Functions of Digestive System:
1. Ingestion: take in food
2. Propulsion: move food through GI tract by swallowing and peristalsis
3. Mechanical processing:
   - chewing, churning, mixing, compacting
4. Chemical digestion: enzymatic breakdown of large molecules into building blocks
5. Secretion: enzymes, acids, mucus, water, cell wastes
6. Absorption: move organic molecules, electrolytes, vitamins, water from gut to blood
7. Excretion: cell waste, secretions, indigestible foodstuffs ejected from body
Defecation of feces

Control of digestive function:
- Digestive activity (gland secretion or lumen movement) controlled by chemical or mechanical stimuli:
  - stretching
  - osmolarity
  - pH
  - substrate concentration
  - end product concentration
Modes of control can be extrinsic or intrinsic
1. Neural control
   Enteric Nervous System (ENS): nerve plexus of the gut
   A. Short reflexes: ENS only “gut brain”
   B. Long reflexes: involve input from ANS (in CNS)
2. Hormonal control
   18 hormones produced by enteroendocrine cells in GI: target may be same organ or distant organ
   (specific hormones for specific foods)
3. Local mechanisms
   Prostaglandins and histamine can trigger localized secretion based on contents of GI tract

Location:
- most in peritoneal cavity in abdomen
- cavity: lined with parietal peritoneum
- organs: covered with visceral peritoneum
- both layers secrete peritoneal fluid to reduce friction during movement
Ascites = excess peritoneal fluid → swelling of abdomen, distortion of organs: can cause heart burn, indigestion, back pain
Peritonitis = inflammation of peritoneum from damage or infection: can cause pain and organ failure
Sheets of peritoneum called mesenteries support bulk of digestive system
- Peritoneal organs = supported by mesenteries (sheets of peritoneum)
- Retroperitoneal organs = anchored to body wall
Mesenteries also hold blood vessels, lymphatic vessels, nerves, & adipose → (protection, insulation, energy reserve)

Special mesentery folds:
- lesser omentum: holds stomach
- falciform ligament: holds liver
- greater omentum: holds intestine

Blood Supply
- digestive organs receive 1/4 cardiac output
- this can increase following a meal
- all venous return from GI enters hepatic portal circulation: delivered to liver
- liver processes or absorbs nutrients from gut before blood returns to circulation

Histology of the Digestive Tract
- four major layers along entire length of GI (on handout)
Movements in the Gut
-coordinated by short local reflex arcs of ENS
Peristalsis = waves of contraction, move food bolus along length of gut
Segmentation = single point contractions, chop up bolus, allow enzymes to access inner regions

ENS also innervated by ANS allowing extrinsic control of digestive activity:
Parasympathetic = ↑ muscle activity + secretion
Sympathetic = ↓ muscle activity + secretion

Most ANS to gut is parasympathetic

Accessory organs of mouth:
A. Tongue
- muscular
- surface covered by papillae: provide friction, house taste buds

Functions:
1. Speech
2. Manipulate food into teeth for mastication
3. Compress food into bolus for swallowing
4. Analyze food for texture, taste, temp
5. Produce secretions:
   A. Mucin - lubrication
   B. Lingual lipase - start lipid digestion

B. Salivary Glands
-produce 1-2 L saliva/day
Saliva = 99% water plus:
   enzymes (amylase for starch digestion),
   electrolyte buffers
   mucin (lubrication)
   antibodies
   antimicrobials (lysozyme and defensins)

Functions of saliva:
1. Cleanse mouth, control oral bacteria
2. Dissolve food chemicals for taste
3. Moisten food for bolus formation
4. Begin chemical digestion of carbohydrates
5. Buffer oral pH

Anatomy of GI by Region:
1. Oral Cavity / Mouth / Buccal Cavity
-connects environment to pharynx
-lined with stratified squamous epithelium
-walls = muscular cheeks
-floor contains tongue
-roof = hard palate (anterior), soft palate (posterior - close off nasopharynx during swallowing)

Functions:
1. Analyze food (taste buds)
2. Mechanically process food (chew)
3. Lubricate food (saliva)
4. Digest starches (amylase)
Three pairs of salivary glands:

