CHAPTER 6

Biochemical Pathways—Cellular Respiration

Mutation Leads to Personal Energy Crisis

Genes You Inherit from Mom Can Be Harmful

CHAPTER OUTLINE

Ten-year-old Latisha Franklin has suffered from her own personal energy crisis since she was four. Latisha has been diagnosed with an uncommon illness, an abnormality called mitochondrial encephalopathy, or MELAS. MELAS is the acronym for *m*itochondrial *e*ncephalopathy, *l*actic *a*cidosis, and *s*troke-like episodes. It is caused by mutations in the DNA found in her mitochondria, mDNA. Mitochondria manufacture proteins using their own DNA. Enzymes help to produce useful chemical bond energy for cells, ATP. mDNA differs from the chromosomes found in the nucleus. They are much smaller and circular. Any changes (mutations) in mDNA can have far-reaching effects on the body's ability to control energy production.

Latisha has suffered encephalopathy in the form of epilepsy-like seizures and migraine-like headaches. She has also had severe muscle pain caused by excess lactic acid in her muscles, and stroke-like symptoms leading to paralysis and confusion.

The mutations that cause MELAS and the chemical changes that occur in mitochondria have been identified; however, there is no cure. Medical professionals can only manage symptoms.

- **In what molecular form do cells use chemical-bond energy?**
- **How are these energy-containing molecules generated by cells?**
- **Why would a strict vitamin regimen be helpful in managing Latisha's symptoms?**

Background Check

Concepts you should already know to get the most out of this chapter:

- Features of oxidation-reduction chemical reactions (chapter 2)
- The structure of carbohydrates (chapter 3)
- The structure and function of mitochondria and the types of cells in which they are located (chapter 4)
- How enzymes work in conjunction with ATP, electron transport, and a proton pump (chapter 5)

6.1 Energy and Organisms

There are hundreds of different chemical reactions taking place within the cells of organisms. Many of these reactions are involved in providing energy for the cells. Organisms are classified into groups based on the kind of energy they use. Organisms that are able to use basic energy sources, such as sunlight, to make energy-containing organic molecules from inorganic raw materials are called **autotrophs** (*auto* = self; *troph* = feeding). There are also prokaryotic organisms that use inorganic chemical reactions as a source of energy to make larger organic molecules. This process is known as **chemosynthesis.** Therefore, there are at least two kinds of autotrophs: Those that use light are called *photosynthetic* autotrophs and those that use inorganic chemical reactions are called *chemosynthetic* autotrophs. All other organisms require organic molecules as food and are called **heterotrophs** (*hetero* = other; *troph* = feeding). Heterotrophs get their energy from the chemical bonds of food molecules, such as carbohydrates, fats, and proteins, which they must obtain from their surroundings.

Within eukaryotic cells, certain biochemical processes are carried out in specific organelles. Chloroplasts are the sites of photosynthesis, and mitochondria are the sites of most of the reactions of cellular respiration (figure 6.1). Because prokaryotic cells lack mitochondria and chloroplasts, they carry out photosynthesis and cellular respiration within the cytoplasm or on the inner surfaces of the cell membrane or on other special membranes. Table 6.1 provides a summary of the concepts just discussed and how they are related to one another.

This chapter will focus on the reactions involved in the processes of cellular respiration. In **cellular respiration,**

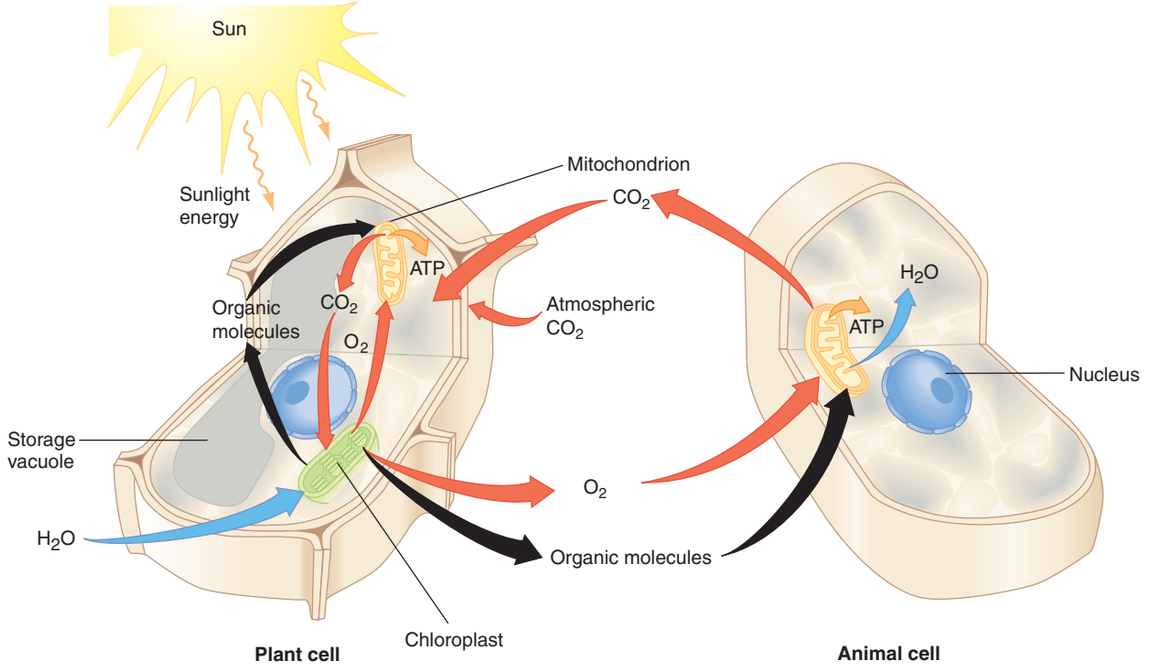


FIGURE 6.1 Biochemical Pathways That Involve Energy Transformation
Photosynthesis and cellular respiration both involve a series of chemical reactions that control the flow of energy. Organisms that contain photosynthetic machinery are capable of using light, water, and carbon dioxide to produce organic molecules, such as sugars, proteins, lipids, and nucleic acids. Oxygen is also released as a result of photosynthesis. In aerobic cellular respiration, organic molecules and oxygen are used to provide the energy to sustain life. Carbon dioxide and water are also released during aerobic respiration.

TABLE 6.1 Summary of Biochemical Pathways, Energy Sources, and Kinds of Organisms

Autotroph or Heterotroph	Biochemical Pathways	Energy Source	Kinds of Organisms	Notes
Autotroph	Chemosynthesis	Inorganic chemical reactions	Certain Bacteria and Archaea	There are many types of chemosynthesis.
Autotroph	Photosynthesis	Light	Certain Bacteria and Archaea	Photosynthesis in Bacteria and Archaea differs from photosynthesis that takes place in the chloroplasts of eukaryotic organisms.
			Eucarya—plants and algae	Photosynthesis takes place in chloroplasts.
Autotroph and heterotroph	Cellular respiration	Oxidation of large, organic molecules	Bacteria and Archaea	There are many forms of cellular respiration. Some organisms use aerobic celluar respiration; others use anaerobic cellular respiration. Cellular respiration in Bacteria and Archaea does not take place in mitochondria.
			Eucarya—plants, animals, fungi, algae, protozoa	Most Eucarya use aerobic celluar respiration and it takes place in mitochondria.

organisms control the release of chemical-bond energy from large, organic molecules and use the energy for the many activities necessary to sustain life. All organisms, whether autotrophic or heterotrophic, must carry out cellular respiration if they are to survive. Because nearly all organisms use organic molecules as a source of energy, they must obtain these molecules from their environment or manufacture these organic molecules, which they will later break down. Thus, photosynthetic organisms produce food molecules, such as carbohydrates, for themselves as well as for all the other organisms that feed on them. There are many variations of cellular respiration. Some organisms require the presence of oxygen for these processes, called *aerobic* processes. Other organisms carry out a form of respiration that does not require oxygen; these processes are called *anaerobic*.

6.1 CONCEPT REVIEW

1. How do autotrophs and heterotrophs differ?
2. What is chemosynthesis?
3. How are respiration and photosynthesis related to autotrophs and heterotrophs?

6.2 An Overview of Aerobic Cellular Respiration

Aerobic cellular respiration is a specific series of enzyme-controlled chemical reactions in which oxygen is involved in the breakdown of glucose into carbon dioxide and water; the chemical-bond energy from glucose is released to the cell in the form of ATP. The following equation summarizes this process as it occurs in your cells and those of many other organisms:

$$\underset{\text{glucose}}{C_6H_{12}O_6} + \underset{\text{oxygen}}{6\ O_2} \rightarrow \underset{\text{carbon dioxide}}{6\ CO_2} + \underset{\text{water}}{6\ H_2O} + \underset{(\text{ATP} + \text{heat})}{\text{energy}}$$

Covalent bonds are formed by atoms sharing pairs of fast-moving, energetic electrons. Therefore, the covalent bonds in the sugar glucose contain chemical potential energy. The removal of the electrons from glucose results in glucose being *oxidized*. Of all the covalent bonds in glucose (O—H, C—H, C—C), those easiest to get at are the C—H and O—H bonds on the outside of the molecule. When these bonds are broken, two things happen:

1. The energy of the electrons can ultimately be used to phosphorylate ADP molecules to produce higher-energy ATP molecules.
2. Hydrogen ions (protons) are released and pumped across membranes, creating a gradient. When they flow back to the side from which they were pumped, their energy is used to generate even more ATP (refer to chapter 5, Proton Pump).

