Endothelium-Derived Contracting Factors


Endothelium-Derived Contracting Factors

Editors
Gabor M. Rubanyi, Cedar Knolls, N.J.
Paul M. Vanhoutte, Houston, Tex.

91 figures and 16 tables, 1990

Karger

Basel · München · Paris · London · New York · New Delhi · Bangkok · Singapore · Tokyo · Sydney

Gabor M. Rubanyi
MD, PhD, Department of Pharmacology, Berlex Laboratories, Inc., Cedar Knolls, N.J., USA

Paul M. Vanhoutte
MD, PhD, Center for Experimental Therapeutics, Baylor College of Medicine, Texas Medical Center, Houston, Tex., USA

Library of Congress Cataloging-in-Publication Data
Contains the second part of the proceedings of the First International Symposium on Endothelium-Derived Vasoactive Factors.
Includes bibliographical references.
I. Endothelium-derived contracting factors - Congresses. I. Rubanyi, Gabor M., 1947-
II. Vanhoutte, Paul M. III. Title.
QV 150 15915e 1989]
ISBN 3-8055-5092-8
Drug Dosage
The authors and the publisher have exerted every effort to ensure that drug selection and dosage set forth in this text are in accord with current recommendations and practice at the time of publication. However, in view of ongoing research, changes in government regulations, and the constant flow of information relating to drug therapy and drug reactions, the reader is urged to check the package insert for each drug for any change in indications and dosage and for added warnings and precautions. This is particularly important when the recommended agent is a new and/or infrequently employed drug.

All rights reserved.
No part of this publication may be translated into other languages, reproduced or utilized in any form or by any means, electronic or mechanical, including photocopying, recording, microcopying, or by any information storage and retrieval system, without permission in writing from the publisher.

© Copyright 1990 by S. Karger AG, P.O. Box, CH-4009 Basel (Switzerland)
ISBN 3-8055-5092-8

Contents

Acknowledgements VIII
Foreword IX

I. Endothelium-Dependent Vasoconstriction

Vanhoutte, P.M.; Luscher, T.M. (Houston, Tex.): Endothelium-Dependent Vasoconstriction 1
Harder, D.R.; Kauser, K.; Lombard, J.H.; Roman, R.J. (Milwaukee, Wise);
Rubanyi, G.M. (Cedar Knolls, N.J.): Pressure-Induced Activation of Renal and Cerebral Arteries Depends upon an Intact Endothelium 8
Pearce, W.J. (Loma Linda, Calif): Hypoxia Promotes the Release of Both Relaxing and Contracting Factors from the Endothelium of Isolated Cerebral Arteries 20
Wadsworth, R.M.; Amatya, M.P.; Kwan, Y.W.; Kane, K.A.; Zeitlin, I.J. (Glasgow): Modulation by Hypoxia of the Release of Endothelium-Derived Mediators from Sheep Coronary Artery Rings 32
Auch-Schwelk, W.; Katusic, Z.S.; Vanhoutte, P.M. (Rochester, Minn.): Endothelium-Dependent Contractions in the SHR Aorta are Inhibited by Thromboxane A2 Receptor Antagonists 39
Toda, N. (Seta): Endothelium-Dependent Contractions in Monkey and Dog Cerebral Arteries - Possible Mechanism Underlying Cerebral Vasospasm 44
Highsmith, R.F.; Schmidt, D.J. (Cincinnati, Ohio); Pang, D.C. (Cedar Knolls, N.J.); Stauderman, K.A.; Rapoport, R.M. (Cincinnati, Ohio): Mechanisms of Action of Endothelial Cell-Derived Constricting Factor(s) 50

II. Endothelin


Contents VI

Pang, O.C.; Johns, ;; Patterson, ;; Parker Botelho, L.H.; Rubanyi, G.M. (Cedar Knolls, N.J.): Cellular Mechanisms of Action of Endothelin in Isolated Canine Coronary Arteries 66

Cocks, T.M.; Angus, J.; Broughton, A. (Prahran, Victoria): Endothelin-1 Is a Selective Vasoconstrictor: Studies on Human, Dog and Rabbit Blood Vessels in vitro and in vivo 73

Miller, V.M.; Vanhoutte, P.M. (Rochester, Minn.): Contractions to Endothelin in Canine Veins: Effects of Calcium Antagonists and Inhibitors of Endothelium-Derived Relaxing Factor(s) 80


Winquist, R.J.; Bunting, P.B.; Lumma, P.K.; Garsky, V.M.; Scott, A.L.; Vlasuk, G.P. (West Point, Pa.): Depressor Response to Endothelin in Normotensive and Hypertensive Rats 104

Hom, G.J.; Touhey, B.; Rubanyi, G.M. (Cedar Knolls, N.J.): Endothelin Is a Potent Coronary Vasoconstrictor in Anesthetized Dogs 110

King, A.J.; Brenner, B.M.; Anderson, S. (Boston, Mass.): Renal Hemodynamic Actions of Endothelin 117

Shigeno, T. (Saitama); Mima, T.; Takakura, K. (Tokyo); Yanagisawa, M.; Saito, ;; Goto, K.; Masaki, T. (Tsukuba): Effects of Endothelin on Cerebral Arteries and Its Possible Role in the Pathogenesis of Cerebral Vasospasm 124

Thiemermann, Ch.; Lidbury, P.S.; Thomas, G.R.; Vane, J.R. (London): Comparison of the Haemodynamic and Platelet-Inhibitory Effects of Endothelin-1 and Endothelin-3 in the Anaesthetized Rabbit 128

