DIGESTIVE SYSTEM PHYSIOLOGY

The Digestive System

Oral cavity→ esophagus →
stomach → small intestine →
large intestine → rectum

Secretions are added by secretory epithelial cells and by **accessory glandular organs**

salivary glands, liver, gallbladder, pancreas

soupy mixture of food and secretions is known as **chyme**

GI tract is a long tube with muscular walls. There are muscle rings that separate tube into segments with different functions. Food moves by the waves of muscle contraction.

chewing and secretion of saliva

swallowed food passes into the esophagus, a narrow tube that travels through thorax to the stomach

Stomach continues digestion by mixing food with acid and enzymes.

Pylorus is the opening between stomach and small intestine. Thickened of smooth muscle relaxes to allow only small amount to pass at one time.

Most digestion takes place in small intestine. It is carried out by intestinal enzymes, aided by exocrine secretions from pancreas and liver.

Secretions from liver and pancreas enter duodenum through **ducts**.

a tonically contracted sphincter to keep pancreatic fluid and bile from entering small intestine except during a meal.

Digestion finishes in small intestine and digested nutrients and secreted fluids are absorbed there .
Leaving 1.5 L of chyme passes into large intestine and in colon.
Watery chyme becomes semisolid feces as water and electrolytes are absorbed.

Primary function of digestive system is to move nutrients, water and electrolytes from external environement to internal environment. Four basic processes:

SECRETION
Movement of material from cells into lumen or ECF

DIGESTION
Chemical and mechanical breakdown of food into absorbable units

ABSORPTION
Movement of material from GI lumen to ECF

MOTILITY
Movement of material through the GI tract as a result of muscle contraction

Three significant challenges that digestive system faces:

•Avoiding autodigestion: digestive enzymes must not digest the cells of GI tract itselt

•Mass balance: by matching fluid input with output , secreted fluid should be reabsorbed

•Defense: protecting from foreign invaders

INTERSTITIAL CELLS OF CAJAL (ICC) ARE THE PACEMAKERS OF THE GUT

Smooth muscle contraction occur automatically.
Graded depolarizations called **slow waves** produced by pacemaker cells called **ICC** produce action potentials in muscle cells.
Action potentials fire when slow wave potentials exceed threshold.
The force and duration of muscle contraction are directly related to the amplitude and frequency of action potentials.
3-12 waves / min

INTERSTITIAL CELLS OF CAJAL (ICC) ARE THE PACEMAKERS OF THE GUT

Slow waves begin automatically , ICCs spread to adjacent smooth muscle layers through gap junctions. The fastest pacemaker sets the pace for the entire group. When a slow wave reaches threshold, Ca channels open, Ca enters the cell fires one or more AP. Depolarization, just like cardiac cells, is the result of Ca entry. Ca netry initates muscle contraction. Longer duration, more Aps, greater contraction force.

GI smooth muscle exhibits different patterns of contraction

Between meals , when tract is largely empty, a series of contraction begins in the stomach and passes slowly from section to section, each series taking about 90 min to reach large intestine.
This pattern is known as **migrating motor complex**, is a housekeeping function that sweeps food remnants and bacteria out of the upper GI tract and intoo the large intestine.

GI smooth muscle exhibits different patterns of contraction

Peristalsis is a progressive waves of contraction that move from one section of the GI tract to the next.
Circular muscles contract just behind a bolus of food. This contraction pushes bolus food forward where the circular muscles are relaxed. Then receiving segment contracts so forward movement continues.

GI smooth muscle exhibits different patterns of contraction

Segments of intestine alternately contract and relax. In the contracting segments, circular muscles contract while longitudinal muscles relax. These contractions may occur randomly or at regular intervals. These contractions mix intestinal contents and keep them in contact with absorptive epithelium.

