

20th Edition



HARRISON'STM
P R I N C I P L E S O F
**INTERNAL
MEDICINE**

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Preface

The Editors are pleased to present the 20th edition of *Harrison's Principles of Internal Medicine*. This 20th edition is a true landmark in medicine, spanning 68 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 and lifelong learning is 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 exams, *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 exam 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 chapter 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 format as well as its content. We have reincorporated chapters that in previous editions were available only online. The 20th edition marks the return of *Harrison's* “Further Reading” citations at the end of each chapter, providing references carefully selected by our contributors. The authors and editors have rigorously curated 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 consistency of format 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 addition to the printed book, *Harrison's* is available on multiple digital platforms, including eBook and app versions, and via an online subscription available through McGraw-Hill’s popular Access Medicine (www.accessmedicine.com) collection. The digital editions feature an array of supplementary videos, databases, and photographic atlases as well as new literature updates, tutorials, animations, and audio discussions covering key topics in medicine. *Harrison's Manual of Medicine* is a condensed pocket version of clinical essentials derived from the more comprehensive *Harrison's Principles of Internal Medicine*. The *Manual* is also available as an eBook and an app and via Access Medicine. Together, these platforms form a potent *Harrison's* collection of reference, test prep, and point-of-care online content.

In the 20th edition, examples of new chapters include “Promoting Good Health,” focusing on prevention and practical lifestyle changes to enhance longevity and well-being; “Health Care Systems in Developed Countries,” providing a comparison of health delivery models from around the world; “Pharmacogenomics,” applying new approaches for selecting precision medicines and appropriate doses; “Bacterial Resistance to Antimicrobial Agents,” highlighting the widespread and often inappropriate use of antibiotics in clinical care and agriculture; “LGBT Health,” outlining strategies to enhance access and care models for populations with distinctive health care needs; “Neuromyelitis Optica,” summarizing disorders with similarities to multiple sclerosis but requiring different treatments; “Worldwide Changes in Patterns of Infectious Disease,” reviewing the dynamic evolution of new infectious diseases and the containment of older disorders, some of which have plagued humankind for centuries; and “Approach to the Medical Consultation,” providing practical advice to ensure that the consultant addresses the needs of the referring clinician. In addition to these and other new topics, the 20th edition presents a fascinating new 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 “Telomere Disease,” “The Role of Epigenetics in Disease and Treatment,” “The Role of Circadian Biology in Health and Disease,” and “Behavioral Economics and Health.”

In addition to these new topics, major advances in each subspecialty of internal medicine have been incorporated into this edition. Of particular note in this 20th edition are critical updates in the classic chapter on HIV/AIDS, which offers a clinically pragmatic focus as well as a comprehensive and analytical approach to pathogenesis. The updates cover the latest treatment protocols and address the issue of combination prevention modalities, making the chapter the most up-to-date treatise on HIV disease available.

Readers will find expanded coverage of neurodegenerative diseases, highlighting important advances in their classification and management and delineating new mechanisms responsible for the deposition and spread of pathogenic protein aggregates in these disorders. Practical guidance for the use of highly effective therapies for multiple sclerosis is another highlight of the new edition. The chapter on chronic hepatitis discusses in detail the dramatic new discoveries in the use of direct-acting antiviral agents for the treatment and cure of chronic hepatitis C virus disease; these agents are responsible for some of the most exciting therapeutic advances in medicine today.

The promise of the Human Genome Project continues to be realized in clinical medicine. This is reflected throughout the book but particularly highlighted by advances in our understanding of genetic heterogeneity of cancers, including molecular nosology that distinguishes distinct entities that share histologic similarities. The tools of genetics also inform the use of therapies targeting specific genetic lesions and immune system activation. Genetic counseling for patients with genetic predisposition to cancer (e.g., BRCA 1/2) is informing prevention strategies and reducing cancer risk. Our understanding of the microbiome, its relevance to normal physiology and disease pathogenesis, and its implications for treatment of a variety of diseases is expanding rapidly, and these advances are captured in a completely rewritten chapter “The Human Microbiome” and a thoroughly updated chapter “Microbial Genomics and Infectious Disease.” The classification and management of diabetes has been thoroughly updated on the basis of new studies, clinical guidelines, and treatments. Updated guidelines for testosterone management and replacement are based on the results of new clinical trials.

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 Patricia Conrad, Patricia L. Duffey, Gregory K. Folkers, Julie B. McCoy, Elizabeth Robbins, Anita Rodriguez, and Stephanie Tribuna. Scott Grillo and James Shanahan, our long-standing partners at McGraw-Hill Education'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 and Armen Ovsepyen oversaw the production of our videos and animations. Jeffrey Herzich, along with other members of the McGraw-Hill Education staff, shepherded the production of this new edition.

We are privileged to have compiled this 20th 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.

The Editors