General Principles of Digestive Physiology

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Digestive Process

- The GI tract is a “disassembly” line
  - Nutrients become more available to the body in each step
- There are six essential activities:
  - Ingestion, propulsion, and mechanical digestion
  - Chemical digestion, absorption, and defecation

Gastrointestinal Tract Activities

- Ingestion – taking food into the digestive tract
- Propulsion –
- Swallowing - Deglutition
- Peristalsis – waves of contraction and relaxation of muscles in the organ walls
- Segmentation – mixing foods with juices by repeatedly moving food back and forth
- Mechanical digestion – chewing, mixing, and churning food
- Chemical digestion – catabolic breakdown of food
- Absorption – movement of nutrients from the GI tract to the blood or lymph
- Defecation – elimination of indigestible solid wastes

Regulation of digestion involves:

- The GI System is “outside” the body and is regulated by:
  - Mechanical and chemical stimulates stretch receptors, osmolarity, and presence of substrate in the lumen
  - Controls of the GI Activity are also
    - Extrinsic control by CNS centers
    - Intrinsic control by local centers

Receptors of the GI Tract

- Mechano- and chemoreceptors respond to:
  - Stretch by the presence of food
  - Osmolarity – solute concentration
  - pH of contents
  - Presence of end products of digestion
- They initiate reflexes that:
  - Activate or inhibit digestive glands to secrete digestive juices
  - Mix lumen contents and move them along

Nervous Control of the GI Tract

- Intrinsic controls
  - Nerve plexuses near the GI tract initiate short reflexes
  - Short reflexes are mediated by local enteric plexuses (gut brain)
- Extrinsic controls
  - Long reflexes arising within or outside the GI tract
  - Involve CNS centers and extrinsic autonomic nerves
  - Involves CNS and ANS

Gut-Brain Axis

- (GBA) consists of bidirectional communication between the central and the enteric nervous system.
- Links emotional and cognitive centers of the brain with intestinal functions.
- Recent advances in research have described the importance of gut microbiota in influencing these interactions.
- Within the gut, there are approximately 10^{14} microorganisms, which is around 10 fold more cells than there are cells in the human body.

What do we process in 24 hours?

Ingestion of Fluid and Food	Secretions into GI Tract	Absorption into GI Tract
2 liters	1.5 L Mouth	
	0.5 L Gallbladder	7.5 L in Small Intestine
	2.0 L Stomach	1.4 L in Large Intestine
	1.5 L Pancreas	
	1.5 L Colon	0.1 L excreted out in feces
	7 liters total	
9 Liters In		9 Liters out

Digestive Processes Occurring in the Mouth, Pharynx, Esophagus

Salivary Glands

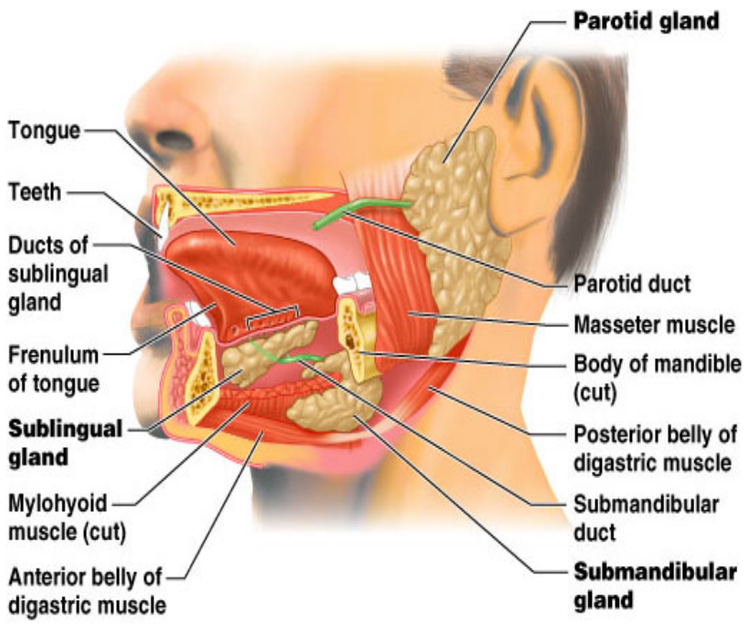
- Produce and secrete saliva at 700-1000cc/day (2.8 - 4 cups)
  - Cleanses the mouth
  - Moistens and dissolves food chemicals
  - Aids in bolus formation
  - Contains enzymes that break down starch
- Three pairs of extrinsic glands – parotid, submandibular, and sublingual
- Intrinsic salivary glands (buccal glands) – scattered throughout the oral mucosa
- Secreted from serous and mucous cells of salivary glands
- A 97-99.5% water, hypo-osmotic, slightly acidic solution containing
  - Electrolytes
  - Digestive enzyme – salivary amylase
  - Proteins – mucin, lysozyme, defensins
  - Metabolic wastes – urea and uric acid

