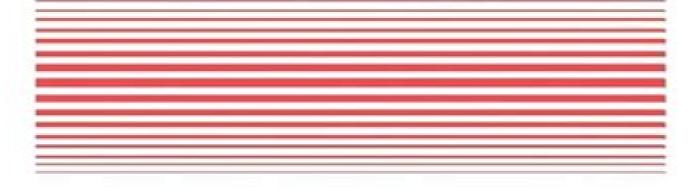
# THE EVALUATION OF NEW ANTIARRHYTHMIC DRUGS

edited by

J. Morganroth, E.N. Moore, L.S. Dreifus, and E.L. Michelson



Developments in Cardiovascular Medicine 11

# The Evaluation Of New Antiarrhythmic Drugs Developments In Cardiovascular Medicine

**C Cleary** 

### The Evaluation Of New Antiarrhythmic Drugs Developments In Cardiovascular Medicine:

The Evaluation of New Antiarrhythmic Drugs J. Morganroth, E. Neil Moore, L.S. Dreifus, E.L. Michelson, 2012-12-06 Thus there are now several chronic canine myocardial infarction ventricular tachyarrhythmia models which are available for the evaluation of new antiarrhythmic drugs Table I The available models fulfill many but not all of the requirements for an ideal chronic arrhythmia model Table 11 The sustained arrhythmias initiated in these models using programmed pacing presumably have the same localized reentrant mechanism that characterizes chronic human myocardial infarction and chronic coronary 26 artery disease However these models are not suitable for determining whether a new drug will abolish spontaneous ly occurring PVCs In addition these models are of unproven value in the study of acute spontaneously occurring sudden death although recently initiated provocative work may shed further light on this subject Most importantly the available models do seem well suited to the evaluation of new drugs intended for use in chronic coronary artery disease patients at risk for sustained reentrant ventricular tachycardia or VF Notably the results of preliminary electropharmacologic studies in these canine models parallel closely those findings reported in human patients with sustained life threatening ventricu lar tachyarrhythmias Table Ill Therefore increased use of these chronic models for new antiarrhythmic drug testing is strongly recommended TABLE II Ideal vs Available Chronic Canine Arrhythmia Models Ideal Available 1 a Arrhythmia mechanism comparable to Yes patients with chronic CAD Reentry b Pathophysiology similar e q atherogenic CAD No 2 Susceptible to a spontaneous PVCs No l No b spontaneous VT VF c inducible VT VF Yes 3 **Current Catalog National** Library of Medicine (U.S.), First multi year cumulation covers six years 1965 70 Surgical Options for the Treatment of Heart Failure R. Masters, 2007-12-14 Despite the significant decline in heart disease mortaht rates over the last 25 years heart failure has remained a significant problem We are now confronted with large numbers of terminally ill patients for whom conventional therapies for heart failure have been exhausted and for whom repeated hospital visits are necessary There now is a major thrust towards a management strategy which embraces a comprehensive approach including vigorous preventive measures and earlier surgical interventions This book outlines the major surgical options for the treatment of heart failure and brings together a very broad base of opinions with contributions from several outstanding individuals With the improved knowledge and techniques to control rejection transplantation has become the central pillar in the surgical management of this group of patients Unfortunately because of limited donor supply the teclmique cannot be applied to large numbers of patients A great deal of excitement however exists in the potential for xenotransplantation as a supplement to homotransplantation The use of cardiac assist devices has become a reality with several hundred LVADS and BiVADS implanted throughout the world and cardiac replacement with total artificial hearts continues to be used successfully as a bridge to transplantation We are on the thieshold of the broad application of assist devices to provide prolonged relief of heart failure and restore patients to an ambulatory home environment and hopefully return to the work force in significant

