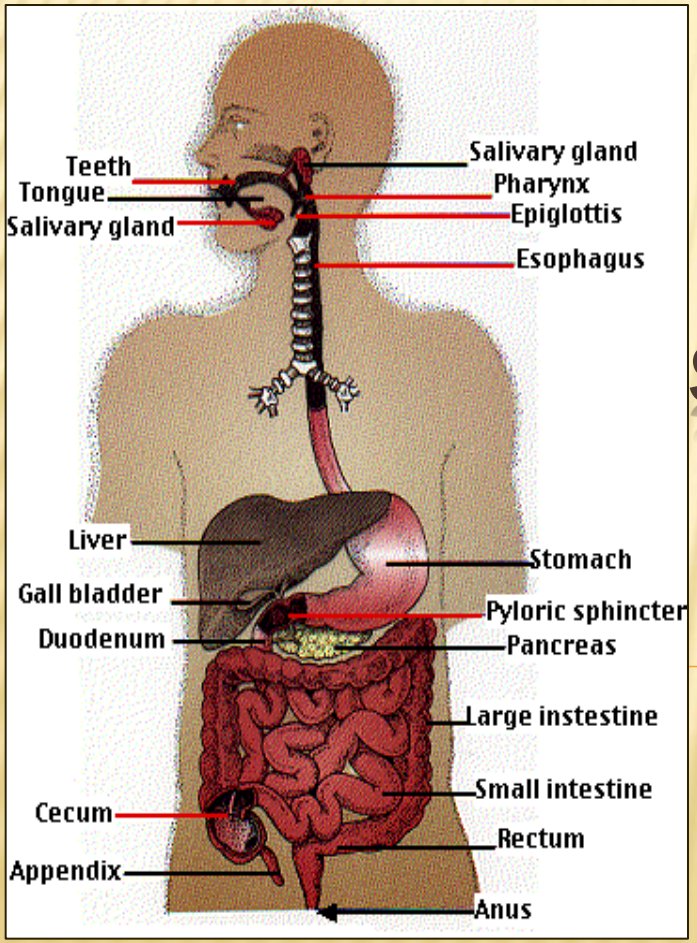
MEDICAL UNIVERSITY – PLEVEN
FACULTY OF MEDICINE
DISTANCE LEARNING CENTER

Lecture № 15



SECRETORY FUNCTIONS OF THE GASTROINTESTINAL TRACT. SECRETION OF THE SALIVA, GASTRIC AND PANCREATIC SECRETION, SECRETION OF BILE BY THE LIVER, SECRETIONS OF THE SMALL INTESTINE.

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Secretion of Saliva

❑ Saliva is secreted by:

1. The principal salivary glands – 90%:

✓ **Gl. Parotis** ✓ **Gl. Submandibularis** ✓ **Gl. Sunlingualis**

2. Many very small *buccal* glands - 10%

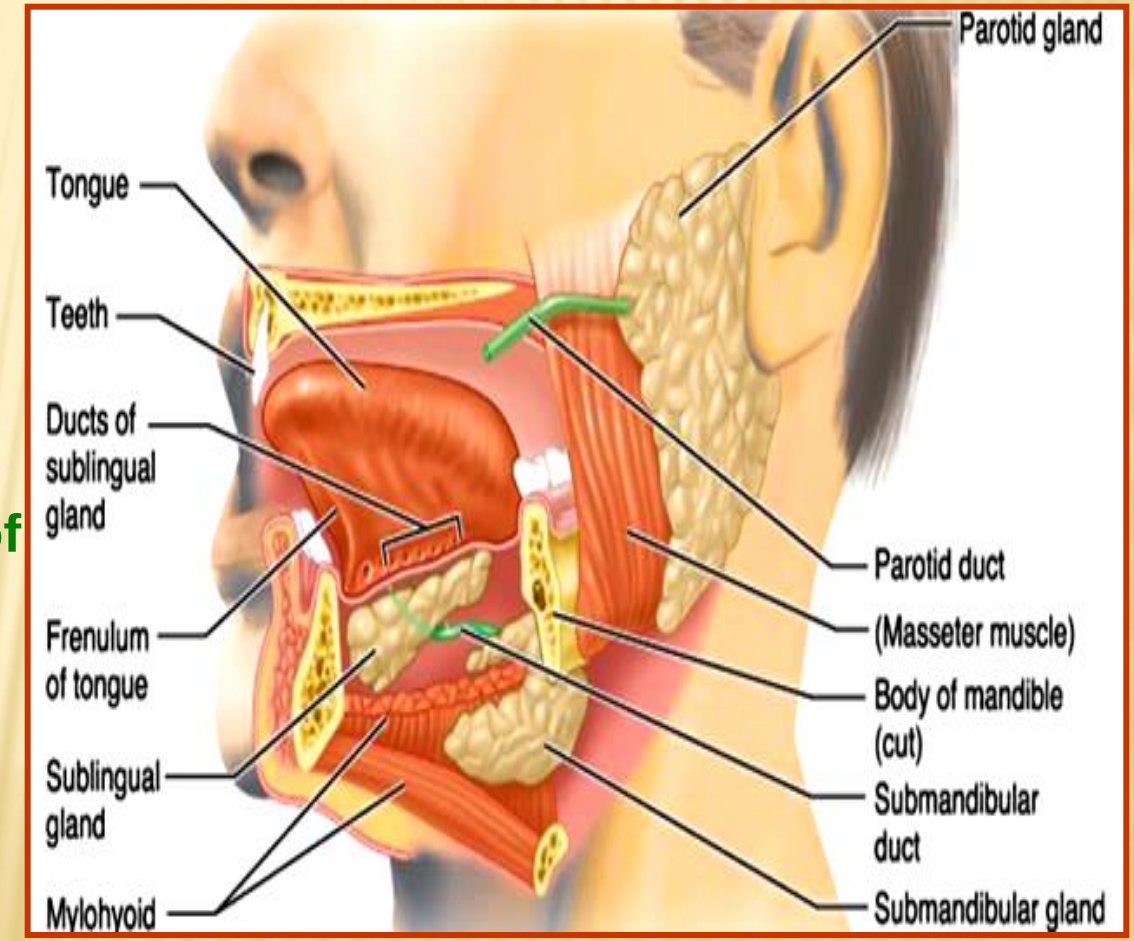
❖ **The salivary glands are charactirizated by:**

✓ **Good blood supplying –** during maximal secretory activity their blood supply is 10 times greater than supplying of working muscle per 1 g of tissue.

✓ **Innervations by two parts of ANS, that have stimulating action**

✓Sympathicus – increases secretion of enzymes

✓Parasympathicus increases secretion of water and electrolytes.



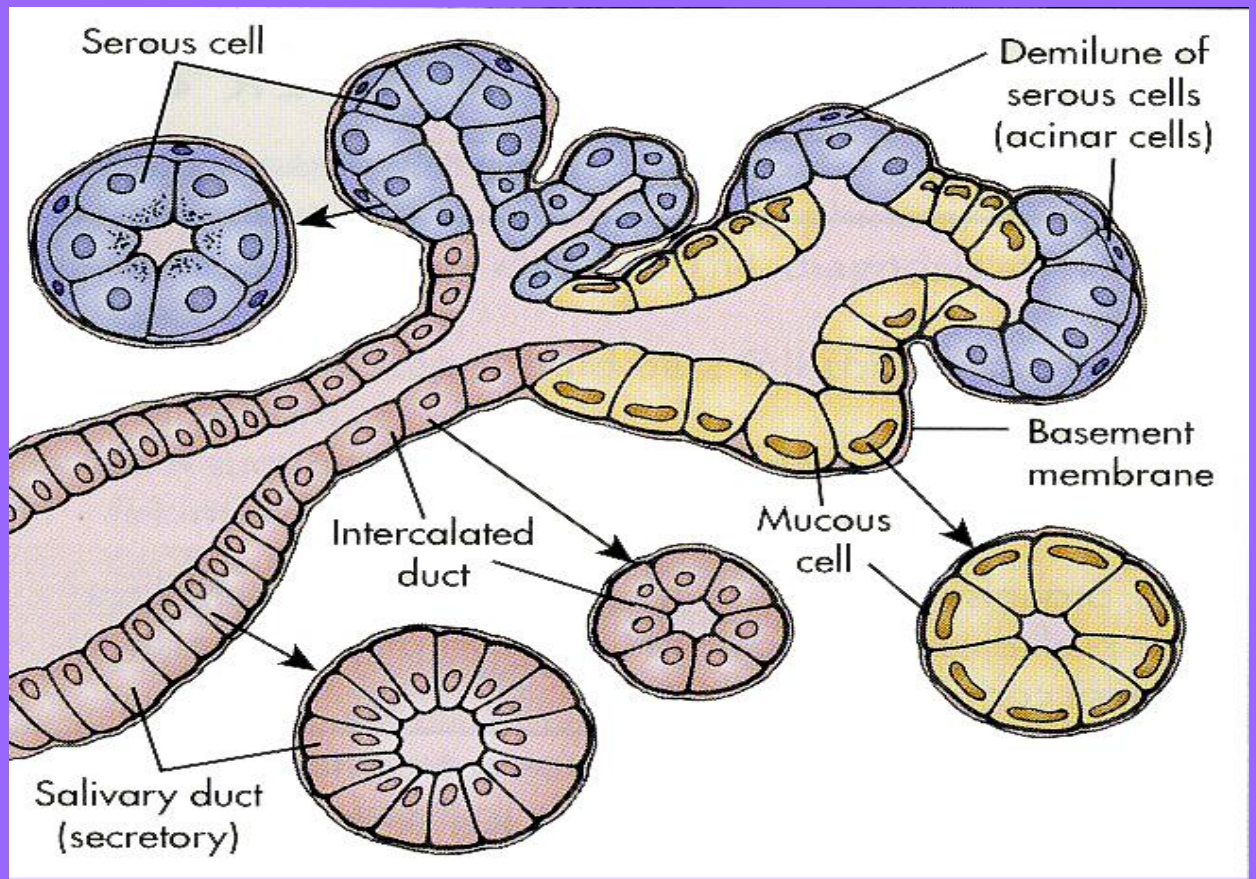
Physiological Morphology of Salivary Glands

- **Salivary glands contain acini and ducts**
  - **Depending of the type of the contained cells and produced secret, primary salivary glands are divided in:**

The glands with serous type of secretion - parotid gland

The glands that secrete both serous secretion and mucus – Submandibular and sublingual glands

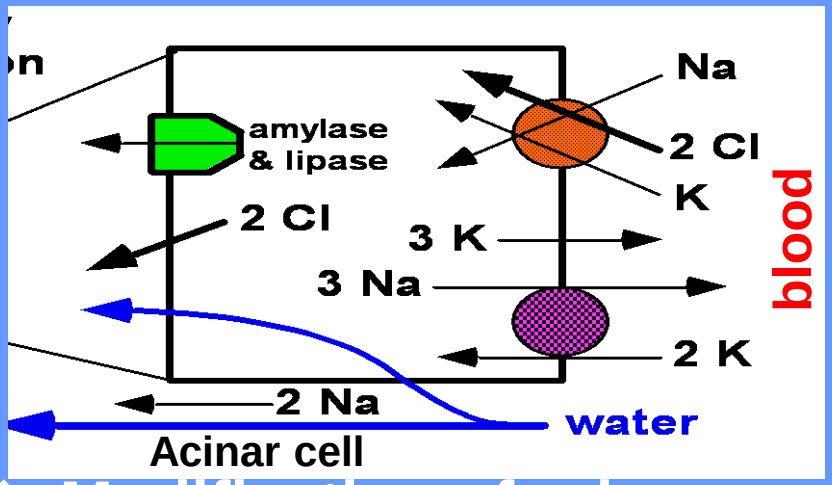
✓**The buccal glands secrete only mucus.**

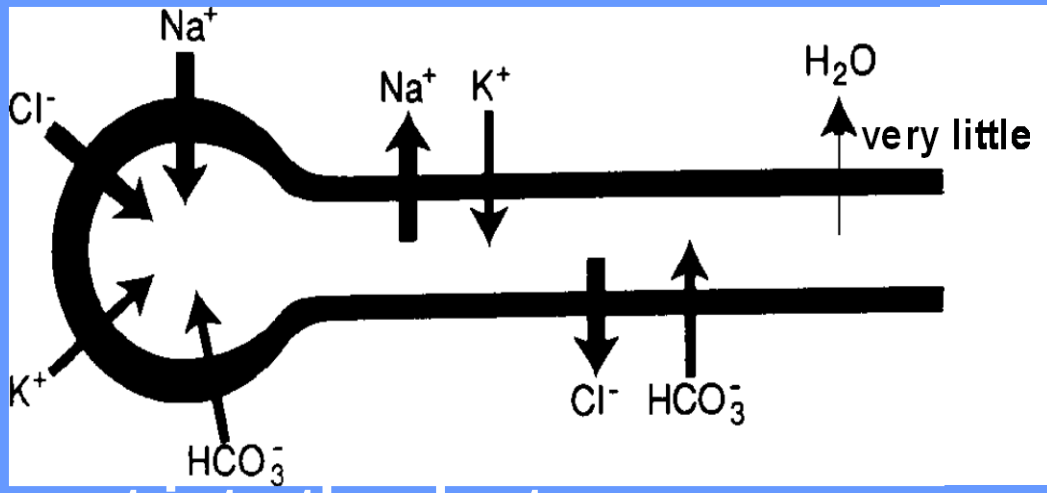


❖ Mechanism of secretion by acinar cells

➢ **Enzymes (α-amylase, lipase) –** exocytose of zymogene granules

➢ **Secretion of ions into the lumen: Cl^- and Na^+ ->** osmosis of water – isotonic secret





❖ Modification of primary secret into the ducts:

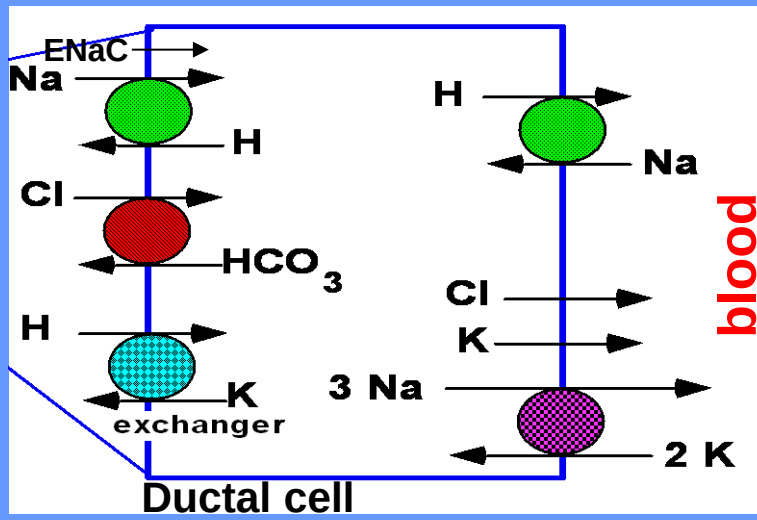
➢ **secretion of HCO_3^- and K^+**

➢ **reabsorption of Na^+ and Cl^-**

✓ the speed of absorption is higher than the speed of secretion

✓ thigh junction between the cells are not permeable for water

❑ Saliva is more hypotonic than the plasma



Quantity and contents of the saliva

Daily secretion of saliva normally ranges between 800 and 1500 ml.

