REVIEWS IN



CARDIOVASCULAR MEDICINE®

accepted for inclusion in MEDLINE and PUBMED

Volume 15, No. 1 • 2014 • Medical Editors: Norman E. Lepor, MD • Peter A. McCullough, MD, MPH

In This Issue

Review Articles

- Use of Microsomal Triglyceride Transfer Protein Inhibitors in Patients With Homozygous Familial Hypercholesterolemia: Translating Clinical Trial Experience Into Clinical Practice Peter P. Toth, MD, PhD, Prediman K. Shah, MD, Michael J. Wilkinson, MD, Michael H. Davidson, MD, Peter A. McCullough, MD, MPH
- Acute and Chronic Cardiovascular Effects of Hyperkalemia: New Insights Into Prevention and Clinical Management Peter A. McCullough, MD, MPH, Thomas M. Beaver, MD, MPH, Elliott Bennett-Guerrero, MD, Michael Emmett, MD, Gregg C. Fonarow, MD, Abhinav Goyal, MD, MHS, Charles A. Herzog, MD, Mikhail Kosiborod, MD, Biff F. Palmer, MD

 Reassessing the Importance of Complete Versus Incomplete Coronary Revascularization Dean I. Kereiakes, MD

 Emerging Treatment Options for Refractory Angina Pectoris: Ranolazine, Shock Wave Treatment, and Cell-Based Therapies Marco Gennari, MD, Elisa Gambini, PhD. Beatrice Bassetti, MS, Maurizio Capogrossi, MD, Giulio Pompilio, MD, PhD

 Prevention and Treatment of No-Reflow Phenomenon by Targeting the Coronary Microcirculation Attila Feher, MD, PhD, Stephen Y. Chen, MD, Zsolt Bagi, MD, PhD, Vishal Arora, MD

L-carnitine for the Treatment of Acute **Myocardial Infarction**

James J. DiNicolantonio, PharmD, Asfandyar K. Niazi, Mark F. McCarty, BA, Carl J. Lavie, MD, Evangelos Liberopoulos, MD, FASA, FRSH, James H. O'Keefe, MD

CA ACC News

Case Review

Literature Reviews





www.medreviews.com for downloadable articles

Medical Editors



NORMAN E LEPOR, MD, FACC, FAHA, FSCAI
Known for his interest in graduate medical education and investigations in the field of
interventional cardiology, Dr. Lepor is cofounder of *Reviews in Cardiovascular Medicine*. He is Clinical Professor of Medicine at The David Geffen School of Medicine at UCLA and an attending interventional cardiologist at Cedars-Sinai Heart Institute. He has directed investigations into the study of interventions in acute myocardial infarction, treatment and prevention of coronary artery disease, contrast nephropathy, oral antiplatelet and anticoagulant agents, atrial arrhythmias, and appropriate use of cardiovascular imaging. Dr. Lepor has lectured widely on such topics as the utility of advanced cardiovascular imaging technologies and the prevention and treatment of cardiovascular disease



PETER A McCullough, MD, MPH, FACC, FAHA, FACP, FCCP, FNKF

After receiving a bachelor's degree from Baylor University, Dr. McCullough completed his medical degree as an Alpha Omega Alpha graduate from the University of Texas Southwestern Medical School in Dallas. He went on to complete his internal medicine residency at the University of Washington in Seattle, cardiology fellowship including service as Chief Fellow at William Beaumont Hospital, and master's degree in public

health at the University of Michigan. Dr. McCullough directs cardiovascular education and research for the Baylor Health Care System and is a Vice Chief of Medicine at Baylor University Medical Center in Dallas, TX. He is an internationally recognized authority on the role of chronic kidney disease as a cardiovascular risk state with over 1000 publications. Dr. McCullough has won numerous awards including in the Simon Dack Award from the American College of Cardiology for outstanding scholarship and the International Vicenza Award for Critical Care Nephrology for his contributions and dedication to the emerging problem of cardiorenal syndromes.

