Metabolism: all the chemical reactions that take place in living cells to break down or build molecules are known as metabolism. The term metabolism refers to all the chemical reactions that provide energy and the substances required for continued cell growth. There are two types of metabolic reactions: catabolic and anabolic.

Catabolic reaction: in catabolic reactions, complex molecules are broken down to simpler ones with an accompanying release of energy.

Anabolic reaction: anabolic reactions utilize energy available in the cell to build large molecules from simple ones.

Stage of metabolism: we can think of the catabolic processes in metabolism as consisting of three stages.

[Diagram of stages of metabolism]
Consider a tuna sandwich for our example. In stage 1 of metabolism, the processes of digestion break down the large macromolecules into small monomer units. The polysaccharides in bread break down to monosaccharides, the lipids in the mayonnaise break down to glycerol and fatty acids, and the proteins from the tuna yield amino acids. These digestion products diffuse into the bloodstream for transport to cells. In stage 2, they are broken down to two- and three-carbon compounds such as pyruvate and acetyl CoA. Stage 3 begins with the oxidation of the two-carbon acetyl CoA in the citric acid cycle, which produces several reduced coenzymes. As long as the cells have oxygen, the hydrogen ions and electrons are transferred from the coenzymes to the electron transport chain, where most of the energy for the cell is produced.

Cell structure for metabolism: in animals, a membrane separates the materials inside the cell from the aqueous environment surrounding the cell. The nucleus contains the genes that control DNA relation and protein synthesis of the cell. The cytoplasm consists of all the materials between the nucleus and the cell membrane. The cytosol, which is the fluid part of the cytoplasm, is an aqueous solution of electrolytes and enzymes that catalyze many of the cell’s chemical reactions. Within the cytoplasm are specialized structures called organelles that carry out specific function in the cell. The mitochondria are the energy producing factories of the cells. A mitochondria consist of an outer membrane and an inner membrane with an intermembrane space between them. The fluid section surrounded by the inner membrane is called the matrix. Enzymes located in the matrix and along the inner membrane catalyze the oxidation of carbohydrates, fats, and amino acids. All of these oxidation pathways lead to CO₂, H₂O, and energy, which is used to form energy-rich compounds.

ATP and energy: in our cells, the energy released from the oxidation of the food we eat is used to form a “high energy” compound called adenosine triphosphate (ATP). The ATP molecule is composed of the nitrogen base adenine, a ribose sugar, and three phosphate groups.
When ATP undergoes hydrolysis, the cleavage of one phosphate group releases energy of 7.3 kcal per mole of ATP. The products are adenosine diphosphate (ADP) and hydrogen phosphate ion (HPO$_4^{2-}$) abbreviated as P$_i$ (inorganic phosphate).

![Diagram of ATP and ADP](image)

We can write this reaction in its simplified form as:

$$\text{ATP} + \text{H}_2\text{O} \rightarrow \text{ADP} + \text{P}_i + 7.3 \text{ kcal/mole}$$

Every time we contract muscles, move substances across cellular membranes, send nerve signals, or synthesize an enzyme, we use energy from ATP hydrolysis. In a cell that is doing work (anabolic processes), 1-2 million ATP molecules may be hydrolyzed in one second. The amount of ATP hydrolyzed in one day can be as much as our body mass, even though only about 1 gram of ATP is present in all our cells at any given time. When we take in food, the resulting catabolic reactions provide energy to regenerate ATP in our cells. Then 7.3 kcal/mole is used to make ATP from ADP and P$_i$:

$$\text{ADP} + \text{P}_i + 7.3 \text{ kcal/mole} \rightarrow \text{ATP}$$

**Stage 1: Digestion:** In the first stage of catabolism, foods undergo digestion, a process that converts large molecules to smaller ones that can be absorbed by the body.

