**DIGESTIVE SYSTEM**

digerere "to separate, divide, arrange," from dis- "apart" + gerere "to carry."

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**Functions Of The Digestive System**

- **Ingestion:** taking food or drink into the mouth
- **Deglutition:** swallowing
- **Digestion:** breaking down food into molecules that are small enough to enter cells
  - **Mechanical Digestion**
    - Mixing: alternate contraction and relaxation of smooth muscle in walls of GI tract mixes food with secretions
    - Propulsion: propelling toward anus ie motility
  - **Chemical Digestion**
    - Secretion: cells in GI tract walls secrete ~ 7L water, acid, buffers, digestive enzymes into GI lumen daily
- **Absorption:** products of digestion enter epithelial cells lining GI tract & pass into **blood or lymph** to circulate to all cells of body
- **Defecation:** substances not absorbed leave body through the anus as **feces**
  - wastes, indigestible substances, bacteria, cells sloughed from the GI tract

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**Mechanical vs Chemical Digestion**

1. **Mechanical digestion**
   - Teeth cut and grind food
   - Smooth muscle in stomach and small intestine churns food to help it dissolve and mix with enzymes

2. **Chemical digestion**
   - Hydrolysis: Water is used to split apart large carbohydrate, lipid, protein, nucleic acid molecules in food. This would take forever w/o:
   - Digestive enzymes produced by salivary glands, tongue, stomach, pancreas, and small intestines catalyze these catabolic reactions

3. **No digestion needed:** amino acids, cholesterol, glucose, vitamins, minerals, and water can be absorbed **without chemical digestion**

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**MOUTH**

Mastication, Taste, Salivation, Deglutition
Mouth (mechanical) – Mastication

- During mastication (chewing) food is manipulated by tongue, mixed with saliva, and ground by teeth.
- 32 permanent teeth grind & cut food:
  - Incisors: chisel-shaped, cut into food
  - Cuspids (canines): pointed surface called cusp. tear or shred food
  - Molars: crush and grind food
- Food becomes a soft, flexible mass called a BOLUS (lump) that is easily swallowed.

Tongue - Taste

- Taste bud receptors are found in:
  1. *Fungiform papillae* - near tip mushroom-like elevations
  2. *Foliate papillae* – lateral margins of tongue in small trenches
  3. *(Circum) Vallate papillae* - in V-shape area at posterior
- Receptors for touch/feel are in:
  4. Filiform papillae – (majority of papillae) lack taste buds.

- SALIVATION: Taste & Feel of food stimulates salivation.
- DIGESTION: Lingual glands secrete mucus, and a watery serous fluid that contains the enzyme, lingual lipase.

Saliva

- Functions of Saliva
  - *Lubricates* & dissolves food to create a bolus that can be swallowed
  - Bacteriolytic: Kills bacteria with enzymes like lysozyme
  - Cleanses mouth & teeth (Saliva continues to be secreted heavily for some time after food is swallowed

Secretion of Saliva from:

1. Major salivary glands: Parotid, Submandibular, and Sublingual glands
2. Minor salivary glands: Labial, Buccal, Palatal, Lingual
Salivation

Salivation (secretion of saliva) is controlled by the autonomic nervous system.

**AFFERENT IMPULSES:**
1. Food stimulates taste bud receptors on tongue & send sensory info by CN VII / CN IX
2. Impulses from sight, smell, taste are also propagated to salivatory nuclei in brain stem

**EFFERENT IMPULSES:**
- Facial (CN VII) & Glossopharyngeal (CN IX) nerves stimulate saliva secretion from major & minor salivary glands
- Or sympathetic stimulation

Saliva - Chemical Digestion

Saliva is 99.5% water, 0.5% solutes.

1. *Ptyalin* salivary α-amylase. Works optimally at pH 6.8 to digest starch.
   - Starches are polysaccharides of glucose that exist in 3 forms:
     - Amylose (linear): Breaks into maltotriose & maltose
     - Amylopectin (branched): breaks into α-limit dextrin
     - Glycogen from animals
2. Contains lingual lipase that activates at pH4 in stomach to digest fat

Mouth to Stomach: Deglutition / Swallowing

- The food bolus stimulates receptors in the oropharynx which sends signals to deglutition (swallow) center in brain stem
- Swallowing (deglutition) forcibly moves food bolus from mouth, to esophagus, to stomach by peristalsis
  - Buccal stage (Voluntary): bolus is passed into oropharynx
  - Pharyngeal stage (Involuntary): pharynx > esophagus
  - Esophageal stage (Involuntary): esophagus > stomach
Deglutition: Pharyngeal & Esophageal Phases

