Table of Contents

Guest Editor for this issue:

Myung H. Park, MD
Assistant Professor of Medicine
Director, Pulmonary Vascular
Diseases Program
Division of Cardiology
University of Maryland
School of Medicine
Baltimore, Maryland

- 75 Advances in Pulmonary Hypertension CME Section
- 77 Epidemiology and Classification of Pulmonary Hypertension
- 78 Summary of Pulmonary Hypertension Genetics and Genomics
- 79 Diagnosis and Assessment of Pulmonary Arterial Hypertension
- 81 Updated Evidence-Based Treatment Algorithm in Pulmonary Arterial Hypertension
- 83 Diagnosis, Assessment, and Treatment of Non-Pulmonary Arterial Hypertension Pulmonary Hypertension
- 85 Future Perspectives for the Treatment of Pulmonary Arterial Hypertension
- 87 CME Self-Assessment Examination
- 89 Pulmonary Hypertension Roundtable: Messages from Dana Point
- 95 Ask the Expert
- 97 Article Reviews
- 99 Clinical Trials Update
- 100 PHRN Corner
- 102 International Corner

Publisher

Pulmonary Hypertension Association Carl Hicks, *Board Chair* Rino Aldrighetti, *President* Sherrie Borden, *Vice President, Medical and Patient Education*

Publishing Staff

Managing Editor Deborah L. McBride McBride Strategic Services mcbridedeb@aol.com Design Director Michael McClain

PHA Office

Pulmonary Hypertension Association 801 Roeder Road., Ste 400 Silver Spring, MD 20910 301-565-3004, 301-565-3994 (fax) www.PHAssociation.org

© 2009 by Pulmonary Hypertension Association. All rights reserved. None of the contents may be reproduced in any form whatsoever without the written permission of PHA.

Advances in Pulmonary Hypertension is circulated to cardiologists, pulmonologists, rheumatologists and other selected physicians by the Pulmonary Hypertension Association. The contents of the articles are independently determined by the Editor and the Editorial Advisory Board.

Cover Image

Beach at Dana Point, California, USA, site of the 4th World Symposium on Pulmonary Hypertension, 2008. Photo credit: Lynn C. Kelly

Guest Editor's Memo

4th World Symposium Makes History



The 4th World Symposium on Pulmonary Hypertension at Dana Point was a historical event. Composed of 11 working groups in areas of basic science, clinical science, and future perspectives, this 3-day event brought experts in pulmonary vascular disease from all over the world to review the past and current literature, update guidelines and recommendations, and discuss and debate issues regarding the controversies and the future directions in pulmonary arterial hypertension (PAH). What was singularly the most remarkable memory for me was witnessing the collective dedication of the group to reach

that elusive, yet definite, goal —finding the cure for PAH, a disease that was recently considered "uniformly fatal." Indeed, one only had to step into the room to feel the incredible energy and excitement of all the participants—we all felt the past, present, and future of PH converging in that moment.

This meeting marked the 35th anniversary of the 1st World Health Organization Meeting on Pulmonary Hypertension held in Geneva in 1973, a meeting prompted by the outbreak of aminorex-induced PH. It is a testimony to the unflagging dedication of all involved that we now have 8 FDA-approved therapies with more treatments targeting novel pathways currently being developed.

In putting this issue together, I have had the privilege of working closely with several key members of the working groups. In addition to bringing you a synopsis of several sections, our goals in this issue were to give you an insider's view on the process of shaping the drafts, personal perspectives on some key controversial issues, and a taste of what we can and should expect at the next World Symposium in 2013. Furthermore, we present a lively roundtable discussion from Drs Robyn Barst, Marc Humbert, Ivan Robbins, and Lewis Rubin, in which they share their experiences and thoughts from the Dana Point meeting and place this symposium in context with the past ones. I hope you enjoy the journey from an insider's look at the 4th World Symposium from Dana Point.

Myung H. Park, MD Guest Editor

Editor's Memo



As a participant in the 4th World Symposium on Pulmonary Hypertension, held February 2008 in Dana Point, California, I was struck by several things—first was the beautiful setting. Although Southern California is no Venice, Italy (site of the 3rd World Symposium), the Pacific Ocean certainly holds its own as far as aesthetics are concerned.

