
Human digestion

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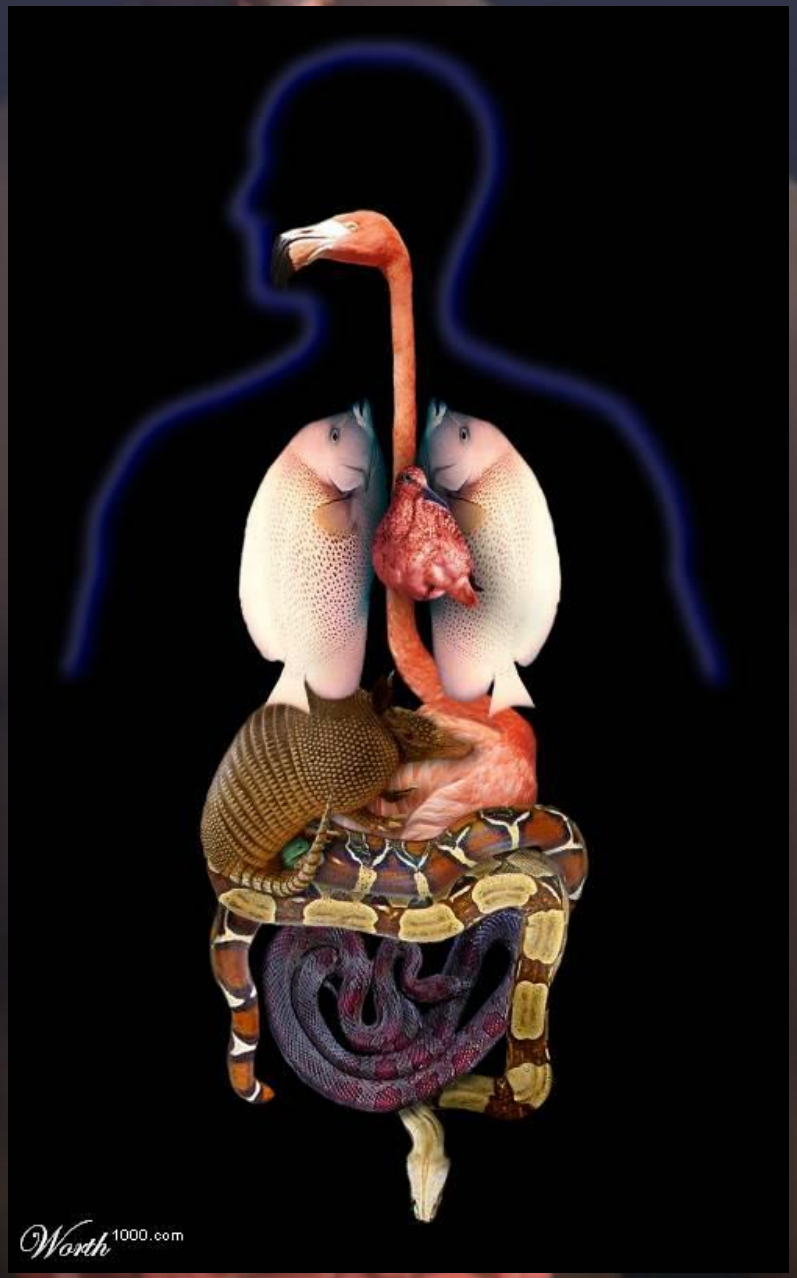
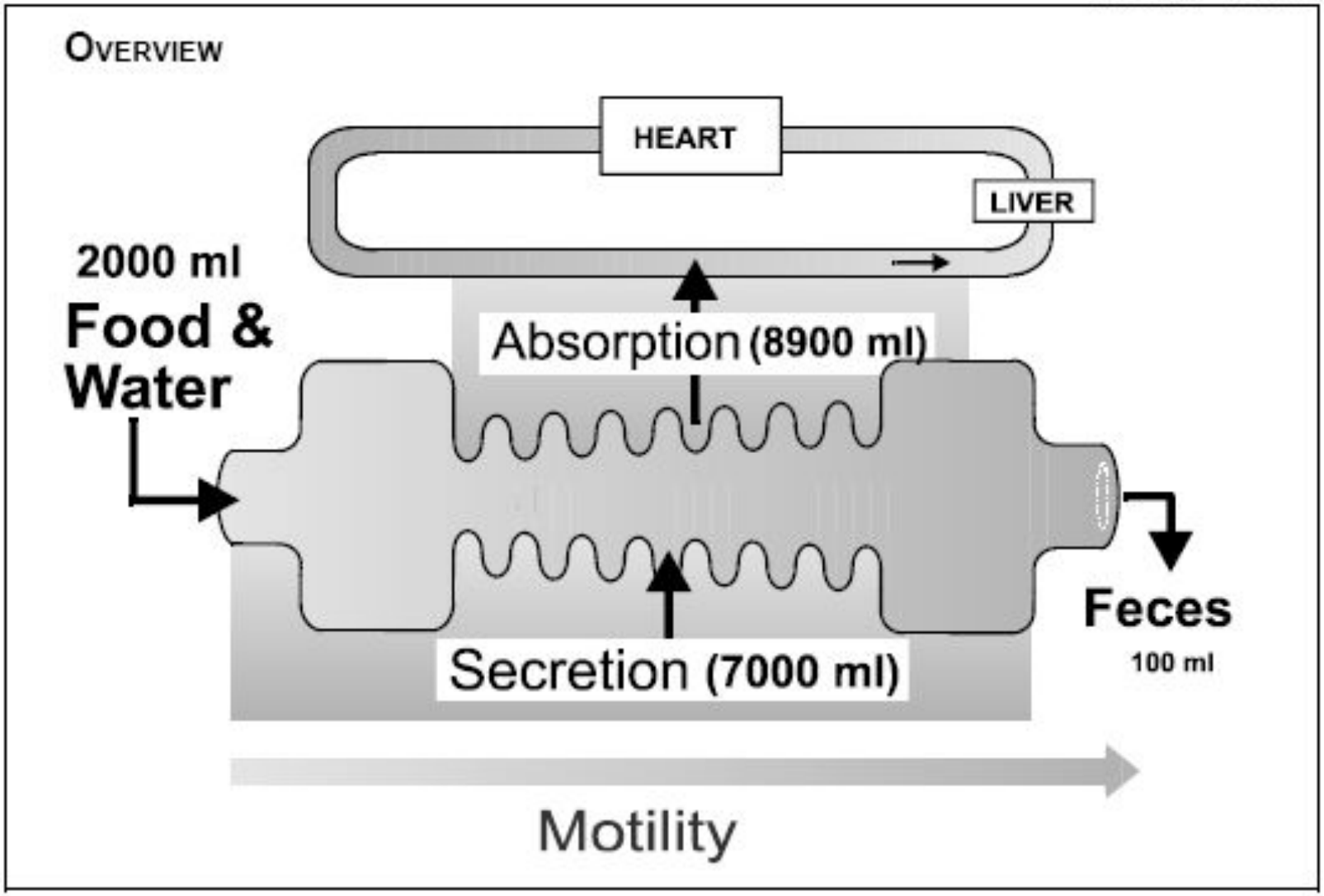



Hardwood Dowels

Пищеварение: физиологические процессы

Subject: GI/OE

These processes were then grouped into five broad categories	The analog of each of these in our digestive systems would be:
Movement of materials from one container to another and mixing	Muscular **MOTILITY** involving primarily *smooth muscle*
Measure the concentration of hydrogen ion, the concentrations of protein, fat, and carbohydrate, and the tonicity of the digest	**CHEMORECEPTORS** and **OSMORECEPTORS** are stimulated by elevated levels of hydrogen ion, protein, fat, and carbohydrate, and by elevated tonicity
Addition of enzymes and fluid	**SECRETION** of enzymes and fluid by *secretory (exocrine) cells*
Extraction of breakdown products	**ABSORPTION** of breakdown products by specialized *absorptive epithelial cells*
Coordination of events and decisions about appropriate responses	**REGULATION** by neural reflexes, hormones, and an extensive *enteric nervous system* found in the wall of the digestive tract

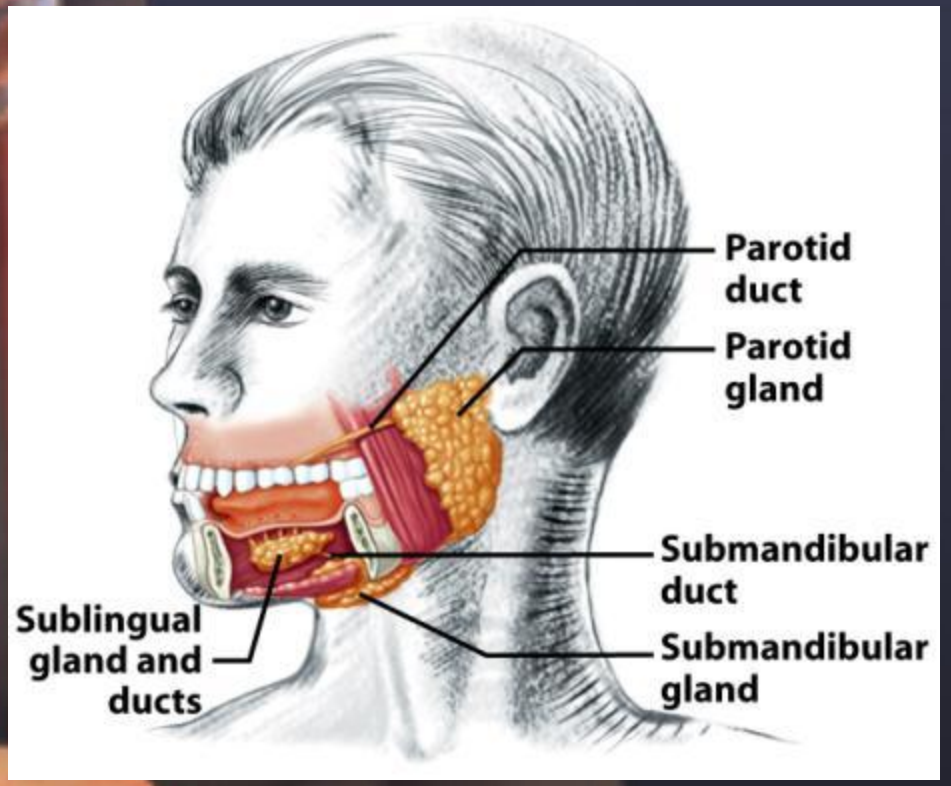

Overview
HEART
LIVER
2000 ml
Food &
Water
Absorption (8900 ml)
Secretion (7000 ml)
Feces
100 ml
Motility

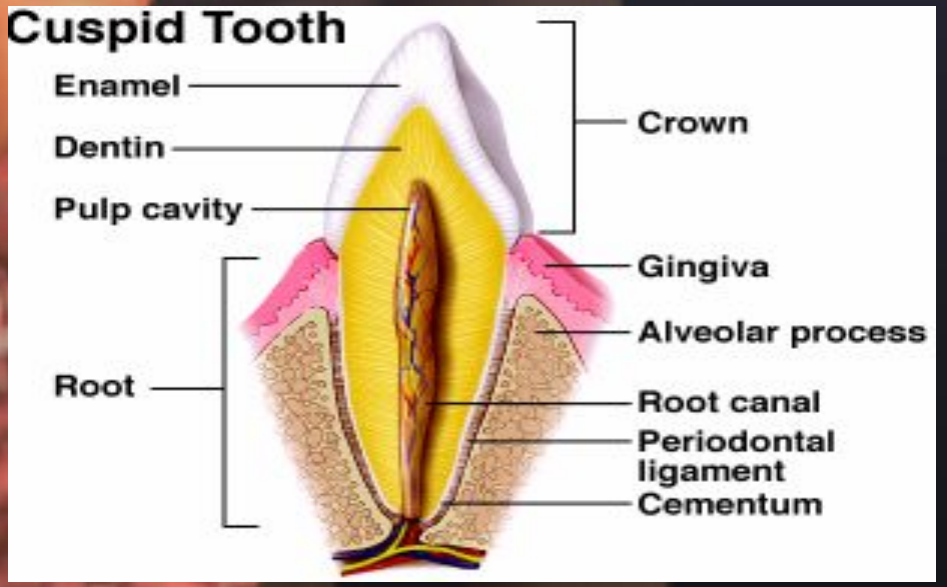
Sites of digestion

Organ/s	Mechanical digestion	Carbohydrate digestion	Protein digestion	Nucleic Acid digestion	Lipid digestion
Oral cavity **Esophagus** **Pharynx**	Chewing Peristalsis	Polysaccharides (starch, glycogen) Disaccharides (sucrose, lactose) ***Salivary amylase*** Smaller polysaccharides, maltose			
Stomach	Churning Mixing Peristalsis		Proteins ***Pepsin*** Small polypeptides		
Small intestine ***Lumen***	Peristalsis Mixing	Polysaccharides ***Pancreatic amylase*** Maltose and other disaccharides	***Pancreatic trypsin and chymotrypsin*** Smaller polypeptides	DNA, RNA ***Pancreatic nuclease*** Nucleotides	Fat globules ***Bile salts*** Fat droplets ***Pancreatic lipase*** **Glycerol, fatty acids, glycerides**
Small intestine ***Epithelium***		***Disaccharidases*** **Monosaccharides**	Small peptides ***Dipeptidases, carboxypeptidase, aminopeptidase*** **Amino acids**	***Nucleotidases*** Nucleosides ***Nucleosidases, phosphatases*** **Nitrogenous bases, sugars, phosphates**	

Digestion in the Mouth

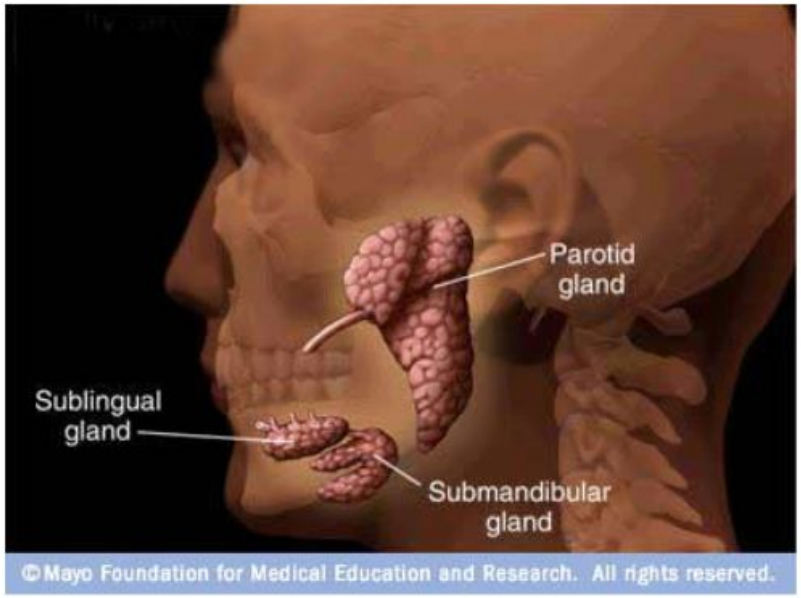
- Salivary glands
  - Produce saliva
    - Mostly water
    - Some enzymes
      - Salivary amylase
      - Lysozyme
    - Mucus or mucin
- Teeth



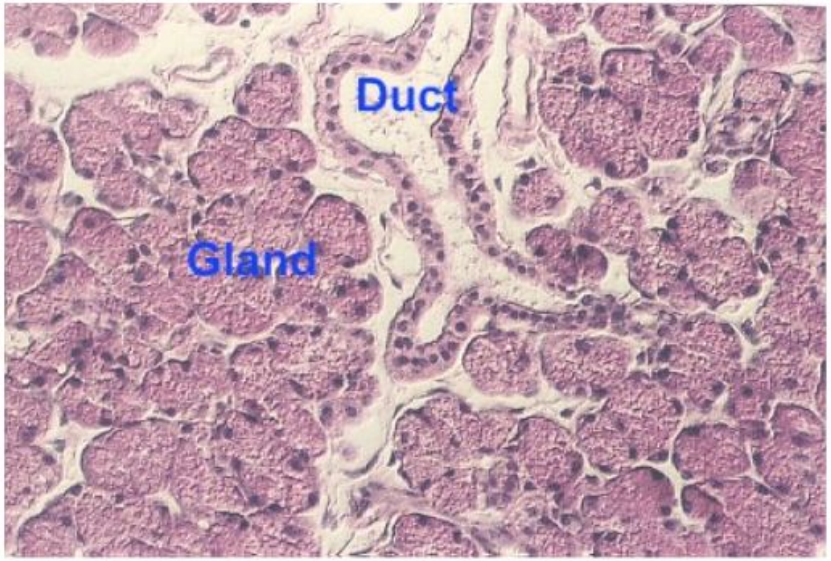


Функции слюны

ˆ увлажняет пищу, облегчает глотание,
ˆпредупреждает аспирацию пищи в трахею, способствуя формированию пищевого комка,
ˆ начинается пищеварение углеводов ,
ˆ облегчает ощущение вкуса расщеплением углеводов – вкусовые почки стимулируются расщепленными углеводами
ˆ нейтрализует желудочную кислоту в случае ее забрасывания в пищевод (рефлюкс, отрыжка)
ˆминерализующая функция и способствует снижению заболевания зубов



http://content.revolutionhealth.com/contentimages/images-image_popup-ah6a192.jpg



http://www.cytochemistry.net/microanatomy/digestive/salivary1.jpg

Contents of saliva:

(about 0.75l produced per day!)

amylase (starch digestion)

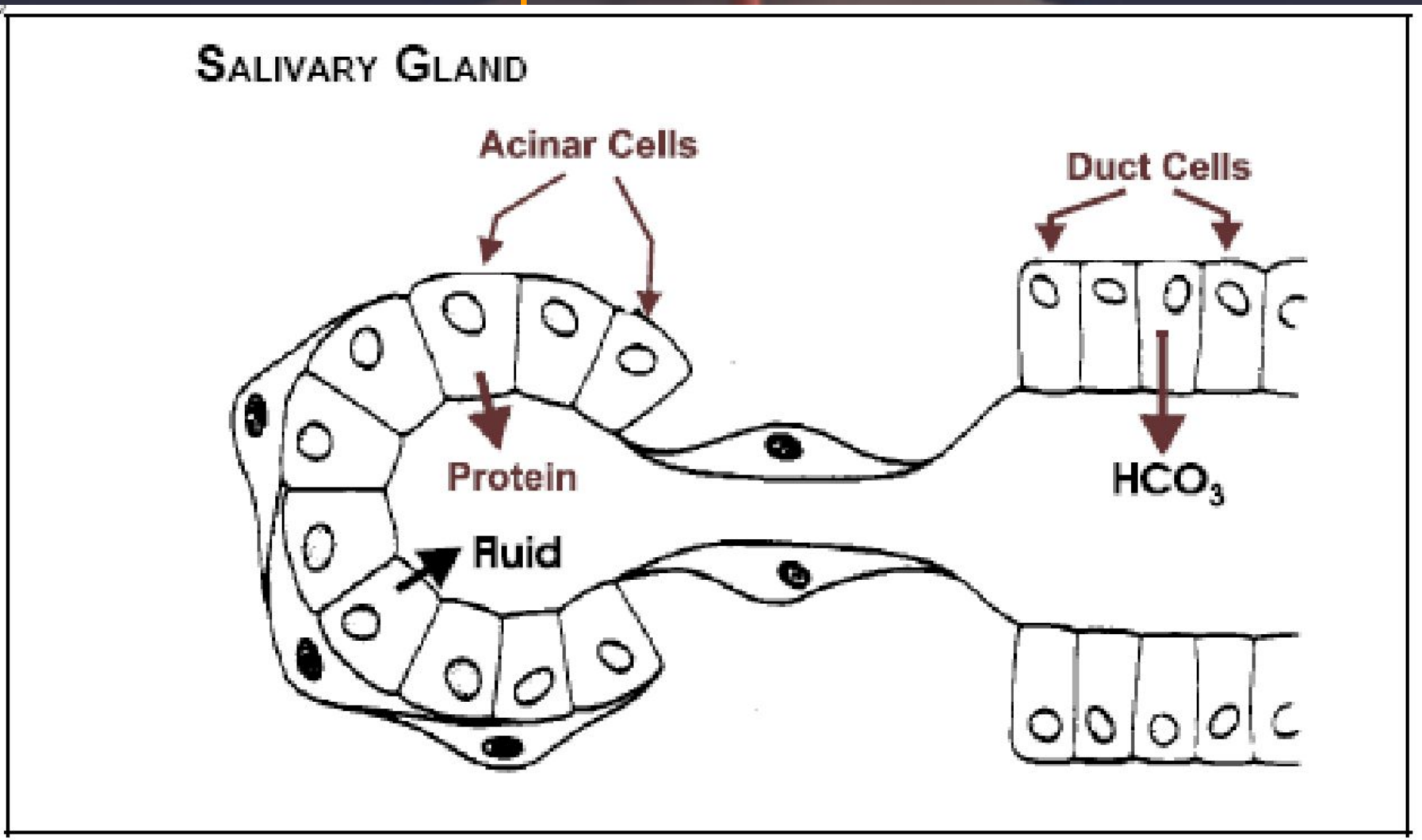
lingual lipase
(break triglycerides into fatty acids)

water & electrolytes
(moistens and lubricates)

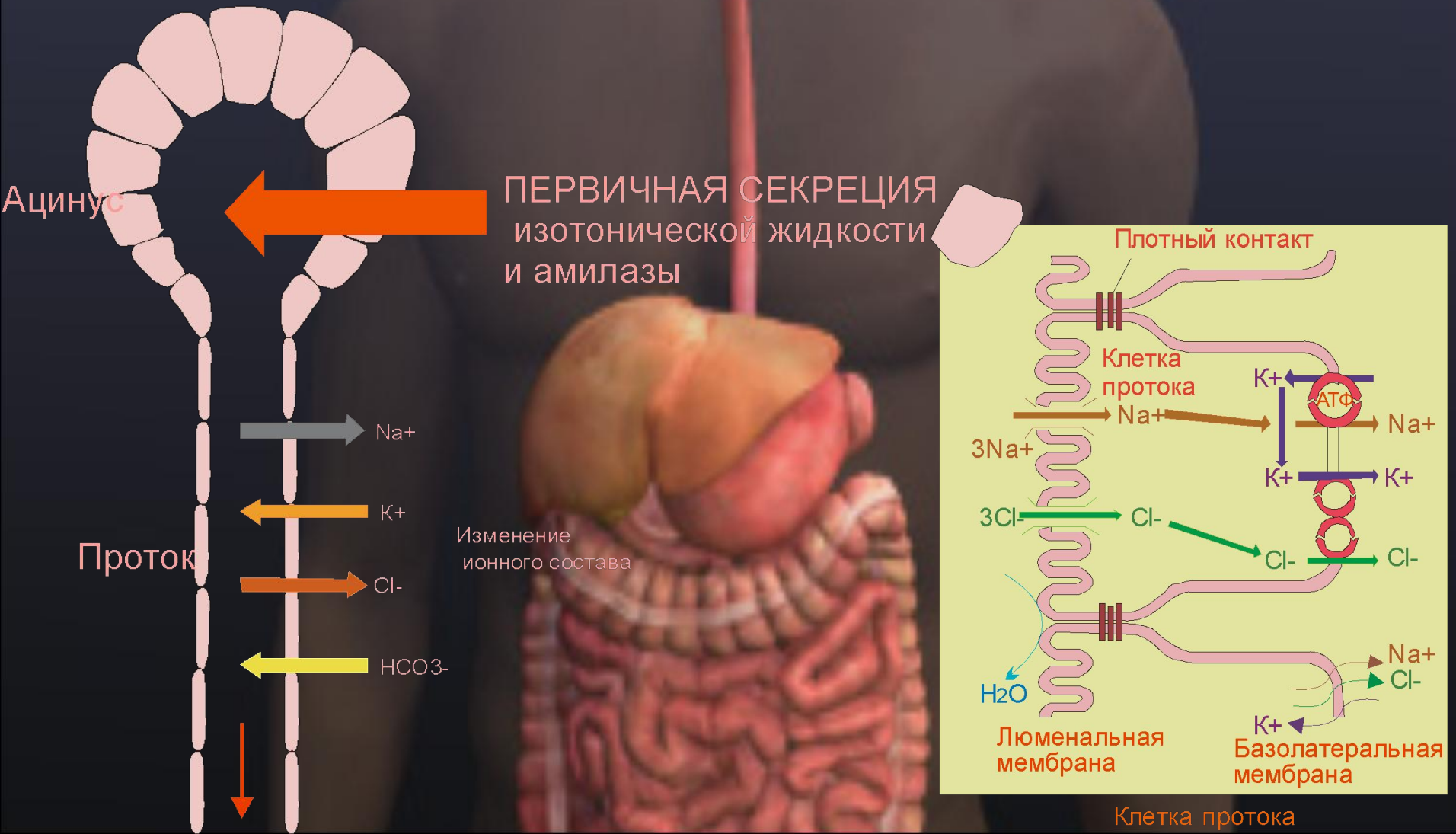
mucus
(lubricates food bolus)

antibacterial compounds
(and bacteria)

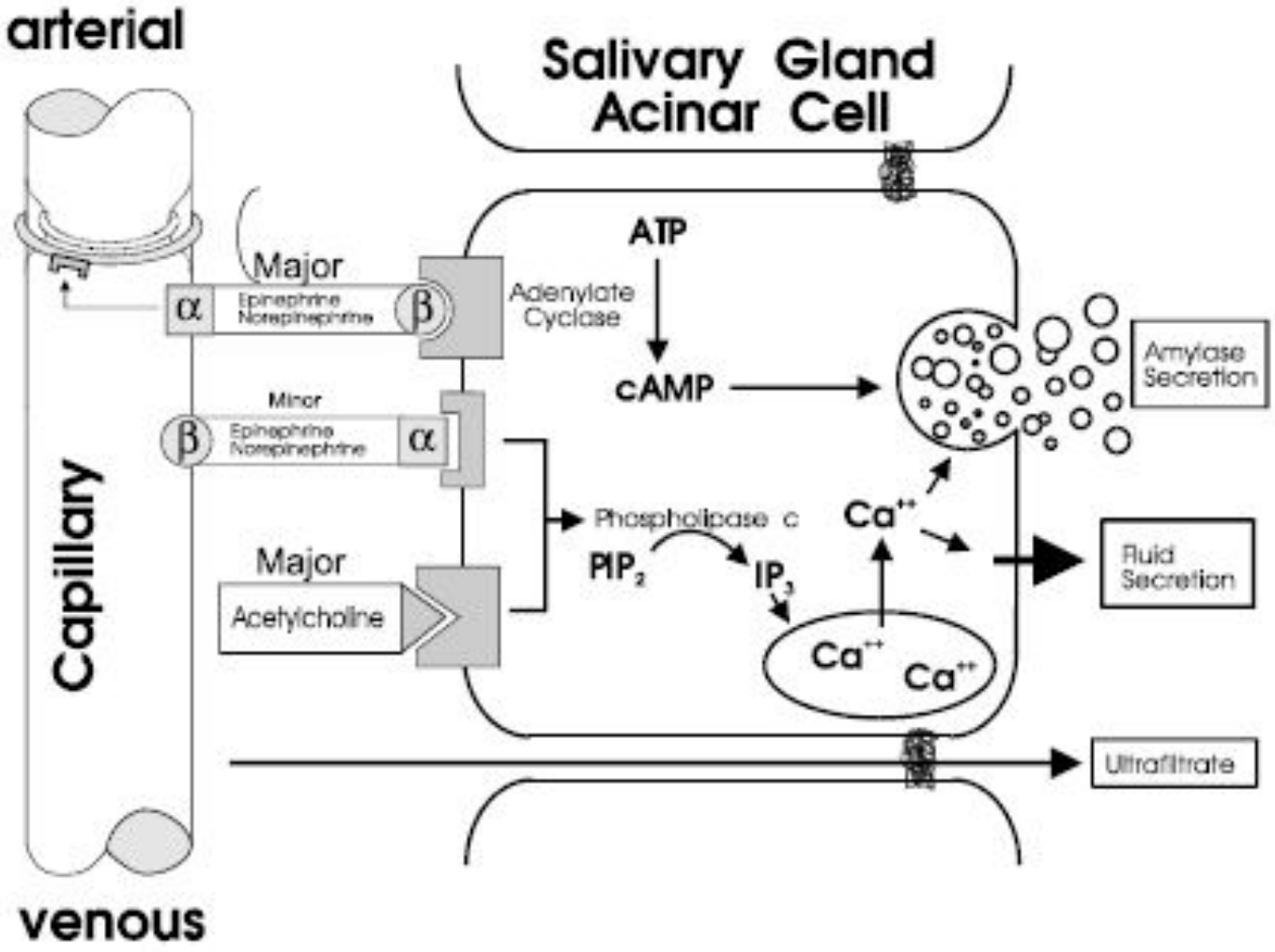
Образование слюны



Функция протоков слюнных желез

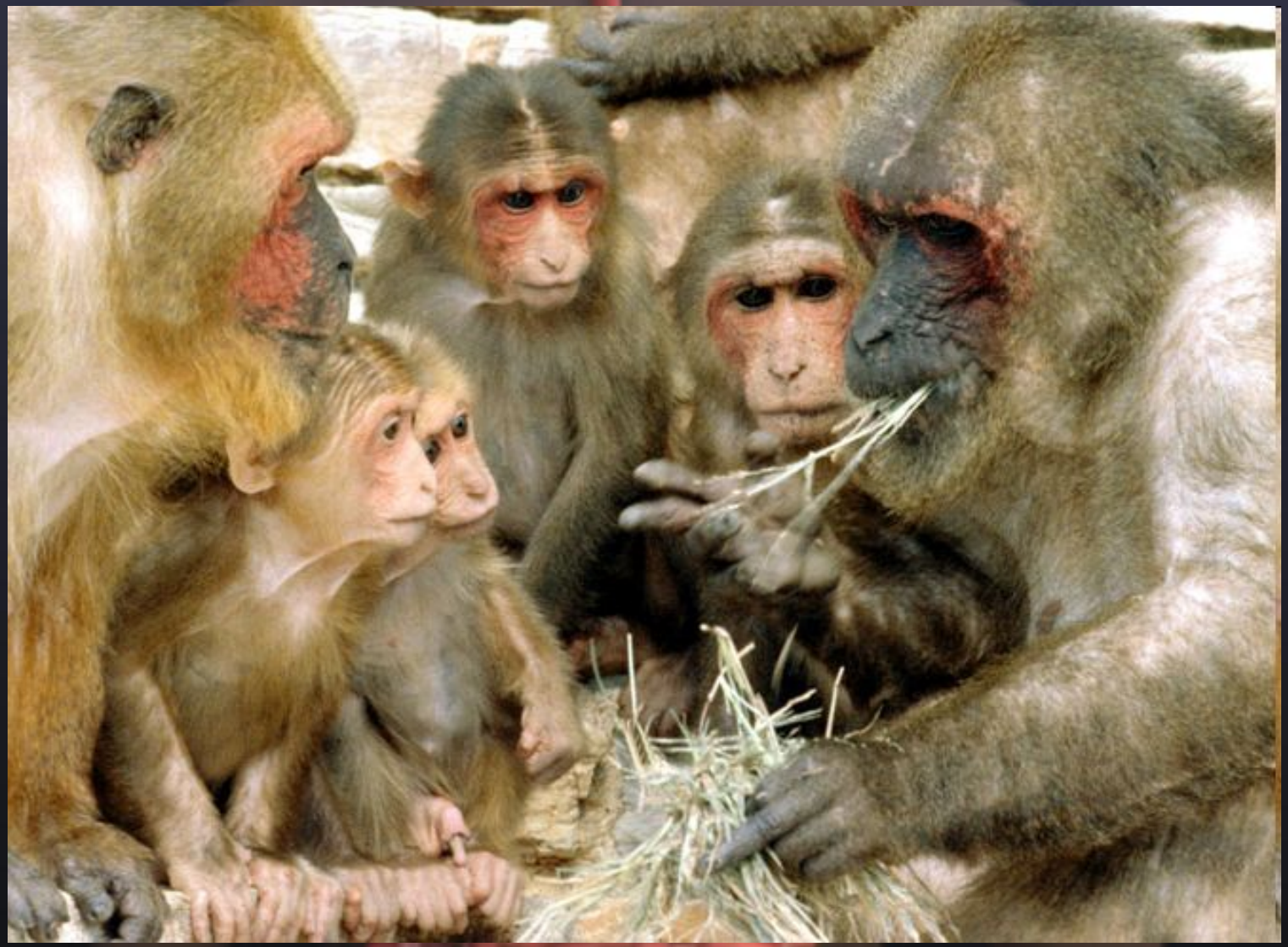


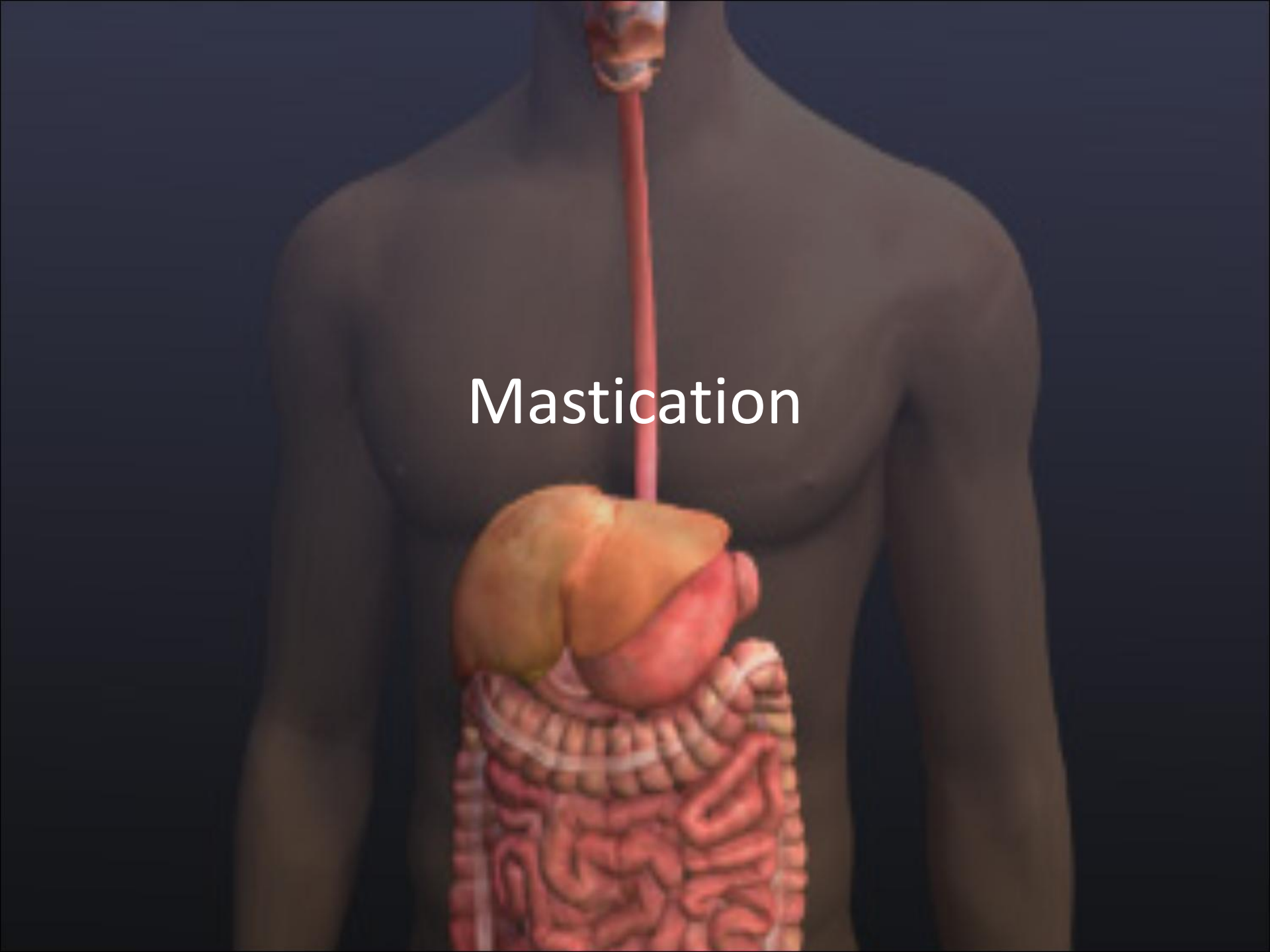
Regulation of Salivary Glands



Takehito Etani, Masticator triptych, 2005.