Peristalsis is triggered by bolus contacting pharynx

- **Uvula + soft palate** rise to close off nasopharynx. Prevents food from entering nasal cavity
- **Epiglottis** folds down, while **Larynx** and **Hyoid** rise, to close off trachea. Prevent food from going down trachea
- Tongue pushes food into pharynx

Deglutition: Esophageal phase

- **Upper esophageal sphincter (UES)** in laryngopharynx regulates entrance of food bolus into esophagus
- Esophagus secretes mucus but not digestive enzymes
- No absorption takes place here
- **Peristalsis**: coordinated contractions & relaxations push bolus to stomach
- **Lower esophageal sphincter (LES)** opens during a swallow

STOMACH

**Stomach Functions (2-4 hrs)**

- Reservoir. Holds food. Slowly releases bits to the Small Intestine
- Mechanical & chemical digestion - makes semisolid food bolus into *liquid chyme*

**Chemical Digestion of:**
1. **Protein**: Secretes **Pepsin**
2. **Triglycerides**: **Gastric lipase** & **Lingual lipase** work here
3. **Starch**: Salivary amylase continues to work until it contacts acid

- Secretes **gastrin** into blood to stimulate HCl secretion. Hydrochloric acid:
  - Kills bacteria
  - Provides an acidic pH for pepsinogen to convert to pepsin
- Secretes **mucus** to protect itself
- Secretes **Intrinsic factor** – makes **B12** absorption possible in Small Intestine
- Absorbs few substances - H₂O, aspirin…
**Stomach - Mechanical Digestion**

- A *gastric pacemaker* in the stomach creates regular depolarizations or ‘slow waves’ (3-5/min)
- When stretched by food, signals from stretch receptors increase force & frequency of contractions producing mixing waves which reduce food bolus to *chyme*
- Rippling, peristaltic movements every 15-25 s macerate food and mix it with secretions from gastric glands

**Stomach - Chemical digestion of Carbohydrates**

- Carbohydrate digestion:
  - Food can remain in fundus without contacting HCl for up to 1hr
  - *Salivary amylase* continues to break down starch into maltose, maltose & dextrins until it comes into contact with acidic HCl

**Stomach - Chemical digestion of Lipids**

- 2 lipases that require an acidic pH(3-6) work in the stomach:
  1. *Lingual lipase* activity peaks when bolus contacts stomach acid, HCl
  2. *Gastric Lipase* secreted by *Chief cells* in fundus
- Lipases cleave dietary triglycerides by hydrolysis, resulting in:
  1. free fatty acids
  2. diglycerides, or monoglycerides

**Storage in the stomach**

- Stomach can hold up to 4L of food - most distensible organ
- A meal can be eaten much faster than the intestines can digest/absorb it
- The *Fundus* serves mainly a distensible storage function.
- Rugae disappear when the stomach is distended
- Food remains in the stomach for 2-4 hours
  - Carb meal stays shortest, then protein, fat stays longest

*Endoscopy videoclip: Peristaltic Wave in the Gastric Antrum*
Stomach - Chemical digestion of Protein

- 2 kinds of cells in Gastric glands participate in protein digestion:
  1. Chief cells secrete Pepsinogen (inactive enzyme so don’t self-digest)
  2. Parietal cells secrete HCl (H⁺ via H/K proton pump & Cl⁻ separately)
- In the presence of HCl (pH 2) or active pepsin, Pepsinogen is activated into pepsin enzyme
- PEPSIN digests protein into amino acids, NOT HCl

Parietal cells secrete H⁺Cl⁻

- Parietal cells take up CO₂ from the blood
- by action of carbonic anhydrase, convert it into Bicarb & H⁺ ions
- The H⁺ ions are then secreted from ducts of the gastric glands
- Bicarb leaves the cell into the blood in exchange for a CI⁻ ion. This is called the (bicarb) alkaline tide

Stomach: ENDOCRINE Regulation of HCl

Increases HCl: 
Gastrin & Histamine

- in the antrum, G cells secrete gastrin into blood, which stimulates:
  1. Parietal cell to secrete HCl
  2. EnteroChromaffin-Like (ECL) Cells = Mast Cells to secrete histamine. Histamine causes Parietal cells to secrete even more HCl

Decreases HCl: 
Somatostatin

- when acid is too high D cells in antrum secrete somatostatin into blood
- which inhibits G cell gastrin release into blood

Control of Acid Summary
Stomach’s Protection from Acid & Enzymes

- mucus neck cells & surface mucus cells secrete Mucus & Bicarbonate, HCO₃⁻
- **Pepsin** cannot penetrate mucus
- H⁺ can penetrate mucus but it is neutralized by bicarb

