Chapter 23.
Digestive System

Overview

- Digestive Anatomy
  - Common histology of GI tract
  - Tour through GI tract: Oral cavity → pharynx → esophagus → stomach → small intestine → large intestine
  - Accessory organs: liver, pancreas

- Digestive Physiology
  - Hormones and reflexes
  - Nutrient digestion and absorption (carbs, proteins, fats)

Metabolism

- Anabolism: Uses raw materials to synthesize essential compounds
- Catabolism: Decomposes substances to provide energy cells need to function
  - Require two essential ingredients:
    1. Oxygen
    2. Organic molecules broken down by intracellular enzymes (e.g., carbohydrates, fats, and proteins)

Components of the Digestive System

Digestive Tract

- Gastrointestinal (GI) tract or alimentary canal
  - A muscular tube that extends from oral cavity to anus
  - Includes: mouth, pharynx, esophagus, stomach, small intestine, large intestine and anus

- Digestive system also includes accessory digestive organs: teeth, tongue, gallbladder, salivary glands, liver, and pancreas

Functions of the Digestive System

- Ingestion:
  - Occurs when materials enter digestive tract via the mouth
- Mechanical processing:
  - Crushing and shearing, increases S.A., makes materials easier to propel along digestive tract
- Digestion:
  - Chemical breakdown of food into small organic fragments for absorption by digestive epithelium (not always necessary e.g., glucose)
Functions of the Digestive System 2

- **Secretion:**
  - release of water, acids, enzymes, buffers, and salts by glandular organs in digestive tract epithelium
- **Absorption:**
  - movement of organic substrates, electrolytes, vitamins, and water across digestive epithelium into interstitial fluid of digestive tract
- **Excretion:**
  - removal of waste products from body fluids

Digestive epithelial defenses

- Bacteria is ingested with food and resides in digestive tract
- Attacked by macrophages, and immune system cells found in the lamina propria (underlying layer of areolar tissue)
- Also acids in the stomach
- Nonspecific immunity
- Also Peyer’s Patches

Peritoneal Cavity

- Located within the abdominopelvic cavity
- Lined with serous membrane consisting of a superficial mesothelium covering a layer of areolar tissue
  - **visceral peritoneum (serosa):**
    - covers organs within peritoneal cavity
  - **parietal peritoneum:**
    - lines inner surfaces of body wall
- **Peritoneal fluid** allows sliding without friction or irritation

Mesenteries

- Double sheets of peritoneal (serous) membrane that suspend portions of digestive tract within peritoneal cavity
- Connect parietal peritoneum with visceral peritoneum
- Stabilize positions of attached organs
- Prevent intestines from becoming entangled
- The areolar tissue between mesothelial surfaces provides an access route to and from the digestive tract for passage of blood vessels, nerves, and lymphatic vessels

Development of Mesenteries
Mesentery Development

- During embryonic development, digestive tract and accessory organs are suspended in peritoneal cavity by:
  - dorsal mesentery remains on ventral surface of stomach and enlarges to form an enormous pouch, called the greater omentum:
    - Extends inferiorly between the body wall and the anterior surface of small intestine
    - Hangs like an apron from lateral and inferior borders of stomach
    - Adipose tissue in greater omentum: conforms to shapes of surrounding organs, pads and protects surfaces of abdomen, provides insulation to reduce heat loss, stores lipid energy reserves
  - ventral mesentery persists in 2 places:
    - between stomach and liver (lesser omentum)
    - between liver and anterior abdominal wall (falciform ligament)

Retroperitoneal Organs

- Retroperitoneal organs – organs outside the peritoneum
- Peritoneal organs (intraperitoneal) – organs surrounded by peritoneum

Adult Mesenteries

Histology of the Digestive Tract

- Major layers of the digestive tract (from lumen out):
  - mucosa
  - submucosa
  - muscularis externa
  - serosa

Mucosa

- Mucous membrane inner lining of digestive tract is made of:
  - Short-lived epithelium, moistened by glandular secretions (protect, lubricate)
  - Lamina propria of areolar tissue
  - Muscularis mucosa

- Mucosal epithelium is simple or stratified depending on location, function, and stresses
  - Stratified squamous epithelium
    - Oral cavity, pharynx, and esophagus (Why?)
  - Simple columnar epithelium with goblet cells
    - Stomach, small intestine, and most of large intestine (Why?)

Digestive Lining

- Folding increases surface area for absorption:
  1. Longitudinal folds, disappear as digestive tract fills
  2. Permanent transverse folds (plicae)
- Enteroendocrine cells are scattered among columnar cells of digestive epithelium in stomach and small intestine
  - Secrete hormones that coordinate activities of digestive tract and accessory glands
**Lamina Propria**

- Consists of a layer of loose areolar tissue (sometimes with reticular CT) contains:
  - blood vessels to nourish epithelium and absorb nutrients and hormone signals
  - sensory nerve endings
  - lymphatic vessels and nodes (MALT)
  - smooth muscle cells
  - scattered areas of lymphoid tissue
  - Muscularis mucosa at the bottom

**Muscularis Mucosae**

- Narrow band of smooth muscle and elastic fibers in lamina propria
- Smooth muscle cells arranged in 2 concentric layers:
  - inner layer encircles lumen (circular muscle)
  - outer layer contains muscle cells parallel to tract (longitudinal layer)

**Other Layers**

- **Submucosa**
  - Layer of dense irregular connective tissue with large blood vessels and lymphatic vessels
  - May contain exocrine (submucosal glands) that secrete buffers and enzymes into digestive tract
  - Contains submucosal plexus
- **Muscularis externa**
  - Tons of smooth muscle arranged into outer longitudinal and inner circular layers (like m. mucosa)
  - Involved in segmentation and peristalsis (mechanical processing and movement of materials along digestive tract)
- **Serosa**
  - Serous membrane covering muscularis externa except in oral cavity, pharynx, esophagus, and rectum
  - In these sites the muscularis externa is covered by a dense sheath of collagen fibers that firmly attaches the digestive tract to adjacent structures called adventitia

