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## Introduction to Part Two: Celebrating the Challenge of Cardiac Arrhythmias

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The field of cardiac arrhythmias has matured dramatically over the past 15 years, initially spurred on by the studies performed on the genetics of arrhythmia disorders. Once the genetic basis of disorders such as the long QT syndrome (LQTS) and Brugada syndrome (BrS) was discovered to occur due to disruption in ion channel encoding genes, basic electrophysiologists joined the fray, opening up a new area of study with significant clinical relevance. This book is a result of such bedside-to-bench collaboration.

Today, the genetic foundation of arrhythmia disorders is known to be based on disruption of a “final common pathway,” now called ion channelopathies. In addition to LQTS and BrS, catecholaminergic polymorphic ventricular tachycardia (CPVT), short QT syndrome (SQTS), atrial fibrillation (AF), and Wolf–Parkinson–White (WPW) syndrome have, at least in part, been defined genetically. Overlap disorders including arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C), dilated cardiomyo-

pathy (DCM), Andersen–Tawil syndrome, and Timothy syndrome are also defined, with ion channel disruption central to the clinical features or secondarily dysfunctional.

These new genetic and biophysical discoveries have opened up several new sciences as well. Drug discovery now requires analysis of potential effects on channel function. Pharmacogenomics is also the key to new approaches to medical therapy of “old” disorders. The concepts of gene-targeted therapies have grown out of this work. The pioneering work by Arthur Moss, Peter Schwartz, G. Michael Vincent, and others on the use of mexilitine and other similar therapies in LQTS, a gain-of-function persistent sodium channel leak treated with a sodium channel blocking agent, as well as the use of potassium supplementation in other forms of treatments to be devised have caused a reawakening to older therapies during studies of outcomes in patients treated with classic modalities such as  $\beta$  (beta) blockers and have resulted in newer approaches such as internal cardioverter defibrillator (ICD) implantation. In addition, fee-for-service genetic testing has finally become available for clinical use.

In the chapters that follow, an excellent group of assembled authors outline the current state of knowledge in the area of arrhythmias, as well as novel new concepts that are likely to define the future of diagnosis and treatment of these high-risk disorders. This has been an exciting field and, as demonstrated in this book by Gussak and Antzelevitch et al., the best is yet to come.

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