Ihor Gussak · Charles Antzelevitch *Editors*
Arthur A.M. Wilde · Brian D. Powell · Michael J. Ackerman
Win-Kuang Shen *Co-Editors*

Electrical Diseases of the Heart

Volume 2: Diagnosis and Treatment

Second Edition

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Ihor Gussak and Charles Antzelevitch (Eds.)

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We dedicate this book to the thousands of investigators whose collective works have brought us to this exciting juncture in the history of science and medicine and on whose shoulders we stand. We are proud to dedicate this compendium to these pioneers of cardiac electrophysiology as well as to our mentors, collaborators and fellows who have assisted us in advancing the field and last but certainly not least to our families, whose understanding and support permitted us to dedicate the time and effort needed to formulate this text.

Ihor Gussak
Charles Antzelevitch

Foreword

I presented the following "case report" in the preface of the first edition of this book to illustrate the progress in cardiac electrophysiology over a period of 20-odd years. The evolution is still relevant:

She was about 35 years old when she first became my patient in 1975. She had suffered from bouts of a supraventricular tachycardia (SVT) as far back as she could remember. "In the early days," she recalled, "when I was a kid, they would give me something in the emergency room that elevated my blood pressure and damn near tore my head off. What a headache I would get! But a lot of times it didn't work. Then they stuck my head in a bucket of cold water and told me to 'bear down.' Finally, they would give me more digitalis in my vein until I started vomiting. That usually stopped the SVT."

But nothing seemed to prevent recurrences. She was on a full dose of digitoxin and was one of the first to try a β(beta) blocker (propranolol) in the late 1960s. Her episodes were fast, around 220/min, and frightened her terribly, so much so that she would ride the tractor alongside her farmer-husband all day long just to be near him in case she had a recurrence.

Then came one of the first breakthroughs. Gordon Moe had published a "case report" of a dog with probable atrioventricular node reentry (AVNRT), showing that such a tachycardia could be started and stopped by external stimuli. Clinical studies followed (though somewhat belatedly) and replicated such responses in humans. Medtronic developed an implantable pacemaker (5998 RF unit) that was triggered by an external battery-driven stimulator held over the passive receiver to deliver a burst of rapid stimuli to the epicardial electrodes implanted on her right atrium. Magic! She terminated her own SVT with unerring reliability and never precipitated atrial fibrillation. Now a free woman, she no longer needed tractor rides. But she never left her house without the RF generator and always carried a spare battery in her pocket.

Over time she discontinued her medications and gradually stopped coming for return visits because she had complete control of her SVT. About 15 years later she showed up unannounced after one of the wires in her hand held unit fractured and she no longer could stop the SVT. "Could I get her a replacement or send the broken unit for repairs?" she asked. The next day she was in the EP laboratory, had a slow pathway ablation, cure of the AVNRT, and eventual removal of the implanted unit.

This patient benefited from knowledge derived from animal and clinical research, as well as technological discoveries, over a period of some 15–20 years. And hundreds of thousands of patients like her have similarly profited from such advances. The work of basic and clinical scientists continues to uncover complex mechanisms and anatomic sites responsible for these and other arrhythmias, providing understanding ranging from molecular to clinical. Such advances, along with new mapping, imaging and recording modalities, and catheter and ablation innovations, help us toward our goal of translating science into improved patient care. We are also beginning to understand the pervasive role of genetics, not just for the classic inherited syndromes, but also for polygenic diseases such as sudden death in coronary disease and heart failure, and to manipulate genes for therapy.

Once again this book captures this new information, with sections on basic electrophysiology and heritable channelopathies, primary and secondary electrical diseases and sudden cardiac death, diagnostic methods and tools, risk stratification, and treatment. It is a tour de force, and one that is certain to fulfill the reading tastes and intellectual demands of both researchers and clinicians.

Congratulations to the editors and authors for creating the second edition of this popular work.

Indianapolis, IN *Douglas P. Zipes, MD*

Preface

In this second edition of *Electrical Disease of the Heart*, our goal was to embrace and highlight the explosion of knowledge that our field has witnessed since the publication of the first edition of this book. Building on the success of our first edition, our approach continues to be one of bridging basic and clinical science in an attempt to meaningfully advance our understanding of heart diseases and identify the knowledge gaps that exist.

Each chapter includes up-to-date results of studies aimed at providing an understanding of the electrical function of the heart in health and disease, established and evidence-based knowledge of clinical outcomes, areas of controversy, and future trends. Our goal is to provide a contemporary and succinct distillation of the state of the art. Although many of the chapters are highly sub-specialized, this book is designed for a broad audience, ranging from medical and graduate students to clinicians and scientists.

The book is the result of a collaboration that has brought together the skills and perspectives of researchers, scientists, and clinicians. We are deeply indebted to our associate editors and to all of the authors for their valuable contributions.

Ihor Gussak
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Part I
Secondary Hereditary and Acquired Cardiac Channelopathies and Sudden Cardiac Death

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1
Introduction to Part Three: Cardiac Remodeling

N.A. Mark Estes III

The concept of remodeling of the heart has evolved to include a broad spectrum of inherited or acquired electrical and structural myocardial alterations that are important in the pathogenesis of multiple cardiac arrhythmias [1–3]. The rhythm abnormalities associated with myocardial diseases discussed in this section include those encountered with hypertrophic cardiomyopathy (HCM), arrhythmogenic right ventricular dysplasia (ARVD), dilated cardiomyopathies (DCM), and skeletal myopathies. Functional electrophysiologic abnormalities frequently develop in association with structural and electrical remodeling with these myocardial diseases [1–3]. Also discussed in this section are functional cardiac alterations that can be inherited as channelopathies, such as the long QT syndromes (LQTS), catecholaminergic polymorphic ventricular tachycardia, Brugada Syndrome, and the early repolarization syndromes. These functional abnormalities of ion channels also can be acquired, as occurs with drug induced QT prolongation and resultant Torsades de Pointes. Brugada type pattern on the electrocardiogram represents another example of an acquired condition induced by pharmacologic agents. These and other abnormalities of electrical activation are considered as forms of electrical remodeling, typically but not always, without significant structural remodeling. Thus when considered from the perspective of cardiac remodeling, the chapters in the section have a common thematic basis. These alterations of electrical depolarization, repolarization and myocardial structure assume clinical significance as they are mechanistically linked to a spectrum of cardiac arrhythmias [1–3]. Understanding the fundamental cellular and molecular mechanisms of remodeling is a requisite to identify novel therapeutic targets for the prevention or treatment of cardiac arrhythmias with the cardiac conditions discussed in this section [1–3].

The remodeling processes associated with HCM, ARVD, dilated cardiomyopathies and cardiac dysfunction associated with skeletal myopathies, as noted in the subsequent chapters are complex and only partially understood [1–4]. Mechanism based prevention and therapy for these conditions, as well as the channelopathies discussed in the ensuing chapters, are not possible with current knowledge [1–4]. Nevertheless, the application of current techniques of cellular and molecular biology has improved the understanding of the multiple factors causing anatomic and functional remodeling [1–4]. It also has resulted in insights into the complex interaction of underlying anatomic or functional substrate abnormalities with triggering mechanisms that determine whether arrhythmias will arise in association with these clinical conditions [1–4].

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