

BRAUNWALD'S HEART DISEASE

A Textbook of Cardiovascular Medicine

Edited by

ROBERT O. BONOW, MD

Max and Lilly Goldberg Distinguished Professor of Cardiology
Department of Medicine
Northwestern University Feinberg School of Medicine
Chicago, Illinois

DOUGLAS L. MANN, MD

Ada L. Steining Professor of Cardiology
Professor of Medicine, Cell Biology, and Physiology
Washington University School of Medicine
St. Louis, Missouri

GORDON F. TOMASELLI, MD

Professor of Medicine (Cardiology)
The Marilyn and Stanley M. Katz Dean, Emeritus
Albert Einstein College of Medicine
Bronx, New York;
Adjunct Professor of Medicine
Johns Hopkins University School of Medicine
Baltimore, Maryland

DEEPAK L. BHATT, MD, MPH, MBA

Director of Mount Sinai Fuster Heart Hospital
Dr. Valentin Fuster Professor of Cardiovascular Medicine
Icahn School of Medicine at Mount Sinai
New York, New York

SCOTT D. SOLOMON, MD

The Edward D. Frohlich Endowed Chair
Professor of Medicine
Harvard Medical School
Senior Physician
Brigham and Women's Hospital
Boston, Massachusetts

PETER LIBBY, MD

Mallinckrodt Professor of Medicine
Harvard Medical School
Brigham and Women's Hospital
Boston, Massachusetts

Founding Editor and Online Editor

**EUGENE BRAUNWALD, MD,
ScD(Hon), FRCP**

Distinguished Hersey Professor of Medicine
Harvard Medical School
Founding Chairman, TIMI Study Group
Brigham and Women's Hospital
Boston, Massachusetts



ELSEVIER

Contents

PART I FOUNDATIONS OF CARDIOVASCULAR MEDICINE

- 1 **Cardiovascular Disease: Past, Present, and Future, 1**
EUGENE BRAUNWALD
- 2 **Global Burden of Cardiovascular Disease, 14**
THOMAS A. GAZIANO, DORAIRAJ PRABHAKARAN,
AND J. MICHAEL GAZIANO
- 3 **Impact of Climate Change and the Environment on Cardiovascular Health, 31**
SADEER AL-KINDI AND SANJAY RAJAGOPALAN
- 4 **Clinical Trials in Cardiovascular Medicine, 43**
SCOTT D. SOLOMON AND JOHN MCMURRAY
- 5 **Clinical Decision-Making in Cardiology, 56**
JOHN E. BRUSH JR AND HARLAN M. KRUMHOLZ
- 6 **Impact of Health Care Policy on Quality, Outcomes, and Equity in Cardiovascular Disease, 66**
KAREN E. JOYNT MADDOX

PART II PERSONALIZED APPROACHES TO CARDIOVASCULAR DISEASE

- 7 **Applications of Genetics to Cardiovascular Medicine, 75**
PRADEEP NATARAJAN
- 8 **Principles of Drug Therapeutics, Pharmacogenomics, and Biologics, 90**
LARISA H. CAVALLARI
- 9 **Biomarkers and Use in Precision Medicine, 99**
PETER LIBBY AND PAUL M. RIDKER
- 10 **Artificial Intelligence in Cardiovascular Medicine, 106**
ZACHI I. ATTIA, SURAJ KAPA, DEMILADE A. ADEDINSEWO,
AND PAUL FRIEDMAN