Associate Editors



GREGG C FONAROW, MD, FACC, FAHA

An eminent specialist in heart failure management, preventive cardiology, quality of care, and outcomes research, Dr. Fonarow holds the Eliot Corday Chair in Cardiovascular Medicine and Science. He is a Professor of Medicine in the Division of Cardiology at The David Geffen School of Medicine at UCLA, Director of the Ahmanson-UCLA Cardiomyopathy Center, and Co-Chief of the UCLA Division of Cardiology.



GREGG W STONE, MD, FACC, FSCAI

Dr. Stone is Professor of Medicine at Columbia University, Director of Cardiovascular Research and Education at the Center for Interventional Vascular Therapies at Columbia University Medical Center, and Co-Director of Medical Research and Education at the Cardiovascular Research Foundation in New York, NY. Dr. Stone has served as the lead principal investigator for more than 60 national and international multicenter random-ized trials, and is the Co-Director of Transcatheter Cardiovascular Therapeutics, the world's largest symposium devoted to interventional cardiology and vascular medicine.

CA ACC Honorary Editor



JOHN B. GORDON, MD, FACC

John Gordon is in private practice and a partner at the San Diego Cardiac Center Medi-cal Group, which he joined in 1989. He is a senior interventional cardiologist at Sharp Memorial Hospital where he launched the peripheral interventions program in the Cardiac Catheterization Laboratory, and the Sharp Memorial STEMI program. He has served as Chief of the Cardiology Subsection and Vice Chair of the Internal Medicine Supervisory Committee at Sharp Memorial Hospital. He has served as President of the American Heart Association, San Diego Chapter.

Dr. Gordon's current research interests include coronary and peripheral interventions, and the late sequelae of Kawasaki Disease in adults. He is Director of the Annual Maui Cardiovascular Symposium, now in its tenth year, which is sponsored by the CA ACC.

Contributing Editors



WILLIAM T ABRAHAM, MD, FACP, FACCDr. Abraham is Professor of Internal Medicine and Chief of the Division of Cardiovascular Medicine at The Ohio State University in Columbus, OH. He earned his medical degree from Harvard University and completed postgraduate training at the University of Colo rado. Dr. Abraham's clinical activities and research interests focus on heart failure. He has received grants from the National Institutes of Health and participated in more than 100 multicenter clinical drug and device trials. In addition to authoring more than 600 original works, Dr. Abraham has co-edited a leading textbook, Heart Failure: A Practica.

Approach to Treatment.



DEAN J KEREIAKES, MD, FACC, FSCAI

An active clinical and scientific investigator, Dr. Kereiakes is Medical Director of The Christ Hospital Heart and Vascular Center and The Lindner Center for Research and Education; and Professor of Clinical Medicine at Ohio State University. Dr. Kereiakes serves on the scientific advisory boards for multiple medical device companies and on the editorial boards of seven major cardiovascular journals. He maintains an active practice in interventional cardiology.



CHRISTOPHER P CANNON, MD, FACC
Dr. Cannon is a Professor of Medicine at Harvard Medical School, and a He is a senior investigator in the Thrombolysis In Myocardial Infarction (TIMI) Study Group in the Cardiovascular Division at Brigham and Women's Hospital in Boston. He has or is leading 14 international trials in the field of acute coronary syndromes and prevention. He is Editor-in-Chief of the journal *Critical Pathways in Cardiology* and Deputy Editor-in-Chief of Clinical Cardiology, as well as Editor-in-Chief of Cardiosource Science and Quality, the American College of Cardiology's Web site (www.cardiosource.org).



MIKHAIL KOSIBOROD, MD, FACC, FAHA
Dr. Kosiborod is a cardiologist and a clinical scholar at Saint Luke's Mid America Heart
Institute, and Associate Professor of Medicine at the University of Missouri-Kansas City.
His main research interests include diabetes and glucose management in patients with acute coronary syndromes. He has authored and co-authored many peer-reviewed publi-cations and abstracts, including several scientific statements and position documents on in-hospital and long-term glucose control. Dr. Kosiborod is a recipient of several American Heart Association research awards. He is actively involved in the work of many commit-tees for the American College of Cardiology and American Heart Association.



