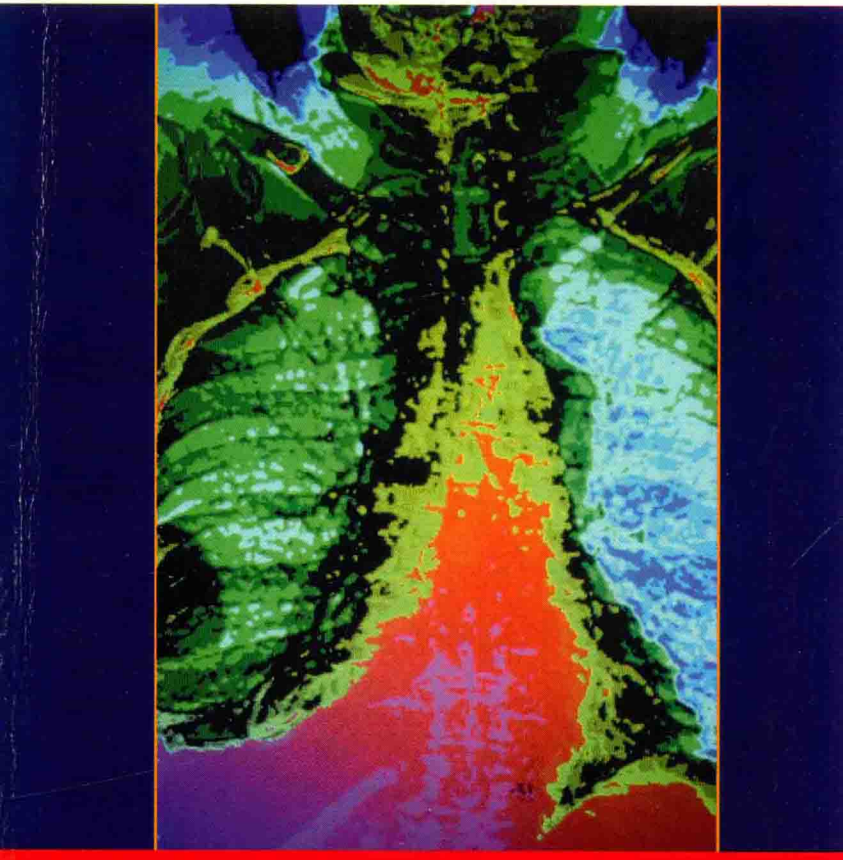
HANDBOOK OF
PATHOPHYSIOLOGY



CAUSES • SIGNS AND SYMPTOMS • DISEASE MANAGEMENT

Foreword by Joan P. Frizzell, RN, PhD

SPRINGHOUSE

Handbook of
PATHOPHYSIOLOGY

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PATHOPHYSIOLOGY

Contributors

Gary J. Arnold, MD, FACS
Assistant Professor of Nursing
University of Louisiana at Lafayette
Lafayette, LA

Deborah Becker, MSN, CRNP, CS, CCRN
Lecturer, Adult Acute Care Practitioner Program
University of Pennsylvania
Philadelphia, PA

Marcy S. Caplin, RN, MSN
Independent Nurse Consultant
Hudson, OH

Susan B. Dickey, PhD, RN,C
Associate Professor
Temple University
Philadelphia, PA

Kay Gentieu, RN, MSN, CRNP
Coordinator Family Nurse Practitioner Program
Thomas Jefferson University
Philadelphia, PA

H. Dean Krimmel, RN, MSN
Independent Nurse Consultant
Collingdale, PA

Nancy LaPlante, RN, BSN
RN-Staff Nurse Emergency Department
The Chester County Hospital
West Chester, PA

Kay Luft, RN, MN, CCRN, TNCC
Assistant Professor
Saint Luke's College
Kansas City, MO

Elaine Mohn-Brown, EdD, RN
Professor, Nursing
Chemeketa Community College
Salem, OR