These high-energy electrons cannot be allowed to fly about at random because they would quickly combine with other molecules, causing cell death. Electron-transfer molecules, such as NAD^+ and FAD, hold electrons temporarily before passing them on to other molecules. ATP is formed when these transfers take place (see chapter 5). Once energy

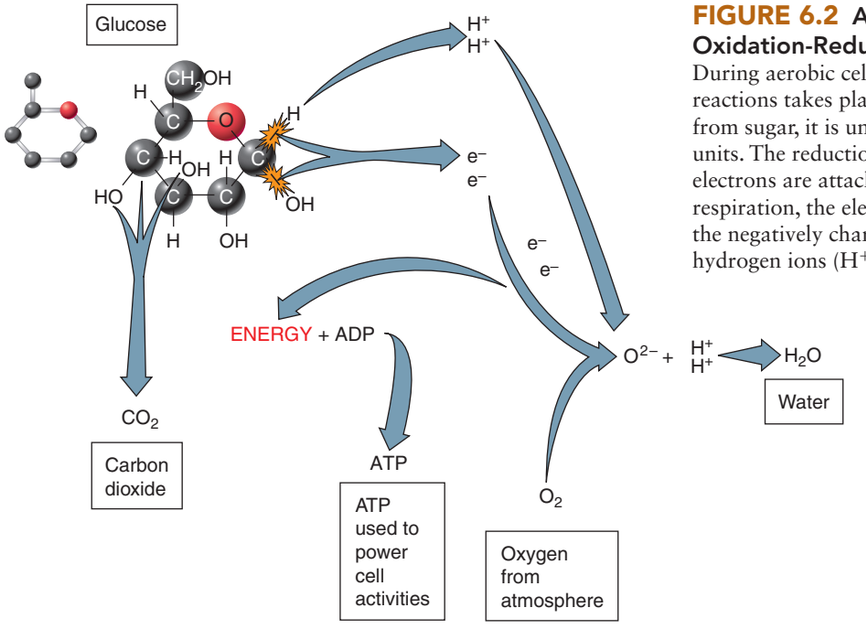


FIGURE 6.2 Aerobic Cellular Respiration and Oxidation-Reduction Reaction
During aerobic cellular respiration, a series of oxidation-reduction reactions takes place. When the electrons are removed (oxidation) from sugar, it is unable to stay together and breaks into smaller units. The reduction part of the reaction occurs when these electrons are attached to another molecule. In aerobic cellular respiration, the electrons are eventually picked up by oxygen and the negatively charged oxygen attracts two positively charged hydrogen ions (H^+) to form water.

has been removed from electrons for ATP production, the electrons must be placed in a safe location. In *aerobic* cellular respiration, these electrons are ultimately attached to oxygen. Oxygen serves as the final resting place of the less energetic electrons. When the electrons are added to oxygen, it becomes a negatively charged ion, $O^=$.

Because the oxygen has gained electrons, it has been *reduced. Thus, in the aerobic cellular respiration of glucose, glucose is oxidized and oxygen is reduced.* A molecule cannot simply lose its electrons—they have to go someplace! If something is oxidized (loses electrons), something else must be reduced (gains electrons). Eventually, the positively charged hydrogen ions (H^+) that were released from the glucose molecule combine with the negatively charged oxygen ion ($O^=$) to form water (H_2O).

As all the hydrogens are stripped off the glucose molecule, the remaining carbon and oxygen atoms are rearranged to form individual molecules of CO_2. All the hydrogen originally a part of the glucose has been moved to the oxygen to form water. All the remaining carbon and oxygen atoms of the original glucose are now in the form of CO_2. The energy released from this process is used to generate ATP (figure 6.2).

In cells, these reactions take place in a particular order and in particular places within the cell. In eukaryotic cells, the process of releasing energy from food molecules begins in the cytoplasm and is completed in the mitochondria. There are three distinct enzymatic pathways involved (figure 6.3): glycolysis, the Krebs cycle, and the electron-transport system.

Glycolysis

Glycolysis (*glyco* = sugar; *lysis* = to split) is a series of enzyme-controlled, anaerobic reactions that takes place in the cytoplasm of cells, which results in the breakdown of glucose with the release of electrons and the formation of ATP. During glycolysis, the 6-carbon sugar glucose is split into two smaller, 3-carbon molecules, which undergo further modification to form pyruvic acid or pyruvate.[1] Enough energy is released to produce two ATP molecules. Some of the bonds holding hydrogen atoms to the glucose molecule are broken, and the electrons are picked up by electron carrier molecules (NAD^+) and transferred to a series of electron-transfer reactions known as the electron-transport system (ETS).

The Krebs Cycle

The **Krebs cycle** is a series of enzyme-controlled reactions that takes place inside the mitochondrion, which completes the breakdown of pyruvic acid with the release of carbon dioxide, electrons, and ATP. During the Krebs cycle, the pyruvic acid molecules produced from glycolysis are further broken down. During these reactions, the remaining hydrogens are removed from the pyruvic acid, and their electrons are picked up by the electron carriers NAD^+ and FAD. These electrons are sent to the electron-transport system. A small amount of ATP is also formed during the Krebs cycle. The carbon and oxygen atoms that are the remains of the pyruvic acid molecules are released as carbon dioxide (CO_2).

The Electron-Transport System (ETS)

The **electron-transport system (ETS)** is a series of enzyme-controlled reactions that converts the kinetic energy of hydrogen electrons to ATP. The electrons are carried to the electron-transport system from glycolysis and the Krebs cycle as NADH and $FADH_2$. The electrons are transferred through a series of oxidation-reduction reactions involving enzymes until eventually the electrons are accepted by oxygen atoms

[1]Several different ways of naming organic compounds have been used over the years. For our purposes, pyruvic acid and pyruvate are really the same basic molecule although technically, pyruvate is what is left when pyruvic acid has lost its hydrogen ion: pyruvic acid → H^+ + pyruvate. You also will see terms such as lactic acid and lactate and citric acid and citrate and many others used in a similar way.

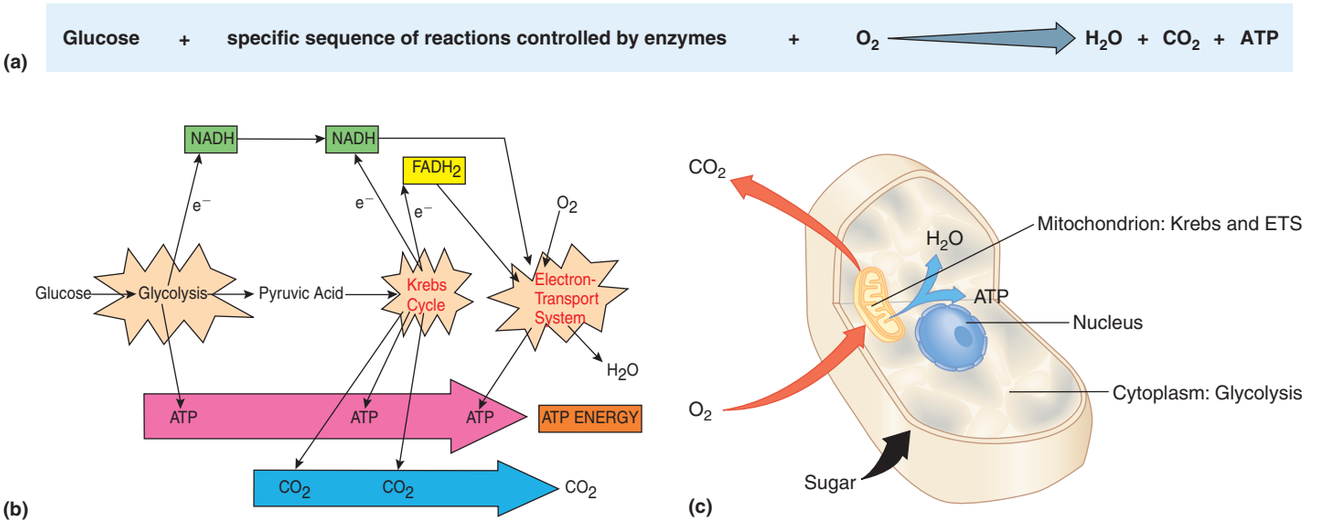


FIGURE 6.3 Aerobic Cellular Respiration: Overview

(a) This sequence of reactions in the aerobic oxidation of glucose is an overview of the energy-yielding reactions of a cell. *(b)* Glycolysis, the Krebs cycle, and the electron-transport system (ETS) are each a series of enzyme-controlled reactions that extract energy from the chemical bonds in a glucose molecule. During glycolysis, glucose is split into pyruvic acid and ATP and electrons are released. During the Krebs cycle, pyruvic acid is further broken down to carbon dioxide with the release of ATP and the release of electrons. During the electron-transport system, oxygen is used to accept electrons, and water and ATP are produced. *(c)* Glycolysis takes place in the cytoplasm of the cell. Pyruvic acid enters mitochondria, where the Krebs cycle and electron-transport system (ETS) take place.

to form oxygen ions ($O^=$). During this process, a great deal of ATP is produced. The ATP is formed as a result of a proton gradient established when the energy of electrons is used to pump protons across a membrane (refer to chapter 5). The subsequent movement of protons back across the membrane results in ATP formation. The negatively charged oxygen atoms attract two positively charged hydrogen ions to form water (H_2O).

Aerobic respiration can be summarized as follows. *Glucose* enters glycolysis and is broken down to pyruvic acid, which enters the Krebs cycle, where the pyruvic acid molecules are further dismantled. The remains of the pyruvic acid molecules are released as *carbon dioxide*. The electrons and hydrogen ions released from glycolysis and the Krebs cycle are transferred as NADH and $FADH_2$ to the electron-transport system, where the electrons are transferred to *oxygen* available from the atmosphere. When hydrogen ions attach to oxygen ions, *water* is formed. *ATP* is formed during all three stages of aerobic cellular respiration, but most comes from the electron-transfer system.

6.2 CONCEPT REVIEW

4. Aerobic cellular respiration occurs in three stages. Name these and briefly describe what happens in each stage.
5. Which cellular organelle is involved in the process of aerobic cellular respiration?

6.3 The Metabolic Pathways of Aerobic Cellular Respiration

It is a good idea to begin with the simplest description and add layers of understanding as you go to additional levels. Therefore, this discussion of aerobic cellular respiration is divided into two levels:

1. **a fundamental description and**
2. **a detailed description.**

Ask your instructor which level is required for your course of study.

Fundamental Description

Glycolysis

Glycolysis is a series of enzyme-controlled reactions that takes place in the cytoplasm. During glycolysis, a 6-carbon sugar molecule (glucose) has energy added to it from two ATP molecules. Adding this energy makes some of the bonds of the glucose molecule unstable, and the glucose molecule is more easily broken down. After passing through several more enzyme-controlled reactions, the 6-carbon glucose is broken down to two 3-carbon molecules known as glyceraldehyde-3-phosphate (also known as PGA, or phosphoglyceraldehyde), which undergo additional reactions to form pyruvic acid ($CH_3COCOOH$).

