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Guest Editors for this issue:

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

Francisco J. Soto, MD, MS
Assistant Professor
Director, Pulmonary Hypertension Program
Medical College of Wisconsin
Milwaukee, Wisconsin

Publisher
Pulmonary Hypertension Association
Michael D. McGoon, MD, *Chair of the Board*
Rino Aldrighetti, *President*
Rachel Pokorney, *Associate Director of Medical Services*

PHA Office
Pulmonary Hypertension Association
801 Roeder Rd. Suite 400
Silver Spring, MD 20910-4496
301-565-3004, 301-565-3994 (fax)
www.phassociation.org

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Editorial Offices
Advances in Pulmonary Hypertension, DataMedica,
P.O. Box 1688, Westhampton Beach, NY 11978
Tel (631) 288-7733 Fax (631) 288-7744
E-mail: sbelsonchapman@aol.com

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Cover Image
Unofficially called "The Case Discussion" by PHA editorial staff, this painting by Jamil Aboulhosn, MD, is one of several for *Advances in Pulmonary Hypertension*. Dr Aboulhosn is an assistant professor of medicine (cardiology) at the UCLA School of Medicine. His clinical interests include pulmonary hypertension and adult congenital heart disease as well as general cardiology. He is a member of the Ahmanson/UCLA Adult Congenital Heart Disease Center. Dr. Aboulhosn paints "for fun," pursuing topics from medicine to landscapes and figures. His medical illustrations have been published in journals and textbooks, including *Circulation* and the latest *Hurst's the Heart* (12th ed).

Editor's Memo

Marking a Milestone for the Journal and Previewing PHA's Upcoming Conference and Scientific Sessions

This issue of *Advances in Pulmonary Hypertension* is a milestone in the journal's history: it is the first to produce a series of clinical cases and expert commentaries since the journal's inception in 2002. The Editorial Board and I were excited when the idea was conceived. Now that the "cases" issue is in print, I am happy to see that we were right to be energized about this issue. Publishing these cases is one of several components introducing new dimensions in PHA's tireless efforts in educating the world about PAH: 1) Formal case presentations presenting practical approaches to PAH diagnosis and management, 2) CD-ROM-based case presentations, with interactive multimedia (coming soon), and 3) On-line "live" case discussions via Pulmonary Hypertension Clinicians and Researchers (you must be a PHCR member to view and participate in these discussions).

The many contributors to this issue deserve a great deal of thanks for their efforts in helping to produce it. These include our Editorial Board members Drs Francisco J. Soto, Robert Schilz, Charles D. Burger, Srinivas Murali, E. Clinton Lawrence, and Micah R. Fisher.

This issue also coincides with the opening of registration for PHA's 8th International Pulmonary Hypertension Conference and Scientific Sessions, which will be held on June 20-22 in Houston, Texas. The theme of the 2008 Scientific Sessions, a daylong educational program specifically for medical professionals who work in the field of pulmonary hypertension, is *Determinants of RV Function on Molecular, Pharmacogenomic, and Metabolic Levels.* PHA's biennial conference is the largest meeting of its kind and is unique in bringing together pulmonary hypertension patients, caregivers, and medical professionals from around the world. For more information on this exciting event, be sure to see the ad in this issue of *Advances*. As someone who has attended past PHA Conferences and worked to develop their programming, as well as the 2008 Conference program, I can assure you that this will be an exceptional weekend.

Ronald J. Oudiz, MD
Editor-in-Chief

Guest Editor's Commentary

Pulmonary Hypertension: Challenges and Controversies in Diagnosis and Management

The case presentations and discussions in this issue of *Advances* illustrate both common and uncommon challenges in the diagnosis and management of patients with pulmonary hypertension. Although significant guidelines and evidence-based recommendations exist for patient evaluation and care, practical application of these guidelines and managing uncertainty in areas where evidence may be sparse are key elements in the daily activities of specialized pulmonary hypertension clinics.

The contributors present case-based analyses exploring important concepts and controversies in pulmonary venous hypertension, transplantation, vasoreactivity, chronic thromboembolic disease, and catastrophic antiphospholipid syndrome. Two of the cases not only illustrate important concepts but are examples of notable

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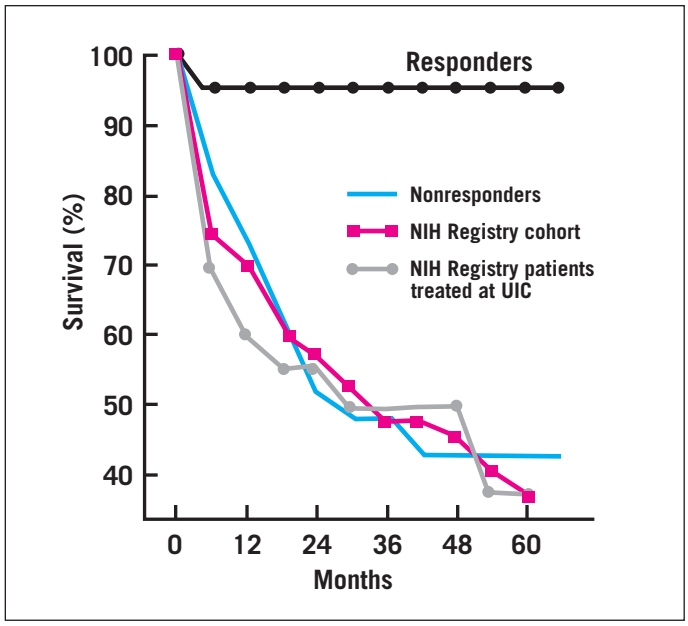

