AI-01911 Weight Loss vs Food Intake Ratio

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Will a human lose weight 50% of weight if a food intake is reduced by 50%? What is the metabolic ratio or relationship between weight loss and food intake. I'm trying to simplify the science of weight loss to human. In third world countries, humans there don't have the over-weight problem.

Understanding weight loss in humans involves understanding the balance between energy intake and expenditure, rather than a simple proportional reduction in body weight based solely on reduced food intake.

Here's a breakdown based on the provided sources:

- **Will a human lose 50% of weight if a food intake is reduced by 50%?**
  A 50% reduction in food intake would lead to weight loss, but it's **not directly proportional** to a 50% loss of body weight. The initial rapid weight loss experienced when significantly reducing food intake is often due to **loss of body water**, not primarily fat. This water loss occurs because muscle tissue and liver glycogen, which are about 80% and 70% water respectively, are degraded to supply energy in the early phases of a diet. As the body adapts to a prolonged caloric deficit (fasting or starvation), it prioritizes preserving vital functions, which involves shifting fuel utilization patterns to spare protein. Therefore, while significant weight loss would occur, it would not necessarily translate to a 50% reduction in overall body weight.
- **What is the metabolic ratio or relationship between weight loss and food intake?**
  The fundamental relationship between weight loss and food intake is governed by
  caloric balance.

- **Caloric Content of Fuels**: The energy content of the major dietary fuels is approximately:
  - **Carbohydrate: 4 kcal/g**
  - **Protein: 4 kcal/g**
  - **Fat (triacylglycerols): 9 kcal/g**
  - **Alcohol: 7 kcal/g**
- **Weight Loss Rate**: To lose weight, a person must consume fewer calories than they expend. The sources state that a person loses **approximately 1 lb of weight for every 3,500 calories expended more than consumed**. For instance, consuming 1,000 calories less than expended per day would lead to a loss of about 2 lb per week.
- **Fuel Mobilization**: When food intake is less than the body's energy needs (negative caloric balance), the body draws on its **fuel stores** to supply the remaining calories. These stores include:
  - **Fat (triacylglycerol)**: The major fuel store, mainly in adipose tissue. It is a very efficient store due to its high caloric content (9 kcal/g) and low water content (15% water in adipose tissue).
  - **Glycogen**: Stored as carbohydrate in muscle and liver, though in much smaller quantities than fat. Liver glycogen helps maintain blood glucose levels between meals, while muscle glycogen supplies energy for muscle contraction during exercise.
  - **Protein**: Body protein, particularly in muscle, also serves as a fuel store to some extent, especially during fasting. However, only a limited amount of body protein can be degraded before vital functions are compromised.

- **Simplifying the science of weight loss to human**:
  The core principle of weight loss is achieving a **negative caloric balance**, meaning the **kilocalories consumed in food are less than the daily energy expenditure (DEE)**.
  - **Daily Energy Expenditure (DEE)** is composed of three main factors:

        - **Resting Metabolic Rate (RMR) / Basal Metabolic Rate (BMR)**: This is the energy required to sustain basic life functions, such as breathing, heart pumping, brain function, and biochemical pathways, at rest. It is affected by factors like body size, age, sex, body temperature, and thyroid status.
        - **Physical Activity**: The energy expended through movement and exercise. This can vary significantly between individuals based on their activity levels.
        - **Diet-Induced Thermogenesis (DIT)**: The energy required for the digestion, absorption, distribution, and storage of nutrients after eating. This component is roughly 10% of ingested calories and is often simplified or ignored in general calculations.
    - In essence, if you consistently take in fewer calories than your body burns, your body will tap into its stored fuels (fat, glycogen, and eventually protein) to make up the deficit, leading to weight loss.
- **In third world countries, humans there don't have the over-weight problem.**
  The provided sources do not make a direct statement about the prevalence of overweight issues in "third world countries." However, they do extensively discuss
  malnutrition, particularly protein-energy malnutrition, which is characterized by an inadequate intake of nutrients and can lead to being underweight.
    - **Malnutrition** is described as occurring in the United States among children in poverty, the elderly, and individuals with poor dietary choices, often leading to conditions like anemia, mild protein and energy malnutrition, and growth retardation.
    - Specific forms of protein-energy malnutrition mentioned include:
        - **Kwashiorkor**: Characterized by protein deficiency, leading to hypoalbuminemia, anemia, edema, pot belly, and hair loss.
        - **Marasmus**: Refers to prolonged protein-calorie malnutrition, especially in young children. Percy Veere is diagnosed with Grade I protein-energy malnutrition (marasmus), while Ann O'Rexia has Grade III malnutrition due to severe calorie and protein restriction.

- These descriptions focus on the consequences of insufficient food and nutrient intake, leading to underweight conditions, rather than overweight problems.

1. How does the human body meet its basic metabolic needs, and what are the four main types of metabolic pathways involved?

The human body has two fundamental metabolic requirements: synthesizing essential cellular components not obtained through diet and protecting its internal environment from toxins and external changes. To achieve these, it employs four primary metabolic pathways:

- **Fuel Oxidative Pathways:** These convert dietary fuels (carbohydrates, fats, proteins) into energy (ATP) for various functions like movement, thought, and reproduction. This is a catabolic process, breaking down larger molecules.
- **Fuel Storage and Mobilization Pathways:** These store excess dietary energy, primarily as triacylglycerol (fat) in adipose tissue and glycogen (carbohydrate) in muscle and liver. These stored fuels can then be mobilized when not eating or when increased energy is needed, for instance, during exercise.
- **Biosynthetic Pathways (Anabolic Pathways):** These construct larger molecules from smaller components, such as synthesizing proteins from amino acids. The diet must supply essential amino acids, vitamins, and fatty acids that the body cannot synthesize itself. Fuel storage is also considered an anabolic process.
- **Detoxification or Waste Disposal Pathways:** These pathways remove toxins from the diet, air, drugs, or those generated internally from metabolism. Dietary components with no value are called xenobiotics and are disposed of.

Cooperation between tissues and responses to environmental changes are managed through transport and intercellular signaling pathways, often involving hormones like insulin.

2. What are the primary dietary fuels, their caloric content, and how are excess fuels managed by the body?

The major dietary fuels are carbohydrates, fats, and proteins.

- **Carbohydrates:** Provide approximately 4 kcal/g. They are digested into monosaccharides like glucose, which is the predominant sugar in blood.
- **Proteins:** Provide approximately 4 kcal/g. They are broken down into amino acids.
- **Fats (Triacylglycerols):** Provide approximately 9 kcal/g, more than twice the energy yield of carbohydrates or proteins, due to their lower oxygen content (meaning they are more reduced and yield more energy upon oxidation). They are digested into fatty acids and glycerol.
- **Alcohol (Ethanol):** Provides approximately 7 kcal/g.

Any dietary fuel exceeding the body's immediate energy needs is stored. Fats are mainly stored as triacylglycerol in adipose tissue, glycogen is stored in muscle and liver, and protein is stored to some extent in muscle. When fasting, fuel is drawn from these stores to provide energy.

3. How does the body's fuel utilization change during fasting and prolonged starvation, and what is the role of the liver in these states?

The body undergoes significant metabolic shifts during fasting and starvation to maintain blood glucose levels, particularly for glucose-dependent tissues like the brain and red blood cells.

- **Fasting State (2-4 hours after a meal to overnight):**
- Blood glucose levels fall, leading to a decrease in insulin and an increase in glucagon.
- **Liver Glycogenolysis:** Liver glycogen is degraded to release glucose into the blood. This is the primary initial source of blood glucose.
- **Lipolysis:** Adipose triacylglycerols are mobilized, releasing fatty acids and glycerol into the blood. Fatty acids become the major fuel oxidized by most tissues (muscle, liver, kidney).
- **Ketone Body Production:** The liver partially oxidizes fatty acids into ketone bodies, which are then released into the blood and can be used as fuel by other tissues (muscle, kidney). The liver itself cannot oxidize ketone bodies.