**Digestion of carbohydrates:** We begin the digestion of carbohydrates as soon as we chew food. An enzyme produced in the salivary glands called amylase hydrolyzed some of the α-glycosidic bonds in amylase and amylopectin. Producing smaller polysaccharides called dextrins, which contain three to eight glucose units; maltose; and some glucose. After swallowing, the partially digested starches enter the acid environment of the stomach, where the low pH soon stops further carbohydrate digestion. In the small intestine, which has a pH of about 8, an α-amylase produced in the pancreas hydrolyzes the remaining polysaccharides to maltose and glucose. Then enzymes produced in the mucosal cells that line the small intestine hydrolyze maltase as well as lactose and sucrose.
**Digestion of lipids (fats):** the digestion of dietary fats begins in the small intestine, when the hydrophobic fat globules mix with bile salts released from the gallbladder. In a process called **emulsification**, the bile salts break the fat globules into smaller droplets called micelles.
Then pancreatic lipases released from the pancreas hydrolyze the triacylglycerols in the micelles to yield monoacylglycerols and free fatty acids. These digestion products are absorbed into the intestinal lining where they recombine to form triacylglycerols, which are coated with proteins to form lipoproteins called chylomicrons. The chylomicrons transport the triacylglycerols through the lymph system and into the bloodstream to be carried to cells of the heart, muscle, and adipose tissues. In the cells, enzymes hydrolyze the triacylglycerols to yield glycerol and free fatty acids, which can be used for energy production. We can write the overall equation for the digestion of triacylglycerols as follows:

\[
\text{Triacylglycerols} + 3\text{H}_2\text{O} \xrightarrow{\text{lipase}} \text{Glycerol} + 3\text{Fatty acids}
\]

The products of fat digestion, glycerol and fatty acids, diffuse into the bloodstream and bind with plasma proteins to be transported to the tissues. Most of the glycerol goes into the liver where it is converted to glucose.

**Digestion of proteins:** in stage 1, the digestion of proteins begins in the stomach, where hydrochloric acid (HCl) at pH 2 denatures proteins and activates enzymes such as pepsin that begin to hydrolyze peptide bonds. Polypeptides from the stomach move into the small intestine where trypsin and chymotrypsin complete the hydrolysis of the peptides to amino acids. The amino acids are absorbed through the intestinal walls into the bloodstream for transport to the cells.

**Oxidation reaction by coenzymes:** when an enzyme catalyzes an oxidation, hydrogen atoms are removed from a substrate as hydrogen ions, \(2\text{H}^+\), and electrons, \(2\text{e}^-\).

\[
2\ \text{H atoms} \text{ (removed in oxidation)} \rightarrow 2\text{H}^+ + 2\text{e}^-
\]

Those hydrogen ions and electrons are picked up by a coenzyme, which is reduced.

**Some important coenzymes:** as we saw in chapter 23, the structures of many coenzymes include the water-soluble B vitamins we obtain from the foods in our diets. There are three important coenzymes:

**NAD\(^+\) (nicotinamide adenine dinucleotide):** is an important coenzyme in which the vitamin niacin provides the nicotinamide group, which is bonded to adenosine diphosphate (ADP). The NAD\(^+\) coenzyme participates in reactions that produce a carbon-oxygen (C=O) double bond such as the oxidation of alcohols to aldehydes and ketones. The NAD\(^+\) is reduced when the carbon in nicotinamide accepts a hydrogen ion and two electrons leaving one H\(^+\). For example ethanol is oxidized in the liver using NAD\(^+\):
FAD (flavin adenine dinucleotide): is a coenzyme derived from adenosine diphosphate (ADP) and fiboflavin. Riboflavin, also known as vitamin B₂, consists of ribitol, a sugar alcohol, and flavin. As a coenzyme, two nitrogen atoms in the flavin part of the FAD coenzyme accept the hydrogen, which reduces the FAD to FADH₂. FAD typically participates in oxidation reactions that produce a carbon-carbon (C=C) double bond such as dehydrogenation of alkanes.
**Coenzyme A (CoA):** is made up of several components: pantothenic acid (vitamin B₅), adenosine diphosphate (ADP), and aminoethanethiol. The main function of coenzyme A is to activate acyl groups (indicated by the letter A in CoA), particularly the acetyl group.

