THE DIGESTIVE SYSTEM

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VI. Regulation of the Digestive System

I. Overview

- **The major parts of the digestive system:**

- Salivary glands
- Pharynx
- Esophagus
- Stomach
- Small Intestine
- Large Intestine
- Rectum
- Accessory digestive organs: liver, gallbladder, pancreas

- The major layers of the gastrointestinal tract:

- *Mucosa:*
    - inner layer
    - lines the gastrointestinal tract
    - simple columnar epithelilium

- *Submucosa:*
    - blood vessels
    - glands
    - nerve plexuses (Meissner's plexus)

- *Muscularis:*
    - peristalsis
    - nerve plexus (Myenteric plexus)

- *Serosa:*
    - Outer layer of connective tissue

- Functions of the GI system
- Motility: movement through the GI tract
- Digestion: breakdown of food or chime
- Secretion and absorption: across and epithelial layer either into the GI tract (secretion) or into blood (absorption)
- Storage and elimination:

II. Esophagus and Stomach

Esophagus

- From pharynx to stomach
- Salivary glands release mucus for lubrication, antimicrobial agents, and amylase to digest starch.
- epiglottis covers respiratory tract during swallowing
- At end of esophagus is the lower esophageal sphincter (LES)
- Propulsion of food occurs through peristalsis: contraction occurs behind the bolus of food and relaxation occurs ahead of the bolus of food.

Stomach

Functions:

1. store food
2. initiate digestion of proteins
3. kill bacteria with the strong acidity (low pH of the gastric juice)
4. make chyme

- Parts of the stomach:

a. Fundus
b. body
c. pyloric region (pyloric sphincter)

- material passed from the stomach to the small intestine is called the chyme.
- The gastric glands of the stomach contain several types of cells:

Cell Type	Secretions
Parietal cells	HCl; intrinsic factor
Chief cells	pepsinogen
Goblet cells	mucus
Enterochromaffin-like (ECL) cells	histamine;serotonin
D cells	Somatostatin
G cells	Gastrin

- pH of gastric juice is 2. The low pH of gastric juice:

1. denatures ingested proteins
2. optimum pH for pepsin activity is 2.0
3. at pH 2.0, weak pepsinogen enzymes digest each other to form pepsin

- The stomach digests only proteins, but not fats and carbohydrates
- There is basically no absoprtion in the stomach
- Acid secretion by parietal cell:

H^+ transport

1. H^+ is converted to CO_2 (blood)
2. CO_2 diffused into parietal cell
3. CO_2 is converted back to H^+
4. H^+ is transported into the GI lumen by a H^+-K^+-ATpase

Cl^- transport

1. Cl^- is transported into the parietal by a Cl^-/HCO_3^- transporter
2. Cl^- diffused into the GI lumen via a Cl^- channel

III. Small Intestine

- small intestine is from the pyloric sphincter to the ileocecal valve
- 12ft in length, small in diameter compared to large intestine
- regions of the small intestine
- duodenum: absoprtion of carbohydrates, lipids, amino acids, Ca^{2+}, iron
- jejuneum: absopriton of carbohydrates, lipids, amino acids, Ca^{2+}, iron
- ileum: absorption of bile salts, vitamin B_{12}, water electrolytes.
- Columnar epithelial cells
- Villi/ microvilli: increases surface area for absorption
- Core of villus
    - blood capillaries: absorption of monosaccharides, amino acids
    - lymphatic vessels (central lacteal): absorption of fats
- Brush border enzymes: dissacharidase, peptidase, phosphatase.

Absorption in the Small Intestine

Caloric content of food is derived mainly from:

- carbohydrates (50%)
- proteins (11-14%)
- lipids (36%-39%)

Carbohydrates

Begins as starch (polysaccharide) and then eventually digested into monosacharides for absorption.

Amylase: Starch digestion begins in the mouth (salivary amylase), and then continues in the duodenum (pancreatic amylase). Amylase digestion of starch produces maltose (disaccharide) and maltriose (trisaccharide) and oliosaccharides.

Brush border enzymes: hydrolyze maltose, maltriose, and oligosaccharides, sucrose, lactose to monosaccharides for absorption.

The three absorbable monosaccharides are glucose, galactose, and fructose.

Transport across epithelial layer

1. Lumen side: Na^{+} cotransporter with monosaccharides
2. Blood side: passive diffusion via a transporter

Proteins

Stomach: Somewhat digested to short-chain polypeptides by pepsin

Duodenum, jejunum: Digested to amino acids, di-peptides, tri-peptides by pancreatic juice enyzmes

Transport across epithelial layer

1. Lumen side: Na^+ co-transporter with amino acids, di-peptides, tri-peptides
2. Blood side: passive diffusion via a transporter

Fats

Absorption of fats takes place in the duodenum and are transported into the lymphatic system.

1. Fat droplets, mainly comprised of triglycerides are first emulsified by bile salts (see later section for discussion of bile salts). Emulsification makes the fat droplets smaller, making them more easily digested enzymatically.
2. Pancreatic lipase digests the smaller, emulsified fat droplets into free fatty acids and monoglycerides.
3. The free fatty acids and monoglycerides form micelles which migrate towards the brush border membrane. The micelles contain bile salts, lecithin, cholesterol and
4. The free fatty acids and monglycerides leave the micelle and enter the epithelial cell.
5. Inside the epithelial cell the free fatty acids and monoglycerides combine with protein to form chylomicrons (lipid + proteins).
6. The chylomicrons are secreted into the lymphatic system.