**Enteric Nervous System (ENS)**

- Composed of two major intrinsic nerve plexuses both containing: sensory neurons, parasympathetic ganglionic neurons, sympathetic postganglionic fibers
- **Submucosal Plexus**
  - Found in submucosa
  - Innervates the mucosa and submucosa and regulates glands and smooth muscle of muscularis mucosa
- **Myenteric plexus**
  - Major nerve supply that controls GI tract mobility
  - Found in between the circular and longitudinal layers of muscle in the muscularis mucosa and innervates it
- Muscle movements coordinated by ENS:
  - Myenteric plexus can coordinate local responses independent of autonomic nervous system or
  - Innervated primarily by parasympathetic division of ANS, when active, increase muscular activity
  - Sympathetic activity decreases muscular activity, constricts blood vessels here

**Digestive Smooth Muscle**

- Smooth Muscle along digestive tract has rhythmic cycles of activity controlled by pacesetter cells
  - Cells undergo spontaneous depolarization, triggering wave of contraction through entire muscular sheet
- Located in muscularis mucosae and muscularis externa surrounding lumen of digestive tract
Peristalsis and Segmentation

**Peristalsis**
- Consists of waves of muscular contractions
- Moves a bolus along the length of the digestive tract
- **Bolus**: small, oval mass of digestive contents
  1. Circular muscles contract behind bolus while circular muscles ahead of bolus relax
  2. Longitudinal muscles ahead of bolus contract shortening adjacent segments
  3. Wave of contraction in circular muscles forces bolus forward

**Segmentation**
- Cycles of contraction:
  - Churn and fragment bolus
  - Mix contents with intestinal secretions
- Does not follow a set pattern
- Does not push materials in any direction
- Occurs in small and part of large intestine

Nervous Control of the GI Tract

**Neural Mechanisms**
- Control the movement of materials along digestive tract and secretory functions
- Motor neurons located in myenteric plexus control smooth muscle contraction and glandular secretion
- **Long reflexes**: CNS coordinates large scale changes in muscular activity via parasymp. NS
- **Short reflexes** (myenteric reflexes) are local, affect only a portion of tract:
  - Material activates sensory neuron (stretch receptor) ➔ interneuron ➔ motor neuron (does not require any other neural input)
  - Prostaglandins, histamine, and other chemicals released into interstitial fluid affect adjacent cells within small segment of digestive tract
**Digestive Hormones**

- At least 18 hormones that affect most aspects of digestive function and also activities of other systems
- Peptides produced by enteroendocrine cells in digestive tract
- Reach target organs after distribution in bloodstream

**Tour Through Digestive Tract**

Oral cavity → pharynx → esophagus → stomach → small intestine → large intestine
Also: liver, pancreas

---

**The Oral Cavity**

- Is bounded by lips, cheeks, palate, and tongue
- Has the oral orifice as its anterior opening
- Is continuous with the oropharynx posteriorly

**Functions of the Oral Cavity**

- **Sensory analysis** of material before swallowing
- **Mechanical processing** through actions of teeth, tongue, and palatal surfaces
- **Lubrication** by mixing with mucus and salivary gland secretions
- **Limited digestion** of carbohydrates and lipids

**Oral Mucosa**

- Lining of oral cavity has a stratified squamous epithelium
- Layer of slightly keratinized cells covers only regions exposed to severe abrasion (gums, hard palate, dorsal tongue)
- Lining of cheeks, lips, and inferior surface of tongue is relatively thin, nonkeratinized, and delicate

**Oral Cavity Structures**

- **Lips (Labia)**
  - overly orbicularis oris
  - mucosa of each cheek is continuous with that of the lips
- **Cheeks**
  - Overly buccinator muscles
- **Vestibule**: space between the cheeks (or lips) and the teeth
- **Gingivae (Gums)**: ridges of oral mucosa
  - surround base of each tooth on alveolar processes of maxillary bones and mandible
- **Uvula**: a dangling process that helps prevent food from entering pharynx prematurely
- **Fauces**: passageway between oral cavity and oropharynx
Tongue and Palate

- **Tongue**
  - Manipulates materials inside mouth
  - Mixes food with saliva and forms bolus
  - Initiates swallowing; speech
  - Secretion by sublingual glands:
    - mucins
    - enzyme lingual lipase
      - Enzyme, works over broad pH range (3.0–6.0)
      - Starts lipid digestion immediately

- **Palate**
  - Soft palate
    - Closes off the nasopharynx during swallowing
    - Uvula projects downward from its free edge
  - Hard palate
    - Underlain by palatine bones and palatine processes of the maxillae
    - Assists the tongue in chewing

Salivary Glands

- 3 pairs secrete into oral cavity
- Each pair has distinctive cellular organization and produces saliva with different properties
- Produce 1.0–1.5 liters of saliva each day:
  - 70% by submandibular glands
  - 25% by parotids
  - 5% by sublingual glands

Functions of Saliva

- 99.4% water
- Rest is electrolytes (Na⁺, Cl⁻, and HCO₃⁻), buffers, mucins, antibodies, enzymes, waste products
- Cleanses and lubricates the mouth
- Aids in bolus formation
- Moistens and lubricates materials in the mouth
- Dissolves chemicals that:
  - stimulate taste buds
  - provide sensory information
- Initiates digestion of:
  - complex carbohydrates by enzyme salivary amylase (alpha-amylase)
  - lipids by enzyme lingual lipase

The Salivary Glands

- **Parotid Salivary Glands**
  - Lies anterior to the ear between the masseter muscle and skin
  - Produce serous secretion:
    - enzyme salivary amylase (breaks down starches)

