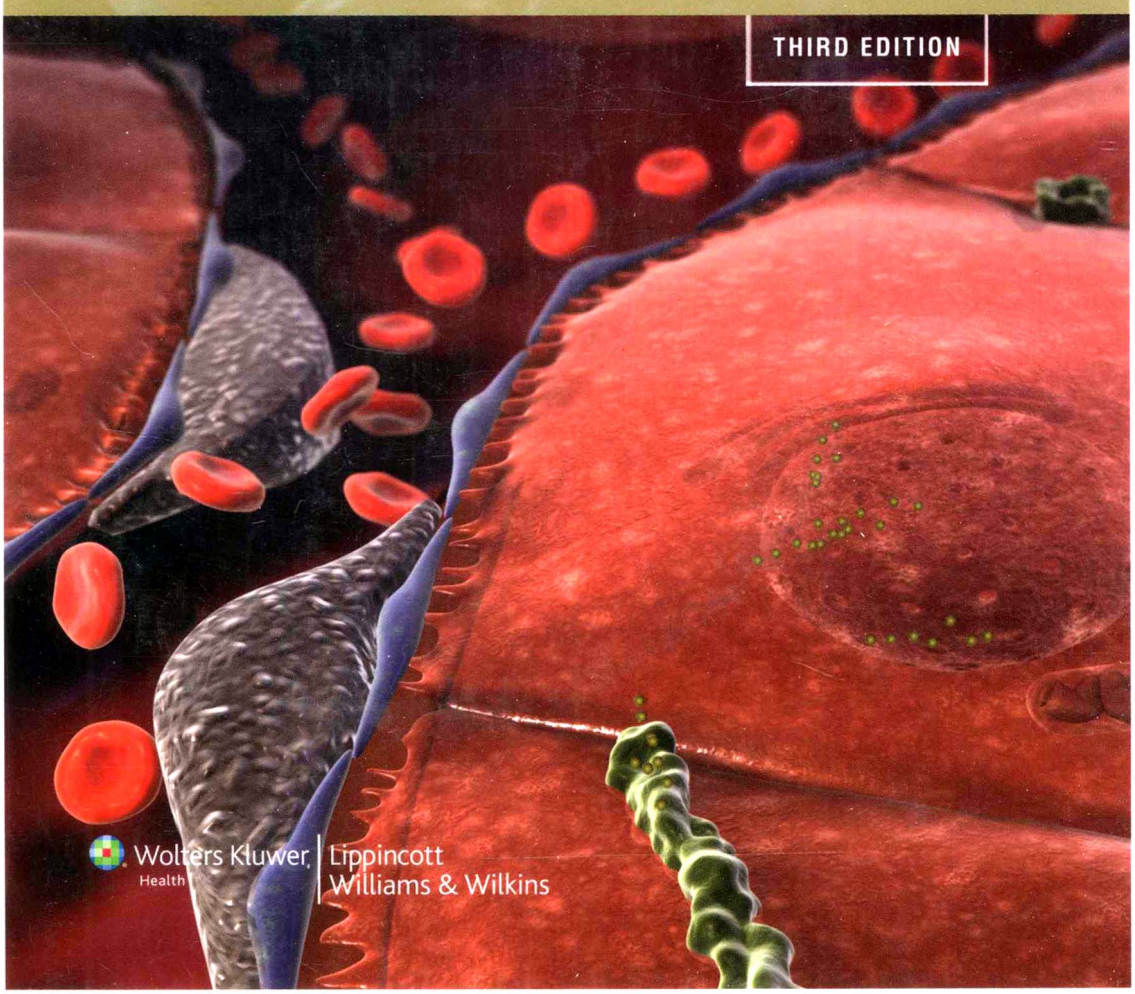
Essentials of Pathophysiology

Carol Mattson Porth

THIRD EDITION



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Essentials of Pathophysiology

CONCEPTS OF ALTERED HEALTH STATES

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This book is dedicated to
All the Students who use the book, for it is for them that the book was written

Carol Mattson Porth

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Preface

The text, which is based on the eighth edition of *Pathophysiology: Concepts of Altered Health,* has been prepared specifically for those students who do not need the extensive breadth or detail of content provided in the larger book. To accomplish this task, content deemed to be less essential has been omitted, while essential content has been reorganized, revised, and condensed.

The integration of full color into the design and illustrations from the eighth edition has been carried over into the third edition of the essentials version. Over 200 of the illustrations that appear in this edition are new or have been extensively modified. The illustrations—line drawings of anatomic structures and pathophysiologic processes, flow charts, and photographic illustrations of disease states—have been carefully chosen to support the concepts that are presented in the text. This offers not only visual appeal but also enhances conceptual learning, linking text content to illustration content A new element, the "clinical feature," uses illustration to depict the clinical manifestations of selected disease states.

The third edition also retains the list of suffixes and prefixes, the glossary, and the table of normal laboratory values that were in the previous edition. The table of laboratory values includes conventional and SI units, as well as conversion units and internet addresses for additional information. The key concept boxes have been retained within each chapter. They are intended to help the reader retain and use text information by providing a mechanism to incorporate the information into a larger conceptual unit as opposed to merely memorizing a string of facts. Review exercises appear at the end of each chapter and assist the reader in using the conceptual approach to solving problems related to chapter content.