Figure 4. Kaplan-Meier survival curves demonstrating excellent long-term survival of patients with sustained response to calcium channel blockers. Contained for reference are survival curves of idiopathic PAH patients within the NIH registry (-). Adapted from Rich S, et al.[8]

channel antagonist use in PAH include documented sensitivity to these agents and significant right heart dysfunction or failure. Agents with a significant negative inotropic effect, such as verapamil, should be avoided.

Long-term follow-up is critical in patients initially treated with calcium channel blockers. Continued sustained response as evidenced by the attainment of functional class I or II is the current suggested goal indicating adequacy of response according to ACCP guidelines.[1] Continued robust clinical follow-up and documentation are important as the initial effects of therapy can wane, creating the need for alternate treatment regimens.

Nonetheless, patients with idiopathic PAH with documented acute vasoreactivity and excellent sustained long-term functional class and hemodynamics have superior survival rates compared with nonresponders even under treatment with other agents[7,8] (**Figures 3** and **4**).

This patient in particular shares a number of these favorable characteristics, at least with the current follow-up. She demonstrates initial vasoreactivity that is recapitulated with calcium channel antagonist therapy with subsequent improvement to WHO functional class I (**Table 2**). Although repeat hemodynamics were not obtained, regression of right ventricular changes on echocardiography suggests that sustained improvements in the initial hemodynamics are likely present. It is important to note that this patient carries a diagnosis of APAH and CREST syndrome. As mentioned, vasoreactivity is infrequently reported in this subset of patients[9] and thus data regarding long-term outcome in vasoreactive APAH patients are lacking. The dramatic response to therapy in this patient, however, appears favorable and at least initially parallels responses that when seen in idiopathic PAH patients are associated with good outcome. Thus, acute vasoreactivity testing must be done using a short-acting vasodilator in all suspected idiopathic PAH patients. Whether it is necessary in all PAH patients is still not settled. ■

References

1. Badesch DB, Abman S, Ahearn G, et al. Medical therapy for pulmonary arterial hypertension: ACCP Evidence Based Clinical Practice Guidelines. *Chest.* 2004;126:35S-62S.
2. McLaughlin VV, Genther DE, Panella RN, Rich S. Reduction in pulmonary vascular resistance with long-term epoprostenol (prostacyclin) therapy in primary pulmonary hypertension. *New Engl J Med.* 1998; 338:273-277.
3. Opitz CF, Wensel R, Bettmann M, et al. Assessment of the vasodilator response in primary pulmonary hypertension: comparing prostacyclin and iloprost administered by either infusion or inhalation. *Eur Heart J.* 2003;24:356-365.
4. Groves BM, Badesch DB, Turkevich D, et al. Correlation of acute prostacyclin response in primary (unexplained) pulmonary hypertension with efficacy of treatment with calcium channel blockers and survival. In: Weir K, ed. *Ion Flux in Pulmonary Vascular Control.* New York: Plenum Press; 1993.317-330.
5. Sitbon O, Humbert M, Jagot JL, et al. Inhaled nitric oxide as a screening agent for safely identifying responders to oral calcium-channel blockers in primary pulmonary hypertension. *Eur Respir J.* 1998; 12:265-270.
6. Schrader BJ, Inbar S, Kaufmann L, et al. Comparison of the effects of adenosine and nifedipine in pulmonary hypertension. *J Am Coll Cardiol.* 1992;19:1060-1064.
7. Sitbon O, Jais X, Ioos V, et al. Long-term response to calcium channel blockers in idiopathic pulmonary arterial hypertension. *Circulation.* 2005;111(23):3105-3111.
8. Rich S, Kaufmann E, Levy PS. The effect of high doses of calcium-channel blockers on survival in primary pulmonary hypertension. *N Engl J Med.* 1992;327:76-81.
9. Sitbon O, Humbert M, Jais X, et al. Acute vasodilator responsiveness and long-term response to calcium channel blockers in different forms of pulmonary hypertension. *Am J Respir Crit Care Med.* 2004;169: A120.

Guest Editor's Commentary

(continued from inside front cover)

educational PHA initiatives: a preview of an upcoming educational CD edited by Todd Bull, MD, and a discussion from the PHCR on-line forums. As with many discussions of patient care, areas of consensus emerge, as well as topics that clearly require additional investigation.

Robert Schilz DO, PhD
Guest Editor