## 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)

- o 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)

- o 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 (HCI) 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.
- o 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.

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## **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 (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 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 (Na^+, 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

- o 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)

- o In the mitochondrial matrix, pyruvate is converted to acetyl-CoA, which enters the TCA cycle.
- Yields CO\_2, NADH, FADH\_2, and GTP/ATP.

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

- $\circ~$  NADH, FADH\_2 donate electrons to the ETC in the mitochondrial inner membrane.
- o 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.
- $\circ \ \ \text{Glycogen breakdown can release glucose (liver) into the bloodstream or supply muscle cells during exercise.}$

## **Lipid Metabolism**

## 1. Beta-Oxidation

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- $\circ\;$  Fatty acids are transported to mitochondria, broken down to acetyl-CoA units.
- o 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 (acetoacetate, β-hydroxybutyrate).

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• Extrahepatic tissues can reconvert ketone bodies to acetyl-CoA for ATP production.

#### 3. Lipid Transport

- o 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

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

## Integration of Metabolism

### 1. Fed State (Postprandial)

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

#### 2. Fasting State

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

### 3. Hormonal Regulation

- o Insulin (anabolic hormone): Lowers blood glucose, promotes storage.
- o **Glucagon** and **Epinephrine** (catabolic hormones): Increase blood glucose, mobilize energy stores.
- o **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, β-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.

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