



ERS | *monograph*

Acute Exacerbations of Pulmonary Diseases

Edited by Pierre-Régis Burgel,
Marco Contoli and
José Luis López-Campos

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Editor in Chief
Robert Bals

This book is one in a series of *ERS 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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Preface

Robert Bals

Many lung diseases have a chronic course, and this in itself can be challenging to manage. Diseases like COPD and IPF, for example, slowly deteriorate and treatment is often limited to relieving symptoms. It is disastrous for the patient if the situation gets out of control and the disease gets much worse within a short time. It is often difficult to understand the underlying biological processes of these deteriorations. Exacerbations frequently result in a faster decline of the underlying disease and can cause the death of the patient. The field of exacerbations in pulmonary diseases is complex and inadequately understood, for a number of reasons: 1) Generally, the pathomechanisms of exacerbations are poorly understood. 2) The definitions of exacerbations are often unclear, which can cause additional difficulties in the diagnosis of these sudden deteriorations. 3) It is often difficult to rule out relevant differential diagnoses and in many cases, these seem to be more than one disease entity, including infections. 4) Treatment options can be very limited, which is largely a result of a lack of basic understanding of what is happening.



Whilst all of this may seem pessimistic, this area actually provides an opportunity to improve the care of our patients. Exacerbations represent an acute-on-chronic condition and it should be possible to focus future research on mechanisms, diagnosis and treatment. In addition, there is clearly a need to raise awareness about these critical conditions in pulmonary medicine. In comparison with the number of chest pain and stroke units, very few departments handle exacerbations of respiratory diseases in a similar treatment structure, despite the fact that pulmonary exacerbations have a significant impact on the patient and on mortality figures overall.

This *Monograph* provides a comprehensive overview of exacerbations in pulmonary diseases. It covers specific disease entities such as COPD, asthma, CF and IPF, and provides detailed information for the clinician. It also discusses the mechanisms of exacerbation development, which is an important for the prevention of and basic understanding about this area.

The Guest Editors, Pierre-Régis Burgel, Marco Contoli and José Luis López-Campos, have selected and integrated the topics covered to create a book that successfully summarises current knowledge in this area. I thank the Guest Editors and all of the authors for their hard work on this excellent book. Together, they have produced a practice-guideline publication, comprising information about scientific background and application at the patient's bedside. I am sure that this comprehensive review will prove useful in the clinical practice of a broad range of respiratory physicians, and will improve the care of patients that experience AEs.

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Guest Editors

Pierre-Régis Burgel

Pierre-Régis Burgel is currently Professor of Respiratory Medicine at Paris Descartes University in Paris, France, where he is also a senior researcher in the Cystic Fibrosis and Chronic Airway Diseases Laboratory. He is a senior consultant at the Respiratory Medicine Department of Cochin Hospital in Paris.

Pierre-Régis Burgel completed his medical training at the University of Paris, School of Medicine (Paris), in 1999. After a post-doctoral fellowship at the University of California in San Francisco (USA) (1999–2001), he obtained a PhD in respiratory cell biology at the University of Paris. His main research interests include COPD phenotypes, CF in adults, and chronic bacterial infection in COPD and CF. He has published over 150 articles in peer reviewed journals in these areas of lung disease.

Pierre-Régis Burgel is a member of several professional societies, including the European Respiratory Society (ERS), the American Thoracic Society (ATS), the European Cystic Fibrosis Society (ECFS), and the Société de Pneumologie de Langue Française (SPLF). He is Vice President of the French Cystic Fibrosis Society and a member of the ERS College of Experts. He is also a member of the Editorial Boards of the *European Respiratory Journal*, *COPD: Journal of Chronic Obstructive Pulmonary Disease* and *Revue des Maladies Respiratoires*. He is the scientific secretary of the French collaborative group INITIATIVES BPCO, which is dedicated to the identification of clinically relevant COPD phenotypes. He was recently an active member of the ATS/ERS task force on Research Questions in COPD and the ERS/ECFS task force on the Provision of Care for Adults with CF in Europe.



Marco Contoli

Marco Contoli is Assistant Professor at the Section of Respiratory Diseases, Dept of Medical Sciences, of the University of Ferrara, Ferrara, Italy. He is also a respiratory consultant at the Respiratory Disease Unit of the Arcispedale Sant'Anna, Azienda Ospedaliero-Universitaria (Ferrara).



He gained his degree in medicine and surgery at the University of Bologna (Bologna, Italy) in 2001. He went on to study respiratory diseases at the University of Ferrara (Ferrara, Italy) and a PhD in Experimental Respiratory Pathophysiology at the University of Parma (Parma, Italy). As a recipient of a European Respiratory Society (ERS) fellowship, he spent 1 year (November 2003–November 2004) working in Professor Sebastian Johnston's laboratory at St Mary's Hospital (Imperial College, London, UK).

