2.2 Cellular Respiration: The Details

The sequence of chemical reactions and energy changes that occurs in aerobic respiration may seem complex, but keep in mind the overall equation:

$$C_6H_{12}O_{6(aq)} + 6O_{2(g)} \longrightarrow 6CO_{2(g)} + 6H_2O_{(l)}$$

It provides you with a reminder of the three overall goals of the process:

1. to break the bonds between the six carbon atoms of glucose, resulting in six carbon dioxide molecules
2. to move hydrogen atom electrons from glucose to oxygen, forming six water molecules
3. to trap as much of the free energy released in the process as possible in the form of ATP

The entire process occurs in four stages and in three different places within the cell:

Stage 1: Glycolysis—a 10-step process occurring in the cytoplasm

Stage 2: Pyruvate oxidation—a one-step process occurring in the mitochondrial matrix

Stage 3: The Krebs cycle (also called the tricarboxylic acid cycle, the TCA cycle, or the citric acid cycle)—an eight-step cyclical process occurring in the mitochondrial matrix

Stage 4: Electron transport and chemiosmosis (oxidative phosphorylation)—a multistep process occurring in the inner mitochondrial membrane

Figure 1 shows the four stages of respiration in graphic form and indicates their locations within the cell. This illustration reappears at certain points within the chapter to remind you of the stage and location of a particular set of reactions.

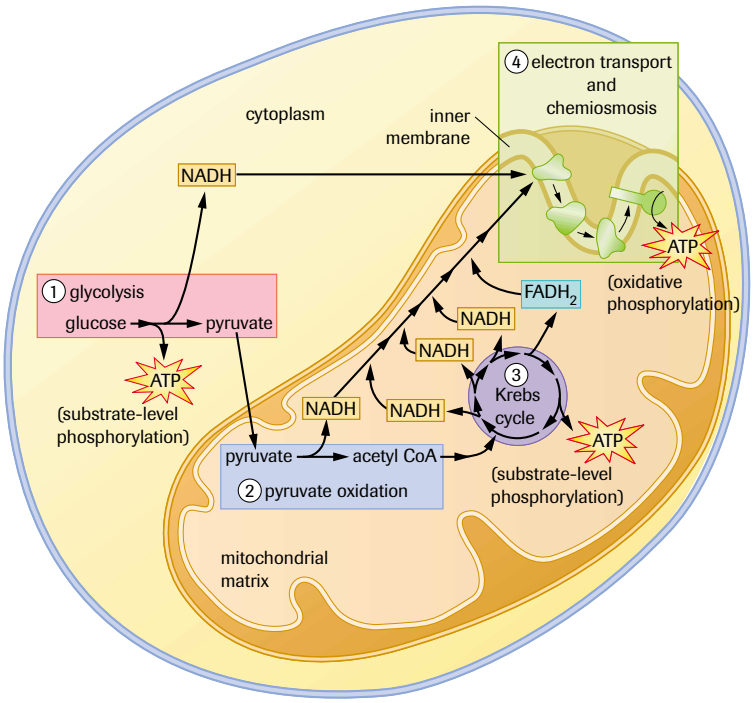


Figure 1
In eukaryotic cells, glycolysis occurs in the cytoplasm (pink), pyruvate oxidation and the Krebs cycle occur in the mitochondrial matrix (blue and purple respectively), and the electron transport chain is embedded in the inner mitochondrial membrane (green).

The ultimate goal of cellular respiration is to extract energy from nutrient molecules and store it in a form that the cell can use for its many and varied energy-requiring activities. In cellular respiration, the primary energy transfer is from glucose to ATP.

Energy Transfer

Before we describe the series of chemical reactions in glycolysis, the first stage of cellular respiration, we will outline the mechanisms used by cells to convert chemical potential energy from one form into another. The first law of thermodynamics tells us that energy cannot be created or destroyed—it can only be changed from one form into another or transferred from one object to another. Many chemical changes take place during cellular respiration, but only some of them transfer significant amounts of energy from one compound to another. The ultimate goal is to capture as much of the available free energy as possible in the form of ATP. This goal is accomplished through two distinctly different energy-transfer mechanisms called **substrate-level phosphorylation** and **oxidative phosphorylation**.

substrate-level phosphorylation mechanism forming ATP directly in an enzyme-catalyzed reaction

oxidative phosphorylation mechanism forming ATP indirectly through a series of enzyme-catalyzed redox reactions involving oxygen as the final electron acceptor

nicotinamide adenine dinucleotide, NAD$^+$ coenzyme used to shuttle electrons to the first component of the electron transport chain in the mitochondrial inner membrane

Substrate-Level Phosphorylation

In substrate-level phosphorylation, ATP is formed directly in an enzyme-catalyzed reaction. In the process, a phosphate-containing compound transfers a phosphate group directly to ADP, forming ATP. During the process, approximately 31 kJ/mol of potential energy is also transferred (**Figure 2**). (The value of 31 kJ/mol is determined under standard laboratory conditions and is used in all calculations in this book. In a living cell, the value is closer to 50 kJ/mol.) For each glucose molecule processed, four ATP molecules are generated this way in glycolysis and two in the Krebs cycle (**Figure 3**, yellow starbursts).

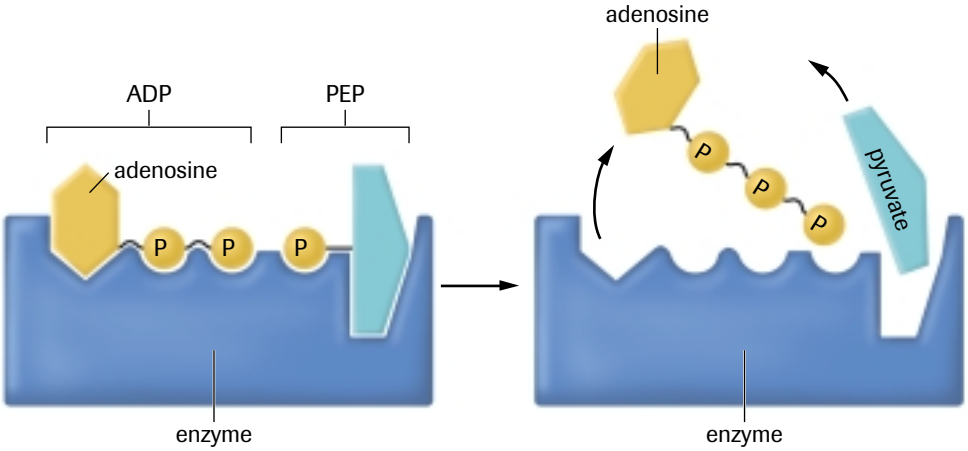


Figure 2
In this example of substrate-level phosphorylation, a phosphate-containing molecule called phosphoenolpyruvate (PEP) transfers its phosphate group to ADP, forming ATP. In the process, 31 kJ/mol of free energy is also transferred. This particular reaction occurs in glycolysis.

Oxidative Phosphorylation

In oxidative phosphorylation, ATP is formed indirectly. This process is oxidative because it involves a number of sequential redox reactions, with oxygen being the final electron acceptor. It is a more complex process than substrate-level phosphorylation and yields many more ATP molecules for each glucose molecule processed.

Oxidative phosphorylation begins when a compound called **nicotinamide adenine dinucleotide, NAD$^+$**, removes two hydrogen atoms (two protons and two electrons) from

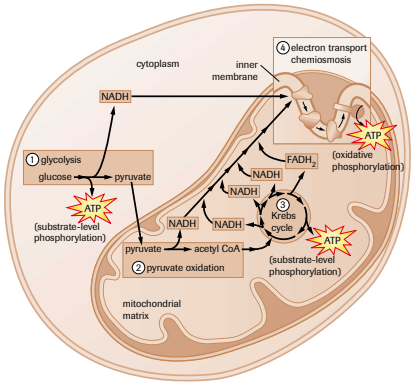


Figure 3
Substrate-level phosphorylation in cellular respiration

DID YOU KNOW ?

Coenzymes and Vitamins

NAD^+ is a derivative of vitamin B_3 (niacin or niacinamide) (**Figure 4**). Vitamins are organic compounds that are required in very small amounts in the diet. Many vitamins, especially B vitamins like niacin, function as coenzymes in energy metabolism.

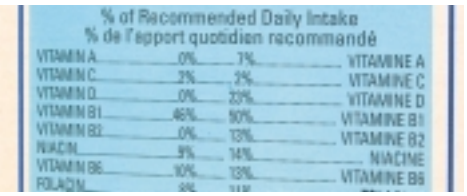
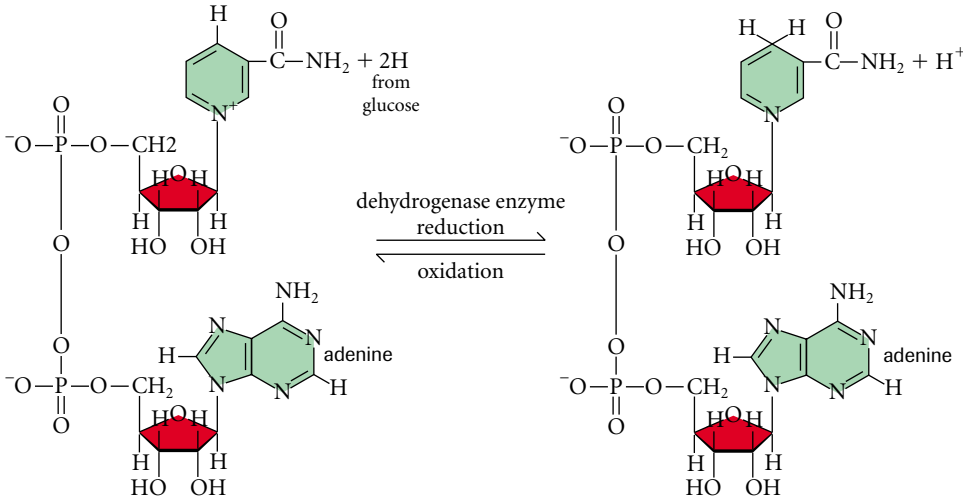


Figure 4
NAD^+ is derived from vitamin B_3 (niacin).



NAD^+: oxidized form of nicotimamide adenine dinucleotide

NADH: reduced form of nicotimamide adenine dinucleotide

Figure 5
NAD^+ is reduced to NADH + H^+ (NADH) by the transfer of two hydrogen atoms from a portion of the original glucose molecule.

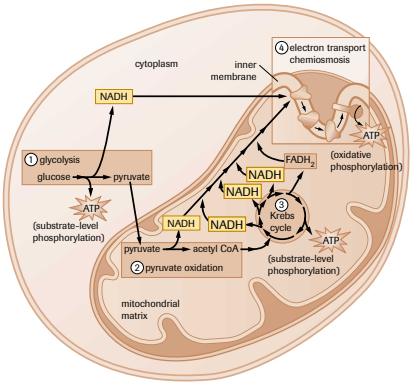


Figure 6
NADH is formed in glycolysis, pyruvate oxidation, and three steps of the Krebs cycle (yellow boxes).

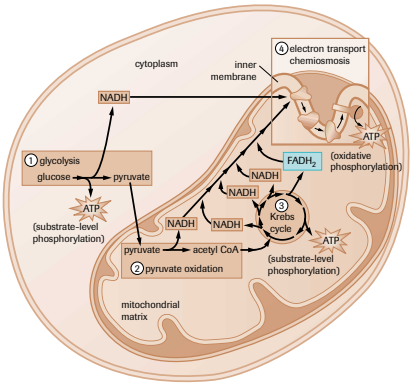


Figure 7
$FADH_2$ is formed in one step of the Krebs cycle (blue box).

a portion of the original glucose molecule. In the process, two electrons and one proton attach to the NAD^+, reducing it to NADH, while the remaining proton dissolves into the surrounding solution as $H^+_{(aq)}$. A dehydrogenase enzyme catalyzes this reaction. Thus, NAD^+ is the oxidized form of nicotinamide adenine dinucleotide and NADH + H^+ (shortened to NADH) is the reduced form (**Figure 5**). NAD^+ reduction occurs in one reaction of glycolysis (stage 1), during the pyruvate oxidation step (stage 2), and in three reactions of the Krebs cycle (stage 3) (**Figure 6**).

