PHYSIOLOGY OF GASTROINTESTINAL TRACT (GIT)

References:

1- Guyton and Hall Textbook of Medical Physiology

2- Ganong Review of Medical Physiology

Lecture One:

Regulation of GASTROINTESTINAL FUNCTION& G.I.T. Motility

Objectives:

Outline the mechanisms regulating G.I.T. functions.

Describe the types of movements of smooth muscles of the gut.

Define Peristalsis.

G.I.T Parts:

1-Oral cavity.

2- Pharynx.

3- Esophagus.

4- Stomach.

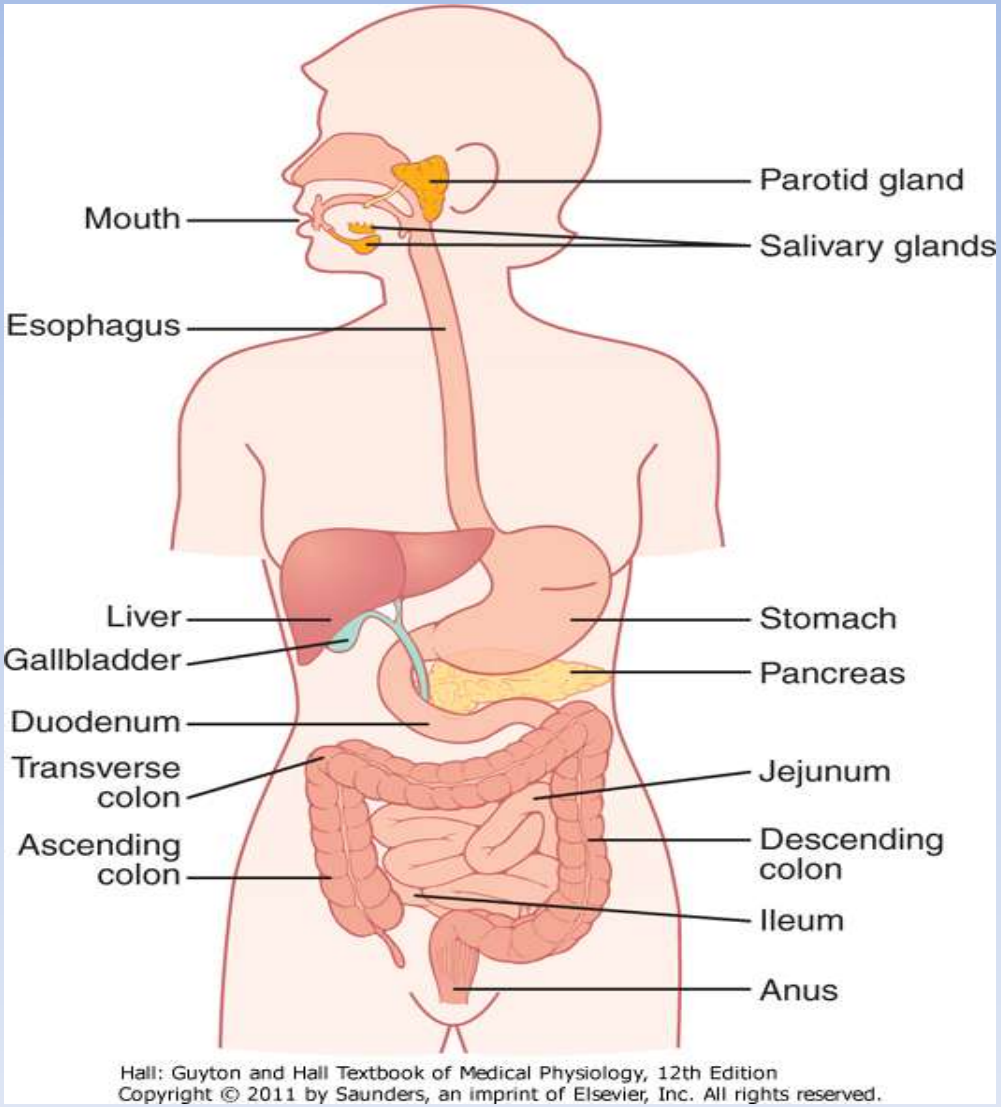
5- Small intestine: Duodenum , Jejunum, Ileum.

6- Large intestine: Caecum, Ascending colon, Transverse colon , Descending colon, Sigmoid, Rectum and anal canal.

The accessory organs are:

1- Salivary glands. 2- Pancreas. 3- Liver.

Parts of GIT



REGULATION OF GASTROINTESTINAL FUNCTION

Some of the mechanisms that regulate the gastrointestinal functions depend on:

- **Intrinsic properties of intestinal smooth muscles.**
- **Nervous:**

  A-Extrinsic.

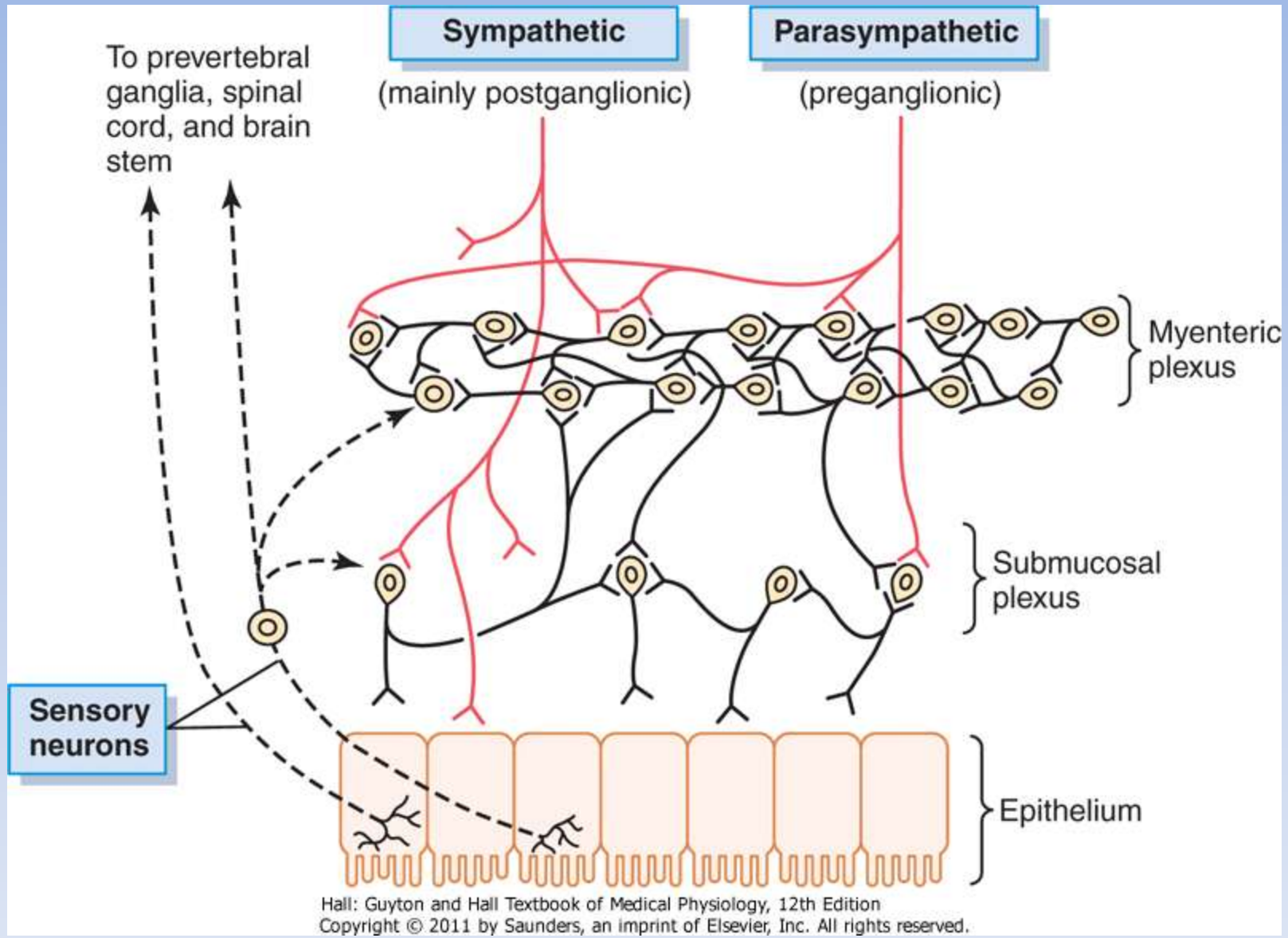
  -Parasympathetic

  -Sympathetic

  B-Intrinsic

  -Auerbach or myenteric plexus

  -Meissner’s or sub mucosal plexus
- **Hormones.**



ELECTRICAL ACTIVITY OF THE G.I. SMOOTH MUSCLES

The smooth muscle of the G.I. tract is excited by almost continual slow intrinsic electrical activity along the membranes of the muscle fibres. This activity has two basic types of electrical waves.

1. **Slow waves**
2. **Spikes.**

- **SLOW WAVES**: these waves are slow undulating changes in the resting membrane potential. Their intensity ranges between 5-15 milli volts, and their frequency range between 3-12 per minute (3 in the body of the stomach and 12 in the duodenum).
- The cause of the slow waves is unknown → might result from slow undulation of the pumping activity of sodium-potassium pump.

- **SPIKE POTENTIALS:** they are true action potentials. They occur automatically when the resting membrane potential of the G.I. smooth muscle becomes more positive than about -40 mille volt (normal resting membrane potential of the gut is -50 to -60 mille volt).

- ***The slow waves do not cause muscle contraction by themselves, but the spike potentials generated at the peak of the slow waves, cause most of the contraction.***
- **(entry of calcium ions into the muscle fibers.)**

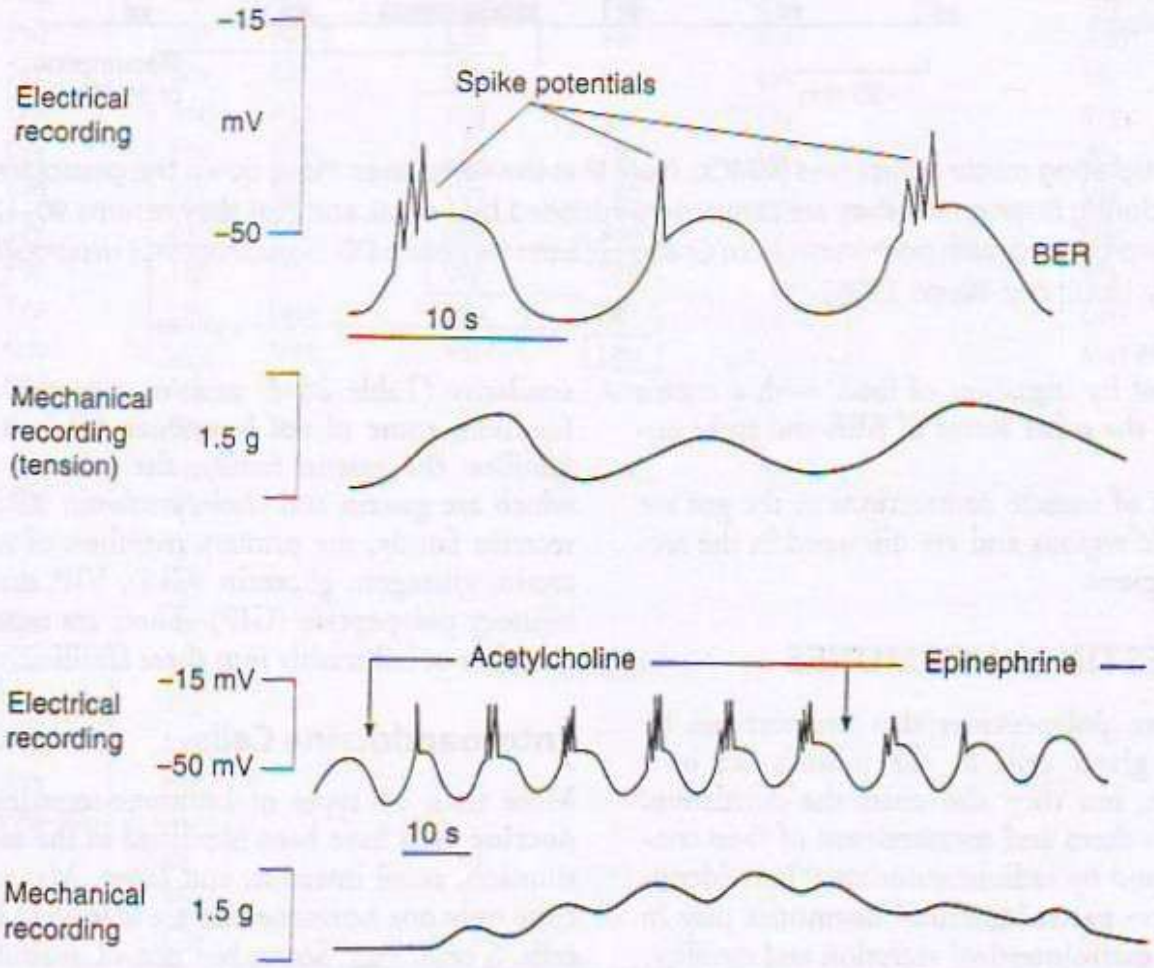
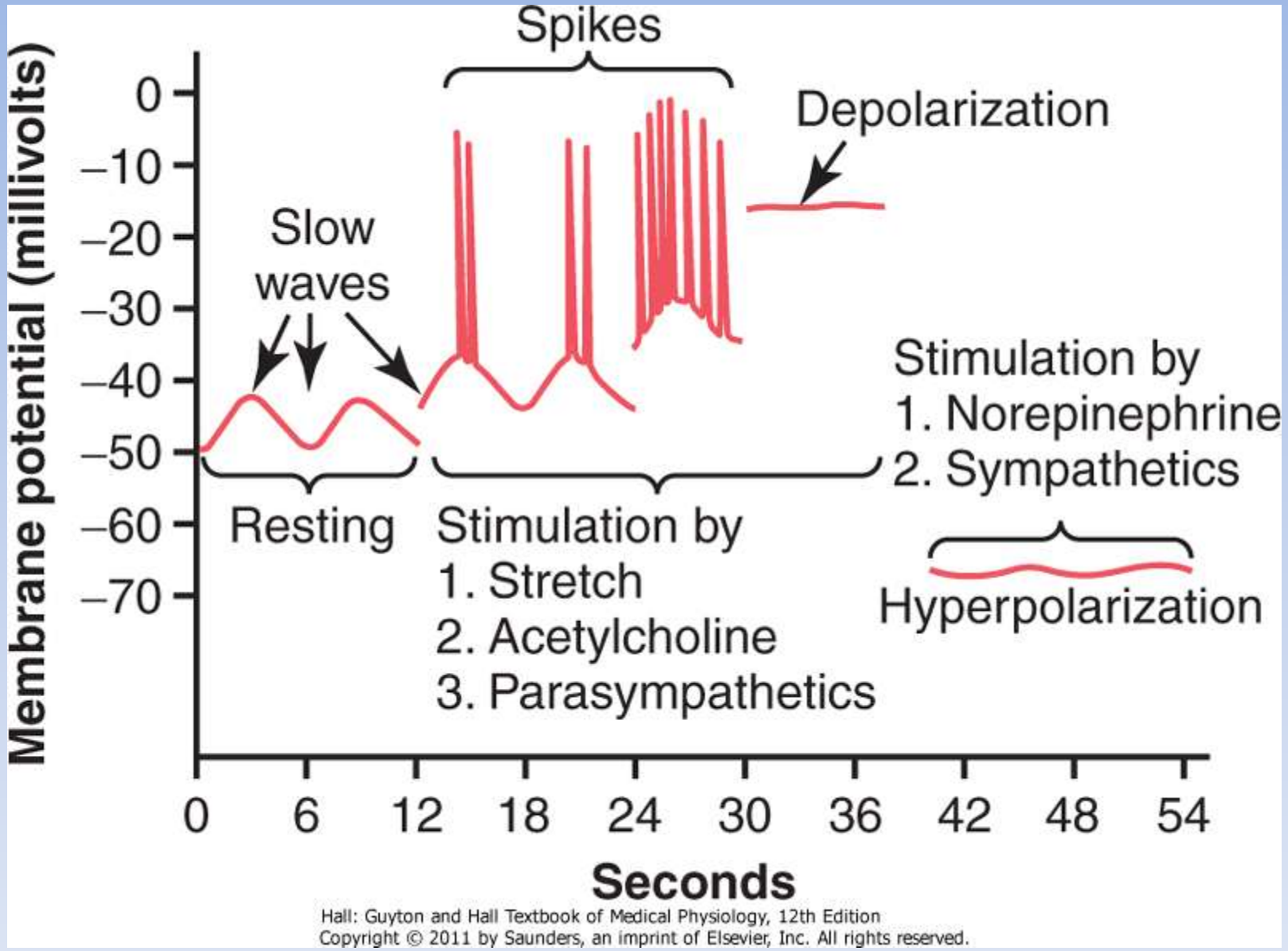


Figure 26–2. Basic electrical rhythm (BER) of gastrointestinal smooth muscle. **Top:** Morphology, and relation to muscle contraction. **Bottom:** Stimulatory effect of acetylcholine and inhibitory effect of epinephrine. (Modified and reproduced, with permission, from Chang EB, Sitrin MD, Black DD: *Gastrointestinal, Hepatobiliary, and Nutritional Physiology.* Lippincott-Raven, 1996.)



AUTONOMIC INNERVATION (extrinsic)
Parasympathetic innervation

- The **vagus nerve** is the main parasympathetic nerve supply to the gut.
- It provides extensive innervations to the **oesophagus**, **stomach**, **pancreas** and **first half of the large intestine**. But to a lesser extent to the small intestine.
- The **pelvic or Nervi erigentes** and comes from 2, 3, 4^{th} sacral segments of the spinal cord. It supplies the distal half of the large intestine.
- The preganglionic parasympathetic nerves will end on ganglion cells in the enteric plexus (Meissner and Auerbach).
- The post ganglionic fibers will pass then to the muscles of the muscular coat and to the muscularis mucosae to **control contraction of the smooth muscles**. Some fibers pass to the secretory cells to **control secretion of mucus or different juices.**
- Stimulation of parasympathetic nerves ***increase the activity of the gastrointestinal tract i.e. increases the motility and increases the secretion***

Sympathetic innervation:

- **The thoraco-lumbar** part of the spinal cord.
- The **preganglionic** fibers after leaving the cord will end in **the celiac** and various **mesenteric ganglia**. From there the post ganglionic fibers will pass to all parts of the G.I. tract.
- Some post ganglionic fibers will end on the myenteric plexus of Auerbach's to **inhibit** its activity. In addition to these axons, other postganglionic sympathetic fibers pass to the circular and longitudinal muscle to **produce relaxation.**
- There are also some fibers going to the blood vessels to cause **vasoconstriction**. Some fibers pass to the **Meissner plexus to inhibit its activity.**
- stimulation of the sympathetic nervous system ***inhibits activity in the G.I.*** tract causing an opposite effect for that of the parasympathetic stimulation. This inhibition is carried out by two ways:

1- **Direct inhibitory effect of nor-epinephrine on the smooth muscle** (except the muscularis mucosae which it excites).

