



METABOLISM AND ENERGY BALANCE

LEARNING OBJECTIVES

- 1 | Explain human energy balance and the components of intake and expenditure.
- 2 | Understand human metabolism at the cellular level.
- 3 | Differentiate between aerobic and anaerobic energy systems in the body.
- 4 | Identify the body's energy currency and how it works within the energy system.

CHAPTER 03 | METABOLISM AND ENERGY BALANCE

METABOLISM:

The process of converting ingested nutrients into energy in the body.

ENERGY:

The usable power derived from nutrient sources.

ENERGY BALANCE:

The symmetry between nutrient consumption and energy demands of the body.

CHEMICAL ENERGY:

The energy released as the bonds that hold chemicals together are broken.

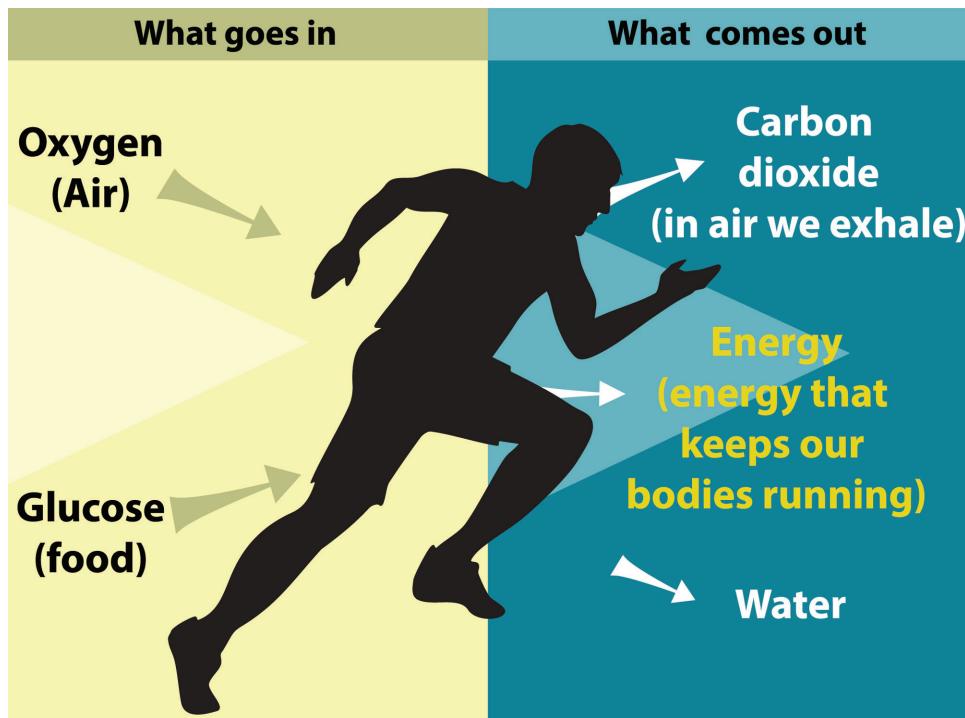
Metabolism is the way the human body converts consumed foods into a source of **energy** to power physiological processes. Energy requirements of the body for physical activity and bodily functions, such as digestion, respiration, and circulation, are met by the digestion and absorption of nutrients and the presence of oxygen. The balance between nutrient consumption and energy demands creates an **energy balance**.

DID YOU KNOW?

Energy exists in six basic forms. These forms are chemical, nuclear, electrical, mechanical, thermal, and radiant. The form of energy humans and animals directly rely upon for survival is **chemical energy**.

The two important aspects of energy production and energy balance are nutrients and oxygen. Both are required to perform the cellular processes producing energy for body function.

Figure 3.1 How Energy Is Created.



NUTRITION AND ENERGY BALANCE

Metabolism is a detailed and complicated chemical process occurring within the cells of the body. When it comes to nutrition, understanding these processes, as well as energy balance, is important. In nutritional terms, energy is provided by a **calorie (cal)**. Technically written as a **kilocalorie (kcal)**, a calorie is the amount of energy needed to raise the temperature of 1 gram of water by 1°C (4.184 joules) at a pressure of 1 atmosphere.

Calories are provided by macronutrients, micronutrients, vitamins, and minerals consumed in the diet. The breakdown of these nutrient sources yields a specific number of calories individually.

CALORIE (CAL):

The amount of energy needed to raise the temperature of 1 gram of water by 1°C (4.184 joules) at a pressure of 1 atmosphere.

KILOCALORIE (KCAL):

Another name for a cal.

Table 3.1 Caloric Content of Macronutrients.

SOURCE	KCAL YIELD
Nutritional carbohydrate	4 kcal
Nutritional protein	4 kcal
Nutritional fat	9 kcal
Stored fat from carbohydrate source (adipose tissue)	3.27 kcal
Alcohol	7 kcal

ENERGY INTAKE

Total calorie intake in a 24-hour period, as compared to total energy expenditure in the same time, is used to measure energy balance. The simple observation for a fitness and nutrition professional is the gain or loss of body mass. If an individual gains weight over time, they are consuming an excess of calories compared to what they are expending. If an individual loses weight over time, they are consuming fewer calories than they are expending.

Excess calories lead to weight gain, while deficiency of calories leads to weight loss.

Research has shown the average American consumes about 3,600 calories a day, an increase of more than 24 percent from the average of 2,880 calories daily in 1961. The current guidelines from the US Department of Health and Human Services declare the average adult female requires 1,600–2,400 calories daily, and the average adult male requires 2,000–3,000 calories daily from all nutritional sources.

CHAPTER 03 | METABOLISM AND ENERGY BALANCE

Table 3.2 Estimated Calorie Needs by Age, Gender, and Physical Activity Level.