Another coenzyme called flavin adenine dinucleotide, FAD, performs a function similar to NAD^+. FAD is also reduced by two hydrogen atoms from a portion of the original glucose molecule. Its reduced form is symbolized as $FADH_2$ because all of the protons and electrons of hydrogen bind directly to the molecule. FAD is reduced to $FADH_2$ in one of the reactions of the Krebs cycle (**Figure 7**).

The reductions of NAD^+ to NADH and FAD to $FADH_2$ are energy-harvesting reactions that will eventually transfer most of their free energy to ATP molecules. The reduced coenzymes act as mobile energy carriers within the cell, moving free energy from one place to another and from one molecule to another. The process by which a cell transfers free energy from NADH and $FADH_2$ to ATP has not yet been discussed. It involves stage 4 of the cellular respiration process (electron transport and chemiosmosis) and requires the use of free oxygen molecules. All the reduced coenzymes are formed in the first three stages (glycolysis, pyruvate oxidation, and the Krebs cycle); therefore, the chemical reactions in these stages will be outlined before the mechanisms by which the reduced coenzymes power ATP synthesis are described. In the discussion, particular attention will be paid to the reactions in which NADH and $FADH_2$ are formed. The reactions in which ATP is produced directly by substrate-level phosphorylation will also be noted.

Stage 1: Glycolysis

The first 10 reactions of cellular respiration are collectively called **glycolysis** (Greek for "sugar splitting") (**Figure 8**). Starting with glucose, a 6-carbon sugar, glycolysis produces two 3-carbon pyruvate (pyruvic acid), molecules (**Figure 9**). The carbon backbone of glucose is essentially split in half. All the reactions in glycolysis occur in the cytoplasm, each step catalyzed by a specific enzyme. Glycolysis is an anaerobic process; it does not require oxygen.

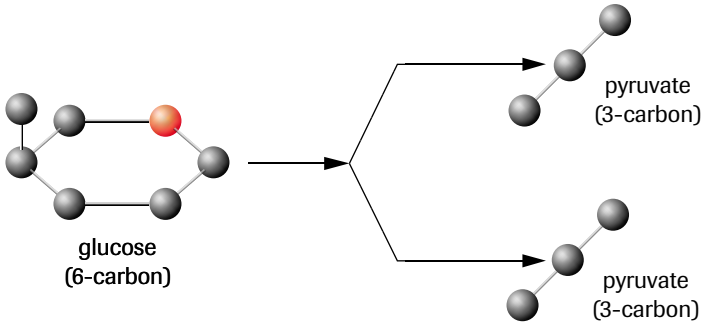


Figure 9
In a series of reactions called glycolysis, a 6-carbon glucose molecule is split into two 3-carbon pyruvate molecules.

Figure 11 (page 98) outlines the 10 reactions of the glycolytic pathway. As you study them, note the following:

- Two ATP molecules are used in the first five steps of the process, one in step 1 and one in step 3. These reactions "prime" the glucose molecule by adding phosphate groups to its structure, which prepares the molecule for cleavage in steps 4 and 5 and a return on the energy investment in the last five steps.
- Fructose 1,6-bisphosphate is split into dihydroxyacetone phosphate (DHAP) and glyceraldehyde 3-phosphate (G3P) in steps 4 and 5. The isomerase enzyme in this step immediately converts DHAP into G3P, resulting in two molecules of G3P. Steps 6 through 10 happen exactly the same way for each of the G3P molecules.
- In step 6, two NADH molecules are produced, one from each of the two G3P molecules processed.
- Two ATP molecules are produced by substrate-level phosphorylation in step 7, one ATP for each of the 1,3-bisphosphoglycerate (BPG) molecules processed.
- In step 10, two more ATP molecules are formed by substrate-level phosphorylation as two molecules of phosphoenolpyruvate (PEP) are converted into two pyruvate molecules.

The overall chemical equation for glycolysis is the following:

$$\text{glucose} + 2\text{ADP} + 2\text{P}_i + 2\text{NAD}^+ \longrightarrow 2\,\text{pyruvate} + 2\text{ATP} + 2(\text{NADH} + \text{H}^+)$$

The following is the energy yield for glycolysis:

4 ATP produced
2 ATP used
2 ATP produced net (may be used by the cell immediately)
2 NADH produced (may be further processed by some cells to obtain more ATP)

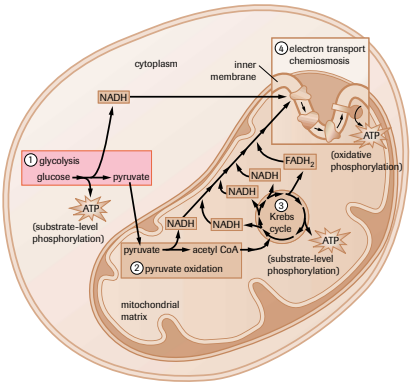


Figure 8
Glycolysis in cellular respiration (pink box)

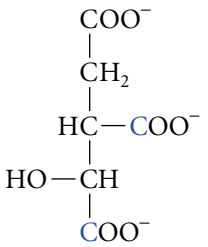
glycolysis a process for harnessing energy in which a glucose molecule is broken into two pyruvate molecules in the cytoplasm of a cell

LEARNING TIP

The Name Game: The Suffix -ate Versus Acid

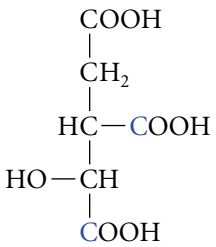
The suffix *-ate* replaces the word *acid* in the name of an organic acid to indicate the ionized form of the acid. Thus, ionized aspartic acid is called *aspartate* (**Figure 10**).

(a)



aspartate

(b)



aspartic acid

Figure 10
(a) Aspartate; **(b)** aspartic acid

1. ATP phosphorylates glucose to G6P

2. G6P rearranged to F6P

3. ATP phosphorylates F6P to F 1, 6-BP

4-5. F 1, 6-BP is split into DHAP and G3P, then DHAP is converted into G3P, resulting in two G3P molecules

6. Two G3P are converted to two BPG. Hydrogen atoms reduce NAD^+ to NADH.

7. BPG is converted toŁ 3PG. A high energy phosphate group onŁ BPG phosphorylatesŁ ADP to ATP

8. 3PG is rearranged to 2PG

9. 2PG is converted to PEP by removal of a water molecule

10. PEP is converted to pyruvate. A high energy phosphate group on PEP phosphorylates ADP to ATP

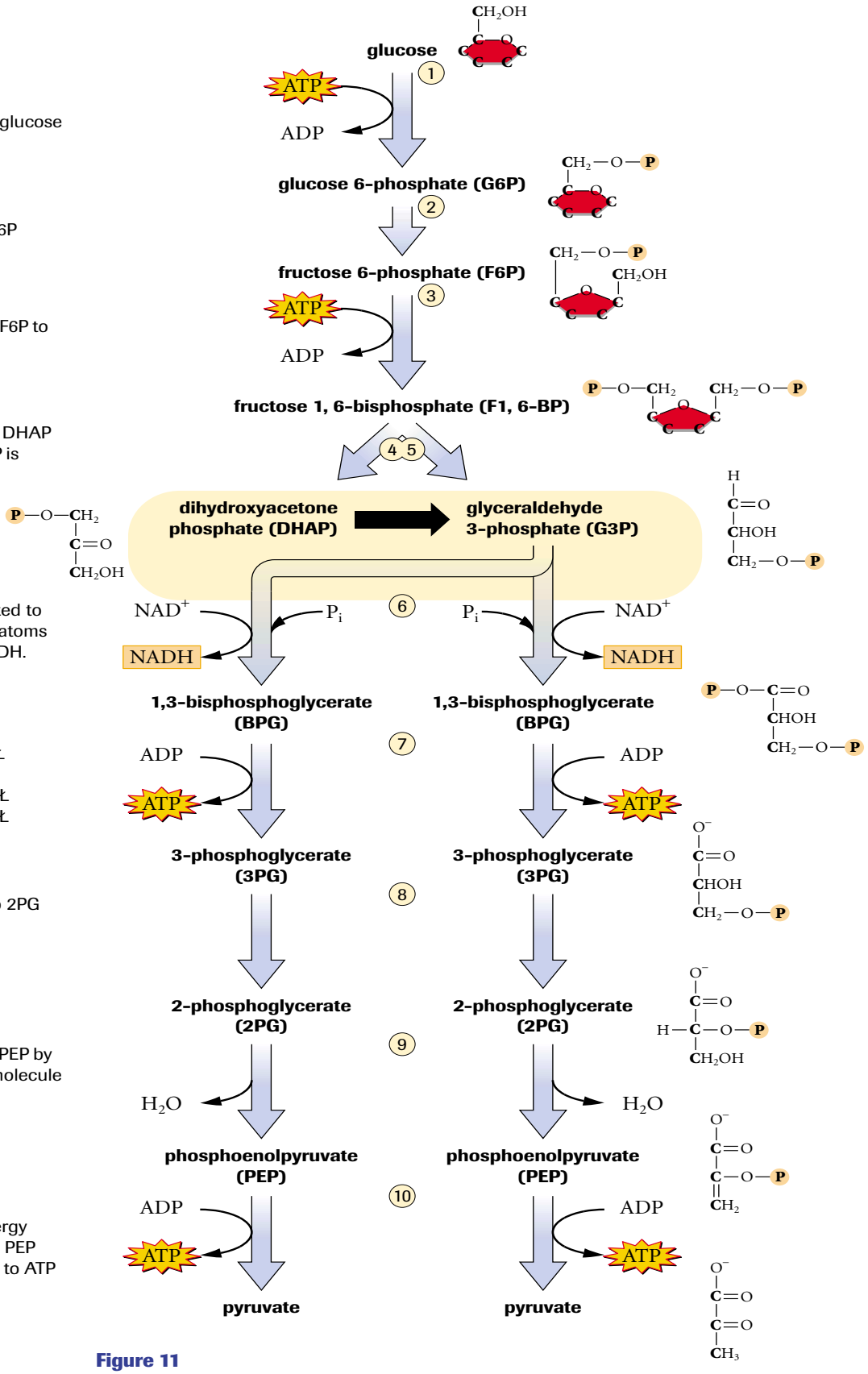


Figure 11
Glycolysis converts a glucose molecule into two pyruvate molecules. Some of the free energy released is captured in the form of ATP and NADH.

The energy conversion efficiency of glycolysis (per mole glucose processed) is calculated as follows:

$$2 \text{ mol ATP} \times 31 \text{ kJ/mol ATP} = 62 \text{ kJ}$$

$$\text{total free energy in 1 mol of glucose} = 2870 \text{ kJ}$$

$$\text{energy conversion efficiency} = \frac{62 \text{ kJ}}{2870 \text{ kJ}} \times 100\% = 2.2\%$$

Glycolysis alone is not a highly efficient energy-harnessing mechanism. It transfers only about 2.2% of the free energy available in 1 mol of glucose to ATP. Some of the energy is released as heat during the process, but the vast majority is still trapped in the two pyruvate and two NADH molecules. The 2.2% conversion efficiency value applies to glycolysis only; it does not take into consideration the possibility of obtaining additional ATP by further processing pyruvate and NADH in the reactions of aerobic respiration (stages 2, 3, and 4).

Glycolysis is thought to be the earliest form of energy metabolism. The first cells to emerge on Earth probably used this process to harness energy and, today, the simplest organisms continue to use it for all their energy needs. Glycolysis yields two ATP molecules from each glucose molecule processed. This may be sufficient energy for the needs of certain microorganisms, but it is not enough to satisfy the energy needs of most multicellular organisms. Nevertheless, all organisms, large and small, multicellular or not, carry out glycolysis either as their only source of ATP or as the first part of a more elaborate and more productive energy-yielding process, such as aerobic respiration. In addition to glycolysis (stage 1), three more processes are associated with aerobic respiration: pyruvate oxidation (stage 2), the Krebs cycle (stage 3), and electron transport and chemiosmosis (stage 4). In eukaryotes, these processes all occur in the cell's mitochondria and require oxygen.

