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TEXTBOOK OF CORONARY THROMBOSIS AND THROMBOLYSIS

Edited by

Richard C. Becker, M.D.

Director, Cardiovascular Thrombosis Research Center

Director, Coronary Care Unit

University of Massachusetts Medical School
Worcester, Massachusetts



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Dedicated to Clinton Frederick, Gillian Martha, and Kristian Charles Deiter — “Seek the truth and devote yourselves to those that have not.”

Dedicated to my colleagues at the Cardiovascular Thrombosis Research Center — “Keep asking questions.”

Dedicated to my soulmate — “Inspiration knows no boundaries and manifests itself in many wonderful and loving ways.”

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PREFACE

Teleologically, the hemostatic mechanism is among the most fundamental yet complex physiologic processes in humans. Early scientists and physicians were fascinated by the blood's ability to remain in a liquid state only to clot in response to vascular injury. The cellular and noncellular components of normal hemostasis took centuries to discover, and the intricacies of their delicate interactions are still being unraveled today. As is so often the case, an in-depth appreciation of physiologic hemostasis, representing a basic life-sustaining sequence of events, paved the way for understanding abnormal hemostasis or pathologic thrombosis. Aristotle, Malpighi, and Osler, representing but a few of the founding fathers in the field, would undoubtedly be honored to see their observations form the template for lifesaving treatments.

The evolution of thrombocardiology, a hybrid of cardiology, hematology, and pathology has proceeded at an extraordinary pace. Fueled by a seemingly insatiable sense of enthusiasm and a "need to know" attitude, modern-day pioneers and visionaries have taken on the challenge of defeating coronary arterial thrombosis, a leading cause of death, disability, and healthcare expenditures in the United States and other industrialized nations worldwide. Now, more than ever before, the timeless links between cellular biology, vascular biology, and the practice of medicine are being recognized and justly exploited through basic investigation and clinical research endeavors, providing answers to fundamental questions and sparking new hypotheses, with the ultimate goal of developing universally applicable and affordable therapies as well as practical guidelines for their use.

The *Textbook of Coronary Thrombosis and Thrombolysis*, in essence, represents a heartfelt gift of knowledge from a dedicated group of scientists and clinicians, who collectively have set out on a mission to minimize the societal impact of "hemostasis in the wrong place." The book is divided into four distinct sections: Part 1, Scientific Principles, lays down the supporting foundation; Part 2, Clinical Application of Scientific Principles, places the knowledge base in a working perspective, directly applying science to patient care; Part 3, New Dimensions, provides a glimpse of tomorrow. Steering the field clear of self-proclaimed victory and the dangers of complacency as we move into the 21st century, Part 4, Evolution of Thrombocardiology, focuses on laboratory standards, clinical trials, and drugs in development.

These major sections are systematically divided into smaller sections, each with a composer who has been asked to assemble the works of the finest scientific minds in the world. When brought together and conducted well, this orchestra plays a symphony for all the world to hear. It is this spirit of coordinated research and clinical practice that has captured the pain of human disease and suffering, and is rising swiftly to meet the needs of humanity in the global village. The *Textbook of Coronary Thrombosis and Thrombolysis* represents the culmination of a long journey designed solely for the purpose of serving basic scientists, clinician-scientists, and practicing clinicians intimately involved with seeking truth through pointed investigation and unconditional clinical application of current concepts in thrombocardiology.

Richard C. Becker, M.D.

FOREWORD

Eric J. Topol

In looking back over the past decade, the progress made in the treatment of patients with acute coronary syndromes has been enormous. The use of intravenous thrombolysis for acute myocardial infarction was first approved by the United States Food and Drug Administration in late 1987, and was implemented in clinical practice over the next 2–3 years. Intravenous heparin was shown to change the natural history in patients with unstable angina, and aspirin was demonstrated in 20 randomized trials to provide important protection from death and myocardial infarction in patients with acute myocardial infarction, unstable angina, and those undergoing percutaneous coronary intervention. In aggregate, in this discipline of cardiovascular medicine — the treatment of patients with acute manifestations of ischemic heart disease — we have been on a steep, ascending climb, acquiring new and vital information, and, coincidentally, it has led to a major transformation in clinical practice. Most of us who cared for these patients before this time fully recognize that this represents a true revolution in medicine.

