



BRAUNWALD'S HEART DISEASE

A Textbook of Cardiovascular Medicine



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A Textbook of Cardiovascular Medicine

NINTH EDITION

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Dedication

We are proud to dedicate the ninth edition of *Braunwald's Heart Disease* to its founder, Eugene Braunwald, MD. The first edition of this work, published 30 years ago, established a standard of excellence that is rarely, if ever, achieved in publishing. Dr. Braunwald personally wrote half of the book and expertly edited the rest. He did the same for the next four editions, taking a 6-month sabbatical every 4 to 5 years to accomplish that. For the sixth edition, published in 2001, he invited two of us (PL, DPZ) to share the experience with him, increasing the editors by one (ROB) for the seventh edition. A new editor (DLM) joined for the eighth edition, and Dr. Braunwald no longer directly participated in the day-to-day editing of the print text, while still contributing some of the key chapters. However, he kept his finger on the pulse of the text and for that edition began *twice-weekly* electronic updates. Incorporating the most recent research, reviews, and opinions into the electronic text has continued through this ninth edition, making *Braunwald's Heart Disease* truly a living work and setting it apart from other texts. Dr. Braunwald, through his research, teaching, and mentorship, has shaped much of contemporary cardiovascular medicine, and it is with gratitude and admiration that we dedicate this edition of *his work* to him.

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PREFACE TO THE NINTH EDITION

Advances in cardiovascular science and practice continue at a breathtaking rate. As the knowledge base expands, it is important to adapt our learning systems to keep up with progress in our field. We are pleased to present the ninth edition of *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine* as the hub of an ongoing, advanced learning system designed to provide practitioners, physicians-in-training, and students at all levels with the tools needed to keep abreast of rapidly changing scientific foundations, clinical research results, and evidence-based medical practice.

In keeping with the tradition established by the previous editions of *Braunwald's Heart Disease*, the ninth edition covers the breadth of cardiovascular practice, highlighting new advances and their potential to transform the established paradigms of prevention, diagnosis, and treatment. We have thoroughly revised this edition to keep the content vibrant, stimulating, and up-to-date. Twenty-four of the 94 chapters are entirely new, including nine chapters that cover topics not addressed in earlier editions. We have added 46 new authors, all highly accomplished and recognized in their respective disciplines. All chapters carried over from the eighth edition have been thoroughly updated and extensively revised. This edition includes nearly 2500 figures, most of which are in full color, and 600 tables. We have continued to provide updated sections on current guidelines recommendations that complement each of the appropriate individual chapters.

A full accounting of these changes in the new edition cannot be addressed in the space of this Preface, but we are pleased to present a number of the highlights. The ninth edition includes two entirely new chapters—ethics in cardiovascular medicine by Paul Mueller and design and conduct of clinical trials by Elliot Antman—that supplement the initial section on the fundamentals of cardiovascular disease. Thomas Gaziano has joined J. Michael Gaziano in authoring the first chapter on the global burden of cardiovascular disease. With recognition of the increasing relevance of genetics, J.G. Seidman joins Reed Pyeritz and Christine Seidman in the updated chapter on inherited causes of cardiovascular disease, and David Tester and Michael Ackerman have contributed a new chapter on the genetics of cardiac arrhythmias.

Acknowledging the unremitting burden and societal impact of heart failure, the section on heart failure receives continued emphasis and has undergone extensive revision, including five new chapters. Barry Greenberg teams with Andrew Kahn in addressing the clinical approach to the patient with heart failure; Mihai Georghiadu, Gerasimos Filippatos, and Michael Felker provide a fresh look at the evaluation and management of acute heart failure; Michael Acker and Mariell Jessup address advances in surgical treatment of the failing heart; Mandeep Mehra and Bartley Griffith discuss the role of device therapy in assisted circulation; and William Abraham reviews the emerging role of devices for monitoring and managing heart failure.

The chapters that address cardiovascular imaging have kept abreast of all of the exciting advances in this field. Raymond Kwong and Allen Taylor have written excellent and comprehensive new chapters on cardiac magnetic resonance and cardiac computed tomography, respectively, with accompanying sections addressing the American College of Cardiology appropriate use criteria for the use of these advanced technologies. Updated ACC appropriate use criteria also follow the chapters on echocardiography and nuclear cardiology. In addition, the imaging section has been further enhanced by the inclusion of two new chapters focusing on the evolving applications of intravascular ultrasound, authored by Jean-Claude Tardif and Philippe


L'Allier, and cardiovascular molecular imaging, provided by Peter Libby, Farouc Jaffer, and Ralph Weissleder.

In recognition of the growing importance of atrial fibrillation in cardiovascular practice, a new chapter devoted to the evaluation and treatment of this rhythm disturbance, authored by Fred Morady and Douglas Zipes, has been added to the section on cardiac arrhythmias. The other updated chapters in the heart rhythm section continue to inform our readers on the current state-of-the-art in this important aspect of heart disease.