PART III EVALUATION OF THE PATIENT

- 11 **History, Physical Examination, and the Virtual Visit, 119**
JAMES C. FANG, THOMAS S. METKUS JR, AND PATRICK T. O'GARA
- 12 **Electrocardiography, 138**
DAVID M. MIRVIS, GORDON F. TOMASELLI, AND ARY L. GOLDBERGER
- 13 **Exercise Physiology and Exercise Testing, 171**
SATYAM SARMA, WILLIAM K. CORNWELL III, KERI SHAFER, AND BENJAMIN D. LEVINE
- 14 **Echocardiography, 189**
JUSTINA C. WU, MAJA CIKES, LINDA D. GILLAM, AND SCOTT D. SOLOMON; ILLUSTRATED BY BERNARD BULWER
- 15 **Chest Radiography in Cardiovascular Disease, 262**
SUMIT GUPTA AND FRANCINE L. JACOBSON
- 16 **Nuclear Cardiology, 271**
SHARMILA DORBALA AND MARCELO F. DI CARLI
- 17 **Cardiovascular Magnetic Resonance Imaging, 307**
CHIARA BUCCIARELLI-DUCCI AND MARIANNA FONTANA
- 18 **Cardiac Computed Tomography, 329**
RON BLANKSTEIN
- 19 **Coronary Angiography and Intravascular Imaging, 361**
GEORGE D. DANGAS AND ROXANA MEHRAN
- 20 **Invasive Hemodynamic Diagnosis of Cardiac Disease, 384**
MORTON J. KERN AND ARNOLD H. SETO

Guidelines Summary (online)
DAVID M. TEHRANI
- 21 **Anesthesia and Noncardiac Surgery in Patients With Heart Disease, 409**
LEE A. FLEISHER AND JOSHUA A. BECKMAN

PART IV PREVENTIVE CARDIOLOGY

22 **The Vascular Biology of Atherosclerosis, 425**

PETER LIBBY

23 **Primary Prevention of Cardiovascular Disease, 442**

SAMIA MORA, PETER LIBBY, AND PAUL M RIDKER

24 **Systemic Hypertension: Mechanisms, Diagnosis, and Treatment, 471**

LUKE J. LAFFIN AND GEORGE L. BAKRIS

25 **Lipoprotein Disorders and Cardiovascular Disease, 502**

LALE TOKGÖZOGLU AND PETER LIBBY

Guideline Highlights: Lipid Management (online)

RAHUL AGGARWAL, PETER LIBBY, AND SAMIA MORA

26 **Cardiovascular Effects of Tobacco and Nicotine Products, 517**

ARUNI BHATNAGAR

27 **Nutrition and Cardiovascular and Metabolic Diseases, 524**

DARIUSH MOZAFFARIAN

28 **Obesity and Cardiovascular Health, 539**

GITANJALI SRIVASTAVA AND CAROLINE M. APOVIAN

29 **Diabetes and the Cardiovascular System, 551**

DARREN K. MCGUIRE, SILVIO E. INZUCCHI, AND NIKOLAUS MARX

Guidelines Highlight: Cardiovascular Disease in Patients With Diabetes (online)

DARREN K. MCGUIRE, SILVIO E. INZUCCHI, AND NIKOLAUS MARX

30 **Comprehensive Cardiac Rehabilitation, 578**

RANDAL J. THOMAS

31 **Integrative Approaches to the Management of Patients With Heart Disease, 583**

STEPHEN DEVRIES

PART V ATHEROSCLEROTIC CARDIOVASCULAR DISEASE

32 **Approach to the Patient With Chest Pain, 589**

MARC P. BONACA AND MARC S. SABATINE

Guidelines Highlight: Chest Pain (online)

RHANDERSON CARDOSO

33 **Coronary Blood Flow and Myocardial Ischemia, 600**

DIRK J. DUNCKER AND JOHN M. CANTY JR

34 **ST-Elevation Myocardial Infarction Pathophysiology and Clinical Evolution, 627**

BENJAMIN M. SCIRICA, PETER LIBBY, AND DAVID A. MORROW

35 **ST-Elevation Myocardial Infarction: Management, 650**

ERIN A. BOHULA AND DAVID A. MORROW

Guideline Highlights: STEMI Management (online)

ERIN A. BOHULA AND DAVID A. MORROW

36 **Non-ST Elevation Acute Coronary Syndromes, 700**

ROBERT P. GIUGLIANO AND EUGENE BRAUNWALD

Guideline Highlights: Non-ST Elevation Acute Coronary Syndromes (online)

MATTHEW I. TOMEY, ROBERT P. GIUGLIANO, DEEPAK L. BHATT, AND EUGENE BRAUNWALD

37 **Stable Ischemic Heart Disease, 725**

NICHOLAS A. MARSTON, DAVID A. MORROW, AND JAMES A. DE LEMOS

38 **Percutaneous Coronary Intervention, 768**

DHARAM J. KUMBHANI AND DEEPAK L. BHATT

Guidelines Summary (online)

