

PROSTAGLANDINS IN CLINICAL MEDICINE

CARDIOVASCULAR AND THROMBOTIC DISORDERS

Edited by

KENNETH K. WU, M.D.

*Professor and Chief
Coagulation and Thrombosis Unit
Rush Medical College
Chicago, Illinois*

ENNIO C. ROSSI, M.D.

*Professor and Chief
Section of Hematology
Northwestern University
School of Medicine
Chicago, Illinois*

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Contributors

- C. ARÉN, Sahlgrenska Sjukhuset, Göteborg, Sweden
NAJAM A. AWAN, University of California, Davis, School of Medicine; Sacramento (Calif.) Medical Center
R. N. BAIRD, Bristol (England) Royal Infirmary
JAMES M. BEATTIE, University of California, Davis, School of Medicine; Sacramento (Calif.) Medical Center
VITTORIO BERTELE, Mario Negri Institute for Pharmacological Research, Milan, Italy
EUGENE H. BLACKSTONE, University of Alabama, School of Medicine, Birmingham
F. WILLIAM BLAISDELL, University of California, Davis, School of Medicine
M. J. BROEKMAN, New York Veterans Administration Medical Center, New York
W. P. BROWN, Upjohn Company, Kalamazoo, Michigan
WILLIAM B. CAMPBELL, University of Texas Health Science Center, Dallas
CHIARA CERLETTI, Mario Negri Institute for Pharmacological Research, Milan, Italy
DENNIS E. CHENOWETH, Scripps Clinic and Research Foundation, La Jolla, California
P. C. CLIFFORD, Bristol (England) Royal Infirmary
F. COCEANI, Hospital for Sick Children, Toronto, Canada
JOANN L. DATA, Burroughs Wellcome Company, Research Triangle Park, North Carolina
GIOVANNI DE GAETANO, Mario Negri Institute for Pharmacological Research, Milan, Italy
GARRY L. DE GRAAF, Upjohn Company, Kalamazoo, Michigan
MRINAL K. DEWANJEE, Mayo Clinic and Foundation, Rochester, Minnesota
P. A. DIEPPE, Bristol (England) Royal Infirmary
GIOVANNI DI MINNO, Mario Negri Institute for Pharmacological Research, Milan, Italy
DONALD W. DUCHARME, Upjohn Company, Kalamazoo, Michigan

- MICHAEL J. DUNN, Case Western Reserve University; University Hospitals of Cleveland (Ohio)
- A. J. DUTKA, Naval Medical Research Institute, Bethesda, Maryland
- H. H. G. EASTCOTT, St. Mary's Hospital, London, England
- N. EGBERG, Karolinska Sjukhuset, Stockholm, Sweden
- ANDERS ERIK EKLUND, Danderyd Hospital, Stockholm, Sweden
- BRITA EKLUND, Karolinska Hospital, Stockholm, Sweden
- GUNNEL ERIKSSON, Danderyd Hospital, Stockholm, Sweden
- MARK K. EVENSON, University of California, Davis, School of Medicine; Sacramento (Calif.) Medical Center
- THOMAS F. FERRIS, University of Minnesota Hospitals, Minneapolis
- BRIAN G. FIRTH, University of Texas Health Science Center, Dallas
- GARRET A. FITZGERALD, Vanderbilt University, Nashville, Tennessee
- F. A. FITZPATRICK, Upjohn Company, Kalamazoo, Michigan
- HO-LEUNG FUNG, State University of New York, Buffalo
- ROBERT R. GORMAN, Upjohn Company, Kalamazoo, Michigan
- L. J. GREENBAUM, JR., Naval Medical Research Institute, Bethesda, Maryland
- RYSZARD J. GRYGLEWSKI, N. Copernicus Academy of Medicine, Krakow, Poland
- J. M. HALLENBECK, Naval Medical Research Institute, Bethesda, Maryland
- KATHLEEN E. HARRIS, Northwestern University Medical School, Chicago
- MICHAEL A. HEYMANN, University of California, San Francisco, School of Medicine
- L. DAVID HILLIS, University of Texas Health Science Center, Dallas
- PAUL D. HIRSH, University of Texas Health Science Center, Dallas
- JOHN C. HOAK, University of Iowa College of Medicine, Iowa City
- JAMES W. HOLCROFT, University of California, Davis, School of Medicine
- STEPHEN J. HUMPHREY, M.D., Upjohn Company, Kalamazoo, Michigan
- E. A. JAFFE, Cornell University Medical College, New York
- TORBJÖRN JORETEG, Karolinska Hospital, Stockholm, Sweden
- LENNART KAIJSER, Karolinska Hospital, Stockholm, Sweden

