Ch 24
Metabolism and Nutrition
*Metabolism* refers to all chemical reactions in an organism

**Cellular Metabolism**

- Includes all chemical reactions within cells
- Provides energy to maintain homeostasis and perform essential functions

Cells break down organic molecules to obtain energy

- Used to generate ATP
- Most energy production takes place in mitochondria
Metabolism

Metabolic turnover

- Periodic replacement of cell’s organic components

Growth and cell division

Special processes, such as secretion, contraction, and the propagation of action potentials
Organic Nutrients

**Nutrients**—carbohydrates, proteins, fats, water, vitamins, minerals

Are building blocks cell need for: Homeostasis – include:

- Energy
- Growth, maintenance, and repair

**Catabolism** (digestion, repair, maintenance)

- Is the **breakdown** of organic substrates
- Releases energy used to synthesize high-energy compounds (e.g., ATP)

**Anabolism** (growth, maintenance)

- Is the **synthesis** of new organic molecules
Organic Nutrients

Functions (all these functions need ATP for energy)

- Perform structural maintenance and repairs
- Support growth
- Produce secretions
- Store nutrient reserves

Glycogen - Most abundant storage carbohydrate
  - A branched chain of glucose molecules

Triglycerides - Most abundant storage lipids
  - Primarily of fatty acids

Proteins - Most abundant organic components in body
  - Perform many vital cellular functions
Generates ATP and other high-energy compounds by breaking down (catabolism) carbohydrates:

\[
glucose + oxygen \rightarrow carbon
dioxide + water
\]

**Glucose Breakdown**
- Occurs in small steps
- **Glycolysis**
  - Breaks down glucose in cytosol into smaller molecules used by mitochondria
  - *Does not require oxygen: anaerobic reaction*

**Aerobic Reactions**
- Also called **aerobic metabolism** or cellular respiration
- Occur in mitochondria, consume oxygen, and produce ATP
Carbohydrate Metabolism

**Glycolysis**
- Breaks 6-carbon glucose
- Into two 3-carbon pyruvic acid

**Pyruvate – 3-carbon**
- Ionized form of pyruvic acid

**Mitochondrial ATP Production**
- If oxygen supplies are adequate, mitochondria absorb and break down pyruvic acid molecules:
  - C and O atoms are removed and released as CO\(_2\) in the process of *decarboxylation in citric acid, tricyclic, Kreb’s*
Pyruvic acid reacts with NAD and coenzyme A (CoA)

- Acetyl group transfers
  - From acetyl-CoA citric acid is produced then goes through *stripping process* – carbon and oxygen removed, electrons, and hydrogens

- Decarboxylation - production of carbon dioxide

In the mitochondrion: 2 (C) acetyl-CoA enters:

**TCA Cycle** (citric acid cycle, Kreb’s)

- Function of the citric acid cycle is
  - Strip electrons and remove hydrogen atoms from organic molecules and transfer them to NAD, FAD
  - Decarboxylate acetyl-CoA as carbon dioxide waste
Carbohydrate Metabolism

Oxidative Phosphorylation and the ETS

- Generates ATP within mitochondria
- Produces more than 90% of ATP used by body
- Results in $2 \text{H}_2 + \text{O}_2 \rightarrow 2 \text{H}_2\text{O}$

Energy Yield of Glycolysis and Cellular Respiration

- For most cells, reaction pathway
  - Begins with glucose
  - Ends with carbon dioxide and water
  - Main method of generating ATP
Aerobic Respiration

**GLYCOLYSIS**
- Glucose (6-carbon) → 2 ATP, 2 ADP, 4 ADP, 4 ATP, 2 NAD, 2 NADH
- Pyruvic acid (3-carbon) → 2 CO₂, 2 NADH, 2 NAD

**SUMMARY**
- **Glycolysis**:
  - 4 ATP by substrate-level phosphorylation
  - 2 ATP used to initiate glycolysis
  - 2 ATP net gain to cell
- **The Electron Transport System and TCA Cycle**:
  - 4 ATP from NADH produced in glycolysis
  - 24 ATP from NADH generated in TCA cycle
  - 4 ATP from FADH₂ generated in TCA cycle
  - 2 ATP via GTP produced by substrate-level phosphorylation
  - 36 ATP net gain to cell from aerobic catabolism of one glucose molecule
Carbohydrate Metabolism - The G’s

**Gluconeogenesis**
- Is the synthesis of glucose from noncarbohydrate precursors
  - Lactic acid
  - Glycerol
  - Amino acids
  - Stores glucose as glycogen in liver and skeletal muscle

**Glycogenogenesis (in liver and skeletal muscles)**
- Is the formation of glycogen from glucose
- Occurs slowly

*Liver and skeletal muscles must have insulin receptors!"
Glycogenolysis - (occurs quickly)

