The Physiology of Exercise

THE PHYSIOLOGY OF EXERCISE

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ABOUT THE TEXTBOOK

The Physiology of Exercise, 3rd Edition

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About the text

The Physiology of Exercise (3rd Edition) is a comprehensive and student-focused resource designed for upper-level undergraduate courses in exercise physiology. Originally authored in 2016 by Rosie Lanphere, PhD, CSCS, this text was created with the goal of making complex physiological concepts accessible and relevant to students preparing for careers in exercise science, health, and human performance. Now in its third edition, the book has been thoroughly revised and updated to reflect current research and best practices in the field.

This edition provides an in-depth exploration of the physiological systems that underpin human movement and performance, including:

1. Metabolism and Energy Systems – Understand how the body produces and utilizes energy during rest and exercise.
2. Measurement of Human Energy Expenditure – Learn the principles and techniques for assessing energy use and efficiency.
3. The Nervous System – Examine the role of neural control in movement and coordination.
4. The Muscular System – Gain insight into muscle structure, function, and adaptations to training.
5. Cardiovascular and Respiratory Systems – Explore how these systems adapt to exercise and support performance.
6. The Endocrine System – Discover hormonal regulation and its impact on metabolism and training

Written in a clear, engaging style, the text integrates foundational science with practical applications, helping students connect theory to real-world exercise training. Each chapter includes learning objectives, key terms, and scholarly questions to reinforce understanding and support academic success.

Whether you are pursuing a degree in exercise science, preparing for professional certifications, or simply passionate about understanding the human body in motion, this book provides the essential knowledge and tools to excel.

Dedication

This textbook is dedicated to my teaching mentor Dr. Len Kravitz. His commitment to student empowerment has been a guiding light in my career as an educator. Thank you Dr. Kravitz for your storytelling, scholarship, and tremendous efforts in the field of Exercise Science. From you I have learned that the bell curve should not be the standard for excellence in teaching.

1.

INTRODUCTION TO EXERCISE PHYSIOLOGY

The First Lady, Michelle Obama, and Ellen DeGeneres dance during a taping of "The Ellen DeGeneres Show" marking the second anniversary of the "Let's Move!" initiative, in Burbank, California. February 1, 2012.

Learning Objectives

- Understand the scope and significance of exercise science, including its various sub-disciplines and related fields.
- Recognize the diverse career paths available within exercise science
- Articulate the personal and professional benefits of pursuing a career in exercise science.
- Comprehend the fundamental concepts of exercise physiology, including the body's

responses and adaptations to different types of physical exercise.
- Describe how environmental factors such as altitude, heat, and cold impact exercise performance and physiology.
- Acknowledge the need for continuous learning, professional relationships, and practical experiences to succeed in the field of exercise science.
- Explain how exercise science contributes to public health initiatives and the prevention and management of chronic diseases.

What is Exercise Science?

Exercise science is a multidisciplinary field that explores the science of movement and the body's responses and adaptations to physical activity. It encompasses various sub-disciplines, including **Biomechanics**, **Exercise and Sport Physiology**, **Kinesiology**, **Sports Psychology**, and **Sports Sociology**. Additionally, related fields such as **Sport Management** and **Health Promotion** offer further specialization opportunities for graduate students pursuing degrees in Exercise Science.

Careers in Exercise Science

Over the past three decades, interest in exercise science and kinesiology has surged, driven by extensive research demonstrating the benefits of exercise in enhancing longevity, reducing disease risk factors, and promoting overall wellness. Initiatives like "Exercise Is Medicine," (http://exerciseismedicine.org) developed by the American College of Sports Medicine and the American Medical Association, have further emphasized the importance of physical activity in health care. Consequently, career opportunities in exercise science have expanded significantly, including roles included in the purple sidebar:

Career Opportunities in Exercise Science

Many of these careers require advanced degrees and specialized certifications. Students should not assume that an undergraduate program alone will provide all the necessary experiences for post-graduation success. Professional or graduate school admissions often require practicum, internships, or research experiences. It is crucial for students to seek these opportunities and build professional

relationships with professors, who can provide valuable letters of recommendation. Additionally, students should research the admission requirements for their desired graduate programs early to ensure they complete the necessary coursework. Pursuing a career in exercise science offers numerous benefits, both personally and professionally:

Personal Benefits

1. **Health and Wellness:** Working in exercise science often means practicing what you preach. You'll have a deeper understanding of how to maintain your own health and fitness, leading to a healthier lifestyle.
2. **Job Satisfaction:** Helping others achieve their fitness and health goals can be incredibly rewarding. Seeing the positive impact of your work on others' lives can provide a strong sense of fulfillment.
3. **Continuous Learning:** The field is constantly evolving with new research and techniques. This means you'll have ongoing opportunities to learn and grow professionally.

Professional Benefits

1. **Diverse Career Opportunities:** As highlighted earlier, exercise science offers a wide range of career paths, from clinical roles like cardiac rehabilitation specialists to academic positions such as college professors.
2. **Growing Demand:** With increasing awareness of the importance of physical activity for health, there is a growing demand for professionals in this field. This can lead to more job opportunities and job security.
3. **Interdisciplinary Work:** Exercise science professionals often work with other health care providers, such as doctors, physical therapists, and nutritionists. This interdisciplinary approach can enhance your skills and

- Applied Research Scientist
- Athletic Director
- Basic Research Scientist
- Cardiac Rehabilitation Specialist
- Cardiovascular Technologist
- Chiropractor
- Clinical Researcher
- College Professor
- Director of Community Relations
- Director of Intramural Sports and Recreation
- Director of Sports Facilities
- Ergonomist
- Exercise Physiologist
- Exercise Program Director
- Exercise Specialist
- Exercise Test Technologist
- Fitness Director
- Fitness Instructor
- General Manager, Pro Sports Team
- Health Club Manager
- Health Educator
- Health/Fitness Instructor
- Kinesiologist
- Marketing Director
- Occupational Therapist
- Occupational Therapy Assistant
- Operations Director
- Personal Trainer
- Performance Coach

- Physical Education Director
- Physical Therapist
- Physical Therapy Assistant
- Physician
- Physician's Assistant
- Promotion Director
- Recreation Therapist
- Rehabilitation Therapist
- Sporting Goods Manufacturing Representative
- Sports Events Coordinator
- Sports Information Director
- Sports Instructor/Coach
- Sports Nutritionist
- Sports Psychologist
- Sports Trainer
- Strength and Conditioning Coach
- K-12 Teacher
- Ticket Manager
- Weight Training Instructor
- Wellness Coordinator

knowledge.

4. **Impact on Public Health:** By promoting physical activity and healthy lifestyles, you can contribute to the prevention and management of chronic diseases, improving public health outcomes.
5. **Flexibility:** Many careers in exercise science offer flexible work environments, including opportunities for self-employment, such as personal training or consulting.

Overall, a career in exercise science can be both fulfilling and impactful, offering a blend of personal satisfaction and professional growth.

Introduction to Exercise Physiology

Exercise Physiology is a branch of both physiology and exercise science. Physiology studies the function of organs, tissues, and cells, with a foundational understanding of anatomy. Exercise physiology focuses on the body's acute responses and chronic adaptations to various physical exercise conditions, such as endurance exercise, high-intensity interval training (HIIT), and resistance training. It also includes environmental exercise physiology, which examines the effects of exercise under stressors like altitude, heat, cold, space flight, and deep-sea diving. Research in exercise physiology spans diverse populations, including healthy and diseased individuals, and different age groups, contributing to the understanding of exercise's role in disease rehabilitation and treatment, such as diabetes mellitus.

Scholarly Questions

1. Define exercise science and list its main sub-disciplines.
2. Identify at least five career paths available to exercise science graduates.
3. Explain the primary focus of exercise physiology.
4. What is environmental exercise physiology, and what are some of the stressors studied in this sub-discipline?
5. What is the “Exercise Is Medicine” initiative, and how does it impact the field of exercise science?

2.

CONTROL OF THE INTERNAL ENVIRONMENT

A Thoroughbred racehorse in full stride during a race at Churchill Downs, the historic racetrack in Louisville, Kentucky. The horse is mid-gallop, with all four hooves off the ground, demonstrating peak speed and muscular exertion. The ability of a racehorse to maintain a steady state internal environment while racing is key to a winning performance.

Learning Objectives

- Define homeostasis and explain its importance in maintaining a stable internal environment.
- List and explain the three major components of a biological control system: receptor, control

center, and effector.
- Differentiate between negative and positive feedback mechanisms with examples.
- Discuss how exercise challenges homeostatic control systems and the body's response to these challenges.
- Describe how exercise training improves homeostatic control through physiological adaptations.
- Explain the process of protein synthesis in response to exercise.
- Identify the different cell-signaling mechanisms involved in cellular adaptations.
- Define stress proteins and their function in protecting cells from damage.
- Analyze how different types of exercise (resistance vs. endurance) lead to specific adaptations in muscle cells.
- Evaluate the effects of environmental stressors on homeostatic control and the concept of acclimation.

Control of the Internal Environment

For over a century, physiologists have recognized that the "milieu intérieur" (internal environment) of the human body remains constant despite changing external conditions. Claude Bernard (1813-1878), a French physiologist and one of the founding fathers of physiology, emphasized the importance of a stable internal environment. Bernard discovered that the liver could synthesize glucose from blood-derived products like lactate and that the nervous system controls vasomotor responses, which can dilate or constrict blood vessels. Maintaining a stable internal environment is crucial for health. This chapter introduces exercise as a challenge to homeostatic control, reviews homeostatic control systems, and explains how adaptations affect these systems. Understanding the challenges exercise poses to homeostasis can help appreciate how exercise-induced adaptations protect the body from future stressors.

Exercise: A Challenge of Homeostatic Control

Exercise significantly challenges homeostatic control. Variables such as pH, core temperature, heart rate, blood pressure, ventilation, and hormone concentrations can deviate greatly from resting values during exercise. **Homeostasis**, a term coined by Walter Cannon in 1932, refers to the maintenance of a relatively constant internal environment, describing a dynamic balance that keeps the body within livable limits during rest. **Steady state**, while also describing a stable internal environment, refers to conditions where

physiological variables are elevated or decreased from resting values. Steady state exercise involves maintaining constant but elevated levels of variables like heart rate, ventilation rate, body temperature, oxygen consumption, blood pressure, hormones, and blood glucose concentration are constant but elevated from rest.

Although homeostasis and steady state imply stability, the internal environment is not constant. These states are maintained through dynamic balance by control systems that make small adjustments to keep physiological variables around a "set" value. For example, blood pressure is a critical variable to control, as it ensures oxygen delivery to tissues. Resting blood pressure can oscillate between 92 and 94 mmHg, with an average arterial pressure around 93 mmHg[1]. During steady state exercise, blood pressure increases from rest and varies depending on individual training and exercise intensity (e.g. speed, resistance, load) of the mode of exercise. If exercise intensity remains constant, small oscillations in blood pressure occur but stay close to the mean steady state value (Figure 2.1). These oscillations result from highly regulated biological control systems that provide feedback to adjust blood pressure when it deviates from the set value[2].

Homeostatic Regulation

Biological Control Systems

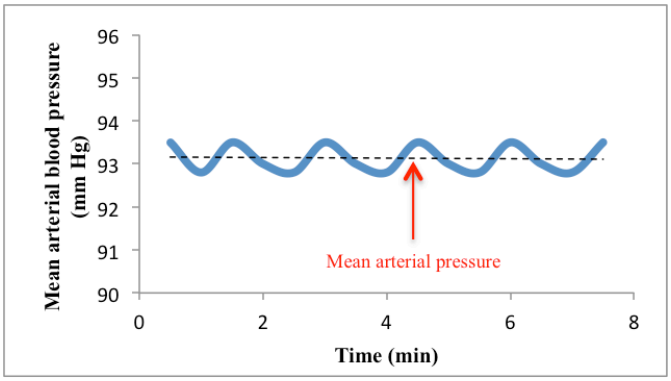


Figure 2.1 Resting arterial blood pressures across time. Notice that the small oscillations revolve around the central mean pressure.

The human body contains thousands of control systems that maintain homeostasis. These systems range from intricate mechanisms within single cells to those regulating entire organs. They also manage interactions between organ systems. For example, the respiratory system, in conjunction with the nervous system, regulates carbon dioxide levels produced during metabolism, especially during exercise. A typical biological control system comprises three main components: the receptor, control center, and effector. The receptor, a specialized sensor, measures the current state of the system. The control center compares this value to the desired "set" value. If a discrepancy is detected, the effector modifies the parameter to correct the disturbance. This process often involves negative feedback, where the response reduces the original stimulus. The three components of a biological control system are:

1. Powers SK, Howley ET, Exercise Physiology (Theory and Application to Fitness and Performance). 9th Edition ed. 2015, New York, NY: McGraw-Hill.

2. Widmaier E, Raff H, Strang K. Vander's Human Physiology. 2013, Boston, MA: McGraw-Hill.

1. Receptor: obtains current information
2. Control center: compares current value and compares it to a desired value
3. Effector: modifies some parameter

Negative Feedback

Most biological control systems operate via **negative feedback**, where the system's response opposes the original stimulus. For instance, consider the regulation of blood glucose after eating shown in Figure 2.2. Following a high-carbohydrate meal, glucose enters the bloodstream, causing hyperglycemia (blood glucose levels above 100 mg/100 ml)[3]. Normal fasting blood glucose levels range from 80-90 mg/100 ml. In response, the pancreas releases insulin, which binds to cell receptors and facilitates glucose uptake into cells, thereby lowering blood glucose levels. This mechanism restores homeostasis by reducing blood glucose to normal levels. Negative feedback is so named because the control system's response is in the opposite direction of the initial stimulus.

During exercise, several physiological control systems operate via negative feedback to maintain homeostasis. These include the regulation of carbon dioxide and oxygen concentrations, arterial blood pressure, body temperature, heart rate, and electrolyte balance. A common household thermostat, as illustrated in Figure 2.3, also employs a negative feedback system. The thermostat can be set to a desired temperature, such as 72°F, and is connected to the heating unit of a dwelling. If the indoor temperature drops below this setting, the thermostat activates the furnace to produce heat until the desired temperature is reached. Once the thermostat measures the set temperature (72°F), the furnace turns off. If the temperature drops again, the thermostat reactivates the furnace. In this example, the furnace's response (producing heat) is opposite to the initial stimulus (a decrease in temperature).

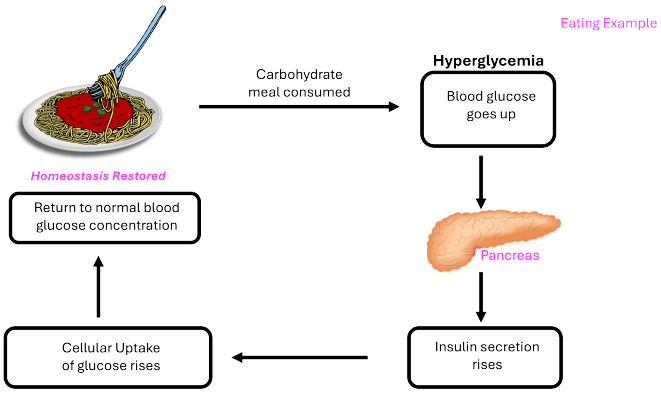


Figure 2.2 Illustration of the negative feedback that is used to regulate blood glucose levels after a high-carbohydrate meal. See text for details of how this system operates.

In general, when a factor becomes excessive or deficient, a control system initiates negative feedback to make adjustments that return the factor toward a certain mean value, thereby maintaining homeostasis.

3. Guyton AC, Hall JE. Textbook of Medical Physiology. 11th ed. 2006, Philadelphia, PA: Elsevier Saunders.

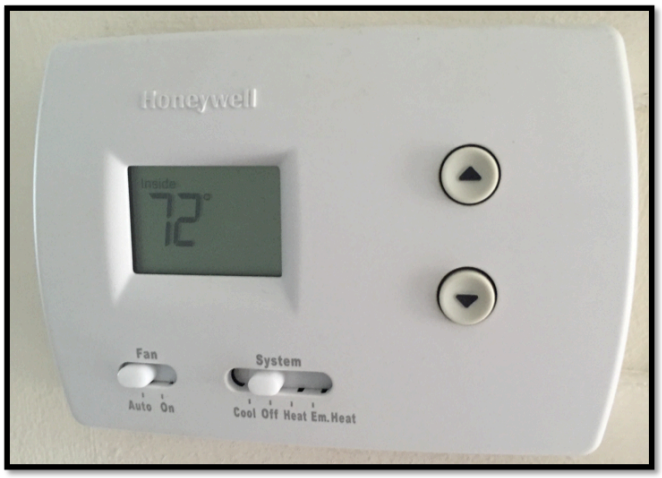


Figure 2.3 A common household thermostat set to 72°F. A thermostat also works by way of negative feedback.

Positive Feedback

Positive feedback mechanisms amplify the original stimulus, meaning the response moves in the same direction as the stimulus. This can sometimes lead to vicious cycles and instability, potentially causing harm or even death. For example, consider body temperature regulation during endurance exercise in hot and humid conditions. Normally controlled by negative feedback, body temperature can rise from its normal level of 98.6°F to 102°F or 103°F (37°C to 40°C) due to heat produced by muscle contractions. In hot and humid environments, the body struggles to dissipate this heat, causing temperatures to potentially rise to 106°F to 108°F (41°C to 42°C). Such high temperatures can damage cells and lead to heatstroke, a dangerous positive feedback loop where the body's temperature-regulating mechanisms fail, and the elevated temperature accelerates chemical reactions, producing even more heat[4]. Without intervention, this cycle can be fatal.

However, positive feedback can be beneficial in certain situations, such as childbirth, blood clotting, and nerve signal generation. For instance, to generate a nerve signal during exercise, a motor neuron must be stimulated, causing sodium ions to leak into the cell. This changes the membrane potential, opening more sodium channels and allowing more sodium to enter, eventually triggering an action potential and nerve transmission to stimulate muscle contraction. This positive feedback process enables neurons to function within numerous negative feedback systems, maintaining overall homeostasis through interconnected control systems.

Gain of the control system

The effectiveness of a control system in maintaining homeostasis through negative feedback varies, described by the term "**gain**." Gain is a term to describe the precision with which a control system maintains homeostasis. Systems with high gain maintain homeostasis more precisely than those with low gain. Gain is determined by

4. Medical aspects of exercise. Benefits and risks. Summary of a Report of the Royal College of Physicians. J R Coll Physicians Lond, 1991. 25(3): p. 193-6.

the system's ability to correct disturbances and the error involved in preventing changes. The gain of a system can be calculated using the following formula:

$$Gain = \frac{Correction}{Error}$$

This formula quantifies the system's precision in maintaining stable conditions.

Exercise Improves Homeostatic Control

Exercise challenges the body's homeostatic control systems by potentially disrupting variables such as core temperature, acid-base balance, and oxygen and carbon dioxide levels. During sub-maximal exercise in a cool environment, control systems can maintain a steady state. However, prolonged or intense exercise in hot or humid conditions can overwhelm these systems, leading to premature fatigue or cessation of exercise. Heavy exercise can cause disturbances too great for even the most effective control systems to manage, preventing a steady state. Exercise training can improve performance under these conditions by enhancing homeostatic control.

Exercise training stimulates physiological adaptations in affected organ systems, improving homeostatic control. Adaptations involve changes in the structure and function of cells, tissues, or organ systems, enhancing the ability to maintain a steady state during stress, such as exercise, and allowing the body to return to homeostasis quickly afterward. The principle of specificity states that exercise adaptations are specific to the muscles involved, the muscle fiber types recruited, and the energy systems used. For example, aerobic exercise leads to adaptations in oxygen transport (increased synthesis of myoglobin) and utilization (more mitochondria) mechanisms, while anaerobic resistance training increases proteins associated with force production (actin and myosin) and anaerobic energy creation (creatine kinase). These adaptations are specific to the type of training and develop over weeks. Exercise improves homeostatic control through adaptation.

Exposure to environmental stressors also causes adaptations, known as **acclimation**, which occur after repeated or chronic exposure to conditions like heat, altitude, cold, deep-sea diving, or space flight. These adaptations are studied in Environmental Exercise Physiology and are of interest to organizations like the National Aeronautics and Space Administration (NASA). Figure 2.4 shows the relationship of heart rate (bpm) at 45 minutes of cycling exercise (50 W) throughout a 7-day acclimation protocol in 40°C. Note that the heart rate is lower during day 7 of the protocol (~118 bpm) when compared to the same time during day 1 (~138). This decrease in heart rate following several days of exercise in the heat demonstrates acclimation of the cardiovascular and associated systems[5]. Acclimation results in the improved function of an existing homeostatic system. When environmental conditions are artificially created, such as in altitude chambers, the

resulting adaptations are called **acclimatization**. Training-induced adaptations enhance performance by improving the body's ability to maintain homeostasis.

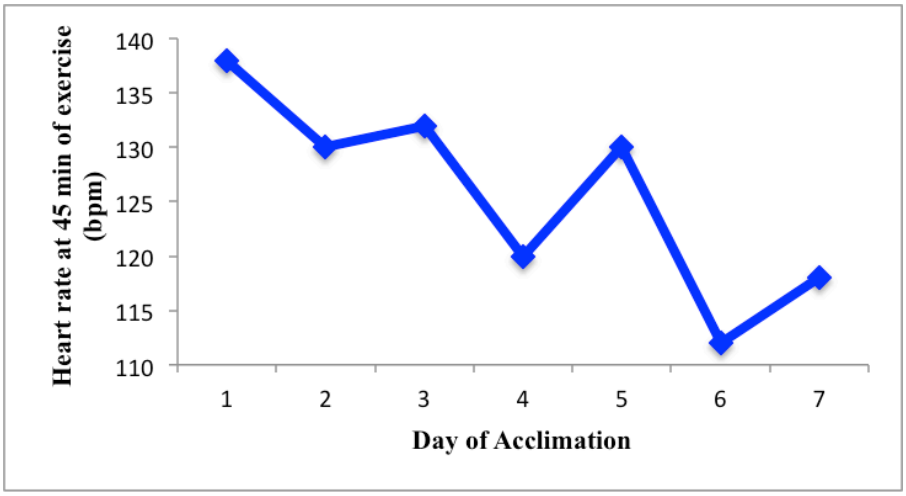


Figure 2.4 The relationship between heart rate at the end of 45 minutes of cycling (50 W) in 40°C and days of acclimation.

Cellular Adaptations

Exercise training induces cellular adaptations that enhance the function of existing homeostatic systems. Cell signaling refers to the communication processes that occur within or between cells, allowing them to coordinate activities. There are five major cell-signaling mechanisms involved in adaptation and homeostasis:

1. **Intracrine signaling.** Chemical messengers within a cell trigger a response in the same cell.
2. **Juxtacrine signaling.** Adjacent cells communicate through transmembrane protein junctions that allow a chemical messenger to travel from one cell to the neighboring cell.
3. **Autocrine signaling.** A cell secretes a chemical messenger into the extracellular fluid, but the receptor for this messenger is on the membrane of the same cell that produced it.
4. **Paracrine signaling.** A cell communicates with nearby cells by secreting a chemical messenger into the extracellular fluid.
5. **Endocrine signaling.** Cells secrete hormones into the bloodstream, affecting downstream cells that have specific receptors for these hormones.

5. Atherton PJ, Smith K, Muscle protein synthesis in response to nutrition and exercise. The Journal of Physiology, 2012. 590(Pt 5): p. 1049-1057.

Exercise Stimulates Protein Synthesis

Regular exercise induces specific cellular adaptations depending on the type of training. **Resistance training** and **endurance training** lead to different adaptations, coordinated by cell signaling mechanisms. The mechanical and metabolic stimuli of exercise activate signaling pathways, leading to protein synthesis and subsequent adaptations within muscle cells. Understanding the process of protein synthesis is crucial, as exercise stimulates structural and metabolic changes in this manner. The process of protein synthesis induced by exercise involves the following steps and is shown in Figure 2.5:

1. The mechanical mechanisms and metabolic stresses of exercise activate a cell-signaling pathway.
2. The pathway activates a transcription factor, which enters the cell nucleus.
3. In the nucleus the transcription factor binds to a gene promoter region, initiating DNA transcription.
4. DNA is transcribed to messenger RNA (mRNA).
5. The mRNA is processed and released into the cytoplasm, where it binds with a ribosome for translation.
6. The mRNA is translated, and a protein is assembled from amino acids according to the mRNA code.

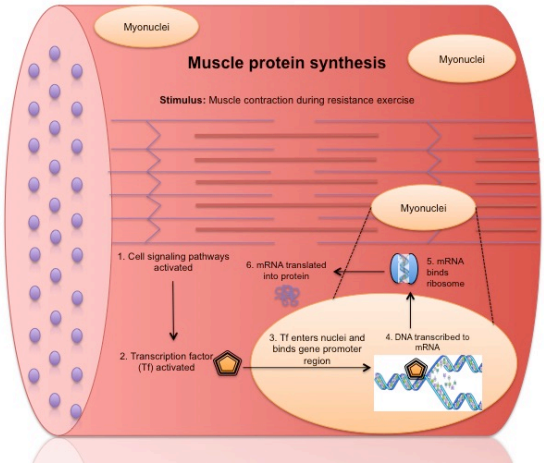


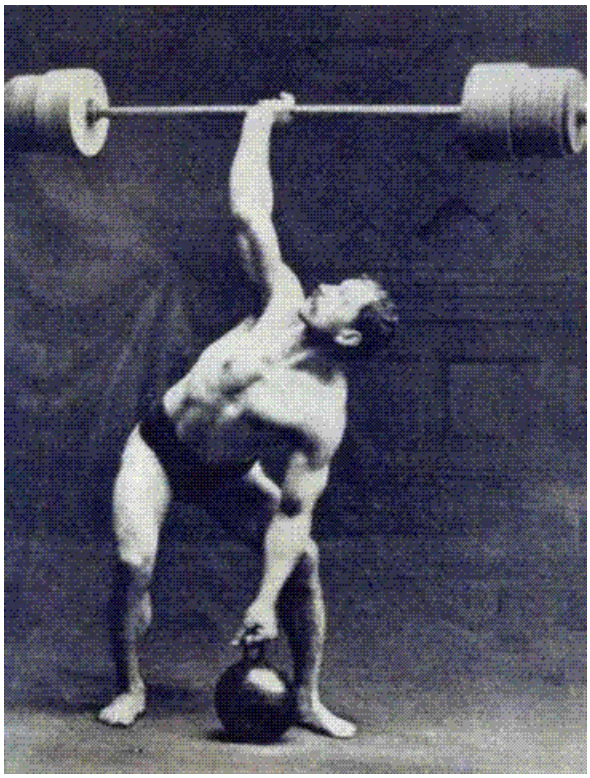
Figure 2.5. Illustration of how resistance training promotes the activation of cell signaling and protein synthesis.

The **workload** and **intensity** of exercise are key determinants of the magnitude of muscle protein synthesis[6]. Resistance and endurance exercises activate distinct signaling pathways, leading to different adaptations. For instance, resistance training causes micro-tears in skeletal muscle fibers, which activate satellite cells. These cells play a crucial role in muscle repair by synthesizing actin and myosin proteins. The addition of new actin and myosin proteins results in muscle hypertrophy, enhancing the muscle's ability to generate additional force.

6. Wingo J, et al. Heat Acclimation of an Adult Female With a Large Surface Area of Grafted Skin. J Burn Care Res, 2008. 29(5): p. 848-851.

Stress Proteins

Stress proteins are a specialized class of proteins synthesized to protect cells from damage. Among these, heat shock proteins (HSPs) are extensively studied. HSPs function as molecular chaperones, refolding damaged or misfolded proteins to conserve energy and prevent unnecessary degradation. They are produced in response to physiological stress, such as exposure to extreme heat, cold, or acidosis. Once synthesized, HSPs provide protective effects against future stress exposures, helping to restore and maintain cellular homeostasis.



Author Saxon performing a "Two Hands Anyhow" with an early kettle bell and plate-loaded barbell. The lift demonstrates exceptional balance, coordination, and unilateral strength. This image captures a foundational moment in the history of strength training and physical culture, showcasing the use of rudimentary equipment and the evolution of lifting techniques.

Chapter Summary

In this chapter, we explored the fundamental concept of homeostasis and the body's intricate systems for maintaining a stable internal environment. We examined the components of biological control systems, including receptors, control centers, and effectors, and discussed how negative feedback mechanisms help regulate homeostasis. The challenges exercise poses to homeostatic control were highlighted and how exercise training induces physiological adaptations that enhance the body's ability to maintain stability. The principle of specificity was emphasized, showing how different types of exercise lead to specific cellular adaptations.

The chapter also covered the role of stress proteins, particularly heat shock proteins, in protecting cells from damage and maintaining homeostasis during stress. Additionally, we discussed the concept of acclimation, where repeated exposure to environmental stressors leads to adaptations that improve homeostatic function. Overall, this chapter provided a comprehensive understanding of how the body maintains homeostasis, the impact of exercise on these processes, and the adaptations that occur to enhance performance and health.

Scholarly Questions

1. What is homeostasis, and why is it important for maintaining a stable internal environment?
2. What is steady state and how is it different than homeostasis?
3. What are the three major components of a biological control system, and what roles do they play in maintaining homeostasis?
4. Describe the process of protein synthesis in response to exercise.
5. What are the five major cell-signaling mechanisms involved in cellular adaptations?
6. What type of feedback system regulates glucose homeostasis?
7. What is acclimation?
8. What kind of proteins respond to heat stress?
9. Name some physiological variables that maintain a steady state during exercise at a low-moderate (constant) intensity?
10. Explain what negative feedback means. Give an example of a negative feedback loop in the body (you may want to do a google search to find additional examples).

3.

BIOENERGETICS AND METABOLISM

The food shown here are those that we consume which are comprised of macronutrients like carbohydrates, proteins, and fats. A healthy diet comprises all of these nutrients as well as minerals, vitamins, and electrolytes. Our body breaks down food in a process called metabolism and the process in which our body transfers energy is called bioenergetics.

Learning Objectives

- Explain the concept of bioenergetics and its importance in cellular functions.
- State and explain the first and second laws of bioenergetics.

- Illustrate how energy is converted and transferred within the body, including examples of exergonic and endergonic reactions.
- Describe the structure and function of the cell membrane, mitochondria, nucleus, and cytoplasm.
- Define metabolism and explain the role of metabolic pathways in energy production.
- Identify the primary substrates used for energy during exercise and describe their metabolic pathways.
- Classify different types of enzymes and describe their specific roles in metabolic reactions.
- Explain the concept of enzyme specificity and the "induced fit" model of enzyme action.
- Define coenzymes and describe their role in assisting enzymatic reactions.
- Explain the importance of high-energy phosphate molecules like ATP and creatine phosphate in energy transfer.
- Discuss how an understanding of bioenergetics can inform exercise professionals about muscle energy generation and body responses to exercise.

Bioenergetics

All living organisms require energy that is generated through chemical reactions. At any given moment, thousands of these reactions are occurring within your cells, enabling your body to produce the energy necessary for sustaining life. This energy can also be stored and used during activities such as physical exercise. Ultimately, all energy on Earth originates from the sun. Plants transform solar energy into carbohydrates, fats, and proteins through photosynthesis. Animals then consume these plants, or other animals, to obtain the energy needed for cellular functions.

Bioenergetics is a branch of biochemistry that examines the flow of energy from one source to another. It explores how foodstuffs are converted into adenosine triphosphate (ATP), the primary energy currency of cells (Figure 3.1). This process is crucial for understanding how organisms' harness and utilize energy to maintain life.

Understanding bioenergetics is crucial because it provides the foundational principles by which metabolism operates. Comprehending metabolism is essential for exercise professionals to understand how skeletal muscles generate energy and how the body responds to exercise. Without a thorough grasp of energy flow within the body, it is impossible to fully understand skeletal muscle functions both at rest and during exercise. **Metabolism** encompasses the chemical reactions responsible for the creation and transfer of energy necessary to sustain exercise.

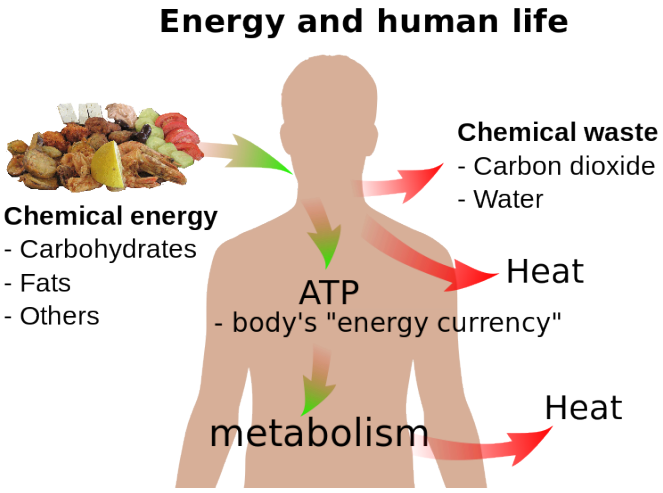


Figure 3.1 Conceptual diagram providing an overview of bioenergetics.

There are two fundamental laws of bioenergetics that govern metabolic processes. The first law states that 1) energy cannot be created or destroyed but is converted from one form to another. In the human body, various reactions convert chemical, electrical, mechanical, and thermal energies into different forms. For instance, light entering the eyes is transformed into a chemical signal, which is then converted into electrical action potentials in the brain. Muscles convert chemical energy (ATP) into mechanical energy during muscle contractions, which can be used to exert force on the external environment. The bioenergetic process of energy conversion involves a series of tightly regulated chemical reactions that release energy stored in the chemical bonds of molecules. Ultimately, all energy is eventually transformed into heat.

The second law of bioenergetics states that 2) energy transfer will proceed in the direction of increased **entropy** and the release of **free energy**. Potential energy is stored in the bonds of molecules, referred to as "high energy" bonds. When these bonds are broken, they release a specific amount of energy known as free energy (ΔG), typically measured in calories per mole. For example, the complete oxidation of one mole of glucose releases 686,000 calories[1]. Cells harvest this free energy to perform work, or it can be lost as heat. In thermodynamics, entropy describes the unavailability of a system's thermal energy for conversion into mechanical work and can also be interpreted as the degree of disorder or randomness in a system. When converting a substrate to a product, by-products such as heat, light, entropy, and free energy are often produced.

1. Guyton AC, Hall JE. Textbook of medical physiology. 11th ed. Philadelphia, PA: Elsevier Saunders; 2006.

Cellular Chemical Reactions

Chemical reactions within cells are categorized into two major types that work together to sustain energy flow. **Exergonic (or exothermic) reactions** release free energy, such as those involved in glucose breakdown. The energy liberated from exergonic reactions can drive other reactions. Conversely, **endergonic (or endothermic) reactions** require an input of energy to proceed. When energy is added to an endergonic reaction, the resulting products contain more free energy than the original substrates.

Exergonic and endergonic reactions are often linked in a process known as coupled reactions. In **coupled reactions**, the free energy released from an exergonic reaction is used to drive an endergonic reaction. This systematic linking of reactions ensures the efficient transfer and utilization of energy within cells. An example of coupled reactions is illustrated in figure 3.2 where the same energy that is liberated from reaction 1, is then used to initiate reaction 2.

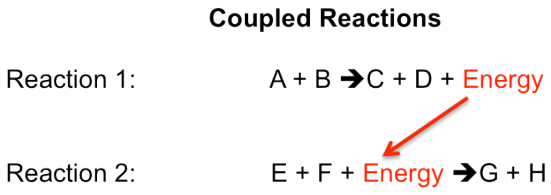


Figure 3.2 Coupled Reactions. Reaction 1 is an exergonic reaction in which substrates A and B are converted into products C and D, releasing free energy. This liberated energy is then used to drive Reaction 2, an endergonic process where substrates E and F are converted into products G and H. Arrows indicate the direction of each reaction, and a connecting line or symbol shows the energy transfer between them. The figure demonstrates how energy-releasing reactions can power energy-requiring processes, a fundamental principle in cellular metabolism.

Redox reactions

Reduction-oxidation (redox) reactionsinvolve the transfer of electrons between two molecules. These reactions are essential to many fundamental life processes, including photosynthesis, respiration, combustion, and metabolism. When a molecule gains electrons, it undergoes a reduction reaction. Conversely, when a molecule loses electrons, it undergoes an oxidation reaction. A helpful mnemonic to remember this is "LEO the lion says GER," which stands for "Loss of Electrons is Oxidation" and "Gain of Electrons is Reduction."

It is important to note that electrons are not free-floating; they are attached to other molecules by their charge. In many metabolic steps, electrons that are removed are bound to a proton (hydrogen). Figure 3.3 illustrates a hydrogen atom, which consists of a proton and a valence electron. Redox reactions involving hydrogen atoms occur in several stages of catabolism. When hydrogen is removed, a carrier molecule transports the hydrogen (a proton and an electron) to later stages in metabolism. These molecules, known as "electron carriers," will be discussed further in the co-enzyme section of this chapter.

Energy Transfer and Cell Anatomy

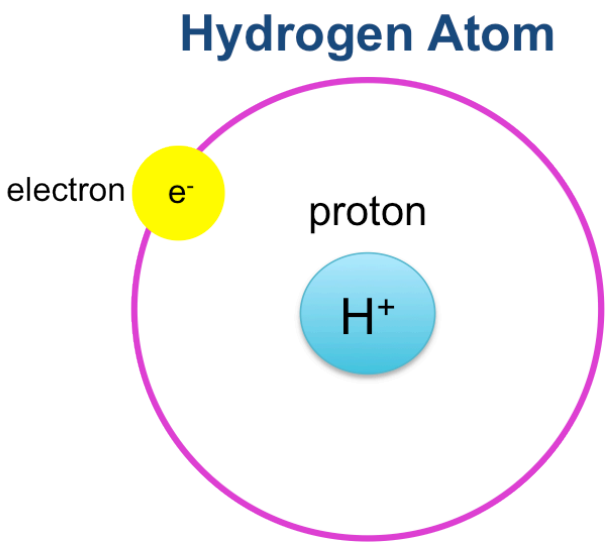


Figure 3.3 A hydrogen atom is composed of a positively charged proton and a negatively charged electron.

Energy transfer occurs within the cells of the body, making an understanding of cell anatomy vital to the study of bioenergetics. Cells were first discovered in the seventeenth century by the English natural philosopher Robert Hooke. Over the past 300 years, advancements in cell microscopy have significantly enhanced our understanding of cell structure. We now know that organisms are primarily composed of four elements: oxygen (65%), carbon (18%), hydrogen (10%), and nitrogen (3%)[2]. These elements make up more than 95% of the human body. Additional chemical substances found in the body include sodium, iron, zinc, potassium, magnesium, chloride, and calcium.

Molecules that contain carbon are known as organic compounds and are often linked with other elements by chemical bonds. For example, glucose ($C_6H_{12}O_6$) is an organic molecule and serves as a source of energy classified as a carbohydrate. In contrast, inorganic compounds are molecules that do not contain carbon atoms. Water (H_2O), for instance, does not contain carbon atoms and is therefore classified as inorganic.

2. Powers SK, Howley ET. Exercise physiology (theory and application to fitness and performance). 9th Edition ed. New York, NY: McGraw-Hill; 2015.

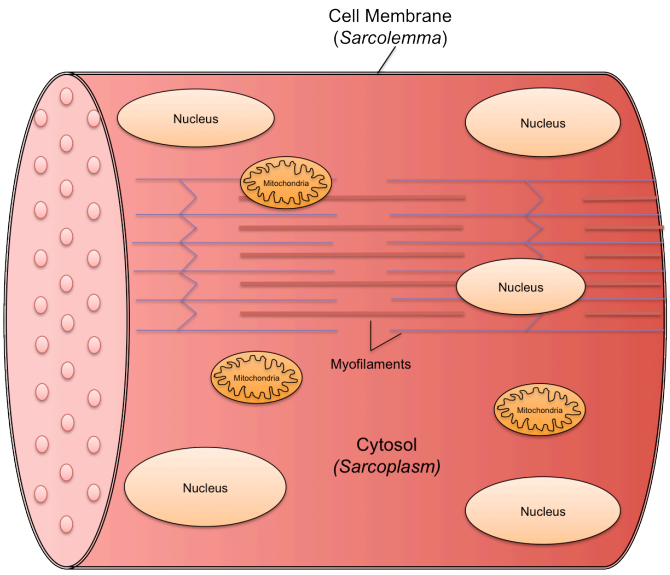


Figure 3.4 The basic structure of a muscle cell (fiber) and its major organelles. The elongated, cylindrical cell is shown with multiple peripheral nuclei and a surrounding sarcolemma (cell membrane). Inside, longitudinally arranged myofilaments are visible, composed of repeating sarcomeres—the contractile units. Mitochondria are scattered throughout the sarcoplasm, indicating sites of ATP production. The diagram emphasizes the structural and functional organization of muscle cells in relation to contraction and energy metabolism.

Cells are highly organized units compartmentalized into smaller organelles that carry out necessary functions. While not all cells have the same function, they share structural similarities. Each cell is surrounded by a semi-permeable membrane composed of a phospholipid bilayer with both hydrophobic and hydrophilic properties. This cell membrane, known as the **sarcolemma** in skeletal muscle, protects the cell from the external environment and provides structural compartments to house the cell's inner contents.

The nucleus is a large, rounded body within the cell that contains the organism's genetic material in the form of deoxyribonucleic acid (DNA). DNA contains genes that code for proteins, regulating protein synthesis, which determines cell composition and controls cellular activity. Muscle cells, also known as muscle fibers, are unique in that they are multi-nucleated, meaning they have more than one nucleus.

Another major component of the cell is the cytoplasm, or **sarcoplasm** in muscle cells. The cytoplasm, also referred to as the cytosol, contains various organelles, including the mitochondria. **Mitochondria**, often called the powerhouse of the cell, are heavily involved in creating energy from foodstuffs. They are particularly important in skeletal muscle bioenergetics and metabolism due to their role in energy generation. Additionally, the sarcoplasm contains essential proteins such as actin and myosin, which promote organization and prevent structural collapse. **Actin** and **myosin** form structures called myofilaments within the muscle cell, providing rigid scaffolding for structure and the ability to produce force. Figure 3.4 illustrates the basic structures of a muscle fiber.

Metabolism

A significant proportion of chemical reactions in cells occur to create energy from food, which is then used to perform cellular work. These reactions are termed **metabolism** and are required to maintain life. Metabolism is typically divided into two categories. **Catabolism** refers to reactions that breakdown molecules to release energy and anabolism are those reactions that synthesize molecules to form larger molecules.

Anabolism requires energy to be inputed into the reaction.

Energy is required for muscle activity, gland secretion, maintenance of nerve and muscle fiber membrane potentials, synthesis of substances in cells, absorption of food from the gastrointestinal tract, and many other functions[3]. A **substrate** is any substance acted upon by enzymes to create a product molecule. The three forms of usable nutrients in the human body are **carbohydrates**, **proteins**, and **fats**. When consumed, these nutrients are metabolized and used as substrates to create usable cellular energy. A **metabolic pathway** is a sequence of enzyme-mediated chemical reactions that convert substrates to products.

During exercise, the primary substances used for energy generation are fats and carbohydrates, with minimal energy contribution from protein metabolism. Therefore, carbohydrate and fat metabolism will be highlighted in this text, along with an explanation of the relationship between carbohydrate, fat, and protein metabolism.

Substrates Used for Energy

Carbohydrates are synthesized during photosynthesis by plants from the interaction of CO_2, water, and solar energy. Composed of carbon (C), hydrogen (H), and oxygen (O_2), carbohydrates exist as **monosaccharides**, **disaccharides**, or **polysaccharides**. Monosaccharides are simple sugars such as fructose and glucose. All carbohydrates are ultimately converted to glucose, which is transported through the blood to all body tissues. **Glucose** is the preferred carbohydrate for muscles due to its high availability in the blood and the substantial energy yield it provides. Glucose yields approximately 4 kcal of energy per gram and has the chemical formula $C_6H_{12}O_6$.

Muscle cells can store small amounts of glucose in the form of glycogen, a polysaccharide also stored in the liver. **Glycogen** is synthesized within cells by linking single glucose molecules together with the enzyme glycogen synthase. Glycogen molecules can consist of hundreds to thousands of glucose molecules. Carbohydrate stores in the liver and skeletal muscle are limited to about 2,500 to 2,600 kcal of energy, equivalent to the energy needed for approximately 25 miles (40 km) of running[4].

3. Guyton AC, Hall JE. Textbook of medical physiology. 11th ed. Philadelphia, PA: Elsevier Saunders; 2006.

4. Kenney LK, Wilmore JH, Costil DL. Physiology of sport and exercise. In. Champaign, IL: Human Kinetics; 2012.

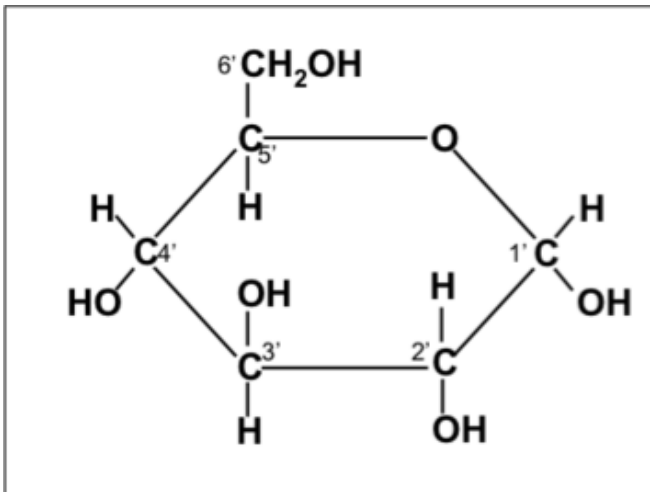


Figure 3.5 The molecular structure of glucose. A glucose molecule is a six-carbon monosaccharide with the molecular formula $C^6H^{12}O^6$. The image shows glucose in its cyclic (pyranose) form, with a six-membered ring composed of five carbon atoms and one oxygen atom. Each carbon is bonded to hydrogen and hydroxyl (–OH) groups in a specific orientation, distinguishing D-glucose as a biologically active isomer. The diagram includes labels for carbon atoms (C1–C6), and hydroxyl groups, highlighting the molecule's role in energy metabolism and cellular respiration.

Fructose, another monosaccharide, is the sweetest of the carbohydrates and is found in fruits and honey. Disaccharides are formed when two monosaccharides combine. A common example is table sugar, or **sucrose**, which consists of glucose and fructose. Sucrose is the most common dietary disaccharide in the United States, accounting for nearly 25% of the total caloric intake for most Americans[5]. Polysaccharides, which are complex carbohydrates, contain three or more monosaccharides. Cellulose and starch are two forms of polysaccharides; however, humans lack the enzymes to digest cellulose, which is excreted as waste. Starch, found in corn, beans, grains, and peas, is easily digested and constitutes a significant portion of the human diet[6]. It is recommended that adults obtain 45% to 65% of their calories from carbohydrates[7].

Fats are also a preferred substrate for energy production during exercise, providing a substantial portion of the energy used during prolonged, less intense activities. Fats contain the same chemical elements as carbohydrates, but with a higher ratio of carbon to oxygen. This higher ratio allows fats to yield more energy per gram than carbohydrates, with 1 gram of fat providing approximately 9 kcal of energy, roughly double that of carbohydrates. Fats are generally classified into three groups: triglycerides, phospholipids, and steroids.

Triglycerides consist of three fatty acid chains and one glycerol molecule. **Fatty acids**, the primary fats used by muscles for metabolism, are stored in the body as triglycerides. They are released into the bloodstream through a process called **lipolysis**, which is regulated by enzymes known as lipases. The glycerol molecule can be used by the liver to synthesize glucose if necessary. **Phospholipids**, which make up the cell membrane's

5. McArdle WD, Katch FI, Katch VL. Exercise physiology: Nutrition, energy, and human performance. In. Exercise physiology: Nutrition, energy, and human performance: LWW; 2014, p 1088.

6. McArdle WD, Katch FI, Katch VL. Exercise physiology: Nutrition, energy, and human performance. In. Exercise physiology: Nutrition, energy, and human performance: LWW; 2014, p 1088.

7. Powers SK, Howley ET. Exercise physiology (theory and application to fitness and performance). 9th Edition ed. New York, NY: McGraw-Hill; 2015.

phospholipid bilayer, provide structural integrity for cells but are not used as an energy source. **Steroids**, derived from dietary cholesterol, are components of cell membranes and are necessary for synthesizing sex hormones. Nutritional guidelines recommend that adults obtain 20% to 35% of their calories from fat[8].

Proteins are not a major energy source during exercise but can be used under certain conditions. To be used for energy, proteins must be converted to glucose through gluconeogenesis or to free fatty acids through lipogenesis in cases of severe energy depletion or starvation. Proteins are composed of **amino acids**, which can be broken down through deamination. There are 20 amino acids needed by the body to synthesize proteins, tissues, and enzymes, nine of which are essential and must be obtained from food. Proteins can also become intermediates in metabolism to help generate ATP. It is recommended that adults obtain 10% to 35% of their calories from protein[9].

Enzymes are biological catalysts that increase the speed of metabolic pathways without becoming part of the final product (Figure 3.6). Chemical reactions occur only when the reacting molecules have sufficient initial free energy, or activation energy, to start the reaction. Enzymes lower the activation energy required, thereby conserving energy and improving reaction time. Many enzymes facilitate the breakdown (catabolism) of chemical compounds. All enzymes are proteins that act upon a substrate to create a product. They are highly specific, interacting only with their designated substrate to form an enzyme-substrate (E-S) complex. This complex temporarily changes shape to facilitate the reaction, after which the enzyme returns to its original shape, remaining virtually unaltered. This process is known as the "induced fit" model of enzyme action. Enzymes rely on maintaining their correct conformation, which can be affected by temperature and pH. The major characteristics of enzymes are listed in Table 3.1.

Table 3.1 A summary of the major characteristics of enzymes

Major characteristics of enzymes
Proteins
Specific
Unaltered
Affected by temperature
Affected by pH
Facilitate the reaction

8. Powers SK, Howley ET. Exercise physiology (theory and application to fitness and performance). 9th Edition ed. New York, NY: McGraw-Hill; 2015.

9. Powers SK, Howley ET. Exercise physiology (theory and application to fitness and performance). 9th Edition ed. New York, NY: McGraw-Hill; 2015.

Other cellular constituents, such as ATP, can regulate enzyme activity. Enzymes can be inhibited through negative feedback, slowing the overall rate of the reaction or pathway. Rate-limiting enzymes, typically found early in the pathway, can be inhibited or stimulated. **Allosteric enzymes**, which bind to effectors, can either stimulate or inhibit enzyme activity at the active site. These enzymes are major regulators of metabolic pathways.

Classification of Enzymes

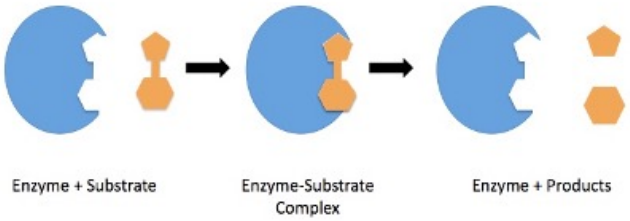


Figure 3.6 The enzyme-substrate complex mechanism of enzymes.

Enzymes play a crucial role in energy transfer and control the rate of free-energy release. Metabolic pathways that produce a product from a substrate typically involve multiple steps, each catalyzed by a specific enzyme with a specific function. Enzymes are named based on their role in rearranging, adding, or cleaving sub-molecules during a reaction.

- **Kinases:** These enzymes add a phosphate group to a molecule.
- **Dehydrogenases:** These enzymes remove hydrogen atoms, such as lactate dehydrogenase.
- **Oxidases:** These enzymes catalyze redox reactions involving oxygen.
- **Isomerases:** These enzymes rearrange molecular substances.

Most enzymes have names ending in "-ase." Additionally, many enzymes require other molecules called coenzymes or cofactors to function.

Coenzymes, also known as cofactors, are non-protein organic substances that assist enzymes. They act as temporary carriers of products and are often considered "helper molecules" in biochemical transformations. The availability of coenzymes can affect enzymatic function and the rate of metabolic reactions. Dietary coenzymes are derived from vitamins. Two important coenzymes in metabolism are **Nicotinamide Adenine Dinucleotide** (NAD+) and **Flavin Adenine Dinucleotide** (FAD). NAD+ is derived from niacin (vitamin B3), while FAD comes from riboflavin (vitamin B2). Both NAD+ and FAD are electron carriers essential for ATP production.

High-Energy Phosphates

High-energy phosphate molecules store potential energy within their chemical bonds, making them vital for energy use in the body. The most immediate source of energy for skeletal muscle contraction is

adenosine triphosphate (ATP), known as the universal energy donor. ATP can be broken down when energy is needed for cellular activities. ATP's middle-range energy potential allows other molecules to donate energy to create ATP from **adenosine diphosphate (ADP)** and **inorganic phosphate (Pi)**. ATP consists of an adenine molecule combined with a ribose (sugar) and three linked phosphates.

When ATP is combined with water (hydrolysis) and acted upon by the enzyme **ATPase**, the last phosphate group is cleaved, releasing approximately 7.3 kcal per mole of ATP under standard conditions [2]. This process reduces ATP to ADP and Pi. To regenerate ATP, a phosphate group is added to ADP in a process called phosphorylation, which requires a considerable amount of energy. Some ATP is generated independently of oxygen availability through substrate-level phosphorylation, while other ATP-producing reactions occur with the aid of oxygen through oxidative phosphorylation. ATP must be continuously synthesized as it is only stored for about 10 seconds in the body, necessitating various metabolic pathways to synthesize ATP from other molecules.

Creatine phosphate (CrP), also known as phosphocreatine (PCr), is another high-energy phosphate molecule stored in muscles in small amounts and used to quickly generate ATP. Creatine phosphate is depleted in less than 15 seconds of exercise but is resynthesized and stored during rest and recovery.

Chapter Summary

In this chapter, we explored the fundamental principles of bioenergetics, emphasizing its critical role in understanding how energy flows through living organisms. We discussed the two primary laws of bioenergetics, which govern energy conversion and transfer, and highlighted the importance of cellular structures such as the cell membrane, nucleus, and mitochondria in energy production. We delved into the metabolic pathways that convert carbohydrates, fats, and proteins into usable energy, focusing on the processes of glycolysis, lipolysis, and gluconeogenesis. The chapter also covered the classification and function of enzymes, including the roles of kinases, dehydrogenases, oxidases, and isomerases, as well as the significance of coenzymes like NAD+and FAD in facilitating biochemical reactions.

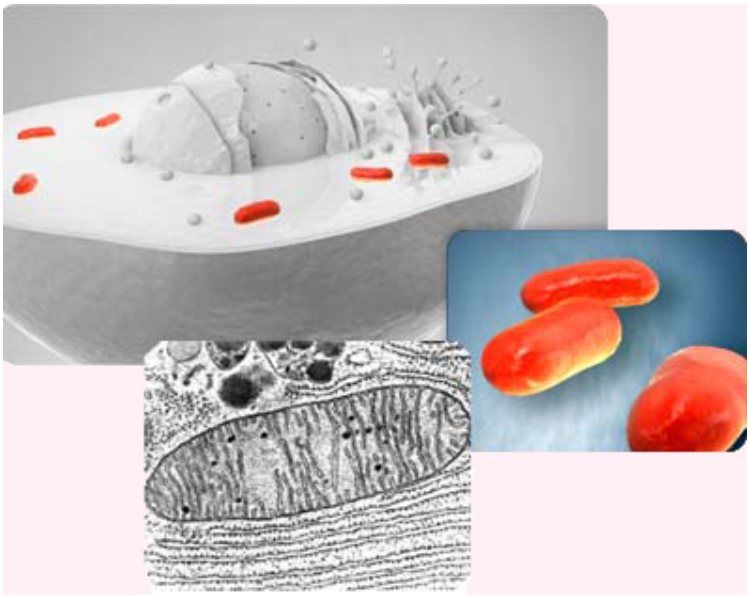
Additionally, we examined the role of high-energy phosphate molecules, particularly ATP and creatine phosphate, in storing and transferring energy within cells. Understanding these concepts is essential for comprehending how the body generates and utilizes energy, especially during physical exercise. By integrating these principles, we gain a deeper insight into the intricate processes that sustain life and enable physical activity, providing a solid foundation for further study in bioenergetics and exercise physiology.

Scholarly Questions

1. What is a substrate?
2. List 6 characteristics of enzymes.
3. What are the 3 substrates we use for fuel?
4. Basic Terms to Know with this section: bioenergetics, glycogen, glucose, metabolism, metabolic pathway, oxidation, reduction, redox reactions, creatine kinase, ATPase, enzyme, co-enzyme, mitochondria, and substrate.
5. What is the difference between anabolism and catabolism?
6. Know the basic structure of a muscle cell. What is the cell membrane called? The fluid portion of the cell? Which organelle is the most energy made? Where is the genetic material (DNA) of the cell located?
7. Can you name some high energy phosphates? Where is the potential energy stored?
8. Name two co-enzymes. How are they different than enzymes? How do they assist enzymes in biochemical reactions?
9. What is the chemical formula for glucose?
10. Approximately how long can ATP be stored?
11. Describe the roles of kinases, dehydrogenases, oxidases, and isomerases in metabolic pathways.

4.

THE BASIC ENERGY SYSTEMS



Transmission electron micrograph showing a mitochondrion (orange) inside a eukaryotic cell. The mitochondrion is enclosed by two membranes: an outer membrane and a highly folded inner membrane. These folds, called cristae, increase the surface area for energy production. Inside the inner membrane is the matrix, which contains enzymes for the citric acid cycle and mitochondrial DNA. This organelle is the primary site of ATP synthesis through oxidative phosphorylation, playing a central role in cellular energy metabolism.

Learning Objectives

- Describe the three basic energy systems: CrP-ATP, glycolysis, and mitochondrial respiration

(oxidative phosphorylation).

- Explain the process of ATP formation and its importance in muscle contraction.
- Identify the stages of carbohydrate metabolism and outline the key steps involved in glycolysis, conversion of pyruvate to acetyl-CoA, the TCA cycle, and the electron transport chain (ETC).
- Compare and contrast glycolysis and glycogenolysis, including their ATP yields and regulatory enzymes.
- Discuss the role of the phosphagen system in ATP production and its regulation by cellular constituents.
- Understand the significance of the electron transport chain in oxidative phosphorylation and the production of ATP.
- Explain the process of beta oxidation and its role in the metabolism of fatty acids to produce ATP.
- Summarize the contribution of protein metabolism to ATP production and the conditions under which it becomes significant.
- Analyze the relationship between carbohydrate, fat, and protein metabolism, highlighting the common intermediate, acetyl-CoA.
- Evaluate the efficiency of different substrates (carbohydrates, fats, and proteins) in ATP production and their utilization during various intensities of exercise.

The Basic Energy Systems

The formation of **adenosine triphosphate (ATP)** is crucial for cellular energy storage and release. Cells have a limited capacity to store ATP, approximately 8 mmol/kg, necessitating its continuous synthesis. During muscle contraction, the demand for ATP can surge by up to 100-fold, depleting resting ATP levels within 2-3 seconds of intense exercise[1]. Consequently, skeletal muscle exhibits precise biochemical control over metabolic pathways through enzymatic regulation. This regulation ensures the production of ATP to replenish resting stores and support muscle contraction. Skeletal muscle cells can generate ATP via three metabolic pathways, either individually or in combination, as depicted in Figure 4.1. These pathways are collectively known as the energy systems. The three energy systems responsible for ATP production are:

1. Robergs RA, Ghiasvand F, Parker D, The biochemistry of exercise-induced metabolic acidosis. Am J Physiol Regul Integr Comp Physiol, 2004. 287: p. R502-R516.

1. CrP-ATP or the Phosphagen system
2. Glycolysis
3. Mitochondrial Respiration

The phosphagen energy system and **glycolysis** are metabolic pathways that can function without oxygen, collectively known as anaerobic metabolism. In contrast, **mitochondrial respiration**, also referred to as the oxidative system or oxidative phosphorylation, requires oxygen and constitutes aerobic metabolism. The energy required for exercise is derived from the interplay of both anaerobic and aerobic pathways. Typically, high-intensity, short-duration activities rely more heavily on anaerobic energy production, whereas prolonged, low to moderate-intensity activities depend on ATP generated from aerobic sources. It is important to note that all three energy systems operate continuously to maintain ATP levels, regardless of oxygen availability. Therefore, these terms are somewhat imprecise. The energy systems should be viewed as three engines that are always active, adjusting their output based on the demands placed upon them. One never exclusively uses "aerobic" or "anaerobic" metabolism but rather shifts reliance among the systems depending on exercise intensity and duration. These energy systems share a common central pathway, such as glycolysis, and function simultaneously.

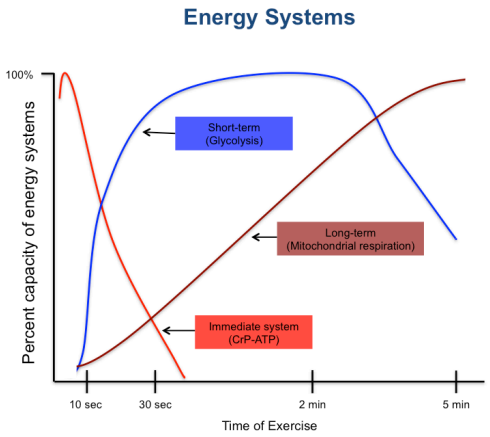


Figure 4.1 A line graph depicting the three basic energy systems (CrP-ATP, glycolysis, mitochondrial respiration) and the percent capacity of each system to generate ATP during 5 minutes of exercise.

CrP-ATP or the Phosphagen System

The phosphagen system is perhaps the simplest of the energy systems. It is the most immediate source of ATP and involves a series of coupled reactions to generate ATP. The phosphagen system operates by transferring phosphate groups to create ATP through two primary reactions: the creatine kinase reaction (CrP) and the adenylate kinase reaction. Cells store another high-energy phosphate molecule, creatine phosphate (CrP), which donates an inorganic phosphate (Pi) to adenosine diphosphate (ADP) to form ATP. Unlike ATP, CrP is not used directly for cellular work; its primary role is to regenerate ATP, ensuring a constant supply under resting conditions. Although the phosphagen system can regenerate ATP at high rates, the limited stores of CrP (approximately 26 mmol/kg wet weight) can be depleted in as little as 10 seconds[2].

The Creatine Kinase Reaction. The cellular store of creatine phosphate, also known as phosphocreatine (CrP), provides an almost immediate source of ATP. Reactions are often named after the

enzyme that catalyzes them; in this case, the creation of ATP from CrP is facilitated by the enzyme creatine kinase, hence the term creatine kinase reaction. This reaction synthesizes ATP from CrP, with creatine kinase acting as the rate-limiting enzyme of the phosphagen system. At the onset of exercise and during the initial seconds, CrP is broken down to produce ATP and creatine from ADP and a **proton (H+)**. Initially, this reaction alkalizes the cell by consuming a proton. A linear representation of the creatine kinase reaction is shown below:

$$\text{Creatine phosphate} + \text{ADP} \rightleftharpoons \text{Creatine} + \text{ATP}$$

During intense exercise, the creatine kinase reaction is driven to the right via the enzyme creatine kinase, resulting in the formation of ATP from creatine phosphate (CrP). In the body, this reaction consists of two coupled processes. The breakdown of CrP into creatine (Cr) and inorganic phosphate (Pi) is an exergonic reaction, which provides the energy needed for the endergonic synthesis of ATP from adenosine diphosphate (ADP), a proton (H+), and Pi. These coupled reactions help to delay acidosis during the initial seconds of intense exercise.

The Adenylate Kinase Reaction. Another high-energy phosphate molecule that can regenerate ATP is **adenosine monophosphate (AMP)**. The adenylate kinase reaction, illustrated below, generates ATP from two ADP molecules with the enzyme adenylate kinase. During intense exercise, this reaction is also driven to the right, increasing the production of AMP. AMP acts as an allosteric activator for the enzyme phosphorylase (involved in glycogenolysis) and phosphofructokinase (involved in glycolysis), thereby enhancing carbohydrate catabolism. Phosphorylase and phosphofructokinase are crucial enzymes for carbohydrate metabolism and will be discussed in detail later in the chapter.

$$2\ \text{ADP} \rightleftharpoons \text{ATP} + \text{AMP}$$

The AMP Deaminase Reaction. Under extreme acidic conditions, the purine nucleotide cycle facilitates the further breakdown of adenosine monophosphate (AMP) to help buffer acidosis with the enzyme, AMP deaminase. This process is known as the AMP deaminase reaction. In this reaction, AMP combines with water and a proton (H+) to produce inosine monophosphate (IMP) and ammonia (NH_4). It is important to note that ammonia is toxic to both cells and the central nervous system. The ammonia generated by this reaction is transported into the bloodstream, where it is metabolized by the liver, excreted by the kidneys, or lost through sweat. This reaction, shown below, highlights the production of ammonia as a byproduct.

$$\text{AMP} + H_2O + H^+ \rightarrow \text{IMP} + NH_4$$

ATP Hydrolysis and Synthesis Reactions. The phosphagen system heavily relies on coupled reactions involving ATP, specifically ATP hydrolysis (ATPase reaction) and ATP synthesis (ATP synthetase reaction). ATP hydrolysis involves the breakdown of ATP with water to release energy for cellular activities. The enzyme ATPase catalyzes this reaction, splitting ATP into adenosine diphosphate (ADP), inorganic phosphate (Pi), a

2. Robergs RA, Ghiasvand F, Parker D, The biochemistry of exercise-induced metabolic acidosis. Am J Physiol Regul Integr Comp Physiol, 2004. 287: p. R502-R516.

proton (H+), and free energy. This process is exergonic, meaning it releases free energy, which is then used for various cellular functions, such as muscle contraction. ATP hydrolysis and its products, highlighting the free energy utilized for cellular activities are shown below:

$$ATP + H_2O \rightarrow ADP + Pi + energy + H^+$$

The ATP hydrolysis reaction can also proceed in reverse, depending on the cell's needs. In this case, ATP is generated, and water is produced as a byproduct. This process is known as ATP synthesis. ATP is synthesized from adenosine diphosphate (ADP), inorganic phosphate (Pi), a proton (H+), and energy, facilitated by the enzyme ATP synthetase or synthase. ATP synthesis is an endergonic reaction, meaning it requires activation energy to proceed. This process is illustrated:

$$ADP + Pi + energy + H^+ \rightarrow ATP + H_2O$$

Regulation of the Phosphagen System. The phosphagen system is regulated by the concentration of cellular constituents. The presence of adenosine diphosphate (ADP) stimulates the phosphagen system, while the presence of cellular adenosine triphosphate (ATP) inhibits or prevents its reactions. The reactions within the phosphagen system are coupled, working together to create ATP during periods of high cellular demand and to store ATP as creatine phosphate (CrP) when ATP is abundant. The combined stores of ATP and CrP can sustain muscle energy needs for only 3 to 15 seconds during an all-out sprint. Beyond this duration, muscles must rely on other energy systems, such as glycolysis and mitochondrial respiration, for ATP generation[3].

Carbohydrate Metabolism

Glucose is a primary substrate for both exercise and resting metabolism. Typically, most carbohydrates used by skeletal muscle during exercise come from blood glucose. However, skeletal muscle can store up to 1 to 3 percent of its weight as glycogen, the storage form of glucose[4]. Upon complete oxidation, a single glucose molecule yields a net of 30 ATP. This complete oxidation occurs through the tricarboxylic acid (TCA) cycle and the electron transport chain. Understanding glucose metabolism is essential for exercise professionals, as it provides insights into the similarities between fat and protein metabolism. Carbohydrate metabolism consists of four stages:

Stage I: Glycolysis
Stage II: Conversion of pyruvate to acetyl-CoA
Stage III: TCA cycle
Stage IV: Electron transport chain (ETC) (Oxidative phosphorylation)

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3. Kenney LK, Wilmore JH, Costil DL, ed., Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

4. Guyton AC, and Hall JE, Textbook of Medical Physiology. 11th ed. 2006, Philadelphia, PA: Elsevier Saunders.

Stage I: Glycolysis

The phosphagen system has a limited capacity to generate ATP beyond the first 15 seconds of exercise. The second method of ATP production involves liberating energy from blood glucose, a process known as glycolysis. **Glycolysis** is an anaerobic metabolic pathway that does not require oxygen. Glycogen, the storage form of glucose in muscles, is broken down through a similar pathway called glycogenolysis.

Glycolysis, which means the splitting of sugar (glucose), occurs in the cytoplasm of the cell. Glucose, with the chemical formula C6H12O6, is arranged in a 6-carbon ring structure and serves as the substrate for glycolysis. This pathway consists of 10 enzymatically catalyzed steps. The purpose of glycolysis is to break down the 6-carbon glucose molecule into two 3-carbon pyruvate molecules, which are then shuttled to the mitochondria for complete oxidation. The reactions in glycolysis can be divided into two phases:

1. **Energy Investment Phase:** The first four steps, where 2 ATP molecules are invested in steps 1 and 3 to provide the necessary activation energy.
2. **Energy Generation Phase:** Steps 5-10, where 4 ATP molecules are generated in steps 7 and 10 from a single glucose molecule.

The net yield of glycolysis (Stage I of carbohydrate metabolism) includes 2 water H_2O molecules, 2 pyruvate molecules, 2 ATP molecules, and 2 $NADH+H^+$ molecules. The rate-limiting enzyme of glycolysis is phosphofructokinase (PFK), an allosteric enzyme that can change its conformation upon binding of effectors such as ATP or ADP. Glycolysis occurs in the sarcoplasm of muscle cells and provides a rapid means of generating ATP anaerobically. Each $NADH+H^+$ produced in the cytoplasm results in the generation of 1.5 ATP equivalents.