Mastication. masticatory cycle (chewing cycle) the complete pathway of the mandible



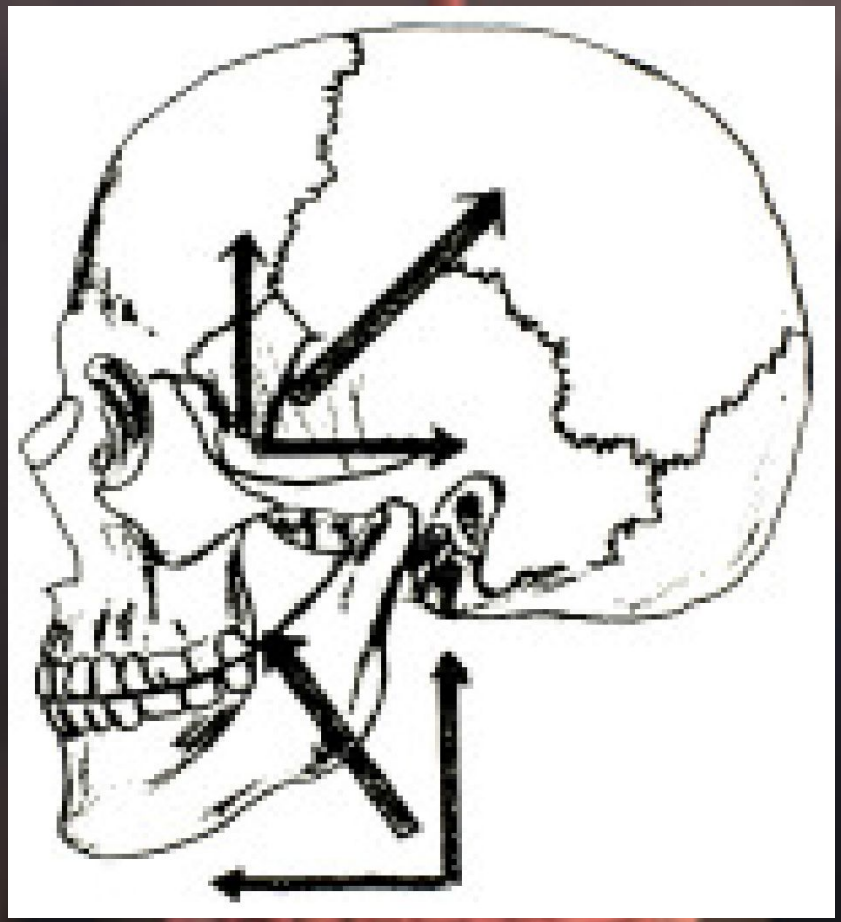

Mastication

The Muscles of Mastication (Chewing)

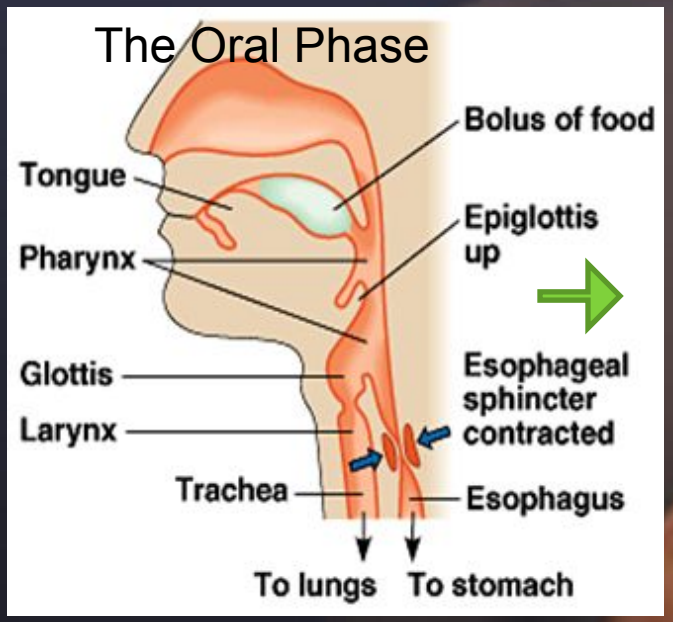
- Перетирание или жевание, выполняется скоординированной функцией четырех важных мышц, которые сжимают зубы вместе в различных направлениях.
- These are:
- The masseter
- The lateral pterygoid
- The medial pterygoid
- The temporalis

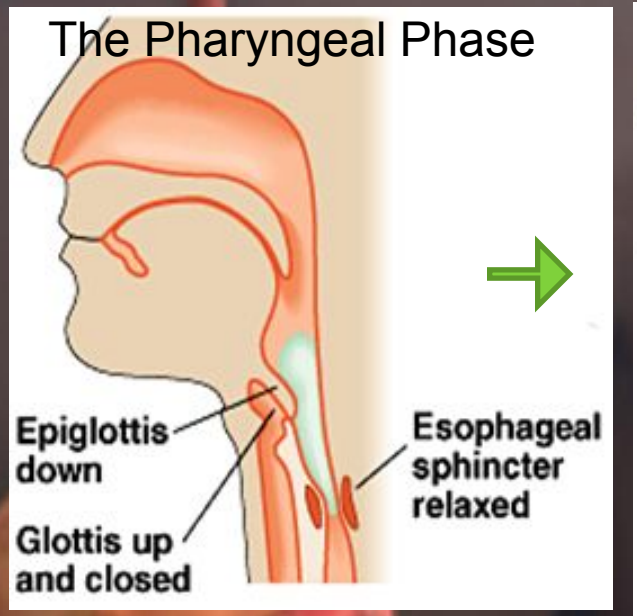
- Каждая из этих мышц - парная и ими управляет мозг через нервные волокна тройничного нерва(cranial nerve V).

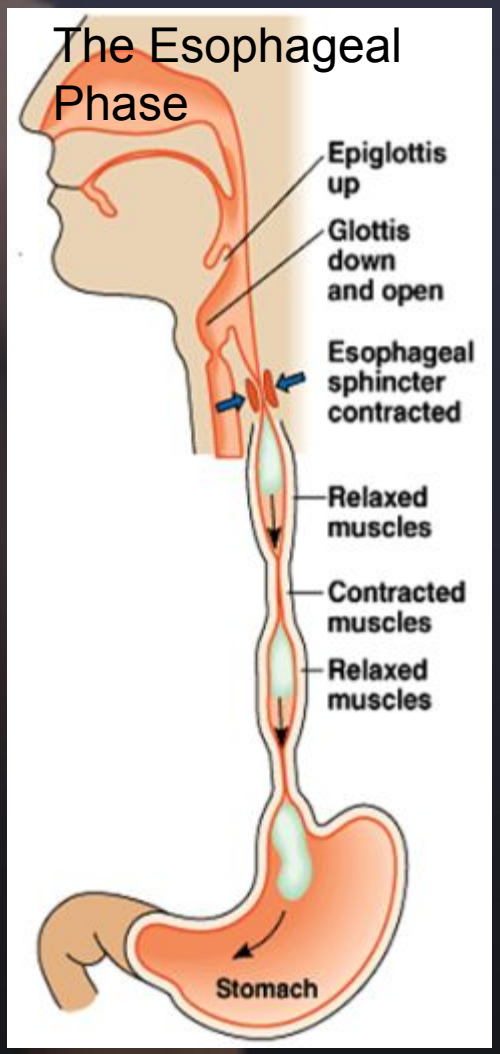
Main force vectors of masticatory muscles

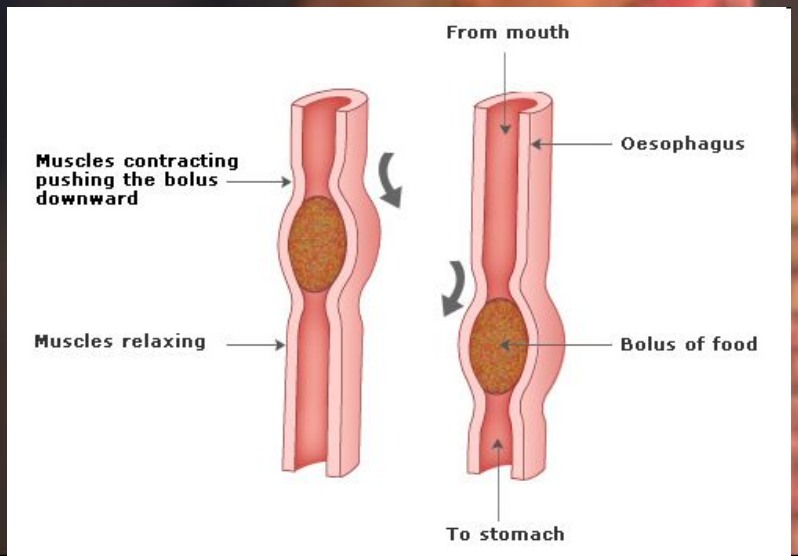


Swallowing: from mouth to stomach









Oral Preparatory Stage

- Ротовая предварительная стадия по существу жевание. Это включает координацию губ, щек, челюсти, языка и движения мягкого нёба, чтобы приготовить пищу для того, чтобы глотать.
- В конце этой фазы формируется пищевой комок, который язык прижимает к твердому небу.
- Самая важная нейромускульная функция в этой фазе - повторяющееся латеральные движение языка, поскольку без нормальной подвижности языка имеются большие затруднения при жевании.

Oral Stage

- Ротовая стадия - вторая стадия глотания. Это длится приблизительно 1 секунду, и не меняется в зависимости от возраста, пола или консистенции пищевого комка.
- Это перемещает еду с передней части полости рта к передним дужкам. .
- Снова, движение языка - самый важный аспект этой фазы глотания, так как это формирует, снимает и сжимает шарик вверх и назад вдоль твердого неба.

Pharyngeal Stage

- The pharyngeal stage begins when the bolus reaches the anterior faucial arches.
- Here, the bolus triggers the swallowing reflex which occurs via the glossopharyngeal nerve.
- The swallowing reflex may also be triggered by the superior laryngeal nerve at the laryngeal inlet.
- When a swallow reflex occurs late by this second mechanism, the patient is said to have a delayed swallowing reflex.
- While the first two phases of swallowing can be bypassed by using liquid feeds and syringing the bolus to the back of the mouth or extending the head, the reflexive stage of swallowing cannot be bypassed.
- The swallowing reflex is mediated in the reticular formation of the brainstem, adjacent to the respiratory center. It is modulated by input from the respiratory center, and cortical areas. The pharyngeal stage lasts a maximum of 1 second and does not vary with food consistency, age or sex.

Swallowing Reflex (Pharyngeal Stage)

- When triggered, the swallowing reflex results in four neuromuscular functions, which occur in rapid sequence in the following order:
- 1) Velopharyngeal closure (to prevent nasopharyngeal reflux)
- 2) Pharyngeal peristalsis (to propel the bolus into the pharynx) Pharyngeal peristalsis occurs in a sequential fashion, from superior to inferior constrictor. It functions to clear material from the pharyngeal recesses. Vallecular or pyriform sinus pooling on modified barium swallow is an indication of reduced pharyngeal peristalsis.
- 3) Elevation and closure of the larynx (for airway protection Laryngeal elevation occurs by contraction of the strap muscles, which positions the larynx anterosuperiorly (under the tongue base).

Laryngeal closure occurs at three sphincters:

- **1) the epiglottis and aryepiglottic folds,**
- **2) the false vocal folds, and**
- **3) the true vocal folds. (Epiglottic closure is probably of relatively minor importance. Closure actually begins at the glottic level, followed soon after by closure of the false cords and epiglottis. Airway protection is the most important aspect of swallowing.)**
- **4) Pharyngoesophageal segment opening (to allow the bolus to pass into the esophagus).**

Pharyngoesophageal segment opening depends on:

- 1) relaxation of the cricopharyngeus,
- 2) the upward, anterior pull of the larynx (probably most important), and
- 3) the bolus pressure. After the bolus passes through the PE segment, this sphincter immediately closes to prevent reflux.

Esophageal Stage

- The fourth and final stage of swallowing is the esophageal stage. It is more variable and prolonged than the other phases of swallowing, lasting from between 8 and 20 seconds. Esophageal transit time significantly increases with age.

Swallowing Centers

- In humans, the development of
- functional magnetic resonance imaging (fMRI) has allowed the identification of the cortical
- regions involved in voluntary swallowing.
- The primary motor and sensory areas are
- consistently active in healthy adults during swallowing. The anterior cingular cortex is also
- activated during swallowing (Hamdy, Mikulis et al. 1999; Humbert and Robbins 2007).

Swallowing Centers

- There is convincing evidence that the sequential and rhythmic patterns of swallowing are
- formed and organized by a central pattern generator (CPG) located within the medulla
- oblongata (Jean 2001). The CPG was first described as a swallowing center that can be
- subdivided into three systems: an afferent system composed of the central and peripheral
- inputs to the center; an efferent system composed of outputs from the center to various
- motor neuron pools involved in swallowing; and an organizing system composed of
- interneuronal networks that program the motor pattern.

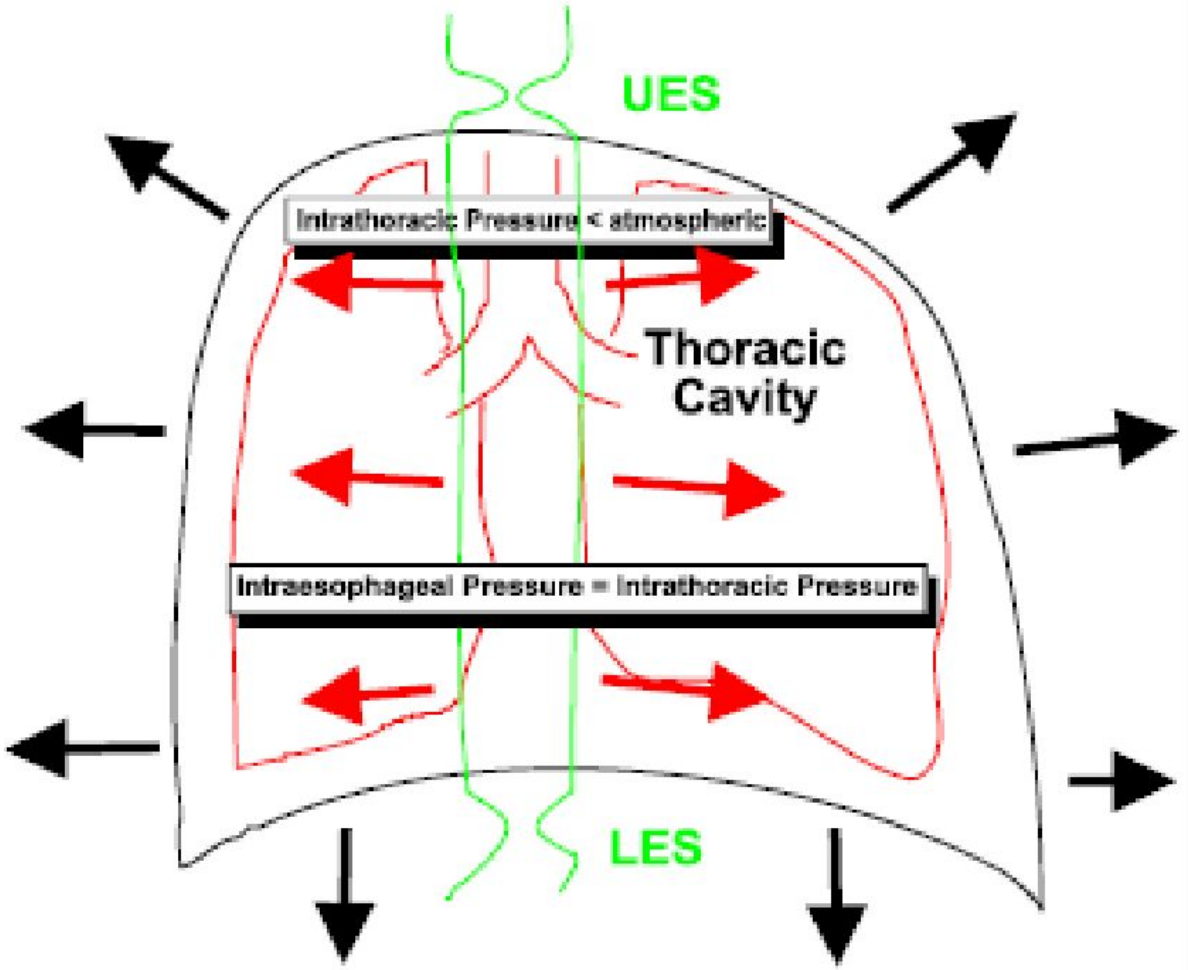
Swallowing Centers

The voluntary initiation of swallowing takes place in special brain areas located in the precentral, posterior-inferior, and frontal- gyri. These structures send orders via axons that travel inside a nerve bundle called the corticobulbar tract, to a third swallowing center in the medulla. These centers include areas located in the cerebral cortex, the medulla oblongata, and the cranial nerve nuclei.

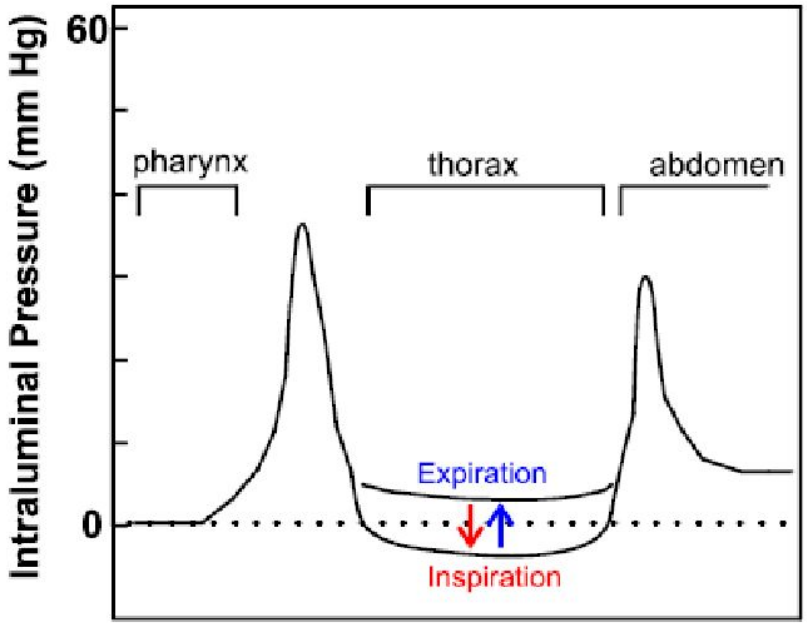
Sensory Nerves
:
Trigeminal (cranial nerve V)
Facial (cranial nerve VII)
Glossopharyngeal (cranial nerve IX)
Vagus (cranial nerve X)

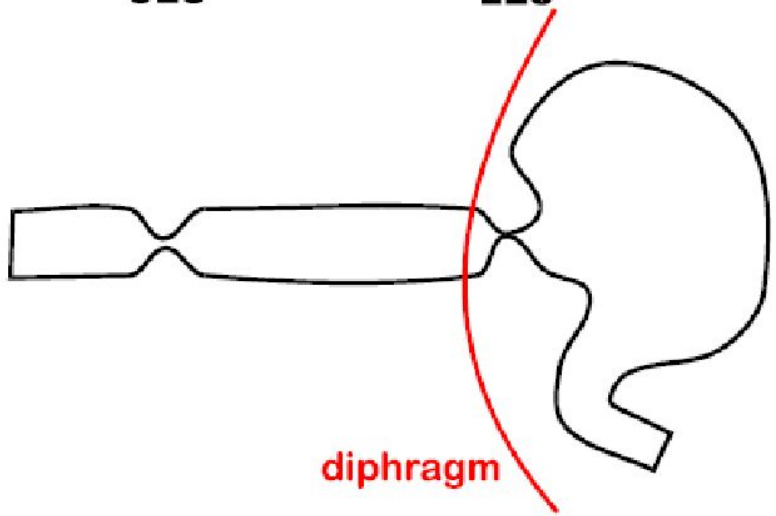
Cranial Nerve Nuclei
The muscles of swallowing are controlled by several cranial nerve nuclei. These are:
The nucleus ambiguous (of the vagus and glossopharyngeal nerves)
The dorsal motor nucleus (of the vagus nerve)
The hypoglossal nucleus (of the hypoglossal nerve)

Esophagus


UES
Intrathoracic Pressure < atmospheric
Thoracic Cavity
Intraesophageal Pressure = Intrathoracic Pressure
LES

Intraesophageal Pressure





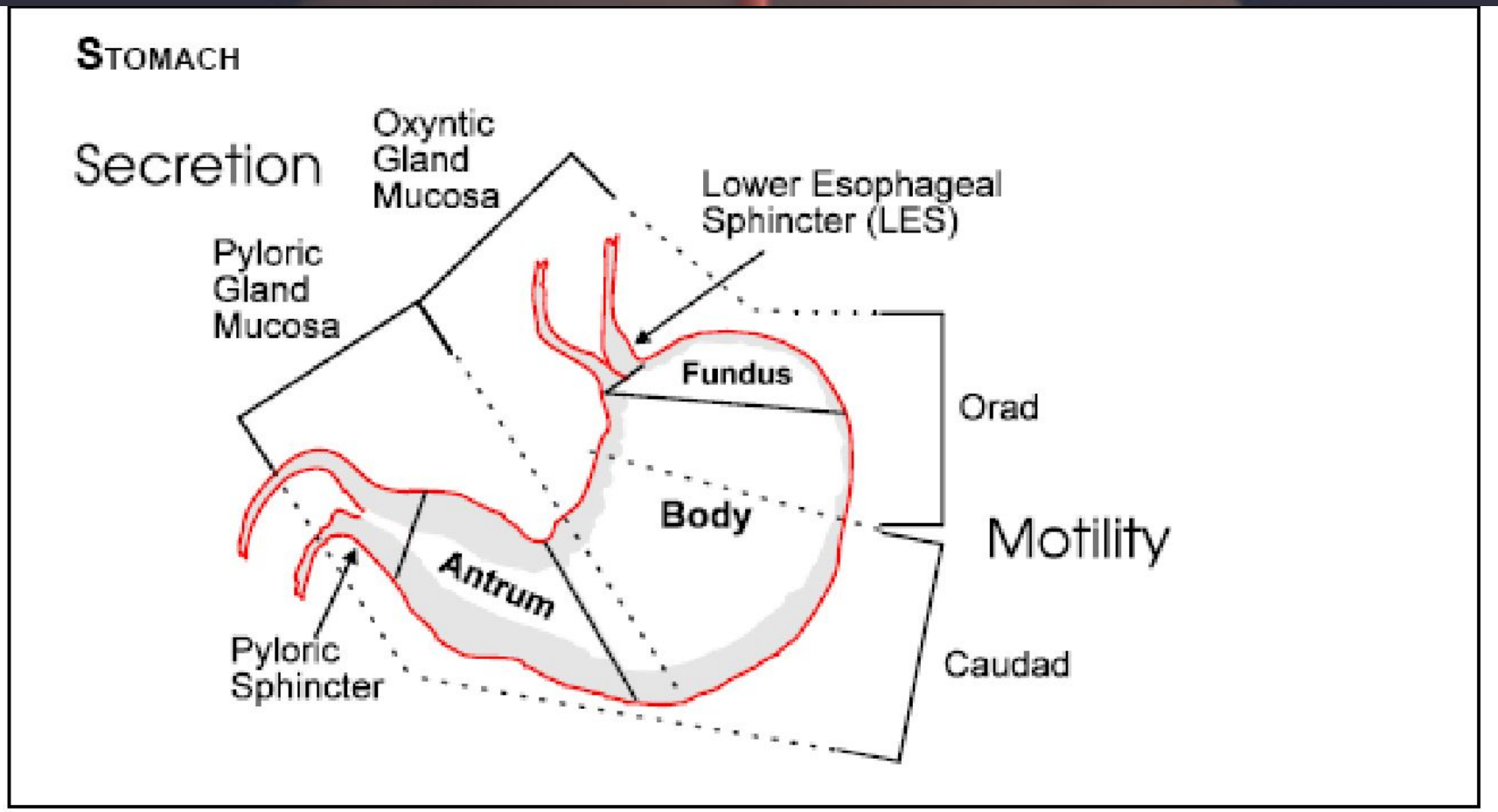
Моторика пищевода

Food is propelled down the esophagus by coordinated contractions of the esophageal muscle called *peristalsis*.

The wave of contraction that is initiated by swallowing, is called *primary peristalsis*

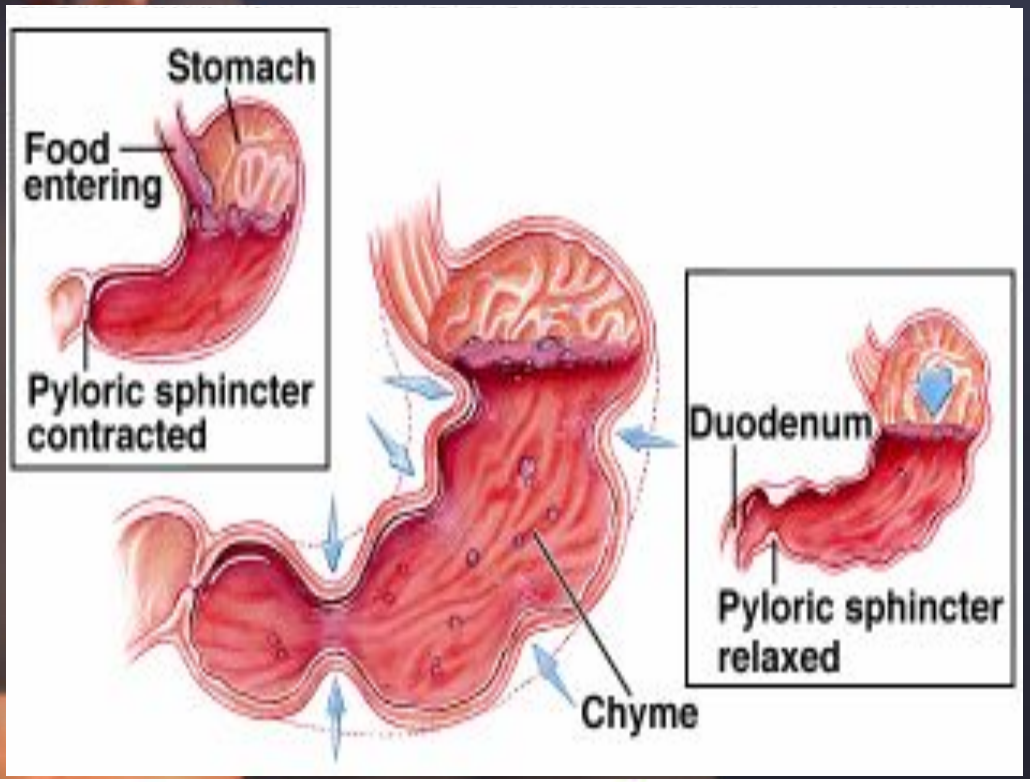
Any food that remains in the esophagus after this initial wave of contraction will activate additional waves of contraction called *secondary peristalsis*.
These contractions are initiated by distention of the esophagus and will continue until the esophagus is empty. Secondary peristalsis will also continue after vagotomy.

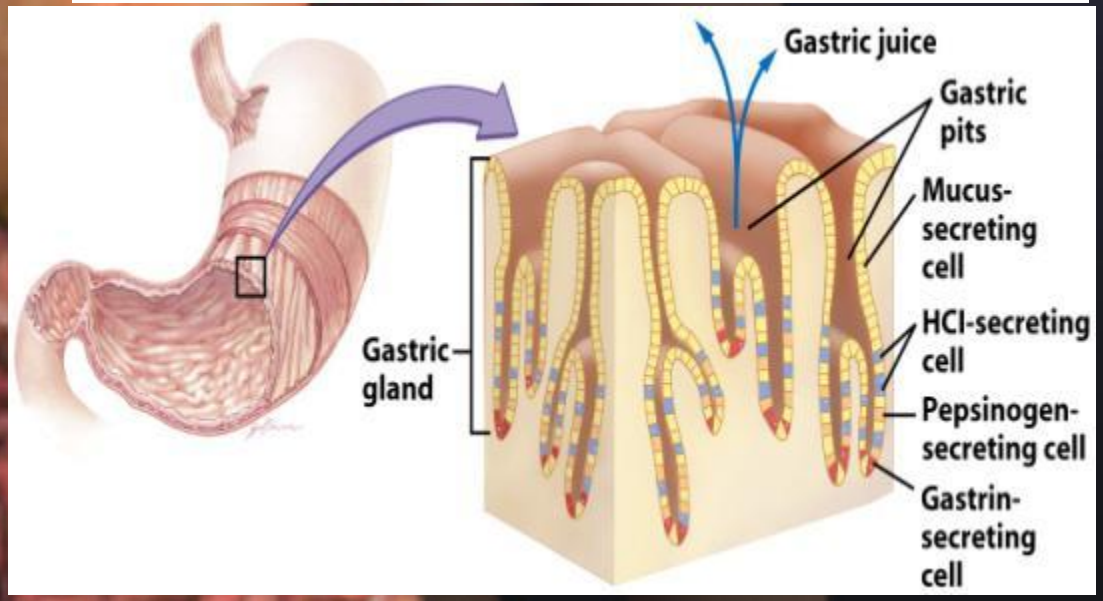
Пищеварение в желудке



Digestion in the Stomach

- Muscular sac
  - Churns & mixes food
- Gastric glands
  - Parietal cells → HCl, intrinsic factor
  - Goblet cells → mucus
  - Chief cells → pepsinogen, weak gastric lipase
  - *Gastrin*
    - *Hormone*
    - *Controls gastric juices*
- Comes out as chyme (2-6 hours)





Функции желудка

^

Serves as a reservoir that allows for the ingestion of food faster than it can be digested and absorbed.

^

Kills some bacteria and parasites

^Begins the process of digestion by exposing food to low pH and pepsin. A major effect of this treatment is the swelling and dissociation of collagen fibers and the proteolysis of extracellular matrix proteins. This, combined with the mixing action of the stomach, causes the breakup of food into smaller particles.

^ Delivers the gastric contents (chyme) to the duodenum at a rate compatible with:

the secretion rate of bile salts, bicarbonate ion, fluid, and digestive enzymes;

the rate of enzymatic breakdown of proteins, lipids, and carbohydrates; and

the rate of chyme transport down the small intestine.

Секреция в желудке

The major components of *gastric juice* are:

ˆ *Hydrochloric acid (HCl)* - denatures proteins

ˆ *Pepsinogen* - proenzyme that is converted to pepsin (protease)

ˆ *Intrinsic factor* - vitamin B12-binding protein

ˆ *Mucous* - protects stomach wall from HCl, pepsin, and mechanical trauma

Secretion	Secretory Cell	Location	Gastric Mucosa
HCl	Parietal	Fundus and Body	Oxyntic Gland Area
Pepsinogen	Chief	Body and Antrum	Oxyntic & Pyloric
Gastrin	G-cell	Antrum	Pyloric Gland Area
Intrinsic Factor	Parietal	Fundus and Body	Oxyntic Gland Area

Contents of gastric juice

pH 1-3

hydrochloric acid
(begins protein digestion and activates pepsin)

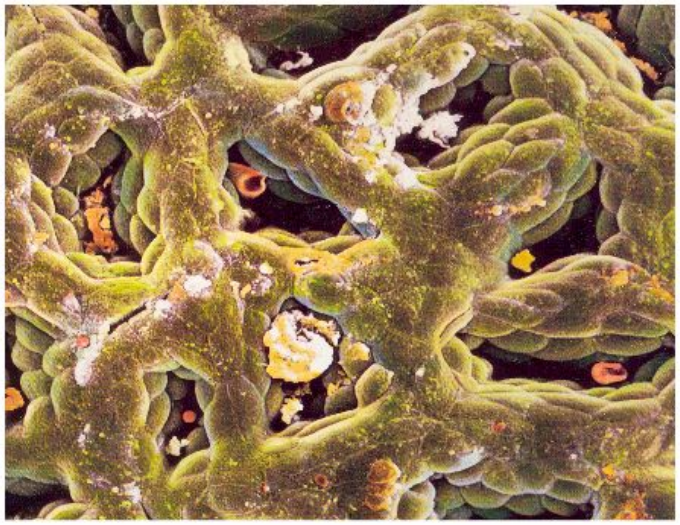
mucus
(protects the stomach lining)

enzymes
(pepsin and rennin)

Gastric juice is produced by the parietal cells in the stomach wall.

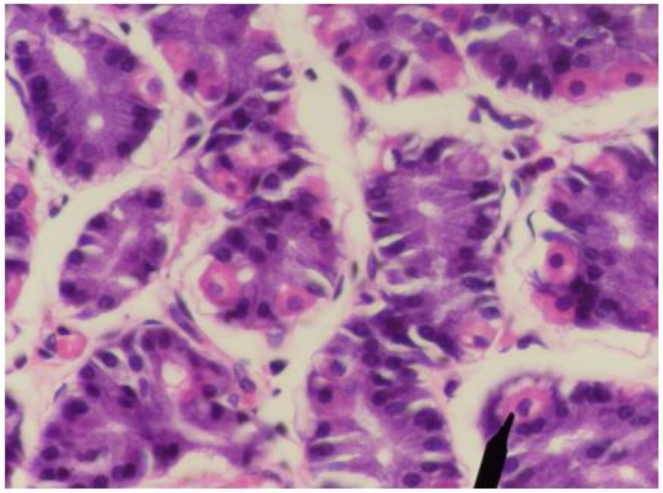
Production is triggered by detection of peptides.

