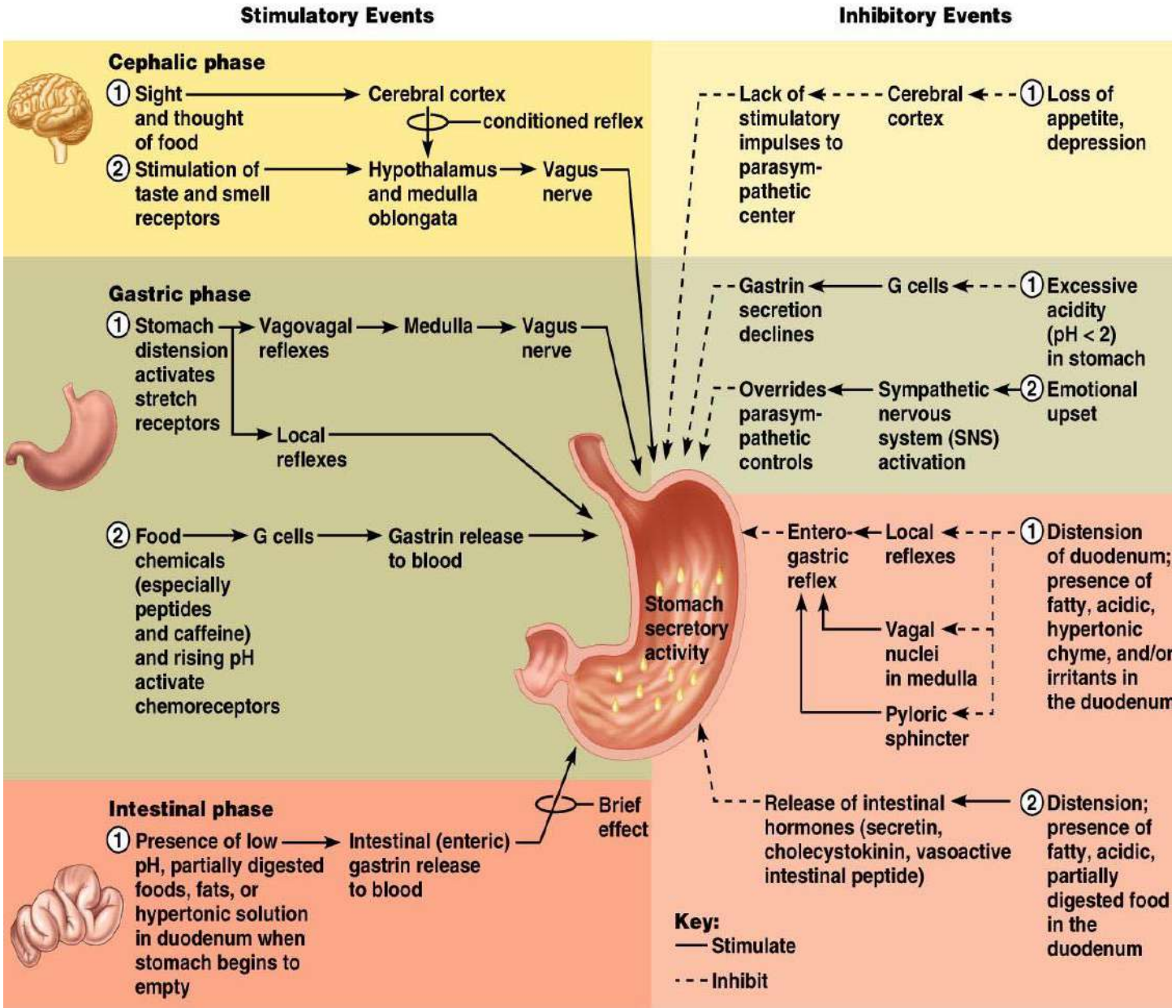
Neural & Hormonal Control of Gastric Secretion

- Vagus nerve (neural effector).
- Gastrin (hormonal effector).
- Enterochromaffin-like cells Histamine ---→H_2 receptor (parietal cells) → acid secretion.

Stomach: Regulation of Secretion and Motility

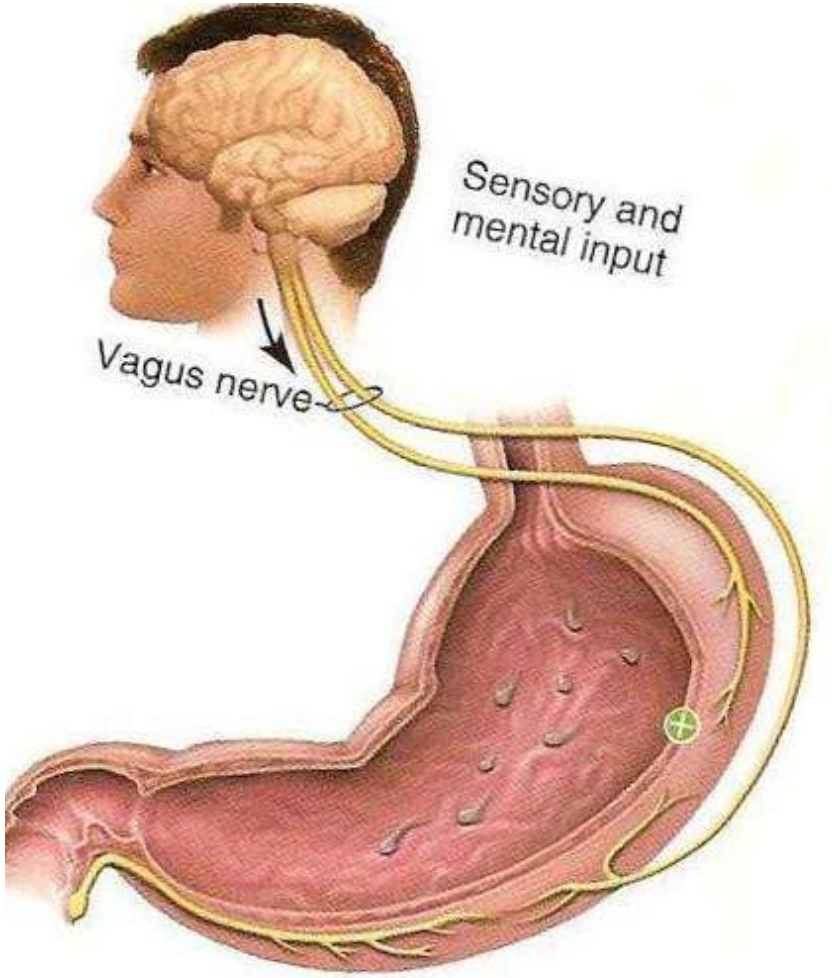
3 phases

- ***Cephalic***
- ***Gastric***
- ***Intestinal***



Stomach: Regulation of Secretion and Motility

1. *Cephalic phase*
   - Stimuli
     - Sight
     - Smell
     - Taste
     - Thoughts/Memories
   - Effect
     - Parasympathetic impulses increase gastric secretion

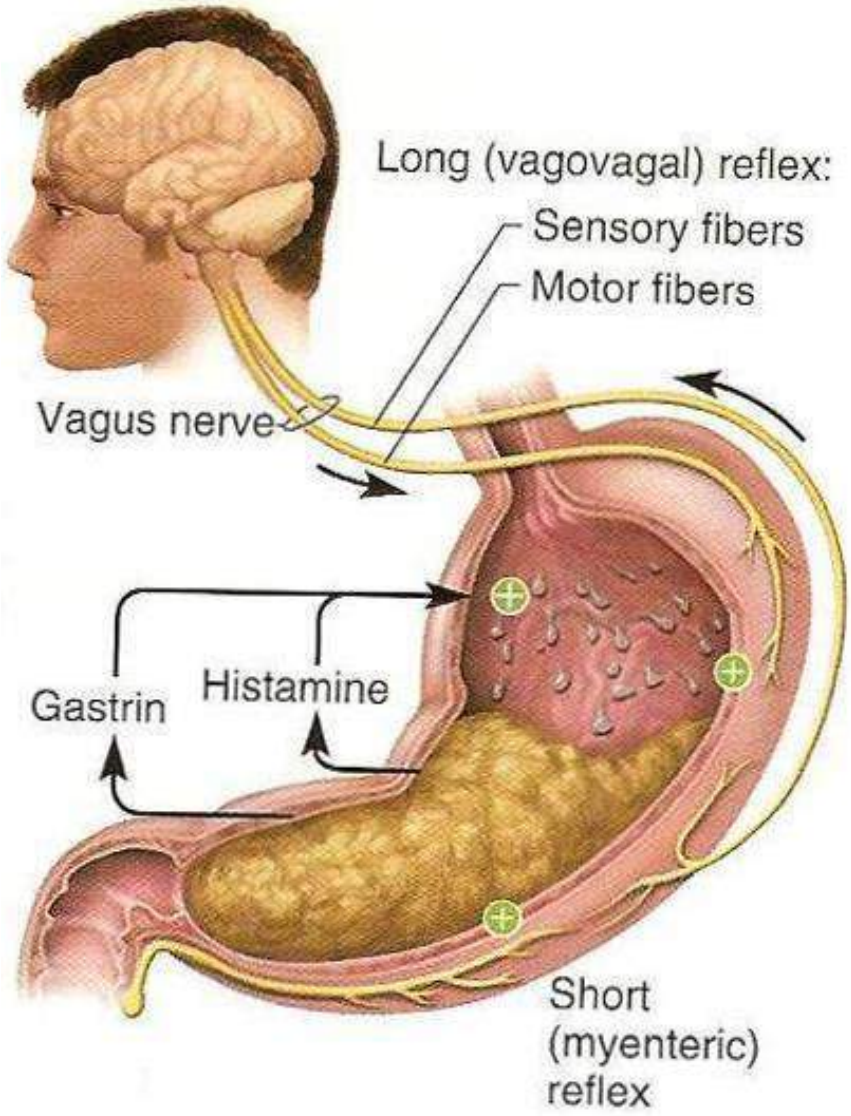


Stomach: Regulation of Secretion and Motility

2. Gastric phase

- ***Neural negative feedback mechanisms***

- **Distension activates stretch receptors causing Myenteric and vago-vagal reflexes to release Ach**
  - **Ach stimulates gastric juice secretion**
- **Chemoreceptor's respond to partially digested proteins, caffeine and rising pH**
  - **Stimulate gastric secretion from G cells**

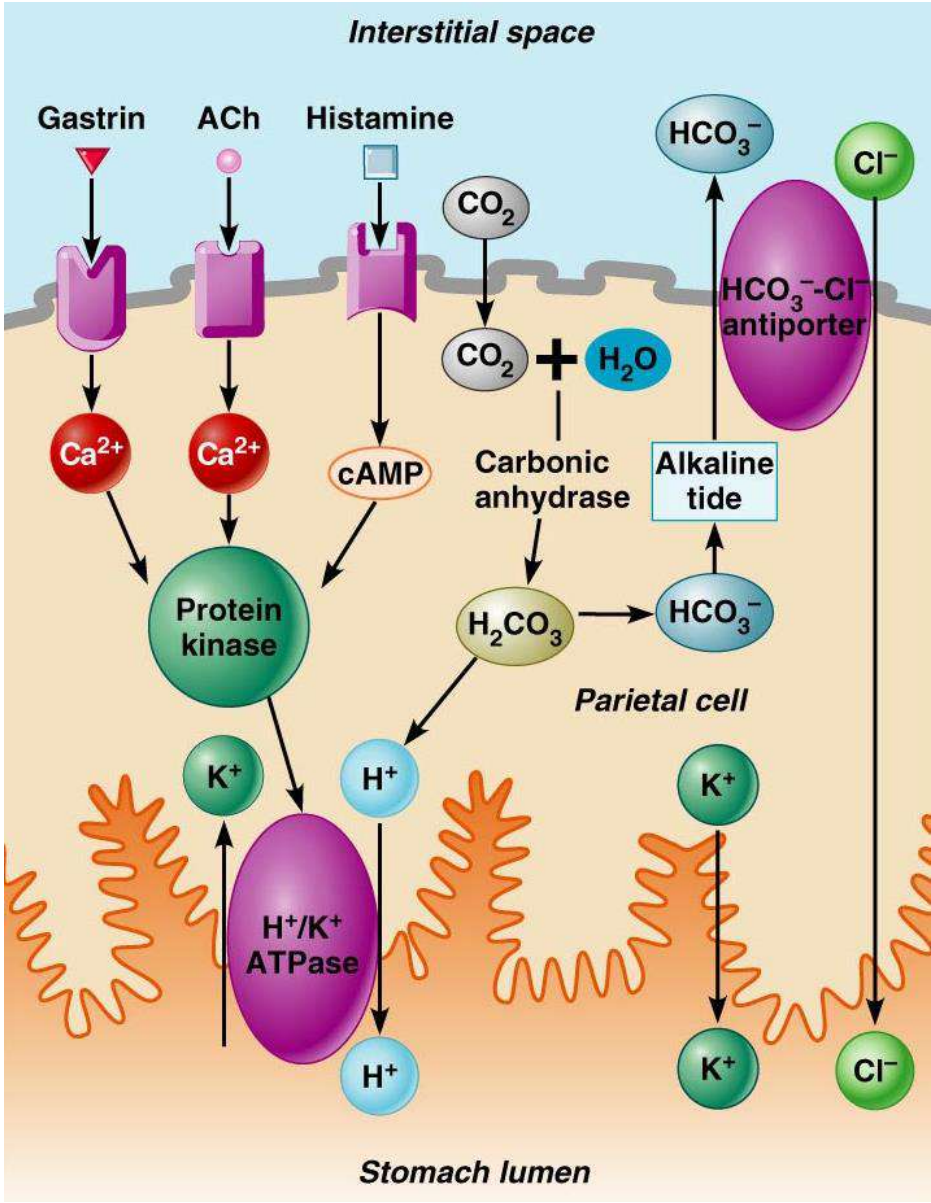


Stomach Regulation of Secretion and Motility

2. Gastric phase (cont.)

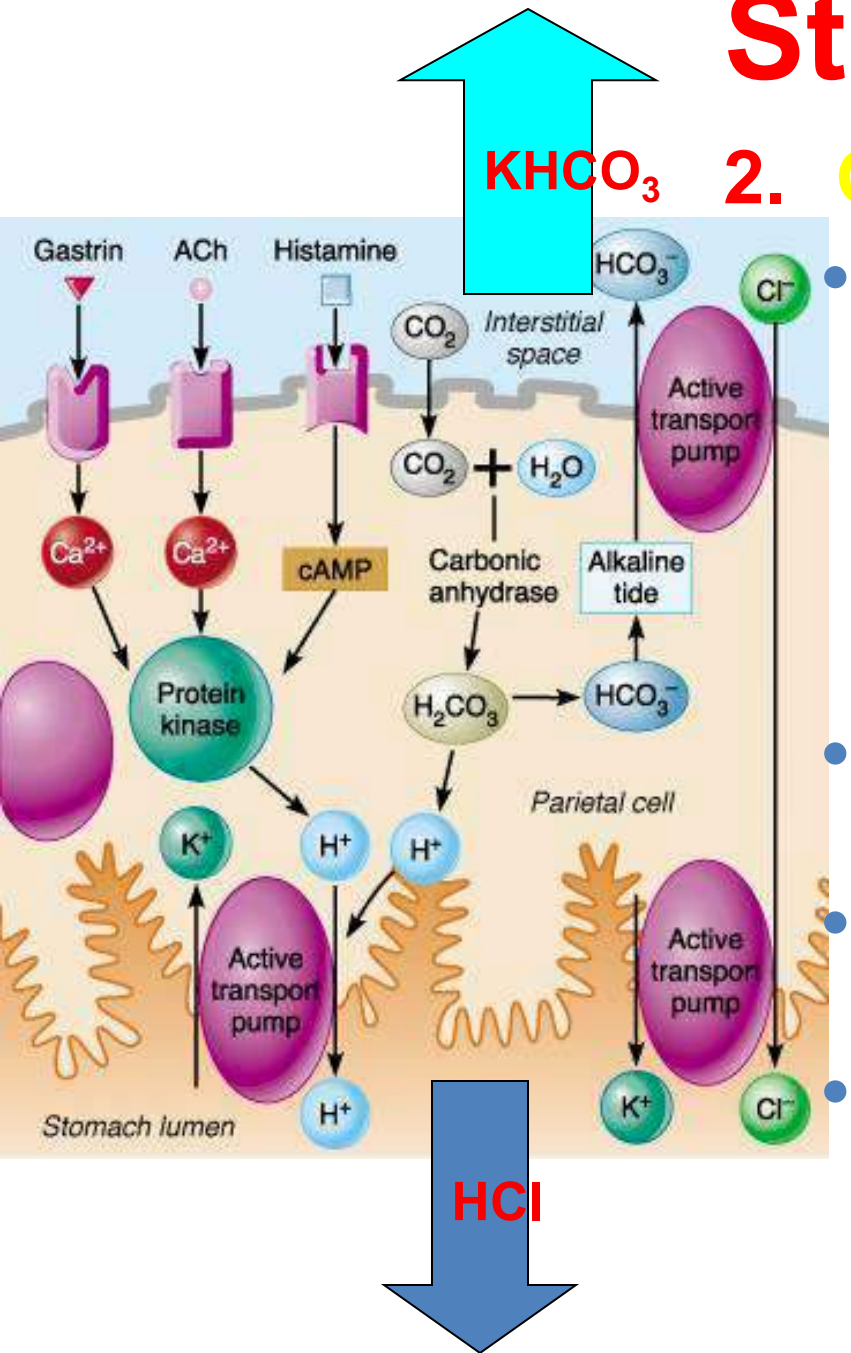
- ***Gastrin***

- Inhibited at pH less than 2
- Gastrin transported in the blood to the gastric glands
- Greatly stimulates HCl secretion
- Stimulates histamine secretion
- Slightly stimulates pepsinogen secretion
- Contracts lower esophageal sphincter
- Relaxes pyloric sphincter
- Increases gastric motility



Stomach

2. Gastric phase (continued)



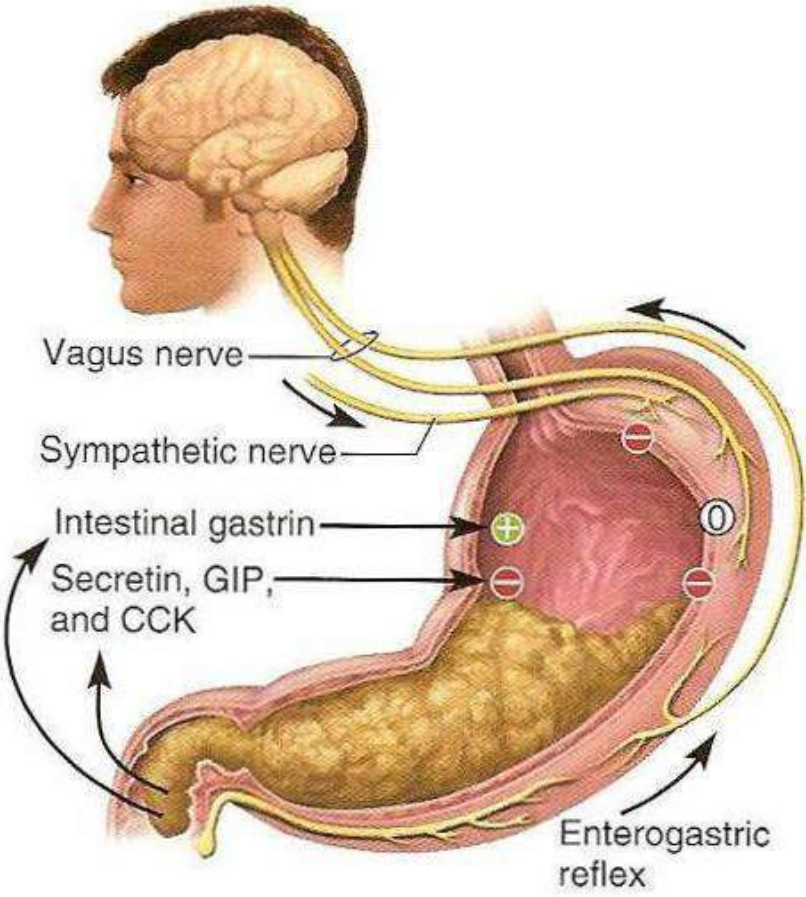
- Control of HCl secreting parietal cells
  - stimulation by three signal chemicals
    - **gastrin**
    - **acetylcholine**
    - **histamine**
- All three needed for strong H^+ secretion
- H^+ pumps work in conjunction with carbonic anhydrase
- blockage of the histamine H_2 receptor decreases HCl secretion
  - Tagamet
  - Zantac

Stomach: Regulation of Secretion and Motility

3. Intestinal phase has excitatory and inhibitory components:

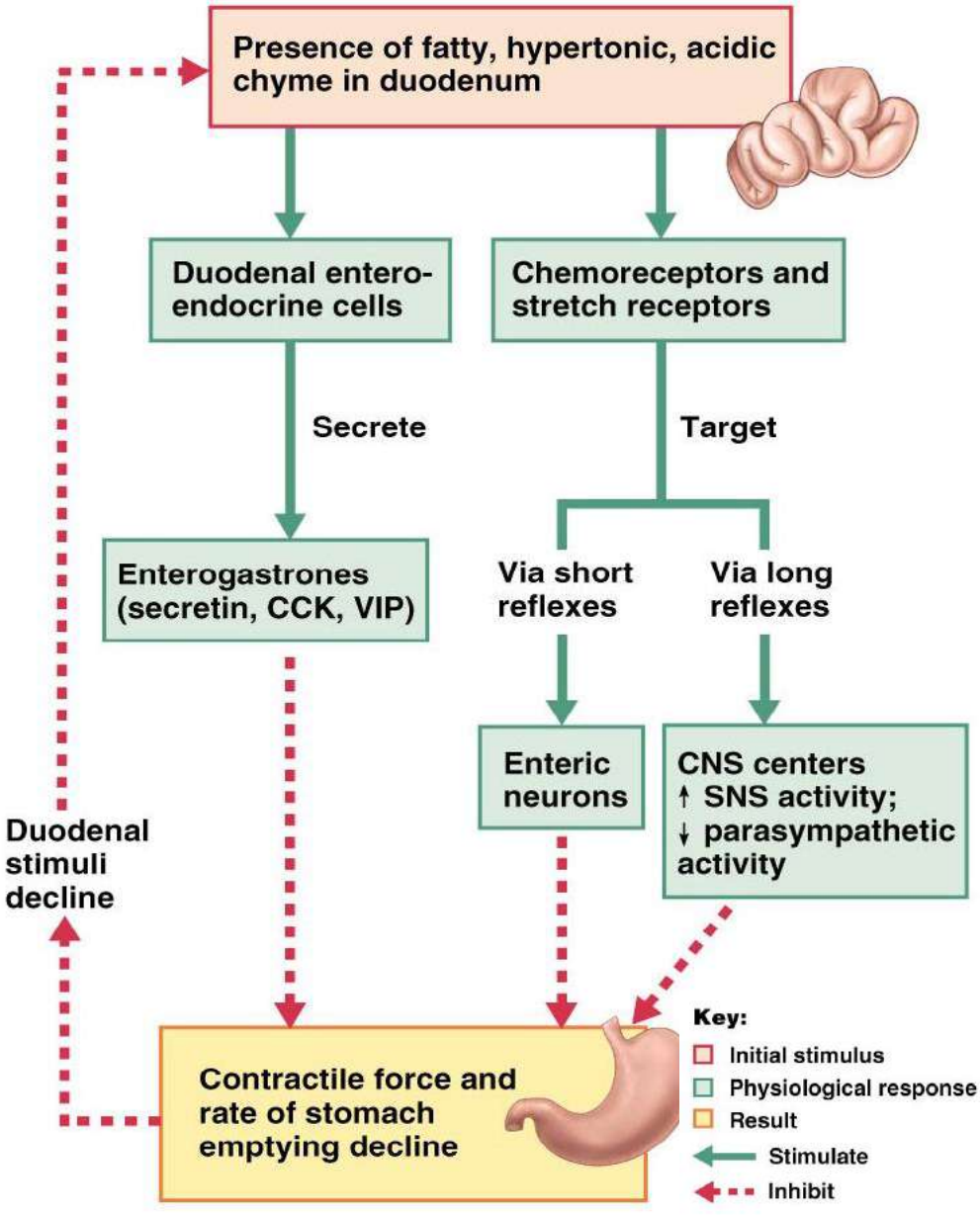
- ***Excitatory***

- **Very short phase**
- **Initiated by chyme entry into duodenum**
- **Stretch receptors stimulate release of intestinal (enteric) gastrin**
- **Chemoreceptor's detect fatty acids, & glucose in the duodenum**
- **Stimulate enteric gastrin release**



Emptying

- Food normally passes through stomach in *4 hours*
- Hormonal/neuronal reflexes regulate gastric emptying
- Large meals and large amounts of liquid increase stomach distension → increasing rate of emptying
- Stomach emptying inhibited by the Enterogastric reflex, enterogastrones, and fat in the duodenum.

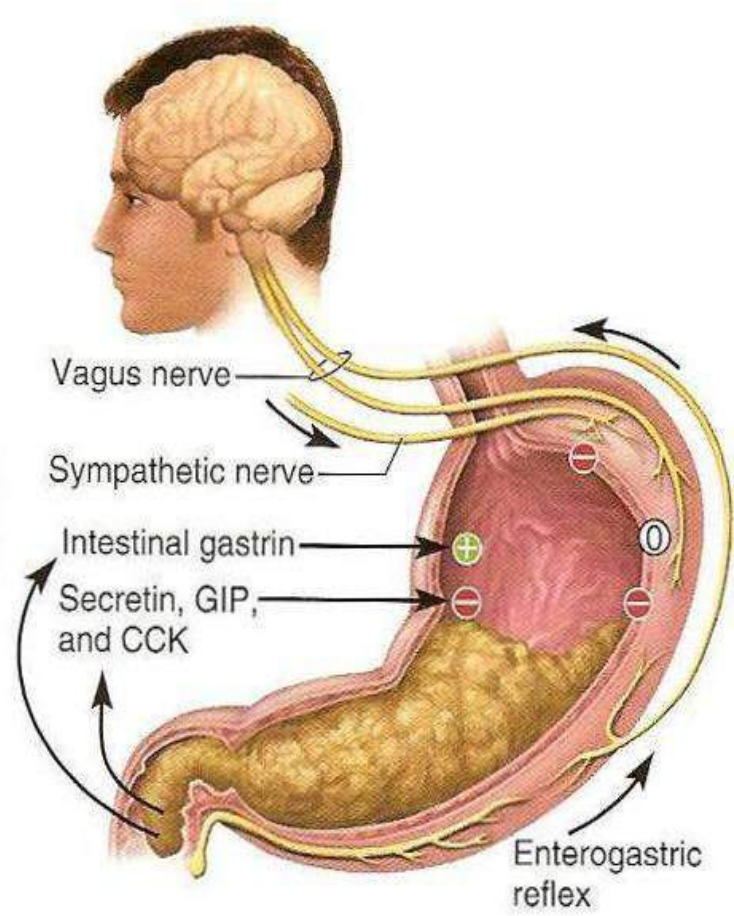


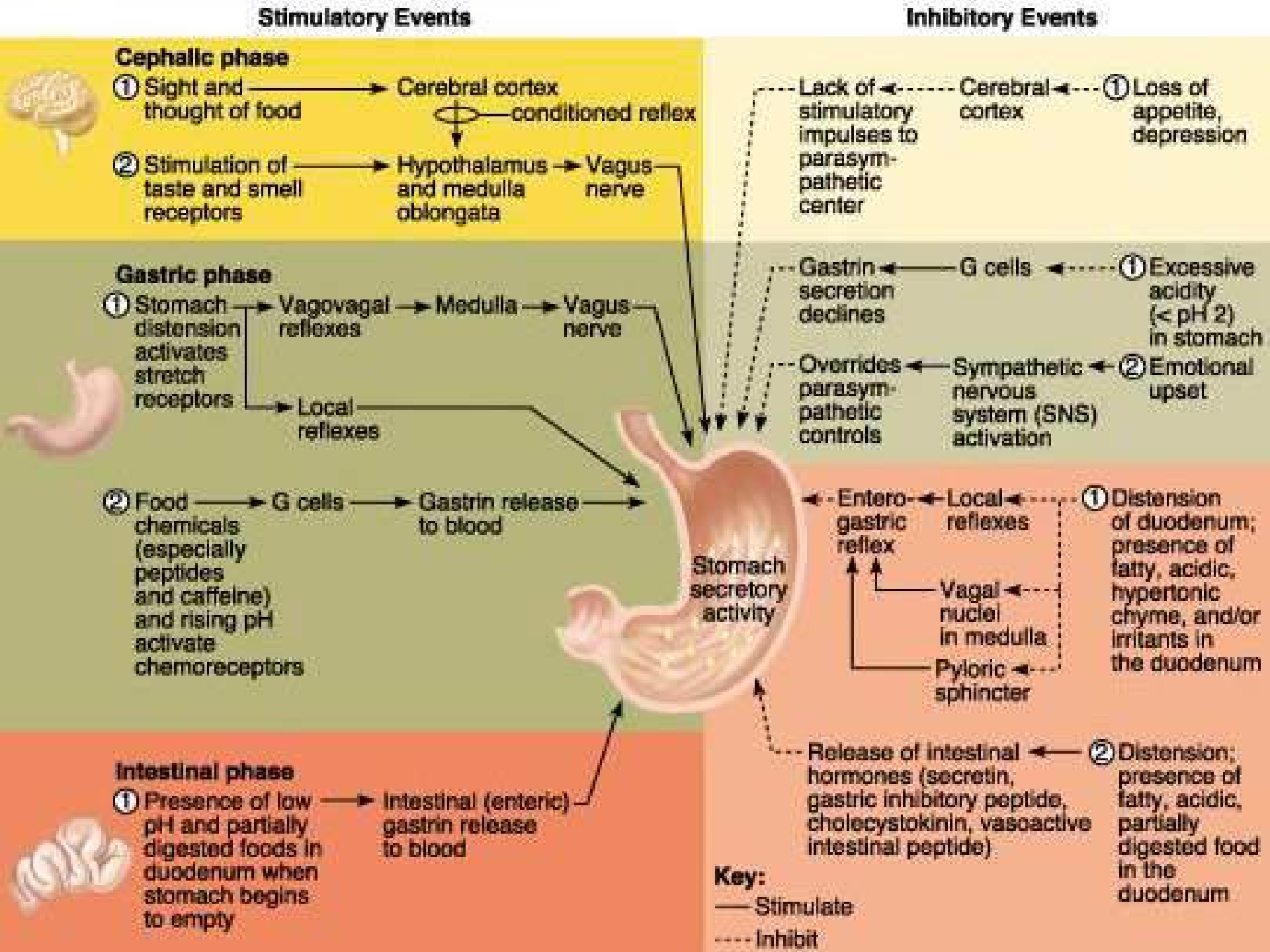
Stomach: Regulation of Secretion and Motility

3. Intestinal phase (cont.)

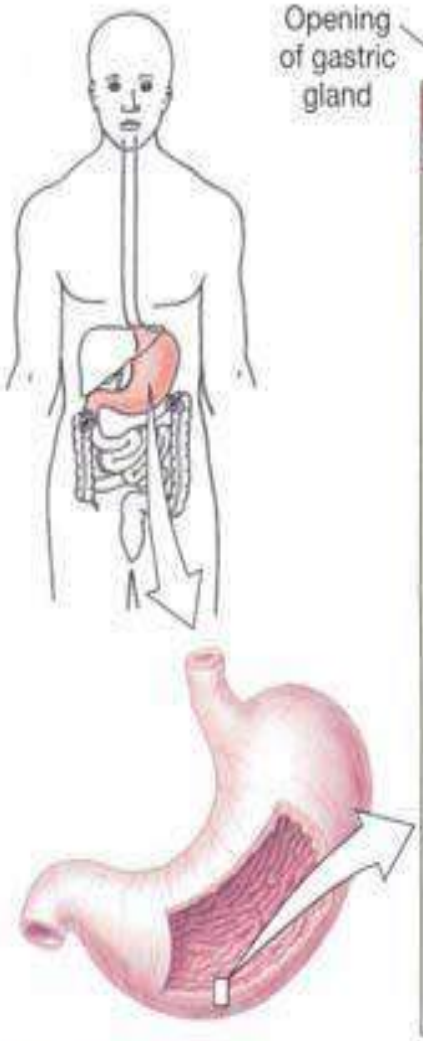
- ***Inhibitory***

- ***Enterogastric reflex:*** **stretch receptors, chemoreceptors trigger 3 reflexes that**
  1. **Inhibit vagovagal reflex**
  2. **Inhibit myenteric reflex**
  3. **Activate sympathetic nervous syste close pyloric sphincter**
  - **Inhibit gastric secretion**
  - **Enterogastrone secretion**
- **Enteroendocrine cells in the small intestine release:**
  - **Cholecystokinin (CCK)**
  - **Gastric inhibitory peptide (GIP)**
  - **Secretin**
  - **Vasoactive intestinal peptide (VIP)**
  - **Hormones inhibit gastric secretion**



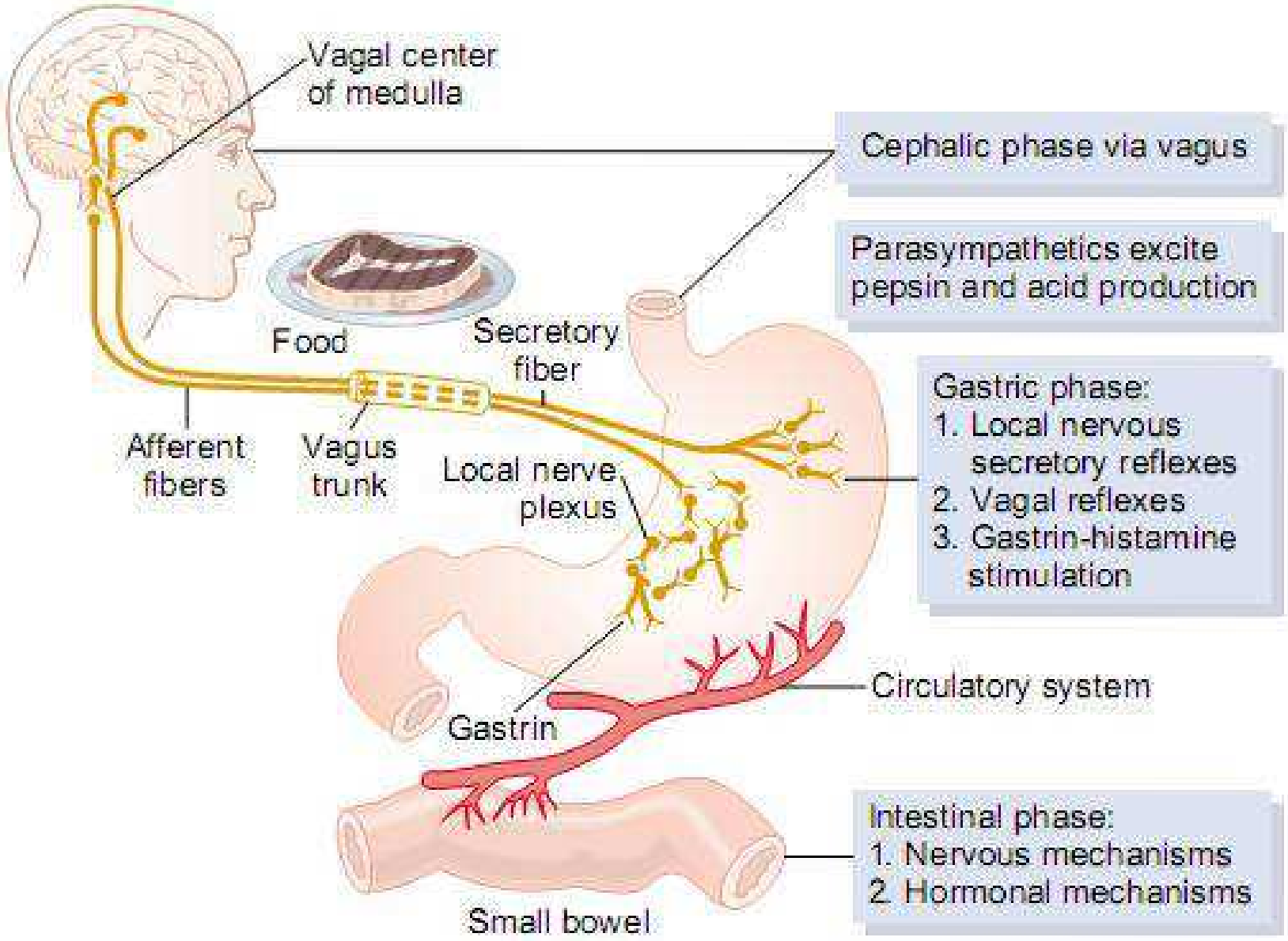

Stimulatory Events
Inhibitory Events
Cephalic phase
① Sight and thought of food
Cerebral cortex
conditioned reflex
② Stimulation of taste and smell receptors
Hypothalamus and medulla oblongata
Vagus nerve
Lack of stimulatory impulses to parasympathetic center
Cerebral cortex
① Loss of appetite, depression
Gastric phase
① Stomach distension activates stretch receptors
Vagovagal reflexes
Medulla
Vagus nerve
Local reflexes
Gastrin secretion declines
G cells
① Excessive acidity (< pH 2) in stomach
Overrides parasympathetic controls
Sympathetic nervous system (SNS) activation
② Emotional upset
② Food chemicals (especially peptides and caffeine) and rising pH activate chemoreceptors
G cells
Gastrin release to blood
Stomach secretory activity
Entero-gastric reflex
Local reflexes
① Distension of duodenum; presence of fatty, acidic, hypertonic chyme, and/or irritants in the duodenum
Vagal nuclei in medulla
Pyloric sphincter
Intestinal phase
① Presence of low pH and partially digested foods in duodenum when stomach begins to empty
Intestinal (enteric) gastrin release to blood
Release of intestinal hormones (secretin, gastric inhibitory peptide, cholecystokinin, vasoactive intestinal peptide)
② Distension; presence of fatty, acidic, partially digested food in the duodenum
Key:
Stimulate
Inhibit

Gastric Glands and secretions



Source	Substance Secreted	Stimulus for Release	Function
Mucous neck cell	Mucus	Tonic secretion; increased with irritation of mucosa	Physical barrier between lumen and epithelium
	Bicarbonate	Secreted with mucus	Buffers gastric acid to prevent damage to epithelium
Parietal cells	Gastric acid (HCl)	Acetylcholine, gastrin, histamine	Activates pepsin; kills bacteria
	Intrinsic factor		Complexes with vitamin B_{12} to permit absorption
Enterochromaffin-like cell	Histamine	Acetylcholine, gastrin	Stimulates gastric acid secretion
Chief cells	Pepsin(ogen)	Acetylcholine, acid, secretin	Digests proteins
	Gastric lipase		Digests fats
D cells	Somatostatin	Acid in the stomach	Inhibits gastric acid secretion
G cells	Gastrin	Acetylcholine, peptides, and amino acids	Stimulates gastric acid secretion

Figure 20-16 Cell types of the gastric mucosa



Figure

Phases

Secretion and Activation of Pepsinogen

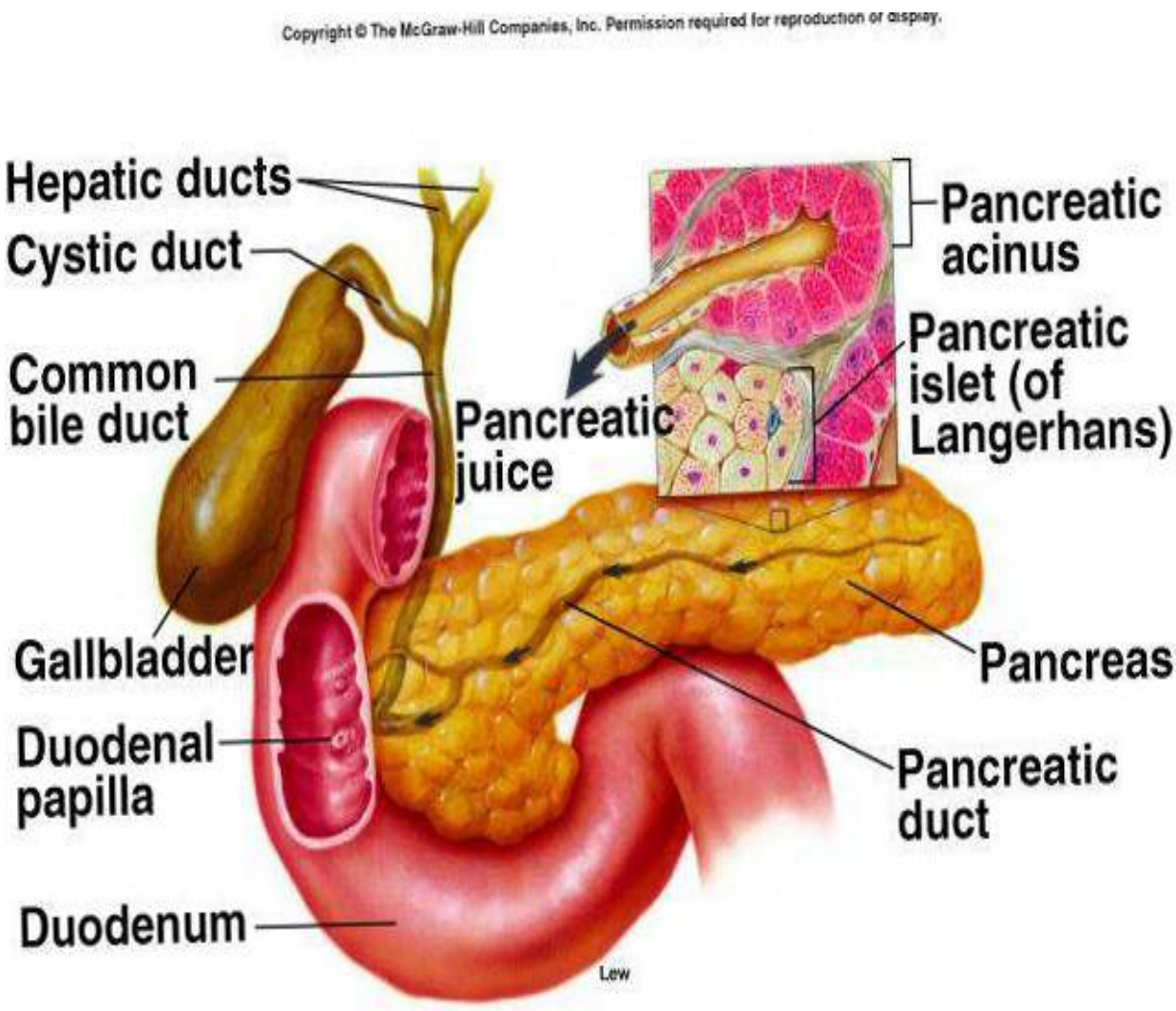
- **Secreted by the peptic and mucous cells of the gastric glands**
- **When pepsinogen is first secreted, it has no digestive activity. However, as soon as it comes in contact with hydrochloric acid, it is activated to form active *pepsin*.**
- **Pepsin functions as an active Proteolytic enzyme in a highly acid medium (optimum pH 1.8 to 3.5), but above a pH of about 5 it has almost no Proteolytic activity and becomes completely inactivated in a short time.**

Regulation of Pepsinogen Secretion

- **(1) stimulation of the *peptic cells* by *acetylcholine* released from the *Vagus nerves* or from the *gastric enteric nervous plexus.***
- **(2) stimulation of peptic cell secretion in response to acid in the stomach. The acid probably does not stimulate the peptic cells directly but instead elicits additional enteric nervous reflexes that support the original nervous signals to the peptic cells.**

Pancreas

- ***Exocrine:***
  - ***Acini:***
- **Secrete pancreatic juice.**
- **Endocrine:**
  - **Islets of Langerhans:**
- **Secrete insulin and glucagon.**



5-Pancreatic Secretion

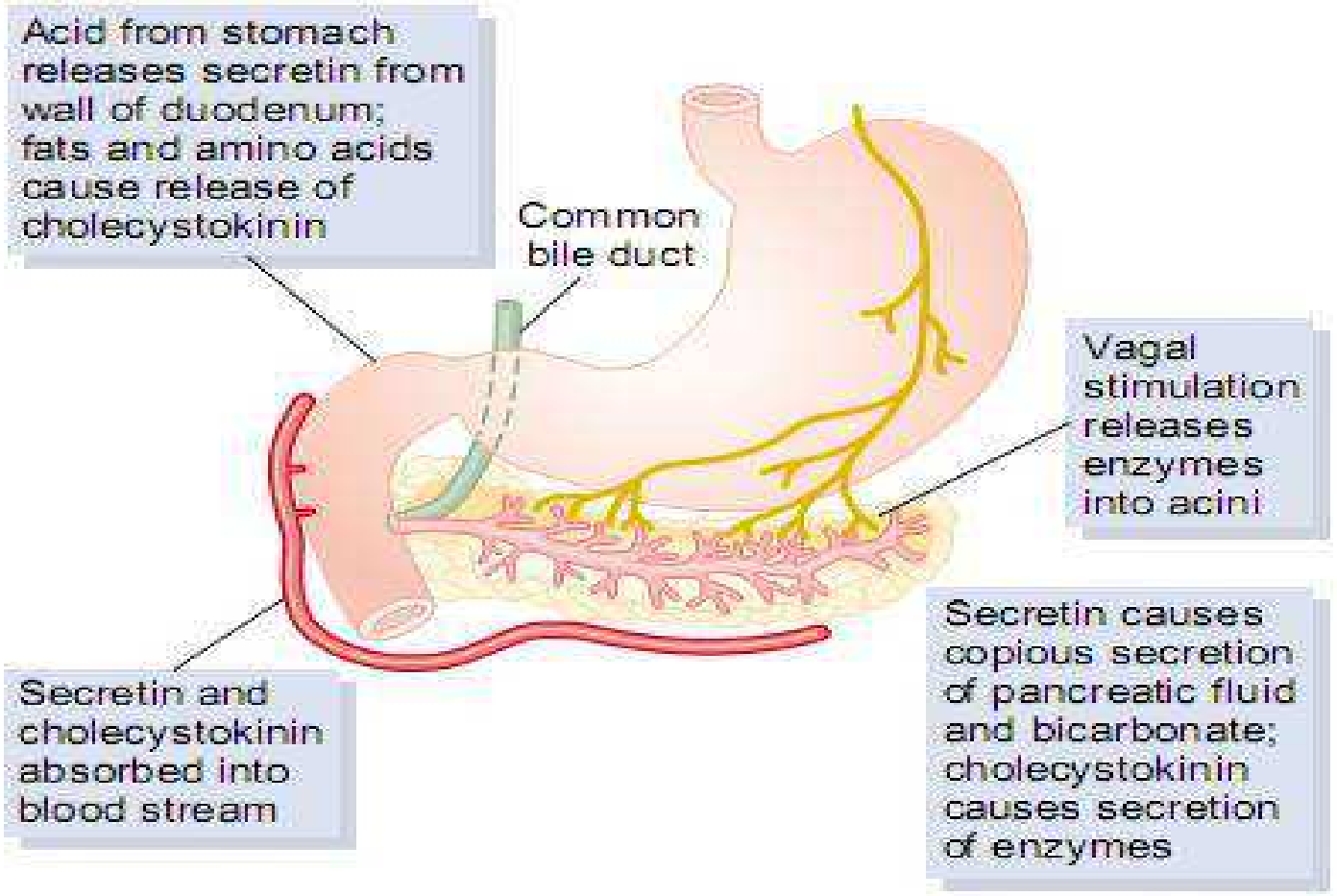
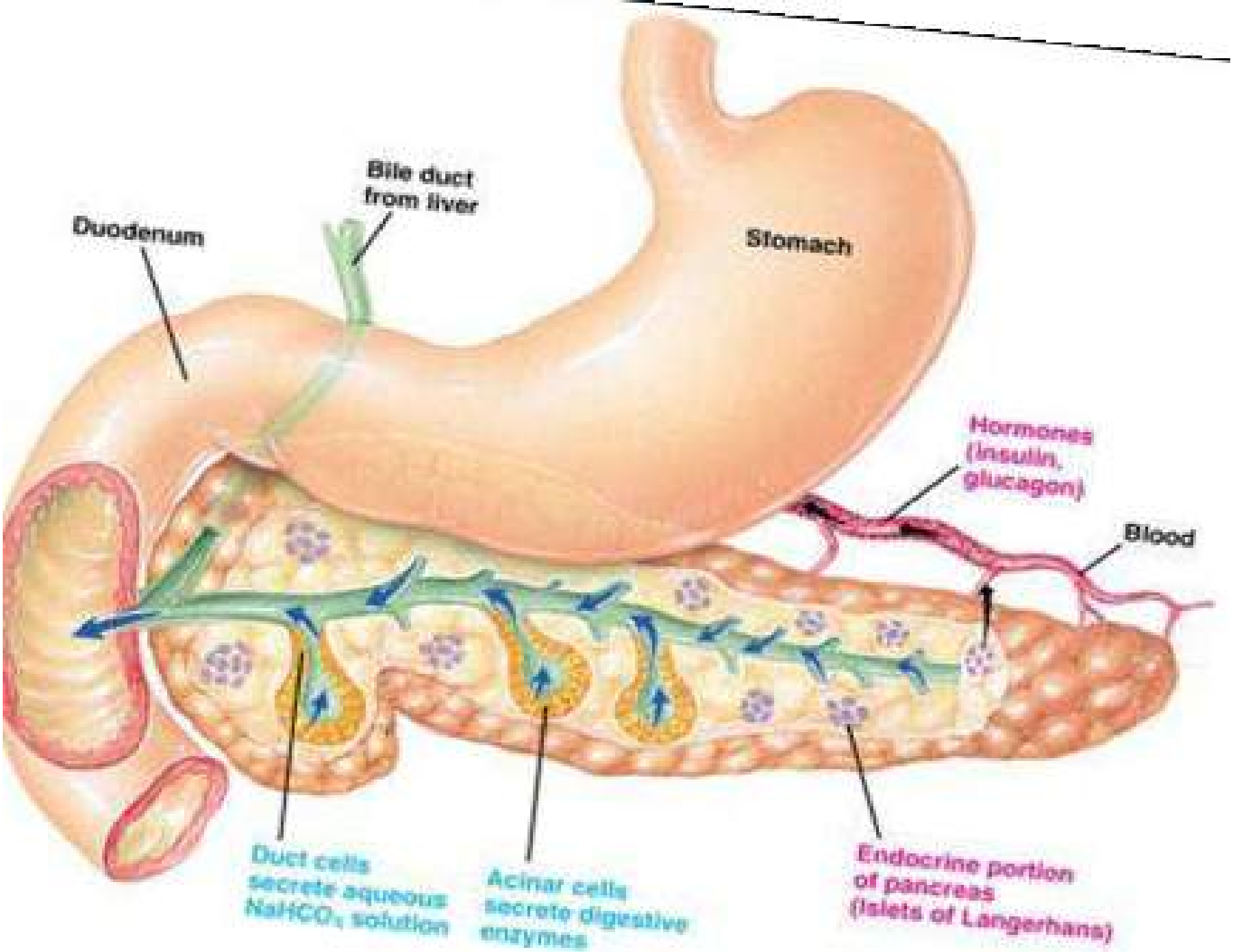


Figure 64–10

Regulation of pancreatic secretion.