- **Sublingual Salivary Glands**
  - Covered by mucous membrane of floor of mouth
  - Produce mucous secretion:
    - buffer and lubricant

Salivary Glands

- **Submandibular Salivary Glands**

Teeth

- Primary – 20 deciduous teeth that erupt at intervals between 6 and 24 months
- Permanent – enlarge and develop causing the root of deciduous teeth to be resorbed and fall out between the ages of 6 and 12 years
  - All but the third molars have erupted by the end of adolescence
  - Usually 32 permanent teeth
The Pharynx

- A common passageway for solid food, liquids, and air
  - Nasopharynx
  - Oropharynx
  - Laryngopharynx
- Food passes through oropharynx and laryngopharynx to esophagus

The Esophagus

- A hollow muscular tube from laryngopharynx to stomach, about 25 cm long and 2 cm wide (narrowest at the top)
- Travels through the mediastinum and pierces the diaphragm
- Joins the stomach at the cardiac orifice
- Conveys solid food and liquids to the stomach
- Resting muscle tone in the circular muscle layer in the superior 3 cm of esophagus prevents air from entering (not a very big hole normally)
- Resting muscle tone at inferior end prevents backflow from stomach (not an actual sphincter)

Histology of the Esophagus

- Wall of esophagus has mucosa, submucosa, muscularis mucosa, adventitia
- Mucosa contains nonkeratinized, stratified squamous epithelium:
  - Mucosa and submucosa both form large folds that extend the length of the esophagus and allow for expansion
  - Muscularis mucosae consists of irregular layer of smooth muscle
- Submucosa contains submucosal esophageal glands:
  - produce mucus secretion which reduces friction between bolus and esophageal lining
- Muscularis externa:
  - has usual inner circular and outer longitudinal layers
  - Superiormost portion has skeletal muscle fibers, changes to smooth muscle inferiorly

Swallowing

- Also called deglutition
- Can be initiated voluntarily but proceeds automatically
- Divided into 3 phases:
  - buccal phase
  - pharyngeal phase
  - esophageal phase
The Swallowing Process

Figure 24–11

Swallowing

- **The Buccal Phase**
  - Compression of bolus against hard palate
  - Retraction of tongue forces bolus into oropharynx:
    - assists elevation of soft palate
    - seals off nasopharynx

- **The Pharyngeal Phase**
  - Bolus contacts:
    - arches along the pharynx
    - posterior pharyngeal wall
  - The Swallowing Reflex: passage of the bolus stimulates tactile receptors on palatal arches and uvula, relayed to cranial nerves which activate pharyngeal muscles

- **The Esophageal Phase**
  - Contraction of pharyngeal muscles forces bolus through entrance to esophagus, peristalsis follows

Esophageal Peristalsis

- **Primary Peristaltic Waves**: movements coordinated by afferent and efferent fibers in glossopharyngeal and vagus nerves
- **Secondary Peristaltic Waves**: local reflexes coordinated in the esophagus

Functions of the Stomach

- Storage of ingested food
- Mechanical breakdown of ingested food
- Disruption of chemical bonds in food by acids and enzymes (chemical digestion)
- Production of **intrinsic factor**: glycoprotein required for absorption of vitamin B₁₂ in small intestine
- When food reaches the stomach it becomes **chyme** = mixture of secretions and food in the stomach

Anatomy of the Stomach

- The stomach is shaped like an expanded J
- Anterior and posterior surfaces are smoothly rounded
- Shape and size vary from individual to individual and from one meal to the next
- **Greater omentum** – drapes inferiorly from the greater curvature to the small intestine
- Stomach typically extends between levels of vertebrae T₇ and L₃
  - **Cardiac region** - surrounds the cardiac orifice within 3cm of esophagus
  - **Fundus** – dome-shaped region beneath the diaphragm
  - **Body** – midportion of the stomach
  - **Pyloric region** – The bottom portion of the “J”, made up of the antrum and canal which terminates at the pyloric sphincter (continues into the duodenum of the S.I.)
  - Glands here secrete **gastrin**

The Stomach
The Stomach Lining

Histology of the Stomach

- Rugae = folds of empty stomach
- Muscularis mucosa and externa contain extra oblique layers of smooth muscle that allow the stomach to churn, mix, and pummel food physically
- Simple columnar epithelium lines all portions of stomach, is a secretory sheet: produces alkaline mucus that covers interior surface of stomach
- Gastric Pits: shallow depressions that

Gastric Glands

- Found in fundus and body of stomach, extend deep into underlying lamina propria
- Secrete gastric juice, mucus, and gastrin
- Each gastric pit communicates with several gastric glands
- Two types of secretory cell: in gastric glands secrete gastric juice:
  - parietal cells
  - chief cells

Gastric Gland cells of Fundus and Body

- Parietal Cells
  - Mostly in proximal portions of glands
  - Secrete intrinsic factor and hydrochloric acid (HCl)
- Chief Cells
  - Most abundant near base of gastric gland:
  - Secrete pepsinogen (inactive proenzyme)
  - Pepsinogen is converted by HCl in the gastric lumen to pepsin (active proteolytic enzyme)
- Enteroendocrine cells (later)

The Secretion of Hydrochloric Acid

- H+ and Cl- are not assembled in the cytoplasm (Why not?)
- H+ from carbonic acid dissociation are active transported into lumen
- Bicarbonate ion countertransported out (with Cl- in) to interstitial fluid (alkaline tide)
- Cl- diffuses though cell and out to lumen

HCl

- Secretion increased by gastrin, ACh, and histamine
- pH = 1.5
- Kills microorganisms
- Denatures proteins, inactivating enzymes present in foods
- Helps break down plant cell walls and connective tissues
- Activates pepsinogen
Stomach Lining
• The stomach is exposed to the harshest conditions in the digestive tract
• To keep from digesting itself, the stomach has a mucosal barrier with:
  – A thick coat of bicarbonate-rich mucus on the stomach wall
  – Epithelial cells that are joined by tight junctions
  – Gastric glands that have cells impermeable to HCl
• Damaged epithelial cells are quickly replaced

