**Summary of Metabolism**

1. Simple molecules such as glucose, amino acids, glycerol, and fatty acids
2. Catabolic reactions transfer energy from complex molecules to ATP
3. Anabolic reactions transfer energy from ATP to complex molecules
4. Heat released

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**Mechanism of Enzyme Action**

1. The substrate contacts the active site
2. The enzyme-substrate complex is formed.
3. The substrate molecule is altered
   (atoms are rearranged, or the substrate is broken into smaller parts, or the substrate is combined with another molecule)
4. Product(s) is/are released from the active site.
5. The enzyme is unchanged and can catalyze a new reaction.
Energy Production In A Cell

Large food molecules contain a lot of potential energy in the form of chemical bonds but it requires a lot of work to liberate the energy. Cells need a quick easy way to get energy for anabolism: this is done with ATP. ATP is an unstable molecule, the bonds of which are easy to break.

\[
\text{ATP} \rightarrow \text{ADP} + P + \text{energy} \\
\text{Food energy} + \text{ADP} + P \rightarrow \text{ATP}
\]

Catabolic reactions generate energy to make ATP, and the ATP energy is used to drive anabolic reactions, such as metabolic turnover (replacement of cell parts), growth and cell division, and special functions (such as secretion, absorption, contraction, or signaling).

Metabolism = the sum of all chemical reactions in the body.

Oxidation-Reduction Reactions (Redox Rxns)

Oxidation = the removal of electrons (or addition of oxygen)  
Reduction = the addition of electrons

These reactions are always coupled: one molecule must be oxidized while another is reduced. The reduced molecule gains energy while the oxidized molecule loses energy.

\[
\text{A-e'} + \text{B} \rightarrow \text{A} + \text{B-e'}  \\
(\text{A is oxidized while B is reduced})
\]

Cells more commonly perform dehydrogenation reactions where a hydrogen (1 proton + 1 electron) is exchanged instead of a free electron. Catabolism results in reduced compounds, which can then be oxidized to generate ATP.

ATP Production

Generation of ATP involves the addition of a phosphate to ADP and can be accomplished one of three ways:
1. **Substrate Level Phosphorylation**: a high-energy phosphate is transferred directly from one substrate to ADP.
2. **Oxidative Phosphorylation**: electrons are transferred from an organic compound to a cofactor carrier molecule (e.g. NAD\(^+\)). The electrons are passed through other carriers (the electron transport chain) to a final acceptor (such as oxygen, nitrate, sulfate, or carbonate) and the passing of the electrons releases energy that is harvested to add a phosphate to ADP in a process called chemiosmosis.
3. **Photophosphorylation**: only occurs in photosynthetic organisms that contain the appropriate light-trapping pigments. Light energy is converted to chemical energy by an electron transport chain to generate the energy to add phosphate to ADP.
Carbohydrate Catabolism

Carbohydrates are the primary source of cellular energy for most organisms. Glucose is the most commonly used carbohydrate. Glucose can be catabolized for ATP production in two ways:

1. **Cellular respiration**: requires oxygen or a similar inorganic molecule to serve as the final electron acceptor in a series of redox reactions that generate ATP by oxidative phosphorylation. This is the most efficient method of ATP production. (1 glucose generates 36 or 38 ATP)

2. **Fermentation**: requires an organic molecule to serve as the final electron acceptor and can be done in the absence of oxygen. ATP is synthesized using substrate level phosphorylation, which is less efficient. (1 glucose generates 2 ATP)

**Aerobic Respiration Of Glucose**

\[
C_6H_{12}O_6 + 6 O_2 \rightarrow 6 CO_2 + 6 H_2O
\]

(energy from 1 glucose \(\rightarrow\) 38 ATP)

Three stages of aerobic respiration:

1. **Glycolysis**: oxidation of glucose to pyruvic acid with some ATP and NADH produced.
2. **Kreb’s Cycle**: oxidation of acetyl to carbon dioxide with some ATP, NADH and FADH\(_2\) produced.
3. **Electron Transport Chain**: NADH and FADH\(_2\) are oxidized providing electrons for redox reactions to generate ATP. The majority of the ATP is produced at this step.

