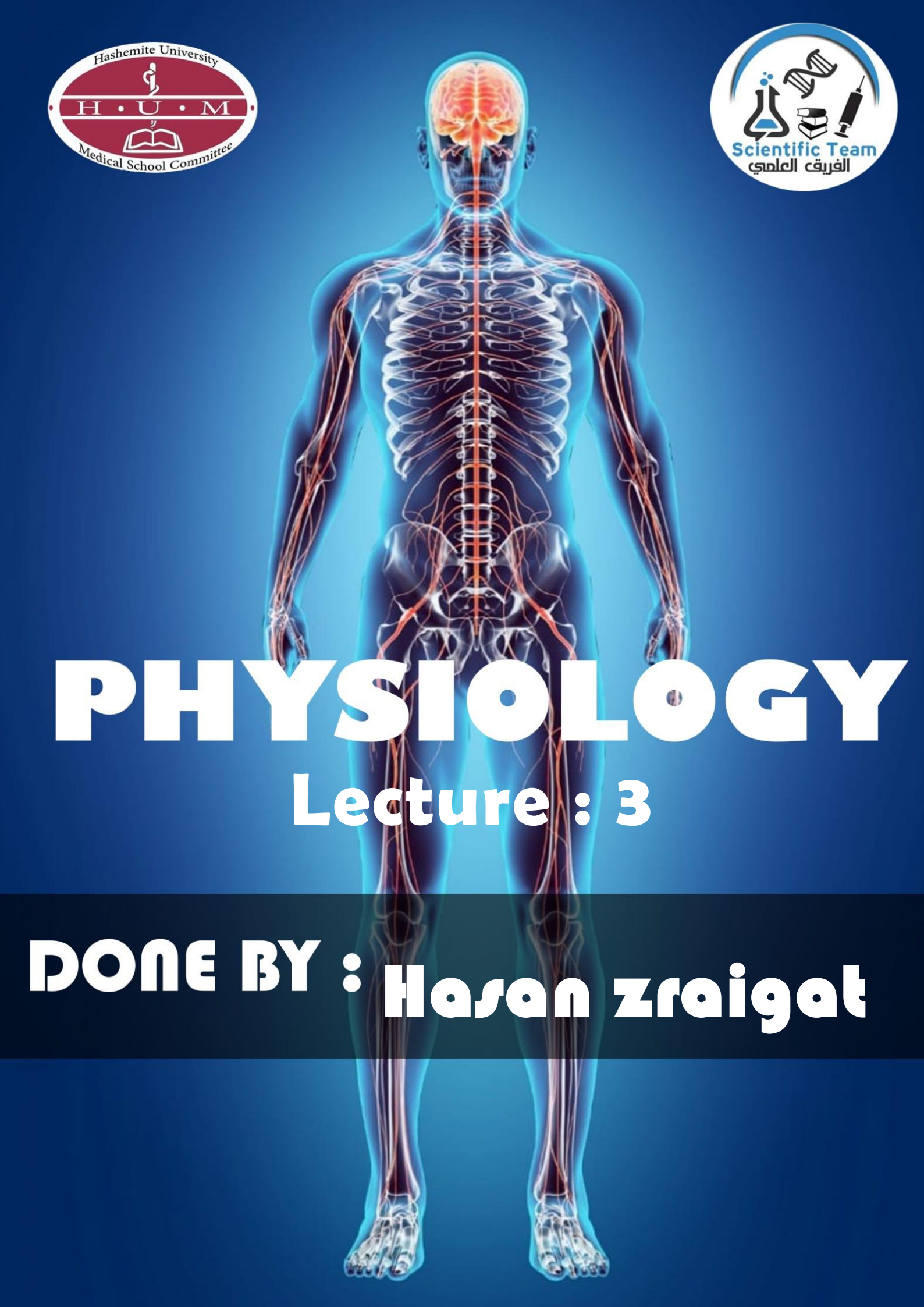


PHYSIOLOGY

Lecture : 3

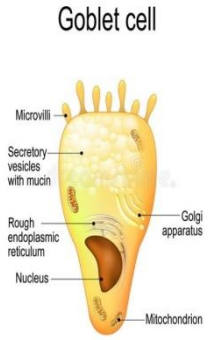
DONE BY : Hasan zraigat

Secretary Functions of the Alimentary Tract

Functions of Secretary Glands

• Digestive enzymes secretion - mouth → distal end of ileum

• Mucus secretion for lubrication & protection- mouth → anus



Types of Secretory Glands

• Single cell mucous glands/ mucous cells/goblet cells- extrude mucus → epithelial surface → lubrication & protection

The importance of mucus in GI

• Mucus is thick secretion composed mainly of water, electrolytes & glycoproteins.