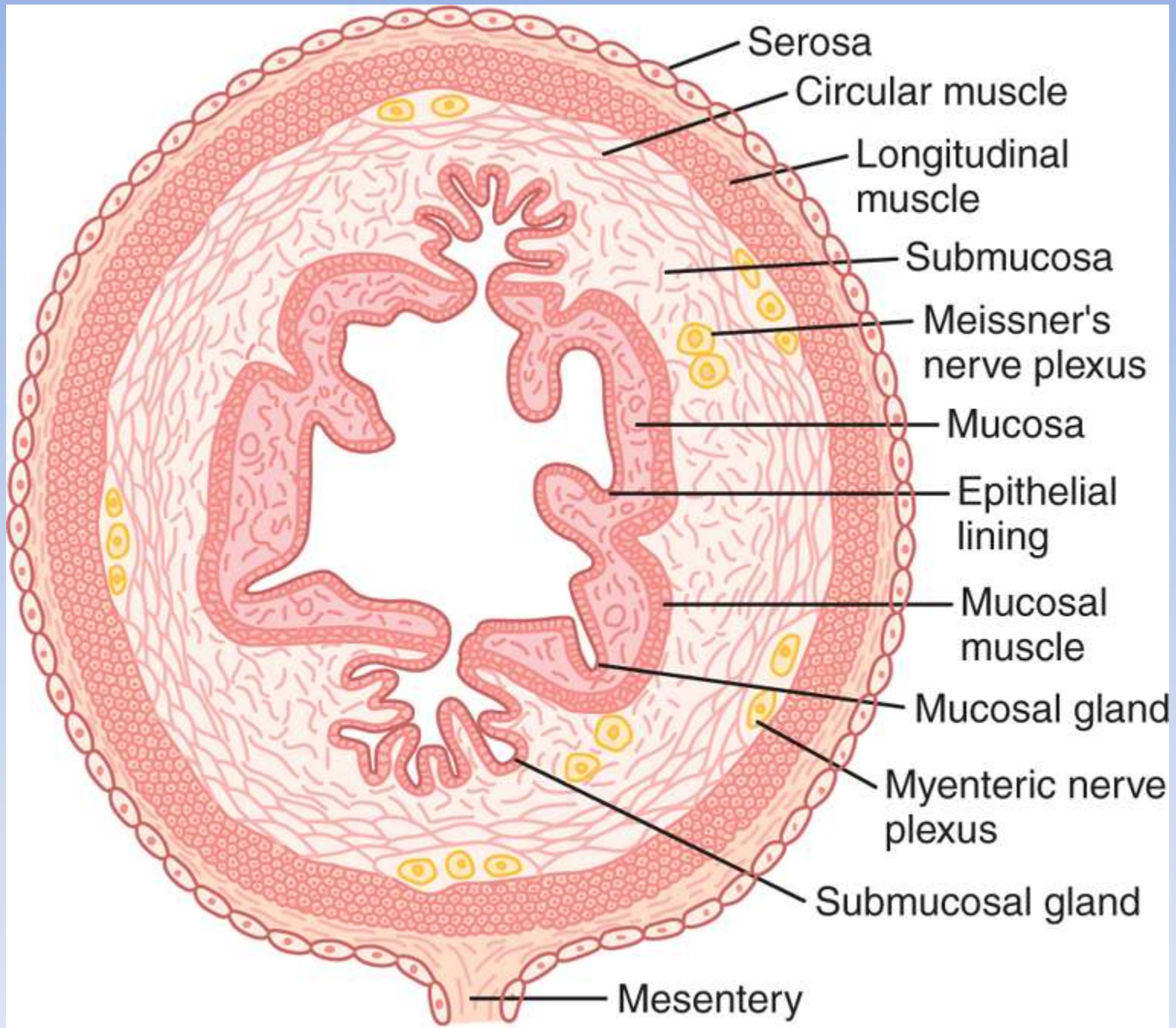
2- By **inhibiting the neurons of the enteric nervous plexus**.

INTRINSIC INNERVATION

- The whole gut from the oesophagus to the anus is supplied by intrinsic nerves which consist of two plexuses.

1. **Meissner's plexus in the submucosa**.
2. **Auebach's or myenteric plexus**. In between the circular and longitudinal muscle layer of the muscular coat.

- Together these plexuses are called **ENTERIC PLEXUSES**. These plexuses are composed of groups of ganglionic cells interconnected by a network of fibers. This system control most gastrointestinal functions and particularly **movement and secretion**. **Auerbach's** plexuses control mainly the ***gastrointestinal movement***, while the **Meissner's** plexus controls mainly the ***secretion***, and also has many sensory functions.



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- The intrinsic nervous system is responsible for many **neurogenic reflexes that occur locally in the gut**, such as reflexes from the mucosal epithelium to increase the activity of the gut muscles or to cause localized secretion of digestive juice by the gastrointestinal glands.
- There are about 100 million neurons in this system. They contain not only Ach and nor-epinephrine but other mediators.

Mediators are:

- **Ach.**
- **Nor-epinephrine.**
- **Nitric oxide (NO).**
- **Carbon monoxide (CO).**
- **Vasoactive intestinal polypeptide (VIP).**
- **Serotonin.**
- **CCK.**
- **Enkephalin.**
- **ATP.**
- **GRP.**
- **Neuropeptide y.**
- **Peptide yy.**
- **Neurotensin.**
- **Somatostatin.**
- **Substance P**
- **Endothelin -2. e.t.c……..**

HORMONAL CONTROL

- There are two major families of gut hormones according to their chemical structure.
  - **Gastrin** family which includes GASTRIN and CCK.
  - **Secretin** family which includes SECRETIN, GLUCAGON, GLICENTIN (GLI), VIP, GIP.
  - Other hormones include Motilin, substance P, Bombesin (GRP), Somatostatin, Neurotensin, e.t.c……

GASTROINTESTINAL MOTILITY

Smooth muscle of the gut exhibits two types of movements

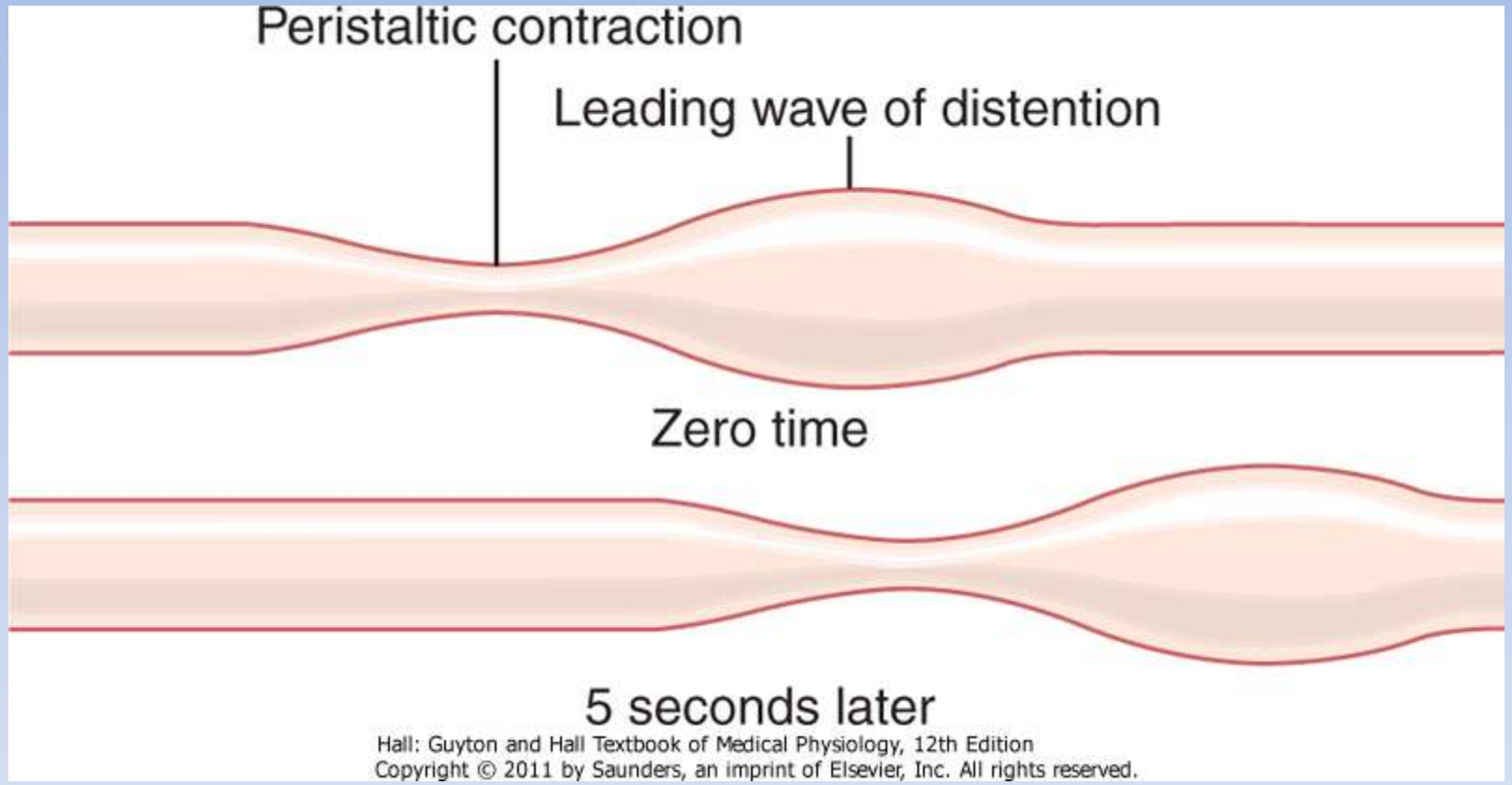
- **Tonic contraction.**
- **Rhythmic contraction.**

- **Tonic contraction:** is continuous contraction lasting for minutes or hours and increasing or decreasing in intensity but the contraction is on. The intensity of tonic contraction in each segment of the gut determines the amount of steady pressure in the segment
- contractions of the sphincters will determine the amount of resistance offered by the sphincters to the movement of intestinal contents. Examples of tonic contractions of sphincters are 1-Pyloric. 2-ileocaecal. 3-internal anal sphincter.

- **Rhythmic contraction:**
- can occur as rapid as 9-12 per minute in the intestine or as slow as 3 per minute in the stomach.
- It is the frequency of the slow wave in these segments that sets the frequency. Rhythmic contraction is important for:
  1. Mixing the food.
  2. Peristaltic propulsion of food.

Peristalsis

- A reflex response that is **initiated when the gut wall is stretched by the contents of the lumen**, and it occurs in all parts of the gastrointestinal tract from the esophagus to the rectum.
- The stretch initiates a **circular contraction behind** the stimulus and an **area of relaxation in front of it**. The wave of contraction then **moves in an oral to caudal direction**, propelling the contents of the lumen forward at rates that vary from 2 to 25 cm/s.
- Peristaltic activity can be increased or decreased by the autonomic input to the gut, ***but its occurrence is independent of the extrinsic innervation.***
- Peristalsis is an excellent example of the integrated activity of the enteric nervous system.



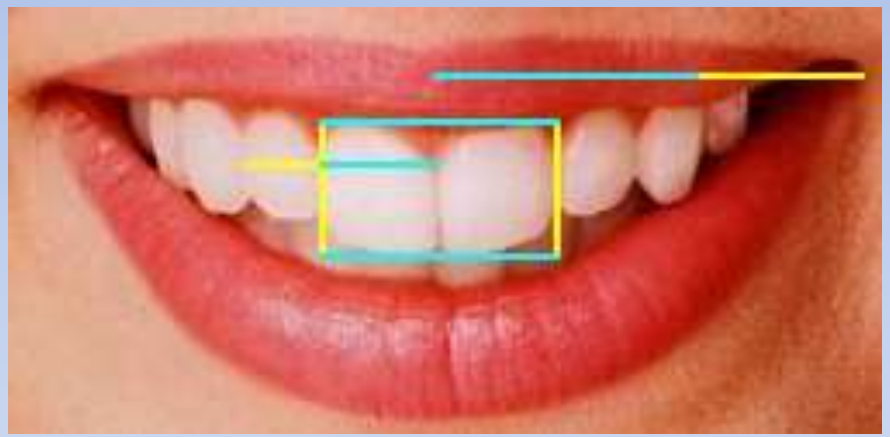
- It appears that local stretch releases **serotonin**, which activates sensory neurons that activate the myenteric plexus. ***Cholinergic neurons passing in a retrograde direction*** in this plexus activate neurons that **release substance P and acetylcholine, causing smooth muscle contraction**.
- At the same time, cholinergic neurons passing in an **anterograde direction activate neurons that secrete NO, VIP, and ATP, producing the relaxation ahead of the stimulus**

Migrating Motor Complex?

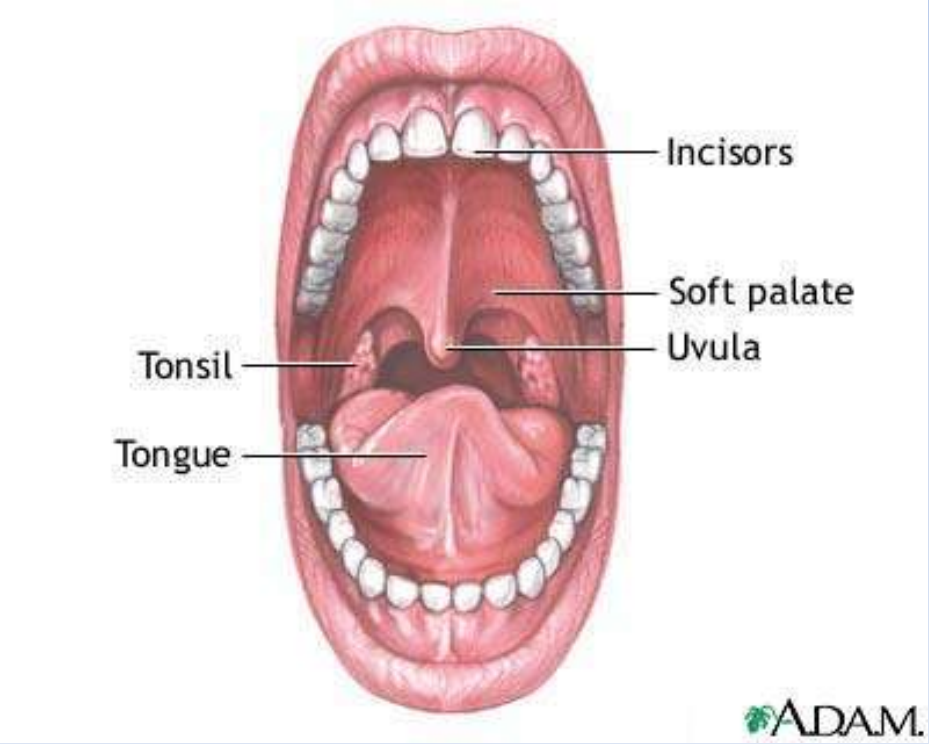
MASTICATION OR CHEWING:

- **The incisors for cutting.**
- **The molars for grinding action.**

<u>TEETH:</u> they are important for the process of mastication (chewing).



<u>TONGUE:</u> this is an extremely mobile mass of striated muscle covered with a mucus membrane. It helps greatly in mastication and swallowing.



Lecture Two: Swallowing & Stomach movements

Objectives:

Define swallowing and its stages.

Define lower esophageal sphincter.

Describe the term Achalasia.

Explain Stomach movements.

DEGLUTITION OR SWALLOWING

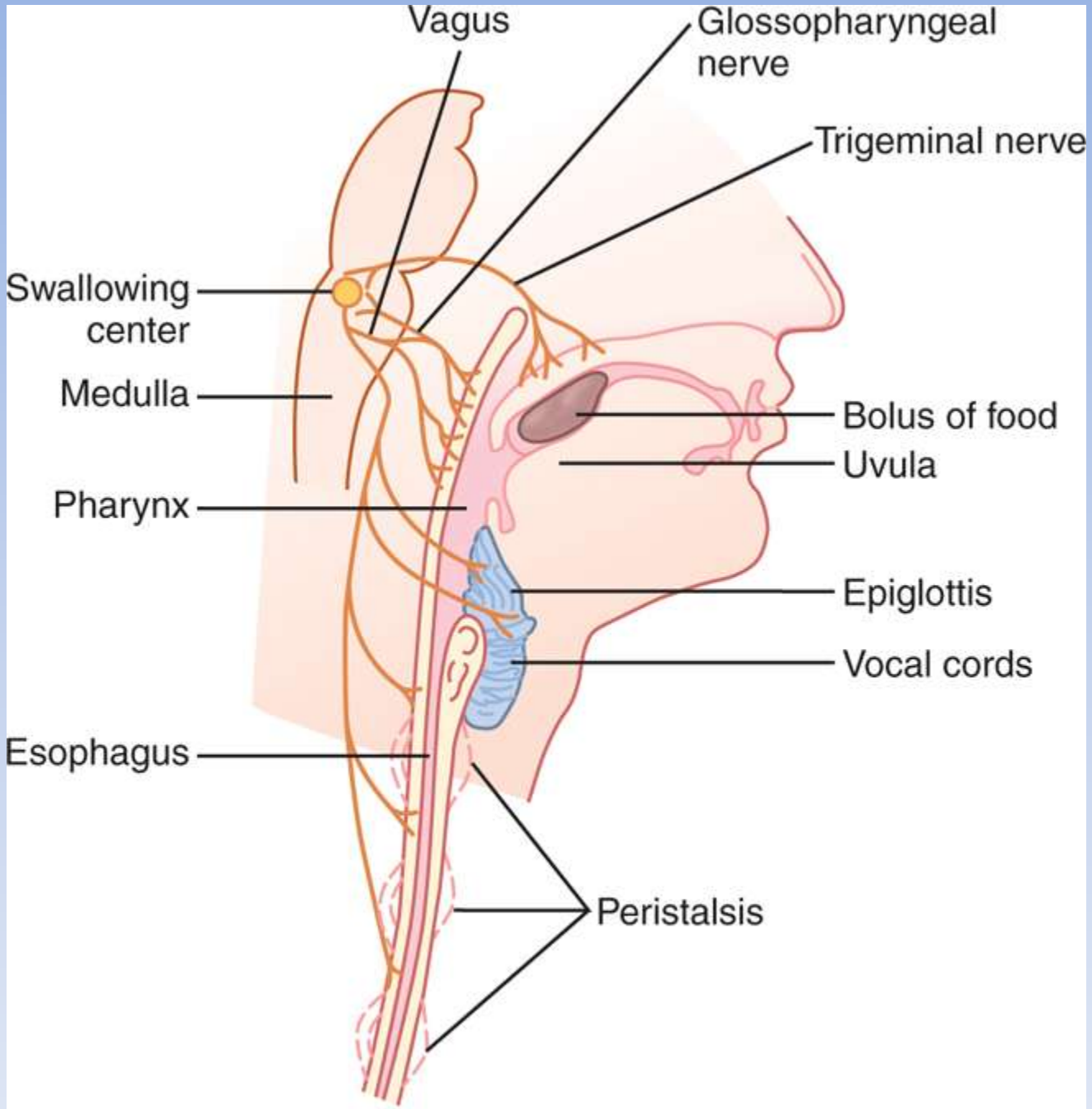
- Deglutition or swallowing is a highly complicated process because it requires the simultaneous activity of a number of structures.
- Swallowing can be divided into 3 stages:
  - Oral stage: voluntary
  - Pharyngeal stage: involuntary
  - Oesophageal stage: involuntary.