Stomach lining:



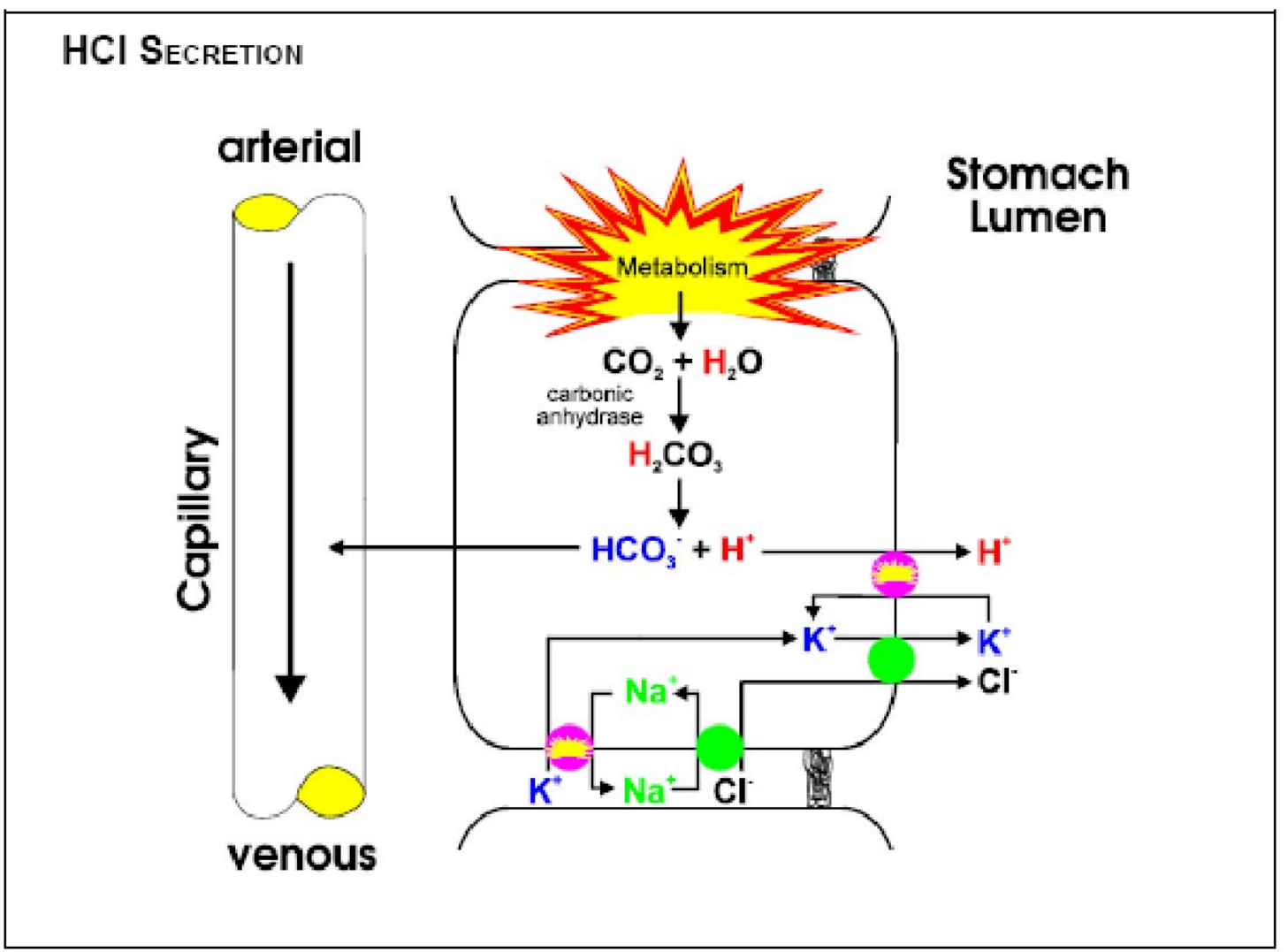
http://www.eytonsearth.org/stomach-lining.jpg

Parietal cells:

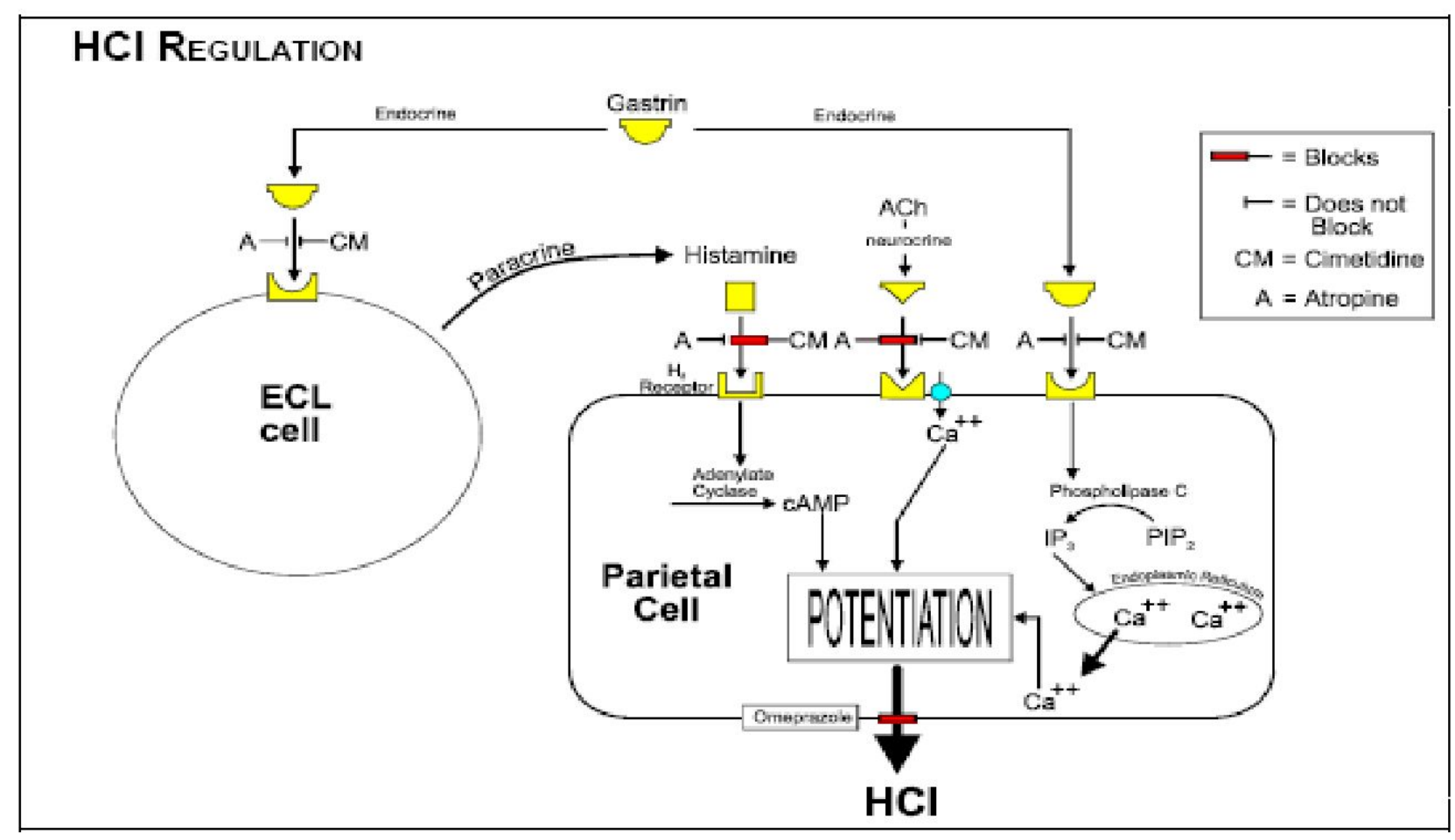


http://en.wikipedia.org/wiki/Image:Parietal_cells.JPG

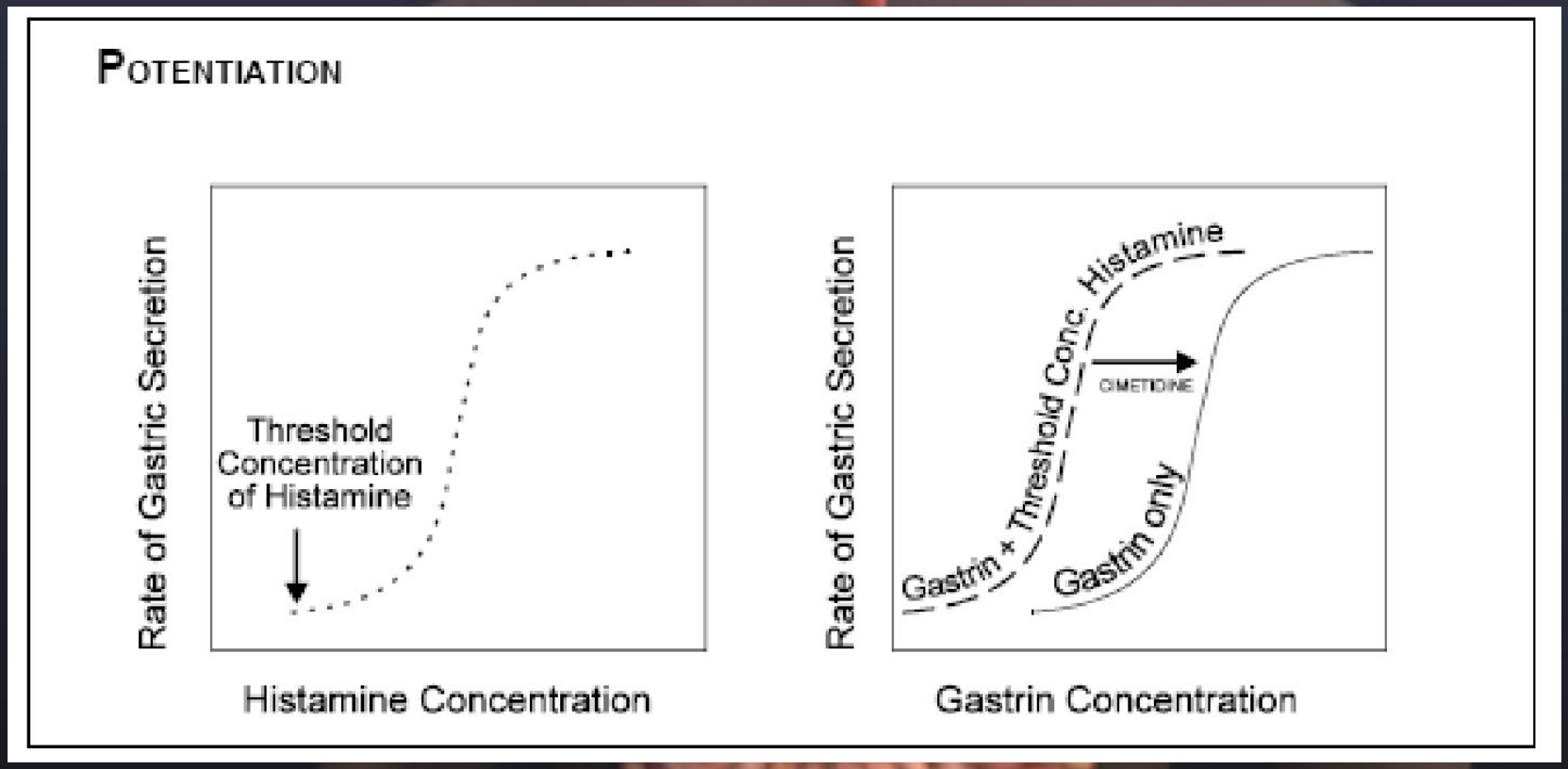
Механизм секреции HCL



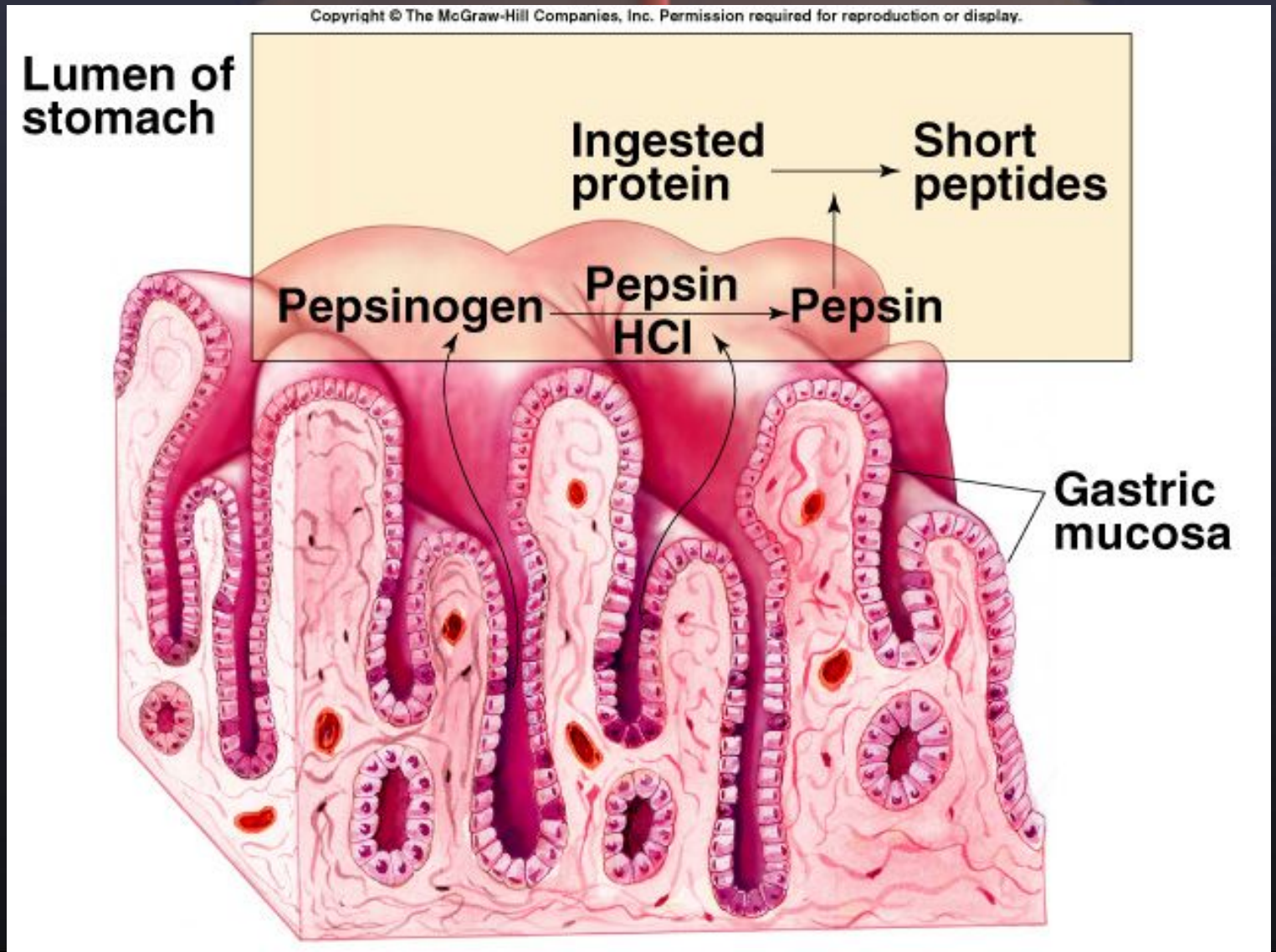
Регуляция секреции HCL



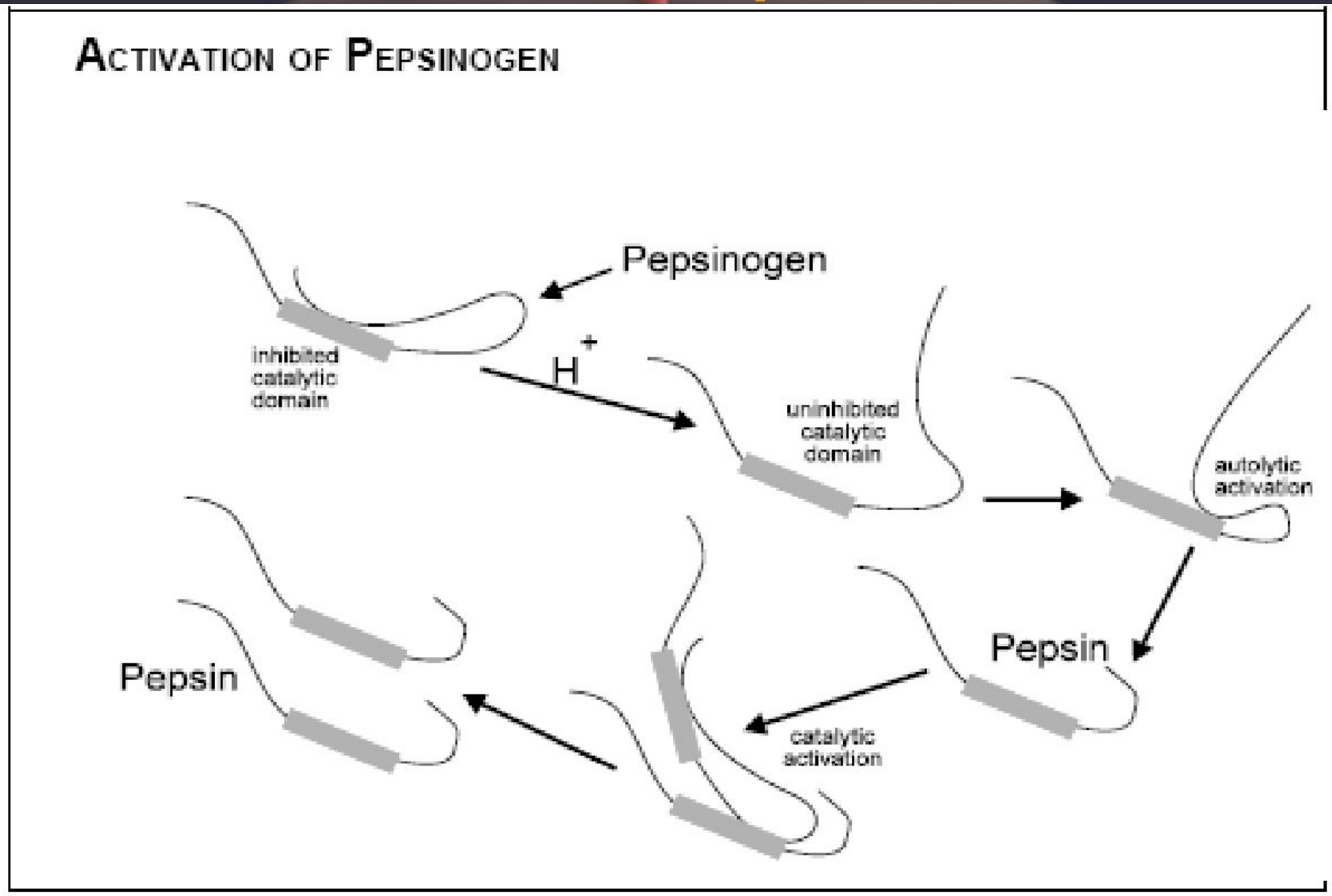
Потенциация секреции HCL



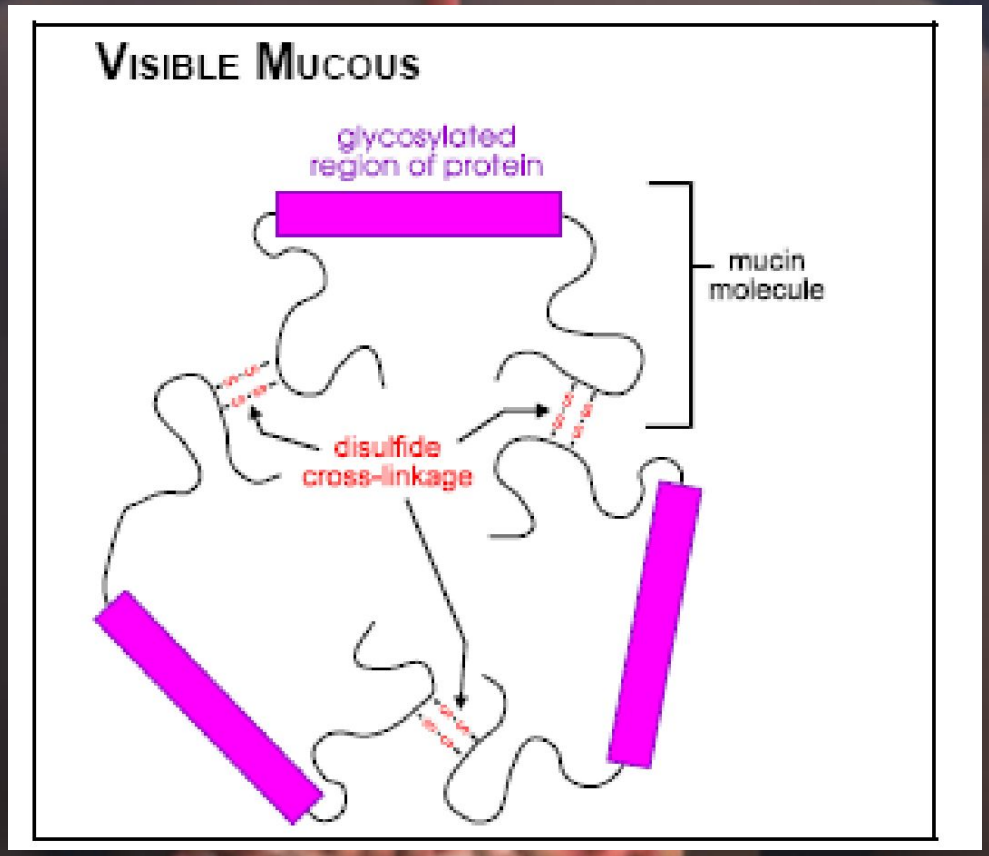
Activation of pepsin in the stomach



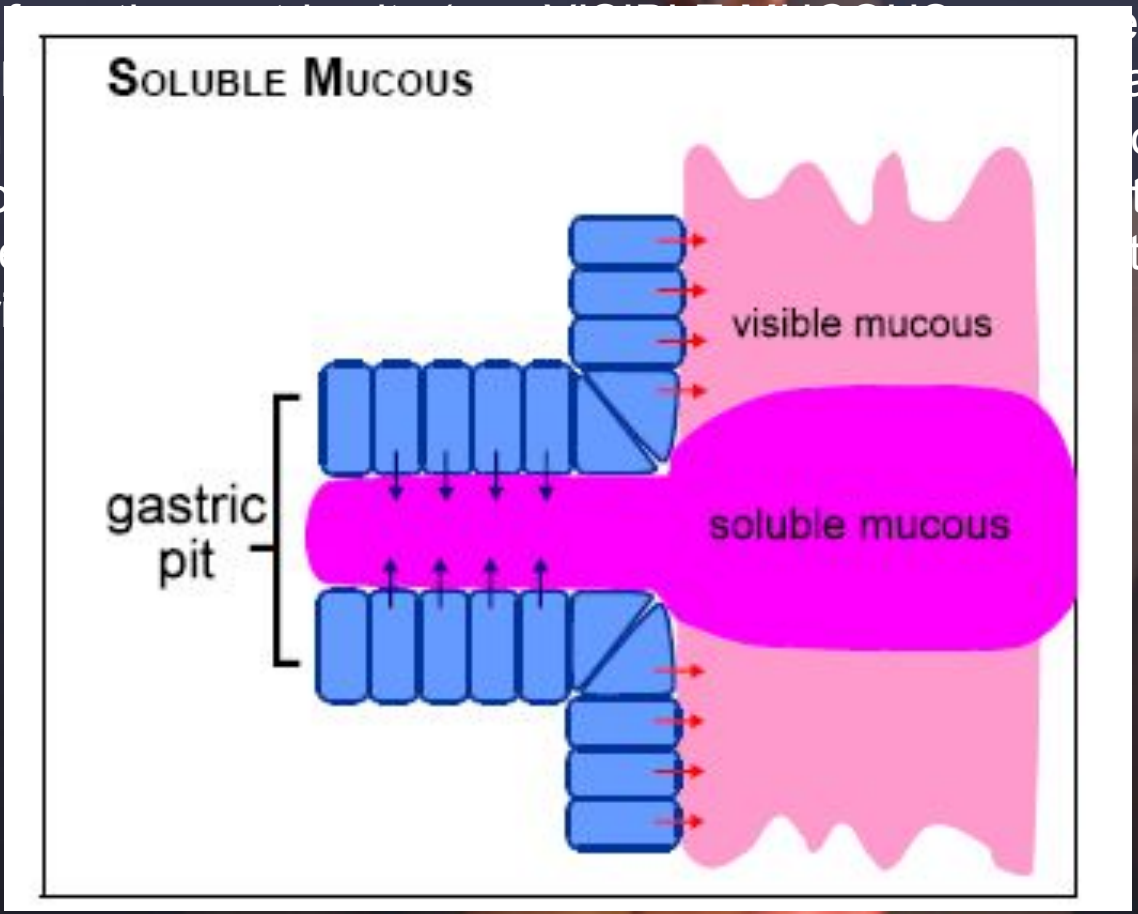
Секреция пепсиногена: активация



Секреция слизи в желудке: типы слизи

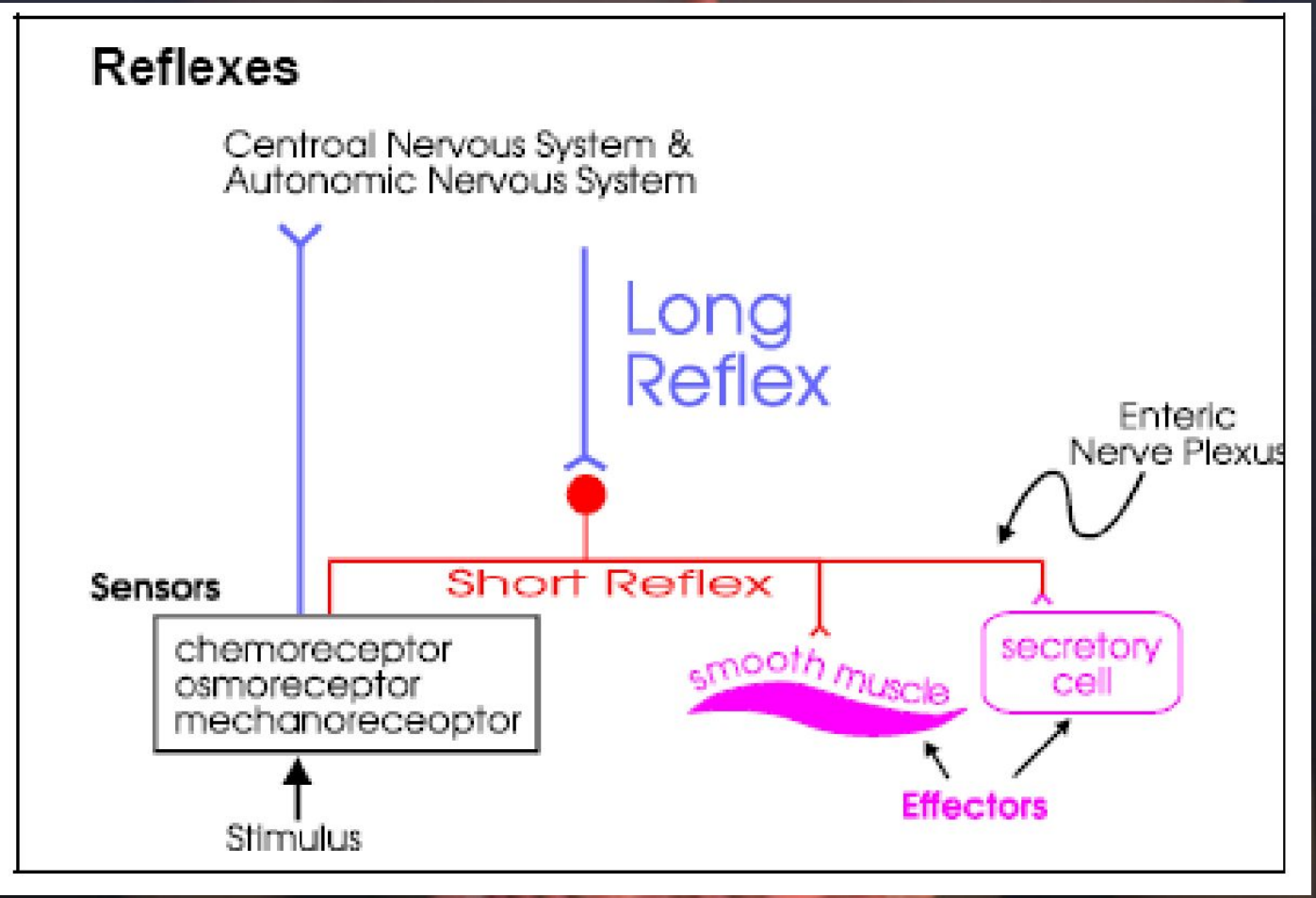


The surface epithelial cells of the stomach secrete *visible mucous* (slightly opaque) that lines the surface of the stomach. Visible mucous contains *crosslinked mucins* (glycoproteins) that form an almost gelatinous coating which contains relatively high concentrations of bicarbonate ion

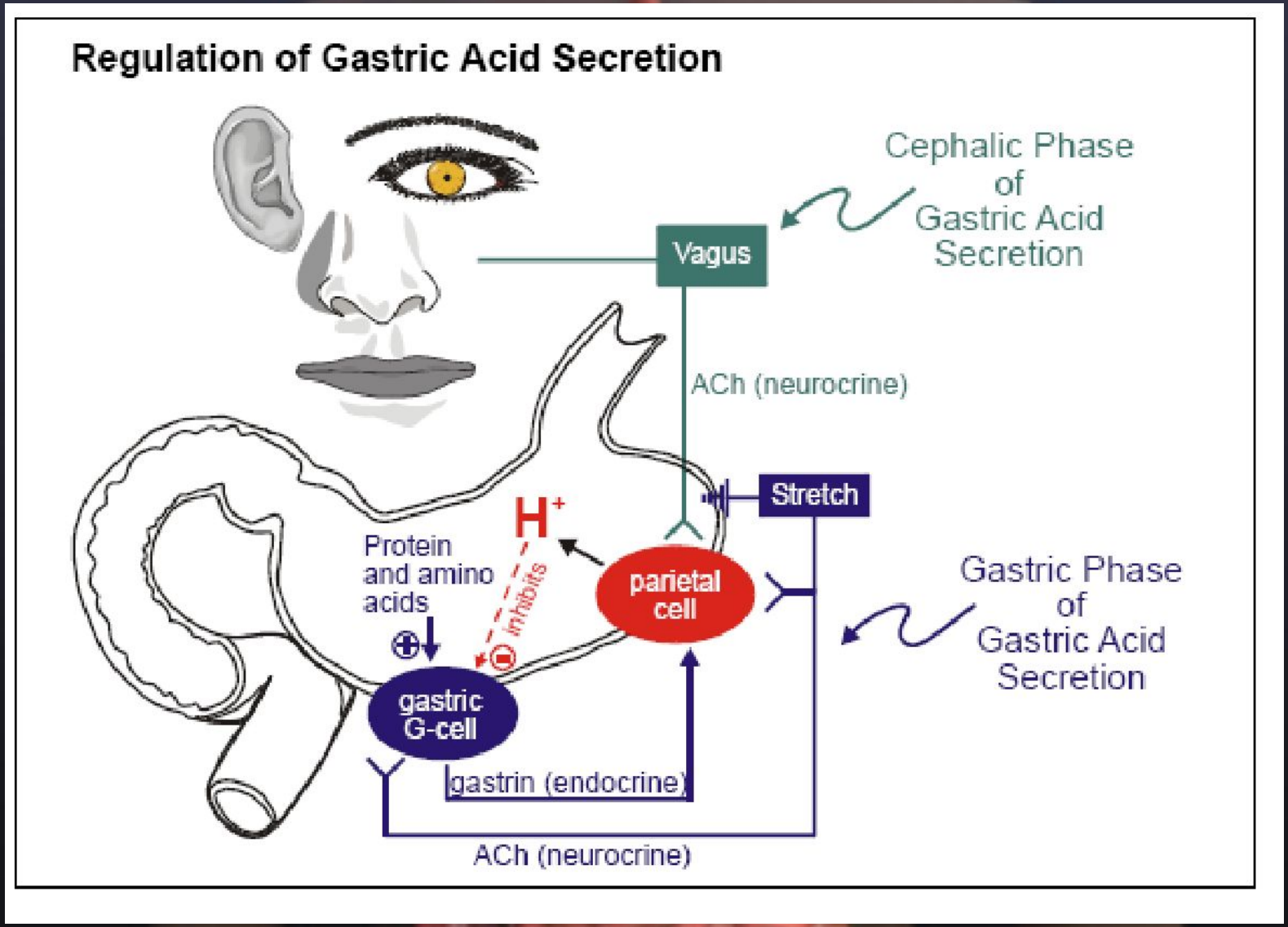


A second type of mucous, *soluble mucous*, is secreted along with the gastric juice from the gastric pits (see VISIBLE MUCOUS on page 22) to lubricate the food bolus and facilitate mixing. Soluble mucous also contains mucins, but they are not crosslinked, and consequently, produce a less viscous fluid. Soluble mucous also restricts the access of gastric juice to the gastric pit epithelial cells by creating an unmixed mobile phase that sweeps the gastric juice out of the gastric pits.

Регуляция секреции в желудке



Регуляция секреции HCL



Фазы желудочной секреции

Anticipation of a meal, or the sight of food activates a long reflex that stimulates secretion of gastric juice (*cephalic phase of gastric digestion*) proteins and amino acids in the stomach directly stimulate the release of gastrin from G-cells in the gastric mucosa, which then travels by way of the general circulation back to the stomach (endocrine) to stimulate gastric juice secretion (*gastric phase of gastric digestion*)

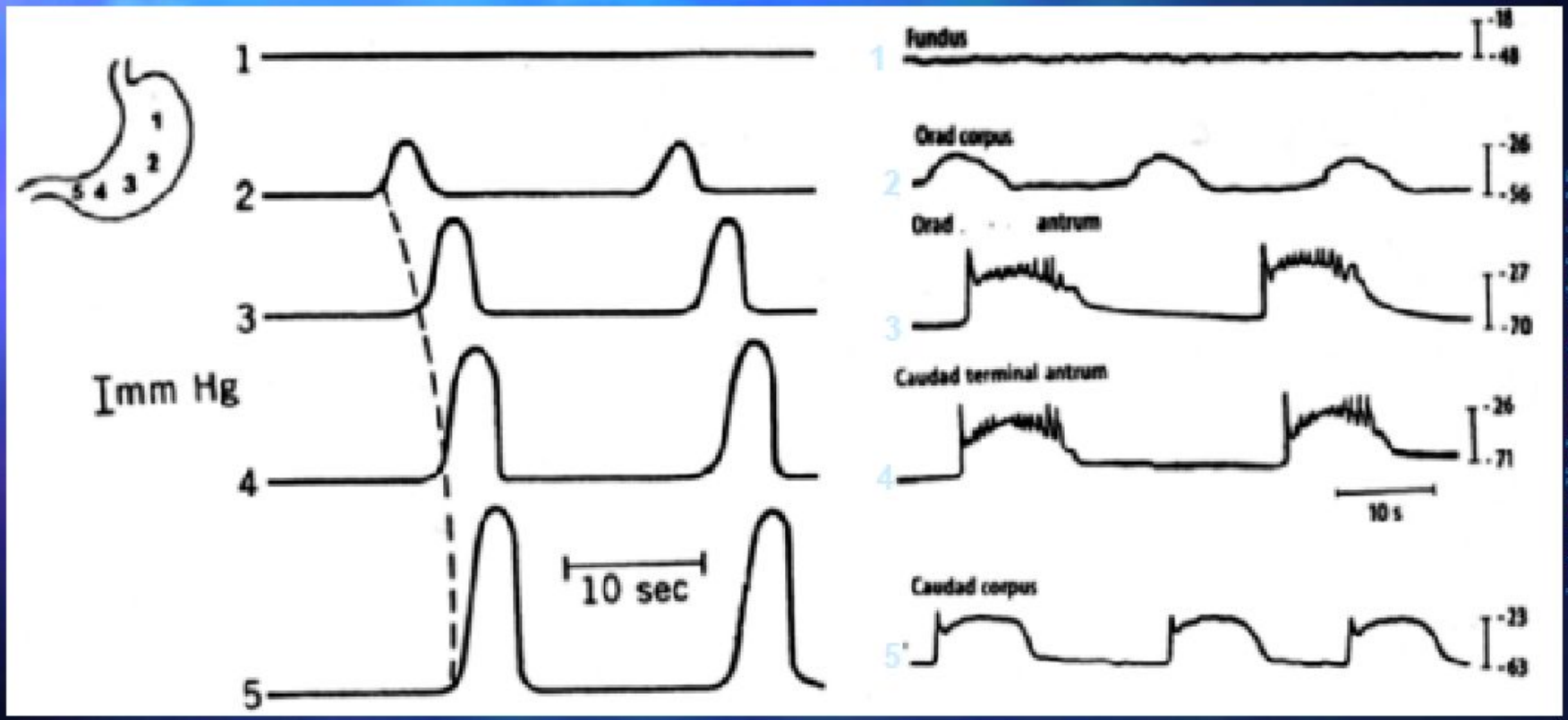
^

Between meals, the secretion of gastric juice is very low. In the absence of protein, which is a good pH buffer, a small amount of gastric juice can reduce the pH to 1.

Hydrogen ions inhibit secretion by directly inhibiting the release of gastrin from gastric mucosal G-cells (*gastric phase of gastric digestion*).
This negative feedback process halts the secretion of gastric juice and prevents the hydrogen ion concentration from reaching levels that would be toxic to the gastric mucosal cells.

Pepsinogen secretion closely parallels the secretion of HCl. This is in part due to a vagal reflex activated by low pH in the stomach that directly stimulates chief cells. ACh released from nerve fibers is a strong stimulant of pepsinogen secretion.

Physiology: Motility



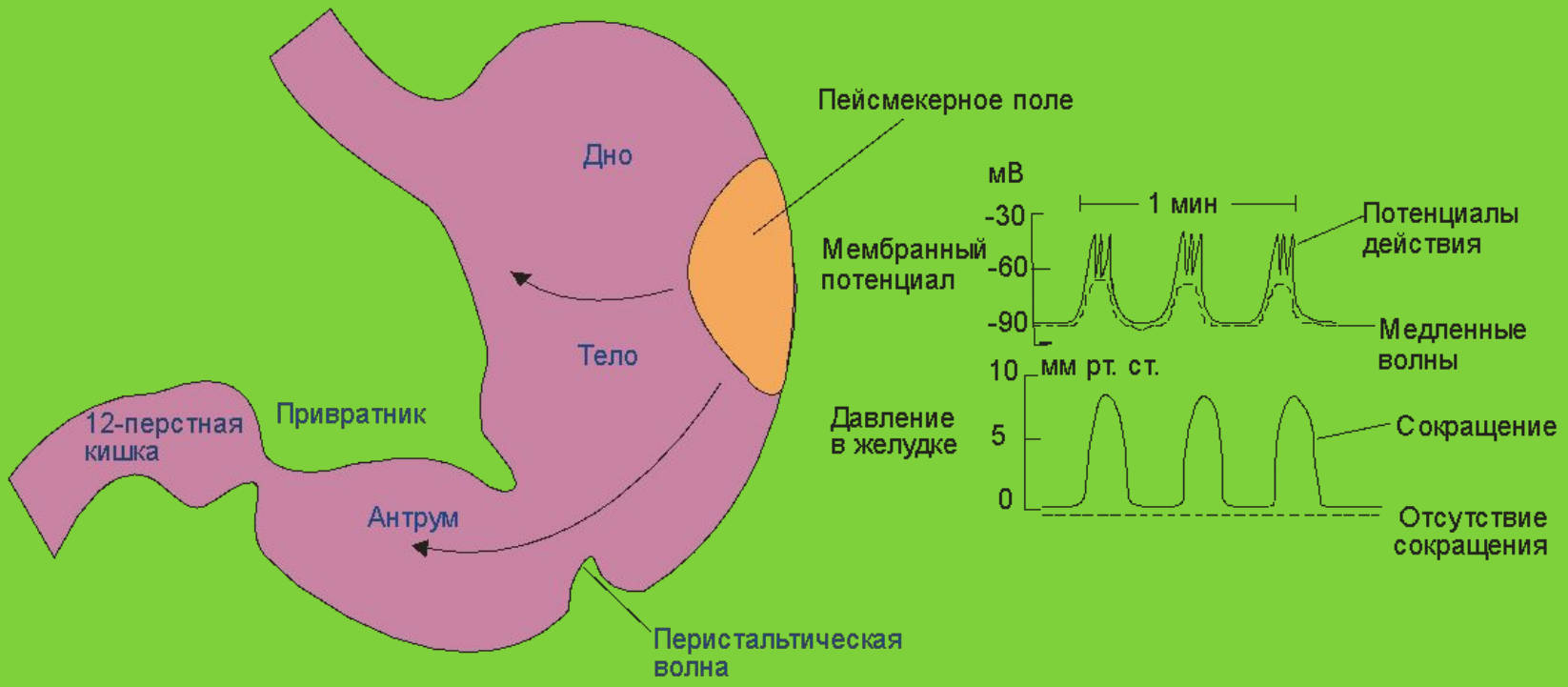
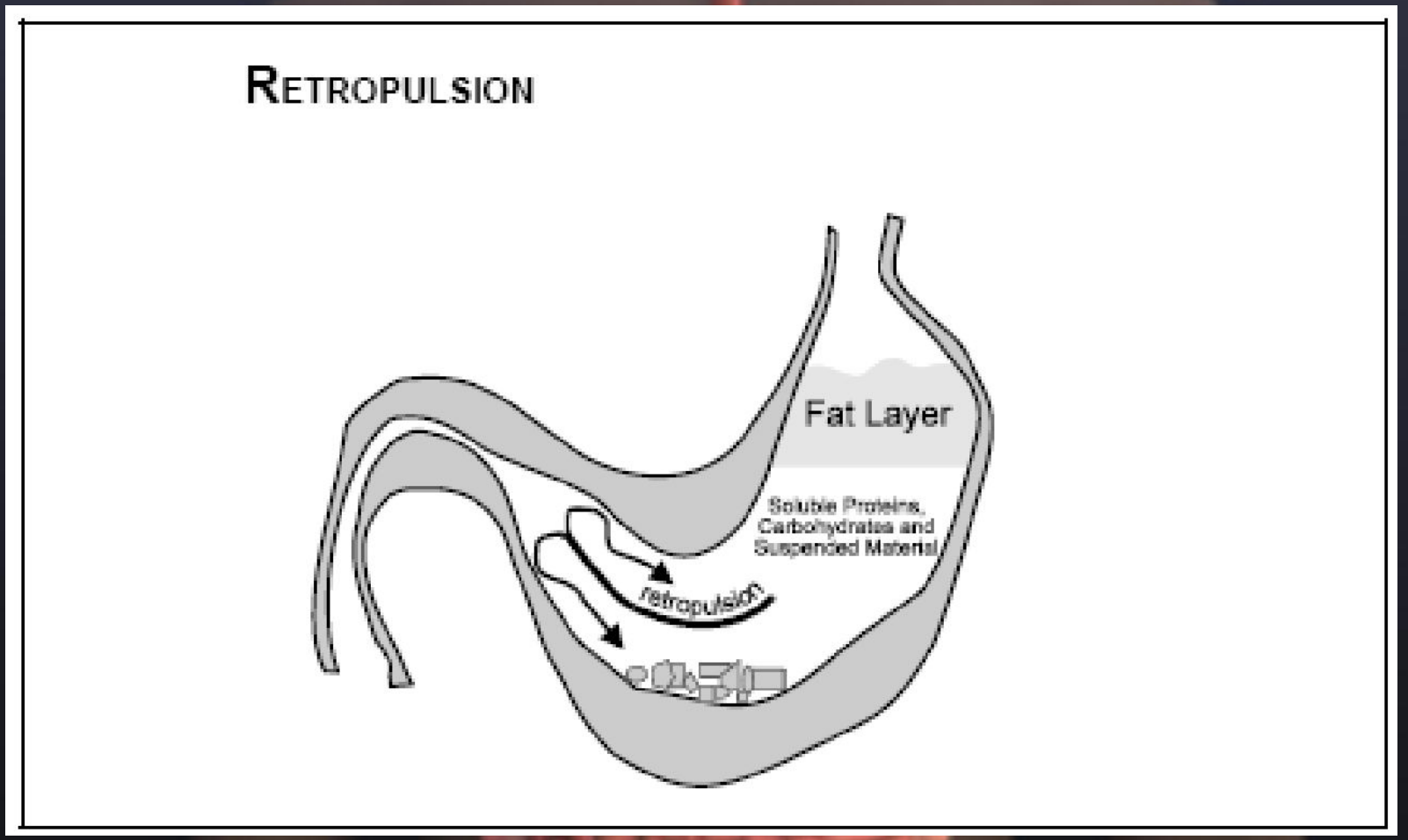


Рис. 10-3. Миоэлектрическая активность желудка во время перистальтики. В проксимальном отделе тела желудка на большой кривизне расположено песмекерное поле желудка. В покое в глакдомышечных клетках пейсмекерного поля возникают медленные волны колебания мембранного потенциала с частотой 3/мин, которые распространяются поперечно и дистально, мигрируя через преддверие до привратника без периодическорй сократительной деятельности желудка (пунктирная линия) . После наполнения желудка пищей клетки п ейсмекерного поля начинают генерировать серии потенциалов действия с частотой 3/мин, которые вызывают перистальтические волны сокращения с той же частотой (сплошная линия). Стрелками показано направление распространения потенциалов действия по гладкомышечным волокнам стенки желудка. Клетки дна желудка не имеют пейсмекерной активности.