• Lubricant & protectant for wall of gut

1. Has adherent qualities. 2. Coats gut wall & prevents contact of food with mucosa.

3. Sliding of food. 4. Adhering fecal particles together forming feces.

5. Resistant to digestion by GI enzymes. 6. Glycoproteins of mucus are capable of buffering small amounts of acids or alkalies.

Types of Secretory Glands

Pits - invaginations of epithelium into submucosa (crypts of Lieberkühn)

Tubular - acid & pepsinogen secreting oxyntic gland-stomach & upper duodenum

Complex - salivary, pancreas → compound acinous glands (acini+ducts) – liver

Not only the food that we have eaten it is found in the intestine. There will be also secretion. GIT starts to secret secretions from the mouth all the way of the track.

What is the purpose of secretion ? To know the purpose , let us know what we secret first.

We secret:

1-water to make fluid format

2-mucous to mix, adhere, to protect and lower resistance

3-proteins that will work as enzymes (we do not secret enzymes) into blood then work on parietal cells.

4-ions

What are the secretions?

starting from mouth, we have salivary, oesophagus has no secretion, then we have stomach, intestinal, biliary and pancreatic secretions. Through All the way of the intestinal wall, there is mucous secretion glands, these are goblet cells which secret as glands. The wall of intestine contain invaginations (pits) of the submucosa, so we can have complex gland. Simple Glands might be:

1- as part of the surface like mucous, or 2- they can be as part of the pits, or may be 3- complex like salivary, pancreas and liver. So the glands are in a range between simple, in pit or complex or even very high complex degree glands and they all secret their components in ducts.

Some of stomach secretion do not go to the lumen, it will go the circulation, so we call it hormone. Secretions to lumen are mucous, water, electrolytes, acid. What we secret in the opposite direction is hormones. How we regulate that? by Neural regulation (when think of or smell food there will be secretion), mechanical local irritation (when eat, try to put anything in the mouth, there will be secretion), chemical.

