Supplement to
Basic Research in Cardiology, Vol. 87, Suppl. 2 (1992)

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Cardiac Adaptation in Heart Failure

Risks due to myocardial phenotype changes
Introduction

Traditionally, cardiac hypertrophy is regarded as an adaptation of the heart to permanent mechanical overload. Regardless of the fact that many different and often unknown primary causes can result in heart failure, mechanical overload and myocardial hypertrophy is found in almost all forms of manifest chronic heart failure (apart from failure due to extramyocardial hindrances to inflow or to relaxation). However, the reactive enlargement of myocardial mass in response to an enhanced hemodynamic burden appears to be a double-edged sword.

Obviously, the hypertrophy helps to reduce the enhanced ventricular wall stress in heart failure by adding contractile units to the overdistended chamber wall. However, in recent years it became clear that this adaptive hypertrophic process is rather complex and may include problematic facets. The adaptive hypertrophy includes proliferation of the nonmyocyte cardiac cells as well as substantial alterations in the phenotype of the growing myocytes due to differential changes in gene expression. Presently open issues in this context are: What is the pathophysiological relevance of this altered phenotype of the myocardial tissue in overload hypertrophy? Does it explain the disturbed diastolic function of the failing myocardium? Does it contribute to the enhanced risk of complex ventricular arrhythmias? What is the relevance of a disproportionate increase in myocardial mass relative to the growth of the coronary vascular tree? Are there hypertrophy-specific alterations in coronary vascular function, even in absence of artherosclerotic coronary heart disease? Facts, concepts and opinions on these questions are under intensive discussion and research in cardiology, worldwide.

Within this volume, three questions out of the complex problem of cardiac adaptation in heart failure will be considered by international experts in clinical and experimental cardiology:

- What do we know about the cellular transduction mechanisms triggering myocyte hypertrophy and phenotype alterations in response to hemodynamic overload?
- Is the fragile Ca\(^{++}\)-homeostasis of hypertrophied cardiocytes a common basis for disturbed diastolic function and for the susceptibility to complex ventricular arrhythmias in heart failure?
- Is there a specific trophic role of the renin-angiotensin-system in cardiac adaptation to chronic overload?

The contributions to this volume resulted from the lectures and discussions of an international symposium devoted to these questions, which took place in Freiburg/Breisgau, Germany, December 5–7, 1991. This symposium was under the auspices of the European Society of Cardiology (Working group: Drug Therapy in Cardiology), of the Deutsche Gesellschaft für Herz- und Kreislaufforschung (Arbeits-
gemeinschaft Vasodilatantien), and of the Society for Cooperation in Medical Sciences, Freiburg. We are very grateful for the generous financial support by Bristol-Myers-Squibb, Munich, and by Schwarz-Pharma, Monheim, which made this symposium possible.

The success of the symposium came from the excellent lectures of the invited experts and from the lively and intensive discussions, which were inspired and directed by the distinguished chairmen of the sessions: W. Kübler (Heidelberg, Germany), A.H. Henderson (Cardiff, United Kingdom), F. Burkart (Basel, Switzerland), H. Krayenbühl (Zürich, Switzerland) and H. Scholz (Hamburg, Germany). Indispensable, however, were the excellent symposium organization in the hands of Mrs. Hedy Woeste, Bristol-Myers-Squibb, Munich, and the skillful help by Mrs. S. Müller, Steinkopff-Verlag, in preparing this volume.

Freiburg, summer 1992

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