Bile duct from liver
Duodenum
Stomach
Hormones (insulin, glucagon)
Blood
Duct cells secrete aqueous $NaHCO_3$ solution
Acinar cells secrete digestive enzymes
Endocrine portion of pancreas (islets of Langerhans)

- **Pancreatic secretion contains *multiple enzymes* for digesting all of the three major types of food: proteins, carbohydrates, and fats. It also contains large quantities of *bicarbonate ions*, which play an important role in neutralizing the acidity of the chyme emptied from the stomach into the duodenum.**

- **Pancreatic enzymes for digesting Proteins are *Trypsin, Chymotrypsin,* and *Carboxypolypeptidase*. By far the most abundant of these is trypsin.**

- **The pancreatic enzyme for digesting Carbohydrates is *pancreatic Amylase*, which hydrolyzes starches, glycogen, and most other carbohydrates (except cellulose) to form mostly disaccharides and a few trisaccharides.**

- **The main enzymes for Fat digestion are:**
- **(1) *Pancreatic lipase*, which is capable of hydrolyzing neutral fat into fatty acids and monoglycerides**
- **(2) *Cholesterol esterase*, which causes hydrolysis of cholesterol esters**
- **(3) *Phospholipase*, which splits fatty acids from phospholipids.**

Pancreas

- **Pancreatic juice**
  - **1.0-1.2 L/day**
  - **Mostly water some salts, bicarbonate, enzymes**
- **Alkaline, pH 7.1-8.2.**
- **Buffers acidic gastric juice, stops pepsin activity, creates proper alkaline pH for enzymes acting in the intestine.**
  - **Enzymes include:**
    - **Pancreatic amylase**
    - **Trypsinogen, Chymotrypsinogen, Procarboxypeptidase (inactive zymogens)**
    - **Pancreatic lipase**
    - **Ribonuclease and deoxyribonuclease**

A-aqueous Pancreatic Secretion

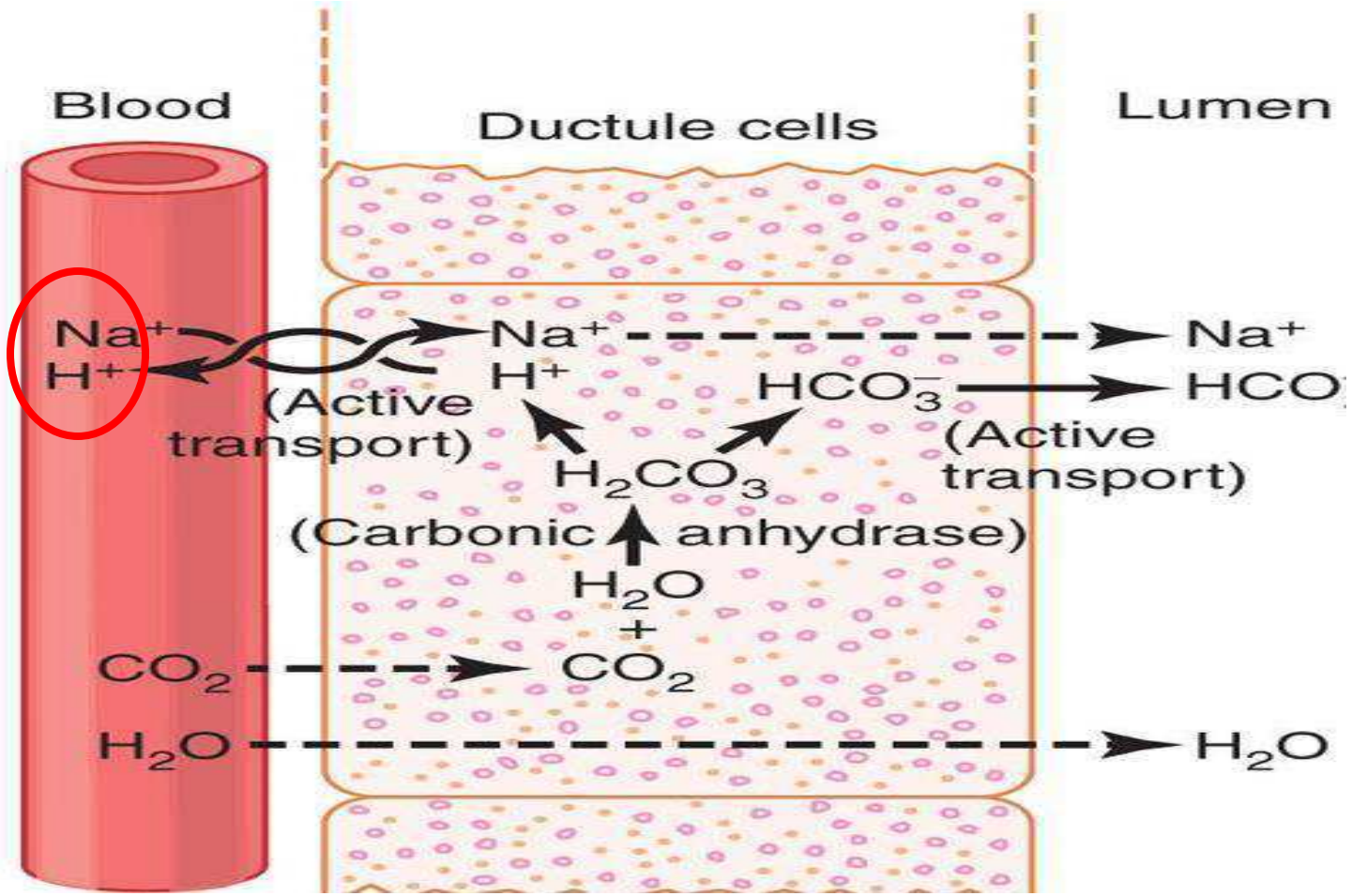
- **Composition;**
  - **Water**
  - **HCO_3^-**
  - **Poor in enzymes.**
- **Secretion;** **Actively by epithelial cells of pancreatic *Ducts***
  It is stimulated by secretin & VIP.
- **Function;**

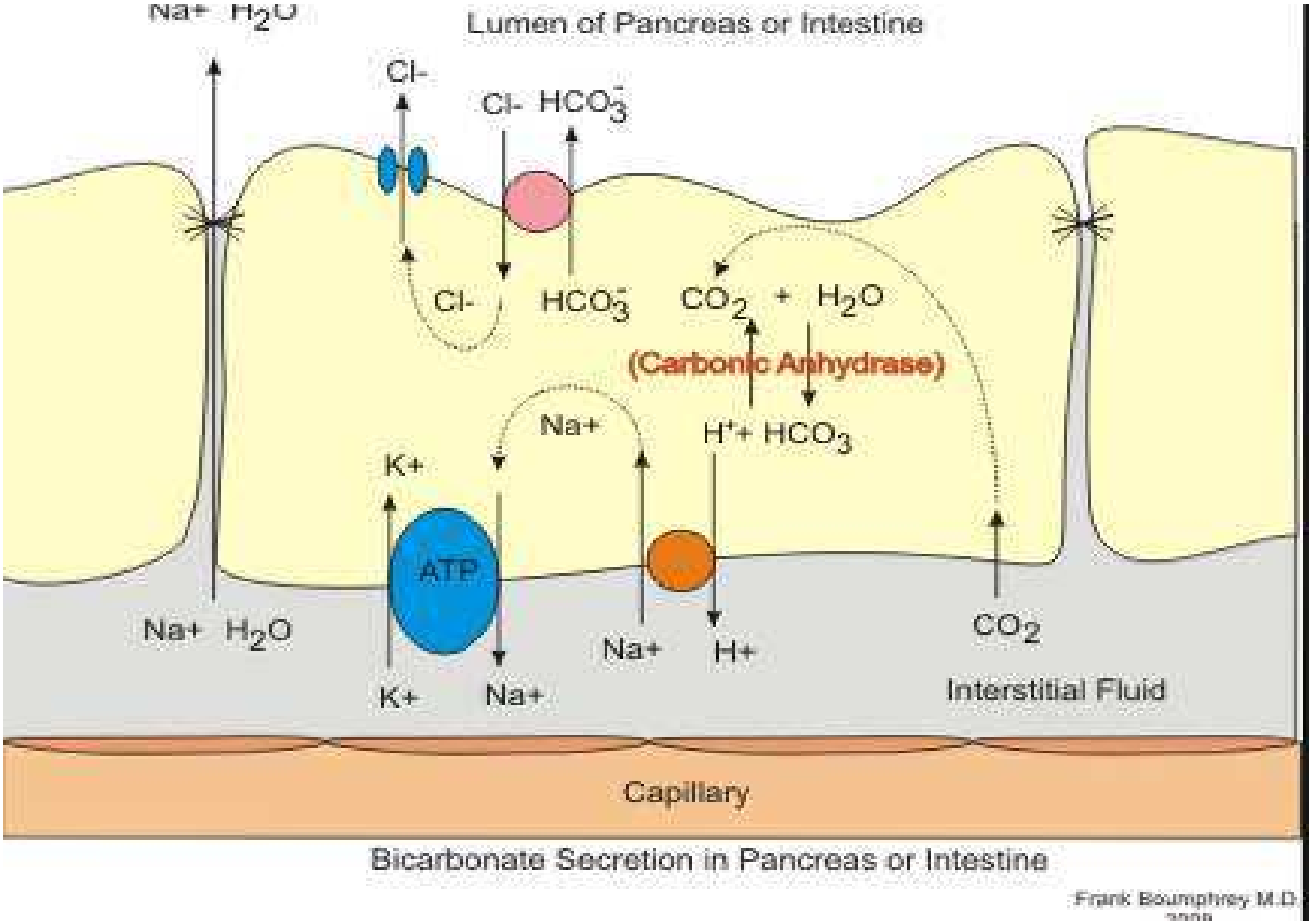
- ***Neutralize the acid chyme emptied by the stomach into the duodenum to protect the delicate duodenal mucosa from harmful effect of acidity&pepsin.***

  $$HcI+NaHco_3=NaCl+H_2Co_3$$

- ***Provide the alkaline pH optimum for the action of pancreatic & intestinal enzymes .***

Mechanism of HCO_3^- secretion





Bicarbonate Secretion in Pancreas or Intestine

Frank Boumphrey M.D.

B-Pancreatic enzymes

- They are fully sufficient for ***complete digestion of food.***
- They are secreted from the ***Acinar cells.***
- The juice is small in volume, poor in HCO_3^- and Rich in the following enzymes:-
  - Pancreatic amylase.
  - Pancreatic lipase.
  - Pancreatic Proteolytic enzymes.

Pancreatic enzymes

1-Proteolytic:

Secreted in inactive form, become activated only in small intestine. *By Enterokinase enzymes secreted by Intestinal mucosa in response to chyme.*

- **Trypsinogen** $\xrightarrow{EK}$ **Trypsin (Endopeptidase)** $\xrightarrow{\text{Trypsin}}$ **peptides**
- **Chymotrypsinogen** → **chymotrypsin (endopeptidase)** $\xrightarrow{\text{Trypsin}}$ **peptides**
- **Procarboxypeptidase** → **carboxypeptidase** → **Amino acids**

It is an Exopeptidase. It is the only Proteolytic enzyme that can release amino acids.

- **d-Proelastase** → **Elastase (acts on elastin).**

2-Lipolytic:

a- **Pancreatic lipase acts on TG → Monoglycerides and fatty acids. It is the only enzyme that accomplish fat digestion. It needs bile salts.**

b-Prophospholipase A2.

c-Cholesteryl ester hydrolase(*cholesterol esterase)*

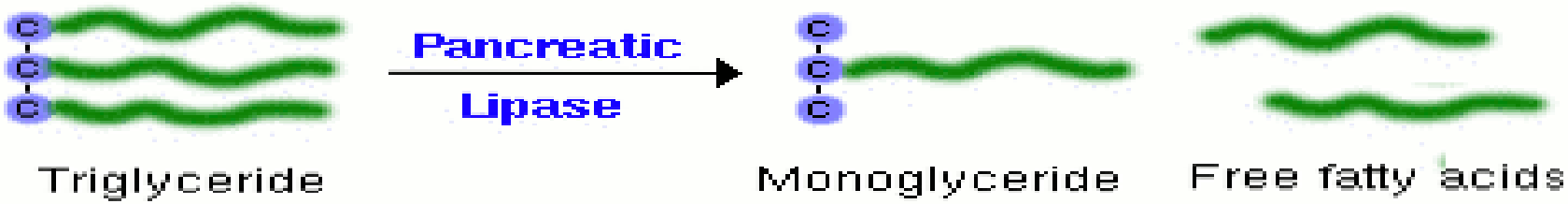
3-α-Amylase:

Act on starch → maltose and maltotriose & dextrins.

More potent than ptyalin.

4-Nucleases:

Act on RNA, DNA → nucleotides.



Protection Of The Pancreas From Autodigestion

- ***All Proteolytic enzymes are secreted in an inactive form to protect the pancreas against Autodigestion, and they become activated only in small intestine under the effect of Trypsin.***

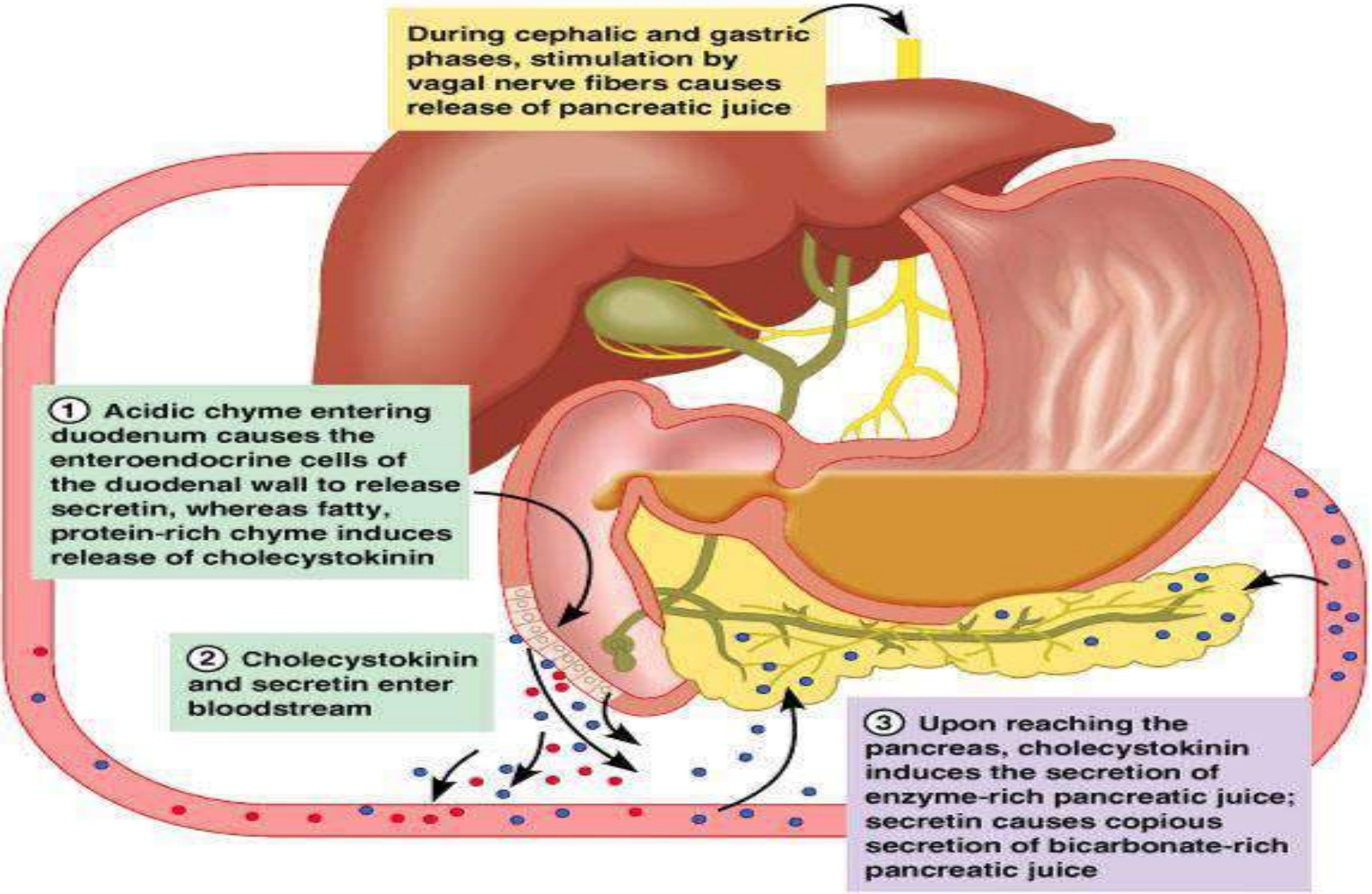
- ***The pancreas also secretes a Trypsin Inhibitor that blocks any trypsin activity inside the pancreas, because normally, some trypsinogen is activated to trypsin in the pancreas.***

Predict the mechanism of pancreatitis?

Regulation of Pancreatic Secretion

- **Basic Stimuli That Cause Pancreatic Secretion:**
- ***Acetylcholine*, which is released from the parasympathetic Vagus nerve endings and from other cholinergic nerves in the enteric nervous system**
- ***Cholecystokinin*, which is secreted by the duodenal and upper jejunal mucosa when food enters the small intestine**
- ***Secretin*, which is also secreted by the duodenal and jejunal mucosa when highly acidic food enters the small intestine**

Regulation of Pancreatic Secretion



- **Secretin, in contrast to the first two basic stimuli, stimulates secretion of large quantities of water solution of sodium bicarbonate by the pancreatic *Ductal epithelium.***

- **Acetylcholine and Cholecystokinin, stimulate the *Acinar cells of the pancreas*, causing production of large quantities of pancreatic digestive enzymes but relatively small quantities of water and electrolytes to go with the enzymes.**

- **Secretin is released from the mucosa of the small intestine when the *pH* of the duodenal contents falls below *4.5 to 5.0,* and its release increases greatly as the pH falls to 3.0.**
- **This immediately causes copious secretion of pancreatic juice containing large amounts of sodium bicarbonate**
- **Because the mucosa of the small intestine cannot withstand the digestive action of acid gastric juice, this is an essential protective mechanism to prevent development of *Duodenal ulcers*.**

- **Bicarbonate ion secretion by the pancreas provides an appropriate pH for action of the pancreatic digestive enzymes, which function optimally in a slightly alkaline or neutral medium, at a pH of 7.0 to 8.0.**
- **Fortunately, the pH of the sodium bicarbonate secretion averages 8.0.**

Regulation of secretion of pancreatic juice (Phases of Pancreatic Secretion)

1-Nervous:

During the Cephalic 20% (both conditioned & unconditioned reflexes) and Gastric phase 10% (presence of food in the stomach), there is stimulation of Vagus nerve → act on acinar cells of pancreas → pancreatic juice (secretion rich in digestive enzymes, poor in fluid).

2-Hormonal:

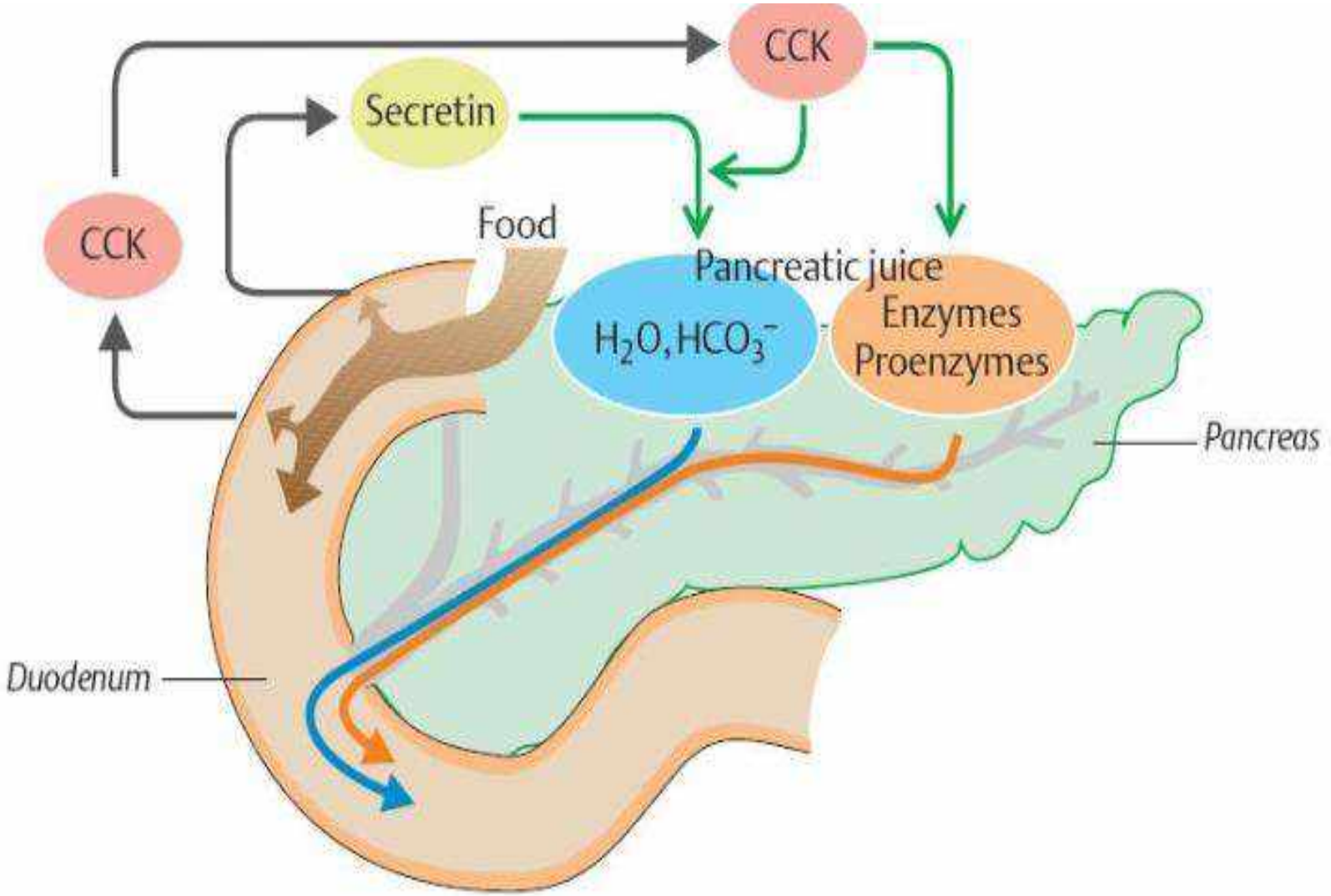
During the Intestinal phase of gastric secretion two important GIT hormones; secreted by duodenal mucosa stimulate the secretion of pancreatic juice:

a-Secretin hormone: It stimulates the secretion of pancreatic juice, large in volume, rich in HCO_3^-.

b-Cholecystokinin hormone (CCK): It stimulates the secretion of pancreatic juice, small in volume, rich in enzymes.

Secretin

- It is a polypeptide hormone secreted from specialized cells called S cells in the glands of the duodenum& jejunum contain 27 amino acid.
- It is secreted in response to:-
  - Acidic chyme in the duodenum.
  - Products of protein digestion.
- Function:-
  - Stimulate secretion of pancreatic juice rich in Hco_3 from pancreatic duct cells.
  - Stimulate secretion of Hco_3 from duct cells of the biliary tract which increase Bile flow *(Choleretic).*
  - Augment the action of CCK on pancreatic cells.
  - Inhibit gastric acid secretion & emptying.
  - Has trophic effect on exocrine pancreas.

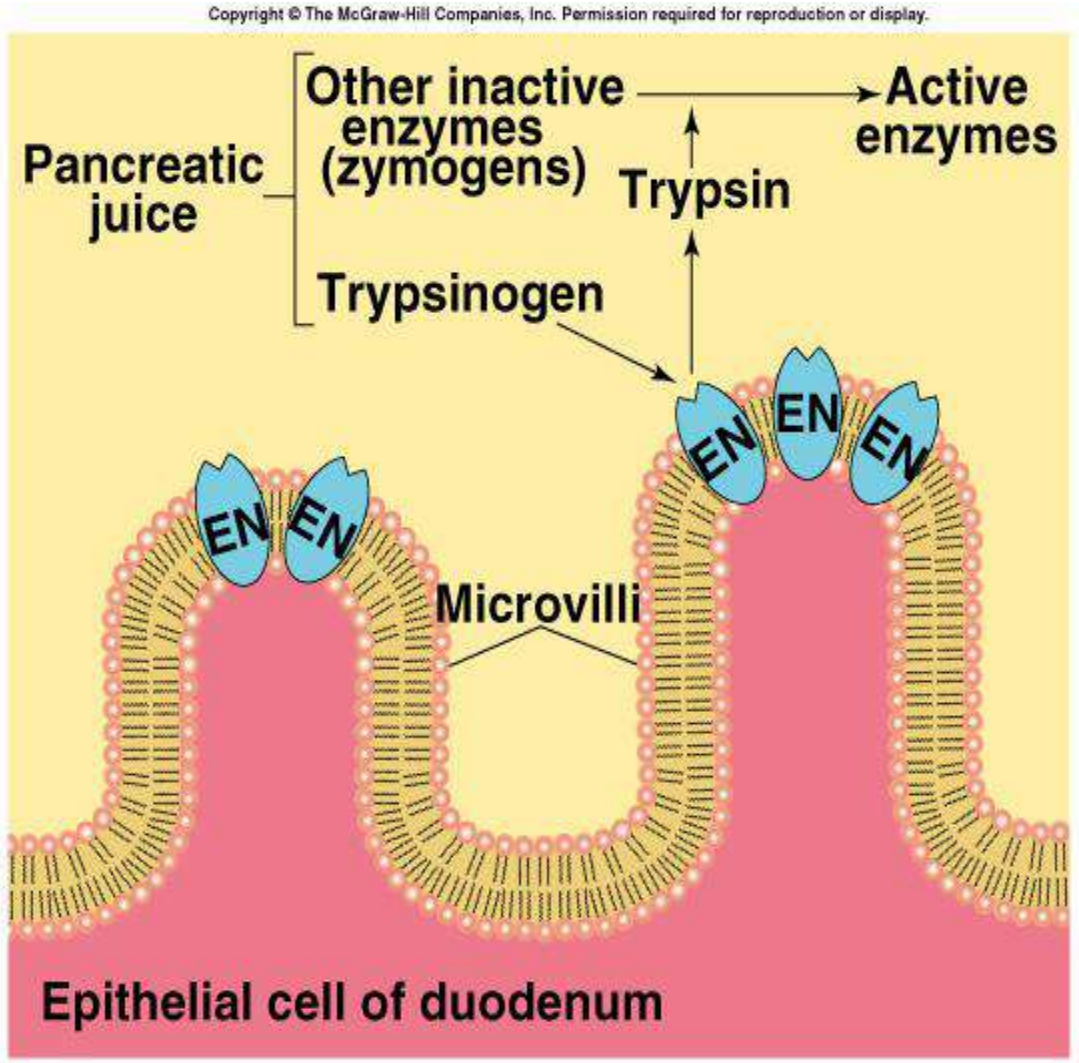

CCK
Secretin
CCK
Food
Pancreatic juice
H_2O, HCO_3^-
Enzymes
Proenzymes
Pancreas
Duodenum

Cholecystokinin

- **It is secreted from:-**
  - **I cells in the upper small intestine contain 33 amino acid.**
  - **Nerves in the distal ileum.**
- **It is secreted in response to products of fat & protein digestion.**
- **Function:-**
  - **Inhibit gastric motility, emptying & secretion.**
  - **Stimulate pancreatic acinar cell to secrete juice rich in enzymes.**
  - **Trophic to exocrine pancreas**
  - **Augment action of secretin.**
  - **Stimulate gall bladder contraction (act as cholagogue).**
  - **Involved in regulation of food intake.**

Pancreatic Juice

- Complete digestion of food requires action of both ***Pancreatic and Brush border enzymes***.
- Most pancreatic enzymes are produced as zymogens.
- Trypsin (when activated by enterokinase) triggers the activation of other pancreatic enzymes.
- Pancreatic trypsin inhibitor attaches to trypsin.
- Inhibits its activity in the pancreas.



Pancreatic Juice

- Contains H_20, $HC0_3^-$ and digestive enzymes.

Table 18.4 Enzymes Contained in Pancreatic Juice

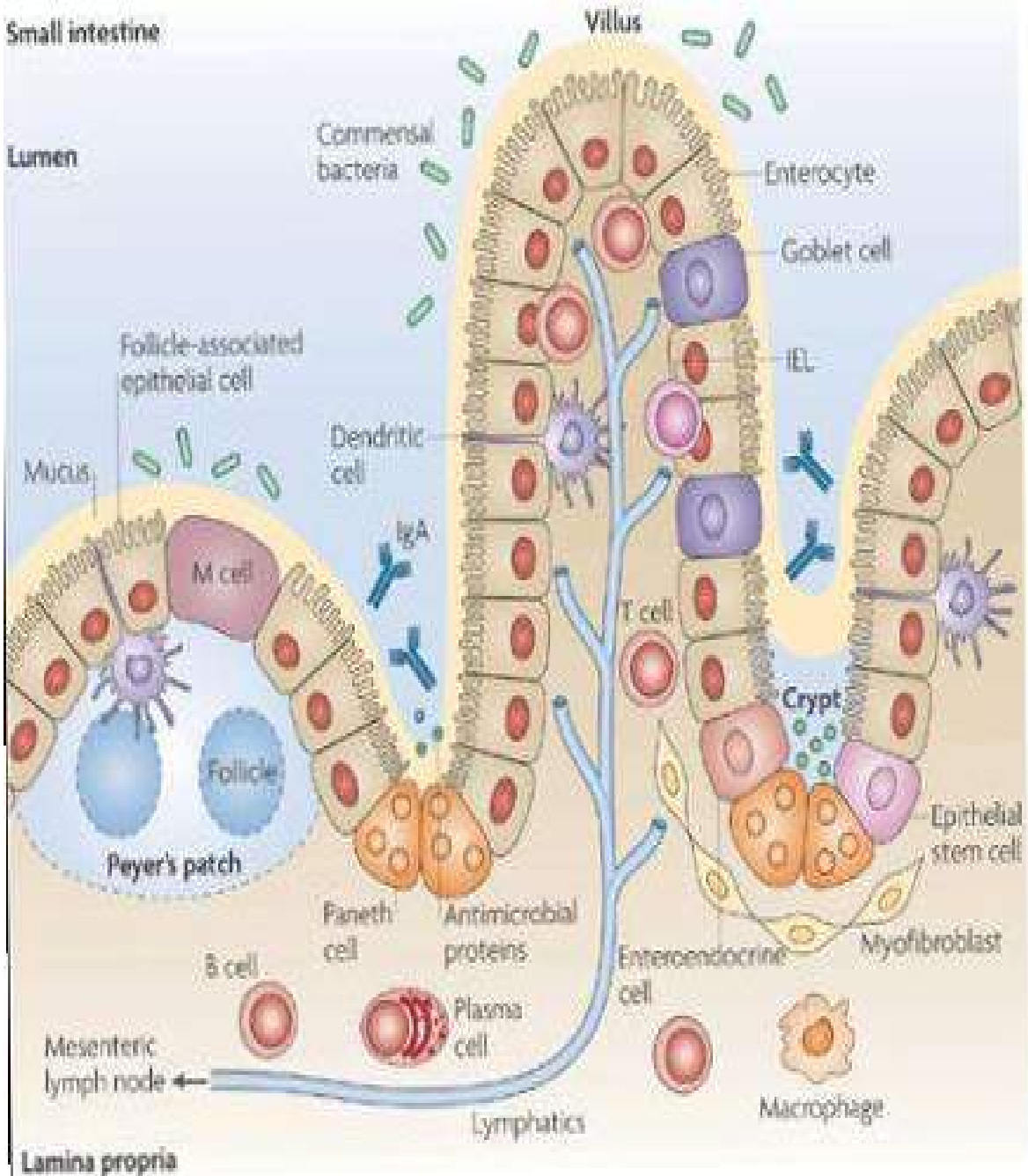
Enzyme	Zymogen	Activator	Action
Trypsin	Trypsinogen	Enterokinase	Cleaves internal peptide bonds
Chymotrypsin	Chymotrypsinogen	Trypsin	Cleaves internal peptide bonds
Elastase	Proelastase	Trypsin	Cleaves internal peptide bonds
Carboxypeptidase	Procarboxypeptidase	Trypsin	Cleaves last amino acid from carboxyl-terminal end of polypeptide
Phospholipase	Prophospholipase	Trypsin	Cleaves fatty acids from phospholipids such as lecithin
Lipase	None	None	Cleaves fatty acids from glycerol
Amylase	None	None	Digests starch to maltose and short chains of glucose molecules
Cholesterolesterase	None	None	Releases cholesterol from its bonds with other molecules
Ribonuclease	None	None	Cleaves RNA to form short chains
Deoxyribonuclease	None	None	Cleaves DNA to form short chains

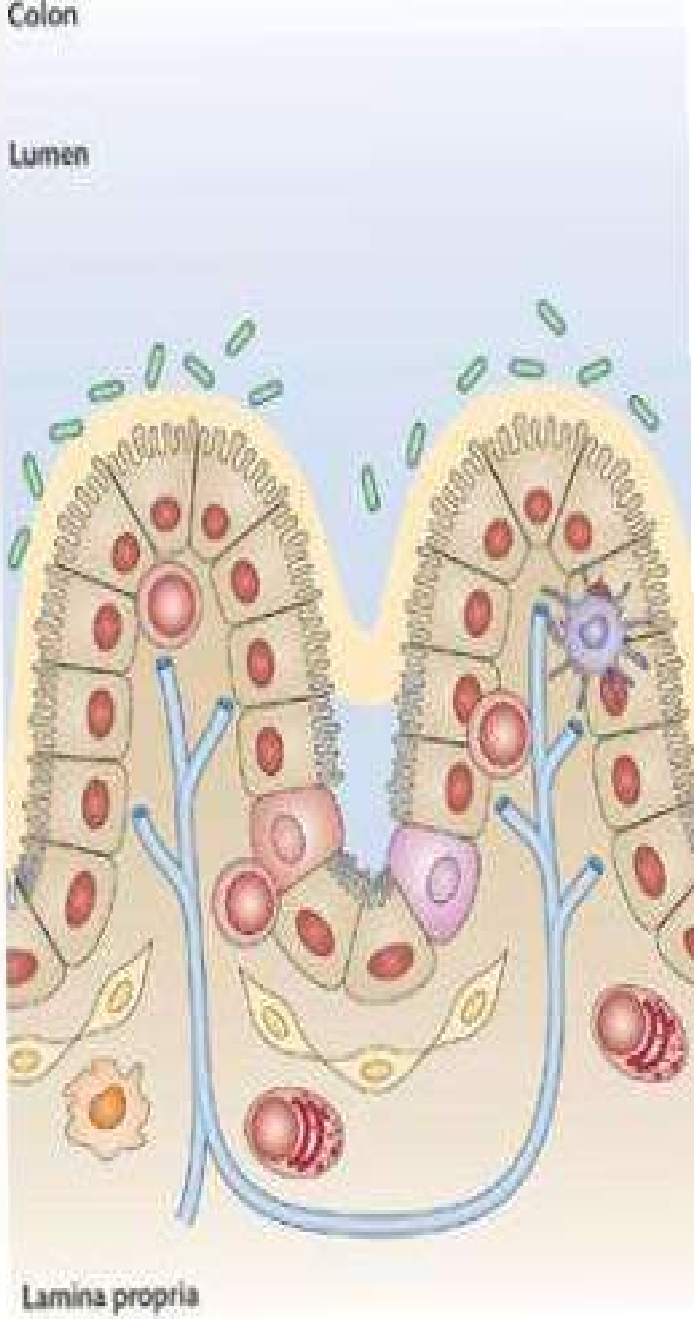
7-Secretions of the Small Intestine

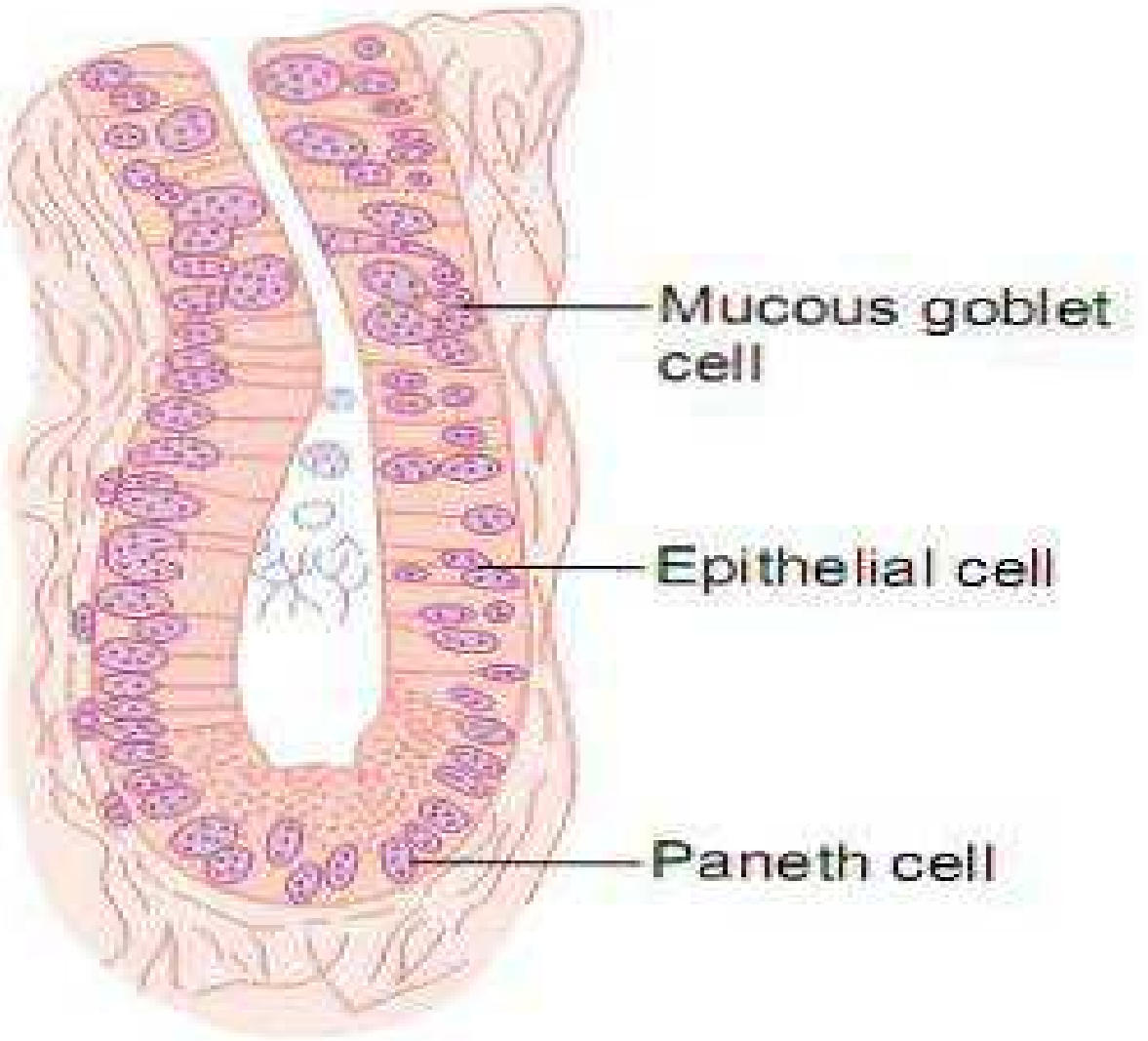
- **Secretion of Mucus by Brunner's Glands in the Duodenum :**
- ***Brunner's Glands***, **is located mainly between the pylorus of the stomach and the ampula of Vater. These glands secrete *large amounts of alkaline mucus* in response to**
  - **(1) *Tactile or irritating stimuli* on the duodenal mucosa**
  - **(2) *Vagal stimulation*, which causes increased Brunner's glands secretion concurrently with increase in stomach secretion.**
  - **(3) Gastrointestinal hormones, especially *secretin*.**
- **Brunner's glands are inhibited by sympathetic stimulation.**

Secretion of Intestinal Digestive Juices by the Crypts of Lieberkühn

- These crypts lie between the intestinal villi Located over the entire surface of the small intestine.
- The surfaces of both the crypts and the villi are covered by an epithelium composed of two types of cells:
- (1) Moderate number of *Goblet cells*, which *secrete mucus* that lubricates and protects the intestinal surfaces, and
- (2) Large number of *Enterocytes,* which, in the crypts, secrete large quantities of water and electrolytes and, over the surfaces of adjacent villi, reabsorb the water and electrolytes along with end products of digestion.