Enough energy is released by this series of reactions to produce four ATP molecules. Because two ATP molecules were used to start the reaction and four were produced, there is a *net gain* of two ATPs from the glycolytic pathway (figure 6.4). During the process of glycolysis, some hydrogens and their electrons are removed from the organic molecules being processed and picked up by the electron-transfer molecule NAD^+ to form NADH. Enough hydrogens are released during glycolysis to form 2 NADHs. The NADH with its extra electrons contains a large amount of potential energy, which can be used to make ATP in the electron-transport system. The job of the coenzyme NAD^+ is to transport these energy-containing electrons and protons safely to the electron-transport system. Once they have dropped off their electrons, the oxidized NAD^+s are available to pick up more electrons and repeat the job.

Fundamental Summary of One Turn of Glycolysis

Glucose + 2 ATP + 2 NAD^+
($C_6H_{12}O_6$)

↓

4 ATP + 2 NADH + 2 pyruvic acid
($CH_3COCOOH$)

The Krebs Cycle

The series of reactions known as the Krebs cycle takes place within the mitochondria of cells. It gets its name from its discoverer, Hans Krebs, and the fact that the series of reactions begins and ends with the same molecule; it cycles. The Krebs cycle is also known as the citric acid cycle and the TriCarboxylic Acid cycle (TCA). The 3-carbon pyruvic acid molecules released from glycolysis enter the mitochondria. These are acted upon by specific enzymes made using genetic information found on DNA located within the mitochondria (mDNA). One of these carbons is stripped off and the remaining 2-carbon fragment is attached to a molecule of *coenzyme A (CoA)*, becoming a compound called **acetyl-CoA.** Coenzyme A is made from pantethine (pantothenic acid), a form of vitamin B_5. Acetyl-CoA is the molecule that proceeds through the Krebs cycle. At the time the acetyl-CoA is produced, 2 hydrogens are attached to NAD^+ to form NADH. The carbon atom that was removed is released as carbon dioxide.

Summary of Changes as Pyruvic Acid is Converted to Acetyl-CoA

Pyruvic Acid + NAD^+ + Coenzyme A

↓

CO + NADH + Acetyl-CoA

During the Krebs cycle (figure 6.5), the acetyl-CoA is completely oxidized (i.e., the remaining hydrogens and their

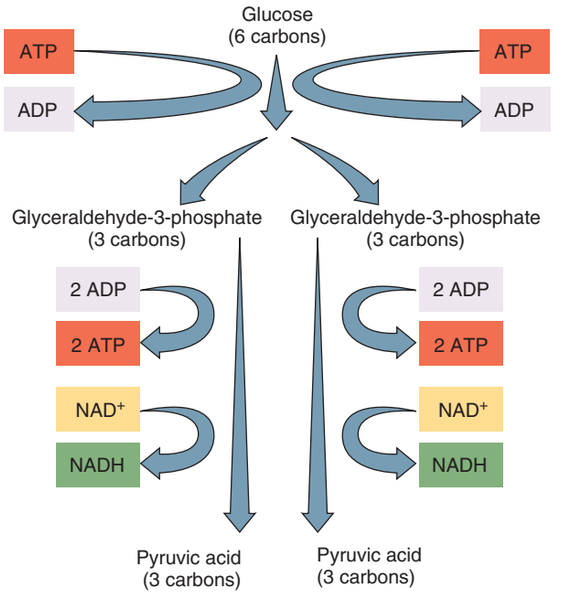


FIGURE 6.4 Glycolysis: Fundamental Description
Glycolysis is the biochemical pathway many organisms use to oxidize glucose. During this sequence of chemical reactions, the 6-carbon molecule of glucose is oxidized. As a result, pyruvic acid is produced, electrons are picked up by NAD^+, and ATP is produced.

electrons are removed). Most of the electrons are picked up by NAD^+ to form NADH, but at one point in the process FAD picks up electrons to form $FADH_2$. Regardless of which electron carrier is being used, the electrons are sent to the electron-transport system. The remaining carbon and oxygen atoms are combined to form CO_2. As in glycolysis, enough energy is released to generate 2 ATP molecules. At the end of the Krebs cycle, the acetyl portion of the acetyl-CoA has been completely broken down (oxidized) to CO_2. The CoA is released and available to be used again. The energy in the molecule has been transferred to ATP, NADH, or $FADH_2$. Also, some of the energy has been released as heat. For each of the acetyl-CoA molecules that enters the Krebs cycle, 1 ATP, 3 NADHs, and 1 $FADH_2$ are produced. If we count the NADH produced during glycolysis, when acetyl-CoA was formed, there are a total of 4 NADHs for each pyruvic acid that enters a mitochondrion.

Fundamental Summary of One Turn of the Krebs Cycle

Acetyl-Coenzyme A + ADP + 3 NAD + FAD
(CH_3OC-CoA)

↓

CoA + ATP + 2 CO_2 + 3 NADH + $FADH_2$

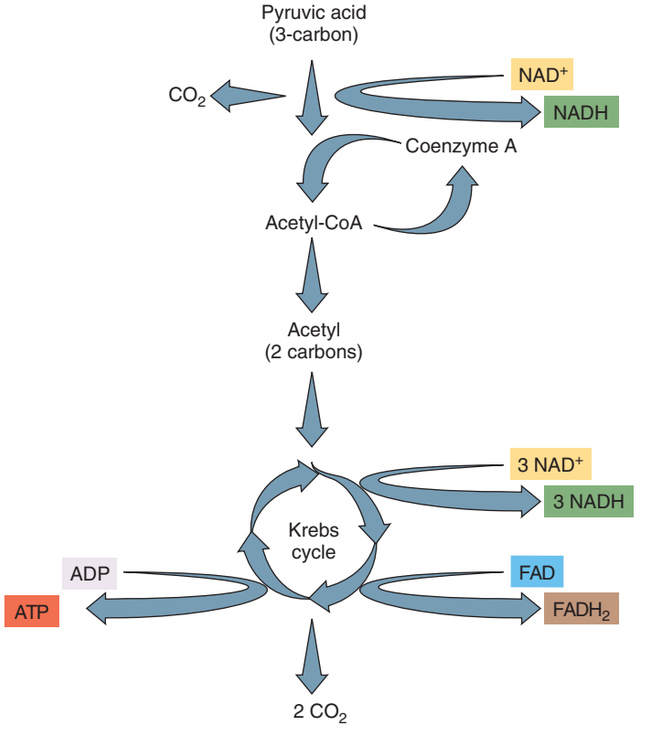


FIGURE 6.5 Krebs Cycle: Fundamental Description
The Krebs cycle takes place in the mitochondria of cells to complete the oxidation of glucose. During this sequence of chemical reactions, a pyruvic acid molecule produced from glycolysis is stripped of its hydrogens. The hydrogens are picked up by NAD^+ and FAD for transport to the ETS. The remaining atoms are reorganized into molecules of carbon dioxide. Enough energy is released during the Krebs cycle to form 2 ATPs. Because 2 pyruvic acid molecules were produced from glycolysis, the Krebs cycle must be run twice in order to complete their oxidation (once for each pyruvic acid).

The Electron-Transport System

Of the three steps of aerobic cellular respiration, (glycolysis, Krebs cycle, and electron-transport system) cells generate the greatest amount of ATP from the electron-transport system (figure 6.6). During this stepwise sequence of oxidation-reduction reactions, the energy from the NADH and $FADH_2$ molecules generated in glycolysis and the Krebs cycle is used to produce ATP. Iron-containing *cytochrome* (*cyto* = cell; *chrom* = color) enzyme molecules are located on the membranes of the mitochondrion. The energy-rich electrons are passed *(transported)* from one cytochrome to another, and the energy is used to pump protons (hydrogen ions) from one side of the membrane to the other. The result of this is a higher concentration of hydrogen ions on one side of the membrane. As the concentration of hydrogen ions increases on one side, a proton gradient builds up. Because of this concentration gradient, when a membrane channel is opened, the protons flow back to the side from which they were pumped. As they

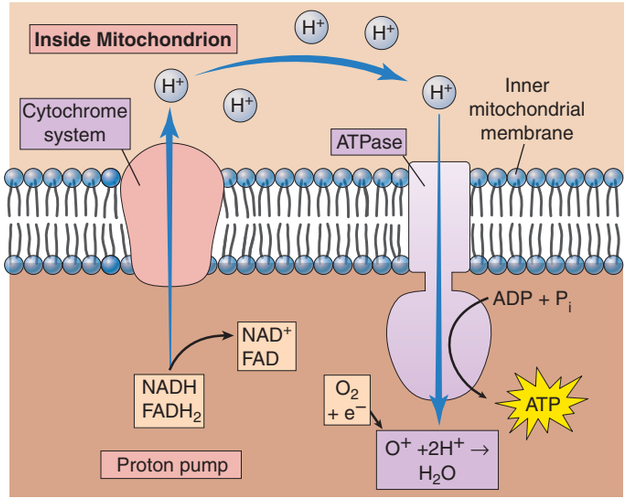


FIGURE 6.6 The Electron-Transport System: Fundamental Description
The electron-transport system (ETS) is also known as the cytochrome system. With the help of enzymes, the electrons are passed through a series of oxidation-reduction reactions. The energy the electrons give up is used to pump protons (H^+) across a membrane in the mitochondrion. When protons flow back through the membrane, enzymes in the membrane cause the formation of ATP. The protons eventually combine with the oxygen that has gained electrons, and water is produced.

pass through the channels, a phosphorylase enzyme (ATP synthetase, also referred to as ATPase) speeds the formation of an ATP molecule by bonding a phosphate to an ADP molecule (phosphorylation). When all the electrons and hydrogen ions are accounted for, a total of 32 ATPs are formed from the electrons and hydrogens removed from the original glucose molecule. The hydrogens are then bonded to oxygen to form water.

Fundamental Summary of the Electron-Transport System

$$32\ ADP + 10\ NADH + 2\ FADH_2 + 6\ O_2\ (\text{free}) \rightarrow 32\ ATP + 10\ NAD^+ + 2\ FAD + 12\ H_2O$$

Detailed Description

Glycolysis

The first stage of the cellular respiration process takes place in the cytoplasm. This first step, known as glycolysis, consists of the enzymatic breakdown of a glucose molecule without the use of molecular oxygen. Because no oxygen is required,

glycolysis is called an anaerobic process. The glycolysis pathway can be divided into two general sets of reactions. The first reactions make the glucose molecule unstable, and later oxidation-reduction reactions are used to synthesize ATP and capture hydrogens.