Along with the extensive changes and revision, every attempt has been made to present content in a manner that is logical, understandable, and that inspires reader interest. The content has been arranged so that concepts build on one another, with concepts from physiology, biochemistry, physics, and other sciences reviewed as deemed appropriate. A conceptual model that integrates the developmental and preventative aspects of health has been used. Selection of content was based on common health problems, including the special needs of children, pregnant women, and elderly persons. Although first and foremost intended as a course textbook, it also serves as a reference book that students can take with them and use in their practice once the course is finished.

And finally, as a nurse–physiologist, my major emphasis with each edition has been to relate normal body functioning to the physiologic changes that participate in disease production and occur as a result of disease, as well as the body's remarkable ability to compensate for these changes. The beauty of physiology is that it integrates all of the aspects of human genetics, molecular and cellular biology, and organ anatomy and physiology into a functional whole that can be used to explain both the physical and psychological aspects of altered health. Indeed, it has been my philosophy to share the beauty of the human body and to emphasize that in disease as in health, there is more "going right" in the body than is "going wrong." This book is an extension of my career and, as such, of my philosophy. It is my hope that readers will learn to appreciate the marvelous potential of the body, incorporating it into their own philosophy and ultimately sharing it with their clients.

Carol Mattson Porth

Student and Instructor Resources

Student Resources

The student resource DVD accompanying this text contains several useful study resources including

- **Animations** of selected pathophysiologic processes
- **Student Review Questions** for every chapter

Resources are also available online at thePoint.lww.com!

Instructor Resources

The instructor resource DVD available to accompany this text is a comprehensive resource including the following:

- **Test Generator** containing over 900 multiple-choice questions
- **PowerPoint** presentations with incorporated images from the book
- **Image Bank** featuring all of the figures from each chapter
- **Lecture Outlines** for presenting key information to your students
- **Assignments** and **Quizzes** for gauging student understanding
- **Discussion Topics** to encourage critical thinking
- **Case Studies** providing real life application of concepts
- **WebCT- and Blackboard-ready materials** for use with your institution's Learning Management System.

Resources are also available online at thePoint.lww.com!

To the Reader

This book was written with the intent of making the subject of pathophysiology an exciting exploration that relates normal body functioning to the physiologic changes that occur as a result of disease, as well as the body's remarkable ability to compensate for these changes. Indeed, it is these changes that represent many of the signs and symptoms of disease.

Using a book such as this can be simplified by taking time out to find what is in the book and how to locate information when it is needed. The *table of contents* at the beginning of the book provides an overall view of the organization and content of the book. The *index,* which appears at the end of the book, can be viewed as a road map for locating content. It can be used to quickly locate related content in different chapters of the book or to answer questions that come up in other courses.

Organization

The book is organized into units and chapters. The *units* identify broad areas of content, such as alterations in the circulatory system. Many of the units have *introductory chapters* that contain information about the normal structure and function of the body systems that are being discussed in the unit. These chapters, which are intended as a review of content from previous courses as well as an update on recent scientific advances in genetic and molecular biology, provide the foundation for understanding the pathophysiology content presented in the subsequent chapters. The *disorder chapters* focus on specific areas of pathophysiology content, such as heart failure and circulatory shock. The *chapter outline* that appears at the beginning of each chapter provides an overall view of the chapter content and organization. *Icons* identify specific content related to infants and children  , pregnant women  , and older adults  .

Reading and Learning Aids

In an ever-expanding world of information you will not be able to read, let alone remember, everything that is in this book, or in any book, for that matter. With this in mind, we have developed a number of special features that will help you focus on and master the essential content for your current as well as future needs.

It is essential for any professional to use and understand the vocabulary of his or her profession. Throughout the text, you will encounter terms in *italics.* This is a signal that a word and the ideas associated with it are important to learn. In addition, in the back of the book are two aids that can be used to help you expand your vocabulary and improve your comprehension of what you are reading: the glossary and the list of prefixes and suffixes.

The *glossary* contains concise definitions of frequently encountered terms. If you are unsure of the meaning of a term you encounter in your reading, check the glossary in the back of the book before proceeding. The *list of prefixes and suffixes,* found in the inside back cover, is a tool to help you derive the meaning of words you may be unfamiliar with and increase your vocabulary. Many disciplines establish a vocabulary by affixing one or more letters to the beginning or end of a word or base to form a derivative word. Prefixes are added to the beginning of a word or base, and suffixes are added to the end. If you know the meanings of common prefixes and suffixes, you can usually derive the meaning of a word, even if you have never encountered it before.

Boxes

Boxes are used throughout the text to summarize and highlight key information. You will frequently encounter two types of boxes: *Key Concept Boxes* and *Summary Boxes.* One of the ways to approach learning is to focus on the major ideas or concepts rather than trying to memorize significant amounts of information. As you have probably already discovered, it is impossible to memorize everything that is in a particular section or chapter of the book. Not only does your brain have a difficult time trying to figure out where to store all the different bits of information, your brain doesn't know how to retrieve the information when you need it. Most important of all, memorized lists of content can seldom, if ever, be applied directly to an actual clinical situation. The *Key Concept Boxes* guide you in identifying the major ideas or concepts that form the foundation for truly understanding the major areas of content. When you understand the concepts in the Key Concept Boxes, you will have a framework for remembering and using the facts given in the text.