While our therapies have indeed improved, there are major residual shortcomings. With the most potent thrombolytics available today, nearly half of patients are left without prompt restoration of infarct vessel patency 90 minutes into therapy. Reocclusion, a manifestation of rethrombosis, occurs in up to 25% of patients within a year from the index event. Furthermore, in patients receiving aspirin, there is an incomplete effect on inhibiting platelet aggregation, and with heparin there is an inconsistent effect owing to lack of inactivation of clot-bound thrombin and the natural inhibitors of heparin, such as platelet factor 4. Accordingly, there is a major gap between the actual therapies of today and, their ideal improved and optimized forms in the future.

The number one killer, the most important manifestation of heart disease today, is still coronary thrombosis. Fundamental to more effectively addressing its treatment in the years ahead is an improved understanding of its principles and the thrombotic

process. In the *Textbook of Coronary Thrombosis and Thrombolysis*, Richard Becker has organized a superb and comprehensive examination of all the relevant basic and clinical information in the field.

In the first section on scientific principles, the leading international authorities have reviewed each major building block in coronary thrombosis and clot lysis, including detailed reviews of the coagulation cascade, platelets, plasminogen activators, atherosclerosis, thrombosis, plaque rupture, and vascular biology. This is followed in Section II by a review of the central concepts pertaining to clinical applications, which include thrombolytic agents, the pathophysiology of the acute coronary syndromes, prehospital and early in-hospital therapy, coagulation and myocardial necrosis serum markers, the use of coronary angiography and percutaneous interventions, along with a systematic review of the complications of therapy and the futuristic approach of gene therapy. These sections are followed by a section dedicated to the future directions of basic and clinical investigation, along with another that provides an exhaustive glossary of relevant clinical trials, terms, and drugs that are in development but not yet commercialized.

Dr. Becker has done a masterful job of soliciting outstanding input from so many of the leading authorities on this subject. The superb content of the book is a direct reflection of the top-notch authors who have contributed to it. All of the pivotal aspects of coronary thrombosis are at least touched on, if not fully reviewed, in this textbook.

The future of improved therapies directed against coronary thrombosis in the years to come is predicated on enhanced understanding of the current state of the art with a visionary eye toward where the field is headed. In this textbook, both of these notable objectives are fully met. There is no other book available that ties together this important wealth of information, and undoubtedly this monograph will prove useful for not only cardiologists but also trainees and internists caring for patients with ischemic heart disease.

CONTRIBUTING AUTHORS

Dr. George S. Abela
Division of Cardiology
Michigan State University
Department of Medicine
B-208 Clinical Center
East Lansing, MI 48824

Dr. Dana Abendschein
Cardiovascular Division
Washington University School of Medicine
St. Louis, MO 63110

Dr. John A. Ambrose
Cardiac Catheterization Laboratory
The Mount Sinai Medical Center
One Gustave L. Levy Place
New York, NY 10029-6574

Dr. Felicita Andreotti
Istituto di Cardiologia
Policlinico A. Gemelli
Largo F. Vito, 1
00168 Roma
Italy

Dr. Alfred Arnold
Department of Cardiology
Medical Center Alkmaar
P.O. Box 501
1800 AM Alkmaar
The Netherlands

Dr. James M. Atkins
University of Texas Southwestern Medical School
5323 Harry Hines Boulevard
Dallas, TX 75235-8890

Dr. Richard C. Becker
Cardiovascular Thrombosis Research Center
University of Massachusetts Medical School
55 Lake Avenue North
Worcester, MA 01655

Dr. Narinder P. Bhalla
Cardiac Catheterization Laboratory
Brooklyn Hospital Center
New York University Medical Center

550 First Avenue
New York, NY 10016

Dr. Christoph Bode
Medizinische Klinik III (Kardiologie)
Bergheimerstrasse 58
69115 Heidelberg
Germany

Dr. Eric Boersma
Department of Cardiology
Medical Center Alkmaar
P.O. Box 501
1800 AM Alkmaar
The Netherlands

Dr. Peter Carmeliet
Center for Transgene Technology and Gene
Therapy
Vlaams Interuniversitair Instituut voor
Biotechnologie
Campus Gasthuisberg
O&N, Herestraat 43
B-3000 Leuven Belgium

Dr. Steffen P. Christow
Virchow Hospitals of the Humboldt University
at Berlin
Franz-Volhard-Hospital
Wiltbergstrasse 50
D-13125 Berlin
Germany

Dr. Richard Cohen
Evans Memorial Department of Clinical Research
Department of Medicine
Boston University Medical Center
Boston, MA 02118

Dr. D. Collen
Center for Molecular and Vascular Biology
Campus Gasthuisberg, O&N Herestraat 49
University of Leuven
B-3000 Leuven
Belgium