![Coenzyme A structure](image)

**Stage 2: Glycolysis:** our major source of energy is the glucose produced when we digest the carbohydrates in our food, or from glycogen, a polysaccharide stored in the liver and skeletal muscle. Glucose in the bloodstream enters our cells for further degradation in a pathway called glycolysis. Early organisms used this pathway to produce energy from simple nutrients long before there was any oxygen in Earth’s atmosphere. Glycolysis is an anaerobic process (no oxygen is required). In glycolysis, which is one of the metabolic pathways in stage 2, a six-carbon glucose molecule is broken down to yield two three-carbon pyruvate molecules. Glycolysis yields two ATP and two NADH for each glucose that is converted to two pyruvates (so it produces a big amount of energy).

![Glycolysis reaction](image)

**Pathways for pyruvate:** the pyruvate produced from glucose can now enter pathways that continue to extract energy. The available pathway depends on whether there is sufficient oxygen in the cell. We have two possibilities:

**Aerobic conditions:** in glycolysis, two ATP molecules were generated when glucose was converted to pyruvate. However, much more energy is still available. The greatest amount of the energy is obtained from glucose when oxygen levels are high in the cells. Under aerobic conditions, pyruvate is oxidized and a carbon atom is removed from pyruvate as CO₂. The coenzyme NAD⁺ is required for the oxidation. The resulting two-carbon acetyl compound is attached to CoA, producing acetyl CoA, an important intermediate in many metabolic pathways.
Anaerobic conditions: When we engage in strenuous exercise, the oxygen stored in our muscle cells is quickly depleted. Under anaerobic conditions, pyruvate is reduced to lactate and NAD$^+$ is produced. The accumulation of lactate causes the muscles to tire rapidly and become sore. After exercise, a person continues to breathe rapidly to repay the oxygen debt incurred during exercise. Most of the lactate is transported to the liver where it is converted back into pyruvate. Bacteria also convert pyruvate to lactate under anaerobic conditions.

Glycogen: we have just eaten a large meal that has supplied us with all the glucose we need to produce pyruvate and ATP by glucolysis. Then we use excess glucose to replenish our energy reserves by synthesizing glycogen that is stored in limited amounts in our skeletal muscle and liver. When glycogen stores are full, any remaining glucose in converted to triacylglycerols and stored as body fat. When our diet does not supply sufficient glucose, or we have utilized our blood glucose, we degrade the stored glycogen and release glucose.

Stage 3: Citric acid cycle: as a central pathway in metabolism, the citric acid cycle uses acetyl CoA from the degradation of carbohydrates, lipids, and proteins. The citric acid cycle is a series of reactions that degrades acetyl CoA to yield CO$_2$, NADH + H$^+$, and FADH$_2$. There are a total of 8 reactions in the citric acid cycle. In one turn of the citric acid cycle, four oxidation reactions provide hydrogen ions and electrons, which are used to reduce FAD and NAD$^+$ coenzymes.

Reaction 1: Formation of Citrate: in the first reaction, the two-carbon acetyl group in acetyl CoA bonds with four-carbon oxaloacetete to yield citrate and CoA.

Reaction 2: Isomerization to Isocitrate: in order to continue oxidation, citrate undergoes isomerization to yield isocitrate. This is necessary because the secondary hydroxyl group in isocitrate can be oxidized in the next reaction, while the tertiary hydroxyl group in citrate cannot be oxidized.