AGE (YEARS)	MALES			FEMALES**		
	Sedentary*	Moderately active*	Active*	Sedentary*	Moderately active*	Active*
2	1,000	1,000	1,000	1,000	1,000	1,000
3	1,000	1,400	1,400	1,000	1,200	1,400
4	1,200	1,400	1,600	1,200	1,400	1,400
5	1,200	1,400	1,600	1,200	1,400	1,600
6	1,400	1,600	1,800	1,200	1,400	1,600
7	1,400	1,600	1,800	1,200	1,600	1,800
8	1,400	1,600	2,000	1,400	1,600	1,800
9	1,600	1,800	2,000	1,400	1,600	1,800
10	1,600	1,800	2,200	1,400	1,800	2,000
11	1,800	2,000	2,200	1,600	1,800	2,000
12	1,800	2,200	2,400	1,600	2,000	2,200
13	2,000	2,200	2,600	1,600	2,000	2,200
14	2,000	2,400	2,800	1,800	2,000	2,400
15	2,200	2,600	3,000	1,800	2,000	2,400
16	2,400	2,800	3,200	1,800	2,000	2,400
17	2,400	2,800	3,200	1,800	2,000	2,400
18	2,400	2,800	3,200	1,800	2,000	2,400
19–20	2,600	2,800	3,000	2,000	2,200	2,400
21–25	2,400	2,800	3,000	2,000	2,200	2,400
26–30	2,400	2,600	3,000	1,800	2,000	2,400
31–35	2,400	2,600	3,000	1,800	2,000	2,200
36–40	2,400	2,600	2,800	1,800	2,000	2,200
41–45	2,200	2,600	2,800	1,800	2,000	2,200
46–50	2,200	2,400	2,800	1,800	2,000	2,200
51–55	2,200	2,400	2,800	1,600	1,800	2,200
56–60	2,200	2,400	2,600	1,600	1,800	2,200
61–65	2,000	2,400	2,600	1,600	1,800	2,000
66–70	2,000	2,200	2,600	1,600	1,800	2,000
71–75	2,000	2,200	2,600	1,600	1,800	2,000
76+	2,000	2,200	2,400	1,600	1,800	2,000

*Sedentary, the activity of independent living; moderately active, independent living and the equivalent of walking 1.5–3 miles per day at 3–4 miles per hour; active, independent living and the equivalent of walking more than 3 miles daily at 3–4 miles per hour.

**Female estimates do not include pregnancy or breastfeeding.

Energy intake is measured by surveying food consumption over a 24-hour period. Typically, it is based on the individual's recall and is subject to the accuracy of reporting. Historical research has found the average human consumes about 3,500 kcal daily, but self-reporting showed average calorie consumption of 2,639 kcal daily for men and 1,793 kcal daily for women.

ENERGY EXPENDITURE

Energy expenditure is measured in a variety of ways. The classic method is a **calorimeter**, which measures heat production. **Direct calorimetry** uses an insulated chamber to measure heat added to the ambient environment, while **indirect calorimetry** measures oxygen consumed and carbon dioxide produced.

Energy expenditure is a result of the cumulation of four main processes in the body: **resting metabolic rate (RMR)**, **thermic effect of food (TEF)**, physical activity, and physical growth.

Resting Metabolic Rate

RMR is, specifically, the energy required to support cardiac function and respiration, repair internal organs, maintain body temperature, and balance water and ion concentrations across cell membranes. It is also referred to as basal metabolic rate (BMR). It consumes about two-thirds of the body's total energy expenditure in a 24-hour period and is the most influential of the physical processes consuming energy.

The RMR is correlated to body size and gender. Determining the exact RMR for an individual is nearly impossible. However, accurate formulas have been developed for health and fitness professionals to closely estimate the overall caloric needs for an individual. Predict an individual's BMR using the Harris-Benedict Formula:

$$\text{Men} = 66.4730 + (13.7516 \times \text{weight in kg}) + (5.0033 \times \text{height in cm}) - (6.7550 \times \text{age in years})$$

$$\text{Women} = 655.0955 + (9.5634 \times \text{weight in kg}) + (1.8496 \times \text{height in cm}) - (4.6756 \times \text{age in years})$$

Remember, resting metabolic rate (RMR) and basal metabolic rate (BMR) are synonymous.

Thermic Effect of Food

The TEF accounts for the heat loss resulting from energy consumed when the body digests carbohydrate, fat, and protein. Also referred to as **diet-induced thermogenesis**, the thermic effect varies based on the macronutrient. For example, fats have a lesser thermic effect during digestion and absorption than protein and carbohydrates. The overall macronutrient composition of food consumed will also affect the TEF. Foods heavier in carbohydrates or protein will increase the body's heat production more than meals heavier in fats.

CALORIMETER:

A tool to measure heat production and energy expenditure.

DIRECT CALORIMETRY:

A way to measure energy expenditure in a chamber measuring ambient heat increases.

INDIRECT CALORIMETRY:

A way to measure energy expenditure by oxygen consumed and carbon dioxide produced.

RESTING METABOLIC RATE (RMR):

The energy expenditure of metabolic and physical processes when the body is at rest.

THERMIC EFFECT OF FOOD (TEF):

The energy expenditure associated with food consumption.

DID YOU KNOW?

Men tend to have higher RMR than women due to differences in body composition and, in older men, their higher levels of sympathetic nervous system activity.

DIET-INDUCED THERMOGENESIS:

The thermic effect of macronutrient digestion and absorption.

Physical Activity

Physical activity is second only to the RMR in terms of its effect on daily energy expenditure. Physical activity, including body movement, is directly related to an individual's body size, physical conditioning, and the amount (or distance) of movement performed. The more someone moves or exercises, the more energy they will expend. Energy expenditure from physical activity can be calculated using the heart rate as compared to resting heart rate data or through diaries of physical activity. Individuals with smart watches and activity trackers can estimate calorie burns from physical activity.

Figure 3.2 Physical Activity Trackers.



Growth

The body is constantly growing. Millions of cells die daily, and millions of cells are created to replace them. For babies, infants, and youth, their bodies are maturing and growing into their adult size at a rapid rate, meaning more cells are being created than are dying daily. The energetic cost of physical growth varies at different stages of life but is an important factor in total energy expenditure of the body.

The aspect of growth applies especially to pregnant women, who are not only supporting their own cell growth and turnover but also growing another human. The energy needs and expenditure of pregnant and lactating females is greater than the average but depends heavily on the stage of pregnancy or lactation.

ENERGY BALANCE

Creating an energy balance involves more than simple weight management. A **positive energy balance** means more energy is consumed than expended. A **negative energy balance** means more energy is expended than consumed. The body naturally seeks a homeostatic balance of the energy system, and this is evident in patterns of weight gain. Research shows individuals who gain body weight over time have periods of time when their weight plateaus, regardless of the positive energy balance.