❖ content: water, organic and inorganic substances

➢ **organic substances**

✓digestive enzymes: **α-amylase, sublingual lipase**

✓ enzymes with defensive action: peroxidase, lisosym

✓ glycoproteins: mucus, calcium binding proteins

✓ growth factors (epidermal and neuronal)

✓ immunoglobulins

✓low molecular weight organic substances: glucose, urea, ammonium, creatinine, uric acid

➢**inorganic substances**

- Compared with the plasma **saliva has** :

✓lower concentration of Na^+ and Cl^-

✓ higher concentration of HCO_3^- and K^+

❖ Saliva is hypotonic secret with pH from 6 to 7.

Functions of the saliva

➢1. Digestive:

✓ alfa-amylase – splits polysaccharides to oligosaccharides
✓sublingual lipase - splits triacilglycerols to diacilglycerols and free fatty acids

➢ 2. Defensive:

✓ mucus, lisosym, lactopherin, peroxidase, thiocianate ions, immunoglobulins, epidermal growth factor, HCO_3^-

➢3. Excretion of:

✓ the end metabolic products of proteins and some hormones

➢ 4.Exchange of electrolytes (Ca, F) with the teeth email

❖ 5. Other functions:

➢ facilitates swallowing acting on the mouthful formation

➢action on the taste sensation dissolving the ingested substances

➢ facilitates speech ensuring humectation of bucal mucosa

Gastric Secretion

❑ The stomach secretes 2-2.5 l of stomach juice/ 24 h, that contains H_2O, enzymes (pepsinogen, lipase), HCl, intrinsic factor of Castle and electrolytes.

❖ The content of stomach juice is secreted by the gastric glands and epithelium:

Pepsinogen
Gastric lipase } by chief cells

HCl
Intrinsic factor of Castle } By parietal cells

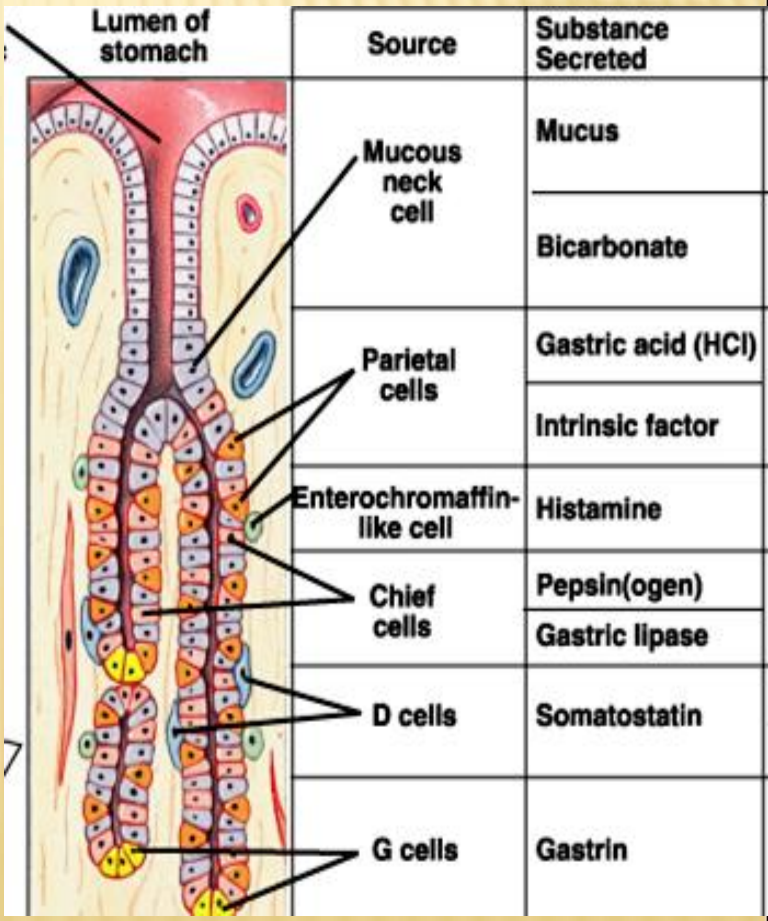
Mucus ⟶ by mucous neck cells

HCO_3^- ⟶ by epithelial cells

➢ The cells of stomach mucosa secrete:

Gastrin
Somatostatin
Grelin } by endocrine cells

Histamine ⟶ by enterochromaffin-like cells



Source	Substance Secreted
Mucous neck cell	Mucus
	Bicarbonate
Parietal cells	Gastric acid (HCl)
	Intrinsic factor
Enterochromaffin-like cell	Histamine
Chief cells	Pepsin(ogen)
	Gastric lipase
D cells	Somatostatin
G cells	Gastrin

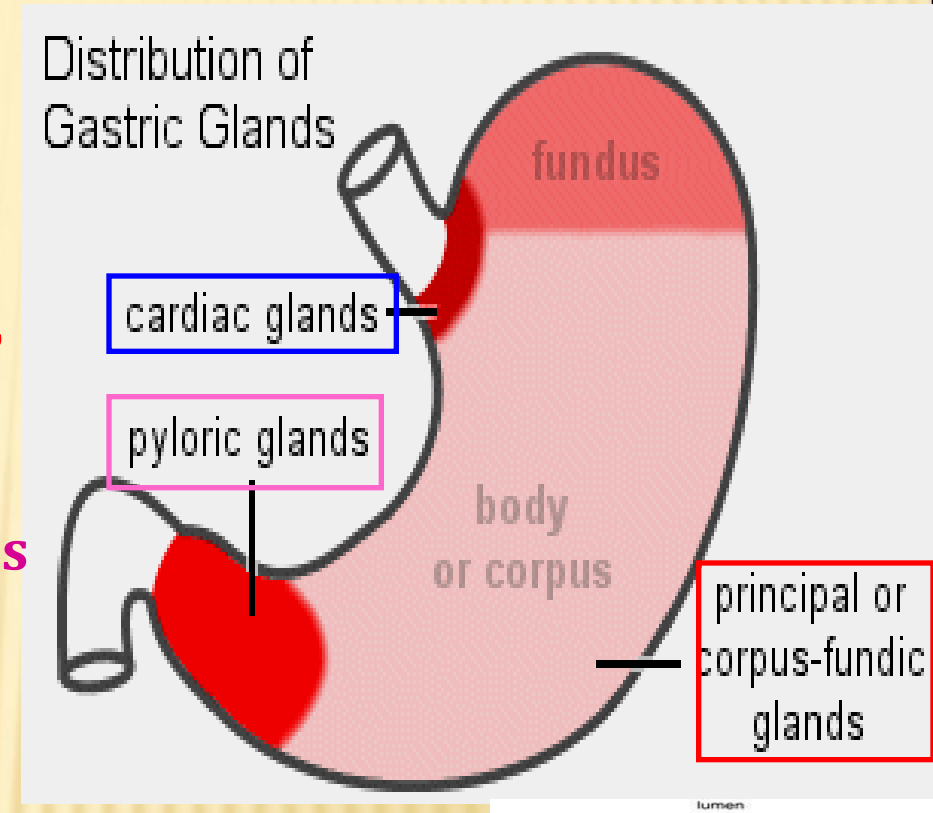
Types of gastric glands

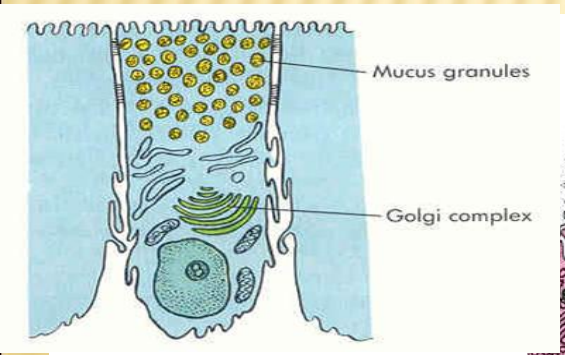
➢There are 3 types depending on their localization in stomach wall:

✓ Cardiac glands, that contain mainly mucous neck cells

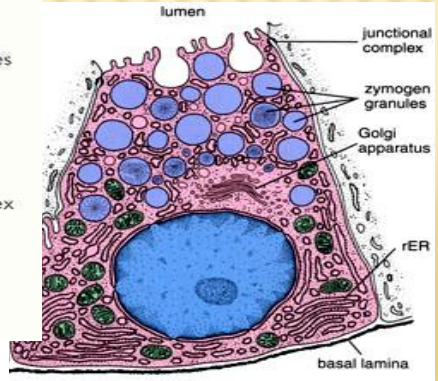
✓ Principal or Corpus-fundic glands, that contain all 4 types of gastric secreting cells

✓ Piloric glands, that contain mucous neck and endocrine cells

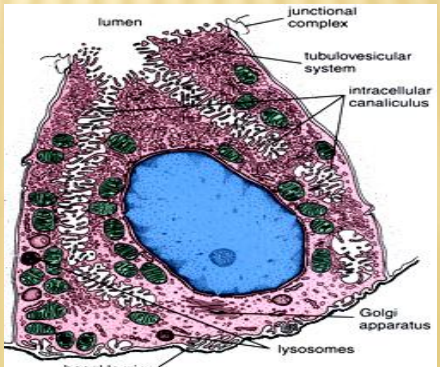




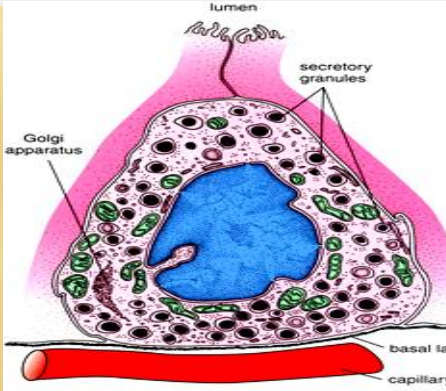
Mucous neck cell



Chief cell



Parietal cell



Endocrine cell

Mechanism of secretion of HCl by parietal cells

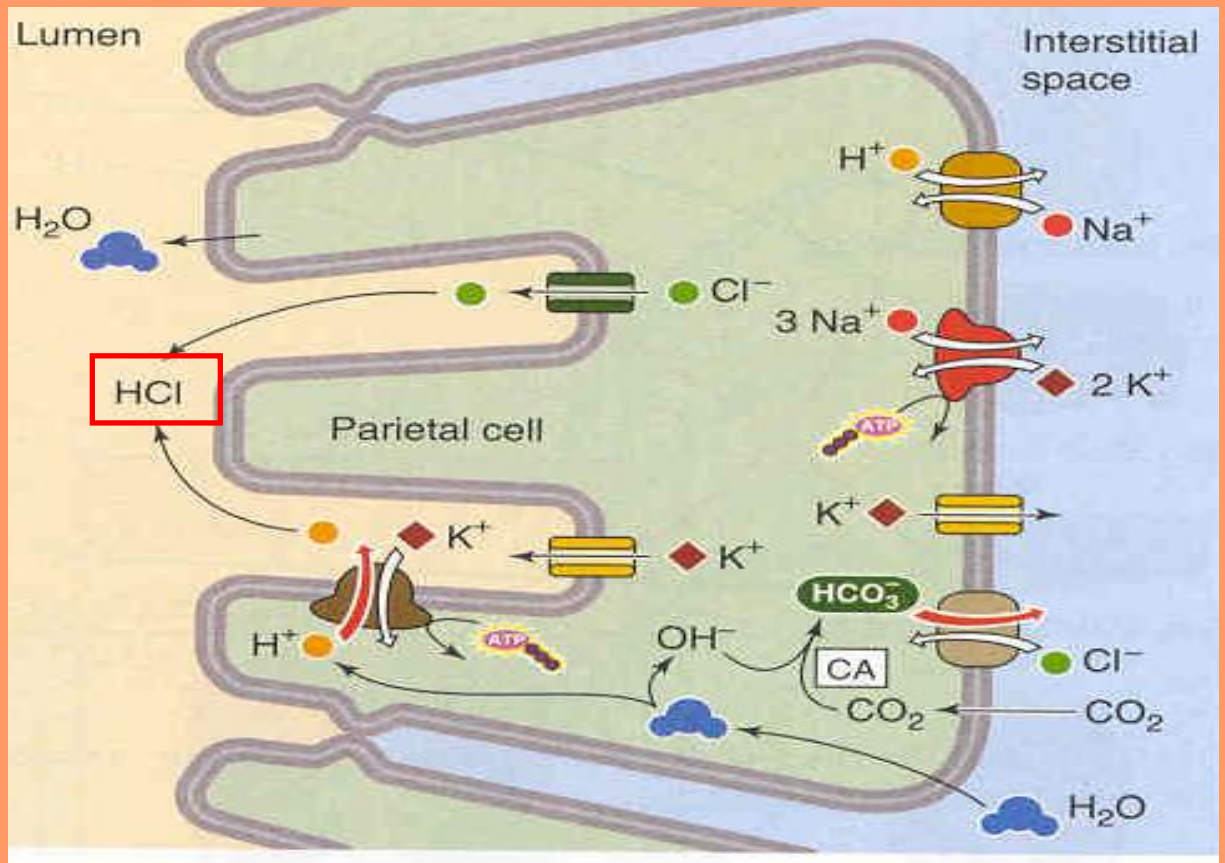
❖ **Secretion is active process (hydrolysis of ATP).**