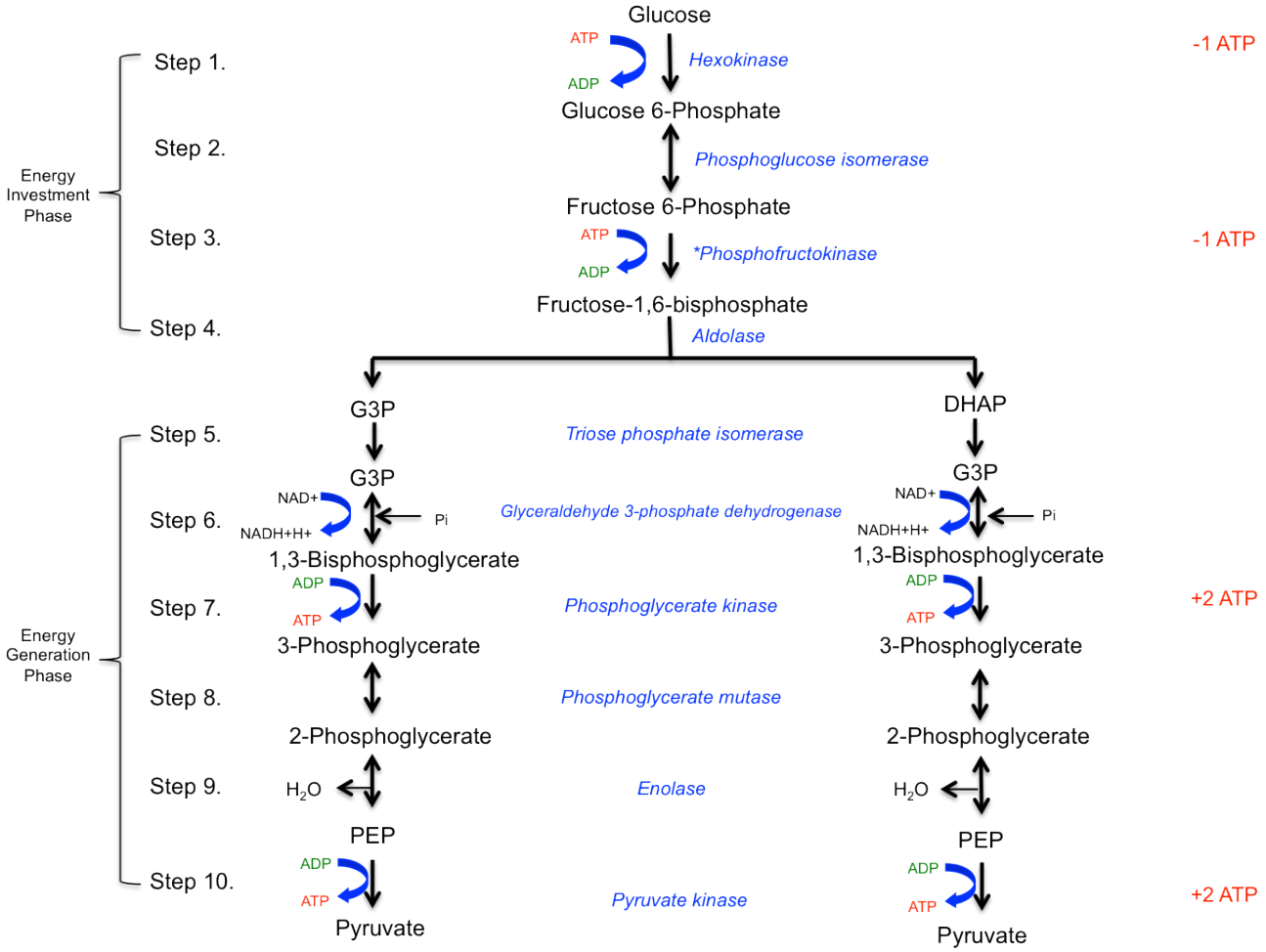

Figure 4.2 Glycolysis. All enzymes are shown in blue text and the energy investment and generation phases are indicated with brackets. Tall of the ATP invested and generated is shown in red text on the right side of the pathway.

Table 4.1 The net yield of glycolysis (stage I of carbohydrate metabolism) from one glucose molecule.

The net yield of glycolysis
2 ATP
2 H_2O
2 $NADH+H^+$
2 Pyruvate

A simplified version of glycolysis is depicted in Figure 4.3, highlighting the major regulatory enzyme, phosphofructokinase (PFK), and the ATP tally. This figure provides a clear visual representation of the glycolytic pathway, emphasizing the key steps and the net production of ATP.

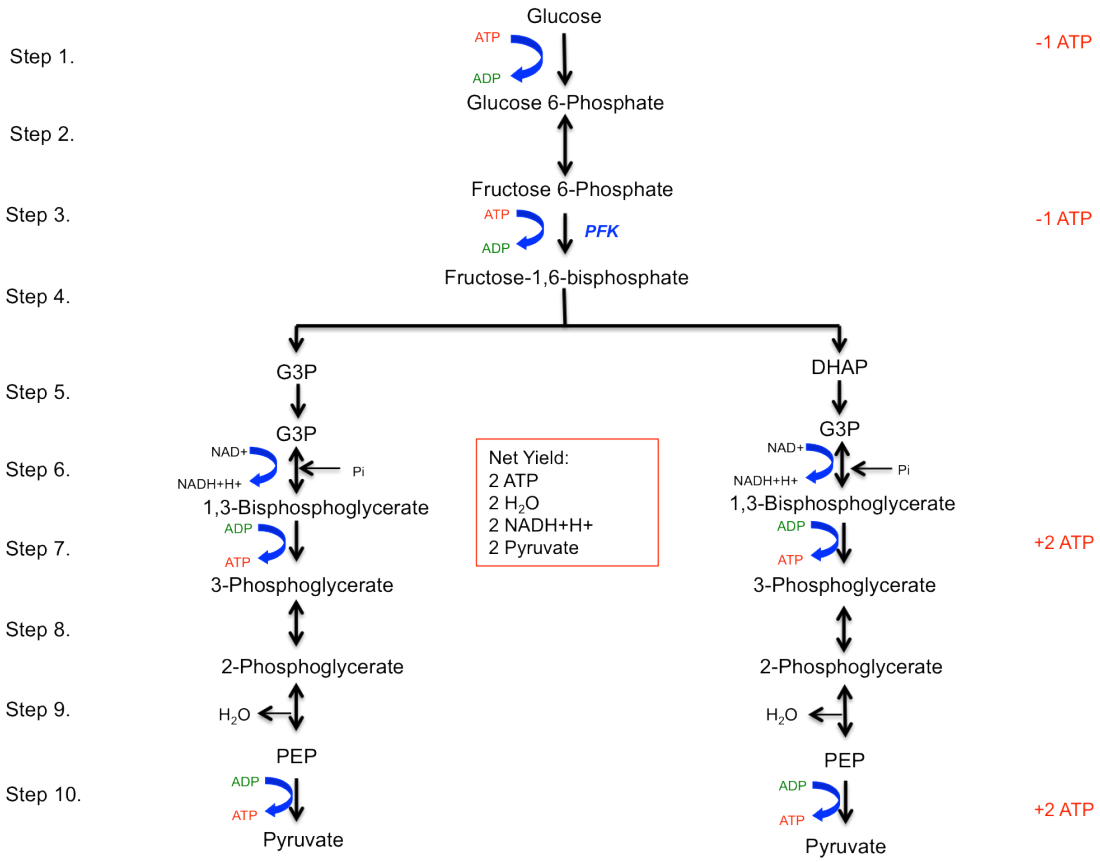

Figure 4.3 The ten steps of glycolysis and the net yield.

Glycogenolysis

Glycogenolysis is the metabolic pathway in which stored muscle glycogen is used as a substrate instead of blood glucose. This pathway involves the breakdown of glycogen into pyruvate and is very similar to glycolysis. However, the first step of glycogenolysis does not require an investment of ATP. Instead, glycogen is converted to glucose 1-phosphate by the enzyme phosphorylase. Phosphorylase adds an inorganic phosphate to the carbon structure, which is then converted to glucose 6-phosphate. From this point, the metabolic pathway follows the same steps as glycolysis. Consequently, the complete oxidation of glycogen yields a net ATP production of 31 ATP. Figure 4.4 illustrates the steps in glycogenolysis that differ from glycolysis.

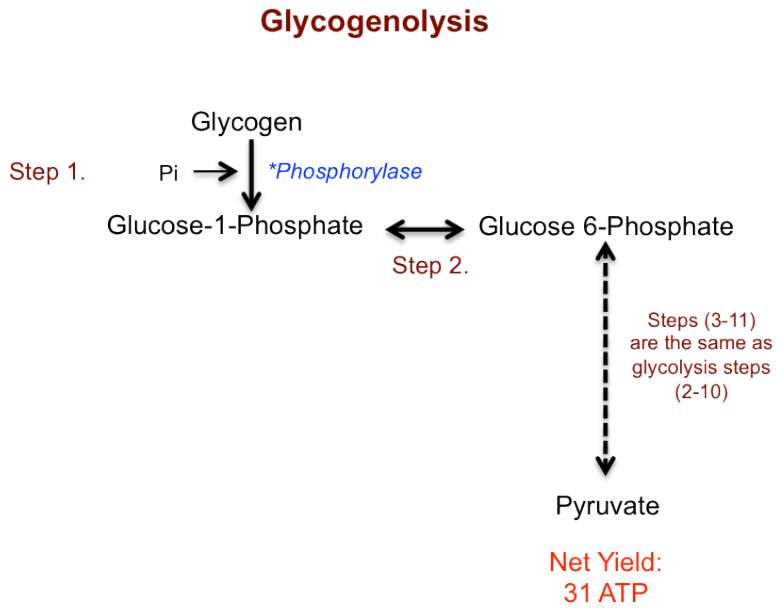

Figure 4.4 The first two steps of glycogenolysis differ from glycolysis but are the same following conversion of the substrates to glucose 6-phosphate.

Comparison of Glycogenolysis and Glycolysis. Figure 4.5 provides a comparison of glycogenolysis and glycolysis. One key difference is that glycogenolysis does not require an ATP investment in the first step. As a result, the net ATP yield from the complete oxidation of glycogen is 31 ATP, compared to the 30 ATP yield from glycolysis. This comparison highlights the efficiency of glycogenolysis in energy production.

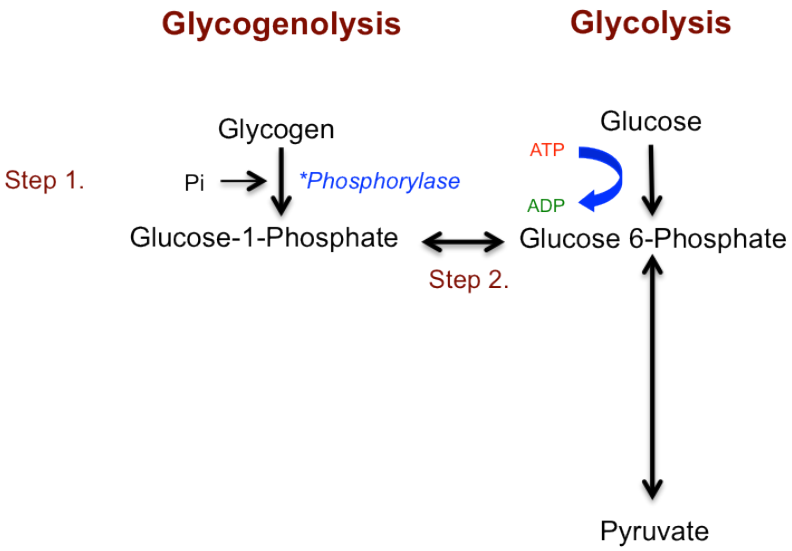

Figure 4.5 Comparison of glycogenolysis and glycolysis. Glycogenolysis does not invest 1 ATP during step 1 and 2. Glucose 1-phosphate is converted to Glucose 6-phosphate and then the following steps are the same as the glycolytic pathway. Thus, glycolysis has an ATP yield of 30 ATP and glycogenolysis has an ATP yield of 31.

Mitochondrial Respiration (Oxidative Phosphorylation)

Mitochondria, illustrated in Figure 4.6, are often referred to as the "powerhouses" of the cell because they are the primary site of ATP production. Mitochondria are distributed throughout the cytoplasm of cells, with their number per cell ranging from fewer than a hundred to several thousand, depending on the cell's energy requirements[5]. Mitochondria can also vary in size and shape. The basic structure of a mitochondrion, shown in Figure 4.11, consists of two lipid bilayer-protein membranes: an outer membrane and an inner membrane. The space between these membranes, known as the intermembrane space, is crucial for creating a proton gradient during the electron transport chain (ETC).

5. Guyton AC, and Hall JE, Textbook of Medical Physiology. 11th ed. 2006, Philadelphia, PA: Elsevier Saunders.

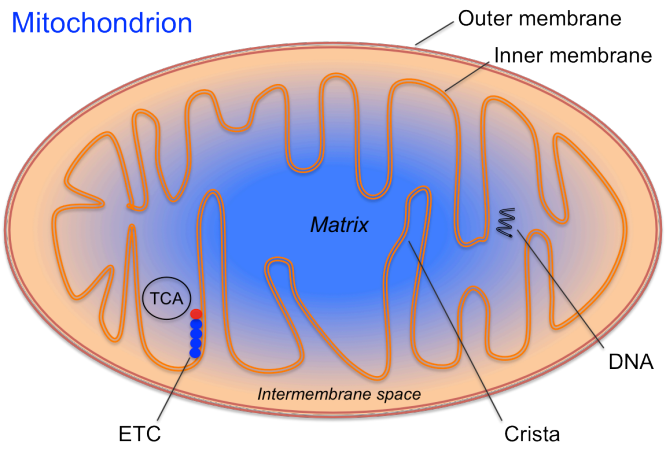

Figure 4.6 The mitochondrion is an organelle inside of the cell and is where mitochondrial respiration (oxidative phosphorylation) occurs.

The inner membrane is characterized by folds called cristae, which extend into the mitochondrial matrix. The matrix, the inner cavity of the mitochondrion, contains a high concentration of enzymes responsible for nutrient oxidation, such as those involved in the tricarboxylic acid (TCA) cycle. Additionally, mitochondria possess their own DNA, enabling them to self-replicate and produce proteins as needed to meet the cell's ATP demands.

Several metabolic pathways within the mitochondria complete the oxidation of substrates. This chapter will discuss three key metabolic processes that occur within the mitochondria:

1) Conversion of Pyruvate to Acetyl-CoA

2) TCA Cycle

3) Electron Transport Chain (ETC)

Stage II: Conversion of Pyruvate to Acetyl-CoA

To complete the oxidation of a single glucose molecule, the two pyruvate molecules formed during glycolysis must undergo further catabolism. This process converts pyruvate into acetyl-coenzyme A (acetyl-CoA), often referred to as the intermediate molecule of metabolism because it is a common product of the catabolism of proteins, fats, and carbohydrates. Pyruvate molecules produced in glycolysis are transported into the mitochondria. Once inside the mitochondrial matrix, pyruvate is converted into acetic acid, releasing a carbon dioxide (CO_2) molecule as a byproduct.

The **conversion of pyruvate to acetyl-CoA** (Stage II of carbohydrate metabolism) occurs within the mitochondria and involves a two-step process, as shown in Figure 4.7. In the first step, pyruvate (a 3-carbon molecule) is converted into acetic acid (a 2-carbon molecule), releasing CO_2. In the second step, acetic acid is converted into acetyl-CoA by coenzyme A (CoA). During this reaction, NAD+ oxidizes acetic acid by removing hydrogen, resulting in the reduction of NAD+ to NADH+H^+.

The net yield from the conversion of pyruvate to acetyl-CoA (Stage II of carbohydrate metabolism) from a single glucose molecule includes 2 CO_2, 2 NADH+H^+, and 2 acetyl-CoA molecules, as summarized in Table 4.2.

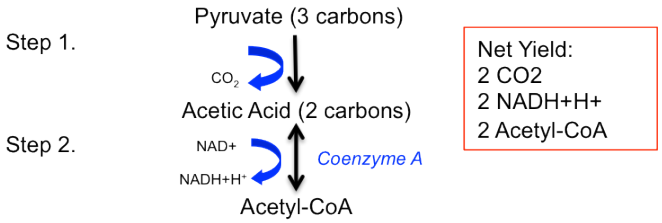

Figure 4.7 Conversion of pyruvate to acetyl-CoA and the net yield.

Table 4.2 The net yield of conversion of pyruvate to acetyl Co-A (stage II of carbohydrate metabolism) from 1 glucose molecule.

The net yield of conversion of pyruvate to acetyl-CoA
2 CO_2
2 $NADH+H^+$
2 Acetyl-CoA

Stage III: TCA Cycle

The **tricarboxylic acid (TCA) cycle**, also known as the citric acid cycle or Krebs cycle, is a series of enzyme-catalyzed chemical reactions that are essential for aerobic respiration. This cycle completes the oxidation of carbohydrates, fats, and proteins within the mitochondrial matrix. Named after Hans Krebs, the 1953 Nobel Prize recipient for his research on these reactions, the TCA cycle is crucial for the complete oxidation of glucose, which does not occur until acetyl-CoA is degraded to carbon dioxide (CO_2) and hydrogen atoms. The hydrogen atoms released from acetyl-CoA are subsequently oxidized in the electron transport chain (ETC), releasing significant amounts of energy to form ATP[6].

Entry into the TCA cycle requires the breakdown of carbohydrates, fats, or proteins into acetyl-CoA. Focusing on the formation of acetyl-CoA from pyruvate, the TCA cycle involves eight steps, beginning with acetyl-CoA (a two-carbon molecule) and ending with the regeneration of oxaloacetate (a four-carbon molecule). Initially, acetyl-CoA combines with oxaloacetate to form citrate (a six-carbon molecule). This is followed by a series of reactions that regenerate oxaloacetate and produce two molecules of CO_2. Due to the cyclic nature of the TCA cycle, oxaloacetate is not a final product but is continuously combined with acetyl-CoA to restart the cycle (Figure 4.8).

Since two acetyl-CoA molecules are formed from one glucose molecule during Stage II of carbohydrate

6. Guyton AC, and Hall JE, Textbook of Medical Physiology. 11th ed. 2006, Philadelphia, PA: Elsevier Saunders.

metabolism, this results in two turns of the TCA cycle. Each turn of the TCA cycle yields one ATP (via GTP), three $NADH+H^+$, one $FADH_2$, and two CO_2 molecules. Therefore, the net yield from one glucose molecule (Table 4.3) is double the yield of a single turn. Each $NADH+H^+$ produced in the TCA cycle will yield 2.5 ATP equivalents in the ETC, and each $FADH_2$ will yield 1.5 ATP equivalents. The rate-limiting enzyme of the TCA cycle is isocitrate dehydrogenase.

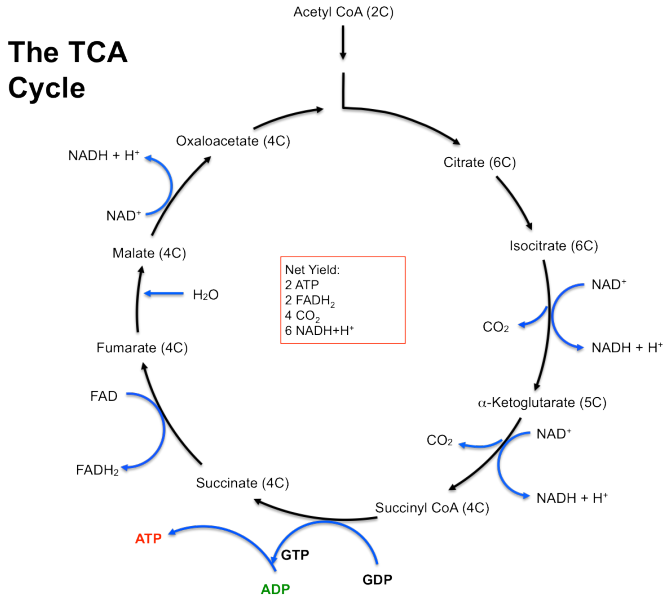

Figure 4.8 The reactions and the net yield of the TCA cycle, also known as the Krebs cycle and the Citric Acid cycle.

As discussed in Chapter 3, hydrogen atoms consist of a proton and an electron. When hydrogen is transferred to NAD+ and FAD, these electron carriers also transport protons. Following the TCA cycle, a single glucose molecule is completely oxidized through a series of redox reactions, where NAD+ and FAD are reduced to $NADH+H^+$ and $FADH_2$, respectively. The $NADH+H^+$ and $FADH_2$ produced in Stages II and III of carbohydrate metabolism shuttle their hydrogens to the electron transport chain (ETC), where they are oxidized back to NAD+ and FAD. Both $NADH+H^+$ and $FADH_2$ return to their oxidized forms by releasing electrons to the electron carriers within the ETC.

Table 4.3 The net yield of the TCA cycle (stage III of carbohydrate metabolism) from one glucose molecule.

Net Yield of the TCA cycle (remember: 2 acetyl-CoA molecules)
2 ATP (by way of GTP)
6 $NADH+H^+$
2 $FADH_2$
4 CO_2

The origin of $NADH+H^+$ determines the number of ATP equivalents produced during the complete oxidation of glucose. Each $NADH+H^+$ created in the cytoplasm yields 1.5 ATP equivalents, while $NADH+H^+$ produced inside the mitochondria yields 2.5 ATP equivalents. Additionally, each $FADH_2$

molecule produced in the mitochondria yields 1.5 ATP equivalents. The difference in ATP yield is due to the double membrane structure of the mitochondria. $NADH+H^+$ created in the cytoplasm must transfer its hydrogen into the mitochondria because it cannot cross the double membrane barrier. This transfer is facilitated by a "shuttle" mechanism that transfers hydrogen from $NADH+H^+$ to a FAD molecule inside the mitochondria, reducing FAD to $FADH_2$, which then carries the hydrogen to the ETC. Consequently, $NADH+H^+$ created in the cytoplasm has the same ATP yield (1.5 ATP) as $FADH_2$.

The mechanism by which hydrogen carried by $NADH+H^+$ and $FADH_2$ is used to generate ATP will be further explained in the ETC section. The total ATP produced from one glucose molecule during carbohydrate metabolism, including ATP equivalents, is summarized and organized by stage in Table 4.4.

Table 4.4 Total ATP produced from one glucose molecule during carbohydrate metabolism.

Total ATP production from one glucose molecule (net yields)	ATP yield
Stage I. Glycolysis:	
ATP	2
2 $NADH+H^+ \Rightarrow$ 2 $FADH_2$ (to ETC)	3
Stage II. Conversion of pyruvate to acetyl CoA:	
2 $NADH+H^+$ (to ETC)	5
Stage III. TCA cycle (remember: 2 cycles):	2
ATP (at one site)	15
$NADH+H^+$ at three steps (to ETC)	3
$FADH_2$ at one step (to ETC)	
Total ATP from one molecule of glucose:	*30 ATP*

Electron Transport Chain (Oxidative Phosphorylation)

The aerobic production of ATP, known as oxidative phosphorylation, occurs within the mitochondria. The pathway responsible for this process is the electron transport chain (ETC), where the majority of ATP is synthesized. The theory of the electron transport chain was proposed by British physiologist Peter Mitchell in 1961 but was not widely accepted until 1978. The mechanism explaining the aerobic formation of ATP is known as the chemiosmotic hypothesis. This hypothesis describes the transfer of electrons along a chain of proteins, releasing energy used to "pump" protons through the inner mitochondrial membrane. This creates

an ion gradient and potential energy within the intermembrane space, which can then be harnessed to recombine inorganic phosphate (P_i) with adenosine diphosphate (ADP) to form ATP. At the end of the chain, oxygen combines with the electrons and two protons to form water, which is why oxygen is essential as the final electron acceptor in the ETC.

Oxidative phosphorylation results from a complex interaction between the TCA cycle and the ETC. The electron carriers $NADH+H^+$ and $FADH_2$ produced in these pathways play a crucial role in ATP synthesis within the ETC. The ETC is located in the inner mitochondrial membrane and consists of four protein complexes, known as the cytochrome chain, two mobile carriers, and ATP synthase. The ETC is illustrated in Figure 4.9. The cytochrome chain includes transmembrane proteins named complex I (NADH dehydrogenase), complex II (succinate dehydrogenase), complex III (cytochrome c reductase), and complex IV (cytochrome c oxidase). The mobile carriers are coenzyme Q10 (mobile carrier Q) and the cytochrome c complex (mobile carrier C). Finally, the enzyme ATP synthase (also known as ATP synthetase) is located at the end of the cytochrome chain and catalyzes the formation of ATP from ADP and Pi. Cytochrome oxidase (complex IV) is the rate-limiting enzyme of the ETC.

The electron transport chain (ETC) involves a series of redox reactions that generate potential energy to synthesize ATP. The process begins with the arrival of $NADH+H^+$ from Stage II (conversion of pyruvate to acetyl-CoA) or Stage III (TCA cycle) of carbohydrate metabolism. $NADH+H^+$ donates two electrons to Complex I of the ETC and is oxidized to NAD+, with its protons being deposited into the matrix. As electrons enter Complex I, a redox reaction occurs, creating a pump that translocates four protons from the matrix into the intermembrane space of the mitochondria.

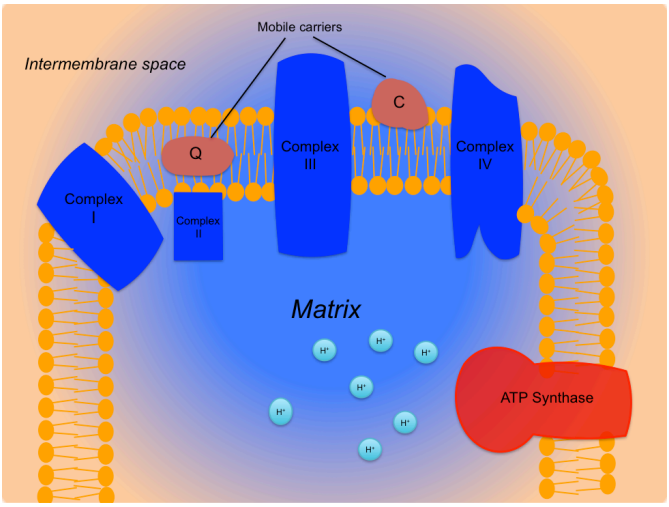

Figure 4.9 The electron transport chain is made up of four protein complexes; complex I (NADH dehydrogenase), complex II (succinate dehydrogenase), complex III (cytochrome c reductase), complex IV (cytochrome c oxidase): two mobile carriers; Q (coenzyme Q10) and C (cytochrome c complex): and ATP synthase. Protons (H+) are represented as blue circles.

The electrons are then transferred to mobile carrier Q, and NAD+ returns to its original source to pick up more hydrogen. The electrons move from mobile carrier Q to Complex III, where another redox reaction occurs, pumping four more protons into the intermembrane space. The electrons are then shuttled from Complex III to Complex IV by mobile carrier C. Upon reaching Complex IV, a redox reaction pumps two additional protons into the intermembrane space. Complex IV, now in its reduced form, transfers the electrons to oxygen, the final electron acceptor. Oxygen combines with the electrons and two protons from the matrix to form water (H_2O), known as "metabolic water," which accounts for 10-20% of total daily fluid intake. Using

$NADH+H^+$ as the electron donor results in ten protons being pumped into the intermembrane space.

A similar process occurs with $FADH_2$ as the electron donor. $FADH_2$ donates two electrons to Complex II, is oxidized to FAD, and releases its protons into the matrix. Complex II passes the electrons to mobile carrier Q, continuing down the ETC towards Complex IV. This process bypasses Complex I, resulting in only six protons being pumped through the chain.

The protons in the intermembrane space create an electrochemical gradient, forming potential energy. This gradient, with a higher proton concentration in the intermembrane space than in the matrix, activates ATP synthase. Protons flow through ATP synthase, causing a rotary action that generates enough free energy to phosphorylate ADP, synthesizing ATP. For every four protons that flow through ATP synthase, one ATP is created. Therefore, each $NADH+H^+$ produced in the mitochondria yields 2.5 ATP, and each $FADH_2$ yields 1.5 ATP[7].

In summary, the ETC is where the greatest amount of ATP is synthesized. It involves the oxidation of $NADH+H^+$ and $FADH_2$ and the phosphorylation of ADP by ATP synthase, facilitating oxidative phosphorylation and aerobic metabolism. Table 4.4 summarizes the ATP yield from one glucose molecule.

Beta Oxidation (Oxidation of Fatty Acids)

Fats are also utilized in mitochondrial respiration to create ATP during exercise. Muscle and liver glycogen stores provide approximately 2,500 kcal of energy, while fat stored in muscle fibers and fat cells can supply 70,000 to 75,000 kcal, even in a lean adult[8]. Fats are stored as triglycerides and broken down by the enzyme hormone-sensitive lipase into free fatty acids and glycerol, a process called lipolysis[9]. Free fatty acids released into the blood can enter muscle fibers for oxidation. A triglyceride consists of one glycerol molecule and three fatty acids, with most triglycerides stored in adipose tissue. Limited quantities are stored in muscle cells, providing an intramuscular source of free fatty acids.

Fat is an excellent storage fuel because it is stored dry, without excess water, unlike glycogen, which is diluted with water. Fat yields about 9.13 kcal/g and contains many oxidizable carbons and hydrogen. Fat stores are substantial compared to glycogen and can last for weeks, even with heavy exercise.

Fatty acids, composed of long carbon chains, must be broken down into acetyl-CoA through beta oxidation to be used as fuel. **Beta oxidation** involves a series of reactions that break down fatty acids into

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7. Powers SK, and Howley ET, Exercise Physiology (Theory and Application to Fitness and Performance). 9th Edition ed. 2015, New York, NY: McGraw-Hill.

8. Kenney LK, Wilmore JH, Costil DL, ed., Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

9. Haff GG, Triplett NT, ed., Essentials of strength training and conditioning, 4th edition/National Strength and Conditioning Association. 2016, Human Kinetics: Champaign, IL.

pairs of carbons, forming acetyl-CoA and hydrogen protons. Acetyl-CoA enters the TCA cycle, and the hydrogen atoms are carried by $NADH+H^+$ and $FADH_2$ to the ETC. Each acetyl-CoA produced by beta oxidation generates 3 $NADH+H^+$, 1 $FADH_2$, and 1 ATP (from GTP) per acetyl-CoA molecule.

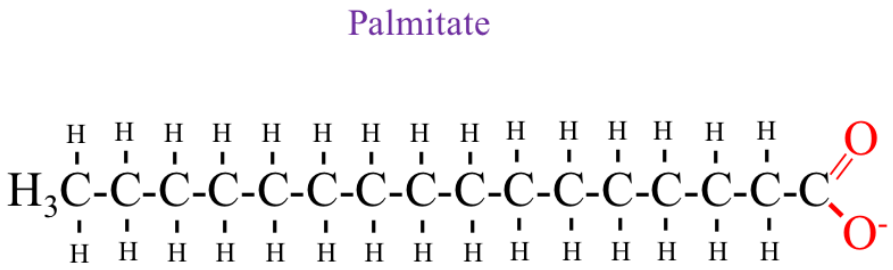

Figure 4.10 Palmitate is a 16-Carbon fatty acid chain commonly used in metabolism. The molecule consists of a straight hydrocarbon chain with 15 methylene (–CH^2–) groups and a terminal carboxyl group (–COOH). Palmitate is a key substrate in β-oxidation, where it is broken down in the mitochondria to generate acetyl-CoA, $NADH+H^+$, and $FADH^2$, contributing to ATP production through the TCA cycle and oxidative phosphorylation.

ATP Production from Fatty Acids. There are various forms of fat, and the amount of ATP produced depends on the specific fatty acid being oxidized. For example, consider palmitate, a 16-carbon fatty acid chain illustrated in Figure 4.10. Theoretically, 106 ATP molecules can be produced from the oxidation of one palmitate molecule. During beta oxidation, palmitate is cleaved seven times to yield eight acetyl-CoA molecules. A helpful equation shown below shows how the number of cleavages required for any fatty acid length is mathematically expressed:

Number of times to cleave = (number of carbons / 2) – 1

To initiate beta oxidation, 2 ATP molecules are required to activate the fatty acid (note: 1 ATP is used for activation, but since it is hydrolyzed to AMP, this is equivalent to 2 ATP). Once activated, the fatty acid does not need to be reactivated. The first reaction, following the metabolism of acetyl-CoA in the TCA cycle, yields 12 ATP. The remaining acetyl-CoA molecules yield 14 ATP each until the last four carbons of the fatty acid chain. The last four carbons yield 4 ATP from beta oxidation and 10 ATP from each acetyl-CoA oxidized in the TCA cycle, totaling 24 ATP. The carboxylate ending of the palmitate molecule decreases the ATP yield of the last four carbons. In total, the complete oxidation of one 16-carbon palmitate molecule yields approximately 106 ATP. This demonstrates the significant capacity of fat oxidation for ATP synthesis compared to carbohydrate and protein oxidation[10].

The advantage of having more carbon and hydrogen atoms in free fatty acids than in glucose is that more

10. Haff GG, Triplett NT, ed., Essentials of strength training and conditioning, 4th edition/National Strength and Conditioning Association. 2016, Human Kinetics: Champaign, IL.

acetyl-CoA is formed from fat metabolism, providing more hydrogens for the ETC. Although fat provides more kilocalories of energy per gram than carbohydrate, fat oxidation requires more oxygen. Oxygen delivery is limited by the oxygen transport system, making carbohydrate the preferred substrate during high-intensity exercise[11]. During high-intensity exercise, the maximum rate of ATP production from fat oxidation is insufficient to match ATP utilization, explaining the reduction in an athlete's pace when carbohydrate stores are depleted, and fat becomes the primary fuel source[12].

Protein Oxidation (Metabolism)

Protein is not a major fuel source during exercise but can be broken down into amino acids through various metabolic processes. These amino acids are converted into glucose (**gluconeogenesis**), pyruvate, acetyl-CoA, or TCA cycle intermediates. Proteins contribute 3% to 18% of energy requirements during prolonged activity, but their contribution to ATP production is minimal during short-term exercise[13]. The major amino acids oxidized in skeletal muscle are branched-chain amino acids (leucine, isoleucine, and valine), along with alanine, aspartate, and glutamate[14]. When degraded, amino acids are eliminated through the formation of urea and ammonia. Ammonia is toxic to cells and is associated with muscle fatigue[15].

The relationship between protein, carbohydrate, and fat metabolism is illustrated in Figure 4.11. This relationship highlights that metabolic pathways converge at acetyl-CoA, a common metabolic intermediate. Carbohydrates, fats, and most proteins used for energy are converted to acetyl-CoA, which then enters the TCA cycle for complete oxidation.

11. Kenney LK, Wilmore JH, Costil DL, ed., Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

12. Kenney LK, Wilmore JH, Costil DL, ed., Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

13. Brooks G, Amino acid and protein metabolism during exercise and recovery. Med Sci Sports Exerc, 1987. 19: p. S150-S156.

14. Graham TE, Rush JWE, MacLean DA, Skeletal muscle oxidative enzyme enhancement with endurance training. Exercise Metabolism, ed. S.L. Hargreaves M. 2006, Champaign, IL: Human Kinetics. 41-72.

15. Haff GG, Triplett NT, ed., Essentials of strength training and conditioning, 4th edition/National Strength and Conditioning Association. 2016, Human Kinetics: Champaign, IL.

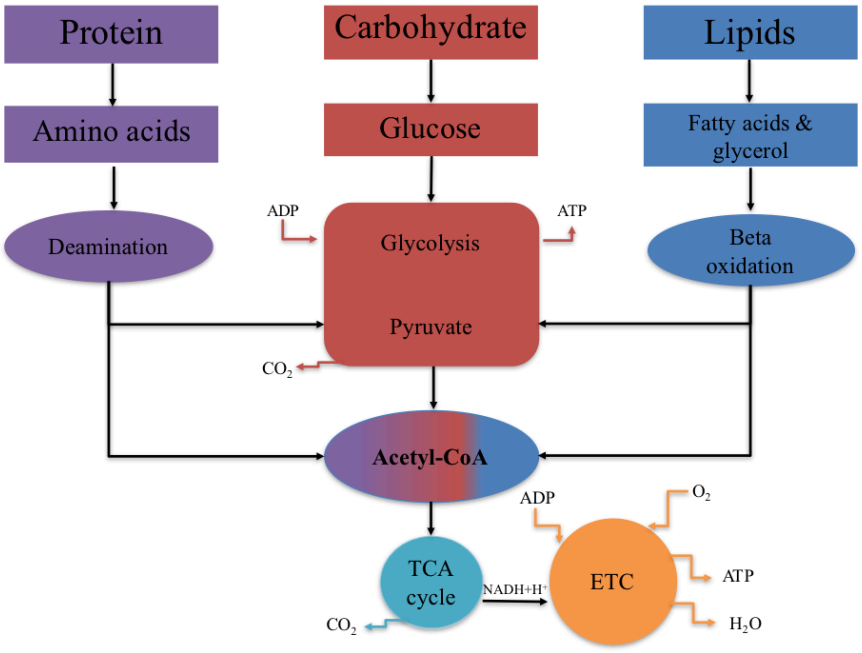

Figure 4.11 The relationship between CHO, FAT, and PROTEIN metabolism. The common metabolic intermediate is acetyl CoA.

When protein is combusted in a laboratory setting, it yields 5.65 kcal/g. However, within the body, energy must be expended to convert nitrogen to urea during protein metabolism, resulting in an energy yield of approximately 4.1 kcal/g[16].

Summary of Substrate Metabolism

The ability to produce muscle contraction depends on ATP synthesis, which is generated through the metabolism of carbohydrates, fats, and, in some cases, proteins. These substrates are broken down through catabolism in three energy systems: the CrP-ATP system, glycolysis, and mitochondrial respiration (oxidative phosphorylation). Carbohydrate metabolism, highlighted in this chapter, is discussed in four stages:

1. Glycolysis
2. Conversion of Pyruvate to Acetyl-CoA
3. TCA Cycle
4. Electron Transport Chain (ETC)

16. Kenney LK, Wilmore JH, Costil DL, ed., Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

The CrP-ATP system and glycolysis occur in the cytosol, while oxidative phosphorylation takes place within the mitochondria. Under aerobic conditions, carbohydrates and fats are reduced to the common intermediate acetyl-CoA, which then enters the TCA cycle for complete oxidation. The hydrogens removed during redox reactions are utilized by the ETC, where the majority of ATP is generated.

Table 4.5 The factors known to affect rate-limiting enzyme activity. The common stimulator of metabolism is ADP. The common inhibitor of metabolism is ATP.

Pathway	Rate-limiting enzyme	Stimulators	Inhibitors
Phosphogen	Creatine Kinase	ADP	ATP
Glycolysis	PFK	AMP, ADP, Pi, decrease in pH	ATP, Creatine Phosphate, Citrate, increase in pH
TCA Cycle	Isocitrate dehydrogenase	ADP, Ca2+, NAD+, ADP, Pi	ATP, NADH+H+
Electron Transport Chain	Cytochrome oxidase	ADP, Pi	ATP

Chapter Summary

In this chapter, we explored the fundamental processes of energy metabolism essential for muscle contraction and overall cellular function. We began by examining the three primary energy systems: the CrP-ATP system, glycolysis, and mitochondrial respiration (oxidative phosphorylation). Each system plays a crucial role in ATP production, with specific pathways and regulatory mechanisms. Carbohydrate metabolism was also discussed, detailing its four stages: glycolysis, conversion of pyruvate to acetyl-CoA, the TCA cycle, and the electron transport chain (ETC). We highlighted the differences between glycolysis and glycogenolysis, emphasizing their ATP yields and regulatory enzymes. The chapter also covered the phosphagen system's role in rapid ATP production and its regulation by cellular constituents.

The electron transport chain was discussed in depth, illustrating its importance in oxidative phosphorylation and ATP synthesis. We also explored beta oxidation, explaining how fatty acids are metabolized to produce ATP, and the significant energy yield from fat oxidation compared to carbohydrates and proteins. Finally, we touched on protein metabolism, noting its contribution to ATP production during prolonged activity and the conditions under which it becomes significant. The chapter concluded by analyzing the interconnectedness of carbohydrate, fat, and protein metabolism, with acetyl-CoA serving as a common metabolic intermediate.

Overall, this chapter provided a comprehensive understanding of the biochemical pathways involved in energy metabolism, highlighting their relevance to exercise physiology and cellular energy production.

Scholarly Questions

1. Identify the rate-limiting enzymes for the CrP-ATP system, glycolysis, the TCA cycle, and the ETC.
2. List the three energy systems that supply ATP.
3. Which energy system is the most immediate? Which system is utilized for long-duration exercise?
4. How long can ATP be stored in the body?
5. What is the chemical formula for glucose?
6. Define the following terms: glycogen, glucose, metabolism, glycogenolysis, gluconeogenesis, metabolic pathway, glycolysis, creatine kinase, ATPase, and PFK.
7. Describe the process where a phosphate is cleaved from the ATP molecule with water. What enzyme catalyzes ATP hydrolysis?
8. Which energy system is used for long-term energy? What metabolic pathways occur in the mitochondria?
9. What is the common metabolic intermediate?
10. What is the preferred substrate (carbohydrate, fat, or protein) for energy in the body, and why?
11. What is the total ATP yield from the metabolism of one glucose molecule? What about glycogen?
12. How many steps are there in glycolysis? In which part of the cell does glycolysis occur?
13. What is a hydrogen atom composed of?
14. Define oxidation and reduction.
15. Explain the function of the coenzyme carriers NAD+ and FAD. Is there a difference between NAD+ function in the cytosol and the mitochondria?
16. How many net ATP are produced in glycolysis?
17. Which energy system can produce ATP both aerobically and anaerobically?
18. What are the four stages of carbohydrate metabolism?
19. How many pyruvate molecules are produced from one glucose molecule?
20. Draw and label the structure of a mitochondrion. What metabolic processes occur inside the mitochondrion?
21. Name the protein complexes in the ETC. How many are there?
22. Diagram all four stages of carbohydrate metabolism and write out the ETC in a complete

essay. Tally the total ATP production from one glucose molecule.

23. What is beta oxidation? How many ATP are produced from a 16-carbon fatty acid? An 18-carbon fatty acid?
24. Can protein be used to create ATP? What must protein be converted to in order to create ATP (hint: common intermediate and ?).

5.

METABOLIC ADAPTATIONS TO EXERCISE TRAINING

French 100 meter runner Christine Arron, a retired track and field sprinter, during her first round heat at the World Athletics Championships on August 26, 2007, in Osaka. In July 2013, she was the world's fifth-fastest female 100-meter sprinter (10.73 sec) and holds the European record for this distance.

Learning Objectives

- Define muscle fatigue and differentiate between central and peripheral fatigue.
- List and explain the primary causes of muscle fatigue, including energy delivery, metabolic by-products, heat production, contractile mechanism failure, and neuromuscular control alterations.
- Discuss the role of lactate production in buffering hydrogen ions during exercise.
- Explain the concept of metabolic acidosis and its impact on muscle performance.
- Describe the lactate threshold and its significance in endurance performance.
- Explain the hypotheses for the lag in oxygen utilization at the onset of exercise.
- Define excess post-exercise oxygen consumption (EPOC) and its physiological significance.
- Describe the exercise principles of specificity and progressive overload.
- Identify the metabolic adaptations to anaerobic and aerobic exercise.

Introduction

Exercise significantly disrupts metabolic homeostasis in skeletal muscle. During intense physical activity, the body's total energy expenditure can surge to levels 15 to 25 times higher than at rest. Skeletal muscles exhibit a remarkable ability to generate and utilize substantial amounts of ATP during exercise, and they can modify their metabolic processes to enhance their energy expenditure capacity. This chapter will explore the following topics:

1. The scientific definition and underlying causes of exercise-induced fatigue.
2. The metabolic responses observed at the onset of exercise and during the recovery phase.
3. The selection of energy substrates used for ATP production.
4. The long-term metabolic adaptations resulting from aerobic and anaerobic exercise training.

Muscle Fatigue and Metabolic Acidosis

Muscle fatigue can be broadly defined as the inability to maintain the required or expected force[1]. It is a complex and multifactorial phenomenon, often described as a decline in muscle performance with continued

1. MacIntosh BR, Gardiner PF, McComas AJ, Skeletal muscle: Form and Function. 2006: Human Kinetics.

effort, accompanied by a sensation of tiredness[2]. The sites of fatigue are generally categorized into two types: central fatigue, which includes any site from the brain to the neuromuscular junction, and peripheral fatigue, which encompasses any physiological site from the neuromuscular junction into the muscle. The specific site of fatigue can vary depending on the type of exercise. For instance, fatigue experienced during a 400-meter run differs significantly from that during a marathon.
Researchers have identified several key areas to determine the underlying causes and sites of fatigue:

1. Decreased rate of energy delivery (PCr-ATP, glycolysis, oxidative phosphorylation).
2. Accumulation of metabolic by-products such as H+.
3. Heat produced as a by-product of energy expenditure.
4. Failure of the muscle fiber's contractile mechanisms.
5. Alterations in neuromuscular control.

The first four causes are often referred to as **peripheral fatigue**. Other mechanisms of peripheral fatigue include acetylcholine breakdown at the neuromuscular junction, H^+ accumulation inside the muscle cell (acidosis), competitive binding of H^+ with calcium, and disruption of ATPase activity. Environmental factors, such as ambient temperature, also affect fatigue. For example, men cycling at 70% VO2max experienced delayed fatigue in cooler environments (11°C) compared to hotter ones (21°C and 31°C)[3]. Pre-cooling muscles can prolong exercise, while preheating can cause earlier fatigue[4].

Other factors that affect fatigue are the types and intensity of exercise, environmental conditions, the fiber types of the involved muscles, the subject's training status, and even the athlete's diet. Changes in the brain or central nervous system may also cause **central fatigue** but none of these alone can explain all aspects of fatigue. Undoubtedly, the central nervous system (CNS) also may be a site of fatigue. It has been shown that verbal encouragement, shouting, playing of music, or even direct electrical stimulation of the muscle can increase the strength of muscle contraction. However, the precise mechanisms underlying the CNS role in fatigue are still not fully understood. Keep in mind that fatigue is rarely caused by a single factor but possibly many factors acting at multiple sites.

2. Kenney LK, Wilmore JH, Costil DL, ed., Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

3. Galloway SDR, and Maughan RJ, Effects of ambient temperature on the capacity to perform prolonged cycle exercise in men. Medicine and Science in Sports and Exercise, 1997. 29: p. 1240-1249.

4. Kenney LK, Wilmore JH, Costil DL, ed., Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

Acidosis

For over 90 years, lactic acidosis has been a classic explanation for acidosis during exercise. This theory posits that lactic acid production during intense exercise causes acidosis, leading to fatigue. However, a 2004 review by Robert Robergs, PhD, and colleagues challenged this view, presenting evidence that lactate production actually retards acidosis rather than causing it[5]. They argued that **acidosis** results from reactions other than lactate production and that the concept of lactic acidosis is a construct rather than a fact.

In skeletal muscle, acidosis is caused by cytosolic catabolism, leading to an accumulation of hydrogen ions (H^+) in the sarcoplasm. This accumulation decreases muscle pH from a resting value of 7.1. It is crucial that muscle pH does not drop below 6.6 to 6.4, as this could cause physiological damage or cell death. An intracellular pH below 6.9 inhibits phosphofructokinase activity, slowing glycolysis and ATP production. At a pH of 6.4, H^+ accumulation halts glycogen breakdown, causing a rapid decrease in ATP and leading to exhaustion. Most researchers agree that low muscle pH is a major limiter of performance and a primary cause of fatigue during maximal, all-out exercise lasting more than 20 to 30 seconds.

Researchers now agree that ATP hydrolysis coupled with glycolysis is the main source of proton (H^+) production, leading to decreased muscle and blood pH[6][7][8]. ATP hydrolysis releases a free proton, contributing significantly to acidosis when proton removal does not balance proton production.

By understanding these mechanisms, we can better appreciate the complex interplay of factors that contribute to muscle fatigue and acidosis during exercise. Recall that ATP hydrolysis (catalyzed by ATPase) results in the release of a free proton as shown below. This reaction is thought to be a major contributor to acidosis under conditions where proton removal is not balanced with proton production.

$$ATP + H_2O \rightarrow ADP + Pi + energy + H^+$$

The second most accepted cause of acidosis is the release of protons from several reactions in glycolysis. While this textbook does not provide an exhaustive examination of the biochemistry of acidosis, it is important to note that specific steps in glycolysis (steps 1, 3, and 6) release protons (H^+). Conversely, step 10 in glycolysis consumes two protons, acting as a buffering reaction that removes protons from the cytosol. Thus, the net proton yield of glycolysis is 2 H^+.

In addition to generating energy, cells possess mechanisms to buffer and remove H^+. These include

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5. Robergs RA, Ghiasvand F, Parker D, The biochemistry of exercise-induced metabolic acidosis. Am J Physiol Regul Integr Comp Physiol, 2004. 287: p. R502-R516.

6. Kenney LK, Wilmore JH, Costil DL, ed., Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

7. Robergs RA, Ghiasvand F, Parker D, The biochemistry of exercise-induced metabolic acidosis. Am J Physiol Regul Integr Comp Physiol, 2004. 287: p. R502-R516.

8. Busa WB, and Nuccitelli R, Metabolic regulation via intracellular pH. Am J Physiol Regul Integr Comp Physiol, 1984. 246: p. R409-R438.

intracellular proteins, mitochondrial transport, bicarbonate (HCO_3^-), lactate production, and the export of H^+ to the blood. It is crucial to understand that metabolic acidosis is not solely caused by proton release from metabolic reactions but by an imbalance between the rate of proton release and the rate of buffering and removal.

Lactate Formation and Redox Potential

The redox potential of muscle cells to continuously produce ATP depends on the availability of NAD+ to accept hydrogen from various metabolic steps. During aerobic metabolism, $NADH+H^+$ shuttles hydrogen to the mitochondria via the glycerol phosphate shuttle, where it is oxidized back to NAD^+, allowing it to continue accepting hydrogen. Chapter 4 detailed the steps of carbohydrate metabolism, including the net yield of glycolysis: two $NADH+H^+$, two pyruvate molecules, two ATP, and two H_2O.

During rest and steady-state exercise, pyruvate is oxidized in the mitochondria into acetyl CoA, and mitochondrial respiration proceeds. Oxygen serves as the final electron acceptor, enabling a steady rate of glycolysis. However, during high-intensity exercise, the oxygen demands of the cell exceed the supply, inhibiting the ability of $NADH+H^+$ to shuttle hydrogen into the mitochondria. When oxygen is unavailable to accept electrons in the mitochondria, $NADH+H^+$ accumulates in the cytosol.

To improve the redox potential (i.e., increase the amount of NAD^+ available for glycolysis), pyruvate can accept hydrogen from $NADH+H^+$, converting into lactate. This redox reaction, catalyzed by the enzyme lactate dehydrogenase, results in the formation of lactate and the reformation of NAD^+. The lactate dehydrogenase (LDH) reaction is a crucial buffering mechanism that allows glycolysis to continue under strenuous exercise conditions. The lactate dehydrogenase reaction important for generating lactate is shown:

$$\text{Pyruvate} + \text{NADH} + H^+ \rightleftharpoons \text{Lactate} + NAD^+$$

The formation of lactate allows NAD^+ to return to step 6 of glycolysis to accept more hydrogen, thereby enabling glycolysis to continue. Importantly, the lactate dehydrogenase reaction does not result in a net production of protons. Consequently, lactate production serves as a crucial H^+ buffering reaction, allowing sustained exercise. Without lactate production, skeletal muscle would rapidly experience acidosis and fatigue, severely diminishing exercise performance[9]. The lactate dehydrogenase (LDH) reaction is reversible, allowing lactate to be converted back to pyruvate under resting conditions.

9. Robergs RA, Ghiasvand F, Parker D, The biochemistry of exercise-induced metabolic acidosis. Am J Physiol Regul Integr Comp Physiol, 2004. 287: p. R502-R516.

Lactate Threshold (LT)

Once produced in the muscle during exercise, lactate can be transported out of the muscle fiber through specialized transport proteins, such as monocarboxylate transporter proteins, into the blood. This export of lactate can be measured during exercise and is used to predict endurance performance in athletes. Historically, **maximal oxygen uptake (VO_{2max})** was considered the best measure of endurance capacity. While VO_{2max} is valid for short-term endurance workloads leading to exhaustion within 3-10 minutes, it is insufficient for assessing performance capacity during middle-term (10-30 minutes) and long-term (> 30 minutes) workloads[10].

A more accurate measure of middle- and long-term endurance exercise capacity is the lactate threshold. Often synonymous with the anaerobic threshold due to the link between anaerobic metabolism and lactate appearance, the term "lactate threshold" is preferred for its accuracy[11]. The **lactate threshold (LT)** is the point at which there is an exponential rise in blood lactate levels during incremental exercise. It indicates an increasing reliance on anaerobic metabolism (i.e., glycolysis) and can predict success in distance running. Figure 5.1 illustrates changes in blood lactate concentration during incremental exercise and identifies the lactate threshold inflection point.

Another term used to describe the systematic rise in blood lactate concentration is the **onset of blood lactate accumulation (OBLA)**. Unlike the lactate threshold (LT), OBLA is defined as the exercise intensity (or oxygen consumption) at which a lactate concentration of 4 millimoles per liter of blood is achieved[12]. The threshold value of 4 mmol/L is not a criterion for the LT, which is usually expressed as a percentage of VO_{2max}. The LT is one of the best determinants of an athlete's optimal pace in events such as cycling or running. It has practical applications for optimizing training

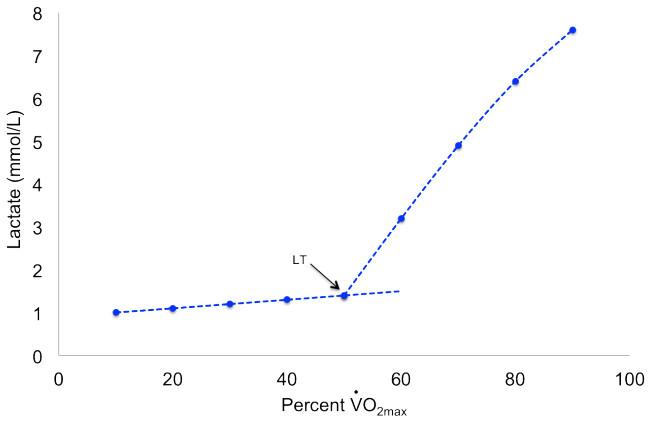

Figure 5.1 The lactate threshold is indicated with an arrow as point where there is a sudden rise in lactate during incremental exercise.

10. . Heck H, Mader A, Hess G, Mucke S, Muller R, and Hollmann W, Justification of the 4-mmol/l Lactate Threshold. Int J Sports Med, 1985. 6: p. 117-130.

11. Powers SK, and Howley ET, Exercise Physiology (Theory and Application to Fitness and Performance). 9th Edition ed. 2015, New York, NY: McGraw-Hill.

12. . Heck H, Mader A, Hess G, Mucke S, Muller R, and Hollmann W, Justification of the 4-mmol/l Lactate Threshold. Int J Sports Med, 1985. 6: p. 117-130.

programs and predicting success in endurance athletes. Generally, the LT occurs at 50-60% VO_{2max} in untrained individuals and at 70-80% VO_{2max} in elite endurance-trained athletes[13]. Coaches can use the LT to plan exercise intensity levels to optimize training results, such as selecting a training heart rate based on the LT. Several mechanisms may contribute to the lactate threshold during increasing exercise intensities:

1. Low muscle oxygen.
2. Accelerated glycolysis.
3. Recruitment of fast-twitch fibers.
4. Reduced rate of lactate removal.

As exercise intensity increases, more muscular force is required, leading to the recruitment of fast-twitch muscle fibers. These fibers rely on **anaerobic metabolism** (i.e., glycolysis), resulting in increased lactate production. Another mechanism involves the balance between lactate production in skeletal muscle and its removal by other tissues, such as the liver and heart. At any given time during exercise, some muscles produce lactate while other tissues remove it. Therefore, blood lactate concentration depends on the rate of lactate entry into the blood and its removal rate[14]. A rise in blood lactate concentration can occur due to either increased lactate production or decreased lactate removal. These mechanisms remain controversial, but it is likely that a combination of factors explains the lactate threshold.

13. Kenney LK, Wilmore JH, Costil DL, ed., Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

14. 5. Powers SK, and Howley ET, Exercise Physiology (Theory and Application to Fitness and Performance). 9th Edition ed. 2015, New York, NY: McGraw-Hill.

Ventilatory Threshold (VT)

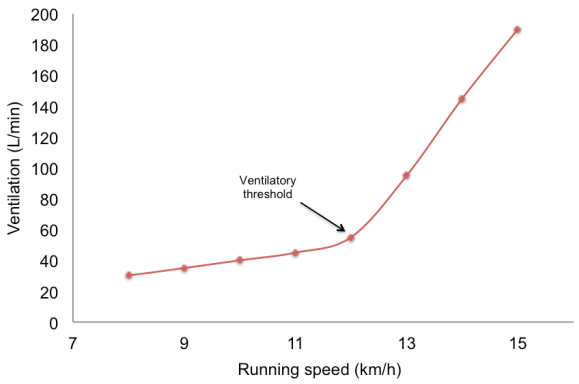

Figure 5.2 Changes in the rate of pulmonary ventilation (VE) during running at increasing speeds, illustrating the ventilatory threshold.

The original purpose of determining the **ventilatory threshold** (Figure 5.2) was to provide a noninvasive alternative to blood sampling for detecting the onset of the "anaerobic threshold" or lactate threshold. Although the term "anaerobic threshold" remains controversial, the ventilatory threshold offers a means to assess changes in exercise metabolism without invasive procedures. During moderate, steady-state exercise, ventilation increases in proportion to the rate of metabolism, paralleling oxygen uptake. The ventilatory equivalent of oxygen (VE/VO_2) is the ratio between the volume of air expired (VE) and the amount of oxygen consumed by the tissues (VO_2) over a given time. At rest, VE/VO_2 ranges from 23 to 28 L of air per liter of oxygen and changes minimally during mild exercise. However, as exercise intensity approaches maximal levels, VE/VO_2 can exceed 30 L of air per liter of oxygen consumed.

The ventilatory threshold is the point during incremental exercise where ventilation increases disproportionately compared to oxygen consumption, typically occurring between 55% to 70% of VO_{2max} [15]. This disproportionate increase in ventilation is likely due to rising carbon dioxide levels during intense exercise, which stimulate chemoreceptors that signal the inspiratory center to increase ventilation. Beyond the ventilatory threshold, ventilation increases dramatically, making it difficult to maintain a steady state of exercise. Exercise physiologists can estimate the lactate threshold by identifying the point where VE/VO_2 starts to increase while VE/VCO_2 continues to decline.

VO_2 Drift

Exercise significantly increases energy requirements beyond resting metabolism. Metabolism rises in direct proportion to exercise intensity during sub-maximal exercise bouts. At higher exercise intensities, the **oxygen uptake (VO_2)** response does not follow the typical steady-state pattern, where oxygen consumption

15. Kenney LK, Wilmore JH, Costil DL, ed., Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

stabilizes within 1 to 2 minutes. Instead, VO_2 continues to increase, a phenomenon known as the slow component of oxygen uptake kinetics, likely due to changes in muscle fiber recruitment[16]. The recruitment of more type II muscle fibers, which are less efficient, necessitates a higher VO_2 to achieve the same power output.

Generally, a **steady-state VO_2** can be maintained during prolonged, moderate-intensity exercise. However, in hot or humid environments or at high work rates, an upward "drift" in VO_2 over time can occur, preventing the attainment of a steady state[17]. VO_2 drift is defined as a slow increase in VO_2 during prolonged sub-maximal, constant power output exercise. It is observed at power outputs well below the lactate threshold, with a smaller magnitude of increase. The exact cause of **VO_2 drift** is not fully understood but is thought to be related to increased circulating catecholamines[18].

Substrate Utilization During Exercise

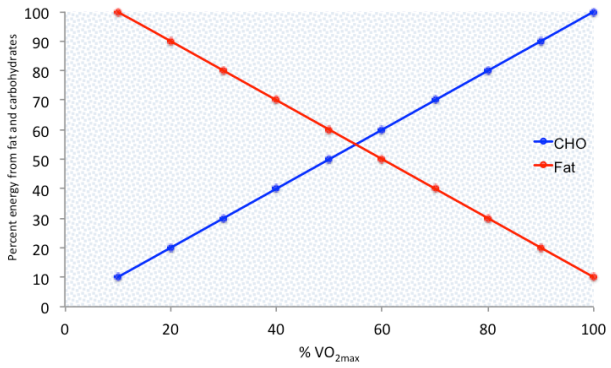

Figure 5.3 Illustration of the crossover concept. As exercise intensity increases, there is a progressive increase in the utilization of carbohydrate (CHO) as a substrate for energy production.

The pattern of substrate utilization during exercise depends on the interaction between exercise intensity and duration. Increased exercise intensity results in greater carbohydrate (CHO) utilization compared to fat[19]. Conversely, endurance training promotes lipid oxidation, making fats the dominant fuel source during prolonged exercise. Brooks and Mercier confirmed that at low exercise intensities (≤ 45% VO_{2max}), lipid is the main substrate, while at high intensities (~75% VO_{2max}), carbohydrate predominates[20]. This shift from fat to carbohydrate metabolism as exercise intensity increases is known as the crossover concept (Figure 5.3).

Physiologically, this change is due to the recruitment of fast-twitch fibers, which contain many glycolytic enzymes and thus utilize more glucose for ATP production. Additionally, increased blood

16. . Kenney LK, Wilmore JH, Costil DL, ed., Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

17. Powers SK, and Howley ET, Exercise Physiology (Theory and Application to Fitness and Performance). 9th Edition ed. 2015, New York, NY: McGraw-Hill.

18. Kenney LK, Wilmore JH, Costil DL, ed., Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

levels of epinephrine associated with higher exercise intensities cause muscle glycogen breakdown.

Recovery from Exercise: Metabolic Responses

At the onset of exercise, metabolic changes in skeletal muscle must occur rapidly to provide the necessary energy for movement. Measuring O_2 consumption during exercise offers an indirect assessment of metabolism. There is a direct relationship between O_2 utilization in the electron transport chain and ATP generation. Research shows that during the transition from rest to light or moderate exercise, O_2 consumption increases rapidly, reaching a steady state within 1 to 4 minutes[2122]. Initially, anaerobic energy sources (CrP-ATP and glycolysis) contribute to ATP production until a steady state is achieved.

Trained individuals reach steady state faster than untrained subjects[23]. It is important to note that all metabolic systems operate with considerable overlap, and no single pathway generates the entire ATP contribution at any time.

Oxygen Deficit

The lag in oxygen consumption at the start of exercise is termed the **oxygen deficit**. This can be measured through indirect calorimetry as the difference between oxygen uptake in the first few minutes of exercise and an equal time period after steady state is reached. The oxygen deficit affects mitochondrial respiration's ability to generate ATP. During this period, ATP demands are met by the phosphagen and glycolytic systems (anaerobic metabolism). The oxygen deficit continues until a steady state of oxygen consumption is achieved. The degree of oxygen deficit can be influenced by exercise intensity and duration, providing insights into the control of oxidative phosphorylation.

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19. Brooks GA, Mercier J, Balance of carbohydrate and lipid utilizaiton during exercise: the "crossover" concept. Journal of Applied Physiology, 1994. 76(6): p. 2253-2261.

20. Brooks GA, Mercier J, Balance of carbohydrate and lipid utilizaiton during exercise: the "crossover" concept. Journal of Applied Physiology, 1994. 76(6): p. 2253-2261.

21. Boutellier U, Glezendanner D, Cerretelli P, and di Prampero PE, After effects of chronic hypoxia on VO2 kinetics and on O2 deficit and debt. Eur J Appl Physiol Occup Physiol, 1984. 53: p. 87-91.

22. Powers SK, Dodd S, Beadle RE, Oxygen uptake kinetics in trained athletes differing in VO2max. Eur J Appl Physiol Occup Physiol, 1985. 54(3): p. 306-8.

23. Powers SK, Dodd S, Beadle RE, Oxygen uptake kinetics in trained athletes differing in VO2max. Eur J Appl Physiol Occup Physiol, 1985. 54(3): p. 306-8.

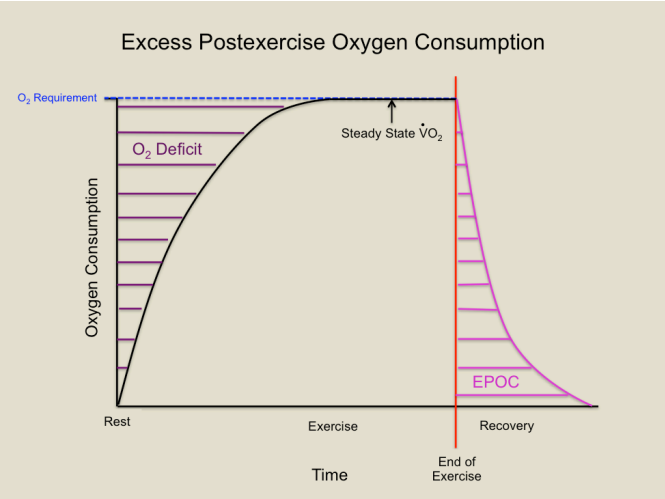


Figure 5.4 The oxygen deficit during moderate exercise and the excess post-exercise oxygen consumption (EPOC) following exercise during recovery. Oxygen requirement and steady state oxygen consumption are also shown.

Two main hypotheses may explain the lag in oxygen utilization at the onset of exercise. The first hypothesis suggests an inadequate supply of oxygen to the muscles, meaning there is insufficient oxygen to accept electrons at the end of the electron transport chain (ETC), thereby restricting whole-body oxygen consumption. The second hypothesis posits that there is a delay because the stimuli for oxidative phosphorylation require time to reach their full effects. Metabolic pathways are highly regulated and often activated when concentrations of ADP and Pi increase due to exercise. As CrP is broken down, ADP and Pi concentrations rise, gradually stimulating oxidative phosphorylation until it meets the energy demands of the exercise. Research supports both hypotheses, suggesting that regulators of oxidative phosphorylation interact to provide the overall stimulus under various exercise conditions.

Excess Post-exercise Oxygen Consumption (EPOC)

Historically, the term "**oxygen debt**" was used to describe the elevated oxygen uptake following exercise, coined by British physiologist Archibald Vivian (A.V.) Hill. He observed that oxygen debt could be divided into a rapid portion (2-3 minutes post-exercise) and a slow portion (persisting for over 30 minutes)[24][25]. The rapid portion was thought to re-synthesize ATP and CrP and replenish tissue oxygen stores (~20% of oxygen debt), while the slow portion (~80% of oxygen debt) was attributed to the oxidative conversion of lactate to glucose in the liver. However, recent evidence shows that only 20% of the oxygen debt is used for lactate to glucose conversion, leading to the term's controversy and eventual replacement.

The term "**excess post-exercise oxygen consumption**" (EPOC) is now used to describe the recovery period after cardiovascular exercise, where oxygen consumption remains elevated. EPOC is the amount of oxygen consumed during recovery beyond what would be consumed at rest. It occurs until physiological

24. null

25. Powers SK, and Howley ET, Exercise Physiology (Theory and Application to Fitness and Performance). 9th Edition ed. 2015, New York, NY: McGraw-Hill

variables return to homeostasis, including CrP replenishment, lactate metabolism, glycogen re-synthesis, and hormone recovery. During this period, increased oxygen demand helps the body achieve homeostasis by lowering body temperature, adjusting heart rate and ventilation, and re-oxygenating hemoglobin.

Exercise intensity affects the duration of the oxygen deficit and EPOC. Compared to moderate-intensity exercise, EPOC is greater during high-intensity, exhaustive exercise due to higher heat production, greater CrP depletion, higher blood lactate levels, and elevated epinephrine and norepinephrine levels. Figure 5.5 illustrates the differences in the duration of EPOC and the oxygen deficit during moderate- and heavy-intensities of exercise.

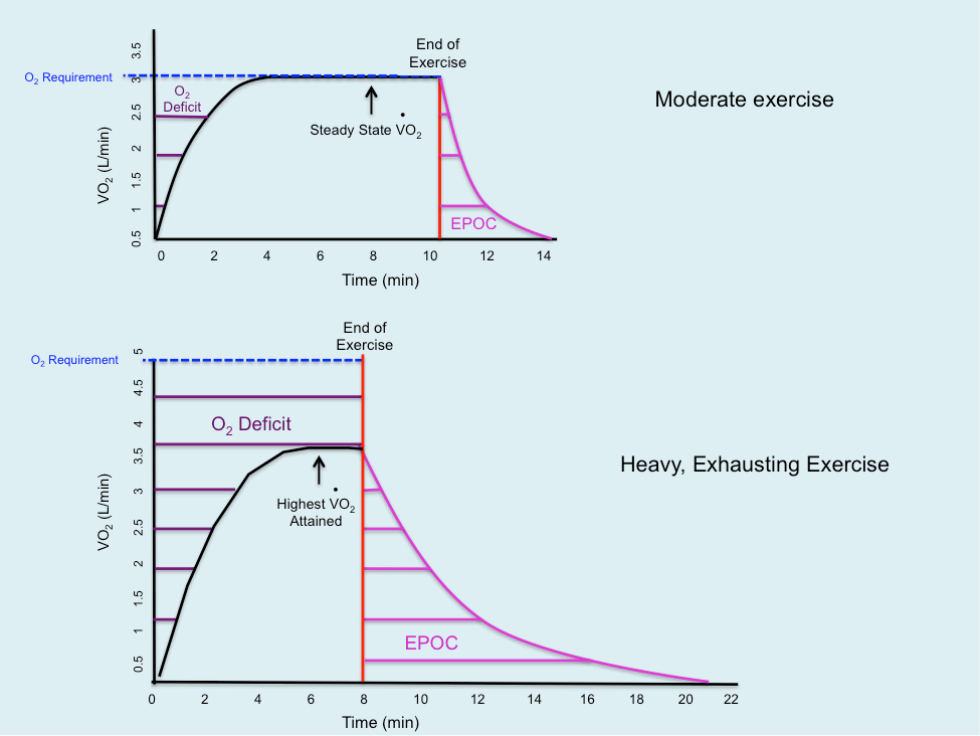


Figure 5.5 A comparison of the oxygen deficit and EPOC at (A) moderate exercise, and (B) heavy, exhausting exercise.

Metabolic Changes with Exercise Training

For exercise professionals, understanding metabolism and distinguishing between exercise duration and intensity is crucial. The exercise principle of specificity states that adaptations are specific to the type of training, which applies directly to training metabolic pathways. Metabolic adaptations result from targeting specific systems through exercise training. Intensity is typically expressed as a **percentage of maximal oxygen consumption (%VO_{2max})**, maximum speed, the **percentage of one repetition maximum (% 1RM)**, or the athlete's maximum heart rate (MHR). Both duration (long or short) and intensity (high or low) should be considered when training for a particular sport or event. Most sports require a combination of

anaerobic and aerobic pathways to produce the ATP needed for performance.