Dr. David P. de Bono
Department of Medicine

University of Leicester, LE3 9QP
UK

Dr. Marco Diaz
Sections of Cardiology and Vascular Medicine
Evans Memorial Department of Clinical Research
Department of Medicine
Boston University Medical Center
Boston, MA 02118

Dr. Sanjay Dixit
Cardiovascular Division
Department of Medicine
State University of New York Health Science Center
at Syracuse
Syracuse, NY 13210

Dr. Paul R. Eisenberg
Cardiac Care Unit
Washington University
School of Medicine
660 South Euclid Avenue
St. Louis, MO 63110

Dr. Daniel Eitzman
University of Michigan Medical School
1301 Catherine Road
Medical Science Building I
Ann Arbor, MI 48109-0624

Dr. Christopher J. Ellis
Cardiologist and Senior Lecturer in Cardiovascular
Medicine
Auckland Hospital
Private Bag 92 024
Auckland 1030
New Zealand

Dr. Mark L. Entman
Section of Cardiovascular Sciences
Department of Medicine
Baylor College of Medicine
The Methodist Hospital and the DeBakey Heart
Center
Houston, TX 77030-3498

Dr. William P. Fay
University of Michigan Medical School
1301 Catherine Road
Medical Science Building I
Ann Arbor, MI 48109-0624

Dr. James Ferguson
Cardiology Research MC 1-191
Texas Heart Institute

P.O. Box 20345
Houston, TX 77225-0345

Dr. Nikolaos G. Frangogiannis
Section of Cardiovascular Sciences
Department of Medicine
Baylor College of Medicine
The Methodist Hospital and the DeBakey Heart
Center
Houston, TX 77030-3498

Dr. David Ginsburg
University of Michigan Medical School
1301 Catherine Road
Medical Science Building I
Ann Arbor, MI 48109-0624

Dr. Robert J. Goldberg
Department of Medicine
University of Massachusetts Medical School
55 Lake Avenue North
Worcester, MA 01655

Dr. Paolo Golino
Division of Cardiology
University of Naples "Federico II"
via S. Pansini 5
80131 Naples
Italy

Dr. Dietrich Gulba
Virchow Hospitals of the Humboldt
University at Berlin
Franz-Volhard-Hospital
Wiltbergstrasse 50
D-13125 Berlin
Germany

Dr. Robert Harrington
Duke Clinical Research Institute
2024 West Main Street
Durham, NC 27705

Patricia K. Hodgson
Department of Medicine
Duke University Medical Center
Durham, NC 27710

Dr. Kurt Huber
Department of Cardiology
University of Vienna
Wahringer Gurtel 18-20
A-1090 Vienna
Austria

Dr. Jeffrey M. Isner
Tufts University School of Medicine
136 Harrison Avenue
Boston, MA 02111

Dr. Allan S. Jaffe
SUNY HSC at Syracuse
750 E. Adams Street
Syracuse, NY 13210

Dr. John F. Keaney, Jr.
Evans Memorial Department of
Medicine
Cardiology Section Room W507
80 E. Concord Street
Boston, MA 02118

Dr. Bruce A. Keyt
Genentech, Inc.
Department of Cardiovascular
Research
460 Point San Bruno Blvd.
South San Francisco, CA 94080

Dr. Reza Khoshnevis
Cardiology Research
MC 1-191
Texas Heart Institute
P.O. Box 20354
Houston, TX 77225

Dr. Benedikt Kohler
Medizinische Klinik III (Kardiologie)
Bergheimerstrasse 58
69115 Heidelberg
Germany

Dr. Willemeijn J. Kollöffel
Pharmacy of St. Anna Hospital
P.O. Box 90
5660 AB Geldrop
The Netherlands

Dr. H. Joost Kruik
Department of Cardiology
University Hospital St. Radboud
Nijmegen, P.O. Box 9101
6500 HB Nijmegen
The Netherlands

Dr. Costas Lambrew
Maine Medical Center
Division of Cardiovascular Medicine
22 Bramhall Street
Portland, ME 04102-3175

Dr. L. Veronica Lee
Washington University School of Medicine
Cardiovascular Division
660 South Euclid Avenue
St. Louis, MO 63110

Dr. H. Roger Lijnen
Center for Molecular and Vascular
Biology
University of Leuven, Campus Gasthuisberg
O&N Herestraat 49
B-3000 Leuven
Belgium

Dr. Joseph Loscalzo
Boston University School of Medicine
Evans Memorial Department of Medicine
Center for Advanced Biomedical Research
700 Albany Street
Boston, MA 02118

Dr. Douglas W. Losordo
St. Elizabeth's Hospital of Boston
736 Cambridge Street
Boston, MA 02135

