



Advanced Physiology and Pathophysiology

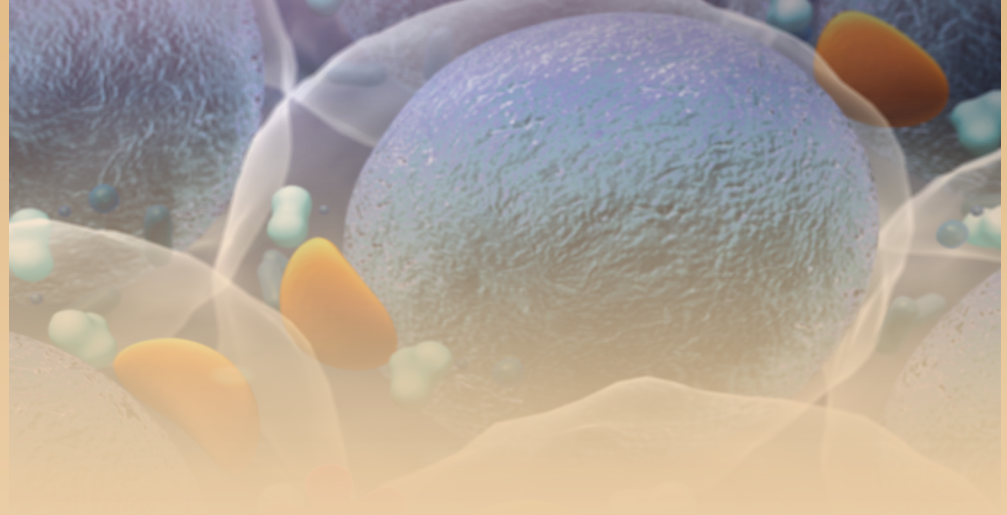
ESSENTIALS FOR CLINICAL PRACTICE

Second Edition

Advanced Physiology and Pathophysiology

Nancy C. Tkacs, PhD, RN, received her BSN and MSN degrees from the University of Pennsylvania School of Nursing and her PhD in physiology with a focus in neuroscience from Loyola University of Chicago Graduate School at the Stritch School of Medicine. She completed postdoctoral training in neuroendocrinology in the laboratory of Dr. William F. (Fran) Ganong at University of California San Francisco. Dr. Tkacs conducted preclinical research on neuroendocrine responses to physiological stressors in rodent models, particularly pertaining to the diabetes complication hypoglycemia unawareness. Dr. Tkacs has been teaching pathophysiology for advanced nursing practice for over 25 years, drawing on her knowledge of organ systems physiology and pathophysiology to provide a strong basic science foundation for advanced nursing practice. As a master's-prepared nurse with a doctorate in physiology, she is able to build a bridge between physiology concepts and the pathophysiology of disease. Students learn how findings from the history and physical examination and diagnostic test results relate to the underlying disease process at the cell and organ level. She taught advanced pathophysiology and neuroscience courses at the University of Medicine and Dentistry of New Jersey and the New Jersey Medical School; she taught advanced pathophysiology and pathogenesis of mental health disorders courses at the University of Pennsylvania; and she directed and taught advanced pathophysiology and advanced pharmacology online courses at the University of Southern California. She also served as assistant dean for Diversity and Inclusivity at the University of Pennsylvania School of Nursing.

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Linda L. Herrmann, PhD, RN, AGACNP-BC,
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Editors



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*To my husband Bill, whose unfailing love and support made the preparation
of this book possible.*

NANCY C. TKACS

*In loving memory of my mother, Dot Herrmann, my guardian angel, who forever
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LINDA L. HERRMANN