Short-Term, Intense Exercise

The energy required for short-term, high-intensity exercise primarily comes from anaerobic metabolic pathways. The CrP-ATP and glycolytic systems both contribute to ATP generation, with their contributions depending on the activity's duration. For example, during a 50-meter dash or a single play in American football, the CrP-ATP system predominantly provides ATP[26]. For events lasting longer than 45 seconds, such as a 400-meter dash or an extended volleyball rally, a combination of CrP-ATP, glycolysis, and mitochondrial respiration generates ATP. Intense exercise lasting about 60 seconds utilizes 70% anaerobic and 30% aerobic systems, while events lasting 2 to 3 minutes use both systems equally.

Anaerobic training, defined as exercise performed at intensities above VO_{2max}, aims to stimulate anaerobic energy pathways. Speed training involves high-intensity anaerobic training lasting 2-10 seconds, while speed endurance training refers to anaerobic training lasting longer than 10 seconds[27]. It is important to target specific muscle groups required by the athlete during competitions. Some research suggests that CrP-ATP efficiency may increase with anaerobic training, though this is debated. Training to improve the CrP-ATP system involves short, high-intensity intervals (5-10 seconds) targeting specific muscles. Other research indicates that enzyme efficiency (phosphorylase, PFK, and LDH) can increase by 10-25% with repeated 30-second training bouts.

A significant factor in high-intensity training is the ability to decrease acidosis and fatigue through matching buffering activity. Buffering capacity can improve by 12-50% with anaerobic training. Buffers such as bicarbonate (HCO_3^-), muscle phosphates (HPO_4^{2-}), and increased lactate production (via lactate dehydrogenase) help delay acidosis, reduce fatigue, and enhance performance.

26. Powers SK, and Howley ET, Exercise Physiology (Theory and Application to Fitness and Performance). 9th Edition ed. 2015, New York, NY: McGraw-Hill. 6. Busa WB, and Nuccitelli R, Metabolic regulation via intracellular pH. Am J Physiol Regul Integr Comp Physiol, 1984. 246: p. R409-R438.

27. Powers SK, and Howley ET, Exercise Physiology (Theory and Application to Fitness and Performance). 9th Edition ed. 2015, New York, NY: McGraw-Hill. 6. Busa WB, and Nuccitelli R, Metabolic regulation via intracellular pH. Am J Physiol Regul Integr Comp Physiol, 1984. 246: p. R409-R438.

Figure 5.6 This figure depicts the legendary Greek athlete Milo of Croton, renowned for his extraordinary strength. In the scene, Milo is shown attempting to tear apart a tree by hand—a feat of hubris. His hand becomes stuck in the partially split trunk, rendering him vulnerable. Wild animals, likely wolves or lions, are depicted encircling him, symbolizing his tragic demise as told in ancient myth.

The exercise principle of **progressive overload** is crucial for metabolic training adaptations. It states that a training program must stress the system beyond its accustomed level to induce adaptations. Muscles increase in strength and energy generation capability by contracting at relatively high tensions and will not adapt unless overloaded[28]. The first application of this principle was by Milo of Crotona, a famous Olympic wrestler from 500 B.C. Milo's training involved carrying a bull calf on his back daily, continuing until the animal matured (Figure 5.6). This story illustrates the principle of progressive overload, which is now applied by athletes through lifting heavy objects. Progressive overload is essential for developing not only strength and performance enhancements but also for adapting metabolic pathways to improve energy generation capabilities.

Prolonged Exercise

The energy for long-term exercise (more than 10 minutes) primarily comes from oxidative phosphorylation (**aerobic metabolism**). A steady-state VO_2 can generally be maintained during sub-maximal, moderate-intensity exercise if body temperature and hormonal concentrations are stable. Oxygen consumed is used in the electron transport chain (ETC) to accept electrons, driving redox reactions that create ATP. Improving VO_2 is key to enhancing endurance performance and involves several physiological factors, from oxygen binding to hemoglobin to utilization within mitochondria.

Endurance training can improve VO_{2max} by 15-20%, depending on initial fitness levels. Typically, endurance training involves prolonged bouts of low-to-moderate intensity exercise that overload the muscles. **Type I muscle fibers**, recruited at this intensity, can increase in size (**muscle hypertrophy**) by 7-22%. A critical adaptation is an increase in capillary supply to trained muscles, enhancing oxygen delivery. **Myoglobin**

28. Powers SK, and Howley ET, Exercise Physiology (Theory and Application to Fitness and Performance). 9th Edition ed. 2015, New York, NY: McGraw-Hill. 6. Busa WB, and Nuccitelli R, Metabolic regulation via intracellular pH. Am J Physiol Regul Integr Comp Physiol, 1984. 246: p. R409-R438.

content, which shuttles oxygen from the cell membrane to mitochondria, increases by 75-80% with endurance training. Mitochondria can also increase in number and size, with cardiovascular training boosting them by 15% and 35%, respectively. Mitochondrial enzymes can increase 2.5 times even after training stops.

Trained muscles can store more glycogen and twice as much intramuscular fat for use during exercise compared to untrained individuals. During prolonged exercise, there is a gradual shift from carbohydrate metabolism to fat oxidation, initiated by epinephrine and norepinephrine hormones that trigger lipolysis. Fat oxidation requires more oxygen than carbohydrate oxidation, making lipolysis a slower process. A study on muscle triglyceride utilization during exercise found that after a 12-week training program, subjects increased their triglyceride utilization and decreased glycogen utilization, demonstrating that fat utilization increases with endurance training [29]. Fatty acid oxidation can increase by up to 30% with training.

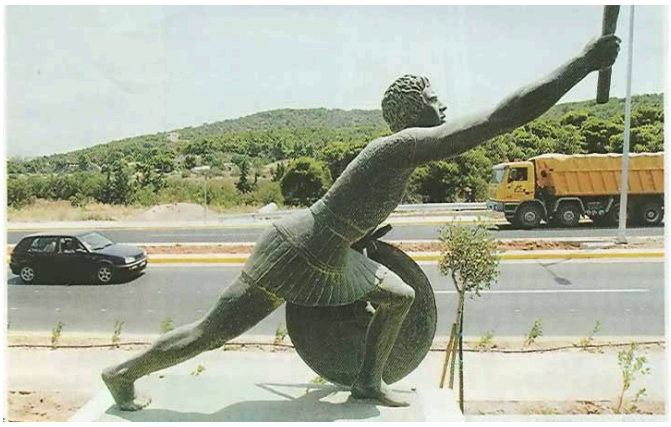


Figure 5.7 This figure shows the bronze statue of Pheidippides, located along the historic Marathon Road in Greece. Pheidippides is depicted in mid-stride, muscular and determined, symbolizing his legendary run from the battlefield at Marathon to Athens to announce the Greek victory over the Persians in 490 B.C. This mythological event is widely regarded as the inspiration for the modern marathon race. The statue stands as a tribute to endurance, athleticism, and the historical roots of long-distance running.

Distance running has seen remarkable performance improvements over the past century. One study hypothesized that a marathon could be completed in under 2 hours by the year 2100, though the results were inconclusive [30]. Nevertheless, the marathon remains one of the most popular commercialized running races. Endurance events like the marathon primarily rely on aerobic ATP production. Proper conditioning of the aerobic systems is crucial for marathon runners to sustain their race pace and recover adequately.

The history of the marathon is an interesting tale that highlights the importance of training for such feats of endurance. The story begins with the Athenian victory over the Persians at the Battle of Marathon. Following the battle, Athens reached new heights of prosperity as democracy blossomed, laying the foundation for Western civilization. According to legend, the Greek messenger Pheidippides ran from the battlefield at Marathon to Athens to relay news of the victory. Upon arriving in Athens, he exclaimed, "We were victorious!" and then collapsed

29. Hurley BF, Nemeth PM, Hagberg M, Dalsky GP, Martin III WH, and Holloszy JO. Muscle triglyceride utilization during exercise: effect of training. JAP, 1986. 60(2): p. 562-567.

30. Weiss M, Newman A, Whitmore C, Weiss S. One hundred and fifty years of sprint and distance running – Past trends and future prospects. European Journal of Sport Science, 2016. 16 (4): p. 393-401.

and died from exhaustion. Figure 5.7 shows a statue commemorating Pheidippides run that inspired the modern marathon event, which was introduced at the 1896 Modern Olympics.

While the story of Pheidippides is tragic and extreme, modern training protocols and methods for endurance training have shown significant benefits. Endurance training improves many cardiovascular risk markers, including body weight, blood lipids, and blood pressure. Additionally, endurance training positively affects metabolic factors and helps delay metabolic diseases.

Chapter Summary

In conclusion, this chapter has provided an in-depth exploration of the metabolic challenges and adaptations associated with exercise. We examined how exercise disrupts metabolic homeostasis in skeletal muscle, leading to significant increases in energy expenditure and necessitating rapid metabolic responses. The causes and sites of muscle fatigue were analyzed, highlighting the complex interplay between central and peripheral factors.

We discussed the critical role of lactate production in buffering hydrogen ions and preventing rapid acidosis, as well as the concept of the lactate threshold and its importance for endurance performance. The chapter also covered the lag in oxygen utilization at the onset of exercise and the significance of excess post-exercise oxygen consumption (EPOC) in recovery.

Metabolic adaptations to both anaerobic and aerobic exercise were explored, emphasizing the principles of specificity and overload. These principles are essential for developing metabolic pathways that enhance energy generation and overall athletic performance. The historical perspective on marathon running underscored the importance of proper training and conditioning for endurance athletes, illustrating how modern training methods have evolved to improve both physiological and metabolic outcomes.

Overall, this chapter has provided a comprehensive understanding of the metabolic processes involved in exercise and training, offering valuable insights for optimizing athletic performance and promoting long-term health.

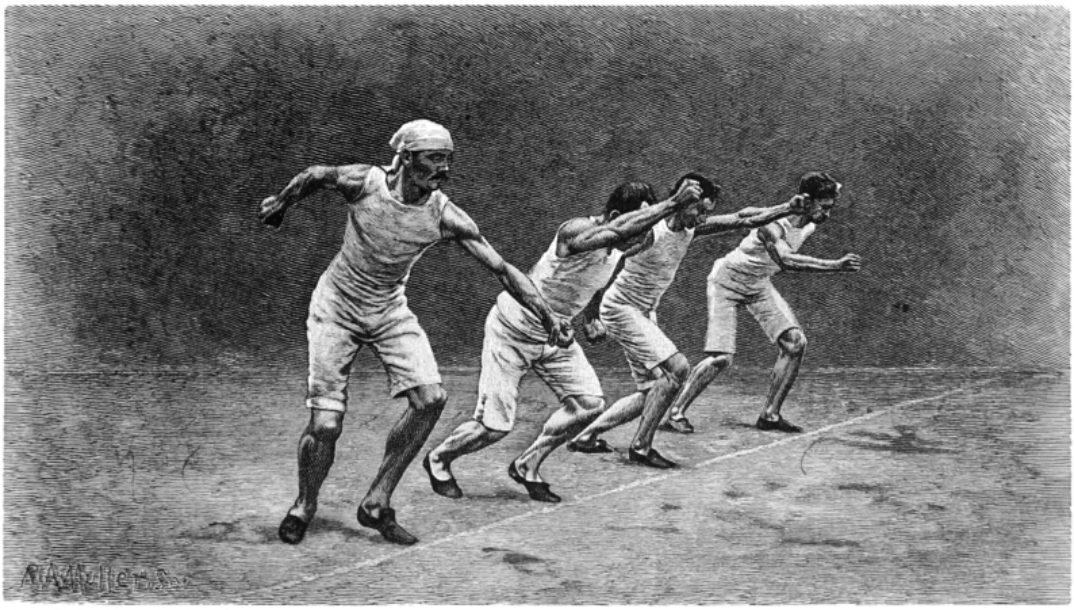
Scholarly Questions

1. What is the ventilatory threshold? How is it different from the lactate threshold?
2. Approximately how long does it take to achieve steady state VO_2?
3. What are the causes of acidosis/H^+ production?

4. So, is lactate really causing the acidosis? If not, what would this be?
5. Explain how with glycolytic training, there is an increase in buffering capacity.
6. What are the names of some buffers? What are they doing?
7. If the pH goes below 7, is the concentration more or less acidic?
8. What two energy systems are providing the majority of ATP during the oxygen deficit? What energy system is providing the majority of ATP during steady state?
9. What are the factors of EPOC? What does EPOC stand for and what does it mean? Be able to graph the following items: oxygen deficit, EPOC, steady state VO_2, and the oxygen requirement.
10. With very short burst training, what adaptations do we see to the phosphagen system?
11. What are the aerobic and anaerobic metabolic adaptations with training? How do these adaptations improve the ability to continue exercise?
12. With aerobic exercise, what VO_{2max} improvement range can be expected?
13. With aerobic training, can Type I fibers hypertrophy? If so, by how much?
14. Of the Type IIa and Type IIb/x fibers, which would be used more in aerobic exercise?
15. A key adaptation of aerobic training is capillary supply. How much of an increase may be seen?
16. If the number of capillaries increases, how does this affect O_2, CO_2, nutrients, and waste products?
17. What does myoglobin do? Which fiber type, Type I or Type II, is higher in myoglobin? How much may myoglobin increase with aerobic training?
18. Does mitochondrial function improve with aerobic training? Explain.
19. How much do mitochondrial oxidative enzymes increase due to aerobic training?
20. Aerobically trained muscle can oxidize fatty acids better. By what percentage does this ability increase?
21. What is the difference between an acute response and a chronic adaptation to exercise? Can you give some examples of each?
22. What are the major types of muscle fibers discussed in class? Which type is recruited for endurance (aerobic) exercise? Which type is recruited for short-term, high-intensity (anaerobic) exercises? Which fiber type has oxidative characteristics? Which has glycolytic characteristics?

6.

MEASURING HUMAN ENERGY EXPENDITURE, WORK AND POWER



Athletes preparing to run the 100-yard dash-THE START. June 1980. The Century Magazine.

Learning Objectives

- Describe the key principles of energy expenditure and its importance in exercise physiology.
- Differentiate between direct and indirect calorimetry and explain how each method measures energy expenditure.
- Calculate energy expenditure using the respiratory exchange ratio (RER) and understand its limitations.

- Explain the significance of measuring RMR in clinical and research settings.
- Describe the methods for measuring VO^2, including closed and open circuit spirometry.
- Define VO^2max and explain its importance in assessing cardiovascular fitness.
- Identify the criteria for achieving VO^2max and understand the protocols for incremental exercise testing.
- Perform calculations to determine work and power output in humans.
- Explain the factors that influence exercise efficiency and the concept of running economy.
- Measure and compare the O^2 cost of different activities to assess exercise efficiency.
- Use the 2011 Compendium of Physical Activity to estimate energy expenditure for various activities.

Introduction

One cannot grasp the fundamentals of exercise physiology without first understanding the key principles of energy expenditure. In Chapter 4, we explored several metabolic pathways involved in the formation of adenosine triphosphate (ATP), the primary chemical energy source for our bodies. ATP can be synthesized using substrates such as sugars, fats, or proteins and is essential for cellular activities, including muscle contraction. The ability to expend energy, particularly during exercise, depends on metabolic function, rate, and the availability of substrates. This chapter will delve into how energy expenditure varies between rest and exercise and how the duration and intensity of exercise influence the amount of energy utilized.

Measuring Energy Expenditure

Energy utilized by contracting skeletal muscles cannot be directly measured. However, several indirect laboratory methods can calculate whole-body energy expenditure. **Energy expenditure (EE)**, measured in kilocalories (kcal) per minute, reflects the body's rate of heat production. A **calorie**, the System International (SI) unit of heat, is the amount of heat required to raise 1 gram of water by 1°C. Given the small size of a calorie, energy content is typically expressed in kilocalories (1 kcal = 1,000 calories). Estimating or measuring energy expenditure is valuable for individuals using activities like walking, running, or swimming for fitness or performance improvement. Additionally, understanding energy expenditure is crucial for weight-loss programs. There are two primary techniques for measuring human energy expenditure: direct calorimetry and indirect calorimetry.

Direct Calorimetry

Direct calorimetry measures the heat produced by the body during rest or exercise. This technique is based on the principle that energy expenditure results in heat production. The rate of heat production is directly proportional to metabolic rate, making heat measurement a direct indicator of energy expenditure. A calorimeter, an insulated chamber allowing free exchange of O_2 and CO_2, measures body heat. The person's body heat raises the temperature of the water or insulation surrounding the chamber, and the temperature difference over time indicates the amount of heat produced. Although scientists have used this technique since the eighteenth century, direct calorimetry is costly due to the size and maintenance of the chamber. While it provides accurate measures of resting metabolism, it is not commonly used by exercise physiologists. Figure 6.1 illustrates a human calorimeter at the School of Human Kinetics in Ottawa, Canada.
The principles of direct calorimetry can be demonstrated by the following relationship:

Foodstuff + O2 → ATP + Heat → Cell Work → Heat

Indirect Calorimetry

Unlike direct calorimetry, **indirect calorimetry** does not measure heat production directly. Instead, it involves measuring whole-body oxygen consumption (VO_2) and **carbon dioxide production (VCO_2)** from expired gases. The principle behind indirect calorimetry is the direct relationship between oxygen consumption and heat production. By measuring an i**oxygen consumption (VO_2)**ndividual's oxygen consumption, we can indirectly estimate their heat production and, consequently, their energy expenditure.

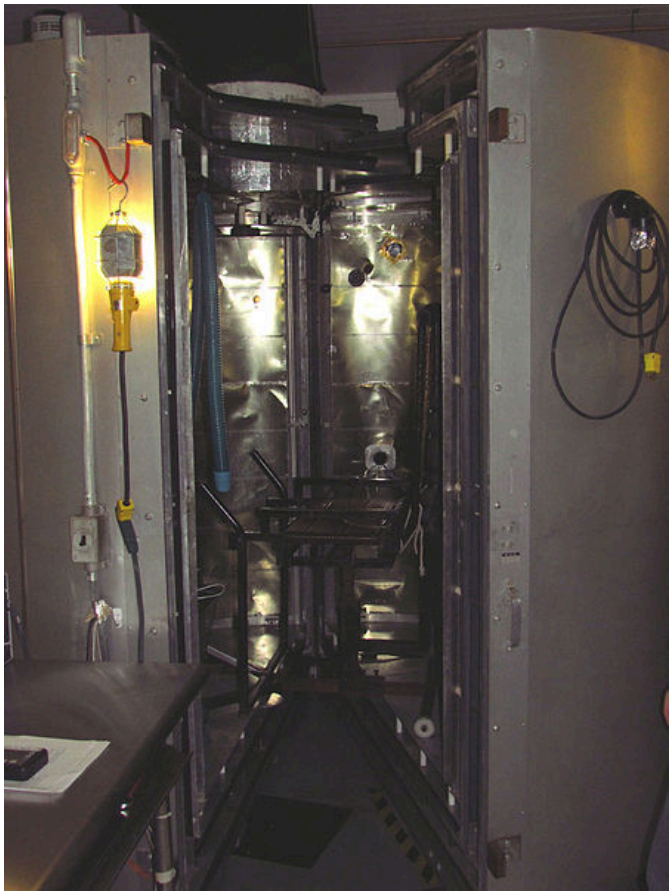


Figure 6.1 The Snellen direct calorimetry chamber, School of Human Kinetics, University of Ottawa, Ottawa, Ontario, Canada.

To convert the amount of oxygen consumed into heat equivalents, it is essential to know the type of nutrient being metabolized—carbohydrates, fats, or proteins. The energy released when fat is the sole metabolized nutrient is approximately 4.7 kcal per liter of oxygen consumed (kcal/LO_2). When only carbohydrates are metabolized, the energy release is about 5.05 kcal/LO_2. For practical purposes, the caloric expenditure of exercise is often estimated at around 5

kcal/LO_2. Therefore, an individual exercising at an oxygen consumption rate of 3.0 LO_2/min would expend approximately 15 kcal of energy per minute.

$$3.0\ LO_2/min \times 5\ kcal/LO_2 = 15\ kcal/min$$

The principle of indirect calorimetry can be explained by the following relationship:

$$Foodstuff + VO_2 \rightarrow CO_2 + Heat + H_2O$$

- VO_2 is the volume of oxygen consumed (in liters per minute).

Energy Equivalent per Liter of Oxygen varies depending on the nutrient being metabolized:

- For fats: approximately 4.7 kcal/LO_2
- For carbohydrates: approximately 5.05 kcal/LO_2
- For mixed substrates: often estimated at 5 kcal/LO_2

This relationship allows us to estimate the total energy expenditure based on the measured oxygen consumption during various activities.

There are two primary methods used to measure VO_2 in humans: closed circuit spirometry and open circuit spirometry.

1. **Closed Circuit Spirometry.** In **closed circuit spirometry**, all the air breathed in and out by the subject is contained within a chamber. Historically, the subject would wear a nose clip to prevent nasal breathing and use a respiratory valve that allowed room air to be inhaled while the exhaled gas was collected in a Douglas bag. Figures 6.2 and 6.3 illustrate this setup. The collected air in the bag was later analyzed for gas volume and the percentages of O_2 and CO_2. Although this technique did not allow for breath-by-breath measurements, it was useful in the early stages of studying exercise energy expenditure.

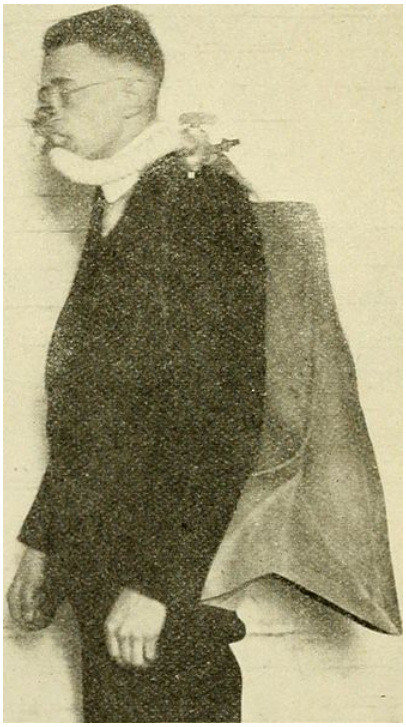


Figure 6.2 The Tissot spirometer, which is a modification of the Douglas bag method for determining the respiratory exchange. The barometric pressure, temperature, and volume of air are important for measurement of the air. The composition of air was determined by the Haldane gas analysis apparatus. The Douglas bag was made of a rubber-lined cloth, and was capable of holding from 50 to 100 liters. It was considered useful for investigations during exercise, since it was fitted with straps so that the bag could be fastened to the shoulders.

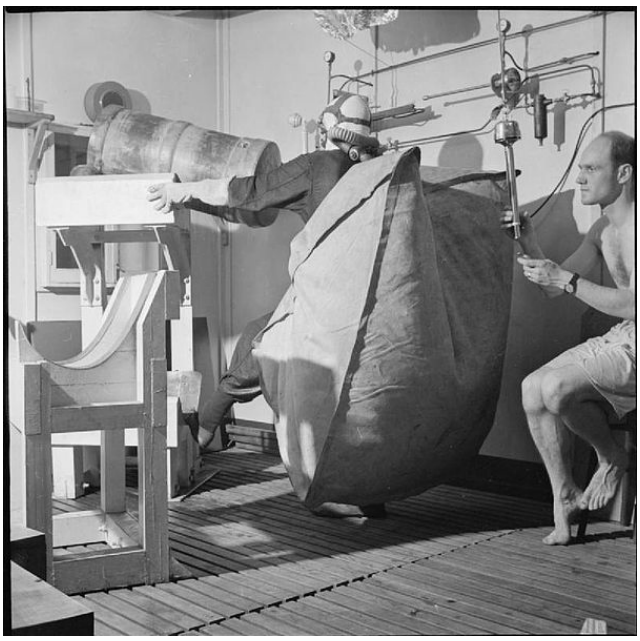


Figure 6.3 A British naval officer takes part in tests to investigate the effect of temperature on efficiency in 1945. The subject is working in a high temperature room and wearing a Douglas oxygen consumption bag. The doctor can be seen on the right-hand side, checking on progress.

2. Open Circuit Spirometry. Open circuit spirometry, on the other hand, involves the subject breathing in ambient air and exhaling into a collection system. This method allows for continuous, breath-by-breath analysis of the expired gases, providing more detailed and immediate data on VO_2 and VCO_2. Open circuit spirometry is more commonly used in modern exercise physiology due to its accuracy and practicality.
The most common technique used to measure oxygen consumption today is open-circuit spirometry. In this method, the subject breathes in environmental air, and the exhaled air is analyzed for CO_2, O_2, and N_2. Modern open-circuit spirometry utilizes advanced computer technology to measure the volume of exhaled gas on a breath-by-breath basis. This exhaled gas is then directed to a mixing chamber where samples are analyzed. Figure 6.4 shows a modern indirect spirometer being used to measure metabolic rate.

Figure 6.4 A sailor stationed at Pearl Harbor uses indirect calorimeter to check his metabolic rate during a Wellness Vehicle visit.

Resting Metabolic Rate

The rate at which the body utilizes energy is known as the metabolic rate. Indirect calorimetry is frequently used to estimate energy expenditure both at rest and during exercise. Under resting conditions, an average person consumes about 0.3 liters of O_2 per minute, which translates to 18 liters of O_2 per hour or 432 liters of O_2 per day. Knowing a person's VO_2 allows for the calculation of their caloric expenditure.

For example, a resting Respiratory Exchange Ratio (RER) value of approximately 0.80 is typical for most individuals on a mixed diet. The caloric equivalent associated with an RER value of 0.80 is 4.80 kcal per liter of O_2 consumed. Energy expenditure can then be calculated using the following formula:

kcal/day = LO2 consumed/day x kcal/LO2

so, kcal/day = 432 LO2 /day x 4.80 kcal/LO2

= 2,074 kcal/day

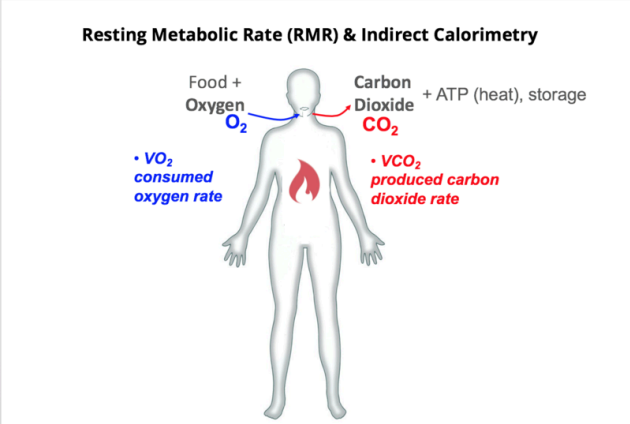


Figure 6.5 How oxygen and carbon dioxide relate to the measure of human energy expenditure.

Measurement of **resting metabolic rate (RMR)** is utilized in both clinical and research settings to provide invaluable information regarding energy requirements and the types of fuels being oxidized at rest. RMR, measured by indirect calorimetry under standard conditions, provides data on oxygen consumption (VO_2), carbon dioxide production (VCO_2), and the respiratory exchange ratio (RER)[1]. Figure 6.5 illustrates the

relationship between oxygen and carbon dioxide in measuring resting metabolic rate.

RMR represents the energy required to maintain essential physiological processes in a relaxed, awake, and reclined state. It is a significant component of **total daily energy expenditure (TEE)**, accounting for 65% to 75% of the total daily energy demands in adults[2]. Practically, RMR indicates the number of calories a person needs per day before considering the calories expended through physical activity. RMR is expressed in kilocalories per day and is also used to calculate physical activity levels (PAL), where PAL = TEE/RMR[3].

RMR can be measured using indirect calorimetry or estimated through prediction equations. One of the most accurate equations for estimating RMR is the Mifflin-St Jeor equation, developed in 1990 to estimate the caloric needs of men and women[4]. The equation is as follows:

Men: 9.99 x weight (kg) + 6.26 x height (cm) – 4.92 x age +5

Women: 9.99 x weight (kg) + 6.26 x height (cm) – 4.92 x age – 161

When measuring RMR, it is crucial that subjects are fasted for at least 5 hours prior to testing. Indirect calorimetry measurements typically occur over approximately 30 minutes while the subject lies supine in a relaxed, awake state. Data is usually collected for 5 minutes once the subject reaches a steady state of oxygen consumption, which is then analyzed to determine the RMR[5].

Metabolic Rate During Exercise

Research has shown that exercise significantly increases energy requirements beyond the resting metabolic rate (RMR). Studies on energy expenditure and **oxygen cost** (O_2 cost = VO_2 at steady state) during exercise have demonstrated that it is possible to estimate energy expenditure with reasonable precision. Detailed studies have been conducted on various exercise types such as walking, running, and cycling[678].

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1. Cooper JA, AC, O'Brian MJ, Luke A, Dobratz JR, Earthman CP, Schoeller DA, Assessing validity and reliability of resting metabolic rate in six gas analysis systems. Journal of the American Dietetic Association, 2009. 109(1): p. 128-132.

2. Ravussin E, Burnand B, Schutz Y, Jequier E, Twenty-four-hour energy expenditure and resting metabolic rate in obese, moderately obese, and control subjects. Am J Clin Nutr, 1982. 35: p. 566-73.

3. Jackson DM, Pace L, Speakman JR, The measurement of resting metabolic rate in preschool children. Obesity, 2007. 15(8): p. 1930-1932.

4. Reidlinger DP, Willis JM, Whelan K, Resting metabolic rate and anthropometry in older people: a comparison of measured and calculated values. J Hum Nutr Diet, 2015. 28(1): p. 72-84.

5. Cooper JA, AC, O'Brian MJ, Luke A, Dobratz JR, Earthman CP, Schoeller DA, Assessing validity and reliability of resting metabolic rate in six gas analysis systems. Journal of the American Dietetic Association, 2009. 109(1): p. 128-132.

6. Daniels J, and Daniels N, Running economy of elite male and elite female runners. Medicine & Science in Sports & Exercise, 1992. 24(4): p. 483-489.

Indirect calorimetry is used to determine VO_2 at different exercise intensities, which is then used to calculate the metabolic rate of that exercise.

VO_2 can be expressed as an absolute value (**absolute VO_2** = L O_2/min) or the relative value, relative to body mass (**relative VO_2** = ml O_2/kg*min). Expressing VO_2 relative to body mass is appropriate when comparing the O_2 cost between individuals or when describing the O_2 cost of weight-bearing activities such as walking, running, or climbing steps. The energy cost of horizontal treadmill walking or running, as well as the O_2 requirement, increases linearly, as shown in Figure 6.6[9]. A similar relationship exists for cycling, up to a power output of about 200 W[10].

Accurately measuring energy expenditure is limited to the time spent in steady state during exercise. This limitation makes it challenging to measure the energy costs of activities other than running, walking, and cycling. Consequently, the energy costs of various activities are often expressed as metabolic equivalents of a task, or METs.

Figure 6.6 The relationship between oxygen cost (VO2) and speed for both walking and running at steady state. Note that the relationship between speed and VO2 in these types of exercise is linear.

The **metabolic equivalent of a task (MET)** represents the energy expended during resting metabolism, with one MET conventionally equal to 3.5 ml O_2/kg/min. The energy cost of activities can be expressed in multiples of the MET unit. METs can also be used to express the number of calories expended per kilogram of body weight per hour.

For example, if a subject is working at 12 METs, or 42 ml O_2/kg/min, and exercises for 60 minutes, the total oxygen consumption would be 2,520 ml/kg/hr. If the person is using a mixture of carbohydrates and fats for fuel, the VO_2 is multiplied by 4.85 kcal per liter of O_2 (the average between 4.7 and 5.05 kcal/LO_2) the energy expenditure would be 12.22 kcal/kg/hr. This method provides a practical way to estimate the energy expenditure of various activities based on MET values and body weight.

7. Moseley L, Jeukendrup AE, The reliability of cycling efficiency. Medicine & Science in Sports & Exercise, 2000. 33(4): p. 621-627.

8. Mian OS, Thom JM, Aridigo LP, Narici MV, Minetti AE, Metabolic cost, mechanical work, and efficiency during walking in young and older men. Acta Physiologica, 2006. 186(2): p. 127-139.

9. Das SK, Dutta A, Relation of speed of a mile run, maximum energy cost of running, and maximum oxygen consumption: a field study. Br J Sports Med, 1995. 4: p. 271-272.

10. Powers SK, and Howley ET, Exercise Physiology (Theory and Application to Fitness and Performance). 9th Edition ed. 2015, New York, NY: McGraw-Hill.

12 MET x 3.5 ml/kg/min = 42 ml/kg/min
42 ml/kg/min x 60 min/hr = 2,520 ml/kg/hr
2,520 ml/kg/hr = 2.52 L/kg/hr
= 2.52 L/kg/hr x 4.85 kcal/LO2
= 12.22 kcal/kg/hr

The following steps outline how to convert metabolic equivalents to the number of calories expended per hour based on body mass:

1. Determine the MET value of the activity.
2. Multiply the MET value by 3.5 to convert to ml O_2/kg/min.
3. Multiply by the duration of the activity in minutes to get ml O_2/kg/hr.
4. Convert to liters by dividing by 1,000.
5. Multiply by the caloric equivalent (4.85 kcal/LO_2) to get kcal/kg/hr.
6. Multiply by body weight in kilograms to get total kcal/hr.

The 2024 Compendium of Physical Activity website is designed to provide an updated resource and MET codes for physical activities used in research[11][12]. It serves as a valuable reference for the energy expenditure associated with various sports, household activities, and other categories. For example, the energy expended for one hour of a basketball game is 8.0 METs, while one hour of competitive volleyball equals 6.0 METs. The Compendium was not intended to determine the precise energy cost of physical activities for individuals but rather to standardize MET intensities. It does not account for differences in body mass, adiposity, age, sex, exercise efficiency, or environmental conditions. Therefore, individual differences in energy expenditure may vary from the MET levels presented in the Compendium.

Calculating Rates of Gas Exchange

Using indirect calorimetry, exercise physiologists can measure the three variables needed to calculate the volume of oxygen consumed (VO_2) and the volume of carbon dioxide produced (VCO_2). The calculation of

11. Ainsworth BE, Haskell WL, Herrmann SD, Meckes N, Bassett Jr DR, Tudor-Locke C, Greer JL, Vezina J, Whitt- Glover MC, Leon AS, 2011 Compendium of Physical Activities: a second update of codes and MET values. Medicine & Science in Sports & Exercise, 2011. 48(8): p. 1575-1581.

12. The 2024 Compendium of Physical Activities and its expansion. Stephen D. Herrmann, Erik A. Willis, Barbara E. Ainsworth. Journal of Sport and Health Science. 13(1), p. 1-2.

the rate of gas exchange involves subtracting the amount of expired gas from the amount of inspired gas. Specifically, VO_2 is equal to the volume of O_2 inspired minus the volume of O_2 expired. To calculate the volume of O_2 inspired, we multiply the volume of air inspired by the fraction of that air composed of O_2 (FIO_2). The volume of O_2 expired is calculated by multiplying the volume of air expired by the fraction of the expired air composed of O_2 (FEO_2). The oxygen consumption, in liters of oxygen consumed per minute, can then be calculated as follows:

$$VO_2 = (VI \times FIO_2) - (VE \times VEO_2)$$

Carbon dioxide production (VCO_2) is calculated in a manner similar to oxygen consumption. To determine the volume of CO_2 produced, we need to account for the inspired and expired fractions of CO_2. Specifically, VCO_2 is equal to the volume of CO_2 inspired minus the volume of CO_2 expired. The volume of CO_2 inspired is calculated by multiplying the volume of air inspired by the fraction inspired of air composed of CO_2 ($FICO_2$). The volume of CO_2 expired is calculated by multiplying the volume of air expired by the fraction of the expired air composed of CO_2 ($FECO_2$). The carbon dioxide production, in liters of CO_2 produced per minute, can then be calculated as follows:

$$VCO_2 = (VI \times FICO_2) - (VE \times VECO_2)$$

These equations provide reasonably good estimations of gas exchange; however, there are limitations. The equations assume that there are no changes in gases stored within the body and that the volume of O_2 consumed equals the volume of CO_2 produced. During exercise, it is known that the volumes of CO_2 increase due to increases in metabolic rate.

More accurate equations have been derived for exercise based on the fact that a third important gas, nitrogen, is also inhaled and exhaled. The volumes of nitrogen inspired (VIN_2) and the volume of nitrogen expired (VEN_2) should also be considered. The following is called the Haldane transformation, and it is used by exercise physiologists to compute the volume of oxygen (VO_2):

$$VO_2 = (VE) \times \{[1 - (FEO_2 \times FECO_2) \times (0.265)] - (FEO_2)\}$$

Where:

- VI is the volume of air inspired.
- VE is the volume of air expired.
- FIO_2 is the fraction of inspired oxygen.
- FEO_2 is the fraction of expired oxygen.
- $FECO_2$ is the fraction of expired carbon dioxide.

The Haldane transformation accounts for the constant volume of nitrogen in inspired and expired air, providing a more accurate measure of VO_2 during exercise.

Computers now calculate VO_2 automatically and correct the expired air concentrations because body temperature (BT), ambient pressure (P), and water vapor saturation (S) can influence the accuracy of the measurements. Therefore, every gas volume is routinely converted by correction equations to its standard

temperature (ST: 0°C or 273 K) and pressure (P: 760 mmHg), dry equivalent (D) or STPD[13].

Respiratory Exchange Ratio (RER)

The amount of oxygen used during metabolism depends on the type of substrate or fuel being oxidized. Generally, the amount of oxygen needed to completely oxidize a molecule of fat or carbohydrate is proportional to the amount of carbon in that fuel. By evaluating the amount of CO_2 released compared with the amount of O_2 consumed, we can estimate the type of fuel being utilized. The ratio between the rate of CO_2 released (VCO_2) and oxygen consumed (VO_2) is termed the respiratory exchange ratio (RER).

$$RER = VCO_2/VO_2$$

The RER is measured by indirect calorimetry. The theoretical RER limits range from 0.70 to 1.00. An RER of 1.00 indicates that 100% of the energy produced in metabolism is derived from carbohydrates, with no contribution from fats. For example, glucose ($C_6H_{12}O_6$) contains six carbon atoms. During the combustion of glucose, six molecules of oxygen are used to produce six molecules of CO_2, six molecules of H_2O, and 30 ATP molecules:

$$6\ O_2 + C_6H_{12}O_6 \rightarrow 6\ CO_2 + 6\ H_2O + 30\ ATP$$

This reaction illustrates the complete oxidation of glucose, where the ratio of CO_2 produced to O_2 consumed is 1:1, resulting in an RER of 1.00.

$$RER = VCO_2/VO_2 = 6\ CO_2/6\ O_2 = 1.0$$

Inversely, an RER of 0.70 indicates that 100% of the energy produced in metabolism is derived from fat, with no contribution from carbohydrates. Fats have considerably more carbon and hydrogen atoms but less oxygen than glucose. Consider palmitic acid ($C_{16}H_{32}O_2$). To completely oxidize palmitic acid, 23 molecules of oxygen are needed:

$$C_{16}H_{32}O_2 + 23\ O_2 \rightarrow 16\ CO_2 + 16\ H_2O + 129\ ATP$$

This reaction shows that the ratio of CO_2 produced to O_2 consumed is lower than 1:1, resulting in an RER of 0.70. This lower RER reflects the greater oxygen requirement for the oxidation of fats compared to carbohydrates. Thus, the RER of palmitic acid is 0.70.

$$RER = VCO_2/VO_2 = 16\ CO_2/23\ O_2 = 0.70$$

Combustion of fat requires significantly more oxygen than a carbohydrate molecule. This results in a substantially lower RER value for fat (e.g., 0.70) compared to carbohydrates (e.g., 1.00). The respiratory exchange ratio chart, shown in Table 6.1, varies with the type of fuels being used for energy. Once the RER value has been determined, the chart can be used to identify the food mixture being oxidized and calculate the amount of energy being expended.

13. Kenney LK, Wilmore JH, Costil DL, ed., Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

For example, if the RER value is 1.00, the cells are using only glucose or glycogen, and each liter of oxygen consumed generates 5.05 kcal/L of O_2. Therefore, if the muscles are using only glucose and the body is consuming 3 L of O_2 per minute, the rate of energy production would be:

$$3L/min * 5.05\ kcal/L = 15.15\ kcal/min$$

Each substrate has a specific energy yield[14]:

- The oxidation of pure fat yields 4.69 kcal/L of O_2 consumed.
- The oxidation of only protein yields 4.46 kcal/L of O_2 consumed.

This information allows for precise calculations of energy expenditure based on the type of substrate being metabolized.

14. Cooper JA, AC, O'Brian MJ, Luke A, Dobratz JR, Earthman CP, Schoeller DA, Assessing validity and reliability of resting metabolic rate in six gas analysis systems. Journal of the American Dietetic Association, 2009. 109(1): p. 128-132.

Table 6.1 Percentage of fat and carbohydrate metabolized as determined by a non-protein respiratory exchange ratio (RER).

RER	FAT %	CHO%
1.00	0	100
.98	6	94
.96	12	88
.94	19	81
.92	26	74
.90	32	68
.88	38	62
.86	47	53
.84	53	47
.82	62	38
.80	68	32
.78	74	26
.76	81	19
.74	88	12
.72	94	6
.70	100	0

The measurement of RER has limitations mainly due to the assumption that the body's O_2 content remains constant and that CO_2 exchange in the lungs is proportional to CO_2 release from the cells. Therefore, calculations of carbohydrate and fat usage based on indirect calorimetry are valid only at rest or during steady-state exercise. Additionally, protein cannot be completely oxidized in the body because nitrogen is not oxidizable, making it impossible to calculate the body's protein use from the RER. As a result, the RER is sometimes referred to as non-protein RER because it ignores protein oxidation. Despite its shortcomings, indirect calorimetry still provides the best estimate of energy expenditure at rest and during steady-state (aerobic) exercise.

Maximal Exercise Testing

The most valid measurement of cardiovascular fitness is the maximal capacity to transport and utilize oxygen during exercise. **Maximal oxygen uptake (VO_2max)** is defined as the maximum rate of VO_2 ($ml \cdot min^{-1} \cdot kg^{-1}$) obtained by working to exhaustion. Simply put, VO_2max is the body's maximal capacity to consume, distribute, and utilize oxygen during an incremental exercise test. VO_2max is also known as the aerobic capacity or maximum physical work capacity[15].

Typically, changes in oxygen uptake are measured during an incremental (graded) exercise test conducted on a treadmill or a cycle ergometer. An incremental exercise test usually begins with a 5-minute warm-up at 60-70% of VO_2max, followed by a brief rest. The protocol then starts with an initial load set at about 60-70% VO_2max and includes a series of planned progressions that increase the work rate at each stage. Each stage can last from 1 to 3 minutes, and the test continues until the subject cannot maintain the desired power output. Excluding the warm-up, subjects should reach the limit of tolerance within 8-12 minutes to ensure that aerobic metabolism is functioning at full capacity. On a treadmill, increasing the grade (incline) or speed are methods used to increase the work rate. On a cycle ergometer, resistance is applied to the flywheel as the subject tries to maintain the required cadence. Fatigue is determined when a subject (under verbal encouragement from the experimenters) can no longer sustain a pedaling cadence of at least 60 rpm or terminates a running test at their own volition. Another type of test progression used by exercise physiologists is called an incremental ramp protocol, where the work rate is rapidly incremented as a "smooth" function of time[16].

Research has shown that oxygen uptake increases linearly with the work rate until VO_2max is reached.

15. Das SK, Dutta A, Relation of speed of a mile run, maximum energy cost of running, and maximum oxygen consumption: a field study. Br J Sports Med, 1995. 4: p. 271-272.

16. Day JR, Rossiter HB, Coats EM, Skasick A, Whipp BJ, The maximally attainable VO2 during exercise in humans: the peak vs. maximum issue. Journal of Applied Physiology, 2003. 95(5): p. 1901-1907.

When VO_2max is reached, an increase in work rate or power output does not result in an increase in oxygen uptake; thus, VO_2max represents a "physiological ceiling" for the oxygen transport system to deliver O_2 to working muscles[17]. Classically, VO_2max levels were thought to exhibit a "plateau" of oxygen consumption at the end of the incremental test. This value is still considered a criterion for achieving VO_2max; however, not all individuals demonstrate this plateau at the end of an incremental test. Perhaps it is because the subject simply cannot complete one more stage beyond the one at which VO_2max was achieved. Nevertheless, other criteria recognized by exercise scientists can also demonstrate that the highest value reached is VO_2max[18]. The major criteria include:

1. A maximal heart rate within 10 beats per minute of the subject's predicted maximum heart rate (predicted max-HR = 220 – age).
2. A rating of perceived exertion (RPE) greater than 17 on the Borg RPE scale (shown in Table 6.2).
3. A respiratory exchange ratio (RER) greater than 1.1.
4. A "plateau" of oxygen consumption less than or equal to 150 ml O_2/min.

If the subject reaches 3 out of the 4 aforementioned criteria, it is said that the highest value of oxygen consumed is the VO_2max. Additionally, some researchers consider high levels of blood lactate to be an additional criterion for achieving VO_2max[19].

Clinically, incremental exercise tests (also called stress testing) are often employed by physicians to examine patients for possible heart disease. Along with an echocardiogram (ECG) assessment of the stress test, a physician can determine various pathophysiological conditions. Often with these patients, a "system-limited" **peak oxygen uptake (VO_2peak)** value, rather than a VO_2max value, is reported. A VO_2peak is reported when a subject or patient only achieves 2 out of the 4 criteria for VO_2max. It is still not known if failure to reach a plateau in VO_2 is due to "insufficient effort" or if plateaus of VO_2 are rarely attained despite "good effort" from the subjects[20]. Knowing an athlete's VO_2max can be valuable for coaches who need to know the maximum speed of athletes under training or of competitors in various sports and games where endurance is a good criterion for selection, training, and improvement. It is also known that greater

17. Powers SK, and Howley ET, Exercise Physiology (Theory and Application to Fitness and Performance). 9th Edition ed. 2015, New York, NY: McGraw-Hill.

18. Day JR, Rossiter HB, Coats EM, Skasick A, Whipp BJ, The maximally attainable VO_2 during exercise in humans: the peak vs. maximum issue. Journal of Applied Physiology, 2003. 95(5): p. 1901-1907.

19. Howley ET, Bassett DR Jr, Welch HG, Criteria for maximal oxygen uptake: review and commentary. Medicine & Science in Sports & Exercise, 1995. 27(9): p. 1292-1301.

20. Day JR, Rossiter HB, Coats EM, Skasick A, Whipp BJ, The maximally attainable VO_2 during exercise in humans: the peak vs. maximum issue. Journal of Applied Physiology, 2003. 95(5): p. 1901-1907.

cardiorespiratory fitness correlates with greater speed in a mile run[21].

Calculating Work and Power in Humans

An ongoing problem in exercise science is the failure to standardize units of measurement in presenting research data. In the United States, the English system of measurement remains in common use despite the standard system of measurement for scientists. The metric system is used in most other countries and is the standard system of measurement. Almost all scientific journals use the metric system, with the basic units of length, volume, energy, and mass being the meter, the liter, the joule, and the gram, respectively. Because of this, a uniform system of reporting scientific measures has been developed. This system, developed through international cooperation, is called System International units, or SI units. SI units have been endorsed by almost all exercise and sports medicine journals for the publication of data to make comparison of published values easy and are summarized in Table 6.3.

Table 6.2 The Borg ratings of perceived exertion scale (RPE).

Rating	Perceived Exertion
6	No exertion
7	Very, very light
8	
9	Very light
10	
11	Fairly light
12	
13	Somewhat hard
14	
15	Hard
16	
17	Very hard
18	
19	Very, very hard
20	Maximum exertion

It is important to understand the terms work and power to compute human work output and exercise efficiencies. **Work** is defined as the product of force and the distance through which the force acts:

Work = force x distance

Human work is quantified in joules (J) and is a function of force expressed in newtons (N) and distance in meters (m). The following example demonstrates how to calculate work for a person lifting a 20 kg weight upward over a distance of 2 meters.

Example: Lifting a 20 kg weight upward over a distance of 2 meters in 60 seconds

The kilopond is a unit of force that represents the effect of gravity on a mass of 1 kilogram. Thus, is important

21. Das SK, Dutta A, Relation of speed of a mile run, maximum energy cost of running, and maximum oxygen consumption: a field study. Br J Sports Med, 1995. 4: p. 271-272.

to realize that at the earth's surface, a mass of 1 kg exerts a force of 9.81 N due to gravity. Therefore, the mass (kg) of the weight must first be converted to a force (N).

Step 1: Convert kg to Newtons (N), where 1 kg = 9.81 N

20 kg x 9.81 m/s2 = 196.2 N

Once the mass is converted to a force, the force can be multiplied by the distance to find the work done, expressed in joules (J).

Step 2: Multiply force (N) by distance (m) to find work

Work = 196.2 N x 2 m

Work = 392.4 Newton-meters or 392.4 joules (J)

An additional step is required to calculate power for the same example. **Power** is expressed in watts (W) and measures the rate at which work is completed. Power describes how much work is accomplished per unit of time.

Then, to calculate power, work must be calculated from weight and distance as in Step 1 and Step 2. Then, power (W) can be determined by dividing work by time in seconds (s):

Power = work/time

Step 3: Divide joules by seconds to find power

Power = 196.2 N x 2 m

Power = 6.54 watts (W)

In some situations, traditional units are used to express both work and energy. Table 6.4 contains a list of terms commonly used today to express work, power, and energy and their conversions to SI units. Note that both work and energy use joules (J). The energy content of commercial food products is often listed on the label in kilocalories (kcals) or Calories (kcals) with a capital letter "C." However, the SI unit for energy content and expenditure is joules, where 1 kilocalorie is equal to 4,186 joules (J) or 4.186 kilojoules (kJ). In the UK and other European countries, energy is expressed as both kilojoules (kJ) and kilocalories (kcals) on food labels. In the United States, food labels often represent energy as Calories (kcals), which may be misleading because the capital "C" represents kilocalories and not calories, which are 1,000 times smaller than one kilocalorie.

Table 6.4 Common units and conversion factors used to express work, power, or energy expended in humans

Unit	SI Unit
Mass	Kilogram (kg)
Distance	Meter (m)
Time	Seconds (s)
Force	Newton (N)
Work, Energy	Joule (J)
Power	Watt (W)
Velocity	Meters per second (m/s)
Torque	Newton-meter (Nm)

The measurement of work output is termed **ergometry**. Several devices measure specific types of work or power in humans. These apparatuses are called ergometers and are used in exercise physiology laboratories. One of the earliest ergometers to measure work in humans was the bench step, where the total work performed was a function of body mass, step cadence, and the height of the step. Other commonly used devices to measure work or power include the cycle ergometer, rowing ergometers, motor-driven treadmills, and arm crank ergometers. Figure 6.7 shows examples of ergometers commonly used to measure human work and power.

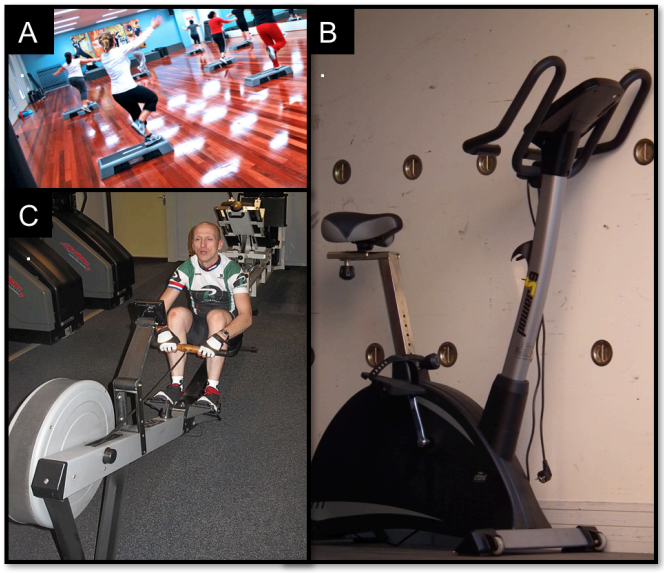


Figure 6.7 Examples of ergometers used in the measurement of human work and power output. A) A bench step ergometer, B) a cycle ergometer, and C) a rowing ergometer.

Exercise Efficiency

Exercise efficiency is the capacity to convert energy expenditure (EE) into work, with some energy inevitably lost as heat. Net efficiency is a function of work output and energy expended.

Net efficiency = (Work output/Energy Expended) x 100

Factors influencing efficiency include the percentage of slow muscle fibers, which display greater efficiency. Slow fibers require less ATP per unit of work. Subjects with increased efficiency generate greater power output at any given EE rate. Horizontal running efficiency cannot be calculated

directly. Instead, the O_2 cost of running at any speed is measured to make comparisons. The O_2 cost is defined as VO_2 at steady state. A runner with poor running economy would require a higher VO_2 at any given running speed. Running economy is the relationship between oxygen consumption (VO_2) and the velocity (v) of running, or the aerobic demands of running[22].

Chapter Summary

In this chapter, we explored the fundamental principles of energy expenditure and its critical role in exercise physiology. We began by examining the metabolic pathways involved in ATP formation and how energy expenditure varies between rest and exercise. We discussed the methods for measuring energy expenditure, including direct and indirect calorimetry, and highlighted the importance of understanding the respiratory exchange ratio (RER) in determining the type of fuel being utilized.

We also delved into the measurement of resting metabolic rate (RMR) and its significance in both clinical and research settings. The chapter covered the methods for measuring VO_2, including closed and open circuit spirometry, and the use of the Haldane transformation for more accurate calculations during exercise. Furthermore, we examined the concept of maximal exercise testing, the criteria for achieving VO_2max, and the practical applications of knowing an athlete's VO_2max. The importance of standardized units of measurement in exercise science was emphasized, along with the calculation of work and power in humans.

Finally, we discussed exercise efficiency, the factors influencing it, and the concept of running economy. By understanding these principles, we can better appreciate the complexities of energy expenditure and its implications for exercise performance and overall health.

Scholarly Questions

1. What is calorimetry?
2. Is VO2 a direct or indirect measure of energy expenditure?
3. What does MET stand for? How would you calculate a MET from a given VO2? How many

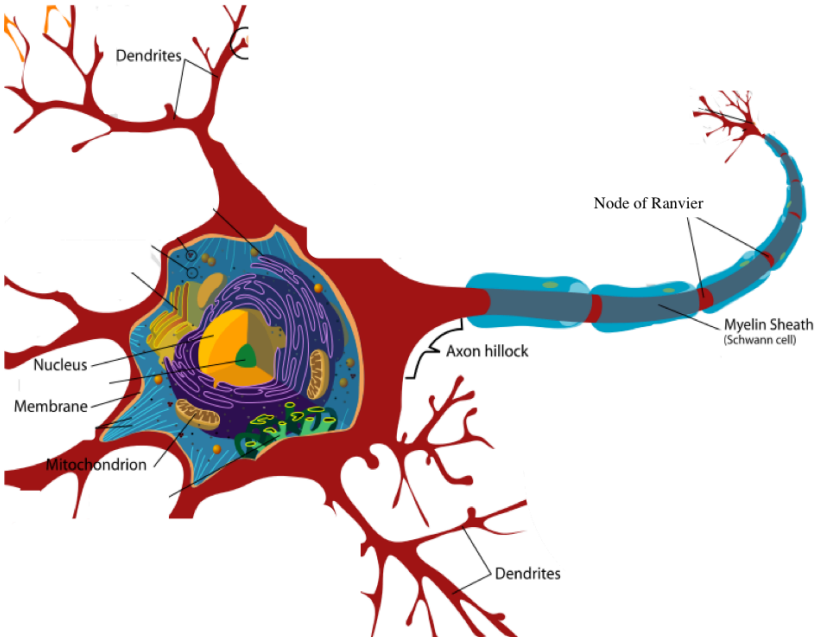
22. Daniels J, and Daniels N, Running economy of elite male and elite female runners. Medicine & Science in Sports & Exercise, 1992. 24(4): p. 483-489.

METs is a person working at if VO2 is 35 ml/kg/min? 60 ml O2/kg/min?

4. What is work?
5. Calculate the work a person does if they lift 40 kg weight upward over a distance of 4 meters.
6. What is power?
7. Calculate the power a person does if they lift 40 kg weight upward over a distance of 4 meters in 30 seconds.
8. What is an ergometer? Can you name an example of an ergometer that is used in the lab?
9. What factors can affect exercise efficiency?
10. What does RER stand for? How is it expressed mathematically? Can you calculate RER if VO2 is 12 ml/kg/min and VCO2 is 10 ml/kg/min?
11. What is the difference between the RQ (Respiratory Quotient) and RER?
12. What are the theoretical limits of RER?
13. What is a VO2 max? What are the 4 criteria to know it has been achieve?
14. What is the average improvement seen with VO2max from endurance training?
15. What is a VO2 peak? What is the difference between VO2max and VO2 peak?
16. What are the two ways for expressing VO2? Which is better for comparison and why?
17. If the caloric expenditure of exercise is 5 kcal/LO2, how many kcals is a person burning if they are exercising at 25 LO2/min?
18. Usually, what type of exercise mode (cycle, treadmill, stepper) will yield the highest VO2max values? Why (hint: which mode utilizes the most muscle mass)?

7.

THE NERVOUS SYSTEM



A complete neuron cell, including the cell body (soma), dendrites, axon, myelin sheath, nodes of Ranvier, axon terminals, and synapse involved in the transmission of electrical impulses. Dendrites receive incoming signals, which are processed in the soma and transmitted along the axon. The myelin sheath, interrupted by nodes of Ranvier, facilitates rapid signal conduction. Axon terminals connect to other neurons or target cells via synapses. This figure represents the fundamental architecture of neurons in the vertebrate nervous system, including the brain, spinal cord, and peripheral nerves.

Learning Objectives

- Describe the role of the central nervous system (CNS) in initiating and coordinating voluntary

movements, including the functions of the primary motor cortex, cerebellum, and basal ganglia.
- Explain the structure and function of the peripheral nervous system (PNS), particularly the motor division, and its role in transmitting impulses to skeletal muscles.
- Understand the concepts of resting membrane potential, graded potentials, and action potentials, including the processes of depolarization, hyperpolarization, and the refractory periods.
- Identify the steps involved in the generation and propagation of an action potential, and how it leads to muscle excitation and contraction cycling.
- Discuss the mechanisms of synaptic transmission, including the roles of neurotransmitters such as acetylcholine and the processes at the neuromuscular junction.
- Recognize the importance of exercise in promoting brain health, and describe the benefits of physical activity on cognitive function and overall well-being.
- Summarize the pathway of force production, from CNS activation to the arrival of the action potential at the neuromuscular junction, and understand its relevance to exercise physiology and fatigue.

The Nervous System: An Overview

The nervous system is a complex network that receives millions of bits of information each minute from various sensory neurons and sensory organs. It integrates these signals to determine the necessary responses of the body. Acting as a central computer, the brain processes this information and selects appropriate responses. All functions within the human body are under the control or influence of the nervous system, which facilitates communication and coordination between different tissues and the external environment.

Generally, the nervous system, along with the endocrine system, promotes homeostasis by communicating with various tissues, organs, and systems, often without our conscious awareness. It also stores information as memories, enabling learning. Besides involuntary control, the nervous system allows volitional control of skeletal muscle locomotion. Reflexes, which can be programmed in the spinal cord, bypass higher brain centers to permit quick responses to stimuli. The nervous system transmits signals throughout the body by converting stimuli into electrical signals, or nerve impulses.

The Neuromuscular System

A single voluntary muscle contraction involves a complex pathway of events starting in the motor cortex of the brain and ending with muscle contraction cycling within a muscle fiber. This intricate process is why the nervous system and the muscular system are often grouped together and referred to as the neuromuscular system. This chapter focuses on the neural control of muscle contraction, providing an overview of the nervous system's functions and presenting the first three steps of the pathway of force production. This pathway, designed for undergraduate students, summarizes the complex systems involved in voluntary muscle contractions. The pathway of force production includes:

1. Central nervous system activation of the primary motor cortex and the spinal cord
2. The action potential
3. Arrival of the action potential at the neuromuscular junction
4. Muscle contraction cycling

The details of processes 1-3 will be discussed in this chapter, with muscle contraction cycling and force production covered in chapter 8.

Organization of the Nervous System

Before delving into the pathway of force production, it is essential to understand the organization of the nervous system and how it integrates and controls movement. The nervous system is divided into two anatomical systems: the **central nervous system (CNS)** and the **peripheral nervous system** (PNS). The CNS, comprising the brain and spinal cord, contains over 100 billion neurons. The PNS includes all neurons outside the CNS and is divided into sensory and motor divisions.

The **sensory division** of the peripheral nervous system relays impulses from receptors in the body to the CNS. Neurons that transmit messages from the body to the CNS are called afferent fibers (sensory fibers). The **motor division**'s nerve cells, termed efferent fibers, carry impulses from the CNS to effector organs. An example of an efferent fiber is a motor neuron that stimulates muscle contraction in the connected muscle fiber.

The motor division of the peripheral nervous system (PNS) is crucial in exercise physiology as it relays messages to skeletal muscles for locomotion. This division is subdivided into systems that control voluntary and involuntary actions of tissues and organs. These systems are the **somatic nervous system**, which pertains to the outer regions of the body, and the **autonomic nervous system**, also known as the visceral nervous system. The somatic nervous system is responsible for voluntary movements, whereas the autonomic nervous system governs involuntary functions. The autonomic nervous system is further divided into the **sympathetic nervous system**, often referred to as the "fight or flight" system, and the **parasympathetic nervous system**, known for "resting and digesting." Figure 7.1 illustrates the organization of the nervous system.

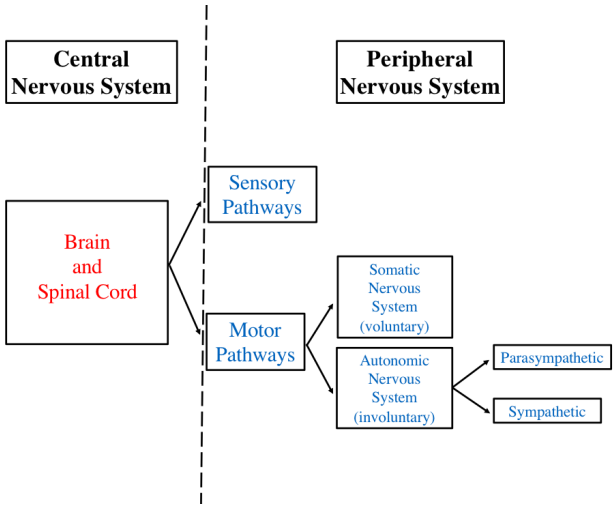


Figure 7.1 Organization of the nervous system including the divisions of the central and peripheral nervous systems.

Anatomy of a Neuron

The fundamental building block of the nervous system is the neuron, or nerve cell, which rapidly conveys signals over long distances to communicate and process information[1]. Neurons are specialized excitable tissues capable of transmitting electrical impulses to communicate with other neurons or tissues in the body. Anatomically, neurons share many components with typical cells, including a cell membrane, nucleus, and mitochondria. Each neuron has an enlarged cell body, known as the soma, which houses the nucleus, endoplasmic reticulum, ribosomes, and other organelles within the cytoplasm. Extending from the soma are several finger-like projections called dendrites, which make contact with neighboring neurons. At the base of the soma is the axon hillock, which integrates impulses received from other cells to determine if an **action potential**, or nerve transmission, will occur.

Neurons also possess a long, thin extension called the axon, which conducts impulses away from the cell body. The axon is insulated by a discontinuous myelin sheath, which facilitates rapid transmission of nerve impulses. The segments of the myelin sheath are known as Schwann cells. Near its end, the axon branches into numerous end branches, with the tips of these branches forming tiny bulbs called axon terminals. These

1. Brodal P, The Central Nervous System. 2010, New York, NY: Oxford University Press.

terminals contain synaptic vesicles filled with acetylcholine, a chemical neurotransmitter. When a signal travels down the axon, acetylcholine is released into the synapse, a 20-30 nanometer gap between cells. Communication between nerve cells occurs at synapses. Synaptic clefts are too small to be observed with a light microscope, and it wasn't until the 1950s that it was demonstrated that neurons are anatomically separate entities[2]. Figure 7.2 provides an illustration of presynaptic and postsynaptic neurons separated by a synapse, highlighting their key anatomical structures.

Specialized Sensory Neurons

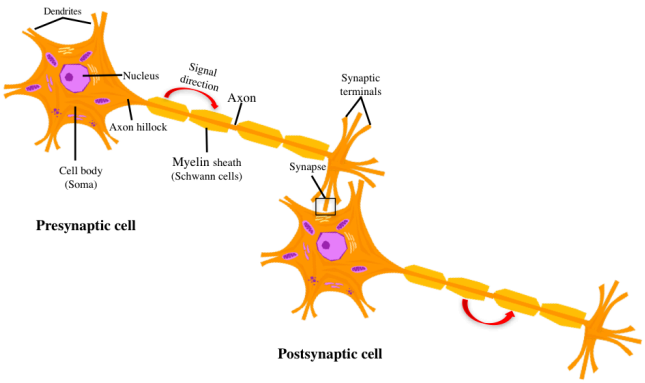


Figure 7.2 An illustration of a neuron and important structures. This also depicts a presynaptic cell and postsynaptic cell which are separated by a synapse.

The central nervous system (CNS) receives constant feedback from receptors throughout the body about changes in both the internal and external environments. These receptors are sensory neurons that monitor everything from environmental sensations to the physiological status of nutrient availability. Sensory neurons include chemoreceptors, which sense changes in the internal chemical environment (e.g., H^+, K^+, CO_2 concentrations), and baroreceptors, which sense changes in blood pressure. Given the vast number of sensory receptor variations, this discussion will focus on sensory organs relevant to exercise physiology and those responsible for body position sense. Sensory stimulation from these receptors is transmitted via sensory nerves to the spinal cord, where it can either trigger a reflex at that level or be transferred to upper regions of the spinal cord or brain.

Skeletal muscle contains several types of sensory receptors. Receptors that provide the CNS with information about the position of body parts with respect to gravity are called **proprioceptors**. Also known as kinesthetic receptors, proprioceptors include **muscle spindles**, **Golgi tendon organs**, and joint receptors. For the nervous system to properly control skeletal muscle movements, it must receive continuous sensory feedback about the tension building in muscles and the amount of muscle length.

The muscle spindle is the muscle's measuring instrument for static muscle length and dynamic length changes[3]. Muscle spindles run parallel with muscle fibers and, when activated, increase the force produced by

2. Brodal P, The Central Nervous System. 2010, New York, NY: Oxford University Press.

3. Henatsch HD, and Langer HH, Basic Neurophysiology of Motor Skills in Sport. Int J Sports Med, 1985. 06(1): p. 2-14.

the muscle. They are composed of several thin muscle cells called intrafusal fibers, which are surrounded by connective tissue sheaths and insert into the connective tissue within the muscle fibers (extrafusal fibers). Muscle spindles have two types of sensory nerve endings: primary endings, which respond to dynamic changes in muscle length, and secondary endings, which continuously provide the CNS with information about static muscle length[4].

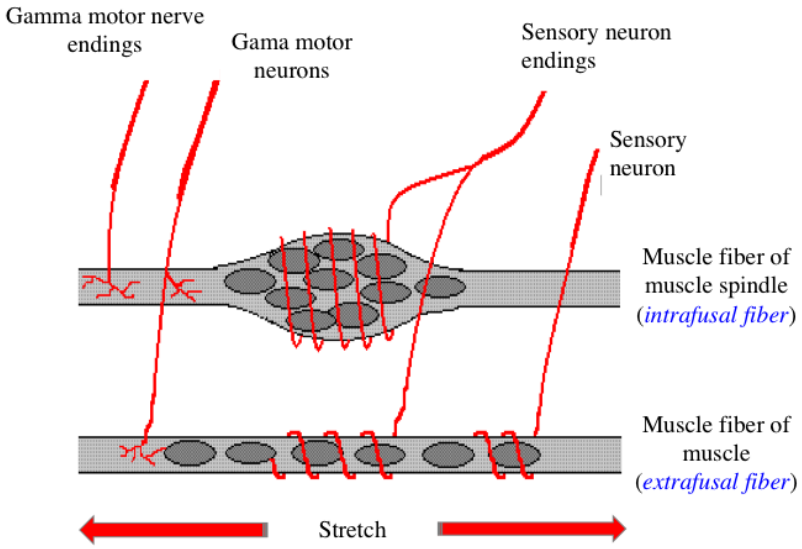


Figure 7.3 The structure of muscle spindles and their location in skeletal muscle.

4. Powers SK, and Howley ET, Exercise Physiology (Theory and Application to Fitness and Performance). 9th Edition ed. 2015, New York, NY: McGraw-Hill.

Muscle spindles are innervated by gamma motor neurons (Figure 7.3), which stimulate the intrafusal fibers to contract simultaneously with the extrafusal fibers. When a muscle is stretched, muscle spindles activate the agonist muscle motor unit to shorten the muscle. Rapid stretching of skeletal muscles results in a reflex contraction, known as the myotatic reflex, which is monitored by the muscle spindles. The knee-jerk reflex is a classic example of the myotatic reflex, often evaluated in a physician's office by tapping the patellar tendon with a rubber mallet. The mallet's blow stretches the entire muscle, exciting the primary nerve endings in the muscle spindles. This stimulation activates the extrafusal fibers of the extensor muscle, the rectus femoris, resulting in the knee jerk action. Muscle spindles also help prevent collapsing or falling when muscle stretch is sensed. They detect both the stretch and the speed of the stretch.

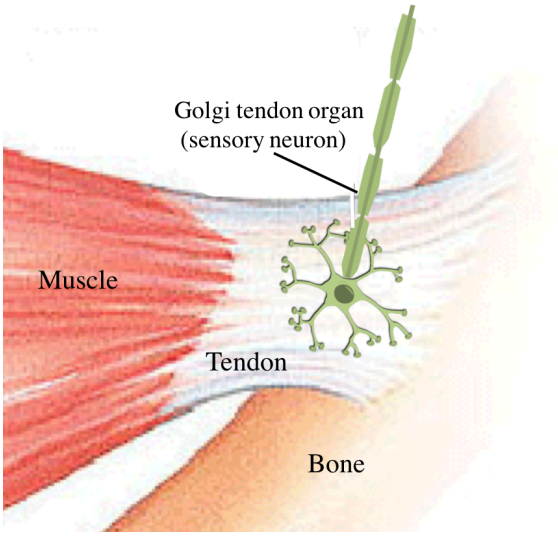


Figure 7.4 The Golgi tendon organ. The Golgi tendon organ is located in series with the muscle and measures tension that acts as a protective mechanism for muscle.

