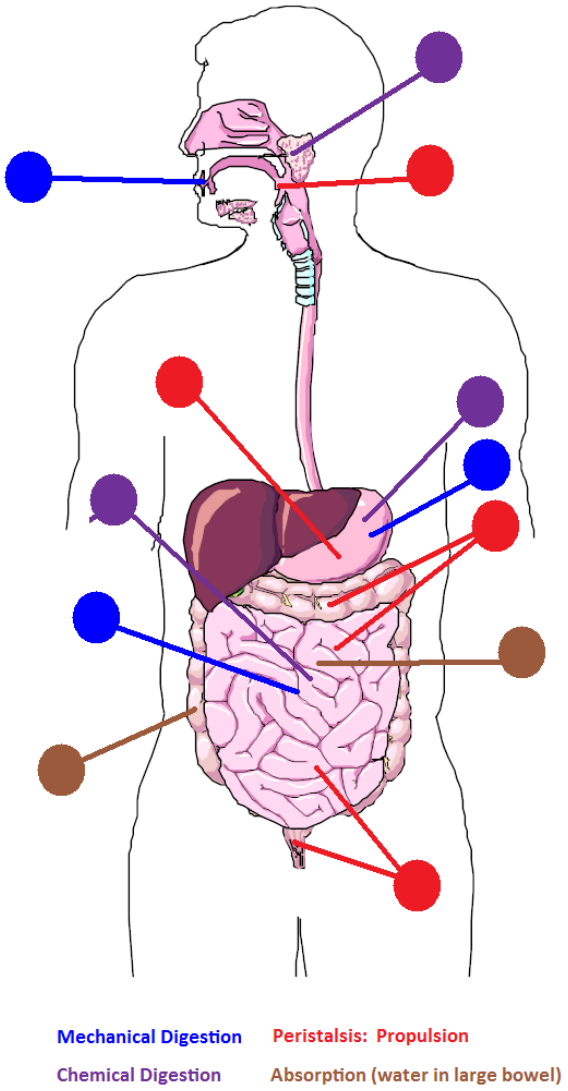
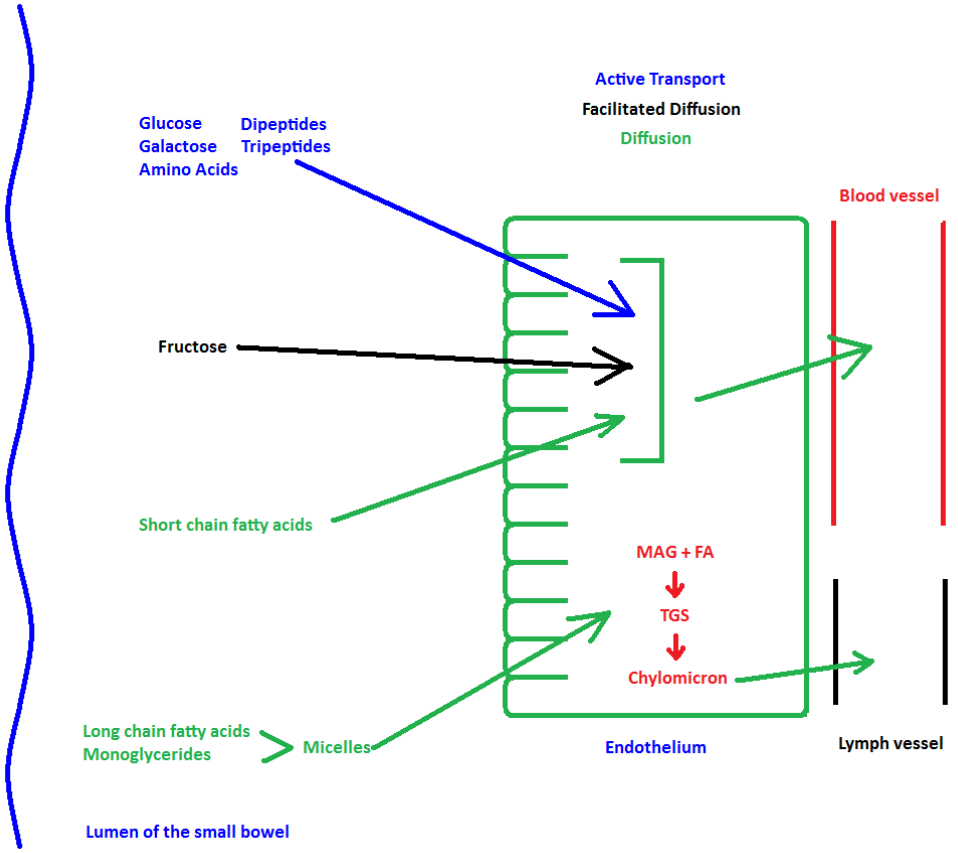
The Digestive System

GI Overview

- **Mechanical digestion** is accomplished by teeth (chewing), grinding (on the rugae ["wash boards"] of the stomach) and segmentation ("churning" in the small bowel).
- **Peristalsis** is the segmental contraction and stricture of the tubular GI system propelling chyme through the tract to be taken in and expelled.
- **Chemical digestion** means that we'll be discussing enzymes.



- **Absorption** is just that: absorption. The uptake of the nutrients for utilization by the organism. The figure illustrates the uptake of various nutrients across the lumen of the small bowel into the endothelium, thence to the blood or lymph vessels. For a review of the types of transport color-coordinated in this graphic, review your A&P I.
- Note, too, that in the cases of amino acids (AA's), di- and tri-peptides and glucose and galactose that, even though they require uptake by active transport and facilitated diffusion, all of these nutrients then undergo diffusion from the endothelium into the blood or lymph vessels.



Digestion is Multi-Faceted

1. Ingestion – putting the food in your mouth, chewing and swallowing
2. Digestion – chemical and physical activities that reduce the food particles to smaller sizes ("break down" – shudder)
3. Assimilation – the smaller particles (di- or tri-peptides; monosaccharides; fatty acids) are taken up across the bowel and placed in the blood
4. Transport – nutrients are transported in the blood to the cells
5. Cellular uptake – the nutrients are transported across the cell membrane
6. Metabolism – the nutrients are either catabolized or anabolized
7. Cellular assimilation – catabolites or anabolites are used by the cell for energy or for growth

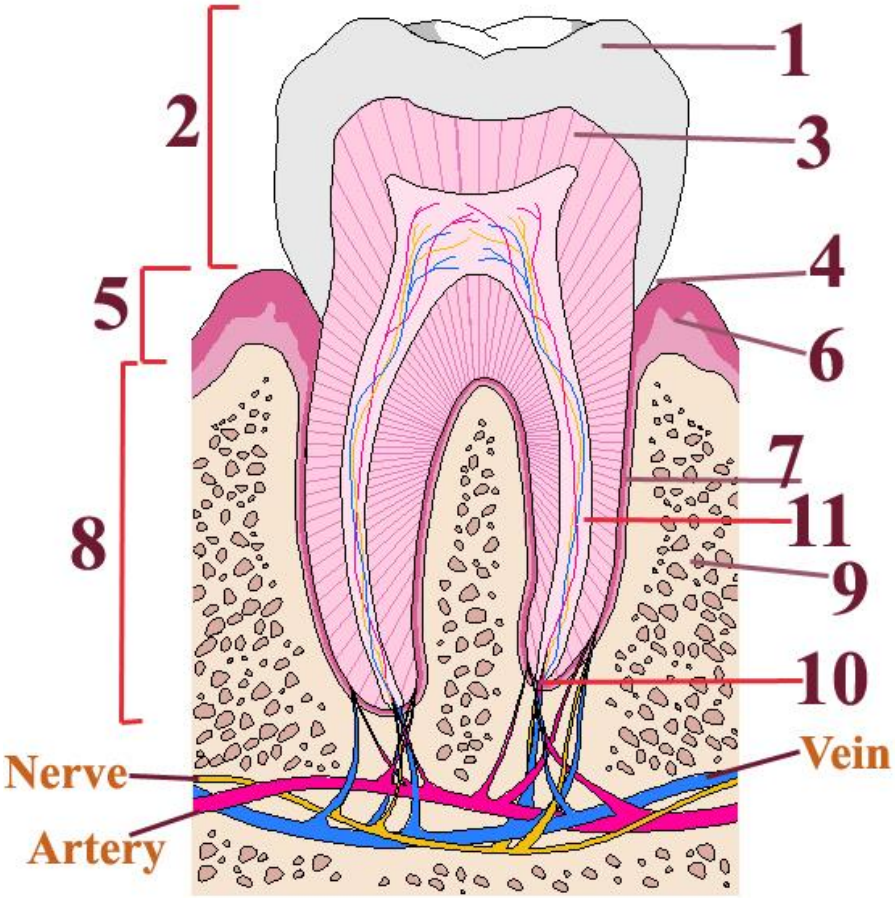
These are saved for the lecture on Metabolism

- Digestion is a multi-faceted process.
- This process involves ingestion (getting the foodstuffs into your digestive system via the mouth, chewing it and swallowing it), metabolism (making the large nutrients smaller for uptake and assimilation), transport and cellular uptake and assimilation.
- You've previously studied metabolism/cellular phenomena in BIOL 223, hence, it's not covered in this lecture.
- In a very broad overview of digestion, there are really two kinds of digestion:
  - mechanical (organs grind the food up into smaller chunks) and
    - Chewing, stomach churning and small bowel segmentation are forms of mechanical digestion.
  - chemical (performed by enzymes that "clip" proteins to smaller peptides, disaccharides to monosaccharides, triglycerides to glycerol and free fatty acids, to mention a few).
    - The parotid gland (salivary gland located over the masseter muscle), lingual tonsil, stomach and small bowel provide for chemical sorts of digestion.
- The small and large bowel [re]absorb water prior to waste excretion so we don't become unduly dehydrated.
- All foodstuffs are propelled from our oropharynx to our anus by peristalsis, a segmental and circular contraction of two muscle layers in our GI system that propels things "down". You can imagine peristalsis by taking a piece of rubber tubing that just fits a marble in it. Encircle the tubing behind the marble with your right hand, hold onto the tubing with your left hand and pull with your right hand -- you've just demonstrated peristalsis.

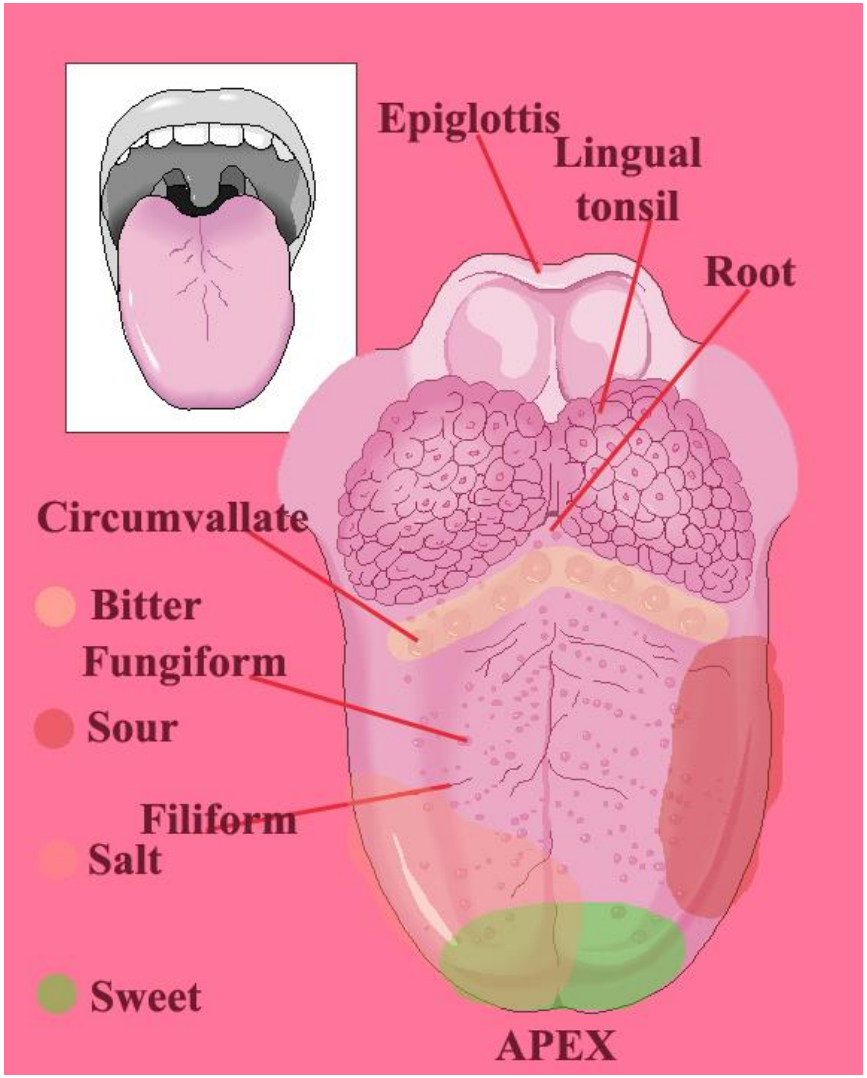
Teeth

- The teeth are what "sees" the food first. The table below summarizes the names of the anatomical parts of the tooth correlated with the numbers on the graphic

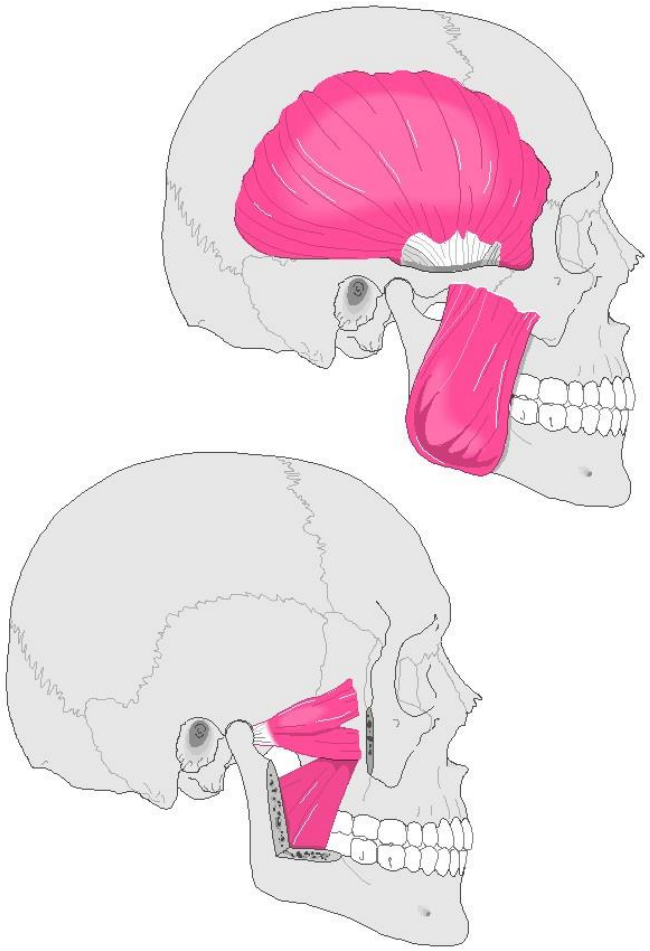
No.	Name	No.	Name
1	Enamel	7	Periodontal ligament
2	Crown	8	Root
3	Dentin	9	Alveolar bone
4	Gingival sulcus	10	Apex/ical foramen
5	Neck	11	Pulp cavity
6	Gingiva		



- The next organ for the initiation of digestion is the tongue (the teeth chew it up and the tongue wallers it around). The tongue (Figure) consists of numerous muscles and is innervated as we discussed with the cranial nerves.
- The tongue is the organ for taste.
- It contains three kinds of papillae:
  - circumvallate,
  - fungiform and
  - filiform.
  - Circumvallate papillae and fungiform papillae contain the taste buds.
  - Filiform papillae do NOT have taste buds.
- Circumvallate papillae are circular and form an inverted V-shaped row on the posterior tongue, anterior to the lingual tonsil (Figure).
- Fungiform papillae are knob-like extension found primarily on the tip and sides of the tongue.
- Circumvallate papillae detect the bitter taste;
- fungiform papillae are more diverse: they detect sweet, salt and sour, in order from anterior to posterior.
- Filiform papillae are pointed, thread-like structures that cover the anterior 2/3 of the tongue.
- They contain NO taste buds.
- A human being inherently prefers sweets.
- We detect bitter tastes (tonic water) with the least amount of stimulus, sour with the next higher stimulus and sweet and salt at about equal higher thresholds.