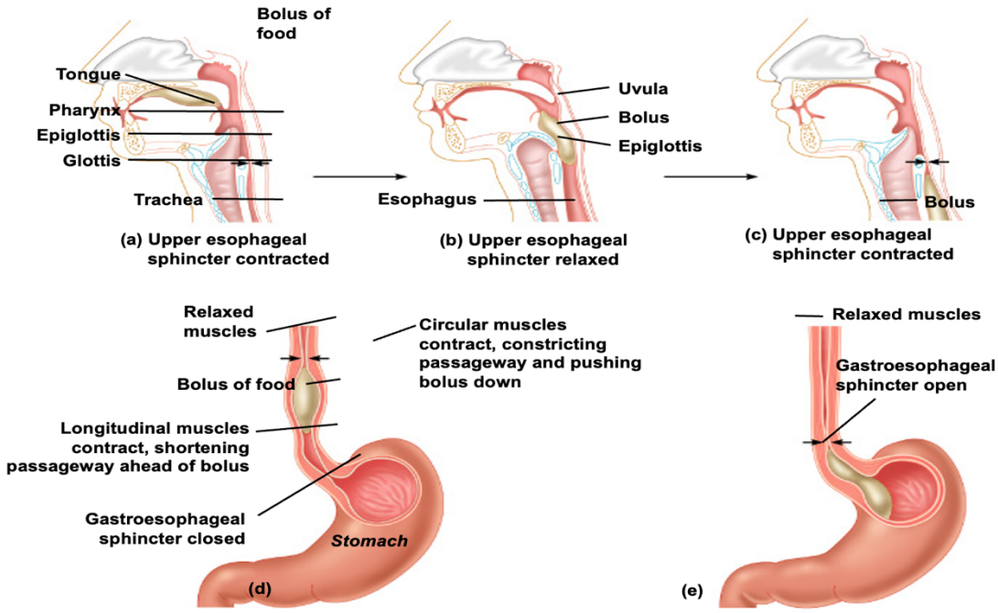
Control of Salivation

- Intrinsic glands keep the mouth moist
- Extrinsic glands secrete serous, enzyme-rich saliva in response to:
  - Ingested food which stimulates chemoreceptors and pressure receptors
  - The thought of food
- Ingestion of foodstuffs →
  activate chemoreceptors and pressoreceptors →
  salivatory nuclei (pons & medulla) →
  PARASYMPATHETIC nerve activation →
  Facial (VII) and Glossopharyngeal (IX) nerves →
  secretion by salivary glands
  SYMPATHETIC nerve activation → decreased salivation

Digestive Process in the Mouth

- Food is ingested
- Mechanical digestion begins (chewing)
- Propulsion is initiated by swallowing
- Salivary amylase begins chemical breakdown of starch
- The pharynx and esophagus serve as conduits to pass food from the mouth to the stomach





Deglutition (Swallowing)

- Involves the coordinated activity of the tongue, soft palate, pharynx, esophagus and 22 separate muscle groups
- Tongue compacts ground food into a "bolus"
- Buccal phase (voluntary)
  - tongue against hard palate
  - tongue contraction
  - bolus forced into oropharynx
- Pharyngeal-esophageal phase (involuntary)
  - tongue blocks off mouth
  - soft palate blocks off nasopharynx
  - controlled by the medulla and lower pons
  - all routes except into the digestive tract are sealed off
  - epiglottis blocks off trachea → peristaltic waves moves food to stomach