ORAL STAGE:

- Swallowing starts by closing the mouth and the bolus will be maneuvered or moved to the postero-dorsal surface of the tongue
- The tongue will squeeze or roll the bolus against the hard palate in an upward and backward direction.
- Thus the bolus will be forced into the pharynx. Saliva is necessary for normal swallowing.

PHARYNGEAL STAGE:

- When the bolus is pushed backwards in the mouth, it stimulates the swallowing receptor areas all around the opening of the pharynx and particularly on the tonsillar pillars→ sensory branch of the trigeminal (5^{th}) and glossopharyngeal (9^{th}) nerves → brainstem where the swallowing or the deglutition center is situated →the pharynx through 5^{th}, 9^{t}, 10^{th} and 12^{th} cranial nerves.
- These motor impulses will produce a series of automatic pharyngeal muscular contractions.



- the swallowing movements have to serve two quiet different functions:
- First is to propel the food through the pharynx and into the oesophagus.
- Second is to protect the airways both above and below form the possible entrance of food particles.

- **The pharyngeal movements that occur in the second stage of swallowing are the followings:-**
- **The soft palate will be pulled upwards in order to close the posterior nares, so that no food or fluid will enter the nasal cavity (protective).**
- **The palate-pharyngeal folds of mucus membranes on either side of the pharynx will be pulled medial wards so that they are approximated. This will change the pharyngeal opening into a slit through which the bolus must pass to the posterior pharynx. This slit will have a selective action allowing the passage of properly masticated food easily while impeding the passage of large objects. This is a protective phenomenon.**

- **Epiglottis will swing backwards over the superior opening of the larynx, in order to prevent the food from getting as far as the vocal cords. This is a protective phenomenon.**
- **Vocal cords of the larynx are approximated in order to prevent the passage of food to the trachea. This is a protective mechanism. Damage to the vocal cords or the muscles that approximate them can cause strangulation.**

- **The larynx will be elevated by muscles attached to the hyoid bone. This will elevate the glottis out of the main stream of food flow so that the food passes on either side of the epiglottis rather than on its surface. Thus it is another protective mechanism against the passage of food to the trachea.**
- **The upper oesophageal sphincter will relax to allow the food to pass from the posterior pharynx to the oesophagus. This sphincter (made from crico-pharyngeus muscle) is in a state of tonic contraction normally between swallows and thus it prevents the air form going to the oesophagus during respiration.**

- **Simultaneously will the elevation of the larynx and relaxation of the upper oesophageal sphincter there will be a contraction of the superior constrictor muscle of the pharynx which will initiate a rapid peristaltic wave passing downward from the pharynx to the oesophagus.**

- **The process of respiration will be inhibited temporarily. The swallowing center will inhibit the respiratory center whether in the process of inspiration or expiration. This is a protective mechanism also.**

- The entire pharyngeal stage of swallowing will take less than 2 seconds, so that temporary inhibition of respiration will take only a small fraction of the respiratory cycle. So in summary of the pharyngeal stage:
- **The trachea is closed.**
- **The oesophagus is open.**
- **Rapid peristaltic wave originate in the pharynx, will force the bolus of food into the upper oesophagus.**

Swallowing can be greatly affected or prevented by:

- Any damage to the cranial nerves (5^{th}, 9^{th}, 10^{th})
- Or to the swallowing center such as in poliomyelitis or encephalitis.
- Or to the swallowing muscle as in muscle dystrophy
- Failure of neuromuscular transmission as in myasthenia gravis.
- One of the most important conditions of paralysis of the swallowing mechanism occurs when the patient is under deep anesthesia.

OESOPHAGEAL STAGE:

- The oesophageal stage of swallowing begins with the relaxation of the upper oesophageal sphincter.
- Immediately after the bolus has passed, the sphincter closes, the glottis opens and breathing returns.
- Once in the oesophagus the bolus is moved towards the stomach by a progressive wave of muscle contraction which is known as peristaltic wave.
- Swallowing can occur while a person is upside down since it is not primarily gravity but the peristaltic wave which moves the bolus to the stomach.

- In upright position liquids and semi-solids foods generally fall by gravity to the lower oesophagus ahead of the peristaltic wave. The oesophagus has two types of movements:

- **Primary peristalsis**: is the continuation of the peristaltic wave that started higher up in the pharynx. It will take about 8-10 seconds to pass from the pharynx to the stomach. The **vagus nerve** is the main nerve that controls this primary peristalsis. If this primary peristalsis fails for some reason to move all the food then secondary peristalsis will start.
- **Secondary peristalsis**: it will be stimulated by the distension of the oesophagus by the retained food. The **myenteric plexus** of the oesophagus are responsible for these secondary peristalsis.

LOWER OESOPHAGEAL SPHINCTER (LOS)

- The lower Oesophageal sphincter (LOS) is a ***physiological sphincter*** rather than an anatomical sphincter.
- When there is no swallowing the sphincter is in state of tonic contraction and thus there is no reflux of food from the stomach to the oesophagus.
- During swallowing, this sphincter will relax to allow the food to enter the stomach.
- LOS is controlled by both nervous and hormonal mechanisms.

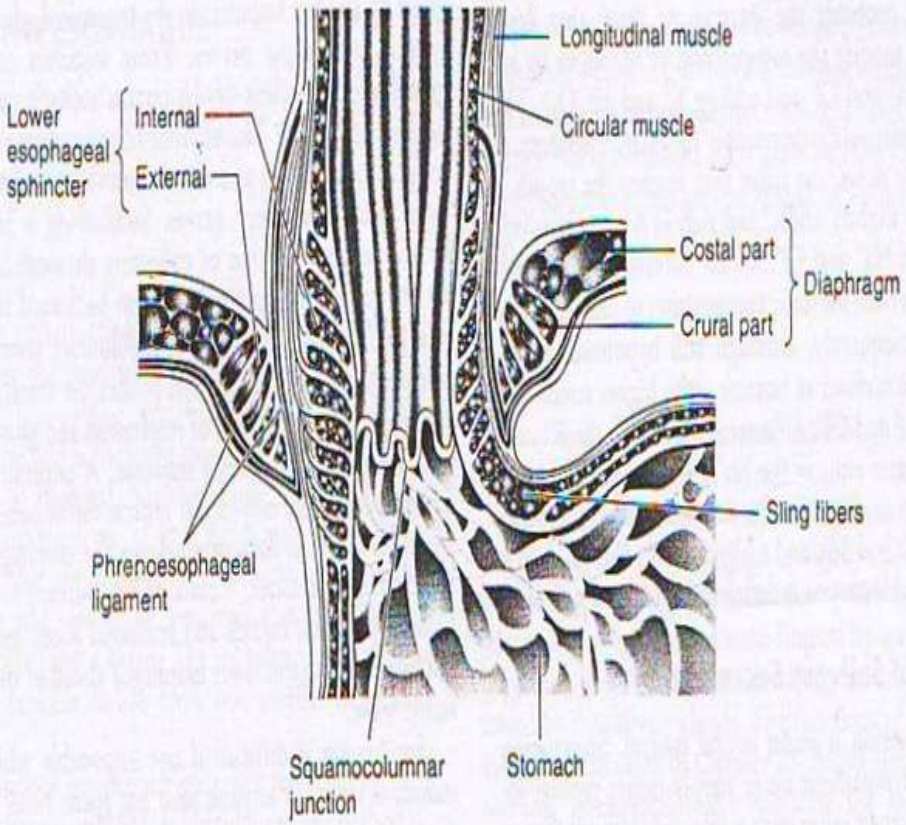


Figure 26–7. Esophagogastric junction. Note that the lower esophageal sphincter (intrinsic sphincter) is supplemented by the crural portion of the diaphragm (extrinsic sphincter), and that the two are anchored to each other by the phrenoesophageal ligament. (Reproduced, with permission, from Mittal RK, Balaban DH: The esophagogastric junction. N Engl J Med 1997;336:924. Copyright 1997 by Massachusetts Medical Society. All rights reserved.)

Nervous control:

- Ach from vagal endings cause increase in tonic contraction.
- Nitric oxide (NO) and VIP released from interneurons innervated by other vagal fibers causes it to relax (non-adrenergic non-cholinergic NANC).

Hormonal control:

- Some hormones ***increase*** the tone of the sphincter such as **gastrin**, and some ***decrease*** the tone of this sphincter such as **secretin and progesterone**.
- Because progesterone decreases the tone of LOS, thus reflux is well documented in the 3rd trimester of pregnancy, and in women taking birth control pills containing progesterone.
- Thus the common problem of heart burn occurring during pregnancy appears to be primarily due to hormonal influence on LOS pressure which will allow a gastro-esophageal reflux to occur particularly when there is an enlarged uterus with increased abdominal pressure.

Several mechanisms operate to prevent reflux of food and fluid from the stomach into the lower oesophagus. The most important are:-

- Lower oesophageal sphincter just above the oesophago-gastric junction.
- The position of this sphincter just below the diaphragm so that it is reinforced by intra-abdominal pressure and
- the angle of entry of the oesophagus into the stomach.

- Thus reflux is prevented by this flutter valve closure of the distal end of the oesophagus which is a valve-like mechanism of that portion of the oesophagus that lies immediately beneath the diaphragm.
- Greatly increased intra-abdominal pressure caves the oesophagus inward at the same time that the abdominal pressure also increases the intra-gastric pressure.
- This flutter-valve closure of the lower oesophagus prevents the high pressure in the stomach from forcing stomach contents into the oesophagus.

- The later two mechanisms are lost when the oesophago-gastric junction slides through the diaphragm.
- This proximal displacement is usually sufficient to allow reflux although the lower oesophageal sphincter may remain operative.

ACHALASIA

- Due to increase in resting LOS tension and incomplete relaxation of this sphincter upon swallowing and motor disorder in the lower 2/3 of the oesophagus.
- The myenteric plexus of the oesophagus is deficient in NO and VIP.
- The patient usually complains from dysphagia. If the condition becomes sever, the emptying of food from the oesophagus to the stomach may take a long time.

Lower Esophageal sphincter incompetence

- This is opposite to Achalasia.
- The incompetence will cause reflux of gastric contents and acids to the oesophagus.
- inflammation of the oesophagus→Oesophagitis by the irritating gastric contents.
- ulceration of the oesophagus and then scarring and stricture of the oesophagus.

RECEPTIVE RELAXATION OF THE STOMACH:

- The normal tonic contraction of the stomach is inhibited by the arrival of food, mediated by a vagal reflex.
- This allows the stomach to accommodate greater quantities of food up to 1-1.5 liter.
- This large increase in volume is accompanied by only a small rise in pressure within the lumen.

BASIC ELECTRICAL RHYTHM (BER) OR GASTRIC SLOW WAVE:

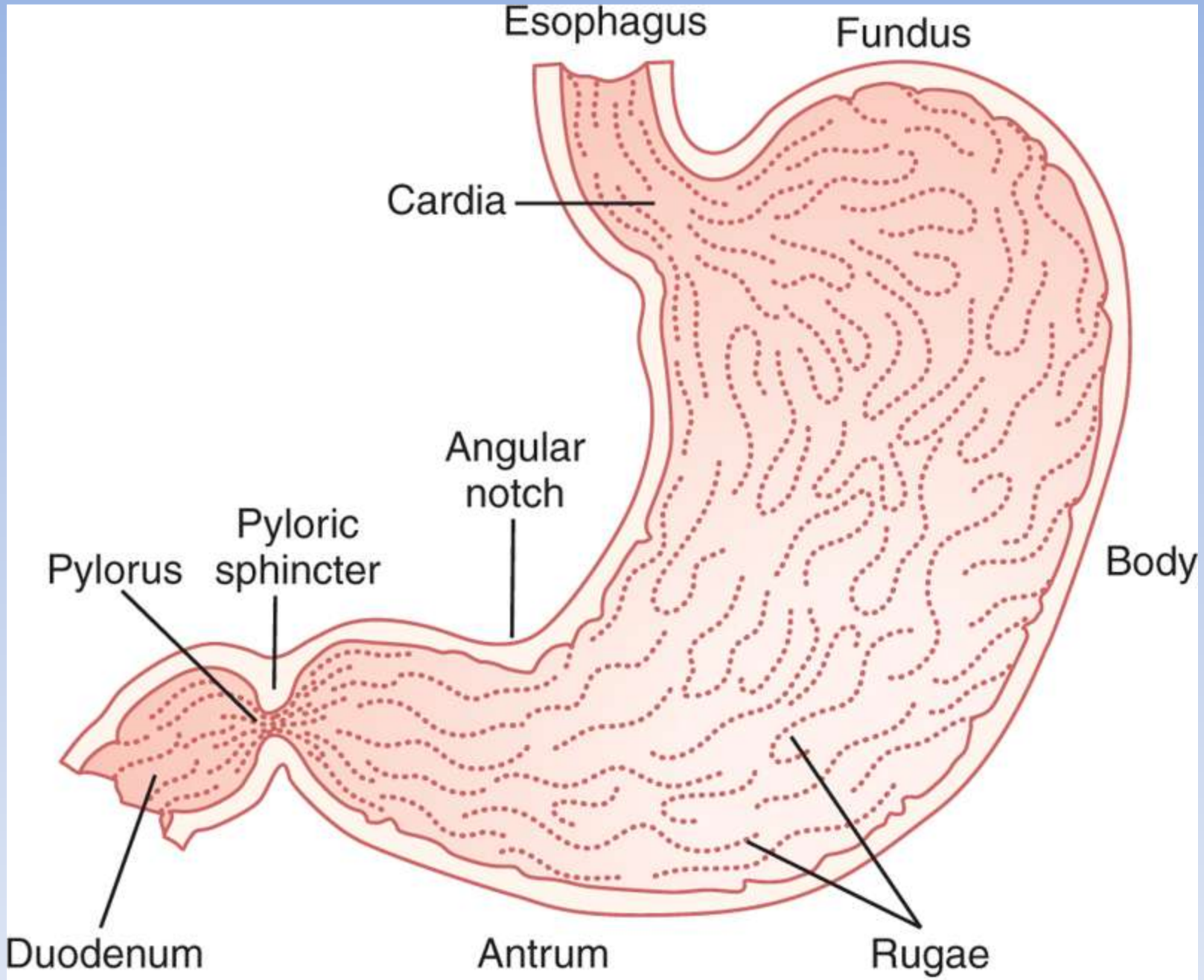
- Consisting of electrical slow wave that occur spontaneously in the stomach wall.
- The BER is a wave of depolarization of smooth muscle cells proceeding from circular muscle of the fundus of the stomach to the pylorus every 15-20 seconds.
- pacemaker for the mixing and peristaltic movement of the stomach.

MOVEMENTS IN THE STOMACH

1-MIXING movement: when the stomach is filled, weak constrictor waves ,at a rate of 3-4/min.

start near midpoint of the stomach and they progress from the body of the stomach to the antrum.

When they reach the antrum, they become more intense in order to mix the food.



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2-PROPULSIVE OR PERISTALTIC waves: strong peristaltic waves occur in the antrum with a rate of 3-4/min.

an extension of the mixing waves that have become more intense as they spread from the body of the stomach to the antrum.

They start at the incisura angularis and spread as strong peristaltic ring-like constriction through the antrum in the direction of the pylorus and duodenum.

They are about 6 times as powerful as the usual mixing waves. The peristaltic waves help in **propulsion and mixing of food.**

3-HUNGER contractions:

This is an intense contraction that occurs in the stomach when it has been empty for a long time.

rhythmic peristaltic contraction which are very strong and they may fuse together to cause a continuing ***TETANIC CONTRACTION*** lasting 2-3 minutes.

in young healthy persons with high degree of gastrointestinal tonus and usually after fasting for 12-24 hours, when the blood sugar is low.

The strong hunger contractions causes **pain** in the area of the stomach called **Hunger pangs** and it is relieved by ingestion of food.

Lecture Three: **Emptying of the Stomach & movements in Small and Large intestine**

Objectives:

Describe the role of the pylorus in stomach emptying.

Outline the factors affecting gastric emptying.

Explain the movements in the small intestine.

Outline the movements in the colon.

Describe defecation reflex.

EMPTYING OF THE STOMACH

- The emptying of the stomach is opposed by the resistance of the pylorus to the passage of food.

- It is promoted by peristaltic waves in the antrum of the stomach.

ROLE OF THE PYLORUS IN THE STOMACH EMPTYING:

- The pylorus is usually **tonically contracted**.
- This tonic contraction is weak enough so that water and fluid can empty with ease.
- While it is great enough to prevent movement of semisolid food (chyme) into the duodenum, **except** when strong antral peristaltic wave force the chyme through the pylorus.

- The degree of constriction of the pyloric sphincter can increase or decreases under the influence of signals from the stomach and duodenum.
- **Gastrin** and distension of the stomach by food by (**nervous** mechanism) will **inhibit** the pylorus.
- While signals from the duodenum depress the pyloric pump and **increase pyloric tone** by both ***nervous*** (***enterogastric)*** and ***hormonal*** (secretin-GIP-VIP-CCK-peptide YY….e.t.c).

ROLE OF ANTRAL PERISTALSIS IN THE STOMACH EMPTYING:

- Antral peristalsis sometimes become so intense and spread as strong peristaltic ring-like constriction.
- Each antral peristaltic wave forces several milliliters of chyme into the duodenum, thus peristaltic waves provides a pumping action that is frequently called **pyloric pump**.

FACTORS AFFECTING GASTRIC EMPTYING

The rate at which food leaves the stomach is determined by various factors:-

1. **Total volume of gastric contents.**
2. **Consistency.**
3. **Chemical composition.**
4. **Osmolar concentration.**
5. **PH.**

- **The total food volume** → the amount evaluated in a unit of time is related to the volume of the gastric contents. Stretch of the stomach wall elicits VAGAL and local MYENTERIC reflexes in the wall that increase the emptying.
- **Consistency:** liquid more than solids, inert liquids that do not stimulate the stomach chemically or osmotically leave the stomach rapidly such as water. Solids are not evacuated until they are reduced to a fluid or semi-fluid consistency.

- **Chemical composition:** CHO leave more rapidly followed by protein and lastly fat. Fat especially if eaten in large quantities remain in the stomach for a long time and in animal experiments up to 24 hours.
- **Osmolar concentration of the gastric contents** → saline in a physiological concentration leaves the stomach more rapidly than do salt solution of either greater or lesser concentrations.
- **Acid:** strong acid solution in the stomach leaves the stomach slowly and the rate of emptying of such solution can be accelerated by neutralizing the acid.

REGULATION OF GASTRIC MOTILITY AND EMPTYING

- **NERVOUS:**
  - **Local reflexes through myenteric plexus.**
  - **Vagal nerve.**
  - **Enterogastric reflex → inhibits activity.**
- **Hormonal:**
  - **Gastrin in the stomach and small intestine → increase emptying.**
  - **INTESTINAL: Enterogastrone, GIP, VIP, Secretin, CCK, Peptide YY…e.t.c.→ inhibit gastric motility and emptying.**

SMALL INTESTINE
Basic electrical rhythm (BER)

- They are initiated by pacemaker cells located in the outer circular muscle layer near the myenteric plexus. It is about 12/min., In the duodenum.
- Falls to about 8/min., In the distal ileum, thus enabling the proximal small bowel to override more distal areas.
- the myenteric plexus and the enteric hormones determine the local response to the slow wave so the contraction may or may not occur depending on the state of the affairs in the lumen at any one time.