Pyloric Glands
• Glands in the pylorus (pyloric glands) produce mucous secretions
• Enteroendocrine Cells are scattered among mucus-secreting cells:
  – G cells
    • Abundant in gastric pits of pyloric antrum
    • Produce gastrin: stimulates both parietal and chief cells and promotes gastric muscle contractions
  – D cells
    • In pyloric glands
    • Release somatostatin, a hormone that inhibits release of gastrin

The Phases 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

3 Phases of Gastric Secretion
• Cephalic phase (a few minutes)
  – Begins when you see, smell, taste, or think of food:
    • Neural, directed by CNS through Para NS
    • prepares stomach to receive food
• Gastric phase (3-4 hours)
  – Begins with arrival of food in stomach, builds on stimulation from cephalic phase
  – Has a neural response (stretch receptors), hormonal response (gastrin), and local response (histamine → stimulates acid secretion)
• Intestinal phase (many hours)
  – Begins when chyme first enters small intestine after several hours of mixing waves
    – Chyme is squirted by contractions though pyloric sphincter in small, controlled amounts (why not all at once?)
      • Neural (stretching stimulates entogastric reflex temporarily inhibits gastrin and gastric contractions)
      • Hormonal (CCK, GIP, and Secretin: all inhibit gastric activity; also tell pancreas to secrete buffers and liver to make bile)
    – Arrival of undigested proteins stimulates G cells in duodenal wall to secrete gastrin to increase acid and enzyme production

Regulation of Stomach Acid and Enzyme Production
• Can be controlled by CNS
• Regulated by short reflexes of ENS which is coordinated locally in wall of stomach
• Regulated by hormones of digestive tract
  – CCK, gastrin, somatostatin, secretin, GIP
• Alcohol, caffeine, large sized meal, low protein content: all speed up gastric processing
• Carbohydrate-rich chyme quickly moves through the duodenum
• Fat-laden chyme is digested more slowly causing food to remain in the stomach longer

Response of the Stomach to Filling
• 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
• Plasticity – intrinsic ability of smooth muscle to exhibit the stress-relaxation response
• Peristaltic waves move toward the pylorus at the rate of 3 per minute (pacemaker cells)
• 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
Digestion in the Stomach

- Stomach performs preliminary digestion of proteins by pepsin
- Some digestion of carbohydrates (by salivary amylase)
- Some digestion of lipids (by lingual lipase)
- Stomach contents:
  - become more fluid
  - pH approaches 2.0
  - pepsin activity increases
  - protein disassembly begins
- Little or no absorption occurs in the stomach (some drugs can be absorbed)

Segments of the Intestine

The Small Intestine

- Plays key role in digestion and absorption of nutrients
- 90% of nutrient absorption occurs in the small intestine

Segments of the S.I.

- S.I. Runs from pyloric sphincter to the ileocecal valve; 3 segments:
  - The Duodenum is the 25 cm (10 in.) long segment of small intestine closest to stomach
    - “Mixing bowl” that receives chyme from stomach, digestive secretions from pancreas and liver
  - The Jejunum is the 2.5 meter (8.2 ft) long middle segment and is the location of most chemical digestion and nutrient absorption

Intestinal Folds and Projections

- Structural modifications of the small intestine wall increase surface area
- Plicae = Largest; deep transverse (circular) folds in intestinal lining; permanent features (they do not disappear when small intestine fills)
- Intestinal Villi: a series of fingerlike projections of mucosa
- Villi are covered with simple columnar epithelium which themselves are have
**Intestinal Histology**

- Absorptive columnar cells
- **Goblet cells** between columnar epithelial cells eject mucins onto intestinal surfaces
- Enteroendocrine cells in intestinal glands produce intestinal hormones:
  - gastrin
  - cholecystokinin
  - Secretin
- Peyer’s patches are found in the submucosa

**Lacteals**

- Each villus lamina propria has ample capillary supply (to absorb nutrients) and nerves
- In addition, each villus has a central lymph capillary called a lacteal. These are larger than the blood capillaries and thus can absorb larger particles into the body, such as lipid droplets.
- Muscle contractions move villi back and forth to facilitate absorption and to squeeze the lacteals to assist lymph movement

**Crypts**

- Openings from intestinal glands to the intestinal lumen at the bases of villi
- Entrances for **brush border enzymes**:
  - Integral membrane proteins on surfaces of intestinal microvilli
  - Break down materials in contact with the brush border
  - **Enterokinase**: a brush border enzyme that activates pancreatic proenzyme trypsinogen

**The Duodenum**

- Has few plicae, small villi
- Duodenal glands in the submucosa called Brunner’s Glands produce lots of mucus and buffers (to protect against acidic chyme)
  - Activated by Para NS during cephalic phase to prepare for chyme arrival, also activated by chyme arrival
- Functions
  - **Mixing bowl**
  - To receive chyme from stomach
  - To neutralize acids before they can damage the absorptive surfaces of the small intestine
  - To mix in pancreatic digestive juices

**Intestinal Secretions**

- Watery intestinal juice (1.8 liters per day enter intestinal lumen) mostly via osmosis
- Moistens chyme
- Assists in buffering acids
- Keeps digestive enzymes and products of digestion in solution

**Intestinal Movements**

- Chyme arrives in duodenum
- Weak peristaltic contractions move it slowly toward jejunum
  - Controlled by local myenteric reflexes, not under CNS control
  - Parasympathetic stimulation accelerates local peristalsis and segmentation
Intestinal Reflexes

- Both stimulated by stretching of stomach
- Preparatory
- The Gastroenteric Reflex stimulates motility and secretion along entire small intestine
- The Gastroileal Reflex Triggers relaxation of ileocecal valve
  - Allows materials to pass from small intestine into large intestine
- Like the opposite of the enterogastic reflex in which chyme entry into S.I. slows gastric movement

