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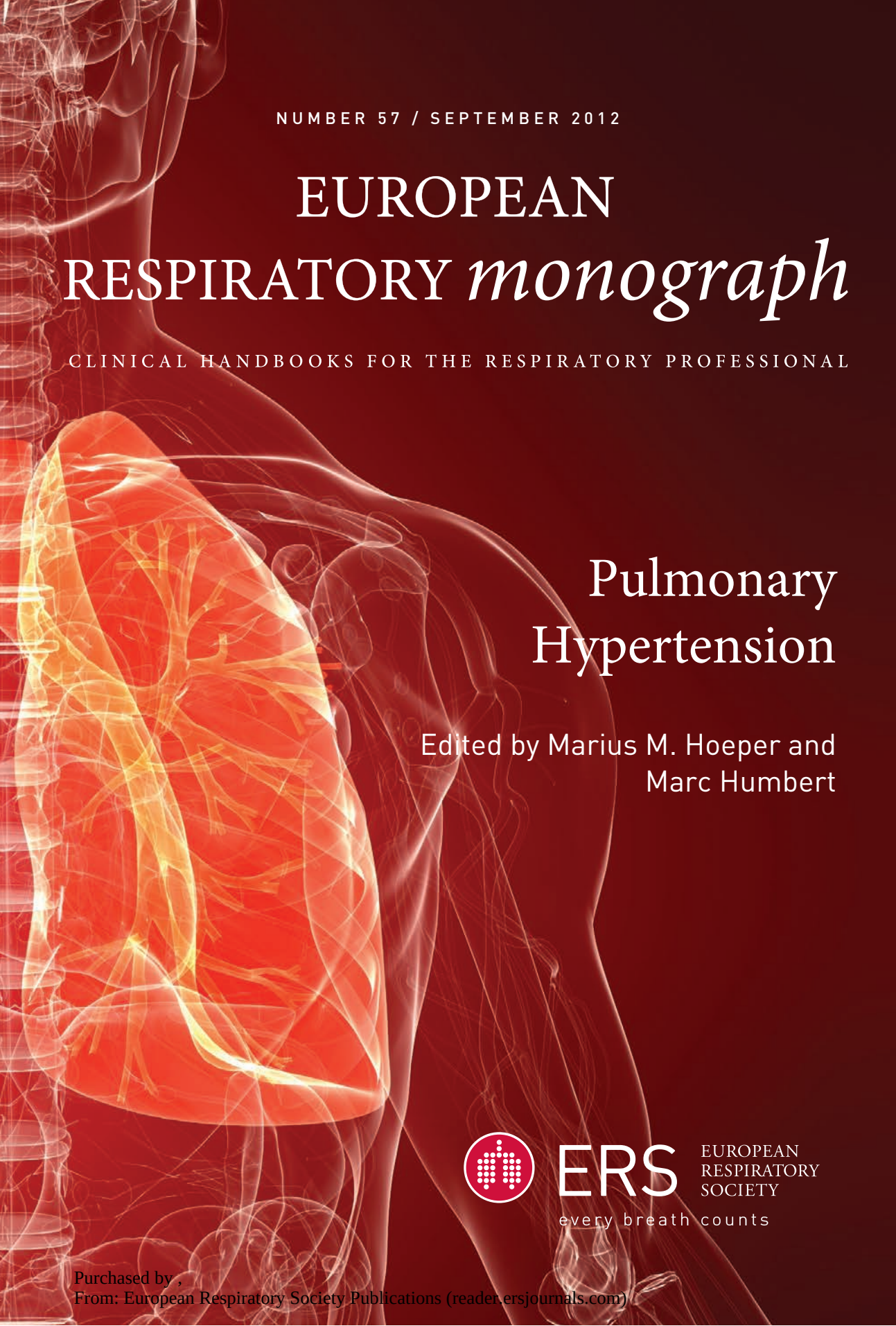

Pulmonary Hypertension

Edited by Marius M. Hoeper and Marc Humbert

ERS EUROPEAN RESPIRATORY SOCIETY
every breath counts

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Pulmonary Hypertension

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Editor in Chief
Tobias Welte

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This book is one in a series of *European Respiratory Monographs*. Each individual issue provides a comprehensive overview of one specific clinical area of respiratory health, communicating information about the most advanced techniques and systems required for its investigation. It provides factual and useful scientific detail, drawing on specific case studies and looking into the diagnosis and management of individual patients. Previously published titles in this series are listed at the back of this *Monograph*.

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Guest Editors

Marius M. Hoeper

Marius M. Hoeper was educated at Hannover Medical School (Hannover, Germany), where he specialised in respiratory medicine and intensive care medicine. In 1992, he received a 2-year grant from Germany's National Research Foundation for a post doctorial training position at the University of Colorado (Denver, CO, USA). Following this he returned to the Hannover Medical School, where he now holds the position of Senior Physician in the Department of Respiratory Medicine. He is in charge of the pulmonary hypertension programme and is the clinical director of the medical intensive care unit. His main scientific interest lies in the field of pulmonary hypertension, where he has published more than 160 papers. In addition, Marius serves as a regular reviewer for major medical journals in his field and is a member of the *American Journal of Respiratory and Critical Care Medicine* editorial board as well as an associate editor for the *European Respiratory Journal (ERJ)*. Marius was a task force member at the 3rd World Symposium on Pulmonary Hypertension held in 2003 (Venice, Italy) and was a task force chair at the 4th World Symposium on Pulmonary Hypertension held in 2008 (Dana Point, CA, USA). In addition, he has been an author and section editor for the 2009 European Guidelines for Pulmonary Hypertension.