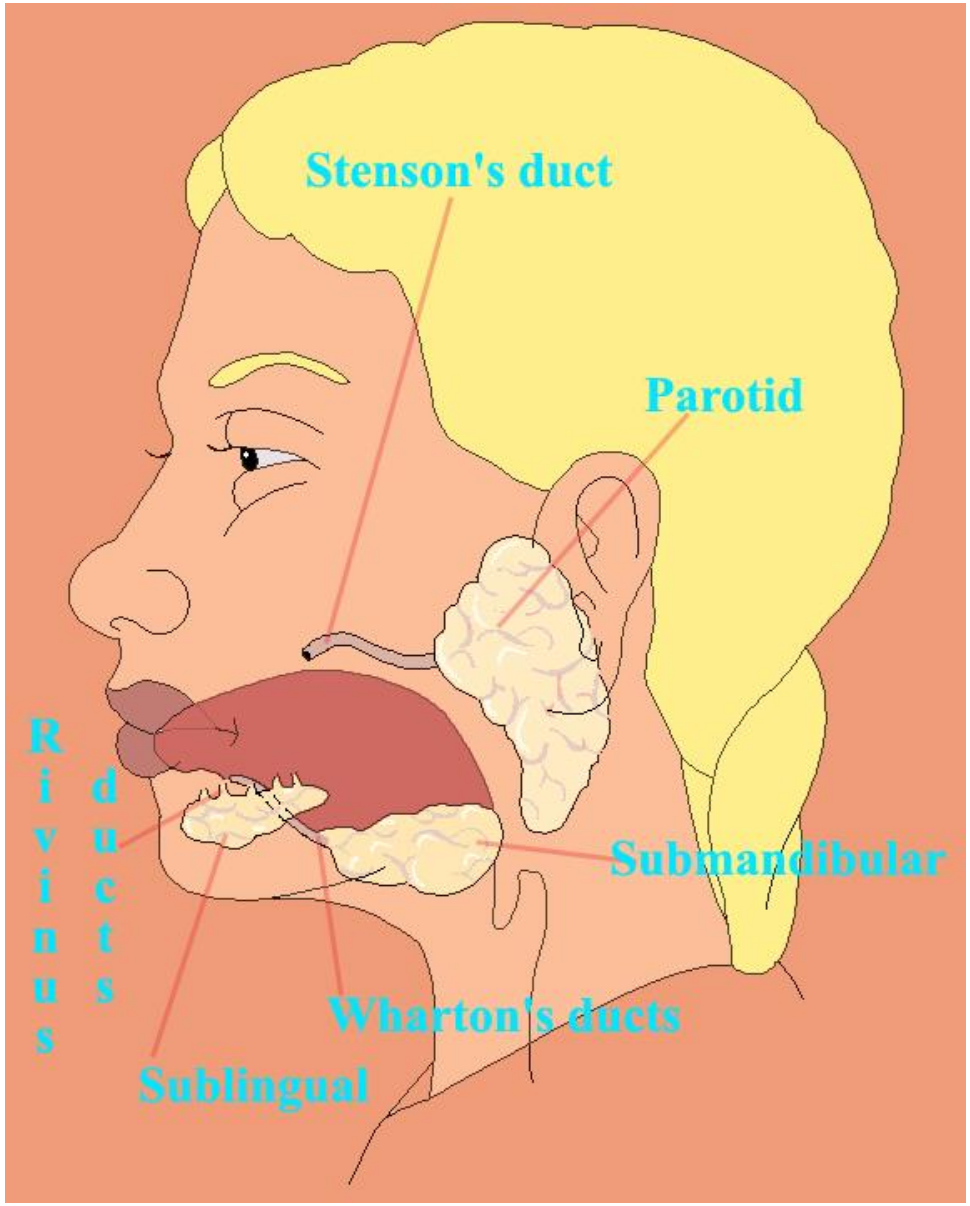


Muscles of Mastication – Physical (Mechanical) Digestion

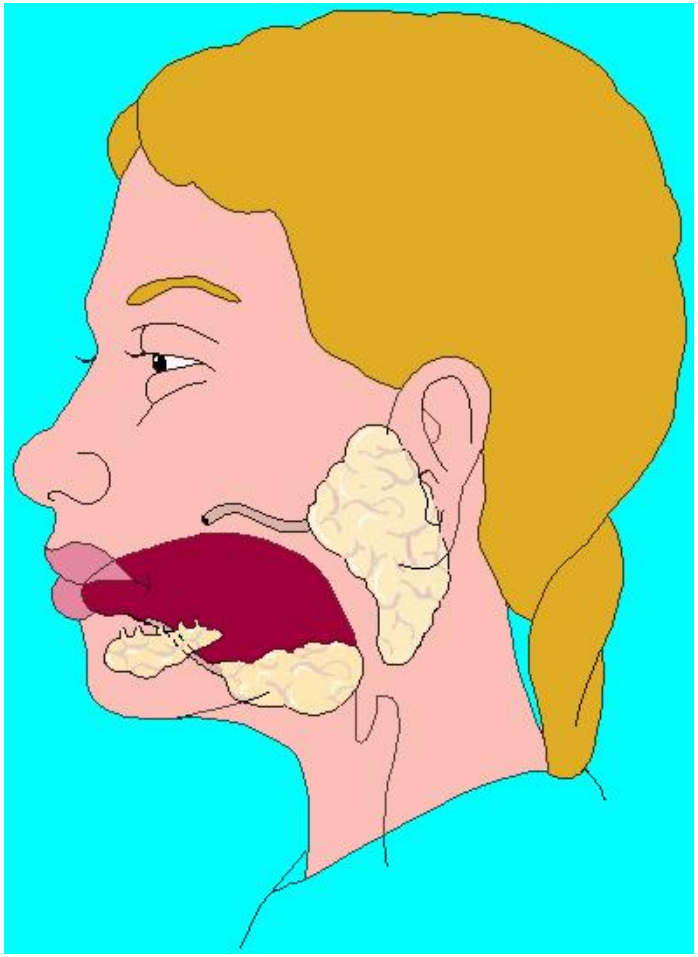


- Temporalis
- Masseter
  - Incisors = 55 psi; molars = 200 psi
- Lateral pterygoid
- Medial pterygoid

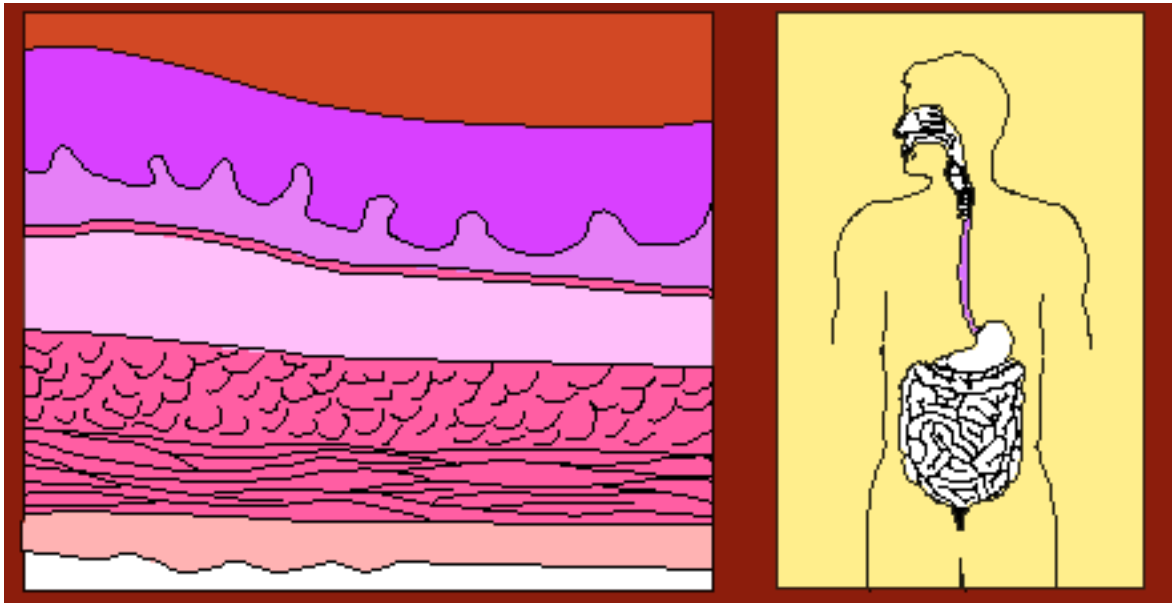
- While the teeth are chewing food and the tongue is wallering it around, we also secrete saliva from 3 salivary glands (illustrated in your text): the parotid gland, sublingual gland and submandibular gland.
- The parotid gland overlies the masseter muscle and secretes an enzyme used to destroy starch (a polysaccharide) to maltose (a disaccharide) called alpha-amylase.
- The parotid gland secretes its saliva through Stenson's duct, a duct about 2.5 inches long that exits opposite #2 and #15.
- The sublingual gland secretes a mucous-like saliva that makes the food bolus slick.
- The sublingual gland exits beneath the tongue via Rivinus ducts. There are between 8 and 20 of these ducts on either side of the frenulum (skin flap that attaches the tongue to the floor of the mouth).
- The sublingual gland is the smallest of the glands and is ahead of the submandibular gland.
- The submandibular gland secretes a watery saliva at a rate of about 1-1.5 liters per day.
- The submandibular is the most posterior and deepest of the glands. It exits via Wharton's ducts. These ducts are about 2 inches long and exit at the side of the frenulum through papillae on each side.



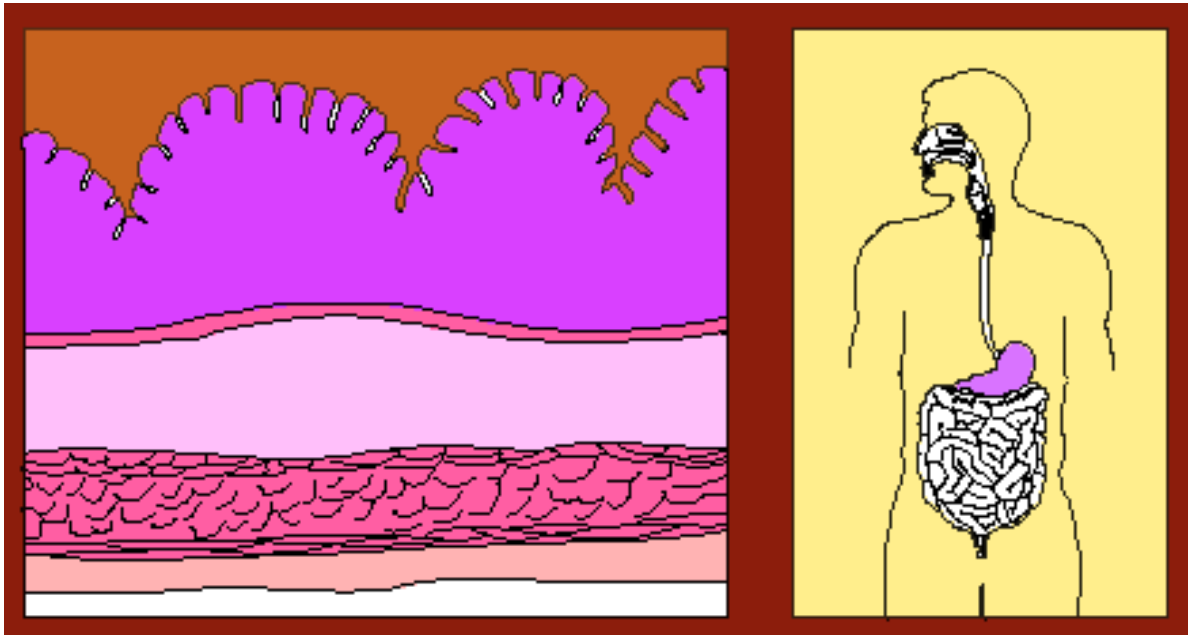
Ingestion



1. Put food in mouth
2. Chew
3. Saliva mixes with food to make a bolus
    1. Amylase drives starch hydrolysis
4. Tongue “pushes” food down to esophagus
5. Food bolus “drug” across lingual tonsil (lipase)
    1. Short and medium chain fatty acids only
6. Carbohydrate and lipid hydrolysis continue down esophagus
7. As food is swallowed, it causes peristalsis, i.e., propagating its own movement from the oropharynx into the esophagus, thence into the stomach.

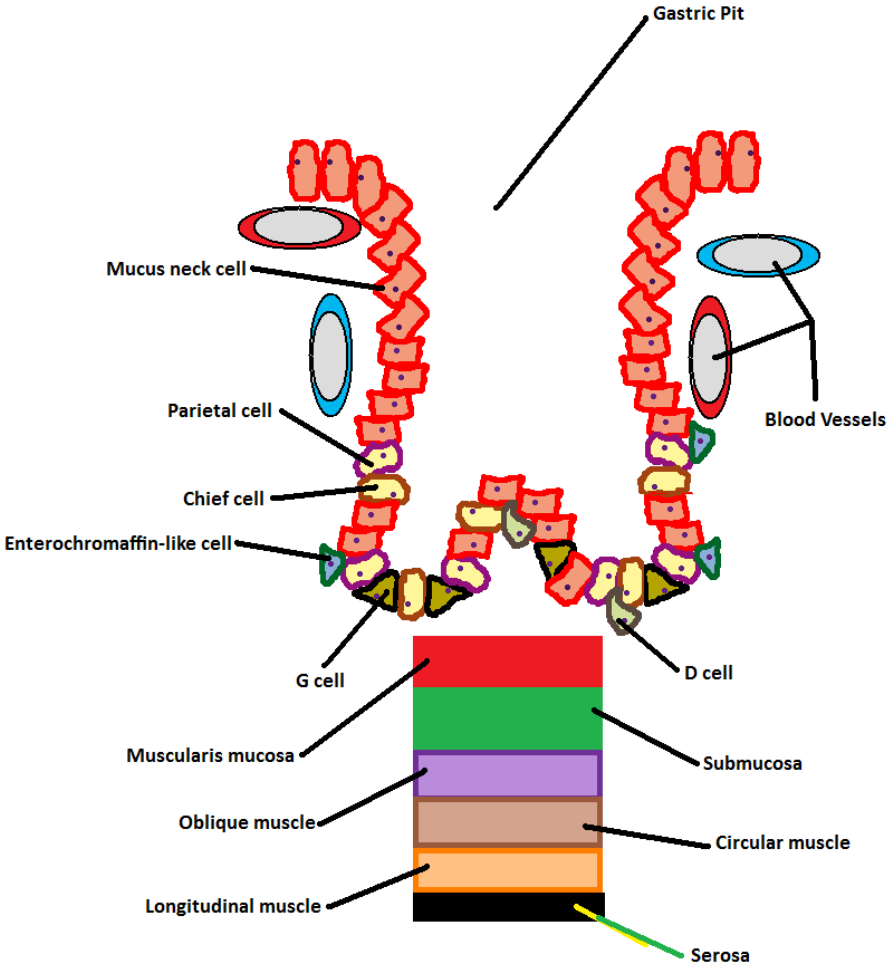


- The esophagus is a tube that consists of 3 layers:
- 1) an outer muscularis layer that consists of a longitudinal and a circular muscle layer,
- 2) a middle layer that consists of areolar tissue that connects the muscle with the inner, mucosal, layer and
- 3) the inner mucosal layer (this is sometimes called the "slider" layer).
- The esophagus has no chemical digestive role in the human body.



- The food bolus enters the stomach through the cardiac valve at the end of the esophagus where it "connects" with the stomach. The stomach has folds along its insides called rugae. These rugae are like washboards: the food bolus is ground between these rugae into smaller particles.
- The stomach absorbs some water, electrolytes, ethyl alcohol (grain alcohol) and aspirin. Indeed, the "best conditions under which to take aspirin is on an empty stomach with refrigerator cold water -- of course this also is the perfect environment for aspirin to "help" you develop an ulcer, too.

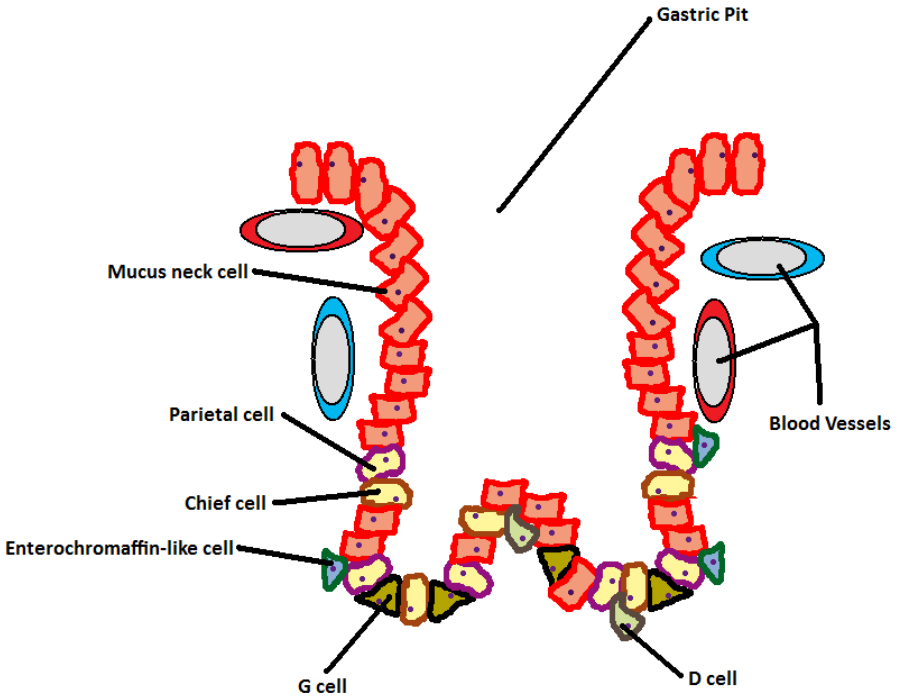
Stomach and Gastric Pits



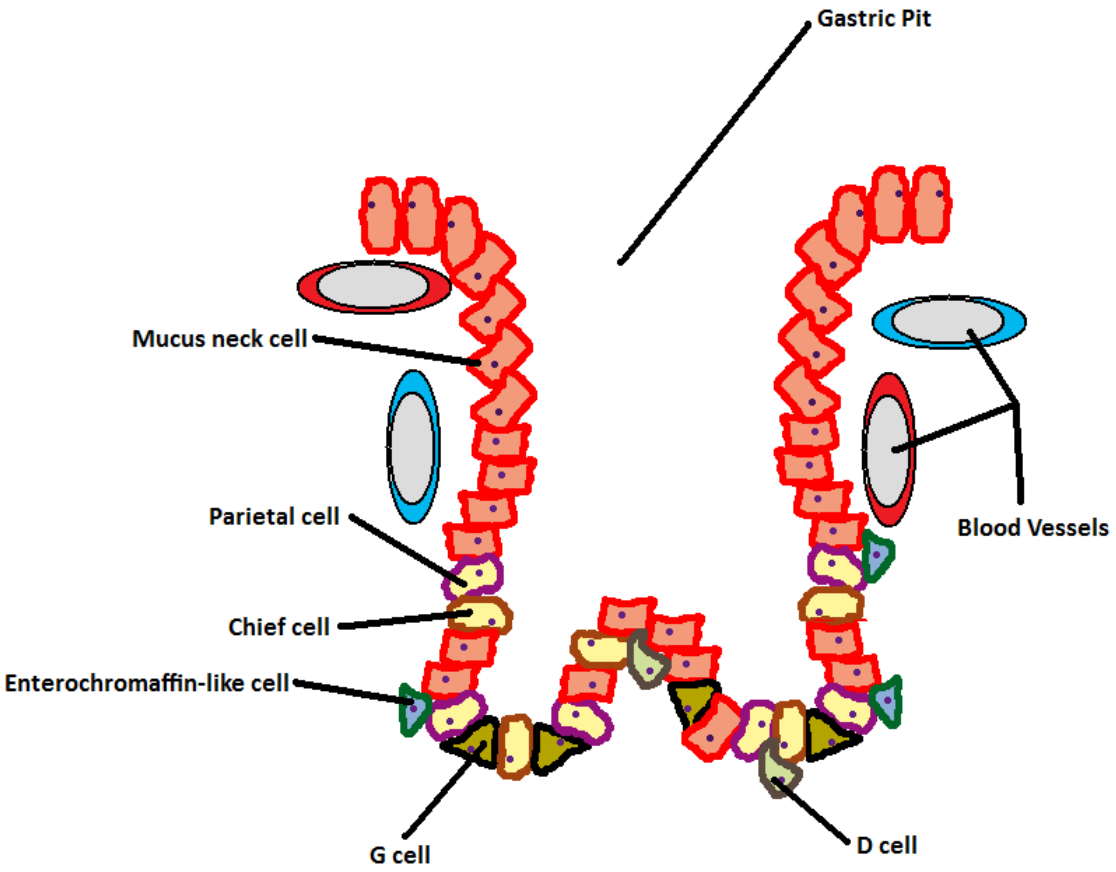
- Mechanical (Physical) Digestion – rugae – folds – churns food
- Absorption – SOME water, electrolytes, ASA and EtOH

Stomach – Chemical/Secretory Digestion

- In terms of the chemical, secretory, part of the digestive function of the stomach, in the walls of the stomach are gastric pits, Figure.
- In these pits are **chief cells** which secrete pepsinogen.
- Pepsinogen is activated at a pH of 2.
- The activation process leaves behind pepsin (active enzyme) and a waste peptide.
- Pepsin is a protease (an enzyme that "clips" proteins into smaller peptides).
- The pits also contain parietal cells.
- **Parietal cells** secrete hydrochloric acid (HCl).
- HCl creates the acidic environment necessary to form active pepsin.
- **Mucous neck cells** are also present in the lining of the gastric pits.
- These cells secrete mucous to protect the gastric lining and gives body and cohesiveness to the churned up food mass.
- Pyloric glands are surface goblet cells that produce a thicker, stickier mucus to coat/protect the stomach wall, as well.