The Pancreas

- Lies posterior to stomach tucked in between it and the duodenum
- Tail extends toward spleen
- Bound to posterior wall of abdominal cavity
- Wrapped in thin, connective-tissue capsule

Functions of the Pancreas

1. Endocrine cells of pancreatic islets
   - secrete insulin and glucagon into bloodstream
2. Exocrine cells
   - Acini: clusters of secretory cells called acinar cells
     - produce digestive enzymes
   - epithelial cells of duct system

Pancreatic Secretions

- 1000 ml (1 qt) pancreatic juice per day
- Contain pancreatic enzymes
- Controlled by hormones from duodenum in response to chyme arrival (when fatty or acidic)
  - secretin → tells pancreas to release juice with buffers, bicarbonate ions
  - CCK → tells pancreas to release dig. enzymes
- Parasympathetic vagus nerve activation during the cephalic phase also causes duodenal cells to release their hormones
  - Especially important for the enzymes because they have to be made ahead of time, takes awhile

The Pancreas

- Pancreatic Duct: large duct that delivers digestive enzymes and buffers to duodenum
- Common Bile Duct from the liver and gallbladder
  - Meets pancreatic duct near duodenum
- Pancreas is divided into lobules:
  - ducts branch repeatedly
  - end in pancreatic acini
  - Blind pockets lined with simple cuboidal epithelium
  - Contain scattered pancreatic islets (1%)
Pancreatic Enzymes

- Pancreatic alpha-amylase:
  - a carbohydrase similar to salivary amylase
  - breaks down starches
- Pancreatic lipase:
  - breaks down complex lipids
  - releases products (e.g., fatty acids) that are easily absorbed
- Nucleases:
  - break down nucleic acids
- Proteolytic enzymes:
  - break certain proteins apart
  - proteases break large protein complexes
  - peptidases break small peptides into amino acids

Proteolytic Enzymes

- 70% of all pancreatic enzyme production
- Secreted as inactive proenzymes
- Activated only after reaching small intestine
  - trypsin a protease activated by enterokinase in duodenum (converts trypsinogen to trypsin)
  - Also: chymotripsinogen, procarboxypeptidase, proelastase

The Liver

- Largest visceral organ (1.5 kg)
- Lies in right hypochondriac and epigastric regions, extends to left hypochondriac and umbilical regions
- Performs essential metabolic and synthetic functions
- Wrapped in tough fibrous capsule
- Covered by visceral peritoneum
- Divided into lobes
- The gallbladder rests in a recess on the inferior surface of the right lobe

Functions of the Liver

1. Metabolic regulation
2. Hematological regulation
   - Largest blood reservoir in body
   - Receives 25% of cardiac output
   - Regulates:
     - Synthesis of plasma proteins
     - Removal of circulating hormones
     - Removal of antibodies
     - Removal or storage of toxins
     - Synthesis and secretion of bile
3. Bile production

Hepatic Blood Supply

- 1/3 of blood supply:
  - arterial blood from hepatic artery proper
- 2/3 venous blood from hepatic portal vein, originating at:
  - esophagus
  - stomach
  - small intestine
- Blood leaving the liver returns to systemic circuit via hepatic veins which open into inferior vena cava
**Liver Histology**
- Hexagonal liver lobules are the basic functional units of the liver.
- Each lobe is divided by connective tissue into about 100,000 liver lobules about 1 mm diameter each.
- Hepatocytes are the main liver cells.
  - Adjust circulating levels of nutrients through selective absorption and secretion.
  - In a liver lobule they form a series of irregular plates arranged like wheel spokes around a central vein.
  - Between them run sinusoids of the hepatic portal system.
- Many Kupffer Cells are located in sinusoidal lining.
- Portal triads are found at each of the six corners.

**Hexagonal Liver Lobule**
- Has 6 portal areas (one per corner).
- Each Portal Area Contains:
  - Branch of hepatic portal vein (venous blood from digestive system).
  - Branch of hepatic artery proper (arterial blood).
  - Small branch of bile duct.
- The arteries and the veins deliver blood to the sinusoids.
  - Capillaries with large endothelial spaces so that even plasma proteins can diffuse out into the space surrounding hepatocytes.

**Hepatic Blood Flow**
- Blood enters liver sinusoids:
  - From small branches of hepatic portal vein.
  - From hepatic artery proper.
- As blood flows through sinusoids:
  - Hepatocytes absorb solutes from plasma.
  - Secret materials such as plasma proteins.
- Blood leaves through the central vein, returns to systemic circulation.
- Pressure in portal system is low, flows slowly.
- This is the blood that can be returned by venoconstriction.

**Bile**
- A yellow-green, alkaline solution containing bile salts, bile pigments, cholesterol, neutral fats, phospholipids, and electrolytes.
- Produced in liver.
- Stored in gallbladder.
- Discharged into small intestine.
- Aids lipid digestion.
- Bile salts are cholesterol derivatives that:
  - Emulsify fat.
  - Facilitate fat and cholesterol absorption.
  - Help solubilize cholesterol.
- Enterohepatic circulation recycles bile salts.
- The chief bile pigment is bilirubin, a waste product of heme.

