

CHAPTER 1

What is physiology?

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After reading this chapter you should understand:

- ◆ The subject matter of physiology
- ◆ The hierarchical organization of the body
- ◆ The concept of homeostasis

1.1 Introduction

Physiology is the study of the functions of living matter. It is concerned with *how* an organism performs its varied activities: how it feeds, how it moves, how it adapts to changing circumstances, how it spawns new generations. The subject is vast and embraces the whole of life. The success of physiology in explaining how organisms perform their daily tasks is based on the notion that they are intricate and exquisite machines whose operation is governed by the laws of physics and chemistry. Although some processes are similar across the whole spectrum of biology—the replication of the genetic code for example—many are specific to particular groups of organisms. For this reason it is necessary to divide the subject into various parts such as bacterial physiology, plant physiology, and animal physiology. The focus of this book is the physiology of mammals, particularly that of humans.

To study how an animal works it is first necessary to know how it is built. A full appreciation of the physiology of an organism must therefore be based on a sound knowledge of its anatomy. Experiments can then be carried out to establish how particular parts perform their functions. Although there have been many important physiological investigations on human volunteers, the need for precise control over the experimental conditions has meant that much of our present physiological knowledge has been derived from studies on other animals such as frogs, rabbits, cats, and dogs. When it is clear that a specific physiological process has a common basis in a wide variety of animal species, it is reasonable to assume that the same principles will apply to humans. The knowledge gained from this approach has given us a great insight into human physiology and endowed us with a solid foundation for the effective treatment of many diseases.

1.2 The organization of the body

The building blocks of the body are the *cells*, which are grouped together to form *tissues*. The principal types of tissue are epithelial, connective (including blood and lymphoid tissue), nervous, and muscular, each with its own characteristics. Many connective tissues have relatively few cells but have an extensive extracellular matrix. In contrast, smooth muscle consists of densely packed layers of muscle cells linked together via specific cell junctions. *Organs* such as the brain, the heart, the lungs, the intestines, and the liver are formed by the aggregation of different kinds of tissue. The organs are themselves parts of distinct physiological *systems*. The heart and blood vessels form the cardiovascular system; the lungs, trachea, and bronchi together with the chest wall and diaphragm form the respiratory system; the skeleton and skeletal muscles form the musculoskeletal system; the brain, spinal cord, autonomic nerves and ganglia, and peripheral somatic nerves form the nervous system, and so on.

Cells differ widely in form and function but they all have certain common characteristics. First, they are bounded by a limiting membrane, the plasma membrane. Secondly, they have the ability to break down large molecules to smaller ones to liberate energy for their activities. Thirdly, at some point in their life history, they possess a nucleus which contains genetic information in the form of deoxyribonucleic acid (DNA). Further details of the fine structure of cells will be considered in Chapter 3.

Living cells continually transform materials. They break down glucose and fats to provide energy for other activities such as motility and the synthesis of proteins for growth and repair. These chemical changes are collectively called *metabolism*. The breakdown of large molecules to smaller ones is called *catabolism* and the synthesis of large molecules from smaller ones *anabolism*.

In the course of evolution, cells began to differentiate to serve different functions. Some developed the ability to contract (muscle cells), others to conduct electrical signals (nerve cells). A further group developed the ability to secrete different substances such as hormones (endocrine cells) or enzymes (e.g. the acinar cells of the salivary glands). During embryological development, this process of *differentiation* is re-enacted as many different types of cell are formed from the fertilized egg.

Most tissues contain a mixture of cell types. For example, blood consists of red cells, white cells, and platelets. Red cells transport oxygen around the body. The white cells play an important role in defense against infection and the platelets are vital components in the process of blood clotting. There are a number of different types of connective tissue but all are characterized by having cells distributed within an extensive non-cellular matrix. Nerve tissue contains nerve cells (of which there are many different kinds) and glial cells.

The principal organ systems

The cardiovascular system

The cells of large multicellular animals cannot derive the oxygen and nutrients they need directly from the external environment. These must be transported to the cells. This is one of the principal functions of the blood, which circulates within blood vessels by virtue of the pumping action of the heart. The heart,

blood vessels, and associated tissues form the cardiovascular system.

