Physiology
Unit 4

DIGESTIVE PHYSIOLOGY
In Physiology Today

Two men walk into a bar.
One man orders H₂O.
The other says, "I'll have H₂O, too."
The second man dies.
Functions

- **Motility**
  - Ingestion
  - Mastication
  - Deglutition
  - Peristalsis
- **Secretion**
  - 7 liters/day!
  - Exocrine/endocrine
- **Digestion**
- **Absorption**
Digestion of Carbohydrates

- Average intake is 250-300 g/day
- Amylase
  - Salivary, pancreatic
  - Products: maltose, short chains of glucose
- Brush border enzymes
  - Products: glucose, galactose, fructose

<table>
<thead>
<tr>
<th>Class</th>
<th>Examples</th>
<th>Made of</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polysaccharides</td>
<td>Starch</td>
<td>Glucose</td>
</tr>
<tr>
<td></td>
<td>Cellulose</td>
<td>Glucose</td>
</tr>
<tr>
<td></td>
<td>Glycogen</td>
<td>Glucose</td>
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<tr>
<td>Disaccharides</td>
<td>Sucrose</td>
<td>Glucose-fructose</td>
</tr>
<tr>
<td></td>
<td>Lactose</td>
<td>Glucose-galactose</td>
</tr>
<tr>
<td></td>
<td>Maltose</td>
<td>Glucose-gluose</td>
</tr>
<tr>
<td>Monosaccharides</td>
<td>Glucose</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fructose</td>
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<tr>
<td></td>
<td>Galactose</td>
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</tbody>
</table>
Absorption of Carbohydrates

- Luminal absorption
  - *Glucose*
  - *cotransport with Na*
    into enterocytes
- Basolateral absorption
  - Monosaccharides enter blood via *facilitated diffusion*
Digestion of Proteins

- Require 40-50g of protein/day
  - Supply essential amino acids
  - We consume 70-90 g/day

- Stomach
  - *Pepsin*
    - Products are short chain polypeptides

- Small intestines from pancreas
  - *Trypsin, chymotrypsin*
    - Products are short chain polypeptides
  - *Carboxypeptidase*
    - Products are free amino acids

- Small Intestines from brush border enzymes
  - *Aminopeptidase*
    - Products are free amino acids
Absorption of Proteins

• Luminal absorption
  – Free amino acids enter enterocytes by *counter-transport with Na*\(^+\)
  – Short polypeptides (2 or 3 amino acids) enter enterocytes by *counter-transport of H*\(^+\)

• Basolateral absorption
  – Free amino acids enter blood by *facilitated diffusion*
Digestion of Fat

- Daily intake 70-100 g/day (mostly triglycerides)
- Emulsification by bile salts
- Pancreatic lipase
  - Monoglyceride + 2 fatty acids
- Formation of micelles by bile salts
Absorption of Fat

• **Luminal Absorption**
  – Monoglycerides and fatty acids enter enterocytes by *diffusion*

• **Basolateral absorption into lacteals**
  – *Exocytosis of chylomicrons*
  – Chylomicrons contain triglycerides, phospholipids, cholesterol, fat-soluble vitamins
Lipid Transport

• From lymphatics to thoracic duct
• Free fatty acids and glycerol into tissues
• Leftovers to liver
  – Remnant particles contain cholesterol
  – Combined with apoproteins *(lipid binding protein)* to produce VLDL’s
    – Deliver triglycerides to other organs
Lipoproteins

• Lipid & protein complexes
  – Transport cholesterol & triglycerides in blood
  – Protein allows hydrophobic lipids to remain in suspension

• Five classes: Based on density, molecular weight, size, chemical composition
  • Chylomicrons
  • VLDL
  • IDL
  • LDL
    – High levels associated with increased risk CVD
  • HDL
    – Low levels associated with increased risk of CVD
    – Best profile = high HDL, low LDL
Absorption of Vitamins

• Fat-soluble vitamins
  – Vitamins A, D, E, K
  – *Exocytosis in chylomicrons*

• Water-soluble vitamins
  – Vitamins B, C
  – Absorbed by *diffusion* or *mediated transport*