Because glucose is a very stable molecule and will not automatically break down to release energy, some energy must be added to the glucose molecule in order to start glycolysis. In glycolysis, the initial glucose molecule gains a phosphate to become glucose-6-phosphate, which is converted to fructose-6-phosphate. When a second phosphate is added, fructose-1,6-bisphosphate (P—C_6—P) is formed. This 6-carbon molecule is unstable and breaks apart to form two 3-carbon, glyceraldehyde-3-phosphate molecules.

Each of the two glyceraldehyde-3-phosphate molecules acquires a second phosphate from a phosphate supply normally found in the cytoplasm. Each molecule now has 2 phosphates attached to form 1,3-bisphosphoglycerate (P—C_3—P). A series of reactions follows, in which energy is released by breaking chemical bonds that hold the phosphates to 1,3-bisphosphoglycerate. The energy and the phosphates are used to produce ATP. Since there are two 1,3-bisphosphoglycerate molecules each with 2 phosphates, a total of 4 ATPs are produced. Because 2 ATPs were used to start the process, a net yield of 2 ATPs results. In addition, 4 hydrogen atoms detach from the carbon skeleton and their electrons are transferred to NAD^+ to form NADH, which transfers the electrons to the electron-transport system. The 3-carbon pyruvic acid molecules that remain are the raw material for the Krebs cycle. Because glycolysis occurs in the cytoplasm and the Krebs cycle takes place inside mitochondria, the pyruvic acid must enter the mitochondrion before it can be broken down further (figure 6.7).

Summary of Detailed Description of Glycolysis

The process of glycolysis takes place in the cytoplasm of a cell, where glucose ($C_6H_{12}O_6$) enters a series of reactions that:

1. requires the use of 2 ATPs,
2. ultimately results in the formation of 4 ATPs,
3. results in the formation of 2 NADHs, and
4. results in the formation of 2 molecules of pyruvic acid ($CH_3COCOOH$).

Because 2 molecules of ATP are used to start the process and a total of 4 ATPs are generated, each glucose molecule that undergoes glycolysis produces a net yield of 2 ATPs.

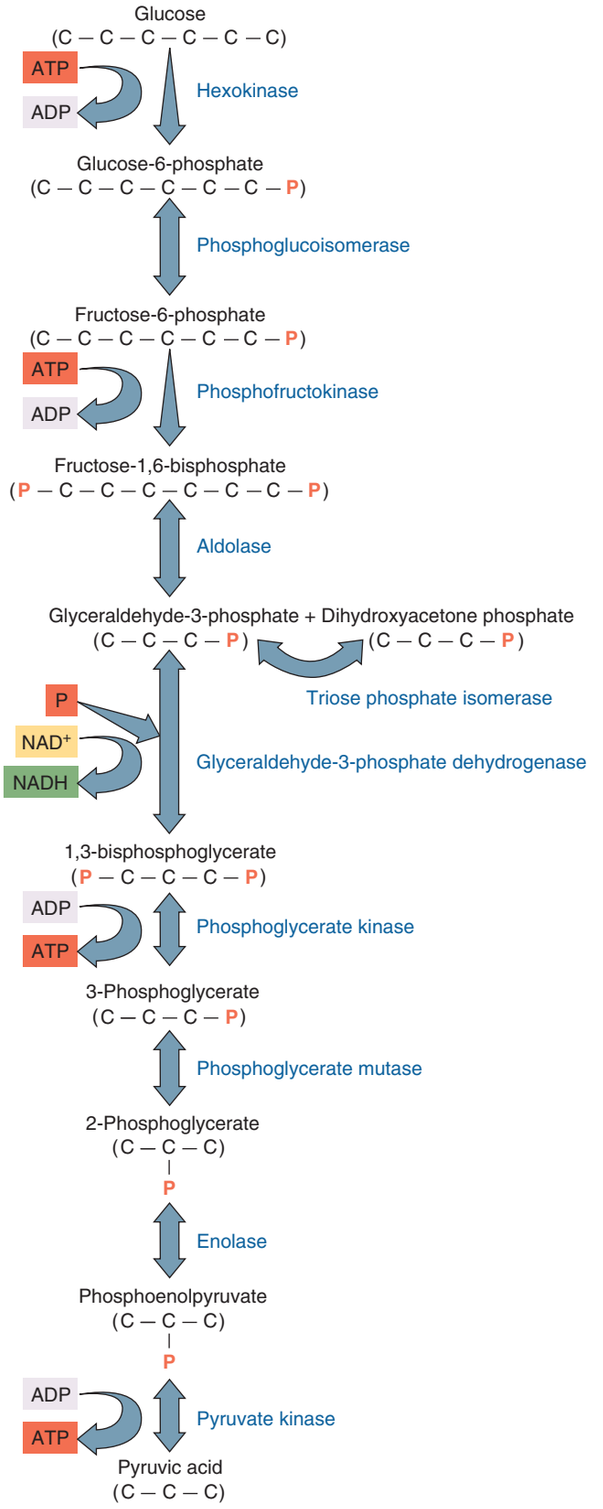


FIGURE 6.7 Glycolysis: Detailed Description
Glycolysis is a process that takes place in the cytoplasm of cells. It does not require the use of oxygen, so it is an anaerobic process. During the first few steps, phosphates are added from ATP and ultimately the 6-carbon sugar is split into two 3-carbon compounds. During the final steps in the process, NAD^+ accepts electrons and hydrogen to form NADH. In addition, ATP is produced. Two ATPs form for each of the 3-carbon molecules that are processed in glycolysis. Because there are two 3-carbon compounds, a total of 4 ATPs are formed. However, because 2 ATPs were used to start the process, there is a net gain of 2 ATPs. Pyruvic acid (pyruvate) is left at the end of glycolysis.

OUTLOOKS 6.1

What Happens When You Drink Alcohol

Ethyl alcohol (CH_3CH_2OH) is a 2-carbon organic compound with a single alcoholic functional group. Because it is soluble in water, it is easily absorbed into the bloodstream. After an alcoholic beverage enters the body, it is spread by the circulatory system rapidly throughout the body and enters the brain. The majority of the alcohol is absorbed from the stomach (20%) and small intestine (80%). The more a person drinks, the higher the blood alcohol level. How fast alcohol is absorbed depends on several factors.

1. Food in the stomach slows absorption.
2. Strenuous physical exercise decreases absorption.
3. Drugs (e.g., nicotine, marijuana, and ginseng) increase absorption.

Ninety percent of ethyl alcohol is oxidized in mitochondria to acetate ($CH_3CH_2OH + NAD^+ \rightarrow CH_3CHO + NADH$). The acetate is then converted to acetyl-CoA that enters the Krebs cycle where ATP is produced. Alcohol is high in calories (1g = 7,000 calories, or 7 *food* calories). A standard glass of wine has about 15 g of alcohol and about 100 kilocalories. The 10% not metabolized is eliminated in sweat or urine, or given off in breath. It takes the liver one hour to deal with one unit of alcohol. A unit of alcohol is:

- 250 ml (1/2 pint) of ordinary strength beer/lager.
- One glass (125 ml/4 fl oz) of wine.
- 47 ml/1.5 oz of sherry/vermouth.
- 47 ml/1.5 oz of liquor.

If alcohol is consumed at a rate faster than the liver can break it down, the blood alcohol level rises. This causes an initial feeling of warmth and light-headedness. However, alcohol is a depressant, that is, it decreases the activity of the nervous system. At first, it may inhibit circuits in the brain that normally inhibit a person's actions. This usually results in a person becoming more talkative and active—uninhibited. However, as the alcohol's effect continues, other changes can take place. These include increased aggression, loss of memory, and loss of motor control.

Long-term, excessive use of alcohol can cause damage to the liver, resulting in the development of a fatty liver, alcoholic hepatitis, and alcoholic cirrhosis. It can also interfere with the kidneys' regulation of water, sodium, potassium, calcium, and phosphate and with the kidney's ability to maintain a proper acid-base balance, and produce hormones. It also causes low blood sugar levels, dehydration, high blood pressure, strokes, heart disease, birth defects, osteoporosis, and certain cancers.

Drinking alcohol in moderation does have some health benefits if the beverage contains antioxidants (for example, red wines and dark beers). The antioxidants in red wine (polyphenols) appear to counteract the negative effect of chemicals called free radicals released during metabolism. Free radicals are known to destroy cell components and cause mutations, damage which can lead to heart disease and cancers. Antioxidants protect against this kind of harm by capturing free radicals.

The Krebs Cycle

After pyruvate (pyruvic acid) enters the mitochondrion, it is first acted upon by an enzyme, along with a molecule known as *coenzyme A* (*CoA*) (figure 6.8). This results in three significant products. Hydrogen atoms are removed and NADH is formed, a carbon is removed and carbon dioxide is formed, and a 2-carbon fragment is formed, which temporarily attaches to coenzyme A to produce acetyl-coenzyme A. (These and subsequent reactions of the Krebs cycle take place in the fluid between the membranes of the mitochondrion.) The acetyl coenzyme A enters the series of reactions known as the Krebs cycle. During the Krebs cycle, the acetyl-CoA is systematically dismantled. Its hydrogen atoms are removed and the remaining carbons are released as carbon dioxide (Outlooks 6.1).

The first step in this process involves the acetyl-CoA. The acetyl portion of the complex is transferred to a 4-carbon compound called *oxaloacetate (oxaloacetic acid)* and a new 6-carbon citrate molecule (citric acid) is formed. The coenzyme A is released to participate in another reaction with pyruvic acid. This newly formed citrate is broken down in a series of reactions, which ultimately produces oxaloacetate, which was used in the first step of the cycle (hence, the names Krebs cycle, citric acid cycle, and tricarboxylic acid cycle). The compounds formed during this cycle are called *keto acids*.

