# Pathophysiology

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The authors and publisher have exerted
every effort to ensure that drug selection and
dosage set forth in this text are in accord with
current recommendations and practice at the
time of publication. However, in view of
ongoing research, changes in government
regulations, and the constant flow of
information relating to drug therapy and
drug reactions, the reader is urged to
check the package insert for each drug for
any change in indications and dosage
and for added warnings and precautions.
This is particularly important when the
recommended agent is a new or infrequently
employed drug.

Disease: A state of altered physiologic functioning
  Manifestations of disease
  Causes of disease
    Developmental and acquired causes of disease
    Multifactorial origins of disease
    Stress as a cause of disease
Adaptation to alterations in function

# 1



# Prologue: Introduction to Health and Adaptation

Health can be described as a dynamic state that includes various aspects of both wellness and illness. Although most of us perceive ourselves as being healthy, few of us can say that we have never been sick. For the most part, health includes (1) well-health, in which wellness may be periodically interrupted by acute illness, (2) modified well-health, in which aspects of chronic illness have been incorporated into a pattern of wellness functioning, and (3) consistent ill-health, which causes marked alterations in body functioning. The discussion in this chapter focuses on disease, or what this book terms altered health, and physiologic adaptation to states of altered health.

## :Disease: A State of Altered Physiologic Functioning

Disease, from a practical point of view, describes a condition of impaired body function. Engel defines disease as failures or disturbances in the growth, development, function, and adjustment of the organism, either as a whole or of any of its systems.[1] Although disease usually includes alterations in body structures or in the composition of body fluids, it is the manifestations of these bodily changes that impair function and lead to an awareness of illness. Likewise, it is the return of normal function that usually marks recovery from illness.

A disease can be acute, subacute, or chronic. An *acute* disorder is one that is relatively severe, but self-limiting. *Chronic* disease refers to a continuous, long-term process. A chronic disease can run a continuous course or it can present with *exacerbations* (aggravation of symptoms and severity of the disease), and *remissions* (a period of time where there is a lessening of severity and a decrease in symptoms). *Subacute* disease is intermediate between acute and chronic; it is not as severe as acute and not as prolonged as a chronic illness.

### Manifestations of Disease

Signs and symptoms are terms that are used to describe the structural and functional changes that accompany disease. A *symptom* is regarded as a subjective complaint that is noted by the person afflicted with the disorder, whereas a *sign* is a manifestation that is noted by an observer. Pain, difficult breathing, and a feeling of lightheadedness are symptoms of disordered function. On the other hand, an elevated temperature, a swollen extremity, and changes in pupil size are objective signs that can be observed by someone other than the person with the disorder. Signs and symptoms may be related to the primary disorder, or they may represent the body's attempt to compensate for the altered function caused by the pathologic condition. For our purposes, physiologic coping mechanisms refer to physiologic responses that counteract or compensate for conditions that tend to disrupt body function. "Anyone who has worked in the health professions for any length of time is aware that most pathological states are not observed directly—one cannot see a sick heart or a failing kidney. What one can see is the body's attempt to compensate for the change in structure and function."[2]

It is important to recognize that a single sign or symptom is frequently associated with a number of different disease states. For example, an elevated temperature can indicate the presence of infection, myocardial infarction, brain injury, or any of a large number of other disorders. A differential diagnosis that describes the origin of a disorder usually requires knowledge of a number of signs and symptoms. The presence of fever, a reddened sore throat, and a positive throat culture, for example, describes a "strep throat" infection, whereas, the previously mentioned presence of fever gave little information about the cause of the alteration in temperature. A syndrome is a *compilation* of signs and symptoms that are characteristic of a specific disease state. One example of a syndrome is the syndrome of inappropriate antidiuretic hormone (SIADH), described in Chapter 22.

*Morphologic* changes refer to changes in cell or tissue structure and *physiologic* changes refer to changes in body function. A demonstrable structural change is sometimes called a *lesion*. Quantitative measurements of structural and functional changes can be obtained through the use of physical measuring devices (thermometer or scale), laboratory tests, x-ray studies, and other scientific methods.

### Causes of Disease

The causes of disease are known as the *etiological* factors while the method by which the lesions or disease develops is its *pathogenesis*. Etiology describes what sets the process in motion, and pathogenesis, how the motion evolves. Although the two terms have quite different meanings, they are often used interchangeably. For example, atherosclerosis is often cited as the cause (or etiology) of a heart attack, while in reality, the atherosclerotic changes that appear in the coronary vessels describe the

pathogenesis of the disease—the etiology of atherosclerosis is still largely uncertain. The term *epidemiology* comes from the word epidemic and refers to the study of diseases in large populations. Epidemiologic studies look for patterns, such as the age, sex, race, or geographic location of persons affected with a particular disorder.

### Developmental and acquired causes of disease

One way to view the factors that cause disease is to group them into categories according to whether they were present at birth or whether they were acquired following birth. The conditions that are present at birth include those that are *inherited* (due to genetic make-up) and *congenital* (due to errors in development). Not all genetic disorders are evident at birth; many take years to develop. *Acquired* defects result from conditions that occur after birth. These include trauma, exposure to injurious physical, chemical, and microbial agents; deficient food and oxygen supplies; immune responses; and neoplasia.

### Multifactorial origins of disease

Most disease-causing agents are *nonspecific* and many different agents can cause disease of a single organ. For example, lung disease can result from trauma, infection, exposure to physical and chemical irritants, or neoplasia. With severe lung involvement, each of these agents has the potential to cause respiratory failure. On the other hand, a *single* agent or traumatic event can lead to disease or dysfunction of a *number* of organs and systems. An example of multisystem involvement occurs in severe circulatory shock when the blood flow to many different organs is decreased. The complications of circulatory shock can, therefore, affect a number of systems. These complications may include respiratory distress syndrome, renal failure, gastrointestinal ulcerations, and disseminated intravascular clotting.

Although a disease agent can affect more than one organ and a number of disease agents can affect the same organ, it is important to recognize that most disease states do not have a single cause. Rather, most diseases are *multifactorial* in origin. This is particularly true of diseases such as cancer, heart disease, and diabetes. The multiple factors that predispose to a particular disease are often referred to as *risk factors*.