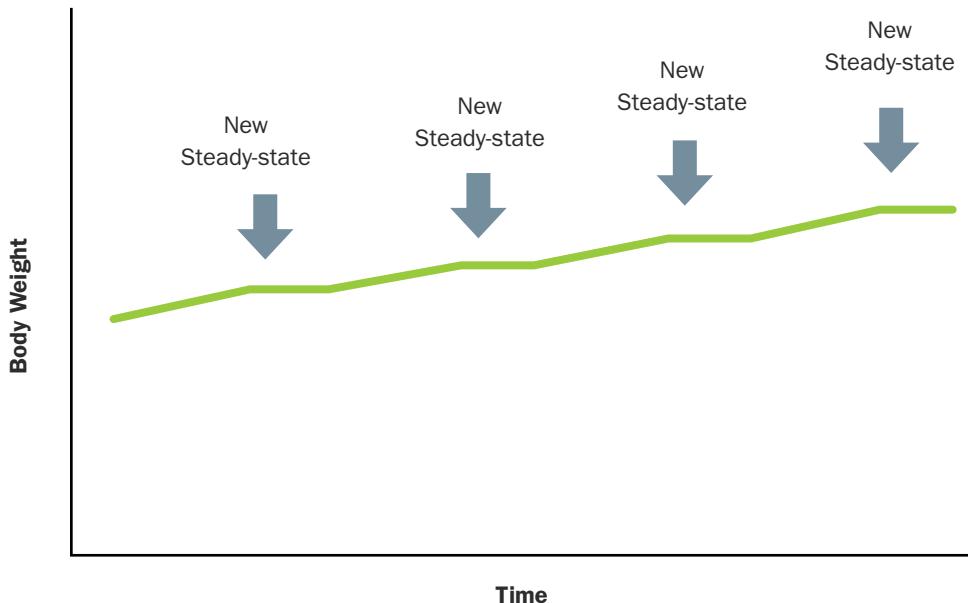
POSITIVE ENERGY BALANCE:

More energy is consumed than expended.

NEGATIVE ENERGY BALANCE:

More energy is expended than consumed.

Figure 3.3 Weight Gain and Energy Balance over Time.



Research has shown how relatively small adjustments in energy consumption and energy expenditure can slow the onset of weight gain and, ultimately, obesity. Simple changes such as a 200–300 kcal reduction in daily intake and incorporating 200–400 kcal of activity three or more times a week can make a difference in energy balance.

On a large scale, nutrition must be balanced—calories out versus calories in. On a cellular level, the way energy is produced is a complicated series of reactions that can be accelerated, decelerated, or limited based on the urgency of energy requirements.

CELLULAR METABOLISM:

The series of reactions converting nutrients to ATP

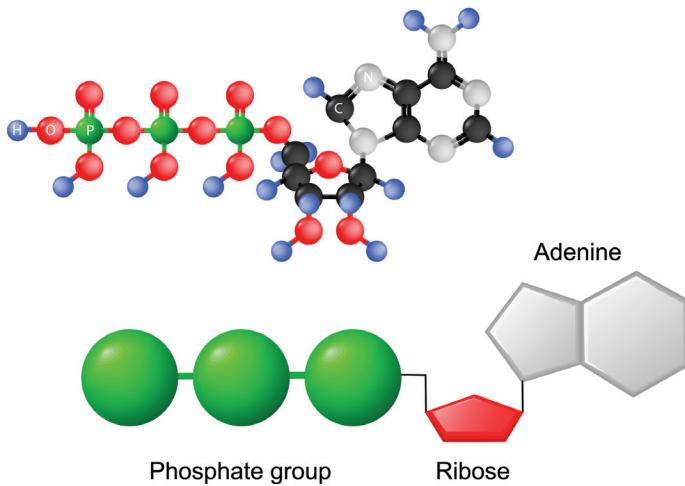
ADENOSINE TRIPHOSPHATE (ATP):

The cellular energy molecule.

CELLULAR ENERGY CURRENCY

Often referred to as cellular respiration, **cellular metabolism** is a series of reactions converting nutrients into the cellular energy currency **adenosine triphosphate (ATP)**.

Figure 3.4 Adenosine Triphosphate.



Adenosine is made up of adenine and ribose. It is attached to three phosphates, and the two bonds between the three phosphates store and release energy.

The body contains all the raw materials needed to produce ATP. Food contains proteins, fats, and carbohydrates that can be broken down into ATP through a series of steps beyond mechanical and chemical digestion and absorption. The ATP is then broken down into smaller components to release energy and heat and then is recycled back to the original ATP structure, much like a puzzle that can be pieced together, taken apart, and then put together again.

This process follows the first law of thermodynamics, also known as the **law of conservation of energy**, which states that energy can be changed from one form to another but cannot be created or destroyed. Metabolism runs on **anabolic** and **catabolic** reactions, forming the cornerstone of human physiology.

LAW OF CONSERVATION OF ENERGY:

The principle stating energy cannot be created or destroyed but only changed from one form to another.

ANABOLIC:

The building process.

CATABOLIC:

The breakdown process.

ENZYME:

A protein catalyzing chemical reactions.

ATPASE:

An enzyme catalyzing the breakdown of ATP to ADP.

DEPHOSPHORYLATION:

The process of removing a phosphate.

CONVERTING ATP INTO ENERGY

ATP by itself does not provide cellular energy. The energy is stored within the bonds between the three phosphates in the ATP molecule, and those bonds need to be broken in the presence of water to release the energy.

ATP TO ADENOSINE DIPHOSPHATE PLUS ENERGY

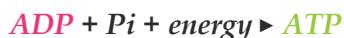
The first step is to break down adenosine triphosphate into its simpler counterpart, adenosine diphosphate (ADP). That break requires an **enzyme**, which causes a chemical reaction to occur. In this case, the enzyme is **ATPase**, which breaks the bond between the second and third phosphates to release the stored energy. The phosphate-removal process, **dephosphorylation**, requires water (H_2O). This is one of the reasons why water makes up two-thirds of the body's weight. Importantly, the breakdown of ATP to ADP releases one acidic proton (H^+).

ATP-ADP CYCLE

The **ATP-ADP cycle** is the process allowing the cleaved ADP to be recycled back into the functional, energy-producing ATP within the cell. The process of reattaching phosphate (Pi), **rephosphorylation**, requires the enzyme **ATP synthase**. The molecule can then be broken down again for quick energy as part of the ATP-ADP cycle.



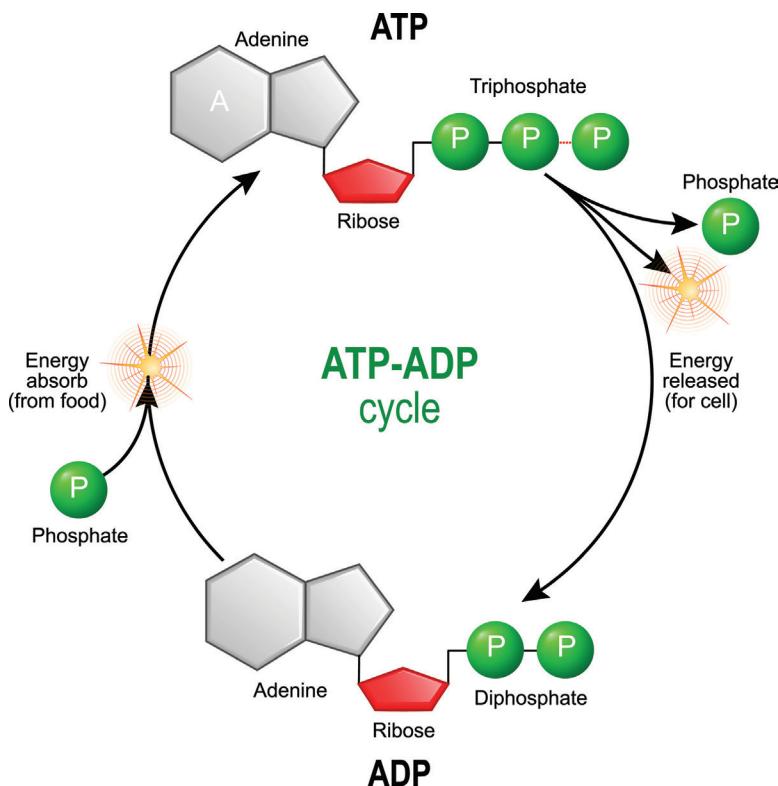
(dephosphorylation by the enzyme ATPase)