Mitochondria

Mitochondria (singular: mitochondrion) are round or sausage-shaped organelles that are usually scattered throughout a cell's cytoplasm. These vital organelles specialize in the production of large quantities of ATP, the main energy-carrying molecule in living cells. The process that produces ATP in mitochondria cannot proceed without free oxygen. Three stages of aerobic cellular respiration take place within mitochondria: pyruvate oxidation, the Krebs cycle, and electron transport and chemiosmosis. Only **eukaryotic cells** contain mitochondria. **Prokaryotic cells** carry out all the stages of cellular respiration within the cytoplasm.

mitochondria eukaryotic cell organelle in which aerobic cellular respiration occurs

eukaryotic cells cells possessing a cell nucleus and other membrane-bound organelles

prokaryotic cells cells possessing no intracellular membrane-bound organelles or nucleus

Mitochondria possess a double membrane (referred to as an envelope) composed of a smooth outer membrane and a highly folded inner membrane (**Figure 12**, page 100). The folds of the inner membrane are called **cristae** (singular: crista). The outer membrane plays a role similar to that of the cell membrane, but the inner membrane performs many functions associated with cellular respiration. It has numerous substances, such as proteins and enzymes, attached to its inner surface or embedded in its phospholipid bilayer that participate in the reactions of respiration. The inner membrane also creates two compartments within the mitochondrion. The mitochondrial **matrix** is a protein-rich liquid that fills the innermost space of a mitochondrion, and a fluid-filled **intermembrane space** lies between the inner and outer membrane. Both these compartments play a critical role in aerobic respiration.

cristae the folds of the inner mitochondrial membrane

matrix the fluid that fills the interior space of the mitochondrion

intermembrane space the fluid-filled space between the inner and outer mitochondrial membranes

Mitochondria have their own DNA (symbolized as mtDNA), RNA, and ribosomes. These components allow them to reproduce. Many of the features of mitochondrial DNA resemble those found in prokaryotes, such as bacteria. For example, mtDNA is

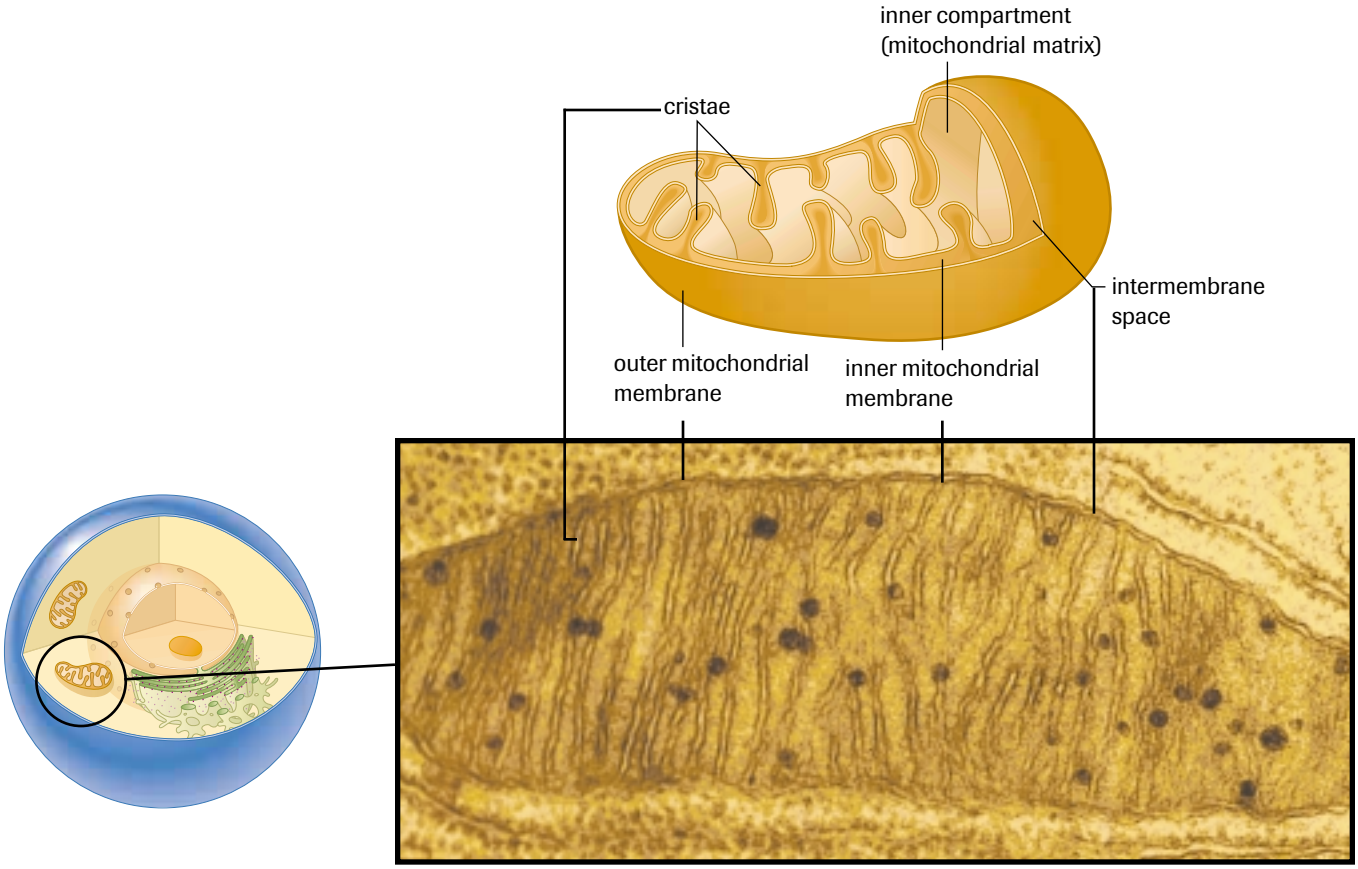


Figure 12
Sketch and transmission electron micrograph (thin section) of a typical mitochondrion

circular like that of bacteria. This observation has strengthened the theory (called the *endosymbiosis hypothesis*) that mitochondria are the evolutionary descendants of prokaryotes that established a symbiotic relationship with the ancestors of eukaryotic cells (discussed further in section 5.7 of Chapter 5).

Stage 2: Pyruvate Oxidation

The two pyruvate molecules formed in glycolysis are transported through the two mitochondrial membranes into the matrix (**Figure 13**). There, a multienzyme complex catalyzes the following three changes (**Figure 14**):

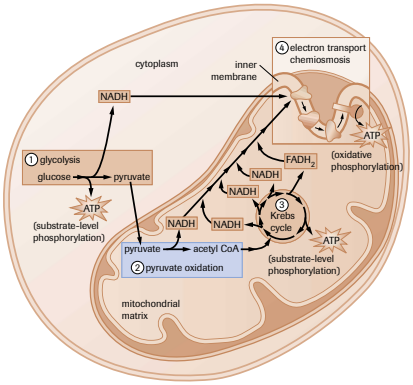


Figure 13
Pyruvate oxidation in cellular respiration

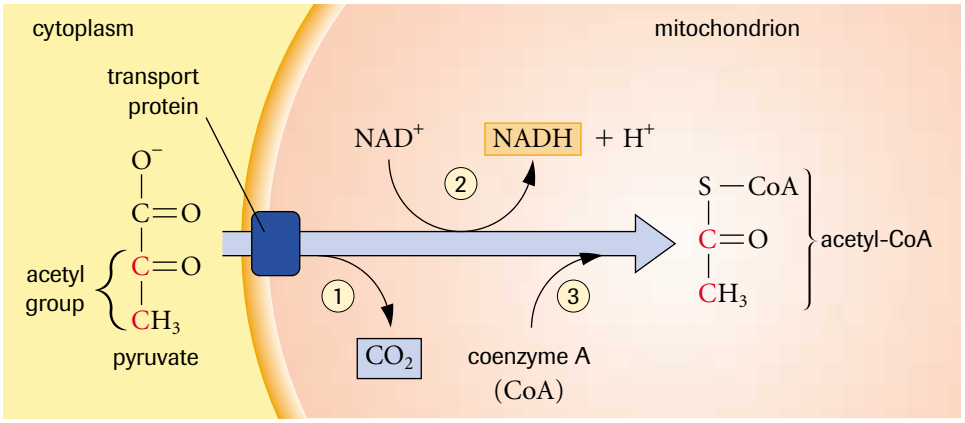


Figure 14
Pyruvate oxidation results in three changes to pyruvate:
1. A CO_2 portion is removed.
2. NAD^+ is reduced by two H atoms, obtained from food.
3. Coenzyme A is attached to the remaining acetic acid portion (acetyl group).

1. A low-energy carboxyl group is removed as CO_2. This is a decarboxylation reaction catalyzed by the enzyme pyruvate decarboxylase.
2. The remaining two-carbon portion is oxidized by NAD^+. In the process, NAD^+ gains two hydrogen atoms (two protons and two electrons) from organic molecules of food, and the remaining two-carbon compound becomes an acetic acid (acetate) group. This reaction transfers potential energy to NAD^+. It is a redox reaction—pyruvate is oxidized, and NAD^+ is reduced.
3. A sulfur-containing compound called coenzyme A (CoA) is attached to the acetate component, forming acetyl-CoA. The carbon–sulfur bond that holds the acetyl group to coenzyme A is unstable. This prepares the two-carbon acetyl portion of this molecule for further oxidation in the Krebs cycle. CoA is a derivative of vitamin B_5, also known as pantothenic acid.

The following is the overall equation for this process. (Remember that glycolysis produces two pyruvate molecules from one glucose molecule.)

$$2\ \text{pyruvate} + 2\ NAD^+ + 2\ \text{CoA} \longrightarrow 2\ \text{acetyl-CoA} + 2\ \text{NADH} + 2H^+ + 2\ CO_2$$

The two molecules of acetyl-CoA enter the Krebs cycle where additional free energy transfers occur. The two molecules of NADH proceed to stage 4 (electron transport and chemiosmosis) to produce ATP by oxidative phosphorylation. The two CO_2 molecules produced during pyruvate oxidation diffuse out of the mitochondrion and then out of the cell as a low-energy waste product. The two H^+ ions remain dissolved in the matrix.

Acetyl-CoA is a central molecule in energy metabolism. Almost all molecules that are catabolized for energy are converted into acetyl-CoA, including proteins, lipids, and carbohydrates. Acetyl-CoA is multifunctional; it can be used to produce fat or ATP. If the body needs energy, acetyl-CoA enters the Krebs cycle, ultimately transferring most of its free energy to ATP. If the body does not need energy, acetyl-CoA is channelled into an anabolic pathway that synthesizes lipids as a way of storing large amounts of energy as fat. The pathway taken by acetyl-CoA depends on the levels of ATP in the cell. If ATP levels are low, acetyl-CoA goes into the Krebs cycle to increase ATP production. If ATP levels are high, acetyl-CoA goes on to produce lipids. This explains why animals accumulate fat when they consume more food than their bodies require to satisfy their energy needs. All nutrients, whether protein, lipid, or carbohydrate, are converted to acetyl-CoA and then channelled toward fat production or ATP production, depending on the organism's immediate energy needs.

Krebs cycle a cyclic series of reactions that transfers energy from organic molecules to ATP, NADH, and $FADH_2$ and removes carbon atoms as CO_2

Stage 3: The Krebs Cycle

In 1937, Sir Hans Krebs (1900–81), a biochemist working at the University of Sheffield in England, discovered the series of metabolic reactions that became known as the **Krebs cycle** (**Figure 15**). He received the 1953 Nobel Prize in Physiology or Medicine for this important discovery. Fritz Albert Lipmann (1899–1986) shared the Nobel Prize with Krebs for his discovery of coenzyme A and the key role it plays in metabolism.

The Krebs cycle is an eight-step process, each step catalyzed by a specific enzyme. It is a cyclic process because oxaloacetate, the product of step 8, is the reactant in step 1 (**Figure 16**, page 102). Key features of the Krebs cycle are outlined in **Table 1** (page 103).

The following is the overall chemical equation for the Krebs cycle:

$$\text{oxaloacetate} + \text{acetyl-CoA} + \text{ADP} + P_i + 3NAD^+ + \text{FAD} \longrightarrow$$
$$\text{CoA} + \text{ATP} + 3\text{NADH} + 3H^+ + FADH_2 + 2CO_2 + \text{oxaloacetate}$$

(Oxaloacetate is shown as reactant and product to indicate that the process is cyclic.)