*(NAD (nicotinamide adenine dinucleotide) and FAD (flavin adenine dinucleotide) are coenzymes that function to transport electrons in the form of hydrogen: NAD\(^+\) carries 2 electrons but only one proton, FAD carries 2 complete hydrogen atoms)*

**Glycolysis**

a.k.a the Embden-Myerhof Pathway

Glycolysis is an anaerobic process (does not involve oxygen) consisting of a 10-step metabolic pathway that converts 1 glucose molecule into 2 pyruvic acid molecules and generates 2 molecules of ATP by substrate level phosphorylation.

Two stages:

1. **Preparatory Stage**: two ATP molecules are used to phosphorylate one 6-carbon glucose and catabolize it into two 3-carbon molecules.
2. **Energy Conservation Stage**: The two 3-carbon molecules are oxidized to generate two 3-carbon pyruvic acid molecules. At the same time two NAD\(^+\) molecules are reduced to two NADH molecules and four ATP molecules are produced by substrate level phosphorylation.
Summary of glycolysis:
\[ \text{1 Glucose} + 2 \text{NAD}^+ + 2 \text{ADP} + 2 \text{P} \rightarrow \text{2 Pyruvic acid} + 2 \text{NADH} + 2 \text{H}^+ + 2 \text{ATP} \]

Decarboxylation (Preparation for the Kreb’s Cycle)

This is the first step in the aerobic process of glucose metabolism. The 3-carbon pyruvic acid is decarboxylated into carbon dioxide and a 2-carbon acetyl. The acetyl is attached to Coenzyme A and one NAD$^+$ is reduced to NADH. (Each glucose generates two pyruvic acid molecules so this will run twice). Coenzyme A functions only as a carrier and is not catabolized.

Summary of decarboxylation:
\[ 2 \text{Pyruvic acid} + 2 \text{NAD}^+ + 2 \text{CoA} \rightarrow 2 \text{Acetyl CoA} + 2 \text{CO}_2 + 2 \text{NADH} \]
\[ (\text{CH}_3\text{-CO-COOH}) \quad (\text{CH}_2\text{CO}) \]

Kreb’s Cycle

a.k.a. The Citric Acid Cycle or The Tricarboxylic Acid Cycle

This part of the aerobic metabolism of glucose involves 8 enzymatic reactions that function to reduce the coenzymes NAD$^+$ and FAD. The 2-carbon acetyl is attached to a 4-carbon oxaloacetic acid creating a 6-carbon citric acid. Oxidation and decarboxylation reactions occur which catabolize the 6-carbon citric acid back into a 4-carbon oxaloacetic acid and two carbon dioxide molecules (the cycle is ready to run again with the addition of acetyl). At the same time three NAD$^+$ and one FAD are reduced into three NADH and one FADH$_2$ respectively, and one ATP is produced by substrate level phosphorylation (remember that for each glucose there are two acetyl molecules so this will run twice).

Summary of the Kreb’s cycle:
\[ 2 \text{Acetyl CoA} + 6 \text{NAD}^+ + 2 \text{FAD} + 2 \text{ADP} + 2 \text{P} + 4 \text{H}_2\text{O} \rightarrow 2 \text{CoA} + 4 \text{CO}_2 + 6 \text{NADH} + 4 \text{H}^+ + 2 \text{FADH}_2 + 2 \text{ATP} \]

Electron Transport Chain

This is the aerobic part of the aerobic metabolism of glucose. Oxidative phosphorylation occurs on a membrane to generate most of the ATP produced from glucose. Coenzymes from the previous reactions pass electrons to a series of electron carrier molecules, which carry out redox reactions resulting in the chemiosmotic generation of ATP.

There are three classes of carrier molecules:
1. Flavoproteins: protein + flavin coenzyme
2. Cytochromes: protein + an iron group
3. Ubiquinones or Coenzyme Q: nonprotein
Events of the electron transport chain:
1. NAD$^+$ and FAD collected hydrogens (electrons) from organic molecules during Glycolysis, Decarboxylation, and the Kreb’s Cycle becoming NADH and FADH$_2$
2. NADH and FADH$_2$ pass hydrogens (electrons and protons) to the electron transport chain consisting of flavoproteins, cytochromes, and coenzyme Q. As electrons are passed along the chain, protons are pushed out through the membrane. This sets up a concentration gradient with protons (positive charge) on the outside and electrons (negative charge) on the inside.
3. At the end of the chain the electrons are accepted by oxygen (or another inorganic if anaerobic) creating an anion (O$^-$) inside, which has a strong affinity for the cation (H$^+$) outside.
4. Chemiosmosis generates ATP: H$^+$ from the outside moves toward O$^-$ on the inside through special membrane channels that are coupled to ATP synthase and the high energy diffusion of H$^+$ drives the reaction ADP + P $\rightarrow$ ATP. The energy from 1 NADH can generate 3 ATP, and that from 1 FADH$_2$ can generate 2 ATP.
5. H$^+$ combines with O$^-$ inside the membrane creating water (H$_2$O).