MICHAEL H DAVIDSON, MD, FACC, FACP

Dr. Davidson is Clinical Professor and Director of Preventive Cardiology at the University of Chicago. He also serves as Chief Medical Officer for Omthera Pharmaceuticals. Dr. Davidson's clinical research background encompasses both pharmaceutical and nutritional clinical trials. His extensive research on statins, novel lipid-lowering drugs, and nonpharmacologic risk factor reduction has established him as a key opinion leader in this area. Dr. Davidson has coordinated more than 1000 clinical trials in areas of preventive cardiology, published more than 250 articles for leading medical journals, and has written three books on lipidology.



GERALD M POHOST, MD, FACC, FAHA

Dr. Pohost is known worldwide for his contributions to cardiovascular imaging. His pioneering efforts led to the development of thallium for clinical myocardial imaging and the field of cardiovascular magnetic resonance imaging. His leadership led to the establishment of the (International) Society for Magnetic Resonance in Medicine and the Society for Cardiovascular Magnetic Resonance. He is a Professor at the Keck School of Medicine and the Viterbi School of Engineering at the University of Southern California, and a Professor at the Loma Linda University School of Medicine. Dr. Pohost has been working on developing and applying approaches for diagnostic image analysis in China and has received professorships at three universities in China.



PRAKASH C DEEDWANIA, MD, FACC, FAHA, FACP, FCCP

Dr. Deedwania is one of the most recognizable figures in the fields of hypertension, heart Tailure, lipid disorders, ischemic heart disease, rhythm disorders and preventive cardiology. He is Professor of Medicine at the University of California -San Francisco (UCSF) School of Medicine and is Chief of the Cardiology Division for the Veterans Administration Central California Health Care System. Dr. Deedwania is also Director of Cardiovascular Research for the UCSF Fresno -Central San Joaquin Valley Medical Education Program and Clinical Professor of Medicine at Stanford University in Palo Alto, CA. He has authored numerous landmark clinical trials and has authored or co-authored more than 350 publications.



MATTHEW J PRICE, MD, FACC, FSCAI

Dr. Price is an interventional cardiologist and currently serves as Director of the Cardiac Catheterization Laboratory in the Cardiovascular Division of Scripps Clinic and Assistant Professor at the Scripps Translational Science Institute. Dr. Price has published numerous papers and chapters on high-risk percutaneous coronary intervention (PCI), drug-eluting stents, and the impact of antiplatelet therapy on outcomes after stent implantation. He is involved in the leadership of several trials examining the safety and efficacy of antiplatelet therapy during and after PCI.



ALICE K JACOBS, MD, FACC, FAHA
Dr. Jacobs is a Professor of Medicine at Boston University School of Medicine and the Director of Invasive Cardiology Services at Boston Medical Center. Her major research interest is in coronary revascularization strategies. Dr. Jacobs is the principal investigator of the MASS COMM trial, which is evaluating the safety and efficacy of coronary angioplasty performed in community hospitals without on-site cardiac. surgery in Massachusetts. She is also interested in cardiovascular disease in women and the sex-based differences in the epidemiology, diagnosis, treatment and prognosis of ischemic heart disease.



Prediman K Shah, MD, FACC, FACP, FCCP

Dr. Shah is Director of the Division of Cardiology and Director of the Oppenheimer Atherosclerosis Research Center at Cedars-Sinai Medical Center in Los Angeles, where he holds the Shapell and Webb Family Chair in Clinical Cardiology at Cedars-Sinai. He is also Professor of Medicine at the David Geffen School of Medicine at the University of California, Los Angeles. Dr. Shah is currently leading several studies that focus on heart disease prevention and treatment. In March, 2012, Dr. Shah received the Distinguished Scientific Achievement award (basic science category) from the American College of Cardiology. He has edited three books on heart disease and published more than 600 scientific papers, reviews, book chapters and abstracts.