Roger M. Morrell, MD, PhD, FACP, FAIC
Neurologist
Lathrup Village, MI

David Toub, MD
Consultant
Lansdale, PA

Tracy S. Weintraub, RN, MSN, CNS
Instructor of Clinical Nursing
University of Southern California
Los Angeles, CA

Patricia A. Wessels, RN, MSN
Assistant Dean
Viterbo College
LaCrosse, WI

Foreword

In today's fast-paced, ever-changing health care environment, health care professionals are required to provide competent, compassionate care that integrates every aspect of prior learning. They must assess patients, relate patients' clinical symptoms to the pathophysiology associated with the disease process, interpret laboratory data, and prepare patients for the expected treatment. These actions must be completed quickly and accurately, making both the science and the art of health care more complex. Thus, clinicians need a reliable, accessible reference that incorporates all of this information, enabling them to feel confident about the quality of their care.

Modern clinical practice includes the domains of patient education and advocacy as well as the more traditional domains of providing and coordinating actual patient care. Additionally, clinical practice has moved from the traditional hospital or long-term care facility to the patient's home or to outpatient centers. Typically, there must be collaboration between physicians and other health care professionals as part of the health care team to discuss the patient's physiologic status and treatment issues. They initiate meetings with patients, families, and other members of the health care team to disseminate information about these same issues. To be confident in these aspects clinicians need a reference that enables them to obtain relevant pathophysiologic information applicable to the patient's disease status.

The *Handbook of Pathophysiology* is designed for the health care professional who enjoys the challenge of science-based practice. It is an easy-to-use reference that provides a synopsis of updated information on the major pathophysiologic disease processes. This handbook presents more than 450 diseases. The basic concepts of altered homeostasis, disease development, and disease progression are presented in an easy-to-read format. Additionally, "Pathophysiology in color" is a special section (located within chapter 9) that contains 16 full-color pages, illustrating asthma, cancer, osteoporosis, and ulcers.

The first chapter of the handbook provides an overview of the cell in health and illness. Various cell types and their normal function are discussed, including muscle and nerve cells. This provides the basis for the review of normal physiology found in each chapter. Information about pathophysiologic changes at the cellular level provides the foundation for describing alterations in the major organ systems that occur during illness.

Subsequent chapters are presented in a systems format, including a discussion of the major disorders associated with that particular body system. The pathophysiologic manifestations are described in relation to the patient's clinical presentation. Thus, the clinician can monitor physical changes and relate them directly to the disease process.

The appropriate diagnostic tests for each disease are included in each chapter. The review of expected results from these tests provides information about disease progression, remission, and resolution. This enables all

members of the health care team to become active participants in the clinical decision-making process as plans are made for future care.

The usually recommended treatments are presented as well. Inclusion of this information enables the clinician to prepare for the next phase of patient care. The rationales for the treatment support the development of individualized patient education about the particular treatment.

Each chapter contains crucial age-related, cultural, or socioeconomic information related to common pathophysiologic conditions for that organ system. For example, Chapter 7, the "Respiratory System," includes a discussion of age-related triggers for asthma. There's also information about asthma triggers that patients may encounter in the workplace and the inner city. This is the type of comprehensive information this handbook includes that's applicable to most patient-care circumstances.

The appendix of the handbook includes flow charts that summarize core information for some of the less common diseases. Thus, important facts are available in a synopsis format. The clinician can readily access and refer to these flow charts when accurate information is needed very quickly.

The *Handbook of Pathophysiology* is a much needed reference for the entire health care team. For students, this handbook will complement other textual material and will be easy to use in the clinical site in conjunction with drug and diagnostic study handbooks. New clinicians will refer to this handbook to enable them to integrate patient-assessment information with the proposed plan of care. Experienced professionals will find that this reference contains information that will provide foundation knowledge to be utilized in coordinating patient care and developing patient-education information.