Summary of the ETC:
2 NADH from Glycolysis + 2 NADH from Decarboxylation + 6 NADH from Kreb’s Cycle + 2 FADH$_2$ from Kreb’s Cycle + 6 O$_2$ + 34 ADP + 34 P $\rightarrow$ 12 H$_2$O + 34 ATP + 10 NAD$^+$ + 2 FAD

Final Summary For Aerobic Respiration:

$$C_6H_{12}O_6 + 6 O_2 + 38 ADP + 38 P \rightarrow 6 CO_2 + 6 H_2O + 38 ATP$$

In Prokaryotes 38 ATP are produced from 1 glucose molecule: 2 from Glycolysis and 2 from Kreb’s cycle by substrate level phosphorylation, and 34 from Electron Transport by oxidative phosphorylation. Electron transport occurs on the inside surface of cell membrane and Glycolysis and the Kreb’s Cycle occur in the cytoplasm.

In Eukaryotes, usually only 36 ATP are produced from 1 glucose molecule: 2 from Glycolysis, 2 from the Kreb’s Cycle and 32 from Electron Transport. Glycolysis occurs in the cytoplasm, the Kreb’s cycle occurs in the matrix of the mitochondria, and Electron Transport occurs on the cristae of the mitochondria. Some energy is lost as electrons are carried from the cytoplasm across the mitochondrial membrane and thus the two NADH from Glycolysis can generate only four ATP instead of six.
Anaerobic Respiration

The organism still carries out Glycolysis, the Kreb’s Cycle and the Electron Transport Chain but the final electron acceptor is an inorganic molecule other than oxygen. These reactions result in less ATP production compared to aerobic respiration. The amount varies per organism and type of acceptor that is used, but as a result, anaerobes grow more slowly than aerobes. As with aerobic respiration, the ATP is generated by both substrate level and oxidative phosphorylation, and is always more than 2 but less than 38 ATP per glucose.

Examples of anaerobic electron acceptors include:
- nitrate (NO$_3^-$) $\rightarrow$ reduced to nitrite (NO$_2^-$), nitrous oxide (N$_2$O), or nitrogen gas (N$_2$)
- sulfate (SO$_4^{2-}$) $\rightarrow$ reduced to hydrogen sulfide (H$_2$S)
- carbonate (CO$_3^{2-}$) $\rightarrow$ reduced to methane (CH$_4$)

Fermentation

Definitions of fermentation:
1. Release energy from sugar or other organic molecules
2. Does not require oxygen
3. Does not require the use of the Kreb’s Cycle or the Electron Transport Chain
4. Uses an organic molecule as the electron acceptor (e.g. acid or alcohol)
5. Produces a small amount of ATP (the two generated during Glycolysis)

Fermentation begins with Glycolysis where sugar is converted into pyruvic acid with production of NADH. Two ATP are generated by substrate level phosphorylation. The pyruvic acid is then reduced by the NADH generated during Glycolysis to create an alcohol or an acid. The resulting reduced molecules are energy rich and could be used to generate more ATP in other metabolic reactions.

- Lactic acid fermentation:
  pyruvic acid + NADH $\rightarrow$ lactic acid + NAD$^+$

- Alcohol fermentation:
  pyruvic acid $\rightarrow$ acetaldehyde + CO$_2$ (decarboxylation) + NADH $\rightarrow$
  ethanol + NAD$^+$ (oxidation)
Lipid and Protein Catabolism

Carbohydrates are always the first choice for energy production but if they are not available, other organic molecules can be catabolized to generate ATP.

Lipids are broken down by lipases into glycerol and fatty acids. The glycerol is converted into pyruvic acid and used in the Kreb’s Cycle. The fatty acids undergo beta-oxidation and enter into the Kreb’s Cycle as 2-carbon fragments. Each 2-carbon fragment can generate 17 ATP. This means that there is more energy stored in lipid molecules than in carbohydrates: one 6-carbon glucose can generate 38 ATP whereas one 6-carbon fatty acid can generate 51 ATP.