✓formation of HCO_3^- and H^+ into the cells under action of carbonic anchydrase

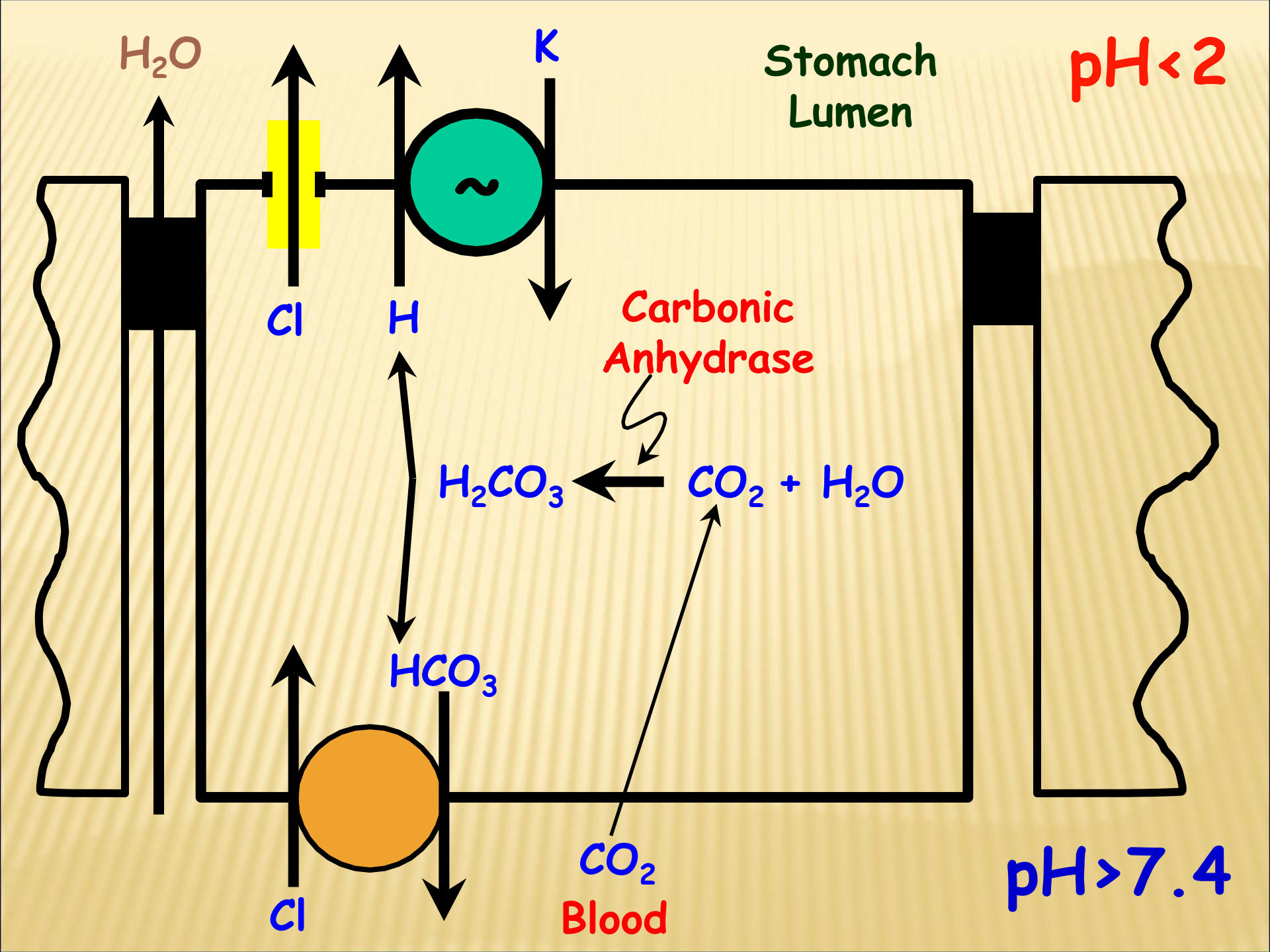
✓H^+ pump out from the cells into the lumen by K^+/H^+ pump (ATPase)

✓ HCO_3^- are reabsorbed into the blood through the basolateral membrane – exchange of Cl^- by HCO_3^-

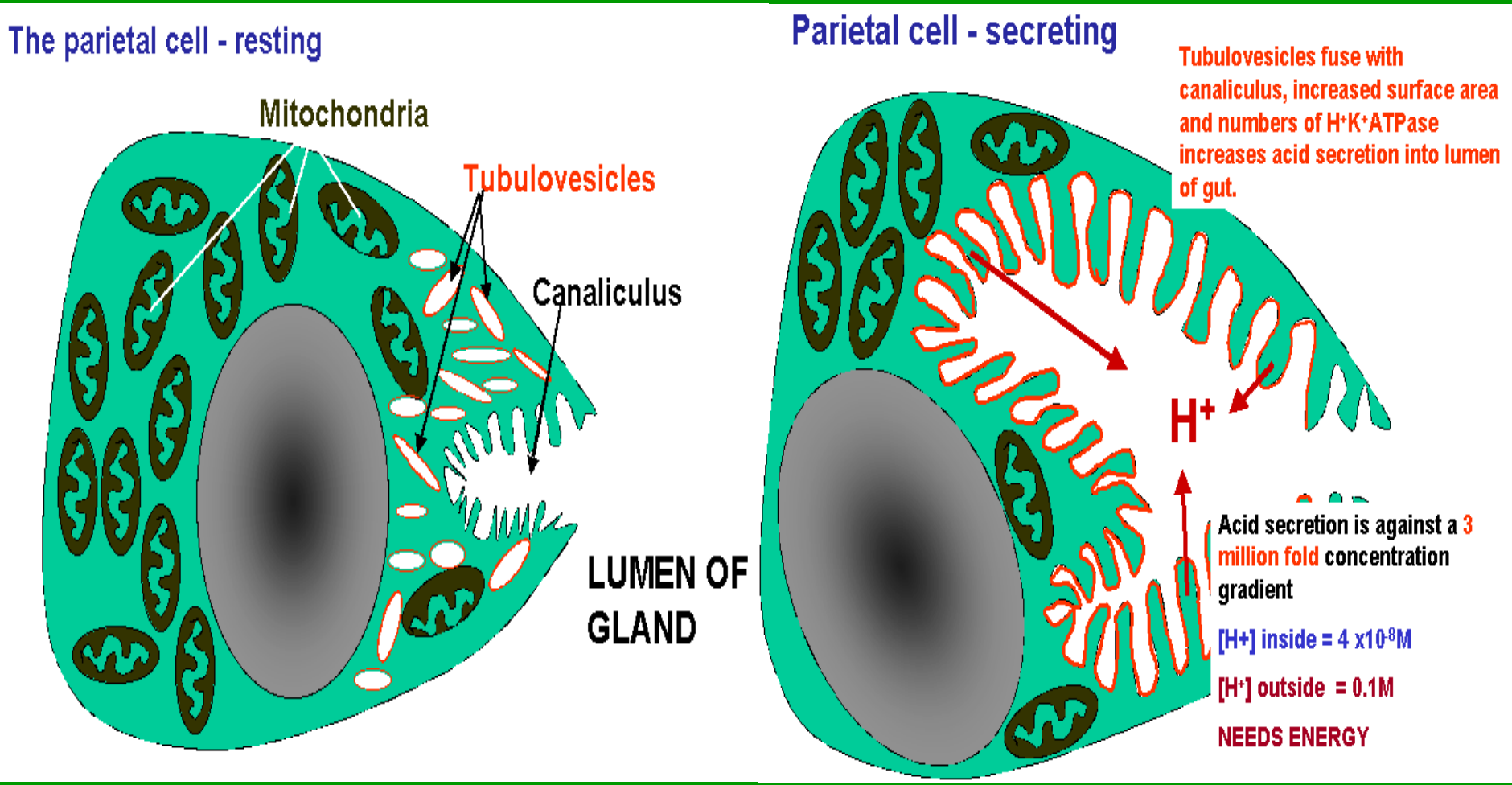
✓ Cl^- go out from the cells trough Cl channels of apical membrane under concentration gradient



❑ **Secretion of H^+ and Cl^- causes going of water out from the cells into the lumen.**


H_2O
K
Stomach
Lumen
pH<2
Cl
H
Carbonic
Anhydrase
H_2CO_3
$CO_2 + H_2O$
HCO_3
Cl
CO_2
Blood
pH>7.4

Secretion of hydrochloric acid



Functions of HCl

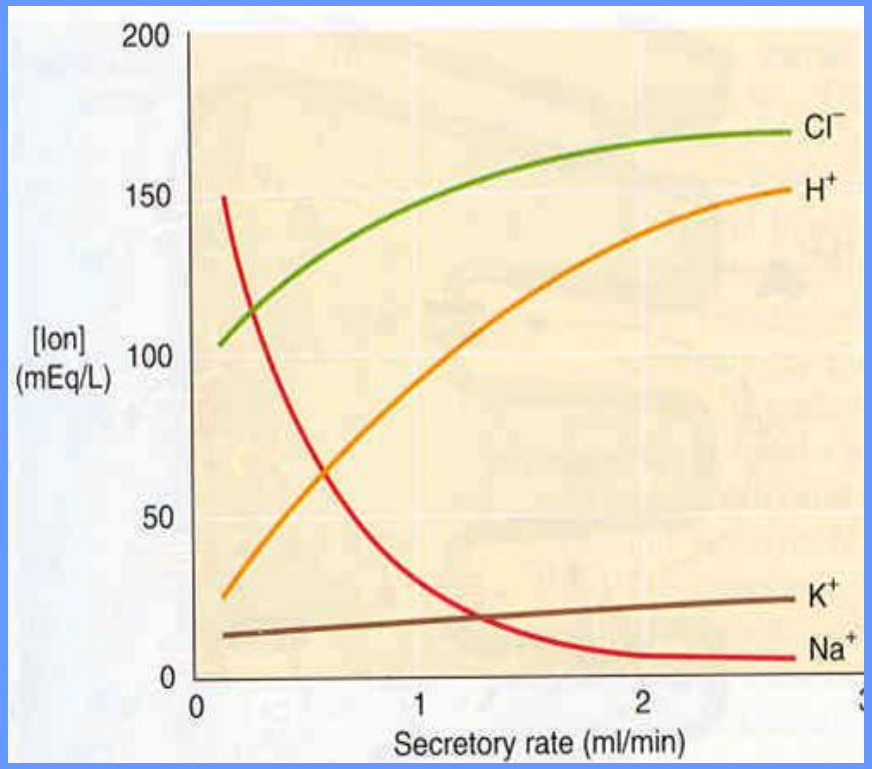
- ✓ denaturation of proteins
- ✓ bactericid action
- ✓ acidic pH causes activation of pepsinogen to pepsin

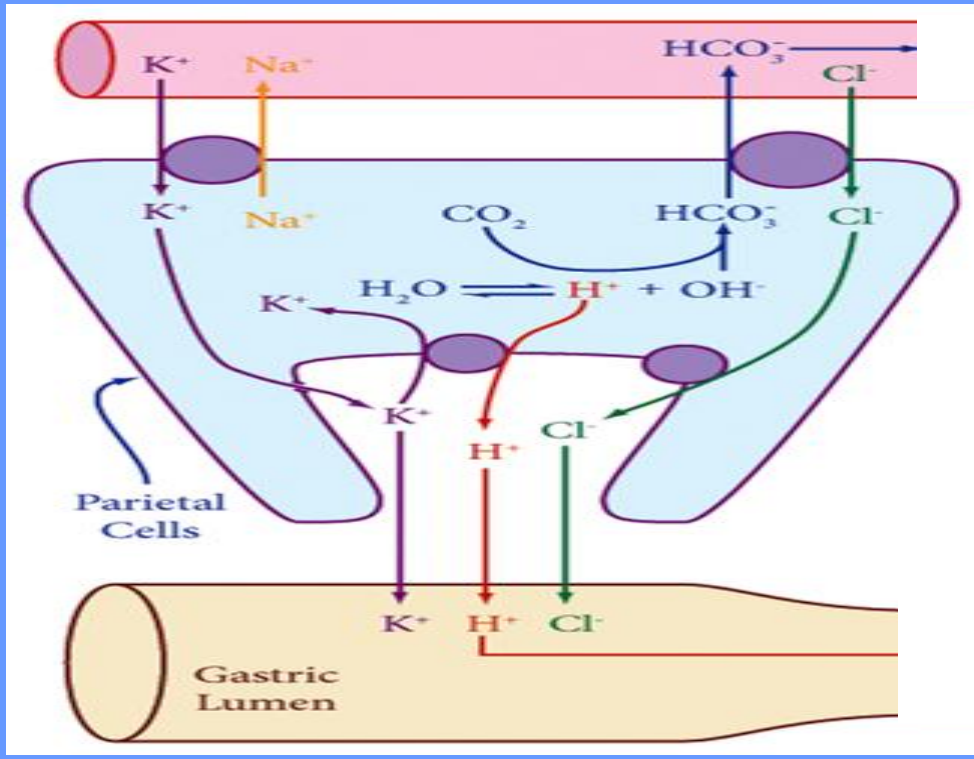
❖ **The content of ions in stomach juice depends on the speed of its secretion.**

➢ **The high rate of secretion increases concentration of H^+, Cl^-, K^+, and decreases Na^+ concentration.**

❑ **During stomach juice secretion HCO_3^- enter the venous blood "alkaline influx".**

During vomiting and loss of stomach juice metabolic alkalosis and hypokalemia occur.