MOVEMENTS IN THE SMALL INTESTINE

1- Mixing or segmentation contraction:

- They are ring-like contractions that occur throughout the length of the small intestine.
- appear at regular or irregular intervals. The length of each segment is about 1 cm.
- causes segmentation of the gut (a chain of sausage). As a set of contraction disappear, a new set appears in the segment

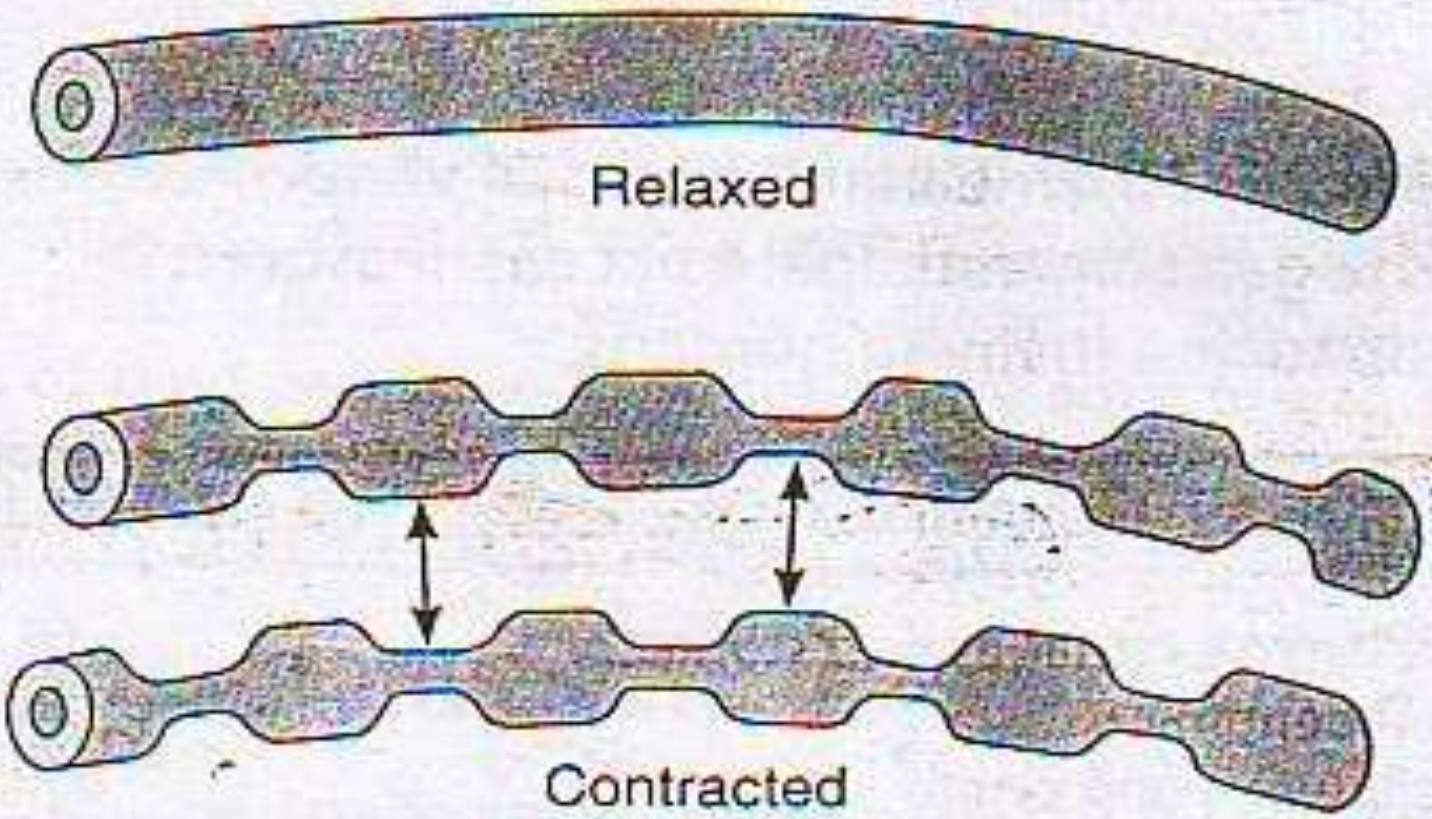


Figure 26–29. Diagram of segmentation contractions of the intestine. Arrows indicate how areas of relaxation become areas of constriction and vice versa.

2-Tonic contractions: are relatively prolonged contractions that in effect isolate one segment of the intestine from another. The segmentation contractions and the tonic contractions slow transit in the small intestine to the point that the transit time is actually longer in the *fed* than in the *fasted* state. This allows longer contact of the chyme with the enterocyte and enhances absorption.

3- Propulsive or peristaltic movement: these will propel the chyme through the small intestine, being faster in the proximal small intestine than in the distal small intestine.

4- Peristaltic rush: very strong peristaltic waves not seen normally but in intestinal obstruction or severe diarrhea.

5- Movements caused by muscularis mucosae and muscle fiber of the villi:

- Muscularis mucosae contract → making mucosal fold → increase absorption.
- Muscle fiber of the villi contract intermittently, thus the villi will shorten and elongate and shorten again.
- This will help in MILKING the villi so that lymph flow is increased from central lacteal to the lymphatic system.

Movements in the colon:

- The movements of the colon are coordinated by BER of the colon.
- The frequency of this wave, unlike the wave in the small intestine, increases along the colon from about 9/min. at the ileo-caecal valve to 16/min. at the sigmoid.

Types of movements of the colon:

- The motor activities in the colon are designed to either:

1. Mix colonic contents and facilitate absorption.

2. Propulsion.

1- Mixing movement → Haustration.

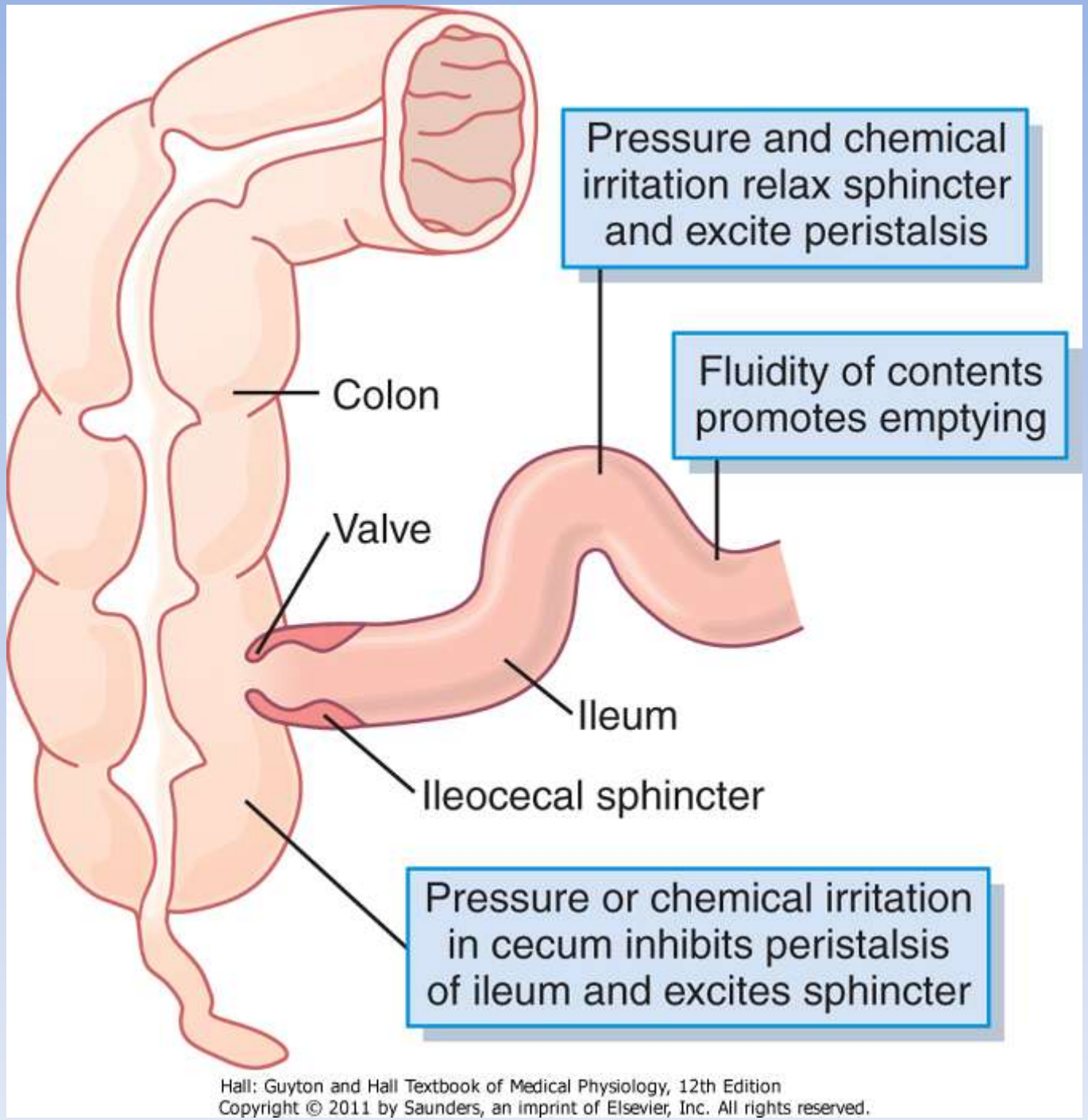
- It is similar to segmentation movement of the small intestine.
- Large circular constriction occurs in the large intestine. These circular constrictions are due to the contraction of circular muscles and also the longitudinal muscles.
- The longitudinal muscles in the colon are aggregated into three longitudinal strips called TAENIA COLI.
- The contraction of these longitudinal and circular muscles will result in that the ***unstimulated portion*** of the large intestine to **bulge outwards into bag-like sacs called Haustration**. The Haustral contraction mixes the colonic contents and exposes them to the mucosa.
- Thus it facilitates absorption by colonic mucosa of water and electrolyte.

2- **Peristaltic movement**: propel the contents towards the rectum.

3- **Mass peristalsis**: most of the peristalsis in the colon is the mass peristalsis. It **occurs only in the colon**. Mass peristalsis occurs only a few times every day and they occur **mostly after eating breakfast**. *The mass peristalsis occur when a point in the colon is distended or irritated, then this will cause a constrictive contraction around this point and simultaneously there will be contraction of 20 cm or more of the colon distally.* This will force the faecal contents in this colonic segment enmasse down the colon. The mass peristalsis can occur anywhere in the colon although they often occur in the transverse or descending colon. ***If mass peristalsis has forced a mass of faeces into rectum, then the desire for defaecation will be felt***.

However **not all mass peristalsis result in the desire to defaecate** because sometimes the movements of the colonic contents stops before emptying the colonic contents into the rectum.

Mass movements occur usually after meal and particularly after breakfast, drinking a glass of coffee, warm water, orange juice or lemon juice in the morning. This is at least due to **Gastro-colic** and **Duodeno-colic reflexes**.These reflexes occur when the stomach or duodenum is distended after eating or drinking. The mechanism behind these reflexes might be due to both **nervous** and **hormonal**. The nervous pathway might be through the autonomic nervous system. The hormonal mechanism might be due to release of the **hormone gastrin** from the antral mucosa in response to distension.



Defecation

The rectum is usually empty from faeces and the faecal masses are stored in the sigmoid colon and not in the rectum.
The desire to defecate occurs when the faeces enter the rectum as a result of mass peristalsis. An increase in the intra-luminal pressure of the rectum by 18 mmHg will usually cause the desire to defecate. The desire to empty the rectum is experienced if the rectum is filled with solid faeces, liquid or gas.
The receptors in the rectal wall are not only able to detect increase in pressure inside the rectum, but they can also differentiate whether the increase in pressure is due to faeces, liquid or gas. This discriminating ability of these receptors will be lost in patients with infectious diarrhea or proctitis due to ulcerative colitis or other inflammatory conditions.

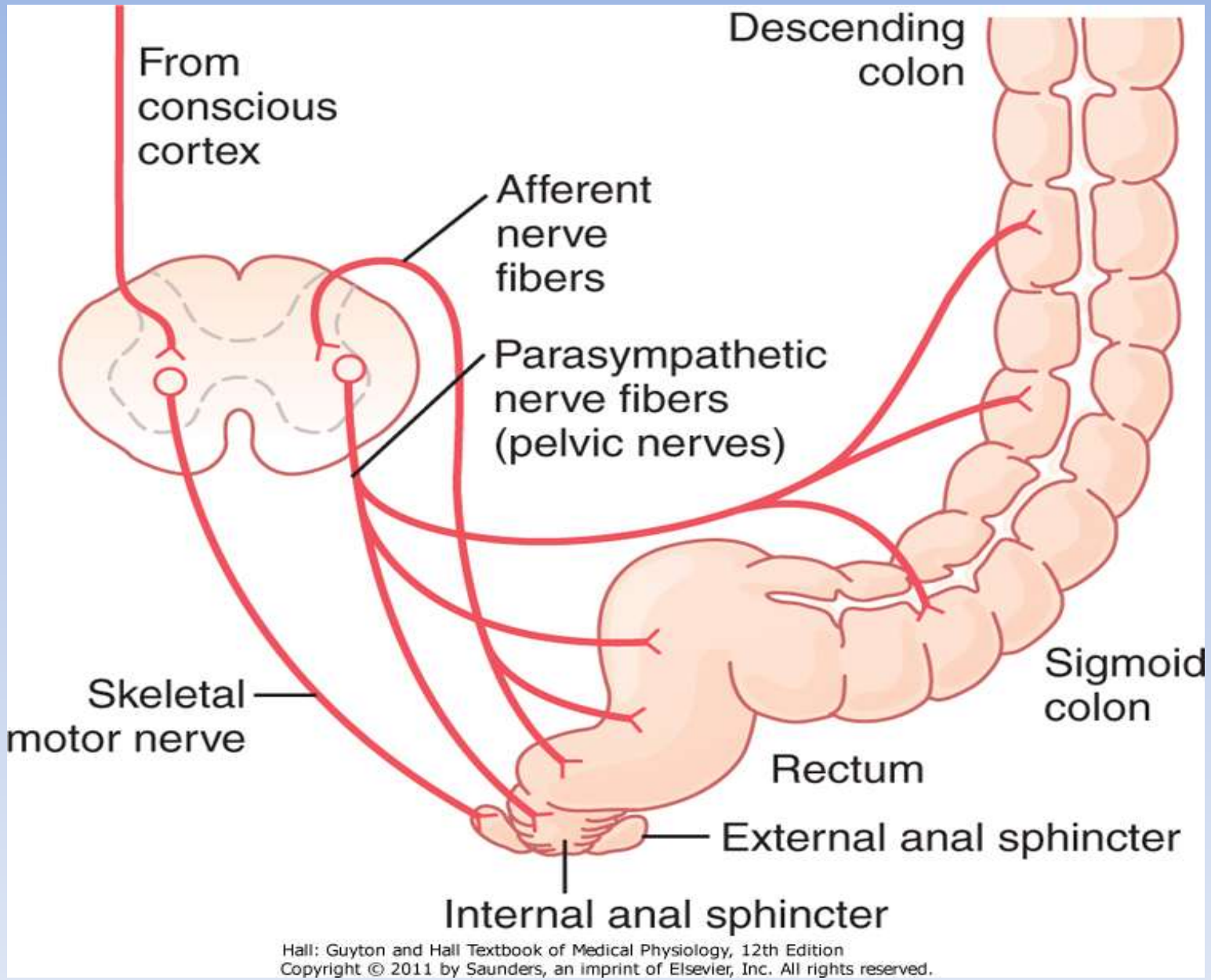
Defaecation will happen as a result of the defaecation reflexes:-

1-Intrinsic defaecation reflex: this occurs when afferent signals spreading to the myenteric plexus will cause peristaltic waves in the descending colon, sigmoid and rectum, and relaxation of the internal anal sphincter (which is a circular mass of smooth muscle lying immediately inside the anus) and if the external anal sphincter is relaxed then defaecation will occur. However this reflex is very weak and in order to be effective it must be supported by the second defaecation reflex →

2- Parasympathetic defaecation reflex: this occurs when afferent signals will pass to the sacral portion of the spinal cord and impulses will be sent back through **Nervi erigentes or pelvic nerve** to cause contraction of the descending colon, sigmoid and rectum and relaxation of internal anal sphincter. This parasympathetic reflex will greatly intensify the intrinsic reflex. However the defaecation reflexes will not produce defaecation unless the external anal sphincter is relaxed.

- External anal sphincter is composed of striated voluntary muscles and it is ***under voluntary control*** from the cerebral cortex through the somatic nerve which is the **pudendal nerve**. Contraction of this sphincter will counteract the defaecation reflex. Except in babies , in the normal adults the conscious mind will take the control of the external anal sphincter and will either cause relaxation of the external anal sphincter if the time is suitable, or will cause contraction of the external anal sphincter to prevent defaecation. Thus if the time is suitable then from cerebral cortex, efferent impulses will be sent through the pudendal nerve to cause relaxation of the external anal sphincter

- At the same time impulses from higher centers will facilitate defaecation by:
- Taking a deep breath
- Closure of the glottis
- Contraction of the abdominal muscles
- All these will increase the intra-abdominal pressure and force the faeces downward.
- If the time was not suitable, then the external anal sphincter will remain contracted and the reflex will die out after a short time and will ***not return until an additional amount of faeces enter the rectum.***



Lecture 4: Salivary secretions & Stomach secretions

Objectives:

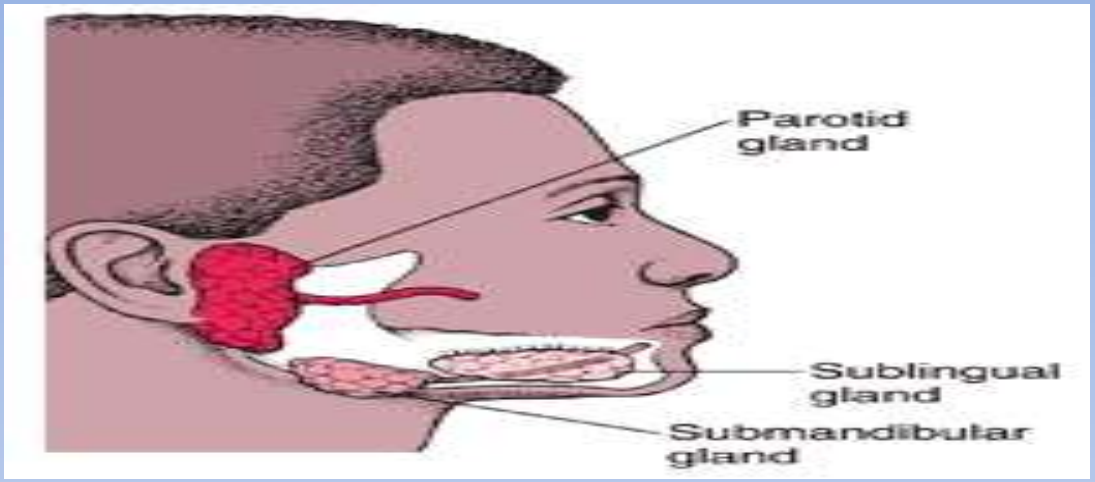
Describe the regulation of salivary secretion.