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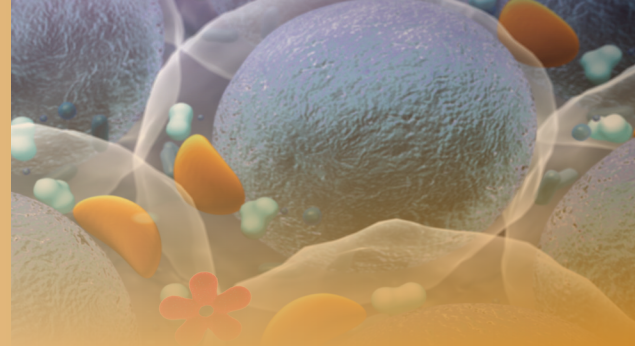
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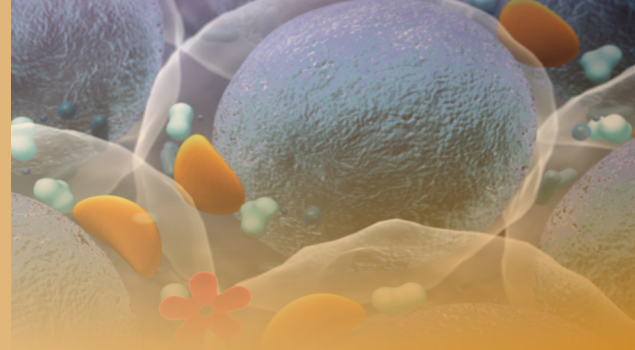
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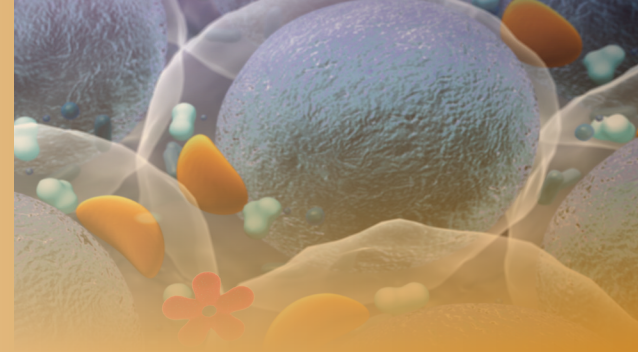
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FOREWORD



In September 2020, I was handed the reins of an advanced pathophysiology course with an average enrollment of 200 students per term, amounting to more than 800 students per year. Conventional wisdom is that the pathophysiology professor can rest on their laurels because the human body and the disease processes that undermine normal function change slowly or not at all. Timely course updates concern the pharmacology professor or the disease management course faculty. The pathophysiology professor must only awaken from their slumber . . . should a global pandemic occur.

The textbook in the course I inherited was due to release a new edition. The time was right to evaluate textbook offerings from all major publishers. Within 2 weeks, I had four copies of different advanced pathophysiology textbooks and supplemental materials to consider. Almost immediately, one product stood clearly above all the other offerings. The organization was stellar, the content was crisp and clear, and the language was purposely inclusive. Dr. Nancy Tkacs's *Advanced Physiology and Pathophysiology: Essentials for Clinical Practice* was the textbook I would write if I had

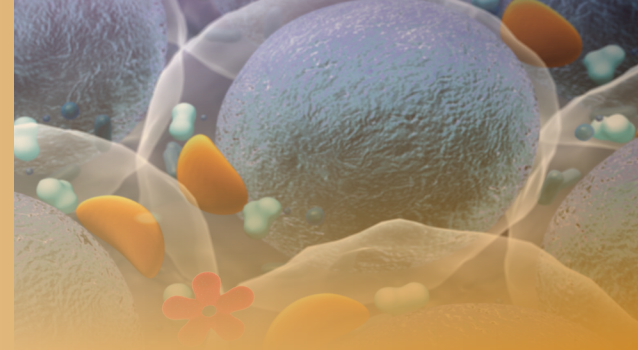
the talent and knowledge of Dr. Tkacs and her team. Adoption was an easy choice.

Ever evolving, the Second Edition increases concept comprehension and decreases cognitive load by providing the student with standardized templates for pediatric and gerontological considerations for each chapter. Endocrinology content offers insight and understanding of gender diversity and incorporates the physiology and pathophysiology of pregnancy for future clinicians caring for mothers and birthing persons. Social determinants of health, including environmental exposures and the lasting effects of adverse childhood experiences, are discussed where appropriate. Most importantly, the focus remains on conveying content to the future advanced practitioner that they can take into the clinic and apply today.

A professor and their students share a special relationship based on mutual trust. I have since welcomed Dr. Tkacs and her team into our small circle. Trust the content, trust the process, and trust that you have the finest advanced pathophysiology textbook available. Place your trust in Dr. Tkacs and her team. I do.