- **Gluconeogenesis:** The liver begins synthesizing new glucose from non-carbohydrate precursors like lactate (from red blood cells/exercising muscle), glycerol (from adipose tissue lipolysis), and amino acids (primarily from muscle protein breakdown). Amino acid nitrogen is converted to urea in the liver for excretion.
- **Starvation State (3 or more days of fasting):**
- **Protein Sparing:** To conserve vital functions, the body decreases the rate of muscle protein degradation. This is achieved because the brain, sensing the high levels of ketone bodies (which continue to rise as the liver produces them from fatty acids), begins to oxidize them for a significant portion of its energy needs. This reduces the brain's demand for glucose, consequently lowering the liver's rate of gluconeogenesis from amino acids.
- **Fatty Acid Reliance:** Fatty acids remain the major fuel for most tissues, including muscle.
- **Decreased Urea Production:** Due to reduced protein degradation and gluconeogenesis from amino acids, urea production in the liver also decreases.

The liver is crucial in both states, maintaining blood glucose homeostasis through glycogenolysis and gluconeogenesis, and providing alternative fuels (ketone bodies) during prolonged starvation.

4. What are lipoproteins, and what are their roles in the digestion, absorption, and transport of dietary and endogenous lipids in the body?

Lipoproteins are soluble particles that transport lipids (which are insoluble in water) through the bloodstream. They consist of a core of hydrophobic lipids (like triacylglycerols and cholesterol esters) surrounded by a monolayer of amphipathic lipids (phospholipids and cholesterol) and proteins called apoproteins.

Their key roles in lipid metabolism include:

- **Chylomicrons:**
- **Production:** Formed in intestinal epithelial cells from digested dietary fats (fatty acids and 2-monoacylglycerol).

- **Function:** Primarily transport dietary triacylglycerols from the intestine, through the lymphatic system, and into the blood circulation to various tissues. They also carry cholesterol and fat-soluble vitamins.
- **Maturation:** Acquire apoproteins (CII and E) from HDL in the lymph and blood to become "mature" chylomicrons.
- **Digestion and Fate:** In capillaries of muscle and adipose tissue, lipoprotein lipase (LPL) (activated by ApoCII) digests their triacylglycerols, releasing fatty acids for energy (muscle) or storage (adipose tissue). The remaining chylomicron remnants are taken up by the liver via ApoE receptors and degraded.
- **Very Low Density Lipoprotein (VLDL):**
- **Production:** Synthesized in the liver, mainly from excess dietary carbohydrates which are converted to fatty acids and then triacylglycerols.
- **Function:** Transports endogenously synthesized triacylglycerols from the liver to peripheral tissues.
- **Intermediate Density Lipoprotein (IDL):**
- **Production:** Formed in the blood as VLDL loses triacylglycerols due to LPL activity.
- **Fate:** Can be taken up by the liver or further converted to LDL.
- **Low Density Lipoprotein (LDL):**
- **Production:** Derived from IDL.
- **Function:** Rich in cholesterol and cholesterol esters; serves as the major carrier of cholesterol to peripheral tissues and the liver.
- **High Density Lipoprotein (HDL):**
- **Production:** Synthesized in the liver and intestine.
- **Function:** Important for "reverse cholesterol transport," moving excess cholesterol from peripheral tissues back to the liver. Also exchanges proteins and lipids with chylomicrons and VLDL, aiding in their maturation.

During fasting, adipose tissue releases fatty acids and glycerol. Fatty acids bind to albumin for transport and are oxidized for energy by various tissues or converted

to ketone bodies by the liver. Glycerol travels to the liver for gluconeogenesis.

5. What are the key functions of the liver in maintaining overall body health and metabolism?

The liver is a central metabolic hub with numerous vital functions:

- **Central Receiving and Recycling Center:** It processes all compounds absorbed from the digestive tract (via the portal vein) and receives blood from the general circulation (hepatic artery). It retrieves useful compounds for metabolism and distribution, and removes toxic or useless compounds (xenobiotics) for excretion.
- **Nutrient Metabolism and Distribution:** It metabolizes dietary carbohydrates (glucose, galactose, fructose), storing excess as glycogen or converting it to fatty acids for storage as triacylglycerols (in VLDL). It is the primary site for the catabolism of all amino acids, converting their carbon skeletons to glucose, fatty acids, or ketone bodies, and their nitrogen to urea.
- **Detoxification and Inactivation:** The liver is the main site for degrading xenobiotic compounds (drugs, pollutants, natural food toxins). It performs Phase I reactions (oxidation, hydroxylation, hydrolysis) and Phase II reactions (conjugation with charged groups like sulfate or glycine) to make these substances more water-soluble for excretion. The cytochrome P450 system is crucial in these processes. It also inactivates many of the body's own metabolic waste products.
- **Blood Glucose Regulation:** It maintains blood glucose homeostasis by performing glycogenolysis (breaking down glycogen) and gluconeogenesis (synthesizing glucose from non-carbohydrate precursors) during fasting, and synthesizing glycogen and fatty acids during fed states.
- **Urea Synthesis:** It is the primary organ for synthesizing urea from toxic ammonia, which is then excreted by the kidneys.
- **Ketone Body Formation:** It is the only organ that produces ketone bodies from fatty acids, serving as an alternative fuel for other tissues (especially the brain during starvation), though the liver itself cannot utilize them for energy.
- **Nucleotide Biosynthesis:** It can synthesize and salvage all ribonucleotides and deoxyribonucleotides, supplying them to other cells that may have lost

this capacity.

- **Blood Protein Synthesis:** It is the primary site for synthesizing most circulating proteins, including albumin (important for osmotic pressure and transport) and clotting factors. Compromised liver function can lead to hypoproteinemia, edema, and clotting issues.
- **Glycoprotein and Proteoglycan Synthesis:** It synthesizes these complex molecules, essential for various cellular functions and structural integrity, using a variety of sugar and amino acid precursors.
- **Pentose Phosphate Pathway:** Highly active in the liver, this pathway generates NADPH (essential for biosynthetic reactions like fatty acid and cholesterol synthesis, and detoxification via cytochrome P450) and five-carbon sugars for nucleotide synthesis.

6. How is muscle metabolism regulated differently from liver metabolism, especially concerning glucose and fatty acid utilization?

Muscle metabolism, while sharing many pathways with the liver, has distinct regulatory mechanisms tailored to its energy demands, particularly during activity:

- **Glucose Utilization:**
- **PFK-2 Regulation:** Unlike liver PFK-2, which is inhibited by phosphorylation (leading to decreased glycolysis during fasting), skeletal muscle PFK-2 is not regulated by phosphorylation. Cardiac PFK-2 is actually *activated* by insulin-stimulated protein kinase, allowing the heart to increase glycolysis when blood glucose is high.
- **Glucose Transport (GLUT4):** Glucose transport into muscle cells is stimulated by both insulin and exercise, due to the translocation of GLUT4 transporters to the cell membrane. This ensures adequate glucose uptake when needed.
- **Glycogen Storage and Mobilization:** Muscle glycogen stores are primarily for the muscle's own use and are not released into the blood. Muscle glycogenolysis is activated by AMP (indicating low energy) and calcium (during contraction), and also by epinephrine during intense exercise. Muscle glycogen is less affected by glucagon compared to liver glycogen.

