Heart Failure

Pathophysiology, Molecular Biology, and Clinical Management

SECOND EDITION
For Phyllis
and
Varda
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Despite the dramatic advances in the care of patients with cardiovascular diseases that have occurred in the past half century, these conditions remain—by far—the most common causes of death in developed nations. Moreover, the prevalence of cardiovascular diseases is now rising rapidly in developing nations as well. It has been projected that within 20 years, cardiovascular disease will, for the first time in human history, be the most common cause of death worldwide.

As the treatment of most cardiovascular disorders—acute myocardial infarction and other acute coronary syndromes, hypertension, valvular disease and many congenital cardiac disorders—improves, early mortality is reduced. However, these patients are rarely “cured,” but instead they often develop myocardial disease and ultimately heart failure. Thus, heart failure has become the most frequent “final common pathway” to death or serious disability in cardiovascular diseases and might be considered to be the price paid for successful early management of these disorders. In the United States, heart failure is also the most frequent hospital discharge diagnosis of patients 65 years of age or older. It is, therefore, mandatory that physicians involved in the care of patients with this very common and serious condition understand its pathogenesis, clinical features, and the mechanisms underlying various therapies. Of equal importance, investigators of heart failure, be they basic or clinical scientists, have a great need to understand the relation between abnormalities at the molecular, cellular, organ, and clinical levels.

Heart failure is actually a much more complex condition than it was thought be 20 years ago. At that time, the pathophysiology of heart failure had been well described, but the responsible alterations in cellular biochemistry and biophysics were just being elucidated. The underlying genetic alterations were a total mystery.

Heart Failure: Pathophysiology, Molecular Biology and Clinical Management provides important insights into this important condition. Comprehensive medical texts on complex subjects are usually multiauthored because few individuals possess the understanding and perspective to do justice to fields as enormous as heart failure. Drs. Katz and Konstam have, by themselves, successfully tackled this Herculean task. In this magnificent book, they have not only reviewed all relevant aspects of this vast subject, but have provided a “grand vision” of how molecular biology provides explanations of the abnormalities of myocardial contraction and relaxation and how abnormalities of myocyte function affect the performance of the cardiac pump. Furthermore, they carefully describe the links between the disturbed pathobiology and both the clinical manifestations and treatment of heart failure. The breadth and depth of understanding provided by these two authorities, who uniquely span the disciplines of genetics, molecular biology, cardiac biochemistry, physiology, clinical cardiology, and therapeutics, are matched by their extraordinary ability to relate these fields to one another and to explain complex concepts clearly, both in words and diagrams.

This book is truly a joy to read and study. It will be equally useful to clinicians, scientists, and their trainees. It will surely stand as a landmark in the field.

Eugene Braunwald, MD
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Knowledge of the pathophysiology and treatment of heart failure has expanded rapidly since the first edition of this text was published in 2000. Discoveries in the basic sciences, notably molecular biology, are increasing the importance of pathophysiology for those who manage this common syndrome and revolutionizing the way we treat these patients. At the same time, new clinical information, by focusing attention on the mechanisms responsible for death and disability in heart failure, is drawing basic science and clinical practice toward one another. Because this expansion is making it increasingly difficult for a single individual to provide informed views of the many important features of this syndrome, this second edition has two authors: Arnold Katz, whose focus is on basic science, and Marvin Konstam, whose chapters describe patient management.

The goal of this text remains unchanged: to describe the molecular mechanisms that cause hearts to fail; the hemodynamic and other functional abnormalities that disable these patients; the neurohumoral and proliferative responses, both adaptive and maladaptive, that modify these disabilities; the clinical manifestations caused by these abnormalities; and therapeutic strategies for patient management.

This second edition covers more information than the first, but the text has been shortened to clarify our descriptions of disease mechanisms and therapeutic strategies. Achieving these goals in a concise text precludes inclusion of many details, so that readers seeking more exhaustive discussions are referred to standard textbooks of medicine and cardiology, reviews (many of which are cited in the present text), and original articles.

A number of changes have been made in this second edition. The historical overview in Chapter 1 includes discoveries made in the 20th century. All of the other chapters have been reorganized. Chapter 2 describes the hemodynamic basis for the clinical manifestations of this syndrome, while Chapter 3 reviews the neurohumoral responses evoked by impaired cardiac performance and key signaling pathways that mediate the functional responses. Chapter 4 describes the proliferative responses in failing hearts, as many of these have been recognized to play a central role in determining long-term prognosis in these patients and so are becoming targets for new therapy. The mechanisms by which cellular and molecular abnormalities impair the performance of failing hearts are reviewed in Chapter 5. Chapter 6 discusses the rationale for the many therapeutic approaches to this syndrome, and Chapter 7, which concludes this text, integrates the material covered in the earlier chapters to describe the management of specific groups of heart failure patients.

The goal of this text remains to aid physicians and other health professionals, along with students of medicine, basic science, nursing, and other fields related to cardiology, in understanding the pathophysiology and treatment of heart failure. We hope that this second edition will explain the pathophysiological mechanisms that are the basis of modern strategies for managing patients with this syndrome, and provide an overview for scientists who seek to apply basic concepts to this important clinical problem.

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