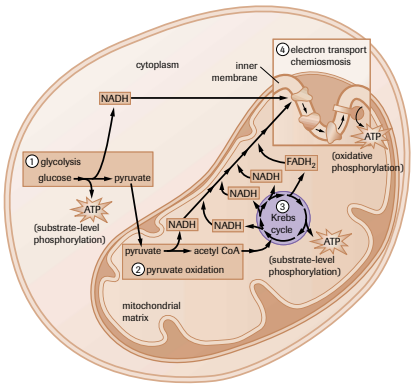


Figure 15
The Krebs cycle in cellular respiration

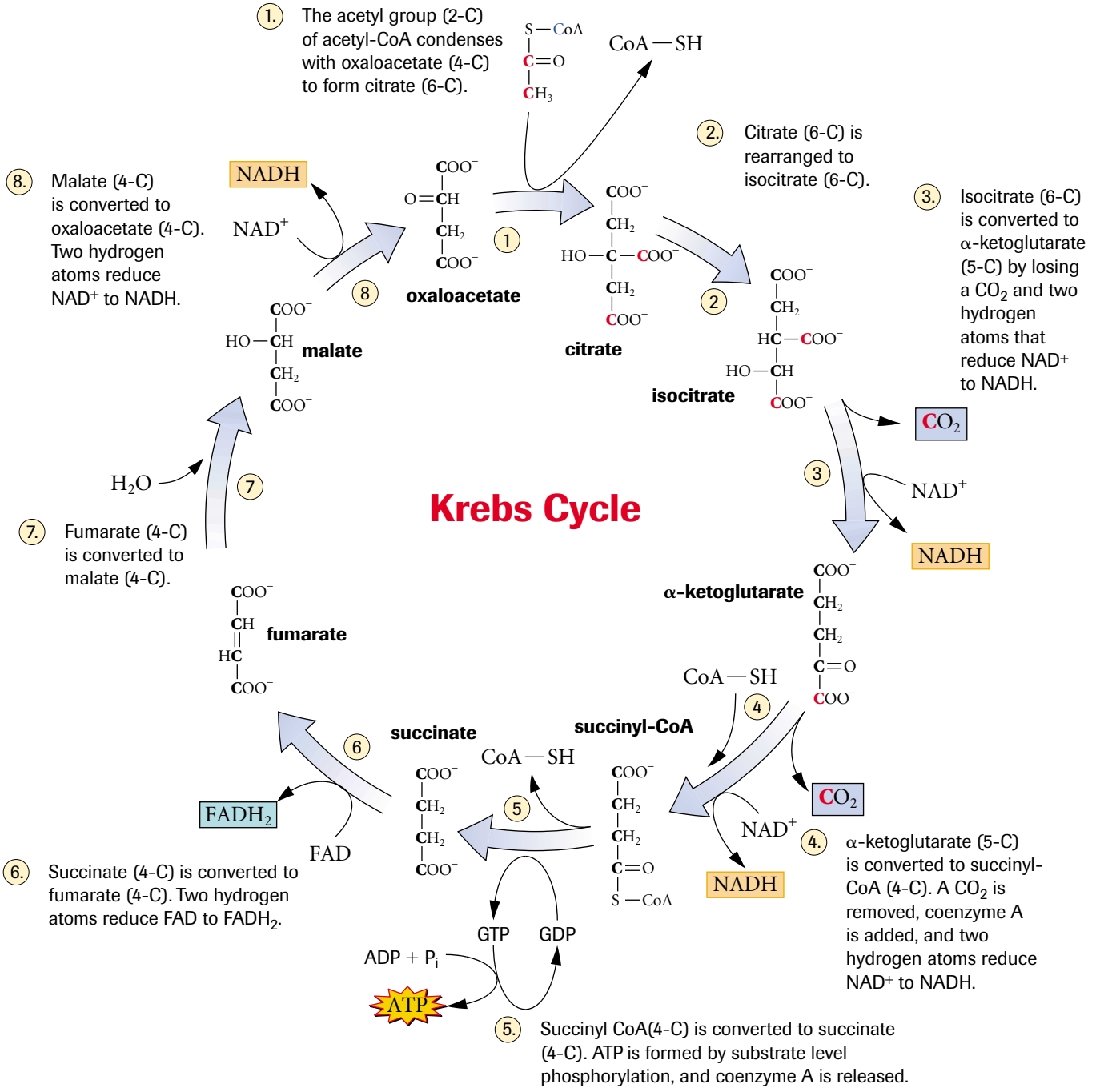


Figure 16
The Krebs cycle begins when acetyl-CoA condenses with oxaloacetate to form citrate. In one turn of the cycle, the last two carbon atoms of the original glucose molecule are removed as CO_2, and free energy is transferred to ATP, NADH, and $FADH_2$.

By the end of the Krebs cycle, the original glucose molecule is entirely consumed. The six carbon atoms leave the process as six low-energy CO_2 molecules, which are released by the cell as waste. All that is preserved of the original glucose molecule is most of its energy, which is stored in the form of four ATP molecules (two from glycolysis and two from the Krebs cycle) and 12 reduced coenzymes (two NADH from glycolysis, two NADH from the pyruvate oxidation step, six NADH from the Krebs cycle, and two

Table 1 Key Features of the Krebs Cycle

• Since two molecules of acetyl-CoA are formed from one molecule of glucose, the Krebs cycle occurs twice for each molecule of glucose processed (**Figure 17**).
• Acetyl-CoA enters the cycle at step 1. It reacts with an existing molecule of oxaloacetate (OAA) to produce a molecule of citrate. This is why the cycle is sometimes called the citric acid cycle. Note that this reaction converts a four-carbon compound (OAA) into a six-carbon compound (citrate) by the addition of the two-carbon acetyl group of acetyl-CoA. This releases CoA, which can be used to process another pyruvate molecule in the pyruvate oxidation step. Thus, CoA is recycled. Also notice that oxaloacetate contains two carboxyl groups and citrate has three carboxyl groups. Because of this, the cycle is sometimes referred to as the tricarboxylic acid cycle (TCA cycle).
• Energy is harvested in steps 3, 4, 5, 6, and 8.
• In steps 3, 4, and 8, NAD^+ is reduced to NADH.
• In step 5, ATP is formed by substrate-level phosphorylation. In this reaction, a phosphate group from the matrix displaces CoA from succinyl-CoA. The phosphate group is then transferred to guanosine diphosphate (GDP), forming guanosine triphosphate (GTP). Next, the phosphate group condenses with ADP, forming ATP. Overall, free energy is transferred from succinyl-CoA to ATP by a form of substrate-level phosphorylation.
• Energy is harvested in step 6. However, this reaction is not exergonic enough to reduce NAD^+ to NADH. Instead, a molecule of FAD is reduced to $FADH_2$, storing free energy in this form. This step is closely linked to the electron transport chain in the inner mitochondrial membrane.
• The last four carbon atoms of the original glucose molecule leave as fully oxidized CO_2 molecules in steps 3 and 4 (remember that it takes two turns of the Krebs cycle to process one glucose molecule). Like the two CO_2 molecules produced in the pyruvate oxidation steps, these four carbon atoms diffuse out of the mitochondrion and eventually out of the cell as low energy metabolic waste.

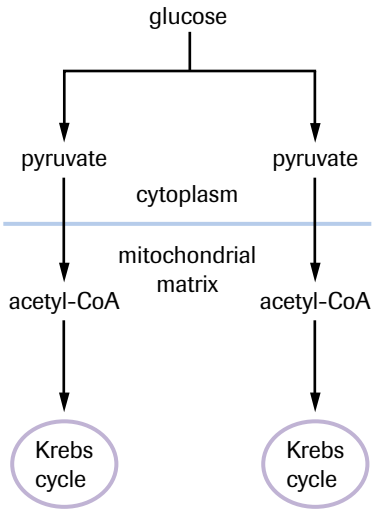


Figure 17

$FADH_2$ from the Krebs cycle). Most of the free energy stored in NADH and $FADH_2$ molecules will eventually be transferred to ATP in the next (and last) stage of cellular respiration—an elaborate series of processes called electron transport and chemiosmosis.

However, before we move to stage 4, let's take a close look at the six carbon atoms of the original glucose molecule and see what happens to them as they move through the reactions of the first three stages of the process. The following summarizes the fate of glucose's carbon atoms:

electron transport chain (ETC) a series of membrane-associated protein complexes and cytochromes that transfer energy to an electrochemical gradient by pumping H^+ ions into an intermembrane space

$$\underset{\text{glucose}}{CCCCCC} \xrightarrow[\text{glycolysis}]{} \underset{\text{2 pyruvate}}{CCC + CCC} \xrightarrow[\text{oxidation}]{\text{pyruvate}} \underset{\text{2 acetyl-CoA + 2CO}_2}{CC + CC + CO_2 + CO_2} \xrightarrow{\text{Krebs cycle}} \underset{\text{4CO}_2}{CO_2 + CO_2 + CO_2 + CO_2}$$

Notice that by the end of the Krebs cycle, all six carbon atoms of glucose have been oxidized to CO_2 and released from the cell as metabolic waste. All that is left of the original glucose molecule is some of its free energy in the form of ATP and the reduced coenzymes, NADH and $FADH_2$. The reduced coenzymes now go on to stage 4 of the process, electron transport and chemiosmosis, where much of their free energy will be transferred to ATP.

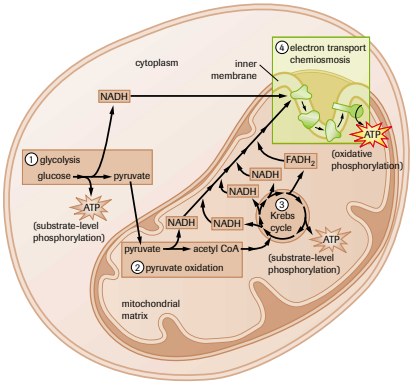


Figure 18
The electron transport chain and chemiosmosis in cellular respiration

Stage 4: Electron Transport and Chemiosmosis

NADH and $FADH_2$ eventually transfer the hydrogen atom electrons they carry to a series of compounds, mainly proteins, which are associated with the inner mitochondrial membrane, called the **electron transport chain (ETC)** (**Figure 18**). The components of the ETC are arranged in order of increasing electronegativity, with the weakest attractor of electrons (NADH dehydrogenase) at the beginning of the chain and the strongest (cytochrome oxidase) at the end. Each component is alternately reduced (by

gaining two electrons from the component before it in the chain) and oxidized (by losing the two electrons to the component after it in the chain); the electrons shuttle through the ETC like a baton handed from runner to runner in a relay race. As the electrons move from molecule to molecule in the ETC, they occupy ever more stable positions relative to the nuclei of the atoms they associate with. The free energy released in the process is used to move protons (H^+ ions) from the mitochondrial matrix. They move through three proton pumps, one in each of three membrane-associated protein complexes, into the fluid-filled intermembrane space. By the time the two electrons reach the last component of the ETC, they are in a very stable position. A highly electronegative substance is required to oxidize this last protein. Oxygen, one of the most electronegative substances on Earth, is used to do this. It strips the two electrons from the final protein complex in the chain and, together with two protons from the matrix, forms water. As such, oxygen acts as the final electron acceptor in the electron transport process. The actual components of the ETC are (in order of increasing electronegativity) NADH dehydrogenase, ubiquinone (Q), the cytochrome b-c_1 complex, cytochrome c, and the cytochrome oxidase complex.

Figure 19 illustrates how the components of the ETC are arranged in the membrane and shows the path taken by electrons (long red arrow) and protons (H^+ ions) (short blue arrows). The process begins with NADH giving up its two electrons to the first protein complex in the ETC, NADH dehydrogenase. The mobile electron carriers, Q and cytochrome c, shuttle the electrons from one protein complex to the next until they reach the final protein complex in the chain, the cytochrome oxidase complex. Finally, the enzyme cytochrome oxidase, which is part of this complex, catalyzes the reaction between the electrons, protons, and molecular oxygen to form water.

The electron transport process is highly exergonic. As mentioned earlier, the free energy lost by the electron pair during electron transport is used to pump three protons into the intermembrane space. This mechanism converts one form of energy into another—the chemical potential energy of electron position is converted to electrochemical potential energy of a proton gradient that forms across the inner mitochondrial membrane.