(rephosphorylation by the enzyme ATP synthase)

The breakdown of ATP to release its stored energy is called **ATP hydrolysis**. When ATP hydrolysis causes the muscle to accumulate protons (H^+) faster than the muscle can remove them as waste, the result is metabolic acidosis. This impairs muscle power and energy production in the short term but may have the long-term effect of reprogramming the cell to recycle ADP faster and reduce the **oxidative stress** of the process.

Figure 3.5 Converting ATP into ADP and Back.



ATP-ADP CYCLE:

A mechanism allowing ATP to be quickly broken into ADP and then re-formed.

REPHOSPHORYLATION:

The process of adding a phosphate.

ATP SYNTHASE:

An enzyme creating ATP

ATP HYDROLYSIS:

The breakdown of ATP while in the presence of water to release energy stored within its bonds.

OXIDATIVE STRESS:

The imbalance of reactive oxygen and the body's ability to detoxify or remove it.

In the presence of water, the bond between the second and third phosphate ions of ATP is broken by the enzyme ATPase, which releases energy and one proton (H⁺). The enzyme ATP synthase reattaches the phosphate in the ATP-ADP cycle.

Muscles constantly generate protons during basic cellular metabolism, whether at rest or during activity. The body manages these hydrogen ions easily during rest or light activity by moving them into the mitochondria of the cells where their energy is harnessed to resynthesize ATP with the use of O₂ and formation of water. But as exercise intensity increases and more energy is required from ATP, many more protons are released, and avoiding acidosis (i.e., lower cellular pH) becomes a priority.

ADP TO ADENOSINE MONOPHOSPHATE

In the compound ADP there are still two remaining phosphate ions, and the bond between them contains stored energy. In extreme circumstances, this bond can be used to generate needed cellular energy as well.

For an individual running at an all-out sprint lasting 10–15 seconds, at that intensity and duration the body has energy needs exceeding what the ATP-ADP cycle can provide. ADP accumulates in the muscle as it cannot rephosphorylate back into ATP fast enough. To meet immediate ATP demands, the enzyme **adenylate kinase** takes two ADP molecules and converts them into one ATP through rephosphorylation and one adenosine monophosphate (AMP) through dephosphorylation. This reaction can occur in both directions.



However, when the cellular demand for energy remains high, ADP is unable to rephosphorylate back into ATP because it is not energetically favorable, meaning the cell cannot support the reaction efficiently at that moment. Instead, the ADP is dephosphorylated to AMP, a phosphate ion, and cellular energy. This reaction can occur in both directions.



AMP is not an ideal molecule to have in the cells. In extreme circumstances and with the addition of other enzymes, it can break down even further and create ammonia, which is toxic to the muscles and blood when produced in large quantities or unfiltered by the urinary system. The lone phosphate can also pose a problem since an accumulation of phosphates can cause muscle fatigue and limit physical performance.

ADENYLATE KINASE:

An enzyme catalyzing the reaction between ATP and AMP to form two ADP molecules and vice versa.

THE ENERGY SYSTEMS

The body has three different energy systems, which can be classified as short-term, intermediate-term, and long-term energy systems. These systems overlap in virtually everything a human does. It is important to understand each system individually and when they are the most active and how nutrients contribute to their energy output.

OVERVIEW OF THE ENERGY SYSTEMS

Muscle tissues have enough stored ATP to last only a couple of seconds. To manufacture more ATP as quickly as possible, muscles turn to **phosphocreatine (PC)**. This process provides an instant source of energy—up to 30 seconds' worth. However, this source is quickly depleted. The muscle's stored ATP plus its phosphocreatine are collectively known as the **phosphagen system**.

As muscle tissue continues using phosphocreatine, **glycolysis**, in which ATP is made from **glucose**, emerges as the primary energy source. This occurs about seven seconds into the run. During glycolysis, a series of chemical reactions allow the body to break the glucose molecule into two **pyruvate** molecules, producing a small amount of ATP for a short amount of time—around two minutes. The process of glycolysis produces protons (H⁺). Once cellular acidity rises, muscle power declines. Research has shown that the end product of glycolysis is always lactic acid.

The phosphagen system and glycolysis are **anaerobic** processes, meaning neither requires the presence of oxygen.

The body begins with the pyruvate made through **anaerobic glycolysis**. With the addition of oxygen, it undergoes a complex series of steps to break down the pyruvate until it ends up in the mitochondria of the cell, where ATP is generated. This **aerobic metabolism** can now manufacture ATP for extended periods of time. Adipose tissue—stored fat—can also be used as a fuel source during aerobic metabolism.

The overview of the three energy systems suggests a relatively clear transition from one system to the next, but the transitions are not so definitive. These energy systems are always working in tandem in the body, but the immediate energy demand will determine which system is dominant.

PHOSPHOCREATINE (PC):

A molecule found in muscle and brain tissue donating its phosphate to ADP to form ATP.

PHOSPHAGEN SYSTEM:

The combination of a muscle's stored ATP plus its phosphocreatine.

GLYCOLYSIS:

The process of splitting a glucose molecule into a pair of pyruvate molecules.

GLUCOSE:

The smallest molecule a carbohydrate can be broken down into and used as an energy source.

PYRUVATE:

A three-carbon structure formed by splitting a glucose molecule.

ANAEROBIC:

A process that can occur without the help of oxygen.

