THE EVALUATION OF NEW ANTIARRHYTHMIC DRUGS

I Morganioth E N Moore I

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

Developments in Cardiovascular Medicine

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The Evaluation Of New Antiarrhythmic Drugs Developments In Cardiovascular Medicine

J. Rick Turner, Dilip R. Karnad, Snehal Kothari

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 Cardiac Arrhythmias, Pacing & Electrophysiology P.E. Vardas,2012-12-06 Europace 97 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 years

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 summary of current opinion Coronary Angioplasty: A Controlled Model for Ischemia P.W. Serruys, G.T. Meester, 2012-12-06 Since the introduction of coronary angioplasty in 1977 this procedure has gained a steadily increasing

position in the treatment of coronary artery obstraction From the available evidence it can be estimated that this thera peutic tool will get even more additional momentum of many ten thousands of patients to be treated in the next few years due to a growing fraction of patients who are candidates for this intervention Information about the indications benefits and risks of coronary angioplasty is accumulating rapidly in addition to publications about refinements of the technique itself Recently a number of investigators have realized that coronary angioplasty is not only a therapeutic tool but can during the procedure be used as a source of diagnostic information When the catheter is placed in a coronary artery obstruction inflation of the balloon produces transient myocardial ischemia Before during and after this period of severe ischemia studies of the perfor mance of the myocardium at risk can be carried out The fact that therapeutic coronary angioplasty is carried out in a cardiac catheterization laboratory which is by definition optimally equipped for the measurement of hemodynamic parameters has probably also contributed to the effectuation of these investigations The combination of hemodynamic and biochemical parameters with morphological information from the coronary angiogram can be utilized for the quantification of myocardial involvement and the success of coronary dilatation with angioplasty Studies of interactions with pharmacological substances Cardiovascular Safety in Drug Development and Therapeutic Use J. Rick Turner, Dilip R. are also feasible and informative Karnad, Snehal Kothari, 2016-07-28 At a time when the field of cardiac safety is going through important changes this unique book provides the rationale for and cutting edge explanations of new regulatory landscapes that will likely govern cardiac safety assessments globally for the foreseeable future Exposure response modeling is already being accepted by regulatory agencies in lieu of the traditional Thorough QT QTc Study and the Comprehensive in vitro Proarrhythmia Assay initiative is well under way Developments in the field of cardiovascular safety are also described and discussed in the book These include the search for more efficient ways to exonerate new drugs for type 2 diabetes from an unacceptable cardiovascular liability how best to address off target blood pressure increases induced by noncardiovascular drugs and the continued evolution of the discipline of Cardio oncology a resource that will likely serve as a standard for years to come Dr Jonathan Seltzer Therapeutic Innovation 51 2 180 I have no hesitation in recommending this book as a valuable reference source Dr Rashmi Shah Journal for Clinical Studies 2017 9 1 62 63 <u>Cardiac Drug Development Guide</u> Michael K. Pugsley, 2008-02-06 Cardiac Drug Development Guide outlines in detail the therapeutics of cardiac medicine currently at the cutting edge of scientific research and development around the world This volume integrates basic and clinical cardiac pharmacology by c bining for the first time both classical and molecular aspects of therapeutic drug development The chapters comprise a broad spectrum of therapeutic areas and hence involve a comprehensive discussion of molecular biochemical and electrophy ological concepts based on years of in vitro as well as in vivo pharmacological st ies In addition the latter part of the book includes comprehensive clinical cardiac chapters that describe important topics in molecular medicine These chapters also discuss current clinical therapeutic trends in medicine and provide an evaluation of the efficacy of novel drugs in these areas

Cardiac Drug Development Guide has many distinctive and outstanding features that set it apart from other cardiac pharmacology books This book introduces topics in an easily understandable format for researchers in many varying disciplines by integrating and thereby simplifying concepts not usually discussed across a broad range of cardiac disciplines and in a highly technical field Each chapter not only introduces and describes the physiology pharmacology and pathophysiology of the disease but also overviews the clinical implications of drug development what stages these areas are currently in and also reviews some of the methodologies involved in drug discovery and development As a result this book provides a comprehensive overview of the most advanced procedures in cardiac pharmacology today