Stomach – Chemical/Secretory Digestion



Enterochromaffin-like cells – secrete histamine for acid production at parietal cells.
G cells – secrete gastrin to stimulate parietal cells to secrete HCl.
D cells – inhibit HCl secretion via somatostatin at parietal cells.
✓Parietal cells also seem to secrete Intrinsic Factor.

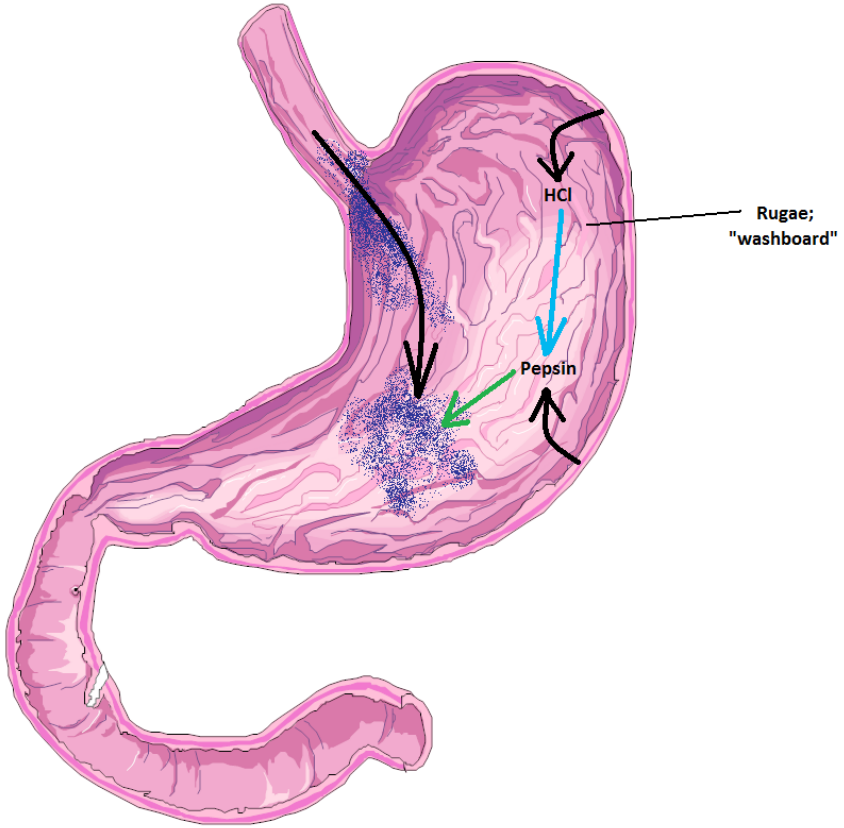
Stomach – Chemical/Secretory Digestion -- REGULATION

Nerve Stimulus

- Due to sensations such as ingested food and hostility
  - Secretions increased due to anger/hostility which lead to diarrhea
  - Fear/depression decreases secretions and decreases blood flow and motility and leads to increased constipation

Hormonal Stimulus

- Due to food in the stomach
  1. Coffee, red meat, alcohol, nicotine increase gastrin secretion from gastroendocrine cells
  2. Gastrin stimulates parietal cells to secrete HCl
  3. At pH 2, feedback inhibits gastrin secretion
  4. Enterogastrone (duodenal glands) decrease acid and pepsin secretion and gastric motility

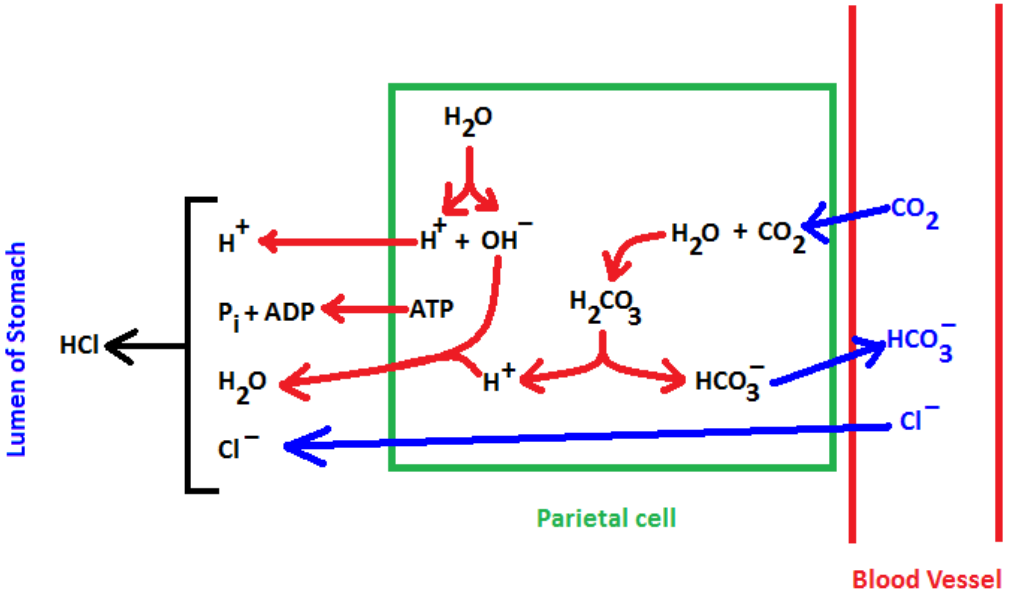


- Once the food bolus enters the stomach, it causes the release of HCl and pepsin.
- Food also causes peristalsis
- The former is an acid and the latter is a protease, i.e., an enzyme that destroys proteins.

HCl Biosynthesis

$$CO_2 + H_2O \xrightarrow[\text{Anhydrase}]{\text{Carbonic}} H_2CO_3$$

$$H_2CO_3 \xrightarrow[\text{Anhydrase}]{\text{Carbonic}} H^+ + HCO_3^-$$



- HCl biosynthesis, while initiated in parietal cells, starts in the blood.
- CO_2 is taken up by the parietal cells and condensed with water to form carbonic acid (the enzyme that does this is called carbonic anhydrase).
- The carbonic acid is then enzymatically de-protonated.

HCl Biosynthesis

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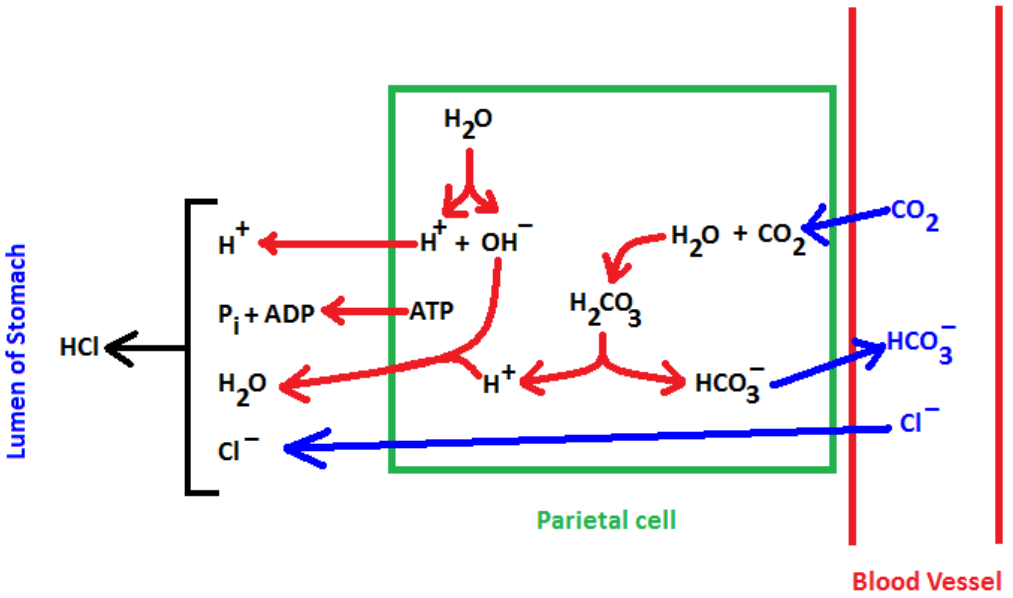


- The resulting bicarbonate is dumped back into the blood while a negatively charged chloride ion (Cl^-) is concurrently taken up into the parietal cell (another “chloride shift”!). The proton gained from the de-protonation of carbonic acid condenses with a hydroxide ion to form water.
- The hydroxide came from the dissociation of water into a proton and hydroxide ion.
- The "left-over" proton from the dissociation of water is enzymatically reacted with the chloride ion to form HCl at the expense of some energy.
- This energy is in the form of ATP (adenosine triphosphate) -- the molecule of energy of life.

- The effects of HCl on both α-amylase and the short chain fatty acid lipase.
- In short, HCl denatures these two enzymes -- while ACTIVATING pepsin -- which stops carbohydrate and lipid digestion at this point. This process does not happen all at once, rather it happens a little bit at a time, i.e., in a step-wise manner.
- This occurs as the HCl penetrates the bolus of food, eventually denaturating the two proteins, stopping their activity.
- Hence, there is no carbohydrate OR lipid digestion in the stomach, proper.

HCl Disorders

HypOchlorhydria

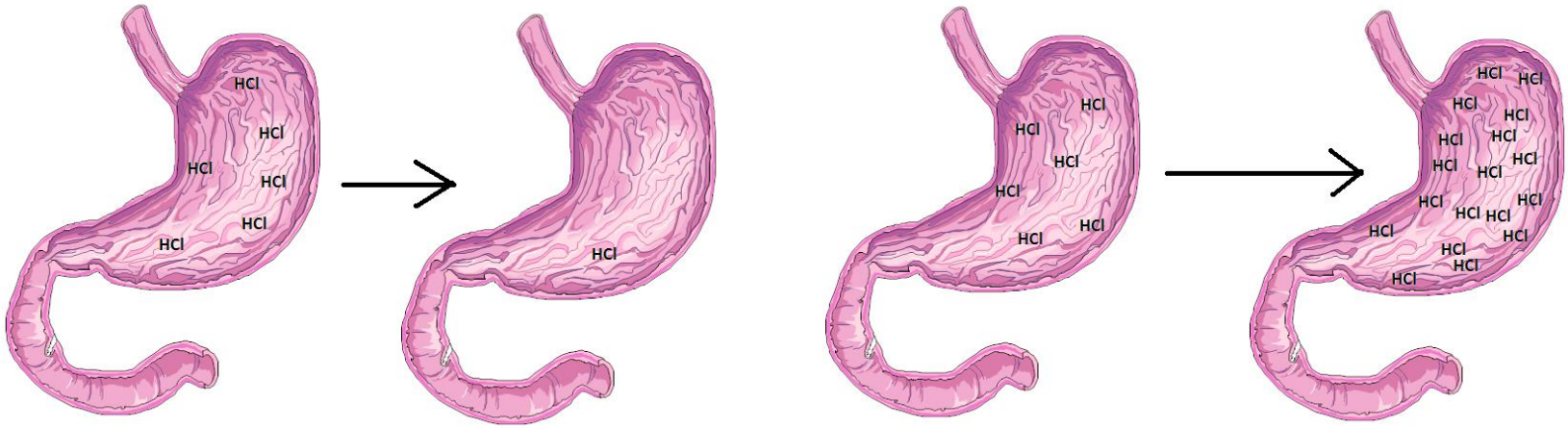
- Aging

PROBLEM:

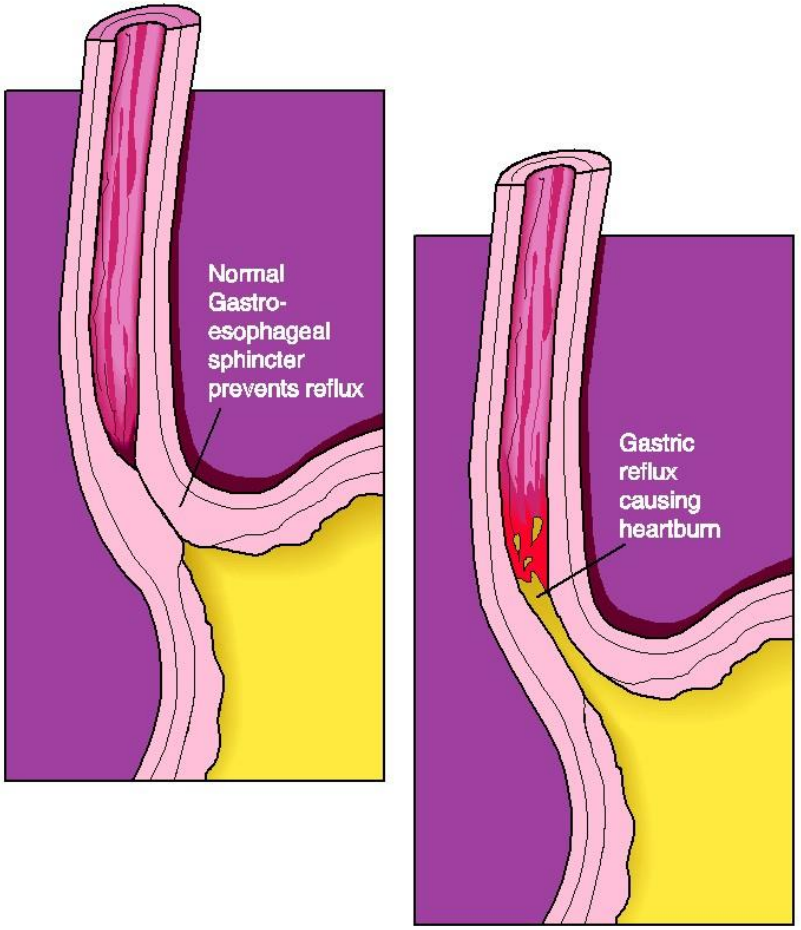
- Reduces efficiency of Ca^{2+} uptake
  - Reduction due to alkaline gastric environment

HypERchlorhydria

- Tx with antacids
  - TUMS is NOT a good Ca^{2+} source – makes stomach too alkaline
- Tx with H_2 antagonists
- Tx with proton pump inhibitors
- Tx with prokinetics



GERD



- Heartburn --two or more days a week
- Bloating/belching
- Repetitive
- Requires intervention
- Only proton pump inhibitors (e.g., prilosec) seem to reverse esophageal changes

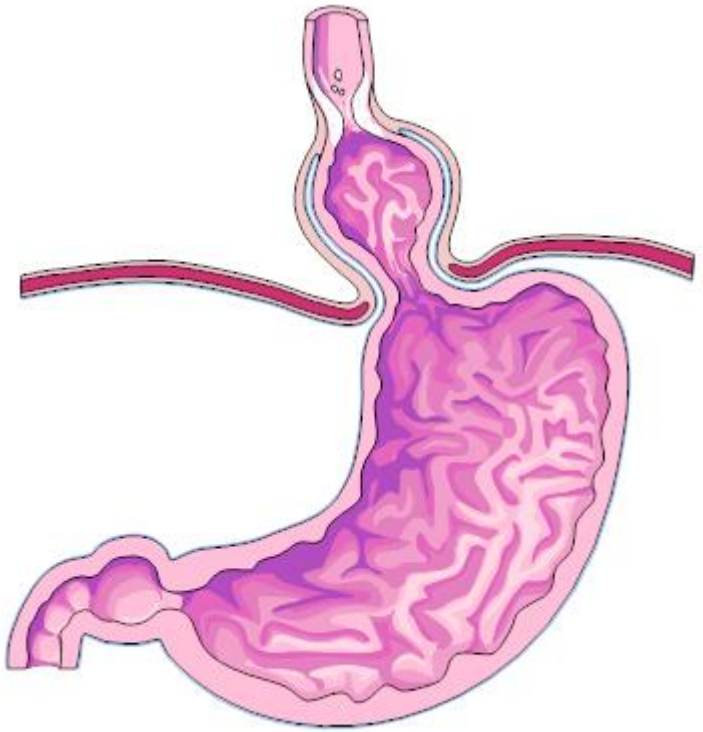
Hiatal Hernia

Symptoms & Causes

In most patients, there are no symptoms, however some experience heartburn and regurgitation. Besides discomfort from acid reflux and dysphagia, hiatal hernias may have severe consequences if not treated.