KAROL E WATSON, MD, PHD, FACC

Dr. Watson is a full-time cardiologist at The David Geffen School of Medicine at UCLA. Currently, Dr. Watson is director of the Women's Cardiovascular Center at UCLA, Co-Director of the UCLA Program in Preventative Cardiology, and director for the Center for Cholesterol and Hypertension Management. A Principal Investigator for several large National Institutes of Health studies, Dr. Watson's more than 80 publications and presentations have addressed many subjects including prevention of heart disease, vascu lar calcification, hormone replacement therapy, the metabolic syndrome, hypertension, hypercholesterolemia, and cardiovascular disease in women and African Americans.





The Instant-Access Resource Center for Today's Practicing Cardiologist

www.medreviews.com provides busy cardiologists with access to a variety of useful tools in one convenient online resource center.

Whether you're looking to keep up to date with the newest trends, further your education, or read articles by prominent experts, www.medreviews.com is the complete Web site for all your needs.

CIVIE ARTICLES
FULL-TEXT ARTICLES
DOWNLOADS
EVENTS AND SEMMARS

accepted for inclusion in MEDLINE and PUBMED

MedReviews®, LLC • 494 Eighth Avenue, Suite 1000 New York, NY 10001 Tel: 212-201-6860 • Fax: 212-201-6850 © 2014 MedReviews®, LLC. All rights reserved.

Reviews in Cardiovascular Medicine is a registered trademark of MedReviews®, LLC.

It was almost fourteen years ago, in Summer 2000, that the first issue of *Reviews in Cardiovascular Medicine* was published. Topics covered in the first few issues included the implications of radiocontrast nephropathy, looking beyond the Framingham risk model, advances in heart failure and acute coronary syndrome management, and, yes, way before others caught on, women's cardiovascular health. In those early years, *Reviews in Cardiovascular Medicine* distinguished itself by providing content that was not just timely but also comprehensive, scholarly, and brought to life with incredible graphics that made the articles more impactful and easier to understand. We are happy to see that over the years we have been emulated by many of our sister journals.

Before I describe the content in this issue, I cannot resist the temptation to use this opportunity to entice the community of cardiologists to become more involved in the political process. The changes we have witnessed over the past several years have been a mixed bag: some positive, most negative. On the positive side, there is a focus on providing health care using more efficient models of delivery. There are only so many dollars available for health care and with Baby Boomers entering the phase in their lives with increasing health resource utilization, there will be fewer dollars available per person. On the negative side, the conversations on health care reform that take place in Washington DC, state capitals, health care policy foundations, and by third-party payors seem to have little to do with quality and more to do with cost. The biggest delusion is that dollars will be saved with health care reform. I predict that, instead of net savings, we will witness a huge shift of dollars and resources from the physicians providing the care to the growing medical bureaucracy. Why would the best and brightest work hard to excel in college, incur a huge debt to attend medical school, and spend up to 10 years in postgraduate medical education when they will no longer be empowered to determine how to care for patients? Where the biggest factor determining job security becomes how little is spent per patient and not quality of the care provided to them? I urge all of my colleagues to become more active in our medical societies and their associated political action committees (ie, American College of Cardiology Political Action Committee). Without your engagement, you become part of the problem.

In this issue, Dr. Toth and colleagues discuss the use of use lomitapide, a novel microsomal triglyceride transfer protein inhibitor, in patients with homozygous familial hypercholesterolemia. Lomitapide does not depend on the ability to upregulate LDL receptors on the surface of hepatocytes and reduces production of apolipoprotein B-containing lipoproteins. Dr. McCullough and associates discuss an old problem with a new solution, and review the acute and chronic cardiovascular effects of hyperkalemia. In addition, the group describes an innovation for treating hyperkalemia using ZS-9, a first-in-class orally administered selective potassium ion trap that is a non-systemically absorbed inorganic compound. It has 10 times the binding capacity of sodium polystyrene sulfonate and is 100 times more selective.

