Endothelium-Derived Contracting Factors


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

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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,

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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.

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