- **Fatty Acid Metabolism:**
- **Acetyl CoA Carboxylase (ACC-2):** Muscle cells contain ACC-2 (different from liver's ACC-1), which produces malonyl CoA. Malonyl CoA inhibits carnitine palmitoyl transferase I (CPT-I), blocking fatty acid entry into mitochondria for oxidation. This mechanism ensures that fatty acid oxidation is inhibited when glucose is abundant.
- **Malonyl CoA Decarboxylase (MCoADC):** Muscle also has MCoADC, which converts malonyl CoA back to acetyl CoA, relieving the inhibition of CPT-I. Both ACC-2 and MCoADC are regulated by AMP-activated protein kinase (AMP-PK), which inhibits ACC-2 and activates MCoADC when energy levels are low (high AMP). This allows muscle to rapidly switch to fatty acid oxidation during periods of high energy demand or fasting.
- **No Fatty Acid Synthesis:** Unlike the liver, muscle cells do not synthesize fatty acids; their ACC-2 is solely for regulatory purposes of fatty acid oxidation.
- **Creatine Phosphate:** Muscle cells uniquely use creatine phosphate as a rapidly accessible store of high-energy bonds, allowing for quick ATP regeneration at the onset of exercise before other oxidative processes fully activate.

These differences enable muscle to effectively manage its fuel sources for contraction, adapting to varying conditions from rest to intense exercise, and preserving glucose for glucose-dependent tissues during fasting.

7. What are the major cell types of the nervous system, and how do they interact to support neural function, especially considering the blood-brain barrier?

The nervous system comprises two main types of cells: neurons and neuroglia (supporting cells).

- **Neurons:** These are the primary cells for transmitting electrical signals (nerve impulses). They consist of a cell body (soma), dendrites (receiving information), and axons (transmitting information). Signals are transmitted across synapses via neurotransmitters. Neurons are terminally differentiated, limiting their ability to repair.
- **Neuroglia (Glial Cells):** These support and protect neurons.

- **Astrocytes (CNS):** Star-shaped cells providing physical and nutritional support for neurons. They guide neuronal migration, regulate the extracellular ionic environment, and take up/metabolize nutrients and waste. They can provide lactate to neurons as a carbon source.
- **Oligodendrocytes (CNS):** Form the myelin sheath around multiple axons in the CNS, acting as electrical insulation to increase signal conduction speed. They have limited replication capacity if damaged, leading to demyelination.
- **Schwann Cells (PNS):** Similar to oligodendrocytes, but myelinate only one axon in the peripheral nervous system. They also clean cellular debris in the PNS.
- **Microglial Cells:** Smallest glial cells, acting as immune cells (macrophages) of the nervous system, destroying invaders and phagocytosing debris.
- **Ependymal Cells:** Ciliated cells lining brain and spinal cord cavities, secreting and circulating cerebrospinal fluid (CSF), which protects the CNS and removes metabolic wastes.

The Blood-Brain Barrier (BBB): This highly restrictive barrier protects the brain from harmful blood-borne substances.

- **Structure:** Composed of tightly joined endothelial cells lining brain capillaries, lacking fenestrations and transpinocytosis mechanisms found in other capillaries. It's further protected by a continuous collagen-containing basement membrane and astrocyte foot processes.
- **Permeability:** Allows passive diffusion of lipophilic substances, water, oxygen, and carbon dioxide. Other molecules require specific transport systems.
- **Fuel Transport:** Glucose, the brain's primary fuel, is transported by GLUT-1 transporters. Monocarboxylic acids (lactate, acetate, pyruvate, ketone bodies) are transported by a slower, stereospecific system. During starvation, ketone body transporters are upregulated, allowing the brain to use them as an alternative fuel.
- **Amino Acid and Vitamin Transport:** Large neutral amino acids use a single transporter, leading to competition. Small neutral amino acids are largely restricted to maintain neurotransmitter balance. Vitamins have specific transporters.

- **Enzymatic Barrier:** Endothelial cells contain drug-metabolizing enzymes and active efflux pumps (P-glycoproteins) to prevent potentially harmful substances from entering the brain.

The BBB's selective permeability ensures that the brain maintains a stable internal environment, while glial cells provide crucial support and maintenance for neurons within this protected space.

8. How are major neurotransmitters synthesized and inactivated in the nervous system, and what factors can impact their metabolism?

Neurotransmitters, crucial for nerve impulse transmission, are primarily small nitrogen-containing molecules or neuropeptides. Their synthesis, storage, release, and inactivation are tightly regulated.

General Features of Small Nitrogen-Containing Neurotransmitter Metabolism:

- **Synthesis:** Most are synthesized from amino acids or intermediates of glycolysis and the TCA cycle in the presynaptic terminal. Synthesis rate generally correlates with neuronal firing.
- **Storage:** Neurotransmitters are actively transported into storage vesicles via ATP-requiring pumps (often linked to proton gradients, like VMAT2 for catecholamines).
- **Release:** Triggered by nerve impulses and Ca2+ influx, leading to exocytosis of vesicles into the synaptic cleft.
- **Termination of Action:** Achieved by reuptake into the presynaptic terminal, uptake into glial cells, diffusion away from the synapse, or enzymatic inactivation (e.g., in the synaptic cleft, presynaptic terminal, adjacent astrocytes, or brain capillary endothelial cells).

Examples of Neurotransmitter Metabolism:

- **Dopamine, Norepinephrine, Epinephrine (Catecholamines):**
- **Synthesis:** Derived from L-tyrosine. The rate-limiting step is tyrosine hydroxylation (requires BH4). Subsequent steps involve decarboxylation (requires pyridoxal phosphate) and further hydroxylation/methylation.

- **Inactivation:** Primarily by reuptake and enzymatic degradation by monoamine oxidase (MAO) and catechol-O-methyltransferase (COMT). MAO-A deaminates norepinephrine and serotonin, while MAO-B acts on phenylethylamines. COMT methylates catecholamines. Both MAO and COMT actions result in various degradation products.
- **Clinical Relevance:** Overproduction (e.g., in pheochromocytomas) causes hyperadrenergic symptoms. MAO inhibitors, if taken with tyramine-rich foods, can lead to hypertensive crises due to increased norepinephrine release.
- **Serotonin:**
- **Synthesis:** From tryptophan, involving hydroxylation (requires BH4) and decarboxylation (same enzyme as DOPA).
- **Inactivation:** Primarily by MAO-A.
- **Clinical Relevance:** Involved in mood and appetite. SSRIs (selective serotonin reuptake inhibitors) block reuptake, increasing serotonin levels in the synapse.
- **Histamine:**
- **Synthesis:** From histidine by histidine decarboxylase (requires pyridoxal phosphate).
- **Inactivation:** In the brain, primarily by methylation by histamine methyltransferase (requires SAM), followed by oxidation by MAO-B. In peripheral tissues, by diamine oxidase.
- **Clinical Relevance:** Excitatory neurotransmitter in the brain; peripheral effects mediate allergic responses. Antihistamines block receptors, causing drowsiness if they cross the BBB.
- **Acetylcholine:**
- **Synthesis:** From acetyl CoA (primarily from glucose oxidation) and choline (from diet or phosphatidylcholine hydrolysis) by choline acetyltransferase.
- **Inactivation:** Rapidly inactivated by acetylcholinesterase in the synaptic cleft.
- **Clinical Relevance:** Major neurotransmitter at neuromuscular junctions. Acetylcholinesterase inhibitors (e.g., nerve gases, some dementia drugs)

prolong its action. Deficiency of thiamine or inherited pyruvate dehydrogenase deficiency can impair its synthesis.