Dariusz Mozaffarian and Edzard Ernst have added expertly authored new chapters on nutrition and complementary medicine, respectively, to the section on preventive cardiology. In the atherosclerotic disease section, Marc Sabatine joins Chris Cannon in the revised discussion of the approach to the patient with chest pain, and William Boden joins David Morrow in a new chapter on stable ischemic heart disease. Deepak Bhatt teams with Jeffrey Popma in creating a new chapter on percutaneous coronary intervention, and he joins Andrew Eisenhauer and Christopher White in updating the discussion on endovascular treatment of noncoronary vascular disease. We welcome John Webb to our authorship team with his new chapter on catheter-based interventions in structural heart disease that includes discussion of the exciting novel catheter-based techniques for repair and replacement of cardiac valves. Our other new chapters include a fresh commentary on diseases of the aorta by Alan Braverman, Robert Thompson, and Luis Sanchez; diabetes and cardiovascular disease by Darren McGuire; hemostasis, thrombosis, and fibrinolysis by Jeffrey Weitz; and psychiatric and behavioral aspects of cardiovascular disease by Viola Vaccarino and Douglas Bremner. Finally, we are delighted that José Ramires, Andrei Sposito, Edécio Cunha-Neto, and Maria de Lourdes Higuchi have expanded our discussion of the global nature of cardiovascular disease by contributing an excellent chapter on the pathophysiology, evaluation, and treatment of Chagas' disease.

We are indebted to all of our authors for their considerable time, effort, and commitment to maintaining the high standards of *Braunwald's Heart Disease*. As excited as we are about bringing this edition of the text to fruition, we are even more energized regarding the expanding *Braunwald's Heart Disease* website. The electronic version of this work on the companion Expert Consult website includes greater content in terms of figures and tables than the print version can accommodate. Figures and tables can be downloaded directly from the website for electronic slide presentations. In addition, we have a growing portfolio of video and audio content that supplements the print content of many of our chapters. Dr. Braunwald personally updates the chapter content on a weekly basis, thus creating a truly unique living textbook with expanding content that includes the latest research, clinical trials, and expert opinion.

Moreover, the family of *Braunwald's Heart Disease* companion texts continues to expand, providing detailed expert content for the subspecialist across the broad spectrum of cardiovascular conditions. These include: *Clinical Lipidology*, edited by Christie Ballantyne; *Clinical Arrhythmology and Electrophysiology*, authored by Ziad Issa, John Miller, and Douglas Zipes; *Heart Failure*, edited by Douglas Mann; *Valvular Heart Disease*, by Catherine Otto and Robert Bonow; *Acute Coronary Syndromes*, by Pierre Thérault; *Preventive Cardiology*, by Roger Blumenthal, JoAnne Foody, and Nathan Wong; *Cardiovascular Nursing*, by Debra Moser and Barbara Riegel; *Mechanical Circulatory Support*, by Robert Kormos and Leslie Miller; *Hypertension*, by Henry Black and William Elliott; *Cardiovascular Therapeutics*, by Elliott Antman and Marc Sabatine; *Vascular Medicine*, by Marc Creager, Joshua



Beckman, and Joseph Loscalzo; and recent atlases on cardiovascular imaging such as *Cardiovascular Magnetic Resonance*, by Christopher Kramer and Gregory Hundley; *Cardiovascular Computed Tomography*, by Allen Taylor; and *Nuclear Cardiology*, by Ami Iskandrian and Ernest Garcia.

The ninth edition of *Braunwald's Heart Disease* does indeed represent the central hub of a burgeoning cardiovascular learning system that can be tailored to meet the needs of all individuals engaged in cardiovascular medicine, from the accomplished subspecialist practitioner to the beginning student of cardiology. *Braunwald's Heart*

Disease aims to provide the necessary tools to navigate the ever-increasing flow of complex information seamlessly.

Robert O. Bonow

Douglas L. Mann

Douglas P. Zipes

Peter Libby

PREFACE—ADAPTED FROM THE FIRST EDITION

Cardiovascular disease is the greatest scourge affecting the industrialized nations. As with previous scourges—bubonic plague, yellow fever, and smallpox—cardiovascular disease not only strikes down a significant fraction of the population without warning but also causes prolonged suffering and disability in an even larger number. In the United States alone, despite recent encouraging declines, cardiovascular disease is still responsible for almost 1 million fatalities each year and more than half of all deaths; almost 5 million persons afflicted with cardiovascular disease are hospitalized each year. The cost of these diseases in terms of human suffering and material resources is almost incalculable. Fortunately, research focusing on the causes, diagnosis, treatment, and prevention of heart disease is moving ahead rapidly.

In order to provide a comprehensive, authoritative text in a field that has become as broad and deep as cardiovascular medicine, I chose to enlist the aid of a number of able colleagues. However, I hoped that my personal involvement in the writing of about half of

the book would make it possible to minimize the fragmentation, gaps, inconsistencies, organizational difficulties, and impersonal tone that sometimes plague multiauthored texts.

Since the early part of the 20th century, clinical cardiology has had a particularly strong foundation in the basic sciences of physiology and pharmacology. More recently, the disciplines of molecular biology, genetics, developmental biology, biophysics, biochemistry, experimental pathology, and bioengineering have also begun to provide critically important information about cardiac function and malfunction. Although *Heart Disease: A Textbook of Cardiovascular Medicine* is primarily a clinical treatise and not a textbook of fundamental cardiovascular science, an effort has been made to explain, in some detail, the scientific bases of cardiovascular diseases.

Eugene Braunwald
1980



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