Joan P. Frizzell, RN, PhD
Assistant Professor
School of Nursing
LaSalle University
Philadelphia

Contents

FUNDAMENTALS OF PATHOPHYSIOLOGY

1

An understanding of pathophysiology requires a review of normal physiology — how the body functions day to day, minute to minute, at the levels of cells, tissues, organs, and organisms.

HOMEOSTASIS

Every cell in the body is involved in maintaining a dynamic, steady state of internal balance, called *homeostasis*. Any change or damage at the cellular level can affect the entire body. When homeostasis is disrupted by an external stressor — such as injury, lack of nutrients, or invasion by parasites or other organisms — illness may occur. Many external stressors affect the body's internal equilibrium throughout the course of a person's lifetime. Pathophysiology can be considered as what happens when normal defenses fail.

MAINTAINING BALANCE

Three structures in the brain are responsible for maintaining homeostasis of the entire body:

- medulla oblongata, which is the part of the brain stem associated with vital functions such as respiration and circulation
- pituitary gland, which regulates the function of other glands and, thereby, a person's growth, maturation, and reproduction
- reticular formation, a network of nerve cells (nuclei) and fibers in the brain stem and spinal cord that help control vital reflexes such as cardiovascular function and respiration.

Homeostasis is maintained by self-regulating feedback mechanisms. These mechanisms have three components:

- a sensor that detects disruptions in homeostasis
- a control center that regulates the body's response to those disruptions
- an effector that acts to restore homeostasis.

An endocrine or hormone-secreting gland usually serves as the sensor. It signals the control center in the central nervous system to initiate the effector mechanism.

Feedback mechanisms exist in two varieties: positive and negative.

- A positive feedback mechanism moves the system away from homeostasis by enhancing a change in the system. For example, the heart pumps at increased rate and force when someone is in shock. If the shock progresses, the heart action may require more oxygen than is available. The result is heart failure.
- A negative feedback mechanism works to restore homeostasis by correcting a deficit in the system.

An effective negative feedback mechanism must sense a change in the body — such as a high blood glucose level — and attempt to return body functions to normal. In the case of a high blood glucose level, the effector mechanism triggers increased insulin production by the pancreas, returning blood glucose levels to normal and restoring homeostasis.

DISEASE AND ILLNESS

Although *disease* and *illness* are often used interchangeably, they aren't synonyms. Disease occurs when homeostasis isn't maintained. Illness occurs when a person is no longer in a state of perceived "normal" health. For example, a person may have coronary artery disease, diabetes, or asthma but not be ill all the time because his body has adapted to the disease. In such a situation, a person can perform necessary activities of daily living. Illness usually refers to subjective symptoms, that may or may not indicate the presence of disease.

The course and outcome of a disease are influenced by genetic factors (such as a tendency toward obesity), unhealthy behaviors (such as smoking), attitudes (such as being a "Type A" personality), and even the person's perception of the disease (such as acceptance or denial). Diseases are dynamic and may be manifested in a variety of ways, depending on the patient or his environment.

Cause

The cause of disease may be intrinsic or extrinsic. Inheritance, age, gender, infectious agents, or behaviors (such as inactivity, smoking, or abusing illegal drugs) can all cause disease. Diseases that have no known cause are called *idiopathic*.

Development

A disease's development is called its *pathogenesis*. Unless identified and successfully treated, most diseases progress according to a typical pattern of symptoms. Some diseases are self-limiting or resolve quickly with limited or no intervention; others are chronic and never resolve. Patients with chronic diseases may undergo periodic remissions and exacerbations.

A disease is usually detected when it causes a change in metabolism or cell division that causes signs and symptoms. Manifestations of disease may include hypofunction (such as constipation), hyperfunction (such as increased mucus production), or increased mechanical function (such as a seizure).

How the cells respond to disease depends on the causative agent and the affected cells, tissues, and organs. The resolution of disease depends on many factors functioning over a period of time, such as extent of disease and the presence of other diseases.