### Stress as a cause of disease

It was pointed out in the previous paragraph that most often a number of factors contribute to the cause and progression of a single disease and there is little doubt that both *physical* and *emotional stress* function as risk factors in the development of many illnesses. For example, the reader can undoubtedly identify the stresses associated with the "catching of" the common cold. Although it is generally agreed that the cold is caused by a virus, the persons most apt to develop a cold are those that have been exposed to the stresses of cold weather or wet feet, or are tired and "run down." Retrospectively, many persons can relate the actual onset of illness to the occurrence of a recent, particularly stressful event. Whether the stress contributed to the illness or the stressful event became more impressive because of its relationship to the illness is a question that remains unanswered.

Stress takes many forms and exerts its effect on many levels. There are changes in neural function, hormone release, and cardiorespiratory responses. Although the effect of stress on health is beyond the scope of this book, it is mentioned here because of its effect on physiologic functioning and its influence on the development of disease.

## Adaptation to Alterations in Function

Health is a dynamic state that requires a continual expenditure of energy. Much of this energy is used to recruit physiologic behaviors that oppose or compensate for changes that are perceived as threats to maintenance of the internal environment. In this respect, the human body is truly an amazing structure. It is able to withstand exposure to a variety of environmental stresses while maintaining its internal environment within the narrow confines of what is termed "normal." For example, we have been able to put men on the moon and send them to the depths of the ocean, yet their vital functions, as reflected by body temperature, blood *p*H, and heart rate, remained remarkably similar to those observed under normal environmental conditions.

The need to adapt is essential because minute changes in the internal environment can be lethal. For example, the normal range of blood *p*H is between 7.35 and 7.45 and even small deviations from these values can cause death. Adaptation is affected by a number of factors including impairment of capacity due to age, disease, or a *sudden* need to adapt. It is most effective when there is no impairment of adaptive capacity due to age or disease, and when the need for adaptation is a gradual process.

Generally speaking, adaptation affects the whole person. When adapting to stress the body

uses those behaviors that are most efficient and effective—the body will not "use a baseball bat to kill a mosquito." Nor will the body use long-term mechanisms when short-term adaptation is sufficient. The increase in heart rate that accompanies a febrile illness is a temporary response designed to deliver additional oxygen to the tissues during the short period of time that the elevated temperature increases the metabolic needs of the tissues. On the other hand, hypertrophy of the left ventricle is a long-term adaptive response that occurs in persons with chronic hypertension.

Adaptation is further affected by the availability of adaptive responses and flexibility in selecting effective responses. The greater the number of available responses, the more effective the capacity to adapt. Adaptive capacity is decreased with extremes of age and when disease conditions limit the availability of adaptive responses. The immaturity of the infant impairs the ability to adapt as does the decline in functional reserve that occurs in the elderly. For example, the infant has difficulty concentrating urine due to the immaturity of the renal tubular structures and is, therefore, less able than an adult to cope with decreased water intake or exaggerated water losses. Similarly, persons with pre-existing diseases of the heart are less able to adapt to stresses that require recruitment of cardiovascular responses.

As indicated, adaptation is most efficient when the changes that occur in body function are gradual rather than sudden. It is possible, for instance, to lose a liter of blood through chronic gastrointestinal bleeding over a period of a week without developing signs of shock. However, a sudden hemorrhage that causes the loss of an equal amount of blood is apt to cause hypotension and shock.

*In summary, disease is usually manifested by an alteration in body function. It is this alteration in function associated with the disease and the body's attempt to compensate for the altered function that causes the signs and symptoms that are associated with specific disease states.*

## :Study Guide

After you have studied this chapter, you should be able to meet the following objectives:

: : State an inclusive definition of *health*.

: : State and give examples of the terms used to describe changes that accompany a disease.

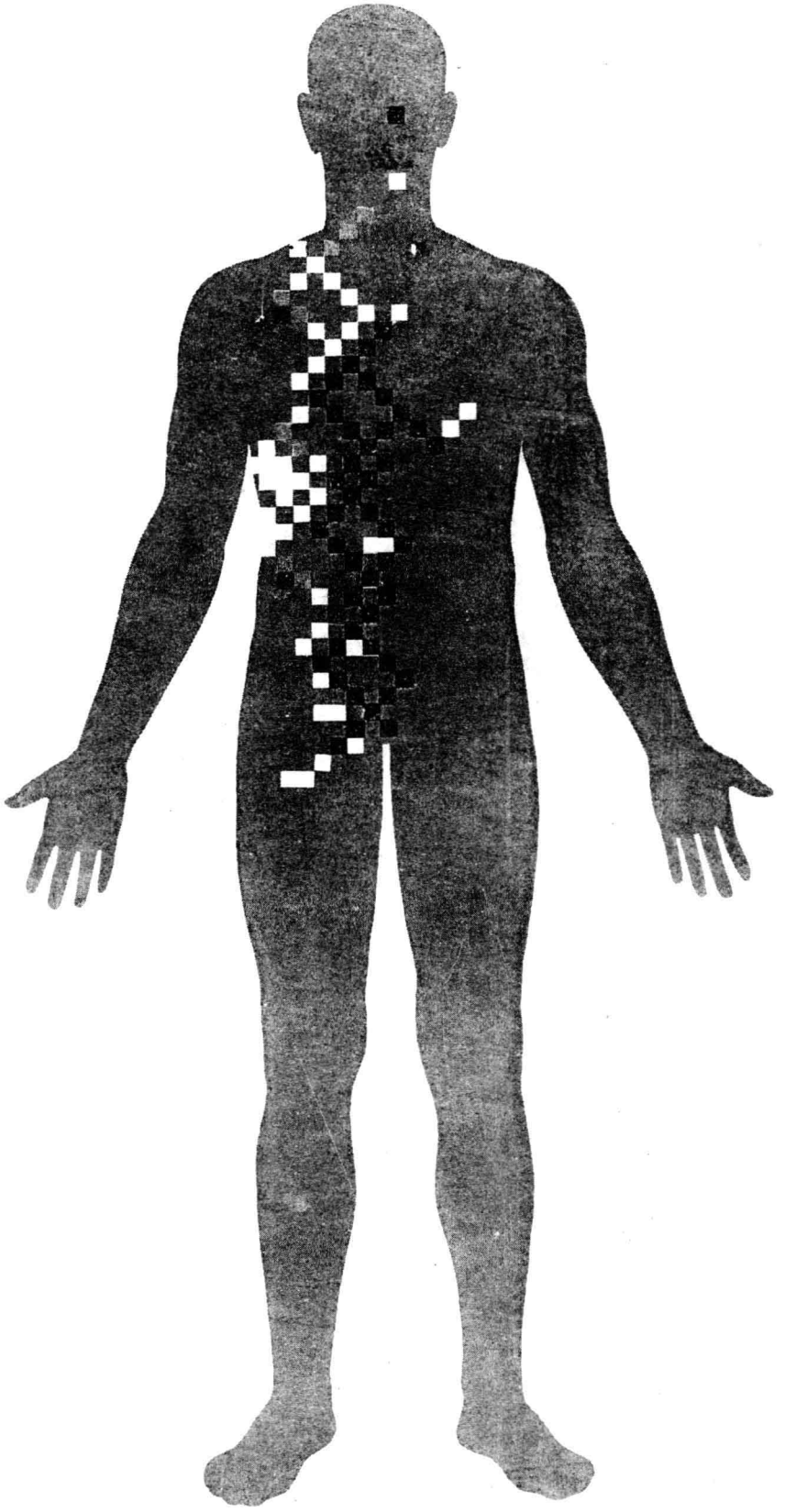
: : State an example of a hereditary disorder; a congenital disorder; an acquired disorder.

