Editor's Memo

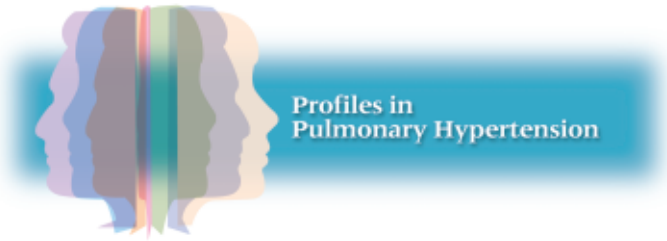
Under the Tent of the New ACCP Guidelines in PAH: Room for Debate, Comment, Analysis

Publication of the new American College of Chest Physicians (ACCP) evidence-based clinical practice guidelines for pulmonary arterial hypertension (PAH) represents a major advance in understanding the diagnosis and management of the disease. For the target audience of cardiologists, pulmonologists, rheumatologists, internists, and other healthcare providers involved in such care, the guidelines are the first revision of an earlier document created 10 years ago. Lewis J. Rubin, MD, who chaired the consensus panel, and the international panel of 19 experts from five medical specialties, deserve our appreciation and praise for the extraordinary work they have done during the last 3 years. We applaud their efforts and commitment to the highest standards of medical care.

If the guidelines cast a long shadow over our practice because of how large they loom in clinical decision-making, they also shed tremendous light on areas where we need more evidence-based information. Under the tent of the guidelines, however, there is plenty of room for debate and comment over how the new criteria should be applied in the myriad decisions we make every day. As clinicians, we must often make decisions in areas in which the evidence base is inadequate because of the need for more data. As our Editorial Board reviewed the guidelines, we wanted to explore various approaches taken by clinicians involved with PAH, especially in areas where the guidelines cannot (of necessity) make strong recommendations.

The experts we have assembled for this issue are not debating the relative merits of the guidelines. Beginning on page 3, they are offering fresh and varied perspectives, whether it is on the use of echocardiography or the benefits of new agents still in phase 3 clinical trials. Gleaned from their own knowledge and practice-based experience, these comments, queries, and insights will, it is hoped, broaden our base of knowledge.

Victor F. Tapson, MD
Editor-in-Chief



From ACCP Guidelines to Pharmacogenomics of PH, Lewis Rubin, MD, Stands Tall as a Prime Mover

Lewis J. Rubin, MD

Lewis J. Rubin, MD, is one of a select group of physicians who have seen pulmonary hypertension from many different perspectives, one of a handful of clinicians worldwide whose experience spans more than 20 years in this clinical setting. Their experience covers a dramatic time in the evolution of therapy—from the years when virtually no treatments were available to the current state-of-the art therapies. Only Dr Rubin, however, was looked to by the American College of Chest Physicians (ACCP) as the physician who should lead the initiative to update its guidelines on the disease in 2004.

Serving as Chair of the ACCP Consensus Panel on Pulmonary Hypertension, Dr Rubin headed a multidisciplinary team to revise the guidelines for the first time in 10 years as the panel produced a landmark document in evidence-based medicine. That document is expected to influence treatment strategies for years to come. In those years ahead, however, new directions pursued by Dr Rubin and his colleagues are also likely to determine the direction of management in pulmonary hypertension. The area he and his research team will be concentrating on is how therapeutic interventions are likely to flow from genomics, how treatment will be based on the genomic profiles of individual patients.

Looking ahead to this next career challenge, Dr Rubin is involved in the study of the pharmacogenomics of pulmonary hypertension, the genetic basis for pharmacologic responses. "Why do some people take diet drugs and develop pulmonary hypertension, why do some people respond to prostacyclin and others don't? Why do others do best with an endothelin blocker or with combination treatment? As part of that direction we're exploring new genetic mechanisms responsible for pulmonary hypertension and trying to identify novel targets that we can go after therapeutically. We've already identified that there are some novel regulatory genes that are abnormal in pulmonary hypertension and that may be targets. This will become an important direction."

These future therapies will be a quantum leap from the early days of his career when he first saw patients with pulmonary hypertension. Every physician on the ACCP panel and other physicians as well surely remember

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Profile *(continued from page 3)*

their first patient who died of pulmonary hypertension, but for Dr Rubin the experience was even more unforgettable because of the bizarre circumstances surrounding the patient's death.

At the time of his residency at Duke University Medical Center, Dr Rubin treated a patient with hydralazine; vasodilators were one of the only therapies available. "He did well for about 2 years but then became sick, developed severe anemia and kidney failure, and he died. We assumed that because he had severe pulmonary hypertension that his death was the final consequence of that."

About 2 months later, however, Dr Rubin received a call from the North Carolina State Board of Investigations. "They said they had reason to believe the cause of death was not natural and were exhuming the body. They wanted some additional information from me. It turned out that this rural North Carolina farmer owned a piece of land in the path of a planned federal highway, and the government wanted to buy it from him. His wife had visions of a big profit but he did not want to sell. His wife had poisoned him with arsenic. So that was my first patient who we thought had died as a result of pulmonary hypertension, but actually of arsenic poisoning."

Coincidentally, Burroughs Wellcome, which had begun developing epoprostenol, had its US offices not far from Duke University and before long, Dr Rubin was immersed in the first clinical trials exploring the role of prostacyclin, an agent that would transform treatment strategies in pulmonary hypertension. Representatives of the company had heard Dr Rubin lecture about pulmonary hypertension and recruited him for their protocol with prostacyclin. Soon afterward, Dr Rubin and colleagues published their first paper on intravenous epoprostenol in pulmonary hypertension. From there numerous other investigations followed as Dr Rubin pursued his research interest for more than 20 years, continuing with work now being done at the University of California, San Diego, where he is Professor of Medicine and Director of the Pulmonary Vascular Center. Prior to that he served as Director of the Division of Pulmonary and Critical Care Medicine.

During the last 10 years, the ACCP has twice turned to him for leadership in establishing guidelines for pulmonary hypertension. Recognizing the dramatic expansion in therapy within the last 10 years, the College issued the new guidelines in a supplement to Chest this year. The 20-member panel received the imprimatur from the ACCP, the American Heart Association, the American College of Cardiology, the American College of Rheumatology, and the Pulmonary Hypertension Association. The charge was to revise guidelines for the diagnosis and treatment of pulmonary hypertension by applying rigorous, evidence-based criteria and Dr Rubin led the effort to assemble international experts whose work is addressed in this issue. Dr Rubin thinks it may be another 5 years before the ACCP considers yet another revision of the guidelines on pulmonary hypertension. When that happens, he will no doubt remain in the forefront of the creation of new evidence-based criteria for treating the disease.