The Golgi tendon organ (GTO) is another specialized sensory neuron that monitors tendon tension. GTOs are measuring devices for changes in muscular tension or force. Located within the tendon and in series with the extrafusal fibers (Figure 7.4), GTOs are controlled by spinal interneurons, which are subject to inhibitory influences [3]. GTOs respond more effectively to active contractile force than to passive tension produced by external pull.

The Golgi tendon organ (GTO) prevents excess force production by the muscle and also prevents muscle tearing. When activated, the GTO sends information to the spinal cord via sensory neurons. These sensory neurons, in turn, excite inhibitory neurons (IPSPs) that prevent the motor neurons from firing. This reduces muscle force production and protects the muscle against contraction-induced injury. In sports, GTOs may play an important role in performance and strength activities. It is thought that GTO influence can be gradually reduced in response to strength training, allowing an individual to produce greater muscle force by voluntarily opposing the inhibition of the GTO.

Motor Reflexes

The level of nervous system involvement in sensory input varies according to the complexity of the movement necessary to respond. Imagine a scenario where an unsuspecting person touches a hot stovetop. Within a second, the person can remove their hand from the danger without consciously thinking about the action. In the case of a reflex, the stimuli of heat and pain are received by the thermoreceptors and nociceptors

in the hand, respectively, and the sensory action potentials travel to the spinal cord. Once in the spinal cord, these action potentials are integrated, and interneurons that connect the sensory and motor neurons are activated in what is referred to as a reflex arc. Once activated, action potentials in the motor neurons are sent to effectors that control the withdrawal of the hand. By the time the person is conscious of the hot surface, the reflex activity is well underway, if not completed.

A **motor reflex** is a rapid, unconscious means of reacting to stimuli and does not depend on higher brain centers for muscle activation. It can be thought of as a preprogrammed response, and any time the sensory nerve transmits a certain impulse, the body's response will be instant and identical to the last. This consistency is advantageous as it eliminates the need for higher brain centers to consider options. In summary, reflexes occur when a sensory nerve sends an impulse to the spinal column. An interneuron in the spinal cord then activates motor neuron depolarization. The motor neuron immediately relays the impulse to the skeletal muscle to withdraw, bypassing higher brain centers, which would delay the reaction.

With the motor reflex activation of the agonist muscle (by **EPSPs**, explained later in the graded potentials section), it is also important that a simultaneous **IPSP** (see **graded potentials**) be sent to the antagonist muscle. This deactivates the antagonist muscle to prevent interference or opposition to the agonist muscle's action. The simultaneous excitatory and inhibitory activity by the spinal cord is known as **reciprocal inhibition**. Along with the motor reflex, reciprocal inhibition demonstrates the spinal cord's contribution to rapid movements. Additionally, emerging evidence suggests that reflexes play a major role in the control of voluntary movement[56]. Some researchers believe that additional refinement of movement occurs at the spinal cord, playing a larger role in volitional movement than initially proposed.

Somatic Alpha Motor Neurons

The somatic motor portion of the PNS is responsible for carrying neural messages from the spinal cord to the effector organs, such as skeletal muscles. The effectors of all motor actions are the skeletal muscles, whose basic properties are viscoelasticity and contractility[7]. Neural messages signal muscle contraction. The somatic neuron that innervates skeletal muscle fibers is called a motor neuron, or specifically, an alpha motor neuron. The cell body of a motor neuron is located in the spinal cord, and its axon extends to the muscle it innervates. At the muscle fiber, the axon splits into collateral branches, each innervating a single muscle fiber. Thus, one motor neuron can innervate many muscle fibers (cells). One motor neuron and all the muscle fibers it

5. Brodal P, The Central Nervous System. 2010, New York, NY: Oxford University Press.

6. Henatsch HD, and Langer HH, Basic Neurophysiology of Motor Skills in Sport. Int J Sports Med, 1985. 06(1): p. 2-14.

7. Henatsch HD, and Langer HH, Basic Neurophysiology of Motor Skills in Sport. Int J Sports Med, 1985. 06(1): p. 2-14.

innervates are collectively known as a **motor unit**.

Motor units are the smallest functional entities of normal motor activity. They contain fewer than ten muscle fibers per motor neuron in the most finely adjustable muscles (e.g., extraocular muscles of the eyes), some hundreds in extremity muscles, and some thousands in very crude muscles (e.g., gluteus maximus)[8]. Mathematically, the **innervation ratio** can be expressed as the number of muscle fibers innervated per motor neuron (i.e., number of muscle fibers/motor neuron). When the motor neuron is activated, all the muscle fibers it innervates will simultaneously contract. Conversely, if the motor neuron ceases to contract, all the fibers it innervates will cease to contract.

Motor Unit Recruitment

The CNS can enhance muscle force production in two ways: 1) by increasing the number of activated motor units, called motor unit recruitment, and 2) by heightening the excitation frequency of individual motor units, leading to growing forces of overlapping and fusing contractions. Recruitment of additional motor units activates more muscle fibers, increasing the strength of a voluntary muscle contraction. Generally, motor units are recruited in an orderly and sequential fashion based on their size. This is called the **size principle** (Henneman size principle) of motor units, where recruitment begins with the smallest motor neurons and progresses to larger and larger motor neurons. For example, when a muscle is initially activated to lift a light weight, the first motor units to fire are smaller in size, as the force generation required by the muscle is low. However, if the weight is increased (heavy lifting) and the force required by the muscle increases, there will be a progressive increase in the recruitment of more and larger motor neurons in addition to the smaller motor neurons. It is also important to note that even in the strongest in vivo contractions, not all motor units of a muscle are simultaneously active[9].

The American scientist Elwood Henneman (1915-1995) discovered that the smallest motor neurons were the most easily excited, whereas the large motor neurons were the least susceptible to excitation. As the discovery of the size principle improved our knowledge of how the nervous system increases force production within the muscular system, motor units were also categorized into different types. Motor units can be divided into three classes based on their metabolic and size properties. **Type S (slow) motor units** are the smallest motor units and are resistant to fatigue. Type S motor units are recruited first. **Type FR (fast-fatigue resistant) motor units** are considered large, have a faster transmission speed of impulse, and innervate type IIa muscle fibers. **Type FF (fast-fatigable) motor units** have the largest motor neurons, are the last to be recruited, and innervate the largest muscle fibers (i.e., type IIx). In general, the larger the motor

8. Henatsch HD, and Langer HH, Basic Neurophysiology of Motor Skills in Sport. Int J Sports Med, 1985. 06(1): p. 2-14.

9. Henatsch HD, and Langer HH, Basic Neurophysiology of Motor Skills in Sport. Int J Sports Med, 1985. 06(1): p. 2-14.

neuron, the faster the neural transmission speed. Additionally, motor neuron size corresponds with the size of the muscle fiber. A comparison of the characteristics of motor units is shown in Table 7.1.

Table 7.1 Characteristics of human motor unit types.

Motor Unit Type	Type S	Type FR	Type FF
Size	Small	Large	Largest
Signal Transmission Speed	Slow	Fast	Fast
Muscle Fiber Innervated	Type I	Type IIa	Type IIx

The Pathway of Force Production

The conscious desire to perform physical exercise of any intensity requires coordination of several body systems, starting in the cerebral cortex of the brain and ending with muscle force production through contraction cycling. The intricate steps in between will be discussed by system as the pathway of force production in the following sections. This pathway is extremely complex, involving the coupling of the nervous and muscular (neuromuscular) systems. It is also of particular interest in the study of fatigue, as several theories have been developed to explain decrements in performance related to neuromuscular physiology. One theory of fatigue suggests that alterations in neural control, or signaling, prevent muscle contraction. It is also thought that the CNS plays a role in most types of fatigue, perhaps limiting exercise performance as a protective mechanism[10]. Other theories propose that muscle fibers' contractile mechanisms fail due to intracellular conditions such as acidosis. Nevertheless, it is important to realize that muscle contraction is extremely complex, and fatigue is most likely caused by multiple factors occurring at several sites along the pathway.

Central Nervous System Activation of the Primary Motor Cortex and the Spinal Cord

To comprehend how even the most basic muscle contractions are initiated, we will first consider the initial step in the pathway of force production: activation of the primary motor cortex and the spinal cord. First and foremost, the complex nature of the CNS must be investigated. In this section, a brief overview of components of the CNS will be introduced, as well as the areas of the brain that are of primary concern to

10. Kenney LK, Wilmore JH, Costil DL, ed., Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

exercise physiology.

The cerebrum is composed of the right and left cerebral hemispheres, connected by the corpus callosum. The cerebral cortex forms the outer portion of the cerebral hemispheres and is the conscious brain, allowing people to think, be aware of sensory stimuli, and voluntarily control movements.

Figure 7.3 A volleyball player serves the ball to the opposing team. The premotor cortex is the part of the brain where learned motor skills, like serving, are stored.

The desire and decision to perform a sport-specific skill or conscious movement of skeletal muscle begins at the primary motor cortex of the cerebrum. The primary motor cortex is the part of the brain where decisions are made about what movement to make. For example, in volleyball, if a player desires to serve the ball to the opposing team (as shown in Figure 7.3), the decision to toss the ball into the air and swing the arm to make contact with the ball is made in the primary motor cortex. Pyramidal cells are housed in the primary motor cortex, and their axons form the extrapyramidal tracts. These are known as the corticospinal tracts because the nerve processes extend from the cerebral cortex down to the spinal cord. These tracts provide the major voluntary control of skeletal muscles[11]. Learned **motor skills** of a repetitious nature, such as those learned in sports, are stored in the premotor cortex. The premotor cortex is located anterior to the precentral gyrus in the frontal lobe. This area of the brain can be thought of as the memory bank for skilled motor activities.

Another brain structure that is important for coordinating movement is the cerebellum. The cerebellum is located behind the brain stem, as shown in Figure 7.4. It is responsible for coordinating the timing of complex muscular activities and helps the rapid progression from one movement to the next. The cerebellum facilitates movement patterns by smoothing out the movement through corrective adjustments via the motor system. From the motor cortex, the decision to perform a movement is relayed to the cerebellum, where the desired movement is compared to the actual movement based on sensory feedback from the muscles and joints[12].

The basal ganglia (nuclei) is another area of primary concern to exercise physiology. The basal ganglia are

11. Kenney LK, Wilmore JH, Costil DL, ed., Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

12. Kenney LK, Wilmore JH, Costil DL, ed., Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

not part of the cerebral cortex but are located in the cerebral white matter, deep within the cortex. It is thought that the basal ganglia are important in initiating movements of a sustained and repetitive nature, such as arm swinging during walking. The basal ganglia control movements such as walking and running and are also involved in maintaining posture and muscle tone. The brain stem, composed of the midbrain, the pons, and the medulla oblongata (see Figure 7.3), connects the brain and the spinal cord. Both sensory and motor neurons pass through the brain stem as they relay information between the brain and spinal cord. The spinal cord is continuous with the medulla oblongata and is composed of tracts of nerve fibers that allow two-way conduction of nerve impulses. Both afferent (towards the brain) and efferent (towards the body) nerve fibers transmit action potentials to end organs from the spinal cord. Sensory-motor integration is also assisted by specialized sensory organs within muscles as well as reflex pathways for quick responses.

In summary, motor responses for complex movement patterns by the CNS originate in the primary motor cortex of the brain. The pathway then continues to the basal ganglia and the cerebellum, which coordinate repetitive movements and smooth out the desired movement patterns. Motor pathways (and sensory pathways) then proceed through the brain stem (midbrain, pons, medulla oblongata) and on to the spinal cord for transmission of the signal to the PNS.

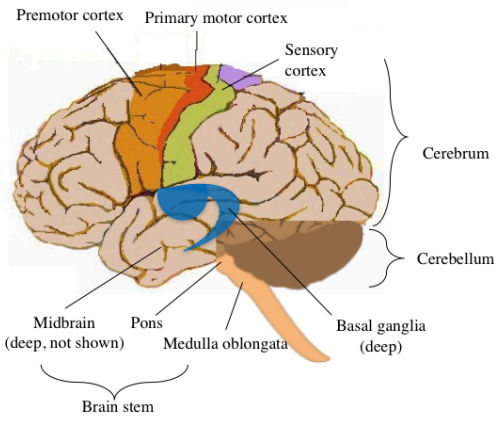


Figure 7.4 The major regions of the brain associated with voluntary control of movement.

Peripheral Nervous System Impulse Transmission

From the CNS, the pathway of force production continues through the motor, or efferent, division of the PNS. Cranial and spinal nerves directly innervate and carry nerve transmissions from the CNS to the skeletal muscles. The PNS contains 43 pairs of nerves. Of these, 12 pairs are cranial nerves that connect with the brain, and the remaining 31 pairs are spinal nerves that connect with the spinal cord[13]. From the brain and spinal cord, intricate networks of neurons extend to all parts of the body, including–and central to exercise and sport physiology–skeletal muscles. Signals are carried through this network by generating action potentials along the PNS until they arrive at the junction where the motor neuron and muscle meet. The

13. Kenney LK, Wilmore JH, Costil DL, ed., Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

details involved in nerve transmission, generation of an action potential, and arrival of the action potential at the neuromuscular junction will be discussed next.

Resting Membrane Potential

Electrical potentials exist across the membranes of virtually all cells in the body. These potentials are caused by an ion concentration difference on the two sides of the membrane. The membrane of nerve cells is polarized, meaning there is a difference in ionic charges across the membrane that creates an electric potential. Understanding the **resting membrane potential** of a neuron is important for understanding how an impulse, or action potential, is generated. The electrical potential difference is known as the resting membrane potential (RMP), and in most resting cells, it is measured at -70 millivolts (mV). This means that the potential inside the fiber is 70 millivolts more negative than the potential in the extracellular fluid outside the fiber[14].

The resting membrane potential is determined by the concentration of sodium (Na+), potassium (K+), and chloride (Cl–) inside and outside the cell. At rest, the inside of a neuron is negatively charged, with a large concentration of potassium inside the membrane along with negatively charged proteins that cannot cross the cell membrane. Additionally, a larger concentration of chloride and sodium exists outside the nerve cell in the extracellular space. The differences in the concentration of these ions create potential energy that can be used to transmit an action potential down the neuron axon.

Ions tend to move to establish equilibrium across the membrane as a general rule of diffusion. However, in the case of the resting membrane potential, it is necessary to maintain a difference in ion concentration across the cell membrane. This difference is maintained in two ways. First, the cell membrane is much more permeable to K+ than Na+. This means that K+ can move more freely, and some of the K+ will move to the area where it is less concentrated, outside the cell. On the other hand, Na+ cannot move inside as easily. Secondly, the membrane potential is maintained by the sodium-potassium pumps (Na+/K+ pump) located in the membrane that actively, requiring ATP, transport potassium ions in and sodium ions out. The Na+/K+ pump moves three Na+ out of the cell for every two K+ it brings in. The end result is a membrane with more positively charged ions outside the cell than inside, creating the potential difference across the membrane.

14. Guyton AC, and Hall JE, Textbook of Medical Physiology. 11th ed. 2006, Philadelphia, PA: Elsevier Saunders.

Graded Potentials, Depolarization, and Hyperpolarization

The nerve cell membrane also contains gated ion channels that act as doorways, allowing ions into and out of the nerve cell. These gates are usually closed; however, if the stimulation is potent enough, the gates open and allow more ions to move from the outside to the inside or vice versa. When ions change positions by crossing the membrane through these gates, the electrical potential will also change. **Graded potentials** are localized changes in the membrane potential that occur from either **depolarization** or **hyperpolarization**. Depolarization reflects any time that the charge difference becomes more positive than the RMP of -70 mV by moving closer to zero[15]. The opposite can also occur. If the charge difference across the membrane increases, this is termed hyperpolarization, which moves the RMP to an even more negative value. Thus, hyperpolarization results in the membrane becoming more polarized.

Neurons receive signals from neighboring nerve cells that can negate an action potential or cause the action potential to be generated. The process of communication between neurons occurs through synaptic transmission. As mentioned previously, signals are transmitted at a junction called synapses via chemical messengers known as neurotransmitters. More than 50 neurotransmitters have been identified as potential candidates to serve as chemical messengers. Neurotransmitters that cause depolarization of membranes, such as acetylcholine and norepinephrine, are termed excitatory transmitters. These types of neurotransmitters bind to receptors on the target cell membrane, producing a graded potential in the dendrites and the cell body of the postsynaptic cell. Excitatory neurotransmitters released from the presynaptic cell cause excitatory postsynaptic potentials in the postsynaptic cell. **Excitatory postsynaptic potentials (EPSP)** cause a depolarization of the nerve cell membrane; however, the threshold is not always reached. If sufficient amounts of the excitatory neurotransmitter are released, the postsynaptic neuron can be depolarized to threshold, and an action potential will occur[16]. It is estimated that the addition of up to 50 EPSPs might be required to produce an action potential[17]. Note that not all neurotransmitters are excitatory; some can cause hyperpolarization of the membrane. Interestingly, norepinephrine can also be an inhibitory neurotransmitter depending on the receptor.

Inhibitory neurotransmitters cause the membrane to become more negative, resulting in an **inhibitory postsynaptic potential (IPSP)**. IPSPs cause hyperpolarization of the nerve cell membrane, moving the

15. Kenney LK, Wilmore JH, Costil DL, ed., Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

16. Powers SK, and Howley ET, Exercise Physiology (Theory and Application to Fitness and Performance). 9th Edition ed. 2015, New York, NY: McGraw-Hill.

17. Powers SK, and Howley ET, Exercise Physiology (Theory and Application to Fitness and Performance). 9th Edition ed. 2015, New York, NY: McGraw-Hill.

membrane potential further away from zero. This hyperpolarization pushes the membrane potential even further from the threshold, thus resisting depolarization. The axon hillock is responsible for determining if an action potential will occur. Impulses from IPSPs and EPSPs are summed at the axon hillock, and often, more than one stimulus will be received. Whether a neuron reaches the threshold depends on the ratio of EPSPs to IPSPs received. For example, if the ratio of EPSPs to IPSPs is equal, the threshold to generate an action potential will not be reached. If the ratio of EPSPs is greater than IPSPs, the membrane potential will be pushed toward the threshold, and an action potential will occur.

Temporal summation occurs when several EPSPs from a single presynaptic neuron are received at the axon hillock over a short period. **Spatial summation** occurs w**Temporal summation**hen EPSPs are received from many presynaptic cells and are summed at several different presynaptic inputs.

Action Potential

Nerve and muscle cells are capable of generating electrochemical impulses at their membranes and can transmit signals along their membranes[18]. Neurons are known as excitable tissue because they are irritable and able to respond to a stimulus. Neurons can transmit an impulse along their axons; however, the stimulus must be large enough to create an impulse. The impulse conducted along the membrane is called an action potential. As mentioned, the RMP in most cells is -70 millivolts (mV). An action potential only occurs when a depolarization threshold of -55 mV (which makes the membrane potential more positive) is reached. Any time depolarization reaches or exceeds the threshold, an action potential will indeed result. This is known as the **all-or-none principle**.

18. Guyton AC, and Hall JE, Textbook of Medical Physiology. 11th ed. 2006, Philadelphia, PA: Elsevier Saunders.

All action potentials begin as graded potentials at portions of the cell membrane[19]. When enough stimulation occurs to cause a depolarization threshold of -55 mV, an action potential will be triggered. Upon reaching the threshold, voltage-gated Na+ channels open, allowing Na+ to enter the cell rapidly. The influx of Na+ depolarizes the cell to a membrane potential of +30 mV and the action potential propagates down the axon membrane at 100 m/s (225 mph). Subsequently, the voltage-gated K+ channels open, but do so more slowly, which allows K+ to exit the cell. As K+ exits from the cell to the extracellular fluid, this causes a **repolarization** and returns the membrane potential to -70 mV. Also note that a slight hyperpolarization of the membrane occurs momentarily following K+ diffusion to the extracellular fluid as shown in figure 7.6. Lastly, as the membrane returns to -70 mV, the voltage-gated K+ channels close. The cell then returns Na+ and K+ back into their intracellular and extracellular resting positions via active transport of the ions by the sodium potassium (Na+K+) pump.

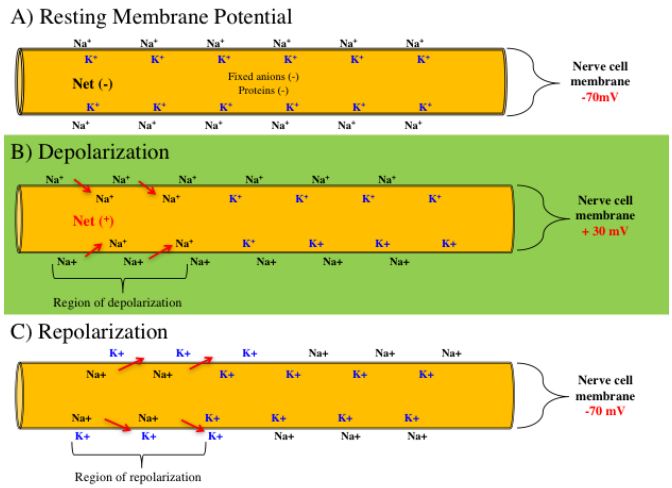


Figure 7.5 (A) The resting membrane potential is about -70 millivolts. (B) When the membrane reaches a threshold of -55 mV, sodium channels open, sodium ions rush in, and the membrane is depolarized to +30 mV. (C) When the potassium channels open, potassium diffuses outward, and the membrane is repolarized to -70 mV.

19. Kenney LK, Wilmore JH, Costil DL, ed., Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

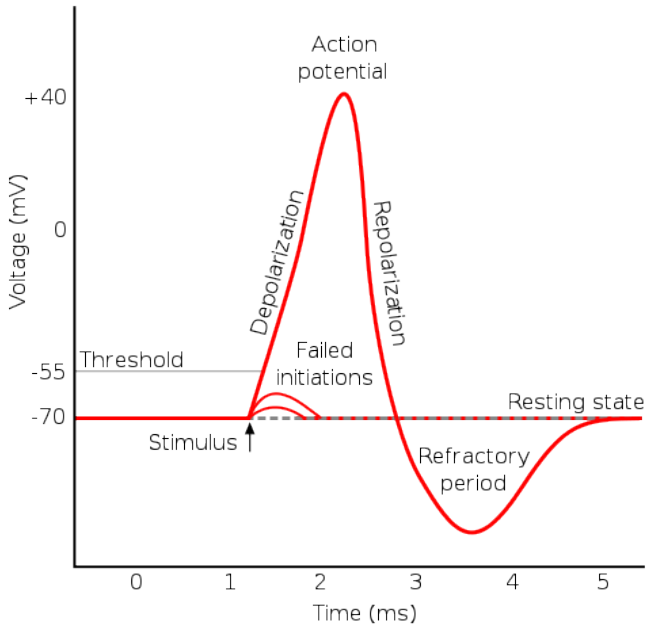


Figure 7.6 Voltage changes during an action potential.

An action potential occurs rapidly and substantially depolarizes the remaining portions of the membrane. Since the signal only travels away from the cell body, the depolarization will travel down the axon towards the axon terminal. When a cell is in the process of generating an action potential and a segment of an axon's sodium gates are open, it will not be able to respond to another stimulus. This is called the absolute refractory period. When the sodium gates close and the potassium gates open (during repolarization), the segment of the axon can potentially respond to a new stimulus if the stimulus is substantially greater in magnitude. This time frame is known as the relative refractory period[20].

Arrival of the Action Potential at the Neuromuscular Junction

The nervous system's involvement in the pathway of force production culminates when the action potential arrives at the axon terminal and interfaces with a muscle fiber. Nerve cells that extend outward from the spinal cord and transmit signals to skeletal muscles are termed alpha (α-) motor neurons. Stimulation from the nervous system via the α-motor neuron is necessary to initiate muscle excitation and contraction cycling. The axon terminal of the α-motor neuron does not physically contact the muscle fiber; instead, a small gap called the synaptic cleft separates the muscle and nerve fibers.

One α-motor neuron can innervate many muscle fibers, all of which will contract if the motor neuron depolarizes (the all-or-none principle applies here too). A single α-motor neuron and all the fibers it innervates are collectively called a motor unit. Figure 7.7 illustrates the neuromuscular junction, the site where the α-motor neuron excites the muscle fiber. The neuromuscular junction functions similarly to a synapse, except the α-motor neuron is communicating with a muscle fiber instead of a postsynaptic neuron.

20. Kenney LK, Wilmore JH, Costil DL, ed., Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

When the action potential arrives at the axon terminal, a series of events occur that lead to the "coupling" of the α-motor neuron and excitation of the muscle fiber membrane. Upon arrival of the nerve impulse at the axon terminal, calcium (Ca2+) ions enter the axon terminal from the extracellular space via voltage-gated calcium channels. Calcium ions diffuse into the axon terminal and interact with synaptic vesicles filled with the neurotransmitter acetylcholine. The synaptic vesicles migrate toward the synaptic cleft and release acetylcholine into the cleft via exocytosis.

Once released, acetylcholine diffuses across the synaptic cleft and binds with acetylcholine receptors (ligand-gated cation channels) on a specialized portion of the muscle cell called the motor end plate. The **motor end plate** is composed of invaginated (folded to form cavities) segments of the sarcolemma. Acetylcholine receptors located on the motor end plate bind acetylcholine, causing the ligand-gated cation channels to open, allowing Na+ ions to enter the fiber and K+ ions to exit. The influx of Na+ causes the motor end plate to depolarize once the threshold has been reached. The depolarization then travels throughout the sarcolemma, down the transverse tubules, and to the sarcoplasmic reticulum of the muscle fiber. **Muscle contraction cycling** is then activated (see Chapter 8 for details about the transverse tubules, sarcoplasmic reticulum, and muscle contraction cycling) and is the final step in the pathway of force production.

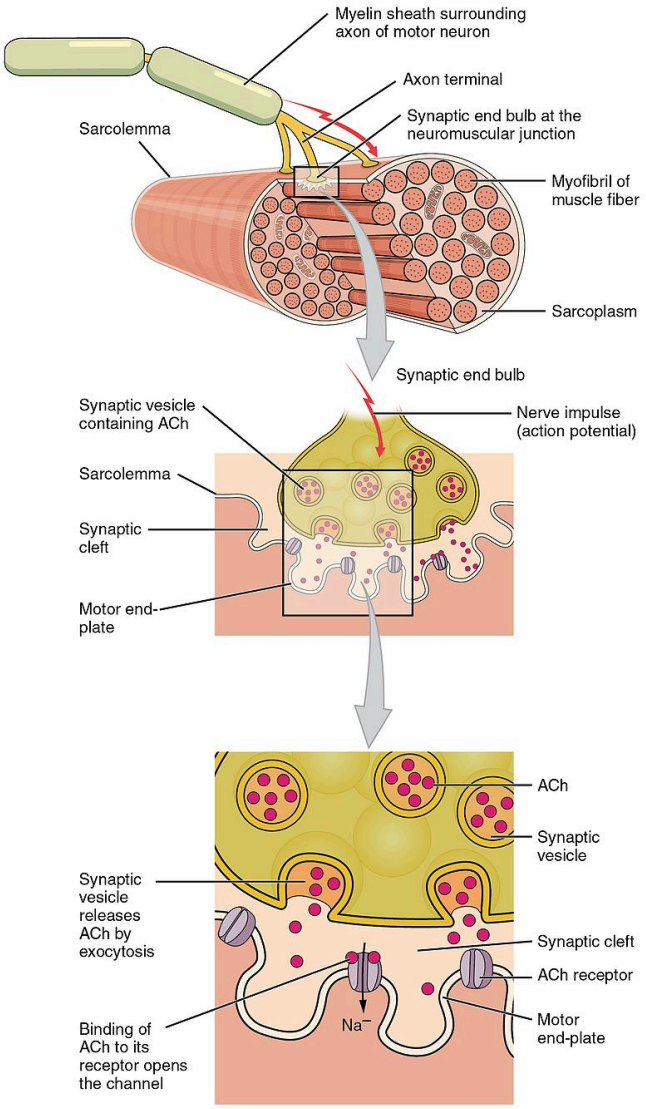


Figure 7.7 Enlarged, detailed diagram of the neuromuscular junction, showing the connection between a motor neuron and a skeletal muscle fiber. The image includes the axon terminal of the motor neuron containing synaptic vesicles filled with acetylcholine, the synaptic cleft, and the motor end plate of the muscle fiber with acetylcholine receptors. The figure illustrates the process of signal transmission from the nervous system to the muscular system, highlighting neurotransmitter release, receptor binding, and initiation of muscle contraction.

Neurotransmission to the muscle fiber ceases when acetylcholine is removed from the synaptic cleft. This occurs when 1) acetylcholine diffuses away from the synapse, or 2) is broken down by the enzyme acetylcholine esterase into acetic acid and choline. Following acetylcholine breakdown, choline is transported back into the axon terminal for the re-synthesis of acetylcholine.

Exercise Promotes Good Brain Health

Extremely strong evidence has revealed that exercise improves brain (cognitive) function, particularly later in life. Both mental stimulation (e.g., reading) and physical exercise are interventions that can contribute to improved brain health. Numerous studies have shown that exercise targets parts of the brain involved in learning, memory, and depression, and has broad positive benefits on overall brain health. Exercise has been shown to protect against several diseases of the nervous system, such as dementia, Alzheimer's disease, and stroke[2122]. Regular aerobic exercise promotes brain growth factor signaling and results in:

1. Enhanced learning and memory
2. Neurogenesis, the formation of new neurons
3. Improved vascular function and blood flow in the brain
4. Attenuation of mechanisms leading to depression

Daily exercise is a simple and inexpensive way to maintain the overall function of the CNS and good brain health.

Chapter Summary

In this chapter, we explored the intricate pathway of force production, beginning with the central nervous system's activation of the primary motor cortex and the spinal cord, and culminating in the arrival of the action potential at the neuromuscular junction. We examined the roles of various brain structures, including the cerebrum, cerebellum, basal ganglia, and brain stem, in coordinating and executing voluntary movements. The peripheral nervous system's role in transmitting impulses to skeletal muscles was also discussed, highlighting the importance of motor neurons and the neuromuscular junction.

We investigated the mechanisms underlying resting membrane potential, graded potentials, and the generation and propagation of action potentials. The concepts of depolarization, hyperpolarization, and the refractory periods were explained to provide a comprehensive understanding of how nerve impulses are generated and transmitted. Furthermore, the critical role of neurotransmitters in synaptic transmission and the processes involved in muscle excitation and contraction cycling were discussed. The chapter also

21. Cotman CW, Berchtold N, Christie LA, Exercise builds brain health: key roles of growth factor cascades and inflammation. Trends Neurosci, 2007. 30(464-472).

22. Marks BL, Katz LM, Smith JK, Exercise and the aging mind: buffing the baby boomer's body and brain. The Physician and Sportsmedicine, 2009. 37: p. 119-125.

emphasized the importance of exercise in promoting good brain health, underscoring the positive effects of physical activity on cognitive function and overall well-being.

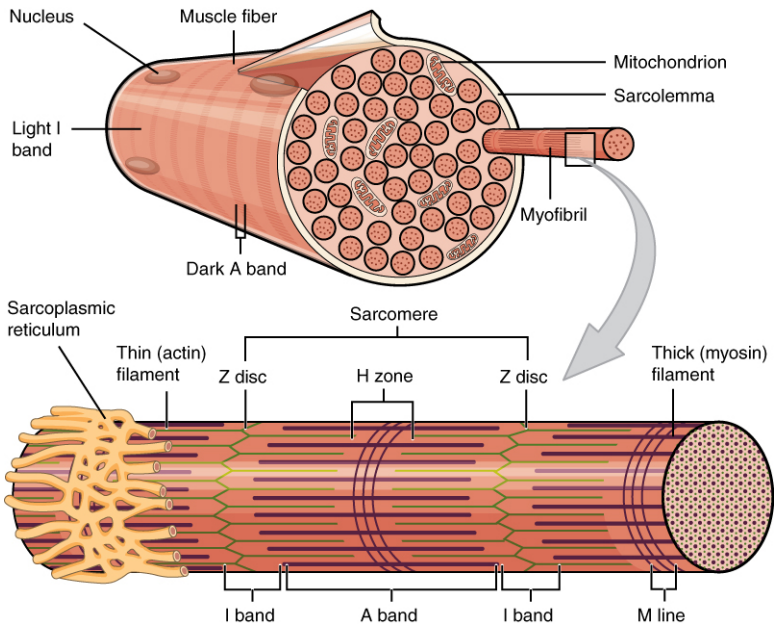
By understanding the complex interactions between the nervous and muscular systems, we gain valuable insights into the physiological processes that enable movement and the factors that can influence performance and fatigue. This foundational knowledge sets the stage for further exploration of muscle contraction cycling and force production in subsequent chapters.

Scholarly Questions

1. What are the two main anatomical nervous systems? How is the PNS divided?
2. Define the following terms: soma, dendrites, axon hillock, myelin sheath, nodes of Ranvier, and synaptic terminal.
3. What does depolarization mean?
4. What is a repolarization?
5. What is a graded potential?
6. Describe the resting membrane potential. What ions have the largest concentrations on the inside and outside of the cell?
7. What is the first step in the pathway of force production?
8. What part of the brain stores learned motor skills?
9. What part of the brain does movement originate?
10. Discuss the steps and processes of an action potential. What does it mean for a nerve cell to reach threshold?
11. Be able to discuss the steps and process of arrival of the action potential.
12. What is a motor neuron? Motor unit?
13. What is the principal that describes how motor units are recruited? Which motor units are recruited first?
14. How do IPSP's work? EPSPs?
15. What is the motor end plate and where is it located?
16. Discuss the following statement: "Calcium has a double role in muscle contraction."
17. What do GTO's monitor? Where are they located?
18. What is the muscle spindle responsible for? How does it function?

8.

STRUCTURE AND FUNCTION OF EXERCISING MUSCLE



The components of a skeletal muscle cell include peripheral nuclei, mitochondrion, myofibrils, and alternating light and dark bands. Striations are visible due to the alignment of actin and myosin proteins as arranged in sarcomeres in series.

Learning Objectives

- Identify and describe the three types of muscle tissue: skeletal, smooth, and cardiac.
- Describe the structure and function of muscle fibers, including the roles of the plasmalemma, sarcolemma, and satellite cells.
- Explain the differences between type I (slow-twitch) and type II (fast-twitch) muscle fibers,

including their metabolic properties and roles in different types of physical activities.
- Explain the sliding filament theory and the process of muscle contraction cycling.
- Describe the role of ATP in muscle contraction and relaxation.
- Understand the sequence of events in excitation-contraction coupling and the role of calcium in muscle contraction.
- Define and differentiate between isotonic, isometric, and isokinetic muscle actions.
- Understand the force-velocity relationship and its implications for muscle performance.
- Explain the power-velocity relationship and identify the optimal speed of movement for maximizing power output.

Introduction to Muscle Physiology

In the preceding chapters, we established a foundational understanding of metabolism and the basic research concepts of energy expenditure. This groundwork is essential for delving into the structure and function of exercising muscle, which is the cornerstone of human movement and a primary focus of research for exercise physiologists. The upcoming sections will explore how the structure and function of exercising muscle and muscle fibers are crucial for comprehending sport performance and maintaining general health. Given the pivotal role of skeletal muscles in sports performance, a comprehensive understanding of muscle physiology is indispensable not only for exercise scientists but also for physical educators, physical therapists, and coaches.

As previously noted, there is significant overlap between organ systems, as they rely on each other to achieve homeostasis, ensure optimal system function, and maintain overall health. Chapter 7 examined the nervous system and its role in initiating and transmitting signals for the activation of skeletal muscle, covering the first three processes in the pathway of force production. With the nervous system responsible for initiating skeletal muscle excitation, this chapter will focus on the final process in the pathway: muscle contraction cycling.

Structure and Function of Exercising Muscle

The muscular system encompasses a variety of functions carried out by three distinct types of muscles: **skeletal muscle**, **smooth muscle**, and **cardiac muscle** (refer to Figure 8.1). Smooth muscle, often referred to as involuntary muscle, operates without direct conscious control. It is located around the walls of luminal areas (i.e., openings in the body), enabling these openings to dilate or constrict. For instance, smooth muscle

encircles the walls of blood vessels, regulating blood flow by either dilating or constricting the vessels. Additionally, smooth muscle is present in the walls of most organs, where it facilitates the movement of food through the digestive tract, the expulsion of urine, and the process of childbirth.

Cardiac muscle is exclusively found in the heart. It is striated like skeletal muscle but operates involuntarily. Essentially, cardiac muscle controls itself, with minor regulation by the nervous and endocrine systems. It features specialized junctions called intercalated discs, which allow electrical impulses to swiftly transfer throughout the heart. A more detailed discussion of cardiac muscle will be provided in Chapter 9.

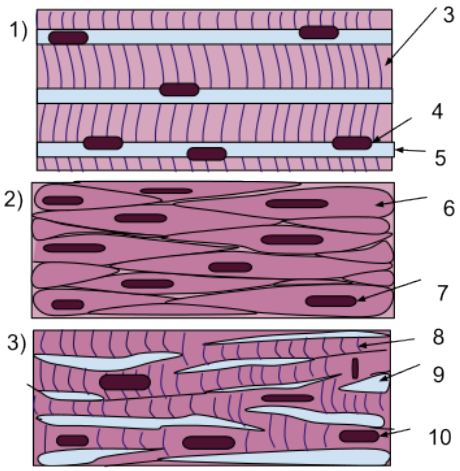


Figure 8.1, Illustrations of the three types of muscle. 1) Skeletal muscle cells are striated (3) and exist as long tubular cells. Skeletal muscles are multi-nucleated (4) and the nuclei are embedded in the cell membrane (5). 2) Smooth muscles are spindle shaped (6), and each cell has a single nucleus (7). There are no striations as in skeletal muscle. 3) Cardiac muscle cells function to pump blood, which is an involuntary action. Unlike skeletal muscles, cardiac muscle cells branch off from each other to allow uniform transmission of depolarization. Specialized junctions exist between adjacent branching cardiac cells (9). Cardiac cells are striated (8), and each cell has a single nucleus (10).

Skeletal muscle, on the other hand, is under conscious control and is named because most of these muscles are attached to the skeleton. Together with the bones of the skeleton, they form the musculoskeletal system. Exercise requires body movement, which is accomplished through the action of the musculoskeletal system. Given that exercise and sport physiology depend on movement, this chapter will primarily focus on the structure and function of skeletal muscle. Despite the anatomical differences between these muscle types, their control mechanisms and principles of action are similar. Figure 8.1 illustrates the different types of muscle in the body and details the differences in their structures.

Gross Structure of Skeletal Muscle

The human body contains over 600 skeletal muscles, which constitute approximately 40% of a person's body weight. Skeletal muscle plays a crucial role in regulating other organ systems. The general functions of skeletal muscles include:

1. Force generation for locomotion and breathing,
2. Force generation for postural support,
3. Heat production during cold and stress,

4. Acting as endocrine organs, as suggested by new evidence.

The most apparent function of skeletal muscle is force production, which is essential for breathing and locomotion. Skeletal muscles enable the movement of bony lever systems, transferring the forces generated within the body to external objects. These muscles are attached to bones by tendons, which are composed of fibrous cords of connective tissue that transmit the force generated by muscle fibers to the bones. One end of the muscle is attached to a bone that does not move, known as the origin of the muscle. The opposite end, called the insertion, is fixed to a bone that moves during contraction. Various types of movements are possible, depending on the type of joint and the muscles involved. Muscles that decrease the angle of a joint are called flexors, while those that increase joint angles are called extensors.

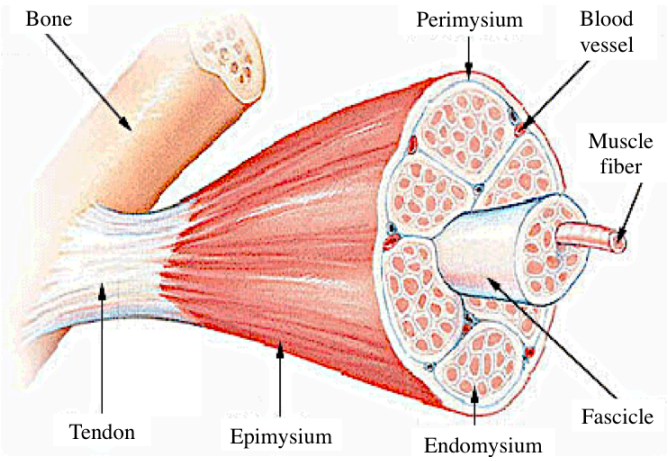


Figure 8.2 The basic structure of skeletal muscle and the connective tissue layers associated within.

Skeletal muscle is composed of various tissues, including muscle fibers, nervous tissue, blood vessels, and different types of connective tissue. Figure 8.2 illustrates the anatomical compartments of skeletal muscle, which are delineated by layers of connective tissues. Individual muscles are separated and held together by a connective tissue called the **fascia**. Beneath the fascia, the most superficial layer of connective tissue surrounding the muscle belly is known as the **epimysium**. Skeletal muscle is further divided into bundles of fibers, each wrapped in a connective tissue sheath. These bundles, called **fasciculi** (or fascicles), are encased in a connective tissue layer called the **perimysium**. Within each bundle, individual muscle fibers (cells) are enveloped by a connective tissue sheet known as the **endomysium**. Due to this compartmentalization, the longest human muscle fibers measure approximately 12 cm (4.7 in.) and contain about 500,000 sarcomeres, the fundamental units of muscle contraction[1].

Muscle Fibers

A single muscle cell, referred to as a **muscle fiber**, can vary in diameter from 10 to 120 μm, making it nearly invisible to the naked eye. Like all other cells in the body, skeletal muscle fibers are surrounded by a plasma membrane called the plasmalemma. The plasmalemma is part of a larger structure known as the **sarcolemma**

1. Kenney WL, Wilmore JH, Costil DL, ed., Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

(see Figure 8.3). The sarcolemma consists of both the plasmalemma and a basement membrane. The plasmalemma plays a crucial role in maintaining acid-base balance and facilitating the transport of metabolites from the capillary blood into the muscle fiber.

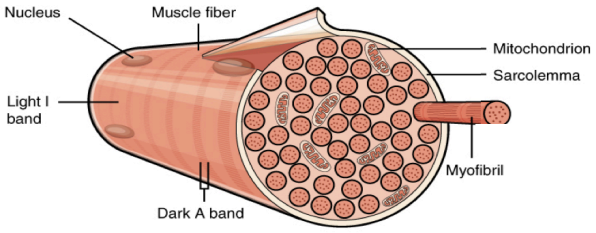


Figure 8.3 The structure of a single muscle fiber.

Between the plasmalemma and the basement membrane resides an important structure for the regeneration and repair of skeletal muscles called the satellite cell. **Satellite cells** play a major role in hypertrophy as well as repair after trauma due to exercise training, immobilization, or injury[2]. These cells, also known as "myogenic stem cells," typically lie dormant. When activated, satellite cells divide and contribute their nuclei to existing fibers, thereby increasing the capacity to synthesize new contractile proteins. Each satellite cell is responsible for a particular domain of the muscle cell. Satellite cells also facilitate muscle hypertrophy by donating extra nuclei to muscle fibers.

Sarcoplasm

A fluid portion of the cell fills the spaces between structures and organelles and is called the **sarcoplasm**—its cytoplasm. Inside the sarcolemma, a muscle fiber contains smaller subunits called myofibrils, the contractile units of the cell, which are described later. The sarcoplasm also contains proteins, minerals, glycogen, and fats. The sarcoplasm differs from the cytoplasm because it contains large amounts of stored glycogen and myoglobin, an oxygen-binding protein that transports oxygen in the muscle cell[3].

2. Schoenfeld BJ, The mechanism of muscle hypertrophy and their application to resistance training. J Strength Cond Res, 2010. 24(10): p. 2857-2872.

3. Kenney WL, Wilmore JH, Costil DL, ed., Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

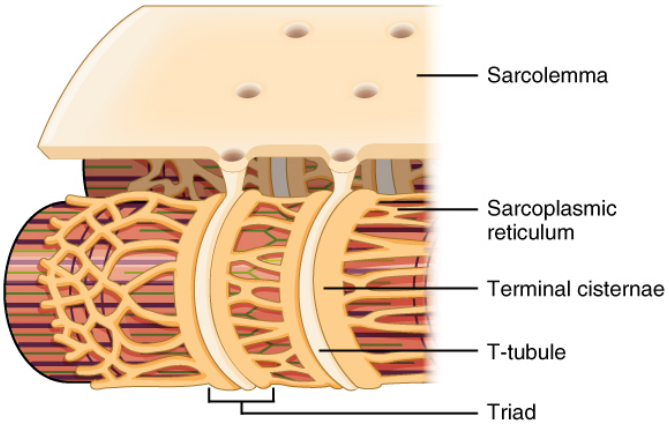


Figure 8.4 The muscle triad is made of a T-tubule surrounded by terminal cisternae on each side. Together, these three structures make up the triad.

The sarcoplasm also houses an extensive network of **transverse tubules** (T-tubules), which are extensions of the sarcolemma that pass laterally through the muscle fiber. The T-tubules allow nerve impulses received by the sarcolemma to be transmitted to individual myofibrils. The T-tubules also provide a pathway for extracellular substances to enter the cell and a path for waste products to leave the cell. Surrounding the T-tubules are enlarged portions of the sarcoplasmic reticulum (SR) called the **terminal cisternae**. Figure 8.4 depicts the sarcoplasmic reticulum, which is a longitudinal network of tubules that run parallel and loop around the myofibrils. Calcium is stored in the **sarcoplasmic reticulum** and terminal cisternae, which is essential for muscle contraction. Often, the structure made by a T-tubule surrounded by terminal cisternae on each side is called the muscle triad and is located at the **A-I junction** (see the Sarcomere section for explanation).

Myofibrils

Each muscle fiber is composed of several hundred to several thousand myofibrils. **Myofibrils** are threadlike strands within muscle fibers and make up the basic contractile elements of skeletal muscle. Each myofibril is composed of numerous sarcomeres joined end to end by a structure called the **Z-disk**. Sarcomeres give skeletal muscles a striated appearance under a microscope (Figure 8.5).

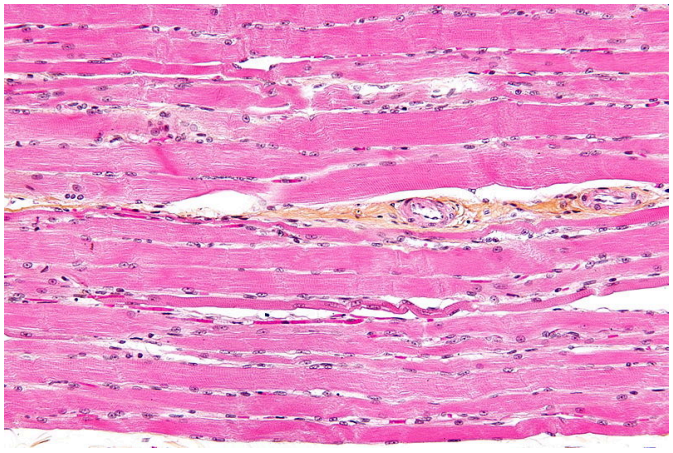


Figure 8.5 A micrograph of striated skeletal muscle from the right fibularis longus. A hematoxylin phloxine saffron stain was used to make the structures visible to the naked eye.

Sarcomeres

A **sarcomere** is the basic unit of muscle contraction that is separated from other sarcomeres by Z-disks. Each sarcomere contains the following zones:

- The I-band (isotropic: light zone)
- The A-band (anisotropic: dark zone)
- The H-zone (in the middle of the sarcomere)
- The M-line (in the middle of the H-zone)

There are two major proteins responsible for muscle contraction, differentiated into thin and thick filaments. The thinner filaments are composed primarily of **actin**, and the thicker filaments are primarily **myosin**. Striations in skeletal muscle result from light passing through these alignments of proteins in the sarcomere, as illustrated in Figure 8.6. The light **I-band** indicates the region of the sarcomere where there are only thin filaments, allowing more light to pass through the tissue under a microscope. Thus, this area of the sarcomere was named the I-band for isotropic. The darker **A-band** (anisotropic) represents the regions of the sarcomere that contain both thick and thin filaments, allowing less light to pass through and giving it a darker appearance. The **H-zone** is the central portion of the A-band and does not contain thick filaments, as myosin does not extend the full length of a sarcomere. The H-zone appears lighter under a microscope and was named for the German word for brighter, heller. The **M-line** resides in the center of the H-zone and is composed of proteins important for structure that will be described later.

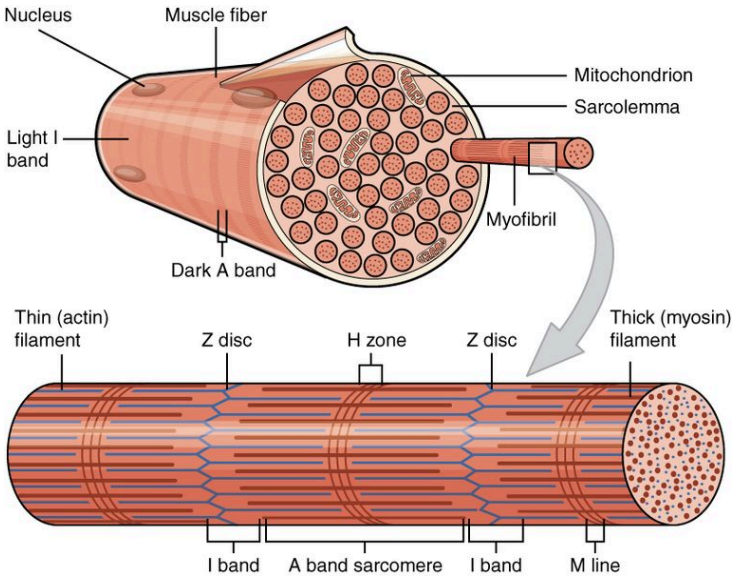


Figure 8.6 The microstructure of a muscle. A skeletal muscle contains numerous myofibrils, each consisting of units called sarcomeres. Each sarcomere is separated by Z-discs and contains an A-band, I-band, H-zone, and M-line.

Myosin is the principal protein of the thick filament and is an ATP-dependent motor protein. Each myosin filament (15 nm) is formed by about 200 myosin molecules that are twisted together in two strands. One end of the strand is folded into a globular structure, called the myosin head (Figure 8.7). Many of these heads

protrude from the thick filament to form cross-bridges that interact with sites on actin. When energized by ATP, myosin heads can rotate on a hinge to move actin filaments toward the center of the sarcomere. Fine filaments composed of the "giant" protein **titin** (also called connectin) extend from the Z-disk to myosin, stabilizing myosin filaments along their longitudinal axis.

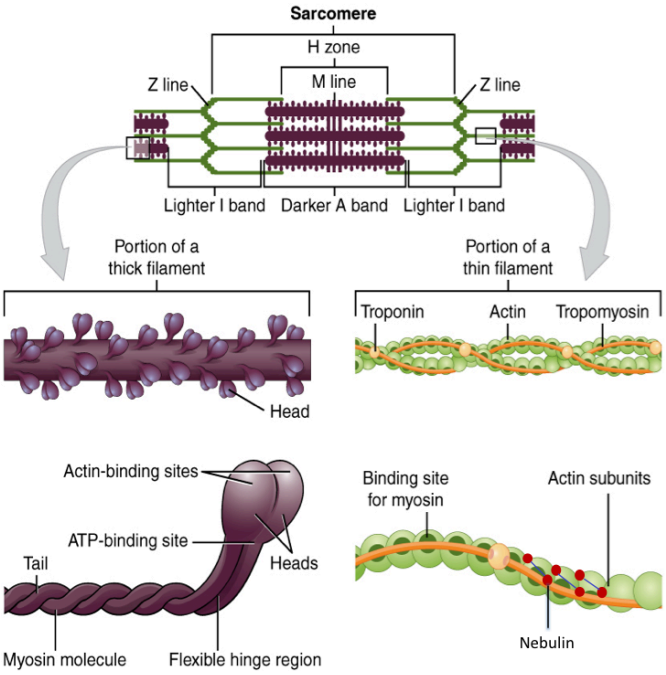


Figure 8.7 Actin (thin filament) and myosin (thick filament) proteins allow association of the filaments to produce force.

Another recently discovered giant protein named **nebulin** (originally called band 3) may also be involved in keeping the thin filaments centered during force generation. Nebulin is thought to play a regulatory role in mediating actin and myosin interactions and is often referred to as an "anchoring protein" because it provides a framework that helps stabilize the position of actin. Together, titin and nebulin are thought to be involved in the passive elasticity of the muscle fiber and provide axial continuity for the production of resting tension[4].

The thin filament of the sarcomere is primarily composed of actin (6 nm), but also includes two other protein molecules called tropomyosin and troponin. Individual subunits of actin are called **G-actin** and are globular proteins. G-actin subunits are joined together to form two strands of actin microfilaments, which are twisted into a helical pattern. Actin microfilaments are present in all cells and are central to conserving cell structure. **Tropomyosin** is a tube-shaped protein that twists around the actin strands and functions to cover actin binding sites. **Troponin** is attached at regular intervals to both the actin strand and the tropomyosin[5]. Tropomyosin and troponin work together to maintain relaxation or contraction (if calcium is present) of the myofibril.

Figure 8.8 demonstrates the specialized arrangement of actin and myosin filaments and associated proteins. The M-band proteins myomesin and **C-protein** crosslink the myosin filaments in the sarcomere. **Myomesin** is found in the M-line and associates with M-protein. Myomesin is found in both slow and fast fibers, whereas M-protein is found only in fast fibers. **Desmin** is another protein that is thought to be important for sarcomere architecture. Desmin is an intermediate filament (8-10 nm) that forms a three-

4. Horowits R, Kemper ES, Bishner ME, Podolsky RJ, A physiological role for titin and nebulin in skeletal muscle. Nature, 1986. 323: p. 160-164.

5. Kenney WL, Wilmore JH, Costil DL, ed., Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

dimensional scaffold around the Z-disc[6]. These proteins are thought to be involved in anchoring myosin to other filaments[7].

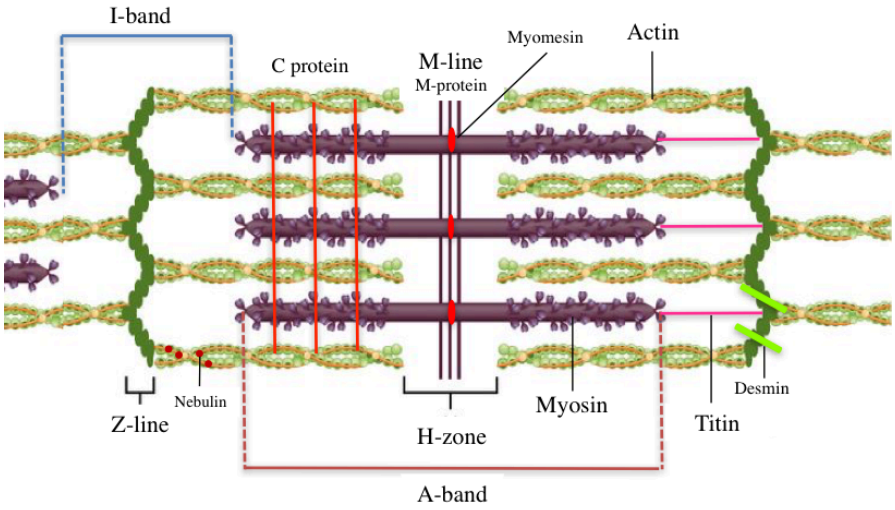


Figure 8.8 The sarcomere contains a specialized arrangement of actin and myosin filaments. Associated proteins important for structure and function of the sarcomere are also illustrated.

Muscle Fiber Types

Not all muscle fibers are alike. A single skeletal muscle contains muscle fibers that differ in key characteristics. These characteristics can include different speeds of shortening velocity, different isoforms of myosin **ATPase** (i.e., the enzyme for breaking down ATP), and different α-motor neuron innervation. These characteristics affect the muscle fibers' ability to generate maximal force.

Type I (also called slow-twitch) fibers take approximately 110 ms to reach peak tension. They are the smallest of the fibers and predominantly use aerobic metabolism to generate ATP. **Type II muscle fibers** (also called fast-twitch), on the other hand, are larger in size and can reach peak tension in about 50 ms[8]. Only one form of type I fiber has been identified; however, there are two major forms of type II fibers, type x (type IIx) and type a (type IIa). Type IIx fibers are equivalent to type IIb in animals and are the largest fibers in humans. Type IIx fibers utilize mainly aerobic metabolism to generate ATP. Type IIa fibers are still considered

6. Paulin D, and Xue Z, Desmin and Other Intermediate Filaments in Normal and Diseased Muscle, in Intermediate Filaments, J. Paramino, Editor. 2006, Landes Bioscience and Springer Science+Business Media.

7. Tskhovrebova L, and Trinick J, Making muscle elastic: the structural basis of myomesin stretching. PLoS Biology, 2012. 10(2): p. e1001264.

8. Kenney WL, Wilmore JH, Costil DL, ed., Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

to be large and use a combination of anaerobic and aerobic metabolism. A third subtype of fast-twitch fiber has also been identified, type IIc, but the differences among the type II fibers are not fully understood. Table 8.1 describes various metabolic, anatomical, and physiological characteristics of human skeletal muscle fiber types.

Table 8.1 Characteristics of human skeletal muscle fiber types.

Characteristic	Type I	Type IIa	Type IIx
Fibers per motor neuron	≤ 300	≥ 300	≥ 300
α-Motor neuron size	Small	Large	Large
Contractile speed	Slow	Fast	Fast
Type of myosin ATPase	Slow	Fast	Fast
Predominant energy system	Aerobic	Combination	Anaerobic
Oxidative capacity	High	Moderately high	Low
Glycolytic capacity	Low	High	Highest
Fatigue resistance	High	Moderate	Low
Fiber size	Small	Large	Large
Myoglobin content	High	Low	Low

As you may recall, the **size principle** describes the orderly and sequential recruitment of motor units from smallest to largest. According to the size principle, type I fibers are recruited the most often and are first to be recruited in the progression. Motor unit recruitment depends heavily on the force or resistance of the exercise. With light intensity exercise, the type I (small) motor units are recruited. When the resistance or load is increased, the type IIa (large) motor units will be recruited with the help of the type I fibers. If the load becomes even greater, the type IIx (largest) fibers will be recruited with the help of type IIa and type I motor units. With additional motor units recruited, the force exerted by each unit is increased, and they exhibit a higher rate of firing due to increases in the impulse firing from the nervous system (called rate coding). As the velocity of any movement increases, the size principle is retained; however, the order is less pronounced.

Most skeletal muscles contain both type I and type II fibers, as depicted in Figure 8.8. On average, most muscles are composed of roughly 50% type I fibers, 25% type IIa fibers, and 25% type IIx fibers (type IIc fibers only make up 1-3%). Because knowledge about type IIc fibers is limited, we will not discuss them further. Generally, arm and leg muscles have similar fiber compositions within an individual. This has been shown in the hip flexors (e.g., gluteus maximus and hamstrings), gastrocnemius, knee extensors (e.g., vastus lateralis), shoulders, and the latissimus dorsi. There are exceptions; however, the soleus muscle has a greater tendency to have a higher percentage of type I fibers in everyone[9]. The rectus femoris, biceps, triceps, and pectoral muscle groups have a greater tendency towards type II proportions [6].

Characteristics of fiber types are genetically determined and appear to be established within the first few years of life. This means that the genes we inherit from our parents determine which α-motor neurons innervate our individual muscle fibers. After innervation is established, muscle fibers differentiate. Some recent evidence, however, suggests that endurance training, strength training, and muscular inactivity may cause a shift in the myosin isoforms. Training may induce a small change, less than 10%, in the percentage of type I and type II fibers. Both endurance and resistance training have been shown to reduce the percentage of type IIx fibers while increasing the fraction of type IIa fibers. Specifically, training can result in a shift from type IIx to IIa, in which the fibers will have more oxidative properties. Aging may also alter the distribution of type I and type II fibers. It is known that as we grow older, muscles tend to lose type II motor units, which increases the percentage of type I fibers.

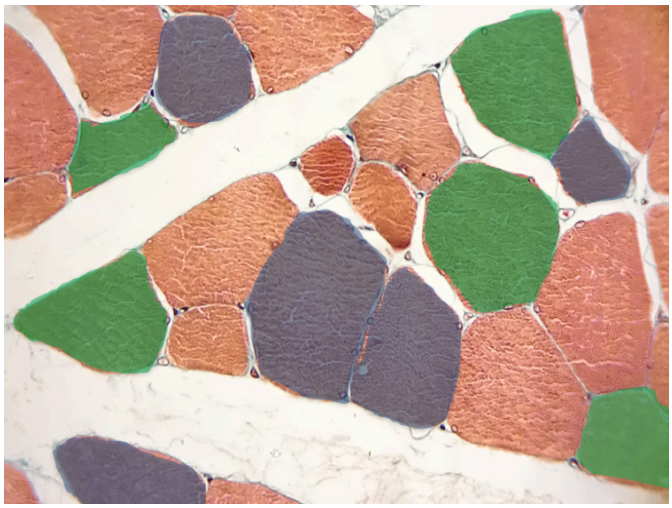


Figure 8.8 Immunohistochemical staining can identify differences in muscle fiber types as illustrated in a cross-sectional area of a skeletal muscle. The blue cells represent type I fibers, whereas the green cells represent type IIa fibers.

Numerous studies have investigated muscle fiber types' role in successful performance in athletes. As mentioned previously, the general population, sedentary individuals, and non-athletes typically have a 50/50 mix of type I to type II muscle fibers. It has been shown that highly successful power athletes (track sprinters) typically possess a high percentage of type II fibers (70-75%) and a lower percentage of type I fibers (25-30%)[10]. On the other hand, highly trained distance runners have been shown to possess a high percentage of type I fibers (70-80%) and a lower percentage of type II fibers (20-30%)[11]. Lastly, there are no apparent sex or age differences in fiber distribution[12]. Nevertheless, considerable variation exists in the percentage of various fiber types even among successful athletes competing in the same event or sport. This demonstrates that an individual's muscle fiber composition is not the only variable that determines success in athletic events[13]. Success in athletic performance is due to many complex interactions, including but not limited to

9. Kenney WL, Wilmore JH, Costil DL, ed., Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

10. Carlson F, and Wilkie D, Muscle Physiology, ed. Prentice-Hall. 1974, Englewood Cliffs, NJ.

11. Costill DL, Fink WJ, Pollock ML, Muscle fiber composition and enzyme activities of elite distance runners. Med Sci Sports, 1976. 8: p. 96-100.

12. Pette D, Plasticity of Muscle, ed. W.d. Gruyter. 1980, New York, NY.

13. Costill DL, Fink WJ, Pollock ML, Muscle fiber composition and enzyme activities of elite distance runners. Med Sci Sports, 1976. 8: p. 96-100.

psychological, biomechanical, and cardiopulmonary factors.

Muscle Contraction

The study of muscle contraction has a long history that has changed rapidly as the original theories of how force is produced have been rejected due to advancements in science. Andrew F. Huxley is credited for developing the sliding filament theory. The **sliding filament theory** explains the phenomenon of the shortening of muscle cells when the myosin cross-bridges are activated. Huxley's original model for muscle contraction was proposed in 1957 but has since been modified[14][15].

We now know that muscle contraction occurs as a cycle. This cycle is referred to as **muscle contraction cycling** and is the last process in the pathway of force production. Force production occurs during a step in the process called the "power stroke," which will be detailed in the following section.

14. Huxley AF, Muscle structure and theories of contraction. Prog Biophys Biophys Chem, 1957. 7: p. 255-318.

15. Jontes JD, Theories of Muscle Contraction. Journal of Structural Biology, 1995. 115: p. 119-143.

Excitation-Contraction Coupling

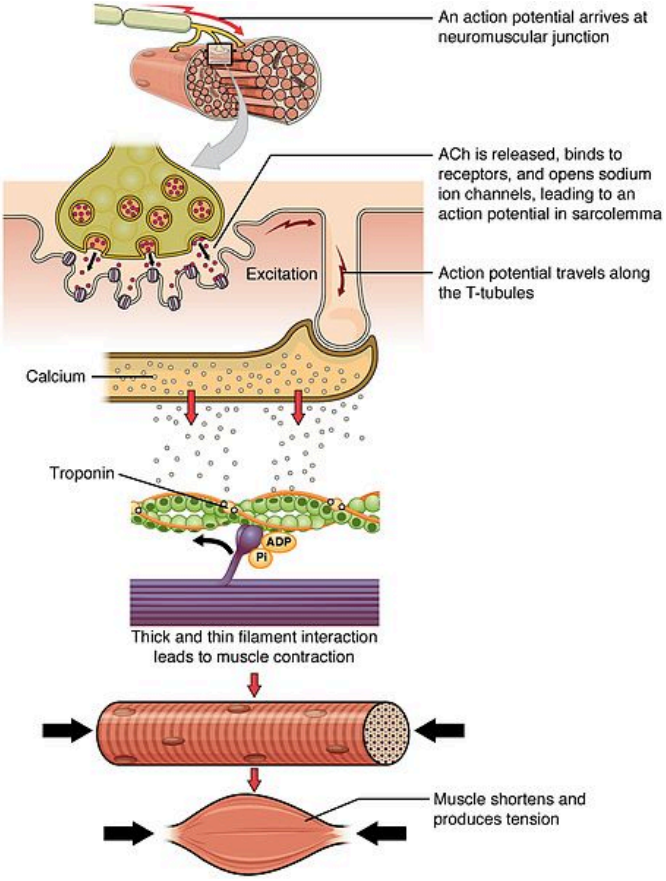


Figure 8.9 Excitation-contraction coupling. Arrival of the action potential at the neuromuscular junction causes excitation of the muscle cell. When activated the sarcoplasmic reticulum releases calcium into the sarcoplasm which reacts with troponin. The reaction allows a thick and thin filament interaction known as a cross-bridge. Cross-bridge formation leads to a muscle contraction, thus shortening of the muscle and creation of tensions.

The complex sequence of events that triggers a muscle contraction is termed **excitation-contraction coupling** because it begins with excitation of an α-motor neuron and results in muscle contraction. Excitation begins at the **neuromuscular junction (NMJ)** when the motor endplate of the muscle is excited by the arrival of an action potential. As the **motor endplate** is excited, the depolarization travels down the T-tubules to the sarcoplasmic reticulum. The details of the neural processes were discussed more fully in Chapter 7. A summary of events that lead to tension production by muscle is illustrated in Figure 8.9.

Muscle Contraction Cycling

In the pathway of force production, skeletal muscle plays the mechanical role in which force or tension is produced by the muscles. The process is called muscle contraction cycling, sometimes also called **cross-bridge cycling**. The energy for muscular contraction comes from the breakdown of ATP by the enzyme myosin ATPase. A single contraction cycle or "**power stroke**" of all the cross-bridges only shortens the muscle by 1% of its resting length. Because of this, it is clear that the contraction cycle must be repeated over and over again as some muscles can shorten up to 60% of their resting length.

Muscle contraction cycling is activated when an action potential impulse is received by the neuromuscular junction. The impulse then travels down the T-tubules and into the sarcoplasmic reticulum. Calcium is released from the sarcoplasmic reticulum (i.e., the terminal cisternae) into the cytoplasm of the cells and binds to troponin. This is the "trigger" step in the control of muscle contraction cycling because troponin and tropomyosin control the interaction of actin and myosin (Figure 8.10).

The thin filament is composed of actin myofilaments, troponin, and tropomyosin proteins that are arranged in a fashion where tropomyosin can be shifted to reveal myosin binding sites.

Calcium release causes troponin to shift, pulling tropomyosin away from the active site on actin. Concurrently, the myosin head on the thick filament is being energized. This occurs when an ATP molecule binds to myosin and is hydrolyzed by ATPase, releasing energy. This activates the myosin head, cocking it into the high-energy, extended position.

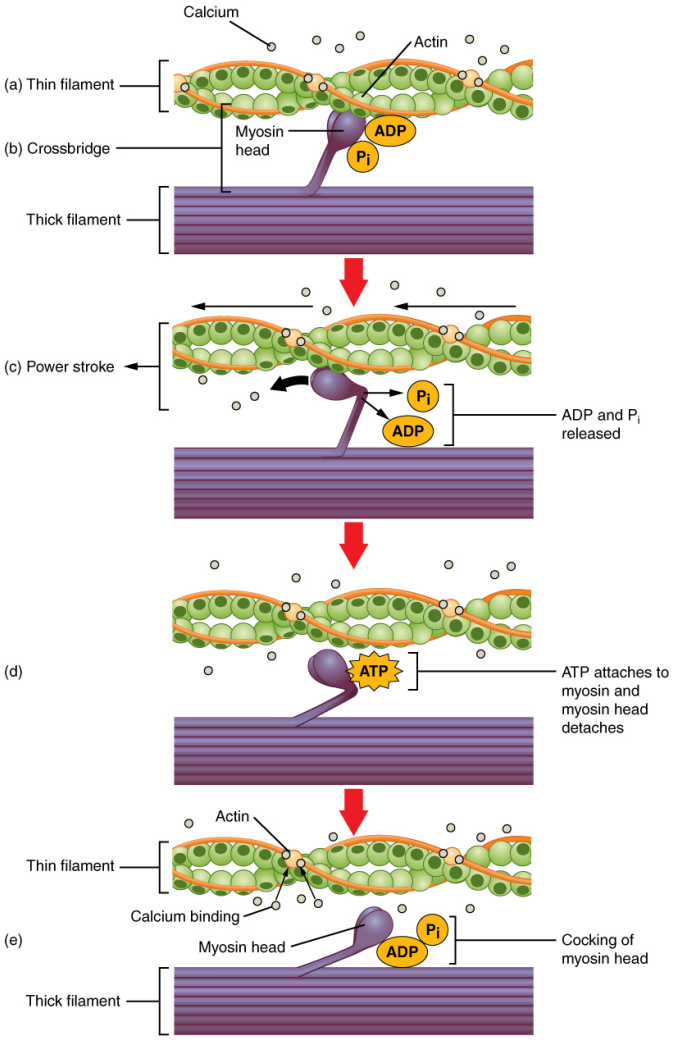


Figure 8.10 Muscle contraction cycling. (a) Calcium released from the SR binds to troponin shifting tropomyosin away from the actin binding sites. Concurrently, ATP binds to the myosin head and is hydrolyzed to ADP and Pi. (b) The myosin head binds to actin creating a cross-bridge. (c) The myosin head pulls on the actin filament which produces force. This is known as the power stroke. (d) A second ATP attaches to myosin and the myosin head detaches. (e) A new ATP binds to the myosin head, cocking it into the high energy, extended position. If the ATP and calcium concentration are maintained, the cycle will revert back to (a). Relaxation occurs when the action potentials are not received by the neuromuscular junction and calcium is actively pumped back into the SR.

