

## ii. Digestive System

### ii. Digestive System - Digestion, Absorption and Metabolism

## Introduction to the Digestive System

### 1. General Function

- The digestive system converts complex macromolecules in ingested food into absorbable units (monosaccharides, amino acids, fatty acids) that can be utilized for energy, growth, and repair.
- **Accessory organs** (salivary glands, liver, gallbladder, pancreas) secrete enzymes, bile, or other substances essential for efficient digestion.

### 2. Organization of the GI Tract

- **Mouth** → **Pharynx** → **Esophagus** → **Stomach** → **Small Intestine (duodenum, jejunum, ileum)** → **Large Intestine (colon)** → **Rectum** → **Anus**
- Four major layers in the GI tract wall: **mucosa**, **submucosa**, **muscularis externa** (with circular and longitudinal layers), and **serosa** (visceral peritoneum).

### 3. Regulatory Systems

- **Enteric Nervous System (ENS)**: "Gut brain" with local reflexes (myenteric plexus for motility, submucosal plexus for secretions and blood flow).
- **Autonomic Innervation**: Parasympathetic stimulation (e.g., vagus nerve) generally increases digestive activity; sympathetic stimulation reduces it.
- **GI Hormones**: Gastrin, Secretin, Cholecystokinin (CCK), Gastric Inhibitory Peptide (GIP), Motilin, etc., coordinate secretions, motility, and appetite.

## Digestion

### Mechanical and Chemical Digestion

#### 1. Mastication (Chewing)

- In the mouth, teeth grind food into smaller pieces, while saliva moistens it.
- **Salivary Enzymes**: Salivary amylase initiates carbohydrate digestion; lingual lipase may begin minimal lipid hydrolysis (especially in infants).

#### 2. Swallowing (Deglutition)

- Coordinated by the swallowing center in the medulla; the epiglottis prevents aspiration into the trachea.
- **Esophagus** uses **peristalsis** to propel the bolus into the stomach.

#### 3. Stomach Digestion

- **Gastric secretions**: Hydrochloric acid (HCl) from parietal cells denatures proteins and activates pepsinogen → pepsin; intrinsic factor is essential for vitamin B12 absorption.
- **Mechanical churning** creates chyme. Regulated emptying into the duodenum prevents overload of the small intestine.

#### 4. Small Intestine Digestion

- **Major site** of enzymatic digestion and absorption.
- **Pancreatic Secretions**: Enzymes (pancreatic amylase, lipases, proteases like trypsin and chymotrypsin) and bicarbonate to neutralize acidic chyme.
- **Bile** (from liver, stored in gallbladder): Emulsifies fats, facilitating micelle formation.
- **Brush Border Enzymes** (on intestinal microvilli): Disaccharidases (lactase, sucrase, maltase), peptidases, etc., finalize nutrient breakdown.

### Key Digestion Pathways

- **Carbohydrates**: Polysaccharides → Oligosaccharides → Disaccharides → Monosaccharides (glucose, fructose, galactose).
- **Proteins**: Polypeptides → Oligopeptides → Amino acids.
- **Lipids**: Triglycerides → Monoglycerides + Free fatty acids (via pancreatic lipase). Emulsification by bile is critical.

## Absorption

### Sites and Mechanisms

#### 1. Small Intestine

- **Primary region** for nutrient absorption—particularly the jejunum and, to some extent, the duodenum and ileum.
- **Surface Area Amplification:** Mucosal folds, villi, and microvilli (brush border) dramatically increase absorptive capacity.

#### 2. Transport Mechanisms

- **Carbohydrates:** Monosaccharides (glucose, galactose) actively transported via SGLT1 ( $\text{Na}^+$ -cotransporter), fructose via GLUT5 (facilitated diffusion). All exit enterocytes by GLUT2 into the bloodstream.
- **Proteins:** Amino acids and di/tripeptides often enter via proton or  $\text{Na}^+$ -dependent carriers (PepT1).
- **Lipids:** Form micelles (with bile salts). At the enterocyte surface, lipids diffuse in, are re-esterified to triglycerides, and packaged into **chylomicrons** which enter lacteals (lymphatic vessels) before reaching the systemic circulation.
- **Vitamins and Minerals:**
  - Fat-soluble vitamins (A, D, E, K) co-absorb with dietary lipids.
  - Water-soluble vitamins are mostly absorbed by specific transporters or diffusion.
  - Mineral absorption (iron, calcium) is tightly regulated; e.g., iron regulated by hepcidin, calcium influenced by vitamin D.

#### 3. Large Intestine

- Primarily absorbs water and electrolytes ( $\text{Na}^+$ ,  $\text{Cl}^-$ ).
- Resident microbiota ferment undigested carbohydrates, producing short-chain fatty acids which can be absorbed and utilized as energy sources.