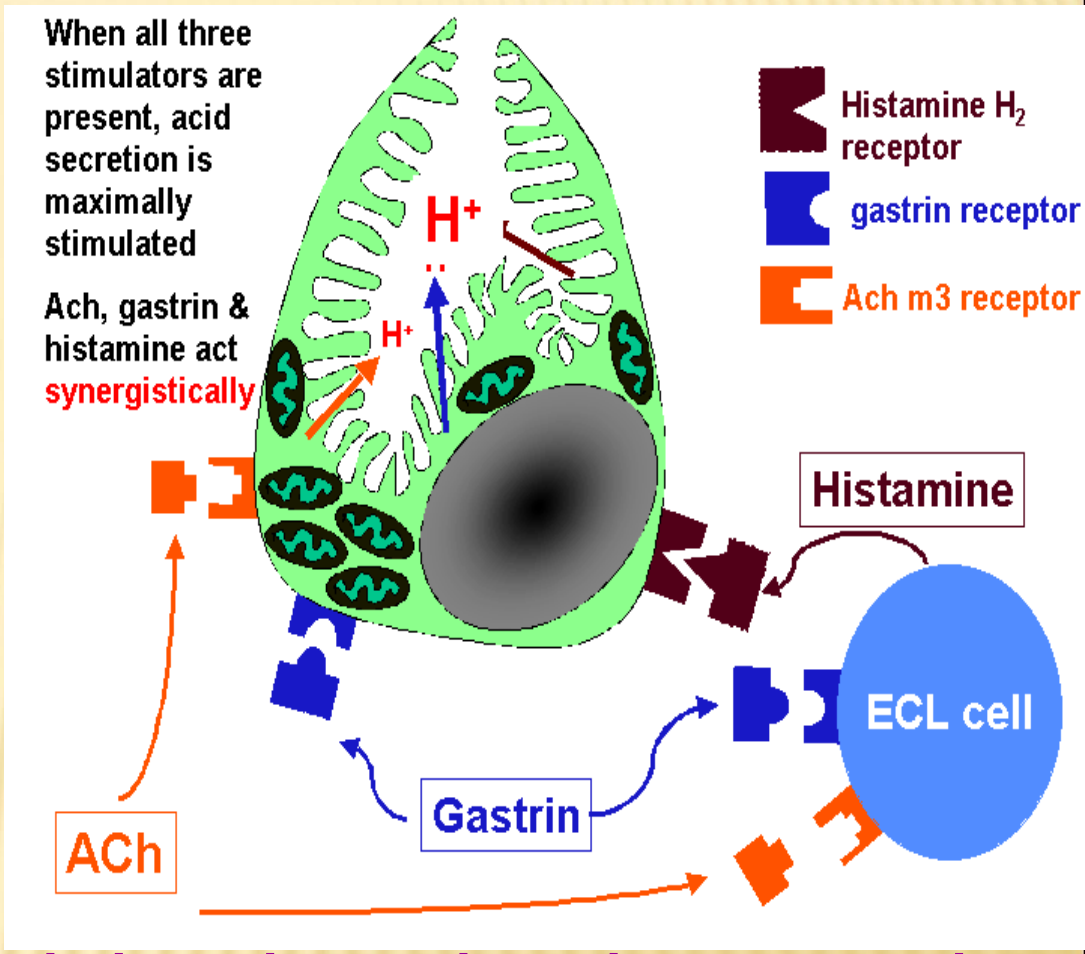
Control of HCl secretion

❖ Activation by:

➢ **Acetylcholine:** directly by ***M_3 receptors*** **(Ca^{2+})** and indirectly by activation of histamine secretion

➢ **Gastrin:** directly by ***CCK_B receptors*** **(Ca^{2+})** and indirectly by activation of histamine secretion

➢ **Histamine:**
H_2 receptors (cAMP)



❑ **These 3 factors have synergistic action and maximum secretion occur during their simultaneous action.**

❑ **Mechanism of activation: fuse of tubulo-vesicular system with membrane of secretory canaliculi.**

▪ **The same stimuli cause activation of intrinsic factor of Castle secretion.**

Secretion of HCl is inhibited by:

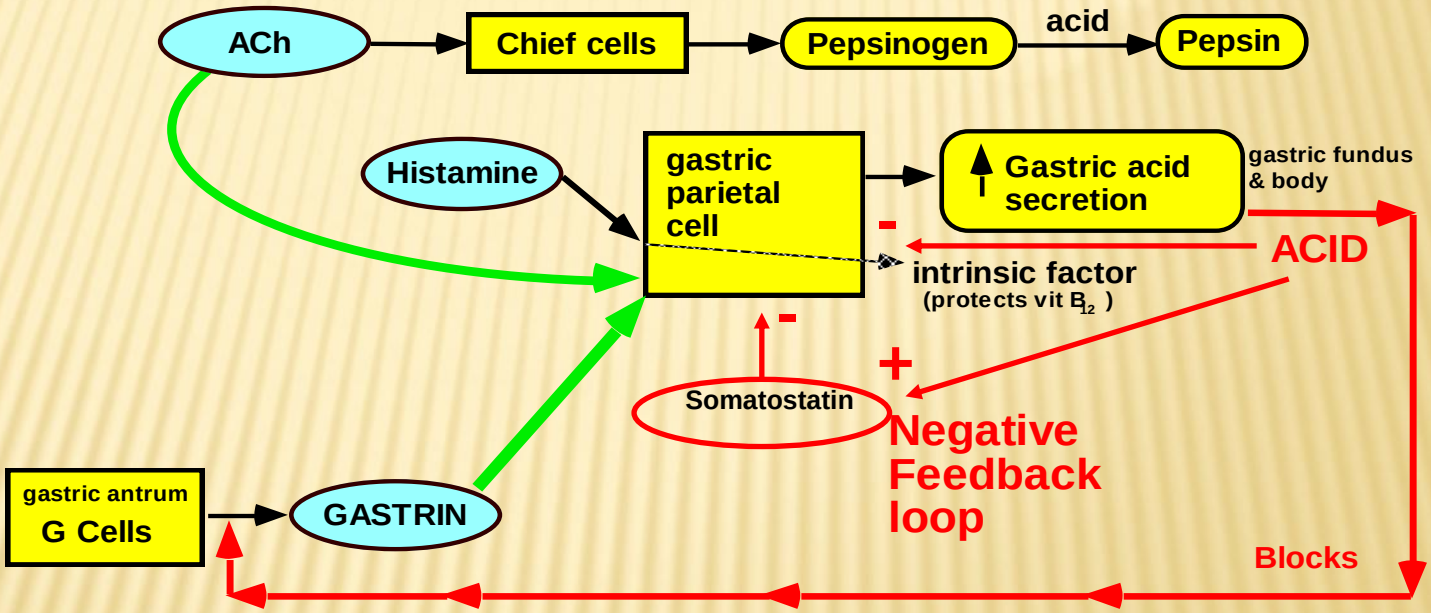
❖ **Gastric factors:**

➢ Somatostatin – direct inhibition (cAMP) and indirect (influence on the secretion of gastrin and histamine)

➢ **Prostaglandin E_2 (↓cAMP)**

➢ **pH < 2 – *negative feedback loop*, direct inhibition**

➢ **reflex and hormonal control by: ↑somatostatin, ↓gastrin**

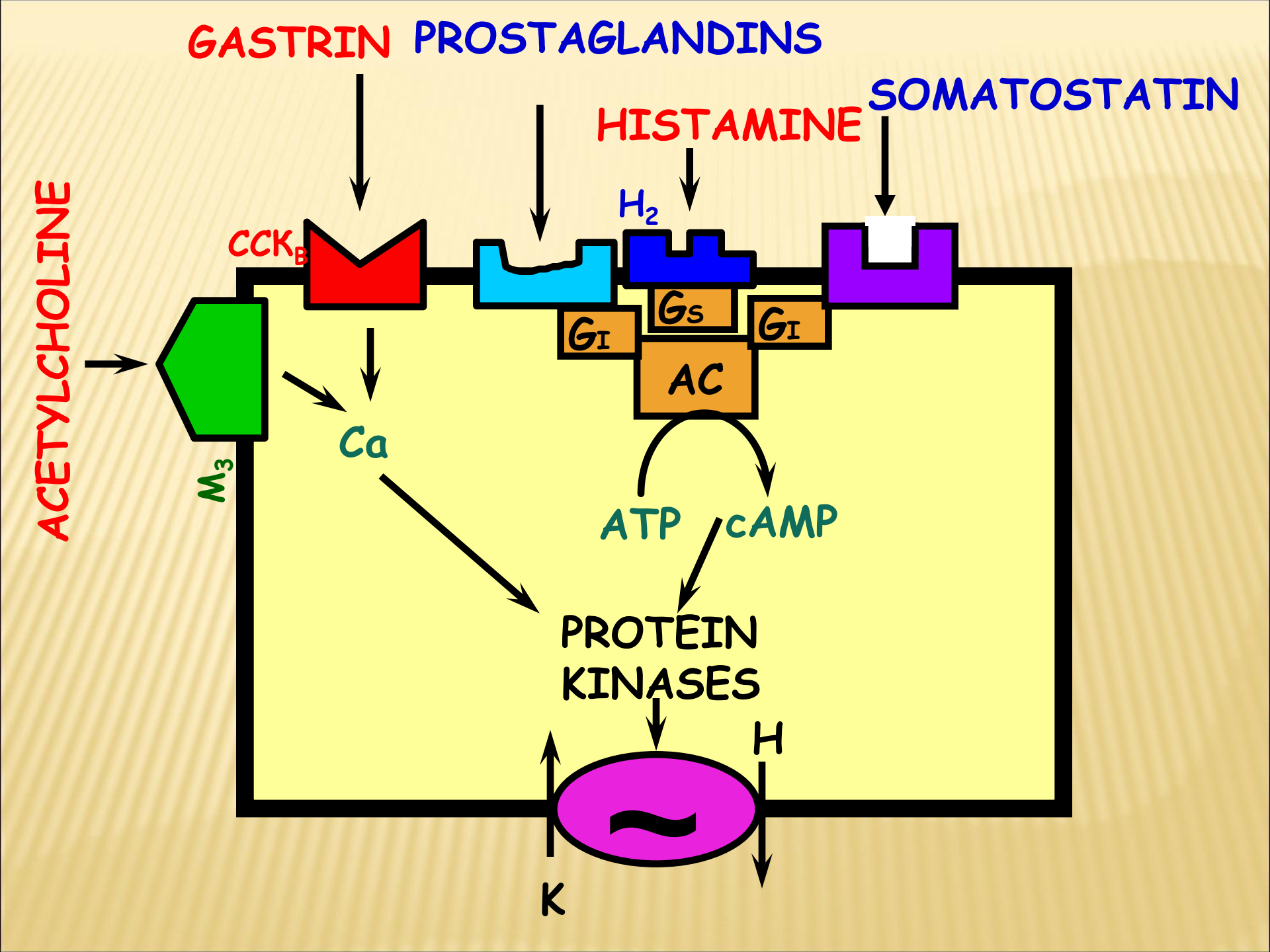


❖ **intestinal factors:**

❖ **low pH; increase of osmolarity and quantity of breakdown products**

hormonal control by:

✓ secretin ✓ cholecystokinine ✓ gastrin inhibitory hormone (GIP)


GASTRIN
PROSTAGLANDINS
SOMATOSTATIN
HISTAMINE
ACETYLCHOLINE
H_2
CCK_B
G_I
G_S
G_I
AC
M_3
Ca
ATP
cAMP
PROTEIN KINASES
H
K

Secretion of pepsinogens

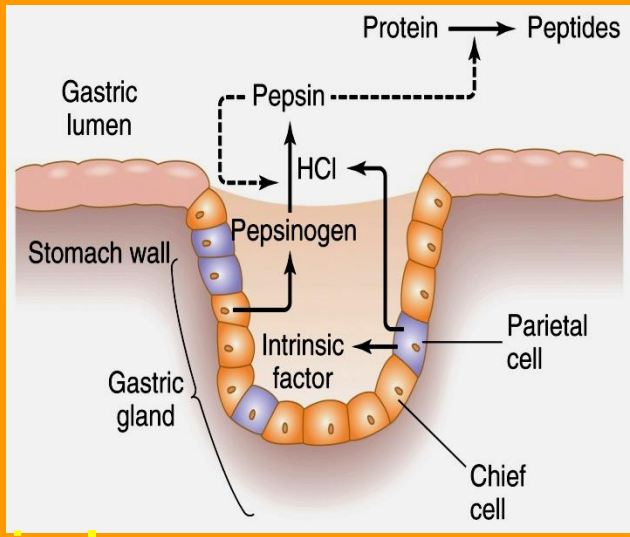
❖ **Pepsinogens, secreted by cheef cells, under low pH covert into pepsin.**

➢ optimum pH for activation is < 3

if pH is > 3,5 – reversible inactivation

if pH is > 7,2 - irreversible inactivation

❑ Pepsin is endopeptidase that splits proteins to oligopeptides and small quantity of amino acids (pH optimum from 1.8 to 3.5).