Stages

Typically, diseases progress through these stages:

- Exposure or injury — Target tissue is exposed to a causative agent or is injured.
- Latency or incubation period — No signs or symptoms are evident.
- Prodromal period — Signs and symptoms are usually mild and nonspecific.
- Acute phase — The disease reaches its full intensity, possibly resulting in complications. This phase is called the subclinical acute phase if the patient can still function as though the disease wasn't present.
- Remission — This second latent phase occurs in some diseases and is often followed by another acute phase.
- Convalescence — The patient progresses toward recovery after the termination of a disease.
- Recovery — The patient regains health or normal functioning. No signs or symptoms of disease remain.

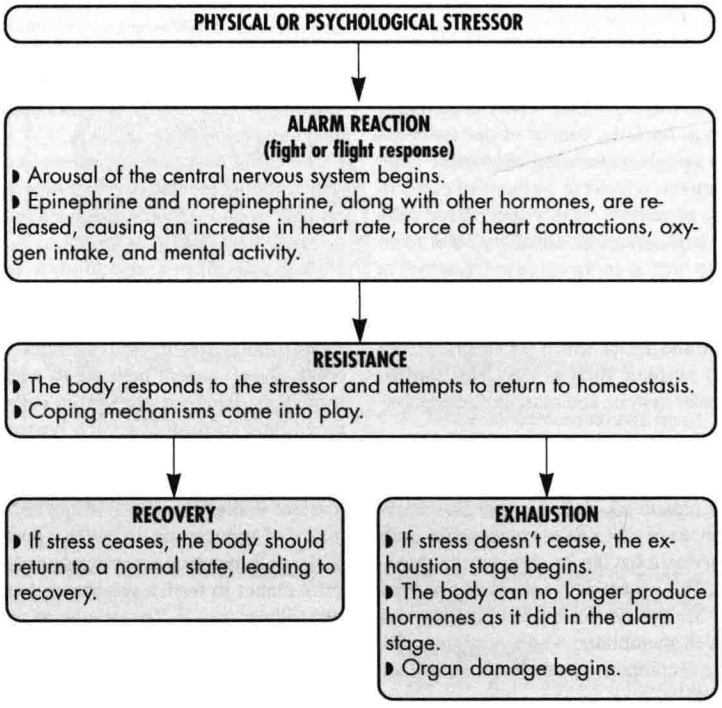
Stress and disease

When a stressor such as a life change occurs, a person can respond in one of two ways: by adapting successfully or by failing to adapt. A maladaptive response to stress may result in disease.

Hans Selye, a pioneer in the study of stress and disease, describes the following stages of adaptation to a stressful event: alarm, resistance, and recovery or exhaustion (See *Physical response to stress.*)

PHYSICAL RESPONSE TO STRESS

According to Hans Selye's General Adaptation Model, the body reacts to stress in the stages depicted below.



In the alarm stage, the body senses stress and arouses the central nervous system (CNS). The body releases chemicals to mobilize the fight-or-flight response. In this dual effort, the sympatho-adrenal medullary response causes the release of epinephrine and the hypothalamic pituitary adrenal axis causes the release of glucocorticoids. Both of these systems work in concert to enable the body to respond to stressors. This release is the adrenaline rush associated with panic or aggression. In the resistance stage, the body either adapts and achieves homeostasis or it fails to adapt and enters the exhaustion stage, resulting in disease.

The stress response is controlled by actions that take place in the cells of the nervous and endocrine systems. These actions try to redirect energy to the organ that is most affected by the stress, such as the heart, lungs, or brain.

Stressors may be physiologic or psychological. Physiologic stressors, such as exposure to a toxin, may elicit a harmful response leading to an identifiable illness or set of symptoms. Psychological stressors, such as the death of a loved one, may also cause a maladaptive response. Stress-

ful events can exacerbate some chronic diseases, such as diabetes or multiple sclerosis. Effective coping strategies can prevent or reduce the harmful effects of stress.