Regulation of GI Function

Enteric nervous system can act independently
GI peptides include hormones, neuropeptides and cytokines

Enteric nervous system

Work independently of the brain and sensory organs, responds to local stimuli in the same manner as lower level organisms.
Intrinsic neurons – neurons that lie completely within the gut wall
Neurotransmitters and neuromodulators – 30 different types that are similar to those in the brain. Examples- serotonin, vasoactive intestinal peptide, nitric oxide.
Support cells – serve a similar function as astroglia cells
Diffusion barrier – capillaries around the ganglia have reduced permeability as in the blood-brain barrier
Integrating center –signals are processed in the ENS and do not go out to the CNS for integration

Enteric nervous system

- **Short reflexes** are originated and are integrated **in ENS** without outside input, take care of local reflexes related to motility, secretion and growth.
- **Long reflexes** are integrated **in CNS** –classic neural reflex, receptors are in or outside GI tract. Feedforward and emotional reflexes. Parasympathetic excites and sympathetic inhibits.

Digestive Hormones

are secreted into the blood and transported throughout the body.

- Gastrin family –hormone families
  - Gastrin and (cholecystokinin)CCK -
- Secretin family –
  - Secretin, vasoactive intestinal peptide (VIP), gastric inhibitory peptide (GIP), and glucagon like peptide-1 (GLP-1) –
- Others -
  - Motilin –

Food processing is divided into three phases:

Cephalic Phase
Gastric Phase
Intestinal Phase

The Cephalic Phase

Digestive process in the body begin before food ever enters the mouth. Simply smelling, seeing or even thinking about food can make our mouths watery and stomach rumble. These long reflexes begin in the brain create a feedforward response known as cephalic phase of digestion. Anticipatory stimuli and stimulus of food in oral cavity begin secretion from stomach, small intestine or accesory glandular organs and increase motility.

The Cephalic Phase

This is the phase of digestion that begins with a stimulus processed by the cerebrum and an efferent response from the medulla oblongata. These are also digestive processes within the head (cephalic) region.

- **Chemical and mechanical digestion begins in the mouth** – chewing and mixing food with saliva
- **Salivary secretion under autonomic control** – sympathetic decreases and parasympathetic increases activity.
  - **Softens and lubricates food** – allows for better swallowing and taste detection
- **Chemical digestion: Salivary amylase and some lipase** – begin the breakdown of *starches* and very little fat
- **Saliva is protection as well** – lysozyme kills bacteria, antibodies disable bacteria and viruses, fluid rinses mouth
- **Chewing: mastication** – creates a bolus appropriate for swallowing

The Gastric Phase

- **Storage** - holding food in one organ and regulating the flow into the next organ to optimize absorption
  - **Stomach** – relaxes its walls to hold about 3.5 L daily, upper half holds food, lower half digest
- **Digestion** – changing food/drinks by chemical or mechanical digestion so that it can be absorbed
  - **Stomach** – Parietal cells secrete gastric acid and intrinsic factor, Chief cells secrete pepsinogens, gastric lipase,
    - **Acid, enzymes, and signal molecules** – the acid activates enzymes, denatures proteins, and targets pathogens, stomach releases signal molecules and digestion progresses
- **Protection** – acid kills pathogen and protects the body, the stomach protects its lining from the strong acid

Lumen of stomach is lined with mucus producing epithelium
Within mucosal layer there are gastric glands.
Gastric acid, enzymes, hormones and paracrine molecules are secreted.

Acid Secretion by Parietal Cells

Their pH is 7.2. It means they pump H+ against concentration gradient. H+ from water inside the cells is pumped into the stomach lumen by an H+*K+-ATPase exchanging K+ entering the cell. Cl- then follow electrical gradient created by H+ by moving through open chloride channels. Net result is the release of HCl

Gastric acid has multiple functions:

- It causes release and activation of pepsin, an enzyme digests protein.
- It triggers somatostatin release from D cells.
- It denaturates proteins.
- It helps kill bacteria etc.
- It inactivates salivary amylase, stopping carbohydrate digestion that began in the mouth.

Paracrine Secretion

Histamine is secreted by enterochromaffin-like cells in response to Ach or gastrin. It diffuses to parietal cells and stimulates acid secretion by combining with H2 receptors.

Somatostatin (SS), hypothalamic growth hormone, inhibiting hormone is secreted by D cells. It is the primary negative feedback signal for gastric phase secretion. It shuts off acid secretion by decreasing gastrin, histamine and pepsinogen secrretion.

Intrinsic factor is a protein secreted by parietal cells that secrete acid. In the lumen, it complexes with vit B12, a step needed for vitamin absorption.