Control of Glandular Secretions

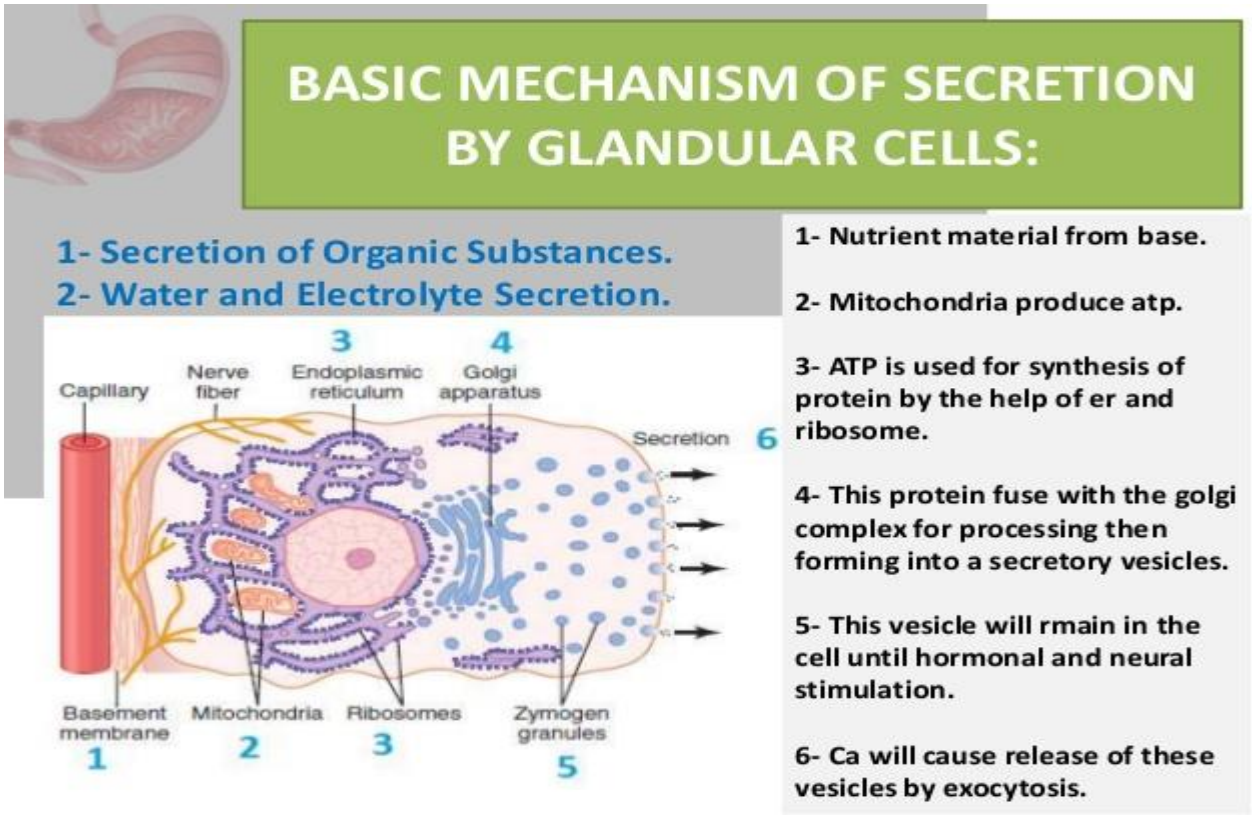
- Local - tactile, distention, irritation
- Reflex - nervous input
- Hormonal - G.I. hormones (stomach & intestine)→gastric & pancreatic juice secretion

Parasympathetic.↑rate of secretion Glossopharyngeal, vagus →salivary, esophageal, gastric, pancreas & Brunner's glands in D Pelvic n.→ glands of distal LI

Sympathetic -↑or↓- (vasoconstriction) rate of secretion

Secretion of organic substance, Water and Electrolyte

Nervous/hormonal stimulation → water and salts to pass through the glandular cells → washing organic substances through the secretory border of the cells at the same time.



MAJOR SALIVARY GLANDS

1. Parotid glands 2. Submaxillary or submandibular glands 3. Sublingual glands

Buccal glands

Secretion of saliva

- Two types of secretion - -

Serous - watery secretion, contain a-amylase (ptyalin), starch digestion enzyme

- Mucous - contains mucin – lubrication & surface protection

- Parotid (serous)
- Buccal (mucus)
- Submandibular + sublingual (mixed)
- Maximum rate of secretion: 4 ml/min
- Flow of saliva decreases during sleep
- Secrete 800-1500 ml/day (avg of 1000) of saliva
- pH 6-7

When saliva secreted, why? Continously All the time, so mouth stay wet. Why? To stand against inflammation, erosion…. What are the contents? Fluid, proteins, ions. Function of the secretion depends on the contents (mucus, serous,..) What is the amount? Litre per day

Functions of Saliva

• Lubrication • Solubilizes dry food • Oral hygiene - (wash bacteria, thiocyanate ions, lysozyme & antibodies destroy bacteria) • Digestive function

Saliva function in digestion Amylase → help in carbohydrate digestion

Can we live without saliva secretion? Yes but with complications

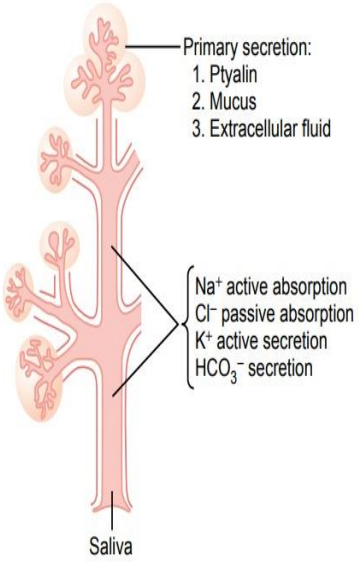
Formation and Secretion of Saliva

• Two Stages :

- Acini - primary secretion similar to plasma

- Salivary Ducts - modified as it passes through ducts

Parotid is the main salivary gland. The structure of the gland consist of acini and duct, so there is acinar secretion and ductal secretion or say modifications . acini secrete proteins and other globulin. In the duct, the process is modifying of the secretions. So what secreted primarily is not necessary ends in the mouth



Formation and secretion of saliva by a submandibular salivary gland.