Small intestine
Villus
Lumen
Commensal bacteria
Enterocyte
Goblet cell
Follicle-associated epithelial cell
IEL
Dendritic cell
Mucus
IgA
M cell
T cell
Crypt
Follicle
Peyer's patch
Epithelial stem cell
Paneth cell
Antimicrobial proteins
Myofibroblast
Enteroendocrine cell
B cell
Plasma cell
Mesenteric lymph node
Lymphatics
Macrophage
Lamina propria


Colon
Lumen
Lamina propria



ure 64–13

- ***The intestinal secretions are formed by the enterocytes of the crypts at a rate of about 1800 ml /day. These secretions are almost pure extracellular fluid and have a slightly alkaline pH in the range of 7.5 to 8.0. The secretions are also rapidly reabsorbed by the villi.***

Digestive Enzymes in the Small Intestinal Secretion

- **The enterocytes of the mucosa, covering the villi, contain digestive enzymes that digest specific food substances *while they are being absorbed* through the epithelium. These enzymes are the following:**

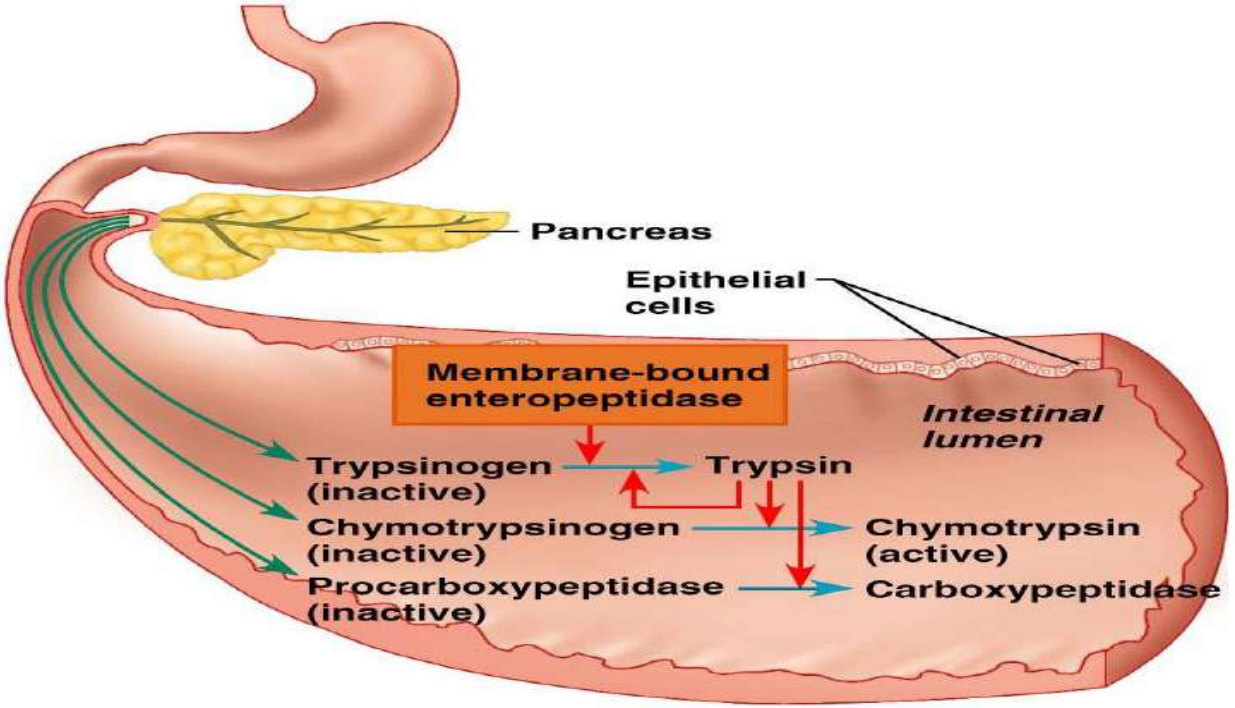
- **(1) *Several peptidases:* for splitting small peptides into amino acids.**
- ***(2) Four enzymes sucrase, maltase, isomaltase, and lactase:* *for* splitting disaccharides into *monosaccharide's.***
- ***(3) Small amounts of intestinal lipase:* for splitting neutral fats into glycerol and fatty acids.**

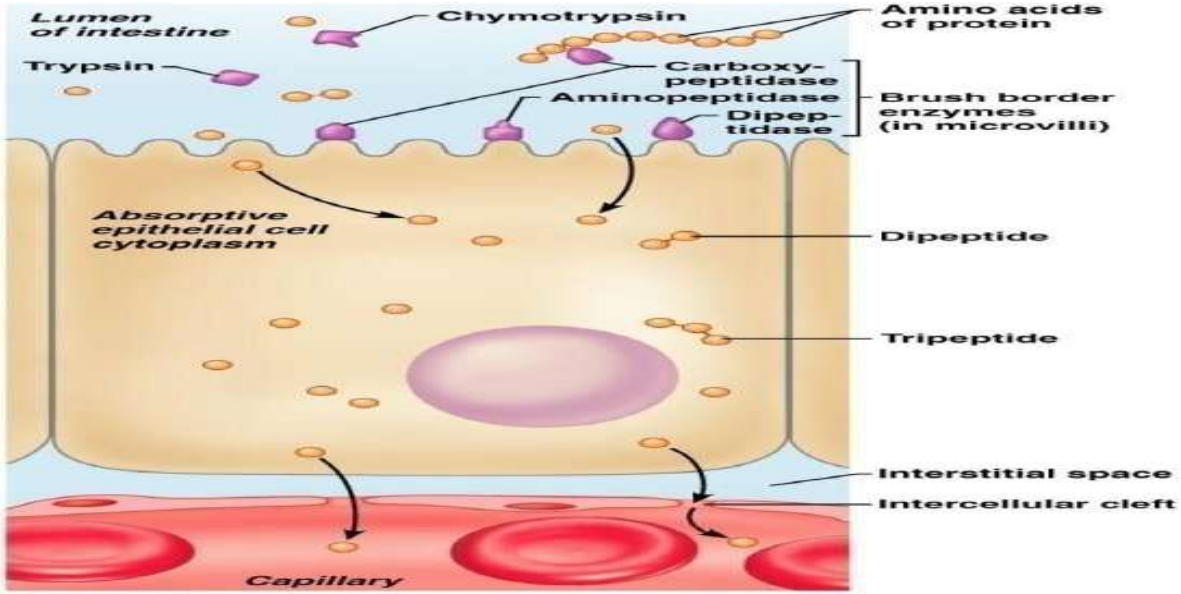
Regulation of Small Intestine Secretion-Local Stimuli

- **The most important means for regulating small intestine secretion *are local enteric nervous reflexes,* especially reflexes initiated by tactile or irritative stimuli from the chyme in the intestines.**
- **The life cycle of an intestinal epithelial cell is about *5 days.***

Small Intestine: Chemical Digestion

Brush border enzymes *Enteropeptidases* (Enterokinase) converts trypsinogen to trypsin Trypsin activates other zymogens Various other brush border enzymes complete digestion of protein and carbohydrate molecules





8-Secretion of Mucus by the Large Intestine

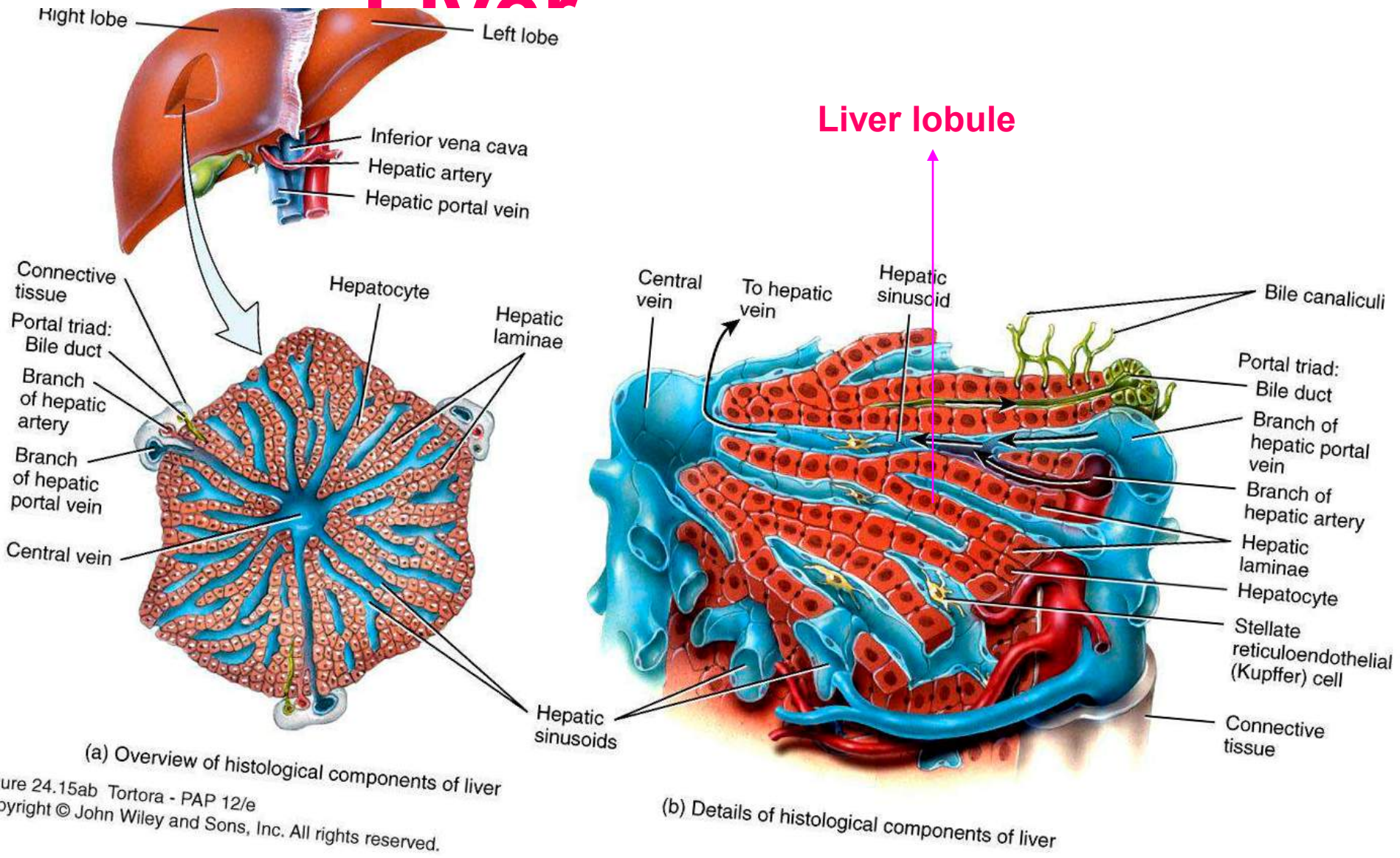
Mucus Secretion:

- **The mucosa of the large intestine has many crypts of Lieberkühn; however, unlike the small intestine, there are *no villi.***
- **The epithelial cells secrete almost *no digestive enzymes*.**
- **Instead, they contain mucous cells that secrete only *mucus.***
- **This mucus contains moderate amounts of bicarbonate ions.**

6-Secretion of Bile by the Liver Functions of the Biliary Tree

- liver is the largest gland in the body (1.5 Kg), essential for life.
- The functional unit is the *liver lobule* (hepatocytes around a central vein separated by blood sinusoids).
- The sinusoids are wide fenestrated, contain large Kupffer cells.
- Hepatic vascular system:
  - 1.5 L/minute (27% of CO) , 1L from portal vein, 500ml from hepatic artery.
  - Rich lymphatic drainage.

Histology of the Liver



(a) Overview of histological components of liver

(b) Details of histological components of liver

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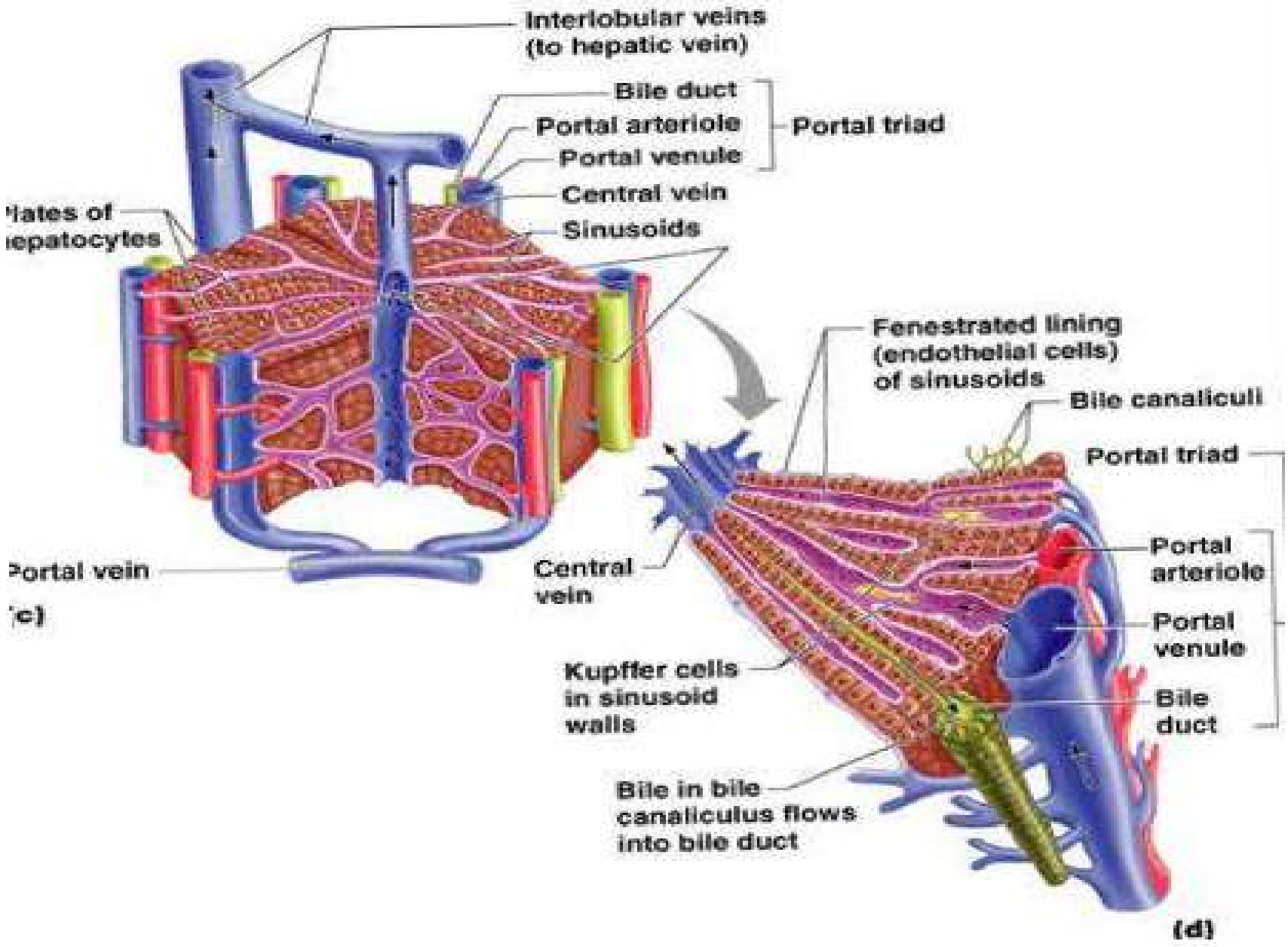
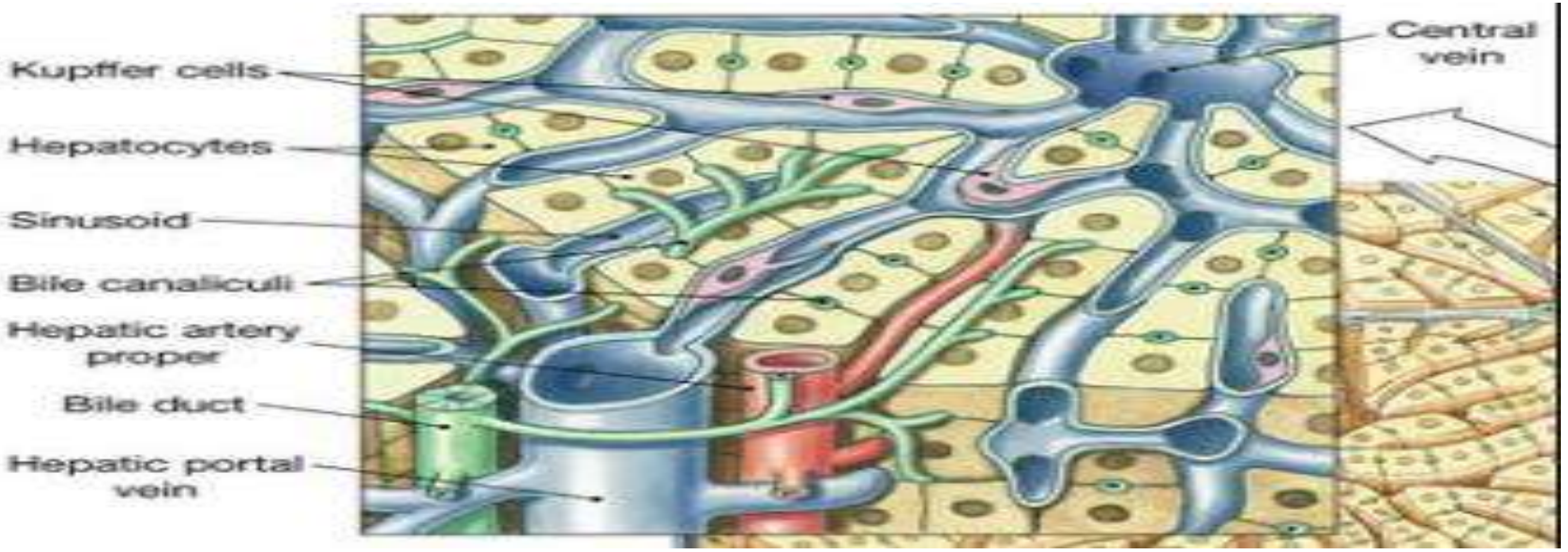
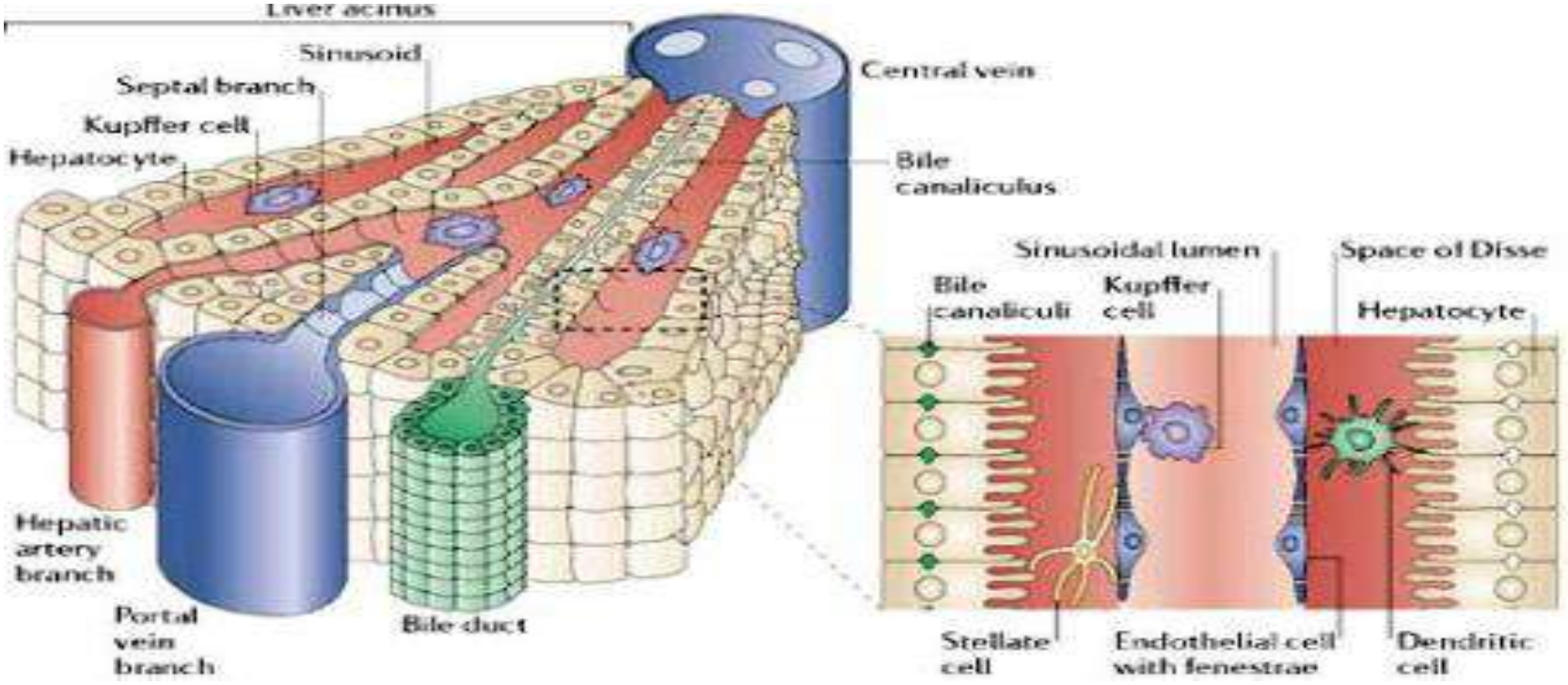
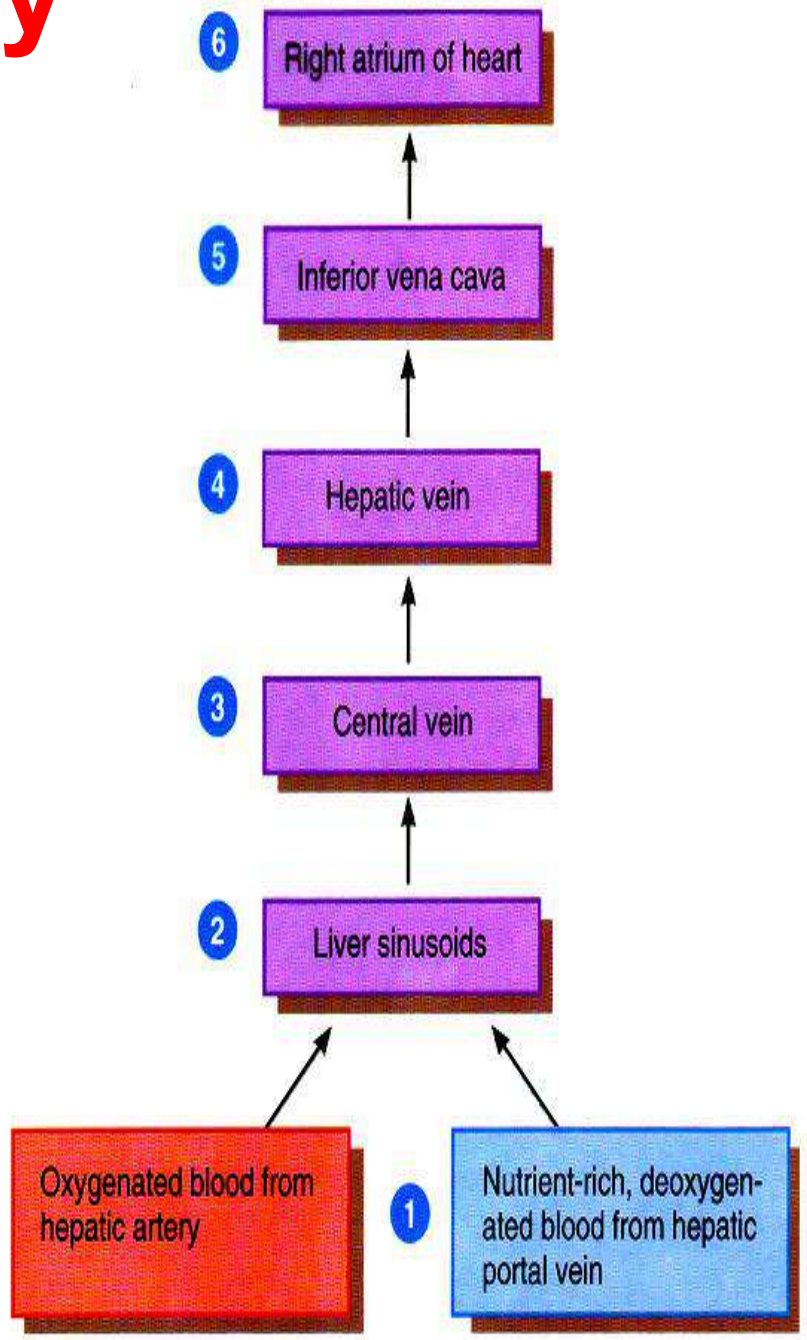

Interlobular veins
(to hepatic vein)
Bile duct
Portal arteriole
Portal venule
Portal triad
Central vein
Sinusoids
lates of
epatocytes
Portal vein
c)
Fenestrated lining
(endothelial cells)
of sinusoids
Bile canaliculi
Portal triad
Portal
arteriole
Portal
venule
Bile
duct
Central
vein
Kupffer cells
in sinusoid
walls
Bile in bile
canaliculus flows
into bile duct
(d)


Kupffer cells
Hepatocytes
Sinusoid
Bile canaliculi
Hepatic artery proper
Bile duct
Hepatic portal vein
Central vein


Liver acinus
Sinusoid
Septal branch
Kupffer cell
Hepatocyte
Central vein
Bile canaliculus
Hepatic artery branch
Portal vein branch
Bile duct
Sinusoidal lumen
Space of Disse
Bile canaliculi
Kupffer cell
Hepatocyte
Stellate cell
Endothelial cell with fenestrae
Dendritic cell

Liver: Blood Supply

- Two sources
  - *Hepatic artery* - oxygenated blood from aorta.
  - *Hepatic portal vein* - deoxygenated blood:
    - Absorbed nutrients and toxins from the stomach and intestines.
    - Hormones from the pancreas.
    - Breakdown products of RBCs from the spleen.
- Blood mixes in the sinusoids
- Hepatocytes (liver cells) modify and exchange molecules with the blood.



Liver functions

1. ***Vascular Function:***
   - ***Blood storage:*** **10% of total blood volume 450ml.**
   - ***Blood filtration:*** **99% of bacteria that enter the portal blood from the intestine, small blood clots by are phagocytosed by Kupffer cells that line hepatic sinusoids.**
   - ***Removal of old red blood cells*** **by Kupffer cells.**
2. ***Secretory function (Bile formation):***

Synthesis & secretion of bile salts & bile pigments.

3. Metabolic functions:

1. **Carbohydrate metabolism: gluconeogenesis, glycogenolysis ,.**
2. **Protein metabolism: Deamination of amino acids → ketoacids.**

Conversion of ammonia to urea.
Formation of uric acid.

Synthesis of non essential amino acids.

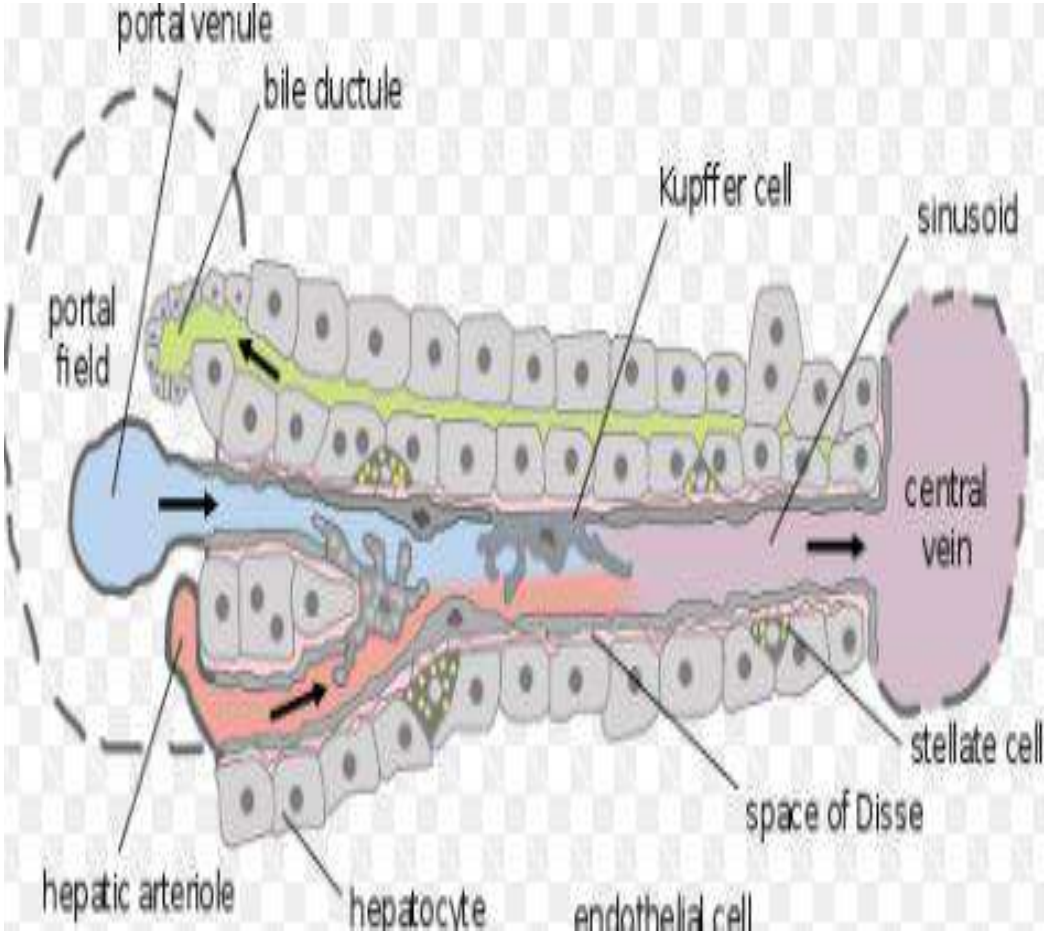
3. **Fat metabolism:**
    1. **Oxidation of fatty acids to supply energy.**
    2. **Synthesis of cholesterol, lipoproteins & phospholipids.**
    3. **Lipogenesis.**
4. **Synthesis of 25 hydroxy-cholecalciferol, plasma proteins (except y globulin), clotting factors.**

4. Storage function:

Glycogen, Vitamin A (ten months), D (3-4 months), B12 (12 months), Iron as ferritin.

5. Excretory function ;bile pigments, cholesterol.

6. **Detoxification of drugs & hormones** (thyroxin, steroid).
7. **Immunity:Kupffer cells.**



Bile

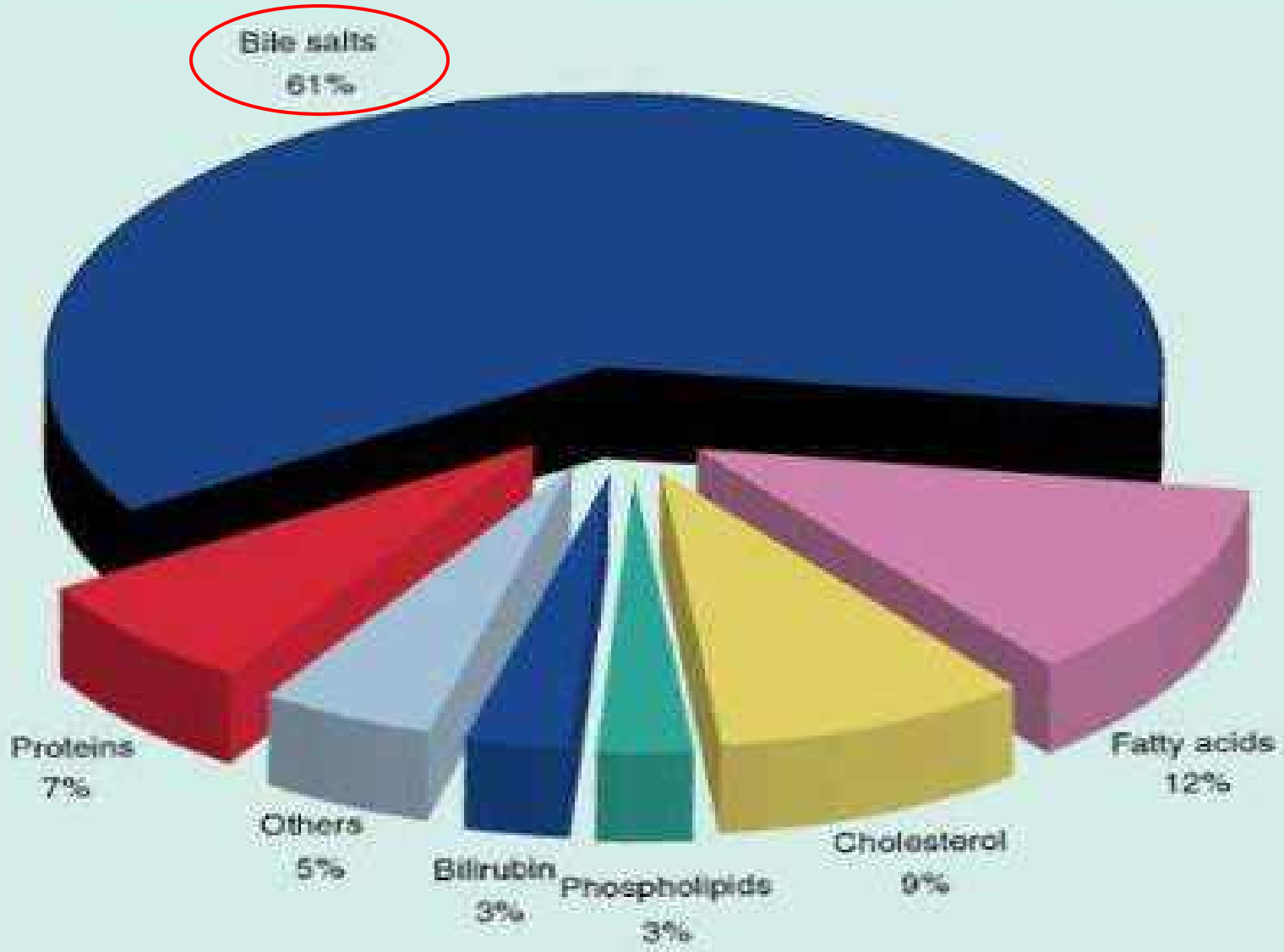
- Bile is an important digestive juice that is secreted by the liver and stored into the gall bladder.
- *Initial secretion* The liver forms and secretes 600-1200 ml of bile/ day by the *liver hepatocytes* into the biliary canaliculi rich in bile acids, cholesterol, lecithin to reach the hepatic duct.
- *Second secretion* by *hepatic ducts* rich in Na&Hco3 then the bile empties into the duodenum or through the cystic duct into the gall bladder.

Composition:

Volume: 600-1200 ml/day.

pH: 7.8- 8.6.

	Liver Bile	Gallbladder Bile
Water	97.5 g/dl	92 g/dl
Bile salts	1.1 g/dl	6 g/dl
Bilirubin	0.04 g/dl	0.3 g/dl
Cholesterol	0.1 g/dl	0.3 to 0.9 g/dl
Fatty acids	0.12 g/dl	0.3 to 1.2 g/dl
Lecithin	0.04 g/dl	0.3 g/dl
Na^+	145.04 mEq/L	130 mEq/L
K^+	5 mEq/L	12 mEq/L
Ca^{++}	5 mEq/L	23 mEq/L
Cl^-	100 mEq/L	25 mEq/L
HCO_3^-	28 mEq/L	10 mEq/L



Constituents:

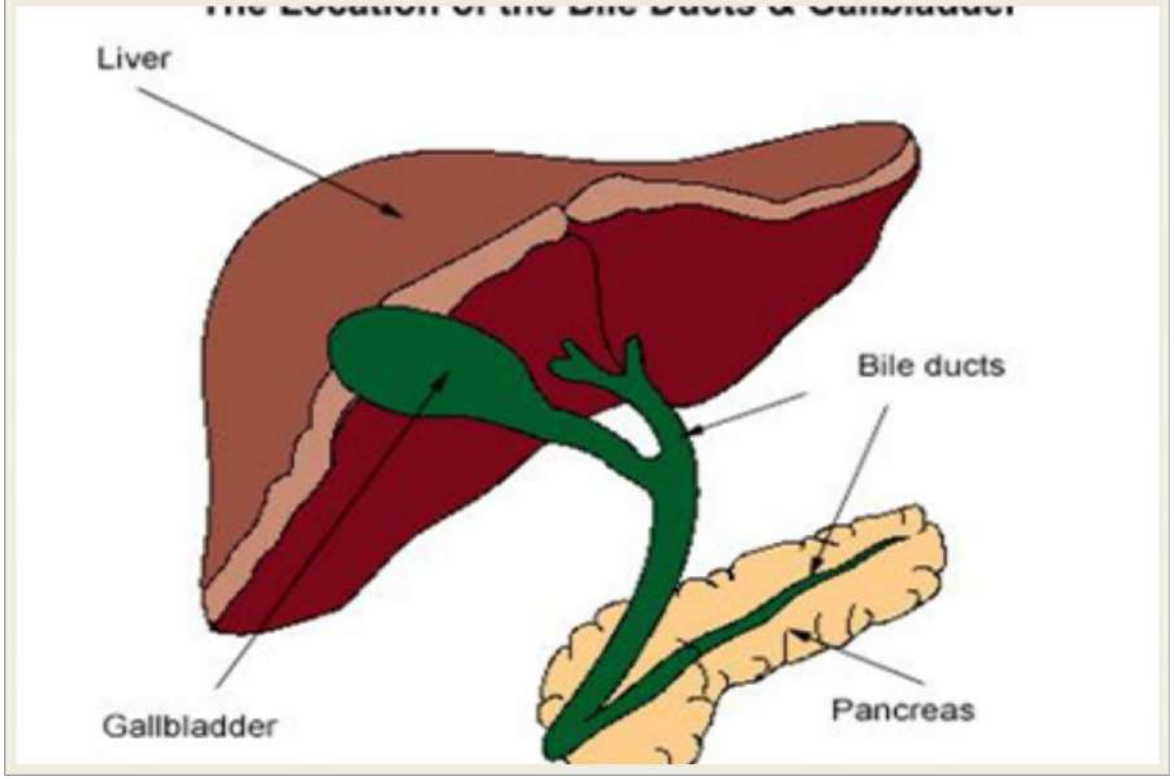
1-Aqueous constituents **(alkaline fluid, 97.5%);**

- **Secreted by *Duct cells.***
- **H_2O, Inorganic salts 0.5% (Na^+, K^+, Ca^{2+}, Cl^-, HCO_3^-).**

2-Organic constituents **(2.5%):**

- **Secreted by *Hepatocytes.***
- **(Bile salts, bile pigments, fatty acids, cholesterol, lecithin).**

3-Alkaline phosphatase enzyme.



Liver continuously synthesize &secretes bile.
Between meals, sphincter of Oddi is closed so secreted bile is moved into the gall bladder to be stored and concentrated.
During meal, bile is secreted from the gall bladder & liver .

Functions of bile

- ***Neutralization of HCl :*** **Share in HCl neutralization in the duodenum due to its high bicarbonate content. Its mucus content protect duodenal mucosa.**

- ***Digestive function:*** **Bile contains bile acids & salts , which are critical for digestion and absorption of fats and fat-soluble vitamins in the small intestine.**

- ***Excretory function:*** **Many waste products *(bilirubin & cholesterol) ,* are eliminated from the body by secretion into bile and elimination in feces.**

Free cholesterol is not soluble in aqueous solutions, but in bile, it is made soluble by *bile acids and lipids like lecithin.*

- **Bile salts are important for cholesterol homeostasis,**
- *Hepatic synthesis of bile acids accounts for the majority of cholesterol breakdown in the body. In humans, roughly **1-2g of cholesterol** are converted to bile acids and eliminated in bile every day*.

Bile salts

- **Bile acids (600 mg daily)are synthesized in the hepatocytes from cholesterol.**
- **Cholesterol is converted into the (primary), bile acids *cholic and chenodeoxycholic acids* which are then conjugated to an amino acid (glycine or taurine) to yield the conjugated form that is actively secreted into canaliculi.**
- **Bile acids contain both hydrophobic (lipid soluble) and polar (hydrophilic) faces. 2ry bile acids deoxycholic , lithocholic acids are formed by *bacterial action in colon.***
- **Tertiary(ursodeoxycholic,sulpholithocholic.**

Functions of bile salts:

1. They help fat digestion by decreasing surface tension of fat globules → *fat emulsification* (*detergent function*) to small droplets.
2. They are essential for absorption of
   - Fatty acids
   - Monoglycerides
   - Cholesterol.
   - Other lipids from the intestinal tract. & fat soluble vitamins (A,D,E, K).

(forming *Micelles* which are water soluble complexes).If absent, 40-50% of fats will lost in feces.

3. They are *cholertics* .i.e. stimulate bile flow.
4. *Laxative action* by stimulating intestinal peristalsis.
5. They are essential for keeping cholesterol dissolved in bile.

Liver Secretion Of Cholesterol And Gallstone Formation

- **Bile acids are formed in the hepatic cells from cholesterol in the blood plasma.**
- **BS are conjugated in liver by amino acids glycine and taurine to glycocholic and taurocholic acids.**
- **Both form salts by binding to Na, K in alkaline bile**
- **In the process of secreting the bile salts about**

1 to 2 grams **of cholesterol are removed from the blood plasma and secreted into the bile each day.**

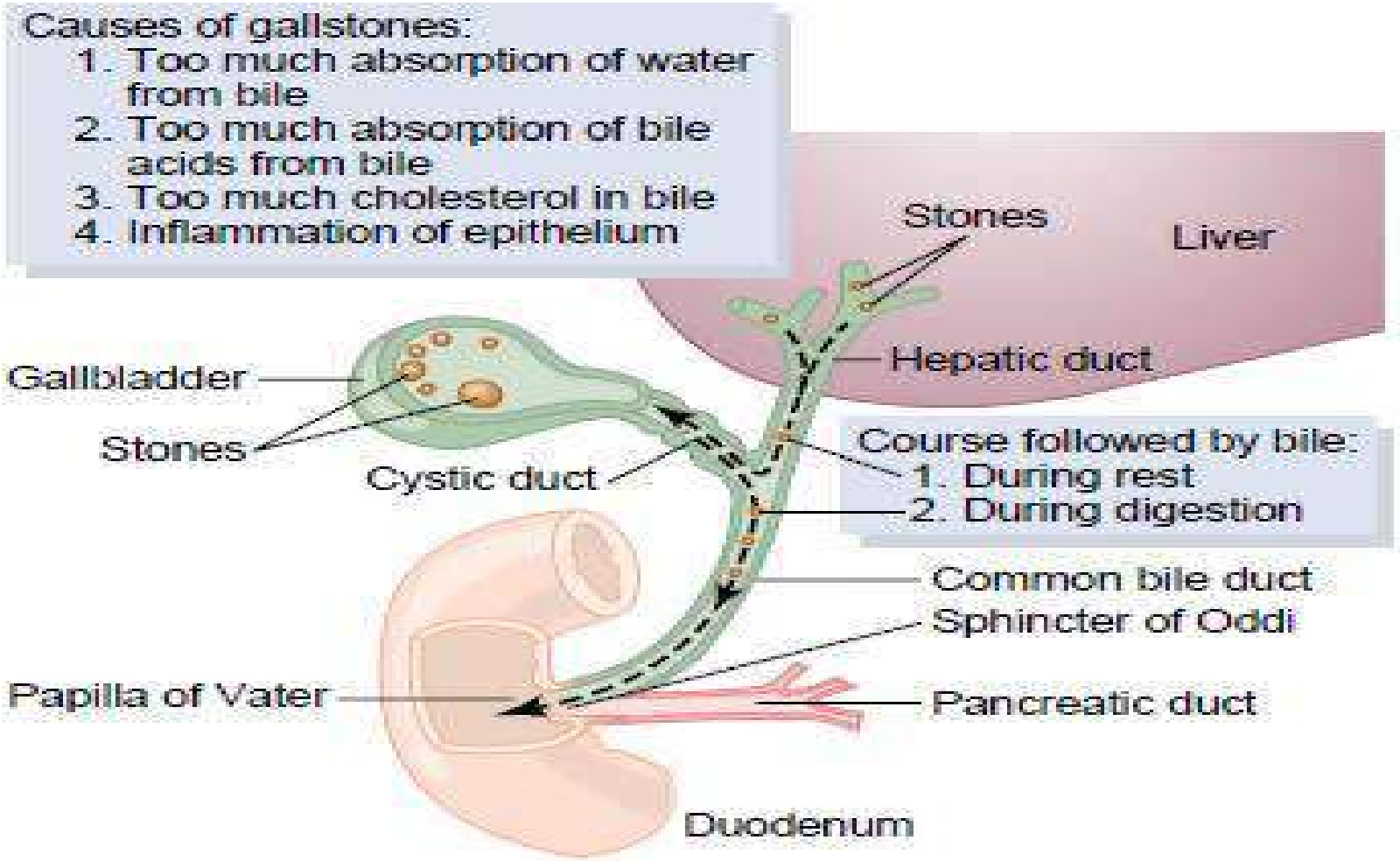
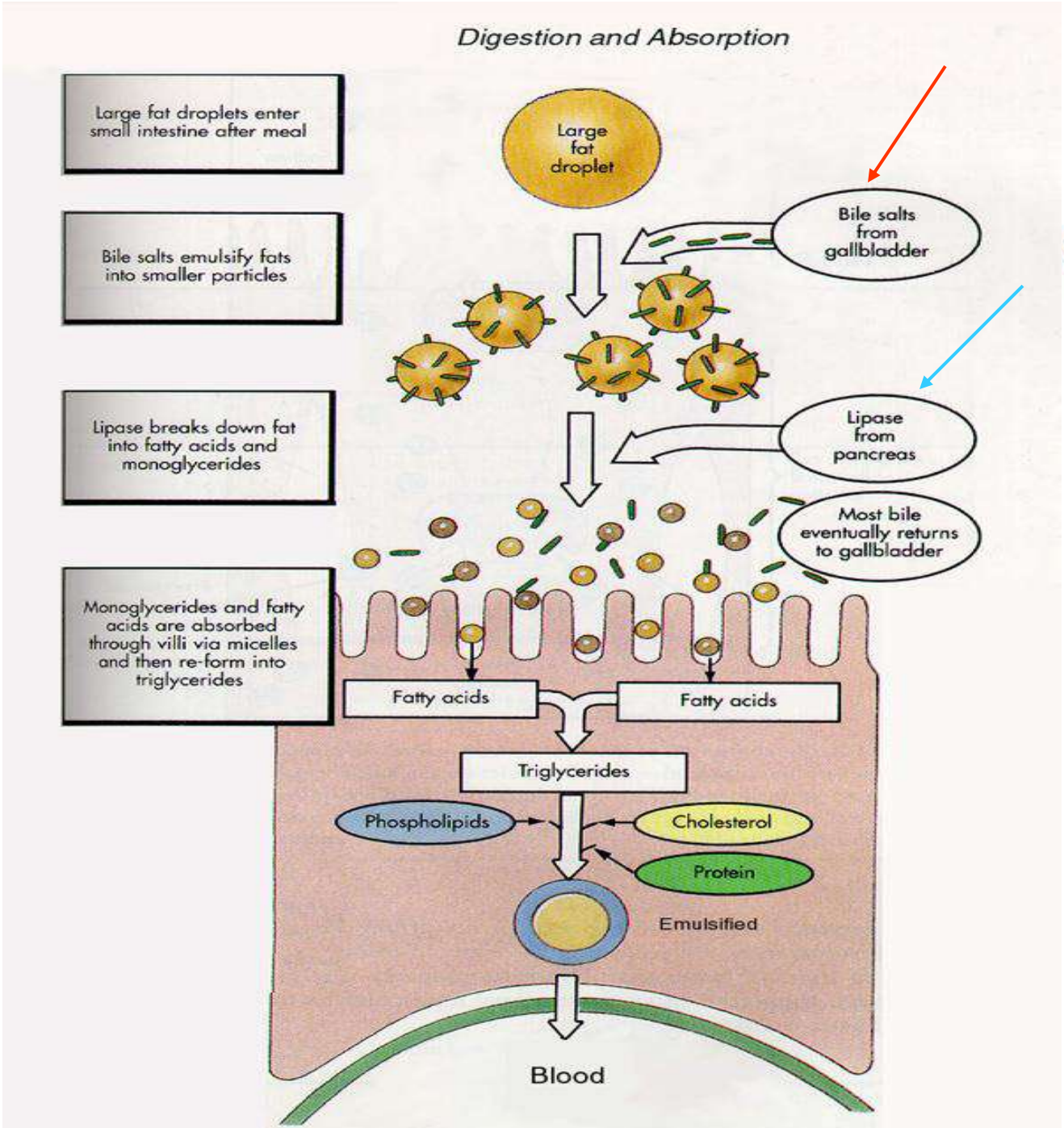
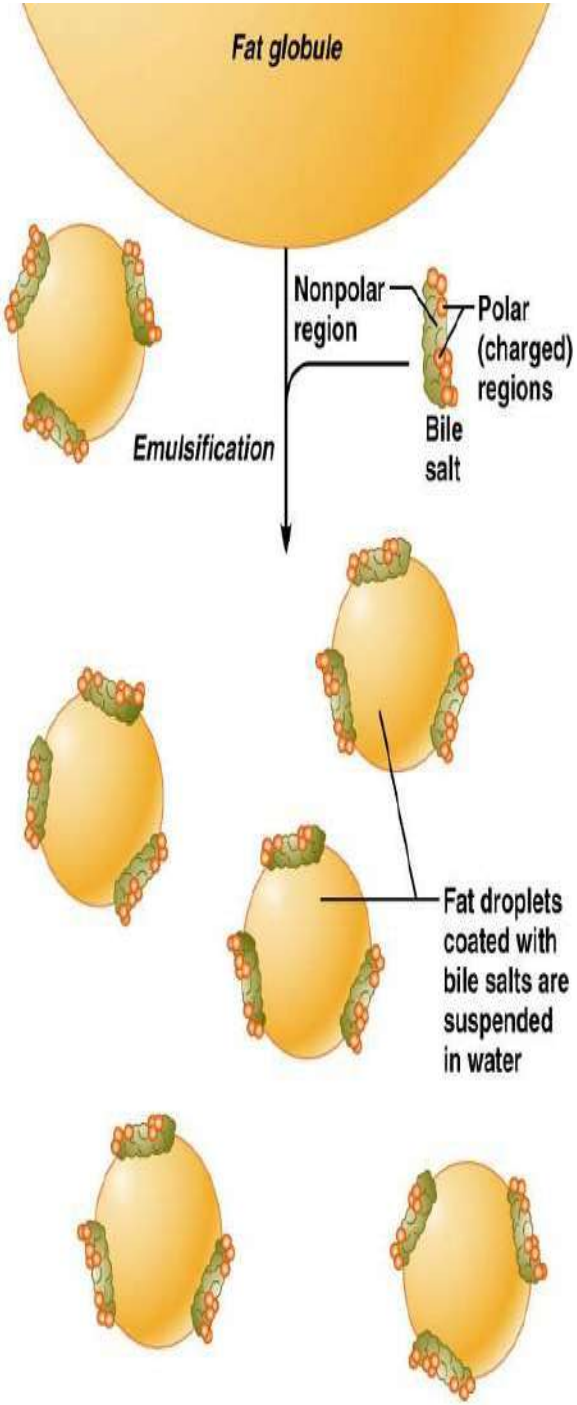
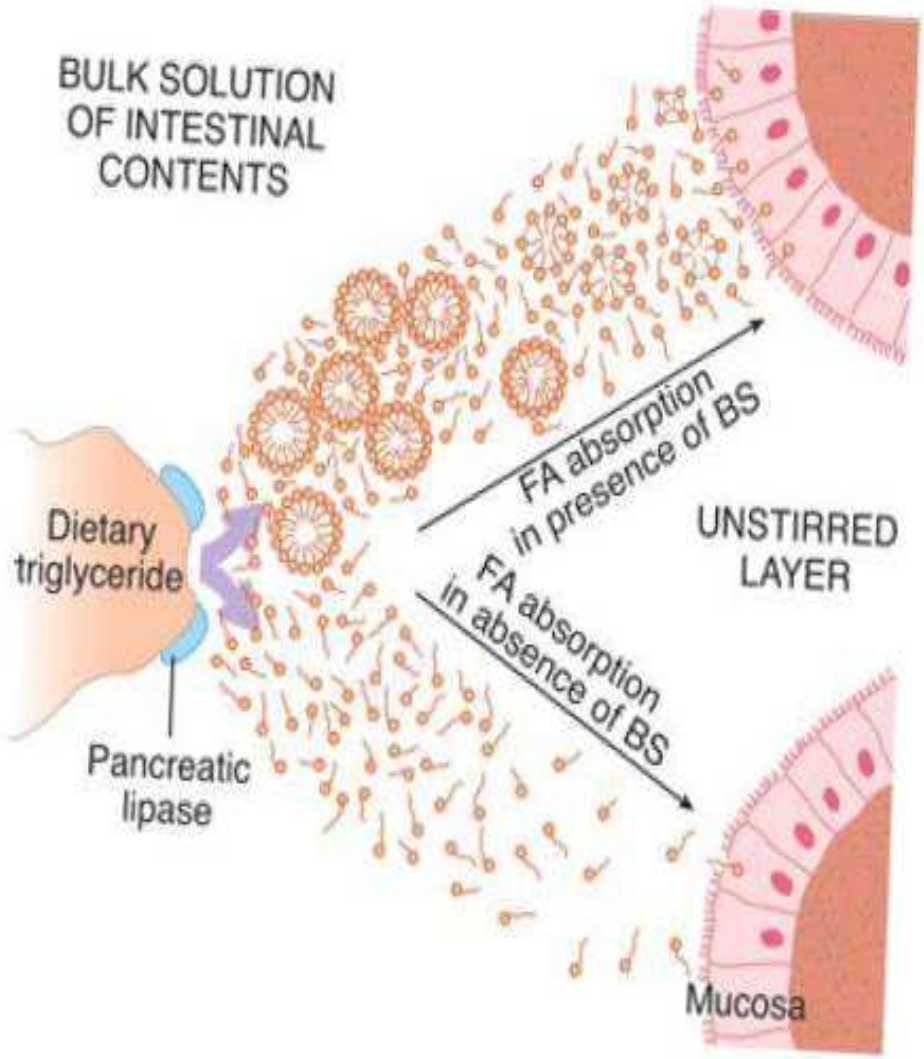


Figure 64–12

Formation of gallstones.