- **Glutamate and GABA:**
- **Glutamate:** Excitatory. Synthesized from α-ketoglutarate (TCA cycle) or glutamine. Removed from synapse by high-affinity uptake systems in nerve terminals and glial cells.
- **GABA:** Inhibitory. Synthesized by decarboxylation of glutamate by glutamic acid decarboxylase (GAD). Recycled via the GABA shunt, involving glial cells converting glutamate to glutamine for transport to neurons.
- **Clinical Relevance:** Imbalances in glutamate or GABA are implicated in many neurological disorders. Drugs like tiagabine inhibit GABA reuptake to treat epilepsy.

Factors Impacting Neurotransmitter Metabolism:

- **Nutrient Availability:** Deficiencies in cofactors like pyridoxal phosphate (B6), thiamine-pyrophosphate (B1), vitamin B12, and folate can impair synthesis.
- **Blood-Brain Barrier:** Limits precursor entry, requiring the brain to synthesize many components locally.
- **Energy Status:** Hypoglycemia or hypoxia severely impair ATP production and neurotransmitter synthesis, leading to brain dysfunction.
- **Genetic Factors:** Mutations affecting enzymes or transporters can lead to neurological disorders (e.g., PKU affecting amino acid transport, GAD autoantigens in type 1 diabetes).
- **Drugs and Toxins:** Many drugs target neurotransmitter systems (e.g., MAO inhibitors, SSRIs), and toxins can interfere with inactivation (e.g., nerve gases).

Detailed Timeline

I. General Metabolic Processes & Dietary Intake

- **Continuous:** Humans require a constant supply of energy (calories) from dietary carbohydrates, fats, and proteins for functions like movement, thinking, and reproduction.

- **Continuous:** Cells synthesize necessary compounds not supplied by diet.
- **Continuous:** Detoxification pathways remove toxins (xenobiotics) from diet and air, or generated internally.
- **Continuous:** Waste disposal pathways excrete xenobiotics and metabolic waste products.
- **Continuous:** Anabolic pathways synthesize larger molecules from smaller components (e.g., protein synthesis, fuel storage).
- **Continuous:** Catabolic pathways break down larger molecules into smaller components (e.g., fuel oxidation).
- **Continuous:** Essential amino acids, essential fatty acids, vitamins, minerals, and water must be supplied by the diet.
- **Continuous:** Dietary components are digested, absorbed, and transported via blood and intercellular signaling.
- **Continuous:** The body maintains fuel stores (triacylglycerol/fat in adipose tissue, glycogen in muscle/liver, protein in muscle) to provide energy between meals or during increased demand.
- **Continuous:** Energy balance is maintained when caloric intake equals daily energy expenditure (DEE). Weight is lost if intake < DEE, and gained if intake > DEE.
- **Continuous:** Resting Metabolic Rate (RMR)/Basal Metabolic Rate (BMR) measures energy for basic life functions, affected by body size, age, sex, temperature, thyroid status, pregnancy, and genetics.
- **Continuous:** Physical activity contributes to DEE, varying greatly between individuals.
- **Continuous:** Diet-induced thermogenesis (DIT) or thermic effect of food (TEF) accounts for energy used to digest, absorb, distribute, and store nutrients (approx. 10% of ingested calories).
- **Continuous:** Body Mass Index (BMI) is a preferred method for assessing healthy weight (18.5-24.9 desirable).

- **Continuous:** Metabolism of lipids and proteins occurs, with liver playing a central role in processing and distributing nutrients, detoxifying compounds, regulating blood glucose, and synthesizing various essential molecules.
- **Continuous:** Muscle cells utilize stored glycogen, circulating glucose, fatty acids, and amino acids for energy, with different regulation than liver metabolism.
- **Continuous:** Creatine phosphate serves as a readily available high-energy phosphate reserve in muscle cells.
- **Continuous:** The nervous system relies heavily on glucose and oxygen, maintaining the blood-brain barrier to restrict entry of potentially harmful substances.
- **Continuous:** Neurotransmitters are synthesized, stored, released, and inactivated to transmit nerve signals.

II. Specific Events and Conditions

- **Early 1900s - 1960s:** Increase in fat content in the typical American diet.
- **1962:** 12.8% of the U.S. population had a BMI ≥ 30 (clinically obese).
- **1970s (approx.):** Photograph taken of a patient with anorexia nervosa (Fig. 3.6).
- **1977:** Evan Applebod successfully loses weight for the only time in his life.
- **1980:** Obesity prevalence in the U.S. increased to 14.5% (BMI ≥ 30).
- **1980s (since):** Incidence of Reye's syndrome in the U.S. decreased dramatically due to awareness of aspirin dangers in children.
- **1997:** Evan Applebod becomes concerned about joint pain and peripheral neuropathy due to his weight. He is prescribed Redux.
- **1997 (late):** Redux is withdrawn from the market due to toxicity (heart valve abnormalities). Evan Applebod is placed on Prozac but regains weight within a year.
- **1998:** Obesity prevalence in the U.S. increased to 22.5% (BMI ≥ 30), with an additional 30% pre-obese (BMI 25.0-29.9).

- **2000:** "Dietary Guidelines for Americans" prepared, merging various recommendations.
- **Present:** Will Sichel experiences severe right upper abdominal pain, vomiting, jaundiced sclerae, and tea-colored urine, leading to a suspected diagnosis of acute cholecystitis or gallstone in the common bile duct.
- **Present:** Al Martini continues alcohol abuse and poor eating, developing severe upper mid-abdominal pain, vomiting, fever, rapid heart beat, and mild reduction in blood pressure, consistent with acute pancreatitis.
- **Present:** Jean Ann Tonich, after a period of sobriety, resumes heavy drinking, leading to chronic alcohol-induced cirrhosis, constant upper mid-abdominal pain, increasing girth, vomiting "coffee ground" material, and bright red blood.
- **Present:** Amy Biasis, a missionary, presents with abrupt onset of fever, chills, and severe pain in the right upper quadrant radiating to her right shoulder, vomiting, and an enlarged, tender liver, diagnosed as amoebiasis (amoebic liver abscesses).
- **Present:** Katie Colamin, a dress designer, experiences alarming heart palpitations, pounding headache, and profuse sweating, with severe hypertension, suggestive of a pheochromocytoma (tumor of the adrenal medulla).
- **Present:** Percy Veere, a 59-year-old school teacher, experiences increasing fatigue and loss of appetite after his wife's death, leading to dehydration and malnutrition; admitted to hospital with BMI 17.5, low hemoglobin, serum iron, folic acid, vitamin B12, and albumin. Diagnosed with mild protein-energy malnutrition (marasmus).
- **Present:** Otto Shape, a 25-year-old medical student, is "out-of-shape" and gaining weight (BMI 27); decides to consult a physician for weight reduction.
- **Present:** Ivan Applebod, a 56-year-old accountant, is morbidly obese (BMI 37.9) with central obesity, slightly elevated blood pressure, and high serum cholesterol; referred to a weight reduction center.
- **Present:** Ann O'Rexia, a 23-year-old buyer, is convinced she is overweight despite being underweight (BMI 15.5); engages in excessive exercise and seeks a weight reduction diet. Later, she is hospitalized with severe

malnutrition (BMI 13.7) secondary to anorexia nervosa, with decreased body core temperature, blood pressure, pulse, and elevated serum ketone bodies.