Primary Immunodeficiency Disorders

- Primary immunodeficiency disorders are congenital or inherited abnormalities of immune function that render a person susceptible to diseases normally prevented by an intact immune system.
- Disorders of B-cell function impair the ability to produce antibodies and defend against microorganisms and toxins that circulate in body fluids (IgM and IgG) or enter the body through the mucosal surface of the respiratory or gastrointestinal tract (IgA). Persons with primary B-cell immunodeficiency are particularly prone to pyogenic infections due to encapsulated organisms.
- Disorders of T-cell function impair the ability to orchestrate the immune response ($CD4^+$ helper T cells) and to protect against viral ($CD8^+$ cytotoxic T cells), intracellular bacterial, fungal, and protozoan infections. T cells also play an important role in surveillance against oncogenic viruses and tumors; hence, persons with impaired T-cell function are at increased risk for certain types of cancers.
- Combined T-cell and B-cell immunodeficiency states affect all aspects of immune function. Severe combined immunodeficiency represents a life-threatening absence of immune function that requires bone marrow or stem cell transplantation for survival.

The *Summary Boxes* at the end of each section provide a review and a reinforcement of the main content that has been covered. Use the summaries to assure that you have covered and understand what you have read.

In summary, heart failure occurs when the heart fails to pump sufficient blood to meet the metabolic needs of body tissues. The physiology of heart failure reflects the interplay between a decrease in cardiac output that accompanies impaired function of the failing heart and the compensatory mechanisms that preserve the cardiac reserve. Compensatory mechanisms include the Frank-Starling mechanism, sympathetic nervous system activation, the renin-angiotensin-aldosterone mechanism, natriuretic peptides, endothelins, and myocardial hypertrophy and remodeling. In the failing heart, early decreases in cardiac function may go unnoticed because these compensatory mechanisms maintain the cardiac output. Unfortunately, the mechanisms were not intended for long-term use, and in severe and prolonged heart failure the compensatory mechanisms no longer are effective, and instead contribute to the progression of heart failure.

Tables and Charts

Tables and charts are designed to present complex information in a format that makes it more meaningful and easier to remember. Tables have two or more columns, and are often used for the purpose of comparing or contrasting information.

TABLE 8-2 Sources of Body Water Gains and Losses in the Adult

Gains		Losses	
Oral intake		Urine	1500 mL
As water	1000 mL	Insensible losses	
In food	1300 mL	Lungs	300 mL
Water of oxidation	200 mL	Skin	500 mL
		Feces	200 mL
Total	2500 mL	Total	2500 mL

Charts have one column and are used to summarize information.

CHART 18-1 Risk Factors for Atherosclerosis

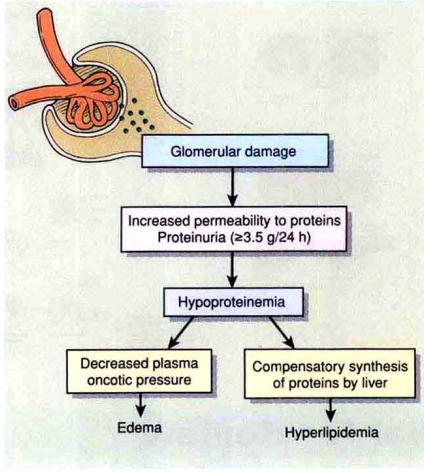
Nonmodifiable
- Increasing age
- Male gender
- Genetic disorders of lipid metabolism
- Family history of premature coronary artery disease

Potentially Modifiable
- Cigarette smoking
- Obesity
- Hypertension
- Hyperlipidemia with elevated low-density lipoprotein and low high-density lipoprotein cholesterol
- Diabetes mellitus

Additional Nontraditional
- Inflammation marked by elevated C-reactive protein levels
- Hyperhomocystinemia
- Increased lipoprotein (a) levels

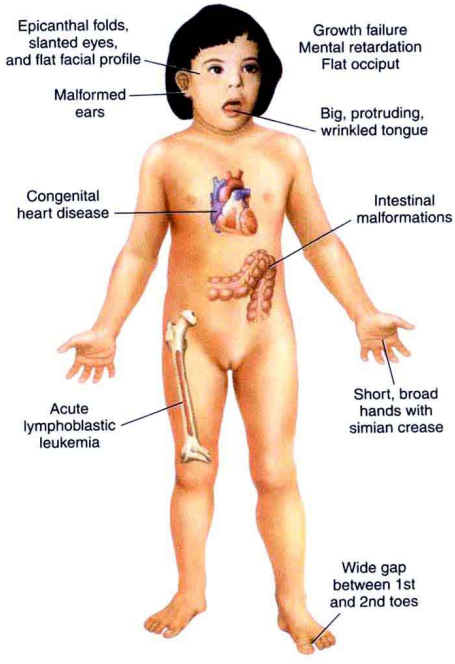
Illustrations and Photos

The full-color illustrations will help you to build your own mental image of the content that is being presented. Each drawing has been developed to fully support and build upon the ideas in the text. Some illustrations are used to help you picture the complex interactions of the multiple phenomena that are involved in the development of a particular disease; others can help you visualize normal function or understand the mechanisms whereby the disease processes exert their effects. In addition, photographs of pathologic processes and lesions provide a realistic view of selected pathologic processes and lesions.