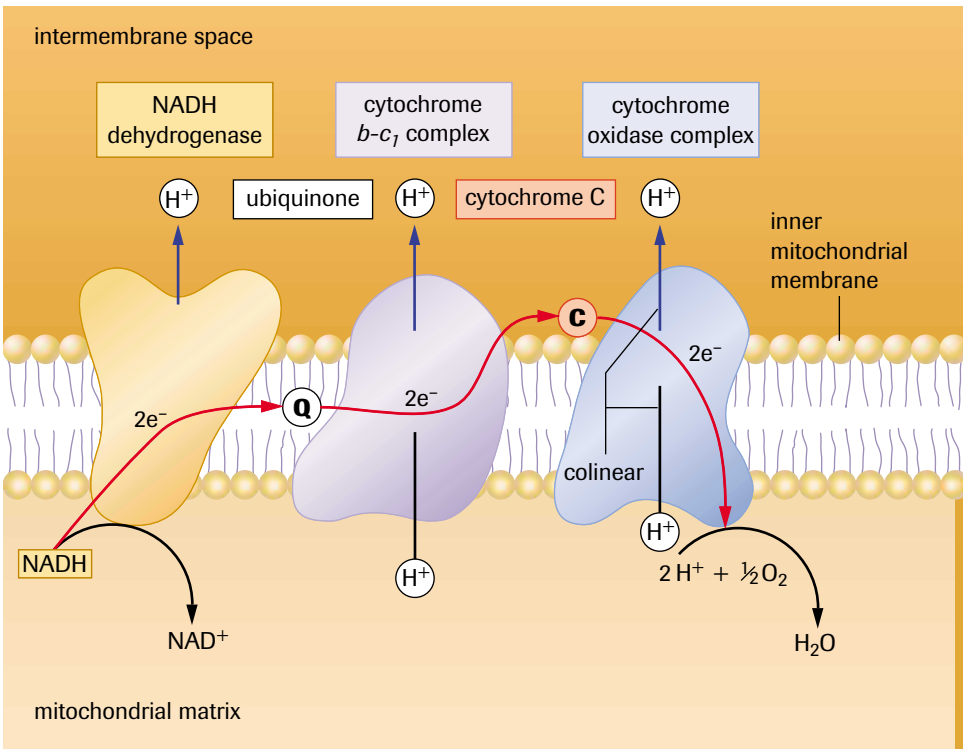


Figure 19
Electron transport chain (ETC)

Electrochemical potential energy is the type of stored energy possessed by a charged battery. It is caused by an accumulation of charged objects (ions, protons, electrons, etc.) on one side of an insulator. (The nature of the proton gradient that forms across the inner mitochondrial membrane will be described in more detail later in this section.) The transfer of a pair of electrons from NADH to oxygen through the electron transport chain is an exergonic process with a free energy change (ΔG) of -222 kJ/mol NADH. Much of this energy becomes stored in the electrochemical gradient and will be used to power ATP synthesis in the next part of the process, called chemiosmosis.

Before chemiosmosis is described, it is important to distinguish between NADH and $FADH_2$ in terms of their relationship with the electron transport system. NADH and $FADH_2$ do not transfer their electrons to the electron transport chain in the same way. NADH passes its electrons on to the first protein complex, NADH dehydrogenase, and $FADH_2$ transfers its electrons to Q, the second component of the chain (**Figure 20**). Thus, the free energy released by the oxidation of $FADH_2$ is used to pump two protons into the intermembrane space, while NADH oxidation pumps three. The result is that two ATP are formed per $FADH_2$ and three ATP molecules are formed per NADH.

Also, a distinction must be made between the NADH molecules produced in glycolysis and those produced in the pyruvate oxidation step and Krebs cycle. NADH produced by glycolysis in the cytoplasm (cytosolic NADH) may diffuse through the outer mitochondrial membrane into the intermembrane space, but not through the inner membrane into the matrix. Since the inner membrane is impermeable to NADH, it has two shuttle systems that pass electrons from cytosolic NADH in the intermembrane space to the matrix. The first and most common shuttle, called the glycerol-phosphate shuttle, transfers the electrons from cystolic NADH to FAD to produce $FADH_2$. Like $FADH_2$ produced in the Kreb's cycle, it transfers its electrons to Q, resulting in the synthesis of two ATP molecules by chemiosmosis. The second shuttle, called the aspartate shuttle, transfers electrons to NAD^+ instead of FAD, forming NADH, and then three ATP molecules. However, in this chapter we will assume that the transfer is made to FAD, using the glycerol-phosphate shuttle.

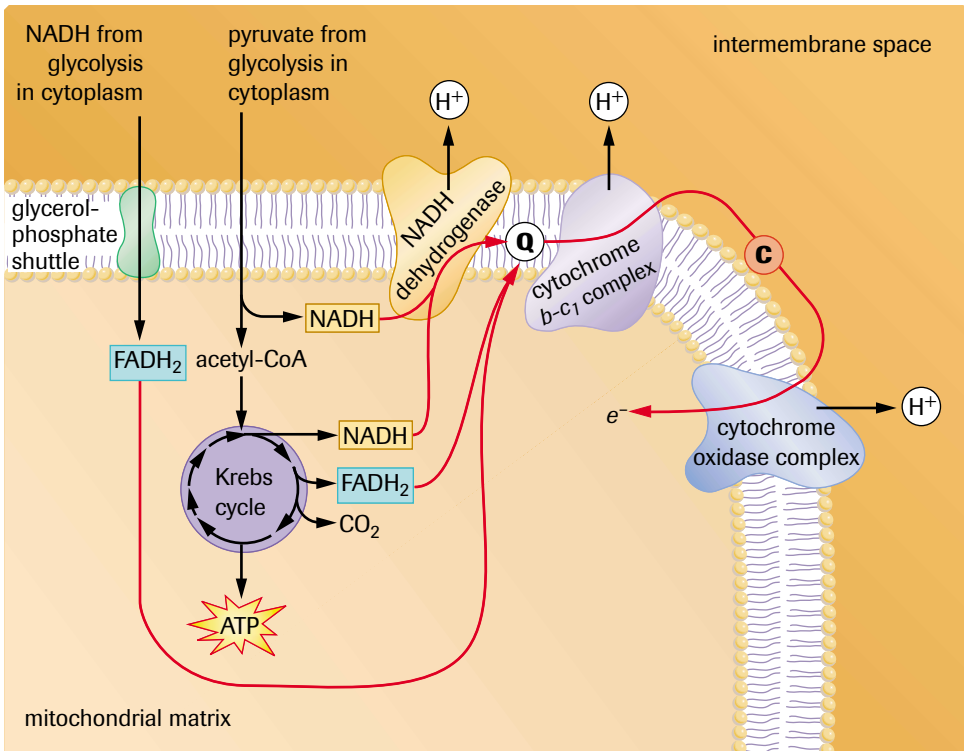


Figure 20
Reduced coenzymes give up their electrons to different components of the electron transport chain.

DID YOU KNOW?

Cyanide Blocks the Electron Transport Chain

Cyanide inhibits cytochrome oxidase activity, preventing oxygen from acting as the final electron acceptor in the electron transport chain. This disruption virtually shuts down ATP production, resulting in coma and death. That is why cyanide is a poison. However, it is not poisonous to all organisms. Anaerobic bacteria called MIT-13 actually live on cyanide—they use it in the same way aerobes use oxygen!

The many folds of the inner membrane increase surface area and allow multiple copies of the ETC to be located throughout the mitochondrion. At any given time, there are a limited number of NAD^+ and FAD molecules in a cell and, therefore, they must be recycled. Once NADH and $FADH_2$ give up their electrons to NADH dehydrogenase and Q, respectively, the resulting oxidized compounds pick up more hydrogen atoms in glycolysis, pyruvate oxidation, or the Krebs cycle.

Chemiosmosis and Oxidative ATP Synthesis

electrochemical gradient a concentration gradient created by pumping ions into a space surrounded by a membrane that is impermeable to the ions

The protons that accumulate in the intermembrane space of the mitochondrion during electron transport create an **electrochemical gradient** that stores free energy. This gradient has two components: an electrical component caused by a higher positive charge in the intermembrane space than in the matrix, and a chemical component caused by a higher concentration of protons in the intermembrane space than in the matrix. The intermembrane space essentially becomes an H^+ reservoir because the inner mitochondrial membrane is virtually impermeable to protons. The electrochemical gradient creates a potential difference (voltage) across the inner mitochondrial membrane similar to that in a chemical cell or battery. Unable to diffuse through the phospholipid bilayer, the protons are forced to pass through special proton channels associated with the enzyme ATP synthase (ATPase). The free energy stored in the electrochemical gradient produces a **proton-motive force (PMF)** that moves protons through an ATPase complex. As protons move through the ATPase complex, the free energy of the electrochemical gradient is reduced. This energy drives the synthesis of ATP from ADP and inorganic phosphate (P_i) in the matrix (**Figure 21**).

proton-motive force (PMF) a force that moves protons through an ATPase complex on account of the free energy stored in the form of an electrochemical gradient of protons across a biological membrane

Thus, some of the free energy lost by the electrochemical gradient is harvested as chemical potential energy in ATP. This mechanism of ATP generation was first worked out by Peter Mitchell in 1961, whose theory started a revolution in the way scientists thought about bioenergetics. However, it took him a long time to convince an initially hostile scientific community that his ideas were reasonable. He received the Nobel Prize

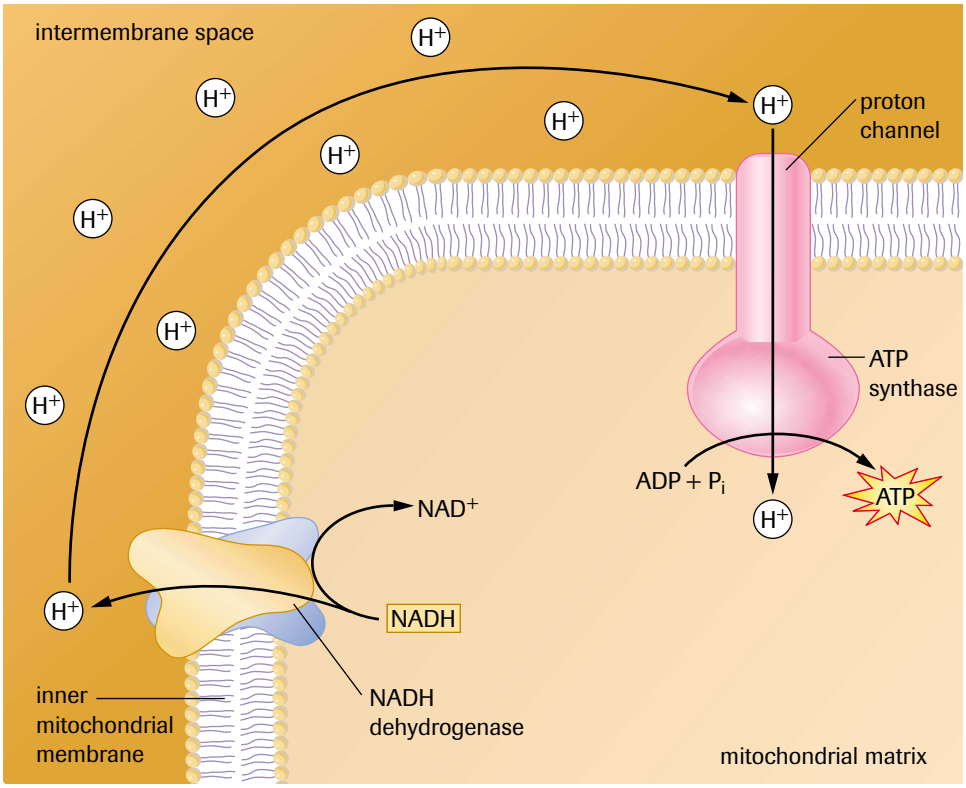


Figure 21
One molecule of ATP is synthesized from ADP and P_i as an H^+ ion passes through the ATPase complex into the mitochondrial matrix from the H^+ reservoir in the intermembrane space.

in Chemistry in 1978 for "his contribution to the understanding of biological energy transfer through the formulation of the chemiosmotic theory." Mitchell called the process **chemiosmosis** because the energy that drives the synthesis of ATP comes from the "osmosis" of protons through a membrane from one compartment into another. Although it is a misnomer according to today's definition of osmosis, the term *chemiosmosis* continues to be used to describe this process.

chemiosmosis a process for synthesizing ATP using the energy of an electrochemical gradient and the ATP synthase enzyme

After they are formed by chemiosmosis, the ATP molecules are transported through both mitochondrial membranes by facilitated diffusion into the cytoplasm, where they are used to drive endergonic processes, such as movement, active transport, and synthesis reactions throughout the cell.