In the process, electrons are removed and, along with protons, become attached to the coenzymes NAD^+ and FAD. Most become attached to NAD^+ but some become attached to FAD. As the molecules move through the Krebs cycle, enough energy

is released to allow the synthesis of 1 ATP molecule for each acetyl-CoA that enters the cycle. The ATP is formed from ADP and a phosphate already present in the mitochondria. For each pyruvate molecule that enters a mitochondrion and is processed through the Krebs cycle, 3 carbons are released as 3 carbon dioxide molecules, 5 pairs of hydrogen atoms are removed and become attached to NAD^+ or FAD, and 1 ATP molecule is generated. When both pyruvate molecules have been processed through the Krebs cycle, (1) all the original carbons from the glucose have been released into the atmosphere as 6 carbon dioxide molecules; (2) all the hydrogen originally found on the glucose has been transferred to either NAD^+ or FAD to form NADH or $FADH_2$; and (3) 2 ATPs have been formed from the addition of phosphates to ADPs (review figure 6.8).

Summary of Detailed Description of the Eukaryotic Krebs Cycle

The Krebs cycle takes place within the mitochondria. For each acetyl-CoA molecule that enters the Krebs cycle:

1. The three carbons from a pyruvate are converted to acetyl-CoA and released as carbon dioxide (CO_2). One CO_2 is actually released before acetyl-CoA is formed.
2. Five pairs of hydrogens become attached to hydrogen carriers to become 4 NADHs and 1 $FADH_2$. One of the NADHs is released before acetyl-CoA enters the Krebs cycle.
3. One ATP is generated.

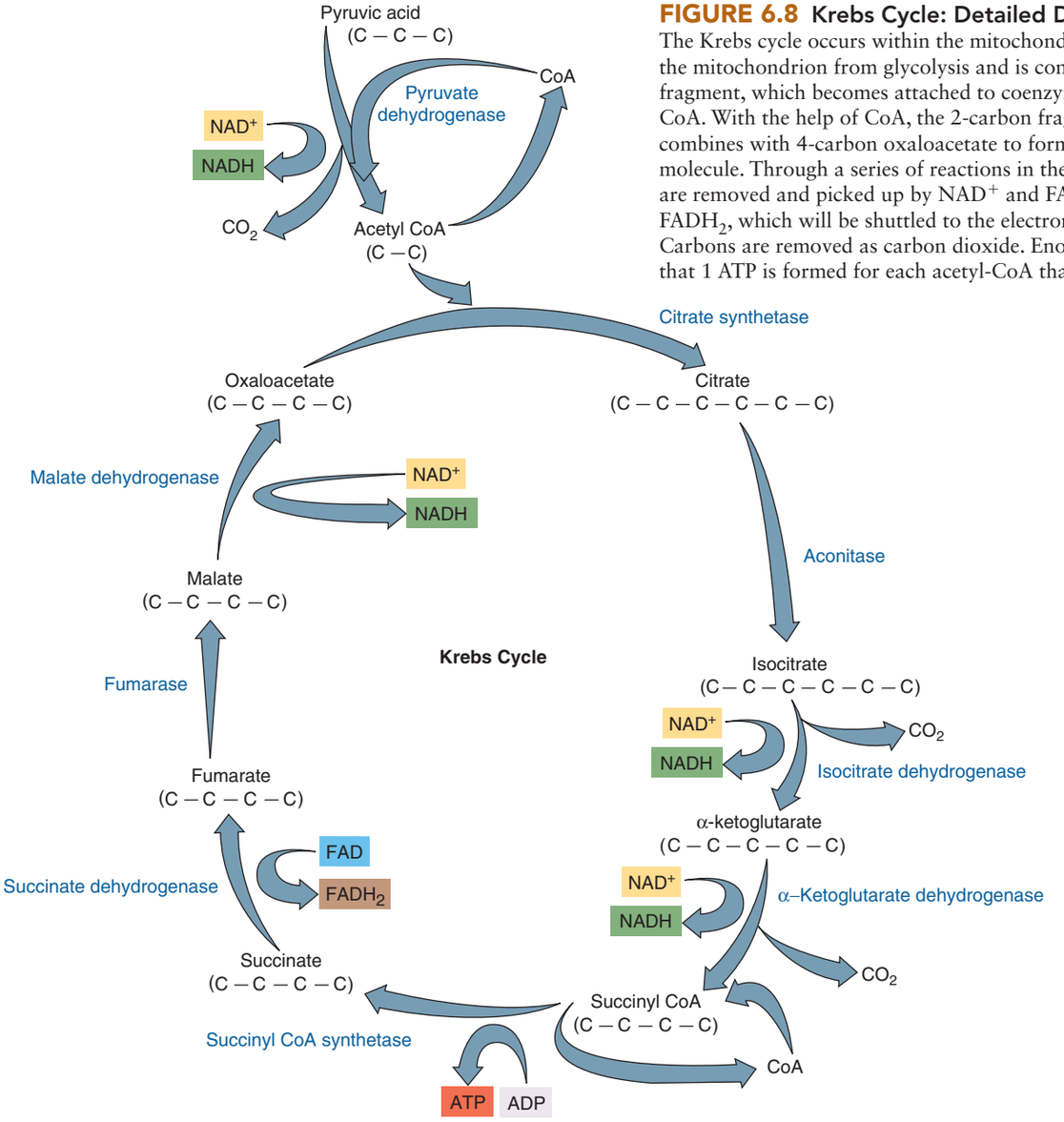


FIGURE 6.8 Krebs Cycle: Detailed Descriptions
The Krebs cycle occurs within the mitochondrion. Pyruvate enters the mitochondrion from glycolysis and is converted to a 2-carbon fragment, which becomes attached to coenzyme A to from acetyl-CoA. With the help of CoA, the 2-carbon fragment (acetyl) combines with 4-carbon oxaloacetate to form a 6-carbon citrate molecule. Through a series of reactions in the Krebs cycle, electrons are removed and picked up by NAD^+ and FAD to form NADH and $FADH_2$, which will be shuttled to the electron-transport system. Carbons are removed as carbon dioxide. Enough energy is released that 1 ATP is formed for each acetyl-CoA that enters the cycle.

The Electron-Transport System

The series of reactions in which energy is transferred from the electrons and protons carried by NADH and $FADH_2$ is known as the electron-transport system (ETS) (figure 6.9). This is the final stage of aerobic cellular respiration and is dedicated to generating ATP. The reactions that make up the electron-transport system are a series of oxidation-reduction reactions in which the electrons are passed from one electron carrier molecule to another until, ultimately, they are accepted by oxygen atoms. The negatively charged oxygen combines with the hydrogen ions to form water. It is this step that makes the process aerobic. Keep in mind that potential energy increases whenever things experiencing a repelling force are pushed together, such as adding the third phosphate to an ADP molecule. Potential energy also increases whenever things that attract each other are pulled apart, as in the separation of the protons from the electrons.

Let's now look in just a bit more detail at what happens to the electrons and protons that are carried to the electron-transport systems by NADH and $FADH_2$ and how these activities are used to produce ATP. The mitochondrion consists of two membranes—an outer, enclosing membrane and an inner, folded membrane. The reactions of the ETS are associated with this inner membrane. Within the structure of the membrane are several *enzyme complexes,* which perform particular parts of the ETS reactions (review figure 6.9). The production of ATPs involves two separate but connected processes. Electrons carried by NADH enter reactions in enzyme complex I, where they lose some energy and are eventually picked up by a coenzyme (coenzyme Q). Electrons from $FADH_2$ enter enzyme complex II and also are eventually transferred to coenzyme Q. Coenzyme Q transfers the electrons to enzyme complex III. In complex III, the electrons lose additional energy and are transferred to cytochrome c, which transfers electrons to enzyme complex IV. In complex IV, the electrons are eventually transferred to oxygen. As the electrons lose energy in complex I, complex III, and complex IV, additional protons are pumped into the intermembrane space. When these protons flow down the concentration gradient through channels in the membrane, phosphorylase enzymes (ATPase) in the membrane are able to use the energy to generate ATP.

A total of 12 pairs of electrons and hydrogens are transported to the ETS from glycolysis and the Krebs cycle for each glucose that enters the process. In eukaryotic organisms, the pairs of electrons can be accounted for as follows: 2 pairs are carried by NADH and were generated during glycolysis outside the mitochondrion, 8 pairs are carried as NADH and were generated within the mitochondrion, and 2 pairs are carried by $FADH_2$ and were generated within the mitochondrion.

- For each of the 8 NADHs generated within the mitochondrion, enough energy is released to produce 3 ATP molecules. Therefore, 24 ATPs are released from these electrons carried by NADH.

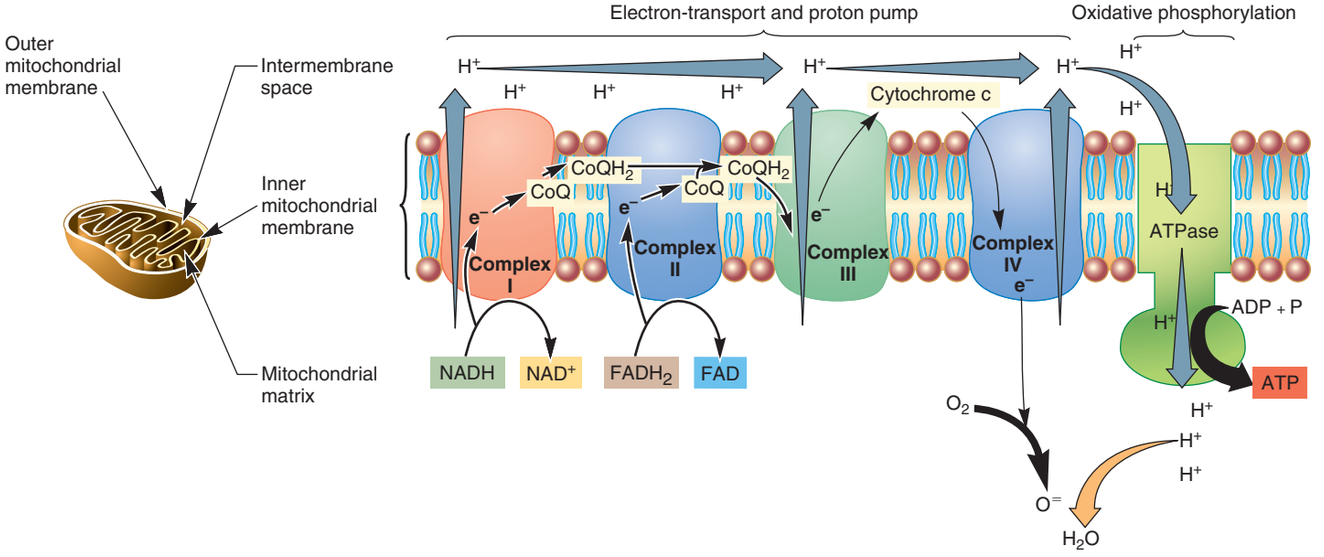


FIGURE 6.9 The Electron-Transport System: Detailed Description
Most of the ATP produced by aerobic cellular respiration comes from the ETS. NADH and $FADH_2$ deliver electrons to the enzymes responsible for the ETS. There are several protein complexes in the inner membrane of the mitochondrion, each of which is responsible for a portion of the reactions that yield ATP. The energy of electrons is given up in small amounts and used to pump protons into the intermembrane space. When these protons flow back through pores in the membrane, ATPase produces ATP. The electrons eventually are transferred to oxygen and the negatively charged oxygen ions accept protons to form water.