: : State the rationale for describing cancer as a disease of multifactorial origin.

: : State a general definition of *adaptation*, and give one example of adaptation to an alteration in function.

## :References

1. Engel GL: A unified concept of health and disease. Perspect Biol Med 3:459, 1960
2. Porth CM: Physiological coping: a model for teaching pathophysiology. Nurs Outlook 25, No. 12:781, 1977



# I

# Alterations in Cell Structure and Function

From conception to death, a continuous process of human development proceeds, despite changes from within and outside the body. The ability to adapt and develop in a world of continuous stress is dependent upon both genetic endowment and the nature of the environmental stresses to which an individual is exposed. Within limits, the body is able to change cell structures so that they can survive—and even thrive—under less-than-optimal conditions. The body is able to resist attack by foreign agents and is able to repair tissue damage that accompanies the normal stresses of living. Only a fine line separates the normal, healthy adaptive responses that allow one to withstand the ravages of everyday life from the exaggerated or defective responses that cause disease.

This unit discusses (1) normal cell structure and function, (2) cellular responses to stress and injury, (3) inflammation and repair, (4) immune responses, (5) genetic and congenital influences on health, and (6) neoplasia.

# 2

# Cell and Tissue Characteristics

The cell is the basic functional unit of the body. Cells, in turn, are organized into larger functional units called tissue. It is tissue that forms body structures and organs. To understand the function of the body, its various organs, and altered function that occurs with disease, it is necessary to understand the basic organization and function of the individual cells and the characteristics of the various tissue types.

## :Cell Structure and Function

Although the cells of different organs vary in both structure and function, there are certain general characteristics that are common to most cells. When seen under a light microscope, three major components become evident—nucleus, cytoplasm, and cell membrane (Fig. 2-1). Within the cytoplasm are a number of physical structures generally called organelles. These are the inner organs of the cell.

### The Nucleus

The nucleus controls cellular activity. Inside the *nuclear membrane* is the *nuclear sap* and *chromatin* that contains the chromosomes. The *chromosomes* contain the *genes*, which are made up of *deoxyribonucleic acid* (DNA). Genes not only control cellular replication, but they also control cellular activity by determining the type of proteins that are made by the cell. Cell activity is largely determined by cell enzymes that are proteins.

Not all genes are active at all times, nor are the same genes active in all cell types. On the contrary, only a small, select group of genes is active in protein synthesis and this group varies from one cell type to another. This difference can be noted in the different types of proteins and enzymes that are found in different tissues of the body. Gene activity and protein synthesis can be altered by hormone actions and by stresses imposed on the cell. Many of the cellular adaptations that are discussed in the latter part of this chapter are mediated by changes in gene expression.

Although DNA determines the type of protein that is synthesized in a cell, the transmission of this information and the synthesis of proteins are carried out by the *ribonucleic acid* (RNA). The nucleus contains one or more rounded bodies known as the nucleoli (Fig. 2-1) and it is within these bodies that RNA is synthesized. There are three types of RNA. *Messenger RNA (mRNA)* is the template for protein synthesis; it carries the information coded on DNA into the cytoplasm. There is an mRNA molecule that corresponds to each gene or group of genes being expressed in the nucleus. *Transfer RNA (tRNA)* transfers the message from mRNA to the ribosomes; it selects and carries the appropriate amino acids to the ribosomes. *Ribosomal RNA (rRNA)* is the major component of the ribosomes in which protein synthesis takes place. These relationships are indicated in the chart on the facing page.