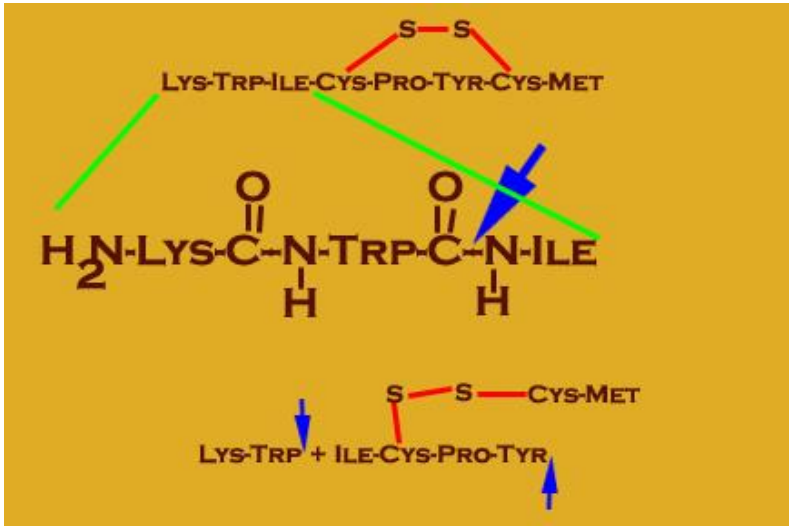
Below is a list of contributing factors which may result in hiatal hernia:

- Congenital defects
- Heredity
- Frequent bending over or heavy lifting
- Frequent coughing
- Obesity
- Poor seated posture
- Smoking
- Straining with constipation



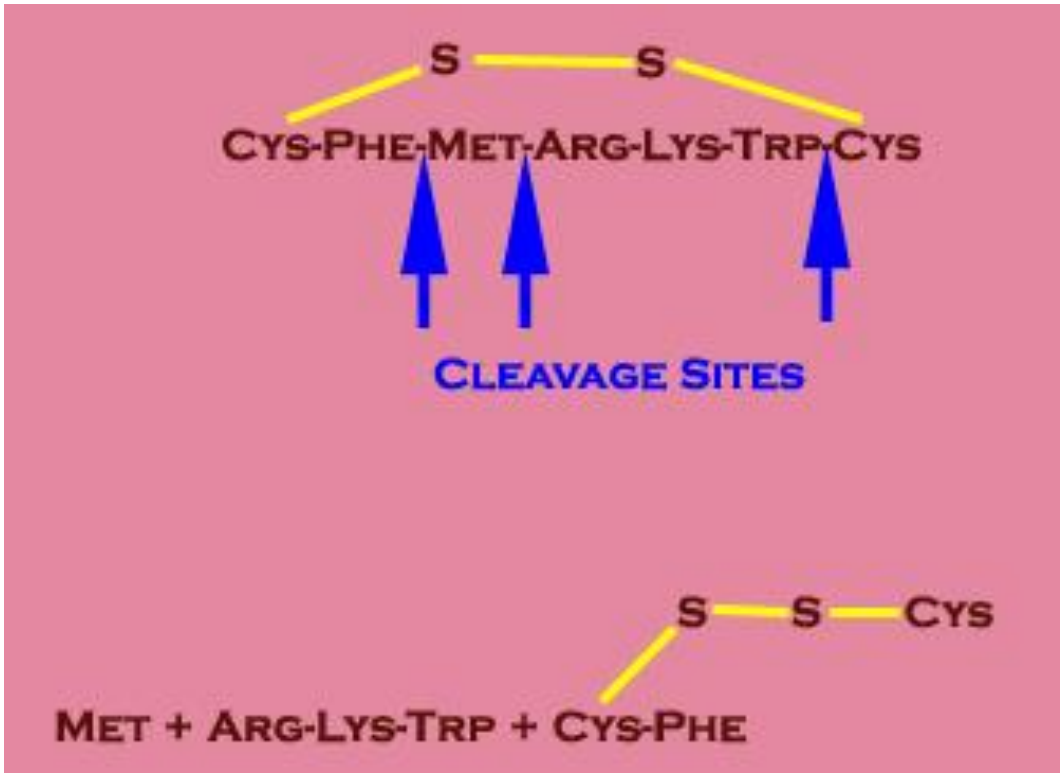
Pepsin -- #1

Pepsin hydrolyzes proteins at the C-terminus of			
Trp	The aromatic amino acids	Met	Sulfur-containing amino acid
Phe		Leu	BCAA
Tyr			



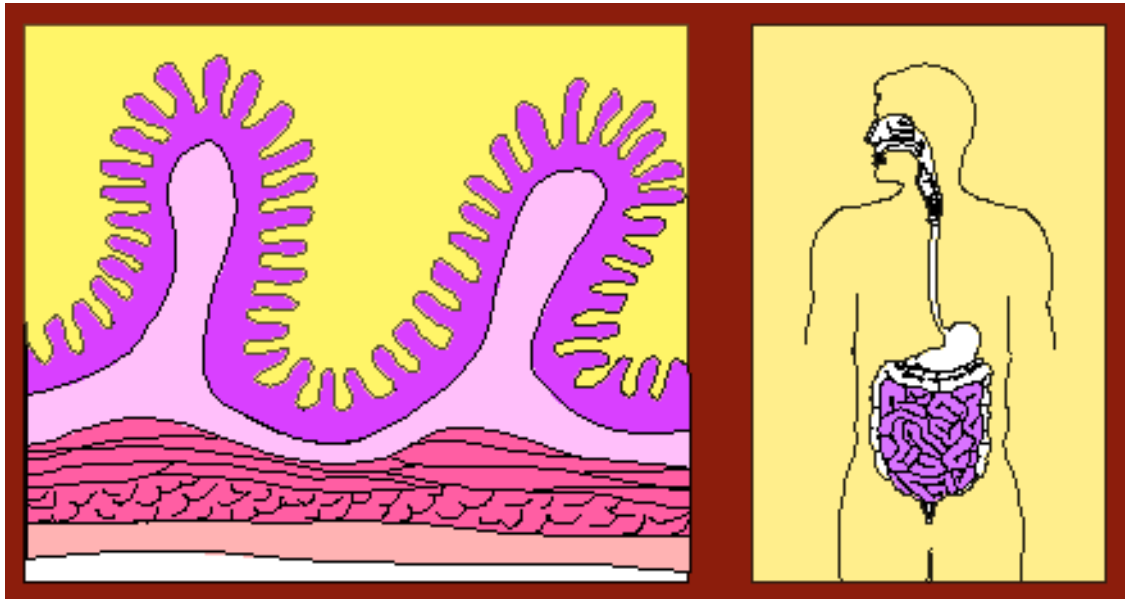
- Note disulfide bond
- Note pepsin cleavage site
- Note products

Pepsin Activity -- #2



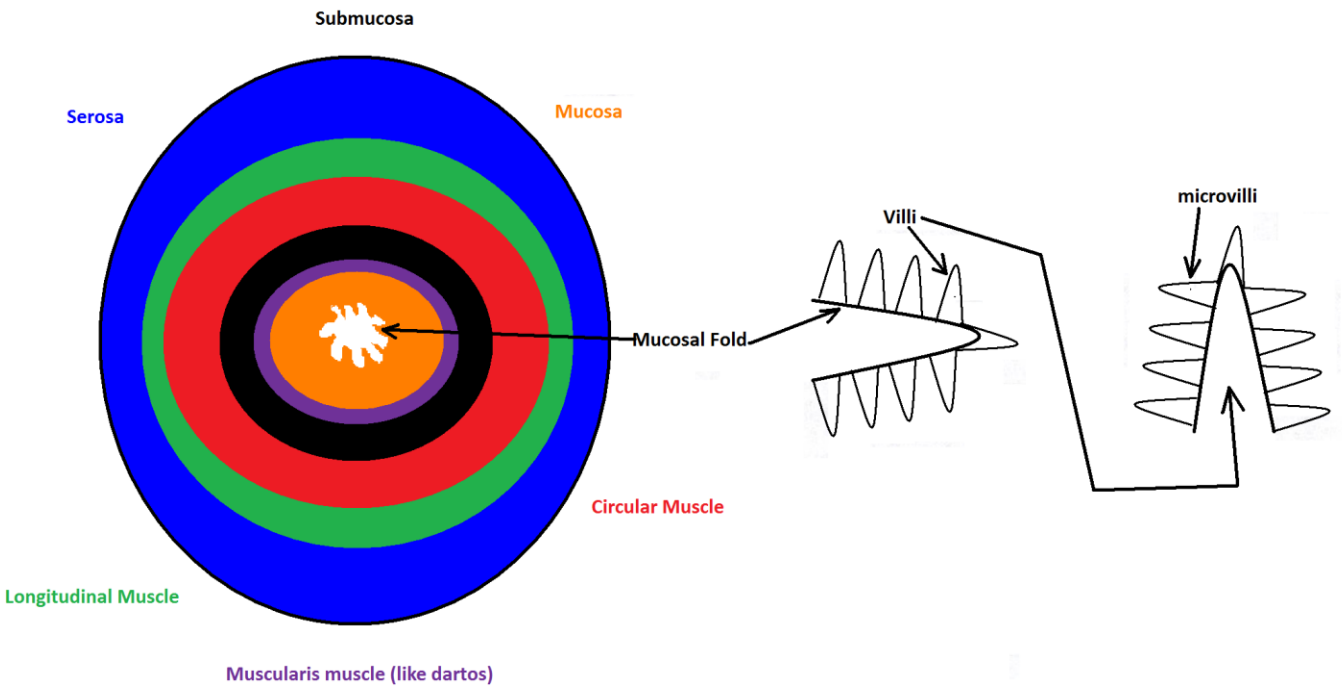
- Note disulfide bond
- Note cleavage sites
- Note products

- In very young animals and humans (babies), the stomach secretes another enzyme called rennin. Rennin (note the spelling) causes milk to curd, to prevent it from "just running out from" the stomach undigested (HCl does the same thing with fat or grease which is why Grandma's turkey gravy sticks with you, repeating for 4-6-8-12 hours).
- Rennin is NOT present in adult's stomachs.



- Once the stomach has done its share of digestion, the chyme is injected into the small bowel through the pyloric valve at the distal end of the stomach.
- The small bowel is in three parts: the duodenum, the jejunum and the ileum.
- The duodenum originates at the pyloric sphincter and is about 25 cm in length.
- The jejunum is the second part and measures about 2.5 meters (jejunum means empty, since it is usually found empty after death.
- The final portion of the small bowel is the ileum. It measures out about 3.6 meters in length and joins the large bowel at the ileocecal valve. By the time the chyme reaches this point, it is about the consistency of creamed corn.
- Almost all absorption and digestion of nutrients occurs in the small bowel.

Layers of the Small Bowel



- Figure illustrates a cross-sectional view of the small bowel.
- Note the two layers of muscle that perpetuate peristalsis -- the esophagus is set up the same way.
- The other significant landmark is the mucosal folds. On the surface of the mucosal folds are villi (little fingers). On the surface of these villi are microvilli (very little fingers).
- All the villi and microvilli increase the surface area of the small bowel to increase the efficiency of nutrient uptake during digestion.
- Although the total length of the small bowel comes to about 6.3 meters, if the surface area of the small bowel is taken into consideration, it would about cover a football field.

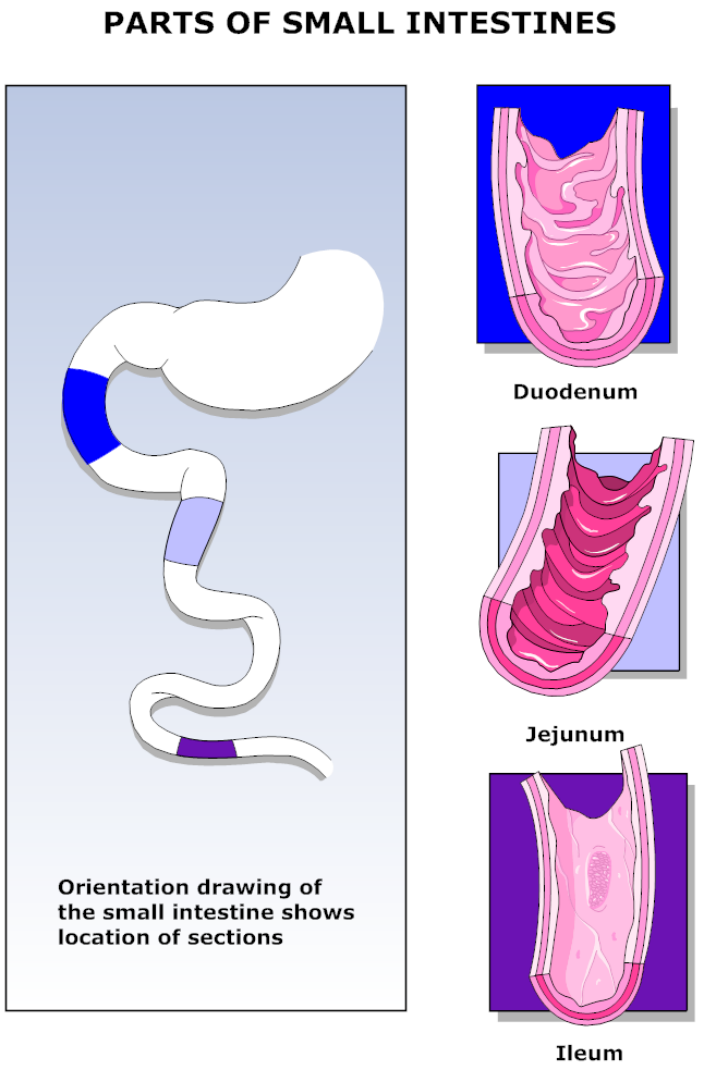
Summary of The Chemical, Secretory Portion of Digestion from The Small Bowel and Accessory Organs of Digestion

Nutrient Digested	Enzyme[s]	Nutrient Digested	Enzyme[s]
Fat	Intestinal lipase "clips" fat to monoglycerides, glycerol and/or free fatty acids	Nucleic acids	Nucleosidase metabolizes nucleosides to a base and [d-]ribose
Protein	Enterokinase (activates trypsin; protease); aminopeptidase; dipeptidase	Carbohydrates	Maltase, lactase, sucrase hydrolyze maltose, lactose and sucrose, respectively, to glucose and glucose, glucose and galactose and glucose and fructose
Hormones			
Secretin	From duodenal mucosa; stimulates pancreatic secretions and regulates the pH of the secretions. The pH of the small bowel is radically higher than the stomach (about 9).	Cholecystokinin (CCK-PZ; CCK)	From the duodenal mucosa, too. Stimulates the gall bladder to contract. It also stimulates the release of pancreatic amylase. CCK stimulates the sphincter of Oddi to relax.

Small Bowel

Divisions

- Duodenum
  - Originates at the pyloric sphincter; is about 25 cm long (means “12” since it is about 12 finger breadths long) in length
- Jejunum
  - 2d part – 2.5 m in length (means empty, since at death it is found empty)
- Ileum
  - Final portion; 3.6 m long and joins large bowel at ileocecal valve

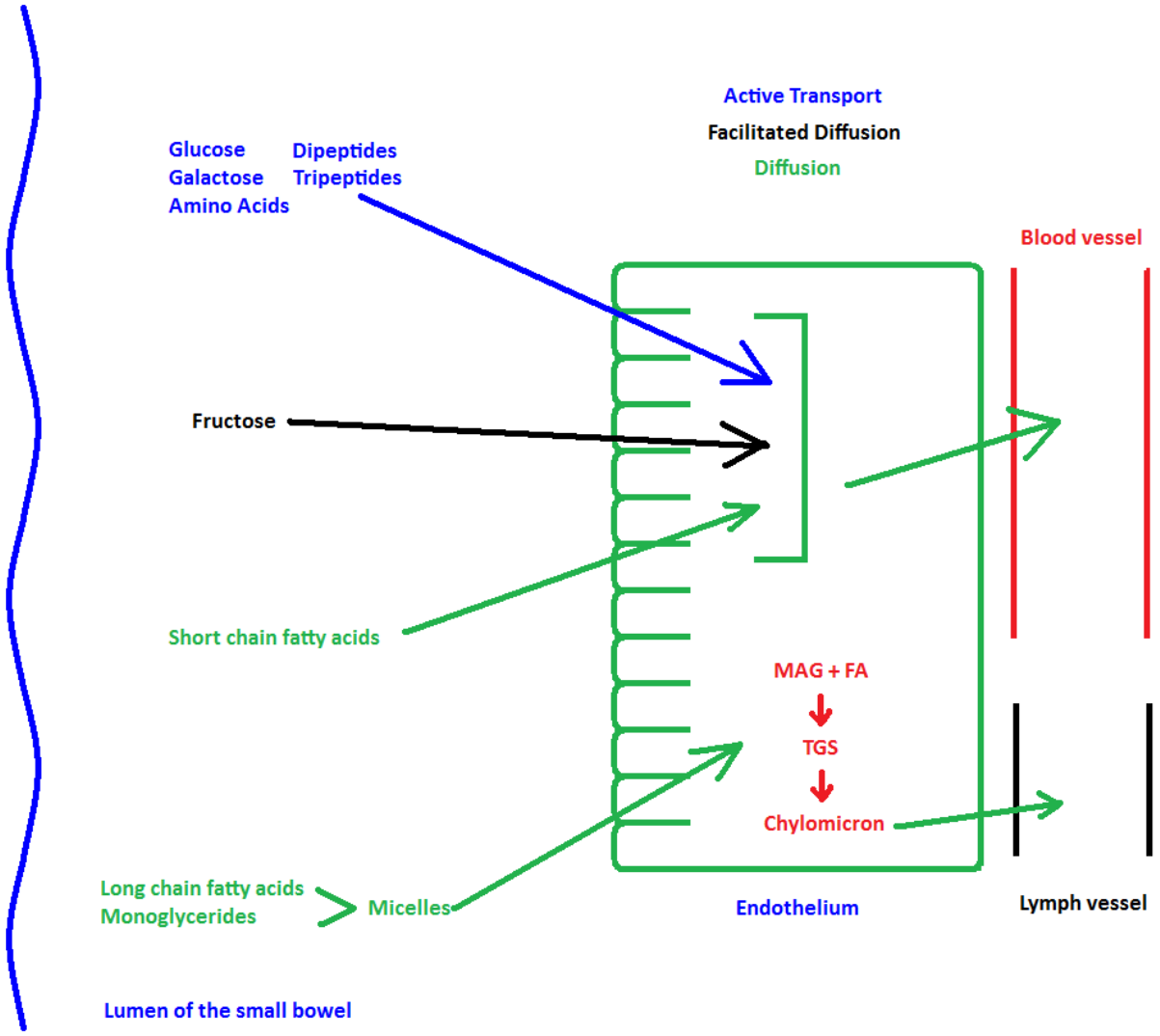


Almost all digestion and absorption of nutrients occurs in the small bowel

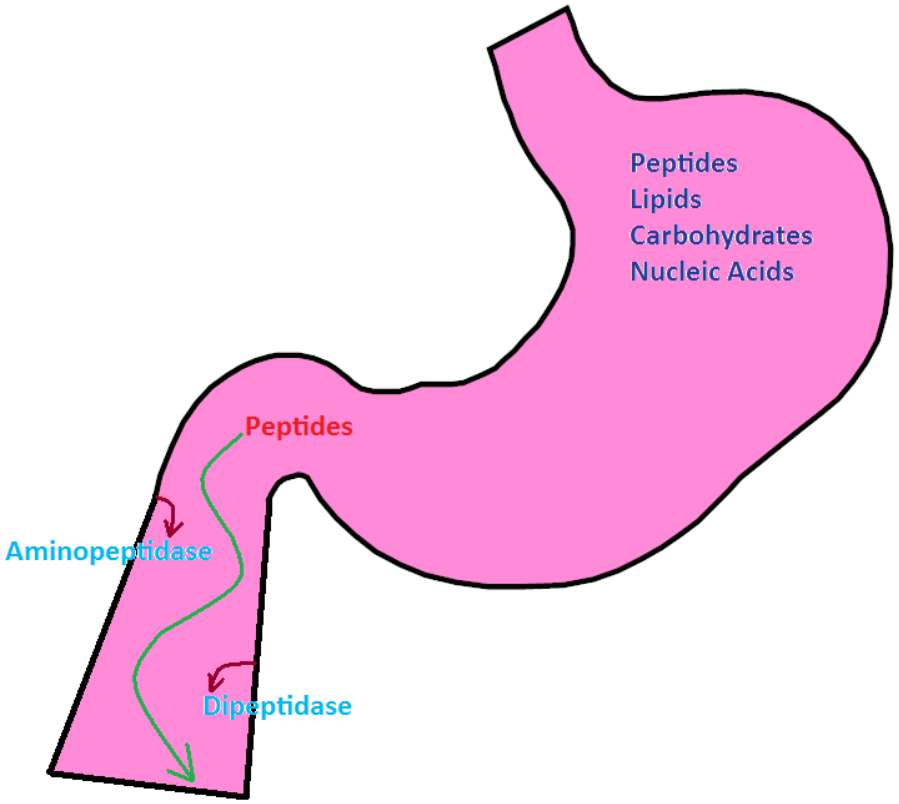
Small Bowel – Chemical/Secretory Digestion – Intestinal Glands in Mucosa

1. Fat: intestinal lipase (fat metabolized to MG's, glycerol and FFA's)
2. Protein: enterokinase activates trypsin; aminopeptidase; dipeptidase; nucleosidase – nucleosides hydrolyzed to a nitrogenous base and [d-]ribose
3. Carbohydrates: maltase, lactase, sucrase (yields glucose, glucose and galactose, glucose and fructose)
4. Secretin: from duodenal mucosa; stimulates pancreatic secretions and regulates pH of the secretions
5. CCK-PZ: from duodenal mucosa; stimulates gall bladder to contract; also stimulates release of pancreatic amylase; stimulates relaxation of Sphincter of Oddi

Nutrient Uptake Across the Small Bowel



Protein Digestion – Small Bowel



- Alkaline pH "opens up" proteins

•Aminopeptidase is secreted from the wall of the small bowel and removes the N-terminal amino acid from the peptide, one at a time.
•Dipeptidase is the last enzyme "seen" by peptides. It is the final protease and hydrolyzes dipeptides to single amino acids. Our body will take up di- and tri-peptides, although it doesn't like to.