DHARAM J. KUMBHANI AND DEEPAK L. BHATT

39 **Diseases of the Aorta, 789**

ALAN C. BRAVERMAN AND MARC SCHERMERHORN

Guidelines Summary for the Evaluation and Management of Aortic Disease (online)

ALAN C. BRAVERMAN

40 **Peripheral Artery Diseases, 818**

MARC P. BONACA, CONNIE N. HESS, AND MARK A. CREAGER

Guidelines Highlights: ACC/AHA Guidelines for the Management of Lower Extremity Peripheral Artery Diseases (online)

MARC P. BONACA, CONNIE N. HESS, AND MARK A. CREAGER

41 **Treatment of Noncoronary Obstructive Vascular Disease, 840**

SCOTT KINLAY AND DEEPAK L. BHATT

42 **Prevention and Management of Ischemic Stroke, 851**

MARK J. ALBERTS

PART VI ARRHYTHMIAS, SUDDEN DEATH, AND SYNCOPE

43 **Approach to the Patient With Cardiac Arrhythmias, 869**

ANNE B. CURTIS AND GORDON F. TOMASELLI

Guidelines Summary (online)

ANNE B. CURTIS AND GORDON F. TOMASELLI

- 44 Mechanisms of Cardiac Arrhythmias, 886**
STANLEY NATTEL AND GORDON F. TOMASELLI
- 45 Genetics of Cardiac Arrhythmias, 912**
JOHN R. GIUDICESSI, DAVID J. TESTER, AND MICHAEL J. ACKERMAN
- 46 Therapy for Cardiac Arrhythmias, 931**
JOHN M. MILLER AND KENNETH A. ELLENBOGEN
- 47 Supraventricular Tachycardias, 969**
JONATHAN M. KALMAN AND PRASHANTHAN SANDERS
- Guideline Highlights: Supraventricular Tachycardias (online)**
YOULIN KOH
- 48 Atrial Fibrillation, 996**
HUGH CALKINS, DAVID D. SPRAGG, AND GORDON F. TOMASELLI
- Guideline Highlights: Atrial Fibrillation (online)**
DAVID D. SPRAGG
- 49 Ventricular Arrhythmias, 1012**
WILLIAM G. STEVENSON AND KATJA ZEPPENFELD
- Guidelines Highlights: Ventricular Arrhythmia (online)**
SEBASTIAAN R.D. PIERS, ARVINDH N. KANAGASUNDRAM, KATJA ZEPPENFELD, AND WILLIAM G. STEVENSON
- 50 Bradyarrhythmias and Atrioventricular Block, 1036**
KRISTEN K. PATTON AND JEFFREY E. OLGIN
- Guidelines Highlights: Bradycardia and Atrioventricular Block (online)**
BEIXIN JULIE HE
- 51 Pacemakers, Conduction System Pacing, Cardiac Resynchronization Therapy, and Implantable Cardioverter-Defibrillators, 1046**
JAMES P. DAUBERT AND MINA K. CHUNG
- 52 Cardiac Arrest and Sudden Cardiac Death, 1076**
JEFFREY J. GOLDBERGER, CHRISTINE M. ALBERT, AND GORDON F. TOMASELLI
- 53 Hypotension and Syncope, 1111**
HUGH CALKINS AND PENG-SHENG CHEN
- Guidelines Highlights: Syncope**
NINO ISAKADZE
- PART VII HEART FAILURE**
- 54 Mechanisms of Cardiac Contraction and Relaxation, 1123**
DONALD M. BERS AND BARRY A. BORLAUG
- 55 Pathophysiology of Heart Failure, 1147**
DOUGLAS L. MANN
- 56 Clinical Assessment of Heart Failure, 1167**
JAMES L. JANUZZI JR AND DOUGLAS L. MANN
- Online Guidelines: Pharmacologic Therapy for the Management of Heart Failure (online)**
MUTHIAH VADUGANATHAN
- 57 Diagnosis and Management of Decompensated Heart Failure, 1180**
G. MICHAEL FELKER AND JOHN R. TEERLINK
- 58 Management of Heart Failure Patients With Reduced Ejection Fraction, 1208**
JANE E. WILCOX AND DOUGLAS L. MANN
- 59 Heart Failure With Preserved or Mildly Reduced Ejection Fraction, 1239**
CAROLYN S.P. LAM, SANJIV J. SHAH, AND SCOTT D. SOLOMON
- 60 The Dilated, Restrictive, and Infiltrative Cardiomyopathies, 1266**
RAY E. HERSHBERGER AND DANIEL P. JUDGE
- 61 Cardiac Amyloidosis, 1287**
FREDERICK L. RUBERG AND MATHEW S. MAURER
- 62 Hypertrophic Cardiomyopathy, 1298**
CAROLYN Y. HO AND SHARLENE M. DAY
- Guidelines Highlight: Management of Hypertrophic Cardiomyopathy (online)**
ANNA AXELSSON RAJA
- 63 Myocarditis, 1313**
LESLIE T. COOPER JR AND BIYKEM BOZKURT
- 64 Cardio-Oncology, 1328**
BONNIE KY
- 65 Devices for Monitoring and Managing Heart Failure, 1343**
JOANN LINDENFELD AND MICHAEL R. ZILE
- 66 Mechanical Circulatory Support, 1358**
EZEQUIEL J. MOLINA AND JENNIFER A. COWGER
- Guidelines Highlights: Mechanical Circulatory Support (online)**
EZEQUIEL J. MOLINA AND JENNIFER A. COWGER
- 67 Cardiac Transplantation, 1370**
RANDALL C. STARLING
- PART VIII DISEASES OF THE HEART VALVES**
- 68 Aortic Valve Stenosis, 1383**
BRIAN R. LINDMAN, ROBERT O. BONOW, AND CATHERINE M. OTTO
- Guidelines Highlight: Aortic Stenosis: Classification, Diagnosis, and Management (online)**
RANYA SWEIS