- Is the breakdown of glycogen (locally in skeletal muscles with need; liver-in response to glucagon)
- Involves a single enzymatic step
Lipid molecules contain carbon, hydrogen, and oxygen

*Triglycerides are the most abundant lipid in the body*

**Lipid Catabolism (also called lipolysis)**

Breaks lipids down into pieces that can be

- Converted to pyruvic acid - *glycerol*
- Channeled directly into TCA/Kreb’s cycle

Hydrolysis splits triglyceride into component parts

- One molecule of *glycerol*
- Three fatty acid molecules
Triglyceride

Fatty Acids

Glycerol
Lipid/ Triglyceride Catabolism

- **Glycerol** - Enzymes convert glycerol to pyruvic acid
  - Pyruvic acid enters TCA cycle

Different enzymes convert **fatty acids to acetyl-CoA** (beta-oxidation)

**Beta-Oxidation (fatty acids)**

- A series of reactions that break fatty acid molecules into **2-carbon fragments**
- Occurs inside mitochondria
  - Generates molecules of **acetyl-CoA** – can enter TCA/Kreb’s cycle
Lipid Metabolism

Fatty acid (18-carbon) → Coenzyme A

\[ \text{Fatty acid (18-carbon)} \rightarrow \text{Coenzyme A} \]

\[ \text{ATP} \rightarrow \text{AMP} + 2 \text{P} \]

Fatty acid (18-carbon) - CoA

\[ \text{Fatty acid (18-carbon)} - \text{CoA} \]

NAD → NADH

\[ \text{NAD} \rightarrow \text{NADH} \]

FAD → FADH₂

\[ \text{FAD} \rightarrow \text{FADH}_2 \]

Coenzyme A

\[ \text{Coenzyme A} \]

ATP

\[ +3 \text{ ATP} \]

Electron Transport System

\[ \text{ELECTRON TRANSPORT SYSTEM} \]

TCA Cycle

\[ \text{TCA CYCLE} \]

Acetyl-CoA

\[ \text{Acetyl-CoA} \]

\[ +12 \text{ ATP} \]

Small carbon chains

Triglycerides → Glycogen → Proteins

\[ \text{Small carbon chains} \]

Fatty acids → Glucose → Amino acids

\[ \text{Fatty acids} \rightarrow \text{Glucose} \rightarrow \text{Amino acids} \]

Coenzymes → Electron transport system

\[ \text{Coenzymes} \rightarrow \text{Electron transport system} \]

ATP → CO₂ → H₂O

\[ \text{ATP} \rightarrow \text{CO}_2 \rightarrow \text{H}_2\text{O} \]
1. For each 2-carbon fragment removed from fatty acid, cell gains:
   - 12 ATP from acetyl-CoA in TCA cycle and 5 ATP from oxidative phosphorylation
2. Cell can gain 144 ATP molecules from breakdown of one 18-carbon fatty acid molecule
3. *Fatty acid breakdown yields about 1.5-2 times the energy of glucose breakdown*

**Lipid Storage is important as energy reserves**
- Can provide large amounts of ATP, but slowly
- Saves space, but hard for water-soluble enzymes to reach
Lipid Synthesis (also called lipogenesis)

Lipids can be made from almost any organic substrate

- Because lipids, amino acids, and carbohydrates can be converted to acetyl-CoA - 2 carbon then the reaction can reverse...... and triglycerides made!!!

- Anabolism by adding carbons from other molecules to make fatty acids and glycerol

- Other Lipids
  - Nonessential fatty acids and steroids are examples can also be synthesized from acetyl-CoA
Lipid Transport

Cells require lipids to maintain plasma membranes

- Steroid hormones must reach target cells in many different tissues

Solubility

Most lipids are not soluble in water (hydrophobic)

- Special transport mechanisms carry lipids from one region of body to another

Circulating Lipids

*Most lipids circulate through bloodstream as lipoproteins*

- Free small chain fatty acids are a small percentage of total circulating lipids - *Free Fatty Acids*
Lipoproteins

Lipid–Protein complexes

- Five classes of lipoproteins
  - Chylomicrons
  - Very low-density lipoproteins (VLDLs)
  - Intermediate-density lipoproteins (IDLs)
  - Low-density lipoproteins (LDLs)
  - High-density lipoproteins (HDLs) (4 Min)

Chylomicrons -produced in intestinal tract

- Are too large to diffuse across capillary wall
- *Enter lymphatic capillaries (Lacteals)*
- Travel through thoracic duct to venous circulation and systemic arteries
Chylomicrons

Lipoprotein lipase converts to fatty acids and glycerol *in packets*
Liver – processes out VLDLs and LDLs to cells - returns to liver as HDLs.
1. Liver cells synthesize VLDLs for discharge into the bloodstream.