### Regulation and Pathophysiological Considerations

- **Hormonal Modulation:** CCK, secretin, GIP, etc., coordinate secretory and absorptive processes.
- **Neural Influences:** Local reflexes and autonomic pathways fine-tune motility, secretion.
- **Malabsorption Syndromes:** Examples include celiac disease (villous atrophy), chronic pancreatitis (enzyme insufficiency), Crohn's disease.

## Metabolism

Once absorbed, nutrients enter metabolic pathways. **Metabolism** comprises all biochemical reactions, including **catabolism** (breakdown for energy) and **anabolism** (synthesis of complex molecules).

### Carbohydrate Metabolism

#### 1. Glycolysis

- Cytoplasmic process splitting glucose into pyruvate; net 2 ATP and 2 NADH per glucose.
- Under anaerobic conditions, pyruvate is reduced to lactate (lactic acid fermentation).

#### 2. Pyruvate Oxidation and TCA Cycle (Citric Acid Cycle)

- In the mitochondrial matrix, pyruvate is converted to acetyl-CoA, which enters the TCA cycle.
- Yields  $\text{CO}_2$ , NADH, FADH<sub>2</sub>, and GTP/ATP.

#### 3. Oxidative Phosphorylation (Electron Transport Chain)

- NADH, FADH<sub>2</sub> donate electrons to the ETC in the mitochondrial inner membrane.
- Proton gradient drives ATP synthase, generating the majority of ATP in aerobic respiration.

#### 4. Glycogenesis and Glycogenolysis

- Glucose is stored as glycogen mainly in the liver and muscle.
- Glycogen breakdown can release glucose (liver) into the bloodstream or supply muscle cells during exercise.

### Lipid Metabolism

#### 1. Beta-Oxidation

- Fatty acids are transported to mitochondria, broken down to acetyl-CoA units.
- High energy yield per molecule of fat but requires sufficient oxygen.

## 2. **Ketogenesis and Ketolysis**

- In carbohydrate deficit (fasting, low-carb diets, uncontrolled diabetes), excess acetyl-CoA in the liver forms ketone bodies (acetone,  $\beta$ -hydroxybutyrate).
- Extrahepatic tissues can reconver ketone bodies to acetyl-CoA for ATP production.

## 3. **Lipid Transport**

- Chylomicrons, VLDL, LDL, HDL move lipids through blood.
- Hormone-sensitive lipase in adipose tissue mobilizes fatty acids for oxidation.

## Protein Metabolism

### 1. **Amino Acid Catabolism**

- Deamination removes nitrogen (excreted as urea), and the carbon skeleton enters gluconeogenesis or TCA cycle.

### 2. **Transamination**

- Transfer of amino groups, key for synthesizing non essential amino acids and for nitrogen disposal.

## Integration of Metabolism

### 1. **Fed State (Postprandial)**

- Insulin promotes glucose uptake, glycogen, and triglyceride synthesis.
- Amino acids used for protein synthesis or deaminated if in excess.

### 2. **Fasting State**

- Glucagon drives glycogenolysis, gluconeogenesis, lipolysis; prolonged fasting shifts to ketone production.
- Muscle protein can be catabolized to supply substrates for gluconeogenesis.

### 3. **Hormonal Regulation**

- **Insulin** (anabolic hormone): Lowers blood glucose, promotes storage.
- **Glucagon** and **Epinephrine** (catabolic hormones): Increase blood glucose, mobilize energy stores.
- **Cortisol**: Affects protein and glucose metabolism, stress response.

## Concluding Remarks

From **mechanical and chemical digestion** in the upper GI tract to **selective absorption** in the small intestine and **fermentation** in the large intestine, the human digestive system is finely tuned to optimize nutrient breakdown and uptake. These nutrients fuel **metabolic pathways** in cells across the body, interfacing with **endocrine** and **nervous** control to maintain **homeostasis** and support essential processes like growth, repair, and energy expenditure.

Understanding the coordinated interplay of **digestion, absorption, and metabolism** is fundamental for addressing nutritional deficiencies, metabolic disorders (e.g., diabetes, obesity), and GI diseases, and forms the basis for many therapeutic interventions and dietary strategies.

## Key Takeaways

- **Mechanical and Chemical Digestion** reduce food to absorbable units.
- **Small Intestine** is the primary site of nutrient absorption, aided by brush border enzymes and bile/emulsification.
- **Metabolic pathways** (glycolysis, TCA cycle,  $\beta$ -oxidation, etc.) under hormonal regulation integrate nutrients into energy production and biosynthesis.
- **Clinical Relevance**: Disorders in any stage (digestion, absorption, metabolic regulation) can compromise nutrient status and systemic health.