Acid degrades meat, releasing vitamin B-12 (cobalamin)
2. **Parietal Cells** secrete intrinsic factor
3. B-12 binds to intrinsic factor in duodenum
4. **Intrinsic Factor shuttles B-12 into the cells of the ileum**
   - (B-12 binds to transcobalamin once in the plasma)

Gastric Emptying

- each mixing wave forces ~3mL (5mL=1tsp) of chyme through the pyloric sphincter every 15-25 sec
- It can take 2-4 hours to empty stomach (more with gastroparesis)
- Different foods empty at different rates. Smaller particle size or liquids empty quicker than larger solids. & fat inhibits gastric emptying most potently

Controlling gastric emptying, Luminal Pancreatic Enzymes

**SMALL INTESTINE LUMEN, PANCREAS & GALLBLADDER**
Small Intestine Functions (3-6 hrs)

- **Enterogastric reflexes & SI hormones** control emptying and acidity of stomach
- **Alkaline environment** due to secretin, Brunner’ s glands, & pancreatic bicarb
- Most major events of digestion and absorption occur in the small intestine
  - Pancreatic enzymes, bile, & brush border enzymes complete digestion of carbohydrates, proteins, and lipids
  - Begins and completes digestion of nucleic acids
  - Absorption of 90% of nutrients and water through plicae, villi, microvilli, lacteals
- **Segmentations** mix chyme with digestive juices, bring food into contact with the mucosa for absorption.
- **Peristalsis** propels food through the SI.
- Protects us from external bacteria
  - Paneth cells, lysozyme, MALT, Peyer’ s patches
  - Secretes mucus - goblet cells

Secreted by the Small Intestine

- Endocrine cells of the small intestine secrete:
  1. **Cholecystokinin (CCK cells)** - stimulated by fatty meal. Enters blood and stimulates pancreas to secrete digestive proenzymes & gallbladder to contract & secrete Bile
  2. **Secretin (S cells)** - stimulated by acidic chyme. Enters blood & stimulates pancreas to secrete sodium bicarbonate
  3. **Glucose-dependent Insulinotropic Peptide (K cells)** - Stimulates B cells of pancreas to secrete insulin. Glucose ingestion induces release of GIP by SI.

Protecting Small Intestine from Acid

- Small intestine protects its own mucosa from stomach acid entering by the following mechanisms:
  - Goblet cells secrete MUCUS
  - Brunner’ s glands (B)- large glands secrete alkaline MUCUS
  - Secretin - recruits pancreas to release alkaline SODIUM BICARB

Small intestine controls Gastric function

- When the SI is first distended by chyme, the SI aids gastric digestion by secreting intestinal Gastrin, which stimulates HCl production
- If chyme is too acidic or fatty, the SI must slow gastric emptying & decrease HCl production by secreting 1. Cholecystokinin (CCK cells), 2. Secretin (S cells), 3. GIP (K cells)
SI Secretin stimulates Pancreatic Bicarb

- When acidic chyme enters the Small Intestine, the SI releases Secretin into the blood.
- Secretin travels via blood to pancreas & stimulates the Duct Cells to secrete alkaline Sodium Bicarbonate (\(\text{NaHCO}_3\)) & \(\text{H}_2\text{O}\) with a pH 7.8–9.0
- Alkalinity buffers the acidic chyme, and deactivates the stomach’s pepsin
- Creates the proper pH for digestive enzymes of the small intestine to work

CCK from the Small Intestine Stimulates the Pancreas to secrete Digestive Enzymes

- CCK from the small intestine stimulates pancreatic Acinar cells (99% of pancreas) to secrete many digestive enzymes & proenzymes activated in the small intestine lumen:
  - STARCH DIGESTION
    - Pancreatic amylase
  - PROTEIN DIGESTION
    - Trypsinogen
    - Chymotrypsinogen
    - Proelastase
    - Procarboxypeptidase
  - LIPID DIGESTION
    - Pancreatic lipase
  - NUCLEIC ACID DIGESTION
    - Ribonuclease
    - Deoxyribonuclease

Pancreatic Islets of Langerhans \(\alpha\) & \(\beta\) cells

1% of pancreatic cells are islets of langerhans that secrete hormones into the blood (endocrine function of the pancreas):
- \(\beta\) cells secrete insulin in response to high glucose levels in blood - allows cells to absorb glucose via glut transporter proteins
- \(\alpha\) cells secrete glucagon in response to low glucose levels - breaks down glycogen stores in liver