.

Моторика желудка: перемешивание, эвакуация



Эвакуация: факторы регуляции

The chyme coming from the stomach is normally hypertonic, acidic, and contains high concentrations of fat, protein, and carbohydrates. Consequently, changing any of the above four rates would change one or more of the following:

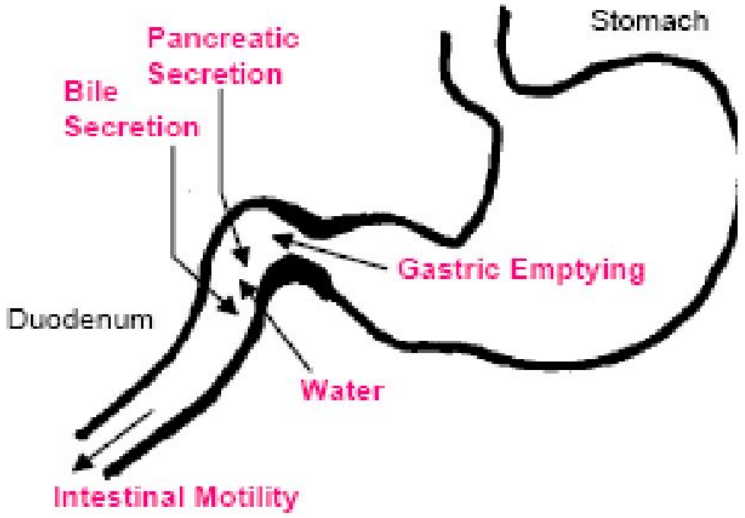
- ^Substrate Concentration
- ^pH
- ^Tonicity
- ^Volume

Состав химуса

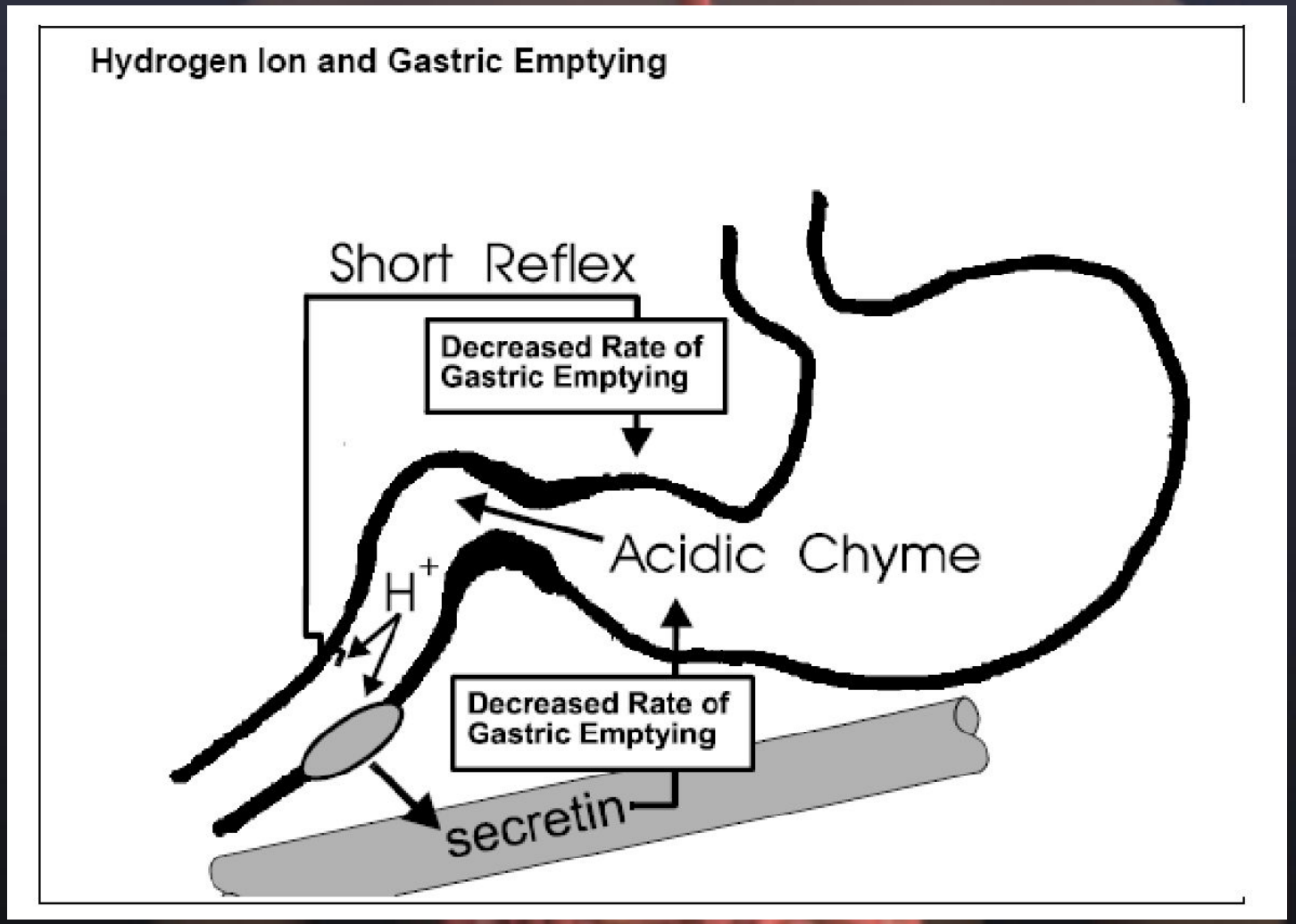
Chyme Composition

Four things determine the final composition of the chyme when it leaves the duodenum:

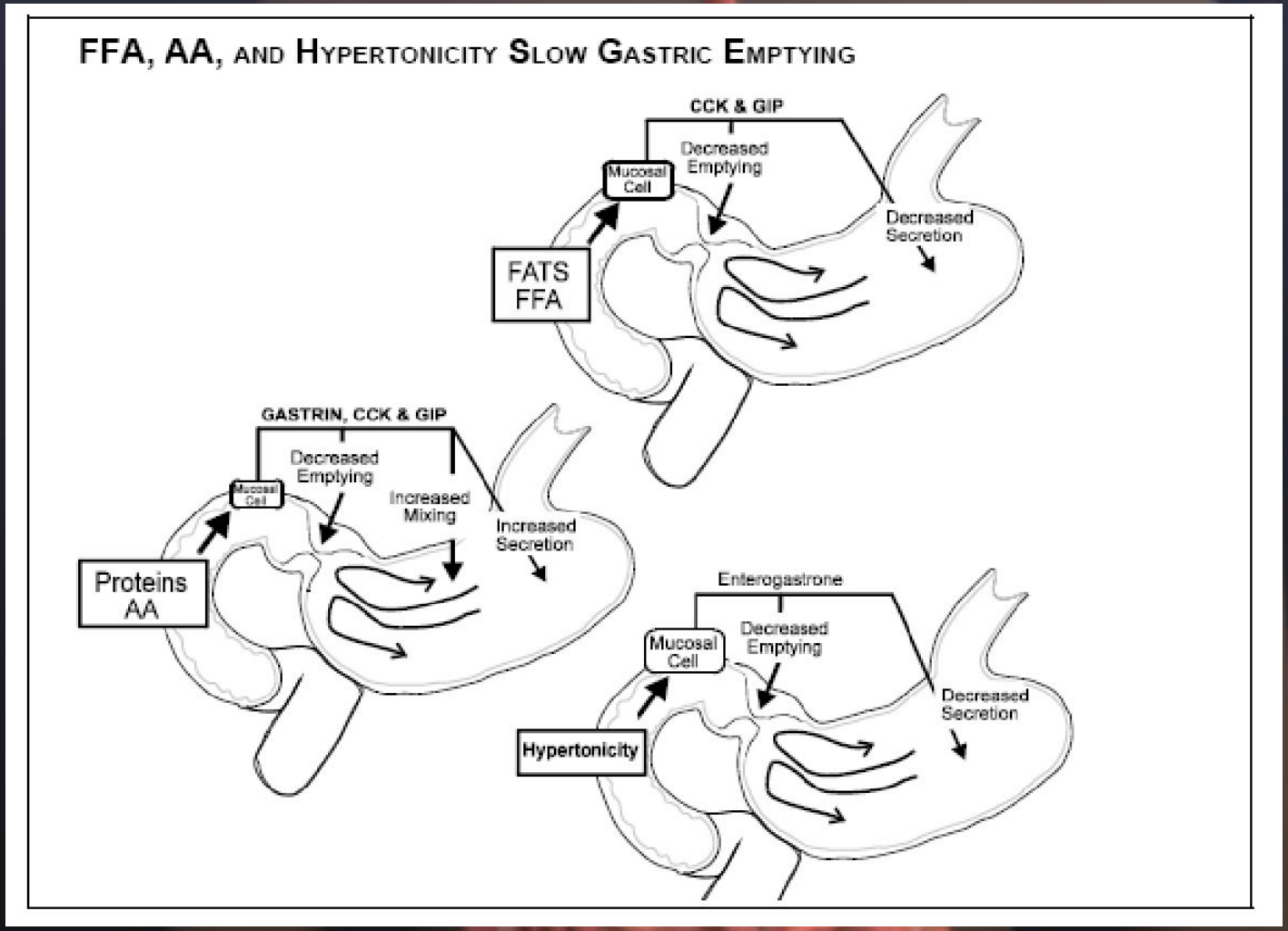
- the rate of gastric emptying
- the rate of pancreatic fluid secretion
- the rate of gall bladder emptying
- the reate of water secretion
- the rate of transport of chyme out of the proximal duodenum (intestinal motility)



Эвакуация: роль H ионов

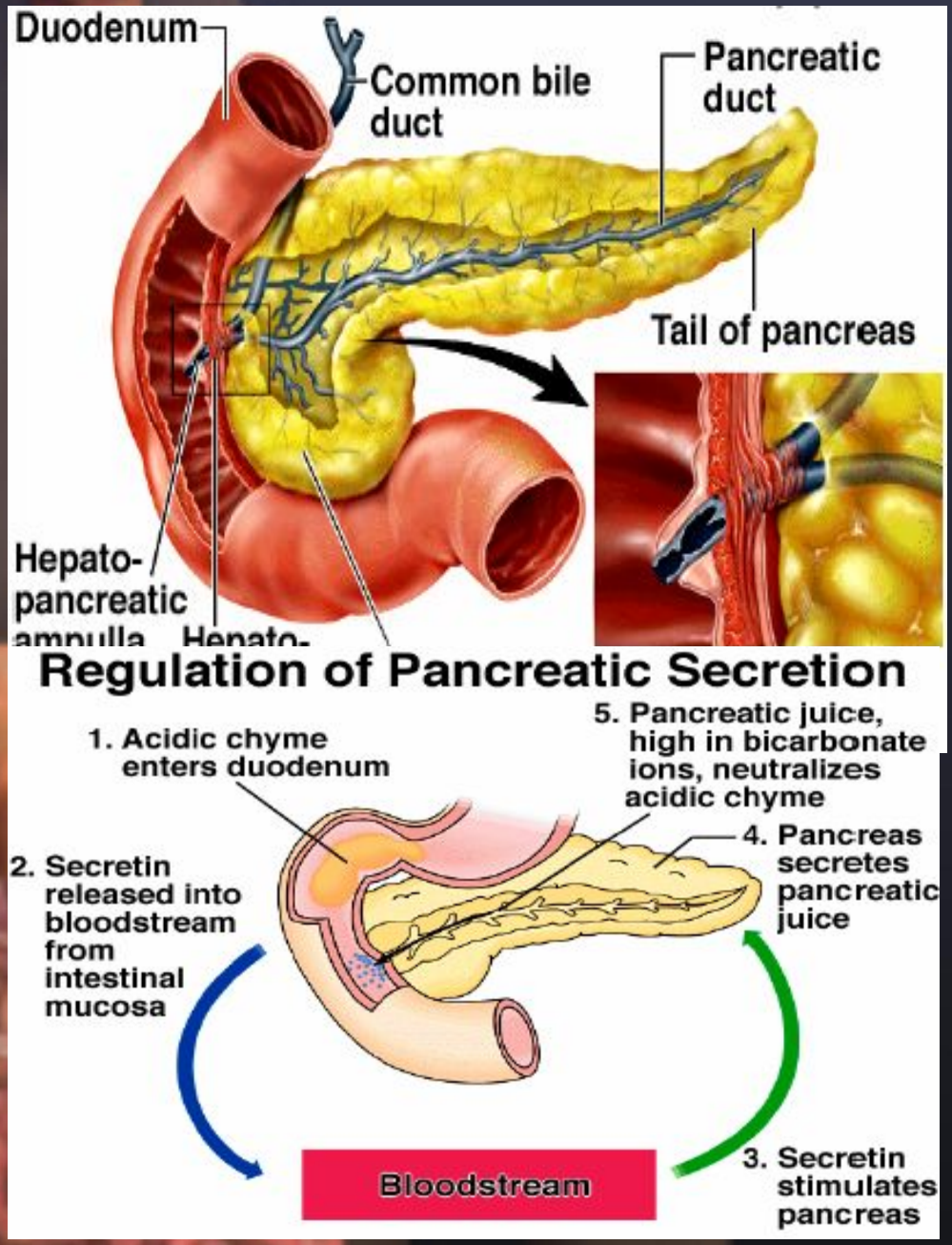


Регуляция эвакуации химуса



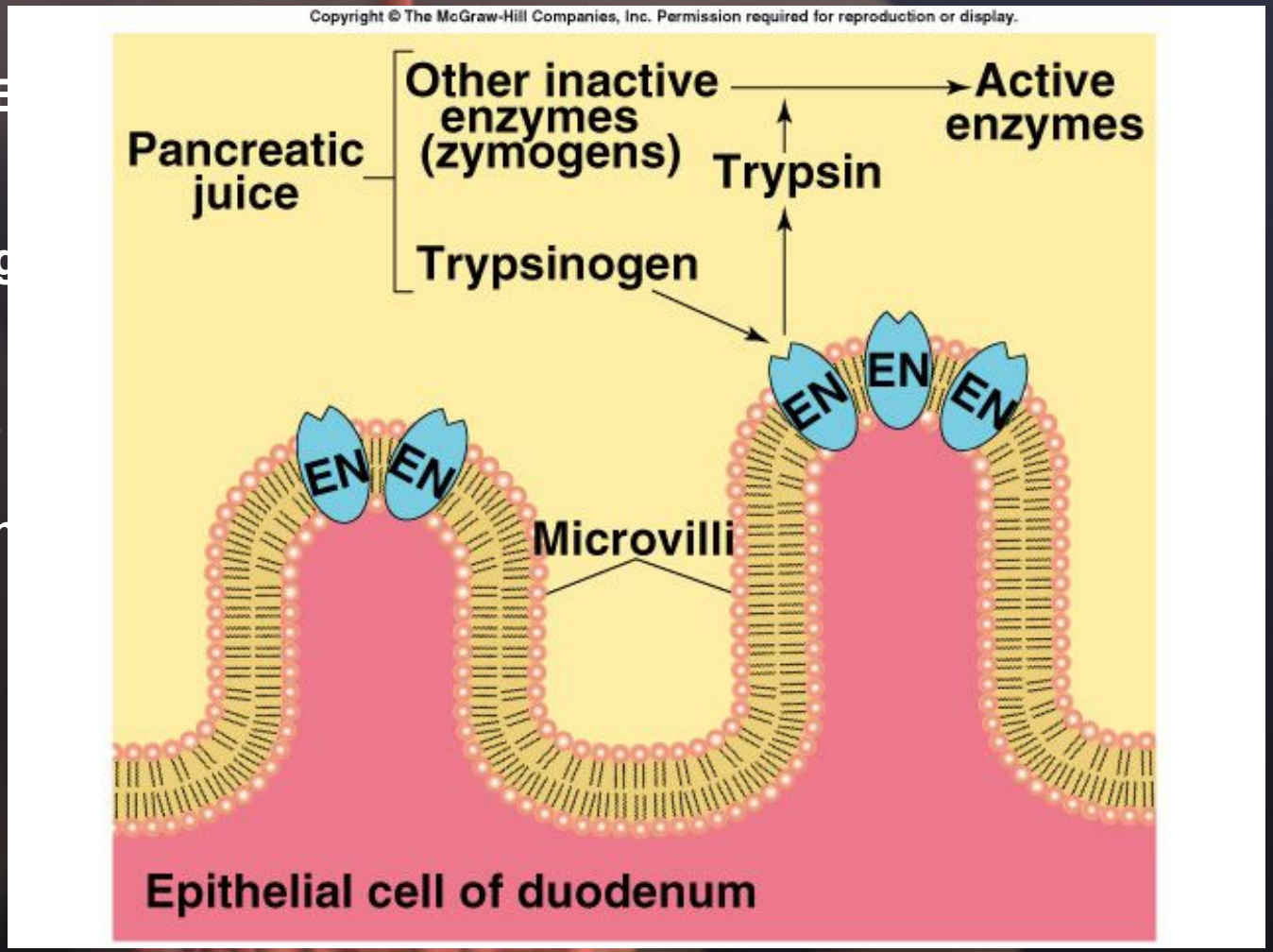
Pancreas

- Exocrine function
- Acinar cells secrete pancreatic juice
  - Amylase
  - Lipase
  - Trypsin
  - Chymotrypsin
  - Carboxypeptidase
  - Nuclease
  - $NaHCO_3^-$
- *Secretin* and *cholecystokinin (CCK)* fr intestinal wall stimulates PJ production

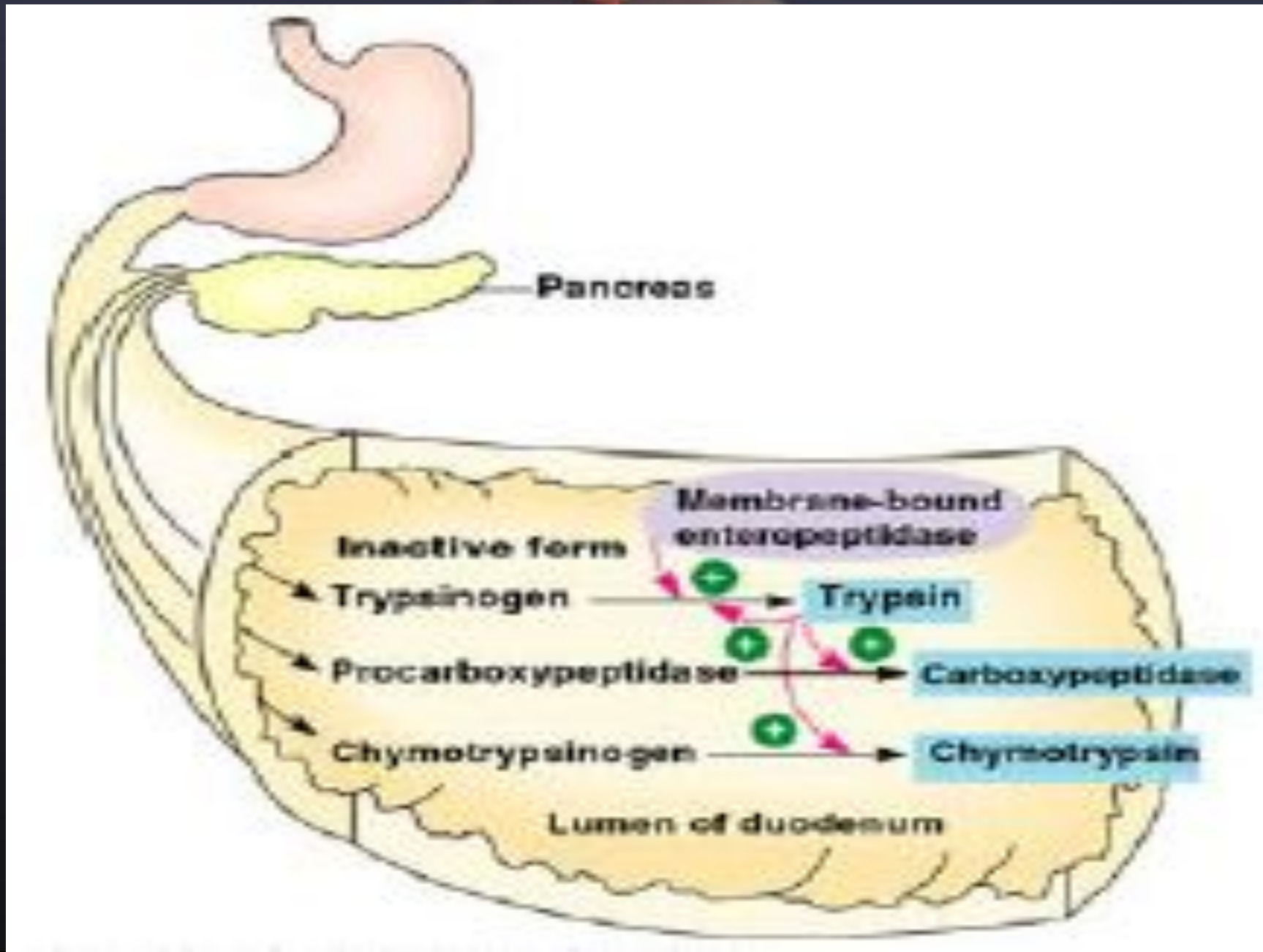


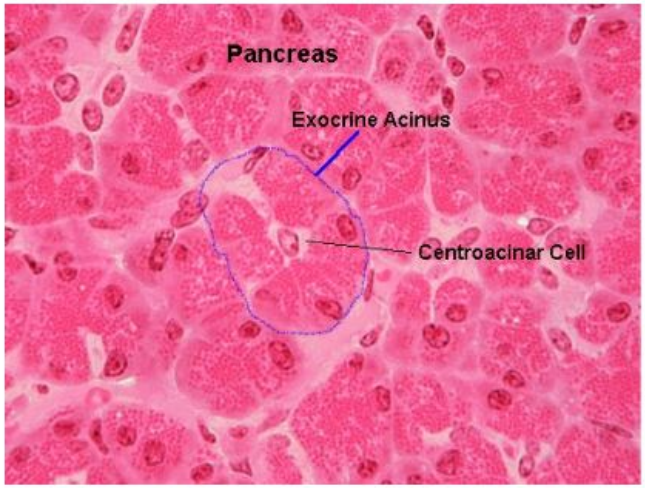
Activation of pancreatic zymogens in the small intestine by brush-border enzymes.

The brushborder enzyme enterokinase (E phosphorylates the protease zymogen trypsinogen, converting to its active form (trypsin). Trypsin, in turn digests other pancreatic zymogens in their active forms.



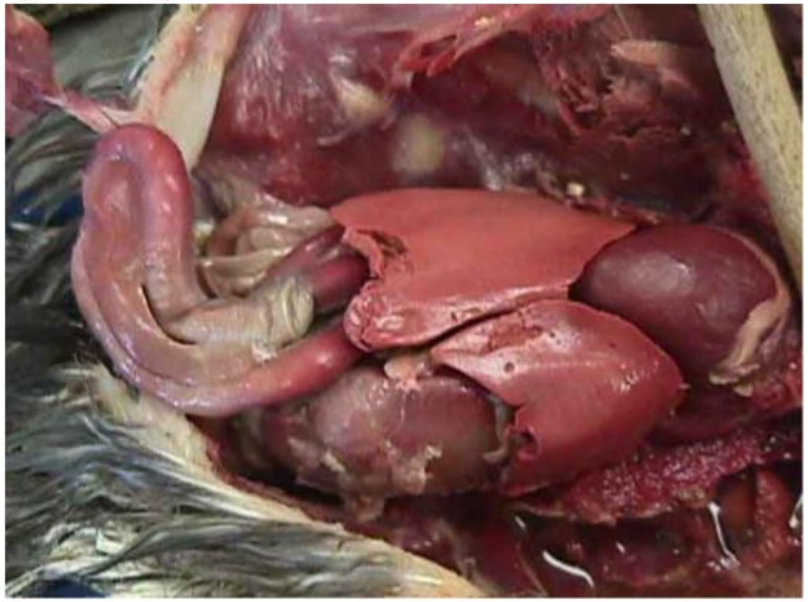
Активация ферментов





http://www.sacs.ucsf.edu/home/cooper/Anat118/GI-Glands/pancreas/pancreas-acinus.jpg

Spot the pancreas!



http://www.nesc.k12.in.us/union/Mr.%20Sly/Pigeon%20Dissection/pancreas%20liver%20gizzard%20www.jpg

Contents of pancreatic juice:

basic (high pH) (bicarbonate ions neutralise acidic gastric products)

Pancreatic juice contains many different enzymes

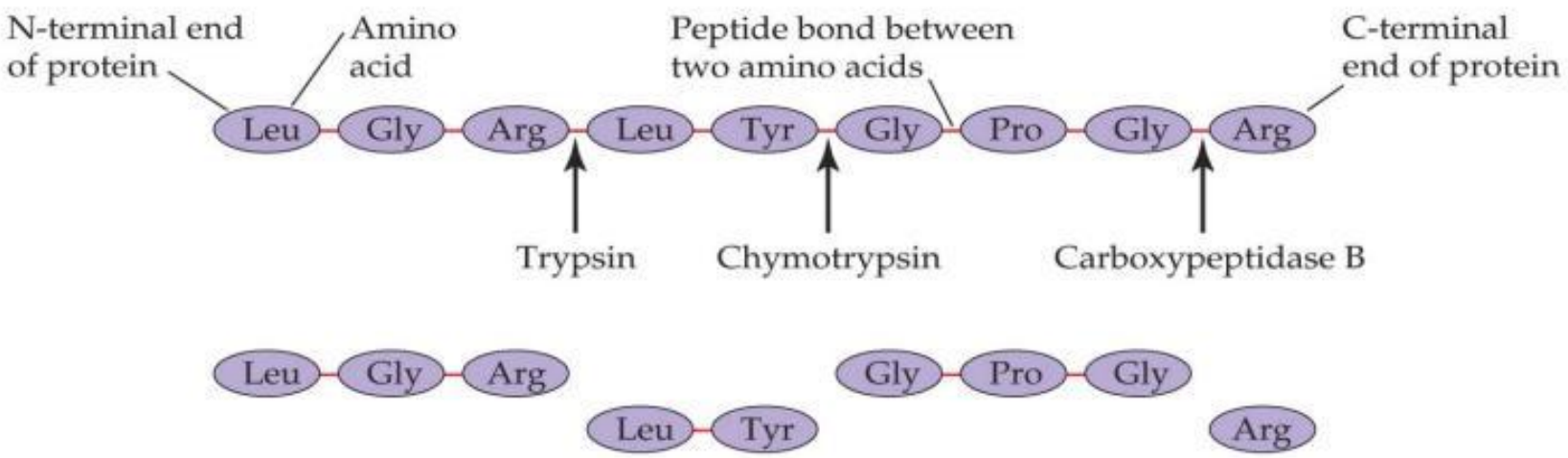
pancreatic lipase

pancreatic amylase

trypsin and chymotrypsin (endopeptidases)

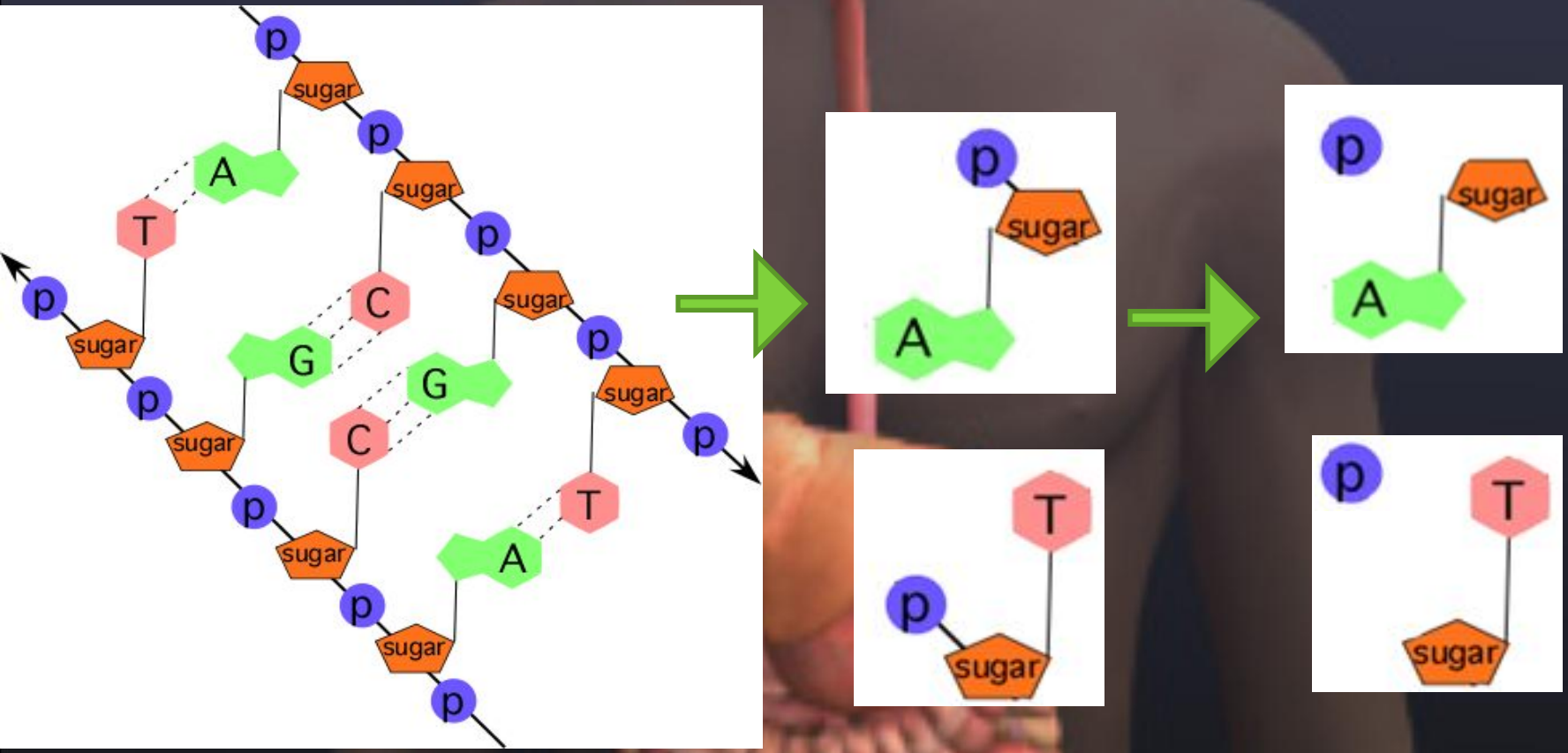
carboxypeptidase and elastase (exopeptidase)

Пищеварение в **duodenum**

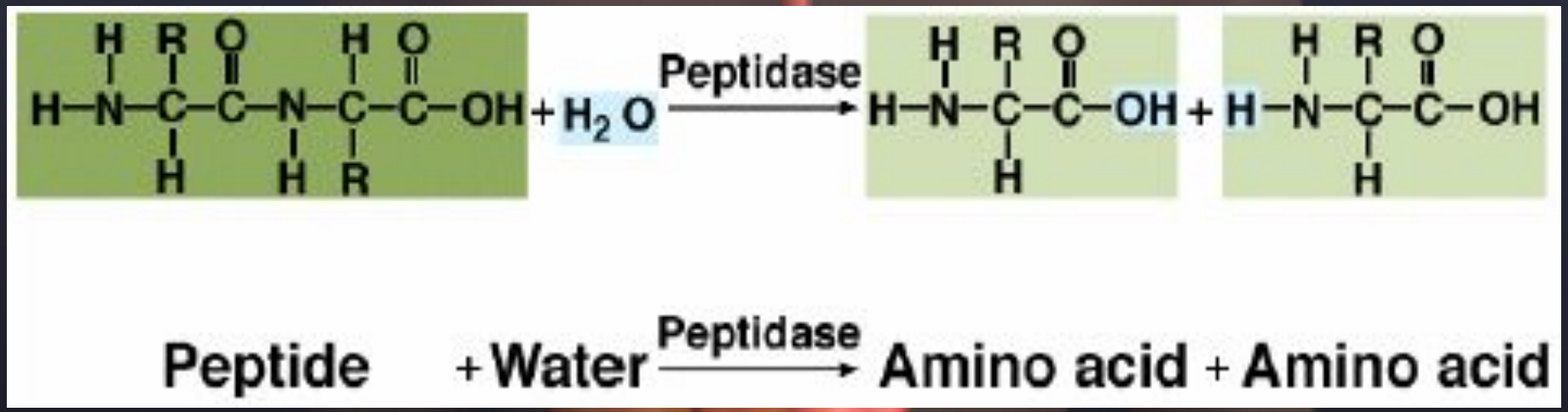


ANIMAL PHYSIOLOGY, Figure 4.18 © 2004 Sinauer Associates, Inc.