Dr. Ted W. Love
Genentech, Inc.
Department of Product Development
460 Point San Bruno Blvd.
South San Francisco, CA 94080

Dr. Elizabeth G. Nabel
Division of Cardiology
University of Michigan Medical School
MSRB III 7220
1150 W. Medical Center Dr.
Ann Arbor, MI 48109-0644

Dr. Thomas K. Nordt
Medizinische Klinik III (Kardiologie)
Bergheimerstrasse 58
69115 Heidelberg
Germany

Dr. Patrick O'Gara
Brigham and Women's Hospital
75 Francis Street
Boston, MA 02115

Dr. Joseph P. Ornato
Internal Medicine Section of Emergency Medical
Services
Virginia Commonwealth of Virginia
Richmond, VA 23298

Dr. Voula Osganian
New England Research Institute
9 Galen Street
Watertown, MA 02172

Dr. Mary Ann Peberdy
Medical College of Virginia
P.O. Box 525, MCV Station
401 North 12th Street
Richmond, VA 23298-0525

Dr. Linda R. Peterson
Division of Cardiology
Washington University School of Medicine
660 S. Euclid Avenue, Box 8086
St. Louis, MO 63110

Dr. Hans J. Rapold
Basel University Medical School
Urichstrasse 27
D-79618 Rheinfelden
Germany

Dr. Robert Roberts
Department of Medicine
Section of Cardiology
6550 Fannin, MS SM 677
Baylor College of Medicine
Houston, TX 77030

Dr. Arie Roth
Intensive Cardiac Care Unit
Tel Aviv Medical Center
Ichilov Hospital
6 Weizman Street
Tel Aviv 64239
Israel

Dr. Una S. Ryan
Vice President of Research
T Cell Sciences, Inc.
115 Fourth Avenue
Needham, MA 02194-2725

Dr. Pamela A. Sakkinen
University of Vermont
Aquetec Bldg. T205
55A South Park Drive
Colchester, VT 05446

Dr. Harsch Sanchorawala
Evans Memorial Department of Medicine
Cardiology Section, Room W507
80 E. Concord Street
Boston, MA 02118

Dr. William P. Santamore
Division of Thoracic and Cardiovascular Surgery
Department of Surgery
University of Louisville
Louisville, KY 40292

Dr. Harry P. Selker
New England Medical Center
Health Services Research
750 Washington Street
Boston, MA 02111

Dr. Maarten L. Simoons
Department of Cardiology
Medical Center Alkmaar
P.O. Box 501
1800 AM Alkmaar
The Netherlands

Dr. Richard Smalling
Division of Cardiology
University of Texas Medical School at
Houston
6431 Fannin, Room 1.246 MSB
Houston, TX 77030

Dr. Frederick A. Spencer
Thrombosis Research Center
University of Massachusetts Medical School
55 Lake Avenue North
Worcester, MA 01655

Dr. David Stump
Genentech, Inc.
I DNA Way
South San Francisco, CA 94080

Dr. Melvin E. Tan
Duke Clinical Research Institute
Division of Cardiology
Duke University Medical Center
Durham, NC 27710

Dr. Cynthia M. Thaik

Dr. Mark C. Thel
Division of Cardiology
Department of Medicine
Duke University Medical Center
Durham, NC 27710

Dr. Russell P. Tracy
University of Vermont
Aquatec Building, T205

55A South Park Drive
Colchester, VT 05446

Dr. Maureen van der Vlugt
Department of Cardiology
Medical Center Alkmaar
P.O. Box 501
1800 AM Alkmaar
The Netherlands

Dr. Steven Vanderschueren
Center for Molecular and Vascular Biology
University of Leuven
Campus Gasthuisberg
O & N, Herestraat 49
B-3000 Leuven
Belgium

Dr. Freek W.A. Verheugt
Department of Cardiology
University Hospital St. Radboud, Nijmegen
P.O. Box 9101
6500 HB Nijmegen
The Netherlands

Dr. W. Douglas Weaver
Division of Cardiology
Henry Ford Hospital
Detroit, MI

Prof. Harvey D. White
Coronary Care and
Cardiovascular Research
Green Lane Hospital
Private Bag 92 189
Auckland 1030
New Zealand

Dr. James M. Wilson
Cardiology Research MC 1-191
Texas Heart Institute
P.O. Box 20345
Houston, TX 77225-0345

Dr. Robert J. Zalenski
Emergency Medicine and Medicine (Cardiology)
School of Medicine
Wayne State University/The Detroit Medical Center
Detroit, MI 48201