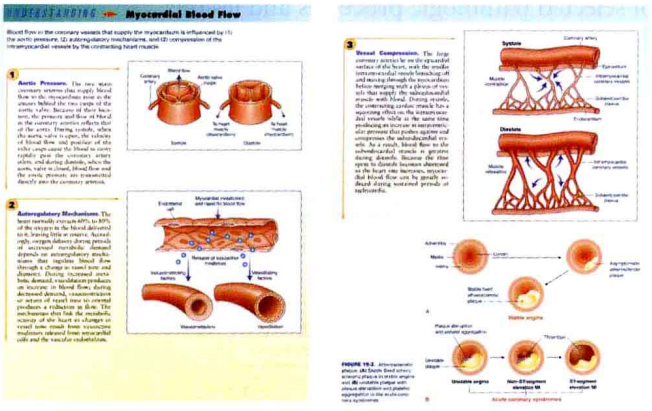
Clinical Features

New to this edition is a new type of illustration that depicts the clinical features of persons with selected diseases. This feature is designed to help you visualize the entire spectrum of clinical manifestations that are associated with these disease states.



Understanding Physiologic Processes

Included in a number of chapters is an "*Understanding*" feature that focuses on the physiologic processes and phenomena that form the basis for understanding disorders presented in the text. This feature breaks a process or phenomenon down into its component parts and presents them in a sequential manner, providing an insight into the many opportunities for disease processes to disrupt the sequence.



Material for Review

An important feature has been built into the text to help you verify your understanding of the material presented. After you have finished reading and studying the chapter, work on answering the *review exercises* at the end of the chapter. They are designed to help you integrate, conceptualize, and apply material from the text. If you are unable to answer a question, reread the relevant section in the chapter.

REVIEW EXERCISES

1. A 6-year-old boy is admitted to the emergency department with nausea, vomiting, and abdominal pain. He is very lethargic; his skin is warm, dry, and flushed; his pulse is rapid; and he has a sweet smell to his breath. His parents relate that he has been very thirsty during the past several weeks, his appetite has been poor, and he has been urinating frequently. His initial plasma glucose is 420 mg/dL (23.1 mmol/L), and a urine test for ketones is strongly positive.

A. What is the most likely cause of this boy's elevated blood glucose and ketonuria?
B. Explain his presenting signs and symptoms in terms of the elevated blood glucose and metabolic acidosis.
C. What type of treatment will this boy require?

Appendix

The *Lab Values table* in the appendix of your book provides rapid access to normal values for many laboratory tests in conventional and SI units, as well as a description of the prefixes, symbols, and factors (e.g., micro, μ, 10^{-6}) used for describing these values. Knowledge of normal values can help you put abnormal values in context.

We hope that this guide has given you a clear picture of how to use this book. Good luck and enjoy the journey!

Acknowledgements

As in past editions, many persons participated in the creation of this work. The contributing authors deserve a special mention. Without their long hours of work preparing the eighth edition of *Pathophysiology: Concepts of Altered Health States,* which served as a foundation, the preparation of this essentials version would not have been possible. I would like to expressly share my gratitude to and esteem of Dr. Edward W. Carroll, who expired during the preparation of this edition. He was with the book from its beginning and played an important role in its genesis and continued development.

I would also like to acknowledge Dr. Kathryn Gaspard and Dr. Kim Noble for their consultation and help in making this edition become a reality. Dr. Gaspard, in particular, deserves special thanks. Her genial nature, wide-breadth of knowledge, and skillful assistance were invaluable in preparing the text and developing the illustrations for the book. Several other persons deserve special recognition. Georgianne Heymann assisted in editing the manuscript. As with previous editions, she provided not only excellent editorial assistance but also encouragement and support when the tasks associated with manuscript preparation became most frustrating.

Special thanks also to those at Lippincott Williams & Wilkins who participated in the development of this edition: Hilarie Surrena, Senior Acquisitions Editor; Katherine Burland, Product Manager; and Brett MacNaughton, Art Director. Acknowledgement also goes to Wendy Beth Jackelow, MFA, CMI, for her talent and expertise in creating and modifying the illustrations; and to Jeri Litteral, Managing Editor, Aptara Corporation, for her dedication in managing the production and printing of the book.

The students in the classes I have taught over the years also deserve a special salute, for they are the inspiration upon which this book was founded. They provided the questions, suggestions, and contact with the "real world" of patient care that directed the organization and selection of content for the book.

And last, but certainly not least, I would like to acknowledge my family and my friends for their unlimited patience, understanding, and encouragement throughout the entire process.

Introduction to Pathophysiology

The term *pathophysiology,* which is the focus of this book, may be defined as the physiology of altered health. The term combines the words *pathology* and *physiology.* Pathology (from the Greek *pathos,* meaning "disease") deals with the study of the structural and functional changes in cells, tissues, and organs of the body that cause or are caused by disease. Physiology deals with the functions of the human body. Thus, pathophysiology deals not only with the cellular and organ changes that occur with disease, but with the effects that these changes have on total body function. Pathophysiology also focuses on the mechanisms of the underlying disease process and provides the background for preventive as well as therapeutic health care measures and practices.

Disease

A *disease* has been defined as an interruption, cessation, or disorder of a body system or organ structure that is characterized usually by a recognized etiologic agent or agents, an identifiable group of signs and symptoms, or consistent anatomic alterations.[1] The aspects of the disease process include etiology, pathogenesis, morphologic changes, clinical manifestations, diagnosis, and clinical course.