Ionic composition of Saliva

• Ionic composition depends upon rate of secretion.

• Resting composition are:

- Na+ & Cl- - 1/7-10 x plasma (15 mEq/L) - K+ - 7 x plasma (30 mEq/L) - HCO3 - 2-3 x plasma (50-70 mEq/L)

We secret ions… what is there concentration and how we manipulate them?

• Saliva is hypotonic

• During maximal salivation rate ↑ by 20-folds (osmolarity increases →[Na+& Cl-] is 1/2 or 2/3 X plasma, [K+] 4X plasma

• Loss of saliva from body can lead to K+ depletion

Here we compare the ions concentrations in plasma and saliva

- The more we have chloride and Na in mouth means that the shorter the time of it stay in ductal system. Lower the chloride, longer stay in ducts and more manipulation occur to it.

- There are two stages of secretion: -

1- at the beginning, secretion from acini and the ion conc is similar to plasma (high Na and low K)

2- ducts modify the acini secretion before release it to the mouth (reabsorbed Na and secret K) - High flow rate = less time stay at duct= no enough time to secret K and reabsorbed Na - Low flow rate= long time stay in duct = high K, HCO3 stay high and less Na and Cl

Nervous Regulation of Salivary Flow

• Controlled mainly by PSN signals from superior and inferior salivatory nuclei in BS (at juncture of M & P)

• Excited by taste & tactile stimuli from tongue, mouth & pharynx

• Appetite area in CNS control salivation

• Sour taste →↑ salivation (8-20 fold ↑)

• Smooth objects→ ↑ salivation, Rough objects→ ↓ salivation

• Reflexes in stomach and upper SI (irritation & nausea)→ ↑ salivation

What stimulate secretion?

neural stimulation (seeing, smiling, thinking of food).

Eating→ increase saliva secretion = stimulate parasympathetic

Fear→ less saliva secretion = stimulate sympathetic = Direct stimulate to acinar cells, indirect due to decrease blood flow to tissue

Other factors increase secretion

= reflex Condition ex. when you start thinking eating a meal at 9 pm and you are accustomed to eat a meal in this hour Also irritants in stomach and intestine (nasua) increase secretion in order to get rid of them

Factors decrees secretion Sleep, dehydration. Fear→ sever sympathetic stimulation

Nervous Regulation of Salivary Flow

• Sympathetic→ ↑ salivation, weaker than parasympathetic stimulation.

• Sympathetic nerves originate from Superior Cervical G. and travel along surfaces of blood vessel walls to salivary glands.

• PSN → blood supply to glands (vasodilation) →↑ salivation

• ↑ Salivation →vasodilation (kallikrein splitting alpha2-globulin, forming VD bradykinin)

Esophageal secretions

• Main body of esophagus → simple mucous glands

• Gastric end & initial portion of esophagus → compound mucous glands

• Mucous secretions only →lubrication for swallowing & protect mucosa (food & acid reflux)

Gastric Secretion

• Glands of stomach:

1- Mucus-secreting cells

2- Oxyntic / gastric/ parietal (acid-forming) glands

-Located on inside surfaces of body & fundus (proximal 80%)

-Secrete HCl, Pepsinogen, Intrinsic factor, Mucus.