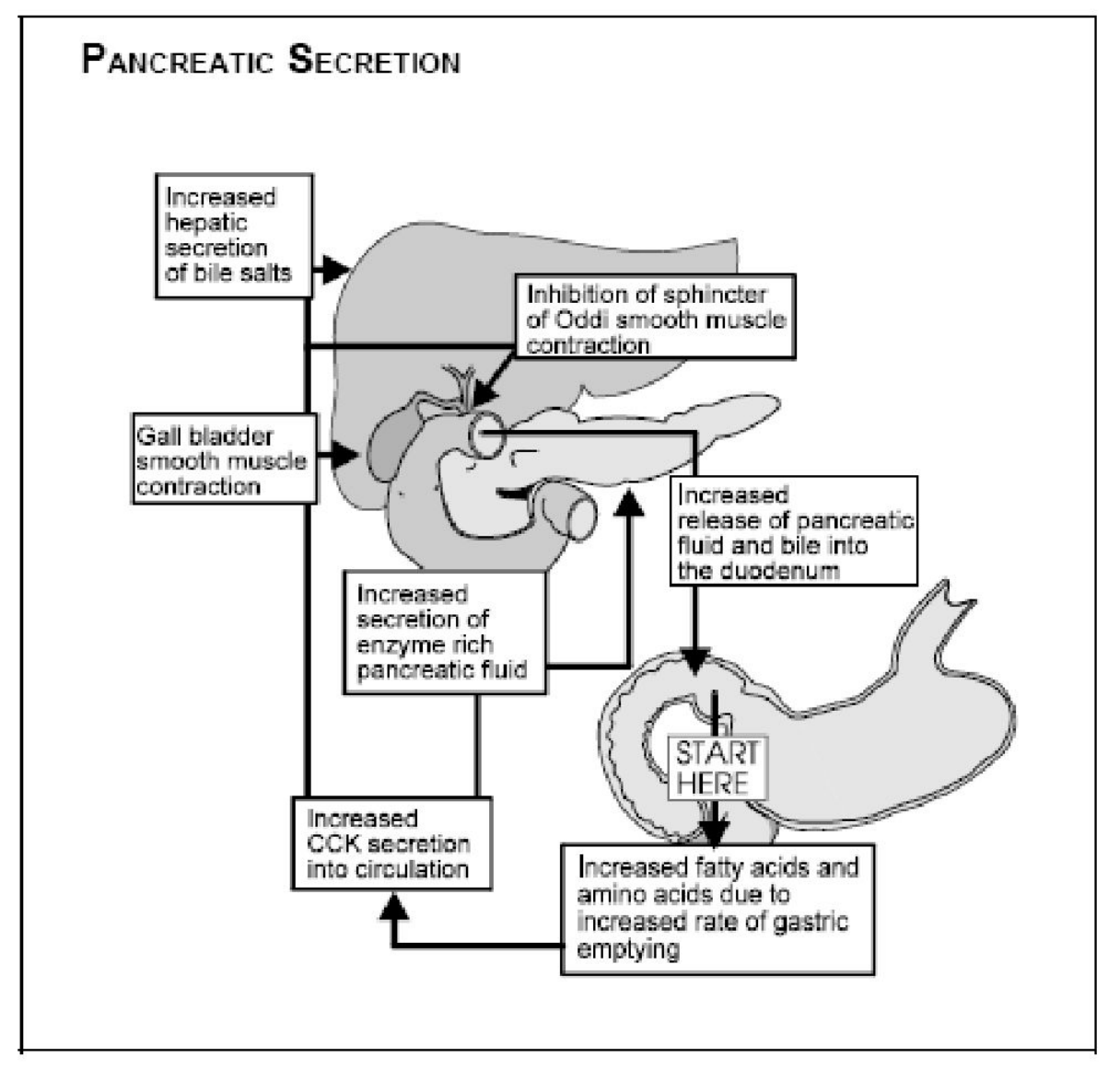
Расщепление углеводов



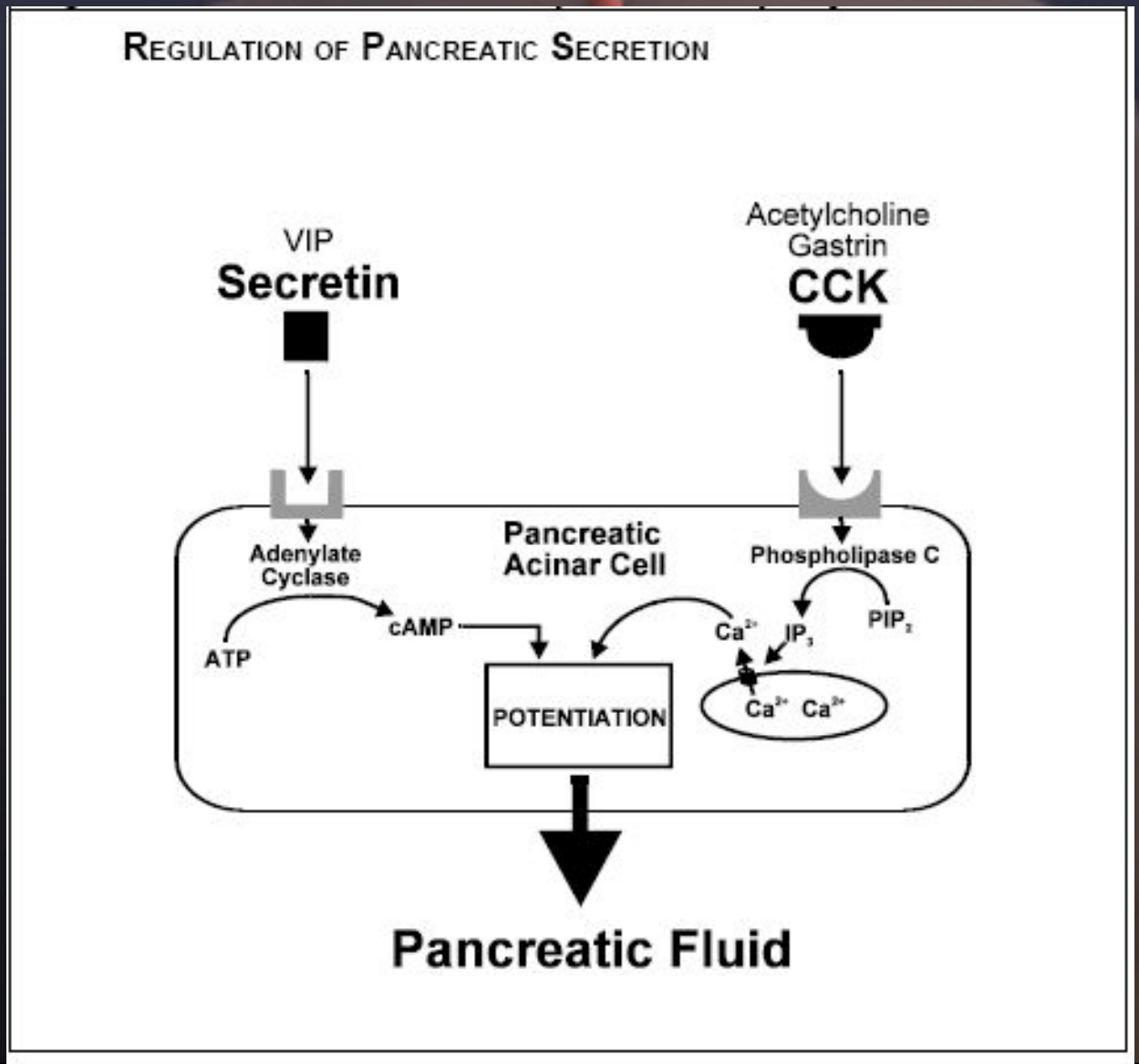
Расщепление белков



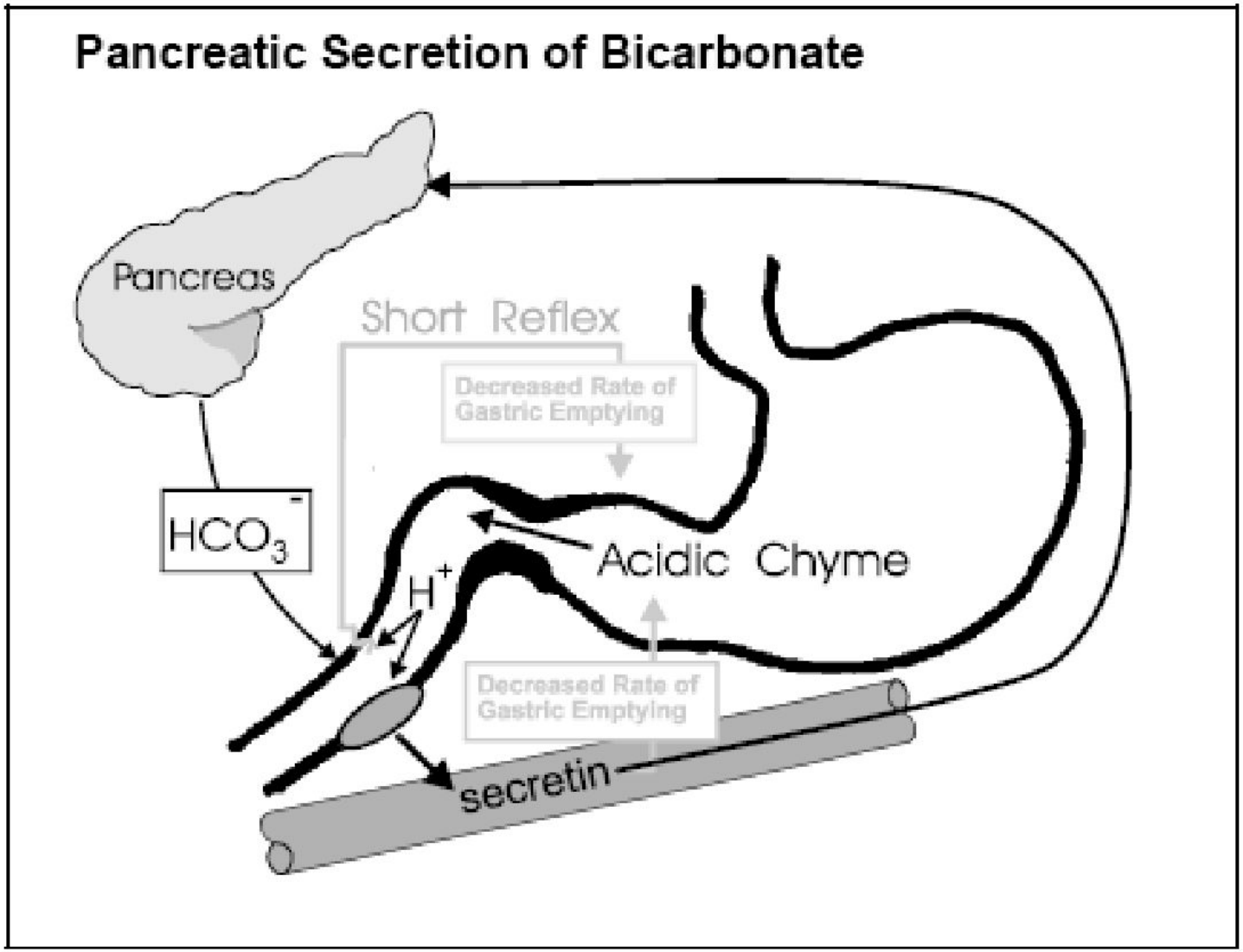
Панкреатическая секреция

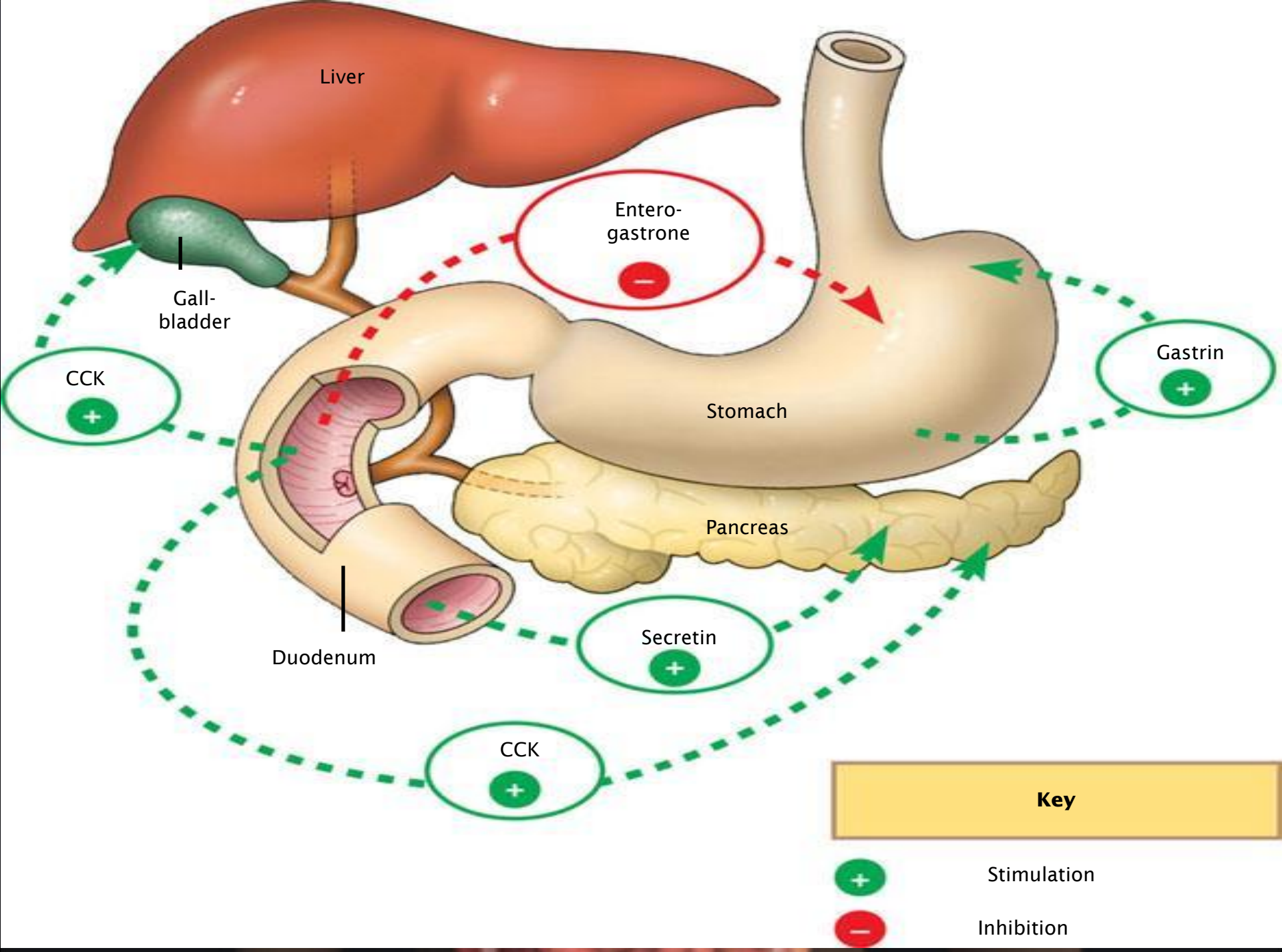


Регуляция панкреатической секреции

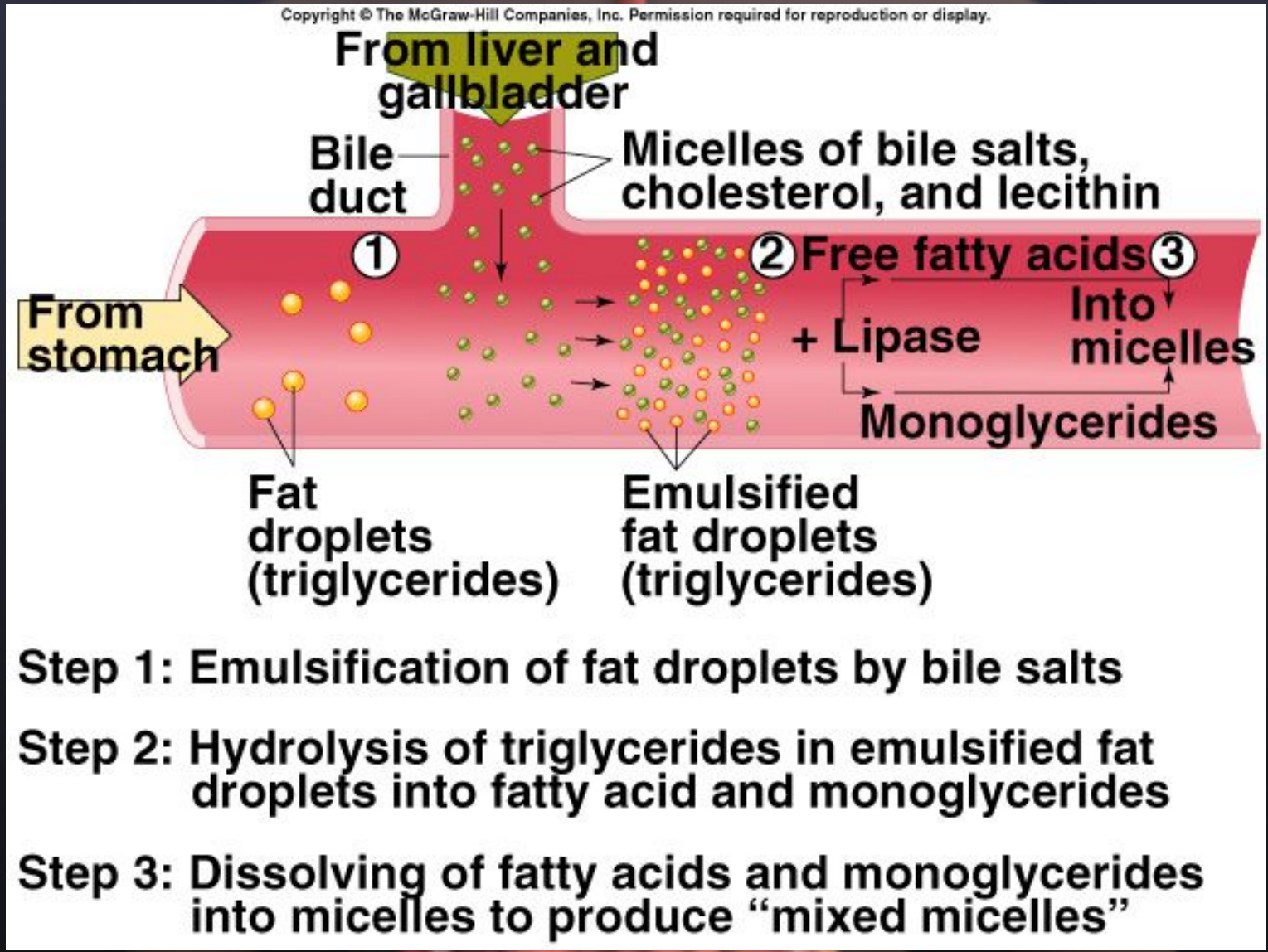


Секреция бикарбоната




Liver
Gall-
bladder
Entero-
gastrone
CCK
Gastrin
Stomach
Pancreas
Duodenum
Secretin
CCK
Key
Stimulation
Inhibition

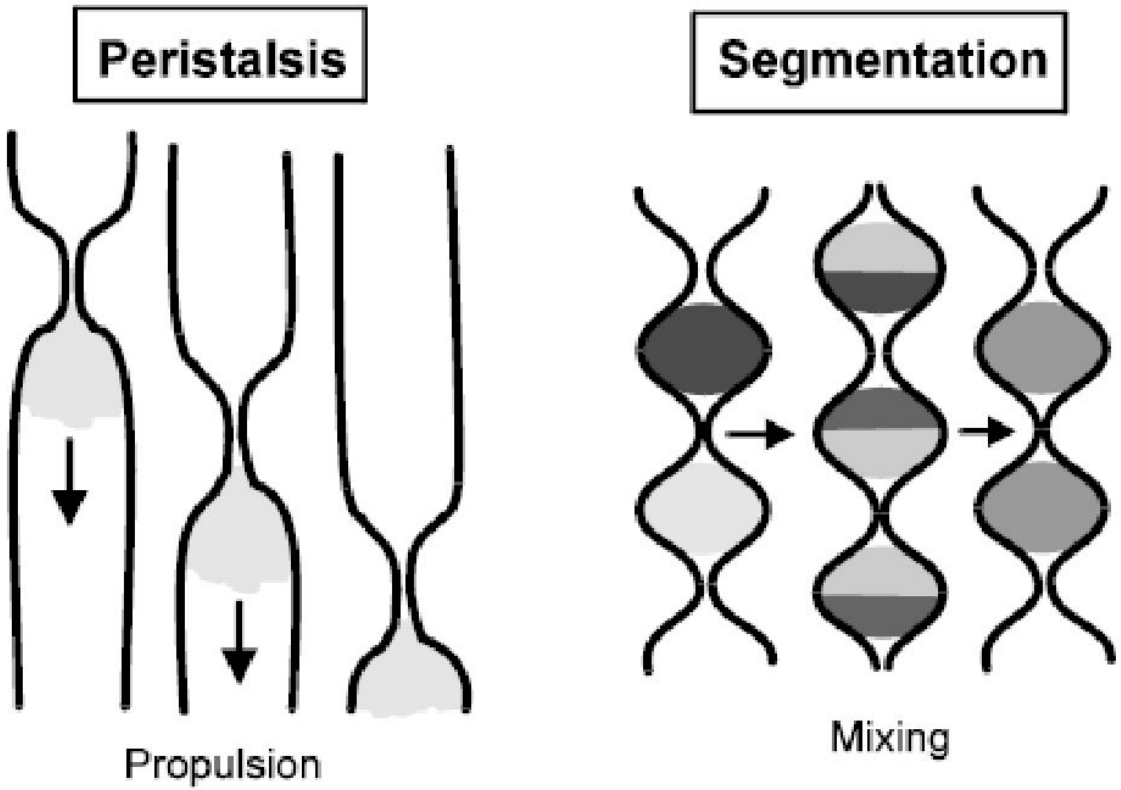
Emulsification and digestion of fat in the small intestine.

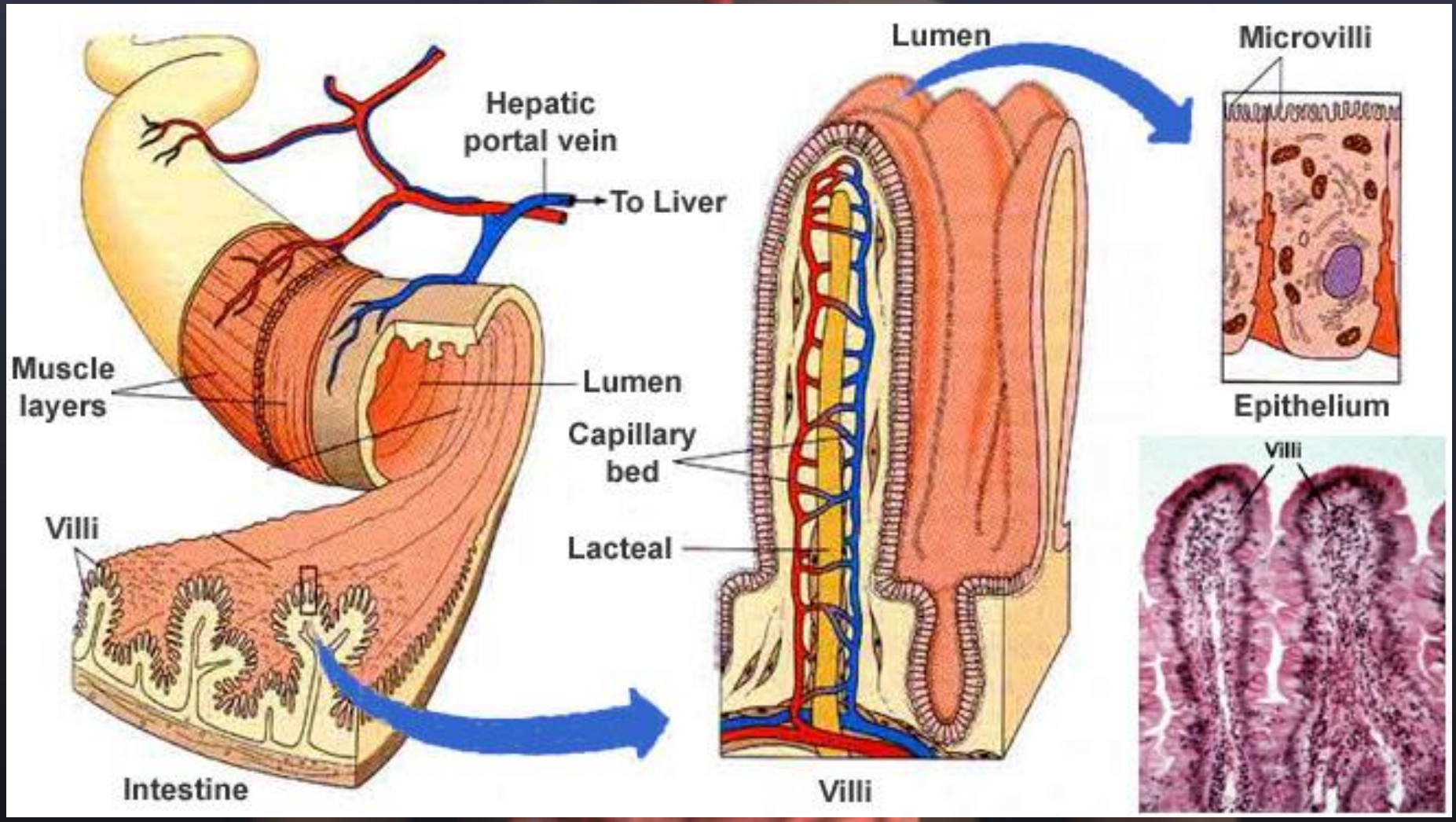


Пищ

Пищеварение и всасывание углеводов и белков

Intestinal Motility



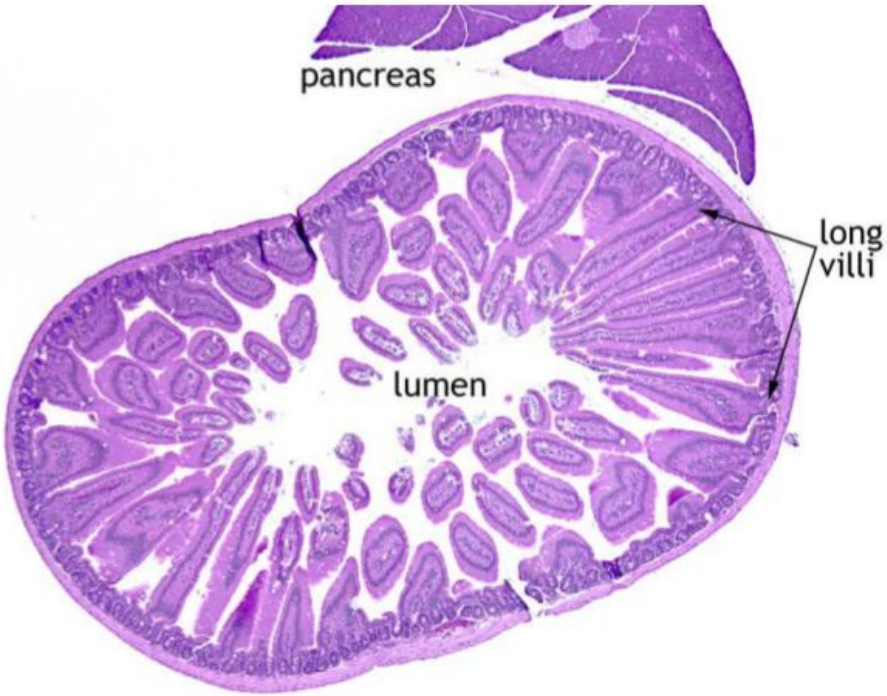

Hepatic
portal vein
To Liver
Muscle
layers
Lumen
Capillary
bed
Villi
Lacteal
Intestine
Lumen
Villi
Microvilli
Epithelium
Villi

The small intestine: digestion and absorption of macromolecules

DUODENUM

Digestion: close association with pancreas, many enzymes released into the lumen.

Membrane-bound enzymes (e.g. maltase) increase efficiency of digestion of some molecules.

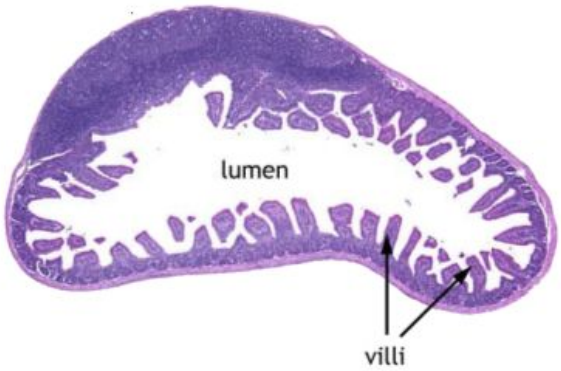


http://www.deltagen.com/target/histologyatlas/atlas_files/digestive/duodenum_4x.jpg

ILEUM

Absorption of digested molecules:

Surface area maximised by villi and microvilli (more on this in the next chapter)



http://www.deltagen.com/target/histologyatlas/atlas_files/digestive/ileum_4x.jpg

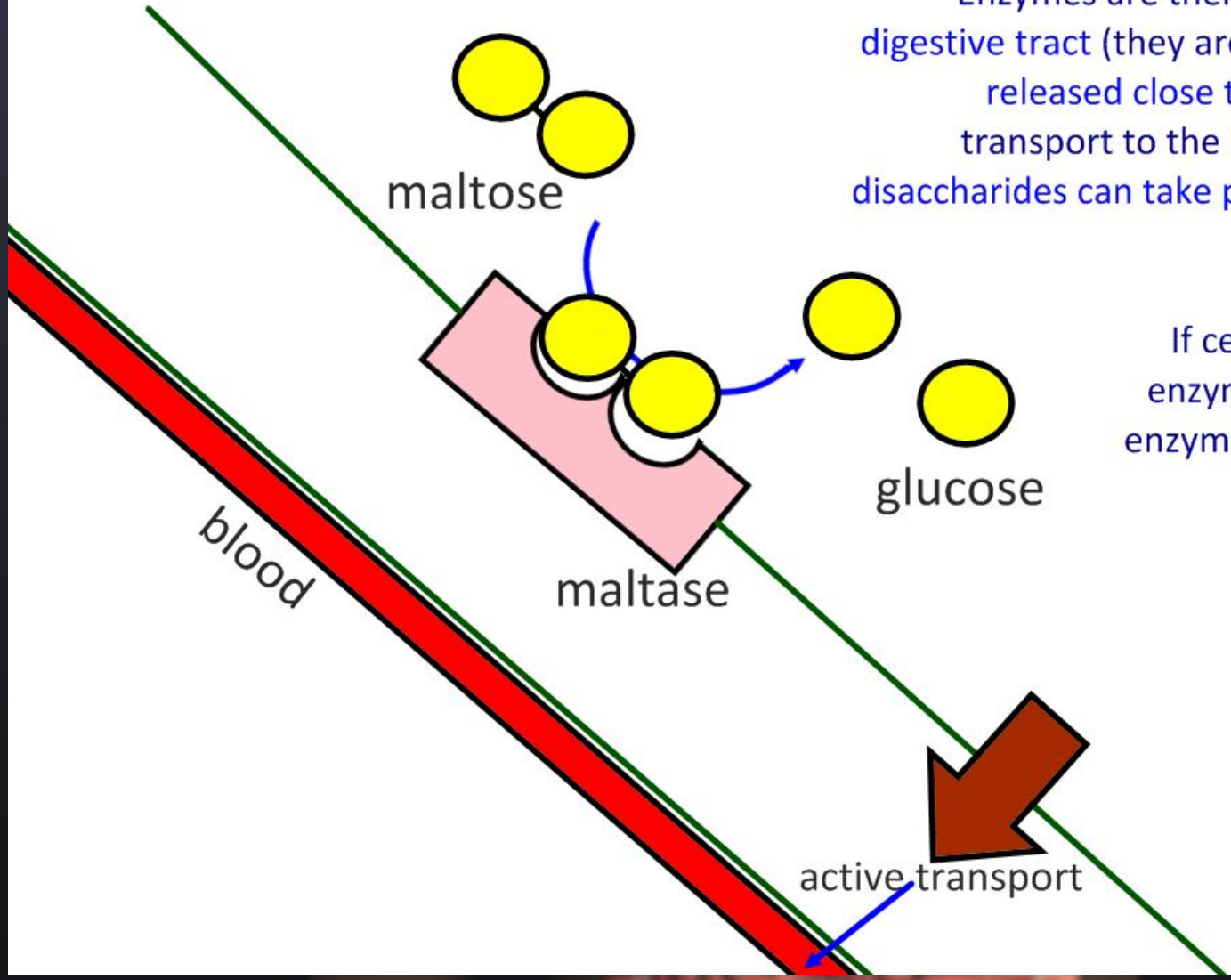
Membrane-bound enzymes

e.g. maltase (maltose → glucose)

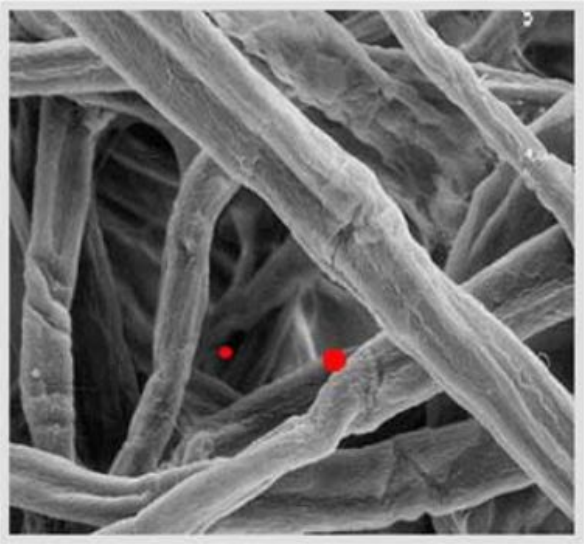
Some digestive enzymes are locked in place on the epithelium of the villi of the duodenum.

Enzymes are therefore not lost through the digestive tract (they are conserved), products are released close to the membrane for rapid transport to the blood and digestion of the disaccharides can take place early in the digestive system.

If cells with membrane-bound enzymes become detached, the enzymes will continue to work in the lumen of the gut.



Cellulose digestion



http://www.amsoil.com/products/ea_filters/images/cellulose1.jpg

Cellulose is a structural polysaccharide found in foods of plant origin.

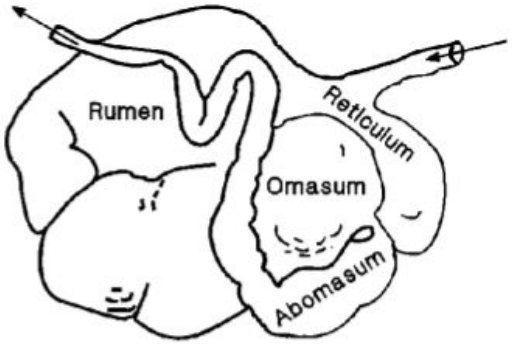
Digestion of cellulose is by cellulase, which is not produced by humans. Therefore, cellulose passes through the digestive system and is egested in faeces.

Darwin proposed that the human appendix is a vestigial organ from our ancestors, allowing digestion of leaves. The appendix harboured cellulase-producing bacteria is a symbiotic relationship.

This adaptation exists in nature in the form of the ruminant stomach. Ruminants, such as cows, have a rumen which houses bacteria, protozoa and fungi. These microbes aid in the digestion of cellulose.

Cellulose (dietary fibre) remains a vital part of the human diet, as it is aids the health of the digestive system, sweeping out dead cells, unabsorbed materials and bacteria.

The ruminant stomach:

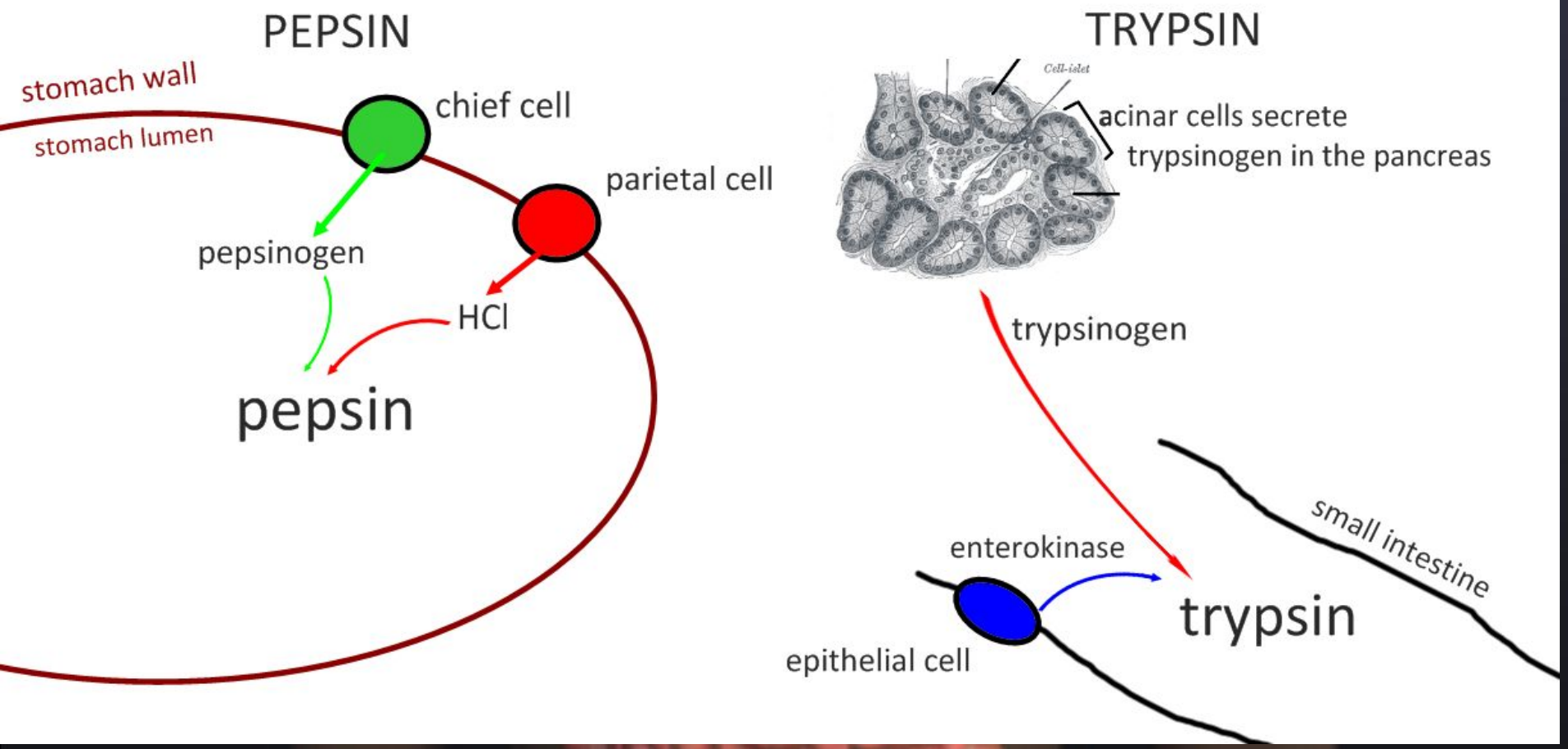


http://spuds.agron.ksu.edu/rumen.gif

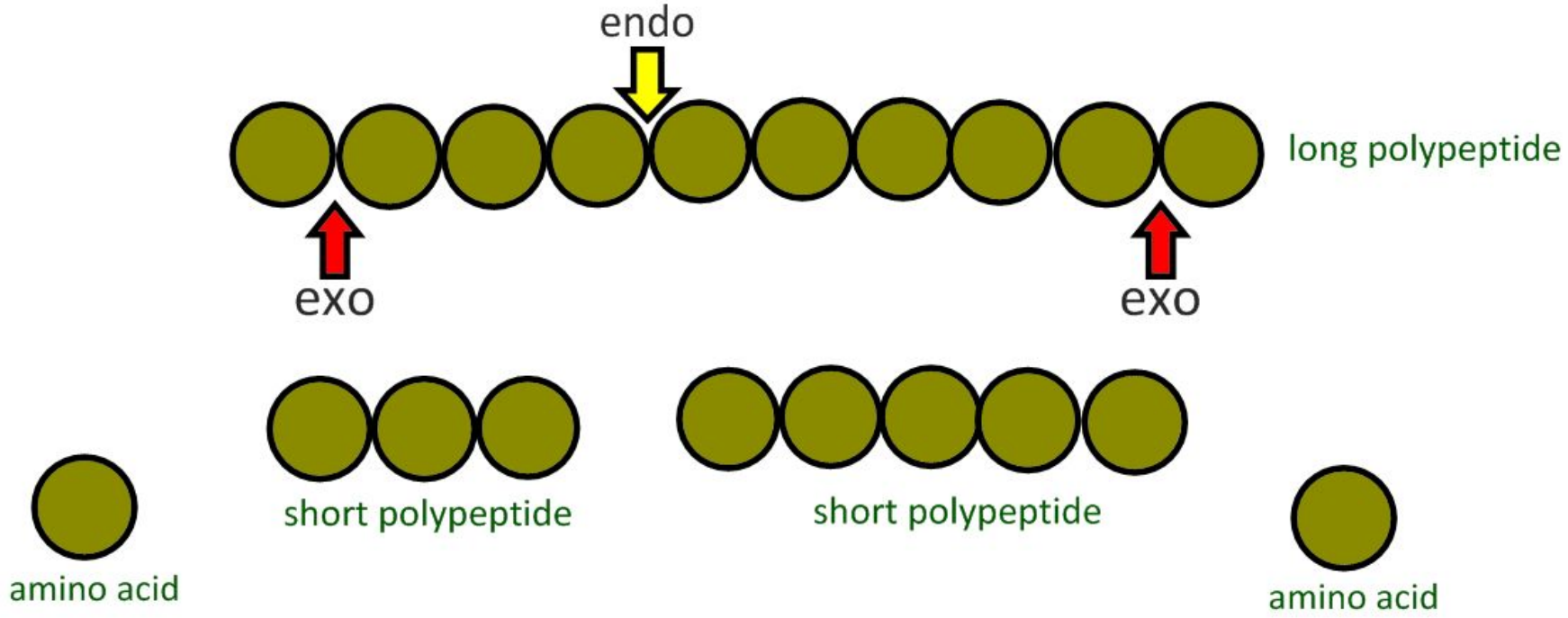
Digestion of Proteins: inactive precursors

Pepsin and trypsin are proteases. If they were secreted as active enzymes, they would cause damage to the exocrine cells (autodigestion).