**The Bile Duct System**
- Liver secretes bile fluid into a network of narrow channels (bile canaliculi) between opposing membranes of adjacent liver cells.
  - Extend outward, away from central vein.
  - Connect with bile ductules in nearest portal area.
  - Right and left hepatic ducts collect bile from all bile ducts of liver lobes.
- Unite to form common hepatic duct which leaves the liver.
- This unites with cystic duct to form common bile duct.
Bile Flow

- From common hepatic duct to either:
  - the common bile duct, which empties into duodenum
  - the cystic duct, which leads to gallbladder

Metabolic Regulation

- The liver regulates:
  1. composition of circulating blood
  2. nutrient metabolism
  3. waste product removal
  4. nutrient storage (fat soluble vitamins)
  5. drug inactivation

Composition of Circulating Blood

- All blood leaving absorptive surfaces of digestive tract enters hepatic portal system and flows into the liver
- Liver cells extract nutrients or toxins from blood before it reaches systemic circulation through hepatic veins
- Liver removes and stores excess nutrients, corrects nutrient deficiencies by:
  - mobilizing stored reserves
  - performing synthetic activities

Metabolic Activities of the Liver

- Carbohydrate metabolism
  - Releases/stores glucose as needed
  - Tells other cells to do the same
- Lipid metabolism
  - Releases/stores fatty acids
- Amino acid metabolism
  - Removes excess from circulation
- Waste product removal
  - Produces urea from nitrogenous wastes
- Vitamin storage (Fat soluble: A, D, E, K)
- Mineral storage (Iron)
- Drug inactivation

Lipid Digestion and Absorption

- Dietary lipids are not water soluble
- Mechanical processing in stomach creates large drops containing lipids
- Pancreatic lipase is not lipid soluble and thus interacts only at surface of lipid droplet
- Bile salts break droplets apart (emulsification):
  - increases surface area exposed to enzymatic attack
  - creates tiny emulsion droplets coated with bile salts

The Gallbladder and Bile Ducts
The Gallbladder

- A pear-shaped, muscular sac
- Stores and concentrates bile by absorbing its water prior to excretion into small intestine
- Releases bile into duodenum via cystic duct only under stimulation of hormone cholecystokinin (CCK)
  - Otherwise, bile is stored (in gallbladder)
- Acidic, fatty chyme causes the duodenum to release CCK and secretin into the bloodstream
- Vagal stimulation causes weak contractions of the gallbladder

CCK

- Is released whenever chyme enters duodenum
- Stimulates contractions in gallbladder: pushes bile into small intestine
- Amount secreted depends on lipid content of chyme (more lipids, more CCK, more bile)
  - (Also causes release of all types of digestive enzymes)

Gallstones

- Are crystals of insoluble minerals and salts
- Form if bile is too concentrated
- Small stones may be flushed through bile duct and excreted
- Can lead to cholecystitis

You can live without a gallbladder but the release of bile will not be as well coordinated with the arrival of lipids (because CCK will no longer cause release of stored bile)

Large Intestine

- Also called large bowel
- Horseshoe-shaped, about 1.5 meters long and 7.5 cm wide
- Extends from end of ileum to anus
- Lies inferior to stomach and liver
- Frames the small intestine
- Functions
  - Reabsorption of water (the last 15-20%)
  - Compaction of intestinal contents into feces
  - Absorption of important vitamins produced by bacteria
  - Storage of fecal material prior to defecation

Parts of the Large Intestine

- Cecum:
  - the pouchlike first portion
  - Has wormlike appendix projecting from it
- Colon:
  - the largest portion
- Rectum:
  - the last 15 cm of digestive tract
- Anal canal
Ileocecal Valve
- Attaches the ileum to the medial surface of cecum
  - an expanded pouch
  - receives material arriving from the ileum
  - stores materials and begins compaction
  - [opened by the gastoroileal reflex to receive material from S.I.]

The Appendix
- Also called vermiform appendix
- A slender, hollow appendage (about 9 cm long), dominated by lymphoid nodules (a lymphoid organ)
- Is attached to posteromedial surface of cecum

The Colon
- Has a larger diameter (this is why it is called large) and thinner wall than small intestine
- The wall of the colon forms a series of pocketlike pouches (haustra) giving it a segmented appearance
- Haustra permit expansion and elongation of colon

Colon Muscles
- 3 longitudinal bands of smooth muscle (taeniae coli) run along outer surfaces of colon deep to the serosa (similar to outer layer of muscularis externa)
- Muscle tone in taeniae coli creates the haustra

Regions of the Colon
- Ascending colon
  - Begins at superior border of cecum
  - Ascends along right lateral and posterior wall of peritoneal cavity to inferior surface of the liver
- Transverse colon
  - Curves anteriorly from right colic flexure
  - Crosses abdomen from right to left
  - Is supported by transverse mesocolon
  - Is separated from anterior abdominal wall by greater omentum

Regions of the Colon
- Descending colon
  - Proceeds inferiorly along left side:
    - to the iliac fossa (inner surface of left ilium)
  - Is retroperitoneal, firmly attached to abdominal wall
- Sigmoid colon
  - S-shaped segment, about 15 cm long
  - Starts at sigmoid flexure
  - Lies posterior to urinary bladder
  - Is suspended from sigmoid mesocolon
  - Empties into rectum
The Rectum

- Forms last 15 cm of digestive tract
- Is an expandable organ for temporary storage of feces
- Movement of fecal material into rectum triggers urge to defecate
- **Anus**: exit of the anal canal
- Has keratinized epidermis like skin [anus]
- [The rest of the rectum is columnar or nonkeratinized stratified squamous]

Anal Sphincters

- **Internal anal sphincter**:
  - circular muscle layer of muscularis externa
  - has smooth muscle cells, not under voluntary control
- **External anal sphincter**:
  - encircles distal portion of anal canal
  - a ring of skeletal muscle fibers, under voluntary control

Mucosa and Glands of the Colon

- Lack villi
- Abundance of goblet cells
- Presence of distinctive intestinal glands in crypts
  - deeper than glands of small intestine
  - dominated by goblet cells
- Mucosa of the large intestine does not produce enzymes
  - Provides lubrication for fecal material
- Large lymphoid nodules are scattered throughout the lamina propria and submucosa
- The longitudinal layer of the muscularis externa is reduced to the muscular bands of **taeniae coli**