2. In peripheral capillaries, lipoprotein lipase removes many of the triglycerides from VLDLs, leaving IDLs.

3. When IDLs reach the liver, additional triglycerides are removed and the protein content is altered. This process creates LDLs.

4. LDLs leave the bloodstream through capillary pores or cross the endothelium by vesicular transport.

5. Once in peripheral tissues, the LDLs are absorbed by means of receptor-mediated endocytosis.

6. The cholesterol not used diffuses out of the cell.

7. The cholesterol then reenters the bloodstream, where it is absorbed by HDLs and returned to the liver.

8. In the liver, the HDLs are absorbed and the cholesterol is extracted. Some of the recovered cholesterol is used in the synthesis of LDLs.

9. The HDLs stripped of their cholesterol are released into the bloodstream to travel to peripheral tissues and absorb additional cholesterol.
Free Fatty Acids

Free Fatty Acids (FFAs)

- Are lipids that diffuse easily across plasma membranes
- Are an important energy source
- In blood, are generally bound to albumin (most abundant plasma protein)

Sources of FFAs in blood

- Fatty acids not used in synthesis of triglycerides diffuse out of intestinal epithelium into blood
- Fatty acids diffuse out of lipid stores (in liver and adipose tissue) when triglycerides are broken down
The body synthesizes 100,000 to 140,000 proteins
  - Each with different form, function, and structure
  - All body proteins are built from the 20 amino acids
  - Amino acids are in protein nutrients eaten. 8 amino acids are essential and cannot be made by the body, so must be in the diet.

Amino acid anabolism- **transamination**

Amino acid catabolism- **deamination**
  - These processes occur in hepatocytes of sinusoids (liver)
Transamination - Attaches amino group of amino acid to keto acid

- Converts keto acid into amino acid
- Available for protein synthesis

Glutamic acid + Keto acid 1 $\xrightarrow{\text{Transaminase}}$ Keto acid 2 + Tyrosine

(a) Transamination
Protein Synthesis

Body synthesizes half of the amino acids needed to build proteins

**Nonessential amino acids**

- Amino acids made by the body on demand

**Ten Essential Amino Acids** *(Must be in diet!)*

- Eight not synthesized: isoleucine, leucine, lysine, threonine, tryptophan, phenylalanine, valine, and methionine
- Two insufficiently synthesized: arginine and histidine
Deamination

- Prepares amino acid for breakdown in TCA cycle
- Removes amine group and hydrogen atom
  - Reaction generates ammonium ion

(b) Deamination

Glutamic acid

Deaminase

H₂O

NAD

NADH

Keto acid

+ NH₄⁺

Ammonium ion
Ammonia (ium) Ions

- Are highly toxic, even in low concentrations
- Liver cells (primary sites of deamination) have enzymes that use ammonium ions to synthesize **urea** (water-soluble compound excreted in urine)

Urea Cycle - the reaction sequence that produces urea

\[
\text{Urea} \quad \xrightarrow{\text{Ammonium ion}} \quad \text{NH}_4^+ + \text{CO}_2 \quad \xrightarrow{\text{Urea cycle}} \quad \text{urea}
\]

\[
\begin{array}{c}
\text{Urea} \\
\text{H}_2\text{N} \quad \text{C} \quad \text{NH}_2 \\
\end{array}
\]
Protein Metabolism

Proteins and ATP Production

- When glucose and lipid reserves are inadequate, liver cells
  - Break down internal proteins
- Amino acids are deaminated and carbon chains broken down to provide ATP

Three Factors Against Protein Catabolism of Proteins for Energy

- Proteins are more difficult to break apart than complex carbohydrates or lipids
- A byproduct, ammonium ion, is toxic to cells
- Proteins form the most important structural and functional components of cells
24-5 Absorptive and Postabsorptive States

Five Metabolic Tissues

- Liver                     Adipose tissue                Skeletal muscle
- Neural tissue               Other peripheral tissues

Liver

- Is focal point of metabolic regulation and control
- Contains great diversity of enzymes that break down or synthesize carbohydrates, lipids, and amino acids
- Hepatocytes
  - Have an extensive blood supply
  - Monitor and adjust nutrient composition of circulating blood
  - Contain significant energy reserves (glycogen deposits)
Absorptive and Postabsorptive States

Body has two patterns of daily metabolic activity

- Absorptive state
- Postabsorptive state

The Absorptive State

- Is the period following a meal when nutrient absorption is under way

The Postabsorptive State

- Is the period when nutrient absorption is not under way
- Body relies on internal energy reserves for energy demands
- Liver cells conserve glucose and engage in glycogenesis
Thermoregulation

- Heat production
  - BMR estimates rate of energy use
  - Energy not captured is released as heat:
    - serves important homeostatic purpose

