

Preface

Many readers may recall a family member, friend, or acquaintance who died suddenly with no history of heart disease or who acutely developed heart failure of unknown cause. These are common clinical presentations of patients who have acute myocarditis. Myocarditis, often related to a viral infection, contributes substantially to dilated cardiomyopathy and the burden of heart failure worldwide. In the 8 years since the last monograph on myocarditis was published, knowledge of viral-induced myocardial injury, autoimmune pathways in the heart, and the clinical treatment of myocarditis has advanced significantly. New cardiotropic viruses have been described. The causal mechanisms between acute viral infection and dilated cardiomyopathy have been elucidated in great detail. It is timely to draw together in one volume the threads of research on viral myocarditis, autoimmune myocardial injury, and clinical advances in myocarditis for the benefit of the practicing physician and the specialized researcher. This book is written equally for the clinician confronted with suspected myocarditis and the specialized investigator. It seeks to give each a framework and greater context for study.

This is the first volume that attempts to cover the entire spectrum of myocarditis from basic research to bedside medicine. The first chapter provides an introduction to experimental myocarditis. Dr. Charles Gauntt is an authority in the field of virology who is well equipped to provide such an overview. The members of Dr. Steven Tracy's premier enteroviral research laboratory contributed the second chapter on viral life cycle and the earliest events in the molecular pathogenesis of experimental coxsackie and adenoviral myocarditis.

Chapters 3 through 6 address the immune reaction that results in postviral myocarditis. The multifaceted immune response is described by several closely related topics. Dr. Sally Huber begins the discussion with a chapter on the cellular immune response, followed by Dr. Bernhard Maisch's chapter on the humoral immune response. These chapters emphasize the central role of Th1 and Th2 lymphocytes in postviral autoimmune myocarditis. In Chapter 5, Dr. Akira Matsumori, discusses the beneficial and detrimental roles of cytokines in postviral myocarditis. The terrific expansion of knowledge of nitric oxide biology justified a separate chapter by Drs. Joshua Hare and Charles Lowenstein on the roles of nitric oxide in viral infection and postviral heart disease.

The next 4 chapters cover translational research and seek to bridge basic biologic investigations and the clinical disorders. Dr. Bruce McManus and his laboratory colleagues cover extensive experimental data on the role of programmed cell death, apoptosis, in viral myocarditis in Chapter 7. Dr. Makoto Kodama describes experimental autoimmune (versus postviral) giant cell and lymphocytic myocarditis in rat and mouse models in Chapter 8. The role of the adrenergic system in experimental and human dilated cardio-

myopathy and the implications for treatment of human disease are described next. This section concludes with a chapter on the latest available data on enteroviral proteases and cardiomyopathy from Dr. Kirk Knowlton's laboratory.

The diagnosis, prognosis, and treatment of nonspecific and specific myocarditides are covered in Chapters 11 through 24. The strengths and limitations of noninvasive tests, including serologic biomarkers, measures of apoptosis, nuclear imaging, and echocardiography, are covered in detail. The technique and interpretation of endomyocardial biopsy are placed at the center of this section. Separate chapters are devoted to major idiopathic clinical entities, including cardiac sarcoidosis, giant cell myocarditis, and the eosinophilic myocarditides. Specific infectious diseases that affect the heart include Chagas disease, rheumatic fever, and human immunodeficiency virus-related cardiomyopathy. The book concludes with state-of-the-art chapters on myocarditis in children and peripartum cardiomyopathy.

A second objective of this book is to foster exchange of new ideas between basic and clinical investigators through a collation of parallel, related research. Leaders in experimental myocarditis can read of their clinical colleagues' latest progress and opinions and vice versa. I hope this book forms a platform for new research collaborations to grow. I am heartened that students of the clinical and basic sciences can glimpse in these chapters the excitement of participation in a decades-long, worldwide, multidisciplinary effort and sense the satisfaction of many investigators.

I thank all of my colleagues who have generously contributed to this work, in particular, Dr. Kirk U. Knowlton for his counsel and encouragement early on, for without him this project would not have started; Dr. Joseph G. Murphy, whose experience I sought on many occasions and who heard my frustrations and shared in the pleasure of the final proof; Dr. Carol L. Kornblith (editor), who read every word at least four times and patiently heard and taught me; and the production staff, including Kathryn K. Shepel (art director), Roberta J. Schwartz (production editor), Virginia A. Dunt (editorial assistant), and John P. Hedlund (proofreader). I thank my dear wife, Jane, without whose support and encouragement (and ruthless editing) this project could not have happened.

Leslie T. Cooper, Jr., MD

Myocarditis

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