Etiology

The causes of disease are known as *etiologic factors.* Among the recognized etiologic agents are biologic agents (e.g., bacteria, viruses), physical forces (e.g., trauma, burns, radiation), chemical agents (e.g., poisons, alcohol), and nutritional excesses or deficits. At the molecular level, it is important to distinguish between abnormal molecules and molecules that cause disease.[2] This is true of diseases such as cystic fibrosis, sickle cell anemia, and familial hypercholesterolemia, in which the genetic abnormality of a single amino acid, transporter molecule, or receptor protein produces widespread effects on health.

Most disease-causing agents are nonspecific, and many different agents can cause disease of a single organ. On the other hand, a single agent or traumatic event can lead to disease of a number of organs or systems. Although a disease agent can affect more than a single organ and a number of disease agents can affect the same organ, most disease states do not have a single cause. Instead, the majority of 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 often are referred to as *risk factors.*

One way to view the factors that cause disease is to group them into categories according to whether they were present at birth or acquired later in life. *Congenital conditions* are defects that are present at birth, although they may not be evident until later in life. Congenital conditions may be caused by genetic influences, environmental factors (e.g., viral infections in the mother, maternal drug use, irradiation, or intrauterine crowding), or a combination of genetic and environmental factors. *Acquired defects* are those that are caused by events that occur after birth. These include injury, exposure to infectious agents, inadequate nutrition, lack of oxygen, inappropriate immune responses, and neoplasia. Many diseases are thought to be the result of a genetic predisposition and an environmental event or events that serve as a trigger to initiate disease development.

Pathogenesis

Pathogenesis is the sequence of cellular and tissue events that take place from the time of initial contact with an etiologic agent until the ultimate expression of a disease. Etiology describes what sets the disease process in motion, and pathogenesis, how the disease process evolves. Although the two terms often are used interchangeably, their meanings are quite different. For example, atherosclerosis often is cited as the cause or etiology of coronary heart disease. In reality, the progression from fatty streak to the occlusive vessel lesion seen in persons with coronary heart disease represents the pathogenesis of the disorder. The true etiology of atherosclerosis remains largely uncertain.

Morphology

Morphology refers to the fundamental structure or form of cells or tissues. *Morphologic changes* are concerned with both the gross anatomic and microscopic changes that are characteristic of a disease. *Histology* deals with the study of the cells and extracellular matrix of body tissues. The most common method used in the study of tissues is the preparation of histologic sections—thin, translucent sections of human tissues and organs—that can be examined with the aid of a microscope. Histologic sections play an important role in the diagnosis of many types of cancer. A *lesion* represents a pathologic or traumatic discontinuity of a body organ or tissue. Descriptions of lesion size and characteristics often can be obtained through the use of radiographs, ultrasonography, and other imaging methods. Lesions also may be sampled by biopsy and the tissue samples subjected to histologic study.

Clinical Manifestations

Diseases can manifest in a number of ways. Sometimes the condition produces manifestations, such as fever, that make it evident that the person is sick. In other cases, the condition is silent at the onset and is detected during examination for other purposes or after the disease is far advanced.

Signs and *symptoms* are terms used to describe the structural and functional changes that accompany a disease. A *symptom* is a subjective complaint that is noted by the person with a disorder, whereas a *sign* is a manifestation that is noted by an observer. Pain, difficulty in breathing, and dizziness are symptoms of a disease. 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 disease. 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. Many pathologic states are not observed directly—one cannot see a sick heart or a failing kidney. Instead, what can be observed is the body's attempt to compensate for changes in function brought about by the disease, such as the tachycardia that accompanies blood loss or the increased respiratory rate that occurs with pneumonia.

A *syndrome* is a compilation of signs and symptoms (e.g., chronic fatigue syndrome) that are characteristic of a specific disease state. *Complications* are possible adverse extensions of a disease or outcomes from treatment. *Sequelae* are lesions or impairments that follow or are caused by a disease.

Diagnosis

A *diagnosis* is the designation as to the nature or cause of a health problem (e.g., bacterial pneumonia or hemorrhagic stroke). The diagnostic process usually requires a careful history and physical examination. The history is used to obtain a person's account of his or her symptoms and their progression, and the factors that contribute to a diagnosis. The physical examination is done to observe for signs of altered body structure or function.

The development of a diagnosis involves weighing competing possibilities and selecting the most likely one from among the conditions that might be responsible for the person's clinical presentation. The clinical probability of a given disease in a person of a given age, sex, race, lifestyle, and locality often is influential in arrival at a presumptive diagnosis. Laboratory tests, radiologic studies, computed tomography (CT) scans, and other tests often are used to confirm a diagnosis.

An important factor when interpreting diagnostic test results is the determination of whether they are normal or abnormal. Is a blood count above normal, within the normal range, or below normal? What is termed a *normal* value for a laboratory test is established statistically from test results obtained from a selected sample of people. The normal values refer to the 95% distribution (mean plus or minus two standard deviations [mean ± 2 SD]) of test results for the reference population.[3,4] Thus, the normal levels for serum sodium (136 to 145 mEq/L) represent the mean serum level for the reference population ± 2 SD. The normal values for some laboratory tests are adjusted for sex or age. For example, the normal hemoglobin range for women is 12.0 to 16.0 g/dL, and for men, 14.0 to 17.4 g/dL.[5] Serum creatinine level often is adjusted for age in the elderly, and normal values for serum phosphate differ between adults and children.

