

NUMBER 60 / JUNE 2013

EUROPEAN RESPIRATORY *monograph*

CLINICAL HANDBOOKS FOR THE RESPIRATORY PROFESSIONAL

The Spectrum of Bronchial Infection

Edited by Francesco Blasi
and Marc Miravittles



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Published by European Respiratory Society ©2013
June 2013
Print ISBN: 978-1-84984-034-7
Online ISBN: 978-1-84984-035-4
Print ISSN: 1025-448x
Online ISSN: 2075-6674
Printed by Page Bros Ltd, Norwich, UK

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The Spectrum of Bronchial Infection

Edited by
Francesco Blasi and Marc Miravittles

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Tobias Welte

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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Preface



The 21st century will be described as the century of infectious diseases. This is not only because of the increasing number of new infections, such as severe acute respiratory syndrome, the H1N1 pandemic or the spread of West Nile virus and dengue fever, but also because the role of infection in the pathogenesis of chronic diseases has been recognised and is now better understood. Chronic bronchial infection plays a role in the progression and prognosis of many lung diseases but also contributes to a systemic inflammatory response, which is a predisposition for extrapulmonary diseases such as arteriosclerosis or diabetes mellitus.

At present, the mechanisms that contribute to chronic pathogenic colonisation of the lower respiratory tract are not entirely clear. Is there a defect of the innate or the adaptive immune system of the lung favouring chronic colonisation? Are there deficits in the innate and/or adaptive immune system on a local pulmonary level that contribute to the primary colonisation and secondary tissue damage? What is the role of air pollution and other environmental factors?

Many questions about chronic bronchial infection are unclear. Is it possible to prevent this condition by early, adequate treatment of the underlying disease or is it better to stimulate an immune response by vaccination or similar immunomodulatory agents? Is it possible to influence the course of the disease by treating chronic pulmonary infection? How long should the treatment period last for? Should the patient receive the same treatment strategy or should different treatment be administered at different time-points?

This issue of the *European Respiratory Monograph (ERM)* summarises the current understanding of chronic bronchopulmonary infections and addresses future needs.

I would like to congratulate the Guest Editors, Francesco Blasi and Marc Miravittles, for their tremendous work in bringing together this cutting-edge *ERM*, which should be of interest for general medical doctors and respiratory physicians, as well as infectious diseases specialists. In addition, it will provide guidance for future basic and clinical research. I am sure that readers from different areas of respiratory medicine will find this *ERM* useful in their daily practice.

Guest Editors



Francesco Blasi

Francesco Blasi is Professor of Respiratory Medicine and Vice-chairman of the Department of Pathophysiology and Transplantation at the University of Milan, Milan, Italy, as well as Director of Respiratory Diseases at the Unit IRCCS Fondazione Cà Granda Ospedale Maggiore Milan. He is currently President of the European Respiratory Society (ERS) (2012–2013).

Professor Blasi has published more than 180 papers in international journals. He is an Associate Editor on the editorial boards of *Pulmonary Pharmacology and Therapeutics*, *Respiratory Research*, *Clinical Respiratory Journal* and *Therapeutic Advances in Respiratory Disease*. His research interests include the effects of atypical bacterial infection on cellular immunity in chronic bronchitis, and the role of atypical bacteria and viral infection in asthma onset. He is also interested in the role of antibiotics in the treatment of chronic obstructive pulmonary disease (COPD) exacerbations and asthma. He is actively working on pneumonia and tuberculosis research trials. Professor Blasi was also involved in the ERS/European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidelines on lower respiratory tract infections. In addition to being a member of the ERS, he is also a member of the American Thoracic Society (ATS) and the Italian Respiratory Medicine Society (SIMeR).



Marc Miravittles

Marc Miravittles is a pulmonologist working in clinical research in the Hospital Universitari Vall d'Hebron in Barcelona, Spain. His primary research interests include COPD, chronic bronchitis, α_1 -antitrypsin deficiency, lung defence mechanisms and respiratory infections.

