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Series Editor: Juan Carlos Kaski

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Editors
Gheorghe-Andrei Dan, MD PhD, FESC, FAHA
Internal Medicine Clinic and Department of Cardiology
Colentina University Hospital
Bucharest
Romania

Department of Internal Medicine and Cardiology
Faculty of Medicine
University of Medicine and Pharmacy Carol Davila
Bucharest
Romania

Antoni Bayés de Luna, MD FESC, FACC
The Catalan Institute of Cardiovascular Sciences
Hospital Santa Creu i Sant Pau
Barcelona, Spain

John Camm, MD, FRCP(London), FRCP(Edin), FACC, FESC, FMedSci, FHRS, CStJ
Cardiovascular Sciences Research Centre
Division of Clinical Sciences
St George's University of London
London, United Kingdom

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Series Preface

Cardiovascular pharmacotherapy is of fundamental importance for the successful management of patients with cardiovascular diseases. Appropriate therapeutic decisions require a proper understanding of the disease and a thorough knowledge of the pharmacological agents available for clinical use. The issue is complicated by the existence of large numbers of agents with subtle differences in their mode of action and efficacy and the existence of national and international guidelines, which sometimes fail to deliver a clear-cut message. Aggressive marketing techniques from pharma industry; financial issues at local, regional, or national levels; and time constraints make it difficult for the practitioner to – at times – be absolutely certain as to whether drug selection is absolutely appropriate. The International Society of Cardiovascular Pharmacotherapy (ISCP) aims at supporting evidence-based, rational pharmacotherapy worldwide. This book series represents one of its vital educational tools. The books in this series aim at contributing independent, balanced, and sound information to help the busy practitioner to identify the appropriate pharmacological tools and to deliver rational therapies. Topics in the series include all major cardiovascular scenarios, and the books are edited and authored by experts in their fields. The books are intended for a wide range of healthcare professionals and particularly for younger consultants and physicians in training. All aspects of pharmacotherapy are tackled in the series in a concise and practical fashion. The books in this series provide a unique set of guidelines and examples that will prove valuable for patient management. They clearly articulate many of the dilemmas

clinicians face when working to deliver sound therapies to their patients. The series will most certainly be a useful reference for those seeking to deliver evidence-based, practical, and successful cardiovascular pharmacotherapy.

Juan Carlos Kaski, DSc, DM (Hons),
MD, FRCP, FESC, FACC, FAHA

Preface

> Atrial fibrillation has been the low man on the totem pole and so we're just trying to get more visibility about this particular disease and how dangerous this could be (Barry Manilow, American singer)

Atrial Fibrillation (AF) has a long history, but in many regards it remains a challenging *terra incognita*. In the oldest medical text written earlier than 400 B.C., the Chinese "Yellow Emperor's Inner Canon" (or better Huang Di Nei Jing Su Wen), we find the following quotation: "*When the pulse is irregular and tremulous and the beats occur at intervals, then the impulse of life fades; when the pulse is slender (smaller than feeble, but still perceptible, thin like a silk thread), then the impulse of life is small*." Much later, in the seventeenth century, it was William Harvey who rediscovered and described the arrhythmia in dogs, but the first electrical characterization was done during the mid-nineteenth century by the French Felix Alfred Vulpian who also baptized the disease "*fremissement fibrillaire*." Other nicknames were "*pulsus irregularis perpetuus*" (Hering) or even more suggestive "*delirium cordis*" (Cushny). Two Austrian doctors, Rothberger and Winterberg, identify "arrhythmia perpetua" as being atrial fibrillation. Shortly after the invention of the electrocardiogram by Einthoven, it was Sir Thomas Lewis to send to his Dutch friend the first tracing from a patient with atrial fibrillation. The mechanism of atrial fibrillation was a longtime subject of debate (and this debate still continues). After Sir Thomas Lewis and his pupil C. C. Iliescu stated that reentry is the main mechanism of AF and atrial flutter, it was Scherf to propose the automaticity as the main mechanism and the reentry as a consequence. Ten years later, Moe put the basis for the multi-