The quality of data on which a diagnosis is based may be judged for their validity, reliability, sensitivity, specificity, and predictive value.[6,7] *Validity* refers to the extent to which a measurement tool measures what it is intended to measure. This often is assessed by comparing a measurement method with the best possible method of measure that is available. For example, the validity of blood pressure measurements obtained by a sphygmomanometer might be compared with those obtained by intra-arterial measurements. *Reliability* refers to the extent to which an observation, if repeated, gives the same result. A poorly calibrated blood pressure machine may give inconsistent measurements of blood pressure, particularly of pressures in either the high or low range. Reliability also depends on the persons making the measurements. For example, blood pressure measurements may vary from one observer to another because of the technique that is used (e.g., different observers may deflate the cuff at a different rate, thus obtaining different values), the way the numbers on the manometer are read, or differences in hearing acuity.

In the field of clinical laboratory measurements, *standardization* is aimed at increasing the trueness and reliability of measured values. Standardization relies on the use of written standards, reference measurement procedures, and reference materials.[7] In the United States, the Food and Drug Administration (FDA) regulates in vitro diagnostic devices, including clinical laboratory instruments, test kits, and reagents. Manufacturers who propose to market new diagnostic devices must submit information on their instrument, test kit, or reagent to the FDA, as required by existing statutes and regulations. The FDA reviews this information to decide whether the product may be marketed in the United States.

Measures of sensitivity and specificity are concerned with determining how likely or how well the test or observation will identify people with the disease and people without the disease.[9] *Sensitivity* refers to the proportion of people with a disease who are positive for that disease on a given test or observation (called a *true-positive* result). If the result of a very sensitive test is negative, it tells us the person does not have the disease and the disease has been excluded or "ruled out." *Specificity* refers to the proportion of people without the disease who are negative on a given test or observation (called a *true-negative* result). Specificity can be calculated only from among people who do not have the disease. A test that is 95% specific correctly identifies 95 of 100 normal people. The other 5% are *false-positive* results. A false-positive test result can be unduly stressful for the person being tested, whereas a *false-negative* test result can delay diagnosis and jeopardize the outcome of treatment.

Predictive value is the extent to which an observation or test result is able to predict the presence of a given disease or condition.[8,9] A *positive predictive value* refers to the proportion of true-positive results that occurs in a given population. In a group of women found to have "suspect breast nodules" in a cancer screening program, the proportion later determined to have breast cancer would constitute the positive predictive value. A *negative predictive value* refers to the true-negative observations in

a population. In a screening test for breast cancer, the negative predictive value represents the proportion of women without suspect nodules who do not have breast cancer. Although predictive values rely in part on sensitivity and specificity, they depend more heavily on the prevalence of the condition in the population. Despite unchanging sensitivity and specificity, the positive predictive value of an observation rises with prevalence, whereas the negative predictive value falls.

Clinical Course

The clinical course describes the evolution of a disease. A disease can have an acute, subacute, or chronic course. An *acute disorder* is one that is relatively severe, but self-limiting. *Chronic disease* implies a continuous, long-term process. A chronic disease can run a continuous course or can present with exacerbations (aggravation of symptoms and severity of the disease) and remissions (a period during which there is a decrease in severity and symptoms). *Subacute disease* is intermediate or between acute and chronic: it is not as severe as an acute disease and not as prolonged as a chronic disease.

The spectrum of disease severity for infectious diseases, such as hepatitis B, can range from preclinical to persistent chronic infection. During the *preclinical stage,* the disease is not clinically evident but is destined to progress to clinical disease. As with hepatitis B, it is possible to transmit a virus during the preclinical stage. *Subclinical disease* is not clinically apparent and is not destined to become clinically apparent. It is diagnosed with antibody or culture tests. Most cases of tuberculosis are not clinically apparent, and evidence of their presence is established by skin tests. *Clinical disease* is manifested by signs and symptoms. A persistent chronic infectious disease persists for years, sometimes for life. *Carrier status* refers to an individual who harbors an organism but is not infected, as evidenced by antibody response or clinical manifestations. This person still can infect others. Carrier status may be of limited duration or it may be chronic, lasting for months or years.

Perspectives and Patterns of Disease

The health of individuals is closely linked to the health of the community and to the population it encompasses. The ability to traverse continents in a matter of hours has opened the world to issues of populations at a global level. Diseases that once were confined to local areas of the world now pose a threat to populations throughout the world.

As we move through the 21st century, we are continually reminded that the health care system and the services it delivers are targeted to particular populations. Managed care systems are focused on a population-based approach to planning, delivering, providing, and evaluating health care. The focus of health care also has begun to emerge as a partnership in which individuals are asked to assume greater responsibility for their own health.

Epidemiology and Patterns of Disease

Epidemiology is the study of disease occurrence in human populations.[8] It was initially developed to explain the spread of infectious diseases during epidemics and has emerged as a science to study risk factors for multifactorial diseases, such as heart disease and cancer. Epidemiology looks for patterns of persons affected with a particular disorder, such as age, race, dietary habits, lifestyle, or geographic location. In contrast to biomedical researchers, who seek to elucidate the mechanisms of disease production, epidemiologists are more concerned with whether something happens than how it happens. For example, the epidemiologist is more concerned with whether smoking itself is related to cardiovascular disease and whether the risk of heart disease decreases when smoking ceases. On the other hand, the biomedical researcher is more concerned about the causative agent in cigarette smoke and the pathway by which it contributes to heart disease.

