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 (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**
   - 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 CO_2, NADH, FADH_2, and GTP/ATP.
3. **Oxidative Phosphorylation (Electron Transport Chain)**
   - NADH, FADH_2 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 (acetoacetate, β-hydroxybutyrate).
   - Extrahepatic tissues can reconvert 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, 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.