1. Parotid salivary glands: inferior to zygomatic arch, thick secretion, high salivary amylase (25% of saliva)
2. Sublingual salivary glands: inferior to tongue, watery secretion, high in buffers (5% of saliva)
3. Submandibular salivary glands: posterior floor of mouth, buffers, mucin, amylase (70% of saliva)

Low levels saliva produced continuously
Parasympathetic stim. = ↑ secretion (food cue)
Sympathetic stim. = ↓ secretion “dry mouth”

C. Teeth
Function: mastication, mechanical digestion
Structure:
- Pulp cavity:
  - soft center, blood vessels & nerves in CT called pulp
- Dentin: bone like, surrounds pulp cavity, contains odontoblasts which secrete and maintain dentin throughout life
- External surface:
  - Crown: exposed region, covered in enamel composed of hydroxyapatite (calcium salt crystals)(like bone but no collagen)
  - Cells that produce enamel degenerate after eruption: no repair of enamel
  - Root: embedded region, covered in cementum, attached to periodontal ligaments: hold tooth in alveolus of jaw

4 types of teeth:
1. Incisors: chisel shaped, single root, 8 total, used for cutting
2. Cuspids / Canines / Eyeteeth:
   - conical shaped, single root, 4 total, used for tearing and piercing
3. Bicuspids / Premolars: 2 ridges/cusps, one or two roots, 8 total, used for crushing, mashing, grinding
4. Molars: 4-5 cusps, three or more roots, 12 total, used for crushing, grinding
   - 3rd molars = wisdom teeth

Under age 12 → 20 deciduous / milk teeth
Replaced by age 21 → 32 permanent teeth

Impacted tooth = fails to erupt, remains in jaw causing pain, surgical fix
Dental caries = demineralization of enamel and dentin by bacteria, exposes nerve, pain
Peridontal disease = infection of gingiva, immune response erodes bone around teeth, teeth fall out

2. Pharynx
   - oropharynx (back of mouth)
   - laryngopharynx (superior to voice box)
   - connects oral cavity to esophagus
   - shared space with respiratory system
   - stratified squamous epithelium
   - lamina propria has tonsils and mucus glands
   - skeletal muscles surround for swallowing
3. Esophagus
- muscular tube, connects pharynx to stomach
- 25 cm long
- passes through diaphragm to abdomen
- at rest superior and inferior regions
  constricted to keep air out and stomach
  contents in
- inferior constriction point =
  gastroesophageal sphincter
“Heartburn” = gastroesophageal reflux disease (GERD): gastric juice regurgitates into esophagus causing erosion

Features of esophagus:
1. Stratified squamous epithelium
2. Large folds in mucosa and submucosa to keep lumen closed during rest
3. Esophageal glands in submucosa secrete mucus to reduce friction
4. Upper 2/3 of muscularis externa contains skeletal muscle
5. Adventitia anchors esophagus

Pharynx and esophagus function in food propulsion from mouth to stomach
Deglutition (swallowing):
1. Buccal phase - voluntary
   - soft palate raised to protect nasopharynx
   - bolus pushed against hard palate
   - bolus pushed into oropharynx

2. Pharyngeal phase - involuntary reflex
   - epiglottis blocks entry to trachea
   - contractions move bolus past glottis

3. Esophageal phase - involuntary reflex
   - peristaltic waves push bolus toward stomach
   - gastroesophageal sphincter opens
   - bolus enters stomach
4. Stomach

*Functions:*

1. Store ingested food (~1 L)
2. Mechanical breakdown of food (churning)
3. Chemical breakdown of food (denature and digest proteins)
4. Produce intrinsic factor for Vitamin B12 uptake (VitB12 necessary for erythropoiesis)

Stomach holds acidic mixture of enzymes and food called chyme: typically 1L but up to 4L
4 regions: cardia, fundus, body, pylorus

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Four Major Regions:

1. Cardia
   
   -where esophagus connects via gastroesophageal sphincter
   
   -gastric glands produce mucus to protect esophagus

2. Fundus
   
   -superior region, contact diaphragm

3. Body
   
   -majority of stomach
   
   -holds chyme
   
   -gastric glands secrete enzymes and acids for digestion

4. Pylorus
   
   -inferior region
   
   -connects to duodenum via pyloric sphincter: regulates chyme entry into duodenum
   
   -gastric glands secrete hormones to stimulate gastric activity

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**Stomach Features:**

-muscularis externa has 3 layers (+ oblique) to assist mixing chyme

-when empty mucosa and submucosa folded into *rugae* (can expand to for large volume)

-mucosa has simple columnar epithelium with goblet cells that secrete alkaline mucus

-mucosa perforated by deep *gastric pits* which connect to *gastric glands* in lamina propria

-stem cells in gastric pits replace stomach epithelium every 3-6 days
Gastric Glands:
- produce 1-3 L gastric juice / day: secretions vary per region:
  1. Cardia gastric glands = mucus
  2. Fundus and Body gastric glands = digestive enzymes and acid
     2 types of cells:
     A. Parietal cell secretions:
        1. Intrinsic factor (VitB12 uptake)
        2. H+ and Cl- ions - combine to make HCl in stomach
     B. Chief cell secretions:
        1. Pepsinogen -converted to pepsin by acid in stomach; hydrolyzes proteins
        2. Rennin -infants only; curdles milk protein to aid digestion

Acid production important to gastric function:
1. Kill microbes
2. Denature proteins (digestion, destroy enzymes in food)
3. Break down plant cell walls and animal CT
4. Activate pepsin

3. Pyloric gastric glands = mucus and hormones
   2 important hormone producing cells:
   A. G cells: produce gastrin
      - stimulates secretion by parietal and chief cells
      - promotes contraction of gastric wall
      - secreted in response to food or parasympathetic stimulation
   B. D cells: produce somatostatin
      - inhibits release of gastrin (thus inhibits gastric activity)
      - secreted in response to sympathetic stimulation

Regulation of gastric activity
- secretion and motility controlled by 3 factors:
  1. Innervation from CNS (ANS)
  2. Reflexes of the ENS
  3. Hormones
- mechanisms rely on stimuli from three regions: head, stomach and small intestine
- 3 Phases of regulation: all may act simultaneously to alter gastric activity (go to handout)
-much digestion occurs in stomach but not much absorption (except alcohol and drugs)

-food does not usually remain in stomach for more than 4 hrs but total time depends on chemical makeup of food (how long it will take to digest in small intestine:
  -carbohydrate rich: pass quickly
  -fatty foods can cause chyme to remain in stomach 6+ hrs

5. Small Intestine
-major digestive organ
-chemical digestion completed
-90% of nutrients absorbed (remaining absorbed in large intestine)
-20 ft long, 3 major subdivisions based on histology (no clear anatomical divisions)

A. Duodenum:
-first 10 inches
-retroperitoneal
-receives chyme from stomach through pyloric sphincter
-receives digestive secretions from pancreas and liver through duodenal ampulla controlled by hepatopancreatic sphincter

-mixing pot

B. Jejunum:
-next 8 ft -peritoneal
-majority of chemical digestion and nutrient absorption occur here

C. Ileum:
-last 12 ft -peritoneal
-mucosa rich in lymphoid tissue
-connects to cecum at ileocecal valve

Histology:
-same 4 layers, but adapted for absorption:
  1. Plicae: mucosa and submucosa folded into circular plicae that cause chyme to spiral slowly
  2. Villi: plicae covered with finger-like projections of mucosa called intestinal villi, base of each has crypt / intestinal gland
  3. Microvilli: simple columnar epithelial cells have microvilli on apical surfaces: membrane collectively called brush border of intestine

Plicae + villi + microvilli = 2200ft² surface area (compare to 3.6ft² for flat wall)
-lamina propria of each villus contains capillaries that carry small nutrient molecules to liver via hepatic portal vein
-larger molecules that cannot enter capillaries (lipid-protein complexes) are collected by special lymphatic capillary called a lacteal