Explain the functions of saliva.

Outline the role of saliva in oral hygiene.

Analyze the functions of the Stomach.

Describe the composition of gastric juice



SALIVARY GLANDS:

There are 3 chief paired salivary glands these are:

Parotid.

Submandibular (submaxillary).

Sublingual.

In addition there are many small salivary glands scattered in the lining of the oral cavity and are named according to their position.

- **COMPOSITION OF SALIVA**
- The daily secretion of saliva is about 1-1.5 liter per day. A large proportion of this 24 hours volume is secreted at meal time. Ordinary mixed saliva contains:
- Water 99.5%.
- Solids 0.5%.

The solid materials are:

- Organic
- Inorganic

Organic constituents of saliva:

1- Protein mucin.

2- Ptyalin or α-amylase for the digestion of starch.

3- Lingual lipase It plays an important role in the hydrolysis of triglycerides. digest as much as 30% of dietary triglycerides

4- Urea, uric acid & creatinine.

5- Kallikrein which is an enzyme that acts on plasma protein to produce a very powerful vasodilator polypeptide called kinin.

6- Specific blood group antigen (ABO system).

7- Somatostatin, glucagon, renin and several growth factors.

8- Lysozyme which can destroy the bacteria by lysis.

9- Lactoferrin which binds to iron and deprive organisms of nutrient iron and it is bacteriostatic.

10- Proline-rich protein that protects tooth enamel and binds toxic tannins.

11- Immunoglobulin A which can destroy the bacteria including those that cause the dental caries.

Inorganic constituents of saliva:

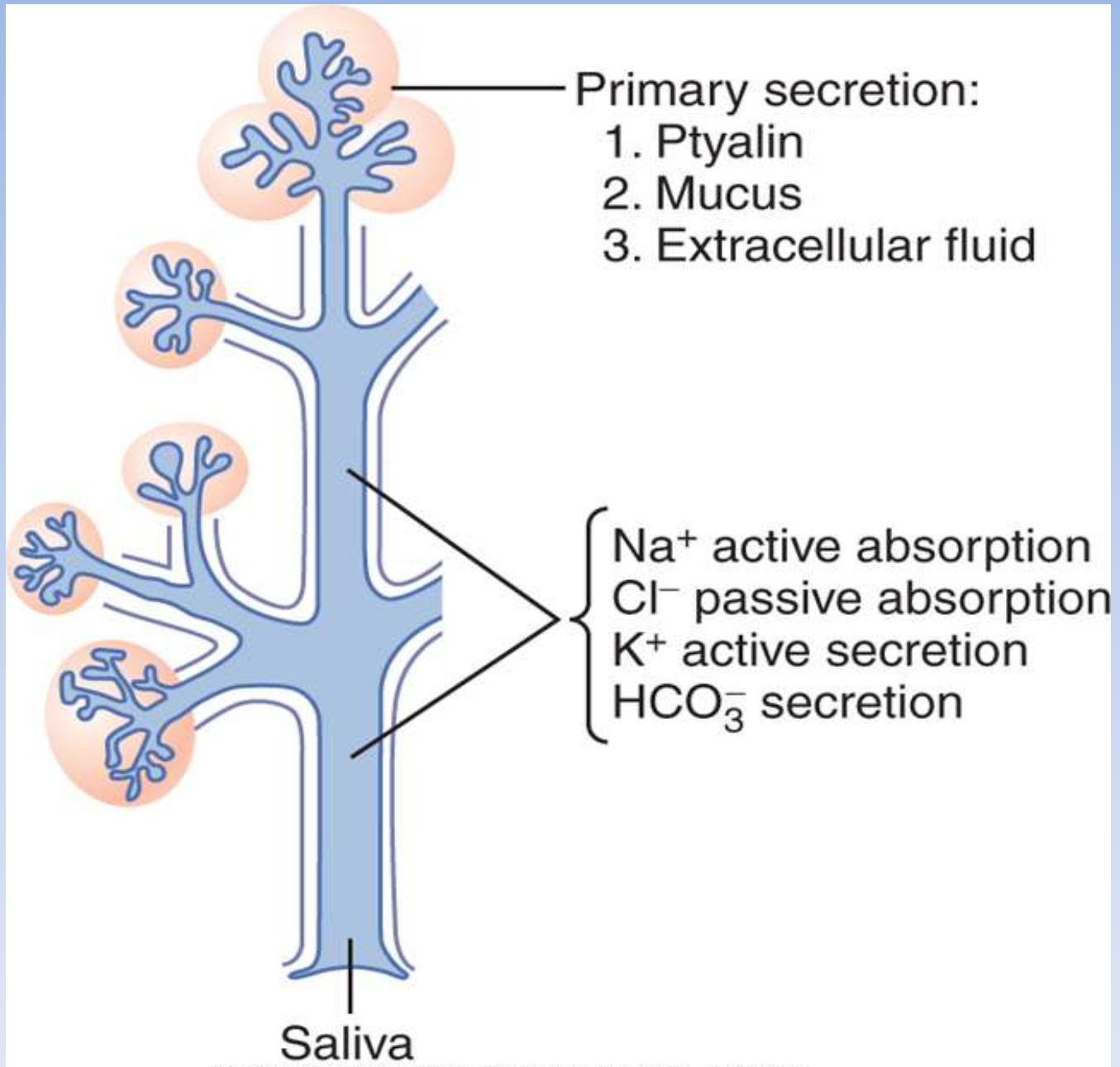
Saliva contains different ANIONS such as chloride, phosphate, bicarbonate, Floride and CATIONS such as calcium, sodium and potassium.

Floride is important to prevent dental caries, calcium salts might be the source of tartar deposits on the teeth.

The concentration of sodium and chloride in the saliva is less than that in the plasma, while potassium concentration in the saliva is higher than that in the plasma.

The absorption of sodium and chloride occurs at a faster rate than the secretion of the potassium thus saliva becomes **hypotonic**.

The PH of the saliva is between (6-7.4).



Regulation of salivary secretion

Salivary secretion is brought about reflexly:

1-Unconditioned salivary reflex due to ***stimulation of the nerves within the mouth*** such as by the presence of food or other substances.Material such as **acid** will cause profuse salivary secretion because it stimulates the taste buds, this stimulus is **chemical** in nature e.g. stimulation of salivary secretion by lemon or sweets.Material such as **dry sand or powder** with no taste will stimulate secretion by acting as a **physical** stimulus.

2-Conditioned reflex the stimulus is received by one or other of the organs of special senses other than that of taste particularly those of ***sight, smell, hearing***, or even ***thought*** of palatable food. The conditioned reflex requires previous training and experience e.g. Pavlov experiment on dogs.

3- In abnormal situations, salivation can occur in response to ***reflexes originating from the esophagus, stomach and the small intestine*** by stimulation of ***the vagal afferent fibers***. Thus when a person eats *a very irritating food* or is *nauseated* there will be an increase salivation which might act as a neutralizing or diluting agent for the irritating substance

FUNCTIONS OF SALIVA

Saliva helps to:

1- moisten, lubricate and soften food, mixes it up and makes it possible to be swallowed.

2-It keeps the mouth wet and facilitates speech.

3-important for the taste sensation because it acts as a solvent. Taste is chemically mediated and therefore any substance must be dissolved in order to stimulate the taste buds.

4-Saliva contains 3 buffering systems and these are bicarbonate, phosphonate, and mucin. The bicarbonate is the most important. These buffers in saliva help in maintaining the oral PH around 7 so that the teeth do not lose calcium to the oral fluid.

5-Saliva has a digestive function through its enzyme ptyalin and lingual lipase.

6-Oral hygiene this is one of the very important functions of the saliva. The ***flow of saliva*** plays a very important role in maintaining healthy oral tissues. The mouth is loaded with many harmful bacteria that can cause tissue damage or dental caries. Salivary secretion helps in preventing these harmful effects by several ways:

Mechanical: the flow of saliva will wash away the pathogenic bacteria and also the remaining food particles and debris that can act as a metabolic support for the bacteria.

Thiocyanate ions which can act as bactericidal.

Lysozyme.

Lactoferrin.

Proline-rich proteins.

Immunoglobulin A.

Disturbance of salivary secretion:

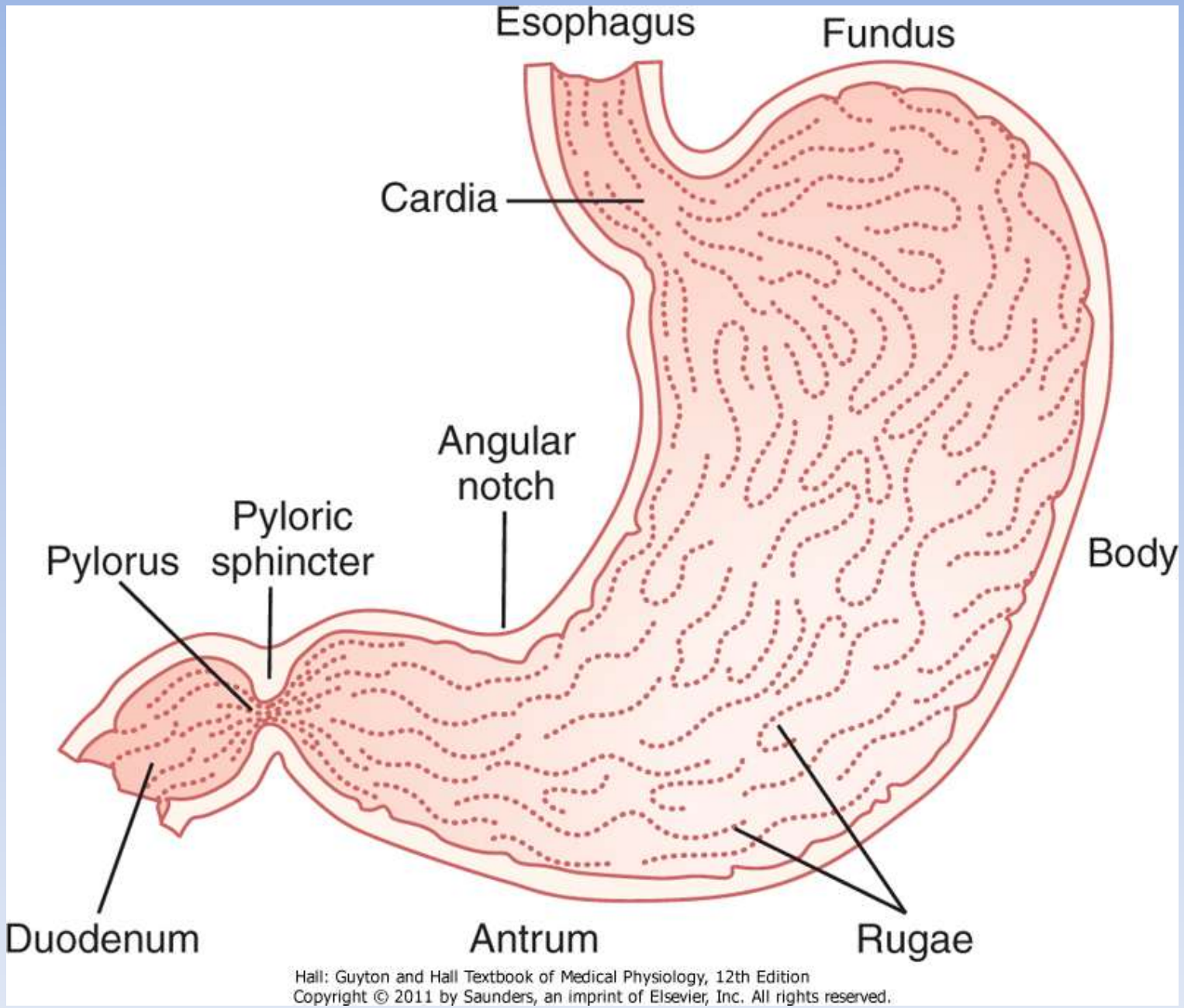
Deficiency of salivary secretion ***(xerostomia)*** can occur after

- Emotional state such as fear or anxiety.
- Dehydration.
- Fever.
- Anticholinergic drugs.

Hyper salivation (sialorhoea) occurs during***:***

- Pregnancy.
- Tumours of the mouth or tongue or even a carious tooth (reflex stimulation of salivary secretion due to local irritation).
- Diseases of the esophagus, stomach, pancreas such as tumor of the esophagus or spasm, gastric or duodenal ulcer, pancreatitis, (esophago-salivary reflex).

- **Esophageal secretion:**
- Mucus only, in the upper esophagus to prevent excoriation and in the lower esophagus to protect from acid



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FUNCTIONS OF THE STOMACH

1. As a reservoir to store the food, we can eat food faster than we can digest.

2. Mechanical degradation and liquification of the food, the stomach mixes the food with gastric secretion until it forms a semi-fluid mixture called **chyme.**

3. Small role as a digestive function by hydrochloric acid and pepsin. Hydrochloric acid cause hydrolysis of food and also activates pepsinogen into pepsin and pepsin begins protein digestion.

4. Antibacterial action, the high acidity of the gastric juice will render the gastric juice sterile.

5. Absorption, no nutritionally important absorption occurs in the stomach, only alcohol, some water and lipid soluble drugs are absorbed across the stomach mucosa.

6. Haemopoiesis, the secretion of intrinsic factor in the body of the stomach is necessary for the normal absorption of vitamin B12 in ileum.

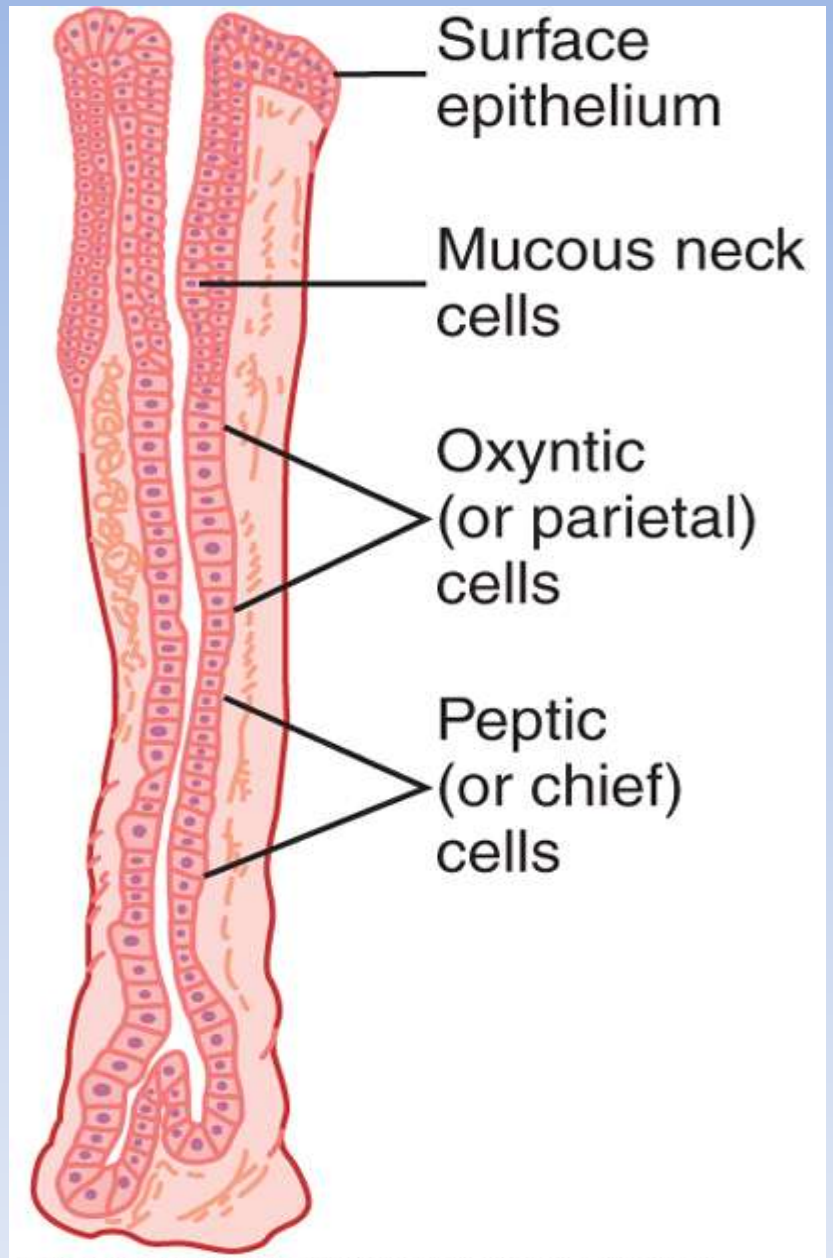
Glands of the Stomach

– Mucus neck cells: these cells secret mainly mucus with some pepsinogen.

- They divide and the new cells which migrate both to the surface to become mucus cells or down into the gland to become parietal cells. Peptic cells are capable of mitosis but they may also come from mucus neck cells.

– Peptic or chief cells: these cells secrets pepsinogen.

– Parietal or oxyntic cells: these cells secrete hydrochloric acid and also the intrinsic factor.



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COMPOSITION OF GASTRIC JUICE

Daily secretion 2-3 liters, the PH is about 0.9-1.0.

Gastric juice consists of water and different organic and inorganic constituents:

1. **Electrolytes like sodium, potassium, magnesium, calcium, chloride, phosphate, sulphate and bicarbonate.**
2. **HCL.**
3. **Mucus.**
4. **Pepsins.**
5. **Lipase.**
6. **Gelatinase.**
7. **Intrinsic factor**

Lecture Five: Gastric juice

Objectives:

Outline the HCL secretion.

Describe the functions of HCL.

Explain the mucus secretion,pepsin,prostaglandins.

Describe the regulation of gastric secretion.