• Vitamin $B_{12}$
  – Binds to intrinsic factor
  – *Endocytosis* (in ileum) into enterocytes
Vitamin $\text{B}_{12}$
Absorption of Water and Minerals

• Water is most abundant substance in *chyme*
  – 8 L of ingested and secreted water enter the small intestine each day!
  – 1.5 L make it to the large intestine
  – 80% absorbed in small intestine

• Minerals
  – Na$^+$
  – HCO$_3^-$
  – Cl$^-$
  – Small concentrations K$^+$, Mg$^{2+}$, Ca$^{2+}$, Fe$^{3+}$, Zn$^{2+}$, I$^-$
Regulation of Gastrointestinal Processes

• Regulation of the conditions of the lumen of the tract (the outside of the body)

• Governed by the volume and composition of the luminal contents rather than the nutritional state of the body (the inside of the body)
Basic Principles

1. Distention of the lumen wall (volume of contents)
2. Chyme osmolarity (solute concentration)
3. Chyme acidity
4. Chyme concentrations
   - Monosaccharides
   - Fatty acids
   - Peptides
   - Amino acids
Neural Regulation

- Enteric Nervous System (ENS)
  - **Myenteric plexus**
    - Influences smooth muscle activity
  - **Submucosal plexus**
    - Influences secretory activity
Neural Regulation

- Neural activity in one plexus influences the activity of the other
- Stimulation at one point in the plexus can lead to impulses that are conducted both up and down the tract
- Neural reflexes independent of CNS
- CNS can influence motility and secretion of the tract
Hormonal Regulation

• Hormones that control the GI system are secreted by cells scattered throughout the epithelium of the stomach and small intestine
• One surface of each endocrine cell is exposed to the lumen of the tract
• Chemicals in chyme stimulate the cell to secrete its hormones from the opposite side of the cell into the blood
Hormonal Regulations

• Each hormone participates in a feedback control system that regulates some aspect of the luminal environment.

• Most GI hormones affect more than one type of target cell.

• Best understood peptide GI Hormones
  – Gastrin
  – Cholecystokinin (CCK)
  – Secretin
  – Glucose-dependent insulino tropic peptide (GIP)
Gastrin

• **Endocrine cell location:**
  – G cells of the antrum of stomach

• **Stimulus for release**
  – Protein in stomach
  – Parasympathetic nervous system

• **Actions**
  – Stimulates
    • Stomach: (+) acid secretion and motility
    • Pancreas: (+) enzyme secretions
    • Intestines: (+) motility in ileum and colon
Cholecystokinin (CCK)

• Endocrine cell location: small intestine
• Stimulus for release
  – amino acids, fatty acids in small intestine
• Actions
  – Stimulates
    • Pancreas: (+) enzyme secretion
    • Gall bladder: (+) contraction
  – Potentiates
    • Pancreas: (+) bicarbonate secretion
    • Liver: (+) bicarbonate secretion
  – Inhibits
    • Stomach: (-) acid secretion, gastric motility
Secretin

- Endocrine cell location: small intestine
- Stimulus for release
  - Acid in small intestine
- Actions
  - Stimulates
    - Pancreas: (+) bicarbonate secretion
    - Liver: (+) bicarbonate secretion
  - Inhibits
    - Stomach: acid secretion, gastric motility
Glucose-Dependent Insulinotrophic Peptide

• Endocrine cell location: small intestine
• Stimulus for release
  – glucose, fat in the small intestine
• Actions
  – Stimulates
    • Pancreas: (+) insulin secretion
Stomach

• Function
  – Initiates protein digestion
  – Kills bacteria
  – Intrinsic factor
    • Secreted by parietal cells
    • Needed for Vitamin B$_{12}$ absorption in ileum
  – Absorption
    • Water
    • Alcohol
    • Aspirin

• 3 functions of pH in stomach
  – Denature ingested protein
  – Convert pepsinogen to pepsin
    • Digests proteins
  – Destroy bacteria
Gastric Glands