When the active site on actin is exposed, it permits the energized myosin head to bind, creating a cross-bridge. Cross-bridge formation is ultimately the most important variable in force generation and tension development by muscles. The cross-bridge binding initiates the release of energy stored within the myosin molecule; this causes the myosin head to pull on the actin filament and slide actin along myosin. This is also known as the "power stroke" and is the step where force is produced. The power stroke results in muscle shortening (Figure 8.11).

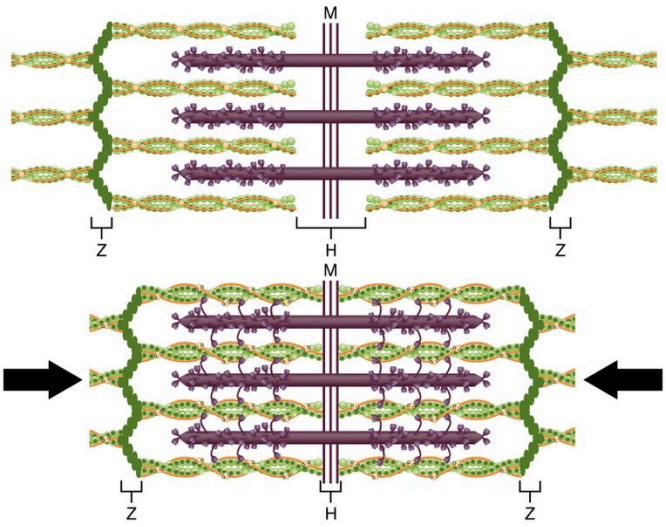


Figure 8.11 When a skeletal muscle contracts individual sarcomeres shorten as thick and thin filaments slide past one another. Shortening of the sarcomere as illustrated by arrows results in a concentric muscle action.

A fresh ATP then arrives and attaches to the cross-bridge; it is needed to release the bond between actin and myosin. The enzyme ATPase again hydrolyzes the ATP attached to the myosin cross-bridge and provides the energy necessary for re-attachment to another active site on actin. If the active site on actin is aligned with the myosin head, then the cycle will continue to repeat. Muscle contraction cycling will then be repeated as long as ATP is available, calcium concentrations are maintained, and action potentials are received by the NMJ.

Muscle Relaxation

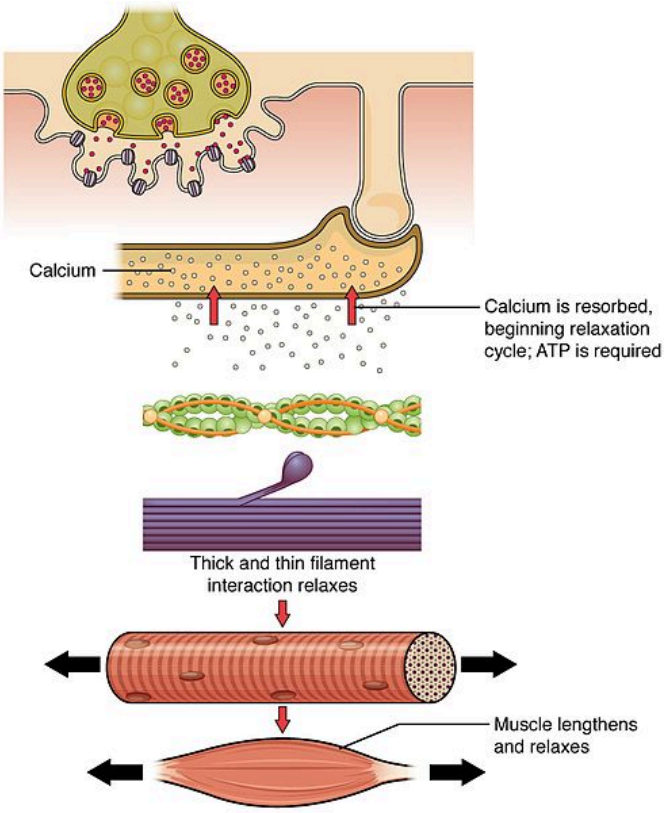


Figure 8.12 Muscle relaxation.

If the cell is no longer activated, everything will return to the resting state (Figure 8.12). Relaxation of the muscle fiber occurs when action potentials are no longer received by the NMJ. When this happens, calcium is actively pumped back into the sarcoplasmic reticulum, which requires ATP. The removal of calcium from troponin causes tropomyosin to move back to cover the binding sites on actin, blocking the cross-bridge binding site on actin. This action results in the relaxation of the muscle fiber.

Types of Muscle Action

The process of skeletal muscle force generation is referred to as "muscle contraction"; however, this terminology suggests that a muscle is always shortening, although muscle is also capable of lengthening or staying the same length while generating force. For this reason, the term muscle action has been proposed to describe muscle force production. There are three major types of muscle actions: **isotonic**, **isometric**, and **isokinetic actions**, which will be described in this section.

Most types of exercise or sport activities require muscle actions that result in dynamic movement of limbs. In the context of a sport movement, muscles will undergo isotonic muscle action (dynamic), where there is a change in muscle length to enable movement. There are two isotonic muscle actions: concentric and eccentric. An isotonic muscle action that results in the shortening of a muscle is called a concentric action. Figure 8.13A shows an example of a biceps curl in which the upward movement of the exercise results in **concentric action**. In contrast, if the muscle action results in the lengthening of a muscle while activated and actively producing force, this is called an **eccentric action**. Eccentric action occurs when the force generated is insufficient to overcome an external load on the muscle, and the muscle fibers lengthen as they produce force. Eccentric actions are also used as a means of decelerating a body part or object, such as lowering a dumbbell during a biceps curl (Figure 8.13B) or lowering grocery bags to the floor.

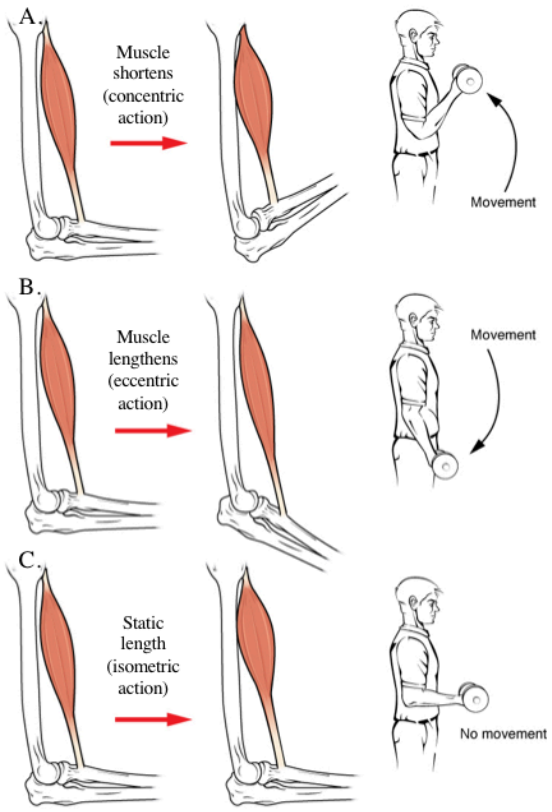


Figure 8.13 A) Concentric muscle action occurs when a muscle shortens, B) Eccentric muscle action occurs when a muscle exerts force bot lengthens, and 3) Isometric muscle action occur when a muscle exerts force but does not shorten.

Isometric actions (static) occur when a muscle is generating force but is not changing lengths. An example of isometric actions is what happens when a person holds a dumbbell without moving it, with their elbow flexed at 90° in front of their body, for a period of time (Figure 8.13C). This action is considered to be a static exercise because the dumbbell does not move, and therefore neither does the body part that applies the force. Isometric actions are also common in postural muscles of the body during periods of standing or sitting.

The last muscle action that will be mentioned is an isokinetic action (same speed). This is a muscle action completed at a constant velocity of movement, or speed. They are similar to isotonic in that the muscle changes length during contraction. Isokinetic actions are studied but not commonly found in sport or exercise because they require specialized equipment to achieve. Isokinetic contractions require a machine called an Isokinetic Dynamometer, which is expensive and bulky. Since this equipment is not practical from the standpoint of transferring the movement to sport or exercise, this muscle action is only used in research settings.

Generation of Force

The amount of force generated by a single muscle fiber is unquestionably related to the number of myosin cross-bridges making contact with actin. If a muscle fiber is given a single stimulus, the muscle will respond with a simple twitch. However, force exerted by a group of muscles is complex and can be affected by more than one factor. The three primary factors are:

1. The number and types of motor units recruited,
2. The length of the muscle when stimulation ensues,
3. The frequency and nature of the neural stimulation of the motor units.

There are variations in the force production capabilities of different muscle fibers. Recall that muscle fibers are recruited based on the size principle and that the larger motor units are recruited last. Fast fibers

exert a greater specific force than slow fibers. Therefore, the types of motor units recruited influence force production. Recruitment of larger motor units results in increases in force production. Additionally, the number of muscle fibers increases as the stimulation increases. As the stimulation increases, the force of contraction also increases due to the recruitment of additional motor units. Therefore, if more motor units are recruited, the force is increased.

The second factor that affects muscle force production is the initial length of the muscle. There exists an ideal length for force generation that is related to the overlap of actin and myosin (Figure 8.14). Production of myosin cross-bridges is necessary for the production of force. If the resting length is longer than optimal, an overlap between actin and myosin will limit cross-bridge attachment. Note that when a muscle is stretched to the point where there is no overlap between actin and myosin, no tension is developed. At the other extreme, when the muscle is shortened to about 60% of its resting length, the Z-lines will lie more closely to the A-band, which will also limit the muscle's ability to shorten and produce additional tension.

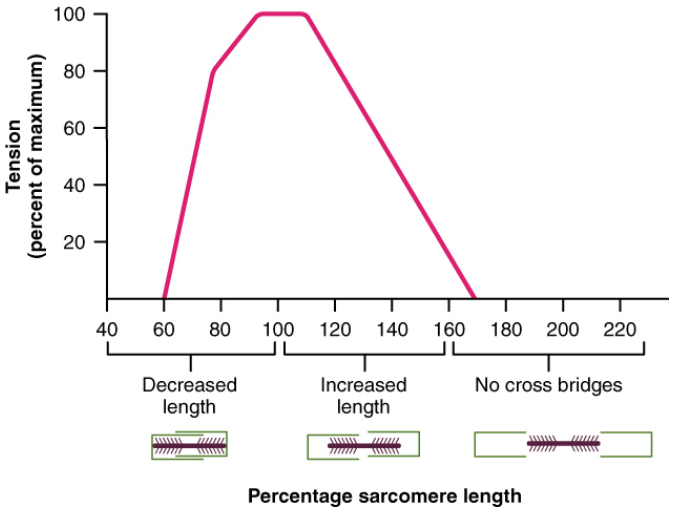


Figure 8.14 The length-tension relationship in skeletal muscle. There is an optimal length of muscle which will produce maximal force when stimulated. Lengths longer or shorter than optimal result in a reduced amount of force when stimulated.

The nature of the neural stimulation can also affect the amount of force produced. Simple muscle twitches examined under experimental conditions reveal fundamental properties about how muscles function. This is useful; however, normal body movements involve sustained contractions that are not simple twitches. A simple **twitch** is a muscle contraction as a result of a single stimulus. If more than one stimulus is delivered to the muscle and the muscle does not have time to relax, the force produced is additive. The addition of successive twitches is called **summation**. If the frequency of stimuli is increased further, the single twitches blend together into a single, sustained contraction called **tetanus**. Increases in stimulation from the nervous system result in tetanus, where peak force production occurs. Figure 8.15 illustrates how the frequency of neural stimulation affects force production during experimental conditions.

The Force-Velocity Relationship

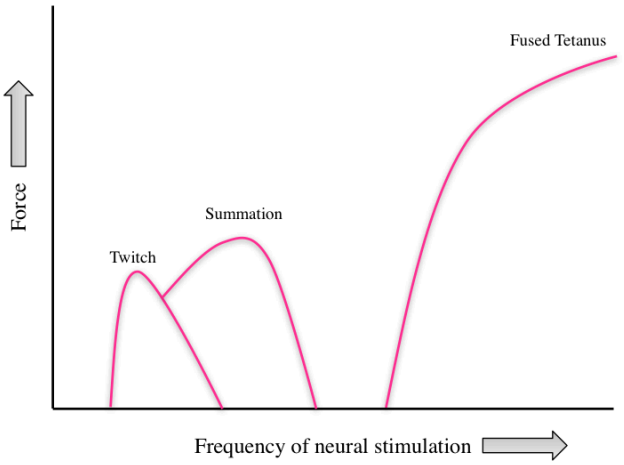


Figure 8.15 A comparison of forces generated by a single twitch, summation of two twitches, and fused tetanus.

In most physical activities, muscular force is applied throughout a range of motion to propel the body or transmit force through external objects. Since in many sporting events speed is a determinant of success, it is important to investigate the basic concepts behind the relationship between muscular force and the speed, or velocity, of movement.

As previously discussed, it is known that fast-twitch muscle fibers exert more force than slow-twitch muscle fibers. In this case, muscle groups that contain a high percentage of fast fibers will also have a greater speed of movement, at any force[16]. Physiologically, this may be explained by the fact that fast fibers possess higher ATPase activity than slow fibers do. Thus, ATP can be more rapidly hydrolyzed in fast fibers. It is also known that the neural stimulation to fast fibers is more quickly delivered. Further, this increases the potential for calcium release from the SR, resulting in more effective excitation-contraction coupling[17].

In practical application to performance, athletes who possess a high percentage of fast fibers would seem to have an advantage in power-type athletic events. This may explain why successful sprinters and weightlifters typically possess a relatively high percentage of fast fibers.

16. Faulker J, Claffin D, McCully K, Power output of fast and slow fibers from human skeletal muscles, in Human Muscle Power, N.M. N Jones, A McComas, Editor. 1986, Human Kinetics: Champaign, IL.

17. Faulker J, Claffin D, McCully K, Power output of fast and slow fibers from human skeletal muscles, in Human Muscle Power, N.M. N Jones, A McComas, Editor. 1986, Human Kinetics: Champaign, IL.

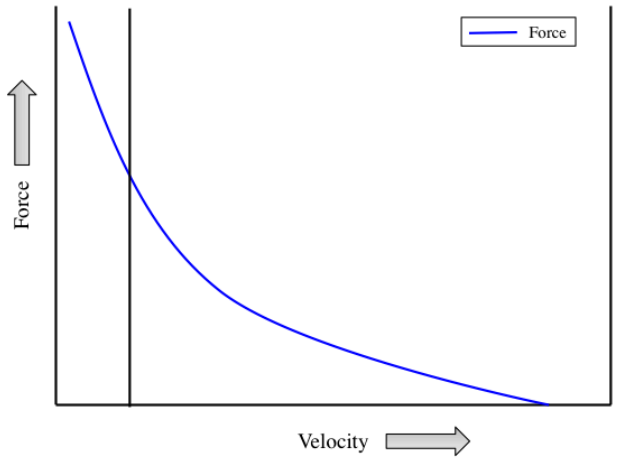


Figure 8.16 Muscle force-velocity relationship.

The force-velocity relationship, as depicted in Figure 8.16, demonstrates that the maximum velocity of muscle shortening occurs at the lowest force. This concept can be easily understood by comparing the lifting of a light load to a heavy load; the light load can be moved more quickly. Therefore, the highest speed of movement is achieved at the lowest workload, regardless of muscle fiber type. Conversely, the maximal velocity of shortening in a muscle fiber is greatest when the force, or resistance against the muscle, is minimal.

The force generated by a muscle is determined by the number of myosin cross-bridges that are attached. However, forming these cross-bridge connections requires time. During rapid muscle shortening, the actin and myosin filaments slide past each other at a faster rate, which limits the number of cross-bridges that can form and, consequently, reduces the muscle's force capacity.

In summary, three key points emerge from examining the force-velocity relationship:

1. Fast-twitch muscle fibers exert the greatest forces at any given velocity.
2. The highest speed of movement is generated at the lowest workloads.
3. Rapid movements limit cross-bridge connections, thereby reducing force production.

Power-Velocity Relationship

Power is defined as the performance of work over a unit of time, with peak power representing the highest power value achieved during a maximal test. Since power is a function of force, distance, and time, there are notable similarities between the force-velocity and power-velocity relationships. The fiber-type composition of a muscle significantly influences its ability to generate power. At any given velocity of movement, muscles with a high percentage of fast-twitch fibers produce greater peak power.

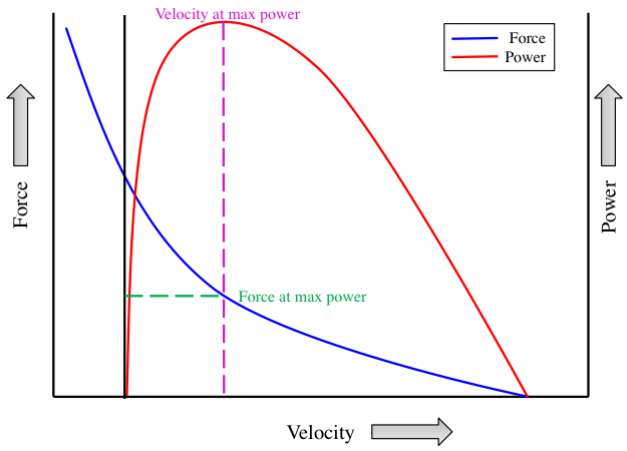


Figure 8.17 Muscle power-velocity relationship. Peak power increases with increasing velocities up to 200 to 300 degrees/second. There is a decline in power beyond this point.

The power-velocity curve, illustrated in Figure 8.17, shows how the velocity of movement influences power output up to a certain point. Similar to force generation, there is an optimal speed of movement that produces the highest power output. Peak power increases with rising velocities, reaching its maximum at approximately 200-300 degrees per second. Beyond this velocity, power output declines rapidly as the speed of movement continues to increase. This decline occurs because muscular force decreases with higher speeds. Consequently, for any given muscle group, there is an optimal speed of movement that maximizes peak power.

Chapter Summary

In this chapter, we examined the intricate structure and function of exercising muscle, emphasizing its pivotal role in human movement and overall health. A detailed examination of skeletal muscle revealed its complex composition, including muscle fibers, connective tissues, and the essential roles of the plasmalemma, sarcolemma, and satellite cells in muscle regeneration and repair.

The mechanisms of muscle contraction, from the sliding filament theory to the processes of excitation-contraction coupling and muscle contraction cycling were discussed. Understanding these mechanisms is crucial for comprehending how muscles generate force and produce movement. We also differentiated between isotonic, isometric, and isokinetic muscle actions, providing practical examples of each.

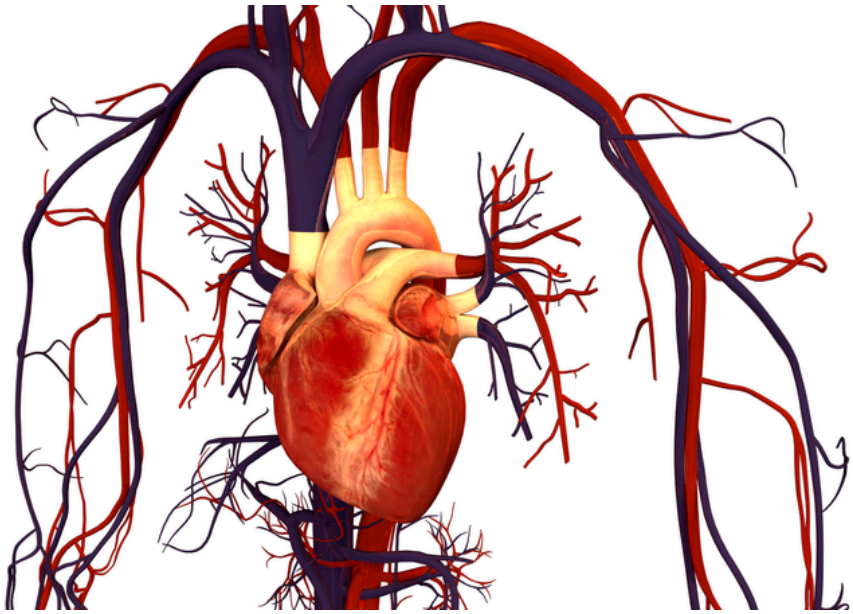
The chapter further explored the force-velocity and power-velocity relationships, illustrating how muscle fiber composition and movement speed influence force and power generation. These concepts are vital for understanding athletic performance and the physiological basis behind different types of physical activities. Finally, we examined how muscle fiber types and their distribution affect athletic performance, noting the impact of training and aging on muscle function. This comprehensive overview equips students with a solid foundation in muscle physiology, essential for careers in exercise science, physical education, physical therapy, and coaching.

Scholarly Questions

1. List the steps of muscle contraction cycling.
2. Pathway of Force Production: Name and describe the four stages of the pathway of force production. This is worth major points on the exam!
3. Define the following muscle actions: isotonic, isometric, and isokinetic.
4. Explain the changes in the H zone length during different muscle actions: Concentric action, Eccentric action, Isometric actions. Also, describe the changes in the I-band, A-band, and the distance between the Z-lines.
5. Identify the most superficial and the deepest layers of connective tissue surrounding the muscle body.
6. Which type of muscle action decreases the angle of a joint?
7. Define the following terms: myofibrils, sarcolemma, plasmalemma, sarcoplasm, T-tubules, muscle triad, sarcoplasmic reticulum, motor endplate, multinucleated, mitochondria, and sarcomere.
8. Explain the importance of satellite cells and their function.
9. Do muscle fibers with a greater percentage of type II fibers exert a faster or slower velocity of contraction?
10. Do muscle fibers with a greater percentage of type I fibers fatigue faster or slower?
11. What is the general percentage of fast-twitch to slow-twitch fiber types in weight lifters and non-athletes?
12. Discuss the factors that affect force production.
13. Define a muscle twitch and fused tetanus.
14. Describe the relationship between force production and the velocity of movement. At what speeds does muscle generate the greatest forces? Why does this happen? (Note: This was not discussed in lecture; please read on your own.)
15. What is the optimal velocity at which muscle generates the greatest peak power? (Note: This was not discussed in lecture; please read on your own.)
16. In class, we broke down the sites of peripheral fatigue into three major areas. What are they, and how might they lead to fatigue?

9.

THE CIRCULATORY RESPONSE TO EXERCISE



Human Heart and Circulatory System Illustration.

Learning Objectives

- Describe the primary functions of the cardiovascular system and explain how it responds to the increased demands of exercise.
- Identify the structural components of the heart, including the atria, ventricles, and major valves, and describe their roles in the cardiac cycle.
- Explain the Frank-Starling mechanism and its significance in regulating stroke volume and cardiac output during exercise.

- Discuss the factors that influence cardiac output, including venous return, ventricular contractility, and total peripheral resistance.
- Interpret an electrocardiogram (ECG), identifying key waveforms (P wave, QRS complex, T wave) and intervals (PR interval, ST segment, QT interval), and explain their significance in diagnosing cardiac conditions.
- Analyze the changes in blood flow distribution during exercise and explain how the body prioritizes oxygen delivery to active muscles.
- Describe the chronic cardiovascular adaptations that occur with regular aerobic training, including changes in heart size, stroke volume, and blood volume.
- Explain the concept of heart rate variability (HRV) and its importance as an indicator of autonomic balance and cardiovascular health.
- Apply the Fick equation to understand the relationship between cardiac output, oxygen delivery, and oxygen consumption during exercise.
- Evaluate the impact of endurance training on resting and submaximal heart rates, and discuss the physiological mechanisms behind these changes.

Introduction

In this chapter, we will explore the heart and circulatory system's response to exercise. Endurance exercise training induces significant adaptations in the cardiovascular system, enhancing performance, longevity, and overall cardiovascular function. These adaptations in the muscles, along with improvements in the oxygen transport system, boost the capacity for oxidative phosphorylation, thereby improving endurance performance. A major challenge to homeostasis during exercise is the increased muscular demand for oxygen, which can rise by 15 to 25 times during intense activity. The cardiovascular system responds through a complex mechanism that ultimately increases cardiac output and redistributes blood flow to the working muscles.

To fully understand the cardiovascular system's response to exercise, it is essential to grasp the fundamentals of resting cardiac function. This chapter will cover the basic functions of the cardiovascular system, the cardiac cycle, and the cardiac conduction system. Additionally, we will introduce the electrocardiogram (ECG) and discuss some clinical measures of cardiac function. Finally, we will examine the cardiovascular adaptations and responses to exercise.

Basic Functions of the Cardiovascular System

The cardiovascular system's primary function is to transport oxygen and nutrients to tissues and remove waste products. Additionally, it plays a crucial role in regulating body temperature. The circulatory and respiratory systems work together as an integrated unit, commonly referred to as the "cardiorespiratory system." Detailed information about the respiratory system will be provided in Chapter 10.

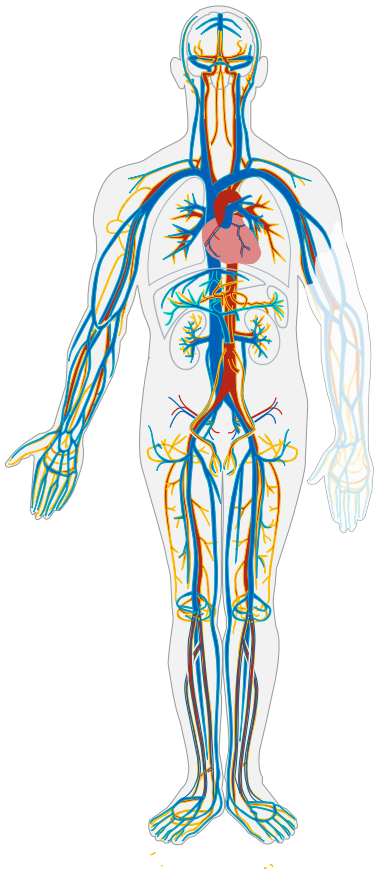


Figure 9.1 The human cardiovascular system.

The heart, as illustrated in Figure 9.1, functions as two distinct pumps: the right heart, which circulates blood through the lungs, and the left heart, which circulates blood through the rest of the body. Each side of the heart operates as a pulsatile two-chamber pump, consisting of a superior atrium and an inferior ventricle. The atria serve as weaker pumps that deliver blood to the ventricles. The ventricles then provide the primary pumping force, propelling blood through the pulmonary circuit via the right ventricle, or through the systemic circuit via the left ventricle.

The human circulatory system operates as a closed circuit, circulating blood to all body tissues. This circulation requires a driving force to generate pressure, enabling blood to move through the body's vessels. Since these vessels are continuous, the system is termed "closed."

Arteries are vessels that transport blood away from the heart, branching into smaller microscopic vessels called **arterioles**. Arterioles further develop into networks of even smaller vessels known as capillaries. **Capillaries** form extensive networks where the exchange of nutrients, including oxygen (O_2) and carbon dioxide (CO_2), occurs with the tissues (see Figure 9.2).

At rest, some muscle capillaries have minimal or no blood flow. However, during strenuous exercise, the number of open capillaries increases two- to three-fold compared to the resting state[1]. This opening of dormant capillaries reduces the distance that oxygen and other nutrients must diffuse through.

Blood transitions from capillaries into small vessels called **venules**, which carry blood back toward the heart. Venules converge into larger **veins** that return blood to the heart. Major veins from both the upper and lower body empty directly into the heart. Due to the mixture of venous blood from the entire body, the blood returning to the right side of the heart is referred to as mixed venous blood[2].

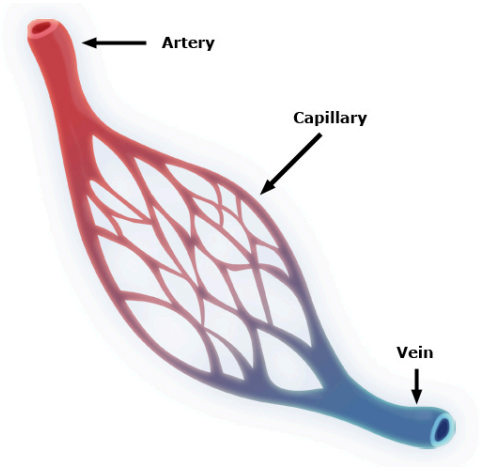


Figure 9.2 A capillary bed and it's relationship to adjoining artery and vein.

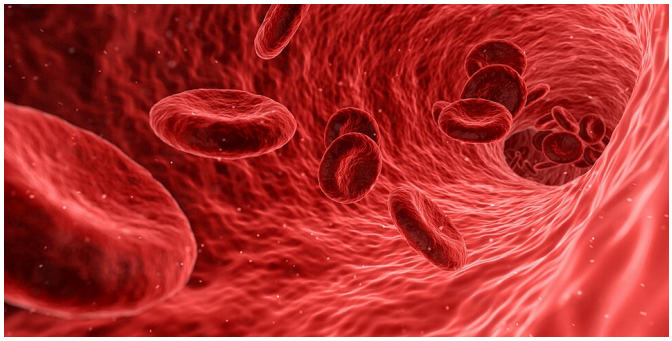


Figure 9.3 Red blood cells inside a blood vessel.

Blood is a crucial component of the cardiovascular system, serving as the vehicle for transporting gases and nutrients. It is primarily composed of plasma, the fluid portion, and cells. Red blood cells (RBCs) are particularly important for gas transport. RBCs have a lifespan of four months and typically constitute 42% of blood in healthy college-aged males and 38% in females. Unique in their lack of a nucleus and mitochondria, RBCs have minimal metabolic needs and derive their energy mainly from glycolysis. Each RBC contains approximately 250 million hemoglobin (Hb) molecules, which are oxygen-carrying proteins. Each hemoglobin molecule has four sites that bind oxygen, and when all sites are occupied, the RBC is considered saturated. This means that each saturated RBC can bind approximately one billion oxygen molecules.

1. Guyton AC, and Hall JE, Textbook of Medical Physiology. 11th ed. 2006, Philadelphia, PA: Elsevier Saunders.

2. Powers SK, and Howley ET, Exercise Physiology (Theory and Application to Fitness and Performance). 9th Edition ed. 2015, New York, NY: McGraw-Hill.

Structure of the Heart

The heart functions as a two-pump system that circulates blood through the lungs and the rest of the body by generating pressure. It has four chambers: two upper chambers called atria and two lower chambers called ventricles (see Figure 9.4). The right atrium and right ventricle form the right pump, while the left atrium and left ventricle form the left pump. The right and left sides of the heart are separated by a muscular wall called the interventricular septum, which prevents the mixing of blood between the two sides.

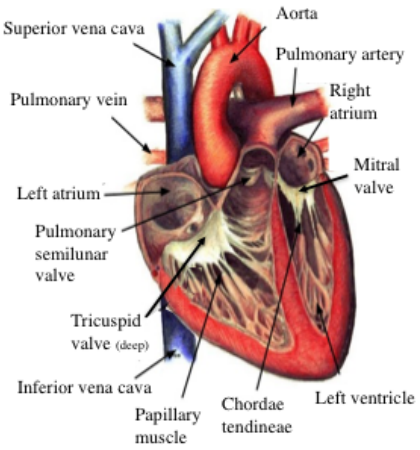


Figure 9.4 A cross-sectional view of anterior structures of the heart.

Blood moves from the atria to the ventricles through one-way valves called **atrioventricular (AV) valves**. These valves, shown in Figure 9.4, include the tricuspid valve (right AV valve) and the mitral valve (left AV valve, also known as the bicuspid valve). Blood then moves from the ventricles to the lungs via the pulmonary semilunar valve and from the ventricles to the aorta via the aortic semilunar valve. These **semilunar valves** prevent the backflow of blood within the heart and from the pulmonary artery and aorta.

Blood Flow Through the Heart

The right side of the heart pumps deoxygenated blood to the lungs through the pulmonary circuit, while the left side pumps oxygenated blood to the systemic circuit. Blood moves along a pressure gradient, flowing from higher to lower pressures. This pressure differential causes the heart valves to open and close, facilitating the movement of blood from one chamber to the next. The pathway of blood flow through the body is as follows:

Blood that has circulated through the body, delivering oxygen and nutrients and collecting waste products, returns to the heart through small venules that branch into larger veins. These veins converge into the great veins, the inferior and superior vena cava, which empty blood into the right atrium. When the blood pressure in the right atrium exceeds that in the right ventricle, blood flows from the right atrium through the tricuspid valve into the right ventricle. The right ventricle then pumps partially deoxygenated blood through the pulmonary semilunar valve into the pulmonary artery and onward to the lungs.

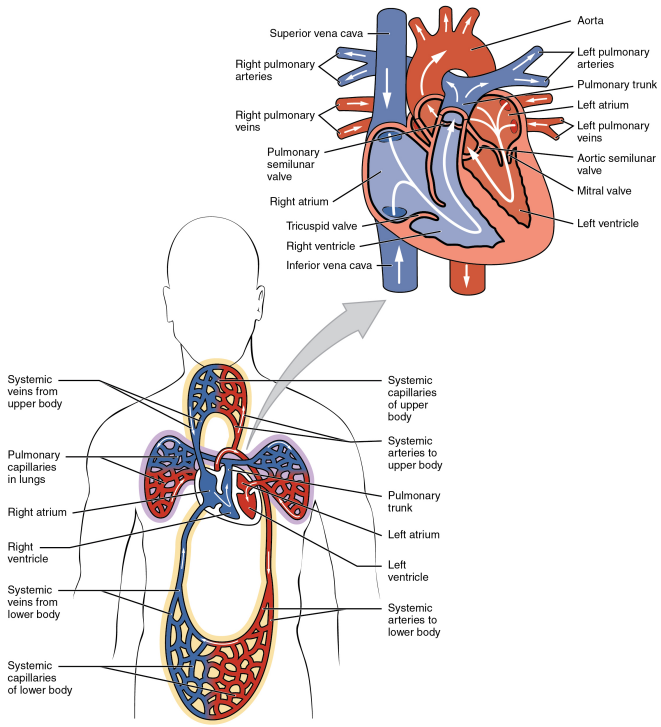


Figure 9.5 The pathway of blood flow throughout the body is a dual system which includes pulmonary and systemic circulation circuits.

In the lungs, external respiration occurs as oxygen is loaded onto red blood cells and carbon dioxide is unloaded. The oxygenated blood returns to the left atrium via the pulmonary veins. When the pressure in the left atrium exceeds that in the left ventricle, blood moves through the mitral valve into the left ventricle. The left ventricle then ejects the blood through the aortic semilunar valve into the systemic circulation. The oxygenated blood travels through the aorta into smaller arteries, which branch into arterioles and eventually reach the capillary beds in the tissues. Here, oxygen is unloaded from the blood to the tissues, and carbon dioxide is loaded into the blood in a process known as internal respiration. As a closed circuit, the deoxygenated blood is then returned to the right side of the heart via the venous system.

Figure 9.5 illustrates the pathway of blood flow through the heart and the systemic vessels of the upper and lower body. During exercise, blood flow increases in proportion to the metabolic needs of the muscles.

Myocardium

The heart walls are composed of three distinct layers: 1) the **epicardium**, 2) the **myocardium**, and 3) the **endocardium**. The outermost layer is the epicardium, a serous membrane that acts as a lubricative outer covering of the heart, containing blood capillaries, lymph capillaries, and nerve fibers. The next layer is the myocardium, which is responsible for the muscular contractions that eject blood from the heart. This layer is separated from the others by connective tissue and also contains blood capillaries, lymph capillaries, and nerve fibers. The innermost layer is the endocardium, which serves as the protective inner lining of the chambers and valves. The endocardium is composed of endothelial tissue and includes a thick layer of elastic and collagenous fibers that allow for stretch (see Figure 9.6).

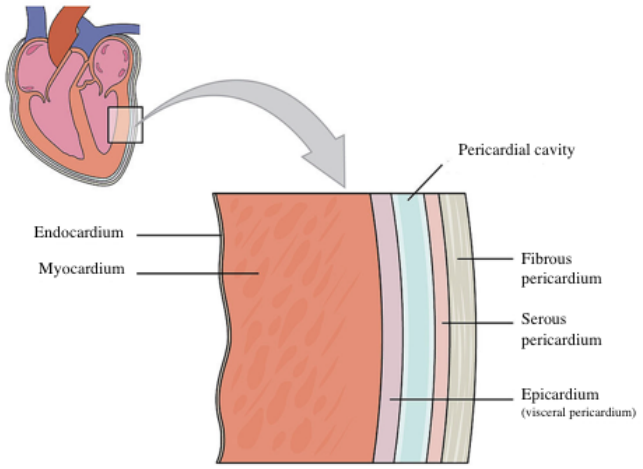


Figure 9.6 The heart wall is composed of three distinct layers: the epicardium, the myocardium, and the endocardium. External to the epicardium are the pericardial cavity, serous pericardium, and the fibrous pericardium.

Cardiac muscle, collectively known as the myocardium, is striated and contains the same contractile proteins as skeletal muscle: actin and myosin. Despite its striated appearance, cardiac muscle differs from skeletal muscle in several ways. Firstly, cardiac muscle fibers are shorter than skeletal muscle fibers and are typically branched[3]. Anatomically, individual cardiac muscle fibers are interconnected end-to-end by regions called **intercalated disks** (see Figure 9.7). These disks contain desmosomes, which are protein structures that anchor neighboring cells together. The myocardium also features gap junctions, allowing for the rapid transmission of action potentials that signal the heart to contract as a single unit. Unlike skeletal muscle, cardiac muscle has only one fiber type, which is similar to type I fibers in that it is highly aerobic, contains a large number of mitochondria, and has a high capillary density[4].

The thickness of the myocardium varies throughout the heart, depending on the amount of stress placed on it. The myocardium in the left ventricle is the thickest because it must generate sufficient pressure to pump blood throughout the entire body. This hypertrophy results from the pressure placed on the left ventricle at rest or under normal conditions of moderate activity. During vigorous aerobic activity, the demand on the left ventricle to deliver blood to the exercising muscles increases significantly, causing the left ventricle to hypertrophy.

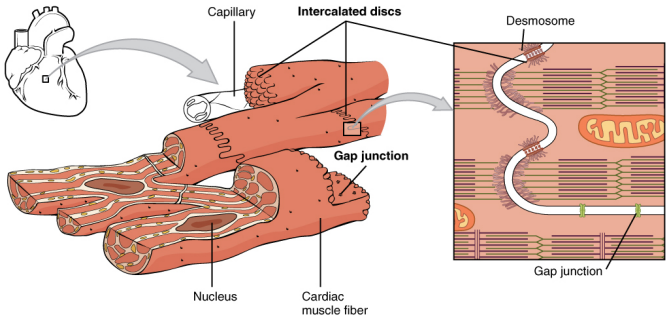


Figure 9.7 Cardiac muscle fibers are continuous and are connected end to end with other cells through intercalated discs. Specialized proteins called desmosomes anchor two neighboring cells together so that they stay connected during contraction of the myocardium.

Hypertrophy of the left ventricle can also result from diseases such as high blood pressure or valvular heart disease. Whether due to exercise training or disease,

3. Powers SK, and Howley ET, Exercise Physiology (Theory and Application to Fitness and Performance). 9th Edition ed. 2015, New York, NY: McGraw-Hill.

4. Kenney WL, Wilmore JH, Costil DL, ed. Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

the myocardium adapts to the condition.

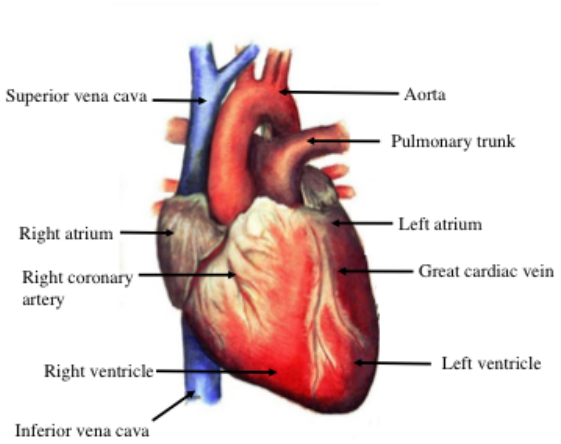


Figure 9.8 The anterior structures of the superficial heart and the associated blood vessels.

The myocardium has its own blood supply, receiving blood via the right and left coronary arteries (see Figure 9.8). Maintaining a constant blood supply to the heart is critical, as deficits in coronary blood flow result in myocardial damage. The heart has a high demand for oxygen and nutrients, and when coronary blood flow is disrupted for more than several minutes, permanent damage to the heart occurs. Unlike skeletal muscle fibers, cardiac muscle fibers do not regenerate because they lack satellite cells, giving heart muscle cells limited regenerative capacity.

Deficits in oxygen due to blockage of coronary blood vessels result in the death of cardiac muscle cells, commonly known as a heart attack or myocardial infarction. Damage to a significant portion of the myocardium greatly diminishes the heart's pumping capacity, making it crucial to minimize injury during a heart attack. Strong evidence indicates that exercise training can provide cardiac protection during a heart attack[5].

Lastly, blood returning from the myocardium drains into the coronary sinus (see Figure 9.11) via the veins of the heart and the great coronary vein. This blood then empties into the right atrium as mixed venous blood.

5. Powers SK, and Howley ET, Exercise Physiology (Theory and Application to Fitness and Performance). 9th Edition ed. 2015, New York, NY: McGraw-Hill.

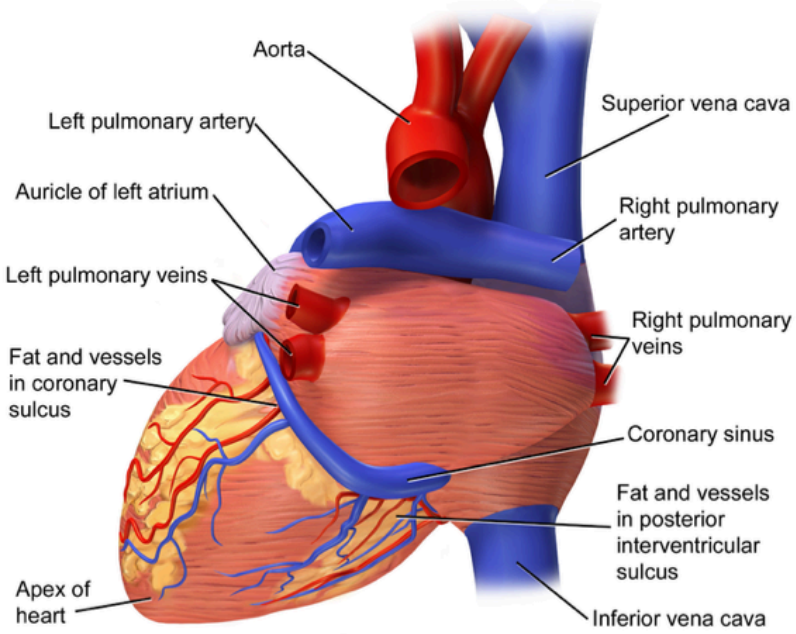


Figure 9.9 The posterior structures of the superficial heart.

The Cardiac Cycle

The **cardiac cycle** encompasses all the events of a single heartbeat, characterized by a repeating pattern of contraction and relaxation of the heart. There are two primary phases of heart function: relaxation, known as **diastole**, and contraction, known as **systole**. During diastole, the heart fills with blood, while systole refers to the period when blood is ejected from the ventricles. These terms can describe the relaxation or contraction of the ventricles, but the atria also undergo systole and diastole. The heart's two-step pumping action allows both atria to contract simultaneously, emptying arterial blood into the ventricles. Approximately 0.1 seconds later, both ventricles contract simultaneously, delivering blood to the systemic and pulmonary circuits.

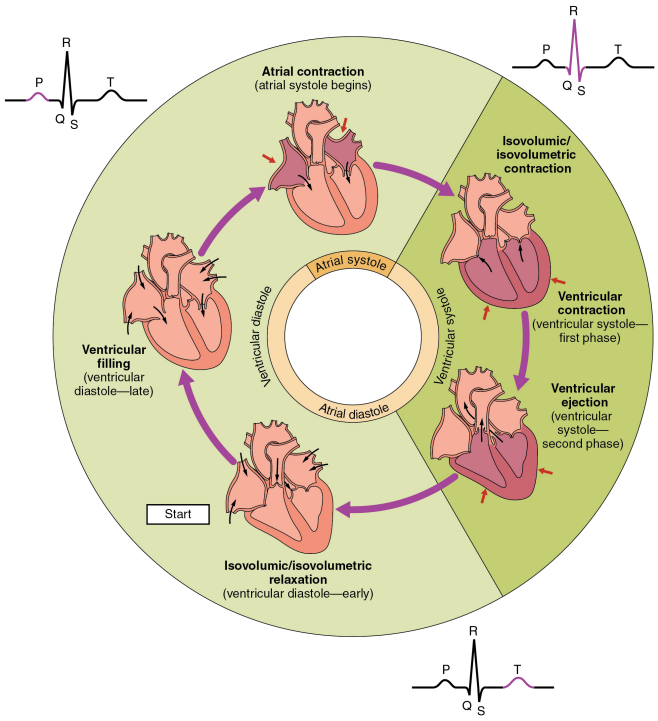


Figure 9.10 The cardiac cycle illustrates all the events of a single heart beat and their corresponding ECG tracings.

The cardiac cycle can be divided into three phases, beginning in mid-to-late diastole, as shown in Figure 9.10. During the first phase, the ventricles fill with blood as the pressure from the atria overcomes the pressure in the ventricles, forcing the atrioventricular valves to open. An atrial contraction then pushes additional blood into the ventricles.

Systole begins in phase two and consists of two periods. The first period is isovolumetric contraction, where the blood volume in the ventricles remains constant, but the pressure builds. During this time, both the atrioventricular and semilunar valves are closed. In the second period of systole, ventricular ejection occurs, forcing the semilunar valves to open while the atrioventricular valves remain closed. Blood is then ejected to the body and lungs.

Phase three is isovolumetric relaxation, occurring during early diastole. At this time, both the atrioventricular and semilunar valves are closed, and the atria begin filling with blood.

Pressure Changes During the Cardiac Cycle

During the cardiac cycle, the pressure within the heart chambers fluctuates. When the atria are in diastole, blood flows into them from venous return. As the atria fill, the internal pressure gradually increases. Approximately 70% of the blood entering the atria during diastole flows directly into the ventricles through the atrioventricular valves before the atria contract. Upon atrial contraction, atrial pressure rises, forcing the remaining 30% of the blood into the ventricles.

A Wiggers diagram, shown in Figure 9.11, illustrates the changes in atrial pressure, ventricular pressure, and aortic pressure throughout the cardiac cycle.

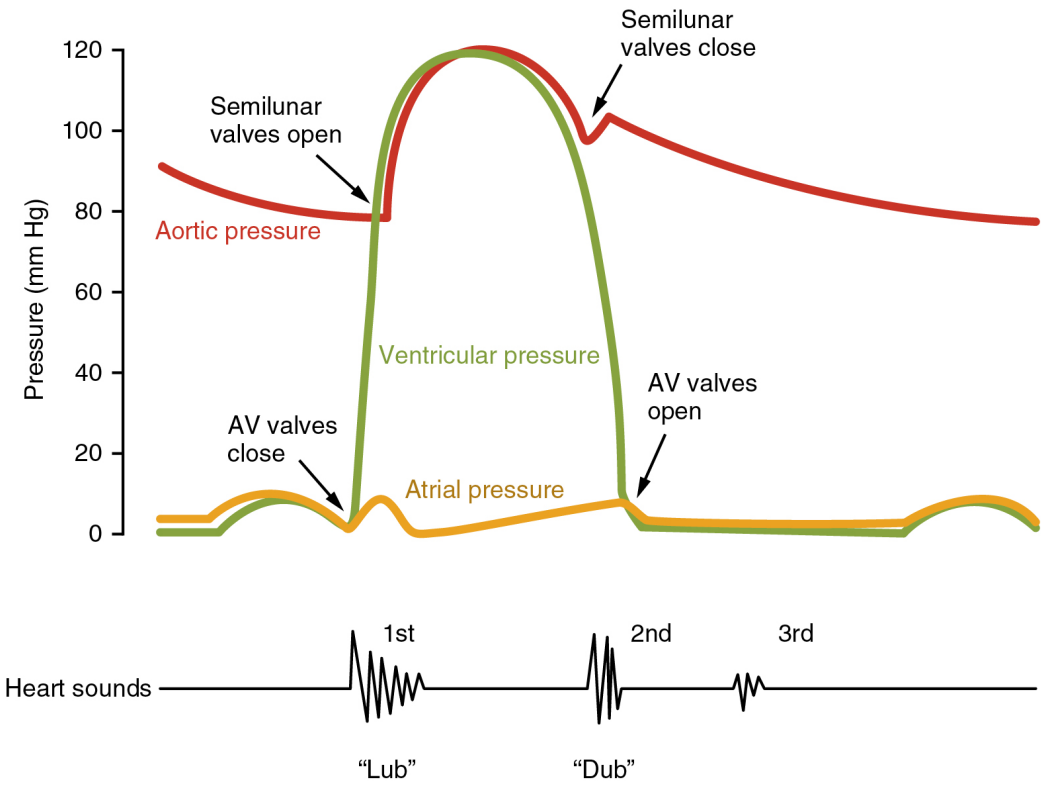


Figure 9.11 A Wiggers diagram, showing the pressure changes during cardiac cycle events. The heart sounds from a phonocardiogram are also shown. The sound labeled 1st contributes to the S1 heart sound and is the reverberation of blood from the sudden closure of the mitral valve and the 2nd contributes to the S2 heart sound and is the reverberation of blood from the sudden closure of the aortic semilunar valve.

Recall that pressure is the most important factor in blood flow through the heart and systemic circulation. As expected, the pressure in the ventricles is low while they are filling. However, when the atria contract, the ventricular pressure increases slightly. As the ventricles contract, the pressure rises sharply, closing the atrioventricular valves to prevent backflow of blood into the atria, as shown in the Wiggers diagram (see Figure 9.11). Once the ventricular pressure exceeds the pressure in the pulmonary artery and the aorta, the semilunar valves open, and blood is forced into both the pulmonary and systemic circuits. Heart sounds are heard as the heart valves close: the "lub" sound is the closing of the atrioventricular valves (first heart sound), and the "dub" sound is the closing of the semilunar valves (second heart sound).

Blood exerts pressure throughout the circulatory system, but it is greatest within the arteries. **Blood pressure**, the force exerted by the blood against the arterial walls, is generally measured as an indication of health. Blood pressure is influenced by the volume of blood pumped and the resistance to flow. A sphygmomanometer can estimate arterial blood pressure. Normal blood pressure for an adult male is 120/80 mmHg, while for an adult female it tends to be lower (110/70 mmHg). High blood pressure is diagnosed if the pressure is greater than 140/90 mmHg. The top number represents systolic blood pressure, the pressure in the arteries during ventricular contraction (systole). Diastolic blood pressure, the bottom number, is the

pressure during cardiac relaxation (diastole). At maximal exercise capacity, systolic blood pressure increases, and diastolic pressure decreases. The difference between these pressures is called **pulse pressure** and can be calculated as follows:

$$\text{Pulse pressure} = \text{SBP} - \text{DBP}$$

The average pressure during a cardiac cycle is called mean arterial pressure (MAP). It is significant because it determines the rate of blood flow through the systemic circuit during rest. The **mean arterial pressure** is determined by the following equation:

$$\text{Mean arterial pressure} = \text{DBP} + 0.33(\text{pulse pressure})$$

It is difficult to find the mean arterial pressure during exercise because the formula assumes that 33% of the total cardiac cycle is spent in systole. During exercise, systole may account for up to 66% of the cardiac cycle; therefore, the formula must be adjusted to reflect the time spent in systole and diastole [2].

The Cardiac Conduction System

At rest, specialized mechanisms in the heart cause a succession of heart contractions called cardiac rhythmicity. This intrinsic rhythm transmits action potentials throughout the heart muscle, causing the heart to beat at regular intervals. The heart is equipped with an electrical conduction system that generates and conducts electrical impulses from the atria to the ventricles. The electrical impulse follows specialized pathways, causing the atria and ventricles to contract at specific times. The system, illustrated in Figure 9.12, consists of the sinoatrial (SA) node, the interatrial tract (Bachmann's bundle), the internodal tracts, the atrioventricular (AV) node, the bundle of His, the right and left bundle branches, and the Purkinje fibers[6].

6. Huff J, ECG workout: exercises in arrhythmia interpretation. Fifth ed. 2006, Philadelphia, PA: Lippincott Williams & Wilkins.

The **sinoatrial (SA) node**, known as the pacemaker of the heart, discharges impulses in a rhythmic fashion at a rate of 60-100 beats per minute (bpm). It possesses the highest level of automaticity, or inherent firing rate. The **atrioventricular (AV) node** can function as a secondary pacemaker at a rate of 40-60 bpm. Additionally, ventricular pacemaker cells can fire at a rate of 30-40 bpm or less. If the SA node fails to generate electrical impulses at its normal rate or if the conduction of these impulses is blocked, pacemaker cells in other sites can assume control of the heart rate, albeit at a much slower rate[7].

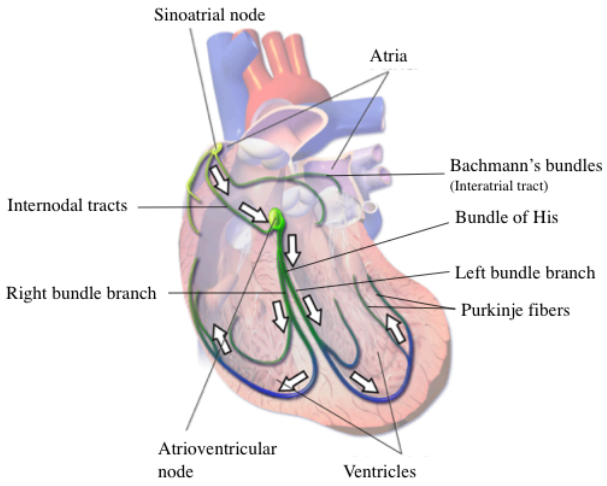


Figure 9.12 The structures of the electrical conduction system of the heart.

The regular impulse sent by the SA node to the myocardium is called an intrinsic rhythm because the impulse originates from within the heart itself. As the impulse leaves the SA node, it is conducted via Bachmann's bundles (interatrial tracts) through the left atrium and passes through internodal tracts down the right atrium. The impulse is then conducted to the AV node, located in the lower right atrium near the septum of the heart, where there is a momentary delay.

The AV node has three main functions. First, it slows the conduction of the electrical impulse to allow time for the atria to contract and empty blood into the ventricles, a process known as the atrial kick, which occurs before the ventricles contract. Secondly, the AV node blocks impulses from being conducted when the atrial rate is too rapid, protecting the ventricles from dangerously fast rates. Lastly, the AV node acts as a backup pacemaker if the SA node fails.

After the delay in the AV node, the impulse moves rapidly through the **bundle of His**, located in the septum region of the heart. The impulse then divides into two important conducting pathways: the right bundle branch (RBB) and the left bundle branch (LBB). Both **bundle branches** terminate in a network of terminal fibers called the **Purkinje fibers**. The signal then penetrates the ventricular muscle mass as the Purkinje fibers form an elaborate web of pathways[8].

7. Huff J, ECG workout: exercises in arrhythmia interpretation. Fifth ed. 2006, Philadelphia, PA: Lippincott Williams & Wilkins.

8. Huff J, ECG workout: exercises in arrhythmia interpretation. Fifth ed. 2006, Philadelphia, PA: Lippincott Williams & Wilkins.

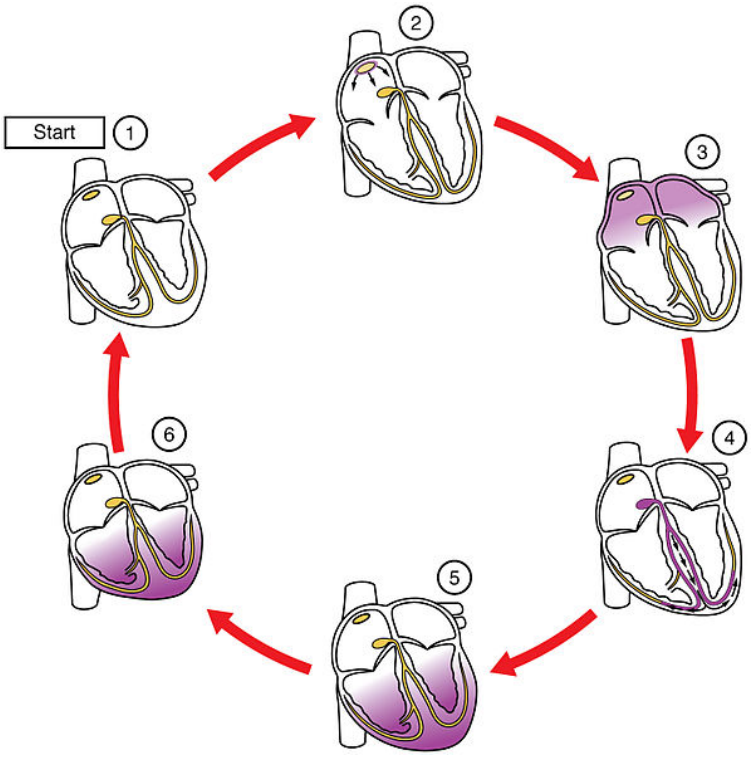


Figure 9.13 An illustration of the heart's electrical events; 1) Resting conditions, 2) SA node causes atria to begin depolarizing, 3) atrial depolarization, 4) depolarization delays at AV node and then quickly travels down the bundle of His, 5) depolarization spreads down LBB and RBB in the ventricles beginning at the apex and progresses superiorly as atria re-polarize, and 6) ventricular repolarization begins at the apex and also progresses superiorly.

Electrocardiogram (ECG)

The **electrocardiogram (ECG)** is a recording of the heart's electrical activity. It captures the electrical processes of depolarization and repolarization in the myocardium. **Depolarization** refers to the spread of the electrical stimulus through the heart, while **repolarization** is the return of the stimulated muscle to its resting state. These electrical processes generate currents that are transmitted to the body's surface and can be detected by electrodes attached to the skin.

The ECG allows for continuous observation of the heart's electrical activity and is used to identify arrhythmias, evaluate pacemaker function, and assess the response to medications. Cardiologists often analyze the ECG during exercise to diagnose coronary artery disease.

To perform ECG monitoring, conductive gel pads (electrodes) are placed on the patient's chest and body and connected to a lead-cable system. This setup allows the electric current to be displayed on a monitor screen (oscilloscope) and recorded on ECG graph paper. In a typical 12-lead ECG, there are six chest lead positions (V1 to V6), two arm positions (RA and LA), and two leg positions (LL and RL). Figure 9.14 shows the electrode positions for a typical 12-lead ECG.

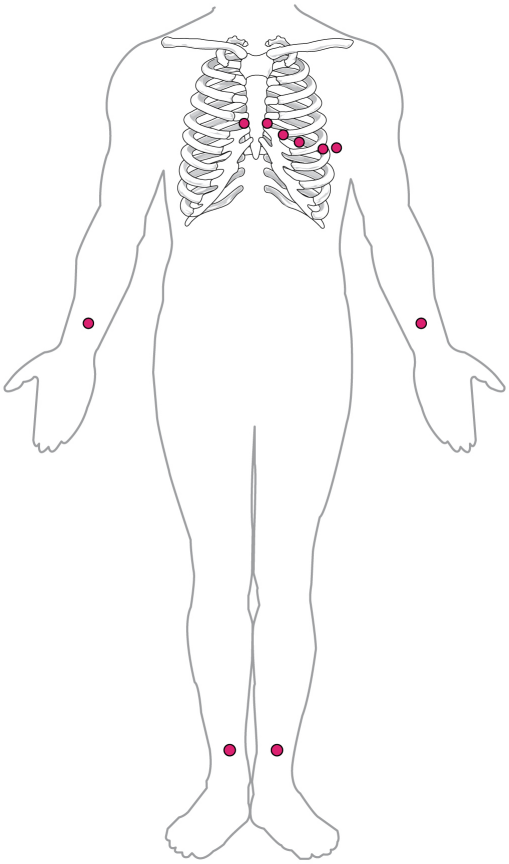


Figure 9.14 Anterior view of monitor lead position in a typical 12-lead ECG.

A monitor lead, or ECG lead, provides a view of the heart's electrical activity between two points and is recorded on specialized graph paper. As shown in Figure 9.15, the flat line represents the baseline of electrical current, known as the isoelectric line. Any waveform above the isoelectric line is considered a positive (upright) deflection, while any waveform below the isoelectric line is a negative (downward) deflection. A deflection with both positive and negative components, such as the QRS complex, is called a biphasic deflection. Biphasic deflections occur when current flowing away from the poles is detected. Electric currents traveling toward the positive pole produce a positive deflection, while currents flowing toward the negative pole result in a negative deflection.

The heart's electrical activity is represented on the ECG tracing by three basic waveforms: the **P wave**, the **QRS complex**, and the **T wave**. Between these waveforms are segments and intervals, such as the **PR interval**, the **ST segment**, and the **QT interval**. Occasionally, a **U wave** is also present. These waves and intervals correspond to different phases of the cardiac conduction system.

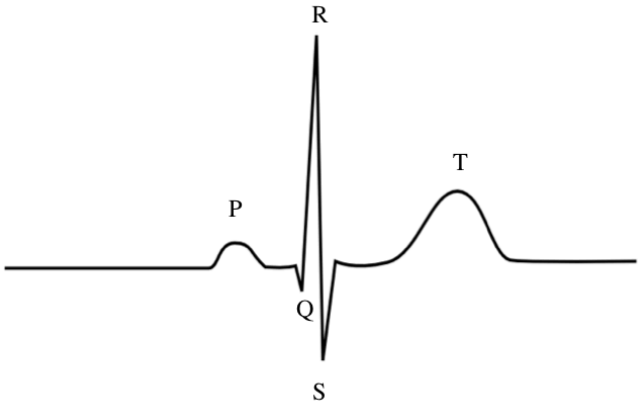


Figure 9.15 An ECG tracing of one cardiac cycle.

- P wave: Depicts atrial depolarization, which is the spread of the impulse from the SA node throughout the atria.
- PR interval: Represents the time from the onset of atrial depolarization to the onset of ventricular depolarization.
- QRS complex: Depicts the spread of the impulse through the ventricles, or ventricular depolarization. Note that atrial repolarization occurs simultaneously with ventricular

depolarization and is masked by the QRS signal.

- ST segment: Represents the end of ventricular depolarization and the beginning of ventricular repolarization.
- T wave: Represents the latter phase of ventricular repolarization.
- U wave: Although not always present, it is thought to represent further repolarization of the ventricles[9].

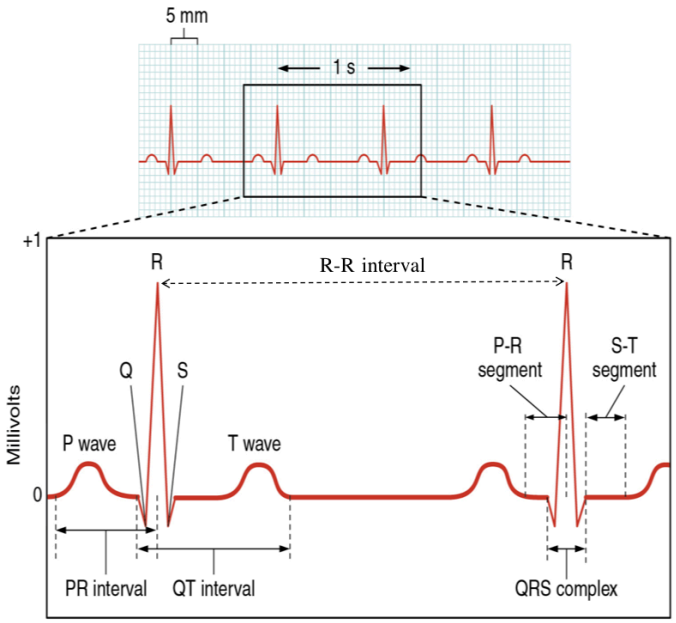


Figure 9.16 Relationship of the electrical conduction system to the ECG. Note that there are 2 cardiac cycles emphasized.

The PQRST sequence is recorded on special graph paper, as shown in Figure 9.16. Each small square measured horizontally represents 0.04 seconds in time. The distance of the **R-R interval** in Figure 9.16 extends across 20 small squares, representing 0.8 seconds (0.04 seconds x 20 squares). Each small square measured vertically indicates the voltage or amplitude in millimeters (mm)[10]. Each square represents 1 mm in height. Therefore, the height of the QRS complex, which spans 14 small squares, represents a voltage of 14 mm (1 mm x 14 squares).

9. Huff J, ECG workout: exercises in arrhythmia interpretation. Fifth ed. 2006, Philadelphia, PA: Lippincott Williams & Wilkins.

10. Huff J, ECG workout: exercises in arrhythmia interpretation. Fifth ed. 2006, Philadelphia, PA: Lippincott Williams & Wilkins.

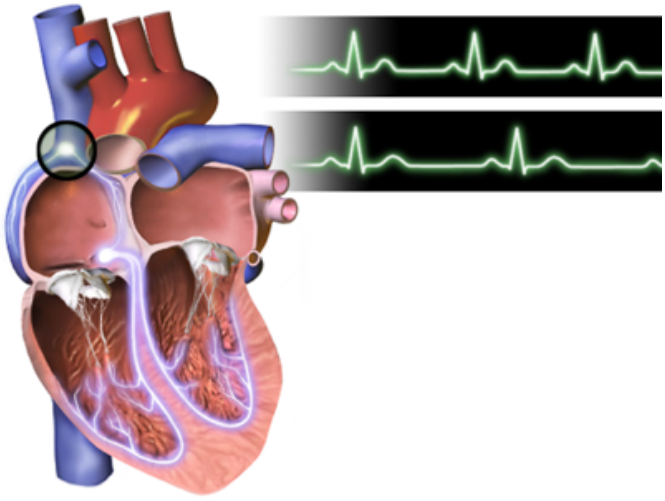


Figure 9.17 The conduction system of the heart and the associated ECG tracings comparing a NSR (top) and sinus bradycardia (bottom).

The ECG is a valuable tool in clinical settings, providing a noninvasive means of assessing heart function. Abnormalities in the ECG can indicate coronary heart disease due to restricted blood flow to the tissues, or ischemia. For instance, ST segment depression may signal myocardial ischemia, while an elevated ST segment can indicate myocardial injury[11]. ECG monitoring is also effective in identifying cardiac arrhythmias. Heart rate, expressed as beats per minute (bpm), is a key metric. A **normal sinus rhythm (NSR)** describes a resting heart rate of 60-100 bpm. **Sinus bradycardia** is identified when a resting heart rate is less than 60 bpm, as illustrated in Figure 9.17. Conversely, **sinus tachycardia** is a resting heart rate over 100 bpm.

Heart Rate Regulation and Variability

Heart rate is regulated by the autonomic nervous system. It can be elevated by increasing sympathetic activity or decreasing parasympathetic (vagal) activity. **Heart rate variability (HRV)** refers to the variation in the time between heartbeats. This interval, measured in milliseconds, can be determined as the R-R interval on an ECG tracing, as shown in Figure 9.16. Although it may seem counterintuitive, a wide variation in HRV is considered a good indicator of health, reflecting a healthy balance between the sympathetic and parasympathetic nervous systems.

The physiological significance of HRV lies in its reflection of autonomic balance, making it an excellent noninvasive screening tool for many cardiovascular diseases. Low HRV has been shown to predict cardiovascular events, such as sudden cardiac death, and generally indicates an imbalance in autonomic regulation.

Terminology of Cardiac Function

Understanding the following measures of cardiac function is essential for discussing the heart's responses to

11. Huff J, ECG workout: exercises in arrhythmia interpretation. Fifth ed. 2006, Philadelphia, PA: Lippincott Williams & Wilkins.

exercise:

- **End-Diastolic Volume (EDV)**: The volume of blood in the ventricles at the end of diastole, also known as the "preload."
- **End-Systolic Volume (ESV)**: The volume of blood remaining in the ventricles after ejection.
- **Stroke Volume (SV)** is the difference between EDV and ESV: SV(ml/beat) = EDV – ESV
- **Ejection Fraction (EF)** is an important clinical term used to assess the heart's pumping ability. It describes the fraction, as a percentage, of blood pumped out of the ventricles relative to the amount of blood in the ventricle before contraction. EF is calculated by dividing the stroke volume by the end-diastolic volume: EF(%) = (SV/EDV) x 100

The average ejection fraction in a healthy adult is 60% at rest, meaning that 60% of the blood in the ventricles is ejected per beat.

- **Cardiac Output (Q)** describes the total amount of blood pumped by the heart per minute. It is the product of heart rate and stroke volume: Q(L/min) = HR x SV

The abbreviation "Q" stands for the "quantity" of blood pumped per minute. The average cardiac output is 4.0 L/min in women and 5.6 L/min in men[12]. In round numbers, it is often stated to be approximately 5 L/min.

Factors Affecting Cardiac Output

During exercise, cardiac output increases proportionally to the metabolic needs of the muscles. Several factors influence cardiac output during exercise, including increased venous blood return, ventricular contractility, ventricular stretch, and resistance to blood flow. These factors are described below.

Exercise enhances blood return from the body through several mechanisms. Figure 9.18 illustrates the muscle pump, which results from the mechanical action of rhythmic skeletal muscle contractions during exercise. When muscles contract, they compress their veins, pushing blood back toward the heart. Veins contain one-way valves that prevent blood from flowing away from the heart. Between contractions, blood fills the veins, and the process repeats. This mechanism accelerates venous blood return, increasing end-diastolic volume (EDV), stroke volume, and cardiac output. However, if the returning blood exceeds the heart's pumping capacity during exercise, the heart becomes the limiting factor for cardiac output.

12. Guyton AC, and Hall JE, Textbook of Medical Physiology. 11th ed. 2006, Philadelphia, PA: Elsevier Saunders.

Additionally, venoconstriction increases venous return by reducing the veins' capacity to store blood, thereby moving blood back toward the heart. This occurs through reflex sympathetic constriction of smooth muscle in veins draining skeletal muscle. Endurance training has been shown to enhance venous blood return, thereby increasing EDV.