3- Pyloric glands

-Located in antrum (distal 20%)

-Secrete mucus, gastrin

Stomach mucosa is not the same in all parts, so secretions are deferent according to the area of the stomach. There are two parts (1- gastric/oral/proximal part

2- pyloric/caudal/distal part)

Gastric Acid

• Three major functions -

- Bacteriostatic - Converts pepsinogen to pepsin - Begins protein digestion (with pepsin)

In gastric/pyloric area of the stomach, the secretions are as following in the slide: All secretions will ends up in lumen

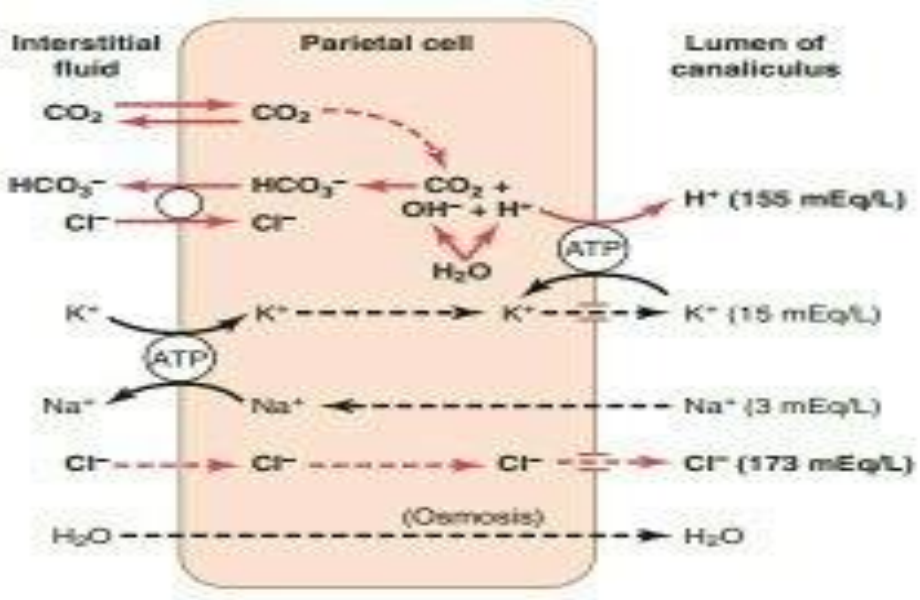
Stomach mucosa is not the same in all parts, so secretions are deferent according to the area of the stomach. There are two parts (1- gastric/oral/proximal part 2- pyloric/caudal/distal part)

Parietal Cell

- Gastric juice contains 160 mmol/L of HCl (isotonic with body fluid)
- pH= 0.8, [H+] 3 million * arterial blood
- HCl is formed at the villus-like membranes of the canaliculi which are continuous with the lumen

Mechanism of HCl Secretion

1. H2O inside parietal dissociate → H+ & OH−
2. H+ is actively secreted into canaliculus in exchange for K+ (catalyzed by H+ -K+ ATPase).
3. K+ transported into cell by Na+ -K+ ATPase pump on the basolateral side
4. K+ leak into lumen but recycled back into cell by H+ - K+ ATPase.
5. Basolateral Na+ -K+ ATPase creates low intracellular Na+ → Na+ reabsorption from lumen of canaliculus.
6. Pumping of H+ out of cell → OH− accumulation +CO2(carbonic anhydrase) →HCO3
7. HCO3 is transported into ECF in exchange for Cl→
8. Cl secreted by Cl channels → canaliculus → Cl+H →HCl secreted to lumen.
9. H2O passes into the canaliculus by osmosis.



Look to the final results in the green box. We get that result when there is high stimulation rate. HCL=155 (cl not that change but a lot of H ions),NA=is almost nothing(remember normally it was 100), K=15 (higher cuz normal was 3-5)

See the picture: we have at the apical membrane H/K pump, so K move in and out through the apical membrane to maintain gradient. These cells have high carbonic and hydras activity and this what will create H and HCO3. H will be bound in replacement of K. we have excess K in the lumen due to Na/K pump in the basilar membrane. Na enters through apical m by active transport in order to be exchanged by K (by Na/K pump in basilar M). Bicarbonate will come out and Cl will come in cell then in to the lumen Purpose of the membranesالناتج النهائيpumps in the apical and basilar

1-To allow K/Na replacement

2- to maintain pumping huge amount of H to lumen and bring K in

Blood that drains gastric part of the stomach will be alkaline, why?? Because the bicarbonate that exit the partial cell will end in the blood vessels (alkaline is on the opposite side to the acidic)

What regulate acid secretion? Ach Gastrin Histamine

Effect of Secretory Rate on Ionic Composition of Gastric Juice

- Low secretion rate (between meals) - high NaCl
- High secretion rate (after a meal) - high HCl
- Always isotonic