Proteases from Small Bowel

- Aminopeptidase – removes N-terminal amino acid from peptide:

Asp-Gly-Pro-Lys-Arg-Cys-Phe + aminopeptidase

Yields

Asp + Gly-Pro-Lys-Arg-Cys-Phe

- If repeated one AA at a time, would disassemble peptide slowly

Proteases from Small Bowel

- Dipeptidase: a final protease that hydrolyzes dipeptides to free amino acids:

Pro-Met + dipeptidase

Yields

Pro + Met

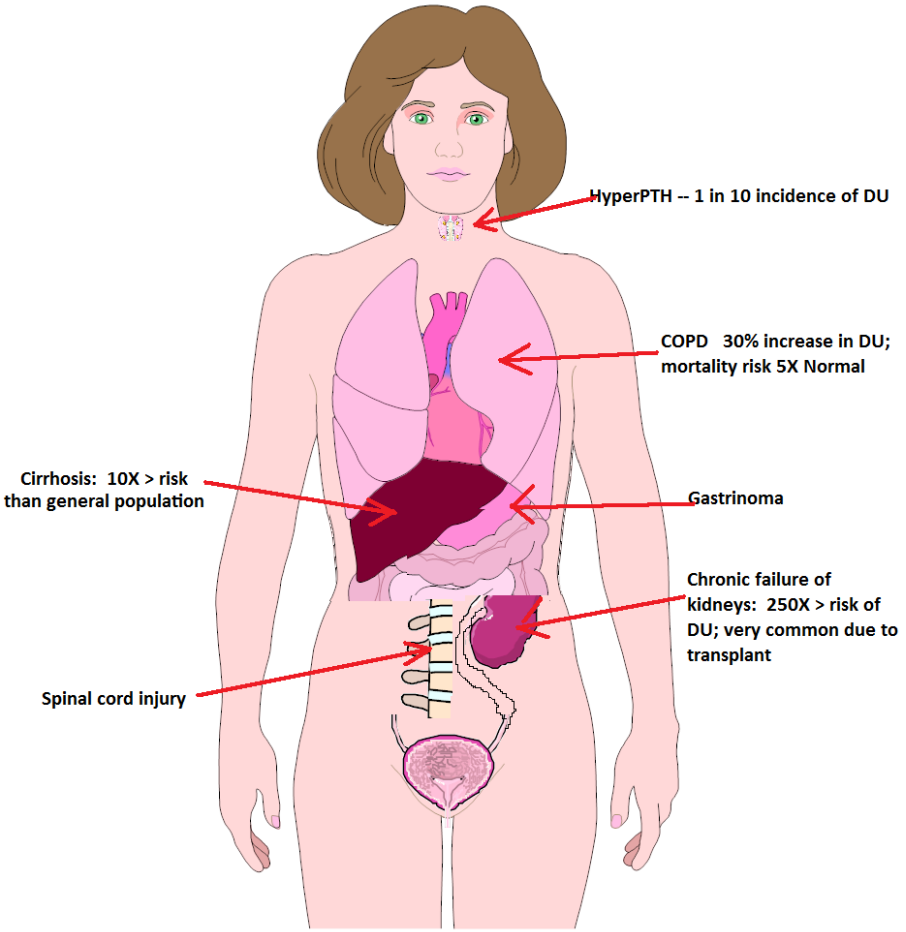
- In a best and worst case scenario, newborns and chronic alcoholics have an "open gut". This means that they can take up larger peptides: for the newborn, this is a positive thing to permit uptake of larger peptides for growth and protection; for the chronic alcoholic, this is a last ditch defense mechanism to attempt to pull as much protein into the body as is possible from ANYTHING an alcoholic is eating or drinking as s/he isn't getting enough protein in his/her diet.

- On a final note, the significance of having multiple proteases is that they can work on different parts of the same protein at the same time making proteolysis incredibly efficient.

Duodenal Ulcers

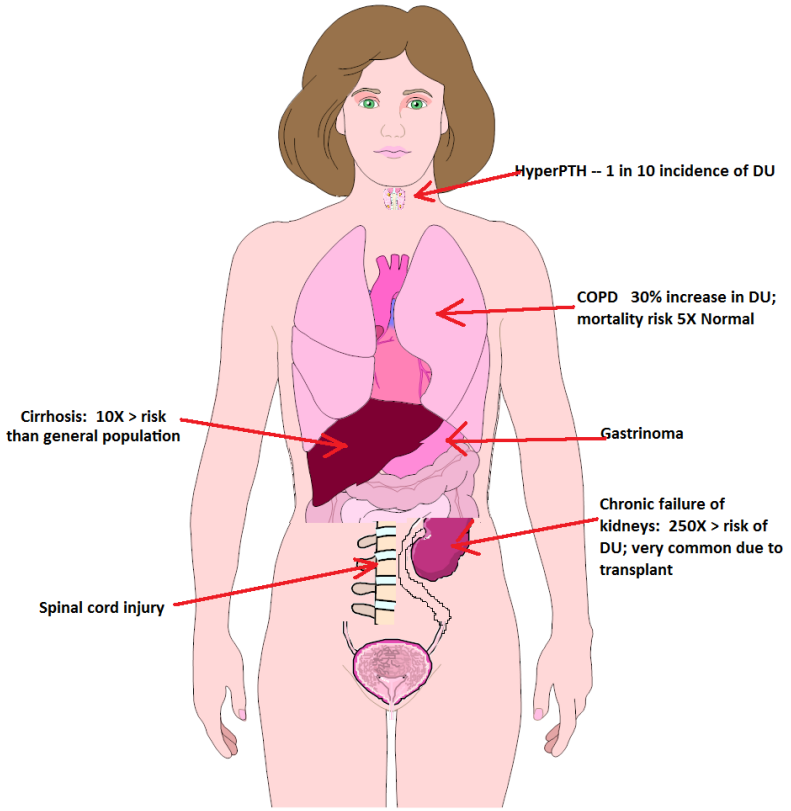
Pathogenesis

- Hyperchlorhydria (increased secretion OR reduced inhibition of its release)
- Smoking
- ASA, NSAID's
- Steroids
- Helicobacter pyloris
- Blood Group O has a 170X> risk of DU -- ????
- 25-50% of ulcer patients have a family hx of ulcers



Duodenal Ulcers

- Recently, a microorganism (*Helicobacter pylori*) has been identified as causative of upwards of 85% of all ulcers. It is generally treated with a bismuth containing compound, H_2 antagonists and either a tetracycline/Flagyl cocktail or an erythromycin derivative coupled with an antacid (just recently gained FDA approval).



- Treatment of H. pylori
- Has changed radically in the last 10 years
- 8 approved FDA regimens:

H. Pylori Treatment Regimens

1. Omeprazole 40 mg QD + clarithromycin 500 mg TID x 2 wks, then omeprazole 20 mg QD x 2 wks
2. Ranitidine bismuth citrate (RBC) 400 mg BID + clarithromycin 500 mg TID x 2 wks, then RBC 400 mg BID x 2 wks
3. Bismuth subsalicylate (Pepto Bismol®) 525 mg QID + metronidazole 250 mg QID + tetracycline 500 mg QID* x 2 wks + H_2 receptor antagonist therapy as directed x 4 wks
4. Lansoprazole 30 mg BID + amoxicillin 1 g BID + clarithromycin 500 mg TID x 10 days
5. Lansoprazole 30 mg TID + amoxicillin 1 g TID x 2 wks**
6. Ranitidine bismuth citrate 400 mg BID + clarithromycin 500 mg BID x 2 wks, then RBC 400 mg BID x 2 wks
7. Omeprazole 20 mg BID + clarithromycin 500 mg BID + amoxicillin 1 g BID x 10 days
8. Lansoprazole 30 mg BID + clarithromycin 500 mg BID + amoxicillin 1 g BID x 10 days

- *Although not FDA approved, amoxicillin has been substituted for tetracycline for patients for whom tetracycline is not recommended.
- **This dual therapy regimen has restrictive labeling. It is indicated for patients who are either allergic or intolerant to clarithromycin or for infections with known or suspected resistance to clarithromycin.
- H_2-receptor antagonist for six to eight weeks to heal the ulcer is also recognized

Ulcer Differentiation -- Broad

Gastric Ulcer

- Pain
- Eat
- Pain

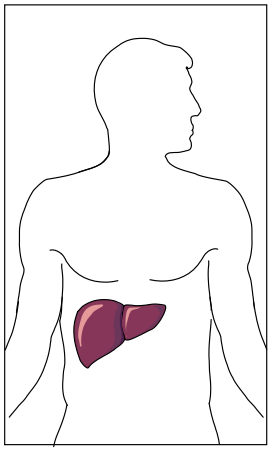
Duodenal ulcer

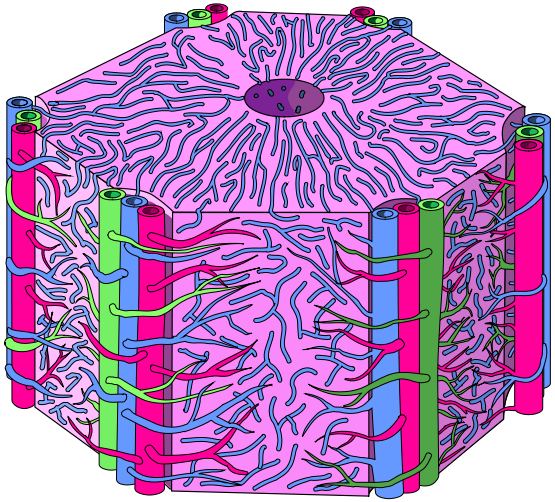
- Pain
- Eat
- NO pain

- Why no pain with duodenal ulcer?
- Alkaline secretions after eating soothe the lesion.

- Three accessory organs play roles in digestion, as well. These are the liver, gall bladder and pancreas. The chemical, secretory contribution of the pancreas is tabulated, below:

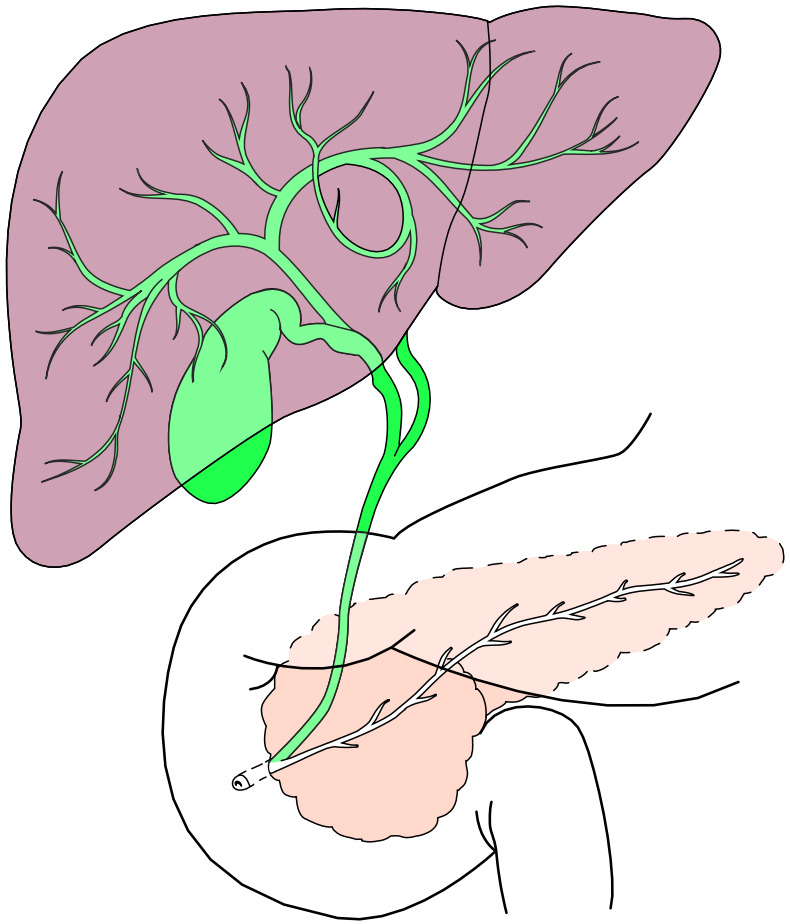
Nutrient Digested	Enzyme[s]	Nutrient Digested	Enzyme[s]
Fat	Pancreatic lipase "clips" fat to monoglycerides, glycerol and/or free fatty acids	Nucleic acids	Nucleases metabolize DNA and RNA to nucleotides.
Protein	Trypsin (protease); chymotrypsin (protease); carboxypeptidase	Carbohydrates	Pancreatic amylase hydrolyzes starch to maltose.



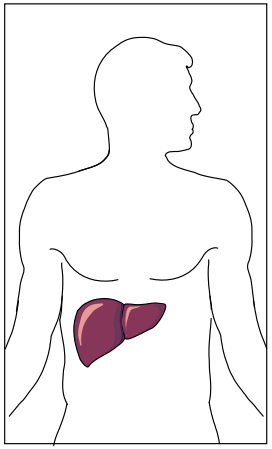


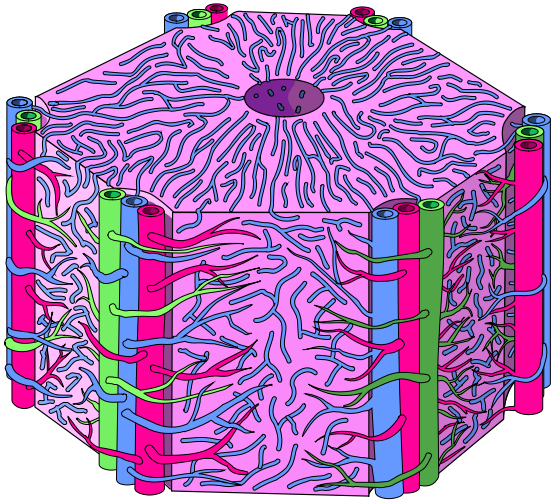
- The liver weighs about 3 lbs. Roughly a third of its weight is glycogen (the storage form of glucose in animals). Its right lobe is made up of an inferior quadrate lobe and a posterior caudate lobe. The left lobe is smaller than the right. It secretes 0.8-1 liter of bile per day. Bile is yellow to brown to OD green in color and has a pH of about 7.6-8.6. Bile breaks down large fat globules into fat droplets/suspension. The primary bile pigment is bilirubin. Bilirubin is a breakdown product of hemoglobin (gives feces its color[s]).

- Returning to more traditional topics for digestion, food regulates the functioning of both the gall bladder and the pancreas.
- When food that is very acidic (even with the addition of the HCl) "hits" the duodenum, it causes the release of CCK (cholecystokinin).
- CCK is released into the blood and travels to both organs.
- In the case of the gall bladder, CCK causes the gall bladder to contract, ejecting bile through the, now, relaxed sphincter of Oddi into the duodenum, Figure.
- Digestion is perpetuated, the bile salts are reabsorbed into the blood and are taken up by the liver for recycling (i.e., to make more bile).
- CCK also causes the pancreas to release enzyme rich pancreatic juices into the duodenum to work with the bile.



- When food is very fatty, it causes the secretion of bicarbonate rich pancreatic juices that further propagates digestion.
- This stimulation comes about via secretin secretion.

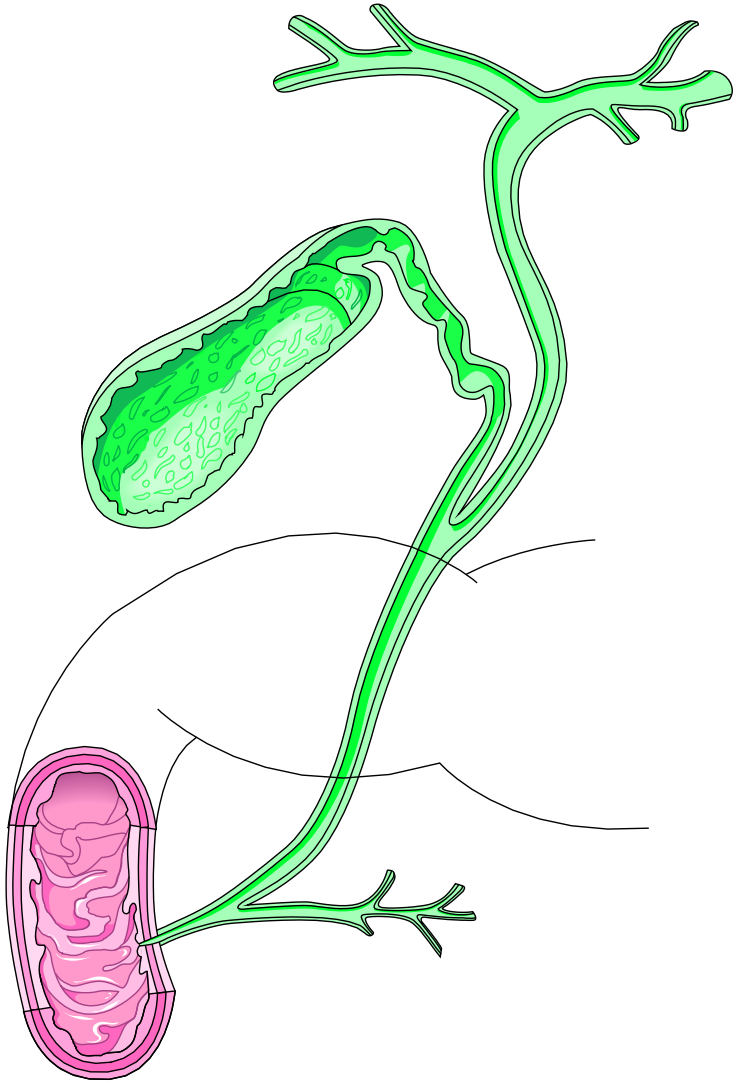




- In terms of liver physiology and metabolism, while most is best kept for BIOL 223, suffice it to say that the liver is a detoxification center of the body. It is also a metabolically active organ, capable of a great deal of anabolic and catabolic pathways. It plays a significant role in blood clotting as it produces the clotting proteins we need to stop hemorrhage. The physiological role to be discussed, next, is that of bile producer.