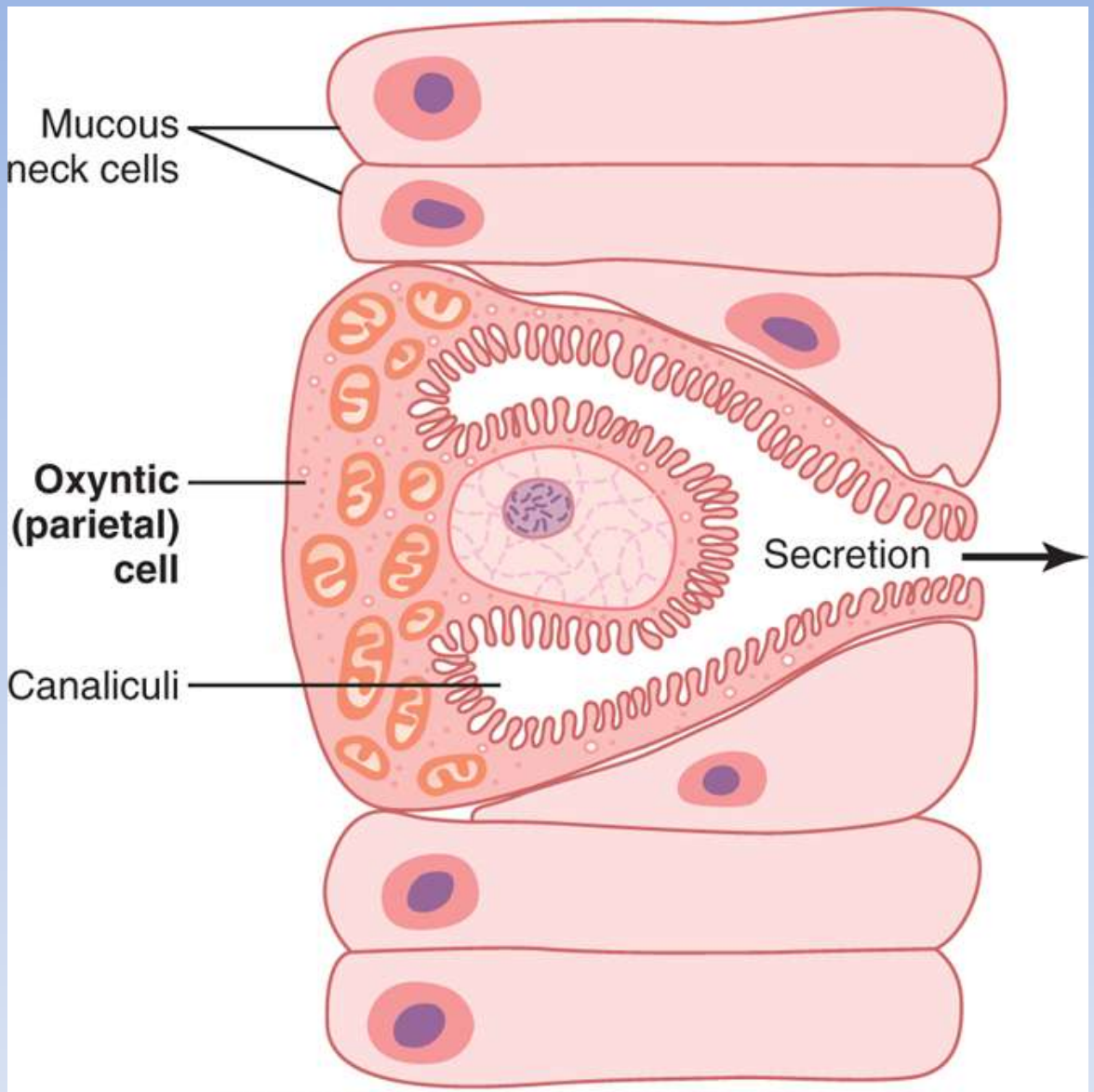
Explain the role of Histamine in acid secretion.

HYDROCHLORIC ACID SECRETION

HCL is secreted by the parietal or oxyntic cells which are found in the main gastric gland or oxyntic gland, the PH of acid solution is about 0.9 and thus it is extremely acidic. To reduce the PH to this level the hydrogen ion concentration of this solution is about 3 million times that of the arterial blood.

Plasma	***Juice***
0.00004 mEq/liter.	***150 mEq/liter.***

To concentrate the hydrogen ion to this tremendous amount, *a great amount of energy is needed*. The hydrochloric acid formed and released by the parietal cells is not formed inside the protoplasm of the cells but it is formed in the intracellular canaliculi that are small channels that communicate with the lumens of the gastric gland. If the parietal cells are stained with certain indicator dyes, the inside of the cells like that of the other body cells has a PH 7-7.2 while the canaliculi has an extremely acid reaction. HCL is formed at the membrane of these canaliculi and then conducted through openings to the outside.



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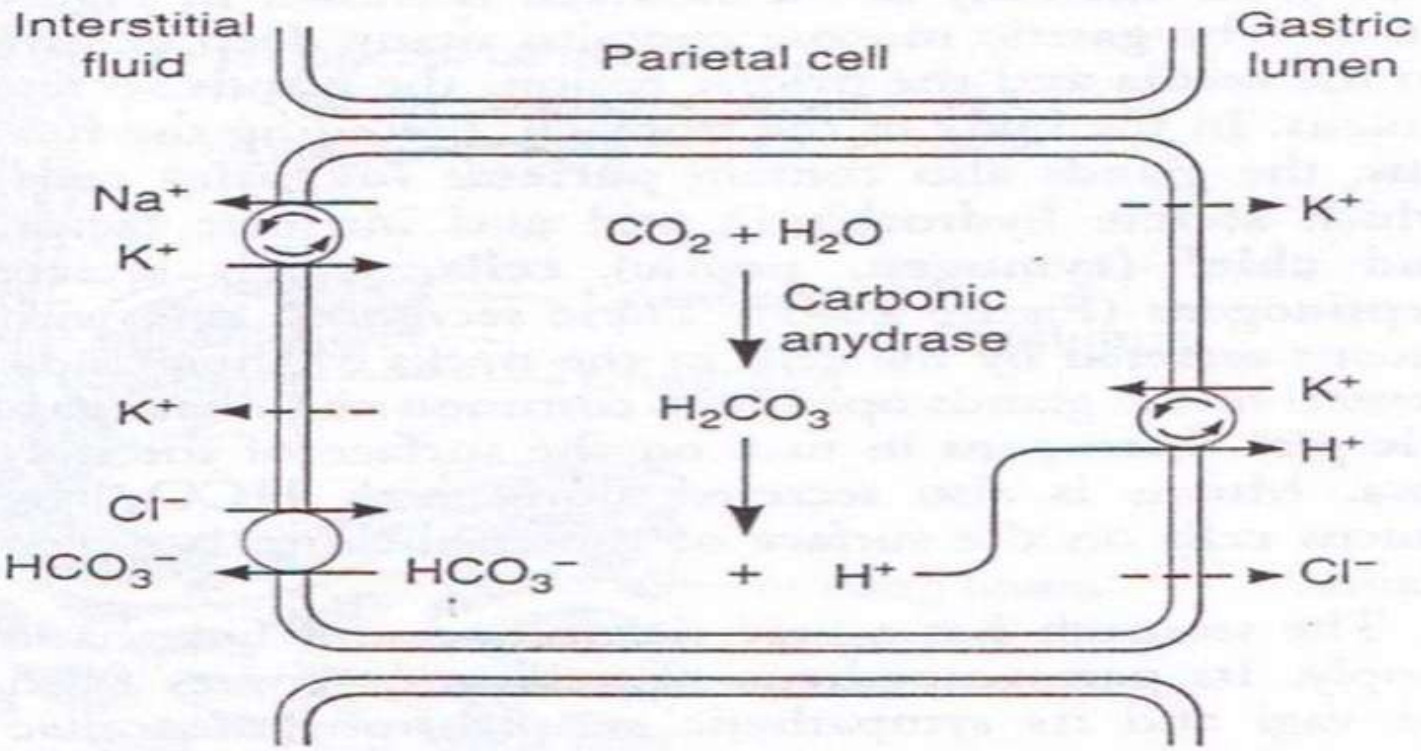


Figure 26–10. HCl secretion by parietal cells in the stomach. Active transport by ATPase is indicated by arrows in circles. H^+ is secreted into the gastric lumen in exchange for K^+ by H^+–K^+ ATPase. HC_3^- is exchanged for Cl^- in the interstitial fluid by an antiport, and Na^+–K^+ ATPase keeps intracellular Na^+ low. Dashed arrows indicate diffusion. Compare with Figure 38–19.

The hydrogen ion (H^+) comes from H2CO3 and by the hydration of CO2.

This reaction is catalyzed by carbonic anhydrase and the parietal cells are particularly rich in this enzyme.

H^+ is pumped out of the parietal cells in exchange for potassium and this is carried out by the **enzyme H^+-K^+ ATPase** .

Omeprazol inhibits H^+-K^+ ATPase and thus inhibit acid secretion and is very effective in the treatment of peptic ulcer.

The bicarbonate $HCO3^-$ formed by the dissociation of H2CO3 is extruded into the interstitial fluid in exchange for Cl^-.

When gastric acid secretion is elevated after a meal (which stimulates acid secretion) sufficient H^+ may be secreted to raise the PH of the systemic blood and make the urine alkaline.

Water moves passively from cell to juice and the gastric juice is isotonic with plasma.

Other suggested mechanism for the formation of HCL is that H^+ comes from the dissociation of water into H^+ and OH^-. And that Cl^- is actively secreted into the lumen of the canaliculus.

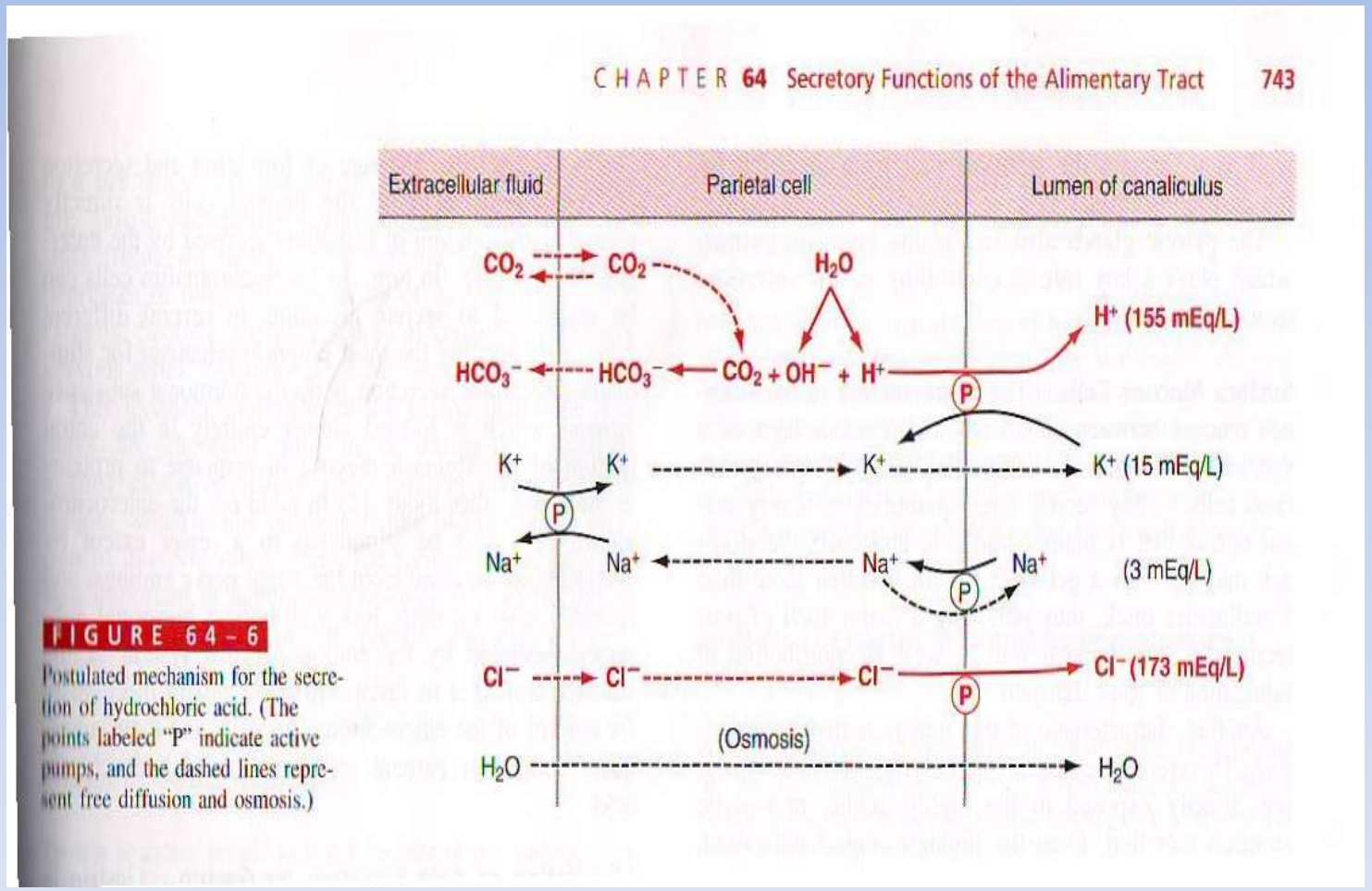


FIGURE 64-6

Postulated mechanism for the secretion of hydrochloric acid. (The points labeled "P" indicate active pumps, and the dashed lines represent free diffusion and osmosis.)

FUNCTIONS OF HYDROCHLORIC ACID

The main functions of HCL are:

1- It causes ***activation of pepsinogen into pepsin***. Pepsin is an active proteolytic enzyme in a high acid medium (PH-2) but above a PH of 5, pepsin has little proteolytic activity and soon becomes completely inactivated.

2- This acidity has some ***antibacterial*** or ***antiseptic*** action against some virulent organisms. The gastric acid will damage these bacteria before they reach the small intestine, thus in normal healthy individuals the duodenal contents are relatively sterile.

3- Reduce iron from ferric to ferrous state.

MUCUS SECRETION BY THE STOMACH

Two types of gastric mucus are secreted by the stomach:

1. **Soluble mucus**

this is secreted by the cells of the pyloric and cardiac gland and also by mucus neck cells of the main gastric gland. These cells secrete large quantities of thin mucus which is soluble and ***helps in protecting the stomach wall from damage by peptic digestion.***

2. **Visible mucus**

this is secreted by the surface epithelial cells of the gastric mucosa and its more alkaline, thick, viscid and even jelly-like. It forms a thick coat (2-3 mm thick) that covers the surface of the gastric mucosa. This mucus will act as an important factor of protection for the stomach wall. The mucus secretion from the surface epithelium is stimulated by various chemical and tactile stimuli. Mucus secreted by neck cells and surface mucus cells in the body and fundus of the stomach and similar cells form a **FLEXIBLE GEL** that coats the mucosa.

The surface mucosal cells also secrete **$HCO3^-$.** The $HCO3^-$ and the mucus form an **UNSTIRRED LAYER** that has a PH around 7.

The unstirred layer plus the surface membrane of the mucosal cells and the **tight junctions** between them constitute the **MUCOSAL BICARBONATE BARRIER** that protects the mucosal surface from damage by gastric acid.

PROSTAGLANDINS:

Act as cyto-protector to gastric mucosa by:-

1. Stimulate mucus production.
2. Increase bicarbonate secretion.
3. Inhibit acid accumulation.
4. Increase mucosal blood flow.

Misoprostol is a prostaglandin analogue is effective in the treatment of duodenal ulcer it has both acid inhibitory and cyto-protective properties. Especially when used in patients with arthritis and duodenal ulcer (DU).

Substances that tend to disrupt the barrier (mucosal bicarbonate barrier) and cause irritation include:

H-pylori (helicobacter pylori) – Aspirin – NSAID'S (non-steroidal anti inflammatory drugs) – ethanol – vinegar – bile salts.

NSAID'S inhibit prostaglandin, the older types are non specific inhibitors of both cyclooxygenase 1 (COX1) which is involved in the production of prostaglandins in the normal GI and cyclooxygenase 2 (COX2) which induce prostaglandin production at inflammatory site. So COX2 specific inhibitor like rofecoxib is used in treating arthritis.

PEPSIN:

secreted as pepsinogen and activated by HCL. Also pepsin itself can activate pepsinogen into pepsin → autocatalytic positive feedback process.

Optimum PH for pepsin is 2, At PH 5 it will be blocked.

Group I pepsinogen: only present in acid secreting region i.e. secreted by peptic and mucus neck cells of the oxyntic gland.

Group II pepsinogen: from pyloric, Brunner's and oxyntic gland.

Maximal acid secretion correlates with pepsinogen I level. Patients with congenitally elevated circulating pepsinogenI levels have a 5 folds greater incidence of peptic ulcer than normal levels.

Gastric lipase: weak lipolytic enzyme acts mainly on butter fat.

Gelatinase: liquefies the protein gelatin.
Intrinsic factor: secreted by the parietal cells, it's a glycoprotein that combines firmly with vitamin B12→protect vitamin B12 from digestion and also this complex will become bound to specific receptors in the ileum and from there vitamin b12 is absorbed by endocytosis.
Trypsin is required for the process of absorption to be efficient and absorption might be decreased in patients with pancreatic insufficiency.
If the acid producing cells of the stomach are destroyed such as after chronic gastritis then the person will develop achlorhydia and also pernicious anaemia due to the failure of maturation of rbcRBC in the absence of vitamin b12 stimulation of the bone marrow.

REGULATION OF GASTRIC SECRETION

The regulation of the gastric secretion is by both nervous and hormonal mechanisms. Thus it is different from that of salivary secretion which is controlled by nervous mechanism only. Gastric secretion associated with a meal can be divided into 3 phases:-

Cephalic phase.

Gastric phase.

Intestinal phase.

1**) Cephalic phase:** also called nervous or appetite phase. Gastric secretion can occur even before the food reaches the stomach and it is controlled by the vagus nerve. It can be divided into to 2 types:

A-unconditioned reflex: the secretion results from the taste of the food. The presence of food in the mouth will stimulate gastric secretion after five minutes and the secretion may persist for half to two hours. The sham feeding technique by Pavlov proves the mechanism of production of appetite juice.

B-conditioned reflex: the cephalic phase of gastric secretion can be brought about not only by the taste of the food but also by the sight, smell or thought of food that's to say by conditioned reflex.

The neural pathway for the cephalic phase is through the vagus and can be abolished by: -Atropine.
-Vagatomy (cutting the vagi).

Gastric secretion in response to this vagal stimulation is ***highly acidic and high in pepsin***. Cephalic phase accounts for 1/3 to ½ of total gastric acid secretion associated with a meal.

Emotional states: anger and hostility is associated with hyper secretion of the gastric mucosa. This is mediated principally by the vagi. Fear and depression decrease gastric secretion

2) Gastric phase: presence of food in the stomach stimulates gastric secretion by both A-Nervous. B-Hormonal.

A-Nervous:

1-Local reflexes in the intrinsic nerve plexus of the stomach (chemoreceptor and stretch).

2-Vagovagal reflexes that passes from the stomach to the brainstem and back to the stomach.

B-Hormonal: →Gastrin

Gastrin is produced by G-cells in the antrum. A second type of gastrin producing cells the TG-cells found throughout the stomach and small intestine. The G-cells are flask shaped and have a small apex which contains micro villi which is in contact with the lumen. This apical portion may serve some type of receptor function.

The presence of food in the stomach causes the release of gastrin by:**1-distention**→the bulk of food distends the pyloric antrum and this causes the release of gastrin

2-certain substances such as peptides and amino acids (meat extract-partially digested proteins).

3-however gastrin is also released in **response to vagal stimulation** which release gastrin-releasing peptide (GRP) or Bombesin to produce gastrin.

Vagal nerve stimulation will inhibit somatostatin which inhibits the G-cells. Thus the nervous and humeral stimulation of gastric secretion interact and are not merely additive but are markedly synergistic.

Gastrin stimulates gastric juice highly acidic but it does not contain high peptic activity.

The gastric phase of secretion accounts for ½ -2/3 of total gastric acid secretion associated with a meal.

ROLE OF HISTAMINE IN ACID SECRETION

Histamine is a powerful stimulant of acid secretion.
There are 3 receptors for histamine H1 – H2 – H3

H2-receptors mediate the stimulatory effect of histamine on acid secretion. So H2-receptors antagonist such as cimitidine – ranitidine – famotidine – e.t.c. are very useful drugs in the treatment of peptic ulcer.

histamine facilitate the action of gastrin and acetylcholine. It is believed that the stimulatory effect of gastrin on acid secretion is mediated by the release of histamine which in turn stimulates the oxyntic cells to produce acid secretion.