- 69 Aortic Regurgitation, 1404**
ROBERT O. BONOW AND RICK A. NISHIMURA

Guidelines Highlights: Aortic Regurgitation (online)
AKHIL NARANG

- 70 Transcatheter Aortic Valve Replacement, 1415**
TAMIM M. NAZIF, MARTIN B. LEON, AND MICHAEL J. MACK

- 71 Mitral Stenosis, 1428**
Y.S. Chandrashekar

Guidelines Highlight: Mitral Stenosis: Classification, Diagnosis, and Management (online)
MOHAMED AL-KAZAZ

- 72 Mitral Regurgitation, 1439**
REBECCA TUNG HAHN AND ROBERT O. BONOW

Guideline Highlights: Mitral Regurgitation (online)
AKHIL NARANG

- 73 Tricuspid, Pulmonic, and Multivalvular Disease, 1457**
PATRICIA A. PELLIKKA AND VUYISILE T. NKOMO

Guidelines Highlight: Tricuspid Valve Disease and Pulmonic Valve Disease (online)
LAURA DAVIDSON

- 74 Transcatheter Therapies for Mitral and Tricuspid Valvular Heart Disease, 1468**
HOWARD C. HERRMANN AND MICHAEL J. REARDON

- 75 Prosthetic Heart Valves, 1479**
PHILIPPE PIBAROT AND PATRICK T. O'GARA

Guidelines Highlights: Prosthetic Valves (online)
MOHAMED AL-KAZAZ

- 76 Infective Endocarditis, 1490**
THOMAS J. CAHILL AND BERNARD D. PRENDERGAST

Guidelines Highlights: Infective Endocarditis (online)
JONATHAN VIBHISHANAN, THOMAS J. CAHILL, AND BERNARD D. PRENDERGAST

- 77 Rheumatic Fever, 1503**
ANA OLGA MOCUMBI

PART IX DISEASES OF THE PERICARDIUM AND PULMONARY VASCULAR BED

- 78 Pericardial Diseases, 1513**
ALLAN L. KLEIN, TOM KAI MING WANG, MARTIN M. LEWINTER, AND PAUL C. CREMER