Electron transport followed by chemiosmosis is the last stage of the oxidative phosphorylation process that began with the reduction of NAD^+ and FAD with hydrogen atoms from the original glucose molecule. But how is chemiosmosis linked to electron transport in the ETC? The electron transport chain gets its electrons from the hydrogen atoms that NADH obtained from glucose. Some of the free energy released by the electrons as they travel through the chain is harnessed by pumping protons into the H^+ reservoir and creating the electrochemical gradient. The energy of the gradient is reduced as the protons pass through the ATPase complex back into the mitochondrial matrix. Although some of the energy dissipates as heat, much of it is captured by condensing ADP and P_i into ATP at the ATPase complex.

The continual production of ATP by this method is dependent on the establishment and maintenance of an H^+ reservoir. This condition requires the continual movement of electrons through the ETC, which, in turn, is dependent on the availability of oxygen to act as the final electron acceptor. This explains why animals have lungs and fish have gills. Oxygen is needed to keep the electrons flowing through the ETC. Electrons are "pulled down" the chain in an energy-yielding "fall," similar to gravity pulling a skydiver down toward the centre of Earth. The energy released in the fall keeps protons moving into the H^+ reservoir so that they can "fall back" into the matrix and drive the synthesis of ATP.

Without food (glucose), there will be no electrons in the first place. This is one of the reasons why heterotrophs must continually eat and why photoautotrophs must continually photosynthesize. If oxygen is not available, or its supply is interrupted, electrons cannot continue to flow through the ETC because there is no substance available to act as the final electron acceptor. Although there are many chemicals in a cell, none is electronegative enough to oxidize the last protein in the chain. Without oxygen to free up that last protein, the chain soon becomes clogged with stationary electrons. H^+ ions cannot be pumped into the intermembrane space, and those that are there soon move into the matrix until protons are equally distributed across the inner membrane of the mitochondrion. If this happens, chemiosmosis stops, and ATP synthesis grinds to a halt. At the other end of the chain, NADH and $FADH_2$ are no longer able to give up their electrons (as hydrogen atoms) to proteins in the ETC because these proteins cannot get rid of the electrons that they are already holding on to. All of the available NAD^+ and FAD remain in reduced form as NADH and $FADH_2$, unable to remove any more hydrogen atoms from glucose.

As you can see, the three stages of oxidative phosphorylation (pyruvate oxidation, the Krebs cycle, and electron transport and chemiosmosis) are all linked to one another and are all dependent on glycolysis for the production of pyruvate. It is said that ATP synthesis by chemiosmosis is *coupled* with electron transport, and both of these are dependent on the availability of electrons (from food such as glucose) and oxygen (for its ability to act as a final electron acceptor).

An overview of the mechanism of oxidative phosphorylation is presented in **Figure 22** (page 108). The illustration shows that NADH shuttles electrons from glucose to the ETC, where they lose potential energy as they are transported from protein to protein in

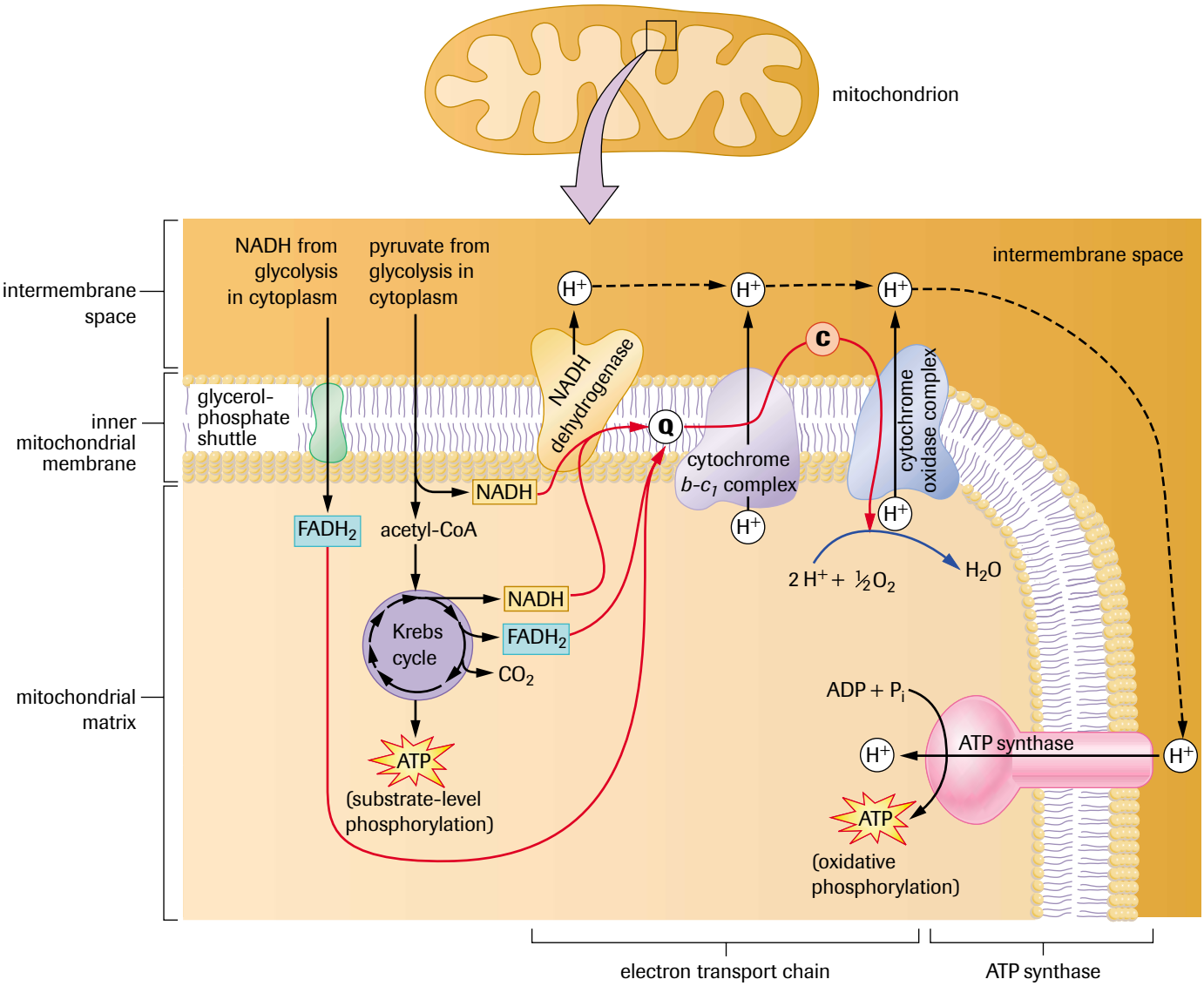


Figure 22
An overview of oxidative phosphorylation

the chain. Some of the energy is harnessed in the form of an electrochemical gradient caused by the accumulation of protons in the intermembrane space of the mitochondrion. The energy of the gradient is used to power ATP synthesis in the matrix as protons diffuse through ATPase complexes back into the matrix. The continual movement of electrons through the ETC is dependent on the availability of molecular oxygen to act as a final electron acceptor. The formation of water using electrons from the ETC and protons from the matrix is catalyzed by cytochrome oxidase, the last protein in the chain.

In oxidative phosphorylation, electrons flow "downhill" (**Figure 23**).

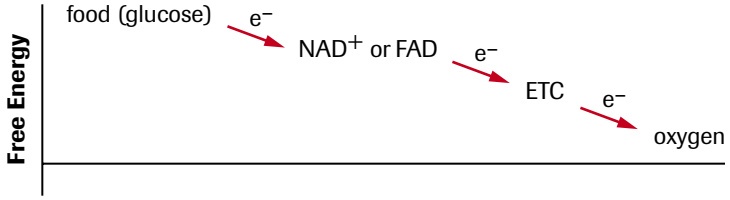


Figure 23
The exergonic ("downhill") flow of electrons in aerobic respiration

The Energetics of Oxidative Phosphorylation

Water can be formed in a test tube by combining hydrogen, $H_{2(g)}$, and oxygen, $O_{2(g)}$, according to the following equation:

$$H_{2(g)} + \frac{1}{2}O_{2(g)} \longrightarrow H_2O_{(l)}$$

This reaction is highly exergonic. In fact, it is explosive! A large amount of energy is released rapidly in the test tube reaction because bonding electrons quickly move much closer to a nucleus in water than they were in the hydrogen and oxygen molecules, as illustrated in **Figure 24(a)**. **Figure 24(b)** shows that the same reaction occurs at the end of the electron transport chain, where an oxygen atom ($\frac{1}{2}O_2$) combines with two electrons and two protons (two H atoms) to form water. As you can see, the same reaction may occur by two totally different mechanisms.

In cellular respiration, the source of hydrogen is glucose. The electron transport chain separates the electrons of the hydrogen atoms from their protons. The protons dissolve in the mitochondrial matrix and the electrons move through the ETC, occupying more stable configurations as they move to ever more electronegative components. Energy is released at each step. Most of the energy dissipates as heat, but a significant amount is harnessed as ATP is synthesized by chemiosmosis. The electrons, already in a much more stable state at the end of the ETC, gain a little more stability when they are captured by oxygen and reunited with protons in the matrix to form water. This removes low-energy electrons from the ETC, and makes room for other electrons coming down the chain.

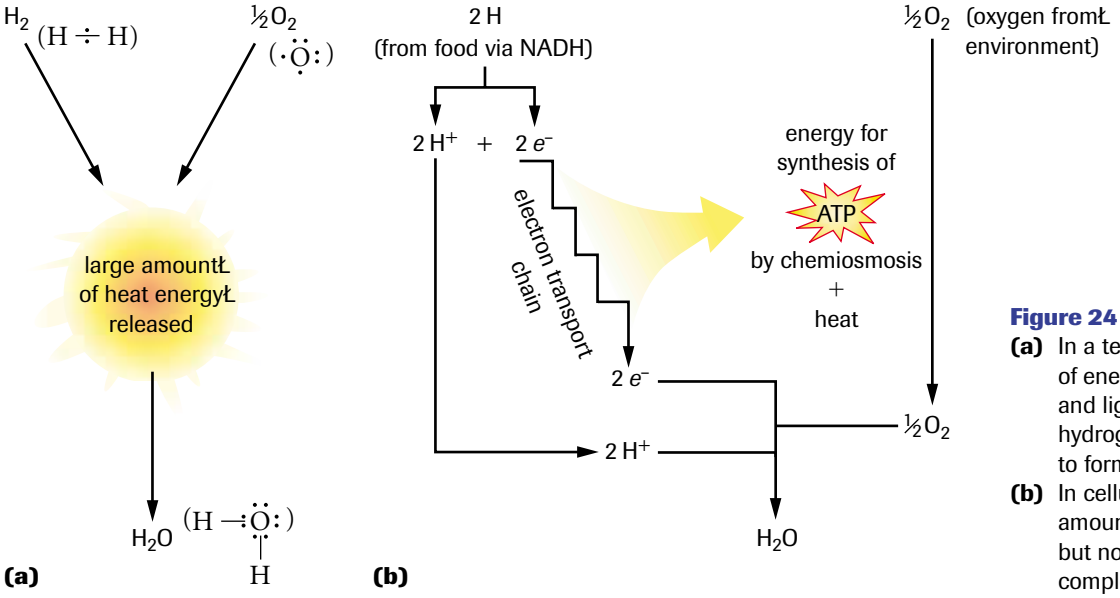


Figure 24
(a) In a test tube, a large amount of energy in the form of heat and light is released when hydrogen and oxygen react to form water.
(b) In cellular respiration, the same amount of energy is released, but not all at once and not completely as heat and light.

The Aerobic Respiration Energy Balance Sheet

How much energy was transferred from glucose to ATP in the entire aerobic respiration process? We may calculate two values in answer to this question: a theoretical value and an actual value. Although the actual value gives a more realistic total, it too varies according to the type of cell and various environmental conditions. **Figure 25** (page 110) summarizes the theoretical yield of 36 ATP and its sources.

The actual ATP yield is less than 36 for the following two reasons:

1. The inner mitochondrial membrane is not completely impermeable to H^+ ions. Thus, some H^+ ions leak through the phospholipid bilayer of the membrane, reducing the number that go through the ATPase complex to produce ATP.

