## EDITOR'S MEMO

For this issue of Advances, we are examining the relationship between societal metabolic abnormalities and the development of pulmonary arterial hypertension (PAH)/pulmonary hypertension (PH) in the United States-and throughout the developed world. These abnormalities, frequently referred to as the metabolic syndrome-central obesity, insulin resistance, dyslipidemia, and systemic hypertension-are common, really epidemic, in the United States and now are even increasing in developing nations. As POGO (created by the cartoonist Walt Kelly) famously observed: "We have met the enemy and he is us." Oh, were that not such a truism! However, beyond the obvious health-related issues associated with these entities,

of equal importance to us is whether they, singly or in various combinations, contribute to the development and/or worsening of PAH/PH and, if so, how?

In this issue, we have attempted to condense decades of observations and research to suggest that they do contribute in some fashion, although exactly how and when in the course of the disease is not yet clear. I thank Anna Hemnes for serving as Guest Editor of this issue; she has assembled an outstanding group of contributors and has presented this subject exceedingly well. I think the concerns, truths, and potential pitfalls of the relationship between the factor(s) of the metabolic syndrome and PAH/PH are very well summarized in the Roundtable: honestly, I think it is a free-wheeling and fascinating look at this topic. Anna and I hope you enjoy this issue and that, after reading it, you form your own opinion as to the importance of these factors. It may even trigger the thought that perhaps the lines between Group 1 PAH and Group 2 PH are even more than somewhat blurred and that we might need to reconsider our classification schemes to accommodate these observations.

## Harrison (Hap) Farber, MD

Professor of Medicine Director, Pulmonary Hypertension Center Boston University/Boston Medical Center Boston, MA

# GUEST EDITOR'S MEMO

Metabolic disease is highly prevalent in the United States and many other countries, with numbers of affected people rising every year.<sup>1</sup> So it is not a surprise that more patients than decades ago present for evaluation of pulmonary hypertension (PH) with comorbid features of the metabolic syndrome-central obesity, insulin resistance, systemic hypertension, and dyslipidemia.<sup>2</sup> The challenge to us, as clinicians and researchers, is to understand if this shift in our population simply reflects society at large or may provide clues to the etiology of pulmonary arterial hypertension (PAH), in particular. Beginning with the initial observations that insulin resistance and features of the metabolic syndrome are more common in PAH patients than controls,<sup>3,4</sup> this work has shaped many basic science and clinical studies that are ongoing today. The questions that were raised were innumerable but can be fundamentally broken down into a few lines of thought: 1) Do features of the metabolic syndrome contribute to PAH on a cellular or physiologic level? 2) Is metabolic syndrome a consequence of or an actual promoter of PAH? 3) How do we identify the features of the metabolic syndrome that are important to PAH? 4) Does reversal of metabolic

syndrome improve PAH? In this issue we have attempted to address these key questions through expert interpretation of relevant studies in the literature.

On a personal level, I am very excited to see where this research leads. Metabolic syndrome has many potential effective therapies, while PAH has far fewer. If we can unlock the keys to metabolic disease in pulmonary vascular disease, perhaps we can tap into the tremendous and existing research of metabolic therapies and basic science. In the field of insulin resistance, there are 3 main interventions known to improve this condition: exercise, weight loss, and medications. These all have potential benefits and risks in PAH, but each is well understood in patients with insulin resistance and has a clear path forward to study in PAH. Harnessing this existing knowledge, applying the techniques to pulmonary vascular disease, and studying its effects in animal models of PAH and one day in affected patients offer a real opportunity to improve lives with this disease.

In addition to the excellent authors represented here, I'd like to end with thanking the patients and their families who have participated in these studies. Without their dedication to learning more about why PAH develops and how best to treat PAH, we never would have come so far. This issue is a testament to the powerful partnership between patients, caregivers, and researchers in this field. Our work continues, and I look forward to seeing what we discover together!

## Anna R. Hemnes, MD

Associate Professor Division of Allergy, Pulmonary and Critical Care Medicine

Vanderbilt University Medical Center

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