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Tuberculosis

Edited by Christoph Lange and
Giovanni Battista Migliori



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Tuberculosis

Edited by
Christoph Lange and Giovanni Battista Migliori

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



With the introduction of tuberculostatic antibiotics and the improvement of living conditions in developed countries, it was generally felt that the problem of tuberculosis (TB) had been overcome. However, the persistent problems caused by the disease that were seen in developing countries were not really noticed beyond expert circles. With the spread of AIDS in the 1980s, TB returned to the forefront of attention as one of the major opportunistic infections in AIDS patients. In the years that followed, the first reports of difficult-to-treat multidrug-resistant (MDR)-TB were published. In the beginning, reports were limited to countries with a high AIDS prevalence; however, after the collapse of the Soviet Union and the opening of the former Communist countries to the West, the full extent of MDR-TB became clear.

The number of presentations that focussed on TB at the 2012 European Respiratory Society (ERS) Congress in Vienna was truly amazing. Many of the contributions reported increasing MDR in different parts of the world. A recently published study from eight countries, including Estonia, Latvia and Russia, demonstrated a dramatic increase in extensively drug-resistant (XDR)-TB [1]. Previous treatment with second-line anti-TB drugs was shown to be the main risk factor. The development of new drugs has been significantly slower than the increase in resistance; 10 years on, there have been no advances specifically for this area. Only antibiotics approved for other indications, such as fluoroquinolones and linezolid, have provided new treatment options. It is thanks to the commitment of the World Health Organization (WHO) and the support of private foundations (primarily the Bill and Melinda Gates Foundation) that there has been research into new tuberculostatic substances. Some of these are currently being tested in early clinical trials, giving hope of improved treatment options in the future.

It is clear, then, that TB is once again a subject of intense interest. This edition of the *European Respiratory Monograph (ERM)* is therefore particularly topical, as it presents current scientific discussion in the practice of TB diagnosis and treatment. I would like to congratulate the Guest Editors of this issue of the *ERM*, who have brought together contributions from the best experts in the field. This book provides an excellent overview of the topic, and should be of interest to general practitioners and chest physicians, as well as those in industry and in public health who are faced with the problem of TB everyday.

References

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Guest Editors



Christoph Lange

Christoph Lange is a physician and biologist. He was appointed as Professor of Medicine at the University of Lübeck (Lübeck, Germany) in 2009 and is currently the Leading Attending Physician at the Medical Clinic/Head of the Division of Clinical Infectious Diseases at the Research Center Borstel (Borstel, Germany). Since 2005, he has been Co-Chair of the Center of Infectious Diseases (DGI) at the Research Center Borstel and the University of Lübeck, and he is Vice-Chair of the Center of Infection and Inflammation at the University of Lübeck (ZIEL). Following clinical training in Cape Town (South Africa), Cleveland, OH (USA), and hospitals in Germany, he is board certified in internal medicine, pulmonary and critical care medicine, infectious diseases, allergology and sleep medicine. His research focus is on tuberculosis (TB), in which he has been principle investigator of national and international multicentre studies, and a coordinator of consensus documents. C. Lange is Head of the Respiratory Infection Assembly (Assembly 10) of the European Respiratory Society (ERS) (2011–2014) and was previously (2008–2011) chair of the Tuberculosis Group (Group 10.2) of this Assembly. He is the Founding Chair of the Tuberculosis Network European Trials Group (TBNET), which he headed from 2006 to 2012. Since 2011, he has been a member of the steering committee of the Mycobacteriology Study Group (ESGMYC) of the European Society for Clinical Microbiology and Infectious Diseases, and from 2009 to 2012, he was the chair of the Mycobacteriology Study Group of the DGI. C. Lange is an Associate Editor of the *International Journal of Tuberculosis and Lung Diseases*, an Associate Editor of *Infection* and Section Editor for Respiratory Infections of the *Clinical Respiratory Journal*. He has been a Guest Editor for TB series in the *European Respiratory Journal (ERJ)* and *Respirology*. C. Lange was appointed a Visiting Professor at the University of Medicine and Pharmacy of the Republic of Moldova in Chisinau (Moldova) in 2011 and a Fellow of the Infectious Diseases Society of America.