❖ **Acetylcholine, realized during parasympathetic stimulation is the main physiological stimulus for secretion of pepsinogens.**

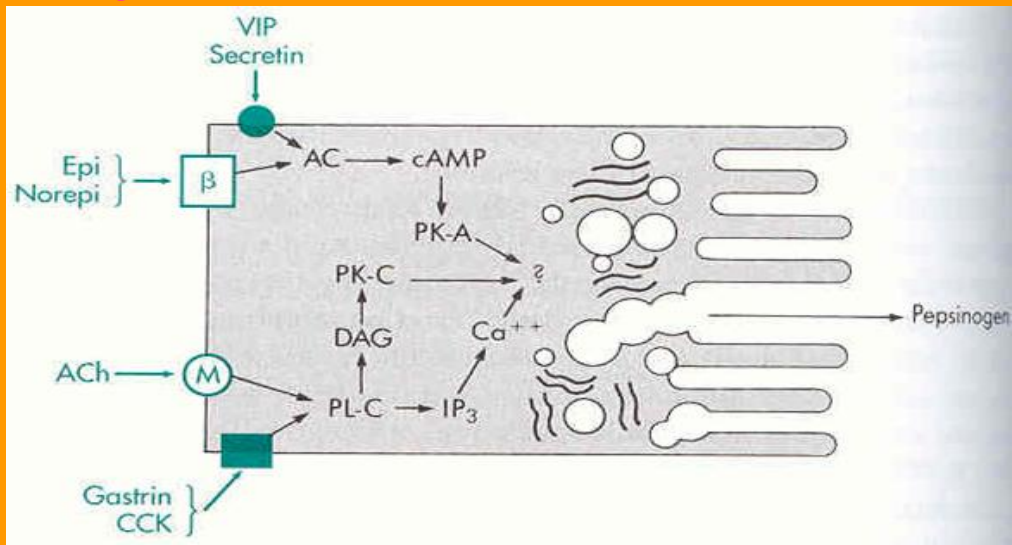
➢ Secretion is stimulated also and by:

✓ Secretin
✓ VIP
✓ Adrenalin and NA (β_2)

} cAMP

✓ Cholecystokinin
✓ Gastrin

} Ca^{2+}

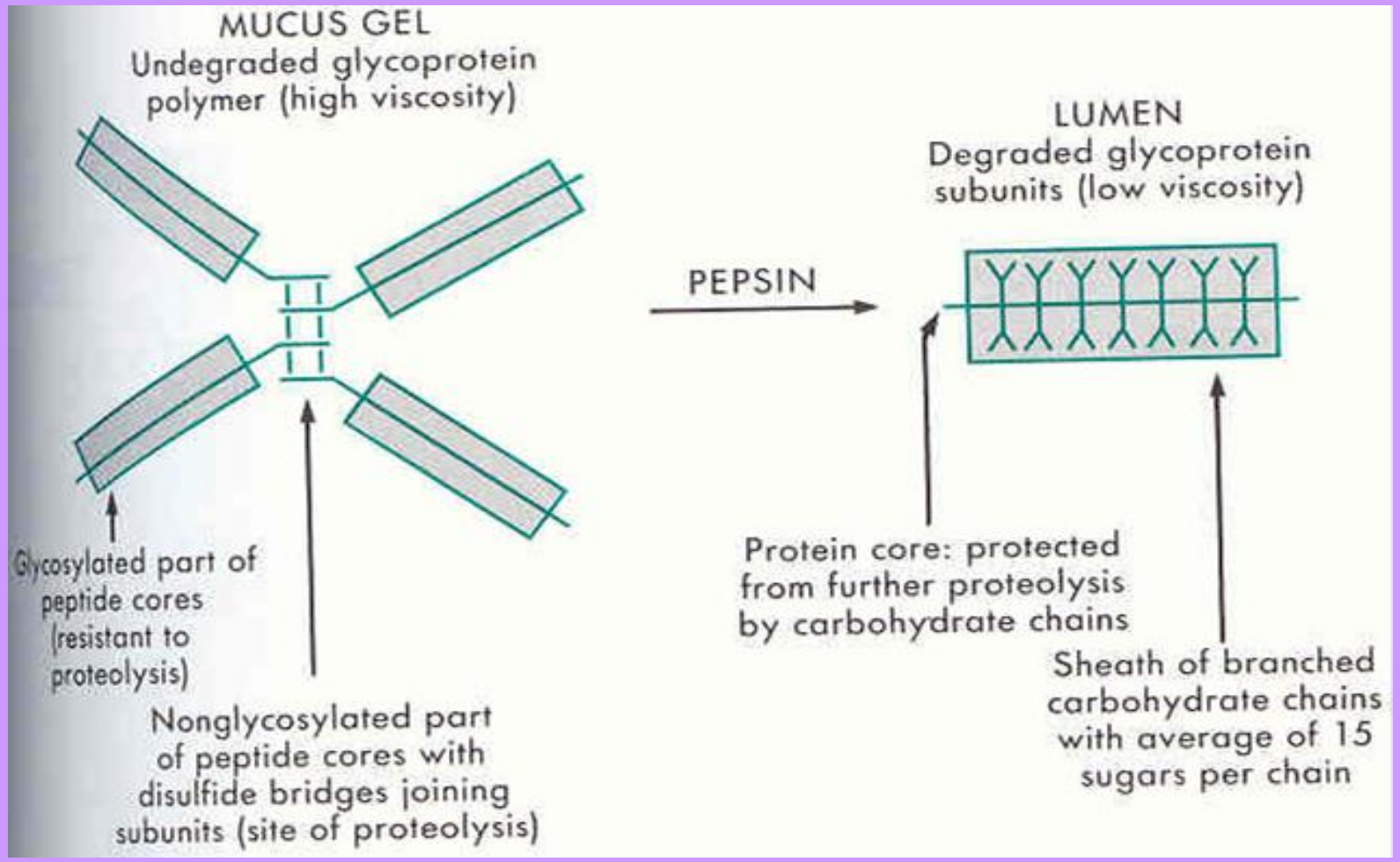


Secretion of mucus into stomach

- Mucus is a glycoprotein.

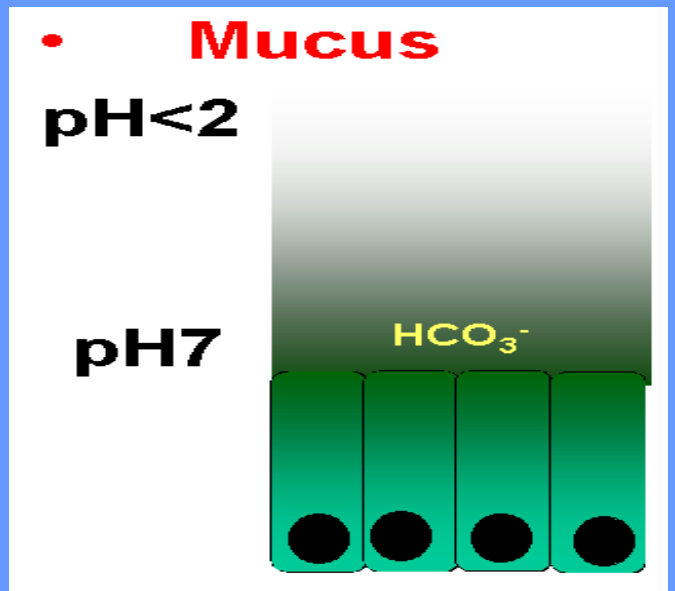
➢Mucus forms gel (50-450 µ) tightly attached to the surface of epithelium.

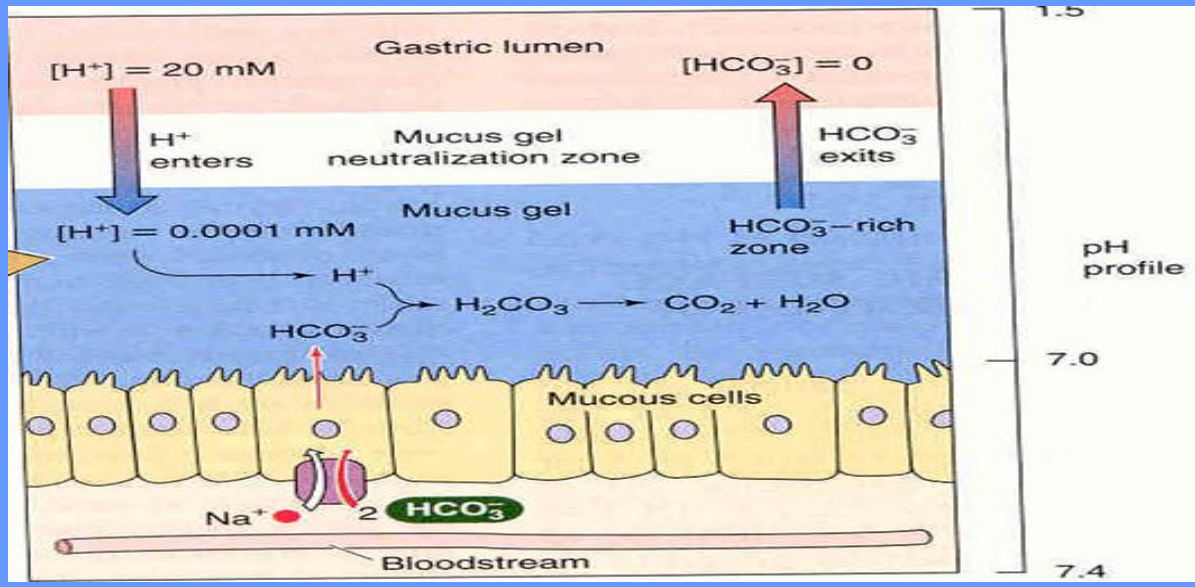
- Its function is protection from the action of enzymes, toxins and cancerogenic agents.



Secretion of HCO_3^- into the stomach

- HCO_3^- are secreted by epithelial cells
  - HCO_3^- diffuse into mucus gel
  - they neutralize H^+, diffused into mucus, and maintain pH near to epithelial cells ~7, whereas pH into the lumen is ~2
- secretion of mucus and HCO_3^- is stimulated by:
  - ✓ Parasympathicus
  - ✓ distension of stomach wall and low pH into the lumen
  - ✓ prostaglandins
- secretion is inhibited by α-adrenomimetics