Digestion and Absorption
Large fat droplets enter small intestine after meal
Large fat droplet
Bile salts from gallbladder
Bile salts emulsify fats into smaller particles
Lipase breaks down fat into fatty acids and monoglycerides
Lipase from pancreas
Most bile eventually returns to gallbladder
Monoglycerides and fatty acids are absorbed through villi via micelles and then re-form into triglycerides
Fatty acids
Fatty acids
Triglycerides
Phospholipids
Cholesterol
Protein
Emulsified
Blood

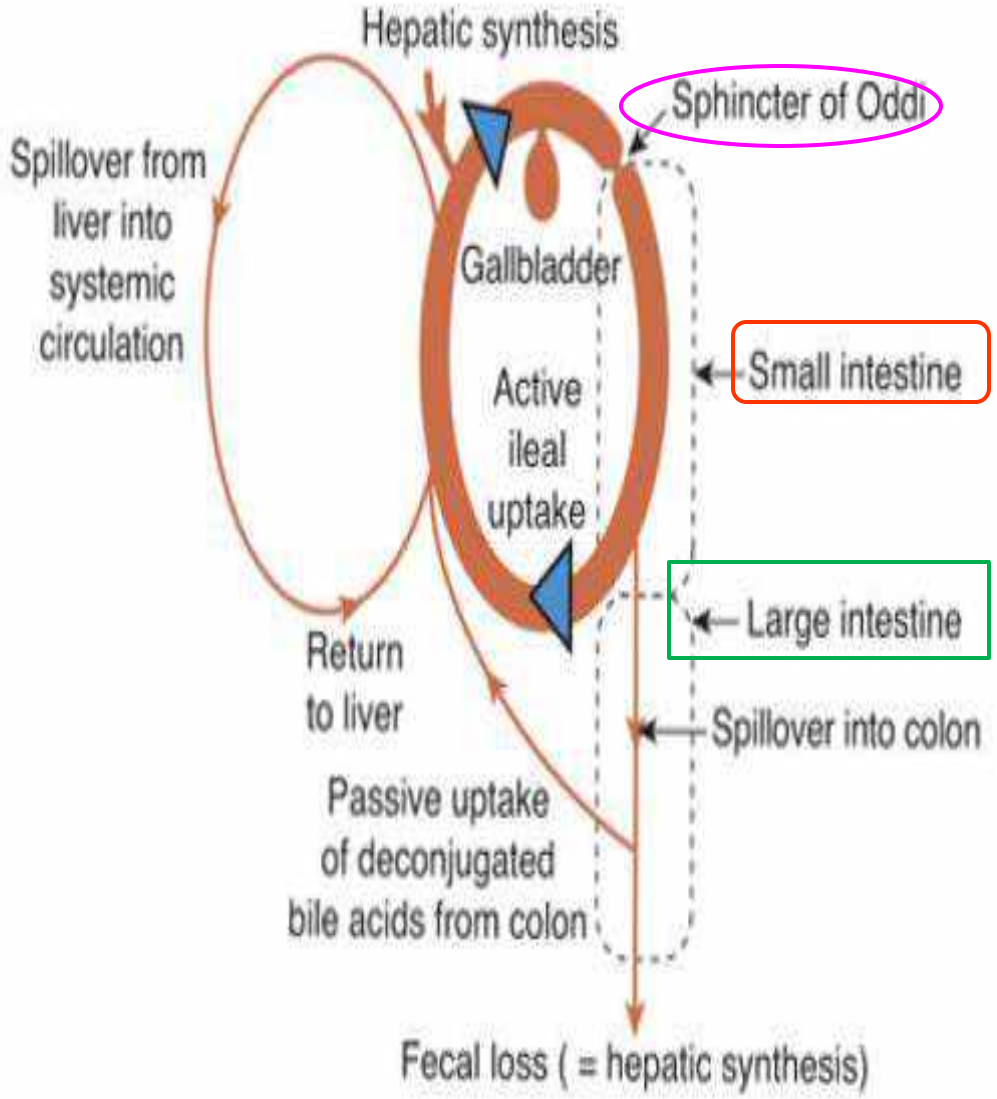

Fat globule
Nonpolar region
Polar (charged) regions
Bile salt
Emulsification
Fat droplets coated with bile salts are suspended in water


BULK SOLUTION
OF INTESTINAL
CONTENTS
FA absorption
in presence of BS
UNSTIRRED
LAYER
Dietary
triglyceride
FA absorption
in absence of BS
Pancreatic
lipase
Mucosa

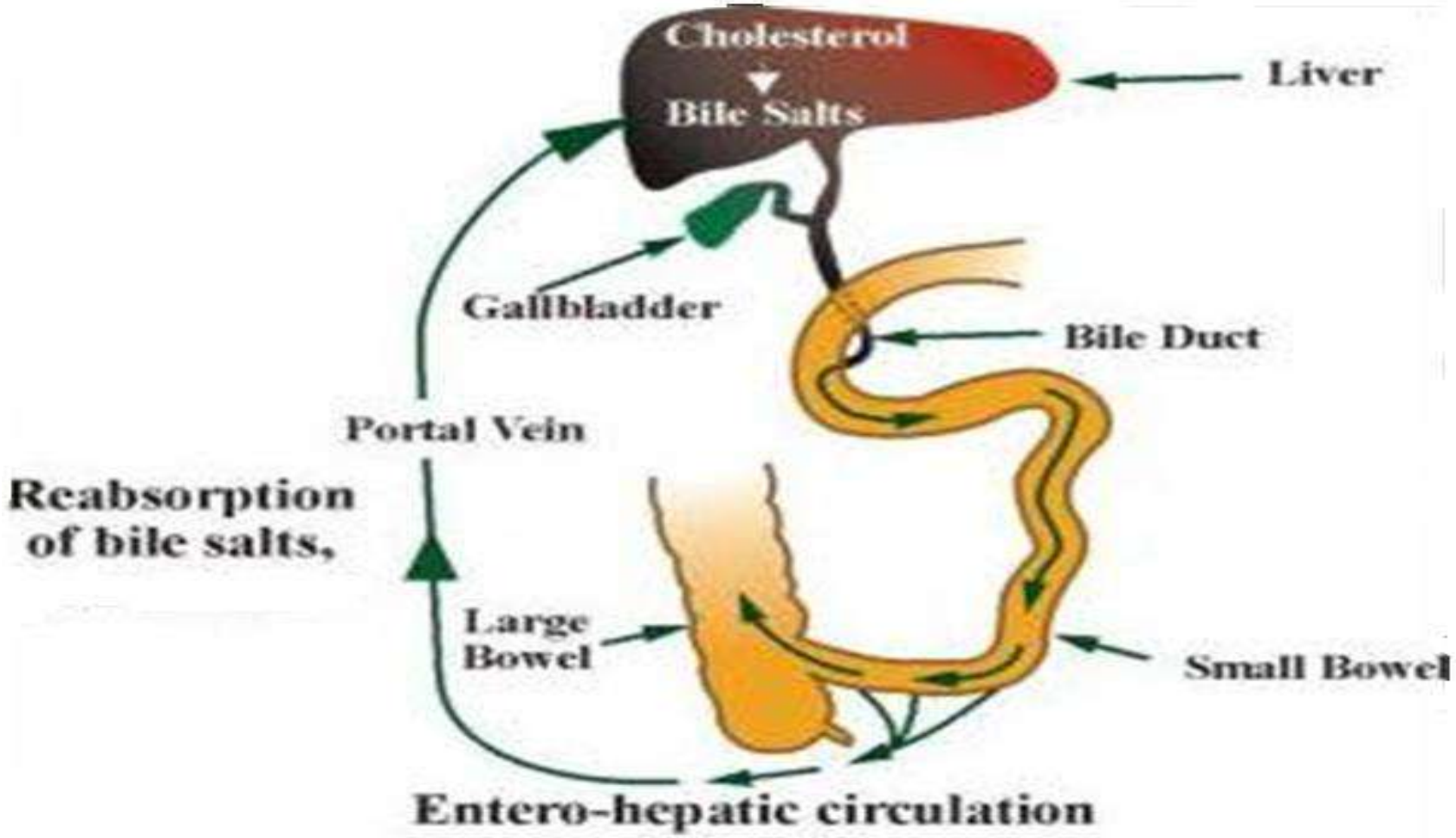
Enterohepatic circulation

- 94% of bile salts are reabsorbed, about one half of this by *Diffusion* through the mucosa in the *early portions of the small intestine* and the remainder by an *Active transport* process from the *Terminal ileum* and returned to the liver to be secreted.

- 5-10% enter the colon → salts of deoxy (reabsorbed) and lithocholic acid (insoluble and excreted in the stool). *2nd bile salts.*
- The total bile salt pool in the body is 3.5 gm (recycles 6-8 times), and the amount lost in stools (0.2-0.4 gm/day) is replaced by new synthesis in the liver.


Hepatic synthesis
Sphincter of Oddi
Spillover from liver into systemic circulation
Gallbladder
Small intestine
Active ileal uptake
Large intestine
Return to liver
Spillover into colon
Passive uptake of deconjugated bile acids from colon
Fecal loss (= hepatic synthesis)

- **If the enterohepatic circulation is interrupted → liver cannot compensate and signs of bile salt deficiency appear** ***(steatorrhea, deficiency of fat soluble vitamins , cholesterol stones).***



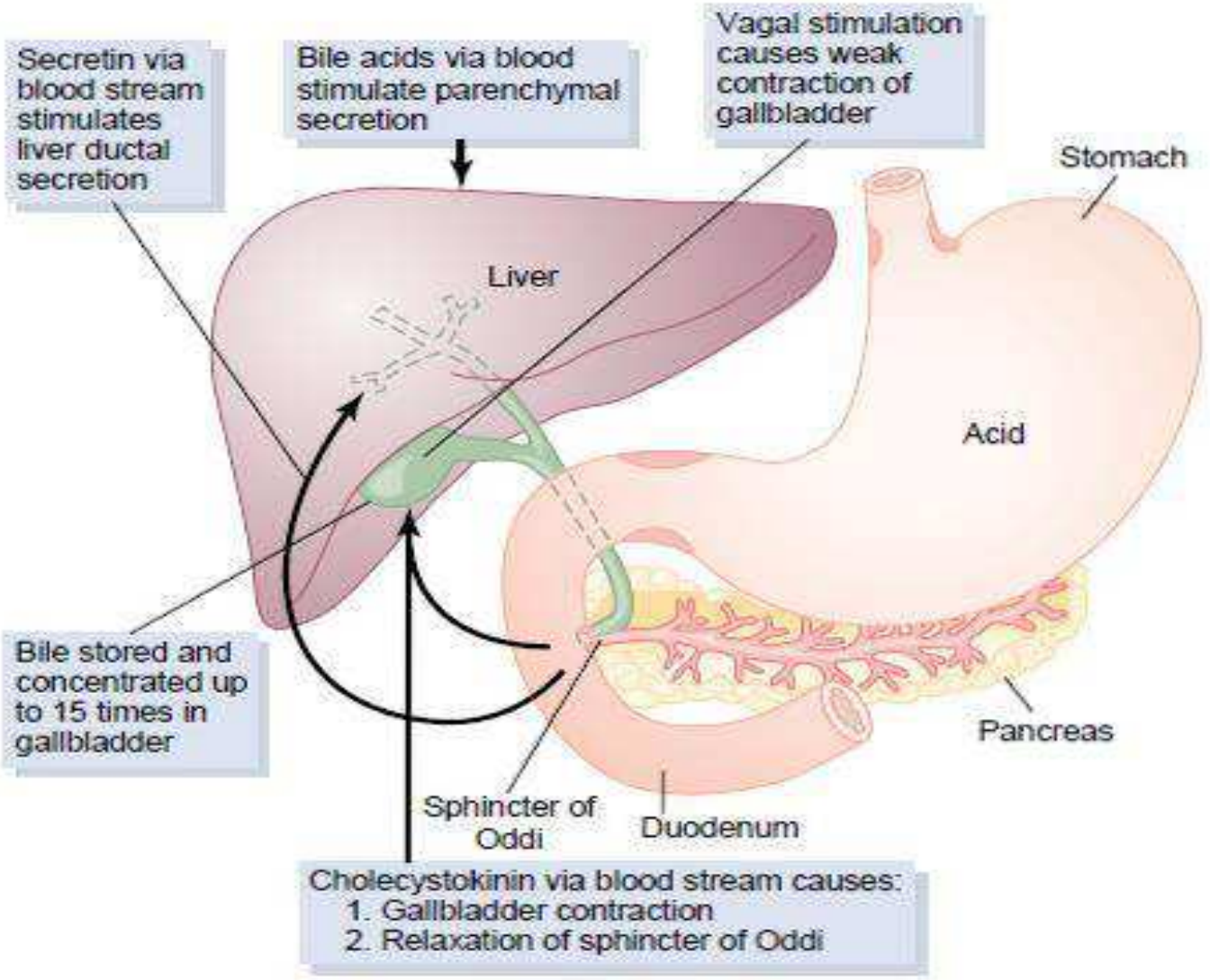
Regulation of bile secretion

Bile secretion by the liver is increased by:-

- ***Chemical mechanism;*** **Bile salts returned to the liver by the enterohepatic circulation stimulate further bile secretion.**
- ***Hormonal mechanism;*** ***Secretin*** **stimulate the aqueous alkaline portion of bile and increase bile flow.**
- ***Neural mechanism;*** **occurs in the cephalic phase of digestion . Mediated via the** ***Vagus nerve*** **& cause increased water & bicarbonate content of bile.**

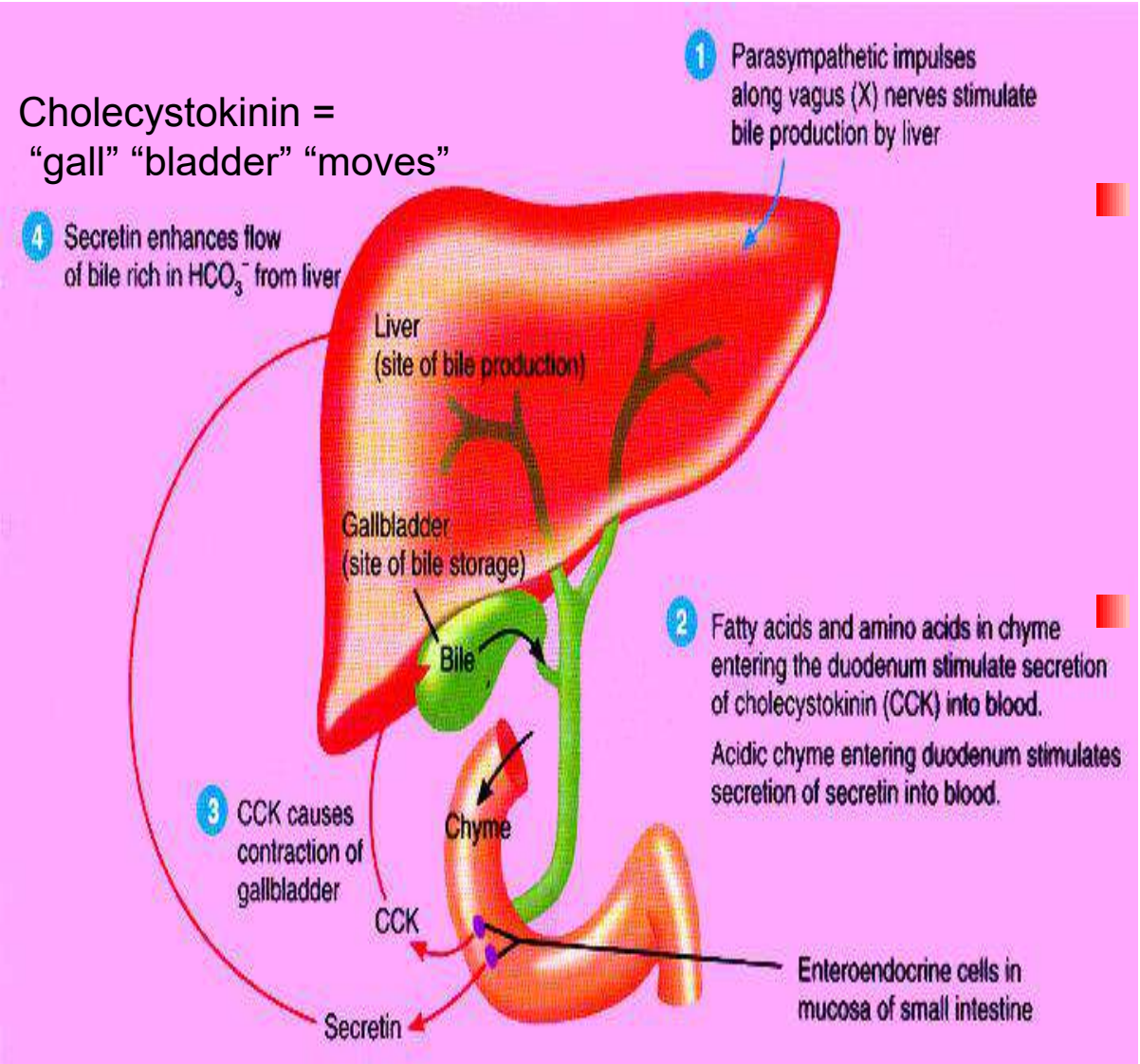
Choleretics ***are substances that increase bile formation by the liver and bile flow .e.g. bile salts &*** **secretin.**

Cholagogue ***are substances that increase move bile from the gall bladder and increase bile flow .e.g.*** **CCK**


Secretin via blood stream stimulates liver ductal secretion
Bile acids via blood stimulate parenchymal secretion
Vagal stimulation causes weak contraction of gallbladder
Stomach
Liver
Acid
Bile stored and concentrated up to 15 times in gallbladder
Pancreas
Sphincter of Oddi
Duodenum
Cholecystokinin via blood stream causes:
1. Gallbladder contraction
2. Relaxation of sphincter of Oddi

ptying.

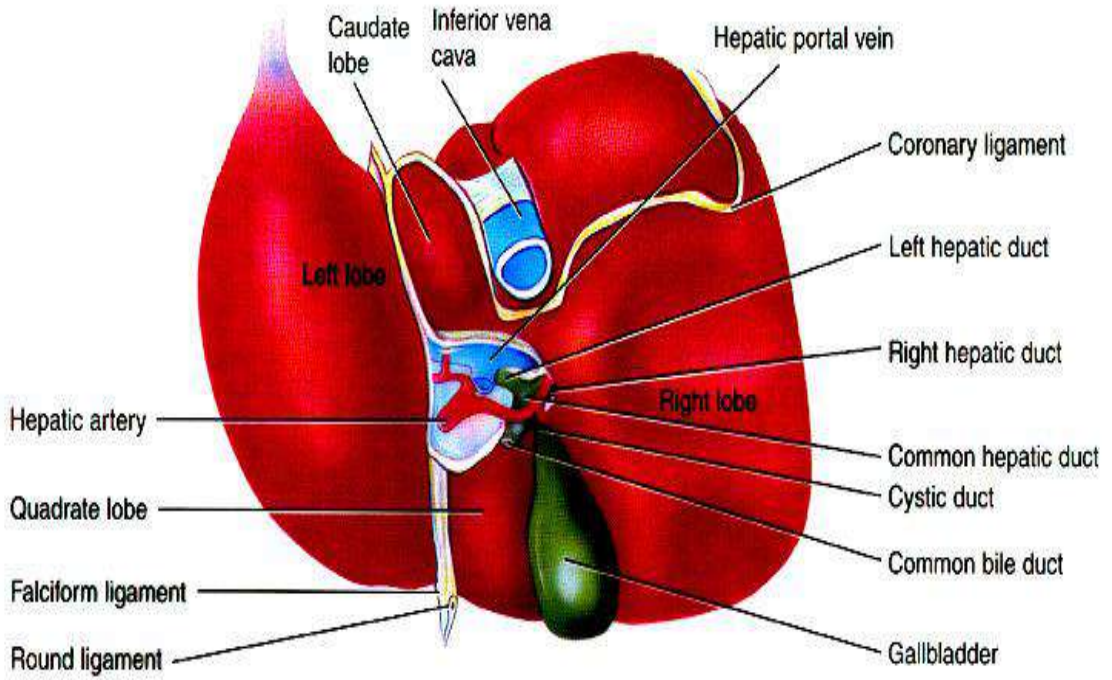
Liver:
Bile Synthesis



- **Regulation of bile production/secretion**
  - ***Nervous control*** **from parasympathetic via Vagus nerve**
  - ***Auto regulation*** **by sensing the presence of fatty acids and amino acids in the acidic chyme**
  - ***Hormonal control*** **by the secretion of the Enteroendocrine, CCK and secretin, from the duodenum**

Gall Bladder

- Pear-shaped sac, 7-10 cm long
- Physiology
  - Stores and concentrates bile between meals
  - CCK stimulates bile release for fatty meals
  - when the small intestine is empty, the hepatopancreatic sphincter closes, forcing bile into the gallbladder for storage



Pathology: gallstones

Functions Gall Bladder

***1-Storage of bile*: between meals, the sphincter of oddi is tonically contracted, so bile flow retrograde upwards through the cystic duct to be stored in the gall bladder.**

***2-Concentration of bile :* by active reabsorption of Na+, followed by passive reabsorption of water and most electrolytes, except calcium (bile salts increase 5-10 times, water content decreases to 89%).**

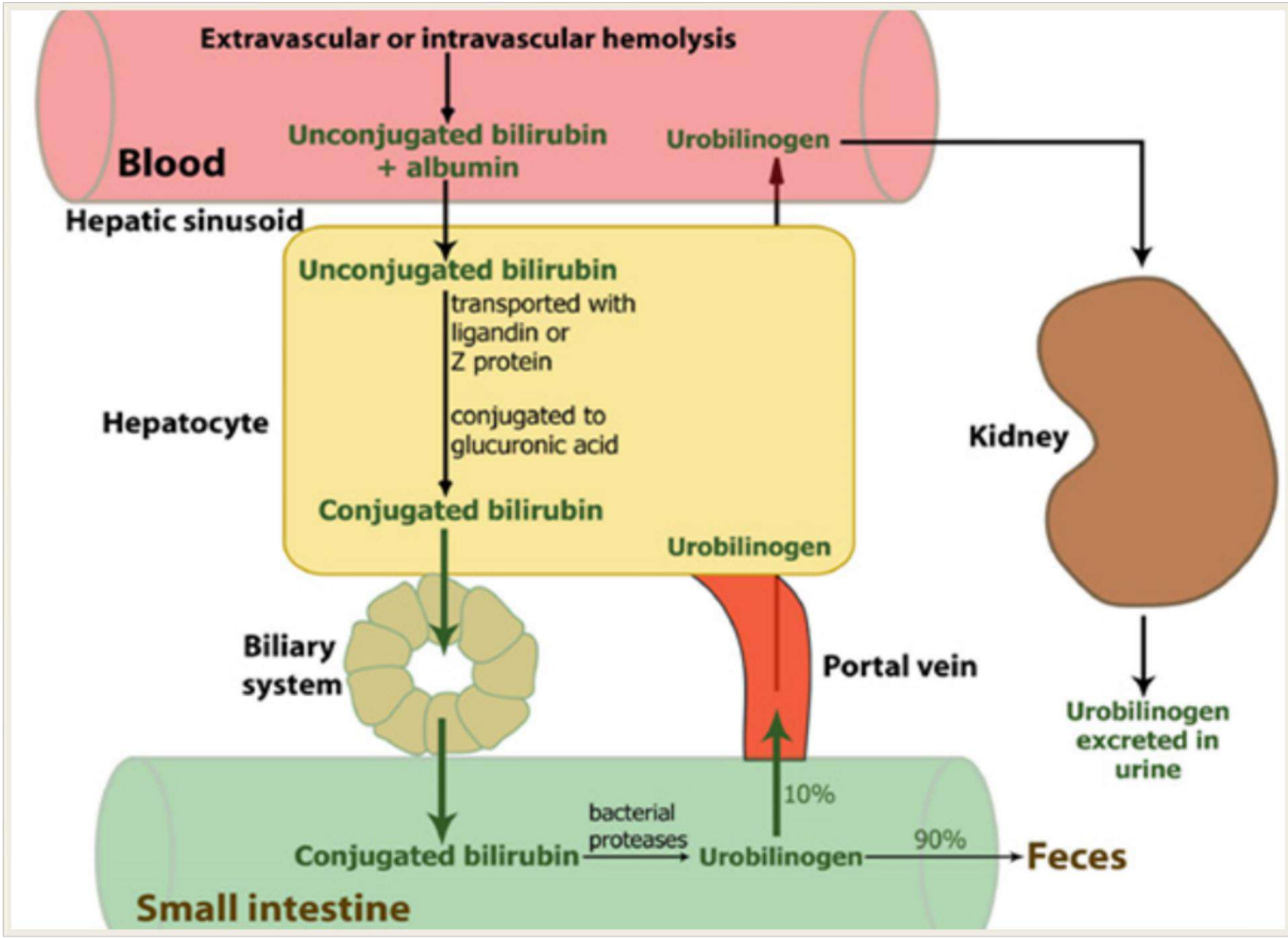
3-Acidification of bile: due to bicarbonate reabsorption during concentration, pH= 7-7.4 (prevents Ca^{2+} ppt and formation of gall stones).

4-Secretion of mucus: (white bile) from mucous glands in the mucosa: it ***Protects*** the gall bladder wall against highly concentrated bile salts, gives the bile a semi fluid consistency, and acts as a lubricant in the small intestine.

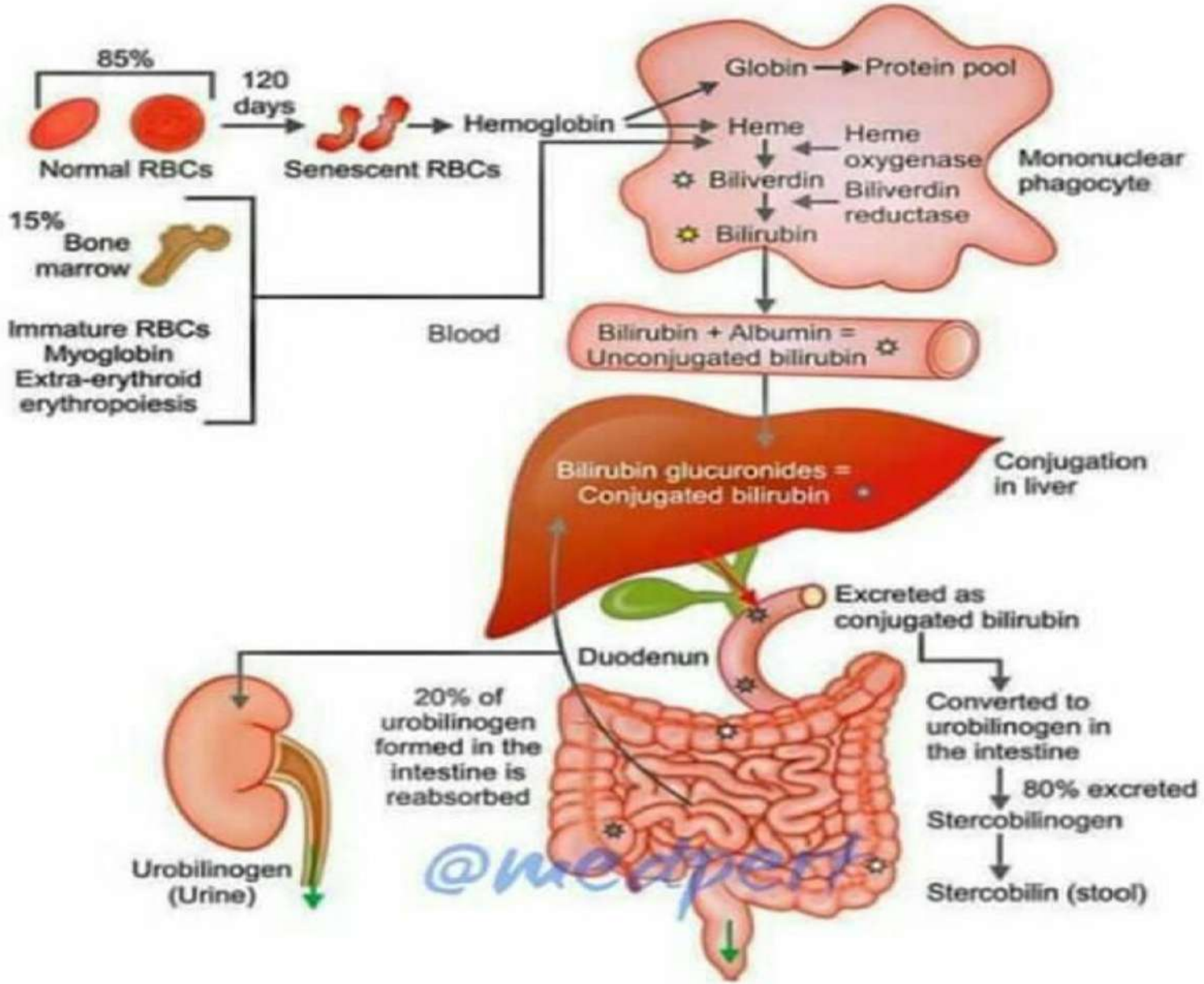
5-Evacuation: by contraction of wall and relaxation of sphincter.

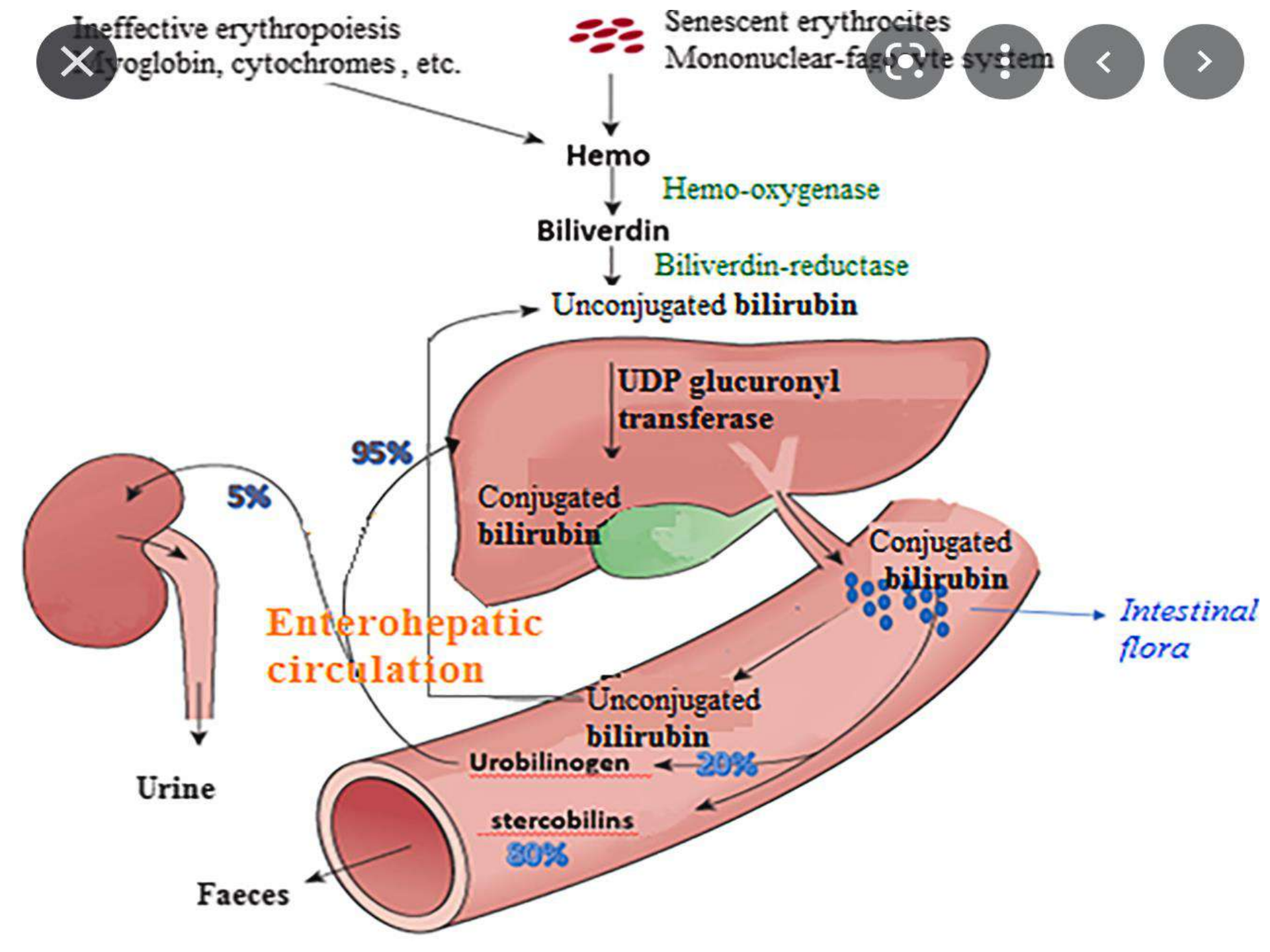
Bile Pigments

- Hb of RBCs is phagocytozed by RES → Heme + Globin.
- Heme ring is opened → Iron is stored in the liver.
- The remaining part of heme is converted to the Green pigment biliverdin → reduced into bilirubin → blood, combine with albumin (haemobilirubin, unconjugated, indirect or free bilirubin)→ liver where albumin is detached, while bilirubin is conjugated with glucuronic acid (Conjugated or direct bilirubin).
  - Conjugated bilirubin is actively transported into the bile canaliculi → golden yellow color of liver bile → Small intestine is converted to urobilinogen → most urobilinogen is converted to sterocoblinogen→Stool (sterocobilin, brown color of stool).
  - 10% enter the general circulation →(urobilinogen) 5%→ kidneys → urine (urobilin).


Extravascular or intravascular hemolysis
Blood
Unconjugated bilirubin
+ albumin
Urobilinogen
Hepatic sinusoid
Unconjugated bilirubin
transported with
ligandin or
Z protein
Hepatocyte
conjugated to
glucuronic acid
Conjugated bilirubin
Urobilinogen
Kidney
Biliary
system
Portal vein
Urobilinogen
excreted in
urine
10%
bacterial
proteases
Conjugated bilirubin
Urobilinogen
90%
Feces
Small intestine

Bilirubin Metabolism




Ineffective erythropoiesis
Myoglobin, cytochromes , etc.
Senescent erythrocites
Mononuclear-fagocyte system
Hemo
Hemo-oxygenase
Biliverdin
Biliverdin-reductase
Unconjugated bilirubin
UDP glucuronyl transferase
95%
5%
Conjugated bilirubin
Conjugated bilirubin
Intestinal flora
Enterohepatic circulation
Unconjugated bilirubin
Urobilinogen
20%
Urine
stercobilins
80%
Faeces

Jaundice

- **Definition:** ***Yellow discoloration of skin and mucus membranes due to presence of excess level of bilirubin (free or conjugated).***

	Hemolytic jaundice	Hepatocellular J	Obstructive J
Causes	Excessive hemolysis of RBCS Hemolytic anemia, drugs, Autoimmune disease	Liver disease Infection viral hepatitis Chemicals chloroform Drugs	Cholestasis Intrahepatic cirrhosis Extra-hepatic GBS Carcinoma stricture
Mechanism	↑ Production of free bill	Liver cannot uptake Conjugate and excreate bill	Liver conjugate but cannot excrete bill to intestine
Blood Bill Bile salts	Haem billi↑ ↑ Absent	Both ↑ Present	Chole bill ↑ ↑ Present
Urine Billi Color	Absent normal	Present Chole billi Dark brown	Present Chole Billi Very dark brown
Stool	Very dark stool	Pale stool	Very pale stool

Physiology of Gastrointestinal Disorders

- ***Disorders of Swallowing and of the Esophagus:***
- **Paralysis of the Swallowing Mechanism :**
- **Damage to the *Fifth, Ninth, or Tenth* cranial nerve**
- ***Poliomyelitis* or *encephalitis.***
- **Paralysis of the swallowing muscles, *muscle dystrophy* , *myasthenia gravis* or *botulism.***

- ***When the swallowing mechanism is partially or totally paralyzed***

- **Swallowing cannot occur.**
- **Failure of the glottis to close food passes into the lungs instead of the esophagus .**
- **Failure of the soft palate and uvula to close the posterior nares so that food refluxes into the nose during swallowing.**

Aspiration under GA.

Achalasia and Mega esophagus

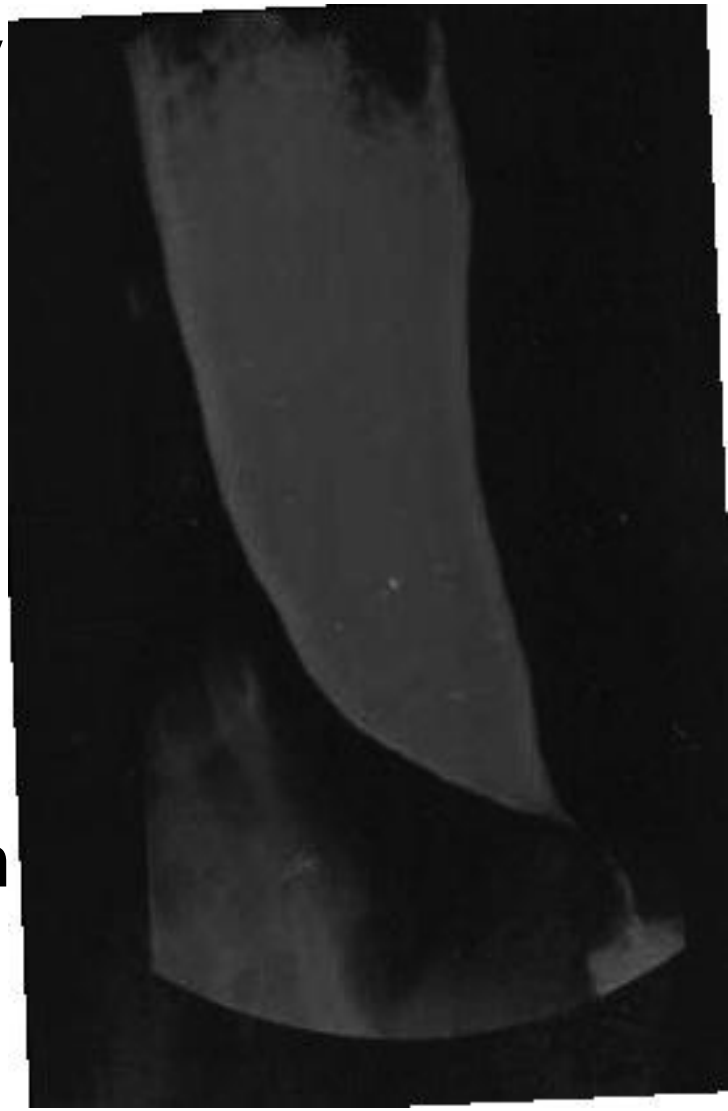
Definition: ***Aprestalsis of muscles of body of esophagus and failure of relaxation of lower esophageal sphincter .***

- **Food fails to pass from the esophagus into the stomach.**
- ***Causes:*** **Damage of the Myenteric plexus in the lower two thirds of the esophagus.**

Muscles remains spastically contracted ,loss receptive relaxation" of the G.E sphincter.

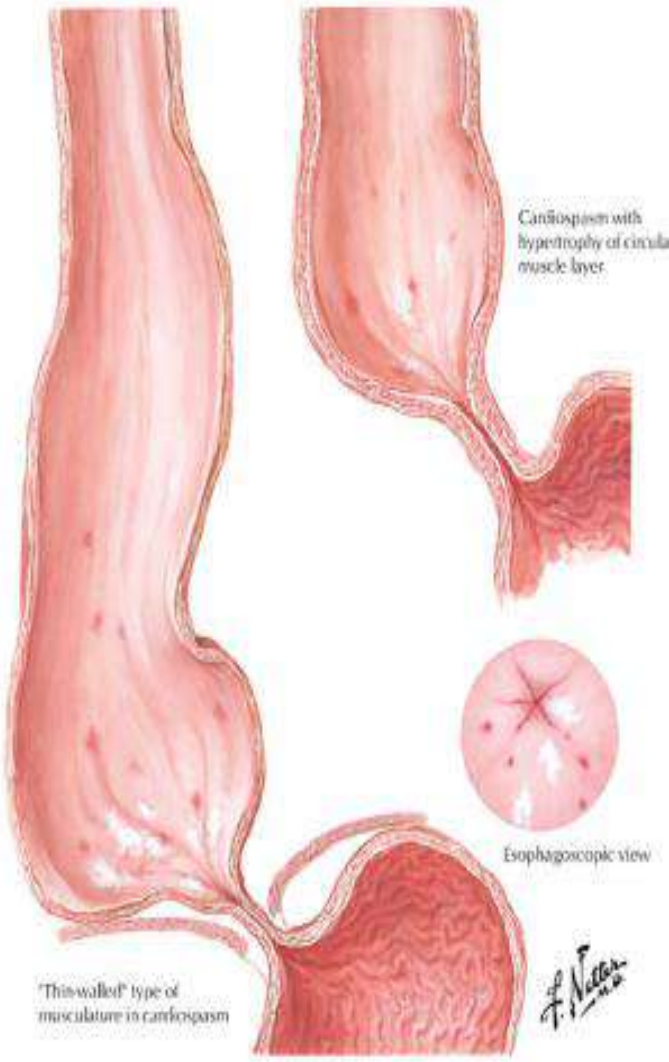
- **Over long periods the esophagus becomes markedly enlarged until it often can hold as much as 1 liter of food, which becomes putridly infected during the long periods of esophageal stasis. The infection may also cause ulceration of the esophageal mucosa, severe substernal pain or even rupture and death**

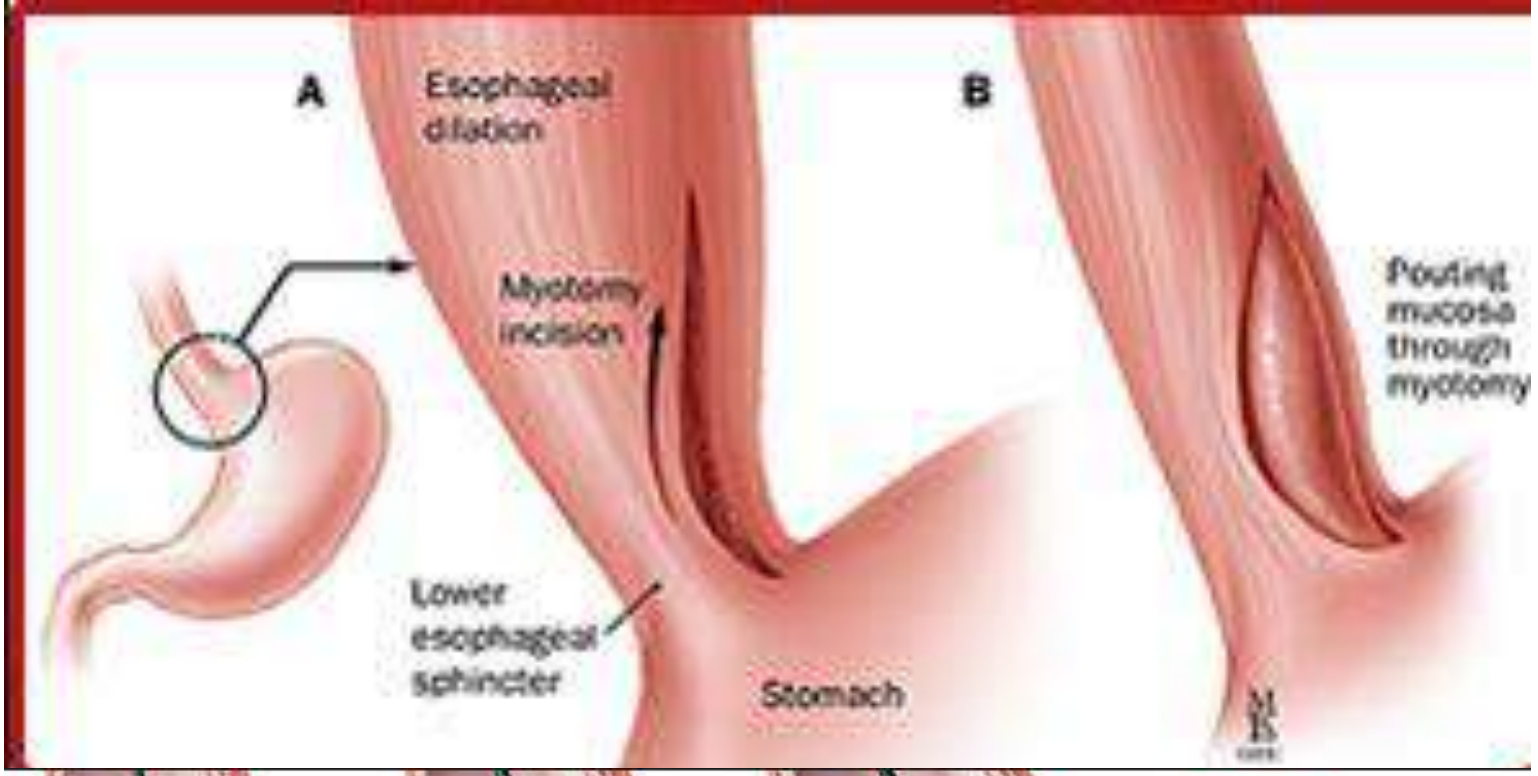
Mega esophagus.

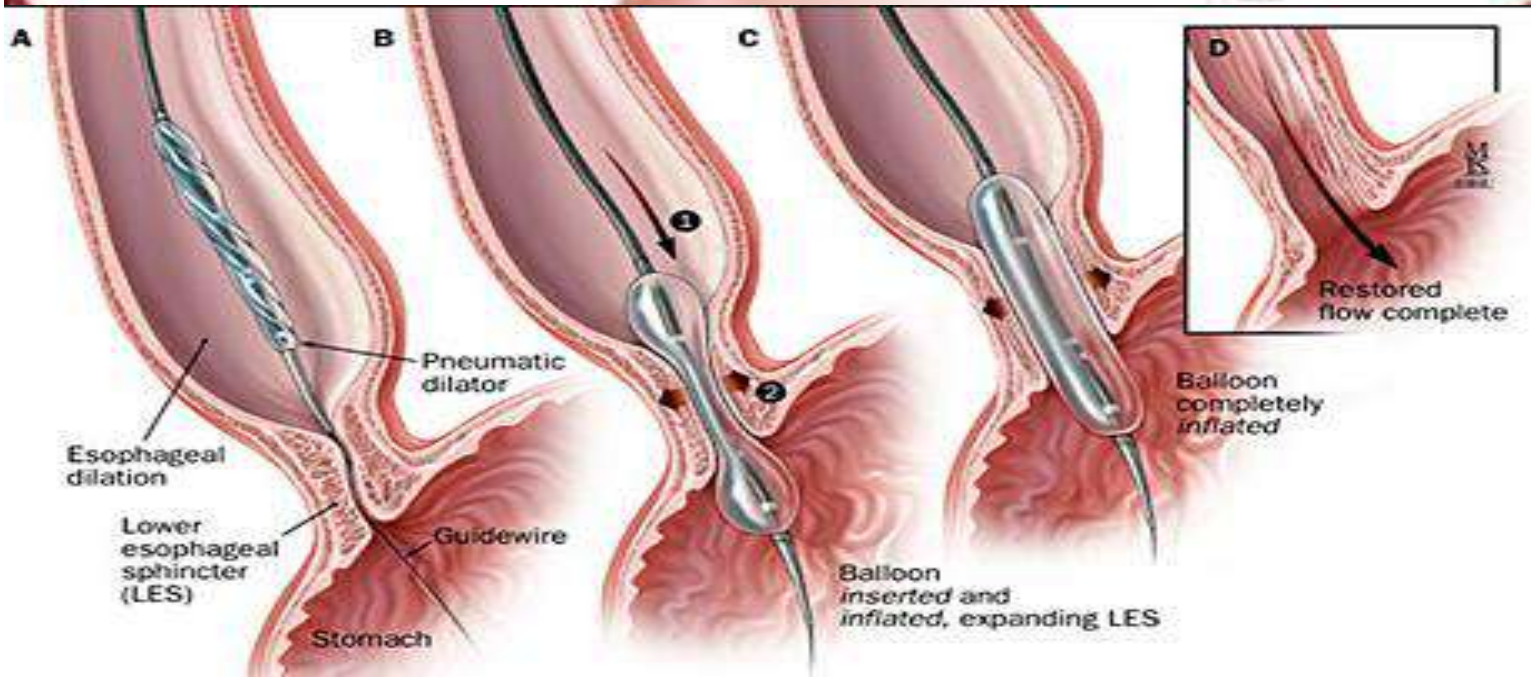


Achalasia

- Primary esophageal motility disorder.
- Peak incidence 20 -50 y.
- Cause progressive dysphagia to solids and liquids.
- Regurgitation undigested food
- Chest pain.
- Loss of weight.
- Increase risk of esophageal cancer.