III. Large Intestine

- large intestine is from the ileocecal valve to the anus
- parts of the large intestine: ascending colon, transverse colon, descending colon, sigmoid colon, rectum, anal canal
- columnar epithelial cells, goblet cells, scattered lymphocytes, lympathic nodules
- contains no villi
- involved in absorption of water, electrolytes, vitamins.
- Contains bacteria which serve a number of functions
- absorption of vitamins (B and K)
- produce small fatty acids used as energy by GI epithelial cells
- help breakdown indigestible molecules
- final water content of feces is about 200 ml

Summary of Water transport in GI tract

	Amount of water entering	Amount reasborbed
Small Intestine	Ingestion: 1.5 liters secretions: 7-9 liters Total: 8.5-10.5 liters	6.5-9 liters
Large Intestine	1.5-2 liters	1.3-1.7 liters
Rectum	200 ml	

- Diarrhea is caused by many problems. The end result in a decrease in water absorption, so the stools are very watery. This can lead to severe dehydration.
- Cholera: Na^+ secretion into GI lumen
- Celiac Sprue: damage to GI wall
- Lactose intolerance: osmolarity of the GI lumen
- Defecation reflex: opening of the external anal sphincter due to pressure in the rectum.

III. Liver, Gallbladder and Pancreas

A. Liver and Gallbladder

Anatomy

- Connected to gallbladder via bile duct and then to small intestine
- Contains sinusoidal capillaries which are permeable to most substances
- Unusual vasculature: G.I. capillaries → Liver → vena cava. This allows filtration of ingested substances.
- Enterohepatic circulation: from liver via bile duct to small intestine and then from small intestine back through portal vein to liver

Major functions

1. production and secretion of bile
2. detoxication of blood
3. secretion and storage of glucose
4. production of albumin

Liver clears substances via the bile duct in a similar manner to the way the kidney clears substances into the nephron.

Production and secretion of bile

- Components of bile:
- bile pigment or bilirubin: removes hemoglobin breakdown products
- bile salts: adds in fat absorption
- phoshpholipids, cholesterol, inorganic ions.

Gallbladder stores bile. Bile entering gallbladder is controlled by the sphincter of Odii.

B. **Pancreas**

Endocrine versus exocrine function:

- endocrine: involves secretion into blood (inside the body, endo): insulin and glucagons (endocrine function not discussed in lecture)
- exocrine: involves secretion into GI system (outside the body, exo).

Pancreatic juice contains:

- water: H_2O
- bicarbonate: HCO_3^-
- amylase: digests starch
- trypsin: digests protein
- lipase: digests fatty acids

I. **Control of the Digestive System**

- Digestive system is controlled by:

- automatic activity
- autonomic nerves
- hormones

- Innervation of the gastrointestinal tract

- *parasympathetic*: rest and digest

- *sympathetic*: fight and flight
- *enteric nervous system*: intrinsic nervous system in GI system

Autonomic Branch	Effect on GI system
parasympathetic	motility, open valves
sympathetic	↓ motility, close valves

Three Phases in Control of Gasric Function

A. Cephalic Phase
B. Gastric Phase
C. Intestinal Phase

A. Cephalic Phase:

Regulation by the vagus nerve: lasts approximately 30 minutes.

The vagus nerve is activated by sight, smell, taste of food.

Activation of the vagus nerve:

1. indirectly causes the parietal cells to secrete HCl
2. directly stimulates chief cells to secreate pepsinogen to digest proteins

A. Gastric Phase

Stimulated by

1. distension of the stomach (i.e. amount of chyme)
2. chemical nature of the chyme

The goal of this phase is to release acid and proteolytic enzymes into the stomach.

Feedback loops

- A positive feedback loop occurs in which peptides cause acid and pepsinogen to be released and this in turn causes more peptides in the stomach, which causes acid and pepsinogen to be released, etc..

- A negative feedback loop occurs in which the low pH of the stomach inhibits gastrin secretion by the G cells which results in less acid secretion.

- Stimulation of HCl secretion:

1. Vagus nerve and amino acids in the stomach lumen stimulate gastrin release by G-cells
2. Gastrin stimulates histamine release by ECL cells

3. Histamine stimulates HCl secretion by parietal cells.

Stimulus for gastric phase

- peptides (particularly phenylalanine and tyrptophan) stimulate pepsinogen and acid secretion
- glucose and fats do not stimulate acid secretion.

A. Intestinal phase

Inhibition of gastric activity due to:

- neural reflex: stretch of the duodenum inhibits gastric motility and secretion
- hormone: fat in the chyme stimulates an inhibitory hormone. It is not clear what this hormone is. Potential candidates include gastric inhibitory peptide, somatostatin, cholecystokinin, glucagon-like.

Control of Intestine

- Chyme in duodenum stimulates

1. gastric inhibition
2. pancreatic secretion
3. bile secretion

- Pancreatic juice secretion is controlled by secretin and cholecystokinin (CCK).

- Secretin: stimulated by a drop in duodenal pH — results in HCO_3^- secretion by pancreas and bile secretion
- Cholecystokinin: stimulated by fats and proteins in duodenum — results in pancreatic secretion of enzymes and bile secretion.