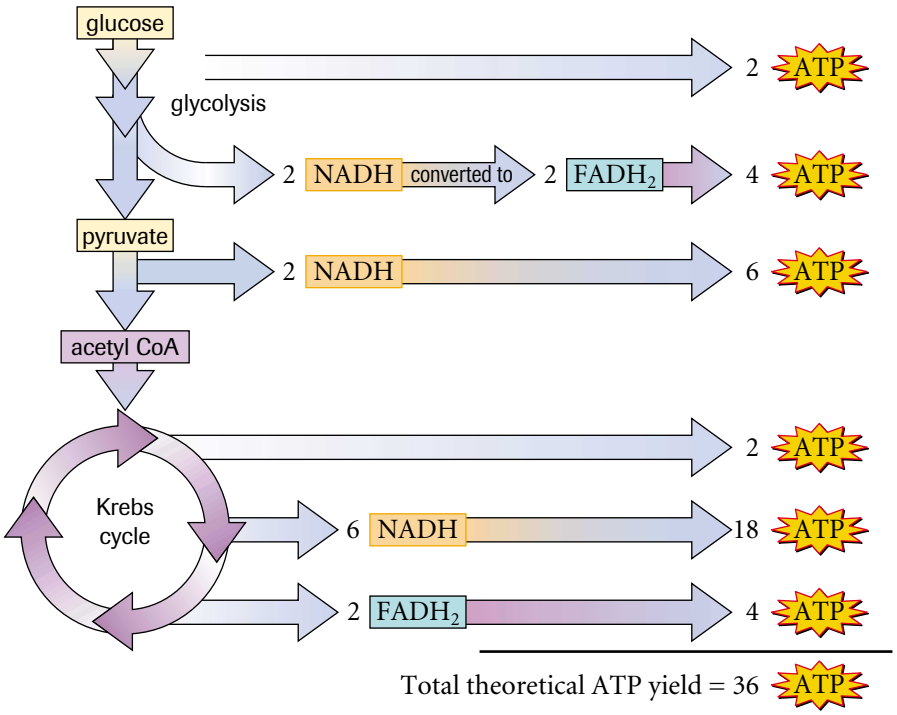


Figure 25
Theoretical coenzyme and ATP yield from the aerobic respiration of one glucose molecule

2. Some of the protons in the H^+ reservoir are used by the cell for other energy-requiring activities. The result is a reduction in the number of ATP molecules produced by chemiosmosis.

It has been estimated that the equivalent of 2.5 ATP molecules (not 3) are realistically produced for every NADH and approximately 1.5 ATP molecules (not 2) are produced for each $FADH_2$. This difference reduces the number of ATP produced from NADH to 25 (10 NADH $\times$ 2.5 ATP/NADH) and the number produced from $FADH_2$ to 3 (2 $FADH_2$ $\times$ 1.5 ATP/$FADH_2$), resulting in an actual yield of 30 ATP per glucose molecule (or 30 mol ATP per mol glucose) molecules from one glucose molecule.

Efficiency of Energy Conversion for Aerobic Respiration

Aerobic respiration is a much more efficient energy conversion mechanism than glycolysis. Aerobic respiration captures approximately 32% of the available free energy in glucose. Using an actual yield of 30 ATP per glucose molecule (or 30 mol ATP per mol glucose), the efficiency may be calculated as follows:

efficiency = 30 mol ATP $\times$ 31 kJ/mol ATP / 2870 kJ $\times$ 100% = 32% (rounded)

The greater ability of aerobic respiration to harness energy from nutrients makes multicellular life possible.

The efficiency of energy conversion for an automobile engine is estimated to be approximately 25%. In both cases, the remainder of the energy is given off as heat.

Metabolic Rate

metabolic rate the amount of energy consumed by an organism in a given time

An organism's **metabolic rate** is the amount of energy consumed by the organism in a given time. This value is also a measure of the overall rate at which the energy-yielding reactions of cellular respiration take place. Metabolic rate will increase when work is done, but even when at rest, an organism uses energy to keep cells alive. In the case of

the human body, energy is used for breathing, maintaining body temperature, contracting muscles, and maintaining brain function. The minimum amount of energy needed to keep an organism alive is called the **basal metabolic rate (BMR)**. The BMR accounts for about 60% to 70% of the energy a human body uses in a day. In general, BMR is measured in units of kilojoules per square metre of body surface per hour: $kJ/m^2/h$.

basal metabolic rate (BMR) the minimum amount of energy on which an organism can survive

The BMR does not remain constant over time but changes with growth, development, and age. A newborn baby's BMR is approximately 100 $kJ/m^2/h$. As the baby grows, the BMR increases, reaching a maximum of about 220 $kJ/m^2/h$ by the end of the first year. After that, as age increases, the BMR gradually decreases (**Figure 26**).

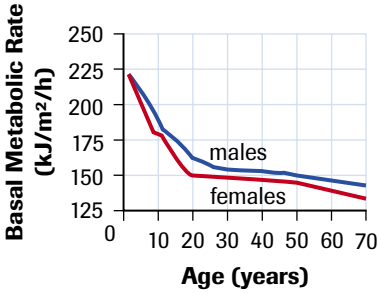


Figure 26
Changes in the human BMR with age

BMR varies not only with age, but also according to gender and health. In general, a healthy adult male has a BMR of about 167 $kJ/m^2/h$, and a healthy woman has a BMR of approximately 150 $kJ/m^2/h$. The BMR may be estimated experimentally by measuring the amount of thermal energy lost by a person's body over a given time. This is done while a person is lying at rest in a human calorimeter, such as the Benzinger calorimeter.

The calorimeter is an insulated vessel containing a known mass of water and a thermometer. As the person lies perfectly still in the calorimeter, thermal energy expended by the body is transferred to the water, causing its temperature to rise. The amount of thermal energy released is calculated on the basis that 4.2 J of energy is required to raise the temperature of 1.0 g of water by 1°C. Since the thermal energy expended by the body comes from the oxidation of food, the calculated energy value is proportional to the person's BMR. To complete the BMR calculation, the person's surface area must be measured. This measurement is made by encasing the person's entire body in a wax mould, and then flattening out the mould and measuring its surface area. As you might imagine, this is a very demanding process for the human subject. Thankfully, such measurements have led to formulas that can estimate a person's surface area without subjecting the individual to the wax mould. The following equation estimates human body surface area (BSA) in square metres (m^2):

$$BSA = m^{0.425} \times h^{0.725} \times 0.007\,184$$

(m = body mass in kilograms, h = height in centimetres)

nomograms graphical methods for determining the value of an unknown quantity when the values of other quantities that it is mathematically related to are known

Calculating Human Body Surface Area (BSA)

SAMPLE problem

Example

(a) Calculate the body surface area of an adult male who is 1.75 m tall and has a mass of 85.0 kg.

(b) Calculate the person's BMR if he dissipates 322 kJ of thermal energy in 1.0 hours while in a Benzinger calorimeter.

Solution

(a) h = 1.75 m = 175 cm

m = 85.0 kg

$BSA = m^{0.425} \times h^{0.725} \times 0.007\,184$

$= 85.0^{0.425} \times 175^{0.725} \times 0.007\,184$

$= 6.46 \times 42.3 \times 0.007\,184$

$= 2.01\ m^2$

The man's body surface area is approximately 2.01 m^2.

(b) BMR = 322kJ ÷ 2.01 m^2 ÷ 1.0 h

= 160 $kJ/m^2/h$

To make things even easier, **nomograms** have been developed that allow the BSA to be determined graphically (**Figure 27**, page 112).

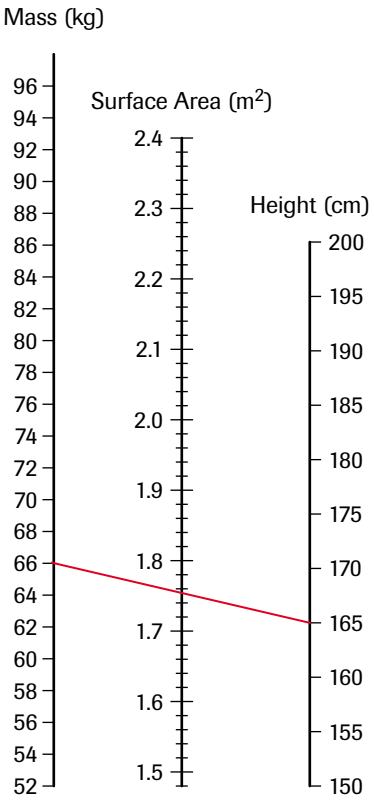


Figure 27
Line up a ruler from the body mass in kg to the body height in cm. The point where the ruler crosses the surface area line gives the body's surface area in m^2, as shown by the red line for a person who is 165 cm tall and has a mass of 66 kg (1.755 m^2).

Answer

2. (a) BSA = 1.89 m^2
   (b) BMR = 155 kJ/m^2/h

INVESTIGATION 2.2.1

Energy Consumption During Exercise (p. 128)
Cellular respiration provides energy in the form of ATP for all the energy-requiring activities of an organism. How many teaspoons of table sugar does a human body have to respire to carry out a specific function? Investigation 2.2.1 provides you with an opportunity to determine the number of teaspoons of table sugar respired when exercising.

The BMR is measured when a person is lying at rest—even the slightest movement will result in a value higher than the basal value. BMR represents a base line for the measurement of metabolic activity. It is not applicable to everyday life. A person's metabolic rate changes according to activity level. The metabolic rate of an active person may be measured in terms of energy expenditure over a given period time. **Table 2** lists the average energy expenditures for different kinds of activities for men and women in kilojoules per minute.

Table 2 Average Energy Expenditures for Different Types of Human Activities

Activity	Average Energy expediture (kJ/min)	
	Woman	***Man***
sleeping	3.8	4.2
sitting	5.0	5.8
light work	15.0	17.0
bicycling (20km/h)	37.0	41.0
heavy work	57.0	63.0

As with BMR, metabolic rates also decrease with age. This is partly because, as we get older, the body becomes more efficient at doing the same tasks over and over again. It is also because in general, people become less physically active as they get older. As level of activity declines, the amount of muscle tissue decreases, and energy requirements diminish.

Practice

Understanding Concepts

1. Why is body surface area used in the determination of basal metabolic rate?
2. (a) Use the BSA equation to determine the body surface area of a teenager whose mass is 78 kg and whose height is 1.70 m. Use the nomogram in **Figure 27** to check your answer.
   (b) Calculate the teenager's BMR as she dissipates 439 kJ of thermal energy in 1.5 hours while in a Benzinger calorimeter.

Controlling Aerobic Respiration

The reactions of aerobic respiration are regulated by various feedback inhibition and product activation loops (**Figure 28**). A major control point is the third reaction of glycolysis, which is catalyzed by the allosteric enzyme phosphofructokinase. The final product of respiration, ATP, inhibits phosphofructokinase, while ADP stimulates its activity. Therefore, less ATP will be produced when ATP levels are high and ADP levels are low, and vice versa. If citrate, the first product of the Krebs cycle, accumulates in the mitochondria, some will pass into the cytoplasm and inhibit phosphofructokinase, thereby slowing down glycolysis. As citrate is used in the Krebs cycle, or in other metabolic processes, its concentration will decrease; phosphofructokinase inhibition will be reduced, and the rate of glycolysis (and the rest of the respiratory process) will increase.

Another important control mechanism involves NADH. A high concentration of NADH in a cell indicates that the electron transport chains are full of electrons and ATP production is high. In this case, NADH allosterically inhibits pyruvate decarboxylase and reduces the amount of acetyl-CoA that is fed into the Krebs cycle, restricting the amounts of NADH produced.

