In 1987 Dr Eugene Robin wrote a critical review in the journal *Chest* entitled, “The Kingdom of the Near-Dead. The Shortened Unnatural Life History of Primary Pulmonary Hypertension”. In the article he described the fragility of patients with primary pulmonary hypertension (PPH) and questioned whether they have a shortened life expectancy in part as a result of ill-advised tests and treatments. Routine open lung biopsy for diagnosis and empiric vasodilator therapy were common at that time. The emerging perception when the article was published was that calcium channel blockers had a significant role to play in the treatment of PPH and offered new hope in this disease. However, we now know that calcium channel blockers, while an easy drug to administer, are beneficial long-term in only a minority of patients. Indeed, it now appears that less than 5% of patients with PPH benefit long-term from calcium channel blocker therapy. Furthermore, there is concern that empiric vasodilator use contributed further to the “shortened unnatural life history” in pulmonary hypertension. A study of death certificates in the United States reveals an increase in mortality from PPH in the early 90s following the publication of a number of high-profile reports on this form of therapy.

Ten years following the Robin article, continuous intravenous epoprostenol was demonstrated to improve hemodynamics and prolong life in PPH and became the first specific therapy for the disease. However, the complex nature of this therapy, requiring an indwelling Hickman catheter and infusion pump as well as a requirement for patients to learn how to reconstitute the medication each day, limited its use to a few specialized centers. Leading specialists from these centers achieved international consensus with a new treatment-based classification system at the World Symposium on PPH held in Evian, France in 1998. The classification grouped patients with PPH in the category of pulmonary arterial hypertension (PAH) along with those with histologically similar conditions such as left-to-right congenital shunts and pulmonary hypertension associated with connective tissue diseases. This new and practical classification system resulted in pulmonary hypertension receiving considerable attention from the pharmaceutical industry. Since the Evian symposium, there have been at least 9 multinational trials with new drugs ongoing or completed in PAH.

The review article in this month’s issue of *ASIM* describes our current understanding of PAH and presents the up-to-date revised classification system agreed to at the recent World Symposium on PAH held in Venice. PPH, now termed idiopathic pulmonary arterial hypertension (IPAH), has come a long way over the past 25 years. Complex therapy with intravenous epoprostenol can now be deferred while new oral-based therapy with endothelin blockers is initiated. Transplantation, once the only option, can also be deferred, often indefinitely. Nevertheless, while great progress has been made, a cure remains elusive. Perhaps now is a good time to re-examine Eugene Robin’s article. His message remains as important today as it was 27 years ago. Patients with PPH and PAH are fragile and, without appropriate treatment—or with inappropriate treatment for that matter—face a life expectancy of only a couple of years. Reiterating Robin’s message, great care must be taken in diagnosis and when initiating treatment. The case for referral to specialized centers remains as strong today as ever. While starting a patient on oral therapy is easy, errors in diagnosis can be costly. Patients with surgically curable chronic thromboembolic pulmonary hypertension can be missed. Delays in initiating epoprostenol, proceeding to septostomy, or referral for transplantation can contribute to early mortality. Recognition of the continuing need for specialized centers with expertise in multinational trials is vital if the current hope and progress are to continue. Only by learning from the past in this disease can we hope to one day finally overthrow the Kingdom of the Near-Dead forever.

References


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