Reaction 3: First Oxidative Decarboxylation (CO$_2$): this is the first time in the citric acid cycle that both an oxidation and a decarboxylation occur together. The oxidation converts the hydroxyl group to a ketone and the decarboxylation removes a carbon as a CO$_2$ molecule. The loss of CO$_2$ shortens the carbon chain to yield a five-carbon α-ketoglutarate. The energy from the oxidation is used to transfer hydrogen ions and electrons to NAD$^+$. We can summarize the reactions as follows:

1. The hydroxyl group (-OH) is oxidized to acetone (C=O).
2. NAD$^+$ is reduced to yield NADH.
3. A carboxylate group (COO$^-$) is removed as CO$_2$. 
Reaction 4: Second Oxidative Decarboxylation (CO$_2$): in this reaction, a second CO$_2$ is removed as α-ketoglutarate undergoes oxidative decarboxylation. The resulting four-carbon group combines with coenzyme A to form succinyl CoA and hydrogen ions and electrons are transferred to NAD$^+$. The two reactions that occur are follows:

1. A second carbon is removed as CO$_2$.
2. NAD$^+$ is reduced to yield NADH.
**Reaction 5: Hydrolysis of Succinyl CoA:** the energy released by the hydrolysis of succinyl CoA is used to add a phosphate group (P_i) directly to GDP (guanosine diphosphate). The products are succinate and GTP, which is a high-energy compound similar to ATP. The hydrolysis of GTP is used to add a phosphate group to ADP, which regenerates GDP for the citric acid cycle. This is only time in the citric acid cycle that a direct substrate phosphorylation is used to produce ATP.

**Reaction 6: Dehydrogenation of Succinate:** in this oxidation reaction, hydrogen is removed from two carbon atoms in succinate, which produces fumarate, a compound with a trans double bond. This is the only place in the citric acid cycle where FAD is reduced to FADH_2.

**Reaction 7: Hydration:** Dehydrogenation forms Oxaloacetate: in the last step of the citric acid cycle, the hydroxyl (-OH) group in malate is oxidized to yield oxaloacetate, which has a ketone group. The coenzyme NAD^+ is reduced to NADH + H^+

We can write the overall chemical equation for one turn of the citric acid cycle as follows:

\[
\text{CH}_3\text{C}-\text{SCoA} + \text{GDP} + P_i + 3\text{NAD}^+ + \text{FAD} + 2\text{H}_2\text{O} \rightarrow 2\text{CO}_2 + \text{CoA} + \text{GTP} + 3\text{NADH} + \text{FADH}_2 + 3\text{H}^+ 
\]

**Electron transport:** in electron transport, hydrogen ions and electrons from NADH and FADH_2 are passed from one electron carrier to the next until they combine with oxygen to form H_2O.

**Electron carriers:** there are four types of electron carriers that make up the electron transport system.

1. **FMN (Flavin Mononucleotide):** is a coenzyme derived from riboflavin (vitamin B_2). In riboflavin, the ring system is attached to ribitol, the sugar alcohol of ribose. The reduced product is FMNH_2.
2. **Fe-S clusters**: is the name given to a group of iron-sulfur proteins that contain iron-sulfur clusters embedded in the proteins of the electron transport chain. The clusters contain iron, inorganic sulfides, and several cysteine groups. The iron in the clusters is reduced to Fe\(^{2+}\) and oxidized to Fe\(^{3+}\) as electrons are accepted and lost.

![Typical Fe-S cluster](image)

3. **Coenzyme Q (Q or CoQ)**: is derived from quinine, which is a six-carbon cyclic compound with two double bonds and two keto groups attached to a long carbon chain. Coenzyme Q is reduced when the keto groups of quinine accept hydrogen ions and electrons.