They are instead secreted as inactive precursors (*pepsinogen* and *trypsinogen*), which are harmless. The enzymes become activated under the right conditions.



Digestion of Proteins: exo- and endo-peptidases



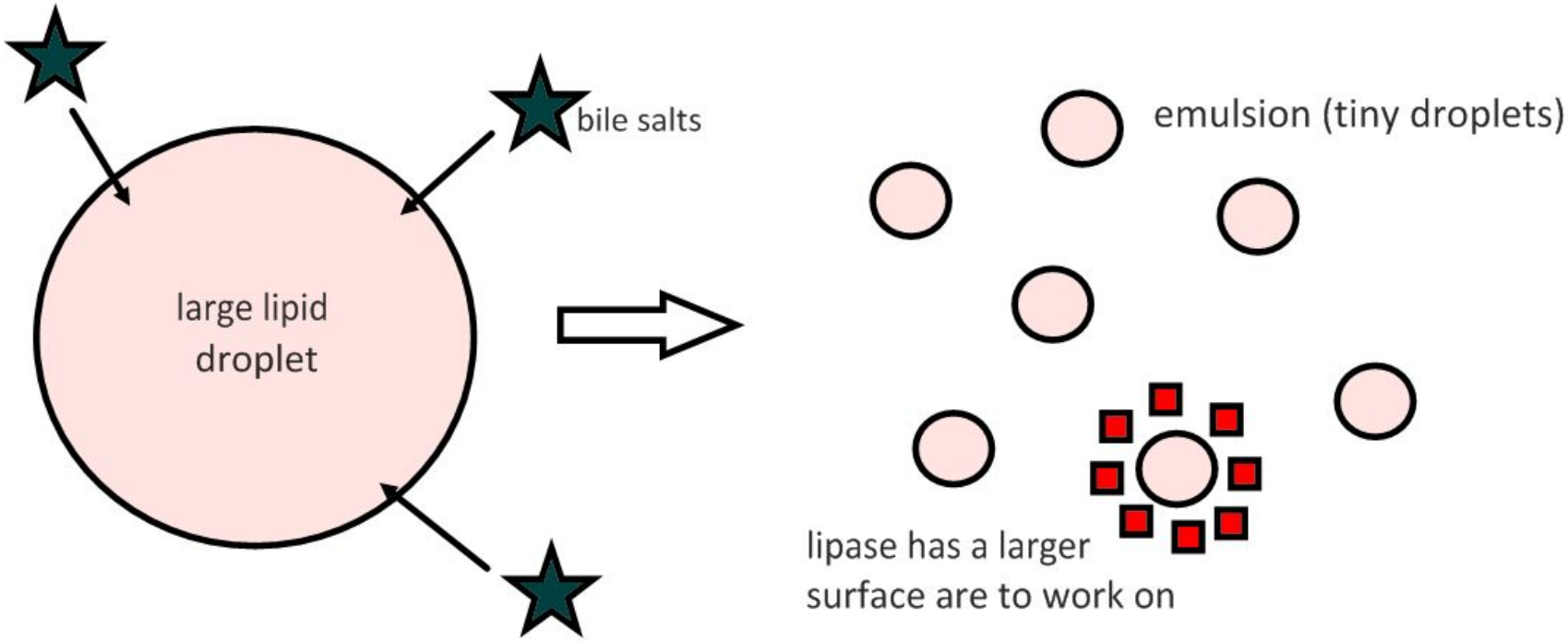
Endopeptidases (e.g. pepsin, trypsin) hydrolyse bonds in polypeptide chains.
They break large polypeptides into smaller ones.
Increased surface area for action of exopeptidases.

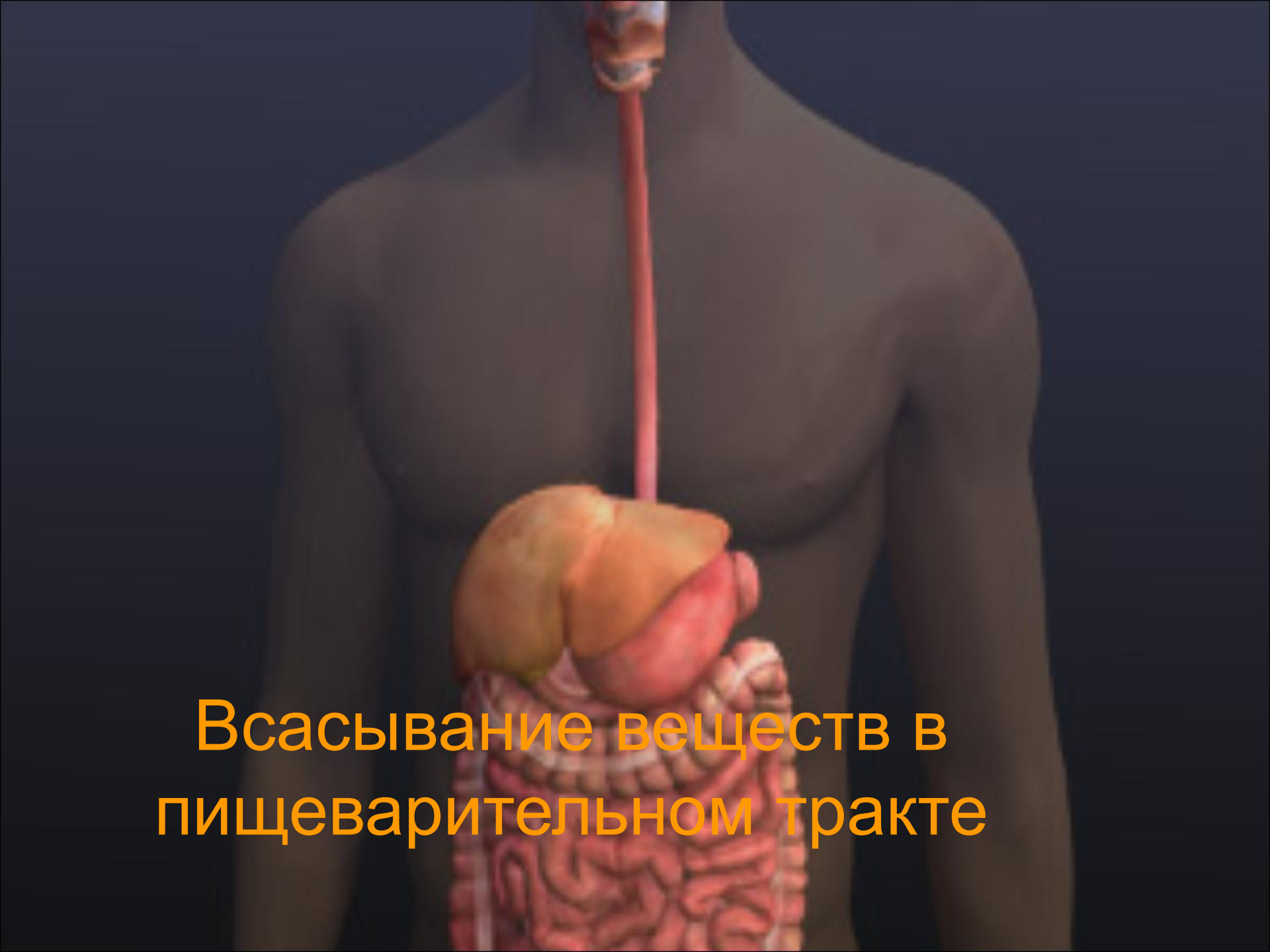
Exopeptidases (e.g. dipeptidase) remove terminal amino acids.
These amino acids are then available for absorption.

Digestion of lipids: the problem of hydrophobia

Problem: Lipids are hydrophobic and form large droplets.
Lipases are water-soluble, so cannot gain access to any more than the outermost lipid molecules in the droplet.
Digestion of lipids would be very slow and inefficient.

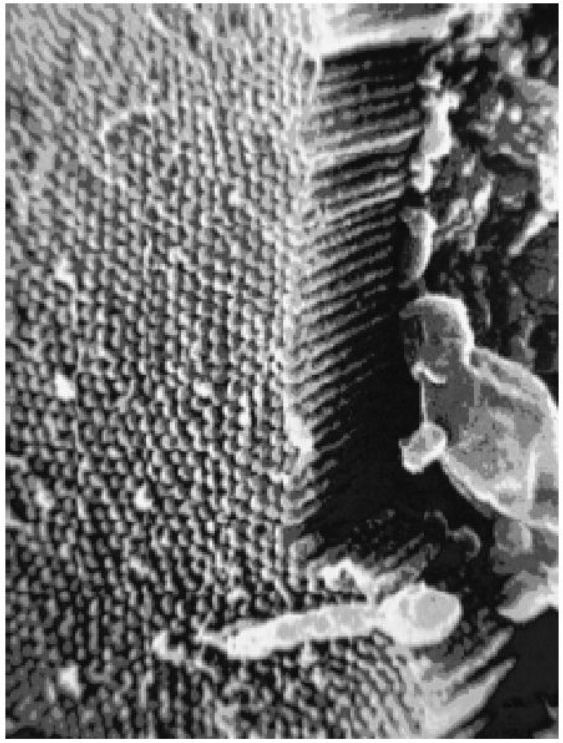
Solution: Use bile salts to emulsify the lipids.
These are secreted by the liver and stored in the gall bladder.
They have both hydrophilic and hydrophobic ends and break them up into smaller droplets, giving increased surface area for lipases to work on.

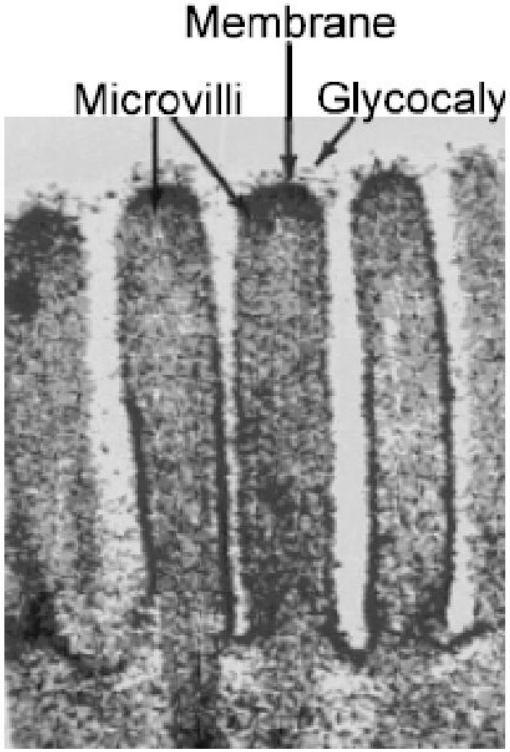


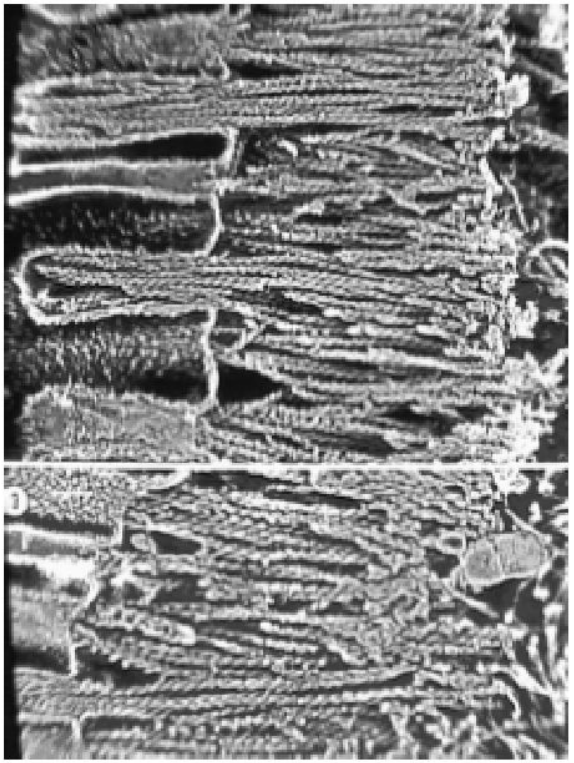


Всасывание веществ в пищеварительном тракте

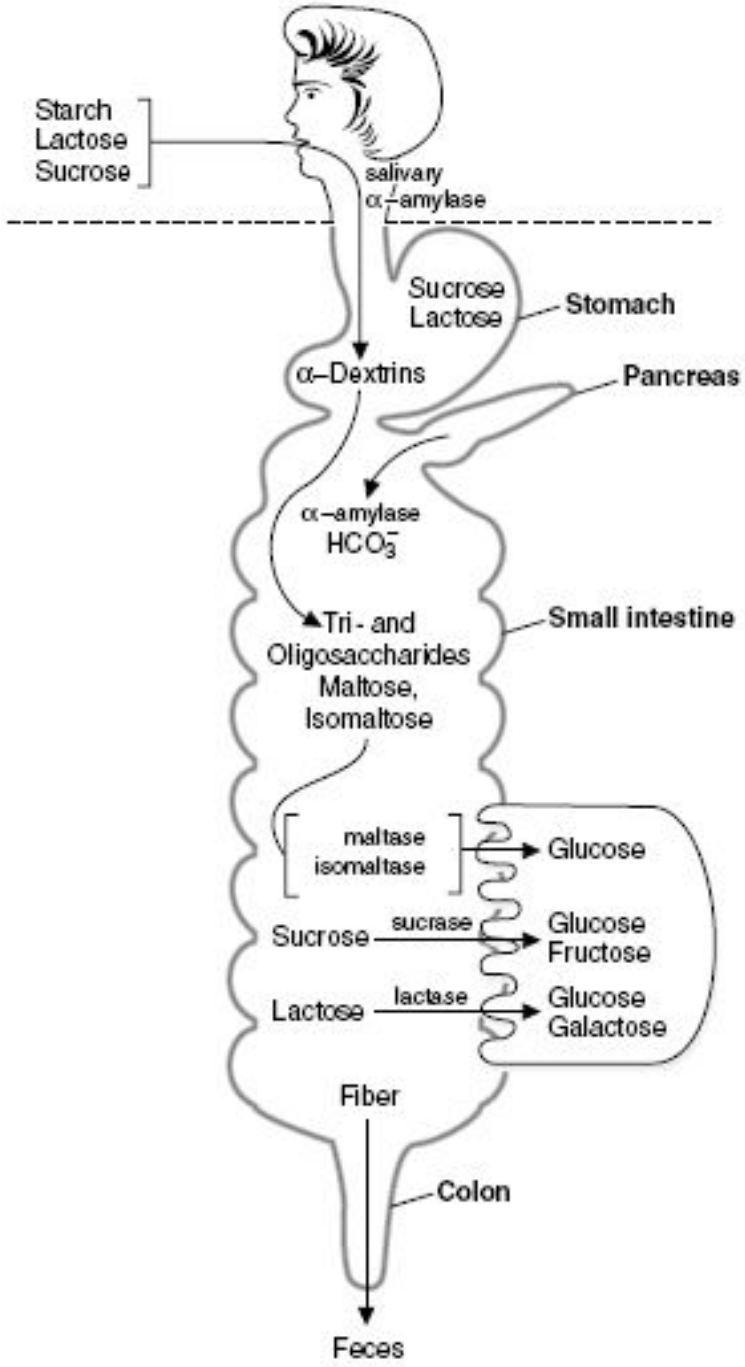
Microvilli





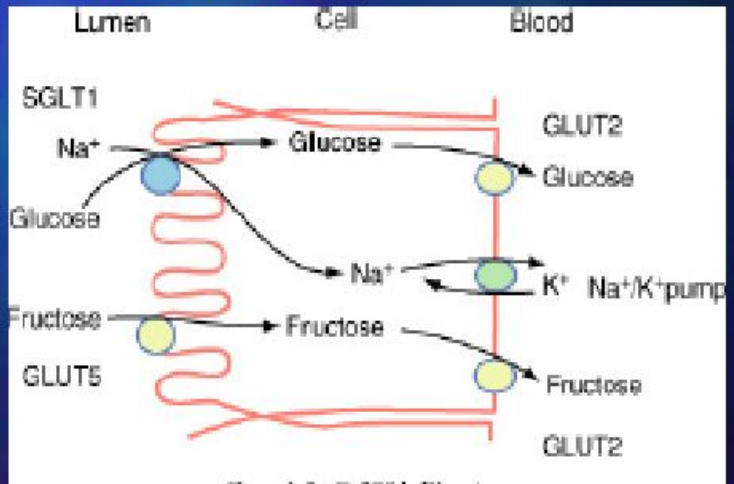


Overview of carbohydrate digestion.

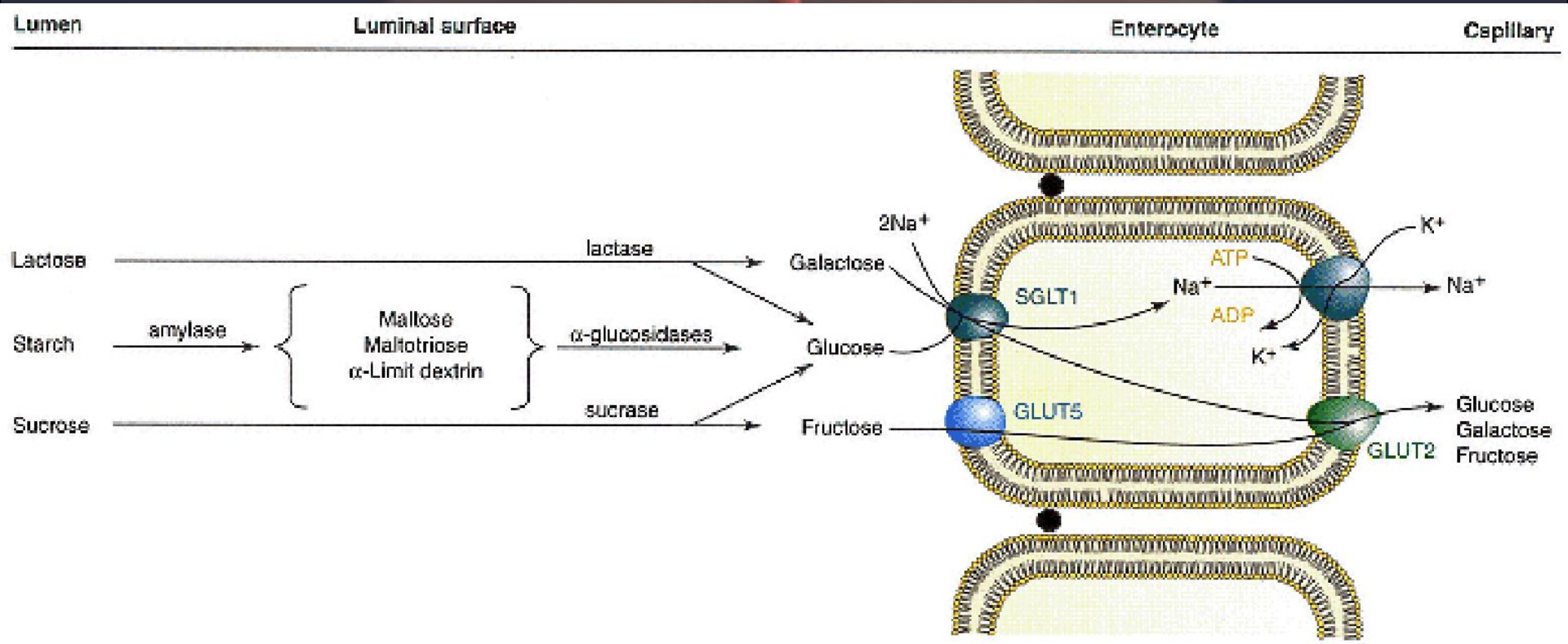


Physiology: Digestion and Absorption

- Carbohydrates
  - Broken down by intra luminal amylase and amylopectin
  - Brush border: maltase, lactase, sucrase, trehalase -> break disaccharides
  - Monosaccharides are absorbed
    - Na cotransport
    - Facilitated diffusion

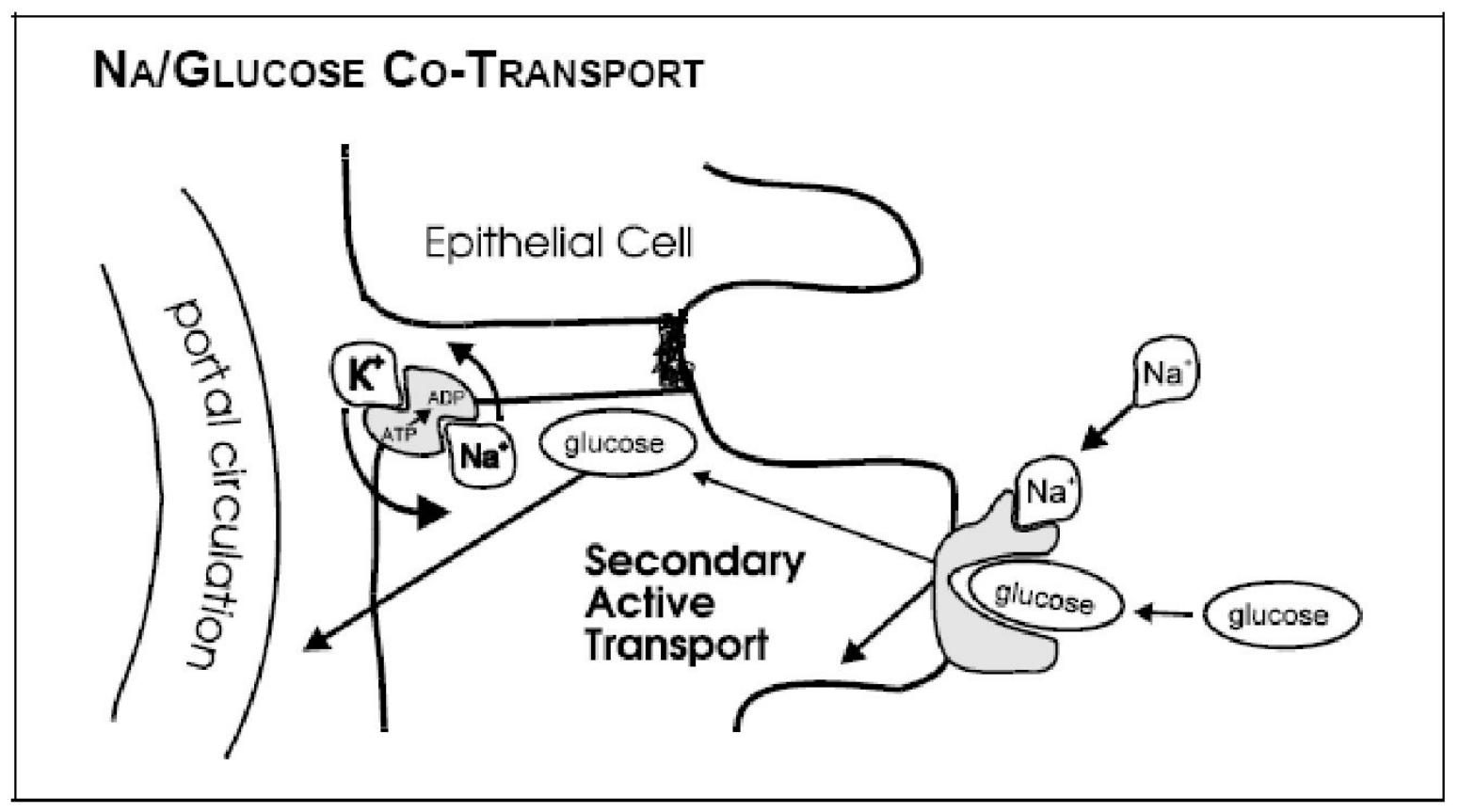


Overview of carbohydrate digestion.



Na_-dependent and facilitative transporters in the intestinal epithelial cells.

Overview of carbohydrate digestion.



Properties of the GLUT 1-GLUT 5 Isoforms of the Glucose Transport Proteins

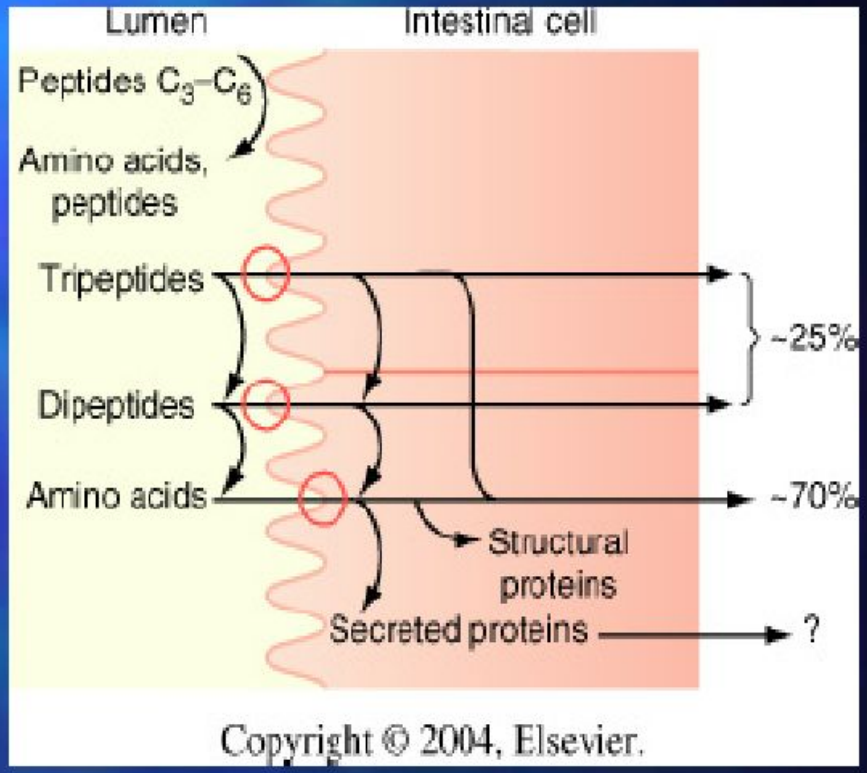
Transporter	Tissue Distribution	Comments
GLUT 1	Human erythrocyte Blood-brain barrier Blood-retinal barrier Blood-placental barrier Blood-testis barrier	Expressed in cell types with barrier functions; a high-affinity glucose transport system
GLUT 2	Liver Kidney Pancreatic β-cell Serosal surface of Intestinal mucosa cells	A high capacity, low affinity transporter. May be used as the glucose sensor in the pancreas.
GLUT 3	Brain (neurons)	Major transporter in the central nervous system. A high-affinity system.
GLUT 4	Adipose tissue Skeletal muscle Heart muscle	Insulin-sensitive transporter. In the presence of insulin the number of GLUT 4 transporters increases on the cell surface. A high-affinity system
GLUT 5	Intestinal epithelium Spermatozoa	This is actually a fructose transporter.

CLINICAL CORRELATION

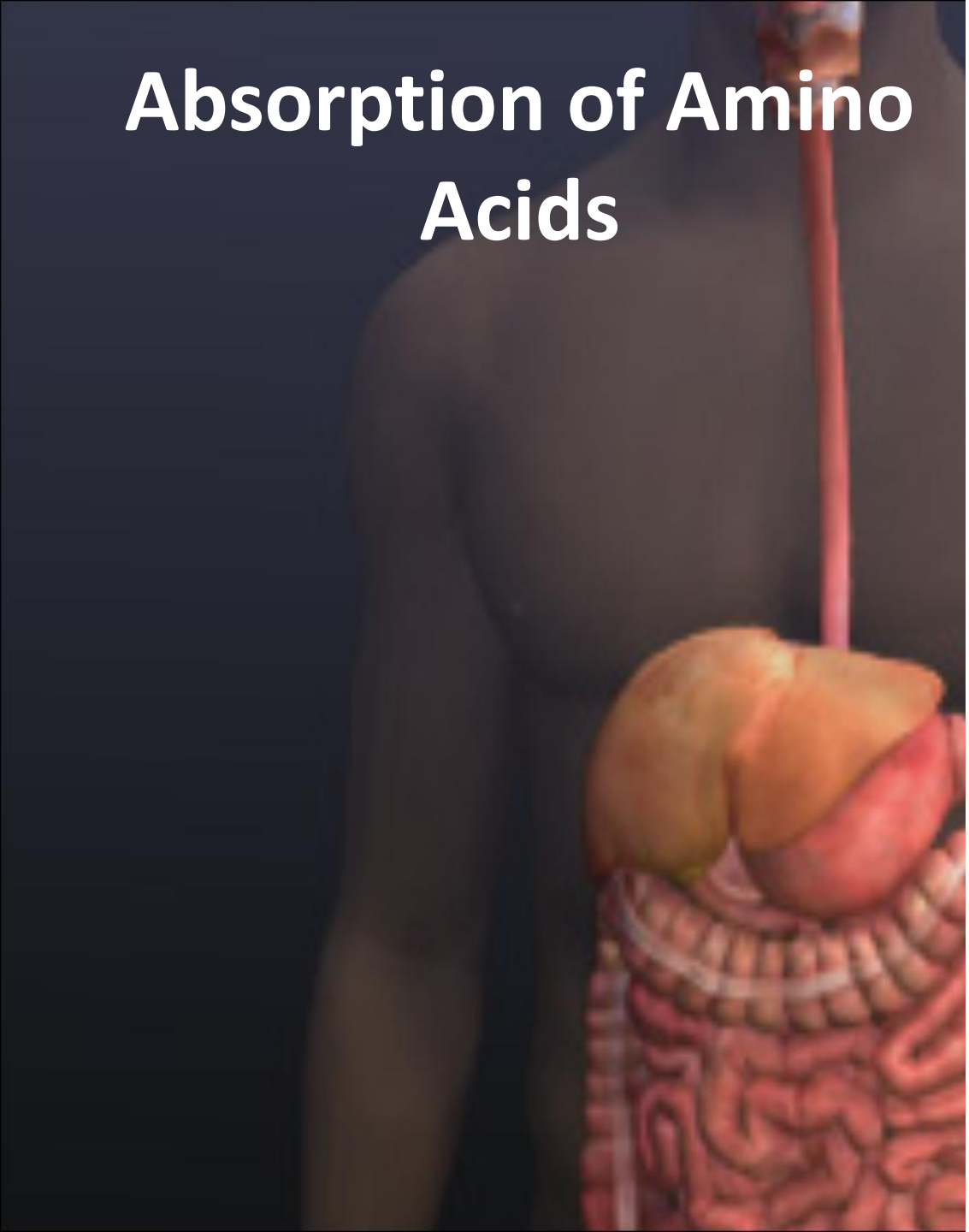
Disaccharidase Deficiency Intestinal disaccharidase deficiencies are encountered relatively frequently in humans. Deficiency can be present in one enzyme or several enzymes for a variety of reasons (genetic defect, physiological decline with age, or the result of "injuries" to the mucosa). Of the disaccharidases, lactase is the most common enzyme with an absolute or relative deficiency, which is experienced as milk intolerance. The consequences of an inability to hydrolyze lactose in the upper small intestine are inability to absorb lactose and bacterial fermentation of ingested lactose in the lower small intestine.