Joshua E. Faucett, DNP, MBA, FNP-BC, CNE
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HOW TO USE THIS BOOK



Physiology and pathophysiology are subjects that are loved by some students even as they scare others! These disciplines cover challenging topics that, while necessary for success in future clinical courses, can be seen as a painful rite of passage or as an enlightening journey to clinical competence. The features of the book were developed by master pathophysiology teachers and clinician faculty members with the goal of helping students to synthesize complex content and extend that synthesis to clinical application. The following features, recognizable by their easy-to-find design elements, appear consistently in the chapters to help reinforce the physiological and pathophysiological concepts discussed in this book.

THE CLINICAL CONTEXT

Each chapter begins with a short introduction that sets the stage for the content's relevance to clinical practice. This section introduces the common disease states of that organ system, briefly highlighting their incidence and prevalence.

THOUGHT QUESTIONS

In each chapter, major subtopics conclude with questions to improve student mastery of information. These open-ended questions require students to pause and reflect on the section they have just read, to recall important facts, and often to use higher-level thinking to synthesize and apply what they have learned.

Thought Question

4. How does smoking-induced damage to lung tissue lead to emphysema?

THE CLINICAL CONTEXT

Cardiovascular disease is the most common cause of adult morbidity and mortality, accounting for about 32% of deaths worldwide, with over 75% of the deaths occurring in low- and middle-income countries.¹ The most common form of cardiovascular disease is hypertension, affecting about 47% of adults in the United States, based on National Health And Nutrition Examination Survey (NHANES) data and using the most recent definition of hypertension.²

Complications of hypertension include accelerated atherosclerosis, myocardial infarction, stroke, kidney failure, and aneurysm. There is substantial overlap between hypertension and atherosclerosis, the second most common vascular disorder. Patients with atherosclerosis are at risk of developing ischemic heart disease (including myocardial infarction), stroke, and peripheral arterial disease (PAD). In the United States, coronary heart disease prevalence is 7.1% in adults over 20 years of age, and the prevalence of stroke is 3.3%.³ This chapter focuses on the structure, function, and diseases of the circulatory system, and Chapter 10, "Heart," focuses on the heart.

PEDIATRIC CONSIDERATIONS

These sections review embryology, prenatal, and postnatal development as it relates to physiology and pathophysiology. The important new field of developmental origins of health and disease led to the inclusion of a new subsection "Prenatal and Postnatal Influences on Organ Function" within the system chapters. Congenital malformations and genetic conditions generally present at birth or in the pediatric population. Additionally, children metabolize therapeutic agents differently than adults—critical information to understand when treating children. All the system chapters as well as Chapter 3, Molecular Biology, Genetics, and Genetic Diseases, provide an in-depth look at the most common conditions, genetic disorders, and important treatment considerations related to this patient population.

PEDIATRIC CONSIDERATIONS

Randall L. Johnson

The lungs are unique in that they have little function during prenatal development, but are required to assume their main physiological role of gas exchange immediately after birth. Lung development occurs in both prenatal and postnatal periods, with most structural development occurring postnatally. Lung function is very vulnerable to prenatal birth, the earlier, the greater the risk of respiratory dysfunction. For the first 2 years of life, alveolar diameter is small relative to that in older children and adults, increasing the risk of atelectasis. Respiratory rate is high at birth (covering about 60 breaths/min), decreasing throughout childhood to approximate adult rates during the teen years.

LUNG DEVELOPMENT

LUNG EMBRYOLOGY AND STRUCTURAL CHANGES DURING DEVELOPMENT

Prenatal and early postnatal lung development is divided into five stages (Figure 17.2). During embryonic development from gestational ages 4 to 6 weeks, the trachea and esophagus are derivatives of the foregut that share a common embryonic origin.

LUNG DEVELOPMENT PHYSIOLOGY AND THE BIRTH TRANSITION

During prenatal development, the lungs are filled with fluid produced by a serous fluid. This fluid supports the growing and developing alveoli and is critical for normal lung development.

Figure 17.2 illustrates the stages of prenatal lung development. Note that surfactant production does not begin until 26 to 28 weeks, after which the lung fluid is replaced by air at birth. The diagram also shows the transition from fetal to neonatal lung function.

KEY POINTS

This feature highlights the important takeaways for which students should be able to demonstrate an understanding at the conclusion of each chapter. These points are not intended as a comprehensive summary of the chapter; instead, they capture the main ideas conveyed throughout the chapter in short bullet points that students can reflect upon as they assess their mastery of the content.

KEY DISORDERS

All disorders reviewed in this book are highlighted within the text to facilitate quick identification and discovery. These disorders are also listed in the List of Disorders to help students locate content rapidly. Highlighted disorders appear throughout each chapter, in the main discussion as well as in the pediatric and geriatric consideration sections.