CELL PHYSIOLOGY

The cell is the smallest living component of a living organism. Many organisms, such as bacteria, consist of one independent cell. Human beings and other large organisms consist of millions of cells. In large organisms, highly specialized cells that perform an identical function form tissue such as epithelial tissue, connective tissue, nerve tissue, and muscle tissue. Tissues, in turn, form organs (skin, skeleton, brain, and heart), which are integrated into body systems such as the CNS, cardiovascular system, and musculoskeletal system.

Cell components

Like organisms, cells are complex organizations of specialized components, each component having its own specific function. The largest components of a normal cell are the cytoplasm, the nucleus, and the cell membrane, which surrounds the internal components and holds the cell together.

Cytoplasm

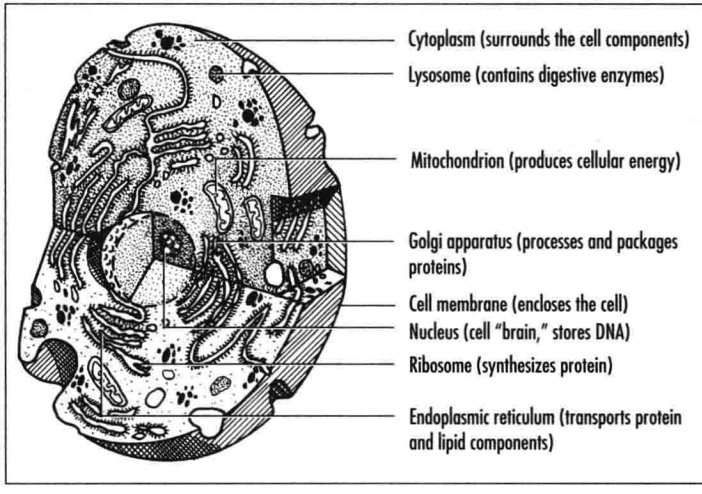
The gel-like cytoplasm consists primarily of cytosol, a viscous, semitransparent fluid that is 70% to 90% water plus various proteins, salts, and sugars. Suspended in the cytosol are many tiny structures called *organelles*.

Organelles are the cell's metabolic machinery. Each performs a specific function to maintain the life of the cell. Organelles include mitochondria, ribosomes, endoplasmic reticulum, Golgi apparatus, lysosomes, peroxisomes, cytoskeletal elements, and centrosomes.

- *Mitochondria* are threadlike structures that produce most of the body's adenosine triphosphate (ATP). ATP contains high-energy phosphate chemical bonds that fuel many cellular activities.
- *Ribosomes* are the sites of protein synthesis.
- The *endoplasmic reticulum* is an extensive network of two varieties of membrane-enclosed tubules. The rough endoplasmic reticulum is covered with ribosomes. The smooth endoplasmic reticulum contains enzymes that synthesize lipids.
- The *Golgi apparatus* synthesizes carbohydrate molecules that combine with protein produced by the rough endoplasmic reticulum and lipids produced by the smooth endoplasmic reticulum to form such products as lipoproteins, glycoproteins, and enzymes.
- *Lysosomes* are digestive bodies that break down nutrient material as well as foreign or damaged material in cells. A membrane surrounding each lysosome separates its digestive enzymes from the rest of the cytoplasm. The enzymes digest nutrient matter brought into the cell by means of endocytosis, in which a portion of the cell membrane surrounds and engulfs matter to form a membrane-bound intracellular vesicle. The membrane of the lysosome fuses with the membrane of the vesicle surrounding the endocytosed material. The lysosomal enzymes then digest the engulfed material. Lysosomes digest the foreign matter ingested by white blood cells by a similar process called *phagocytosis*.
- *Peroxisomes* contain oxidases, which are enzymes that chemically reduce oxygen to hydrogen peroxide and hydrogen peroxide to water.
- *Cytoskeletal elements* form a network of protein structures.
- *Centrosomes* contain centrioles, which are short cylinders adjacent to the nucleus that take part in cell division.
- *Microfilaments* and *microtubules* enable the movement of intracellular vesicles (allowing axous to transport neurotransmitters) and the formation of the mitotic spin-

A LOOK AT CELL COMPONENTS

The illustration below shows the components and structures of a cell. Each part has a function in maintaining the cell's life and homeostasis.



dle, which connects the chromosomes during cell division.