A
Esophageal dilation
Myotomy incision
Lower esophageal sphincter
Stomach
B
Pouting mucosa through myotomy


A
Pneumatic dilator
Esophageal dilation
Lower esophageal sphincter (LES)
Guidewire
Stomach
B
1
2
Balloon inserted and inflated, expanding LES
C
Balloon completely inflated
D
Restored flow complete

Disorders of the Stomach

- ***Gastritis*** **Inflammation of the Gastric Mucosa**
- **Gastritis is caused by chronic *Bacterial infection* of the gastric mucosa.**
- **Damage to the protective gastric mucosal barrier by *Alcohol, Aspirin , NSAIDS .Steroids, Viniger .***
- ***Gastric Barrier and Its Penetration in Gastritis:***
- **low level of stomach absorption is mainly due to two specific features of the gastric mucosa:**

(1) It is lined with highly resistant mucous cells that secrete viscid and adherent mucus.

(2) It has tight junctions between the adjacent epithelial cells*. "Gastric Barrier."*

- **The gastric barrier normally is resistant enough to diffusion of highly concentrated hydrogen ions of the gastric juice.**

- **In gastritis, the permeability of the barrier is greatly increased. The H^+ diffuse into mucosa causing damage and atrophy.**

- **It also makes the mucosa susceptible to digestion by the peptic digestive enzymes, thus frequently resulting in a *Gastric ulcer.***

Chronic Gastritis Can Lead to Gastric Atrophy and Loss of Stomach Secretions

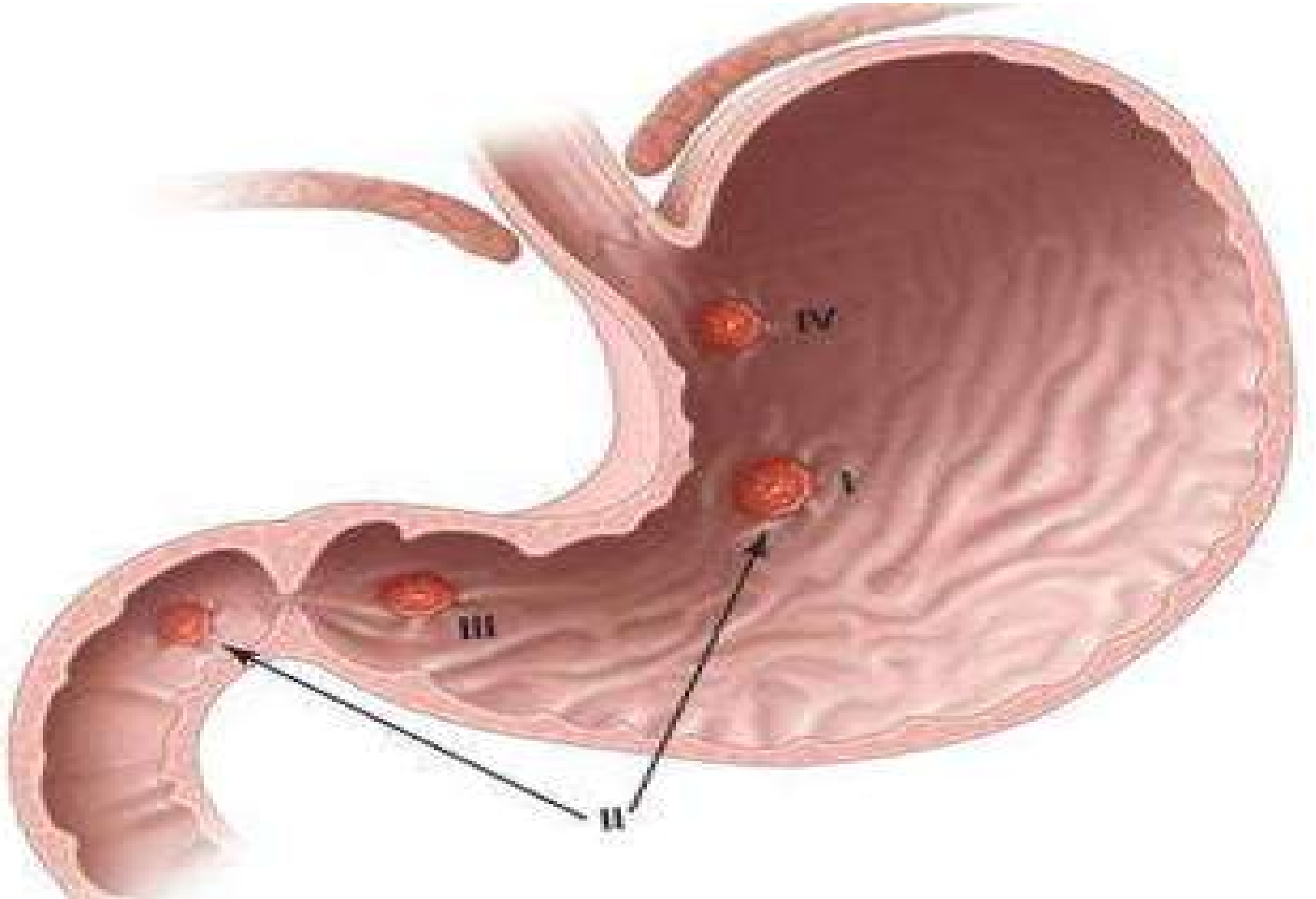
Achlorhydria (and Hypochlorhydria):

- ***Achlorhydria:*** **means simply that the stomach fails to secrete hydrochloric acid; it is diagnosed when the pH of the gastric secretions fails to decrease below 6.5 after maximal stimulation.**
- **Hypochlorhydria: means diminished acid secretion. When acid is not secreted, pepsin also usually is not secreted; even when it is, the lack of acid prevents it from functioning because pepsin requires an acid medium for activity.**

Gastric Atrophy May Cause Pernicious Anemia

- **In the absence of intrinsic factor, only about 1/50 of the vitamin B_{12} is absorbed. And, without intrinsic factor, an adequate amount of vitamin B_{12} is not made available from the foods to cause young, newly forming red blood cells to mature in the bone marrow. The result is *Pernicious Anemia.***

Types of gastric ulcers



- ***A Surface Breach*** **of mucosal lining of GIT (excoriated area of stomach or intestinal mucosa) occurring as a result of *acid and pepsin* attack.**
- ***Sites:***
  - **Duodenum (DU)**
  - **Stomach (GU)**
  - **Oesophagus**
  - **Gastro-Enterostomy stoma *(Marginal ulcer).***
  - **Related to ectopic gastric mucosa (e.g. in Meckel's diverticulum).**
  - **Acute peptic ulcer Like acute erosion but breaching muscularis mucosa.**

Peptic Ulcer

Causes:

1. High acid and peptic content
2. Irritation
3. Poor blood supply
4. Poor secretion of mucus
5. Infection, *H. pylori*

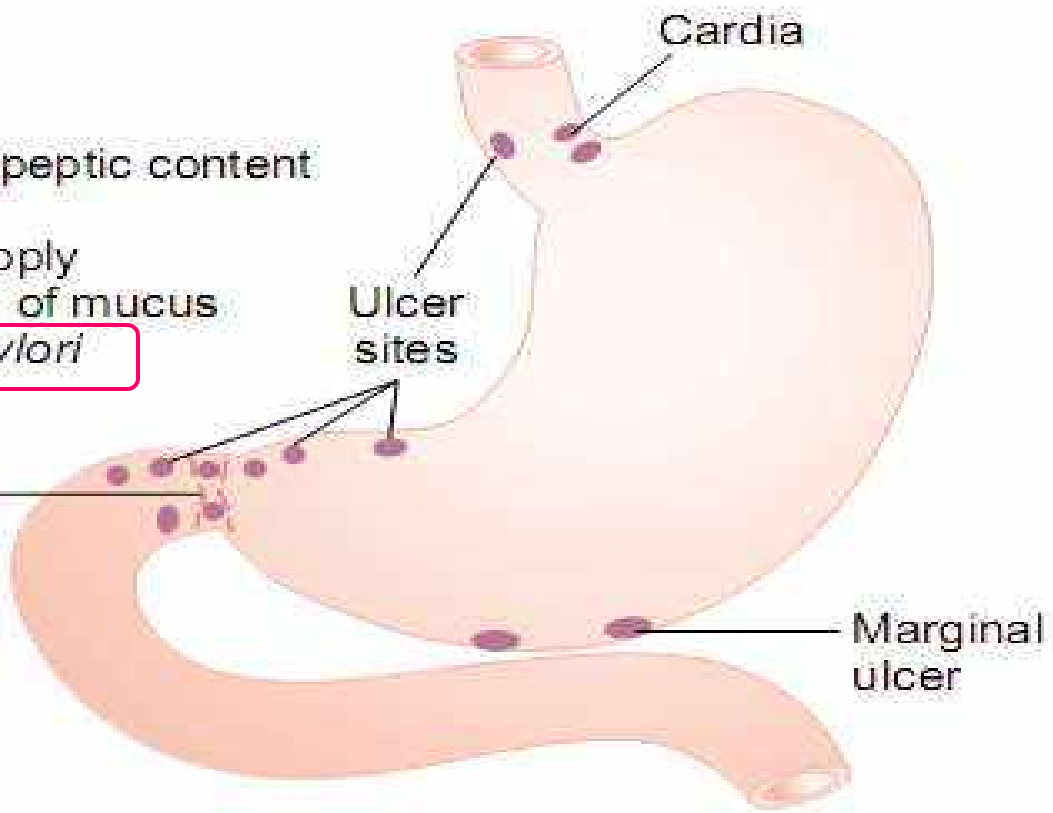


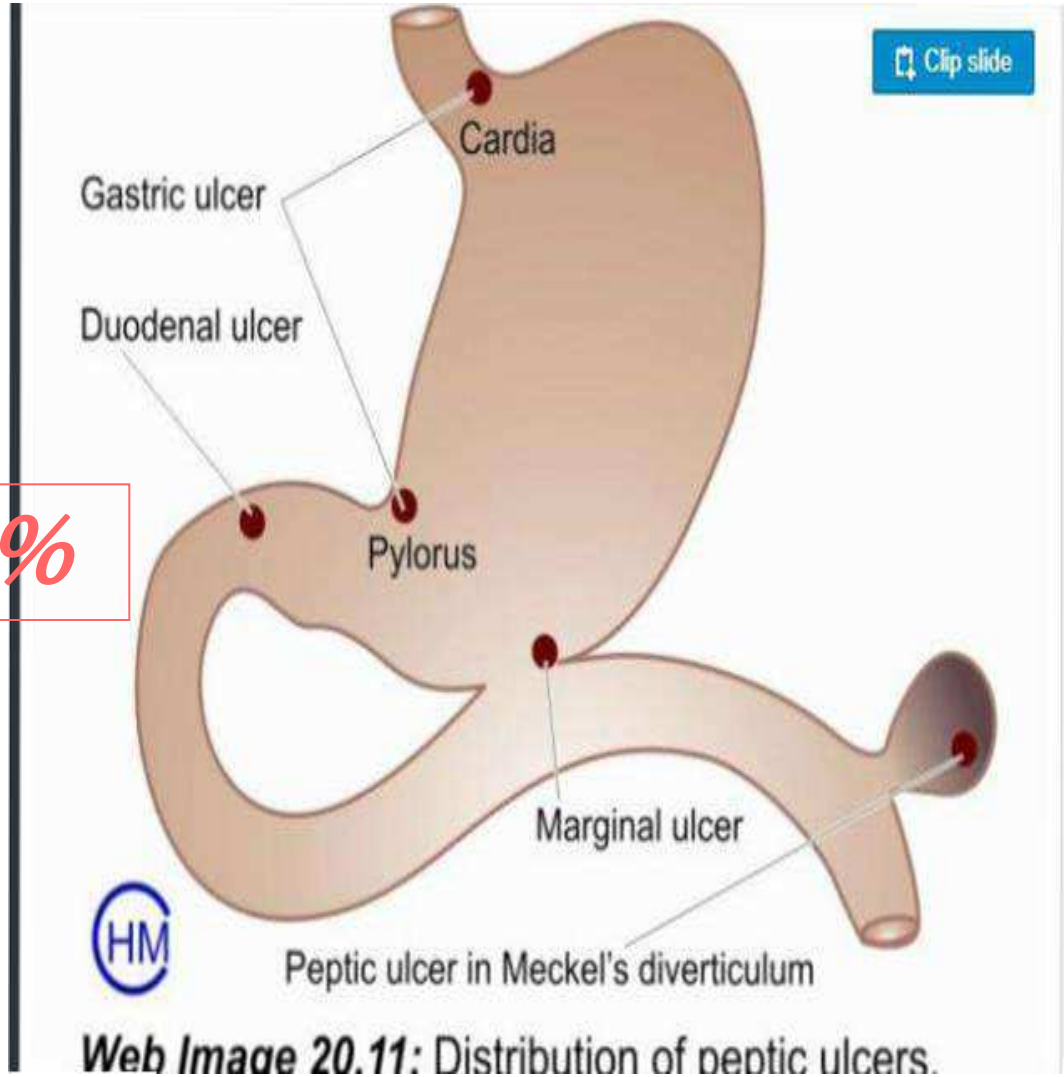
Figure 66–1

Peptic ulcer. *H. pylori*, *Helicobacter pylori*.

Sites of PUD

- **Duodenum:80%**
- ***Gastric:* 15%**
- ***D1, Stomach:* 4%**
- ***O-G Junction :***
- ***Meckel's D:***
- ***Marginal :***

1 %



Web Image 20.11: Distribution of peptic ulcers.

Basic Cause of Peptic Ulceration

The usual cause of peptic ulceration is an *Imbalance* between the Rate of secretion of gastric juice and the Degree of protection afforded by

- **The gastro duodenal mucosal barrier .**
- **The neutralization of the gastric acid by duodenal juices.**

MUCUS : **all areas normally exposed to gastric juice are well supplied with mucus glands(compound mucous glands in the lower esophagus plus the mucous cell coating of the stomach mucosa, the mucous neck cells of the gastric glands, the deep pyloric glands that secrete mainly mucus, and, finally, the glands of *Brunner's of the upper Duodenum*, which secrete a highly alkaline mucus).**

ALKALINE SECRETIONS

- **The duodenum is protected by the *Alkalinity of small intestinal secretions.***
- ***Pancreatic secretion,* which contains large quantities of $Nahco_3$ that neutralize the Hcl of the gastric juice, also *Inactivating Pepsin* and preventing digestion of the mucosa.**
- **In addition, large amounts of bicarbonate ions are provided in the secretions of the large Brunner's glands in the first *few centimeters of the duodenal wall* and In bile coming from the liver.**

Aggressive Factors

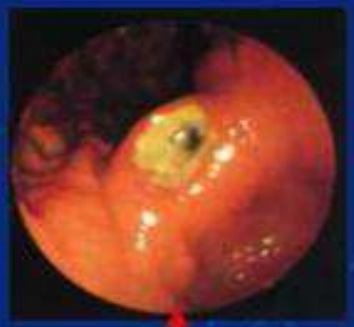
Acid/Pepsin

- H. pylori infection
- NSAIDs
- Smoking

Defensive Factors

- Mucus-bicarbonate barrier
- Barrier of apical membrane
- Mucosal blood flow
- Prostaglandins
- Epithelial cell restitution

I — Aggressive Factors ↑



II — Defensive Factors ↓

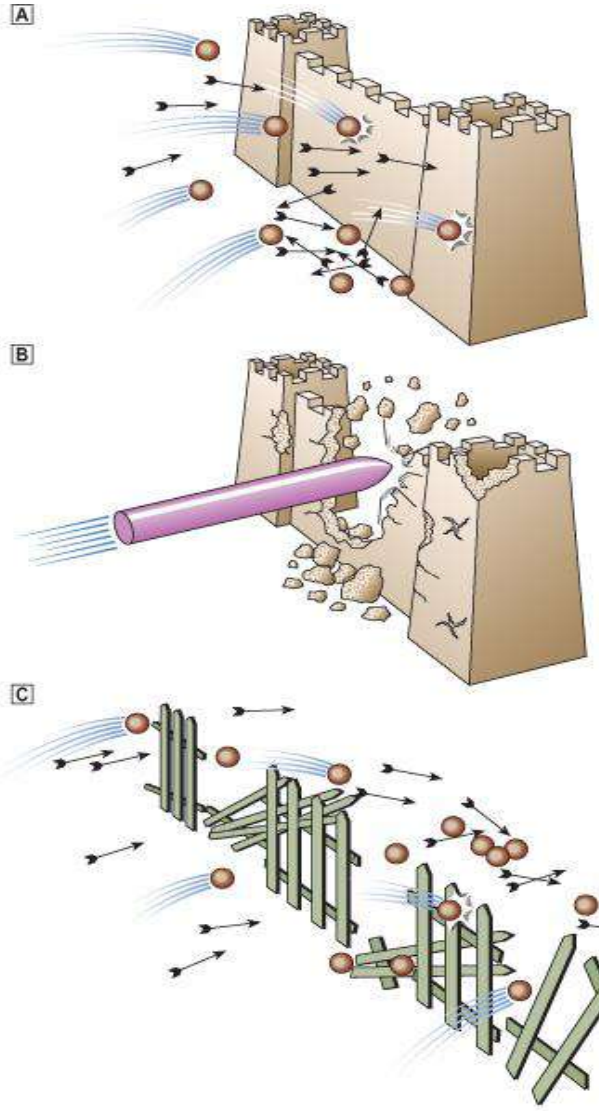
III — Aggressive Factors ↑ + Defensive Factors ↓

REFLEXES

- ***Two feedback control mechanisms*** **normally ensure that this neutralization of gastric juices is complete.**
- **When excess acid enters the duodenum, it inhibits gastric secretion and peristalsis in the stomach, both by nervous reflexes and by hormonal feedback from the duodenum, thereby *decreasing the rate of gastric emptying.***
- **The presence of acid in the small intestine liberates *Secretin* from the intestinal mucosa, which then passes by way of the blood to the pancreas to promote rapid secretion of pancreatic juice.**

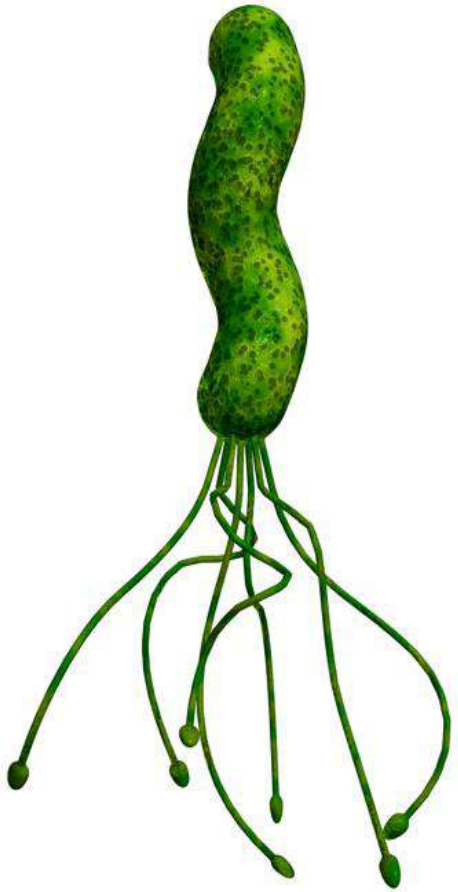
Causes

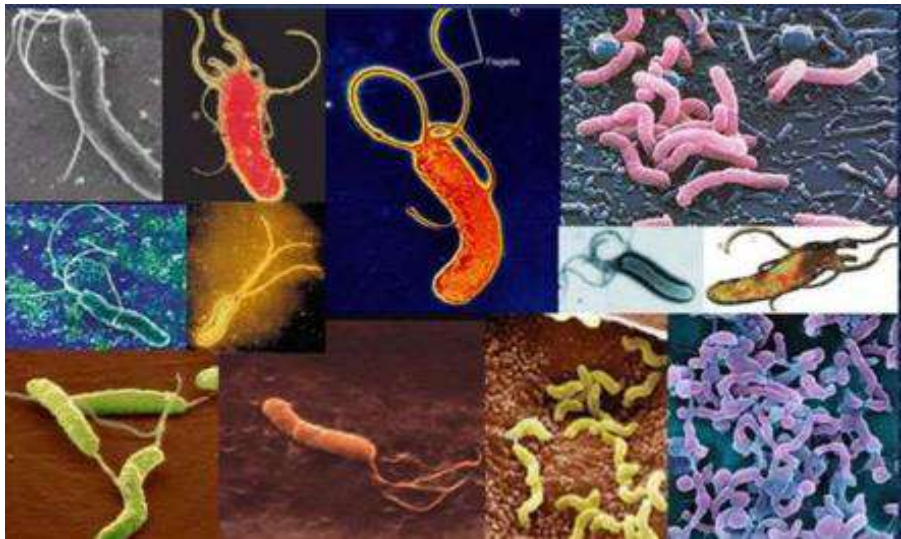
- In normal acid/pepsin attack is balanced by mucosal defences
- Increased attack by hyperacidity Weakened mucosal defence – the major factor *(H. pylori Related)*



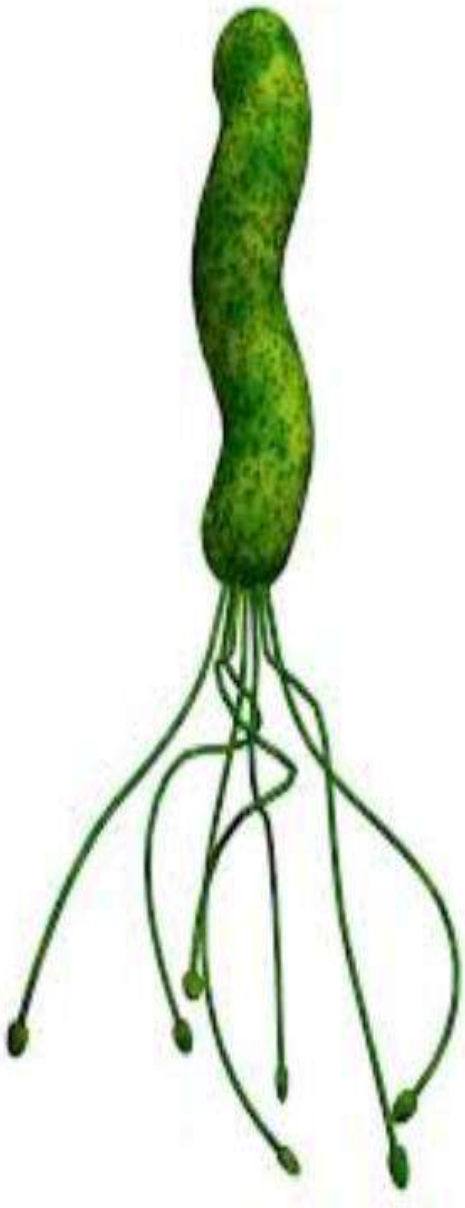
Helicobacter pylori

- Gram -ve Comma Shaped Bacteria Micro Aerophilic with 4-6 Flagella .
- Is most common cause of PUD.
- Transmission is Feco - Oral.
- Secrete urease convert Urea to Ammonia.
- Produce alkaline environment to survive in stomach.
- Higher prevalence in low socio economic.
- Almost all patient with DU and 2/3 of GU are HLO +.

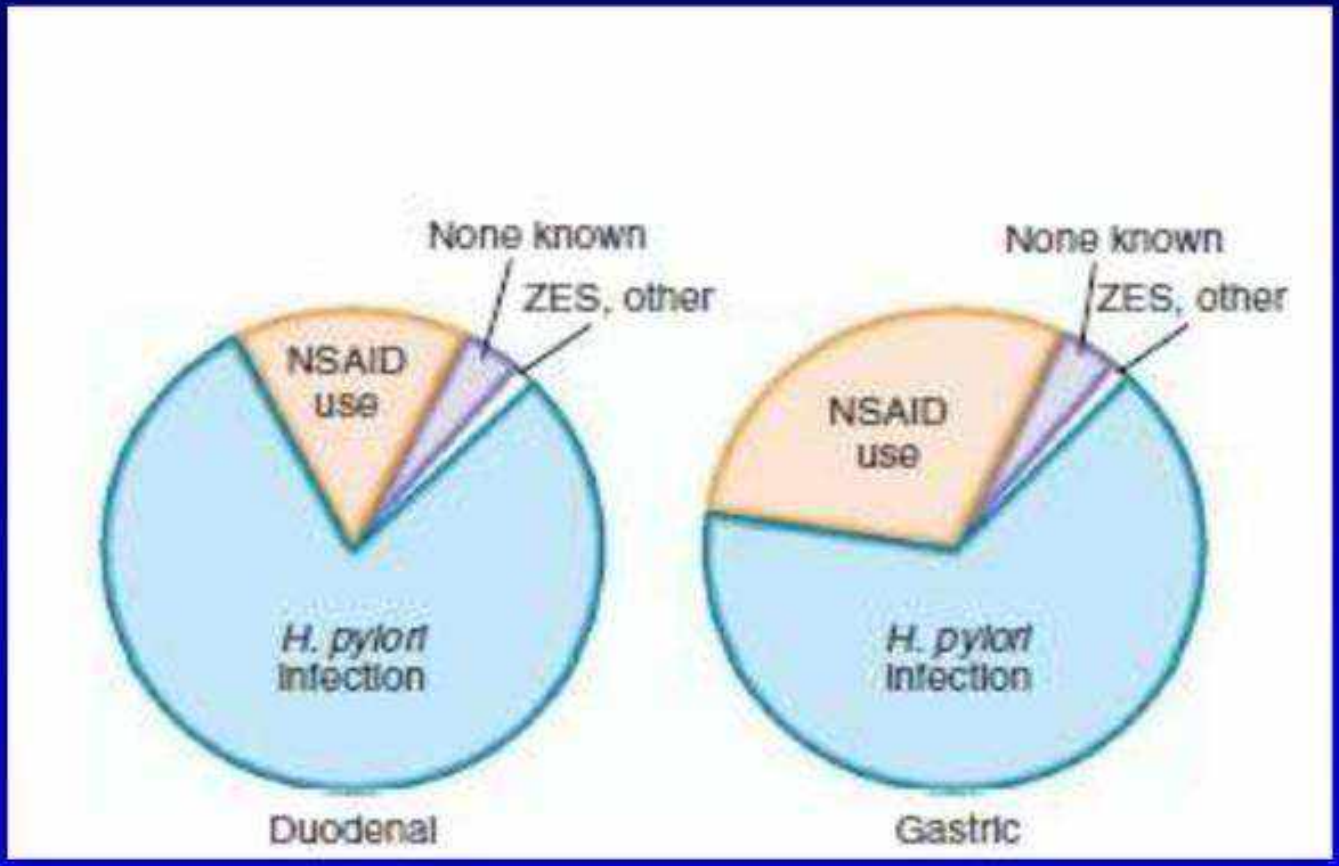




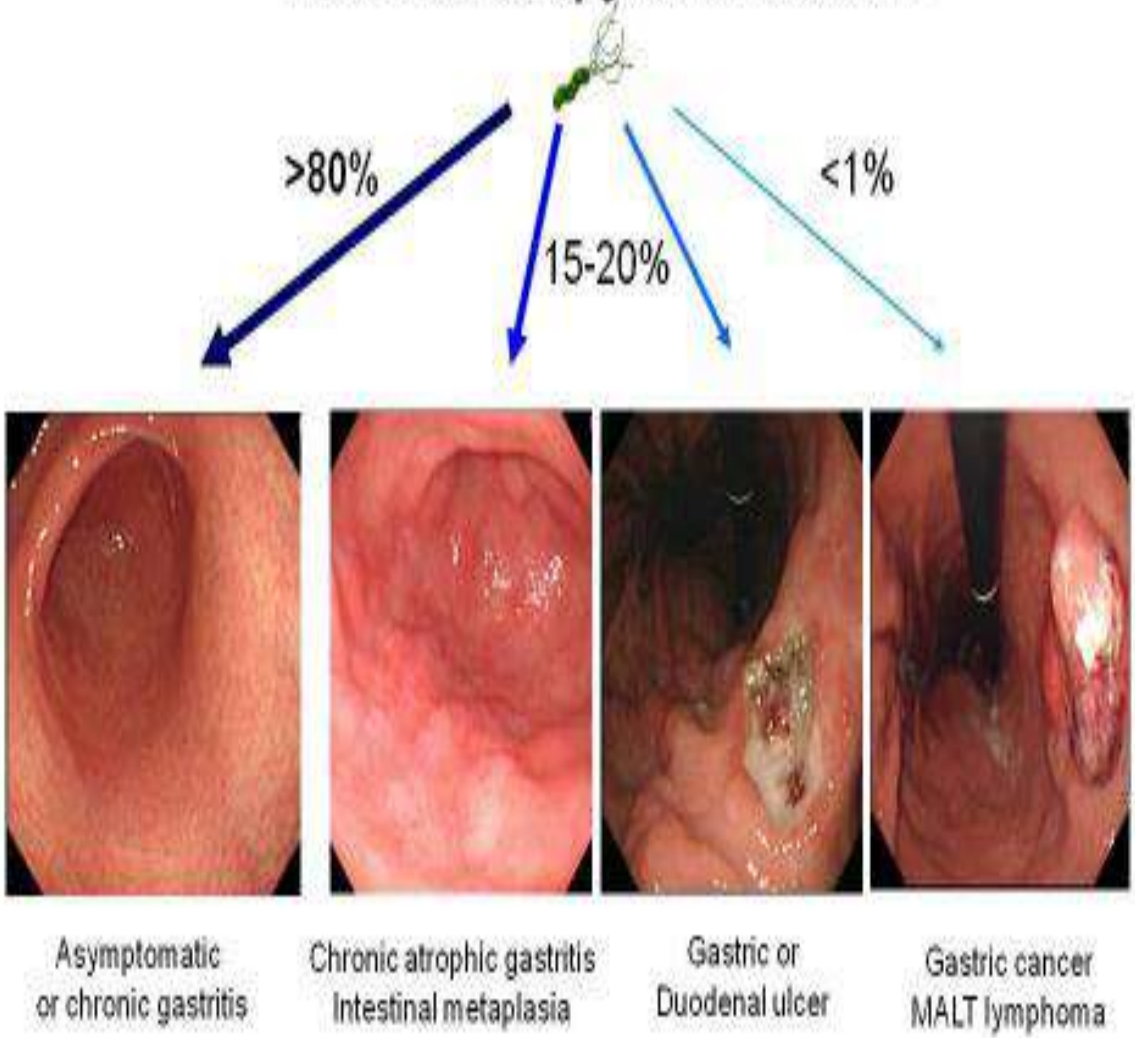
- **Bacterial Infection by *Helicobacter pylori* Breaks Down the Gastro duodenal Mucosal Barrier and Stimulates Gastric Acid Secretion.**
- **At least 75 percent of peptic ulcer patients have been found to have chronic infection of the terminal portions of the gastric mucosa and initial portions of the duodenal mucosa, most often caused by the bacterium *Helicobacter pylori***
- **In *DU*, the rate of gastric acid secretion is greater than normal, sometimes as much as twice normal.**
- **Excess secretion of gastric juices for any reason may cause peptic ulceration.**

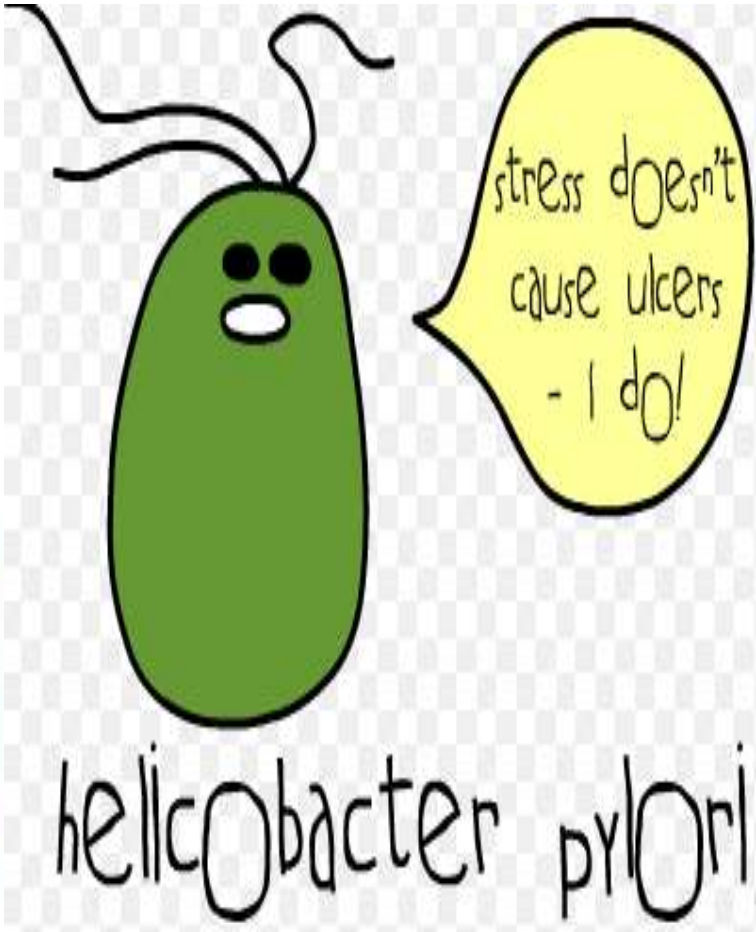


Conditions associated with PUD

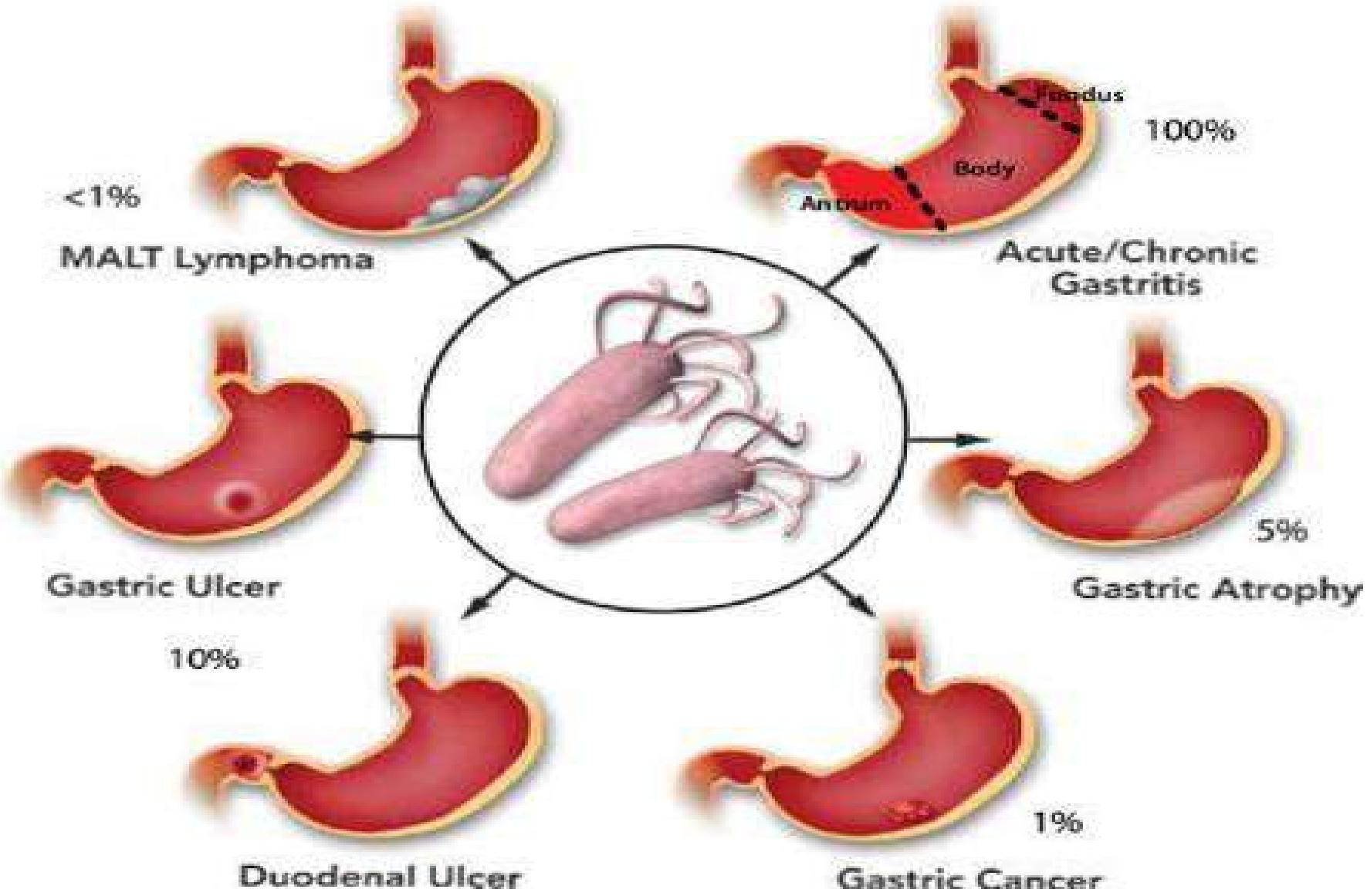


The Clinical Outcomes of *Helicobacter pylori* Infections





HLO OUTCOME


<1%
MALT Lymphoma
Fundus
Body
Antrum
100%
Acute/Chronic Gastritis
Gastric Ulcer
10%
5%
Gastric Atrophy
Duodenal Ulcer
1%
Gastric Cancer

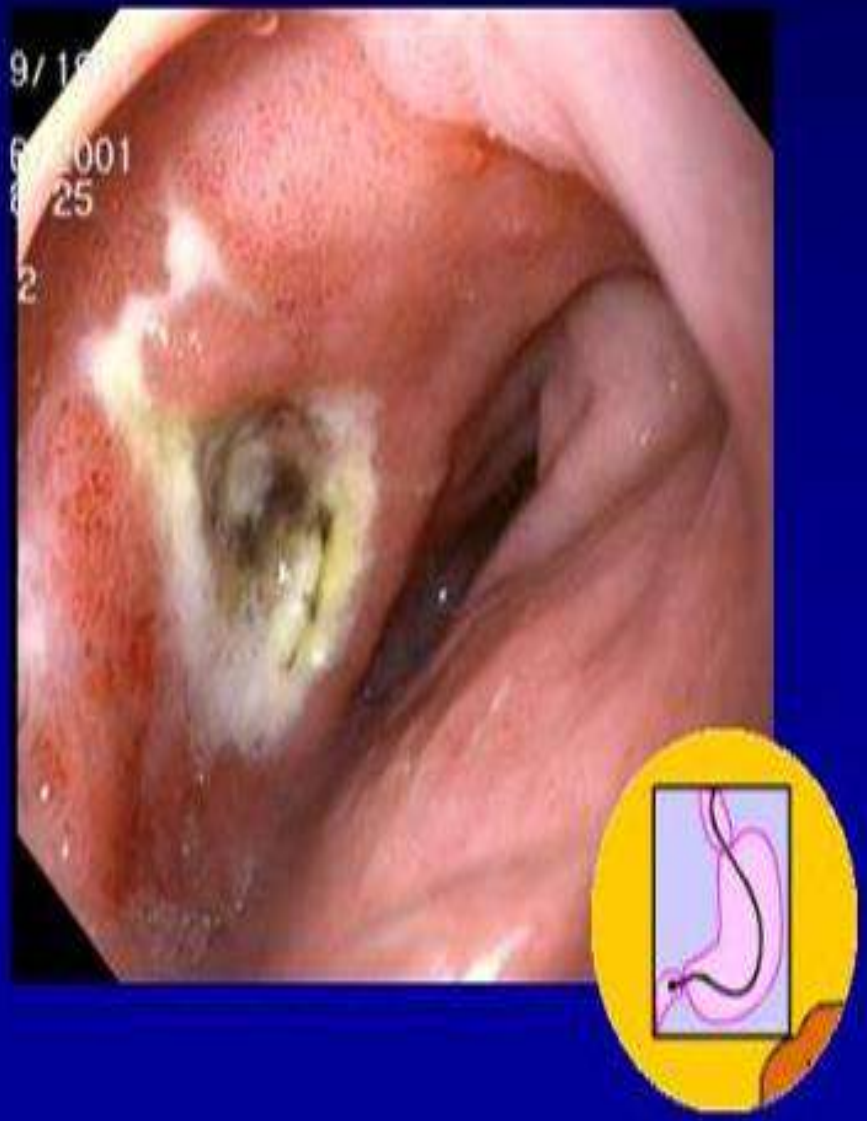
Other factors that predispose to ulcers include

- ***Smoking:*** **presumably because of increased nervous stimulation of the stomach Secretory glands.**
- ***Alcohol:*** **because it tends to break down the mucosal barrier.**
- ***Aspirin and other NSAIDS:*** **drugs that also have a strong propensity for breaking down this barrier.**

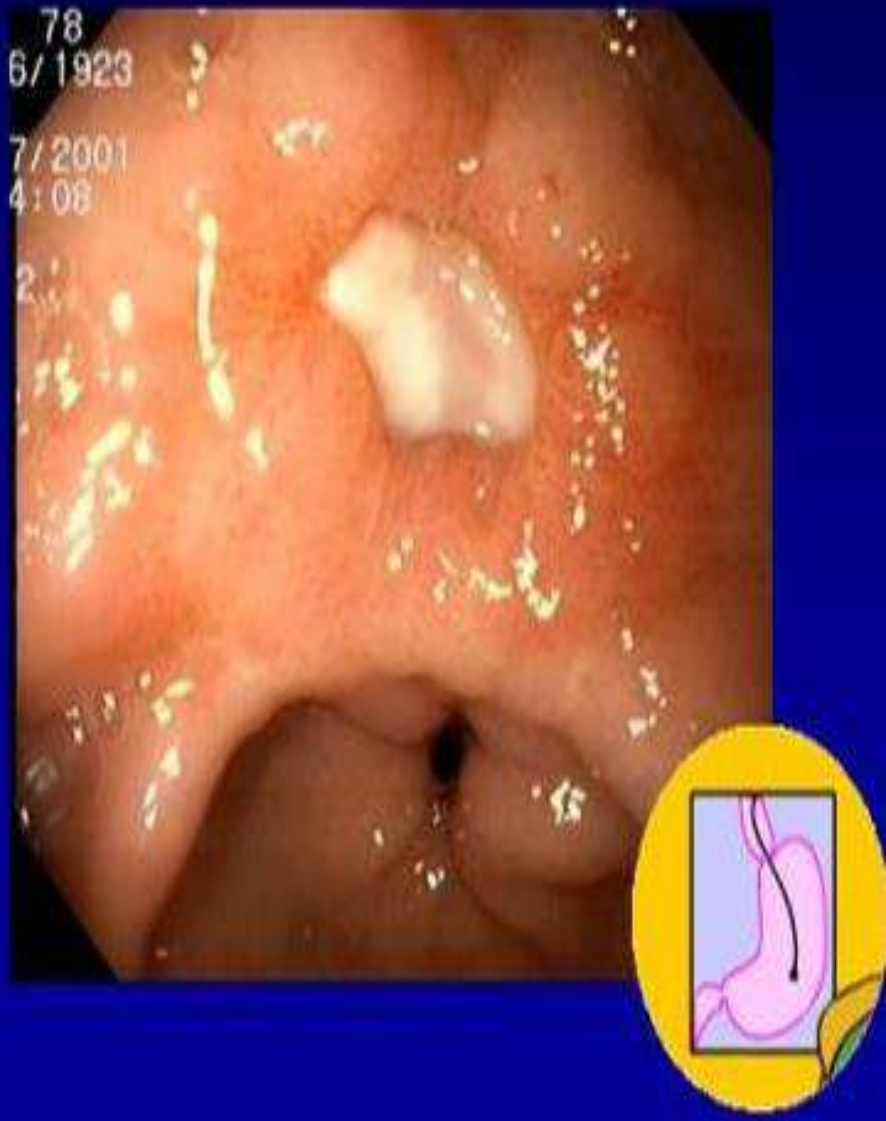
Physiology of Treatment

- **Use of Antibiotics along with other agents to kill infectious bacteria.**
- **Proton pump inhibitors (PPI)are used now as their antacid effect is better and duration of action is longer e.g. *Omeprazole.***
- **Administration of an acid-suppressant drug, especially *ranitidine*, an antihistaminic that blocks the stimulatory effect of histamine on gastric gland histamine$_2$ *(H_2) receptors antagonist,* thus reducing gastric acid secretion by 70 to 80 per cent.**
- **Triple Therapy is the recent approach in treatment of peptic ulcer. It includes 2 antibiotics (Clarithromycin + Amoxicillin or metronidazole) and an acid-suppressant (Omeprazole).**

Duodenal Ulcer (DU)



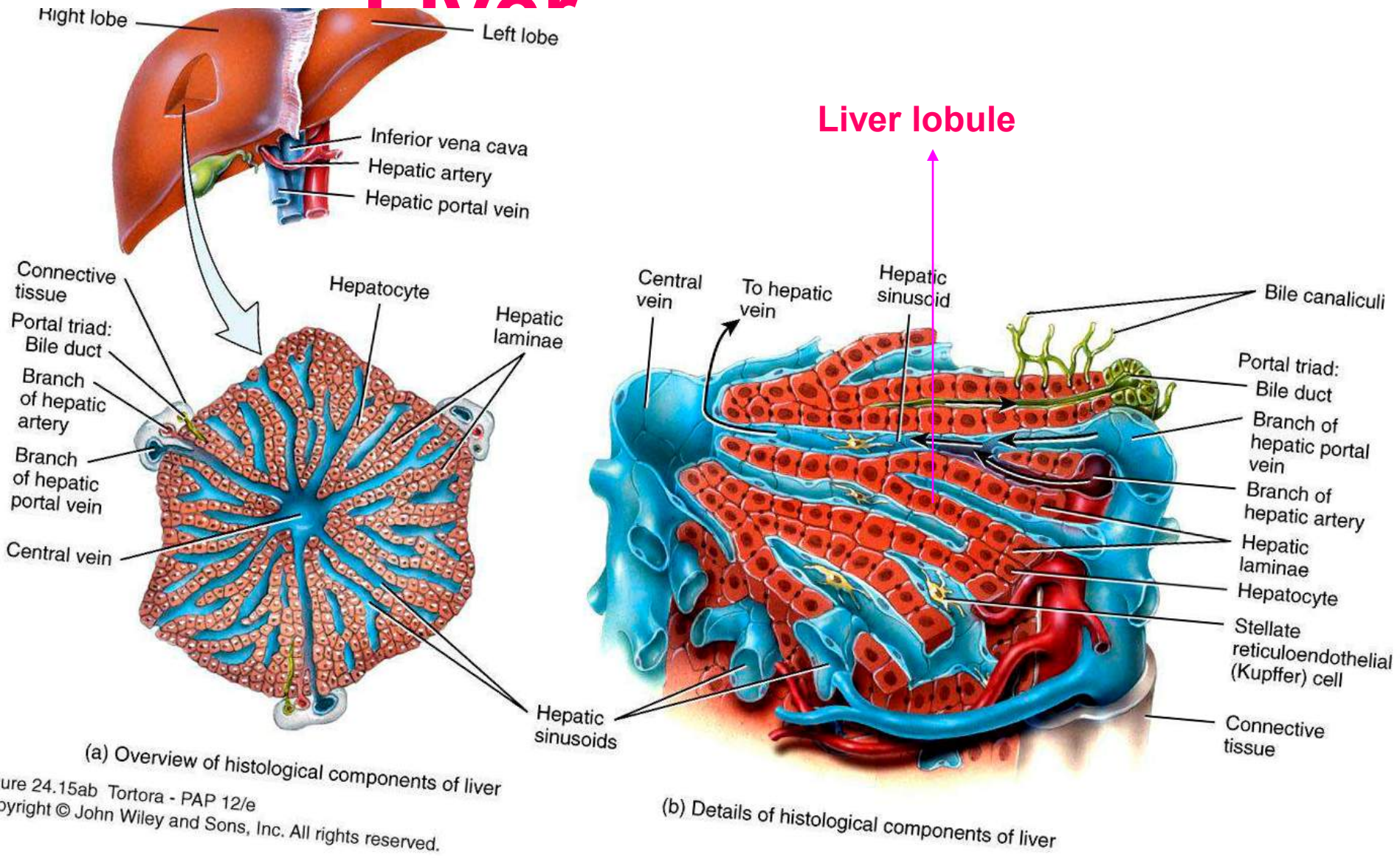
Gastric Ulcer (GU)



6-Secretion of Bile by the Liver Functions of the Biliary Tree

- liver is the largest gland in the body (1.5 Kg), essential for life.
- The functional unit is the *liver lobule* (hepatocytes around a central vein separated by blood sinusoids).
- The sinusoids are wide fenestrated, contain large Kupffer cells.
- Hepatic vascular system:
  - 1.5 L/minute (27% of CO) , 1L from portal vein, 500ml from hepatic artery.
  - Rich lymphatic drainage.