...toring, particularly of the size of the aortic root, the rate of increase in size. The use of β -adrenergic blockade may slow the rate of enlargement, and surgery of the aorta may be necessary. Treatment may also be necessary for mitral valve regurgitation and dissection (ectopia lentis) as well as other complications.



Hereditary Breast and Ovarian Cancer
Mutations in the *BRCA1* and *BRCA2* genes provide a genetic basis for one monogenic form of **hereditary breast and ovarian cancer**. Although mutations in *BRCA2* genes impart a heightened lifetime risk for breast or ovarian cancer, the percentages of all breast and ovarian cancers caused by these mutations remain small—5% to 10% of breast cancers and 10% of ovarian cancers. The balance of these cancers is caused by sporadic mutations that are generally mutations in other genes. *BRCA1* is found at 17q12-21, and more than 20 mutations have been identified in this gene. *BRCA2* is found at 13q12-13 and is subject to a similar number of mutations.

Type 1: Immediate Hypersensitivity

Type 1 reactions are known as immediate hypersensitivity (Figures 6.31a and 6.32). This response is mediated by the production of IgE that recognizes an environmental antigen (in this case, referred to as an *allergen*). Once synthesized and secreted by B cells, IgE circulates throughout the body and binds to high-affinity IgE receptors on the membranes of mast cells and basophils. Upon later exposures, the allergen binds to IgE, causing mast cell and basophil degranulation with immediate release of histamine and development of allergic inflammation. The conditions that develop from type 1 reactions include **hives**, **eczema**, **allergic rhinoconjunctivitis** (hay fever, allergic rhinitis), **allergic asthma**, **food allergy**, and **anaphylaxis**. Although the initial allergic reaction occurs immediately, late-stage reactions occur several hours after allergen exposure as newly synthesized effector molecules take effect. Sustained allergic inflammation can occur, for example, in chronic asthma and eczema.

KEY POINTS

- The body is composed of molecules that are made by chemical bonds between individual atoms. Properties of atoms depend on their atomic weight and structure. The nucleus of an atom is made up of protons and neutrons with a surrounding shell of electrons. Electrons are arranged in orbitals, and atomic properties depend on the extent to which the outermost orbital shell (the valence shell) is occupied by electrons.
- Biomolecules are formed when covalent bonds are made between atoms and molecules, building up from simple to very complex macromolecular structures.
- The elements found in highest amounts in biomolecules are carbon, hydrogen, oxygen, and nitrogen. Several other elements are found in lesser amounts. Elements that are stabilized by



GENETIC CONDITIONS

As the fields of molecular biology and genetics provide ever more understanding of the genetic basis of disease and disease risk factors, the book uses an easily identifiable icon next to all genetic conditions described throughout the text for quick reference and discovery. These disorders are also included among the key disorders found in the List of Disorders.

RARE DISEASE CASE VIGNETTES

Chapters 11 and 16 each have a vignette describing a rare disorder. The purpose of including these rare conditions is to highlight the importance of considering an atypical cause when a patient presents with symptoms and signs that are not easily explained by a common diagnosis. In both of the conditions highlighted, early diagnosis is key to preventing mismanagement.

RARE DISEASE CASE VIGNETTE: LYMPHANGIOLEIOMYOMATOSIS

A 35-year-old woman has been experiencing mild shortness of breath for the past 5 years. She first noticed that her shortness of breath became worse at the time she smoked. She delivered her first child 3 months prior to coming to the clinic, and noticed that her shortness of breath worsened considerably during pregnancy. Pulmonary function testing results are consistent with an obstructive defect and modest diffusion impairment. A lung CT scan shows multiple small nodules (cysts) in both lungs. She is subsequently diagnosed with lymphangioleiomyomatosis (LAM).

LAM is a rare lung disease that primarily affects women. LAM is a low-grade neoplastic condition characterized by abnormal proliferation of smooth muscle cells in the lung. Mutations in one of the two known tuberous sclerosis complex (TSC) genes, *TSC1* or *TSC2*, are found in patients with underlying TSC, an autosomal dominant condition characterized by germ cell tumors that can cause abnormal tumors in multiple organ systems, or occur sporadically without concomitant TSC. LAM is very rare and believed to affect four to eight women per million. The numbers are almost certainly an underestimation.