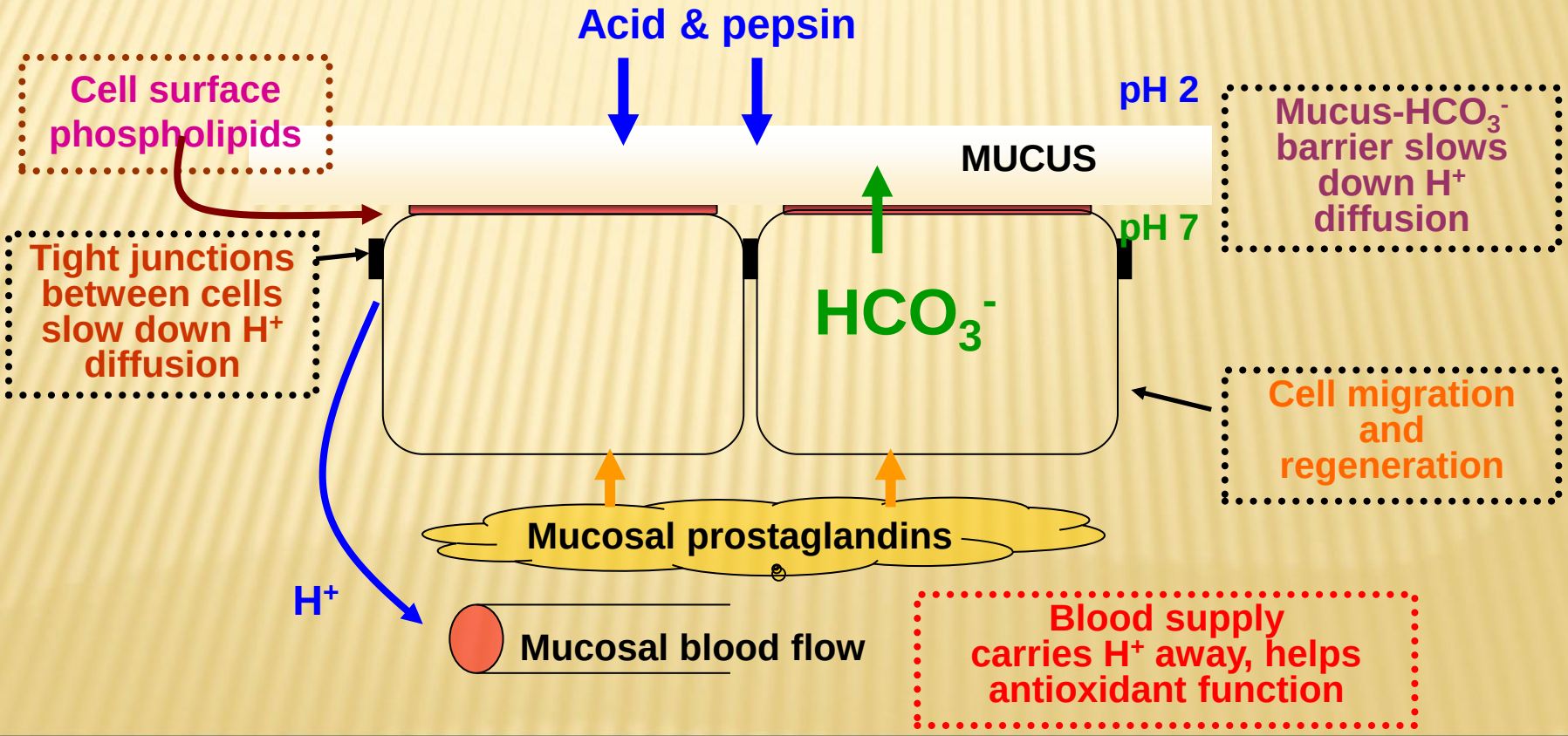


The stomach epithelial barrier

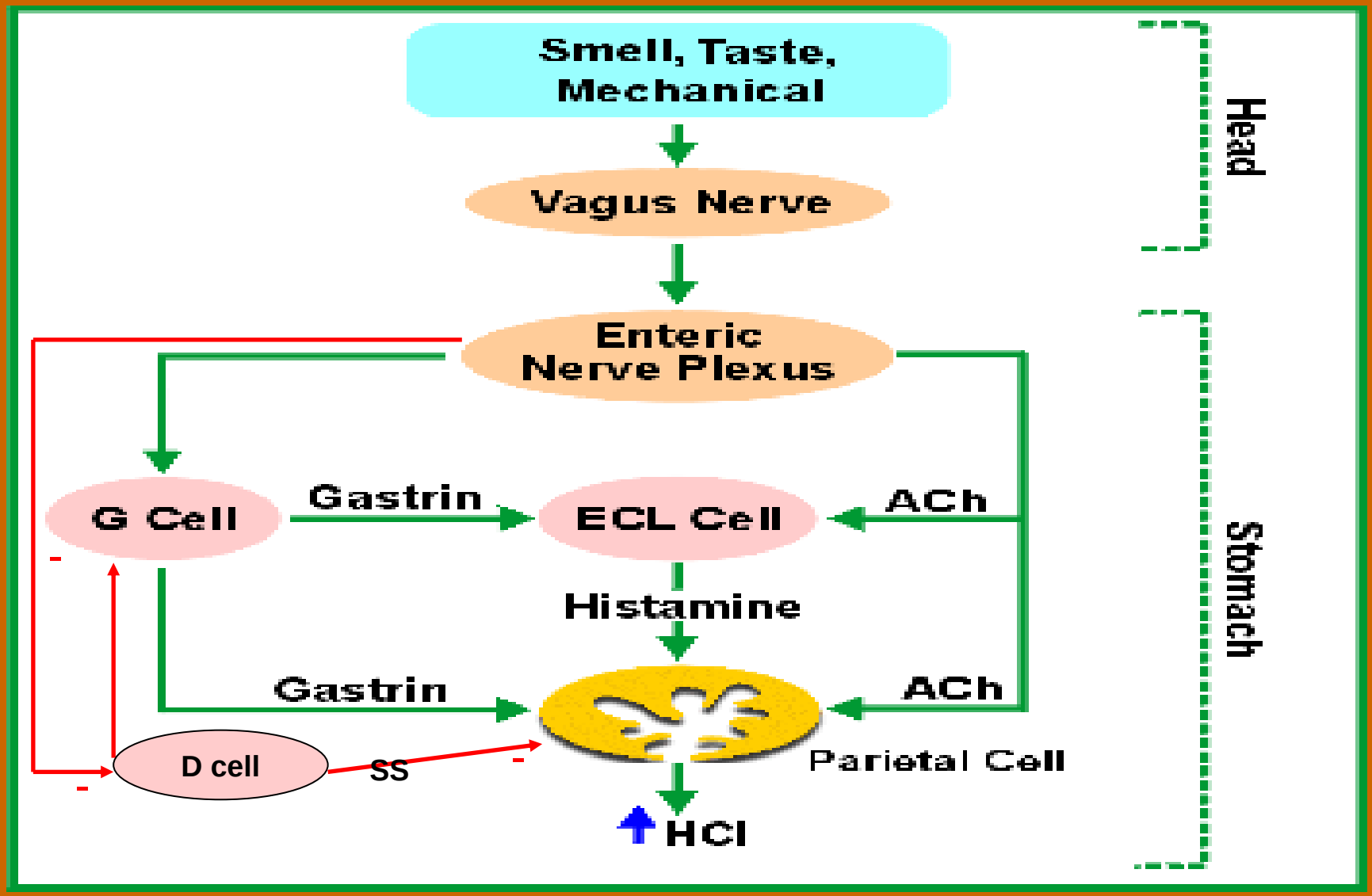
❖ protection of stomach mucosa from action of HCl, pepsin, toxins and the other injuring agents

➢ Barrier is due to:

* relative impermeability of apical membrane of epithelial cells for H^+
* mucus gel
* secretion of HCO_3^-
* Mucosal blood flow
* cell regeneration
* production of prostaglandins



Control of gastric juice secretion



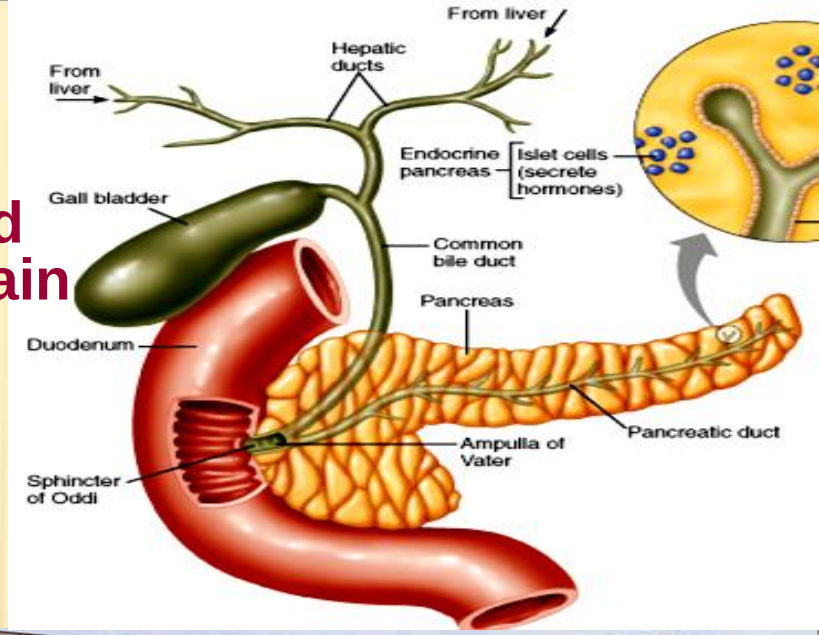
CONTROL OF STOMACH JUICE SECRETION

- **Cephalic phase** (30% of secretion)
  type, smell or mind for food
  signals from taste or mechanoreceptors of mouth

- **Gastric phase** (60% of secretion)
  stimuli: n. vagus (Ach), gastrin, histamine, caffeine
  inhibition by increased tone of simpathicus

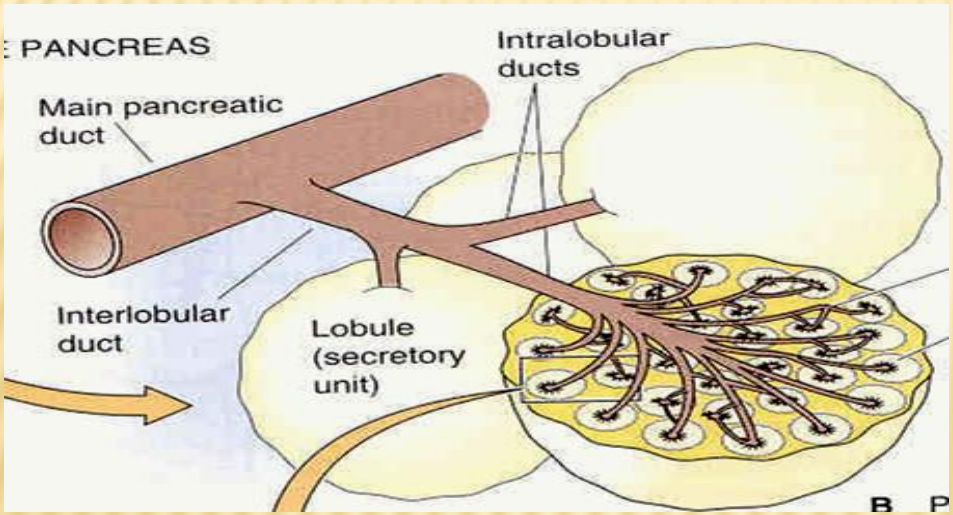
- **Entheral phase** (10% of secretion)
  stimulation by gastrin
  inhibition by: secretin,CCK, VAP, GIH, somatostatin

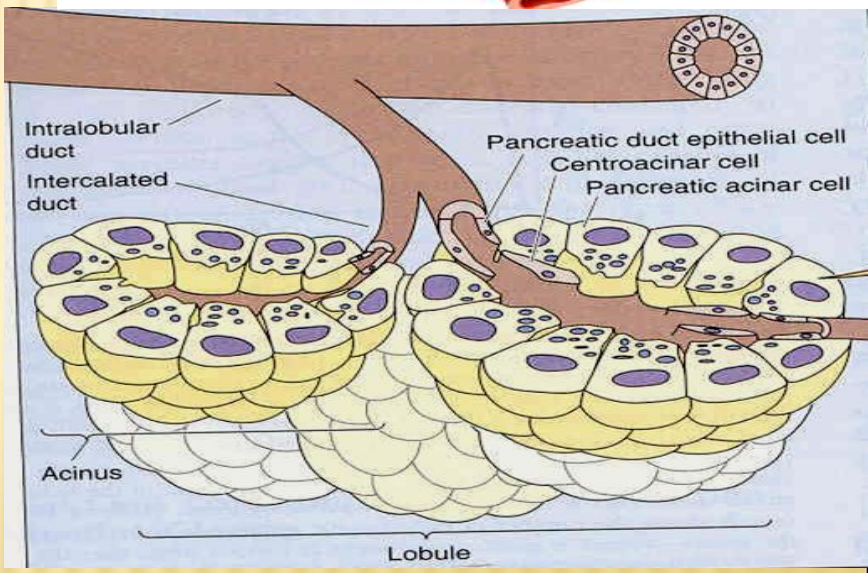
Pancreatic juice



- **Exocrine pancreas contains acini and ducts: intercaleted, intralobular and main pancreatic duct.**

- **basic unit – lobule: acini, connected with 1 intralobular duct**





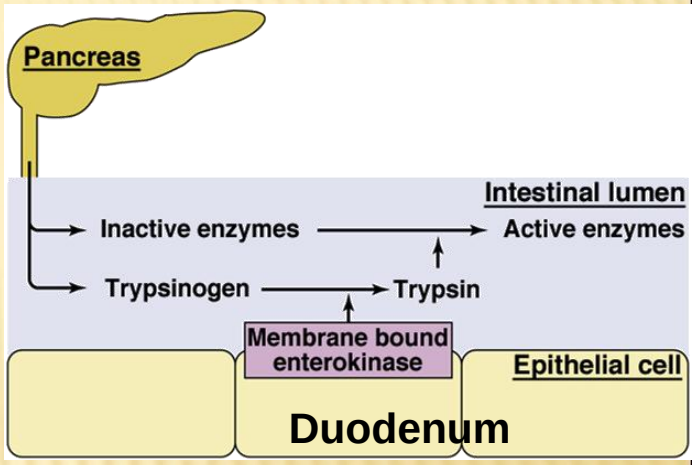
Innervation:

Parasympathicus – n.vagus (Ach and VAP); effect: activation of secretion

Sympathicus (NA); effect inhibition of secretion

Volume, content and functions of pancreatic juice

- volume – 1.5- 2.5 l/ 24h, pH 7,1 - 8,8
- content - water, electrolytes, enzymes



➢ enzymes:

Proteolytic enzymes - trypsin, chymotrypsin, elastase-split proteins to polypeptids; carboxipeptidases A and B-cleft end AA from protein chain. They are secreted in inactive state that protects pancreas from autodigestion. They are activated into duodenum by enterokinase.

Lipolytic enzymes –lipase,cholesterolesterase,phospholipase A_2.

Amilolytic enzyme – alfa-amilase splits polysaccharides to glucose and maltose

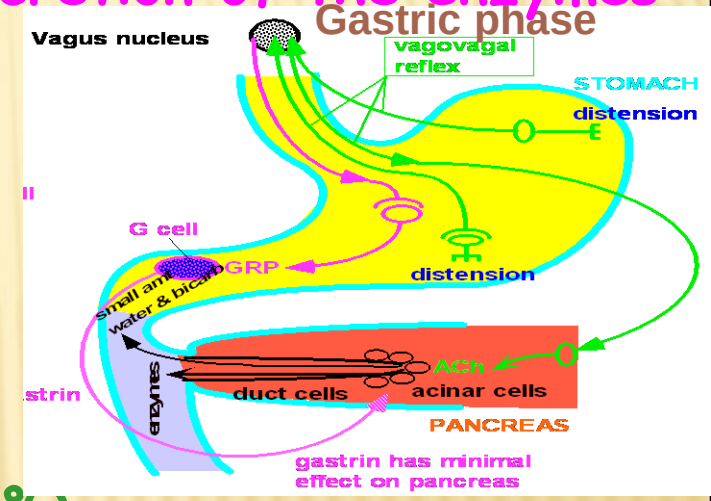
Nucleases –ribonuclease and desoxiribonuclease

- the other proteins of pancreatic juice:
  - tripsin inhibitor
  - immunoglobulins