Wang, Y.N.; Chou, J.C.; Chang, D.; Chang, J.K. (Belmont, Calif.); Avila, C; Romero, R. (New Haven, Conn.): Endothelin-1 in Human Plasma and Amniotic Fluid 143

III. Atherosclerosis/Ischemia

Vrints, C; Verbeuren, T.J.; Snoeck, J.; Herman, A.G. (Antwerp-Wilrijk): Effects of Hypercholesterolemia on Coronary Vascular Reactivity. Impaired Endothelium-Dependent Vasodilation Leads to Unmasking of 5-HT2-Serotonergic Vasoconstriction in Hypercholesterolemic Rabbits 162
Boulanger, C; Shimokawa, H.; Schini, V.B.; Vanhoutte, P.M. (Houston, Tex.): Vascular Endothelium and -3 Unsaturated Fatty Acids 169

Contents VII

Lefer, A.M.; Tsao, P.S.; Johnson, G., III (Philadelphia, Pa.): Role of Endothelium-Derived Relaxing Factor as a Cardioprotective Agent in Myocardial Ischemia 190
Muller, B.; Schmidtke, M. (Berlin/Bergkamen): Effects of Iloprost on Ischemia-Induced Necrosis in the Hairless Mouse Ear 205
Stewart, D.J.; Baffour, R. (Montreal): Ischemia-Reperfusion Potentiates Endothelin-Induced Constriction in the Coronary Resistance Bed 212

Subject Index 232

The first part of these proceedings appears under the title 'Endothelium-Derived Relaxing Factors'.

Acknowledgements

The success of the International Symposium on Endothelium-Derived Vasoactive Factors and the publishing of this book were made possible by the
support and efforts of many organizations and individuals.
We would like to thank the professional staff of International Business
Communications, Inc., for the highly competent organization of the symposium
with special thanks to Ms. Kim Todd, who was the driving force
behind the organizational effort.
We wish to acknowledge the valuable sponsorship of the Physiological
Society of Philadelphia and the generous support of Schering AG, West
Berlin (FRG), and Berlex Laboratories, Inc., Cedar Knolls, N.J. (USA).
The outstanding contribution of the Scientific Advisory Board in preparing
the program and the excellent and exciting presentations and chapter
contributions by the speakers and chairpersons to the symposium and to this
book are gratefully appreciated.
We would like to express our gratitude to Mrs. Susan Packie for her help
in the organization of the symposium and editing of this book.
Finally, the editors would like to thank the staff of S. Karger, Basel
(Switzerland), for their very efficient handling and swift publication of the
monograph.

November 1989 Gabor
M. Rubanyi, MD, PhD
Paul M. Vanhoutte, MD, PhD

Foreword

This monograph contains the second part of the proceedings of the
International Symposium on Endothelium-Derived Vasoactive Factors,
which was held in Philadelphia from May 1 to May 3, 1989. Whereas the first
part, Endothelium-Derived Relaxing Factors, focuses on endothelium-dependent
relaxations, this book addresses mainly the issue of contracting factors of
endothelial origin. Soon after the discovery of endothelium-dependent relaxation,
it appeared that under given conditions and in certain blood vessels,
the endothelial cells generated contractions rather than relaxations [De Mey
and Vanhoutte, Circulation Res. 51: 439, 1982]. Bioassay studies revealed
that the endothelium can release very labile [Rubanyi and Vanhoutte, J.
Physiol., Lond. 364: 45, 1985] and more stable polypeptide-like contracting
factors [Hickey et al., Am. J. Physiol. 248: C550, 1985] which, in analogy
with the relaxing factors, were termed endothelium-derived contracting
factor(s) [EDCF(s)]. Interestingly, as is the case for the release of prostacyclin
and endothelium-derived relaxing factor (EDRF), one type of endothelium-dependent
contraction is prevented by inhibitors of cyclooxygenase, while
the other is not. The identity of EDCF is not firmly established yet, but the
cyclooxygenase-dependent factor appears to be superoxide anion; again the
analogy with relaxing factors is striking, as the most important EDRF also appears to be a radical species, nitric oxide.
The physiological role of endothelium-dependent contractions is more difficult to define than that of EDRF; they may contribute to responses such as cerebral autoregulation and hypoxic pulmonary vasoconstriction. However, under pathological conditions EDCF(s) may become very important. Whereas blood vessels progressively lose the ability to release or to respond to EDRF, endothelium-dependent contractions are well maintained,

Foreword

or even reinforced in a variety of models of vascular disease. The field of endothelium-dependent contractions has been expanded considerably by the discovery of endothelin [Yanagisawa et al., Nature 332:411, 1988], a 21-amino-acid peptide that not only contracts vascular smooth muscle, but can affect the function of many other cells as well. As such, it is a prime candidate of prolonged vasospastic episodes.

This second monograph consists of three parts. The first gives an overview of the experiments which have defined the existence of endothelium-dependent contractions and hence of EDCF(s), determined the stimuli that cause its release, and attempted to determine the nature of the factor. The second part discusses the current knowledge on endothelin for as far as we can cover such a rapidly-moving field in science. The third part discusses the dysfunctional endothelium of atherosclerotic and ischemic blood vessels as it is characterized by a reduced production of EDRF and prostacyclin, and the facilitated production of EDCF(s). Like the first monograph, this book is of relevance, not only for the cardiovascular physiologists and pharmacologists, but also for the cardiologist and the cardiovascular surgeon, as it discusses phenomena which probably play a key role in ischemic disorders and vascular occlusions.

November 1989
Gabor M. Rubanyi, MD, PhD
Paul M. Vanhoutte, MD, PhD