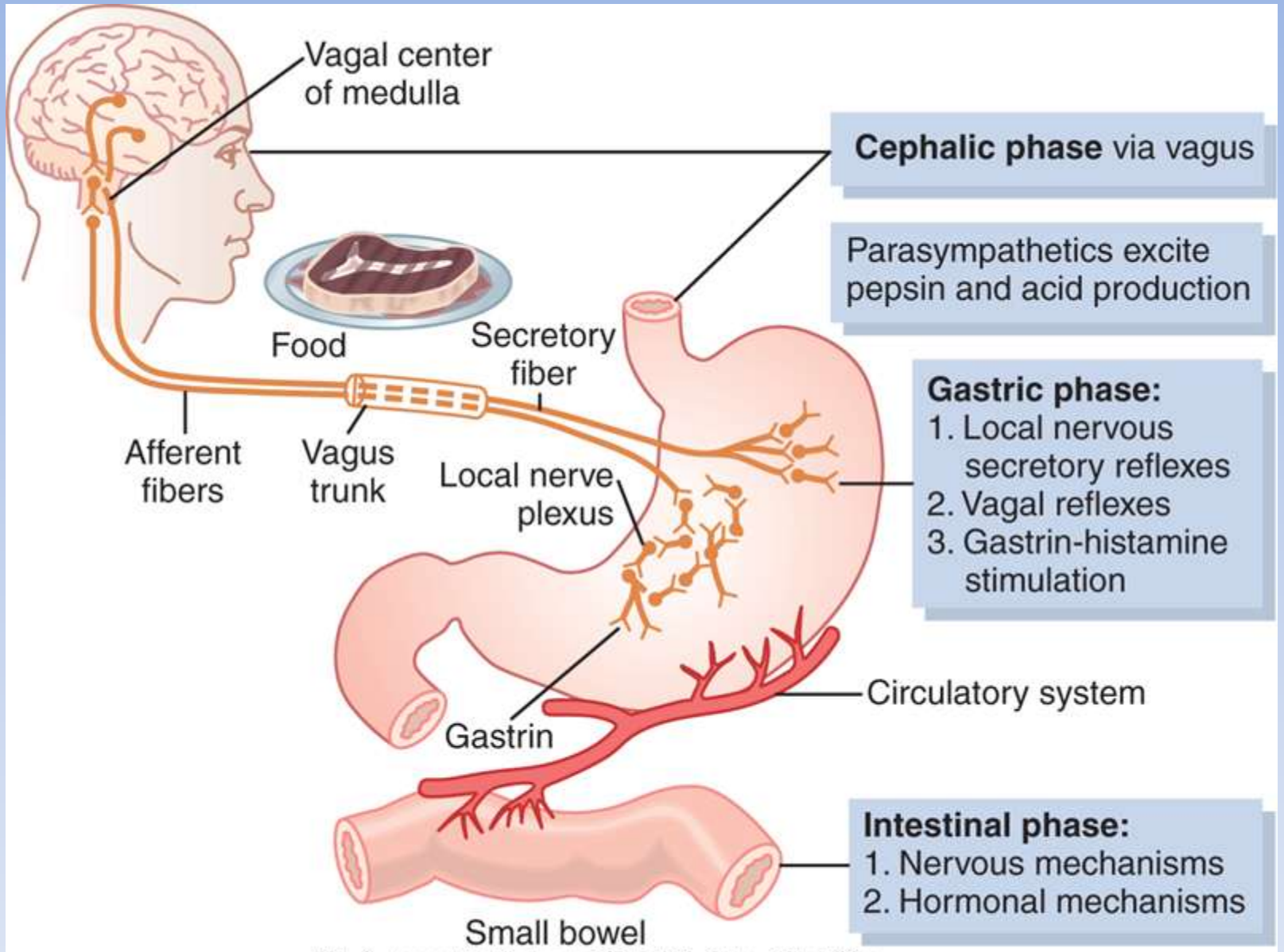
Feedback inhibition of gastric acid secretion by antral factors:

If the PH in the antrum falls to 1.5 or 2 (highly acidic) then there will be inhibition of the gastrin mechanism and thus there will be inhibition of acid secretion induced by gastrin. This will protect the stomach against very high acid secretion. When the PH rises gastrin will be secreted again.

3-Intestinal phase:

Certain food in the small intestine will cause small release of enteric or intestinal gastrin from duodenal mucosa which will cause small increase in acid secretion. The intestinal phase accounts for the least of the total acid gastric secretion.

Inhibition of gastric secretion by intestinal factors: gastric secretion can be inhibited also by certain substances in the upper small intestine for e.g. **1-Acid. 2-Fat. 3-Hyper/Hypo-osmotic fluids. 4-Any irritating substance in the upper small intestine.**



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- **The inhibition of gastric secretion can be brought about in 2 ways:**

- **Enterogastric reflex:** reflex nervous signals are transmitted from the duodenum back to the stomach to cause inhibition of gastric secretion and gastric emptying. This reflex is stimulated by many factors for e.g. acid in the duodenum will stimulate this reflex. If the PH in the duodenum falls to 3.5 or 4 this will stimulate this reflex to inhibit gastric secretion and thus protects the duodenal mucosa from high acidity.

- **Inhibitory hormones**: the presence of acids, fat, hypo/hyper osmotic fluids, e.t.c. causes the release of several intestinal hormones that are:

-Secretin.

-Gastric inhibitory peptide (GIP).

-Vasoactive intestinal polypeptide (VIP).

-Somatostatin.

-Peptide YY

Enterogastrone: refers to the inhibitory hormones that inhibit gastric acid secretion. Peptide YY is a good candidate to be Enterogastrone. Fat causes its release from the jejunum and it is an effective inhibitor of gastrin-stimulated acid secretion.

Gastric secretion is increased following the removal of a large part of the small intestine, due to the removal of the source of these inhibitory hormones.

The purpose of inhibition of gastric secretion and emptying is to slow the release of chyme from the stomach to the small intestine when the small intestine is already filled.

Secretion of the stomach during the interdigestive period

The stomach secrets only a few milliliters of gastric juice per hour during the interdigestive phase when little or no digestion is occurring anywhere in the gut. The secretion is usually of the non-oxyntic type i.e. **composed mainly of mucus, little pepsin and almost no acid and sometimes it is usually slightly alkaline with sodium bicarbonate**. During emotional stress there will be an increase of the interdigestive secretion up to 50 ml. or more per hour like that of the cephalic phase. So emotional stimuli is believed to be one of the factors for the development of peptic ulcer.

Lecture six: Pancreas, Biliary,Small and Large intestinal secretions

Objectives:

Describe the regulation of pancreatic secretion.

Outline the phases of pancreatic secretion.

Explain the importance of secretin mechanism and CCK.

Describe biliary secretions and its regulation.

Describe the Small and Large intestinal secretions.

Pancreas

- **Another part of the GI that is present outside the GI but connected to it by a duct. The pancreas has two components**

- **Endocrine: produces hormones such as insulin, glucagon.**

- **Exocrine: produces several digestive enzymes that help in the digestion of protein, fat and carbohydrates (CHO). The enzymes are secreted by the acini of the pancreas.**

- **In addition the epithelial cells lining the ducts will secret an electrolyte solution that contains large amounts of water and bicarbonate ions which is important in neutralizing the acid chyme emptied by the stomach, into the small intestine.**

Composition of the pancreatic juice:

The volume is 1-1.5 liter per day. PH is 8

It contains water and different electrolyte - CATIONS (Na^{+}, K^{+}, Ca^{++}, Mg^{++})

- ANIONS ($HCO3^{-}$, Cl^{-}, $SO4^{=}$, $HPO4^{=}$)

The organic constituents: different digestive enzymes for the digestion of protein, fat and CHO.

Protein digesting enzymes:

1. **Trypsin.**
2. **Chymotrypsin.**
3. **Elastase.**
4. **Carboxypeptidase.**

These enzymes will become activated only after they are secreted into the intestinal tract and not while they are present in the pancreas.

Enzymes for the digestion of carbohydrates:

1. **α-amylase:** the pancreas secrets an α-amylase similar to that of salivary secretion. It splits starches and glycogen into disaccharides such as maltose and isomaltose.

Fat splitting enzymes:

1. **Lipase.**
2. **Bile salts-activated lipase:**
3. **Procolipase (colipase):** it is secreted from the pancreas as procolipse (inactive form) and activated into active form by trypsin.
4. **Cholesterol ester hydrolase.**
5. **Phospholipase A2** secreted as inactive form (prophospholipase A2) and activated by trypsin into phospholipase A2
6. **Trypsin inhibitor:** This substance is secreted by the same cells that secrete the proteolytic enzymes and at the same time. It surrounds the enzyme granules and prevents its activation both inside the acini or the ducts of the pancreas. In the small intestine it will be diluted and loss its effect.

REGULATION OF PANCREATIC SECRETION

- **Nervous by the vagus and other cholinergic nerves in the enteric nervous system.**
- **Hormonal:**

  a- Cholecystokinin-pancreozymin CCK.

  b- Secretin.

PHASES OF PANCREATIC SECRETION

- **Cephalic and Gastric phase.**
- The same nervous signals that cause the secretion in the stomach also cause acetylcholine release by the vagal nerve endings in the pancreas. It will cause moderate amount of enzymes to be secreted into the pancreatic acini and ducts, so the pancreatic juice secreted is **rich in enzymes** and **poor in water and bicarbonate.**
- As the amount of water secreted is little then the pancreatic secretion to the intestine is small because there is no fluid medium to transport the enzymes to the intestine. So most of the enzymes are temporarily stored in the pancreas itself. This phase accounts for 20% of the total secretion of pancreatic enzymes after a meal.

Intestinal phase

- After the chyme enters the small intestine, it will cause copious secretion mainly in **response to secretin**. Also **CCK** causes more increase in the secretion of enzymes.
- **SECRETIN:** Secretin is present in the mucosa of the upper small intestine and it's secreted when chyme enters the intestine. The most important factor in chyme that causes the release of secretin is:
- ACID→ hydrochloric acid → causes release of secretin → absorbed by blood → to the pancreas.
- Secretin causes copious secretion of pancreatic juice that contains little enzymes and chloride ions. Secretin acts on the epithelial cells lining of the small ducts and not on the acinar cells (that secrete the enzymes) and the duct cells will secrete water and bicarbonate ions thus the ***response of the pancreas to secretin is a watery, alkaline juice poor in enzymes and chloride.***

Importance of the secretin mechanism

1-Secretin is released in large quantities from the mucosa of the small intestine whenever the PH of the duodenal contents falls below 4.5-5. This will cause the secretion of large amounts of watery-alkaline pancreatic juice which will neutralize the acid in the duodenum.

HCL + NaHCO3→ NaCl + H2CO3.The carbonic acid will then dissociate into CO2 + H2O and CO2 will be absorbed by blood and expired through the lungs leaving a neutral solution of NaCl in the duodenum. Thus:

a-Excessive acidity is neutralized.

b-Peptic activity of gastric juice is stopped.

This is a protective mechanism against the development of peptic ulcer in the duodenum.

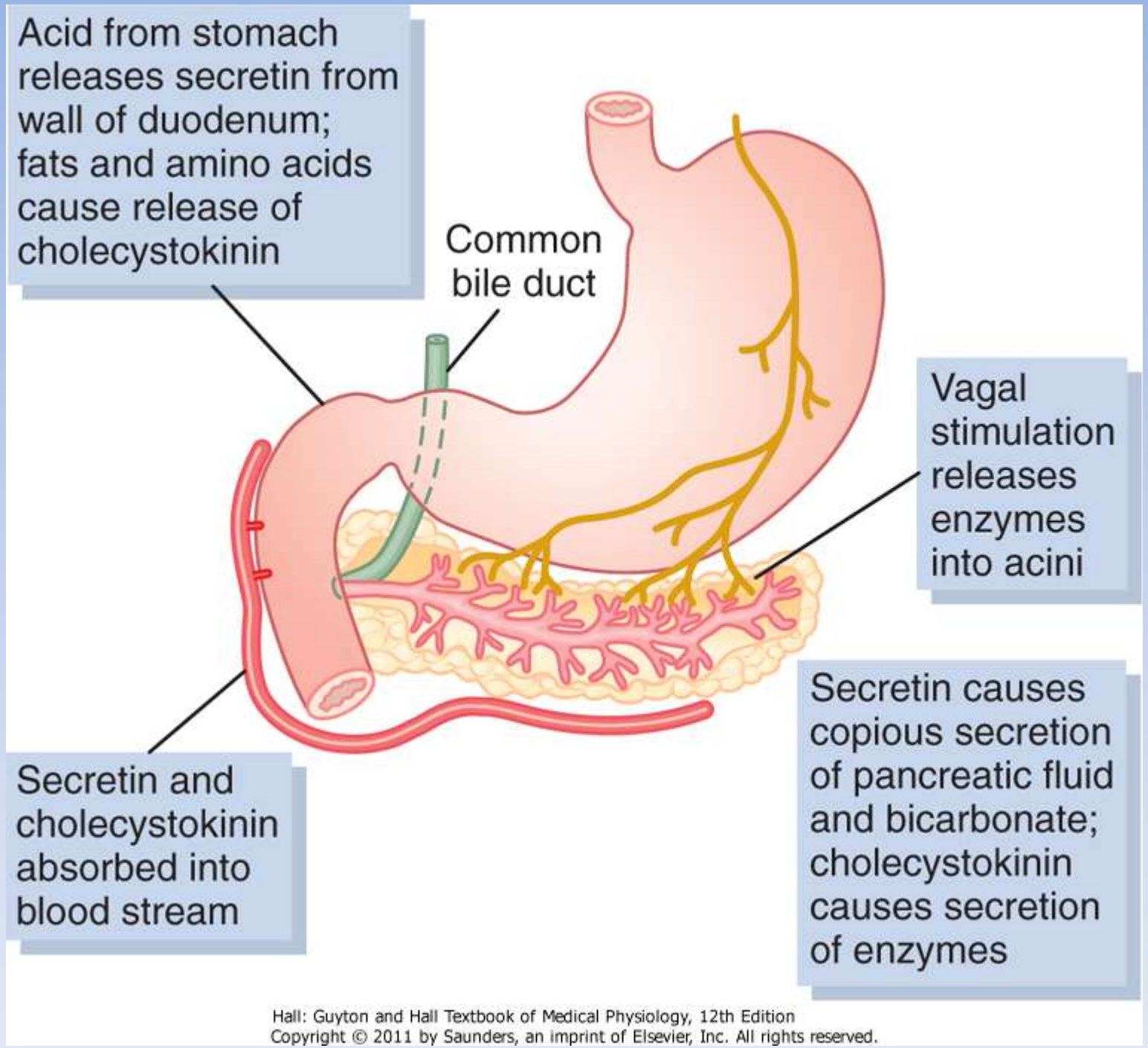
2-The bicarbonate ions will provide a suitable PH for the action of the pancreatic enzymes, since all these enzymes act optimally in a slightly alkaline or neutral medium at a PH of 7-8.

3- Secretin will also provide the fluid medium to wash out the enzymes that are secreted into the acini without large accompanying osmotic equivalent of water.

CHOLECYSTOKININ-PANCREOZYMIN (CCK)

- This hormone is released from the mucosa of the upper small intestine in ***response to fat and partial byproducts of protein digestion*** such as proteoses and peptones and also to a lesser extent in response to acid (HCL).
- CCK when released will be absorbed by the blood and then will go to the pancreas to cause the secretion of pancreatic juice ***rich in enzymes but poor in water and bicarbonate.***

- CCK accounts for about ***70-80% of the total secretion of pancreatic digestive enzymes*** after a meal.



SECRETION OF BILE

Bile serves two important functions:

1. Very important for the digestion and absorption of fat although it does not contain any digestive enzymes.
2. Bile serves as a mean for excretion of several waste products from blood e.g. bilirubin (end product of haemoglobin destruction) and excess of cholesterol.

The daily secretion of bile from the liver is 500-1000 ml. however the gall bladder has the capacity of 40-50 mills only so the hepatic bile is concentrated in the gall bladder by the absorption of water and electrolytes. So we have two types of bile:

Hepatic bile → secreted by the liver.

the gall bladder bile → which is the hepatic bile that has been stored and concentrated by bladder.

Main functions of bile salts in the intestinal tract:

Detergent function (emulsification).

Bile salts through their detergent effect will decrease the surface tension of fat particles in the food and allow the agitation in the intestine to break the fat globules into smaller sizes thus it will increase the total surface area of fat particles exposed to the action of the digestive enzymes, this emulsification function is very important for the digestion of fat.

Formation of micelles.

This is a very important effect by which bile salts help in the absorption of fatty acids, monoglycerides, cholesterol and other lipids from the intestinal tract. Bile salts will form small complexes with lipids particles called micelles; they are highly soluble in the water of the digestive fluid. The lipids are then ferried (transported) to the mucosa to be absorbed. *Without the presence of bile salts 40-50% of lipids are lost in the stool, and there is important loss of fat soluble vitamins such as vitamin A, D, E, and K.*

Activate lipases in the intestine.

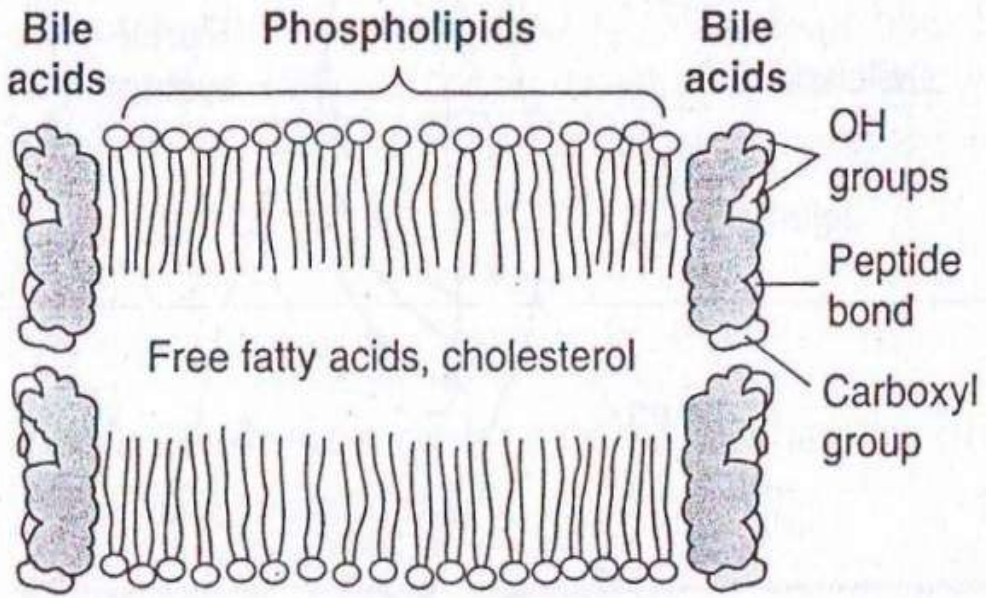


Figure 26–23. Cross section of disk-shaped bile acid–lipid mixed micelle with free fatty acids and cholesterol in its hydrophobic interior. The surface of each bile acid that faces outward is hydrophilic because of the polar peptide bond and the carboxyl and OH groups.