Regulation of Gastric Secretion, Motility, and Emptying

Regulation of Gastric Secretion

- Neural and hormonal mechanisms regulate the release of gastric juice
- Stimulatory and inhibitory events occur in three phases
  - Cephalic (reflex) phase: prior to food entry
  - Gastric phase: once food enters the stomach
  - Intestinal phase: as partially digested food enters the duodenum

Cephalic Phase

- Excitatory events include:
  - Sight or thought of food
  - Stimulation of taste or smell receptors
- Inhibitory events include:
  - Loss of appetite or depression
  - Decrease in stimulation of the parasympathetic division
- sight, aroma, taste, thought → hypothalamus
- gustatory centers → vagal nuclei of medulla →
- vagus nerve (parasympathetic) → increased gastric secretion

Gastric Phase

- Excitatory events include:
  - Stomach distension
  - Activation of stretch receptors (neural activation)
  - Activation of chemoreceptors
  - Release of gastrin to the blood
- Inhibitory events include:
  - A pH lower than 2
  - Emotional upset that overrides the parasympathetic division

Neural mechanism		**Hormonal mechanism**	
Distention & low acidity	→	Digested proteins	→
Vagal afferents	→	Increase in pH	→
Vagal efferent to stomach	→	Gastrin released	→
Parasympathetic Ach release	→	Enzymes & HCl released	→
Increased gastric secretion			

Intestinal Phase

- Excitatory phase – low pH; partially digested food enters the duodenum and encourages gastric gland activity
- Inhibitory phase – distension of duodenum, presence of fatty, acidic, or hypertonic chyme, and/or irritants in the duodenum
  - Initiates inhibition of local reflexes and vagal nuclei
  - Closes the pyloric sphincter
  - Releases enterogastrones that inhibit gastric secretion

Excitatory phase		**Inhibitory phase**	
chyme enters the duodenum	→	inhibition of vagal nuclei	→
release of intestinal gastrin	→	inhibition of local reflexes	→
continued gastric secretion	→	activation of sympathetic	→
release of inhibitory neurons			

Response of the Stomach to Filing

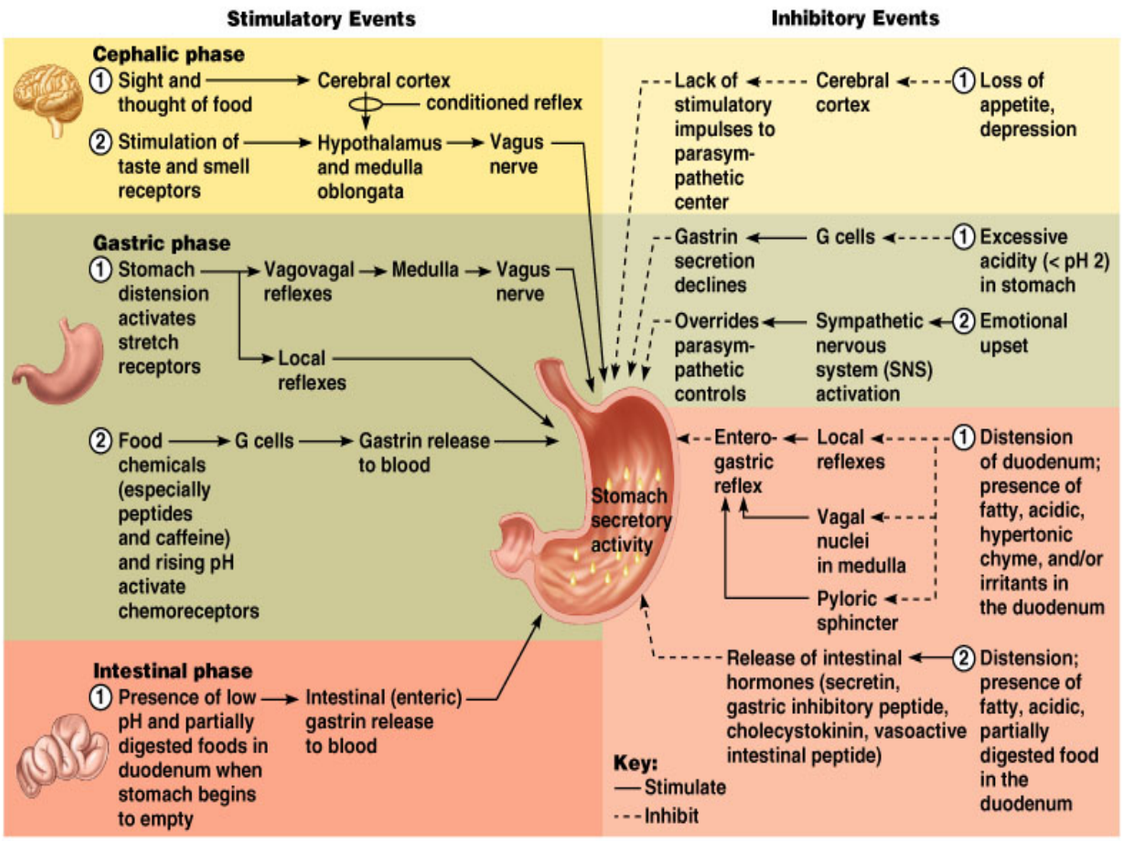
- Stomach pressure remains constant until about 1L of food is ingested
- Relative unchanging pressure results from reflex-mediated relaxation and plasticity
- Reflex-mediated events include:
  - Receptive relaxation – as food travels in the esophagus, stomach muscles relax
  - Adaptive relaxation – the stomach dilates in response to gastric filling