- **Ongoing (Hospitalization):** Percy Veere's fasting blood glucose is 72 mg/dL; serum ketone body level 110 µM (slightly elevated); no ketone bodies in urine. CHI is 85%. Later, he resumes normal eating and shows signs of recovery.
- **Ongoing (Hospitalization):** Ann O'Rexia's blood glucose is 65 mg/dL; serum ketone body concentration is 4,200 µM; urine test positive for ketone bodies. She is placed on enteral nutrition and psychotherapy.
- **Ongoing (Hospitalization):** Will Sichel's ultrasound shows a large gallstone. Scheduled for ERCP.
- **Ongoing (Hospitalization):** Al Martini's serum amylase and lipase are elevated. His stools become bulky, glistening, yellow-brown, and foul-smelling (steatorrhea), consistent with pancreatic insufficiency.
- **Ongoing (Hospitalization):** Amy Biasis's CT scan shows cystic masses in her liver. Serum antibodies against *Entamoeba histolytica* are strongly reactive. Treatment with nitroimidazole amoebicides initiated.
- **Ongoing (Hospitalization):** Katie Colamin's plasma and urine catecholamine levels are elevated. She is prescribed phenoxybenzamine and scheduled for surgical resection of the tumor. Post-surgery, she is symptom-free with normal blood pressure.

III. Post-Meal to Starvation Metabolic Stages

- **~1 hour after meal:** Blood glucose levels begin to fall.
- **2-4 hours after meal (Fasting State begins):** Blood glucose returns to basal levels (80-100 mg/dL). Insulin levels decline, glucagon levels rise.
- **Fasting State:** Liver glycogenolysis and adipose lipolysis (releasing fatty acids and glycerol) begin. Fatty acids become major fuel. Glucose-dependent tissues (brain, red blood cells) continue to oxidize glucose. Liver partially oxidizes fatty acids to ketone bodies. Muscle, kidney, and other tissues oxidize fatty acids and ketone bodies. Liver starts gluconeogenesis from lactate, glycerol, and amino acids (from muscle protein).

- **~12 hours (Overnight Fast/Basal State):** Liver glycogen stores are significantly reduced (approx. 80g remaining). Gluconeogenesis becomes increasingly important. Fatty acids are the major fuel for most tissues; liver produces ketone bodies.
- **~30 hours (Prolonged Fasting/Starved State begins):** Liver glycogen stores are depleted. Gluconeogenesis is the sole source of blood glucose.
- **3-5 days of fasting (Starved State):** Muscle decreases ketone body use, relying mainly on fatty acids. Ketone body concentration in blood rises significantly. Brain begins to oxidize ketone bodies for energy, reducing glucose need. Liver decreases gluconeogenesis rate, sparing muscle protein. Urea production decreases.
- **Extended Periods (Starvation):** Humans can survive extended periods due to these fuel utilization shifts. Death occurs with significant loss of body weight (approx. 40%) or body protein (30-50%), typically at very low BMIs (13 for men, 11 for women).

Cast of Characters

- **Percy Veere:** A 59-year-old school teacher who developed severe reactive depression, fatigue, and loss of appetite after his wife's sudden death and a child moving away. Admitted to the hospital with dehydration and malnutrition, diagnosed with mild protein-energy malnutrition (marasmus), iron deficiency anemia, and low folic acid and vitamin B12 levels. His BMI was 17.5 (underweight). He eventually resumed normal eating patterns.
- **Otto Shape:** A 25-year-old medical student who was formerly athletic but is now "out-of-shape" and gaining weight (BMI 27, overweight). He consults a physician for weight reduction and plans to improve his diet and exercise habits, using online tools to track his intake.
- **Ivan Applebod:** A 56-year-old accountant who has been morbidly obese for years (BMI 37.9, obese), exhibiting central obesity ("apple shape"). He leads a sedentary lifestyle with occasional gardening, elevated blood pressure, and high cholesterol. He is referred to a weight reduction center.
- **Evan Applebod:** Ivan Applebod's brother, who is severely overweight (425 pounds). He experienced joint pain and peripheral neuropathy. He took the

weight-loss drug Redux, lost significant weight, but regained it after Redux was withdrawn due to toxicity, even after switching to Prozac.

- **Ann O'Rexia:** A 23-year-old buyer for a clothing store who, despite being severely underweight (BMI 15.5, later 13.7), believes she is overweight. She engages in excessive exercise and seeks a weight reduction diet. She is diagnosed with early anorexia nervosa, experiences amenorrhea, and is hospitalized for severe malnutrition.
- **Will Sichel:** A patient who experienced mild back and lower extremity pain, likely due to sickle cell crises, but then developed severe upper abdominal pain, vomiting, and jaundice, indicating acute cholecystitis or a gallstone in the common bile duct.
- **Al Martini:** An individual with a history of alcohol abuse and poor eating habits. He developed severe upper abdominal pain, vomiting, and signs of acute pancreatitis, leading to steatorrhea (fat-laden stools) due to decreased pancreatic enzyme secretion.
- **Jean Ann Tonich:** A patient with a history of alcohol abuse who resumed heavy drinking after a period of sobriety. She developed chronic alcohol-induced cirrhosis, leading to constant abdominal pain, distention, and vomiting blood ("coffee ground" material and bright red blood), indicative of a severe, diffuse hepatic disease with complications like esophageal varices and hepatic encephalopathy.
- **Amy Biasis:** A 23-year-old missionary who presented with acute fever, chills, and severe right upper quadrant abdominal pain. Her symptoms and travel history in Belize led to a diagnosis of amoebiasis (amoebic liver abscesses).
- **Katie Colamin:** A 34-year-old dress designer who experienced episodic heart palpitations, pounding headaches, and profuse sweating, accompanied by severe hypertension. She was diagnosed with a pheochromocytoma, a tumor of the adrenal medulla that secretes excessive catecholamines, and underwent successful surgical resection.
- **Rena Felya:** A 9-year-old girl who developed a severe sore throat, fever, and then swollen eyes and legs with "Coca-Cola" colored urine, elevated blood pressure, and protein/red blood cells in her urine. Diagnosed with acute poststreptococcal glomerulonephritis.

II. Quiz

Instructions: Answer each question in 2-3 sentences.

1. What are the two fundamental metabolic requirements humans must meet for survival, and what broad categories of metabolic pathways are involved in meeting these?
2. Compare and contrast anabolic and catabolic pathways, providing an example of each from the provided text.
3. Why are triacylglycerols a more efficient fuel storage form compared to carbohydrates like glycogen, considering both caloric content and water association?
4. Briefly explain the role of the liver during the initial stages of fasting, focusing on glucose and fatty acid metabolism.
5. During prolonged fasting (starvation), how does the brain's fuel usage change, and what is the metabolic consequence of this shift for muscle tissue?
6. Describe the sequential process of dietary triacylglycerol digestion in the intestinal lumen, highlighting the roles of bile salts and pancreatic lipase.
7. What are chylomicrons, where are they assembled, and what is their primary function in lipid transport?
8. Explain the dual role of the liver in xenobiotic metabolism, differentiating between Phase I and Phase II reactions.
9. How do muscle cells quickly regenerate ATP during the onset of exercise before increased blood flow and aerobic metabolism can fully kick in?
10. Describe the key structural features of the blood-brain barrier and how they restrict the entry of substances into the central nervous system.

III. Answer Key (Quiz)

1. Humans must synthesize cellular components not from diet and protect against toxins/external changes. Fuel oxidative, fuel storage/mobilization, biosynthetic, and detoxification pathways are involved.