- MICHAEL P. KAYE, Mayo Clinic and Foundation, Rochester, Minnesota
- JOHN W. KIRKLIN, University of Alabama, School of Medicine, Birmingham
- D. R. LEITCH, Naval Medical Research Institute, Bethesda, Maryland
- PETER R. LICHTENTHAL, Northwestern University Medical School, Chicago
- O. I. LINET, Upjohn Company, Kalamazoo, Michigan
- JOHN E. LUND, Upjohn Company, Kalamazoo, Michigan
- JOHN C. MC GIFF, New York Medical College, Valhalla
- A. J. MARCUS, New York Veterans Administration Medical Center, New York
- M. F. R. MARTIN, Bristol (England) Royal Infirmary
- DEAN T. MASON, University of California, Davis, School of Medicine; Sacramento (Calif.) Medical Center
- LAWRENCE L. MICHAELIS, Northwestern University School of Medicine, Chicago
- KATHLEEN E. NEEDHAM, University of California, Davis, School of Medicine; Sacramento (Calif.) Medical Center
- PHILIP NEEDLEMAN, Washington University Medical School, St. Louis
- MARK NEMEROVSKI, UCLA School of Medicine; Cedars-Sinai Medical Center, Los Angeles
- CARL R. NOBACK, Mayo Clinic and Foundation, Rochester, Minnesota
- P. M. OLLEY, Hospital for Sick Children, Toronto, Canada
- ANDERS G. OLSSON, Karolinska Sjukhuset, Stockholm, Sweden
- C. PAPACONSTANTINOU, Karolinska Sjukhuset, Stockholm, Sweden
- BRUCE J. PARDY, St. Mary's Hospital, London, England
- ROY PATTERSON, Northwestern University Medical School, Chicago
- NORBERTO PERICO, Ospedali Riuniti di Bergamo, Bergamo, Italy
- KEVIN A. PETERSON, Mayo Clinic and Foundation, Rochester, Minnesota
- CH. PUNZENGRUBER, University of Vienna, Vienna, Austria
- K. RADEGRAN, University of Göteborg (Sweden)
- GIUSEPPE REMUZZI, Ospedali Riuniti de Bergamo, Bergamo, Italy
- ENNIO C. ROSSI, Northwestern University School of Medicine, Chicago

- L. B. SAFIER, New York Veterans Administration Medical Center,
New York
- EDWIN W. SALZMAN, Beth Israel Hospital, Boston
- WILLIAM E. SHELL, UCLA School of Medicine, Cedars-Sinai Medical Center, Los Angeles
- K. SILBERBAUER, University of Vienna, Vienna, Austria
- H. SINZINGER, University of Vienna, Vienna, Austria
- ERIC G. SPOKAS, New York Medical College, Valhalla
- ROBERT W. STEWART, University of Alabama School of Medicine, Birmingham
- ANDREW SZCZEKLIK, N. Copernicus Academy of Medicine, Krakow, Poland
- K. TACK-GOLDMAN, New York Veterans Administration Medical Center, New York
- A. C. TEGER-NILSSON, Sahlgrenska Sjukhuset, Göteborg, Sweden
- L. TREGERMAN, Upjohn Company, Kalamazoo, Michigan
- H. L. ULLMAN, New York Veterans Administration Medical Center, New York
- B. B. WEKSLER, Cornell University Medical College, New York
- J. T. WHICHER, Bristol (England) Royal Infirmary
- JAMES T. WILLERSON, University of Texas Health Science Center, Dallas
- PATRICK Y. K. WONG, New York Medical College, Valhalla
- KENNETH K. WU, Rush Medical College, Chicago
- M. A. WYNALDA, Upjohn Company, Kalamazoo, Michigan
- EDWARD J. ZAMBRASKI, Rutgers University, New Brunswick, New Jersey

Preface

Fifty-one years ago, human seminal fluid was shown to produce contraction of smooth muscle. Von Euler found this activity in extracts of the prostate gland and named the active principle "prostaglandin." These early observations, which introduced a new era, did not receive much attention for two decades. Subsequently, however, prostaglandins have been characterized, and their biological actions have been well described. They appear to play an important role in the regulation of many physiologic systems, and the steady flow of new information continually broadens the arena in which prostaglandins appear to act. Important clinical applications seem inevitable.

On the 7th, 8th, and 9th of May, 1981, an international symposium sponsored by Rush Medical College and the Northwestern University School of Medicine, was held in Chicago to explore the clinical applications of prostaglandins in cardiovascular and thrombotic disorders. This volume contains the proceedings of that symposium. The first two sections deal with the basic principles and physiologic effects of prostaglandins. They are followed by sections that describe clinical trials of prostaglandins in peripheral vascular and coronary artery disease; their potential role in asthma, persistent fetal pulmonary circulation, and thrombotic disorders; and the use of prostacyclin in cardiopulmonary bypass surgery.

Frequently, the goal of symposia proceedings is limited to the gathering and organization of previously published information. We believe these proceedings may exceed this limitation. Because of the rapid progress in prostaglandin research, a significant amount of the information presented—especially on clinical trials—is new. We hope the reader will share our view that the clinical data obtained to date confirm the promise of prostaglandin research and foreshadow clinical applications yet to come.

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KENNETH K. WU
ENNIO C. ROSSI

PART I

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M. J. BROEKMAN, L. B. SAFIER, H. L. ULLMAN,
K. TACK-GOLDMAN

*Divisions of Hematology/Oncology, Departments of
Medicine, New York Veterans Administration Medical
Center, and Cornell University Medical College,
New York*

Introduction

Lipids can be broadly defined as a chemically heterogeneous group of biomolecules with the common property of insolubility in water but solubility in nonpolar solvents.¹ In this chapter, we will mainly confine our discussion to lipids that are esters of long-chain fatty acids. Three major classes of lipids contain esterified fatty acids: phospholipids, glycolipids, and neutral lipids.¹

Phospholipids serve as structural components in mammalian cells and tissues. In addition, phospholipids can be conceived as metabolic storage depots for essential fatty acids (EFA). Some phosphoglycerides, such as phosphatidyl-inositol (PI) and phosphatidic acid (PA), turn over rapidly when the cell is stimulated.² Tissue fractionation studies have indicated that phospholipids in subcellular compartments usually have similar fatty acid compositions.³ These similarities may relate to a requirement of phospholipids for normal cell structure and function. Turnover of intact phosphoglyceride molecules is slow. Only the fatty acid moiety is renewed rapidly by intracellular fatty acid transfer. Although arachidonate is the precursor of prostaglandins and hydroxy acids, it may also lend a certain degree of stability to phospholipid components in cell membranes.

Glycolipids contain one or more sugar molecules, and some also have a sialic acid moiety (gangliosides). In human platelets the major