The heart consists of four chambers, two atria and two ventricles, which form a pair of pumps arranged side by side. The right ventricle pumps deoxygenated blood to the lungs where it absorbs oxygen from the air, while the left ventricle pumps oxygenated blood returning from the lungs to the rest of body to supply the tissues. Physiologists are concerned with establishing the factors responsible for the heartbeat, how the heart pumps the blood around the circulation, and how it is distributed to perfuse the tissues according to their needs. Fluid exchanged between the blood plasma and the tissues passes into the *lymphatic system*, which eventually drains back into the blood.

The respiratory system

The energy required for performing the various activities of the body is ultimately derived from respiration. This process involves the oxidation of foodstuffs (principally sugars and fats) to release the energy they contain. The oxygen needed for this process is absorbed from the air in the lungs and carried to the tissues by the blood. The carbon dioxide produced by the respiratory activity of the tissues is carried to the lungs by the blood in the pulmonary artery where it is excreted in the expired air. The basic questions to be answered include the following: How is the air moved in and out of the lungs? How is the volume of air breathed adjusted to meet the requirements of the body? What limits the rate of oxygen uptake in the lungs?

The digestive system

The nutrients needed by the body are derived from the diet. Food is taken in by the mouth and broken down into its component parts by enzymes in the gastrointestinal tract (or gut). The digestive products are then absorbed into the blood across the wall of the intestine and pass to the liver via the portal vein. The liver makes nutrients available to the tissues both for their growth and repair and for the production of energy. In the case of the digestive system, key physiological questions are: How is food ingested? How is it broken down and digested? How are the individual nutrients absorbed? How is the food moved through the gut? How are the indigestible remains eliminated from the body?

The kidneys and urinary tract

The chief function of the kidneys is to control the composition of the extracellular fluid (the fluid which bathes the cells). In the course of this process, they also eliminate non-volatile waste products from the blood. To perform these functions, the kidneys produce urine of variable composition which is temporarily stored in the bladder before voiding. The key physiological questions in this case are: how do the kidneys regulate the composition of the blood? How do they eliminate toxic waste? How do they respond to stresses such as dehydration? What mechanisms allow the storage and elimination of the urine?

The reproductive system

Reproduction is one of the fundamental characteristics of living organisms. The gonads (the testes in the male and the ovaries in the female) produce specialized sex cells known as gametes. At the core of sexual reproduction is the creation and fusion of the male

and female gametes, the sperm and ova (eggs), with the result that the genetic characteristics of two separate individuals are mixed to produce offspring that differ genetically from their parents. Key questions are: How are the sperm and eggs produced? What is the mechanism of fertilization? How does the embryo grow and develop? How is it delivered and nourished until it can fend for itself?

The musculoskeletal system

This consists of the bones of the skeleton, skeletal muscles, joints, and their associated tissues. Its primary function is to provide a means of movement, which is required for locomotion, for the maintenance of posture, and for breathing. It also provides physical support for the internal organs. Here the mechanism of muscle contraction is a central issue.

The endocrine and nervous systems

The activities of the different organ systems need to be coordinated and regulated so that they act together to meet the needs of the body. Two coordinating systems have evolved: the nervous system and the endocrine system. The nervous system uses electrical signals to transmit information very rapidly to specific cells. Thus the nerves pass electrical signals to the skeletal muscles to control their contraction. The endocrine system secretes chemical agents, *hormones*, which travel in the bloodstream to the cells upon which they exert a regulatory effect. Hormones play a major role in the regulation of many different organs and are particularly important in the regulation of the menstrual cycle and other aspects of reproduction.

The *immune system* provides the body's defenses against infection both by killing invading organisms and by eliminating diseased or damaged cells.

Although it is helpful to study how each organ performs its functions, it is essential to recognize that the activity of the body as a whole is dependent on the intricate interactions between the various organ systems. If one part fails, the consequences are found in other organ systems throughout the whole body. For example, if the kidneys begin to fail, the regulation of the internal environment is impaired which in turn leads to disorders of function elsewhere.

