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Community-Acquired Pneumonia

Edited by James D. Chalmers,
Mathias W. Pletz and Stefano Aliberti



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Community-Acquired Pneumonia

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Edited by
James D. Chalmers, Mathias W. Pletz and
Stefano Aliberti

Editor in Chief
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



Tobias Welte
Editor in Chief

Community-acquired pneumonia (CAP) is the leading cause of death due to infectious disease worldwide. As the incidence of CAP increases with increasing age, the number of cases of pneumonia is increasing steadily, in parallel with changes in demography. In recent years, we have learned a lot, primarily from data from large multicentre networks in Spain, the UK, Germany and the USA, about the course of this disease, its complications, risk factors for increased mortality and the effectiveness of various antibiotics. In addition, the understanding of the pathogenic mechanisms of bacteria and the role of pathogen–host interaction has improved considerably.

Despite the enormous progress in the understanding of CAP, the hospital mortality rate is as high as it was 50 years ago. Unlike hospital-acquired pneumonia, however, an increasing development of resistance of the most important respiratory pathogens does not play a significant role. The key factor for the increased mortality is, along with the rising age and the increased number of comorbidities of the patients, the virulence of the pathogens. The introduction of antibiotic therapy in the 1940s has meant that pathogens are reliably killed, reducing the mortality rate dramatically. However, the increase of pathogenic factors caused by destroying the pathogen or late onset of effective therapy has not been successfully tackled to date.

The future of the treatment of CAP is, therefore, not related to the improvement of diagnostics or the development of new antibiotics. Instead, it will focus on two other fields: prevention and immune modulation. Vaccines as an essential preventive measure are already available for some pathogens, but their further development, in particular to improve immunogenicity in the elderly, is a major subject of research. Modulation of the immune response, both to limit overshooting reactions as well as to improve lack of immune response, has not been successful despite many different attempts in the past. Due to the rapid development of sequencing technology, it will be possible to determine risk profiles of patients quickly and this will allow individualised therapy according to the immune status of the patient. This is the music of the future, although a new form of anti-infective therapy, including pharmacokinetic considerations and a risk stratification approach, stands out already on the horizon.

I want to thank the three guest editors, James Chalmers, Mathias Pletz and Stefano Aliberti, for their tremendous work in preparing this issue of the *European Respiratory Monograph (ERM)*, which summarises the current knowledge about the prevention, diagnosis, risk stratification and therapy of CAP and gives an outlook to the future. The book represents an ideal basis for all clinicians, basic scientists and people operating in this field in the pharmaceutical industry to gain an overview of the state of knowledge. I am convinced that they will find this *ERM* useful for further considerations.

Guest Editors



James D. Chalmers

James D. Chalmers is a Wellcome Trust Postdoctoral Fellow and Lecturer in Respiratory Medicine at the University of Dundee, UK. He trained in Glasgow and Edinburgh, performing his PhD studies at the Medical Research Council (MRC) Centre for Inflammation Research in Edinburgh investigating the role of innate immunity in non-cystic fibrosis (CF) bronchiectasis. His research and clinical interests are in respiratory infections, particularly community-acquired pneumonia (CAP), bronchiectasis and chronic obstructive pulmonary disease (COPD). He now leads a research group at the University of Dundee investigating the mechanisms of pulmonary bacterial infections, supported by grants from the Wellcome Trust, MRC, Scottish Government and charities.

James Chalmers has been awarded several prestigious young investigator awards, including from the European Respiratory Society (ERS) and British Thoracic Society (BTS). He has published widely on respiratory infections, with over 60 articles in peer reviewed journals since 2008. He is a member of the international advisory board of *The Lancet Respiratory Medicine*. He is heavily involved in international respiratory societies, being a current member of the BTS Science and Research Committee, the ERS Long-Range Planning Committee and the American Thoracic Society Microbiology, Tuberculosis and Pulmonary Infections Program Committee.



Mathias W. Pletz

Mathias W. Pletz, Professor for Infectious Diseases, is a board-certified physician for internal medicine, pulmonology and infectious diseases and the head of the Center for Infectious Diseases and Infection Control of the University Hospital in Jena, Germany. He also leads a clinical research group focusing on novel diagnostic and therapeutic strategies against multidrug-resistant bacterial pathogens, funded by the German Ministry for Science and Education.

Mathias Pletz received his PhD in Virology at the University of Leipzig, Germany. During his thesis he worked as a guest researcher at the Food and Drug Administration Laboratory of Parasitic Pathology and Biochemistry in Bethesda, MD, USA. After his medical training at the University of Leipzig, Baylor College of Medicine (Houston, TX, USA) and the University of Basel (Switzerland), he started his residency at the Chest Hospital in Berlin, Germany. Subsequently, he spent 2 years as a postdoctoral researcher at Emory University (Atlanta, GA, USA), working with Keith Klugman's group on the spread of multi-resistant pneumococci. In addition he served as a guest researcher at the Centers for Disease Control and Prevention (CDC) in Atlanta, exploring the severe acute respiratory syndrome (SARS) epidemics.