Gastric Contractile Activity

- Peristaltic waves move toward the pylorus at the rate of 3 per minute
- Most vigorous peristalsis and mixing occurs near the pylorus
- Chyme is either:
  - Delivered in small amounts to the duodenum or
  - Forced backward into the stomach for further mixing

Regulation of Gastric Emptying

- Receptive relaxation - trilayer of muscles in wall of the stomach relax to allow filling to occur
- Plasticity - smooth muscle tension specially regulated to prevent regurgitation of food
- Basic electrical rhythm - pacemaker cells of longitudinal muscle allow rhythmic contractions
- Emptying to duodenum - regulated by amount and type of chyme entering into the duodenum; faster with high carbo, slower with higher fats
- Vomiting (emesis) - irritants activate neurons which stimulate the "emetic center" of medulla



Content of Bile and Bile Release into Small Intestine

Content of Bile

- Made in Liver and released by Gall Bladder
- Bile salts, bile pigments, cholesterol, neutral fats, phospholipids, electrolytes
- Bile salts - derivatives of cholesterol (cholic acid, chenodeoxycholic acid)
    - emulsify fats - separate fats into tiny droplets for digestion & absorption
    - enterohepatic circulation - conservation of bile salts by re-processing
        - reabsorbed in distal small intestine
        - to liver via hepatic portal blood
        - resecreted as bile from gall bladder
- bile pigment (bilirubin) - waste product of heme from broken-down erythrocytes
    - urobilinogen - breakdown product of bilirubin, causes darker coloration of feces

Regulation of Bile Release

- Hepatocytes - cells of the liver that produce 0.5-1.0 liters of bile each day
- Parasympathetic - stimulates gall bladder release (contraction and bile release due to relaxed muscle)
- Cholecystokinin (CCK) - hormone released by cells of the mucosa of the duodenum
    - acidic, fatty chyme enters duodenum →
    - duodenal mucosa secretes CCK →
        - gall bladder contracts to release bile
        - pancreas secretes pancreatic juices
        - hepatopancreatic sphincter opens
- Gallstones - crystallized formation of cholesterol and salts, causing obstruction of bile release

Composition of Pancreatic Juice and Regulation of Secretions

Pancreatic Juices
- 1200-1500 ml per day (42to 53 oz)
- 1.2 to 1.5 liters per day
- Water solution of enzymes and electrolytes
    - Neutralizes acid chyme
    - Provides environment for pancreatic enzymes
- Enzymes are released in inactive form and activated in the duodenum
- Active enzymes secreted
    - Amylase, lipases, and nucleases
    - These enzymes require ions or bile for optimal activity
- **Amylase (carbohydrates)**
    - Converts starch and glycogen into simple sugars
- **Lipases (fats)**
    - Enzyme that catalyzes the hydrolysis of fats (lipids)
    - Transport and processing of dietary lipids (e.g. triglycerides, fats, oils).
- **Nucleases (nucleic acids)**
    - Enzyme that splits the chains of nucleotides in nucleic acids into smaller units.