Much of our knowledge about disease comes from epidemiologic studies. Epidemiologic methods are used to determine how a disease is spread, how to control it, how to prevent it, and how to eliminate it. Epidemiologic methods also are used to study the natural history of disease, to evaluate new preventative and treatment strategies, to explore the impact of different patterns of health care delivery, and to predict future health care needs. As such, epidemiologic studies serve as a basis for clinical decision making, allocation of health care dollars, and development of policies related to public health issues.

Measures of disease frequency are an important aspect of epidemiology. They establish a means for predicting what diseases are present in a population and provide an indication of the rate at which they are increasing or decreasing. A *disease case* can be either an existing case or the number of new episodes of a particular illness that is diagnosed within a given period. *Incidence* reflects the number of new cases arising in a population at risk during a specified time. The population at risk is considered to be persons without the disease but who are at risk for developing it. It is determined by dividing the number of new cases of a disease by the population at risk for development of the disease during the same period (e.g., new cases per 1000 or 100,000 persons in the population who are at risk). The cumulative incidence estimates the risk of developing the disease during that period of time. *Prevalence* is a measure of existing disease in a population at a given point in time (e.g., number of existing cases divided by the current population).[8] The prevalence is not an estimate of risk of developing a disease because it is a function of both new cases and how long the cases remain in the population. Incidence and prevalence are always reported as rates (e.g., cases per 100 or cases per 100,000).

Morbidity and mortality statistics provide information about the functional effects (morbidity) and death-producing (mortality) characteristics of a disease. These statistics are useful in terms of anticipating health care needs, planning of public education programs, directing health research efforts, and allocating health care dollars.

Mortality statistics provide information about the causes of death in a given population. In most countries, people are legally required to record certain facts such as age, sex, and cause of death on a death certificate. Internationally agreed on classification procedures (the International Classification of Diseases [ICD] by the WHO) are used for coding the cause of death, and the data are expressed as death rates.[10] Crude mortality rates (i.e., number of deaths in a given period) do not account for age, sex, race, socioeconomic status, and other factors. For this reason, mortality often is expressed as death rates for a specific population, such as the infant mortality rate. Mortality also can be described in terms of the leading causes of death according to age, sex, race, and ethnicity.

Morbidity describes the effects an illness has on a person's life. Many diseases, such as arthritis, have low death rates but a significant impact on a person's life. Morbidity is concerned not only with the occurrence or incidence of a disease but with persistence and the long-term consequences of the disease.

Determination of Risk Factors

Conditions suspected of contributing to the development of a disease are called *risk factors*. They may be inherent to the person (high blood pressure or overweight) or external (smoking or drinking alcohol). There are different types of studies used to determine risk factors, including cross-sectional studies, case-control studies, and cohort studies. *Cross-sectional studies* use the simultaneous collection of information necessary for classification of exposure and outcome status. They can be used to compare the prevalence of a disease in those with the factor (or exposure) with the prevalence of a disease in those who are unexposed to the factor, such as the prevalence of coronary heart disease in smokers and nonsmokers. *Case-control studies* are designed to compare persons known to have the outcome of interest (*cases*) and those known not to have the outcome of interest (*controls*).[8] Information on exposures or characteristics of interest is then collected from persons in both groups. For example, the characteristics of maternal alcohol consumption in infants born with fetal alcohol syndrome (cases) can be compared with those in infants born without the syndrome (controls).

A *cohort* is a group of persons who were born at approximately the same time or share some characteristics of interest.[8] Persons enrolled in a cohort study (also called a *longitudinal study*) are followed over a period of time to observe a specific health outcome. A cohort may consist of a single group of persons chosen because they have or have not been exposed to suspected risk factors; two groups specifically selected because one has been exposed and the other has not; or a single exposed group in which the results are compared with the general population.

One of the best-known examples of a cohort study is the Framingham Study, which was carried out in Framingham, Massachusetts.[11] Framingham was selected because of the size of the population, the relative ease with which the people could be contacted, and the stability of the population in terms of moving into and out of the area. This longitudinal study, which began in 1950, was set up by the U.S. Public Health Service to study the characteristics of people who would later develop coronary heart disease. The study consisted of 5000 persons, aged 30 to 59 years, selected at random and followed for an initial period of 20 years, during which time it was predicted that 1500 of them would develop coronary heart disease. The advantage of such a study is that it can explore a number of risk factors at the same time and determine the relative importance of each. Another advantage is that the risk factors can be related later to other diseases such as stroke.

A second well-known cohort study is the Nurses' Health Study, which was developed by Harvard University and Brigham and Women's Hospital. The study began in 1976 with a cohort of 121,700 female nurses, 30 to 55 years of age, living in the United States.[12] Initially designed to explore the relationship between oral contraceptives and breast cancer, nurses in the study have provided answers to detailed questions about their menstrual cycle, smoking habits, diet, weight and waist measurements, activity patterns, health problems, and medication use. They have collected urine and blood samples, and even provided researchers with their toenail clippings. In selecting the cohort, it was reasoned that nurses would be well organized, accurate, and observant in their responses, and that physiologically they would be no different from other groups of women. It also was anticipated that their childbearing, eating, and smoking patterns would be similar to those of other working women.