2. Anabolic pathways synthesize larger molecules from smaller ones (e.g., protein synthesis from amino acids, fuel storage). Catabolic pathways break down larger molecules into smaller components (e.g., fuel oxidative pathways converting fuels to energy).
3. Triacylglycerols are more efficient because they yield 9 kcal/g (more than double carbohydrates' 4 kcal/g) and adipose tissue, where they are stored, contains very little water (about 15%), making the fuel storage lighter and more compact.
4. During initial fasting, the liver first degrades its glycogen stores (glycogenolysis) to supply blood glucose. Concurrently, adipose tissue mobilizes triacylglycerols via lipolysis, releasing fatty acids for other tissues and glycerol for hepatic gluconeogenesis.
5. During prolonged fasting, the brain shifts to oxidizing ketone bodies as a major fuel. This reduces the brain's demand for glucose, leading to a decreased rate of gluconeogenesis in the liver and thus sparing muscle protein degradation.
6. Dietary triacylglycerols are first emulsified by bile salts in the small intestine, increasing their surface area. Then, pancreatic lipase, aided by colipase, hydrolyzes the emulsified triacylglycerols into free fatty acids and 2-monoacylglycerol.
7. Chylomicrons are soluble lipoprotein particles assembled in intestinal epithelial cells from re-synthesized triacylglycerols, apoB-48, phospholipids, and cholesterol esters. Their primary function is to transport dietary lipids from the intestine into the lymphatic system and eventually the bloodstream.
8. The liver performs Phase I reactions (e.g., oxidation, hydroxylation) to introduce reactive sites into lipophilic xenobiotics, making them more polar. Subsequently, Phase II reactions conjugate these intermediates with charged groups (e.g., glucuronidation, sulfation) to facilitate their excretion.
9. At the onset of exercise, muscles rapidly regenerate ATP by drawing on pre-existing ATP stores and then primarily by converting creatine phosphate to ATP via creatine phosphokinase. Anaerobic glycolysis of stored muscle glycogen also quickly provides ATP before aerobic metabolism fully activates.

10. The blood-brain barrier is characterized by tight junctions between endothelial cells of brain capillaries, preventing free diffusion of polar molecules. It also lacks fenestrations and transcytosis mechanisms, and is further protected by a continuous basement membrane and astrocyte foot processes.

IV. Essay Format Questions (No Answers)

1. Discuss the interplay between insulin and glucagon in regulating fuel metabolism during fed, fasting, and prolonged starvation states. Include the major metabolic adjustments in the liver and adipose tissue in response to these hormonal changes.
2. Describe the complete journey of a dietary triacylglycerol molecule from ingestion to its utilization or storage in a peripheral tissue like muscle or adipose tissue. Highlight the key enzymes, transport mechanisms, and lipoprotein particles involved.
3. Analyze the liver's multifaceted role as a central metabolic hub. Elaborate on at least three distinct metabolic functions (e.g., detoxification, glucose homeostasis, protein synthesis) and explain how its unique anatomical and cellular features support these roles.
4. Compare and contrast the fuel utilization strategies of skeletal muscle during rest, high-intensity anaerobic exercise, and moderate-intensity aerobic exercise. Discuss the regulatory mechanisms that dictate the preference for specific fuels in each scenario.
5. Explain the concept and physiological significance of the blood-brain barrier. Describe how the brain obtains its primary fuels and neurotransmitter precursors despite this barrier, and discuss the metabolic consequences of disruptions to these transport systems.

V. Glossary of Key Terms with Definitions

- **Abetalipoproteinemia:** A disease resulting from the lack of microsomal triglyceride transfer protein (MTP) activity, affecting chylomicron and VLDL assembly, leading to lipid malabsorption.

- **Acetyl CoA Carboxylase (ACC-2):** An enzyme in muscle cells that produces malonyl CoA, regulating the rate of fatty acid oxidation by inhibiting carnitine palmitoyl transferase I.
- **Acetylcholine:** An excitatory neurotransmitter synthesized from acetyl CoA and choline, inactivated by acetylcholinesterase.
- **Acetylcholinesterase:** An enzyme that inactivates acetylcholine by hydrolysis.
- **Adenosine Triphosphate (ATP):** The primary energy currency of the cell, generated from fuel oxidation and used for various cellular processes.
- **Adipose Tissue:** Specialized connective tissue for the storage of fat (triacylglycerols).
- **Albumin:** A major blood protein synthesized by the liver that transports fatty acids and other hydrophobic compounds in the blood.
- **Anabolic Pathways:** Metabolic pathways that synthesize larger, complex molecules from smaller precursors, typically requiring energy.
- **Anaplerotic Reactions:** Reactions that replenish intermediates of metabolic pathways, such as the TCA cycle, that have been drawn off for other syntheses.
- **Anorexia Nervosa:** A behavioral disorder characterized by severe emaciation and a distorted body image, leading to severe malnutrition.
- **Apolipoprotein B-48 (apoB-48):** The major protein component of chylomicrons, synthesized in intestinal epithelial cells.
- **Apolipoprotein B-100 (apoB-100):** A major protein component of VLDL and LDL, synthesized in the liver.
- **Apoproteins:** The protein components of lipoproteins.
- **Apoprotein CII (apoCII):** An apoprotein acquired by nascent chylomicrons and VLDL from HDL, activating lipoprotein lipase.
- **Apoprotein E (apoE):** An apoprotein acquired by nascent chylomicrons and VLDL from HDL, recognized by liver receptors for remnant uptake.
- **Aspartate:** An excitatory neurotransmitter synthesized from oxaloacetate.

- **Astrocytes:** Star-shaped glial cells in the CNS that provide physical and nutritional support for neurons and help regulate the extracellular ionic environment.
- **Basal Metabolic Rate (BMR):** The energy expenditure of a person mentally and bodily at rest, reflecting the energy required to maintain basic life functions.
- **Beri-beri:** A disease caused by thiamine deficiency, characterized by edema, anorexia, muscle weakness, and neurological symptoms.
- **Bile Salts:** Amphipathic compounds synthesized in the liver and secreted into the small intestine, that emulsify dietary fats for digestion.
- **Blood-Brain Barrier:** A highly restrictive barrier formed by tight junctions of endothelial cells in brain capillaries, limiting the passage of many substances from blood to the brain.
- **Body Mass Index (BMI):** A measure used to classify body weight categories, calculated as weight/height^2.
- **Calorie (kcal):** A unit of energy often used in metabolism and nutrition; 1 kcal = 4.18 kJ.
- **Carnitine Palmitoyl Transferase I (CPT-I):** An enzyme that controls the entry of fatty acids into mitochondria for oxidation.
- **Catabolic Pathways:** Metabolic pathways that break down larger molecules into smaller components, often releasing energy.
- **Catecholamines:** Neurotransmitters including dopamine, norepinephrine, and epinephrine, synthesized from tyrosine.
- **Cholecystokinin:** A gut hormone secreted by intestinal cells that stimulates gallbladder contraction and pancreatic enzyme secretion.
- **Choline Acetyltransferase (ChAT):** The enzyme that synthesizes acetylcholine from acetyl CoA and choline.
- **Cholestasis:** A condition where the flow of bile from the liver to the small intestine is obstructed.

- **Chromogranins:** Acidic proteins found in storage vesicles alongside catecholamines, involved in vesicle biogenesis.
- **Chylomicron Remnant:** The portion of a chylomicron that remains after lipoprotein lipase action, taken up by the liver.
- **Chylomicrons:** Large lipoprotein particles assembled in intestinal epithelial cells, primarily transporting dietary triacylglycerols through the lymph to the bloodstream.
- **Cirrhosis:** End-stage liver disease characterized by diffuse scarring, loss of hepatic cells, and formation of regenerative nodules.
- **Colipase:** A protein secreted by the pancreas that binds to dietary fat and pancreatic lipase, increasing lipase activity.
- **COMT (Catechol-O-methyltransferase):** An enzyme involved in the inactivation and degradation of catecholamines.
- **Cori Cycle:** A metabolic pathway involving the conversion of lactate (produced in muscle) to glucose in the liver, which can then be returned to muscle.
- **Creatine:** A compound synthesized in the kidney and liver, which is phosphorylated to creatine phosphate for energy storage in muscle.
- **Creatine Phosphokinase (CPK or CK):** An enzyme that catalyzes the reversible transfer of a high-energy phosphate between ATP and creatine to form creatine phosphate.
- **Creatinine:** A spontaneous degradation product of creatine phosphate, excreted in urine at a constant rate proportional to muscle mass.
- **Creatinine-Height Index (CHI):** A measure of muscle mass depletion, calculated from 24-hour urinary creatinine excretion relative to height.
- **Cytochrome P450 (CYP) Enzymes:** A family of mixed-function oxidases in the liver (and other tissues) critical for Phase I xenobiotic detoxification reactions.
- **Daily Energy Expenditure (DEE):** The total energy expended by the body each day, including resting metabolic rate, physical activity, and diet-induced thermogenesis.