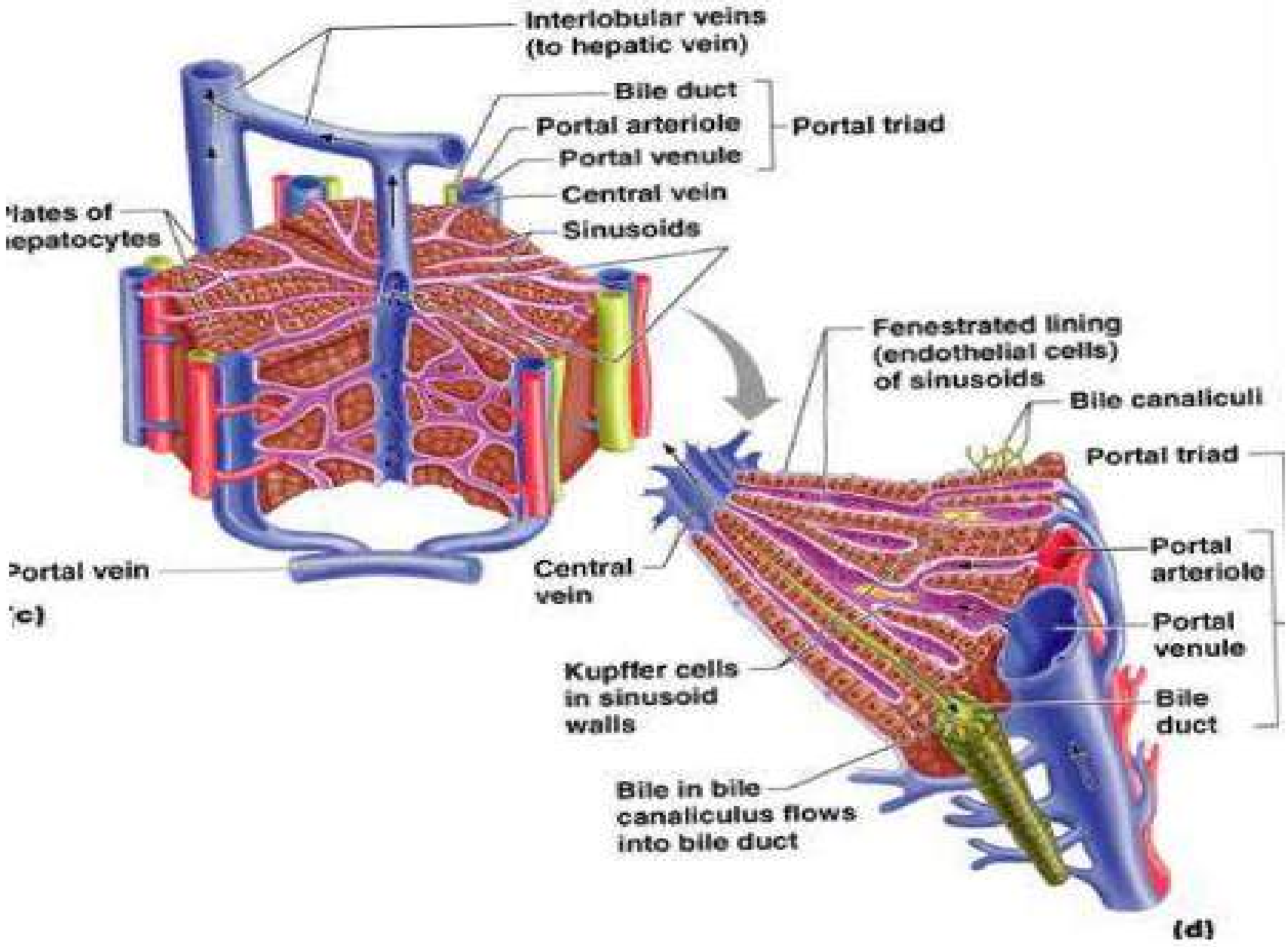
Histology of the Liver

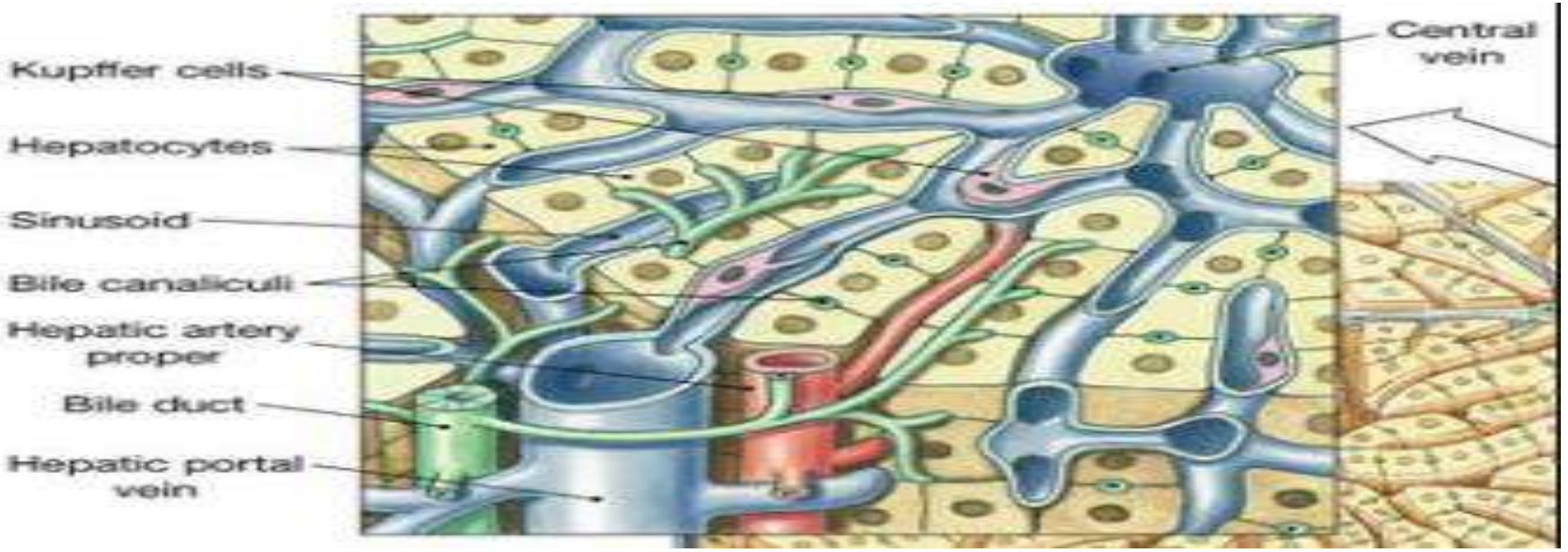


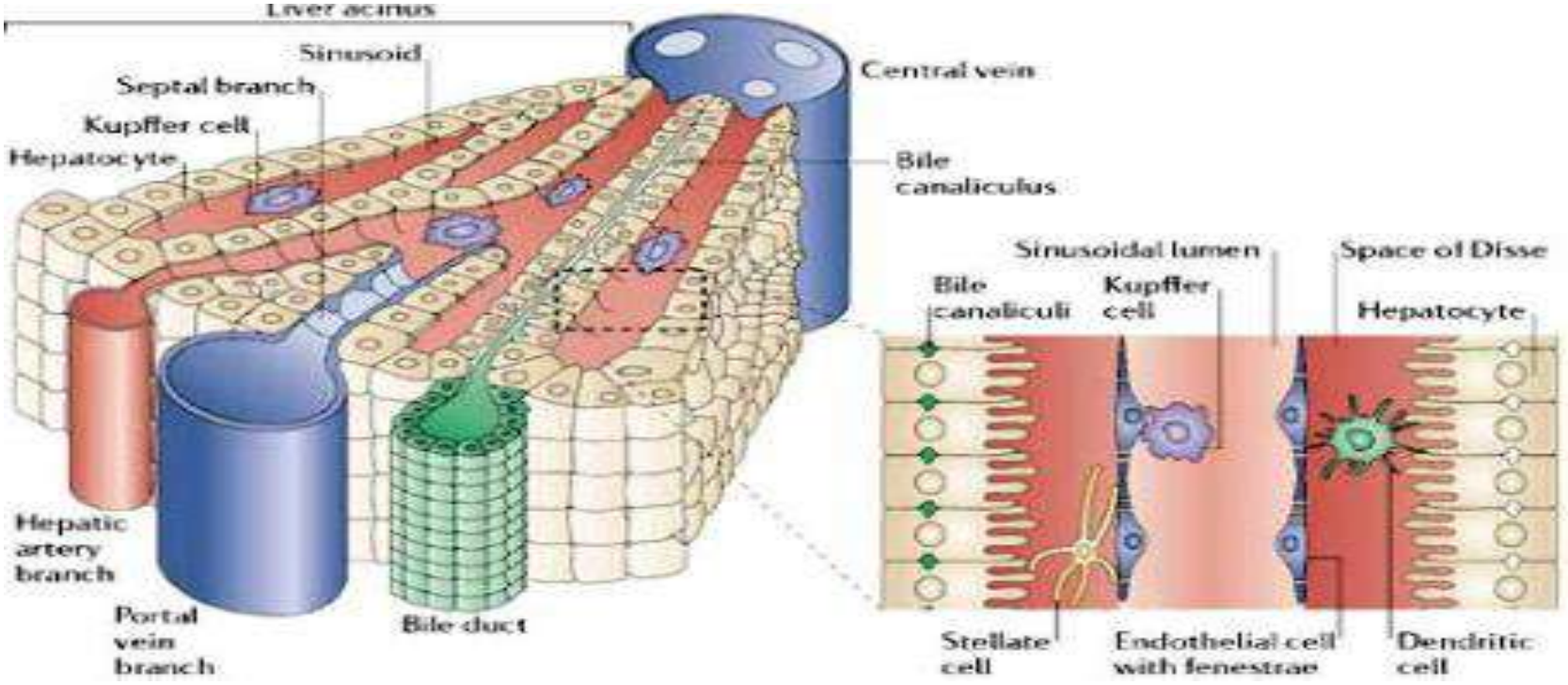
(a) Overview of histological components of liver

(b) Details of histological components of liver

ure 24.15ab Tortora - PAP 12/e

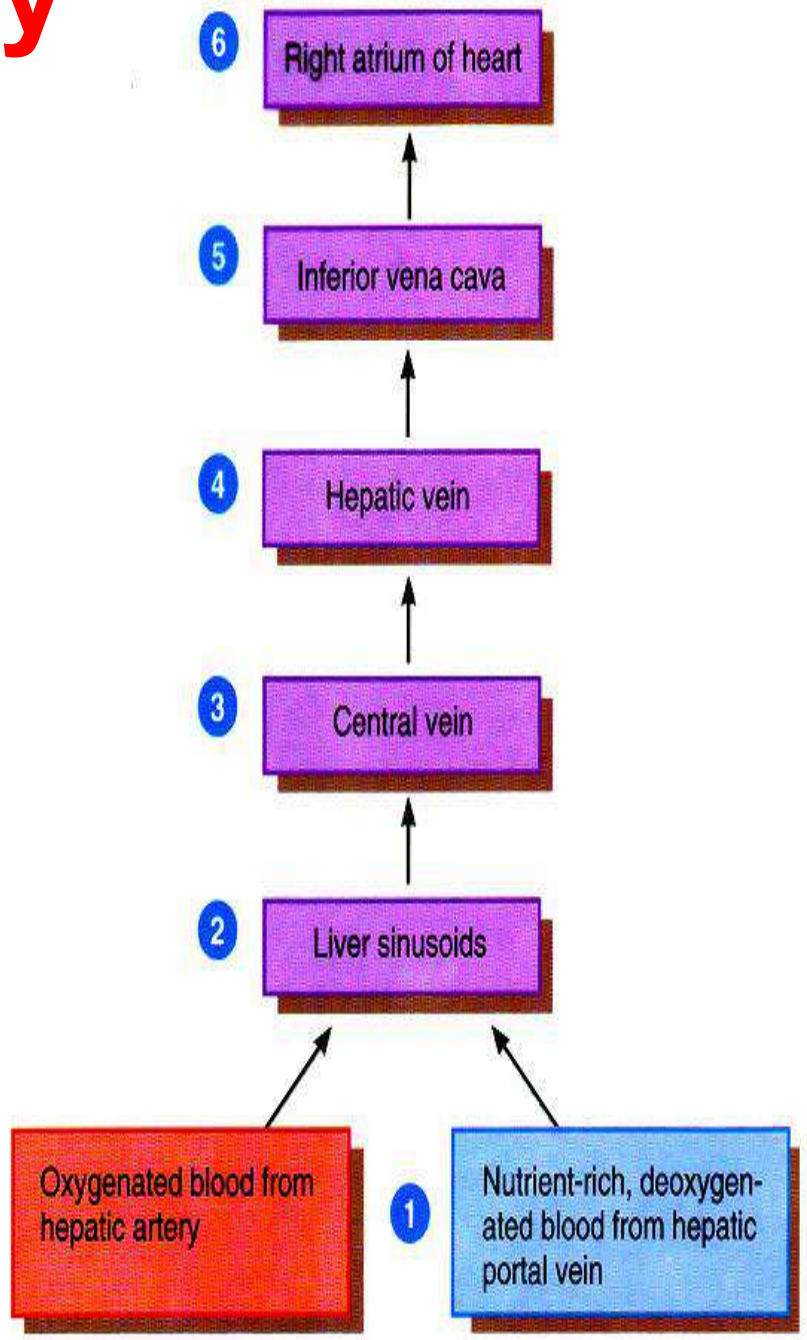

Interlobular veins
(to hepatic vein)
Bile duct
Portal arteriole
Portal venule
Portal triad
Central vein
Sinusoids
lates of
epatocytes
Portal vein
c)
Fenestrated lining
(endothelial cells)
of sinusoids
Bile canaliculi
Portal triad
Portal
arteriole
Portal
venule
Bile
duct
Central
vein
Kupffer cells
in sinusoid
walls
Bile in bile
canaliculus flows
into bile duct
(d)


Kupffer cells
Hepatocytes
Sinusoid
Bile canaliculi
Hepatic artery proper
Bile duct
Hepatic portal vein
Central vein


Liver acinus
Sinusoid
Septal branch
Kupffer cell
Hepatocyte
Central vein
Bile canaliculus
Hepatic artery branch
Portal vein branch
Bile duct
Sinusoidal lumen
Space of Disse
Bile canaliculi
Kupffer cell
Hepatocyte
Stellate cell
Endothelial cell with fenestrae
Dendritic cell

Liver: Blood Supply

- Two sources
  - *Hepatic artery* - oxygenated blood from aorta.
  - *Hepatic portal vein* - deoxygenated blood:
    - Absorbed nutrients and toxins from the stomach and intestines.
    - Hormones from the pancreas.
    - Breakdown products of RBCs from the spleen.
- Blood mixes in the sinusoids
- Hepatocytes (liver cells) modify and exchange molecules with the blood.



Liver functions

1. ***Vascular Function:***
   - ***Blood storage:*** **10% of total blood volume 450ml.**
   - ***Blood filtration:*** **99% of bacteria that enter the portal blood from the intestine, small blood clots by are phagocytosed by Kupffer cells that line hepatic sinusoids.**
   - ***Removal of old red blood cells*** **by Kupffer cells.**
2. ***Secretory function (Bile formation):***

Synthesis & secretion of bile salts & bile pigments.

3. Metabolic functions:

1. **Carbohydrate metabolism: gluconeogenesis, glycogenolysis ,.**
2. **Protein metabolism: Deamination of amino acids → ketoacids.**

Conversion of ammonia to urea.
Formation of uric acid.

Synthesis of non essential amino acids.

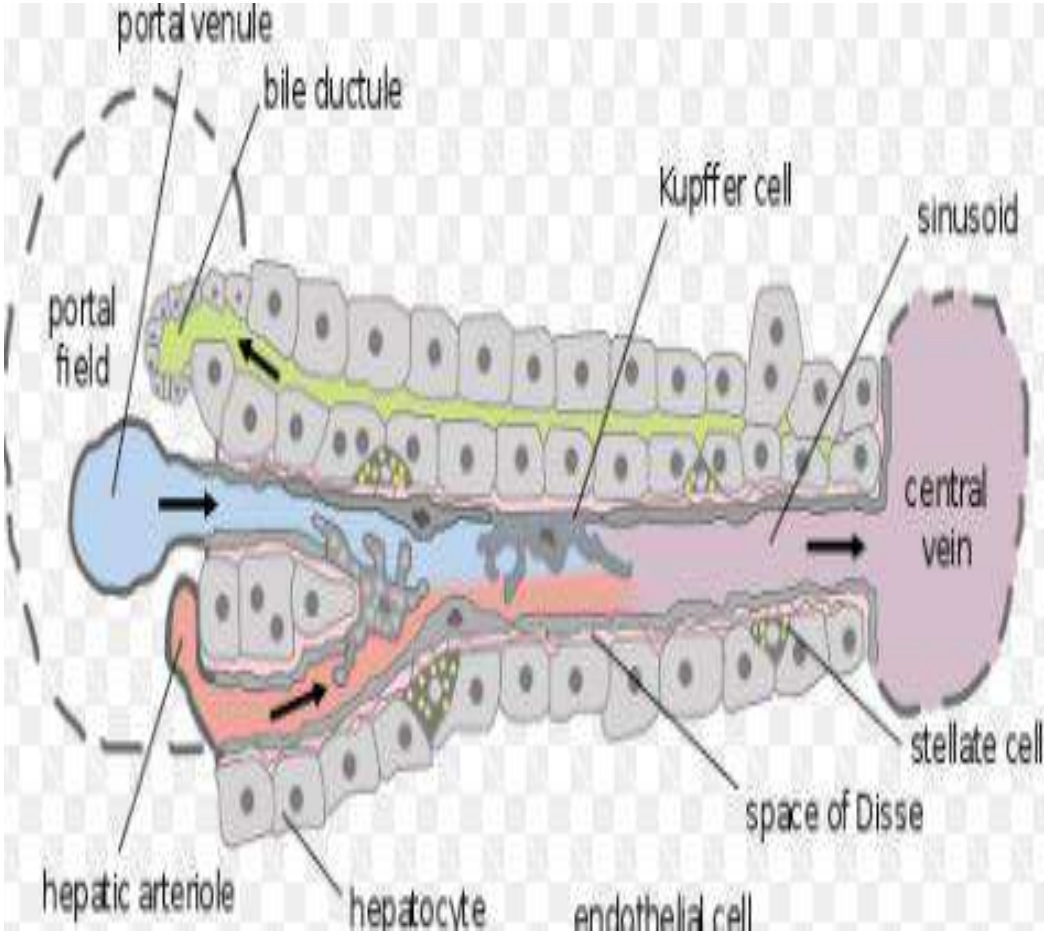
3. **Fat metabolism:**
    1. **Oxidation of fatty acids to supply energy.**
    2. **Synthesis of cholesterol, lipoproteins & phospholipids.**
    3. **Lipogenesis.**
4. **Synthesis of 25 hydroxy-cholecalciferol, plasma proteins (except y globulin), clotting factors.**

4. Storage function:

Glycogen, Vitamin A (ten months), D (3-4 months), B12 (12 months), Iron as ferritin.

5. Excretory function ;bile pigments, cholesterol.

6. **Detoxification of drugs & hormones** (thyroxin, steroid).
7. **Immunity:Kupffer cells.**



Bile

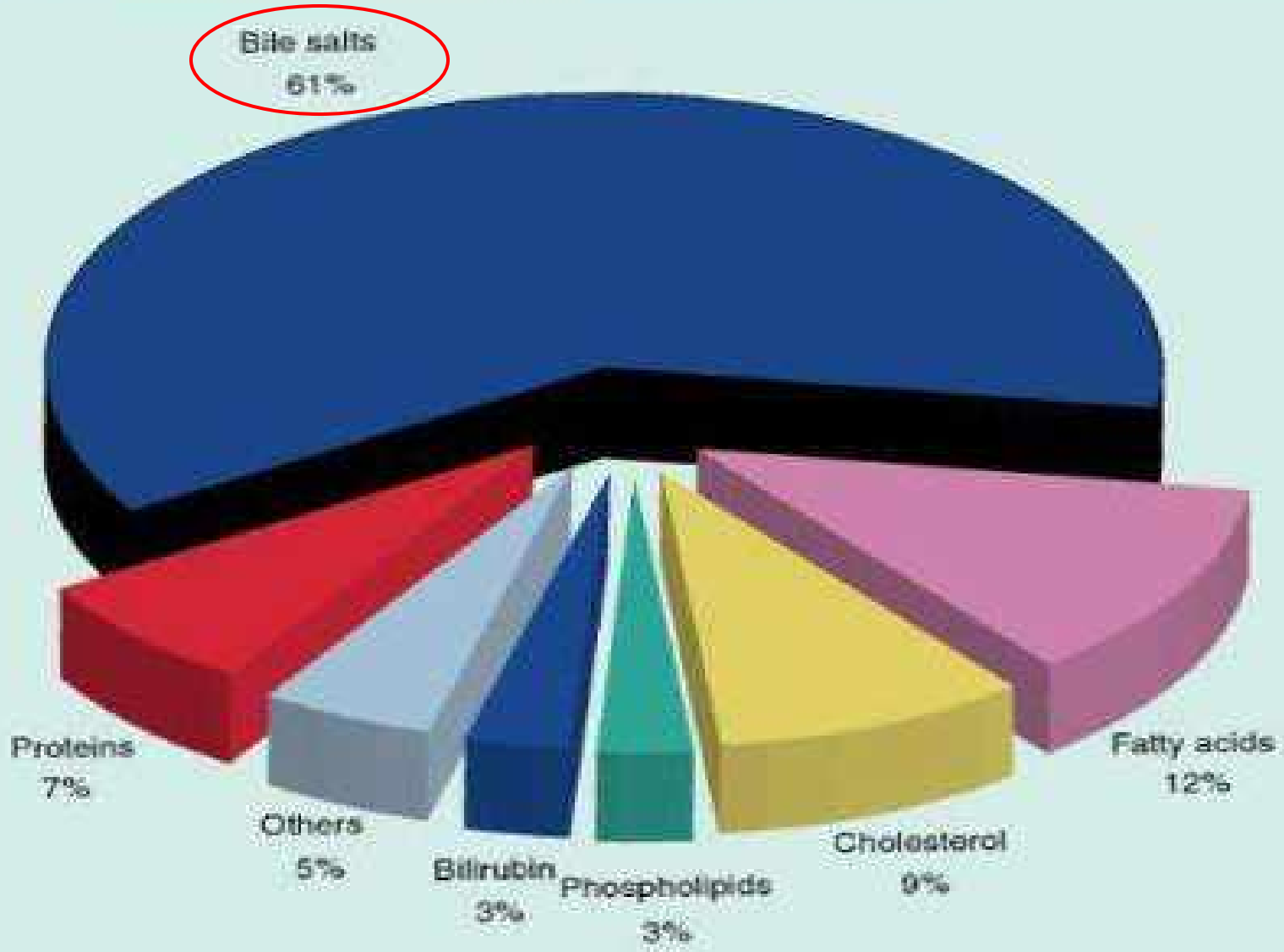
- Bile is an important digestive juice that is secreted by the liver and stored into the gall bladder.
- *Initial secretion* The liver forms and secretes 600-1200 ml of bile/ day by the *liver hepatocytes* into the biliary canaliculi rich in bile acids, cholesterol, lecithin to reach the hepatic duct.
- *Second secretion* by *hepatic ducts* rich in Na&Hco3 then the bile empties into the duodenum or through the cystic duct into the gall bladder.

Composition:

Volume: 600-1200 ml/day.

pH: 7.8- 8.6.

	Liver Bile	Gallbladder Bile
Water	97.5 g/dl	92 g/dl
Bile salts	1.1 g/dl	6 g/dl
Bilirubin	0.04 g/dl	0.3 g/dl
Cholesterol	0.1 g/dl	0.3 to 0.9 g/dl
Fatty acids	0.12 g/dl	0.3 to 1.2 g/dl
Lecithin	0.04 g/dl	0.3 g/dl
Na^+	145.04 mEq/L	130 mEq/L
K^+	5 mEq/L	12 mEq/L
Ca^{++}	5 mEq/L	23 mEq/L
Cl^-	100 mEq/L	25 mEq/L
HCO_3^-	28 mEq/L	10 mEq/L



Constituents:

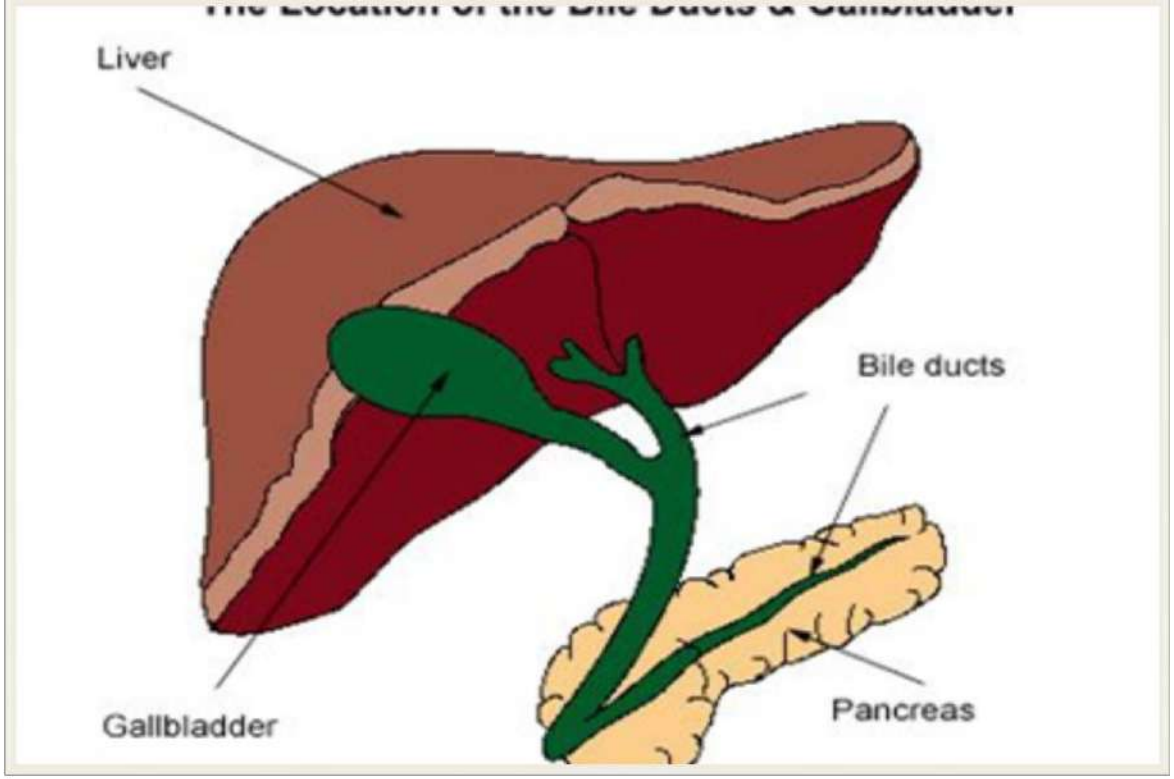
1-Aqueous constituents **(alkaline fluid, 97.5%);**

- **Secreted by *Duct cells.***
- **H_2O, Inorganic salts 0.5% (Na^+, K^+, Ca^{2+}, Cl^-, HCO_3^-).**

2-Organic constituents **(2.5%):**

- **Secreted by *Hepatocytes.***
- **(Bile salts, bile pigments, fatty acids, cholesterol, lecithin).**

3-Alkaline phosphatase enzyme.



Liver continuously synthesize &secretes bile.
Between meals, sphincter of Oddi is closed so secreted bile is moved into the gall bladder to be stored and concentrated.
During meal, bile is secreted from the gall bladder & liver .

Functions of bile

- ***Neutralization of HCl :*** **Share in HCl neutralization in the duodenum due to its high bicarbonate content. Its mucus content protect duodenal mucosa.**

- ***Digestive function:*** **Bile contains bile acids & salts , which are critical for digestion and absorption of fats and fat-soluble vitamins in the small intestine.**

- ***Excretory function:*** **Many waste products *(bilirubin & cholesterol) ,* are eliminated from the body by secretion into bile and elimination in feces.**

Free cholesterol is not soluble in aqueous solutions, but in bile, it is made soluble by *bile acids and lipids like lecithin.*

- **Bile salts are important for cholesterol homeostasis,**
- *Hepatic synthesis of bile acids accounts for the majority of cholesterol breakdown in the body. In humans, roughly **1-2g of cholesterol** are converted to bile acids and eliminated in bile every day*.

Bile salts

- **Bile acids (600 mg daily)are synthesized in the hepatocytes from cholesterol.**
- **Cholesterol is converted into the (primary), bile acids *cholic and chenodeoxycholic acids* which are then conjugated to an amino acid (glycine or taurine) to yield the conjugated form that is actively secreted into canaliculi.**
- **Bile acids contain both hydrophobic (lipid soluble) and polar (hydrophilic) faces. 2ry bile acids deoxycholic , lithocholic acids are formed by *bacterial action in colon.***
- **Tertiary(ursodeoxycholic,sulpholithocholic.**

Functions of bile salts:

1. They help fat digestion by decreasing surface tension of fat globules → *fat emulsification* (*detergent function*) to small droplets.
2. They are essential for absorption of
   - Fatty acids
   - Monoglycerides
   - Cholesterol.
   - Other lipids from the intestinal tract. & fat soluble vitamins (A,D,E, K).

(forming *Micelles* which are water soluble complexes).If absent, 40-50% of fats will lost in feces.

3. They are *cholertics* .i.e. stimulate bile flow.
4. *Laxative action* by stimulating intestinal peristalsis.
5. They are essential for keeping cholesterol dissolved in bile.

Liver Secretion Of Cholesterol And Gallstone Formation

- **Bile acids are formed in the hepatic cells from cholesterol in the blood plasma.**
- **BS are conjugated in liver by amino acids glycine and taurine to glycocholic and taurocholic acids.**
- **Both form salts by binding to Na, K in alkaline bile**
- **In the process of secreting the bile salts about**

1 to 2 grams **of cholesterol are removed from the blood plasma and secreted into the bile each day.**

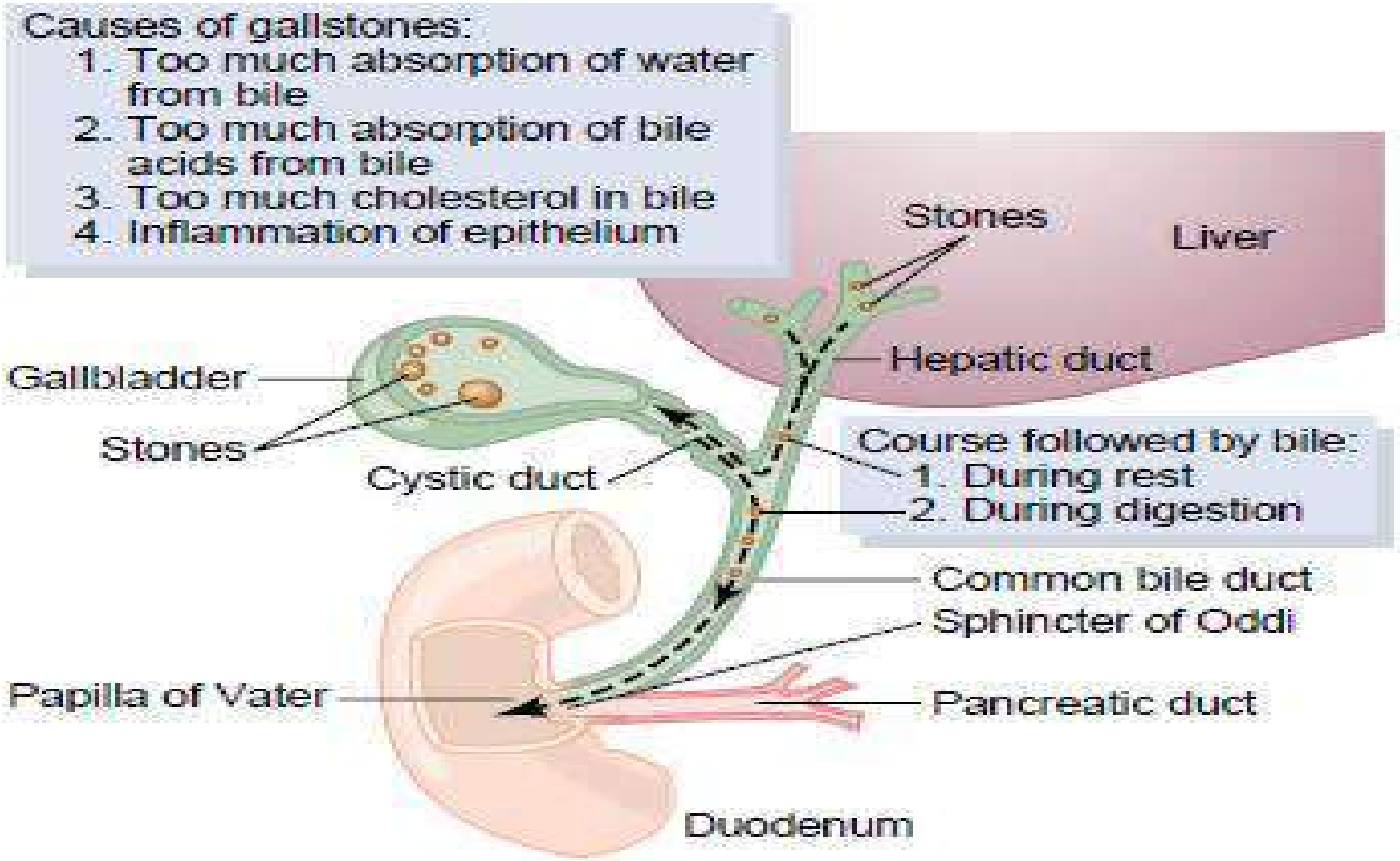
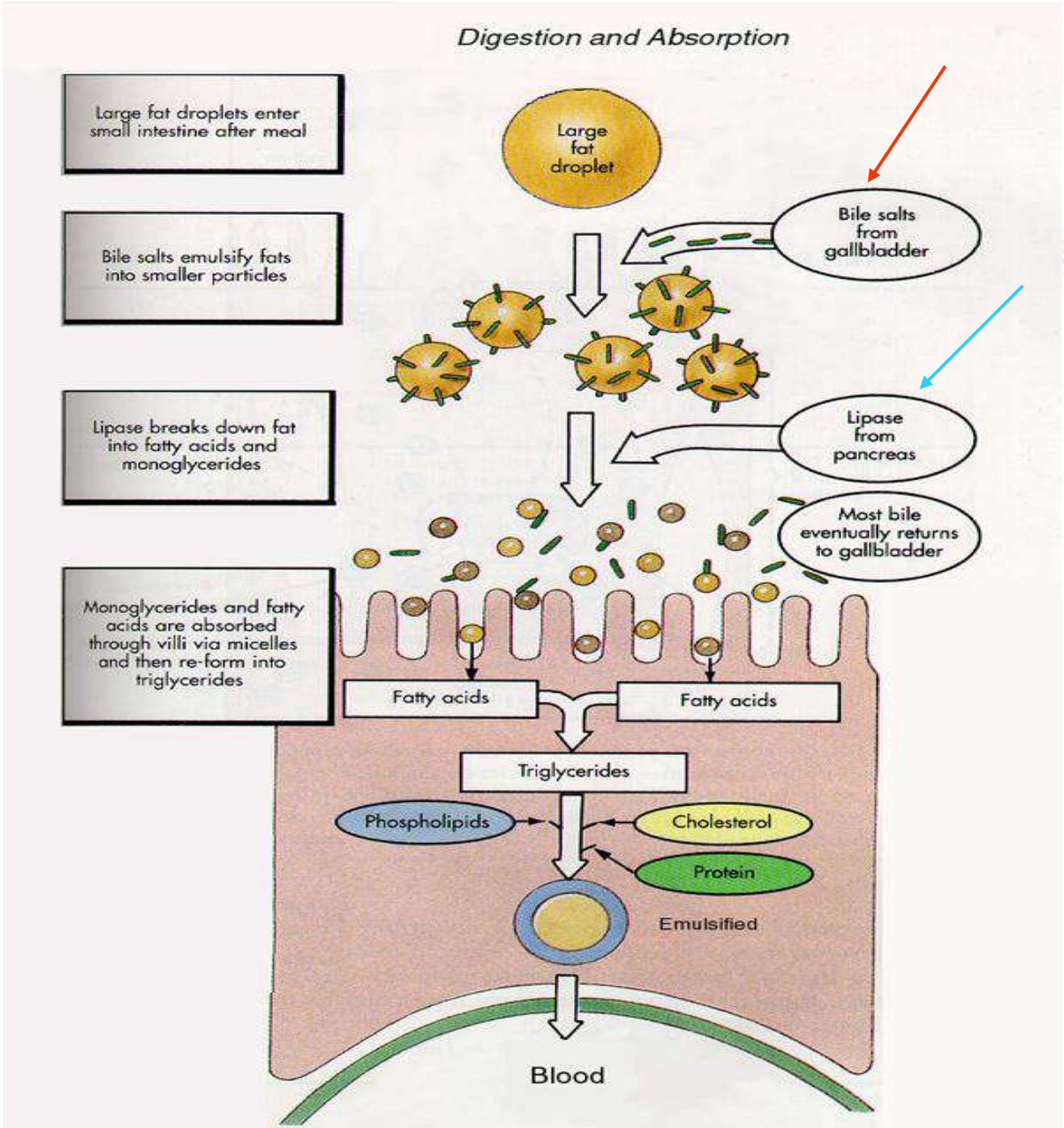
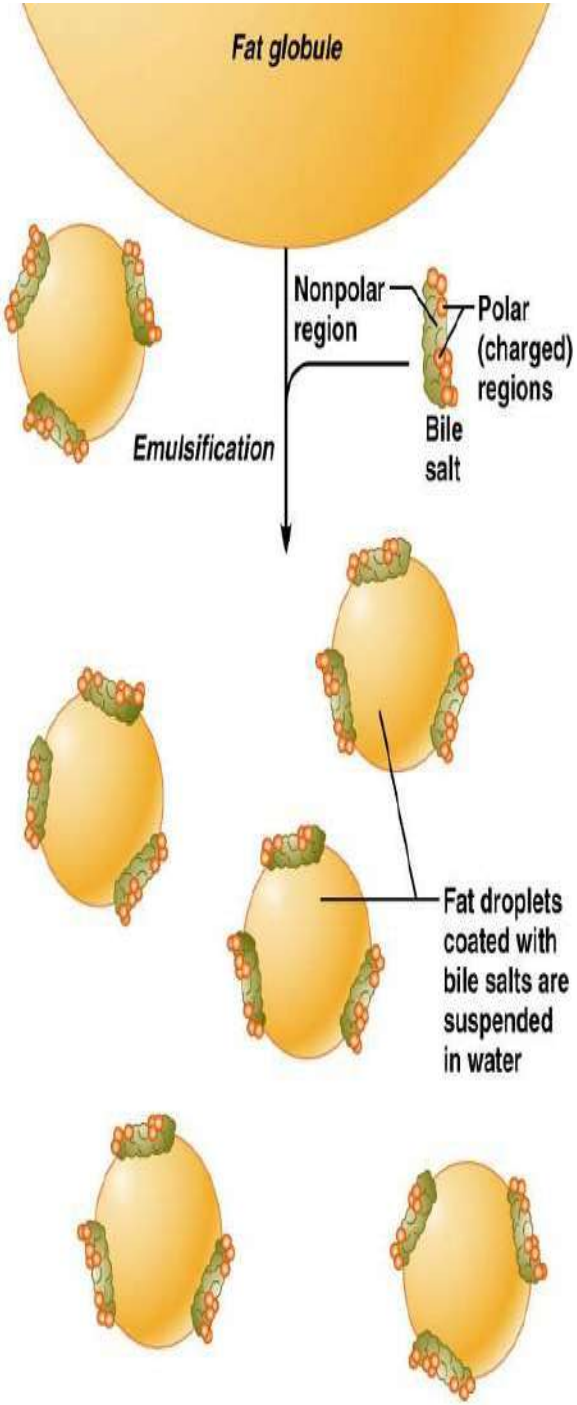
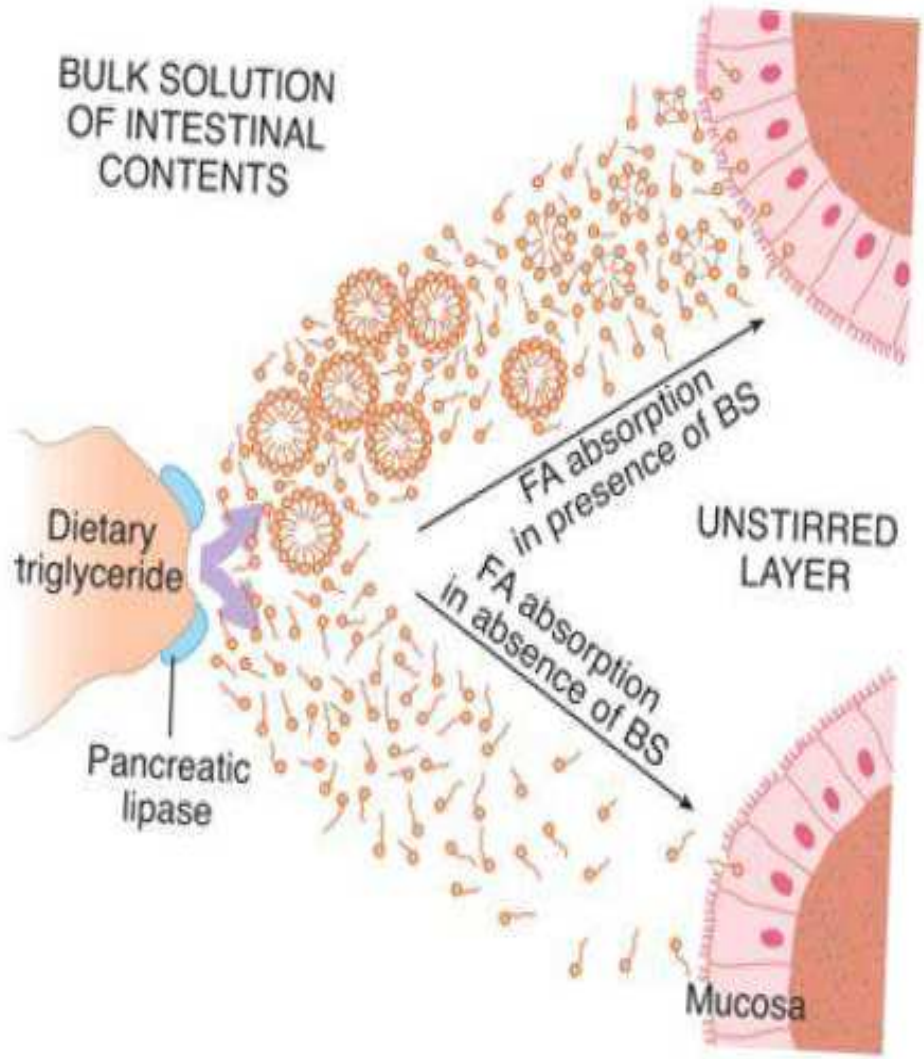


Figure 64–12

Formation of gallstones.