The Gastric Phase

Two sources stimulate the secretion by stomach cells. G-cells are activated to release gastrin by stretching walls, protein presence, and vagus stimulation. Gastrin is inhibited by low pH and somatostatin

Enterochromaffin-like cells (ECL) is stimulated by gastrin and ENS to secrete histamine that stimulates parietal cells

Acid secretion by parietal cells stimulates a chemoreceptor that signals a short reflex to activate cheif cells to release pepisogen (protease)

D cells stimulated by low pH release somatostatin that inhibits secretion of gastrin, histamine, and pepsinogen. This process integrates cephalic and gastric secretion.

- Under normal conditions, gastric mucosa protects itself from autodigestion by acid and enzymes with a mucus-bicarbonate barrier.
- Mucous cells secrete both substances. The mucus forms a physical barrier and the bicarbonate creates a chemical buffer.

The Intestinal Phase

Once chyme passes into the small intestine, intestinal phase of digestion begins. Forward movement of chyme through the intestine must be slow enough to allow digestion and absorption to go to completion. Parasympathetic innervation and GI hormones gastrin and CCK promote intestinal motility; sympathetic innervation inhibits it.

Hepatic Portal System

Most fluid is absorbed in the small intestine

Venous blood from digestive tract does not go directly back to the heart. Instead it passes into the hepatic portal system. This specialized region of the circulation has two sets of capillary beds: one that picks up absorbed nutrients at the intestine, and another that delivers the nutrients directly to the liver.

Intestinal Secretions

- **Digestive enzymes –** by intestinal epithelium and exocrine pancreas
  - **Enteropeptidase** – converts inactive trypsinogen to trypsin that changes others into active forms
- **Bile –** made in liver and released from gall bladder, facilitates digestion of fats
- **Bicarbonate neutralizes gastric acid** – produced by the pancreas it is secreted into the doudenum as the chyme enters to neutralize the acid
- **Goblet cells secrete mucus for protection and lubrication** – the thin mucus layer also contains bicarbonate
- **Isotonic NaCl solution-** mixes with mucus to help lubricate the contents

Isotonic NaCl secretion

Crypt cells in the small intestine and colon secrete an isotonic NaCl solution.

CTFR; cystic fibrosis transmembrane conductance regulator

Bicarbonate Secretion

The bicarbonate secreted mostly from pancreas neutralizes the acid as it enters the duodenum.

Cells that produce bicarbonate have high concentrations of carbonic anhydrase (CA).

Bicarbonate produced from CO2 and water is secreted by an Cl-HO3 exhanger.

H+ reabsorbed helps balance HCO3- put into the blood when parietal cells secrete H+.

Bile is a nonenzymatic solution secreted from hepatocytes. Key component of bile are:

- Bile salts, which facilitate enzymatic fat digestion
- Bile pigments, such as bilirubin, which are the waste products of Hb degradation
- Cholesterol, which is excreted by feces.

The Intestinal Phase

- **Most digestion occurs in small intestine** – a samll amout of starch is brokendown in mouth and incomplete protein digestion in the stomach. When chyme enters the small intestine, protein digestion stops when pepsin is inactivated at higher pH. Pancreatic and brush border enzymes finish digestion of peptides, carbohydrates and fats.

Fat soluble vitamins are absorbed with fats in small intestine. Water soluble vitamins are absorbed by mediated transport. Vitamin B12 is an exception, is transported via intestinal transporter which recognized intrinsic factor.

Large intestine concentrates waste for excretion – 1.5L of unabsorbed chyme moves to large intestine, water is absorbed until there is about 0.1L of water left

Motility in large intestine– segmentation contractions continue

- **Mass movement triggers defecation** – colonic contraction that moves chyme along colon
- **Defecation reflex** –removes undigested feces
- **Digestion and absorption in large intestine** – bacteria perform fermention to digest complex carbs to provide energy molecules for colonocytes. They produce vitamin K and other vitamins and gas.

Diarrhea can cause dehydration – lose stools contain a large amount of unabsorbed water. Sometimes it is cause by osmotic diarrhea, or copious diarrhea or secretory diarrheas

Immune Function

Specialized M cells provide information about the contents of the lumen. Antigens bind to its receotrs and by transcytosis they are transported into the interstitial fluid where they meet eith macrophages and lymphocytes.