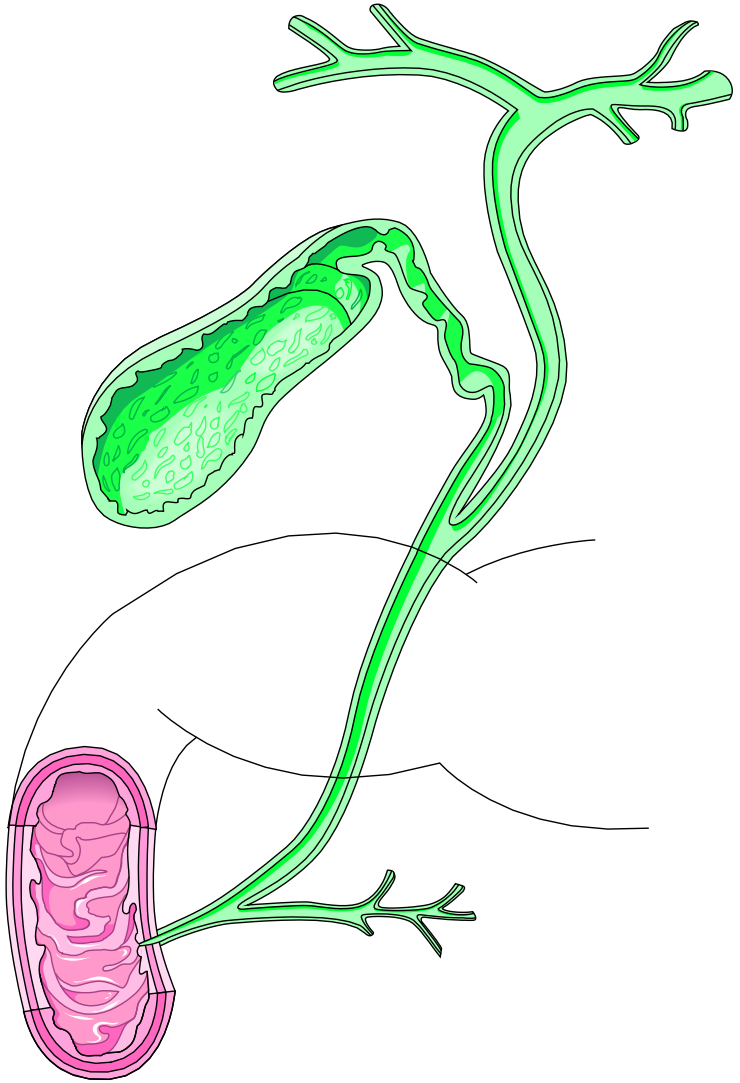
Gall Bladder

- A pear-shaped sac about 7-10 cm long
- Stores/concentrates bile (up to 10-fold) until needed in small bowel
- The gall bladder also plays a role in lipid digestion. It secretes (more like "squirts") bile (a detergent required for lipase activity, too) into the small bowel to emulsify the fat.

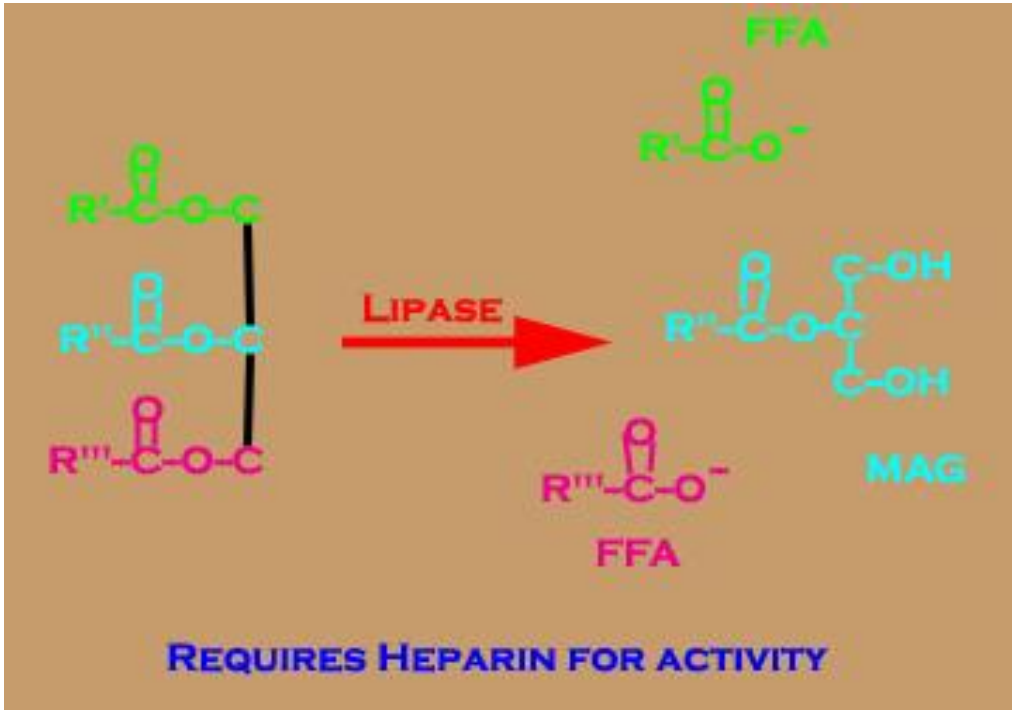


Bile Flow from Liver to GB

1. Bile secreted from liver to hepatic duct
2. Bile flows from hepatic duct into common duct
3. Bile splashes against closed Sphincter of Oddi
4. Bile “backflows” up common duct into cystic duct
5. Bile fills GB
6. GB dehydrates (concentrates) bile and stores it until needed

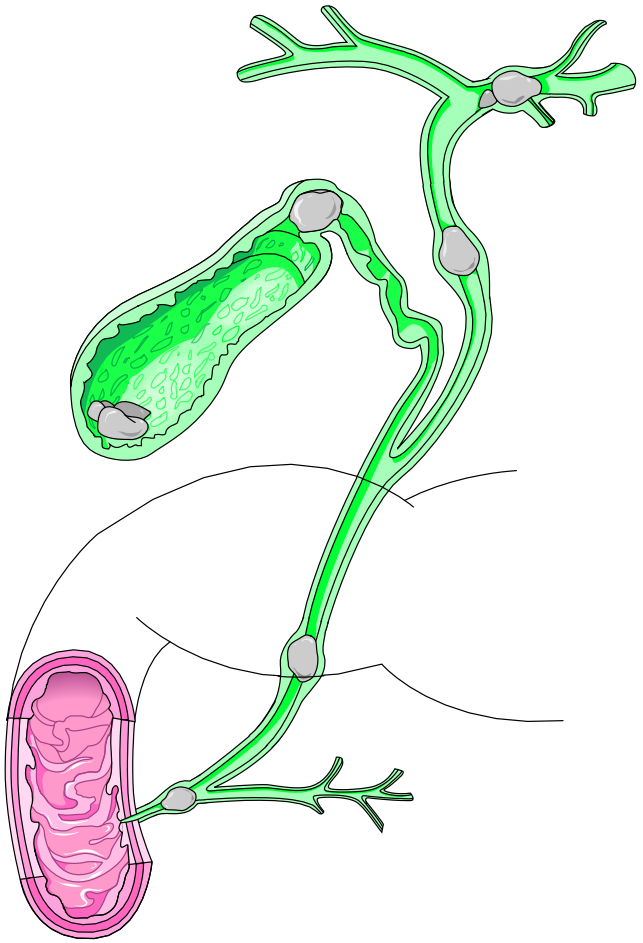


Gall Bladder -- Lipids



- Bile = detergent to emulsify the fat for lipase activity
- Both intestinal and pancreatic lipase hydrolyze TAG's to MAG's, FFA and glycerol

- Gallstones
- Dieting
- Hydration



Thus Far

Are the three Proteases (pepsin, aminopeptidase, dipeptidase) enough for proper protein digestion?

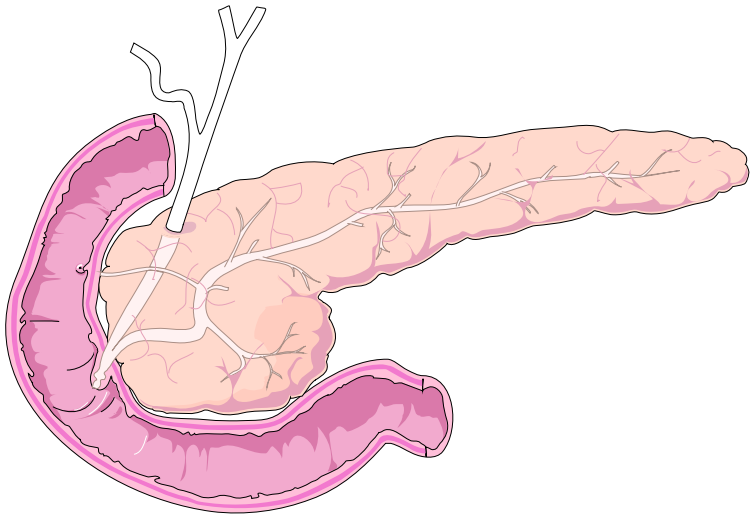
- NO!!!!!!!!!!!!!

- What else is there? Pancreatic Enzymes!

- Trypsin
- Chymotrypsin
- Elastase
- Carboxypeptidase

Pancreas

- The pancreas plays a very important role in protein digestion, as well.
- The pancreas release enzymes into the small bowel to further facilitate protein digestion.

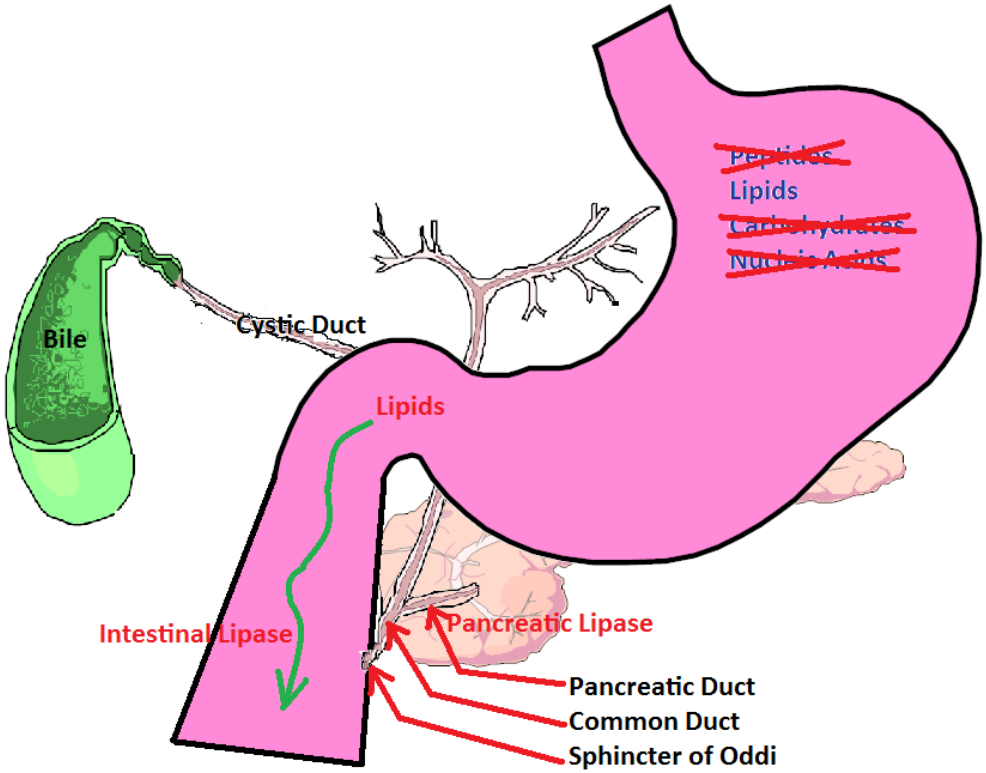


- Enzymes
- Bicarbonate
- Glucagon
- Insulin
- Somatostatin

Pancreas

- Pancreatic lipase – like intestinal lipase
- Protein: trypsin (activates chymotrypsin from chymotrypsinogen); chymotrypsin; carboxypeptidase; nucleases (hydrolyze RNA and DNA to nucleotides)
- Carbohydrates: pancreatic amylase degrades starch to disaccharides (maltose)

Lipase Activities



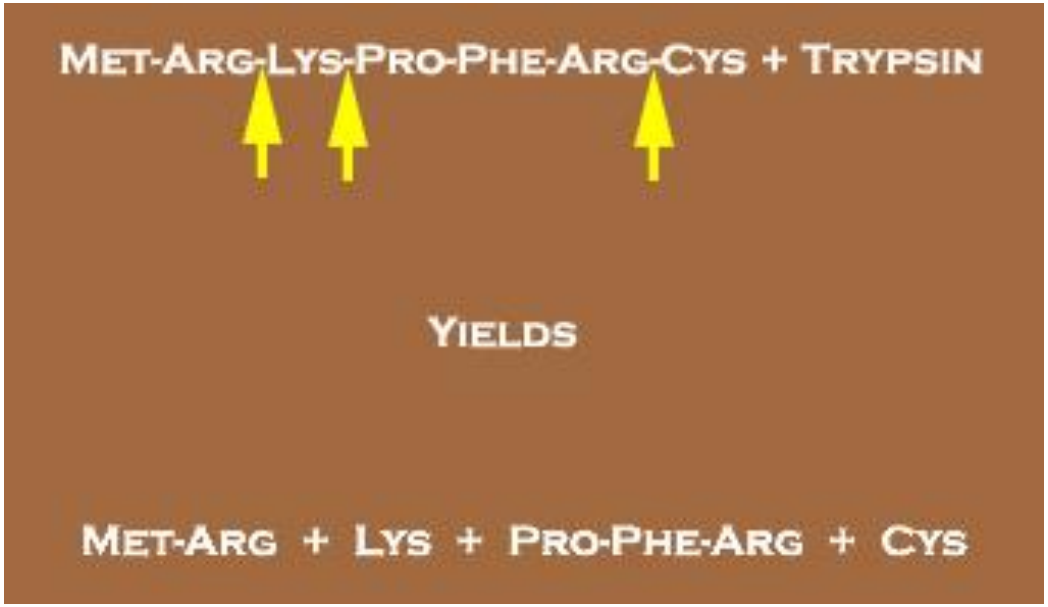
- Besides the short chain fatty acid lipase secreted at the lingual tonsil, the small bowel and pancreas also secrete lipase, Figure.
- Both require heparin for full activation and hydrolyze tri-acyl glycerols (TAG's; TGS') to mono-acyl glycerols (MAG's), free fatty acids (FFA's) and glycerol for uptake as described, earlier.

Pancreatic Proteases

Trypsin	Chymotrypsin	Carboxypeptidase	Elastase
Cleaves at the C-terminus of Arg and Lys	Cleaves at the C-terminus of Phe, Trp, Tyr	Removes the C-terminal amino acid -- one at a time	Cleaves at the C-terminus of Ser, Thr, Tyr, Asn, Gln and Cys

- Note that chymotrypsin has some of the same activity of pepsin. Pepsin, though, functions BEST at a pH of around 2. It STILL has SOME function at higher pH's, although it "prefers" the acidic conditions for its "pH optimum".
- The pH optimum is the pH at which optimal activity is attained.
- Chymotrypsin functions best at an alkaline pH, as is found in the small bowel.
- Pancreas also secretes bicarbonate rich juices

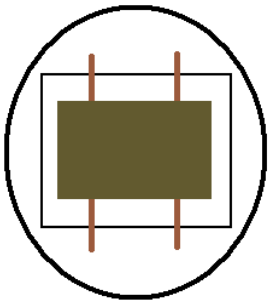
Trypsin



- Secreted as trypsinogen and activated by enterokinase
- Cleaves at the C-terminus of Arg and Lys – the positively charged amino acids

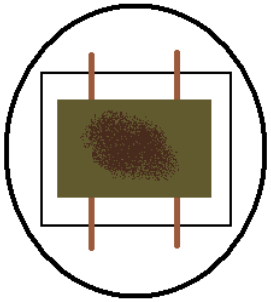
Cystic Fibrosis

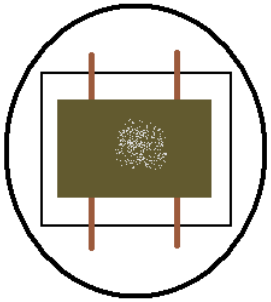
- A quick and dirty lab test to detect the potential for a newborn patient to develop cystic fibrosis (CF). Although we usually think of CF as a pulmonary disease, it has multiple ramifications, including bowel disorders. This disorder comes about because the pancreas gets plugged by this disease in its process, rendering digestion difficult, to say the least. Since the pancreas gets plugged, it can not secrete digestive enzymes like trypsin.
- To perform this easy screening procedure, you need to perform the following. Place the bottom of a Petri dish flat on a lab surface, break one of the applicator sticks in two and place them in the dish on top of a moistened paper towel. With another applicator stick, smear a little baby poop on the piece of x-ray film and mix it with normal saline.
- Place the film on the applicator sticks and cover with the top of the Petri dish. Incubate at 37° C. After incubation, rinse off the film and examine it.