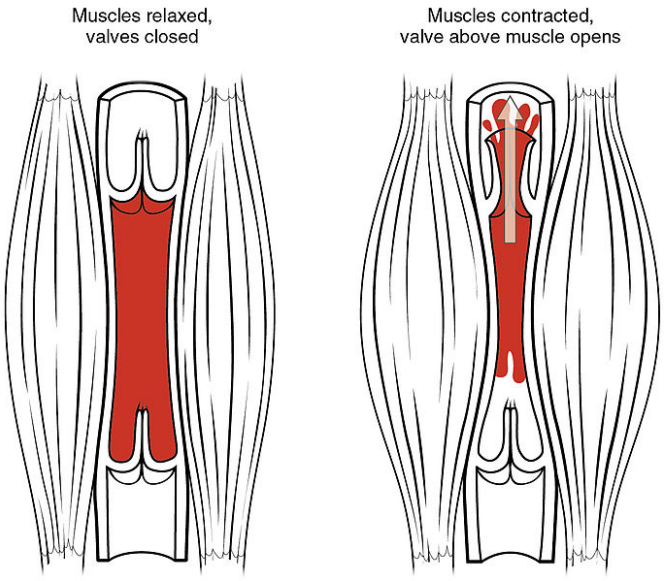


Figure 9.18 The muscle pump. The action of the one-way venous valves imbedded in skeletal muscle ensure the unidirectional flow of blood back to the heart. Contractions of the skeletal muscles help to pump blood toward the heart, preventing blood from flowing away from the heart or pooling in the lower extremities due to gravity.

Venous blood return is the primary controller of cardiac output and is more important than the heart itself in controlling cardiac output [1]. This is because the heart has a built-in mechanism that allows it to pump automatically whatever amount of blood flows into the right atrium from the veins. This mechanism is called the **Frank-Starling law** of the heart. Essentially, when increased quantities of blood flow into the heart and stretch the walls of the heart chambers, the Frank-Starling mechanism is triggered. As a result, the cardiac muscle contracts with increased force. Like any other muscle, the myocardium can contract with greater force, known as ventricular contractility, which directly affects stroke volume. Therefore, the Frank-Starling mechanism leads to a more powerful ventricular contraction, emptying the extra blood that has returned from systemic circulation. This amount of blood return from the body is also referred to as the "preload."

Cardiac output levels also vary with changes in total peripheral resistance, especially long-term levels. To eject blood, the pressure generated by the left ventricle must exceed the pressure in the aorta. Therefore, aortic pressure or mean arterial pressure (called afterload) represents a barrier to the ejection of blood and cardiac output. Total peripheral resistance from smaller openings or diseased vessels greatly affects cardiac output. This can be understood by considering **Ohm's law**: Q = arterial pressure/total peripheral resistance

The meaning of this formula is that any time the level of total peripheral resistance changes, the cardiac output changes quantitatively in the opposite direction. Aortic and pulmonary artery resistance to blood flow can adversely affect cardiac output. Healthy arteries have better vasodilation, allowing blood to travel more efficiently through the systemic circuit. Maintenance of normal arterial pressure usually occurs via nervous reflexes and is essential to achieving high cardiac outputs during exercise when the muscles dilate their vessels to increase blood flow and venous return[13]. It is noteworthy that afterload is minimized during exercise due to arteriole dilation. The arteriole dilation in working muscles decreases aortic pressure, making it easier for the heart to pump large volumes of blood[14].

The final factor influencing cardiac output is the effect of circulating epinephrine and norepinephrine (catecholamines). In addition to increases in sympathetic nervous system stimulation, catecholamines increase muscle contractility by increasing the amount of calcium available to the myocardial cells. As you may recall, calcium is necessary for muscle contraction activation. Calcium release into the muscle cell increases cross-bridge activation and force production.

In summary, cardiac output is regulated by venous blood return (EDV), cardiac contractility, and cardiac afterload. During upright exercise, there is an increase in EDV, contractility, and cardiac output due to the rhythmic mechanical contraction of skeletal muscles and influence from the nervous system. Catecholamines also play a role in increasing contractility and cardiac output during exercise.

Cardiovascular Responses to Exercise

Improvements in endurance resulting from regular aerobic training, such as running and swimming, stem from multiple adaptations to the training stimulus. Aerobic training, or cardiorespiratory endurance training, enhances cardiac function and peripheral blood flow. It significantly boosts the capacity of muscle fibers to generate ATP, which is dependent on oxygen supplied and transported via the cardiovascular system.

During maximal exercise, the metabolic need for oxygen in skeletal muscle can increase up to 25 times the resting values. Increased oxygen delivery to exercising skeletal muscle is achieved by 1) increasing cardiac output and 2) redistributing blood flow from inactive organs to the working muscles. Blood is also directed away from the gut by decreasing blood flow to the splanchnic area (i.e., liver, kidneys, GI tract). These mechanisms are facilitated by the cardiorespiratory system.

Cardiac output and blood flow increase in direct proportion to the metabolic requirements of the tissues. At rest, approximately 15% to 20% of total cardiac output is directed toward skeletal muscle. However, during maximal exercise, 80% to 85% of total cardiac output goes to contracting skeletal muscle [5]. Increased blood flow allows more oxygen delivery to the working skeletal muscles, achieved by increasing arteriole vasodilation in vessels supplying the muscles. During heavy exercise, the percentage of blood going to the brain is reduced compared to the percentage at rest, but the absolute blood flow to the brain is slightly increased above resting values, thus improving blood flow to the brain. Additionally, total coronary blood flow increases during heavy exercise due to increased cardiac output, supplying the myocardium with enough oxygen to meet the demands of increased contraction necessary to amplify heart rate. Both light and moderate intensities of exercise increase blood flow to the skin, but this decreases during maximal exercise. Finally, compared to

13. Guyton AC, and Hall JE, Textbook of Medical Physiology. 11th ed. 2006, Philadelphia, PA: Elsevier Saunders.

14. Powers SK, and Howley ET, Exercise Physiology (Theory and Application to Fitness and Performance). 9th Edition ed. 2015, New York, NY: McGraw-Hill.

resting values, blood flow to abdominal organs decreases during maximal exercise. Increases in muscle blood flow during exercise and the decrease in splanchnic blood flow change as a linear function of $\%VO_{2max}$ [5].

To utilize the oxygen delivered by the cardiovascular system, there must also be changes in oxygen uptake by muscles during exercise. Oxygen uptake by muscles increases during exercise and can be measured by determining the **arterial-(mixed blood) venous O_2 difference (a-vO_2 difference)**. The a-vO_2 difference represents the amount of O_2 taken up from 100 ml of blood by the tissues during one cycle of the systemic circuit. To find the a-vO_2 difference, the change in O_2 blood content between the arteries and veins is determined. During intense exercise, an increase in the a-vO_2 difference indicates enhanced oxygen extraction at the muscle capillaries. This increase is due to a rise in the amount of O_2 taken up and used for oxidative phosphorylation (i.e., utilization of O_2 in skeletal muscle) by skeletal muscle. Endurance exercise training has been shown to increase muscles' O_2 extraction abilities.

Chronic Cardiovascular Adaptations to Aerobic Training

Multiple chronic cardiovascular adaptations occur in response to exercise training, including changes in heart size, cardiac output, blood volume, and others. To fully understand these changes, it is important to review how these components relate to oxygen transport. Much of endurance performance is related to the cardiovascular and respiratory systems' ability to deliver sufficient oxygen to meet the needs of metabolically active muscles. **The Fick equation** (1870), developed by Adolf Eugene Fick, describes the relationship between oxygen delivery and utilization by the tissues with whole-body oxygen consumption. The product of cardiac output and the (a-v)O_2 difference determines the rate at which oxygen is being consumed: $VO_2 = Q \times (a - v)O_2$ difference

Cardiac muscle, like skeletal muscle, can undergo morphological changes when stimulated by exercise training. Cardiac hypertrophy of the left ventricle can be induced by exercise, resulting in an increase in chamber size. This allows for increased filling and, consequently, an increase in stroke volume and cardiac output. In concert with this, a decrease in heart rate at rest is caused by increased parasympathetic tone, and during exercise at the same rate of work, this adaptation allows a longer diastolic filling period. As mentioned, endurance training results in hypertrophy of the left ventricular wall, increasing its thickness. Increased ventricular mass results in increased contractile force, in turn causing a lower end-systolic volume (ESV). It was once thought that cardiac hypertrophy was dangerous because experts erroneously believed that enlargement of the heart always reflected a pathological state, as seen in cases of severe hypertension and myopathies. It is now known that endurance training-induced cardiac hypertrophy is a normal adaptation to chronic training and that left ventricular mass is highly correlated with VO_{2max} and, therefore, improved performance[15].

Aerobic training affects stroke volume through adaptations to the left ventricular dimensions, increases in

contractility, and a greater blood volume. Following a program of endurance training, stroke volume at rest is substantially higher than it was prior to training. This is known as a chronic adaptation. Stroke volume can be greatly affected by the volume of blood that enters the ventricle during diastole. Plasma volume has been shown to expand with training, increasing the end-diastolic volume (EDV). Additionally, an increase in red blood cell volume also contributes to the overall increase in blood volume, though this finding is inconsistent[16]. Although the actual number of red blood cells may increase, the hematocrit may decrease. Hematocrit is the ratio of red blood cell volume to total blood volume. A trained athlete's hematocrit can decrease due to a greater increase in plasma volume. However, this may be beneficial. One physiological benefit of decreasing hematocrit is reduced blood viscosity, which decreases peripheral resistance to blood flow. Both increases in plasma and hematocrit result in more blood entering the ventricles. Recall that increased blood volumes stretch the ventricular walls, resulting in an increased force of contraction (i.e., the Frank-Starling mechanism). Therefore, if more blood enters the left ventricle, a greater percentage of it is ejected with each contraction with greater force, resulting in an increase in stroke volume.

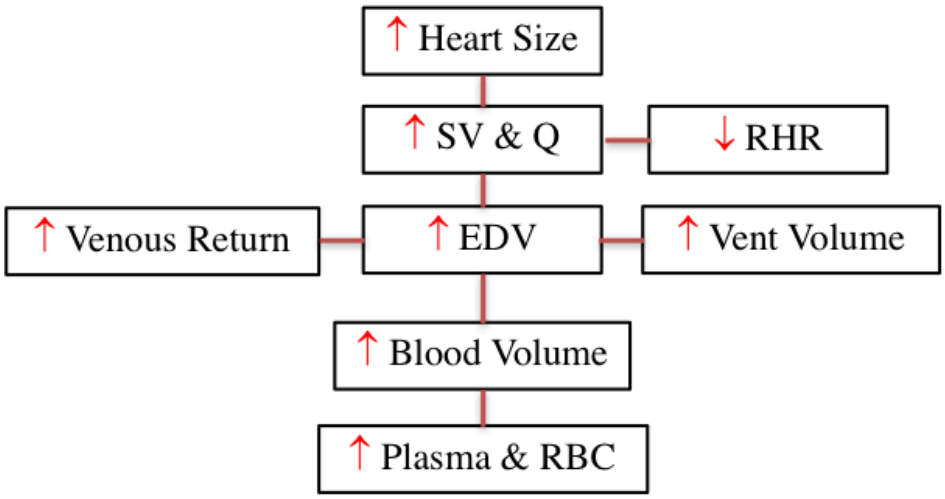


Figure 9.19 A flow chart of factors that increase cardiovascular endurance performance including heart size, stroke volume, cardiac output, resting heart rate, venous return, end diastolic volume, ventricular volume, blood volume, plasma and red blood cell content.

Studies have shown that a sedentary individual with an initial resting heart rate (RHR) of 80 bpm can decrease their resting heart rate by approximately 1 bpm per week of aerobic training, at least for the first few

15. Milliken MC, Stray-Gundersen J, Left ventricular mass as determined by magnetic resonance imaging in male endurance athletes. American Journal of Cardiology, 1988. 62: p. 301-305.

16. Kenney WL, Wilmore JH, Costil DL, ed. Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

weeks. After 10 weeks of training, resting heart rate can decrease from 80 to 70 bpm or lower[17]. Similarly, after endurance training, submaximal heart rate is 10 to 20 bpm lower during exercise at the same absolute workload. This reflects increased cardiac output, higher stroke volumes, and increased blood volume, indicating that a trained heart performs less work than an untrained heart at the same workload. On the other hand, maximal heart rate generally does not change or may decrease slightly with endurance training. The mechanisms responsible for this decrease in RHR are not fully understood, but training appears to influence parasympathetic activity in the heart, while a decrease in sympathetic activity may play a small role.

In summary, blood flow to active muscles increases with endurance training due to several factors. Figure 9.19 summarizes the factors that enhance cardiovascular endurance performance. Increases in blood volume, stroke volume, ventricular muscle mass, and venous blood return ultimately result in increased cardiac output and a decreased resting heart rate. Endurance training programs improve the consumption, distribution, and utilization of oxygen within skeletal muscles, with the cardiorespiratory system adapting to the training stimulus to facilitate these developments.

Chapter Summary

This chapter explored the heart and circulatory system's response to exercise, highlighting the significant adaptations that occur with endurance training. Key points include:

- Cardiovascular Adaptations: Endurance exercise training enhances cardiac function and peripheral blood flow, increasing the capacity for oxidative phosphorylation and improving endurance performance. The cardiovascular system responds to increased muscular demand for oxygen by increasing cardiac output and redistributing blood flow to working muscles.
- Heart Structure and Function: The heart functions as a two-pump system, with the right side pumping blood to the lungs and the left side pumping blood to the rest of the body. The myocardium, the heart's muscular layer, adapts to exercise by increasing in thickness and contractile force, particularly in the left ventricle.
- Blood Flow and Pressure: Blood flow through the heart and systemic circulation is driven by pressure changes. The cardiac cycle, consisting of systole and diastole, regulates the movement of blood through the heart's chambers and valves. The ECG is a crucial tool for monitoring the heart's electrical activity and diagnosing conditions such as arrhythmias and myocardial ischemia.
- Cardiac Output: Cardiac output, the total amount of blood pumped by the heart per minute, is influenced by factors such as venous return, ventricular contractility, and resistance to blood flow. The

17. Kenney WL, Wilmore JH, Costil DL, ed. Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

Frank-Starling mechanism and the effects of catecholamines play significant roles in regulating cardiac output during exercise.

- Chronic Adaptations: Regular aerobic training induces chronic cardiovascular adaptations, including increased heart size, stroke volume, and blood volume. These changes enhance the heart's efficiency and capacity to meet the metabolic demands of active muscles. Endurance training also improves the body's ability to extract and utilize oxygen, as reflected in increased a-vO2 difference.
- Heart Rate and Blood Flow: Endurance training lowers resting and submaximal heart rates, reflecting improved cardiac efficiency. Blood flow to active muscles increases during exercise, facilitated by arteriole vasodilation and enhanced venous return. These adaptations support greater oxygen delivery and utilization during physical activity.

Overall, the chapter emphasized the intricate relationship between the cardiovascular system and exercise, detailing how regular aerobic training leads to significant improvements in cardiovascular health and performance.

Scholarly Questions

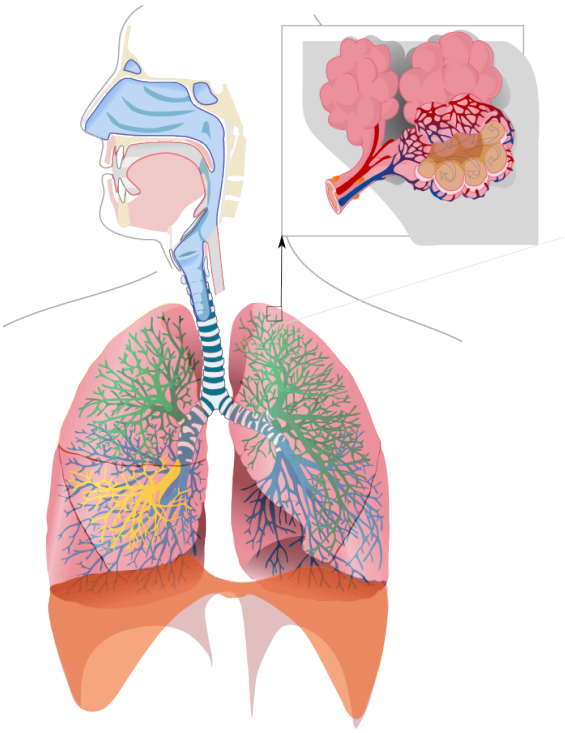
1. What are the three primary functions of the cardiovascular system?
2. Define the following terms: arteries, arterioles, capillaries, veins, venules, hemoglobin, epicardium, myocardium, endocardium, and pericardium.
3. Trace the pathway of blood flow through the body, starting with blood returning in the venules.
4. What are the two phases of the cardiac cycle? Describe which valves are open and closed during each phase.
5. Trace the cardiac conduction system from the SA node to the Purkinje fibers. Where is the SA node located? What is the term for the heart's ability to generate its own electrical signal?
6. How do the chordae tendineae prevent backflow of blood into the atria?
7. Identify the major components of the ECG. What occurs during each wave?
8. What is the range for normal sinus rhythm? Define sinus bradycardia and sinus tachycardia.
9. Which part of the nervous system plays the largest role in decreasing resting heart rate (RHR)?
10. What is a normal stroke volume in milliliters?
11. Define the following terms: end-diastolic volume, end-systolic volume, stroke volume, cardiac

output, contractility, systolic blood pressure, diastolic blood pressure, and ejection fraction.

12. What are the unique metabolic needs of red blood cells? Why is this important for oxygen transportation?
13. Describe the heart rate response to exercise. Is there an anticipatory response, and what causes it?
14. Which is better for predicting exercise intensity, heart rate or VO2? Explain why.
15. Discuss the factors that affect stroke volume.
16. How is blood redirected during exercise?
17. List some cardiovascular adaptations that occur with endurance training.
18. How does exercise affect blood pressure?
19. What is the arterial-(mixed) venous O2 difference? What does it represent?
20. What is the Fick equation?
21. What causes the heart sounds?
22. Which valves are open or closed when pressure in the ventricles is greatest?

10.

THE RESPIRATORY SYSTEM



The major components of the respiratory system and a magnified view of the alveoli and its associated capillary beds.

Learning Objectives

- Explain the interdependence of the pulmonary and cardiovascular systems.
- Identify the four processes involved in the transportation of oxygen and carbon dioxide in the body.

- Define pulmonary ventilation and pulmonary diffusion and the processes of external and internal respiration.
- Identify the major organs of the respiratory system and their locations.
- Outline the pathway of environmental air from the nose to the alveoli.
- Explain the roles of the conducting and respiratory zones.
- Explain the principles of Boyle's Law and Fick's Law of diffusion as they apply to respiration.
- Identify Factors Affecting Oxygen and Carbon Dioxide Transport.
- Explain the Bohr and Haldane effects.
- Define and measure tidal volume, vital capacity, residual volume, and total lung capacity.
- Describe the changes in ventilation during incremental exercise and the concept of the ventilatory threshold.
- Explain the effects of exercise in hot environments on ventilation.
- Discuss the neural and chemoreceptor control of ventilation during and after exercise.

Introduction

The pulmonary and cardiovascular systems work in tandem to form an efficient delivery mechanism that transports oxygen to tissues and removes carbon dioxide. Due to their close interdependence, these systems are often collectively referred to as the cardiopulmonary system. The transportation of oxygen and carbon dioxide within the body encompasses four distinct processes:

1. Pulmonary Ventilation
2. Pulmonary Diffusion
3. Transportation via the Blood
4. Capillary Diffusion

Pulmonary ventilation, commonly known as breathing, involves the movement of air into and out of the lungs. During **pulmonary diffusion**, the exchange of oxygen and carbon dioxide occurs between the lungs and the blood. This process replenishes the blood's oxygen supply, which is depleted at the tissue level for oxidative energy production, and removes carbon dioxide from the systemic venous blood. In the lungs, oxygen is loaded into the blood while carbon dioxide is unloaded and exhaled. Both pulmonary ventilation and pulmonary diffusion are forms of **external respiration**, which refers to gas exchange occurring in the alveoli and capillary beds of the lungs[1]. Following pulmonary diffusion, gases are transported by the blood to various tissues. Upon reaching the tissues, gases diffuse through the capillaries into the tissues. This gas

exchange process at the tissue level is known as **internal respiration** or cellular respiration. The circulatory system links both internal and external respiration, highlighting the integral role of the pulmonary system in gas exchange.

Understanding lung function is crucial due to its significant role in this process. This chapter will explore the design and components of respiration and describe the ventilatory responses to exercise.

Anatomy of the Respiratory System

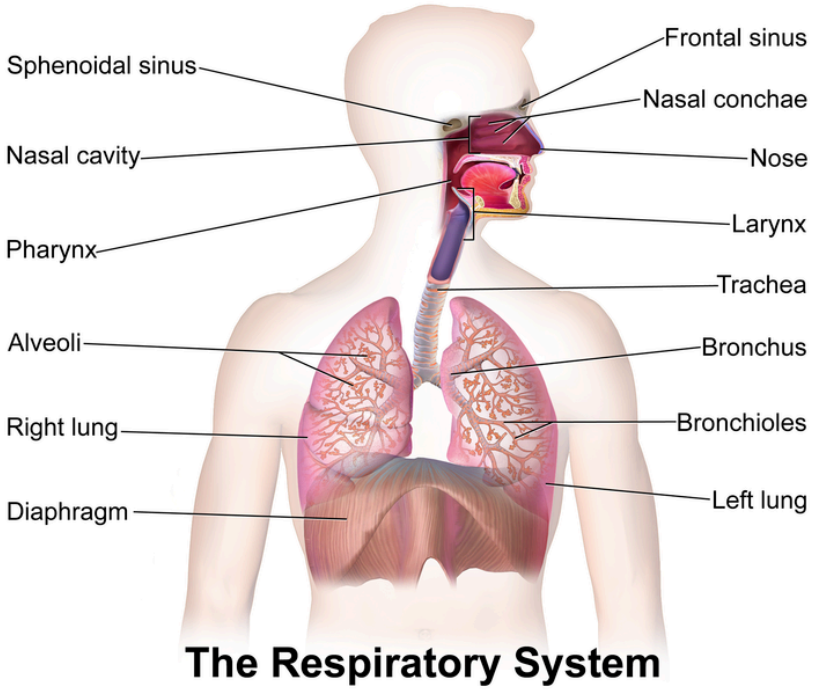


Figure 10.1 The major organs of the respiratory system.

The lungs consist of a network of respiratory passages that facilitate the close association of lung capillaries with environmental air. This proximity enables the efficient exchange of oxygen and carbon dioxide with the atmosphere. The primary organs of the respiratory system are illustrated in Figure 10.1.

Located in the thoracic cavity, the lungs flank the heart laterally and are the main organs of the respiratory system. They are not directly attached to the ribs but are suspended by connective tissue sacs known as pleural sacs. The **pleura** is a slick, sticky, semi-transparent serous membrane that provides lubrication for the movable lungs and heart (Figure 10.2). The pleurae produce a watery fluid called pleural fluid. The pleurae

1. Kenney WL, Wilmore JH, Costil DL, ed. Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

serve three main purposes:

1. Reducing Friction: Since the heart, lungs, and diaphragm are in constant motion, the pleurae minimize friction between the ribs and these organs.
2. Creating a Pressure Gradient: The pressure within the pleurae is lower than atmospheric pressure, creating a pressure gradient essential for gas exchange (to be discussed later in the chapter).
3. Compartmentalization: The pleurae separate the abdominal cavity from the thoracic cavity, compartmentalizing the heart and lungs and preventing infections from spreading from other organs to the thoracic cavity.

When the pleurae do not function correctly, it can result in painful and difficult breathing.

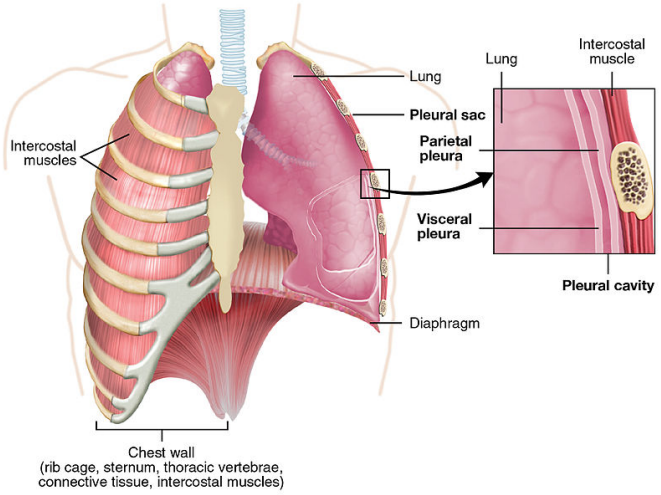


Figure 10.2 The anatomy of the lungs, the pleural sack.

Figure 10.2 illustrates the three components of the pleurae. The most superficial layer is the **parietal pleurae**, which covers the diaphragm and attaches to the internal walls of the thoracic cavity. Beneath the parietal pleurae lies the **pleural cavity**, containing serous fluid. Each thorax holds approximately 16 ml of serous fluid, which drains from the chest via the lymphatic vessels. This fluid lubricates the moving parts within the chest. The deepest layer is the **visceral pleurae**, which attaches directly to the lungs. Together, the pleurae connect the surfaces of the lungs and ribs, preventing lung collapse when the ribs expand.

The lung tissue, or **spongy parenchyma**, contains the bronchial tree and allows for the elastic recoil of the lungs after expansion during inspiration. This tissue includes a significant proportion of elastic fibers, which aid in this recoil.

The Pathway of Environmental Air into the Body

Environmental air enters the body through the nose and nasal cavity. As the air travels through the body, it is warmed, cleansed, and humidified by swirling through the irregular sinus surfaces, causing dust and other particles to adhere to the nasal mucosa. This process filters out most particles that could infect the respiratory tract. From the nasal cavity, air moves down a series of rigid pathways commonly known as the “windpipe,” which includes the pharynx, larynx, and trachea. These structures are lined with cartilage, providing an open airway for the passage of gases.

Air travels from the trachea into the left and right lungs, entering the **bronchial tree**. The bronchial tree consists of progressively smaller airways, culminating in approximately 65,000 terminal bronchioles. The primary bronchus is the largest airway, which then branches into secondary bronchioles. These secondary bronchioles further divide into tertiary bronchi and smaller bronchioles. These structures form the conducting zone of the lungs, responsible for directing air towards the **respiratory zone** (Figure 10.3). It is important to note that gas exchange does not occur in the **conducting zone**; its primary function is to maintain an open pathway for air to reach the respiratory zone.

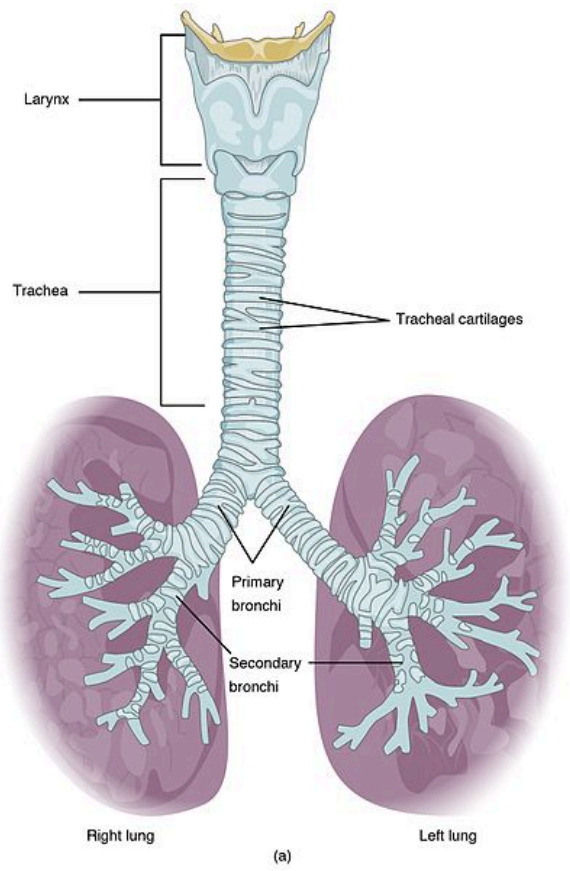


Figure 10.3 The conducting zone is composed of the trachea, bronchial tree, and bronchioles.

From the bronchioles, air moves into the terminal bronchioles (also known as respiratory bronchioles), which have scattered alveoli in their walls. Unlike the windpipe, terminal bronchioles are lined with smooth muscle, allowing the airways to dilate or constrict. The ends of the terminal bronchioles consist of "sacs" of **alveoli** that line the alveolar ducts. These alveolar sacs are surrounded by capillary networks, facilitating the oxygenation of blood and the release of carbon dioxide into the lungs as waste. Together, the terminal bronchioles and alveolar sacs constitute the respiratory zone (Figure 10.4). The respiratory zone is where gas exchange between air and blood occurs, and where external respiration takes place.

Gas exchange in the lungs occurs across approximately 300 million alveoli. Due to their vast number, these tiny alveoli provide the lungs with a large surface area for diffusion. Each alveolus is only one cell thick, which enhances the diffusion of gases at the respiratory membrane. According to Fick's law of diffusion, the rate of gas diffusion across tissues is inversely proportional to the tissue thickness.

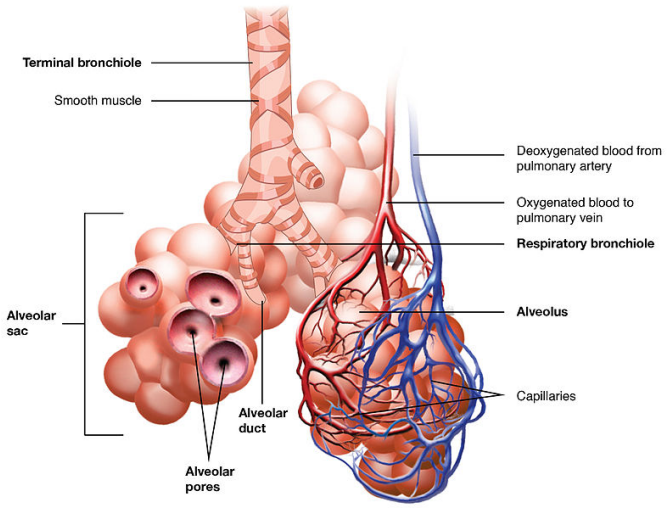


Figure 10.4 The respiratory zone is comprised of the terminal bronchioles and the alveolar sacs.

Alveolar macrophages, also known as "dust cells," play a crucial role in eliminating bacteria, dust, pollen, and pollutants that reach the respiratory zone. The air in the alveoli is humidified before arrival, which creates a challenge for the lungs. The surface tension of the liquid in the air is relatively high, posing a risk of alveolar collapse.

To counteract this, **type II alveolar cells** produce a substance called **pulmonary surfactant**. Surfactant reduces the surface tension of water in the alveoli, preventing their collapse due to the attractive forces of water[2]. Figure 10.5 illustrates the relationship between the different types of cells that make up an alveolus.

Alveoli contain specialized cells that facilitate their function. The cells lining the alveoli are known as simple **squamous cells**, which also form the **respiratory membrane** between the pulmonary capillaries. The respiratory membrane, measuring 0.5 micrometers in diameter, consists of two basement membranes sandwiched between a simple squamous cell lining the alveolus and a simple squamous cell lining the capillary wall. This membrane is only two cells thick, making it very fragile and susceptible to damage from smoking, pollution, and disease.

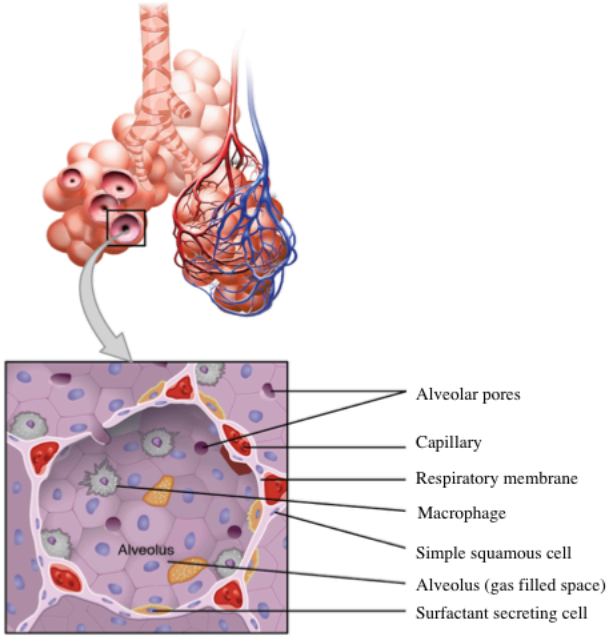


Figure 10.5 The enlarged view of an alveolus showing its components and the regions of gas exchange between the alveolus and the pulmonary blood in the capillaries.

The Respiratory Muscles

Respiratory muscles are skeletal muscles that act upon the chest wall to facilitate the movement of gas in and out of the lungs. During resting ventilation,

2. Powers SK, and Howley ET, Exercise Physiology (Theory and Application to Fitness and Performance). 9th Edition ed. 2015, New York, NY: McGraw-Hill.

the **diaphragm** and **external intercostal muscles** drive the volume changes in the thoracic cavity essential for breathing.

The external intercostal muscles are the most superficial layer of muscles located between the ribs. When they contract, they assist in lifting the rib cage away from the abdomen. Unfortunately, spinal cord injuries that damage the phrenic nerve can result in the inability to operate the diaphragm, leading to an inability to ventilate.

The diaphragm is the most important muscle for ventilation and is the only skeletal muscle considered essential for life. It is a concave-shaped muscle located beneath the lungs and attached to the ribs (Figure 10.6). When the diaphragm contracts, it moves downward, forcing the abdominal contents downward and forward.

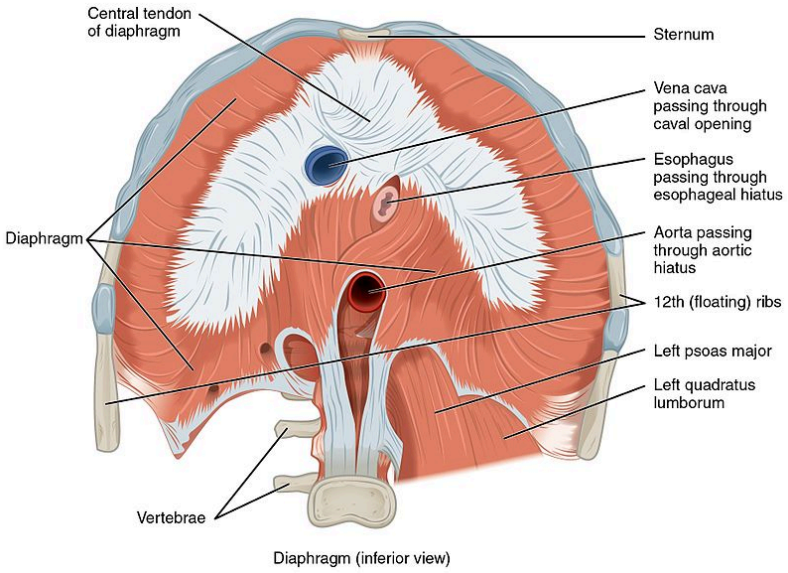


Figure 10.6 The inferior view of the diaphragm and associated anatomical features.

During resting ventilation, the external intercostal muscles and the diaphragm are the primary muscles involved in breathing. However, during exercise, ventilation increases to meet the muscles' oxygen demands and to expel carbon dioxide. This results in an increase in pulmonary ventilation, placing a greater workload on the respiratory muscles.

During exercise and deep breathing, accessory muscles also contribute to the intake and expulsion of air. The muscles involved in deep inspiration include the **scalene muscles**, **pectoralis minor**, and the **sternocleidomastoid**, in addition to the diaphragm and external intercostal muscles [2]. These muscles assist the diaphragm in increasing the volume of the chest, thereby aiding in inspiration (see pulmonary ventilation).

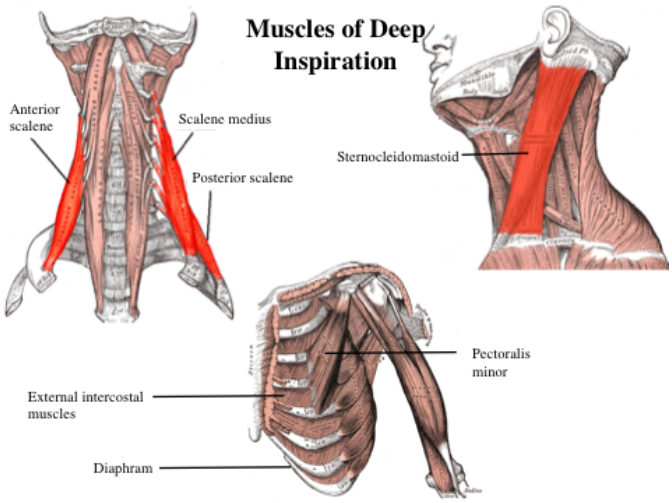


Figure 10.7 The muscles of deep inspiration.

Typically, expiration is a passive process that does not require ATP. However, during deep expiration and expiration associated with exercise, accessory muscles are engaged, making it an active process. The muscles involved in deep expiration are those of the abdominal wall, including the **internal intercostal muscles**, **external oblique**, **internal oblique**, and **transverse abdominis** (Figure 10.8). When these muscles contract, they push the diaphragm upward and pull the ribs downward and inward. This action decreases the dimensions of the thoracic cavity, aiding in the expulsion of air.

Ventilation Physiology

The movement of air from the environment into the lungs is known as pulmonary ventilation and occurs due to changes in pressure and volume. Resting inhalation is an active process that requires ATP, as it involves the contraction of the diaphragm and external intercostal muscles. Conversely, resting exhalation is a passive process that does not require ATP, as it involves the relaxation of these muscles.

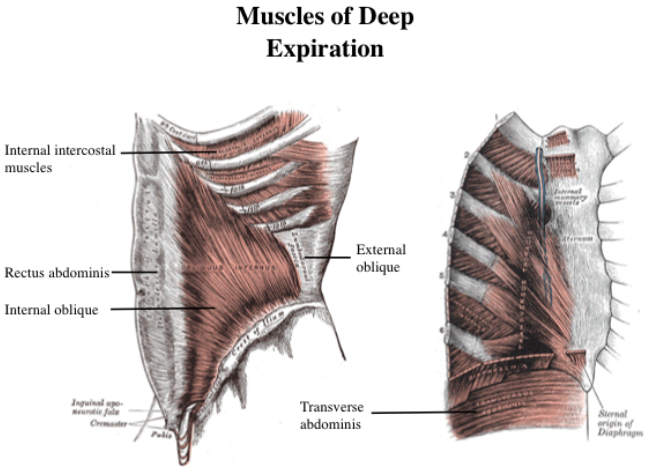


Figure 10.8 The muscles of deep expiration.

To understand the mechanics of ventilation, it is essential to grasp **Boyle's Law**. Boyle's Law states that the absolute pressure exerted by a given mass of an ideal gas is inversely proportional to the volume it occupies, provided the temperature and the amount of gas remain constant within a closed system (i.e., ($P_1V_1 = P_2V_2$))[3].

Figure 10.9 illustrates Boyle's Law using containers of specific volumes and a precise number of particles. In a larger container with a fixed number of particles, the pressure exerted by the particles is relatively low due to their interactions with each other and the container. When the volume of the container decreases while maintaining the same number of particles, the pressure exerted by the particles on themselves and the container increases. Thus, pressure and volume are inversely related.

3. Levine IN, Physical Chemistry. 1978, Boston, MA: McGraw Hill.

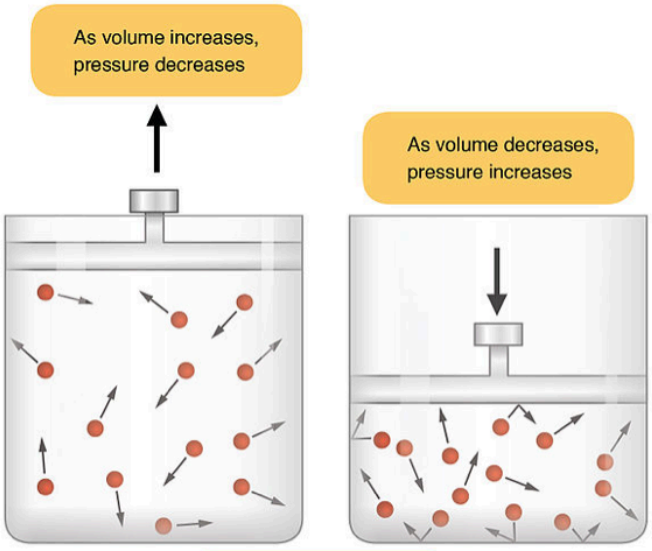


Figure 10.9 Containers of particles that demonstrate Boyle's law by showing the inverse relationship between pressure and volume.

Simple diffusion refers to the process by which gases, such as carbon dioxide and oxygen, pass through a membrane without the assistance of intermediary molecules like integral membrane proteins. The driving force behind this movement is the force of diffusion. In terms of gas pressures, this means that gases will diffuse from an area of higher pressure to an area of lower pressure until the pressures on both sides of the membrane are equal, a state known as equilibrium.

Therefore, based on the principles of simple diffusion, a **pressure gradient** (i.e., the difference in pressures across a membrane) is essential for gas exchange to occur.

By applying the principles of Boyle's Law and simple diffusion to the lungs, the mechanisms of ventilation can be understood (Figure 10.10). During resting inhalation, the diaphragm contracts and moves downward, enlarging the volume of the thoracic cavity. The external intercostal muscles also contribute to this enlargement. This increase in cavity volume reduces intrapulmonary pressure below the environmental air pressure, creating a suction force that draws air into the lungs to equalize the pressure difference.

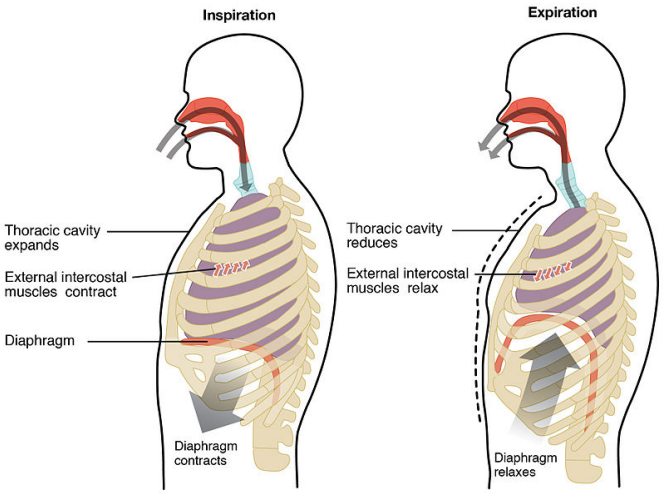


Figure 10.10 The physiological mechanisms of inspiration and expiration.

Expiration occurs in the opposite manner. During expiration, the diaphragm and external intercostal muscles relax, decreasing the volume of the thoracic cavity and increasing intrapulmonary pressure. This makes the pressure inside the lungs greater than the environmental pressure, resulting in the expulsion of air from the lungs.

During forced or labored breathing, such as during heavy exercise, inspiration and expiration are assisted by accessory muscles (see respiratory muscles). The pressure changes required for ventilation at rest are relatively small. The standard atmospheric pressure at sea level is 760 mmHg. Inspiration may decrease the pressure in the lungs by 2 to 3 mmHg. However, during exhaustive exercise, intrapulmonary pressure can decrease by up to 100 mmHg[4].

Partial Pressures of Physiological Gases

Before discussing the diffusion of gases across membranes in the body, it is essential to understand the concept of **partial pressures**. Atmospheric air is a mixture of oxygen, carbon dioxide, nitrogen, and trace amounts of other gases. Each gas exerts its own pressure, known as the partial pressure (P). According to **Dalton's Law**, the total pressure of a mixture of gases is equal to the sum of the partial pressures of the individual gases.

This concept is illustrated in Figure 10.11, where the total pressure of two gases in the same container can be calculated by adding their partial pressures. For example, if the partial pressure of oxygen is 159 mmHg and the partial pressure of nitrogen is 593 mmHg, the total pressure of the gas mixture is 752 mmHg (i.e., 593 mmHg + 159 mmHg = 752 mmHg).

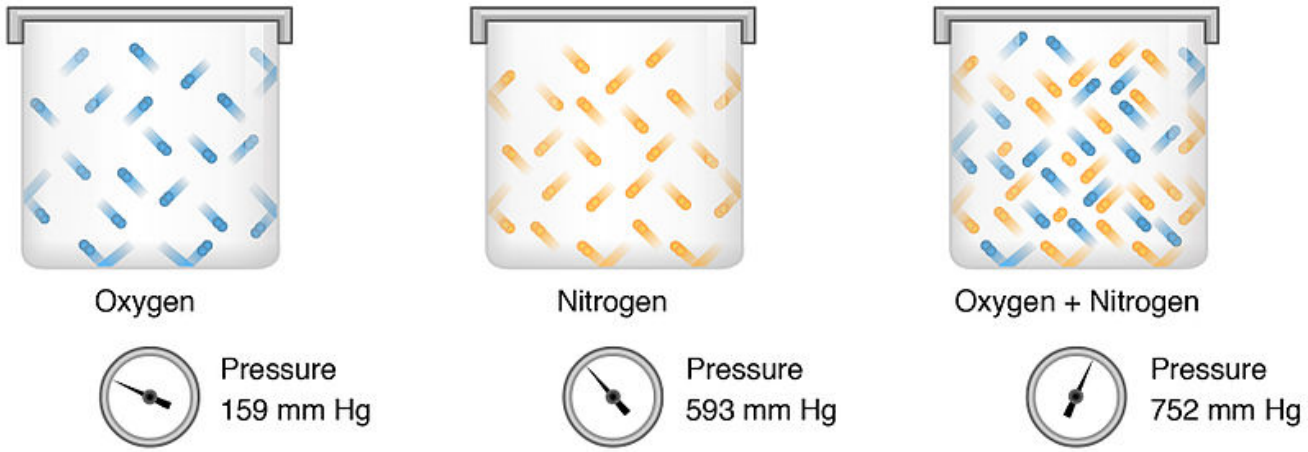


Figure 10.11 Three containers of oxygen, nitrogen, and mixed gas particles and their additive pressures demonstrating partial pressures, total pressure, and Dalton's law.

The partial pressure of a gas is proportional to its concentration. Atmospheric air is generally composed of 20.93% oxygen, 79.04% nitrogen, and 0.03% carbon dioxide, totaling 100%. To determine the partial pressures of each gas, it is necessary to know the barometric pressure (P_B), which is the force exerted by the weight of the gas in the atmosphere. At sea level, the barometric pressure is typically 760 mmHg.

For example, to calculate the partial pressure of oxygen (PO_2) in air at sea level, first determine the fraction of air composed of oxygen. Since oxygen makes up 20.93% of the air, the fraction is 0.2093 (20.93/100). The partial pressure of oxygen at sea level can then be computed as:

$$PO_2 = 760 \text{ mmHg} \times 0.2093$$

$$PO_2 = 159 \text{ mmHg}$$

4. Kenney WL, Wilmore JH, Costil DL, ed. Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

Fick's Law of Diffusion

Another important concept in the diffusion of gases in the body is Fick's Law of Diffusion. **Fick's Law of Diffusion** states that the rate of gas transfer (V) is proportional to the tissue area (A), the diffusion coefficient of the gas (D), and the difference in the partial pressure of the gas on the two sides of the tissue ($P_1 - P_2$), and is inversely proportional to the membrane thickness (T):

$$V_{gas} = (A/T) \times D \times (P_1 - P_2)$$

Therefore, a pressure gradient is necessary to move gases from one part of the body to another. A pressure gradient is the difference in partial pressures on opposite sides of a membrane. The lung is well-designed for the diffusion of gases across the alveolar membrane, with an estimated surface area of 60 to 80 square meters (approximately the size of a tennis court). Additionally, the alveolar membrane is extremely thin. Together, these features make the lung an ideal organ for gas exchange. This is crucial because gas exchange throughout the body depends on the factors of diffusion, primarily driven by pressure gradients.

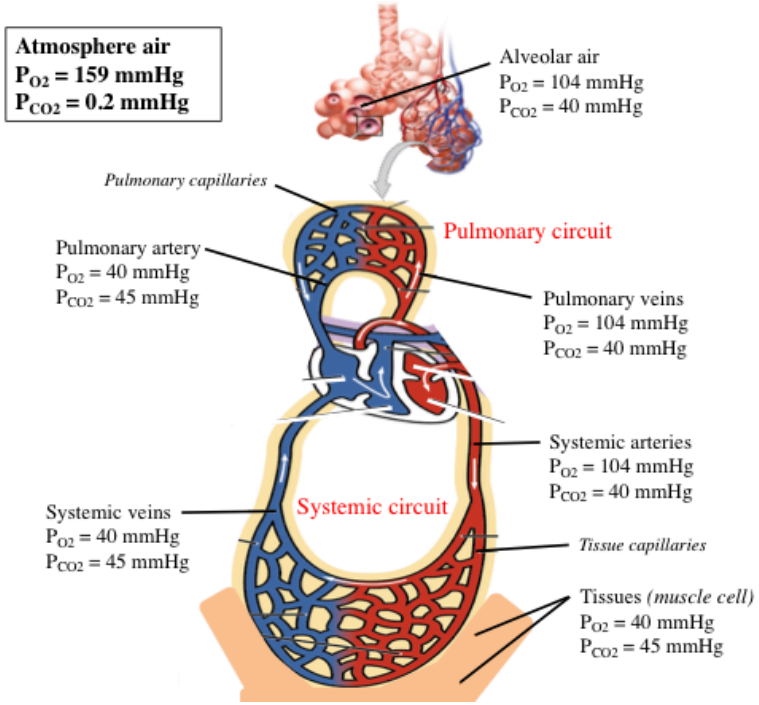


Figure 10.12 Partial pressure changes of the atmosphere air, alveolar air, pulmonary circuit, and systemic circuit.

Figure 10.12 illustrates gas exchange via diffusion across the alveolar-capillary membrane and at the capillary-tissue membranes. The partial pressure of carbon dioxide (PCO_2) and the partial pressure of oxygen (PO_2) in the alveolar capillaries are 40 mmHg and 104 mmHg, respectively. In contrast, the PCO_2 in the atmosphere is 0.2 mmHg, and the PO_2 is 159 mmHg. This creates a PO_2 difference of 55 mmHg in the alveoli and a PCO_2 difference of 39.8 mmHg in the atmosphere. Consequently, due to the pressure gradient,

carbon dioxide leaves the alveoli and diffuses into the alveolus, while oxygen diffuses into the alveoli.

Oxygen Transport

Hemoglobin, a protein in red blood cells, transports oxygen. When bound to oxygen, it is called oxyhemoglobin; when not bound to oxygen, it is referred to as deoxyhemoglobin. The loading and unloading of hemoglobin are reversible reactions:

$$\text{Deoxyhemoglobin} + O2 \Leftrightarrow \text{Oxyhemoglobin}$$

Approximately 98% of oxygen in the blood is transported as oxyhemoglobin, while the remaining 2% is dissolved in the plasma, as oxygen is a poor solute. Oxygen unloading from hemoglobin is determined by the partial pressures of the tissues and other factors.

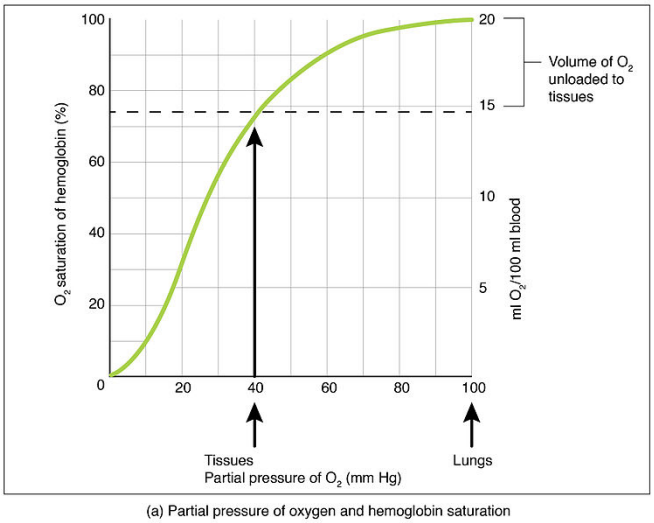
Each hemoglobin molecule can bind four oxygen molecules, and the amount of oxygen transported per volume of blood depends on the concentration of hemoglobin. In healthy males, the concentration of hemoglobin is approximately 150 grams per liter of blood, and in females, it is about 130 grams per liter[5]. When fully saturated, each gram of hemoglobin can transport 1.34 ml of oxygen. Therefore, at 100% saturation, a healthy adult can transport between 174-200 ml of oxygen per liter of blood.

The oxygen-hemoglobin (O_2-Hb) dissociation curve, shown in Figure 10.13, demonstrates the relationship between oxygen and hemoglobin binding. The O_2-Hb dissociation curve is sigmoidal (S-shaped) and describes the amount of oxygen unloaded at the tissues. The percent hemoglobin saturated with oxygen increases sharply up to an arterial PO_2 of 40 mmHg. At PO_2 values above 40 mmHg, hemoglobin saturation rises slowly to a plateau around 90-100 mmHg, where hemoglobin is approximately 98% saturated.

At rest, the body's oxygen requirements are relatively low, and only about 25% of oxygen is unloaded at the tissues, as shown in Figure 10.13 when the PO_2 at the tissues is 40 mmHg. However, during strenuous exercise, the muscles' demand for oxygen increases, which can drop the PO_2 in the tissues to 20 mmHg. In such cases, the muscles and peripheral tissues can extract up to 90% of the oxygen bound to hemoglobin.

5. Levitsky M, Pulmonary Physiology. 2007, New York, NY: McGraw Hill.

Several factors influence both blood PO_2 and the unloading of oxygen at the tissues. Changes in acidity, increases in PO_2, temperature, and levels of 2-3-diphosphoglyceric acid (2,3-DPG) all enhance oxygen unloading (i.e., oxygen dissociation from hemoglobin) at the tissues. This is particularly important during exercise, as efficient oxygen unloading is crucial for the continued production of ATP.



(a) Partial pressure of oxygen and hemoglobin saturation

Figure 10.13 The oxyhemoglobin dissociation curve.

The bond strength between oxygen and hemoglobin is weakened by a decrease in blood pH, leading to increased oxygen unloading to the tissues. This phenomenon is represented by a "rightward" shift in the oxyhemoglobin dissociation curve and is known as the **Bohr effect** (Figure 10.14). During heavy exercise, the rise in blood hydrogen ion levels contributes to this effect. Physiologically, hydrogen ions in the blood compete for binding sites on hemoglobin, reducing its oxygen transport capacity. High concentrations of hydrogen ions (e.g., during acidosis) cause a reduction in hemoglobin's affinity for oxygen.

An increase in core temperature also causes a rightward shift in the curve, as this condition weakens the bond between oxygen and hemoglobin. Conversely, a decrease in blood temperature results in a stronger bond, hindering oxygen release at the tissues. As shown by the resting curve (green line) in Figure 10.14, the curve can shift to the left or right depending on these factors.

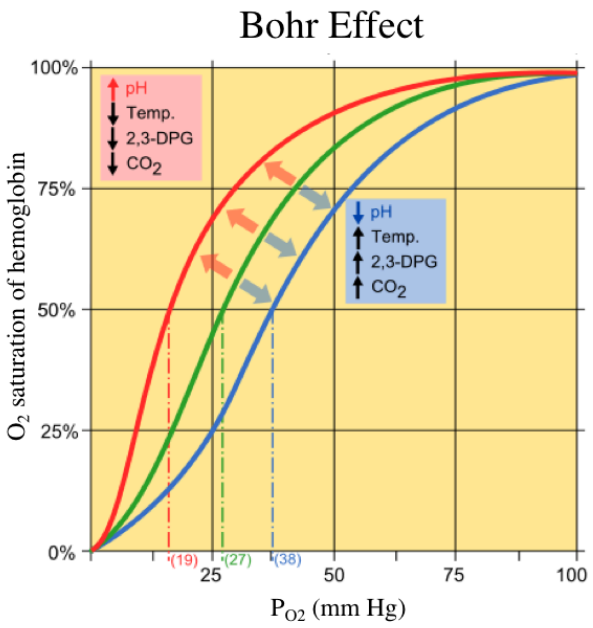


Figure 10.14 The Bohr effect and factors that affect the oxygen hemoglobin disassociation curve.

Carbon dioxide in the blood can displace oxygen from hemoglobin by binding with the amine radicals of the hemoglobin molecule. This increase in blood PCO2 contributes to the Bohr effect, which enhances oxygen unloading at the tissues. Conversely, the binding of oxygen to hemoglobin tends to displace carbon dioxide from the blood, known as the **Haldane effect**. This occurs because the combination of oxygen with hemoglobin in the lungs makes hemoglobin a stronger acid, which displaces carbon dioxide from the blood. As a result, the increased acidity of hemoglobin causes excess hydrogen ions transported by red blood cells to be released in the lungs. These hydrogen ions bind with bicarbonate to form carbonic acid, which then dissociates into water and carbon dioxide. The carbon dioxide is subsequently released from the blood into the alveoli and finally exhaled[6]. Thus, oxygen loading in the lungs facilitates carbon dioxide unloading.

Another factor affecting the hemoglobin dissociation curve is 2,3-diphosphoglycerate (2,3-DPG), a byproduct of glycolysis. Red blood cells rely exclusively on glycolysis for energy production, leading to the creation of 2,3-DPG when they are metabolically active. 2,3-DPG binds with hemoglobin and reduces its affinity for oxygen. The production of 2,3-DPG increases with exposure to anemia and high altitudes, due to the reliance on glycolysis under lower PO2 conditions.

When oxygen is delivered to muscles, **myoglobin**, another oxygen-binding protein, shuttles oxygen from the muscle cell membrane to the mitochondria. Myoglobin is one-fourth the weight of hemoglobin and has a higher affinity for oxygen, even at lower PO_2. Myoglobin releases its oxygen only at very low PO_2, compatible with the PO_2 of exercising muscle, which can be as low as 1 to 2 mmHg[7]. Type I muscle fibers have a higher concentration of myoglobin than Type II fibers. Myoglobin may serve as an "O_2 reservoir" for muscles during the transition from rest to exercise. It is thought that at the end of exercise, myoglobin oxygen stores are replenished, contributing to the oxygen debt (EPOC).

6. Guyton AC, and Hall JE, Textbook of Medical Physiology. 11th ed. 2006, Philadelphia, PA: Elsevier Saunders.

7. Kenney WL, Wilmore JH, Costil DL, ed. Physiology of Sport and Exercise. 5th ed. 2012, Human Kinetics: Champaign, IL.

Carbon Dioxide Transport

Carbon dioxide, produced by tissues during cellular respiration, diffuses out of cells in its dissolved molecular form. Upon entering the tissue capillaries, carbon dioxide undergoes instantaneous physical and chemical reactions for transport. Carbon dioxide is transported in the blood in three forms:

1. Approximately 10% is dissolved in the plasma.
2. 20% is bound to hemoglobin (forming carbaminohemoglobin).
3. 70% is transported as bicarbonate ion (HCO^{3-}).

Most of these processes occur within red blood cells (Figure 10.15). Carbon dioxide can be transported in far greater quantities than oxygen, significantly influencing the acid-base balance of body fluids. Under resting conditions, an average of 4 ml of carbon dioxide is transported from the tissues to the lungs per 100 ml of blood[8]. The majority of carbon dioxide produced by active muscles is transported back to the lungs as bicarbonate ion.

A high PCO_2 in the blood causes carbon dioxide to combine with water to form carbonic acid. This reaction would occur too slowly without the enzyme carbonic anhydrase inside red blood cells, which catalyzes the reaction and accelerates its rate approximately 5,000 times. Carbonic acid (H_2CO_3) quickly dissociates into bicarbonate ion (HCO^{3-}) and a hydrogen ion (H^+). The hydrogen ion binds to hemoglobin in red blood cells, as hemoglobin is a powerful acid-base buffer. The bicarbonate ion then diffuses into the plasma, where it is transported. Chloride ions diffuse into red cells to replace the bicarbonate, a phenomenon known as the chloride shift. This results in a higher chloride content in venous red blood cells compared to arterial red cells.

8. Guyton AC, and Hall JE, Textbook of Medical Physiology. 11th ed. 2006, Philadelphia, PA: Elsevier Saunders.

In addition to reacting with water, some carbon dioxide reacts directly with the hemoglobin molecule to form carbaminohemoglobin (CO_2Hgb). This reaction is reversible, allowing carbon dioxide to be easily released into the alveoli where PCO_2 is lower than in the pulmonary capillaries. However, this reaction is much slower than the reaction between carbon dioxide and water, so under normal conditions, the carbamino-mechanism of transport accounts for no more than 20% of the total carbon dioxide transported[9].

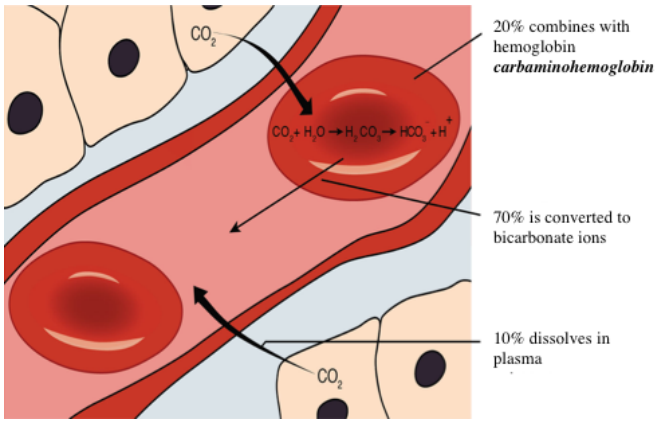


Figure 10.15 Summary of carbon dioxide transport in the blood from the tissues.

At the lungs, the PCO_2 of the blood is greater than that in the alveolus, causing carbon dioxide to diffuse out of the blood across the membrane. When the blood reaches the pulmonary capillaries, carbonic acid dissociates into carbon dioxide and water, with the carbon dioxide being exhaled.

Pulmonary Volumes and Capacities

The volume of air in the lungs can be measured using a technique called **spirometry**. In this method, the subject breathes into a device capable of measuring both inspired and expired gas volumes. Spirometry assesses the rate of expired airflow and lung capacity, making it a valuable tool for diagnosing lung diseases such as chronic obstructive pulmonary disease (COPD) and asthma.

A modern spirometer, shown in Figure 10.16, includes a mouthpiece similar to the one used in indirect calorimetry. Several measures of pulmonary function can be obtained through spirometry, including the **total lung capacity** and **tidal volume** of an individual.

9. Guyton AC, and Hall JE, Textbook of Medical Physiology. 11th ed. 2006, Philadelphia, PA: Elsevier Saunders.

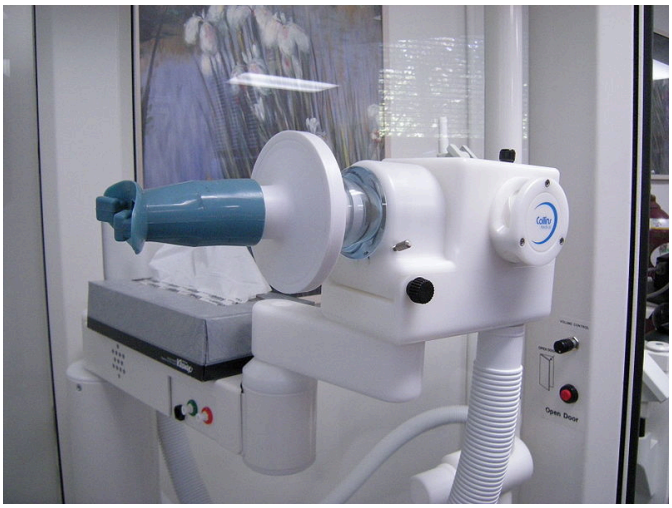


Figure 10.16 Device into which a patient breathes for Spirometry, Body Plethysmography and other related medical tests. Photographed at Swedish Hospital Ballard Campus, Seattle, Washington.

The volume of air that enters and leaves the lungs during normal, resting conditions with each breath is called the tidal volume (VT) . Tidal volume typically displaces about 500 ml of air between inhalation and exhalation. **Pulmonary ventilation (VE)** refers to the volume of air moved in or out of the lungs per minute. It is the product of tidal volume (VT) and **breathing frequency (f)**. Mathematically, ventilation can be expressed as:

$$VE = VT \times f$$

This equation helps quantify the amount of air exchanged in the lungs over a given period, providing valuable insights into respiratory function.

Figure 10.17 graphically illustrates the measurement of tidal volumes during normal quiet breathing and the various lung volumes and capacities. The **vital capacity (VC)** is the greatest amount of air that can be expired following a maximal inspiration, typically about 4,700 ml. Even after a maximal voluntary expiration, a small volume of air remains in the lungs, known as the **residual volume (RV)**, which is about 1,300 ml and cannot be voluntarily exhaled. The sum of the residual volume and the vital capacity constitutes the total lung capacity (TLC), which is approximately 6 liters in healthy individuals:

$$TLC = RV + VC$$

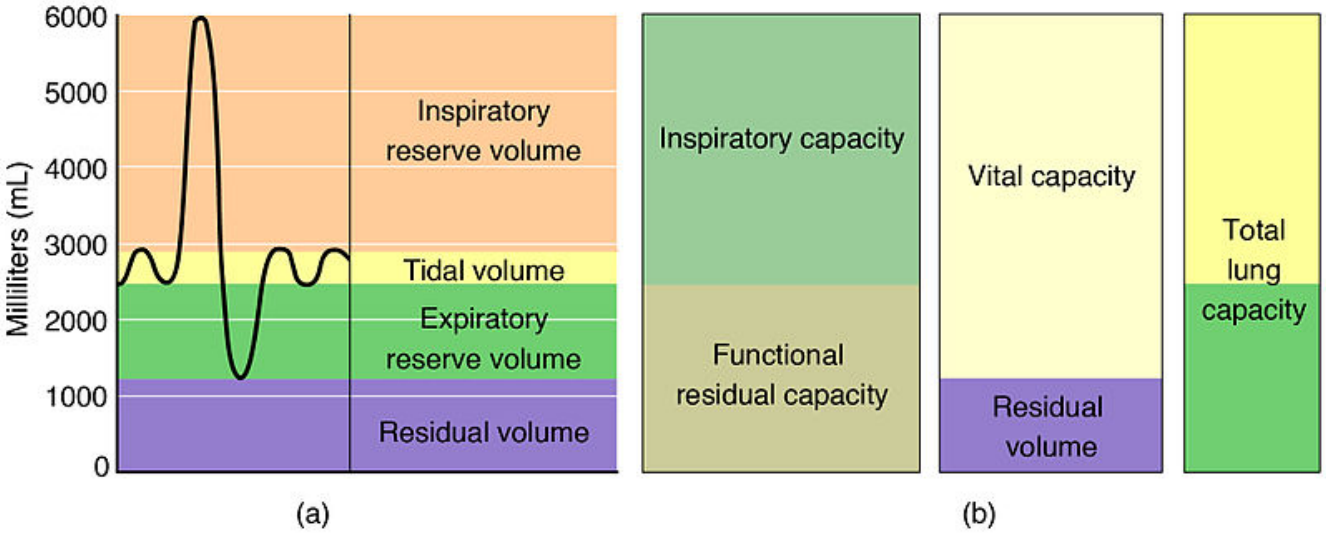


Figure 10.17 Lung volumes at rest measured by spirometry (a). Inspiratory capacity, functional capacity vital capacity, residual volume, and total lung capacity are shown (b).

Pulmonary Ventilation During Dynamic Exercise

The onset of exercise is accompanied by an increase in ventilation. Initially, ventilation increases rapidly and then rises more slowly towards a steady state, even without an initial increase in arterial PCO_2. The initial rise in ventilation is controlled by the nervous system and mediated by respiratory control centers in the brain. The more gradual rise towards steady-state exercise is controlled by changes in the chemical status of the arterial blood. Increased metabolism in skeletal muscles raises blood PCO_2. Increases in PCO_2 and hydrogen ions are sensed by chemoreceptors in the brain, carotid bodies, and lungs, which stimulate the inspiratory center to increase the frequency and depth of respiration. Similar to heart rate, there may also be an anticipatory effect where ventilation rises before exercise commences.

During strenuous exercise, oxygen consumption and carbon dioxide formation can increase up to 20-fold[10]. Maximal ventilation rates of approximately 100 L/min are common for smaller individuals but may exceed 200 L/min in larger individuals [1]. During mild, steady-state exercise, ventilation increases to match the rate of energy expenditure. The ratio of air ventilated to oxygen consumed in a given time is the ventilatory equivalent for oxygen (VE/VO_2). At rest, this ratio ranges from 23-28 L of air per liter of oxygen. This value changes very little during low-intensity exercise, such as walking. However, at near-maximal exercise intensities, the ventilatory equivalent for oxygen can exceed 30 L of air per liter of oxygen. Generally, the ventilatory equivalent for oxygen remains relatively constant, indicating that the control of breathing is properly matched to the muscles' demand for oxygen.

Ventilation must also match cardiac output for optimal blood perfusion, known as the **ventilation-perfusion relationship (V/Q)**:

$$VE(L/min) = \text{blood flow (Q, perfusion)}$$

Where (Q) is blood flow, or perfusion. The ideal ventilation-perfusion ratio is 1.0, indicating a perfect match between ventilation and cardiac output. However, gas exchange is not always perfect in the exercising lung[11]. Light-to-moderate exercise intensities improve ventilation-perfusion matching. During heavy exercise, small ventilation-perfusion inequalities may occur because red blood cells do not have enough transit time in the lung capillaries due to high heart rates. This can impair gas exchange and cause a condition known as exercise-induced hypoxemia.

10. Guyton AC, and Hall JE, Textbook of Medical Physiology. 11th ed. 2006, Philadelphia, PA: Elsevier Saunders.

11. Dempsey JA, Wagner PD, Exercise-induced arterial hypoxemia. Journal of Applied Physiology, 1999. 87(6): p. 1997-2006.

During incremental exercise with increasing speeds, ventilation increases linearly up to 50-70% of VO_{2max}. Beyond this point, there is a disproportionate increase in ventilation, known as the **ventilatory threshold**, illustrated in Figure 10.18. The ventilatory threshold reflects the respiratory response to increased carbon dioxide levels, causing a dramatic rise in ventilation. In trained runners, the ventilatory threshold occurs at a higher work rate. Trained individuals can also maintain their pH and have lower lactate levels at higher work rates compared to untrained individuals[12].