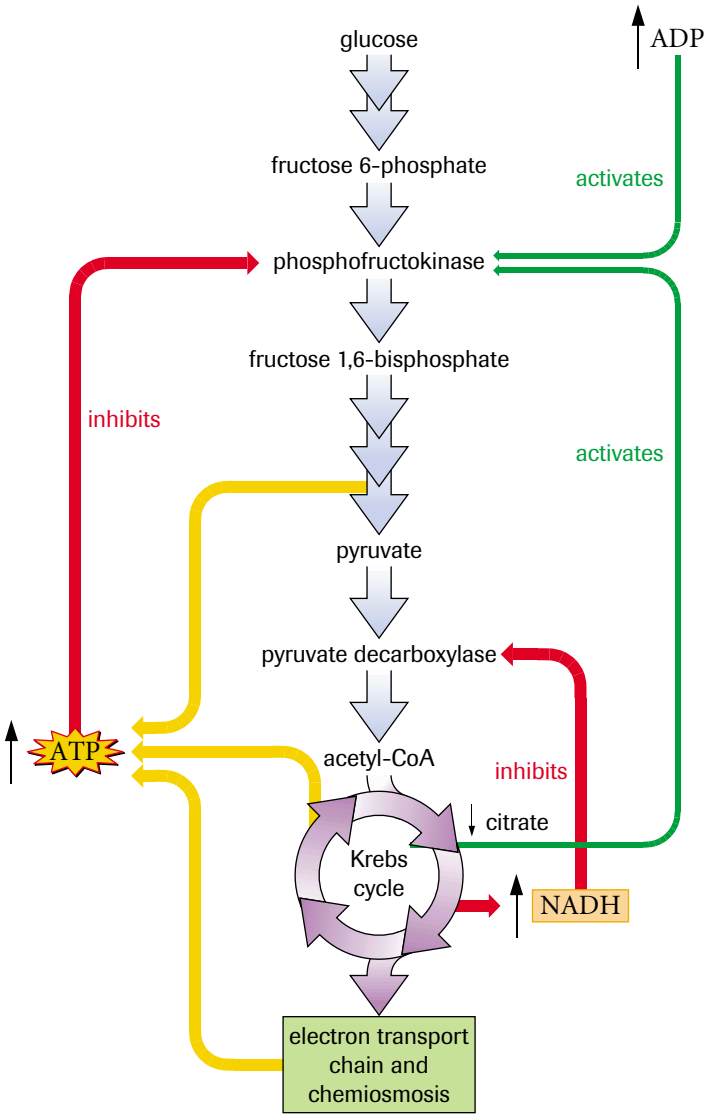


Figure 28
Aerobic respiration is regulated by the relative concentrations of ATP and ADP and the concentrations of citrate and NADH.

SUMMARY Cellular Respiration: The Details

- Cellular respiration begins in the cytoplasm and, in the case of aerobic respiration, is completed in mitochondria in eukaryotes; it takes place in the cytoplasm of prokaryotes.
- Mitochondria possess two membranes: a smooth outer membrane and a highly folded inner membrane that contains many proteins used in cellular respiration.
- ATP may be formed by substrate-level phosphorylation or oxidative phosphorylation. Substrate-level phosphorylation does not require oxygen; oxidative phosphorylation does. In substrate-level phosphorylation, a phosphate group is attached to ADP in an enzyme-catalyzed reaction. Oxidative phosphorylation is made up of redox reactions involving NAD^+, FAD, an electron transport chain, the inner mitochondrial membrane, ATPase, and oxygen as the final electron acceptor.
- Glycolysis occurs in the cytoplasm. It produces two three-carbon pyruvate molecules from a six-carbon glucose molecule. Glycolysis produces two ATP (net) and two NADH.

- Pyruvate oxidation occurs in the mitochondria. In the process, a CO_2 portion is cleaved from pyruvate and removed from the cell as waste. The remaining two-carbon acetyl group attaches to coenzyme A to produce acetyl-CoA. In this reaction, two NADH and two CO_2 are formed (one for each of the two pyruvate molecules).
- The Krebs cycle occurs in the mitochondrial matrix. It begins when acetyl-CoA reacts with oxaloacetate to produce citrate. The two carbon atoms introduced by acetyl-CoA are removed as two CO_2, one ATP molecule is produced by substrate-level phosphorylation, one $FADH_2$ and three NADH are produced, and the final step regenerates oxaloacetate.
- The electron transport chain, associated with the inner mitochondrial membrane, transports electrons through a series of redox reactions that release the free energy used to pump protons into the mitochondrial intermembrane space, creating an electrochemical gradient that is a source of free energy.
- In chemiosmosis, protons move through ATPase complexes embedded in the inner membrane, releasing free energy that drives the synthesis of ATP.
- Oxygen is the final acceptor of electrons that pass through the electron transport chain. If oxygen is not available, the Krebs cycle, electron transport, and chemiosmosis come to a halt.
- **Table 3** summarizes the inputs (reactants) and outputs (products) of cellular respiration. Compare the reactants and products in the table with the figures that illustrate the various stages of the process.

Table 3 Summary of Cellular Respiration

	Glycolysis (per glucose)	Pyruvate oxidation (per glucose)	Krebs cycle (per glucose)	Electron transport and chemiosmosis (per glucose, theoretical yield)
Location	cytoplasm	mitochondrial matrix	mitochondrial matrix and inner membrane	inner mitochondrial membrane and intermembrane space
Reactants	glucose 2 ATP 2 NAD^+ 4 ADP 2 P_i	2 pyruvate 2 NAD^+ 2 CoA	2 acetyl-CoA 2 oxaloacetate 6 NAD^+ 2 ADP 2 P_i 2 FAD	6 NADH (Krebs) 2 NADH (pyruvate oxidation) 2 $FADH_2$ (Krebs) 2 $FADH_2$ (from 2 cytosolic NADH) 32 ADP 32 P_i 6 O_2 12 H^+
Products	2 pyruvate 4 ATP 2 NADH 2 H^+ 2 ADP	2 acetyl-CoA 2 NADH 2 H^+ 2 CO_2	2 CoA 4 CO_2 2 oxaloacetate 6 NADH 6 H^+ 2 $FADH_2$ 2 ATP	8 NAD^+ 4 FAD^+ 24 H^+ 32 ATP 6 H_2O
ATP required	2	none	none	none
ATP produced	4	none	2	32
Net ATP produced	2	none	2	32

Total ATP produced by aerobic respiration of 1 glucose molecule = 36

- The theoretical yield of ATP in aerobic respiration is 36; however, the actual yield is about 30 ATP because some free energy is lost by the permeability of the inner mitochondrial membrane to protons and by the use of some energy for other endergonic reactions. The efficiency of energy conversion is approximately 32%.
- Phosphofructokinase, the enzyme that catalyzes step 3 of glycolysis, controls cellular respiration. It is activated by ADP and citrate and inhibited by ATP. NADH inhibits pyruvate decarboxylase, an enzyme that catalyzes the conversion of pyruvate to acetyl-CoA.
- An organism's metabolic rate is the amount of energy consumed in a given time, and a measure of the overall rate at which the energy-yielding reactions of cellular respiration take place.

Section 2.2 Questions

Understanding Concepts

1. What raw materials are needed for a cell to produce a molecule of ATP by substrate-level phosphorylation?

2. (a) In eukaryotic cells, where does glycolysis occur?
(b) What does *glycolysis* mean?

3. Which stores more potential energy: one molecule of glucose or two molecules of pyruvic acid? Explain.

4. (a) List the final products of glycolysis.
(b) What two products of glycolysis may be transported into mitochondria for further processing?

5. Compare substrate-level phosphorylation and oxidative phosphorylation.

6. How do ADP and ATP differ in structure? in free energy content?

7. Arrange the following types of cells in order of increasing number of mitochondria in the cytoplasm: nerve cell, skin cell, fat cell, heart muscle cell. Provide a rationale for your sequence.

8. Describe two functions that mitochondrial membranes serve in energy metabolism.

9. (a) Why is every reaction of cellular respiration catalyzed by a specific enzyme?
(b) What would happen to an organism that lacked the gene for hexokinase, the enzyme that catalyzes the first reaction in glycolysis?

10. Describe the function of NAD^+ and FAD in cellular respiration.

11. What are the final products of aerobic cellular respiration?

12. Why is aerobic respiration a more efficient energy-extracting process than glycolysis alone?

13. As a result of glycolysis, pyruvate oxidation, and the Krebs cycle, only a small portion of the energy of glucose has been converted to ATP. In what form is the rest of the usable energy found at this stage of the process?

14. (a) What part of a glucose molecule provides electrons in cellular respiration?
(b) Describe how electron transport complexes set up a proton gradient in response to electron flow.
(c) How is the energy used to drive the synthesis of ATP?
(d) What is the name of this process?
(e) Who discovered this mechanism?

15. (a) Distinguish between an electron carrier and a terminal electron acceptor.
(b) What is the final electron acceptor in aerobic respiration?

16. Explain how the following overall equation for cellular respiration is misleading:

$$C_6H_{12}O_6 + 6O_2 \longrightarrow 6CO_2 + 6H_2O$$

17. Explain why CO_2 does not serve as a source of free energy in living systems.

18. (a) Distinguish between metabolic rate and basal metabolic rate.
(b) Explain how and why metabolic rate changes as we grow older.

Applying Inquiry Skills

19. (a) How could a pH meter be used to support Peter Mitchell's chemiosmotic theory?
(b) What other common laboratory apparatus could be used to test the theory? Briefly describe a procedure that uses the instrument.
(c) Strong detergents disrupt and rupture phospholipid bilayers. When a suspension of mitochondria in a test tube is treated with detergents, electron transport is detected, but ATP is not produced. Explain how this supports the theory of chemiosmosis.

20. (a) Use the nomogram in **Figure 29** on page 116 to determine the surface area of a teacher who is 180 cm tall and has a mass of 80 kg.
(b) If the basal energy requirement for this individual is 160 $kJ/m^2/h$, calculate the total energy content of the food the teacher must consume to function at rest for 24 h.
(c) Predict the BMR of a student whose height is 165 cm and whose mass is 90 kg.
(d) Determine the solution for (c) and evaluate your prediction.

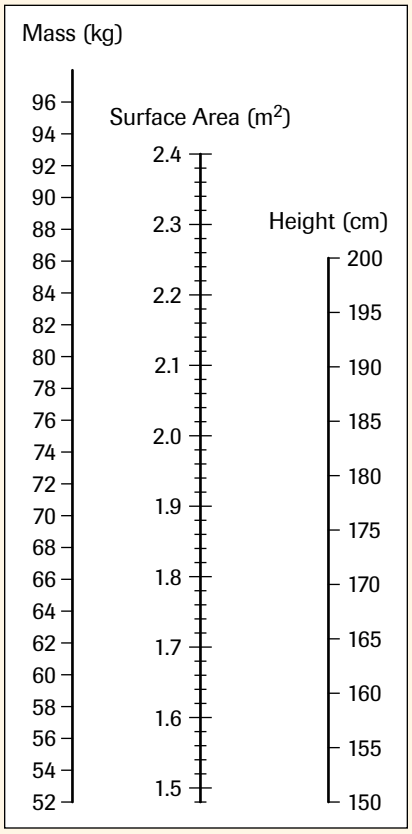


Figure 29

Making Connections

21. (a) Why must mitochondria be able to reproduce?
(b) At conception, only the nucleus of a sperm cell enters the egg cell. Considering this, how are all of the mitochondria in a fully grown individual genetically related?
(c) One class of metabolic disorders is caused by defective mitochondria. Research at the library or on the Internet to find out about two mitochondrial diseases. Describe the symptoms of the disorders, the part(s) of the mitochondrion that are defective, and treatments that are available for the conditions.

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22. Several vitamins, especially the B vitamins, play key roles in energy metabolism. A number of vitamin B deficiencies, if left unchecked, can cause serious illness. Conduct library and/or Internet research to answer the following questions:
(a) What is meant by the term vitamin B complex? List the names of the vitamins that are part of this group.
(b) Why are these vitamins called water-soluble vitamins? What other water-soluble vitamins are there?
(c) Select two B vitamins and briefly describe
(i) their function in energy metabolism;
(ii) functions not directly associated with energy metabolism;
(iii) good natural sources;
(iv) deficiency symptoms.

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23. Hummingbirds (**Figure 30**) have the highest metabolic rate of any animal.

Figure 30
The male rufus hummingbird, like many diminutive animals, must consume relatively large quantities of food to maintain body temperature and meet its body's demands for energy.

(a) Conduct library or Internet research to complete the comparison chart shown in **Table 4**.

Table 4

Function	Hummingbird	Human
Resting heart rate (beats/min)		
Breathing rate (breaths/min)		
Fastest speed (km/h)		
Average lifespan (yrs.)		

(b) Determine the mass of hamburger meat that a human would have to consume in one day to obtain as much energy as a hummingbird uses in one day.

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