Proteins are broken down by proteases and peptidases into individual amino acids. The amino acids are deaminated and the amino group in the form of an ammonium ion (NH$_4^+$) is excreted as a waste product. The remaining organic acid is processed for entry into the Kreb’s Cycle as either a 2-carbon fragment or some intermediate step later in the pathway with varying amounts of ATP produced.

Photosynthesis

Photosynthesis involves the conversion of light energy into chemical energy. Energy from the sun is used to convert carbon dioxide gas into reduced solid compounds by using electrons from water in a process called carbon fixation. Carbon fixation is carried out only by plants, algae, cyanobacteria and green and purple sulfur bacteria.

Summary of photosynthesis:

$$6 \text{ CO}_2 + 6 \text{ H}_2\text{O} + \text{light} \rightarrow \text{C}_6\text{H}_{12}\text{O}_6 + 6 \text{ O}_2$$

Photosynthesis occurs in two stages:

1. **The Light-Dependent Reaction**: this is where light is used to convert ADP into ATP. Usually, NADP$^+$ is reduced into NADPH concurrently.
2. **The Dark or Light-Independent Reaction**: electrons from NADPH and energy from ATP generated during the Light-Dependent Reaction are used to reduce CO$_2$ into sugar.

**Light-Dependent Reactions**

Light energy is absorbed by chlorophyll molecules. Chlorophyll a is used in plants, algae, and cyanobacteria, and Bacteriochlorophylls are used in the other photosynthetic bacteria groups. Electrons are excited by the light energy and jump from the chlorophyll to the electron transport chain. ATP is generated by chemiosmosis. This is an oxidative phosphorylation reaction, but because the process was started with light it is said that the ATP is generated by photophosphorylation.
There are two types of photophosphorylation:

1. Cyclic photophosphorylation: The electron ultimately returns to the chlorophyll which acts as both the electron donor and its final acceptor. (These organisms do not reduce NADP⁺ and cannot carry out carbon fixation, e.g. green and purple non-sulfur bacteria.)

2. Non-cyclic photophosphorylation: The electron released from chlorophyll gets incorporated into NADPH (and ultimately into the sugar). Electrons must be replaced to the chlorophyll by water (e.g. plants, algae, cyanobacteria) or some other oxidizable compound such as hydrogen sulfide (H₂S) (e.g. green and purple sulfur bacteria).

**Light-Independent Reactions**

a.k.a. The Calvin-Benson Cycle. This is the series of reactions that result in carbon fixation. Carbon dioxide from the air is synthesized into sugar molecules using energy from ATP and electrons from NADPH. It takes six turns of the cycle to generate one glucose molecule.

Summary of the light-independent reaction:

\[
6 \text{CO}_2 + 18 \text{ATP} + 12 \text{NADPH} \rightarrow C_6\text{H}_{12}\text{O}_6 + 18 \text{ADP} + 18 \text{P} + 12 \text{NADP}^+ 
\]

**Summary of Cellular Energy Production**

All the energy for life ultimately comes from redox reactions.

1. An electron donor is needed to begin the process. This is either an organic molecule or a photosynthetic pigment.
2. Electrons are transferred to electron carriers such as NAD⁺, NADP⁺, and FAD.
3. Electrons are transferred from the carriers to final acceptors and this is where the majority of ATP is produced.
   - Aerobic final acceptors = oxygen
   - Anaerobic final acceptors = inorganic other than oxygen
   - Fermentation final acceptors = organic molecules
Nutritional classification of organisms

All organisms

Energy source

Chemical

Chemotrophs

Carbon source

Organic compounds

Chemoheterotrophs

Final electron acceptor

O₂

All animals; most fungi, protozoa, bacteria

Not O₂

Organic compound

Fermentative Streptococcus, for example

Inorganic compound

Electron transport chain Clostridium, for example

CO₂

Hydrogen-, sulfur-, iron-, nitrogen-, and carbon monoxide-oxidizing bacteria

Light

Phototrophs

Carbon source

Organic compounds

Photoheterotrophs

Use H₂O to reduce CO₂?

Yes

Green nonsulfur bacteria, purple nonsulfur bacteria

Oxycyclic photosynthesis (plants, algae, cyanobacteria)

No

Photoautotrophs

CO₂

Anoxic photosynthetic bacteria (green and purple bacteria)