![Reduction of Coenzyme Q](image)

4. **Cytochromes (cyt)**: are proteins that contain an iron ion in a heme group. The different cytochromes are indicated by the letters following the abbreviation for cytochrome (cyt): cyt b, cyt c₁, cyt c, cyt a, and cyt a₃. In each cytochrome, the Fe\(^{3+}\) accepts a single electron to form Fe\(^{2+}\), which is oxidized back to Fe\(^{3+}\) when the electron is passed to the next cytochrome.

\[
\text{Fe}^{3+} + 1 \; \text{e}^- \leftrightarrow \text{Fe}^{2+}
\]

**Electron transfer**: a mitochondrion consists of inner and outer membranes with the matrix located between. Along the highly folded inner membrane are the enzyme and electron carriers required for electron transport. Two electron carriers, coenzyme Q and cytochrome c, are not firmly attached to the membrane. They function as mobile carriers shuttling electrons between the protein complexes that are tightly bound to membrane.

![Electron transport diagram](image)
**Complex I: NADH Dehydrogenase:** at complex I, NADH transfers hydrogen ions and electrons to FMN. The reduced FMNH$_2$ forms, which NADH is reoxidized to NAD$^+$, which returns to oxidative pathways such as the citric acid cycle to oxidize more substrates.

\[
\text{NADH} + H^+ + \text{FMN} \rightarrow \text{NAD}^+ + \text{FMNH}_2
\]

Within complex I, the NADH electrons are transferred to iron-sulfur (Fe-S) clusters and then to coenzyme (Q).

\[
\text{FMNH}_2 + Q \rightarrow \text{QH}_2 + \text{FMN}
\]

The overall reaction sequence in complex I can be written as follows:

\[
\text{NADH} + H^+ + Q \rightarrow \text{QH}_2 + \text{NAD}^+
\]

**Complex II: Succinate Dehydrogenase:** complex II is specifically used when FADH$_2$ is generated by the conversion of succinate to fumarate in the citric acid cycle. The electrons from FADH$_2$ are transferred to coenzyme Q to yield QH$_2$. Because complex II is at a lower energy level than complex I, the electrons from FADH$_2$ enter transport at a lower energy level than those from NADH.

\[
\text{FADH}_2 + Q \rightarrow \text{FAD} + \text{QH}_2
\]

**Complex III: Coenzyme Q-cytochrome c Reductase:** the mobile carrier QH$_2$ transfers the electrons it has collected from NADH and FADH$_2$ to an iron-sulfur (Fe-S) cluster and then to cytochrome b, the first cytochrome in complex III.

\[
\text{QH}_2 + 2 \text{cyt b (Fe}^{3+}) \rightarrow Q + 2 \text{cyt b (Fe}^{2+}) + 2H^+
\]

From cyt b, the electron is transferred to an Fe-S cluster and then to cytochrome c$_1$ and the to cytochrome c. Each time an Fe$^{3+}$ ion accepts an electron, it is reduced to Fe$^{2+}$, and the oxidized back to Fe$^{3+}$ as the electron is passed on along the chain. Cytochrome c is another mobile carrier; it moves the electron from complex III to complex IV.

**Complex IV: Cytochrome c Oxidase:** at complex IV, electrons are transferred from cytochrome c to cytochrome a, and then to cytochrome a$_3$, the last cytochrome. In the final step of electron transport, electrons and hydrogen ions combine with oxygen (O$_2$) to form water.

\[
4H^+ + 4e^- + O_2 \rightarrow 2H_2O
\]

**Oxidative phosphorylation:** energy is generated when electrons from the oxidation of substances flow through electron transport. This energy is used in the production of ATP for the cell, which is a process called oxidative phosphorylation.

**Chemiosmotic model:** this model links the energy from electron transport to a proton gradient that drives the synthesis of ATP. In this model, three of the complexes (I, III, and IV) extend through the inner membrane with one end of each complex in the matrix and the other end in the intermembrane space. In the chemiosmotic model, each of these complexes act as a proton pump by pushing protons (H$^+$) out of the matrix and into the intermembrane space.
This increase in protons in the intermembrane space lowers the pH and creates a proton gradient. To equalize the pH between the intermembrane space and the matrix, there is a tendency by the protons to return the matrix. However, protons cannot diffuse through the inner membrane. The only way protons can return to the matrix is to pass through a protein complex called \textbf{ATP synthase}. We might think of the flow of protons as a stream or river that turns a water wheel. As the protons flow through ATP synthase, energy generated from the proton gradient is used to drive the ATP synthesis. Thus the process of oxidative phosphorylation couples the energy from electron transport to the synthesis of ATP from ADP and P\textsubscript{i}.