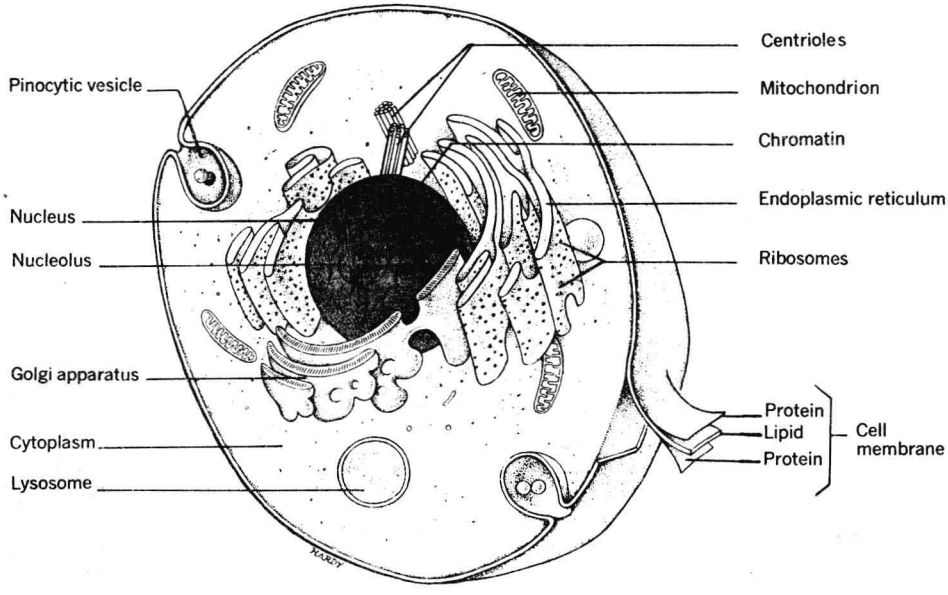
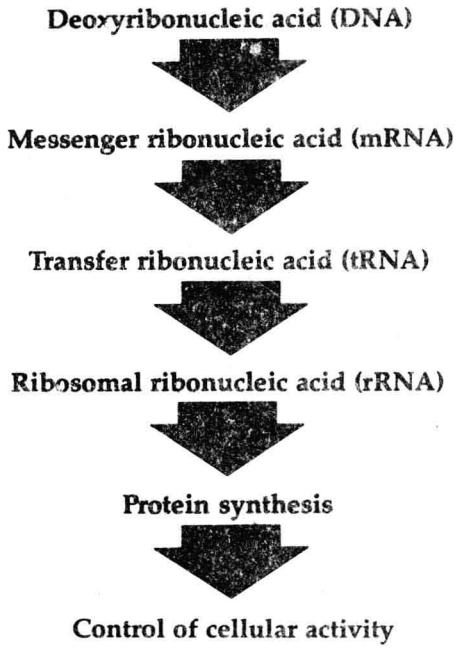



Figure 2–1. A composite cell designed to show, in one cell, all of the various components of the nucleus and cytoplasm.




The nuclear contents are surrounded by a double walled *nuclear membrane*. The large number of nuclear pores in this membrane permit diffusion of fluids, metabolites, mRNA, and tRNA to move between the nuclear and cytoplasmic compartments.

## The Ribosomes

The ribosomes serve as sites of protein synthesis in the cell. As previously mentioned, the ribosomes are small particles of nucleoproteins (rRNA and proteins) that are synthesized in the cell nucleus and can be found as free ribosomes or attached to the wall of the endoplasmic reticulum (see Fig. 2-2). The free ribosomes are singly scattered in the cytoplasm or are joined to form functional units called polyribosomes.

## The Endoplasmic Reticulum

The endoplasmic reticulum (ER) is an extensive system of paired parallel membranes that connect various parts of the inner cell. There are two types of ER—rough and smooth. The rough ER is studded with ribosomes and functions in synthesis of proteins (Fig. 2-2).

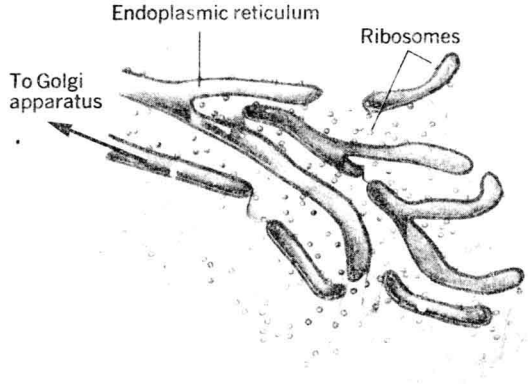
Hormone synthesis by glandular cells and plasma protein production by liver cells takes place in the rough ER. The smooth ER is free of ribosomes, but is often attached to the rough ER. Functions of the smooth ER vary in different cells. The sarcoplasmic reticulum of skeletal and cardiac muscle cells is a form of smooth ER. Calcium ions needed for muscle contraction are stored and released from cisterns located in the sarcoplasmic reticulum of these cells.

In the liver, the smooth ER is involved in glycogen storage and drug metabolism. There is an interesting form of adaptation that occurs in the smooth ER of the liver cells responsible for metabolizing certain drugs such as phenobarbital. It is known that repeated administration of phenobarbital leads to a state of increased tolerance to the drug, such that the same dose of drug no longer produces the same degree of sedation. This response has been traced to increased drug metabolism due to increased synthesis of drug-metabolizing enzymes by the ER membrane. This system is sometimes called the microsomal system because the ER can be fragmented in the laboratory, and when this is done, small vesicles called microsomes are formed. The microsomal system responsible for metabolizing phenobarbital has a cross-over effect that influences the metabolism of other drugs that use the same metabolic pathway.

## The Golgi Complex

The Golgi complex consists of flattened, membranous saccules and cisterns that communicate with the ER, and acts as a receptacle for hormones and other substances that the ER produces. It then collects and packages these substances into secretory granules and vesicles. The secretory granules move out of the Golgi complex, into the cytoplasm, and, following an appropriate signal, are then released from the cell through the process of exocytosis or

Figure 2-2. Diagram of the endoplasmic reticulum and related ribosomes. (Chaffee EE, Lytle IM: Basic Physiology and Anatomy, 4th ed. Philadelphia, JB Lippincott, 1980)