Between meals = low stimulation. See food, smell.. Stimulate vagal Low K and H concentration+ high Na (cuz of no secretion) during meals (In case of stimulate acid secretion) → increase K inside due to increase pump activity. Na concentration will be next to nothing. H is very high. Cl increased in very little amount

Regulation of Gastric Secretion

- Gastric secretion is stimulated by neural, paracrine and endocrine mechanisms

- Acetylcholine - HCl secretion - mucus, pepsinogen, and gastrin - Histamine - HCl secretion - Gastrin - HCl secretion (1500x more powerful compared to histamine)

The nervous system , and endocrine system collaborate in the digestive system to control gastric secretions, and motility associated with the movement of food throughout the gastrointestinal tract, including peristalsis, and segmentation contractions.

Gastric activity involved in digestion is divided into three stages known as the cephalic phase, the gastric phase, and the intestinal phase. These phases overlap and all three can occur simultaneously.

A fourth phase of acid secretion is known as the basal state which occurs in the times between meals (interdigestive phase). The level of acid secretion during these times is regulated by body weight, individual, number of parietal cells, and time of day. Acid secretion is lowest in the morning before awakening and highest at night.

Pepsinogen

• Secreted by peptic and mucous cells of gastric glands

• Pepsinogen is an inactive, secreted form of pepsin

- HCl converts pepsinogen to pepsin - Pepsin (35 kDa) converts more pepsinogen to pepsin
- proteolytic enzyme - optimal pH 1.8 - 3.5 - reversibly inactivated >pH 5.0
- irreversibly inactivated >pH 7-8

- Secreted in inactive form from gastric part - Activated by H
- It will stop working if environment become alkaline

Intrinsic Factor

• Secreted by parietal cells

• Essential for absorption of vit. B12 in ileum.

• When the acid-producing parietal cells of the stomach destroyed (Ileal disease, resection, atrophic gastritis) → achlorhydria & pernicious anemia.

• Pernicious anemia → failure of maturation of RBC in absence of vit. B12

-It is a protein secreted from the same cells that secret acids –helps in absorption of B12 in terminal ilium

Intrinsic Factor

• Stomach - Dietary vitamin B12 bound by B12 -binding proteins present in gastric juice

• Duodenum - pancreatic proteases digest binding proteins, releasing vitamin B12 which binds to intrinsic factor

• Ileum - intrinsic factor - vitamin B12 complex absorbed

Secretion from pyloric glands

Ø Structurally similar to the oxyntic glands.

Ø Few peptic cells, no parietal cells.

Ø Contain mostly mucous cells, identical with mucous neck cells of oxyntic glands. Ø Secrete small amount of pepsinogen

Ø Secrete large amount of thin mucus → lubricate food & protect stomach wall from digestion by gastric enzymes

Ø Secrete Gastrin→ controlling gastric secretion.

See this video

https://www.youtube.com/watch?v=as44dSTv8z0

Gastric barrier

• Surface mucous cells → thick (1 ml), alkaline, viscid mucus

• Alkaline mucus & tight junctions between epithelia cells→ protect stomach mucosa from acidic gastric juice

• Barrier is damaged by excessive use of aspirin or alcohol → causing stomach mucosal damage.

The **gastric mucosal barrier** is the property of the stomach that allows it to safely contain the gastric acid required for digestion.

If the barrier is broken, as by acetylsalicylic acid (ASA, aspirin) in acid solution, acid diffuses back into the mucosa where it can cause damage to the stomach itself.

The barrier consists of three protective components.[1] These provide the additional resistance for the mucosal surface of the stomach. The three components include:

- A compact epithelial cell lining. Cells in the epithelium of the stomach are bound by tight junctions that repel harsh fluids that may injure the stomach lining.
- A special mucus covering, derived from mucus secreted by surface epithelial cells and oveolar cells. This insoluble mucus forms a protective gel-like coating over the entire surface of the gastric mucosa. The mucus protects the gastric mucosa from autodigestion by e.g. pepsin and from erosion by acids and other caustic materials that are ingested.
- Bicarbonate ions, secreted by the surface epithelial cells. The bicarbonate ions act to neutralize harsh acids.