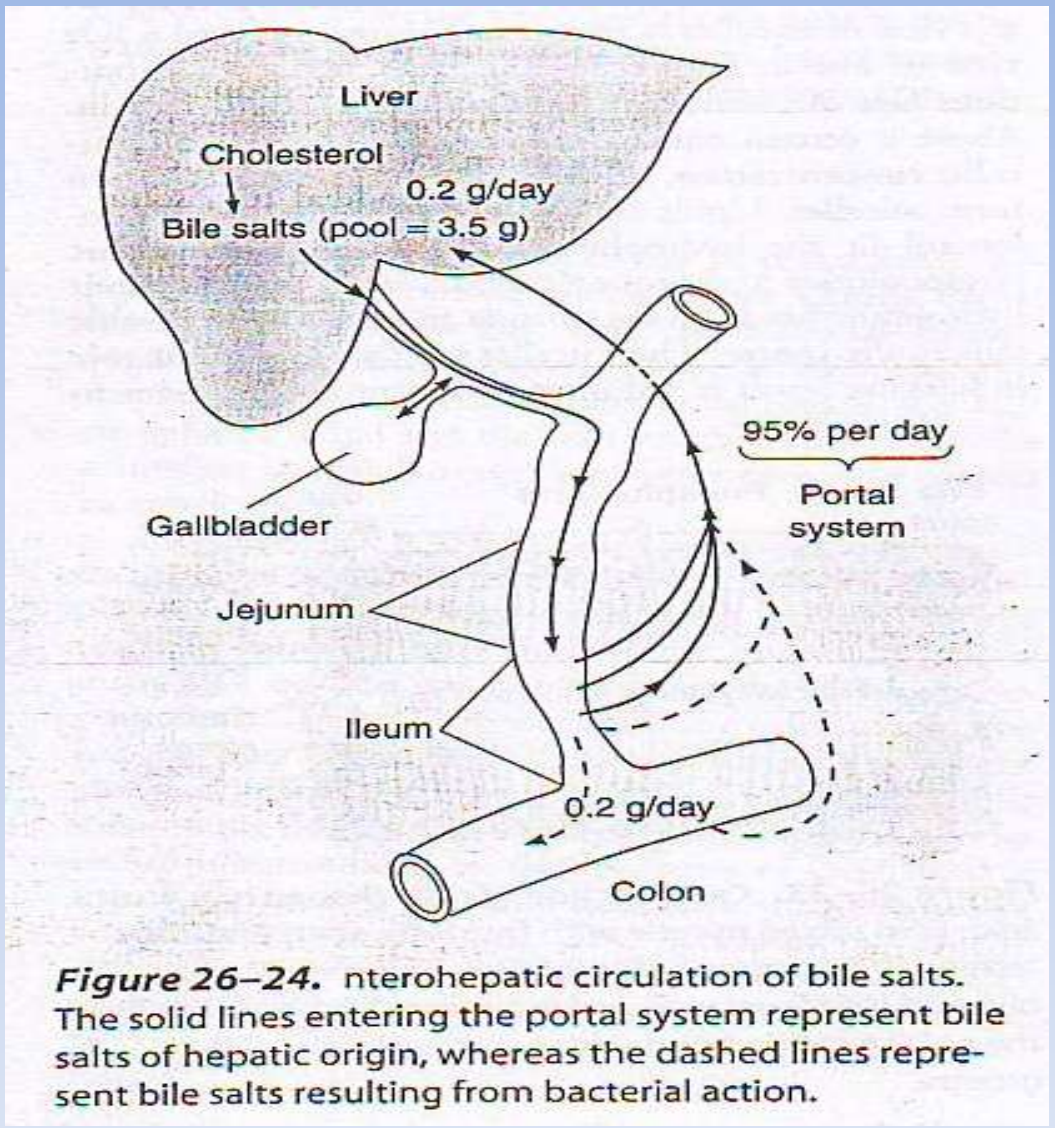


Figure 26–24. nterohepatic circulation of bile salts. The solid lines entering the portal system represent bile salts of hepatic origin, whereas the dashed lines represent bile salts resulting from bacterial action.

REGULATION OF BILIARY SECRETION

Bile is continuously formed by the liver and is stored and concentrated by the gall bladder until it is needed. Any agent that causes an increase in the production of bile by the hepatic cells is called **CHOLERETICS. The most important choleretic substances:**

1-Bile salts: They are the most important choleretic substance. the amount of bile salts secretion is controlled by the concentration of bile salts in the blood. The greater the plasma concentration of bile salts, the greater is the stimulus for their secretion. Thus between meals when there is little bile salts in the intestine and little absorbed , the plasma concentration of bile salts is low and there is little bile salts available to be transported into the bile ducts i.e. the enterohepatic cycling of bile salts is minimal. During a meal the higher plasma concentration of absorbed bile salts leads to an increased rate of bile salts secretion. The liver synthesizes new bile salts to replace the bile salts that escaped absorption in the small intestine (0.2-0.4 grams/day). The uptake by hepatocyte of bile salts from the plasma inhibits the synthesis of bile salts.

2-Vagal stimulation: increases the flow??

3-Secretin: increases the bile secretion. This is due mainly to the stimulation of the small bile ducts to secret sodium bicarbonate solution, the same effect that secretin has on the pancreas. The bicarbonate ions in the bile help to neutralize the acid in the duodenum. This electrolyte solution is stimulated by secretin in response to the presence of acid in the duodenum (just like the pancreas), so secretin does not stimulate the secretion of the bile salts by the hepatocyte.

Control of gall bladder Contraction and emptying

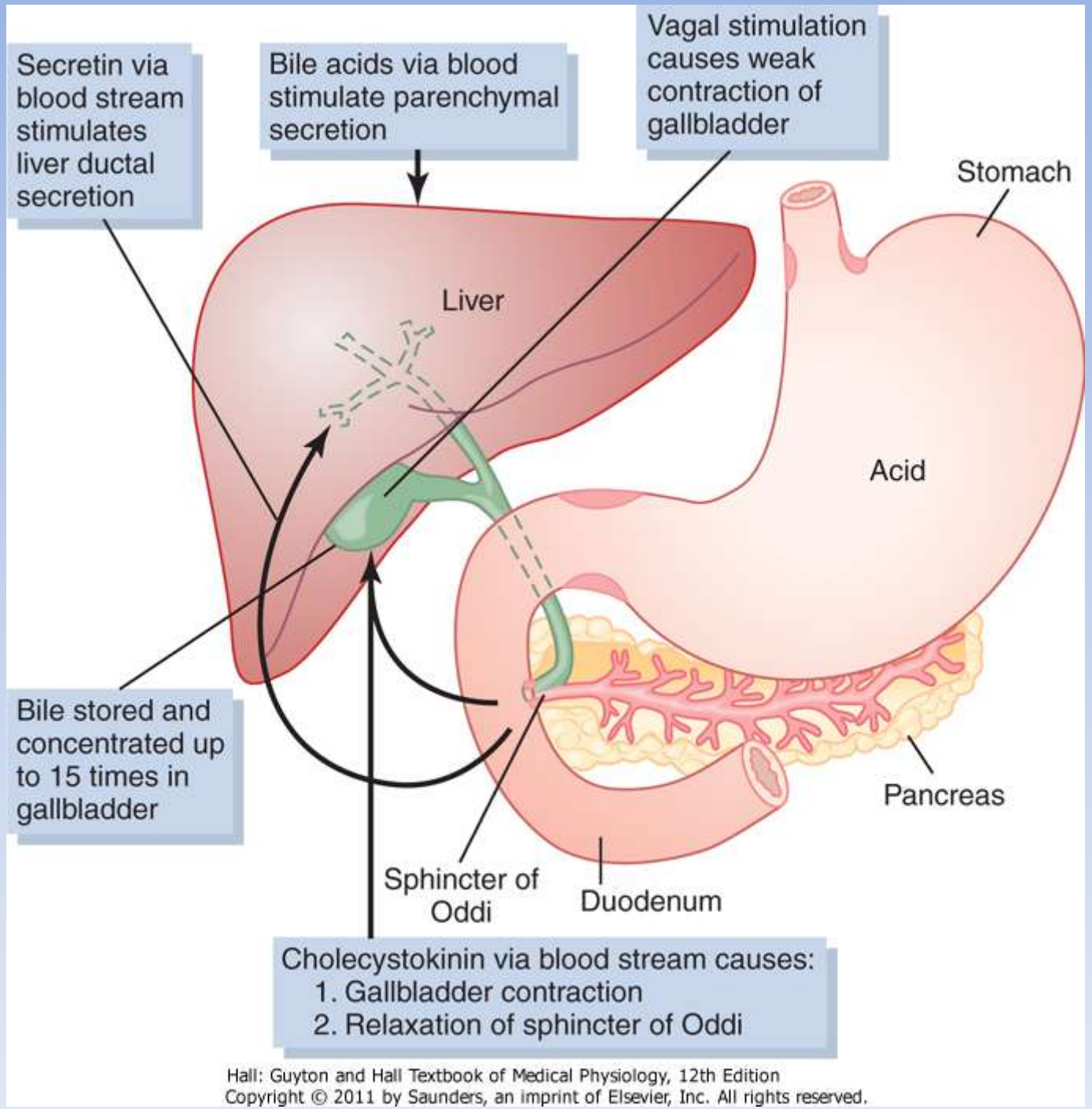
Substances that cause contraction of the gall bladder and expulsion of bile from the gall bladder are called CHOLAGOGUES, for example CCK. The contraction of gall bladder is under control of two types of control:

1- Nervous. **2- Hormonal.**

The hormonal mechanism is more important.

Nervous mechanism: is by parasympathetic (vagus nerve) which causes contraction of the gall bladder and relaxation of the sphincter of Oddi.

Hormonal mechanism: CCK is secreted from the duodenal mucosa in response mainly to fat and byproducts of protein digestion such as proteoses and peptones and to a lesser extent to acid. CCK will be absorbed to the blood then to the gall bladder and will cause emptying of the gall bladder (contraction of the gall bladder and relaxation of the sphincter of Oddi).



Hall: Guyton and Hall Textbook of Medical Physiology, 12th Edition

SMALL INTESTINE

- **The small intestine consists of the duodenum, jejunum, and ileum.**
- **The small intestine is the major site for digestion and absorption. Within the small intestine the hydrolysis of every major type of food molecules is completed and the resulting smaller molecules are absorbed into the circulating blood or lymph.**
- **The secretion of 2 major accessory glands, that's to say the pancreas and the liver enter the small intestine and help in the digestive process.**
- **We have two types of glandular secretions in the small intestine:**
  - **Brunner's gland secretion.**
  - **Crypts of Lieberkühn secretion**

Small intestinal secretions

- The secretions contain almost no digested enzymes. In the duodenum there are extensive numbers of mucus secreting glands called Brunner's glands. They are only present in the duodenum and are located mainly in the first few cm. of the duodenum between the pylorus and the duodenal papillae (where the bile and pancreatic juice empty in the duodenum). ***Brunner's gland secrete special type of mucus which is thick, viscid, alkaline and helps in protecting the duodenum against the acid chyme emptied by the stomach***. There is also an appreciable secretion of $HCO3^-$ that is independent of Brunner's gland. Decreased duodenal $HCO3^-$ secretion may play a role in the genesis of duodenal ulcer.

- The secretion of Brunner's gland can be stimulated by:-
  - Direct tactile or irritating stimuli of the overlying mucosa.
  - Vagal stimulation.
  - Intestinal hormones: Especially secretin.

- These glands are ***inhibited by sympathetic stimulation***, and therefore sympathetic stimulation over a long time might leave the duodenal bulb unprotected and is perhaps one of the reasons for the development of peptic ulcer.

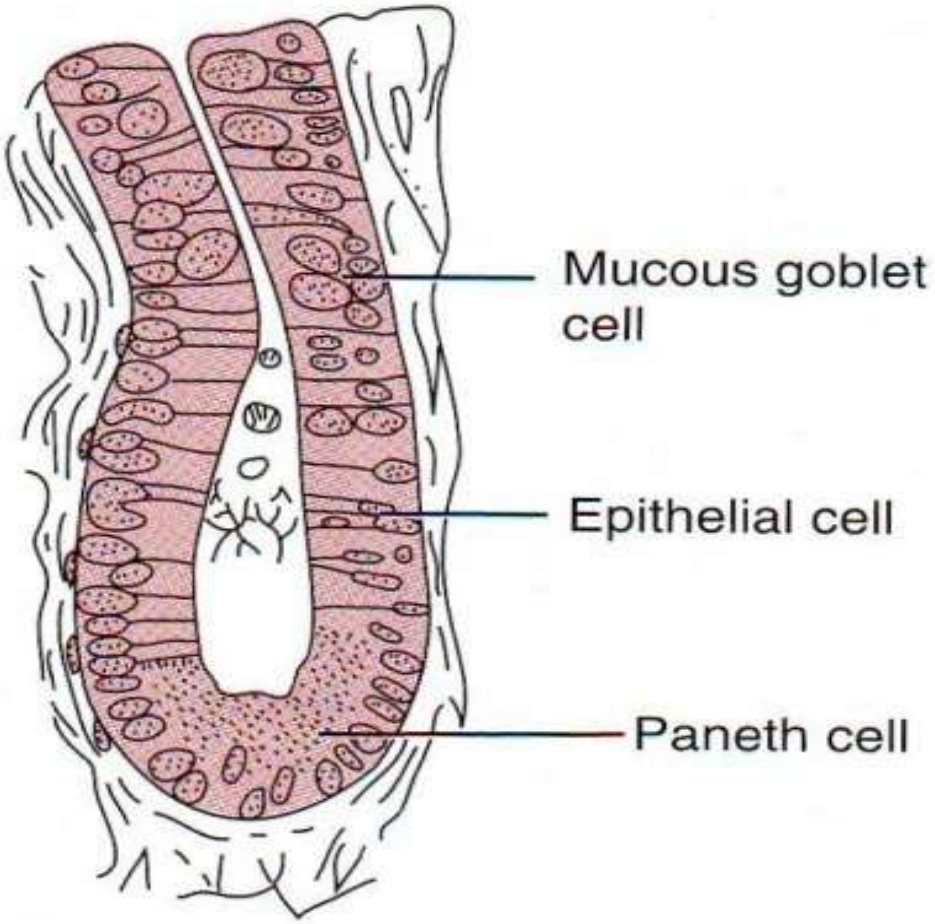


FIGURE 64–13

Crypt of Lieberkühn, found in all parts of the small intestine between the villi, which secretes almost pure extracellular fluid.

COMPOSITION OF THE INTESTINAL JUICE OR SUCCUS ENTERICUS

- The crypts of Lieberkühn secrets the intestinal juice or succus entericus. secreted at a rate of about 1-2 liters by day. It is similar to extracellular fluids and has a PH slightly alkaline 7.5-8. The secretion is rapidly reabsorbed by the villi. The circulation of fluid from the crypts to the villi will provide a fluid medium for the absorption of substances from the chyme as it comes in contact with the villi.
- If we collect any enzymes in the juice then it's from desquamated epithelial cells. The epithelial cells of the mucosa contain digestive enzymes on the Brush border of the epithelial cells. These enzymes will digest the food as they come in contact with the microvilli prior to the absorption of the end products of digestion.
- The enzymes are:-Peptidases, Disaccharidases.

Cholera toxin seems to have a specific effect in increasing active transport of Cl^- ions into the crypts. This will lead to massive loss of fluid into the intestinal tract.

REGULATION OF SECRETION OF THE SMALL INTESTINE

- **Local stimuli→ local nervous reflexes: this is the most important regulatory mechanism. Thus local nerve reflexes initiated by various stimuli will cause the secretion of the small intestinal juice. Of these stimuli are:-**

  A-Tactile B-Irritative C-Distension.

- **Therefore the secretion of the small intestine occurs mainly in response to chyme, the greater amount of chyme→ the greater response.**
- **hormonal regulation: some hormones that increase secretion in other parts of the gastrointestinal tract will increase the small intestinal secretion of these hormones:**

  A-Secretin B-CCK

C-VIP (vasoactive intestinal polypeptide).

- **Vagal stimulation has probably <u>No effect</u> on intestinal glands.**

LARGE INTESTINE

- **The main function of the large intestine is to *absorb water and electrolytes from the chyme, and to store the faecal matter until it can be expelled by defaecation.***
- **The mucosa of the large intestine contains No villi. There are crypts of Lieberkühn but they are composed largely of goblet cells that secrete mucus. Also there are no enzymes in the epithelial cells. Thus the most important secretion in the large intestine is mucus. The main functions of mucus secreted by the large intestine are:**

1. **Provide an adherent medium to hold the faecal mass together.**
2. **Protect the mucosa against excoriation or damage, against bacterial activity inside the faecal mass, against the acid formed deep in the faeces (PH 8 caused by large amount of sodium bicarbonate in colonic secretion) and thus neutralize the acid formed by the bacterial activity in the large intestine.**

REGULATION OF SECRETION OF THE LARGE INTESTINE:

- **Direct tactile stimulation of the goblet cells.**
- **Local nerve reflexes through the intrinsic nerve plexus to the goblet cells.**
- **Parasympathetic nerve stimulation through stimulation of Nervi erigentes (pelvic nerve) will cause marked increase in mucus secretion and also it causes an increase in motility. Therefore during excessive parasympathetic stimulation such as after emotional stress there might be frequent bowel motions with a large amount of ropy mucous quality→ psychogenic or emotional diarrhea.**

Large intestinal bacteria

The large intestine of the newborn child is bacteriologically sterile. This sterility will last for a few days only and thereafter the intestine will be invaded and colonized by ingested bacteria. The bacteria will flourish mainly in the large intestine, while the small intestine contains much less bacteria. The reasons why the small intestine contains less bacteria than the large intestine might be due to:

1. Acid gastric secretion.
2. Rapid transit time in the small intestine will allow less time for the growth of bacteria.

Effect of intestinal bacteria

Intestinal bacteria have a complex effect on their host (man). Some of these effects are useful and others are harmful:

1. Antibiotics improve growth rates in a variety of species including man, that's the reason why antibiotics are frequently added to the diets of domestic animals and the reason is unsettled?.
2. Nutritionally important substances such as vitamin C and cyanocobalamine and choline are utilized by some intestinal bacteria. On the other hand some bacteria synthesize vitamin K and some B-complex vitamin. Folic acid was shown to be absorbed in significant amounts.

3. Intestinal bacteria form a number of amines such as indole – skatole, which contribute to the odor of the faeces, as do sulfides.
4. Change primary bile acids in to secondary bile acids.
5. Partly responsible for the formation of gases in the large intestine .the amount of gases entering or forming in the large intestine each day is about 7 – 10 liters where as the average amount expelled is only 0.6 liters. The reminder is absorbed through the intestinal mucosa. Most often the person expels large amount of gases not because of excessive bacterial activity but because of excessive motility of the large intestine, the gases being moved on through the large intestine before they can be absorbed.
6. Intestinal bacteria appear to play a role in cholesterol metabolism, since the poorly absorbed antibiotic neomycin that modifies the intestinal flora lowers plasma LDL and cholesterol levels.
7. Colonic bacteria produce short chain fatty acids (SCFA) by acting on undigested complex carbohydrates from fruits and vegetables, and the major site of their production and absorption is the colon. They appear to be trophic to the colonic mucosa and they promote the absorption of Na^+ by Na^+ - SCFA coupled absorption.

   SCFAs when absorbed will be metabolized and make a significant contribution to the total caloric intake.

   SCFAs combat inflammation. SCFAs are absorbed in part by exchange for H^+ helping to maintain acid – base equilibrium.