- In eukaryotic cells, the electrons released during glycolysis are carried by NADH and converted to 2 $FADH_2$ in order to shuttle them into the mitochondria. Once they are inside the mitochondria, they follow the same pathway as the other 2 $FADH_2$s from the Krebs cycle.

The electrons carried by $FADH_2$ are lower in energy. When these electrons go through the series of oxidation-reduction reactions, they release enough energy to produce a total of 8 ATPs. Therefore, a total of 32 ATPs are produced from the hydrogen electrons that enter the ETS.

Finally, a complete accounting of all the ATPs produced during all three parts of aerobic cellular respiration results in a total of 36 ATPs: 32 from the ETS, 2 from glycolysis, and 2 from the Krebs cycle.

Summary of Detailed Description of the Eukaryotic Electron-Transport System

The electron-transport system takes place within the mitochondrion, where:

1. Oxygen is used up as the oxygen atoms accept hydrogens from NADH and $FADH_2$ forming water (H_2O).
2. NAD^+ and FAD are released, to be used over again.
3. Thirty-two ATPs are produced.

6.3 CONCEPT REVIEW

6. For glycolysis, the Krebs cycle, and the electron-transport system, list two molecules that enter and two that leave each pathway.
7. How is each of the following involved in aerobic cellular respiration: NAD^+, pyruvic acid, oxygen, and ATP?

6.4 Aerobic Cellular Respiration in Prokaryotes

The discussion so far in this chapter has dealt with the process of aerobic cellular respiration in eukaryotic organisms. However, some prokaryotic cells also use aerobic cellular respiration. Because prokaryotes do not have mitochondria, there are some differences between what they do and what eukaryotes do. The primary difference involves the electrons carried from glycolysis to the electron-transport system. In eukaryotes, the electrons released during glycolysis are carried by NADH and transferred to FAD to form $FADH_2$ in order to get the electrons across the outer membrane of the mitochondrion. Because $FADH_2$ results in the production of fewer ATPs than NADH, there is a cost to the eukaryotic cell of getting the electrons into the mitochondrion. This transfer is not necessary in prokaryotes, so they are able to produce a theoretical 38 ATPs for each glucose metabolized, rather than the 36 ATPs produced by eukaryotes (table 6.2).

TABLE 6.2 Aerobic ATP Production: Prokaryotes vs. Eukaryotic Cells

Stage of Aerobic Cellular Respiration	Prokaryotes	Eukaryotes
Glycolysis	Net gain 2 ATP	Net gain 2 ATP
Krebs cycle	2 ATP	2 ATP
ETS	34 ATP	32 ATP
Total	38 ATP	36 ATP

6.4 CONCEPT REVIEW

8. How is aerobic cellular respiration different in prokaryotic and eukaryotic organisms?

6.5 Anaerobic Cellular Respiration

Although aerobic cellular respiration is the fundamental process by which most organisms generate ATP, some organisms do not have the necessary enzymes to carry out the Krebs cycle and ETS. Most of these are Bacteria or Archaea, but there are certain eukaryotic organisms, such as yeasts, that can live in the absence of oxygen and do not use their Krebs cycle and ETS. Even within multicellular organisms, there are differences in the metabolic activities of cells. For example some of your cells are able to survive for periods of time without oxygen. However, all cells still need a constant supply of ATP. An organism that does not require O_2 as its final electron acceptor is called *anaerobic* (*an* = without; *aerob* = air) and performs **anaerobic cellular respiration.** Although some anaerobic organisms do not use oxygen, they are capable of using other inorganic or organic molecules as their final electron acceptors. The acceptor molecule might be sulfur, nitrogen, or other inorganic atoms or ions. It might also be an organic molecule, such as pyruvic acid ($CH_3COCOOH$). Anaerobic respiration is an incomplete oxidation and results in the production of smaller electron-containing molecules and energy in the form of ATP and heat (figure 6.10).

Many organisms that perform anaerobic cellular respiration use the glycolytic pathway to obtain energy. **Fermentation** is the word used to describe anaerobic pathways that oxidize glucose to generate ATP by using an organic molecule as the ultimate hydrogen electron acceptor. Electrons removed from sugar in the earlier stages of glycolysis are added to the pyruvic acid formed at the end of glycolysis. Depending on the kind of organism and the specific enzymes it possesses, the pyruvic acid can be converted into lactic acid, ethyl alcohol, acetone, or other organic molecules (figure 6.11).

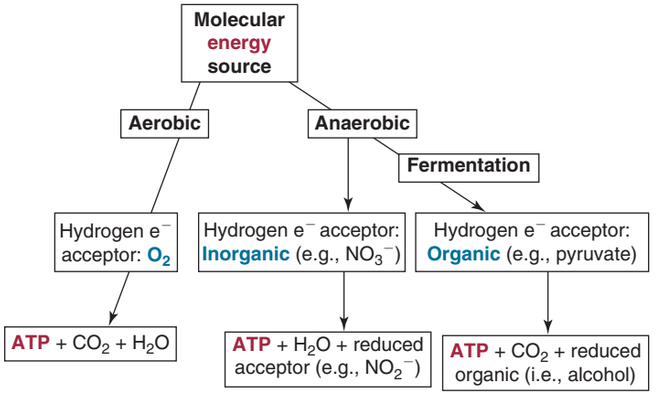
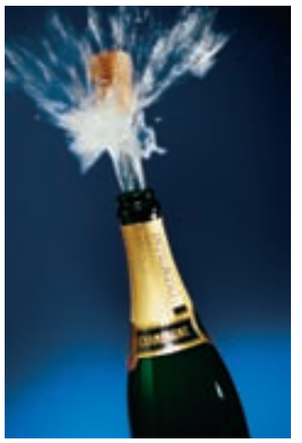


FIGURE 6.10 Anaerobic Cellular Respiration in Perspective
This flowchart shows the relationships among the various types of cellular respiration and the descriptive terminology used. Notice that all begin with a molecular source of energy and end with the generation of ATP.

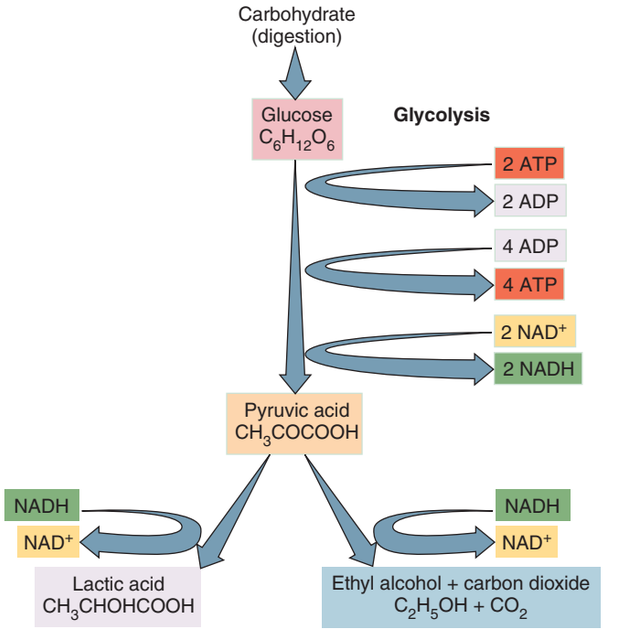
Organisms that produce ethyl alcohol have genes for the production of enzymes that guide electrons onto pyruvic acid. This reaction results in the conversion of pyruvic acid to ethyl alcohol (ethanol) and carbon dioxide. Other organisms have different genes, produce different enzymes, carry out different reactions, and, therefore, lead to the formation of different end products of fermentation. The formation of molecules such as alcohol and lactic acid is necessary to regenerate the NAD^+ needed for continued use in glycolysis. It must be done here, because it is not being regenerated by an ETS, as happens in aerobic respiration. Although many products can be formed from pyruvic acid, we will look at only two fermentation pathways in more detail.

Alcoholic Fermentation

Alcoholic fermentation is the anaerobic respiration pathway that yeast cells follow when oxygen is lacking in their environment. In this pathway, the pyruvic acid ($CH_3COCOOH$) is converted to ethanol (a 2-carbon alcohol, CH_3CH_2OH) and carbon dioxide. Yeast cells then are able to generate only 4 ATPs from glycolysis. The cost for glycolysis is still 2 ATPs; thus, for each glucose a yeast cell oxidizes, it profits by 2 ATPs.



Although during alcoholic fermentation yeasts get ATP and discard the waste products ethanol and carbon dioxide, these waste products are useful to humans. In making bread, the carbon dioxide is the important end product; it becomes trapped in the bread dough and makes it rise—the bread is *leavened*. Dough that has not undergone this process is called *unleavened*. The alcohol produced by the yeast evaporates during the baking process. In the brewing industry, ethanol is the desirable product produced by yeast cells. Champagne, other sparkling wines, and beer are products that contain both carbon dioxide and alcohol. The alcohol accumulates, and the carbon dioxide in the bottle makes them sparkling (bubbly) beverages. In the manufacture of many wines, the carbon dioxide is allowed to escape, so these wines are not sparkling; they are called "still" wines.