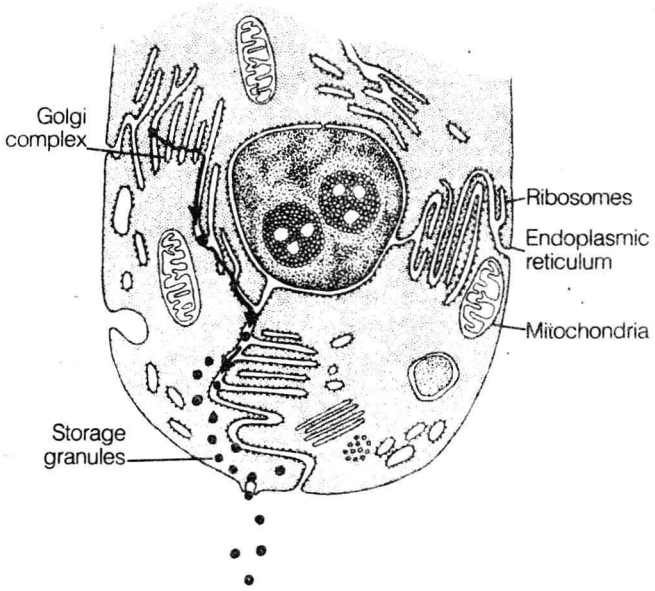
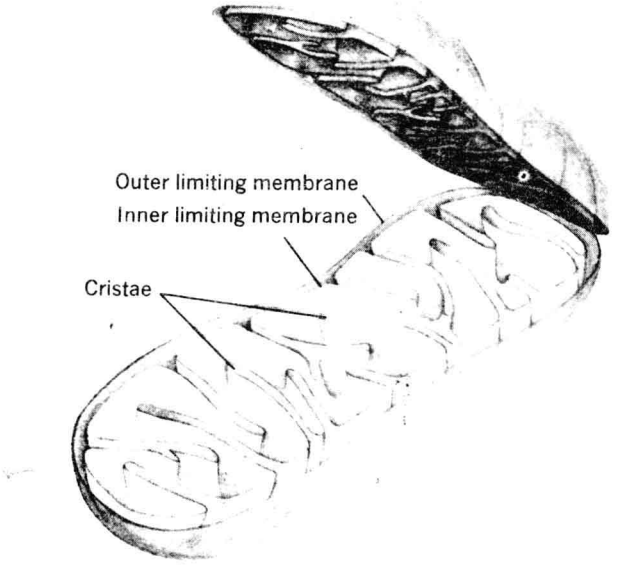



Figure 2–3. Schematic diagram for hormone secretion. The hormone is synthesized by the ribosomes. It moves from the rough endoplasmic reticulum to the Golgi complex where it forms secretory granules. These leave the Golgi complex and are stored within the cytoplasm until released from the cell in response to an appropriate signal.

Figure 2–4. Diagram of a mitochondrion. The inner membrane forms transverse folds called the cristae. It is here that the enzymes needed for the final step in ATP production (oxidative phosphorylation) are located. (Chaffee EE, Lytle IM: Basic Physiology and Anatomy, 4th ed. Philadelphia, JB Lippincott, 1980)




reverse phagocytosis. Figure 2-3 is a diagram of the synthesis and movement of a hormone through the endoplasmic reticulum and Golgi complex. In addition to secreting proteins, the Golgi complex is thought to produce some of the large carbohydrate molecules that are needed to combine with proteins produced in the rough ER to form glycoproteins.

## The Cytoplasm and Its Organelles

The cytoplasm surrounds the nucleus and it is here that the work of the cell takes place. The cytoplasm is essentially a colloidal solution that contains water, suspended proteins, neutral fats, and glycogen molecules. Although they do not contribute to the cell's function, there are pigments that may also accumulate in the cytoplasm. The cytoplasm contains the organelles, or inner organs of the cell, which include the mitochondria, lysosomes, microtubules, microfilaments, and centrioles.

### The mitochondria

The mitochondria are literally the "power plants" of the cell, for it is here that energy from foodstuffs is transformed into an energy-rich compound, adenosine triphosphate (ATP), which powers the various activities that take place within the cell. The mitochondria capture energy contained in glucose, fatty acids, and amino acids through both the tricarboxylic acid or Krebs cycle and the electron-transport system that requires the presence of oxygen for its operation (see Chap. 34 for discussion of metabolic process). The mitochondria are encased in a double membrane. An outer membrane encloses the periphery of the mitochrondria and an inner membrane is enfolded to form the cristae which aid in the production and temporary storage of ATP (Fig. 2-4). The mitochrondria are located close to the site of energy consumption in the cell, i.e., near the myofibrils in muscle cells. The number of mitochrondria in a given cell type is largely determined by the type of activity that the cell performs and the amount of energy that is needed to perform this activity.

### The lysosomes

The lysosomes essentially form the digestive system of the cell. The lysosomes consist of small vesicles or sacs which contain hydrolytic enzymes capable of breaking down worn-out cell parts and foreign material that enters the cell. The enzymes contained in the lysosomes are so powerful that they are often called "suicide bags" because under abnormal conditions their contents can be released, causing lysis and the destruction of cellular contents. Under other conditions their contents can be released into the

extracellular spaces, destroying the surrounding cells. One of the theories of irreversible shock suggests that this stage of shock is caused, at least in part, by widespread release of lysosomal enzymes from cells that have been damaged by lack of oxygen.

### The microtubules and microfilaments

Because they control cell shape and movement, the microtubules and microfilaments are often called the cytoskeletal system.

The *microtubules* are long, rigid, threadlike structures that are dispersed throughout the cytoplasm and are usually arranged in bundles. In cilia and sperm, the microtubules occur in doublets. The centrioles, which will be discussed next, contain microtubules arranged in triplets. It appears that microtubules can be rapidly assembled and disassembled according to the needs of the cell. The assembly of microtubules is halted by the action of the plant alkaloid, colchicine. In the laboratory this compound is used to halt cell mitosis, and it is also used in the treatment of gout. It is thought that the drug interferes with microtubular function and leukocyte motility and, therefore, leads to a decrease in the inflammatory reaction that occurs with this condition.

The *microfilaments* occur in association with the microtubules. The contractile proteins—actin, myosin, and troponin—are examples of microfilaments found in muscle cells.

Abnormalities of the cytoskeletal system may constitute important causes of alterations in cellular function. Robbins suggests that in certain disease conditions, such as diabetes mellitus, alterations in leukocyte mobility and migration may interfere with the inflammatory response and predispose to the development of bacterial infection.[1]

### The centrioles

The centrioles, found in cells capable of reproducing themselves, are composed of nine bundles of microfilaments, each of which contains three microfilaments. The microfilaments aid in movement of the chromosomes during cell division.