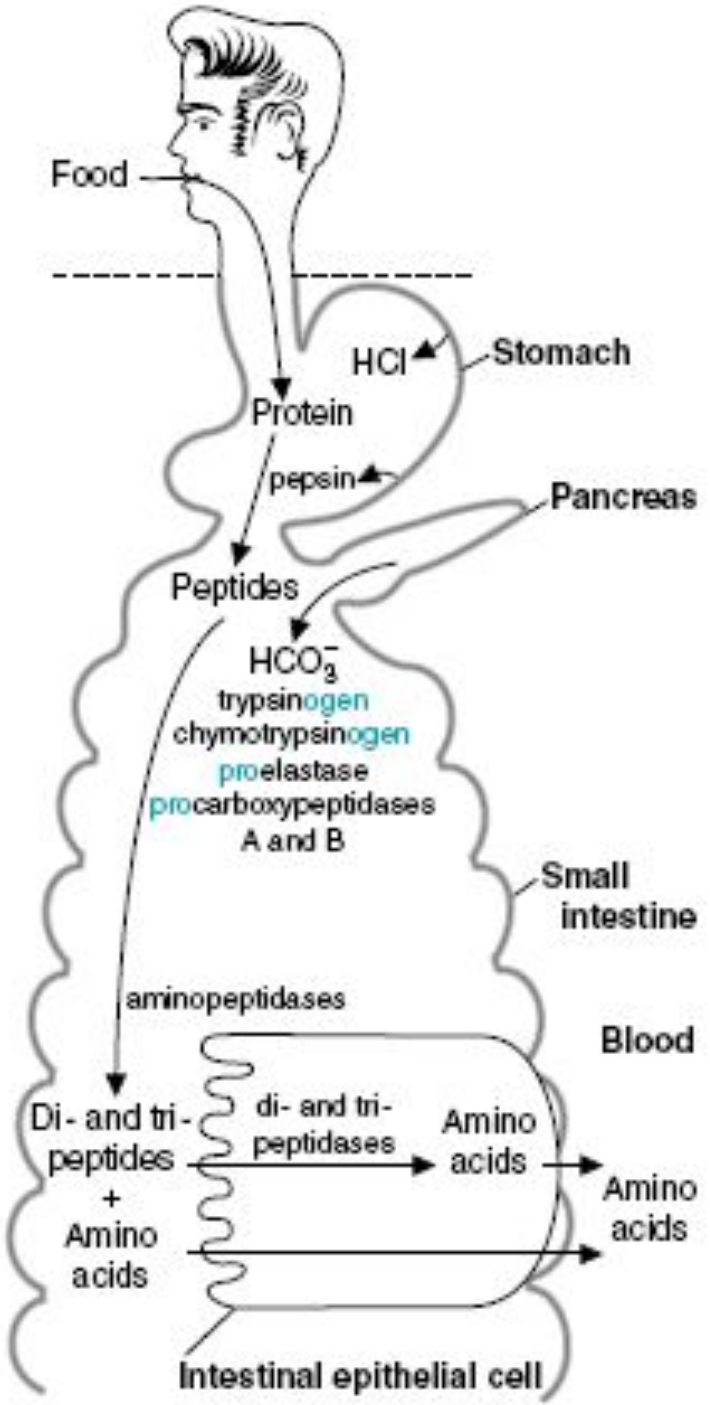
Physiology: Digestion and Absorption

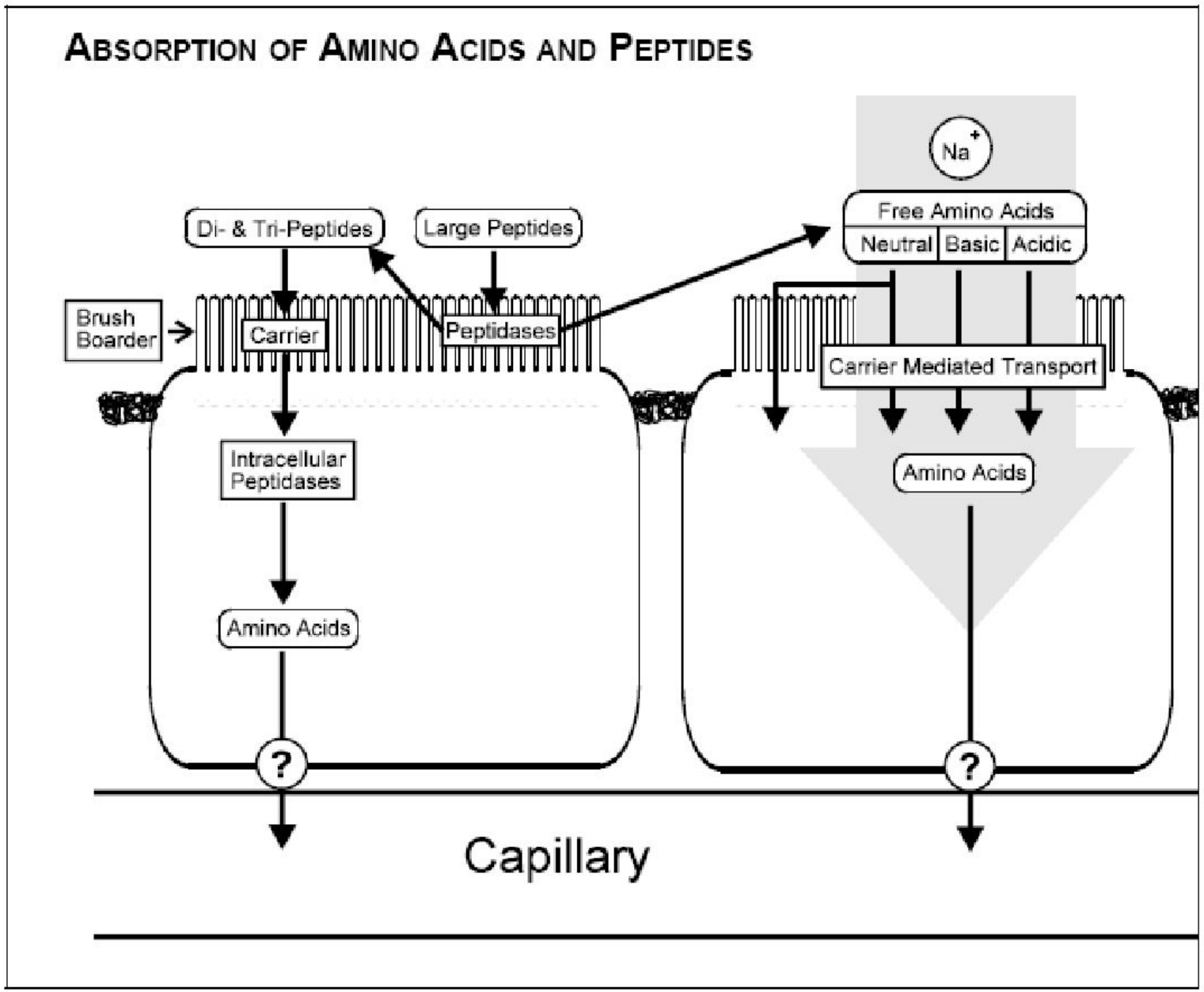
- Protein
  - 80-90% is absorbed in the jejunum
  - Pancreatic trypsinogen (ENTEROKINASE)
  - Endopeptidases: trypsin, chymotrypsin, elastase



Absorption of Amino Acids






ABSORPTION OF AMINO ACIDS AND PEPTIDES
Na+
Free Amino Acids
Neutral
Basic
Acidic
Di- & Tri-Peptides
Large Peptides
Brush Boarder
Carrier
Peptidases
Carrier Mediated Transport
Intracellular Peptidases
Amino Acids
Amino Acids
?
?
Capillary

CLINICAL CORRELATION

Neutral Amino Aciduria (Hartnup Disease)

Transport functions, like enzymatic functions, are subject to modification by mutations.

An example of a genetic lesion in epithelial amino acid transport is Hartnup disease, named after the family in which the disease entity resulting from the defect was first recognized.

The disease is characterized by the inability of renal and intestinal epithelial cells to absorb neutral amino acids from the lumen. In the kidney, in which plasma amino acids reach the lumen of the proximal tubule through the ultrafiltrate, the inability to reabsorb amino acids manifests itself as excretion of amino acids in the urine (amino aciduria).

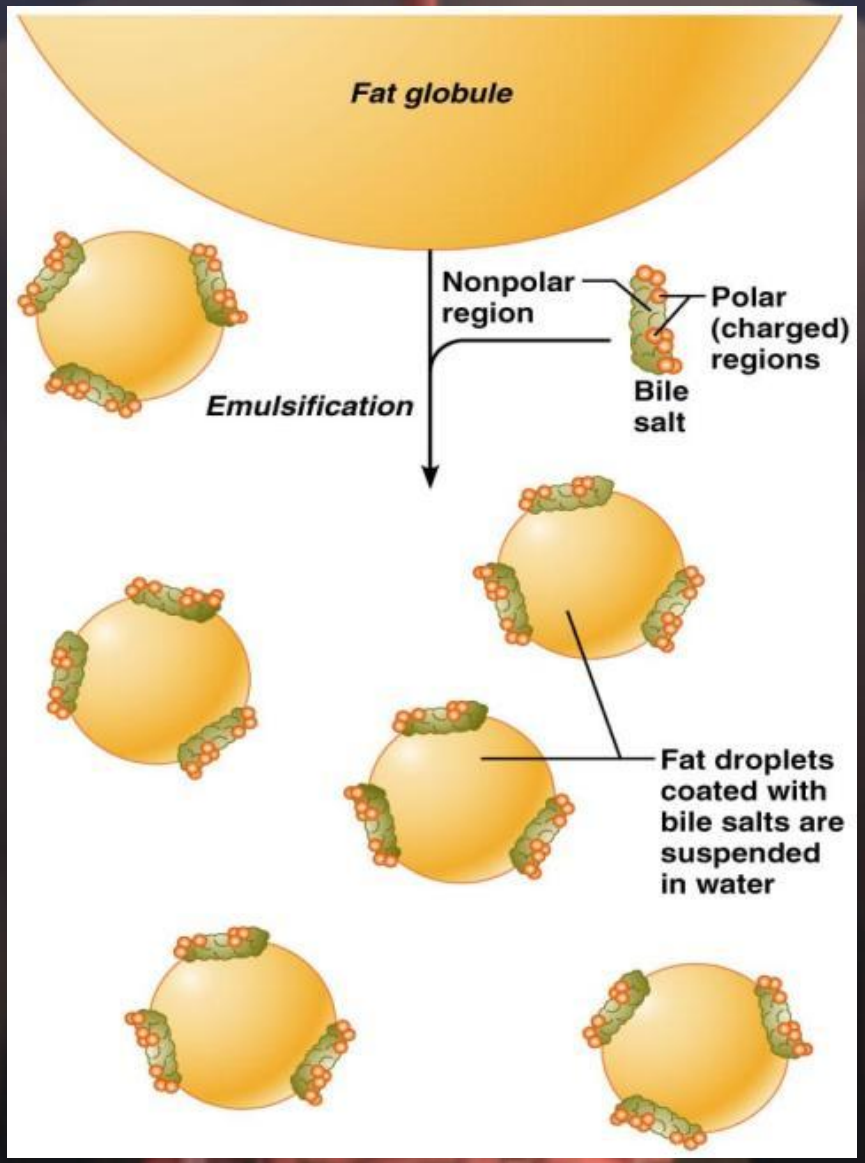
The intestinal defect results in malabsorption of free amino acids from the diet.

Kwashiorkor

Kwashiorkor, A common problem of children in Third World countries, is caused by a deficiency of protein in a diet that is adequate in calories. Children with kwashiorkor suffer from muscle wasting and a decreased concentration of plasma proteins, particularly albumin.

The result is an increase in interstitial fluid that causes edema and a distended abdomen that make the children appear “plump”.

Расщепление жиров

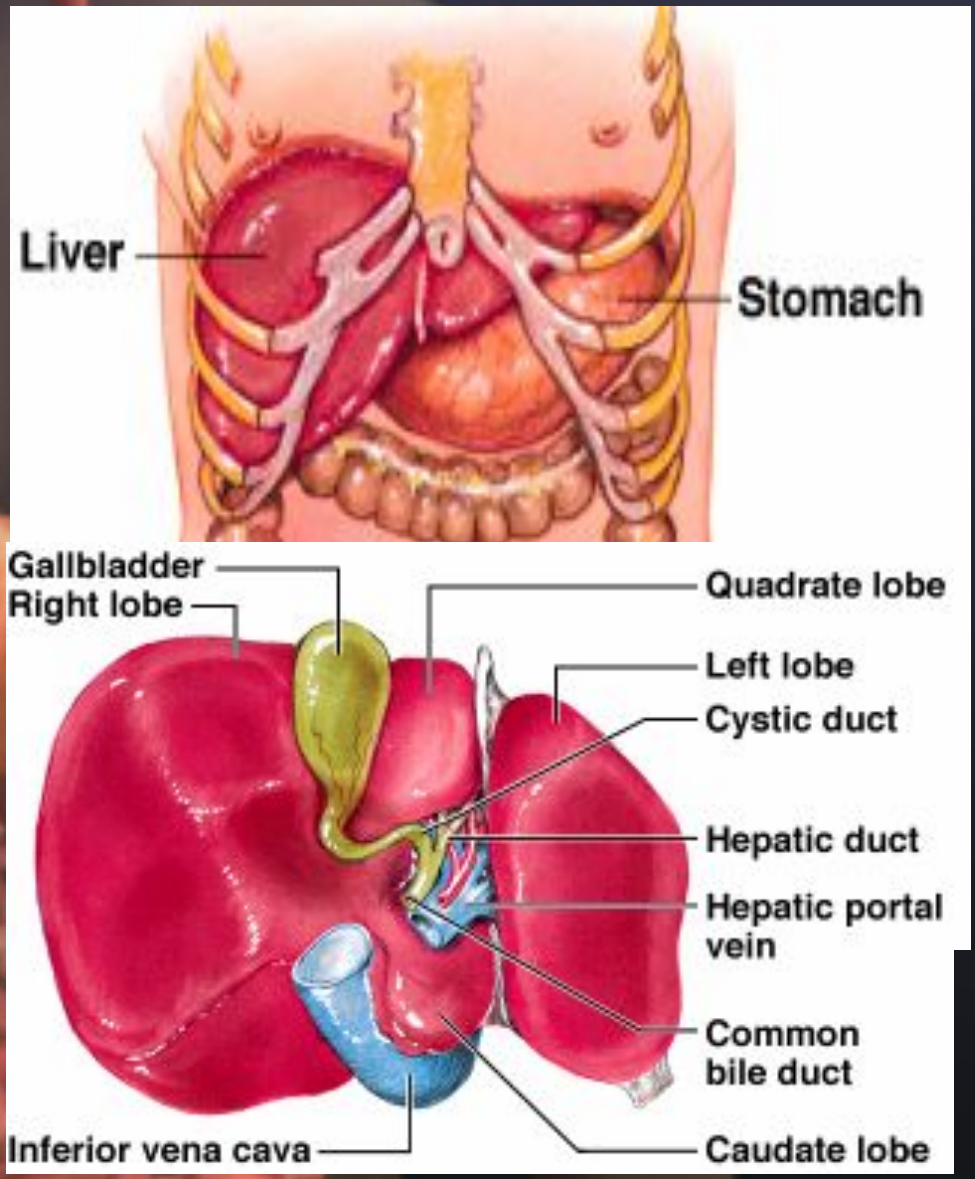


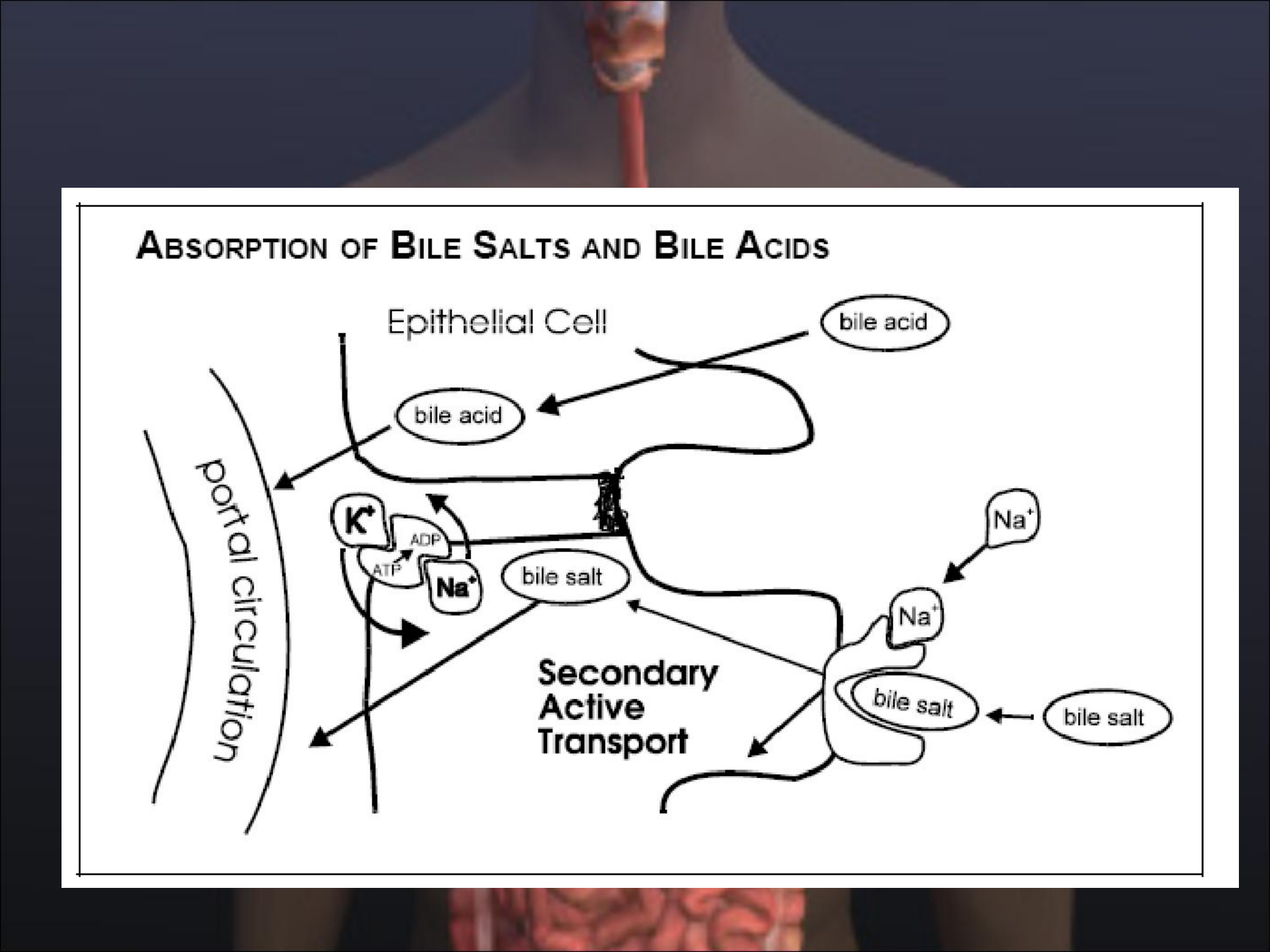
Liver

- Secretes bile (stored in gall bladder)
- Emulsifies fats

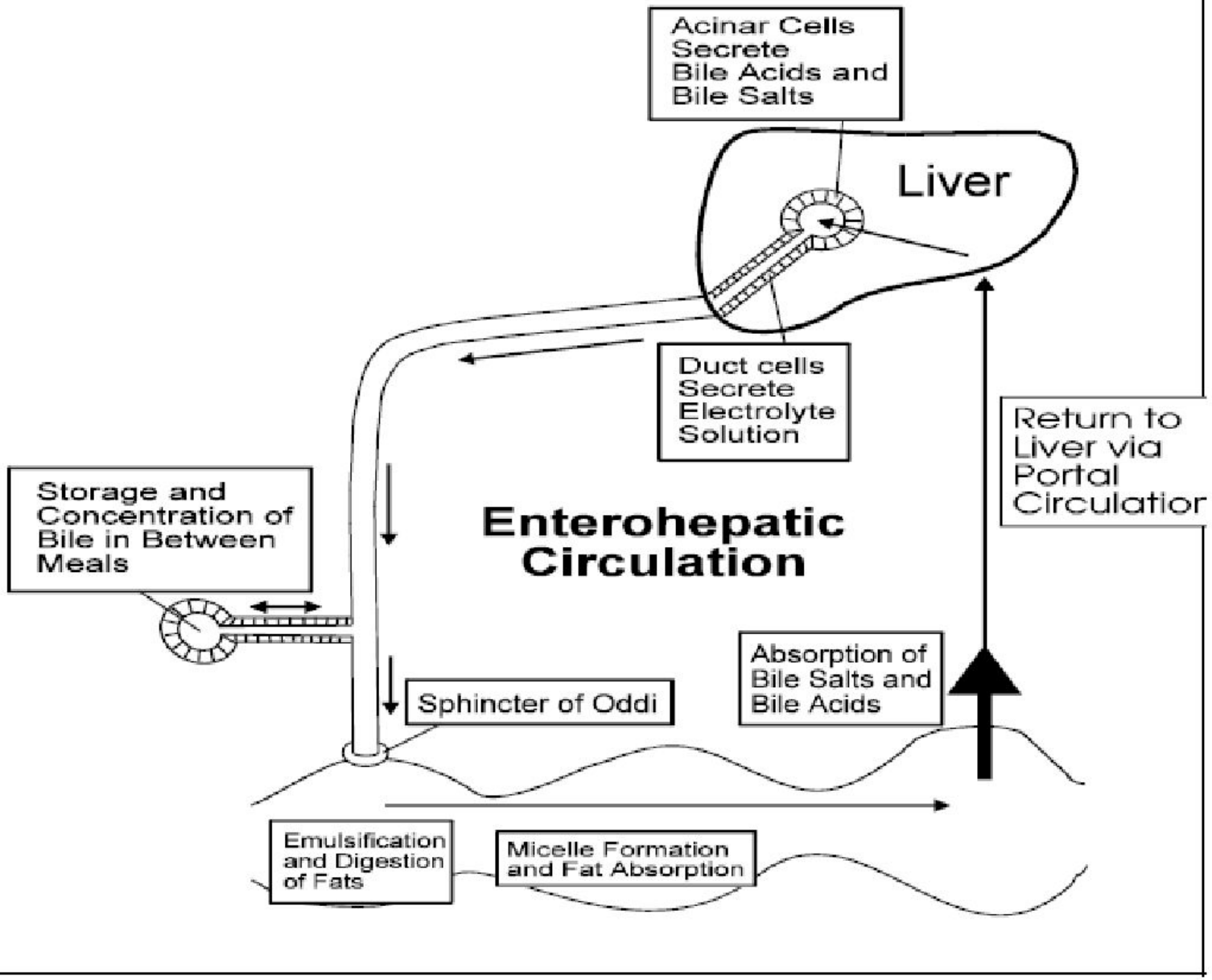
Gallbladder

- Stores, concentrates, and releases bile into duodenum
- Stimulated by the hormone cholecystokinin (CCK)

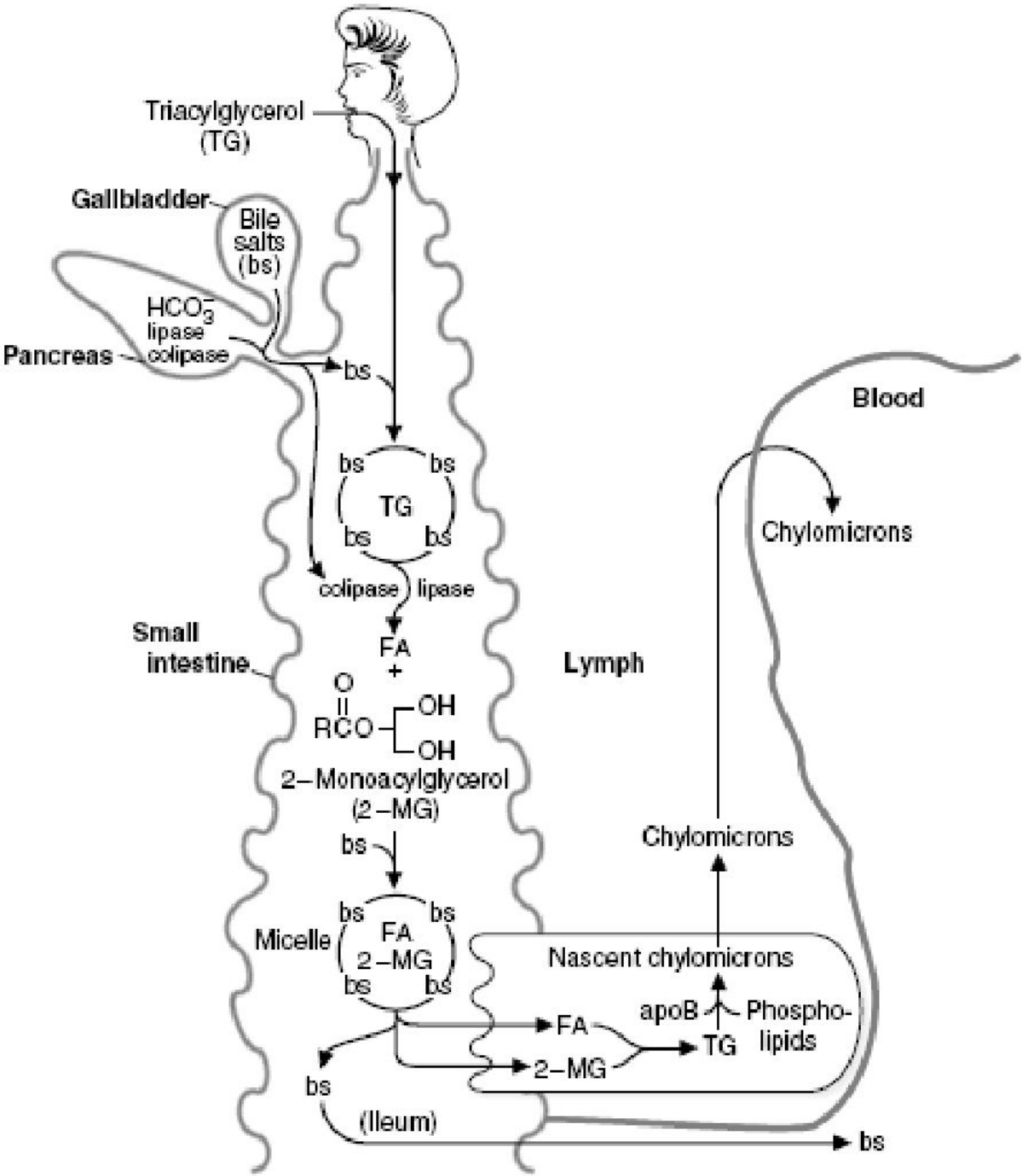



ABSORPTION OF BILE SALTS AND BILE ACIDS
Epithelial Cell
bile acid
bile acid
portal circulation
K+
ADP
ATP
Na+
bile salt
Na+
Na+
Secondary
Active
Transport
bile salt
bile salt

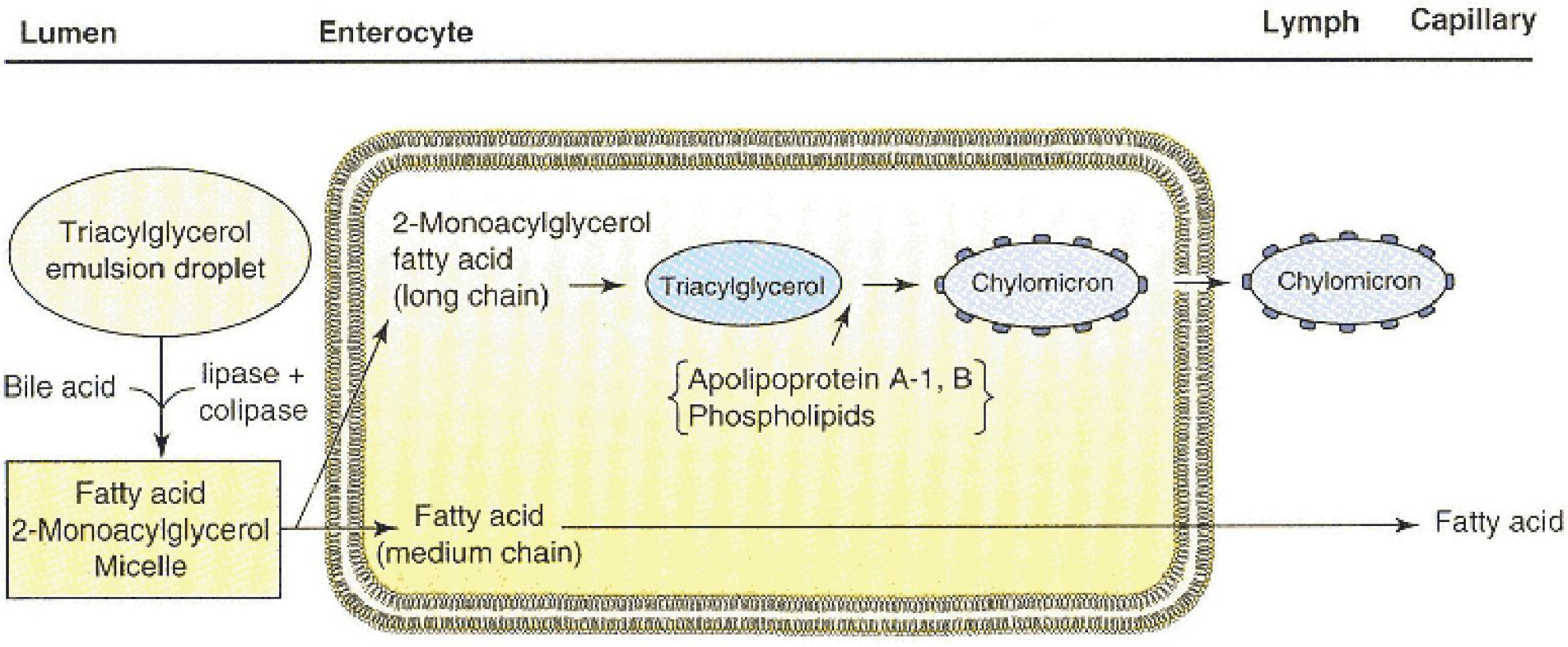
Enterohepatic Circulation



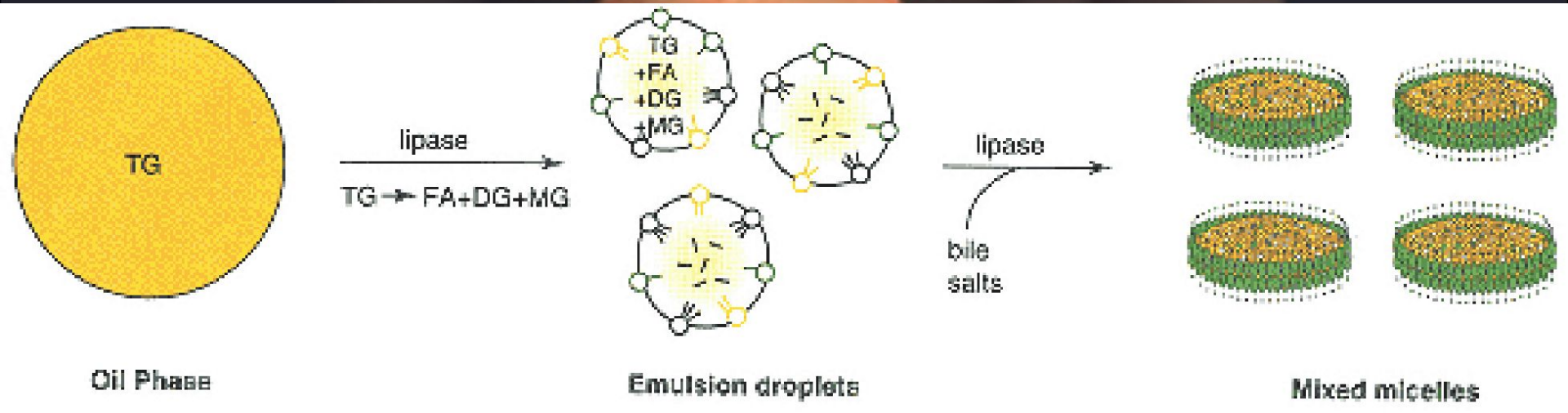
Digestion of triacylglycerols in the intestinal lumen. TG _ triacylglycerol; bs _ bile salts; FA _ fatty acid; 2-MG _ 2-monoacylglycerol



Digestion and absorption of lipids



Changes in physical state during triacylglycerol digestion. Abbreviations: TG, triacylglycerol; DG, diacylglycerol; MG, monoacylglycerol; FA, fatty acid



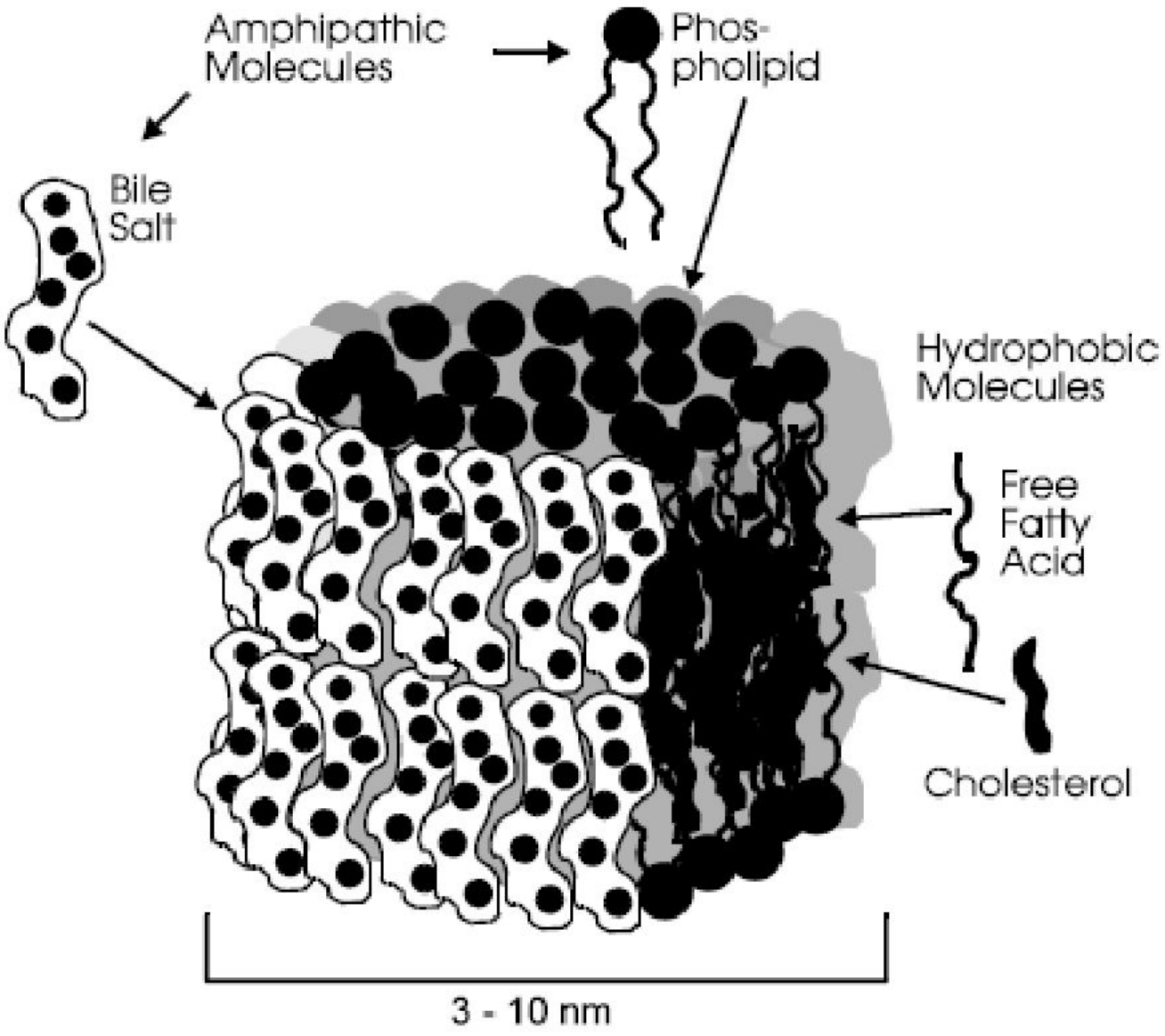
Physiology: Digestion and Absorption

- Fat
  - Emulsification:
    - breakdown of fat globules into smaller sizes
    - Facilitated by bile (bile salts, lecithin)
    - Allows action of pancreatic lipase
  - Micelle formation
    - Bile salts are amphipathic
    - Core of free fatty acids and monoglycerides
    - They simply diffuse into the interior of the cell, without the bile salts

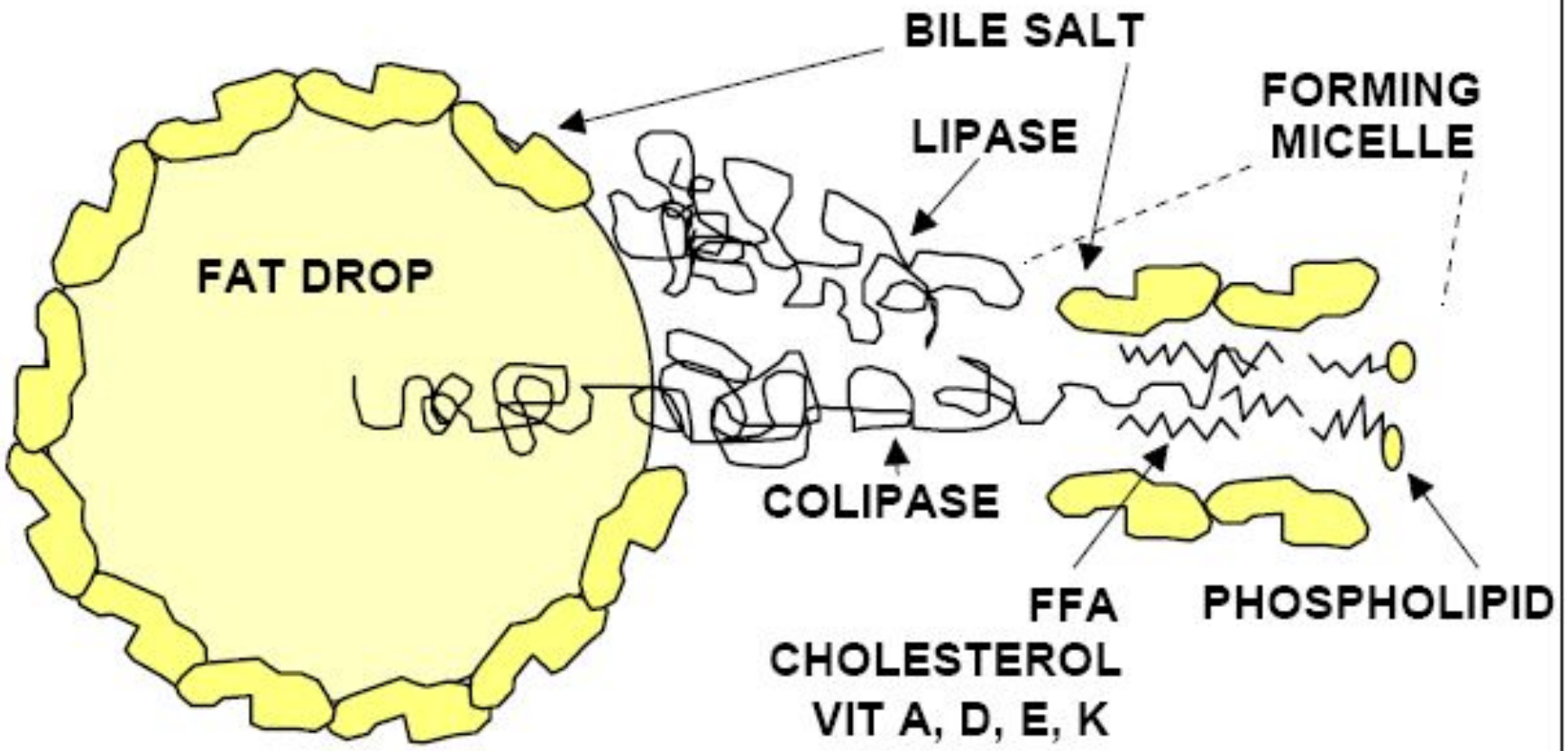
Physiology: Digestion and Absorption

- Fat
  - Intracellular processing
    - Reformation of triglycerides
    - Combination with lipoproteins
      - Short and medium-chain FA may be diluted in blood (portal system)
      - Chylomicrons to lacteals and then lymphatics
  - Enterohepatic circulation
    - Conjugated bile acids are absorbed in the distal ileum -> portal system -> back to the liver
    - Pool of 2-3 g
    - Recirculates 6 times every day
    - 5% lost: resynthesis from cholesterol