Dean Kerieakes, MD, a giant in the field of interventional cardiology, reassesses the importance of complete versus incomplete coronary revascularization in patients with multi-vessel obstructive disease. This article provides guidance on how to approach this clinical scenario commonly faced in the cardiac catheterization laboratory. Dr. Pompilio and colleagues review emergent options for the treatment of refractory angina pectoris using ranolazine, shock wave treatment, and cell based therapies. With limited options available to these patients, we look to regenerative medicine and cell-based therapies as possibilities that may benefit the patients who suffer significant disability. Dr. Fehrer and colleagues report on the prevention and treatment of the no-reflow phenomenon in the coronary circulation, and Dr. DiNicolantonio and colleagues review the data regarding the therapeutic effectiveness of L-carnitine.

From the California Chapter of the American College of Cardiology, Dr. Gordon and Margo Minissian report on the recent ACC Board of Governors meeting and views on a team-based approach to care. Finally, there is an interesting case review on left main coronary artery perforation during PCI in a patient with noninfectious aortitis and two literature reviews.

Enjoy the issue!

We would like to acknowledge the efforts of our external reviewers who have assisted in the careful evaluation of original papers submitted for consideration in 2013. We receive many high quality manuscripts; unfortunately, we can only accept a fraction of them for publication each year. Our academic peer reviewers are a valued resource and we are indebted to their skill and expertise.

A Afzal T Larsen M Diloreto K Akrawinthawong A Falcone C Lavie S Ali P Fazel M Nasser F Al-Qa Hanna A Gopal G Patankar H Assad R Gorges C Piyaskulkaew D Haines JS Bhuller K Rajmani S Hussain R Shah H Chugtai A Daraghmeh J Kachner S Steigerwalt S Darda O Kashlan A Wladis G Degheim Y Khouri

CARDIOVASCULAR MEDICINE®

Medical Editors

Norman E. Lepor, MD, FACC, FAHA, FSCAI

The David Geffen School of Medicine at UCLA and Cedars-Sinai Medical Center, Los Angeles, CA

Peter A. McCullough, MD, MPH, FACC, FAHA, FACP, FCCP, FNKF

Baylor University Medical Center, Baylor Heart and Vascular Institute, Baylor Jack and Jane Hamilton Heart and Vascular Hospital, Dallas, TX, The Heart Hospital, Plano, TX

Associate Editors

Gregg C. Fonarow, MD, FACC, FAHA

The David Geffen School of Medicine at UCLA, Los Angeles, CA

Gregg W. Stone, MD, FACC, FSCAI

Columbia University Medical Center, New York, NY

CA ACC Honorary Editor

John B. Gordon, MD, FACC

San Diego Cardiac Center Medical Group, San Diego, CA

Contributing Editors

William T. Abraham, MD, FACP, FACC

Ohio State University College of Medicine, Columbus, OH

Christopher P. Cannon, MD, FACC

Brigham and Women's Hospital, Boston, MA

Michael H. Davidson, MD, FACC, FACP

University of Chicago, Chicago, IL

Prakash C. Deedwania, MD, FACC, FAHA, FALP, FCCP

Veterans Administration Central California Health

Care System/UCSF Program, Fresno, CA, and Stanford University, Palo Alto, CA

Alice K. Jacobs, MD, FACC, FAHA

Boston University School of Medicine and Boston University Medical Center, Boston, MA

Dean J. Kereiakes, MD, FACC, FSCAI

The Christ Hospital Heart and Vascular Center and

The Lindner Center for Research and Education, Cincinnati, OH

Mikhail Kosiborod, MD, FACC, FAHA

Saint Luke's Mid America Heart and Vascular Institute and University of Missouri-Kansas City, Kansas City, MO

Gerald M. Pohost, MD, FACC, FAHA

Keck School of Medicine and the Viterbi School of Engineering, University of Southern California, Los Angeles, CA, and Loma Linda University