1.3 Homeostasis

Complex mechanisms are at work to regulate the composition of the extracellular fluid and individual cells have their own mechanisms for regulating their internal composition. The regulatory mechanisms stabilize the internal environment despite variations in both the external world and the activity of the animal. The process of stabilization of the internal environment is called *homeostasis* and is essential if the cells of the body are to function normally.

To take one example, the beating of the heart depends on the rhythmical contractions of cardiac muscle cells. This activity depends on electrical signals which, in turn, depend on the concentration of sodium and potassium ions in the extracellular and intracellular fluids. If there is an excess of potassium in the extracellular fluid, the cardiac muscle cells become too excitable and may contract at inappropriate times rather than in a coordinated manner. Consequently, the concentration of potassium in

the extracellular fluid must be kept within a narrow range if the heart is to beat normally.

How does the body regulate its own composition?

The concept of balance

In the course of a day, an adult consumes approximately 1 kg of food and drinks 2–3 liters of fluid. In a month, this is equivalent to around 30 kg of food and 60–90 liters of fluid. Yet, in general, body weight remains remarkably constant. Such individuals are said to be *in balance*; the intake of food and drink matches the amounts used to generate energy for normal bodily activities plus the losses in urine and feces. In some circumstances, such as starvation, intake does not match the needs of the body and muscle tissue is broken down to provide glucose for the generation of energy. Here, the intake of protein is less than the rate of breakdown and the individual is said to have a *negative nitrogen balance* (nitrogen is a characteristic component of the amino acids that make up the protein—see Chapter 2). Equally, if the body tissues are being built up, as is the case for growing children, pregnant women and athletes in the early stages of training, the daily intake of protein is greater than the normal body turnover and the individual is in *positive nitrogen balance*.

This concept of balance can be applied to any of the body constituents including water and salt (NaCl) and is important in considering how the body regulates its own composition. Intake must match requirements and any excess must be excreted for balance to be maintained. Additionally, for each chemical constituent of the body there is a desirable concentration range, which the control mechanisms are adapted to maintain. For example, the concentration of glucose in the plasma (the fluid part of the blood) is about 4–5 mmol.l⁻¹ between meals. Shortly after a meal, plasma glucose rises above this level and this stimulates the secretion of the hormone insulin by the pancreas, which acts to bring the concentration down. As the concentration of glucose falls, so does the secretion of insulin. In each case, the changes in the circulating level of insulin act (together with other mechanisms) to maintain the plasma glucose at an appropriate level. This type of regulation is known as *negative feedback*. During the period of insulin secretion, the glucose is being stored as either glycogen (mainly in the liver and muscles) or fat (in specialized fat cells in adipose tissue).

A *negative feedback loop* is a control system that acts to maintain the level of some variable within a given range following a disturbance. Although the example given above refers to plasma glucose, the basic principle can be applied to other physiological variables such as body temperature, blood pressure, and the osmolality of the plasma.

A negative feedback loop requires a *sensor* of some kind that responds to the variable in question but not to other physiological variables. Thus an osmoreceptor should respond to changes in osmolality of the body fluids but not to changes in body temperature or blood pressure. The information from the sensor must be compared in some way with the desired level (known as the 'set point' of the system) by some form of *comparator*. If the two do not match, an error signal is transmitted to an *effector*, a system that can act to restore the variable to its desired level. The basic features of a negative feedback loop are summarized

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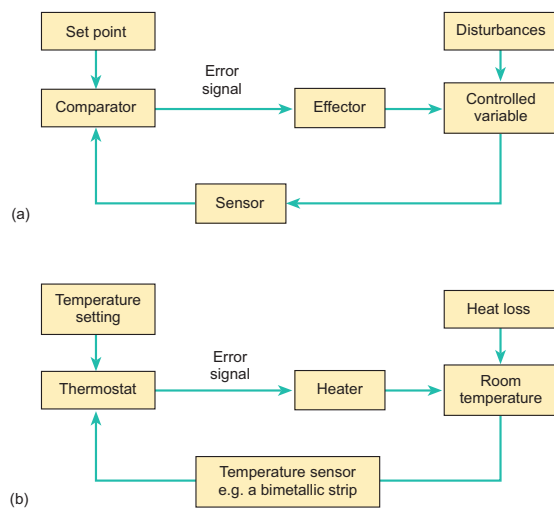