Secondly, I was amazed at how much new knowledge has been garnered since the 3rd World Symposium. Dedicated investigators have continued to help unravel the pathogenesis of pulmonary arte-

rial hypertension (PAH) at the cellular and molecular levels. What happens inside the pulmonary vascular cells that drives the disease process is becoming increasingly clear. Although the complexities of this process are daunting, new "targets" for therapy are being identified in a classic demonstration of "bench-to-bedside" research. On the classification front, increased understanding of specific disease entities and drug exposures and their association with PAH have led to important changes in the classification system. On diagnosis, newer modalities such as biomarkers and advanced imaging (MRI) are gaining a foothold in the evaluation and follow-up of the pulmonary hypertension (PH) patient. Great advances have been made with treatment: at the 3rd World Symposium, 3 drugs were FDA-approved for PAH; at the time of the Dana Point meeting, 6 approved therapies were available. These new options lead to an expanded, evidence-based treatment algorithm.

Perhaps most importantly, I was struck by the sheer number and diversity of

(continued on page 63)

Editorial Advisory Board

Editor-in-Chief

Richard Channick, MD

Professor of Clinical Medicine Pulmonary and Critical Care Division University of California, San Diego Medical Center San Diego, California

Immediate Past Editor

Ronald J. Oudiz. MD

Associate Professor of Medicine The David Geffen School of Medicine at UCLA

Director, Liu Center for Pulmonary Hypertension

LA Biomedical Research Institute at Harbor-UCLA Medical Center Torrance, California

Editor-in-Chief Elect

Erika Berman Rosenzweig, MD

Associate Professor of Clinical Pediatrics (in Medicine) Columbia University, College of Physicians and Surgeons Morgan Stanley Children's Hospital of New York New York, New York

Associate Editors Kristin Highland, MD

Assistant Professor of Medicine Division of Pulmonary, Critical Care, Allergy and Sleep Medicine

Medical University of South Carolina Charleston, South Carolina

Francisco Soto, MD, MS

Director, Pulmonary Hypertension Program

Pulmonary and Critical Care Medicine Medical College of Wisconsin Milwaukee, Wisconsin

Todd Bull, MD

Associate Professor of Medicine Division of Pulmonary Sciences and Critical Care Medicine University of Colorado Health Sciences Center Denver, Colorado

Robert Schilz, DO, PhD

Medical Director of Lung Transplantation and Pulmonary Vascular Disease University Hospital of Cleveland Case Western Reserve University Cleveland, Ohio

Editorial Board Charles Burger, MD

Chair, Pulmonary and

Critical Care Medicine Associate Professor of Medicine Medical Director, PH Clinic Mayo Clinic Florida Jacksonville, Florida

Karen Fagan, MD

Chief, Division of Pulmonary and Critical Care Medicine University of South Alabama Mobile, Alabama

Eli Gabbay, MD

Lung Transplant Unit Royal Perth Hospital Western Australia, Australia

Nick Kim, MD

Associate Clinical Professor of Medicine University of California, San Diego La Jolla, California

Deborah Jo Levine, MD

University of Texas Health Science Center at San Antonio San Antonio, Texas

Omar Minai, MD

Dept of Pulmonary, Allergy and Critical Care Medicine Cleveland Clinic Cleveland, Ohio

Myung Park, MD

Assistant Professor of Medicine Director, Pulmonary Vascular Diseases Program Division of Cardiology University of Maryland School of Medicine Baltimore, Maryland

Fernando Torres, MD

Director, Pulmonary Hypertension Clinic University of Texas Southwestern Medical Center Dallas, Texas

Glenna Traiger, RN, MSN

Pulmonary & Critical Care Pulmonary Hypertension CNS University of California, Los Angeles Los Angeles, California

R. James White, MD, PhD

Assistant Professor of Medicine, Pharmacology & Physiology Division of Pulmonary and Critical Care Medicine University of Rochester Rochester, New York

Roham Zamanian, MD

Division of Pulmonary and Critical Care Medicine Stanford University Medical Center Stanford, California

Program Description

The mission of Advances in Pulmonary Hypertension is to serve as the premiere forum for state of the art information regarding diagnosis, pathophysiology, and treatment of pulmonary hypertension. The 2003 Venice revision of the World Health Organization Classification serves as a guide to categories of pulmonary hypertension addressed by the Journal. While focusing on WHO Group I PAH, the other categories (Group II, Left heart disease; Group III, Associated with lung disease and/or hypoxemia; Group IV, Thrombotic and/or Embolic Disease; Group V, Miscellaneous) are also addressed. This mission is achieved by a combination of invited review articles. Roundtable discussions with panels consisting of international experts in PH, and original contributions. In addition, a special section in selected issues entitled "Profiles in Pulmonary Hypertension" recognizes major contributors to the field and serves as an inspiring reminder of the rich and collegial history of dedication to advancing the field.