Digestion and Absorption
Large fat droplets enter small intestine after meal
Large fat droplet
Bile salts from gallbladder
Bile salts emulsify fats into smaller particles
Lipase breaks down fat into fatty acids and monoglycerides
Lipase from pancreas
Most bile eventually returns to gallbladder
Monoglycerides and fatty acids are absorbed through villi via micelles and then re-form into triglycerides
Fatty acids
Fatty acids
Triglycerides
Phospholipids
Cholesterol
Protein
Emulsified
Blood

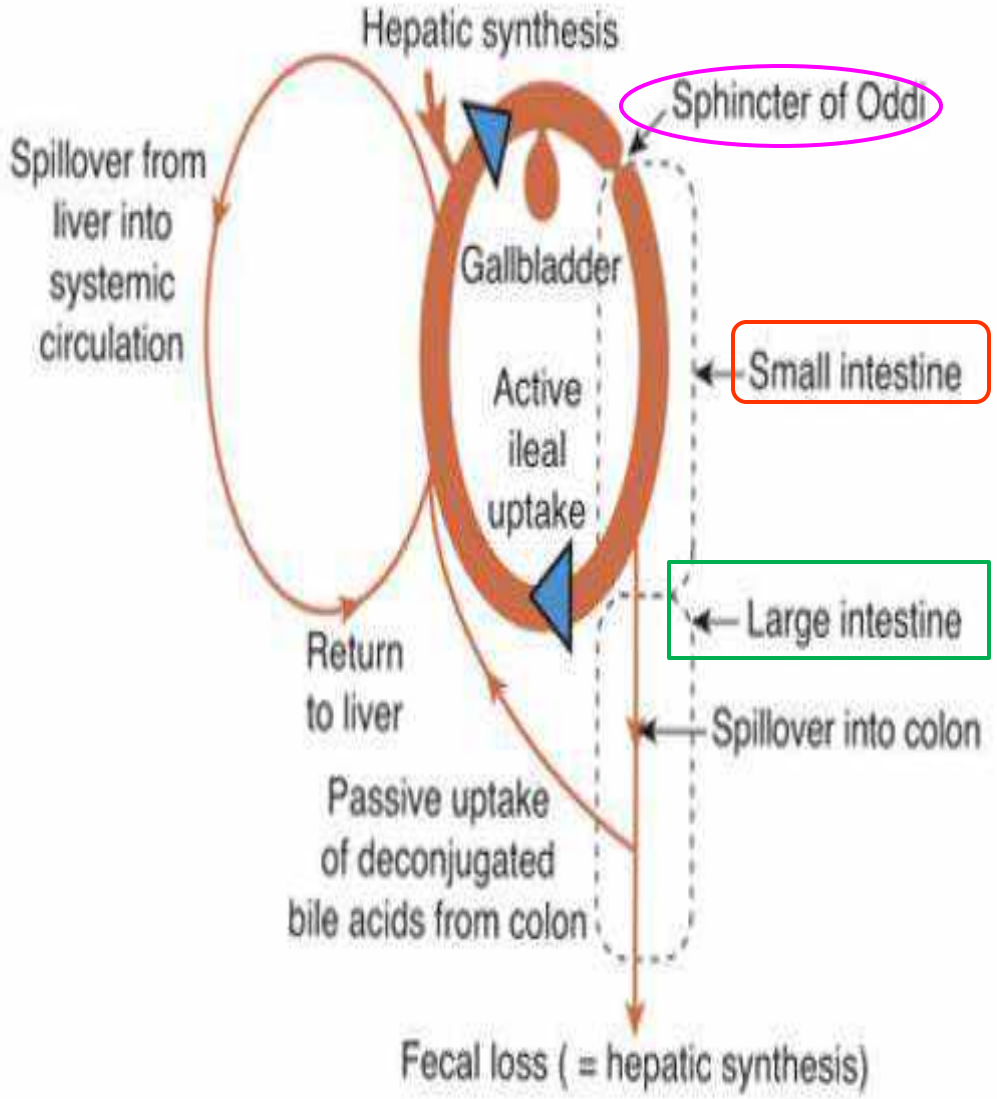

Fat globule
Nonpolar region
Polar (charged) regions
Bile salt
Emulsification
Fat droplets coated with bile salts are suspended in water


BULK SOLUTION
OF INTESTINAL
CONTENTS
FA absorption
in presence of BS
UNSTIRRED
LAYER
Dietary
triglyceride
FA absorption
in absence of BS
Pancreatic
lipase
Mucosa

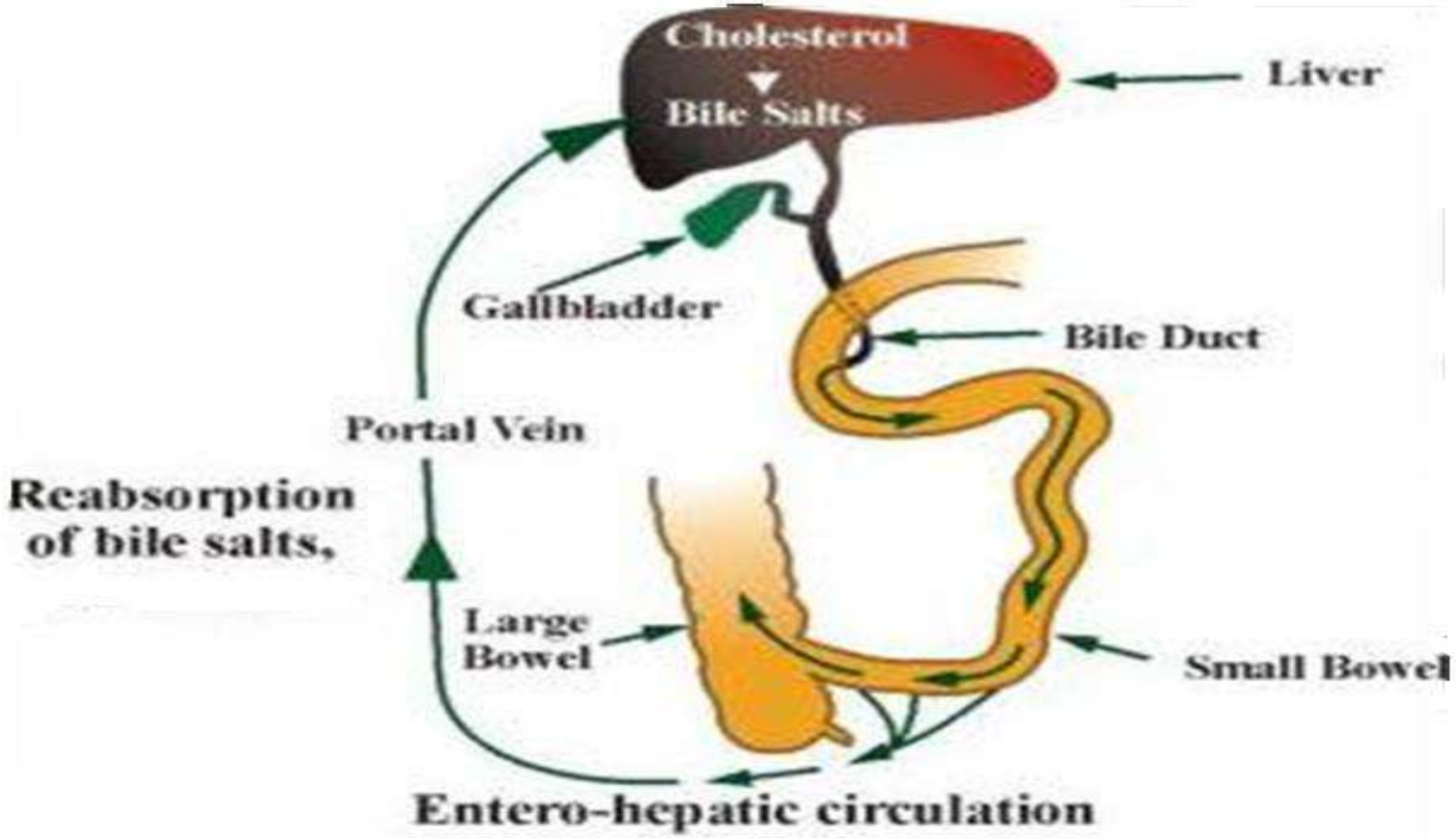
Enterohepatic circulation

- 94% of bile salts are reabsorbed, about one half of this by *Diffusion* through the mucosa in the *early portions of the small intestine* and the remainder by an *Active transport* process from the *Terminal ileum* and returned to the liver to be secreted.

- 5-10% enter the colon → salts of deoxy (reabsorbed) and lithocholic acid (insoluble and excreted in the stool). *2nd bile salts.*
- The total bile salt pool in the body is 3.5 gm (recycles 6-8 times), and the amount lost in stools (0.2-0.4 gm/day) is replaced by new synthesis in the liver.


Hepatic synthesis
Sphincter of Oddi
Spillover from liver into systemic circulation
Gallbladder
Small intestine
Active ileal uptake
Large intestine
Return to liver
Spillover into colon
Passive uptake of deconjugated bile acids from colon
Fecal loss (= hepatic synthesis)

- **If the enterohepatic circulation is interrupted → liver cannot compensate and signs of bile salt deficiency appear** ***(steatorrhea, deficiency of fat soluble vitamins , cholesterol stones).***



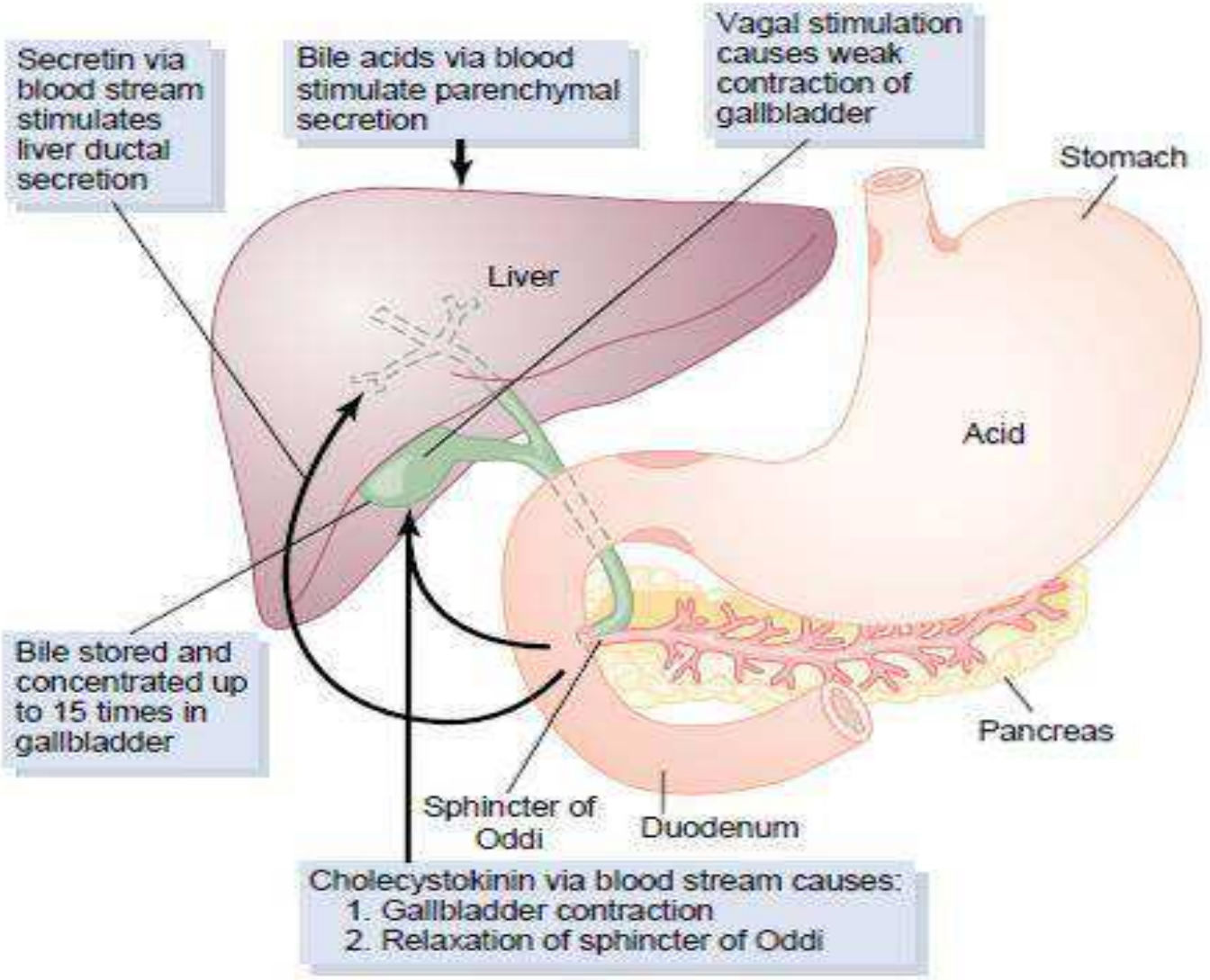
Regulation of bile secretion

Bile secretion by the liver is increased by:-

- ***Chemical mechanism;*** **Bile salts returned to the liver by the enterohepatic circulation stimulate further bile secretion.**
- ***Hormonal mechanism;*** ***Secretin*** **stimulate the aqueous alkaline portion of bile and increase bile flow.**
- ***Neural mechanism;*** **occurs in the cephalic phase of digestion . Mediated via the** ***Vagus nerve*** **& cause increased water & bicarbonate content of bile.**

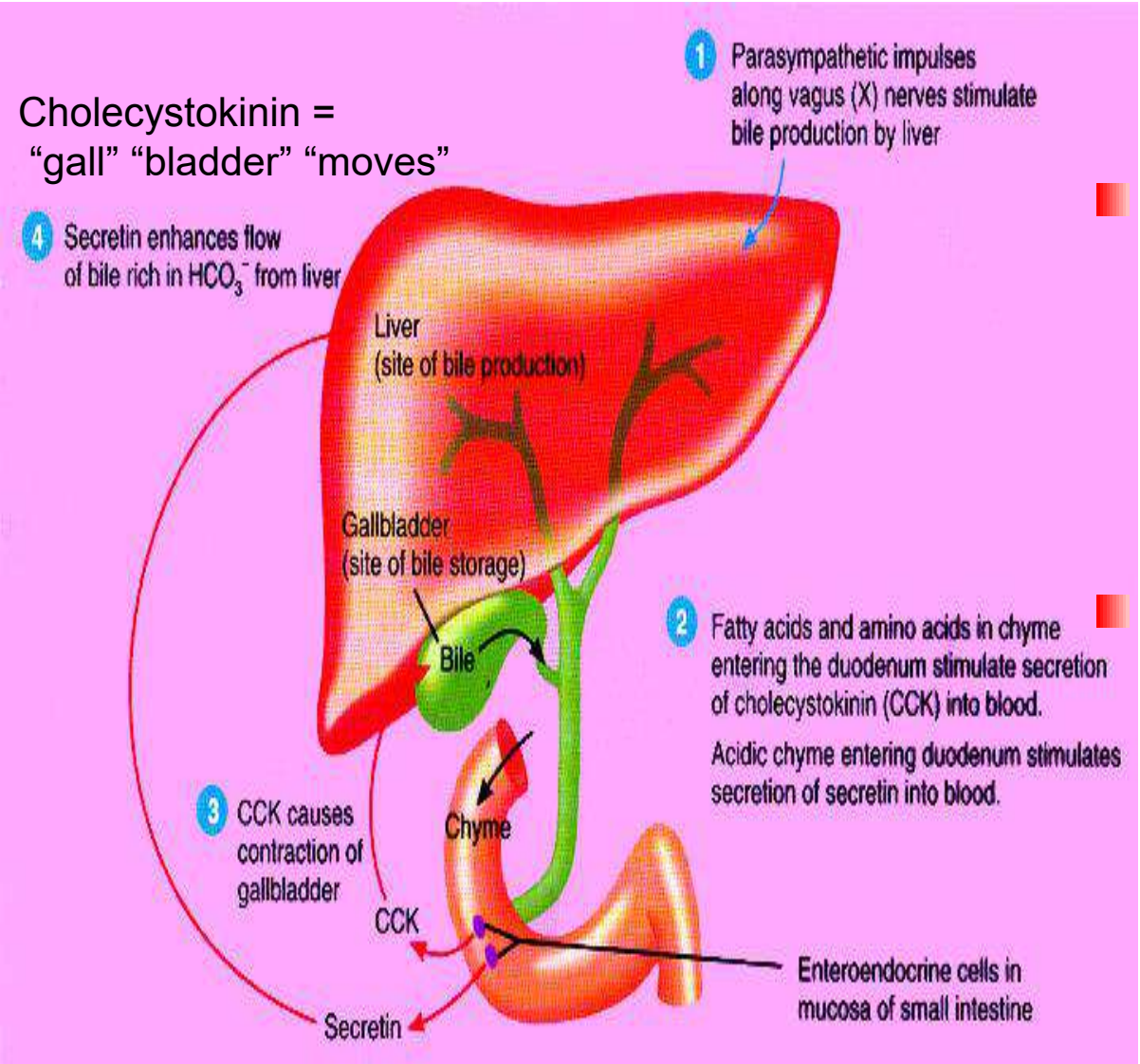
Choleretics ***are substances that increase bile formation by the liver and bile flow .e.g. bile salts &*** **secretin.**

Cholagogue ***are substances that increase move bile from the gall bladder and increase bile flow .e.g.*** **CCK**


Secretin via blood stream stimulates liver ductal secretion
Bile acids via blood stimulate parenchymal secretion
Vagal stimulation causes weak contraction of gallbladder
Stomach
Liver
Acid
Bile stored and concentrated up to 15 times in gallbladder
Pancreas
Sphincter of Oddi
Duodenum
Cholecystokinin via blood stream causes:
1. Gallbladder contraction
2. Relaxation of sphincter of Oddi

ptying.

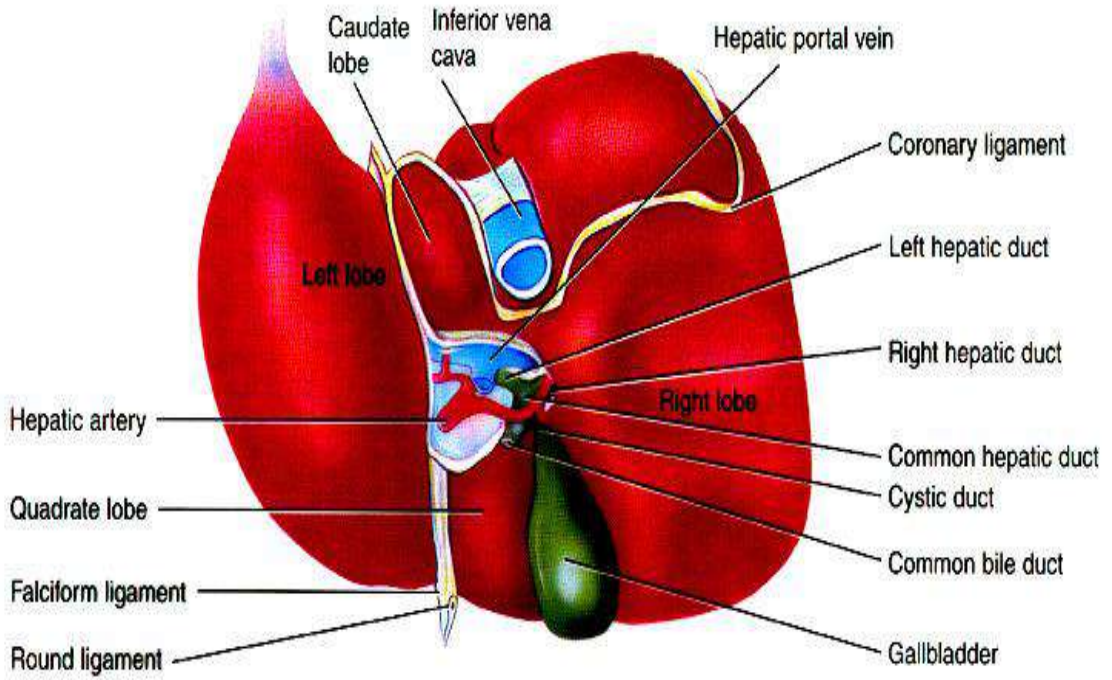
Liver:
Bile Synthesis



- **Regulation of bile production/secretion**
  - ***Nervous control*** **from parasympathetic via Vagus nerve**
  - ***Auto regulation*** **by sensing the presence of fatty acids and amino acids in the acidic chyme**
  - ***Hormonal control*** **by the secretion of the Enteroendocrine, CCK and secretin, from the duodenum**

Gall Bladder

- Pear-shaped sac, 7-10 cm long
- Physiology
  - Stores and concentrates bile between meals
  - CCK stimulates bile release for fatty meals
  - when the small intestine is empty, the hepatopancreatic sphincter closes, forcing bile into the gallbladder for storage



Pathology: gallstones

Functions Gall Bladder

***1-Storage of bile*: between meals, the sphincter of oddi is tonically contracted, so bile flow retrograde upwards through the cystic duct to be stored in the gall bladder.**

***2-Concentration of bile :* by active reabsorption of Na+, followed by passive reabsorption of water and most electrolytes, except calcium (bile salts increase 5-10 times, water content decreases to 89%).**

3-Acidification of bile: due to bicarbonate reabsorption during concentration, pH= 7-7.4 (prevents Ca^{2+} ppt and formation of gall stones).

4-Secretion of mucus: (white bile) from mucous glands in the mucosa: it ***Protects*** the gall bladder wall against highly concentrated bile salts, gives the bile a semi fluid consistency, and acts as a lubricant in the small intestine.

5-Evacuation: by contraction of wall and relaxation of sphincter.

Physiology of Gastrointestinal Disorders

- ***Disorders of Swallowing and of the Esophagus:***
- **Paralysis of the Swallowing Mechanism :**
- **Damage to the *Fifth, Ninth, or Tenth* cranial nerve**
- ***Poliomyelitis* or *encephalitis.***
- **Paralysis of the swallowing muscles, *muscle dystrophy* , *myasthenia gravis* or *botulism.***

- ***When the swallowing mechanism is partially or totally paralyzed***

- **Swallowing cannot occur.**
- **Failure of the glottis to close food passes into the lungs instead of the esophagus .**
- **Failure of the soft palate and uvula to close the posterior nares so that food refluxes into the nose during swallowing.**

Aspiration under GA.

Achalasia and Mega esophagus

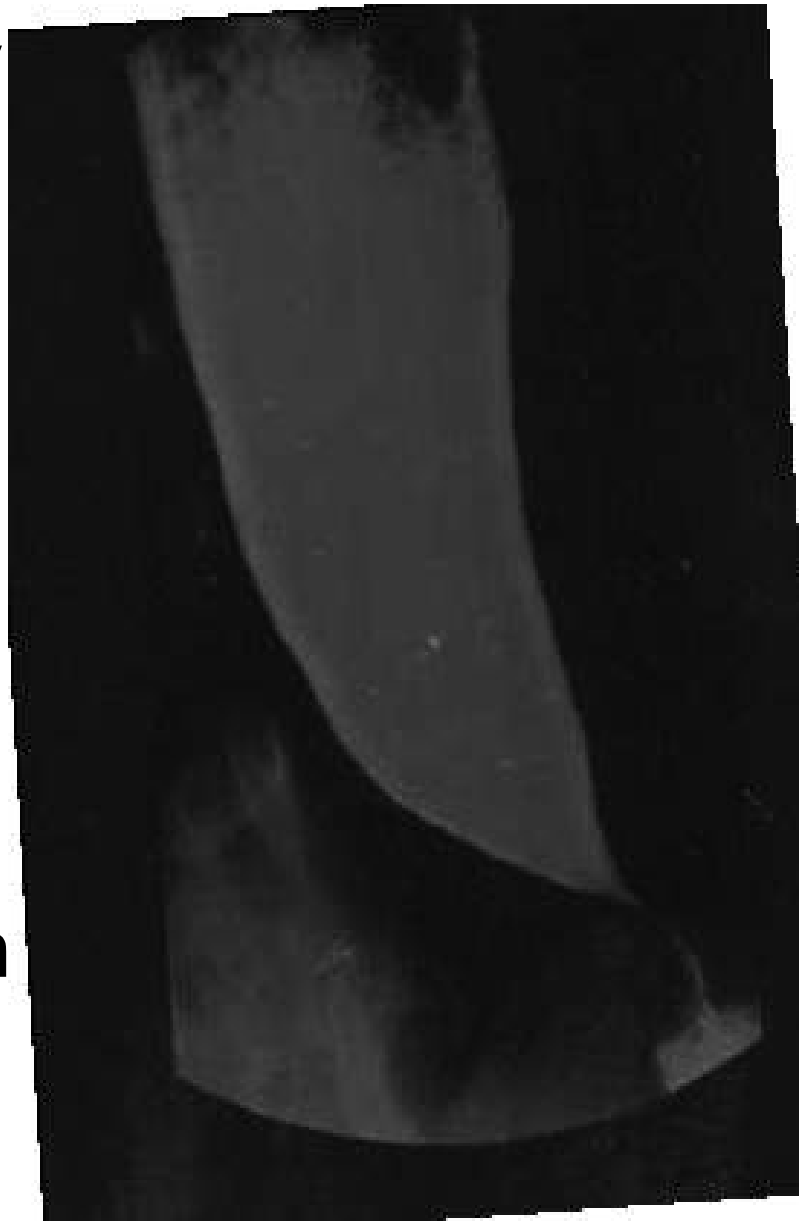
Definition: ***Aprestalsis of muscles of body of esophagus and failure of relaxation of lower esophageal sphincter .***

- **Food fails to pass from the esophagus into the stomach.**
- ***Causes:*** **Damage of the Myenteric plexus in the lower two thirds of the esophagus.**

Muscles remains spastically contracted ,loss receptive relaxation" of the G.E sphincter.

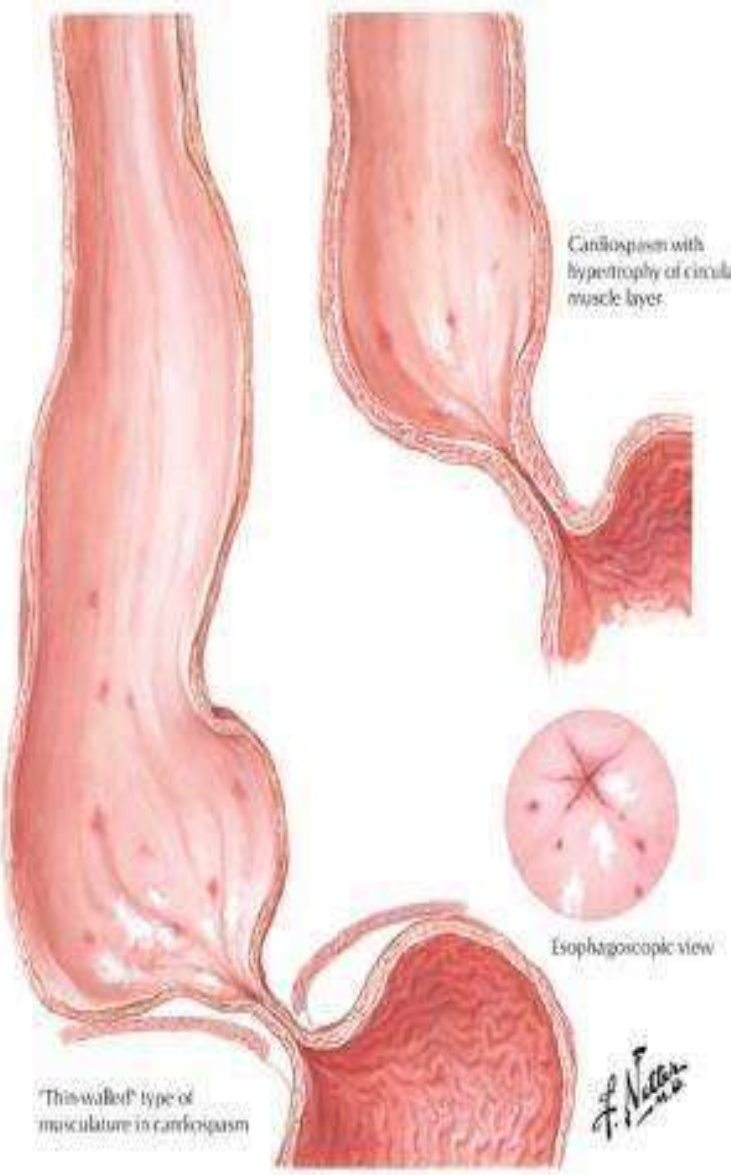
- **Over long periods the esophagus becomes markedly enlarged until it often can hold as much as 1 liter of food, which becomes putridly infected during the long periods of esophageal stasis. The infection may also cause ulceration of the esophageal mucosa, severe substernal pain or even rupture and death**

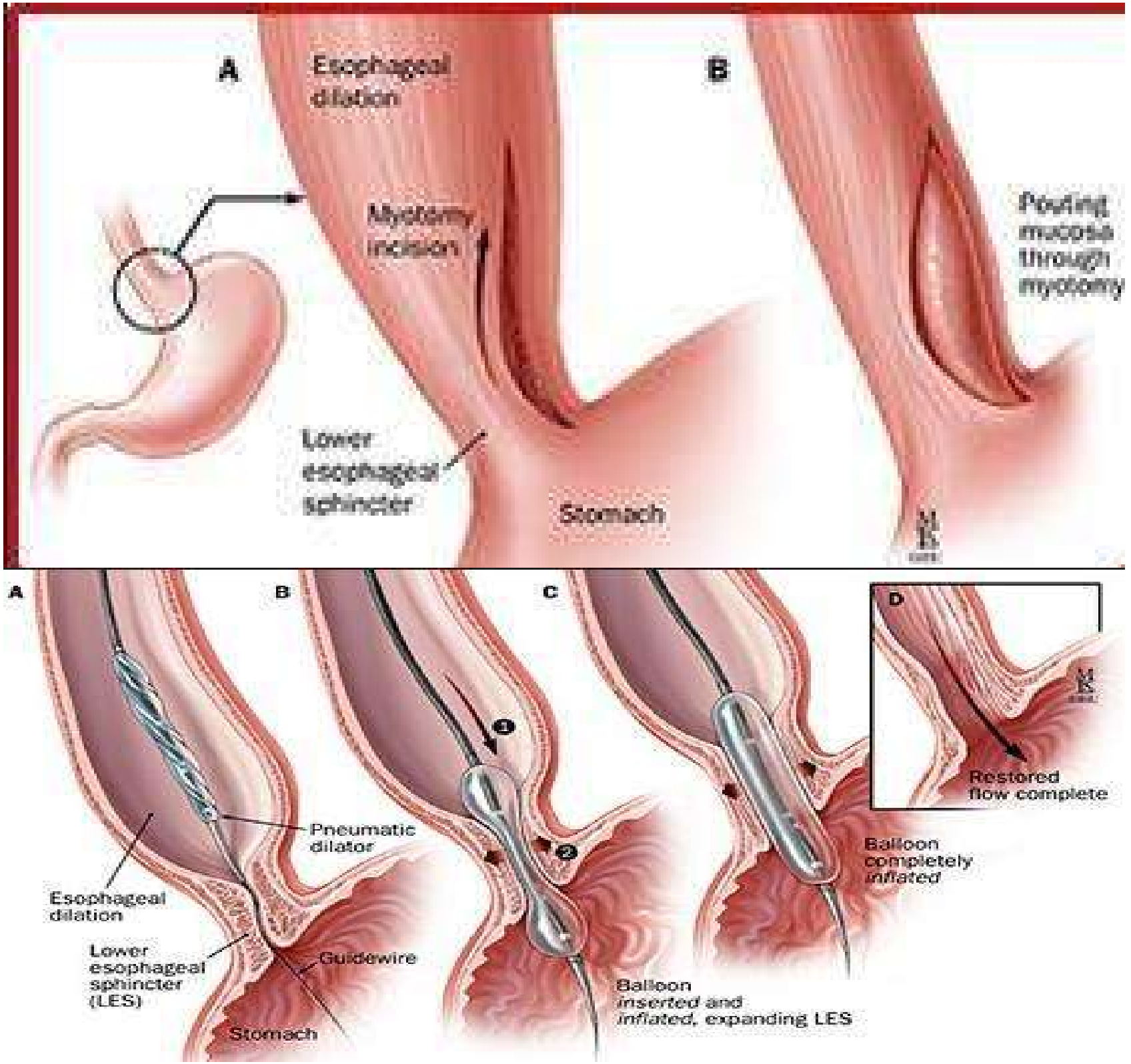
Mega esophagus.



Achalasia

- Primary esophageal motility disorder.
- Peak incidence 20 -50 y.
- Cause progressive dysphagia to solids and liquids.
- Regurgitation undigested food
- Chest pain.
- Loss of weight.
- Increase risk of esophageal cancer.




A
Esophageal dilation
Myotomy incision
Lower esophageal sphincter
Stomach
B
Posting mucosa through myotomy
A
B
C
D
Pneumatic dilator
Esophageal dilation
Lower esophageal sphincter (LES)
Guidewire
Stomach
Balloon inserted and inflated, expanding LES
Balloon completely inflated
Restored flow complete

Disorders of the Stomach

- ***Gastritis*** **Inflammation of the Gastric Mucosa**
  - **Gastritis is caused by chronic *Bacterial infection* of the gastric mucosa.**
  - **Damage to the protective gastric mucosal barrier by *Alcohol, Aspirin , NSAIDS .Steroids, Viniger .***
- ***Gastric Barrier and Its Penetration in Gastritis:***
  - **low level of stomach absorption is mainly due to two specific features of the gastric mucosa:**

(1) It is lined with highly resistant mucous cells that secrete viscid and adherent mucus.

(2) It has tight junctions between the adjacent epithelial cells*. "Gastric Barrier."*

- **The gastric barrier normally is resistant enough to diffusion of highly concentrated hydrogen ions of the gastric juice.**

- **In gastritis, the permeability of the barrier is greatly increased. The H^+ diffuse into mucosa causing damage and atrophy.**

- **It also makes the mucosa susceptible to digestion by the peptic digestive enzymes, thus frequently resulting in a *Gastric ulcer.***

Chronic Gastritis Can Lead to Gastric Atrophy and Loss of Stomach Secretions

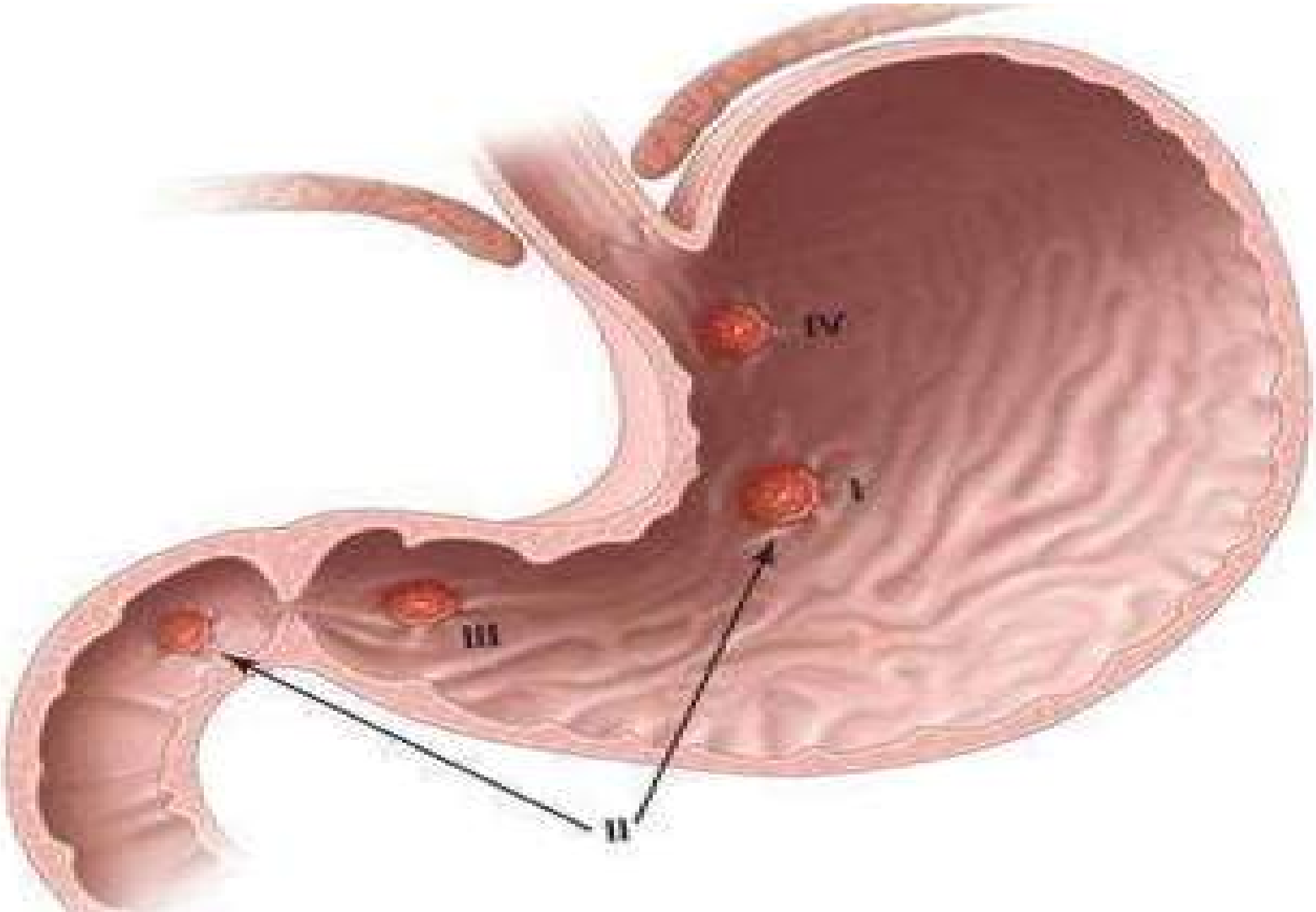
Achlorhydria (and Hypochlorhydria):

- ***Achlorhydria:*** **means simply that the stomach fails to secrete hydrochloric acid; it is diagnosed when the pH of the gastric secretions fails to decrease below 6.5 after maximal stimulation.**
- **Hypochlorhydria: means diminished acid secretion. When acid is not secreted, pepsin also usually is not secreted; even when it is, the lack of acid prevents it from functioning because pepsin requires an acid medium for activity.**

Gastric Atrophy May Cause Pernicious Anemia

- In the absence of intrinsic factor, only about 1/50 of the vitamin B_{12} is absorbed. And, without intrinsic factor, an adequate amount of vitamin B_{12} is not made available from the foods to cause young, newly forming red blood cells to mature in the bone marrow. The result is *Pernicious Anemia.*

Types of gastric ulcers



- ***A Surface Breach*** **of mucosal lining of GIT (excoriated area of stomach or intestinal mucosa) occurring as a result of *acid and pepsin* attack.**
- ***Sites:***
  - **Duodenum (DU)**
  - **Stomach (GU)**
  - **Oesophagus**
  - **Gastro-Enterostomy stoma *(Marginal ulcer).***
  - **Related to ectopic gastric mucosa (e.g. in Meckel's diverticulum).**
  - **Acute peptic ulcer Like acute erosion but breaching muscularis mucosa.**

Peptic Ulcer

Causes:

1. High acid and peptic content
2. Irritation
3. Poor blood supply
4. Poor secretion of mucus
5. Infection, *H. pylori*

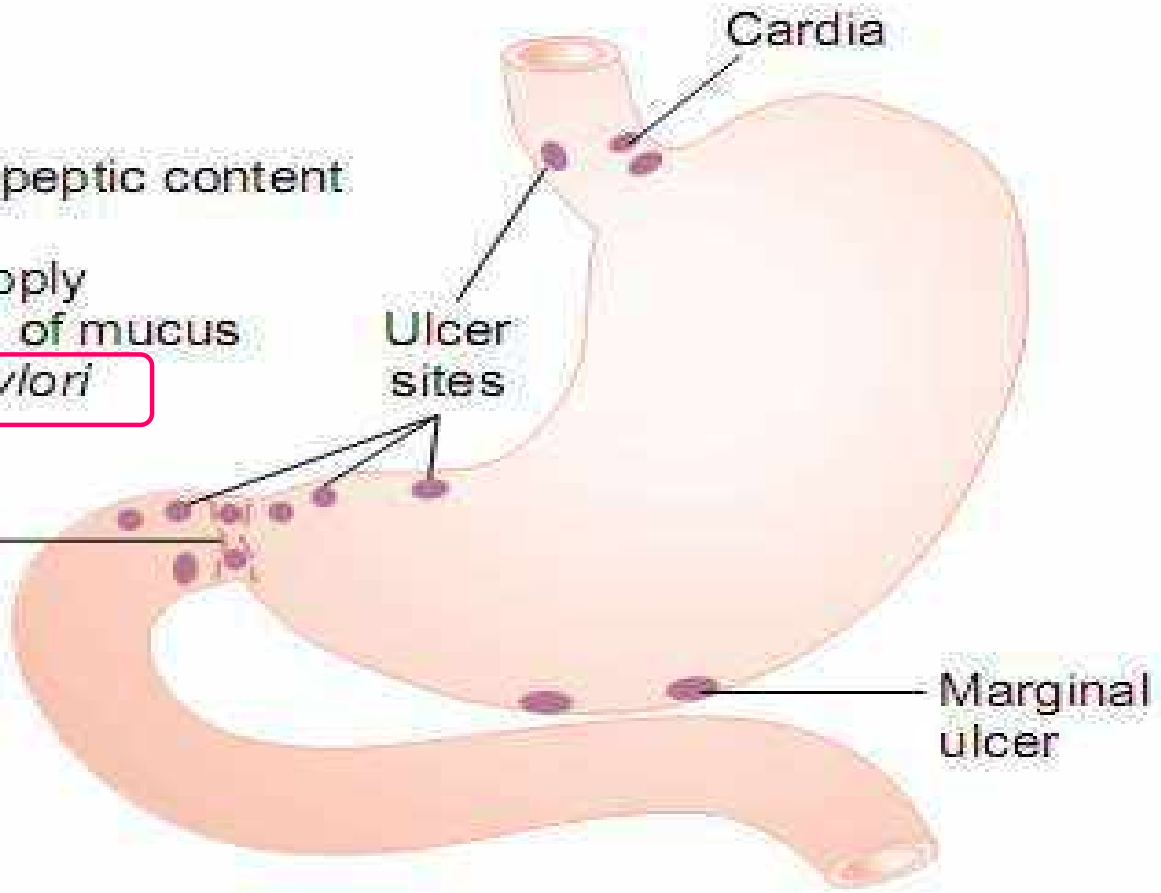


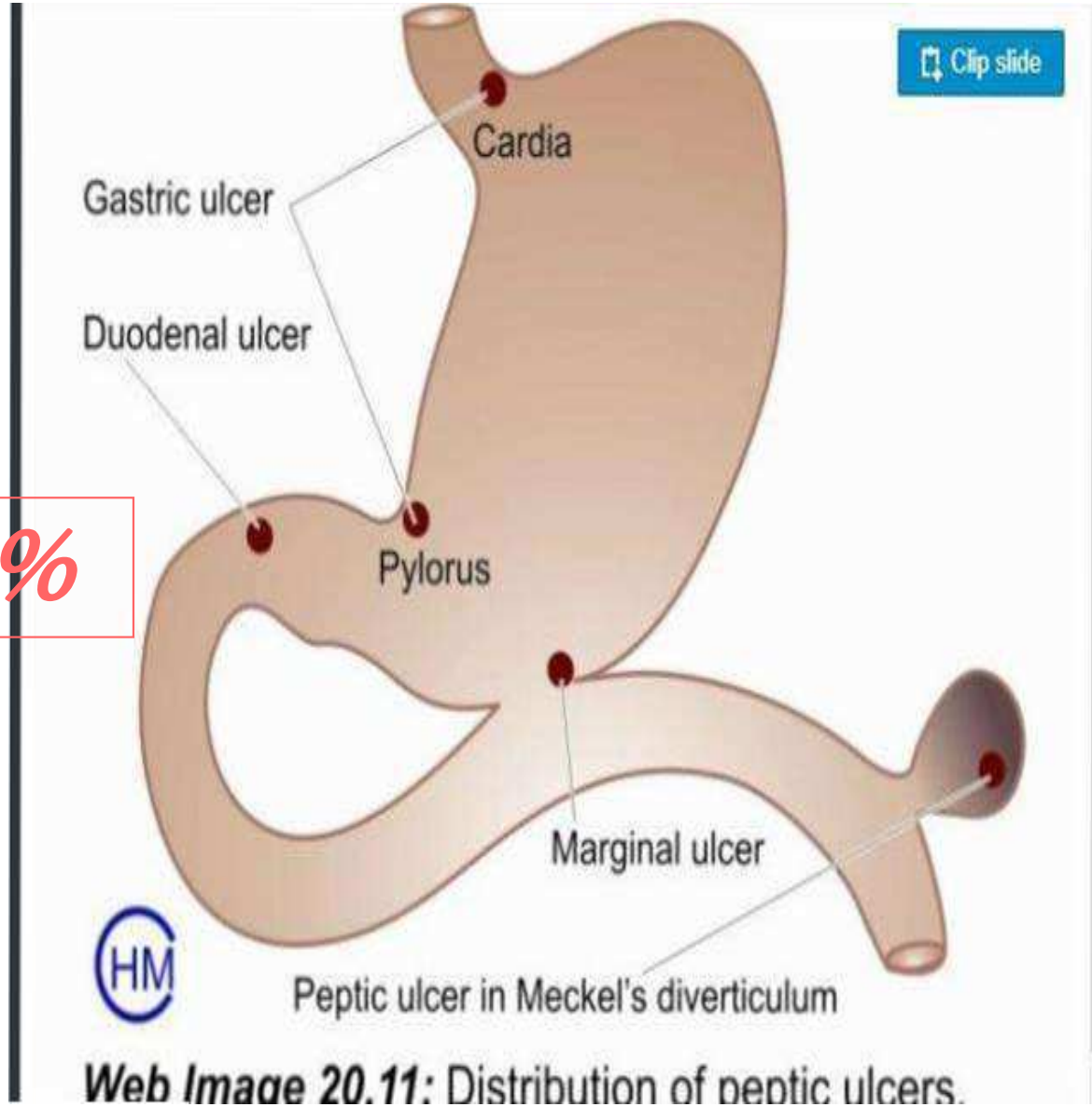
Figure 66–1

Peptic ulcer. *H. pylori*, *Helicobacter pylori*.

Sites of PUD

- **Duodenum:80%**
- ***Gastric:*** **15%**
- ***D1, Stomach:*** **4%**
- ***O-G Junction :***
- ***Meckel's D:***
- ***Marginal :***

1 %



Web Image 20.11: Distribution of peptic ulcers.