Note: 6 ATP molecules are produced from glycolysis (step 2), 6 ATP from pyruvate (step 2) and 24 ATP from citric acid cycle (12 ATP for each acetyl CoA, we have two acetyl CoA, so 24 ATP in step 3). Total ATP molecules for the complete oxidation of glucose is 36 ATP.

\[
\text{C}_6\text{H}_{12}\text{O}_6 + 6\text{O}_2 + 36 \text{ADP} + 36 \text{P}_i \rightarrow 6\text{CO}_2 + 6\text{H}_2\text{O} + 36 \text{ATP}
\]

**Oxidation of fatty acids:** a large amount of energy is obtained when fatty acids undergo oxidation in the mitochondria to yield acetyl CoA. In stage 2 of fat metabolism, fatty acids undergo \textbf{beta oxidation (β oxidation)}, which removes two-carbon segments, one at a time, from a fatty acid.

Each cycle in β oxidation produces acetyl CoA and a fatty acid that is shorter by two carbons. The cycle repeats until the original fatty acid is completely degraded to two-carbon acetyl CoA units. Each acetyl CoA can then enter the citric acid cycle in the same way as the acetyl CoA units derived from glucose.

**Fatty acid activation:** before a fatty acid can enter the mitochondria, it undergoes activation in the cytosol. The activation process combines a fatty acid with coenzyme A to yield fatty acyl CoA. The energy released by the hydrolysis of two phosphate groups from ATP is used to drive the reaction. The products are AMP and two inorganic phosphates (2P\textsubscript{i}).
**Reaction of β oxidation cycle:** in the matrix, fatty acyl CoA molecules undergo β oxidation, which is a cycle of four reactions that convert the -CH₂- of the β carbon to a β-keto group. Once the β-keto group is formed, a two-carbon acetyl group can be split from the chain, which shortens the fatty acyl group.

**Reaction 1: Oxidation (dehydrogenation):** in the first reaction of β oxidation, the FAD coenzyme removes hydrogen atoms from the α and β carbons of the activation fatty acid to form a trans carbon-carbon double bond and FADH₂.

**Reaction 2: Hydration:** a water molecules now add across the trans double bond, which places a hydroxyl group (-OH) on the β carbon.

**Reaction 3: Oxidation (Dehydrogenation):** the hydroxyl group on the β carbon is oxidized to yield a ketone. The hydrogen atoms removed in the dehydrogenation reduce coenzyme NAD⁺ to NADH + H⁺. At this point, the β carbon has been oxidized to a keto group.

**Reaction 4: Cleavage of Acetyl CoA:** in the final step of β oxidation, the α-Cβ bond splits to yield free acetyl CoA and fatty acyl CoA molecule that is shorter two carbon atoms. This shorter fatty acyl CoA is ready to go through the β oxidation cycle again.

**Note:** the number of carbon atoms in a fatty acid determines the number of times the cycle repeats and the number of acetyl CoA units it produces. For example, the complete β oxidation of myristic (C₁₄) produces seven acetyl CoA groups, which equal to one-half the number of carbon atoms in the chain. Because the final turn of the cycle produces two acetyl CoA groups, the total number of times the cycle repeats is one less than the number of acetyl groups it produces.