Regulation of Pancreatic Secretions
- Secretin and CCK are released when fatty or acidic chyme enters the duodenum
- CCK and secretin enter the bloodstream
- Upon reaching the pancreas:
    - CCK induces the secretion of enzyme-rich pancreatic juice
- Vagal stimulation also causes release of pancreatic juice
- parasympathetic causes release during cephalic and gastric phases of gastric secretion
- secretin - hormone that causes release of "bicarbonate-rich" pancreatic juices in response to the presence of HCl
- cholecystokinin - hormone that causes release of "enzyme-rich" pancreatic juice in response to the presence of proteins and fats

Digestive Processes of the Small Intestine

Optimal Conditions for Digestion & Absorption
- Pancreatic juice & bile - enzymes, emulsifying fats, and pH are essential for proper intestinal processes
- Small intestine is PRIMARY site for absorption of nutrients into the cardiovascular system

Digestion in the Small Intestine
- As chyme enters the duodenum:
    - Carbohydrates and proteins are partially digested
    - No fat digestion has taken place
    - Chyme is released slowly into the duodenum
    - Mixing is required for proper digestion
    - Virtually all nutrient absorption takes place in the small intestine

Motility in the Small Intestine
- The most common motion of the small intestine is segmentation
    - Initiated by intrinsic pacemaker cells
    - Moves contents steadily toward the ileocecal valve
- After nutrients have been absorbed:
    - Peristalsis begins with each wave starting distal to the previous
    - Meal remnants, bacteria, mucosal cells, and debris are moved into the large intestine

Digestive Processes of the Large Intestine

Bacterial Flora

- The bacterial flora (over 700) of the large intestine consist of:
  - Bacteria surviving the small intestine that enter the cecum and
  - Those entering via the anus
- These bacteria:
  - Colonize the colon
  - Ferment indigestible carbohydrates
  - Release irritating acids and gases (flatus)
  - Synthesize B complex vitamins and vitamin K

Functions of the Large Intestine

- Other than digestion of enteric bacteria, no further digestion takes place
- Vitamins, water, and electrolytes are reclaimed
- Its major function is propulsion of fecal material toward the anus
- Though essential for comfort, the colon is not essential for life

Motility of the Large Intestine

- Haustral contractions
  - Slow segmenting movements that move the contents of the colon last about 1 minute every 30 minutes
  - Haustra sequentially contract as they are stimulated by distension
- Mass movements
  - Long slow moving powerful contractions that move large parts of the colon 3-4 times per day forcing contents to the rectum
- Presence of food in the stomach:
  - Activates the gastrocolic reflex
  - Initiates peristalsis that forces contents toward the rectum

Defecation

- Distension of rectal walls caused by feces
  - Stimulates contraction of the rectal walls
  - Relaxes the internal anal sphincter
- Voluntary signals stimulate relaxation of the external anal sphincter and defecation occurs
- defecation reflex when feces (stool) enters rectum, spinal cord reflex is triggered
  - internal sphincter (involuntary)
  - external sphincter (voluntary
- Valsalva's maneuver - contraction of diaphragm and abdominal muscles
- diarrhea - too much water in the stool
- constipation - insufficient water or fiber

Chemical Digestion

- Carbohydrates
  - Enzymes used: salivary amylase, pancreatic amylase, and brush border enzymes
- Proteins
  - Enzymes used: pepsin in the stomach
  - Enzymes acting in the small intestine
- Fats
  - Absorption via diffusion into intestinal cells
  - Enzymes used: bile salts and pancreatic lipase

Enzymatic Hydrolysis (“water” “breaking”)
- Hydrolysis - a water molecule is added between two "monomers" of a complex organic molecule in order break it down into its component parts