Fig. 1.1 Schematic drawings of a negative feedback control loop (a) compared with a simple heating system (b).

in Fig. 1.1. These features of negative feedback can be appreciated by examining a simple heating system. The controlled variable is room temperature, which is sensed by a thermostat. The effector is a heater of some kind. When the room temperature falls below the set point, the temperature difference is detected by the thermostat which switches on the heater. This heats the room until the temperature reaches the pre-set level whereupon the heater is switched off.

Although negative feedback is the principal mechanism for maintaining a constant internal environment, it does have certain disadvantages. First, negative feedback control can only be exerted after the controlled variable has been disturbed. Secondly, the correction to be applied can only be assessed by the magnitude of the error signal (the difference between the desired value and the displaced value of the variable in question). In practice, this means that negative feedback systems provide incomplete correction. Thirdly, overcorrection has the potential for causing oscillations in the controlled variable. These disadvantages are largely overcome in physiological systems by means of multiple regulatory processes. In the example above, blood glucose is maintained within a narrow range by two mechanisms that act in opposition (push-pull). Insulin acts to lower plasma glucose while another pancreatic hormone, glucagon, acts to mobilize glucose from the body's stores.

While it is difficult to overemphasize the importance of negative feedback control loops in homeostatic mechanisms, they

are frequently reset or overridden in stresses of various kinds. For example, arterial blood pressure is monitored by receptors, known as baroreceptors, which are found in the walls of the aortic arch and carotid sinus. These receptors are the sensors for a negative feedback loop that maintains the arterial blood pressure within close limits. If the blood pressure rises, compensatory changes occur that tend to restore it to normal. In exercise, however, this mechanism is reset. Indeed, if it were not, the amount of exercise we could undertake would be very limited.

Negative feedback loops operate to maintain a particular variable within a specific range. They are a stabilizing force in the economy of the body. However, in some circumstances *positive feedback* occurs. In this case, the feedback loop is inherently unstable as the error signal acts to increase the initial deviation. An example from everyday life is the howling that occurs when a microphone is placed near one of the loudspeakers of a public address system. The microphone picks up the initial sound and this is amplified by the electronic circuitry. This drives the loudspeaker to emit a louder sound, which is again picked up by the microphone and amplified so that the loudspeaker makes an even louder sound, and so on until the amplifying circuitry reaches the limit of its power—and the hearers run for cover!

An example of the interaction between negative and positive feedback mechanisms is the hormonal regulation of the menstrual cycle. Cyclical alterations in the plasma levels of two hormones from the pituitary gland known as follicle-stimulating hormone (FSH) and luteinizing hormone (LH) are involved in the regulation of fertility. Steroid hormones from the ovaries can exert both negative and positive feedback control on the output of FSH and LH, depending upon the concentration of hormone present. Low or moderate levels of a hormone called estradiol-17 β , tend to inhibit secretion of FSH and LH (negative feedback). However, if estradiol-17 β is present in high concentrations for several days, it stimulates the secretion of FSH and LH (positive feedback). As a result, there is a sharp increase in the output of both FSH and LH just before midcycle. This rise is responsible for ovulation. Once ovulation has taken place, estrogen levels fall sharply and the output of FSH and LH drops as negative feedback reasserts control.

Recommended reading

- Houk, J.C. (1980). Homeostasis and control principles. In *Medical physiology* (14th edn) (ed. V.B. Mountcastle), Chapter 8, pp. 246–267. Mosby, St Louis, MO.
- Paton, W.D.M. (1993). *Man and mouse. Animals in medical research* (2nd edn). Oxford University Press, Oxford.