

Harrison's

# PRINCIPLES OF INTERNAL MEDICINE

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*10<sup>th</sup> Edition*



# *Harrison's* **PRINCIPLES OF INTERNAL MEDICINE**

Tenth Edition

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Guatemala Hamburg Johannesburg Lisbon London  
Madrid Mexico Montreal New Delhi Panama Paris  
San Juan São Paulo Singapore Sydney Tokyo Toronto

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## Harrison's **Principles of Internal Medicine**

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234567890 DOW DOW 89876543

### **Foreign Editions**

**FRENCH** (Ninth Edition)—Flammarion, © 1982

**ITALIAN** (Ninth Edition)—Piccin Editore, S.A.S., © 1983 (est.)

**PORTUGUESE** (Ninth Edition)—Editoria Guanabara Koogan, S.A., © 1983 (est.)

**SPANISH** (Eighth Edition)—La Prensa Medica Mexicana, © 1979

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**GREEK** (Eighth Edition)—Parissianos, © 1979

**INDONESIAN** (Eighth Edition)—E.G.C., JL, © 1983 (est.)

**GERMAN** (Tenth Edition)—Schwabe and Company, Ltd., © 1983 (est.)

This book was set in Times Roman by Rocappi, Inc.  
The editors were J. Dereck Jeffers and Moira Lerner.  
The indexer was Philip James; the production supervisor was Jeanne Skahan.  
R. R. Donnelley & Sons Company was printer and binder.

### **Library of Congress Cataloging in Publication Data**

Main entry under title:

Harrison's principles of internal medicine.

Includes bibliographies and index.

1. Internal medicine. I. Petersdorf, Robert G.

II. Title: Principles of internal medicine.

RC46.H323 1983 616 82-23981

ISBN 0-07-049603-X (1-vol. ed.)

ISBN 0-07-079309-3 (2-vol. ed.)

**A salute to Maxwell M. Wintrobe by the editors of  
*Harrison's***

This edition is dedicated to Professor Maxwell Wintrobe as an expression of gratitude for his contributions to *Harrison's* and to American medicine.

One of the founders of this book, along with Tinsley Harrison, George Thorn, William Resnik, and Paul Beeson, he inculcated his high standards of succinct and lucid exposition, gained through writing his own textbook, *Clinical Hematology*. More than any other of the early editors, he insisted on every chapter's being mercilessly criticized with complete objectivity and impartiality by peers of the contributor in another university department. This peer review method which he was instrumental in initiating continues to be used as a way of maintaining the standards of *Harrison's* to this day.

In the swift current of scientific progress it is easy to forget the people who make fundamental contributions. The current vogue is to cite only the most recent reference. Max Wintrobe, it will be remembered, in one of his first scientific endeavors, while still a PhD candidate, introduced a quantitative methodology for evaluating the volume, size, and hemoglobin content of red blood cells. These measurements became the basis for the classification of the anemias into macrocytic, microcytic, and hypochromic. He also standardized the measurement of the sedimentation rate by using tubes of a constant caliber, the Wintrobe tubes. Fundamental contributions to the role of trace elements in red blood cell metabolism, as well as the original studies of the effects of thiamine, pyridoxine, and pantothenic acid deficiencies, followed in rapid succession.

But the time and energy spent on these and innumerable other scientific works did not prevent or deter him from founding one of the fine medical schools and departments of medicine in the United States, at the University of Utah; guiding a generation of students to careers in scientific medicine; and giving his colleagues on *Harrison's* the benefits of his wise counsel and clinical experience over a period of nearly thirty years.



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## PREFACE

This is the Tenth Edition of *Harrison's Principles of Internal Medicine* to appear in the short span of thirty-three years. As has been the case with previous editions, the editors have attempted to incorporate into this edition the latest advances in pathophysiology, diagnosis, and treatment. The attempt has been made, where possible, to build a bridge between basic science and clinical medicine and to emphasize the advances in biomedicine while retaining those facts which, while not new, remain clinically useful.

In adherence to the principles of those who founded the book, the section dealing with the cardinal manifestations of disease remains a mainstay of this edition. Its 56 chapters form a comprehensive introduction to clinical medicine. The next part deals with disorders that affect multiple organs and includes genetics, clinical immunology, clinical pharmacology, neoplasia, and, in this edition for the first time, the biology and diseases of aging. These multisystem disorders are then followed by a predominantly etiologically oriented section on infections and the traditional discussion of diseases of the major organ systems.