numbers Interventions in the Acute Phase of Myocardial Infarction J. Morganroth, E. Neil Moore, 2012-12-06 In the 1980 s a primary focus for intense cardiovascular research is in the treatment of patients with acute myocardial infarction Although the prevalence of this syndrome has been decreasing in the United States still over 1.5 million patients develop myocardial infarction per year There is about a 20% chance of a North American male developing myocardial in farction before the age of 65 The in hospital mortality still remains at ap proximately 10070 15070 and advances in pharmacologic and device therapy have allowed for the intensification of research in the treatment of patients with acute myocardial infarction The following manuscripts represent the collective efforts of academic in vestigators in the United States and abroad as well as members of the phar maceutical industry and the Food and Drug Administration to address the issues involved in interventions in the acute phase of myocardial infarction State of the art papers addressing important topics are followed by discus sion sections which have allowed participants to express their own viewpoints leading to a consensus opinion The first part of this Symposium addresses the models of experimental myocardial infarction followed by the important issue of how one defines myocardial infarction size The latter is extremely important to be certain that endpoints of therapeutic or device interventions are objective and reproducible A detailed description of the pharmacological interventions to reduce myocardial infarction size as well as newer devices to effect mechanical and electrical disorders provide an up to date Cardiac Arrhythmias, Pacing & Electrophysiology P.E. Vardas, 2012-12-06 Europace 97 summary of current opinion was held in Athens Greece on 8 11 June Leads were as usual an important topic with the earl 1997 in the city of classical civilisation and learning iest mention of the then new polyurethane leads Future Though now held in modem surroundings and meeting conferences elaborated on these basic topics while pro facilities the influence of the ancient city state was un gressively adding sensors and sensor function dual mistakable with the architecture and learning of antiquity chamber pacing and recognising the development of looming over the city by its influence over the intellectual clinical cardiac electrophysiology activities of the symposium The ancient magnificence of Clinical cardiac electrophysiology and compre the site was matched by the novelty of modem art and hension of arrhythmias has been largely a development science Europace is a European symposium begun in of the twentieth century With the description and 1979 and has occurred every second year since Con recording of the bundle of His depolarisation by direct sistent with its importance and continental reach the actual access and by catheter modem clinical investigation of symposium has moved to different cities throughout arrhythmias and cardiac electrophysiology began The Western Europe The first symposium was held in London disciplines of cardiac stimulation and of investigation of and subsequent symposia have been held in Torremolinos arrhythmias impulse formation and A V conduction Ostend Florence Istanbul and other cities Because of the were essentially separate for many Cardiovascular Nuclear Medicine and MRI Johan H. C. Reiber, Ernst E. van der Wall, 2012-12-06 In recent years vears there have been major advances in the fields of cardiovascular nuclear medicine and cardiac magnetic resonance imaging In

nuclear cardiology more adequate tomographic systems have been designed for routine cardiac use as well as new or improved quantitative analytic software packages both for planar and tomographic studies implemented on modern state of the art workstations In addition artificial intelligence techniques are being applied to these images in attempts to interpret the nuclear studies in a more objective and reproducible manner Various new radiotracers have been developed such as antimyosin labeled isonitriles metabolic compounds etc Furthermore alternative stress testing with dipyridamole and dobutamine has received much attention in clinical cardiac practice Magnetic resonance imaging is a relative newcomer in cardiology and has already shown its merits not only for anatomical information but increasingly for the functional aspects of cardiac performance This book covers almost every aspect of quantitative cardiovascular nuclear medicine and magnetic resonance imaging It will assist the nuclear medicine physician the radiologist the physicist image processing specialist and the clinical cardiologist in understanding the nuclear medicine techniques used in cardiovascular medicine and in increasing our knowledge of cardiac magnetic resonance imaging Maximal Myocardial Perfusion as a Measure of the Functional Significance of Coronary Artery Disease N.H. Pijls, 2012-12-06 Coronary flow reserve is a functional measure of stenosis severity reflecting the integrated effects of its geometry including percent stenosis absolute lumen area length and shape Its clinical application has been primarily qualitative in non invasive perfusion imaging Measurement of coronary flow reserve during routine coronary arteriography has been an elusive goal Transit time and indicator dilution techniques for assessing coronary flow reserve at cardiac catheterization are associated with marked variability compared to microspheres or flow meters thereby making their use questionable in comparison to the precision of good quantitative arteriography Coronary flow reserve measured by special Doppler catheters as an adjunct to coronary arteriography shows in man the value of this integrated functional measure of stenosis severity and the limitations of percent diameter narrowing as a measure of its physiologic significance However Doppler catheters require additional instrumentation that is not yet an integral part of coronary arteriography and provide measures of absolute coronary flow reserve only Relative maximum flow or relative flow reserve has been demon strated to be an important independent complimentary descriptor of stenosis severity independent of fluctuating hemodynamic conditions The method developed for DSA by Nico Pijls described in this book is the first approach for assessing relative coronary flow reserve as a part of routine coronary arteriography by DSA The theory and basic con cepts are well developed experimental validation thorough and clinical applications timely PTCA An Investigational Tool and a Non-Operative Treatment of Acute Ischemia P.W. Serruys, Rüdiger Simon, Kevin J. Beatt, 2012-12-06 Obstruction of coronary blood flow and the resultant consequences are the center stage pathophysiologic events in cardiology today The speculations of Jenner Burns Heberdin McKenzie Prinzmetal and many others had until now been left to observations of isolated tissue and intact animal experimentation Only with the advent of Gruentzig's technique which allowed us to work safely inside the coronary arteries are we able to observe the effects of coronary occlusion in living