SI lumen - Chemical Digestion of Carbs

- Pancreatic \(\alpha\)-Amylase breaks down carbs - both starch & now glycogen in alkaline environment
- Like salivary amylase, pancreatic \(\alpha\)-Amylase breaks polysaccharides into
  1. oligosaccharides: malthose, limit dextrins
  2. disaccharides: maltose
Enzymes from the pancreas, *Ribonuclease* & *Deoxyribonuclease*, degrade DNA & RNA into nucleotides

1. Pancreas secretes several proenzymes into duodenum in response to CCK
2. Enteropeptidase of duodenum starts the chain reaction, by converting
3. Trypsinogen into Trypsin, which activates other proteolytic proenzymes:
   - Chymotrypsinogen ⇒ Chymotrypsin
   - Procarboxypeptidase ⇒ Carboxypeptidase
   - Proelastase ⇒ Elastase
   - Each protease cleaves a protein at a different point resulting in peptides

* CCK stimulates gallbladder contraction thus Bile / bile salt secretion into SI through duodenal papilla
* Bile salts *emulsify* dietary fats (mainly triglycerides), because they have both hydrophobic & hydrophilic portions (amphipathic). Hydrophobic faces fat side. Hydrophilic faces water side.
* Before they can be digested by lipases, lipids must be *emulsified* into small lipid droplets to increase digestible surface area

- Bile is made in the liver cells, hepatocytes
- Bile contains mostly Bile Salts (see pie chart)
  - Bile salts are made from cholesterol
- Bile drains from hepatocytes into bile canaliculi & out ducts
Chemical Digestion in SI lumen - Lipids into Micelles

- Emulsified fat can be broken down by **Pancreatic Lipase** into
  - free fatty acids &
  - monoglycerides

- The Free fatty acids, monoglycerides, & bile salts aggregate into droplets called **MICELLES** in SI lumen

*BRUSH BORDER DIGESTION & ABSORPTION*

Brush Border of the small intestine

- Plica circularis folds are covered in projections called villi
- Absorptive cells on the villi have microvilli at their apical end
- Absorptive cells make enzymes & store them in their microvilli, also known as the "brush border"
- Brush border enzymes are the **last step** in the digestion of carbs, lipids & proteins. After this, the products can be absorbed

Conversion to monosaccharides, amino acids, and chylomicrons

**BRUSH BORDER DIGESTION & ABSORPTION**

- Disaccharides are broken into **monosaccharides**
- brush border enzymes: lactase, maltase, sucrase
  - Lactose (lactase) → galactose + glucose
  - Maltose (maltase) → glucose + glucose
  - Sucrose (sucrase) → glucose + fructose
- Monosaccharides can now be absorbed by absorptive cells
- Monosaccharides exit absorptive cells from basolateral surface via facilitated diffusion & enter villi capillaries
Brush border digestion & absorption of Protein

- Brush border enzymes: endopeptidase, aminopeptidase, dipeptidase, tripeptidase complete breakdown of proteins into amino acids
- Amino acids, dipeptides and tripeptides can be absorbed via 2nd active transport by absorptive cells
- Amino acids exit basolateral surface mainly by active transport to enter villus capillary

Chylomicron

- The Protein coat around chylomicrons prevents them from sticking to each other
- Lipoprotein lipase secreted by capillaries breaks chylomicrons down into FA & glycerol again
  
  FA & glycerol can diffuse into hepatocytes or adipose cells

Once inside cells, FA & glycerol again reassemble into triglycerides

Digestion summary
Absorption in the Small Intestine

- Nutrients exit the basolateral surface of absorptive cells into villus capillaries or lacteals
  - Blood filled with nutrients (proteins & sugars) flows to liver via hepatic portal vein
  - Chylomicrons dump into lacteals, travel through the lymphatic system until it dumps into the left subclavian vein & then the heart

The GI tract is a lymphoid organ

- Gut Associated Lymphoid Tissue (GALT):
  - Peyer’s patches - similar to lymph nodes in wall of intestine. B cells (plasma) predominate. Secrete IgA
  - Lamina propria lymphocytes
  - Intraepithelial lymphocytes

Water absorption in the SI

- Nutrients moving from intestinal cells into capillaries create an osmotic gradient for water
- Water absorption from the GI occurs via osmosis into capillaries
- About 9.3L of water enters the Small Intestine daily from ingested + secreted juices
- All except ~1L is reabsorbed in SI

SI nutrient absorption

- Nutrients exit the basolateral surface of absorptive cells into villus capillaries or lacteals
  - Blood filled with nutrients (proteins & sugars) flows to liver via hepatic portal vein
  - Chylomicrons dump into lacteals, travel through the lymphatic system until it dumps into the left subclavian vein & then the heart
Venous blood from the small intestine, filled with amino acids & monosaccharides, gathers into the superior mesenteric vein and enters the liver through the hepatic portal vein.