- 79 Pulmonary Embolism and Deep Vein Thrombosis, 1533**
GREGORY PIAZZA AND SAMUEL Z. GOLDBER

Guidelines Highlight: Diagnosis and Management of Pulmonary Embolism (online)
BEHNOOD BIKDELI AND GREGORY PIAZZA

- 80 Pulmonary Hypertension, 1557**
BRADLEY A. MARON

Guidelines Highlight: Managing Pulmonary Hypertension (online)
BRADLEY A. MARON AND GAUTAM V. RAMANI

- 81 Sleep-Disordered Breathing and Cardiac Disease, 1580**
SUSAN REDLINE

PART X CARDIOVASCULAR DISEASE IN SELECT POPULATIONS

- 82 Endemic and Pandemic Viral Illnesses and Cardiovascular Disease: Influenza and COVID-19, 1589**
ORLY VARDENY, MOHAMMAD MADJID, AND SCOTT D. SOLOMON

- 83 Cardiovascular Abnormalities in HIV-Infected Individuals, 1607**
MATTHEW S. DURSTENFELD AND PRISCILLA Y. HSUE

- 84 Exercise and Sports Cardiology, 1620**
PAUL D. THOMPSON AND AARON L. BAGGISH

- 85 Cardiovascular Disease in Women, 1629**
MARTHA GULATI AND C. NOEL BAIREY MERZ

- 86 Pregnancy and Heart Disease, 1643**
SAMUEL C. SIU AND CANDICE K. SILVERSIDES

Guidelines Highlight: Pregnancy and Heart Disease (online)
CANDICE SILVERSIDES AND SAMUEL SIU

- 87 Congenital Heart Disease in the Adolescent and Adult, 1667**
ERIC V. KRIEGER, ADAM L. DORFMAN, SONYA V. BABU-NARAYAN, AND ANNE MARIE VALENTE

Guidelines Highlight: Management of Adults with Congenital Heart Disease (online)
CHARMAINE SIN MAN LAM

- 88 Heart Disease in Various Populations, 1710**
ALANNA A. MORRIS AND MICHELLE A. ALBERT

- 89 Cardiovascular Disease in Older Adults, 1717**
DANIEL E. FORMAN, KAREN ALEXANDER, PARAG GOYAL, AND MICHAEL W. RICH

90 Cardiovascular Effects of Drugs and Toxins, 1739

RHONDALYN C. MCLEAN AND LEE R. GOLDBERG

PART XI CARDIOVASCULAR DISEASE AND DISORDERS OF OTHER SYSTEMS

91 Hemostasis, Thrombosis, Fibrinolysis, and Cardiovascular Disease, 1749

JEFFREY I. WEITZ

92 Endocrine Disorders and Cardiovascular Disease, 1774

BERNADETTE BIONDI

93 Rheumatic Diseases and the Cardiovascular System, 1794

TARYN YOUNGSTEIN, PETER LIBBY, AND BRITTANY WEBER

94 Tumors Affecting the Cardiovascular System, 1815

MARVIN D. ATKINS, SACHIN S. GOEL, AND MICHAEL J. REARDON

95 Psychiatric and Psychosocial Aspects of Cardiovascular Disease, 1827

KENNETH E. FREEDLAND, ROBERT M. CARNEY, ERIC J. LENZE, AND MICHAEL W. RICH

96 Neuromuscular Disorders and Cardiovascular Disease, 1839

ELIZABETH M. MCNALLY, GORDON F. TOMASELLI, AND WILLIAM J. GROH

Guideline Highlights: Neuromuscular Disorders (online)

UPASANA JARORI AND DEEPAK BHAKTA

97 Interface Between Kidney, Metabolic, and Cardiovascular Diseases, 1858

CLARE ARNOTT, RADICA Z. ALICIC, VLADO PERKOVIC, AND KATHERINE R. TUTTLE

98 Cardiovascular Manifestations of Autonomic Disorders, 1879

VARUN MALIK, JASON S. BRADFIELD, AND KALYANAM SHIVKUMAR