After his return to Germany, he finished his medical training at the Dept of Respiratory Medicine at the Hannover Medical School.

Mathias Pletz is the deputy director of the German Competence Network for Community-Acquired Pneumonia (CAPNETZ), a member of the board of directors of the German-Austrian-Swiss Paul-Ehrlich-Society for antimicrobial chemotherapy, and scientific advisor for the German Robert Koch Institute. He has published more than 100 papers on pneumonia, pneumococcal vaccines, respiratory infections, antimicrobial resistance and pharmacokinetics of antibiotics in the critically ill. He has also received numerous scientific awards, *e.g.* the Honor Award Certificate from the CDC, the Kass-Award of the Infectious Diseases Society of America and the Respiratory Infections Awards from the ERS.



Stefano Aliberti

Stefano Aliberti is Assistant Professor in Respiratory Medicine at the University of Milan-Bicocca, Milan, Italy, and consultant at the San Gerardo Hospital in Monza, Italy. He trained at the Institute of Respiratory Diseases at the University of Milan, under the mentorship of Professor Francesco Blasi. During his fellowship, he received research grants to investigate the epidemiology of non-CF bronchiectasis and COPD, and he worked as a visiting research fellow at the Division of Infectious Diseases at the University of Louisville, KY, USA. He has been an active member of the Community-Acquired Pneumonia Organization (CAPO) international study group since 2006, and a member of the Community-Acquired Pneumonia Inflammatory Study Group (CAPISG). His research and clinical interests are in both acute and chronic respiratory infections, including CAP, non-CF bronchiectasis and atypical mycobacteria. He was awarded the young researcher award in respiratory infections from the ERS in 2007. During the past 10 years, he has been involved in several clinical and translational studies on these topics at both national and international level. Stefano Aliberti has published over 60 articles on CAP in peer-reviewed journals since 2006. He is associate editor of *Breathe* and the *European Journal of Internal Medicine*. He has been heavily involved in the ERS, as Secretary of the Respiratory Infection Group and Secretary of the Assembly of Respiratory Infections.

Introduction

James D. Chalmers^{*}, Mathias W. Pletz[#] and Stefano Aliberti[¶]

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The morbidity and mortality of respiratory tract infections in Europe throughout history is incalculable, but when the English writer John Bunyan coined the phrase “Captain of all these men of death” to describe tuberculosis (TB) in 1680, TB was estimated to cause 15–20% of all deaths in Europe. It was hard to imagine at that time that another infection might one day take this crown. In 1918, the father of modern medicine, Sir William Osler, observed that pneumonia had overtaken TB as one of the leading causes of death in Europe and described pneumonia as the “Captain of the men of death”, an appellation it still justifies today.

While improvements in public health and sanitation reduced mortality from many, mostly food-borne, infections, it was not until the widespread introduction of antibiotics after the Second World War that mortality from pneumonia in Europe began to fall significantly. Since then, there have been few new treatments and limited progress in reducing mortality from pneumonia. While mortality rates for cardiovascular diseases and many cancers are falling in Europe, the rates for hospitalisation and deaths from pneumonia are static or rising. This is a disease of huge clinical and public health importance.

It is for this reason we are delighted to introduce the 63rd issue of the *European Respiratory Monograph (ERM)*, dedicated to the epidemiology, pathophysiology, microbiology, investigation, management and prevention of community-acquired pneumonia (CAP). The 20 chapters of this *ERM* serve as a comprehensive text, describing the modern approach to this disease, each chapter written by internationally recognised experts in their field. Major changes in our understanding and management of pneumonia have been emphasised, including the new microbiology techniques that are set to change how we detect and diagnose infection, the emerging role of anti-inflammatory therapies and the current controversy over inhaled corticosteroids as a cause of pneumonia in patients with chronic obstructive pulmonary disease. The changing face of pneumonia reflects the world around us, with an increasing impact of antibiotic resistance and an ageing population with comorbidities to the fore. We now recognise the important impact of this disease on long-term outcomes. Previously regarded as a purely “acute” condition, new evidence shows that pneumonia can destabilise the precarious balance in patients with comorbidities and poor performance status, even after apparent recovery from the acute episode.

This is a broad and multidisciplinary book, covering diverse specialities from epidemiology to the basic science of pneumococcal infection, and reviewing CAP in children, in primary care and in the intensive care unit.

As much as in any other disease, CAP requires improvements in clinical care and to achieve progress through innovative research. Every clinician in every speciality will encounter pneumonia in their daily practice and we hope that this *ERM* will serve as a complete and up-to-date reference for our colleagues.