Despite their efforts to present as much new material in this edition as possible, the amount of information that is coming to the fore exceeds the editors' abilities to keep within the confines of one volume. Therefore, following publication of the ninth edition, the editors and the publisher embarked on a new venture and have published four volumes entitled *Updates to Harrison's Principles of Internal Medicine* (Volumes I through IV). Each of these volumes contains between 15 and 18 articles, written by an expert in the field but not necessarily the author of the article in the ninth or tenth editions. The subject matter, which varies widely, was chosen to augment discussion of the same subject in the ninth edition or consists of important new topics in which there have been exciting advances since the publication of the ninth edition. These *Updates* complement the *Harrison* textbook in every sense of the word. Cognizant of the continued requirements for continuing education for licensure and relicensure, as well as the emphasis on certification and recertification, the editors and the publisher have embarked on two efforts to help the reader stay abreast of the broad field of internal medicine. The *PreTest Self-Assessment and Review* to accompany the ninth edition of *Principles of Internal Medicine* appeared shortly after the ninth edition, and a radically revised version will appear simultaneously with the tenth edition. *PreTest Self-Assessment and Review* consists of several hundred questions based upon the textbook, along with answers and explanations for the answers. A CME examination multiple-choice test which may be taken for CME credit is an optional companion to the *PreTest*. Some months after the appearance of *PreTest*, a self-assessment examination book dealing with patient management problems was published under the editorial guidance of Dr. Alfred J. Bollet. These patient management problems also refer to *Principles of Internal Medicine*.

This quadripartite effort—*Principles of Internal Medicine*, the four *Updates*, and the two examination books—represents a continuous learning system and reflects the editors' conviction that medicine is an ever-changing science and that multiple modalities of presenting new information and learning are essential if physicians want to keep up with the rapid changes in their field.

The tenth edition also pays close attention to updated and current references. Although space constraints require that references be kept to a modest number, the editors have made particular efforts to include papers that were published in 1981, 1982, and even 1983. Although this has required omission of some important older papers, these almost always appear in the bibliographies of the newer ones. The reverse is, of course, not the case and, hence, our effort to keep the references up-to-date.

Although we cannot highlight in this short preface all of the new and extensively updated parts of the tenth edition, we would like to call the reader's attention to some.

- In the section on gastroenterology, the chapters on dysphagia and diseases of the esophagus have been completely revised; there is an entirely new and comprehensive chapter on inflammatory bowel disease; the chapter dealing with diseases of the gallbladder and biliary tract is entirely new; the diagnosis, prevention, and treatment of viral hepatitis have been completely updated in line with newer advances in the field; the chapter on diseases of the pancreas has been revised to take into account the current state of imaging procedures, endoscopy, and serologic tests in the diagnosis of acute and chronic pancreatitis, as well as cancer of the pancreas; and the chapters on absorption and malabsorption have been completely revised.

- The section on metabolic pathways has been changed to emphasize the clinical relevance of the cyclic AMP system, the prostaglandins, the endorphins, and cell surface phagocytosis. In the expanded genetic section, there are new chapters on the HLA system and an essay on the implications of recombinant DNA technology for medicine. There are major new chapters on ovarian disorders, nutritional therapy, disturbances in glycogen metabolism, and pheochromocytoma. There is a totally new chapter on the autonomic nervous system, resulting from an appreciation of the importance of the autonomic nervous system in a wide variety of disease states and in understanding the responses to a variety of drugs.

- One of the spectacular advances in clinical cardiology has been the application of electrophysiologic techniques to the study of arrhythmias. Two new chapters on the brady- and tachyarrhythmias, respectively, emphasize this new approach. Cardiac surgery is playing an increasingly important role in the management of cardiac diseases and its role is emphasized in the chapters on arrhythmias, congenital heart disease, valvular heart disease, infective endocarditis, coronary heart disease, acute myocardial infarction, cardiac tumors, and pericardial disease.

- Hypersensitivity pneumonitis and environmental air pollution have been increasingly recognized in the production of interstitial lung disease, and these two topics have been emphasized in two important new chapters by new authors. Likewise, the emergence of the adult respiratory distress syndrome (ARDS) as the major cause of death in a variety of medical and surgical illnesses is now recognized, and a new chapter on this syndrome has been included.

- The section on disorders of the nervous system includes completely new chapters on coma, epilepsy, multiple sclerosis, and sleep and its abnormalities. A new chapter on commonly abused drugs has been added. New chapters on psychiatry, including the neuroses, manic-depressive psy-

choses, and schizophrenia have been included. Extensive revisions have also been made in the chapters on faintness, syncope and seizures, abnormalities in movement and posture, and traumatic diseases of the brain. The chapter on diagnostic methods has been extensively updated to include a consideration of evoked potentials and of nuclear magnetic resonance.