Stimulation of gastric acid secretion

• Secretion of gastric acid is controlled by endocrine and nervous signals.

• Enterochromaffin-like (ECL) cells

..Lie in deep recesses of oxyntic glands

.. Stimulated by gastrin

.. Secrete histamine → partial cells → HCl.

Regulation of pepsinogen secretion

Stimulation of pepsinogen secretion:

(1) Acetylcholine released from vagus nerves/ENS

(2) Acid in stomach (indirect effect-ENS reflexes)

- Secreted in inactive form from gastric part - Activated by H

- It will stop working if environment become alkaline

Phases of Gastric Secretion/Cephalic Phase

• Seeing, smelling and anticipating food is perceived in CC & appetite center)→vagus → stomach

• Accounts for 30% of acid response to meal –

- Stimuli - Mechanoreceptors Chemoreceptors (smell and taste) Central pathway (thought) Hypoglycemia

Gastric Phase

• When meal enters stomach.

• Accounts for 60% of acid response (1500 ml) to a meal

• Stimuli

(1) Vagovagal reflexes from stomach →brain → stomach

(2) Local enteric reflexes

(3) Gastrin mechanism

Intestinal Phase

• Accounts for 10% of acid response to a meal

- presence of food in upper portion of SI (esp. D)

- small amounts of gastric juice

- Stimulated by gastrin release by D mucosa.

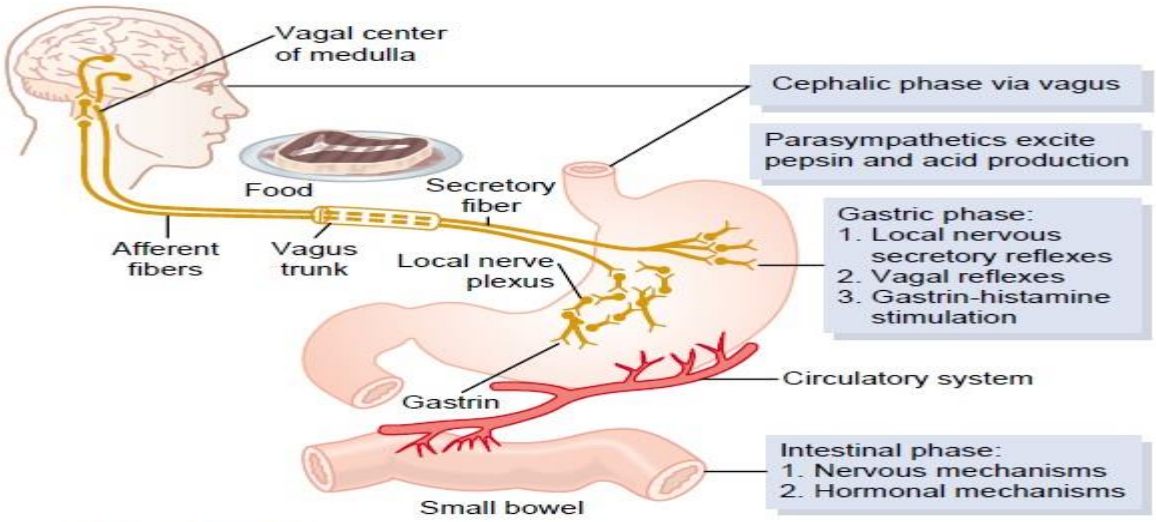


Figure 64–7

Phases of gastric secretion and their regulation.

Inhibition of Gastric Secretion by Other Intestinal Factors

ØEnterogastric reflex: transmitted through MNS, sympathetic and vagus nerves→ ↓stomach secretion.

ØStimuli for enterogastric reflex:

(a)SI distention (b)Presence of acid in upper I (c) Protein breakdown products (d) Irritation of mucosa

ØAcid, fat, protein breakdown products, hyperosmotic or hypo-osmotic fluids, irritating factor in upper I → secretin → pancreatic secretion control & ↓stomach secretion.
ØGlucose-dependent insulinotropic peptide (gastric inhibitory peptide), vasoactive intestinal polypeptide, and somatostatin ↓stomach secretion.