- Provide up-to-date information regarding diagnosis, pathophysiology, and treatment of pulmonary hypertension.
- Serve as a forum for presentation and discussion of important issues in the field, including new paradigms of disease under-
- standing and investigational trial design.
 Recognize and preserve the rich history of individuals who have made major contributions to the field via dedication to patient care, innovative research, and furthering the mission of the PH community to cure pulmonary hypertension.

The Scientific Leadership Council of the Pulmonary Hypertension Association

The scientific program of the Pulmonary Hypertension Association is guided by the association's Scientific Leadership Council. The Council includes the following health care professionals:

Vallerie V. McLaughlin, MD

Chair, SLC University of Michigan Health System Ann Arbor, Michigan

David B. Badesch, MD

SLC Immediate Past-Chair University of Colorado Health Sciences Center Aurora, Colorado

John H. Newman, MD

SLC Vice-Chair Vanderbilt Medical School Nashville, Tennessee

Raymond L. Benza, MD

Allegheny General Hospital Pittsburgh, Pennsylvania

Todd Bull, MD

University of Colorado Health Sciences Center Denver, Colorado

Richard Channick, MD

Editor-in Chief, Advances in Pulmonary Hypertension **UCSD Medical Center** La Jolla, California

C. Gregory Elliott, MD

University of Utah School of Medicine Murray, Útah

Karen A. Fagan, MD

University of South Alabama Mobile, Alabama

Robert Frantz, MD

Mayo Clinic College of Medicine Rochester, Minnesota

John Granton, MD

Toronto General Hospital Toronto, Canada

Nicholas S. Hill, MD

Tufts-New England Medical Center Boston, Massachusetts

Marius Hoeper, MD University of Hanover Medical School Hanover, Germany

Dunbar Ivy, MD

University of Colorado Denver Health Sciences Center Denver, Colorado

Zhi-Cheng Jing, MD Shanghai Pulmonary Hospital Shanghai, China

Anne M. Keogh, MD

St. Vincent's Public Hospital Sydney, Australia

Michael J. Krowka, MD

Mayo Clinic Rochester, Minnesota

James E. Loyd, MD

Vanderbilt University Medical Center Nashville, Tennessee

Michael Mathier, MD

University of Pittsburgh Medical Center Pittsburgh, Pennsylvania

Michael D. McGoon, MD

Immediate Past-Chair, PHA Board of Trustees Mayo Clinic Rochester, Minnesota

Srinivas Murali, MD

Allegheny General Hospital Pittsburgh, Pennsylvania

Ronald J. Oudiz, MD

Immediate Past Editor-in-Chief, Advances in Pulmonary Hypertension Liu Center for Pulmonary

Hypertension at Harbor - UCLA Medical Center Torrance, California

Andrew Peacock, MD

Western Infirmary Glasgow, Scotland, United Kingdom

Erika Berman Rosenzweig, MD

Editor-In-Chief Elect. Advances in Pulmonary Hypertension Columbia Presbyterian Medical Center New York, New York

Ivan Robbins, MD

Chair, Scientific Sessions Committee Vanderbilt University Nashville, Tennesee

Julio Sandoval, MD

National Institute of Cardiology of Mexico Tlalpan, Mexico

Richard Silver, MD

Medical University of South Carolina Charleston, South Carolina

Victor F. Tapson, MD

Duke University Medical Center Durham, North Carolina

Jason Yuan, MD, PhD

Chair, PHA Research Committee University of California, San Diego La Jolla, California

Liaisons

Arlene Schiro, NP (voting) Chair, PH Resource Network Massachusetts General Hospital Boston, MA

Harry Rozakis Board Liaison

Emeritus Members

Bruce H. Brundage, MD St. Charles Medical Center - Bend Bend, Oregon

Alfred P. Fishman, MD

University of Pennsylvania Health System Philadelphia, Pennsylvania

The Mission of the Scientific Leadership Council is to provide medical and scientific guidance and support to the PHA by:

 Developing and disseminating knowledge for diagnosing and treating pulmonary hypertension

researchers and practitioners

 Advocating for patients with pulmonary hypertension · Increasing involvement of basic and clinical

More information on PHA's Scientific Leadership Council and associated committees can be found at: www.PHAssociation.org/SLC/