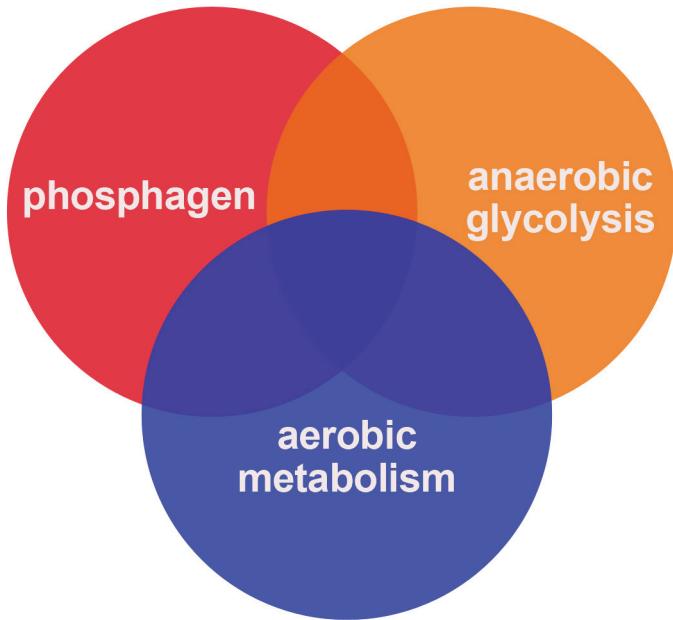
ANAEROBIC GLYCOLYSIS:

The process of splitting a glucose molecule into a pair of pyruvate molecules to produce ATP when oxygen is low.

AEROBIC METABOLISM:

The breakdown of fuels to form ATP in the presence of oxygen.

Figure 3.6 Overlap of Energy Systems during Exercise.



The energy system most heavily recruited will depend on the immediate energy demand, but all three systems work in cooperation.

Energy Sources and Cellular Metabolism

KETONES:

By-product of fatty acid metabolism that can be used for energy.

There are four primary sources of energy: glucose, fatty acids, lactate, and **ketones**. Whether from dietary sources or supplements or naturally occurring in the body, ketones play one key role in cellular metabolism: producing ATP. The energy system primarily in use will determine which fuel source is the most efficient for energy production.

PHOSPHAGEN SYSTEM (ATP-PC SYSTEM)

Every cell within the human body contains cytoplasm, a semiliquid material. Like water inside an aquarium, cytoplasm surrounds and supports all the living material and organelles in the cell. The nucleus, which contains the deoxyribonucleic acid (DNA) used for growth, development, functioning, and reproduction, is the only part of the cell that is not considered part of the cytoplasm.

SARCOPLASM:

The cytoplasm of striated muscle fiber.

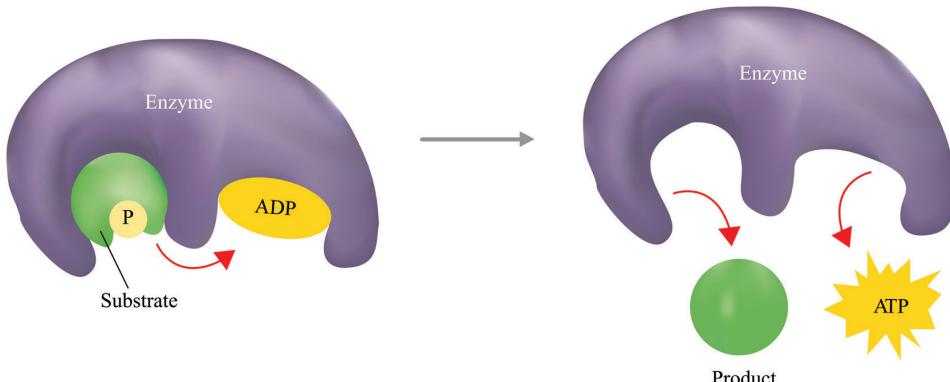
In muscle cells, cytoplasm is referred to as **sarcoplasm**. It serves the same purpose as the cytoplasm in a normal cell. The sarcoplasm of muscle cells is important, as it is where the actions of the phosphagen system and the reaction components take place. This process within muscle fibers puts ATP and released energy in a prime location to be used quickly for

muscle contraction.

Phosphocreatine includes one phosphate molecule connected to one molecule of **creatine**. Creatine is naturally found in muscle tissue, and maintaining average creatine stores will depend on overall muscle mass. For that reason, the ATP-PC system of energy production occurs only in muscle tissue, donating its phosphate to ADP to form ATP with the help of the **creatine kinase** enzyme.

All chemical reactions in the body require an enzyme to occur at a speed making them biologically viable. The enzyme serves as a lock, and the substrate—a substance like phosphocreatine—serves as the key. Every enzyme has binding sites for a substrate that are specific to that molecule. For example, glucose cannot bind at the site where phosphocreatine can bind and cause the same reaction. When the correct substrate binds to the enzyme, a reaction can occur, and a product can be created.

Figure 3.7 Creatine Kinase Enzymatic Reaction.



The substrate (creatine) plus a phosphate binds to the enzyme (creatine kinase), which is also bound to a molecule of ADP. The phosphate is donated to the ADP when both are bound. The donation of the phosphate group to ADP immediately creates a molecule of ATP—and a single proton as a by-product of the phosphate-bond creation—which is released and stimulates the release of the lone creatine attached to the proton.

The creatine kinase reaction is critical for muscular contraction as it keeps the ATP-ADP cycle running. The more this cycle runs, the more protons will build up in the cytoplasm, reducing the pH of the muscle cell. The reduction of cellular pH is referred to as **metabolic acidosis**.

CREATINE:

A molecule synthesized in the liver and kidneys assisting reformation of ATP from ADP

CREATINE KINASE:

An enzyme catalyzing ADP to ATP and creatine to phosphocreatine.

METABOLIC ACIDOSIS:

The reduction of cellular pH.

Replenishing Phosphocreatine

The phosphagen system is limited by the supply of phosphocreatine in the body. Naturally, creatine is synthesized in the kidney, pancreas, and liver from the amino acids methionine, glycine, and arginine. Creatine is stored in muscle tissue but also in the brain and has been identified as a major substrate in the immune response, the epithelial cells of the airway, and in neurotransmission. Once creatine reaches the inside of the muscle cells, it is bound to phosphate through rephosphorylation and becomes the active form of phosphocreatine needed for the ATP-ADP cycle.

GLYCOGEN:

The body's stored form of glucose.

Glucose is the muscle's next fastest source of ATP. **Glycogen** is the stored form of glucose in the body, and it is stored in the liver and skeletal muscle. When stored glycogen runs low, glucose in the bloodstream is forced into the muscle cells and broken down in a process called glycolysis (glyco means "glucose"; lysis means "breakdown"). Glycolysis can occur both in the presence of oxygen (aerobically) or without oxygen (anaerobically). In the presence of oxygen, the process is called oxidative phosphorylation. In the absence of oxygen, the process is called anaerobic glycolysis. Both processes produce many times more ATP than the phosphagen system.

ANAEROBIC GLYCOLYSIS

Nicotinamide Adenine Dinucleotide (NAD⁺):

A coenzyme participating in glycolysis.