Marco Contoli's main clinical expertise is in the diagnosis, management and treatment of asthma and COPD. His research interests include mechanisms of virus-induced exacerbations of asthma and COPD, markers of airway inflammation and mechanisms of airways obstruction, and the impact of comorbid conditions in asthma and COPD. He has served as co-investigator in several clinical and pharmacological international trials conducted according to good clinical practice guidelines in the field of asthma and COPD. He has published research in leading international journals and serves as invited reviewer for the most important respiratory journals. He is a member of the ERS.

José Luis López-Campos



José Luis López-Campos is a pulmonologist at the Hospital Universitario Virgen del Rocío (Seville, Spain), and is the head of the monographic COPD and the bronchiectasis outpatient clinic. He also serves as Associate Professor of Medicine at the University of Seville (Seville) and tutors residents of pneumology at the Hospital Universitario Virgen del Rocío. He is head of a research group linked to the CIBER of Respiratory Diseases, Ministry of Economy, Spain. His research projects include epidemiology, clinical audits and translational research in COPD.

As well as serving as an Associate Editor of *Archivos de Bronconeumología*, José Luis Lopez-Campos is Chair of the Monitoring Airway Disease group of the European Respiratory Society (ERS) and is a member of the ERS College of Experts. He was previously: secretary of the COPD Assembly at the Spanish national society (SEPAR); Web Director at SEPAR; and ERS Clinical Assembly web coordinator.

Recent publications have included research on T-helper type 2 signatures in chronic airway diseases (with the CHACOS study group), results from the Andalusian COPD audit and a study of the effects of smoke-free legislation on lung cancer mortality trends.



Introduction

Pierre-Régis Burgel^{1,2}, Marco Contoli³ and José Luis López-Campos^{4,5}

Chronic non-communicable respiratory diseases (*e.g.* asthma, COPD, CF, bronchiectasis and IPF) are responsible for high morbidity and mortality. These diseases represent a significant burden to patients and healthcare systems, and are considered a major challenge in the currently ageing population worldwide. Despite their differences in nature, chronic respiratory diseases all have one thing in common: a considerable impact on patient health status, which mainly derives from the impact of symptoms in the short and the long term. AEs of chronic respiratory diseases are also no longer considered to be just an increase in symptoms. On the contrary, it has now been established that exacerbations are associated with significant immediate risks (*e.g.* hospitalisation and/or death) and are responsible for a deep long-term impact with prognostic implications.

The field of AEs in chronic respiratory diseases is challenging. Definitions of AEs differ amongst the diseases, as investigators have used various combinations of symptoms and/or biomarkers (*e.g.* imaging, lung function), which were often based on expert opinion or data availability. Similarly, the severity of exacerbations has proven challenging to define, as these definitions of severity often rely on therapeutic management (*e.g.* the need for specific drugs and/or hospitalisation), which may have varied in different countries with different healthcare systems. Major progress has therefore been the establishment of a consensus for diagnosing and establishing the severity of exacerbations in each individual disease, allowing for comparisons among studies and the development of therapeutic strategies. In this regard, some fields have evolved rapidly (*e.g.* asthma and COPD), whereas the concept of exacerbations is emerging more slowly in other diseases (*e.g.* CF, bronchiectasis and IPF).

In the present issue of the *ERS Monograph*, we have brought together a series of articles from internationally recognised experts in the field of exacerbations in chronic lung diseases. The book is separated into three sections: the first section considers the definition, severity and consequences of exacerbations in each disease. The second section looks at exacerbation triggers, including bacterial and viral infections, air pollution and allergen exposure; part of this section is also dedicated to the difficult problem of differential diagnosis of exacerbations, which should not be confounded with other acute conditions (*e.g.* left heart failure or pulmonary embolism). The last section discusses the treatment and

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prevention of exacerbations using pharmacological and non-pharmacological interventions (e.g. pulmonary rehabilitation and strategies aimed at improving physical activity).

The book's originality lies in the fact that it covers AEs in various respiratory diseases, allowing comparisons between definitions, short- and long-term consequences, triggers and therapeutic management. As such, this book will serve as a complete and up-to-date reference that will raise awareness on the importance of exacerbations in patients with chronic lung diseases and will promote further research in this area.

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List of abbreviations

AE	acute exacerbation
CF	cystic fibrosis
COPD	chronic obstructive pulmonary disease
CRP	C-reactive protein
CT	computed tomography
FEV ₁	forced expiratory volume in 1 s
FVC	forced vital capacity
HRCT	high-resolution computed tomography
ICU	intensive care unit
IL	interleukin
IPF	idiopathic pulmonary fibrosis
MRSA	methicillin-resistant <i>Staphylococcus aureus</i>
NTM	nontuberculous mycobacteria
P_{aCO_2}	arterial carbon dioxide tension
P_{aO_2}	arterial oxygen tension
QoL	quality of life
RCT	randomised controlled trials
S_{aO_2}	arterial oxygen saturation
TNF	tumour necrosis factor