Nucleus

The cell's control center is the nucleus, which plays a role in cell growth, metabolism, and reproduction. Within the nucleus, one or more nucleoli (dark-staining intranuclear structures) synthesize ribonucleic acid (RNA), a complex polynucleotide that controls protein synthesis. The nucleus also stores deoxyribonucleic acid (DNA), the famous double helix that carries genetic material and is responsible for cellular reproduction or division. (See *A look at cell components.*)

Cell membrane

The semipermeable cell membrane forms the cell's external boundary, separating it from other cells and from the external environment. Roughly 75Å (3/10 millionths of an inch) thick, the cell membrane consists of a double layer of phospholipids with protein molecules embedded in it.

Cell division

Each cell must replicate itself for life to continue. Cells replicate by division in one of two ways: mitosis (division that results in two daughter cells with the same DNA and chromosome content as the mother cell) or meiosis (division that creates four gametocytes, each containing half the number of chromosomes of the original cell). Most cells undergo mitosis; meiosis occurs only in reproductive cells.

Mitosis

Mitosis, the type of cell division that leads to tissue growth, creates an equal division of material in the nucleus (karyokinesis) followed by division of the cell body (cytokinesis). This process yields two exact duplicates of the original cell. (See Chap-

ter 4 for a detailed discussion of mitosis and meiosis.)

Cell functions

The basic functions of a cell are movement, conduction, absorption, secretion, excretion, respiration, and reproduction. In the human body, different cells are specialized to perform only one function; muscle cells, for example, are responsible for movement.

Movement

Some cells, such as muscle cells, working together produce movement of a specific body part or the entire organism. Muscle cells attached to bone move the extremities. When muscle cells that envelop hollow organs or cavities contract, they produce movement of contents, such as the peristaltic movement of the intestines or the ejection of blood from the heart.

Conduction

Conduction is the transmission of a stimulus, such as a nerve impulse, heat, or sound wave, from one body part to another.

Absorption

This process of absorption occurs as substances move through a cell membrane. For example, food is broken down into amino acids, fatty acids, and glucose in the digestive tract. Specialized cells in the intestine then absorb the nutrients and transport them to blood vessels, which carry them to other cells of the body. These target cells, in turn, absorb the substances, using them as energy sources or as building blocks to form or repair structural and functional cellular components.

Secretion

Some cells, such as those in the glands, release substances that are used in another part of the body. The beta cells of the islets of Langerhans of the pancreas, for example, secrete insulin, which is transported by the blood to its target cells, where the insulin facilitates the movement of glucose across cell membranes.

Excretion

Cells excrete the waste that is generated by normal metabolic processes. This waste includes such substances as carbon dioxide and certain acids and nitrogen-containing molecules.

Respiration

Cellular respiration occurs in the mitochondria, where ATP is produced. The cell absorbs oxygen; it then uses the oxygen and releases carbon dioxide during cellular metabolism. The energy stored in ATP is used in other reactions that require energy.

Reproduction

New cells are needed to replace older cells for tissue and body growth. Most cells divide and reproduce through mitosis. However, some cells, such as nerve and muscle cells, typically lose their ability to reproduce after birth.

Cell types

Each of the four types of tissue (epithelial, connective, nerve, and muscle tissue) consists of several specialized cell types, which perform specific functions.

Epithelial cell

Epithelial cells line most of the internal and external surfaces of the body, such as the epidermis of the skin, internal organs, blood vessels, body cavities, glands, and sensory organs. The functions of epithelial cells include support, protection, absorption, excretion, and secretion.