Natural History

The *natural history* of a disease refers to the progression and projected outcome of the disease without medical intervention. By studying the patterns of a disease over time in populations, epidemiologists can better understand its natural history. Knowledge of the natural history can be used to determine disease outcome, establish priorities for health care services, determine the effects of screening and early detection programs on disease outcome, and compare the results of new treatments with the expected outcome without treatment.

There are some diseases for which there are no effective treatment methods available, or the current treatment measures are effective only in certain people. In this case, the natural history of the disease can be used as a predictor of outcome. For example, the natural history of hepatitis C indicates that 80% of people who become infected with the virus fail to clear the virus and progress to chronic infection.[13] Information about the natural history of a disease and the availability of effective treatment methods provides directions for preventive measures. In the case of hepatitis C, careful screening of blood donations and education of intravenous drug abusers can be used to prevent transfer of the virus. At the same time, scientists are striving to develop a vaccine that will prevent infection in persons exposed to the virus. The development of vaccines to prevent the spread of infectious diseases such as polio and hepatitis B

undoubtedly has been motivated by knowledge about the natural history of these diseases and the lack of effective intervention measures. With other diseases, such as breast cancer, early detection through use of breast self-examination and mammography increases the chances for a cure.

Prognosis refers to the probable outcome and prospect of recovery from a disease. It can be designated as chances for full recovery, possibility of complications, or anticipated survival time. Prognosis often is presented in relation to treatment options—that is, the expected outcomes or chances for survival with or without a certain type of treatment. The prognosis associated with a given type of treatment usually is presented along with the risk associated with the treatment.

Levels of Prevention

Basically, leading a healthy life contributes to the prevention of disease. There are three fundamental types of prevention: primary prevention, secondary prevention, and tertiary prevention.[8,14] It is important to note that all three levels are aimed at prevention. *Primary prevention* is directed at keeping disease from occurring by removing all risk factors. Examples of primary prevention include the administration of folic acid to pregnant women and women who may become pregnant to prevent fetal neural tube defects, giving immunizations to children to prevent communicable disease, and counseling people to adopt healthy lifestyles as a means of preventing heart disease.[8] Primary prevention is often accomplished outside the health care system at the community level. Some primary prevention measures are mandated by law (e.g., wearing seat belts in automobiles and helmet use on motorcycles). Other primary prevention activities (e.g., use of earplugs or dust masks) occur in specific occupations. *Secondary prevention* detects disease early when it is still asymptomatic and treatment measures can affect a cure or stop it from progressing. The use of a Papanicolaou (Pap) smear for early detection of cervical cancer is an example of secondary prevention. Screening also includes history taking (asking if a person smokes), physical examination (blood pressure measurement), laboratory tests (cholesterol level determination), and other procedures (colonoscopy) that can be "applied reasonably rapidly to asymptomatic people."[8] Most secondary prevention is done in clinical settings. All types of health care professionals (e.g., physicians, nurses, dentists, audiologists, optometrists) participate in secondary prevention. *Tertiary prevention* is directed at clinical interventions that prevent further deterioration or reduce the complications of a disease once it has been diagnosed.

Evidence-Based Practice and Practice Guidelines

Evidence-based practice and evidence-based practice guidelines have recently gained popularity with clinicians, public health practitioners, health care organizations, and the public as a means of improving the quality and efficiency of health care.[15] Their development has been prompted, at least in part, by the enormous amount of published information about diagnostic and treatment measures for various disease conditions, as well as demands for better and more cost-effective health care.

Evidence-based practice has been defined as "the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients."[15] It is based on the integration of the individual expertise of the practitioner with the best external clinical evidence from systematic research.[15] The term *clinical expertise* implies the proficiency and judgment that individual clinicians gain through clinical experience and clinical practice. The best external clinical evidence relies on the identification of clinically relevant research, often from the basic sciences, but especially from patient-centered clinical studies that focus on the accuracy and precision of diagnostic tests and methods, the power of prognostic indicators, and the effectiveness and safety of therapeutic, rehabilitative, and preventive regimens.

Clinical practice guidelines are systematically developed statements intended to inform practitioners and clients in making decisions about health care for specific clinical circumstances.[16,17] They not only should review but also must weigh various outcomes, both positive and negative, and make recommendations. Guidelines are different from systematic reviews. They can take the form of algorithms, which are step-by-step methods for solving a problem, written directives for care, or a combination thereof.

The development of evidence-based practice guidelines often uses methods such as meta-analysis to combine evidence from different studies to produce a more precise estimate of the accuracy of a diagnostic method or the effects of an intervention method.[18] It also requires review: by practitioners with expertise in clinical content, who can verify the completeness of the literature review and ensure clinical sensibility; from experts in guideline development who can examine the method by which the guideline was developed; and by potential users of the guideline.[16]

Once developed, practice guidelines must be continually reviewed and changed to keep pace with new research findings and new diagnostic and treatment methods. For example, the Guidelines for the Prevention, Evaluation, and Treatment of High Blood Pressure (see Chapter 23), first developed in 1972 by the Joint National Committee, have been revised seven times, and the Guidelines for the Diagnosis and Management of Asthma (see Chapter 22), first developed in 1991 by the Expert Panel, have undergone four revisions.

Evidence-based practice guidelines, which are intended to direct client care, are also important in directing research into the best methods of diagnosing and treating specific health problems. This is because health care providers use the same criteria for diagnosing the extent and severity of a particular condition such as hypertension, and because they use the same protocols for treatment.

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