Giovanni Battista Migliori

Giovanni Battista Migliori, MD, FRCP (Lond) is Director of the World Health Organization (WHO) Collaborating Centre for TB and Lung Diseases (Fondazione S. Maugeri, Tradate, Italy), a Professor in the Applied Health Sciences Department of the University of Pavia (Pavia, Italy) and a Visiting Professor at the Mayo Clinic (Rochester, MN, USA).

He originally specialised in respiratory medicine in Pavia and then in medical statistics and epidemiology. He has developed global experience in TB, TB/HIV and HIV/AIDS care and control in Africa (Benin, Burkina, Democratic Republics of Congo, Egypt, Ethiopia, Mozambique and Tanzania), Asia (India and Thailand), Europe (Croatia, Estonia, Kosovo, Latvia, Moldova, Romania, Russia, Turkey and Ukraine) and Latin America (Mexico). G.B. Migliori has served as ERS Tuberculosis Group Chair (Group 10.2), as Head of the Respiratory Infections Assembly (Assembly 10) (2008–2010), Long Range Planning Committee Chair (2011–2013), and is presently the ERS WHO and European Centre for Disease Control Liaison Officer and Secretary General Elect.

Since 2007, he has been an Associate Editor of the *ERJ* and since 2011 of the *International Journal of Tuberculosis and Lung Diseases*, having previously served in the same capacity at *BMC Infectious Disease*.

He is an author of more than 250 publications (including the 1999 ERS Guidelines on TB Management and the 2012 EU Standards for TB care) with a personal H-Index of 38 and average impact factor of more than 220 over the last 3 years. As Guest Editor, he was responsible for two *ERJ* TB Series (2010 and

2011) and the *Respirology* TB Series (2010), and has collaborated in the *Lancet* TB Series (2011).

Within the International Union against Tuberculosis and Lung Disease (IUALTD), he was Secretary General and President (2008–2009) of the Europe Region.

He currently serves WHO as a member of STAG (Scientific Technical Advisory Group, 2010–2012), WHO EURO as a member of TAG (Technical Advisory Board) as well as the GFATM (Global Fund Against AIDS, Tuberculosis and Malaria) as Rotating Member, TRP (Technical Review Panel and Consultant), the GDF (Global Drug Facility) and the European Commission (TACIS programme, Expert Group and the Scientific Committee of EDCTP (European and Developing Countries Clinical Trials Partnership)).

G.B. Migliori is former Secretary of TBNET (2006–2011).

Introduction

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Although the global incidence of tuberculosis (TB) is slowly declining, the disease still remains one of the leading causes of morbidity and mortality worldwide. In many regions of the world, including parts of Europe, the high incidence of TB is an indicator of poverty and healthcare inequalities. In countries with a low incidence of TB, the disease is mainly related to risk group; for example, recent close contacts of infected index patients, migrants from high-incidence countries, HIV-infected individuals, and those with other immunodeficiencies and co-morbidities. Targeting these groups in order to prevent TB is particularly important if the ultimate goal of eliminating the disease is to be achieved.

The emergence of antimicrobial drug resistance in *Mycobacterium tuberculosis* strains with multidrug- (MDR) and extensively drug-resistant (XDR) profiles has become a major obstacle to achievement of the Millennium Development Goal of TB, which aims for the elimination of the disease by 2050. However, for the first time in many centuries, new drugs for the treatment of TB will soon become available. These new weapons must be used wisely.

There may be a further barrier to disease elimination: medical students and even residents of internal medicine from industrialised countries may complete their education without seeing a single patient with TB. This lack of experience is reflected in the diagnostic delay seen in these countries.

However, important advances have been achieved in the prevention, diagnosis and treatment of TB in recent years. This has been due to the hard work and dedication of leaders in the field, many of whom have kindly agreed to contribute to this issue of the *European Respiratory Monograph (ERM)*. We are very grateful for their commitment to the field and for their support in the compilation of this publication.

This issue of the *ERM* includes up-to-date information on TB epidemiology, as well as control and elimination strategies. TB prevention, including the latest developments in novel vaccine research, and recent advances in the diagnosis and treatment of latent infection with *M. tuberculosis*, are also presented. The issue also covers state-of-the-art diagnosis of TB and the treatment of active TB in patients from different risk groups, including cases of *M. tuberculosis* drug resistance and complications of therapy.

We hope that this issue of the *ERM* will prove a useful and valuable reference source to our colleagues, and will inspire young clinicians and scientists to enter this fascinating field.