Connective tissue cell

Connective tissue cells are found in the skin, the bones and joints, the artery walls, the fascia around organs, nerves, and body fat. The types of connective tissue cells include fibroblasts (such as collagen,

elastin, and reticular fibers), adipose (fat) cells, mast cells (release histamines and other substances during inflammation), and bone. The major functions of connective tissues are protection, metabolism, support, temperature maintenance, and elasticity.

Nerve cell

Two types of cells — neurons and neuroglial cells — comprise the nervous system. Neurons have a cell body, dendrites, and an axon. The dendrites carry nerve impulses to the cell body from the axons of other neurons. Axons carry impulses away from the cell body to other neurons or organs. A myelin sheath around the axon facilitates rapid conduction of impulses by keeping them within the nerve cell. Nerve cells:

- generate electrical impulses
- conduct electrical impulses
- influence other neurons, muscle cells, and cells of glands by transmitting those impulses.

Neuroglial cells, also called glial cells, consist of four different cell types: oligodendroglia, astrocytes, ependymal cells, and microglia. Their function is to support, nourish, and protect the neurons.

Muscle cell

Muscle cells contract to produce movement or tension. The intracellular proteins actin and myosin interact to form crossbridges that result in muscle contraction. An increase in intracellular calcium is necessary for muscle to contract.

There are three basic types of muscle cells:

- *Skeletal (striated) muscle cells* are long, cylindrical cells that extend along the entire length of the skeletal muscles. These muscles, which attach directly to the bone or are connected to the bone by tendons, are responsible for voluntary movement. By contracting and relaxing, striated muscle cells alter the length of the muscle.
- *Smooth (nonstriated) muscle cells* are present in the walls of hollow internal organs, such as the gastrointestinal (GI) and genitourinary tracts, and of blood vessels and bronchioles. Unlike striated muscle, these spindle-shaped cells contract involuntarily. By contracting and relaxing, they change the luminal diameter of the hollow structure, and thereby move substances through the organ.
- *Cardiac muscle cells* branch out across the smooth muscle of the chambers of the heart and contract involuntarily. They produce and transmit cardiac action potentials, which cause cardiac muscle cells to contract. Impulses travel from cell to cell as though no cell membrane existed.

AGE ALERT In older adults, muscle cells become smaller and many are replaced by fibrous connective tissue. The result is loss of muscle strength and mass.

PATHOPHYSIOLOGIC CHANGES

The cell faces a number of challenges through its life. Stressors, changes in the body's health, diease, and other extrinsic and intrinsic factors can change the cell's normal functioning (homeostasis).

Cell adaptation

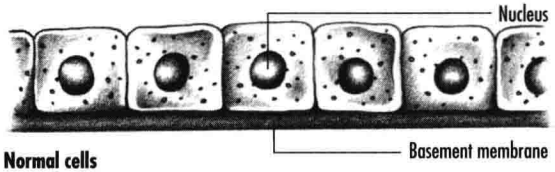
Cells are generally able to continue functioning despite changing conditions or stressors. However, severe or prolonged stress or changes may injure or even kill cells. When cell integrity is threatened — for example, by hypoxia, anoxia, chemical injury, infection, or temperature extremes — the cell reacts in one of two ways:

- by drawing on its reserves to keep functioning
- by adaptive changes or cellular dysfunction.

If enough cellular reserve is available and the body doesn't detect abnormalities, the cell adapts. If cellular reserve is insufficient, cell death (necrosis) occurs.

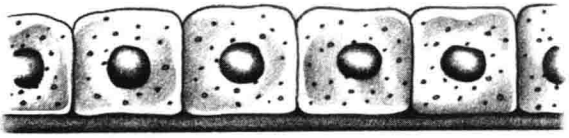
ADAPTIVE CELL CHANGES

Cells adapt to changing conditions and stressors within the body in the ways shown below.