## The Cell Membrane

The cell is enclosed in a thin membrane that separates the intracellular contents from the extracellular environment. To distinguish it from the other cell membranes, such as the mitochondrial or nuclear membranes, the cell membrane is often called the plasma membrane. In many respects, the plasma membrane is one of the most important parts of the cell. The functions of the cell membrane include (1) acting as a semipermeable membrane that separates the intracellular and extracellular environments, (2) carrying receptors for hormones and other biologically active substances, (3) participating in the electrical events that occur in nerve and muscle cells, and (4) aiding in the regulation of growth and proliferation. It is also thought that the cell membrane may play an important role in the cancerous behavior of cells,[2] which function will be discussed in Chapter 7.

The cell membrane consists of an organized arrangment of lipids, carbohydrates, and proteins (Fig. 2-5). According to current theories, the lipids

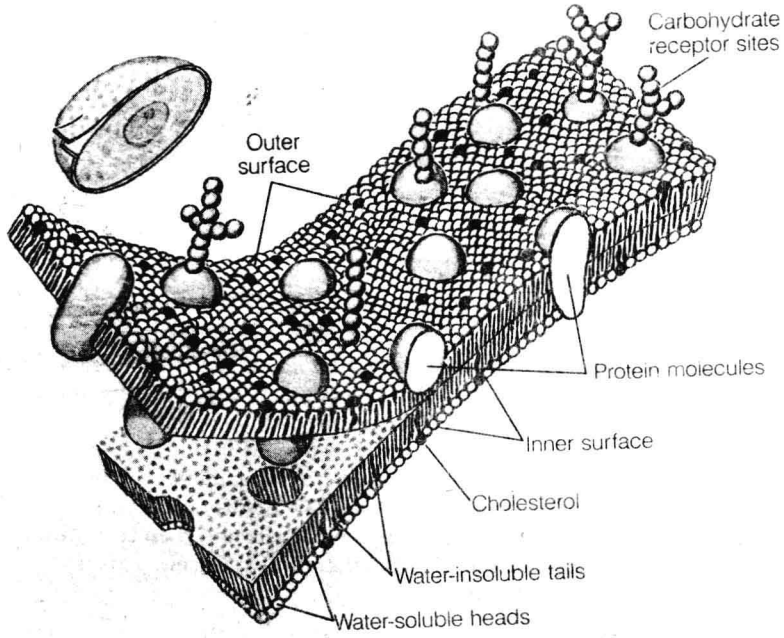



Figure 2–5. Diagram of a cell membrane. The right end is intact, but the left end has been split along the plane of the lipid tails. (Chaffee EE, Lytle IM: Basic Physiology and Anatomy, 4th ed. Philadelphia, JB Lippincott, 1980)

form a bilayer structure that is essentially impermeable to all but the lipid-soluble substances. It is believed that globular proteins are embedded in this lipid bilayer and that these proteins participate in the transport of lipid-insoluble particles. According to this schema, some of the globular proteins move within the membrane structure acting as carriers, some are attached to either side of the membrane, and others pass directly through the membrane, communicating with both the inside and the outside of the cell. It is probable that these latter proteins form channels that permit passage of substances such as water and specific ions such as sodium, hydrogen, and chloride.

The cell surface has been observed, under the electron microscope, to be surrounded by a fuzzy-looking layer called the cell coat or *"glycocalyx."* This layer is made up of glycolipid and glycoprotein molecules (Fig. 2-5) that participate in cell membrane interactions. The cell coat contains the sites for hormone recognition, the ABO blood group, and other tissue antigens.

*Microvilli* are elongated protrusions of the cell membrane that are arranged as a series of tubular extensions. These extensions greatly increase the surface area of the cell membrane. This specialized cell membrane arrangement facilitates the absorption of fluids and other materials. Microvilli are found in the lumen of the small intestine.

*Cilia* are long protuberances of the cell membrane with the tapered ends that are characteristic of many cell types, particularly the epithelium. They are anchored in the cytoplasm by a structure similar to the centriole, and extending from this structure is a series of microtubules that are surrounded by the cell membrane. By sliding the microfilaments on each other, the cilia are capable of a sweeping type of movement. Longer cilia are called flagella. The cilia provide a mechanism for cell movement, or if the location of the cell is fixed, as in the respiratory tract, for the movement of adjacent fluids.

## Membrane transport

There is a constant movement of molecules and ions across the cell membrane. This movement is facilitated by diffusion, osmosis, facilitated diffusion, active transport, and pinocytosis. Each of these mechanisms is depicted in Figure 2-6.

*Diffusion* refers to the process whereby molecules of gases and other substances move from an area of higher to lower concentration, and become equally distributed across the cell membrane. Lipid-soluble molecules such as carbon dioxide cross the cell membrane rapidly by diffusion.

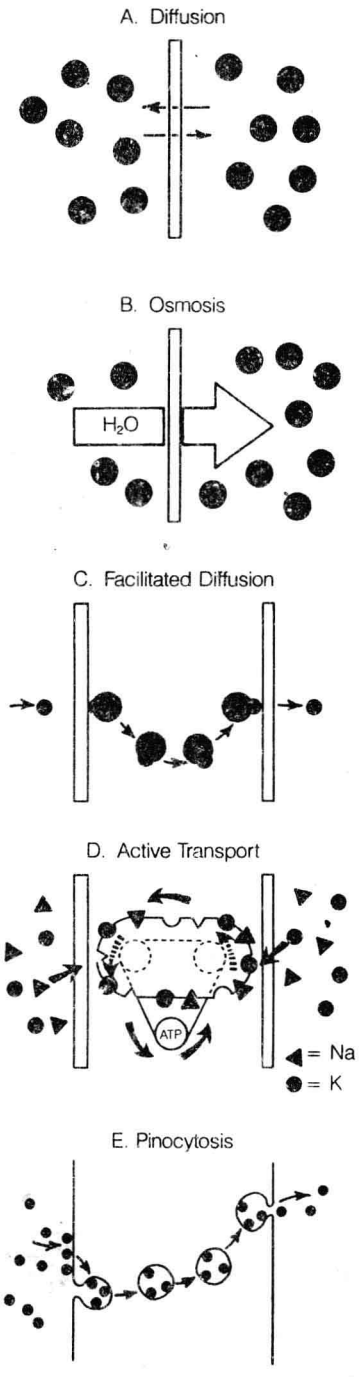



Figure 2–6. Mechanisms of membrane transport. Figure *A* represents diffusion in which the molecules are equally distributed across the membrane. In figure *B* the osmotically active particles regulate the flow of water. In figure *C*, facilitated diffusion uses a carrier system. Figure *D* represents active transport in which selected molecules are transported across the membrane using the energy driven (ATP) pump. The membrane forms a vesicle in *E* that engulfs the particle and then transports it across the membrane where it is released. This is called pinocytosis.