School of Medicine, Loma Linda, CA

Matthew J. Price, MD, FACC, FSCAI Cardiac Catheterization Laboratory, Scripps Clinic, and

Scripps Translational Science Institute, La Jolla, CA Prediman K. Shah, MD, FACC, FACP, FCCP

The David Geffen School of Medicine at UCLA, Los Angeles, CA

Karol E. Watson, MD, PhD, FACC

The David Geffen School of Medicine at UCLA, Los Angeles, CA

Editorial Consultants

Bernard J. Gersh, MB, ChB, DPhil, FRCP, FACC Bradley P. Knight, MD, FACC, FHRS

Richard W. Nesto, MD, FACC

Statement of Editorial Purpose

REVIEWS IN CARDIOVASCULAR MEDICINE

is designed to review the latest advances in the diagnosis and treatment of a wide range of cardiovascular conditions to help the busy, practicing cardiologist keep up to date with the rapidly evolving field of cardiology.

Published by

MedReviews®, LLC 494 Eighth Avenue, Suite 1000 New York, NY 10001 Phone: 212-201-6860 Fax: 212-201-6850 www.medreviews.com

Publications

Merilee Croft

Director, Editorial Production Managing Editor

> **Jeanette Simmons** Art Director

Client Services

Jeff Arnold

Vice President

Programming

Steven Black

Executive Vice President

Blaine Vella

Director of Programming

Trenton Clark

Program Manager

Danielle Wagner Traffic Manager

REVIEWS IN CARDIOVASCULAR MEDICINE (ISSN 1530-6550 [print]; ISSN 2153-8174 [online]) is published 4 times a year by MedReviews®, LLC, 494 Eighth Avenue, Suite 1000, New York, NY 10001. Copyright \circledcirc 2013 by MedReviews®, LLC. Reproduction by magnetic, electronic, or other means is strictly prohibited by law. Violation of copyright will result in legal action. Fees may be subject to change. Reviews in Cardiovascular Medicine is an independent publication under the editorial control of MedReviews®, LLC and its editorial board. Scientific rigor is enforced through a process of review that evaluates information presented for fair balance, objectivity, independence, and relevance to educational need. All articles are reviewed by the medical editors of the journal. The opinions expressed in this publication are those of the contributors and are not attributable to the publisher, editor, editorial board, or advertisers of *Reviews in Cardiovascular Medicine*. The authors, editors, publisher, their servants, assigns, or agents, shall not be in any way liable for the currency of information or for any errors, omissions, or inaccuracies in the publication. Clinical judgment must guide each physician in weighing the benefits of treatment against the risk of toxicity. Information in this publication should not be relied upon in the care of patients. The publisher cannot be held responsible for any injury or damage to persons or property from any use of methods, products, instructions, or ideas contained in this publication. Although articles in this issue of the journal may contain discussion of investigational uses of agents that are not approved by the FDA, these are the authors' views and do not necessarily represent those of MedReviews®, LLC. Please refer to the official prescribing information for each product for indications, contraindications, and warnings. MedReviews®, LLC does not recommend the use of any agent outside of the labeled indications. Every effort has been made by the authors and contributors to contact holders of copyright to obtain permission to reproduce copyrighted material. However, if any have been inadvertently overlooked, the publication will be pleased to make the necessary arrangements at the first opportunity. The appearance of advertising has no influence on editorial content or presentation and does not imply endorsement of products by the publication or its editors.

Reprint requests: Please contact Merliee Croft at 212-201-6860 or mcroft@medreviews.com.

Reviews in Cardiovascular Medicine has been accepted for inclusion in PubMed and Medline and is indexed in EMBASE, the Excerpta Medica database; Science Citation Index Expanded; Current Contents®/Clinical Medicine; and Journal Citation Reports/Science Edition. It is monitored for selective inclusion in Cambridge Scientific Abstracts' Physician Education Index.

This paper meets the requirements of ANSI/NISO Z39.48-1992 (Permanence of Paper) effective with Volume 2, Issue 2, Spring 2001.