NADH:

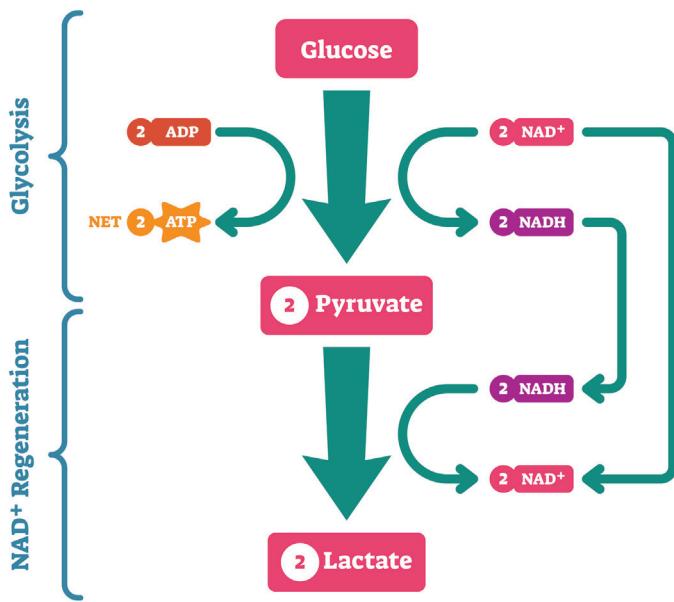
The reduced form of NAD⁺ necessary for energy production.

Lactate Dehydrogenase (LDH):

An enzyme catalyzing the conversion of pyruvate and NADH into lactate and NAD⁺, and vice versa.

Unlike the phosphocreatine system, glycolysis occurs in the cytoplasm of nearly all cells in the human body, not just in muscle cells. During glycolysis, the glucose molecule is split into two pyruvate molecules. The split is regulated by the coenzyme **nicotinamide adenine dinucleotide (NAD⁺)**. NAD⁺ is found in all living cells and is essential for glycolysis. After going through glycolysis, it is converted to **NADH**. Importantly, glycolysis not only forms pyruvate and NADH but also releases an acidic proton, H⁺. The enzyme **lactate dehydrogenase (LDH)** is found in the walls of cellular mitochondria. This enzyme acts with pyruvate, NADH, and the excess proton (H⁺) to catalyze the release of the NADH proton and donate it to pyruvate, which forms lactate and NAD⁺. This secondary process is known as NAD⁺ regeneration, and the entire process is referred to as lactic acid fermentation.

Figure 3.8 Lactic Acid Fermentation.



The coenzyme NAD⁺ and glucose create two pyruvate molecules and an excess proton and release two ATP molecules (energy) in the process. The pyruvate reacts with LDH and NADH to create lactate and NAD⁺, which can return to the beginning of the process and continue to break down glucose.

There are distinct differences in the ATP generation processes thus far. Glycolysis is acidifying to the muscle, unlike the phosphagen system, which is alkalinizing to the muscle. Protons are released in both glycolysis and ATP hydrolysis. In the first few seconds of maximal activity, the protons from ATP hydrolysis (phosphorylation) are buffered by the creatine kinase reaction. Anaerobic glycolysis has a similar buffer in place, but the buffer cannot consume all the newly released protons when lactate is formed and NADH is recycled back to NAD⁺.

AEROBIC METABOLISM

The **aerobic metabolism** produces ATP in the presence of oxygen. The process of aerobic metabolism begins with **acetyl coenzyme A (acetyl-CoA)** after the pyruvate molecule enters the mitochondria. This molecule must be formed no matter what source of fuel is used to make ATP. It is the “shuttle” triggering the first stage of aerobic metabolism, the **Krebs cycle**. The second stage is the **electron transport chain**, also called **oxidative phosphorylation**, which forms most of the ATP produced during aerobic metabolism. The outputs of aerobic metabolism are ATP, carbon dioxide (cellular waste expelled during respiration), and water.

AEROBIC METABOLISM:

The breakdown of fuels to form ATP in the presence of oxygen.

ACETYL COENZYME A (ACETYL-COA):

The molecule entering the Krebs cycle to start aerobic metabolism.

KREBS CYCLE:

A series of chemical reactions within mitochondria to form ATP from the oxidation of acetyl-CoA.

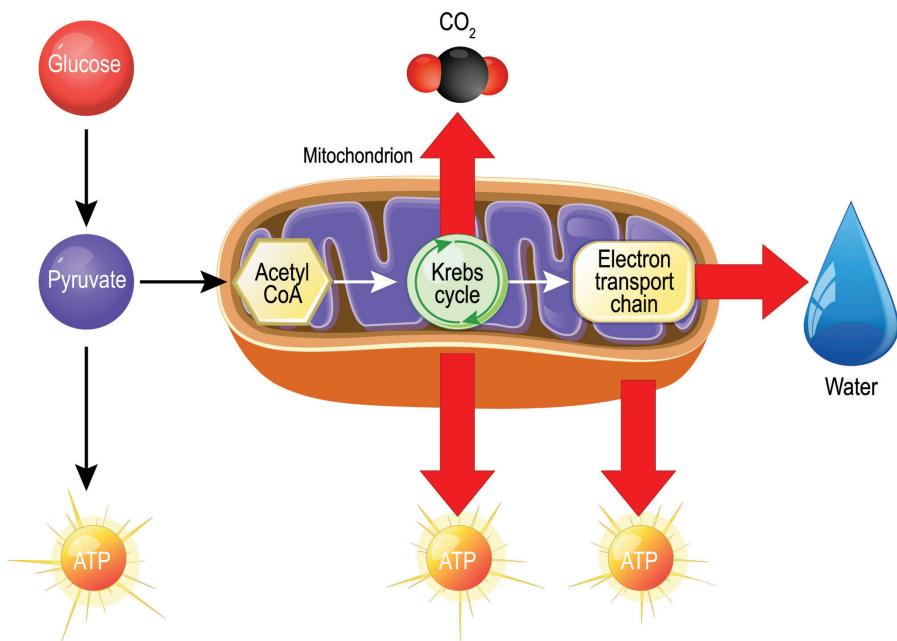
ELECTRON TRANSPORT CHAIN:

A metabolic pathway within mitochondria where most ATP molecules are formed during aerobic metabolism.

OXIDATIVE PHOSPHORYLATION:

Another name for the electron transport chain.

Figure 3.9 Aerobic Metabolism.



An overview of aerobic metabolism is shown. In the presence of oxygen, the initial pyruvate moves into the mitochondria, interacts with acetyl-CoA, enters the Krebs cycle, and moves through the electron transport chain.

Mitochondria

Mitochondria (singular is mitochondrion) are essential cell organelles generating most of the chemical energy needed for cellular processes. Some cells in the human body have more mitochondria than others (e.g., liver and muscle cells), and there are a few cell types lacking them altogether (e.g., red blood cells).

