Endothelium-Derived Contracting Factors


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91 figures and 16 tables, 1990

Karger

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Library of Congress Cataloging-in-Publication Data
International Symposium on Endothelium-Derived Vasoactive Factors
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.

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ISBN 3-8055-5092-8

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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
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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, 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
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