Characteristics of the Colon

- Lack villi
- Abundance of goblet cells
- Presence of distinctive intestinal glands in crypts
  - deeper than glands of small intestine
  - dominated by goblet cells
- Mucosa of the large intestine does not produce enzymes
  - Provides lubrication for fecal material
- Large lymphoid nodules are scattered throughout the lamina propria and submucosa
- The longitudinal layer of the muscularis externa is reduced to the muscular bands of **taeniae coli**

Physiology of the Large Intestine

- Other than digestion of enteric bacteria, no further digestion takes place
- Less than 10% of nutrient absorption occurs in large intestine
- Prepares fecal material for ejection from the body
- [most of the absorption is of vitamins produced by colonic bacteria, along with water and electrolytes]

Absorption in the Large Intestine

- Reabsorption of **water** (15% or so)
- Reabsorption of **bile salts** in the cecum
  - transported in blood to liver
- Absorption of **vitamins** produced by bacteria
- Absorption of **organic wastes**
Vitamins

- Are organic molecules
- Important as cofactors or coenzymes in metabolism
- Normal bacteria in colon make 3 vitamins that supplement diet
  - Vitamin K
  - Biotin
  - Pantothenic acid

Organic Wastes

- Bacteria convert bilirubin to urobilinogens and stercobilinogens:
  - Urobilinogens absorbed into bloodstream are excreted in urine
  - Urobilinogens and stercobilinogens in colon convert to urobilins and stercobilins by exposure to oxygen

Organic Wastes

- Bacteria break down peptides in feces and generate:
  - Ammonia:
    - As soluble ammonium ions
  - Indole and skatole:
    - Nitrogen compounds responsible for odor of feces
  - Hydrogen sulfide:
    - Gas that produces "rotten egg" odor
- Bacteria feed on indigestible carbohydrates (complex polysaccharides):
  - Produce flatus, or intestinal gas, in large intestine

Organic Wastes

- Gastroileal and gastroenteric reflexes: move materials into cecum while you eat
- Movement from cecum to transverse colon is very slow allowing hours for water absorption
- Peristaltic waves move material along length of colon [mass movements, stimulated by arrival of food into stomach and duodenum, force feces into rectum]
- Segmentation movements (hastral churning) mix contents of adjacent haustra
- Food in the stomach activates the gastrocolic reflex: Initiates peristalsis that forces contents toward the rectum

Movements of the Large Intestine

The Defecation Reflex

- Requires relaxation of internal and external anal sphincters
- Reflexes open internal sphincter, close external sphincter [when rectum receives feces]
- Opening external sphincter requires conscious effort
- [If this doesn’t occur, pressure will build until the external sphincter is forced open]

Elimination of Feces
Coordination of Secretion and Absorption

- Neural and hormonal mechanisms coordinate activities of digestive glands
- Regulatory mechanisms center around the duodenum where acids are neutralized and enzymes added

Neural Mechanisms involving CNS control

- Prepare digestive tract for activity (parasympathetic innervation)
- Inhibit gastrointestinal activity (sympathetic innervation)
- Coordinate movement of materials along digestive tract (the enterogastric, gastroenteric, and gastroileal reflexes)

Activities of Major Digestive Tract Hormones

- Neural and hormonal mechanisms coordinate activities of digestive glands
- Regulatory mechanisms center around the duodenum where acids are neutralized and enzymes added

Neural Mechanisms involving CNS control

- Prepare digestive tract for activity (parasympathetic innervation)
- Inhibit gastrointestinal activity (sympathetic innervation)
- Coordinate movement of materials along digestive tract (the enterogastric, gastroenteric, and gastroileal reflexes)

Duodenal Enteroendocrine Hormones

- Intestinal tract secretes peptide hormones with multiple effects in several regions of digestive tract and in accessory glandular organs
  - Secretin
    - Released when chyme arrives in duodenum
    - Increases secretion of bile and buffers by liver and pancreas
  - cholecystokinin (CCK)
    - Secreted in duodenum when chyme contains lipids and partially digested proteins
    - Accelerates pancreatic production and secretion of digestive enzymes
    - Ejects bile and pancreatic juice into duodenum
  - gastric inhibitory peptide (GIP)
    - Secreted when fats and carbohydrates enter small intestine
    - ALL of these also reduce gastric activity

Duodenal Enteroendocrine Hormones

- vasoactive intestinal peptide (VIP)
  - Stimulates secretion of intestinal glands
  - Dilates regional capillaries (remove absorbed nutrients)
  - Inhibits acid production in stomach
- Gastrin
  - Secreted by G cells in duodenum when exposed to incompletely digested proteins
  - Promotes increased stomach motility
  - Stimulates acid and enzyme production [stomach]
- Enterocrinin
  - Released when chyme enters small intestine
  - Stimulates mucin production by submucosal glands of duodenum (WHY?)

Intestinal Absorption

- It takes about 5 hours for materials to pass from duodenum to end of ileum
- Movements of the mucosa increases absorptive effectiveness:
  - stir and mix intestinal contents
  - constantly change environment around epithelial cells
- Microvilli: are moved by supporting microfilaments
- Individual villi are moved by smooth muscle cells
Digestion and Absorption

- Digestive system handles each nutrient differently:
  - large organic molecules must be digested before absorption can occur
  - water, electrolytes, and vitamins can be absorbed without processing, but may require special transport

Processing Nutrients

- The digestive system:
  - breaks down physical structure of food
  - disassembles component molecules
- Molecules released into bloodstream are
  - absorbed by cells
  - broken down to provide energy to make ATP
  - used to synthesize carbohydrates, proteins, and lipids

Digestive Enzymes

- Divided into classes by targets:
  - carbohydrases:
    - break bonds between simple sugars
  - proteases:
    - break bonds between amino acids
  - lipases:
    - separate fatty acids from glycerol
  - Nucleases
    - Brush border enzymes break nucleotides into: sugars, phosphates, and nitrogenous bases