Carbohydrate Digestion
- Monosaccharides - "monomers" such as glucose, fructose, and galactose
- Disaccharides - sucrose (table sugar), lactose (milk sugar), and maltose (grain sugar)
- Polysaccharides - starch (grains), glycogen (muscle)
- Carbohydrate hydrolyzing enzymes
    - salivary amylase - produces "oligosaccharides"
    - pancreatic amylase - in small intestine
    - intestinal enzymes - dextranase & glucoamylase (> 3 sugars), maltase, sucrase, and lactase
- Lactose intolerance - decreased ability to digest lactose in the diet (use "lactase" supplements)

Protein Digestion
- Amino acids - the "monomer" components of protein
- Stomach - pepsinogen >>>>>>>>>> pepsin (low pH)
- Small intestine
    - enzymes that cleave throughout the protein

trypsinogen >>>>>>>>>> trypsin
chymotrypsinogen >>>>>>>>>> chymotrypsin

Lipid (Fat) Digestion
- Lipid structure - glycerol + 3 triglycerides
- Lipases - enzymes that break down lipids
- Bile salts - "emulsify" fats in 1 micron "micelles”

Nucleic Acid Digestion
- Pancreatic nucleases - break down DNA and RNA

Absorption of Nutrients
- Up to 10 L of food, drink, and GI secretions enter the GI tract daily
- Only 1 L or less reaches the large intestine
- Virtually all food, 80% of electrolytes and water absorb in the small intestine
- It is nearly impossible to exceed the absorptive capacity if the GI tract
- At the end of the ileum, all that remains is some water, indigestible food materials, and millions of bacteria
- The debris is passed on into the large intestine
- Transepithelial transport - nutrients must pass across the epithelial lining of the small intestine
- Active transport - most nutrients must be transported across membrane using ATP of the cells

Water Absorption
- Approximately 9 L of water (14 oz/hour), mostly derived from GI tract secretions, enter the small intestine daily
- Water is the most abundant substance in chyme
- 95% of water is absorbed in the small intestines by osmosis
- Normal rate of water absorption is 300-400 ml/hour
- Water moves in both directions across intestinal mucosa
- Small intestine - 95% of water absorbed by small intestine following transport of solutes
- Large intestine - absorbs remaining water before moving the chyme on to the rectum

Carbohydrate Absorption
- Facilitated diffusion - glucose and galactose (coupled with active transport of Na
    - "carrier molecule" has binding sites for both sugar and Na^+; relies on Na^+ gradient

Protein (Amino Acid) Absorption
- Facilitated diffusion - amino acids and small peptides (coupled with Na+ active transport)
    - "carrier molecule" has binding sites for both amino acid and Na+; relies on Na+ gradient
- Food allergies - absorption of proteins in infant gut causes early immune reaction

Lipid Absorption
- Micelles - tiny balls of fats that result from bile salt emulsification and "lecithin"
    - contain cholesterol and fat-soluble vitamins
    - diffuse through lipid bilayer of membrane
    - chylomicrons - micelles combined with associated proteins within the cell; enter the lacteals of the lymphatic system

Nucleic Acid Absorption
- Pentoses, nitrogen bases, phosphates - absorbed by similar processes as sugars and amino acids

Vitamin Absorption
- Fat soluble - Vitamins A, D, E, K are absorbed by epithelial cells along with lipid micelles
    - OLESTRA - will carry fat-soluble vitamins out in feces with it
- Water soluble - Vitamins B & C absorbed by diffusion
    - Vitamin B_{12} - large and electrically charged, must bind with "intrinsic factor" before being taken into the cell by endocytosis

Electrolyte Absorption
- Fe and Ca - primarily absorbed in small intestine
    - ferritin - sequesters Fe in intestinal cells
    - transferrin - transfers Fe into circulation when need is present (menstruation)
    - Vitamin D - facilitates Ca absorption
- Na - exchanged for sugars and amino acids
- Cl - absorbed into cells and exchanged for HCO_3^-
- K - absorbed into cells due to osmotic gradients

Malabsorption of Nutrients
- Results from anything that interferes with delivery of bile or pancreatic juice
- Factors that damage the intestinal mucosa (e.g., bacterial infection)
- Gluten enteropathy (adult celiac disease) – gluten damages the intestinal villi and reduces the length of microvilli (1 in 100 people)
    - Treated by eliminating gluten from the diet (all grains but rice and corn)