Ischemia-reperfusion in cardiac surgery Hans Michael Piper, C.J. Preusse, 2012-12-06 In open heart surgery protection of the myocardium against injury by ischemia reperfusion is an issue of utmost clinical interest. The knowledge on the causal mechanisms of myocardial injury in ischemia reperfusion has greatly progressed in recent years both to clinical and experimental research This book provides a critical and comprehensive overview on the current discussion of myocardial protection in cardiac experimental research and surgery Leading groups from Europe the U S and Japan have contributed reviews of their special fields On the basic science side major topics discussed are the mechanisms of stunning and lethal reperfusion injury the role of the endothelium and leukocyte activation in postischemic myocardial dysfunction and the differences between the adult and neonatal myocardium On the clinical side the major concepts and procedures for cardioplegic myocardial protection their rationales application and respective merits are discussed In a third part of the book possible approaches for the monitoring of myocardial injury during ischemia and reperfusion are evaluated with particular attention to their intraoperative use This book brings together the scientific discussions on ischemia reperfusion in experimental cardiology and cardiac surgery a task needed for a long time It is of general interest for clinicians as well as research workers and students in the cardiac field Drug Discovery Toxicology Yvonne Will, J. Eric McDuffie, Andrew J. Olaharski, Brandon D. Jeffy, 2016-04-18 As a guide for pharmaceutical professionals to the issues and practices of drug discovery toxicology this book integrates and reviews the strategy and application of tools and methods at each step of the drug discovery process Guides researchers as to what drug safety experiments are both practical and useful Covers a variety of key topics safety lead optimization in vitro in vivo translation organ toxicology ADME animal models biomarkers and omics tools Describes what experiments are possible and useful and offers a view into the future indicating key areas to watch for new predictive methods Features contributions from firsthand industry experience giving readers insight into the strategy and execution of predictive toxicology practices Cardiovascular Nuclear Medicine and MRI Johan H. C. Reiber, Ernst E. van der Wall, 2012-12-06 In recent years 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 Index ,1987 Integrated Cardiac Safety J. Rick Turner, Todd A. Durham, 2008-11-26 The serious nature of cardiovascular adverse drug reactions occurring in patients makes assessment of a drug s cardiac safety profile a high priority during both development and post approval monitoring Integrated Cardiac Safety provides necessary guidance and methodology for professionals assessing cardiac safety of drugs throughout all stages of the drug s life from discovery and development through postmarketing research This self contained reader friendly text is valuable to professionals in the pharmaceutical biotechnology and CRO industries pharmacologists toxicologists government officials and students Index National Institutes of Health (U.S.). Division of Research Grants, 1973 Molecular Physiology and Pharmacology of Cardiac Ion Channels and Transporters M. Morad, S. Ebashi, W. Trautwein, Yoshihisa Kurachi, 2012-12-06 Knowledge of cardiac ion channels and transporters has advanced remarkably in the last two decades with the development of patch clamp and molecular biological techniques This textbook offers a comprehensive overview of structures and functions of ion channels and transporters in the heart Readers are first introduced to the molecular biology and electrophysiology of all the important ion channels After discussing their developmental changes the pharmacology and pathophysiology of clinically relevant ion channels are reviewed Molecular aspects of the cardiac excitation contraction coupling and intracellular Ca2 regulation by ion transporters are also described The book will be useful to electrophysiologists cardiac physiologists and pharmacologists and molecular biologists interested in ion channels at all levels For research specialists the book will provide a perspective of the field The book can be used as a reference source for working scientists in the fields of ion channels biophysics cardiac electrophysiology and pharmacology It is aimed at graduate and medical students designed for Animal models in cardiovascular research D.R. Gross, 2013-04-17 use as a textbook for graduate and medical courses Interest in the humane and scientifically justifiable use of research animals has intensified since the publication of the first edition of this textbook This completely revised and updated text provides information essential to any researcher interested in using animal models for cardiovascular research or any research which requires normal cardiovascular function The