Control of pancreatic secretion

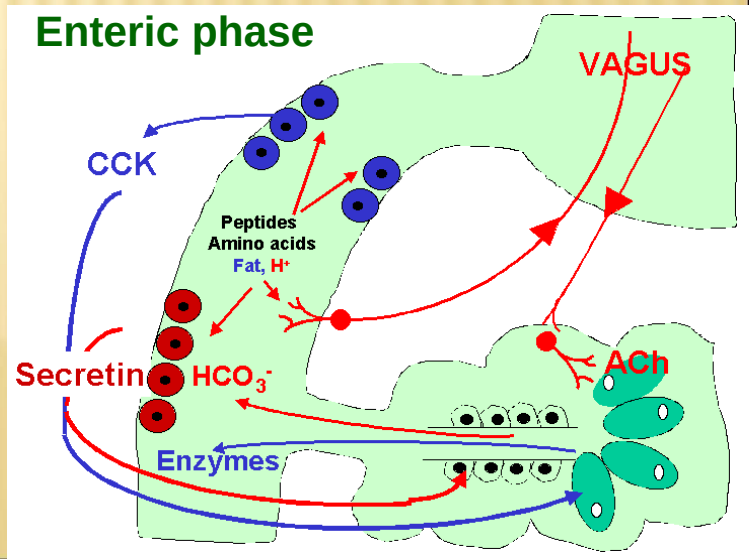
- **Cephalic phase:** the same stimuli that control gastric secretion (25% of secreted juice)

eff. Pathway = n. vagus -> increases secretion of the enzymes



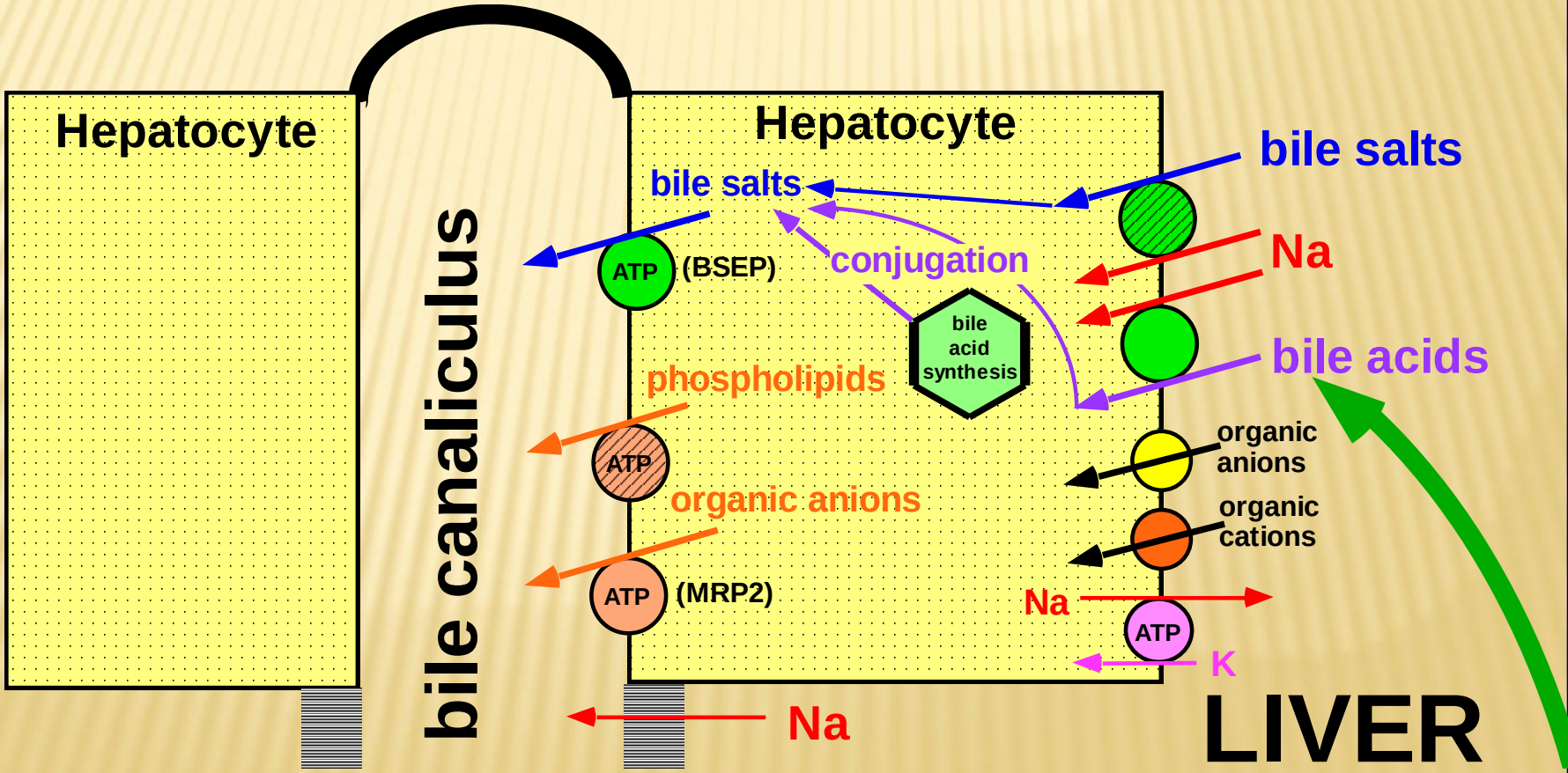
- gastric phase: irritation of mechanical and chemical receptors into stomach wall (10% of secreted juice)
  - is controled by:
    - ✓ n. vagus
    - ✓ Gastrin
- **enteral phase:** chyme into duodenum (65%)

- **stimuli for secretion:**
  - ✓ increased volume and osmolarity of duodenal content
  - ✓ acidic pH
  - ✓ breakdown products of lipids and proteins
  - control:
    - ✓ nervous control - n. vagus
    - ✓ hormonal control - CCK-pancreosimin and secretin



Secretion of bile - 500 -1200 ml / 24h

- **Formation of primary secret by hepatocytes :**
  - **active secretion of organic and inorganic substances into intralobular bile canaliculi following by passive transpot of water trough tight junctions**
- **The primary secret contains bile acids, pigments, cholesterol, phospholipides, organic ions and electrolytes.**

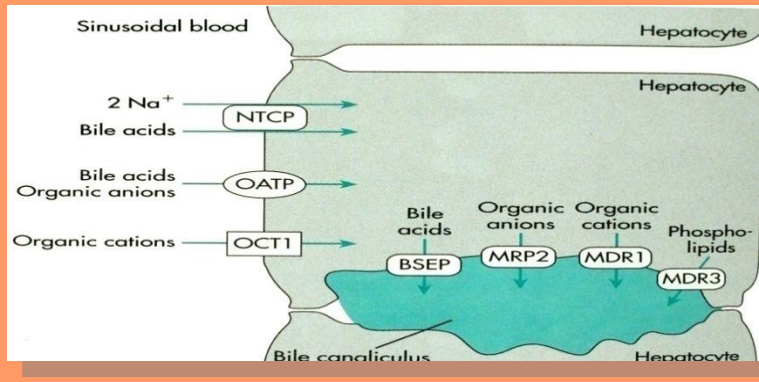


❖ **the rate of primary secret formation depends on the bile salts (BS) concentration**

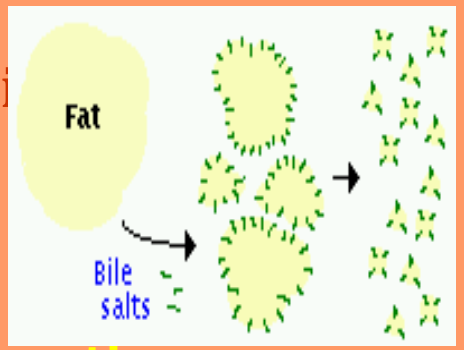
Bile acids (cholic and chenodeoxycholic) are synthesised from cholesterol.

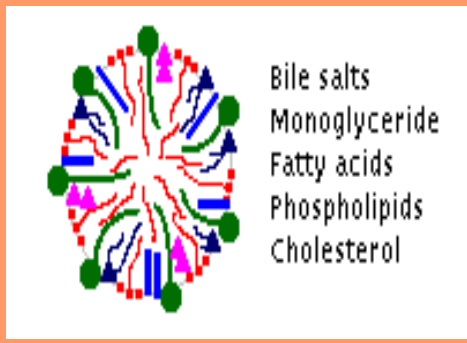
✓ secretion of bile acids (BA) across the apical membrane of hepatocytes uses ABC (ATP-Binding Cassette)transportes

✓ In GIT BA are conjugated with glycin and taurine and form BS with Na and K



▪ **BS are necessary for fats emulsifying and reabsorption of thei end breakdown products**





❑ **Stimulation of primary secret formation:**

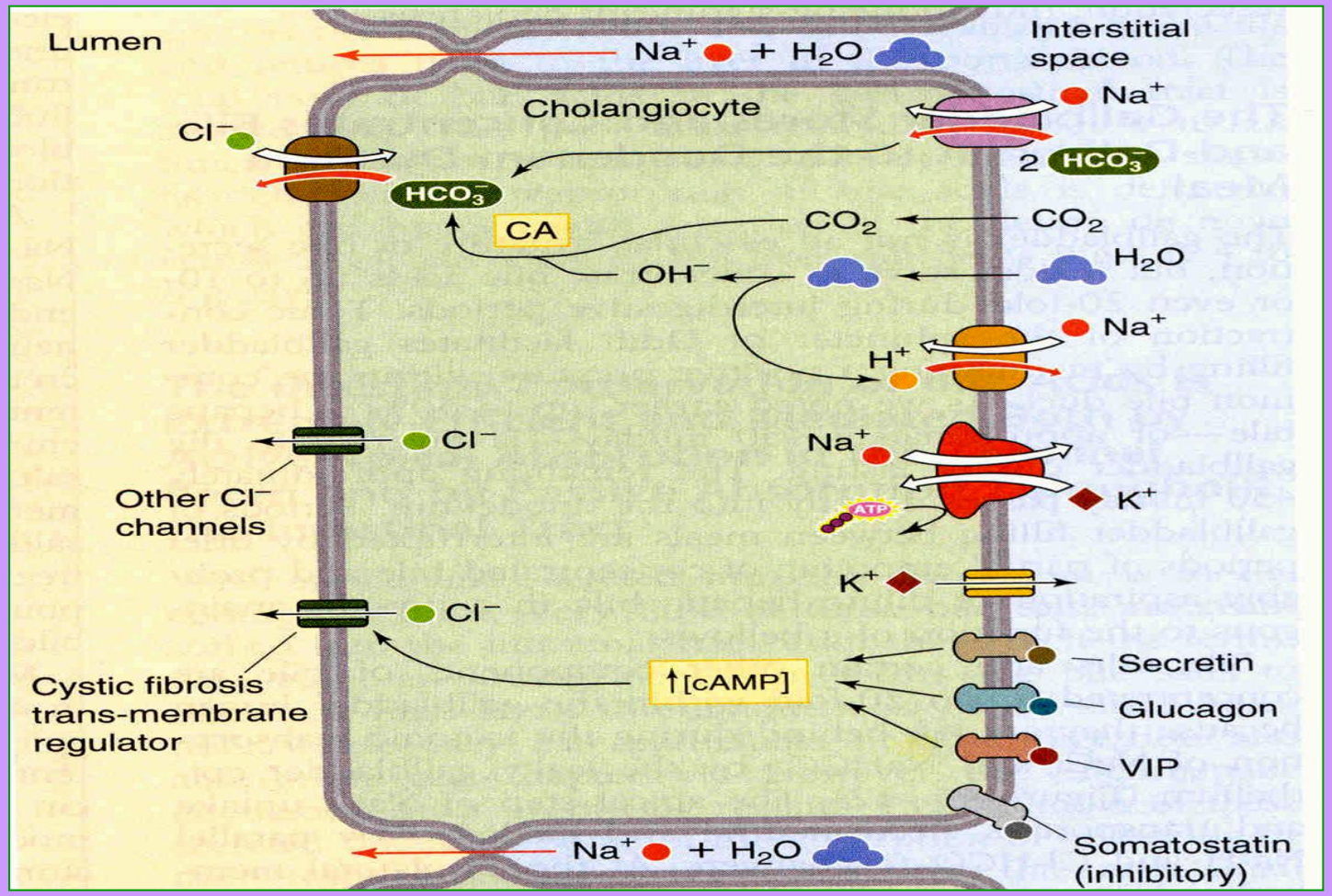
✓secretin

substances that increase bile secretion are called choleretics

✓inhibition of BA synthesis - by high BS concentration in the blood of vena portae, because of their reabsorption at ileum (enterohepatic circulation)

❖ **transformation of primary secret by the cells of extralobular ducts:**

➢ **their secret contains high [HCO_3^-] and low [Cl^-] ions concentration**

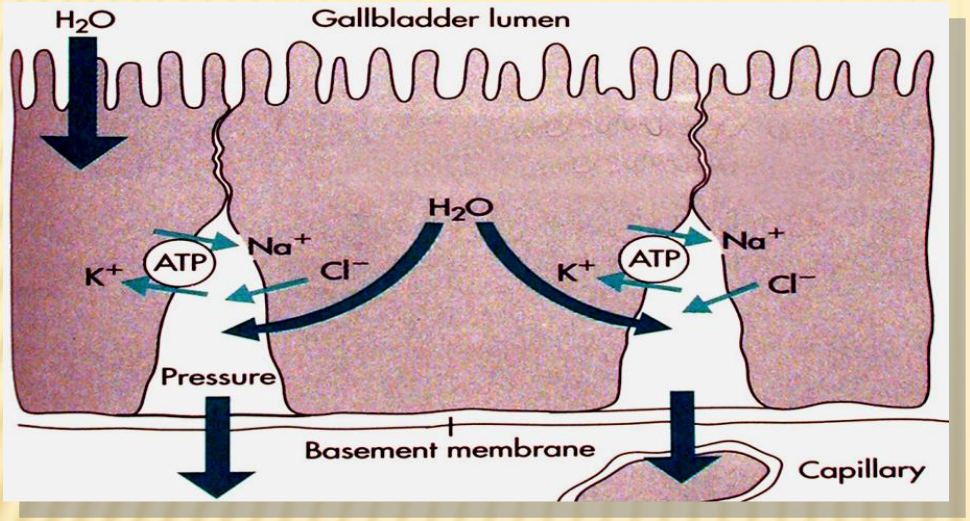


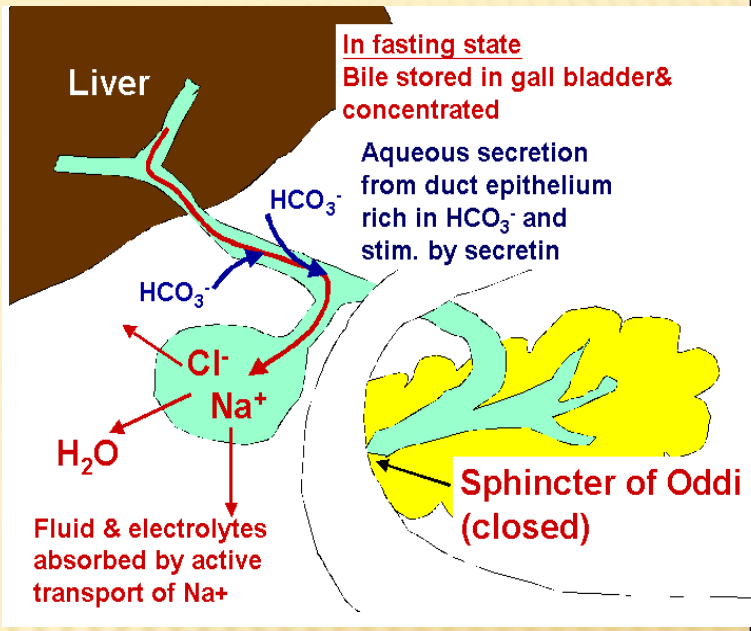
❑ **stimulating factors –secretin and VIP**