Contractions of muscularis mucosae:
-move villi to expose surface to new chyme
-squeeze lacteals to move lymph
Glands of small intestine:
1. Goblet cells - between columnar epithelial cells, secrete mucus (mucin)
2. Intestinal glands: variety of cells in the crypts, located in the lamina propria at the base of each villus, produce many products:
   A. Intestinal juice: 1-2L/day, watery mucus, aids solubilization and absorption of nutrients
   B. Lysozyme: from Paneth cells, lyse bacteria
   C. Hormones: enteroendocrine cells
      - intestinal gastrin
      - cholecystokinin
      - secretin
      - gastric inhibitory peptide
      - vasoactive intestinal peptide
      - somatostatin
      - enterocrinin
      (all control GI activity)

D. Epithelial cells: stem cells in glands
   - New cells created, migrate up villus, shed at tip, complete turnover 3-6 days.
   - Shed cells carry digestive enzymes in plasma membrane that function in lumen:
     **brush border enzymes**: complete digestion of carbohydrates and proteins

Specializations in small intestine:
- duodenum has duodenal glands in submucosa: produce mucus to protect against acidic chyme from stomach
- number and size of crypts decreases along length of small intestine
- number of goblet cells increases along length
- jejunum has most plicae and villi
- ileum has aggregated lymphoid nodules called Peyer’s Patches for immune defense

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**Secretion**
~ 2 L intestinal gland secretions per day
- secretion begins before chyme enters due to parasympathetic stimulation
- When chyme present, stretch receptors and enterocrinin stimulate secretions of mucus, hormones and juice (no digestive enzymes in liquid secretions)
- sympathetic stimulation inhibits secretion (stress → ulcers, no mucus)

**Small Intestinal Movements**
1. Myenteric reflexes (ENS) → peristalsis to move chyme slowly through small intestine
2. Parasympathetic reflexes (stretch receptors) to accelerate movement
   A. **gastroenteric reflex**: stimulates motility and secretion along whole small intestine
   B. **gastroileal reflex**: relaxes ileocecal valve, materials pass from ileum to cecum (large intestine)

Irritation to GI triggers reflexes to empty quickly:

**Emesis/Vomiting reflex**
- controlled by emetic center of medulla oblongata
1. Pyloric sphincter relaxes, contents of duodenum and upper jejunum discharged into stomach
2. Salivary secretion enhanced (buffer stomach acid)
3. Soft palate rises to close off nasopharynx
4. Diaphragm and abdominal wall muscles contract; stomach contents regurgitated
6. Pancreas
- retroperitoneal
- inferior to stomach
- exocrine and endocrine

A. **Pancreatic islets** (endocrine) (1%)
cells secrete **insulin** and **glucagon** to control blood sugar
B. **Pancreatic acini** (exocrine) (majority)
- acinar cells (simple cuboidal epithelium)
  produce digestive enzymes and buffers:
  **pancreatic juice**

Pancreatic Juice
~ 1.5 L/day in response to parasympathetic and hormonal control
- water + proenzymes + electrolytes (buffer)

Hormonal control from duodenum:
1. Secretin: released in response to acid chyme, triggers pancreas to secrete bicarbonate and phosphate buffers
2. Cholecystokinin: released in response to lipids and peptides in chyme or parasympathetic stimulation, triggers pancreatic enzyme secretion

Pancreatic Enzymes
~70% secreted as proenzymes, activated in gut
1. Pancreatic alpha-amylase:
  hydrolyzes starch
2. Pancreatic lipase:
  hydrolyzes lipids and fatty acids

3. Nucleases:
  hydrolyze nucleic acids (RNA, DNA)
4. Proteolytic enzymes (majority):
  many, each digests specific peptide bond
  2 main classes:
  A. proteases: hydrolyze large proteins into peptides
  B. peptidases: hydrolyze peptide chains into amino acids
All proteolytic enzymes are secreted inactive, must be activated in gut (prevent autolysis)
Enterokinase, a brush border enzyme, activates pancreatic trypsinogen → trypsin
Trypsin activates all other pancreatic proteolytic pro-enzymes via cleavage