Body Temperature

- Enzymes operate in a limited temperature range
- Homeostatic mechanisms keep body temperature within limited range (thermoregulation)
Metabolic Rate

Thermoregulation

- The body produces heat as byproduct of metabolism
- Increased physical or metabolic activity generates more heat
- Heat produced is retained by water in body
- For body temperature to remain constant
  - Heat must be lost to environment
- Body controls heat gains and losses to maintain homeostasis
Mechanisms of Heat Transfer

Heat exchange with environment involves four processes

- **Radiation** - Warm objects lose heat energy as infrared radiation
  - Depending on body and skin temperature
  - About 50% of indoor heat is lost by radiation

- **Conduction** - is direct transfer of energy through physical contact
  - Is generally not effective in heat gain or loss

**Convection** - Results from conductive heat loss to air at body surfaces

**Evaporation** - Cools surface where evaporation occurs
Metabolic Rate

Body Size and Thermoregulation

- Heat is produced by body mass (volume)
- Surface-to-volume ratio decreases with size

Basal Metabolic Rate (BMR) – the amount of daily energy expended at rest in a temperate environment in the post-absorptive state

- Measuring BMR
  - Involves monitoring respiratory activity
  - Energy utilization is proportional to oxygen consumption
Homeostasis can be maintained only if digestive tract absorbs enough fluids, organic substrates, minerals, and vitamins to meet cellular demands.

Nutrition is the absorption of nutrients from food.

The body’s requirement for each nutrient varies.

A balanced diet contains all components needed to maintain homeostasis:

- Substrates for energy generation
- Essential amino acids and fatty acids
- Minerals and vitamins
- Must also include water to replace urine, feces, evaporation
Minerals and Vitamins

- Are essential components of the diet
- The body does not synthesize minerals
- Cells synthesize only small quantities of a few vitamins

Fat-Soluble Vitamins

- Vitamins A, D, E, and K
  - Are absorbed primarily from the digestive tract along with lipids of micelles into cells and processed as chylomicrons
  - Normally diffuse into plasma membranes and lipids in liver and adipose tissue
Vitamins

- Vitamin A
  - A structural component of epithelial cells and visual pigment retinal

- Vitamin D
  - Is converted to calcitriol, which increases rate of intestinal calcium and phosphorus absorption

- Vitamin E
  - Stabilizes intracellular membranes

- Vitamin K
  - Helps synthesize several proteins, including three clotting factors
Vitamins

Vitamin Reserves

The body contains significant reserves of fat-soluble vitamins

- Normal metabolism can continue several months without dietary sources

- Water-Soluble Vitamins

  - Are components of coenzymes (like NAD, FAD)
  - Are rapidly exchanged between fluid in digestive tract and circulating blood
    - Excesses are excreted in urine
    - Include B vitamins, biotin, folic acid, and C (ascorbic acid)
Vitamins and Bacteria

- Bacterial inhabitants of intestines produce small amounts of
  - Fat-soluble vitamin K
  - Five water-soluble vitamins

Vitamin $B_{12}$

- Intestinal epithelium absorbs all water-soluble vitamins except $B_{12}$
  - $B_{12}$ molecule is too large:
    - must bind to intrinsic factor before absorption
Minerals

- Inorganic ions released through dissociation of electrolytes
- Most common in body are calcium and phosphorus.

Mineral Reserves

- The body contains significant mineral reserves
  - That help reduce effects of variations in diet

Ions such as sodium, chloride, and potassium determine osmotic concentrations of body fluids
- Ions are essential
  - Cofactors in many enzymatic reactions
Metals or Trace Minerals

Metals

- Each component of ETS requires an iron atom
- Final cytochrome of ETS requires a copper ion
Diet and Disease

- Average U.S. diet contains excessive amounts of sodium, calories, and lipids
- Poor diet contributes to
  - Obesity
  - Heart disease
  - Atherosclerosis
  - Hypertension
  - Diabetes
Calories

- **Calorimetry** - measures total energy released when bonds of organic molecules are broken
- Food is burned with oxygen and water in a calorimeter

**Calories**

- Energy required to raise 1 g of water 1 degree Celsius is a **calorie (cal)**
- Energy required to raise 1 kilogram of water 1 degree Celsius is a **Calorie (Cal) = kilocalorie (kcal)**

**The Energy Content of Food**

- Lipids release 9.46 Cal/g
- Carbohydrates release 4.18 Cal/g
- Proteins release 4.32 Cal/g
Metabolic Rate

Energy Expenditure: Metabolic Rate

- Clinicians examine metabolism to determine calories used and measured in
  - Calories/hour or per day
  - Calories per unit of body weight per day

- Energy Expenditure: Metabolic Rate
  - Is the sum of all anabolic and catabolic processes in the body
  - Changes according to activity