Fermentation Product	Possible Source	Importance
Lactic acid	Bacteria: *Lactobacillus bulgaricus*	Aids in changing milk to yogurt
	Homo sapiens Muscle cells	Produced when O_2 is limited; results in pain and muscle inaction
Ethyl alcohol $+CO_2$	Yeast: *Saccharomyces cerevisiae*	Brewing and baking

FIGURE 6.11 Fermentations
The upper portion of this figure is a simplified version of glycolysis. Many organisms can carry out the process of glycolysis and derive energy from it. The ultimate end product is determined by the kinds of enzymes the specific organism can produce. The synthesis of these various molecules is the organism's way of oxidizing NADH to regenerate NAD^+ and reducing pyruvic acid to a new end product.

Summary of Alcohol Fermentation

1. Starts with glycolysis
   a. Glucose is metabolized to pyruvic acid.
   b. A net of 2 ATP is made.
2. During alcoholic fermentation
   a. pyruvic acid is reduced to form ethanol.
   b. carbon dioxide is released.
3. Yeasts do this in
   a. leavened bread.
   b. sparkling wine.

Lactic Acid Fermentation

In **lactic acid fermentation,** the pyruvic acid ($CH_3COCOOH$) that results from glycolysis is converted to lactic acid ($CH_3CHOHCOOH$) by the transfer of electrons that had been removed from the original glucose. In this case, the net profit is again only 2 ATPs per glucose. The buildup of the waste product, lactic acid, eventually interferes with normal metabolic functions and the bacteria die. The lactic acid waste product from these types of anaerobic bacteria are used to make yogurt, cultured sour cream, cheeses, and other fermented dairy products. The lactic acid makes the milk protein coagulate and become pudding-like or solid. It also gives the products their tart flavor, texture, and aroma (Outlooks 6.2).

In the human body, different cells have different metabolic capabilities. Nerve cells must have a constant supply of oxygen to conduct aerobic cellular respiration. Red blood cells lack mitochondria and must rely on the anaerobic process of lactic acid fermentation to provide themselves with energy. Muscle cells can do either. As long as oxygen is available to skeletal muscle cells, they function aerobically. However, when oxygen is unavailable—because of long periods of exercise or heart or lung problems that prevent oxygen from getting to the skeletal muscle cells—the cells make a valiant effort to meet energy demands by functioning anaerobically.

When skeletal muscle cells function anaerobically, they accumulate lactic acid. This lactic acid must ultimately be metabolized, which requires oxygen. Therefore, the accumulation of lactic acid represents an *oxygen debt*, which must be repaid in the future. It is the lactic acid buildup that makes muscles tired when we exercise. When the lactic acid concentration becomes great enough, lactic acid fatigue results. As a person cools down after a period of exercise, breathing and heart rate stay high until the oxygen debt is repaid and the level of oxygen in the muscle cells returns to normal. During this period, the lactic acid that has accumulated is converted back into pyruvic acid. The pyruvic acid can then continue through the Krebs cycle and the ETS as oxygen becomes available. In addition to what is happening in the muscles,

OUTLOOKS 6.2

Souring vs. Spoilage

The fermentation of carbohydrates to organic acid products, such as lactic acid, is commonly called *souring*. Cultured sour cream, cheese, and yogurt are produced by the action of fermenting bacteria. Lactic-acid bacteria of the genus *Lactobacillus* are used in the fermentation process. While growing in the milk, the bacteria convert lactose to lactic acid, which causes the proteins in the milk to coagulate and come out of solution to form a solid curd. The higher acid level also inhibits the growth of spoilage microorganisms.

Spoilage, or putrefaction, is the anaerobic respiration of proteins with the release of nitrogen and sulfur-containing organic compounds as products. Protein fermentation by the bacterium *Clostridium* produces foul-smelling chemicals such as putrescine, cadaverine, hydrogen sulfide, and methyl mercaptan. *Clostridium perfringens* and *C. sporogenes* are the two anaerobic bacteria associated with the disease gas gangrene. A gangrenous wound is a foul-smelling infection resulting from the fermentation activities of those two bacteria.

much of the lactic acid is transported by the bloodstream to the liver, where about 20% is metabolized through the Krebs cycle and 80% is resynthesized into glucose.

Summary of Lactic Acid Fermentation

1. Starts with glycolysis
   a. Glucose is metabolized to pyruvic acid.
   b. A net of 2 ATP is made.
2. During lactic acid fermentation
   a. pyruvic acid is reduced to form lactic acid.
   b. no carbon dioxide is released.
3. Muscle cells have the enzymes to do this, but brain cells do not.
   a. Muscle cells can survive brief periods of oxygen deprivation, but brain cells cannot.
   b. Lactic acid "burns" in muscles.

6.5 CONCEPT REVIEW

9. Why are their different end products from different forms of fermentation?

6.6 Metabolic Processing of Molecules Other Than Carbohydrates

Up to this point, we have discussed only the methods and pathways that allow organisms to release the energy tied up in carbohydrates (sugars). Frequently, cells lack sufficient carbohydrates for their energetic needs but have other materials from which energy can be removed. Fats and proteins, in addition to carbohydrates, make up the diet of many organisms. These three foods provide the building blocks for the cells, and all can provide energy. Carbohydrates can be digested to simple sugars, proteins can be digested to amino acids, and fats can be digested to glycerol and fatty acids. The basic pathways organisms use to extract energy from fat and protein are the same as for carbohydrates: glycolysis, the Krebs cycle, and the electron-transport system. However, there are some additional steps necessary to get fats and proteins ready to enter these pathways at several points in glycolysis and the Krebs cycle where fats and proteins enter to be respired.

Fat Respiration

A triglyceride (also known as a neutral fat) is a large molecule that consists of a molecule of glycerol with 3 fatty acids attached to it. Before these fats can be broken down to release energy, they must be converted to smaller units by digestive processes. Several enzymes are involved in these steps. The first step is to break the

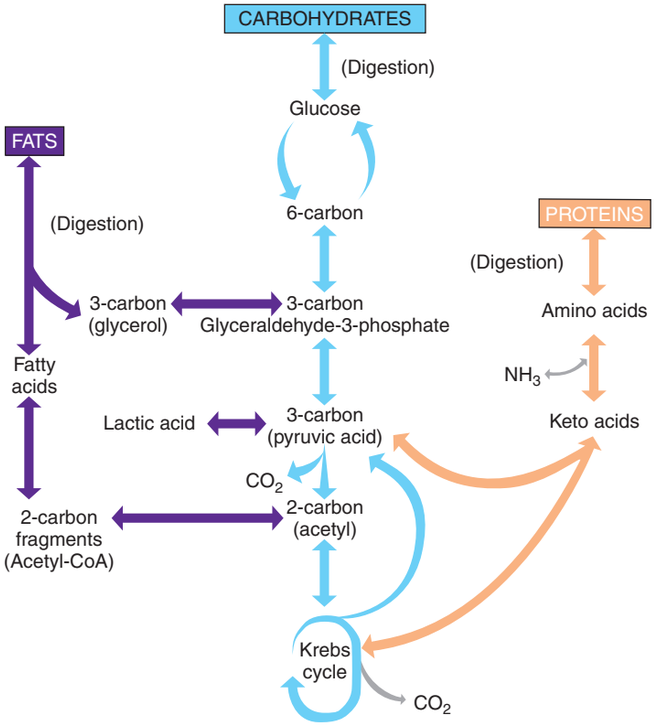


FIGURE 6.12 The Interconversion of Fats, Carbohydrates, and Proteins
Cells do not necessarily use all food as energy. One type of food can be changed into another type to be used as raw materials for the construction of needed molecules or for storage. Notice that many of the reaction arrows have two heads (i.e., these reactions can go in either direction). For example, glycerol can be converted into glyceraldehyde-3-phosphate and glyceraldehyde-3-phosphate can become glycerol.

bonds between the glycerol and the fatty acids. Glycerol is a 3-carbon molecule that is converted into glyceraldehyde-3-phosphate. Because glyceraldehyde-3-phosphate is involved in one of the steps in glycolysis, it can enter the glycolysis pathway (figure 6.12). The remaining fatty acids are often long molecules (typically 14 to 20 carbons long), which also must be processed before they can be further metabolized. First, they need to enter the mitochondrion, where subsequent reactions take place. Once inside the mitochondrion, each long chain of carbons that makes up the carbon skeleton is hydrolyzed (split by the addition of a water molecule) into 2-carbon fragments. Next, each of the 2-carbon fragments is carried into the Krebs cycle by coenzyme A molecules. Once in the Krebs cycle, they proceed through the Krebs cycle just like the acetyl-CoAs from glucose (Outlooks 6.3).

By following the glycerol and each 2-carbon fragment through the cycle, you can see that each molecule of fat has the potential to release several times as much ATP as does a molecule of glucose. Each glucose molecule has 6 pairs of hydrogen, whereas a typical molecule of fat has up to 10 times that number. This is why fat makes such a good long-term energy

OUTLOOKS 6.3

Body Odor and Bacterial Metabolism

In our culture, natural body odor is considered by most to be undesirable. Body odor is the result of bacteria metabolizing chemicals released by glands called aprocrine glands. These glands are associated with hair follicles and are especially numerous within the scalp, underarms, and genitals. They produce fatty acids and other compounds that are secreted onto the skin when people sweat as a result of becoming overheated, exercising, or being stressed. Bacteria metabolize these compounds in perspiration, releasing other compounds responsible for body odor.

A number of factors affect how bacteria metabolize fatty acids and, therefore, the strength and nature of a person's body odor. Hereditary factors can play an important role, as evidenced by the genetic abnormality, hyperhidrosis. People with this condition experience excessive perspiration. Diabetes, low blood sugar, menopause, kidney disease, or liver disease can lead to profuse sweating in some cases. Foods, such as garlic and onions, and spices, such as curry, can lead to stronger body aroma. Caffeine, in coffee, tea, sodas, and chocolate, also affects body odor. People with an imbalance of magnesium and zinc are also more likely to generate more pungent body odors.

These bacteria are usually controlled with commercially available products. Deodorants mask the odors, antiperspirants reduce the flow of perspiration, antiseptics destroy the microorganisms, and soaps remove them. Most antiperspirants work by using aluminum compounds (aluminum chlorhydrate) that reduce the flow of sweat and are moderately antibacterial. If a person is allergic to such compounds, it may be necessary to use deodorant soaps with more powerful antimicrobials, such as chlorhexidine.

storage material. It is also why it takes so long for people on a weight-reducing diet to remove fat. It takes time to use all the energy contained in the fatty acids. On a weight basis, there are twice as many calories in a gram of fat as there are in a gram of carbohydrate.