**Pancreatitis** = inflammation of pancreas, ducts blocked → injury to acinar cells,
Necrotic cells release lysosome enzymes → activate pro-enzymes → autolysis
**Diabetes mellitus** = destruction of Islet cells, due to pancreatitis or autoimmune attack results in loss of regulation of blood sugar levels

7. Liver
- right side, inferior to diaphragm
- largest visceral organ
- four lobes:
  - on anterior: large right and left lobes separated by falciform ligament (fetal umbilical vein)
  - on posterior: tiny caudate lobe and quadrate lobe
- functional units = lobules

Blood flow in lobule:
- Blood from arteries and veins of triads flows through sinusoids
- Allows molecule exchange with hepatocytes
- Blood flows out through central vein
Sinusoids also contain Kupffer cells (fixed macrophage), functions:
1. Remove pathogens, cell debris, damaged erythrocytes
2. Remove and store iron
3. Remove and store lipids
4. Remove and store heavy metals

Lobule: hexagonal functional unit
- separated by interlobular septa
- central vein in middle
- six portal triads on hexagonal corners:
  1. Hepatic artery: O₂ rich blood
  2. Hepatic portal vein: nutrient rich blood from small intestine
  3. Bile duct: collect bile produced by hepatocytes
- hepatocytes: function in nutrient regulation and bile production, arranged in rows around central vein, sinusoids between rows

Bile flow:
- bile secreted by hepatocytes
- flows through bile canaliculi between cells

Canaliculi → Bile ducts of triads → merge into common hepatic duct
Hepatic duct exits liver, joins cystic duct from gallbladder creating common bile duct
Common bile duct connects to duodenum at duodenal ampulla, controlled by hepatopancreatic sphincter
Liver / Hepatocyte Functions:

1. **Metabolic Regulation**
   - hepatocytes regulate blood nutrient levels
   - nutrient rich blood from GI goes to liver so excess can be removed and deficits can be corrected
     e.g. Carbohydrate metabolism:
     - too much glucose → hepatocytes store glucose as glycogen
     - too little → hepatocytes break down glycogen or perform gluconeogenesis (synthesis from non-carb) to release glucose
   
Hepatocytes also carry out: lipid metabolism, amino acid metabolism, waste removal, vitamin storage, mineral storage, and drug and toxin inactivation

2. **Hematological Regulation**
   - Liver serves as blood reservoir
   - Kupffer cells recycle RBCs
   - Kupffer cells perform antigen presentation to lymphocytes
   - Hepatocytes remove / recycle hormones
   - Hepatocytes remove antibodies
   - Hepatocytes and Kupffer cells remove, inactivate, or store toxins, drugs, and heavy metals
   - Hepatocytes produce plasma proteins

3. **Digestion: Bile Synthesis and Secretion**
   
   **Bile components:**
   - water
   - electrolytes
   - bilirubin
   - cholesterol
   - phospholipids
   - bile salts (lipids)

   **Bile functions:**
   - A. buffer chyme (electrolytes)
   - B. emulsify fats: break large lipid globs into small droplets (phospholipids and bile salts)

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Function of emulsification:
- allow enzymes to access lipids
- promote solubilization and absorption of lipids in blood and lymph

Enterohepatic circulation of bile:
- bile salts absorbed in lipid droplets and recycled back to liver, not metabolized

Secretin from duodenum promotes secretion of bile from liver

**Hepatitis** = inflammation of liver, due to viral infection, restricts blood flow to liver, six known viruses with different severity

**Cirrhosis** = chronic inflammation due to severe hepatitis or alcoholism: damaged hepatocytes replaced by fibrous tissue and adipose, can cause portal hypertension → veins swell and rupture

8. **Gallbladder**
   - anterior and inferior to liver
   - functions to concentrate and store bile produced by liver
   - Cholecystokinin from duodenum causes release of bile by stimulating contraction of gallbladder and relaxation of hepatopancreatic sphincter

**Gall stones** = crystallizations of over concentrated bile

**Cholecystitis** = inflammation caused by large gall stones that block or damage the gallbladder
Coordination of Secretion and Absorption in the Small Intestine:
(on handout)

