

# **SpringerBriefs in Public Health**

SpringerBriefs in Public Health present concise summaries of cutting-edge research and practical applications from across the entire field of public health, with contributions from medicine, bioethics, health economics, public policy, biostatistics, and sociology.

The focus of the series is to highlight current topics in public health of interest to a global audience, including health care policy; social determinants of health; health issues in developing countries; new research methods; chronic and infectious disease epidemics; and innovative health interventions.

Featuring compact volumes of 50 to 125 pages, the series covers a range of content from professional to academic. Possible volumes in the series may consist of timely reports of state-of-the art analytical techniques, reports from the field, snapshots of hot and/or emerging topics, elaborated theses, literature reviews, and in-depth case studies. Both solicited and unsolicited manuscripts are considered for publication in this series.

Briefs are published as part of Springer's eBook collection, with millions of users worldwide. In addition, Briefs are available for individual print and electronic purchase.

Briefs are characterized by fast, global electronic dissemination, standard publishing contracts, easy-to-use manuscript preparation and formatting guidelines, and expedited production schedules. We aim for publication 8–12 weeks after acceptance.

More information about this series at <http://www.springer.com/series/10138>

Dorothee Heemskerk · Maxine Caws  
Ben Marais · Jeremy Farrar

# Tuberculosis in Adults and Children

 Springer Open

Dorothee Heemskerck  
Tuberculosis (TB) Group  
Oxford University Clinical Research Unit  
Ho Chi Minh City  
Vietnam

Ben Marais  
Paediatrics and Child Health  
The Children's Hospital at Westmead  
Sydney  
Australia

Maxine Caws  
School of Clinical Sciences  
Liverpool School of Tropical Medicine  
Liverpool  
UK

Jeremy Farrar  
Gibbs Building  
WellcomeTrust  
London  
UK

ISSN 2192-3698

SpringerBriefs in Public Health

ISBN 978-3-319-19131-7

DOI 10.1007/978-3-319-19132-4

ISSN 2192-3701 (electronic)

ISBN 978-3-319-19132-4 (eBook)

Library of Congress Control Number: 2015943842

Springer Cham Heidelberg New York Dordrecht London

© The Author(s) 2015. The book is published with open access at SpringerLink.com.

**Open Access** This book is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

All commercial rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

The publisher, the authors and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, express or implied, with respect to the material contained herein or for any errors or omissions that may have been made.

Printed on acid-free paper

Springer International Publishing AG Switzerland is part of Springer Science+Business Media  
(www.springer.com)

# Preface

This monograph is written for healthcare workers in any setting who are faced with the complex care for patients with tuberculosis. Prevention, diagnosis and treatment of tuberculosis are fraught with challenges that are often reflective of problems in society as a whole. Significant progress has been made since the millennium; Global TB incidence has been reduced, access to rapid molecular diagnosis for both TB and drug resistance has been scaled up, and two new TB drugs have been approved in Europe and the USA. However, major political and socio-economic obstacles remain in the translation of these and other advances into equitable TB healthcare access for all. Access to information on developments in TB care is one such barrier, and by summarizing the most recent advances in disease epidemiology, scientific achievements in treatment and diagnosis and current recommendations for all forms of tuberculosis, we hope to improve the dissemination of access to the latest evidence base for the care of individuals with tuberculosis.

# Contents

<b>1</b>	<b>Epidemiology</b> . . . . .	1
1.1	Tuberculosis in History . . . . .	1
1.2	Pathogen . . . . .	2
1.3	Epidemiology . . . . .	4
1.4	Prognosis . . . . .	7
<b>2</b>	<b>Pathogenesis</b> . . . . .	9
2.1	Transmission . . . . .	9
2.2	The Innate Immune Response . . . . .	10
2.3	The Adaptive Immune Response . . . . .	12
2.4	The Complex Role of TNF and Its Genetic Control . . . . .	12
2.5	The Tuberculoma . . . . .	13
2.6	Vitamin D and the Immune Response . . . . .	14
2.6.1	Vitamin D Metabolism . . . . .	14
2.6.2	Antimicrobial Effects of Vitamin D . . . . .	15
2.6.3	Vitamin D Deficiency and Susceptibility to Tuberculosis . . . . .	15
<b>3</b>	<b>Clinical Manifestations</b> . . . . .	17
3.1	Primary Tuberculosis . . . . .	17
3.2	Pulmonary Tuberculosis . . . . .	18
3.2.1	Parenchymal Disease . . . . .	18
3.2.2	Endobronchial Tuberculosis . . . . .	19
3.2.3	Intra-Thoracic Lymphnode Disease . . . . .	20
3.3	Extra-Pulmonary Tuberculosis . . . . .	20
3.3.1	Pleural Tuberculosis . . . . .	21
3.3.2	Miliary Tuberculosis . . . . .	21
3.3.3	Extra-Thoracic Lymphnode Disease . . . . .	22
3.3.4	Central Nervous System Tuberculosis . . . . .	23

3.3.5	Tuberculous Pericarditis . . . . .	25
3.3.6	Spinal Tuberculosis . . . . .	25
3.3.7	Other Forms of Extra-Pulmonary Tuberculosis . . . . .	26
<b>4</b>	<b>Diagnosis . . . . .</b>	<b>27</b>
4.1	Smear Microscopy . . . . .	27
4.2	Mycobacterial Culture . . . . .	31
4.3	Nucleic Acid Amplification Tests . . . . .	32
4.4	Diagnosing Drug-Resistant Tuberculosis . . . . .	34
4.5	Other Diagnostic Methods . . . . .	35
4.6	Diagnosing Latent Tuberculosis Infection . . . . .	36
<b>5</b>	<b>Treatment . . . . .</b>	<b>39</b>
5.1	First-Line Antituberculous Treatment . . . . .	39
5.2	HIV Associated Tuberculosis . . . . .	43
5.3	Treatment of Drug-Resistant Tuberculosis . . . . .	44
5.4	The Role of Fluoroquinolones . . . . .	47
5.5	Bedaquiline . . . . .	48
5.6	Delamanid . . . . .	49
<b>6</b>	<b>Prevention . . . . .</b>	<b>51</b>
6.1	Prophylactic Treatment . . . . .	51
6.2	Prophylactic Treatment in Multi-drug Resistant Tuberculosis . . . . .	52
6.3	Vaccines . . . . .	53
6.4	Concluding Remarks . . . . .	54
	<b>References . . . . .</b>	<b>57</b>
	<b>Index . . . . .</b>	<b>65</b>