CRISTAE:

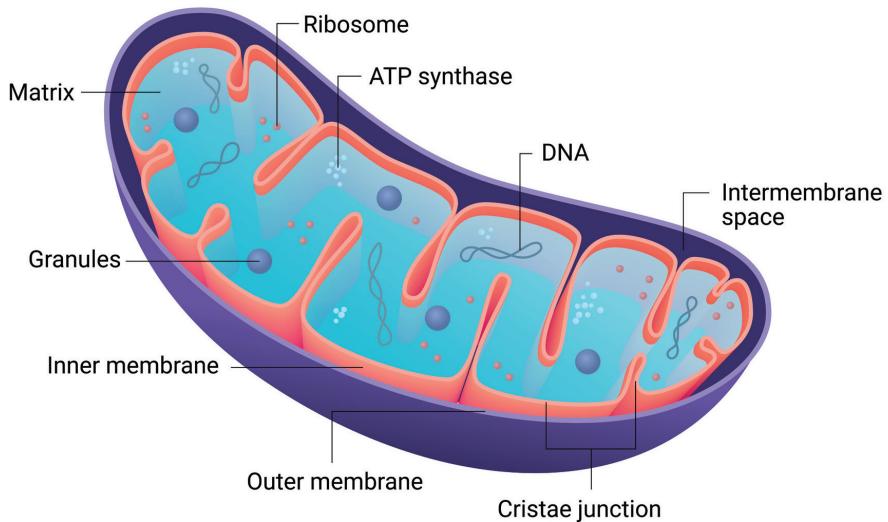
Folds of the inner membrane of a mitochondrion.

MATRIX:

Part of the mitochondria that is filled with enzymes, water, and proteins as well as the organelle's own unique DNA and ribosomes.

This specialized organelle has a dual membrane. The outer membrane of the organelle acts as a skin, while the inner membrane is folded—like the folds in the epithelial tissue of the intestines—many times over to increase the surface area. These folds are called **cristae**. The inner **matrix** of the mitochondria is filled with enzymes, water, and proteins as well as the organelle's own unique DNA and ribosomes. These organelles use their proteins, including pyruvate and acetyl-CoA, to break down oxygen and glucose—and other fuel sources—into energy, water, and carbon dioxide.

Figure 3.10 Mitochondrion Structure.



Aerobic metabolism can use four potential sources of fuel: glucose, fatty acids, lactate, and ketones. Each can be converted into acetyl-CoA, which can then enter the Krebs cycle, followed by the electron transport chain to complete aerobic metabolism.

Glucose for Fuel

Glycolysis splits glucose into a pair of pyruvates in the sarcoplasm of the muscle cell. With sufficient oxygen, pyruvate moves from the sarcoplasm into the mitochondria, where aerobic metabolism begins. Pyruvate is a three-carbon structure, and it must be converted into acetyl-CoA, which is a two-carbon structure.

Fatty Acids for Fuel

Fat is stored throughout the body in three different locations. Around the midsection, in the area between the abdominals and organs, is **visceral fat** (i.e., belly fat). Directly beneath the skin is **subcutaneous fat**, the most widely distributed fat in the body. And within the muscles are small amounts of **intramuscular fat**.

Fat is stored in all three locations as **triglycerides**. Before they can be used for energy, triglycerides are broken down into fatty acids through a process called **lipolysis**. Although it works differently, it is the equivalent of glycolysis, which breaks down glucose.

DID YOU KNOW?

When cellular energy needs are high, mitochondria can reproduce by growing in size and dividing. When they are not needed, they may die or become inactive in the cell.

VISCEERAL FAT:

Fat stored around the midsection and major intra-abdominal organs.

SUBCUTANEOUS FAT:

Fat stored directly beneath the skin.

INTRAMUSCULAR FAT:

Fat stored within the muscles.

TRIGLYCERIDES:

The stored form of fatty acids.

LIPOLYSIS:

The breakdown of triglycerides into fatty acids.

Lactate for Fuel

Muscle tissue produces lactate during short-term contraction, even when there is sufficient oxygen. The lactate can then be used for energy through one of these two processes:

- Remain in the muscle: Lactate can stay inside the muscle, where it converts back to pyruvate. It then enters the mitochondria and produces ATP.
- Move to other areas: Some of the lactate will leave the sarcoplasm and go into the bloodstream. From there it can flow into another working muscle, including the heart. Or it can move to the liver, where it is converted to pyruvate, then to glucose, and then sent back through the bloodstream to wherever it is needed. If it is not needed, the glucose can be converted to glycogen and stored in the muscles or liver to fuel future activity.

Ketones for Fuel

GLUCAGON:

A hormone produced in the pancreas, increasing levels of glucose and fatty acids in blood.

KETOACIDOSIS:

A metabolic state where high levels of ketones are in the blood due to fatty acid metabolism.

Ketones are an acidic by-product of fatty acid metabolism, produced in the liver when glucose is not available. They are a normal part of human metabolism and usually well controlled by the hormones insulin and **glucagon**.

Trouble arises when starvation, a severe illness, infection, or a chronic disease such as diabetes forces the liver to metabolize large amounts of fatty acids. Supraphysiological blood ketone levels can cause metabolic acidosis and put stress on the kidneys. If ketones remain elevated too long, it can lead to **ketoacidosis**, a potentially fatal health problem.

Ketones will have an effect in extreme circumstances, including the following:

- A diet low in carbohydrates
- An ultralow-calorie diet
- An extreme physical endurance event

Ketones are also a significant source of ATP for the brain in those circumstances. After three days on a low-carbohydrate nutrition plan, for example, ketones provide as much as 30 percent of the brain's needs. After weeks without carbohydrates, ketones could supply up to 70 percent. The heart can also use ketones for energy.

When ketone levels are high during physical activity, they can easily travel from the blood into the muscle and then into the mitochondria, where they are converted to acetyl-CoA, enter the Krebs cycle, and produce ATP.

Acetyl-CoA

Regardless of the fuel source, acetyl-CoA is the central metabolite initiating the aerobic metabolism process within the mitochondria. In the initial step of the Krebs cycle, acetyl-CoA donates an acetyl group to a substrate called oxaloacetate to form the substrate citrate and two ATP molecules, thus entering the energy production cycle.