✓ **inhibiting factor - somatostatin**

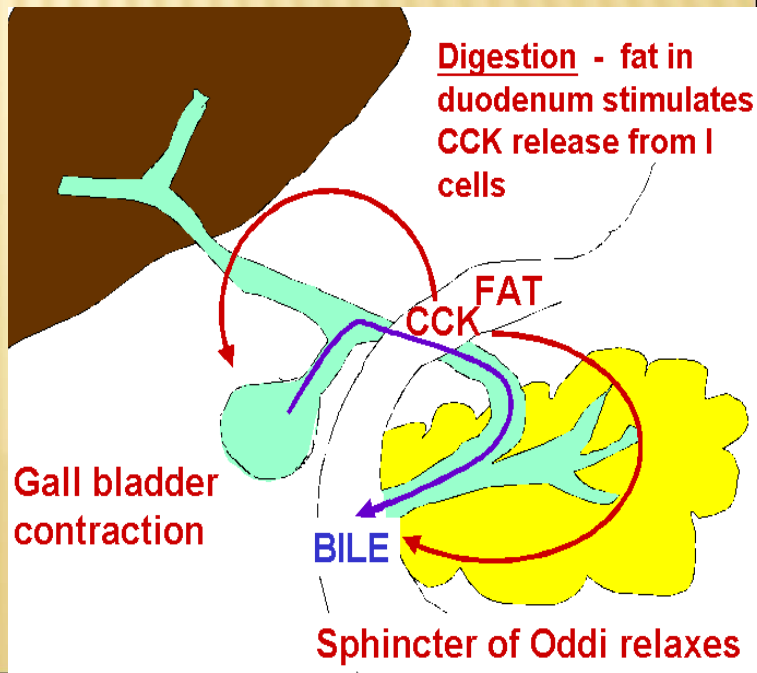
Function of gallbladder

- storage of the bile between having of meal
- concentration of the bile av. 20 tymes because of reabsorption of water and NaCl





- During digestion gallbladder contracts, spincter of Oddi is relaxed and bile enters duodenum.



Control by:

- ✓ N. Vagus
- ✓ Cholecystokinin

Volume, content and functions of small intestine juice

❖ volume – av. 1,5 l/24h ❖ content- mucus, electrolytes, water

❖ functions:

❖ 1. participation in digestive processes

✓maintenance of optimal pH into intestinal lumen for enzyme activation

✓ maintenance of appropriate surrounding on the bruch border of enterocytes for normal digestion and reabsorption

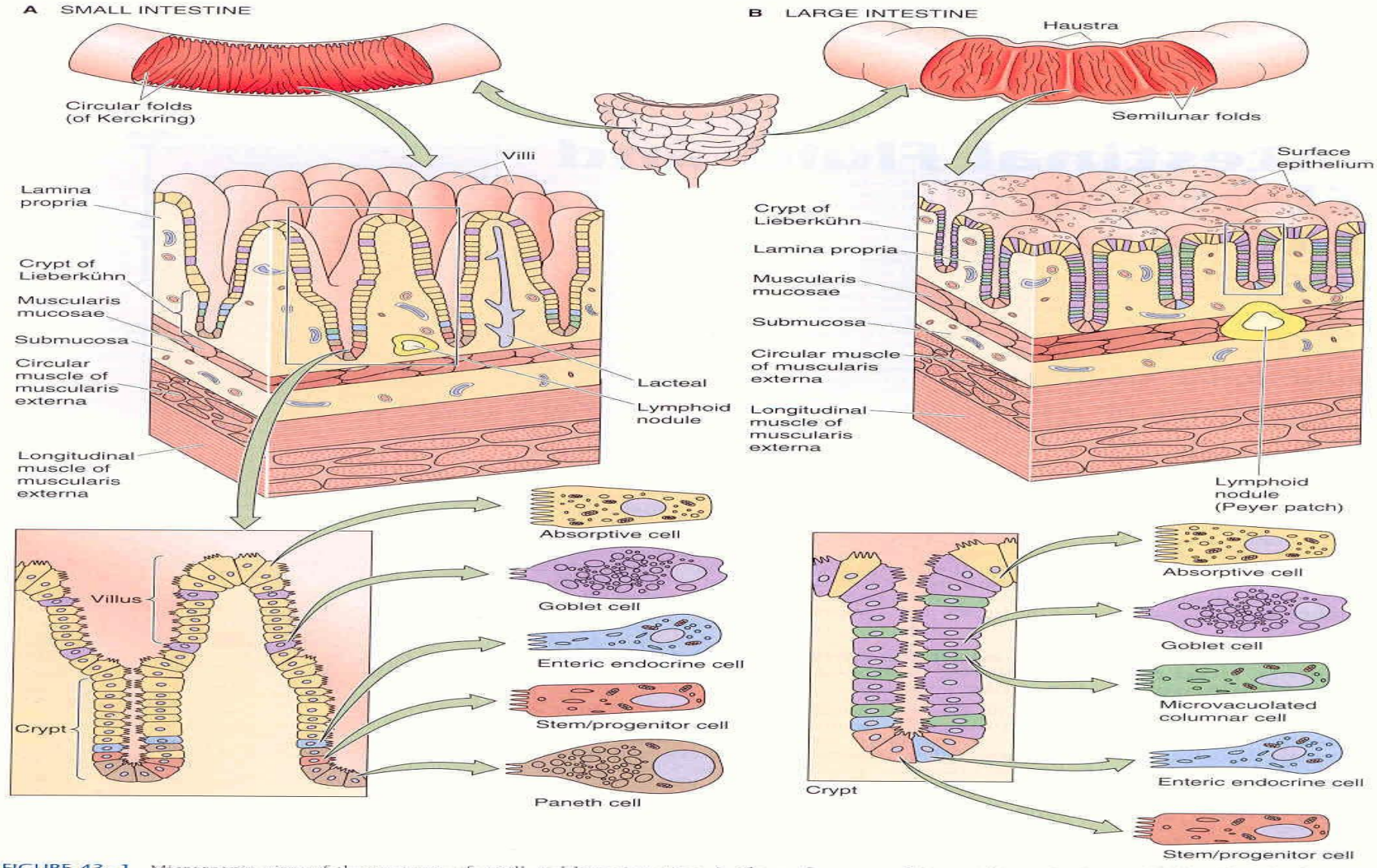
❖ 2. defensive function:

✓mucus- barrier for mechanical and chemical harmful agents

✓ water-electrolyte secretion – accelerates elimination of irritative agents, bacteria and their toxins

✓ antimicrobial substances – defensine, lisosym, that are secreted by the cells of Paneth

- secretion of mucus – by the Goblet·s cells
- secretion of water and electrolytes – by enterocytes



❖ **Into duodenum is secreted rich of HCO_3^- juice by the glands of Brunner**

❖ **The cells of Lieberkuhn's crypts secrete NaCl and water**

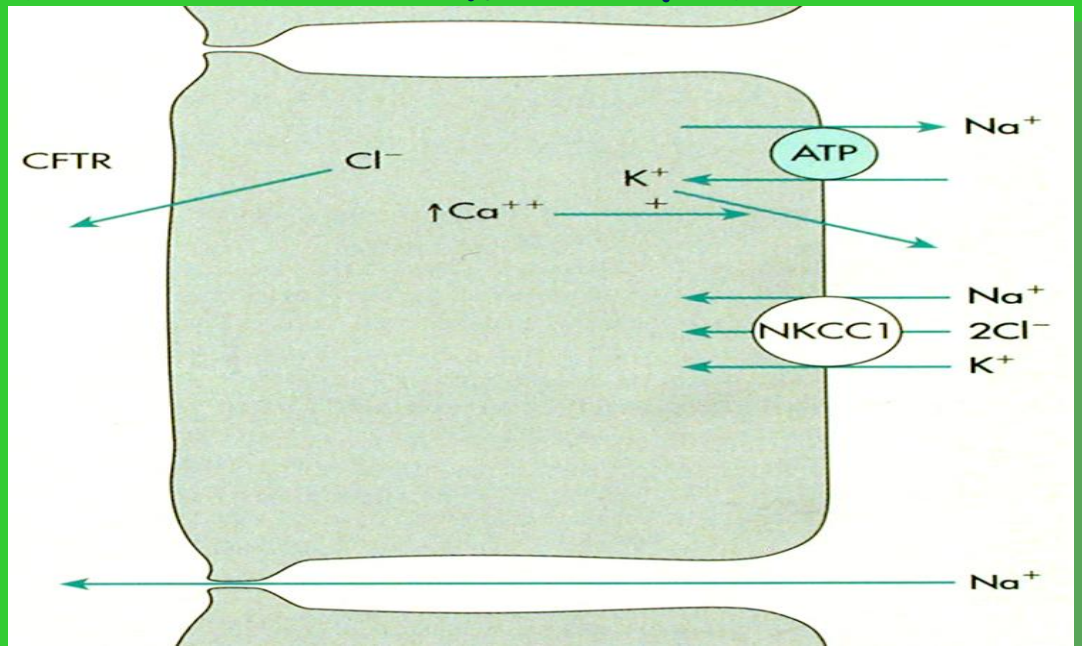
➢ **mechanism of secretion is similar to mechanism of secretion in salivary and pancreatic glands**

✓ **influx of Cl^- across basolateral membrane using secondary active transport mechanism (Na-K-2Cl transporter)**

✓ **eflux of Cl^- across apical membrane via Cl chanels (CFTR)**

➢ **secretion of Cl^- creates lumenal potential that causes paracellular secretion of Na^+**

➢ **secretion of NaCl causes osmosis of water**

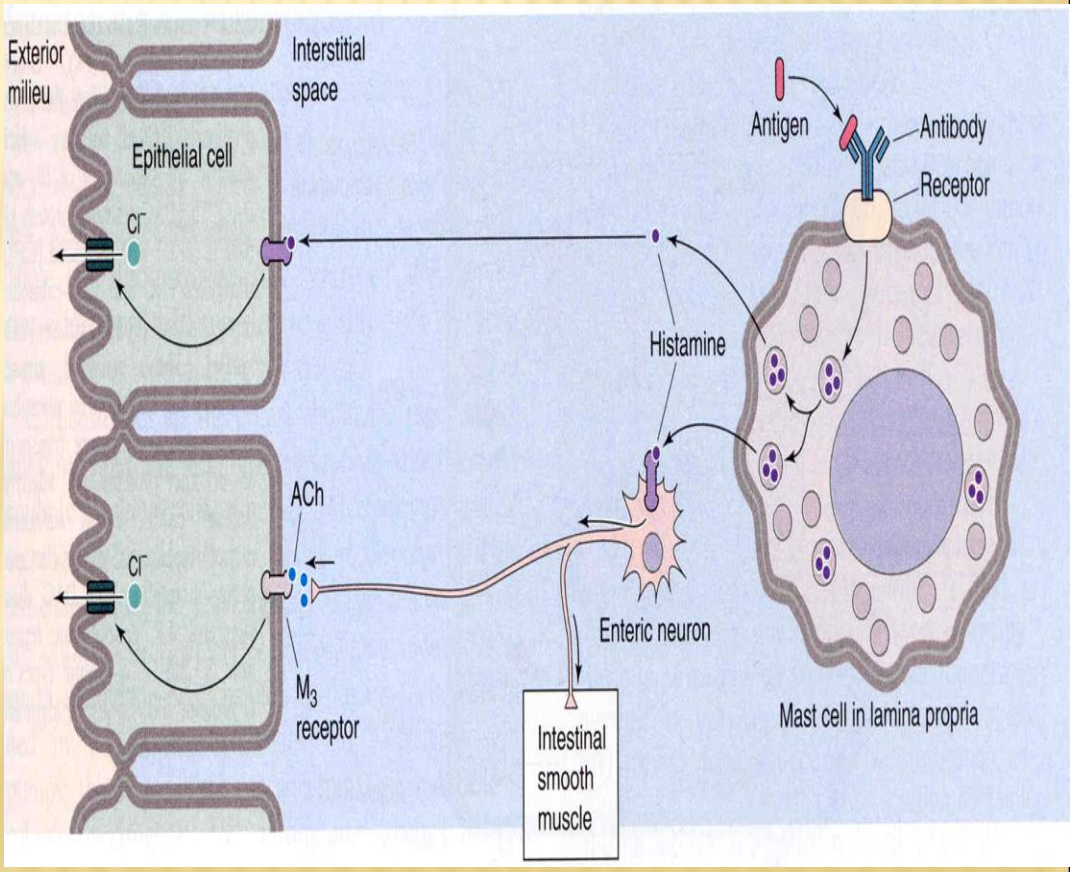


Control of intestinal secretion

❖ **Stimulation by:**

- mechanical and chemical agents into intestines
- substances, secreted by mass cells at lamina propria: histamine, prostaglandins, bradikinine
- bacterial exotoxins of Vibrio cholerae, E. coli
- bile salts, castor oil

❖ Intestinal secretion is inhibited by sympathicus and somatostatin.



Thanks for your attention!