- **Demyelinating Diseases:** A group of neurological disorders characterized by the loss or damage of the myelin sheath surrounding nerve fibers, impairing nerve conduction.
- **Diet-Induced Thermogenesis (DIT):** The energy required to digest, absorb, distribute, and store nutrients from food.
- **Dopamine Beta-Hydroxylase (DBH):** An enzyme that catalyzes the conversion of dopamine to norepinephrine, found in storage vesicles.
- **Dopamine:** A catecholamine neurotransmitter synthesized from L-DOPA.
- **DOPA Decarboxylase:** An enzyme that decarboxylates L-DOPA to dopamine (and 5-hydroxytryptophan to serotonin), requiring pyridoxal phosphate.
- **Eicosanoids:** Hormone-like molecules (e.g., prostaglandins, thromboxanes, leukotrienes) derived from polyunsaturated fatty acids, involved in regulating various cellular processes.
- **Electron Transport Chain:** A series of proteins that transfers electrons from oxidized fuels to oxygen, generating a proton gradient used for ATP synthesis (oxidative phosphorylation).
- **Emulsification:** The process of suspending fats in small particles in an aqueous environment, primarily by bile salts, to increase surface area for enzyme action.
- **Endothelial Cells:** Cells that line blood vessels; in the brain, they form the tight junctions of the blood-brain barrier.
- **Enterohepatic Circulation:** The circulation of bile acids from the liver to the small intestine, where they are reabsorbed and returned to the liver.
- **Ependymal Cells:** Ciliated cells lining brain cavities and the spinal cord, involved in CSF production and circulation.
- **Epinephrine:** A catecholamine neurotransmitter and hormone, synthesized from norepinephrine.
- **Essential Amino Acids:** Amino acids that the human body cannot synthesize and must obtain from the diet.

- **Essential Fatty Acids:** Fatty acids that the human body cannot synthesize due to specific double bond arrangements and must obtain from the diet.
- **Fasting State:** The metabolic state that begins approximately 2-4 hours after a meal when blood glucose levels return to basal levels.
- **Fenestrations:** Pores or "windows" in endothelial cells, particularly in liver sinusoids, that allow for the free passage of small molecules.
- **Fuel Oxidative Pathways:** Catabolic pathways that convert dietary fuels (carbohydrates, fats, proteins) into usable energy (ATP).
- **GABA (gamma-aminobutyric acid):** The major inhibitory neurotransmitter in the central nervous system, synthesized from glutamate.
- **GAD (Glutamic Acid Decarboxylase):** The enzyme that synthesizes GABA from glutamate.
- **Gastric Lipase:** An enzyme produced in the stomach that hydrolyzes short- and medium-chain fatty acids from dietary triacylglycerols.
- **Glial Cells:** Supporting cells of the nervous system (astrocytes, oligodendrocytes, Schwann cells, microglia).
- **Glucagon:** A hormone secreted by the pancreas in response to low blood glucose, signaling fuel mobilization from stores.
- **Gluconeogenesis:** The metabolic pathway for the synthesis of glucose from non-carbohydrate precursors, primarily in the liver and kidney.
- **Glucose-6-Phosphatase:** An enzyme found in the liver (and kidney) that dephosphorylates glucose-6-phosphate to free glucose, allowing glucose export into the blood.
- **Glutamate:** An excitatory neurotransmitter in the CNS, synthesized from α-ketoglutarate.
- **Glycine:** An inhibitory neurotransmitter in the spinal cord.
- **Glycogen:** A branched polysaccharide of glucose, serving as a storage form of carbohydrate in animals, primarily in the liver and muscle.
- **Glycogenolysis:** The breakdown of glycogen into glucose or glucose-6-phosphate.

- **Glycolysis:** The metabolic pathway that breaks down glucose to pyruvate, generating ATP.
- **HDL (High-Density Lipoprotein):** A lipoprotein involved in reverse cholesterol transport (from peripheral tissues to liver) and in exchanging proteins/lipids with other lipoproteins.
- **Hepatobiliary Transport:** The transport of substances within the liver and into the bile.
- **Hepatocytes:** The primary functional cells of the liver, responsible for most metabolic processes.
- **Hepatic Stellate Cells (Ito Cells):** Lipid-filled cells in the liver that store vitamin A and, when activated, contribute to liver fibrosis.
- **Histamine:** A neurotransmitter synthesized from histidine, involved in allergic responses and CNS excitation.
- **Homovanillylmandelic Acid (HVA):** A degradation product of dopamine, used as an indicator of dopamine degradation.
- **Hypoglycemia:** A condition of abnormally low blood glucose levels.
- **Hypoxic Encephalopathy:** Brain dysfunction caused by insufficient oxygen supply to the brain, impairing neurotransmitter synthesis and ATP production.
- **IDL (Intermediate-Density Lipoprotein):** A remnant of VLDL after triacylglycerol digestion, taken up by the liver or converted to LDL.
- **Insulin:** A hormone secreted by the pancreas in response to high blood glucose, signaling fuel storage.
- **Ketone Bodies:** Fuel molecules (acetoacetate, β-hydroxybutyrate) produced by the liver from partial oxidation of fatty acids during fasting, used by other tissues for energy.
- **Kupffer Cells:** Specialized macrophages located in the liver sinusoids, responsible for phagocytosis of debris and microorganisms.
- **Kwashiorkor:** A form of protein malnutrition characterized by edema, hypoalbuminemia, and tissue injury, often seen in children.
- **Lactate Dehydrogenase:** An enzyme that interconverts pyruvate and lactate.

- **Lactate:** A metabolic end-product of anaerobic glycolysis, which can be used as a fuel by some tissues or converted to glucose in the liver.
- **LCAT (Lecithin Cholesterol Acyltransferase):** A plasma enzyme synthesized in the liver that catalyzes cholesterol ester formation.
- **LDL (Low-Density Lipoprotein):** A lipoprotein rich in cholesterol, responsible for transporting cholesterol to peripheral tissues.
- **Lingual Lipase:** An enzyme produced in the mouth that initiates digestion of short- and medium-chain fatty acids.
- **Lipogenesis:** The metabolic process of synthesizing fatty acids, typically from carbohydrates.
- **Lipolysis:** The breakdown of lipids (e.g., triacylglycerols) into fatty acids and glycerol.
- **Lipoprotein Lipase (LPL):** An enzyme attached to capillary endothelial cells that hydrolyzes triacylglycerols in chylomicrons and VLDL, releasing fatty acids for tissue uptake.
- **Lipoproteins:** Complexes of lipids and proteins that transport hydrophobic lipids in the aqueous blood plasma.
- **Malonyl CoA Decarboxylase (MCoADC):** An enzyme in muscle that converts malonyl CoA to acetyl CoA, relieving inhibition of fatty acid oxidation.
- **Malonyl CoA:** A molecule produced by ACC-2 that inhibits carnitine palmitoyl transferase I, thus blocking fatty acid entry into mitochondria.
- **Marasmus:** A severe form of protein-energy malnutrition, particularly in young children, characterized by prolonged protein and calorie deficiency.
- **Melatonin:** A neurotransmitter synthesized from tryptophan, produced in the pineal gland in response to light-dark cycles.
- **Micelles:** Small, lipid-soluble microdroplets formed by digestion products and bile salts in the intestinal lumen, facilitating absorption.
- **Microsomal Triglyceride Transfer Protein (MTP):** An enzyme required for the assembly of chylomicrons and VLDL in the endoplasmic reticulum.