**Ketone bodies:** when carbohydrates are not available to meet energy needs, the body breaks down body fat. However, the oxidation of large amounts of fatty acids cause acetyl CoA molecules to accumulate in the liver. Then acetyl CoA molecules combine to form keto compounds called ketone bodies. Ketone bodies are produced mostly in the liver and transported to cells in the heart, brain, and skeletal muscle, where small amounts of energy can be obtained by converting acetoacetate or β-hydroxybutyrate back to acetyl CoA.

$$\beta\text{-hydroxybutyrate} \rightarrow \text{acetoacetate} + 2 \text{CoA} \rightarrow 2 \text{acetyl CoA}$$
Ketosis: when ketone bodies accumulate, they may not be completely metabolized by the body. This may lead to a condition called ketosis, which is found in severe diabetes, diets high in fat and low in carbohydrates, and starvation. Because two of the ketone bodies are acids, they can lower the blood pH below 7.4, which is acidosis, a condition that often accompanies ketosis. A drop in blood pH can interfere with the ability of the blood to carry oxygen and cause breathing difficulties.

Fatty acid synthesis: When the body has met all its energy needs and the glycogen stores are full, acetyl CoA from the breakdown of carbohydrates and fatty acids is used to form new fatty acids. Two-carbon acetyl units are linked together to give a 16-carbon fatty acid, palmitic acid. Several of the reactions are the reverse of the reactions we discussed in fatty acid oxidation. However, fatty acid oxidation occurs in the mitochondria and uses FAT and NDA⁺, whereas fatty acid synthesis occurs in the cytosol and uses the reduced coenzyme NADPH. NADPH is similar to NADH, except it has a phosphate group. The new fatty acids are attached to glycerol to make triacylglycerol, which are stored as body fat.

Degradation of amino acids: when dietary protein exceeds the nitrogen needed by the body, the excess amino acids are degraded. The degradation of amino acids occurs primarily in the liver.

Transamination: in the transamination reaction, an α-amino group is transferred from an amino acid to an α-keto acid, usually α-ketoglutarate. A new amino acid and a new α-keto acid are produced. We can write an equation to show the transfer of the amino group from alanine to α-ketoglutarate to yield glutamate, the new amino acid, and the α-keto acid pyruvate.
Oxidative deamination: in a process called oxidative deamination, the amino group in glutamate is removed as an ammonium ion $\text{NH}_4^+$. This reaction is catalyzed by glutamate dehydrogenase, which use either NAD$^+$ or NADP$^+$ as a coenzyme. Then the ammonium ion is converted to urea.

![Chemical structure of glutamate deamination](image)

Urea cycle: ammonium ion is highly toxic. In a series of reactions called the urea cycle, $\text{NH}_4^+$ combines with $\text{CO}_2$ to yield urea, which is excreted in the urine. There are several steps of the urea cycle with several intermediates, but the overall reaction converts ammonium ion into urea.

![Chemical structure of urea cycle](image)

Note: in one day, a typical adult may excrete about 25-30g of urea in the urine. This amount increases when a diet is high in protein. If urea is not properly excreted, it builds up quickly to a toxic level. To detect renal disease, the blood urea nitrogen (BUN) level is measured. If the BUN is high, protein intake must be reduced, and hemodialysis may be needed to remove toxic nitrogen waste from the blood.

Fates of the carbon atoms from amino acids: the carbon skeletons from the transamination of amino are used as intermediates of the citric acid cycle or other metabolic pathways. We can classify the amino acids according to the number of carbon atoms in those intermediates. The amino acids with the carbons, or those that are converted into carbon skeletons with three carbons, are converted to pyruvate. The four-carbon group consists of amino acids that are converted to oxaloacetate, and the five-carbon group provides $\alpha$-ketoglutarate. Some amino acids can enter different pathways to form citric acid cycle intermediates.

Energy from amino acids: normally, only a small amount (about 10%) of our energy needs is supplied by amino acids. However, more energy is extracted from amino acids in condition such as fasting or starvation, when carbohydrates and fat stores are exhausted. If amino acids remain the only source of energy for a long period of time, the breakdown of body proteins eventually leads to a destruction of essential body tissues.