- **Goblet cells**
  - mucus
- **Parietal cells**
  - HCl
  - Intrinsic factor
- **Chief cells**
  - Pepsinogen
- **Argentaffin cells**
  - Serotonin
  - Regulate intestinal movements
- **G cells**
  - Gastrin
Pancreas

- Pancreatic acini
  - Pancreatic juice
    - water
    - bicarbonate
    - digestive enzymes
  - Activation by enterokinase
# Pancreatic Enzymes

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Substrate</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trypsin, chymotrypsin, elastase</td>
<td>Proteins</td>
<td>Break peptide bonds in proteins to form peptide fragments</td>
</tr>
<tr>
<td>Carboxypeptidase</td>
<td>Proteins</td>
<td>Splits off terminal amino acid from carboxyl end of protein</td>
</tr>
<tr>
<td>Lipase</td>
<td>Fats</td>
<td>Splits off two fatty acids from triglycerides, forming free fatty acids and monoglycerides</td>
</tr>
<tr>
<td>Amylase</td>
<td>Polysaccharides</td>
<td>Splits polysaccharides into glucose and maltose</td>
</tr>
<tr>
<td>Ribonuclease, deoxyribonuclease</td>
<td>Nucleic acids</td>
<td>Split nucleic acids into free mononucleotides</td>
</tr>
</tbody>
</table>
Energy Regulation by Islets of Langerhans

- Three cell types produce peptide hormones
  - Beta cells: insulin
    - Stimulates cellular uptake of glucose
    - In liver, activates glycogenesis
    - Stimulates lipid synthesis
    - Stimulates cellular uptake of amino acids
  - Alpha cells: glucagon
    - Encourages liberation of reserves
    - Prevents glucose uptake by liver, muscle, adipose
  - Delta cells: somatostatin
    - Not sure
Regulation of Insulin and Glucagon Secretion

- **Effects of glucose and amino acids**
  - Increase in plasma glucose
    - Stimulates b cells
    - Inhibits a cells
  - Decrease in plasma glucose
    - decreased insulin production
    - increased glucagon production
  - Meals high in protein
    - stimulates insulin
  - Meals high in protein and low in carbohydrate
    - stimulates glucagon
    - result: increase in blood glucose and increased incorporation of amino acids into tissues
Regulation of Insulin and Glucagon Secretion

• **Effects of autonomic nerves**
  – Parasympathetic activation
    • increased insulin
  – Sympathetic activation
    • increased glucagon, inhibits insulin
  – **Goal**: Keep blood glucose between
  – 50-170mg/100ml
    • higher = glycosilation; lower = brain damage
Functions of the Liver

- Exocrine
- Endocrine
- Clotting functions
- Synthesizes plasma proteins
- Organic metabolism
- Cholesterol metabolism
- Excretory and degradative functions
Exocrine & Endocrine Functions

**Exocrine Functions**
- Synthesis and secretion of bile salts
  - 250-1500ml/day
- Adds bicarbonate rich solution to bile

**Endocrine Functions**
- Secretes IGF-1
  - promotes cell division
- Forms T₃ from T₄
- Secretes angiotensinogen
  - Increases BP
  - Stimulates aldosterone secretion
- Metabolizes hormones
- Secretes immune cytokines
Clotting and Plasma Proteins

• Produces
  – Prothrombin
  – Fibrinogen
  – Plasma albumin
    • Regulates blood volume
  – Acute phase proteins
  – Binding proteins
  – Lipoproteins
Organic Metabolism

- Converts plasma glucose to glycogen and triglycerides
- Converts amino acids to fatty acids
- Produces triglycerides and secretes them as lipoproteins
- Gluconeogenesis and glycogenolysis
- Converts fatty acids into ketones
- Produces urea
Cholesterol Metabolism/Excretory & Degradative Functions

• Synthesizes cholesterol
• Converts plasma cholesterol into bile salts
  – Bile salts needed for vitamin K absorption
• Excretes toxins via bile
• Destroys old erythrocytes
• ...and lots, lots more!