*Osmosis* is concerned with the passage of water across the semipermeable membrane. Osmosis is regulated by the concentration of osmotically active particles that are present on either side of the membrane (see Chap. 21).

*Facilitated diffusion* involves a carrier system. Substances that are not lipid-soluble and cannot pass readily through the cell membrane depend on their ability to combine with special carriers for transport across the membrane.

*Active transport* moves substances through the cell membrane against a concentration gradient (from a lower to a higher concentration). Active transport requires expenditure of ATP. The sodium and potassium membrane transport system, sometimes called the sodium and potassium pump, is an example of active transport. The sodium concentration within the cell is about 14 times less than the extracellular concentration, and the potassium concentration outside the cell is about 28 times less than that within the cell. The sodium and potassium pump extrudes sodium from the cell and then returns potassium to the cell. Were it not for the activity of the sodium and potassium pump, sodium would accumulate within the cell, and the cell would swell as water movement into the cell increased.

*Pinocytosis* is a mechanism by which the cell membrane engulfs particles and forms a pinocytic vesicle. The vesicle then breaks away from the inner surface of the cell membrane and moves into the cytoplasm where it is eventually freed by the action of lysosomes or other cytoplasmic enzymes. Pinocytosis is important to the transport of proteins and strong solutions of electrolytes.

*Endocytosis* is a mechanism for secretion of intracellular fluid into the extracellular spaces. It is the reverse of pinocytosis in that a fluid-filled vacuole fuses to the inner side of the cell membrane and an opening occurs to the outside of the cell surface, allowing the contents of the vacuole to be released into the extracellular fluid.

*Phagocytosis* is a mechanism similar to pinocytosis, except that larger indentations occur in the cell membrane, allowing the cell to ingest large particles such as bacteria and cell debris.

### Intercellular junctions

Intercellular attachments join cell membranes of adjacent cells to form a unit. *Desmosomes* serve as a "spot weld" to hold the cell membranes of two cells together. The zonula occludens or *tight junction* is another form of intercellular junction by which the cell membranes are actually fused together. A less common form of intercellular adhesion involves the close approximation of the cell membranes with the formation of apparent pores between the cytoplasms of the two cells. These junctions or *nexus* possess low electrical-resistance properties and permit electrical communication between cells. The type of cell junction varies with the function of the tissue type. Tissues that facilitate absorption of fluids usually have cells that are connected by desmosomes. The intercalated discs that join the myocardial fibers of the heart are nexus with low resistance properties.

*In summary, the cell is a remarkably autonomous structure that functions in a manner strikingly similar to that of the total organism. Cells are separated from their external environment by a semipermeable cell membane that aids in regulating the osmotic and ionic homeostasis of the cells' interior. The cell nucleus controls cell function and is the master-mind of the cell, while the cytoplasm contains the cell's inner organs and is the cell's work site. The cell transforms foodstuffs into a high-energy chemical compound, ATP, and uses ATP as a power source for its functions. Cells contain other structures such as microtubules and microfilaments that are needed for the specific functions which they perform.*

## Tissue Types

In the preceding section we discussed the individual cell. Although cells are similar, their structure and function vary according to the needs of the tissues. While an extensive discussion of tissue types is beyond the scope of this text, a brief overview is offered in preparation for understanding the subsequent chapters in this unit.

### Cell Differentiation

The formation of different types of cells and the disposition of these cells into tissue types is called cell differentiation. Following conception, the fertilized ovum divides and subdivides and ultimately forms over a hundred different cell types. The process of cell differentiation normally moves forward and is irreversible, producing cells that are more specialized than their predecessors. This means that once differentiation has occurred, the tissue type does not move backward to an earlier stage of differentiation.

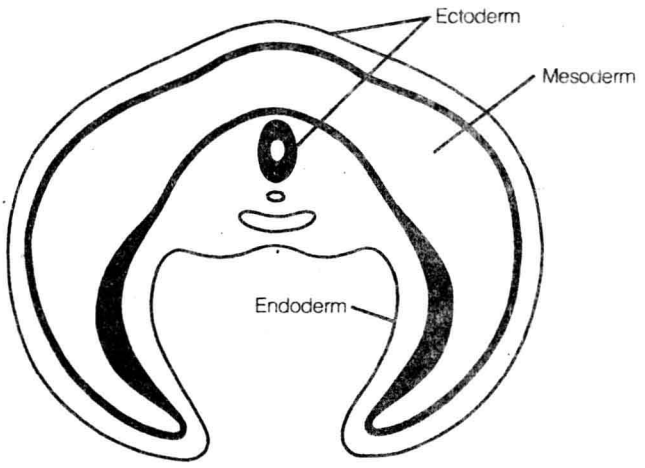
Although most cells proceed through differentiation into specialized cell types, many tissues contain a few cells that apparently are only partially differentiated. These cells are still capable of cell division and serve as a stem cell source for continued

production of specialized cells throughout the life span of the organism. This is one of the major processes by which regeneration is possible in some but not all tissues. Skeletal muscle, for example, has relatively few undifferentiated cells to serve as a reserve supply. Cancer cells can originate from stem cells, or, in special cases, from cells that undergo undifferentiation or revert to earlier stages of differentiation (see Chap.7 for further discussion).

## The Embryonic Origin of Tissue Types

The four basic tissue types are often described in terms of embryonic origin. The very young embryo is essentially a three-layered tubular structure (Fig. 2-7). The outer layer of the tube is called the ectoderm, the middle layer, the mesoderm, and the inner layer, the endoderm. All of the adult body tissues originated from these three cellular layers. Epithelium has its origin in all three embryonic layers, connective tissue and muscle develop from the mesoderm, and nervous tissue develops from the ectoderm. Mesenchymal tissue is a precursor to connective tissue and has its origin in the mesoderm. The epithelial lining of the gut, the respiratory tract, and much of the urinary system is derived from the endoderm.