- **Monoamine Oxidase (MAO):** An enzyme on the outer mitochondrial membrane that inactivates catecholamines and serotonin by deamination.
- **Multiple Sclerosis (MS):** A progressive autoimmune disease of the CNS characterized by demyelination of neurons.
- **Myelin Basic Proteins (MBP):** Proteins found on the cytoplasmic face of myelin membranes in the CNS, helping to stabilize myelin structure.
- **Myelin Sheath:** A multilayered lipid and protein structure that insulates axons, increasing the speed of nerve impulse conduction.
- **NADPH:** A reduced coenzyme primarily used in anabolic reactions (e.g., fatty acid synthesis, cholesterol synthesis) and detoxification reactions.
- **Nascent Chylomicrons:** Newly synthesized chylomicrons as they leave intestinal cells before acquiring additional apoproteins.
- **Negative Nitrogen Balance:** A state where nitrogen excretion exceeds nitrogen intake, indicating net protein loss from the body.
- **Neuroglia:** Non-neuronal supporting cells of the nervous system.
- **Neurons:** The primary signaling cells of the nervous system.
- **Neurotransmitters:** Chemical messengers that transmit signals across synapses between neurons or from neurons to other target cells.
- **Nitric Oxide (NO):** A gaseous biological messenger involved in vasodilation, neurotransmission, and immune responses.
- **Nitrogen Balance:** The difference between daily nitrogen intake (mainly protein) and nitrogen excretion.
- **Norepinephrine:** A catecholamine neurotransmitter synthesized from dopamine.
- **Oligodendrocytes:** Glial cells in the CNS that form myelin sheaths around multiple axons.
- **Oxidative Phosphorylation:** The process of ATP synthesis that occurs in mitochondria, driven by the energy released from electron transport.
- **Pancreatic Lipase:** The major enzyme secreted by the pancreas into the small intestine, responsible for digesting dietary triacylglycerols.

- **Pentose Phosphate Pathway:** A metabolic pathway that generates NADPH and 5-carbon sugars (pentoses).
- **Peroxisomal Oxidation:** A pathway of fatty acid oxidation that occurs in peroxisomes, particularly for very-long-chain fatty acids.
- **Peroxisome Proliferator Activated Receptors (PPARs):** Nuclear receptors that, when activated by fatty acids, regulate genes involved in fatty acid metabolism.
- **Pheochromocytoma:** A tumor of the adrenal medulla that episodically secretes large amounts of catecholamines, leading to symptoms like palpitations and hypertension.
- **Phosphofructokinase-2 (PFK-2):** An enzyme that produces fructose-2,6-bisphosphate, a regulator of glycolysis; its regulation differs in liver and muscle.
- **Phospholipase A2:** An enzyme secreted by the pancreas that hydrolyzes phospholipids.
- **Pit Cells:** Liver-specific natural killer cells, part of the immune defense in the liver.
- **Plasma Protein Binding:** The binding of substances in the blood to plasma proteins, which can affect their transport and availability.
- **Po:** The major glycoprotein found in the myelin of the Peripheral Nervous System (PNS).
- **Positive Nitrogen Balance:** A state where nitrogen intake exceeds nitrogen excretion, indicating net protein gain (e.g., during growth, pregnancy).
- **Proteolipid Protein (PLP):** A very hydrophobic protein that is a major structural component of myelin in the CNS.
- **Pyridoxal Phosphate (PLP):** The active coenzyme form of vitamin B_6, required for many amino acid metabolism reactions, including decarboxylation.
- **Reactive Oxygen Species (Free Radicals):** Highly reactive molecules containing oxygen that can cause cellular damage.

- **Recommended Dietary Allowance (RDA):** The average daily dietary intake level sufficient to meet the nutrient requirements of most healthy individuals in a specific group.
- **Resting Metabolic Rate (RMR):** See Basal Metabolic Rate (BMR).
- **Reye's Syndrome:** A rare, severe condition characterized by vomiting, CNS damage, and hepatic injury, epidemiologically associated with aspirin use in children during viral illnesses.
- **RNA Editing:** A molecular process that alters the nucleotide sequence of an RNA molecule post-transcription, as seen in the production of apoB-48 from the apoB gene.
- **Ryanodine Receptor:** A calcium release channel found in the sarcoplasmic reticulum of muscle cells, involved in muscle contraction.
- **S-Adenosyl Methionine (SAM):** A universal methyl donor in many biochemical reactions, including catecholamine and histamine inactivation and creatine synthesis.
- **Sarcolemma:** The cell membrane surrounding muscle fibers.
- **Sarcoplasmic Reticulum (SR):** An internal membrane system in muscle cells that stores and releases calcium ions for contraction.
- **Schwann Cells:** Supporting cells of the peripheral nervous system (PNS) that form myelin sheaths around axons.
- **Secretin:** A hormone released from the intestine that stimulates bicarbonate secretion from the pancreas.
- **Serotonin:** A neurotransmitter synthesized from tryptophan, involved in mood and appetite regulation.
- **SERCA (Sarcoplasmic Reticulum Ca^{2+} ATPase):** A protein that pumps calcium ions back into the sarcoplasmic reticulum, essential for muscle relaxation.
- **Sinusoids:** Expandable vascular channels in the liver, lined with leaky endothelial cells, allowing plasma access to hepatocytes.

- **Specific Dynamic Action (SDA):** Former term for Diet-Induced Thermogenesis (DIT).
- **Sphingolipids:** A class of lipids, including cerebrosides and sphingomyelin, that are abundant in myelin.
- **Starvation:** A prolonged fasting state (3 or more days) where major metabolic shifts occur to conserve protein.
- **Steatorrhea:** Fat-laden stools, caused by malabsorption of dietary fats.
- **TCA Cycle (Tricarboxylic Acid Cycle):** Also known as the Krebs cycle or citric acid cycle; a central metabolic pathway for the complete oxidation of fuels to CO_2.
- **Thiamine Pyrophosphate (TPP):** The active coenzyme form of vitamin B_1, required for various enzymatic reactions, including decarboxylations.
- **Thoracic Duct:** A major lymphatic vessel through which chylomicrons enter the bloodstream.
- **Tolerable Upper Intake Level (UL):** The highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all individuals.
- **Transcytosis:** The process of transporting substances across a cell by enclosing them in vesicles.
- **Triacylglycerol (TG):** The major form of fat storage in the body and the most abundant dietary lipid, consisting of three fatty acids esterified to a glycerol backbone.
- **Tyrosine Hydroxylase:** The rate-limiting enzyme in catecholamine biosynthesis, converting tyrosine to DOPA.
- **Urea Cycle:** The metabolic pathway in the liver that converts toxic ammonia into non-toxic urea for excretion.
- **VLDL (Very Low-Density Lipoprotein):** A lipoprotein produced in the liver, mainly from dietary carbohydrate, that transports endogenously synthesized triacylglycerols in the blood.

- **VMAT2 (Vesicle Membrane Transporter 2):** A protein that transports catecholamines into storage vesicles in neurons.
- **Xenobiotics:** Chemical compounds that are foreign to the body, have no nutritional value, and may be toxic.