Endothelium-Derived Contracting Factors


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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 Constrictions in the SHR Aorta are Inhibited by Thromboxane A2 Receptor Antagonists 39
Toda, N. (Seta): Endothelium-Dependent Constrictions 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


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'.

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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,

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
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