Mutations in TSC genes drive abnormal growth and proliferation of neoplastic smooth muscle cells (LAM cells) via activation of the mechanistic target of rapamycin (mTOR) signaling pathway.

SHARE YOUR FEEDBACK WITH DR. TKACS



The editors would like to hear your feedback on this book. If you would like to share your thoughts on potential additions, corrections, or updates that you believe should be incorporated into this book, please contact Nancy Tkacs at tkacs@nursing.upenn.edu.

ACKNOWLEDGMENTS

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INSTRUCTOR RESOURCES

A complete set of resources is available to qualified instructors by contacting textbook@springerpub.com for access.

Available resources include:

- **LMS COMMON CARTRIDGE WITH ALL INSTRUCTOR RESOURCES**
- **INSTRUCTOR MANUAL**
 - Chapter Outline
 - Chapter Summary
 - Objectives
 - Connecting the Dots (Tips and Pointers for Faculty on How to Approach the Content of the Chapter With Their Students)
 - Key Points
 - Thought Questions and Suggested Answers
 - Case Studies Suggested Answers
 - Discussion Questions
 - Assignment Suggestions (Individual and Group) and Suggested Answers
 - Additional Resources
- **INSTRUCTOR TEST BANK**
 - Multiple Choice Questions With Rationales
 - Essay Questions and Suggested Answers
- **INSTRUCTOR POWERPOINT PRESENTATIONS**
- **INSTRUCTOR IMAGE BANK**
- **MAPPING TO AACN ESSENTIALS: CORE COMPETENCIES FOR PROFESSIONAL NURSING EDUCATION**
- **TRANSITION GUIDE: FIRST EDITION TO SECOND EDITION**

THE FOUNDATIONAL CONCEPTS OF CLINICAL PRACTICE

Nancy C. Tkacs, Linda L. Herrmann, and Joshua E. Faucett

Pathophysiology and the Process of Clinical Decision-Making

Building From a Basic Science Foundation:
Chapters 2 to 4

Advanced Physiology and Pathophysiology:
Chapters 5 to 17

Connecting the Dots

Pathophysiology and the Independent Clinician

PATHOPHYSIOLOGY AND THE PROCESS OF CLINICAL DECISION-MAKING

Clinicians' ability to correctly identify disease processes and develop management plans with their patients relies on a deep knowledge of the pathophysiology of disease. This book was developed to meet that clinical need. Physiology seeks to understand the mechanisms of body function, and pathophysiology seeks to understand the mechanisms of altered body function due to pathological states. People, whether patients or clinicians, often fail to appreciate the fine-tuned machine that is the human body until they experience alterations in function that lead to signs and symptoms of disease. Pathophysiology can be viewed with the same lens: Studying the manifestations of body function *loss* can illuminate the exquisite and intricate functions of our organs that we do not even think about when we are healthy. For every physiological function, there is a pathophysiological consequence when that normal function goes awry. Clinicians-in-training are well positioned to reinforce their knowledge of normal physiological principles when they are presented as the context for disease development, as we have in this book.

In disease states, one or more normal homeostatic mechanisms malfunction, and the organism increasingly relies on compensatory mechanisms to maintain homeostasis. The clinician must know the principles of normal function, the alteration of these functions during disease states, and the benefits and risks of compensatory mechanisms. In addition, one cannot study physiology and pathophysiology in isolation: To understand the complex mechanisms of body function requires application of fundamental principles from chemistry, genetics, cell biology, and other basic sciences.

The data gathered during the clinical encounter include details from the history and physical examination, comprising both subjective and objective findings; results of laboratory studies; results of imaging studies; and other measurements. The clinician must then evaluate these data, consider the differential diagnosis, and formulate a plan. At each step, knowledge of pathophysiology is integral to the process. The aims of this book are to:

- Provide a foundation of core *principles* of physiology for each system and organ discussed.
- Link the pathophysiology of common and selected less common disorders to those core principles.
- Alternate discussion of each core principle with the clinical applications, sequencing the content to emphasize the application of those core principles and mechanisms.
- Present in-depth life-span considerations for each organ and system as developed by pediatric and geriatric content experts who
 - Emphasize developmental aspects of organ structure and function and their relationships to congenital defects and disorders commonly encountered in infants, children, and adolescents.
 - Describe organ and system structural and functional alterations of normal healthy aging and