The Third World Symposium on Pulmonary Arterial Hypertension (PAH) created the opportunity to evaluate multiple new findings into the causes and management of this life-threatening and devastating disease. Led by task force members, the scientific presentations allowed a collective sharing of knowledge and provided a specialized forum by which to establish new benchmarks in the pathogenesis, pathophysiology, diagnosis, treatment, and monitoring of PAH.

Although mysteries still surround the trigger factor(s) initiating the pathological changes seen in PAH, we now understand more of the mechanisms involved. A genetic mutation of bone morphogenetic protein receptor-2, part of the transforming-growth-factor-beta superfamily, appears to have some association with familial and idiopathic PAH. With much still unknown, research has allowed us to consider that genetic elements may play a fundamental role, although this could cover a broad range of factors such as endothelin (ET), prostacyclin (PGI₂) synthase, nitric oxide (NO) synthase, the serotonin transporter, and voltage-gated potassium channels.

Superficially, it may appear that the disease process is driven by vasoconstriction, but it now appears that pulmonary vascular proliferation and remodeling are the primary forces of pathogenesis. Endothelial dysfunction is a key element of the manifestation of disease pathophysiology, marked by prolonged elevation of ET coupled with chronic reductions in NO and PGI₂. Identification of these processes has allowed the development of specific pharmacologic targets.

Regardless of the etiology, PAH presents as an extremely serious disease state that is difficult to identify early owing to the insidious nature of early-stage symptoms. A heightened awareness of patients at risk, or of early-stage disease manifestation, is necessary to allow for diagnosis before significant pathophysiological changes. The diagnostic process is now more clearly defined, with consensus reached on an algorithm of various investigative tests and procedures to exclude other causes and to ensure that an accurate diagnosis of PAH can be reached.

Advances in medical therapies over the past decade reflect the inroads made into our understanding of PAH. Co-administered with conventional supportive therapy, new drug classes such as endothelin receptor antagonists and prostanoids are now offering viable treatment options for these patients. A focused session on medical therapy during the Third World Symposium on PAH has led to an updated treatment algorithm to guide treating clinicians on the best practice options for PAH patients.

The dilemma remains as to whom best to treat these patients, given that the patient population is spread across a broad range of disciplines, such as respiratory, cardiology, rheumatology, and immunology. The global trend is moving toward a system of designated centers for PAH care, with medical teams including all specialties working in a shared-care approach to patient management. It is no coincidence that the collaborative approach to this World Symposium reflects the cooperation required across specialty groups in the broader medical community, to ensure that best possible care is delivered to this orphan disease state. To this end, we appreciate the opportunity to disseminate the proceedings of this symposium by means of this supplement to the *Journal of the American College of Cardiology*, and we hope that the readership finds it informative and useful.

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