● The last three or four years have seen exciting developments in infectious disease. Following the discovery of *Legionella*, a number of other new as well as previously described agents were shown to cause pneumonia. These are summarized in a new chapter. The toxic-shock syndrome and the acquired immune deficiency syndrome (AIDS) in homosexuals represent two exciting developments in human biology which have been included in the tenth edition.

One of the strengths of this textbook is the close-knit character of the editors. But just as medicine progresses, the old guard must give way to the new. With the tenth edition, Dr. Raymond D. Adams, who was the editor of the section on neurology from the second through the tenth editions—giving him more seniority than any other editor who has ever been with the book—is retiring as editor. We are fortunate to welcome as a new editor Dr. Joseph B. Martin, Neurologist-in-Chief at Massachusetts General Hospital and Professor of Neurology at Harvard Medical School, as Dr. Adams's successor. In order to ensure a smooth transition, Drs. Martin and Adams worked together on the Neurology Section of the tenth edition. The editors are grateful to Ray Adams for the continuing high quality that he has given to the section on neurological medicine; more importantly, he has been a valuable critic, a wise counselor, and a warm friend. While we shall miss him as an active editor, we consider ourselves fortunate in having attracted an outstanding academic neurologist like Joseph Martin to the editorial board.

We also wish to express our appreciation to our many associates and colleagues who, as experts in their fields, have helped us with constructive and valuable criticisms of the chapters in the tenth edition. We wish to thank the following for many helpful suggestions: Drs. Elliott Antman,

David W. Bilheimer, Kurt J. Bloch, Neil Breslau, H. Franklin Bunn, George Canellos, Norman Carter, Jack L. Clausen, Wayne E. Crill, J. Donald Easton, Richard W. Erbe, Clement A. Finch, Daniel W. Foster, William Franklin, Eugene Frenkel, Lawrence Friedman, Peter L. Friedman, Theodore Friedmann, Bruce Gilliland, Stephen E. Goldfinger, Joseph L. Goldstein, John L. Gollan, Mehron Goulian, Mark R. Green, Gabriel Gregoratos, James E. Griffin, Frederick G. Guggenheim, Robert I. Handin, John A. Hanson, Donald H. Harter, Lee W. Henderson, Fred Hendler, Roland H. Ingram, Jr., Jon I. Isenberg, Charles Jablecki, Robert N. Jones, Lewis L. Judd, Vern H. Kerchberger, William Kovacs, Guenther Krejs, S. Lakshminarayanan, Alexander R. Lawton, Mark Leshin, John D. Loeser, Kenneth L. Luskey, Paul C. MacDonald, Raymond J. Maciewicz, Jamie Maguire, Roger J. May, Robert J. Mayer, Donald B. McCormick, E. Regis McFadden, Alfred Merrill, Kenneth M. Moser, Robert Munford, Barbara Nath, David Nathan, Charles Y. C. Pak, Alan S. Pearlman, James E. Pennington, James Plorde, Daniel K. Podolsky, Charles E. Pope II, Samuel I. Rapaport, Joel M. Rapoport, Robert W. Rebar, Peter Reich, Herbert Y. Reynolds, James Richter, R. Paul Robertson, Russell Ross, John W. Rowe, Daniel Rudman, Martin A. Samuels, Stuart F. Schlossman, Jerry A. Schneider, William J. Schwartz, J. E. Seegmiller, Ralph Shabetai, Marc A. Shuckit, Sheldon R. Simon, Frank E. Speizer, Paul E. Strandjord, Christina M. Surawicz, Steven I. Wasserman, Henry O. Wheeler, W. C. Wiederholt, Robert R. Young, Jerome Zeldis, and Ms. Mary Ellen Collins.

This book could not be edited without the dedicated help of our coworkers in the editorial offices of the individual editors. We are especially indebted to Kristin Ahlman, Martha Conant, Rebecca Frost, Hilda Gardner, Brenda H. Hennis, Patricia Higgins, Mary Jackson, Patricia Kadlick, Kathy Kreatz, Cynthia Reid, Barbara Ann Rumson, Ruth R. Simonds, Janice Stearns, Trisha C. Walker.

Finally, we need to say a word of thanks to the senior editors at McGraw-Hill, Mr. Dereck Jeffers and Mr. Richard Laufer. They formed a most effective team who gave the editors constant encouragement and kept them on the straight and narrow.

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