Marc Humbert

Marc Humbert is Professor of Medicine at the South Paris University (Le Kremlin-Bicêtre, France). In addition to his academic responsibilities, he is consultant and specialist at the National Referral Centre for Pulmonary Hypertension, Department of Respiratory and Intensive Care Medicine, Hôpital Bicêtre, Assistance-Publique Hôpitaux de Paris, (Paris, France). Marc is Director of the INSERM UMR-S 999 "Pulmonary Hypertension: Pathophysiology and Innovative Therapies" and Director of the ''Thorax Innovation'' University Hospital Department. Marc is Vice Dean of the South Paris University School of Medicine, President of the Research Committee and Vice President of the Board of Directors of the Assistance-Publique Hôpitaux de Paris. He was the Editor of the proceedings for 4th World Symposium on Pulmonary Hypertension held in 2008. He is currently Chief Editor for the *European Respiratory Review* (*ERR*) and is an Associate Editor for the *European Respiratory Journal* (*ERJ*). He has published widely in the fields of pulmonary hypertension and pulmonary inflammation, and was awarded the European Respiratory Society Cournand Lecture in 2006 with a lecture on "The Burden of Pulmonary Hypertension". Marc has also received the Descartes-Huygens Prize from the Royal Netherlands Academy of Arts and Sciences.

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Preface

Ten years ago, the prognosis of patients with pulmonary hypertension (PH) was poor. At that time, no pharmaceutical treatment was effective in all patients. This has changed dramatically with the introduction of inhaled prostacyclin as maintenance therapy. Endothelial antagonists and phosphodiesterase inhibitors, both based on pathophysiological considerations and used as monotherapy or in combination, have extended the spectrum of treatment possibilities. All of the drugs used have been shown to be efficient with regard to the different outcome measures, including haemodynamic parameters, exercise tolerance and life quality. As a result, observational studies have demonstrated an incredible increase in the life expectancy of patients with PH.

When the development of new therapies began, idiopathic pulmonary arterial hypertension (IPAH) was the focus of research. The therapeutic success in this field initiated studies in patients with different forms of secondary PH, starting with PH associated with connective tissue disease, followed by patients with interstitial lung fibrosis or chronic thromboembolism, and then moving on to those with chronic obstructive pulmonary disease (COPD) or congestive heart failure. Huge randomised controlled trials have been performed for most of these indications, meaning it has been possible to establish very specific algorithms for diagnosis and treatment with regard to the baseline disease causing PH. Due to the intensive collaboration of PH researchers all over the world and a special effort within the PH community, guidelines have been developed and quickly corrected in the light of new experiences and findings, making PH an example of standardised management of disease on a worldwide scale.

However, the story of PH continues. Basic research in PH has raised interesting new concepts for further treatment options. The pharmaceutical industry and public research institutes are also working together to consider different methods of diagnosis and treatment. And personalised medicine based on pathophysiological concepts and risk stratification is no longer just a vision, as work is underway to improve outcome of patients with PH.

This issue of the *European Respiratory Monograph* summarises the current pathophysiology, diagnosis, and pharmacological and non-pharmacological treatment of PH. The best experts in the field have contributed to this book, which should be of interest not only to basic scientists and clinicians, but also to those in the pharmaceutical industry, as it provides in-depth consideration of the future of PH. The issue is also the first to include continuing medical education (CME) questions (accredited by the European Board for Accreditation in Pneumology (EBAP)), meaning it will be particularly attractive to those in training. To earn 5 CME credits, simply read the issue and answer the questions at the back of the book and provided online.

I want to personally congratulate the Guest Editors of this excellent *Monograph*, which provides an excellent overview of PH. Marius and Marc, thank you very much for a fantastic collaboration. I am convinced that this *Monograph* will be a major success.

Editor in Chief
Tobias Welte

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Introduction

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Pulmonary arterial hypertension (PAH) is characterised by vasoconstriction, thrombosis and remodelling of the small pulmonary arteries, leading to chronic pre-capillary pulmonary hypertension (PH) and fatal right heart failure. PAH is a rare and devastating condition with a prevalence of less than 50 cases per million adults in the European Union and a median survival of less than 5 years after diagnosis. As emphasised in the updated PH classification, there are many other causes of PH and its global burden is currently unknown and certainly underestimated. Indeed, common diseases such as chronic obstructive pulmonary disease (COPD), pulmonary embolism and hepatosplenic schistosomiasis are frequent causes of PH worldwide. In addition, post-capillary PH due to chronic cardiac diseases is very common in general and specialised practice. Altogether, PH and its consequences on the right heart contribute markedly to the global burden of chronic cardiopulmonary diseases.

Initial symptoms of PH are nonspecific and often unspectacular, and may delay diagnosis and appropriate management. Lack of awareness often explains why symptoms are attributed to a more common cardiorespiratory disease. As a result, there is a substantial delay of more than 1 year in the diagnosis and initiation of appropriate therapy. It is important to highlight that management requires a thorough diagnostic work-up, including right heart catheterisation (RHC), which is the gold standard to confirm diagnosis, define whether PH is pre- or post-capillary and evaluate its severity. It is widely accepted that early intervention (and prevention, whenever possible) of PH is of utmost importance to improve quality of life and long-term outcomes.

The current issue of the *European Respiratory Monograph* provides updated information on the various forms of PH from respected leaders in the field of pulmonary vascular medicine. Our ambition is to help healthcare professionals and medical students to better understand and manage PH in the modern era. The more we learn about these diseases, the more we understand how complex the management of these patients can be. Advanced therapies are often beneficial in patients with PAH but can worsen other forms of PH. Delaying appropriate treatment can have detrimental, sometimes life threatening, consequences that should remind us that the management of patients with severe PH should always involve expert centres.

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