Blood vessels to & from the small intestine run through fatty tracts in the mesentery.

**Mesentery & Hepatic portal vein**

- The hepatic portal vein branches into liver sinusoids.
- Blood flows from liver sinusoids towards central vein of lobule.
- Phagocytic Kupffer cells in the sinusoids destroy any bacteria, old WBCs, RBCs...

**Hepatic blood flow**

- Nutrient use in the liver in fed state

  **In the fed state (after a meal):**

- **Carbs:**
  - Glucose is converted to glycogen for storage
- **Lipids:**
  - Some triglycerides are stored
  - Lipoprotein transporters are made
  - Cholesterol is synthesized
  - Cholesterol is used to make bile salts
  - Fatty acids are broken down to make ATP
  - Bile salts are recycled
- **Protein**
  - Deamination of amino acids
  - Deaminated amino acids can be used to make ATP, carbs or fats
  - Toxic ammonia NH3 results
  - Conversion of ammonia to less toxic urea
  - Synthesis of plasma proteins (globulin, albumin etc)
- **Vitamins**
  - A, D, E, K, B12 are stored

  **Small intestine Mechanical Digestion**

- **Segmentation** - alternating contraction of circular muscle fibers spirals chyme with digestive juice & brings food in contact with mucosa for absorption
- **Migrating Motility Complex (MMC)** - contraction of circular & longitudinal muscle fibers moves chyme from stomach to ileocecal sphincter after most of a meal has been absorbed
Enteric Nervous System: a 2nd brain

- These neurons can all function independently of the ANS
- The Myenteric plexus lies in the muscularis, between longitudinal and circular muscle layers - controls GI tract motility
- The Submucosal plexus lies in the submucosa - controls secretory cells of epithelium
- Interneurons connect myenteric & submucosal plexi
- Sensory neurons are chemoreceptors or stretch receptors

Large Intestine Functions (3-10 hrs)

- Haustral churning
- Peristalsis/ mass peristalsis
- Water absorption
- Mucus secretion
- Bacterial activity
- Defecation reflex

Chyme passes ileocecal valve

- Chyme passes from the small intestine, ileum, into the large intestine, cecum, through the ileocecal valve
- after a meal, secretin relaxes the sphincter
- & a gastro-ileal reflex (stomach stretch increases ileal activity) increases ileal peristalsis to push chyme through valve
Mechanical digestion in LI

• **Haustral churning** - when 1 haustra fills & distends, it will contract & pass its content to the next one

• Peristalsis still occurs here but slowly

• **Mass peristalsis** is triggered by food entering & stretching stomach (gastro-colic reflex). It starts in the middle of the transverse colon, & quickly moves the contents into the rectum

Mucus secretion & Water absorption in LI

• LI Crypts of Lieberkuhn only have absorptive cells & goblet cells (no other secretory cells):
  - Absorptive cells absorb all but 100-200mL of water from LI via osmosis (nearly 1L)
  - Goblet cells secrete mucus to lubricate passage of feces

Chemical digestion in LI by Bacteria

• Bacteria do the following:
  - Ferment undigested carbs, releasing methane, H+, CO2 gasses (flatus)
  - Break down undigested proteins to Amino acids
  - Break down amino acids to indole & skatole (poop smell), hydrogen sulfide
    - Some indole & skatole are converted to less toxic substances, then excreted in urine
  - Synthesize vitamins: Biotin, K.

Defecation reflex

1. Mass peristalsis pushes fecal material into rectum
2. Distended stretch receptors in rectum triggers defecation reflex
3. Sensory impulses go to sacrum
4. Parasympathetic motor nerves from sacrum contracts longitudinal muscles & opens involuntary internal smooth muscle sphincter
5. External sphincter can be voluntarily controlled to delay defecation
Feces

- Feces consist of:
  - Water
  - Inorganic salts
  - Sloughed off epithelial cells from GI
  - Bacteria (60%)
  - Products of bacterial decomposition
  - Unabsorbed but digested materials
  - Indigestible parts of food eg FIBER: indigestible plant carbohydrates like cellulose, lignin, pectin...

- Diarrhea: increased frequency, volume and fluid content due to increased motility and decreased absorption of intestines

- Constipation: infrequent or difficult defecation with decreased water content due to decreased intestinal motility