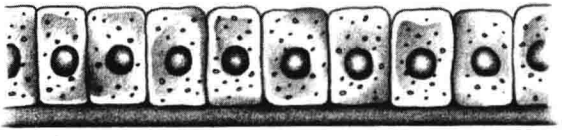


Normal cells

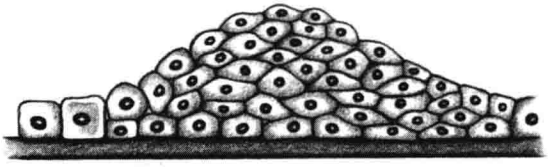
Atrophy



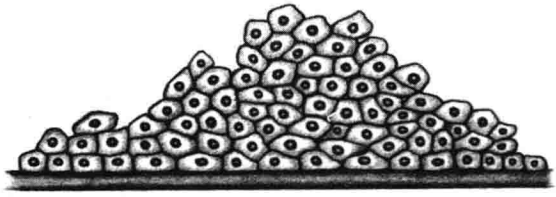
Hypertrophy



Hyperplasia



Metaplasia



Dysplasia

Necrosis is usually localized and easily identifiable.

The cells' methods of adapting include atrophy, hypertrophy, hyperplasia, metaplasia, and dysplasia. (See *Adaptive cell changes.*)

Atrophy

Atrophy is a reduction in the size of a cell or organ that may occur when cells face reduced workload or disuse, insufficient blood flow, malnutrition, or reduced hormonal and nerve stimulation. Examples of atrophy include loss of muscle mass and tone after prolonged bed rest.

Hypertrophy

In contrast, hypertrophy is an increase in the size of a cell or organ due to an increase in workload. The three basic types of hypertrophy are *physiologic*, *compensatory*, and *pathologic*.

- *Physiologic hypertrophy* reflects an increase in workload that is not caused by disease — for example, the increase in muscle size caused by hard physical labor or weight training.
- *Compensatory hypertrophy* takes place when cell size increases to take over for nonfunctioning cells. For instance, one kidney will hypertrophy when the other is not functioning or is removed.
- *Pathologic hypertrophy* is a response to disease. An example is hypertrophy of the heart muscle as the muscle pumps against increasing resistance in patients with hypertension.

Hyperplasia

Hyperplasia is an increase in the number of cells caused by increased workload, hormonal stimulation, or decreased tissue density. Like hypertrophy, hyperplasia may be *physiologic*, *compensatory*, or *pathologic*.

- *Physiologic hyperplasia* is an adaptive response to normal changes. An example is the monthly increase in number of uterine cells that occurs in response to estrogen stimulation of the endometrium after ovulation.
- *Compensatory hyperplasia* occurs in some organs to replace tissue that has been removed or destroyed. For example, liver cells regenerate when part of the liver is surgically removed.
- *Pathologic hyperplasia* is a response to either excessive hormonal stimulation or abnormal production of hormonal growth factors. Examples include acromegaly, in which excessive growth hormone production causes bones to enlarge, and endometrial hyperplasia, in which excessive secretion of estrogen causes heavy menstrual bleeding and possibly malignant changes.

Metaplasia

Metaplasia is the replacement of one cell type with another cell type. A common cause of metaplasia is constant irritation or injury that initiates an inflammatory response. The new cell type can better endure the stress of chronic inflammation. Metaplasia may be either *physiologic* or *pathologic*.

- *Physiologic metaplasia* is a normal response to changing conditions and is generally transient. For example, in the body's normal response to inflammation, monocytes that migrate to inflamed tissues transform into macrophages.
- *Pathologic metaplasia* is a response to an extrinsic toxin or stressor and is generally irreversible. For example, after years of exposure to cigarette smoke, stratified squamous epithelial cells replace the normal ciliated columnar epithelial cells of the bronchi. Although the new cells can better withstand smoke, they don't secrete mucus nor do they have cilia to protect the airway. If exposure to cigarette smoke continues, the squamous cells can become cancerous.

Dysplasia

In dysplasia, abnormal differentiation of dividing cells results in cells that are abnormal in size, shape, and appearance. Al-