

The Editors are pleased to present the 21st edition of *Harrison's Principles of Internal Medicine*. This 21st edition is a true landmark in medicine, spanning 71 years and multiple generations of trainees and practicing clinicians. While medicine and medical education have evolved, readers will appreciate how this classic textbook has retained enduring features that have distinguished it among medical texts—a sharp focus on the clinical presentation of disease, expert in-depth summaries of pathophysiology and treatment, and highlights of emerging frontiers of science and medicine. Indeed, *Harrison's* retains its conviction that, in the profession of medicine, we are all perpetual students with lifelong learning as our common goal.

Harrison's is intended for learners throughout their careers. For *students*, Part 1, Chapter 1 begins with an overview of “The Practice of Medicine.” In this introductory chapter, the editors continue the tradition of orienting clinicians to the *science* and the *art* of medicine, emphasizing the values of our profession while incorporating new advances in technology, science, and clinical care. Part 2, “Cardinal Manifestations and Presentation of Diseases,” is a signature feature of *Harrison's*. These chapters eloquently describe how patients present with common clinical conditions, such as headache, fever, cough, palpitations, or anemia, and provide an overview of typical symptoms, physical findings, and differential diagnosis. Mastery of these topics prepares students for subsequent chapters on specific diseases they will encounter in courses on pathophysiology and in clinical clerkships. For *residents* and *fellows* caring for patients and preparing for board examinations, *Harrison's* remains a definitive source of trusted content written by internationally renowned experts. Trainees will be reassured by the depth of content, comprehensive tables, and illuminating figures and clinical algorithms. Many examination questions are based on key testing points derived from *Harrison's* chapters. A useful companion book, *Harrison's Self-Assessment and Board Review*, includes over 1000 questions, offers comprehensive explanations of the correct answer, and provides links to the relevant chapters in the textbook. *Practicing clinicians* must keep up with an ever-changing knowledge base and clinical guidelines as part of lifelong learning. Clinicians can trust that chapters are updated extensively with each edition of *Harrison's*. The text is an excellent point-of-care reference for clinical questions, differential diagnosis, and patient management. In addition to the expanded and detailed Treatment sections, *Harrison's* continues its tradition of including “Approach to the Patient” sections, which provide an expert's overview of the practical management of common but often complex clinical conditions.

This edition has been modified extensively in its structure as well as its content and offers a more consistently standardized format for each disease chapter. The authors and editors have curated rigorously and synthesized the vast amount of information that comprises general internal medicine—and each of the major specialties—into a highly readable and informative two-volume book. Readers will appreciate the concise writing style and substantive quality that have always characterized *Harrison's*. This book has a sharp focus on essential information with a goal of providing clear and definitive answers to clinical questions.

In the 21st edition, examples of new chapters include “Precision Medicine and Clinical Care,” focusing on the ever-growing pool of “big data” used to provide individualized genotype-phenotype correlations; “Mechanisms of Regulation and Dysregulation of the Immune System,” focusing on the extraordinary advances made over the past 5 years in understanding the complex and subtle mechanisms whereby the immune system is regulated and how perturbations in this regulation lead to disease states as well as targets for therapeutic intervention; new chapters on Alzheimer's disease and related conditions, with a special focus on vascular dementia, a common and treatable cause of cognitive

loss; and a new chapter on marijuana and marijuana use disorders, as well as updated management guidelines for multiple sclerosis and the expanding array of other autoimmune nervous system diseases that can now be identified and treated.

Other new chapters include “Vaccine Opposition and Hesitancy,” “Precision Medicine and Clinical Care,” “Diagnosis: Reducing Errors and Improving Quality,” “Approach to the Patient with Renal or Urinary Tract Disease,” “Interventional Nephrology,” “Health Effects of Climate Change,” and “Circulating Nucleic Acids as Liquid Biopsies and Noninvasive Disease Biomarkers.” In addition, many chapters have new authors.

The chapter, “Vaccine Opposition and Hesitancy,” provides an overview of the current antivaccination crisis, the issues involved, and specific strategies to utilize within the clinical setting to address the lack of confidence that many patients feel toward the health care system. The chapter, “Metabolomics,” outlines an emerging and important new and sensitive approach to measuring perturbations within a system or patient that will likely become a routine part of the clinical armamentarium for diagnosing, monitoring, and treating disease.

In addition to these and other new topics, the 21st edition presents important updates in the established chapters, such as the microbiology and clinical management of SARS-CoV-2 infection, the use of gene editing for sickle cell anemia and thalassemia, gene therapy for hemophilia, new immunotherapies for autoimmune diseases and cancers, and novel approaches to vaccine development, among many others. Our focus on forward-looking issues of emerging clinical importance continues with the series of chapters entitled “Frontiers,” which foreshadows cutting-edge science that will change medical practice in the near term. Examples of new Frontier chapters include “Machine Learning and Augmented Intelligence,” “Metabolomics,” “Protein Folding Disorders,” and “Novel Approaches to Disease of Unknown Etiology.”

Harrison's content is available in a variety of print and digital formats, including eBooks, apps, and a popular, widely used online platform available at www.accessmedicine.com.

We have many people to thank for their efforts in producing this book. First, the authors have done a superb job of producing authoritative chapters that synthesize vast amounts of scientific and clinical data to create informative and practical approaches to managing patients. In today's information-rich, rapidly evolving environment, they have ensured that this information is current. We are most grateful to our colleagues who work closely with each editor to facilitate communication with the authors and help us keep *Harrison's* content current. In particular, we wish to acknowledge the expert support of Lauren Bauer, Patricia Conrad, Patricia L. Duffey, Gregory K. Folkers, Julie B. McCoy, Elizabeth Robbins, Marie Scurti, and Stephanie C. Tribuna. Scott Grillo and James Shanahan, our long-standing partners at McGraw Hill's Professional Publishing group, have inspired the creative and dynamic evolution of *Harrison's*, guiding the development of the book and its related products in new formats. Kim Davis, as Managing Editor, has adeptly ensured that the complex production of this multi-authored textbook proceeded smoothly and efficiently. Priscilla Beer oversaw the production of our videos and animations; Jeffrey Herzich, Elleanore Waka, and Rachel Norton, along with other members of the McGraw Hill staff; and Revathi Viswanathan of KnowledgeWorks Global Ltd., shepherded the production of this new edition.

We are privileged to have compiled this 21st edition and are enthusiastic about all that it offers our readers. We learned much in the process of editing *Harrison's* and hope that you will find this edition uniquely valuable as a clinical and educational resource.

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