Figure 2–7. Diagram of the embryonic tissue layers.




## Four Types of Tissue

All of the more than 100 different types of body cells can be classified under four basic or primary tissue types: epithelium, connective, muscle, and nervous. Each of the primary tissue types has various subdivisions. The four tissue types and the major subdivisions are summarized in Table 2-1.

**Table 2-1 Classification of Tissue Types**

| Tissue Type | Location* |
|---|---|
| **Epithelium** | |
| Covering and lining of body surfaces | |
| Simple epithelium | |
| squamous | Lining of blood vessels and body cavities |
| cuboidal | Covering of ovaries and thyroid gland |
| columnar | Lining of intestine and gall bladder |
| Pseudostratified epithelium | Trachea and respiratory passages |
| Stratified epithelium | |
| squamous keratinized | Skin |
| squamous nonkeratinized | Mucous membranes of mouth, esophagus, and vagina |
| transitional | Bladder |
| Glandular | |
| Endocrine | Pituitary, thyroid, adrenal, others |
| Exocrine | Sweat glands and glands in gastrointestinal tract |
| **Connective Tissue** | |
| Loose | Fibroblasts, adipose tissue, endothelial vessel lining |
| Hematopoietic | Blood cells, myeloid tissue (bone marrow), lymphoid tissue |
| Supporting tissues | Connective tissue and cartilage, bone and joint structures |
| **Muscle** | |
| Striated | Skeletal muscles |
| Cardiac | Myocardium |
| Smooth | Gastrointestinal tract, blood vessels, bronchi, bladder, others |
| **Nervous Tissue** | Central and peripheral nerves |

*Not inclusive

## Epithelium

Epithelial tissue covers the body's outer surface, lines the internal surface, and forms the glandular tissues. The epithelium protects (skin and mucous membranes), secretes (glandular tissue and goblet cells), absorbs (intestinal mucosa), and filters (renal glomeruli). The epithelial cells are avascular, that is, they have no blood vessels of their own and must receive oxygen and nutrients from the capillaries of the connective tissue upon which the epithelium rests. To survive the epithelial cells must be kept moist. Even the seemingly dry skin epithelium is kept moist by a nonvitalized waterproof layer of keratin which prevents evaporation of moisture from the deeper living cells. Epithelium is able to quickly regenerate when injury occurs.

The epithelium can be divided into three types: simple, stratified, and pseudostratified. The terms squamous (thin and flat), cuboidal (cube shaped), and columnar (resembling a column) refer to the cell shapes (Fig. 2-8).

*Simple epithelium* contains a single layer of cells. *Simple squamous epithelium* is adapted for filtration; it is found lining the blood vessels, lymph nodes, and alveoli of the lung. *Simple cuboidal epithelium* is found on the surface of the ovary and in the thyroid. *Simple columnar epithelium* lines the intestine. One form of simple columnar epithelium has hairlike projections called *cilia*, and another produces mucus and is called a *goblet* cell.

*Stratified epithelium* contains more than one layer of cells and is designed to protect the body surface. *Keratin* is a tough fibrous protein that is formed from flattened dead cells. *Stratified squamous keratinized epithelium* makes up the epidermis of the skin and *nonkeratinized cells* are found on wet surfaces such as the mouth and tongue.

*Pseudostratified columnar epithelium* is a mixture of columnar cell types. As some of these do not reach the surface of the tissue, it gives the appearance of stratified epithelium. Pseudostratified columnar ciliated epithelium with goblet cells forms the lining of most of the upper respiratory tract.

*Glandular epithelium* can be divided into two types: exocrine and endocrine. The *exocrine glands* have ducts and discharge their secretions directly onto the epithelial surface where they are located. Sweat glands and alveolar glands are examples of exocrine glands. The *endocrine glands* produce secretions that move directly into the blood stream.

## Connective tissue

Connective tissue is the most abundant tissue in the body. As its name indicates, it connects and holds

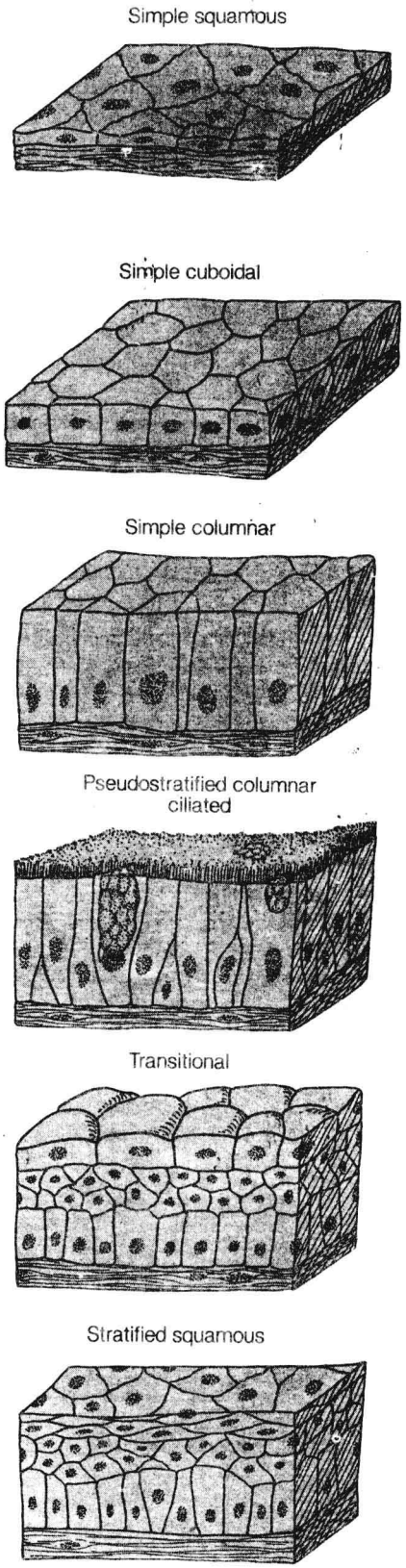



Figure 2–8. Representation of the various epithelial tissue types.