conscious man PTCA provides not only a therapeutic modality for non operatively opening coronary obstructions but has also provided the best model for studying the effects of acute ischemia on the heart The procedure also lead the way to all other interventional cardiology developments including modern thrombolysis in the setting of acute myocardial infarction In his previous works Serruys has examined how PTCA can serve as a model for studying acute ischemia In this book he and his co authors discuss the effects of balloon induced ischemia on the electrocardiographic changes coronary blood flow dynamics cardiac muscle metabolism and left ventricular function as well as measures to counter these effects and provide for reperfusion in unstable angina and acute myocardial infarction Technology has expanded the eyes of the observer of these events The authors use many techniques including ECG recording from surface endocardium and intracoronary electrodes angiographic assessment of coronary flow pattern using digital techniques as well as doppler flow measurements biochemical assessment of metabolic products stimulated by ischemia and digital angiographic and echo doppler assessment of left ventricular function What's New in Cardiac Imaging? Ernst E. van der Wall, H. Sochor, A. Righetti, M.G. Niemever, 2012-12-06 Since the introduction of myocardial perfusion imaging and radionuclide angiography in the mid seventies cardiovascular nuclear medicine has undergone an explosive growth The use of nuclear cardiology techniques has become one of the cornerstones of the noninvasive assessment of coronary artery disease In the past 15 years major steps have been made from visual analysis to quantitative analysis from planar imaging to tomographic imaging from detection of disease to prognosis and from separate evaluations of perfusion metabolism and function to an integrated assessment of myocardial viability. In recent years many more advances have been made in cardiovascular nuclear imaging such as the development of new imaging agents reevaluation of existing procedures and new clinical applications. This book describes the most recent developments in nuclear cardiology and also addresses new contrast agents in MRI What s New in Cardiac Imaging will assist the clinical cardiologist the cardiology fellow the nuclear medicine physician and the radiologist in understanding the most recent achievements in clinical cardiovascular nuclear imaging Lifelong Management of **Hypertension** H. Mitchell Perry Jr., 2012-12-06 In the thirty years since the advent of effective pharmacologic treatment for hypertension the world of the hypertensive has been transformed beyond recognition. The first change involved only malignant hypertensives with enough residual renal parenchyma to survive Such a hypertensive could trade inevitable renal failure unless an intracerebral bleed occurred first for a rigid regimen which prevented his blood pressure from destroying him but which was asso ciated with nearly intolerable side effects Over the next 20 years increasing numbers of patients with hypertension of decreasing severity were treated with drugs that had fewer and fewer side effects In 1970 with the medical world finally ready to accept the concept the well known Veterans Administration Study demonstrated that morbidity and mortality could be diminished in mode rately hypertensive patients by antihypertensive therapy that had minimal side effects As a result there has been a major attempt to bring everyone with elevated blood pressure under lifelong pharmacologic

control It is difficult however to know what levels ofblood pressure deserve treatment many who when therapy first became available would not have even been considered hypertensive are now candidates for treatment The lower the pressure the larger the potential population to be treated but the smaller the individual risk and hence the smaller the possible benefit The point where decades of diminished quaiity of life from treatment begins to outweigh a possible late life complication is yet to be de termined

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