9. Large Intestine
~ 5 feet long
-Functions:
  1. Reabsorb any remaining water and compact feces
  2. Absorb vitamins and electrolytes
  3. Storage of feces and defecation
- No digestion, except by microbes
- Water absorption important to feces consistency:
  too much water = diarrhea
  too little water = constipation

Bacteria of Large Intestine:
(Fun fact: ~2 lb bacteria in gut)

Some produce vitamins:
- Vitamin K: clotting factor synthesis
- Biotin: glucose metabolism
- Vitamin B5: steroid hormone and neurotransmitter synthesis

Bacterial metabolism produces characteristics of feces:
- Bilirubin → urobilins and stercobilins = brown
- Fermentation of organics → ammonia, indole, \( \text{H}_2\text{S} \) = odor
- Fermentation of carbs → methane, \( \text{CO}_2 \) = flatus
(You will produce ~500ml flatus /day, more with complex carb rich diet)

Histology specializations:
- Muscularis externa made up of three longitudinal bands of smooth muscle called taeniae coli
- Contraction of taeniae coli produces pouches called haustra
- Mucosa has deep crypts with intestinal glands that produce mucus
- No plicae or vili
- Lamina propria has large lymphoid nodules
- Epithelium is simple columnar with abundance of goblet cells
Subdivisions:

A. Cecum
- attached to ileum via ileocecal valve
- functions to begin compaction of feces
- appendix on side: has lymphoid nodules that are part of the MALT

Appendicitis = blockage of appendix, results in bacterial growth causing inflammation and swelling, rupture will release bacteria into abdomen → peritonitis → sepsis → death

B. Colon
-absorbs water, vitamins, electrolytes
- four major regions:
  1. Ascending colon
  2. Transverse colon
  3. Descending colon
  4. Sigmoid colon

Diverticulitis = pockets form in colon wall and are site of recurrent inflammation and infection: due to lack of fiber

C. Rectum
- store feces
- has 3 valves to separate feces and flatus
- exits at anal canal
- lined with stratified squamous epithelium

Defecation controlled by two sphincters:
  1. Internal anal sphincter: smooth muscle from muscularis externa, involuntary
  2. External anal sphincter: skeletal muscle under voluntary control

Large Intestinal Movements:
1. Hastral contractions: local, slow, segmenting contractions, shift feces for water absorption
2. Mass movements: powerful peristaltic contractions, force feces toward rectum, occur few times per day, can trigger defecation reflex via stretch receptors in rectum
3. Defecation reflex: stretch receptors → parasympathetic stimulation → contraction of sigmoid colon and rectum and relaxation of internal anal sphincter. Voluntary control of external anal sphincter controls timing of defecation

Time in colon controls water absorption:
- Movement through large intestine too fast = too much water in feces = diarrhea
- Movement too slow = too little water in feces = constipation

Chemical Digestion
- Large molecules catabolized into monomers
- Monomers absorbed by mucosa
- Enzymatic breakdown = hydrolysis

Carbohydrate Digestion and Absorption (on handout)
- Cellulose not digested: “bulk” fiber, aids intestinal mobility

Lactose intolerant = fail to produce lactase (brush border enzyme), undigested lactose creates osmotic gradient that causes feces to remain hydrated (diarrhea), bacteria ferment lactose producing flatus
Lipid Digestion and Absorption
(on handout)

Protein Digestion and Absorption
(on handout)

Nucleic Acid Digestion and Absorption
(on handout)

Water Absorption
(on handout)

Ion Absorption
-ions from food and secretions
-must be regulated for homeostasis
-control osmosis and pH, needed for enzyme function
(on handout)

Vitamin Absorption
(on handout)

Age related Changes:
1. Epithelium division rates decline, ulcers more likely
2. Smooth muscle tone decreases;
   -constipation from slow movement
   -diverticulitis and hemorrhoids from weak walls
   -GERD from open sphincters
3. Cumulative damage
   -teeth (wear, caries)
   -liver (toxin, lipid build up)
4. Increased cancer rate