Fats are an excellent source of energy and the storage of fat is an important process. Furthermore, other kinds of molecules can be converted to fat. You already know that people can get fat from eating sugar. Notice in figure 6.12 that both carbohydrates and fats can enter the Krebs cycle and release energy. Although people require both fats and carbohydrates in their diets, they need not be in precise ratios; the body can make some interconversions. This means that people who eat excessive amounts of carbohydrates will deposit body fat. It also means that people who starve can generate glucose by breaking down fats and using the glycerol to synthesize glucose.

Summary of Fat Respiration

1. Fats are broken down into
   a. glycerol.
   b. fatty acids.
2. Glycerol
   a. is converted to glyceraldehyde-3-phosphate.
   b. enters glycolysis.
3. Fatty acids
   a. are converted to acetyl-CoA.
   b. enter the Kreb's cycle.
4. Each molecule of fat fuels the formation of many more ATP than glucose.
   a. This makes it a good energy-storage molecule.

Protein Respiration

Proteins can be catabolized and interconverted just as fats and carbohydrates are (review figure 6.12). The first step in using protein for energy is to digest the protein into individual amino acids. Each amino acid then needs to have the amino group (—NH_2) removed, a process (deamination) that takes place in the liver. The remaining non-nitrogenous part of the protein is converted to keto acid and enters the respiratory cycle as acetyl-CoA, pyruvic acid, or one of the other types of molecules found in the Krebs cycle. As the acids progress through the Krebs cycle, the electrons are removed and sent to the ETS, where their energy is converted into the chemical-bond energy of ATP. The amino group that was removed from the amino acid is converted into ammonia. Some organisms excrete ammonia directly; others convert ammonia into other nitrogen-containing compounds, such as urea (humans) or uric acid (birds). All of these molecules are toxic, increase the workload of the liver, can damage the kidneys and other organs, and must be eliminated. They are transported in the blood to the kidneys, where they are eliminated. In the case of a high-protein diet, increasing fluid intake will allow the kidneys to remove the urea or uric acid efficiently.

When proteins are eaten, they are digested into their component amino acids. These amino acids are then available to be used to construct other proteins. Proteins cannot be stored; if they or their component amino acids are not needed immediately, they will be converted into fat or carbohydrates or will be metabolized to provide energy. This presents a problem for individuals who do not have ready access to a continuous source of amino acids in their diet (e.g., individuals on a low-protein diet).

HOW SCIENCE WORKS 6.1

Applying Knowledge of Biochemical Pathways

As scientists have developed a better understanding of the processes of aerobic cellular respiration and anaerobic cellular respiration, several practical applications of this knowledge have developed:

1. Newborn human infants have a modified respiratory plan that allows them to shut down the ATP production of their mitochondria in certain fatty tissue. Even though ATP production is reduced, it allows them to convert fat directly to heat to keep them warm.
2. Studies have shown that horses metabolize their nutrients 20 times faster during the winter than the summer.
3. Although for centuries people have fermented beverages such as beer and wine, they were often plagued by sour products that were undrinkable. Once people understood that there were yeasts that produced alcohol under anaerobic conditions and bacteria that converted alcohol to acetic acid under aerobic conditions, it was a simple task to prevent acetic acid production by preventing oxygen from getting to the fermenting mixture.
4. When it was discovered that the bacterium that causes gas gangrene is anaerobic and is, in fact, poisoned by the presence of oxygen, various oxygen therapies were developed to help cure patients with gangrene. Some persons with gangrene are placed in hyperbaric chambers, with high oxygen levels under pressure. In other patients, only the affected part of the body is enclosed. Under such conditions, the gangrene-causing bacteria die or are inhibited (see figure 4.22).
5. When physicians recognized that the breakdown of fats releases ketone bodies, they were able to diagnose diseases such as diabetes and anorexia more easily, because people typically have low amounts of carbohydrates and therefore metabolize fats. The ketones produces by excess breakdown of fats results in foul-smelling breath.

Winter Baby and Blanket

No Blanket Needed

If they do not have a source of dietary protein, they must break down proteins from important cellular components to supply the amino acids they need. This is why proteins and amino acids are considered an important daily food requirement.

Summary of Protein Respiration

1. Proteins are digested into amino acids.
2. Then amino acids have the amino group removed,
   a. generating a keto acid (acetic acid, pyruvic acid, etc.), and
   b. entering the Kreb's cycle at the appropriate place.

One of the most important concepts is that carbohydrates, fats, and proteins can all be used to provide energy. The fate of any type of nutrient in a cell depends on the cell's momentary needs. An organism whose daily food-energy intake exceeds its daily energy expenditure will convert only the necessary amount of food into energy. The excess food will be interconverted according to the enzymes present and the organism's needs at that time. In fact, glycolysis and the Krebs cycle allow molecules of the three major food types (carbohydrates, fats, and proteins) to be interchanged.

As long as a person's diet has a certain minimum of each of the three major types of molecules, a cell's metabolic machinery can manipulate molecules to satisfy its needs. If a person is on a starvation diet, the cells will use stored carbohydrates first. When the carbohydrates are gone (after about 2 days), the cells begin to metabolize stored fat. When the fat is gone (after a few days to weeks), proteins will be used. A person in this condition is likely to die (How Science Works 6.1).

6.6 CONCEPT REVIEW

10. What are the differences between fat and protein metabolism biochemical pathways?
11. Describe how carbohydrates, fats, and proteins can be interconverted from one to another.

Summary

In aerobic cellular respiration, organisms convert foods into energy (ATP) and waste materials (carbon dioxide and water). Three distinct metabolic pathways are involved in aerobic cellular respiration: glycolysis, the Krebs cycle, and the electron-transport system. Glycolysis takes place in the cytoplasm of the cell, and the Krebs cycle and electron-transport system take place in mitochondria. Organisms that have oxygen can perform aerobic cellular respiration. Organisms and cells that do not use oxygen perform anaerobic cellular respiration (fermentation) and can use only the glycolysis pathway. Aerobic cellular respiration yields much more ATP than anaerobic cellular respiration. Glycolysis and the Krebs cycle serve as a molecular interconversion system: Fats, proteins, and carbohydrates are interconverted according to the cell's needs.

Key Terms

Use the interactive flash cards on the ***Concepts in Biology****, 14/e website to help you learn the meaning of these terms.*

acetyl-CoA 120
aerobic cellular respiration 117
alcoholic fermentation 127
anaerobic cellular respiration 126
autotrophs 116
cellular respiration 116
chemosynthesis 116
electron-transport system (ETS) 118
fermentation 126
glycolysis 118
heterotrophs 116
Krebs cycle 118
lactic acid fermentation 128

Basic Review

1. Organisms that are able to use basic energy sources, such as sunlight, to make energy-containing organic molecules from inorganic raw materials are called
   a. autotrophs.
   b. heterotrophs.
   c. aerobic.
   d. anaerobic.
2. Cellular respiration processes that do not use molecular oxygen are called
   a. heterotrophic.
   b. anaerobic.
   c. aerobic.
   d. anabolic.
3. The chemical activities that remove electrons from glucose result in the glucose being
   a. reduced.
   b. oxidized.
   c. phosphorylated.
   d. hydrolysed.
4. The positively charged hydrogen ions that are released from the glucose during cellular respiration eventually combine with _____ ion to form _____.
   a. another hydrogen, a gas
   b. a carbon, carbon dioxide
   c. an oxygen, water
   d. a pyruvic acid, lactic acid
5. The Krebs cycle and ETS are biochemical pathways performed in which eukaryotic organelle?
   a. nucleus
   b. ribosome
   c. chloroplast
   d. mitochondria
6. In a complete accounting of all the ATPs produced in aerobic cellular respiration in eukaryotic cells, there are a total of _____ ATPs: _____ from the ETS, _____ from glycolysis, and _____ from the Krebs cycle.
   a. 36, 32, 2, 2
   b. 38, 34, 2, 2
   c. 36, 30, 2, 4
   d. 38, 30, 4, 4
7. Anaerobic pathways that oxidize glucose to generate ATP energy by using an organic molecule as the ultimate hydrogen acceptor are called
   a. fermentation.
   b. reduction.
   c. Krebs.
   d. electron pumps.
8. When skeletal muscle cells function anaerobically, they accumulate the compound _____, which causes muscle soreness.
   a. pyruvic acid
   b. malic acid
   c. carbon dioxide
   d. lactic acid

9. Each molecule of fat can release _____ of ATP, compared with a molecule of glucose.
   a. smaller amounts
   b. the same amount
   c. larger amounts
   d. only twice the amount
10. Some organisms excrete ammonia directly; others convert ammonia into other nitrogen-containing compounds, such as
   a. urea or uric acid.
   b. carbon dioxide.
   c. sweat.
   d. fat.
11. The ATP generating process in mitochondria works by using which of the following?
   a. proton pump
   b. DNA
   c. oxygen pump
   d. chlorophyll
12. Which best explains the need to reduce pyruvic acid in fermentation?
   a. Fermenting cells cannot produce water.
   b. Not enough energy would be produced to keep them alive.
   c. There is no oxygen available to accept the electrons.
   d. NAD^+ needs to be regenerated for continued use in glycolysis.
13. Why don't human muscle cells produce alcohol and CO_2 during anaerobic respiration?
   a. They only carry out aerobic respiration.
   b. We do not have the genes to produce the enzymes needed to generate alcohol and CO_2.
   c. The cells would blow up with the gas produced.
   d. There is no way to destroy the alcohol.
14. What is the ultimate destination of hydrogen electrons in aerobic cellular respiration?
   a. pyruvic acid
   b. lactic acid
   c. oxygen
   d. water
15. Which electron carrier releases the most potential during the ETS?
   a. NADH
   b. FAD
   c. oxygen
   d. NAD^+

Answers
1. a 2. b 3. b 4. c 5. d 6. a 7. a 8. d 9. c 10. a 11. a 12. d 13. b 14. c 15. a

Thinking Critically

Personalizing Your Pathway
Picture yourself as an atom of hydrogen tied up in a molecule of fat. You are present in the stored fat of a person who is starving. Trace the biochemical pathways you would be part of as you moved through the process of aerobic cellular respiration. Be as specific as you can in describing your location and how you got there, as well as the molecules of which you are a part. Of what molecule would you be a part at the end of this process?