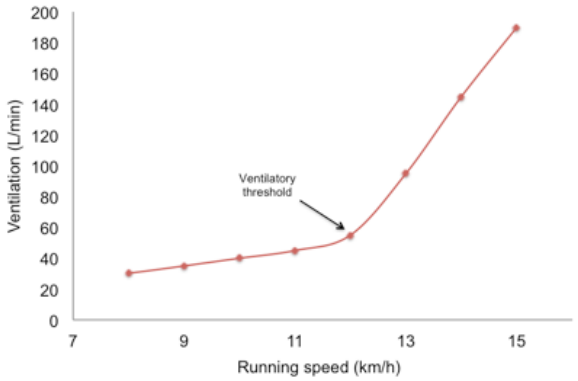


Figure 10.18 Changes in pulmonary ventilation during running at increasing speeds, illustrating the concept of the ventilatory threshold. Ventilatory threshold (Tvent) is the inflection point where ventilation increases exponentially.

Ventilation in Hot Environments

Exercise in a hot environment makes it challenging to maintain steady-state ventilation. During prolonged sub-maximal exercise in the heat, ventilation may drift upward despite little to no change in PO_2. This increase is not due to elevated PCO_2 but is likely caused by catecholamines and increased core temperature. This phenomenon is known as **VO_2 drift**.

Neural and Chemoreceptor Control of Ventilation

Input to the respiratory control center to increase ventilation can come from both neural and chemoreceptor sources. Central chemoreceptors in the medulla sense changes in PCO_2 and hydrogen ion concentration. Peripheral chemoreceptors located in the aorta and carotid artery detect changes in PCO_2, hydrogen ion concentration, and PO_2.

At the end of exercise, pulmonary ventilation returns to normal more slowly than the decrease in the muscles' energy demands. Post-exercise breathing rate remains elevated, primarily regulated by acid-base balance, PCO_2, and blood temperature.

12. Acevedo EO, Goldfarb AH, Increased training intensity effects on plasma lactate, ventilatory threshold, and endurance. Medicine & Science in Sports & Exercise, 1989. 21(5): p. 563-568.

Chapter Summary

This chapter provides a comprehensive overview of the cardiopulmonary system, emphasizing the interdependence of the pulmonary and cardiovascular systems in transporting oxygen and carbon dioxide. It outlines the four key processes involved in gas transportation: pulmonary ventilation, pulmonary diffusion, transportation via the blood, and capillary diffusion. Pulmonary ventilation, or breathing, involves the movement of air into and out of the lungs, while pulmonary diffusion refers to the exchange of gases between the lungs and blood. These processes are crucial for replenishing blood oxygen levels and removing carbon dioxide.

The lungs, located in the thoracic cavity, are suspended by pleural sacs that provide lubrication and reduce friction. The pleurae also create a pressure gradient essential for gas exchange and compartmentalize the thoracic cavity to prevent infections. Air travels from the nose through the nasal cavity, pharynx, larynx, trachea, and bronchial tree, eventually reaching the alveoli where gas exchange occurs. The conducting zone directs air to the respiratory zone, where oxygen and carbon dioxide are exchanged.

Gas exchange in the alveoli is facilitated by a large surface area and thin respiratory membrane. Boyle's Law and Fick's Law explain the mechanics of ventilation and the rate of gas diffusion, respectively. The Bohr and Haldane effects describe how changes in blood pH and (PCO_2) levels influence oxygen and carbon dioxide transport. 2,3-DPG and myoglobin also play roles in oxygen transport, particularly during exercise.

Spirometry measures lung volumes and capacities, such as tidal volume, vital capacity, residual volume, and total lung capacity. These measurements are essential for diagnosing respiratory conditions. Ventilation increases during exercise to meet the muscles' oxygen demands and expel carbon dioxide. The ventilatory threshold marks a disproportionate increase in ventilation, reflecting the body's response to increased (PCO_2) levels. Exercise in hot environments and the role of neural and chemoreceptor control in regulating ventilation are also discussed.

Overall, this chapter equips students with a thorough understanding of respiratory physiology, the mechanics of pulmonary function, and the factors influencing gas exchange and transport in the body.

Scholarly Questions

1. What is the difference between internal and external respiration?
2. Can you name three functions of the pleurae?
3. Review the pathway of environmental air into the body. How is oxygen transported in the

blood once it is loaded?

4. How is carbon dioxide transported in the body?
5. What are the components of the respiratory zone and the conducting zone?
6. Approximately how many terminal bronchioles are there in a healthy adult?
7. Explain Boyle's Law and how it helps to explain ventilation.
8. Discuss the mechanisms of inspiration and expiration. Which muscles are involved in resting inhalation and expiration? Which muscles are involved in deep inspiration and expiration?
9. Is deep expiration an active or passive process?
10. What is a pressure gradient? What is a partial pressure?
11. Discuss Dalton's Law.
12. Calculate the following pressure gradient: Atmospheric PO_2 = 159 mmHg; Alveolar PO_2 = 104 mmHg.
13. What are the partial pressures of nitrogen, oxygen, and carbon dioxide at the standard barometric pressure (760 mmHg)? Calculate the partial pressures at a barometric pressure of 640 mmHg.
14. Based on the principles of simple diffusion, will gas concentrations flow from lower to higher, or higher to lower?
15. How many hemoglobin molecules are present in one red blood cell?
16. How many oxygen molecules can bind to each hemoglobin molecule?
17. If the PO_2 is low, will the hemoglobin be more or less saturated?
18. How do scientists represent the relationship between oxygen and hemoglobin binding?
19. According to the oxyhemoglobin dissociation curve, if the PO_2 is 40 mmHg, what is the hemoglobin saturation? How much oxygen has been unloaded at the tissues?
20. If the PO_2 is 20 mmHg, how much hemoglobin is saturated?
21. What does equilibrium mean? What is the equilibrium reached at the tissues?
22. What is the PO_2 in the alveoli, tissues, and systemic veins?
23. What is the PCO_2 in the alveoli, tissues, and systemic veins?
24. What factors affect oxygen loading? What is the effect called that causes a shift in the oxygen-hemoglobin dissociation curve? Discuss how exercise helps oxygen unloading.
25. What is the Haldane effect?
26. Determine the PO_2 and PCO_2 as blood travels through the pulmonary and systemic circuits.
27. How does exercise affect ventilation and perfusion?

11.

THE ENDOCRINE RESPONSE TO EXERCISE

Exercise and the Endocrine System.

Learning Objectives

- Identify the three classes of hormones based on their chemical makeup.
- Discuss how the chemical composition of hormones affects their transport in the blood and interaction with tissues.
- Describe how hormones like insulin facilitate glucose uptake in cells.

- Explain the G protein-coupled receptor mechanism and its significance in cellular responses.
- Identify the endocrine glands most affected by exercise and the hormones they secrete.
- Explain how changes in plasma volume and osmolality during exercise influence hormone secretion.
- Describe the primary hormones secreted by the adrenal medulla and cortex and their roles during exercise.
- Explain the renin-angiotensin-aldosterone system and its importance in maintaining plasma volume during exercise.
- Explain the functions of testosterone and estrogens in the body and their influence on exercise performance.
- Describe how anabolic hormones like testosterone, GH, insulin, and IGF-1 contribute to muscle hypertrophy and remodeling during resistance training.
- Compare the acute and chronic hormonal responses to resistance training and their significance.

Introduction

As discussed in previous chapters, exercise acts as a stressor on the body, disrupting homeostasis and leading to various acute and chronic changes. Two major homeostatic systems involved in regulating bodily functions are the nervous and endocrine systems. These systems work together to sense information, organize appropriate responses, and send messages to tissues to maintain or regain homeostasis. The term neuroendocrinology is often used to describe the systematic study of these control systems, as endocrine organs receive neural input. The nervous system relays messages via action potentials and neurotransmitters, whereas the endocrine system communicates by releasing hormones (chemical messengers) into the blood to circulate and exert effects. Hormones attach to highly specific receptors to trigger cellular responses. In the context of exercise physiology, hormones are crucial for mobilizing fuel for exercise, stimulating protein synthesis, and initiating muscle hypertrophy. The specific responses of the endocrine system to acute and chronic exercises will be discussed in this chapter.

Categories of Hormones

Hormones can be categorized into three classes based on their chemical makeup: amino acid derivatives, peptides/proteins, and steroid hormones. The chemical composition of hormones determines their transport

in the blood and interaction with tissues. Steroid hormones, being lipid-like, require that they are transported bound to plasma proteins and can diffuse through cell membranes to affect the nucleus. The effect of a hormone on a tissue is directly related to its plasma concentration and the number of active receptors. For example, steroid hormones like thyroxine use transport proteins, and their concentration is influenced by the availability of these proteins. Factors such as secretion rates, metabolism or excretion rates, and changes in plasma volume can affect free plasma hormone concentration and the magnitude of their effects. During exercise, plasma volume decreases due to sweating, increasing the hormone concentrations in the plasma and leads to enhanced metabolic and cellular changes.

Endocrine hormones are carried by the blood to various tissues but only affect those with specific protein receptors. The number of receptors on each cell can range from 500 to 100,000 and can change based on chronic hormone levels. Receptor numbers may decrease (down-regulation) with chronically elevated hormone levels or increase (up-regulation) with low hormone concentrations. High hormone levels can saturate receptors, preventing additional hormonal effects. When a hormone binds to its receptor, it modifies cellular activity through three main mechanisms: altering DNA activity, altering membrane transport activity, and activating second messenger proteins. These mechanisms will be discussed in further detail in the next sections.

Altering DNA activity

Hormones that alter DNA activity initiate protein synthesis in the nucleus. **Steroid hormones**, due to their lipid-like structures, can easily diffuse through cell membranes. These hormones, originating from the adrenal cortex and gonads, bind to protein receptors in the cytoplasm, forming a steroid-receptor complex. This complex then enters the nucleus and binds to a hormone response element on the DNA, leading to gene transcription to mRNA, subsequent protein synthesis, finally resulting in metabolic effects. Although thyroid hormones are not steroids, they also act by altering DNA. This process is slow but results in long-lasting effects compared to hormones that work through second messengers. Figure 11.1 illustrates this process.

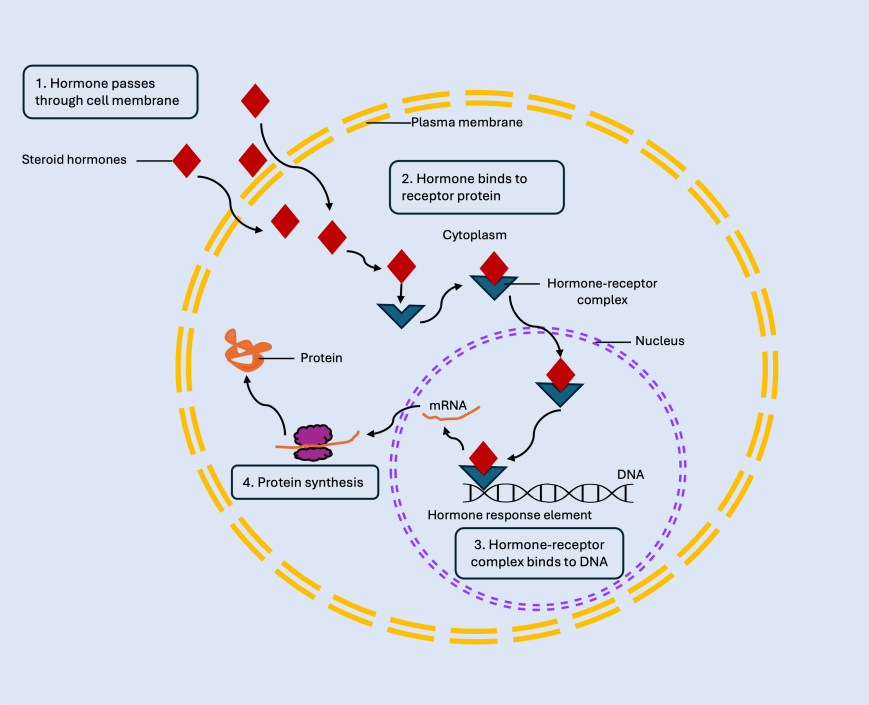


Figure 11.1 The mechanism by which steroid hormones alter DNA activity. Steroid hormones, being lipophilic, diffuse through the cell membrane (1) and bind to a protein receptor in the cytoplasm. This binding creates a hormone-receptor complex (2) that translocates to the nucleus. Within the nucleus, the (3) hormone-receptor complex binds to the hormone response element on the DNA, regulating protein transcription. Messenger RNA (mRNA) is then transcribed, exits the nucleus, and is (4) translated into a functional protein by transfer RNA (tRNA) and ribosomes.

Altering membrane transport activity

Polypeptide hormones exert their primary effects by binding to receptors on the cell surface, thereby altering membrane transport activity. Composed of chains of amino acids, these hormones are not fat-soluble and cannot cross the cell membrane. When polypeptide hormones bind to their receptors, they can activate carrier molecules or increase the movement of ions or substrates from outside to inside the cell. A prime example of this mechanism is the action of insulin. Insulin facilitates the influx of glucose into cells by binding to the extracellular domain of the insulin receptor. Due to its size, glucose cannot naturally diffuse into cells, yet it is an essential nutrient for all tissues. In cases of inadequate insulin response, such as in uncontrolled diabetes, glucose accumulates in the blood, leading to complications in various organ systems and tissues. The specific mechanism by which insulin enables glucose entry into cells involves several steps:

1. Insulin binds to the alpha subunit of a tyrosine kinase receptor located outside the cell.
2. Binding causes the beta subunits inside the cell to phosphorylate themselves.

3. The activation of these subunits leads to the movement of glucose transporters, known as GLUT4 transporters, to the cell membrane.
4. GLUT4 transporters then facilitate the entry of glucose into the cell.

Additionally, **insulin** activates glycogen synthase, an enzyme that converts glucose molecules into glycogen within the cell. Figure 11.2 illustrates the translocation of GLUT4 glucose transporters to the cellular membrane following insulin signaling.

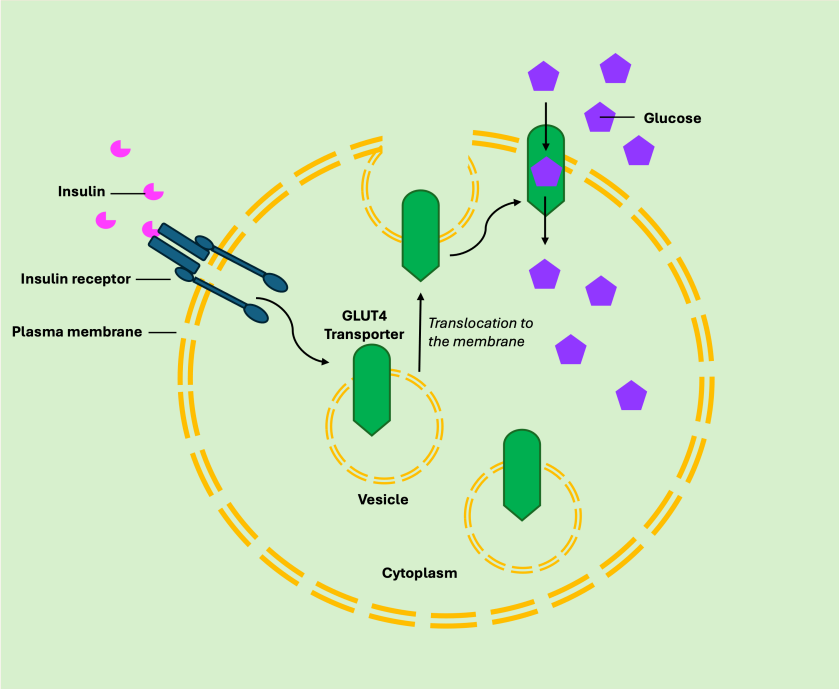


Figure 11.2. Transport of glucose following GLUT4 translocation to the cell membrane after insulin signaling. Insulin binds to its receptor on the cell surface, triggering a signaling cascade that results in the translocation of GLUT4 transporters to the cell membrane. Once at the membrane, GLUT4 transporters facilitate the entry of glucose into the cell, allowing it to be used for energy or stored as glycogen.

Second Messenger Receptor Mechanism

Due to their solubility, size, or specific function, some hormones cannot cross the cell membrane. Instead, they bind to receptors coupled to G proteins on the cell surface. The **G protein**, acting as a secondary messenger, can then activate enzymes within the cell, open ion channels, and ultimately lead to a cellular response. This mechanism serves as the link between the hormone-receptor interaction on the cell membrane and the subsequent intracellular events.

When a hormone binds to its receptor, the G protein is activated, which can trigger a cascade of activities.

One significant pathway involves the activation of adenylate cyclase, an enzyme that converts ATP to cyclic AMP (cAMP). Cyclic AMP then activates protein kinase A, which in turn activates response proteins that alter cellular activity. This pathway can lead to the activation of phosphorylase, which breaks down glycogen into glucose, and hormone-sensitive lipase, which breaks down triglycerides into free fatty acids. Figure 11.3 illustrates the cyclic AMP secondary messenger mechanism. Cyclic AMP is eventually inactivated by the enzyme phosphodiesterase, which converts it to 5' AMP. Caffeine is known to inhibit phosphodiesterase activity, thereby prolonging the effects of cAMP. This prolonged activity can enhance the breakdown of triglycerides in adipose tissues, demonstrating caffeine's impact on metabolic processes.

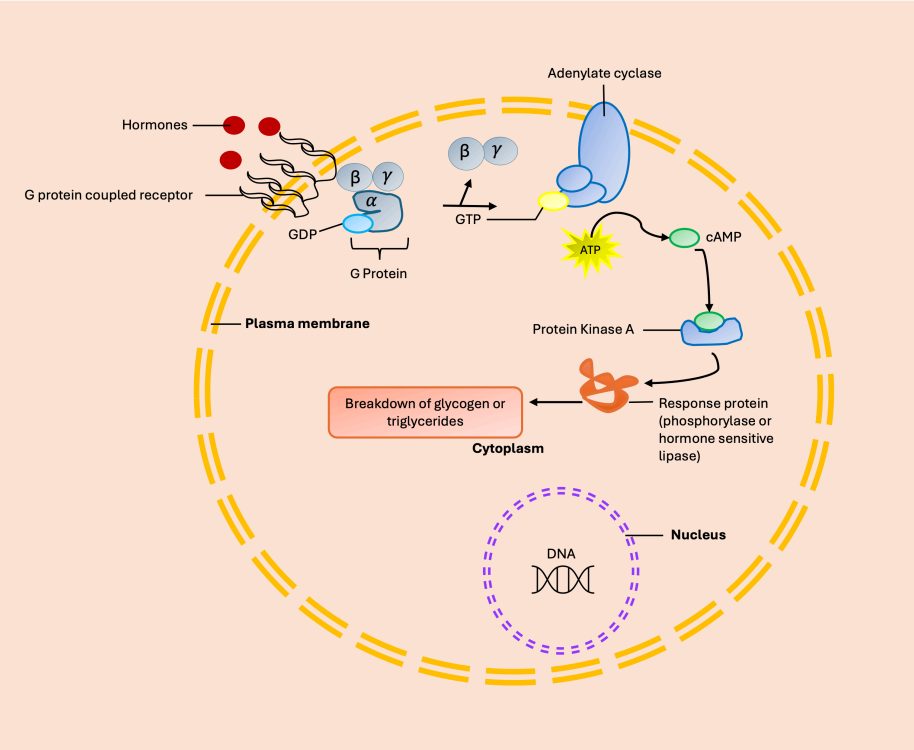


Figure 11.3 The cyclic AMP (cAMP) secondary messenger mechanism. Hormones bind to the G protein-coupled receptor on the plasma membrane, activating a G protein. The G protein then activates adenylate cyclase, which converts ATP to cyclic AMP. Cyclic AMP activates protein kinase A, which in turn activates a response protein, leading to the breakdown of fuels for exercise.

Secretion of Hormones and the General Exercise Response

This section highlights the key endocrine glands involved in the body's response to exercise and training. Understanding these glands, their regulatory mechanisms, and the hormones they release is crucial for discussing the role of the endocrine system in fuel mobilization during exercise. While this overview is not

exhaustive, it focuses on the glands and hormones most affected by exercise.

The rate of hormone secretion is influenced by both inhibitory and stimulatory signals from the nervous system. For instance, changes in calcium ion (Ca^{2+}) concentration or substrate levels, such as blood glucose, can stimulate hormone release. Additionally, the rate of hormone secretion is affected by the liver's ability to inactivate hormones and the kidneys' role in hormone metabolism and excretion. During exercise, blood flow to these organs decreases, which slows the metabolism of hormones, thereby affecting their concentration and activity in the body. Figure 11.4 illustrates the major endocrine organs affected by exercise and their anatomical location.

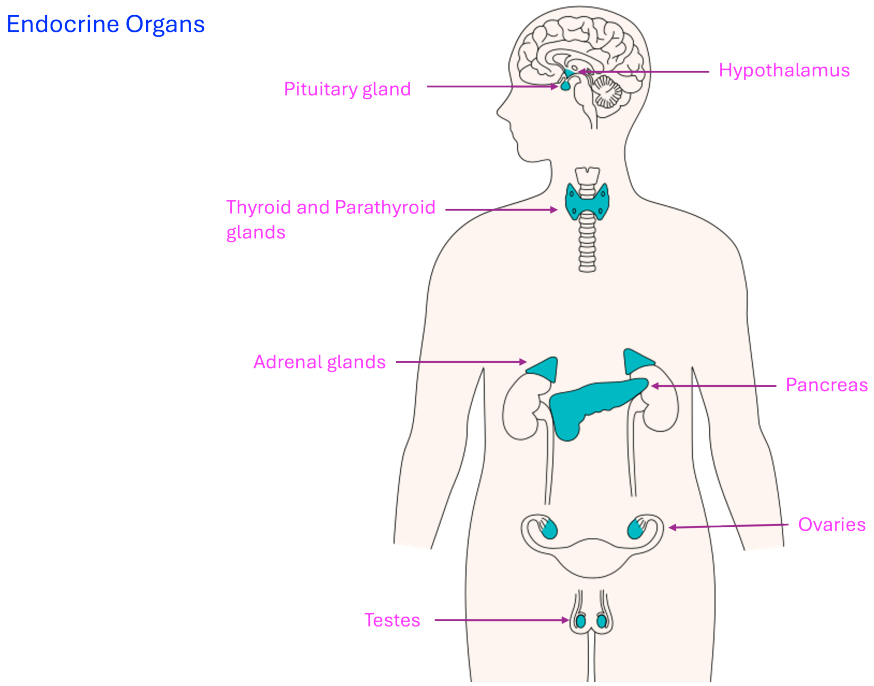


Figure 11.4 Anatomical Locations of Major Endocrine Organs in the Human Body.

Hypothalamus and the Pituitary Gland

The **hypothalamus**, located in the brain, plays a crucial role in maintaining general homeostasis by controlling various body functions and is shown in Figure 11.5. During exercise, the regulation of hormone release, fluid intake, and temperature control becomes increasingly important, as exercise acts as a stressor to these systems. The hypothalamus exerts its control over the **pituitary gland**, which is situated at the base of the brain and is attached to the hypothalamus. The pituitary gland is divided into two lobes: the **anterior pituitary (adenohypophysis)** and the **posterior pituitary (neurohypophysis)**. These lobes are responsible for the secretion of hormones that play vital roles in the body's response to exercise and overall homeostasis.

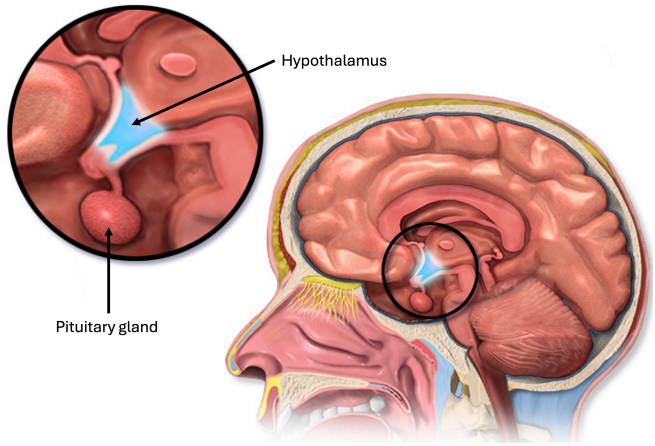


Figure 11.5 The hypothalamus and pituitary glands in the brain. The hypothalamus regulates vital bodily functions such as temperature, hunger, and thirst, while the pituitary gland, often termed the "master gland," controls various endocrine functions by releasing hormones that influence growth, metabolism, and reproductive processes.

Anterior pituitary and its hormones

The anterior pituitary gland is primarily regulated by chemical releasing hormones originating from neurons in the hypothalamus. Most hormones secreted by the anterior pituitary control the release of other hormones throughout the body. Key anterior pituitary hormones include **adrenocorticotrophic hormone (ACTH)**, **luteinizing hormone (LH)**, **thyroid-stimulating hormone (TSH)**, and **growth hormone (GH)**. Other hormones such as melanocyte-stimulating hormone (MSH), follicle-stimulating hormone (FSH), and prolactin are less relevant to the direct changes associated with exercise.

- Adrenocorticotrophic Hormone (ACTH): Stimulates the production and secretion of cortisol in the adrenal cortex in response to stress.
- Luteinizing Hormone (LH): Stimulates the production of testosterone and estrogen.
- Thyroid-Stimulating Hormone (TSH): Regulates the rate and secretion of thyroid hormones.
- Growth hormone (GH) stimulates the release of **insulin-like growth factors (IGFs)** from the liver and other tissues, promoting protein synthesis and tissue growth.

The anterior pituitary plays a crucial role during exercise by secreting key hormones necessary for the body's response.

Growth Hormone (GH) and its regulation

Growth hormone (GH) stimulates the release of insulin-like growth factors (IGFs) from the liver and other tissues, promoting protein synthesis and tissue growth. The hypothalamus controls GH release in response to stimuli such as exercise, sleep, stress, and low plasma glucose levels. When stimulated, the hypothalamus releases growth hormone-releasing hormone (GHRH), which then prompts the anterior pituitary to release GH. GH is particularly important during exercise as it aids in energy mobilization. Specifically, GH increases liver gluconeogenesis and inhibits glucose entry into adipose tissue, favoring fat mobilization. Conversely, **somatostatin**, another hormone secreted by the hypothalamus, inhibits GH

release from the anterior pituitary. The levels of GH and IGFs in the blood exert a negative feedback effect on the hypothalamus, regulating the continued secretion of GH. This negative feedback loop ensures that GH levels are maintained within an optimal range, as illustrated in Figure 11.6.

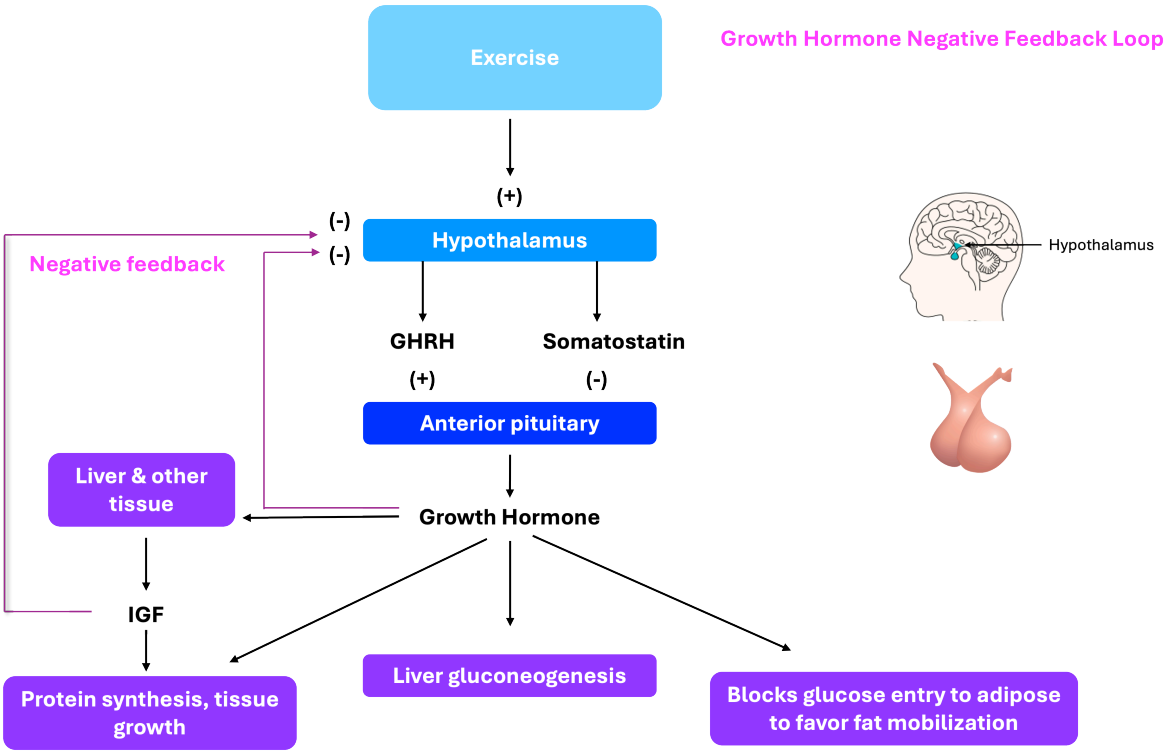


Figure 11.6 The Growth Hormone (GH) Negative Feedback Loop Stimulated by Exercise. Growth hormone release is controlled by the hypothalamus through the secretion of growth hormone-releasing hormone (GHRH). Somatostatin inhibits GH release from the anterior pituitary. When released, GH targets various tissues in the body, including the liver, adipose tissue, and others. Additionally, the release of GH stimulates the production of insulin-like growth factors (IGFs), which have downstream effects.

Posterior pituitary gland

The posterior pituitary gland stores hormones produced by specialized neurons in the hypothalamus. It primarily stores and releases **oxytocin** and **antidiuretic hormone (ADH)**. Oxytocin is a potent stimulator of smooth muscle, playing a crucial role in childbirth and milk release from the breast. ADH, on the other hand, reduces water loss by promoting water reabsorption in the kidney tubules. High plasma osmolality (low water concentration) due to sweating without fluid replacement and low plasma volume can stimulate ADH secretion by the hypothalamus. During exercise, as plasma volume decreases and osmolality increases due to sweating, ADH secretion is elevated. Studies indicate that at exercise intensities above 60% VO2max stimulate ADH secretion to conserve water and maintain plasma volume [1]. These responses are vital for maintaining blood pressure and cardiovascular function during exercise.

Thyroid and Parathyroid Glands

The **thyroid gland** is essential for establishing metabolic rate through the secretion of thyroid hormones. Stimulated by TSH from the anterior pituitary, the thyroid synthesizes two iodine-containing hormones: **triiodothyronine (T_3)** and **thyroxine (T_4)**. T3 contains three iodine atoms, while T_4 contains four. Although T_4 is released in larger quantities, T_3 is more potent. Thyroid hormone secretion is regulated by a negative feedback mechanism. During exercise, the concentration of free thyroid hormones increases due to changes in the binding characteristics of transport proteins, leading to faster uptake by tissues. To counteract the higher rate of hormone removal, **thyroid-stimulating hormone (TSH)** secretion increases. Exercise-induced secretion of prolactin and cortisol can also influence TSH release, affecting metabolism and enhancing the effects of other hormones. Figure 11.7 illustrates the location of the thyroid and **parathyroid glands**.

Calcium regulation and parathyroid hormone

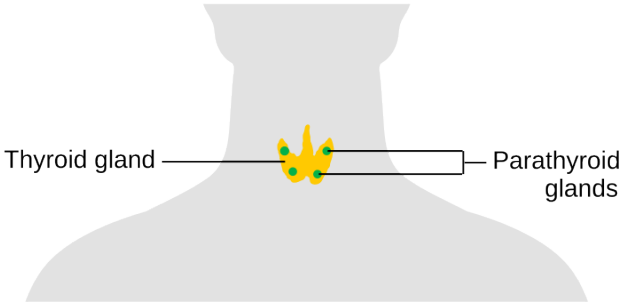


Figure 11.7 Diagram Showing the Position of the Thyroid and Parathyroid Glands. The thyroid gland produces hormones that regulate metabolism, energy levels, and growth. The parathyroid glands, located behind the thyroid, produce parathyroid hormone (PTH), which is crucial for maintaining stable calcium levels in the blood and bones.

Calcium ions (Ca^{2+}) play a crucial role in muscle force production, making their regulation vital during exercise. The primary hormone involved in calcium regulation is parathyroid hormone (PTH), secreted by the parathyroid glands in response to low plasma calcium levels. PTH stimulates the release of calcium from bones into the plasma and enhances renal calcium reabsorption. Additionally, PTH promotes the conversion of vitamin D_3 into its active form in the kidneys, which increases calcium absorption from the gastrointestinal tract. During both intense and prolonged exercise, PTH levels rise, which is also associated with increased plasma hydrogen ion (H^+) and catecholamine concentrations [2]. The thyroid gland also secretes calcitonin, a hormone with a lesser role in calcium regulation. Calcitonin helps control plasma calcium levels by inhibiting calcium release from bones

1. Convertino VA, Keil LC, and Greenleaf JE. Plasma volume, renin, and vasopressin responses to graded exercise after training. Journal of Applied Physiology: Respiratory, Environmental and Exercise Physiology. 54: 508-514.

2. Bouassida A, Latiri I, Bouassida S, Zalleg D, Zaouali M, Feki Y, et al. Parathyroid hormone and physical exercise: a brief review. J Sport Science and Medicine. 5: 367-374, 2006.

and promoting calcium excretion by the kidneys. Unlike PTH, calcitonin secretion is not significantly influenced by exercise.

Pancreas

The **pancreas** functions as both an exocrine and endocrine gland. It secretes digestive enzymes and bicarbonate into the small intestine and contains endocrine tissues known as the islets of Langerhans. These islets release insulin, glucagon, and **somatostatin**. Somatostatin, secreted by delta cells, modulates gastrointestinal activity to regulate the entry rate of nutrients into the bloodstream. Insulin and glucagon, which are significantly affected by exercise, will be discussed in more detail in this section.

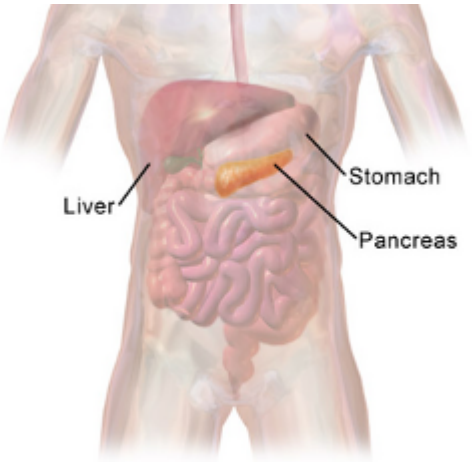


Figure 11.8 The Location and Functions of the Pancreas. The pancreas is in the abdomen behind the stomach. It plays a crucial role in digestion by producing enzymes that help break down carbohydrates, fats, and proteins. Additionally, it regulates blood sugar levels by secreting hormones such as insulin and glucagon.

Insulin and its role in glucose regulation

Insulin, released from the beta cells of the islets of Langerhans in the pancreas, is the most crucial hormone during the absorptive state of digestion. It stimulates tissues to uptake nutrient molecules such as glucose and amino acids, promoting their storage as glycogen, proteins, and fat. Insulin is essential for facilitating the diffusion of glucose across cell membranes, as glucose cannot naturally diffuse across these membranes due to its size. When the insulin response is impaired, plasma glucose accumulates, leading to systemic issues in various organs and tissues. High plasma glucose levels overwhelm the kidneys' reabsorption mechanisms, resulting in glucose loss in the urine along with large volumes of water, a condition known as diabetes mellitus.

Insulin release is regulated by several factors, including plasma glucose concentration, plasma amino acid concentration, sympathetic and parasympathetic nerve stimulation, and various hormones. Blood glucose concentration is a major excitatory input to the beta cells of the pancreas and is part of the negative feedback loop that regulates insulin secretion. Following carbohydrate consumption and absorption, a temporary state of hyperglycemia occurs, with blood glucose levels rising above 100 mg/100 ml, compared to the normal fasting levels of 80-90 mg/100 ml. In response, the beta cells in the pancreas rapidly release insulin into the bloodstream. Insulin then binds to cell receptors, allowing glucose to be transported into the cells, thereby lowering blood glucose concentrations. This process restores blood glucose levels to normal, maintaining

homeostasis through a negative feedback mechanism. In summary, insulin release in response to high blood glucose levels works by opposing the stimulus, reducing the amount of circulating blood glucose. After consuming carbohydrates, plasma glucose levels rise, prompting the beta cells to secrete insulin. Figure 11.9 illustrates the negative feedback response following a high-carbohydrate meal.

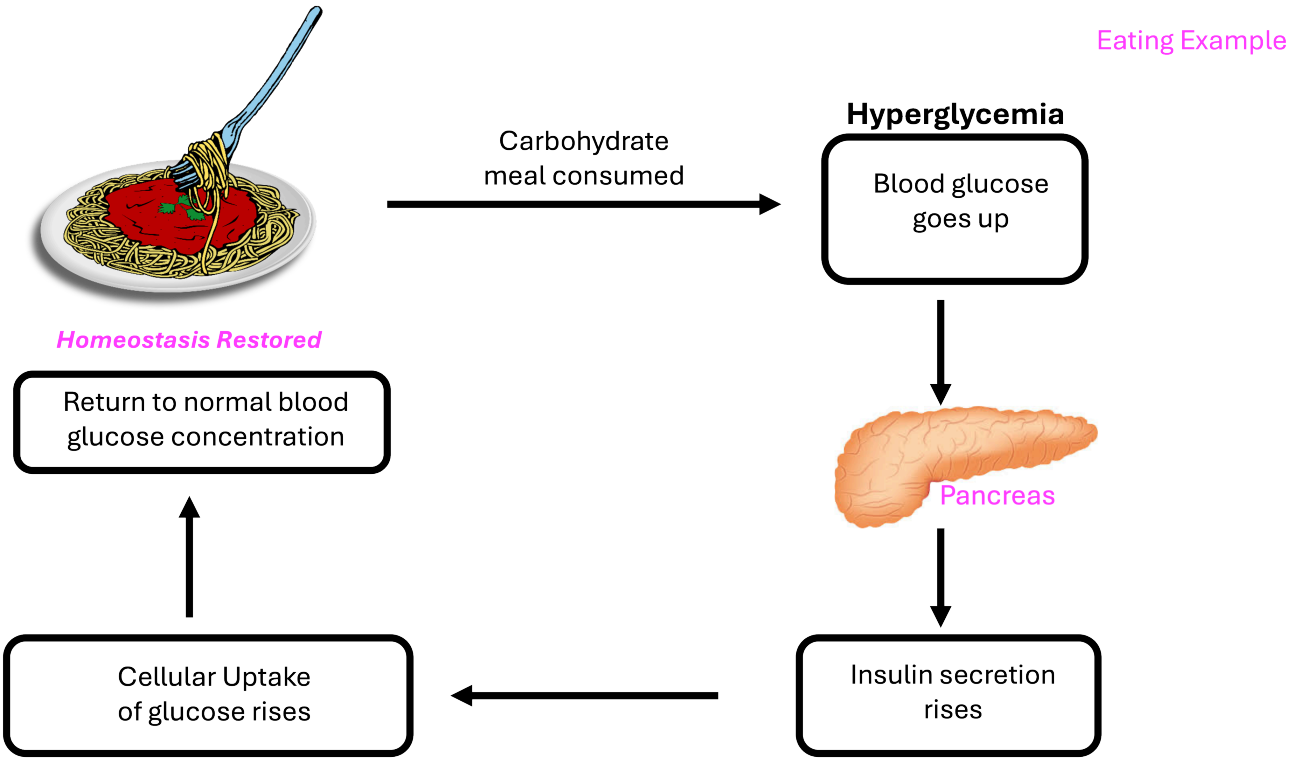


Figure 11.9 Illustration of the Negative Feedback Mechanism Regulating Blood Glucose Levels After a High-Carbohydrate Meal. This diagram illustrates how blood glucose levels are regulated through a negative feedback loop. After a high-carbohydrate meal, blood glucose levels rise, prompting the pancreas to release insulin. Insulin facilitates the uptake of glucose by cells, lowering blood glucose levels. When glucose levels drop, the pancreas releases glucagon, which signals the liver to release stored glucose, maintaining homeostasis.

Insulin and glucagon responses during exercise

During exercise, glucose uptake by muscles can increase significantly, ranging from 7- to 20-fold. Consequently, insulin concentration decreases during exercises of increasing intensity to conserve blood glucose for the exercising muscles. If insulin secretion were to increase during exercise, all tissues would uptake glucose more rapidly, potentially leading to hypoglycemia. Lower insulin concentrations during exercise favor the mobilization of glucose from the liver and free fatty acids (FFAs) from adipose tissues. This mobilization helps maintain plasma glucose concentrations during moderate-intensity and long-term exercise bouts.

As plasma insulin decreases during exercise, **glucagon** levels increase. Secreted by the alpha cells of the

islets of Langerhans, glucagon has effects opposite to those of insulin. In response to low plasma glucose concentrations, glucagon stimulates the mobilization of glucose from the liver, gluconeogenesis, and the release of FFAs from adipose tissues. These actions help spare blood glucose for use as fuel by the tissues. Thus, glucagon increases during exercise to favor the mobilization of FFAs from adipose tissue and glucose from the liver, maintaining plasma glucose concentrations for muscles that are using glucose at a higher rate.

Adrenal Glands

The **adrenal glands**, located above the kidneys, are responsible for producing a variety of steroid and adrenal hormones. The gland consists of two sections: the inner adrenal medulla and the outer adrenal cortex. The **adrenal medulla** secretes **epinephrine (E)**, **norepinephrine (NE)**, and **catecholamines**, while the **adrenal cortex** secretes steroid hormones. These hormones play crucial roles in the body's response to stress, including exercise, by regulating metabolism, cardiovascular function, and other physiological processes.

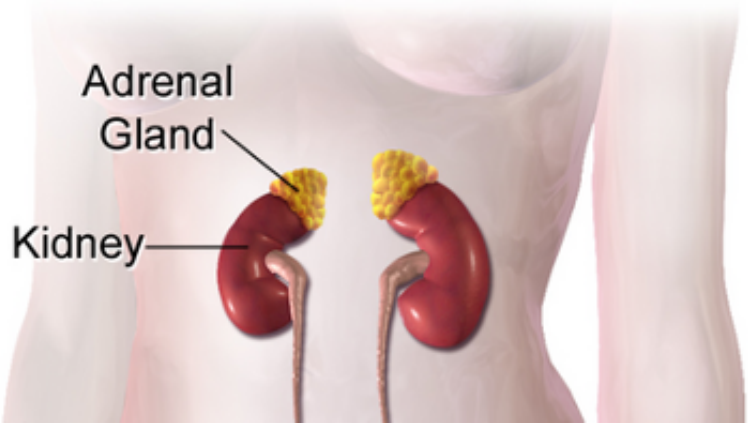


Figure 11.10 The Location and Functions of the Adrenal Glands. The adrenal glands are located on top of each kidney. They produce essential hormones such as cortisol, aldosterone, and adrenaline, which help regulate metabolism, blood pressure, and the body's response to stress. Photo credit (13).

Adrenal medulla and its hormones

The adrenal medulla is regulated by the sympathetic nervous system, with approximately eighty percent of its hormonal secretion being epinephrine. Epinephrine has widespread effects on various systems, including the cardiovascular, respiratory, gastrointestinal, liver, muscle, and adipose tissues. Both epinephrine and norepinephrine are crucial for mobilizing substrates during exercise and are released in response to strong emotional stimuli as part of the "fight or flight" response. These hormones also play a significant role in regulating blood pressure and plasma glucose concentration.

Epinephrine (E) and norepinephrine (NE) bind to adrenergic receptors on target tissues. These receptors are classified into two major classes: **alpha adrenergic receptors (α)** and **beta adrenergic receptors (β)**, with their respective subgroups (α1, α2; β1, β2, and β3). E and NE operate via a secondary messenger mechanism and can have inhibitory or stimulatory effects depending on the receptor type. Different receptors alter cell activity by changing cyclic AMP or Ca++ concentrations.

Adrenal cortex and its hormones

The adrenal cortex, the outer portion of the adrenal gland, secretes cholesterol-derived hormones, including **mineralocorticoids (aldosterone)**, **glucocorticoids (cortisol)**, **androgens**, and **estrogens**. Aldosterone is involved in maintaining Na+ and K+ concentrations in blood plasma, directly influencing Na+/H_2O balance, plasma volume, and blood pressure. Aldosterone release can be triggered by decreases in plasma volume or increases in plasma K+ concentration. Elevated K+ levels stimulate aldosterone secretion, which then prompts the kidneys to actively transport K+.

When plasma volume decreases, the kidneys secrete an enzyme called **renin**. Renin converts **angiotensinogen** in the plasma to **angiotensin I**, which is then converted to angiotensin II by **angiotensin-converting enzyme (ACE)** in the lungs. **Angiotensin II** is a potent vasoconstrictor and stimulates **aldosterone** release, increasing Na+ reabsorption in the kidneys. As water follows Na+ to balance osmolality, this process conserves water and increases blood plasma volume. During exercise intensities greater than 50% VO2max, renin, angiotensin, and aldosterone levels increase in parallel to maintain plasma concentration necessary for sweating and blood pressure regulation [3].

3. Terjung R. Endocrine Response to Exercise. New York, NY: Macmillan, 1979.

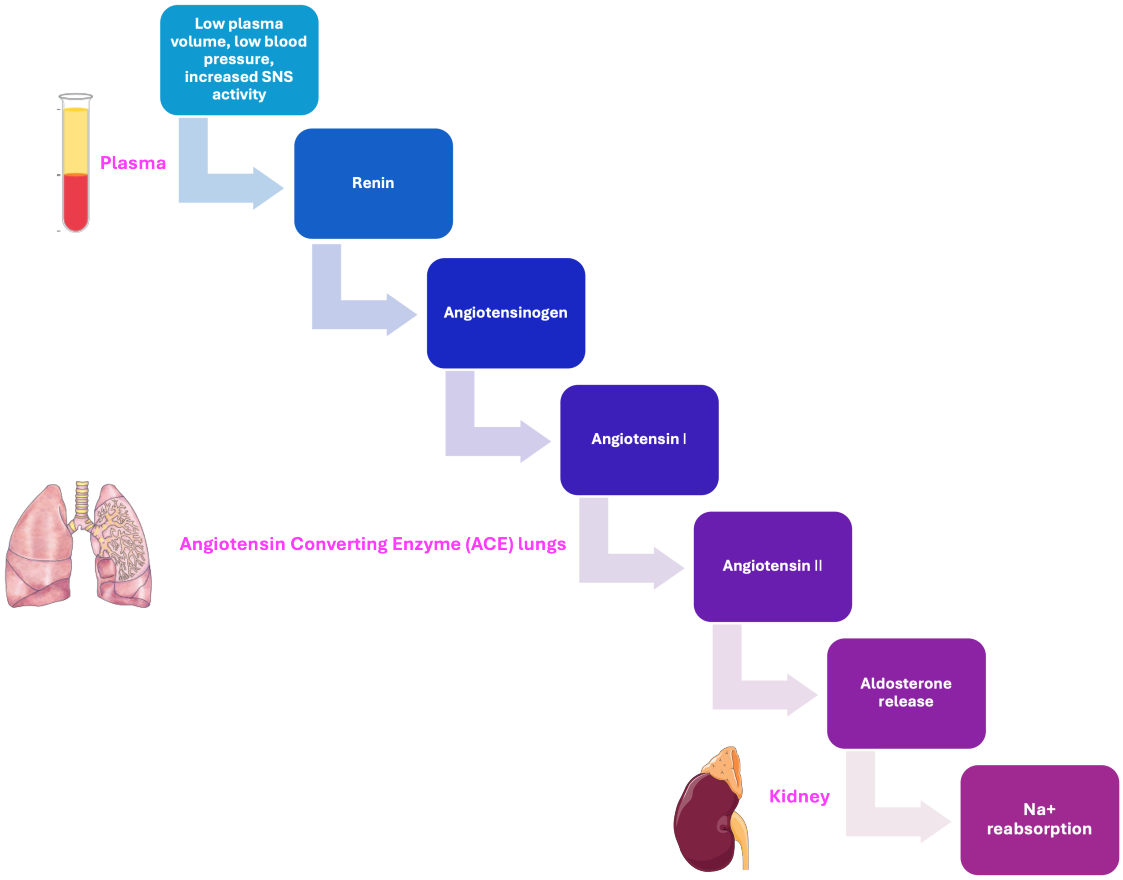


Figure 11.11 The Renin-Angiotensin Pathway. This pathway illustrates the steps involved in regulating blood pressure and fluid balance. When blood pressure drops, the kidneys release renin, which converts angiotensinogen from the liver into angiotensin I. Angiotensin I is then converted to angiotensin II by the angiotensin-converting enzyme (ACE) primarily in the lungs. Angiotensin II acts to constrict blood vessels, increasing blood pressure, and stimulates the release of aldosterone from the adrenal glands, which promotes sodium and water retention by the kidneys.

Cortisol and its role in metabolism

Cortisol is the primary glucocorticoid secreted by the adrenal cortex, playing a crucial role in regulating plasma glucose levels during exercise and long-term fasting. Cortisol targets various tissues, including adipose and liver tissues. Upon secretion, cortisol inhibits glucose entry into tissues and promotes the breakdown of tissue proteins to release amino acids. These amino acids are then utilized by the liver to produce glucose through a process known as gluconeogenesis. Additionally, cortisol stimulates liver enzymes involved in gluconeogenesis. Cortisol also facilitates the mobilization of free fatty acids (FFAs) from adipose tissue, providing an alternative energy source. The release of cortisol is regulated by a negative feedback mechanism, ensuring that its levels remain balanced to meet the body's metabolic demands. This regulatory process is depicted in Figure 11.12.

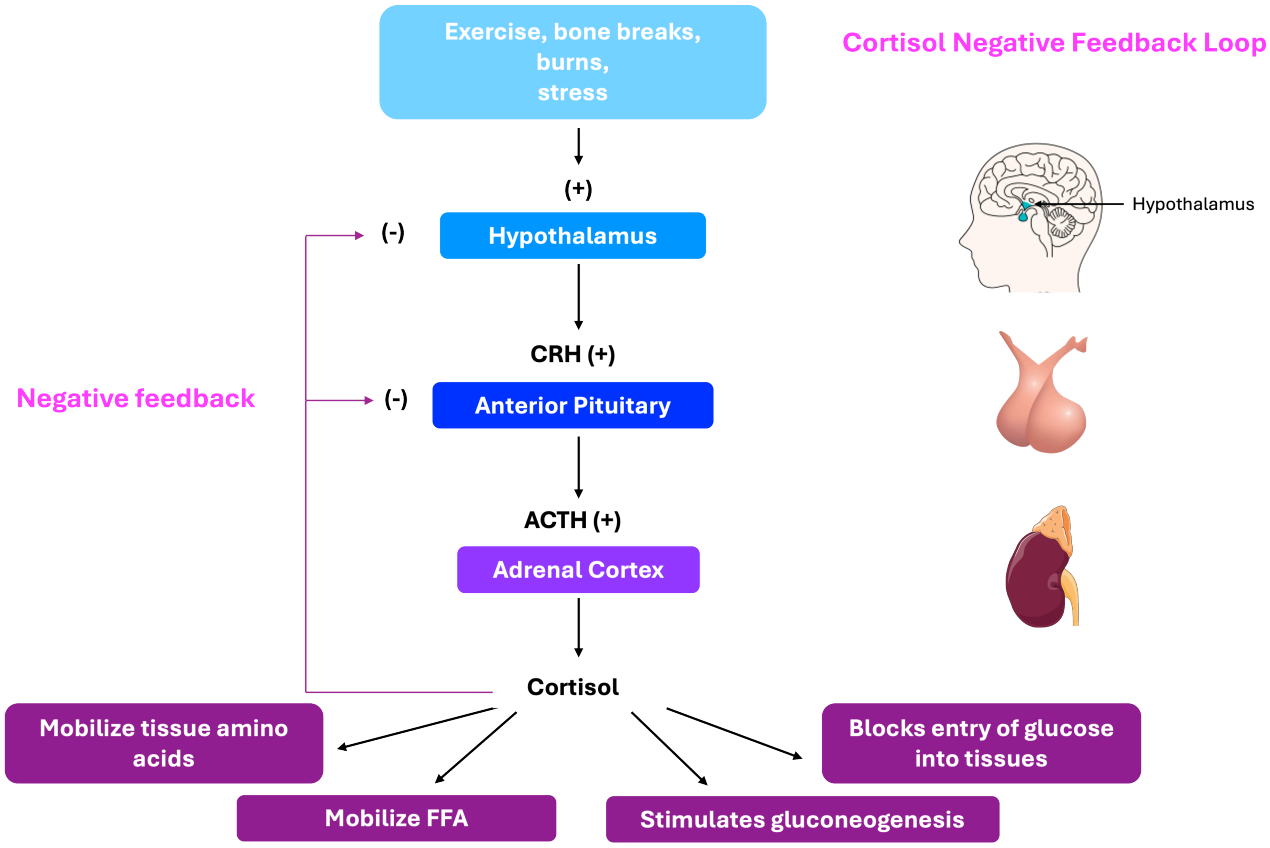


Figure 11.12 Effects of Exercise and Stressors on Cortisol Release and Regulation. This diagram illustrates how exercise and stressors influence cortisol release and its regulation. Exercise can act as a controlled stressor, initially increasing cortisol levels. Cortisol, produced by the adrenal glands, plays a crucial role in managing substrate mobilization and utilization.

Testes and Ovaries

The most well-known hormones produced by the **testes** and **ovaries** are **testosterone** and **estrogens**, respectively. These hormones promote secondary sex characteristics, are crucial for establishing and maintaining reproductive function, and can influence exercise performance based on various metabolic and chronic factors. Androgens and estrogens also support prepubescent growth and female sex drive.

Testosterone is secreted by the interstitial cells of the testes and is regulated by **luteinizing hormone (LH)**, also known as interstitial cell-stimulating hormone (ICSH). LH release is controlled by a releasing hormone from the hypothalamus. Testosterone is both an anabolic and androgenic steroid, stimulating protein synthesis and causing changes during adolescence that lead to a high muscle-mass to fat-mass ratio. Studies have shown that plasma testosterone concentrations increase by 10-37% during prolonged submaximal work, maximal exercise, and endurance and strength training workouts [45]. While exercise-induced testosterone secretion was once thought to be the primary stimulus for muscle protein synthesis and hypertrophy, this effect varies individually and may only account for about 10% of changes [6]. Due to its

muscle-building properties, testosterone and synthetic variants are among the most abused substances to enhance muscle mass and performance.

Estrogens and **progesterone** are hormones with similar effects, secreted by the ovaries. Estrogens, including **estradiol**, **estrone**, and **estriol**, are responsible for breast development, female fat deposition, and other secondary sex characteristics. LH stimulates the production of androgens in the follicle, which are then converted to estrogens under the influence of follicle-stimulating hormone (FSH). Following ovulation, the luteal phase of the menstrual cycle begins, during which both estrogens and progesterone are produced by the corpus luteum. The effect of the menstrual cycle on exercise performance is still unclear, but current evidence suggests that anaerobic performance is not affected by the menstrual cycle phase [7]. Additionally, glucose-regulatory hormones appear to be unaffected by the menstrual cycle during prolonged exercise [8]. Studies also indicate no significant effects on VO_{2max}, lactate production, plasma volume, risk of heat illness, heart rate, or ventilatory responses to exercise due to the menstrual cycle [9].

Exercise-induced menstrual cycle irregularities, particularly in endurance, aesthetic, and weight-class athletes, can lead to chronically low estradiol levels, negatively impacting bone mineral content and increasing the risk of osteoporosis. **Osteoporosis** is common in athletes who experienced secondary amenorrhea (onset of amenorrhea after menarche) due to high volumes of exercise training. The prevalence of amenorrhea in college-aged women is 2-5%, but in collegiate runners, the incidence can range from 3-60% as training volume increases from less than 10 miles (16 km) to more than 68 miles (113 km) per week [10].

A summary of the hormones discussed in this section, including their actions, stimuli, controlling factors, and the effects of acute and chronic exercise, is shown in Table 11.1.

4. Jensen J, Oftebro H, Breigan B, Johnsson A, Ohlin K Meen HD, et al. Comparison of changes in testosterone concentrations after strength and endurance exercise in well trained men. European Journal of Applied Physiology and Occupational Physiology. 63:467-471, 1991.

5. Vogel RB, Books CA, Ketchum C, Zauner CW, and Murray FT. Increase of free and total testosterone during submaximal exercise in normal males. Medicine and Science in Sports and Exercise. 17: 119-123, 1985.

6. Schoenfeld BJ. Postexercise hypertrophic adaptations: a reexamination of the hormone hypothesis and its applicability to resistance training program design. Journal of Strength and Conditioning Research. 27: 1720-1730, 2013b.

7. Oosthusysee T, and Bosch AN. The effect of the menstrual cycle on exercise metabolism. Sports Medicine. 40: 207-227, 2010.

8. Kraemer RR, Francois M, Webb ND, Worley JR, Rogers SN, Norman RL, et al. No effect of menstrual cycle phase on glucose and glucoregulatory endocrine responses to prolonged exercise. European Journal of Applied Physiology. 113: 2401-2408, 2013.

9. Xanne A, and Janse de Jonge X. Effects of the menstrual cycle on exercise performance. Sports Medicine. 33: 833-851, 2003.

10. Redman LM, and Louchs AB. Menstrual disorders in athletes. Sports Medicine. 35: 747-755, 2005.

Table 11.1 Summary of Endocrine Hormones: Actions, Secretion Control, Stimuli Factors, and Effects of Acute and Chronic Exercise Training. This table provides an overview of various endocrine hormones, detailing their primary actions, the factors controlling their secretion, the stimuli that influence their release, and the effects of both acute and chronic exercise training on these hormones.

Gland	Hormone	Action	Control Factors	Stimuli	Acute Exercise Effect	Chronic Exercise Effect
Anterior pituitary	Growth Hormone (GH)	Growth, FFA mobilization, gluconeogenesis; decreases glucose uptake	GH-releasing hormone; somatostatin	Exercise; stress; low blood glucose	Increase	Attenuated response at same rate of work
	Thyroid-stimulating hormone (TSH)	Increases T_3 and T_4 production and secretion	TSH-releasing hormone	Low plasma, T_3 and T_4	Increase	No known effect
	Adrenocorticotrophic hormone (ACTH)	Increases cortisol synthesis and secretion	ACTH-releasing hormone	Stress; bone breaks; heavy exercise; burns	Increase	Attenuated response
	Follicle-stimulating hormone (FSH); luteinizing hormone (LH)	Female: Estrogen and progesterone production and ovum development Male: testosterone production and sperm development	Hypothalamic gonadotrophic-releasing hormone Females: plasma estrogen and progesterone Males: plasma testosterone	Firing of neurons in the hypothalamus	Small or no change	No known effect
	Endorphins	Block pain in opiate receptors in the brain	ACTH-releasing hormone	Stress	Increases in exercise > or = 70% VO_{2max}	Unknown
Posterior pituitary	Antidiuretic hormone (ADH) (vasopressin)	Decrease water loss at kidney; increases peripheral resistance	Hypothalamic neurons	Plasma volume; plasma osmolality	Increase	Attenuated response
Thyroid	Triiodothyronine (T_3); thyroxine (T_4)	Increase metabolic rate, mobilization of fuels, growth	TSH; plasma T_3 and T_4	Low T_3 and T_4	Increase in "free" T_3 and T_4	Increase turnover of T_3 and T_4 at same work rate
	Calcitonin	Decreases plasma calcium	Plasma calcium	Elevated plasma calcium	Unknown	Unknown

	Parathyroid hormone	Increase plasma calcium	Plasma calcium	Low plasma calcium	Increase	Unknown
Adrenal cortex	Cortisol	Increases gluconeogenesis, FFA mobilization, heart rate, stroke volume, and peripheral resistance	ACTH	Stress; bone breaks; heavy exercise; burns	Increases in heavy exercise; decreases in light exercise	Slight increase
	Aldosterone	Increases potassium secretion and sodium reabsorption at kidney	Plasma potassium concentration and renin-angiotensin system	Low blood pressure, low plasma volume, elevated K+	Increase	Unchanged
Adrenal medulla	Epinephrine (E) (80%); norepinephrine (NE) (20%)	Increases glycogenolysis, FFA mobilization, heart rate, stroke volume, and peripheral resistance	Output of baroreceptors; glucose receptor in hypothalamus; brain and spinal centers	Low blood pressure and blood pressure; stress and emotion	Increase	Attenuated response
Pancreas	Insulin	Increases glucose amino acid, and FFA uptake into tissues	Plasma glucose and amino acid concentration; autonomic nervous system	Elevated plasma glucose and amino acid concentration; decreased E and NE	Decrease	Attenuated response
Testes	Testosterone	Protein synthesis; secondary sex characteristics	FSH and LH (ICSH)	Increased FSH and LH	Small increase	Resting levels decreased
Ovaries	Estrogens and progesterone	Fat deposition; secondary sex characteristics; ovum development	FSH and LH	Increased FSH and LH	Small increase	Resting levels may be decreased in trained women

Endocrine Responses to Resistance Exercise

Hormones play a crucial role in protein synthesis and degradation processes that are part of muscle adaptations to resistance exercise. Anabolic hormones promote tissue building and contribute to various

aspects of muscle remodeling. These hormones include testosterone, insulin, insulin-like growth factors (IGFs), and thyroid hormone. These also aid in hypertrophy and inhibit catabolic hormones such as cortisol and progesterone that cause muscle protein breakdown. Resistance training induces significant hormonal changes essential for muscle adaptations. Changes in acute muscular force, power generation, tissue growth, and remodeling would not be possible without these hormonal changes. The short-term effects of resistance training on anabolic hormone release depend on the type of stimulus. Studies have shown that intensity, volume, the amount of muscle mass targeted, recovery, and training frequency are critical elements that stimulate muscle and tissue remodeling [11]. Long-term adaptations in these hormones are minimal compared to acute changes but are also related to the intensity and volume of training [12]. The main anabolic and catabolic hormones of interest during and following resistance training are discussed below.

Acute Hormonal Response to Resistance Training

The acute hormonal response to resistance training is more critical to tissue growth and remodeling than chronic changes in resting hormone concentrations. Anabolic hormones such as testosterone and growth hormone (GH) have been shown to elevate for 15-30 minutes post-resistance exercise when an adequate stimulus is achieved [13]. High volumes of training at moderate to high intensities, short rest intervals, and targeting large muscle groups produce the greatest acute hormonal elevations in testosterone, GH, and cortisol compared to low-volume, high-intensity protocols with long rest intervals. Testosterone targets include augmentation of hormonal mechanisms, such as stimulating GH and IGF-1, and interacting with receptors on neurons and neurotransmitter release. GH encourages muscle growth through protein synthesis and aids in energy generation by increasing free fatty acid mobilization and gluconeogenesis. Studies have shown inconsistent results in chronic resting levels of testosterone and GH, with most showing no change following long-term training protocols [14].

11. Kraemer WJ, Ratamess NA, Hormonal Responses and Adaptations to Resistance Exercise and Training. Review Article. Sports Medicine, 2005. 35(4): p. 339-361.

12. Kraemer WJ, Ratamess NA, Hormonal Responses and Adaptations to Resistance Exercise and Training. Review Article. Sports Medicine, 2005. 35(4): p. 339-361.

13. Kraemer WJ, Ratamess NA, Hormonal Responses and Adaptations to Resistance Exercise and Training. Review Article. Sports Medicine, 2005. 35(4): p. 339-361.

14. Kraemer WJ, Ratamess NA, Hormonal Responses and Adaptations to Resistance Exercise and Training. Review Article. Sports Medicine, 2005. 35(4): p. 339-361.

Insulin and Insulin-Like Growth Factor-1 (IGF-1)

Insulin and IGF-1 are critical anabolic hormones for skeletal muscle growth. Insulin significantly affects muscle protein synthesis when adequate amino acids are available, helping to reduce protein catabolism. Without protein and carbohydrate supplementation, insulin concentrations decrease during acute resistance exercise as serum concentrations parallel changes in blood glucose levels. Research indicates that supplementation before or during resistance exercise is beneficial for maximizing protein synthesis and muscle hypertrophy.

IGFs are small polypeptide hormones secreted by the liver in response to GH-stimulated DNA synthesis. Their main role is to increase protein synthesis following resistance training, resulting in muscle hypertrophy. Recent evidence suggests that IGF-1 increases gene and protein expression due to the stretch and tension associated with resistance training. However, the response is delayed until GH-stimulated synthesis and secretion from the liver occur, with peak values not reached until 16-28 hours post-GH release [15]. Thus, the short-term responses of IGF-1 remain unclear. Chronically, training volume and intensity are important for chronic resting IGF-1 adaptations.

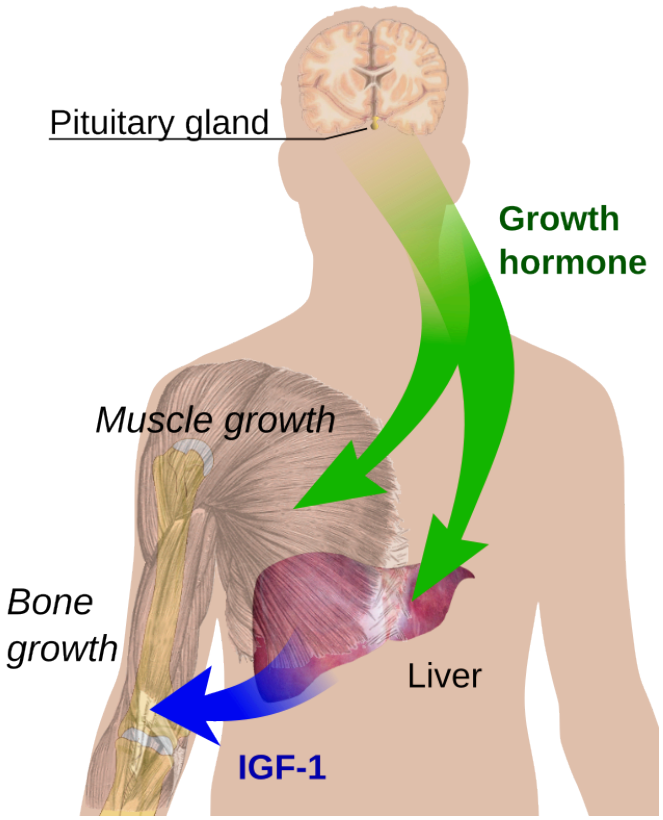


Figure 11.13 Growth Hormone Response in the Liver. The release of growth hormones stimulates the liver to produce insulin-like growth factor 1 (IGF-1), which promotes bone and muscle growth.

Catecholamines

Catecholamines are critical for force production, muscle contraction rate, energy liberation during exercise, and can affect other hormones such as testosterone. Acute exercise increases plasma concentrations of epinephrine (E), norepinephrine (NE), and dopamine. Significant elevations in plasma E and NE have also been observed before exercise, demonstrating an anticipatory or emotional response. Chronic adaptations to catecholamine release remain unclear, but it is suggested that training reduces the

15. Kraemer WJ, Ratamess NA, Hormonal Responses and Adaptations to Resistance Exercise and Training. Review Article. Sports Medicine, 2005. 35(4): p. 339-361.

catecholamine response to resistance exercise.

Glucocorticoids

Glucocorticoids are released from the adrenal cortex in response to the stress of resistance exercise, with cortisol accounting for 95% of this activity. Cortisol has catabolic functions that have greater effects on type II muscle fibers [16]. In peripheral tissues, cortisol stimulates lipolysis in adipose cells, increases protein degradation, and decreases protein synthesis in muscle cells, resulting in a greater release of lipids and amino acids into circulation. Several studies have shown significant elevations in cortisol and adrenocorticotropic hormone (ACTH) during acute resistance exercise in both men and women [17].

A summary of the acute and chronic changes in important anabolic and catabolic hormone concentrations targeted during resistance exercise can be found in Table 11.2.

Table 11.2 Effects of Resistance Training on Acute and Chronic Changes in Notable Anabolic and Catabolic Hormones. This table summarizes the impact of resistance training on the acute and chronic changes in key anabolic hormones, such as testosterone and growth hormone, and catabolic hormones, such as cortisol. It highlights how different training protocols can influence hormone levels immediately after exercise and over prolonged periods, contributing to muscle growth, strength, and overall metabolic health.

Hormone	Acute response	Chronic response
Testosterone	Increase in men, no change or elevation in women	No change or inconsistent results
Growth Hormone	Increases in both sexes	No change
Cortisol	Increases in both sexes	No change or inconsistent results
IGF-1	No change	Increases with high volumes and intensities
Insulin	Decreases without supplementation	No change
Catecholamines (Epinephrine, Norepinephrine, Dopamine)	Increase	Unclear

Resistance training induces a complex array of hormonal changes that are crucial for muscle hypertrophy, force production, and energy liberation. Research indicates that the short-term effects of resistance training

16. Kraemer WJ, Ratamess NA, Hormonal Responses and Adaptations to Resistance Exercise and Training. Review Article. Sports Medicine, 2005. 35(4): p. 339-361.

17. Kraemer WJ, Ratamess NA, Hormonal Responses and Adaptations to Resistance Exercise and Training. Review Article. Sports Medicine, 2005. 35(4): p. 339-361.

are influenced by factors such as intensity, volume, the amount of muscle mass targeted, recovery, and training frequency. These elements are essential for stimulating muscle and tissue remodeling. While long-term hormonal adaptations are minimal, they are closely related to the volume and intensity of training. Understanding these hormonal responses is key to optimizing resistance training outcomes.