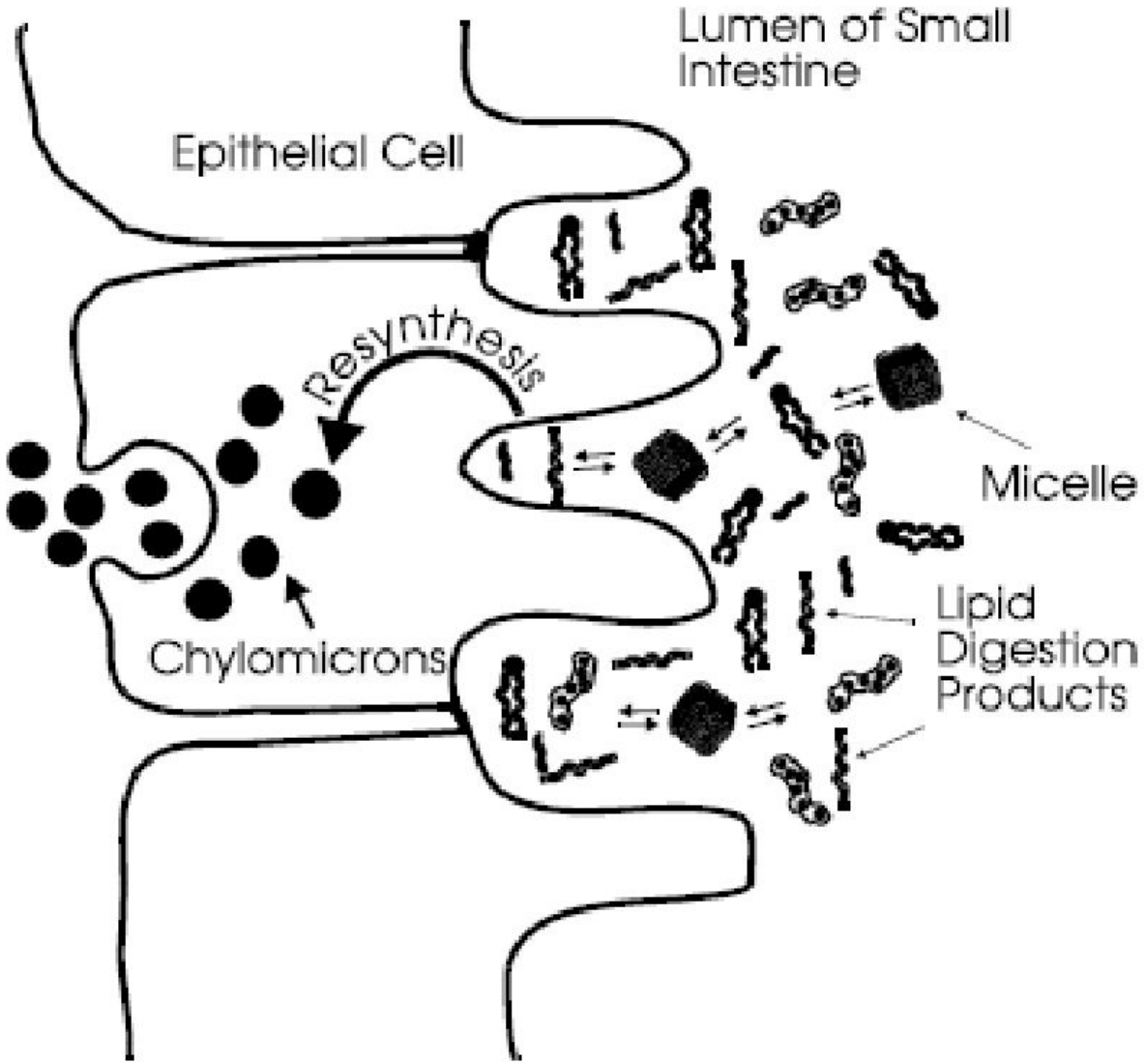
MIXED MICELLE



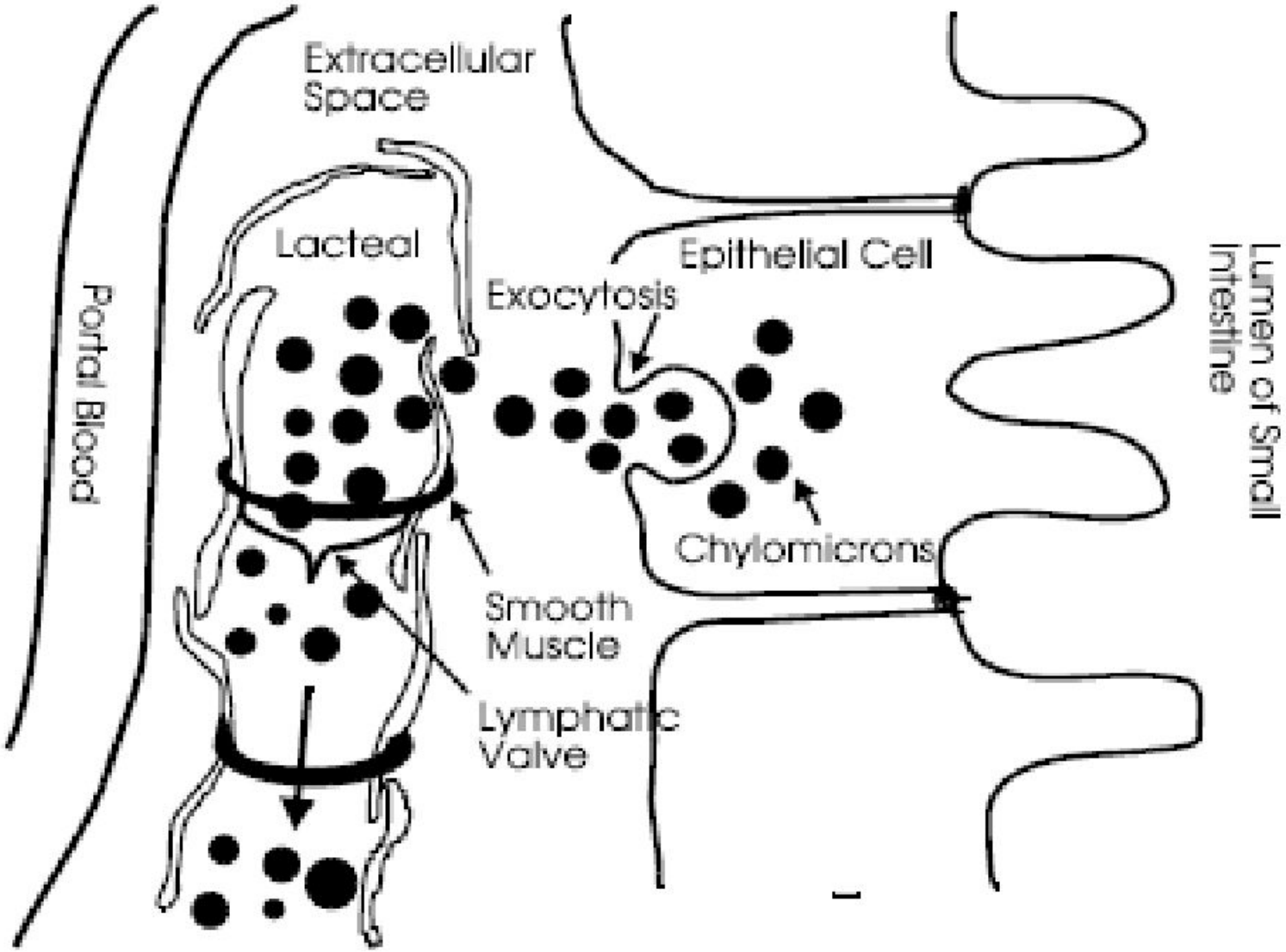
MICELLE FORMATION



Formation of Chylomicrons



Lymphatic Transport of Chylomicrons

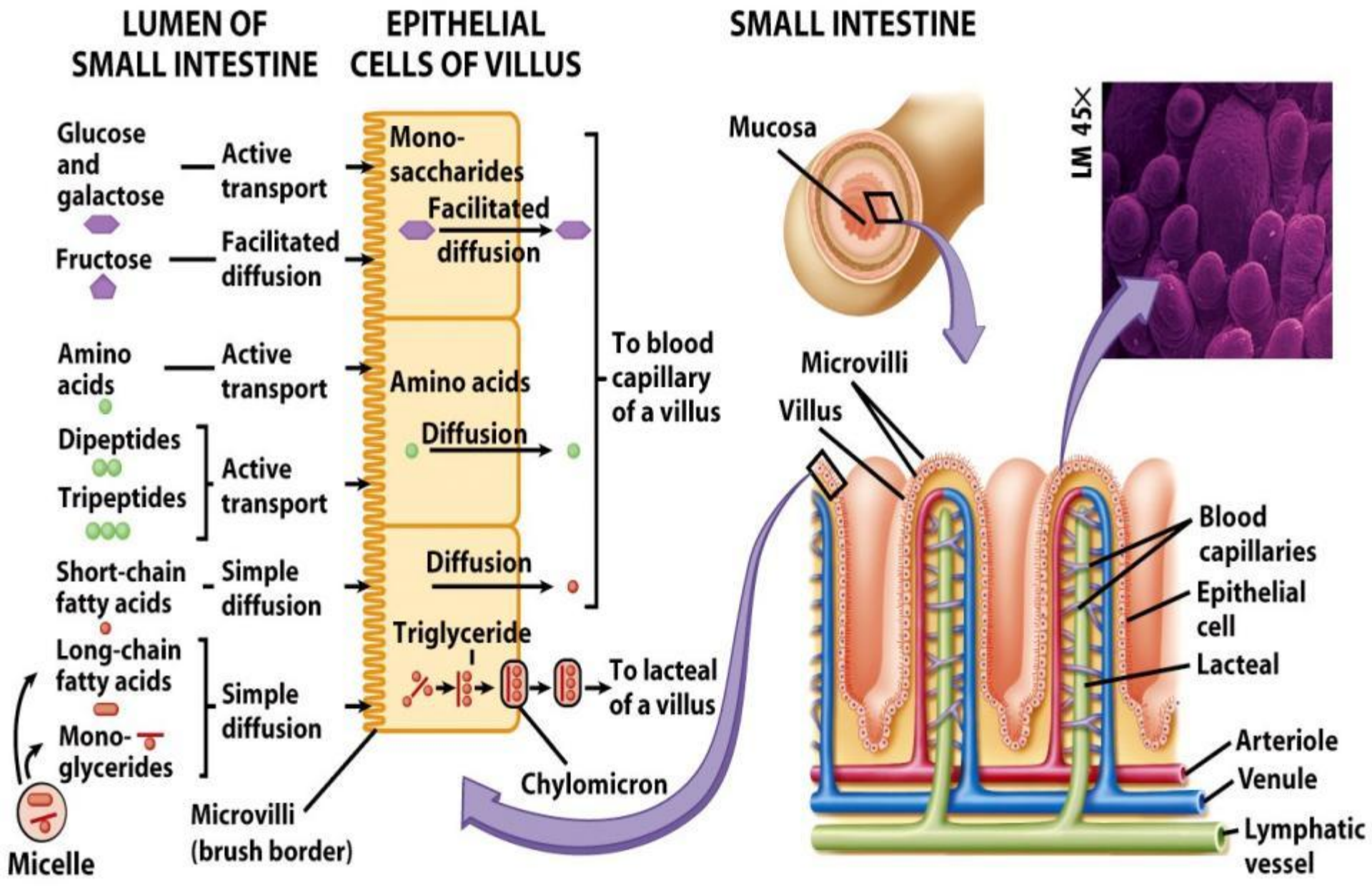


CLINICAL CORRELATION

A-β-Lipoproteinemia

A-*b*-lipoproteinemia is an autosomal recessive disorder characterized by the absence of all lipoproteins containing apo-β-lipoprotein, that is, chylomicrons, very low density lipoproteins (VLDLs), and low density lipoproteins (LDLs). Serum cholesterol is extremely low. This defect is associated with severe malabsorption of triacylglycerol and lipid-soluble vitamins (especially tocopherol and vitamin E) and accumulation of apo B in enterocytes and hepatocytes.

Absorption in the small intestine



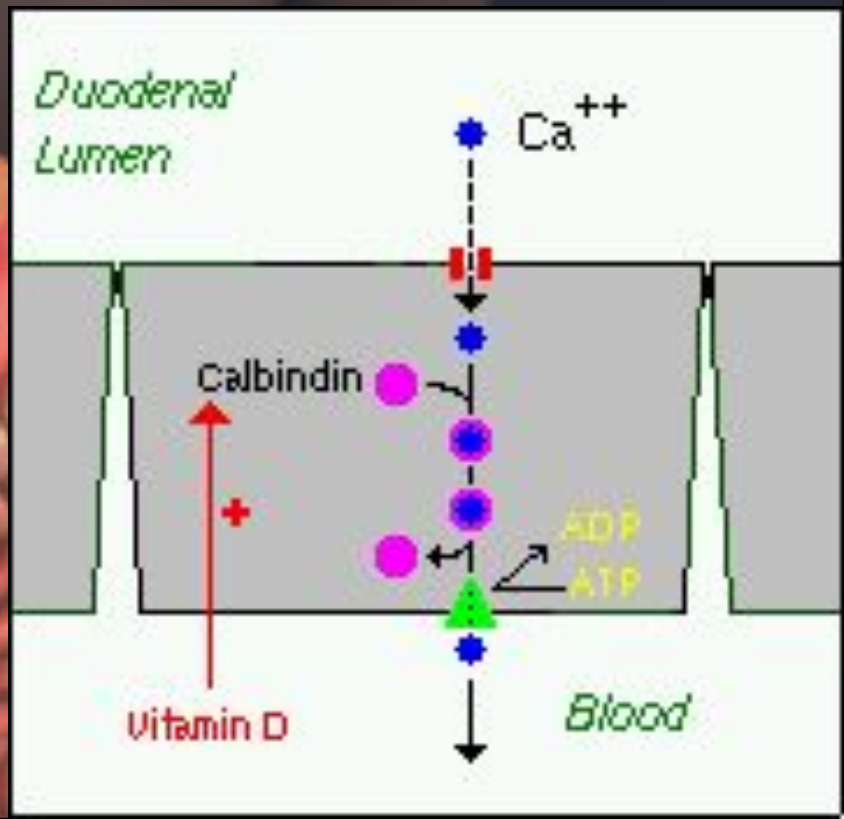
Absorption of Minerals and Metals

Calcium

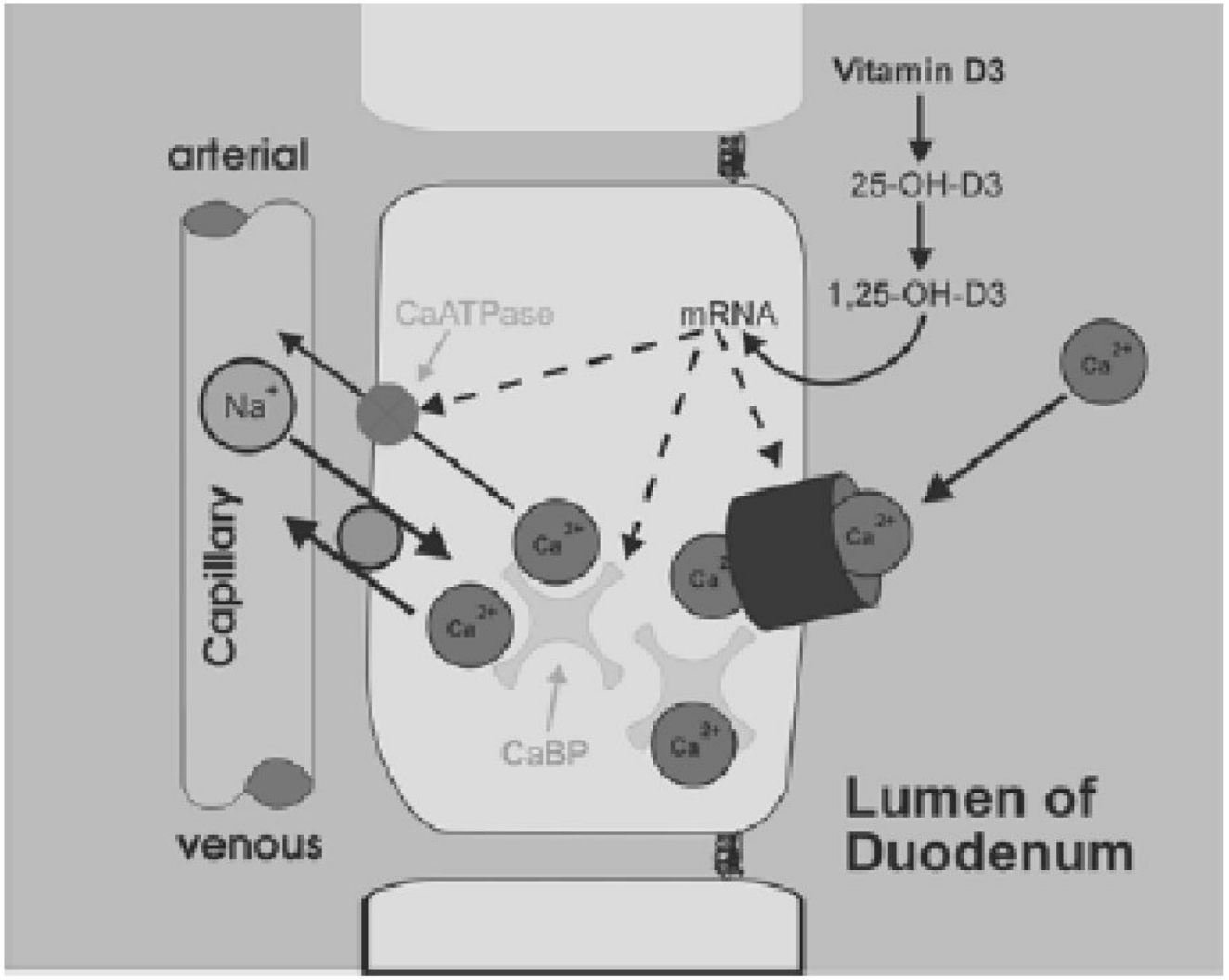
Active, transcellular absorption occurs only in the duodenum when calcium intake has been low.

This process involves import of calcium into the enterocyte, transport across the cell, and export into extracellular fluid and blood.

The rate limiting step in transcellular calcium absorption is transport across the epithelial cell, which is greatly enhanced by the carrier protein calbindin, the synthesis of which is totally dependent on vitamin D.



Calcium Absorption



Calcium

- *Passive, paracellular absorption* occurs in the jejunum and ileum, and, to a much lesser extent, in the colon when dietary calcium levels have been moderate or high. In this case, ionized calcium diffuses through tight junctions into the basolateral spaces around enterocytes, and hence into blood. Such transport depends on having higher concentrations of free calcium in the intestinal lumen than in blood.

Phosphorus

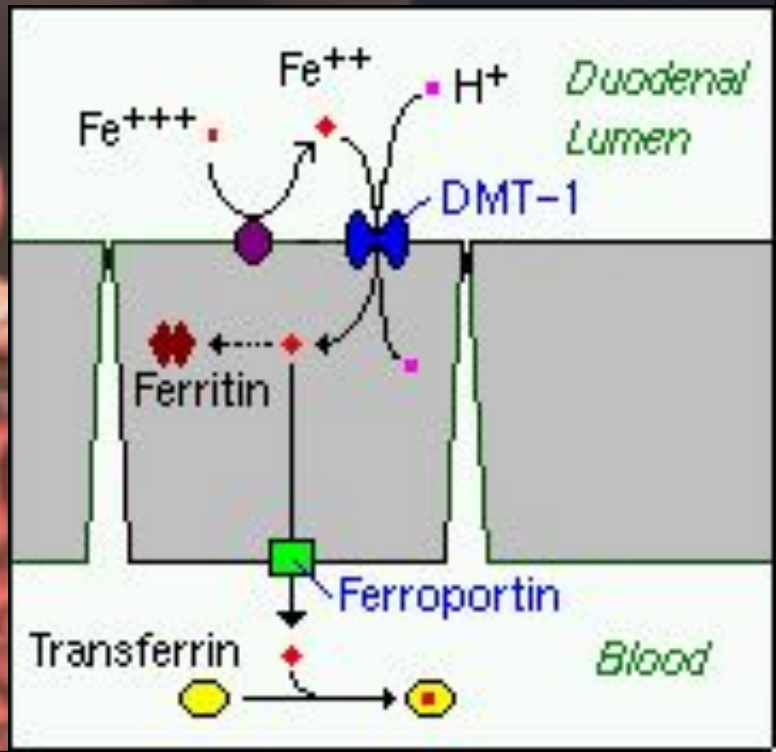
Phosphorus is predominantly absorbed as inorganic phosphate in the upper small intestine.

Phosphate is transported into the epithelial cells by cotransport with sodium, and expression of this (or these) transporters is enhanced by vitamin D.

Iron

Iron is absorbed by villus enterocytes in the proximal duodenum. Efficient absorption requires an acidic environment.

Ferric iron (Fe+++) in the duodenal lumen is reduced to its ferrous form through the action of a brush border ferrireductase. Iron is then co transported with a proton into the enterocyte via the divalent metal transporter DMT-1. This transporter is not specific for iron, and also transports many divalent metal ions.



Iron

- Once inside the enterocyte, iron follows one of two major pathways:
- • *Iron abundance states*: iron within the enterocyte is trapped by incorporation into ferritin and hence, not transported into blood. When the enterocyte dies and is shed, this iron is lost.
- • *Iron limiting states*: iron is exported out of the enterocyte via a transporter (ferroportin) located in the basolateral membrane. It then binds to the iron-carrier transferrin for transport throughout the body.

Copper

- There appear to be two processes responsible for copper absorption:
- i) a rapid, low capacity system and
- ii) a slower, high capacity system, which may be similar to the two processes seen with calcium absorption.

- Many of the molecular details of copper absorption remain to be elucidated.
- A number of dietary factors have been shown to influence copper absorption. For example, excessive dietary intake of either zinc or molybdenum can induce secondary copper deficiency states.

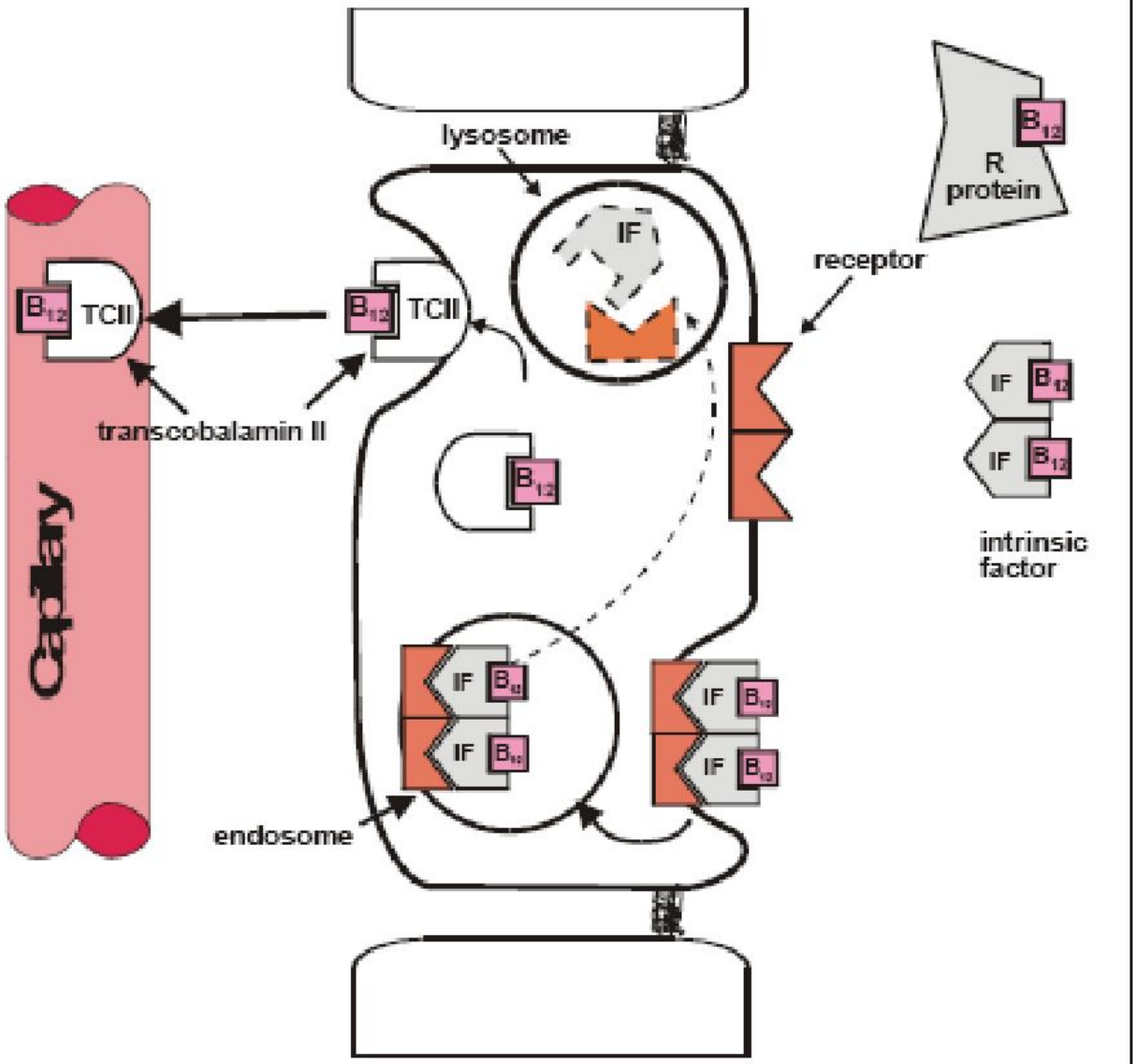
Zinc

- Zinc homeostasis is largely regulated by its uptake and loss through the small intestine. Although a number of zinc transporters and binding proteins have been identified in villus epithelial cells, a detailed picture of the molecules involved in zinc absorption is not yet in hand.
- A number of nutritional factors have been identified that modulate zinc absorption. Certain animal proteins in the diet enhance zinc absorption. Phytates from dietary plant material (including cereal grains, corn, rice) chelate zinc and inhibit its absorption. Subsistence on phytate-rich diets is thought responsible for a considerable fraction of human zinc deficiencies.

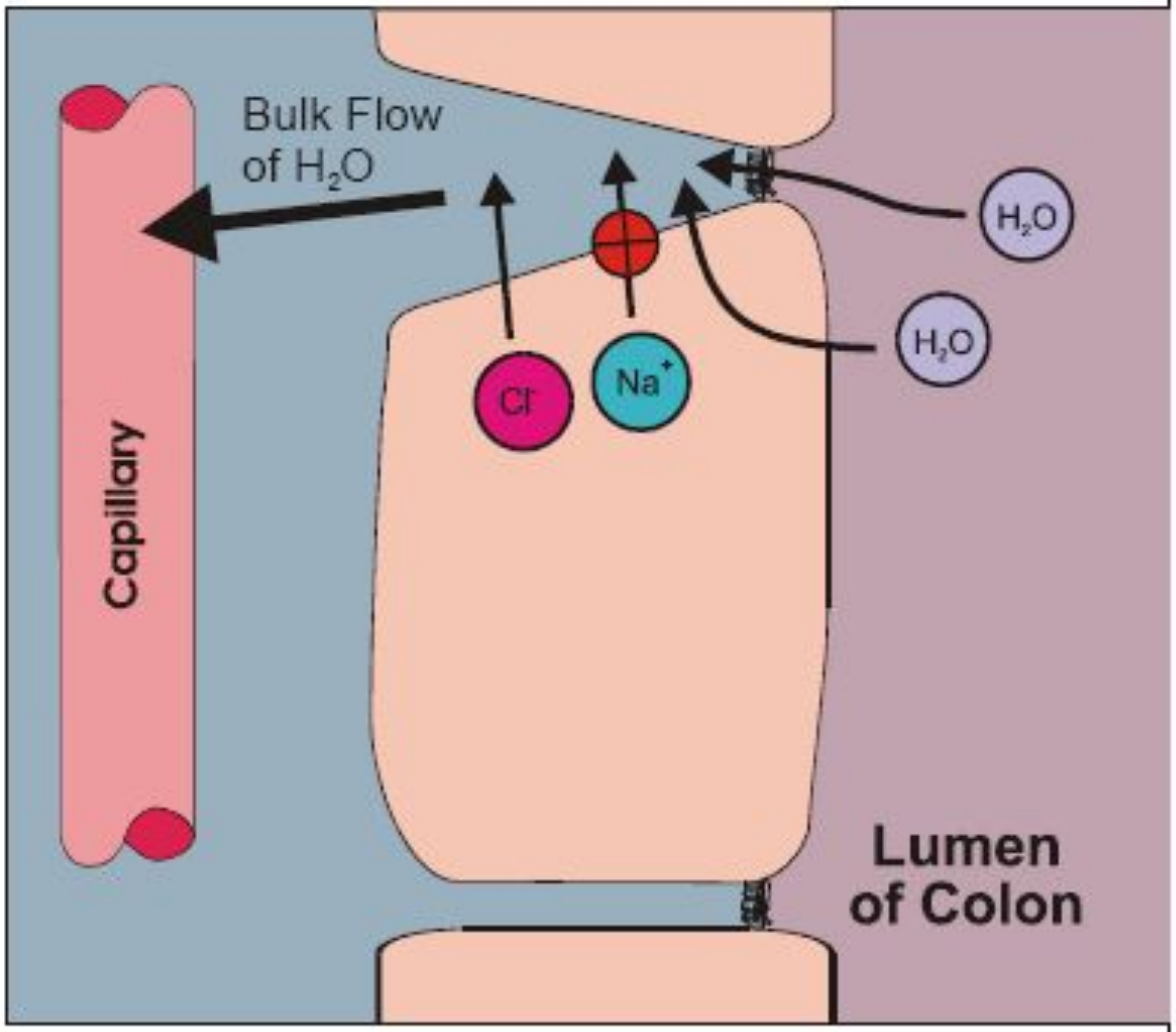
Physiology: Digestion and Absorption

- Water, Electrolytes, and Vitamins
  - Daily: 10 liters water in; 500 cc out
  - Water is absorbed by simple diffusion
  - Na: active transport
  - Cl: passive diffusion
  - HCO3: indirect active transport (Na)
  - Ca: active transport in duod and jejunum
  - Iron: active transport in duodenum
  - Vitamins:
    - Fat soluble (K,A,D,E): distal ileum
    - Water soluble: variable

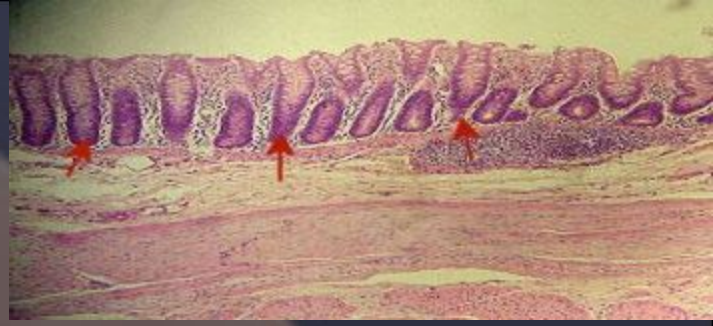
VITAMIN B_{12} ABSORPTION

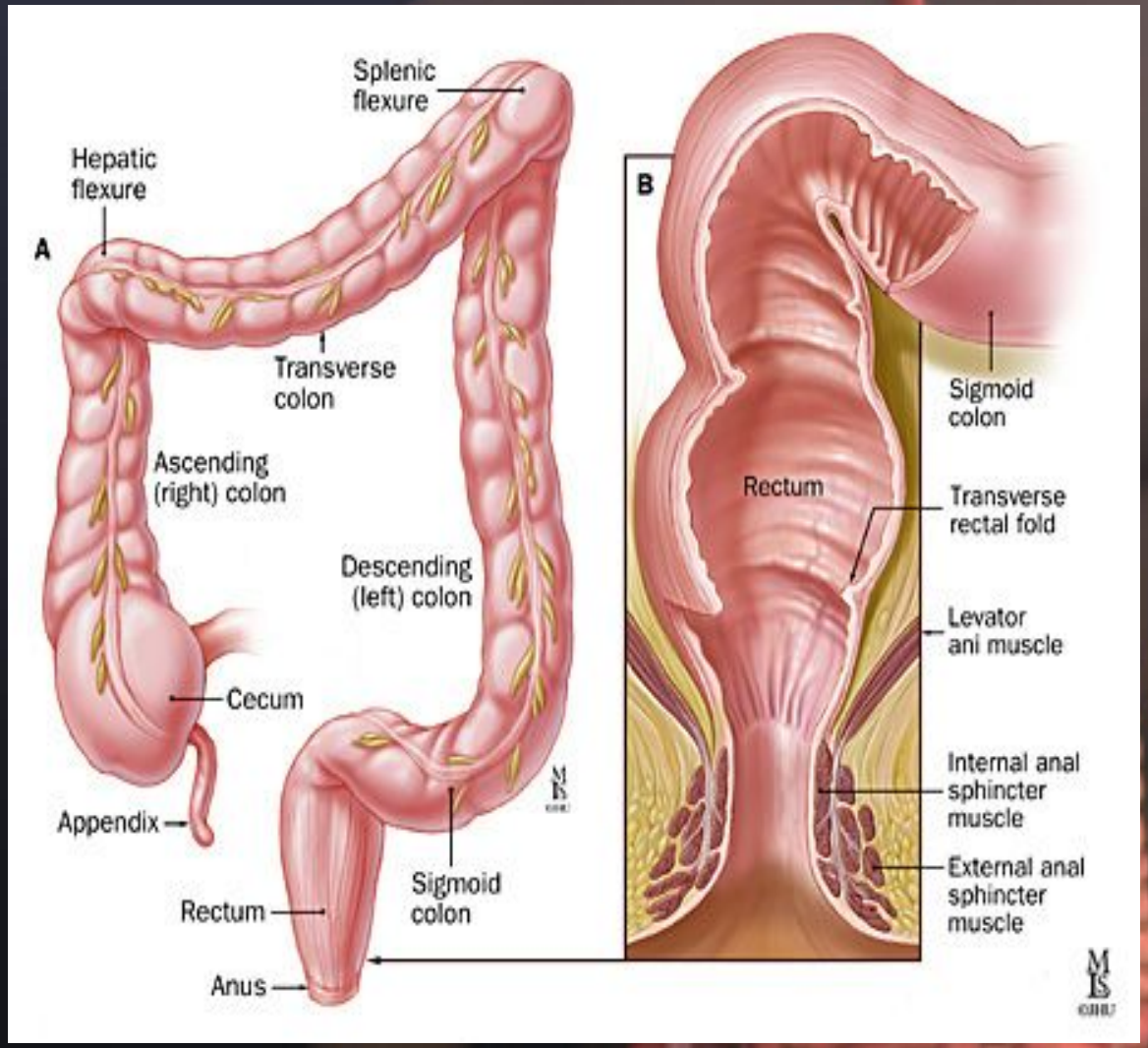


Water Absorption



Reabsorption and elimination in the large intestine





- Areas of the colon
  - Cecum
  - Rectum
  - Anus
- Absorption of **water and electrolytes**
- Concentration & elimination of solids
- Home for **bacteria** that produce biotin, folic acid, vitamin K, several B-vitamins, gases

The Large Intestine: Introduction

- **Recovery of water and electrolytes from ingesta: By the time ingesta reaches the terminal ileum, roughly 90% of its water has been absorbed, but considerable water and electrolytes like sodium and chloride remain and must be recovered by absorption in the large gut.**
- **Formation and storage of feces: As ingesta is moved through the large intestine, it is dehydrated, mixed with bacteria and mucus, and formed into feces. The craftsmanship (for want of a better term) with which this is carried out varies among species.**
- **Microbial fermentation: The large intestine of all species teems with microbial life. Those microbes produce enzymes capable of digesting many of molecules that to vertebrates are indigestible, cellulose being a premier example. The extent and benefit of fermentation also varies greatly among species.**

Large Intestinal Motility

- **Segmentation** contractions which chop and mix the ingesta, presenting it to the mucosa where absorption occurs. These contractions are quite prominent in some species, forming sacculations in the colon known as hausta.
- **Antiperistaltic** contractions propagate toward the ileum, which serves to retard the movement of ingesta through the colon, allowing additional opportunity for absorption of water and electrolytes. Peristaltic contractions, in addition to influx from the small intestine, facilitate movement of ingesta through the colon.
- **Mass movements** constitute a type of motility not seen elsewhere in the digestive tube. Known also as giant migrating contractions, this pattern of motility is like a very intense and prolonged peristaltic contraction which strips an area of large intestine clear of contents.

Fermentation

- Fermentation is the enzymatic decomposition and utililization of foodstuffs, particularly carbohydrates, by microbes.
- Large intestinal epithelial cells do not produce digestive enzymes, but contain huge numbers of bacteria which have the enzymes to digest and utilize many substrates. In all animals, two processes are attributed to the microbial flora of the large intestine:
- Digestion and metabolism of carbohydrates not digested in the small intestine (e.g. cellulose, residual starch)
- Synthesis of vitamin K and certain B vitamins
- Synthesis of vitamin K by colonic bacteria provides a valuable supplement to dietary sources and makes clinical vitamin K deficiency rare. Similarly, formation of B vitamins by the microbial flora in the large intestine is useful to many animals.


THE END