Plain film

- No trypsin in poop
- Plugged pancreas
- Test further for CF



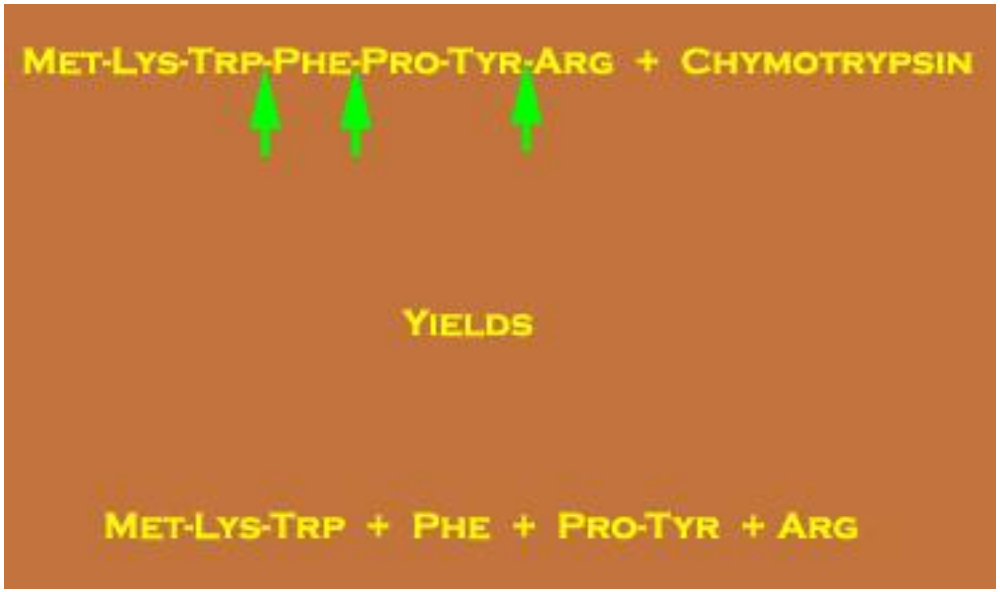


“Hole” in film

- Trypsin in poop
- Pancreas ok
- No further tests for CF

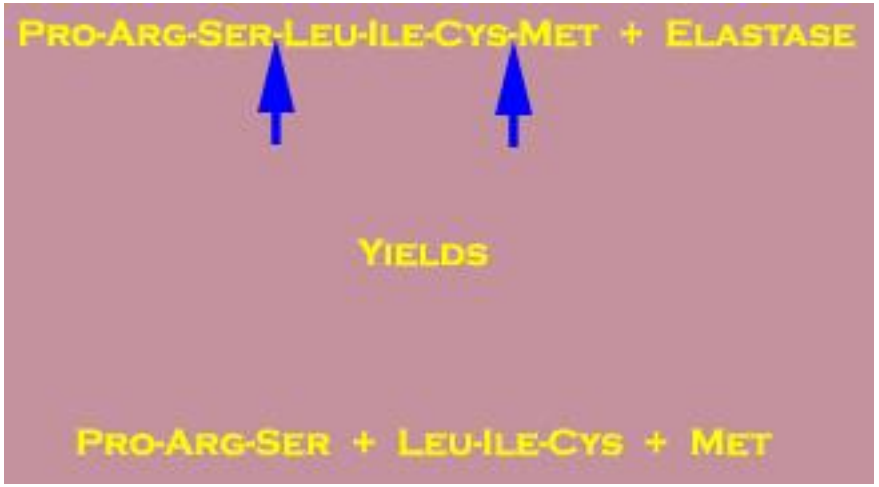
Chymotrypsin[ogen] – Activated by Trypsin

- Cleaves at C-terminus of Trp, Phe, Tyr – the aromatic amino acids



Elastase

- Cleaves at the C-terminus of the neutral amino acids: Ser, Thr, Tyr, Cys, Asn, Gln



Elastase Aside

- Elastase is present in high quantities in lung tissue
- Elastase activity is inhibited under normal conditions by α1-PI – alpha one-protease inhibitor
- This allows lungs to remain pliable and “stretchy-able”
- Smoking inhibits α1-PI – alpha one-protease inhibitor
- Elastase is activated and the lungs lose pliability and the patient is working on “getting” COPD

Carboxypeptidase

- Removes the C-terminal amino acid from a peptide

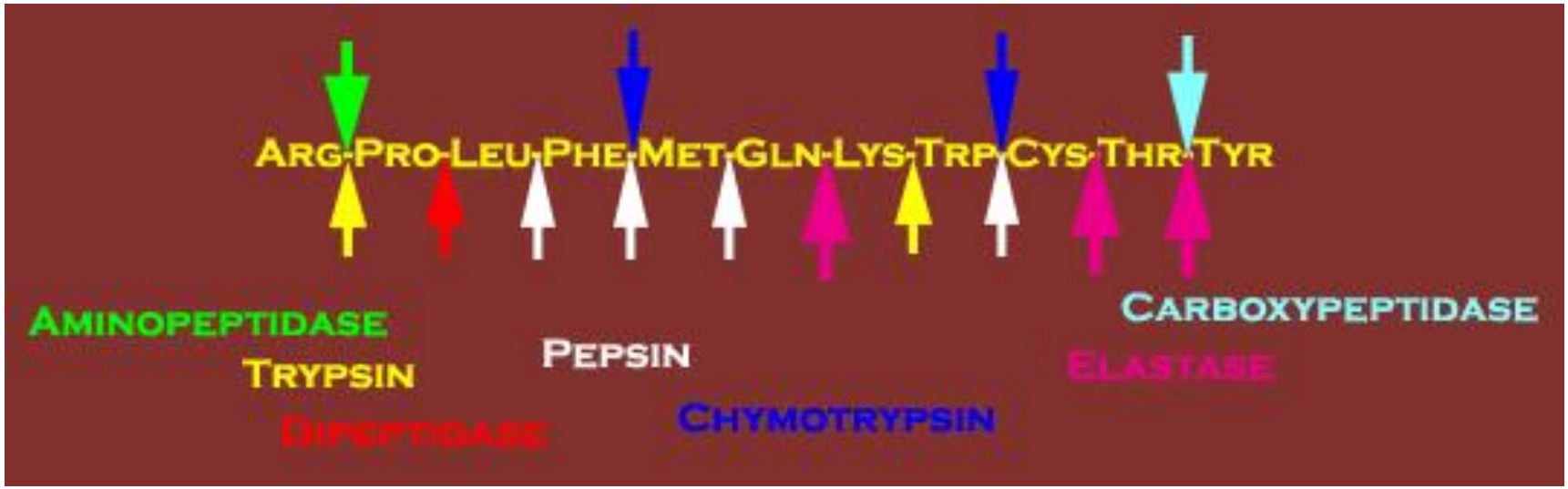
Cys-Pro-Leu-Arg-Gly-Lys + Carboxypeptidase

Yields

Cys-Pro-Leu-Arg-Gly + Lys

Protease Perspective

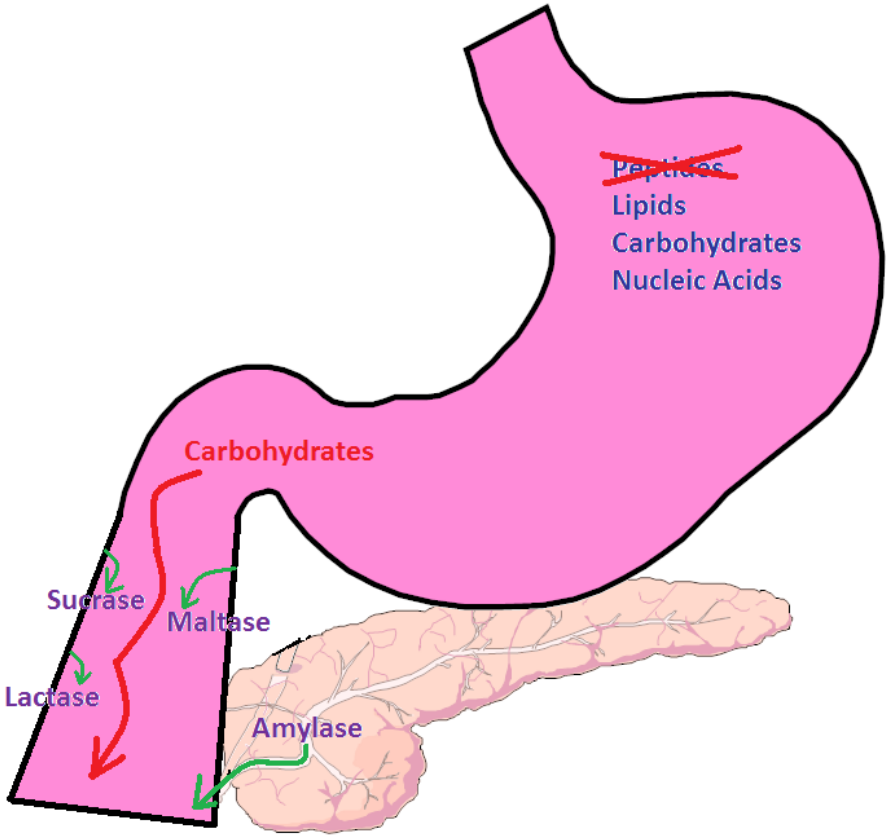
- If each enzyme were to work one at a time, this process would take forever
- Therefore
- All these enzymes (small bowel and pancreas) work at the same time to disassemble proteins



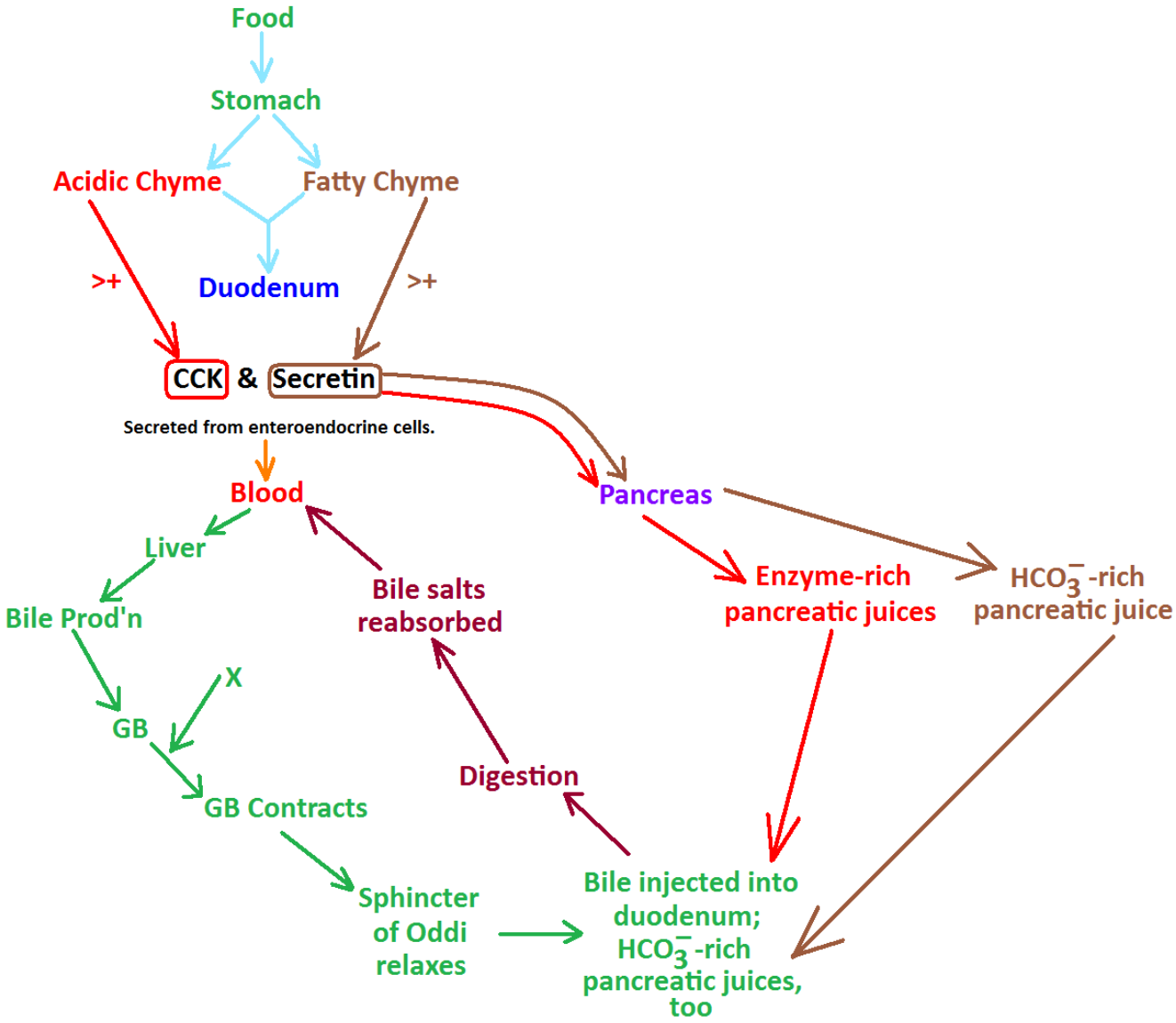
- Note back-up enzymes and specificity

Carbohydrates – Pancreatic Digestion

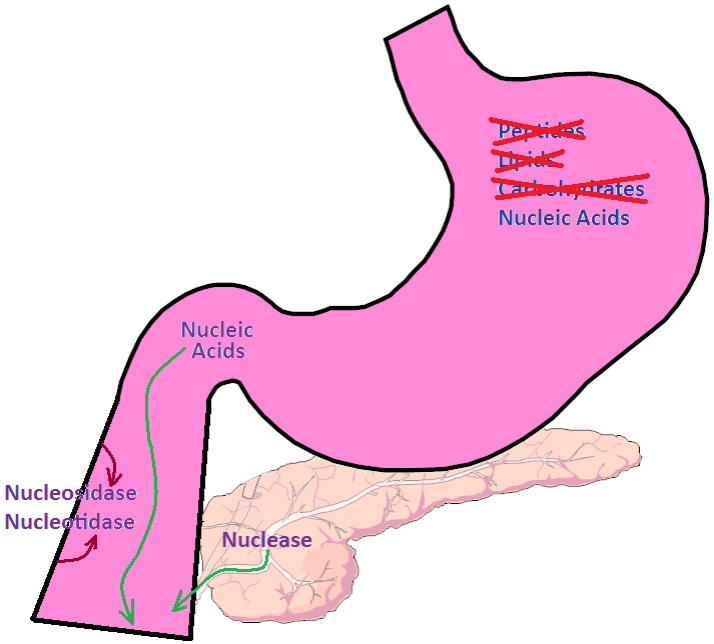
- **Carbohydrate digestion is pretty straight-forward: it starts in the mouth, as mentioned, above. α-Amylase hydrolyzes amylose from starch to a disaccharide, maltose..**
- **MaltAse (remember, if it ends in "ase" it's an enzyme) hydrolyzes maltOse to two molecules of glucose.**
- **SucrAse hydrolyzes sucrOse to a molecule of glucose and a molecule of fructose.**
- **LactAse hydrolyzes lactOse to a molecule of glucose (for rapid, short-term energy) and a molecule of galactose (for longer term energy; stored in the liver in glycogenesis).**
- **Note, too, that the pancreas secretes amylase into the small bowel.**
- **Like pepsin and chymotrypsin, the two amylase's are sort of back-ups to each other.**
- Amylase hydrolyzes starch to MALTOSE not to glucose