Chapter Summary

This chapter explored the intricate relationship between exercise and the endocrine system, emphasizing the roles of various hormones in maintaining homeostasis and facilitating muscle adaptations. Key points include:

- **Introduction to Exercise and Homeostasis:** Exercise disrupts homeostasis, prompting acute and chronic changes regulated by the nervous and endocrine systems. Hormones play a vital role in mobilizing fuel, stimulating protein synthesis, and initiating muscle hypertrophy.
- **Categories of Hormones:** Hormones are classified into amino acid derivatives, peptides/proteins, and steroid hormones. Their chemical makeup influences their transport in the blood and interaction with tissues.
- **Mechanisms of Hormone Action:** Hormones modify cellular activity through altering DNA activity, membrane transport, and activating second messenger proteins. Examples include insulin's role in glucose uptake and the G protein-coupled receptor mechanism.
- **Secretion of Hormones During Exercise:** The chapter highlighted the endocrine glands most affected by exercise, including the hypothalamus, pituitary gland, thyroid, parathyroid glands, and pancreas. Hormonal regulation during exercise involves complex feedback mechanisms to maintain plasma glucose and calcium levels.
- **Adrenal Glands:** The adrenal medulla and cortex secrete hormones like epinephrine, norepinephrine, cortisol, and aldosterone, which are crucial for stress response, metabolism, and maintaining plasma volume during exercise.
- **Testes and Ovaries:** Testosterone and estrogens are essential for reproductive function and influence exercise performance. The chapter discussed their roles in muscle hypertrophy, secondary sex characteristics, and the impact of menstrual cycle irregularities on bone health.
- **Endocrine Responses to Resistance Exercise:** Resistance training induces significant hormonal changes, particularly in anabolic hormones like testosterone, GH, insulin, and IGF-1, which are critical for muscle growth and remodeling. The chapter also covered the role of catecholamines and glucocorticoids in exercise. Resistance training elicits hormonal changes essential for muscle hypertrophy, force production, and energy liberation. Short-term effects depend on training intensity, volume, muscle mass targeted, recovery, and frequency, while long-term adaptations are minimal but

related to training volume and intensity.

Understanding these hormonal responses is key to optimizing exercise performance and achieving desired training outcomes.

Scholarly Questions

1. How does exercise act as a stressor on the body, and what are the acute and chronic changes it induces?
2. What roles do the nervous and endocrine systems play in maintaining homeostasis during exercise?
3. What are the three classes of hormones based on their chemical makeup, and how does this affect their transport and interaction with tissues?
4. How do steroid hormones differ from peptide/protein hormones in terms of their mechanism of action?
5. Describe the process by which insulin facilitates glucose uptake in cells.
6. Explain the G protein-coupled receptor mechanism and its significance in hormone action.
7. Which endocrine glands are most affected by exercise, and what hormones do they secrete?
8. How do changes in plasma volume and osmolality during exercise influence hormone secretion?
9. What are the primary hormones secreted by the adrenal medulla and cortex, and what are their roles during exercise?
10. How does the renin-angiotensin-aldosterone system help maintain plasma volume during exercise?
11. What are the functions of testosterone and estrogens in the body, and how do they influence exercise performance?
12. Discuss the impact of menstrual cycle irregularities on bone health in female athletes.
13. How do anabolic hormones like testosterone, GH, insulin, and IGF-1 contribute to muscle hypertrophy and remodeling during resistance training?
14. What are the acute and chronic hormonal responses to resistance training, and how do they differ?
15. Why is the acute hormonal response to resistance training more critical than chronic changes in resting hormone concentrations?
16. How do catecholamines and glucocorticoids influence exercise performance and muscle

adaptation?

GLOSSARY OF TERMS

A-band

The dark region of a sarcomere that spans the entire length of thick (myosin) filaments, including areas where they overlap with thin (actin) filaments.

A-I junction

The region within a sarcomere where the A band (containing thick myosin filaments) meets the I band (containing thin actin filaments).

absolute VO^2

The total volume of oxygen consumed by the body per unit of time, expressed in liters per minute (L/min), without adjusting for body weight.

acclimation

The process by which an individual organism adjusts to a change in its environment—such as temperature, altitude, or humidity—over a short period of time.

acclimatization

The process by which an organism adjusts to changes in its environment over time, improving its ability to function under new environmental conditions.

acidosis

A physiological condition characterized by an excessive accumulation of hydrogen ions (H^+) in body fluids, leading to a decrease in blood pH below the normal range (7.35–7.45).

actin

A globular protein that plays a central role in the structure and function of muscle cells and many other types of cells.

action potential

A rapid, temporary change in the electrical membrane potential of a neuron or muscle cell that allows the transmission of signals along the cell membrane. It occurs when a stimulus causes the membrane potential to reach a threshold, triggering the opening of voltage-gated ion channels. This results in a sequence of depolarization (influx of sodium ions) and repolarization (efflux of potassium ions), followed by a return to the resting potential.

adenosine diphosphate (ADP)

A nucleotide composed of: adenine (a nitrogenous base), ribose (a five-carbon sugar), and two phosphate groups.

adenosine monophosphate (AMP)

A nucleotide composed of three components: adenine (a nitrogenous base), ribose (a five-carbon sugar), and one phosphate group.

adenosine triphosphate (ATP)

The primary energy carrier in all living organisms. It is a nucleotide composed of: adenine (a nitrogenous base), ribose (a five-carbon sugar), and three phosphate groups linked by high-energy bonds.

adrenal cortex

The outer region of the adrenal gland, responsible for producing steroid hormones. It consists of three zones: the zona glomerulosa (produces aldosterone), zona fasciculata (produces cortisol), and zona reticularis (produces androgens). These hormones regulate metabolism, immune function, blood pressure, and sexual development.

adrenal glands

A pair of endocrine glands located above each kidney. Each adrenal gland consists of two distinct regions: the adrenal cortex, which produces steroid hormones such as cortisol, aldosterone, and androgens; and the adrenal medulla, which secretes catecholamines like adrenaline (epinephrine) and noradrenaline (norepinephrine). These hormones help regulate metabolism, immune response, blood pressure, and the body's response to stress.

adrenal medulla

The inner region of the adrenal gland, responsible for producing and secreting catecholamines, primarily

epinephrine (adrenaline) and norepinephrine (noradrenaline). These hormones are released in response to stress and help initiate the "fight-or-flight" response by increasing heart rate, blood pressure, and energy availability. The adrenal medulla functions as part of the sympathetic nervous system.

adrenocorticotrophic hormone (ACTH)

A peptide hormone produced and secreted by the anterior pituitary gland in response to corticotropin-releasing hormone (CRH) from the hypothalamus. ACTH stimulates the adrenal cortex, particularly the zona fasciculata, to produce and release glucocorticoids, primarily cortisol.

aerobic metabolism

The process of generating ATP (energy) through the oxidation of carbohydrates, fats, and, to a lesser extent, proteins in the presence of oxygen.

aldosterone

A steroid hormone produced by the zona glomerulosa of the adrenal cortex. Aldosterone plays a key role in maintaining blood pressure and electrolyte balance by promoting sodium reabsorption and potassium excretion in the kidneys. Its release is primarily stimulated by angiotensin II, elevated potassium levels, and ACTH.

all-or-none principle

A fundamental property of excitable cells stating that once the threshold stimulus is reached, an action potential is generated and propagated along the membrane at full amplitude without decreasing in size. If the stimulus does not reach threshold, no action potential occurs.

allosteric enzymes

Enzymes whose activity is regulated by the binding of molecules (called effectors or modulators) at a site other than the active site, known as the allosteric site. This binding causes a conformational change in the enzyme, which can either increase (activation) or decrease (inhibition) its catalytic activity.

alpha adrenergic receptors (α)

A class of G protein-coupled receptors that respond to catecholamines such as norepinephrine and epinephrine. These receptors are primarily involved in vasoconstriction, pupil dilation, and other sympathetic nervous system responses.

alveolar macrophage

Specialized immune cells located within the alveoli of the lungs. They play a critical role in the respiratory system's defense by engulfing and digesting airborne particles, pathogens, and cellular debris through a process called phagocytosis.

alveoli

Tiny, balloon-like air sacs located at the ends of the bronchioles in the lungs.

amino acids

Organic molecules that serve as the building blocks of proteins.

anabolism

The synthesis of complex molecules from simpler ones, which requires energy.

anaerobic metabolism

The process of generating energy (ATP) without the use of oxygen, primarily through the breakdown of glucose or glycogen.

androgens

A group of steroid hormones that regulate the development and maintenance of male characteristics. Although produced in greater amounts by the testes, androgens such as testosterone are also secreted by the adrenal cortex and ovaries. They influence muscle mass, libido, and secondary sexual traits.

angiotensin I

An inactive precursor formed when renin cleaves angiotensinogen. Angiotensin I is converted into the active hormone angiotensin II by the enzyme angiotensin-converting enzyme (ACE), which plays a key role in blood pressure regulation.

angiotensin II

A potent vasoconstrictor formed from angiotensin I through the action of angiotensin-converting enzyme (ACE). Angiotensin II increases blood pressure by narrowing blood vessels and stimulates the release of aldosterone from the adrenal cortex. It also promotes thirst and the release of antidiuretic hormone (ADH), contributing to fluid retention and blood pressure regulation.

angiotensin-converting enzyme (ACE)

An enzyme primarily found in the lungs and vascular endothelium that converts angiotensin I into angiotensin II, a potent vasoconstrictor. ACE also degrades bradykinin, a vasodilator, thereby contributing to increased blood pressure.

angiotensinogen

A plasma protein produced by the liver that serves as the precursor to angiotensin I. When acted upon by renin, angiotensinogen is converted into angiotensin I, beginning a cascade that leads to vasoconstriction and increased blood pressure.

anterior pituitary (adenohypophysis)

A portion of the pituitary gland that produces hormones such as growth hormone (GH), thyroid-stimulating hormone (TSH), adrenocorticotropic hormone (ACTH), follicle-stimulating hormone (FSH), luteinizing hormone (LH), and prolactin.

antidiuretic hormone (ADH)

Also known as vasopressin, it is a peptide hormone produced by the hypothalamus and released by the posterior pituitary gland. It regulates water balance in the body by increasing water reabsorption in the kidneys, thereby reducing urine output and conserving body fluids.

arterial-(mixed blood) venous O2 difference (a-vO2 difference)

The difference in oxygen content between arterial blood and mixed venous blood, reflecting the amount of oxygen extracted by tissues during circulation. It is a key indicator of tissue oxygen utilization and, along with cardiac output, determines oxygen consumption according to the Fick principle.

arteries

Blood vessels that carry oxygenated blood away from the heart to the tissues and organs of the body. They have thick, elastic walls composed of three layers (tunica intima, tunica media, and tunica externa) that allow them to withstand and regulate high blood pressure generated by the heart's contractions.

arterioles

Small-diameter blood vessels that branch from arteries and lead to capillaries. They play a critical role in regulating blood flow and blood pressure by adjusting their diameter through vasoconstriction and vasodilation, which control resistance within the circulatory system.

ATPase

An enzyme that catalyzes the hydrolysis of ATP (adenosine triphosphate) into ADP (adenosine diphosphate) and inorganic phosphate (Pi), releasing energy that can be used to power various cellular processes.

atrioventricular (AV) node

A cluster of specialized cardiac cells located in the interatrial septum near the tricuspid valve. The AV node receives electrical impulses from the sinoatrial (SA) node and delays them briefly before transmitting them to the bundle of His and Purkinje fibers. This delay ensures that the atria contract and empty blood into the ventricles before ventricular contraction begins.

atrioventricular (AV) valves

Heart valves located between the atria and ventricles that prevent backflow of blood into the atria during ventricular contraction. There are two AV valves: the tricuspid valve on the right side of the heart and the bicuspid (mitral) valve on the left side.

autonomic nervous system

The division of the peripheral nervous system that regulates involuntary physiological functions, including heart rate, blood pressure, digestion, and respiratory rate. The ANS operates largely without conscious control and is divided into three branches: the sympathetic nervous system (prepares the body for "fight or flight"), the parasympathetic nervous system (promotes "rest and digest" functions), and the enteric nervous system (controls gastrointestinal activity).

beta adrenergic receptors (β)

A class of G protein-coupled receptors that respond to catecholamines such as epinephrine and norepinephrine. These receptors are involved in the regulation of heart rate, smooth muscle relaxation, and metabolic processes.

beta oxidation

The catabolic process by which fatty acids are broken down in the mitochondria (or peroxisomes) to generate acetyl-CoA, which then enters the TCA cycle for energy production.

bioenergetics

The study of how energy flows through living systems, particularly how organisms acquire, convert, store, and use energy to perform biological work.

biomechanics

The mechanics of biological and especially muscular activity (as in locomotion or exercise).

blood pressure

The force exerted by circulating blood on the walls of blood vessels, typically measured in the arteries.

Bohr effect

Describes how changes in blood pH and carbon dioxide concentration influence hemoglobin's affinity for oxygen. Specifically, a decrease in pH (more acidic) or an increase in CO_2 causes hemoglobin to release oxygen more readily—a rightward shift in the oxygen-hemoglobin dissociation curve.

Boyle's Law

A fundamental principle in gas physics that describes the inverse relationship between the pressure and volume of a gas at constant temperature.

breathing frequency (f)

The number of breaths taken per minute.

bronchial tree

Refers to the branching system of airways within the lungs that conducts air from the trachea to the alveoli

bundle branches

One of the two main pathways (right and left bundle branches) that conduct electrical impulses from the atrioventricular (AV) bundle (bundle of His) down the interventricular septum toward the Purkinje fibers. These branches ensure coordinated contraction of the right and left ventricles by rapidly transmitting the action potential to the ventricular myocardium.

bundle of His

A specialized group of cardiac muscle fibers located in the interventricular septum that conducts electrical impulses from the atrioventricular (AV) node to the right and left bundle branches. The bundle of His is a critical component of the heart's conduction system, ensuring that the ventricles receive the signal to contract after the atria have contracted.

C-protein

A structural and regulatory protein located in the thick filament region of the sarcomere, near the M-line. It helps stabilize thick filaments and modulates cross-bridge formation between actin and myosin, influencing the speed and strength of muscle contraction.

calorie

A unit of energy commonly used to quantify the amount of energy provided by food and expended by the body. In nutrition, the term "calorie" typically refers to a kilocalorie (kcal), which equals 1,000 small calories and represents the amount of energy required to raise the temperature of 1 kilogram of water by 1°C.

capillaries

The smallest and thinnest blood vessels in the circulatory system, forming networks that connect arterioles to venules. Their walls consist of a single layer of endothelial cells, allowing efficient exchange of gases, nutrients, and waste products between blood and surrounding tissues.

carbohydrates

Organic molecules composed of carbon (C), hydrogen (H), and oxygen (O), typically in a ratio close to 1:2:1. They are one of the main classes of biomolecules and serve as a primary source of energy for living organisms.

carbon dioxide production (VCO^2)

The volume of carbon dioxide generated by the body per unit of time, typically expressed in liters per minute (L/min). VCO_2 reflects the rate of metabolic processes that produce CO_2 as a byproduct.

cardiac cycle

The sequence of mechanical and electrical events that occur during one complete heartbeat, including

atrial contraction (atrial systole), ventricular contraction (ventricular systole), and relaxation of all chambers (diastole).

cardiac muscle

A specialized type of striated, involuntary muscle found only in the walls of the heart. Cardiac muscle fibers are branched, interconnected, and typically contain a single nucleus.

cardiac output (Q)

The volume of blood pumped by a ventricle per minute, typically expressed in liters per minute (L/min). It is calculated as the product of stroke volume (SV) and heart rate (HR): $Q=SV \times HR$.

catabolism

The breakdown of molecules to release energy.

catecholamines

A group of related hormones and neurotransmitters that include epinephrine, norepinephrine, and dopamine. These compounds are derived from the amino acid tyrosine and are involved in the body's response to stress, regulating heart rate, blood pressure, and metabolism.

central fatigue

The reduction in voluntary muscle activation caused by processes within the central nervous system (CNS), rather than within the muscle itself. It limits the ability to fully recruit motor units during sustained or intense exercise.

central nervous system (CNS)

The part of the nervous system consisting of the brain and spinal cord. The CNS integrates sensory information, processes signals, and coordinates responses by controlling voluntary and involuntary activities throughout the body.

closed circuit spirometry

A method of measuring oxygen consumption (VO_2) in which the subject breathes from a sealed system containing a known volume of oxygen. The system absorbs exhaled carbon dioxide, and the decrease in oxygen volume over time is used to calculate metabolic rate.

coenzymes

Small, organic, non-protein molecules that assist enzymes in catalyzing biochemical reactions.

concentric muscle action

A type of isotonic muscle contraction in which the muscle shortens while generating force, typically occurring when lifting a load or moving against resistance.

conducting zone

The portion of the respiratory system responsible for transporting air to the lungs but not directly involved in gas exchange. It includes the nose, nasal cavity, pharynx, larynx, trachea, bronchi, and bronchioles (up to the terminal bronchioles). These structures serve to warm, humidify, and filter incoming air, ensuring that it reaches the respiratory zone in optimal condition for gas exchange.

conversion of pyruvate to acetyl-CoA

A critical metabolic step that links glycolysis to the TCA cycle (citric acid cycle; Krebs cycle) in aerobic respiration. This process occurs in the mitochondrial matrix.

cortisol

A glucocorticoid hormone produced by the zona fasciculata of the adrenal cortex. Cortisol plays a vital role in the body's response to stress by increasing blood glucose levels, enhancing metabolism of fats, proteins, and carbohydrates, and suppressing inflammation and immune responses. Its secretion is regulated by the hypothalamic-pituitary-adrenal (HPA) axis and follows a diurnal rhythm, peaking in the early morning.

coupled reactions

Pairs of chemical reactions that occur together, where one reaction releases energy (exergonic) and the other requires energy (endergonic).

creatine phosphate (CrP)

Also called phosphocreatine, it is a high-energy compound found primarily in muscle cells. It serves as a rapid energy reserve for the regeneration of ATP (adenosine triphosphate) during short bursts of intense activity, such as sprinting or heavy lifting.

cross-bridge cycling

The repetitive sequence of events during muscle contraction in which myosin heads bind to actin, perform a power stroke, release, and reset.

Dalton's Law

Also known as the Law of Partial Pressures, this states that the total pressure exerted by a mixture of gases is equal to the sum of the partial pressures of each individual gas in the mixture.

depolarization

A phase in which the membrane potential of a cell becomes less negative (moves toward zero) compared to the resting membrane potential.

desmin

An intermediate filament protein found in muscle cells that forms part of the cytoskeleton. It links adjacent myofibrils at the Z-disks and connects them to the cell membrane, providing structural integrity and maintaining alignment during contraction.

diaphragm

A dome-shaped sheet of skeletal muscle that separates the thoracic cavity from the abdominal cavity. It plays a crucial role in respiration

diastole

The phase of the cardiac cycle during which the heart muscle relaxes after contraction, allowing the chambers (atria and ventricles) to fill with blood.

direct calorimetry

A method of measuring energy expenditure by directly quantifying the amount of heat produced by the body in a controlled environment, such as a calorimeter chamber.

disaccharides

Two monosaccharides linked together (e.g., sucrose, lactose).

eccentric muscle action

A type of isotonic muscle contraction in which the muscle lengthens while generating force, typically occurring when lowering a load or resisting an external force.

ejection fraction (EF)

The percentage of blood ejected from a ventricle during systole relative to its end-diastolic volume (EDV). EF is calculated as (stroke volume/EDV) × 100% and is a key indicator of ventricular function; normal values for the left ventricle are typically 50–70%.

electrical potentials

Differences in electric charge across a membrane or between two points, creating a voltage that can drive the movement of ions.

electrocardiogram (ECG)

A diagnostic test that records the electrical activity of the heart over time using electrodes placed on the skin. The ECG produces a waveform with characteristic components (P wave, QRS complex, and T wave) that represent atrial depolarization, ventricular depolarization, and ventricular repolarization, respectively. It is commonly used to assess heart rhythm, detect arrhythmias, and evaluate cardiac health.

electron transport chain (ETC)

A series of protein complexes and associated molecules located in the inner mitochondrial membrane that drive oxidative phosphorylation, the final stage of aerobic respiration.

end-diastolic volume (EDV)

The volume of blood in a ventricle at the end of diastole, just before ventricular contraction. EDV reflects the heart's preload and is a key determinant of stroke volume and cardiac output according to the Frank–Starling mechanism.

end-systolic volume (ESV)

The volume of blood remaining in a ventricle at the end of systole, after ventricular contraction. ESV reflects the heart's afterload and contractility and, together with end-diastolic volume, determines stroke volume and ejection fraction.

endergonic (or endothermic) reactions

Chemical reactions that require an input of free energy to proceed.

endocardium

The innermost layer of the heart wall, composed of a thin layer of endothelial cells and connective tissue. It lines the heart chambers and covers the heart valves, providing a smooth surface that minimizes friction and reduces the risk of blood clot formation during cardiac function.

endomysium

A delicate layer of connective tissue that surrounds each individual muscle fiber within a fasciculus.

endurance training

A type of physical activity typically involving aerobic activities, aimed at improving the efficiency and capacity of the cardiovascular and respiratory systems to sustain prolonged physical activity.

energy expenditure (EE)

The total amount of energy, measured in calories or kilojoules, that an organism uses to maintain basic physiological functions, perform physical activity, and process food. EE is typically divided into three components: basal metabolic rate (BMR), the thermic effect of food (TEF), and energy used during physical activity.

entropy

A measure of disorder or randomness in a system. In thermodynamics and biology, it reflects how energy is distributed and how much of it is available to do useful work.

enzymes

Biological catalysts, typically proteins (and sometimes RNA molecules called ribozymes), that speed up chemical reactions in living organisms without being consumed in the process.

epicardium

The outermost layer of the heart wall, forming part of the pericardium. It consists of a thin layer of connective tissue and fat covered by mesothelium, providing a protective layer and reducing friction between the heart and surrounding structures during contraction.

epimysium

A dense layer of irregular connective tissue that surrounds an entire skeletal muscle.

epinephrine (E)

Also known as adrenaline, epinephrine is a catecholamine hormone and neurotransmitter produced by the adrenal medulla. It plays a central role in the body's "fight-or-flight" response by increasing heart rate, dilating airways, enhancing blood flow to muscles, and promoting the breakdown of glycogen to glucose for quick energy.

ergometry

The measurement of work output during controlled exercise, typically using specialized equipment called ergometers (e.g., cycle ergometer, treadmill). Ergometry is used to assess physical performance, energy expenditure, and physiological responses under standardized conditions.

estradiol (E2)

The most potent and predominant form of estrogen in non-pregnant, reproductive-age females. Produced mainly by the ovaries, estradiol plays a central role in regulating the menstrual cycle, maintaining reproductive tissues, and supporting bone and cardiovascular health.

estriol (E3)

The weakest of the three major estrogens, estriol is produced in significant amounts during pregnancy by the placenta. It plays a role in maintaining pregnancy and preparing the body for childbirth, but has minimal effects outside of gestation.

estrogens

A class of steroid hormones primarily produced by the ovaries, with smaller amounts secreted by the adrenal glands and other tissues. Estrogens regulate the development of female secondary sexual characteristics, reproductive function, and menstrual cycle. The most prominent estrogen is estradiol.

estrone (E1)

A weaker form of estrogen that is primarily produced in adipose (fat) tissue and the adrenal glands. Estrone becomes the dominant estrogen after menopause and can be converted into estradiol or estriol depending on physiological needs.

excess post-exercise oxygen consumption

The elevated oxygen uptake that persists after exercise has ended, compared to resting levels. It reflects the body's effort to restore physiological balance and recover from the metabolic stress of exercise.

excitation-contraction coupling

The physiological process linking the electrical excitation of a muscle fiber (action potential) to its mechanical contraction. It involves calcium release from the sarcoplasmic reticulum, which enables actin–myosin interaction and sarcomere shortening.

excitatory postsynaptic potential (EPSP)

Small, temporary depolarizations of the postsynaptic membrane that occur when excitatory neurotransmitters bind to receptors, causing positively charged ions (such as Na^+) to enter the cell. EPSPs increase the likelihood that the postsynaptic neuron will reach threshold and generate an action potential.

excitatory postsynaptic potentials (EPSP)

Temporary depolarizations of the postsynaptic membrane caused by the flow of positively charged ions (typically sodium, Na^+) into the neuron following the activation of excitatory neurotransmitter receptors. EPSPs increase the likelihood that the postsynaptic neuron will reach the threshold to fire an action potential. They are graded potentials, meaning their strength depends on the amount of neurotransmitter released and the number of receptors activated.

exercise and sport physiology

A field that investigates the effect of exercise on the function and structure of the body.

exercise efficiency

The ratio of mechanical work output to the total energy expended during exercise, usually expressed as a percentage. It reflects how effectively the body converts metabolic energy into external work. Higher efficiency means less energy is wasted as heat for a given workload.

exercise physiology

The study of how the body reacts to physical exercise, in both the long and short term, and how the body adapts to ongoing exercise and any changes to a routine.

exercise science

A multidisciplinary field that explores the science of movement and the body's responses and adaptations to physical activity. It encompasses various sub-disciplines, including Biomechanics, Exercise and Sport Physiology, Kinesiology, Sports Psychology, and Sports Sociology.

exergonic (or exothermic) reactions

Chemical reactions that release free energy into the surroundings.

external intercostal muscles

A group of skeletal muscles located between the ribs that play a key role in the mechanics of breathing, particularly during inhalation

external oblique

A broad, flat muscle located on the lateral and anterior parts of the abdomen. It contributes to forced exhalation by compressing the abdominal cavity, which pushes the diaphragm upward and helps expel air from the lungs.

external respiration

The exchange of gases between the air in the alveoli of the lungs and the blood in the pulmonary capillaries.

fascia

A continuous band or sheet of connective tissue, primarily composed of collagen, that surrounds, stabilizes, and separates muscles, organs, and other internal structures.

fasciculi

Bundles of skeletal muscle fibers grouped together within a muscle, surrounded by a connective tissue sheath called the perimysium.

fats

A type of lipid, a class of hydrophobic (water-insoluble) molecules primarily composed of carbon (C), hydrogen (H), and a small amount of oxygen (O). They serve as a major source of long-term energy storage, provide insulation and protection for organs, and are essential components of cell membranes.

fatty acids

A carboxylic acid with a long hydrocarbon chain, which can be either saturated (no double bonds) or unsaturated (one or more double bonds). Fatty acids are the building blocks of many lipids, including triglycerides and phospholipids, and play a critical role in energy storage, membrane structure, and signaling.

Fick equation

A principle used to calculate oxygen consumption (VO2) based on cardiac output (Q) and the arterial–venous oxygen difference (a-vO_2 difference).

Fick's Law of Diffusion

This describes the rate at which a gas moves across a membrane. It states that the rate of gas transfer is directly proportional to the surface area of the membrane and the difference in partial pressures across it, and inversely proportional to the thickness of the membrane.

flavin adenine dinucleotide

A redox-active coenzyme derived from riboflavin (vitamin B_2).

Frank-Starling law

A physiological principle stating that the strength of ventricular contraction increases with greater end-diastolic volume (EDV), within physiological limits. This relationship ensures that the heart pumps out the volume of blood it receives, maintaining balance between venous return and cardiac output.

free energy

The amount of energy in a system that is available to do useful work. The most commonly used form is Gibbs Free Energy (G), defined by the equation: $\Delta G=\Delta H-T\Delta S$
Where:
ΔG = change in free energy
ΔH = change in enthalpy (total energy)
T = temperature in Kelvin
ΔS = change in entropy (disorder)

fructose

A simple sugar (monosaccharide) with the molecular formula $C_6H_{12}O_6$, like glucose, but with a different structural arrangement.

G protein

Guanine nucleotide-binding proteins, are molecular switches that play a critical role in transmitting signals from cell surface receptors to intracellular effectors. They are activated when a signaling molecule (e.g., a hormone or neurotransmitter) binds to a G protein-coupled receptor (GPCR), causing the G protein to exchange GDP for GTP. This activation triggers downstream signaling pathways that regulate various cellular responses.

G-actin

A monomeric form of actin that polymerizes to form filamentous actin (F-actin) in muscle and non-muscle cells.

gain

The precision with which a control system maintains homeostasis.

glucagon

A peptide hormone secreted by the alpha cells of the pancreas. Glucagon raises blood glucose levels by stimulating the liver to convert stored glycogen into glucose (glycogenolysis) and to produce glucose from non-carbohydrate sources (gluconeogenesis). It acts as a counter-regulatory hormone to insulin.

glucocorticoids

Steroid hormones produced by the adrenal cortex that influence metabolism, immune response, and stress adaptation. The primary glucocorticoid is cortisol, which increases blood glucose levels, suppresses inflammation, and helps the body respond to physical and emotional stress.

gluconeogenesis

The metabolic pathway that synthesizes glucose from non-carbohydrate precursors, ensuring a continuous supply of glucose during fasting, prolonged exercise, or low-carbohydrate intake. It primarily occurs in the liver (and to a lesser extent in the kidney cortex).

glucose

A simple sugar (monosaccharide) with the molecular formula $C_6H_{12}O_6$.

glycogen

The primary storage form of glucose in animals and humans, mainly found in the liver (for maintaining blood glucose levels) and skeletal muscles (for energy during activity).

glycogenolysis

The biochemical process of breaking down glycogen into glucose molecules to provide energy for cellular metabolism. It primarily occurs in the liver (to maintain blood glucose levels) and skeletal muscle (to supply energy during muscle activity).

glycolysis

A metabolic pathway that breaks down glucose ($C_6H_{12}O_6$) into two molecules of pyruvate, producing a small amount of energy in the form of ATP and NADH.

Golgi tendon organs

Specialized proprioceptive sensory receptors located at the junction between muscle fibers and tendons. They detect changes in muscle tension and force rather than length. When tension becomes too high, GTOs send inhibitory signals to the spinal cord to reduce muscle contraction, protecting muscles and tendons from potential damage. They play a key role in reflexes that regulate muscle force and maintain posture.

graded potentials

Localized changes in the membrane potential of a neuron that vary in size (amplitude) depending on the strength of the stimulus. Unlike action potentials, graded potentials are not all-or-none; they can be depolarizing (excitatory) or hyperpolarizing (inhibitory) and diminish in strength as they spread from the point of origin. They occur mainly in the dendrites and cell body and play a key role in initiating action potentials when summed at the axon hillock.

growth hormone (GH)

Also known as somatotropin, is a peptide hormone secreted by the anterior pituitary gland. It plays a vital role in stimulating growth, cell reproduction, and regeneration. GH promotes the growth of bones and muscles, increases protein synthesis, and mobilizes fat stores for energy. It also influences metabolism by

increasing blood glucose levels and stimulating the production of insulin-like growth factor 1 (IGF-1) in the liver and other tissues.

H-zone

The central region of the A-band in a sarcomere that contains only thick (myosin) filaments and no thin (actin) filaments.

Haldane effect

The phenomenon where deoxygenated hemoglobin has a greater capacity to bind carbon dioxide (CO_2) than oxygenated hemoglobin. This effect facilitates the transport of CO_2 from tissues to the lungs.

health promotion

A behavioral social science that draws from the biological, environmental, psychological, physical, and medical sciences to promote health and prevent disease, disability, and premature death through education-driven voluntary behavior change activities.

heart rate variability (HRV)

The physiological variation in the time interval between consecutive heartbeats, typically measured as fluctuations in the R-R intervals on an electrocardiogram (ECG). HRV reflects autonomic nervous system activity, with higher variability generally indicating better cardiovascular health and adaptability, while reduced HRV is associated with stress, fatigue, and certain disease states.

hemoglobin

A complex iron-containing protein found in red blood cells that is essential for oxygen transport in the body

high-energy phosphate

Molecules that store and transfer energy within cells through phosphate bonds that release a large amount of free energy when hydrolyzed.

homeostasis

The process by which a biological system maintains internal stability despite changes in the external environment. It involves a dynamic balance of physiological variables—such as body temperature, pH, blood glucose levels, and water balance—within a narrow, optimal range.

hormones

Chemical messengers produced by endocrine glands and released into the bloodstream to regulate various physiological processes

hyperpolarization

A change in membrane potential that makes the inside of the cell more negative than the resting membrane potential.

hypothalamus

A small but crucial region of the brain located below the thalamus and above the pituitary gland. It serves as a major control center for the autonomic nervous system and the endocrine system, maintaining homeostasis by regulating body temperature, hunger, thirst, sleep, and emotional activity.

I-band

The light region of a sarcomere that contains only thin (actin) filaments and spans across two adjacent sarcomeres, intersected by the Z-disk.

indirect calorimetry

A method of estimating energy expenditure by measuring oxygen consumption (VO_2) and carbon dioxide production (VCO_2) during respiration. These values are used to calculate metabolic rate and substrate utilization, based on the principle that energy metabolism is linked to gas exchange.

inhibitory postsynaptic potential (IPSP)

A temporary hyperpolarization of the postsynaptic membrane that occurs when inhibitory neurotransmitters bind to receptors, causing negatively charged ions (such as Cl^-) to enter the cell or positively charged ions (such as K^+) to leave. IPSPs decrease the likelihood that the postsynaptic neuron will reach threshold and generate an action potential.

innervation ratio

The number of muscle fibers controlled by a single motor neuron within a motor unit. It reflects the degree of fine motor control: muscles requiring precise movements (e.g., eye muscles) have a low innervation ratio (few fibers per neuron), while muscles generating large, powerful movements (e.g., quadriceps) have a high innervation ratio (many fibers per neuron).

inorganic phosphate (Pi)

A free phosphate ion (PO_4^{3-}) that is not bound to an organic molecule.

insulin

A peptide hormone produced by the beta cells of the pancreatic islets (Islets of Langerhans). It plays a central role in regulating blood glucose levels by promoting the uptake of glucose into cells, especially in muscle and adipose tissue, and by stimulating glycogen synthesis in the liver.

insulin-like growth factors (IGFs)

A peptide hormone primarily produced by the liver in response to stimulation by growth hormone (GH). IGF-1 plays a key role in promoting cell growth, differentiation, and tissue repair, especially during childhood and adolescence. It mimics some of the actions of insulin and is essential for mediating many of the growth-promoting effects of GH.

intensity

How hard the body is working during physical activity.

intercalated disks

Specialized junctions between cardiac muscle cells that contain desmosomes and gap junctions. These structures provide strong mechanical attachment and allow electrical impulses to pass rapidly between cells, enabling the heart muscle to contract as a coordinated unit (functional syncytium).

internal intercostal muscles

Located between the ribs, deep to the external intercostals. They assist in forced exhalation by pulling the ribs downward and inward, which decreases the volume of the thoracic cavity and helps push air out of the lungs. These muscles are especially active during vigorous breathing or physical exertion.

internal oblique

A muscle that lies just beneath the external oblique and runs in the opposite direction. Like the external oblique, it aids in forced exhalation by compressing the abdominal contents and assisting in diaphragm elevation.

internal respiration

The exchange of gases between the blood in systemic capillaries and the body's tissues.

isokinetic muscle action

A type of muscle contraction in which the muscle changes length at a constant speed throughout the entire range of motion, typically achieved using specialized equipment that controls the velocity of movement while accommodating resistance.

isometric

A type of muscle contraction in which the muscle generates force without changing its length, resulting in no visible movement of the joint. This occurs when the force produced equals the external load, such as holding a weight stationary.

isometric muscle actions

Muscle contractions in which tension is generated without a change in muscle length, resulting in no visible joint movement. These occur when the force produced equals the external resistance, such as holding a weight in a fixed position.

isotonic

A type of muscle contraction in which the muscle changes length while producing constant tension, resulting in movement of a load. It includes concentric contractions (muscle shortens) and eccentric contractions (muscle lengthens).

kinesiology

The study of the principles of mechanics and anatomy in relation to human movement

lactate threshold (LT)

The exercise intensity at which blood lactate concentration begins to rise significantly above resting levels, typically around 2–4 $mmol \cdot L^{-1}$. It represents the point where lactate production exceeds clearance, signaling a shift toward greater reliance on anaerobic metabolism.

lipolysis

The metabolic process by which triglycerides (stored fats) are broken down into glycerol and free fatty acids. This occurs primarily in adipose tissue and is triggered when the body needs energy, such as during fasting, exercise, or low-carbohydrate intake.

luteinizing hormone (LH)

A glycoprotein hormone secreted by the anterior pituitary gland that plays a key role in regulating reproductive function.

M-line

The central region of the A-band in a sarcomere where thick (myosin) filaments are linked together by supporting proteins. It helps stabilize the arrangement of thick filaments and maintains sarcomere structure during contraction.

maximal oxygen uptake (VO2max)

The maximum rate at which an individual can consume oxygen during intense, whole-body exercise, expressed in liters per minute (L/min) or milliliters per kilogram of body weight per minute ($mL \cdot kg^{-1} \cdot min^{-1}$). It reflects the integrated capacity of the cardiovascular, respiratory, and muscular systems to deliver and utilize oxygen for energy production.

mean arterial pressure (MAP)

The average pressure in a patient's arteries during one cardiac cycle. It represents the perfusion pressure delivered to organs and tissues.

metabolic equivalent of a task (MET)

A standardized unit used to estimate the energy cost of physical activities, expressed as a multiple of resting metabolic rate. One MET is defined as the energy expenditure at rest, approximately 3.5 mL of oxygen per kilogram of body weight per minute ($mL \cdot kg^{-1} \cdot min^{-1}$). Activities are assigned MET values to indicate how many times more energy they require compared to resting conditions.

metabolic pathway

A series of interconnected biochemical reactions within a cell, where the product of one reaction serves as the substrate for the next.

metabolism

The sum of all chemical reactions that occur within a living organism to maintain life.

mineralocorticoids (aldosterone)

A class of steroid hormones produced by the adrenal cortex, primarily involved in regulating electrolyte

and fluid balance. The most well-known mineralocorticoid is aldosterone, which promotes sodium retention and potassium excretion by the kidneys, helping to maintain blood pressure and volume.

mitochondria

Membrane-bound organelles found in most eukaryotic cells, often referred to as the "powerhouses of the cell" because they produce the majority of the cell's usable energy in the form of ATP (adenosine triphosphate).

mitochondrial respiration

The series of biochemical processes that occur within the mitochondria of eukaryotic cells to produce energy in the form of ATP (adenosine triphosphate).

monosaccharides

Simple sugars (e.g., glucose, fructose).

motor division

The component of the peripheral nervous system responsible for transmitting signals from the central nervous system (CNS) to muscles and glands, initiating movement and regulating bodily functions. It is divided into the somatic nervous system (controls voluntary skeletal muscle movements) and the autonomic nervous system (controls involuntary functions such as heart rate, digestion, and glandular activity).

motor end plate

A specialized region of the muscle fiber's sarcolemma (cell membrane) at the neuromuscular junction where the motor neuron communicates with the muscle.

motor reflex

An automatic, involuntary response of a muscle or group of muscles to a specific stimulus, mediated by the nervous system without conscious control. Motor reflexes are typically organized through reflex arcs, which involve sensory receptors, afferent neurons, interneurons (in some cases), efferent neurons, and effectors. Examples include the stretch reflex (knee-jerk) and withdrawal reflex.

motor skills

Learned abilities that enable the execution of coordinated movements involving muscles and the nervous system.

motor unit

A functional unit of the neuromuscular system consisting of a single motor neuron and all the skeletal muscle fibers it innervates.

muscle contraction cycling

Also known as the cross-bridge cycle, it is the repeating sequence of events that occurs during muscle contraction at the molecular level.

muscle fatigue

The decline in the ability of a muscle to generate force or power during sustained or repeated activity. It is a complex, multifactorial phenomenon involving both peripheral and central mechanisms.

muscle fiber

A single, elongated, multinucleated cell that makes up skeletal muscle tissue. Muscle fibers contain myofibrils, which are composed of repeating units called sarcomeres—the basic contractile units of muscle.

muscle hypertrophy

An increase in the size of skeletal muscle fibers resulting from resistance training or other stimuli that promote protein synthesis and muscle growth. Hypertrophy occurs primarily through the enlargement of individual muscle fibers rather than an increase in fiber number.

muscle spindles

Specialized proprioceptive sensory receptors located within skeletal muscles that detect changes in muscle length and the rate of length change. They consist of intrafusal fibers wrapped by sensory nerve endings. When a muscle is stretched, muscle spindles send signals to the central nervous system to trigger reflexive muscle contraction (stretch reflex), helping maintain muscle tone and posture.

myocardium

The thick, muscular middle layer of the heart wall composed primarily of cardiac muscle tissue. It is

responsible for the contractile force that pumps blood throughout the body. The myocardium varies in thickness, being thickest in the left ventricle to generate the high pressure needed for systemic circulation.

myofibrils

A long, cylindrical organelle found in muscle fibers, composed of repeating units called sarcomeres that contain actin and myosin filaments.

myoglobin

A small, oxygen-binding protein found primarily in muscle tissue. Myoglobin stores and facilitates the transport of oxygen within muscle cells, enabling sustained energy production during periods of high metabolic demand. It consists of a single polypeptide chain and a heme group that binds oxygen molecules.

myomesin

A structural protein located in the M-line of the sarcomere that crosslinks thick (myosin) filaments and titin molecules. It provides mechanical stability to the sarcomere and helps maintain the alignment of thick filaments during muscle contraction.

myosin

A motor protein that plays a central role in muscle contraction and various types of cell movement.

nebulin

A large structural protein associated with thin (actin) filaments in skeletal muscle. It runs along the length of the actin filament, acting as a molecular ruler to regulate filament length and contribute to sarcomere stability.

negative feedback

A regulatory mechanism in which a change in a system triggers a response that counteracts or reduces that change, helping to maintain stability or equilibrium.

neuromuscular junction

The specialized synapse between a motor neuron and a skeletal muscle fiber where nerve impulses trigger muscle contraction. It includes the motor neuron terminal, synaptic cleft, and motor end plate, and relies on acetylcholine as the primary neurotransmitter.

nicotinamide adenine dinucleotide

A coenzyme found in all living cells that plays a critical role in redox reactions.

norepinephrine (NE)

Also called noradrenaline, norepinephrine is a catecholamine that functions both as a hormone and a neurotransmitter. It is produced by the adrenal medulla and sympathetic nerve endings. Norepinephrine increases blood pressure by constricting blood vessels and is involved in alertness, arousal, and the stress response.

normal sinus rhythm (NSR)

A heart rhythm originating from the sinoatrial (SA) node, characterized by a regular rate of 60–100 beats per minute in adults, with consistent P waves preceding each QRS complex and a normal PR interval. NSR indicates normal electrical conduction through the heart.

Ohm's law

A fundamental principle in electricity stating that the current (I) through a conductor between two points is directly proportional to the voltage (V) across the two points and inversely proportional to the resistance (R).

onset of blood lactate accumulation (OBLA)

The exercise intensity at which blood lactate concentration reaches approximately 4 $mmol \cdot L^{-1}$, marking a significant shift toward anaerobic metabolism.

open circuit spirometry

A method of measuring oxygen consumption (VO_2) and carbon dioxide production (VCO_2) in which the subject breathes ambient air, and exhaled gases are collected and analyzed.

osteoporosis

A chronic condition characterized by decreased bone mass and deterioration of bone tissue, leading to increased fragility and risk of fractures. It occurs when bone resorption outpaces bone formation, often due to aging, hormonal changes (especially reduced estrogen levels in postmenopausal women), nutritional deficiencies, or lack of physical activity.

ovaries

The female gonads that produce ova (eggs) and secrete female sex hormones, including estrogens and progesterone. Located on either side of the uterus, the ovaries contain follicles at various stages of development and are responsible for regulating the menstrual cycle, fertility, and the development of female secondary sexual characteristics.

oxygen consumption (VO^2)

The volume of oxygen used by the body per unit of time, typically expressed in liters per minute (L/min) or milliliters per kilogram per minute ($mL \cdot kg^{-1} \cdot min^{-1}$).

oxygen cost

The amount of oxygen consumed by the body to perform a specific activity or produce a given amount of work, typically expressed in milliliters of O_2 per kilogram of body weight per minute ($mL \cdot kg^{-1} \cdot min^{-1}$) or per unit of work. Oxygen cost reflects the energy demand of an activity and is commonly used to assess exercise efficiency and metabolic requirements.

oxygen debt

(Now more commonly referred to as Excess Post-Exercise Oxygen Consumption, EPOC) is the elevated oxygen uptake that persists after exercise has ended, compared to resting levels. It represents the body's effort to restore homeostasis and repay the "oxygen deficit" incurred at the start of exercise.

oxygen deficit

The difference between the oxygen required for a given exercise intensity and the actual oxygen uptake (VO_2) during the initial phase of exercise. It occurs because mitochondrial respiration takes time to fully activate, so energy demand is temporarily met by anaerobic pathways (ATP-PC system and anaerobic glycolysis).

oxygen uptake (VO2)

The rate at which the body consumes oxygen during rest or exercise, expressed in liters per minute (L/min) or milliliters per kilogram of body weight per minute ($mL \cdot kg^{-1} \cdot min^{-1}$).

oxytocin

A peptide hormone produced by the hypothalamus and released by the posterior pituitary gland. It plays a key role in reproductive and social behaviors.

P wave

The first deflection on an electrocardiogram (ECG) representing atrial depolarization, which triggers atrial contraction. It reflects the electrical activity as the impulse originates in the sinoatrial (SA) node and spreads through the atria.

pancreas

A dual-function gland located in the upper abdomen, behind the stomach. It has both exocrine and endocrine roles.

parasympathetic nervous system

A branch of the autonomic nervous system that promotes "rest and digest" functions, conserving energy and maintaining homeostasis during restful states. It decreases heart rate, stimulates digestion, and supports processes such as glandular secretion and nutrient absorption.

parathyroid glands

Four small endocrine glands located on the posterior surface of the thyroid gland. They produce parathyroid hormone (PTH), which plays a critical role in calcium homeostasis.

parietal pleurae

The outer layer of the pleural membrane that lines the inner surface of the thoracic cavity, including the chest wall, diaphragm, and mediastinum

partial pressures

Refers to the pressure exerted by a single gas in a mixture of gases. It is a measure of how much of that gas is present and contributes to the total pressure of the mixture.

peak oxygen uptake (VO^2peak)

The highest rate of oxygen consumption measured during an exercise test, regardless of whether a true VO_2max is achieved. VO_2peak is often used as an indicator of cardiorespiratory fitness when maximal effort or physiological criteria for VO_2max cannot be met, such as in clinical populations or submaximal testing.

pectoralis minor

A thin, triangular muscle located beneath the pectoralis major in the upper chest. It attaches from the ribs (usually the 3rd to 5th) to the coracoid process of the scapula.

percentage of maximal oxygen consumption (%VO2max)

The relative exercise intensity expressed as a percentage of an individual's VO_2max.

percentage of one repetition maximum (% 1RM)

The relative load used in resistance training expressed as a percentage of the maximum weight an individual can lift for one complete repetition of a given exercise (1RM).

perimysium

A sheath of connective tissue that surrounds and binds together bundles of muscle fibers, known as fasciculi, within a skeletal muscle.

peripheral fatigue

Decline in muscle performance caused by processes occurring within the muscle fibers themselves, rather than in the nervous system. It is a major component of overall muscle fatigue and is typically associated with metabolic and ionic changes during intense or prolonged exercise.

peripheral nervous system

The part of the nervous system located outside the brain and spinal cord, consisting of cranial nerves, spinal nerves, and associated ganglia. The PNS connects the central nervous system (CNS) to the rest of the body and is divided into the somatic nervous system (controls voluntary movements) and the autonomic nervous system (regulates involuntary functions such as heart rate and digestion).

phospholipids

A class of lipids that are major components of cell membranes. They are amphipathic molecules, meaning they have both water-loving (hydrophilic) and water-fearing (hydrophobic) components.

pituitary gland

Often called the "master gland," is a small, pea-sized endocrine gland located at the base of the brain, beneath the hypothalamus. It regulates many vital body functions by secreting hormones that control other endocrine glands.

pleura

A double-layered serous membrane that surrounds each lung and lines the chest cavity.

pleural cavity

A thin space filled with pleural fluid that reduces friction during breathing and allows the lungs to expand and contract smoothly.

polypeptide hormones

Also called "peptide hormones", polypeptide hormones are composed of short chains of amino acids that are water-soluble and typically bind to receptors on the surface of target cells, triggering intracellular signaling cascades rather than directly altering gene expression. Peptide hormones regulate a wide range of physiological functions including growth, metabolism, and reproduction.

polysaccharides

Long chains of monosaccharides (e.g., starch, glycogen, cellulose).

positive feedback

A regulatory mechanism in which a change in a system triggers a response that amplifies or reinforces that change, rather than reversing it.

posterior pituitary (neurohypophysis)

A portion of the pituitary gland that stores and releases oxytocin and antidiuretic hormone (ADH), which are produced by the hypothalamus.

power

Power (muscular power) reflects how quickly force can be applied to produce movement, making it a key measure of performance in activities requiring speed and strength.

power stroke

The force-generating step of the cross-bridge cycle in which the myosin head pivots after releasing inorganic phosphate, pulling the actin filament toward the center of the sarcomere. This movement shortens the sarcomere and contributes to muscle contraction.

PR interval

The time interval on an electrocardiogram (ECG) from the beginning of the P wave to the start of the QRS complex. It represents the period of atrial depolarization and the delay in the atrioventricular (AV) node before ventricular depolarization begins. Normal duration is typically 0.12–0.20 seconds.

pressure gradient

The difference in pressure between two regions, which drives the movement of gases or fluids from areas of higher pressure to areas of lower pressure.

progesterone

A steroid hormone primarily produced by the corpus luteum in the ovary after ovulation, and in smaller amounts by the adrenal glands and placenta during pregnancy. Progesterone prepares the endometrium (lining of the uterus) for potential implantation of a fertilized egg, supports early pregnancy, and helps regulate the menstrual cycle. It also plays a role in modulating immune responses and maintaining pregnancy.

progressive overload

A principle of exercise training that involves gradually increasing the stress placed on the body's musculoskeletal and cardiovascular systems to stimulate adaptation and improve performance.

proprioceptors

Specialized sensory receptors located in muscles, tendons, and joints that detect changes in body position, movement, and muscle tension. They provide the central nervous system with information about limb position and movement (proprioception), enabling coordination, balance, and posture control.

proteins

Large, complex biomolecules made up of chains of amino acids linked by peptide bonds.

proton (H^+)

A subatomic particle found in the nucleus of an atom. It carries a positive electric charge of +1 elementary charge and has a mass of approximately 1 atomic mass unit (1.67×10^{-27} kg).

pulmonary diffusion

The process by which gases are exchanged between the alveoli in the lungs and the blood in the pulmonary capillaries.

pulmonary surfactant

A lipoprotein substance that reduces surface tension within the alveoli. This surfactant prevents alveolar collapse during exhalation and helps maintain lung compliance, making breathing more efficient.

pulmonary ventilation

The process of moving air into and out of the lungs. It involves two phases: inhalation (inspiration), where air is drawn into the lungs, and exhalation (expiration), where air is expelled from the lungs.

pulmonary ventilation (VE)

The total volume of air moved in and out of the lungs per minute. It is calculated as the product of tidal volume (VT) and breathing frequency (f): $VE = VT \times f$

pulse pressure

The difference between systolic and diastolic blood pressure. It reflects the force the heart generates with each contraction and is an indicator of arterial compliance. Normal pulse pressure is typically around 40 mmHg in healthy adults.

Purkinje fibers

Specialized conductive fibers located in the inner ventricular walls of the heart. They rapidly transmit electrical impulses from the bundle branches to the ventricular myocardium, ensuring a coordinated and efficient contraction of both ventricles during systole.

QRS complex

A series of deflections on an electrocardiogram (ECG) representing ventricular depolarization, which triggers ventricular contraction. It typically consists of a small downward deflection (Q), a large upward spike (R), and a subsequent downward deflection (S).

QT interval

The time interval from the start of the QRS complex to the end of the T wave on an ECG. It represents

the total time for ventricular depolarization and repolarization. The QT interval varies with heart rate and is clinically important for detecting arrhythmia risk.

R-R interval

The time between two consecutive R waves on an electrocardiogram (ECG), representing one complete cardiac cycle. It is commonly used to calculate heart rate and assess rhythm regularity; shorter intervals indicate faster heart rates, while longer intervals indicate slower rates.

reciprocal inhibition

A neural mechanism in which the activation of a muscle (agonist) is accompanied by the simultaneous inhibition of its opposing muscle (antagonist) to allow smooth and coordinated movement. This process is mediated by spinal interneurons within reflex arcs, such as during the stretch reflex, where contraction of the quadriceps is paired with relaxation of the hamstrings.

reduction-oxidation reactions

Reactions (redox) that involve the transfer of electrons between substances.

relative VO^2

The volume of oxygen consumed per unit of body weight per unit of time, typically expressed in milliliters per kilogram per minute ($mL \cdot kg^{-1} \cdot min^{-1}$). Relative VO_2 accounts for body size, allowing for fair comparisons of aerobic capacity and exercise intensity between individuals of different weights.

renin

An enzyme secreted by the juxtaglomerular cells of the kidneys in response to low blood pressure, reduced sodium levels, or sympathetic nervous system stimulation. Renin initiates the renin-angiotensin-aldosterone system (RAAS) by cleaving angiotensinogen into angiotensin I, ultimately helping regulate blood pressure and fluid balance.

repolarization

The process by which the membrane potential of a cell returns to its resting negative value after depolarization. In neurons and muscle cells, repolarization occurs primarily when voltage-gated potassium (K^+) channels open, allowing K^+ ions to exit the cell, restoring the negative internal environment.

residual volume (RV)

The amount of air remaining in the lungs after a maximal exhalation. This air cannot be voluntarily expelled and serves to keep the alveoli open, maintaining gas exchange between breaths. RV typically accounts for about 1.2 liters in a healthy adult and is a critical component of total lung capacity (TLC).

resistance training

(Also known as strength training or weight training) is a form of physical exercise designed to improve muscular strength, endurance, and size by working against a force or resistance. This resistance can come from: Free weights (e.g., dumbbells, barbells), Resistance bands, Weight machines, Body weight (e.g., push-ups, squats).

respiratory membrane

The thin barrier through which gas exchange occurs between the air in the alveoli and the blood in the pulmonary capillaries

respiratory zone

The portion of the respiratory system where gas exchange occurs. It includes the respiratory bronchioles, alveolar ducts, alveolar sacs, and alveoli. These structures contain thin walls and are closely associated with pulmonary capillaries, allowing oxygen to diffuse into the blood and carbon dioxide to diffuse out.

resting membrane potential

The electrical potential difference across the plasma membrane of a cell when it is not actively sending signals, typically around –70 mV in neurons.

resting metabolic rate (RMR)

The amount of energy expended by the body at rest to maintain essential physiological functions such as breathing, circulation, and cellular processes. RMR is typically measured under less strict conditions than basal metabolic rate (BMR) and accounts for the largest portion of total daily energy expenditure.

sarcolemma

The cell membrane that surrounds a muscle fiber (muscle cell).

sarcomere

The basic functional unit of striated muscle, defined as the segment between two Z-disks. It contains

organized thick (myosin) and thin (actin) filaments whose sliding interaction during contraction shortens the sarcomere, producing muscle movement.

sarcoplasm

The cytoplasm of a muscle fiber (muscle cell). It is the gel-like substance that fills the space between the sarcolemma (muscle cell membrane) and the myofibrils (contractile structures).

sarcoplasmic reticulum

A specialized form of smooth endoplasmic reticulum found in muscle fibers, responsible for storing, releasing, and reabsorbing calcium ions (Ca^{2+}) during the process of muscle contraction and relaxation.

satellite cells

Specialized stem cells located between the sarcolemma and the basal lamina of skeletal muscle fibers. They play a key role in muscle growth, repair, and regeneration by proliferating and differentiating into new muscle fibers or fusing with existing ones following injury or stress.

scalene muscles

A group of three paired muscles (anterior, middle, and posterior) located in the lateral neck. During forced inhalation, they assist in elevating the first and second ribs, helping to expand the thoracic cavity and facilitate airflow into the lungs.

semilunar valves

Heart valves located at the bases of the large arteries leaving the ventricles—the aortic valve and the pulmonary valve. They prevent backflow of blood into the ventricles after ventricular contraction.

sensory division

The part of the peripheral nervous system responsible for transmitting sensory information from receptors in the body (e.g., skin, muscles, joints, and organs) to the central nervous system (CNS). It enables the perception of stimuli such as touch, temperature, pain, and body position (proprioception).

sinoatrial (SA) node

A specialized cluster of pacemaker cells located in the right atrium of the heart that initiates electrical impulses, setting the rhythm for the heartbeat. The SA node generates action potentials that spread

through the atria, causing atrial contraction and establishing the heart's intrinsic rate, typically 60–100 beats per minute in adults.

sinus bradycardia

A heart rhythm originating from the sinoatrial (SA) node with a rate of less than 60 beats per minute in adults. It is characterized by normal P waves preceding each QRS complex and a regular rhythm. Sinus bradycardia can be normal in well-conditioned athletes or occur due to medications, increased vagal tone, or certain medical conditions.

sinus tachycardia

A heart rhythm originating from the sinoatrial (SA) node with a rate greater than 100 beats per minute in adults. It maintains normal P wave morphology and a regular rhythm, with each P wave preceding a QRS complex. Sinus tachycardia often occurs as a physiological response to exercise, stress, or fever, but can also indicate underlying conditions such as anemia, hyperthyroidism, or hypovolemia.

size principle

A fundamental rule of motor unit recruitment stating that motor units are activated in order of increasing size of their motor neurons. Smaller motor units, which typically contain slow-twitch (fatigue-resistant) fibers, are recruited first for low-force activities. As force demands increase, progressively larger motor units with fast-twitch fibers are recruited. This ensures efficient, smooth, and energy-conserving muscle activation.

skeletal muscle

A type of striated muscle tissue attached to bones via tendons, responsible for voluntary movements of the body.

sliding filament theory

A model explaining muscle contraction, stating that actin (thin) and myosin (thick) filaments slide past each other within the sarcomere without changing length. This sliding shortens the sarcomere, producing contraction, and is powered by ATP-driven cross-bridge cycling.

smooth muscle

A type of non-striated, involuntary muscle tissue found in the walls of hollow organs such as the intestines, blood vessels, bladder, and uterus.

somatic nervous system

The division of the peripheral nervous system responsible for voluntary control of skeletal muscles and the transmission of sensory information to the central nervous system (CNS). It includes motor neurons that activate muscles and sensory neurons that convey information such as touch, pain, and proprioception.

somatostatin

A peptide hormone that functions primarily as an inhibitory regulator of hormone secretion. It is produced in several tissues, including the hypothalamus, pancreas (delta cells), and gastrointestinal tract.

spatial summation

The process by which multiple postsynaptic potentials (EPSPs or IPSPs) from different presynaptic neurons combine at the same time on a postsynaptic neuron. When these simultaneous inputs occur at different synapses on the dendrites or cell body, their combined effect can bring the membrane potential to threshold, triggering an action potential.

spirometry

A common pulmonary function test that measures the volume and speed of air a person can inhale and exhale. It is used to assess lung function and diagnose respiratory conditions such as asthma, chronic obstructive pulmonary disease (COPD), and restrictive lung disease.

spongy parenchyma

The functional tissue of the lungs that has a soft, porous, and elastic structure, primarily composed of alveoli, bronchioles, and associated capillaries.

sport management

The field of business dealing with sports and recreation. Sports management involves any combination of skills that correspond with planning, organizing, directing, controlling, budgeting, leading, or evaluating of any organization or business within the sports field.

sports psychology

A specialty that uses psychological knowledge and skills to address optimal performance and well-being of athletes, developmental and social aspects of sports participation, and systemic issues associated with sports settings and organizations.

sports sociology

A sub-discipline of sociology which focuses on sports as social phenomena.

squamous cells

A type of epithelial cell characterized by their thin, flat shape and single-layer arrangement.

ST segment

The flat section of the ECG tracing between the end of the QRS complex and the beginning of the T wave. It represents the period when the ventricles are depolarized and in the early phase of repolarization. Abnormalities in the ST segment can indicate myocardial ischemia or infarction.

steady state

A condition in which the key variables of a system remain constant over time, even though energy or matter may be continuously entering and leaving the system. It is a dynamic equilibrium, not a static one.

steady-state VO2

The condition during submaximal, constant-load exercise where oxygen uptake (VO_2) plateaus and remains stable, indicating that aerobic energy supply meets the energy demand of the activity.

sternocleidomastoid

A prominent neck muscle that extends from the sternum and clavicle to the mastoid process of the skull. In addition to its role in head rotation and flexion, it assists in elevating the sternum during forced inhalation, thereby increasing the volume of the thoracic cavity.

steroid hormones

A class of hormones derived from cholesterol that are lipid-soluble and capable of passing through cell membranes to bind with intracellular receptors. They regulate a wide range of physiological processes including metabolism, immune response, salt and water balance, and reproductive functions.

steroids

A class of lipids characterized by a core structure of four fused carbon rings (three six-membered rings and one five-membered ring). Unlike triglycerides, steroids are not composed of fatty acids and glycerol, but they are still classified as lipids because they are hydrophobic and insoluble in water.

stress proteins

A group of proteins that are produced by cells in response to stressful conditions, such as: Heat (e.g., fever or high environmental temperatures); Oxidative stress; Toxins or heavy metals; Inflammation; Exercise; Infection or injury.

stroke volume (SV)

The amount of blood ejected by a ventricle during a single contraction, typically measured in milliliters. Stroke volume is calculated as the difference between end-diastolic volume (EDV) and end-systolic volume (ESV) and is a key determinant of cardiac output.

substrate

A substrate is the specific reactant that an enzyme acts upon during a chemical reaction.

sucrose

A disaccharide of glucose and fructose.

summation

The additive effect of multiple muscle twitches occurring in rapid succession, leading to a greater overall force of contraction. It occurs because the muscle does not fully relax between stimuli, allowing calcium levels to remain elevated.

sympathetic nervous system

A branch of the autonomic nervous system that prepares the body for "fight or flight" responses during stress or emergency situations. It increases heart rate, dilates airways, mobilizes energy stores, and redirects blood flow to skeletal muscles, enhancing the body's ability to respond to perceived threats.

systole

The phase of the cardiac cycle during which the heart muscle contracts, causing the ventricles (and to a lesser extent the atria) to eject blood into the arteries.

T wave

The deflection on an electrocardiogram (ECG) that represents ventricular repolarization, the process by which the ventricles recover electrically after contraction. It follows the QRS complex and precedes the next cardiac cycle.

temporal summation

The process by which multiple postsynaptic potentials (EPSPs or IPSPs) from a single presynaptic neuron accumulate over time at the same synapse. If these signals occur in rapid succession, their combined effect can bring the postsynaptic membrane to threshold, triggering an action potential.

terminal cisternae

Enlarged regions of the sarcoplasmic reticulum located adjacent to the transverse tubules in skeletal and cardiac muscle fibers. They serve as major calcium storage sites and release calcium ions rapidly during excitation-contraction coupling, enabling efficient muscle contraction.

testes

The male gonads responsible for producing sperm and secreting male sex hormones, primarily testosterone. Located in the scrotum, the testes consist of seminiferous tubules (where spermatogenesis occurs) and interstitial (Leydig) cells that produce androgens. They play a central role in male reproductive function and secondary sexual characteristics.

testosterone

The primary male sex hormone, classified as an androgen. It is produced mainly by the testes and in smaller amounts by the adrenal cortex. Testosterone plays a key role in the development of male reproductive tissues, secondary sexual characteristics (such as increased muscle mass and body hair), and the regulation of libido and sperm production.

tetanus

A sustained and continuous contraction of a muscle resulting from rapid, repeated stimulation without sufficient relaxation between stimuli. It occurs when the frequency of nerve impulses is high enough that individual muscle twitches fuse into a smooth, prolonged contraction.

the phosphagen energy system

(Also called the ATP–PCr system) is the body's fastest energy system, providing immediate energy for short-duration, high-intensity activities (e.g., sprinting, heavy lifting).

thyroid gland

A butterfly-shaped endocrine gland located in the front of the neck, just below the larynx. It produces the hormones thyroxine (T_4) and triiodothyronine (T_3), which regulate metabolism, growth, and

development. The gland also secretes calcitonin, which helps regulate calcium levels in the blood. Thyroid hormone production is controlled by thyroid-stimulating hormone (TSH) from the anterior pituitary, forming part of the hypothalamic-pituitary-thyroid axis.

thyroid-stimulating hormone (TSH)

A glycoprotein hormone produced by the anterior pituitary gland that stimulates the thyroid gland to produce and release thyroxine (T_4) and triiodothyronine (T_3). These thyroid hormones regulate metabolism, growth, and development.

thyroxine (T4)

One of the two primary hormones produced by the thyroid gland, the other being T_3 (triiodothyronine). T_4 is the predominant form of thyroid hormone circulating in the blood, but it is less biologically active than T_3. Most T_4 is converted into T_3 in peripheral tissues such as the liver and kidneys.

tidal volume

The amount of air inhaled or exhaled during a normal, resting breath. It represents the baseline volume of air exchanged in the lungs without conscious effort and is typically around 500 milliliters in a healthy adult.

titin

A giant elastic protein that spans from the Z-disk to the M-line within a sarcomere, anchoring thick (myosin) filaments and providing structural stability and elasticity.

total daily energy expenditure (TEE)

The total amount of energy an individual expends in a 24-hour period, encompassing all physiological and physical activities. TEE is composed of three main components: basal or resting metabolic rate (BMR/RMR), the thermic effect of food (TEF), and energy expended during physical activity. It represents the overall energy requirement for maintaining body weight and supporting daily functions.

total lung capacity

The maximum volume of air the lungs can hold after a full, deep inhalation. It includes all the air in the lungs, comprising tidal volume, inspiratory reserve volume, expiratory reserve volume, and residual volume.

transverse abdominis

The deepest of the abdominal muscles, wrapping horizontally around the abdomen. It plays a key role in forced exhalation by compressing the abdominal cavity, which increases intra-abdominal pressure and helps elevate the diaphragm.

transverse tubules

Invaginations of the sarcolemma that penetrate into the interior of skeletal and cardiac muscle fibers, forming a network of membranous channels.

tricarboxylic acid (TCA) cycle

Also known as the citric acid cycle or Krebs cycle, is a central metabolic pathway that takes place in the mitochondrial matrix of eukaryotic cells. It oxidizes acetyl-CoA (derived from carbohydrates, fats, and proteins) into carbon dioxide (CO_2) while generating high-energy electron carriers and a small amount of ATP.

triglycerides

The most common type of fat (lipid) found in the body and in food. They are composed of one glycerol molecule bonded to three fatty acids through ester bonds. Triglycerides serve as a major form of long-term energy storage, provide insulation, and protect organs.

triiodothyronine (T3)

One of the two primary hormones produced by the thyroid gland, the other being T_4 (thyroxine). Although T_3 is produced in smaller quantities than T_4, it is the more biologically active form and is responsible for regulating metabolism, growth, development, and body temperature.

tropomyosin

A regulatory protein that runs along the length of actin filaments in muscle fibers, blocking myosin-binding sites on actin in a relaxed state.

troponin

A regulatory protein complex attached to tropomyosin on actin filaments. It controls muscle contraction by binding calcium ions, which triggers a shift in tropomyosin to expose myosin-binding sites on actin.

twitch

A single, brief contraction and relaxation cycle of a muscle fiber in response to one action potential. It consists of three phases: latent period, contraction phase, and relaxation phase.

Type FF (fast-fatigable) motor units

Motor units composed of large motor neurons and fast-twitch glycolytic (Type IIx or IIb) muscle fibers. These fibers contract very rapidly and generate high force but fatigue quickly because they rely primarily on anaerobic metabolism. Type FF units are recruited last, during short-duration, high-intensity activities like sprinting or heavy lifting.

Type FR (fast-fatigue resistant) motor units

Motor units composed of medium-sized motor neurons and fast-twitch oxidative-glycolytic (Type IIa) muscle fibers. These fibers contract quickly and produce moderate force, with greater fatigue resistance than fast fatigable units due to their mixed oxidative and glycolytic metabolism. Type FR units are recruited for activities requiring both speed and endurance, such as running or cycling at moderate intensity.

Type I muscle fibers

(Also called slow-twitch fibers) are skeletal muscle fibers specialized for endurance and continuous, low-intensity activity. They rely primarily on aerobic metabolism for ATP production and are highly resistant to fatigue.

type II alveolar cells

Specialized epithelial cells found in the alveoli of the lungs. Their primary function is to produce and secrete pulmonary surfactant, a lipoprotein substance that reduces surface tension within the alveoli. This surfactant prevents alveolar collapse during exhalation and helps maintain lung compliance, making breathing more efficient. In addition to surfactant production, these cells also play a role in alveolar repair and regeneration.

type II muscle fibers

Skeletal muscle fibers specialized for rapid, powerful contractions. They rely primarily on anaerobic metabolism, fatigue quickly, and are suited for short bursts of high-intensity activity. Subtypes include Type IIa (fast oxidative-glycolytic) and Type IIx (fast glycolytic).

Type S (slow) motor units

Motor units composed of a small motor neuron and slow-twitch (Type I) muscle fibers. These fibers contract slowly, generate low force, and are highly resistant to fatigue due to their rich supply of mitochondria, capillaries, and oxidative enzymes. Type S motor units are primarily recruited for sustained, low-intensity activities such as posture maintenance and endurance exercise, following the size principle.

U wave

A small, rounded deflection on an electrocardiogram (ECG) that follows the T wave and precedes the next P wave. It is thought to represent repolarization of the Purkinje fibers or papillary muscles. Prominent U waves may indicate conditions such as hypokalemia, bradycardia, or certain drug effects.

veins

Blood vessels that carry blood toward the heart, typically deoxygenated (except in pulmonary and umbilical veins). Veins have thinner walls and larger lumens than arteries, and they contain valves that prevent backflow of blood, aiding its return to the heart under low pressure.

ventilation-perfusion relationship (V/Q)

The ratio between the amount of air reaching the alveoli (ventilation) and the amount of blood reaching the alveoli via the capillaries (perfusion).

ventilatory threshold

The exercise intensity at which ventilation (breathing rate and volume) increases disproportionately to oxygen uptake (VO_2). This occurs because carbon dioxide (CO_2) production rises sharply due to increased buffering of hydrogen ions (H^+), signaling a greater reliance on anaerobic metabolism.

venules

Small blood vessels that collect blood from capillary beds and transport it to veins. Venules have thin walls composed of endothelium and a small amount of smooth muscle, allowing them to facilitate the exchange of some substances and serve as a transition point between the microcirculation and the larger venous system.

visceral pleurae

The inner layer of the pleural membrane that directly covers the surface of each lung. It closely adheres to the lung tissue, following its contours and fissures.

vital capacity (VC)

The maximum amount of air a person can exhale after a full, deep inhalation. It represents the total volume of air that can be voluntarily moved in and out of the lungs and includes the inspiratory reserve volume (IRV), tidal volume (TV), and expiratory reserve volume (ERV).

VO2 drift

The gradual increase in oxygen uptake (VO_2) during prolonged, steady-state exercise at a constant submaximal workload, typically observed after 10–15 minutes of exercise, even though the external workload remains unchanged.

work

Refers to the product of force applied to an object and the distance over which the force is applied, typically expressed in joules (J).

workload

The total amount of physical effort or stress placed on the body during a bout of exercise.

Z-disk

A dense protein structure that defines the boundary of a sarcomere in striated muscle.