Digestive Enzymes

- Break molecular bonds in large organic molecules:
  - carbohydrates, proteins, lipids, and nucleic acids in a process called hydrolysis
- Secreted by:
  - salivary glands
  - tongue
  - stomach
  - pancreas

Complex Carbohydrate Digestion

- Proceeds in 2 steps:
  1. carbohydrases (from salivary glands and pancreas)
  2. brush border enzymes
Complex Carbohydrate Digestion

- Salivary and pancreatic carbohydrases function at pH 6.7–7.5:
  - salivary amylase [actually can withstand much lower pH]
  - pancreatic alpha-amylase
- Break down large carbohydrates into:
  - disaccharides (2 simple sugars)
  - trisaccharides (3 simple sugars)

Lingual Lipase

- Begins triglycerides breakdown in mouth
- Continues for limited time within stomach
- Digests 20% of lipids before chyme enters duodenum

Brush Border Enzymes

- Fragment disaccharides and trisaccharides into monosaccharides (simple sugars):
  - maltase splits maltose into 2 glucose
  - sucrase splits sucrose into glucose and fructose
  - lactase splits lactose into glucose and galactose
- Intestinal epithelium absorbs monosaccharides:
  - by facilitated diffusion and cotransport
  - via a carrier protein
- [No lactase means lactose not digested or absorbed in small intestine: lactose intolerance]

Facilitated Diffusion and Cotransport

- Facilitated diffusion:
  - moves only 1 molecule or ion through cell membrane
  - does not require ATP
  - will not occur against opposing concentration gradient
  - Simple sugars transported into cell at apical surface (transcytosis):
    - diffuse through cytoplasm
    - reach interstitial fluid by facilitated diffusion across basolateral surfaces
    - diffuse into capillaries of villus for transport to liver
- Cotransport:
  - moves more than 1 molecule or ion at the same time
  - transported materials move in same direction
  - May require ATP
  - can occur against opposing concentration gradient
  - For simple sugars and amino acids: bring in sodium ions with them that must be ejected by the sodium–potassium exchange pump
- Either way, next step is:
  - Enter the capillary bed in the villi
  - Transported to the liver via the hepatic portal vein

Lipid Digestion

- Involves:
  - lingual lipase from glands of tongue
  - pancreatic lipase from pancreas
- Break off 2 fatty acids, leaving monoglycerides [plus fatty acids]
- These enzymes Water-soluble
- Attack only exposed surfaces of lipid drops

Bile Salts

- Improve chemical digestion:
  - by emulsifying lipid drops into tiny droplets
  - providing better access for pancreatic lipase
  - Breaks apart triglycerides:
    - to form fatty acids and monoglycerides
Lipid Absorption
• Intestinal cells absorb glycerol and fatty acids
• They synthesize new triglycerides from monoglycerides and fatty acids
• Triglycerides and other absorbed molecules are coated with proteins: creating chylomicrons
  [these are large, soluble lipid/protein particles]
• Intestinal cells secrete chylomicrons into interstitial fluid by exocytosis
• Enter lacteals (lymph) then to circulation and finally to liver after passing through the system once

Protein Digestion
• Complex and time-consuming:
  – mechanical processing in oral cavity (mastication) and chemical processing in stomach acid (HCl) begins digestion, allows proteolytic enzymes to attack proteins
  – Stomach:
    • Pepsin proteolytic enzyme
    • works at pH 1.5–2.0
    • breaks peptide bonds within polypeptide chain
  – Duodenum receives chyme:
    • enterokinase from small intestine [a brush border enzyme] triggers conversion of trypsinogen to trypsin
    • chymotrypsin, and carboxypeptidase also activated
    • When pH is adjusted to 7–8, pancreatic proteases begin working

Absorption of Amino Acids
• aminopeptidases, carboxypeptidases, and dipeptidases:
  – Brush border enzymes on epithelial surfaces of small intestine
  – break short peptide chains (created by proteolytic enzymes like pepsin) into individual amino acids
• After diffusing to basal surface of cell:
  – amino acids are released into interstitial fluid
  – by facilitated diffusion and cotransport

Electrolyte Absorption
• Most ions are actively absorbed along the length of small intestine
  – Na⁺ is coupled with absorption of glucose and amino acids
  – Ionic iron is transported into mucosal cells where it binds to ferritin
• Anions passively follow the electrical potential established by Na⁺
• K⁺ diffuses across the intestinal mucosa in response to osmotic gradients
• Ca²⁺ absorption:
  – is related to blood levels of ionic calcium
  – is regulated by vitamin D and parathyroid hormone (PTH)

Water Absorption
• Cells cannot actively absorb or secrete water
• All movement of water across lining of digestive tract:
  – 90% in S.I. (mostly ileum)
  – involves passive water flow down osmotic gradients
  – Water follows solutes out of the intestines and into the blood and lymph [because solutes are constantly diffusing out of the lumen]
  – Thus water uptake is coupled with solute uptake, and as water moves into mucosal cells, substances follow along their concentration gradients
Overview

- Digestive Anatomy
  - Common histology of GI tract
  - Tour through GI tract: Oral cavity → pharynx
    → esophagus → stomach → small intestine
    → large intestine
  - Accessory organs: liver, pancreas

- Digestive Physiology
  - Hormones and reflexes
  - Nutrient digestion and absorption (carbs, proteins, fats)

Digestive Secretion and Absorption

Vitamins

- Are organic compounds required in very small quantities
- Are divided in 2 major groups:
  - fat-soluble vitamins
    - Vitamins A, D, E, and K
    - Their structure allows them to dissolve in lipids
  - water-soluble vitamins
    - all B vitamins (common in milk and meats)
    - vitamin C (found in citrus)
    - All but 1 of water-soluble vitamins easily diffuse across digestive epithelium (which one does not?)