ple wavelets theory, and the reentrant theory dominated our understanding of the AF mechanism. Although initially considered mutually exclusive, we know now, after the discovery by Haissaguerre of the role of pulmonary foci in triggering AF, that reentry and focal triggering mechanisms are complementary in the mechanisms of AF initiation and perpetuation. After Bouilland discovered that digitalis may reduce the heart rate in AF (without abolishing irregularity) and Bootsma revealed by means of a computer modeling that the mechanism of random concealed conduction of atrial impulses within the AV node is responsible for an irregular ventricular rate, it was only during the late 1960's when Lown recommended cardioversion of AF. After 1980, the Framingham study emphasized the link between AF and stroke and on prognostic implications of this arrhythmia. We know now that AF became an epidemic disease because of aging population and because of increase in the prevalence of chronic heart disease and risk factors. By 2050 as many as 30 million may suffer from this disease. Overall, the mortality for patients with AF is double that in patients in sinus rhythm, and the divergence in the survival curves was noted from the moment of AF diagnosis. The most important contributor to the worse outcome in patients with AF is represented by the ischemic stroke, five times more prevalent in patients with AF and carrying the worst mortality and functional impact among all ischemic strokes. There are several accepted pharmacologic management strategies in AF: prevention of atrial remodeling or reverse remodeling (upstream therapy), systemic embolism prevention, and arrhythmia therapy (heart rate control and/or rhythm control including conversion to sinus rhythm and prevention of recurrences). The aim of therapy is to improve survival and quality of life, to improve symptoms, to reduce consequences (stroke, embolism, or heart failure), to reduce hospitalizations, to restore atrial function (reverse remodeling), and to minimize the adverse effects of medication. Despite huge progress made in understanding mechanisms responsible for initiation and perpetuation of atrial fibrillation and of complex pathophysiology of this complex disease, the actual treatment of AF is far

from being perfect. The same is true about the awareness of the disease impact among medical and patient milieu. Refinement in the research of the subtle molecular targets for newer and safer antiarrhythmics, new diagnostic tools for revealing global AF burden, establishing better targets of primary prophylaxis, and further progress in interventional therapy (ablation) will improve the management and the outcome of AF. Ablation of AF (through removal of triggers and substrate modification) improved substantially the management of AF. However, at least at this moment, AF ablation cannot be seen as a substitute of the pharmacologic therapy. Prevention of ischemic stroke in AF patients with oral anticoagulants represents a huge challenge, and the enormous amount of research is revealing new treatment opportunities at a dizzying pace. A new era has begun for the prevention of stroke, one of the most devastating complications of AF. While new classes of antithrombotic drugs for AF treatment are still in their infancy, recent research is revealing how these can be applied with optimal efficacy in clinical practice.

The present book, *Atrial Fibrillation Therapy*, includes practical information for readers on applying the guidelines developed as a result of the increased pharmacotherapeutic understanding. This book also aims to guide trainees, recertifying physicians, and practicing physicians in internal medicine, cardiology, emergency medicine, and clinical pharmacology to apply the new diagnostic tools for selecting the best treatment options for AF patients. The intention of the authors is more to discuss and emphasize the current aspects of AF therapy than to draw definite conclusions because, as was once said, "*drawing definite conclusions means that the author became too tired to think*."

Gheorghe-Andrei Dan
Antoni Bayés de Luna
John Camm

Contents

Contributors List

Cristian Baicus, MD, PhD Carol Davila University of Medicine and Pharmacy Bucharest, Bucharest, Romania

Department of Internal Medicine, Colentina University Hospital Bucharest, Bucharest, Romania

Gheorghe-Andrei Dan, MD, PhD, FESC, FAHA University of Medicine "Carol Davila", Bucharest, Romania

Internal Medicine Clinic, Cardiology Department, Colentina University Hospital, Bucharest, Romania

Dan Dobreanu, MD, PhD Department of Physiology and Institute of Cardiovascular Disease and Transplant, University of Medicine and Pharmacy of Tîrgu Mures, Tîrgu Mures, Romania

Yuri Gluzman Heart Institute, Edith Wolfson Medical Center, Holon, Israel

Sackler Faculty of Medicine, Tel-Aviv University, Tel Aviv, Israel

Antoni Bayés de Luna, MD, FESC, FACC Catalan Institute of Cardiovascular Sciences, Hospital Santa Creu i Sant Pau, Barcelona, Spain

Antoni Martínez-Rubio, MD, PhD, FESC, FACC Department of Cardiology, University Hospital of Sabadell, Sabadell, Barcelona, Spain