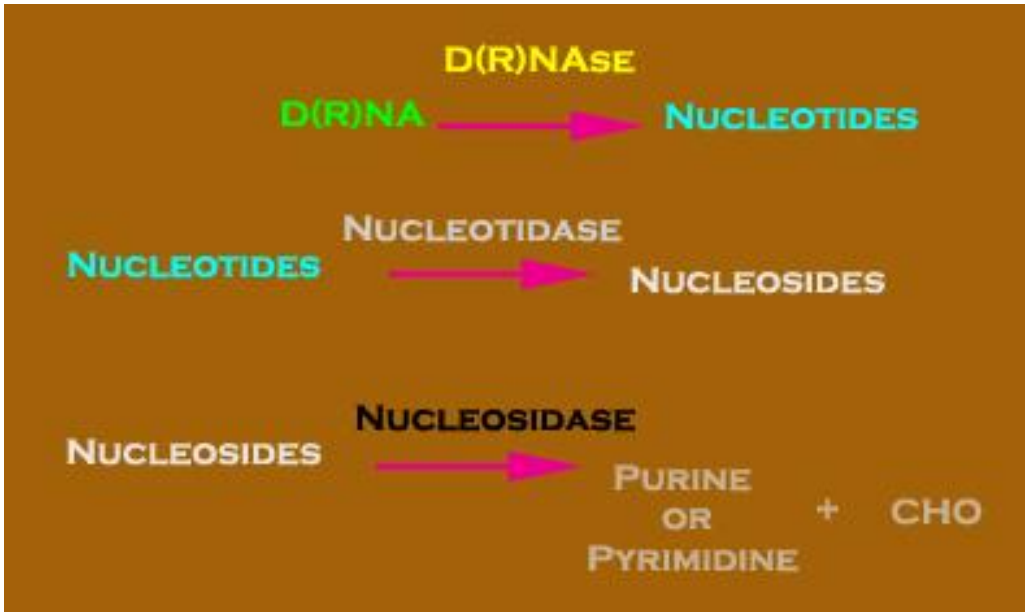


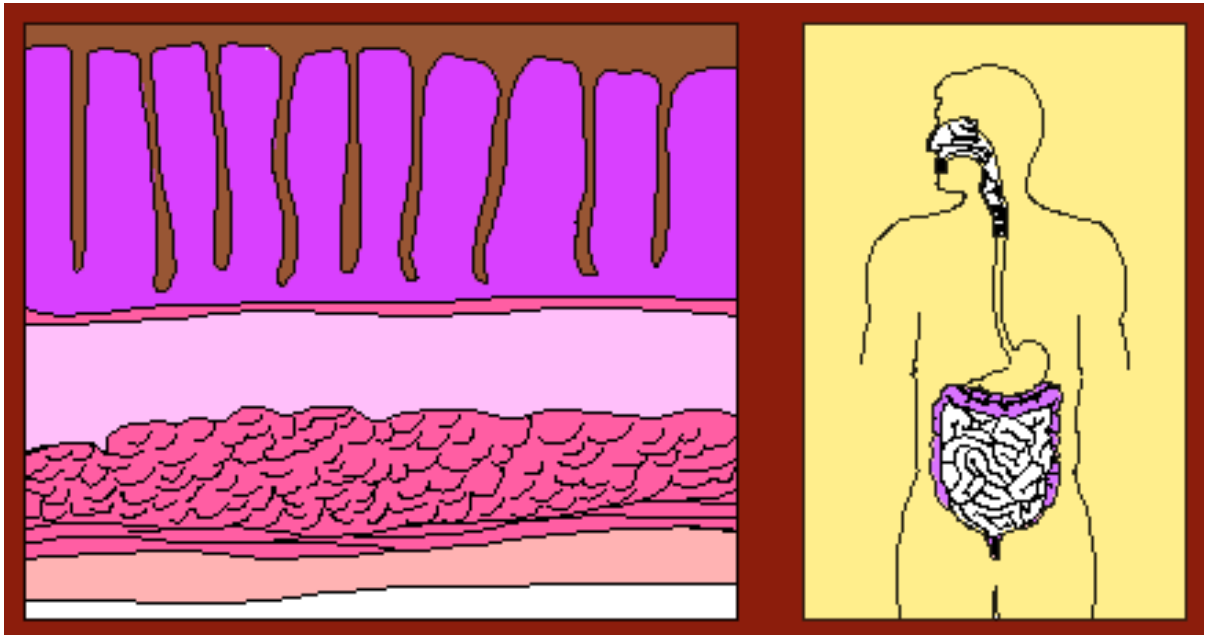
GB and Pancreas Regulation



Nucleases, Nucleotidase and Nucleosidase

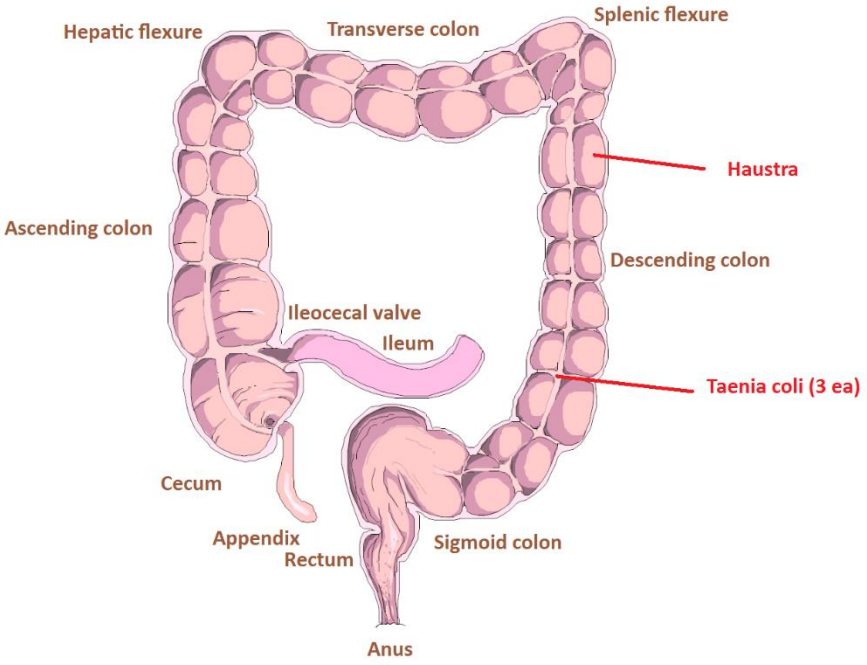


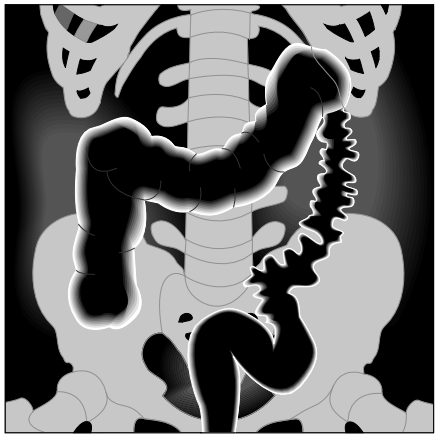




- The small bowel, remember, enters the large bowel at the ileocecal valve -- a one-way valve out into the large bowel. Your meal is usually at the ileocecal valve about 4 hours after it's been eaten (this depends on the composition of your diet: high carbohydrate or high protein diets are there in about 4 hours; high fat diets may take 8-10 hours).

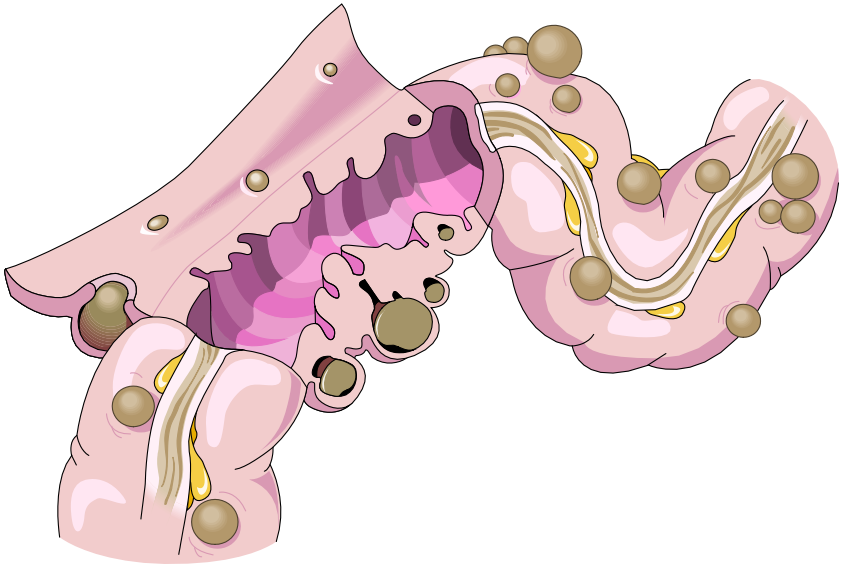
- Below the valve is a pouch.
- This pouch is called the cecum and to it is attached the appendix.
- The large bowel is about 1.5 meters in length and 6.5 cm in diameter.
- It runs from the ileum to the anus. It traverses the bowel from the right side upwards as the ascending colon (Figure coming up).
- It bends (hepatic flexure) across the abdomen (transverse colon) to the left side and bends down (splenic flexure) as the descending colon until it runs into the "S"-shaped colon (sigmoid colon) which terminates in the rectum (last 20 cm of GI tract; last 2-3 cm is the anal canal) and, thence, into the anus.



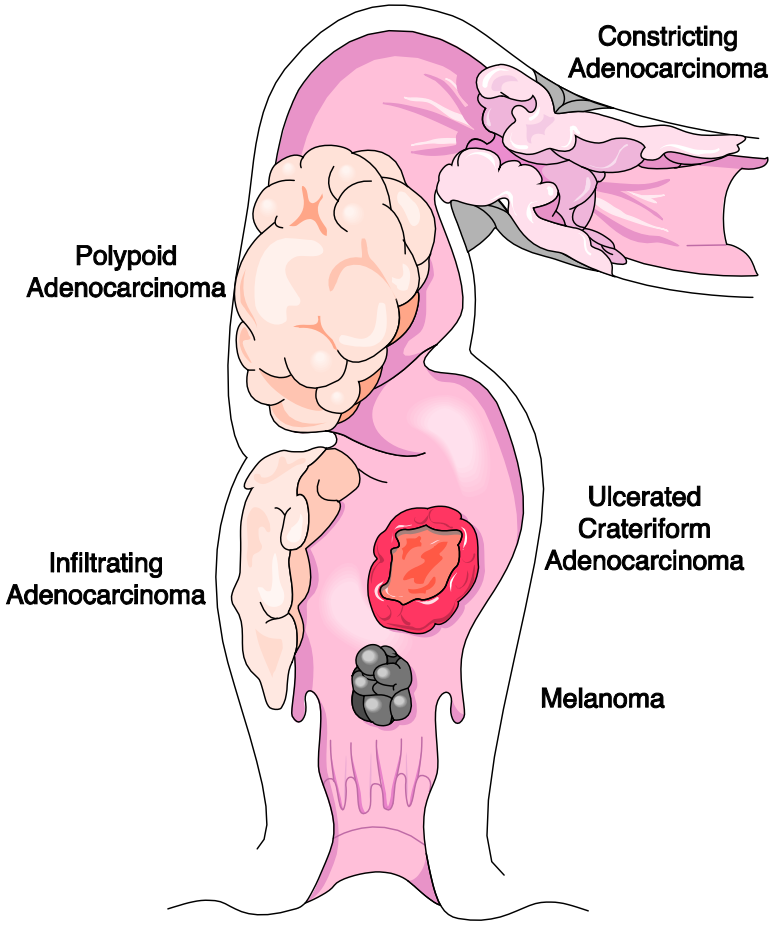


- Haustra
  - Contractions of the bowel caused by the taenia coli; a series of pouches
- Taenia coli
  - 3 longitudinal bands of tissue – like elastic – contributes to contractions of the bowel

- Diverticular disease



Bowel Cancers

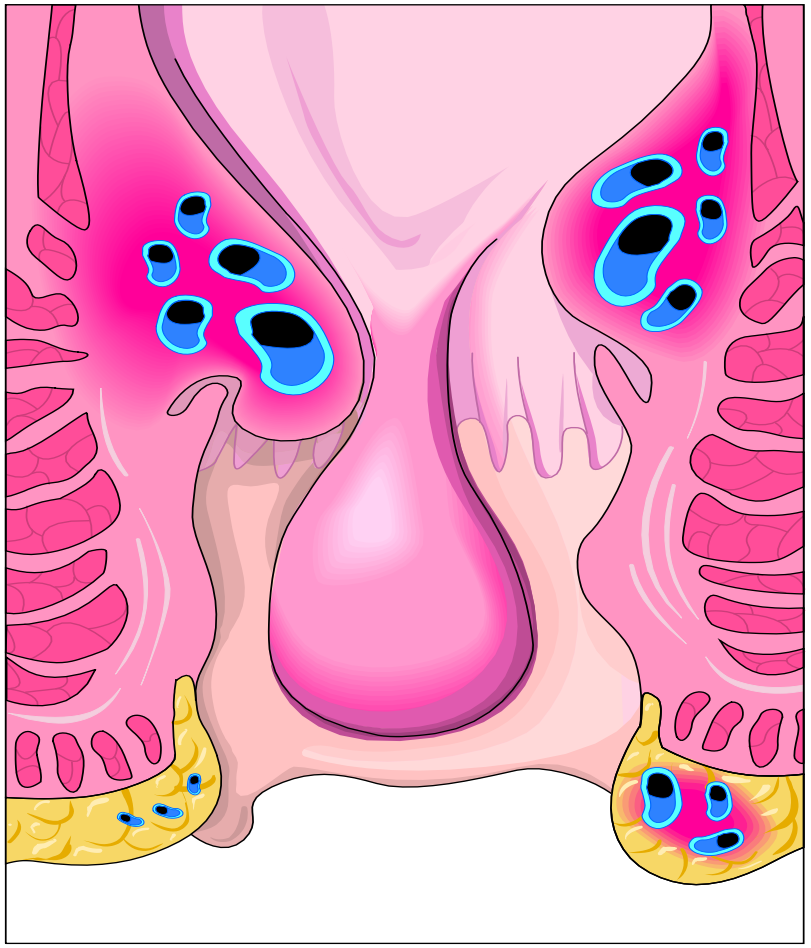


Ibid

- Anus has 2 sphincters:
  - Involuntary – internal
  - Voluntary -- external
- Normally, the anus is closed except during defecation

Rectum and Hemorrhoids

- The rectum is the last 20-cm of the GI tract; the last 2-3 cm is the anal canal.
- The anus has two sphincters (review muscles): the internal and external anal sphincters.
- Normally, the anus is closed except during defecation.
- Mechanically, the only thing the colon does is peristalsis.



Bowel -- Physiology

- Mechanical: peristalsis
- Chemical (enzymes): from bacteria – NOT from colon enzymes
- Primary task of large bowel is water reabsorption – the colon reabsorbs all but 100-150 mL/day
- Large bowel does secrete mucus

Water Reabsorption

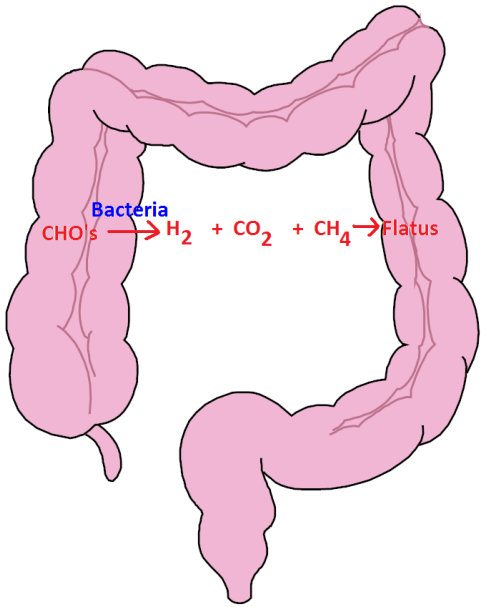
- As a general rule, we take in around a liter and a half per day from the food we eat.
- Water from GI secretions comes from the stomach, the small bowel and the large bowel (the primary function of the large bowel is water reabsorption).
- This water amounts to around 8.5 liters per day.
- Around 9.5 liters of water per day are reabsorbed by the small bowel and the large bowel reabsorbs about 400 mL (0.4 L).
- This totals 9.9 liters of water that is reabsorbed per day.
- ONLY 100 mL is excreted in the feces, i.e., 99% of the water we [re-]absorb is retained by our body.

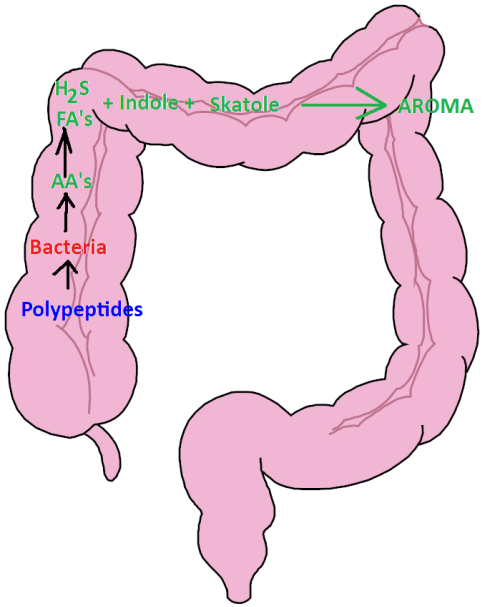
Bowel Physiology

- Minerals:
  - 20-70% of ingested Ca^{2+} is eliminated here
  - 80-85% of ingested iron is eliminated here
  - Na^{+} and Cl^{-} is absorbed here – with the water

- Physiologically, the colon has no enzymes of its own -- any further metabolism that occurs here is due to bacterial enzymes.
- The primary task of the colon is water reabsorption.
- The colon does secrete mucous.

- Bowel material is prepared for elimination by bacterial action:
- They ferment any remaining CHO's;
- They release hydrogen gas, CO_2 gas and methane (natural gas -- no pun intended) which contribute to **flatus**. Bacteria convert the remaining polypeptides to amino acids and them to indole, skatole, hydrogen sulfide (rotten egg odor) and volatile fatty acids. These are simpler and **smellier**. Indole and skatole contribute to the odor of feces.
- The remainder of the compounds are returned to the liver for excretion in different forms via the urine.
- After residing in the bowel for 3-10 hours, the bowel material has become solid or semi-solid due to the reabsorption of water and is called feces. Feces consists of water, inorganic salts, sloughed off epithelial cells from GI tract mucosa, bacteria, bacterial decomposition products and portions of undigested food.





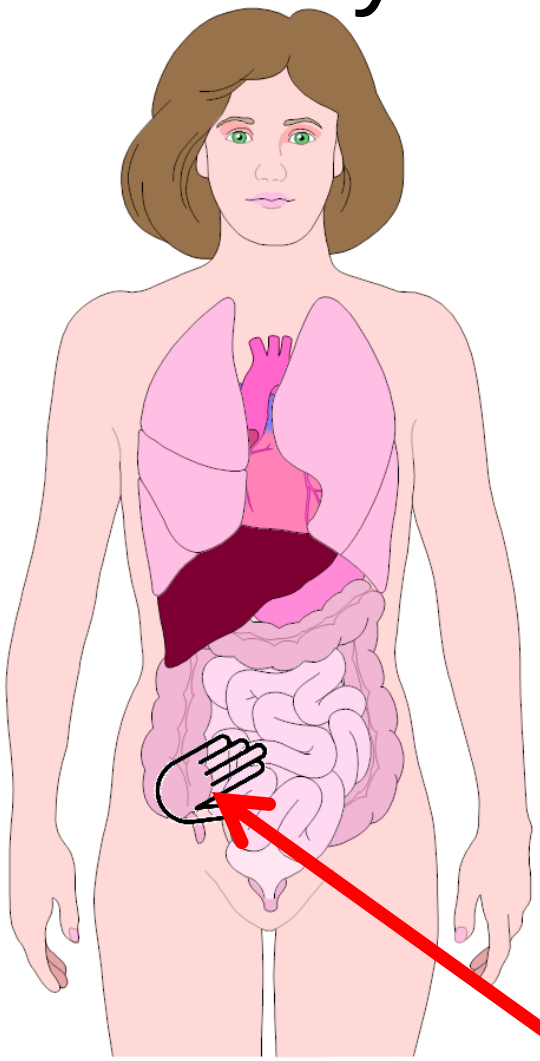
Bowel Physiology

- To avoid passing flatus:
  - Decrease simple CHO's in diet
  - Decrease beans, onions and cabbage in diet
  - Decrease high fiber wheat in diet
- Colon bacteria decompose bilirubin to simpler pigments to give the brown color to feces
- Colon bacteria synthesize vitamin K for our absorption

Irritable Bowel Syndrome (IBS)

- IBS is a well-defined entity that took years to be recognized by the U.S.' medical community. The biggest problem was that the patient didn't look sick.

- “spastic colon”, pain, constipation
- “nervous diarrhea”, painless diarrhea, mucus
- Or 6 of one and a half dozen of the other
- May feel anorexic, N/V, Bloated/distended
- Flatulence



- Associated with stress, subjective depression, recent loss
- Young and middle-aged females more than males (This may simply reflect men's unwillingness to talk about "these sorts of things" with their physician.)
- NO bowel lesions; is due to abnormal motility; rules out origins from microorganisms.
- Non-specific px findings
- Clue: with IBS, pain DECREASES on continuous manual pressure

Irritable Bowel Syndrome

- R/O GB disease, ulcers, infections, diabetes, drug effects
- Patient GENERALLY doesn’t LOOK sick and is why it took so long to get it classified as a disease
- IBS is WELL defined as a syndrome, now.

GI Secretions – Or: Pavlov Revisited

- Lastly, the secretions of the GI system are all regulated, one way or another, by FOOD.
- All we have to do is SEE food, and our GI system goes on alert.
- Physical, oral, contact with food starts us salivating, and turns on nervous regulatory pathways.
- As we look at food, in anticipation of eating it, our pancreas is turned on to begin releasing insulin into our blood; it also begins to secrete secretin and CCK.
- Cholinergic control of the pancreas is turned on.
- In the liver, bile salts are formed under the influence of secretin; they are released as bile by CCK.
- The bowel reacts to food, as well: the nervous system inhibits its activity; it is under physical control (ya ever tried to put more food in your belly than your body will let you?), i.e., if the stomach gets distended, you feel "full".
- In the stomach, gastrin is turned on to cause the release of HCl; it also distends and is under parasympathetic control (like the gall bladder by X).