Marc Miravittles serves on various medical committees and is a member of numerous professional societies, including the Spanish Society of Pneumology and Thoracic Surgery (SEPAR), where he served as Secretary (1999–2003), and was responsible for international relationships from 2006 to 2011. Dr Miravittles acted as the Chair of the Respiratory Infections Group of the ERS (2008–2011). He has also acted as a consultant for the development of different international guidelines for COPD, such as the ATS/ERS Task Force on outcomes in COPD. He was also a consultant of the Spanish Ministry of Health for the development of the national strategy against COPD (2009 onwards) and is the coordinator of the Spanish national guidelines for COPD. Dr Miravittles is Editor in Chief of *Hot Topics in Respiratory Medicine*, Editor in Chief of *Therapeutic Advances in Respiratory Diseases* and serves as an Associate Editor for *Respiration*, the *International Journal of COPD* and the *Clinical Respiratory Journal*. Dr Miravittles has published over 200 articles in a number of peer-reviewed international medical journals, which were largely related to COPD, infection in COPD and α_1 -antitrypsin deficiency.

Introduction

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Optimistically, by the middle of the last century there was the idea that the battle against infections would be won. However, it soon became evident that the mechanisms of adaptation of bacteria to new conditions, including the widespread use of antibiotics, would help them to survive even in hostile environments. Now, it is clear that the battle continues and that the advances of treatments in other areas have changed the battlefield.

This is particularly true in respiratory infections. The different forms of pneumonia are still a clinical challenge and their mortality is still significant in the elderly or immunosuppressed, but other forms of respiratory infections are responsible for a great burden of disease. In particular, infections of the bronchial tree, which include a spectrum of clinical manifestations from benign acute bronchitis in otherwise healthy individuals, to severe exacerbations of patients affected by chronic obstructive pulmonary disease (COPD) or bronchiectasis that are probably the most frequent types of infections in adults. It is no exaggeration to say that everybody has suffered some (or several) form(s) of bronchial infection, fortunately most of them are self-limited, but even the milder forms represent a major cause of morbidity, use of healthcare resources and work absenteeism. The major pathogens involved are the respiratory viruses and bacteria such as *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Pseudomonas aeruginosa*, among others. The aetiological agents will vary depending on the characteristics and baseline respiratory health of the host.

This issue of *European Respiratory Monograph (ERM)* covers the spectrum of bronchial infection, from the milder to the most severe. After explaining the mechanisms of defence within the bronchial tree, the different chapters will elegantly show the clinical manifestations, treatment and prognosis of these frequent diseases.

A number of chapters are dedicated to the chronic bronchial infection in COPD. Up to 10% of adults over the age of 40 years are affected by COPD. The impaired host defences in COPD allow the establishment and proliferation of potentially pathogenic microorganisms (PPMs). Repeated isolation of PPMs in bronchial secretions in stable patients was defined as colonisation; however, it is well documented that the presence of PPMs in the lower airways is associated with increased exacerbation frequency and severity, a faster lung function decline and worse health status. Therefore, the term chronic bronchial infection (CBI) has been proposed to define this clinical situation. The presence of CBI in COPD is characterised by increased chronic inflammation not only in the airways and lung parenchyma, but also at a systemic level. Current evidence indicates that a significant amount of local and systemic inflammatory response in COPD may be attributable to the presence of PPMs. Since atherosclerosis is also characterised by chronic inflammation and oxidative stress, it has been hypothesised that CBI may be responsible for some extrapulmonary manifestations of COPD, particularly the high prevalence of cardiovascular comorbidities.

CBI is linked to acute episodes of increased symptoms, the so-called exacerbations of COPD, which is also covered in this current issue of the *ERM*, from the point of view of: the different infective aetiologies; viruses and bacteria and their interrelationships; the impact of exacerbations

in the course of the disease; antimicrobial treatment and prevention; and along with new evidence for the use of long-term antibiotics in a selected group of patients with COPD and frequent exacerbations.

Finally, there are a number of chapters dedicated to bronchiectasis, once considered an orphan lung disease. In contrast, there is an increased interest in the aetiology, natural history and treatment of bronchiectasis, either as an isolated disease or as a complication of another respiratory condition, such as COPD. The innovative administration of antibiotics by inhalation may represent an advance in the treatment of CBI in bronchiectasis, and the development of new formulations of old antibiotics to be administered by this route will provide a new therapeutic option for some of the most difficult-to-treat severe patients with bronchial infections.

We are sure that clinicians will find this *ERM's* summary of the existing evidence within this field, alongside some of the most relevant and new information that has arisen to date, as a great aid to them in improving their practice and care for patients with these very frequent respiratory problems.