Introduction to the Arrhythmogenic Disorders of Genetic Origin Series

Peter J. Schwartz, MD

That young people with anatomically abnormal hearts, but even with normal hearts, could die suddenly has been reported for a long time. However, until 40 or 50 years ago, little was known and little was done. In my possibly skewed view, 2 events played a major role in catapulting interest and knowledge forward. The first was the report by Professor Anton Jervell and his colleague Fred Lange-Nielsen1 of a family affected by a recessive form of what became later referred to as the long-QT syndrome (LQTS); the second was the identification within 1 year by Mark Keating’s group2-5 of the first disease-causing genes for LQTS.

The Jervell and Lange-Nielsen report opened our eyes to what could lie behind sudden death in childhood under conditions of physical or emotional stress. Keating’s discoveries opened the era of molecular genetics in cardiology in an unprecedented way and, with the rapid connection made by Al George’s group between specific mutations and ionic control of ventricular repolarization,6 established a direct link and productive partnership among clinical cardiologists, molecular biologists, geneticists, and cellular electrophysiologists.

From LQTS, these joint ventures rapidly spread to other diseases, from cardiomyopathies to those that became known as channelopathies. New diseases emerged, from the Brugada syndrome to catecholaminergic polymorphic ventricular tachycardia to the short-QT syndrome. The progress in the genetic understanding of these diseases, with significant implications also for sudden death occurring in other more common conditions, has been mind-boggling. On the other hand, progress in clinical management has developed at different speeds in different circles. Academic groups, partly motivated by the implications of new findings for research grants and funding, have rather rapidly digested the new information. It is still often the case, all over the world, that general practitioners and even cardiologists in busy clinical practices outside academic hospitals are less attuned to suspect these diagnoses and to initiate the most appropriate management strategies. There are also curious geographic differences. In the northeastern part of Italy, close to Padua, whenever an athlete experiences syncope, every physician will suspect the presence of arrhythmogenic right ventricular cardiomyopathy. In every Norwegian town, whenever a deaf-mute child falls to the ground, the presence of the recessive form of LQTS will immediately be suspected. Unfortunately, however, in most cases the diagnoses are made late, or too late, and management often is not optimal.

The academic community, with a penchant for writing, has been producing a number of reviews dealing with these diseases, and some are excellent. Frequently, however, they try to deal with all the many different causes of sudden death in a single monograph; the authors are frequently, but not always, experts in one of these diseases and not in the others. The not uncommon result is a sort of catalog of what has been published without a direct message by the authors to the readers of what should or should not be done. With the present series of reviews on arrhythmogenic disorders of genetic origin, the Editors and I are trying a somewhat different route. I wanted to engage experts and groups with experience both in the clinic and in translational research who are well equipped to take basic science concepts into clinical application. Accordingly, I have asked individuals well recognized for their highly specific expertise not only to review current knowledge, but also to express their unabashed views on the most controversial aspects of the specific disease for which they have been invited to write, from mechanisms to clinical management. The results can never be fully uniform because some are more coy than others (I am not at all), but everyone has made a serious effort to express their personal views that, hopefully, will be appreciated by the readership.

Last but not least, the successful completion of this series was also made possible by the wonderful editorial collaboration of Kristina Sine to whom goes my personal acknowledgement and appreciation.

The series begins with the Brugada syndrome reviewed by Yuka Mizusawa and Arthur A. M. Wilde,7 long recognized as leading experts for this intriguing disease. It continues with LQTS that I review together with Lia Crotti, who for the past 10 years has been in charge of my LQTS clinic and molecular genetics laboratory.8 Then comes catecholaminergic polymorphic ventricular tachycardia reviewed by the French group headed by Antoine Leenhardt, who 35 years ago, with

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(Circ Arrhythm Electrophysiol. 2012;5:604-605.)

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Circ Arrhythm Electrophysiol is available at http://circep.ahajournals.org

DOI: 10.1161/CIRCEP.112.971846
our late friend Philippe Coumel, provided the first description of the disease. The experience of the Padua group led by Gaetano Thiene in all aspects of arrhythmogenic right ventricular cardiomyopathy, from morphology and genetics to clinical management, remains unsurpassed. The series ends with hypertrophic cardiomyopathy reviewed by Bill McKenna, a man whose name has been associated with this disease for as long as I can recall, and his associates.

The Editors and I trust that this series by Circulation: Arrhythmia and Electrophysiology will stimulate young cardiologists to actively contribute to the field, will be of interest to expert electrophysiologists, and will help clinical cardiologists to make early diagnoses and the right choices for the most appropriate management of these complex disorders. Especially, we hope that it will contribute to reducing the number of avoidable tragedies because most of these deaths by ventricular fibrillation can be prevented.

Disclosures
None.

References
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_Circ Arrhythm Electrophysiol_. 2012;5:604-605
doi: 10.1161/CIRCEP.112.971846

_Circulation: Arrhythmia and Electrophysiology_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-3149. Online ISSN: 1941-3084

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