Basic Cause of Peptic Ulceration

The usual cause of peptic ulceration is an *Imbalance* between the Rate of secretion of gastric juice and the Degree of protection afforded by

- **The gastro duodenal mucosal barrier .**
- **The neutralization of the gastric acid by duodenal juices.**

MUCUS : **all areas normally exposed to gastric juice are well supplied with mucus glands(compound mucous glands in the lower esophagus plus the mucous cell coating of the stomach mucosa, the mucous neck cells of the gastric glands, the deep pyloric glands that secrete mainly mucus, and, finally, the glands of *Brunner's of the upper Duodenum*, which secrete a highly alkaline mucus).**

ALKALINE SECRETIONS

- **The duodenum is protected by the *Alkalinity of small intestinal secretions.***
- ***Pancreatic secretion,* which contains large quantities of $Nahco_3$ that neutralize the Hcl of the gastric juice, also *Inactivating Pepsin* and preventing digestion of the mucosa.**
- **In addition, large amounts of bicarbonate ions are provided in the secretions of the large Brunner's glands in the first *few centimeters of the duodenal wall* and In bile coming from the liver.**

Aggressive Factors

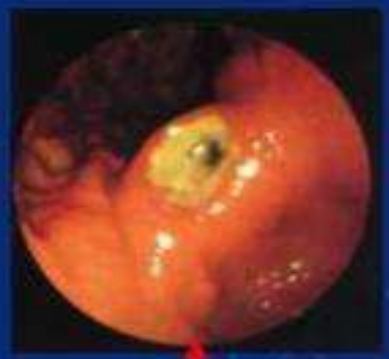
Acid/Pepsin

- H. pylori infection
- NSAIDs
- Smoking

Defensive Factors

- Mucus-bicarbonate barrier
- Barrier of apical membrane
- Mucosal blood flow
- Prostaglandins
- Epithelial cell restitution

I Aggressive Factors ↑



Defensive Factors ↓ II

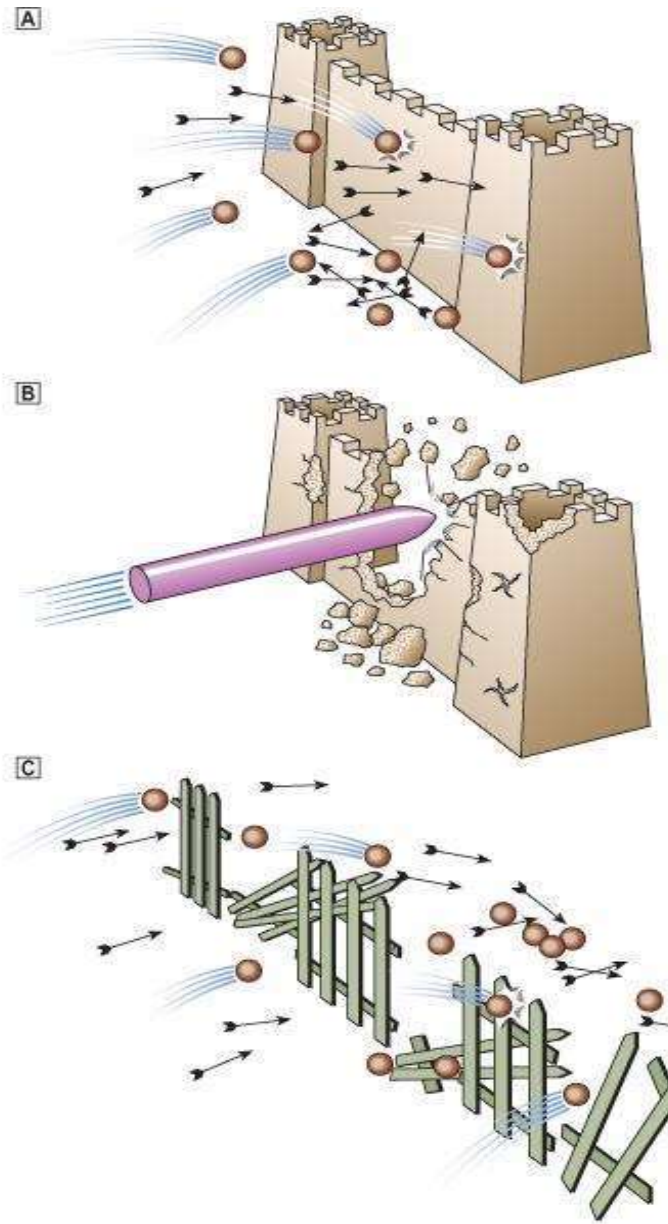
III Aggressive Factors ↑ + Defensive Factors ↓

REFLEXES

- ***Two feedback control mechanisms*** **normally ensure that this neutralization of gastric juices is complete.**
- **When excess acid enters the duodenum, it inhibits gastric secretion and peristalsis in the stomach, both by nervous reflexes and by hormonal feedback from the duodenum, thereby *decreasing the rate of gastric emptying.***
- **The presence of acid in the small intestine liberates *Secretin* from the intestinal mucosa, which then passes by way of the blood to the pancreas to promote rapid secretion of pancreatic juice.**

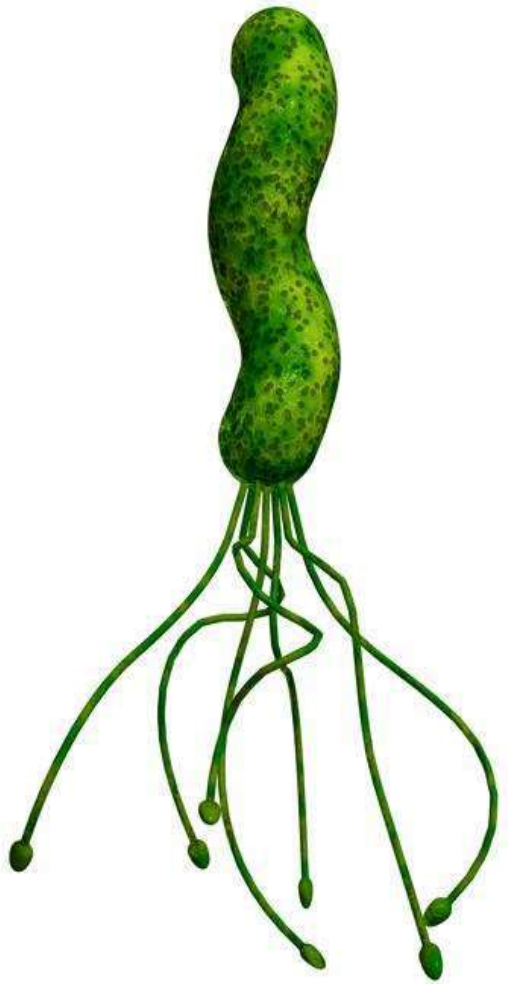
Causes

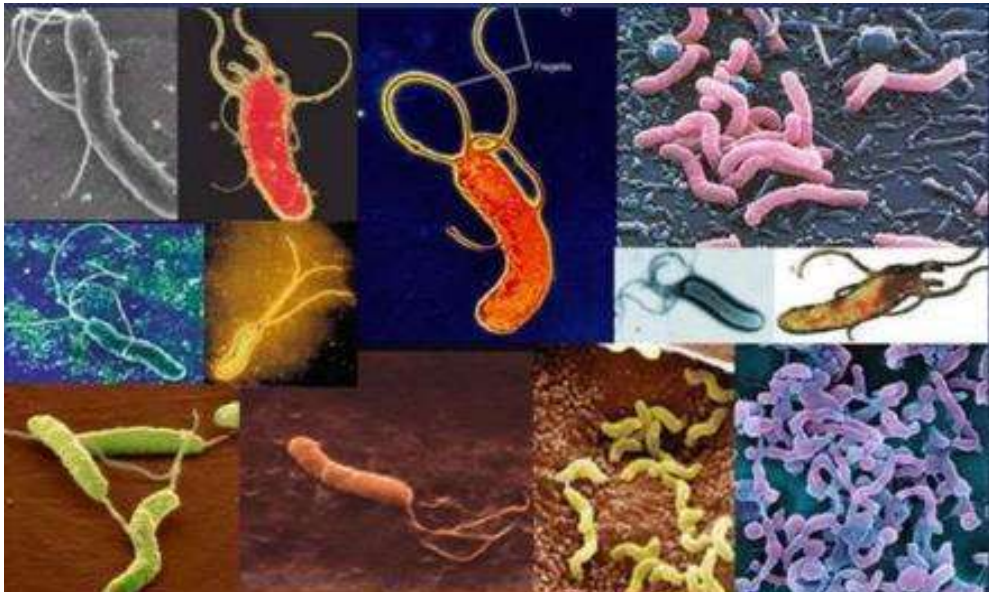
- In normal acid/pepsin attack is balanced by mucosal defences
- Increased attack by hyperacidity Weakened mucosal defence – the major factor *(H. pylori Related)*



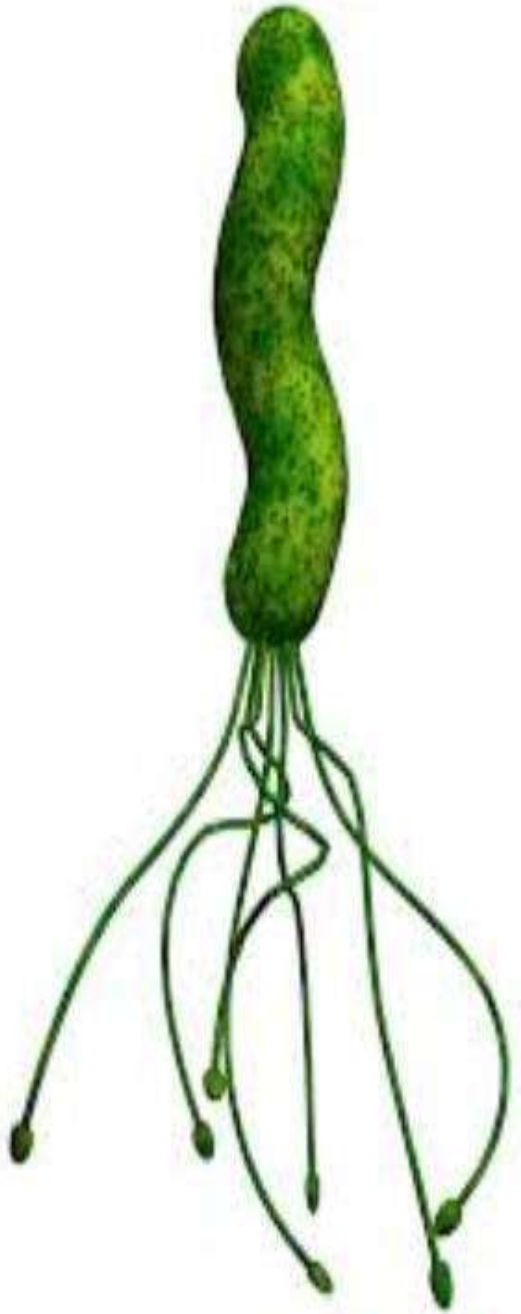
Helicobacter pylori

- Gram -ve Comma Shaped Bacteria Micro Aerophilic with 4-6 Flagella .
- Is most common cause of PUD.
- Transmission is Feco - Oral.
- Secrete urease convert Urea to Ammonia.
- Produce alkaline environment to survive in stomach.
- Higher prevalence in low socio economic.
- Almost all patient with DU and 2/3 of GU are HLO +.

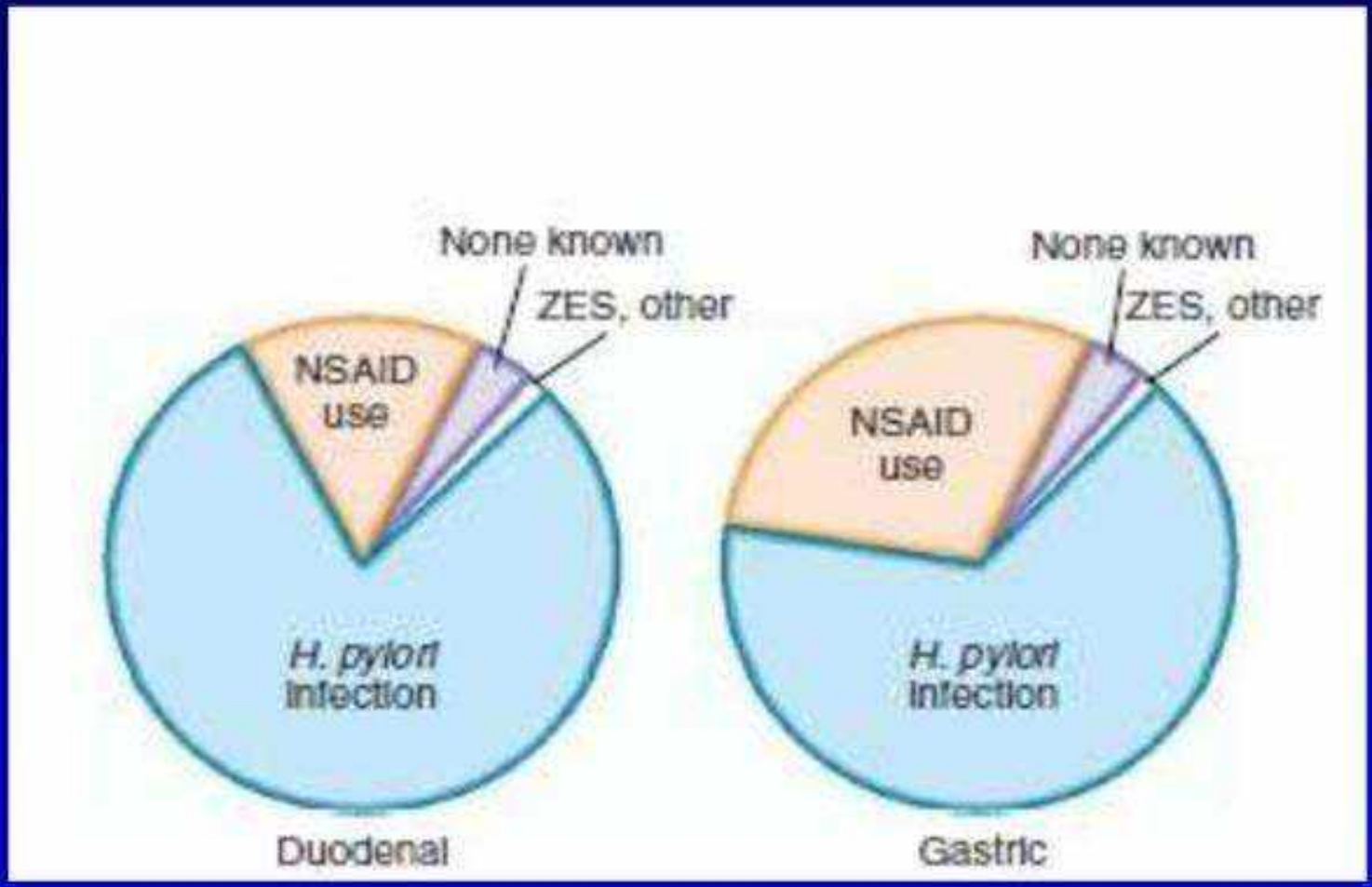




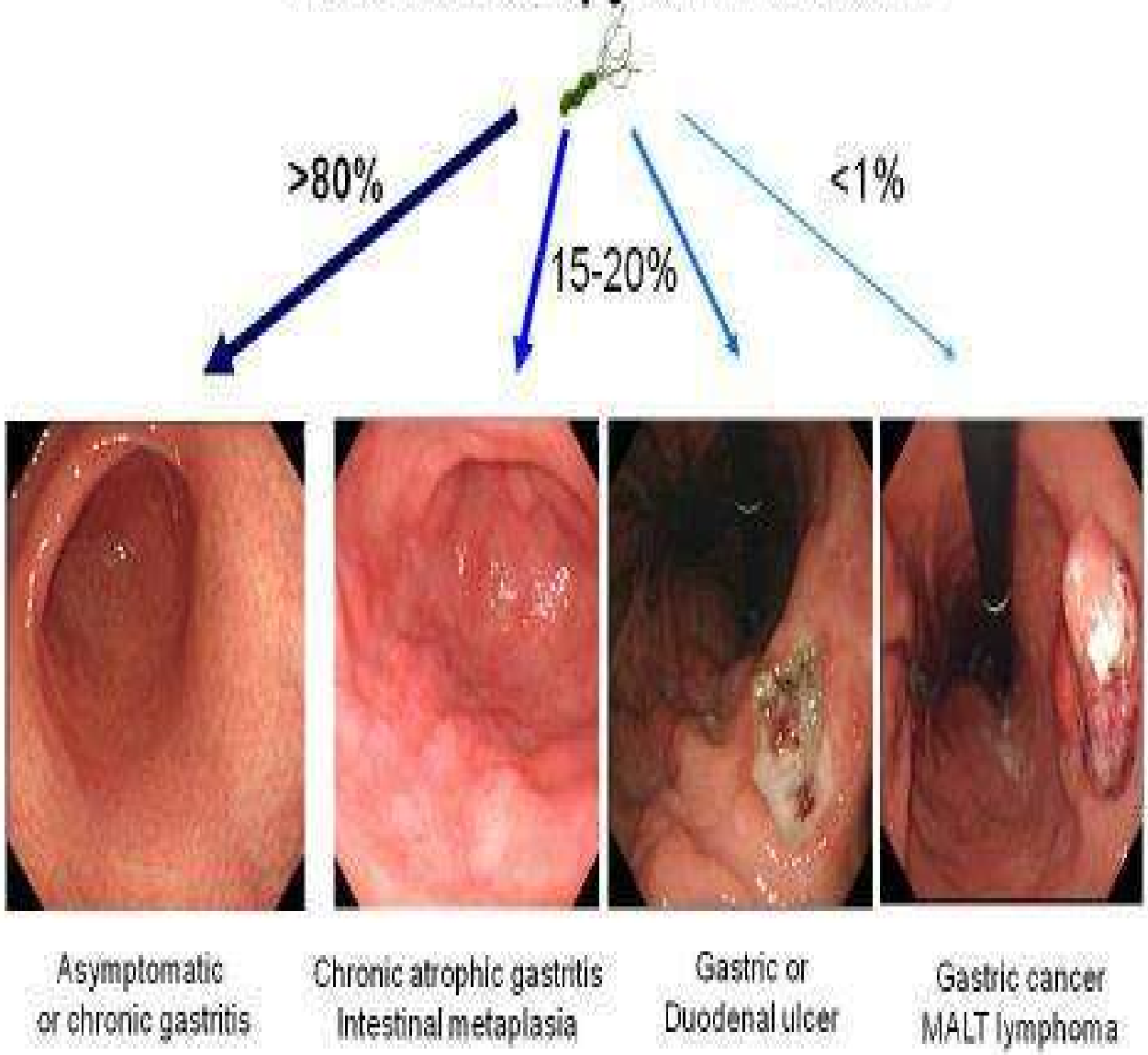
- **Bacterial Infection by *Helicobacter pylori* Breaks Down the Gastro duodenal Mucosal Barrier and Stimulates Gastric Acid Secretion.**
- **At least 75 percent of peptic ulcer patients have been found to have chronic infection of the terminal portions of the gastric mucosa and initial portions of the duodenal mucosa, most often caused by the bacterium *Helicobacter pylori***
- **In *DU*, the rate of gastric acid secretion is greater than normal, sometimes as much as twice normal.**
- **Excess secretion of gastric juices for any reason may cause peptic ulceration.**

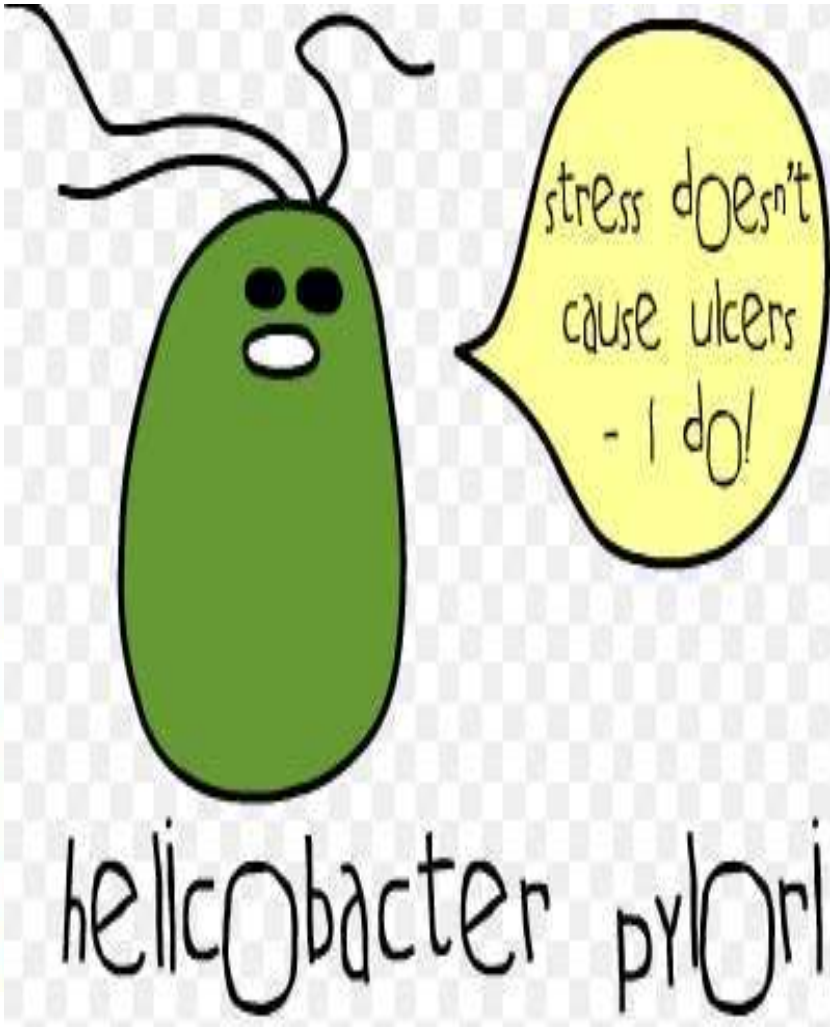


Conditions associated with PUD

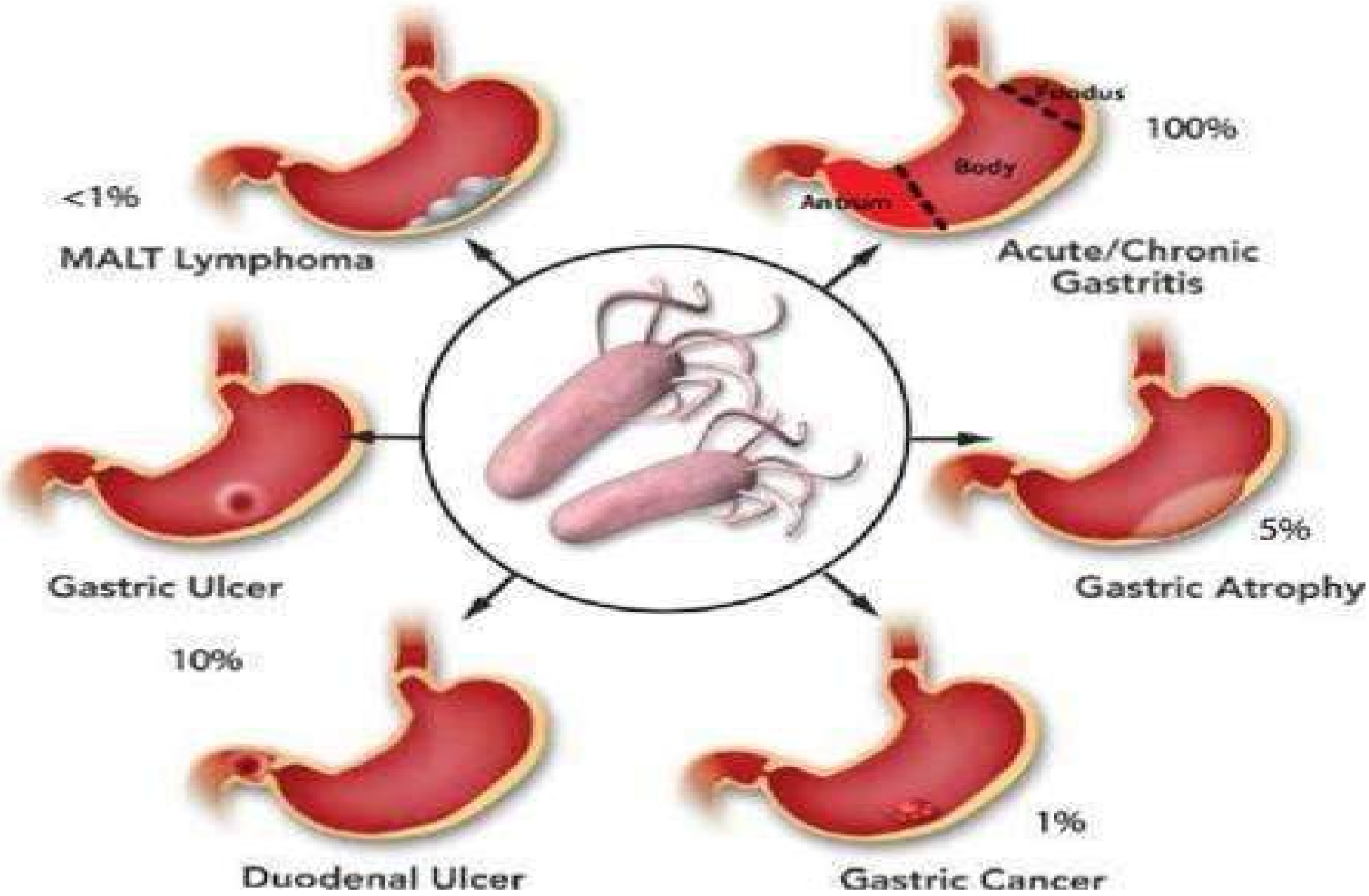


The Clinical Outcomes of *Helicobacter pylori* Infections





HLO OUTCOME


Fundus
Body
Antrum
100%
<1%
MALT Lymphoma
Acute/Chronic Gastritis
Gastric Ulcer
5%
Gastric Atrophy
10%
Duodenal Ulcer
1%
Gastric Cancer

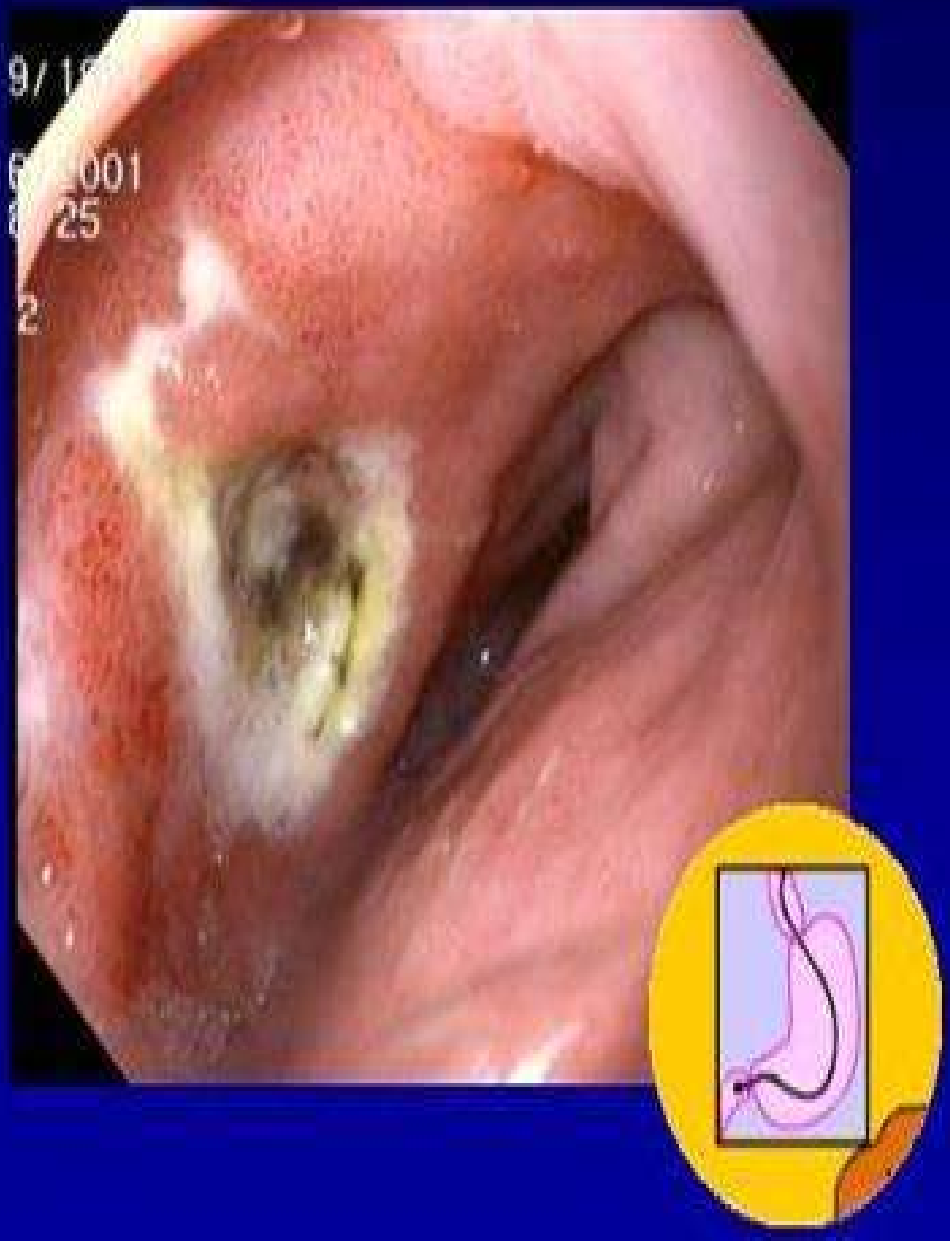
Other factors that predispose to ulcers include

- ***Smoking:*** **presumably because of increased nervous stimulation of the stomach Secretory glands.**
- ***Alcohol:*** **because it tends to break down the mucosal barrier.**
- ***Aspirin and other NSAIDS:*** **drugs that also have a strong propensity for breaking down this barrier.**

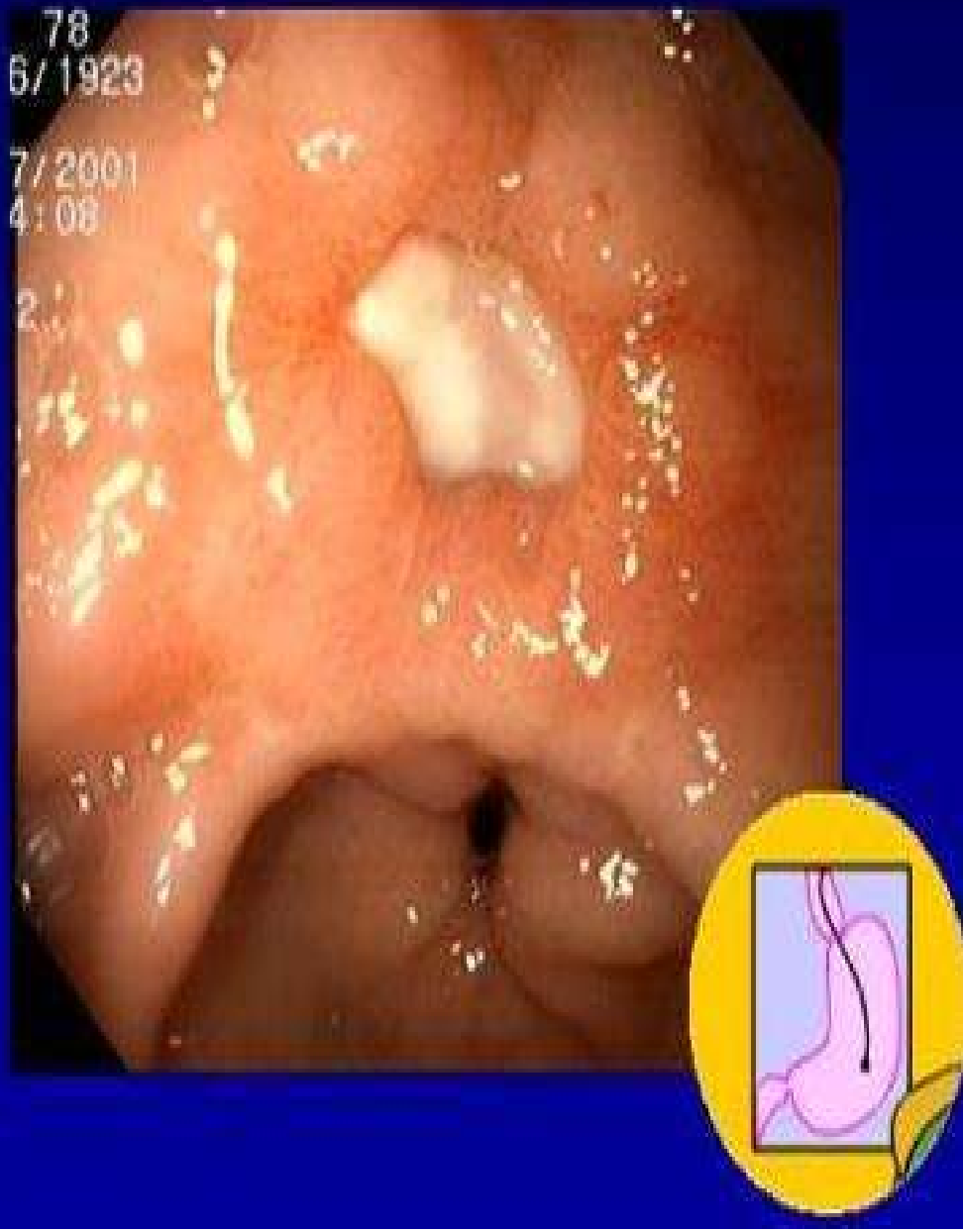
Physiology of Treatment

- Use of Antibiotics along with other agents to kill infectious bacteria.
- Proton pump inhibitors (PPI)are used now as their antacid effect is better and duration of action is longer e.g. *Omeprazole.*
- Administration of an acid-suppressant drug, especially *ranitidine*, an antihistaminic that blocks the stimulatory effect of histamine on gastric gland histamine$_2$ *(H_2) receptors antagonist,* thus reducing gastric acid secretion by 70 to 80 per cent.
- Triple Therapy is the recent approach in treatment of peptic ulcer. It includes 2 antibiotics (Clarithromycin + Amoxicillin or metronidazole) and an acid-suppressant (Omeprazole).

Duodenal Ulcer (DU)



Gastric Ulcer (GU)



Disorders of the Small Intestine

- ***Abnormal Digestion of Food in the Small Intestine(Pancreatic Failure)***
- **Lack of pancreatic secretion frequently occurs**
  - **In *pancreatitis***
  - **When the *pancreatic duct is blocked* by a gallstone at the ampulla of Vater.**
  - **When *head of the pancreas has been removed* because of malignancy.**

- **Loss of pancreatic juice means loss of trypsin, chymotrypsin, carboxypolypeptidase, pancreatic amylase, pancreatic lipase, and still a few other digestive enzymes.**
- **Without these enzymes, up to *60* percent of the *fat* entering the small intestine may be unabsorbed, as well as *one third to one half* of the *proteins and carbohydrates*.**
- **As a result, large portions of the ingested food cannot be used for nutrition and copious, fatty feces are excreted. *(Steatorrhea).***

Pancreatitis-Inflammation of the Pancreas

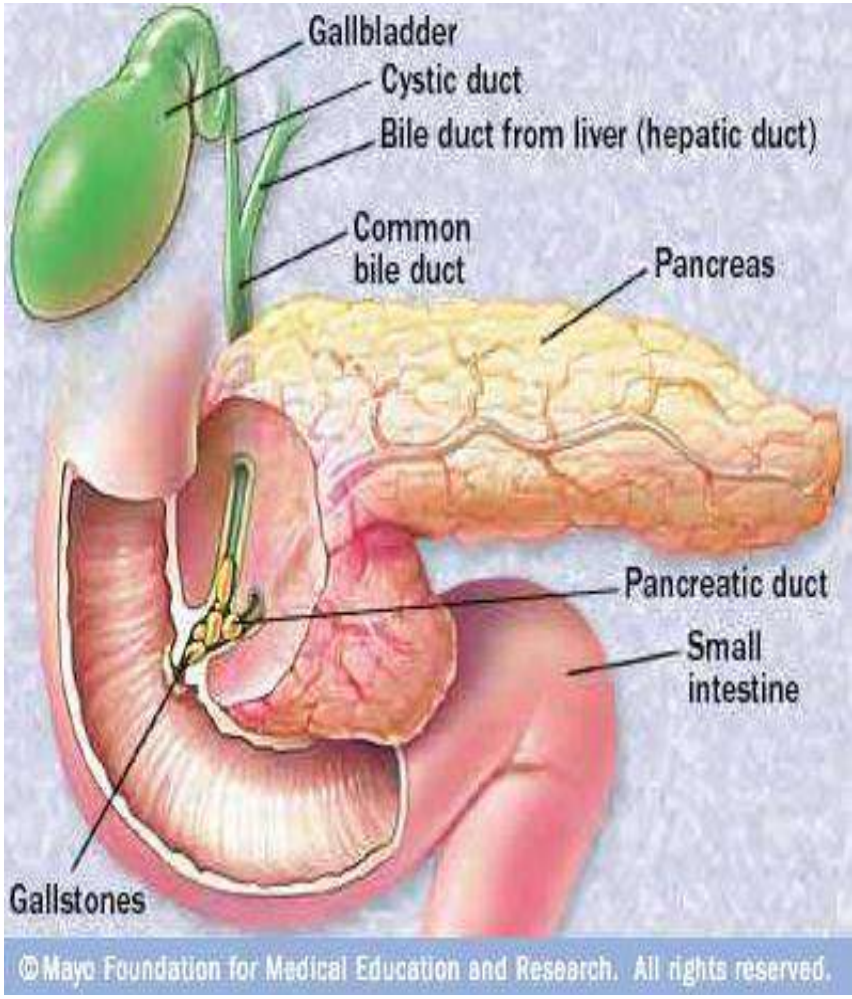
- **Pancreatitis can be either *acute pancreatitis* or *chronic pancreatitis.***

The most common cause of acute pancreatitis are:

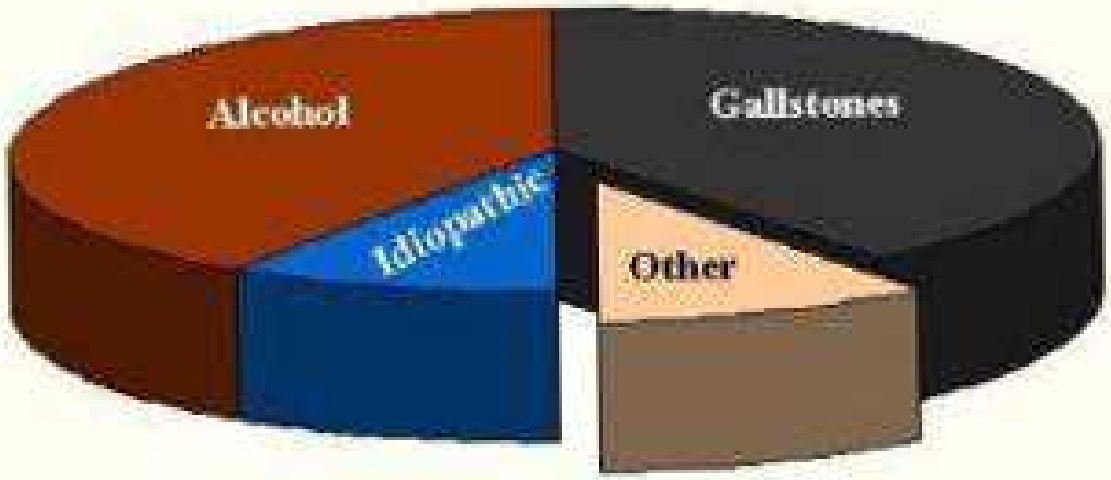
- **B*lockage of the papilla of Vater* by a *Gall bladder stone***
- ***Drinking excess Alcohol.***

The two together account for more than *90 percent* of all cases.

(Auto-digestion)



Pancreatitis: Etiology



- Drugs
- Infectious agents
- Hyperlipidemia
- Hypercalcemia
- Ductal obstruction
- Trauma
- Hypotension
- Post-operative
- Miscellaneous

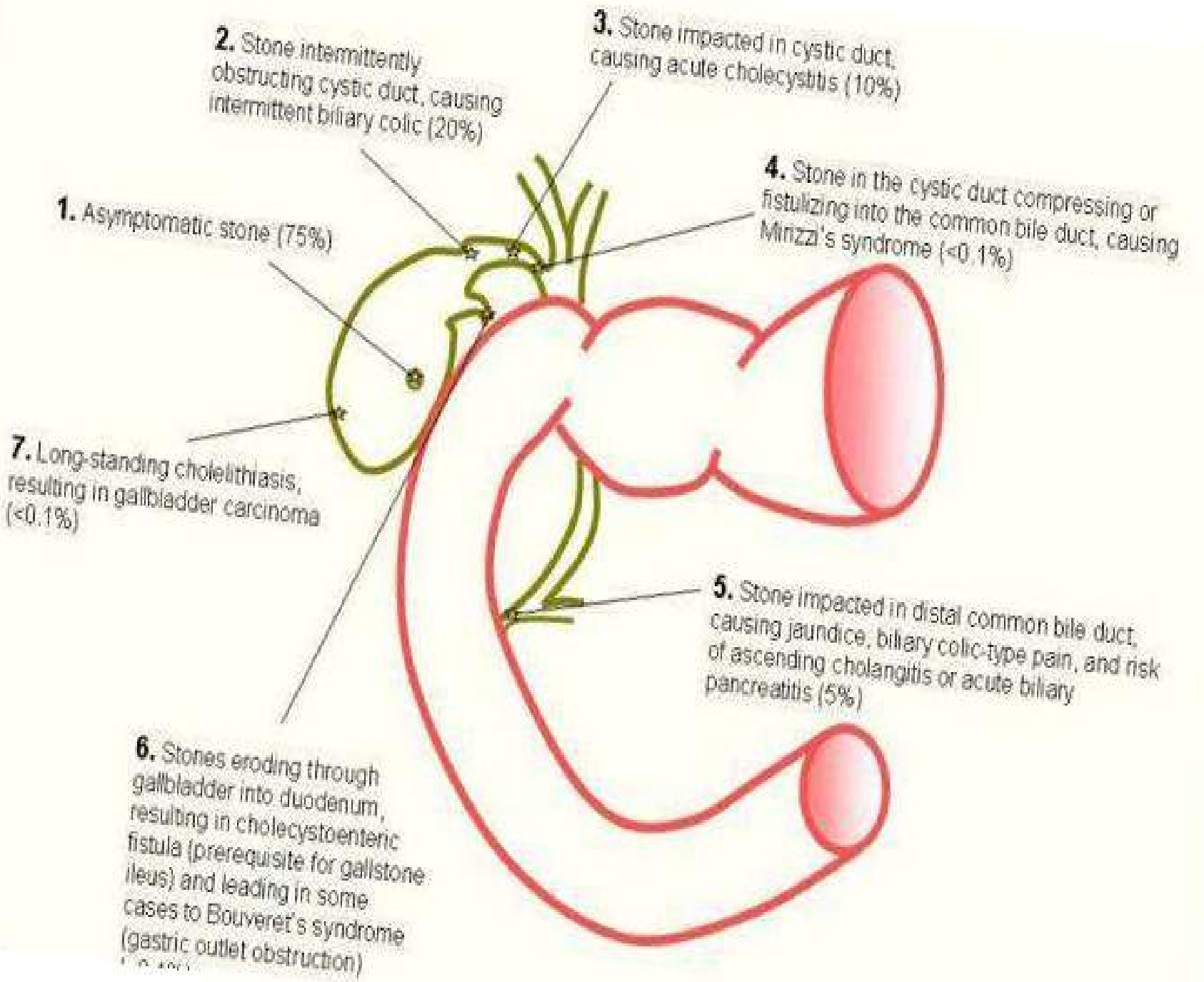
PREV : Pancreatitis: Local Effects of Enzymes

NEXT : Chronic Pancreatitis: Etiology

Author: Laurence Scott Bailen, M.D.

Pancreatitis: Clinical Features

Signs & Symptoms	Lab Tests	Differential Diagnosis
Abdominal pain	↑ WBC	Choledocholithiasis
Abdominal tenderness	↑ Serum amylase	Perforated ulcer
Nausea and vomiting	↑ Serum lipase	Mesenteric ischemia
Fever		Intestinal obstruction
Tachycardia		Salpingitis
		Ectopic pregnancy


2. Stone intermittently obstructing cystic duct, causing intermittent biliary colic (20%)
3. Stone impacted in cystic duct, causing acute cholecystitis (10%)
1. Asymptomatic stone (75%)
4. Stone in the cystic duct compressing or fistulizing into the common bile duct, causing Mirizzi's syndrome (<0.1%)
7. Long-standing cholelithiasis, resulting in gallbladder carcinoma (<0.1%)
5. Stone impacted in distal common bile duct, causing jaundice, biliary colic-type pain, and risk of ascending cholangitis or acute biliary pancreatitis (5%)
6. Stones eroding through gallbladder into duodenum, resulting in cholecystoenteric fistula (prerequisite for gallstone ileus) and leading in some cases to Bouveret's syndrome (gastric outlet obstruction)

Malabsorption by the Small Intestinal Mucosa-Sprue

- ***Sprue:*** **are diseases which lead to decrease mucosal absorption.**
- **Malabsorption also can occur when large portions of the small intestine have been removed.**
- ***Non Tropical Sprue :*** **(*Idiopathic Sprue, celiac disease* (in children), or *gluten enteropathy*)**

Results from the toxic effects of *gluten* present in certain types of grains , especially wheat& rye.

- **Gluten has a direct destructive effect on *Intestinal Enterocytes.***
- **In milder forms of the disease, only the *Microvilli* of the absorbing enterocytes on the villi are destroyed, thus decreasing the absorptive surface area as much as *Two Folds*.**
- **In the more severe forms, the *Villi* themselves become blunted or disappear altogether, thus still further reducing the absorptive area of the gut**
- **Treatment**

Villi

INCREASE THE SURFACE AREA

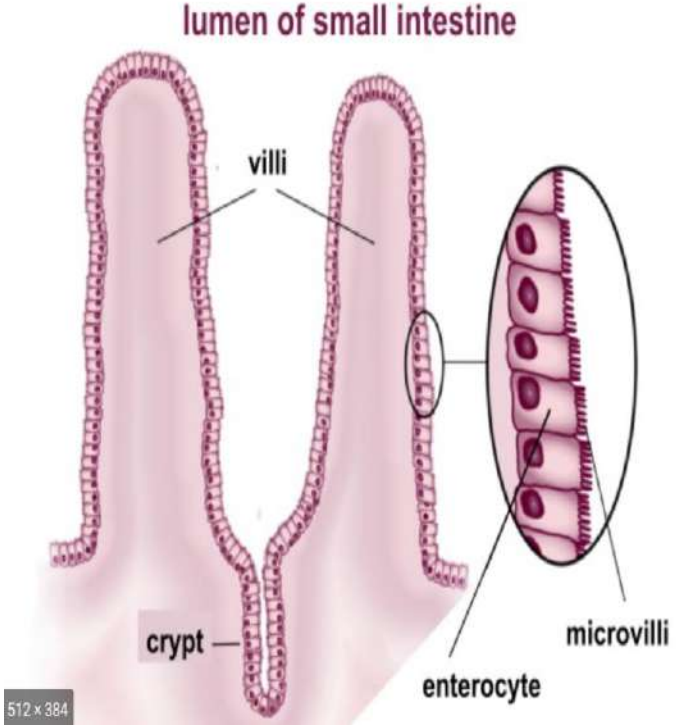
NOTE: THE VILLUS IS MADE UP OF MANY CELLS

CAPILLARY NETWORK

EACH CELL IN THE VILLUS HAS MICROVILLI ON ITS SURFACE

LACTEAL

FOUND IN THE SMALL INTESTINE



Tropical Sprue

Caused by inflammation of the intestinal mucosa resulting from *Unidentified Infectious Agents.*

Malabsorption in Sprue

In the early stages of Sprue, there is impaired absorption of *Fat Only* .

The fat that appears in the stools is almost entirely in the form of *Salts of Fatty Acids Rather than Undigested Fat* , demonstrating that the problem is one of *Absorption, not of Digestion.* In fact, the condition is frequently called *Steatorrhea* which means simply excess fats in the stools.

- **In severe cases of Sprue, there is impaired absorption of *Fat, Proteins, Carbohydrates, Calcium, Vitamin K, Folic acid, and vitamin B_{12}*. As a result, the person suffers from:**
- **Severe nutritional deficiency, developing wasting of the body.**
- **Osteomalacia (demineralization of the bones because of lack of calcium).**
- **Inadequate blood coagulation caused by lack of vitamin K.**
- **Macrocytic anemia of the pernicious anemia type, due to diminished vitamin B_{12} and folic acid absorption.**

Disorders of the Large Intestine

Constipation:

Constipation means *slow movement of feces through the large intestine.*

It is often associated with large quantities of dry, hard feces in the descending colon that accumulate because of *overabsorption of fluid.*

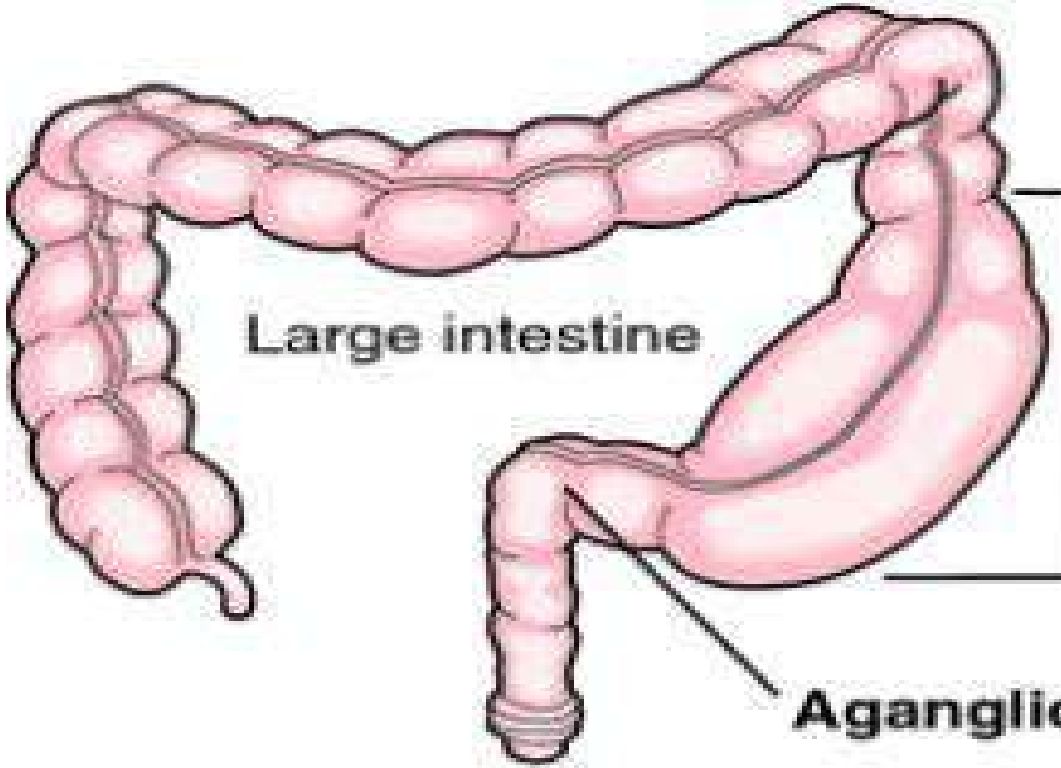
- **Tumors, Adhesions ,Ulcers(Organic), *Atony*, Spasm(IBS) Functional.**
- **If a person establishes regular bowel habits early in life, defecating when the *Gastro Colic and duodenocolic reflexes cause mass movements* in the large intestine, the development of constipation in later life is much less likely.**
- **Alternating constipation and diarrhea.**

Mega Colon (Hirschsprung's Disease)

- **The colon sometimes distend to a diameter of *3 to 4 inches.* (severe constipation) The condition is called *mega colon*, or *Hirschsprung's disease.***

- **The cause of mega colon is lack of or deficiency *of ganglion cells in the Myenteric Plexus in a segment of rectum and lower sigmoid.***

- **The sigmoid itself becomes small and almost spastic while feces accumulate proximal to this area, causing mega colon in the ascending, transverse, and descending colons.**



Megacolon

Dilated with feces and gas

Ganglion cells present (normal in function)

Aganglionic region

Tonic contraction and inadequate peristalsis

Partial obstruction

Chronic constipation

Enterocolitis

Enlargement of proximal segment

Complete bowel obstruction

3.Ulcerative Colitis

- **Extensive areas of the walls of the large intestine become inflamed and ulcerated.**
- **The motility of the ulcerated colon is often so great that Mass Movements occur much of the day rather than for the usual 10 to 30 minutes.**
- **Also, the colon's secretions are greatly enhanced. As a result, the patient has repeated diarrheal bowel movements *(Bloody).***

Ulcerative Colitis

- Unknown etiology , confined to large bowel, auto antibodies or infection triggers inappropriate immune response → destruction of mucosa
- Stress, psycho somatic.
- Infective E.coli
- Immunological lymphocytes
- ***Chronic bloody diarrhea, feces mixed with blood ,mucus and pus.***

- **Proctitis:** involves only the rectum (a)
- **Proctosigmoiditis:** involves the rectum and sigmoid colon (b)
  (the lower segment of the colon before the rectum
- **Distal colitis:** involves only the left side of the colon (c)
- **Pancolitis:** involves the entire colon (d)
- **Backwash ileitis:** involves the distal ileum