format and presentation have been changed to make the text more easy to read and use An introductory chapter offers general principles of animal selection pre and post operative care preanesthesia chemical restraint analgesia and the recognition of pain The number of references cited has been almost doubled over the previous text and the chapter tabulating normal cardiovascular parameters from intact awake animals of those species commonly used in research has been greatly expanded Other chapters providing comprehensive data on the cardiovascular effects of opioids tranquilizers anesthetic agents and other drugs commonly used in cardiovascular research have been expanded with special emphasis on species variability to drug effects The chapters on both naturally occurring and iatrogenic models of cardiovascular disease have also been expanded and updated XIII Mediterranean Conference on Medical and Biological Engineering and Computing 2013 Laura M. Roa Romero, 2013-10-01 The general theme of MEDICON 2013 is Research and Development of Technology for Sustainable Healthcare This decade is being characterized by the appearance and use of emergent technologies under development This situation has produced a tremendous impact on Medicine and Biology from which it is expected an unparalleled evolution in these disciplines towards novel concept and practices The consequence will be a significant improvement in health care and well fare i e the shift from a reactive medicine to a preventive medicine This shift implies that the citizen will play an important role in the healthcare delivery process what requires a comprehensive and personalized assistance In this context society will meet emerging media incorporated to all objects capable of providing a seamless adaptive anticipatory unobtrusive and pervasive assistance The challenge will be to remove current barriers related to the lack of knowledge required to produce new opportunities for all the society while new paradigms are created for this inclusive society to be socially and economically sustainable and respectful with the environment In this way these proceedings focus on the convergence of biomedical engineering topics ranging from formalized theory through experimental science and technological development to practical clinical applications Physiology and Pathophysiology of the Heart Nicholas Sperelakis, 2013-06-29 could go on for several pages Thus the book edited This book emphasizes the fundamental functional aspects of cardiology Within the last thirty years by Sperelakis IS a potent reminder of the almost for the rift between clinical and investigative cardiology gotten fact that cardiology has twO sites inextrica has widened because of the overwhelming devel bly related opment of new clinical procedures both diagnostic The book deals with subjects in which Dr Sper and therapeutic Almost forgotten is the fact that elakis has pioneered ultrastructure of heart muscle we owe most of the clinical advances to theoretical electrophysiology cardiac contractility and ion ex and experimental observations I need not remind change An extension of these subjects is the chapter the reader of the work of Carrel who performed the dealing with fundamental topics of the coronary cir first experimental coronary bypass in 1902 or the culation work of the brothers Curie in 1880 both physicists This book is indeed a timely reminder of the im who discovered piezoelectricity the keystone in ech portance of the fundamental aspects of cardiology ogradiography of the works of Langley who intro Emphasis on clinical

aspects of cardiology alone will duced the receptors concept of Ahlquist in 1946 result in a sterile and unproductive future for a field who first differentiated between alpha and beta re that has made such stunning advances during the ceptors of Fleckenstein a physiologist who pi last thirty years to the benefit of millions of people Cardiovascular Disease in the Elderly Franz H. Messerli, 2013-04-17 After a certain age one is elderly aged venerable and patriarchal Or just plain old When I became old I did not know it I do know it now because of a syndrome of which I had previously been unaware It is quite simple when it hurts it works when it doesn t hurt it doesn t work Writing about the old is a preoccupation of the young and that is as it should be because it is the young who must carry the burden of the old I don't know the average age of the contributors to Franz Messerli's book but I would guess it to be less than 50 which to me is positively pubescent For many years I thought geriatric medicine was nonsense and today I still think some of it is What changes with age are principally the attitude and purposes of the individual and how much energy he or she has to carry out those purposes It isn t so much that the goals ambitions and desire to alter or improve the world disappear they just diminish along with what it takes to accomplish them Which brings me to one particular aspect of aging that is the cardiovascular system The first evidence of the cardiovascular system's aging is the failure of the heart to respond to the demands placed on it What's New in Cardiac Imaging? Ernst E. van der Wall, H. Sochor, A. Righetti, M.G. Niemeyer, 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

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