The Citric Acid Cycle

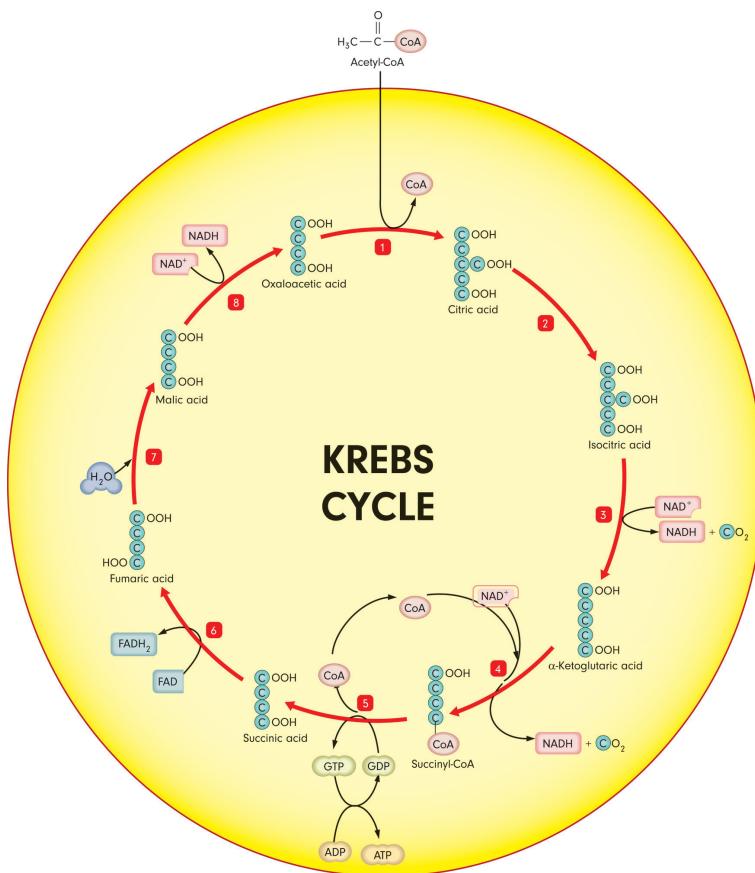
The Krebs cycle is also referred to as the citric acid cycle, named for one of its by-products. The cycle consists of eight consecutive steps in a closed loop, meaning the final step of the process re-creates the compound used in the initial step of the cycle.

The cycle is a series of hydration, dehydration, redox, and decarboxylation reactions, resulting in the formation of carbon dioxide, ATP, NADH, and **flavin adenine dinucleotide (FADH₂)**. NADH and FADH₂ are crucial products, as they are required to contribute electrons to the next step in aerobic metabolism.

FLAVIN ADENINE DINUCLEOTIDE (FADH₂):

A compound produced in the Krebs cycle supporting ATP formation.

Figure 3.11 The Krebs Cycle (Citric Acid Cycle).



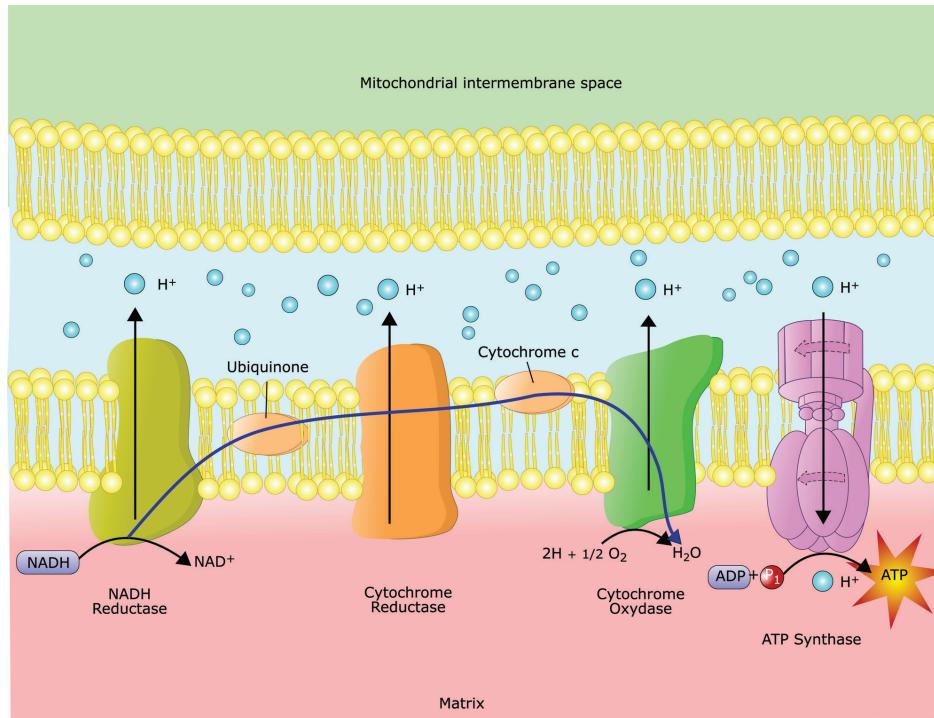
An overview of the energy-producing cycle is shown. It is a closed loop, meaning the initial compound is created by the final step of the cycle.

For the purposes of this course, the details of the reactions occurring at each step in the citric acid cycle are unnecessary. However, the results of the cycle feed into the next step of ATP production. Each citric acid cycle produces one ATP molecule, three NADH molecules, one FADH₂ molecule, two carbon dioxide molecules, and three protons (H⁺).

The Electron Transport Chain

This is the stage where most of the ATP is produced in aerobic metabolism—32 ATP molecules, in fact. The electron transport chain uses the FADH₂ and NADH from the citric acid cycle to release electrons through a series of three intermembrane transporters. In the process, protons (H⁺) are moved into the intermembrane space, and oxygen is reduced to produce water as a by-product. The final intermembrane transporter is ATP synthase. This enzyme moves the protons back into the mitochondrial matrix from the intermembrane space and, in the process, phosphorylates one ADP into one ATP molecule for each proton transported across the membrane.

Figure 3.12 The Electron Transport Chain and ATP Synthase.



NADH and FADH₂ contribute electrons to the three intermembrane transporters (olive, orange, and green). The resulting protons (H⁺) are pulled back into the cell via ATP synthase (purple) to drive the phosphorylation of ADP and produce ATP.

The various sources of fuel for aerobic metabolism will ultimately determine how much ATP can be produced. Glucose, fatty acids, lactate, and ketones each supply a different number of carbon molecules to the initial carbon donation to the citric acid cycle.

Table 3.3 ATP Production from Various Fuel Sources.

FUEL TYPE	MOLECULE DONATING	NUMBER OF CARBONS DONATED	ATP PRODUCTION
Glucose	2 pyruvate	6 (3 for each pyruvate)	30–32 ATP
Fatty acids	1 palmitic acid	16	106 ATP
Lactate	Lactate	6	30–32 ATP
Ketones	Amino acids	2	22 ATP

The use of different initial fuel sources will dictate how much ATP will be produced. Fats are the most effective at producing ATP.

